100

Real-time monitoring of drugs, metabolites and biomarkers: recent advances in in vivo biosensors

Dr Kevin Plaxco

Biography:
Kevin Plaxco, a Distinguished Professor at the University of California, Santa Barbara, holds appointments in the Departments of Chemistry and Biochemistry and of BioEngineering. Prior to joining UCSB in 1998 Dr. Plaxco received his Ph.D. from Caltech and performed postdoctoral studies at Oxford and the University of Washington. Dr. Plaxco's research focus is on the physics of biomolecular folding and its engineering applications. A major aim of the group's applied research is to harness the speed and specificity of folding in the development of sensors, adaptable surfaces, and smart materials. Dr. Plaxco has co-authored more than 250 papers and two dozen patents on protein folding, protein dynamics, and folding-based sensors and materials. He serves on the scientific boards of a half dozen biotechnology firms, several of which are commercializing technologies developed by his group, and has also written a popular science book on Astrobiology.

The availability of technologies capable of tracking the levels of drugs, metabolites, and biomarkers in real time in the living body would revolutionize our understanding of health and our ability to detect and treat disease. To this end, recent years have seen the development of Electrochemical Aptamer-based (EAB) sensors, an in vivo molecular sensing strategy supporting seconds- to sub-second resolution, real-time drug and biomarker measurements. Composed of an electrode-bound, redox-reporter-modified aptamer that generates a signal via a binding-induced conformational change, EAB sensors do not rely on the chemical transformation of their targets. Thus, unlike, for example, the continuous glucose monitor, EAB sensors are adaptable to any of a wide range of targets, with two dozen drugs, metabolites, neurotransmitters, and proteins having been successfully measured in the veins, brains, and solid peripheral tissues of live animal models. In this talk, I highlight both recent technological development of the EAB platform and a number of advances in pharmacology and physiology enabled by this uniquely high-time-resolution, real-time window into the body's molecular status.

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

200

Feasibility of TDM of 5-flurouracil in tertiary-care cancer centre in western India

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Biography:

Dr. Preeti Kulkarni is working as the Principal of Gahlot Institute of Pharmacy since September 2024. She has a M.Pharm degree in Pharmaceutical Quality Assurance and PhD in Pharmaceutical Sciences. Dr. Kulkarni has six years of industry experience and more than 15 years of experience in the field of pharmacy education and research. She has guided 25 M.Pharm students in her career so far. Dr. Kulkarni's research interests include development of analytical methods for biomonitoring and pharmaceutical quality control. She has more than 30 research publications in peer-reviewed journals. Apart from her professional accomplishments, Dr. Kulkarni is a trained singer with a senior diploma in Indian classical music and post graduation degree in light music.

Background: TDM of 5-flurouracil (5FU) is standard practice at many centres globally, although, not commonly practiced in India. Lack of infrastructure and evidence supporting TDM from within the country is vastly responsible for this.

Aim: A feasibility study to assess the utility of 5FU TDM in a tertiary care cancer hospital in western India.
Methods: Patients diagnosed with gastrointestinal malignancies wherein 5FU was administered as a 48 hour infusion were enrolled. All patients were treated with one of the two generic brands of 5FU available in our pharmacy. A single blood sample was collected between 44-48 hour of infusion to measure 5FU concentration. Plasma 5FU was measured by HPLC. AUC of 5FU was calculated for each patient using non compartmental analysis. Toxicity was assessed using CTCAE v5.0.
Results: Between November 2023 to January 2024, 29 patients (4F/25M) were enrolled. Median age was 48(18-67) years. Carcinoma of the stomach and rectum were the most common diagnosis (11 each). The average AUC was 16.7±21.7 mg*35;h/L. Only 6 patients achieved AUC in the therapeutic range of 20-30 mg*35;h/L. 20 patients and 3 patients achieved AUC below and above the therapeutic range respectively. Four patients suffered grade ≥3 toxicity, however, no correlation was observed between 5FU AUC and toxicity.
Conclusions: Frequent sub-therapeutic exposure and low incidence of grade ≥3 toxicity was noted, raising concerns about the quality of drugs. A potential application of TDM in our setting could be to identify patients with very low exposures and make a brand switch early-on in treatment.

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

201

Pharmacokinetics of Cytarabine in Acute Myeloid Leukemia: A Noncompartmental and Multivariate Analysis

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Biography:
Pharmacy resident since November 2020 and currently resident in the pharmacology and toxicology laboratory of Angers university hospital, I'm interested in clinical pharmacology and pharmacometrics. During my residency, I also was trained in poison control center, drug compounding and drug quality control.

Background: Cytarabine is a key drug in acute myeloid leukemia (AML) treatment, where its pharmacokinetics (PK) influence therapeutic efficacy.
Aims: This study evaluates the PK of cytarabine and explores the impact of clinical covariates using multiple linear regression and principal component analysis (PCA).
Methods: Thirty AML patients (13 women, 17 men) received intravenous cytarabine over 2 hours in two dosing regimens: high dose (HD, 3000 mg/m², n=21) and intermediate dose (ID, 1500 mg/m², n=9). Plasma concentrations were measured using LC-MS/MS, with 4–5 samples collected up to 2 hours post-infusion. PK parameters, including dose-normalized area under the curve (AUC/D), maximum plasma concentration (Cmax), and half-life (t½), were estimated using Pkanalix 2024R1. Covariate effects were assessed via multiple linear regression, and PCA was conducted to explore global variability.
Results: Cmax was 19.14 mg/L (CV% = 37.9%) in the HD group and 8.23 mg/L (CV% = 30%) in the ID group, confirming dose-proportionality. AUC/D was similar in both groups (HD: 0.3316, ID: 0.308), suggesting linear PK. Hematocrit significantly influenced AUC/D (p = 0.0067), while higher blast counts correlated with prolonged half-life. PCA showed that the first principal component explained 23% of total variance, with seven components required to capture 80%.
Conclusions: This study confirms the linear PK of cytarabine and highlights the role of hematocrit and blast counts in drug exposure and elimination. PCA underscores the complexity of PK variability, advocating for personalized dosing in AML treatment.
Keywords: Cytarabine, AML, PK

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

202

TDM-Guided Imatinib Dose Adjustment in GIST Patients Undergoing Adjuvant Therapy

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Biography:

Hong Zhou is a clinical pharmacist in the Department of Pharmacy at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (HUST). My research interests primarily focus on individualized therapy for heart transplantation, particularly utilizing pharmacogenomics and pharmacometrics methodologies. I have led a study funded by the National Natural Science Foundation of China (NSFC), investigating the mechanisms underlying tacrolimus-induced new-onset diabetes after transplantation. Additionally, I have served as the principal investigator for a National Key Research and Development Program of China focused on Precision Medicine Research. Furthermore, I hold the position of Deputy Chairman within The Youth Committee of Therapeutic Drug Monitoring Committee under the Chinese Pharmacological Society and am honored to be recognized as a fellow by the International Society for Therapeutic Drug Monitoring and Toxicology (IATDMCT). She participate the development of the Chinese Expert Consensus on Therapeutic Drug Monitoring for Targeted Treatment of Gastrointestinal Stromal Tumor

Background: The IATDMCT guideline have emphasized the necessity of TDM for gastrointestinal stromal tumors (GIST) patients and recommend 1100 μg/L as the concentration thresholds for advanced or metastatic patients. Notably, the concentration threshold for adjuvant population still remain unreported.
Aims: To investigate the efficacy of IM dose adjustment guided by TDM in GIST patients with adjuvant therapy after complete resection.
Methods: Patient who received IM for adjuvant therapy, TDM-guided dose adjustment and had complete follow-up data were enrolled. Dose adjustment was determined through comprehensive consideration of the presence of grade 3 or higher intolerable adverse reactions, current concentration levels, and the threshold range of 760–1100 μg/L. The impact of TDM-guided dosage on relapse-free survival (RFS), adverse reaction, and health-related quality of life were evaluated
Results: A total of 70 patients were included and received an initial IM dose of 400 mg/d, with a mean C0 of 1900±568 μg/L and a median treatment duration of 8.3 months. After adjustment, 60 patients received 300 mg/day (C0: 1216±350 μg/L), and 10 patients received 200 mg/day (C0: 1023±269 μg/L). TDM-guided dosage showed significant reductions in the incidence of bone marrow suppression, edema, cutaneous reactions, and gastrointestinal symptoms. Total physical and mental health scores were improved. The 3-year overall survival was 100%, 3-year RFS was 92.8%, and high-risk patients achieved 89.8% 3-year RFS.
Conclusions: TDM-guided dose reduction effectively mitigates toxicity, improves quality of life, and enhances long-term prognosis in GIST patients with severe adverse reactions during adjuvant therapy.
Keywords: GIST, Imatinib, Dose adjustment, TDM

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

203

Model-based dose optimisation of Anti-Thymocyte Globulin in Allogeneic Stem Cell Transplantation

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Biography:
Elias Biris is a PhD candidate at the University of South Australia and a senior haematology pharmacist at the Royal Adelaide Hospital in Adelaide, Australia. Working closely with patients with haematological malignancy, his research focus is to improve supportive care therapies for patients undergoing chemotherapy. He is currently undertaking his PhD with the aim of optimising dosing of Anti-Thymocyte Globulin in allogeneic stem cell transplant recipients.

Background: Anti-Thymocyte Globulin (ATG) is a polyclonal antibody used as an immunosuppressant to prevent graft-versus-host-disease in haematopoietic stem cell transplantation. While recent studies have worked toward understanding the pharmacokinetic-pharmacodynamic relationship via population pharmacokinetic modelling, dosing remains weight-based and largely empirical in clinical practice.
Aims: To evaluate current ATG dosing regimens and improve pharmacokinetic target attainment by utilising therapeutic drug monitoring.
Methods: Conventional and novel ATG regimens were examined using Monte Carlo simulation with an existing population pharmacokinetic model and an in-silico population of 10,000 representative patients. Individualised ATG dosing regimens were simulated with sparse sampling, empirical Bayesian estimation of pharmacokinetic parameters, and a dose optimisation function. Post-transplant AUC and probability of target attainment was determined for each regimen.
Results: No conventional ATG dosing regimen was able to dose >25% of individuals within the defined target range of 60-95AU.day/mL. Model-based dose optimisation was only able to improve target attainment by up to 9%. In all cases, pharmacokinetic parameter estimation was poor, with ETA shrinkage of >30% noted on three of the five variable pharmacokinetic parameters influencing ATG elimination.
Conclusions: Wide inter-individual variability of ATG leads to universally poor target attainment with current weight-based dosing regimens. Improving attainment by means of Bayesian estimation and dose optimisation leads to minor improvements only and is unlikely to be of clinical benefit in stem cell transplant recipients. Further research into factors influencing the pharmacokinetic parameters of ATG is required to allow for dose individualisation and optimisation.
Keywords: anti-thymocyte globulin, haematological malignancy, dose optimisation, population pharmacokinetics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

204

Bioinformatics analysis of glycolysis-driven drug desistance prognosis in lung adenocarcinoma

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Biography:

Dr. Zhang Lei, Chief Pharmacist and Doctoral Supervisor, serves as the Deputy Director of the Pharmacy Department at the First Affiliated Hospital of University of Science and Technology of China (Anhui Provincial Hospital) and is also the Director of the Infectious Disease Division. Recognized as an outstanding technical backbone within the institution, her primary research focuses on pharmacogenomics, traditional Chinese medicine in oncology pharmacology, and the design and development of polymeric nanomedicines. She has led two projects each funded by the National Natural Science Foundation, Anhui Province Key Research and Development Program, Anhui Provincial Natural Science Foundation, as well as two multicenter clinical trials for medical devices. As either first author or corresponding author, she has published 24 SCI papers (with a highest impact factor of 29.4; five papers with an impact factor above 10; twelve papers in JCR Q1), and has been granted one patent authorization.

Background: Most non-specific anticancer treatment options can cause serious toxicities. Currently, the response rate to clinical treatment for lung adenocarcinoma (LUAD) is not ideal, and the poor prognosis severely affects patients' quality of life. Therefore, there is an urgent need to explore models that can be used as personalized therapy for LUAD patients to improve the efficiency of drug application, reduce irrational drug use, and improve clinical prognostic outcomes.
Aims: To develop predictive models for personalized therapy in lung adenocarcinoma (LUAD) patients, aiming to enhance the efficiency of drug application, minimize irrational drug use, and improve clinical prognostic outcomes.
Methods: Using bioinformatics/statistics, we analyzed cancer markers to build genetic profiles predicting LUAD therapy responses; developed a nomogram incorporating genetic and clinicopathological factors for risk stratification and quantified assessment. Finally, in vivo and in vitro experimental validation of analyses was performed.
Results: Our study demonstrated that high and low-risk levels of glycolysis were important indicators for differentiating the prognosis of LUAD patients and could be used as an independent risk factor for survival, effectively differentiating high-risk patients. The nomogram prediction model showed high predictive accuracy and was a good predictor of patient sensitivity to three commonly used targeted chemotherapeutics.
Conclusions: This research helps to optimize the survival risk stratification of LUAD patients and predict the sensitivity of commonly used chemotherapeutic agents for precision treatment.
Keywords: lung adenocarcinoma, glycolysis, prognosis, precise treatment, therapeutic resistance

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

205

Active Pharmacovigilance trial Integrating Pharmacogenetics, TDM, and Drug-Drug Interaction analyses in Oncology

Dr Bianca Posocco[1], Dr Sara Gagno[1], Dr Eleonora Cecchin[1,2], Dr Diletta Pasin[1], Dr Riccardo Cecchin[1], Dr Elena Peruzzi[1], Dr Rossana Roncato[1,2], Dr Elena De Mattia[1], MD Angela Buonadonna[3], MD Lucia Fratino[3], MD Fabio Puglisi[2,3], Dr Paola Rossi[4], Dr Erika Cecchin[1]
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Biography:

Bianca Posocco has been a healthcare researcher at the Experimental and Clinical Pharmacology Unit of CRO Aviano since 2019. She holds a Master's degree in Chemistry from the University of Padua (2011) and earned a PhD in Pharmaceutical Sciences and Technology from the University of Trieste (2015). She is a licensed chemist and a member of the FVG Chemists and Physicists Association. Her research focuses on developing LC-MS/MS analytical methods for quantifying anticancer drugs in plasma and dried blood spots, supporting pharmacokinetic studies in precision medicine. She contributes to Phase Ib clinical trials and therapeutic drug monitoring (TDM). Bianca has participated in major national (AIRC 5x1000) and international (Horizon 2020) projects aimed at developing point-of-care systems for anticancer drug analysis.

Background: Integrating pharmacogenetics (PGx), therapeutic drug monitoring (TDM), and drug-drug interaction (DDI) assessments (MedReview) into routine clinical practice of oral anticancer drugs (OADs) may enhance their appropriate use.
Aims: A prospective observational clinical trial (NCT06822959) is underway at our center to implement an active pharmacovigilance approach for optimizing OADs treatment (palbociclib, ribociclib, abemaciclib, olaparib, niraparib, imatinib, sunitinib).
Methods: Consenting adult OAD-treated patients, underwent PGx analysis and periodic TDM. Co-medications, co-morbidities, adherence, and ADRs were recorded through interviews. DDI assessment used Lexicomp, and oncologists received integrated pharmacological counseling reports.
Results: 160 patients were enrolled, covering 69% of those on treatment, with higher rates for drugs with available TDM guidelines. TDM found 56% of measurements outside the therapeutic range, while PGx analysis identified 27% of cases with variant genotypes. DDIs were detected in 24% of cases, including grade D (therapy modification recommended). These findings led to 227 pharmacological consultations. ADR review (completed for 29% of cases) showed 58% of patients that experienced clinically relevant toxicity, resulting in dose reduction (84%), therapy discontinuation (9%), or treatment change (7%). An association between comorbidities (e.g. COVID-19) and increased exposure and toxicity was observed. Eleven ADRs were reported to Italian Drug Agency (AIFA)
Conclusions: The interim analysis supports this approach in identifying cases of under- or over-exposure and detecting potentially harmful drug-drug, drug-comorbidity, and drug-gene interactions. It also improved ADR reporting. Completion of data collection will provide further insights. The study was funded by AIFA and Italian Ministry of Health (RF-2021-12374355).
Keywords: pharmacogenetics, TDM, DDI, pharmacovigilance

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

206

Seconds-resolved measurements of the transport of methotrexate into the interstitial fluid

Ms Jennifer Marie Gibson[1], Dr. Nicole Emmons[2,3], Dr. Julian Gerson[6], Ms. Danielle Sogbesan[2,3], Dr. Kon Son[6], Dr. Tod Kippin[2,3], Dr. Kevin Plaxco[4,5]
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Biography:

Jennifer Gibson is a graduate student researcher, with her research focused on the development of electrochemical aptamer-based (EAB) sensors for real-time, minimally invasive pharmacokinetic measurements. By investigating the transport kinetics of drugs between plasma and interstitial fluid (ISF), she aims to improve therapeutic drug monitoring and expand the potential of subcutaneous biosensors as an alternative to traditional blood sampling.

Her recent work includes applying EAB sensors to monitor methotrexate simultaneous in dual body compartments, with a particular emphasis on evaluating ISF as a potential proxy for plasma drug levels. Through her interdisciplinary approach, Ms. Gibson contributes to advancing biosensing technologies for precision medicine and real-time drug monitoring.

Background: Ideally, therapeutic drug monitoring (TDM) would be performed using minimally invasive, real-time, wearable sensors (analogous to glucose sensing). Achieving this vision requires improved understanding of how drugs are transported between blood into the interstitial fluid (ISF) of these solid tissues. Here we employ seconds-resolved measurements collected simultaneously in blood and subcutaneous ISF to study this relationship for methotrexate (MTX), a drug that requires TDM to optimize efficacy and minimize toxicity, particularly in high-dose chemotherapies. However, the relation between MTX pharmacokinetics in plasma versus those in ISF remains poorly understood.

Aims: Here, we determine the relationship between plasma and ISF concentrations of MTX following intravenous infusion employing electrochemical aptamer-based (EAB) sensors.

Methods: EAB sensors functionalized with an MTX-detecting aptamer were placed in the jugular vein and subcutaneously (ISF) in live rats. Following rapid intravenous infusion of MTX, the sensors were electrochemically interrogated to generate seconds-resolved measurements in situ.

Results: Plasma and ISF MTX concentrations showed a modest correlation (R2 = 0.37), which improved considerably post-Cmax in the ISF (R2 = 0.66). Body-mass adjusted dose correlated with plasma Cmax (R2 = 0.75), but was a poor predictor of overall drug exposure (AUC) in plasma and ISF. In contrast, ISF AUC strongly correlates with plasma AUC (R2 = 0.80, p = 0.0070), suggesting ISF measurements as a potential proxy for predicting plasma exposure.

Conclusions: The strong relationship between plasma and ISF pharmacokinetics suggests the potential value of EAB sensors as a means of predicting plasma drug exposure with high-precision through minimally-invasive subcutaneous measurements.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

207

Voriconazole Dosing in Liver Dysfunction: From Population Models to Clinical Practice

Prof Miao Yan[1]
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Biography:

The presenter is the Vice President of the Second Xiangya Hospital of Central South University and the Academic Leader of Clinical Pharmacy in Hunan Province. Previously, the presenter served as a Council Member of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and currently holds the position of Education Chair.

*With a long-standing dedication to research in Therapeutic Drug Monitoring (TDM) and Clinical Toxicology (CT), the presenter focuses on drug-induced liver injury (DILI) and precision medicine. The main research interests include elucidating the mechanisms of DILI induced by drugs such as Thunder God Vine (*Tripterygium wilfordii*) and anticancer agents like Crizotinib, investigating the hepatoprotective effects of Traditional Chinese Medicine (TCM) compounds such as Licorice, and advancing TDM technologies to enhance clinical medication safety and efficacy.*

Objective: Liver dysfunction affects drug metabolism, including voriconazole, used for treating fungal infections. This study evaluated the effectiveness and safety of a voriconazole dosing regimen adjusted for liver dysfunction (VALID) compared to standard dosing.
Methods: The study included liver dysfunction patients hospitalized between January 2020 and December 2023. Patients were divided into the VALID group and a control group. Data on demographics, medication, liver and kidney function, and adverse events were collected. Propensity score matching was used to balance the groups. Voriconazole levels were measured using liquid chromatography.
Results: The study analyzed 182 patients with 375 voriconazole measurements—39 in the VALID group and 143 in the control group. After matching, both groups were similar in baseline characteristics. The VALID group had a significantly higher target trough concentration achievement (89.7% vs. 48.7%, P<0.0001) and lower initial voriconazole levels (2.46 mg/L vs. 4.13 mg/L, P=0.0004). The VALID group also had fewer adverse events (15.4% vs. 38.5%, P=0.02159). Efficacy between the two groups was similar (P=0.9132). Factors like CYP2C19 phenotype and liver function influenced voriconazole levels.
Conclusion: The VALID regimen improved target trough levels and reduced adverse events compared to standard dosing. These findings support individualized dosing for better voriconazole therapy in liver dysfunction patients. Further research is needed to confirm these results in larger studies.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

208

Exploring cumulative amikacin exposure to prevent ototoxicity

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Biography:
Work experience
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Background: Although amikacin-induced ototoxicity is associated with cumulative exposure, the specific amount of exposure that may induce ototoxicity remains unknown.

Aims: This study aimed to clarify the relationship between amikacin exposure and ototoxicity.
Methods: This retrospective observational study included patients with non-tuberculous mycobacterial pulmonary disease. TDM data for amikacin, audiogram records, and patient characteristics were obtained from electronic medical records. Amikacin exposure was calculated from the TDM data, and the relationship between cumulative exposure and change from baseline in the audiogram was analyzed. The population pharmacokinetics/pharmacodynamics model was constructed using NONMEM version 7.5.0. This study was approved by our Ethics Committee.
Results: We enrolled 185 patients. Median amikacin dose and observation period were 500 (interquartile range [IQR]; 500–600) mg/day and 6.4 (IQR; 2.8–22.2) months, respectively. The patients underwent an average of five TDM measurements and four audiograms. Although the peak and trough amikacin concentrations were not significant predictors of ototoxicity, cumulative exposure was associated with audiogram changes. The estimated slope of audiogram change against cumulative amikacin exposure was 0.085 (95% confidence interval [CI]; 0.055–0.12) [dB* L/days/g/h] at 4000 Hz and 0.16 (95% CI; 0.11–0.21) [dB*L/days/g/h] at 8000 Hz. No hearing loss was observed at frequencies < 2000 Hz.
Conclusions: Ototoxicity was related to cumulative amikacin exposure of 117.6 [days*g*h/L], not to peak and trough amikacin concentrations.
Key Words: Amikacin, TDM, cumulative AUC, Ototoxicity.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

209

Optimising Difficult-to-treat Gram-negative Bacterial Infection Outcomes with Individualised Fosfomycin-Based Combination Therapy

Assist Prof Tze-Peng Lim[1,2,3], Yvonne Ng[4], Clarissa Jia Xi Song[4], Dr Nathalie Grace Sy Chua[1], Jun Jie Tan[1], Dr Kelvin Kau Kiat Goh[1,2], Li Jiao Sin[1], Jayden Ho[1], Chen Sing Lim[1], Jovial Si Ying Tan[1], Tami Lee, Winnie Hui Ling Lee[1], Assoc Prof Andrea Lay Hoon Kwa[1,3,5]
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Biography:

Lim Tze Peng, PhD, is a Senior Principal Pharmacist Researcher at Singapore General Hospital (SGH) and Assistant Professor at SingHealth Duke-NUS Pathology Academic Clinical Programme. With over a decade of experience in antimicrobial resistance research, he focuses on optimising antimicrobial dosing to improve clinical outcomes in drug-resistant infections.

A recipient of the National Medical Research Council Clinician Scientist Award (2022), Dr. Lim has secured numerous research grants to investigate antimicrobial resistance mechanisms, develop novel therapeutic drug monitoring (TDM) approaches, and advance precision medicine. He spearheaded the mass spectrometry facility at SGH for antimicrobial research and led practice-changing strategies in antibiotic administration.

Dr. Lim's current initiatives include developing a diagnostic assay for real-time antibiotic monitoring and a cloud-based antibiotic combination testing (ACT) platform to increase clinical adoption of ACT for multidrug-resistant infection

Background: Fosfomycin-based combination therapy is a promising approach against difficult-to-treat Gram-negative bacteria (DT-GNB), but regimen selection remains challenging due to bacterial diversity and patient-specific side effects. Our in-house in vitro antibiotic combination testing (iACT) service identified effective fosfomycin-based combinations with high bactericidal activity within 24 hours, enabling tailored clinical implementation.
Aims: We assessed the side-effect profiles and clinical outcomes of iACT-guided fosfomycin-based combination therapy.
Methods: This prospective observational cohort study (2023-2025) included adult inpatients with DT-GNB infections. iACT was conducted using 96-well plates containing various antibiotics in mono, dual or triple combinations (>170 unique combinations) at clinically unbound concentrations. Bactericidal activity was defined as ≥3log10 CFU/mL reduction at 24 hours.
Results: Twenty-nine subjects who received iACT-guided fosfomycin-based combination therapy were evaluated. All 29 DT-GNB isolates were carbapenem-resistant. The most common bactericidal regimens were Fosfomycin+Aztreonam+Levofloxacin(7/29), Fosfomycin+Aztreonam+Meropenem(4/29) and Fosfomycin+Levofloxacin+Meropenem(3/29).

Adverse effects occurred in 34.5%(10/29) of subjects, including hematologic (3), dermatologic(2), non-C. difficile-associated diarrhea(2), nausea/vomiting(1), hepatobiliary(1), and neurologic(1) events. All were well tolerated without regimen modifications, and no electrolyte imbalances were reported. Positive microbiological outcomes were achieved in 82.8%(24/29), with a 30-day all-cause mortality of 6.9%(2/29). Antibiotic TDM was performed in eight subjects receiving fosfomycin doses of 4–8g every 8h, except one hemodialysis patient who received an 8g load followed by 4g pre- and post-dialysis. Fosfomycin concentrations were observed to range from 13.61—1156.39 mg/L.
Conclusion: A two-pronged employing iACT-guided fosfomycin-based combination therapy for strain-specific treatment and TDM for real-time dose optimization can enhance clinical outcomes while minimizing toxicity in DT-GNB infections.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

210

DNAzyme-functionalized Nanoparticles Counteract HMGB1 Toxicity, Mitigating Sepsis Liver Injury and Multi-organ Failure

Mr MingXuan Xiao[1], Dr Yang Xi[1], Dr Miao Yan[1]
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Biography:

Xiao is a dedicated doctoral candidate specializing in mechanism-based research of drug toxicology and the development of novel small nucleic acid therapies. Integrating advanced biochemical approaches with nanotechnology, Xiao aims to enhance the stability, targeting, and therapeutic efficacy of small nucleic acids. His research focuses on unraveling the molecular underpinnings of drug toxicity, with the ultimate goal of minimizing effects and optimizing clinical potential. A strong advocate for interdisciplinary collaboration, Xiao engages with experts across pharmacology and materials science. He has authored multiple peer-reviewed articles and presented findings at international conferences, reflecting his commitment to academic excellence. By uniting biology and materials science, he seeks to revolutionize healthcare. Through his work, Xiao continues to explore new avenues in nanomaterial-assisted small nucleic acid therapeutics, envisioning targeted therapies to improve patient outcomes.

Background: Sepsis is a life-threatening condition arising from a dysregulated immune response to infection, culminating in multi-organ dysfunction and often organ failure, with a high mortality rate. The liver is notably susceptible to these “toxic” insults early in sepsis, exacerbating systemic inflammation and driving multi-organ failure (MOF). Recent evidence identifies the HMGB1–Caspase-11 axis as a critical endogenous “toxin” pathway in sepsis-related inflammation and liver injury, yet effective interventions targeting this pathway remain elusive.
Methods: Here, we developed DNAzyme-functionalized, pH-responsive glycyrrhizinic acid/zinc@polydopamine (GA/Zn@PDz) nanoparticles designed to release glycyrrhizinic acid and Zn^{2+} in weakly acidic conditions. These nanoparticles concurrently deliver a DNAzyme specifically targeting HMGB1, aiming to inhibit HMGB1-Caspase-11–mediated inflammation and pyroptosis via multiple mechanisms. By blocking this “endogenous toxin,” the system seeks to alleviate sepsis-induced liver injury and prevent progression toward MOF.
Results: In vitro, GA/Zn@PDz nanoparticles displayed excellent cellular uptake and biostability, significantly reducing HMGB1 expression and inflammatory factor release. In a septic mouse model, GA/Zn@PDz prolonged survival, attenuated histopathological liver damage, and reduced inflammatory and coagulation markers. Importantly, safety evaluations demonstrated minimal adverse effects on healthy tissues, indicating good biocompatibility.
Conclusion: We successfully constructed a pH-responsive, DNAzyme-functionalized GA/Zn@PDz nanomaterial to counteract HMGB1, an endogenous “toxin,” in sepsis-induced liver injury. By effectively interfering with the HMGB1–Caspase-11 axis, this strategy suppresses toxic inflammation, alleviates multi-organ damage, and offers a promising new avenue for combined gene silencing and small-molecule therapy in sepsis management.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

211

Beta-Lactam dosing in critically ill children: predictors for failure of target attainment

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Biography:
Stef Schouwenburg is a Pharmacist-Researcher from Rotterdam, The Netherlands. He works at the Department of Hospital Pharmacy in the Erasmus University Medical Center.

Background: Beta-lactam antibiotics are among the most prescribed antibiotics on the pediatric intensive care unit (PICU). For beta-lactam antibiotics, the unbound plasma concentrations above at least one to four times the minimum inhibitory concentration (MIC) for 100% of the dosing interval (100%ƒT>1-4×MIC) has been proposed as pharmacodynamic target to maximize bacteriological.
Aims: To determine the probability of target attainment of beta-lactam antibiotics in PICUs and to identify predictors and clinical outcomes associated with target nonattainment.
Methods: This prospective observational study was performed in two PICUs in the Netherlands. We enrolled pediatric patients treated with the following beta-lactam antibiotics: cefotaxime, ceftazidime, ceftriaxone, cefuroxime, flucloxacillin, and meropenem. Based on multiple samples within consecutive days of treatment, ƒT>MICECOFF and ƒT>4×MICECOFF were determined. Secondary endpoints were estimated regression models for examining the association of target nonattainment with patient characteristics and clinical outcomes.
Results: A total of 116 patients were included, of whom 27.6% achieved 100%ƒT>MICECOFF and 13.7% achieved 100%ƒT>4×MICECOFF. Regression analysis identified estimated glomerular filtration rate (eGFR)≥90mL/min./1.73m2 as risk factors for target nonattainment. In addition, no significant association between the 100%ƒT>MICECOFF target attainment and ICU length of stay (LOS) was found.
Conclusions: Plasma concentrations for beta-lactam antibiotics are frequently subtherapeutic in critically ill children (100%ƒT>MIC). We found an eGFR≥90mL/min./1.73m2 to be associated with target nonattainment, indicating kidney function should be taken into account when identifying individuals which may require higher dosages. These results may help identify subpopulations requiring higher dosages or continuous infusion in order to achieve adequate antibiotic exposure.
Key Words: Beta-lactams, Target-attainment

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

212

Comparative evaluation of machine learning models for predicting vancomycin-associated acute kidney injury

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Biography:

Mr. Yasuhiro Horita received his Master's degree and Doctor of Philosophy (Pharmacy) at the Department of Molecular Health Sciences, Graduate School of Pharmaceutical Sciences, Nagoya City University in 2011. He worked at the Research Institute of Tuberculosis, JATA from 2011 to 2019. He has currently worked as a pharmacist at the Department of Pharmacy, Nagoya City University Hospital since 2019. His official position is a lecturer of the Department of Clinical Pharmaceutics, Graduate School of Medical Sciences, Nagoya City University. His main theme is to conduct clinical studies related to TDM and pharmacokinetic-pharmacodynamic analyses of antimicrobial agents such as anti-MRSA drugs and anti-tuberculosis drugs. Recently, he works on a project to construct machine learning-assisted population pharmacokinetic models for AUC-guided vancomycin dosing.

Background: A machine learning model for predicting vancomycin-associated acute kidney injury (AKI) based on the area under the concentration-time curve (AUC) at an early stage of administration has not been devised.
Aims: To construct a risk prediction model involving related risk factors such as concomitant drugs and comorbidities.
Methods: A multicenter, retrospective, cohort study was conducted among hospitalized patients treated with vancomycin at three hospitals between April 1, 2019 and March 31, 2024. Based on previous studies, 21 variables were included in the model building. After selecting important features, risk prediction models were built using eight machine learning algorithms. The performances of machine learning models were evaluated by using accuracy, precision, recall, and F1 scores.
Results: Five important features were selected: day 2 AUC, trough concentrations, and concomitant use of piperacillin/tazobactam, diuretics, or vasopressors. Among the evaluated machine learning models, Naïve Bayes and a random forest with class weights exhibited equal best prediction performances in terms of accuracy (97.4%, 95% CI 93.4%–99.3%), precision (83.3%), recall (62.5%), and F1 score (71.4%).

Conclusions: We constructed a machine learning-based risk prediction model for vancomycin-associated AKI at an early time of administration. Our results underscore the importance of considering both day 2 AUC and trough levels in the development of such risk prediction models. Furthermore, our findings contribute to the construction of machine learning-assisted population pharmacokinetic models for precise vancomycin dosing.
Key Words: vancomycin, acute kidney injury, machine learning, initial dosing design

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

213

Predictive factors for 30-day-mortality after polymyxinB treatment of carbapenem-resistant Gram-negative bacilli infections

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Biography:

Deputy Chief Pharmacist of the Pharmacy Department, currently serving as the leader of the Therapeutic Drug Monitoring (TDM) Group, specializing in research on individualized dosing through TDM and the clinical safety/efficacy of drugs. Currently holding the positions of Vice Chairman of the Clinical Pharmacist Subgroup under the Therapeutic Drug Monitoring Professional Committee of the Chinese Pharmacological Society, Standing Committee Member and Secretary of the Youth Committee of the Therapeutic Drug Monitoring Professional Committee of the Chinese Pharmacological Society, Standing Committee Member of the Precision Testing Work Committee of the China Association for Promoting Optimal Maternity and Child Health Care, and Standing Committee Member of the Experimental Diagnosis and Social Service Branch of the China Medical and Health Culture Association.

Objectives: This study aimed to investigate the associated factors predicting 30-day mortality of carbapenem-resistant Gram-negative bacilli (CR-GNB) infections, with focus on polymyxin B AUCss,24h/MIC.
Methods: This prospective cohort study included patients with CR-GNB infections from January 2022 to January 2024. The primary outcome was 30-day mortality. Classification and regression tree (CART) analysis was used to calculate the AUCss,24h/MIC threshold for 30-day mortality. Multivariate analysis was conducted to assess risk factors affecting this outcome.
Results: We enrolled 107 patients, among which 30-day mortality occurred in 31 (29.0%) cases. The CART-derived AUCss,24h/MIC breakpoint was 51.3, and patients in the below-breakpoint group had 3.4-fold higher 30-day mortality than those in the above-breakpoint group (58.1% vs 17.1%, $P < 0.001$). On multivariate analysis, polymyxin B AUCss,24h/MIC of ≥ 51.3 (aOR 0.08, $P = 0.001$) predicted a lower risk for 30-day mortality. This survival benefit of AUCss,24h/MIC target attainment remained stable in patients with high risk of mortality or carbapenem-resistant Acinetobacter baumannii infections.
Conclusions: Polymyxin B AUCss,24h/MIC of ≥ 51.3 independently predicted lower 30-day mortality in treating CR-GNB infections. Future studies are required to confirm the reliability of AUCss,24h/MIC target in randomized controlled trials.
Keywords: polymyxin B; carbapenem-resistant gram-negative bacilli; 30-day mortality; predictors; AUCss,24h/MIC

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

214

Risk factors for tacrolimus AUC-trough concentrations discrepancies among transplant patients

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Biography:
Dr Florian Lemaitre has been trained as a pharmacist and pharmacologist during its residency in Rennes and Poitiers, France. In 2014, he received his PhD on the pharmacological optimization of immunosuppressive therapy during his pharmacology fellowship at the Pitié-Salpêtrière Hospital in Paris and the Rennes University Hospital.
His main research topic is the precision medicine in transplantation and he has been authored or co-authored 120+ articles. .
Since 2022, he is the president of the TDM-working group of the Société Française de Pharmacologie et de Thérapeutique (SFPT), the French national learning society of pharmacology. He is also the actual secretary of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and the Chair of the immunosuppressive drugs scientific committee of the IATDMCT.
He has dedicated his career to drug individualization for patients' care notably for solid organ transplant patients and patients with acute or chronic infections.

Background: Due to its narrow therapeutic range, tacrolimus requires therapeutic drug monitoring (TDM) to minimize risks of over- or under-exposure. While the AUC is the most reliable measure of drug exposure, trough concentration (Cmin) is commonly used in clinical practice. However, Cmin may not always accurately reflect true exposure, leading to potential unexpected effects.
Aims: This study aims to identify risk factors associated with AUC-Cmin discrepancies in transplant recipients treated with tacrolimus.
Methods: This retrospective study included patients who benefited from full microsampling tacrolimus PK profiles between one and six months post-transplantation. Age, weight, transplantation date, dose, creatinine, liver enzymes, hematocrit, proteins and co-treatments were collected. AUC-Cmin discrepancy was defined as a difference >20% between AUC calculated using the trapezoidal method and AUC estimated from Cmin using a linear regression equation. A logistic regression was conducted to identify risk factors for discrepancy.
Results: Ninety-eight patients were included in the study (68 kidney, 29 liver and 1 kidney-liver transplant recipients). Discrepancies were observed in 28.6% of patients with a lower Cmin/dose ratio (p=0.03), hematocrit (p=0.007) and total protein (p=0.01) and higher Alanine Aminotransferase (p=0.007) in the group presenting a discrepancy. No covariate remained statistically significant in the multivariate analysis.
Conclusions: No risk factor for AUC-Cmin discrepancy has been evidenced underlining the need for systematic AUC monitoring to detect patients with discrepancies and exposure-targeted

individualization of tacrolimus treatment. Significant discrepancies between AUC and Cmin was experienced in 28.6% of patients, highlighting that Cmin may not reliably reflect tacrolimus exposure.
Keywords: Immunosuppressants; pharmacokinetics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

215

Evaluation of model-based strategies for tacrolimus AUC estimation: Man versus Machine study

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Biography:

Dr Florian Lemaitre has been trained as a pharmacist and pharmacologist during its residency in Rennes and Poitiers, France. In 2014, he received his PhD on the pharmacological optimization of immunosuppressive therapy during his pharmacology fellowship at the Pitié-Salpêtrière Hospital in Paris and the Rennes University Hospital.

His main research topic is the precision medicine in transplantation and he has been authored or co-authored 120+ articles. .

Since 2022, he is the president of the TDM-working group of the Société Française de Pharmacologie et de Thérapeutique (SFPT), the French national learning society of pharmacology. He is also the actual secretary of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and the Chair of the immunosuppressive drugs scientific committee of the IATDMCT.

He has dedicated his career to drug individualization for patients' care notably for solid organ transplant patients and patients with acute or chronic infections.

Background: Pharmacokinetic (PK) population models can be used to estimate tacrolimus area-under-the-curve (AUC) using limited sampling strategies (LSS). Microsampling approaches now makes it feasible to obtain a full PK-profile and determine AUC. While combining these methods is appealing, the clinical applicability of using LLS developed on microsampling has never been evaluated.

Aim: The aim of the Man versus Machine study is to compare the performance of model-based strategies for tacrolimus AUC estimation to gold standard trapezoidal AUCs using a dataset of microsample full PK profiles in solid organ transplant patients.

Method: Five different model-based strategies aiming at estimating AUCs from a LSS (0,1,3 hours for immediate-release and extended-release tacrolimus and 0,8,10 hours for LCP-tacro) were blindly tested. AUCs estimated using model-based strategies were then compared with the corresponding observed reference trapezoidal AUCs. Model performances were deemed appropriate if less than 10% of profiles were estimated with a bias above 20%.

Results:
One-hundred and twenty-one patients were included in the study. The proportion of individual AUCs with bias >20% (failure) for each five models were: 6.6, 6.6, 7.1, 9.9 and 15.3%, respectively, meaning that between 1/6 and 1/15 has an inappropriate AUC estimation with the LSS approach.
Conclusion:
Four of five the five tested models displayed appropriate estimation of AUC when compared with reference AUCs using microsampling. A combined approach using limited microsampling strategy with PK modeling appears clinically feasible in most cases for tacrolimus AUC monitoring.
Keywords: transplantation; immunosuppressants; pharmacokinetics; drug monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

216

Machine Learning and Population Pharmacokinetics: A Hybrid Approach for Optimizing Vancomycin Therapy

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Biography:

Dr. Wang Yan is a highly regarded researcher and associate professor at the Department of Pharmacy, First Affiliated Hospital of Xi'an Jiaotong University. He holds a Doctorate in Pharmacy from Xi'an Jiaotong University and has postdoctoral experience at the University of Queensland, Australia. His research focuses on precision medicine for critically ill patients, especially in drug pharmacokinetics and pharmaco-economics. He is also exploring the application of machine learning methods to analyze critical patient data for optimizing drug use.

Dr. Wang has contributed significantly to the development of novel models for drug selection in critically ill patients, with funding from national scientific foundations. He has published over 40 academic papers. In addition to his research contributions, Dr. Wang has been involved in mentoring younger researchers and is dedicated to advancing the field of pharmacy.

Background: Predicting vancomycin exposure is critical for optimizing dosing regimens in sepsis patients. While population pharmacokinetic (PPK) models are commonly used, their performance is limited. Machine learning (ML) models may offer advantages, but it is unclear which model—PPK, Bayesian, ML, or hybrid PPK-ML—best predicts vancomycin exposure across clinical scenarios.
Aims: This study compares the performance of PPK, Bayesian, ML, and hybrid PPK-ML models in predicting the 24-hour area under the blood concentration curve (AUC24) to support precision dosing in sepsis.
Methods: Data from sepsis patients treated with intravenous vancomycin were sourced from the MIMIC-IV database. The dataset was split into training and testing sets to develop the four models. AUC24 was predicted using all models, and performance was evaluated with mean absolute error, mean squared error, root mean squared error, mean absolute percentage error (MAPE), and R^2.
Results:A total of 4,059 patients were included. In the absence of vancomycin concentration data, the hybrid model outperformed PPK and Bayesian models, with MAPE improvements of 58% and 17%, respectively. When concentration data were available, the Bayesian model performed best (MAPE: 13.37% vs. 68.17%, 34.17%, and 28.52% for PPK, Random Forest, and hybrid models).
Conclusions: The hybrid model is recommended when concentration are unavailable, while the Bayesian model is preferred when concentration are available, offering robust strategies for precise vancomycin dosing in sepsis patients.
Keywords: Population pharmacokinetics, Machine learning, Sepsis, Vancomycin, Drug exposure

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

217

Awareness, Attitudes, and Barriers to Clinical Utilization of Bayesian Dose Prediction Software

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Biography:

Dr.Sarah Alghanem, is currently an Assistant Professor of Pharmacy Practice College of Pharmacy, Kuwait University. Her research focuses on clinical pharmacometrics (PKPD modelling and simulations) and outcome studies to evaluate and optimize the use of antimicrobial and immunosuppressant therapy. In addition, Dr.Alghanem is studying the development, implementation, and evaluation of advanced pharmacy services within the country. She is an active member at reginal and international organizations. She had significant contribution in shaping and transforming pharmacy profession in Kuwait by working closely with Kuwait Ministry of Health to expand pharmacy scope of practice and develop clinical pharmacy services policies and procedures to align with international standards.

Background: Bayesian dose prediction software is designed to aid clinicians in optimizing medication dosing in clinical settings.
Aims: This study evaluated clinicians' awareness and use of Bayesian dose prediction software, their attitudes toward its application, and the barriers to its clinical implementation, addressing the limited literature on its adoption in practice.
Methods: A cross-sectional, multi-organizational study was conducted using a validated electronic questionnaire distributed to 360 members across 8 organizations. Descriptive analyses were performed using SPSS version 28.
Results: The response rate was 65% (n=234) with most respondents from North America (67.4%). Forty-four participants who did not provide direct patient care were excluded, resulting in 190 eligible respondents. Among these, 82.6% (n=157) were aware of Bayesian dose prediction software, but only 65% (n=102) used it in their practice. The most commonly used software were InsightRx (40.2%), DoseMe (22.5%), and MWPharm (18.6%), primarily for dosing vancomycin (94.1%), aminoglycosides (50%), and tacrolimus (10.8%). The overall median (IQR) attitude score toward the software was 4.0 (2.0), indicating a positive attitude. The top three perceived barriers to clinical implementation among those aware of the software were the prohibitive cost of software licensing (65%), lack of healthy facility administrative support for the use and maintenance of the software (50.3%), and lack of awareness of how to use software into clinical practice (49.7%).
Conclusions: Findings indicate that while Bayesian dose prediction software is being utilized, its adoption remains limited to a few medications. The results highlight the need for targeted interventions to overcome the perceived barriers.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

218

Population Pharmacokinetics and Concentration-QTc Analysis of Bedaquiline in Patients with Multidrug-resistant Tuberculosis

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Biography:

Li Jinmeng, a clinical pharmacist at Zhejiang Integrated Traditional Chinese and Western Medicine Hospital, has been actively engaged in the treatment and prevention of tuberculosis in recent years. Together with her team members, she has developed plasma concentration detection methods for 30 drugs, including 15 anti-tuberculosis drugs, 12 anti-infective drugs, and 3 anti-psychotic drugs. These methods have been successfully applied in clinical therapeutic drug monitoring (TDM), and significantly improved clinical treatment outcomes of these drugs. In addition, she specializes in methods related to population pharmacokinetic and pharmacodynamic studies in quantitative pharmacology. The long-term goal is to improve the effectiveness of anti-TB drugs and control the progression of MDR-TB based on therapeutic drug monitoring and quantitative pharmacology. Her current research focuses on optimizing the efficacy of second-line anti-TB drugs and reducing the occurrence of adverse reactions and drug resistance.

Background: Bedaquiline (BDQ) has shown great value in the treatment of multidrug-resistant tuberculosis (MDR-TB) in recent years. However, large pharmacokinetic variability was observed in patients following standard BDQ dosing. BDQ is also reported to induce cardiac QT interval prolongation.
Aims: This study aims to perform a population pharmacokinetic-pharmacodynamic (PPK-PD) analysis of BDQ in Chinese MDR-TB patients to enable model-based precision dosing and investigate the concentration-QTc relationships of BDQ.
Methods: Blood samples and therapeutic drug monitoring (TDM) results of BDQ were collected for PK evaluation, and ECGs were recorded for QTc calculation at the designed timepoints. The PPK-PD model was developed using nonlinear mixed effects modeling (NONMEM) software. An effect compartment model was utilized to explain the relationship between BDQ concentrations and ΔQTc.
Results: A total of 211 BDQ concentrations and 350 QTc measurements were obtained from 105 Chinese MDR-TB patients. The PK characteristics of BDQ was adequately described using a two-compartment model with first-order absorption and elimination. The estimated apparent clearance and volume of distribution were 1.77 L/h and 52.4 L, respectively. Body weight and albumin were significant covariates for clearance of BDQ, with body weight also affecting the apparent volume of distribution. ΔQTc exhibited a linear relationship with BDQ concentration. A linear model properly characterized BDQ-induced QTc prolongation.
Conclusions: A PPK-PD model based on sparse data was established for prediction of BDQ exposure in patients with MDR-TB. TDM and PPK modeling provide valid evidence on the precision dosing of bedaquiline.
Keywords: Bedaquiline; PPK-PD model; concentration-QTc relationship; multidrug-resistant tuberculosis; TDM

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

219

Model-informed precision dosing of linezolid: a model averaging vs single-model approach

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Biography:

Antonia Leonhardt studied pharmacy at the University of Bonn, Germany, from 2016 to 2021. Following her graduation, she moved to Hamburg to work as a pre-registration pharmacist at a public pharmacy and at the University Medical Center Hamburg-Eppendorf (UKE). In July 2022, she obtained her license to practice as a pharmacist. Since October 2022, she has been pursuing a PhD in Clinical Pharmacy with a focus on Pharmacometrics at the Institute of Pharmacy, University of Hamburg, under the supervision of Prof. Dr. Sebastian G. Wicha. Her doctoral research is centered on optimizing anti-infective pharmacotherapy, specifically investigating the pharmacokinetics of antibiotics and strategies for dose individualization.

Background: The pharmacokinetics of linezolid can vary significantly, particularly in critically ill patients. Model-informed precision dosing (MIPD) enables dose individualization by employing one or several population pharmacokinetic (popPK) models to optimize drug exposure, thereby enhancing therapeutic success and minimizing adverse effects.
Aims: To compare the performance of MIPD of linezolid using a single-model and model averaging algorithm (MAA) approach.
Methods: The predictive performance (PP) of popPK models of linezolid (n=30) was externally evaluated. Theoretical target attainment (TTA) was selected as the indicator of PP, demonstrating the percentage of expected trough concentrations within 2-8 mg/L when using popPK models for MIPD. MAA was analyzed in TDMx for two groups. Group one comprised models exhibiting the highest and lowest TTA (three each). In group two, the three models with the highest tendency to overpredict or underpredict were included, respectively.

Results: Averaging across the six models in group one led to a TTA of 69.3%, while the TTA of each single model ranged from 44.3% to 72.3%. MMA in group two exhibited a TTA of 70.8%, compared to a TTA of 44.3% to 66.6% with the six single models.
Conclusions: High variability in PP underscores the importance of model selection within MIPD for linezolid. The MAA achieved a TTA similar to or higher than the best performing single model without user intervention. The MAA is a promising alternative to the single-model approach, particularly in absence of external evaluation or if existing popPK models display unsatisfactory PP.
Keywords: Linezolid, MIPD, Pharmacokinetics, popPK, Model averaging

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

220

Pharmacokinetic-based Bayesian approach to Assess Medication Adherence via Therapeutic Drug Monitoring

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Biography:

Xiao-Qin Liu earned her Bachelor's Degree (2018) and Ph.D. (2022) from Fudan University. She is Member of Quantitative Pharmacology Committee, Chinese Pharmacology Society, Member of Shanghai Anticoagulation Pharmacist Alliance and Youth Member of Therapeutic Drug Committee, Shanghai Pharmaceutical Association. Specializing in pharmacometrics, her research focuses on model-informed precision dosing through population pharmacokinetic approaches. She has published 9 SCI-indexed papers as first/co-first author and currently serves as Principal Investigator of a National Natural Science Foundation of China (NSFC) research grant.

Background: Adherence to long-term pharmacotherapy plays a pivotal role in achieving optimal therapeutic outcomes. While therapeutic drug monitoring (TDM) is widely adopted for evaluating medication adherence, the current guidelines do not offer, or lack patient-specific reference range, potentially compromising the accuracy of adherence assessments.
Aims: The study aims to evaluate a pharmacokinetic-based Bayesian approach utilizing TDM measurements for evaluating medication adherence.
Methods: Taking neuropsychiatric drugs as an example for illustration, including anti-seizure medication, antipsychotic medication, anti-anxiety medication and others. Concentration-time profiles for virtual cohorts with monotherapy were simulated, including full adherence and diverse non-adherence patterns, based on population pharmacokinetic parameters derived from previous studies. Subsequently, a Bayesian framework was implemented to evaluate medication adherence based on TDM data. A systematic investigation of critical factors influencing adherence assessment was also conducted.
Results: By leveraging essential patient-specific data and dosing regimens, the integration of Bayesian approach with TDM data enables evaluation of recent medication adherence patterns. The concentration thresholds for adherence assessment demonstrated significant variability across different classes of neuropsychiatric medications, with notable influences from patients' characteristics, concomitant pharmacotherapy, temporal sampling variations, dosing intervals, and prior probability distributions. To facilitate personalized adherence monitoring, an interactive web-based dashboard incorporating these critical variables was developed, which could be accessed via https://mipd.shinyapps.io/adherence_assessment/.

Conclusion: Pharmacokinetic-based Bayesian approach significantly enhances the capacity of TDM data in identifying distinct non-adherence patterns. These findings advocate for paradigm shift in therapeutic management toward personalized adherence assessment protocols.

Key words: anti-seizure medication, medication adherence, therapeutic drug monitoring, Bayesian method, population pharmacokinetics

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

221

Effects of antimicrobial drugs on microbiome-derived reactivation of mycophenolic acid

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Biography:

Pharmacist by education and a PhD on cyclosporine in kidney transplants. Head of Laboratory for Renal Physiology at Oslo University Hospital – Rikshospitalet and professor at University of Oslo, Norway. Chair of the Pharmacometrics committee and Vice-Chair of the European section committee of the IATDMCT.

Has more than 30 years of research experience in pharmacokinetics and kidney transplantation, with a special interest in using population models for improved diagnostics and dosing of patients.

Background: The gut microbiome may contribute to variations in the pharmacokinetics of mycophenolic acid (MPA). Hepatic glucuronidation converts MPA to the inactive metabolite, mycophenolate glucuronide (MPAG), which can be excreted into the gastrointestinal tract via the bile. In the gut, bacterial β-glucuronidase enzymes convert MPAG back into MPA, which is reabsorbed, contributing to a secondary plasma peak. Antimicrobial drugs can alter gut microbiome composition and potentially influence MPA reactivation.

Aims: This project investigated whether different antimicrobial drugs influence ex vivo microbiome-derived MPA reactivation.

Methods: Fecal samples from healthy individuals were inoculated in anaerobic Gifu media with six antimicrobial drugs (50 µM) individually added to separate samples and incubated (24-hr). Protein lysates were prepared from fecal cultures through bead beating, sonication and ultrafiltration, then standardized after protein determination. To assess the reactivation of MPA, MPAG was added to the lysates, followed by 37°C incubation with samples collected at 0, 0.25, 0.5, 1, 1.5 and 2-hr. MPA concentrations were quantified by UHPLC-MS/MS, and fitted to a linear regression function, with the slope representing the reactivation rate of MPA.

Results: Ciprofloxacin and erythromycin showed higher MPA reactivation rates compared to controls, with mean±SD relative difference of 84±22% and 94±56%, respectively. Ampicillin and sulfamethoxazole had lower reactivation rates, with relative difference of -25±21% and -27±4%, respectively. Trimethoprim and vancomycin showed no difference compared to controls.

Conclusions: Antimicrobial drugs appear to influence microbiome-derived MPA reactivation to varying degrees. Microbiome composition changes will be assessed to investigate antibiotic-induced shifts to explain these effects.

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

222

Tacrolimus Trough Concentration to Dose Ratio: Peak Concentration and Trough-Exposure Relationship

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Biography:
Amar Levens is a hospital outpatient pharmacist and researcher specializing in pharmacogenomics and therapeutic drug monitoring. He has been an outpatient pharmacist at Leiden University Medical Center (LUMC) since 2016 and is currently pursuing a PhD at the Department of Clinical Pharmacy & Toxicology under the supervision of Prof. Dr. Jesse Swen and Dr. Dirk Jan Moes.
Beyond his clinical and research work, Amar is Chair of Leiden Academic Network of Pharmacists (https://www.lananet.nl/) and Young Medical Delta (https://www.youngmedicaldelta.nl/en) , where he promotes healthcare innovation and interdisciplinary collaboration. Additionally, as PR Person of LUMC Association for PhD Candidates (https://www.laplumc.org/), he works to enhance the visibility of PhD candidates and their research.

Background: In kidney transplantation, recipients with a low trough concentration/dose (C0/D) ratio of tacrolimus (<1.05 ng/ml/mg), identified as fast metabolizers, face higher risks of nephrotoxicity, BK-viremia, and graft loss. These patients require higher doses to maintain therapeutic C0, potentially increasing peak tacrolimus concentrations (Cmax) and total drug exposure (AUC24), which may contribute to poorer outcomes (Van Gelder et al., 2020).
Aim: To assess whether fast metabolizers have higher Cmax and to evaluate the C0-AUC24 relationship compared to intermediate and slow metabolizers.
Methods: This retrospective study at Leiden University Medical Centre (2010-2024) included stable kidney transplant recipients with C0 and AUC24 measurements at 12 months post-transplantation. Recipients were categorized as fast (<1.05 ng/ml/mg), intermediate (1.05-1.54 ng/ml/mg), or slow (≥1.55 ng/ml/mg) metabolizers by C0/D ratio. Kruskal-Wallis and Wilcoxon tests compared Cmax and AUC24 across groups. Linear regression assessed the C0-AUC24 relationship.
Results: Among 359 recipients (Fast: n=87, Intermediate: n=97, Slow: n=175), no differences in Cmax were observed (p=0.418). Observed C0 differed significantly (p<0.0001), with fast metabolizers having lower C0 than both intermediate and slow metabolizers. The observed AUC24 was lower in fast vs. slow metabolizers (p=0.025). Linear regression predicted AUC24 at C0=5 and C0=7 as 182 and 246 (Fast), 166 and 230 (Intermediate), and 154 and 217 ng·h/mL (Slow).
Conclusion: Compared to intermediate and slow metabolizers at the same C0, fast metabolizers have a higher AUC24 (but a similar Cmax). The higher tacrolimus exposure may explain poorer outcomes. The difference in AUC24 supports AUC24-based monitoring to optimize tacrolimus dosing in these patients.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

223

Plasma p-cresol sulfate and tacrolimus pharmacokinetic variability in liver transplant recipients

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Biography:

Dr. Huaijun Zhu is a Chief Pharmacist, Master's Advisor, and Director of the Clinical Pharmacology Division at the Pharmacy Department of Nanjing Drum Tower Hospital. His research specializes in precision medication for immunosuppressants and antimicrobial drugs, contributing significantly to advancements in pharmacotherapy. Dr. Zhu has been awarded competitive grants from prestigious programs, including the National Natural Science Foundation of China, the 7th "333 Project" of Jiangsu Province, and the Jiangsu Provincial Medical Youth Talent Program, among others.

Dr. Zhu holds prominent academic and professional roles, serving as a Member of the Therapeutic Drug Monitoring Committee under the Chinese Pharmacists Association and a Standing Committee Member of the Model-Driven Drug Development Committee within the Jiangsu Pharmaceutical Association. His scholarly contributions include the publication of over 70 SCI-indexed papers, and he has been recognized with two provincial-level and five municipal-level new technology awards for his innovative work in the field.

Background: Therapeutic drug monitoring (TDM) plays a crucial role in adjusting tacrolimus (Tac) doses. However, Tac dosing is complicated by various factors that influence its pharmacokinetics. Our previous untargeted metabolomics study indicated that plasma microbial toxins may affect Tac trough concentrations, providing new insights for optimizing Tac dosing.
Aims: To quantitatively examine the correlation between plasma microbial toxin levels and Tac dose-adjusted trough concentrations in adult liver transplant recipients, as well as to explore the in vitro interactions of these toxins with P-glycoprotein (P-gp) and CYP3A4/5 enzymes.
Methods: Plasma samples from 124 liver transplant recipients were analyzed for seven microbial toxin levels using liquid chromatography tandem mass spectrometry. Linear regression was performed to assess the relationship between Tac trough concentrations and microbial toxins. MDCK-MDR1 cells were used to assess Tac uptake, and P-gp expression was measured in HepG2 and Huh-7 cells. The effects of microbial toxins on CYP3A4/5 activity were evaluated using recombinant enzymes.
Results: Regression analysis identified microbial toxin P-cresol sulfate (PCS) (β=-0.192, p=0.036), total bilirubin (β=0.018, p=0.048), and diabetes (β=1.294, p=0.015) as independent factors influencing Tac trough concentrations. In vitro, PCS did not affect Tac uptake in MDCK-MDR1 cells but induced P-gp mRNA and protein expression in a time-dependent manner. PCS showed a minor inhibitory effect on CYP3A4 activity, indicated by decreased 1-hydroxymidazolam metabolites.
Conclusions: Plasma PCS levels negatively correlate with Tac trough concentrations in liver transplant recipients. The interaction between PCS and P-gp may inform Tac dose adjustments.
Key Words: tacrolimus, pharmacokinetics, liver transplantation, P-cresol sulfate

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

224

RSRC1 hydroxymethylation in circulating cfDNA: A novel epigenetic biomarker for UC diagnosis

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Biography:
Pharmacology PhD and Deputy Chief Pharmacist. Lecturer at Peking University and advanced pharmacy practice mentor at the University of Michigan. Research focuses on clinical pharmacology and biomarkers of intestinal inflammatory diseases, and therapeutic drug monitoring of biologics. Published 12 SCI papers, including one ESI highly-cited paper. Awards: "Science and Technology Award" from the China Pharmaceutical Association in 2020, "Science and Technology Innovation Award" from the China Hospital Association in 2021, "Promotion Award" of "Management Science Award" from the Chinese Institute of Management Science in 2022. Second prize award for teaching achievements from Peking University, and outstanding teacher of Peking University Third Hospital.

Background: Ulcerative colitis (UC) diagnosis currently relies on clinical symptoms, endoscopic findings, and histopathology, yet lacks a specific gold-standard biomarker, often leading to delayed or uncertain diagnoses. 5-Hydroxymethylcytosine (5hmC), an epigenetic regulator of gene expression, exhibits chemical stability and disease-specific modifications, positioning it as a promising biomarker to address this unmet need.
Aims: To identify genome-wide 5hmC signatures in circulating cell-free DNA (cfDNA) and develop non-invasive diagnostic biomarkers for UC.
Methods: Utilizing 5hmC-Seal technology, we profiled 5hmC in cfDNA from 49 UC patients and 74 healthy controls. The cohorts were stratified into training (33 UC/50 healthy) and validation (16 UC/24 healthy) sets. An elastic-net logistic regression model was trained on differentially hydroxymethylated regions (DhMRs) and validated for diagnostic performance.
Results: UC patients exhibited globally reduced 5hmC levels ($p<0.0001$) and distinct DhMR patterns compared to controls. A 9-DhMR model attained high accuracy (AUC=0.919, sensitivity=0.812, specificity=1) in validation. Notably, a single DhMR within RSRC1 achieved comparable accuracy (AUC=0.924, sensitivity=0.812, specificity=0.958). Functional analysis linked DhMRs to UC-relevant pathways (e.g., Wnt signaling, platelet activation). RSRC1 5hmC levels inversely correlated with C-reactive protein ($p<0.05$), supporting its role in inflammation. Digital PCR confirmed the reduced RSRC1 5hmC copies in UC ($p<0.0001$), allowing for simplified detection.
Conclusions: Genome-wide 5hmC profiling in cfDNA effectively distinguishes UC patients from healthy individuals. The RSRC1-centric model provides a robust, minimally invasive diagnostic tool with high clinical translatability, addressing critical unmet needs in UC management.
Keywords: Ulcerative colitis, cell-free DNA, 5-hydroxymethylcytosine, diagnosis, RSRC1

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

225

Tacrolimus Levels Compared in PBMCs and Whole Blood Among Kidney Transplant Recipients

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Biography:

Dr. Wang, an Associate Chief Pharmacist, comes from the Department of Pharmacy, Shanghai Children's Hospital, affiliated with Shanghai Jiao Tong University School of Medicine. As a clinical pharmacist and Master's Supervisor, he specializes in TDM and has published 34 academic papers, highlighting his significant contributions to the field.

Background: Tacrolimus monitoring in kidney transplant recipients traditionally relies on whole-blood trough levels, but this approach may inadequately reflect lymphocyte drug exposure, limiting its ability to predict graft outcomes. This study evaluated whether tacrolimus monitoring in peripheral blood mononuclear cells (PBMCs) improves clinical utility by analyzing its correlation with allograft function and de novo donor-specific antibody (dnDSA) status.
Aims: In a single-center prospective observational study, 60 kidney transplant recipients underwent paired tacrolimus measurements in PBMCs and whole blood at six timepoints within the first post-transplant year.
Methods: In a single-center prospective observational study, 60 kidney transplant recipients underwent paired tacrolimus measurements in PBMCs and whole blood at six timepoints within the first post-transplant year.
Results: PBMC tacrolimus levels averaged 3.6% of whole-blood concentrations ($P<0.01$) and correlated with whole-blood levels at early and mid-term follow-ups. Notably, PBMC tacrolimus levels demonstrated stronger associations with creatinine clearance and estimated glomerular filtration rate at multiple timepoints compared to whole-blood measurements. Patients with dnDSA exhibited significantly higher intrapatient variability in PBMC tacrolimus levels than dnDSA-negative counterparts ($P<0.05$), a pattern not observed in whole-blood analyses.
Conclusions: These findings suggest that PBMC-based tacrolimus monitoring better reflects drug bioavailability in target immune cells, offering enhanced insights into graft function and immunological risk. By linking PBMC tacrolimus variability to dnDSA status, this study highlights the potential of lymphocyte-level monitoring to optimize immunosuppression management and improve long-term transplant outcomes.
Key Words: kidney transplantation; tacrolimus; intra-patient variability; peripheral blood mononuclear cell; allograft function; de novo donor-specific antibody

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

226

Compensatory dosing of tacrolimus after vomiting in kidney transplantation: A model-based approach

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Biography:
Dr. Caroline Monchaud, PharmD, PhD, is a hospital practitioner in pharmacology and toxicology at the University Hospital of Limoges, where she heads the Clinical Research Unit in Pharmacology and Toxicology. She is also a researcher within the INSERM UMR 1248 "Pharmacology & Transplantation" unit. Her academic background spans clinical harmacokinetics and therapeutic drug monitoring, with a focus on immunosuppressive therapy in solid organ transplantation. She has coordinated or participated in over 20 clinical research projects in this field and actively mentors graduate students.
She has authored or co-authored more than 60 peer-reviewed publications and contributed to national and international guidelines and educational initiatives in transplant pharmacology. She is a board member of the Société Francophone de Transplantation (French-speaking Transplantation Society) and an active member of the Société Française de Pharmacologie et de Thérapeutique (French Society of Pharmacology and Therapeutics) and the International Association of Therapeutic Drug Monitoring and Clinical Toxicology. Her work combines translational research and patient-centered education to optimize therapeutic strategies and improve long-term transplant outcomes.

Background: Tacrolimus is used for lifelong treatment in kidney transplant recipients, with vomiting being a common complication due to infections or side effects. Vomiting can reduce tacrolimus absorption, potentially decreasing its efficacy.
Aims: To develop a tool that calculates the required additional tacrolimus dose needed after vomiting episodes, to maintain appropriate drug exposure, ensuring therapeutic efficacy and preventing overexposure.
Methods: A published population pharmacokinetics (PK) model for immediate-release tacrolimus in adult kidney transplant recipients (Woillard et al, 2011) was implemented in R software. Ten thousand PK profiles at steady-state, with various vomiting delays and doses, were simulated. Only profiles with a trough concentration (C0) between 4–12 µg/L (Brunet et al, 2019) were considered. Vomiting was assumed to completely empty the depot compartment, and the AUC and C0 were used to evaluate the impact of vomiting and compensatory doses.
Results: A total of 3253 profiles were selected, with mean AUC0-12h and C0 of 128.9 ± 39. h.µg/L and 7.89 ± 2.30 µg/L. Vomiting at 15, 30, and 45 minutes after IR-tac intake led to a decrease in AUC0-12h by 16.9 ± 9.4, 6.0 ± 4.2, and 2.3 ± 2.1%, respectively. Underexposure was corrected (AUC within ± 20 % of steady-state AUC) by adding a half or a full dose.
Conclusions: This study provides a novel and original solution to managing vomiting episodes in kidney transplant recipients. An app under development will offer individualized compensation based on recent C0 values, estimating personal PK parameters.
Keywords: Tacrolimus, Vomiting, Kidney transplant patients, Population pharmacokinetics, Compensatory dosing, AUC

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

227

MPA Exposure in Renal Transplantation and Clinical Outcomes in Early Post-Transplantation Period

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Biography:
I am a physician-scientist passionate about making small differences in patients' lives whether it is providing clinical services or through research. My areas of research include clinical pharmacology of immunosuppressant and anticancer drugs. I focus mostly on investigator-initiated clinical trials involving therapeutic drug monitoring, pharmacogenomics and translational molecular biomarker research, drug repurposing and new drug delivery systems that cater to unmet needs. I am closely involved in postgraduate teaching, and teach courses : clinical research methodology, biostatistics, new drug development and pharmacotherapeutics.

Background: Mycophenolic acid (MPA) is used in fixed doses of 2-3 grams/day. in renal transplantation This has been shown to result in variable patient outcomes. In Indian patients, optimal MPA exposure remains elusive. The recommended therapeutic range of AUC0-12h is 30-60mg.h/L underscores the need for precise dosing to balance efficacy and safety. This study aimed to explore the extent of MPA exposure in renal transplant recipients prescribed standard MMF doses, and to assess its association with rejection and infection episodes at day 30 post-transplantation.
Methods: We enrolled 120 renal transplant recipients with 94 males and 26 females who were prescribed 1g MMF twice daily post-transplantation. The mean age of the renal transplant recipients was 48.2±6.7 years and mean BMI was 20.13±3.58 kg/m². The MPA exposure quantification was done using HPLC. Patients were monitored for rejection and infection episodes at day-30.
Results: Patients with MPA exposure >60mg.h/L (n=68) exhibited mean AUC of 82.65±19.01 mg.hr/L, while those <30mg.h/L (n=13) showed 23.06±5.25, and within therapeutic range (n=39) displayed 64.96±26.73 AUC. Notably, rejection rates did not significantly differ based on MPA exposure (p=0.44), patients with infections had significantly difference in mean AUC 53.61± 20.15) compared to those without infection (mean AUC 66.19±26.59; p=0.008).
Conclusion: Our findings underscore the importance of therapeutic drug monitoring (TDM) in renal transplant care. While MPA exposure did not significantly impact rejection, it significantly influenced infection rates. TDM-guided dosage adjustments may mitigate infection-related complications post-transplantation, emphasising the necessity of personalized immunosuppressive therapy.

229

Leveraging on TDM to Fight Against Antimicrobial Resistance

Dr Nathalie Grace Sy Chua

Biography:
Dr Nathalie Chua is an infectious disease specialist pharmacist at the Singapore General Hospital (SGH). She is involved in antimicrobial stewardship and works with physicians in managing difficult-to-treat infections through antimicrobial therapeutic drug monitoring (TDM) and in vitro antibiotic combination testing as a form of precision medicine. She also currently leads the antiretroviral stewardship service and co-leads the antimicrobial TDM services in SGH. Her research interests include personalised therapy for infectious diseases, pharmacokinetic/pharmacodynamics, therapeutic drug monitoring and managing antimicrobial resistance. She is the principal investigator for the Beta-lactam TDM project in SGH and is a co-investigator for various antimicrobial TDM projects in Singapore. She serves as an infectious disease preceptor for the national pharmacy residency programmes and is a pharmacist representative in the national workgroups for Surgical Antibiotic Prophylaxis Guidelines and Antiretroviral Therapy Recommendations in Singapore. She also currently represents Singapore in the Regional Asia Pacific Section and the Young Scientist Committee of IATDMCT.

With rising antibiotic resistance and limited novel antibiotic armamentarium, infections caused by multidrug-resistant bacterial infections are increasingly challenging to treat. In such dire situations, clinicians may need to resort to currently available antimicrobials but the dosing regimens may have to exceed conventional dosing recommendations to ensure adequate antimicrobial exposures for efficacy. This narrows the therapeutic windows for several antimicrobials, such as beta-lactams, which originally did not require therapeutic drug therapeutic monitoring (TDM) due to their excellent safety profile. In addition, patients often have complex pharmacokinetics and conventional dosing recommendations derived from healthy volunteers may be irrelevant and potentially inadequate. Conversely, subtherapeutic antimicrobial exposures due to inadequate dosing may encourage further resistance development. Hence, antimicrobial TDM becomes a valuable tool to individualise dosing regimens to ensure maximal efficacy and minimal toxicity. In this session, Nathalie shares her experience in utilising TDM as a form of precision medicine in infectious diseases to help prevent resistance development and manage multidrug resistant infections.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

230

Current situation of mass spectrometry analysis of toxins in clinical toxicology

Ms Aline Christin Vollmer

Biography:

Working on my MSc thesis "Cardiovascular drugs: Quantitative adherence monitoring in blood plasma" which I finished in 2020, allowed me to gain first experiences within the field of clinical toxicology. In the same year, I graduated as a licensed pharmacist from the Saarland University and first started working in a public pharmacy afterwards until I joined the group of Prof. Markus R. Meyer at the Department of Experimental and Clinical Toxicology and Pharmacology (Homburg, Germany) in 2021 for my PhD. My research mainly focuses on method development and validation by means of (dual) liquid chromatography (LC)-high-resolution tandem mass spectrometry including small molecule and peptide analysis. Different extraction approaches as well as concepts towards LC miniaturization are also being investigated. For me, it is also a pleasure to be a member of national and international societies including the DPhG, GT, GTFCh, TIAFT, and IATDMCT.

The exposure to toxic plants or mushrooms whether by accident, misuse, or intention can lead to serious health risks or even death. The assessment of suspected poisoning remains a major challenge in clinical toxicology due to the considerable variety of toxic plants and mushrooms, containing different harmful constituents. Depending on the ingested toxin, clinical diagnosis can be difficult as first symptoms are often unspecific and occur with a delayed onset. Treatment must often be symptomatic and supportive as a specific antidote is not always available. Currently, straightforward sample preparation procedures combined with liquid chromatography mass spectrometry (LC-MS)-based analysis may allow for fast, sensitive, and unambiguous toxin detection and/or quantification in plasma and urine. The analysis spectrum should cover non-peptide toxins such as aconitine (Aconitum napellus), atropine (Atropa belladonna), colchicine (Colchicum autumnale), cytisine (Laburnum anagyroides), digoxin and digitoxin (Digitalis purpurea/lanata), muscarin and muscimol (Amanita muscaria), nicotine (Nicotiana tabacum), or yew constituents (Taxus baccata) but also peptide toxins such as ricin (Ricinus communis), abrin (Abrus precatorius), and amanitin (Amanita phalloides, death cap). Extraction can be performed either by conventional techniques including protein precipitation, liquid-liquid extraction, and solid-phase extraction or via antibody-based enrichment using magnetic beads. The talk will give an overview of plant and mushroom toxins relevant in clinical toxicology with a focus on current LC-MS-based approaches that are used to assess suspected poisoning.

231

Establishment of TDM Service in India

Prof Sumith K Mathew

Biography:
Sumith K Mathew is a clinical pharmacologist working in Believers Church Medical College Thiruvalla, Kerala. Working in the field of Therapeutic Drug Monitoring for past 10 years, he developed interest in Therapeutic Drug Monitoring, Analytical Chemistry, Pharmacometrics, Model-informed Precision Dosing and alternative sampling techniques. Currently, he is the Vice Chair of Regional Asia Pacific Section of International Association of Therapeutic Drug Monitoring and Clinical Toxicology. Prof Sumith has contributed extensively to research and publications on antimicrobial dosing regimens, as well as analytical methods for antineoplastics and immunosuppressants.

Therapeutic Drug Monitoring (TDM) services are not widely available in India. This talk will address the existing gap in TDM service availability and the barriers to establishing these services in India, a low- and middle-income country (LMIC). The speaker will outline the processes involved in setting up TDM services within hospitals and will provide details on the logistics required for successful implementation. This includes the collaborative efforts of pharmacologists, clinical pharmacists, analytical chemists, molecular biologists, and clinicians, all working together to integrate TDM into treatment protocols and enhance patient care.

232

The production of reactive metabolites may be one of the main causes of clinical drug-induced liver injury mediated by ALK inhibitors

Dr Yicong Bian

Biography:
Dr. Yicong Bian, an associate chief pharmacist and master's supervisor, works at the First Affiliated Hospital of Soochow University, Suzhou, China. Specializing in the field of therapeutic drug monitoring and clinical pharmacology, Dr. Bian actively contributes as a young member of the Therapeutic Drug Monitoring Specialized Committee of the Chinese Pharmacological Society. Over the years, she has been dedicated to the study of drug metabolism and hepatotoxicity and has published many papers in scientific journals. She has also been selected for the "333 Project" High-Level Talents Program in Jiangsu Province.

Anaplastic lymphoma kinase (ALK) inhibitors are the first-line treatment for ALK mutation-positive non-small cell lung cancer. The second-generation ALK inhibitors, which overcome crizotinib-resistance and are effective for lung cancer with brain metastases, are widely used in clinic. However, the hepatotoxic mechanism of ALK inhibitors remains unclear. Reactive metabolite (RM) is one of the risk factors for drug-induced liver injury. This lecture will provide the metabolic characteristics of three of the second-generation ALK inhibitors both in vitro and in vivo, to show that chemically reactive metabolites were formed and oxidative stress occurred. This lecture may provide new insights into the mechanism of hepatotoxic adverse reactions of ALK inhibitors from drug metabolism perspectives.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

233

Minimising Adverse Drug Reactions and Verifying Economic Legitimacy Pharmacogenomics Implementation in Children (MARVEL- PIC): protocol for a national randomised controlled trial of pharmacogenomics implementation

A/Prof Rachel Conyers

Biography:
A/Prof Conyers is Clinical lead of HCT and Group Leader of Cancer Therapies within the world-renowned Murdoch Children's Research Institute (MCRI) and has recognition as a Level D Associate Professor at The University of Melbourne. CI Conyers is regarded as an international expert in paediatric oncology and HCT; leading inter/national pharmacogenomics and advanced therapy trials. A/Prof Conyers set up and lead the Australian Cardio-Oncology Registry and Biobank which has pioneered the implementation of cardio-oncology clinical research in Australia. In addition she established MARVEL-PIC consortium of pharmacogenomics research in paediatric oncology; this includes MRFF funded clinical trials in pre-emptive PGx implementation, phenoconversion, and population PK models for solid organ transplants. Finally, she has led the design and co-ordination of BANDICOOT a first-in world adaptive platform trial for children receiving haematopoetic transplant across Australia, New Zealand, Netherlands and United States.

The Australian MARVEL-PIC consortium encompasses a body of research into pharmacogenomics implementation in paediatric immunocompromised cohorts. The flagship trial for the consortium is a national randomized controlled, the first trial of its kind internationally in paediatrics aiming to prove that pharmacogenomic informed prescribing reduces adverse drug reactions and is cost effective (MRF/202400 NCT 05667766). Since commencement in 2023 MARVEL-PIC has created a national network for advanced pharmacogenomics practice enrolling > 250 children with provision of comprehensive pharmacogenomics report and prospective adverse drug reactions grading. This session will summarise results to date and barriers and enablers to implementation.

234

Clinical implementation of next generation sequencing derived 18-gene pharmacogenomic panel for personalized drug therapy in a general hospital

Prof Yusuke Tanigawara

Biography:
Prof. Yusuke Tanigawara is Professor Emeritus at Keio University and currently Advanced Research Project Professor of pharmacometrics and systems pharmacology at Keio University, Japan.
His research interests include PK/PD modelling, pharmacogenomics, therapeutic drug monitoring and their translation into clinical practice. He served as President of the IATDMCT for the period 2019-2021.

A novel pharmacogenomic panel test “PKseq” developed by RIKEN in Japan, uses a next-generation sequencing technology and allows the simultaneous analysis of 100 genes related to drug response (Drug Metabolism and Pharmacokinetics, 37 (2021) 100370). “corePGseq” is a subset of PKseq which targets clinically important 18 genes. The genes analysed are CYP2A6, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A5, DPYD, NAT2, NUDT15, TPMT, UGT1A1, SLCO1B1, ABCG2, VKORC1, HLA-A, HLA-B, HLA-DRB1 and HLA-DQA1.
As these are germline genes, we are working to implement PGx panel testing into clinical practice in a general hospital, taking advantage of the fact that only a single test provides useful medical information that can be used throughout life.
The results of the preemptive PGx panel test are stored in the hospital's electronic medical record. When the patient is prescribed medication, the choice of drug and dose is automatically checked against the patient's genotype, and any necessary warnings are displayed to the prescribing physician and dispensing pharmacist. We expect that the introduction of the preemptive PGx panel test using NGS technology will contribute to more effective and safer drug therapy.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

235

Integration of pharmacokinetic, pharmacogenetic and pharmacodynamic data in cancer pain management – the example of oxycodone

Prof Andrew Somogyi

Biography:
Andrew Somogyi graduated in Pharmacy from Tasmania and completed a PhD from the University of Sydney (Pharmacy-Anaesthetics). He then undertook postdoctoral clinical pharmacology training in Bonn (Germany) under the guidance of Michel Eichelbaum, and for the past 40 years has been at the University of Adelaide. Apart from teaching in medical, dental, health sciences, nursing and physiotherapy courses, he has an active research programme examining interindividual variation in drug response through clinical pharmacokinetic, pharmacodynamic and outcomes studies underpinned by pharmacogenomics. His current research covers the fields of acute postoperative and cancer pain and psychiatry with a specific focus on ketamine and opioids and, HIV therapy in Papua New Guinea. He is a contributing member of the Clinical Pharmacogenetics Implementation Consortium (CPIC) and an honorary fellow of the Faculty of Pain Medicine (FFPMANZCA), a Fellow of the British Pharmacological Society and an ASCEPT Fellow.

Opioids are the mainstay of cancer pain management with oxycodone the most widely-prescribed opioid. However the dosage range for optimal pain control and tolerable adverse effects can vary over 70-fold due to patient, biochemical, pharmacokinetic, neuronal, neuroimmune and genetic factors.
We aimed to determine whether variability in the pharmacogenetics and pharmacokinetics of oxycodone and its metabolites (CYP2D6 oxymorphone- opioid active and (CYP3A4 noroxycodone- opioid inactive)) contribute to variability in efficacy and adverse effects. We conducted a multi-centre prospective longitudinal study in 33 people with advanced cancer taking oxycodone. The higher the oxycodone dose, the higher the likelihood of uncontrolled average pain [OR 4.32 (95%CI: 1.1-17), P=0.04] and breakthrough pain episodes [OR 6.4 (1.4-29, P=0.02)]. Higher plasma noroxycodone was associated with uncontrolled pain [OR 2.44 (95% CI 1.0 – 6.0), P=0.05; median 29 ng/ml vs 7 ng/m] and higher plasma noroxycodone/oxycodone concentration ratio [OR 10.5, P=0.02; 1.6 vs 0.45]. The plasma noroxycodone/oxycodone ratio was inversely correlated with serum CRP (r=-0.38; P=0.06), a measure of inflammation. Plasma oxycodone and oxymorphone had no effect on pain or adverse effects. Neuronal (OPRM1, COMT) and neuroimmune gene variants (IL6, IL2, TLR4, BDNF) were associated with dose, pain severity and adverse effects (nausea, drowsiness).
In cancer patients managed with oxycodone, noroxycodone contributes to variability in oxycodone likely due to an immunomodulatory effect via TLR4 glial activation and the production of pro-inflammatory mediators. In addition, neuronal and neuroimmune genetic markers play an important role in contributing to pain severity and adverse effects, implicating a targeted genotyping neuroimmune strategy.

236

Pharmacogenomics Implementation for Clinical Practice in Korea: Current Status and Perspectives

Prof Yong Soon Cho, Junk Sook Kwak[2]
[2]SPMED Co, ,

Biography:

Prof. Yong Soon Cho holds a B.S. in Molecular Biology from Dankook University, an M.S. in Life Sciences from POSTECH, a Ph.D. in Systems Biology from Yonsei University, and an M.D. from Chung Ang University. He began his career as a Senior Scientist at Crystalgenomics Inc. (2002–2011) before completing an internship at the Korea Cancer Hospital and a residency in Clinical Pharmacology and Therapeutics at Asan Medical Center. From 2019 to 2024, he served as Assistant Professor in the Department of Pharmacology and Clinical Pharmacology at Inje University, Busan, where he is now Associate Professor.

His major research interests include TB/NTM clinical cohort establishment, translational research on adverse drug reactions of anti-TB drugs, model-informed precision dosing, and Phase I clinical trials.

Pharmacogenomics (PGx) plays a pivotal role in precision medicine by optimizing drug therapy based on genetic variations. In Korea, the National Health Insurance (NHI) system reimburses PGx testing for selected genes (CYP2D6, CYP2C19, CYP2C9, VKORC1, NUDT15, UGT1A1, etc.), but coverage is not structured around targeted genotyping services for specific drugs. Meanwhile, multi-gene PGx panels for psychiatric, cardiovascular, and other therapeutic areas remain non-reimbursed, restricting the adoption of prospective genotyping in individual patient care. Additional barriers include extremely short outpatient consultation times, limited clinician and patient awareness, and the high cost of testing relative to Korea's highly affordable healthcare system.

Currently, targeted pharmacogenotyping remains the most feasible approach for PGx-guided personalized medication, employing technologies such as PCR-based and SNaPshot genotyping. Clinical implementation is being facilitated by Personalized Medicine CDSS (PDSS), which integrates PGx data, renal/hepatic function, and drug-drug interactions (DDIs) into a real-time clinical decision support system (CDSS). Most hospitals rely on external pharmacogenomic testing services provided by specialized PGx service providers or central diagnostic laboratories, while only a few university hospitals perform in-house PGx testing, and even then, only for a limited set of genes.

As clinical and regulatory frameworks evolve, targeted pharmacogenotyping will remain the predominant approach for PGx implementation in Korea for a considerable period. Once a solid infrastructure is established, NGS-based PGx panels are expected to be increasingly adopted, allowing for broader applications in personalized medicine. Future advancements in AI-driven PGx-CDSS, expanded reimbursement policies, and enhanced clinician education and experience will be fundamental to accelerating the integration of PGx into routine clinical practice in Korea.

237

Delivery of TB drugs to the infection site: Insights from pathogenesis and immunopathology

Prof Catherine Ong

Biography:
Dr. Catherine ONG PhD FAMS FRCP is Associate Professor with Tenure at NUS and Assistant Dean for Research in School of Medicine. She leads as the Head of the Clinician-Scientist Academy and is Senior Consultant in Infectious Diseases at the National University Hospital. Her research and clinical interests focus on Tuberculosis, serving in top editorial boards of the European Respiratory Journal and the IJTLD. She serves as an expert reviewer for international funding agencies eg. UK Research Institute and the Wellcome Trust. Her lab explores TB host-pathogen interactions and therapies in multi-country trials, with multiple prestigious awards globally.
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The hallmark of TB disease is the necrotising granuloma, a site where the live mycobacteria reside amidst necrotic cell death. For TB drugs to be effective, drugs have to be delivered to the infection site which may pose a challenge in granulomas. This talks will describe the immunopathology of TB, the process of dysregulated angiogenesis and how the process can be augmented to improve drug delivery.

238

How to measure TB drug concentrations in limited resources settings; challenges and opportunities

Ms Anh Thi Nguyen

Biography:
Ms Nguyen is an early career researcher with a bachelor's degree from Can Tho University of Medicine and Pharmacy (Vietnam) and master's degree in pharmaceutical science (Master of Mekong Pharma, France). She is finishing her PhD candidature in 2025 at the Sydney Pharmacy School, the University of Sydney, Australia. Her research focus is on developing new point of care assays to be used in the community, especially in high burden and resource-limited settings, and developing statistical models to guide dosing. She has co-led two systematic reviews outlining research priorities areas for fungal infections to inform WHO surveillance and to support treatment and research. She is also an academic in the Sydney Pharmacy School, where she has contributed to curriculum development and tutored undergraduate and Master pharmacy students throughout her PhD candidature.

Optimising tuberculosis (TB) treatment requires ensuring appropriate drug exposure to maximise efficacy, minimise side effects, and prevent drug resistance. However, blood-based therapeutic drug monitoring (TDM) remains largely inaccessible in resource-limited settings due to the need for specialised laboratory infrastructure.
Alternative approaches such as saliva- and urine-based TDM offer practical solutions. Saliva sampling enables non-invasive prediction of plasma drug concentrations, while urine testing provides qualitative or semi-quantitative assessments with minimal technical requirements.
Despite these innovations, important challenges remain, including the need for standardised sampling protocols, validation of alternative matrices against clinical outcomes, acceptance of patients and healthcare workers as well as integration into programmatic care. Opportunities exist to leverage mobile health platforms, point-of-care technologies, and collaborative networks to support the adoption of simplified TDM frameworks. In this presentation, we will discuss the current landscape, highlight key research findings from saliva and urine-based TDM, and outline the critical steps needed to move from innovation to implementation in resource-constrained environments.

239

Implementing TDM in programmatic TB care

Prof Rovina Ruslami

Biography:
Prof Rovina Ruslami, MD, PhD is an internal medicine specialist and clinical pharmacologist by training at the Faculty of Medicine, Universitas Padjadjaran, Bandung, and Hasan Sadikin Teaching Hospital. Her research focuses on tuberculosis pharmacotherapy. She is dedicated to establishing TDM services in Indonesia, recognising TDM as essential for improving better patient care, including for people with tuberculosis.

In high burden countries, TB treatment mainly done in the primary health care (PHC) within the National TB Program. Even with successful programmatic treatment, people treated for TB may experience severe side effects, respond slowly to treatment, or develop antimicrobial resistance. It is imperative that TDM is available for those people. This session will discuss feasibility of implementation of TDM in TB programs, different type of TDM service in different settings, what are the challenges, what technology & innovation can help us, and how to move forward including to face the barriers.

240

What evidence do we need to get TDM into WHO guidelines

Prof Jan-Willem Alffenaar

Biography:
Prof Jan-Willem Alffenaar is a hospital pharmacist and clinical pharmacologist at the School of Pharmacy, Faculty of Medicine and Health at the University of Sydney. He is theme lead AMR and novel therapies of the University of Sydney Infectious Diseases Institute and member of the antimicrobial stewardship committee at Westmead Hospital. He is an internationally recognized expert in therapeutic drug monitoring and dose optimization of antimicrobial therapy. He is the current President of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology. He is a member of the WHO's Technical Advisory Group on TB drug dosing. Prof Alffenaar led systematic reviews for WHO on various antimicrobial drugs informing the WHO TB treatment policy review meeting as well as the WHO Fungal Priority Pathogen List. He has led the education on antimicrobial stewardship to pharmacy students since 2019 as well clinical auditing in Westmead Hospital. His research is focussed on personalized dosing in a programmatic setting using innovative sampling techniques and point-of-care saliva testing.

After diagnosis, providing each tuberculosis (TB) patient with the right drugs at the right dose for the right duration in the right combination is important to effectively reduce transmission, prevent relapse and control the risk of development of drug resistance. A better understanding of the relationship between drug exposure and antimicrobial kill and acquired drug resistance has helped to design more appropriate dosing regimens for antituberculosis drugs. Despite the success of TB treatment programs, patients still experience side effects, slow response to treatment, or acquire drug resistance. Therapeutic drug monitoring (TDM) is intended to optimize treatment efficacy and reduce side effects by performing drug concentration guided dose adjustments. Such individualised strategy clashes with current programmatic TB treatment which recommends general dosing strategies. Identifying patients receiving programmatic TB care who are at risk for suboptimal treatment is key to improve treatment outcomes. The use of new technology and new approaches to TDM can help overcome hurdles for implementation of TDM. In this presentation a TDM framework feasible to be implemented in programmatic care will be presented as well as the evidence required for uptake of TDM in TB treatment guidelines.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

241

Setting up a LC-MS/MS assay for a new therapeutic drug - Lessons learnt

Dr Danijela Kocic

Biography:

Dr. Kocic is the Scientific Head of Clinical Pharmacology and Toxicology at SydPath, St. Vincent's Hospital in Sydney, Australia. She oversees the analysis of Therapeutic Drug Monitoring (TDM) results to optimize patient outcomes in complex clinical settings and trials. As an active member of the TDM Matters Multi-Disciplinary Team, she significantly advances clinical practices. Since 2020, she has also served as a Conjoint Senior Lecturer at St Vincent's Clinical School, University of NSW. Dr. Kocic is a leading committee member of the NSW Health Pathology Clinical Mass Spectrometry Forum, connecting with peers in prominent healthcare institutions across Sydney. Additionally, she chairs the Special Drugs Advisory Committee for The Royal College of Pathologists of Australasia Quality Assurance Programs, providing expert insights to laboratories globally. Dr. Kocic also leads the newly established Analytical Committee with IATDMCT, focusing on enhancing the role of analytical methods in TDM and clinical toxicology.

The implementation of mass spectrometry (MS) assays for new therapeutic drugs necessitates careful consideration of several key factors that vary with the laboratory's pre-existing capabilities. This presentation will discuss the essential lessons learned from different laboratory scenarios .
As laboratories integrate new analytical instruments, particularly LC-MS/MS, it is crucial to prioritize effective training and adaptations in methodology to ensure accurate data interpretation. This presentation will explore the challenges and strategies involved in transitioning from conventional techniques, such as HPLC, to advanced methods like liquid chromatography-tandem mass spectrometry (LC-MS/MS). We will discuss the significance of method adaptation for optimizing analytical performance and the necessity for existing facilities to refine protocols for new applications to facilitate efficient integration. Additionally, we will strongly emphasize the critical importance of maintaining regulatory compliance and validating methods across diverse laboratory settings, underscoring the need for robust methodological development tailored to specific research and clinical objectives. This presentation aims to provide insights applicable to a variety of laboratory scenarios, enhancing overall analytical capabilities and ensuring the highest quality of work. Additionally, cost considerations will be addressed to encompass both initial equipment investment and ongoing operational expenditures. A thorough engagement with these aspects is crucial for the successful establishment and operation of MS assays, ultimately facilitating the advancement of therapeutic drug development.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

242

Pushing the limits: Biomarkers and bioanalytical assays for paediatric patient care in low- and middle-resource settings

Dr Paula Schaiquevich

Biography:
Dr Paula Schaiquevich is Pharmacists with a PhD in Pharmacology from the University of Buenos Aires. She completed her postdoctoral training at St Jude Children´s Research Hospital (US). Upon returning to Argentina in 2009, she established the Unit of Innovative Treatments at Hospital de Pediatria JP Garrahan where she leads preclinical and clinical pharmacological and pharmacokinetic research. Dr Schaiquevich has supervised seven completed doctoral theses, with four currently in progress. She has authored 119 peer-reviewed scientific articles, contributed to three book chapters, and received national and international prizes including the Victor Armstrong Young Investigator Award, IATDMCT (2013). She is the past-president of the Argentinean Society of Experimental Pharmacology and currently serves on the Executive Committee of IUPHAR.

Therapeutic drug monitoring (TDM) offers a valuable strategy for personalising drug treatment in paediatric populations. Children undergo significant physiological changes due to rapid growth that affect drug disposition. These developmental changes require dynamic optimization of drug dosing to maximize therapeutic benefits while minimizing toxicity risks. Monitoring paediatric patients presents several challenges including difficult peripheral blood access and limited blood sample volumes. Microsampling techniques like dried blood spots offer alternatives but require sensitive equipment, seldom available in low- and middle-income countries where most children live. Less sophisticated analytical methods can present challenges, including unexpected interferences as seen with voriconazole during photopheresis.
Alternative matrices like urine and saliva reduce patient discomfort and infection risks, despite technical limitations. Beyond traditional TDM, other fluids like cerebrospinal fluid (CSF) may provide more informative data. Our experience includes quantification of anticancer drugs in CSF and urinary 3-indoxyl sulphate as a dysbiosis biomarker in stem cell transplant patients.
This presentation addresses challenges and solutions for paediatric TDM in resource-limited settings. We will discuss local innovations using biomarker quantification methods adapted to available resources, including cone-rod homeobox for minimally disseminated disease in retinoblastoma and cell-free DNA with immunosuppressant TDM to optimize paediatric liver transplant outcomes.
These approaches demonstrate how locally adapted analytical solutions can bridge the gap between resource-limited settings and optimal care, advancing our goal of ensuring that all children, regardless of geographic or economic circumstances, have access to the benefits of precision medicine.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

243

Using Pharmacokinetics as a Surrogate Marker for Pharmacogenetics to Optimize Resource Allocation

Dr Azucena Aldaz

Biography:
Dr Azucena is a Specialist Pharmacist in Hospital Pharmacy with a PhD in Pharmacy, working at Clínica Universidad de Navarra (CUN) since 1984. She established and leads the Clinical Pharmacokinetics Unit at CUN and has played a key role in multiple institutional and national initiatives, including the Cardiorespiratory Care Group and the PROA antimicrobial stewardship program.
She is actively involved with several scientific societies, including SEFH, SIO, and IATDMCT, and has coordinated the PKgen group of SEFH since 2007. An Associate Professor since 2013, she teaches Clinical Pharmacy and Pharmacotherapy and has supervised 15 doctoral theses.
Her academic contributions include 50 published articles, 14 book chapters, 4 books, and 187 conference presentations. She has led 15 R&D projects and serves as a peer reviewer for several scientific journals.

The integration of pharmacokinetics (PK) and pharmacogenetics (PGx) represents the most comprehensive approach to optimizing the dosing of drugs with a narrow therapeutic index. PGx is particularly valuable for guiding initial dosing, offering a personalized starting point that reduces the risk of adverse effects or subtherapeutic exposure. In contrast, PK plays a critical role in ongoing dose adjustment, ensuring that drug levels remain within the therapeutic range as patient-specific variables evolve.
In theory, the combined use of PGx and PK maximizes both safety and efficacy. However, the routine implementation of PGx in clinical practice remains limited, primarily due to concerns about cost-effectiveness and the strength of supporting evidence. These challenges are particularly relevant in resource-constrained healthcare settings, where PK may serve as a pragmatic surrogate for PGx to support individualized therapy while minimizing resource utilization.
Pharmacokinetics does not directly determine the genotype of a specific enzyme isoform, as it reflects only the phenotype. This phenotype represents the net outcome of multiple contributing factors, including but not limited to genetic variability. Other influencing variables include age, body weight, co-medications, organ function, and environmental factors.
Therefore, relying exclusively on genetic data to guide dosage regimens can, at times, be imprudent, as co-medications may significantly influence genotype-phenotype relationships, potentially leading to dosing decisions that pose a risk to patient safety.
Using PK as a surrogate for PGx may represent a cost-effective strategy in specific contexts—particularly for drugs with well-characterized PK-PGx relationships—but it cannot serve as a universal substitute for genetic testing.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

244

Phenotyping of DPD enzyme: A practical approach to make 5-FU chemotherapy safer in resource-limited settings

Dr Binu Susan Mathew

Biography:
Dr Binu Susan Mathew is Professor in the Department of Pharmacology and Clinical Pharmacology at the Christian Medical College, Vellore in South India. Her work initiated with Therapeutic Drug Monitoring of immunosuppressants, which progressed to include anti TB drugs, antibiotics and antifungals. Past few years she is working on the phenotyping of 5-FU and TDM of anticancer drugs. She was involved in the progression of TDM services in this premier tertiary care hospital and has organized regional national conferences and annual workshops in TDM. She was instrumental in setting up multiple assays on the LC MS/MS. She is currently involved in alternate sampling strategies which would enable TDM services to be offered to remote hospitals and from a distance.

Partial or complete deficiency of the dihydropyrimidine dehydrogenase (DPD) enzyme activity is responsible for most serious adverse events, including mortality associated with 5-FU. While genotyping of the DPYD gene is the most popular approach to identify DPD deficiency, the ideal approach would be to use both phenotypic and genotypic information. Although this multiparametric approach for the dosing of 5-FU is practised in some centres, most rely solely on DPYD genotyping. However, genotyping of DPD, whilst widely acceptable, is impractical in low-resource settings.
In view of the cost constraints associated with performing pharmacogenomic testing for every patient requiring 5-FU at our hospital, a phenotypic approach to indirectly estimate DPD activity by measuring plasma uracil concentration and the ratio of dihydrouracil/uracil (DHU/U) concentrations is being employed.
This talk will focus on the phenotypic approaches available for pretherapeutic screening of DPD, prior to initiating 5-FU. A proposed algorithm for dose optimisation based on phenotyping results before 5-FU administration will also be discussed. In addition, issues related to the stability of plasma uracil and the feasibility of offering the phenotype test to distant hospitals will be addressed.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

245

Altered pharmacokinetics and pharmacodynamics during infection in the post-transplant period

A/Prof Christine Staatz

Biography:
Associate Professor Christine Staatz is a pharmacist and member of academic staff in the School of Pharmacy at the University of Queensland, Brisbane Australia. The major goal of her research work to date has been to obtain in-depth information on the pharmacokinetics and pharmacodynamics of medicines to be able to personalise treatment and improve patient outcomes. She has been involved in studies directed towards optimizing usage of immunosuppressant drugs in solid organ transplant recipients, chemotherapy agents in bone marrow transplant recipients and antibiotics in patients with life-threatening infections. Christine has published over 120 peer-reviewed papers and 150 conference abstracts on these topics. She has been a member of IATDMCT since 2016 and enjoys participating in activities championed by the Immunosuppressive Drugs Committee and Regional Asia-Pacific Section of this organisation.

