CONGRATULATIONS TO THE CONGRESS ORGANIZERS, IATDMCT OFFICE, SPONSORS, ATTENDEES AND TO EVERYONE INVOLVED IN MAKING THE 17TH INTERNATIONAL CONGRESS OF IATDMCT A SUCCESS AT FOZ DO IGUASSU, BRAZIL.
STATISTICS OF THE CONGRESS

Congratulations to the congress organizers, IATDMCT office, sponsors, attendees and to everyone involved in making the 17th International Congress of IATDMCT a success at Foz do Iguassu, Brazil!

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THE PATSALOS PRIZE WAS AWARDED AT THE IATDMCT CONGRESS IN FOZ DO IGUASSU, BRAZIL

The winner was Dr. Kristine Hole with her co-authors, for the manuscript entitled “Comparison of CYP3A4-Inducing Capacity of Enzyme-Inducing Antiepileptic Drugs Using 4ß-Hydroxycholesterol as Biomarker”

Authors: Kristine Hole, Birgit M. Wollmann, Camilla Nguyen, Tore Haslemo, EspenMolden. Ther Drug Monit. 40(4): 463–468, August 2018

The Patsalos Prize was established by Professor Philip Patsalos and his wife Ellie for the best original research manuscript in TDM in a two-year calendar period, and this was the sixth time the prize was awarded.

Kristine Hole is a pharmacist and researcher at Center for Psychopharmacology, Diakonhjemmet Hospital, Oslo, Norway. Center for Psychopharmacology runs a specialized TDM service for CNS drugs analyzing 50,000 patient samples annually. Hole completed her PhD in 2019 on the use of the endogenous biomarker 4ß-hydroxycholesterol for measurement of in vivo CYP3A activity. The awarded manuscript was part of her PhD thesis, which was supervised by Prof. Espen Molden at Department of Pharmacy, University of Oslo and Center for Psychopharmacology.

The topic of the present manuscript was enzyme-inducing antiepileptic drugs. These drugs are among the clinically most important inducers of CYP3A4, both due to their frequent use in combination with other drugs and their strong enzyme inducibility. The most potent enzyme-inducing antiepileptic drugs comprise phenobarbital, phenytoin and carbamazepine, and their induction effects are often considered equal in the literature. However, there is limited evidence regarding the actual comparative capacity of each drug in raising CYP3A4 activity. The aim of the present study was to compare the CYP3A4-inductive capacity of the three enzyme-inducing antiepileptic drugs in question.

This was a retrospective, naturalistic study. Serum samples from patients using phenobarbital, phenytoin, and carbamazepine were collected from the TDM service at Center for Psychopharmacology over nine months. Serum samples from patients using levetiracetam were included as a non-induced control-group. In total, serum was collected from 343 patients treated with enzyme-inducing antiepileptic drugs and 339 patients using the non-inducing drug levetiracetam. To measure in vivo CYP3A4 activity, serum samples were analyzed for the endogenous biomarker 4ß-hydroxycholesterol, which is metabolized from cholesterol by CYP3A4. Compared with levetiracetam users, CYP3A4 activity was 3-fold, 6-fold and 7-fold higher in patients using phenobarbital, phenytoin, and carbamazepine, respectively (p<0.0001)(figure1). The results indicate that phenytoin and carbamazepine have approximately twice the CYP3A4-inducing capacity of phenobarbital, which questions the existing understanding where the three drugs are customarily listed together as

Dr. Kristine Hole at the Award lecture.
strong CYP3A4 inducers. According to these findings, recommendations on dose adjustments of CYP3A4-metabolized drugs should be differentiated with respect to which enzyme-inducing antiepileptic drug is being used.

Figure 1. Scatterplot of 4ß-hydroxycholesterol concentrations in patients using levetiracetam (n = 339), phenobarbital (n = 28), phenytoin (n = 65), carbamazepine (n = 225), and 2 enzyme-inducing antiepileptic drugs (n = 25). Medians are expressed as solid lines, and P-values are estimated from Mann-Whitney tests.

CONGRATULATIONS TO THE 2019 AWARDEES AT THE 17TH INTERNATIONAL CONGRESS OF THE IATDMCT

The Irving Sunshine Prize was awarded at the IATDMCT Congress in Foz do Iguassu, Brazil
The winner was Dr. Amadeo Pesce

By Loralie J Langman

The Irving Sunshine Award is one of our society’s highest honours; it is presented for Outstanding Contributions to Clinical Toxicology. Dr. Irving Sunshine was a world-renowned pioneering toxicologist for more than half a century and an