This presentation explores how infection and use of anti-infective agents may alter drug pharmacokinetics and pharmacodynamics in the post-transplant period. Transplant recipients are inherently immunocompromised due to the use of immunosuppressive drugs, making them more susceptible to infections. Infections, in turn, may alter the pharmacokinetic and pharmacodynamic properties of both immunosuppressive agents and medicines used to manage infections in transplant recipients. Infectious episodes can potentially lead to changes in gut motility, flora and pH affecting drug absorption and enterohepatic recirculation; altered fluid status and plasma protein levels affecting drug distribution; and altered liver enzyme activity and hepatic and kidney function altering drug elimination. Such alterations may subsequently result in either subtherapeutic drug concentrations or toxicity, complicating the management of both the transplant and the infection. Furthermore, use of antibiotics, antivirals, antifungals with immunosuppressive agents can lead to pharmacokinetic or pharmacodynamic drug-drug interactions. Many drug-drug interactions occur secondary to effects on drug metabolizing enzymes or drug transporters. Certain anti-infective and immunosuppressant drug combinations can also increase the risk of drug toxicity including nephrotoxicity. Infections can additionally exacerbate the inflammatory response, leading to changes in immune system function. In some instances, infections may coexist with, or be difficult to distinguishable from, graft rejection and more studies examining infectious outcomes relative to immunosuppressant level targets are needed. Clinicians need to consider the unique challenges presented by infections in transplant recipients and employ strategies such as therapeutic drug monitoring and careful selection of antimicrobial agents to optimize therapeutic outcomes.

246

Individualized immunosuppressive dosing in transplant patients: how the net state evaluation can help

Prof Klemens Budde

Biography:
Klemens Budde MD is Deputy Medical Director of the Department of Nephrology and Medical Intensive Care at Charité Universitätsmedizin Berlin, Germany, where he holds an endowed professorship for pharmacodynamics on immunosuppression after kidney transplantation since 2006. After receiving his medical degree from Tübingen University, Germany, Dr. Budde completed training in Nephrology at Friedrich-Alexander University, Erlangen-Nürnberg and subsequently at the Charité, Humboldt University. Dr. Budde also completed a postdoctoral fellowship in Nephrology at Yale University, New Haven, Connecticut, USA. He possesses a board certification in Internal Medicine, in Nephrology and a Certification for Hypertensiology. He is a board member in several commissions of national and international societies.

Professor Budde had received the Hans-U.-Zollinger Research Prize of the German Association for Nephrology in 2004 for outstanding achievement in his field. In 2018 he became working group chair for Medicine and Care of the platform "Lernende Systeme", Germany´s platform for artificial intelligence.

Prof. Budde's main research interests include kidney transplantation, eHealth and genetic diseases of the kidney. He is the author or co-author of more than 450 journal articles, and has lectured nationally and internationally on numerous topics in transplantation.

The aim of this symposium in to highlight the duality between a required immunosuppression in solid organ transplant recipients and the associated risk of infection. The symposium will first decipher the alteration of drugs PK and PD during infections in transplant patients. Indeed, a lot of pathophysiological modification can change drugs exposure and effect during infections and their mechanism and clinical impact will be highlighted as a first step. Then, the strategies for immunosuppressive dosing adjustment for infection prevention and the latest immunosuppression net state evaluation approach will be presented and the main results on these topics will be discussed. In the second part of the symposium, a comprehensive overview will be provided to the audience regarding therapeutic drug monitoring and dosing adjustments of immunosuppressive and anti-infective drugs in two clinical situations: bacterial infections, in particular when antituberculous drugs has to be used, and viral infections with a special focus on cytomegalovirus and COVID-19 and their treatment interplay with patient's immunosuppressive therapy.

247

Use of TDM to improve treatment of nontuberculous mycobacteria in vulnerable populations

Dr Joy Gibson

Biography:
Joy Gibson, MD, PhD, is an Assistant Professor of Pediatric Infectious Diseases at Children's Hospital Los Angeles (CHLA). As a physician-scientist funded by the Cystic Fibrosis Foundation and National Institutes of Health, she has clinical and research expertise on the management of challenging pathogens in cystic fibrosis. In the laboratory, Dr. Gibson uses the hollow fiber infection model to optimize treatment regimens for Mycobacterium abscessus, Staphylococcus aureus, and Pseudomonas aeruginosa. She is an investigator in the Innovative Synergistic Pediatric Infection Research group, collaboratively leading the first pediatric center in the United States with hollow fiber capabilities to improve treatment of children with complex infections.

Infections with nontuberculous mycobacteria (NTM) are associated with significant disease in vulnerable hosts, including immunocompromised patients and patients with cystic fibrosis (CF). These infections can be challenging to treat due to high rates of resistance and the need for complex multi-drug regimens with prolonged courses. Despite the use of intensive regimens, rates of NTM treatment failure are high. Treatment is further complicated in vulnerable populations due to drug-drug interactions resulting in increased toxicity and altered drug levels. Notable interactions impacting drug metabolism occur between rifamycins and macrolides with immunosuppressive medications such as tacrolimus and cyclosporine. There are also significant interactions of rifamycins with the cystic fibrosis transmembrane conductance regulator modulator therapy elexacaftor-tezacaftor-ivacaftor. Further, numerous potential interactions of antimycobacterial agents and immunosuppressive therapies lead to increased risk of toxicity. Treatment of NTM is further complicated by a lack of PK-PD evidence to support current dosing strategies. Most dosing recommendations are based on typical pathogens such as Pseudomonas, but recent studies indicate that these approaches may not be effective for NTM. More precise TDM is needed in this population, with consideration of unique PK-PD and interactions with other medications, but guidance regarding this approach is sparse. This session will discuss how closer TDM may improve clinical outcome and reduce toxicity during treatment of NTM in immunosuppressed patients and in patients with CF.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

248

TDM and dosing adjustments during antiviral (CMV and Covid) infections in the transplant recipients

Dr Kristina Nadrah

Biography:
Dr Kristina Nadrah MD, MPharm, PhD is a senior specialist in infectious diseases and clinical pharmacology at the Department of Infectious Diseases at the University Medical Centre Ljubljana. She received her PhD in pharmaceutical chemistry from Faculty of Pharmacy in Ljubljana and did her postdoc in immunology at Yale Immunobiology department. Her research interests include antimicrobial stewardship, PKPD of antimicrobials and intersection of infectious diseases and immunology. In her clinical work she is treating patients and consulting on a wide variety of infectious diseases including in immunocompromised host. Dr. Nadrah has been actively involved in treatment of Covid-19 patients including immunocompromised and pregnant patients in Slovenia. She is a member of the Committee for Medicinal Products for Human Use (CHMP) at the European Medicines Agency, representing Slovenia and a member of professional societies, including the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), ESCMID PK/PD study group (EPASG), and the Slovenian Immunology Society.

Treatment of viral infections in transplant recipients is challenging due to high inter-and intrapatient pharmacokinetic variability of immunosuppressive and antiviral drugs, their narrow therapeutic window and many clinically significant drug-drug interactions. Insufficient exposure can lead to clinical failure or even graft rejection, while overexposure can lead to heightened risk of adverse events and toxicity.
Nirmatrelvir/ritonavir which is used for treatment of early Covid-19 can significantly increase the concentration of immunosuppressants which undergo hepatic metabolism via CYP450. On the other hand overexposure to some antiviral drugs for treatment of CMV can lead to enhanced nephrotoxicity and neurotoxicity, while others can increase the levels of immunosuppressive drugs. With therapeutic drug monitoring we can tailor antiviral and immunosuppressive treatments to the individual patient. With TDM we can mitigate risk for under-or overexposure. Therapeutic drug monitoring (TDM) of some immunosuppressive drugs, such as calcineurin inhibitors and mammalian target of rapamycin (mTOR) inhibitors used in transplant patients is performed routinely, while TDM of antivirals is not available in all institutions. Management of concurrent treatment with antiviral drugs for treatment of Covid-19 and CMV will be presented with a synthesis of current advances in this field.
Regarding the title, I have made just a small change: TDM and dosing adjustments during viral (CMV and Covid) infections in the transplant recipients.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

249

Pharmacogenetics and metabolic phenotyping for precision anticancer treatment

Prof Nuala Helsby

Biography:

Nuala Helsby (FBPhS) is a Professor in Pathology at the University of Auckland. Her research focus is on understanding how both inherited and environmental factors influence the safe and effective use of drugs. Nuala has more than 35 years of experience in the field of drug metabolism and pharmacogenetics (orcid.org/0000-0001-6570-5368). She has a particular interest in the factors which result in discordance between genotype and phenotype. Her research also focusses on understanding the role of inter-individual variation in the formation of toxic metabolites to improve the safety of drugs in current clinical use. She teaches extensively in the Biomedical Science and Pharmacology programmes and also serves on a number of NZ-based grant assessment panels.

Much of the recent success of “precision medicine’ in Oncology has been the identification of somatic mutations and development of “targeted” therapies. However, inherited (germline) differences can affect the safety or effectiveness of drugs by altering the metabolic elimination of a drug or by altering the activation of prodrugs. The use of SNP-based genetic biomarkers (pharmacogenetics) to predict metabolism and therapeutic outcome has many advocates. However, there are many layers of regulatory control of genes, as well as environmental and clinical factors which can alter phenotype and influence therapeutic outcomes. My talk will highlight the role of phenotype-based approaches to help understand and clarify whether inherited (pharmacogenetic) risk factors are associated with poor bioactivation of cyclophosphamide and the excessive toxicity of 5-fluorouracil.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

250

Pharmacogenetically Informed Therapeutic Drug Monitoring of 5-Fluorouracil: A Swiss Perspective on Implementation and Clinical Experience

Prof Carlo Largiader

Biography:
Carlo R. Largiadèr (CRL), PhD, has been an Associate Professor of Pharmacogenetics at the Department of Clinical Chemistry (UKC) and the Center of Laboratory Medicine (ZLM) at the Inselspital (Bern University Hospital) since 2010. He received his habilitation in 2002 from the University of Bern in the field of population genetics.
He currently serves as Deputy Director of both the UKC and the University Center for Laboratory Medicine (ZLM), and is the Director of the Liquid Biobank Bern (LBB; www.biobankbern.ch) at the Inselspital. As Deputy Director, he is responsible for clinical research services as well as diagnostic services in pharmacogenomics, therapeutic drug monitoring, and toxicology.
Since 2006, he has been teaching at the Medical and the Faculty of Science (Phil.-nat.) at the University of Bern, and has been leading a research group in pharmacogenomics and drug metabolism at the UKC.ukc.insel.ch). His research focuses on genetic and non-genetic factors underlying inter-individual variability in drug response, with a strong emphasis on translational aspects.
He currently serves as Vice-President of the Governing Board of the Swiss Biobanking Platform (SBP; https://swissbiobanking.ch), the national coordination platform for human and non-human biobanks in Switzerland. See www.webofscience.com/wos/author/record/1181271 for a list of publications.

Fluoropyrimidines (FPs), including 5-fluorouracil (5FU), have been widely used since the 1950s, with over two million cancer patients treated annually. Despite their efficacy, severe or fatal toxicities occur in approximately 10% of patients. Dihydropyrimidine dehydrogenase (DPD) inactivates ~85% of administered 5FU, making it a key determinant of systemic drug exposure and toxicity. Four common DPYD gene variants account for ~20% of early-onset FP-related toxicity, leading to the implementation of routine genotyping and genotype-guided dosing in several European countries, including Switzerland, as recommended by the European Medicines Agency (EMA).
To address the remaining, largely non-genetic variability and to avoid underdosing, the Swiss Group of Pharmacogenomics and Personalised Therapy recommends the integration of therapeutic drug monitoring (TDM). Similar recommendations were issued by the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) in 2019. However, despite reimbursement by the Swiss healthcare system, clinical uptake of 5FU TDM remains limited due to practical barriers. Currently, individualized dosing is based on body surface area (BSA), a method that has proven inadequate in preventing FP-related toxicities. Additionally, venous blood sampling for 5FU TDM is considered cumbersome and a barrier to routine implementation. Here, I present initial findings from two Swiss studies: one validating a dried blood spot (DBS)-based TDM method as a more patient-friendly and logistically feasible alternative; the other investigating demographic, biochemical, and anthropometric factors contributing to interindividual variability in 5FU exposure to support more accurate, personalized chemotherapy dosing.

251

Implementation of pharmacogenetics guided Therapeutic Drug Monitoring in ethnically diverse communities

Prof Stephen Ackland

Biography:
Dr. Stephen P Ackland is a senior academic medical oncologist and Professor in the School of Medicine and Public Health, University of Newcastle Australia; Editor-in-Chief, Asia Pacific Journal of Clinical Oncology since 2005; and Director, Australasian GastroIntestinal Trials Group. He is author of >160 peer-reviewed publications in oncology and pharmacology, with a H-index of 39, in subjects ranging from pre-clinical pharmacology and pharmacogenomics to clinical trials and implementation science. He has previously been Director of Medical Oncology at Calvary Mater Newcastle Hospital; Director of Hunter Cancer Research Alliance; Director and Chairman of ANZ Breast Cancer Trials Group; and Director of Cancer Council NSW. He has participated in many committees of NFP cancer organisations in Australia and elsewhere, including MOGA, COSA, ASCO, Cancer Council, and NSW Office of Health and Medical Research. As EIC of APJCO he has led a team of 20-30 voluntary Associate Editors in evaluation and acceptance of manuscripts in clinical and translational oncology. This task has become an increasing challenge in this technological and pandemic age.www.newcastle.edu.au/profile/stephen-ackland

Pharmacogenomically-guided dose personalisation is one of the advancing strategies of cancer medicine. Genotyping of DPYD is leading the way to refinements in fluoropyrimidine (FP; 5-fluorouracil and capecitabine) dosing to reduce the risk of severe toxicity and death. Four variants in the DPYD gene, present in 7-8% of Caucasian (European) patients, are known to contribute to 30-60 % of severe toxicity when treated with standard doses of FP, which are commonly prescribed for advanced or adjuvant therapy for a range of malignancies of the GI tract, head and neck, breast and other sites. PGx screening of patients can lead to personalized dose reduction of the first cycle of FP chemotherapy with reduced high-grade toxicity risk. A strategy of increasing subsequent doses in patients who do not develop toxicity can maintain anti-cancer benefit. One challenge in Asia-Pacific countries is the diverse ethnicities, different to Europe, including north-Asian, south-Asian and south-east Asian, many indigenous peoples, Pacifika, and Maori. There is a relative lack of data about the range of deleterious DPYD variants in these populations, their effects on DPYD activity, and the risk of severe toxicity. In particular there is limited data on safe dosing of heterozygote variant carriers; it is uncertain whether homozygotes can be treated with FP at all. In Australia, the population is ethnically diverse with a unique indigenous people, and limited genomic data. We are undertaking a national study to describe the spectrum of deleterious DPYD variants in Australians, and to determine the enablers and barriers to DPYD genotyping and FP dose personalisation in our communities. The longterm aim is to implement DPYD genotyping equitably throughout our diverse communities to minimise severe toxicity from FPs in all Australian cancer patients without compromising the benefits. An understanding of the predominant genetic variants causing severe toxicity will facilitate equity. Inclusion of community champions in the conduct of research will be required to ensure safe and culturally sensitive conduct of pharmacogenomics research to achieve these aims. This presentation will discuss the challenges in implementing this research study throughout Australia, to ensure equity and inclusion, and to maximize its value.

252

Tamoxigenomics and monitoring of endoxifen levels to tailor tamoxifen prescription in ER positive breast cancer patients

Prof Balram Chowbay, PhD

Biography:
*Prof Chowbay is the Principal Clinical Pharmacologist and Senior Principal Investigator at the National Cancer Center Singapore (NCCS). He is one of the leading researchers in pharmacogenomics in Singapore and his research focuses on applying pharmacokinetics (PK) and pharmacodynamics (PD) principles for dose optimization and using pharmacogenomics to understand the inter-individual and inter-ethnic variability in clinical outcomes, especially in Asian ethnic groups. He has co-authored over 100 publications and is an editorial board member for numerous drug metabolism and pharmacology-based journals. Dr. Chowbay holds multiple academic appointments at Duke-NUS Medical School, Singapore Immunology Network, Agency for Science, Technology and Research (A*STAR) Singapore and Universitas Sumatera Utara, Singapore and currently serves on advisory committees, grant review boards and research councils both nation and institution-wide.*

We conducted a genome-wide association study (GWAS) on steady-state Z-endoxifen levels in 636 hormone-receptor positive breast cancer patients from Singapore, Lebanon, and Germany who have received 20mg tamoxifen daily for at least 8 weeks prior to their pharmacokinetic (PK) blood sampling. Significant associations (P<5×10-8) were followed up in a validation cohort comprising 859 participants from the UK, France, and Singapore. We also evaluated the association between genetic markers surpassing genome-wide significance and CYP2D6 metabolizer status on the survival outcomes of 1326 non-metastatic hormone-receptor positive breast cancer patients treated with adjuvant tamoxifen . The outcomes evaluated were disease-free survival, relapse free survival and distant relapse free survival.
In the PK GWAS, genome-wide significant association with steady-state Z-endoxifen levels was observed on chromosome 22 at CYP2D6 and at TCF20 rs932376 A>G. Scrutiny of TCF20 rs932376 A>G and CYP2D6 metabolizer status using multivariable Gaussian generalized linear model with log link function showed that both are independent predictors of steady-state endoxifen levels. Each additional copy of the TCF20 rs932376-G allele was associated with a 10.79nM reduction (95% CI -13.39 to -8.20) in mean endoxifen level (P=3.26×10-16). Adjustment for CYP2D6 metabolizer status, age, ethnicity, weight, and menopausal status still resulted in a significant association between TCF20 rs932376-G and serum levels of endoxifen, with each copy of the G allele associated with a 7.48nM reduction (95% CI -10.58 to -4.39, P=2.16×10-6) in mean endoxifen level. This finding was validated (adjusted 6.30nM reduction in mean endoxifen level per-copy of the G allele [95% CI -9.51 to -3.09], P=1.00×10-4) in independently ascertained collections. Neither TCF20 rs932376 nor CYP2D6 metabolizer status was significantly associated with breast cancer outcomes in a model adjusting for age, ethnicity, body mass index,tumour size, nodal status, and tumour grade.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

253

Setting the scene-A clinical perspective on the opioid epidemic

A/Prof Bridin Murnion

Biography:

Associate Professor Murnion is a Clinical Pharmacologist/Toxicologist working in an inner city hospital in Sydney, Australia. She also has fellowships in Pain and Addiction Medicine. Her clinical and research interests are in use and harms of medicines used in pain management.

There are multiple factors underlying the development and maintenance of the opioid crisis in North America. Policy decisions, healthcare standards and their impact on clinical practice and unscrupulous marketing have all contributed. The response to the crisis has occurred in multiple domains. This presentation will discuss the policy and clinical evolution and response to this crisis and the challenges relating to providing care in this population.

This session will

1. Provide an overview of the opioid crisis, with a focus on the evolving patterns of opioid use, including the rise of synthetic opioids like fentanyl, across different global regions.
2. Describe the clinical realities faced by healthcare professionals, including challenges in diagnosis and management of opioid use disorder (OUD), overdose, and associated comorbidities.
3. Identify gaps in current healthcare responses, such as limitations in screening tools, access to treatment, and health system preparedness and the burden for health systems.
4. Set the foundation for interdisciplinary dialogue, by framing the clinical challenges that necessitate innovative solutions in toxicology, monitoring, public health, and policy— some topics which will be explored in subsequent sessions of the symposium.

254

Detection and monitoring fentanyl use and misuse in patients presented in emergency room and out-patient substance use clinic

Dr Lei Fu

Biography:
Dr. Lei Fu is a clinical biochemist, in the Precision Diagnostics and Therapeutics Program (Laboratory Medicine), at the Sunnybrook Health Sciences Centre, and assistant professor at the Department of Laboratory Medicine and Pathobiology, University of Toronto. She is certified by the Canadian Academy of Clinical Biochemistry, and American Board of Clinical Chemistry in all three disciplines, Clinical Chemistry, Toxicological Chemistry, and Molecular Diagnostics. She is actively engaged in clinical service, teaching, and research. Her research interests are in two areas, biomarkers in maternal and fetal health, and clinical applications of pharmacogenomics.

Opioid toxicity crisis is a major public health and safety concern. Fentanyl is one of the most commonly used or misused synthetic opioids. Clinical diagnostic laboratories play important role in managing poisoned patients, reducing the risks and harms associated with drug use. In this session, we will discuss the laboratory technologies and strategies in drug screen and confirmatory testing for emergency room and out-patient substance use clinics.
Learning objectives:
- Describe the assays used for routine screening and confirmatory detection of fentanyl, the advantages and limitations of each method.
- Describe the patterns of drugs detected in patients presented in emergency room and out-patient substance use clinic, and the prevalence of fentanyl use/misuse in these patient population
- Discuss the laboratory roles in better management and reduction of fentanyl related harm

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

255

Leveraging pharmacogenetics for tailored fentanyl overdose prevention and response

Dr Guillaume Drevin

Biography:

Guillaume Drevin, MD, is a medical biologist and clinical pharmacologist at Angers University Hospital, France. His work focuses on clinical and forensic toxicology, with a particular interest in toxicogenetics and its integration into routine practice to refine the interpretation of toxicological findings and personalize overdose risk assessment. He also serves as a court-appointed expert.

The fentanyl crisis continues to drive opioid-related morbidity and mortality globally, necessitating innovative, precision-based strategies. Pharmacogenetics represents a critical tool to personalise both prevention and therapeutic approaches across the spectrum of opioid use and misuse. Genetic susceptibility to opioid dependence is increasingly recognized, particularly in patients prescribed opioids for chronic non-cancer pain. Variants in genes such as OPRM1, CNIH3, and ion channel genes (KCNC1, KCNG2) have been associated with increased vulnerability to opioid use disorder (OUD). Integrating genetic risk screening into pain management could enable anticipatory identification of high-risk individuals, allowing for closer monitoring, non-opioid alternatives, or early addiction intervention. In the context of overdose prevention, pharmacogenetic profiling may identify individuals with altered opioid receptor function or impaired fentanyl metabolism—such as carriers of OPRM1 A118G or CYP2B6*6 alleles—who are at elevated risk for fentanyl toxicity. In such individuals, pharmacogenetic data could inform both clinical and community-based interventions: priority access to take-home naloxone kits, education of lay responders, and the potential for genotype-guided adjustments in naloxone dosing strategies to improve reversal outcomes in high-potency exposures. Moreover, rapid genotyping during overdose emergencies may further enhance individualized naloxone administration, particularly in refractory or atypical presentations. Finally, pharmacogenetic-guided personalization of maintenance therapies (e.g. methadone or buprenorphine) has shown promise in improving adherence, reducing withdrawal symptoms, and enhancing long-term treatment outcomes. To conclude, embedding pharmacogenetics into clinical and harm reduction frameworks represents a paradigm shift toward more precise, equitable, and effective responses to the fentanyl crisis. Further translational research and infrastructure development are imperative for clinical implementation.

256

Fentanyl use and misuse – forensic cases, laboratory biomarkers

Dr Fredric Hellman, M.D., M.B.A.

Biography:
Dr. Fredric Hellman, M.D., M.B.A. currently serves as the Deputy Chief Medical Examiner for Dekalb County, Georgia, where he has been employed since May, 2022. He also serves as a locums forensic pathologist for the Allegheny County (Pittsburgh, PA) Medical Examiner's Office and the Rhode Island State Medical Examiner's Office. Prior to these engagements, Dr. Hellman was the Chief Medical Examiner for Delaware County, Pennsylvania, a large suburb of Philadelphia, where he served for well over 21 years. During that time, Dr. Hellman assumed a variety of leadership roles both in public health and in organized medicine for both Delaware County and Pennsylvania. He also designed and directed/co-directed for fifteen years the Master's Degree Program in Forensic Medicine at Drexel University College of Medicine, at the time the first forensic science graduate program within an allopathic medical school. He is a military veteran, having been assigned to the Armed Forces Institute of Pathology in Washington, D.C. and having served as a Deputy Medical Examiner for the Armed Forces Medical Examiner's Office and as a U.S. Army Flight Surgeon. Dr. Hellman investigated twenty aircraft accidents, many as mission chief as well as served as a forensic pathology consultant for many high-profile U.S. federal government medicolegal death investigations. Dr. Hellman was also the forensic pathologist in charge for the 9/11 investigation of United Airlines Flight 93 in Shanksville, Pennsylvania. Dr. Hellman is the author and/or co-author of 21 scientific publications, numerous resolutions in public health for organized medicine, both at the state and national levels, and has served as a speaker at numerous regional, national and international medical conferences. He is a Fellow of the National Association of Medical Examiners, a Member of the American Academy of Forensic Sciences and a Fellow of the College of American Pathologists. Dr. Hellman is Board Certified by the American Board of Pathology in Anatomic, Clinical and Forensic Pathology.

Four waves of opioid overdose deaths have gripped the United States, beginning in the 1990s with a rise in the incidence of prescription opioid overdose deaths. A rise in heroin overdose deaths began in 2010, followed in 2013 by an escalation in synthetic opioid overdose deaths (illegally made fentanyl (IMF) and its congeners). The fourth wave is defined by the increased prevalence of IMF mixed with potent illicit stimulants like methamphetamine and cocaine. This most recent development has led to a surge in polysubstance overdose deaths, a consequence of the potency of fentanyl and the unpredictable effects of mixing such substances. We present five cases of fentanyl-related overdose, one of an adult whose death is a consequence of polysubstance fentanyl and stimulant abuse. The other four cases are of neonates and infants, the most vulnerable casualties of this epidemic. Young children whose parent(s) engage in drug-seeking behavior are at great risk for inadvertent drug overdose through the consumption of drug-tainted breast milk and the oral consumption of illicit drug(s) left within the proximity of the child. Physiological effects of combined IMF and illicit stimulant use during pregnancy also portend significant gestational complications, including placental abruption. Each of these cases considers routes of administration, maternal influences, physiologic effects, and considerations for both cause and manner of death. Laboratory tests play a major role in monitoring fentanyl to identify co-use with other drugs of misuse and guide informed patient care decisions. Moreover, the possible hypersensitivity reaction to fentanyl must be taken into consideration.

257

TDM research in the digital age?

Miss Amy Legg

Biography:
Amy Legg is an experienced clinical pharmacist in infectious diseases and antimicrobial stewardship. She undertook a PhD with Menzies School Of Health Research in nephrotoxicity related to Staphylococcus aureus bacteraemia. Her research interests include urinary biomarkers for diagnosis of AKI, and antimicrobial therapeutic drug monitoring to ensure efficacy and safety. She was the inaugural Herston Infectious Diseases Research Fellow and authored their Therapeutic Drug monitoring Guidelines. Amy serves as a member of the Australian Prescriber editorial advisory committee and an expert group member of the Australian Therapeutic Guidelines Antimicrobial edition.

Therapeutic drug monitoring (TDM) is a critical tool for optimising antimicrobial therapy, yet its uptake in clinical practice varies widely across institutions and drug classes. Understanding and monitoring patterns of TDM uptake not only supports local quality improvement but also informs the national research agenda by identifying gaps in evidence and practice. Large digital drug concentration datasets, generated through routine TDM, offer unique opportunities to address important clinical questions that are otherwise difficult to study, including rare drug interactions, population-specific pharmacokinetics, and exposure-response relationships. Successful examples of embedding research within digital electronic health records (EHR) systems, such as pragmatic clinical trials and real-world data studies, highlight the potential of integrating research into routine care. Emerging applications of machine learning further enhance this potential, with models being developed to provide patient-specific, data-driven drug dosing recommendations based on TDM results. Together, these approaches demonstrate the power of digital health infrastructure and big data to advance precision antimicrobial therapy and improve patient outcomes.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

258

Real-World Big Data Insights for Advancing Therapeutic Drug Monitoring and Clinical Toxicology

Dr Tomoyuki Yamada

Biography:
Tomoyuki Yamada, PhD, is the Head Pharmacist at the Department of Pharmacy, Osaka Medical and Pharmaceutical University Hospital. His primary areas of expertise include therapeutic drug monitoring for antimicrobial chemotherapy and pharmacovigilance. He is actively involved in promoting the safe and effective use of medications through both research and clinical practice. He is a member of the following academic societies: the International Association of Therapeutic Drug Monitoring & Clinical Toxicology (IATDMCT), the Japanese Society of Therapeutic Drug Monitoring (JSTDM), the Japanese Society of Pharmaceutical Health Care and Sciences (JSPHCS), the Japanese Society of Chemotherapy (JSC), and the Japanese Society for Infection Prevention and Control (JSIPC).

The utilization of real-world big data (RWD) from adverse event report databases and clinical healthcare records is advancing therapeutic drug monitoring (TDM) and clinical toxicology. This presentation introduces case studies demonstrating key applications of big data analytics in evaluating drug safety, optimizing dosing, and improving patient outcomes.
Adverse event report databases are widely used to detect safety signals and generate hypotheses regarding drug-adverse reaction associations. Building on this, we have explored the increased frequency of adverse events due to drug-drug interactions and validated hypotheses derived from preclinical studies using RWD. A major focus is the assessment of daptomycin-statin interactions. We examined how statin co-administration influences daptomycin-related muscle toxicity, underscoring the role of pharmacovigilance in detecting interactions and guiding clinical decisions. For non-steroidal anti-androgens, we investigated liver injury mechanisms through basic research and confirmed the findings with RWD. This integrative approach bridges experimental toxicity models with real-world patient data, offering insights into drug-induced liver injury and the potential hepatoprotective effects of steroids. We also analyzed hospital-based clinical databases to evaluate follow-up TDM following initial vancomycin monitoring. Our findings indicate that ongoing TDM assessments contribute to reducing toxicity risks.
The presentation highlights RWD-based approaches for TDM and clinical toxicology, ultimately advancing safer and more effective pharmacotherapy.

259

Model Informed (precision) dosing of biologics in (hemato)oncology: challenges and opportunities?

Assoc Prof Dirk Jan Moes

Biography:
Dr. Moes is an associate professor of clinical pharmacometrics, a clinical pharmacologist & hospital pharmacist in the laboratory of therapeutic drug monitoring and toxicology affiliated to department of clinical pharmacy and toxicology of the Leiden University Medical Center. He has a strong interest and conducting research in the domain of optimizing pharmacotherapy, specifically in oncology, hematology and transplantation medicine using pharmacometrics and model informed precision dosing.

At the end of this session participants will be able to:

- Explain the mechanism of action of Biologics and sources of variability in exposure of biologics.
- Cite examples of several Biologics in hemato(oncology) where the dose can be optimized using model informed precision dosing and their specific challenges.
- Discuss which model informed precision dosing strategies can be used to personalize the dose in order to reduce financial and clinical toxicity.

Biologics are more and more used in hemato oncology. Evidence is growing that a more personalized dose individualization is beneficial for clinical outcome as well as reduction of clinical and financial toxicity. Combining therapeutic drug monitoring with PK-PD modelling has opened a new way of dose and therapy optimization called model-informed precision dosing. Model-informed precision dosing (MIPD) is an more advanced quantitative approach focusing on individualized dosage optimization, integrating complex mathematical and statistical models of drugs and disease combined with individual demographic and clinical patient characteristics. In this session challenges and opportunities of MIPD of Biologics in (hemato)oncology will be discussed. Several traditional biologics will be discussed, Alemtuzumab, Daratumab, Pembrolizumab, Nivolumab, as well as more complex biologics such as AT(L)G and Antibody drug conjugates (ADCs)

260

Leveraging machine learning and decision support dashboard to facilitate precision dosing in pediatric patient care

A/Prof Tomoyuki Mizuno

Biography:
Tomoyuki Mizuno, PhD, is an Associate Professor of Pediatrics in the Division of Translational and Clinical Pharmacology at Cincinnati Children's Hospital Medical Center (CCHMC) and the University of Cincinnati College of Medicine. Dr. Mizuno also serves as director of the Pharmacometrics Center of Excellence Program and the Clinical Pharmacokinetics Consultation Service. Additionally, he holds a visiting professorship at Kyoto University, Japan.
Dr. Mizuno's research focuses on pharmacometrics, systems pharmacology, and AI/machine learning-driven precision dosing for pediatric patients. Dr. Mizuno also provides strategic clinical pharmacology and model-informed drug development (MIDD) consulting to pharmaceutical companies, optimizing clinical trial designs and pediatric dose findings for FDA submissions.
He has authored or co-authored nearly 110 peer-reviewed publications and delivered more than 35 invited presentations. He has received several prestigious awards, including the Victor Armstrong Young Investigator Award from the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) in 2021, the Young Scientist Award and Commendation for Science and Technology from the Japanese Minister of Education, Culture, Sports, Science and Technology (MEXT) in 2023, and the Tanabe Young Investigator Award from the American College of Clinical Pharmacology (ACCP) in 2024.

Optimizing medication dosing for children presents unique challenges due to rapid developmental changes in body size, physiology, and organ function, significantly impacting drug disposition and responses. This presentation discusses the application of model-informed approaches to personalizing medication dosing tailored to individual needs. Specifically, the talk will explore clinical implementations of model-informed precision dosing (MIPD) and highlight how machine learning approaches can be used to enhance the MIPD framework. Additionally, the presentation introduces a decision support dashboard as an innovative bedside tool designed to assist clinicians in integrating MIPD effectively into routine pediatric care.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

261

MS-Based Quantification of Gemcitabine in Porcine Models: Application to Drug-Eluting Stent Development

Dr Kelvin Goh[1,2], Ms Li-Jiao Sin[1], Ms Wen Qi Chiang[1], Ms Celine Sim[1], Dr Kenneth Chen[3], Assistant Prof. Tze-Peng Lim[1,2,4]
[1]Singapore General Hospital, Division of Pharmacy, Singapore, Singapore, [2]SingHealth Duke-NUS Pathology Academic Clinical Programme, Singapore, Singapore, [3]Singapore General Hospital, Department of Urology, Singapore, Singapore, [4]Singhealth Duke-NUS Medicine Academic Clinical Programme, Singapore, Singapore

Biography:

Dr. Kelvin Goh is a Principal Medical Laboratory Scientist in the Division of Pharmacy at the Singapore General Hospital. He has a wide range of skillsets in Organic/Inorganic Chemistry, Analytical Chemistry and Medicinal Chemistry. His current interests include mass spectrometry assay development and metabolomics approaches towards tackling real-world problems revolving around antimicrobial resistance, cancer, chronic diseases and other healthcare related challenges. He is also interested in implementation science, with most of his current works revolving around translating innovation from bench to bedside through development of lab-developed test kits and accredited lab services.

Background: Advanced urothelial carcinomas, particularly in upper urinary tract, can cause significant morbidity, including bleeding, obstructive uropathy, and kidney failure. Endourological treatments often result in high recurrence rates. Adjuvant localized chemotherapy using indwelling stents can reduce recurrences. However, the absence of well-designed drug-eluting stents makes this approach vulnerable to challenges such as constant urine flow, peristalsis, and an impermeable lining, which hinder effective ureteral drug delivery.
Aims: We seek to evaluate the pharmacokinetics, safety, and toxicity of administering gemcitabine via a 3D-printed, gemcitabine-infused ureteral stent in a porcine model. This approach aims to achieve targeted drug delivery to ureteral tissues, with gemcitabine detection facilitated by mass spectrometry.
Methods: Calibration curves were developed using Gemcitabine spiked in blank porcine plasma(3-1500µg/L), urine(3-1500µg/L) and tissue(0.3-500ng/g) and analyzed with a Shimadzu LCMS 9030 mass spectrometer. Tissue samples from bilateral ureters were harvested via open surgery(laparotomy) and segregated between the left ureter (drug-loaded stent) and right ureter (control stent). Pre-sacrifice and post-sacrifice bloods were drawn. Urine was collected on the day of sacrifice.
Results: Quantification of gemcitabine in plasma, urine and tissue was achieved within 4.5mins with excellent linearity(R^2=0.998). Accuracy and precision were ±15% across the specified range. Gemcitabine was detected in left ureter tissues and urine but mostly absent in plasma and right ureter tissues.
Conclusion: We developed a rapid, sensitive LCMS assay to quantify gemcitabine in porcine urine, plasma, and tissue samples. Results from our assay demonstrated the utility of our novel drug-eluting stent for safe, targeted gemcitabine delivery to ureteral tissues.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

262

Development of a Multi-Triazole UPLC-UV Assay in Plasma for Antifungal TDM

Ms Celine Sim[1], Ms Wen Qi Chiang[1], Ms Li-Jiao Sin[1], Mr Jun Jie Tan[1], Ms Yvonne Zhou[1], Assoc. Prof. Andrea Kwa[1,3,4], Miss Celine Sim, Assistant Prof. Tze-Peng Lim[1,2,3]
[1]Singapore General Hospital, Division of Pharmacy, Singapore, Singapore, [2]SingHealth Duke-NUS Pathology Academic Clinical Programme, Singapore, Singapore, [3]Singhealth Duke-NUS Medicine Academic Clinical Programme, Singapore, Singapore, [4]Emerging Infectious Diseases, Duke-National University of Singapore Medical School, Singapore, Singapore

Biography:
Celine Sim is a research officer at Singapore General Hospital, where she supports clinical studies in Therapeutic Drug Monitoring to enhance patient safety and treatment efficacy. She holds a bachelor's degree in Chemistry and Biological Chemistry from Nanyang Technological University and previously interned at Shimadzu (Asia Pacific), gaining experience in spectrometry and chromatography. Her interests lie in analytical and medicinal chemistry with a focus on clinical applications.

Background: Triazole antifungal drugs (TADs) are pivotal in treating invasive fungal infections (IFIs) due to their broad-spectrum efficacy and relatively low toxicity. However, improper dosing can lead to adverse effects or therapeutic failure, underscoring the importance of therapeutic drug monitoring (TDM) to tailor treatments effectively. While mass spectrometry has become a preferred method for TDM assay development because of its high sensitivity, many existing high-performance liquid chromatography systems with ultraviolet detection (HPLC-UV) remain underutilized.
Aims: This study aims to develop and validate a simple, fast, and low-cost HPLC-UV method for quantifying multiple TADs in plasma.
Methods: Plasma samples containing isavuconazole(ISV), posaconazole(PCZ), voriconazole(VOC), itraconazole(ITZ) and hydroxy-itraconazole(HICZ) underwent protein precipitation with acetonitrile and separation on a C18 column using gradient elution with 10mM potassium phosphate pH2.61 buffer and acetonitrile; and quantified via UV at 270nm using naproxen as internal standard. The method was validated on accuracy, precision, limit-of-quantification(LOQ), specificity, carryover, and short-term stability based on US-FDA guidelines. The feasibility of the assay was tested in 20 clinical samples.
Results: Quantification of all TADs in plasma was achieved within 4.5 mins with excellent linearity(R^2=0.998) over 0.5-40mg/L range. Accuracy and precision were ±15% across the specified range. The method fulfilled acceptance criteria according to US-FDA guidelines and successfully measured TAD in all 20 samples.
Conclusion: We developed a simple, fast, low-cost HPLC-UV assay to measure multiple TADs in plasma that can be translated for routine antifungal TDM. Continual development of HPLC-UV assay helped us to maximize existing infrastructure for TDM implementation in clinical practice.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

263

Antibody-Based Enrichment of Albumin-Cys34 Adducts to Monitor Drug Exposure

Ms Laura Boffel[1], Dr. Bart Van Puyvelde[2], Mr Ruben Almey[2], Dr. Maarten Dhaenens[2], Prof. Dr. Christophe Stove[1]
[1]Laboratory Of Toxicology, Department Of Bioanalysis, Faculty Of Pharmaceutical Sciences, Ghent University, Ghent, Belgium, [2]ProGenTomics, Laboratory of Pharmaceutical Biotechnology, Ghent University, Ghent, Belgium

Biography:
In 2021, Laura graduated as a pharmacist at Ghent University. Mainly due to the interesting research she was involved in during her Master's thesis at the Laboratory of Toxicology of prof. Christophe Stove, she decided to pursue a career in research. Shortly after graduating, she started a PhD at the Laboratory of Toxicology. Her research is mainly focused on two topics. First, she is setting up an LC-(HR)MS-MS method to monitor drug-protein adducts (in plasma), which are formed upon exposure to (illicit) drugs. Second, she is also working on different microsampling-related topics (i.e., the evaluation of novel technologies, conversion approaches, Hct determination methodologies,…).

Background: Although current analysis of drug biomarkers in blood and urine is well-established, compounds are only detectable for a small time period (several days). Analysis of a keratinized matrix (hair) is the only option to detect biomarkers over a longer time period (several months). However, hair analysis faces crucial technical and interpretative obstacles, complicating unambiguous interpretation of drug exposure. Monitoring drug-protein adducts, serving as biomarkers with an extended window of detection (several weeks), may offer an alternative to hair analysis.
Aims: This study aimed to develop an LC-(HR)MS/MS method to monitor and identify potential protein adducts between the Cys34 residue of human serum albumin (HSA) and drugs, with paracetamol chosen as a model analyte.
Methods: To simplify the biological matrix and improve sensitive monitoring of HSA-Cys34 adducts, a polyclonal antibody assay was designed to capture HSA-Cys34 adducts in trypsin-digested plasma. The enrichment assay and both targeted and untargeted LC-(HR)MS/MS-based detection were optimized based on monitoring of a known HSA-Cys34 adduct with N-acetyl-p-benzoquinone imine (NAPQI, a highly reactive metabolite of paracetamol).
Results: As proof-of-principle, an 'addition-only' protocol was optimized for 100 µL of plasma, allowing successful detection of both in vitro and in vivo (i.e., present in a post-mortem sample) generated NAPQI-Cys34 adducts using the antibody-based assay. Additionally, the presence of NAPQI-Cys34 adducts was successfully confirmed using an LC-HRMS method, enabling untargeted detection of unknown Cys34 adducts.
Conclusions: An antibody-based enrichment assay was successfully developed, optimized and applied to monitor drug-Cys34 adducts in plasma.
Key Words: Drug-Protein Adducts, Long-Term Biomarkers, LC-(HR)MS/MS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

264

Utilizing Waste Plasma as a Sustainable Resource in Antibiotic TDM Assay Applications.

Ms Wen Qi Chiang[1], Ms Celine Sim[1], Ms Li-Jiao Sin[1], Dr Nathalie Chua[1], Mr Jun Jie Tan[1], Miss Wenqi Chiang, Assoc. Prof. Andrea Kwa[1,3,4], Assistant Prof. Tze-Peng Lim[1,2,3]
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Biography:
Chiang Wenqi is a Research Officer in the Division of Pharmacy at Singapore General Hospital. She holds a Bachelor's degree in Biological Sciences and Psychology from Nanyang Technological University. Her current research interests include Analytical Chemistry and therapeutic drug monitoring, with a focus on advancing personalised treatment in clinical settings.

Background: Bioanalytical assays are crucial for antibiotic therapeutic drug monitoring (TDM) in plasma, supporting effective antimicrobial stewardship. Plasma serves as the ideal matrix-matched standard (MMS) for calibration curves in bioanalytical assays, ensuring accurate antibiotic level measurements by minimizing matrix effects that compromise assay robustness. However, the rising cost of commercial plasma (CP) hinders the rapid adoption of TDM. TDM labs frequently generate excess leftover plasma, which is typically discarded. We propose recycling this leftover plasma to produce in-house carbon-stripped plasma (ih-CSP), reducing the reliance on fresh CP and potentially saving an estimated S$50,000 and 324kg of CO2-equivalent emission annually for a TDM service operating 2600 assays in a year.
Aims: This study evaluates ih-CSP, made from recycled leftover plasma, as a feasible alternative to fresh CP in TDM applications.
Methods: ih-CSP was prepared by treating leftover research plasma with crushed charcoal pills. Piperacillin(35mg/L), aztreonam(24mg/L), meropenem(20mg/L), doripenem(13mg/L), and tazobactam(12mg/L) were spiked into CP and ih-CSP from six patient sources. Samples were processed via protein precipitation with acetonitrile and analyzed using a Shimadzu-8060 LCMS system. Antibiotic concentrations in spiked CP and ih-CSP were compared to nominal values.
Results: All five antibiotics were quantified in CP and ih-CSP with excellent linearity (R^2=0.999) across 1–400mg/L. Mean accuracies and precision were within ±15%, with negligible concentration differences (0.4–8.9%) between CP and ih-CSP.
Conclusion: Recycling leftover plasma into ih-CSP provides a cost-effective and viable alternative to CP for TDM assay application, promoting sustainable healthcare. Future research will explore its hospital-wide implementation for TDM.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

265

Rethinking Calibration: A Scientific Dive into Diverse Strategies and Their Efficacy

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Biography:

Dr. Kocic is the Scientific Head of Clinical Pharmacology and Toxicology at SydPath, St. Vincent's Hospital in Sydney, Australia. She oversees the analysis of Therapeutic Drug Monitoring (TDM) results to optimize patient outcomes in complex clinical settings and trials. As an active member of the TDM Matters Multi-Disciplinary Team, she significantly advances clinical practices. Since 2020, she has also served as a Conjoint Senior Lecturer at St Vincent's Clinical School, University of NSW. Dr. Kocic is a leading committee member of the NSW Health Pathology Clinical Mass Spectrometry Forum, connecting with peers in prominent healthcare institutions across Sydney. Additionally, she chairs the Special Drugs Advisory Committee for The Royal College of Pathologists of Australasia Quality Assurance Programs, providing expert insights to laboratories globally. Dr. Kocic also leads the newly established Analytical Committee with IATDMCT, focusing on enhancing the role of analytical methods in TDM and clinical toxicology.

Background: Accurate calibration of analytical methods is crucial for ensuring the reliability of quantitative results in clinical laboratories. Calibration frequency and the number of calibrators used can significantly impact the performance of quality controls (QCs) and overall assay stability.
Aims: The objective of this study is to evaluate the stability of calibration curves for various analytes, including azoles, beta-lactams, and immunosuppressants, and to assess the suitability of different calibration frequencies and internal standards for optimal QC performance.
Methods: A comprehensive review of in-house QC data over six months was performed. We compared the stability of calibration curves using QCs with weekly and monthly calibration methods. Additionally, we analyzed QCs from single curves for azoles, beta-lactams, and immunosuppressants. Different numbers of calibrators (6, 3, and 2(1)) were examined across 10 runs to evaluate their impact on QC performance. We also assessed the use of different deuterated internal standards within the same run to evaluate matrix effects and calibration curve performance.
Results: The maximum bias using 3 calibrators (compared to 6 calibrators) was 1.9% and using 2 calibrators was 3.4%, and generally much lower. Repat azole assay referring to previous calibration showed stability for one or more weeks provided no change in instrument conditions.
Conclusions: This study emphasizes the importance of calibration frequency and the number of calibrators in maintaining laboratory assay accuracy. It recommends a balanced calibration strategy considering cost, precision, and stability, highlighting deuterated internal standards to reduce matrix effects in patient samples, which enhances laboratory efficiency and improves patient diagnoses.
Mass Spectrometry, calibration, QCs

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

266

Therapeutic Drug Monitoring of Everolimus in Cancer Patients: A Single-Centre Experience

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Biography:

Eugene is an early-career clinical pharmacist currently working at Flinders Medical Centre. With a strong foundation in clinical pharmacy, Eugene is dedicated to optimising patient care through evidence-based medication management. He professional interests lie in oncology, where he has gained valuable research experience exploring the effectiveness and safety of various cancer therapies. Currently, Eugene is being mentored by Dr Kichenadasse with funding support from the Ryan Hodges Foundation to investigate precision dosing methods for anticancer medicines. His research focuses on optimising treatment strategies to enhance efficacy while minimising toxicity. Actively collaborating with oncologists, pharmacologists, and consumers, Eugene works to bridge the gap between clinical practice and research, ensuring that patient-centered approaches drive advancements in oncology therapeutics. Through this collaboration, he aims to develop evidence-based dosing strategies that improve treatment outcomes and enhance the safety of anticancer medications.

Purpose: Everolimus, a targeted therapy is used in various cancers and transplant medicine. While therapeutic drug monitoring (TDM) of everolimus is standard practice in transplant settings to optimise dosing and manage toxicity, its application in oncology is not mandated. This single-centre review investigates the potential benefits of TDM, a precision dosing method, in cancer patients prescribed everolimus.
Methods: Medical records from a public hospital in South Australia, were retrospectively reviewed for patients treated with everolimus for cancer indications between January 1, 2013, and December 31, 2023. Data on whole blood everolimus concentrations, cancer diagnoses, dosing regimens, survival outcomes, and demographics were collected and analysed.
Results: During the study period, 53 patients with a median age of 64 years (range:38 – 85) were treated with everolimus. Diagnoses included metastatic breast cancer (MBC, n=41), metastatic renal cancer (n=6), neuroendocrine tumours (n=4), and recurrent ovarian cancer (n=2). Among these, 14 patients (26%) underwent at least one everolimus blood level assessment. In the MBC cohort, the median overall survival was 20.5 months for patients with TDM-guided treatment (n=10) compared to 15.1 months for those without TDM (n=31), a difference that was not statistically significant (HR=0.87, 95% CI:0.42 – 1.79, p=0.70). Importantly, all MBC patients who underwent TDM-guided dose adjustments avoided treatment discontinuation due to adverse effects.

Conclusion: This study highlights the underutilisation of TDM in oncology and its potential to optimise everolimus dosing and minimise toxicity. Prospective studies are warranted to establish therapeutic ranges and confirm the clinical benefits of TDM in cancer care.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

267

HDMTX: Risk Factors of Delayed Excretion and Related ADR in NHL Patients

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Biography:
Zhang Min, Master of Clinical Pharmacy. Engaged as a clinical pharmacist specializing in hematologic oncology in department of pharmacy, Chongqing University Cancer Hospital.

Background: High-dose methotrexate (HDMTX), a important treatment for non-Hodgkin lymphoma (NHL), is often complicated by delayed excretion and associated adverse reactions, significantly impacting patient safety.
Aims: This study aims to investigate the influencing factors for delayed excretion and its correlation with adverse reactions (ADR) in NHL patients receiving HDMTX chemotherapy, offering insights for the safe use of MTX.
Methods: From January 26, 2021 to August 18, 2024, the NHL patients who received HDMTX chemotherapy from Chongqing University Cancer Hospital were collected. Using univariate and multivariate logistic regression, the study investigated the factors affecting the delayed excretion of HDMTX and ADR of grade 2 or higher associated with delayed excretion.
Results: This study included 137 patients,comprising 437 courses of HDMTX. Delayed excretion of HDMTX occurred in 55 patients (40.1%), and 31 patients (56.4%) of patients with delayed excretion at 72-hour. Interestingly, the MTX concentrations of 5 patients dropped to the target range but then rose again to exceed the safe concentration. ADR associated with delayed excretion included white blood cell reduction, acute kidney injury, elevated uric acid, and infection. The number of HDMTX treatment courses (p=0.002) and white blood cell levels (p=0.032) were identified as independent risk factors for delayed excretion. Additionally, independent risk factors for delayed excretion with grade 2 or higher ADR included the MTHFR T allele (p=0.008) and weight ≤50 kg (p=0.029).
Conclusions: When using HDMTX, patients with the MTHFR T allele and weight ≤50 kg should be closely monitored for MTX levels and ADR.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

268

Implementation of TDM Guideline-based Standardized Supportive Care Improves Safety of Methotrexate Treatment

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Biography:

Prof. Zhao is a Doctoral Supervisor at Peking University and Macau University of Science and Technology, an Honorary Professor at the University of Manchester (UK), and a Member of the ACCP Board of Regents.

As a leading expert in hospital pharmacy and clinical pharmacy, Prof. Zhao holds key positions in national and international organizations, including: Chinese Pharmacopoeia Commission (Member); Committee on Pharmacy Administration and Pharmacotherapy, National Health Commission of China (Member); Pharmaceutical Specialized Committee, Chinese Hospital Association (Chair); Committee on Patient Education and Science Popularization, Chinese Pharmacists Association (Chair); Hospital Pharmacy & Evidence-Based Pharmacy Committees, Chinese Pharmaceutical Association (Vice Chair); Therapeutic Drug Monitoring Research Committee, Chinese Pharmacological Society (Vice Chair).

He serves as Editor-in-Chief of AJHP (Chinese Edition) and Deputy Editor-in-Chief of multiple prestigious journals, including China Pharmacy, Evaluation and Analysis of Drug-Use in Hospitals of China, Chinese Journal of New Drugs, Clinical Medication Journal and China Pharmaceuticals.

Prof. Zhao's research focuses on precision medicine, therapeutic drug monitoring, and evidence-based pharmacy practice. He has led 38 research projects (including National Natural Science Foundation grants), published over 310 academic papers (3 ESI highly cited), and obtained 20 national invention patents. He has been honored with the Wu Jieping-Paul Janssen Award, China Pharmaceutical Association Science and Technology Award, and other distinguished accolades for his contributions to pharmaceutical sciences and clinical pharmacy.

Background: High-dose methotrexate (HDMTX) is an essential component of treatment protocols in hematologic malignancies. However, common toxicities during HDMTX therapy still remain to be further managed. Herein, to promote individualized medication and supportive care of HDMTX, the Division of TDM of Chinese Pharmacological Society launched the TDM guideline of HDMTX therapy in November 2021.

Aims: To investigated the effect of implementing TDM guideline-based standardized supportive care on patient safety during HDMTX therapy.

Methods: A seven-year ambidirectional cohort study including a 5-year retrospective (367 Cycles) and 2-year prospective study (244 Cycles) was conducted between January 2017 and December 2023. The TDM guideline-based standardized supportive care was provided initially in January 2022 (Intervention group), and it was defined as empirical therapy before this (Empirical group). Adult patients with hematologic malignancies received HDMTX chemotherapy were included. Outcomes measured included adverse drug events (ADEs) (including liver function damage and

myelosuppression), unreasonable co-combinations with proton pump inhibitors (PPIs) and delayed elimination.

Results: In intervention group, a significant decrease of myelosuppression (51.2% vs 60.8%, P=0.02) and liver function damage (18.4% vs 25.3%, P=0.046) was observed in comparison to empirical cohort. The incidence of unreasonable co-combinations with PPIs was also significantly reduced (37.3%. vs. 52.3%, P<0.001). Delayed elimination was observed in 11.1% of cycles in intervention cohort opposed to 13.4% in empirical group.

Conclusions: The implementation of TDM guideline-based standardized supportive care during HDMTX therapy is recommended to improve patient safety. More attention should be paid to TDM guidelines' implementation.

Key Words: Methotrexate, ADEs, TDM, guideline implementation

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

269

Pharmacogenomic influence on high dose methotrexate pharmacokinetics, outcomes, adverse effects in leukaemia

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Biography:

Completed the super speciality (DM, Clinical Pharmacology) from prestigious institute of India, PGIMER, Chandigarh. Journey of academician started just 15 days back in new place, Manipal institute. Holding degrees from 2 prestigious institute of India (MBBS, MD and DNB , DM from JIPMER and PGIMER) gives immense pleasure to serve the community with greatest motivation.
Starting the TDM work in new place, as its the most interested area to build the knowledge and shorten the gaps between TDM team and prescriber.
Also very much interested in personalised medicine, MIPD, Pharmacometrics and machine learning. Diving into modelling and simulation along with population PK to dose optimisation were explored since past 10 years of academic career. Lastly wish to continue learning in the TDM field as its utmost important to contribute to patient service and research for future.

Background: Acute lymphoblastic leukemia (ALL) is a common hematological cancer in the pediatric age group, accounting for 30%. Similarly, incidence among AYA population (Young adolescence and adults) has raised in recent decades. High dose Methotrexate (HDMTX), is one of the important chemotherapeutic agent administered in consolidation phase of Berlin-Frankfurt-Munster (BFM) protocol. Routine therapeutic drug monitoring of plasma HDMTX levels has been strongly recommended.
Aims: We aimed to determine the correlation of Influence of pharmacogenetics polymorphism of genes encoding MTX enzymes and transporters (SLCO1B1, MTHFR, SLC19A1) with plasma levels, clinical outcome and adverse effects of HDMTX.
Methods: We recruited 112 patients with ALL who received 4 cycles of HDMTX administration with interval of 15 days between the each cycle. The 2 ml blood samples were collected at following time points: 24 hours, 48 hours and 72 hours post HDMTX infusion in each cycle. The following parameters were assessed : genetic polymorphisms by Sanger sequencing, plasma methotrexate levels by LCMS/MS, clinical outcome by minimal residual disease (MRD) at end of consolidation and adverse events by Common Terminology Criteria for Adverse Events (CTCAE) version 5.
Results: We observed a wide inter-individual variability in levels of methotrexate at 24 hours, 48 hours and 72 hours in all 4 cycles. The correlation of SNPs (SLCO1B1, SLC19A1) with plasma MTX at 48 and 72 hours of delayed elimination of HDMTX (P value : <0.05) was significant.
Conclusions: Pharmacogenomics and pharmacokinetics are vital for individualized therapy to optimize efficacy and minimize toxicity of high dose methotrexate.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

270

Melatonin and Chrono-Modulation affect Gemcitabine Pharmacokinetics and CDA activity (MEGA-CLOCK)

Assist Prof Khushboo Bisht[1,2], Professor Nusrat Shafiq[3], Professor Shailendra Handu[2], Professor Puneet Dhamija[2]
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Biography:

Dr Khushboo Bisht is an enthusiastic Clinical Pharmacologist from India, MD (Pharmacology) from AIIMS, Delhi and DM (Clinical Pharmacology) from AIIMS, Rishikesh. She has obtained membership of the British Pharmacological Society (UK) and South-Asian College, an affiliate of American College of Clinical Pharmacology. Dr Khushboo joined Amrita Institute of Medical Sciences, Faridabad since 2024. She is Assistant Professor, Department of Pharmacology, training undergraduates and postgraduates with her experience in the field of Clinical Pharmacology. Her areas of interest in research work are cardiovascular pharmacology, onco-therapeutics, geriatric pharmacology antimicrobial stewardship, patient safety and medical ethics. She excels in designing and conducting clinical trials. She is actively engaged in academic roles and clinical research with multiple publications in international peer-reviewed journals, book chapters and awards to her credit.

Background: The timing of chemotherapy administration and adjunctive therapies like melatonin may influence drug metabolism, efficacy, and tolerability. This study evaluates the effects of chrono-modulated gemcitabine infusion and melatonin supplementation on gemcitabine pharmacokinetics and cytidine deaminase (CDA) activity in metastatic cancer patients.
Aims: To assess the impact of chrono-modulated gemcitabine administration and melatonin supplementation on gemcitabine elimination kinetics, CDA activity, and chemotherapy-related adverse effects.
Methods: This study included 14 metastatic cancer patients receiving gemcitabine (1000 mg/m² over 30 minutes) at either 09:00 or 15:00 hours. A subgroup received melatonin supplementation. Plasma gemcitabine concentrations and CDA activity were measured. Adverse effects were assessed using CTCAE 5.0. Ethical approval was obtained, and the study was registered with the Clinical Trials Registry of India (CTRI).
Results: Chrono-modulated administration did not significantly impact gemcitabine elimination kinetics or CDA activity. However, evening administration was associated with a higher incidence of adverse effects. Melatonin supplementation did not significantly alter CDA activity but increased % extrapolated AUMC (10.29% vs. 4.71%, p = 0.011), indicating altered drug elimination dynamics.
Conclusions: While chrono-modulation did not affect gemcitabine pharmacokinetics, evening administration correlated with increased adverse effects. Melatonin influenced gemcitabine disposition without significantly altering overall pharmacokinetics or CDA activity. Further research is required to determine the clinical implications of these findings.
Key Words: Chrono-modulation, gemcitabine, melatonin, cytidine deaminase, pharmacokinetics, chemotherapy

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

271

Indoor dust: Indirect approach to characterize human exposure to a pesticide cocktail

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Biography:

Eloïse is a second-year PhD student at the University of Poitiers, France. Her research focuses on population biology and ecology, with a particular interest in pesticide exposure assessment. The aim of her work is to develop techniques for dosing pesticides in human, animal and environmental matrices, and to link all the data obtained to study the links between exposure levels in these different matrices. Before starting her thesis, she studied analytical chemistry. She has presented her research work at several national conferences, including last year's 22nd IATDMCT.

Background: Intensive use of pesticides in agriculture has led to widespread contamination of the environment. A number of studies suggest ubiquitous exposure of the population, with potential health effects. However, characterizing pesticide exposure in natural conditions is not straightforward because of the many sources of exposure, the high diversity of pesticide molecules, their low doses and the spatio-temporal dynamic of the pesticide uses.
Aims: In this study, we focus on household dust to assess home contamination by pesticides in a rural area and indirectly estimate residents pesticide exposure.
Methods: Indoor dust samples were collected on wipes in houses of residents of four villages in a cereal plain of western France, the Zone Atelier Plaine & Val de Sèvre. Three samples were collected at three different locations per house at two seasons. A total of 459 dust were collected. Pesticides in the wipe-dust were extracted by liquid/liquid extraction and analyzed by UHPLC-MS/MS (Qtrap6500;Sciex) with a qualitative and quantitative method validated in accordance with the European Medicines Agency guidelines.
Results: Preliminary results from two villages revealed the presence of 4 to 22 pesticides per wipe. The most frequently detected pesticides were dichlorodiphenyltrichloroethane (DDT), carbendazim, imidacloprid and pendimethalin. The same pesticides were found in both seasons, but with different contamination levels.
Conclusions: This study demonstrates the feasibility of an indirect and inexpensive measurement of pesticide indoor contamination. Further studies should be conducted to understand the links between pesticide exposure from indoor dusts and human pesticides exposure.
Key words: pesticides, dust, mass spectrometry, cohort

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

272

LCN2 Promotes Liver Regeneration in APAP-Induced Injury via Kupffer Cell Reprogramming

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Biography:

Bowen Zhai is currently conducting research at the Department of Pharmacy at the Second Xiangya Hospital of Central South University, with a research focus on the pathogenesis of Drug-induced liver injury and the pharmacological research of natural active substances.

Background: Acetaminophen (APAP) overdose is a leading cause of drug-induced liver injury. Lipocalin-2 (LCN2), an acute-phase protein, has emerged as a potential modulator of inflammatory responses, but its role in APAP hepatotoxicity and Kupffer cells (KCs) dynamics remains unclear.
Aims: This study aimed to elucidate the mechanism by which LCN2 protects against APAP-induced liver injury (AILI), focusing on liver regeneration through KCs polarization reprogramming.
Methods: We performed time-course transcriptome sequencing on the livers of AILI mice. The polarization level of KCs was analyzed by flow cytometry. The regenerative phenotypes and the paracrine HGF/c-MET pathway were detected using molecular biology techniques.
Results: We found that the LCN2 were significantly elevated in the livers under AILI, and the injection of LCN2 recombinant protein before injury could significantly reduce the levels of ALT/AST. Flow cytometry showed that the ratio of CD206+ KCs were significantly increased after LCN2 administration. Meanwhile, the expression of regeneration indicators was significantly upregulated. Mechanistically, LCN2 could activate the polarization reprogramming of KCs, which releasing HGF to paracrine to hepatocytes, targeting c-MET to activate the downstream nuclear translocation of β-catenin. In addition, the protective effect of LCN2 was reversed by depletion of macrophages with clodronate liposomes, injection of LCN2 neutralizing antibodies, or antagonism with a c-MET inhibitor.
Conclusions: LCN2 protects against AILI by reprogramming KCs toward an M2 phenotype to release HGF, which stimulates hepatocyte proliferation via c-Met/β-catenin signaling. Targeting the LCN2-HGF-β-catenin axis may offer therapeutic strategies for liver regeneration post-injury.
Key Words: APAP,LCN2,Kupffer cells,DILI,liver regeneration

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

273

Cisplatin Interaction with Calmodulin and Its Impact on MLCK: Implications for Neurotoxicity

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Biography:
Dr. Siming Yuan obtained Ph.D. in Chemical Biology from University of Science and Technology of China and now is a deputy researcher at the First Affiliated Hospital of the University of Science and Technology of China. His work is centered on understanding drug-protein interaction mechanisms, particularly in cancer treatment, providing valuable insights into the behavior of metal-based drugs in biological systems.

Background: Cisplatin has been widely used in clinical, however, its toxic side effects are poorly understood. Understanding how cisplatin interacts with proteins in cells is crucial for unravelling the complex mechanisms underlying its toxic side effects.
Aims: To explore the reaction between cisplatin and calmodulin (CaM), a pivotal protein in signal transduction pathways and gain insights into how cisplatin disrupt normal cellular functions, which could be related to its neurotoxicity.
Methods: 19F and 2D HSQC NMR were employed to analyze the interaction of cisplatin with CaM in vitro. 13CH3 - methionine selective labeling and ICP-MS were used to detect protein - drug interactions within cells.
Results: The results revealed that cisplatin readily reacts with CaM, leading to the mobilization of bound calcium ions and inhibition of CaM/MLCK complex formation. The preformed CaM/MLCK complex exhibited greater resilience to cisplatin compared to free CaM, due to the more embedded methionine residues within the complex. Although the complex survived platination, some destabilization occurred, as evidenced by the mobilization of some calcium ions and collapse of the complex under chromatographic conditions. In-cell NMR indicates that cisplatin can enter cells and react with CaM and CaM/MLCK complex. Notably, the 1H-13C HSQC NMR spectra obtained in cell were directly comparable to those obtained in vitro.
Conclusions: Cisplatin can disrupt the interaction between CaM and the kinase, implying that the platination of CaM could underlie the mechanism of cisplatin induced neurotoxicity.
Keywords: CaM, CaM/MLCK complex, Cisplatin, In-cell NMR, Selective labeling, Neurotoxicity

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

274

Toxicological investigations of suspected spiking cases in Ghent, Belgium: a prospective study

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Biography:
Nick Verougstraete has been working as a clinical biologist at Ghent University Hospital since 2019, where he is responsible for the toxicology lab. He obtained his PhD in 2023 at Ghent University. His main research interests include the detection of NPS, TDM of antimicrobial and oncology drugs and alternative sampling strategies.

Background: Spiking involves intentionally administering a substance to someone without their knowledge or consent, aiming to make the person unconscious or incapacitated. Despite widespread public and media attention, scientific research involving studies with comprehensive toxicology testing remains limited.
Aims: This prospective multicenter-study aims to investigate the characteristics and outcomes of suspected spiking incidents in Ghent, Belgium.
Methods: Over a two-year period, patients presenting after a suspected spiking incident at the emergency department were included in the study. Urine samples were collected within 5 and blood samples within 2 days of the alleged spiking. Toxicological testing included screening for alcohol (blood only), benzodiazepines, opiates, amphetamines, cocaine, cannabinoids, and GHB. Additionally, a comprehensive HRMS-screening method was applied to detect other drugs, medications, and NPS.
Results: To date, 76 patients (median age 26 years; female-to-male ratio 0.67) have been included. The median time between the incident and sample collection was 5 hours. Most incidents (92%) were reported at pubs/nightclubs or events. Common symptoms included nausea, sleepiness, dizziness, and amnesia. Alcohol was detected in 54/71 blood samples, with an average concentration of 1.16 g/L. Illicit and medicinal drugs were detected in samples of 27 participants, most of which were reported as voluntary use. Six plausible spiking cases were retained, involving cannabis, MDMA, ketamine, diazepam, and zolpidem.
Conclusions: Spiking suspicion is common in Ghent, and it's essential to take victims seriously with prompt sample collection and thorough toxicological analysis. However, even when substances are detected, determining if they were administered involuntarily remains challenging.
Keywords: spiking,drink-spiking,toxicology-testing,ER-presentations,multi-center-study

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

275

Risk Stratification for Relapse After Intravenous-to-Subcutaneous Infliximab Switching in Inflammatory Bowel Disease

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Biography:

Yannick Hoffert is a pharmacist by training with a degree from Freie Universität Berlin and a research stay at the Center of Pharmacometrics and Systems Pharmacology at the University of Florida. Since 2022 he has been a PhD researcher in the Pharmacometrics research group at the Department of Pharmaceutical and Pharmacological Sciences at KU Leuven in Belgium. His research focuses on PK/PD modeling of therapeutics in gastrointestinal disorders with a particular interest in intestinal transplantation medicine and inflammatory bowel disease. He is a member of the European Network on Optimising Treatment with Therapeutic Antibodies in chronic inflammatory diseases (ENOTTA). Yannick was awarded a strategic basic research fellowship from the Research Foundation Flanders-FWO.

Background: A subcutaneous formulation of infliximab was recently approved for maintenance therapy of inflammatory bowel disease (IBD). However, limited clinical experience, particularly with escalated intravenous infliximab regimens, poses challenges for transitioning to subcutaneous therapy.
Aims: To investigate the pharmacokinetics and pharmacodynamics of subcutaneous infliximab to identify early predictors of relapse upon switching.
Methods: We repurposed data from a prospective, multicenter trial involving patients switching from intravenous to subcutaneous infliximab. We estimated each patient's infliximab clearance using Bayesian forecasting from a pre-switch sample and a population pharmacokinetics model. We performed pharmacodynamics modeling to evaluate pre-switch predictors of post-switch relapse. Relapse was defined as clinical recurrence (partial Mayo score >2 or Harvey–Bradshaw Index >4 leading to therapeutic escalation) or an increase in fecal calprotectin (fCal) ≥150 µg/g upon switching.
Results: Using data from 98 patients with IBD, we identified infliximab clearance and fCal as independent predictors of relapse. A two-item risk score stratified patients into low-risk (<19% probability of relapse; 75/98; 77%) and high-risk (≥19% probability of relapse; 23/98; 23%) groups (sensitivity 0.52 [95%CI 0.31−0.73], specificity 0.95 [95%CI 0.87−0.99], positive predictive value 75% [95%CI 48−93%], negative predictive value 87% [95%CI 77−93%]). Our pharmacokinetics–pharmacodynamics model classified patients with and without relapse (p <0.0001), with area under the receiver operating characteristic curve of 0.83 (95%CI 0.71−0.93).
Conclusions: Pre-switch infliximab clearance and fCal are accurate predictors of relapse after switching to subcutaneous infliximab. An interactive risk stratification tool facilitates confirmation of a stratified medicine approach to improve infliximab therapy in IBD.
Keywords: Infliximab, TDM, Risk-stratification

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

276

Model-Informed Dosage De-Escalation of Infliximab in Patients With Inflammatory Bowel Diseases

Dr Zhigang Wang[1], Ine De Greef[1,2], Dr Wannee Kantasiripitak[1], Prof Sebastian G Wicha[3], Sophie Tops[1], Melissa Nigro[2], An Outtier[1,2], Prof Bram Verstockt[1,2], Prof João Sabino[1,2], Dr Debby Thomas[1], Prof Séverine Vermeire[1,2], Prof Marc Ferrante[1,2], Assist Prof Erwin Dreesen[1]
[1]KU Leuven, Leuven, Belgium, [2]UZ Leuven, Leuven, Belgium, [3]University of Hamburg, Hamburg, Germany

Biography:
Erwin Dreesen is an assistant professor at KU Leuven in Belgium where he leads the Pharmacometrics research group at the Department of Pharmaceutical and Pharmacological Sciences. His research is focused on optimizing drug dosing in vulnerable patient populations. Applications are mainly situated in the areas of model-informed precision dosing of monoclonal antibodies, anti-infectives, and immunosuppressives. Erwin currently supervises seven Ph.D. students. Erwin is the vice-chair of the TDM of Biologics Scientific Committee and a member of the Pharmacometrics Scientific Committee of IATDMCT. He is a member of the Ethics Committee Research at UZ / KU Leuven, works as a scientific expert for the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), and leads Working Group 2 of the ENOTTA COST Action. Erwin is the coordinator of the KU Leuven - UCLouvain joint Master of Pharmacometrics.

Background: Extending the infliximab infusion interval has been attempted in patients with Crohn's disease (CD) and ulcerative colitis (UC) who sustained treatment response after an earlier interval shortening.
Aims: To compare therapeutic drug monitoring (TDM) and model-informed precision dosing (MIPD) for de-acceleration of infliximab dosage.
Methods: In this prospective, historically controlled Phase 4 trial, patients with steroid-free clinical and biological remission on accelerated infliximab dosing underwent interval extension guided either by TDM (historical control) or MIPD (prospective intervention), targeting an infliximab trough concentration (TC) of 5 mg/L. The primary endpoint was sustained steroid-free clinical and biological remission over one year. Infliximab concentrations were measured at each study visit. Bayesian forecasting was performed using the TDMx Infliximab module (www.tdmx.eu).
Results: The study enrolled 52 patients: 21 patients (11 CD, 10 UC) in the TDM arm and 31 patients (19 CD, 12 UC) in the MIPD arm. MIPD achieved a numerically higher rate of sustained steroid-free clinical and biological remission (52% vs. 29%, p=0.17) and a significantly higher rate of sustained steroid-free clinical remission (81% vs. 38%, p<0.01) over one year compared to TDM. The infliximab dose per infusion over the one-year period was comparable between the TDM arm (7.5 [7.4–8.2] mg/kg) and the MIPD arm (8.8 [6.6–10.9] mg/kg).
Conclusions: MIPD-guided dosage de-acceleration of infliximab resulted in similar rates of sustained steroid-free clinical and biological remission compared to TDM. ClincialTrials.gov, number NCT04982172.
Keywords: anti-TNF therapy; biologics; inflammatory bowel disease; model-informed precision dosing; pharmacometrics; therapeutic drug monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

277

A population pharmacokinetic model of bevacizumab in Japanese cancer patients with proteinuria

Prof Atsushi Yonezawa[1], Dr Takashi Masuda[2], Dr Taro Funakoshi[2], Dr Takahiro Horimatsu[2], Dr Sho Masui[1], Dr Daiki Hira[2], Miss Marin Inoue[1], Dr Kodai Yajima[1], Dr Shunsaku Nakagawa[2], Mr Yasuaki Ikemi[2], Dr Junzo Hamanishi[2], Dr Atsushi Takai[2], Dr Shinya Yamamoto[2], Dr Takeshi Matsubara[2], Prof Masaki Mandai[2], Prof Hiroshi Seno[2], Prof Motoko Yanagita[2], Prof Manabu Muto[2], Prof Tomohiro Terada[2]
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Biography:
2023- present Professor, Division of Integrative Clinical Pharmacology, Faculty of Pharmacy, Keio University
2016- 2022 Associate Professor, Graduate School of Pharmaceutical Sciences, Kyoto University
2014-2015 Visiting Assistant Professor, Stanford University
2013- 2016 Senior Lecturer, Dept. of Clinical Pharmacology & Therapeutics, Kyoto University Hospital
2007-2013 Assistant Professor, Dept. of Clinical Pharmacology & Therapeutics, Kyoto University Hospital
Dr. Yonezawa is the author or co-author of 126 original articles and reviews in peer-reviewed journals with the total citation numbers of 4160, H-index of 31 (as of September 2024 by Scopus).
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Scopus: https://www.scopus.com/authid/detail.uri?authorId=7006444596

Backgrounds: A multitude of factors can play a role in the observed interindividual variability in pharmacokinetics of therapeutic antibodies including bevacizumab (BV). In our previous case series, some patients with proteinuria had decreased trough serum BV concentrations (Masuda T, Cancer Chemother Pharmacol, 2024). This study aimed to develop a population pharmacokinetic (PopPK) model and to evaluate the effect of proteinuria on BV pharmacokinetics.
Methods: Seventy Japanese cancer patients newly starting BV were enrolled in this study. Serum BV concentrations in 368 samples were measured using an LCMS-8060 quadrupole mass spectrometer. PopPK analysis was conducted using a nonlinear mixed-effects modeling program (NONMEM version 7.5.1) employing the first-order conditional estimation method with interaction. This study was approved by the Ethics Committee (No. R2643).
Results: Serum albumin concentration, body weight, and urinary protein to creatinine ratio (UPCR) were identified as significant covariates on BV clearance. BV clearance increased with decreasing serum albumin concentration or increasing UPCR. The simulated median trough concentrations of BV decreased by 12, 21, and 32 % in patients with proteinuria CTCAE Grade 1, Grade 2, and Grade 3, respectively, compared to those with no proteinuria.
Conclusion: We successfully established a PopPK model to predict serum BV concentrations in Japanese cancer patients with proteinuria. PopPK analysis revealed that proteinuria as well as serum albumin concentration and body weight were factors associated with BV clearance.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

278

Assessing the Utility of TDM for Biologics in Inflammatory Bowel Disease Management

Assoc Prof Hong Zhou[1], Miss Chen Shi[1], Miss Li Liu[1], Miss Ying Zhou[1], Mr Jiaqiang Xu[1], Professer Liangru Zhu[2], Professer Rong Lin[2], Professer Yu Zhang[1]
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Biography:

Hong Zhou is a clinical pharmacist in the Department of Pharmacy at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (HUST). My research interests primarily focus on individualized therapy for heart transplantation, particularly utilizing pharmacogenomics and pharmacometrics methodologies. I have led a study funded by the National Natural Science Foundation of China (NSFC), investigating the mechanisms underlying tacrolimus-induced new-onset diabetes after transplantation. Additionally, I have served as the principal investigator for a National Key Research and Development Program of China focused on Precision Medicine Research. Furthermore, I hold the position of Deputy Chairman within The Youth Committee of Therapeutic Drug Monitoring Committee under the Chinese Pharmacological Society and am honored to be recognized as a fellow by the International Society for Therapeutic Drug Monitoring and Toxicology (IATDMCT).

Background: TDM have been employed in the use of anti-TNFα drugs with the aim of optimizing their use. However, use of TDM in clinical practice is variable, possibly due to conflicting results in the literature
Aims: We aimed to evaluate whether the use of TDM in inflammatory bowel disease (IBD) patients on biologic therapy results in improved clinical outcomes.
Methods: A systematic search strategy was developed and conducted across PubMed, EMBASE, Web of Science, and Cochrane Library from database inception to December 12, 2023. Articles which matched the inclusion criteria were included. For controlled study data conforming to a normal distribution, meta-analysis was performed using RevMan 5.3 software
Results: We included eight RCTs and fifteen cohort studies with regard to infliximab and adalimumab. RCT results demonstrated comparable efficacy between the TDM group and conventional clinical management in clinical remission rates, clinical response rates, endoscopic remission, and mucosal healing rates. In contrast, cohort studies revealed opposing trends. RCT evidence indicated significantly lower levels of C-reactive protein and fecal calprotectin in the TDM group. Cohort study findings further showed reduced surgical intervention rates and hospitalization rates in TDM-managed patients. No controlled studies comparing TDM with standard/conventional therapy were identified for ustekinumab, vedolizumab, golimumab, or certolizumab pegol.
Conclusions: Current evidence supporting TDM for biologics in IBD remains limited and inconclusive, which maybe a barrier for implement. More studies with larger RCTs and standardized assays are needed to substantiate these results and validate the cost-effectiveness of TDM.
Keywords: Biologics, TDM, IBD

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

279

Personalized Infliximab Dosing For Acute Severe Ulcerative Colitis: A Multi-Center Pharmacometrics Analysis

Emmanuel Niyigena[1], Yannick Hoffert[1], Prof Laurent Peyrin-Biroulet[2], Prof Waqqas Afif[3], Alessandro Pedicelli[3], Prof Xavier Roblin[4], Prof Jurij Hanžel[5], Prof Konstantinos Papamichael[6], Prof Taku Kobayashi[7], Dr Zhigang Wang[1], Prof Bram Verstockt[8,9], Prof Séverine Vermeire[8,9], Prof Niels Vande Casteele[10], Prof Robert Battat[11], Mr Yannick Hoffert
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Biography:

Yannick Hoffert is a pharmacist by training with a degree from Freie Universität Berlin and a research stay at the Center of Pharmacometrics and Systems Pharmacology at the University of Florida. Since 2022 he has been a PhD researcher in the Pharmacometrics research group at the Department of Pharmaceutical and Pharmacological Sciences at KU Leuven in Belgium. His research focuses on PK/PD modeling of therapeutics in gastrointestinal disorders with a particular interest in intestinal transplantation medicine and inflammatory bowel disease. He is a member of the European Network on Optimising Treatment with Therapeutic Antibodies in chronic inflammatory diseases (ENOTTA). Yannick was awarded a strategic basic research fellowship from the Research Foundation Flanders-FWO.

Background: Infliximab is a safe and effective rescue therapy for patients with steroid-refractory acute severe ulcerative colitis (ASUC). There is no evidence that intensified/accelerated infliximab regimens are superior to standard induction dosing.
Aims: To develop a risk stratification algorithm that assigns patients with ASUC into risk groups of colectomy within 90 days after the start of infliximab therapy and inform personalized infliximab rescue dosing.
Methods: We performed a multicenter, retrospective population pharmacokinetics (popPK) and exposure–response study using pooled data from ASUC patients. Time-to-event modeling was used to describe colectomy within 90 days. Patient characteristics and pharmacokinetics projections were evaluated as predictors of colectomy. The popPK model and regression coefficients of the time-to-event model were used to develop an algorithm for risk stratification and personalized infliximab rescue dosing.
Results: Eight medical centers contributed data from 74 ASUC patients, providing 157 infliximab concentrations. Eleven patients (15%) underwent colectomy within 90 days. The log-transformed ratio of the posterior, Bayesian forecasted area under the infliximab concentration–time curve between weeks 2 and 4 (AUCw2–w4; modifiable risk factor) over the estimated infliximab clearance

(unmodifiable risk factor) was the best predictor of colectomy (AUROC, 0.79 [95%CI 0.53–1.00]). Patients with an AUCw2-w4/CL below 5.81 were defined as at high risk for colectomy (sensitivity 83%, specificity 85%). Classification accuracy was 84% [95%CI 73%–92%].
Conclusions: Personalized dosing of infliximab may achieve lower colectomy rates in patients with ASUC. An interactive tool is provided to facilitate decision-making based on therapeutic drug monitoring.
Keywords: Infliximab, Personalized dosing, Pharmacometrics, Therapeutic drug monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

301

TDM of LAI antipsychotics: an example to follow for LAI anti-infectives?

A/Prof Georgios Schoretsanitis

Biography:

I am a psychiatrist and the head of the outpatient unit of the Department of Psychiatry, Psychotherapy and Psychosomatics, Hospital of Psychiatry, University of Zurich, Zurich, Switzerland, whereas I also am appointed associate Professor in the Barbara Zucker School of Medicine at Northwell/Hofstra, Hempstead, NY, USA. Over the past decade I have been working on big therapeutic drug monitoring (TDM) datasets for different neuropsychotropic agents including clozapine. I am member and vice-president of the task force for TDM of the German Collegium of Neuropsychopharmacology (AGNP), which regularly publishes updates of consensus works for TDM in Neuropsychopharmacotherapy.

Long-acting injectable (LAI) formulations of second-generation antipsychotics (SGA) are emerging as a mainstay in the treatment of schizophrenia-spectrum patients, as their use essentially improves adherence and contributes to reduced relapse risk. We provide pharmacokinetic considerations as a cornerstone of a smooth transition from oral to LAI SGAs based on works previously identified in a systematic manner. Quantifying antipsychotic exposure during baseline oral SGA-treatment based on the patient's SGA blood (plasma or serum) levels may often provide a more appropriate orientation method when selecting the equivalent LAI dose over dose selection based on population-based data. Specifically, oral dose adjustment during LAI transition can be guided by regularly assessing SGA levels right before the next LAI injection.

While LAI SGAs increasingly dominate the maintenance treatment of schizophrenia-spectrum disorders, the development of novel formulations with longer injection intervals is expected to provide increased administration ease. Nevertheless, transitioning from oral SGA to LAIs remains a challenge in clinical routine. Personalizing LAI-based treatment involves tailoring the transition from oral to LAIs taking the individual and drug-related pharmacokinetic peculiarities into consideration.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

302

PopPK Modelling and TDM for Individualized Dosing of Long-Acting Antiretrovirals

Dr Paul Thoueille

Biography:
Dr. Paul Thoueille is a clinical pharmacometrician and hospital pharmacist who completed his PhD in 2024. His main focus is the development of Therapeutic Drug Monitoring (TDM) as a tool for individualized dosage adjustment of drugs. He is an expert in population pharmacokinetic modelling, which he applied notably for the analysis of long-acting intramuscular antiretrovirals. He currently leads the TDM Unit at the Service of Clinical Pharmacology of the University Hospital of Lausanne, Switzerland.

Long-acting injectable antiretroviral drugs are a paradigm shift in the treatment and prevention of HIV infection by eliminating the need of daily medication. However, real-world data have revealed substantial pharmacokinetic (PK) variability, challenging the one-size-fits-all dosing approach.
Key factors affecting long-acting antiretrovirals exposure after intramuscular administration were identified, including bodyweight, sex, as well as significant intra- and inter-individual variability in absorption and elimination. In particular, model-based simulations highlighted sex-related differences in cabotegravir PK: females had lower trough concentrations at treatment initiation but significantly higher levels during the late maintenance phase. These findings have direct clinical implications, particularly for individuals with additional risk factors – such as obesity – who may benefit from individualized TDM where feasible.
This presentation will explore how population pharmacokinetic (popPK) modelling and TDM can refine dosing strategies for long-acting antiretrovirals by tailoring dosing intervals based on individual PK data. It will discuss the integration of popPK models and Bayesian approaches into routine clinical practice, aiming to optimize drug exposure, minimize the risk of under-exposure, and sustain virologic suppression while reducing treatment burden.

303

LAI formulations of anti-infectives in adults

Dr Ethel Weld

Biography:
Dr. Ethel D. Weld, MD, PhD is an assistant professor of medicine, pharmacology, and molecular sciences at the Johns Hopkins University School of Medicine. She earned her medical degree from the University of Chicago and her PhD in Clinical Investigation from the Johns Hopkins Bloomberg School of Public Health. She is board certified in Internal Medicine and Pediatrics and subspecialty board certified in Infectious Diseases and Clinical Pharmacology, and serves as an attending Infectious Diseases physician at the Johns Hopkins Hospital and the Johns Hopkins Bayview Medical Center. She is the recipient of Johns Hopkins Center for AIDS Research (CFAR) faculty retention funding, a CFAR Faculty Development Award for her study "Feasibility, Development and Validation of a Non-cold-chain-requiring Assay to Measure Long-acting Antiretrovirals in Blood", and an NIH K23 mentored career award for her project entitled "Optimizing the Use of Long-Acting Antiretrovirals for Youth with HIV". She chairs the IMPAACT 2005 and 2034 trials, both multi-site international studies of novel TB therapeutics in children. Her primary research focus is on developing HIV and TB therapeutics in special populations, and optimizing long-acting therapeutics for individuals with HIV and adherence challenges.

This session will cover the state of the field of existing approved long-acting anti-infectives, with a primary focus on HIV therapeutics. The clinical trial evidence for efficacy and safety, the influence of long-acting drug exposures on efficacy and toxicity, ideal use cases, and the factors contributing to PK variability between occasions and between individuals will all be discussed. Selected case scenarios of clinical virological failures while receiving long-acting antiretrovirals will be presented and discussed, as well as potential strategies to mitigate these. The talk will also touch on long-acting anti-infective therapeutics in the late pipeline, including oral formulations dosed less frequently than daily, and on formulations in development that hold high promise as long-acting strategies.

304

Long Acting treatment of anti-infectives in paediatrics

Prof Natella Y. Rakhmanina

Biography:
Dr. Natella Rakhmanina is a Professor of Pediatrics at George Washington University and serves as an Associate Chief of the Division of the Pediatric Infectious Diseases and a Director of the HIV Prevention and Treatment Services at Children's National Hospital in Washington, DC, USA. Dr. Rakhmanina obtained her MD degree at People's Friendship University in Moscow, Russia, and her PhD degree in clinical pharmacology at the Erasmus University in Rotterdam, the Netherlands. For more than 25 years she has been providing care for infants, children and adolescents affected by the HIV epidemic. She is a successful clinical researcher, focusing her studies on the treatment and prevention of HIV in children and adolescents and serving as a principal investigator of NIH, CDC and industry funded pediatric and adolescent HIV studies. Dr. Rakhmanina has held multiple regional, national, and international professional roles including serving as immediate past Chair of the Committee on Pediatric AIDS at the American Academy of Pediatrics. For over a decade, she has been serving and continues to serve as a member of the US Department of Health and Human Services Panel on the Pediatric Antiretroviral Therapy and Management Guidelines at the Office of AIDS Research Advisory Council in National Institutes of Health and the Pediatric Advisory Working Group at the World Health Organization. She also has more than a decade experience in global health serving as a Senior Technical Advisor at Elizabeth Glaser Pediatrics AIDS Foundation where she led diverse projects on pediatric and adolescent HIV treatment in Sub-Saharan African countries.

Dr. Rakhmanina will review the current developments in the long-acting formulations of anti-infective drugs for pediatric populations. The session will focus on the current pipeline in the development of the novel antiviral, antibacterial and antiparasitic agents to treat most common pediatric health conditions globally such as HIV infection, tuberculosis, bacterial pneumonia, osteomyelitis, malaria, and other infections. The audience will learn about specific challenges in the developmental pharmacology that affect the formulations and dosing considerations of the long-acting anti-infective formulations for infants and children.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

305

The pharmacological effects of using cabozantinib with a light breakfast: The SKIPPY1 study

Ms Amy Rieborn

Biography:
Amy Rieborn is a PhD candidate at the departments of Clinical Pharmacy and Toxicology and Medical Oncology of Leiden University Medical Center. Her research is focused on therapeutic drug monitoring (TDM) and personalized medicine in oncology. Trained as a medical doctor with previous work experience in the field of internal medicine, she aims to translate the theoretics of TDM and pharmacokinetic modelling into a direct benefit for the patient in daily practice.

Introduction: Cabozantinib is a tyrosine kinase inhibitor approved for treatment of renal cell carcinoma. Cabozantinib is started at 60 mg daily, ingested in fasted state. Dose reductions are needed in 67% of patients due to toxicity, without reduce in treatment costs due to a flat pricing model. Alternative dosing strategies are warranted to improve the toxicity profile and reduce treatment costs. Previous studies have shown cabozantinib AUC increased 57% after taking cabozantinib with a high fat meal. The increase in bioavailability when taken with a light breakfast is still unknown. In this study we aim to determine the increase of cabozantinib AUC when taken with a light breakfast.
Methods: A multicentre, open label, randomized cross-over pharmacokinetic evaluation study was performed. In the standard regimen, patients took cabozantinib in fasted condition. In the experimental regimen, patients took cabozantinib with a light breakfast. After 4 weeks on the allocated regimen, pharmacokinetic samples were obtained at t=0,1,2,3,4,6,8 and 24 hours after dose intake and patients thereafter switched to the other regimen. Patients were monitored for (S)AEs.
Results: Twelve patients completed study procedures. AUC0-24 for taking cabozantinib in fasted and fed state were 11530 ug/L and 12530 ug/L respectively (CV 10.1%). Mean difference was 8.3% (ratio 90% CI 100.9 – 117.12). No differences in adverse events were established.
Discussion and conclusion: This study demonstrates taking cabozantinib with a commonly used breakfast leads to a slight increase in exposure, but with no apparent impact on adverse events. These results support to ingest cabozantinib with food without clinically relevant influence on exposure.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

306

Gastrointestinal Environment and Drug Interactions in Cancer Patients: Insights from Clinical Trial Data

A/Prof Ashley Hopkins

Biography:

Associate Professor Ashley Hopkins leads the Clinical Cancer Epidemiology Lab at Flinders University, South Australia. His research harnesses large-scale clinical trial data to understand how commonly used medications, including those affecting the gastrointestinal environment, influence cancer treatment outcomes. Through industry collaborations, he has negotiated access to individual participant data from over 100 oncology trials, enabling world-first analyses on the impact of antibiotics, antacids, and body composition on immunotherapy efficacy and toxicity. Ashley is a strong advocate for data transparency, contributing to international frameworks through roles with the Clinical Oncology Society of Australia and the Society for Immunotherapy of Cancer. His work has shaped clinical guidelines, featured in high-impact journals such as JAMA Oncology, Journal of Clinical Oncology, and The BMJ, and earned recognition through the Tall Poppy Award, Certara New Investigator Award, and prestigious fellowship grants. He is also committed to mentoring emerging researchers and embedding consumer perspectives in cancer research.

This presentation showcases research underpinned by data transparency frameworks that enabled negotiation of access to patient-level data from over 100 industry-sponsored oncology trials. These rich datasets have facilitated investigations into how gastrointestinal-modifying concomitant medicines influence survival and adverse event outcomes in cancer.

Key findings from Associate Professor Ashley Hopkins' work demonstrate that proton pump inhibitor (PPI) use is associated with poorer survival benefit from immunotherapies, such as atezolizumab, in non-small cell lung cancer. Large-scale prognostic analyses further reveal that PPI exposure correlates with reduced overall survival and worsened toxicity in colorectal and breast cancer cohorts. Methodological approaches include multivariable Cox regression and pooled post hoc trial evaluations, illustrating how systematic analyses of participant-level data can uncover clinically meaningful drug interactions.

These results underscore the urgent need to advocate for and expand transparent access to trial data. Findings highlight that GI modulating drugs can alter the gut microbiota and gastric pH, affecting drug absorption, pharmacokinetics, and pharmacodynamics—factors of growing importance as oncology shifts toward orally administered targeted therapies.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

307

Effect of dietary proteins on the pharmacokinetics and toxicity of 5-flurouracil

Prof Jennifer Martin

Biography:
Professor Jennifer Martin is a senior physician and clinical pharmacologist with 30 years clinical, Government, industry and research experience in optimising drug choice and dose. One aspect of this work is therapeutic drug monitoring to optimise individual dosing. Although the genetic makeup of some individuals explains some of the exposure, it doesn't explain most of the variation in clinical exposure and outcomes. Recently, the effects of diet (which may be a surrogate for culture, geography or microbiome) are seen to contribute significant effects on clinical exposure, and/or clinical outcomes. This may be particularly relevant to the use of purine, pyrimidine and other metabolic analogues such as 5FU. This talk will highlight the literature in this space drawing from the Cancer Council funded 5FU dose optimisation studies in Newcastle.

In humans, dietary intake is known to have effects on the pharmacokinetics of many drugs including cancer therapeutics. In fact over half of the chemotherapy approved by the FDA has shown significant effects of diet and dietary composition. Different diets can differentially alter gastric pH, splanchnic and hepatic blood flow, bile production and release, and influence gastrointestinal transit times. Diet also affects the microbiome. Collectively, these factors can impact the pharmacokinetics of oral drugs. In the case of some chemotherapy e.g. those that involve interruptions to protein synthesis or incorporation into DNA, such as 5FU – a fluorinated pyrimidine analogue of uracil that inhibits a key enzyme, the mechanisms are not well understood.
In the case of 5FU, protein malnutrition, which is highly prevalent in cancer, particularly with later stage cancer, increases toxicity. The mechanisms are several, however it has long been known that in animals, protein depletion reduces hepatic metabolism of 5FU and also reduces DPD activity significantly increasing toxicity (1,2).
This abstract will summarise both older animal and current human phenotype data to understand the inter and intra-patient variability in 5FU exposure and the role of diet.

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23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

308

Clinical implications of food–drug interactions with small-molecule kinase inhibitors

Prof Frank Jansman

Biography:

Frank Jansman is professor in clinical pharmacy, in particular oncology-pharmacy at the University Groningen. In addition, he is head and certified trainer hospital pharmacy of the department of clinical pharmacy of the Deventer Teaching Hospital. He combines his activities in the hospital with research and education for the Groningen Research Institute of Pharmacy and for the study pharmacy. Reseach lines include medication surveillance and pharmaceutical care for cancer patients and factors influencing anti-cancer drug exposure in patients. Given his chair of the Dutch Expertgroup Anticancer Drug Interactions, research to co-medication, alternative medicines, and food in combination with anti-cancer drugs is a major topic. Frank Jansman is a hospital pharmacist and a clinical pharmacologist.

During the past decades, small-molecule kinase inhibitors have proven to be valuable in the treatment of solid and haematological tumours. However, because of their oral administration, the intrapatient and interpatient exposure to small-molecule kinase inhibitors (SMKIs) is highly variable and is affected by many factors, such as concomitant use of food and herbs. Food–drug interactions are capable of altering the systemic bioavailability and pharmacokinetics of these drugs. The most important mechanisms underlying food–drug interactions are gastrointestinal drug absorption and hepatic metabolism through cytochrome P450 isoenzymes. As food–drug interactions can lead to therapy failure or severe toxicity, knowledge of these interactions is essential.
Therefore, general principles involving food–drug interactions and herb–drug interactions for SMKIs will be presented. For illustration, the design and results of specific studies will be discussed more extensively. Also, US Food and Drug Administration (FDA) and European Medicines Agency (EMA) recommendations concerning food-drug interactions are considered. Based on current available information, clear recommendations for their management will be provided, and suggestions for performing food-drug studies during drug development phases and thereafter.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

309

Food effect on the bioavailability of abiraterone and its implications for dosing and mitigating financial toxicity: Results of a randomized controlled trial

Dr Vikram Gota

Biography:

Dr. Vikram Gota completed his MD in pharmacology from Christian Medical College, Vellore, following which he briefly worked as a Clinical Investigator in BA/BE studies. Thereafter, he joined the INDOOxford (INDOX) Cancer Trials Network at Tata Memorial Centre, Mumbai, where he received training in the design and conduct of phase I clinical trials. During this time, he also obtained the post graduate diploma in clinical trials from the London School of Hygiene and Tropical Medicine, University of London. He is presently the officer-in-charge of the department of clinical pharmacology at the Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Tata Memorial Centre. His research interests include early clinical development and pharmacokinetics driven optimization of drugs used in cancer, including the development of pediatric-friendly formulations for childhood cancers. He is currently the Chair of the TDM in Oncology sub-committee of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT). He is involved with the geriatric clinic at TMH since 2019 focusing on rational therapeutics, potentially inappropriate medications and drug-drug interactions, among other things. He has worked as an investigator in several phase I clinical trials including first-in-human studies of investigational new drugs.

Abiraterone acetate is a cornerstone in the management of metastatic castration-resistant prostate cancer (mCRPC). Given its food effect on absorption, we compared outcomes between a low-dose (250 mg daily- Arm A) and standard-dose (1000 mg daily – Arm B) abiraterone regimen. The low-dose abiraterone was administered with a low-fat meal, whereas the standard dose was administered in fasting state as per standard recommendations. The objective of the study was to assess whether lower dosing could maintain efficacy and safety while improving cost-effectiveness. In this study, overall survival (OS) and median prostate-specific antigen progression-free survival (PSA-PFS) were comparable between the two arms [PSA-PFA = 5.7 vs 3.8 months, HR=0.95; OS = 18.1 vs 15.1 months, HR=0.99]. Similarly, the incidence of grade ≥3 adverse events did not differ significantly [36.6% vs 31.6%, p=0.51]. Pharmacokinetic (PK) analysis showed that both area under the concentration-time curve (AUC) and maximum plasma concentration (Cmax) were lower in the low-dose arm compared to the standard-dose arm [AUC = 28.7 vs 226 ng/ml*h], indicating reduced systemic exposure. Importantly, the anticipated improvement in bioavailability with a low-fat diet was not observed in the low-dose group. Despite lower PK exposure, clinical outcomes and toxicity remained similar between low-dose and standard-dose treatments. These findings suggest that administering low-dose abiraterone with a low-fat meal does not enhance bioavailability but achieves comparable survival and safety outcomes to the standard regimen. This approach could represent a meaningful strategy for substantial cost savings without compromising patient care.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

310

Modelling of red blood cell turnover to determine safe dosing strategies for treatment of vivax malaria patients

Prof Julie Simpson

Biography:
Professor Julie Simpson is Head of Biostatistics at the Melbourne School of Population and Global Health and Director of the Methods and Implementation Support for Clinical and Health research (MISCH) Hub at the University of Melbourne, and a Visiting Professor of the University of Oxford. She has 30 years' experience collaborating on multidisciplinary research projects with clinicians, laboratory scientists, epidemiologists and health policy-makers at universities and hospitals worldwide. Her main area of research is the integration of biostatistics and mathematical modelling to improve the treatment of malaria.

Background: Primaquine is the only widely available drug that targets Plasmodium vivax malaria parasites in the liver. However, primaquine is underused because of concerns that this drug can cause dose-dependent haemolysis in glucose-6-phosphate dehydrogenase (G6PD) deficient individuals. We developed and calibrated a within-host Bayesian pharmacodynamic model of red blood cell (RBC) production and turnover to explore the safety of primaquine regimens for individuals with G6PD deficiency.
Methods: The within-host RBC model captured deviations from the RBC normal process by assuming a dose-dependent effect of primaquine on the lifespan of circulating erythrocytes and the compensatory response of precursor cells and reticulocytes. The compartmental mechanistic RBC model was fitted to data from a regimen-adaptive trial of ascending primaquine doses in 23 G6PD hemizygote deficient volunteers using a Bayesian hierarchical framework. Detailed serial haemoglobin and reticulocyte count data were available, 1523 individual measurements over 656 unique time points.
Results: Our model estimated that primaquine doses of ~0.75 mg base/kg reduce the circulating lifespan of deficient erythrocytes by ~30 days in individuals with common Southeast Asian G6PD variants. We predict that a total dose of 5 mg/kg of primaquine can be administered safely to G6PD deficient individuals over 14 days with expected drops in haemoglobin of 2.7 to 6.5 g/dL from a baseline of 15 g/dL.
Discussion: Our within-host RBC model captured the effect of primaquine on G6PD deficient volunteers' haemoglobin and reticulocyte profiles. This mechanistic model suggests safe and effective primaquine dosing schemes can be administered within two weeks to G6PD deficient individuals.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

311

In silico modelling of triple artemisinin-based combination therapies to inform dosing in areas with emerging antimalarial drug resistance

Ms Meg Tully

Biography:
Meg Tully has a Masters of Biostatistics from the University of Melbourne and is currently undertaking a PhD specialising in novel antimalarial combination therapies to combat the ongoing threat of drug resistance. She is based in the Centre for Epidemiology and Biostatistics within the Melbourne School of Population and Global Health and supervised by Prof Julie Simpson, A/Prof David Price and Dr Robert Commons. Her research is currently focused on pharmacokinetic-pharmacodynamic modelling of the within-host dynamics of novel malaria treatments.

Declining antimalarial drug efficacy poses a significant threat to malaria control worldwide. The firstline treatment for P. falciparum malaria combines artemisinin derivatives with a long-acting partner drug. These artemisinin-based combination therapies (ACT) have proven very successful in maintaining high cure-rates. However, recent decreases in ACT efficacy have led to the necessary development and testing of new drugs and therapies, such as triple ACTs (TACT), where the ACT is administered alongside a third antimalarial drug.
Some promising candidate TACTs are currently in clinical trials; and whilst essential, clinical trials are an extremely time and resource intensive way to learn more about candidate regimens.
Mathematical modelling of the underlying drug-parasite dynamics can be a cost-effective and ethical way to simulate efficacy of novel regimens, informing effects in varied scenarios.
We have developed an in silico pharmacokinetic-pharmacodynamic model that incorporates parent-metabolite profiles, drug-drug interactions, parasite life-cycle and age-specific killing effects. It was previously applied to dihydroartemisinin-piperaquine-mefloquine and was able to accurately estimate efficacy in the populations where clinical trials were conducted. We have performed a simulation study of the TACT artemether-lumefantrine-amodiaquine, using published pharmacokinetic and pharmacodynamic parameters to explore treatment outcomes in a variety of settings.
This flexible model allows for evaluation of potential cure rates at different levels of resistance to each of the three antimalarials, and for a variety of possible interaction scenarios. This model framework can be used to explore likely efficacy in different populations and inform TACT dosing schedules and local treatment policy.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

312

Dose-optimisation of a novel co-formulated triple combination antimalarial therapy: Artemether-lumefantrine-amodiaquine

Prof Joel Tarning

Biography:
Professor Joel Tarning leads a large and diverse team of 30 people studying clinical pharmacology at the Mahidol Oxford Tropical Medicine Research Unit (MORU) in Thailand. The main scientific directions within the department are pharmacometric data analysis, bioanalytical method development, drug quantification of clinical study samples, omics-based research, falsified/substandard medicine, and basic pharmacology. He is a Professor of Clinical Pharmacology at the University of Oxford, UK and a visiting Professor at the Faculty of Tropical Medicine, Mahidol University, Thailand. Professor Tarning has published >250 peer-reviewed articles resulting in >18,000 citations. His main research is focused on dose-optimisation of drugs used to treat neglected tropical diseases in under-served populations at risk of treatment failure and resistance development, such as children and pregnant women. His work on antimalarial drugs has already had a global impact.
www.ndm.ox.ac.uk/principal-investigators/researcher/joel-tarning

There were an estimated 263 million cases of malaria worldwide, leading to 597,000 deaths, in 2023. Children under the age of five accounted for 74% of all malaria-related deaths. Artemisinin-based combination therapy (ACT) is the first-line therapy for uncomplicated falciparum malaria, but artemisinin resistance in Asia and now sub-Saharan Africa is threatening our ability to control and eliminate malaria. Triple-ACTs have emerged as a viable alternative treatment to combat declining ACT efficacy due to drug-resistant malaria. In this study, we developed and evaluated an optimal fixed-dose regimen of artemether-lumefantrine-amodiaquine through population pharmacokinetic modeling and simulation. Three published population-based pharmacometric models and two large cohorts of observed adult subjects and pediatric malaria patients were used to simulate pharmacokinetic profiles of different dosing strategies. Based on simulated total exposure and peak concentrations, an optimal dose regimen was developed resulting in an extension of the current 4 weight bands to a total of 5 weight bands to generate equivalent exposures in all body weight groups and minimize the fluctuation in exposure between patients. The proposed drug-to-drug ratio of artemether-lumefantrine-amodiaquine (20:120:40 mg) was kept constant throughout the dosing bands in order to simplify manufacturing, implementation, and further development of a fixed-dose co-formulated product.
Key words: malaria, resistance, dose-optimisation, triple combination therapy, pharmacokinetics, pharmacometrics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

313

Mechanistic pharmacokinetic modelling of primaquine in lactating women and breastfed infants for the radical treatment of maternal P. vivax malaria

Dr Thanaporn Wattanakul

Biography:
Dr. Wattanakul is an experienced pharmacometrics researcher specializing in tropical diseases, particularly malaria. Currently, she serves as the Deputy Head of the Pharmacometrics Group in the Department of Clinical Pharmacology at the Mahidol Oxford Tropical Medicine Research Unit, Bangkok, Thailand. Her research focuses on malaria and aim to optimize treatments for underserved populations, including children, lactating women, and pregnant women, through pharmacokinetic/pharmacodynamic (PK/PD) modelling.

Introduction: Primaquine is one of two drugs available for the radical cure of vivax malaria. Lactating women are excluded from receiving primaquine due to a perceived risk of haemolysis in breastfeeding infants with glucose-6-phosphate-dehydrogenase(G6PD)-deficiency.
Methods: Twenty-one lactating women who received a standard dose of primaquine (0.5mg/kg/day) for 14 days were included in this analysis. Primaquine and its metabolite (carboxyprimaquine) concentrations were measured in maternal venous plasma, capillary plasma, breastmilk, and in breastfeeding infant capillary plasma. Population pharmacokinetic analysis was performed using nonlinear mixed-effects modelling (NONMEMv7.4). A mother-to-infant model incorporating feeding pattern observed in the studied population was developed to predict infant drug exposure. Maternal exposure after a single low dose of primaquine (0.25mg/kg) served as a safety reference that does not cause clinically significant haemolysis in G6PD-deficient individuals.
Results: A one-compartment disposition models for both primaquine and carboxyprimaquine accurately described the maternal concentration data across all measurement matrices. Primaquine absorption followed a transit absorption model with first-pass metabolism. Primaquine and its metabolite were excreted into breastmilk, but the estimated infant dose and total drug exposure were <1% of maternal levels. The predicted infant exposures were also well below the safety reference for G6PD-deficient individuals in all evaluated dosing scenarios.
Conclusion: Modelling and simulations demonstrated negligible infant drug exposure, suggesting that even in infants with the most severe G6PD-deficient variants, standard primaquine doses given to mothers are unlikely to cause clinically significant haemolysis in infants through milk consumption. Thus, lactating women should not be excluded from radical cure for vivax malaria.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

314

Role of TDM in model-based individual predictions for treatment of NTDs in breastfeeding mothers

Dr Francis Williams Oraja

Biography:
Francis is a Lecturer of pharmacology at Gulu University (Uganda) and currently a Postdoc at the Infectious Diseases Institute (Uganda).
He holds a Bachelors of Science degree in Biochemistry and a Masters of Science degree in pharmacology, both from Makerere University, and a Doctoral degree in pharmacometrics from the Freie Universitaet Berlin (Germany). Francis's research has applied pharmacometrics in different therapeutic areas, including paediatrics and adult oncology, and infectious diseases such as malaria and HIV, characterising the relationship between treatment and treatment outcome (safety and efficacy). His current research focuses on pharmacometrics-based optimisation of treatment in special populations including pregnant and breastfeeding mother-infant pairs. He is passionate about teaching and mentoring junior scientists into pharmacometrics and increasing the role of pharmacometrics in clinical pharmacology research in Uganda and Africa. https://www.linkedin.com/in/ojara-williams-francis-38993822 / https://scholar.google.com/citations?user=Wc77s50AAAAJ

Introduction: Breast milk offers health benefits to both the mother and infant but also poses a threat for infant exposure to maternal drugs. Only 22% of first-line drugs used for treating malaria, tuberculosis and neglected tropical diseases (NTDs) have breastmilk data [1], limiting informed treatment and potentiating negative efficacy and safety outcomes. We explore the opportunity for Therapeutic Drug Monitoring (TDM) in breastfeeding mothers based on the Maternal to Infant Lactation pharmacoKinetic (MILK) program.
Methods: Breastfeeding mothers plus their infants were enrolled across different observational studies in Kampala, Uganda. Maternal blood and breastmilk, and infant blood were sampled across time within dosing intervals. Bioanalysis of blood and breastmilk used validated liquid chromatography-tandem mass spectrometry. Plasma and breastmilk concentration data were jointly modelled to characterize milk-to plasma ratios, quantify inter-individual variability and identify influential patient/treatment factors, using the population approach in NONMEM 7.4.1.
Results: Overall 200 mothers-infant pairs have been recruited, representing therapeutic areas of HIV (n=152) [2, 3], tuberculosis (n=20) [4] and malaria (n=30) [5]. Workflows for bioanalysis and population pharmacokinetic analysis have fully been developed for lamivudine, a first-line antiretroviral agent, reporting a milk-to-plasma ratio of 1.77 and infant exposure of 179.3 µg/kg/day (range: 125.8, 282.3). Bioanalytical methods for quantification of antituberculosis and antimalarial plasma and breastmilk drug concentrations are under development.
Conclusions: The lactation pharmacokinetic workflows can be leveraged for TDM for the reported antiinfectives, and drugs for NTDs, possessing high milk-to-plasma ratios and high interindividual pharmacokinetic variability to support treatment optimization in breastfeeding mother-infant pairs.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

315

From big data to better dosing: Optimizing patient-specific PK model selection

Dr Jasmine Hughes

Biography:
Dr Jasmine Hughes is the Head of Clinical Data Science at InsightRX, a San Francisco-based company that makes model-informed precision dosing and clinical analytics software. She received her Bachelor's in Chemical Engineering from McGill University and her PhD in Bioengineering from the University of California, San Francisco and the University of California, Berkeley, and is currently based in Toronto, Canada. Her current research focus is creating and improving models, statistical methods and software tools for improving dose individualization in clinical practice.

Background: Successful model-informed precision dosing (MIPD) depends on the ability of the model to describe the patient. However, models may not fully capture the diversity of patients, with some models being more predictive in certain subpopulations than others. In current practice, model selection is often manual, based on simplistic rules (e.g., BMI cutoffs), or defaulted to a single model without empirical validation across diverse cohorts.
Aims: We developed a data-driven, pre-TDM model selection algorithm guided by expert-derived design principles and grounded in real-world experience supporting vancomycin dosing.
Methods: We defined seven principles to guide model selection: (1) evaluate models as used in clinical workflows (stepwise, without future data); (2) emphasize a priori predictive performance; (3) favor models that minimize the risk of underexposure; (4) prefer models developed in clinically similar populations; (5) reflect known drug PK structure (e.g., two-compartment models); (6) incorporate clinical implementation experience; and (7) optimize based on error magnitude, bias, and prediction accuracy. Seven vancomycin PK models were evaluated across 129 patient archetypes defined by age, renal function, BMI, and sex, in a data set of 384,000 treatment courses.
Results: Evaluated in a 145,000-patient hold-out cohort, the algorithm reduced bias by 85–88%, improved prediction accuracy by up to 50%, and lowered RMSE by 10–22% compared to general-use, single-model approaches.
Conclusions: Expert-informed, data-backed model selection improves predictive performance while maintaining transparency required for clinical adoption. Future work may explore integrating machine learning methods capable of leveraging high-dimensional EHR data to further refine model selection, particularly for complex or underrepresented subpopulations.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

316

Does it need a team to win? Model averaging in model-informed precision dosing

Prof Sebastian Wicha

Biography:
Sebastian Wicha is a tenured Full Professor of Clinical Pharmacy. He is leading the research group Clinical Pharmacy at the Institute of Pharmacy, University of Hamburg, Germany since 2017. He is a pharmacist by training holding a Ph.D. in Clinical Pharmacy from the Freie Universität Berlin, Germany (2015) and gained experience as a postdoctoral researcher at the Pharmacometrics Research Group at Uppsala University, Sweden (2015-2017). His research group aims to improve and individualize drug therapy by means of pharmacokinetic-pharmacodynamic and pharmacometric techniques with a special focus on anti-infectives. In this field, he has published >110 peer-reviewed papers. His research group has expertise in bioanalysis, pharmacometric data analysis, and develops open-access web-based software to foster model-informed precision dosing (TDMx.eu). Sebastian is the currently the chairperson of the PK/PD study group of the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) as well as an ESCMID Fellow. Moreover, he is an external expert for pharmacometrics for the German Federal Institute for Drugs and Medical Devices (BfArM) and the European Medicines Agency (EMA).

Model-informed precision dosing (MIPD) integrates population pharmacokinetic (PK) models with drug concentration data obtained through therapeutic drug monitoring to optimize individualized dosing. A critical determinant of accurate and precise predictions is the selection of an appropriate population PK model—ideally, one that closely matches the patient's characteristics. However, identifying the most suitable model for a given patient can be challenging in routine clinical practice. Model averaging has been proposed as a strategy to address this challenge. Rather than relying on a single model, model averaging incorporates multiple candidate models, estimates the individual pharmacokinetic profile using each, and then computes a weighted average of the forecasts based on model performance metrics.
This presentation will begin with an overview of the principles of model averaging and its application in clinical pharmacology. We will review and critically evaluate the current literature on the use of model averaging in MIPD. Finally, we will present findings from a simulation study conducted by our research group, offering practical insights into the selection of a meaningful set of candidate models for model averaging.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

317

Using models in clinical practice – How to get there through retrospective and prospective evaluations

Dr Nynke Jager

Biography:
Dr. Nynke Jager is a hospital pharmacist and clinical pharmacologist at Radboud University Medical Center (Radboudumc) in Nijmegen, the Netherlands. She leads the laboratory and therapeutic drug monitoring (TDM) processes and serves as president of the hospital's Antibiotics Committee.
Her research is centered on optimizing antimicrobial therapies, with a particular focus on critically ill patients. Dr. Jager is the principal investigator of several multicenter clinical trials, including the SNAP trial on the treatment of Staphylococcus aureus bacteremia and the HIT HARD trial, which explores antibiotic dosing strategies in ICU settings.
In addition, her work encompasses bioanalytical assay development, TDM implementation and model-informed precision dosing (MIPD), aiming to personalize and improve antibiotic therapy for better patient outcomes.

Model-Informed Precision Dosing (MIPD) is increasingly recognized as a valuable tool for enhancing individualized pharmacotherapy. By combining mathematical pharmacological information on drugs and diseases (i.e. population pharmacokinetic models) with patient-specific clinical data, MIPD enables more precise dosing decisions in routine clinical practice.
Despite its potential, widespread adoption of MIPD in clinical settings remains limited. Before this approach can be routinely applied, the predictive performance of specific drug modules must be evaluated in the target patient population to ensure reliability.
This lecture will explore strategies to assess the clinical viability of MIPD, aiming to equip healthcare professionals with practical guidance for its adoption and implementation.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

318

Implementing model-based dosing to improve clinical outcomes: Results of external evaluation of vancomycin popPK models and implementation in a NZ hospital

Dr Guangda Ma

Biography:
I studied pharmacy and clinical pharmacometrics at the University of Auckland. My current research interests focus on the implementation and evaluation population models to improve clinical outcomes, clinical trial simulation, and model informed drug development.

Following model selection (1), we conducted a prospective before-after study to evaluate the effectiveness, safety, and acceptability of vancomycin management using an area under the curve (AUC)-target concentration dosingapproach, compared to historical trough therapeutic window dosing approach. AUCdosing used the web-based Bayesian dosing tool NextDose. Each cohort consisted of 200 patients from Auckland City and Starship Children's hospitals.
The primary effectiveness endpoint compared the proportion of AUCss24 between 400-600 mg/L·h in the AUC and trough guided cohorts. The secondary endpoint for effectiveness was based on reasons for vancomycin cessation. The primary safety endpoint compared the hazard of vancomycin-associated nephrotoxicity (VAN). and the secondary endpoint for safety was all-cause mortality. Acceptable AUCss24 values were more likely to be achieved in the AUC guided cohort (59% vs 39.4%, $P < 0.001$). The hazard of VAN was lower in the AUC guided cohort (HR: 0.318; 95% CI: 0.123 – 0.823; $P = 0.01$). No difference was observed in clinical effectiveness based on reasons for vancomycin cessation nor in safety based on all-cause mortality. Prescribers accepted 87% of NextDose recommendations. A dose adjustment followed 34.9% of acceptable NextDose recommendations. AUC guided vancomycin management, supported by NextDose, was associated with improved target attainment and marked reduction in VAN. This confirms the clinical benefits of a Bayesian model-based, target concentration intervention approach to dose individualisation.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

319

Predicting ciprofloxacin target non-attainment in critically ill patients with two machine-learning models

Mr Andre Wieringa[1,2], PhD Angelique Egberts[3], Mr Ravish Gangapersad[2], PhD Reinier van Hest[4], PhD Evert-Jan Wils[3], Prof Birgit Koch[2], PhD Alan Abdulla[2]
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Biography:

Andre Wieringa is hospital pharmacist and clinical pharmacologist and trainer of clinical pharmacology in a large teaching hospital in Zwolle, the Netherlands. In the Erasmus University Medical Center he is conducting research as PhD candidate in optimising anti-infective medication in critically ill patients, specialising in 1. Pharmacokinetic (PK) studies in patients undergoing continous renal replacement therapy and 2. developing PK/PD models which can identify critically ill patients at risk of target non-attainment for Beta-lactam antibiotics and ciprofloxacin on the ICU.

Background: Ciprofloxacin target attainment (TA) is not achieved in 60-80% of adult critically ill patients admitted to Intensive Care (IC; using a minimal inhibitory concentration (MIC) of 0.5mg/L (Pseudomonas aeruginosa). Antibiotic dose optimization can be achieved by therapeutic drug monitoring (TDM) and should ideally only be performed in patients at risk of target non-attainment (TNA).
Aims: Develop ciprofloxacin TNA models in critically ill patients.
Methods: Data from the DOLPHIN, EXPAT studies, and Amsterdam UMC were combined to develop and validate models to predict TNA the day after antibiotic initiation. TA was defined as a plasma concentration ƒ area-under-the-curve 0–24/MIC≥125. We randomly divided 185 patients into a training and validation set (80/20%). Covariates were obtained using the Boruta and elastic net (EN) algorithm. Models were trained using the random forest (RF) and EN. The main metrics used for performance were the area-under-the-receiver-operator-curve (AUROC), sensitivity, specificity, and calibration.
Results: The covariates age, weight, frequency, and Sequential Organ Failure Assessment score (SOFA), albumin, and creatinine were good TNA predictors. In the validation, the RF and EN models showed good calibration and an AUROC of 0.81 and 0.75, a sensitivity of 0.8 and 0.61, and a specificity of 0.70 and 0.77, respectively, without the covariates SOFA score and albumin.
Conclusions: Both ciprofloxacin TNA models showed good performance in the validation set, using 4 readily available predictors in the ICU setting. These -easy to implement- models may improve the allocation of TDM resources in the ICU.
Keywords: PK/PD, TDM, critical care, target attainment, ciprofloxacin, fluoroquinolones

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

320

Beta-lactams Therapeutic Drug Monitoring in intensive care patients: a prospective, comparative study.

Dr Wael Alkassab[2], Dr Elisabeth Jouve[1,3], Ms Eva Foinet[1], Pr Lionel Velly[4], Pr Marc Leone[2], Dr Gary Duclos[2], Dr Romain GUILHAUMOU[1,3]
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Biography:

Romain Guilhaumou (PharmD, PhD, HDR), 41 yo, is Assistant Professor of Pharmacology at Aix-Marseille University and Hospital Practitioner in biological Pharmacology (Therapeutic Drug Monitoring and Pharmacogenetics).

He is currently working in the Clinical Pharmacology & PharmacoSurveillance Department, Marseille University Hospital (APHM, Pr J. Micallef) and is member of the UMR AMU-INSERM 1106, Institut de Neuroscience des Systèmes, INS. His clinical activity is focus on the optimization of treatment of antinfective in vulnerable population (intensive care, pediatric, hematology …). His research activity is focus on personalization treatment in psychiatric disorders and on the development on a Virtual Brain Twin of schizophrenic patient (Virtual Brain Twin – for personalized treatment of psychiatric disorders).

Background: Previous studies have shown that more than a third of intensive care units (ICU) patients do not reach the target concentrations of beta-lactams, despite administration through continuous infusion.
Aims: The objective was to evaluate the impact of a systematic and protocolized Therapeutic Drug Monitoring (TDM) to optimize antibiotic treatment in ICU.
Methods: This prospective, non-randomized, bicentric, comparative interventional study was conducted on 172 ICU patients treated with continuous infusion of five beta-lactams. The pharmacokinetic/pharmacodynamics (PK/PD) target was a free concentration greater than four times the minimum inhibitory concentration of the implicated pathogen. One group of patients received systematic TDM (days 1, 4, and 7), while the control group did not. The primary objective was to evaluate the impact of TDM on PK/PD target attainment.
Results: No difference has been identified regarding the achievement of target concentrations between cohorts with and without TDM. Reaching target concentrations at D1 allows better achievement of targets concentrations at D4 and D7 (OR=8.8 [3.5; 22.3], p<0.001). Several factors were associated with PK/PD target attainment at D1: creatinine serum, age, cefepim treatment, body surface area and sex. No significant impact of TDM was observed on clinical outcomes (ICU free days, SOFA score, neurotoxicity). A toxic concentration was associated with EEG neurotoxicity (p=0.005) and the development of renal failure (p=0.002).

Conclusions: This study highlights the interest of moving towards a better dosage personalization from initiation to the whole treatment of beta-lactams antibiotics in ICU patients.
Keywords: beta-lactams, TDM, pharmacokinetics, ICU, neurotoxicity.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

321

Point-of-Care Therapeutic Drug Monitoring of Levofloxacin Using Saliva in Multidrug-resistant Tuberculosis Patients

Ms Anh Thi Nguyen[1], Dr Thu Anh Nguyen[1,3,4], Dr Van Luong Dinh[5], Associate Professor Binh Hoa Nguyen[5], Associate Professor Dinh Hoa Vu[6], Ms Ngoc Bao Tram Nguyen[4], Mr Dang Vu[4], Professor Greg J Fox[1,3], Associate Professor Sophie Stocker[1,2], Professor Jan-Willem Alffenaar[1,2]
[1]The University Of Sydney, Westmead, Australia, [2]Westmead Hospital, Westmead, Australia, [3]Woolcock Institute of Medical Research, Hanoi, Vietnam, [4]The University of Sydney Vietnam Institute, Ho Chi Minh City, Vietnam, [5]National Lung Hospital, Hanoi, Vietnam, [6]National Drug Information and Adverse Drug Reactions Monitoring Centre, Hanoi University of Pharmacy, Hanoi, Vietnam

Biography:
Ms Thi Nguyen is a PhD student in the Sydney Pharmacy School with a Vietnamese Bachelor's degree from Can Tho University of Medicine and Pharmacy, and French Master's degree in Pharmaceutical Science (Master of Mekong Pharma). Coming from a low-resource country, she values equity, transparency with respect and so, she is interested in facilitating personalised drug dosing worldwide, especially in high burden and resource-limited settings through education and research.
As an academic, she co-supervises junior students. Her research focus is on developing new point of care assays for antimicrobials to be used in the community, and subsequently developing pharmacokinetic models that describe and predict drug levels in patients to inform dosing. She has contributed to several systematic reviews of emerging microbial pathogens to inform WHO surveillance and to support treatment and research.

Background: Underexposure of levofloxacin, a key multidrug-resistant tuberculosis (MDR-TB) drug, can lead to treatment failure and acquired drug resistance. Levofloxacin therapeutic drug monitoring (TDM) optimises dosing to ensure efficacy while minimising toxicity. However, plasma-based TDM is invasive and resource-intensive, limiting its use particularly in high-burden, low-resource settings.
Aims: To assess the feasibility of saliva-based TDM for levofloxacin in MDR-TB patients.
Methods: Adults receiving levofloxacin for ≥7 days had blood and saliva samples collected at 0, 2, and 5 hours post-dose at steady state (ACTRN12620000681954). Levofloxacin concentrations were quantified using both HPLC-MS and UV-spectrophotometry. Saliva and plasma concentrations and the two analytical methods were compared via Passing-Bablok regression, Bland-Altman analysis and Pearson's correlation test.
Results: Of the 60 patients, 70% were male, with a mean age of 44 years and weight of 50 kg. Among 360 paired samples, saliva and plasma concentrations on average showed a proportional bias of 1.13, a constant bias of -0.52 and strong correlation ($r = 0.86$, $P < 0.05$), with only 3.3% of values outside the 95% limits of agreement. Saliva concentrations were, on average, 0.98 times lower than in plasma. UV-spectrophotometry showed reasonable agreement with HPLC-MS, with an average proportional bias of 1.34, a constant bias of -1.15 and moderate correlation ($r = 0.777$, $P < 0.05$).
Conclusion: Levofloxacin concentrations in plasma and saliva were strongly correlated. A simple saliva-based UV-spectrophotometry could be a semiquantitative tool for screening patients at risk of levofloxacin underexposure in resource-limited settings.
Keywords: Levofloxacin, pharmacokinetics, therapeutic drug monitoring, saliva.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

322

Levofloxacin: how choosing the right dose in osteoarticular infections ?

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Biography:
Marie-Clémence Verdier is assistant professor in Rennes University Hospital. Her work is focused on TDM with a special interest in the study of exposure-relationship of anti-infectious drugs.

Background: Levofloxacin is a cornerstone of oral antibiotic therapy for osteoarticular infections (OAI) caused by Staphylococcus spp. It presents significant pharmacokinetics variability, which may lead to underexposure or unnecessary overexposure. As a result, dosing decisions are challenging for clinicians. To optimize dosing schedule, our center has introduced systematic therapeutic drug monitoring (TDM) using AUC0-24h estimation (target 62.5 to 150 µg.h/mL).
Aims: This monocentric retrospective study describes the dose-exposure relationship in OAI patients and try to determine covariates that could help choosing the right dose.
Methods: AUCs were estimated from three samples (pre-dose, 1h, and 3h post-dose) using popPK modeling. Data from TDM (Sept 2018–Nov 2024) were used to calculate the percentage of target attainment. Thereafter, considering the dose required to reach the target, we classified the patients according to bodyweight (> or < 70kg) and eGFR, or according to sex and eGFR, to determine whether we could determine a priori the right dose for the majority of patients according to these criteria.
Results: 230 patients were included. The median age, weight, and eGFR were 68y, 78kg, and 94.5mL/min/1.73m², respectively. Sixty-five percent of patients reached the target AUC with their initial dose. Our classification according to weight or sex and eGFR helped us to select the right dose for only 35% to 70% of patients, depending on the category.
Conclusion: Estimating the dose according to two parameters remains inaccurate but could be optimised using sex and weight and eGFR. No PK-model currently considers them together in OAI.
Keywords: levofloxacin, osteoarticular infection

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

323

External evaluation of population pharmacokinetic models of vancomycin in neonates

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Biography:

Dr. Erin Chung is a Clinical Pharmacy Specialist, Therapeutic Drug Monitoring Coordinator and a Neonatal Intensive Care Unit Pharmacist at The Hospital for Sick Children (SickKids) in Toronto, Canada. Dr. Chung is also an Assistant Professor at the Leslie Dan Faculty of Pharmacy, University of Toronto and a Project Investigator at the SickKids Research Institute. Dr. Chung has a BSc in Biochemistry and Pharmacy, and completed a Hospital Pharmacy Residency at SickKids, and has a MSc and PhD in Pharmaceutical Sciences from the University of Toronto. Her main research interest is using pharmacokinetic modelling to improve precision of dosing in neonatal and paediatric populations.

Background: Vancomycin dosing in the neonatal intensive care unit (NICU) is challenging. Recently, a population pharmacokinetics (popPK) model and dosing app were developed and implemented by our research group for a Level IV (highest acuity level) NICU. However, external validation is necessary to ensure its generalizability in other NICUs.
Aims: To externally evaluate our derived popPK model and compare to 32 other popPK models with a Level III NICU cohort within the same geographic region.
Methods: This retrospective cohort study included neonates until a postmenstrual age (PMA) of 44 weeks and postnatal age of 4 weeks, who had ≥1 vancomycin concentration. The predictive model performance was compared by evaluating the differences between the predicted and observed vancomycin concentrations. The optimal popPK model was determined based on five criteria: mean error (ME)<0.5mg/L, mean absolute prediction error (MAPE)<15%, median absolute prediction error (mdAPE)<15%, root mean squared error (RMSE)<10, and percentage within 30% of observed value (p30)>45%.
Results: A total of 366 neonates (55% male, PMA: 28.9±3.81weeks, weight 1.06±0.6kg) with 661 vancomycin concentrations were included. Among 33 popPK models, only our popPK model met all five criteria (ME=0.46mg/L, MAPE=12.2%, mdAPE=4.2%, RMSE=8, p30=49.3%). Five other models (Jung 2021, Germovsek 2019, Oudin 2011, Marques-Minana 2010, DeHoog 2000) met at least three criteria. All six were one-compartment models and most incorporated weight, PMA and/or serum creatinine.
Conclusions: Our popPK model had robust predictive performance, outperforming 32 other models. This supports the broader application of this popPK-derived vancomycin dosing app in neonates.
Keywords: vancomycin, neonates, population pharmacokinetics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

324

Prophylactic Posaconazole in preventing Invasive Fungal Diseases in Leukemia and BMT patients

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Biography:

Dr Serin is working as an assistant professor in the Department of Pharmacology and Clinical Pharmacology at Christian Medical College Vellore. She completed her MBBS degree in Kerala and did post-graduation in Pharmacology at Christian Medical College Vellore. After One year, she worked as a Regional Medical Officer in an MNC. After recognising her keen interest in patients and the clinical side, joined in clinical pharmacology unit in CMC Vellore in August 2023

Background: A study in our institution showed an incidence of invasive fungal disease (IFD) of 38.7% in patients undergoing chemotherapy for AML. Despite Posaconazole prophylaxis, the incidence of IFD in AML and transplant patients in our institution is about 21.3%. Main challenges in posaconazole prophylaxis are lack of fatty meal intake due to Ill health, Intestinal mucositis and Intraday variability of levels.

Aims: To evaluate the role of posaconazole (in tablet or suspension form) in the prevention of IFD in AML patients and bone marrow transplant recipients.

To compare the proportion of patients who get IFD with posaconazole levels.

Methods: A prospective observational cohort study was done over a period of two years. 63 patients were recruited to determine the correlation between PCZ plasma concentration and its effectiveness and adverse effects. Blood samples are collected in 2 visits, and the patient is followed up till end of treatment for IFD.

Results: The overall incidence of IFD among the 63 patients was 28.6%. 90% of patients using oral PCZ suspension did not achieve the recommended concentration (above 700 ng/ml) in visit 2. A higher proportion of patients ($p < 0.01$) administered PCZ tablets achieved recommended prophylactic concentrations. Subgroup analysis showed that patients with PCZ trough of >700 ng/ml in both visits, did not develop IFD.

Conclusions: Median PCZ concentrations were significantly lower in those who developed IFD than in those who did not develop fungal infections. Routine TDM in frequent intervals for PCZ for dose optimization is needed.

Key Words: Posaconazole, IFD

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

325

Impact of augmented renal clearance on vancomycin pharmacokinetics in paediatric patients

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Biography:

Lee Jian Lynn is an experienced clinical pharmacist with almost 20 years of expertise in hospital pharmacy services. Specializing in paediatric pharmacy practices and clinical pharmacokinetics, she is dedicated to advancing patient care through her research and clinical work. She currently leads the Clinical Pharmacokinetic Unit at the Pharmacy Department at Hospital Tunku Azizah (Women and Children Hospital) in Kuala Lumpur, Malaysia. She oversees the clinical pharmacokinetic services and plays a key part in training junior pharmacists in pharmacokinetics. She also organizes and conducts various workshops and training sessions to enhance knowledge in this critical field.

Jian Lynn holds a Master of Pharmacy degree from the University of Strathclyde (2005), a Master in Clinical Pharmacy degree (2012), and a Doctor of Philosophy degree (2022) from Universiti Kebangsaan Malaysia. Through her dedication to research and professional development, she continues to contribute to the advancement of clinical pharmacy practices in Malaysia.

Background: Augmented renal clearance (ARC) enhances vancomycin elimination and potentially compromising therapeutic efficacy.
Aims: This study evaluates the impact of ARC on vancomycin pharmacokinetics (PK) and pharmacodynamics (PD) in paediatric patients and identifies factors associated with ARC.
Methods: A retrospective cohort study analyzed steady-state vancomycin levels in 201 children admitted to a tertiary paediatric hospital between January 2022 and December 2023. PK parameters were estimated using the Sawchuk-Zaske method, while the 24 hours-area under the curve (AUC24H) was calculated using the trapezoidal method. Patients were categorized into ARC and non-ARC groups for comparison.
Results: ARC was observed in 62.7% of patients at the initiation of vancomycin therapy. Children with ARC had significantly lower vancomycin PK/PD indices despite receiving similar initial doses. Compared to non-ARC patients, those with ARC had a significantly lower minimum concentration (Cmin: 6.96mg/L [IQR: 8.31] vs. 11.01mg/L [IQR: 12.90], p<0.001), lower AUC24H (270.35mg·h/L [IQR: 142.41] vs. 392.76mg·h/L [IQR: 289.12], p<0.001), and lower AUC24H/MIC (223.88mg·h/L [IQR: 358.63] vs. 334.36mg·h/L [IQR: 435.22], p=0.031). To achieve target AUC24H, patients with ARC required significantly higher vancomycin doses than those in the non-ARC group (61.20mg/kg/day [IQR: 16.00] vs. 45.00mg/kg/day [IQR: 28.80], p<0.001). ARC was associated with younger age and admission to general wards.
Conclusions: ARC is prevalent in paediatric patients and correlates with lower vancomycin exposure, thus potentially increasing the risk of treatment failure. Higher vancomycin doses are required to achieve optimal PK/PD targets in patients with ARC.
Keywords: vancomycin, pharmacokinetics, pharmacodynamics, augmented renal clearance, paediatrics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

326

Lipopolysaccharide-linked endotoxemia correlates with cyclosporine A exposure in transplant patients

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Biography:

Roland Lawson, PharmD, PhD, is an Associate Professor of Pharmacology at the University of Limoges and a researcher at the INSERM-U1248 unit, led by Professor Pierre Marquet. His research focuses on precision medicine in transplantation, particularly on the interplay between the microbiota, host, and immunosuppressant drugs, aiming to understand their impact on the variability of transplant outcomes.

After completing his pharmaceutical studies and earning a Master's in pharmacology in 2010, Dr. Lawson received a grant to pursue a PhD at the University of Strasbourg, where he explored the serotonergic system's role in cardiovascular remodeling, solidifying his expertise in both preclinical and clinical pharmacology. His postdoctoral work at the Universities of Franche-Comté and Paris further expanded his knowledge in biochemistry and cellular biology.

Since joining INSERM U1248 in 2016, Dr. Lawson has focused on immunosuppressant drug interactions, especially the gastrointestinal effects of mycophenolate, contributing significantly to the emerging field of pharmacomicrobiomics.

Background: Endotoxemia, characterized by elevated plasma lipopolysaccharide (LPS), is associated with gut microbiota dysbiosis and increased intestinal permeability. In transplant patients, immunosuppressive drugs may contribute to or exacerbate endotoxemia. LPS can modulate hepatic metabolic enzymes and drug transporters, potentially altering the pharmacokinetics of immunosuppressants.
Aims: Understanding these interactions is crucial for optimizing therapy and improving transplant outcomes.
Methods: We analyzed plasma samples from 48 transplant recipients at one-year post-transplantation, sourced from the CRBIOLIM biobank (Limoges University Hospital) through the PIGREC (heart), STIMMUGREP (lung), and BIOMARGIN (kidney) studies in organ transplant recipients. In addition, samples from 24 healthy volunteers were obtained with informed consent through the Clinical Investigation Center (Limoges University Hospital). Patients included were on a standard immunosuppressive regimen with mycophenolate mofetil (MMF), known to disrupt gut microbiota and promote endotoxemia. Plasma LPS levels were quantified using ELISA and compared between groups (Mann-Whitney test). Patient area under the concentration-time curve (AUC) of MMF, tacrolimus, and cyclosporine was extracted from databases, and correlations with LPS levels were assessed using Spearman’s rank correlation coefficient.
Results: Transplant recipients had significantly higher plasma LPS concentrations than healthy volunteers (99 ± 22 pg/mL vs. 257 ± 32 pg/mL; mean ± SEM; $p < 0.01$), confirming endotoxemia.

Among immunosuppressants, only cyclosporine AUC correlated with LPS levels (Spearman's ρ=0.818, p=0.002).

Conclusion: The strong correlation between cyclosporine exposure and LPS plasma levels suggests that endotoxemia may influence cyclosporine metabolism by modulating hepatic enzymes and transporters. Further research is needed to elucidate the mechanisms.

Keywords: endotoxemia, lipopolysaccharide, cyclosporine A

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

327

Exploring Gut Microbiota as Novel Biomarkers for Azathioprine Therapeutic Drug Monitoring

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Biography:

Shuai Song is an Assistant Professor in the department of Pharmacy at the First Affiliated Hospital of Anhui Medical University. Holding a Ph.D. in Medicine, Shuai Song specializes in herbal medicine pharmacology and therapeutic drug monitoring. Since 2018, he has led projects funded by the National Natural Science Foundation of China and Anhui Provincial University, authoring over 10 peer-reviewed papers.

Beyond academic research, Shuai Song is an active member of the Chinese Pharmaceutical Association (CPA), where he participates in national conferences and collaborates with peers to advance pharmaceutical knowledge.

Background: The metabolism of azathioprine, an immunosuppressive drug used in inflammatory bowel disease treatment, is significantly influenced by the gut microbiota. This study aims to identify novel gut microbiota biomarkers for the therapeutic drug monitoring of azathioprine.
Methods: The research combines animal experiments and clinical studies. Germ-free rats were employed to establish a model evaluating the impact of gut microbiota on azathioprine pharmacokinetics. Simultaneously, stable Crohn's disease patients receiving azathioprine for over three months were enrolled to explore the correlations between gut microbiota structure and active metabolite levels (6-thioguanosine nucleotides, 6-TGN). Both 16S RNA sequencing and metagenomic sequencing were utilized to identify potential gut microbiota biomarkers for azathioprine's therapeutic drug monitoring.
Results: Variations in gut microbiota composition correlated with differences in 6-TGN levels. Prevotella emerged as indicative bacteria influencing both exposure (AUC, 3148.8±515.4 hour·ng·mL-1 in control group vs. 2078.0±290.5 hour·ng·mL-1 in germ-free group) and steady-state concentrations of 6-TGN (6-TGN_L: 151.7±29.7, 6-TGN_M: 290.7±58.2, 6-TGN_H: 529.7±130.4; unit: pmol/8×108RBC). Metagenomic analysis revealed significant enrichments of key metabolic enzymes (guanine-methylation-sensitive endonuclease, hypoxanthine phosphoribosyltransferase, and inosine monophosphate dehydrogenase) in the genera Clostridium and Roseburia, potentially contributing to 6-TGN level variations. Known butyrate-producers, including Clostridium and Roseburia, demonstrated a positive correlation with 6-TGN levels (correlation coefficient: 0.483, $P < 0.05$), suggesting azathioprine alleviates intestinal inflammation through an intrinsic mechanism involving these genera.
Conclusion: Prevotella, Roseburia, and Clostridium constitute novel biomarkers for azathioprine therapeutic drug monitoring, potentially offering implications for personalized treatment strategies.
Keywords: Azathioprine, Gut microbiota, Biomarker, 6-TGN

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

328

Capillary Dried Blood Spot Sampling for Tacrolimus and Creatinine Monitoring at Home

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Biography:
Hanna De Baets studied Pharmaceutical Sciences at Ghent University. She obtained her degree as Master in Drug Development in June 2022 and started her PhD at the Laboratory of Toxicology of Professor Stove at the Faculty of Pharmaceutical Sciences at Ghent University in september that year. The focus of her PhD is the development of dried blood microsampling-assisted LC-MS/MS methods for steroid testing. Currently, she is also working on a study evaluating the applicability of dried blood microsampling for therapeutic drug monitoring of patients taking immunosuppressant drug therapy.

Background: Tacrolimus, essential for allogeneic stem cell transplant patients, requires therapeutic drug monitoring (TDM) due to high variability and a narrow therapeutic window. Finger-prick dried blood spots (DBS) could replace venous blood draws, enabling home monitoring and improving patients' quality of life.
Aims: This study aimed at evaluating the clinical applicability of capillary finger-prick sampling for tacrolimus TDM and creatinine determination in the hospital (part 1), and in a homesampling context (part 2), using DBS and Capitainer® qDBS devices.
Methods: Patients collected qDBS samples at home at trough levels over three days. LC-MS/MS analysis methods were used. Analytical and intra-patient variation based on home-sampled duplicates were evaluated as well as therapy adherence. For each homesampling participant, tacrolimus levels were compared to their individual target ranges. Patients' experience was assessed via questionnaires.
Results: Assisted sampling confirmed the clinical applicability of capillary (q)DBS for tacrolimus TDM and creatinine determination, with qDBS showing better clinical agreement (98% of tacrolimus and 93% of creatinine results within 20% of reference values). Homesampling using qDBS is feasible, with the CV below 8%. In stable-dose patients, within-subject variation for tacrolimus ranged from 4.1% to 24.7%, suggesting strong adherence. Homesampling improved tacrolimus trough level resolution and enabled closer monitoring after dose changes, with positive patient feedback.
Conclusions: Capillary qDBS show great potential as a complement to venous blood draws for tacrolimus TDM and creatinine determination. Homesampling is promising for this patient population, addressing the need for individualized TDM.
Key Words: Therapeutic Drug Monitoring, Tacrolimus, Creatinine, Dried Blood Microsampling

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

329

Extracellular Vesicles as a Liquid Biopsy to Characterize Variability in Medicine Exposure

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Biography:
Andrew is a Professor of Clinical Pharmacology at Flinders University. He leads a dynamic team of scientists at the forefront of advancing extracellular vesicle isolation and analysis platforms for use with biospecimens. Andrew's team is world leading in the isolation and characterization of tissue specific EVs from blood and works closely with industry and clinicians to apply this technology to improve patient outcomes by enhancing medicine efficacy and minimize harms.

Introduction: Cytochromes P450 (CYP) regulate exposure to medicines and hence medicine efficacy and safety. Understanding variability in CYP abundance and activity caused by physiological and pathological factors is useful for safe and effective dosing of medicines. Liver-derived extracellular vesicles (EVs) offer a novel strategy to characterise CYP abundance and predict variability in exposure to medicines.
Aim: Investigate liver EVs as a strategy to account for variability in CYP enzyme activity associated with physiological and pathological conditions.
Methods: The abundance of 8 CYP enzymes in liver EVs and tissue homogenates prepared from eleven human livers were quantified by LCMS. Linear regression assessed EV-tissue protein correlations. CYP3A4 abundance was quantified in liver-derived EVs isolated from plasma of pregnant (n=9) and non-pregnant (n=3) females, patients with metabolic associated fatty liver disease (MAFLD; n=14) and controls (n=14).
Results: Strong correlations were observed in paired liver EVs and homogenates for all CYP ($r = 0.654$ to 0.962) supporting EVs as a robust surrogate of hepatic enzyme expression. CYP3A4 expression in liver EVs was significantly elevated in third-trimester pregnancy (3.2-fold, $P = 0.003$) compared to non-pregnant controls. CYP3A4 abundance was 30 to 70% lower in MAFLD patients, consistent with reported reduced metabolism in liver disease. The reduction in CYP3A4 abundance in MAFLD patients was associated with the severity of disease.
Conclusion: These data support liver EVs as a non-invasive liquid biopsy to characterize variability in medicine exposure cased by physiological and pathological changes. EV protein abundance may complement genotype to enable a comprehensive ADME genomic profile.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

330

Pharmacodynamic biomarker evaluation in renal transplant recipients with/without anti-thymocyte globulin induction

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Biography:

I am Ritika Panwar. final-year PhD researcher specializing in renal transplantation, with a focus on the pharmacokinetics and pharmacodynamics of immunosuppressive therapy. My research explores the impact of tacrolimus on gene expression, LC-MS/MS and genotyping techniques to optimize treatment strategies. Passionate about precision medicine and aim to improve personalized immunosuppression protocols for transplant recipients. My work contributes to understanding drug metabolism and individual variability in response to therapy, enhancing long-term transplant outcomes.

Introduction: Tacrolimus (Tac) is a key immunosuppressant in renal transplantation, often combined with anti-thymocyte globulin (ATG) for induction therapy. However, ATG may be obviated in low-risk patients. Tac inhibits nuclear factor of activated T cells (NFAT), reducing gene expression (IL-2, TNF-α, GM-CSF, IFN-γ). Study examines the in-vitro and in-vivo pharmacodynamic (PD) effects of Tac using NFAT residual gene expression (NFAT-RGE) in renal-transplant recipients with/without ATG.
Methods: Sixty patients (≥18 years), planned for de-novo renal-transplant. Blood samples were collected pre-transplant (10ml) and on post-transplantation day 7 (POD 7) (2ml at Tac-C0 and C1.5). Samples were spiked with varying concentrations of Tac (0, 2.5, 5, 10, or 20 ng/ml) and ex-vivo immune activation was done with RPMI 1640 medium, phorbol myristate acetate (PMA), and ionomycin. Total RNA was extracted, cDNA was synthesized. Real-time PCR was performed for gene expression quantification. Fold change was calculated using ΔCt and ΔΔCt. Tac concentration was estimated in whole blood samples using LC-MS/MS system with TAC-13C-d2 as the internal standard.
Results: Recipients (n=60) had an average NFAT-RGE of 53.7±21.8% (2.5ng/ml), 36.6±18.7% (5ng/ml), 24.8±16.2% 10ng/ml) and 13.5±11.6% (20ng/ml) in-vitro. In comparison, the POD7 NFAT-RGE was 46.9±22.3% at C0 (11.15±2.7ng/ml) and 19.5±13.1% at C1.5 (16.6±4.3ng/ml). The NFAT-RGE in ATG-induced patients (n=34) at POD7 was 25.13±30.83% compared to 37.68±34.36% in the non-ATG (n=26) at C0. The corresponding values were 11.92±13.11% and 14.29±15.76% for C1.5.
Conclusions: NFAT-RGE could be used as potential biomarker in individualizing immunosuppression in non-ATG triple drug-induced patients.
Keywords: Renal transplantation, Pharmacodynamic biomarkers, tacrolimus, residual gene expression, NFAT

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

331

Feasibility of Salivary Mycophenolic Acid for Therapeutic Monitoring in Renal Transplant Patients

Ms Bahaar Manro[1], Dr Ashwin Kumar[3], Mr Sunil Sharma[4], Dr Varun Dhir[5], Prof Ashish Sharma[6], Dr Deepesh Kanwar[7], Dr Sarbpreet Singh[8], Dr Shivakumar Patil[9], Ms Sheetal Singh, Prof Smita Pattanaik[10]
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Biography:

I am Sheetal Singh, final year phd scholar, working in the area of renal cell carcinoma along with renal transplantation.

Background: Mycophenolic Acid (MPA), an ester prodrug of Mycophenolate Mofetil i.e. is an immunosuppressive agent, used with tacrolimus to prevent organ rejection in transplant patients. Traditionally, Therapeutic Drug Monitoring (TDM) relies on plasma measurements, but alternative matrices like saliva offers a non-invasive approach for assessing drug exposure. This study investigates the feasibility of estimating MPA from saliva and explores its potential as a surrogate for plasma measurements in renal transplant recipients.

Aims: The study aims to evaluate the feasibility of measuring MPA in saliva, assessing salivary and plasma MPA exposure through area under curve (AUC) and finding their concentration correlation for further clinical outcomes.

Methods: Saliva and plasma samples were collected from 10 adult renal transplant patients with stable allograft ≥4 weeks. Salivary MPA (sMPA) was quantified using High Performance Liquid Chromatography-Fluorescence Detector (HPLC-FLD) and plasma MPA by established HPLC-UV method. The correlation between salivary and plasma MPA concentrations and mean AUC0-12h was calculated.

Results: The mean plasma MPA AUC0-12h was 88.21 ± 35.03 µg*h/mL, while the mean sMPA AUC0-12h was 195.82 ± 126.81 ng*h/mL. In our study, the correlation between plasma and sMPA concentrations was 0.903±0.133,concluding sMPA concentrations may reflects its plasma concentrations.

Conclusions: Out of the 10 patients, 7 exhibited a strong correlation between plasma and sMPA concentrations (>0.900). These findings suggest that saliva may serve as a potential alternative matrix for TDM of MPA, which could aid in non-invasive assessment and optimization for further clinical outcomes.

Keywords: Mycophenolate, Saliva, Therapeutic Drug Monitoring, Area under the Curve, HPLC-FLD

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

332

Blood and plasma tacrolimus concentrations and gestational outcomes in pregnant patients.

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Biography:

Dr Sallustio is Principal Medical Scientist in the Department of Clinical Pharmacology at The Queen Elizabeth Hospital, where she leads the Therapeutic Drug Monitoring Laboratory. She is Affiliate Professor in the Discipline of Pharmacology at the University of Adelaide, and a Fellow of the Faculty of Science of the Royal College of Pathologists of Australia (RCPA). Her research interests include drug metabolism and transport, particularly understanding how inter-individual differences in these processes impact on drug toxicity and clinical efficacy. Her current research focusses on therapeutic drug monitoring in oncology and solid organ transplantation. Dr Sallustio currently serves as Convenor of the Adelaide Pharmacology Group, and on the executives of the Special Drugs Working Party of the RCPA, and on the Toxicology Special Interest Group of ASCEPT.

Background: Tacrolimus is one of few immunosuppressants used in pregnancy. Therapeutic drug monitoring often prompts dose increases due to decreasing trough blood concentrations (BC0) throughout pregnancy. Given high erythrocyte-binding, decreasing BC0 may reflect changes in haematocrit, rather than clearance.
Aims: To investigate relationships between BC0, trough plasma concentrations (PC0) and pregnancy outcomes.
Methods: BC0 and PC0 were measured by LC-MS/MS. Biochemistry and outcomes were obtained from clinical records. Relationships between BC0 and PC0 were investigated by linear mixed effect models adjusting for repeated measures and confounders. Effects of BC0 and PC0 on neonatal birth weight, gestational age and maternal plasma creatinine were investigated by linear regression or mixed effects models.
Results: In 9 participants (6 kidney transplant, 3 lupus nephritis) median BC0 and PC0 were 5.4ng/mL (1.6-23.1ng/mL, n=97) and 0.88ng/mL (0.28-4.27ng/mL, n=88). BC0 and PC0 were moderately correlated (R^2=0.51; P<0.0001). The PC0/BC0 ratio increased during pregnancy (P<0.01) and with higher albumin (P<0.05). Maternal creatinine increased during third trimester (P<0.001) and with higher dose (P<0.05). 6/8 neonates were <37 weeks gestation, 5/6 weighed <2.5kg. Weight was inversely associated with BC0 (P<0.0001, Padj<0.0004). For every 100ng/L increase in BC0, weight decreased by 60g (95%CI: -90, -30).
Conclusions: BC0 were highly variable in pregnancy and often subtherapeutic. However, routinely increasing dose may be unwarranted given the only moderate relationship between BC0 and PC0, and our preliminary observation of a relationship between high dose, BC0 and poor outcomes (decreased maternal renal function and neonatal weight), which warrants further investigation.
Key words: tacrolimus, pregnancy, immunosuppression

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

333

An End-to-end Bioinformatics Solution to Support Next Generation Sequencing Based Pharmacogenetic Testing

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Biography:

Dr. David Yu Yuan has been working at European Bioinformatics Institute, European Molecular Biology Laboratory (EMBL-EBI) for over 6 years. He has played the roles of Data Coordination Centre and Cloud Computing Manager, Genomics Software Development Project Lead, and Cloud Bioinformatics Application Architect. David has a PhD degree in Molecular Biology and a BSc degree in Software Engineering. David deployed an efficient Machine Learning platform based on Kubeflow at EBI. He also applied Kubeflow for cardiomyocyte image classification and for non-Machine Learning pipeline for genomic variant calling. During the pandemic, he led the development and operation of the systematic analysis of six million SARS-CoV-2 genomes and published the analysis results on the COVID-19 Data Portal. He is now leading the development and operation of the European Nucleotide Archive. His research interest is the application of genomics tools in Pharmacogenetic testing, and discovering novel algorithms of genomic analysis with quantum computing.

Background: The pharmacogenetic testing based on next generation sequencing (NGS) allows better coverage of pharmacogenetic (PGx) alleles present in diverse populations and provides opportunities to reanalyze the data when new PGx relevant genes/variants are discovered.
Aims: To create an end-to-end bioinformatics solution to support NGS data analysis and clinical decisions aligned with Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines.
Methods: The CPIC database was integrated with Pgxtools, our pharmacogenetic data analysis and reporting pipeline developed in-house via the Representational State Transfer Abstract Programming Interface (RESTful APIs). It expanded the coverage to 131 genes and 322 drugs with comprehensive variant annotations. The accuracy of variant calls, PGx diplotyping, and clinical interpretation was verified by both long and short read datasets.
Results: A graphical user interface (GUI) was designed for simplicity, secure user management, and access control over input data and output reports. Users can choose three categories for analysis and reporting: “Actionable” (25 genes well characterized by CPIC guidelines), “Twist PGx” (50 genes included in Twist PGx panel) and “All CPIC” (131 genes in CPIC database). The pipeline can accommodate both BAM and VCF data files. Preliminary results of variant calls and genotypes on 15

genes from 12 reference genomes showed very high concordance between PacBio HiFi long read sequencing datasets, corresponding Whole Genome Sequences (WGS) on GRCh38 in the 1000 Genomes Project (G1K), and previously reported PGx star allele assignment.
Conclusions: This bioinformatics pipeline, Pgxtools, provides a comprehensive computational solution to support NGS data analysis and PGx clinical decisions.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

334

Clinical integration of pre-emptive DPYD genotype testing services in a tertiary hospital

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Biography:
Deirdre Landsberg is a clinical pharmacist with an interest in the translation of pharmacogenomics to clinical practice. Deirdre is currently undertaking her PhD examining the clinical application of DPYD genotype screening to guide dosing of fluoropyrimidines in cancer patients. Deridre is also currently employed as a pharmacogenomics pharmacist at the Women's and Children's Hospital (Adelaide, Australia) working under the MARVEL-PIC study, which aims to use pre-emptive pharmacogenomic testing to guide the prescribing of supportive care medicines in paediatric oncology patients.

Background: DPYD genotype screening for targeted variants prior to fluoropyrimidine treatment represents a critical advancement in personalised chemotherapy. Despite availability of pre-emptive genetic testing to identify individuals with dihydropyrimidine dehydrogenase enzyme deficiency, clinical implementation remains limited within Australia.
Aims: To evaluate integration of a pre-emptive DPYD genotyping service in real-world clinical practice, including utility of DPYD genotype-based fluoropyrimidine dosing strategies and impact on short-term patient clinical outcomes.
Methods: Targeted DPYD genotype testing was implemented in a tertiary hospital, from which service and short-term patient outcomes were examined. Data collected included administered fluoropyrimidine doses, toxicity, patient and disease characteristics. Toxicity was assessed using the Common Terminology Criteria for Adverse Events. Clinical dosing of fluoropyrimidines was evaluated against recommendations from the CPIC guideline.
Results: Between 1 June 2022 and 31 December 2023, a total of 225 patients were screened, of whom 20 (8.89%) patients were DPYD variant carriers. Of the 20 patients, 19 were heterozygous carriers and received fluoropyrimidine chemotherapy; one patient was a homozygous c.1236G>A/HapB3 carrier and received alternate treatment. Initial (Cycle 1) dose reductions were reported in 17/19 variant carriers; however, significant variation in dose intensities was observed. Most variant carriers did not report grade ≥3 toxicity and completed their planned treatment.
Conclusions: The clinical integration of DPYD genotype-based dosing to personalise fluoropyrimidine chemotherapy was successful. However, given the heterogeneity in dosing requirements, additional strategies such as expanded DPYD testing and/or quantification of fluoropyrimidine exposure may be required to comprehensively inform personalised dosing for fluoropyrimidines.
Keywords: pharmacogenomics, DPYD genotyping, fluoropyrimidine

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

335

Unravelling Pharmacogenetic Risks in Cardiovascular Drug Safety: Four-Years Study Insights

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Biography:
Livija Šimičević is a medical biochemist and researcher specializing in pharmacogenomics. She graduated in 1998 from the Faculty of Pharmacy and Biochemistry, University of Zagreb, and later pursued a career in both academia and the pharmaceutical industry. She has held key roles in clinical research, marketing, and drug development at international pharmaceutical companies, including Pliva, Novo Nordisk, and Sanofi-Aventis.
After returning to the healthcare sector, she completed a specialization in medical biochemistry and laboratory medicine and earned a PhD in biomedicine and health sciences. She is currently a Senior Assistant at the University of Zagreb School of Medicine and a researcher at the Department of Laboratory Diagnostics, UHC Zagreb, focusing on pharmacogenomics, adverse drug reactions, and personalized medicine. She has co-authored numerous scientific papers, participated in international projects, and serves as an editor and reviewer for renowned scientific journals.

Background: The PGx-CardioDrug study investigates the impact of drug-drug-gene interactions on cardiovascular drug adverse reactions (ADRs).
Aim: To assess the influence of pharmacogenomics and drug-drug interactions (DDIs) on ADR risk in patients prescribed direct oral anticoagulants (DOACs), platelet aggregation inhibitors (PAIs), and statins over a four-years period.
Methods: Patients newly prescribed DOACs, PAIs, or statins were enrolled. Cases experienced ADRs (haemorrhage, myotoxicity, hepatotoxicity, or other severe reactions) within three months; controls had no ADRs. Relevant ADME gene variants (CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, CYP2J2, CES1, ABCB1, ABCG2, SLCO1B1) were genotyped. DDIs were assessed using Lexicomp®.
Results: Among 1,586 analysed patients (980 statin, 710 DOAC, 296 PAI users), 312 ADRs were recorded: myotoxicity (n=159, 16%), hepatotoxicity (n=57, 6%), bleeding (n=126, 13%). High-risk DDIs were identified in 380/980 statins, 580/710 DOACs, and 205/296 PAIs users. Patients were genotyped for relevant ADME genes: CYP2C9 (38%), CYP2C19 (52%), CYP3A4 (76%), CYP3A5 (68%), CYP2D6 (8%), CYP2J2 (36%), CES1 (6%), ABCB1 (45%), ABCG2 (67%), and SLCO1B1 (47%). So far, the study has resulted in five publications on pharmacogenomics in cardiovascular therapy and has contributed to three master's and two PhD theses.
Conclusion: Interim findings suggest that drug-drug-gene interactions play a significant role in ADRs risk, highlighting the potential of pharmacogenomics for therapy individualization. However, further research is essential to refine predictive models and enhance clinical implementation.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

336

Pharmacogenetics of brivaracetam: CYP2C9 and CYP2C19 variants impact on TDM real-life data

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Biography:

Asst. Prof. Lana Ganoci, MMedBiochem, graduated from the Faculty of Pharmacy and Biochemistry University of Zagreb with a degree in Medical Biochemistry, specializing in Analytical Toxicology. Holds a Ph.D. in pharmacogenomics from the University of Zagreb School of Medicine. Currently heads the Division of Pharmacogenomics and Individualization of Therapy at the University Hospital Center Zagreb's Department of Laboratory Diagnostics. She is an Assistant Professor at the University of Rijeka and a postdoctoral researcher at the University of Zagreb School of Medicine. Teaches graduate and postgraduate courses across multiple institutions in Croatia and has supervised several theses She has published over 40 scientific papers cited in reputable databases and collaborates on various domestic and international research projects. Her research interests include pharmacogenomics, personalized medicine, metabolomics, drug interactions, toxicology, and high-throughput methods in molecular biology and toxicology.

Background: Brivaracetam is an antiepileptic drug metabolized primarily through hydrolysis, with minor pathways involving CYP2C19 and CYP2C9, and their genetic variability may influence brivaracetam pharmacokinetic.
Aims: To investigate the association between CYP2C9 and CYP2C19 genotypes/phenotypes and brivaracetam serum concentrations in a real-life clinical setting.
Methods: This retrospective study analysed data from epilepsy patients treated with brivaracetam. Patients were genotyped for CYP2C9*2, CYP2C9*3, CYP2C19*2, CYP2C19*17 using TaqMan Real-Time PCR, their serum steady-state trough brivaracetam concentrations were measured by HPLC-DAD, all methods validated in clinical laboratory. Brivaracetam concentrations, dose-adjusted concentration (D/C) ratios, clinical data, drug interactions, and genotype/phenotype data were analysed in univariate statistical analysis.
Results: We analysed data from 50 patients (29 males, 21 females) aged 6-76 years (mean=31), receiving brivaracetam doses 50-200 mg/day, brivaracetam concentrations ranged 0-21.6 µmol/L. CYP2C19 poor metabolizers (*2/*2, n=2) exhibited 55% higher D/C ratios compared to normal metabolizers (*1/*1, n=20; p=0.02), while intermediate metabolizers (*1/*2/*17, n=11) showed 20%

higher exposure (p=0.04), ultra-rapid metabolizers (*17/*17, n=3) had subtherapeutic concentrations (median: 2.8 µmol/L at 200 mg; p=0.03).
CYP2C9 heterozygous carriers (*1/*2, *1/*3, n=18) demonstrated 22% higher D/C ratios compared to wild-type (*1/*1, n=32; p=0.12), reaching significance in patients on CYP2C9 inhibitors (valproate) (Δ=38%, p=0.01). Enzyme inducers (carbamazepine, phenobarbital) reduced brivaracetam concentrations by 40–60% in normal metabolizers (p<0.01).
Conclusions: This small real-life study showed that genetic variations in CYP2C19, and less in CYP2C9, influence brivaracetam concentrations, and their interaction with inducers/inhibitors necessitates vigilance. These findings warrant further investigation in larger cohorts.
Keywords: brivaracetam, pharmacogenetics, CYP2C9, CYP2C19, therapeutic drug monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

337

MiRNA expressions and DPYD polymorphisms in colorectal cancer patients treated with 5-fluorouracil

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Biography:

Asst. Prof. Dr. Phatchariya Phannasil is an Assistant Professor at the Institute of Molecular Biosciences, Mahidol University, Thailand. She earned her Ph.D. in Biochemistry from Mahidol University in 2015. Her research focuses on metabolic reprogramming in diseases, with a particular emphasis on cancer and thalassemia. Dr. Phannasil has made significant contributions to understanding the role of pyruvate carboxylase in breast cancer, showing that its suppression inhibits cancer cell growth and metastasis. Additionally, her current research involves developing novel therapeutic strategies for thalassemia using metabolomics and single-cell RNA sequencing. She is also exploring microRNA regulation in cancer metastasis and the toxicity of chemotherapeutic drugs. Dr. Phannasil has received numerous awards, including the Outstanding Oral Presentation Award at the RGJ-Ph.D. Congress XV and Outstanding Employee of Institute of Molecular Biosciences, Mahidol University. Her work aims to discover new drugs and biomarkers to improve patient outcomes in cancer and blood disorders.

Background: miRNAs are small non-coding RNAs that regulate gene expression and are implicated in drug resistance and toxicity in cancers such as colorectal cancer (CRC). miR-145, miR-106a, and miR-17-3p show significant differential expression between pre- and post-operative stage II/III CRC patients. High levels of miR-17-3p and miR-106a correlate with shorter disease-free survival, suggesting their potential as biomarkers for prognosis and recurrence. Additionally, miR-27a and miR-27b may regulate dihydropyrimidine dehydrogenase (DPD), an enzyme involved in 5-fluorouracil (5-FU) metabolism, with miR-27a rs895819 potentially predicting fluoropyrimidine toxicity.
Aims: This study aimed to evaluate miRNA expression profiles in colorectal cancer patients carrying DPYD variants (DPYD 85T>C and DPYD 1896T>C) who are treated with 5-FU.
Methods: EDTA blood samples were collected from 16 CRC patients for DNA extraction. TaqMan® RT-PCR detected three DPYD gene SNPs: 85T>C, 1627 A>G, and 1896T>C. For miRNA extraction, 100 µL of plasma was used, and cDNA was synthesized from 200 ng RNA. miRNA profiles associated with the 5-FU pathway were analyzed using a customized miRNA array, real-time PCR, and QIAGEN's GeneGlobe portal.
Results: Differential miRNA expression was observed between DPYD 85T>C variants and wild-type patients, with 9 up-regulated and 11 down-regulated miRNAs. A similar expression pattern was noted in DPYD 1896T>C variants, with 5 up-regulated and 9 down-regulated miRNAs.
Conclusions: The findings suggest that miRNAs could serve as biomarkers for predicting 5-FU toxicity, facilitating personalized treatment strategies for CRC patients.
Keywords: miRNA, DPYD polymorphisms, 5-FU, colorectal cancer, toxicity.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

338

Pharmacogenetics for mavacamten treatment individualization in patients with obstructive hypertrophic cardiomyopathy

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Biography:
Sylvie QUARANTA (PharmD, PhD), 48 yo, is Hospital Practitioner in Molecular Biology and Biological Pharmacology (Pharmacogenetics and Therapeutic Drug Monitoring). She is currently working in the Molecular Biology laboratory / Pharmacokinetics laboratories, Marseille University Hospital (APHM, Pr A. Barlier / Pr C. Solas) and is vice-president of the French National Network of Pharmacogenetics. Her activity is focus on personalization treatment in different fields, as cardiology, neurology, neuropsychiatry, immunology, by combining pharmacogenetics with therapeutic drug monitoring and clinical outcome.

Background: Mavacamten is currently used as early access drug in obstructive hypertrophic cardiomyopathy and its exposure is affected by CYP2C19 polymorphisms. Genotyping of CYP2C19 is then recommended before treatment initiation.
Aims: The objective of this study was to describe CYP2C19 genetic polymorphisms and evaluate their impact on clinical outcomes.
Methods: A retrospective study was performed during 2024 in the Cardiology Unit of Timone hospital (Marseille, France). CYP2C19*2, *3 and *17 alleles were determined using LAMP assays. Patients were categorized as poor, intermediate (IM), extensive (EM), rapid (RM) or ultra-rapid (UM) metabolizers. Impact of CYP2C19 metabolic profiles on clinical outcomes at the end of the titration period were studied (Kruskal-Wallis/Dunn tests).
Results: Allelic frequencies of 40% and 14% were described for CYP2C19*17 and CYP2C19*2, respectively (n=101 patients). Titration period was achieved in 56 patients (33/23 females/males), with a median age of 66 years (20-88). We identified 14(25%) IM, 13(23%) RM, 1(2%) UM and 28(50%) EM patients (initial dose of 5mg/d). Titration period delay, dose at the end of titration and Left Ventricular Ejection Fraction were not different between metabolic profiles. Good response to therapy (residual Left Ventricular Outflow Tract gradient < 30mmHg) was achieved in 52 of 56 patients. A significant difference of residual LVOT obstruction after titration was observed between RM and IM (residual gradient= 19.2 vs 11.6mmHg; p=0.029).
Conclusion: Although regression of LV obstruction was achieved in most patients, our results suggest that CYP2C19 genotyping profile may impact the degree of response to mavacamten.
Keywords: pharmacogenetics, CYP2C19, mavacamten, HOCM

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

339

Association of TLR4 rs11536889 Polymorphism with Increased Risk of Tuberculosis in Thai

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Biography:

Prin Chaiyakit is a medical student at the Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand. He serves as Vice President of the Faculty's Medical Student Union (2024–2025) and has held leadership roles in The International Federation of Medical Students' Associations-Thailand, previously held key roles in IFMSA-Thailand, including Deputy and Vice President for Internal Affairs (2022–2024). He has overseen numerous projects and collaborated with the Thai Health Promotion Foundation to advance student-led initiatives. He has also served as a rapporteur at major forums, including the International Universal Health Coverage Day 2023 and the Prince Mahidol Awards 2024. A passionate communicator and policy advocate, he was a finalist in the British Council's FameLab Thailand 2022 and IFMSA-Thailand's Thai Youth Policy Initiative. His research focuses on the link between diet and mental health; he presented a meta-analysis on dietary lifestyles and depression at the International Medical Student Research Conference 2024.

Background: The TLR4 rs11536889 polymorphism may influence tuberculosis (TB) susceptibility. This study evaluates the association between TLR4 rs11536889 and TB risk in Thai patients to clarify genetic contributions to TB susceptibility.
Aims: To assess the genotypic distribution of the TLR4 rs11536889 polymorphism and its influence on TB susceptibility in a healthy Thai population.
Methods: This case-control study included 38 Thai TB patients and 51 healthy controls. Following ethical approval and informed consent, 3 mL of whole blood was collected in EDTA tubes, and genomic DNA was extracted using the PureLink™ Genomic DNA Mini Kit. Genotyping was performed using TaqMan® SNP assays on the QuantStudio™ 3 Real-Time PCR System. Logistic regression analysis compared genotypic frequencies between groups, adjusting for age, sex, and BMI ($p < 0.05$).
Results: In the TB group, genotype frequencies were 37% Homozygous G/G, 53% Heterozygous C/G, and 10% Homozygous C/C, while the control group showed 39% G/G, 43% C/G, and 18% C/C. Allele frequencies were 63% G and 37% C in the TB group, compared to 61% G and 39% C in the control

group. There were no significant differences in the C/C genotype compared to the wild-type G/G ($p = 0.548$), suggesting no association between the TLR4 rs11536889 polymorphism and TB susceptibility. **Conclusions:** The TLR4 rs11536889 polymorphism may not significantly influence TB susceptibility in the Thai population. Further research with larger sample size is needed to validate these findings and draw more definitive conclusions.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

340

Xylazine Positivity Trends in Drug Screens at a Large Academic Medical Center

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Biography:

Dr. Carmen Gherasim is Associate Professor of Pathology at Michigan Medicine, University of Michigan, Ann Arbor where she serves as the Section Director of Clinical Core Laboratories which includes oversight of Chemistry, Toxicology and ED Laboratories. Dr. Gherasim interests are in translation of biomarkers into clinical diagnostic tests, clinical assay development for toxicology and therapeutic drug monitoring, and personalized medicine.

Background: Xylazine, also called “tranq”, is a veterinary sedative increasingly present in illicit fentanyl supplies across the U.S. Unlike opioids, its effects are not reversed by naloxone leading to increased overdose risks. Chronic xylazine use has been associated with necrotic wounds raising public health and regulatory concerns. In this study, we have investigated the trends in xylazine positivity from the first reported identification in our clinical laboratory in 2020, and its co-occurrence with other drugs in urine drug screens performed at a large academic institution in the U.S.

Methods: Retrospective analysis of untargeted urine drug screens results over five years (2020-2024) included patient testing performed for both acute exposure and compliance monitoring. Presence of xylazine and other drugs and metabolites was determined by gas chromatography – mass spectrometry (GCMS). Overall positivity was calculated as a percentage of total reported results.

Results: Of the 25,580 urine drug screens analyzed, 0.44% of the specimens were positive for xylazine. Positivity increased over time from 0.06% in 2020 to 1% in 2024. Specimens containing xylazine were also positive for fentanyl (100%), cocaine (44.6%), methamphetamine (29.5%), 6-monacetylmorphine/heroin (10.7%). In specimens positive for fentanyl, co-positivity with xylazine increased from 1.55% in 2020 to 25.19% in 2024.

Conclusions: Untargeted drug screens are critical for detection of emerging drugs and adulterants. Our data reveals that fentanyl mixed with xylazine accounted for ~25% of the fentanyl positive specimens in 2024, despite a slight decrease in overall fentanyl positivity.

Key words: Xylazine, Fentanyl, Adulterants, Urine Drug Screens, Clinical Toxicology

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

341

Findings of urine drug screening in the US South region 2020- 2024

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Biography:

Dr. Jing Cao received her Ph.D. degree in Biochemistry, Molecular Biology and Biophysics from the University of Minnesota, Twin Cities, and is board certified in Clinical Chemistry after completion of fellowship training at the University of Minnesota Medical Center. She is currently an Associate Professor of Pathology at the University of Texas Southwestern Medical Center, Director of clinical chemistry, mass spectrometry and point of care testing. She serves on a number of committee positions, including Chair of the Association of Diagnostics and Laboratory Medicine (ADLM) Cardiovascular Health division 2022-2025 and Chair of ADLM Texas Section 2023-2025. Dr. Cao has over 50 peer-reviewed articles in journals including Clinical Chemistry, Nature Nanotechnology. She has been invited to present at the ADLM Annual Meeting consecutively for years.

Background: Immunoassay (IA) remains the primary method for urine drugs of abuse (DOA) screening (UDS) despite significant limitations including false positives (FP) and false negatives (FN). Our laboratories offer IA UDS reflexed to LC-MS/MS, as well as IA paired with LC-QTOF MS (QTOF) for patients in the US South region.
Aims: To understand clinical needs for UDS in opiate/opioid and amphetamine classes 2020-2024.
Methods: IA UDS (Siemens Emit on Beckman AU) reflexed to LC-MS/MS and IA UDS (Siemens Atelicca or Abbott Alinity) paired with QTOF (Sciex 4600 or 5600) were analyzed. IA reporting followed SAMHSA cutoff guidelines. Opiate/opioid class on QTOF mainly includes opiates, oxycodone, fentanyl, levorphanol, methadone (reporting cutoffs 2.5 to 50 ng/mL). IA FP and FN rates were derived using MS methods as reference.
Results: Among 114731 IA UDS, positive rate was 10% for opiate/opioid and amphetamine with a FP rate of 23.5%. In 13612 paired IA/QTOF, 840 (6.2%) were positive for amphetamine and 1102 (8.1%) for opiate/opioid on QTOF. FN rates were 79.3, 67.3, 67.9,57.9 and 64.0% for amphetamine class, 83.9, 83.2, 85.8, 76.5 and 67.1% for opiate/opioid in year 2020-2024, respectively. The lab implemented fentanyl IA in 2024 which reduced FN rates while other major opioids contributing to FN IA were levorphanol and methadone.
Conclusions: Our study demonstrates limitations of IA UDS with the well-known FP and the alarmingly high FN rates in common drug classes, underscoring the need for comprehensive and sensitive UDS, including broader adoption of MS methods.
Keywords: UDS, DOA, fentanyl, opioid, amphetamine

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

342

Metabolic Toll of Atypical Antipsychotics: AGEs Accumulation, Mitochondrial Dysfunction and Cognitive Decline

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Biography:

HuaLin Cai is a doctoral supervisor at the Second Xiangya Hospital, Central South University, and Deputy Director of the International Research Center for Precision Medicine, Hunan, China. He is also an Associate Professor at the National Clinical Research Center for Mental Disorders, China. Dr. Cai's research focuses on biomarkers for therapeutic drug monitoring and clinical toxicology. After completing his Ph.D. in China, he pursued postdoctoral studies at the University of Pittsburgh, specializing in neuropsychopharmacology. As a clinical pharmacist in psychiatry, he leads a research group at Second Xiangya Hospital to evaluate drug metabolism and biomarker use in patient diagnosis and monitoring. He has received funding from the National Natural Science Foundation of China, Hunan Provincial Natural Science Foundation, and the Specialized Research Fund for Doctoral Programs. Dr. Cai has authored 115 peer-reviewed publications and received several prestigious awards, including the High Level Talents Award and Servier Young Investigator Award.

Background: Metabolic disturbances in glucose metabolism, induced by atypical antipsychotic drugs, are linked to the accumulation of advanced glycation end products (AGEs) in tissues. In the brain, AGEs accumulation impairs mitochondrial function, disrupts energy metabolism, and contributes to cognitive decline.
Aims: This study aims to explore the relationship between atypical antipsychotics, particularly clozapine, and AGEs accumulation, with a focus on their toxicological impact on brain metabolism and cognitive function.
Methods: Clinical part: Plasma AGEs levels were measured in 57 antipsychotic-naive first-episode schizophrenia (FE-SZ) patients and 54 healthy controls (HC). Additionally, 66 chronic relapsing schizophrenia (RE-SZ) patients on clozapine and 85 HC were enrolled. Plasma AGEs levels were measured before and after 4 weeks of clozapine treatment, alongside PANSS scores. In vivo: 18F-FDG-PET imaging assessed brain glucose uptake in rats, and mitochondrial ATP production, Krebs cycle intermediates, and related enzyme expression were analyzed.
Results: No significant difference in plasma AGEs was found between FE-SZ and HC. However, baseline AGEs levels were higher in RE-SZ patients, and these levels increased after 4 weeks of clozapine treatment, correlating with cognitive decline. 18F-FDG-PET imaging revealed reduced glucose uptake in the prefrontal cortex, accompanied by increased AGEs accumulation, reduced ATP production, and altered Krebs cycle intermediates and enzymes.
Conclusions: Chronic clozapine exposure disrupts brain glucose metabolism and mitochondrial function, leading to AGEs accumulation. AGEs and Krebs cycle biomarkers could help monitor metabolic side effects of antipsychotics and improve cognitive outcomes in schizophrenia.
Key Words: AGEs, clozapine, schizophrenia, mitochondrial dysfunction, glucose metabolism, cognitive impairment.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

343

In Vitro Biotransformation of Six Compounds Derived from the Stimulant Prolintane

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Biography:
Lea Wagmann is currently working as a postdoc at the Department of Experimental and Clinical Toxicology and Pharmacology (Prof. Markus R. Meyer, Saarland University) in Homburg (Germany). She received her PhD in 2018 for her thesis entitled "Psychoactive Substances as Substrates or Inhibitors of Enzymes in Drug Metabolism and Transport" supervised by Prof. Hans H. Maurer (Saarland University). Lea is Clinical Toxicologist GTFCh and actively involved in the laboratory's emergency toxicology service. She also teaches students of medicine and pharmacy. Her research mainly focuses on the toxicokinetics of new psychoactive substances and on the development of bioanalytical procedures for therapeutic drugs to assess a patient's adherence or detect intoxications.

Background: Prolintane (1-(1-phenylpentan-2-yl)pyrrolidine), a synthetic central nervous system stimulant, was used for the treatment of several diseases in the past. Due to its close structural relationship with pyrrolidinophenones and the previous detection of prolintane on the drugs of abuse market, the future emergence of prolintane derivatives as new psychoactive substances cannot be excluded.
Aims: Investigation of the in vitro metabolic fate of 2-, 3-, and 4-fluorprolintane and 2-, 3-, and 4-methylprolintane.
Methods: Metabolites were tentatively identified in incubations with pooled human liver S9 fraction after 1h and 6h containing cofactors for most phase I and II reactions and 25 µM of the prolintane derivative. Individual incubations with 11 human phase I isozymes were included in a monooxygenases activity screening. Analyses were performed by reversed-phase liquid chromatography-high-resolution tandem mass spectrometry.
Results: Hydroxylations were identified as most frequent phase I reactions. Subsequent oxidation led to the formation of oxo metabolites. Combination and multiple-reactions metabolites were also observed. Only few phase II metabolites were identified in vitro and included glucuronidation and sulfation of hydroxy metabolites. The isozyme mapping revealed the contribution of various isozymes including CYP1A2, CYP2B6, CYP2C19, CYP2D6, and CYP3A4.
Conclusions: All compounds showed metabolic reactions similar to those observed for related compounds including prolintane. The contribution of several isozymes to their metabolism minimizes the risk of drug-drug interactions. The identified metabolites should be considered as analytical targets in human biosamples, especially in urine screening procedures frequently used in clinical and forensic toxicology.
Keywords: Toxicokinetics, drugs of abuse, screening targets, isozyme mapping

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

344

Magnesium Isoglycyrrhizinate alleviates crizotinib-induced liver injury by inhibiting ferroptosis via FOXO3/LPCAT3 pathways

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[1]Department Of Pharmacy, The Second Xiangya Hospital, Central South University, Changsha, China

Biography:

Zhiyu Hu is a Master's student at the Second Xiangya Hospital of Central South University, under the supervision of Professors Miao Yan and Bikui Zhang. His research focuses on the mechanisms and therapeutic strategies for drug-induced liver injury (DILI). In particular, his work explores the role of ferroptosis in crizotinib-induced hepatotoxicity and demonstrates that magnesium isoglycyrrhizinate (a glycyrrhizinate formulation) mitigates this damage by modulating the FOXO3/LPCAT3 signaling pathway. His findings offer new insights into protective strategies for the prevention and management of DILI. He has co-authored three peer-reviewed publications to date.

Background: Crizotinib, as first-line treatment for advanced ALK-positive NSCLC, induces liver injury through ferroptosis, an iron-dependent form of cell death. Magnesium isoglycyrrhizinate (MgIG), a bioactive compound derived from licorice, has shown hepatoprotective effects. However, its protective role and mechanism in crizotinib-induced liver injury remains unclear.
Aims: This study aims to investigate the protective effects of MgIG against crizotinib-induced liver injury, focusing on the modulation of the FOXO3/LPCAT3 signaling pathway.
Methods: In vitro hepatocyte models and in vivo crizotinib-induced liver injury models were used. Cell survival, lipid peroxidation, and ferroptosis-related markers were assessed. The expression of FOXO3 and LPCAT3 was analyzed using Western blotting, qPCR, and immunofluorescence. FOXO3 phosphorylation and nuclear translocation were also evaluated to examine the regulatory effect of MgIG.
Results: MgIG treatment significantly alleviated crizotinib-induced liver injury, reduced lipid peroxidation, and promoted hepatocyte survival. Mechanistically, MgIG inhibited the phosphorylation level of FOXO3 and the expression of LPCAT3. In the absence of MgIG, FOXO3 activated LPCAT3 expression, but following MgIG treatment, FOXO3's suppressive effect on LPCAT3 transcription was amplified, contributing to ferroptosis inhibition.
Conclusions: MgIG protects against crizotinib-induced liver injury by enhancing FOXO3-mediated suppression of LPCAT3 expression, thereby inhibiting ferroptosis. These findings highlight MgIG as a potential therapeutic approach for treating drug-induced liver toxicity.
Keywords: Magnesium isoglycyrrhizinate, crizotinib, liver injury, ferroptosis, FOXO3, LPCAT3

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

345

Phosphatidylethanol: Detecting Alcohol in General Population and Transplant Patients

Clinical Chemistry Fellow Jacob Nielsen[1], HLA Pathology Fellow Jacob Kinskey[1], Assoc Prof Xin Yi[1,2]
[1]Houston Methodist Hospital, Houston, USA, [2]Weill Cornell Medical College , New York , USA

Biography:

Dr. Yi is a board-certified clinical chemist, currently serving as the Co-director of Clinical Chemistry at Houston Methodist Hospital and Associate Professor at Weill Cornell Medical College. She is also a fellow of the AACC Academy and the Co-director of the clinical chemistry fellowship program at Houston Methodist Hospital. Dr. Yi completed her clinical chemistry fellowship training at the University of Chicago after completing her PhD in clinical- bioanalytical chemistry at Cleveland State University/Cleveland Clinic. Dr. Yi served as the president of NACCCA in 2021-2022 and is currently the chair of AACC personalized medicine division and chair of AACC Texas session. She is also on several editorial boards, including American Journal of Clinical Pathology, Archives of Pathology & Lab Med, Encyclopedia of Analytical Chemistry, as well as CLSI document development committees. Her work appears in reputable journals and is showcased at major conferences.

Background: Alcohol consumption can lead to serious health consequences, including motor impairments and organ failure. Testing for short-term alcohol use is typically done using blood ethanol. Gamma-glutamyl transferase (GGT), though nonspecific, is used to indicate liver disease and can serve as an indirect alcohol marker. However, more reliable biomarkers are needed, especially for transplant patients. Phosphatidyl ethanol (PEth), a group of abnormal phospholipids formed in cell membranes, has emerged as a more sensitive and specific marker for detecting heavy alcohol use.

Aims: We aimed to compare ethanol, GGT, and PEth results over three years in both general and transplant populations, focusing on transplant patients' adherence to pre- and post-surgery abstinence.

Methods: We retrospectively analyzed the positive rates of ethanol, GGT, and PEth (18:1 and 18:2) to assess alcohol use patterns. Additionally, we compared PEth 18:1 and PEth 18:2 to determine if PEth 18:2 provides additional diagnostic value.

Results: Among the three markers, PEth identified chronic alcohol use more accurately (28% positivity) than ethanol (19%) and GGT (48%). All samples that tested positive for PEth 18:2 also had positive PEth 18:1 results, but the reverse was not true, indicating that PEth 18:1 is a more sensitive marker. Although PEth 18:1 and PEth 18:2 showed a fair correlation, no fixed percentage ratio was observed between them.

Conclusions: PEth 18:1 alone may be sufficient for detecting alcohol consumption. These findings highlight PEth's clinical utility over ethanol and GGT, particularly for monitoring transplant patients.

Key Words: alcohol consumption, biomarkers, phosphatidyl ethanol, gamma-glutamyl transferase, transplant.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

346

In-silico DrugBank® database: does CFM-ID-4.0 outperform CFM-ID-2.0 at generating clinical toxicology databases?

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Biography:

I studied Pharmacy at the University René Descartes (France) and received my Pharm.D. degree in 2002 in the field of toxicology/analytical chemistry.
I pursued my formation at University of Geneva (Switzerland) and received my Ph.D. degree in 2007 in the field of pharmaceutical sciences and mass spectrometry.
For three years, I worked in UCB pharmaceutical company (Belgium) as bioanalysis support for preclinical and clinical studies. I moved to public research and hospital clinical laboratories where I specialized in clinical toxicology and nowadays in pharmacology (anti-infective drugs). Teaching is also present with responsibility in toxicology at the school of Pharmacy (Université Paris Cité).
My research efforts focus on the development of new methods using LC-MS/MS for quantitation and screening of small molecules in biological fluids.

Background: Analysts face challenging problems in toxicology that lead to clinical issues. LC-MS/MS screening is difficult due to the number of molecules to be detected and the lack of MS/MS databases.
Aims: in silico DrugBank® database creation using CFM-ID_v2_v4 for clinical toxicology.
Methods: A python script was used to create an in-silico database of DrugBank® (www.go.drugbank.com, ver.5.1.12). Biotech drugs were excluded. Molecules with molecular weight, molecular formula, and Inchi structure were retained. MS/MS spectra were generated with Competitive_Fragmentation_Modeling_for_Metabolite_IDentification (CFM-ID) 2.0 or 4.0. Standards, patients or databases were queried using Metgem®, with cosine ≥ 0.2and 3 common fragments.
Results: Of the 11’928 molecules listed in DrugBank®, around 94% could be generated by CFM-ID 2.0 and 4.0. Ionized molecules or MS/MS spectra taking too long to generate are the main reasons for failure. The v.2.0 database was queried with v.4.0, 8648(77%) molecules were recognized; 10%(1195) incorrectly annotated and 13%(1387) unrecognized. Using different GNPS databases and querying DrugBank®v2/4, annotations remained similar or v4 had more hits. v2 annotated 49% of the 377 molecules in "nih_part_1" while v4 53%. v2 annotated 27% of the 1460 molecules in "small_molecules_pharmacologically_active" and v4 annotated 40%. The two training algorithms ensure the two databases remain useful and complementary.
Conclusions: Databases are a bottleneck in drug identification. The 11’000 in-silico DrugBank® database generated with CFM-ID v2 and v4 can help expand drug annotation. The two training algorithms ensure that both databases are useful to fully annotate unknown molecules in polyintoxicated patients.
Keywords: in-silico database, CFM-ID, clinical toxicology, Untargeted screening

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

347

How to predict renal function from premature neonates to adults

Dr Conor O'Hanlon

Biography:

Conor completed his PhD in pharmacometrics and clinical pharmacology at the University of Auckland, New Zealand. He investigated the impact of renal function on drug pharmacokinetics and pharmacodynamics (PKPD), with a focus on paediatric populations and cardiopulmonary bypass. He is currently a Postdoctoral Scientist at F. Hoffmann-La Roche in Basel, Switzerland, working on development of PKPD informed machine learning models.

Quantifying the effect of kidney disease on glomerular filtration rate (GFR) is important when describing variability in the clearance of drugs eliminated by the kidney. We developed a continuous model for renal function (RF) from prematurity to adulthood based on consistent models for fat-free mass (FFM), creatinine production rate (CPR), and GFR. A model for fractional FFM in premature neonates to adults was developed using pooled data from 4462 subjects and 2847 FFM observations. Girls were found to have an FFM higher than that predicted from adult women based on height, total body mass, and sex. Boys have an FFM lower than adult men until around the onset of puberty, when it approaches adult male values. Data from 108 subjects with measurements of GFR and serum creatinine (Scr) were used to construct a model for CPR, predicted using FFM, postmenstrual age, and sex. Individual CPR may then be used with individual Scr to predict the estimated GFR (eGFR; eGFR = CPR/Scr). A previously published model for human GFR based on 1153 GFR observations in 923 subjects without known kidney disease was updated using the model for fractional FFM to predict individual size and age-consistent values for the expected normal GFR (nGFR). Individual renal function was then calculated using RF = eGFR/nGFR.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

348

A physiological approach to renal clearance informed by renal function

Prof Nick Holford

Biography:
Professor Holford obtained his medical qualifications (MBChB, MRCP) in the United Kingdom. In 1983 he moved to Auckland, New Zealand to join the University of Auckland in the Dept of Pharmacology & Clinical Pharmacology. Until 1989 he had a part time appointment as a Specialist in Internal Medicine at Auckland Hospital. During this period he was elected Fellow of the Royal Australasian College of Physicians. He retired from the University of Auckland as Professor Emeritus of Clinical Pharmacology at the end of 2021.
His interests are in applying pharmacokinetics and pharmacodynamics to clinical pharmacology and developing tools to aid dose individualization (www.nextdose.org).
http://holford.fmhs.auckland.ac.nz

Background: By analogy with hepatic clearance, glomerular filtration rate (GFR) provides an upper limit for the filtration component of renal clearance.
Aims: To describe how GFR and renal function (RF) provide a physiological basis to distinguish clearance constrained by GFR and a component, not associated with GFR, also linked to RF.
Methods: Methods for estimation of normal GFR (nGFR) RF have been described (1). A population pharmacokinetic analysis was used to quantitate components of plasma clearance as a function of RF (2).
Equation 1: CLGFRplasma=fu×nGFR×asymmetrical sigmoid function(RF)
Equation 2: CLNGFRplasma=POP_CLNGFR×RF
Results: Plasma GFR clearance was described by the unbound fraction (fu), nGFR and an asymmetrical sigmoid function of RF (Equation 1). Plasma non-GFR clearance based on a population estimate (POPCLNGFR) used a linear function of RF (Equation 2).
Conclusions: The unbound fraction in plasma is an important determinant of plasma clearance based on nGFR. The use of nGFR as the physiological determinant of filtration.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

349

Pharmacokinetics during haemodialysis and haemodiafiltration, application to amikacin

Dr Laila Nassar

Biography:
Dr. Laila Nassar is a clinical pharmacologist and pharmacometrician with extensive experience in clinical practice, research, and academic teaching. She holds a Doctor of Pharmacy degree from the Hebrew University of Jerusalem and recently completed her PhD in pharmacometrics at the Technion – Israel Institute of Technology in collaboration with the University of Auckland and under the supervision of Professor Nick Holford and Professor Daniel Kurnik. Her doctoral research focused on pharmacokinetic modeling to support target concentration intervention. Her symposium presentation, titled "Pharmacokinetics during haemodialysis and haemodiafiltration: application to amikacin", highlights key findings from this work. Dr. Nassar currently holds a clinical and research position at Rambam Health Care Campus in Haifa. She has also taught pharmacokinetics and clinical pharmacology at several universities and has a strong background in hospital and community pharmacy practice.

A single-center, prospective study in haemodialysis (HD) or haemodiafiltration (HDF) patients was used to describe amikacin pharmacokinetics. The theory describing dialyser blood clearance [1] was extended to HDF. Target exposures (area under the concentration time curve for 24 hours from the start of dialysis (AUC24h), peak (Cpeak) and trough concentrations (Ctrough), were used to evaluate alternative dosing designs. The current recommended dosing regimen (5 mg/kg 4 hours of dialysis) achieves neither the target AUC24h nor the target peak with either HD or HDF. For HD, increasing the dose to 17.5 mg/kg achieves AUC24h, Cpeak and Ctrough within the acceptable range. For HDF, 25 mg/kg achieves AUC24h and Ctrough but not Cpeak within the acceptable range, 30 mg/kg achieves Cpeak within the acceptable range but leads to higher Ctrough, which may be associated with toxicity [2]. The principles used to develop target exposure based dosing in patients on dialysis are not limited to amikacin but are generally applicable to other drugs. The consequences on dosing in HDF when compared with HD are better predicted by considering dialyser clearance rather than dialysis efficiency because of the additional effects of dialyser blood flow on elimination.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

350

Disposition of colistin in critically ill patients on sustained low-efficiency dialysis: a population pharmacokinetic study and Monte Carlo simulations

Ms Dominika Fuhs

Biography:
Dominika is a PhD candidate at the Monash Institute of Pharmaceutical Sciences, Monash University. Her PhD research focuses on the development of novel mechanism-based mathematical models as well as population pharmacokinetic models. She's passionate about investigating ways to treat resistant bacterial "superbugs" by optimising dosing regimens of currently available antibiotics in the fight against antimicrobial resistance

Colistin (administered as the inactive prodrug colistin methanesulphonate [CMS]) is often used to treat infections in critically-ill patients undergoing sustained low-efficiency dialysis (SLED).
We aimed to develop a population pharmacokinetic (popPK) model for colistin in patients undergoing SLED, and evaluate the probabilities of antibacterial benefit and colistin nephrotoxicity for different dosing regimens via simulations.
A prospective popPK study included 13 critically-ill patients treated with CMS and receiving SLED (6-8h) for renal support. The PK of formed colistin was studied on both a nonSLED and a SLED day. Colistin plasma concentrations were analysed using the popPK approach. Monte Carlo simulations (MCS) for dosing regimen evaluation were performed.
A linear one-compartment PK disposition model best described the data. The total body clearance of colistin (excluding SLED clearance) was 1.69L (21%) [population mean (between subject variability)] with 42% interoccasion variability. Colistin clearance during the SLED period was estimated to be 3.49L (42%). We evaluated the probability of target attainment defined as percentage of patients achieving relevant average colistin plasma concentration (Cavg) targets: >80% for Cavg ≥2 mg/L, >90% for Cavg ≥1.5 mg/L and <30% for Cavg ≥4 mg/L for the first 24h of therapy initiation on a SLED or nonSLED day as well as maintenance therapy.
Colistin clearance was substantially higher during SLED; therefore, SLED should be accounted for in CMS dosing regimens. This analysis provides comprehensive information regarding the achievement of clinically desirable average plasma colistin concentrations (including evaluation of loading doses) for two dosing regimens and six different SLED administration scenarios.
Key words:
Population pharmacokinetic modelling, colistin, sustained low-efficiency dialysis

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

351

Model-informed precision dosing of anti-infective drugs in paediatrics

A/Prof Xiao Zhu

Biography:

Dr. Zhu is an Associate Professor in Pharmacometrics at Fudan University since 2021. He obtained PhD from University of Otago in 2019 under the supervision of Prof. Stephen Duffull and worked as Postdoc Fellow during 2019-2020 under the sponsorship of Murdoch Children's Research Institute. His current research involves the development of pharmacological models, population analysis of pharmacokinetic (PK) and pharmacodynamic (PD) data, and the optimal design of clinical studies. He has successfully applied pharmacometrics techniques in a range of therapeutic areas, primarily for oncology, bacterial infections, and neuroscience. His research facilitates the model-informed precision dosing (MIPD) for special populations (e.g., pediatrics and critically ill patients), as well as model-informed drug development (MIDD) through close collaborations with local biotech companies. He was awarded the ASCEPT Fred Fastier Prize and selected for the Shanghai Overseas Talent Program, and has published over 30 SCI papers as the first or corresponding author in leading journals such as Lancet Reg Health West Pac, Br J Pharmacol, J Antimicrob Chemother, and Antimicrob Agents Chemother.

Model-informed precision dosing (MIPD) has been a topic of growing interest in clinical pharmacology in recent years. However, there is still a significant challenge to make the MIPD results more readily accepted by physicians and to demonstrate its impact on clinical practice. During the upcoming presentation, Dr. Zhu will discuss his experience using MIPD to improve dosing for renally eliminated anti-infective drugs in pediatric patients. He will also share insights gained through years of collaboration with pediatricians and highlight the bridging role that clinical pharmacometricians play in implementing MIPD.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

352

The Impact of Inter-individual variation of anti-infective drug exposure and delay in achieving the target concentration on clinical outcome

Dr Lee Lee Low

Biography:
Dr Lee Lee Low is an Infectious Disease Physician and Head of the Department of Medicine at Hospital Sultanah Bahiyah, Alor Setar, Kedah, Malaysia. She is also the Chief Coordinator of Infection Control and Antimicrobial Stewardship (AMS) program for the state of Kedah, Malaysia.
Dr Low currently sits on the committee of the Asia Fungal Working Group, under the International Society for Human and Animal Mycology (ISHAM). She is also involved in various societies in Malaysia, including the Malaysian Society of HIV Medicine, the Malaysian Society of Infectious Disease and Chemotherapy, The Malaysian Society of Infection Control and Infectious Diseases, and IATDMCT.
An avid researcher, Dr Low has served as the co-investigator of several major studies in the field of infectious diseases and has published many peer-reviewed articles on the subject.

The inter-individual variability of anti-infective agents arises from both pharmacokinetics (PK) and pharmacodynamics (PD) of the drugs. Integrating PK and PD is essential to define the dose-exposure-response relationship, which plays a critical role in maximizing efficacy,
preventing toxicity and reducing the risk of drug resistance. Optimizing antibiotic doses in critically ill patients is particularly challenging due to the significant inter-patient variability, even for drugs with linear PK. Critical illness has been linked to reduced anti-infective exposure, and delays in achieving the target drug concentration may lead to inadequate clinical response and the development of drug resistance. This lecture aims to highlight and present clinical evidence supporting dose optimization as a strategy to mitigate interpatient pharmacokinetic variability, and to improve treatment outcome.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

353

Use of dose optimization programs in achieving target anti-infective drug concentrations early and maintaining it for the duration of anti-infective drug treatment

Dr Anne-Grete MÃrtson

Biography:

Anne-Grete Märtson is an assistant professor at the Leiden Academic Centre for Drug Research, Leiden University. She is leading a research group focusing on translational antiviral pharmacology. The group focuses on clinical studies, laboratory experiments such as the hollow fibre infection model and use computational methods to find best treatment regimens and translate results back to the clinical setting. The research topics include optimizing ganciclovir therapy for cytomegalovirus (CMV), therapeutic drug monitoring of antivirals, relating antiviral drug exposure to dose-related toxicity, dosing in extremes of organ function and in special populations, delay in antiviral therapy in SARS-CoV-2.

Achieving optimal tissue penetration and maintaining therapeutic concentrations of anti-infective agents are critical for successful treatment. Dose optimization integrating pharmacokinetic/pharmacodynamic (PK/PD) principles, patient-specific variables and therapeutic drug monitoring (TDM) are needed to improve drug distribution to infection sites. Utilizing model-informed precision dosing (MIPD) provides a systematic approach to optimizing drug therapy. This method incorporates population PK/PD modeling, while also integrating patient-specific covariates (e.g., age, weight, disease state) to guide treatment optimization. This talk will explore MIPD and other modelling approaches that are used for dose optimisation, with a focus on maintaining effective drug levels in target tissues, ultimately supporting optimized treatment of infectious diseases.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

354

Strategies to Improve Therapeutic Target Attainment for Anti-Infectives: Leveraging Advanced Tools and Technologies

Prof Birgit Koch

Biography:
Birgit CP Koch is Hospital Pharmacist-Clinical Pharmacologist and Full Professor of Clinical Pharmacometrics, working at Erasmus MC in Rotterdam. She supervises the education program for residents in Clinical Pharmacology.
Nowadays, she is member of the executive board of EPASG, the PK/PD group of ESCMID, council member of IATDMCT, member the pharmacology committee of UEMS, the specialist registration committee for hospital pharmacists and clinical pharmacologists in the Netherlands, member of ISAP, ASCPT, EACPT, the SWAB committee, the medical ethical board, the editorial board of therapeutic drug monitoring, British Journal of Clinical Pharmacology and Clinical Pharmacokinetics. She is member of the alternative sampling and infections committees of IATDMCT and NWO VIDI member. She is chair of the Young Investigator Grant Committee and chair of the expert team Knowledge security of Erasmus MC. She authored > 230 publications on PK/PD, TDM and toxicology and she is the PI of several studies on model-based dosing, TDM and PK in antibiotics and psychoactive drugs, with funding > 2000 K. Her research focuses on alternative matrices, pharmacokinetics and pharmacodynamics of drugs in special populations and toxicology during pregnancy. At the moment, she supervises 21 PhD students (and 9 finished).

Achieving optimal therapeutic target attainment in anti-infective therapy is essential for maximizing efficacy, reducing toxicity, and minimizing the development of resistance. This session will explore innovative strategies that aim to improve the precision of anti-infective dosing through the integration of advanced technologies and methodologies.

Goals/Objectives:
1. Understand the Role of Therapeutic Drug Monitoring (TDM) in individualizing dosing and improving patient outcomes by adjusting drug levels for optimal therapeutic response.
2. Explore Model-Informed Precision Dosing (MIPD) as a cutting-edge approach to predict individualized drug doses based on pharmacokinetic (PK) models and patient-specific data, ensuring better efficacy and safety.
3. Examine the Importance of Target Site Concentrations in achieving effective drug exposure at the site of infection, highlighting the need for enhanced PK models that incorporate tissue penetration data.
4. Discuss Alternative Sampling Techniques such as saliva and dried blood spots, offering less invasive and more frequent options for monitoring anti-infective drug concentrations.
5. Delve into the Potential of Improved PK Models and how they can provide more accurate dosing recommendations through population-based approaches and dynamic modeling.
6. Review the Future of Machine Learning and Real-Time Monitoring, which could revolutionize anti-infective therapy by enabling continuous, real-time dosing adjustments based on patient-specific data.

By the end of this session, participants will gain a comprehensive understanding of the evolving landscape of anti-infective therapy, equipped with the tools necessary to implement these advanced strategies to optimize therapeutic target attainment.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

355

A randomized controlled trial of therapeutic monitoring-based dosing strategy versus standard dosing strategy of sunitinib in metastatic renal cell carcinoma

Dr Vikram Gota

Biography:

Dr. Vikram Gota completed his MD in pharmacology from Christian Medical College, Vellore, following which he briefly worked as a Clinical Investigator in BA/BE studies. Thereafter, he joined the INDOOxford (INDOX) Cancer Trials Network at Tata Memorial Centre, Mumbai, where he received training in the design and conduct of phase I clinical trials. During this time, he also obtained the post graduate diploma in clinical trials from the London School of Hygiene and Tropical Medicine, University of London. He is presently the officer-in-charge of the department of clinical pharmacology at the Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Tata Memorial Centre. His research interests include early clinical development and pharmacokinetics driven optimization of drugs used in cancer, including the development of pediatric-friendly formulations for childhood cancers. He is currently the Chair of the TDM in Oncology sub-committee of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT). He is involved with the geriatric clinic at TMH since 2019 focusing on rational therapeutics, potentially inappropriate medications and drug-drug interactions, among other things. He has worked as an investigator in several phase I clinical trials including first-in-human studies of investigational new drugs.

Background: Sunitinib, a multi-targeted tyrosine kinase inhibitor, is a standard first-line treatment for metastatic renal cell carcinoma (mRCC). We evaluated whether TDM-guided dosing of sunitinib improves treatment outcomes compared to conventional dosing in mRCC patients.

Methods: This randomized, controlled trial enrolled patients with mRCC and randomized them in a 1:1 ratio to receive sunitinib (50 mg/day) either with TDM-guided dose optimization or conventional dose adjustments based on observed toxicity. In both arms, total trough levels (TTL) of sunitinib were measured between days 10–14 of cycle 1. In the TDM Arm, suitable dose adjustments were made, where necessary, to maintain TTL within the therapeutic range of 60–100 ng/mL. In the Standard Arm dose modifications were initiated only in case of intolerable side effects as per standard institutional practice. The primary endpoint was progression-free survival (PFS), while the key secondary endpoint was the incidence of grade ≥3 adverse events.

Results: A total of 125 patients were enrolled, with 64 and 61 patients randomized to the Standard and TDM arms, respectively. TTL in cycle 1 were comparable between the arms (142 ng/mL vs. 145 ng/mL), but by cycle 4, median TTL of sunitinib decreased to 84 ng/mL in the TDM arm, reflecting dose adjustments, as against 124 ng/mL in the Standard Arm. The median PFS was 14.9 vs 14.7 months in the Standard arm and TDM arm (HR = 1.0, 95% CI: 0.669–1.493) respectively. Notably, grade ≥3 adverse events were markedly lower in the TDM arm (16.6%) compared to Standard Arm (49.2%).

Conclusion: TDM did not significantly impact PFS. However, it markedly reduced the incidence of grade ≥3 adverse events, supporting its role in personalized dosing of sunitinib.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

356

Mechanisms and Implications of Maternal-Fetal Exposure to Drugs and Environmental Toxins

Adj A/Prof Laure Ponthier

Biography:
Laure Ponthier is a professor associate in neonatal intensive care unit , Limoges universitary hospital, France, MD, PhD, Inserm U1248 "pharmacology&transplantation"

Maternal-fetal exposure to medications and environmental toxins represents a major issue in public health and developmental biology. Numerous toxic substances can cross the placental barrier via passive diffusion or active transport, thereby exposing the fetus to compounds that its still-immature organism struggles to eliminate.
The placenta, a vital interface between mother and fetus, ensures the supply of oxygen and nutrients essential for fetal development. It also plays a partial role in the elimination of xenobiotics. These foreign substances must be metabolized before they can be excreted—a process that primarily takes place in the liver but can also involve the kidneys, skin, and lungs. This metabolism occurs in two phases: Phase I, mainly carried out by the cytochrome P450 enzyme system, produces often reactive metabolites; Phase II involves conjugation reactions that make these metabolites water-soluble for urinary excretion.
In the fetus, hepatic immaturity limits the biotransformation of xenobiotics, making elimination largely dependent on maternal liver and kidney function. The placenta, which also expresses certain CYP450 enzymes, contributes to this detoxification process, particularly regarding pesticides during gestation. However, this protection is not absolute: transplacental passage remains possible, as evidenced by the detection of toxic residues in newborn urine, meconium, or cord blood.
Fetal vulnerability is further increased by the heightened permeability of the developing blood-brain barrier. The agents involved include certain medications (e.g., antiepileptics), illicit drugs (cocaine, heroin), environmental toxins (heavy metals, endocrine disruptors, pesticides), as well as alcohol and tobacco. Such exposures can lead to congenital malformations, neurodevelopmental disorders, intrauterine growth restriction, prematurity, or even fetal death.
The effects may extend well beyond birth. Prenatal exposures have been linked to the later development of chronic diseases in adulthood, such as obesity, diabetes, and cognitive disorders. Prevention relies on proactive patient education, strict regulation of teratogenic and polluting substances, and public health policies aimed at minimizing risk exposures during pregnancy.

357

Human Studies on Prenatal Exposures: Evidence, Trends, and Advances

Dr Melissa Bennett

Biography:
Melissa Bennett is the Associate Clinical Director of the Alberta Centre of Toxicology in the Department of Physiology and Pharmacology at the University of Calgary. She holds a PhD in biochemistry and molecular biology from the University of Calgary and is board-certified in toxicological chemistry by the American Board of Clinical Chemistry. She is also a Fellow of the Academy of Diagnostics and Laboratory Medicine.

Prenatal exposures to environmental factors have garnered significant attention due to their potential impact on fetal development and long-term health outcomes. This presentation reviews current evidence from human studies exploring prenatal exposures to various environmental stressors, including chemicals, pollutants, and lifestyle factors. Emphasizing recent trends and advancements in research methodologies, the session will highlight key findings linking prenatal exposures to developmental outcomes, neurobehavioral effects, and diseases. Attendees will gain a comprehensive understanding of the current state of prenatal exposure research, its implications for maternal and child health, and future directions for advancing knowledge.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

359

Evolving Chemical Risk Assessment in Maternal-Child Health

Dr Souleiman El Balkhi

Biography:
Dr. Souleiman El Balkhi is a hospital practitioner at Limoges teaching hospital of Limoges, France. He is the head of the Professional Toxicology and Environmental Health in the hospital laboratory and is chair of Committee of Toxicology and Environmental. He is also recognized as a legal expert in toxicology.
His research interests encompass analytical toxicology, with a particular focus on the detection and impact of environmental contaminants on human health. He has contributed to studies investigating the association between pesticide and metals and their health implications. Dr. El Balkhi's work integrates also advanced analytical techniques and biomarker development on posttranslational proteins modifications to enhance the early diagnosis of liver injuries. He wrote more than 60 articles, 3 books chapters and hold 3 patents.

Risk assessment for maternal and child health in relation to chemical exposures has evolved slowly in recent years. Traditional approaches have largely focused on individual chemicals and dose-response relationships, neglecting the complexity and ubiquity of real-world exposures. However, growing evidence on the developmental impacts of multiple, low-dose exposures is prompting a gradual shift toward more integrative frameworks.
Modern methodologies increasingly incorporate cumulative exposure models and consider emerging contaminants, as well as previously overlooked windows of susceptibility such as the preconception period and paternal exposures. These approaches recognise that chemical impacts can occur through diverse pathways and across life stages. Technological advances, including real-time monitoring and machine learning, offer new possibilities for improving exposure detection and data integration. Nonetheless, significant challenges remain, particularly in assessing risks from chemical mixtures and substances with limited toxicological data. In this context, toxicology laboratories are pivotal to progress. By refining specimen analysis techniques and expanding biomarker panels, they enhance the detection of emerging contaminants and support the development of more robust cumulative risk models.
To further strengthen these frameworks, toxicology laboratories should play a greater role in integrating biomonitoring data with computational models and machine learning platforms. Additionally, clinical studies evaluating antenatal interventions to mitigate chemical exposures could provide critical insights into the long-term health consequences of early-life chemical burdens. Such efforts are essential for advancing public health strategies aimed at protecting vulnerable populations from complex chemical exposures.

400

Personalised Medicine of Immunosuppressants

Xiaoman (Alexis) Liu

Biography:
Xiaoman Liu is a clinical pharmacist at the First Affiliated Hospital, Sun Yat-sen University (FAH-SYSU), China. She received her Ph.D. from the niversity of Sydney, Australia. Dr. Liu's research focuses on pharmacogenetics- and pharmacokinetics-based personalised medicine, with a particular emphasis on immunosuppressive therapy. She is a co-author of the International Pharmaceutical Federation (FIP) consensus on the management of immunosuppressants and has contributed to multiple journal articles and book chapters. The FAH-SYSU pharmacy research team is dedicated to investigating the effects of genetic polymorphisms and pharmacokinetic variability on drug levels, efficacy, and side effects, with the aim of improving the safety and effectiveness of medications for pediatric patients and individuals with immunocompromised conditions.

Immunosuppressants are foundational in the management of autoimmune diseases and organ transplantation, yet their clinical use is frequently complicated by substantial inter-individual variability in pharmacokinetics, pharmacodynamics, and toxicity profiles. This variability, driven by genetic and disease-related factors, underscores the critical need for personalised dosing strategies to maximize therapeutic efficacy while minimizing adverse effects. Recent advances in model-informed precision dosing, pharmacogenomics, and data-driven predictive analytics have accelerated the evolution of individualized immunosuppressant therapy, moving the field towards a more precise and patient-centered paradigm. In this talk, I will highlight the recent progress in the personalised medicine of mycophenolic acid for pediatric lupus nephritis, focusing on integrating pharmacokinetic modeling, pharmacogenomic profiling, and machine learning models that leverage multi-dimensional patient data to refine therapeutic drug monitoring and support clinical decision-making.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

417

Well-validated models adequately describe vancomycin pharmacokinetics in patients with acute kidney injury

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Biography:

Dr Jasmine Hughes is the Head of Clinical Data Science at InsightRX, a San Francisco-based company that makes model-informed precision dosing and clinical analytics software. She received her Bachelor's in Chemical Engineering from McGill University and her PhD in Bioengineering from the University of California, San Francisco and the University of California, Berkeley, and is currently based in Toronto, Canada. Her current research focus is creating and improving models, statistical methods and software tools for improving dose individualization in clinical practice.

Background: Patients on vancomycin often develop acute kidney injury (AKI), altering pharmacokinetics (PK). Due to vancomycin's narrow therapeutic index, model-informed precision dosing (MIPD) is widely used, however model predictive performance during AKI remains uncertain. Aims: We evaluated the performance of select vancomycin PK models in patients with AKI.
Methods: Patient data entered into the InsightRX Nova MIPD app between January 1 2023 and August 1 2024 were de-identified and analyzed retrospectively. For each age group (adult, pediatric, neonatal) 3-4 models validated for use in that patient population were selected. Measured drug concentrations were iteratively predicted using MAP Bayesian estimation with regular or flattened model priors. AKI rates were determined according to KDIGO criteria. Prediction error was assessed based on if the patient was not in AKI, or was in AKI for one ("rising") or more ("sustained") consecutive serum creatinine levels, quantified by root mean square error (RMSE).
Results: The data set included 454,671 adults, 6198 children and 2117 neonates, who experienced AKI rates of 5.4%, 3.4% and 5.2%, respectively. Relative to model performance in patients without AKI, models performed similarly or slightly worse in patients with sustained AKI (RMSE = -1-10%, +8-39%, +2-64% respectively) but performed considerably worse in patients with rising AKI (RMSE: +13%-27%, +23-73%, +45-105%). Using flattened priors improved predictions overall, and reduced the discrepancy in predictive performance between patients with or without AKI.
Conclusions: Predictive performance in patients with AKI varies between models. Flattened priors improves model prediction, particularly for patients in worsening condition.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

418

AntibioMIC: a dynamic Web_App helping clinicians interpret antibiotic concentrations for drug monitoring

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Biography:

I studied Pharmacy at the University René Descartes (France) and received my Pharm.D. degree in 2002 in the field of toxicology/analytical chemistry.
I pursued my formation at University of Geneva (Switzerland) and received my Ph.D. degree in 2007 in the field of pharmaceutical sciences and mass spectrometry.
For three years, I worked in UCB pharmaceutical company (Belgium) as bioanalysis support for preclinical and clinical studies. I moved to public research and hospital clinical laboratories where I specialized in clinical toxicology and nowadays in pharmacology (anti-infective drugs). Teaching is also present with responsibility in toxicology at the school of Pharmacy (Université Paris Cité).
My research efforts focus on the development of new methods using LC-MS/MS for quantitation and screening of small molecules in biological fluids.

Background: Therapeutic Drug Monitoring (TDM) of antibiotics is based on pharmacokinetic-pharmacodynamic (PK-PD) indices that compare antibiotic exposure to the minimum inhibitory concentration (MIC) of the targeted pathogen. This latter information is often not available, and worst-case scenarios are then assumed.
Aims: Creation of a webapp (www.antibiomic.com) to improve TDM interpretation of antibiotic/microbial combinations.
Methods: Developed with a Vue.js front-end and Node.js back-end (using Express for endpoints), this site pulls MIC data for various pathogens/anti-infectives from EUCAST (European Committee on Antimicrobial Susceptibility Testing) and computes free fractions via DruMAP (Drug Metabolism and pharmacokinetics (DMPK) Analysis Platform). Therapeutic targets come from literature or consensus.
Results: First, the time-dependent class of beta-lactam antibiotics is interpreted. Once the patient form is completed, a 100% ft>4 x MIC target was selected for results interpretation. In terms of efficacy, the free active concentration (fu.p) is relevant, and was used to compare the antibiotic exposition to the ECOFFs (highest MICs in a wild bacterial population). The prediction site https://adme.nibiohn.go.jp was used to calculate fu.p of each antibiotic. The MIC histogram distribution and ECOFF are daily uploaded from the website (https://mic.eucast.org/search/). Finally, the tab “interpretation” provides three essential indications: (i)efficacy via the calculated free concentration versus ECOFF, (ii)total concentration versus the usual pharmacological targets and (iii)notion of toxicity.
Conclusion: For TDM, this app allows results individualization and supports clinical/biological diagnosis. Antibiomic.com is successfully used for time-dependent antibiotics. Work is in progress on AUC-dependent antibiotics, aminoglycosides, and a patient history.
Keywords: Antibiotics, MIC, TDM, Web_App, personalized biology.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

419

Mechanistic PBPK Modeling Predicts Population-Specific Voriconazole-Tofacitinib Interaction Risks

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Biography:

Dr. Shasha Jin is an Assistant Researcher at Ren Ji Hospital, Shanghai Jiao Tong University School of Medicine, specializing in clinical pharmacology, pharmacokinetics, and pharmacogenomics. She earned her Ph.D. in Clinical Pharmacy from Fudan University.

Dr. Jin's research leverages advanced methodologies, including physiologically based pharmacokinetic (PBPK) modeling, metabolomics, and molecular biology techniques, to address clinically significant issues such as DDI risks, drug-induced liver injury, and personalized dosing. She currently leads a National Natural Science Foundation of China (NSFC) Youth Project exploring methimazole-induced hepatotoxicity through metabolic activation and mTORC1 signaling. Her prior work as a co-investigator on NSFC projects includes dynamic PK/PD modeling of tyrosine kinase inhibitors and herbal medicine mechanisms.

Dr. Jin has authored multiple peer-reviewed publications and actively contributes to the scientific community as a Youth Committee Member of the Therapeutic Drug Monitoring Research Professional Committee and a reviewer for the Chinese Journal of Clinical Pharmacy.

Background: Tofacitinib (JAK inhibitor) and voriconazole (triazole antifungal) are frequently co-administered in immunocompromised patients with autoimmune disorders. Voriconazole and its metabolite N-oxide inhibit CYP enzymes, while tofacitinib is metabolized by CYP3A4. However, the pharmacokinetic relationship between them remains poorly characterized, especially in populations with organ impairment or CYP2C19 polymorphisms.

Aims: To (1) establish physiologically based pharmacokinetic (PBPK) models for voriconazole/N-oxide and tofacitinib; (2) elucidate the CYP-mediated DDI mechanisms; (3) quantify exposure risks in clinical subpopulations.

Methods: PBPK models were developed in Simcyp® using physicochemical/ADME parameters from literature and optimized to match observed plasma profiles. Voriconazole/N-oxide models incorporated CYP2C19/3A4 metabolism and renal elimination; tofacitinib models included CYP3A4/2C19 clearance. DDI predictability was validated using midazolam (victim) and fluconazole/ketoconazole (perpetrators). Virtual trials (n=1,000) simulated interactions in healthy, hepatic/renal impairment, and CYP2C19 phenotypes (extensive [EM], intermediate [IM], poor metabolizers [PM]).

Results: Predicted/observed AUC and Cmax ratios fell within twofold error. Voriconazole/N-oxide increased tofacitinib exposure most markedly in severe renal impairment (AUCR 4.55, 95% CI: 4.21–4.93) and CYP2C19 PM (AUCR 4.18 vs. EM 3.58), driven by N-oxide accumulation. Rheumatoid arthritis patients showed reduced AUCR (2.14). Dose-normalized AUC inversely correlated with CYP2C19 activity (R^2=0.89, $p<0.001$).

Conclusions: This study demonstrates metabolite-amplified CYP2C19 inhibition by voriconazole, elevating tofacitinib toxicity risks in renal impairment and CYP2C19 PM populations. Proactive dose reductions (≥50%) are recommended for these subgroups.

Keywords: physiologically based pharmacokinetics, drug-drug interaction, CYP2C19 polymorphism, voriconazole, tofacitinib, organ impairment

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

420

Levofloxacin in osteoarticular infections: could we determine a therapeutic range?

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Biography:

Marie-Clémence Verdier is assistant professor in Pharmacology in Rennes University Hospital since 2012.

Her work focuses on therapeutic drug monitoring and the assessment of exposure-effect relationships, with a particular interest in anti-infective drugs.

Background: Osteoarticular infections (OAI) frequently require long-term oral levofloxacin treatment. This antibiotic is associated with numerous adverse drug reactions (ADR), the mechanism of which remains poorly understood. The literature identifies the levofloxacin area under the curve of concentrations (AUC0-24h) /MIC ratio as the best PK-PD biomarker for efficacy. However, no study has investigated the link between levofloxacin exposure and the occurrence of ADR.
Aims: This monocentric retrospective study aims at evaluating the relationship between exposure parameters of levofloxacin (AUC0-24h, Cmax, Cmin) and the risk of ADR in the context of OAI.
Methods: Exposure data were collected from our TDM activity between July 2018 and July 2024. ADR occurring during the treatment were extracted from patients' records and levofloxacin imputability was assessed by the regional pharmacovigilance center.
Results: Preliminary results of the first 79 patients of the study are presented. The most frequently dosing schedule were 500, 750 and 1000 mg/d (n=24, 30, 20, respectively) . The average duration of treatment was 83 days. Eleven patients presented at least one ADR attributed to levofloxacin (tendon and joint pain, neurological, hepatic or cardiological disorders). Median AUC0-24h, Cmax and Cmin in case of ADR were 161.6µg.h/mL [123.9;182.7], 10.5µg/mL [7.9;12.8] and 4.4µg/mL [2.4;5.4], respectively, vs 109.0µg.h/mL [83.9;163.6], 9.8µg/mL [7.1;12.1] and 1.9µg/mL [1.1;4.7] in the group without ADR.
Conclusions: These preliminary results show a significantly higher Cmin (p=0.01) and a trend to higher AUC0-24h (p=0.07) in patients developing ADR . These results are promising for refining the therapeutic range of levofloxacin.
Keywords: Levofloxacin, safety, exposure

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

421

Real-world experience optimising vancomycin dosing in paediatric ICU using model-informed precision dosing

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Biography:
Michael is a senior Pharmacist in the Paediatric Palliative Care service for the Sydney Children's Hospitals Network. He has substantial experience in Paediatric Intensive Care medicines and is a PhD candidate under the supervision of Assoc. Prof. Sophie Stocker.

Background: Model-informed precision dosing(MIPD) is now the preferred method for vancomycin TDM. However, its impact on reducing vancomycin-associated acute-kidney-injury (AKI) and attainment of area under the curve (AUC) targets has not been specifically examined in a real-world, paediatric ICU setting where resourcing for the MIPD service is limited.
Aim: To assess the impact of real-world vancomycin MIPD implementation on vancomycin-associated AKI rates and therapeutic target attainment in critically ill children.
Methods: Vancomycin courses from patients admitted to a paediatric ICU (2020-2022) were retrospectively reviewed. All courses with at least 2 doses and ≥ 1 vancomycin concentration were included. From January 2020 to June 2021, vancomycin dosing was determined solely by trough concentration monitoring. From July 2021, MIPD was increasingly used to guide vancomycin dosing by targeting a 24-hour AUC of 400-600mg·h/L. AKI severity was determined by modified KDIGO criteria. Due to resource constraints MIPD was generally not applied a priori and was not applied for all courses.
Results: In total, 648 vancomycin courses were identified. The average patient age was 3.9 years (range; 1.5 days - 19.1 years). The median (range 100 – 1838 mg·h/L) AUC24 was 452mg·h/L in 2020, 411.97mg·h/L in 2021, and 388mg·h/L in 2022. The vancomycin-associated AKI rate was 13% in 2020, 12% in 2021 and 9% in 2022 ($p = 0.4$). Severe AKI reduced from 8.6% in 2020, 7.8% in 2021, to 3.7% in 2022 ($p = 0.4$).
Conclusion: There was a non-significant trend towards a reduction in vancomycin-associated AKI with the implementation of MIPD.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

422

Real-World Free Fractions and Probability Target Attainment of Cefoperazone/Sulbactam

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Biography:

Yu-Ting is a clinical pharmacist at National Taiwan University Hospital (NTUH), specializing in integrated medicine and general internal medicine. Their clinical practice focuses on managing patients with multiple comorbidities, geriatric populations, and complex polypharmacy in integrated care wards. They provide comprehensive pharmaceutical care, including antibiotic selection and therapeutic drug monitoring for acute infections, medication reconciliation, and drug interaction management. In addition to clinical service, Yu-Ting is actively engaged in research on antibiotic efficacy and adverse effects. Their work also includes database analysis of drug interactions involving novel oral anticoagulants, contributing to safer and more effective medication use. With a commitment to both patient care and clinical research, they strive to optimize pharmacotherapy and improve treatment outcomes through evidence-based practice.

Background: Cefoperazone/Sulbactam (CPZ/SUL) has distinct protein-binding properties, affecting free drug concentrations and probability of target attainment (PTA).
Aim: This study reports real-world free fractions (F) of CPZ/SUL and investigates physiological factors influencing free drug concentrations.
Methods: An observational study was conducted at a tertiary hospital in Taiwan (June–December 2024). Patients receiving CPZ/SUL (1:1) were enrolled to measure free (fCPZ/fSUL) and total concentrations via ultra-high-performance liquid chromatography. Measured fCPZ/fSUL was compared to estimated values (EF: 0.2 for CPZ, 0.8 for SUL). Linear regression analyzed factors affecting free drug levels.
Results: Thirty-three patients (48.5% male, mean age 75.2 ± 13.8) provided 66 CPZ/SUL concentrations. Median F was 0.07 (0.05,0.09) for CPZ and 0.95 (0.87,1.01) for SUL. fCPZ correlated with total-bilirubin ($p < 0.01$), and fSUL with creatinine ($p < 0.01$). PTA for 50% fT>MIC (MIC = 8) was lower using measured vs. estimated fCPZ/fSUL (21.2% vs. 52.5%, $p = 0.01$).
Conclusions: CPZ/SUL free fractions deviated from estimates, reducing PTA. Direct fCPZ/fSUL measurement is crucial for patients with hyperbilirubinemia or renal impairment to optimize dosing and improve treatment outcomes.
Key word: unbound fraction, free drug concentration, probability of target attainment (PTA)

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

423

Should Beta-lactams and Beta-lactamase-Inhibitors Be Co-Formulated? Insights from Beta-lactam Therapeutic Drug Monitoring

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Biography:

Dr Nathalie Chua is a specialist pharmacist (infectious diseases) at the Singapore General Hospital (SGH). She completed her infectious disease residency at Singhealth Post Graduate Allied Health Institute in 2013 and obtained her PharmD at National University of Singapore in 2018. She is a board certified infectious disease pharmacy specialist under US Board of Pharmacy Specialties and a registered specialist pharmacist under Singapore Pharmacy Council since 2021.

She is involved in antimicrobial stewardship and in the research and clinical implementation of antimicrobial therapeutic drug monitoring (TDM) services in SGH to manage difficult-to-treat infections. Her research interests include pharmacokinetics and pharmacodynamics, TDM and antimicrobial resistance.

She is an infectious disease preceptor for the national pharmacy residency programmes in Singapore and a guest lecturer for infectious diseases at the NUS PharmD programme.

She currently represents Singapore as a committee member of the Regional Asia Pacific Section and Young Scientists Committee of IATDMCT.

Background: Beta-lactamase-inhibitors (BLI) are co-formulated with beta-lactams (BL). However, changes in pharmacokinetics and drug exposures may not remain proportional for both components.
Aims: We evaluated percentage of subtherapeutic BLI exposure and compared plasma BL:BLI ratio against original product formulation ratio (8 for piperacillin-tazobactam, 4 for ceftazidime-avibactam and 2 for ceftolozane-tazobactam).
Methods: We retrospectively reviewed patients (≥16 years old) on BL/BLI TDM service in a quaternary hospital
from Oct-2019 to Jan-2025. Blood samples (maximum 4 timepoints within a dosing interval, including peaks and troughs) were collected and assayed using liquid-chromatography-tandem-mass-spectrometry. Unbound BLI troughs>4mg/L were considered subtherapeutic.
Results: Seventy-eight patients were included: 57 males, mean age 60.1 ± 15.0 years; mean body weight 69.8
± 24.6 kg. They received 44 piperacillin-tazobactam, 32 ceftazidime-avibactam, 6 ceftolozane-tazobactam courses, which yielded 395 plasma concentrations (208 piperacillin-tazobactam, 154 ceftazidime-avibactam, 33 ceftolozane-tazobactam). Median (IQR) total drug concentrations were: piperacillin 125.4 (58.1-217.1) mg/L, ceftazidime 74.2 (49.0-108.1) mg/L, ceftolozane 54.8 (44.7-103.2) mg/L, tazobactam 17.7 (8.0-32.0) mg/L, avibactam 14.6 (9.3-21.3) mg/L. Median (IQR) BL:BLI ratios were 7.1 (6.0-8.1), 5.3 (4.1-7.0), and 4.2 (2.8-7.5) for piperacillin-tazobactam, ceftazidime-

avibactam and ceftolozane-tazobactam respectively. Unbound BLI were subtherapeutic for 20 of 62 (32%) tazobactam troughs and 12 of 37 (32%) avibactam troughs.
Conclusion: BLI concentrations were low especially for ceftazidime-avibactam and ceftolozane-tazobactam.
Original BL:BLI ratios were not achieved in plasma. BL TDM alone does not guarantee adequate BLI exposure. TDM should be performed for both BL and BLI. BLIs should be formulated as standalone products for easier dose adjustments.
Keywords: beta-lactam, beta-lactamase inhibitor, tazobactam, avibactam

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

424

Relationship between pharmacokinetics, pharmacogenetics and adverse events in women treated with tamoxifen

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Biography:
Fabienne Thomas graduated from the University Paul Sabatier of Toulouse, France as a pharmacist in 2007. From 2003 to 2007, she was resident and PhD student at the Toulouse Cancer Center (Institut Claudius Regaud) in the Pharmacology lab directed by Prof. Etienne Chatelut. She specialized herself in clinical pharmacology of anticancer drugs with a focus on pharmacogenetics and defended her PhD in 2007. Since 2008, she is professor assistant at the Faculty of Pharmacy in Toulouse where she teaches pharmacology. She has a clinical activity in the Pharmacology lab of the Toulouse Cancer Center as a clinical pharmacologist. Some major activities of her lab are: TDM of anticancer drugs and population PK analyses, DPD phenotyping test (UH2/U) and the pharmacogenetic testing of patients (DPYD, UGT1A1, and TPMT). She was president of the French Clinical Oncopharmacology Group (GPCO) from 2019 to 2022 (now secretary) and is member of RNPGx.

Background: The impact of genetic polymorphisms (SNP) and plasma levels of tamoxifen (TAM) and endoxifen (ENDO) on adverse events (AE) remains controversial.
Aims: This prospective, multicenter, 3-year follow-up study (PHACS, NCT01127295) of adjuvant TAM (20 mg/day) in patients with breast cancer (n=880) aimed to evaluate the relationships between pharmacogenetics, pharmacokinetics of TAM and ENDO and AE.
Methods: Patients were genotyped for 92 SNPs selected from literature in 23 genes including CYP2D6. Each 6-month post-inclusion, residual concentrations for TAM and metabolites were measured and patients were assessed for 28 types of AE (NCI-CTC grade), over 3 years. For each AE, visit and patient a binary (increase in severity since inclusion) and a continuous toxicity variable (increase in severity since inclusion multiplied by grade) were created. Mixed effects generalised linear models were used to explore the relationship between the toxicity variables and TAM and ENDO concentrations, adjusting for genetic polymorphisms, weight and hormonal status.
Results: For the 8 most frequent AE, no statistically significant association was found between ENDO (or TAM) concentrations or CYP2D6 metabolizer status and an increase of severity. SNPs in CYP19A1, UGT2B17 were significantly associated with the risk of having an increase in the severity of sweating or depression since inclusion respectively. CYP2C19*2 allele had a significant protective effect on the occurrence of thrombo-embolic events.
Conclusions: No clear relationship was observed between pharmacokinetics and toxicity. Some genetic polymorphisms may be involved in the occurrence of AE but this requires confrmation in future studies.
Keywords: Tamoxifen, adverse events, pharmacokinetics, pharmacogenetics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

425

Optimizing Busulfan Exposure in Chinese Pediatric Patients Undergoing Allogeneic Hematopoietic Cell Transplantation

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Biography:

Chenrong Huang, Ph.D., is an Associate Professor and Deputy Director of the Department of Pharmacy at the First Affiliated Hospital of Soochow University. In 2011, she conducted research as a visiting scholar at the Japan Clinical Pharmacology Research Association (J-CLIPNET).

Dr. Huang is actively involved in numerous professional organizations, including serving as Standing Committee Member of the division of Therapeutic Drug Monitoring of the Chinese Pharmacological Society, and holding leadership roles in the Jiangsu Provincial Medical Association and Pharmacological Society.

Her research focuses on therapeutic drug monitoring (TDM) and personalized medicine, as well as clinical pharmacology. She has led nine research projects, including grants from the National Natural Science Foundation of China, and has published over 20 SCI-indexed papers as the first or corresponding author. Dr. Huang has contributed to expert consensus documents on TDM and chromatographic techniques and has received many awards.

Background: Therapeutic drug monitoring (TDM)-guided busulfan (BU) dosing improves outcomes in hematopoietic stem cell transplantation (HSCT), but optimal BU exposure (AUC) in Chinese pediatric patients remains unclear.

Aims: This multicenter study aimed to develop a population pharmacokinetic (Pop-PK) model for BU and identify optimal AUC for clinical outcomes in Chinese pediatric HSCT recipients.

Methods: Pediatric patients (n=455) from five Chinese centers receiving BU-based conditioning (2018–2023) were analyzed. A Pop-PK model was constructed to estimated cumulative AUC. Outcomes included event-free survival (EFS), overall survival (OS), and toxicities (hemorrhagic cystitis, acute GVHD, oral mucositis). Exposure-outcome relationships were assessed using restricted cubic spline, Cox proportional hazards, and logistic regression models.

Results: For 3-day regimens, cumulative AUC (AUCs)≥54 mg·h/L was associated with superior 2.7-year EFS vs. AUCs <54 mg·h/L [86.4% (80.1–90.9) vs. 77.7% (70.4–83.5); HR=0.58 (0.34–0.99), P=0.045]. For 4-day regimens, AUCs 70–90 mg·h/L yielded higher 2.7-year EFS (88.9% [75.3–95.2]) vs. AUCs <70 mg·h/L (68.3% [54.2–78.9]; HR=2.94 [1.09–7.92], P=0.033) and AUC >90 mg·h/L (66.1% [43.4–81.4]; HR=3.22 [1.05–9.85], P=0.040). Multivariate analysis identified BU AUC, age, and anti-thymocyte globulin use as predictors of grade ≥2 hemorrhagic cystitis in 3-day regimens.

Conclusion: Targeting BU AUC ≥54 mg·h/L for 3-day regimens and 70–90 mg·h/L for 4-day regimens may improve EFS in Chinese pediatric HSCT patients, supporting TDM-based BU optimization.

Keywords: hematopoietic stem cell transplantation; pediatric pharmacotherapy; population pharmacokinetics; busulfan therapeutic drug monitoring; clinical outcomes

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

426

Clinical Validation of Capillary Microsampling for Venetoclax Pharmacokinetic Monitoring and Home-Based Self-Sampling

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Biography:
Amar Levens is a hospital outpatient pharmacist and researcher specializing in pharmacogenomics and therapeutic drug monitoring. He has been an outpatient pharmacist at Leiden University Medical Center (LUMC) since 2016 and is currently pursuing a PhD at the Department of Clinical Pharmacy & Toxicology under the supervision of Prof. Dr. Jesse Swen and Dr. Dirk Jan Moes.
Beyond his clinical and research work, Amar is Chair of Leiden Academic Network of Pharmacists (https://www.lananet.nl/) and Young Medical Delta (https://www.youngmedicaldelta.nl/en) , where he promotes healthcare innovation and interdisciplinary collaboration. Additionally, as PR Person of LUMC Association for PhD Candidates (https://www.laplumc.org/), he works to enhance the visibility of PhD candidates and their research.

Background: Venetoclax, a potent and expensive oral therapy for hematological malignancies, follows a fixed dosing approach, often leading to suboptimal exposure and both clinical and financial toxicity. Its variable pharmacokinetics (PK) highlight the need for exposure-guided dosing. Capillary microsampling enables easier, more intensive PK assessment beyond trough levels, offering a practical, less invasive alternative to venipuncture.
Aims: To clinically validate the interchangeability of microsampling with venous plasma sampling and evaluate the feasibility of home-based self-microsampling for venetoclax PK-monitoring.
Methods: A bioanalytical assay was validated for venetoclax using the HemaXis DB10 device to collect a fixed blood volume (~10 µL). Clinical validation included 65 paired microsamples and venous plasma samples from 25 venetoclax-treated patients. Method agreement was assessed via Passing–Bablok regression and Bland–Altman analysis. Home-based feasibility was evaluated using both the HemaXis DB10 and Mitra Clamshell devices, based on sample acceptability and usability (System Usability Scale, SUS).
Results: After hematocrit correction, Passing–Bablok analysis showed strong agreement between methods with a regression slope of 0.96 (95% CI: 0.92–1.01) and an intercept of 13.13 (95% CI: −22.02 to 45.64). Bland–Altman analysis showed no significant bias (mean difference: 0.68% [95% CI: −2.46% to 3.81%]), with 95% of concentrations within ±20% of the mean. A total of 76% of home-based self-microsamples were successfully sampled, with median SUS scores of 75 and 78.
Conclusions: Capillary microsampling is a feasible, patient-friendly alternative to venous sampling for venetoclax PK monitoring. Strong agreement with venous sampling and successful home-based implementation support its use for decentralized PK self-monitoring.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

427

Real-world pharmacokinetically guided food intervention optimizes abiraterone treatment in mCRPC

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Biography:

Meike Lunenburg (27) is a pharmacist with a special interest in oncology and therapeutic drug monitoring. During her master thesis, she conducted clinical research at OLVG, where she now works part-time as a researcher in the Department of Pharmacy. Alongside her research activities, she works full-time as a pharmacist at St Antonius Ziekenhuis, focusing on pharmaceutical compounding and oncology patient care. Her research primarily involves optimizing drug exposure in oncology patients through pharmacokinetically guided interventions. With her combined clinical and scientific expertise, she aims to translate research findings into clinical practice applications that improve treatment outcomes.

Background: Taking 1000 mg Abiraterone (Abi) on an empty stomach is an effective treatment for metastatic castration-resistant prostate cancer (mCRPC), improving survival by 4 to 15 months. Abi trough concentrations (Cmin) ≥ 8.4 µg/L are associated with prolonged progression-free survival (12 vs. 7 months). Standard Abi administration resulted in Cmin < 8.4 µg/L in 63% of patients in a tertiary academic hospital, while pharmacologically (TDM) guided Abi with a light meal (food intervention) improved Cmin ≥ 8.4 µg/L in 87.5% [1].
Aims: This prospective study evaluates the feasibility of this Abi TDM food intervention in a secondary hospital setting.
Methods: mCRPC patients from two non-academic hospitals underwent three-monthly Abi Cmin monitoring. Those with Cmin < 8.4 µg/L received a food intervention.
Results: Among 47 included patients (median 2 Cmin samples per patient), 14 (30%) had Cmin < 8.4 µg/L: median 6.1 µg/L (range 2.0–8.3). In 9 patients with follow-up post-intervention, Cmin improved from 6.3 (2.0–8.3) to 9.8 µg/L (3.9–688 µg/L); p = 0.021, achieving Cmin ≥ 8.4 µg/L in 7 (78%) patients (p = 0.016), without added toxicity. Among patients with Cmin ≥ 8.4 µg/L throughout the study, 11 had Cmin > 100 µg/L.
Conclusions: Although the group with subtherapeutic Abi exposure was smaller, presumably due to more non-trough sampling, the food intervention demonstrated comparable efficacy in our community hospital setting. These findings support integrating the TDM-guided Abi food intervention into routine clinical practice for mCRPC management.
[1]Eur J Cancer 2020;130:32
Keywords: Abiraterone, TDM, Pharmacokinetics, Clinical Practice, Prostate Cancer, Real-World

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

428

Real-World Pharmacokinetics of Pembrolizumab in Cancer Patients: A Serial Sampling Study

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Biography:
Dr. Maring is hospital pharmacist - clinical pharmacologist at the Isala Hospital Zwolle and has been involved in many clinical studies on precision dosing in oncology during the last decades.

Background: The dosing of pembrolizumab has been established in phase I-III clinical studies. Based on these studies, flat dose treatment regimens have been developed with the aim of achieving 95% target engagement in at least 90% of patients. A minimum plasma concentration of 10-15 µg/ml has been suggested for adequate target engagement.
Aim: The main objective of this study was to determine the variation in trough levels in cancer patients treated with pembrolizumab during 4 consecutive cycles.
Methods: Patients were treated with pembrolizumab according to the standard schedule for their disease. In one group trough samples were collected at the end of treatment cycle 1-4, just before the next dose. In a second group trough samples were obtained during 3 consecutive cycles after at least 2 earlier treatment cycles.
Results: Patients were treated for lungcancer n=20 (100-200mg/3weeks or 400mg/6 weeks), melanoma n=19 (200-400mg/6weeks) or other cancers n=7 (100-200mg/3weeks or 200-300mg/6weeks).
Trough levels increased from 11±6 µg/ml (n=27) during cycle 1 to respectively 16±8 µg/ml (n=31), 18±8 µg/ml (n=22) and 20±9 µg/ml (n=17) during cycles 2-4. In >2 cycles pretreated patients trough levels were 28±11 µg/ml (n=41), 27±12 µg/ml (37) and 27±10 µg/ml (n=28) during three consecutive cycles.
In at least 87% of all treated patients the trough level was above 15 µg/ml after at least three treatment cycles.
Conclusion: In a high proportion of all pembrolizumab treated patients trough plasma levels were a above 15 µg/ml. This suggests that stretching of dosing intervals might be possible without losing treatment efficacy.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

429

Real-World Exposure-Response Analysis of Abiraterone in Metastatic Castration-Resistant Prostate Cancer

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Biography:

Merin Babu is currently a Ph.D. scholar (former ICMR Senior Research Fellow) in the Department of Medical Oncology at Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi since 2020. With a background in Pharmacology (M.Pharm), she has combined her clinical and pharmacological expertise to focus on optimizing cancer treatment through therapeutic drug monitoring (TDM). Her primary focus lies in Therapeutic Drug Monitoring (TDM) in Oncology, particularly in optimizing the use of targeted therapies for solid tumors. Her contribution to real-world data generation on exposure-toxicity relationships of multi-kinase inhibitors such as Lenvatinib in hepatocellular carcinoma (HCC) was recently awarded both the ICMR International Travel Grant and the IATDMCT Travel Grant to present her oral research at the 22nd International Congress of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT 2024) in Banff, Canada. Her work aims to bridge the gap between clinical pharmacology and personalized cancer treatment, ensuring safe and effective dosing strategies for patients. Merin is passionate about translating pharmacological insights into personalized oncology care, aiming to enhance treatment outcomes and minimize adverse effects through the application of TDM into routine oncology practice in India

Background: The NCCN recently endorsed low-dose abiraterone as a cost-effective alternative to the standard dose, potentially improving access and reducing costs globally.
Aim: To evaluate the exposure-response relationship of low-dose (250 mg/day with food) versus standard-dose abiraterone (1000 mg/day fasting) in metastatic castration-resistant prostate cancer (mCRPC) patients and assess the feasibility of achieving the target abiraterone concentration (8.4 ng/mL).
Methods: A prospective observational pilot study (2023–2025) included 20 patients in each dosing cohort. Plasma abiraterone trough concentrations were analyzed using LC-MS. The primary objective was to compare therapeutic drug levels and clinical efficacy.
Results: Among twenty patients receiving low dose, 15 (75%) achieved >50% PSA decline at 3 months. Similarly, in the standard dose group (n=18), 15 (83%) demonstrated >50% PSA reduction (p=0.397). PFS was 24.8 vs. 19.54 months in the low dose vs standard dose group and OS was 27.1 vs. 24.78 months respectively. The abiraterone plasma trough level was 4.1 ± 1.71ng/mL and 21.6 ± 7.96 ng/mL in the low dose and standard dose respectively. This analysis showed a weak positive relationship (r = 0.26, p = 0.575) between concentration and PSA levels at low dose, while at standard dose, a moderate negative correlation (r = -0.57, p = 0.433) was observed.

Conclusion: Low-dose abiraterone demonstrated a comparable PSA response to standard dosing, suggesting potential non-inferiority, with slightly better survival outcomes. Further studies, including RCTs are needed to confirm these findings and optimize dosing strategies.
Keywords: Abiraterone Acetate, mCRPC, Exposure-Response Relationship

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

430

Towards model-informed precision dosing and optimal sampling of 5-FU for gastrointestinal cancers

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Biography:

Zhiyuan Tan is currently a PhD candidate in quantitative clinical pharmacology at Division of System Pharmacology and Pharmacy, Leiden Academic Center for Drug Research, Leiden University and Department of Clinical Pharmacy & Toxicology, Leiden University Medical center since 2021. His research is focused on optimizing dosing in oncology patients by analyzing available pharmacokinetics and pharmacodynamics data from routine clinical setting. Before moving to the Netherlands, he was trained as a pharmacist within the field of TDM in oncology and hematology, as well as a one-year intern in clinical CRO company. His aim is to expose and close the dosing gap between clinical trials and the real-world setting with different modeling and simulation approaches.

Background: 5-Fluorouracil (5-FU) is the cornerstone of first-line chemotherapy for various gastrointestinal cancers. 5-FU has due to myelosuppression and other toxicities, a narrow therapeutic window, for which recently an area under the curve (AUC0-inf) target 20–30 mg·h/L was proposed.
Aims: Primary aim was to develop a 5-FU population pharmacokinetic (POPPK) model and identify covariates. Secondary aims were to develop a limited sampling strategy (LSS) to estimate individual AUC0-inf and to develop an MIPD application to facilitate both initial dose and subsequent dose individualization.
Methods: Retrospective data from multiple centers was collected to establish the 5-FU POPPK model with non-linear mixed effect modelling. A workflow to identify LSS was developed using simulated data from 1000 virtual patients of the final model. The final POPPK model was integrated into a user-friendly shiny application to provide individualized dosing recommendations.
Results: 140 individuals with 435 PK samples were best described using a two-compartment model with Michaelis-Menten elimination. Body surface area (BSA) significantly influenced the maximum rate of reaction (Vmax) and was implemented using allometric scaling with an exponent of 1.14 (RSE24%). For bolus and 46h continuous infusion, the LSS was T=0.1(end-of-bolus),1,3 hours after treatment initiation, while for 46h continuous infusion, the LSS was T=2,3,5 hours. MIPD algorithms were developed and implemented in a shiny application(https://tanzy1995.shinyapps.io/5FU-shiny-app/).

Conclusions: The developed POPPK model effectively described 5-FU pharmacokinetics with BSA as covariate. In addition, the LSS and the shiny MIPD application demonstrated the potential for dose individualization of 5-FU.
Key Words: 5-Fluorouracil, population pharmacokinetics, MIPD, optimal sampling

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

431

A joint target-mediated drug disposition/time-to-event model of ramucirumab in gastric cancer

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Biography:
I am an assistant teacher of pharmacology in Tours, France. I defended my thesis on the influence of antigen mass on monoclonal antibodies elimination using target-mediated drug disposition models. My field of study is optimizing the use of monoclonal antibodies using therapeutic drug monitoring and model-informed precision dosing.

Background: Ramucirumab is an anti-VEGFR2 monoclonal antibody used in gastric and gastroesophageal junction cancers. A pharmacokinetic-pharmacodynamic (PK-PD) relationship has been highlighted in these cancers (Kim 2018, Tabernero 2017) as well as non-small cell lung cancer (Akagi 2023), using Kaplan-Meier and Cox proportional hazards analyses. However, these approaches are subject to confounding factors as disease activity can also influence drug levels (Lobet 2023).
Aims: This study aimed to assess the relationship between ramucirumab pharmacokinetics, target occupancy and overall survival (OS) using joint population target-mediated drug disposition (TMDD) and parametric survival modeling.
Methods: Data were obtained from a phase II clinical trial (SOCRATE, EudraCT 2024-513515-27-00), including 70 patients receiving ramucirumab every 2 weeks up to progression or grade 3 toxicity. Ramucirumab concentrations were measured using an ELISA method (Desvignes 2021). Ramucirumab PK and hazard function for survival were described using a TMDD and a log-logistic model, respectively.
Results: Estimated parameters were volumes of distribution (V1=2.03L, V2=2.89L), clearances (CL=0.23L/d, Q=2.01L/d), baseline target level (R0=30.2nM), immune complex elimination rate (kout=0.91d-1) and dissociation constant (KSS=0.47nM). Overall survival significantly increased with ramucirumab exposure, using either concentrations or target occupancy in the model (Δ-2LL = -42.46 and -45.10, respectively).
Conclusions: This study is the first to simultaneously depict the relationship between ramucirumab PK, target occupancy and OS, and demonstrated target-mediated nonlinear PK and an association between ramucirumab exposure and clinical efficacy. A nonlinear PK was previously suspected but never described (O'Brien 2017). These results show that TDM of ramucirumab could be promising.
Key words: Ramucirumab, oncology, pharmacokinetics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

432

Model-Based Precision Dosing and Non-Adherence Remediation of Isoniazid in Chinese Tuberculosis Patients

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Biography:

Mr Cheng studies the clinical pharmacy and clinical pharmacokinetics. He has a master degree of pharmacy from Soochow University. Now he is a clinical pharmacist in Zhejiang Hospital of Integrated Traditional Chinese and Western Medicine (also named Zhejiang Tuberculosis Diagnosis and Treatment Center). His research has been published in Cell Reports, Journal of Neuroinflammation, Infection and Drug Resistance and other journals.

Background: Isoniazid (INH), a first-line drug to treat tuberculosis (TB) for more than 50 years. However, large inter-individual variability was found in its pharmacokinetics, and effects of non-adherence to INH treatment and optimal remedial dosing remains unclear.
Aims: This study aimed to develop a population pharmacokinetics (PPK) model of INH in Chinese patients with TB, to provide model-informed precision dosing and explore appropriate remedial dosing regimens for non-adherent patients.
Methods: 1012 INH therapeutic drug monitoring (TDM) results from 736 TB patients were included. A nonlinear mixed-effects modeling was used to analyze the PPK of INH. Using Monte Carlo simulations to determine optimal dosage regimens and design remedial dosing regimens.
Results: A two-compartmental model, including first-order absorption and elimination with allometric scaling, was found to best describe the PK characteristics of INH. A mixture model was used to characterize dual rates of INH elimination. Estimates of apparent clearance in fast and slow eliminators were 28.0 and 11.2 L/h, respectively. Monte Carlo simulations determined optimal dosage regimens for slow and fast eliminators with different body weight. For remedial dosing regimens, the missed dose should be taken as soon as possible when the delay does not exceed 12 h, and an additional dose is not needed. On delaying a INH dose exceed 12 h, only need to take the next single dose normally.
Conclusions: TDM and PPK modeling and simulation provide valid evidence on the precision dosing and remedial dosing regimen of INH.
Keywords: Isoniazid; PPK; model-based precision dosing; remedial dosing; tuberculosis; TDM

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

433

Intravenous cefuroxime target attainment in neonates and infants: pooled population pharmacokinetic study

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Biography:
Stef Schouwenburg is a Pharmacist-Researcher from Rotterdam, The Netherlands. He works at the Department of Hospital Pharmacy in the Erasmus University Medical Center.

Background: Cefuroxime is a widely prescribed beta-lactam antibiotic, particularly in pediatric cardiac and medical-surgical intensive care units.
Aims: To describe intravenous cefuroxime disposition in critically ill pediatric patients. Moreover, target attainment of currently applied dosing regimens were evaluated and suggestions for improvement of these dosing regimens were provided.
Methods: This pooled population pharmacokinetic (popPK) study combined two datasets for analysis in NONMEM v7.5. Cefuroxime exposure was simulated using the percentage of time above the minimum inhibitory concentration (%T>MIC). PK profiles of different dosage regimens (intermittent/continuous) were simulated with the developed popPK model. A target of 90% of cases 100%T>(4x)MIC8mg/L was used.
Results: The cohort consisted of 45 pediatric patient's with a median (range) age of 391 days (0-6131), and bodyweight of 9.0 kg (2.8-70.0). A two-compartment popPK model with first-order elimination and allometric scaling best described cefuroxime disposition. Postnatal age and creatinine clearance were the best descriptive covariates for cefuroxime clearance. Simulations evaluating the current cefuroxime dosing regimens stratified for eGFR levels illustrated moderate (eGFR <30 and 30-80 mL/min./1.73m2) and poor (eGFR 80-120 and >120 mL/min/1.73m2) cefuroxime target attainment across the entire age range. Alternative dosing regimens, including four times daily schedules and continuous infusion, improved target attainment, particularly in older children and those with augmented renal clearance.
Conclusions: While applying the current dosing regimens, underexposure due to enhance renal functions is possible. Future research should focus on individualized dosing strategies to optimize cefuroxime exposure and efficacy in pediatric populations.
Key Words: Cefuroxime, Pediatrics, Population pharmacokinetics, PICU

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

434

Reinforcement Learning for Generalized Dose Optimization

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Biography:

Dr. Neely is a Professor of Pediatrics and Clinical Scholar in the Department of Pediatrics at the Keck School of Medicine of the University of Southern California. He is a Board-certified pediatric infectious disease specialist physician with more than 20 years of experience in patient care, research, and mentoring of over 50 undergraduates, medical students, residents, fellows, PhD students, post-docs, and visiting scholars in clinical pharmacology and pharmacometrics. He serves as the Chief of Infectious Diseases at the Children's Hospital of Los Angeles (CHLA) and the director of the CHLA Laboratory of Applied Pharmacokinetics and Bioinformatics. Dr. Neely's lab created and maintains the Pmetrics population modeling and simulation package for R and the BestDose software to optimize individual patient dosing through applied pharmacometric and machine learning techniques. His lab is increasingly involved in the use of artificial intelligence to enhance the use of drug therapies. He has recently expanded his lab to include hollow fiber capabilities, focusing on optimizing treatment of serious infections in pediatric patients such as Mycobacterium abscessus, Staphylococcus aureus, cytomegalovirus, and resistant Gram-Negative bacteria. His research has been continually funded by the NIH since 2000, with additional funding from FDA and private foundations. He lectures and conducts pharmacometric workshops internationally and has published almost 200 peer-reviewed publications and ten book chapters.

Background: PopPK models are drug and population specific and combining them for model informed personalized dosing (MIPD) has thus far been limited to averaging dose recommendations from different models made for one drug in similar populations.
Aims: Use reinforcement learning (RL) to combine diverse popPK models for optimized dosing
Methods: We developed non-parametric population models for theophylline in adults and voriconazole in children and adult and from these models simulated 50 patients and concentration-time profiles for each drug after standard dosing, splitting the data into training (60%) and validation (40%) subsets. With one simulated concentration and set of covariates (drug, weight, age for voriconazole, drug for theophylline), we trained a deep RL agent to predict the optimal loading and maintenance doses to achieve specified concentration targets within a therapeutic window.
Results: In the validation data, the agent found loading and maintenance doses that achieved therapeutic concentrations in 90.5% of episodes overall. Specifically, therapeutic concentrations were achieved in 84% of episodes for voriconazole and 98% for theophylline.
Conclusions: We present a completely novel approach to MIPD that learns across drugs and populations, with subsequent creation of a single, generalized model where the drug itself becomes a

covariate. Our results suggest that the method is feasible from typical popPK models and can be extended to more drugs and populations.
Keywords: Dose optimization, patient individualization, reinforcement learning.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

435

An optimised fluconazole dosing strategy in critically ill patients

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Biography:

Luong Vuong holds a Pharm.D. from Hanoi University of Pharmacy, Vietnam, along with a Master's in Epidemiology from the University of Antwerp, Belgium. He is passionate about combatting antimicrobial resistance, a significant healthcare challenge in his home country Vietnam. He's currently doing a PhD in pharmacometrics at Leuven Pharmacometrics Research Group, KU Leuven, where his research focuses on utilizing pharmacometrics to optimise antimicrobial dosing in intensive care unit patients to improve their clinical outcomes. Besides, he is also interested in enhancing the methodological aspect of pharmacometrics research.

Background: Invasive candidiasis, particularly candidaemia, is a life-threatening complication in critically ill patients. Fluconazole is the recommended step-down therapy from echinocandins for fluconazole-susceptible Candida spp. However, standard fluconazole dosing does not achieve adequate exposure in critically ill patients.
Aims: This study aimed to identify factors that impact fluconazole target attainment and provide a dosing regimen ensuring adequate pharmacokinetic–pharmacodynamic (PKPD) target attainment in critically ill patients.
Methods: An individual patient data meta-analysis was conducted, combining fluconazole concentration data from eight published studies. We developed a population pharmacokinetics (popPK) model and used multiple imputation to handle missing covariate data. We performed Monte Carlo simulations to identify a dosing strategy with at least a 90% probability of PKPD target attainment (PTA) in every patient.
Results: Data from 177 critically ill patients were included. A two-compartment popPK model with linear elimination best described the data. Continuous renal replacement therapy (CRRT) status, estimated glomerular filtration rate, and total body weight (BW) were statistically significant covariates. However, with standard dosing, only CRRT status and BW were clinically relevant with the PTA dropping below 90% for all patients on CRRT, and for patients not undergoing CRRT weighing more than 60 kg. An optimised dosing regimen considering the patient's CRRT status and BW is proposed.

Conclusion: We have developed a fluconazole dosing regimen that could achieve adequate population-wide PKPD target attainment in critically ill patients. Confirmation that the proposed dosing regimen achieves optimal fluconazole exposure is required.

Keywords: Population pharmacokinetics, Monte Carlo simulation, Individual patient data meta-analysis

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

436

Performance evaluation of ceftriaxone population pharmacokinetic models in children

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Biography:
Stef Schouwenburg is a Pharmacist-Researcher from Rotterdam, the Netherlands. He works at the Erasmus University Medical Center and is finishing up his PhD-trajectory.

Background: Sepsis affects approximately 8% of pediatric intensive care unit (PICU) admissions in high-income countries. Ceftriaxone, a broad-spectrum beta-lactam antibiotic, is widely used for treating severe infections and bacterial meningitis in children. Despite its frequent use, limited studies address the population pharmacokinetic (popPK) of ceftriaxone in pediatrics.
Aims: To externally evaluate pediatric ceftriaxone popPK model peformance, enabling selection of the model best suited to this population.
Methods: This study used data from the EXPAT Kids study, a prospective PK/PD study. Included popPK models were implemented in NONMEM, with diagnostic goodness-of-fit and visual predictive check analyses performed to assess model accuracy. Predictive performance was evaluated using the relative prediction error, relative root mean square error, and mean (absolute) percentage error.
Results: The predictive performance of the evaluated models varied widely. Included models showed only modest performance and generally seem to overpredict ceftriaxone concentrations. Unbound ceftriaxone popPK models did not perform adequately. None of the models met all the predefined thresholds for accuracy and precision.
Conclusion: Our external dataset comprised high ceftriaxone trough concentrations, indicating re-evaluation of current ceftriaxone dosing regimens to minimize the risk of overdosing and prevent toxicity. Future research should focus on the fine dosing balance for ceftriaxone (especially in meningitis patients) considering adequate exposure but preventing high trough concentrations. Model informed precision dosing may enhance the use of the optimal individual dosage for critically ill children. However, our findings highlight the importance of externally evaluating ceftriaxone popPK models in the PICU population.
Key words: Ceftriaxone, Population Pharmacokinetics, Pediatrics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

437

Clozapine optimal timing for optimal monitoring (COTTON)

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Biography:

Afnan is training to become both a hospital pharmacist and a clinical pharmacologist, with a strong interest in therapy optimization. She has always been driven by a desire to make a meaningful societal contribution, which led her to the medical field. Combining her analytical mindset with a passion for patient care, she found her place in clinical pharmacology and hospital pharmacy, where she works to refine drug therapy and improve patient outcomes.

Driven by her commitment to individualized pharmacotherapy, she chose a traineeship that provides extensive experience in wards where therapeutic drug monitoring (TDM) and pharmacokinetic/pharmacodynamic (PK/PD) relationships are particularly relevant. Through her work in psychiatry, intensive care, and infectious diseases, she continues to develop a deeper understanding of drug exposure variability and its clinical implications. By integrating research with hands-on clinical experience, she strives to enhance medication management and contribute to safer, more effective pharmacotherapy.

Background: Therapeutic drug monitoring (TDM) is essential for optimizing clozapine treatment. Current guidelines recommend blood sampling 12 (±2) hours after intake for once-daily dosing. However, this timing is primarily based on twice-daily dosing regimens and its suitability for once daily dosing remains uncertain.
Aims: This study aims to evaluate the validity of current TDM practice for once-daily clozapine dosing.
Methods: This retrospective, single-center study includes patients with treatment-resistant schizophrenia spectrum disorders on stable once-daily clozapine, with TDM performed as part of standard care. Bayesian analysis was used to predict individual concentration-time profiles. Predicted clozapine concentrations at 10, 11, 13, and 14 hours post-intake were compared to the 12-hour reference value, with deviations exceeding 20% considered clinically significant.
Results: Data were collected from seven patients (86% male, 14% non-smoker) with a clozapine dose of 246±109 mg (mean±SD). A total of 22 clozapine samples were analyzed, of which two outliers were excluded. The mean clozapine concentration at t=12 was 608±255 µg/L. The mean percentage differences from the 12-hour reference value were 6.4±2.0%, 3.1±1.0%, -2.9±1.0%, and -5.7±1.8% at t=10, 11, 13 and 14 hours, respectively.

Conclusions: These preliminary findings suggest that the current sampling window of 12 (±2) hours post-intake is appropriate for the clinical interpretation of clozapine levels in once-daily dosing. However, given the limited dataset and absence of the consideration of inter-occasion PK variability (IOV), additional data and further analysis is required to confirm the sampling window for once-daily clozapine dosing.

Keywords: Clozapine, therapeutic drug monitoring, population pharmacokinetics, sampling time, schizophrenia

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

438

Comparative Evaluation of Approaches to Convert Microsampled Capillary Blood-Based to Plasma-Based Results

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Biography:
In 2021, Laura graduated as a pharmacist at Ghent University. Mainly due to the interesting research she was involved in during her Master's thesis at the Laboratory of Toxicology of prof. Christophe Stove, she decided to pursue a career in research. Shortly after graduating, she started a PhD at the Laboratory of Toxicology. Her research is mainly focused on two topics. First, she is setting up an LC-(HR)MS-MS method to monitor drug-protein adducts (in plasma), which are formed upon exposure to (illicit) drugs. Second, she is also working on different microsampling-related topics (i.e., the evaluation of novel technologies, conversion approaches, Hct determination methodologies,…).

Background: The past decades have witnessed a growing interest in patient-centric sampling, including capillary blood microsampling. Despite its advancements, a key issue lies in interpreting capillary blood results against existing plasma-based reference ranges. To address this challenge, various methodologies to convert capillary blood concentrations to plasma equivalents have been proposed.
Aims: This study aimed at systematically evaluating and comparing different methodologies for converting capillary blood-based to venous plasma-based results using clinical pharmacokinetic (PK) data of paracetamol and metabolites.
Methods: Paired finger-prick volumetric absorptive microsampling (VAMS) and venous blood samples were collected from 55 patients. For each analyte, VAMS-based results were converted using multiple approaches, including conversion based on the hematocrit (Hct), the median (time-dependent) capillary-to-plasma ratio, Passing-Bablok regression analysis, and linear mixed-effects modeling. Performance was assessed by comparing the agreement between converted capillary blood-based and actual plasma-based results to predefined analytical and clinical acceptance criteria.
Results: All approaches, except Hct-based conversion, yielded acceptable results, with minor variations in analytical performance. Additionally, the time after paracetamol dosing proved to be a significant covariate for adequate conversion for all except one analytes. Predicted Cmax and AUC0-t values using converted VAMS-based results were within bio-equivalence criteria (80–125%) for all, but one (i.e., Hct), conversion approaches.
Conclusions: Both from analytical and clinical perspectives, this study demonstrated the reliability of different approaches to convert capillary blood-based to plasma-based results. Additionally, this study framework may guide future microsampling-based studies aiming at converting capillary blood concentrations.
Key Words: Microsampling, Conversion Approaches, VAMS, Pharmacokinetics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

439

Does microsampling enhance preanalytical stability of uracil in dihydropyrimidine dehydrogenase (DPD) phenotyping?

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Biography:

Kevin Vandenbroucke graduated as a pharmacist at Ghent University and obtained his Master's degree in Drug Development in 2023. A few months later, he started a PhD at the Laboratory of Toxicology headed by Professor Christophe Stove. His main focus lies on the development of innovative LC-MS/MS based methods to determine small molecule metabolic biomarkers, implementing dried blood microsampling. Secondly, he is also exploring automation approaches to improve the bioanalytical workflow.

Background: Over 80% of the rate-limiting step in 5-fluorouracil degradation is catalysed by the pivotal DPD enzyme. Known risk factors for severe toxicity are (partial) DPD deficiencies, which are currently evaluated prior to chemotherapy by DPD phenotyping. The latter encompasses determination of the endogenous analytes uracil and dihydrouracil, with elevated plasma uracil indicating impaired DPD functionality, requiring treatment adjustment. However, challenges arise in the preanalytical phase, as uracil levels quickly rise after blood sampling, risking false positive results.
Aims: Assess whether dried blood spots (DBS) offer improved preanalytical stability in uracil determination.
Methods: An LC-MS/MS method, targeting uracil, dihydrouracil and uridine, was developed to analyse (dried) blood samples. Stability in venous DBS was assessed after one week storage at ambient conditions and compared with liquid microsamples. A study in healthy volunteers was performed to evaluate differences between venous and capillary DBS.
Results: Analyte concentrations in liquid whole blood exceeded the 15% threshold within 5h, with uracil rising to 700% after 48h. In venous DBS, uracil levels only slightly increased upon drying, stabilizing at a mean increase of 36%±17 for at least one week. Uracil concentrations were significantly higher in capillary than in venous DBS (264%±42) and showed large within-subject variation (26%). Variability in venous DBS remained limited.
Conclusion: Capillary DBS showed both higher and inconsistent uracil levels compared to venous DBS. However, as preanalytical stability is significantly improved, with limited variation, this study suggests that venous DBS are possibly suitable for DPD phenotyping.
Key Words: Microsampling, uracil, DPD, phenotyping, stability

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

440

Reducing Healthcare's Carbon Footprint: Environmental Benefits of Transporting Microsamples vs. Frozen Plasma

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Biography:

Janice Johnstone is a Lab Manager at the University of Newcastle, specializing in pharmacology and toxicology. With qualifications in environmental science, she is able to effectively connect health and environmental research. Janice is involved in research focused on therapeutic drug monitoring (TDM), clinical pharmacokinetics, and the environmental impact of microsampling.
Her work includes developing strategies to reduce pharmaceutical waste, minimize environmental impact, and promote sustainable practices within healthcare. She is currently collaborating on multiple projects aimed at educating clinicians and healthcare professionals about sustainability in their practice. Janice advocates for greener management practices and improved pharmaceutical disposal methods, ensuring that patient care aligns with both health and environmental goals.

Background: Healthcare accounts for 4-5% of the world's carbon footprint. The carbon emissions associated with blood tests are predominantly generated through the transportation of the patient to a collection centre, the equipment used for sample collection and the transport of the sample to the laboratory. Transportation emissions are significant in countries like Australia where patients live in remote areas which are long distances from laboratories.
Aims: To calculate the carbon emissions from transportation of a Telimmune® card and frozen plasma sample from collection site to the laboratory (888km) and the total carbon savings in a pilot study.
Methods: The transportation carbon emissions were calculated using the Carboncare CO_2 Emissions Calculator (based on ISO 14083:2023) and the total carbon savings was based on 50 patients.
Results: The carbon emissions of transporting a frozen plasma sample and a Telimmune® Card were 2.56 and 0.01 kg Co_2e, respectively. The transport of the card produced 99.6% less carbon compared to plasma, a total savings of 127.4 kg of Co_2e.
Discussion: The use of microsampling devices for Therapeutic Drug Monitoring can reduce the carbon footprint of blood sampling with transport alone. A comprehensive Life Cycle Assessment of blood collection to include patient travel, sample collection, sample transport, sample packaging and storage conditions (before, after and during transport), and other microsampling devices is required to have a full understanding of the carbon savings of microsampling compared to traditional blood collection methods.
Keywords: Microsampling, Carbon Emissions, Sustainability in Healthcare, Environmental Impact, Blood Sample Transport, Therapeutic Drug Monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

441

Volumetric absorptive microsampling (VAMS) for therapeutic drug monitoring of antiepileptics in children

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Biography:
Raffaele Simeoli is a pharmacologist working on Therapeutic Drug Monitoring (TDM) in pediatric field. Following his bachelor's degree in Pharmacy and Ph.D in Pharmacological Sciences, he has spent four years in London working on different pre-clinical areas. Actually, he works as Researcher at Bambino Gesù Children's Hospital in Rome (Italy).

Background: Epilepsy is a chronic neurologic disorder that significantly impacts on the everyday quality of life of patients. The use of multiple concomitant medications is associated to drug-drug interactions (DDIs) and highlights the utility of therapeutic drug monitoring (TDM). Volumetric absorptive microsampling (VAMS) are emerging tools for TDM of several drugs including antiepileptics (AEs).
Aim: To compare the concentrations of carbamazepine (CBZ), levetiracetam (LEV), lacosamide (LCS), topiramate (TPR) in both plasma and VAMS samples.
Methods: VAMS were collected by fingerprick in pediatric patients followed at our Centre. Patients were also subjected to conventional venous blood sampling. Plasma and VAMS samples were analysed by UHPLC-MS/MS using a validated kit for determination of AE (ClinMass LC-MS/MS Complete Kit®, RECIPE+). A cross-validation analysis was performed by using Spearman correlation coefficient (r), Deming regression and Bland-Altman plot.
Results: A positive significant correlation ($p<0.001$) was found between VAMS and plasma concentrations for CBZ (r=0.80) with its metabolites Diol (r=0.92) and Epoxide (r=0.90), LEV (r=0.87), LCS (r=0.91) and TPR (r=0.95). Bland-Altman analysis showed a % bias of -0.90 for CBZ, 7.76 for Diol, -0.55 for Epoxide, 4.56 for LEV, -13.09 for TPR and -12.22 for LCS.
Conclusions: Our results show a good agreement between plasma and VAMS, suggesting their use for TDM of AEs during the routine clinical practice. Due to the low blood volume required, VAMS are a compliant alternative to conventional venipuncture for pediatric patients, and, following an adequate cross-validation, they could represent a valid opportunity for promoting remote TDM.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

442

Volumetric Absorptive Microsampling (VAMS) to Measure Steroids in Congenital Adrenal Hyperplasia Patients

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Biography:

Hanna De Baets studied Pharmaceutical Sciences at Ghent University. She obtained her degree as Master in Drug Development in June 2022 and started her PhD at the Laboratory of Toxicology of Professor Stove at the Faculty of Pharmaceutical Sciences at Ghent University in september that year. The focus of her PhD is the development of dried blood microsampling-assisted LC-MS/MS methods for steroid testing. Currently, she is also working on a study evaluating the applicability of dried blood microsampling for therapeutic drug monitoring of patients taking immunosuppressant drug therapy.

Background: Steroid hormone measurement in blood is crucial for diagnosing and monitoring endocrine disorders, including congenital adrenal hyperplasia (CAH), which results from enzymatic defects in the steroidogenesis pathway. CAH patients require lifelong hormone replacement therapy to manage adrenal insufficiency and regulate excess androgen levels. Microsampling provides a less invasive alternative to frequent venous blood sampling, particularly in paediatric CAH patients, enabling at-home follow-up.
Aims: The aim of this study was to set up a microsampling method utilizing 20 µL VAMS samples for determining androstenedione, 17α-hydroxyprogesterone and 11-ketotestosterone to follow-up CAH patients.
Methods: LC-MS/MS methods were developed and optimized for a broad panel of endogenous steroids, including testosterone, androstenedione, 17α-hydroxyprogesterone and 11-ketotestosterone, allowing broad applicability of the method. An extraction protocol for VAMS samples was optimized to maximize the sensitivity of the method and samples from healthy volunteers were analysed.
Results: Two separate LC-MS/MS methods were developed, allowing detection in either positive or negative ionization mode and allowing separation of all isomeric compounds. A liquid-liquid extraction protocol was optimized resulting in an LLOQ as low as 20 pg/mL for androstenedione and 500 pg/mL for 17α-hydroxyprogesterone. Endogenous levels of androstenedione and 17α-hydroxyprogesterone could be measured in 20 µL VAMS samples from healthy volunteers.
Conclusions: A sensitive LC-MS/MS method was developed to determine a broad panel of endogenous steroids in 20 µL VAMS samples. Endogenous levels in healthy volunteers could be determined, confirming adequate sensitivity for use in CAH patients.
Key Words: Volumetric Absorptive Microsampling, Steroid profiling, Congenital Adrenal Hyperplasia

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

443

Plasma-To-DBS Ratio As transversal Conversion Factor For DBS-Methods: The Case Of Imatinib

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Biography:

Bianca Posocco has been a healthcare researcher at the Experimental and Clinical Pharmacology Unit of CRO Aviano since 2019. She holds a Master's degree in Chemistry from the University of Padua (2011) and earned a PhD in Pharmaceutical Sciences and Technology from the University of Trieste (2015). She is a licensed chemist and a member of the FVG Chemists and Physicists Association. Her research focuses on developing LC-MS/MS analytical methods for quantifying anticancer drugs in plasma and dried blood spots, supporting pharmacokinetic studies in precision medicine. She contributes to Phase Ib clinical trials and therapeutic drug monitoring (TDM). Bianca has participated in major national (AIRC 5x1000) and international (Horizon 2020) projects aimed at developing point-of-care systems for anticancer drug analysis.

Background: Various DBS-based methods, both volumetric and non-volumetric, have been published for imatinib quantification, each proposing a unique correction factor (CF). Since CF represents the plasma-to-whole blood concentration ratio (or vice versa), it should ideally remain consistent across different assays.
Aims: This study aims to determine whether different DBS-methods for imatinib quantification yield the same CF, enabling cross-validation of conversion strategies across methods and patient samples, addressing the common challenge of limited sample size in clinical validation.
Methods: A DBS-based LC-MS method quantified imatinib in patient samples (NCT06822959) using Capitainer B and HemaXis DB10. Plasma concentrations were estimated using a blood-to-plasma CF. Statistical analyses included Passing–Bablok and Bland–Altman tests, with CF comparisons to previously published DBS-methods.
Results: An haematocrit independent (22-55%) LC-MS method for imatinib quantification in Capitainer B and HemaXis DB10 was developed and validated. Seventy five paired DBS and plasma samples were collected from 28 patients and used to calculate the CF (0.78 for Capitainer, 0.82 for HemaXis). A strong correlation (percentage difference within ±20% in > 90%) between the estimated and actual plasma concentrations for both devices was observed and statistically demonstrated. The same agreement (> 90%) was observed when using the CFs previously proposed in different DBS-methods (2 non-volumetric assays and 1 using VAMS).
Conclusions: All the calculated CFs accurately represent the relationship between plasma and DBS concentrations across various DBS-based methods, making them applicable to future methods regardless of characteristics such as volumetric/non-volumetric DBS or collection device type.
Keywords: imatinib, TDM, DBS, LC-MS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

444

Microsampling for adherence monitoring of coronary artery disease drugs: Method development

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Biography:
Diana Kretschmer studied pharmacy at the University of Greifswald, Germany, and graduated in 2022. She then completed her diploma thesis in the field of Pharmaceutical Biology in Greifswald under the supervision of Prof. Günther. After that she spent her research stay at the University of Florida, Gainesville, USA, at the Department of Pharmacotherapy and Translational Research in the working group of Prof. Markowitz. She received her license to practice as a pharmacist in 2023. Since June 2024, she is a PhD student at the Saarland University in the Department of Experimental and Clinical Toxicology and Pharmacology in Homburg, Germany, under the supervision of Prof. Meyer. Her research area there is LC/MS method development.

Background: Microsampling is an alternative sampling strategy for adherence monitoring. Some devices like volumetric absorptive microsampling (VAMS) and Capitainer-B allow the collection of defined volumes of capillary blood. Both have already been successfully applied for therapeutic drug monitoring and adherence assessment.
Aims: The aim was to develop a microsampling procedure to be used for adherence monitoring of 15 drugs in the context of coronary artery disease (CAD). Sampling by VAMS and Capitainer-B should be evaluated and compared.
Methods: Amlodipine, atenolol, atorvastatin, bisoprolol, carvedilol, clopidogrel, diltiazem, lercanidipine, metoprolol, nebivolol, prasugrel, rosuvastatin, salicylic acid, simvastatin hydroxy acid, and verapamil were included. VAMS-tips and Capitainer-B-disks loaded with 10 µL capillary blood were extracted by adding 200 µL of methanol. After shaking and centrifugation, the supernatant was evaporated, reconstituted, and analyzed using an LC-Orbitrap system. Isotope dilution mass spectrometry was used for quantification and the validation was based on recommendations of e.g., the European Medicines Agency and the IATDMCT.
Results: Both devices were found to be suitable for sample collection and extraction. Selectivity was given for all analytes except for prasugrel. Matrix effects for Capitainer-B were higher for most analytes compared to VAMS. Isotope dilution mass spectrometry allowed the quantification of all analytes except prasugrel. Accuracy and precision data were acceptable with exception of lercanidipine (both devices) and atorvastatin (only Capitainer-B).
Conclusions: A quantitative method for analysis of 15 drugs used for the treatment of CAD was successfully developed and validated, and shall be applied for future adherence monitoring.
Keywords: Microsampling, LC-MS, Adherence, Validation

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W200

Determination of methotrexate polyglutamates (MTXPGs) in VAMS microsamples for monitoring adult adherence

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Biography:

Dr. Arkadiusz Kocur is an associate professor of pharmacokinetics and bioanalysis in the Department of Drug Chemistry and Pharmaceutical and Biomedical Analysis at the Medical University of Warsaw, Poland. He also works in clinical pharmacokinetics related to therapeutic drug monitoring and the toxicology unit at the Children's Memorial Health Institute. Dr. Kocur leads the pharmacokinetics of the AntiSepsis study. His research interests encompass bioanalysis, immunosuppressants, pharmacokinetics, pharmacodynamics, and therapeutic drug monitoring.

Background: Due to rapid methotrexate (MTX) metabolism, particularly in patients receiving low doses (standard in rheumatoid arthritis (RA) patients), methotrexate polyglutamate (MTXPGs) serve as informative biomarkers of drug exposure. The MTXPGn(2-7) are predominantly present in red blood cells, and whole/capillary blood is the preferred matrix for MTXPG determination.
Aims: This study's primary objective was to quantify MTXPGs (following EMA guidelines) in Mitra™ samples collected from adults with RA taking MTX.
Methods: The Synergi-FUSION-RP column was maintained at 30^{o}C, with a gradient flow of mobile phase (water/acetonitrile with 0.1% formic acid and 10mM NH_4HCO_3). A 20µL capillary blood sample was extracted using 0.1% formic acid enriched with MTXPG-d_5/d_7. The sample underwent purification with perchloric acid and was then neutralised with an equivalent amount of potassium acetate. The LC-MS/MS platform (Shimadzu-LC40/QTRAP-6500+) was employed for method optimisation and sample processing.
Results: The methodology was validated within the 0.1-100nM calibration range for each MTXPG. All precisions and accuracies were maintained within ±15% of their nominal values. The purification using perchloric acid exhibited the highest recovery; however, it required neutralisation due to significant matrix effects. Elevated levels of hematocrit (HT>60%) adversely affected the recovery of analytes from the VAMS sample. The MTXPGs remained stable in microsamples during storage for 10 days at room temperature (sunlight-protected).
Conclusions: The analytical technique has been optimised and validated in accordance with EMA standards. This assay could facilitate home-based monitoring of MTXPGs in capillary blood collected with the Mitra™ microsampling device.
Key Words: methotrexate, MTXPGs, LDMTX, rheumatoid arthritis, adherence

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W201

6β-Hydroxycortisol/cortisol ratio in dried blood spots for CYP3A phenotyping in healthy participants

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Biography:
Hiromi Shibasaki-Hirano is an Associate Professor of Laboratory of Clinical Pharmacy and Experimental Therapeutics at the Tokyo University of Pharmacy and Life sciences (Japan). In 1992, she obtained her PhD on the synthesis of multiply deuterium-labeled glucocorticoids and the development of stable isotope dilution mass spectrometry analysis of glucocorticoids in human plasma. She teaches pharmacokinetics and personalized pharmacotherapy. She and laboratory colleagues developed a new index of in vivo cytochrome P450 3A (CYP3A) phenotyping in human as probed by endogenous cortisol 6β-hydroxylation clearance. Using this method, she investigated human CYP3A activity in vivo throughout the menstrual cycle, as well as the inter and intra-individual variability of CYP3A activity in Japanese subjects. Furthermore, she is developing 6β-hydroxylation to cortisol ratio as a minimally invasive CYP3A activity assessment. Outside of her research activity, Hiromi enjoys going for a walk with friends and family.

Background: Cytochrome P450 3A (CYP3A) metabolizes approximately 50% of human drugs, making CYP3A phenotyping crucial for personalized medicine. We developed the 6β-hydroxycortisol to cortisol concentration ratio (6β-OHF/F) in dried blood spots (DBS) as a minimally invasive CYP3A activity assessment. To apply this method clinically, establishing the 6β-OHF/F range in healthy individuals is necessary.
Aims: We aimed to investigate the normal range of the 6β-OHF/F ratio in DBS samples obtained from healthy participants.
Methods: 6β-OHF and cortisol concentrations in DBS were quantified using LC–MS/MS. The study population consisted of 37 healthy participants (21 men, aged 22–61 years, 16 women, aged 22–58 years). The study protocol was approved by the Tokyo University of Pharmacy and Life Sciences Human Subjects Review Board, and written informed consent was obtained from all participants.
Results: The measured concentrations of 6β-OHF and cortisol in four DBS spots were 0.0112–0.182 ng/80 µL and 1.05–7.77 ng/80 µL, respectively. The resulting 6β-OHF/F ratios in DBS from the 37 healthy participants ranged from 0.00627 to 0.0321, reflecting a 5-fold interindividual variability in CYP3A activity. The mean 6β-OHF/F ratio in women (0.0151 ± 0.0075) was higher than that in men (0.0138 ± 0.0034).
Conclusions: This minimally invasive index allows pre-treatment identification of patients with extremely low CYP3A activity, enabling optimized initial drug dosing and reduced adverse reaction risk. We propose a 6β-OHF/F value of <0.005 in DBS to identify patients requiring reduced doses of CYP3A-metabolized drugs.
Keywords: biomarker, dried blood spots, 6β-hydroxycortisol/cortisol ratio, CYP3A, phenotyping

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

W202

Validation of Toxicological Test of 135 Drugs in VAMs Using LC-MSMS

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Biography:

Wanzhu Zhao holds a Master of Science Degree in Toxicology from the University of Colorado, School of Pharmacy. She is currently a research instructor managing the daily operation of iC42 Clinical Toxicology Laboratory affiliated with University of Colorado, School of Medicine.

Background: Although drug abuse has increased substantially over the last decade to reach the level of a national crisis in the United States, little progress in drug of abuse monitoring and treatment has been made. Recently, dried blood spots (DBS) have emerged as a promising alternative that do not have the drawbacks of IV blood samples. DBS are collected after a finger prick, thus, eliminating the need for a phlebotomist, however, DBS are currently not yet used for toxicology screening.
Aims: It was the aim to develop and validate a DBS-based toxicology screening/ therapeutic drug monitoring strategy. The assay developed during the present thesis includes 135 drugs of abuse and pain drugs including key metabolites.
Methods: The validation followed applicable FDA and Clinical Laboratory Standards Institute guidelines. For the drugs for which the assay worked, matrix effects and autosampler stability were also established. Transport stability at increased temperature and moisture still needs to be established.
Results: 94 drugs across 18 drug classes worked well on the platform with clinical assay criteria, 27 will work as a semi-quantitative screening assay while 13 drugs do not work on the current platform.
Conclusions: The resulted validated assay has great potential to become commercialized with endless possibilities from forensic testing to therapeutic drug monitoring purposes. The fact that it is done meeting regulatory requirements also helps it become a marketable product.
Keywords: Toxicology, VAMS, Alternative Sample Strategy, Validation, LC-MSMS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W203

VAMS is promising method for evaluating the pharmacokinetics of (val)ganciclovir in neonates

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Biography:

Dr. Arkadiusz Kocur is an associate professor of pharmacokinetics and bioanalysis in the Department of Drug Chemistry and Pharmaceutical and Biomedical Analysis at the Medical University of Warsaw, Poland. He also works in clinical pharmacokinetics related to therapeutic drug monitoring and the toxicology unit at the Children's Memorial Health Institute. Dr. Kocur leads the pharmacokinetics of the AntiSepsis study. His research interests encompass bioanalysis, immunosuppressants, pharmacokinetics, pharmacodynamics, and therapeutic drug monitoring.

Background: (Val)ganciclovir is the first-choice agent for treating congenital cytomegalovirus infection, particularly in neonates. Due to potential toxic side effects and the physiological challenges associated with neonates, therapeutic drug monitoring with dosing adjustments is essential to ensure the safety and efficacy of pharmacotherapy.
Aims: This study aimed to evaluate the pharmacokinetics of VGCV using the microsampling technique in neonates with cCMV infection.
Methods: For GCV monitoring, the previously validated HILIC-LC-MS/MS method was employed. Simultaneously with GCV, creatinine levels were determined in a single analytical run. Mitra™ volumetric-absorptive microsamples were collected at the following time points: C_0 (30 minutes before drug administration) and at C_2, C_4, C_8, and C_{12} (after oral administration of Valcyte®). The patients received a dose of 16 mg/kg every 12 hours. In this preliminary study, 10 neonates were included.
Results: The mean AUC value was approximately 56.67±24.88 mgxh/L, with more than 70% of patients achieving the target AUC(0-24) value within the 40-60 mgxh/L range. Interestingly, clinical manifestations of side effects were not observed. For patients with toxic or subtherapeutic AUC levels, the clinical pharmacist suggested a dosing adjustment for Valcyte®. The accuracy of sampling using Mitra™ was greater than 95%, and the evaluated sample stability was established at a minimum of 2 weeks under ambient conditions (RT).
Conclusions: The Mitra™ VAMS is a suitable tool for multi-point individual drug exposure and pharmacokinetic evaluation of VGCV in neonates treated in hospitals and at home (after appropriate training of caregivers).
Key Words: (val)ganciclovir, CMV, AUC, VAMS, neonates, LC-MS/MS, TDM

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W204

Saliva-based therapeutic drug monitoring of oxazolidinone antibiotics

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Biography:

Yuki Inoue obtained her Doctor of Philosophy degree from the Graduate School of Life Science, Hokkaido University, in 2025 and currently works as a clinical pharmacist at Hokkaido University Hospital. Her research focuses on oxazolidinone antibiotics. She aims to enhance the safety of drug therapy and seeks to establish a non-invasive therapeutic drug monitoring method using saliva as an alternative to blood sampling, reducing the burden on both patients and healthcare professionals.

Background and Aims: Oxazolidinones such as linezolid and tedizolid are active against methicillin-resistant Staphylococcus aureus infections. Thrombocytopenia caused by linezolid is a concern, and therapeutic drug monitoring (TDM) has been reported to help prevent this condition. Although plasma concentrations provide valuable information for treatment decisions, plasma sample collection can be burdensome for both patients and healthcare providers. Therefore, there is an interest in saliva as an alternative to TDM.
Methods: To establish a monitoring method using saliva, we collected saliva and plasma samples from rats after linezolid or tedizolid administration. Subsequently, a prospective study was conducted to evaluate the potential clinical application of TDM for linezolid and tedizolid using saliva. Patients who received linezolid or tedizolid were enrolled in the study. We analyzed the concentration profiles of linezolid and tedizolid in saliva and examined their correlation with plasma concentrations.
Results: The saliva/plasma (S/P) concentration ratio of linezolid in rats and patients were 0.66 and 1.03, respectively. The S/P ratio of tedizolid in rats and patients were 0.05 and 0.33, respectively. Strong correlations were found between the saliva and plasma concentrations of linezolid (r=0.945 in rats, r=0.83 in patients) and tedizolid (r=0.964 in rats).
Conclusions: Considering the correlation between saliva and plasma concentrations of linezolid and tedizolid as well as the characteristics of saliva, our results suggest that saliva is a useful matrix for TDM. Notably, the concentrations of linezolid in the plasma and saliva of patients were similar, indicating its potential applicability in clinical settings.
Keywords: Oxazolidinones, saliva, alternative sampling

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W205

DBS sampling for TDM during OPAT: qualitative analysis of facilitators and barriers

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Biography:
Moska Hassanzai is a hospital pharmacist and PhD student, currently working at the Hospital Pharmacy department of the Erasmus MC hospital. Her research focus is mainly on alternative sampling strategies and OPAT services.

Background: Dried blood spot (DBS) sampling is considered an alternative sampling strategy for TDM in patients receiving OPAT.
Aims: To provide insights in the barriers and facilitators of DBS sampling for OPAT patients.
Methods: A qualitative study was conducted in patients performing DBS sampling for TDM of vancomycin and creatinine during OPAT. Patients were interviewed using a semi-structured interview guide based on the theoretical domains framework and consolidated framework for implementation research. The results were transcribed verbatim and analysed inductively by two researchers according to thematic analysis.
Results: 15 barriers and 15 facilitators were classified in four domains: information, technique, process and patient. The overall view on DBS sampling was very positive. Patients mentioned the added value of DBS sampling for healthcare and society in terms of health care personnel and time. Involvement and control over their own healthcare was also mentioned as a positive attribute of DBS sampling. Facilitators included training including the information to warm the hands, DBS properties (simple and quick to perform, easy integration in routine, time- and cost saving) and previous experience with finger prick. The patient's sense of responsibility is crucial for DBS success. Barriers included insufficient information on the background of DBS sampling, the limitation of assays available with DBS sampling, posting and mail delivery and aversion towards needles.
Conclusions: This study addressed barriers and facilitators of DBS sampling for TDM during OPAT and provides multiple advices for proper DBS implementation.
Key Words: OPAT, TDM, dried blood spot sampling, vancomycin, qualitative analysis

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W206

Quantification of creatinine as endogenous analyte in qDBS and VAMS microsampling devices

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Biography:
Dr. Arkadiusz Kocur is an associate professor of pharmacokinetics and bioanalysis in the Department of Drug Chemistry and Pharmaceutical and Biomedical Analysis at the Medical University of Warsaw, Poland. He also works in clinical pharmacokinetics related to therapeutic drug monitoring and the toxicology unit at the Children's Memorial Health Institute. Dr. Kocur leads the pharmacokinetics of the AntiSepsis study. His research interests encompass bioanalysis, immunosuppressants, pharmacokinetics, pharmacodynamics, and therapeutic drug monitoring.

Background: Creatinine (CRE) is the most popular renal function biomarker, and venous plasma/serum collection is necessary to monitor it in routine clinical practice. Our centre successfully introduced home-based self-sampling for immunosuppressant monitoring, and optimizing the methodology for additional determination of CRE in a single sample seems highly valuable.
Aims: The study aimed to evaluate the EMA's approach to determining creatinine (an endogenous molecule) in qDBS (Capitainer B) and VAMS (Mitra) samples collected from pediatric renal transplant recipients.
Methods: During HILIC-based (Luna chromatographic column from Phenomenex), LC-MS/MS (6500TQ AB Sciex) method optimization and validation, the surrogate followed approaches were evaluated: surrogate analyte, surrogate matrix, the background subtraction approach and the standard addition protocols. The extraction of CRE (or surrogate) was achieved using a water/methanol medium, while protein was precipitated using a zinc sulphate/acetonitrile mixture.
Results: The methodology has been evaluated in the 0.1 - 40 mg/L calibration range. The accuracies and precision were within nominal values. Despite high ion suppression, sample dilution must be done before analysis. Signal-to-noise ratios were lower than 20% for each evaluated approach. The ^{13}C-CRE compensated matrix effects were more satisfactory than d_5-CRE.
Conclusions: The surrogate analyte approach (d_3-CRE) produced the most reliable results among those proposed by the EMA in the ICH M10 bioanalytical validation guidelines. The optimized method may be used to determine creatinine in VAMS and qDBS samples concomitantly with immunosuppressants, but it requires two different analytical runs.
Key Words: creatinine, renal transplantation, LC-MS/MS, surrogate analyte, VAMS, qDBS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W207

Novel TDM strategy for prediction of pulmonary drug deposition via soft-mist inhaler

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Biography:

Dr. Daiki Hira is a Senior Lecturer / Junior Associate Professor at Department of Clinical Pharmacology and Therapeutics, Kyoto University Hospital and a specialist in clinical pharmaceutics and pharmacology.

EDUCATION

2012: PhD: Pharmaceutical Sciences at Meijo University, Nagoya, Japan

ACADEMIC APPOINTMENTS

2012-2017: Assistant Professor, Department of Pharmacy, Shiga University of Medical Science Hospital

2017-2021: Assistant Professor, College of Pharmaceutical Sciences, Ritsumeikan University, Kusatsu, Japan

2021-2022: Assistant Professor, Department of Clinical Pharmacology and Therapeutics, Kyoto University Hospital.

2023-Present: Senior Lecturer / Junior Associate Professor, Department of Clinical Pharmacology and Therapeutics, Kyoto University Hospital.

Background: Soft-mist inhalers (SMIs) are used to treat respiratory diseases. Because SMI has a long drug mist emission time of approximately 1.5 seconds, some patients are unable to keep inhaling during drug mist emission. However, information regarding the impact of improper use on pulmonary drug deposition is lacking. Our previous study demonstrated that a particle emission monitoring can be used to estimate pulmonary drug deposition via dry powder inhaler [Hatazoe S, AAPS PharmSciTech, 2024].
Aims: This study aimed to evaluate whether the particle emission monitoring can be used to estimate pulmonary drug deposition via SMI.
Methods: Spiriva® Respimat® was selected as the SMI model. Pulmonary deposition of inhaled tiotropium was evaluated using an Andersen cascade impactor, an in vitro aerodynamic particle size analyzer. The inhalation flow rate and particle emission profile were measured using an inhalation flow meter and a photo reflection method, respectively. Inhalation performance was characterized by the fine particle fraction deposited on the whole lung (FPF-WL; aerodynamic dimeter < 4.7 µm).
Results: The particle emission monitoring device successfully visualized the differences in timing between inhalation and drug mist emission. FPF-WL via SMI was increased by less difference in the timing between inhalation and drug mist emission and longer inhalation duration time. An inhalation duration shorter than 1.2 seconds reduced pulmonary drug deposition to 25% of the maximum.
Conclusions: Particle emission monitoring is applicable for the prediction of pulmonary drug deposition via SMI as well as dry powder inhalers.
Keywords: alternative sampling strategy, soft-mist inhaler, pulmonary drug delivery

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W208

Determination of direct oral anticoagulants (DOACs) in qDBS and VAMS microsampling devices

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Biography:
Dr. Arkadiusz Kocur is an associate professor of pharmacokinetics and bioanalysis in the Department of Drug Chemistry and Pharmaceutical and Biomedical Analysis at the Medical University of Warsaw, Poland. He also works in clinical pharmacokinetics related to therapeutic drug monitoring and the toxicology unit at the Children's Memorial Health Institute. Dr. Kocur leads the pharmacokinetics of the AntiSepsis study. His research interests encompass bioanalysis, immunosuppressants, pharmacokinetics, pharmacodynamics, and therapeutic drug monitoring.

Background: Direct oral anticoagulants (DOACs), such as rivaroxaban (RVX), apixaban (APX), dabigatran (DAB), and edoxaban (EDX), are commonly used in clinical practice to prevent blood clots and strokes. However, they are characterised by a wide therapeutic range, and monitoring these medications may be beneficial for specific populations, including children, elderly patients with renal function difficulties, and those with obesity.
Aims: This study aimed to develop and validate a novel LC-MS/MS method for determining EDX, RVX, APX (and its metabolite, O-desmethylapixaban), and DAB in Mitra™ and SEP10® microsampling devices.
Methods: The in vitro/ex vivo methods have been optimised and validated using the LC-MS/MS system QTRAP6500+ from AB Sciex. An Agilent column C18-XDB was used with a 0.5 mL/min mobile phase flow in gradient mode. Various solvents were employed to extract dried matrices, supported by sonication and cold-induced phase extraction.
Results: Each analyte validated the LC-MS/MS method in the 0.5 - 500 ng/mL calibration range. The methanol/water mixture was used to extract analytes, while acidified acetonitrile was used for protein precipitation. The stable isotope-labelled IS satisfactorily compensated for the matrix effects for each analyte. All acceptance criteria proposed by the EMA and FDA were fulfilled, and analyte recovery did not affect the hematocrit effect (>95%).
Conclusions: The method for determining DOACs was successfully validated in accordance with EMA and FDA guidelines. Moreover, the technique has been standardised through four rounds of IPT. The assay will be implemented for PK-monitoring in paediatric patients undergoing anticoagulant treatment.
Key Words: apixaban, rivaroxaban, dabigatran, edoxaban, microsampling

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W209

Saliva-Based Therapeutic Drug Monitoring of Linezolid in Multidrug-Resistant Tuberculosis Patients

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Biography:
Ms Thi Nguyen is a PhD student in the Sydney Pharmacy School with a Vietnamese Bachelor's degree from Can Tho University of Medicine and Pharmacy, and French Master's degree in Pharmaceutical Science (Master of Mekong Pharma). Coming from a low-resource country, she values equity, transparency with respect and so, she is interested in facilitating personalised drug dosing worldwide, especially in high burden and resource-limited settings through education and research.
As an academic, she co-supervises junior students. Her research focus is on developing new point of care assays for antimicrobials to be used in the community, and subsequently developing mathematical models that describe and predict drug levels in patients to inform dosing. She has contributed to several systematic reviews of emerging microbial pathogens to inform WHO surveillance and to support treatment and research.

Background: Multidrug-resistant tuberculosis (MDR-TB) remains a major global health challenge, due to increasing resistance rates and few well-tolerated anti-TB drugs. Linezolid, a key MDR-TB drug, causes haematological and neurological adverse events with prolonged treatment or higher doses. Therapeutic drug monitoring (TDM) is recommended to optimise dosing, but traditional plasma-based TDM is invasive and resource-intensive, limiting its use particularly in high-burden low-resource settings.
Aims: To investigate the feasibility of using saliva as an alternative for linezolid TDM in MDR-TB.
Methods: Adults receiving linezolid for MDR-TB for ≥7 consecutive days had blood and saliva samples collected at 0, 2, and 5 hours post-dose at steady-state (ACTRN12620000681954). Plasma and saliva linezolid concentrations were quantified using liquid chromatography–mass spectrometry. Saliva-plasma correlations were compared via Passing-Bablok regression, Bland-Altman analysis and Pearson's correlation test.
Results: Of the 17 patients, 76% were male, with a mean age of 46 years and weight of 49 kg. A total of 102 saliva and plasma linezolid concentrations were analysed as 54 concentrations were below the limit of quantification. Saliva concentrations were, on average, 1.34 times higher (95% CI, 0.08–2.61) than in plasma. There was good agreement between saliva and plasma concentrations ($r = 0.90$; $P < 0.05$) with only 1.9% of concentrations falling outside the 95% limits of agreement.

Conclusion: Saliva linezolid concentrations are strongly correlated with those in plasma, suggesting saliva is a potential non-invasive alternative matrix for linezolid TDM to minimise toxicity and improve MDR-TB treatment outcomes.
Keywords: Linezolid, pharmacokinetic, therapeutic drug monitoring, saliva.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W210

Performance evaluation of LM1010 in determining the serum concentration of linezolid

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Biography:

Mr. Hashimoto has been working as a clinical pharmacist in the Department of Pharmacy at the University of Tsukuba Hospital since April 2011. He obtained his PhD in 2023 from the University of Tsukuba by investigating the effects of serum lipids on the serum concentration of antiarrhythmic drugs. Since April 2024, he has been working as a clinical assistant professor in the Department of Infectious Diseases at the University of Tsukuba Hospital. His research focuses on therapeutic drug monitoring (TDM) in the fields of cardiology and infectious diseases. Currently, he is collaborating with physicians, nurses, and clinical laboratory technicians to establish a novel approach for TDM of anti-MRSA agents, which aims to optimize drug dosing strategies and improve patient outcomes.

Background: LM1010, a high-performance liquid chromatography system designed for therapeutic drug monitoring (TDM) of various drugs in clinical practice, is currently approved in Japan. LM1010 enables rapid measurement of drugs in serum specimens and performs fully automated data analysis based on the absolute calibration curve method. We evaluated the analytical performance of the LM1010 for determining serum concentrations of linezolid (LZD).
Aims: The present study aimed to evaluate the analytical performance of LM1010 and investigate the long-term stability of LZD in serum specimens stored at −30°C.
Methods: A total of 148 serum specimens were collected from 25 patients (17 males and 8 females) who were treated with LZD. Serum concentrations of LZD were measured using LM1010 and liquid chromatography-tandem mass spectrometry (LC-MS/MS). The measured values were also compared among three LM1010 instruments at different institutions to validate the analytical performance.
Results: A Passing–Bablok regression analysis demonstrated a strong correlation in the measured values between LM1010 and LC-MS/MS (r = 0.991), and comparable results were observed among the three LM1010 instruments (r = 0.982–0.998). Bland–Altman analyses revealed that the difference in the average between LM1010 and LC-MS/MS methods was 1.7%, and similar results were observed among the three LM1010 instruments. The long-term stability of serum LZD was also confirmed in LZD-spiked serum specimens stored at −30°C for 48 weeks.

Conclusions: The present results confirm that LM1010 can be used for TDM of LZD in serum specimens even in those stored at −30°C.

Key Words: linezolid, therapeutic drug monitoring, high-performance liquid chromatography

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W211

Simultaneous LC-MS/MS Analysis of 35 Anti-Psychotics in Human Plasma for Clinical Research

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Biography:

Fionn Quinlan is the Asia Clinical Market Manager for Waters Corporation and is based in Taiwan. Since Fionn completed his post graduate studies in Dublin City University and Trinity College Dublin in the fields of molecular genetics, he has been continuously involved in the life science, diagnostics and forensic field for over 20 years.

Fionn works closely with leading hospitals, national reference laboratories, universities and forensic labs throughout Asia supporting the education and awareness of LCMS applications.

He is a serving member of the Asia Pacific Federation of Clinical Biochemistry commercial committee. His focus areas are New Born Screening, Therapeutic Drug Monitoring, Endocrinology, Forensic and Clinical Toxicology.

Background: Antipsychotic drugs (APDs) are frequently used in combination with other drugs, leading to potential drug interactions.
Aim: Here we present a simple, cost-effective and robust protein precipitation and LC-MS/MS method for the simultaneous analysis of 35 APDs in human plasma for clinical research.
Methods: In brief, to 50µL of plasma, 100µL of protein precipitation solvent containing internal standards was added. The samples were mixed, centrifuged for five minutes and 100µL of the supernatant was diluted with water. Samples were injected onto a Waters XSelect™ HSS C18 SB XP Column using an ACQUITY™ UPLC™ I-Class PLUS FL System and eluted using a water/methanol/formic acid/ ammonium acetate gradient. APDs were quantified using a Xevo™ TQ-S micro Mass Spectrometer.
Results: The method was demonstrated to be linear across calibration range for all analytes, with analytical sensitivity investigations showing precise quantification (<20% CV, ≤15% bias). Non-linearity was less than 10% across all the analytes. Coefficients of variation (CV) for total precision and repeatability of QCs were ≤8.7% CV and ≤7.4%, respectively. Recoveries for all analytes were within ±15%. Mean extraction efficiencies for the 35 APDs ranged from 52.2%-96.9%.
Conclusions: A fast and inexpensive LC-MS/MS clinical research method was developed for 35 APDs, based on protein precipitation and requiring only 50µL of plasma. The method demonstrated acceptable analytical sensitivity, recovery, linearity and precision for all analytes.
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Key words: LC-MS/MS, Anti-psychotics, robust

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W212

Enhancing Mass Spectrometry Efficiency: Increasing Assay Capacity for Cost-Effective Analysis

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Biography:

Dr. Kocic is the Scientific Head of Clinical Pharmacology and Toxicology at SydPath, St. Vincent's Hospital, Sydney. She manages Therapeutic Drug Monitoring (TDM) analyses, providing crucial support to clinicians and patients to optimize outcomes in complex clinical scenarios and trials. Since 2020, she has served as a Conjoint Senior Lecturer at the University of NSW's Clinical School. Dr. Kocic is also a leading committee member of the NSW Health Pathology Clinical Mass Spectrometry Forum, which hosts discussions for clinical scientists and clinicians with esteemed speakers. Additionally, she chairs the Special Drugs Advisory Committee for the Royal College of Pathologists of Australasia Quality Assurance Programs, offering expert insights for laboratories globally. In her role as chair of the newly established Analytical Committee with IATDMCT, she focuses on enhancing analytical methods in TDM and clinical toxicology, with research interests in improving sample throughput using LC-MS/MS technology.

Introduction: In the past decade, liquid chromatography-tandem mass spectrometry (LC-MS/MS) has emerged as a crucial analytical tool in clinical chemistry laboratories. However, the high cost of these machines often limits their routine use. This research demonstrates how a consolidated LC-MS/MS approach can replace multiple HPLC methods, thereby streamlining turnaround times, reducing costs, and conserving resources.
Methods: To enhance the analysis of 29 drug assays, our laboratory implemented a mass spectrometry strategy that combined these into four efficient workflows. Each workflow underwent stringent validation to ensure reliability, focusing on parameters such as linearity, trueness, precision, specificity, and matrix effects. A comprehensive method comparison was conducted against traditional HPLC protocols to evaluate performance metrics. The effectiveness of the new methodologies was further confirmed through participation in external quality assessments (EQA).
Results: The new methods demonstrated high efficiency, with run times ranging from 1 to 4 minutes. This combined approach resulted in significant cost savings by reducing both instrument and scientist time. Improved service delivery was noted from two assays running multiple times per week, significantly enhancing turnaround times in comparison to weekly HPLC methods.
Discussion: This innovative strategy enhances analytical efficiency and the quality of results while optimizing service delivery. Furthermore, the refined methodology is adaptable for various applications, meeting different laboratory requirements. These results highlight the potential of this integrated approach to transform laboratory practices and elevate analytical capabilities across multiple domains.

Mass Spectrometry, LC-MS/MS, Efficiency, Cost effective, Multiplexing

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W213

24/7 fully automated therapeutic drug analysis for research projects by LC/MS/MS

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Biography:
n/a

Background: Simplifications in LCMS instrumentation have made MS a viable option for clinical research. The ability to support various analysis methods on a single system is a key feature. However, the automation of sample preparation, automatic transfer to LCMS, and standardization of analytical conditions have been considered challenging.
Aims: The purpose is the development and the validation of a unified methods set for LC/MS/MS, for 24/7 therapeutic drug analysis, with a fully automated platform.
Methods: The evaluated analytical system was a fully automated platform, CLAM-LC/MS/MS (Shimadzu, Japan). HL-7 interface standards were used for bidirectional communication between LIS (Dedalus, Germany) and the platform. Target applications were Antibiotics, DOAC, Antiepileptics, Neuroleptics, Tricyclic Antidepressants, Other Antidepressants, Benzodiazepines, Antifungals, and several other drugs. All methods use similar analytical conditions. The fitness for purpose for 24/7 use was evaluated by requesting measurements for several methods in random alternance.
Results: Each method was evaluated based on the following validation items and met the criteria: isobars resolution, accuracy, repeatability, intermediate precision, mobile phase stability, LLOQ confirmation, carryover and ring trial analysis. Also, repeated measurements for several methods in random alternance showed results within the acceptance criteria.
Conclusion: This strategy proved its fitness for purpose. The fast LCMS methods which can alternate smoothly, and the automated sample extraction enable robust therapeutic drug analysis with a high throughput and at low cost, without compromising the user comfort. For research use only.
Key words:24/7, automated, TDM, analysis, RUO, LCMS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W214

UHPLC-MS/MS Analysis of Traditional and Novel Benzodiazepines in Urine

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Biography:

Around 30 years in Mass Spectrometry applications in both Europe and Asia. Currently working as head of APAC customer success in Clinical and Forensics application areas.

Background: Benzodiazepines are important forensic toxicology drugs which are prescribed for neurological and psychiatric disorders but also have a high potential for abuse.
Aims: The aim was to develop a forensic toxicology research method for confirmatory analysis of 26 traditional and designer benzodiazepines via UHPLC-MS/MS.
Methods: Urine samples (100µL) were added to a Waters Oasis™ MCX µElution™ Plate followed by 100 µL of a solution containing recombinant beta-glucuronidase enzyme, hydrolysis buffer and internal standards. The sample was loaded, washed and then eluted using 50:50 acetonitrile:methanol containing 5% ammonia. Samples were diluted with 2% acetonitrile: 1% formic acid prior to analysis.
Samples were injected onto an ACQUITY™ UPLC™ BEH™ C18 Column using an ACQUITY UPLC I-Class PLUS System and eluted using a water/formic acid/acetonitrile gradient with detection on a Xevo™ TQ-S micro Mass Spectrometer.
Results: The panel of benzodiazepines were well separated, with baseline resolution for most compounds. The extraction recovery was within 80-120% for the majority of compounds. The matrix effects were mostly minimized to ±20% after internal standard correction. Calibration curves were linear with r2≥0.99 and coefficients of variation were less than 15% for all analytes. The data for proficiency samples showed excellent agreement to existing research methods.
Conclusion: Leveraging SPE sample preparation and UHPLC-MS/MS with the Xevo TQ-S micro Mass Spectrometer, a rapid, accurate and precise method was demonstrated for analyzing benzodiazepines in urine.
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Keywords: Benzodiazepines, Urine, LC-MS/MS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W215

Evaluating the performance of commercial nitazene immunoassay test strips

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Biography:
Marthe graduated from Ghent University (Belgium) in 2019 as a pharmacist with a Master's in Drug Development. Later that year, she started working at the UGent Laboratory of Toxicology under the supervision of Prof. Christophe Stove. In 2024, she defended her PhD thesis entitled 'The old, the new, the (un)expected: a pharmacological perspective on new synthetic opioids of the post-fentanyl analogue era'. As a postdoctoral researcher at the UGent Laboratory of Toxicology, she continues her research on the activity-based detection and pharmacological characterization of new psychoactive substances with a special focus on synthetic opioids.

Background: 2-Benzylbenzimidazole 'nitazene' opioids pose a growing threat to public health, and are increasingly mixed with or (mis)sold as heroin and present in falsified (non-)opioid medications. Lateral flow immunoassay nitazene test strips (NTS; BTNX Rapid ResponseTM) became commercially available in Q1-2024, aiming to enable rapid detection of nitazene analogues in drug samples.
Aims: This lab-based study aimed at evaluating the potential of NTS for drug checking applications.
Methods: Following dilution of drug standards in water, the NTS readouts were analyzed independently by two individuals and by ImageJ. The limit of detection for isotonitazene was determined using two manufacturing lots of NTS. Cross-reactivity with 32 additional nitazene analogues was evaluated. Six sourced drug samples were tested to explore the ability of NTS to detect the presence of a nitazene analogue in authentic samples.
Results: The limits of detection for isotonitazene were 2000 or 3000 ng/mL, depending on the lot. 24/33 nitazene analogues cross-reacted with the NTS at concentrations ≤ 9000 ng/mL. Structural analysis indicated that either substitution or removal of the 5-nitro group, or lengthening the linker between the two aromatic rings, generally hampered detection. All six authentic drug samples consistently tested positive.
Conclusions: Our findings indicate that NTS can theoretically alert to the presence of most nitazene analogues that have emerged on recreational drug markets. However, in practice, factors like specificity, lot-to-lot variability, nitazene content in drug samples, solubility, and different testing conditions should be considered.
Keywords: New synthetic opioids, Nitazenes, Harm reduction, Drug checking, Immunoassay test strips

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W216

Towards standardized measurement of free valproic acid concentrations: variability in ultrafiltration protocols

Ms Cathérine Van herteryck[1], Dr. PharmD Sigrid Deprez[2], MD Eva Willems[2], Dr. PharmD Nick Verougstraete[2], Dr. PharmD Matthijs Oyaert[2], Prof. Dr. PharmD Veronique Stove[2]
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Biography:

Cathérine Van herteryck obtained her masters degree in Pharmaceutical Sciences from Ghent University, Belgium, in 2024. During her master dissertation, she investigated the measurement of the unbound concentration of flucloxacillin in plasma, sparking her enthusiasm for further research at doctoral level.

She is currently pursuing a PhD at Ghent University, within the Department of Diagnostic Sciences at Ghent University Hospital. Her research focuses on optimizing therapeutic drug monitoring of beta-lactams, with a particular interest in measuring unbound drug concentrations, the only pharmacologically active concentration. She is especially intrigued by the various factors influencing ultrafiltration and their impact on concentration measurements.

Her ultimate goal is to enhance patient care by individualising therapy, hence ensuring more precise and effective treatment strategies.

Background: Conventional assays measure total valproic acid (VPA) concentrations to guide epilepsy therapy, but only unbound VPA is pharmacologically active. Free VPA concentrations correlate better with efficacy and toxicity, especially since VPA is highly protein-bound (90–95%). Hypoalbuminemia or drug-drug interactions can elevate unbound VPA levels despite normal or low total VPA levels, highlighting the need for free VPA measurement.

Aims: Determining ultrafiltration variables and setting up an optimized protocol to measure unbound VPA concentrations.

Methods: Since no IVDR-compliant method exists for free VPA concentrations, an in-house ultrafiltration protocol was developed at Ghent University Hospital using Centrifree devices (500µL serum, incubation and centrifugation at 37°C, 1990g, 30 minutes). Ultrafiltrate and total VPA concentrations were analyzed using Chemiluminescent Microparticle ImmunoAssay (Abbott Architect i2000SR). Validation included assessing matrix effects across a broad VPA range (±4–125mg/L) and evaluating filter device type, temperature, serum volume, centrifugation time, and buffer (pH 7.5).

Results: A ~15% matrix effect was observed, with higher recoveries in ultrafiltrate versus serum. Key centrifugation variables affecting results included: filter membrane type (10kD vs. 30kD), temperature (concentrations 37°C > 22°C), serum volume (400µL vs. 500µL), centrifugation time, and phosphate buffer use. Vivacon® filters yielded different results than Centrifree, underlining the importance of consistent device selection.

Conclusions: Free VPA measurements are influenced by multiple variables, necessitating standardized ultrafiltration protocols. Variability in filter devices and processing conditions emphasize the importance of robust guidelines and external quality controls to improve accuracy and comparability.

Key words: Hypoalbuminemia, drug-drug interactions, ultrafiltration, unbound concentration, valproic acid

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W217

Selective and sensitive quantitation of 18 steroids using Thermo Scientific™ Stellar™ MS

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Biography:
Dr. Jingshu Guo is a trained mass spectrometrist with 15 years of experience in LC-MS-based qualitative and quantitative analyses of small molecules, nucleosides, peptides, and intact protein. After joining Thermo Fisher Scientific, she worked on the method development, implementation, and optimization in clinical and toxicology-related fields. One of her current focuses is to develop fast quantification methods in small molecules, such as biomarkers, therapeutic drugs, and drugs of abuse in biofluids using LC coupled to triple quadrupole MS, quadrupole-linear ion trap MS, or high-resolution MS, and LC-free MS platforms.

Background: Successful biomarker quantitation in complex matrices requires sensitivity and specificity. The Stellar™ mass spectrometer (MS) is a hybrid quadrupole, dual-pressure linear ion trap MS that offers alternative fragmentation mechanisms and/or MS3 fragmentation as an efficient solution to reduce background interferences and provide greater specificity.
Aims: To demonstrate the advantages of utilizing multiple collision activations and MS3 provided by Stellar MS to the selective and sensitive quantification of 18 steroids in serum.
Method: Commercially available 18 steroids standards and their corresponding internal standards were serially diluted in blank human serum to generate calibrator samples over 4-orders of magnitude concentration range. Quality control human serum samples were purchased from Chromsystem. Steroids were extracted with protein precipitation for the LCMS analysis. Multiple fragmentation schemes were evaluated and optimized on the Stellar MS, and the data was analyzed in TraceFinder™ software for the quantitative performance.
Results: The detection of 18 steroids were optimized in Stellar MS under multiple fragmentation mechanisms (beam-type CID, resonance-type CID, and MS3 in different combinations) with polarity switching. Excellent analytical performance of the calibration curves were achieved for all steroids. Comparing to the MS2 beam-type CID commonly used in contemporary triple quadruple MS, steroids such as cortisone, estradiol, and dihydrotestosterone benefited from the alternative, resonance-type CID and MS3 acquisition modes, resulting in a 2-10 fold increase of the LOQ values.
Conclusions: Stellar MS provides unique selectivity allied to fast acquisition for high-throughput and sensitive biomarker quantitation optimal for routine analysis
Key words: Alternative fragmentation mechanism, Stellar MS, steroids, serum

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W218

Selection of internal standards for quantitation of surufatinib

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Biography:

Ms. Tiantian Tang is a TDM pharmacist with a Master's degree. Her primary research focuses on the development of sample pretreatment techniques, optimization of analytical methods, and therapeutic drug monitoring. In this study, she explored the selection of isotope-labeled internal standards for quantitation of surufatinib.

Background: The internal standard (IS) is key in LC-MS/MS for drug analysis. There is no commercially available isotope-labeled internal standards for surufatinib due to the challenges of chemical synthesis and high cost. Thus, it is very important to select an appropriate IS for the accurate quantitative detection of surufatinib.
Aims: The optimization of various parameters was conducted to obtain the optimal IS of surufatinib.
Methods: The 15 IS candidates include 10 TKIs and 5 other drugs. Parameter optimization consists of signal crossing in the MS ion channels, the influence of IS concentration, and the influence of the matrix effect. The resolution (R), correlation coefficient (r^2), and matrix effect were used as evaluation indexes.
Results: In the ion signal channel of surufatinib, only imatinib showed a weak response. The r^2 values could reach 0.990, except for gefitinib. Zanbrutinib, ritonavir, nirmatrelvir and gabapentin were most significantly inhibited in hemolytic plasma. The IS with the least R is PRA (0.08). Regorafenib exhibited high variability (CV% > 30%) in different standard curves. Only osimertinib, crizotinib, praseltinib and olaparib fell within the acceptable ranges of 15% in QC. In short, the praseltinib was the most optimal choice as IS for surufatinib.
Conclusions: The praseltinib was selected as the best IS for surufatinib, as it exhibited smaller R and As, better stability and linearity, and less affected by the matrix.
Key Words: Surufatinib, Internal standard, Selection

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W219

Meropenem PK/PD targets in ICU: attainment and factors for non-achievement

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Biography:
Dr Florian Lemaitre has been trained as a pharmacist and pharmacologist during its residency in Rennes and Poitiers, France. In 2014, he received his PhD on the pharmacological optimization of immunosuppressive therapy during his pharmacology fellowship at the Pitié-Salpêtrière Hospital in Paris and the Rennes University Hospital. His main research topic is the precision medicine in transplantation and he has been authored or co-authored 120+ articles. Since 2022, he is the president of the TDM-working group of the Société Française de Pharmacologie et de Thérapeutique (SFPT), the French national learning society of pharmacology. He is also the actual secretary of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and the Chair of the immunosuppressive drugs scientific committee of the IATDMCT.
He has dedicated his career to drug individualization for patients' care notably for solid organ transplant patients and patients with acute or chronic infections.

Background: Critically ill patients often have altered pharmacokinetics that complicate achieving adequate meropenem exposure. Therapeutic drug monitoring (TDM) can guide dosing and improve outcomes by ensuring appropriate PK/PD targets.
Aims: This study evaluates the achievement of pharmacokinetic/pharmacodynamic (PK/PD) targets for meropenem and identifies factors associated with failing to meet these targets in ICU patients.
Methods: We retrospectively studied ICU patients who had meropenem TDM from September 2022 to December 2024. Patients with incomplete data or invalid assays were excluded. We collected demographic, laboratory (creatinine, estimated glomerular filtration rate (eGFR)), therapeutic (dose, administration mode), vasopressor, renal replacement therapy (RRT), and microbiological data. The PK/PD targets (ƒCmin(or ƒCss)≥4×MIC; Cmin(or Css)<16mg/L) were assessed using the first TDM. Patients were categorized as below-target, on-target, or above-target. Univariate and multivariable regressions were performed.
Results: Eighty-four patients were included: 51.2% had documented MIC, 19.0% had no MIC, and 29.8% were treated empirically. Only 39.3% were on-target, while 60.7% were off-target (31.0% below, 29.8% above). Median Cmin|Css was 9.75µg/mL[3.88-17.40], with median dose of 4g/24h[3.0-6.0]. Higher dose (OR=1.84; 95%CI [1.23-2.75]; p=0.003) and prolonged/continuous infusion (OR=6.09; 95%CI [1.12-33.14]; p=0.036) increased the risk of above-target exposure, whereas higher eGFR (OR=0.96; 95%CI [0.94-0.98]; p=0.003) reduced it. RRT (OR=0.147; 95%CI [0.03-0.82]; p=0.029) decreased risk of below-target exposure.

Conclusions: About two-thirds of ICU patients had meropenem exposures outside recommended PK/PD targets at first TDM. Higher doses and prolonged/continuous infusions may increase above-target risk, underscoring the need for early TDM to optimize dosing.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W220

Beyond the Limits: Therapeutic Drug Monitoring-Guided High-Dose Ceftazidime-Avibactam Therapy For Brain Abscess

Dr Nathalie Grace Sy Chua[1], Dr Jocelyn Qi Min Teo[1], Dr Kelvin Kau-Kiat Goh[1,2], Celine Ting Xuan Sim[1], Wenqi Chiang[1], Dr Tze Peng Lim[1,2,3], Winnie Hui Ling Lee[1], Dr Jai Prashanth Rao[4,5], Dr Ying Ying Chua[6], Associate Professor Andrea Lay Hoon Kwa[1,3,7]
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Biography:

Dr Nathalie Chua is a specialist pharmacist (infectious diseases) at the Singapore General Hospital (SGH). She completed her infectious disease residency at Singhealth Post Graduate Allied Health Institute in 2013 and obtained her PharmD at National University of Singapore in 2018. She is a board certified infectious disease pharmacy specialist under US Board of Pharmacy Specialties and a registered specialist pharmacist under Singapore Pharmacy Council since 2021.
She is involved in antimicrobial stewardship and in the research and clinical implementation of antimicrobial therapeutic drug monitoring (TDM) services in SGH to manage difficult-to-treat infections. Her research interests include pharmacokinetics and pharmacodynamics, TDM and antimicrobial resistance. She is an infectious disease preceptor for the national pharmacy residency programmes in Singapore and a guest lecturer for infectious diseases at the NUS PharmD programme. She currently represents Singapore as a committee member of the Regional Asia Pacific Section and Young Scientists Committee of IATDMCT.

Background: Ensuring adequate antibiotic exposure for central nervous system (CNS) infections remains a dilemma. Standard dosing regimens are suboptimal for CNS infections, particularly for carbapenem-resistant infections.
Aims: We describe the first case of TDM-guided high-dose ceftazidime-avibactam therapy at 15g/day, exceeding conventional dosing recommendations, to treat Klebsiella pneumoniae Carbapenemase (KPC)-producing Klebsiella pneumoniae brain abscess.
Methods: Ceftazidime and avibactam concentrations in plasma and brain abscess were assayed using liquid chromatography tandem mass spectrometry (LCMS). Free drug concentrations in plasma were estimated using published protein binding values.
Results: A 55 year-old, 53.6kg, male developed KPC-producing Klebsiella pneumoniae left basal ganglial abscess [ceftazidime-avibactam minimum inhibitory concentration (MIC) 1/4 mg/L]. IV ceftazidime-avibactam 2.5g q8h, IV Levofloxacin 750mg q24h and IV Fosfomycin 8g q8h were initiated based on in vitro antibiotic combination testing results. His free ceftazidime and avibactam trough levels in the plasma were 22.6 mg/L and 4.5 mg/L respectively. Assuming 32% avibactam CNS penetration 6 , his CNS avibactam level was estimated to be 3mg/L, which was inadequate. Hence, ceftazidime-avibactam was increased to 2.5g q4h (each dose infused over 3h) and maintained for 5 weeks. Weekly trough concentrations ranged between 63.7 to 104.8 mg/L (ceftazidime) and 8.9 to

16.1 mg/L (avibactam). After 3 weeks of high-dose-therapy, brain abscess was aspirated. This sample showed no bacterial growth and yielded ceftazidime concentration of 57 mg/g; avibactam concentration of 8.6 mg/g. The patient completed therapy without major adverse events.
Conclusion: TDM enabled safe use of ultra-high-dose antibiotics.
Keywords: central nervous system infection, carbapenem-resistant infection, beta-lactam, ceftazidime-avibactam

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W221

Effect of ARC and FN on trough level and clearance of teicoplanin

Assoc Prof Ryota Tanaka[1], Ms Nozomi Kondo[1], Mr Ryosuke Tatsuta[1], Ms Haruka Tsushita[1], Dr Takehiro Hashimoto[2], Prof Kazufumi Hiramatsu[2], Prof Hiroki Itoh[1]
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Biography:

Dr. Ryota Tanaka, Ph.D., is an Associate Professor & Deputy Director at the Department of Clinical Pharmacy at Oita University Hospital in Japan. He earned his Ph.D. from Kumamoto University in 2014. Since joining the current department, he has contributed to the antimicrobial stewardship team and TDM work, providing novel evidence, particularly for antimicrobial TDM. He has acquired expertise in PK-PD modeling and simulation through his tenure as a visiting scientist at the Division of Translational and Clinical Pharmacology at Cincinnati Children's Hospital Medical Center. His current major research focuses on PK-PD analysis to optimize dosing strategy in special populations.

Background and Aims: Augmented renal clearance (ARC) and febrile neutropenia (FN) elevate the clearance of drugs excreted primarily by glomerular filtration. This study aimed to evaluate the influence of ARC and FN on dose-normalized trough concentration (C/D) and clearance of teicoplanin (TEIC) by comparing C/D between ARC and non-ARC patients as well as C/D and clearance between FN and non-FN patients.
Methods: This retrospective, single-center, observational cohort study enrolled 309 patients who received an intravenous injection of TEIC. Of the 94 patients who met the selection criteria, 25 satisfied the definition of ARC and 31 the definition of FN. ARC was defined as an estimated glomerular filtration rate ≥ 96.5 mL/min/1.73 m2 using the CKD-EPI formula. FN was defined as an axillary temperature ≥ 37.5°C and neutrophil count < 500/μL. TEIC clearance was estimated using a population pharmacokinetic model for Japanese adult patients with Bayesian estimation.
Results: Compared to the non-ARC group (n = 69), the ARC group (n = 25) had significantly lower first trough concentration (p = 0.014) and lower C/D (p = 0.009). In contrast, the FN (n =31) and non-FN groups (n = 63) did not differ significantly in the first trough concentration, C/D, or clearance. Forced entry multiple regression analysis identified only ARC as the independent factor associated with C/D (p = 0.001).
Conclusions: A higher TEIC loading dose may be required for patients with ARC, regardless of the presence or absence of FN.
Keywords: Teicoplanin, augmented renal clearance, febrile neutropenia

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W222

Cycloserine-Induced Neuropsychiatric Toxicity in Multidrug-Resistant Tuberculosis: Association with Peak Plasma Concentration

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Biography:

Mr Cheng studies the clinical pharmacy and clinical pharmacokinetics. He has a master degree of pharmacy from Soochow University. Now he is a clinical pharmacist in Zhejiang Hospital of Integrated Traditional Chinese and Western Medicine (also named Zhejiang Tuberculosis Diagnosis and Treatment Center). His research has been published in Cell Reports, Journal of Neuroinflammation, Infection and Drug Resistance and other journals.

Background: Cycloserine (Cs) is a crucial anti-drug-resistant tuberculosis medication with significant clinical efficacy. However, its clinical application is limited by neuropsychiatric-related adverse reactions (ADRs).
Aims: Develop a prediction model that accurate identification of high-risk populations for Cs-related neuropsychiatric ADRs.
Methods: This study retrospectively evaluated the peak plasma concentration (Cmax) of Cs and Cs-related neuropsychiatric ADRs, and analyzed the risk factors of developing neuropsychiatric ADRs. A multivariable ordinal logistic regression model was built to predict the incidence of neuropsychiatric ADRs.
Results: This study enrolled a total of 136 participants, with a cumulative incidence of neuropsychiatric ADRs of 12.5% (17/136). Patients with ADRs had significantly higher Cs Cmax (26.50 mg/L vs. 18.11 mg/L, P=0.0003). The incidence of ADRs increased with higher Cs exposure, particularly when Cmax exceeded 30 mg/L. ROC analysis demonstrated the strong predictive value of Cmax for neuropsychiatric ADRs (AUC=0.726, 95%CI: 0.6118-0.8396). Notably, the predictive efficacy of the logistic regression model significantly improved after incorporating drinking history as a covariate, achieving a final predictive accuracy of 87.6%. The model demonstrated good calibration (Hosmer-Lemeshow test p=0.563).
Conclusions: Cs Cmax serves as a critical indicator for predicting Cs-related psychiatric ADRs, with higher Cmax correlating with an increased likelihood of psychiatric ADRs. Dynamic monitoring of Cs Cmax combined with drinking history assessment in clinical practice enables accurate identification of high-risk populations for psychiatric ADRs, thereby providing a scientific basis for developing individualized medication regimens and implementing early interventions.
Keywords: Cycloserine, peak plasma concentration, neuropsychiatric-related adverse reactions

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W223

Evaluating Meropenem TDM Reliability in OPAT Settings: A New Sampling Strategy

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Biography:
Eliza Milliken is an Infectious Diseases Physician and Advanced Trainee in Clinical Pharmacology. Her research interests include the pharmacokinetics of antibiotics in severe bacterial infection and precision dosing in the outpatient parentral antibiotic (OPAT) setting

Background: Meropenem, a broad-spectrum beta-lactam antibiotic, is increasingly used amid rising antimicrobial resistance. Its variable pharmacokinetics and limited heat stability challenge maintaining therapeutic plasma levels in OPAT, though TDM may mitigate this. Clinicians often use convenience sampling from vascular access devices (PIVC, PICC, CVC) instead of venepuncture from TDM, though evidence questions its reliability. This study evaluates reliability of meropenem TDM via PICC sampling.
Aims: Assess whether meropenem TDM via convenience sampling from PICC lines yields reliable plasma concentrations, potentially improving OPAT availability for meropenem therapy and patient comfort.
Methods: A benchtop experiment was conducted using Bard polyurethane PICCs modified to varying lengths. Human plasma was spiked with meropenem to a target concentration of 20 mg/L. Samples were collected directly (no line) and after passage through segments of 5 cm, 10 cm, 25 cm, and 55 cm. Meropenem concentrations were measured via a validated UHPLC-MS/MS method over a 0.2–100 mg/L range. This process was repeated in triplicate.
Results: The assay performed reliably within a calibration range from LLOQ 0.2 mg/L to ULOQ 100 mg/L. Meropenem concentrations in plasma remained consistent across varying PICC lengths. Sample 0 (no PICC) had a mean concentration of 18.5 mg/L Sample 1 (shortest) had a mean concentration of 19.1 mg/L, Sample 2 showed 19.0 mg/L, Sample 3 19.0 mg/L, and Sample 4 (longest) 19.4 mg/L.
Conclusions: Convenience sampling via PICC reliably reflects meropenem plasma concentrations, supporting its use for TDM in OPAT. Further clinical studies are warranted.
Keywords: meropenem, TDM, OPAT, PICC, convenience sampling, pharmacokinetics.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W224

Correlation of Plasma Pharmacokinetics with Hair Drug Concentrations of Linezolid in MDR-TB

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Biography:

Aadil is a CSIR-SRF (Direct) Fellow pursuing Ph.D. in Pharmaceutical Analysis at the School of Pharmacy, Jamia Hamdard, New Delhi. His research focuses on pharmacometrics, pharmacokinetics, therapeutic drug monitoring (TDM), and pharmacogenomics, particularly in tuberculosis and cancer. He specializes in LC-MS/MS-based bioanalysis, population PK/PD modeling, and precision medicine approaches. Aadil has contributed to multiple research projects, including TDM of monoclonal antibodies in breast cancer and PK/PD modeling of anti-TB drugs. He is currently working on TDM and PK/PD modeling of linezolid in Indian MDR TB patients. He aims to integrate the PK/PD modeling in real clinical practice with special emphasis on TB and cancer.

Background: TDM for linezolid plays a crucial role in optimizing treatment outcomes in multidrug-resistant tuberculosis (MDR-TB) while minimizing toxicity. In contrast to plasma pharmacokinetics (PK), hair analysis provides a non-invasive method to assess long-term drug accumulation and adherence.
Aims: To assess hair's potential as a matrix for long-term drug monitoring, we compared plasma PK parameters (AUC, Cmax, Cmin) with hair concentrations of linezolid in Indian MDR-TB patients.
Methods: With the approval of the human ethics committee, plasma PK analysis was performed on 92 patients with MDR-TB, while hair drug concentrations were assessed on 90 patients. The quantification of plasma and hair samples was conducted using UPLC-MS. Plasma PK parameters and hair concentrations of the drugs were evaluated using non-compartmental analysis, and Spearman's correlation was applied for an assessment of their relationship.
Results: Hair drug concentrations correlated significantly with plasma AUC ($\rho = 0.81$, $P = 0.02$), indicating that hair drug levels reliably reflect plasma exposure. Based on these findings, hair analysis may serve as a non-invasive method for long-term adherence monitoring and TDM in MDR-TB patients.
Conclusion: It is clear that plasma PK correlates strongly with hair drug concentrations, which is supportive of the potential for hair as a complementary biomatrix for long-term TDM in MDR-TB prevention and treatment. Incorporating hair analysis in clinical practice could aid in adherence monitoring and individualized dosing strategies for optimizing treatment outcomes.
Key Words: Linezolid, MDR-TB,TDM, LC-MS/MS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W225

Amikacin in critically ill paediatric patients: A pharmacokinetics analysis

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Biography:

Toh is a clinical pharmacist with more than 15 years of experience in pediatric care, including neonatal and pediatric intensive care. He received his Bachelor of Pharmacy from Taipei Medical University in 2008, followed by a Master in Clinical Pharmacy from Universiti Kebangsaan Malaysia in 2014. With a deep commitment to improving therapeutic outcomes, Toh focuses on meticulous dosing strategies and effective treatment optimization for the vulnerable pediatric population. Driven by his passion for precision medicine, he is currently pursuing a PhD at Universiti Kebangsaan Malaysia, where his research centers on antibiotic pharmacometrics modeling to enhance individualized dosing in critically ill children. Toh's work aims to advance pediatric care through targeted, data-informed therapeutic interventions. Guided by his dedication to patient well-being, he strives to ensure that children receive the most appropriate treatments, ultimately contributing to healthier, happier futures. Outside of his professional pursuits, Toh remains an advocate for continuous education.

Background: Amikacin is widely used in critically ill paediatric patients but presents dosing challenges due to developmental pharmacokinetics (PK) variations. Factors such as age, body weight, organ maturation, and concurrent therapies profoundly impact therapeutic efficacy.
Aims: This study aimed to characterize current prescribing practices, determine the PK parameters of amikacin, and identify factors influencing serum levels in critically ill paediatric patients.
Methods: A retrospective analysis was performed from January 2022 through December 2023 on patients admitted to the Paediatric Intensive Care Unit who received intravenous amikacin. Trough and peak concentrations were obtained at the third dose. The elimination rate constant (Ke), volume of distribution (Vd), and clearance (CL) were estimated using a one-compartment model based on both concentrations. Clinical and laboratory data were collected to identify the factors affecting PK parameters.
Results: Of 214 patients, the mean dose administered was 14.06±2.11mg/kg/day over an average duration of 7.8±3.95days. The mean Ke was 0.14±0.26hr^{-1}, the mean Vd was 0.59±0.30L/kg, and the mean clearance (CL) was 0.08±0.03L/kg/hr. Nearly a quarter (24.3%) of Cmax values and 7.5% of Cmin values fell outside the therapeutic range. Notably, Vd significantly associated with age, creatinine clearance, alkaline phosphatase, and alanine aminotransferase levels, while CL was significantly associated with age, dose, and creatinine clearance.
Conclusion: A substantial proportion of critically ill paediatric patients do not achieve optimal amikacin levels with current dosing. Further refinement of amikacin dosing in this population is warranted, and the development of a pharmacometrics model is needed to optimize treatment outcomes and minimize toxicity.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W226

Determination of ganciclovir in patients after lung transplantation

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Biography:

Assoc. Prof. MSc. Eva Klapková, Ph.D. has been working at the Institute of Medical Chemistry and Clinical Biochemistry, Second Faculty of Medicine, Charles University, and Motol University Hospital since 2005. In 2009, she passed her board certification in Investigative Methods in Clinical Biochemistry, and in 2021, she was appointed Associate Professor (habilitation) in Medical Chemistry and Biochemistry at the Second Faculty of Medicine, Charles University. She currently serves as Deputy Head for Research and Science. Her professional focus is primarily on the development of chromatographic methods.

Background: Ganciclovir (GCV) is a nucleoside analogue used for the systemic treatment and prevention of infections caused by DNA viruses belonging to the Herpesviridae family. Severe manifestations of diseases caused by these viruses occur in patients with weakened immunity due to factors such as chemotherapy, acquired immunodeficiency from HIV infection, or immunosuppressive therapy following organ transplants. This drug is characterized by high inter- and intra-individual variability.
Aims: The aim of this work was to develop sensitive and rapid analytical method for the determination of ganciclovir and to evaluate the importance of therapeutic monitoring of ganciclovir in patients after lung transplantation.
Methods: An LC-MS/MS method was developed for the determination of GCV using electrospray ionization on an Agilent 1290 Triple Quad 6470 system. The internal standard used was isotopically labeled ganciclovir-d5. The analysis was performed on an Eclipse Plus C18 column using a gradient of mobile phases (A – water with buffer (5%), B – acetonitrile with buffer (5%)). The method was successfully validated. For sample preparation, only protein precipitation with acetonitrile was used.
Results: Patients after lung transplantation are always prophylactically administered by valganciclovir, and ganciclovir is given in the case of a confirmed infection. Levels were determined in 60 lung transplant patients. In more than 80% of cases, optimal serum levels of ganciclovir were not achieved with the initial dosing regimen.
Conclusions: The results demonstrated that therapeutic drug monitoring (TDM) is essential for all lung transplant patients to establish individualized optimal pharmacotherapy.
Key Words: ganciclovir, LC-MS, lung transplantation

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W227

Association between vancomycin renal clearance and sarcopenic conditions in critically ill patients

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Biography:
Dr. Injin Jang is a professor of f Clinical Pharmacology and Therapeutics at Seoul National University College of Medicine and Seoul National University Hospital. His research and clinical expertise span early-phase clinical trials and therapeutic drug monitoring (TDM), with a particular focus on optimizing drug development and precision dosing strategies. Dr. Jang has led numerous Phase I clinical trials, contributing to the advancement of both novel therapeutics and the scientific foundations of clinical pharmacology in Korea. He is actively involved in investigator-initiated and sponsor-driven studies, and has played a pivotal role in translating pharmacological science into clinical application through interdisciplinary collaborations.

Background: Vancomycin is a narrow therapeutic index drug primarily eliminated through renal excretion. Serum creatinine is commonly used to estimate renal clearance, but it may be overestimated in sarcopenic conditions, particularly in critically ill patients. Sarcopenic conditions can be assessed by evaluating muscle strength using the Medical Research Council Sum Score (MRC-SS).
Aims: The study aimed to investigate the association between muscle strength and vancomycin renal clearance in critically ill patients.
Methods: Patients in the intensive care unit (ICU) at Seoul National University Hospital in 2024, without renal diseases and with at least one vancomycin trough concentration and an MRC-SS, were included. Patients were classified into two categories based on MRC-SS: normal muscle strength (MRC-SS ≥ 36) and muscle weakness (MRC-SS < 36). The correlation between vancomycin trough concentrations and serum creatinine levels was analyzed using Spearman's rank correlation coefficients in both groups.
Results: A total of 28 patients were identified, with 12 in the normal strength group and 16 in the muscle weakness group. The serum creatinine levels (mean ± standard deviation) were 0.79 ± 0.28 mg/dL in the normal muscle strength group and 0.61 ± 0.22 mg/dL in the muscle weakness group, respectively. Vancomycin trough level was moderately correlated with serum creatinine levels in patients with normal muscle strength ($\rho = 0.412$, $p = 0.008$), but not in those with muscle weakness ($\rho = 0.118$, $p = 0.428$).
Conclusions: Serum creatinine may not accurately reflect vancomycin renal clearance in sarcopenic conditions among critically ill patients.
Keywords: Vancomycin, Sarcopenia

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

W228

The Illicit Fentanyl Landscape: Trends, Concentrations and Co-Occurrences

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Biography:

Melissa Bennett has a PhD in Biochemistry and Molecular Biology from the University of Calgary and is certified in Toxicological Chemistry by the American Board of Clinical Chemistry. She is a Fellow of the Academy of Diagnostics and Laboratory Medicine and serves as Associate Clinical Director at the Alberta Centre for Toxicology, within the Department of Physiology and Pharmacology at the University of Calgary. Additionally, she is the President of the Alberta Society for Human Toxicology.

Background: The drug landscape has shifted significantly in North America with changes in the availability, use and types of Illicit fentanyl analogs. Despite their presence, there remains a substantial gap in understanding these fentanyl analogs.

Aims: This study aims to characterize the trends, concentrations and co-occurrences of fentanyl, carfentanil, para-fluorofentanyl (pFF) and ortho-methylfentanyl (oMF) in urine samples from an opioid dependant population. Additionally, it seeks to evaluate cross-reactivities with a fentanyl immunoassay.

Methods: Urine samples were collected and analyzed over nine-months for fentanyl, norfentanyl, carfentanil, norcarfentanil and pFF. oMF testing was conducted over four months. Immunoassay data was obtained using an Olympus AU480 with the Thermo Scientific DRI Fentanyl assay. Mass spectrometry analysis was performed using an internally developed method on an Agilent 6470 triple quadrupole instrument.

Results: Among 5280 urine samples, 27% tested positive for fentanyl. Of these, 79% contained pFF, 75% oMF, 4% carfentanil, and 8% norcarfentanil. A trend indicated declining prevalence of pFF and oMF, while carfentanil is increasing. Concentrations are decreasing for pFF and oMF and increasing for fentanyl and carfentanil. Co-occurrence is common, with norfentanyl detected in 98% of carfentanil-positive, 97% of pFF-positive, and 98% of oMF-positive samples. pFF demonstrated 41% cross-reactivity with the fentanyl immunoassay, while OMF had <2% cross-reactivity.

Conclusions: Our findings highlight the widespread presence of fentanyl analogs in opioid-dependent populations, with pFF, oMF and carfentanil frequently co-occurring with each other and fentanyl. We observed fluctuations in the prevalence and concentrations of these analogs over time. Cross-reactivity varies among the fentanyl analogs.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W229

Cost Comparison Standard versus Extended N-Acetylcysteine Therapy in Non-Paracetamol-Induced Acute Liver Failure

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Biography:

Ezazaya binti Othman is a highly skilled and experienced Pharmacist, currently holding the position of Pegawai Farmasi at Hospital Sultan Ismail, Johor Bahru. She specializes in Clinical Pharmacokinetics and Geriatric Pharmacotherapy. Starting her career in 2007 as a Provisional Registered Pharmacist at Hospital Bukit Mertajam, Pulau Pinang, Ezazaya has steadily advanced through various roles, reaching her current position. She earned her Bachelor of Pharmacy from Universiti Teknologi MARA in 2007 and later obtained a Master's degree in Clinical Pharmacy from Universiti Kebangsaan Malaysia in 2013. Throughout her career, she has made notable contributions to professional publications, research and clinical practice guidelines. She is highly respected for her impactful work in enhancing patient care, particularly in the fields of Clinical Pharmacokinetics, Geriatric and Cardiology Pharmacotherapy.

Background: N-acetylcysteine (NAC) is commonly used to treat non-paracetamol-induced acute liver failure (ALF). While it is an established therapy, prolonged use can lead to significant financial costs. However, its cost-effectiveness in improving clinical outcomes remains unclear.
Aims: This study aims to compare the direct medical costs of standard (≤72 hours) and extended (>72 hours) NAC therapy, focusing on drug acquisition, laboratory tests, and hospitalization expenses.
Methods: This retrospective study analyzed hospital data from 2018 to 2024. Drug acquisition costs, including the drug and administration-related personnel expenses, were calculated. Hospitalization costs covered ward charges and laboratory investigations.
Results: Patients receiving extended NAC therapy had longer hospital stays (13.5 vs. 8 days, p=0.004) and delayed INR normalization (4 vs. 1 day, p<0.001). They also presented with higher MELD scores (29 vs. 15, p=0.007), indicating more severe liver disease. The total direct cost for extended NAC therapy was RM7371.06, compared to RM3567.47 for standard therapy (p=0.02).
Conclusions: In Malaysia, extended NAC therapy significantly increases direct medical costs due to longer hospital stays and delayed INR normalization. Despite the higher costs, the improvement in MELD scores suggests that extended therapy improves patient survival, making it a valuable option for critically ill patients.
Keywords: N-acetylcysteine (NAC), Acute liver failure (ALF), cost comparison, hospitalization costs, MELD score

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W230

The effect of the TGA's labelling requirements on reporting andrographis adverse reactions

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Biography:

Dr Musgrave is a molecular pharmacologist/toxicologist. He obtained his PhD from the University of Melbourne in 1989, postdoctoral work in the Institute of Pharmacology at the Free University of Berlin in 1991-1994, returning to Australia in 1994 on a CJ Martin Fellowship. He was appointed as Senior Lecturer in Pharmacology at the University of Adelaide in 2001. He has a broad interest in neuronal function and survival, natural product pharmacology and drug design. Current research work includes safety of herbal medicines and natural products as anti-amyloid medications. Ian has consulted with State Health and the TGA on herbal medicine safety.

Background: Andrographis paniculata and echinacea are herbal medicines popular for COVID-19 symptoms. These medicines can elicit hypersensitivity adverse drug reactions (ADRs), including anaphylaxis, in susceptible individuals. The Therapeutic Goods Administration (TGA) legislated new warning labels for andrographis and echinacea in Dec-2019 to combat ADRs. The effectiveness of these new labels in ADR prevention is poorly understood.
Aims: This study investigated the prevalence of hypersensitivity ADRs to these medications in the Australian population from 2015-2024; before and after implementation of the TGA's new label requirements.
Methods: Data from the TGA Database of Adverse Event Notifications (DAEN) was exported to Excel. Reports from 2015-2024 with hypersensitivity symptoms, defined by the Brown Scale, were included (n=513). ADR reports of glucosamine/chondroitin were used as a control given their usage should not have increased due to COVID-19 (n=25). Data was analysed alongside Australian influenza and COVID statistics.
Results: Five years before legislation change in May 2020, there was an average of 2.3 ADRs reported per month, compared to 7.3 per month after legislation, revealing an increase in hypersensitivity ADRs. The ADR rates were not constant but formed distinct peaks. Most peaks in ADR reports correlate with preceding increases in influenza-like illnesses. Average ADR reports for glucosamine and chondroitin remain stable.
Conclusions: Despite the TGA's new warning label requirements, influenza-like illnesses peaks are associated with an increase in andrographis/echinacea hypersensitivity ADRs.This indicates the need for a review of TGA warning label sizing and placement, and educating the public of ADRs associated with andrographis and echinacea use.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W231

Afatinib activates inflammasome leading to afatinib-induced nephrotoxicity

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Biography:
Ms. Yuka Sakai is a student of Faculty of Pharmacy at Osaka Medical and Pharmaceutical University. Her research focuses on elucidating the mechanisms of idiosyncratic reactions, including nephrotoxicity induced by molecular-targeted drugs, and identifying potential biomarkers.

Background: Endotherial growth factor receptor (EGFR) tyrosine kinase inhibitors (EGFR-TKI) is known to cause drug-induced nephrotoxicity (DIN). We have reported that covalent binding of drugs induces the release of damage-associated molecular patterns (DAMPs) that activate immune cells, leading to the idiosyncratic drug-induced serious adverse effects. Afatinib, dacomitinib, and osimertinib have a covalent group in their structural formula, which may cause immune related DIN.
Aims: In this study, we examined whether EGFR-TKI can activate inflammasomes in the human renal proximal tubule epithelial cells (RPTECs) and the human macrophage cell line (THP-1 cell).
Methods: Human RPTECs were respectively added afatinib, dacomitinib, erlotinib, gefitinib, and osimertinib and cultured at 37ºC, 5% CO2 for 28 days. The supernatant from the RPTECs was added to human macrophage cell line (THP-1 cell), which was incubated for 24 hr. IL-1β concentration of the culture supernatants and caspase-1 activity of THP-1 cells were measured. The protein of heat shock protein（HSP）40, HSP60, HSP70, HSP90, S100A6, S100A8, S100A9 and S100A11 were measured by the western blotting.
Results: The supernatant from an incubation of RPTECs with afatinib increased the IL-1β production and caspse-1 activity of THP-1 cells. In addition, the production of IL-1β and caspase-1 activation were inhibited by adding YVAD. HSP90 was significantly increased in the supernatants from RPTECs incubated with afatinib.
Conclusions: These results demonstrated that the covalent binding of afatinib can cause the release of HSP 90 and activate inflammasomes, which can cause immune-related adverse events including DIN.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W232

Elucidation of the mechanism of lorlatinib-induced liver injury

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Biography:
Ms. Chihiro Otsubo is a fifth-year pharmacist candidate at Faculty of Pharmacy, Osaka Medical and Pharmaceutical University. She has been a member of the Laboratory of Pharmacotherapeutics and Toxicology since her fourth year. She became interested in drug-induced liver injury as severe adverse events after reading a paper on drug induced liver injury written by her supervisor. Her research interests include elucidation of the pathogenesis of idiosyncratic drug-induced liver injury caused by lorlatinib and identification of potential biomarkers.

Background: Lorlatinib, which is approved for non-small cell lung cancer, might cause idiosyncratic liver injury as severe adverse events. However, the details of the mechanism are unknown. In our previous study, it is reported that reactive metabolites may cause the release of damage-associated molecular patterns (DAMPs), which leads to activate immune cells.
Aims: We evaluated whether lorlatinib or its reactive metabolites can activate inflammasomes in the human macrophage cell line (THP-1 cell).
Methods: Three-dimensional cultured human hepatocarcinoma functional liver cell-4 (FLC-4) cells were incubated with 0.01-3.0 μM lorlatinib for 7 days. The supernatants from the FLC-4 cells was added to THP-1 cells, which was incubated for 24 hr. IL-1β production in the supernatants of THP-1 cells and caspase-1 activity of THP-1 cells were measured. One-aminobenzotriazole (ABT, 1 mM) and Ac-YVAD-cmk (YVAD, 1 μM) were used to inhibit cytochromes P450 activities and caspase-1 activity, respectively. DAMPs and IL-6 levels in the culture medium of FLC-4 cells were measured by western blotting.
Results: The supernatant from FLC-4 cells treated with lorlatinib significantly increased IL-1β production and caspase-1 activity of THP-1 cells. These increase were inhibited by ABT or YVAD. In addition, IL-6 expression in the supernatant from FLC-4 cells treated with lorlatinib was significantly increased.
Conclusions: There results suggested that reactive metabolites of lorlatinib can cause the release of IL-6 and activate inflammasome in THP-1 cells. IL-6 may be predictive biomarkers of liver injury with lorlatinib.
Key Words: ALK tyrosine kinase inhibitors, Lorlatinib, Reactive metabolites, Danger-related molecular patterns, Inflammasome

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W233

Serum concentration of eltrombopag-acyl glucuronide is associated with eltrombopag-induced liver dysfunction

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Biography:

Mr. Oda is a PhD student at the Department of Pharmaceutical Sciences, Graduate School of Comprehensive Human Sciences, University of Tsukuba, and a pharmacist at the Department of Pharmacy, University of Tsukuba Hospital. He is a member of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology. He is the first author of a study on eltrombopag-induced interference in bilirubin assays, published in Therapeutic Drug Monitoring in 2025. His research focuses on pharmacokinetics, therapeutic drug monitoring and pharmacogenetic evaluations of drug-induced toxicity for thrombopoietin receptor agonists. His research aims to optimize drug therapy through advancing the understanding of drug disposition and safety.

Background: Eltrombopag is metabolized to its acyl glucuronide (AG) by uridine diphosphate glucuronosyltransferase (UGT) 1A1. Although several AGs have the potential to cause drug-induced liver injury, the impact of eltrombopag-AG on liver injury is unclear.
Aims: We examined the effects of serum eltrombopag and its AG concentrations on the occurrence of liver dysfunction in patients with aplastic anemia.
Methods: Serum eltrombopag and its AG concentrations, UGT1A1 genotype, and liver dysfunction (elevations in aminotransferases or bilirubin) were examined in 41 patients with aplastic anemia. The association of eltrombopag and its AG concentrations with prediction of liver dysfunction was assessed using receiver operating characteristic (ROC) analysis.
Results: Higher serum eltrombopag and its AG concentrations were observed in patients with liver dysfunction compared with those with the normal function (eltrombopag: 25.8 ± 20.2 vs. 11.0 ± 9.9 μg/mL, $P < 0.001$; eltrombopag-AG: 5.5 ± 4.3 vs. 1.7 ± 1.2 μg/mL, $P < 0.001$). Eltrombopag-AG concentration demonstrated a higher predictive performance for liver dysfunction compared with eltrombopag (area under the ROC curve: 0.81 vs. 0.71, both $P < 0.001$), with the cut-off values of 3.1 and 17.7 μg/mL, respectively. UGT1A1 extensive metabolizers (*1/*1) exhibited higher eltrombopag-AG concentrations than intermediate and poor metabolizers (*6, *28 carriers) (3.7 ± 3.9 vs. 2.1 ± 1.9 μg/mL, $P = 0.082$), and had a higher occurrence rate of liver dysfunction (43% vs. 10%, $P = 0.018$).
Conclusions: Serum eltrombopag-AG concentrations, especially in UGT1A1 extensive metabolizers, are associated with eltrombopag-induced liver dysfunction.
Key Words: eltrombopag, acyl glucuronide metabolite, liver dysfunction

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W234

Investigating New Prophylactic Agents for Vancomycin-induced Nephrotoxicity by using Japanese Medical Big-data

Ms. Megumi Saito, Assoc Prof Shungo Imai, Dr. Hayato Kizaki, Dr. Satoko Hori
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Biography:

Shungo Imai is a Associate Professor of Keio University of Faculty of Pharmacy, Japan. In addition to therapeutic drug monitoring, he specialize in medical big data analysis and machine learning. By applying these data science methods to therapeutic drug monitoring research, he is trying to produce valuable findings.

Background: Nephrotoxicity is a typical adverse effect of vancomycin (VCM). Although several drugs have been reported to prevent vancomycin-induced nephrotoxicity (VIN) in basic research, their real-world effectiveness remains unclear.
Aims: This study aimed to identify novel drugs that prevent VIN using medical big data.
Methods: We used a large Japanese electronic medical record database with information on approximately 20 million individuals. Patients who underwent intravenous VCM between April 1996 and March 2022 were included in this study. Several known VIN risk factors (covariates) and potential protective drugs based on basic studies were selected as explanatory variables, and a multivariate logistic regression analysis was performed. Propensity score matching was used to validate the prophylactic effects of the candidate drugs extracted using logistic regression analysis. The study protocol was approved by the Ethics Committee of Keio University (Number 221125–1).
Results: Among 12,411 eligible patients, VIN occurred in 2,267 (18.3%). Seventeen factors affecting VIN were identified, replicating previous findings. Vitamin E preparations [odds ratio (OR): 0.459, 95% confidence interval (CI): 0.239–0.883] and ramelteon (OR: 0.691, 95% CI: 0.556–0.858) were observed as preventive effects against VIN. After propensity score matching, vitamin E and ramelteon reduced VIN by approximately 8% (17.46% to 9.52%) and 6% (21.38% to 15.38%), respectively. Sensitivity analyses, using different definitions of concomitant drug use, revealed consistent trends.
Conclusions: Vitamin E and ramelteon have been identified as potential prophylactic agents for VIN. Further investigations are necessary to verify these novel findings.
Keywords: vancomycin, nephrotoxicity, medical big data, ramelteon, vitamin E

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W235

The Outcome of Standard versus Extended N-Acetylcysteine Therapy on Non-Paracetamol-Related Liver Injury

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Biography:
Wan Farhah Adiba binti Wan Abd Ghafar is a highly experienced clinical pharmacist specializing in pharmacokinetics and emergency ward pharmacy. She holds a Bachelor of Pharmacy (Hons) from Cyberjaya University College of Medical Sciences (2012) and a Master of Clinical Pharmacy from Universiti Kebangsaan Malaysia (2020). Currently serving at Hospital Sultan Ismail, Johor Bahru, she has over a decade of expertise in clinical pharmacokinetics, therapeutic drug monitoring (TDM), and emergency medicine. Throughout her career, Wan Farhah has contributed significantly to pharmaceutical research, serving as the principal investigator for multiple studies on pain management, toxicology, and cardiology. She is also actively involved in clinical training, having delivered lectures and workshops on antidotes, pharmacokinetics, and therapeutic drug monitoring. Recognized for her excellence, she has received awards for outstanding service and professional contributions. Her dedication to advancing clinical pharmacy continues to impact patient care and medical research in Malaysia.

Background: The optimal duration of N-acetylcysteine (NAC) therapy in non-paracetamol-induced acute liver failure (ALF) remains uncertain. While NAC is widely used, its impact on clinical and biochemical outcomes with prolonged therapy is not well established.
Aims: This study aims to evaluate patient outcomes following NAC treatment for non-paracetamol-induced liver injury by comparing standard (≤72 hours) and extended (>72 hours) NAC therapy. It specifically examines patient characteristics, time to INR normalization, and biomarkers of hepatic recovery between both treatment durations.
Methods: A retrospective cohort study was conducted on patients receiving NAC for non-paracetamol-induced ALF. Clinical outcomes, including hospital length of stay (LOS) and time to INR normalization (<1.5), were analyzed. Kaplan-Meier survival analysis was performed to assess time to INR normalization and all-cause mortality at 3 weeks, with statistical significance determined by the log-rank test.
Results: Patients in the extended NAC group had a longer hospital stay (13.5 vs. 8 days, p=0.004) and delayed INR normalization (4 vs. 1 day, p<0.001). Kaplan-Meier analysis showed a lower probability of early INR normalization (log-rank p<0.001). The extended group had higher MELD scores (25 vs. 12, p=0.004), elevated serum creatinine (250 vs. 76 µmol/L, p<0.001), and higher ALP and bilirubin levels, suggesting more severe liver dysfunction and cholestasis. However, Kaplan-Meier analysis also showed no significant difference in survival the two groups (log-rank p=0.473).
Conclusions: Extended NAC therapy was linked to prolonged hospitalization, delayed INR normalization, and greater hepatic and renal dysfunction. Tailoring NAC duration based on disease severity may help optimize patient management.

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W236

Innovative Therapeutic Drug Monitoring and Pharmacogenetics for Fentanyl Management and Overdose Prevention

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Biography:

Dr. Ofelia Noceti, PharmD, PhD is a distinguished Clinical Pharmacologist and Researcher with expertise in Metabolomics, Biomarkers in Solid Organ Transplantation, Immunobiology, Cell Signaling, and Pharmacology (PK, PD, PGx, Pharmacovigilance). Passionate about Patient Empowerment, Adherence, Health Technology Assessment (HTA), Pharmacoeconomics, and Digital Transformation. Dr. Noceti has led groundbreaking research projects improving personalized medicine, medication adherence, and therapeutic drug monitoring in liver transplant patients.

Currently serving as Deputy General Manager at Uruguay's HTA Agency, she drives research on health technology evaluation and patient engagement. As a Clinical Pharmacologist at the National Center for Liver Transplantation and Liver Disease, she pioneers pharmacovigilance, clinical research, and quality assurance initiatives. With a Ph.D. in Pharmacology from Université de Limoges, Dr. Noceti continues to shape the future of healthcare innovation and policy.

Background: Fentanyl, a synthetic opioid with a narrow therapeutic window, has become a major challenge due to its high potency and the increasing prevalence of illicitly manufactured fentanyl, leading to rising overdose fatalities. Traditional monitoring methods are often inadequate in distinguishing between therapeutic use, misuse, and toxicity. A therapeutic drug monitoring and pharmacogenetics-based approach could provide a precision medicine framework to optimize fentanyl use and improve patient safety.

Aims: This study evaluates TDM strategies, pharmacogenomic applications, and real-time toxicology innovations for fentanyl monitoring and overdose prevention. Additionally, we analyze global policy gaps in integrating these strategies into clinical practice.

Methods: A systematic review of fentanyl pharmacokinetics, drug metabolism variability, and TDM methodologies was conducted, incorporating clinical case studies from hospitals, forensic laboratories, and harm reduction programs.

Results: Four key findings emerged:

1. TDM advancements, such as real-time biosensors and LC-MS/MS assays, improve fentanyl exposure assessment.
2. Pharmacogenetics (CYP3A4, ABCB1 polymorphisms) predicts individual fentanyl metabolism and overdose risk.
3. Forensic toxicology biomarkers differentiate between therapeutic and illicit fentanyl use, guiding clinical interventions.
4. Harm reduction strategies integrating TDM enhance naloxone distribution and overdose reversal outcomes.

Conclusions:
TDM, combined with pharmacogenetics, can revolutionize fentanyl management, ensuring precision dosing and reducing opioid-related harms. Integrating these tools into clinical protocols and global policies will enhance patient safety and regulatory efforts.

Keywords: fentanyl, therapeutic drug monitoring, pharmacogenetics, opioid toxicity, forensic toxicology, overdose prevention

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W237

Prolonged urinary detection time of 11-nor-9-carboxy-Δ9-tetrahydrocannabinol in a pregnant occasional cannabis user

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Biography:

Siri Amundsen obtained her medical degree from the University of Bergen (UiB), Norway. She is a specialist in clinical pharmacology and currently works as a senior consultant at the University Hospital of North Norway. Her research interests include pharmacotherapy, pharmacokinetics and therapeutic drug monitoring (TDM), with a special focus on drug use during pregnancy and breastfeeding.

Background: Limited data exist on pharmacokinetics of cannabinoids in pregnancy and how altered disposition may affect results of drug testing. This case-report describes a woman detained in an addiction treatment ward in late pregnancy due to admitted occasional use of cannabis. She was subjected to urine drug testing every 3 to 8 days, extending into the postpartum period. The woman denied any further use following admission.
Aims: To emphasize challenges in interpreting cannabinoid drug test results in a largely unstudied population, where positive results may have severe consequences.
Methods: 11-nor-9-carboxy-Δ9-tetrahydrocannabinol (THCCOOH) was quantified in urine by liquid chromatography-tandem mass spectrometry with a cut-off ≥10.3 ng/ml. Creatinine-normalization was applied for comparison.
Results: THCCOOH concentrations decreased from 276.6 ng/ml to 10.3 ng/ml, over a period of 78 days. Creatinine-normalized levels did not decline as steadily as expected and fluctuated in the low concentration range. The observed excretion pattern would have indicated recent use had traditional algorithms for interpretation been applied. Drug testing was continued for 10 weeks after the last positive specimen, with negative results.
Conclusions: Assuming that the woman's account is reliable, urinary detection-time of THCCOOH was >11 weeks after the last consumption, which is prolonged compared to what has previously been reported in occasional cannabis users. Further research is needed to assess whether established algorithms for interpretation are applicable to a pregnant population in differentiating residual cannabis excretion from recent use. We suggest interpreting urine THCCOOH test results, especially at low-range concentrations, with caution.
Keywords: Pharmacokinetics, pregnancy, cannabis, drug testing

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W238

Impact of Diseases and Renal Function on Serum Levetiracetam Concentrations

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Biography:

Assistant Professor Dr. Denpong Patanasethanont is a faculty member in the Department of Clinical Pharmacy at the Faculty of Pharmaceutical Sciences, Khon Kaen University, Thailand. He holds a Ph.D. and specializes in clinical pharmacokinetics, therapeutic drug monitoring, and pharmacotherapy. His research interests include pharmacokinetics, therapeutic drug monitoring, pharmacotherapy, pharmacology, and toxicology. He has contributed to several national and international journals. Notable publications include studies on methotrexate monitoring in osteosarcoma patients and the modulation of P-glycoprotein function by Thai plant extracts

Background: Levetiracetam is widely used for seizure prophylaxis, focal and generalized seizures, status epilepticus, subarachnoid hemorrhage, and traumatic brain injury. It has nearly 100% bioavailability, low protein binding, linear pharmacokinetics, and a wide therapeutic index. However, as levetiracetam is primarily eliminated via the kidneys, the impact of renal function and other factors on its pharmacokinetics remains unclear.
Aims: This study aimed to assess levetiracetam pharmacokinetics, determine the prevalence of sub-therapeutic and over-therapeutic levels, and evaluate factors affecting drug concentrations.
Methods: A retrospective study was conducted using medical records from January 2020 to December 2024. Data collected included demographics, renal function, underlying diseases, concomitant medications, dosage regimen, and measured drug levels. A one-compartment, first-order pharmacokinetic model was used, and statistical analyses identified factors influencing drug concentrations.
Results: Among 177 patients (380 serum concentrations), sub-therapeutic and over-therapeutic levels were observed in 128 (72.32%) and 4 (2.82%) patients, respectively. Age, sex, and weight had no significant impact. Enzyme-inducing drugs increased sub-therapeutic levels (71.83% vs. 57.07% in monotherapy). Patients with epilepsy, status epilepticus, and traumatic brain injury had higher sub-therapeutic rates. Notably, 95.24% of patients with augmented renal clearance had sub-therapeutic levels, with eGFR ≥ 95 ml/min/1.73m² strongly associated with drug levels below the therapeutic range (12–46 mg/L).
Conclusions: High renal function and certain diseases significantly affect levetiracetam pharmacokinetics, increasing sub-therapeutic levels. Therapeutic drug monitoring may optimize dosing, and further research is needed to improve treatment in high-risk populations.
Key Words: Levetiracetam, Therapeutic Drug Monitoring, Renal function, Augmented Renal Clearance, Traumatic Brain Injury, Epilepsy

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W239

Weight gain associated with automated vs other insulin delivery methods

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Biography:
Hesham Al-Sallami is an associate professor of clinical pharmacy practice. He holds a PhD (University of Otago) in quantitative clinical pharmacology and pharmacometrics. Hesham's research interests include drug dose individualisation in special populations, with a focus on paediatrics and in obesity.

Background: Exogenous insulin treatment is known to cause excess weight gain, but its impact may vary with different insulin dosing methods. It is unclear whether automated insulin delivery (AID) impacts weight gain differently compared to conventional care. It is hypothesised that AID, by more closely mimicking the body's natural insulin response, may result in less weight gain and potentially lower insulin total daily dose (TDD) compared to conventional methods.
Aims: To evaluate the effect of AID systems compared to conventional insulin therapy on body weight, body mass index (BMI), and insulin TDD in patients with type 1 diabetes mellitus.
Methods: A comprehensive systematic literature search was conducted in PubMed, Scopus, Embase, and Cochrane databases to identify randomised controlled or crossover studies comparing AID to conventional care for T1DM, with a minimum duration of 12 weeks.
Results: In total 14 studies met the inclusion criteria, with data extracted for BMI (6 studies), BMI z-score (5 studies), body weight (12 studies), insulin TDD per kilogram of body weight (9 studies). The only statistically significant finding was related to body weight, where participants using AID gained a modest amount more than those in the control groups during the study period (Cohen's d = 0.19, p <0.001).
Conclusion: The findings do not support the hypothesis that AID systems lead to reduced weight gain in T1DM patients, at least in the short- to medium-term. Longer follow-up studies may be needed to detect any potential long-term differences in weight management or insulin requirements.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

W240

The Rational Basis for Personalized Treatment using Concentration Guided Dosing

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Biography:

Professor Holford obtained his medical qualifications (MBChB, MRCP) in the United Kingdom. In 1983 he moved to Auckland, New Zealand to join the University of Auckland in the Dept of Pharmacology & Clinical Pharmacology. Until 1989 he had a part time appointment as a Specialist in Internal Medicine at Auckland Hospital. During this period he was elected Fellow of the Royal Australasian College of Physicians. He retired from the University of Auckland as Professor Emeritus of Clinical Pharmacology at the end of 2021. His interests are in applying pharmacokinetics and pharmacodynamics to clinical pharmacology and developing tools to aid dose individualization (www.nextdose.org).

Background: The principles of Concentration Guided Dosing (CGD) provide a rational basis for personalized dosing. Existing terminology such as Therapeutic Drug Monitoring (TDM) or Model Informed Precision Dosing (MIPD) may have multiple meanings or be imprecisely defined.
Aims: The purpose of this presentation is to explain and encourage the use of terminology that distinguishes between the steps of measurement and reporting of concentrations, interpretation of the measurements and subsequent prediction of individualised doses.
Methods: A brief history of CGD reveals the evolution of more accurate terminology focused on using concentration observations to provide individual drug dose guidance to clinicians.
Results: CGD is commonly implemented using either the Therapeutic Window Approach (TWA) or the Target Concentration Approach (TCA). However, only the latter approach offers a truly personalized treatment aimed at an optimally effective and safe dose for each patient.
Conclusions: CGD approaches should include a clear description of how concentrations are used to individualise dosing to achieve a clinical outcome.
Key Words: Clinical Pharmacology, Concentration Guided Dosing, Target Concentration Intervention, Therapeutic Drug Monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W241

TDM of Erythrocyte Methotrexate Polyglutamates in Rheumatoid Arthritis? A Prospective Study

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Biography:

Yi Ma, PhD in Pharmacology, is a Pharmacist-in-charge and Clinical Pharmacist specializing in Rheumatology and Immunology at the Pharmacy Department of Peking University Third Hospital. His main research areas include pharmacokinetics, systems omics, personalized therapeutic drug monitoring, and pharmaceutical services. He is the Principal Investigator for two projects, including one funded by the Beijing Natural Science Foundation, and has contributed to multiple national and provincial projects, including the National Natural Science Foundation. Yi Ma has played a key role in developing four national clinical practice guidelines/expert consensus documents. He has presented his work at international conferences such as IATDMCT, ACCP, and the Chinese Pharmacological Society Therapeutic Drug Monitoring Academic Annual Meeting. He was also a second author recipient of the Capital Medical University Science and Technology Award.

Background: Methotrexate (MTX) is the first-line treatment for rheumatoid arthritis (RA), whereas it plays a significant role in inter-individual variability regarding the efficacy and toxicity. Methotrexate polyglutamates (MTXPGn) in erythrocytes may serve as biomarkers for treatment response, but there is still a gap in current evidence to guide MTX TDM in RA.
Aims: To investigates the correlation between MTXPGn concentrations and clinical outcomes in Chinese RA patients, and finally to optimize individualized therapy of MTX.
Methods: A prospective, single-center cohort study was designed and conducted. Efficacy outcomes were assessed using 28-joint Disease Activity Score (DAS28) and Simplified Disease Activity Index (SDAI). Safety outcomes included hepatotoxicity (defined by CTCAE) and Gastrointestinal Symptom Rating Scale (GSRS). MTXPG1-5 concentrations in erythrocytes were measured at 1, 3, and 6 months using LC-MS/MS.
Results: Currently, 59 treatment-naive RA patients receiving MTX (12.5–17.5 mg/week) was enrolled. MTXPGn concentrations increased over time, with a significant rise at 3 months. MTXPG3 was the predominant form (43.2%). At 3 and 6 months, ΔDAS28% and ΔSDAI% were significantly correlated with total and specific MTXPGn levels ($P<0.05$). Patients achieving ΔSDAI ≥50% had significantly higher MTXPGn concentrations ($P<0.05$). Specific MTXPGn concentrations were significantly elevated in patients with hepatotoxicity ($P<0.05$), while GSRS scores showed no significant difference.
Conclusion: Erythrocyte MTXPGn concentrations associate with MTX efficacy and hepatotoxicity in Chinese RA patients, supporting their potential role in dose optimization. Erythrocyte MTXPGn-based TDM would be expected to guide dose adjustment and improve outcomes of MTX therapy.
Keywords: Rheumatoid arthritis, methotrexate, therapeutic drug monitoring, Individualized medication

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W242

Ellagic acid's potential for treating chemotherapy-induced neuropathy: a therapeutic assessment.

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Biography:

Ms. Krishnalekha Bandyopadhyay is a PhD Research Scholar at JSS College of Pharmacy, JSS AHER, Mysuru, as of January 2024. She holds on M.Pharm in Pharmacology from JSS College of Pharmacy, Mysuru, and a Bachelor's degree in Pharmacy from Siksha 'O' Anusandhan University, Bhubaneswar, Odisha. She has gained one month of clinical training experience at SUM Hospital in Bhubaneswar, Odisha, and one month of Industrial experience at Santis Pharmaceutical in Sikkim. Her research focuses on Pharmacology, particularly the synthesis of novel molecules, and she is currently working on projects related to CNS disorders. Ms.Krishnalekha Bandyopadhyay has published two research and five review articles, and has participated in eight conferences at esteemed institutions such as JSS SFEC, APTICN, IPSCON, Sarada Vilas College Mysuru, and the Dhara Ayurvedic Conference in Bangalore. She actively contributes to the scientific community through her presentations at academic conferences.

Introduction: Chemotherapy-Induced Peripheral Neuropathy (CIPN), commonly caused by Paclitaxel, significantly affects patients' quality of life by inducing neuropathic pain through abnormal sensory signal processing. This pain is challenging to treat due to its complex pathophysiology, involving altered ion channel functions like TRPV1 and neuroinflammation. Ellagic acid, a natural polyphenol known for its antioxidant and anti-inflammatory properties via the Nrf2 pathway, shows promise in alleviating CIPN symptoms. This study explores its therapeutic potential in managing neuropathy.
Aim and Objectives: This study aims to evaluate the effectiveness of ellagic acid in alleviating chemotherapy-induced neuropathy. Specific objectives include assessing its impact on thermal and cold allodynia, antioxidant activity, inflammation, and histopathological changes in nerve tissues, comparing its efficacy with pregabalin.
Methods: Neuropathy was induced in male Swiss albino mice using Paclitaxel (2 mg/kg, i.p.) for 5 days. Mice were then treated with ellagic acid (100 mg/kg and 200 mg/kg, orally) and pregabalin (5 mg/kg, orally) for 11 days. Behavioral tests measured thermal and cold allodynia, while biochemical markers assessed antioxidant levels and inflammatory mediators. Histopathological analysis of nerve tissues and in vitro studies using SH-Sy5Y neuroblastoma cells were also conducted.
Results: Ellagic acid significantly reduced thermal and cold allodynia, enhanced antioxidant levels, and decreased proinflammatory cytokines (TNF-α, IL-6). Histopathological analysis showed neuroprotection.
Conclusion: Ellagic acid alleviates chemotherapy-induced neuropathy by reducing oxidative stress and inflammation, demonstrating neuroprotective properties. Its comparable efficacy to pregabalin suggests potential as a natural therapeutic option for CIPN, meriting further clinical exploration.
Keywords: Neuropathy, Inflammation, Ellagic Acid, Pregabalin

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W243

Therapeutic Drug Monitoring of lacosamide concentration in paediatric population with epilepsy

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Biography:

Dr. Silvia is a Senior Resident at Christian Medical College (CMC), Vellore, where she is committed to therapeutic drug monitoring services and advancing clinical research.

Dr. Silvia completed her postgraduate education in Pharmacology and has done a fellowship in Applied Pharmacokinetics. Her clinical interests lie in Therapeutic Drug Monitoring, Pharmacogenomics and Pharmacometrics .In addition to this , Dr. Silvia is involved in academic teachings to medical students.

Background: Lacosamide, a third-generation antiepileptic drug, is approved as adjunctive therapy for adults, adolescents, and children (>4 years) with partial-onset epilepsy. Despite its clinical utility, experience with therapeutic drug monitoring of lacosamide remains limited.
Aim: To assess the pharmacokinetic variability of plasma lacosamide concentrations and to evaluate the impact of concomitant antiepileptic therapy on these concentrations in pediatric patients with focal epilepsy.
Methods: Steady-state trough concentrations of lacosamide were determined in 52 epileptic patients attending the Pediatric Neurology Outpatient Clinic. Plasma lacosamide levels were quantified using a validated high-performance liquid chromatography (HPLC) assay. Furthermore, the correlation between plasma lacosamide concentration and clinical outcomes, specifically the reduction in seizure frequency over a six-month period will be assessed.
Results: A total of 52 children (mean age 10.43 ± 5.13 years) were enrolled in the study. The findings from the initial TDM visit are reported herein. The median daily dose of lacosamide was 200 mg (range: 50–400 mg). The mean plasma lacosamide concentration and concentration-to-dose ratio were 6.2 ± 2.1 mg/L and 0.04 ± 0.02, respectively, indicating a significant interindividual variability of 61.3%. Comparisons of the dose-normalized concentrations between patients receiving valproic acid and those not receiving it revealed no statistically significant differences.
Conclusion: This study demonstrates considerable pharmacokinetic variability in lacosamide plasma concentrations among pediatric patients. Moreover, our findings suggest that concomitant valproic acid therapy does not exert a significant effect on plasma lacosamide levels. This study is ongoing, with two lacosamide measurements scheduled for each patient, and further analyses will be conducted.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W244

Exploring the Place of Therapeutic Drug Monitoring in RNA Drugs

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Biography:

Marc Labriffe, MD (2020), holds a Master's in Clinical Pharmacology, Biostatistics, and Epidemiology (2019) and a PhD in Pharmacology of Immunosuppressive Drugs (2023). He is Associate Professor of Medical Pharmacology at the Faculty of Medicine, Limoges, and Head of the "Pharmacology" unit in the Department of Pharmacology, Toxicology and Pharmacovigilance at Limoges University Hospital. As a member of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT), the European Association for Clinical Pharmacology and Therapeutics (EACPT), the French College of Medical Pharmacology (CNPM) and of the French Society of Pharmacology and Therapeutics (SFPT), he researches treatment personalization at Inserm U1248, focusing on immunosuppressants in transplantation, pharmacoepidemiology, and machine learning models for drug optimization. He also explores antibiotic modeling and dose individualization. Dr. Labriffe has 31 publications in peer-reviewed journals and has delivered numerous national and international presentations, including invited talks.

Background: RNA-based therapeutics represent a groundbreaking approach for treating genetic disorders, cancers, and infectious diseases. Despite their growing clinical application, the pharmacokinetics of RNA drugs and their potential for therapeutic drug monitoring (TDM) remain underexplored. Up to now, its role in RNA drug therapy has not well been established.
Aims: This review assesses the feasibility and requirement of TDM for RNA therapeutics, evaluating their pharmacokinetic variability and current measurement strategies.
Methods: A narrative literature review was conducted to identify key RNA drugs and their pharmacokinetic profiles. Data were gathered on measurement techniques, target concentrations, and inter-individual variability. AI-assisted tools such as Consensus, SciSpace, Litmaps, and Connected Papers facilitated article selection and comparison.
Results: RNA drugs exhibit diverse mechanisms, including RNA interference (-siran), mRNA-based protein synthesis, and antisense oligonucleotide activity (-rsen). Administration varies, requiring intravenous or subcutaneous delivery. Currently, TDM data are only available for a few RNA drugs: e.g. vutrisiran (polyneuropathy of hereditary transthyretin-mediated amyloidosis), remdesivir (antiviral), and mipomersen (familial hypercholesterolemia). Liquid chromatography-tandem mass spectrometry is the primary method for concentration measurement. Pharmacokinetic variability arises from enzymatic degradation, immune response differences, and variations in cellular uptake and distribution, influenced by genetic and metabolic factors.
Conclusions: While TDM has been successfully explored for a limited number of RNA therapeutics, the absence of standardized and validated target concentrations remains a significant challenge. Further clinical research is needed to refine monitoring strategies, ensuring safe and effective use of RNA drugs in precision medicine.
Key Words: RNA drug, oligonucleotide, pharmacokinetics, inter-individual variability

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W245

Population pharmacokinetics and exposure-response analysis of rivaroxaban in patients with atrial fibrillation

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Biography:

Nian-Shiuan Lai holds a Master's degree from the Graduate Institute of Clinical Pharmacy, National Taiwan University. His academic training and research experience have centered on population pharmacokinetics and exposure-response analysis to evaluate the potential application of therapeutic drug monitoring in pharmacotherapy.

Background: Rivaroxaban, a factor Xa inhibitor, is used for stroke prevention in atrial fibrillation (AF) patients. With identical dosing regimen, interindividual variability in pharmacokinetics may result in differences in rivaroxaban exposure and clinical outcomes.
Aims: To establish a population pharmacokinetic (PPK) model of rivaroxaban, identify factors influencing its concentration, and investigate the association between drug exposure and clinical outcomes.
Methods: This retrospective study enrolled AF patients receiving rivaroxaban therapy to measure steady-state drug concentrations. PPK modeling was performed using the Monolix 2023R1 (Lixoft SAS), with covariate selection based on a stepwise forward inclusion and backward elimination approach. The primary outcome was intracranial hemorrhage (ICH). Kaplan-Meier survival analysis and Cox proportional hazards modeling were used to analyze the exposure-response relationship.
Results: A total of 226 patients were enrolled and contributed 452 rivaroxaban concentrations during 2016 to 2023. A one-compartment model with first-order absorption and elimination adequately described the rivaroxaban pharmacokinetics. The estimated apparent clearance (CL/F) and volume of distribution (V/F) were 5.89 L/h and 45.96 L, respectively. Lean bodyweight significantly influenced V/F, while creatinine clearance and co-administration of cytochrome P450 3A4 or P-glycoprotein inhibitors affected CL/F. High rivaroxaban trough concentrations (>137 µg/L) was associated with an increased ICH risk (aHR: 28.3 [2.09 to 383]; P = 0.012).
Conclusions: The pharmacokinetics of rivaroxaban is influenced by bodyweight, renal function, and drug interactions. Additionally, elevated rivaroxaban concentrations may lead to an increased ICH risk. Measurement of rivaroxaban concentration may be helpful in selected populations.
Keywords: Rivaroxaban, atrial fibrillation, population pharmacokinetics, exposure-response analysis

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W246

Dabigatran Trough Concentrations: Should We Monitor?

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Biography:
Dr. Shamin Mohd Saffian is a senior lecturer at Universiti Kebangsaan Malaysia. His research focuses on precision dosing, therapeutic drug monitoring (TDM), dose optimization and population PKPD modeling with interest in the areas of anticoagulants, antiinfectives and oncology.

Background: Dabigatran is an anticoagulant with a fixed dosing regimen. Interindividual variability in exposure may impact efficacy and safety, increasing the risk of thromboembolism or bleeding. Monitoring dabigatran concentrations may help optimize therapy in certain patients.
Aims: To evaluate dabigatran trough concentrations in Malaysian patients and explore factors influencing variability.
Methods: A prospective cohort study was conducted at a tertiary hospital in Malaysia. Adult patients (≥18 years) prescribed dabigatran 110mg or 150mg between March 2021 and June 2022 were recruited. Plasma trough concentrations were measured using the Hemoclot Thrombin Inhibitor assay. Pearson's correlation assessed relationships between dabigatran concentrations and clinical variables. Mann-Whitney U and chi-square tests compared subgroups. Variability was quantified using the coefficient of variation and interquartile range. Point-biserial correlation evaluated associations between dabigatran concentrations and categorical variables.
Results: Sixty-nine patients were included, with a mean±SD dabigatran trough concentration of 65 ± 52.3 ng/mL. A 20-fold interindividual variability was observed, with concentrations ranging from 13.5-280 ng/mL. Significant correlations were found with CHA2DS2-VASc score (p=0.022), adherence (p=0.04), eGFR (p=0.019), diabetes (p=0.019), and calcium channel blocker use (p=0.021). No stroke events were observed, but six bleeding cases were reported (6.2%), primarily within the first six months of therapy.
Conclusion: Dabigatran is generally safe, but its efficacy and safety could be improved with concentration monitoring. Renal function, adherence, drug interactions, and comorbidities influence exposure and outcomes. While a direct correlation between bleeding risk and dabigatran concentrations was not confirmed, an exceedingly high concentration did result in bleeding.
Keywords: dabigatran, bleeding, thrombosis, concentration monitoring

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W300

Bioenergetic biomarkers in First-episode Bipolar Disorders: Linking Mitochondrial Dysfunction with Cognitive Decline

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Biography:

Yue Shen is a Ph.D. Candidate in Clinical Pharmacy at Central South University Second Xiangya Hospital, China, supervised by Professor HuaLin Cai. Her research focuses on therapeutic drug monitoring and clinical toxicology, with particular emphasis on identifying biomarkers for cognitive dysfunction in neurological disorders and investigating the regulatory mechanisms of cerebral glucose metabolism. She has published two first-author papers in journals in Journal of Drug Targeting and Genes & Diseases, with five collaborative publications in high-impact journals including Advanced Healthcare Materials. She presented her research findings at the ACCP 2024 international conference. She has successfully completed a Hunan Provincial Graduate Innovation Project and is currently participating in research funded by the National Natural Science Foundation of China as well as patent development initiatives.

Background: Mitochondrial dysfunction and disrupted bioenergetic processes are critical in the pathogenesis of bipolar disorder (BD), with cognitive impairment being a prominent symptom linked to mitochondrial anomalies. The Krebs cycle, integral to mitochondrial energy production, may be implicated in this cognitive dysfunction, yet its specific association with BD remains underexplored.
Aims: To investigate the association between Krebs cycle disruptions, mitochondrial dysfunction, and cognitive decline in first-episode, drug-naive BD patients, and to explore the potential of bioenergetic metabolites as biomarkers for BD diagnosis and therapeutic monitoring.
Methods: In this cross-sectional study, 144 first-episode, drug-naive BD patients and 51 healthy controls were assessed. Serum Krebs cycle biomarkers were quantified using liquid chromatography-tandem mass spectrometry. Cognitive function was evaluated through the Repeatable Battery for the Assessment of Neuropsychological Status and the Stroop Color-Word Test.
Results: BD patients exhibited significantly elevated serum levels of several Krebs cycle biomarkers compared to healthy controls, alongside lower cognitive function scores. Correlational analyses revealed that certain bioenergetic metabolites were significantly positively associated with anxiety and negatively correlated with cognitive performance in BD patients. Notably, succinic acid, α-Ketoglutaric acid, and malic acid emerged as independent risk factors for BD, with their combined profile demonstrating diagnostic utility.
Conclusions: These findings underscore the potential of serum bioenergetic intermediates as biomarkers for BD, providing insights into the mitochondrial dysfunction underlying cognitive impairment. The study offers a basis for early diagnosis and targeted therapeutic strategies.
Key Words: Bipolar disorder, bioenergetic metabolites, Krebs cycle, mitochondrial dysfunction, cognitive impairment, biomarkers

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W301

Gut Microbiota Characteristics of Tacrolimus-Induced DILI in Renal Transplant Patients

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Biography:

Dongke Yu is an associate researcher at the Sichuan Academy of Medical Sciences & Sichuan People's Hospital. Her main research focuses on discovering new targets and new drug development for liver fibrosis and cholestatic liver disease, funded by multiple projects such as Sichuan Provincial Department of Science and Technology, Sichuan Provincial Health Commission, etc. She has published over 30 SCI papers in well-known journals like "Liver International", "Journal of Hepatology", and "British Journal of Pharmacology".

Background: Research shows a link between gut microbiota and drug-induced liver injury (DILI). Renal transplant patients on Tacrolimus (Tac) therapy often suffer from DILI, but the exact mechanism is unclear.
Aims: To compare gut microbiota differences between renal transplant patients on Tac regimen with DILI and those with stable liver function, explore the DILI-flora relationship, find specific DILI-related microbiota, and provide potential biomarkers for early DILI identification.
Methods: Patients from Sichuan Provincial People's Hospital's Organ Transplant Center on Tac regimen were included. DILI diagnosis followed the "Chinese Guidelines for the Diagnosis and Treatment of Drug-induced Liver Injury (2023 Edition)". Fecal samples were collected, and 16S rRNA gene sequencing was done to analyze gut microbiota differences and their correlation with Tac-induced DILI.
Results: 32 DILI patients and 40 with normal liver function were included. Alpha diversity analysis showed lower Chao1 (P = 0.038) and ACE (P = 0.043) indices in the DILI group, indicating reduced species richness. Beta diversity analysis showed differences in Unweighted UniFrac (P = 0.041), Bray - Curtis (P = 0.001) and Jaccard (P=0.001) distances. Oscillibacter and Ruminococcus gnavus groups were more abundant in the DILI group, while 10 types including Bacteroidetes were less abundant.
Conclusion: Significant gut microbiota composition differences exist between DILI patients and controls. These changes suggest gut microbiota's important role in Tac-induced DILI and potential as DILI biomarkers for early diagnosis and prevention.
Key Words: Gut Microbiota; DILI; Tacrolimus; Renal Transplant.

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W302

Continuous subcutaneous ketamine infusion induces tacrolimus and sirolimus clearance: a case report

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Biography:

Dr. Jana Stojanova is a Senior Scientist at St Vincent's Hospital Sydney and holds a conjoint Senior Lecturer appointment at the University of New South Wales (UNSW). Her research focuses on optimizing medicine use through clinical pharmacology, therapeutic drug monitoring, and pharmacogenomics. She completed her PhD at INSERM's Pharmacology of Immunosuppressants in Transplantation Unit in Limoges, France, investigating pharmacogenetic risk factors in post-transplant lymphoproliferative disease. Her work spans multiple international settings, having held positions in Australia, France, and Chile, including as Associate Professor of Pharmacology at the University of Valparaiso Medical School. Dr. Stojanova is an active member of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and currently serves as co-chair of the 2025 Congress.

Background: Drug interactions involving immunosuppressants can compromise transplant outcomes. While repeated ketamine administration is known to induce hepatic enzymes in experimental models, there are no clinical reports of induced clearance of cytochrome P450 (CYP) substrates. Continuous subcutaneous (SC) ketamine infusions are increasingly used in opioid-sparing strategies for acute pain management.
Aims: To describe a case of induced changes in tacrolimus and sirolimus clearance in a heart transplant recipient following administration of a continuous subcutaneous ketamine infusion.
Methods: A 55-year-old male heart transplant recipient had thrombectomy for extensive left lower limb deep vein thrombosis. Post-operatively, the patient received rivaroxaban, clopidogrel, and ketamine infusion (5mg/h SC, increased to 10mg/h) for severe post-operative pain over four days. Immunosuppressant trough concentrations (C0) were monitored before, during, and after ketamine, with sequential dose adjustments made in response to the observed concentrations.
Results: Following ketamine initiation, tacrolimus and sirolimus C0 were noted to be low, however dose escalations failed to achieve proportional responses: 2.3- and 3.5-fold dose increases resulted in 0- and 2-fold C0 increases, respectively. Approximately three weeks after ketamine discontinuation, drug clearances appeared to return to pre-ketamine values, resulting in supratherapeutic C0 and transient renal dysfunction, which resolved with dose decreases. There was no evidence of transplant rejection over the period.
Conclusions: This case provides clinical evidence of ketamine's enzyme-inducing impact on immunosuppressants. Prescribers should anticipate this interaction, particularly in transplant recipients. This phenomenon may extend to other CYP450 substrates where reduced effectiveness might go unrecognized.
Keywords: Ketamine, tacrolimus, sirolimus, drug interaction, pharmacokinetics, transplantation

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W303

Population Pharmacokinetics and Limited Sampling Strategies for Mycophenolic Acid after Liver Transplantation

Assoc Prof Jiake He[1], Xiaoyu Han[1,2,3], Yun Xiao[1,2,3], Chao Zheng[1,2,3], Jiaqi Yang[1,2,3], Yu Fu[1], Hanbin Xiong[1], Baolin Wang[1], Bin Zou[1], Hailang Liu[4], Jingsheng Ma[4], Wentao Yang[4], Qian Hu[4], Wenwen Lai[4], Na Deng[4], Guohui Li[4], Xiaohui Guo[4], Zhong Lin[4], Yongbin Wu[5]
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Biography:

Dr. Jiake He is a distinguished researcher and educator specializing in clinical pharmacokinetics and personalized drug therapy. She currently serves as an Associate Chief Pharmacist at the 2nd affiliated hospital of Nanchang University, holding the academic rank of Associate Professor and Master's Supervisor at Nanchang University.

Professional Leadership

Dr. He holds leadership roles in multiple national academic committees:

Young Committee Member, Drug Metabolism Committee, Chinese Pharmacological Society

Young Committee Member, Clinical Pharmacology Committee, Chinese Pharmacological Society

Young Committee Member, Therapeutic Drug Monitoring Research Committee, Chinese Pharmacological Society

Young Committee Member, Analytical Pharmacology Committee, Chinese Pharmacological Society

Research Expertise

Dr. He's research focuses on clinical pharmacokinetics, personalized drug therapy particularly in organ transplantation. Key areas include:

Clinical Pharmacokinetics: Mechanisms of drug transport and metabolism

Personalized Drug Therapy: Optimization of immunosuppressive regimens for transplant patients and model-assisted individualized treatment

Objectives: Mycophenolic acid (MPA), a potent immunosuppressant, is widely used in solid organ transplantations to prevent rejection. The aim of this study is i) to establish a population pharmacokinetic (PPK) model and limited sampling strategies (LSSs) to estimate the area under the curve of the dosing interval (AUC0-12h) of MPA and ii) to find the covariates that significantly affect the pharmacokinetics of MPA exposure and iii) to assist therapeutic drug monitoring(TDM) and dosage optimization of MPA during the perioperative period in Chinese liver transplant recipients.
Methods: Population pharmacokinetic analysis was performed using with data obtained from 48 adult patients at steady states during the perioperative period. Various demographic variables were investigated as potential covariates for PPK modeling. The LSSs were established based on multiple linear regression for estimating the AUC0-12h of MPA.

Results: A two-compartment model with first-order absorption and elimination with a lag time was chosen as the structure model in PPK modeling. Non-linear mixed-effects models were developed. The covariate analysis identified liver transplantation donor ABCC2 24C>T genotype as an individual factor influencing central volume of distribution of MPA. The LSSs showed the four-point model (C1.5h, C2h, C4h, C12h) (R2=0.897) performed best in predicting MPA AUC0-12h.
Conclusion: In conclusion, this study successfully developed a PPK model and LSSs that could be applied in real clinical settings to assist TDM and dosage optimization of MPA during the perioperative period in Chinese liver transplant recipients.
Keywords: mycophenolic acid, population pharmacokinetics, limited sampling strategy, liver transplant recipient, perioperative period, therapeutic drug monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W304

Population Pharmacokinetics and Limited Sampling Strategies for Mycophenolic Acid after Renal Transplantation

Assoc Prof Jiake He[1,2,3], Xiaoyu Han[1,2,3], Yun Xiao[1,2,3], Chao Zheng[1,2,3], Jiaqi Yang[1,2,3], Hanbin Xiong[1], Yu Fu[1], Bin Zou[1], Baolin Wang[1], Hua Zou[4], Zhengyao Jiang[4], Chenglong Yin[4], Wenwen Lai[4], Na Deng[4], Guohui Li[4], Xiaohui Guo[4], Zhong Lin[4], Yongbin Wu[5]
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Biography:

Dr. Jiake He is a distinguished researcher and educator specializing in clinical pharmacokinetics and personalized drug therapy. She currently serves as an Associate Chief Pharmacist at the 2nd affiliated hospital of Nanchang University, holding the academic rank of Associate Professor and Master's Supervisor at Nanchang University.

Professional Leadership

Dr. He holds leadership roles in multiple national academic committees:

Young Committee Member, Drug Metabolism Committee, Chinese Pharmacological Society

Young Committee Member, Clinical Pharmacology Committee, Chinese Pharmacological Society

Young Committee Member, Therapeutic Drug Monitoring Research Committee, Chinese Pharmacological Society

Young Committee Member, Analytical Pharmacology Committee, Chinese Pharmacological Society

Research Expertise

Dr. He's research focuses on clinical pharmacokinetics, personalized drug therapy particularly in organ transplantation. Key areas include:

Clinical Pharmacokinetics: Mechanisms of drug transport and metabolism

Personalized Drug Therapy: Optimization of immunosuppressive regimens for transplant patients and model-assisted individualized treatment

Objectives: The aim of this study is i) to establish a population pharmacokinetic (PPK) model and limited sampling strategies (LSSs) to estimate the area under the curve of the dosing interval (AUC0-12h) of MPA and ii) to find the covariates that significantly affect the pharmacokinetics of MPA exposure and iii) to assist dosage optimization of MPA during the perioperative period in Chinese renal transplant recipients.

Methods: Population pharmacokinetic analysis was performed using with data obtained from 120 adult patients at steady states during the perioperative period. Various demographic variables were investigated as potential covariates for PPK modeling. The LSSs were established based on multiple linear regression for estimating the AUC0-12h of MPA.

Results: A two-compartment model with first-order absorption and elimination with a lag time was chosen as the structure model in PPK modeling. Non-linear mixed-effects models were developed. The covariate analysis identified delayed graft function (DGF) as an individual factor influencing

central volume of distribution and identified uric acid as individual factors influencing apparent oral clearance (CL/F) of MPA. The LSSs showed the four-point model (C0.5h, C1.5h, C2h, C8h) (R2=0.946) and the three-point model (C1.5h, C2h, C8h) (R2=0.913) were both effective in predicting MPA AUC0-12h.

Conclusion: In conclusion, this study successfully developed a PPK model and LSSs that could be applied in real clinical settings to assist TDM and dosage optimization of MPA during the perioperative period in Chinese renal transplant recipients.

Keywords: mycophenolic acid, population pharmacokinetics, limited sampling strategy, renal transplant recipient, perioperative period, therapeutic drug monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W305

Significance of Time in Therapeutic Range of Tacrolimus in Acute GVHD Prophylaxis

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Biography:

Naoki Yoshikawa is associate professor of Department of Clinical Pharmacy at Oita University Hospital. His work focuses specifically on the individualized pharmacokinetic management of immunosuppressive drugs.

Background: Intra-patient variability in immunosuppressive blood drug concentrations is a potential biomarker in managing organ transplant patients. However, the association between the time in therapeutic range (TTR) of tacrolimus blood concentrations and its efficacy in preventing graft-versus-host disease (GVHD) remains unknown.
Aims: This study aimed to analyze the relationship between the TTR of tacrolimus blood concentrations and acute GVHD prophylaxis in allogeneic hematopoietic stem cell transplantation (HSCT) recipients to establish a new concept for managing tacrolimus blood concentrations post-HSCT.
Methods: Eligible patients administered tacrolimus were categorized into two groups based on the grade of acute graft-versus-host disease, and propensity score matching was performed using graft-versus-host disease prophylaxis protocols and days to the disease onset to compare time in therapeutic range.
Results: In patients with tacrolimus blood concentration therapeutic range ≥10 ng/mL, time in therapeutic range during the first 4 weeks post-transplantation was significantly lower in the Grade II–III group than in the Grade 0–I group. Among propensity score matching-extracted patients, the Grade II–III group had significantly lower time in therapeutic range during the first 2 and 4 weeks post-transplantation.
Conclusions: This study showed that maintaining a higher tacrolimus TTR in the early post-transplantation period averts severe acute GVHD development. Our data reiterates the need to control deviations in blood concentrations as much as possible and to control them within the therapeutic range when using tacrolimus for acute GVHD prophylaxis after allogeneic HSCT.
Keywords: tacrolimus, therapeutic drug monitoring, time in therapeutic range, hematopoietic stem cell transplantation, graft-versus-host disease

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W306

Continuous quality improvement in immunosuppressant testing: be cautious of clotting samples

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Biography:
Dr. Wang is a Research and Development Scientist at Vancouver Coastal Health, specializing in mass spectrometry method development and quality improvement in clinical laboratories. She is also a Clinical Instructor in the Department of Pathology and Laboratory Medicine at the University of British Columbia.Dr. Wang earned her PhD in Chemistry from the University of British Columbia, where she focused on marine natural products research. She then worked as a Research Scientist at IntelliSyn Pharma, contributing to drug discovery and medicinal chemistry projects. Afterward, she completed postdoctoral training at the University of British Columbia (St. Paul's Hospital), where her research focused on developing new mass spectrometry protein assays. Her current research interests include clinical mass spectrometry, therapeutic drug monitoring, automated sample preparation, and clinical laboratory quality improvement.

Background: Immunosuppressant therapeutic drug monitoring is routinely used in clinical practice. While first-generation mass spectrometry assays rely on manual sample preparation, many laboratories have transitioned to automated preparation with liquid handlers. A local quality program comparing patient samples across different laboratories uncovered significant discrepancies. Further investigation revealed that these discrepancies were linked to clotting errors during processing with the liquid handler.
Methods: Immunosuppressant concentrations were quantified using LC-MS/MS. Sample preparation was automated with a liquid handler, where 20µL of whole blood was mixed with 80µL of 0.1M $ZnSO_4$, followed by protein precipitation using 200µL of acetonitrile. The mixture was filtered and injected into the LC-MS/MS. For patient samples exhibiting clotting errors, they were manually processed following the above protocol. Various manual pipetting techniques from different technologists were assessed.
Results: Reverse pipetting and positive displacement pipetting techniques produced results most consistent with the automated liquid handler, regardless of the operator. In contrast, standard pipetting methods yielded more variable results between technologists. Notably, during initial method validation of this automated sample preparation, prior to clinical implementation, the comparison between manual and automated preparation showed minimal bias.
Conclusions: While automated liquid handlers generally outperform manual preparation, challenges remain with clotting samples. Re-collection of samples is not always feasible due to the time-sensitive nature of sample collection/testing. A standardized workflow should be developed for handling clotting samples. Additionally, this highlights the importance of interlaboratory comparisons using real patient samples, which can complement proficiency testing.
Key Words: Immunosuppressant, LC-MS/MS, Liquid handler, Analytical error, Sample preparation

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W307

Genotype-guided dosing of aripiprazole in Chinese adolescents with psychiatric disorders

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Biography:

Dr. Fan Li, a master's supervisor, is currently employed at the Clinical Pharmacy Research Center of the First Affiliated Hospital of Zhejiang University School of Medicine. She serves as the Pharmacist-in-charge and holds the position of Special Associate Researcher at the Zhejiang University School of Medicine. With a long-term commitment to the research of psychotropic drug therapy, in the past five years, Dr. Fan has been the (co-) first author of numerous research papers published in renowned international professional academic journals, including Phytomedicine, Journal of Ethnopharmacology, International Journal of Biological Macromolecules, and Journal of Agricultural and Food Chemistry. Additionally, she has independently led the Youth Project of the National Natural Science Foundation of China, Zhejiang Provincial Natural Science Foundation of China and Class A Science and Technology Plan Project of Traditional Chinese Medicine in Zhejiang Province respectively.

Background: Aripiprazole, an atypical antipsychotic, is widely prescribed for psychiatric disorders. While the relationship between its pharmacokinetic variability and genetic polymorphisms has been extensively studied in adults, the data on the genotype-guided dosing of aripiprazole in adolescents with psychiatric disorders remain scarce.
Aims: To examine the feasibility of using genotype-guided strategy to determine aripiprazole dose in adolescents with psychiatric disorders and investigate the key role of gene polymorphisms.
Methods: Data from electronic health records and opportunistic sampling of aripiprazole-treated adolescents (12~18 years) were analyzed. A genotype-guided study was conducted, including a pharmacogenetic association analysis of 13 single nucleotide polymorphism loci in genes involved in aripiprazole disposition. Associations were assessed using analysis of covariance, and population pharmacokinetic parameters were estimated via nonlinear mixed-effects modeling.
Results: A total of 175 TDM points from 134 adolescents were analyzed, in which CYP2D6 rs1135840 and rs1065852 showed closer relationship with plasma aripiprazole concentration, total plasma concentrations of aripiprazole and dehydroaripiprazole, and metabolic ratio (dehydroaripiprazole/aripiprazole). Additionally, ABCB1 rs1128503 was significantly linked to evelated plasma concentration of aripiprazole, and total plasma concentrations of aripiprazole and dehydroaripiprazole. Meanwhile, the population pharmacokinetics analysis of aripiprazole estimated a clearance of 2.32 L/h and volume of distribution of compartments of 56.9 L, in which CYP2D6 rs1065852 TT genotype especially reduced aripiprazole clearance by 24.5%.
Conclusions: This study successfully established genotype-guided dosing framework for aripiprazole in Chinese adolescents with psychiatric disorders, emphasizing the critical role of CYP2D6 and ABCB1 polymorphisms in optimizing aripiprazole therapy.
Keywords: aripiprazole; pharmacogenetics; psychiatry; adolescents; genotypes-guided dosing

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W308

Clinical validation of a DPD deficiency assay solution

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Biography:
n/a.

Background: Fluoropyrimidine-based chemotherapy is one of the useful treatments for many cancers. On the other hand, it could cause severe side effects due to a dihydropyrimidine dehydrogenase (DPD) deficiency. Therefore, European health authorities strongly recommend screening for DPD deficiency. However, the standardization of this method has not yet been established.
Aims: The purpose is to evaluate the analytical performance and clinical performance of LC/MS/MS assay with reagent kit for confirming DPD deficiency.
Methods: Clinical evaluation by LC/MS/MS assay with reagent kit developed by Alsachim was conducted at a site in France, already routinely performing indirect DPD phenotyping with their own laboratory-developed test. Both methods are used to measure uracil and dihydrouracil concentrations using reverse-phase LC coupled to a triple quadrupole mass spectrometer. The same samples and the same equipment were used for the method comparison. A total of 229 samples were analyzed and the evaluation of the results was conducted based on CLSI EP09c, using the Bland-Altman method and Deming regression.
Results: Accuracies of calibration curves were assessed on each series and were within the acceptance criteria defined during method validation. A good correlation between methods was obtained with a limited bias for both compounds. However, it should be noted that bias evaluation can be limited as, currently, only LDTs are available as reference methods.
Conclusion: The LC/MS/MS assay with reagent kit was clinically validated to provide reliable diagnostic of DPD deficiency prior to chemotherapy with fluoropyrimidines.
Key words: DPD, phenotyping, 5-FU, chemotherapy, LC/MS/MS, clinical validation

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W309

CYP2C19 genotype-guided voriconazole dosing increases target range attainment and reduces toxicity

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Biography:

Dr. Yoshiki Katada is a chief pharmacist at the department of clinical pharmacology and therapeutics, Kyoto University Hospital in Japan. He is a board certified infection control pharmacy specialist and a certified infectious disease chemotherapy pharmacist. His expertise lies in infectious disease pharmacotherapy, antimicrobial stewardship, and clinical pharmacokinetics.

Background and Aims: Voriconazole (VRCZ) is metabolized by hepatic cytochrome P450 (CYP) isozyme CYP2C19, with genetic polymorphisms causing variability in its efficacy and safety. Poor metabolizer alleles of CYP2C19 are more prevalent in Asian populations, which increases the risk of supratherapeutic VRCZ use in Japanese patients. This study aimed to evaluate whether CYP2C19 genotype-guided VRCZ therapy reduces toxicity.
Methods: This retrospective study included 64 patients (38 controls and 26 genotype-guided). The initial VRCZ dose in the genotype-guided group was determined using a nomogram developed at our hospital in accordance with current guidelines and literature. The primary objective was to determine whether genotype-guided dosing reduced hepatotoxicity and visual symptoms. Secondary outcomes included the percentage of patients within the therapeutic VRCZ trough concentration range (1–4 μg/mL).
Results: Hepatotoxicity (grade ≥2) and visual symptoms were significantly lower in the genotype-guided group (42.1% vs. 11.5%, P=0.008 and 44.7% vs. 7.7%, P=0.001, respectively). VRCZ discontinuation due to adverse events occurred in 9 patients (23.7%) in the control group and in 1 patient (3.8%) in the genotype-guided group (P=0.039). A higher proportion of patients in the genotype-guided group achieved therapeutic range of trough concentrations on 3–5 days after VRCZ initiation (37% vs. 77%, P=0.002).
Conclusion: CYP2C19 genotyping can reduce VRCZ adverse effects while maintaining therapeutic efficacy. Genotype-guided dosing can also facilitate the achievement of the therapeutic range. These results indicate the necessity of CYP2C19 genotyping in VRCZ treatment for Japanese patients.
Keywords: Voriconazole, CYP2C19, Pharmacogenetics, Genotype-guided, Precision medicine

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W310

Establishment of a novel method to assess CYP1A2 activity using melatonin clearance

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Biography:

Dr. Akitomo Yokokawa is an Associate Professor at the Laboratory of Clinical Chemistry and Experimental Therapeutics, School of Pharmacy, Tokyo University of Pharmacy and Life Sciences. He holds both a Master's and Doctorate in Pharmacy from Tokyo University of Pharmacy and Life Sciences. Dr. Yokokawa's research interests include personalized drug therapy, pharmacokinetics, clinical pharmacy, and analytical chemistry techniques like LC-MS and GC-MS. His work focuses on CYP1A2 enzyme activity and drug interactions, aiming to develop new methods for evaluating drug metabolism. His goal is to optimize pharmacotherapy by integrating personalized approaches into clinical practice.

Background: CYP1A2 activity varies significantly among individuals, highlighting its importance in personalized medicine. Currently, caffeine clearance (CLCA) and the paraxanthine/caffeine ratio (PX/CA) are used to access CYP1A2 activity. However, these methods require caffeine intake restrictions and multiple blood samples, making them inconvenient. We developed a novel method to assess CYP1A2 activity—melatonin partial metabolic clearance (CLm(MEL))—based on endogenous melatonin (MEL) and its CYP1A2-mediated metabolite, 6-hydroxymelatonin (6-O-MEL). However, it has not yet been evaluated.
Aims: This study aimed to establish a new CLm(MEL) method by examining its correlation with CLCA and PX/CA.
Methods: Blood samples were collected at 4, 6, 24, and 26 h after caffeine ingestion. Urine samples were collected over 2-hour periods at 4–6 hours and 24–26 hours from 18 healthy participants who provided informed consent. Plasma MEL, CA, PX, and urinary 6-O-MEL concentrations were analyzed using LC–MS/MS. CLCA was calculated from the plasma CA concentrations, while CLm(MEL) was determined by dividing urinary 6-O-MEL excretion by plasma MEL AUC.
Results: CLCA ranged from 1.38 to 12.32 L/h, and PX/CA from 0.41 to 4.55. CLm(MEL) varied between 25.81 and 83.09 L/h. The correlation coefficients of CLm(MEL) with CLCA and PX/CA were 0.72 and 0.60, respectively, indicating the validity of the new assessment method.
Conclusions: The new CLm(MEL) method provides a simple and effective approach to assessing CYP1A2 activity and can be applied in clinical practice for personalized dosing.
Keywords: CYP1A2, 6-hydroxymelatonin, LC–MS/MS, phenotyping, caffeine clearance

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W311

The Correlation Between TDM and CYP2C19 polymorphisms in Voriconazole using

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Biography:

Lixian Li obtained her Ph.D. from Chongqing University in 2013 and has served as a visiting scholar at the University of Waterloo and UBC， Canada. She is currently the Deputy Director of the Clinical Pharmacy Teaching and Research Office at Chongqing Cancer Hospital. Her primary research focuses on the development of methodologies for therapeutic drug monitoring and personalized medicine, the investigation of new magnetic nano drug-loading and detection systems, as well as chromatographic separation and analysis. She has published 25 SCI articles and chaired 7 projects.

Background: To explore the clinical significance of CYP2C19 polymorphisms in therapeutic drug monitoring of voriconazole.
Objective: To investigate the relationship between CYP2C19 polymorphisms and the trough concentration of voriconazole.
Methods: A retrospective, single-center study was conducted, collecting data from patients who underwent voriconazole polymorphism testing and therapeutic drug monitoring between 2023.1 and 2024.5. The primary endpoint was whether the trough concentration of voriconazole was within the normal range. Data from enrolled patients were analyzed using multivariate logistic regression.
Results: A total of 65 patients were included. Single-factor regression included 15 variables, and multivariate logistic regression revealed significant differences in total bilirubin and alcohol history (P = 0.039, P = 0.023).
Conclusion: The single-center retrospective analysis did not find a significant effect of voriconazole genetic polymorphisms on patients' blood drug concentrations. A history of alcohol consumption and abnormal baseline total bilirubin levels may be key factors influencing voriconazole blood concentrations.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W312

Personalized Tacrolimus Dosing Strategies in Kidney Transplantation Optimizing Dosing through Pharmacogenomics

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Biography:
Yi-Jen Huang holds a degree in Pharmacy and a Master of Public Health (MPH). Currently serving as a clinical pharmacist at National Taiwan University Hospital, She has specialized in transplant pharmacotherapy since 2017, focusing on liver and kidney transplantation. Her expertise includes therapeutic drug monitoring of immunosuppressants, personalized dosing strategies, and aiming to improve patient adherence.

Background: Tacrolimus exhibits significant pharmacokinetic variability, requires precise dosing to balance efficacy and toxicity. Its blood levels are influenced by differences in absorption and metabolism. This study explores alternative strategies for individualized dose adjustments to optimize therapeutic outcomes.
Aims: To establish a personalized tacrolimus dosing strategy by integrating pharmacogenomic testing with pharmacokinetic analysis.
Methods: 57 kidney transplant recipients were studied, with pharmacogenomic testing performed on 23 patients. Tacrolimus pharmacokinetics were assessed via blood concentrations at five time points (C0, C1, C2, C4, C8). CYP3A5 and ABCB1 polymorphisms were analyzed.
Results: CYP3A5 polymorphisms influenced tacrolimus clearance, with *1/*1 carriers exhibiting a faster metabolism and requiring higher doses to achieve therapeutic levels. In contrast, *3/*3 carriers more frequently reached the therapeutic range at standard dosing. When using the area under the concentration-time curve (AUC) calculated from cumulative blood sampling points, *3/*3 carriers were more likely to achieve an AUC >100 ng*hour/mL, whereas *1/*1 and *1/*3 carriers were more likely to remain below this threshold. Further analysis of individual blood concentrations revealed that C4 and C8 levels were strongly correlated with AUC and were significantly associated with CYP3A5 genotype. Additionally, ABCB1 mutations, which influence P-glycoprotein function, may alter tacrolimus absorption and impact drug exposure. However, analysis of blood concentrations at absorption-phase (C1 and C2) did not show a significant correlation with genotype.
Conclusions: Pharmacogenomic testing optimizes tacrolimus dosing: *1/*1 (0.2 mg/kg/day), *1/*3 (0.15 mg/kg/day), *3/*3 (0.1 mg/kg/day). C4 and C8 concentration serve as a valuable marker for drug exposure and genotype prediction.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W313

Genotype informed Bayesian dosing of tacrolimus in children undergoing solid organ transplantation

Ms Dhrita Khatri[1,2], Dr David Metz[1,3,4], Dr Andreas Halman[1,6], Dr Joshua Kausman[3], Dr Jacob Mathew[3], Dr Elizabeth Bannister[3], Prof Nicholas Holford[5], Ms Tayla Stenta[1,2], Ms Claire Moore[1,2], Ms Roxanne Dyas[1,2], Ms Elizabeth Williams[1,2], A/Prof Rachel Conyers[1,2,3]
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Biography:
Dhrita Khatri is a pharmacist and researcher with experience in hospital settings in Melbourne, Australia, and Auckland/Wellington, New Zealand. She joined the Murdoch Children's Research Institute (MCRI) in early 2023 as part of the Cancer Therapies Group. Her focus is on applying pharmacogenomics to enhance paediatric care. Through her collaborations with MCRI, the Royal Children's Hospital, Clinical Pharmacogenetics Implementation Consortium, the University of Melbourne, the Victorian Paediatric Cancer Centre, and reNEW, Dhrita's research has a strong translational aspect, aiming to improve clinical practices.

Background: Tacrolimus, a potent immunosuppressant, is widely used in solid organ transplantation (SOT). Despite its effectiveness, highly variable pharmacokinetics lead to inadequate drug concentrations leading to under- or over-dosing, increasing risks of early acute rejection, de novo donor-specific antibody formation and graft loss, as well as toxicities including infection and malignancy, respectively. While genotype-informed and Bayesian dosing has shown to improve outcomes in adults, paediatric data is limited.
Aim: To evaluate the effectiveness of genotype-informed Bayesian dosing of tacrolimus in paediatric SOT compared to standard weight-based dosing.
Methods: A serial cohort study, with single prospective intervention arm, will assess feasibility and benefit of genotype-informed Bayesian dosing of tacrolimus in a paediatric SOT cohort. Participants (n=45) will receive initial dosing informed by CYP3A4 and CYP3A5 genetic variants. From day 4 post-transplant, Bayesian estimation using NextDose will inform dose adjustments.
Results: The effectiveness of the intervention will be assessed by comparing the proportion of participants with therapeutic tacrolimus concentrations to a retrospective cohort who received standard weight-based dosing. Specifically, we will compare the proportion with therapeutic concentrations at day 4 (initial dose prediction) and at weeks 3 and 8 (Bayesian-adapted dosing). Secondary outcomes will include time within therapeutic range over the 8-week period.
Conclusions: BRUNO-PIC will assess the benefits of a precision dosing strategy; combining genotype-informed dosing, Bayesian dose adjustment, and exposure-target dosing on improving tacrolimus concentrations and clinical outcomes in the initial 8 weeks post-transplant, across all SOT procedures in our young patients.
Key Words: Genotype, Pharmacogenomics, Bayesian Prediction, Transplant, Paediatrics.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W314

Pharmacogenetics and pharmacokinetics as useful tools for posaconazole personalization in leukemia patients

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Biography:

Born in Turin on November 22, 1986, she graduated in Health Biology, specialized in Microbiology and Virology, and obtained a PhD in Complex Systems for Life Sciences at the University of Turin.
She was a researcher (RTD-B from 2019 to 2022) and is currently an Associate Professor of Pharmacology. She is affiliated with the ASL Città di Torino as a senior biologist.
She received some awards, including:

- *The "Società Italiana di Farmacologia e Farmindustria" award for pharmacological research (2018).*
- *The second prize of "The Binding Site" by SIBIOC for pharmacological research (2019).*
- *The IATDMCT Victor Armstrong Young Investigator Award 2024 for Exceptional Scientific Achievements Early in her Career.*
- *The Podium Selected Communication at the 42nd SIF Congress (2024).*

Her areas of excellence include clinical pharmacology, pharmacogenetics, therapeutic drug monitoring, drug interactions, and biomarker quantification. She published approximately 170 articles, with an H-index of 28.

Background: antifungal prophylaxis with posaconazole in patients with acute myeloid leukemia (aml) is recommended to reduce the risk of invasive fungal infections (ifi). a few studies described the clinical impact of suboptimal posaconazole exposure during prophylaxis, other than pharmacogenetics, in this clinical setting.
Aims: to analyze if posaconazole exposure and genetics could impact on the ifi onset in patients with aml.
Methods: posaconazole plasma concentrations (cut-off 0.7 mg/l) were evaluated weekly (7/14/21/28 days) through chromatography, whereas polymorphisms of genes encoding enzymes, transporters and transcription factors through real-time pcr.
Results: 100 patients were analyzed (4 were excluded for missing clinical data): 56(58%) were women and median age was 66 years. ifi developed in 18 patients: 5 at 7, 5 at 14 and 8 at 21 days. posaconazole concentrations at 14 days influenced ifi development, when considered as linear variable (p=0.031), whereas at 7 (p=0.015) and 14 (p=0.049) days, when considered lower than 0.7 mg/l. regarding pharmacogenetics, car540tt was associated with posaconazole trough concentrations>0.7 mg/l at every analzyed timing and ugt1a1829tt with ifi development.
an algorithm for the clinical routine including car540tt and ugt1a1829tt analysis before starting therapy (in order to understand which patients are at high risk of having posaconazole exposure<0.7 mg/l or ifi development) has been proposed.

Conclusions: this is the first study reporting a useful tool helping clinicians to identify patients with a higher risk for under-effective posaconazole exposure and it can be used to improve antifungal stewardship approach in this setting.
Keywords: therapeutic drug monitoring, genetic variants, antifungals.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W315

Drug absorption in pulmonary arterial hypertension patients, one sampling time fits all?

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Biography:

Paweł K. Kunicki, PhD,
He is (since 2016) - Assistant Professor at the Department of Drug Chemistry, Pharmaceutical and Biomedical Analysis, Faculty of Pharmacy, Medical University of Warsaw, Poland. He graduated as Master of Pharmacy (M.Pharm. 1990) and as Doctor in Pharmaceutical Sciences (Pharm.D., Ph.D. 2002). He was (1990–2019) - at the Institute of Cardiology in Warsaw, recently the Head of Clinical Pharmacology Unit, and acting Head of Department of Clinical Biochemistry.
He is a clinical pharmacist as well as a laboratory diagnostician, specialist in Public Health (2011) and in Laboratory Medical Toxicology (2021).
Consultant and expert on the field of drug analysis, pharmacokinetics and bioequivalence studies. He is an author of 53 original and review papers and of 202 oral or poster scientific presentations and lectures; h-index: 12. He is a member of IATDMCT (Immunosuppressive Drugs Committee), as well as Editorial Board member of Therapeutic Drug Monitoring.

Background: The effectiveness of pharmacotherapy for pulmonary arterial hypertension (PAH) can be improved by monitoring adherence to treatment, including assessment of drug absorption after oral administration.
Aims: The aim was to determine the concentrations of sildenafil (SIL), bosentan (BOS), macitentan (MAC) and riociguat (RIO) in plasma collected from PAH patients before and after drug administration.
Methods: The study group was 85 PAH patients (27 M, 58 F), of whom 58 received SIL, 16 RIO, 28 BOS and 30 MAC. Blood samples were collected prior to (C0) and 3 h after drug administration (C3). HPLC-UV method was used for drug measuring in plasma. The analyzed drugs significantly differ in tmax value, therefore C3 usually meets the PK profile after (SIL and RIO) around (BOS) or before (MAC) reaching the maximum.
Results: Drug concentrations (with great variability) were determined in every sample, but in only 38 of 58 C0 samples for SIL. The median C0 was: 5.2, 83.5, 166.0, 183.2 ng/mL, while C3 was: 28.7, 155.6, 798.4, 296.4 ng/mL for SIL, RIO, BOS, MAC, respectively. Absorption expressed as (C3-C0) value was: 28.4±23.1 ng/mL (SIL), 45.5±53.5 ng/mL (RIO), 688.5±637.0 ng/mL (BOS) and 150.1±334.1 ng/mL (MAC). The swing (C3 instead of Cmax) showed: 801±829% (SIL), 93±94% (RIO), 1093±1765% (BOS) and 69±71% (MAC). Some negative values observed for (C3-C0) and swing indicate possible cases of non-adherence.

Conclusions: Paired C0 and C3 measurements is a useful tool to control PAH patient adherence. SIL monitoring cannot be successfully guided by C0.

Keywords: Sildenafil, Riociguat, Bosentan, Macitentan, Absorption

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

W316

Simulation-Driven Pharmacometric Modeling for Bioequivalence Using Partial AUC in Pediatric Transplants

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Biography:

Dr. Catherine M. Sherwin, Ph.D., MPharm., CPI., FCP., DABCP., FAAPS, is a globally recognized leader in clinical pharmacology and toxicology with 20 years of experience spanning academia, industry, and regulatory science. She is Vice President of Clinical Pharmacology and Pharmacometrics at Differentia Bio and Discipline Lead for Clinical Pharmacology at the UWA Medical School, University of Western Australia. Additionally, she serves as an adjunct professor at Wright State University, Boonshoft School of Medicine, Ohio, where she advances research and education in pediatric and maternal-fetal health. Dr. Sherwin earned her Ph.D. in Medicine and Pediatric Clinical Pharmacology from the University of Otago, New Zealand, and an MPharm in Clinical Toxicology from the University of Florida. Her research focuses on translational medicine, pediatric pharmacology, model-informed drug development, and precision medicine. A widely published expert, she has co-authored over 200 peer-reviewed articles, contributing to FDA and EMA guidelines on pediatric and maternal-fetal therapeutics.

Background: Immunosuppressants like tacrolimus prevent transplant rejection but show high variability in pediatric populations. Traditional bioequivalence (BE) assessments rely on total AUC, but partial AUC (pAUC) may better evaluate early drug absorption.

Aims: This study aimed to assess BE using pAUC for tacrolimus in pediatric transplant recipients through pharmacometric modeling and simulation.

Methods: A prospective observational study included 25 pediatric solid organ and 10 hematopoietic stem cell transplant recipients. Pharmacokinetic (PK) data were collected during the absorption phase (0-4 hours post-dose). Population PK modeling using NONMEM 7.4.2 applied a one-compartment model with first-order absorption and elimination. Simulations evaluated inter-individual variability, CYP3A5 polymorphisms, and dosing strategies. pAUC4 and pAUC8 were compared with Cmax and AUCT last using Phoenix WinNonlin.

Results: The PK model described tacrolimus disposition, with absorption rate constant (Ka) of 4.23 hr^{-1} (RSE 78.5%) and bioavailability of 23.3% (RSE 37.9%). Model simulations demonstrated that CYP3A5 expressers exhibited significantly higher variability in pAUC compared to non-expressers. Dose-normalized median pAUC4 was 7.44 hr*ng/mL/mg, and pAUC8 was 7.95 hr*ng/mL/mg. pAUC metrics exhibited strong correlation ($r=0.99$, $p<0.0001$) but showed distinct patterns compared to Cmax and AUCT last. Adjusted dosing for CYP3A5 expressers reduced variability and improved BE assessment.

Conclusions: This study supports pAUC as an additional BE metric in pediatric immunosuppressant therapy. Simulations highlight CYP3A5 polymorphisms' impact on BE, suggesting dosing adjustments. Findings support further validation and potential regulatory integration of pAUC. Pharmacometric modeling aids drug assessment and therapeutic equivalence in vulnerable populations.

Key Words: bioequivalence, pharmacometrics, partial AUC, pediatric transplants, CYP3A5, tacrolimus

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W317

Leveraging Deep Q-networks for Starting Dose Optimization: Case Study of Infliximab

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Biography:
I am a associate staff scientist specializing in pharmacometrics in the Division of Translational and Clinical Pharmacology. With over ten years of experience as a clinical pharmacist and academic faculty member, I have studied clinical pharmacodynamics. I implement PK/PD modeling and machine learning models for model-informed precision dosing and model-informed drug development.

Background: Model-informed precision dosing (MIPD) optimizes the initial dosing regimens to achieve therapeutic targets by integrating patient-specific covariates. While this process involves simulations and manual dose selections, reinforcement learning (RL), specifically Deep Q-Networks (DQN), offers the potential to automate and standardize this process by learning optimal strategies across numerous scenarios.
Aims: This study aimed to evaluate the feasibility of applying DQN to automate the selection of initial dosing regimens to achieve predefined PK targets. The study focuses on infliximab as a case example, training the algorithm using model-based synthetic data.
Methods: A pediatric population PK model (Samuels, CTS 2025) was used to simulate infliximab PK. A virtual cohort of 10,000 pediatric patients was generated with random assignments of four key covariates: weight, albumin, erythrocyte sedimentation rate, and neutrophil CD64. The Q-learning algorithm was trained with a reward function designed to achieve infliximab concentrations of 5–10 µg/mL at 14 weeks within a dosing range of 1–20 mg/kg. A DQN model was developed to approximate the relationship between reward and covariate data across different dose levels.
Results: With the standard weight-based dosing (5 mg/kg), only 29.4% of virtual patients achieved the target concentrations. By contrast, using the DQN model, 96.1% of patients reached the target, while 3.9% of patients who did not reach the target concentration even at the highest dose (20 mg/kg).
Conclusion: This study demonstrated that DQN can be used to optimize initial dosing regimens in MIPD. Further model refinement and validation in real-world settings are warranted.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W318

Pharmacokinetic-Pharmacodynamic Modeling of Infliximab in children and young adults with Crohn's Disease

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Biography:
Wen Rui is a clinical pharmacologist specializing in population pharmacokinetics and pharmacodynamics (Pop-PKPD) modeling, with expertise in nonlinear mixed-effects modeling for precision dosing across diverse medications. He is currently a Ph.D. student at Cincinnati Children's Hospital Medical Center (CCHMC), where his research focuses on optimizing the use of monoclonal antibodies such as infliximab in pediatric Crohn's disease. Additionally, he has worked on pharmacokinetic modeling of small molecules, including piperacillin, and is exploring the integration of machine learning techniques to enhance predictive modeling. At CCHMC, Wen Rui is gaining experience in pharmacokinetic consultation for immunosuppressive therapies, including infliximab, mycophenolic acid, sirolimus, and tacrolimus, contributing to model-informed precision dosing (MIPD) research. His work has been presented at leading conferences such as ASCPT and ACOP, and he is continuously learning to contribute to the field through peer-reviewed publications and professional service, including abstract reviewing for pharmacometric conferences and engaging in research mentorship opportunities.

Background: Infliximab is a first-line therapy for pediatric Crohn's disease (CD). While pediatric-specific population pharmacokinetic (PK) models have been developed for model-informed precision dosing (MIPD), no pharmacokinetic/pharmacodynamic (PK/PD) model has been published to describe the infliximab exposure-response relationship in pediatric CD.
Aims: This study aimed to develop a PK/PD model incorporating fecal calprotectin (FCAL) as a biomarker of gut inflammation to characterize the exposure-response relationship of infliximab.
Methods: A total of 186 pediatric and young adult patients (median age 13.8 years, range 1.4–21.7) were included. A total of 1,091 infliximab concentrations and 497 FCAL measurements were available for PK/PD modeling. Area under the concentration-time curve (AUC) was estimated using the established pediatric PK model (Xiong et al., CPT 2021). An indirect response PK/PD model was developed to describe the relationship between infliximab AUC and FCAL levels using NONMEM.
Results: The PK/PD model, parameterized with baseline FCAL (BASE), Imax, EC50, Kin, and Kout, described FCAL dynamics during infliximab treatment. C-reactive protein was identified as a predictor of FCAL levels for both baseline and time-varying manners (dOFV = - 49.787, p-value < 0.001). Large interindividual variability in EC50 (>170 CV%) suggested substantial variability in exposure-response relationship. Diagnostic plots including visual predictive check (VPC) indicate that the final model has no systemic bias and specifications.

Conclusions: The PK/PD model successfully characterized the dynamic interactions between infliximab exposure and FCAL, demonstrating its potential to support MIPD based on not only PK but also PD targets in pediatric patients with CD.

Keyword: Pediatrics

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W319

Smart Dosing: A Line Chatbot Revolutionizing Initial Vancomycin Therapy in Thailand.

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Biography:

I am a clinical pharmacist at Queen Savang Vadhana Memorial Hospital, Thai Red Cross, Chonburi, Thailand. My primary responsibility is therapeutic drug monitoring (TDM) to optimize medication therapy for hospitalized patients. I monitor drug levels, assess pharmacokinetic parameters, and adjust dosages to ensure both efficacy and safety.I have expertise in vancomycin dosing and monitoring, ensuring appropriate therapeutic levels while minimizing toxicity risks. I am actively involved in developing a pharmaceutical care project to improve patient outcomes in this area. In addition to clinical practice, I integrate digital tools such as Google Apps Script and Dialogflow to enhance medication-related chatbot services.Currently, I am working on AI-driven clinical decision support tools to assist healthcare professionals in optimizing patient care. My passion lies in improving patient safety, medication effectiveness, and the integration of technology into clinical pharmacy practice.

Background: Accurate initial dosing of intravenous vancomycin requires careful consideration of weight and renal function. In obese patients, body mass index (BMI) further complicates dosing. Although web and mobile tools are available, many Thai clinicians remain unaware of these resources or face barriers to their use. LINE, a widely used messaging platform in Thailand, offers a user-friendly solution for vancomycin dosing support. However, its accuracy requires validation.
Objective: This study aimed to develop and evaluate a LINE-based chatbot for initial vancomycin dosing in Thai adults.
Methods: The study consisted of three phases: (1) chatbot development using the LINE Messaging API and UpToDate guidelines to generate dosing recommendations based on patient demographics, including sex, age, weight, height, and serum creatinine, while also calculating pharmacokinetic parameters; (2) data collection from patients aged ≥18 years who received intravenous vancomycin, including a loading dose and at least two maintenance doses, excluding those undergoing renal replacement therapy; and (3) evaluation of dosing accuracy by comparing predicted and actual trough levels using root mean square error (RMSE) and mean absolute error (MAE).
Results: The chatbot's dosing recommendations were evaluated in 34 patients, with an average processing time of 31.3 ± 4.4 seconds per case. The predicted trough concentrations demonstrated an RMSE of 2.13 (95% CI = 1.39–2.87) and an MAE of 1.58 (95% CI = 1.10–2.07).
Conclusion: The LINE chatbot provides an accurate and efficient tool for initial vancomycin dosing with minimal prediction error. As a user-friendly tool, it has the potential to improve clinical decision-making.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W320

MIPD Performance Assessment and Model Re-evaluation in Children and Adults

Dr Jordan Brooks[1], Dr Jasmine Hughes[1], Dr Stephanie Hughes[1], Dr Christopher Dvorak[2], Dr Janel Long-Boyle[2], Dr Ron Keizer[1]
[1]InsightRX, San Francisco , United States, [2]University of California, San Francisco, San Francisco, United States

Biography:
Dr. Jordan Brooks, a Senior Pharmacometrician and Data Scientist at InsightRX, focuses on improving the predictive ability of precision dosing models and enhancing their usability for bedside clinicians. His work originated in pediatric hematopoietic cell transplantation with conditioning agents and immunosuppression, but now spans patients of all ages and various drug classes requiring precise dosing.

Background: Model-informed precision dosing (MIPD) is crucial for optimizing busulfan therapy. We previously developed a population pharmacokinetic model using data from 188 children and young adults (Shukla et al. 2020). After implementation, some biases were observed which were potentially related to the covariate effects identified in the original model.
Aims: 1. Assess target attainment of busulfan MIPD in children and adults. 2. Refit the Shukla model with an expanded, multicenter dataset including both children and adults.
Methods: Data were collected from 1062 individuals and 9123 busulfan concentration samples across 11 US medical centers using the InsightRX Nova platform from 2017-2024. The data were modeled using NONMEM and R, comparing performance with the previously published model.
Results: For individuals undergoing busulfan MIPD, 84.4% achieved a cAUC within 80 to 120% of the target. Model refinement included adding a peripheral compartment and an exponential decay function for clearance, while the previously reported regimen effect on clearance was found insignificant. The refined model outperformed the original model in forecasting prediction (mean percent error: -2.9% vs -6.8%; normalized root mean square error: 23.2% vs 27.8%).
Conclusions: MIPD of busulfan improves therapeutic target attainment and continuous refinement of models is essential to improve predictive performance. The refined model represents an improvement in forecasting performance and generalizability across centers and ages.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W321

Exposure – response relationship of adalimumab in Chinese patients with ankylosing spondylitis

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Biography:
I'm an associate chief pharmacist in the department of clinical pharmacology, the First Affiliated Hospital of Soochow University, Suzhou, China. Now I'm serving as vice-chair of young scientist committee, division of TDM, Chinese Pharmacological Society. My work focuses on TDM and clinical pharmacology of biological, specializing in bioanalysis, pharmacokinetics and pharmacodynamics of adalimumab and infliximab.

Background: Therapeutic drug monitoring of adalimumab has been recommended for the management of inflammatory bowel disease.
Aims: This study aimed to investigate the exposure – response relationship of adalimumab in patients with ankylosing spondylitis.
Methods: A prospective cohort study was conducted in patients with ankylosing spondylitis who were initiating adalimumab treatment. Plasma samples were collected prior to the next drug adaministration. Adalimumab concentrations were quantified using an in-house ELISA, and anti-drug antibodies (ADA) were measured using Meso Scale Discovery. Exposure – response modeling was performed using logistic regression.
Results: Ninety-eight patients with 12-24 weeks of follow-up were included, of whom 39 were classified as primary non-responders. Steady-state trough concentrations (Css-min) were significantly higher in primary responders compared to non-responders (6.27 vs. 1.17 μg/mL, P<0.0001). The exposure – response model indicated that a Css-min target of 5.4 μg/mL was associated with an 80% probability of response. Additionally, week 4 trough concentrations (Ctrough-wk4) were higher in primary responders, and a target of 2.5 μg/mL was predictive of primary response (sensitivity 0.81, specificity 0.88). ADA development was observed in 8/41 (19.5%), 38/58 (65.5%), and 90/98 (91.8%) patients at week 2, week4, and during follow-up, respectively. ADA positivity at week 4 was significantly associated with primary non-response (odds ratio=5.5).
Conclusions: A statistically significant exposure – response relationship and an optimal adalimumab concentration target were identified. ADA formation was the primary determinant of low drug concentrations and primary non-response.
Keywords: adalimumab, exposure – response relationship, therapeutic drug monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W322

Development and Visualization of a Generalizable Pharmacokinetics Model

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Biography:
Kanoko Okuba is a specially appointed assistant professor at The University of Osaka with several years of clinical experience as a pharmacy pharmacist. While working in pharmacy, she followed up with individual patients to ensure the success of their drug therapy and contributed to their treatment and health maintenance. She entered the Graduate School of Pharmaceutical Sciences at The University of Osaka in 2024 to conduct research on pharmacometrics and the effects of drugs on pregnant women and fetuses, and began her current position in April 2025.

Background & Aims: In Japan, promoting self-medication is vital for reducing medical costs and extending healthy life expectancy. A broader public understanding of pharmaceuticals is necessary. This study aims to develop an accurate and generalizable pharmacokinetic (PK) model and create a visualization tool for drug kinetics.
Methods: Literature on PK/PD models beyond TDM drugs is limited. We extracted data from the Interview Form graphs to develop PK Model 1 and reconstructed PK Model 2 based on previous research. A PBPK simulation using Simcyp® simulator was conducted with fexofenadine's physicochemical properties. Simcyp® simulator generated plasma concentration data were incorporated into both models, and RMSE was compared to assess PK Model 1's accuracy and generalizability. Additionally, a web-based visualization tool was developed for PK Model 1.
Results: The RMSE between the simulated values obtained from Simcyp® simulator and PK Model 1 was 0.106, while that for PK Model 2 was 0.098. Based on these RMSE values, PK Model 1 demonstrated comparable accuracy to the established PK Model 2 in performing PK simulations. Furthermore, PK Model 1 was visualized using Python and Matplotlib.
Conclusion: The results indicate that an accurate and generalizable PK model can be developed using data from the interview form and Simcyp® simulator. Additionally, while this study focused on visualizing pharmacokinetics, we aim to integrate it with a PD model to develop a tool that allows individuals without pharmaceutical knowledge to understand when a drug takes effect and how long its effects last.
Keywords: Self-medication, Pharmacokinetic Simulation, Visualization

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W323

Application of a population model for procalcitonin in adults in intensive care

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Biography:
Jacqui is Associate Professor at the University of Auckland, with research interests in pharmacometrics, modelling biomarkers, dosing for special populations and anaesthesia. She is President of PAGANZ, treasurer for ASCEPT NZ and runs the Auckland Pharmacometrics Group.

Background: Over 14,000 patients are admitted to intensive care each year in New Zealand. About half have or develop infections. Differentiating bacterial infections which require antibiotics from viral or other causes of inflammation is a longstanding challenge. Procalcitonin is a biomarker that may help diagnose bacterial infections, typically using a single threshold approach but its utility in intensive care is unclear. A population model describing procalcitonin dynamics during sepsis and infection in adults (1) may provide an alternative.
Aims: To determine whether reference ranges for procalcitonin, as determined by a population model, capture concentrations measured in adult ICU patients.
Methods: 100 adult patients, either admitted to the ICU with clinical infection or at increased risk of developing infection (receiving mechanical ventilation for > 48 h), were observed. Clinical data, including infection status over time, were collected. Procalcitonin concentrations were quantified from residual clinical samples and assessed against the reference ranges generated by a model incorporating common covariates including patient characteristics, disease severity and time following admission, for patients with infection, sepsis, or severe sepsis.
Results: Patients were 67% male, with average age 53.9 ± 15.1 years, and weight of 91.1 ± 30.4 kg. 33% were infected at admission, with 80% of those diagnosed with sepsis. Expected procalcitonin concentration reference ranges (10th and 90th percentile) generated by the model are assessed against 707 observed concentrations.
Conclusions: Model-predicted reference ranges of expected procalcitonin concentrations can be generated to support interpretation of procalcitonin concentrations.

1. Bokor et al. [Abstract] PAGANZ 2023; Australia.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W324

Population Pharmacokinetics of Rifampicin: Supporting Model-Assisted TDM in Tuberculosis Treatment

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Biography:

Yuan Pétermann is a pharmacist with a background in clinical pharmacokinetics and pharmacometrics modeling. After earning a pharmacist degree in 2019, he gained experience across preclinical and clinical research, as well as in community pharmacy practice over the years. In 2023, he began a PhD in clinical pharmacokinetics, focusing on population modeling and therapeutic drug monitoring (TDM) to optimize drug dosing strategies. With experience in pharmacokinetic analysis and model-informed precision dosing, he aims to leverage pharmacometric modeling for real-world clinical applications, notably through development of clinical decision support system relying on model-informed precision dosing software

Background: Rifampicin is essential for tuberculosis treatment, but its efficacy is often limited by high inter-individual variability (IIV) subject to demographic, clinical and environmental factors potentially leading to subtherapeutic exposure, emphasizing the need for a model-assisted therapeutic drug monitoring (TDM).
Aims: This study aimed to develop a population pharmacokinetic model to support rifampicin TDM.
Methods: Plasma concentrations were prospectively collected from tuberculosis patients in Tanzania at day 1-3 and 12-16 after treatment initiation and retrospectively from a South African cohort sampled at day 7 and 14. A classical stepwise approach in MonolixSuite™ was used to study rifampicin pharmacokinetics (PK) and explore differences due to populations characteristics.
Results: Rifampicin PK was best described by a one-compartment model with linear absorption (rate of 2.64 h-1), delayed by a lag time of 0.32 h, a volume of distribution of 41 L and a saturable Michaelis-Menten elimination with a Km of 27.5 mg/L and Vm values of 124 mg/h and 419 mg/h for the South-African and Tanzanian populations, respectively. The autoinduction was depicted by an Emax time-dependent function, with a steady state reached after a month of treatment (autoinduction half-life of 157 h), and a corresponding elimination increase of 1.38-fold in Tanzanians and 3.76-fold in South Africans. A large IIV was associated with all PK parameters.

Conclusions: Substantial IIV with population differences in autoinduction amplitude and maximum elimination rates associated to ethnic specific metabolic pathways call for a personalized tuberculosis management, such as model-assisted TDM.

Keywords: rifampicin, tuberculosis, population pharmacokinetics, therapeutic drug monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W325

A nonparametric population pharmacokinetic model of selumetinib administered to pediatric neurofibromatosis-I patients

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Biography:
Zoltan Kollo is a PhD student and a resident physician specializing in laboratory medicine. His research interests include the therapeutic drug monitoring of protein kinase inhibitors.

Background: Selumetinib (SLT) is an oral, selective mitogen-activated protein kinase inhibitor administered twice daily to pediatric neurofibromatosis patients. Adverse effects are common, prompting physicians to switch to smaller or alternating doses. Ingestion in the fasted state is recommended, placing a burden on patients. Concentrations show substantial intraindividual fluctuations, exposure is highly variable, and the drug is eliminated almost entirely between intakes. TDM-based therapy guidance may help overcome these issues.
Aims: To construct a nonparametric population pharmacokinetic model based on rich sampling and to perform Monte-Carlo simulations to facilitate a tighter control of exposure to SLT.
Methods: Twenty-two pediatric outpatients [median age (range): 11.5 (5-16) years], receiving doses based on clinical evaluation and follow-ups, were included. Plasma SLT concentrations obtained in 156 samples were used for modeling using PmetricsTM. Monte-Carlo simulation was performed with 40-mg daily doses to evaluate the interindividual variability in exposure and compare concentration fluctuations seen with q6h, q8h, or q12h regimens.
Results: A three-compartment model best fitted the observations. The median half-life was 1.42 (range: 0.36-3.74) hours. Monte-Carlo simulations estimated a 32.7-fold variability in areas under the concentration-time curves with standard q12h dosing and trough/peak concentration ratios of 12.6%, 10.4%, and 6.5% for q6h, q8h, or q12h dosing, respectively.
Conclusions: The substantial interindividual variability of SLT exposure and the intraindividual fluctuations demonstrate the importance of individualizing dosing regimens.
Key Words: Therapeutic drug monitoring, oncology, paediatrics, selumetinib, nonparametric pharmacokinetic modeling

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W326

The toxicities of regorafenib are correlated with M5 trough concentration

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Biography:

Yukitaka Shibata is a clinical pharmacist at the National Cancer Center Hospital. With a strong passion for pharmacogenomics (PGx), He is dedicated to optimizing cancer treatment through personalized medicine. After earning a doctoral degree, he has been actively involved in research on the genetic factors influencing anticancer drug efficacy and toxicity. Beyond professional life, he recently purchased a new home, marking an exciting personal milestone. With a keen interest in continuous learning and innovation, he strives to bridge the gap between genomic science and real-world clinical applications, ultimately contributing to the advancement of precision oncology.

Background: Regorafenib, a multi-targeted tyrosine kinase inhibitor (TKI), has approved for metastatic colorectal cancer (mCRC) and gastrointestinal stromal tumors (GIST). Regorafenib is converted to M2 and further to M5 by CYP3A4. Regorafenib is difficult to be administered in full doses because of toxicity, including hand-foot skin reactions (HFSR). Therapeutic drug monitoring (TDM) of regorafenib may predict the occurrence of toxicity and contribute to treatment continuation.
Methods: TDM study was prospectively recruited from patients who received several TKIs. Blood samples collected at each visit and the concentrations were measured using liquid chromatography-tandem mass spectrometry. Patients treated with regorafenib between September 2022 and November 2024 were analyzed. The association between toxicities in cycle 1 and plasma concentrations of regorafenib and its metabolites at 7days in cycle 1 was assessed.
Results: Twenty-nine patients were recruited, and the median age was 64 years, with mCRC (n=25) and GIST (n=4). Initial dose (mg/day) was 40 (n=1), 80 (n=22), 120 (n=5), and 160 (n=1). Regorafenib, M2, and M5 concentrations throughout the analysis were 356-8617, 31-1755, and 41-1033 ng/mL, respectively, with large individual differences at the same dose. Patients with ≧ grade 2 HFSR of M5 concentrations showed significantly higher than those with < grade 2 HFSR (251ng/ml vs 520ng/ml, p=0.0475).
Conclusions: We found a significant association between M5 concentrations and HFSR in patients treated with regorafenib. TDM of M5 may be applicable to predict HFSR in clinical practice; studies are needed on differences in M5 concentration by CYP3A4 polymorphisms and their association with HFSR.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W327

Impact of cancer cachexia progression on OATP1B activity: Quantitative analysis using coproporphyrin-I

Mr Takahiro Sumimoto[1], Dr Ryota Tanaka[1], Dr Yosuke Suzuki[2], Mr Jun Negami[2], Mr Yoshio Sueshige[1], Dr Ayako Oda[2], Dr Ken Shiraiwa[1], Dr Takashi Inagaki[3], Dr Kazuo Nishikawa[3], Mr Ryosuke Tatsuta[1], Dr Satoshi Otsu[3], Prof Masao Ogata[3], Prof Keiko Ohno[2], Prof Hiroki Itoh[1]
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Biography:

Takahiro Sumimoto is a manager of Clinical Pharmacy at Oita University Hospital. His work focuses specifically on therapeutic drug monitoring for anticancer and antipsychotic drugs, as well as studies exploring factors that cause fluctuations in pharmacokinetics using endogenous substrates as biomarkers. He graduated from Oita University Graduate School of Medicine in 2023 with a Doctor's Degree of Medicine. He is inspired daily by his wife and their daughter. In his free time, he likes to climb a mountain and camping.

Background: Genetic factors, inflammatory cytokines such as interleukin (IL)-6 and tumor necrosis factor-α (TNF-α), and uremic substances such as 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF) have been reported to affect organic anion transporting polypeptide (OATP)1B activity. However, the relationship between OATP1B activity and these factors in patients with cancer cachexia has not been reported.
Aims: This study aimed to identify the factors contributing to individual differences in OATP1B activity in patients with cancer cachexia, using coproporphyrin- I (CP-I) as an endogenous biomarker of OATP1B activity.
Methods: The study included patients with cancer cachexia attending the Oita University Hospital. After obtaining written informed consent, plasma CP-I and CMPF levels were measured by ultra-high performance liquid chromatography coupled to quadrupole time-of-flight mass spectrometry, inflammatory cytokines by ELISA, and OATP1B genetic polymorphisms by real-time PCR.
Results: The study recruited 114 patients; 40 with pre-cachexia, 39 with cachexia, and 35 with refractory cachexia. Plasma CP-I levels were higher in patients with pre-cachexia compared with the data in general population reported previously, and tended to be higher in patients with refractory cachexia than in the others. Plasma CP-I correlated positively with IL-6 and TNF-α, but did not correlate with OATP1B polymorphisms or CMPF. Multiple regression analysis identified the refractory cachexia as a significant factor independently affecting plasma CP-I levels.
Conclusions: Reduction in OATP1B activity in patients with cancer cachexia may be attributed to inflammatory cytokines or some other factors that are elevated by cancer cachexia progression, rather than OATP1B polymorphisms and CMPF.
Keywords: cancer cachexia, OATP1B, coproporphyrin-I, biomarker

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W328

Relationship between osimertinib concentration and toxicity: preliminary assessment in a prospective study

Ms Reiko Ando Makihara[1], Dr Yuki Katsuya[2], Dr Yasushi Goto[3], Mr Kohei Yoshikawa[4], Mr Keisuke Ikegami[1], Mr Yukitaka Shibata[1], Mr Takuma Suzuki[1], Mr Makoto Maeda[1], Dr Ken Masuda[3], Dr Yuki Shinno[3], Dr Yusuke Okuma[3], Dr Tatsuya Yoshida[3], Dr Hidehito Horinouchi[3], Mr Daisuke Watabe Watabe[1], Mr Tomohisa Asano[1], Mr Yoshimasa Saito[1], Dr Noboru Yamamoto[2], Mr Hironobu Hashimoto[1]
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Biography:
Reiko Ando Makihara is a pharmacist at National Cancer Center Hospital. My work focuses specifically TDM in oncology.

Backgrounds: Osimertinib is an orally, third-generation epidermal growth factor receptor (EGFR)-TKI that acts by irreversibly binding EGFR activating mutations. Although some patients need dose reduction, efficacy has not been demonstrated. We are conducting a prospective observational study of TDM in patients receiving various TKIs. This is a preliminary assessment of osimertinib.
Methods: Patients treated with osimertinib between March 2022 and May 2024 were analyzed. Blood samples collected at each visit. The plasma concentration was measured using LC-MS/MS.
Results: A total of the 26 was enrolled, of which 25 were evaluable. Of these, 8 (31%) were male, the median age was 74 (range 36-88). the initial dose was 40 mg in 3 patients and 80 mg in 22 patients. In the initial blood sampling of 22 patients who started with 80 mg, the concentrations in patients who required a dose reduction within two months tended to be higher than those in patients who were able to continue treatment without a dose reduction (594ng/mL vs 210 ng/mL, p=0.001). The mean concentrations were comparable between 14 patients who continued 80mg and 8 patients who received 40mg either initially or after dose reduction. (204ng/mL vs 223ng/mL).
Conclusions: The group that started at 80mg, the group that switched to 40mg due to adverse events, and the group that started at 40mg due to concerns about adverse events ultimately showed the same plasma concentration. TDM from the initiation of treatment may help prevent adverse events, and could facilitate the optimization of the dose of osimertinib.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W329

Plasma concentrations of imatinib in elderly patients with gastrointestinal stromal tumor

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Biography:

My name is Takuma Suzuki. I am a pharmacist in the Department of Pharmacy at the National Cancer Centre Central Hospital and have been engaged in TDM work for haematopoietic stem cell transplantation and immunosuppressive drugs for about four years. In addition, as part of the field of pharmaceutical administration, I have been engaged in new drug review and post-marketing safety operations for anticancer drugs at the regulatory authority, the Pharmaceuticals and Medical Devices Agency, for about four years. As a personal interest, I am interested in TDM of antibiotics and immunosuppressive agents in haematopoietic stem cell transplant patients and hopes to gain new knowledge in this field at IATDMCT2025.

Background: Imatinib is a representative tyrosine kinase inhibitor for the treatment of gastrointestinal stromal tumor (GIST). Elderly patients are more likely to experience imatinib-related adverse events and dose reductions compared with non-elderly patients. The aim of this study was to investigate the relationship between plasma concentrations of imatinib and age in patients with GIST, and to determine the optimal dose in elderly patients.
Methods: This study analyzed the data of the patients receiving imatinib for GIST enrolled between Sep 2022 and Feb 2025 in a prospective observational study. The correlation between age and C/D ratio (plasma concentration normalized by daily dose) at steady-state was evaluated using Pearson linear correlation coefficients. C/D ratio of imatinib were used to determine differences between two groups: the elderly group (aged 75 ≥, E group), and the non-elderly group (aged <75, NE group).
Results: A total of 34 patients (E: 9, NE: 25) were included. A significant correlation between age and C/D ratio was observed (R^2=0.496, p=0.028). The trough C/D ratios for imatinib were 5.86±5.06 for E group and 2.94±2.59 (p=0.17) for NE group, respectively, indicating a wide variation in the E groups. The starting doses required to achieve target concentrations, based on the median trough C/D ratio, were 400 mg for NE group and 100-200 mg for E group .
Conclusions: This study showed that age was associated with a higher imatinib C/D ratio. Almost two-fold higher C/D ratio in the E group suggests that imatinib was initiated at half the standard dose.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W330

Association of Initial Drug Concentrations with Age and Sex in Cancer Therapy

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Biography:

Keisuke Ikegami is a third-year PhD student at the Graduate School of Pharmaceutical Sciences, Keio University, specializing in pharmacoepidemiology and diagnostic research. His research focuses on predictive model development and evaluating model performance across different institutions. In addition to his academic work, he has been measuring blood concentrations as a research assistant at the National Cancer Center Hospital. With a strong interest in statistical analysis and evidence-based medicine, he aims to contribute to the advancement of precision medicine and healthcare optimization.

Background: TDM for oral molecular targeted anticancer drugs (MTAs) helps individualize dosing regimens and maintain therapeutic target range but is not implemented in routine clinical practice. In addition, age and sex are known to be factors that influence pharmacokinetics for many drugs, but their influence is not clear for MTAs. In this study, we prospectively examined the association of plasma concentrations of various MTAs with age and sex.
Methods: Patients who started treatment with MTAs between March 2022 and January 2025 were included. Plasma concentrations of MTAs were measured by LC-MS/MS at each visit. Patient characteristics were collected on treatment initiation date.
Results: Of the 155 included patients, 37 started imatinib, 25 osimertinib, 23 abemaciclib, and 7 fruquintinib, while the remaining 63 received other MTAs. Of these, 84 patients (54%) were female and the median age was 65 (range: 34-89). The geometric mean ratio (elderly [≥65] to non-elderly) was greater than 1 for imatinib (1.38, 95% CI: 0.95–2.02), abemaciclib (1.85, 0.77–4.44), and fruquintinib (1.39, 0.89–2.19), whereas it was 0.90 (0.55–1.49) for osimertinib. Female receiving osimertinib had significantly higher concentrations than male, regardless of age (p = 0.029). The geometric mean ratio (female to male) for osimertinib was 1.68 (1.15–2.44).
Conclusions: This study suggested certain drug concentrations are associated with age- and sex-related differences in real-world settings. It is expected to validate the impact of TDM by evaluating the relationship between drug concentration and toxicity in the future.
Keywords: Cancer treatment, Oral molecular targeted agents, Therapeutic Drug Monitoring, Plasma concentration

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W331

Busulfan Therapeutic Drug Monitoring in Allogeneic HSCT Patients in Singapore

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Biography:
Ms Sin Li Jiao is a Medical Laboratory Scientist in the Division of Pharmacy at the Singapore General Hospital. She graduated from National University of Singapore with Bachelor of Science with Honours in Life Sciences and continues to pursue ongoing professional development in the fields of Analytical and Bioanalytical Chemistry. She is actively involved in the development and maintenance of LC-TQMS, LC-QTOF-MS and UHPLC assays used for the quantification of drugs and biomolecules related to antimicrobial resistance, cancer, and chronic diseases. Together with her team, Li Jiao is working on the translation of lab innovations from bench to bedside through development of lab-developed test kits and accredited lab services."

Background: Allogeneic haematopoietic stem-cell transplantation (HSCT) is offered to selected patients with blood cancers at Singapore General Hospital (SGH), a leading transplant center in Asia. A key component of the preparative regimen is Busulfan (BU), a chemotherapy agent. However, weight-based dosing of BU results in significant variability in drug exposure among patients. Achieving therapeutic BU concentrations is essential to prevent graft failure, disease relapse, and reduce toxicities like veno-occlusive disease. Despite this, real-time BU therapeutic drug monitoring (TDM) is unavailable in Singapore.
Aims: This study aims to develop a rapid and accurate assay using liquid chromatography-tandem mass spectrometry (LCMS/MS) to optimize BU dosing in patients receiving BU-based HSCT in Singapore.
Methods: BU concentrations of 0.02–5mg/L was spiked in commercial plasma to create the calibration curve. Four adults with haematological malignancies and three children with underlying non-malignant conditions (2 thalassemia, 1 mucopolysaccharidosis type II) were recruited with consent. Samples underwent protein precipitation with zinc sulphate, followed by hexane extraction. Data was acquired using an LCMS 8060 mass spectrometer. BU area-under-the-concentration-time-curve-at-steady-state(AUCss,24hr) was calculated using Pmetrics software to evaluate efficacy.
Results: Excellent linearity(R^2 = 0.999) was demonstrated within tested range. 6 subjects were successfully engrafted, 1 paediatric patient with underlying mucopolysaccharidosis type II had graft rejection despite achieving target BU exposure after dose adjustment. All subjects with underlying haematological malignancies remained in remission with no adverse effects related to BU-TDM.
Conclusion: A validated, rapid, and accurate LCMS/MS method was developed for BU-TDM, enabling optimized dosing for BU-based HSCT at SGH and KKH.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W332

Therapeutic Drug Monitoring for early dose personalization of Sunitinib in mRCC

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Biography:

Eleonora Cecchin is a PhD student at the Università degli Studi di Udine and a researcher at the Centro di Riferimento Oncologico (CRO) in Aviano, Italy. Her research focuses on gender pharmacogenetics in oncology, aiming to optimize therapy through therapeutic drug monitoring (TDM). She investigates sex- and genetics-related differences in drug exposure and toxicity, particularly for oral anticancer drugs. Eleonora has expertise in SNP genotyping, LC-MS/MS analysis, and pharmacokinetic studies. She actively collaborates with hospitals to expand patient recruitment and enhance clinical applications. Committed to advancing precision medicine, she strives to improve personalized cancer treatment by integrating pharmacogenetics and TDM

Background: Sunitinib at a fixed dose may lead to under- or over-exposure which in Italy is currently adjusted over time based only on trial and error clinical practice. Integrating Therapeutic Drug Monitoring (TDM), pharmacogenetics (PGx), and drug-drug interaction (DDI) assessment could lead to a more rational and faster dose personalization.
Aims: To evaluate sunitinib exposure in patients treated at different drug dosage as an effect of successive toxicity-driven dose adjustments over time.
Methods: Steady-state plasma samples (Cmin) from CRO-2022-14 trial (NCT06822959) patients were analyzed for sunitinib levels using validated LC-MS/MS. Target Cmin ranges were 37.5–60/75 ng/mL (continuous) and 50–80/87.5 ng/mL (intermittent). Genetic polymorphisms affecting sunitinib metabolism and transport were assessed, and DDIs were evaluated via UpToDate Lexi-Drug.
Results: Fourteen patients already on sunitinib therapy (median 28 months) were enrolled. As an effect of toxicity-driven dose reductions eight patients on 50 or 37.5 mg/day had Cmin levels (53–79 ng/mL) within target. Two females on 25 mg/day still exceeded 80 ng/mL with recurrent G2–G3 toxicities, suggesting the need for lower doses. Two others on 25 mg/day had Cmin < 40 ng/mL without severe toxicity, indicating 37.5 mg/day might be optimal. Females (81 ng/mL) had higher exposure than males (65 ng/mL). PGx analysis was limited by sample size, and no significant DDIs were identified.
Conclusions: Toxicity-driven dose adjustments ensured adequate sunitinib exposure over 28 months. Females showed higher plasma levels than males, though sample size limited conclusions. Early TDM could have optimized dosing, improving tolerability, adherence, and exposure.
Keywords: sunitinib, toxicity, plasma exposure

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W333

Cost-Effectiveness of TDM and Personalized Interventions in Psychiatric Care: A Comprehensive Review

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Biography:

An assistant professor in pharmaceutical care, the PhD in Clinical Pharmacy Program director. Faculty of Pharmacy, Silpakorn University, Thailand. The member of IATDMCT.

Background: The Cost-effectiveness of Therapeutic Drug Monitoring (TDM) in Psychiatric care is questionable
Aims: To review the cost-effectiveness of TDM in psychiatric care.
Methods: This review synthesizes findings from 12 studies exploring the cost-effectiveness of therapeutic drug monitoring (TDM) and related interventions in psychiatric care by using the Pubmed database 2000-2025.
Results: The studies collectively highlight the economic and clinical benefits of TDM and other tailored strategies for managing mental health conditions. Research on clozapine monitoring emphasizes its role in reducing adverse effects and healthcare costs for schizophrenia. Similarly, TDM of citalopram and atypical antipsychotics demonstrates improved therapeutic outcomes and economic efficiency. Studies on Alzheimer's disease treatments, including cholinesterase inhibitors and the rivastigmine transdermal patch, underscore the cost-effectiveness of regionally tailored practices. Interventions like dementia care management and self-management education programs for epilepsy showcase the dual advantages of enhanced clinical outcomes and cost savings. Additionally, pharmaceutical care models in psychiatric hospitals and contingency management programs for heroin abstinence provide evidence for reducing healthcare costs while improving patient care. Research comparing long-acting and monthly formulations of antipsychotics, such as paliperidone palmitate, further supports the utility of cost-effective formulations in improving adherence and outcomes.
Conclusion: These findings collectively emphasize the importance of personalized, cost-effective strategies in optimizing psychiatric care and resource utilization.
Keywords: Cost-effectiveness, Comprehensive review, TDM in Psychiatric medications,

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W334

Trace Analysis of Alpha-Amanitin in Human Urine: Implications for Poisoning Detection.

dr Rafał Szewczyk[1], dr Katarzyna Krupczyńska-Stopa[1], Maciej Stopa[1,2], dr Adrian Soboń[1], Mrs Karina Izdebska, Anastasiia Shyian[1], Karina Izdebska[2]
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Biography:
n/a

Background: Alpha-amanitin, a toxin from Amanita fungi, causes severe liver damage. Early detection improves survival rates, however detection in urine is challenging due to matrix variability. Accurate identification and quantification at low concentrations requires LC-MS.
Aims: This study focuses on the development of a reproducible and sensitive method for detecting alpha-amanitin in human urine samples.
Methods: Sample preparation was performed using solid-phase extraction (SPE) with DAU sorbent (200 mg/10 mL, UCT Inc). Urine sample was diluted with phosphate buffer (pH 6.0) before loading onto the SPE column, which was conditioned with methanol, water, and phosphate buffer. After sample application, the matrix was washed with water, 0.1% acetic acid, and methylene chloride-methanol. Alpha-amanitin was eluted with methanol, evaporated under nitrogen, and reconstituted in an injection-ready solvent. Data acquisition was done using a QTRAP 6500+ mass spectrometer (SCIEX) with LC-40XR (Shimadzu), and processed with SciexOS software. LC-MS/MS analysis was performed in positive ionization MRM mode.
Results: The development of a sensitive method development was challenged by the lack of stable isotope-labeled analogs and suitable internal standards. The focus was placed on optimizing the solid-phase extraction (SPE) procedure to achieve sensitivity, specificity, linearity, and reproducibility without internal standards. The method met performance criteria with an LLOQ below 0.25 ng/ml, linearity from 0.25–100 ng/ml (R = 0.998), reproducibility below 5% RSD, and no interference at the analyte's retention time.
Conclusion: Preliminary data confirm the method's effectiveness in detecting alpha-amanitin, surpassing ELISA limitations.
Key Words: Alpha-amanitin, Poisoning detection, LC-MS.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W335

Boerhavia diffusa extract exhibits monoamine oxidase inhibition but lacks neuroprotective effects

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Biography:

Professor Vanessa Steenkamp is the Deputy Dean of Teaching & Learning and Professor in Pharmacology in the Faculty of Health Sciences, University of Pretoria. She has made groundbreaking strides in her career, which has had a significant impact in the field of pharmacology, both as a member of committees, through her participation and engagement with students, scientists and the community and her research contributions. She specializes in researching traditional herbal medicine and toxicology, with her focus being drug-development for the treatment of neurodegenerative diseases. Not only is her research comprehensive and multifaceted, but innovative, and incorporates the use of advanced technology. Her recognition both locally and internationally is confirmed by her multiple invitations as plenary/guest speaker, awards received and honorary positions. She has successfully supervised >70 postgraduate students to completion and is actively involved in mentoring emerging scientists.

Background: Parkinson's disease (PD) involves progressive dopaminergic cell loss in the substantia nigra with associated oxidative stress. Boerhavia diffusa is consumed as a tea for its general health benefits.
Aim: This study aimed to assess the neuroprotective potential and safety profile of a proprietary Boerhavia diffusa extract in cellular (SH-SY5Y) and larval zebrafish models of PD.
Methods: The proprietary extract was assessed for cytotoxicity and neuroprotection against 6-hydroxydopamine (6-OHDA)-induced damage in neuroblastoma cells. The Amplex® Red Monoamine Oxidase Assay Kit was used to determine monoamine oxidase (MAO) activity. Antioxidant activity was measured using the ferric reducing antioxidant power (FRAP) assay. Behavioural analysis and determination of protein expression levels of the neurodegeneration markers, tyrosine hydroxylase (TH) and neuronal differentiation 1 (neuroD1), were employed to evaluate neuroprotective potential of the extract in zebrafish.
Results: The extract exhibited cytotoxicity, without apparent protection from 6-OHDA. Low antioxidant activity was observed. All extract concentrations exhibited MAO inhibition; ≥80%, ≥79% and ≥55% for MAO-A, MAO-B and non-specific inhibition, respectively. Zebrafish larvae exposed to 6-OHDA, exhibited significant ($p<0.001$) hypo-locomotion. Treatment with the extract did not reinstate 6-OHDA-induced decreases in brain TH or NeuroD1 protein expression. Independent of 6-OHDA, significant toxicity (lack of swim bladder, edema) was observed for 2.5, 5 and 10 µg/mL of the extract.
Conclusion: The plant extract did not exhibit benefit in the context of PD. Future research should focus on subjecting isolated compounds to the battery of tests.
Keywords: Parkinson's disease, cytotoxicity, neuroprotection, zebrafish, SH-SY5Y cells

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W336

Establishment and Safety Assessments of Micro/Nanoplastic Libraries 5: Focus on Polyvinyl Chloride

Prof Yasuo Tsutsumi[1,2,3,4,5], Dr Yuya Haga[1,2], Sota MANABE[2], Wakaba IDEHARA[2], Mii HOKAKU[1], Phyo Bo Bo Aung[1], Yuto MOTOYAMA[1], Ayaha MORI[2], Dr Ryotaro TSUTSUMI[6], Prof. Kazuya NAGANO[6], Dr Haruyasu ASAHARA[1,2,3], Dr Hirofumi TSUJINO[1,2,7], Dr Kazuma HIGASHISAKA[1,2,8]
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Biography:

Dr. Yasuo TSUTSUMI is a professor at the Graduate School of Pharmaceutical Sciences, Osaka University, Japan. Prof. Tsutsumi specializes in toxicology and public health in the field of pharmaceutical sciences. Especially, he interested in the toxicity and safety of micro- and nanoparticles. Prof. Tsutsumi received a B.S. and M.S., Ph.D. in pharmaceutical sciences from Osaka University, Japan. He has been a state licensed pharmacist. He began work at Graduate School of Pharmaceutical Sciences, Osaka University in the Laboratory of Pharmaceutics in 1994. Dr. Tsutsumi was promoted to professor in 2008 at Graduate School of Pharmaceutical Sciences, Osaka University in the Laboratory of Toxicology and Safety Science.

Background: As highlighted in the SDGs, plastic waste leakage is a critical issue, with concerns over microplastics (MPs, <5 mm) and nanoplastics (NPs, <1 µm) affecting human health. These MPs/NPs (MNPs) have been detected in human tissues such as lung, blood, and placenta, indicating inevitable exposure. Environmental MNPs vary in polymer type, size, shape, and surface characteristics, yet most safety assessments rely on spherical particles with smooth surface, which do not reflect real conditions. To address this, we developed MNPs library considering environmental physicochemical properties.
Aims: This study aimed to characterize our MNPs library including PE, PS, PP, PVC, and PET as model polymers and assess its similarity to environmental samples. Additionally, we tried to evaluate the cellular response especially focusing on Polyvinyl Chloride (PVC) among MNPs library samples.
Methods: Spherical, fragmented, fiber and surface-oxidized MNPs were prepared to mimic environmental conditions. ATR-IR analysis and SEM confirmed their properties. MTT assay was used to measure cell viability.
Results: Surface oxidation was induced via vacuum UV exposure (172 nm), forming hydroxy and carbonyl groups. NPs were produced using a precipitation-based method referring to previous study. Our MNPs exhibited morphology and surface characteristics similar to environmental samples. Additionally, surface oxidized PVC-MNPs exhibited cytotoxicity compared to non-degraded PVC-MNPs.
Conclusions: We developed MNPs library considering environmental condition. This library facilitates comprehensive safety evaluations, including oral and inhalation exposure tests, and is available for collaboration. For inquiries, please contact Yuya Haga at haga-y@phs.osaka-u.ac.jp.
Keywords: Microplastics, Nanoplastics, Environment relevance, Physicochemical properties, Cytotoxicity, Polyvinyl Chloride

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

W337

Profiles of bacterial communities and antibiotic resistance genes in the Lahasa River

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Biography:

Lv yayao is a chief pharmacist at Tianjin First Central Hospital, specializing in Therapeutic Drug Monitoring. Focusing on establishing analytical methods and conducting drug concentration monitoring using LC-MS/MS.

Background: There have been few research reports on the analysis of bacterial communities and the distribution characteristics of ARGs in the Lhasa River.
Aims: To study the distribution characteristics of the resident bacterial communities and the pollution status of ARGs in the Lhasa River, and to provide a theoretical basis for the prevention and control of drinking water safety for the regional population.
Methods: Samples were collected from 5 sampling points in the Lhasa River Basin, and the distribution characteristics of bacterial communities were analyzed by 16sRNA sequencing technology. The contents of 19 kinds of ARGs were detected and analyzed by fluorescence quantitative PCR technology. Statistical analysis was carried out using SPSS 22.0.
Results: Proteobacteria was the predominant resident bacterial phyla, among which Acinetobacter, Aeromonas and Pseudomonas were the three dominant genera. All 19 kinds of ARGs were detected at a relatively high level. Among them, the concentration of aadA was the highest. Among the 8 kinds of last resort antibiotic resistance genes (LARGs), the concentration of blaOXA-48 was the highest. Overall, concentrations of LARGs were lower than those of "conventional" ARGs, and there was a statistically significant difference between the two.
Conclusion: The results of this study expand people's understanding of the distribution of bacterial communities and ARGs in the water of the Lhasa River. Given the potentially serious adverse effects of ARGs, especially LARGs, the pollution of ARGs in the Lhasa River should be given due attention.
Key words: The Lhasa River; Bacterial community; Antibiotic resistance genes

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P500

Patient-centered design of immunosuppressant point-of-care tests for transplant recipients in remote settings

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Biography:
Kelsey is a first year Bioengineering PhD student in the Olanrewaju lab at the University of Washington. She has previous training in both biomedical engineering and material science engineering from the University of Virginia and completed her Master of Science in material science engineering at the University of Washington. Prior to completing her Master's, Kelsey worked in a hospital in the emergency department where she encountered the need for more patient-centric healthcare tools and resources to relieve the burden on medical providers and provide better health outcomes for patients. Her interdisciplinary background aligns nicely with her current research focus: 3D-printing user-friendly microfluidic devices for decentralized diagnostic access. Her research involves interfacing with clinicians, patients, and community engagement committees to develop robust prototypes of diagnostic devices which can be used in decentralized areas around the Pacific Northwest for therapeutic drug monitoring.

Background: Therapeutic drug monitoring (TDM) of immunosuppressant drugs is a necessary component of post-transplant care to prevent graft rejection. Nevertheless, current testing modalities are limited to centralized laboratories and unavailable in point-of-care (POC) settings, including rural and underserved urban areas. This results in time and resource expenditures for patients to obtain routine tests and can be especially harmful in acute situations where fast turn-around times are essential. POC tests may alleviate these burdens and there is growing recognition of the importance of active user engagement, to increase usability, effectiveness, and enthusiastic adoption of such technologies.
Aim: Conduct stakeholder engagement meetings to identify context, attitudes, requirements, and potential unintended consequences for an immunosuppressant TDM POC test.
Methods: We conducted interviews with 9 transplant providers and 11 organ transplant recipients, including members of the community engagement committee of the Center for Innovations in Cancer & Transplant and the Transplant Recipient Advisory Council.
Results: Patients had strong interest in an accurate, quantitative POC test to reduce financial and time burdens. Providers wanted faster turn-around times than available with current modalities, especially for managing patients in remote settings. Both groups agreed that a POC test could enhance patient engagement and empowerment in healthcare, and they expressed concerns about potential increased work a POC device would create for caregivers and healthcare workers.
Conclusions: We will incorporate these findings into our POC test engineering and continue iterative stakeholder engagement to co-design a device that can transform post-transplant care.
Keywords: point-of-care, immunosuppression, expanding healthcare access, design methodologies

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P501

In-depth Study of TDM Data for Tacrolimus in Transplant Patients

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Biography:

Wei-Jian Ni, Ph.D. in Medicine, is a high-level talent at the First Affiliated Hospital of University of Science and Technology of China, serving as an Associate Chief Pharmacist, Associate Researcher, and Master's Supervisor. He has led multiple research projects funded by the National Natural Science Foundation of China, the Anhui Provincial Natural Science Foundation, the Anhui Provincial Clinical Medicine Transformation Research Program, and the Hefei Comprehensive National Science Center. Dr. Ni also holds editorial roles at Clinical Immunology and the Chinese Journal of Antibiotics and is a Youth Committee Member of the Chinese Association of Traditional Chinese Medicine. Specializing in hospital pharmacy, therapeutic drug monitoring, and research in liver and kidney pharmacology and epigenetics, he has published over 30 SCI papers, including high-impact studies as first or corresponding authors in journals such as Clinical and Translational Medicine, Cell Death & Disease, and British Journal of Pharmacology.

Background: Tacrolimus, an immunosuppressive agent, is widely used to treat various types of transplants, and controlling its blood concentration and therapeutic efficacy has always been a particularly critical issue of concern.
Aims: This retrospective analysis evaluated tacrolimus therapeutic drug monitoring (TDM) data to determine the optimal therapeutic window and guide treatment adjustments for transplant patients in real-world settings.
Methods: TDM data from outpatient and inpatient transplant patients (liver, kidney, cardiac, and hematopoietic stem cell transplants) at the First Affiliated Hospital of University of Science and Technology of China (Jan. 1, 2024–Dec. 31, 2024) were analyzed. Tacrolimus steady-state blood concentrations were monitored in 12,539 patients (10,718 outpatients and 1,821 inpatients).
Results: The interquartile range (P25–P75) of tacrolimus blood concentrations was 4.60–7.31 ng/mL. The outpatient concentrations ranged from 4.60–7.10 ng/mL (66.64% compliance), whereas the inpatient concentrations ranged from 4.77–9.25 ng/mL (70.35% compliance). Patients with multiple TDM sessions had significantly higher compliance rates than those with single sessions ($P < 0.01$). The interquartile ranges (compliance rates) of blood concentrations varied by transplant type: kidney (4.70–7.07 ng/mL, 68.71%), liver (3.97–8.11 ng/mL, 61.30%), hematopoietic stem cell (3.60–9.20 ng/mL, 60.84%), cardiac (5.55–8.98 ng/mL, 81.71%), and lung (4.80–10.19 ng/mL, 69.76%), and the differences were significant ($P < 0.05$).
Conclusions: The optimal tacrolimus therapeutic window may need re-evaluation for different transplant types to improve compliance and guide precision therapy.
Key Words: Transplant; Tacrolimus; Therapeutic drug monitoring; Therapeutic window; Individualized therapy

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P502

What gets measured gets managed: multiplex assay for mycophenolate monitoring

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Biography:

Dr. Wang is a Research and Development Scientist at Vancouver Coastal Health, specializing in mass spectrometry method development and quality improvement in clinical laboratories. She is also a Clinical Instructor in the Department of Pathology and Laboratory Medicine at the University of British Columbia. Dr. Wang earned her PhD in Chemistry from the University of British Columbia, where she focused on marine natural products research. She then worked as a Research Scientist at IntelliSyn Pharma, contributing to drug discovery and medicinal chemistry projects. Afterward, she completed postdoctoral training at the University of British Columbia (St. Paul's Hospital), where her research focused on developing new mass spectrometry protein assays. Her current research interests include clinical mass spectrometry, therapeutic drug monitoring, automated sample preparation, and clinical laboratory quality improvement.

Background: Mycophenolate mofetil (MMF) is widely used with other immunosuppressants to prevent organ rejection. It is hydrolyzed to its active form, mycophenolic acid (MPA), which is further metabolized into inactive mycophenolic acid glucuronide (MPAG) and active acyl-glucuronide (AcMPAG). MPA is extensively bound to albumin, and only free MPA is pharmacologically active. MPAG reflects UDP-glucuronosyltransferase activity, and AcMPAG is associated with gastrointestinal toxicity. Simultaneous quantification of free MPA and its metabolites provides comprehensive insight into MPA metabolism, potentially enhancing dose individualization to optimize immunosuppression while minimizing toxicity.
Aims: To develop and validate a multiplex liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay for the simultaneous quantification of free MPA, along with MPA metabolites, in plasma and saliva.
Methods: Absolute quantification of MPA, MPAG, and AcMPAG in plasma was achieved using LC-MS/MS. Analytical validation included assessments of sensitivity, linearity, precision, recovery, matrix effects, and carryover, following clinical laboratory guidelines.
Results: The developed assay enables the simultaneous quantification of MPA, MPAG, and AcMPAG with imprecision of 3.4%, 2.2%, and 1.8% for low, mid, and high MPA QCs; 5.9%, 1.8%, and 1.7% for MPAG QCs; and 9.1%, 2.2%, and 1.8% for AcMPAG QCs. LLOQs were 0.01 mg/L for MPA and MPAG and 0.05 mg/L for AcMPAG, with linear ranges of 50 mg/L (MPA), 150 mg/L (MPAG), and 4 mg/L (AcMPAG).
Conclusions: This validated assay enables accurate monitoring of MPA and its metabolites. Further studies will assess saliva as a non-invasive alternative for TDM in transplant patients.
Keywords: Immunosuppressant, mycophenolic acid, metabolites, LC-MS/MS, therapeutic drug monitoring, saliva

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P503

Model-Informed Precision Dosing (MIPD) for tacrolimus in heart transplant recipients

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Biography:
I am a clinical pharmacist in the Department of Pharmacy at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (HUST). My research interests primarily focus on individualized therapy for heart transplantation, particularly utilizing pharmacogenomics and pharmacometrics methodologies. I have led a study funded by the National Natural Science Foundation of China (NSFC), investigating the mechanisms underlying tacrolimus-induced new-onset diabetes after transplantation. Additionally, I have served as the principal investigator for a National Key Research and Development Program of China focused on Precision Medicine Research. Furthermore, I hold the position of Deputy Chairman within The Youth Committee of Therapeutic Drug Monitoring Committee under the Chinese Pharmacological Society and am honored to be recognized as a fellow by the International Society for Therapeutic Drug Monitoring and Toxicology (IATDMCT).

Background: Tacrolimus is cornerstone in immunosuppressive regimens for heart transplantation, with narrow therapeutic index and large inter- and intra- variabilities. Therapeutic drug monitoring is important for tacrolimus personalized dosing, but have some limitation for clinical application.
Aims: We aimed to establish and validate a population pharmacokinetic (PPK) model of tacrolimus, develop the model into a clinical decision support system (CDSS) for convenient use, and further compare the outcome of MIPD and traditional dosage.
Methods: Tacrolimus data were retrospectively collected from the records of 100 patients who received first heart transplantation. Tacrolimus PPK model was established by NONMEM. Information technology and Bayesian method are used to establish CDSS. The C0 and obtained rate for desired C0 of tacrolimus were compared between MIPD and empiric dosing.
Results: A one-compartment model with first order absorption and elimination was used to describe the disposition of tacrolimus in whole blood. Tacrolimus apparent clearance was significantly reduced in CYP3A5 nonexpressers (CYP3A5*3/*3), concomitant with azole antifungal drugs and Wuzhi capsule (WZ). Recommended dose regimens were obtained by simulations based on the established model. Based on MIPD, the percentage of achieved the therapeutic target is higher, the time to reach the target concentration is faster, and fewer dose adjustments are required.
Conclusions: MIPD for tacrolimus in heart transplantation is superior to the clinic-based dosage to achieve the therapeutic target.
Keywords: Model-Informed Precision Dosing, Tacrolimus, Heart transplantation

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P504

Association of TLR4 rs7873784 polymorphism with Tuberculosis susceptibility in healthy Thai population

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Biography:

Ms.Thanaporn Chaturachumroenchai is a third-year medical student at the Faculty of Medicine, Srinakharinwirot University, Thailand. She has researched under a professor in university since 1st-year. Beyond academia, she has experience in conducting labs and knowledge about medical science. She was used to do an oral presentation in high school because she studied in science project class.

Background: Tuberculosis (TB) is an infectious disease transmitted through airborne, causing it highly contagious. Toll-like receptor 4 (TLR4) plays a crucial role in the pathogen destruction, including Mycobacterium tuberculosis.
Aims: This study aims to determine genotyping frequency of the TLR4 gene rs7873784 polymorphism and its impact on TB susceptibility in the healthy Thai population.
Methods: A total of 43 Thai TB patients and 54 healthy Thai control subjects were included in this study. After obtaining informed consent, 3 ml of whole blood was collected in EDTA tubes. Genomic DNA was then extracted by PureLink™ Genomic DNA Mini Kit and analyzed using QuantStudio™ 3 Real-Time PCR system. The association between TLR4 gene rs7873784 polymorphism and TB susceptibility was assessed by logistic regression analysis.
Results: The allele frequencies in TB group were approximately 85% for G and 15% for C, while in control group, they were approximately 91% for G and 9% for C. The CC genotype was associated with an approximately threefold increased risk of TB susceptibility compared to the GG genotype (wild-type carriers), although this finding was not statistically significant (p = 0.407).
Conclusions: The genetic variation of TLR4 rs7873784 may influence TB susceptibility in Thai population. Although the association was not statistically significant, the findings suggest a clinically potential link to increased TB risk in the Thai population. Future studies with larger sample sizes are warranted to confirm these finding and provide more definite conclusions.
Key words: Tuberculosis, Toll-like receptor 4, gene polymorphism, Thai population, SNPs rs7873784

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P505

Influence of ABCB1 rs1045642 Gene Polymorphism on Prognosis of Platinum-based Chemotherapy

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Biography:
Associate Chief Pharmacist at the First Affiliated Hospital of USTC (Anhui Provincial Hospital). Leading or participating in research projects related to Anhui Provincial Higher Education Quality Engineering, National Natural Science Foundation of China General Projects, and Anhui Provincial Major Science and Technology Special Projects. Published 10 SCI and Peking University core papers as the first author, holds one patent and one software copyright as the primary inventor, and has contributed to the formulation of 2 expert consensus documents and 1 local standard.
Won the second prize in the National Final of the 'National Oncology Pharmacy Service Case Competition,' the Silver Award in the '7th China Hospital Management Award - Pharmacy Management Group,' and the third place in the National Final of the '6th Pharmacy Service Innovation Competition,' among other awards.

Background: Lung cancer is the leading cause of cancer-related deaths in China, with 19% of deaths, totaling 3.62 million cases. Non-small cell lung cancer (NSCLC) accounts for 85% of cases. ABCB1 gene polymorphism (rs1045642) may influence chemotherapy efficacy in NSCLC, particularly with platinum-based treatments, yet studies are limited, especially in Chinese populations.
Objective: To explore the correlation between the ABCB1 rs1045642 genotype and the progression-free survival of patients with advanced non-small cell lung cancer (NSCLC) receiving platinum-containing treatment regimens.
Methods: Clinical data such as age, gender, tumor metastasis, etc. of newly - diagnosed patients with stage IIIB - IV lung cancer admitted to the First Affiliated Hospital of the University of Science and Technology of China (Anhui Provincial Hospital) between August 2020 and April 2022 were collected and the patients were followed up. The genotyping of ABCB1 rs1045642 polymorphism was performed using a fluorescence-based detection method. Kaplan-Meier survival analysis and COX proportional-hazards regression model were employed to analyze the influencing factors of prognosis.
Results: Patients with the CC genotype of ABCB1 rs1045642 (n=34) exhibited a significantly better median progression-free survival (PFS) compared to those with the CT/TT genotype (n=49) (P=0.032). The ABCB1 rs1045642 genotype was identified as an independent factor affecting PFS in lung cancer patients treated with platinum-based regimens (P=0.018).
Conclusion: The ABCB1 rs1045642 genotype can be used to predict the efficacy of platinum-containing treatment regimens in patients with stage IIIB-IV lung cancer, providing a reference for the personalized administration of platinum-based drugs.
Key words: Non-small cell lung cancer; ABCB1 rs1045642; Platinum resistance

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P506

NUDT15 polymorphism increases the risk of early neutropenia due to valganciclovir

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Biography:

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Dr Yurie Katsube is a Program-Specific Assistant Professor. Their research focuses on clinical pharmacology, drug metabolism, pharmacogenomics. After gaining five years of experience as a pharmacist in Kyushu university hospital, she transitioned into a research-focused role, specializing in pharmacokinetics and drug metabolism.

Background: Cytomegalovirus (CMV) disease is a life-threatening complication after lung transplantation. Valganciclovir (VGCV) is safe and highly effective in prophylaxis of CMV infection. However, early cessation by VGCV-induced myelosuppression leads to serious CMV disease. Recently, Nudix hydrolase (NUDT) 15 was identified as a key metabolic enzyme in the active metabolite of VGCV. Although genetic polymorphisms in NUDT15 are prevalent in East Asians, the impact of these polymorphisms on VGCV-induced myelosuppression remains to be unclear.
Aims: This study aims to assess the effect of NUDT15 single nucleotide polymorphisms on the incidence of neutropenia and valganciclovir cessation in lung transplant recipients.
Methods: We recruited 28 lung transplant patients with VGCV prophylaxis therapy. Genotyping in exon1–3 of NUDT15 was performed by Sanger sequencing. The cumulative incidence of neutropenia (neutrophil count < 1,500 /mm³) and neutropenia-related cessation within the one-year follow-up period were assessed in the wild-type group and the reduced-function group, which consisted of patients with NUDT15 single nucleotide polymorphisms.
Results: Of 28 patients, 9 (32.1%) were identified as carrying NUDT15 reduced-function polymorphisms. The nadir of the neutrophil count within the one-month observation period following treatment initiation was significantly lower in the reduced-function group (median, WT 4.01/mm³; reduced-function group 2.60/mm³). In the analysis of covariance using GCV trough levels as a covariate, the NUDT15 polymorphism was found to have a significant effect on the nadir of the neutrophil count ($p<0.05$).
Conclusions: NUDT15 polymorphisms increase the risk of neutropenia due to VGCV prophylaxis in lung transplant recipients.
Keywords: NUDT15, valganciclovir, lung transplantation

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P507

Genetic Variants and Oxypurinol Levels: Investigating Allopurinol Response in Gout

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Biography:

Dr. Shamin Mohd Saffian is a senior lecturer at Universiti Kebangsaan Malaysia. His research focuses on precision dosing, therapeutic drug monitoring (TDM), dose optimization and population PKPD modeling with interest in the areas of anticoagulants, antiinfectives and oncology.

Introduction: Allopurinol and its active metabolite oxypurinol is the primary treatment for gout. ATP-binding cassette subfamily G member 2 (ABCG2) functions as an efflux transporter for uric acid excretion, while human aldehyde oxidase 1 (hAOX1) is a uric acid-metabolizing enzyme sharing homology with xanthine oxidase. Genetic polymorphisms in ABCG2 rs2231142 and hAOX1 rs3731722 have been linked to variability in allopurinol response.
Aims: To investigate the relationship between ABCG2 rs2231142 and hAOX1 rs3731722 polymorphisms and plasma oxypurinol concentration to explain variability in allopurinol treatment response
Method: This cross-sectional study examined 37 gout patients from Hospital Canselor Tuanku Mukhriz. Plasma oxypurinol levels were analyzed using high-performance liquid chromatography with ultraviolet detection, while genotyping was performed through PCR-Sanger sequencing.
Results: All participants (86.5% male, mean age 58.0±14.2 years) carried the homozygous TT variant of ABCG2 rs2231142, while for hAOX1 rs3731722, 81.1% had the wild-type allele and 18.9% carried the heterozygous AG variant. No significant association was observed between hAOX1 rs3731722 and oxypurinol concentration in both unadjusted and adjusted models. However, allopurinol dose and creatinine clearance significantly influenced oxypurinol concentration ($p=0.001$, $p=0.013$). Notably, hAOX1 rs3731722 showed significant association with daily allopurinol dose ($p<0.001$).
Conclusion: While hAOX1 rs3731722 had no direct impact on oxypurinol concentration, its significant association with allopurinol dosing suggests potential influence on treatment requirements. The homogeneity of ABCG2 rs2231142 in our population prevented assessment of its impact on oxypurinol levels limiting our ability to evaluate its role in allopurinol therapy effectiveness
Keywords: ABCG2, hAOX1, allopurinol, oxypurinol, genetic polymorphism

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P508

Association between TLR-4 genetic variation and Tuberculosis susceptibility in Thai Diabetic patients

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Biography:

Mr. Pornpawit Phuangruankaew is a Third-year medical student at Srinakharinwirot University, Thailand. He graduated from Kamnoetvidya Science Academy, which is one of the most prestigious high schools for science, mathematics, and research. He had experience with Lab and Data science since high school. He was excellent at mathematics and received many awards for mathematics competitions both at national and international levels. He was elected as the president of the class of 2024 and selected to be the head of faculty activities. His special skill is being an MC with outstanding characteristics. Now he is preparing for clinical years to expose patients in the hospital.

Background: Tuberculosis remains a high-burden disease in Thailand, with immunocompromised individuals, particularly those with diabetes mellitus, being at increased risk. Previous studies have suggested that the TLR4 variants rs11536889 and rs7873784 may be associated with TB susceptibility in diabetic patients. However, the available research is limited and inconclusive.
Aims: To determine the association between the genotype frequencies of rs11536889 and rs7873784 in the TLR4 gene and the risk of developing TB in Thai diabetic patients.
Methods: Diabetic patients were divided into two groups: Group 1 (without TB), and Group 2 (with TB). Blood samples were collected and processed using PureLink™ Genomic DNA Mini Kit for DNA extraction. Genotyping was performed by RT-PCR, and the associations were analyzed using logistic regression.
Results: Although statistical significance was not observed, carriers of CC genotype for rs11536889 had a 1.6-fold higher risk compared to wild-type carriers (p=0.633). For rs7873784, the CC genotype was absent in the TB group, so the association could not be analyzed. Meanwhile, the CG genotype was associated with decreased risk, but this finding was not statistically significant in either SNP.

Conclusions: Although the results were not statistically significant, they suggest a potential protective effect of the CC genotype for rs11536889. Further studies with larger sample sizes are needed to establish a reliable association and support the development of genetic screening measures for early intervention in diabetic patients in Thailand.
Key Words: TLR4, Diabetes mellitus, Tuberculosis, SNPs, Thai population

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P509

Effect of recombinant CYP3A4 variants and interaction on imatinib metabolism in vitro

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Biography:

He is a chief pharmacist, deputy director of the Medical Department, master's supervisor at the First Affiliated Hospital of Wenzhou Medical University, a key figure in the clinical Chinese pharmacy discipline under the "Twelfth Five-Year" plan of the State Administration of Traditional Chinese Medicine, and the head of the national key research and development program project sub-center. He has long been dedicated to CYP450 research, particularly in the fields of clinical pharmacology, pharmacogenetics, and pharmacokinetics, and has conducted TDM for multiple drugs. He has published over 30 SCI papers as the first author and corresponding author. He has hosted several research projects, including those funded by the National Natural Science Foundation, the National Key Research and Development Program Sub-center Project, and the Zhejiang Provincial Natural Science Foundation, and holds 2 authorized patents. He has received the Chinese Medical Science and Technology Award and the Beijing Science and Technology Award.

Background: CYP3A4 is an important drug-metabolizing enzyme, and its genetic variants may affect drug metabolism and drug-drug interactions. Imatinib is a commonly used anti-cancer drug, and CYP3A4 polymorphisms may influence its metabolism.
Aims: To investigate the catalytic activity of 26 CYP3A4 variants on imatinib metabolism and their drug interactions.
Methods: Ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS) was used to measure the concentration of imatinib's metabolite N-desmethyl imatinib. The study was conducted using an appropriate incubation system under constant temperature water to evaluate the impacts of CYP3A4 genetic polymorphisms and drug interactions on imatinib metabolism.
Results: Compared to CYP3A4.1, the intrinsic clearance (CLint) values of the 26 variants varied significantly, ranging from 2.34% to 120.57%. CYP3A4.14 showed an increase in CLint compared to CYP3A4.1, while the remaining 24 variants exhibited decreased catalytic activity for imatinib metabolism. Additionally, the metabolism of imatinib was inhibited to varying degrees by ketoconazole, itraconazole, and fluconazole in both CYP3A4.1 and CYP3A4.18. Most CYP3A4 variants showed similar enzyme activity patterns with different substrates, imatinib and cabozantinib, except for six variants (CYP3A4.3, .4, .10, .15, .29, and .31).
Conclusions: This study is the first to investigate the effects of 26 CYP3A4 variants on imatinib metabolism. The findings will contribute to the clinical evaluation of imatinib and assist in the personalization of therapy in clinical practice.
Key Words: Imatinib, CYP3A4 variants, metabolism , cabozantinib, microsomes

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P510

Individualising insulin bolus dosing in children diagnosed with type 1 diabetes mellitus

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Biography:

Hesham Al-Sallami is an associate professor of clinical pharmacy practice. He holds a PhD (University of Otago) in quantitative clinical pharmacology and pharmacometrics. Hesham's research interests include drug dose individualisation in special populations, with a focus on paediatrics and in obesity.

Background: Insulin dose requirements vary among patients with type 1 diabetes mellitus (T1DM). Bolus doses are typically determined by a patient's insulin to carbohydrate ratio (ICR), for meal-time dosing, and the correction factor (CF), for elevated blood-glucose correction. Accurately determining a patient's ICR and CF values often requires several days of iterative dose adjustments, guided by blood glucose monitoring and carbohydrate counting.
Aims: To develop and evaluate predictive models of ICR and CF to improve insulin dosing strategies in newly diagnosed paediatric T1DM patients.
Methods: A retrospective analysis of clinical, laboratory, and insulin dosing data was conducted on 70 children (≤ 18 years old) hospitalised for newly diagnosed T1DM. Linear regression models were developed to predict ICR and CF based on clinical characteristics, with model accuracy assessed using mean error (bias) and root mean squared error (precision).
Results: Based on the developed ICR and CF prediction models, for patients < 6 years old, total daily dose of insulin administered on first day (TDD_first) was the only significant predictor for ICR and CF ($p < 0.05$).
For patients ≥ 6 years old, patient's TDD_first and age were found to be significant predictors for both ICR and CF ($p < 0.05$).
Conclusion: Accounting for a patient's age and initial insulin total daily dose allows for better estimation of true (i.e. asymptotic) ICR and CF values. This can potentially provide better glycaemic control sooner during hospital stay. These findings suggest a data-driven approach to personalising insulin therapy in newly diagnosed paediatric T1DM patients.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

P511

Lessons in Real-Time Communication of Potentially Erroneous Data in MIPD Software

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Biography:

Dr. Jordan Brooks, a Senior Pharmacometrician and Data Scientist at InsightRX, focuses on improving the predictive ability of precision dosing models and enhancing their usability for bedside clinicians. His work originated in pediatric hematopoietic cell transplantation with conditioning agents and immunosuppression, but now spans patients of all ages and various drug classes requiring precise dosing.

Background: Real-time communication of potential data errors in Model-Informed Precision Dosing (MIPD) software is crucial for clinical decision making, but it presents challenges. Flagging questionable data against a popPK model's residual error terms introduces biases, as some models have larger magnitude ("lenient") and others smaller magnitude ("stringent"). This study compares data flagging methods used in the InsightRX Nova platform.

Aim: Evaluate the impact of using drug-module-wide error magnitude versus model-specific error magnitude on data flagging and model selection bias.

Methods: We explored mechanisms for flagging questionable data based on residuals (IWRES), comparing model-specific residual error with a constant residual error magnitude across all popPK models for a given drug. This was conducted in both adult vancomycin (N = 55,646) and pediatric busulfan (N = 650) patients from the InsightRX Nova platform where data are flagged as “good”, “intermediate”, or “poor” fit in relation to their calculated residual.

Results: Using model-specific residual error magnitude for flagging questionable observations may lead to user selection bias towards more lenient models, even if those models are less accurate for a patient. Switching to module-wide residual error magnitude reduced bias and provided more consistent flagging across stringent and lenient models. In adult vancomycin data, "poor" flags decreased by 16.9%, and "intermediate" flags increased by 14.1%. In pediatric busulfan data, both "poor" and "intermediate" flagging decreased by 6.7% and 8.5%, respectively.

Conclusions: For MIPD solutions utilizing multiple published models, module-wide residual calculation improves the consistency of data flagging and reduces bias towards lenient models.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P512

A new scoring methodology for implementation of POPPK models for TDM

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Biography:
Pharmacologist at the University Hospital of Rennes. I specialise in therapeutic drug monitoring of anti-infective and immunosuppressive drugs, as well as population pharmacokinetics.

Background: Population pharmacokinetics (popPK) models are increasingly used in therapeutic drug monitoring. In some therapeutic areas, many models are available. Thus, selecting the most relevant model can be challenging, especially when no external evaluation dataset is available.
Aims: The objective was to develop a systematic scoring methodology to identify the most relevant popPK models and to showcase its use with tacrolimus models.
Methods: Mandatory inclusion/exclusion criteria were defined to exclude less relevant models and to focus on original models, reproducibility, and full PK profiles based-models. A generic scoring system based on literature guidelines, good practices in pharmacokinetic modeling and clinical relevance was developed. Then, a systematic review of the literature was conducted to identify candidate popPK models to be scored.
Results: Twenty-three criteria were selected. Dataset (patients/sample size), design (prospective, multicentric, analytical assay, data availability), methodology (methods/results of evaluation) and estimation of parameters (RSE%, residual error, shrinkage) had a score assigned based on weighted criteria. Thirty-two (of 180) models were included in the final scoring process. Median score was 25/61 (range: 7-41), mean±SD was 24.65±7.77. Only 7/32 models scored above 30. Shortcomings included limited sampling, lack of external evaluation, missing covariates of interest, and limited methodological details.
Conclusions: This scoring system identifies best popPK models and is designed to be adaptable across different use-cases. This work also highlighted the heterogeneity and insufficiencies of reporting in popPK articles. Future work involves comparing these results to a statistical external evaluation to further validate the methodology.
Keyword: pharmacokinetics, external evaluation, scoring methodology.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P513

Optimizing doxorubicin dosing in Asian patients with ABCB1*13 polymorphisms

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Biography:
Dr. Janice Goh graduated from NUS Pharmacy and is a registered pharmacist with the Singapore Pharmacy Council. She recently completed her PhD in the lab of Professor Rada Savic at the University of California, San Francisco (UCSF) School of Pharmacy. She joined the Research Data Integration group, Bioinformatics Institute as a Senior Scientist in Aug 2023. Her work focuses on utilizing pharmacokinetic and pharmacodynamic modeling and simulation tools to evaluate the impact of pharmacogenomics on drug disposition in real world settings.

Background: Doxorubicin is a narrow therapeutic index chemotherapeutic. ABCB1 is a major clearance pathway, making doxorubicin susceptible to variations in clearance due to pharmacogenomic (PGx) polymorphisms. However, pharmacogenomic clinical trials are resource intensive, making pharmacogenomic guided dose optimization difficult. Pharmacokinetic (PK) modelling and simulation tools help us evaluate drug-gene interaction (DGI) impact, and suggest optimized doses specific for Asian populations, saving resources.
Aims: We developed a PK model to evaluate doxorubicin-ABCB1 DGI, and suggest an optimized dose for ABCB1 polymorphisms.
Methods: Doxorubicin levels was simulated by merging information from a population PK (PPK) model and a noncompartmental analysis (NCA) pharmacogenomic PK study (NCA-informed PPK) to determine the impact of ABCB1*13 on drug exposure. 1000 simulations were run using Asian breast cancer demographics at a single intravenous dose of 60mg/m2.
Results: The NCA-informed PPK model was able to describe both wild type and ABCB1*13 changes in drug exposure per the NCA study. ABCB1*13 alone increased overall drug exposure (AUC) by 1.70 fold (1.38 – 2.03 fold, 95% confidence interval (CI)) compared to wild type ABCB1. Age > 60y/o with ABCB1*13 further increased AUC, with a 1.92 fold (1.58-2.30 fold, 95% CI) putting patients 13 at high risk of toxicity. Alternative dosing simulations suggest 35mg/m2 for people with ABCB1*13 polymorphisms.
Conclusions: The NCA-informed PPK model has helped us evaluate the impact of ABCB1*13 polymorphism on doxorubicin drug exposure and suggest new doses that might help patients with this polymorphism still benefit from the drug with lower risk of toxicity.
Keywords: Pharmacokinetics, pharmacogenomics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P514

Population pharmacokinetics of tacrolimus in renal transplant recipients combined with posaconazole

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Biography:
Dr Nan Hu, Deputy Director of the Pharmacy Department, the third affiliated hospital of Soochow University.

Background: Posaconazole can prevent and treat invasive fungal infections, but the combination will increase the blood concentration of tacrolimus, requiring dose adjustments to avoid side effects.
Aims: This study aimed to establish a PopPK model of tacrolimus in renal transplant patients combined with posaconazole.
Methods: We conducted a retrospective study of hospitalized patients who received posaconazole treatment or prevention of invasive fungal infection after renal transplantation in our hospital from January 2018 to December 2024, and performed pharmacokinetic analysis and Monte Carlo simulation.
Results: A total of 24 patients were included, and a one-compartment model of first-order absorption and elimination was established using the collected 202 blood samples to describe the pharmacokinetic characteristics of tacrolimus. The final model population typical values of tacrolimus apparent distribution volume (V/F) and apparent oral clearance rate (CL/F) were 957 L and 29.1 L/h, respectively. The key covariates in the final model included posaconazole combination time, serum creatinine, patient age, and CYP3A5 genotype. Monte Carlo simulations suggested initial tacrolimus doses of 9.5 mg for CYP3A5*1 carriers (*1/*1, *1/*3) and 8 mg for *3/*3 homozygotes before posaconazole initiation. During coadministration, doses required immediate reductions (21% for *1 carriers vs 31.25% for *3/*3), followed by daily 1 mg decreases for 2-4 days to maintain therapeutic levels (8-15 ng/mL).
Conclusions: A PopPK model of tacrolimus in renal transplant patients with posaconazole was developed and model-devised dosage regimens with tacrolimus concentrations provide a practical strategy for achieving the therapeutic range.
Keywords: tacrolimus; posaconazole; renal transplantation; PopPK; Monte Carlo simulations

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P515

Incorporating Metabolic Transformation into Pharmacokinetic Models for Clozapine to Improve Dosage Prediction.

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Biography:

Prof David Joyce is a clinical pharmacologist with interests in understanding sources of variability in drug response. The output of a busy drug monitoring laboratory and enthusiastic collaborators provide the opportunity and basis for population pharmacokinetic studies aimed at extending the value of therapeutic drug monitoring. The work presented here focuses on clozapine, an efficacious but commonly toxic psychotropic drug that is reserved for resistant schizophrenia.

Background: Clozapine ameliorates severe schizophrenia but with high risk of toxicity. The relationship between drug dose and blood concentration of clozapine varies appreciably over time within individuals. Pharmacokinetic models have had limited success in countering variability over time. A model that incorporated sex, smoking and fluvoxamine treatment showed clinically useful capacity to predict dosage requirements in the same patients over the ensuing 6 months, but not later than that. Norclozapine is measured as part of clozapine TDM because it shares some activities with clozapine. The ratio of norclozapine to clozapine is therefore an index of metabolic transformation.

Aims: We explored whether incorporating the ratio of norclozapine to clozapine serum concentrations into pharmacokinetic models improved model fitting and thus offered the prospect of a model that better predicted future dose requirements.

Methods: Norclozapine/clozapine ratio was introduced into an existing model that incorporated sex, smoking and fluvoxamine treatment. Improvements in model fitting were assessed by objective function values, goodness of fit plots and visual predictive checks.

Results: Adding norclozapine/clozapine ratio to the existing model significantly improved fitting. Sex, smoking and co-treatment with fluvoxamine remained significantly influential. Models incorporating norclozapine/clozapine ratio were then tested for clinical utility in extending its predictive validity beyond 6 months.

Conclusions: Models incorporating the norclozapine/clozapine ratio model clozapine pharmacokinetics more closely and offer prospects for better prediction of doses needed to meet therapeutic target concentrations later in treatment.

Key words: norclozapine/clozapine ratio, population pharmacokinetics, dosage prediction.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P516

Propofol brain concentration during intraoperative awakening in awake craniotomy

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Biography:
Kyoto University Hospital, Kyoto (April 2012 - present)
Education: Bachelor of Pharmacy, Kyoto Pharmaceutical University, Kyoto (2012)

Background: During awake craniotomy, patients are awakened from anesthesia intraoperatively to allow for brain mapping and monitoring of brain functions. Therefore, individualized regulation of effect-site propofol concentration is crucial. However, there is significant inter-individual variability in the time requiring for intraoperative awakening.
Aims: This study aimed to establish a new pharmacokinetic model to describe plasma and brain propofol concentrations and to analyze the relationship between predicted concentrations and delayed intraoperative awakening.
Methods: Propofol concentrations in plasma and homogenized brain at 0, 5, 15, 25, and 75 min after cessation of administration to induce intraoperative awakening were quantified using HPLC with a fluorescence detector. Population pharmacokinetic modeling was conducted using NONMEM, based on the concentrations. Bispectral index (BIS), reflecting the depth of sedation, was extracted from surgical records. Delayed awakening was defined based on BIS values. Wilcoxon test was used to compare the predicted concentrations in patients with or without delayed awakening.
Results: A three-compartment model with effect-compartment and brain/plasma partition coefficient effectively described the concentrations. Delayed awakening was occured in 6 of 57 patients. The median predicted brain concentration at BIS>60 in the delayed-awakening patients was 1.03 μg/mL (range 0.16–4.41), which was significantly lower than that in the non-delayed patients (2.47 μg/mL, 0.18–7.79, $P<0.05$).
Conclusions: Given the concentrations at the time of awakening was sufficiently low in patients with delayed awakening, it is suggested that the delay is more likely due to pharmacodynamic factors rather than delayed drug elimination from pharmacokinetic reasons.
Key Words: Propofol, Brain concentration, Population pharmacokinetic model

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P517

Population Pharmacokinetics of Cycloserine: A Systematic Review

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Biography:
Li Jinmeng, a clinical pharmacist at Zhejiang Integrated Traditional Chinese and Western Medicine Hospital, has been actively engaged in the treatment and prevention of tuberculosis in recent years. Together with her team members, she has developed plasma concentration detection methods for 30 drugs, including 15 anti-tuberculosis drugs, 12 anti-infective drugs, and 3 anti-psychotic drugs. These methods have been successfully applied in clinical therapeutic drug monitoring (TDM), and significantly improved clinical treatment outcomes of these drugs. In addition, she specializes in methods related to population pharmacokinetic and pharmacodynamic studies in quantitative pharmacology. The long-term goal is to improve the effectiveness of anti-TB drugs and control the progression of MDR-TB based on therapeutic drug monitoring and quantitative pharmacology. Her current research focuses on optimizing the efficacy of second-line anti-TB drugs and reducing the occurrence of adverse reactions and drug resistance.

Background: Cycloserine (CS) plays a key role in the treatment of multi-drug resistant tuberculosis. However, limited pharmacokinetic (PK) data on cycloserine in TB patients and individual differences in drug use have led to unsatisfactory therapeutic outcomes and uncontrolled adverse events.
Aims: To review the published PK models of CS and identify important covariates affecting CS PK differences by comparing the published CS population pharmacokinetic models, so as to provide guidance for clinical drug use.
Methods: A systematic search was made of PubMed and Web of Science databases from establishment to December 2024 on the pharmacokinetics of CS populations. The PK characteristics and significant covariates included in the study were systematically summarized.
Results: Six studies that met the criteria were included in our review. These studies were all conducted in adults, and the apparent clearance and volume of distribution of CS to homeostasis ranged from 0.75 to 3.51 L/h and 4.86 to 34.56 L, respectively. Weight and creatinine clearance were important covariates affecting clearance, with CL/F estimates (2.00 L/h) about twice as high in healthy subjects as in TB patients (1.03 L/h) and smoking increasing CS clearance by 41%.
Conclusions: This article reviews the covariates that may be responsible for individual differences among patients taking CS, which is helpful to provide clinical recommendations for doctors. However, further research is needed to verify the effects of these covariates and to explore other possible covariates.
Keywords: cycloserine, multidrug-resistant tuberculosis, population pharmacokinetics, nonlinear mixed-effect modeling

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P518

Understanding inter-individual variability of lurasidone pharmacokinetics: a population model in Chinese patients

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Biography:

Meihua Lin, Deputy Chief Clinical Pharmacist, graduated from Zhejiang University and served as a Visiting Scholar at Rutgers University, USA. Member of the Youth Branch, Therapeutic Drug Monitoring Research Committee, Chinese Pharmacological Society. Member of the Youth Branch, Clinical Pharmacy Committee, Zhejiang Pharmaceutical Association, Youth Editorial Board Member of Electronic Journal of Tumor Metabolism and Nutrition. Research Focus: Pharmacogenomics/TDM-guided rational clinical drug use, and clinical research on novel antitumor drugs. Research Projects: Presided over 1 project funded by the National Natural Science Foundation of China for Young Scholars. Participated in the National Major New Drug Discovery and Development Program during the 13th Five-Year Plan, and other National Natural Science Foundation projects. Publications: Published over 40 academic papers, including 7 SCI-indexed articles as first/corresponding author. Contributed to the translation of Pharmacology (7th Edition) and Poisoning and Drug Overdose (7th Edition).

Background: Lurasidone is an effective treatment for bipolar disorder (BD), but its pharmacokinetics exhibit significant variability, leading to inconsistent therapeutic efficacy. Understanding the sources of this variability is crucial for optimizing treatment.
Aims: This study aimed to develop a population pharmacokinetic (PPK) model to investigate the impact of physiological and genetic factors on inter-individual variability of lurasidone.
Methods: BD patients who were dispensed lurasidone and underwent therapeutic drug monitoring were included. Clinical data, including demographics, genetic information (e.g., CYP3A4*1G, HTR1A), drug concentrations and medication information, were collected. A PPK model was developed using NONMEM software.
Results: A total of 241 plasma concentrations from 133 patients were adopted for PPK model development. A one-compartment model with first-order kinetics best described lurasidone's pharmacokinetics. CYP3A4*1G genotype and height significantly influenced apparent clearance (CL/F) ($P < 0.01$), reducing variability from 40.5% to 36.7%. CL/F in CYP3A4*1G CC carriers (329 L/h) was 14.3% lower than that in TC carriers (384 L/h) and 25.4% lower than in TT carriers (441 L/h). However, HTR1A genotype was not notably associated with lurasidone clearance in our study.
Conclusions: Lurasidone PPK model in BD patients was established for the first time, hightlighting the effect of CYP3A4*1G genotype on pharmacokinetic variablility of lurasidone. This finding emphasizes the need for individualized dosing of lurasidone to optimize efficacy in BD treatment.
Keywords: lurasidone, cytochrome P450 3A4, population pharmacokinetics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P519

Comparison of 1-point and 2-point sampling for vancomycin Bayesian AUC estimation

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Biography:

EDUCATION

- *2023-Present: Ph.D. in Pharmacy, Kobe Gakuin University, Hyogo*
- *2015-2021: Bachelor of Pharmacy, Kobe Gakuin University, Hyogo*

WORK EXPERIENCE

- *April 2022-Present: Clinical Pharmacist, Kobe City Medical Center General Hospital*
- *April 2021-May 2022: Pharmacy Residency, Kobe City Medical Center General Hospital*

Background: Vancomycin (VCM) therapeutic drug monitoring (TDM) has undergone a paradigm shift from trough-guided to AUC-guided TDM. Due to the clinical complexity of AUC measurement, Bayesian AUC estimation based on peak and trough sampling has been recommended in clinical practice. However, the actual impact of additional peak sampling on AUC estimation, compared to conventional trough sampling, remains unclear.
Aims: This study aimed to compare Bayesian AUC estimations based on trough levels with those based on both peak and trough levels in clinical practice.
Methods: Patients who had both peak and trough levels measured as part of routine TDM practices were retrospectively enrolled. Bayesian AUC estimations using both peak and trough levels (AUCpt) and trough levels only (AUCt) were performed with a published population pharmacokinetic model. The correlation between AUCt and AUCpt was calculated, and the AUCt ratio to AUCpt was assessed in relation to patient characteristics, dosing regimen, and the TDM timing.
Results: A total of 208 patients were included. A strong correlation was observed between AUCpt and AUCt, and AUCt ratios ranged from 0.8 to 1.2. The AUCt ratio tended to increase with early TDM timing (<4 days), whereas no clear trend was observed in relation to patient characteristics or dosing regimen.
Conclusions: Bayesian AUC estimations based on trough levels demonstrated comparable performance to those based on both peak and trough levels. The clinical benefits of additional peak sampling may be limited, particularly under steady-state conditions.
Keywords: vancomycin, Bayesian estimation, TDM

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P520

Stochastic Differential Equations for Modeling Nonparametric Inter-Occasion Variability (IOV) in Pharmacokinetics (PK)

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Biography:

Dr. Neely is a Professor of Pediatrics and Clinical Scholar in the Department of Pediatrics at the Keck School of Medicine of the University of Southern California. He is a Board-certified pediatric infectious disease specialist physician with more than 20 years of experience in patient care, research, and mentoring of over 50 undergraduates, medical students, residents, fellows, PhD students, post-docs, and visiting scholars in clinical pharmacology and pharmacometrics. He serves as the Chief of Infectious Diseases at the Children's Hospital of Los Angeles (CHLA) and the director of the CHLA Laboratory of Applied Pharmacokinetics and Bioinformatics. Dr. Neely's lab created and maintains the Pmetrics population modeling and simulation package for R and the BestDose software to optimize individual patient dosing through applied pharmacometric and machine learning techniques. His lab is increasingly involved in the use of artificial intelligence to enhance the use of drug therapies. He has recently expanded his lab to include hollow fiber capabilities, focusing on optimizing treatment of serious infections in pediatric patients such as Mycobacterium abscessus, Staphylococcus aureus, cytomegalovirus, and resistant Gram-Negative bacteria. His research has been continually funded by the NIH since 2000, with additional funding from FDA and private foundations. He lectures and conducts pharmacometric workshops internationally and has published almost 200 peer-reviewed publications and ten book chapters.

Background: PK IOV is typically modeled as a stepwise random parameter based on sampling occasions using Ordinary Differential Equation (ODE) solvers. In contrast, SDEs allow more physiologic, continuously time-dependent PK parameters. However, due to computational complexity, SDEs are rarely used in parametric popPK modeling and have not been implemented in a nonparametric framework.

Aims: Develop a practical nonparametric SDE popPK solver.

Methods

We implemented a custom SDE solver with particle filtering in Pmetrics. From this, we simulated 4 PK parameter datasets for a 1-compartment IV model (Ke, V) with/without inter-individual variability (IIV) and/or IOV. All datasets comprised 100 subjects. We compared SDE fits to true simulated values.

Results:

#	CONDITIONS	TRUE			FITTED		
		Mean	SD	IOV	Mean	SD	IOV
1	Ke +IIV, -IOV	0.96	0.5	0%	1.16	0.47	0
	V fixed						
2	Ke +IIV, +IOV	0.96	0.5	104%	1.07	0.51	63%
	V fixed						
3	Ke +IIV, -IOV	0.96	0.5	0%	1.08	0.50	0
	V +IIV, -IOV	1.04	0.2	0%	1.05	0.20	0
4	Ke +IIV, +IOV	0.96	0.5	104%	0.97	0.56	108%
	V +IIV, +IOV	1.04	0.2	96%	1.07	0.21	85%

As further validation for #1 (no IOV), with ODE we found mean (SD) Ke of 1.23 (0.5196) and the same likelihood of 920.76 that we obtained for SDE.

Conclusions: SDEs with particle filtering provide a robust framework for modeling nonparametric IOV in pharmacokinetics. This approach accurately estimates parameter values in the presence of continuous IOV and may enhance individualized dosing strategies.

Keywords: pharmacokinetics, nonparametric methods, inter-occasion variability, parameter evolution

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P521

Evaluation of apixaban dose reduction algorithm based on creatinine clearance levels

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Biography:
Yuko Shimamoto, PhD is a senior clinical pharmacist at the National Cerebral and Cardiovascular Center in Osaka, Japan. Dr. Shimamoto's research focuses on the clinical pharmacokinetics, pharmacometrics, and precision dosing of antibiotics in special populations. She received her PhD in Medicine from Osaka University with research on the pharmacokinetics and model-informed precision dosing (MIPD) of vancomycin in pediatric patients with congenital heart disease. She has provided over 15 invited presentations at national and international scientific conferences. Dr. Shimamoto received the Best Presentation Awards for 4 times from academic societies including the Japanese Society of Therapeutic Drug Monitoring (JSTDM). She has been a Board-Certified Infection Control Pharmacy Specialist (certified by the Japanese Society of Hospital Pharmacists) since 2009 and an Infectious Disease Chemotherapy Pharmacist (certified by the Japanese Society of Chemotherapy) since 2011. She is a member of board of trustees of JSTDM since 2024.

Background: Dose reduction of apixaban (APX) is recommended for patients who meet at least two of the following three criteria: age ≥ 80 years, body weight (BW) ≤ 60 kg and serum creatinine (Scr) ≥ 1.5 mg/dL. The Scr-based criterion may overestimate renal function in elderly patients with low BW, potentially leading to overdosing.
Aims: This study aimed to compare the Scr criterion with the creatinine clearance (CLcr) criterion for APX dose reduction algorithms.
Methods: Patients who received 2.5 or 5.0 mg BID according to the Scr-based dose reduction algorithm were retrospectively enrolled. APX concentrations were measured by LC-MS/MS, and individual pharmacokinetic parameters were estimated using a Bayesian approach. A dosing simulation at the standard dose (5.0 mg BID) was performed, and the relationship between the simulated trough concentration and Scr levels was assessed. The CLcr-based dose reduction algorithm was simulated, and the number of patients with trough concentrations ≥ 230 ng/L was evaluated.
Results: Of the 84 patients, only 8 met the Scr criterion, and 40 received a reduced dose according to the Scr-based dose reduction algorithm. The simulated trough concentrations at the standard dose correlated poorly with Scr levels but strongly with CLcr, with 45 mL/min suggested as the cutoff value. The CLcr-based dose reduction algorithm decreased the number of patients with trough concentrations ≥ 230 ng/L from 12 to 10.
Conclusions: The CLcr criterion may be superior to the Scr criterion for the APX dose reduction algorithm, with limited impact in this population.
Keywords: Apixaban, Bayesian approach

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P522

A Scoping review of the Paediatric Population Pharmacokinetic Models of Morphine

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Biography:
Michael is a senior Pharmacist in the Paediatric Palliative Care service for the Sydney Children's Hospitals Network. He has substantial experience in Paediatric Intensive Care medicines and is a PhD candidate under the supervision of Assoc. Prof. Sophie Stocker.

Background: Morphine dosing in paediatrics is dependent on imprecise measures of pain and clinician experience. Multiple population pharmacokinetic models have been developed to identify and quantify factors contributing to variability in morphine pharmacokinetics with the aim of guiding dosing decisions.
Aim: To summarise available population pharmacokinetic models of morphine and its metabolites (M3G and M6G) in paediatric patients to describe how morphine exposure changes across paediatric age groups.
Methods:EMBASE and MEDLINE databases were systematically searched from inception to 8th March 2024 for articles containing paediatric population pharmacokinetic models of morphine and its metabolites. Two independent reviewers (MS and NK) screened abstracts, full texts, and extracted data, which was then summarised. The review was conducted according to PRISMA scoping review guidelines.
Results: Overall, 21 paediatric population pharmacokinetic models of morphine were identified, with 12 studies including morphine metabolite (M3G and/or M6G) pharmacokinetics. Neonates and young children (< 6 years) were the most studied age groups (18/21; 86%), while older children (> 6 years) and adolescents were included in only 6/21 (29%) models. Age, post-natal age for neonates, and bodyweight were found to be significant covariates for morphine clearance. Additional covariates relating to body temperature, duration-of-stay, and genetic variation in drug transporters which mediate the uptake of morphine (e.g. OCT1) were also identified.
Conclusion: Several population pharmacokinetic models of morphine and its metabolites in the paediatric population exist, but the influence of organ dysfunction, atypical disease states, including critical illness, and the effect of long-term treatment on morphine pharmacokinetics remains underexplored.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P523

Machine Learning for Identifying Factors of Delayed Methotrexate Elimination in High-Dose Therapy

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Biography:

Dr. Suetsugu earned a Ph.D. from Kyushu University. He is a hospital pharmacist engaged in Therapeutic Drug Monitoring (TDM). With extensive experience and dedication, Dr. Suetsugu has significantly contributed to optimizing pharmacotherapy and improving patient outcomes. His commitment to research and clinical practice has led to various publications and presentations at national and international conferences. Dr. Suetsugu remains passionate about advancing the field of clinical pharmacy and fostering collaborations among healthcare professionals to enhance patient care.

Background: High-dose methotrexate (MTX) therapy is used for the treatment of gliomas, malignant lymphomas, acute lymphoblastic leukemia, and osteosarcoma. Nevertheless, delayed MTX elimination can occur, resulting in prolonged elevated plasma concentrations and severe adverse effects such as bone marrow suppression. The definitive factors contributing to this delay remain unclear.
Aims: This study aims to identify the factors influencing delayed MTX elimination through the application of machine learning techniques.
Methods: A total of 353 patients who received high-dose MTX at Kagoshima University Hospital between January 2015 and March 2021 were analyzed. Delayed elimination was defined as serum MTX levels of ≥0.1 µmol/L at 72 hours post-administration. Machine learning models were applied to analyze laboratory data and concomitant medication usage.
Results: Neural network analysis revealed that delayed elimination was not attributed to a single factor but rather to multiple interacting factors. The predictive accuracy was enhanced when patients with albumin measurements were selected. Moreover, the discontinuation of diuretics and NSAIDs in certain patients was associated with reduced MTX plasma concentrations.
Conclusions: Machine learning-based analysis suggests that early detection of delayed MTX elimination is feasible, which could lead to improved management of high-dose MTX therapy.
Key Words: High-dose methotrexate therapy, Delayed elimination, Machine Learning, Albumin

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P524

Formulation and evaluation of capecitabine embedded self-dissolving microneedle in breast cancer

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Biography:

Ms. Krishnalekha Bandyopadhyay is a PhD Research Scholar at JSS College of Pharmacy, JSS AHER, Mysuru, as of January 2024. She holds on M.Pharm in Pharmacology from JSS College of Pharmacy, Mysuru, and a Bachelor's degree in Pharmacy from Siksha 'O' Anusandhan University, Bhubaneswar, Odisha. She has gained one month of clinical training experience at SUM Hospital in Bhubaneswar, Odisha, and one month of Industrial experience at Santis Pharmaceutical in Sikkim. Her research focuses on Pharmacology, particularly the synthesis of novel molecules, and she is currently working on projects related to CNS disorders. Ms.Krishnalekha Bandyopadhyay has published two research and five review articles, and has participated in eight conferences at esteemed institutions such as JSS SFEC, APTICON, IPSCON, Sarada Vilas College Mysuru, and the Dhara Ayurvedic Conference in Bangalore. She actively contributes to the scientific community through her presentations at academic conferences.

Background and Purpose: The incidence of breast cancer has surged in the past decade, affecting six out of ten households. Despite advancements, a complete cure remains elusive, necessitating novel therapeutic approaches. This study aims to formulate and evaluate the efficacy of self-dissolving microneedles embedded with capecitabine in treating breast cancer using a DMBA-induced Swiss albino mice model.

Experimental Approach: Breast cancer was induced in Swiss albino mice by administering DMBA orally at a dose of 55 mg/kg for three weeks. Following tumor induction, capecitabine was delivered using a microneedle patch for 14 days. Body weight was measured before and after treatment, accompanied by hematology studies. Tumor size and volume were evaluated at the end of the study. Liver function tests, including SGOT and SGPT, were conducted, and histopathological analysis was performed to assess tissue changes.

Key Results: The developed tumor model was consistent and suitable for evaluating therapeutic efficacy. Mice treated with DMBA showed a significant increase in body weight before capecitabine administration. However, body weight decreased when treated with capecitabine embedded microneedles, indicating effective therapeutic activity. Hematology parameters also increased following DMBA administration but normalized post-treatment. Histopathological analysis confirmed the reduction in tumor volume and improved tissue integrity, supporting the anticancer potential of capecitabine-loaded microneedles.

Conclusion: Capecitabine embedded in self-dissolving microneedles demonstrated effective therapeutic activity against DMBA-induced breast cancer in Swiss albino mice, suggesting its potential as a novel and efficient treatment strategy.

Key words: Breast Cancer, Microneedle, DMBA, Capecitabine

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P525

Busulfan limited sampling strategy evaluation in pediatric HSCT patients using Bayesian CDSS

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Biography:
Othmar Korn has enjoyed a 20 year career in computational biology support for life science research and now medical technology. After graduating with a bachelor's degree in Software Engineering (Griffith University) he was introduced to bioinformatics in the mid-2000s while supporting "eResearch" (as it was then known) activities at Griffith University's Eskitis Institute for Cell and Molecular Therapies then later at the Australian Institute for Bioengineering and Nanotechnology at University of Queensland. Othmar specialised in providing computational biology support for multi-omics projects leveraging skills in large data analysis, parallel computing pipelines and software development.
A sideways career change to precision drug dosing in 2020 saw Othmar joining DoseMe LLC, producers of Bayesian dosing platform DoseMeRx (TM), contributing bioinformatics and software development expertise to help improve patient outcomes.

Background: Intravenous busulfan, a key component of pediatric hematopoietic stem cell transplantation (HSCT) conditioning regimens, has a narrow therapeutic range requiring precise dose adjustments. Standard clinical practice involves obtaining five to eight post-infusion plasma concentrations to estimate patient-specific exposure, but frequent sampling increases patient discomfort and venipuncture-related risks.
Aims: To evaluate the feasibility of limited sampling strategies and assess their predictive accuracy with model-informed precision dosing (MIPD) through a retrospective analysis of pediatric busulfan courses from Children's Healthcare of Atlanta.
Methods: MIPD of intravenous busulfan was conducted using exemplar one- and two-compartment population pharmacokinetic (PK) models from the literature within the Bayesian Clinical Decision Support System (CDSS) DoseMeRx™. Individualized model performance was assessed by fitting varying subsets of post-peak plasma concentrations from the first dose and comparing their goodness-of-fit and predictive accuracy against models individualized with all first-dose samples for predicting subsequent concentrations after the second dose.
Results: Most limited sampling strategies demonstrated high predictive accuracy in both one- and two-compartment models, with those incorporating both early and later time points performing best. The optimal strategy included an initial level between three- and four-hours post-infusion, an optional second level between four and six hours, and a final level between five- and nine-hours post-infusion.
Conclusion: This study demonstrates that a Bayesian CDSS, when combined with a limited sampling strategy, can accurately predict future busulfan plasma concentrations in pediatric HSCT patients, achieving comparable performance to fully-informed PK models currently used in clinical practice.
Keywords: Bayesian, limited sampling, busulfan, pediatric, HSCT

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P526

The Application of Aptamer-Based Sensor in Point-of-Care Therapeutic Drug Monitoring

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Biography:

Lixian Li obtained her Ph.D. from Chongqing University in 2013 and has served as a visiting scholar at the University of Waterloo and UBC, Canada. She is currently the Deputy Director of the Clinical Pharmacy Teaching and Research Office at Chongqing Cancer Hospital. Her primary research focuses on the development of methodologies for therapeutic drug monitoring and personalized medicine, the investigation of new magnetic nano drug-loading and detection systems, as well as chromatographic separation and analysis. She has published 25 SCI articles and chaired 7 projects.

Therapeutic drug monitoring (TDM) is a clinical practice used for optimizing and individualizing drug therapy, and it is essential for ensuring the safety and efficacy of drugs and achieving precision medicine. As a result of the ongoing advancement of TDM, there is an urgent desire for a fast, simple, and easy-to-operate technology to achieve point-of-care testing for TDM. In recent years, aptamers have frequently been employed as biorecognition elements due to their high specificity, good stability, low cost, and ease of modification. Aptamers can be combined with various signal transduction methods (such as optics and electrochemistry) to form aptamer sensors (aptasensors), which are extensively applied in different fields including environmental monitoring, food safety, and clinical diagnosis. Aptamer sensors are increasingly becoming an attractive tool for immediate TDM, yet there is currently no comprehensive review on this topic. Consequently, we intend to provide a thorough overview of the applications of aptamer sensors in point-of-care TDM over the past five years and analyze its development trend, aiming to promote the continuous advancement of point-of-care testing technologies for TDM.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P527

The relationship between sunitinib exposure and toxicity in real-world patient with mRCC

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Biography:

Li Qiaoqiao, Chief Pharmacist, holds a Master's degree in Pharmaceutical Chemistry from Chongqing University. She primarily focuses on the development of new technologies and methods for therapeutic drug monitoring, as well as real-world studies exploring the correlation between blood concentrations of tyrosine kinase inhibitors (TKIs) and toxicity and efficacy.

Background: High plasma levels of sunitinib exposure can lead to severe toxicity; therefore, exploring the relationship between exposure and toxicity may provide a valuable reference basis for the precise administration of sunitinib.
Aims: This study aims to investigate the relationship between sunitinib exposure and toxicity in a real-world patient cohort.
Methods: We conducted a retrospective observational cohort study involving 39 patients diagnosed with metastatic renal cell carcinoma(mRCC) who were treated with sunitinib. The steady-state trough concentrations of sunitinib and its active metabolite were quantified using HPLC-MS/MS. Sunitinib-induced toxicity was evaluated based on the Common Terminology Criteria for Adverse Events version 4.0.
Results: A total of 33 patients (85%) reported experiencing sunitinib-induced toxicity. The mean exposure in patients with toxicity was significantly higher (87.10 ± 30.85 ng/mL) than in those without toxicity (58.16 ± 22.27 ng/mL) (P = 0.035). However, in individuals experiencing grade 3-4 toxicities, the exposure level (73.78 ± 18.69 ng/mL) was not significantly different from that in the no-toxicity group (55.24 ± 18.72 ng/mL (P = 0.196).
Conclusions: This study confirms a positive association between sunitinib exposure and toxicity in Chinese patients with mRCC in a real-world cohort. The absence of a significant relationship between grade ≥3 toxicity and exposure may be attributed to poor medication adherence, potentially leading to decreased blood concentrations due to self-discontinuation of the drug. In future studies, we will expand the sample size and enhance the management of patient medication adherence.
Key Words: sunitinib; exposure; toxicity; real-world; mRCC

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P528

Exposure-response analyses of venetoclax combined with hypomethylating agents in myelodysplastic syndromes

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Biography:
Education:
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Current Position:
Associate Chief Pharmacist, Department of Pharmacy, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences
Expertise:
Pharmaceutical Quality Control Systems
Medication Therapy Risk Management
Precision Pharmacotherapy for Hematologic malignancies
Quantitative Pharmacology Research
Research Achievements:
Published >20 peer-reviewed papers in pharmaceutical sciences
Led/participated in 10+ research projects including:
Population Pharmacokinetics of Hematologic Malignancies
Dose-Response Relationship Studies in Antineoplastic Therapy

Background: Venetoclax (VEN) combined with hypomethylating agents (HMAs) has shown promising activity in patients with myelodysplastic syndromes (MDS).
Aims: The aim of the current study was to evaluate the exposure-efficacy/safety relationships of the VEN + HMAs regimen in Chinese MDS patients.
Methods: This study retrospectively collected the predose (C0) and 6 hours post-oral dosing plasma concentration (C6) of VEN for exposure-response analyses, using receiver operator characteristic (ROC) curves and logistic regression.
Results: The average C0 and C6 of VEN were 1990.60 ± 1591.12ng/mL and 2966.66 ± 1406.96ng/mL, respectively, with large inter-individual variability. The use of azole antifungals was the only significant factor influencing VEN concentration ($P < 0.05$). Compared to VEN 400mg administered without azole antifungals, concomitant use of azole antifungals with VEN 100mg resulted in a 100.03% and 18.50% increase in VEN C0 and C6, respectively. Based on logistic regression and ROC curve analyses, a plasma threshold of 2858.80ng/mL for C6 was found to be significantly associated with treatment success. Other factors, including C0, demographics, and disease characteristics (e.g., molecular mutations, baseline grade III/IV neutropenia, and prior therapies), were not associated with the probability of marrow remission. In the safety analyses, higher VEN concentrations were not associated with an increased probability of grade ≥ 3 infection or a more serious decrease in platelets and neutrophils.

Conclusions: This study provides insights into the VEN exposure threshold that predicts efficacy but not adverse events, offering valuable guidance for optimizing treatment strategies.
Keywords: venetoclax, hypomethylating agents, myelodysplastic syndromes, exposure-response

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P529

Clinical significance of measuring free lenvatinib concentrations in patients with hepatocellular carcinoma

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Biography:

Ken Shiraiwa, Ph.D., is a pharmacist at the Department of Clinical Pharmacy, Oita University Hospital. Since being appointed to his current position, he has been engaged in clinical work, including preparing anticancer drugs and providing pharmaceutical guidance for cancer patients, and obtained the qualification of Board certified Oncology Pharmacist from the Japanese Society of Pharmaceutical Health Care and Sciences in 2025. His current main research interests are related to pharmacokinetics, therapeutic drug monitoring, and pharmaceutical oncology. This presentation is the result of research conducted to address clinical questions arising from his routine clinical practice.

Background: Lenvatinib has a high protein binding rate, resulting in high variability of free lenvatinib concentration (FLC) depending on patient conditions and drug interactions.
Aims: In this study, an ultra-high performance liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS) assay was established to measure FLC in plasma of hepatocellular carcinoma (HCC) patients, and the effect of hepatic dysfunction on FLC was evaluated.
Methods: We studied 31 HCC patients treated orally with lenvatinib. Blood samples were collected at seven time points on the first day of lenvatinib administration to measure total lenvatinib concentrations (TLC) and FLC using UHPLC-MS/MS.
Results: Pharmacokinetic (PK) parameters were calculated, and hepatic function was assessed using Child-Pugh (CP) classification and score. Patients were divided into CP class A (n = 22) and class B (n = 9), and PK parameters were compared between the two groups. The CP class B group had significantly higher trough concentrations (Ctrough) of total and free lenvatinib as well as Ctrough normalized to dose (Ctrough/Dose) compared to the class A group. A significant positive correlation was found between CP score and both Ctrough and Ctrough/Dose of total and free lenvatinib. Interestingly, FLC tended to reflect the effects of hepatic function decline more sensitively than TLC. In addition, plasma albumin concentration correlated significantly with protein binding rate.
Conclusions: FLC may reflect the effects of hepatic dysfunction more sensitively than TLC. Therefore, measuring FLC may be clinically useful in patients with hepatic dysfunction.
Keywords: Free lenvatinib concentration, UHPLC-MS/MS, Hepatic dysfunction

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P530

Exploring Novel Therapeutic Strategies for Cholangiocarcinoma Using Cell Culture Models

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Biography:
n/a

Background: Cholangiocarcinoma (CCA) is a highly aggressive bile duct cancer with limited treatment options and poor prognosis. Current therapies often fail due to late-stage diagnosis and drug resistance, highlighting the need for novel treatments. Natural compounds from Thai traditional plants offer promising anticancer potential.
Aim: This study aims to explore new agents for CCA treatments and evaluating mechanisms of action in CCA cell lines.
Methods: The cytotoxic effects of Thai traditional plants, and chamuangone, a phytochemical from Thai medicinal plants, on CCA using KKU-100 and KKU-452 cell was evaluated through the MTT assay. The effects of chamuangone on cell apoptosis and Ki67 expression were performed using Muse® flow cytometry.
Results: Methanolic extracts of Elaeagnus latifolia barks showed inhibitory cell proliferation of KKU-100 with IC50 values of 134.6 and 219.8 µg/ml for 24 and 48 h. Methanolic extracts of Hylocereus cacti, Averrhoa bilimbi, and Phyllanthus acidus -barks showed inhibitory cell proliferation of KKU-452 with IC50 values of 269.8 and 154.1, 194.5 and 52.27, 169.2 and 157.4 µg/ml for 24 and 48 h. Interesting, chamuangone demonstrated a strong inhibitory effect on CCA cells, with an IC50 value of 1 µg/ml, and effectively induced apoptosis also significantly suppressed the Ki67 expression.
Conclusions: Chamuangone significantly induces cytotoxic effects, highlighting its potential as a more effective component of methanolic extracts from the barks of Thai traditional plants. These findings suggest that chamuangone could serve as a promising therapeutic candidate for cancer drug development.
Keywords: Cholangiocarcinoma, Cell Culture, Apoptosis, Cancer Drug Development, Thai Traditional Plants

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21–24 September
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P531

Deconjugation of methotrexate polyglutamates to methotrexate monoglutamate for therapeutic drug monitoring

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Biography:

Janani Sudnaresan is a PhD candidate with a passion for methotrexate. She did her masters in the University of Amsterdam and is currently a PhD candidate at the laboratory specialized diagnostics & research in the department of laboratory medicine, in Amsterdam medical center. Her research focuses on therapeutic drug monitoring of low-dose methotrexate in immune mediated inflammatory diseases, focusing mainly on rheumatoid arthritis.

Background: Methotrexate is converted to its active metabolite, methotrexate polyglutamate (MTX-PG1to6) intracellularly, by adding up to 5 glutamate moieties. MTX-PG1to5 can be detected accurately using UPLC-MS/MS, but the pre-analytics is time-intensive. Erythrocyte MTX-PGtotal (the sum of MTX-PG1to6) is useful for therapeutic drug monitoring (TDM) of MTX. We investigated the efficiency of folate deconjugation protocol in converting MTX-PG2to6 to MTX-PG1 quantified on the UPLC-MS/MS.
Methods: Whole blood QCs were prepared by spiking MTX-PG1to6 with a target concentration of 1200 nmol/L MTX-PGtotal, stored at -80ºC. MTX-PG2to6 in the QCs were deconjugated using Folate RBC hemolyzing reagent (Roche), with 90 minute incubation at room temperature. Lysates were further processed per den Boer et al.(1), and individual MTX-PG1to6 were quantified by UPLC-MS/MS. Deconjugation (%) was calculated as the ratio of the measured concentration of MTX-PG1 to the calculated concentration of MTX-PGtotal. Efficiency was high if >70% and moderate between 50–70%
Results: QCs had a mean MTX-PGtotal concentration of 1637 ± 94.7 nmol/L. MTX-PG1 accounted for 70% MTX-PGtotal while MTX-PG2 and MTX-PG3to6 were 20% and 10% respectively.
Conclusion: Folate RBC Hemolyzing reagent deconjugates MTX-PG2to6 to MTX-PG1 with moderate efficiency. A therapeutic window of 60-100 nmol/L MTX-PGtotal in packed erythrocytes is reported for rheumatoid arthritis. Higher MTX-PG1to6 increases MTX-PGtotal and can support both TDM and compliance monitoring. Analysers like the Cobas c-module offer a cost-efficient option for clinical implementation. Optimizing incubation time and temperature may improve deconjugation efficiency.
Keywords: Methotrexate, Methotrexate polyglutamates, therapeutic drug monitoring

Reference

(1)Den Boer E et al., Anal Bioanal Chem. 2013;405(5):1673-81

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21–24 September
Grand Copthorne Waterfront Hotel

P532

Review of 2 and 3 points of Busulfan monitoring, which is accurate?

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Biography:

Assistant Professor in Pharmaceutical care and PhD in Clinical Pharmacy Program Director. Department of Pharmceutical care, Faculty of Pharmacy, Silpakorn University, Meaung, NakhonPathom, Thailand. Interested field are Pharmaceutical care, Pharmacokinetics, Therapeutic Drug Monitoring, Pharmacogenetics and Pharmacoeconomics.

Background: This study aims to assess the accuracy of 2-point and 3-point blood sampling methods for Busulfan.
Methodology: A comprehensive review was conducted using the PubMed database spanning from 1989 to March 2024, with keywords including Busulfan, limited sampling, and therapeutic drug monitoring. Accuracy was evaluated based on the percentage of root mean square error (%RMSE) and the percentage of Mean Prediction Error (%MPE). The analysis included forest plots and a heterogeneity test.
Results: Nine studies comprising 44 results were included in the analysis, revealing no significant heterogeneity. A notable difference in mean accuracy was observed between 2-point and 3-point sampling for both %RMSE (3.177 ± 0.182, 95% CI 2.818 to 3.535, $p < 0.001$) and %MPE (-52.47 ± 3.916, 95% CI -60.256 to -44.689).
Conclusion: The findings suggest that 3-point sampling offers significantly higher accuracy and is therefore preferable for limited sampling in Busulfan monitoring.

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P533

Inhibitory effects of dihydropyridine drugs on tamoxifen metabolism and molecular docking

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Biography:

He is a chief pharmacist, deputy director of the Medical Department, master's supervisor at the First Affiliated Hospital of Wenzhou Medical University, a key figure in the clinical Chinese pharmacy discipline under the "Twelfth Five-Year" plan of the State Administration of Traditional Chinese Medicine, and the head of the national key research and development program project sub-center. He has long been dedicated to CYP450 research, particularly in the fields of clinical pharmacology, pharmacogenetics, and pharmacokinetics, and has conducted TDM for multiple drugs. He has published over 30 SCI papers as the first author and corresponding author. He has hosted several research projects, including those funded by the National Natural Science Foundation, the National Key Research and Development Program Sub-center Project, and the Zhejiang Provincial Natural Science Foundation, and holds 2 authorized patents. He has received the Chinese Medical Science and Technology Award and the Beijing Science and Technology Award.

Background: Tamoxifen, a selective estrogen receptor modulator, is widely used in breast cancer therapy. Its effectiveness requires metabolic activation by the enzyme CYP3A4. Calcium channel blockers are often co-administered with tamoxifen in clinical settings, but their potential interactions with tamoxifen metabolism have not been fully investigated.
Aims: To evaluate the effects of the calcium channel blockers nimodipine, nitrendipine, and felodipine on tamoxifen metabolism in vitro and in vivo, particularly their interactions with CYP3A4 and their impact on tamoxifen's pharmacokinetics.
Methods: To evaluate the inhibitory effects of nimodipine, nitrendipine, and felodipine on tamoxifen metabolism, 28 cardiovascular drugs were screened. Kinetic assays identified the inhibition type. Pharmacokinetic studies in rats assessed the impact of pretreatment with these drugs on tamoxifen's AUC, Cmax, and clearance. Additionally, molecular docking studies explored the interactions between the blockers and the active site of CYP3A4.
Results: Kinetic assays revealed competitive inhibition by nimodipine and felodipine in both RLM and HLM, while nitrendipine exhibited non-competitive inhibition in RLM and competitive inhibition in HLM. Pharmacokinetic studies in rats showed that pretreatment with nimodipine and nitrendipine significantly increased tamoxifen's AUC and Cmax, while reducing its clearance. Molecular docking confirmed interactions between these drugs and the active site of CYP3A4.
Conclusions: The study demonstrated that nimodipine, nitrendipine, and felodipine can inhibit tamoxifen metabolism, leading to increased systemic exposure. The observed drug interactions may require careful monitoring and potential dose adjustments of tamoxifen in clinical practice when co-administered with these calcium channel blockers.
Key Words: tamoxifen; calcium channel blockers; pharmacokinetic; molecular docking

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P600

Enhancing Patient Outcomes: Vancomycin Therapeutic Drug Monitoring in Critically Ill Patients

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Biography:
Jefman is a clinical pharmacology physician at Ubaya Hospital and also a lecturer at Faculty of Medicine Universitas Surabaya, Indonesia. He currently serves as the Chairperson of Indonesian Association of Clinical Pharmacology Specialist (PERDAFKI). He is driven to bring personalized therapy services in Indonesia, including optimizing antimicrobial treatments for better patient outcomes.

Background: Vancomycin is essential for treating severe Gram-positive infections in adult critically ill patients, but its narrow therapeutic index requires therapeutic drug monitoring (TDM) to optimize efficacy and minimize toxicity. The debate between trough concentration (Cmin)-based dosing and area under the curve (AUC)-based dosing remains unresolved, impacting mortality, nephrotoxicity, and clinical outcomes.
Aims: This meta-analysis evaluates the impact of TDM on mortality, nephrotoxicity, and clinical cure rates in adult critically ill patients receiving vancomycin.
Methods: A systematic search in PubMed, Scopus, Google Scholar, ProQuest, and Cochrane Library identified nine studies assessing vancomycin TDM in adult critically ill patients. These included three studies each for mortality, nephrotoxicity, and clinical cure rates.
Results: TDM significantly reduced mortality in three studies (N = 11,587 vs. 11,150; RR 0.84 [95% CI: 0.79, 0.89]). Subgroup analysis of Cmin <15 mg/L vs. Cmin >15 mg/L (N = 11,737) showed improved survival with lower trough levels (RR 0.65 [95% CI: 0.54, 0.78]). Nephrotoxicity risk (N = 156 vs. 150) showed no significant difference (RR 0.83 [95% CI: 0.48, 1.44]). Clinical cure rates (N = 22 vs. 48) comparing AUC <400 vs. >400 mg·h/L found no clear benefit (RR 1.80 [95% CI: 0.41, 7.98]).
Conclusions: This meta-analysis confirms TDM significantly reduces mortality, especially with Cmin <15 mg/L, challenging high-trough strategies. However, nephrotoxicity and clinical cure rates were not significantly impacted, supporting a shift to AUC-based dosing. Further randomized trials are needed to refine vancomycin TDM protocols.
Keywords: vancomycin, therapeutic drug monitoring, critically ill, sepsis, AUC, mortality

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P601

Pharmacokinetic analysis of linezolid and its metabolite PNU-142586 in healthy volunteers

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Biography:

Takahiko Aoyama is an Associate Professor at the School of Pharmacy, Nihon University, specializing in clinical pharmacometrics. He earned his Bsc from Showa Pharmaceutical University in 2002 and completed his Msc in 2004. After serving as an assistant at Showa Pharmaceutical University, he joined Nihon University in 2006, where he became an Associate Professor in 2023. He obtained his Ph.D. in Pharmacy in 2018 for his research on mathematical modeling for drug efficacy prediction. His work focuses on optimizing drug dosing through pharmacokinetic-pharmacodynamic modeling and simulations. In addition to research, he is dedicated to teaching pharmacokinetics and clinical pharmacology, contributing to the education of future pharmacists and researchers.

Background: Linezolid (LZD), used to treat infections caused by multidrug-resistant Gram-positive cocci, has been associated with concentration-dependent risk of thrombocytopenia. The metabolite PNU-142586, derived from LZD, is suspected to contribute to this toxicity. However, the pharmacokinetics of PNU-142586 remain unclear.
Aims: This study aimed to characterize the pharmacokinetics of LZD and PNU-142586 following a single intravenous dose of LZD.
Methods: Six healthy adult subjects received a single 600 mg intravenous infusion of LZD. Blood samples were collected for up to 10 hours after administration. LZD and PNU-142586 concentrations were measured using high-performance liquid chromatography. Pharmacokinetic parameters were estimated using non-compartmental analysis. This study was approved by the research ethics review committees of Toyama University Hospital and Nihon University School of Pharmacy (R2020147, R23A-005).
Results: LZD exhibited the maximum concentration (Cmax) of 20.4 mg/L and the area under the concentration-time curve from 0 to 10 hours (AUC0-10) of 102.6 mg·h/L. PNU-142586 exhibited Cmax of 1.6 mg/L, AUC0-10 of 109.0 mg·h/L, and time to Cmax (Tmax) of 4.5 hours. The coefficient of variation (CV) for AUC0-10 was 6.1% for LZD and 19.4% for PNU-142586. The formation rate constant for PNU-142586 was 0.40 /h.
Conclusions: The pharmacokinetics of LZD were consistent with previous reports. The higher CV of PNU-142586 AUC0-10 indicates greater inter-individual variability compared to LZD. The Tmax and formation rate constant of PNU-142586 was relatively consistent among subjects. This study provides the first detailed characterization of the formation rate of PNU-142586 from LZD following intravenous administration.
Keywords: linezolid, PNU-142586, metabolite, pharmacokinetics.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P602

Dual β-lactam therapy for high-risk Pseudomonas aeruginosa ST235-clone clinical isolates

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Biography:

Siobhonne Breen is a PhD candidate at the Monash Faculty of Pharmacy and Pharmaceutical Science, rationally optimising antibiotic combinations against resistant bacterial 'superbugs'. Siobhonne's project encompasses a range of laboratory work as well as mechanism-based mathematical modelling, both of which she has a strong interest in. Siobhonne has a passion for improving patient outcomes through drug research and development. Siobhonne has won multiple poster presentation awards and received oral presentations at international and national conferences.

Background: Pseudomonas aeruginosa (Pa) isolates from the ST235-clone are high-risk as they are often extensively drug-resistant and prevalent in endemics. Innovative personalised treatment for the pathogen and patients is needed to optimise patient outcomes.
Aims: To investigate ceftolozane/tazobactam (C/T) and meropenem (MER), in monotherapy and combination, against ST235-clone Pa isolates using the dynamic in vitro hollow-fibre infection model (HFIM), quantitative and systems pharmacology (QSP) modelling, whole genome sequencing (WGS) and Monte Carlo simulations (MCS).
Methods: Three multidrug-resistant isolates from hospitalised patients were investigated in 240-h HFIM studies (n=1-2 replicates; inoculum ~106.8 CFU/mL) against intermittent C/T (1.5/0.5g 3h infusion 8-hourly, t1/2=2h) and continuous infusion MER (6g/day). Quantified total viable and resistant bacterial counts were QSP modelled. Whole genome sequencing and MCS were performed.
Results: All MER and 2 of 3 C/T monotherapy treatments failed and amplified resistance. The combination performed successfully against all isolates. The model, informed by the resistance mechanisms present, well-described antibacterial effects of the monotherapy and combination regimens, without estimating strain-specific drug effect parameters. MCS predicted the combination would supress regrowth against all isolates for 95% of simulated patients.
Conclusions: The combination of C/T and MER enhanced bacterial killing, consistently suppressing regrowth and resistance against all tested isolates. The QSP model is the first model to characterise the different bacterial responses to an antibiotic combination, only by the resistance mechanisms present and their complex interplay; representing an initial step towards pathogen-specific personalised medicine. MCS predicted the likely effectiveness of tested regimens for patients with normal renal function.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P603

Oxidative stress influence on plasma and intracellular antiretroviral drugs exposure in PWH

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Biography:

Born in Turin on November 22, 1986, she graduated in Health Biology, specialized in Microbiology and Virology, and obtained a PhD in Complex Systems for Life Sciences at the University of Turin.
She was a researcher (RTD-B from 2019 to 2022) and is currently an Associate Professor of Pharmacology. She is affiliated with the ASL Città di Torino as a senior biologist.
She received some awards, including:
•The "Società Italiana di Farmacologia e Farmindustria" award for pharmacological research (2018).
•The second prize of "The Binding Site" by SIBIOC for pharmacological research (2019).
•The IATDMCT Victor Armstrong Young Investigator Award 2024 for Exceptional Scientific Achievements Early in her Career.
•The Podium Selected Communication at the 42nd SIF Congress (2024).
Her areas of excellence include clinical pharmacology, pharmacogenetics, therapeutic drug monitoring, drug interactions, and biomarker quantification. She published approximately 170 articles, with an H-index of 28.

Background: HIV infection triggers oxidative stress by producing reactive oxygen species (ROS), neutralized by antioxidant molecules, such as glutathione. Both ROS and antioxidants could influence the expression of genes encoding enzymes and transporters involved in systemic and intracellular antiretroviral drug pharmacokinetics, with a potential effect on the clinical outcome of people with HIV (PWH). No studies investigating the role of oxidative stress and antioxidant molecules in affecting antiretroviral drug exposure are present.
Aims: To quantify antioxidant molecules, evaluating their impact on plasma and intracellular (PBMCS) drug exposure.
Methods: Plasma and PBMCS drug concentrations and mitochondrial and cytosol oxidative stress biomarker levels were evaluated through liquid chromatography.
Results: 25 PWH with a median age of 42.5 years and BMI of 23.3 kg/m² were analyzed. BIC/TAF/FTC (48%) and RPV/TAF/FTC (40%) were the most frequent antiretroviral therapies, whereas PWH in dual therapy were mostly given DTG/3TC (80%). Three different patterns were identified: associations between antioxidant molecules and a) only systemic (i.e. cytosol n-acetylcysteine with DTG plasma levels), b) only intracellular (i.e. mitochondrial s-adenosylmethionine with intracellular BIC exposure) and c) both systemic and intracellular antiretroviral drug concentrations (i.e. mitochondrial glycine and FTC plasma-PBMCS concentrations or mitochondrial glutathione and RPV plasma-PBMCS).
Conclusions: This is the first study showing the potential role of oxidative stress-related factors impacting on systemic and/or intracellular antiretroviral drug exposures. Overall, mitochondrial oxidant molecules seem to regulate the intracellular antiretroviral concentrations compared to cytosol biomarkers. The clinical relevance of these different associations is currently under evaluation.
Keywords: antioxidants, ros, haart, antiretroviral treatment

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P604

Finding a new therapeutic drug monitoring pathway for ganciclovir in transplant recipients

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Biography:

Pharmacologist at the University Hospital of Rennes. I specialise in therapeutic drug monitoring of anti-infective and immunosuppressive drugs, as well as population pharmacokinetics.

Background: Therapeutic drug monitoring of Ganciclovir is routinely performed using trough concentration (C0), while no studies found a clear relationship with efficacy. Besides, area under the curve (AUC) is increasingly used in therapeutic drug monitoring of ganciclovir.
Aims: The aim of this study was to explore the variation of pharmacokinetics indices and target attainment of GCV in transplantation.
Methods: Transplanted patients who received ganciclovir/valganciclovir and had C0 and AUC0-24h performed between 2022 and 2025 were retrospectively included in the study. Pharmacokinetic variability was assessed using AUC0-24h/C0 linear regression, inter- and intra-patients dose-adjusted coefficient of variation for C0 and AUC0-24h and percentage of patients reaching the therapeutic range (C0=1-2µg/mL, AUC0-24h=40-60µg.h/mL).
Results: Thirty-one transplanted patients (8 children/23 adults, 6 universal prophylaxis/20 preemptive therapy/5 curative treatment) contributed to 54 occasions. A poor AUC0-24h/C0 correlation was found (adults: r^2=0,44, children: r^2=0,55). A high (CV=144%) and mild (CV=41%) interindividual variability were found for C0/D and AUC0-24h/D, respectively. A mild (CV=56%) and low (CV=20%) interindividual variability were found for C0/D and AUC0-24h/D, respectively. Ten percent of adults had AUC0-24h within the range (41% for C0) while 45% of children had AUC0-24h within the range (0% for C0).
Conclusions: C0 does not seem to be the best parameter to monitor ganciclovir treatment and could be replaced by the estimation of AUC for a more precise therapy. Further studies are needed to better define the relationship between AUC0-24h and ganciclovir pharmacodynamics/clinical outcomes.
Key words: area under the curve, trough concentration, cytomegalovirus, antivirals, pharmacokinetics.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P605

Sub-optimal clindamycin dosing induces small colony variant phenotype in Staphylococcus aureus

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Biography:

Joy Gibson, MD, PhD, is an Assistant Professor of Pediatric Infectious Diseases at Children's Hospital Los Angeles (CHLA). As a physician-scientist funded by the Cystic Fibrosis Foundation and National Institutes of Health, she has clinical and research expertise on the management of challenging pathogens in cystic fibrosis. In the laboratory, Dr. Gibson uses the hollow fiber infection model to optimize treatment regimens for Mycobacterium abscessus, Staphylococcus aureus, and Pseudomonas aeruginosa. She is an investigator in the Innovative Synergistic Pediatric Infection Research group, collaboratively leading the first pediatric center in the United States with hollow fiber capabilities to improve treatment of children with complex infections.

Background: Clindamycin is commonly used for treatment of both methicillin susceptible and resistant S. aureus (MSSA, MRSA). Recurrent infections are often attributed to small colony variants (SCV), which tolerate otherwise inhibitory antibiotic concentrations.
Methods: To expose MSSA to a mean pediatric free clindamycin 24-h area under the concentration-time curve (AUC) of 7.2 mcg*h/mL reported after standard dosing, we inoculated 10^5 CFU/mL into broth with clindamycin 0.3 mcg/mL, and 0.5, 2, and 4 times AUC. We quantified CFU on standard agar and agar containing clindamycin at the MIC (0.25 mcg/mL) over 21 days. We identified SCVs phenotypically based on size and slow growth.
Results: All concentrations of clindamycin initially inhibited growth relative to clindamycin-free control. This inhibition was sustained at 2x and 4x AUC, but rebound growth appeared by day 6 in the 0.5x and 1x AUC flasks. Emergence of SCV phenotypes comprising 39-52% of the population occurred by day 8 in all conditions. With low dose clindamycin, the entire population had converted to SCVs by day 14 (0.5x AUC) or day 17 (1x AUC). These SCVs grew on clindamycin agar and randomly selected colonies had MICs that had become resistant per CLSI criteria.
Conclusions: Inadequate dosing and exposure of clindamycin in humans in the treatment of MSSA may promote growth of tolerant and/or resistant SCV with subsequent treatment failure or recurrence following cessation of therapy. We are conducting further experiments to optimize dosing and exposure of clindamycin to reduce the emergence of SCVs.
Keywords: Pharmacokinetics, pharmacodynamics, clindamycin, MSSA, SCV, resistance

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P606

Vancomycin concentrations, treatment outcomes and nephrotoxicity in patients with coagulase-negative Staphylococcus infections

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Biography:

Siriluk Jaisue is an Associate Professor at the Faculty of Pharmaceutical Sciences, Khon Kaen University, Thailand. She is also affiliated with the university hospital, where she provides recommendations for drug dosing as part of Therapeutic Drug Monitoring (TDM). Her research primarily focuses on pharmacokinetic and pharmacodynamic (PKPD) correlations in infectious diseases. She has published several works in this area, collaborating both domestically and internationally. Her current research investigates the PKPD of anti-infective agents, using TDM as a tool. Siriluk aims to further enhance her knowledge in pharmacokinetics and TDM through this conference, exchange ideas with experts, and explore new research approaches. Attending this event will contribute to the ongoing development of her research and strengthen collaborations within the scientific community.

Background: Coagulase-negative staphylococci (CoNS) are commonly found on human skin and can cause hospital-acquired bloodstream infections, typically treated with vancomycin. Vancomycin dosing for methicillin-resistant Staphylococcus aureus (MRSA) infections was traditionally based on maintaining trough concentrations (Ctrough) between 10–20 mg/L. However, current recommendations emphasize targeting a 24-hour area under the curve to minimum inhibitory concentration (AUC24/MIC) ratio of 400–600 mg.h/L. There are no specific guidelines for vancomycin dosing in CoNS infections.
Aim: To investigate relationships between Ctrough, treatment outcomes, and nephrotoxicity in patients with CoNS infections.
Methods: Data were retrieved for adult patients treated at Srinagarind Hospital, Thailand between 2010 and 2023. Treatment outcomes, including 30-day mortality, early clinical response (ECR), and clinical response at the end of therapy (CRend), as well as vancomycin trough concentrations and nephrotoxicity were analyzed.
Results: Fifty-one patients met the study criteria. Ctrough levels were higher in the mortality group (n=6) (32.11 mg/L vs 18.64 mg/L, p = 0.010) and in patients with nephrotoxicity (n=12) (30.71 mg/L vs 18.64 mg/L, p = 0.013). No correlation was observed between Ctrough and ECR or CRend. There was no correlation between achieving vancomycin Ctrough 10-20 mg/L and treatment outcomes or nephrotoxicity.
Conclusion: Vancomycin levels positively correlated with mortality and nephrotoxicity in CoNS-infected patients but not clinical response. Maintaining Ctrough 10-20 mg/L may not ensure therapeutic effects. Due to the small sample size, conclusions on optimal CoNS dosing cannot be made and further research is required to determine an optimal AUC24/MIC ratio.
Keywords: vancomycin,CoNS,PKPD,TDM

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P607

The Use of Antibiotics in Patients' Pneumonia at secondary hospital Indonesia 2020

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Biography:

Dr. Linggom Kurniaty, Sp.FK. was born in Bandung, on July 21 1974. She is a Lecturer at the Faculty of medicine Universitas Kristen Indonesia since 2018. She is also The Head of the PPRA and KFT Team at a Private Hospital in West Java since 2019. She has acquired a Bachelor's degree and is a professional doctor at the Faculty of medicine Universitas Kristen Indonesia, Clinical Pharmacology Specialist Graduate (Sp. FK) the Faculty of medicine Universitas Indonesia. She is Actively participating in social activities in the health sector in the church and other community

Background: Pneumonia is an acute respiratory infection that attacks the lungs caused by viruses, bacteria, parasites, and fungi, which can be transmitted through coughing and sneezing droplets, direct contact with sufferers, and environmental factors. Community-acquired pneumonia is pneumonia that often occurs and can be serious or even fatal. According to PDPI 2014, pneumonia is a disease that has a high crude fatality rate (CFR), which is around 7.6%, in 2020 pneumonia is ranked fifth with a percentage of 52%. Therefore, pneumonia requires proper attention and treatment because this disease is still a major health problem in Indonesia.
Aims: This study was conducted to determine the Characteristics and accuracy of using antimicrobials in pneumonia patients (March-Agustus 2020).
Methods: The research design is in the form of a description analysis study who had met the parameters of the right indication, the right patient, the right drug, and the right dose according to the Indonesian Association of Pulmonary Doctors assesses using medical record data of outpatient adult Pneumonia patients during the period March 2020 - August 2020
Results: The study concluded that out of 34 samples have the correct indication was 100%, right drug 100%, right patient 100%, and right dose 91,2%.
Conclusion: The study showed that all or up to 34 samples diagnosed accurately and given medication according to guidelines.
Keywords: Antimicrobial, Rationality, Pneumonia, secondary hospital

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P608

Mechanism-based modelling of antibiotic effects on Pseudomonas strains with different resistance mechanisms

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Biography:
Assoc Prof Cornelia Landersdorfer leads a research group on dosing regimen optimisation of antibiotics at the Monash Institute of Pharmaceutical Sciences in Melbourne, Australia. Her group conducts dynamic in vitro infection models and mathematical modelling to translate optimised treatment regimens to patients. Research outcomes have informed regulatory decisions, and clinical guidelines and practice. She is also the Scientific Director of the Monash-Moderna Quantitative Pharmacology Accelerator.

Background: Pseudomonas aeruginosa has a large armamentarium of resistance mechanisms, enabling resistance emergence against almost all antibiotics in monotherapy.
Aims: To evaluate regimens of meropenem (MER) and ciprofloxacin (CIP), alone and combined, against isogenic P. aeruginosa strains with different resistance mechanisms in a dynamic hollow fibre infection model (HFIM) and develop a mechanism-based mathematical model (MBM) accounting for the resistance mechanisms.
Methods: Four isogenic strains were used: PAOD1 (spontaneous oprD mutation/loss of porin OprD), PAΔADmexR (ampD knock-out/AmpC overexpression and mexR knockout/MexAB-OprM overexpression), PAOD1ΔmexR and PAOD1ΔAD (other combinations of the resistance mechanisms). Regimens were: MER continuous infusion (CI, 6g/day, 12g/day additionally against MER-resistant strains), CIP intermittent infusions (400mg, 8-hourly as 1-h infusions), and both combinations. The HFIM was run for 240h. MBM was performed.
Results: All monotherapies resulted in regrowth with amplification of resistant subpopulations. The combination regimens suppressed total and resistant counts of PAOD1, PAΔADmexR and PAOD1ΔAD. Against PAOD1ΔmexR, MER 6g + CIP performed synergistically from 24h-120h, while MER 12g + CIP was synergistic from 24h-192h. MER-resistant counts emerged from 72h and 168h for the respective combination regimens; CIP-resistant colonies emerged from 216h with the low-dose combination only. An MBM with subpopulation synergy was developed that described the bacterial response to antibiotic based on the resistance mechanisms for all mono- and combination therapies.
Conclusions: Combination regimens enhanced bacterial killing and suppressed regrowth and resistance overall. An MBM accounting for different resistance mechanisms well-described the impact of double mutations and combination therapies on bacterial response.
Keywords: mathematical modelling, combination, pharmacodynamics, genomics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P609

Therapeutic drug monitoring is essential for managing complex polymicrobial infections: case report

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Biography:
Cindy is the Antimicrobial Stewardship Pharmacist at St Vincent's Hospital, Sydney, Australia. Her interests include clinical implementation of antimicrobial therapeutic drug monitoring, and treatment optimisation of infections in immunocompromised hosts.

Background: The clinical application of antimicrobial therapeutic drug monitoring (TDM) improves achievement of pharmacokinetic/pharmocodynamic targets while minimising toxicity. However, literature describing complex drug interactions and unexpected drug disposition in polymicrobial infections remains scarce
Aim: To describe a case where TDM played a critical role in identifying and managing multiple unexpected drug disposition scenarios, including a possible novel drug-drug interaction between voriconazole and piperacillin/tazobactam.
Methods: A 54-year-old man with gastrointestinal graft-versus-host-disease post allogeneic stem cell transplant for high-risk myelofibrosis developed resistant polymicrobial infections of the blood stream, psoas abscess and prosthetic hip joint. Pathogens isolated included Lomentospora prolificans, Morganella morganii, vancomycin-resistant Enterococcus and AmpC beta-lactamase Escherichia coli. Treatment initially comprised of voriconazole, linezolid and piperacillin/tazobactam. Intensive TDM was performed, targeting trough concentrations between 2-5 mg/L for voriconazole, 2-7 mg/L for linezolid, and 4× minimum inhibitory concentrations for beta-lactam agents.
Results: TDM revealed persistently subtherapeutic trough voriconazole concentrations (mean 0.5mg/L) despite dose escalation to 1500mg/day (triple standard dose) during piperacillin/tazobactam treatment. A subsequent switch to cefepime improved voriconazole concentrations (mean 2.3mg/L). Linezolid concentrations were initially subtherapeutic (mean 1.1mg/L), requiring double standard dosing, suggesting CYP2J2 induction by a pathophysiological mechanism. Dose adjustments maintained antimicrobial concentrations within target ranges, contributing to treatment success without toxicity.
Conclusions: Proactive TDM represents a valuable clinical tool for antimicrobial stewardship by enabling swift detection of drug disposition anomalies, and antimicrobial optimization. The interaction identified here between voriconazole and piperacillin/tazobactam, putatively mediated through CYP450 enzyme induction, has important implications for beta-lactam selection in patients requiring triazole antifungals.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P610

Vancomycin pharmacokinetics and clinical outcomes in children with methicillin-resistant Staphylococcus aureus infection

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Biography:

Lee Jian Lynn is an experienced clinical pharmacist with almost 20 years of expertise in hospital pharmacy services. Specializing in paediatric pharmacy practices and clinical pharmacokinetics, she is dedicated to advancing patient care through her research and clinical work. She currently leads the Clinical Pharmacokinetic Unit at the Pharmacy Department at Hospital Tunku Azizah (Women and Children Hospital) in Kuala Lumpur, Malaysia. She oversees the clinical pharmacokinetic services and plays a key part in training junior pharmacists in pharmacokinetics. She also organizes and conducts various workshops and training sessions to enhance knowledge in this critical field. Jian Lynn holds a Master of Pharmacy degree from the University of Strathclyde (2005), a Master in Clinical Pharmacy degree (2012), and a Doctor of Philosophy degree (2022) from Universiti Kebangsaan Malaysia. Through her dedication to research and professional development, she continues to contribute to the advancement of clinical pharmacy practices in Malaysia.

Background: Vancomycin is the first-line treatment for methicillin-resistant Staphylococcus aureus (MRSA) infections, and achieving the recommended AUC24H/MIC target is crucial for optimal clinical outcomes.
Aims: This study is a sub-analysis of a larger pharmacokinetic study population and focuses on vancomycin pharmacokinetics/pharmacodynamics (PK/PD) and treatment outcomes in paediatric patients with MRSA infections.
Methods: A retrospective cohort analysis was conducted in 23 children admitted to a tertiary paediatric hospital between January 2022 and December 2023. Data were collected from pharmacokinetic and medical records. PK parameters were estimated using established equations. Clinical outcomes were assessed based on clinical and microbiological parameters at the end of treatment.
Results: Among 23 paediatric patients with MRSA infections, two cases (8.7%) were non-responders. The initial vancomycin dose used was 58.40mg/kg/day (IQR: 15.00). The majority of patients (73.9%) had a vancomycin minimum inhibitory concentration (MIC) of ≤1mg/L. Sub-therapeutic pre-levels were observed in 82.6% of patients, with a median level of 8.40mg/L (IQR: 5.22). Additionally, 87% had a sub-therapeutic 24 hours-area under the curve (AUC24H), with a median value of 313.45mg·h/L (IQR: 181.58), while 52.2% had a sub-therapeutic AUC24H/MIC, with a median value of 286.05mg.h/L (IQR: 341.14). To achieve the target AUC24H of 426.30mg·h/L (IQR: 129.62), patients required a median dose of 66.67mg/kg/day (IQR: 18.61).

Conclusion: A large proportion of paediatric MRSA patients received sub-therapeutic vancomycin dosing, failing to meet the AUC24H/MIC targets. Optimized dosing and individualized TDM are needed to improve outcomes, warranting further research in a larger study population.
Keywords: MRSA, vancomycin, therapeutic drug monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P611

Managing High-Risk Drug Interactions with Nirmatrelvir/Ritonavir: Experience from a Pharmacology Advice Service

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Biography:
Dr Florian Lemaitre has been trained as a pharmacist and pharmacologist during its residency in Rennes and Poitiers, France. In 2014, he received his PhD on the pharmacological optimization of immunosuppressive therapy during his pharmacology fellowship at the Pitié-Salpêtrière Hospital in Paris and the Rennes University Hospital. His main research topic is the precision medicine in transplantation and he has been authored or co-authored 120+ articles.Since 2022, he is the president of the TDM-working group of the Société Française de Pharmacologie et de Thérapeutique (SFPT), the French national learning society of pharmacology. He is also the actual secretary of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and the Chair of the immunosuppressive drugs scientific committee of the IATDMCT.
He has dedicated his career to drug individualization for patients' care notably for solid organ transplant patients and patients with acute or chronic infections.

Background: Nirmatrelvir/ritonavir is an antiviral regimen for patients at high risk for severe COVID-19, but it poses significant risks of drug-drug interactions (DDIs), primarily due to ritonavir's potent inhibition of cytochrome-P450 3A4.
Aims: This study aimed to assess the impact of nirmatrelvir/ritonavir-related DDIs and evaluate an expert-driven approach for their management.
Methods: We conducted a retrospective observational study of all pharmacology expert opinions regarding nirmatrelvir/ritonavir-related DDIs, between February 2022 and December 2024. Data on patient demographic and clinical characteristics, concomitant medications, and expert recommendations were systematically collected and analyzed.
Results: Among 455 patients (median age 75 years), 6% received an expert recommendation of contraindication to Nirmatrelvir/ritonavir prescription due to unmanageable DDIs or severe renal impairment. Of the 429 eligible patients, 86.7% had at least one clinically significant DDI, with a median of eight concomitant medications per patient. The most frequent DDIs involved statins (17.7%), immunosuppressants (12.0%), and direct oral anticoagulants (10.5%). Expert recommendations included continuing therapy without modification (76%), temporary interruption (14%), dosage adjustment (6%), or changing treatment (3%). Close clinical monitoring was advised for 8%, and therapeutic drug monitoring for 6%. The majority of requests in 2022 came from hospital specialists (71%), whereas general practitioners accounted for 45% in 2023 and 50% in 2024.
Conclusions: A specialized pharmacology service can effectively support safe prescribing of nirmatrelvir/ritonavir in a high-risk, predominantly older and polypharmacy-prone population. Our service has expanded beyond tertiary centers, enhancing access for a wider range of healthcare professionals and ensuring safer treatment management.
Keywords: nirmatrelvir/ritonavir, drug-drug interaction

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P612

Comparison of Vancomycin Therapeutic Drug Monitoring (TDM) Methods in Neonates

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Biography:
Selina is a Senior Clinical Pharmacist in KKH and has taken up various roles in the Children's Inpatient Pharmacy, Antimicrobial Stewardship Programme (ASP) and Intensive Care Unit (ICU) Pharmacy team. She is also actively involved in clinical research, with a special interest in antibiotic pharmacokinetics.

Background: The Area-Under-the-Curve/Minimum Inhibitory Concentration(AUC/MIC)-based vancomycin TDM has been recommended over trough-based TDM for neonates. However, this recommendation was based on extrapolations from pediatric and pharmacokinetic models. Neonates have unique pharmacokinetic differences due to their immature renal function and rapidly changing fluid status.
Aims: This study aims to compare the (1)percentage of patients attaining subtherapeutic, therapeutic and supra-therapeutic targets; (2)dose required for target attainment (AUC 400-600, assuming MIC 1, or trough 10-20mg/L); (3)culture-directed treatment efficacy (microbiological resolution, clinical efficacy) using vancomycin trough-vs. AUC/MIC-based TDM.
Methods: This was a single-center, retrospective observational study conducted at KK Women's and Children's Hospital, Singapore(KKH) from January 2020 to December 2024. Neonates [post-menstrual age(PMA) <45 weeks] who received intravenous vancomycin, with at least two vancomycin serum concentrations obtained during steady state, were included. Neonates with acute kidney injury, on dialysis or extracorporeal membrane oxygenation(ECMO) are excluded. Using Adult and Pediatric Kinetics(APK©) software, 24-hour AUC was determined using a one-compartmental model.
Results: Of the 22 neonates included, a larger proportion of patients achieved therapeutic targets when the AUC/MIC-based method (40.9%) was used, compared to the trough-based method (22.7%, p=0.2). This resulted in lower adjusted doses of vancomycin when AUC/MIC-based TDM was used(p=0.03). Almost all patients attained clinical improvement and microbiological clearance regardless of whether their serum vancomycin concentrations were therapeutic at initial steady state (95%). Two patients (9%) developed acute kidney injury after vancomycin therapy.
Conclusions: AUC/MIC-based vancomycin TDM resulted a larger proportion of neonates achieving therapeutic targets with potentially lower adjusted doses of vancomycin.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P613

Importance of beta-lactam therapeutic drug monitoring for sepsis in Asia.

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Biography:
Tat Ming NG is a infectious disease specialist pharmacist registered with the Singapore Pharmacy Council. He has more than a decade of experience in antimicrobial stewardship and has established the beta-lactam therapeutic drug monitoring service at Tan Tock Seng Hospital. Most recently, he is pursuing a PhD in physiologically-based pharmacokinetics at the National University of Singapore.

Background: Beta-lactam therapeutic drug monitoring (TDM) is recommended for critically ill patients and those with less susceptible organisms but evidence for non-critically ill patients with lower pharmacokinetic variations, is limited.
Aims: To evaluate the need for beta-lactam TDM in the Asian population with sepsis.
Methods: An observational study at Tan Tock Seng Hospital from January 2022 to August 2023 assessed patients with Gram-negative bacteraemia receiving empiric piperacillin-tazobactam or meropenem. Minimum inhibitory concentrations (MIC) were determined using gradient-diffusion tests. The MIC¬90 of Gram-negative bacteria from a historic cohort (Oct 2022 – Dec 2023) was extracted to represent antibiotic susceptibility from other specimen sources. Therapeutic concentration was defined as an fCmin/MIC≥1.
Results: Out of 293 eligible participants, 68 were enrolled with 16.0% critically ill. Median age was 67, inter-quartile range (IQR) 57-74 years. 30-day mortality of 7.4%. Median MIC of the bacteraemia isolates to meropenem was 0.032, IQR 0.032-0.064 mg/L and to piperacillin-tazobactam was 2, IQR 1-4 mg/L. Overall, median fCmin/MIC was 17.51, IQR 2.88-57.57 with 8% (n=6) with fCmin/MIC<1. Comparisons using MIC90 data and Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility and Testing (EUCAST) breakpoints showed that up to 44% and 3.1% in those receiving piperacillin-tazobactam and meropenem respectively will achieve Cmin/MIC<1.
Conclusion: Asian patients with Gram-negative bacteraemia have a low risk of sub-therapeutic levels of piperacillin-tazobactam and meropenem. Significant risks arise when considering other sources of sepsis. Further studies are needed to identify who would benefit from beta-lactam TDM in this population.
Beta-lactam, TDM, Asian

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P614

Significance of continuous infusion of vancomycin in adults

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Biography:
I am currently a pharmacist at Kumamoto University Hospital, dedicated to the Antimicrobial Stewardship Program. My area of expertise in therapeutic drug monitoring (TDM) focuses on the appropriate use of antibiotics through model-informed precision dosing. Notably, I have authored papers on vancomycin, a glycopeptide antibiotic used to treat methicillin-resistant Staphylococcus aureus (MRSA). I am also a contributing member of the Japanese guidelines for antimicrobial TDM.

Background: Continuous infusion (CI) of vancomycin has been proposed as a method to enhance therapeutic drug levels while minimizing nephrotoxicity compared to intermittent infusion (IntI). However, data on the clinical significance of CI in Japan remain limited.
Aims: This study presents a scoping review along with a case series analysis to assess the significance of CI in Bayesian-assisted, area under the concentration-time curve (AUC)-guided vancomycin dosing.
Methods: A scoping review was conducted using PubMed, Web of Science, and the Cochrane Library to identify studies published between 2018 and 2024. Additionally, a retrospective analysis was performed on 15 patients treated with CI at Kumamoto University Hospital, examining demographics, nephrotoxicity incidence, and mortality rates.
Results: The review identified 10 studies, including one randomized controlled trial. Many studies relied solely on trough concentrations as a surrogate for AUC estimation in IntI regimens without Bayesian assistance. CI target exposure levels varied, with only a few studies adhering to the recommended AUC range of 400–600 µg·h/mL. In the case series, four patients with high creatinine clearance required dose adjustments and achieved therapeutic targets without nephrotoxicity or mortality. Among the remaining 11 patients, only 45.1% reached therapeutic targets, while 54.5% experienced nephrotoxicity.
Conclusions: The findings highlight the need for further research to refine dosing strategies and clarify the advantages of CI compared to Bayesian-assisted IntI. However, CI may be particularly beneficial for patients requiring higher doses (≥3–4 g/day), as it could improve target attainment while mitigating nephrotoxicity risks.
Key Words: Vancomycin,Continuous infusion,Scoping review,Case series,Nephrotoxicity

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P615

Pharmacokinetics of first-line antituberculosis drugs in Thai elderly patients with tuberculosis infection

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Biography:

Weeraya Phaisal is a researcher at the Center of Excellence in Clinical Pharmacokinetics and Pharmacogenomics and the Center for Medical Diagnostic Laboratories, Faculty of Medicine, Chulalongkorn University. Her research focuses on clinical pharmacokinetics and pharmacogenomics. She earned her Ph.D. from Chulalongkorn University and has five years of experience in method development and therapeutic drug monitoring of anti-infective drugs.

At this conference, Weeraya will present her study on the pharmacokinetics of first-line antituberculosis drugs in elderly Thai patients with tuberculosis infection, which investigates the pharmacokinetics of four first-line anti-TB drugs in this patient population. She looks forward to engaging with others, exchanging knowledge, and fostering future collaborations.

Background: Elderly patients with tuberculosis (TB) are at increased risk of adverse reactions to anti-TB drugs. With the growing number of elderly population and rising TB incidence in advanced age, managing anti-TB therapy in older adults presents unique challenges compared to younger patients.
Aims: This study aims to characterize the pharmacokinetics of four first-line anti-TB drugs in elderly Thai patients with active TB.
Methods: Twenty elderly TB patients receiving isoniazid (INH), rifampicin (RIF), ethambutol (EMB), and pyrazinamide (PZA) for at least four weeks underwent serial blood sampling at pre-dose (0) and 1, 2, 4, 6, 8, and 12 hours post-dose. Drug concentrations were quantified using a fully validated LC-MS/MS method, and pharmacokinetic parameters were analyzed via non-compartmental analysis. Adverse reactions were also assessed.
Results: INH reached peak plasma concentration (Cmax) in 1 hour with an apparent oral clearance (CL/F) of 0.48 L/hr/kg. RIF, EMB, and PZA had a median Tmax of 2 hours, with CL/F values of 0.25, 0.58, and 0.05 L/hr/kg, respectively. Considerable inter-individual variability was observed in drug plasma concentrations. Adverse reactions were reported in 30% of patients, including mild maculopapular rash (20%), mild transaminitis (5%), and asymptomatic drug-induced liver injury (5%).
Conclusions: This study provides pharmacokinetic data on first-line antituberculosis drugs in elderly Thai patients. Given the variability in drug exposure, therapeutic drug monitoring is recommended to optimize efficacy and minimize complications.
Keywords: Pharmacokinetics, Antituberculosis drugs, Elderly, Therapeutic Drug Monitoring

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P616

Therapeutic Drug Monitoring on Vancomycin Levels in Adult Patients at HuaHin Hospital

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Biography:
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Background: Therapeutic Drug Monitoring (TDM) of vancomycin is essential for optimizing efficacy and minimizing toxicity, particularly in renal impairment patients. The role of pharmacists in monitoring vancomycin levels and adjusting doses.
Aims: To evaluate the impact of pharmacist-led TDM on vancomycin monitoring and dosing appropriateness in empiric and documented therapy across different renal function groups.
Methods: A retrospective study was conducted on 347 hospitalized patients. Patients were categorized based on renal function. Pharmacists monitored vancomycin levels and provided recommendations to physicians. The proportion of patients achieving target therapeutic levels was compared across groups, and the influence of renal function impairment on drug levels was analyzed.
Results: Among 347 patients with 782 prescriptions. Mean age of 59.78 ± 17.30 years. ICU admissions accounted for 27.67%. Renal function distribution included 40.35% normal, 35.73% CKD, and 23.92% ESRD. Empiric treatment was indicated in 74.04% of cases. Vancomycin levels were within the target in 25.96%, below target in 32.35%, and above target in 41.69%. Patients with normal renal function had subtherapeutic levels in 45.80% ($p < 0.001$), while CKD and ESRD groups had supratherapeutic levels of 51.04% and 47.72% ($p < 0.001$), respectively. Renal impairment significantly influenced vancomycin levels.
Conclusions: Vancomycin TDM is crucial for optimizing treatment outcomes, particularly in renal impairment. Implementing pharmacist-guided initial dose adjustments may improve target level attainment, especially in renal impairment patients, reducing toxicity risks and enhancing therapeutic success. This study supports the importance of standardized monitoring protocols for vancomycin therapy.
Keywords: Vancomycin, Therapeutic Drug Monitoring, Pharmacist

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P617

Prediction of Trough-Based Vancomycin Area-under-the-curve: Performance Evaluation of Pediatric Population Pharmacokinetic Models

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Biography:
Stef Schouwenburg is a Pharmacist-Researcher from Rotterdam, The Netherlands. He works at the Department of Hospital Pharmacy in the Erasmus University Medical Center.

Background: In pediatric patients, vancomycin plays a pivotal role in combating infections, necessitating precise therapeutic drug monitoring to ensure efficacy and safety. The adoption of model-informed precision dosing (MIPD) has demonstrated potential in optimizing dosing strategies based on the area under the concentration-time curve (AUC24h).
Aims: To evalute predictive performance of population pharmacokinetic models using only trough concentrations to estimate AUC24h.
Methods: Predictive performance of 23 vancomycin population pharmacokinetic models was retrospectively evaluated in two cohorts; (A) 21 subjects with PNA<50 days, (B) 124 subjects with PNA≥50 days. Multiple scenarios were investigated using; (a) peak and trough concentration, (b) using either peak or (c) trough concentration solely, (d) covariate information (a priori). The median AUC24h per subject across all models was used as 'true' AUC24h.
Results: For both cohorts, relative root mean square error (rRMSE) for the AUC24h precision using only trough concentrations was similar to the rRMSE using both a peak and trough sample. For cohort A, the model by Chen, Colin, and Mehrotra showed best trough-based performance with the lowest relative Bias (rBias) (-3.3% and -2.6%) and rRMSE (6.8% and 7.3%). For cohort B, the models from Alsultan and Lv illustrated the lowest rBias (1.75% and -5.4%) and rRMSE (16.6% and 15.1%).
Conclusions: This study illustrates that trough concentration-based AUC24h estimation is a feasible approach in vancomycin MIPD. These findings endorse the selected models for advanced MIPD vancomycin therapy in pediatrics, though further investigation into clinical outcomes is recommended.
Key Words: Vancomycin, External evaluation, Population pharmacokinetics, AUC, Pediatrics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P618

Comparing bioavailability of two itraconazole formulations in transplant recipients

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Biography:

Dr. Jana Stojanova is a Senior Scientist at St Vincent's Hospital Sydney and holds a conjoint Senior Lecturer appointment at the University of New South Wales (UNSW). Her research focuses on optimizing medicine use through clinical pharmacology, therapeutic drug monitoring, and pharmacogenomics. She completed her PhD at INSERM's Pharmacology of Immunosuppressants in Transplantation Unit in Limoges, France, investigating pharmacogenetic risk factors in post-transplant lymphoproliferative disease. Her work spans multiple international settings, having held positions in Australia, France, and Chile, including as Associate Professor of Pharmacology at the University of Valparaiso Medical School. Dr. Stojanova is an active member of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and currently serves as co-chair of the 2025 Congress.

Background: Itraconazole is commonly prescribed for antifungal prophylaxis in transplant recipients. Two capsule formulations (Lozanoc® and Sporanox®) are available with a suggested 2:1 bioavailability ratio, but this relationship has not been confirmed in complex patients.
Aims: To compare the relative bioavailability between Lozanoc® and Sporanox® in transplant recipients and identify factors influencing itraconazole concentrations.
Methods: We constructed a relational database using retrospective therapeutic drug monitoring (TDM) data from transplant recipients at St. Vincent's Hospital Sydney (2016-2024). Trough concentrations, administration data, and patient characteristics were analysed when both formulations were administered at 200mg twice daily. Generalized linear mixed models (GLMMs) were used to account for repeated measurements within patients and to identify factors influencing dose-normalized concentrations over time.
Results: We included 362 trough concentrations from 103 patients in analyses. The mean first concentration ratio (Lozanoc®/Sporanox®) was 1.06, suggesting similar initial bioavailability despite the expected 2:1 ratio. The weighted mean concentration normalized to dose ratio was 1.85. GLMM analysis revealed Lozanoc® concentration increased significantly over time (0.069 ng·mL^{-1}/mg daily), while Sporanox® decreased (-0.054 ng·mL^{-1}/mg daily). H2 antagonists and food/fluid intake symptoms reduced Sporanox® concentrations but had less impact on Lozanoc®.
Conclusions: The theoretical 2:1 bioavailability ratio between formulations does not apply in complex patients, particularly early post-transplant. These findings highlight the importance of TDM for both formulations and suggest current dosing equivalence recommendations need reconsideration in this context.
Keywords: itraconazole, bioavailability, transplant, therapeutic drug monitoring, antifungal, pharmacokinetics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P619

Flucloxacillin induces itraconazole clearance: three illustrative cases

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Biography:
Dr. Jana Stojanova is a Senior Scientist at St Vincent's Hospital Sydney and holds a conjoint Senior Lecturer appointment at the University of New South Wales (UNSW). Her research focuses on optimizing medicine use through clinical pharmacology, therapeutic drug monitoring, and pharmacogenomics. She completed her PhD at INSERM's Pharmacology of Immunosuppressants in Transplantation Unit in Limoges, France, investigating pharmacogenetic risk factors in post-transplant lymphoproliferative disease. Her work spans multiple international settings, having held positions in Australia, France, and Chile, including as Associate Professor of Pharmacology at the University of Valparaiso Medical School. Dr. Stojanova is an active member of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and currently serves as co-chair of the 2025 Congress.

Background: Itraconazole is a triazole antifungal metabolized by CYP3A4. Drug interactions resulting in increased metabolism can lead to subtherapeutic concentrations and treatment failure. Flucloxacillin is known to induce CYP450 enzymes, and the impact on voriconazole, a CYP2C19 substrate, is particularly marked; however, the interaction continues to be disputed. Case reports (posaconazole, isavuconazole) and case series (tacrolimus) suggest CYP3A4 substrates are affected. There are currently no reports about the interaction affecting itraconazole.
Aims: To describe the impact of concurrent flucloxacillin therapy on itraconazole concentrations and provide evidence for this clinically significant drug interaction.
Methods: We identified three patients receiving concurrent itraconazole and flucloxacillin, with itraconazole concentrations available pre-, during and post-flucloxacillin treatment. All patients had methicillin-sensitive Staphylococcus aureus infections requiring flucloxacillin. Itraconazole trough concentrations were measured regularly and analysed in relation to dose adjustments.
Results: Two patients had therapeutic itraconazole concentrations (500-1000ng/mL) before flucloxacillin, however all demonstrated subtherapeutic concentrations despite standard or increased dosing during co-treatment. Similar to voriconazole, a notable impact on itraconazole concentrations became apparent approximately one week after flucloxacillin initiation. The interaction occurred independently of the flucloxacillin administration route. One case exhibited undetectable itraconazole concentrations despite standard dosing. The interaction was consistent across different formulations (Sporanox, Lozanoc).
Conclusion: This case series provides evidence that flucloxacillin significantly reduces itraconazole concentrations through CYP3A4 induction. An alternative anti-staphylococcal agent, such as cefazolin, is recommended as metabolic induction affects most alternative antifungal agents.
Keywords: itraconazole, flucloxacillin, drug interaction, CYP3A4, therapeutic drug monitoring, antifungal

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P620

Inflammation-driven variability in drug metabolism: Insight from voriconazole treatment

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Biography:

Jesse Swen PharmD, PhD is a full professor of clinical pharmacy, in particular translational pharmacogenetics. He works as a clinical pharmacist-clinical pharmacologist at the Department of Clinical Pharmacy & Toxicology, Leiden University Medical Center where he is the chair of the laboratory of the hospital pharmacy.

The long-term central goal of his career is to improve the outcomes of drug treatment by gaining a better understanding of the genetic mechanisms that result in inter-individual variability in drug response. To this end, he is working on the following research topics:

•Dissecting the impact of rare, structural and regulatory variants on drug absorption, distribution, metabolism, and excretion (ADME)

•Elucidating the mismatch between the drug metabolizer genotype and the capacity of an individual to metabolize drugs (phenoconversion).

•Translating pharmacogenomics to patient care.

This work is seamlessly integrated with his work as chair of the pharmacy laboratory. He has (co-) authored more than 200 (Web of Science indexed) articles in international peer reviewed scientific journals and several chapters in books. He is one of the primary investigators of the "Ubiquitous Pharmacogenomics" project (www.upgx.eu) and leader of the PREPARE trial that assessed the clinical utility of pharmacogenetics panel testing across 7 European sites. In addition, he is an active member of the Dutch Pharmacogenetics Working Group (DPWG) and the US Clinical Pharmacogenetics Implementation Consortium (CPIC).

Background: Voriconazole is widely used to prevent fungal infections in patients receiving a hematopoietic stem cell transplantation (HSCT). The drug shows highly variable pharmacokinetics, and TDM is used to guide dosing. Voriconazole is extensively metabolized by CYP2C19. Both genetic variation and inflammation have been shown to influence CYP2C19-activity. Together these factors can lead to phenoconversion. However, both factors are currently disregarded and not incorporated into hematologic guidelines.

Aim: Here, we investigated the effect of CYP2C19 drug metabolizer phenotypes in HSCT patients receiving voriconazole in absence and presence of inflammation. Moreover, the influence of inflammation on target attainment and the association between inflammation and CYP2C19 activity was explored.

Methods: We analyzed CYP2C19 metabolizer phenotypes of 126 HSCT patients from the Biobank Hematologische Ziekten (LUMC) receiving voriconazole in the absence and presence of inflammation defined as CRP >10 mg/L .

Results: Higher (dose-corrected) voriconazole concentrations were observed during inflammation (LMM p=<2e-16, effect size of phenotype β=-5.99e-02 mg/L per mg voriconazole; CRP β=1.54e-03 mg/L). During inflammation, the frequency of supra-therapeutic levels of voriconazole increased, while the frequency of sub-therapeutic levels decreased (χ2-test p=0.0080). Finally, a subgroup analysis of 25 patients with longitudinal follow-up including data prior- during, and post-inflammation, showed that voriconazole levels changed in parallel to inflammatory status.
Conclusions: Our data confirm the combined effect of inflammation and CYP2C19 genotype on voriconazole metabolism, and suggest TDM to prevent supra-therapeutic voriconazole levels during inflammation is most beneficial in CYP2C19 IMs and RMs.
Key: Voriconazole, CYP2C19, Inflammation, phenoconversion, TDM, HSCT

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P621

Trough Targets for Amikacin and Gentamicin in Clinical Setting: A Scoping Review

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Biography:

Jian Wei is a dedicated pharmacist with two years of experience at Sengkang General Hospital. He has a strong passion for clinical pharmacy, where he plays an active role in the medication management for patients. Jian Wei ensures that each patient receives optimal and safe pharmaceutical care by tailoring medication plans to meet individual needs. His close collaboration with healthcare professionals allows him to contribute meaningfully to patient care, offering his expertise to optimize treatment outcomes. During his time at Sengkang General Hospital, Jian Wei has earned recognition for his meticulous approach and unwavering attention to detail in patient care. His dedication to enhancing patient well-being is evident in his work, from medication counseling to managing complex treatment regimens. Though early in his career, Jian Wei is driven by a strong commitment to excellence, continuously striving to make a lasting, positive impact on the lives of his patients.

Background: Amikacin and gentamicin are key aminoglycosides against multidrug-resistant infections, with trough monitoring used to minimize toxicity. These target recommendations vary due to outdated pharmacokinetic data and differing dosing strategies across patient populations. This inconsistency is compounded by differences in dosing strategies based on monotherapy or synergistic therapy.

Aims: This scoping review examines trough targets and their clinical implications, aiming to reconcile pharmacokinetic and clinical evidence to enhance the precision of amikacin and gentamicin trough monitoring in practice.

Methods: Search on PubMed and EMBASE were conducted from inception till 01/10/2024 using keywords that encompassed “aminoglycosides”, “therapeutic drug monitoring”, “ototoxicity” and “nephrotoxicity”. Articles reporting the trough levels with pharmacokinetic parameters and/or patient-related clinical outcomes (adults) were included.

Results: A total of 22 clinical studies were identified. For the context of this study, extended interval dosing of aminoglycosides is considered over the traditional multiple-daily doses. Intravenous amikacin (15mg/kg/dose) achieving an optimal trough of <5mg/L, and gentamicin (7mg/kg/dose) achieving an optimal trough of <1mg/L; both levels were associated with reduced nephrotoxicity and ototoxicity while maintaining efficacy. Higher doses respectively, often exceed the toxicity threshold. Extending dosing intervals, rather than dose reduction, in renal-impaired patients can help achieve target peak concentration for optimal killing effect while minimizing toxicity.

Conclusion: Optimal trough targets for amikacin (<5mg/L) and gentamicin (<1mg/L) at recommended doses reduce toxicity while preserving efficacy. Extending dosing intervals, rather than dose reduction, is a key strategy to mitigate toxicity, particularly in renal-impaired patients.

Keywords: Aminoglycosides, Amikacin, Gentamicin, therapeutic drug monitoring, trough targets, infections

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P622

Safety and Efficacy of High-Dose Novel Beta-Lactam/Beta-Lactamase Inhibitor (HDNBLBLI) Combinations

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Biography:

Mr Tan Jun Jie graduated with a Bachelor's Degree in Pharmacy (Distinction) from the National University of Singapore (NUS) in 2019, and is board certified in Pharmacotherapy (BCPS) since November 2024. An Infectious Diseases enthusiast with a heart for the people, he now practices as an Antimicrobial Stewardship Unit pharmacist in Singapore General Hospital, where he is a strong advocate for the appropriate use of antimicrobials for patients. Mr Tan has published peer-reviewed manuscripts, including the safety and efficacy of ceftazidime in patients labelled with penicillin allergy. He aspires to be a specialist pharmacist (Infectious Diseases) in the future, and intends to pursue the NUS Doctor of Pharmacy programme.

Background: Adequate antibiotic exposure is crucial when managing multidrug-resistant infections. HDNBLBLI may improve tissue penetration, clinical outcomes and prevent further resistance development. However, there is limited data on HDNBLBLI usage exceeding literature recommendations (ELR).

Aims: We evaluated safety and efficacy of HDNBLBLI.

Methods: Adult patients (≥16 years) receiving ceftazidime-avibactam or ceftolozane-tazobactam ELR, who underwent therapeutic drug monitoring (TDM) in Singapore General Hospital from 2020 to 2025 were included. Primary efficacy outcome was achieving personalized therapeutic unbound serum BLBLI targets (PT). Secondary efficacy outcome was 30-day infection-related mortality (IRM) after HDNBLBLI initiation. Safety outcomes included adverse drug reaction from HDNBLBLI usage (hepatotoxicity, neurotoxicity, diarrhea).

Results: There were 21 patients (median age 58 years [IQR:55-64]); 33% were bacteremic. Most were on culture-directed HDNBLBLI for multi-drug resistant organisms (carbapenem-resistant Enterobacterales [47.6%], Pseudomonas aeruginosa [23.8%], Acinetobacter baumannii [14.3%]) - Ceftazidime MIC 0.5-4mg/L; Ceftolozane MIC 4-8mg/L. Most patients had soft tissue infection and pneumonia (28.6% each). 61.9% patients had renal impairment (9 hemodialysis [HD]; 4 continuous renal replacement therapy [CRRT]). Majority (80.9%) received ceftazidime-avibactam: Ceftazidime-avibactam daily doses [DD] were 10-15g (normal renal function [NRF]), 2.5-7.5g (HD) and 7.5g (CRRT); Ceftazidime (median peak 92.7mg/L [IQR:72.5-113.5mg/L]; median trough 53.2mg/L [IQR:34.6-66.2mg/L]), Avibactam (median peak 19.4mg/L [IQR:13.1-27.4mg/L]; median trough 11.6mg/L [IQR:5.7-14.7mg/L]). Ceftolozane-tazobactam DD were 12-24g (NRF), 2.25g (HD) and 12g (CRRT);

Ceftolozane (peak 52.6-218.9mg/L; trough 33.4-114.8mg/L); Tazobactam (peak 12.9-86.3mg/L; trough 2.3-41.1mg/L). Most (85.7%) patients achieved PT. None developed adverse reactions or IRM.
Conclusions: TDM-guided HDNBLBLI is safe and efficacious.
Keywords: Ceftazidime-avibactam, Ceftolozane-tazobactam, Beta-lactam, Beta-lactamase inhibitor, High-dose therapy, Multidrug resistance

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P623

Exceeding conventional recommendations: safety of high-dose-beta-lactam (HDBL) in renal replacement therapy (RRT)

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Biography:
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Background: Renal impairment, either acute kidney injury (AKI) or chronic end-stage renal failure (ESRF), is common among septic patients. While renal dose adjustment recommendations exist for beta-lactams, they may not be relevant due to rising antimicrobial resistance and technological advancements in RRT.
Aims: We evaluated safety of HDBL exceeding literature recommendations (ELR), in patients requiring RRT.
Methods: Adult patients (≥16 years old) who required RRT, and received therapeutic drug monitoring (TDM)-guided HDBL ELR in Singapore General Hospital were recruited from 2016 to 2025. Safety outcomes included adverse drug reaction (hepatotoxicity, neurotoxicity, diarrhea and death within 30 days of HDBL initiation).
Results: Thirty-eight patients (median age 59 years [IQR:55.3-73]) were included. Majority were Chinese (57.9%) and male (63.2%). Patients required RRT due to AKI (50%) or ESRF (50%). Most (52.6%) had residual urine and/or extrarenal output >500mL daily; 47.4% were on culture-directed therapy for multi-drug resistant organisms; 34.1% had body mass index >30kg/m². Forty-three beta-lactam levels were drawn: 20 meropenem (median trough [MT]:25.2mg/L [IQR:19.7-28mg/L]; daily dose (DD) 2g for peritoneal dialysis [PD] and hemodialysis [HD], 4-8g for continuous renal replacement therapy [CRRT]); 11 ceftazidime-avibactam (ceftazidime MT:53.2mg/L [IQR:39.8-63.8mg/L]; avibactam MT:14.2mg/L [IQR:11.1-17.8mg/L]; DD 7.5g [CRRT], 2.5-7.5g [HD]); 5 aztreonam (MT:143.6mg/L [IQR:99-181.6mg/L]; DD 6g [PD], 3-8g [HD]); 3 piperacillin-tazobactam (piperacillin trough range 126.7-140.2mg/L, tazobactam trough 32mg/L; DD 13.5g [HD]); 2 cefepime (DD 2g [HD]); 2 ceftolozane-tazobactam (trough 114.8/41.1mg/L; DD 2.25g [HD], 12g [CRRT]). None developed safety concerns.
Conclusions: TDM-guided HDBL ELR is safe for patients requiring RRT.
Keywords: Dialysis, High-dose, Beta-lactam, Safety

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P624

High-dose-beta-lactam (HDBL) in patients without renal impairment: How high can we go?

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Biography:

Mr Tan Jun Jie graduated with a Bachelor's Degree in Pharmacy (Distinction) from the National University of Singapore (NUS) in 2019, and is board certified in Pharmacotherapy (BCPS) since November 2024. An Infectious Diseases enthusiast with a heart for the people, he now practices as an Antimicrobial Stewardship Unit pharmacist in Singapore General Hospital, where he is a strong advocate for the appropriate use of antimicrobials for patients. Mr Tan has published peer-reviewed manuscripts, including the safety and efficacy of ceftazidime in patients labelled with penicillin allergy. He aspires to be a specialist pharmacist (Infectious Diseases) in the future, and intends to pursue the NUS Doctor of Pharmacy programme.

Background: With rising antimicrobial resistance, beta-lactam dosing regimens recommended by literature may no longer be relevant. HDBL exceeding conventional recommendations (ECR) may increasingly be necessary to ensure adequate tissue penetration and clinical success.
Aims: We evaluated safety of HBDL in patients without renal impairment.
Methods: Adult patients (≥16 years old) with creatinine clearance ≥50mL/min, who received HDBL ECR, and underwent therapeutic drug monitoring (TDM) in Singapore General Hospital from 2016 to 2024 were included. Safety outcome includes adverse drug reaction (hepatotoxicity, neurotoxicity, diarrhea and death within 30 days of HDBL initiation).
Results: Sixteen patients (median age 45 years [IQR:32-59]) were included. Majority were Chinese (62.5%) and male (68.8%). Most (87.5%) were on culture-directed therapy for multi-drug resistant organisms; 25% had body mass index >30kg/m². Median daily urine and extrarenal output were 2680mL [IQR:1930-3050mL] and 640mL [IQR:110-1295mL] respectively. Nine (56.3%) patients had inadequate beta-lactam levels on conventional beta-lactam dosing regimen and require HDBL. A total of 20 beta-lactam levels were drawn while patients were on HDBL (i.e. total daily dose of 8-24g for meropenem, 10-15g for ceftazidime-avibactam, 8-12g for cefepime, 27g for piperacillin-tazobactam, 12-24g for ceftolozane-tazobactam). There were eight meropenem levels (median trough (MT):17.4mg/L [IQR:10.4-25.1mg/L]); 5 ceftazidime-avibactam levels (ceftazidime MT:57.2mg/L [IQR:37.2-78.5mg/L]; avibactam MT:7.9mg/L [IQR:4.9-10.5mg/L]); 3 cefepime levels (cefepime MT:41.3mg/L [IQR:36.4-60.7mg/L]); 2 piperacillin-tazobactam levels (piperacillin trough range (TR) 28.2-125mg/L; tazobactam TR 6.1-60mg/L); 2 ceftolozane-tazobactam levels (ceftolozane TR 33.4-70.8mg/L; tazobactam TR 2.3-9.5mg/L). None developed adverse concerns.
Conclusions: TDM-guided HDBL ECR is safe.
Keywords: Augmented clearance, Therapeutic drug monitoring, High-dose, Beta-lactam, Safety

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P625

Trovafloxacin activates inflammasome leading to trovafloxacin induced immune related liver injury

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Biography:
Dr. Saori Tanaka is an Associate professor of Department of Pharmacotherapeutics and Toxicology at Faculty of Pharmacy, Osaka Medical and Pharmaceutical University. She completed her master's degree in 2008 at Osaka Medical and Pharmaceutical University and began her career as a researcher at the Shin Nippon Biomedical Laboratories, Ltd. She then moved to Osaka Medical and Pharmaceutical University as an Assistant Professor. In 2016, she received her PhD in pharmaceutical Sciences.
Her research focuses on elucidating the mechanisms of idiosyncratic drug induced liver injury using human cell lines or PD-1 functional knockout mice model and identifying potential biomarkers.
She is the author or co-author of approximately 20 peer-reviewed manuscripts. Dr. Tanaka is a member of the following academic societies: International Association of Therapeutic Drug Monitoring & Clinical Toxicology (IATDMCT), Japanese Society of Therapeutic Drug Monitoring (JSTDM), Society of Toxicology (SOT), and Pharmaceutical Society of Japan.

Background: Trovafloxacin (trova), which is a quinolone antibiotic agent, was withdrawn from a global market because of serious liver injury. Trova is known to cause idiosyncratic liver injury as severe adverse events. However, the mechanism of pathogenesis is unknown. On the other hand, we have reported that reactive metabolite induces the release of damage-associated molecular patterns （DAMPs） that activate immune cells, which causes the idiosyncratic drug-induced serious adverse effects.
Aims: We tested whether trova or its reactive metabolites can activate inflammasomes in the human hepatocarcinoma functional liver cell-4 (FLC-4) cells and the human macrophage cell line (THP-1 cell).
Methods: FLC4-cells were cultured with 3.0-30 μM trova for 7 days. The supernatant from the FLC-4 cells was added to THP-1 cells, which was incubated for 24 hr. These supernatants were used for measurement of IL-1β production and caspase-1 activity. One-aminobenzotriazole (ABT, 1 mM) and Ac-YVAD-cmk (YVAD, 1 μM) were used to inhibit cytochromes P450 activities and caspase-1 activity, respectively. The protein of DAMPs were measured by the western blotting.
Results: The supernatant from an incubation of FLC-4 cells with trova increased the IL-1β production and caspse-1 activity of THP-1 cells. In addition, this increases were inhibited by adding ABT or YVAD. HSP40 was significantly increased in the supernatants from FLC-4 cells incubated with trova.
Conclusions: These results demonstrated that the reactive metabolite of trova can cause the release of HSP40 and activate inflammasomes, which can cause immune-related adverse events.
Keyword: trovafloxacin, idiosyncratic drug induced liver injury, reactive metabolite, DAMPs, inflammasome

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P626

Using daptomycin in neonates: exposure and target attainment

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Biography:
Marie-CLémence VErdier is assistant professor in Rennes university hospital since 2012. Her activity is focused on TDM with a special interest in the exposure-effect relationship study of anti-infectious drugs.

Background: Due to an epidemic of vancomycin-resistant Staphylococcus haemolyticus infections in neonatology, daptomycin is increasingly used in this population in probabilistic treatment. Little is known about daptomycin exposure in this context.
Aim: We report on a case series of patients who benefited from therapeutic drug monitoring (TDM) of daptomycin in our hospital between oct2024 and Jan2025.
Method: Neonates suspected of having a low-susceptibility to vancomycin, daptomycin-susceptible infection were treated with daptomycin 6 mg/kg/12h, in 1h infusions. Trough (Cmin) and 1h post-infusion (Cmax) plasma concentrations were measured by LC-MS/MS whereas AUC0-24h (=AUC0-12h*2) were approximated by trapezoidal method (no pop-PK-model available in neonates). The PK-PD targets were Cmin<24.3µg/mL for toxicity and AUC/MIC>666µg.h/mL for efficacy.
Results: Fifteen neonates benefited from TDM (4♀, 11♂), one child was treated for 2 separate infectious episodes. S.haemolyticus was identified in 9 cases with an MIC of 0.25mg/L (no germ found in the other 7 cases). Median [min-max] Cmax was 36.7µg/mL [12.4-60.6] (n=10). Median Cmin was 14.9µg/mL [4.8-41.9], 4/16 were above the recommended threshold. Median AUC0-24h was 541.6µg.h/mL [206.4-1134] (n=10). The PK-PD target for efficacy was achieved in 9 patients but can't be evaluated for the others. No adverse events attributable to daptomycin were identified during treatment or up to the end of hospitalization. Daptomycin was never discontinued for lack of efficacy, two children died unrelated to the infection.
Conclusion: Daptomycin was safely used in children, but the appropriateness of the dosing regimen still needs to be assessed to ensure PK-PD target attainment.
Keywords: daptomycin, neonates, exposure

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P627

Pharmacokinetic analysis of tedizolid on protein binding in humans and in vitro

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Biography:

Tomona Yamada is an undergraduate student in the Laboratory of Clinical Pharmacometrics at the School of Pharmacy, Nihon University. She has been accepted into the doctoral program starting next year. Under the mentorship of Professor Yasuhiro Tsuji, she specializes in clinical pharmacology and pharmacometrics. Her research focuses on optimizing antimicrobial therapy through target concentration intervention, aiming to individualize dosing strategies based on patient-specific infection characteristics and treatment responses.

Background: Tedizolid (TZD) is a novel oxazolidinone anti-MRSA agent that primarily binds to plasma albumin. Approximately 90% of TZD is protein-bound, leaving about 10% unbound. As albumin levels decrease due to pathological conditions, the unbound fraction (fuB) of TZD is hypothesized to increase.
Aims: This study aimed to quantitatively evaluate TZD protein binding by modeling the relationship between bound (Cb) and unbound (Cu) concentrations using both clinical and in vitro data.
Methods: A total of 93 plasma samples were analyzed from six healthy adults and five patients. Additionally, 72 in vitro samples were prepared by adding TZD to albumin solutions. TZD concentrations were measured using high-performance liquid chromatography. Nonlinear mixed-effects modeling was used to compare linear and nonlinear binding models. This study was approved by the ethics committees of Toyama University Hospital and Nihon University.
Results: Both clinical and in vitro analyses indicated that the relationship between Cb and Cu was best described by a linear model. For clinical data, the model was Cb = Slope × Cu, while for in vitro data, it was Cb = Slope × Alb × Cu. The estimated Slope was 5.64 (clinical) and 0.00406 L/μmol (in vitro). fuB was 0.15 in clinical samples and 0.40 in vitro.
Conclusion: TZD exhibited linear plasma protein binding at clinically relevant concentrations. The 2.7-fold higher fuB in vitro suggests additional plasma protein binding, indicating that TZD also binds to proteins other than albumin.
Keywords: Unbound concentration, NONMEM, Pharmacokinetics, Protein binding, Tedizolid

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P628

Evaluation of Intravenous Vancomycin Pharmacokinetics in Japanese Peritoneal Dialysis Patients

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Biography:

Yoshiki Yamamoto is a clinical pharmacist and the deputy head of department of pharmacy in Sakai City Medical Center. He strives to contribute to improving patient outcomes by supporting infectious disease treatment through blood concentration measurement using HPLC, pharmacokinetic analysis, and drug administration design. He is also a researcher with a strong interest in clinical pharmacology, particularly focused on anti-infective drugs at Osaka University. Currently, he is a member of two committees of IATDMCT: the Anti-Infective Drugs Committee and the Regional Asia-Pacific Section.

Background: Limited information is available regarding the pharmacokinetic parameters of intravenous vancomycin (VCM) in peritoneal dialysis patients.
Aims: This study aimed to investigate the pharmacokinetic parameters of VCM in Japanese peritoneal dialysis patients.
Methods: This study included peritoneal dialysis patients who received intravenous VCM at Sakai City Medical Center from January 2022 to December 2024. Patients undergoing hemodialysis or without serial serum VCM concentration measurements were excluded. Patient data (age, sex, renal function, VCM administration history, and serum VCM concentrations) were extracted from medical records, and pharmacokinetic parameters were calculated.
Results: Seven patients were included. The initial VCM dose was 21.6 ± 2.2 mg/kg, and the administration interval from the second dose was 52.5 ± 13.0 hours. Pharmacokinetic parameters were calculated based on serum concentration measurements, assuming a distribution volume of 1.07 L/kg. The mean elimination rate constant was 0.00583 ± 0.00132 hr^{-1}, mean clearance was 6.58 ± 1.48 mL/min, and the mean half-life was 127.9 ± 29.7 hours. The AUC was 529.9 [277.3–1147.9] mg·hr/mL, with 61.1% (11/19) within the target range of 400 < AUC < 600.
Conclusion: VCM was administered approximately every 48 hours. Frequent serum concentration monitoring may have contributed to stable VCM administration. Larger studies are needed to confirm these results.
Key Words: vancomycin, pharmacokinetic parameters, peritoneal dialysis

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P629

Optimizing Meropenem Regimens in RICU Patients: A Real-World Efficacy Study

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Biography:

The presenter is the Vice President of the Second Xiangya Hospital of Central South University and the Academic Leader of Clinical Pharmacy in Hunan Province. Previously, the presenter served as a Council Member of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT) and currently holds the position of Education Chair.

*With a long-standing dedication to research in Therapeutic Drug Monitoring (TDM) and Clinical Toxicology (CT), the presenter focuses on drug-induced liver injury (DILI) and precision medicine. The main research interests include elucidating the mechanisms of DILI induced by drugs such as Thunder God Vine (*Tripterygium wilfordii*) and anticancer agents like Crizotinib, investigating the hepatoprotective effects of Traditional Chinese Medicine (TCM) compounds such as Licorice, and advancing TDM technologies to enhance clinical medication safety and efficacy.*

Background: It is inadequate to direct evaluation of meropenem pharmacokinetic targets and clinical efficacy. This study aimed to investigate the predictors of meropenem clinical effectiveness and to optimize dosing regimens precisely in the Department of Respiratory and Intensive Care Unit (RICU).
Methods: Patients with severe pneumonia using meropenem in RICU were included. Blood samples were assayed using two-dimensional high-performance liquid chromatography. Logistic regression analysis was conducted to identify predictors of efficacy. Population pharmacokinetics analysis was performed to optimize dosing regimens.
Results: 396 meropenem concentrations from 111 patients were measured. The joint predictor of total protein, platelet, Cpeak, and APACHE Ⅱ score had a good predictive performance on the clinical efficacy ($P < 0.001$). Model-based simulation suggested to administer 2000 mg of meropenem every 8 hours at a 2-hour infusion for the patient with a minimum inhibitory concentration (MIC) of 8 mg/L and a creatinine clearance (CrCL) of 30 ml/min, or at 3-hour infusion for the patient with a MIC of 4 mg/L and a CrCL of 60 ml/min, respectively, which could achieve a probability of target attainment (PTA), with 100% of the time between doses at which the free fraction concentration remains above MIC (%fT>MIC) ≥ 80%. And only at specific MICs and pharmacodynamic targets, did PTAs of the prolonged infusion be significantly different ($P < 0.05$).
Conclusion: High Cpeak caused potential unfavorable outcomes. 2000 mg of meropenem every 8 hours with 2-hour or 3-hour infusion was recommended for patients with severe pneumonia in RICU. The benefits of prolonged infusion were limited.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P630

Analysis of factors affecting posaconazole serum concentration in patients with haematological malignancies

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Biography:

1990 Graduation from Kobe Pharmaceutical University
1991-2025 Department of Pharmacy, Sakai City Medical Center
2007 Master's degree of Mukogawa Women's University School of Pharmacy and Pharmaceutical Sciences
2025- Osaka Medical and Pharmaceutical University Faculty of pharmacy

Background: Posaconazole (PSCZ) is a triazole antifungal agent for the prevention of invasive fungal infections in patients undergoing hematopoietic stem cell transplantation and with hematological malignancies. When the serum concentration is low, there is a possibility of breakthrough infection, insufficient therapeutic effect, or induction of resistant bacteria. When the serum concentration is high, there is a possibility of adverse events such as hypokalemia.
Aims: We investigated the factors affecting the PSCZ serum concentration.
Methods: 39 patients with hematological malignancies were studied. PSCZ serum concentration was determined by HPLC-UV. Univariate and multivariate analyses were used to investigate the factors affecting significantly trough concentration. Genetic polymorphisms of transporters affecting the pharmacokinetics of PSCZ were analyzed.
Results: Patients with diarrhea or a higher PSCZ-glucuronic rate showed low blood concentrations. Based on Spearman's rank correlation coefficient, trough serum concentration was positively correlated with age and total bilirubin and negatively correlated with metabolic rate and diarrhea. From multiple regression analysis, the similar results were obtained.
In patients with a homozygous mutant for SNPs in MRP2 C3972T or two homozygous variants of SNPs in 'MDR1 T3435C, MDR1 T1236C, BCRP G34A', the PSCZ serum concentration was significantly higher, suggesting the possible lower activity of both the inhibition of gastrointestinal absorption and hepatic-biliary excretion of PSCZ.
Conclusions: In order to achieve safe and effective treatments in patients receiving posaconazole, we recommend that TDM be performed taking into account the age, liver function and the occurrence of diarrhea.
Key Words: Posaconazole, diarrhea, glucuronic metabolism, genetic polymorphism of transporters, hypokalemia

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P631

Pharmacokinetics of Imipenem in Critically Ill Patients: Continuous Infusion Versus Extended infusion

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Biography:
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Background: No study has yet explored whether there are differences between the extended infusion (EI) and continuous infusion (CI) dosing regimens in achieving pharmacokinetic/pharmacodynamic (PK/PD) targets and clinical bacteriological effectiveness for imipenem.
Aims: The study aimed to compare the PK/PD parameters of imipenem administered via EI (administered continuously for 2h) versus CI, and to compare the target PK/PD indices.
Methods: Forty critically ill ICU patients, who were administered imipenem either as a targeted or empirical treatment, were divided into two groups: the EI group (1.5g/d [0.5g, q8h] [n=5], 2.0g/d [0.5g, q6h] [n=8], 3.0g/d [1g, q8h] [n=7]) and the CI group (1.5g/d [n=5], 2.0g/d [n=8], 3.0g/d [n=7]), based on their daily dosage. Pharmacokinetic parameters for imipenem were calculated using the Winnonlin software. The primary outcome was to compare the attainment of PK/PD targets.
Results: There were no significant differences in PK parameters between the CI and EI groups (P ＞ 0.05). Overall target attainment of PK/PD indices was higher with CI compared to EI. When the PKPD target value is set to %fT>MIC, with MIC≥4, there is a significant difference between the two groups (75% vs. 100%; P=0.024). When the PKPD target value is %fT>4MIC, with MIC≥1, there is a significant difference between the two groups %fT>4×MIC (75% vs. 100%; P=0.024).
Conclusions: Even though the stability of imipenem limits its use for continuous infusion, continuous infusion of imipenem can better achieve PKPD targets for critically ill patients or pathogens with higher MICs.
Keywords: Imipenem, extended infusion, Continuous Infusion, PK/PD

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P632

Exploring Involvement of the Immune System and Biomarkers in Brigatinib-Induced Liver Injury

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Biography:
Mr. Takumi graduated from the Faculty of Pharmaceutical Sciences at Osaka Medical and Pharmaceutical University. After graduation, he worked as a hospital pharmacist and is currently practicing at Department of Pharmacy, Osaka National Hospital. He is a Board-Certified Oncology Pharmacy Specialist with advanced knowledge and extensive clinical experience in cancer pharmacotherapy. He collaborates with multidisciplinary teams to contribute to the safe and effective delivery of pharmacological treatments for patients. In addition to his clinical practice, he is a PhD candidate at the Laboratory of Pharmacotherapy, Faculty of Pharmaceutical Sciences, Osaka Medical and Pharmaceutical University. His research focuses on elucidating the mechanisms of idiosyncratic reactions, including liver injury induced by molecular-targeted drugs, and identifying potential biomarkers.

Background: Brigatinib is widely used to treat Anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer. However, severe adverse effects associated with brigatinib, such as liver dysfunction, may involve immune system activation.
To evaluate whether brigatinib activates the immune system, we investigated inflammasome activation using THP-1 cells. Additionally, we analyzed whether reactive metabolites activate inflammasomes in THP-1 cells.
Methods: Differentiated THP-1 cells were cultured with brigatinib for 24 hours. FLC-4 cells were cultured with brigatinib for 7 days, and then the supernatant was added to differentiated THP-1 cells and incubated for 24 hours. IL-1β concentration in the THP-1 culture medium was measured using an ELISA kit. Caspase-1 activity was also measured using the Caspase-Glo® 1 Inflammasome Assay. Damage-associated molecular patterns (DAMPs) were evaluated by western blotting using the hepatocyte supernatant.
Results: Treatment of THP-1 cells with brigatinib significantly increased IL-1β production and caspase-1 activity. The supernatant from FLC-4 cells treated with brigatinib also increased IL-1β production and caspase-1 activity. Brigatinib significantly increased the release of heat shock proteins (HSP) 90 and S100A6 from FLC-4 cells.
Conclusions: Brigatinib demonstrated inflammasome activation in THP-1 cells, both directly and through its reactive metabolites. The release of HSP90 and S100A6 from hepatocytes was caused by the reactive metabolites of brigatinib, suggesting a potential role in the development of idiosyncratic liver injury. Serum levels of HSP90 and S100A6 may be potential biomarkers for brigatinib-induced liver injury.
Keywords: Brigatinib, inflammasome, damage-associated molecular patterns, immune-related adverse effects

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P633

Relationship of 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid concentration with OATP1B activity in patients with CKD

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Biography:

*Hiroyuki Ono, B. Pharm., is a pharmacist at the Department of Clinical Pharmacy at Oita University Hospital in Japan. He enrolled in the Ph.D. program at the Oita University Graduate School of Medicine in 2022. In addition to his daily work as a pharmacist, he has been engaged in research in clinical pharmacology and therapeutic drug monitoring. His current research focuses on elucidating the factors behind individual differences in OATP1B activity during pathological conditions using CP-I. He has previously identified OATP1B1*15 and CMPF concentrations as factors influencing OATP1B activity in patients with rheumatoid arthritis (Clin Pharmacol Ther. 2021 Oct;110(4):1096-1105).*

Background and Aims: Organic anion-transporting polypeptides (OATP)1B are drug transporters mainly expressed in the sinusoidal membrane. Many studies have suggested that OATP1B activity is affected by genetic factors, the uremic toxin 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF), and inflammatory cytokines, such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6). This study evaluated the influence of these factors on OATP1B activity in patients with chronic kidney disease (CKD) using coproporphyrin-I (CP-I), an endogenous substrate of OATP1B.
Methods: The study recruited 73 patients with CKD who were not taking OATP1B inhibitors. CP-I and CMPF concentrations were measured by ultra-high-performance liquid chromatography coupled to tandem mass spectrometry, inflammatory cytokines by ELISA, and OATP1B1*15 by real-time PCR.
Results: Plasma CP-I concentration was higher in OATP1B1*15 carriers than in non-carriers (p = 0.003). In all patients, CP-I did not correlate significantly with CMPF, IL-6, TNF-α, or eGFR. However, when the dataset was cut off at CMPF concentrations of 8 μg/mL, 4 μg/mL, 3 μg/mL, or 2 μg/mL, CMPF correlated positively with CP-I, and correlation coefficient tended to be higher as plasma CMPF concentration was lower (rs = 0.264, p = 0.047; rs = 0.344, p = 0.018; rs = 0.342, p = 0.031; rs = 0.409, p = 0.042, respectively).
Conclusions: OATP1B1*15 impacted OATP1B activity in patients with CKD, but IL-6 and TNF-α did not. However, the impact of CMPF on OATP1B activity was limited to low CMPF concentrations, and the effect could be saturated at high concentrations.
Keywords: Organic anion-transporting polypeptides 1B, Coproporphyrin-I, uremic toxin 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P634

Identifying Biomarkers for Acute Diquat Poisoning: Integrated Clinical and Lipidomic Analysis

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Biography:

Shuai Song is an Assistant Professor in the department of Pharmacy at the First Affiliated Hospital of Anhui Medical University. Holding a Ph.D. in Medicine, Shuai Song specializes in herbal medicine pharmacology and therapeutic drug monitoring. Since 2018, he has led projects funded by the National Natural Science Foundation of China and Anhui Provincial University, authoring over 10 peer-reviewed papers. Beyond academic research, Shuai Song is an active member of the Chinese Pharmaceutical Association (CPA), where he participates in national conferences and collaborates with peers to advance pharmaceutical knowledge.

Objective: This study aims to discover predictive biomarkers for acute diquat (DQ) poisoning by analyzing clinical characteristics and lipidomic profiles, ultimately advancing our understanding of toxicological mechanisms and improving patient prognosis
Method: A retrospective study was conducted on 50 cases of acute DQ poisoning admitted or presenting at the First Affiliated Hospital of Anhui Medical University between February 2022 and October 2024. High-resolution mass spectrometry was used to analyze lipid profiles from serum samples of 32 patients. Cox proportional hazards regression models were employed to assess factors associated with prognosis.
Results: Multivariate Cox regression analysis, adjusting for potential confounders such as gender and the need for continuous renal replacement therapy, identified serum DQ levels (HR: 1.379, 95% CI: 1.194–1.593), oral dose (HR: 1.003, 95% CI: 1.002–1.092), and age (HR: 1.063, 95% CI: 1.015–1.114) as significant independent predictors of prognosis. Furthermore, in cases where serum DQ concentrations were unavailable, urine DQ levels (HR: 1.002, 95% CI: 1.001–1.003) and HCO3- levels (HR: 0.865, 95% CI: 0.761–0.984) emerged as significant predictors. Additionally, novel lipid biomarkers were identified, including PC (16:0/20:4) (HR: 1.203, 95% CI: 1.030–1.406), PC (16:0e/18:2) (HR: 0.742, 95% CI: 0.604–0.911), and PE (18:0p/20:3) (HR: 1.151, 95% CI: 1.053–1.257).
Conclusion: Elevated DQ levels and disruptions in kidney function and lipid metabolism significantly impact the prognosis of acute DQ poisoning. The identification of specific lipid biomarkers provides valuable insights for developing personalized treatment strategies to improve patient outcomes.
Keywords: Diquat poisoning, Biomarkers, Clinical analysis, Lipidomics, Prognosis

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P635

Management of Methotrexate (MTX) Toxicity with DILI using TDM Guide

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Biography:

Primary Role ; Quality System Pharmacist (Pharmacy Department,Queen Savang Vadhana Memorial Hospital)

Additional Responsibilities;

- Secretary of the Drug Risk Management Committee (Year 2010-Present)

- Oversight of Medication Error and Adverse Drug Reaction Systems

Background: Methotrexate (MTX) is widely used in autoimmune diseases; however, its narrow therapeutic index increases the risk of toxicity, particularly when misadministration occurs. This case report highlights the management of MTX toxicity with drug-induced liver injury (DILI) in a 24-year-old female with relapsing-remitting multiple sclerosis (RRMS).

Case Presentation: A 24-year-old female with RRMS presented with upper respiratory infection symptoms, mucositis, and elevated liver enzymes after inadvertent ingestion of MTX instead of azathioprine for approximately three weeks. Laboratory findings confirmed significant hepatic transaminitis (AST 128 U/L, ALT 293 U/L) and MTX toxicity. Therapeutic drug monitoring (TDM) guided treatment, showing declining MTX levels. Management included intravenous leucovorin rescue therapy, aggressive IV hydration, serial liver function monitoring, and supportive care. The patient exhibited gradual improvement in liver function and mucositis, with MTX levels declining to <0.01 µmol/L.

Conclusion: This case emphasizes the critical role of TDM and prompt intervention in MTX toxicity. Vigilant medication reconciliation and patient education are essential to prevent dosing errors.

Key Words: Methotrexate toxicity,drug induced liver Injury (DILI),relapsing-remitting multiple sclerosis (RRMS),Methotrexate level,TDM guided treatment

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P636

Internal Quality Control Evaluation of TDM of Levetiracetam by Westgard Multi-rule Theory

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Background: To establish a simple, effective, accurate analysis method forTDM of levetiracetam in serum of patients with epilepsy. Meanwhile, an internal quality control method for TDM of levetiracetam aim to developed to guarantee the analytical quality of the assays.
Methods: HPLC-DAD method for the quantitative determination of levetiracetam has been developed and validated. Levetiracetam quality control products were self-made. The internal quality control results in our laboratory accompanying with TDM of levetiracetam were collected and retrospectively studied. The control charts for Levey-Jennings quality and Z-score were generated using Microsoft Excel. Westgard multi-rules were applied for quality assessment of TDM of levetiracetam.
Results: Calibration curves were linear over a levetiracetam concentration range of 1-80 μg/mL, with a correlation coefficient equal or greater than 0.997. The intra-day and inter-day coefficient of variations of low, medium, and high concentration of levetiracetam were 1.03-6.9%, 1.63-8.19%, respectively, while the extraction recovery rate were 63.72-83.85%, 67.15-83.72%, respectively. The accuracy ranged from 96.26% to 109.31%. Levery-Jennings and Z-score combined with Westgard multi-rules were used to evaluated 20 batches of quality control products and none of them were out of control.
Conclusion: This method is simple, effective and accurate for daily routine use in TDM of levetiracetam. The reliability and accuracy for levetiracetam measurement were improved though developing internal quality control method and the levetiracetam plasma concentration is helpful for further promotion the clinical rational use of the drug.
Key Words: Levetiracetam; therapeutic drug monitoring; HPLC-DAD; internal quality control; Westgard multi-rule theory

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P637

Pharmacokinetic variability of valsartan in a large cohort of hypertensive patients

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Biography:

Tord B. Amundsen is a doctor at the Department of Pharmacology, Oslo University Hospital, Norway. His clinical responsibilities include assessing drug concentrations in patient blood samples and interpreting therapeutic drug monitoring results. Dr. Amundsen's current research focuses on pharmacokinetics-driven personalized medicine in the context of antihypertensive treatment. He is part of a research group working on the optimization of drug therapy using TDM, pharmacogenetic analyses and other outcome measures, as well as the relationship between serum concentrations and effects/side effects of drugs and toxic substance.

Background: Hypertension is one of the leading risk factors for morbidity and mortality. Guidelines recommend lifetime antihypertensive drug therapy to reduce organ damage. Despite lifestyle modifications and pharmacological treatment, a large percent of patients fail to achieve satisfactory blood pressure control - so-called resistant or uncontrolled hypertension. Possible causes include poor adherence and pharmacokinetic variability, both of which can be evaluated objectively with serum drug concentrations.
Valsartan is an angiotensin II receptor antagonist (ARB) and is one of the most prescribed antihypertensives in Norway. Few studies have described the interindividual pharmacokinetic variability of valsartan, and its blood pressure lowering effect, although limited data suggests that high variability for valsartan.
Aims: The main aim of the study was to study the pharmacokinetic variability of valsartan in a large patient population with controlled and uncontrolled hypertension.
Methods: Data was collected between 2017 and 2022 as part of the Individualized blood pressure treatment study (IDA), a national hypertension project. Patients prescribed two or more antihypertensive drugs, one of which was valsartan, were studied. Patient parameters included age, sex, BMI, hip-waist ratio, prescribed medication history, measured serum levels of valsartan, additional biomarkers, blood sample time, blood pressure levels (office and ambulatory), heart rate and cytochrome genotype.
Results: Pharmacokinetic variability for N=1147 hypertensive patients prescribed with valsartan, and the effect of multiple covariates on this variability, will be illustrated. Further results pending.
Conclusions: The study illustrated the pharmacokinetic variability of valsartan based on serum concentration measurement in a large patient population.
Keywords: hypertension, valsartan, TDM

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P638

Association of Leptin rs7799039 with Dyslipidemia and Hypertension: Unraveling Cardiovascular Risk Factors

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Biography:

I'm Asst. Prof. Chalirmporn Atasilp, Ph.D. is a lecturer specializing in hematology and pharmacogenetics at Chulabhorn International College of Medicine, Thailand. My research focuses on pharmacogenetics in 5-fluorouracil (5-FU), specifically investigating the relationship between uracil and dihydrouracil levels and genetic polymorphisms in colorectal cancer patients. Currently, I'm working on genetic polymorphisms associated with cardiovascular disease in metabolic syndrome, aiming to enhance personalized treatment strategies and improve patient outcomes. Through my research, I and my research teams contribute to advancing precision medicine in oncology and cardiovascular diseases, optimizing therapeutic efficacy and patient care.

Background: Leptin is a key hormone involved in energy homeostasis and metabolism, with genetic variations influencing its role in disease susceptibility. The leptin gene polymorphism rs7799039 (G2548A) has been implicated in metabolic disorders, including dyslipidemia and hypertension.
Aims: This study aims to explore the association between rs7799039 of Leptin gene and dyslipidemia and hypertension, which are related to induced cardiovascular disease.
Methods: The rs7799039 polymorphism was genotyped using Real-Time PCR, and clinical outcome data, including lipid profiles and blood pressure measurements, were recorded.
Results: The results reported that patients carrying the homozygous variant (AA) related significantly to dyslipidemia and hypertension (P-value = 0.032, 0.008, respectively).
Conclusions: Evidence suggests that genetic variations in leptin signaling may contribute to lipid metabolism disturbances and blood pressure regulation, potentially leading to an increased risk of cardiovascular diseases.
Key Words: Leptin gene, Metabolic syndrome, Dyslipidemia, Hypertension

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P639

Drug-Drug Interaction Mechanism Between Imatinib and Amlodipine via Four Dimension Analysis

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Biography:

Chen Yan, Ph.D. in Medicine, Associate Chief Pharmacist, and Post-doctoral Researcher at University of Electronic Science and Technology of China (UESTC). She serves as a Master's supervisor at UESTC and an industry adjunct supervisor at Chengdu Medical College, specializing in Pharmacy.
She has been engaged in research on the synergistic reversal mechanism of tumor drug resistance and targeted delivery through integrated Chinese and Western medicine for nearly 10 years. During this period, she has completed one major scientific and technological achievement transformation project (valued at 22.5 million yuan) recognized by the Ministry of Science and Technology; led two general projects of Sichuan Provincial Natural Science Foundation, one project from Sichuan Traditional Chinese Medicine Administration, and over 10 projects from Sichuan Provincial Health Commission, with total funding exceeding 1 million yuan.

Background: In middle-aged and elderly patients predisposed to gastrointestinal stromal tumors, amlodipine (AML) is often used to control blood pressure due to underlying conditions.
Aims: However, the mechanisms underlying the interaction between AML and the anti-tumor drug imatinib (IM) have not been thoroughly investigated.
Methods: Herein, we designed administration a single administration model and a continuous administration model in rats, respectively. Pharmacokinetic parameters and plasma metabolomics were analyzed. Additionally, network pharmacology, molecular dynamics simulations and traditional interaction cell experiments were performed later.
Results: The results indicated that both AUC and Cmax increased when IM and AML were combined. The bile acid pathway was identified as a common pathway for both drugs, and molecular dynamics simulations suggested some degree of self-assembly aggregation between IM and AML. The changes in membrane permeability and organic cation transporter (OCT1) expression confirmed that the interaction of the two drugs not only affected the resistance of the cell membrane, but also received OCT1 regulation.
Conclusions: This study provides important insights and theoretical support for enhancing the clinical efficacy of treatments for gastrointestinal stromal tumors with hypertension for the first time. We suggest that when the two drugs are used together in the clinic, the dosage should be payed more attention.
Keywords: Drug-drug interaction, pharmacokinetic, metabolomics, network pharmacology, molecular dynamics, imatinib

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P640

Application of TDM to pediatric patients treated with Ivacaftor/Tezacaftor/Elexacaftor combination.

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Background: Cystic fibrosis (CF) is an autosomal recessive genetic disorder caused by sequence variations in the gene encoding for the CF transmembrane regulator (CFTR). Pharmacological therapies are mainly symptomatic. “CFTR modulators” have been developed to partially restore defective CFTR protein function.
Aims: Application of TDM to pediatric patients treated with ivacaftor/tezacaftor/elexacaftor combination.
Methods: Samples were collected from n=33 pediatric patients affected by cystic fibrosis with age comprised between 6-18 years. Ivacaftor (IVA), tezacaftor (TEZ) and elexacaftor (ELX) concentrations were simultaneously measured using LC-MS/MS system, in plasma samples collected before (T0) and 4 hours after (T4) a daily drug assumption. For IVA, the area under the curve 0-12 hours (AUC0-12) was calculated after estimating plasma concentration at 12 hours.
Results: For IVA, TEZ and ELX, median concentrations at T0 were 0.85 µg/mL, 1.39 µg/mL and 8.87 µg/mL, respectively. Median concentrations at T4 were 1.57 µg/mL for IVA, 5.02 µg/mL for TEZ and 20.14 µg/mL for ELX. Evaluation of AUC0-12h for IVA revealed a median drug exposure of 12.50 µg/mL*h. A positive linear correlation was found between Cmin and AUC0-24 values for IVA with a Spearman r correlation coefficient of 0.93 (95% CI=0.83-0.97, P<0.001).
Conclusions: Number of blood samples per patient may be reduced since exposure to IVA may be monitored by assessment of Cmin levels. TDM program could improve our knowledge on the sources of PK variability and the safety profile of these drugs in real life, facilitate a more cost-effective patients’ management.
Keywords: TDM, pediatric patients, Cystic fibrosis, LC-MS/MS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P641

Vitamin K2 - a new treatment option for patients with calcific tendinitis

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Biography:

Assoc. Prof. MSc. Eva Klapková, Ph.D. has been working at the Institute of Medical Chemistry and Clinical Biochemistry, Second Faculty of Medicine, Charles University, and Motol University Hospital since 2005. In 2009, she passed her board certification in Investigative Methods in Clinical Biochemistry, and in 2021, she was appointed Associate Professor (habilitation) in Medical Chemistry and Biochemistry at the Second Faculty of Medicine, Charles University. She currently serves as Deputy Head for Research and Science. Her professional focus is primarily on the development of chromatographic methods.

Background: Vitamin K2 (VK2) is a fat-soluble vitamin which plays an irreplaceable role in bone mineralization, and soft tissue calcification. In the process of calcification of soft tissues and bone mineralization, matrix Gla proteins (MGP) and osteocalcin are crucial. VK2 functions as a cofactor of gamma-glutamyl carboxylase, an enzyme which activates vitamin K-dependent proteins.
Aims: The aim of this study was to assess the effect of VK2 on ectopic calcifications, with special regard to the rotator cuff calcification in patients with calcific tendinitis.
Methods: 60 subjects with confirmed diagnosis of calcific tendinitis were supplemented with 120 g/day of VK2 (30 patients) or placebo (30 patients) for 6 months. The subjects were invited periodically every 3 months for blood collection (ALP, creatinine, Ca, P, 25-OH vitamin D, VK2, MGP, dp-uc MGP), X-ray study and clinical examination.
Results: Calcifications disappeared completely or were significantly reduced in 90% of patients supplemented with VK2. After three months of VK2 supplementation we observed significantly increased levels of VK2 ($p < 0.001$). The VK2 median concentration after three months was 1.830 ng/mL in comparison with pre-treatment levels 0.274 ng/mL. Calcifications were reduced in 20% of patients supplemented with placebo. The median VK2 concentration before the treatment was 0.500 ng/mL in comparison with median (0.418 ng/mL) after three months of supplementation.
Conclusions: According to our research VK2 supplementation significantly accelerates the resorption of calcifications in the rotator cuff tendon and muscle tissue.
Keywords: calcific tendinitis, dp-ucMGP, LC-MS, MGP, MK-7, vitamin K2

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P642

Identification of adverse drug reactions as a pharmacovigilance activity at secondary healthcare

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Biography:

Dr. Linggom Kurniaty, Sp.FK. was born in Bandung, on July 21 1974. She is a Lecturer at the Faculty of medicine Universitas Kristen Indonesia since 2018. She is also The Head of the PPRA and KFT Team at a Private Hospital in West Java since 2019. She has acquired a Bachelor's degree and is a professional doctor at the Faculty of medicine Universitas Kristen Indonesia, Clinical Pharmacology Specialist Graduate (Sp. FK) the Faculty of medicine Universitas Indonesia. She is Actively participating in social activities in the health sector in the church and other community

Background: Unwanted drug reactions (Adverse Drug Reactions) are problems that occur unintentionally when administering drugs at therapeutic doses to humans. This undesirable drug reaction can also occur in the hospital. The pharmacy and therapy committee, one of whose tasks is to identify every unwanted drug event, needs to provide education and monitoring so that side effects do not harm patients.
Aims: To identify the incidence of unwanted drug reactions (ADR) in secondary health services and to understand the description of drug side effects that can occur.
Methods: This was a prospective, descriptive qualitative study, by providing education to health workers about the signs or symptoms of unwanted drug reactions and filling out the yellow sheet for reporting side effects of drugs which is submitted to the BPOM Pharmacovigilance Center. The data used is an existing data from a one-year period in 2023
Result: There were 36 patients experienced side effects from the drug. The incidence in children 8/36 (22%) and adults 30/36 (78%). The drug classes that caused the most side effects were NSAIDs (13/40) and cephalosporin antibiotics (11/40).The most incidents were skin: itching, bumps, redness 28/36 (78%). The treatment obtained in this cases were: observation without an additional therapy, antihistamines, corticosteroids or combination therapy.
Conclusion: Adverse Drug Reactions can occur in children and the elderly. From the Data NSAIDs and cephalosporin antibiotics are the two main classes of drugs that cause side effects.
Keywords: Adverse Drug Reactions, Pharmacovigillans, NSAID, Cephalosporin, descriptive qualitative study

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P643

An Audit of Therapeutic-Drug-Monitoring for Older Anti-Seizure Medications in Tertiary Care, India

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Biography:

Dr. Rachna is working as Assistant Professor in department of Pharmacology, AIIMS Bathinda. She has done her MD Pharmacology and DM Clinical Pharmacology from PGIMER Chandigarh. She has interest in PK-PD, Clinical Trials, Therapeutic Drug Monitoring and Evidence based Medicine in patient care. She has various publications in both national and international indexed journals.

Background: The availability of therapeutic drug monitoring (TDM) service is an invaluable resource for individualizing drug therapy for older Antiseizure medication (ASM). In resource-constrained setting, when allocation of funds demands distributive justice, it is imperative to rationalize need for TDM services.
Aims: This audit was intended to evaluate effectiveness of TDM services provided by our center for phenytoin, phenobarbitone or carbamazepine to make process and performance improvements.
Methods: The present study is an audit of TDM requisitions received by the Department of Pharmacology for antiepileptic drugs between Jan 2015 to June 2021. The study was conducted with approval from Institutional Ethics Committee (INT/IEC2017/673).
Results: In total, 934 samples were tested for TDM from 798 patients between January 2015 and June 2021. Phenytoin was most common older ASM for which TDM was requested (59.8%), followed by phenobarbitone (27.4%) and carbamazepine (12.7%). Phenytoin is most common drug for which TDM requests were received from all age groups {adults (68.4%), children (64.7%) and infants (45.3%)} except the neonates. In 54.5% of instances, it was prescribed as monotherapy and in 15.5% as a part of combination ASM regimen. TDM requests received from 31.5% patients exhibited inadequate response. Out of these, nearly 50% of the patients were observed to have drug levels in the previously reported statistical therapeutic range for the drug.
Conclusion: TDM in our study was found to be instrumental in differentiating between drug toxicity and worsening of disease, especially in neonates, where the signs of meningitis would overlap with phenobarbitone toxicity signs.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P644

Characteristics of Metformin Side Effects in Primary Health Care Kramat Jati Indonesia

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Biography:

Hidekel Tambunan, S.Ked, graduated from Universitas Kristen Indonesia in 2024. He is currently pursuing his professional medical education at the same institution. His primary research interest lies in pharmacology, where he aims to contribute to the advancement of innovative treatments and therapeutic approaches.

Mr. Tambunan is an active member of the Asian Medical Students' Association and a participant in the Regional Medical Olympic organized by ISMKI. His experience includes significant involvement in "Organizing Community Participation In Humanitarian Blood Donation Activities," demonstrating a strong commitment to community engagement and public health initiatives. He is highly motivated to leverage his skills and knowledge in support of this research project, with the goal of making a meaningful contribution to the field.

Background: Diabetes Mellitus (DM) is a chronic disease characterized by high blood glucose levels due to insufficient insulin production or ineffective insulin use. According to the International Diabetes Federation (IDF), in 2021, there were 537 million DM cases in adults aged 20-79 years, with a projected increase to 643 million by 2030. DM treatment focuses on medication and lifestyle changes, but research on anti-DM drug side effects remains limited in Indonesia.
Aims: to identify the characteristics of metformin side effects in Type 2 Diabetes Mellitus (T2DM) patients.
Methods: A descriptive study was conducted at Kramat Jati Community Health Center in February 2024. Primary data were collected through direct interviews using questionnaires with 83 T2DM patients who met the inclusion criteria.
Result: The majority of subjects were women 54/83 (65.1%) subjects. The largest age group was 51-60 years (37/83 subjects, 44.6%). Diagnosis duration was mostly 1-3 years and >3 years (35/83 subjects each, 42.2%). Metformin was the most commonly used drug, either as monotherapy (45 subjects, 54.2%) or combined with glimepiride (33 subjects, 39.8%), with the highest dose being 2 × 500 mg/day (45/83 subjects, 54.2%). The most reported side effects were metallic taste and bloating (9/83 subjects each, 10.8%), occurring mostly within six months (30/32 subjects, 93.8%).
Conclusions: in using Metformin for T2DM patients, the common side effects were metallic taste and bloating, mainly occurring within six months.
Key Word: Side effect, Metformin, Metallic taste, Bloating, anti diabetes Oral, Characteristic, Primary Health Care

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P645

Purifying bacteriophages for safe therapeutic applications

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Biography:

Joseph Tucci is a practicing pharmacist and Professor in Clinical Pharmacy at La Trobe University Bendigo. Professor Tucci completed his PhD at the Howard Florey Institute of Experimental Physiology and Medicine, Melbourne, Australia, and then took up a post-doctoral fellowship in the Department of Biochemistry, University of Leicester, U.K. His research interests include:

- *Bacteriophages as alternatives to antibiotics*
- *Personalising medicines for HIV/TB patients in Papua New Guinea*

Background: Bacteriophages, viruses that kill bacteria, are tested in clinical trials as alternatives to antibiotics. Bacteriophage purification is vital to ensure they ‘re free of bacterial endotoxins to prevent adverse events in therapy. There is no gold-standard method for bacteriophage purification. There are several methods for endotoxin detection and quantification. Interleukin Receptor Associated Kinase 3 (IRAK3) is a negative regulator of inflammation.
Aims: Develop novel endotoxin quantification assay
Evaluate effectiveness of bacteriophage purification methods in removing endotoxins.
Determine whether bacteriophage morphotypes impact endotoxin purification efficacy.
Methods: Purification of bacteriophages using Triton X-100, CsCl ultracentrifugation, Pierce™ Endotoxin Removal Resin columns. IL-6 & TNF-α cytokine responses from IRAK3 knockout THP-1 (human monocyte) cells used to measure endotoxin concentrations of crude and purified bacteriophages.
Results: Triton X-100 and CsCl were most effective in reducing cytokine production.
Biphasic standard curves of cytokine production by IRAK3 knockout THP-1 cells: IL-6 had better correlation with low endotoxin concentrations; TNF-α had better correlation with higher concentrations. Endotoxin concentrations in bacteriophage preparations calculated from standard curves: Triton X-100 and CsCl were most effective in endotoxin removal. Bacteriophage morphology did not impact purification efficacy. Triton X-100 resulted in lowest bacteriophage titre loss.
Conclusions: Triton-X 100 was effective at reducing endotoxin concentration and bacteriophage recovery. Novel assay based on IRAK3 knockout THP-1 cells is robust method of predicting immune responses to bacteriophage preparations with wider range of endotoxin detection limits than commercial kits. Bacteriophage morphology didn’t influence efficacy of purification.
Keywords: Bacteriophages, endotoxins, immune response, IRAK3

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P646

Effects of enteral nutrition and components on the valproate pharmacokinetics in rats

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Biography:

She is a scientist with specialized experience in the field of pharmaceutical science focusing on pharmacokinetics and toxicology. Based on her experience working as a clinical pharmacist, she has conducted a lot of research to clarify problems in clinical practice through basic research, and to apply these results in clinical practice. She has mainly researched "Influence of oral enteral nutrients or food administered on many drugs pharmacokinetics", and has published several results. Since 2022, she has been a member of Communication Committee of IATDMCT, creating advertisements for IATDMCT to be published in the TDM journal and other advertising materials.

Background: The interactions between co-administered enteral nutrients (ENs) and drugs reportedly affect the absorption of the respective drugs. However, the gastrointestinal absorption of Valproate (VPA), an antiepileptic drug used worldwide, co-administered with liquid ENs has not been clarified.
Aims: This study measured the plasma VPA level in rats after oral co-administration of VPA with liquid ENs and its components
Methods: VPA 100 mg/kg, dissolved in different ENs (F2α, Racol NF, Ensure Liquid, and Renalen LP) or other components (dextrin, sucrose, degraded guar gum and indigestible), were administered to 7–8-week-old male Sprague Dawley rats. Blood samples were collected from the cannula inserted into the right jugular vein, 0.083, 0.25, 0.5, 0.75, 1, 1.5, and 2 h after VPA administration, then the plasma VPA concentration was measured using high-performance liquid chromatography. The control group was simultaneously administered with water.
Results: The VPA area under the plasma concentration-time curve from 0 to 2 h (AUC0→2h) was significantly lower for the group co-administered with Renalen LP than that of the control group. Furthermore, dextrin and indigestible dextrin especially contained in the Renalen LP also decreased VPA AUC0→2h; however, other liquid ENs and components did not affect the VPA pharmacokinetics.
Conclusions: Co-administration with Renalen LP decreased the gastrointestinal absorption of VPA. Moreover, dextrin and indigestible dextrin in Renalen LP likely contributed to the reduced absorption. Therefore, the composition of liquid ENs may affect the absorption of VPA differently, and these findings would guide the future selection of liquid ENs for orally administered VPA.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P647

Long-term steroid effects on atopic skin: case report of acne and striae.

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Biography:
Dr. Syahfori, a dedicated lecturer at Christian University of Indonesia's Faculty of Medicine, significantly impacts aspiring medical professionals. Her role extends beyond academia, encompassing clinical practice at UKI General Hospital and other medical facilities, demonstrating her unwavering commitment to patient well-being. Her expertise is widely recognized, evidenced by her frequent invitations as a speaker at various events. Notably, she contributed to a dermatology emergency webinar hosted by the Indonesian Ministry of Health, sharing vital knowledge with a broad audience. Furthermore, Dr. Syahfori actively participates in professional development through her membership in the Indonesian Society of Dermatology and Venereology (PERDOSKI). This involvement underscores her dedication to staying abreast of the latest advancements in her field. Through her teaching, clinical practice, and public engagement, Dr. Syahfori consistently works towards advancing dermatological care and empowering both medical practitioners and the general public with valuable knowledge.

Introduction: Inappropriate and unsupervised topical oral corticosteroid use can cause significant dermatologic side effects. We report a case of a 38-year-old female with atopy who developed acneiform eruptions and striae after prolonged misuse of these medications.
Case Presentation: A 38-year-old female with a history of atopy presented with acneiform eruptions and striae. These developed after a year of using topical oral corticosteroids (including 8 mg Methylprednisolone and 0.5 mg Dexamethasone) and 2% Ketoconazole cream to self-treat red patches. The initial lesions, appearing on the chest, were pinhead-sized, reddish, and accompanied by a burning sensation. Lesions increased daily, with itching worsening at night. She also had a history of gastritis, allergies, and asthma. Physical examination revealed multiple discrete miliary-sized monomorphic erythematous maculopapular eruptions on the chest, thighs, back, and left femoral region, with an erythematous plaque on the left brachial region.
Treatment involved stopping corticosteroids and addressing potential complications with antibiotics (100 mg Doxycycline) and topical therapies (3 gr of Clindamycin combined with 110 ml of Acne Feldin as a topical solution). Acneiform eruptions improved, but striae persisted, likely due to decreased collagen synthesis, increased extracellular matrix degradation, epidermal thinning, oxidative stress, and vascular dysfunction.
Conclusion: This case highlights the risks of unsupervised topical oral corticosteroid use, especially in atopic patients. Clinicians should educate patients about proper use and potential side effects, including long-term skin damage, to prevent such complications.
Keywords: Oral Corticosteroids, Adverse Drug Reactions, Acneiform Eruptions, Striae

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P648

Developed and validated LC-MS method for simultaneous detection of bisphenols in saliva.

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Biography:
n/a

Background: Bisphenols, widely used in plastics, epoxy resins, and paper coatings, are endocrine-disrupting chemicals associated with an increased risk of cancer and metabolic disorders.
Aims: This study aimed to develop and validate a liquid chromatography-mass spectrometry (LC-MS) method for detecting BPA, bisphenol S (BPS), and bisphenol F (BPF) in human saliva.
Methods: Saliva samples were spiked with bisphenols and extracted using acetonitrile. An internal standard and ammonium acetate (10 mM) were added, followed by vortexing and centrifugation (3000 rpm,15 min). The supernatant was filtered (0.22 µm nylon syringe filter) and injected into the LC-MS system. Analytes were separated under gradient conditions at a flow rate of 0.4 mL/min and detected at m/z 227.05>212.05 (BPA), 249.0>108.0 (BPS), and 199.10>105.05 (BPF).
Results: The method demonstrated high accuracy (92.7-105.8%) with a linear calibration range of 0.01-100 ng/mL (r2 = 0.995). The lower limits of quantification were 0.01 ng/mL for BPS and BPF, and 0.5 ng/mL for BPA. Accuracy at 0.03, 30, and 70 ng/ml was 102.15 (11.85 %CV), 98.28 (3.23 %CV), and 96.52 (5.39 %CV) for BPS and 107.26 (13.27 %CV), 95.05 (5.37 %CV), and 92.79 (7.98 %CV) for BPF. BPA showed accuracy values of 100.29 (6.87 %CV), 100.71 (5.06 %CV), and 100 (4.73 %CV) at 1.5, 30, and 70 ng/ml, respectively. Matrix effects were 90-116.4% (1-16.5 %CV).
Conclusions: This validated method offers a simple and reliable approach for simultaneously measuring bisphenols exposure in saliva, making it a valuable tool for biomonitoring environmental exposure.
Keyword: Bisphenol, LC-MS, Saliva

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025

21–24 September

Grand Copthorne Waterfront Hotel

P649

Confirming and Quantifying 31 Oral Fluid Drugs of Abuse using Stellar MS

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Biography:

Dr. Jingshu Guo is a trained mass spectrometrist with 15 years of experience in LC-MS-based qualitative and quantitative analyses of small molecules, nucleosides, peptides, and intact protein. After joining Thermo Fisher Scientific, she worked on the method development, implementation, and optimization in clinical and toxicology-related fields. One of her current focuses is to develop fast quantification methods in small molecules, such as biomarkers, therapeutic drugs, and drugs of abuse in biofluids using LC coupled to triple quadrupole MS, quadrupole-linear ion trap MS, or high-resolution MS, and LC-free MS platforms.

Background: As the clinical and forensic communities adopt oral fluid testing for ease of collection and on-site evaluations, the need to detect a broad range of analytes with sufficient sensitivity becomes paramount. Meeting the LOQ targets outlined by SAMHSA demands robust extraction methods and high-performance analytical instrumentation.

Aims: Confirm and quantitate 31 drugs in oral fluid using a 4.5-minute LC-MS method.

Methods: Calibration levels, 0.5 to 200ng/mL, were made in human oral fluid. Calibrators and 10 case study samples were diluted with a preserving buffer and spiked with the internal standards. 500µL of sample were extracted using DPX SPE tips. Analytes were separated on a Vanquish™ Horizon UHPLC system. Data was acquired on the Stellar™ mass spectrometer using targeted-MS2 (tMS2) mode with an inclusion list for the 31 target drugs. Optimized HCD or CID fragmentation was used to provide unique and high-intensity fragments.

Results: Limits of quantitation (LOQ) were determined for the 31 drugs as low as 0.5ng/mL. LOQ was defined as the back calculated concentration where %difference and %RSD were less than 20%. All 31 drugs were confirmed with retention times and MS2 ion ratios. The ability to use HCD or CID fragmentation allowed for optimizing each compound based on most favorable energies and fragments.

Conclusions: This fast, quantitative Stellar mass spectrometry method detected and confirmed 31 drugs of abuse in oral fluid. A complete workflow was presented with LOQ's as low as 0.25ng/mL up to 1,000ng/mL.

Key Words: Drugs of Abuse, Mass Spectrometry, Oral Fluid, Toxicology

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P650

Improved Homogeneous Enzyme Immunoassay for the Quantitative Determination of Methotrexate

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Biography:
Thomas Houts has been leading assay product development for over 20 years. He is currently Sr. Director of Project Management & Special Projects at ARK Diagnostics.

Background: Methotrexate (MTX) is used at high doses (HDMTX, 1,000-33,000 mg/m² by prolonged i.v. infusion) with leucovorin (LV) rescue for a variety of cancers. HDMTX safety is improved by monitoring serum creatinine and MTX levels during renal clearance of MTX, which can initially exceed 1000 µmol/L. Delayed clearance can cause acute kidney injury, further delaying clearance and severe toxicity. MTX is monitored at 12-24h intervals until it drops to a safe level for discharge, ≤0.05 µmol/L. MTX levels during clearance also inform LV dosing. Accurate measurement of MTX, especially at 0.050 µmol/L is an important clinical tool.
Methods: The ARK™ Methotrexate II Assay is a recombinant antibody based homogeneous enzyme immunoassay for the quantitative determination of methotrexate in human serum or plasma on automated clinical chemistry analyzers with an analytical measurement interval (AMI) of 0.030 to 1.30 µmol/L and reportable range up to 1,200 µmol/L by dilution. Performance was demonstrated on the Beckman AU680 analyzer using CLSI evaluation protocols.
Results: Within-lab precision (%CV) at control levels from 0.070 to 0.800 µmol/L was ≤3.0%; Limit of Quantitation (LoQ) was 0.030 µmol/L; deviations from linearity <8% over the AMI. Results for manual and on-instrument dilutions of supplemented samples up to 1200 µmol/L fell within 10% of nominal values. Passing Bablok analysis of the results for 90 patient specimens of the assay vs (LC-MS/MS) was 1.0278 + 0.0000 (r2 = 0.977).
Conclusion: The FDA-cleared ARK™ Methotrexate II Assay demonstrated excellent performance over an expanded AMI of 0.030 to 1.30.
Key words: Methotrexate, Immunoassay

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P651

Cross-Site Validation of LC-MS/MS Assay for Antibiotic Therapeutic Drug Monitoring in Singapore

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Biography:

Emi Ishikawa is a Research Fellow in the Division of Pharmacy at Singapore General Hospital. She received her Ph.D. from Keio University Graduate School of Pharmaceutical Sciences in Japan in 2023. Her current research focuses on developing bioanalytical assays and investigating the pharmacokinetics/pharmacodynamics (PK/PD) of antibiotics to optimise dosing strategies for patients with difficult-to-treat gram-negative bacteria (DT-GNB) infections. She was awarded the "Best Presentation by a Young Researcher Award" at the 31st Annual Meeting of the Japanese Society of Therapeutic Drug Monitoring in 2021.

Background: Difficult-to-treat gram-negative bacteria (DT-GNB) infections pose challenges in antibiotic therapy due to antimicrobial resistance, requiring TDM to optimise antibiotic dosing. LC-MS/MS is a gold-standard technique for antibiotic quantification, but cross-validation between laboratories is essential to ensure reproducibility and clinical implementation. This study evaluates the cross-site transferability of an in-house LC-MS/MS assay for routine TDM in Singapore.
Aims: To assess the inter-laboratory performance of an LC-MS/MS assay for 11 key antibiotics by cross-validating between a research laboratory and the SGH Antibiotic TDM service laboratory.
Methods: The LC-MS/MS assay, which includes common β-lactams, β-lactam/β-lactamase inhibitors, fosfomycin, tigecycline, and levofloxacin, was evaluated using calibration curves, quality control (QC) samples, and patient samples analysed at both sites. Linearity, intra- and inter-laboratory accuracy and precision (A&P) were evaluated. Acceptance criteria followed European Medicine Agency (EMA) guidelines (2011), requiring QC accuracy within 15% and at least 67% of the repeats to show a measurement difference within 20% of the mean.
Results: Calibration curves (n=3) for all antibiotics showed excellent linearity ($R^2 \geq 0.997$), and QC (n=3) A&P were within 15% in both laboratories. A total of 56 out of 60 antibiotic measurements (93.3%) in 24 patients' plasma samples achieved the acceptance criteria (% concentration difference: ±0.11-19.8%).
Conclusions: Cross-validation of our in-house antibiotic assay met EMA acceptance criteria, indicating that the method is reproducible at different laboratory sites, supporting the clinical implementation of antibiotic TDM in Singapore.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P652

Quantification of vancomycin and clindamycin in synovial tissue and bone using UPLC-MS/MS

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Biography:
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Background: Approximately 1-2% of patients undergoing hip or knee arthroplasty will encounter a periprosthetic joint infection (PJI). Presently, treatment involves revision surgeries alongside long-term antibiotic therapy. Although optimal dosing is very important, there remains insufficient understanding regarding the relationship between plasma concentrations and target-site concentrations of the antibiotics.
Aims: Our aim was to develop a novel ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) technique for quantifying two frequently prescribed antibiotics, vancomycin and clindamycin, in synovial tissue and bone samples.
Method: Method validation was performed based on the FDA and EMA guidelines.
Results: The method was found linear for vancomycin from 0.8 to 25 µg/g and for clindamycin from 0.5 to 25 µg/g in bone and from 1 to 25 µg/g for both compounds in synovial tissue (r2 >0.990). The results of the validation for precision, accuracy and carry-over were all within acceptance range. All clindamycin extracts showed to be stable in the autosampler for bone and synovial tissue samples after 24 hours. The vancomycin extracts were stable for synovial tissue after 24 hours but not for extracts of bone samples.

Conclusions: A quantification method for vancomycin and clindamycin in synovial tissue and bone using UPLC-MS/MS was successfully developed and validated. To our knowledge, this is the first validated method for quantifying vancomycin and clindamycin in synovial tissue and bone using UPLC-MS/MS. This method has already been applied in a clinical research study.

Key words: antibiotics, periprosthetic joint infection, synovial tissue and bone, chromatography, mass spectrometry

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P653

The QuEChERS method efficiently extracts immunosuppressants from whole blood for LC-MS/MS analysis

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Background: Immunosuppressive therapy with tacrolimus (TAC), cyclosporine (CsA), sirolimus (SIR), and everolimus (EVE) requires therapeutic drug monitoring (TDM) due to its narrow therapeutic range. Thus, reliable analytical methods are essential for high-quality results. The QuEChERS method has shown excellent recovery rates for various analytes, serving as a viable alternative to traditional extraction methods for determining IMDs.
Aims: The study aimed to develop and validate a novel, robust, and rapid LC-MS/MS method for determining immunosuppressants in the whole blood of pediatric liver transplant recipients.
Methods: During method development, the various QuEChERS mixtures were tested, supported by acetonitrile and/or methanol. The Luna PhenylHexyl column was used for chromatographic separation with mass spectrometry detection in MRM mode with a QTRAP6500+ device. The method was applied to TDM of clinical samples from pediatric patients after liver transplantation.
Results: The MgSO4, NaCl, di-/trisodium citrate with C18e sorbent composition was employed as the final QuEChERS mixture. Acetonitrile was selected as the suitable solvent, and extraction was facilitated by cold-induced phase-extraction. The method has been successfully validated within the 0.5–60 ng/mL (TAC, SIR, EVE) and 1–2000 ng/mL (CsA) calibration ranges. The mean intra- and interday accuracies and precision (<±15% and <10%, respectively) met the acceptance criteria. The matrix effect factors observed for the method were more satisfactory than those of a previously validated method based only on simple protein precipitation.
Conclusions: The QuEChERS method is distinguished by its high-recovery extraction of immunosuppressants from whole blood for LC-MS/MS analysis.
Key Words: QuEChERS, immunosuppressants, LC-MS/MS, TDM, liver transplantation

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P654

Simultaneous determination of six cephalosporins in critically ill paediatric patients using VAMS

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Background: Cephalosporins (CEPs) are bactericidal β-lactam antibiotics commonly used for prophylaxis and antimicrobial treatment in children following surgeries, sepsis/septic shock, or SIRS. Their pharmacokinetics are complex, particularly in critically ill paediatric patients, and the drug concentration is crucial for PK/PD evaluation, as is routine TDM.
Aims: This study aimed to optimise and validate a novel LC-MS/MS-based assay for determining six CEPs (cefazolin, cefotaxime, ceftazidime, cefuroxime, ceftriaxone, and cefepime) in capillary blood collected using the Mitra™ microsampling device.
Methods: The Kinetex-F5 column from Phenomenex was employed for CEPs separation in LC-MS/MS analysis (IVDR system/Citrine-6500+). Simple protein precipitations were facilitated by a 2-propanol/acetonitrile mixture with isotope-labelled internal standards corresponding to the analytes. The EMA, FDA, and IATDMCT guidelines were applied for validation purposes. The 10µL Mitra™ VAMS device was used to sample paediatric patients hospitalised in intensive care units at The Children's Memorial Health Institute in Warsaw, Poland.
Results: The method was successfully validated within the 0.1-50mg/L calibration range for each CEP. The accuracy and precision were within the acceptance ranges proposed by the EMA. The hematocrit effect did not influence the extraction/recovery of each analyte. The stability of the dried matrix in Mitra™ samples was established as 7 days at RT. The quantitative and qualitative matrix effects were not significant for each analysed CEPs.
Conclusions: The successfully validated method (alongside a previously validated method for the unbound fraction of CEP quantification) has been employed for PK/PD-monitoring of CEPs (fT%>4xMIC) in the AntiSepsis study.
Key Words: cephalosporins, β-lactams, sepsis, microsampling, paediatrics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P655

Keeping neonates calm and safe: a novel LC-MS/MS method for dexmedetomidine monitoring

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Background: Dexmedetomidine (DEX) is a multipotent and highly selective agonist of α_2-adrenergic receptor, commonly utilized for sedation and analgesia in neonatal intensive care units (NICUs). It provides effective sedation with minimal respiratory depression and neuroprotective properties. Nevertheless, the pharmacokinetics of DEX in neonates are highly variable, and optimal dosing remains uncertain. Therapeutic drug monitoring (TDM) could support personalized dosing by ensuring appropriate drug exposure and minimizing the risk of adverse effects.
Aims: The study aimed to develop and validate a sensitive and specific LC-MS/MS method for the quantification of DEX in plasma, whole blood, and VAMS-collected capillary blood to support TDM in neonates.
Methods: Sample preparation involved protein precipitation using an acetonitrile-methanol mixture containing an internal standard (DEX-D4). Chromatographic separation was achieved on a C18 column using a gradient elution with 0.1% formic acid in water and 0.1% formic acid in acetonitrile. Detection was performed in MRM mode on a triple quadrupole mass spectrometer with ESI in positive mode. The monitored transitions were m/z 205 → 99 (DEX-D4) and 201 → 95 (DEX).
Results: The method showed linearity in the range of 0.5–50 ng/mL (R^2 = 0.995) with high precision and accuracy. Stability was confirmed for 5 days at 4°C. The validated method demonstrated reliable performance across all matrices, supporting its use in neonatal TDM.
Conclusions: The developed LC-MS/MS method provides a reliable tool for DEX quantification in neonatal TDM, enabling individualized dosing and improved therapeutic outcomes.
Keywords: dexmedetomidine, LC-MS/MS, VAMS, TDM, neonatal sedation, pharmacokinetics

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Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P656

Small Samples, Big Impact: LC-MS/MS Quantification of Ketamine in Neonates

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Background: Ketamine (KET) is widely used for rapid and effective anesthesia, particularly in Neonatal Intensive Care Units (NICUs). As an NMDA receptor antagonist, it provides strong analgesic and sedative effects without causing respiratory depression. Despite its clinical benefits, the optimal dosing regimen remains unclear, and individual pharmacokinetic variability significantly impacts both efficacy and the risk of toxicity. Therapeutic drug monitoring (TDM) of ketamine and its metabolite, norketamine (NOR), can facilitate personalized dosing by ensuring target concentrations are achieved. Measurements in whole blood, plasma, and capillary blood (VAMS) offer a promising approach for optimizing ketamine dosing in neonates.
Amis: This study aimed to develop and validate a sensitive, specific, and accurate method for simultaneous quantification of KET and NOR in various biological matrices.
Methods: Protein precipitation was performed using an acetonitrile-methanol mixture containing the internal standard (KET-D4), and the supernatant was directly injected into the chromatographic system. Separation was achieved with gradient elution using 0.1% formic acid in water and 0.1% formic acid in acetonitrile on a C18 column. Detection was conducted in MRM mode on a triple quadrupole mass spectrometer with ESI in positive mode. Transitions m/z 242 → 183 (KET-D4), 238 → 179 (KET), and 224 → 125 (NOR) were monitored.
Result: The method demonstrated linearity from 2–500 ng/mL (R^2 = 0.989) with high precision and accuracy. Stability was satisfactory for 7 days at 4°C.
Conclusion: This method is a reliable and practical tool for improving pain management in neonates.
Keywords: analgesics, LC-MS/MS, VAMS, TDM

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P657

HPLC-UV method for monitoring sildenafil concentration in pulmonary arterial hypertension patients

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Biography:

Paweł K. Kunicki, PhD,

He is (since 2016) - Assistant Professor at the Department of Drug Chemistry, Pharmaceutical and Biomedical Analysis, Faculty of Pharmacy, Medical University of Warsaw, Poland. He graduated as Master of Pharmacy (M.Pharm. 1990) and as Doctor in Pharmaceutical Sciences (Pharm.D., Ph.D. 2002). He was (1990–2019) - at the Institute of Cardiology in Warsaw, recently the Head of Clinical Pharmacology Unit, and acting Head of Department of Clinical Biochemistry. He is a clinical pharmacist as well as a laboratory diagnostician, specialist in Public Health (2011) and in Laboratory Medical Toxicology (2021). Consultant and expert on the field of drug analysis, pharmacokinetics and bioequivalence studies. He is an author of 53 original and review papers and of 202 oral or poster scientific presentations and lectures; h-index: 12. He is a member of IATDMCT (Immunosuppressive Drugs Committee), as well as Editorial Board member of Therapeutic Drug Monitoring.

Background: Sildenafil (SIL) is one of the essential drugs in pulmonary arterial hypertension (PAH). A considerable percentage of ineffective treatment in PAH may be related to subtherapeutic dosage or non-adherence.
Aims: The aim of the study was to develop a simple analytical method enabling the determination of SIL in plasma of PAH patients.
Methods: An isocratic HPLC-UV system with a manual injector was applied. The separation of SIL and internal standard gallopamil (GAL) was performed on Supelcosil LC-CN column (150x4.6 mm, 5 µm) at ambient temperature. The mobile phase: CH3CN:H2O:0.5M KH2PO4:85% H3PO4 (172:324.2:3.7:0.1, v/v) was pumped at a flow rate of 1.8 mL/min. Diisopropyl ether (3 mL) was used for 3-min liquid-liquid extraction from 0.4 mL plasma sample buffered with 0.5M glycine. The sample was then re-extracted into 0.01 M HCl. The analytical wavelength was 290 nm.
Results: SIL and GAL were eluted at retention times of 3.4 and 7.3 min, respectively. The extraction yield was: 88.5% for SIL and 84.7% for GAL. The method was calibrated in the range: 2-500 ng/mL. For intraassay, the inaccuracy ranged from -18.1% to +1.0% and imprecision ranged 2.6-6.1% while for interassay, the inaccuracy was from 9.6% to +13.0% and the imprecision ranged 3.9-9.9%. The method has been successfully used in pilot study in 66 PAH patients, enabling SIL monitoring at steady-state.

Conclusions: The method can be used for both therapeutic drug monitoring (TDM) and adherence studies as an economical alternative to the LC-MS/MS technique.

Keywords: HPLC-UV, Sildenafil, Adherence, Pulmonary Arterial Hypertension

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P658

Development and Validation of an HPLC Method for Brivaracetam Therapeutic Drug Monitoring

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Biography:

Mila Lovrić graduated in medical biochemistry from the Faculty of Pharmacy and Biochemistry, University of Zagreb, in 1992. She earned an MSc in biomedicine in 2001 and a PhD in 2010. That same year, she passed the specialist exam in analytical toxicology. Since 1992, she has worked at University Hospital Centre Zagreb, becoming head of the Division for Multidisciplinary Application of Chromatography in 2010. She was appointed research associate in 2011, promoted to senior research associate in 2013, and became an associate professor in 2023. Her research focuses on complex chromatographic techniques, method validation, therapy individualization, and analytical toxicology. She has authored 39 CC-indexed scientific papers and has over 885 citations. She is a member of multiple professional societies, including the Croatian Society for Medical Biochemistry and Laboratory Medicine.

Background: Brivaracetam belongs to the third generation of antiepileptic drugs and is a structural analogue of levetiracetam but has higher lipophilicity. Interindividual variability necessitates therapeutic drug monitoring, especially when used in polytherapy and in patients with altered pharmacokinetics. Currently, brivaracetam measurement relies solely on complex chromatographic methods, limiting their availability in many laboratories.
Aim: of this study is to develop and validate an HPLC method with a diode array detector (HPLC-DAD) that is sufficiently sensitive and suitable for therapeutic monitoring of brivaracetam.
Methods: The HPLC method was validated according to CLSI and ICH guidelines. Preparation of serum samples was performed by liquid–liquid extraction using ethyl acetate:hexane (1:1) with chloramphenicol as internal standard. Separation was achieved using a 5µm 4.6 x 250mm C18 Shim-pack GIST column with the mobile phase consisted of a 50 mM phosphate buffer (pH=4.5) and organic mixture of acetonitrile and methanol (8/3; v/v). Brivaracetam was quantified at 210 nm.
Results: The developed HPLC-DAD method is linear over a concentration range of 0.4-20 µmol/L. Repeatability showed a relative standard deviation lower than 6.6% and intermediate precision lower than 6,7%, except for the value at the lower limit of quantification (0.4 µmol/L) which was 12.6 %. Bias was lower than 8 %. The method has satisfactory specificity and greenness.
Conclusions: The validation parameters were within the acceptance criteria of the ICH guidelines. The developed method is simple, reproducible, more sensitive than other published HPLC method and suitable for the therapeutic drug monitoring of brivaracetam.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P659

A UPLC-MS/MS assay of tasurgratinib and an active metabolite in human plasma

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Biography:

After graduating from the University of Tokyo, Dr. Mano joined Astellas Pharma Inc. In 2007, then he joined Eisai Co., Ltd. and is currently leading the DMPK laboratory as a senior director. He also works as a professor at Graduate School of Comprehensive Human Sciences, University of Tsukuba. His current interest is to establish innovative bioanalytical methods to support exploratory and regulated drug monitoring of new chemical entities. As a scientist in the industry, he has published >50 papers as a corresponding author in peer reviewed journals.

Background: Tasurgratinib is a novel fibroblast growth factor receptor inhibitor that has recently been approved for the treatment of patients with unresectable biliary tract cancer with FGFR2 gene fusions or rearrangements. In vitro studies have demonstrated that a dealkylated metabolite, M2, exhibits comparable pharmacological activity to tasurgratinib.
Aims: To evaluate the pharmacokinetic (PK) profiles of tasurgratinib and M2 in humans, it is necessary to develop a sensitive and robust assay. The objective is to establish and apply a simultaneous assay using ultra-performance liquid chromatography with tandem mass spectrometry (UPLC-MS/MS) to PK sample assays in support of clinical trials.
Methods: The analytes were extracted from 0.1 mL of plasma by protein precipitation and separated on a reverse-phase analytical column utilizing an at-column dilution configuration. The analytes were detected by selected reaction monitoring in electrospray ionization in the positive ion mode. The validation study assessed the following parameters: Linearity, selectivity, carryover, reproducibility (accuracy and precision), dilution integrity, extraction recovery, matrix effects, and stability. The plasma concentrations of tasurgratinib and M2 following an oral dose of tasurgratinib at 35 mg were determined. In order to guarantee the reproducibility of the assay, incurred sample reanalysis (ISR) was conducted.
Results: Tasurgratinib and M2 were quantifiable from 0.025 ng/mL, with accuracy and precision falling within the accepted range. The PK of tasurgratinib and M2 exhibited comparable systemic exposures, and the ISR results satisfied the acceptance criteria.
Conclusions: An established LC-MS/MS assay was validated and successfully applied to a clinical PK study.
Keywords: Tasurgratinib, Metabolite, Pharmacokinetics

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P660

Preliminary Study: Correlation of Fully Automated LC-MS/MS in Tacrolimus and Everolimus Quantification

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Biography:
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CHUO PECK HAM's career highlights include technical management, active participation in professional organizations like the Malaysia Association of Clinical Biochemists (MACB), and involvement in numerous committees and taskforces. She has also contributed to publications and presented at conferences.

Therapeutic drug monitoring (TDM) for kidney transplant patients on Tacrolimus and Everolimus has become more efficient with recent advancements in Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) automation, allowing simultaneous testing.
This study evaluates two methods for quantifying Tacrolimus and Everolimus: LC-MS/MS and immunoassay. The quantification of both drugs was performed utilizing the fully automated Clinical Laboratory Automated Module (CLAM) integrated with the Shimadzu LC-MS/MS system, in addition to conventional immunoassay methods. For Tacrolimus, Chemiluminescence Immunoassay (CMIA) was employed, while Everolimus was tested in batches using Particle Enhanced Turbidimetric Inhibition Immunoassay (PETINIA).
Blood samples from kidney transplant patients were collected at the Department of Nephrology, Hospital Kuala Lumpur, between Aug to Nov 2021. Measurement was obtained using a commercially available kit by Alsachim DOSIMMUNE™ for automated immunosuppressant analysis. The results were compared using Passing-Bablok regression and Bland-Altman analysis.
The Passing-Bablok regression analysis showed systematic biases in Tacrolimus ($y = 0.508 + 0.812x$) and Everolimus ($y = -0.739 + 1.370x$). Spearman correlation coefficients were 0.978 for Tacrolimus and 0.622 for Everolimus ($P < 0.0001$). Bland-Altman analysis revealed a mean bias of -0.7 for Tacrolimus (limits: -2.1 to 0.8) and 0.8 for Everolimus (limits: -3.6 to 5.2). Proportional bias and outliers at higher concentrations suggest measurement inconsistencies. While general agreement exists, further validation and calibration are needed for optimal clinical and analytical use.
The study supports adopting the Shimadzu CLAM-LC-MS/MS system for more accurate and reliable TDM with simultaneous reporting, pending further validation.
Therapeutic Drug Monitoring (TDM), LC-MS/MS, Kidney Transplant, Immunosuppressants, Automation, Method Comparison

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P661

Investigating specificity of 11-nor-9-Carboxy-Δ9-THC mass spectrometry confirmation methods

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Biography:
A Medical Scientist with a wealth of experience and specialisation in clinical biochemistry (pharmacology, and toxicology). With a decade of work in medico-legal toxicology and therapeutic drug monitoring I expertise in LCMSMS and GCMS chromatography. I have developed a deep understanding of laboratory diagnostics and analysis techniques. My interest lies in research or cases related to medico-legal drug testing and analysis but not limited to therapeutic drugs.

Background: Delta 9-tetrahydrocannabinol (Δ9-THC) metabolises to a glucuronide conjugate, 11-nor-9-carboxyΔ9-THC (Δ9-THCCOOH), which is detected in urine specimens. Two isobaric compounds, Δ8-THCCOOH and a carboxylic acid metabolite of cannabidiol (7-CBDCOOH), are potential interferents in mass spectrometry analytical methods and are increasingly apparent in toxicology cases due to internet-availability of Δ8-THC products and increases in the medicinal use of cannabidiol in Australia, respectively.
Aims: To assess the specificity of GCMS and LCMSMS methods for the confirmation of Δ9-THCCOOH in the presence of these isobaric compounds.
Method: Reference material for Δ8-THCCOOH and 7-CBDCOOH were spiked, alone and with Δ9-THCCOOH, into blank urine. All specimens were analysed with GCMS method as well as an alternative LCMSMS method. Authentic urine samples suspected of containing an isobaric interferent were also assessed.
Results: Δ8-THCCOOH was insufficiently chromatographically resolved using the GCMS method from Δ9-THCCOOH. This resulted in the spiked Δ8-THCCOOH samples failing the qualifier ion ratio criterion (>30%) for one of the ion pairs, as did the suspected authentic urines. Baseline resolution was able to be achieved with an increased chromatographic run-time, which demonstrated that Δ8-THCCOOH was the interferent in the authentic specimens. 7-CBDCOOH did not produce a signal for the selected ions. The LCMSMS method was similar, with insufficient chromatographic separation and failure of qualifier ion ratio criterion (>30%).
Conclusion: Δ8-THCCOOH should be assessed as a part of validation of Δ9-THCCOOH confirmation methods. Adjustments to the established methods was able to identify this interferent in authentic urine samples.
Key words: Δ9-THC, Δ9-THCCOOH, Δ8-THCCOOH, 7-CBDCOOH

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P662

Method comparison of human antibiotic concentrations between two diagnostic assays

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Background: Interest in Therapeutic Drug Monitoring (TDM) of antibiotics for critically ill patients has grown, yet it remains underutilized in clinical practice. Rapid, accurate, and user-friendly diagnostic assays are essential for routine implementation.
Aims: The study assessed comparability of TDM results between a new automated assay under development at Roche Diagnostics and the routinely used Chromsystems method at the Medical University of Vienna (MUV).
Methods: Human blood samples of intensive care units obtained for TDM of meropenem, piperacillin and linezolid were routinely analyzed at the MUV using a High Performance Liquid Chromatography (HPLC) assay. Residual material was then remeasured on a prototype of the Cobas® i 601 analyzer at Roche Diagnostics, which recently received CE-mark. The High Performance Liquid Chromatography Tandem Mass Spectrometry (HPLC-MS/MS) based assays are still under development. Weighted Deming regression and Pearsons's R were used for method comparison.
Results: Meropenem samples (n=90) showed mean concentrations (range) of 25.3 µg/ml (1.3 – 78.6) vs. 25.6 µg/ml (1.3 – 72.0) for Cobas i 601 analyzer and MUV results, respectively, r=.989. Piperacillin samples (n=112) showed mean concentrations (range) of 46.5 µg/ml (0.3 – 181.0) vs. 49.1 µg/ml (0.3 – 175.0) for Cobas i 601 and MUV results, respectively, r=.991. Linezolid samples (n=90) showed mean concentrations (range) of 7.0 µg/ml (0.2 – 22.7) vs. 7.6 µg/ml (0.2 – 24.6) for Cobas i 601 analyzer and MUV measurements, respectively, r=.997.
Conclusions: Cobas i 601 analyzer and MUV measurements demonstrate a high level of agreement supporting the transferability of results between the two assays.
Keywords: Therapeutic Drug Monitoring; Intensive Care Unit; Antibiotic Stewardship
Disclaimer: Cobas i 601 analyzer is CE-marked. Ionify® Antibiotics reagents are still under development as of August 2025. These products are not cleared or available for use in the US. COBAS and IONIFY are trademarks of Roche. This study was funded by Roche Diagnostics International Ltd.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P663

Development of a method of LC/MS-MS for simultaneous determination of hyaluronan oligosaccharides

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Biography:

Yuki Sato became a pharmacist and has been a lecturer in the Faculty of Pharmaceutical Sciences, Hokkaido University since 2020. She has been an assistant professor at Hokkaido University since 2009, and a special-appointed assistant professor at Kyoto University Hospital since 2018 and continues to conduct research at the Faculty of Pharmaceutical Sciences involving with pharmacist's work. One of her main research themes is the elucidation of the gastrointestinal absorption mechanism and improvement of absorption of functional food ingredients. By clarifying the pharmacokinetics of not only medicines but also food ingredients, it may be able to avoid unexpected interactions and propose more efficient ways of intaking food ingredients. She believes that this research could contribute to the maintenance and promotion of people's health, and additionally to preventive medicine.

Background: Hyaluronan (HA) is a repeating disaccharide structure of N-acetyl-D-glucosamine and D-glucuronic acid and widely exists at various molecular weights. It has been reported that most of an orally administered HA, regardless of its molecular weight, is degraded by intestinal microflora into HA oligosaccharides of less than octa saccharides and absorbed. However, there will not be a method for simultaneous determination.
Aims: We focused on HA 8-mer or less and aimed to establish a simultaneous quantification method of LC/MS-MS with a simple pretreatment to clarify the absorption properties of orally administered HA oligosaccharides.
Methods: First, carboxy groups of HA oligosaccharides were derivatized with a condensing reagent and Girard's reagent P. After pretreatment by solid-phase extraction using hydrophilic interaction, peaks of HA 2, 4, 6 and 8-mer were detected by LC/MS-MS. Validation studies were conducted for this method and plasma concentrations of HA were determined after oral administration of HA formulation to rats.
Results: We confirmed by an MS scan that the derivatized HA oligosaccharides could be analyzed by the newly developed quantitative method and we identified the peak of derivatized HA oligosaccharides. The MS/MS conditions were optimized, and a calibration curve was generated. Plasma concentrations of HA 4, 6 and 8-mer were determined after oral administration of HA formulation.
Conclusions: The calibration curve showed good linearity for HA 4, 6, and 8-mer. This method is valid and enables measurement of plasma concentrations of HA oligosaccharides.
Key Words: hyaluronan; absorption; oligosaccharides; LC/MS-MS; validation; simultaneous determination.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P664

Method validation for simultaneous quantification of MPA and MPAG in human plasma.

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Biography:
I am sheetal singh, final year phd scholar, working in the area of renal cell carcinoma along with renal transplantation.

Background: Mycophenolic acid (MPA) is a widely used immunosuppressant in transplant recipients, primarily administered as mycophenolate mofetil (MMF). Despite its clinical efficacy, MPA exhibits significant inter- and intra-individual pharmacokinetic variability, necessitating therapeutic drug monitoring (TDM). The primary metabolite, mycophenolic acid glucuronide (MPAG), contributes to the drug's pharmacokinetics but lacks pharmacological activity.
Aim: Study aimed to develop and validate a simple, reliable, and cost-effective high-performance liquid chromatography with ultraviolet detection (HPLC-UV) method for simultaneous quantification of MPA and MPAG in human plasma.
Methods: The method employed a C18 analytical column and an isocratic mobile phase consisting of 20mM phosphate buffer (pH 2.3-2.4) and acetonitrile (62:38, v/v). Carbamazepine was used as an internal standard. Sample preparation involved protein precipitation with acetonitrile. The retention times for MPAG, MPA, and the internal standard were 1.5, 7.2, and 3.2 minutes, respectively.
Results: Linearity was established over the concentration range of 0.39-50 mg/L for MPA and 1.56-400 mg/L for MPAG ($R^2 > 0.999$). The method demonstrated acceptable within-day and between-day precision (CV% < 15%) and accuracy (> 94%). Absolute recoveries of MPA and MPAG were above 97%, with no significant matrix effects.
Conclusion: This validated HPLC-UV method is suitable for routine TDM of MPA and MPAG in clinical settings. It provides an alternative to LC-MS/MS, offering a cost-effective, simple, and robust approach for monitoring MPA therapy in transplant patients. The method ensures high sensitivity, specificity, and reproducibility, facilitating individualized dose adjustments to optimize therapeutic outcomes.
Keywords: Mycophenolic acid, MPAG, HPLC-UV, therapeutic drug monitoring, pharmacokinetics, immunosuppressant

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P665

High Specificity Homogeneous Enzyme Immunoassay for Ketamine

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Biography:

Raj Singh, leads the strategy, next generation assays and new platform development at ARK Diagnostics. At Baebies expanded biochemical and molecular tests for newborn and pediatric screening using DMF. As Senior Director at Caliper Lifesciences (Perkin Elmer), created content to all of PKI technology platforms using microfluidics, automation, preclinical imaging and next gen sequencing. As Head of Chemistry at DiscoveRx, took 40+ products from concept to commercialization for drug discovery. As Manager of Clinical Assays at Surromed, devised and set up the infrastructure to perform MS, laser scanning cytometry, protein and genomic array based screening of biological fluids for biomarker discovery targeted towards patient stratification for precision medicine. At Syntex/Roche invented reagents and new chemical entities for medical diagnostics and nucleic acid analysis. Coauthor in several publications, presentations and coinventor in 30+ patents. Dr. Singh's doctoral work was done under Prof. Ronald Breslow at Columbia University.

Background: Ketamine, a nonbarbiturate and rapid-acting dissociative anesthetic is FDA cleared for use in human and veterinary surgical procedures. Structurally and pharmacologically similar to phencyclidine (PCP) it is less potent, has a faster onset and shorter duration of action. Recently it has attracted attention due to its utility as an adjunctive, opioid-sparing analgesic with sustained antidepressant effects, in patients with acute suicidal ideation or behavior. Besides medical use ketamine is commonly abused as a recreational drug because of its ability to induce an altered state of consciousness. First generation immunoassays to detect ketamine suffered from cross reactivity yielding false positives, necessitating highly specific assays to circumvent difficulties encountered in laboratories performing urine drug screens.
Methods: The performance characteristics of ARK Ketamine II assay, including precision, spiked recovery, specificity were evaluated on the Beckman Coulter AU680 automated clinical analyzer employing two reagents in a homogeneous immunoassay format.
Results: The assay demonstrated acceptable precision, with no overlap at 50 ng/mL cutoff using ± 50% controls, and at 100 ng/mL cutoff using ± 25% controls. Recovery was between 103.7% and 106.1% of the spiked ketamine from 20.0 to 500.0 ng/mL. The cross-reactivity to several structurally similar derivatives was minimal. Human urine samples (N=223) were confirmed negative by both immunoassay and LC-MS/MS, additionally for positive patient samples (N=50), ARK Ketamine II assay showed 100 % sensitivity and 100 % specificity for both cutoffs.
Conclusion: The ARK Ketamine II Assay provides a highly specific, sensitive, rapid, and reliable measurement of ketamine in human urine.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P666

LC-HRMS/MS Quantitative Analysis of Psychoactive Compounds in Blood and VAMS Samples

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Biography:
For several years, he worked as a research scientist at the Medical University of Gdańsk in the Department of Medical Laboratory Diagnostics. After concluding his academic collaboration, he began supporting laboratories in selecting equipment and technical solutions. For the past few years, he has been a co-owner of a laboratory specializing in method development, training, and scientific projects.

Background: High-resolution tandem mass spectrometry (HR-MS/MS) offers unmatched specificity due to superior mass accuracy, combined with broad linearity and high scanning speed in the latest instrumentation. In this study, we present a robust HR-MS/MS method for the sensitive detection of 27 psychoactive compounds in blood and blood collected on volumetric absorptive microsampling (VAMS) devices.
Aims: Accurate confirmation of compound presence is essential for targeted and quantitative toxicology analysis.
Methods: Sample preparation involved internal standard spiking, protein precipitation, extraction with acetonitrile: methanol (1:1, 0.1% formic acid), nitrogen evaporation, and reconstitution in the LC mobile phase. Quantitative analysis was performed using reversed-phase chromatography on an ExionAC LC system coupled with a ZenoTOF 7600 (SCIEX), operating in positive electrospray ionization mode with scheduled MRMhr acquisition. Compound confirmation was based on a multi-criteria approach, emphasizing MS/MS spectral matching, precursor and quantifier ion mass defect, isotope pattern, and retention time.
Results: Transitioning from a QQQ to HR-MS/MS improved data interpretation, particularly at low analyte concentrations, minimizing matrix interferences and false positives. A multi-level confirmation scoring system was developed, assigning weighted contributions to five parameters, with a 60% cut-off ensuring reliable compound identification. The method was validated for blood and VAMS samples, demonstrating excellent linearity ($R \geq 0.995$), precision (%CV ≤ 15%), accuracy (80–120%), and recovery (%CV ≤ 15%). The lower limit of quantification (LLOQ) ranged from 0.001–0.05 ng/ml.
Conclusions: This HR-MS/MS method provides high sensitivity, specificity, and robustness, enabling accurate quantification of psychoactive compounds in forensic applications.
Key Words: HR-MS/MS, psychoactive compounds, blood, VAMS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

667

Development and Validation of an LC-MS/MS Method for Tigecycline in Human Plasma

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Biography:
n/a

Background: Tigecycline (TIG), a broad-spectrum glycylcycline antibiotic, is commonly used for treating multidrug-resistant infections. To facilitate therapeutic drug monitoring and pharmacokinetic studies, a robust and fully validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) method was developed for the quantification of tigecycline in human plasma.
Objectives: This study aimed to develop and validate an LC-MS/MS method for the quantification of TIG in human plasma.
Methods: Plasma samples were spiked with TIG and an internal standard, then extracted using 0.1% trifluoroacetic acid in acetonitrile, followed by vortexing and centrifugation at 12,000 rpm for 10 minutes. Chromatographic separation was achieved on an ACE® C18 column (3 × 100 mm, 3 µm) using 0.1% formic acid in acetonitrile and 0.1% formic acid in water as mobile phases at a flow rate of 0.4 mL/min. The analyte was quantified by multiple reaction monitoring in positive mode.
Results: The method demonstrated high accuracy with a linear calibration range of 0.05–2.5 mg/L (r^2 = 0.997). The intra- and inter-day relative standard deviations of tigecycline were less than 15%, and the accuracy ranged from 87.50% to 111.20%.
Conclusions: This study successfully established a simple, rapid, and highly sensitive method for detecting tigecycline plasma concentrations. The method can be applied to therapeutic drug monitoring.
Keyword: Tigecycline, LC-MS/MS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P668

Resource limited setting experience of voriconazole and posaconazole therapeutic drug monitoring bioassay

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Biography:
Prof Dr T Karuna
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70 Publications , 3 book chapters
Area of Interest : Clinical Mycology, Antifungal Stewardship, Healthcare associated Infections

Background: Therapeutic drug monitoring interpretation for antifungal in central India is resource limited. iMARC AIIMS Bhopal caters antifungal management and TDM Bioassay.
Aims: Analysis of iMARC TDM database of routine reports for plasma range of voriconazole and posaconazole.
Objectives:
a.Monitor clinico-mycological characteristics of patients indicated for routine TDM voriconazole or posaconazole.
b.Evaluate the target plasma concentration range of each azole routinely tested voriconazole or posaconazole for three years.
Methods: Prospective hospital based cross-sectional study. Data extraction and analysis conducted from database of routine patient TDM reports of iMARC. Further enrolled TDM results in study, bedside patient record monitoring was done
Results: Total enrolled sample requisition for voriconazole 36/53 and posaconazole 17/53.
Trough samples predominant compared to random sample TDM requests, voriconazole 28/44 (0.6%), posaconazole 16/44 (0.36%). Random voriconazole 8/9 (0.89%), posaconazole 1/9 (0.1%). Mean voriconazole trough concentration 3.85ug/ml, mean random voriconazole concentration 6.8ug/ml. Mean posaconazole trough concentration 0.56 ug/ml. All posaconazole concentration subtherapeutic in mucormycosis, attributed and empty stomach. Voriconazole prescribed in invasive aspergillosis had subtherapeutic level 8/28 (0.28%) due to simultaneous prescription of few interfering medications.
Conclusion: Resource limited setting without HPLC or LCMS may not deter from antifungal stewardship and optimal patient with conventional bioassay.

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P669

Development and Validation of an HPLC-UV Method for Cisplatin in Peritoneal Fluid

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Biography:
-

Background: Intraperitoneal administration of cisplatin provides superior pharmacological effects against peritoneal metastatic cancer cells compared to intravenous administration. However, analyzing cisplatin levels in peritoneal fluid using high-performance liquid chromatography (HPLC) is challenging due to cisplatin's low light absorption and the complex peritoneal fluid matrix, which can interfere with detection.
Objectives: This study aims to develop and validate a simple, accurate, and reproducible HPLC-UV method for quantifying cisplatin levels in peritoneal fluid samples.
Methods: Cisplatin concentrations were measured using a fully validated HPLC-UV method. Peritoneal fluid (50 µL) was diluted 20-fold with 0.9% saline. A 100 µL aliquot of the diluted sample was mixed with 25 µL of 5% sodium diethyldithiocarbamate, followed by vigorous mixing and incubation at 45°C for 10 minutes in the dark. The reaction was terminated with 200 µL of cold acetonitrile and centrifuged at 4°C, 14,000 rpm for 10 minutes. A 50 µL supernatant aliquot was injected into the HPLC-UV system. Analytes were eluted under gradient conditions at a 1.4 mL/min flow rate and detected at 254 nm.
Results: The total analysis time per sample was 23 min. The method demonstrated no endogenous interference, a linear range of 1-40 µg/mL (r2 = 0.999), and high accuracy (97.1-104.4%). Intra- and inter-day precision and accuracy were within acceptable limits [99.6% (10.15%CV) and 96.1% (9.72%CV)]. Recovery was 97.9-101.9%.
Conclusions: This fast and simple HPLC-UV method reliably quantifies cisplatin in peritoneal fluid and can be used to monitor therapeutic drugs in cancer patients receiving intraperitoneal cisplatin.
Keywords: Cisplatin, Peritoneal Fluid, HPLC

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology

Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P670

Towards implementation of measured unbound flucloxacillin concentrations in routine patient care

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Biography:

Cathérine Van herteryck obtained her masters degree in Pharmaceutical Sciences from Ghent University, Belgium, in 2024. During her master dissertation, she investigated the measurement of the unbound concentration of flucloxacillin in plasma, sparking her enthusiasm for further research at doctoral level. She is currently pursuing a PhD at Ghent University, within the Department of Diagnostic Sciences at Ghent University Hospital. Her research focuses on optimizing therapeutic drug monitoring of beta-lactams, with a particular interest in measuring unbound drug concentrations, the only pharmacologically active concentration. She is especially intrigued by the various factors influencing ultrafiltration and their impact on concentration measurements. Her ultimate goal is to enhance patient care by individualising therapy, hence ensuring more precise and effective treatment strategies.

Background: Flucloxacillin, a beta-lactam (BL) antibiotic, is commonly used to treat Gram-positive infections. To optimize dosing, TDM is performed by measuring total flucloxacillin plasma concentrations, subsequently estimating unbound concentrations, using a fixed free fraction (fu, 5%). However, hypoalbuminemia, common in ICU patients, alters the equilibrium between bound and unbound drug, making total concentrations unreliable.
Aims: Validate and implement an in-house method to measure unbound flucloxacillin concentrations.
Method: Methods for quantifying bound and unbound flucloxacillin concentrations in plasma were validated using an Ultimate 3000 with a Q-Exactive hybrid quadrupole-Orbitrap (UHPLC-HRMS). Total and unbound concentrations were measured in 75 samples from 46 patients (ICU, surgery and internal medicine). Ultrafiltration was performed using Centrifree 30 kDa devices (incubation and centrifugation at 37°C, 1900g, 30 minutes). Therapeutic ranges were 50-100 mg/L (total) and 2-20 mg/L (unbound).
Results: Mean (range) total and unbound flucloxacillin concentrations were 61.9 mg/L (3.76-154 mg/L) and 8,86 mg/L (0.218-28.1 mg/L), respectively (fu 14.0% (4.74% - 40.3%)). Mean albumin concentration was 28.3 g/L (19.8-45.0 g/L). When classified into subtherapeutic, therapeutic and toxic concentrations, total concentrations resulted in 25, 51 and 2 samples, respectively, while unbound concentrations identified 12, 58 and 8 samples in these categories. In 21 cases, total concentration resulted in a different classification than unbound concentration, potentially leading to inaccurate dose adjustments.
Conclusion: For highly protein-bound drugs, like flucloxacillin, total concentrations do not provide reliable guidance for dose adaptations in these patients. Unbound concentrations should be measured using a standardized protocol.
Key Words: unbound concentration, ultrafiltration, hypoalbuminemia, flucloxacillin

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P671

UPLC-MS/MS assay development for linezolid and application to patients with renal insufficiency

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Biography:
He is a chief pharmacist, deputy director of the Medical Department, master's supervisor at the First Affiliated Hospital of Wenzhou Medical University, a key figure in the clinical Chinese pharmacy discipline under the "Twelfth Five-Year" plan of the State Administration of Traditional Chinese Medicine, and the head of the national key research and development program project sub-center. He has long been dedicated to CYP450 research, particularly in the fields of clinical pharmacology, pharmacogenetics, and pharmacokinetics, and has conducted TDM for multiple drugs. He has published over 30 SCI papers as the first author and corresponding author. He has hosted several research projects, including those funded by the National Natural Science Foundation, the National Key Research and Development Program Sub-center Project, and the Zhejiang Provincial Natural Science Foundation, and holds 2 authorized patents. He has received the Chinese Medical Science and Technology Award and the Beijing Science and Technology Award.

Background: Linezolid, an antibiotic, is known to be metabolized in the liver, but the specific role of its metabolites, particularly PNU-142300, in causing adverse effects such as myelosuppression has not been fully established, especially in patients with renal dysfunction.
Aims: To develop a rapid ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS) assay for the simultaneous determination of linezolid and its metabolite, PNU-142300, in human serum. This would enable the investigation of their concentrations and their potential link to myelosuppression in patients with renal insufficiency.
Methods: The method involves preparing human serum samples using acetonitrile for protein precipitation, followed by separation on a Waters Acquity UPLC BEH C18 column with gradient elution. Detection is performed using UPLC-MS/MS with multiple reaction monitoring (MRM) for linezolid, PNU-142300, and tedizolid (internal standard, IS).
Results: The method demonstrates good linearity, precision, accuracy, and stability for quantifying linezolid and its metabolite in serum.
Conclusions: A fast, accurate UPLC-MS/MS assay was developed to measure linezolid and its metabolite PNU-142300 in serum. With a quick 3-minute analysis and simple sample preparation, this method is ideal for routine therapeutic drug monitoring. The study also found that linezolid-induced myelosuppression is more common in patients with renal impairment, and the PNU-142300 to linezolid ratio may reduce this toxicity.
Key Words: Linezolid, PNU-142300, myelosuppression, human serum, UPLC-MS/MS

23rd International Congress of Therapeutic Drug Monitoring & Clinical Toxicology
Singapore 2025
21–24 September
Grand Copthorne Waterfront Hotel

P672

LC-MS/MS for the determination of apalutamide and application in castration-resistant prostate cancer

A/Prof Lijuan Zhang[1], Assoc Prof Jun Li[2], Prof Lu Chen[1,3], Assoc Prof Yuxuan Zhu[1], Mr. Wenqiang Cheng[4], Mr. Dingyuan Yang[5]
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Biography:

Zhang Lijuan, female, Associate Professor; working in the Department of Pharmacy, Department of Pharmacy, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, School of Medicine, University of Electronic Science and Technology of China. Mainly focus on therapeutic drug monitoring and clinical pharmacy related work. She is currently a young member of division of Therapeutic Drug Monitoring of the Chinese Society of Pharmacology; committee member of Therapeutic Drug Monitoring of the Sichuan Society of Pharmacology; member of Organic Mass Spectrometry Committee, Sichuan Society of Analytical Testing.

Background: Apalutamide is used in the treatment of castration-resistant prostate cancer. A simple, specific, selective, and effective liquid chromatography tandem mass spectrometry method for quantifying apalutamide and its active metabolite concentration in human plasma was developed and validated according to the FDA and EMA validation guidelines.
Methods: 24 patients diagnosed with NM-CRPC were recruited. Blood samples were drawn after 4 weeks' administration with Apalutamide at a dose of 180 mg once daily to ensure steady therapeutic blood levels were achieved. Apalutamide and N-desmethyl apalutamide were analyzed by quantitative liquid chromatography tandem mass spectrometry to identify the concentrations among individuals and the effect on the baseline level of PSA and adverse events.
Results: The linear range, precision, accuracy, matrix effect, recovery, carryover, and stability were appropriate according to regulatory agencies. The apalutamide blood concentration range of the 24 patients was 0.517–7.27 µg/mL, and the median value was 4.92 µg/mL. The N-desmethyl apalutamide blood concentration range was 1.78–8.32 µg/mL, and the median value was 5.71 µg/mL. The median serum PSA level decreased from 61.03 (range 0.57–885.93) ng/mL at baseline to 0.970 (range 0.01–47.9) ng/mL at week 4.
Conclusions: Therapeutic drug monitoring can help evaluate the individual differences between patients taking apalutamide. A dose of 180 mg could reduce baseline PSA level significantly ($p < 0.05$), and the incidence of skin rash was less compared to a dose of 240mg.
Key Words: Apalutamide, N-desmethyl apalutamide, Therapeutic drug monitoring, LC-MS/MS, Castration-resistant prostate cancer, Human plasma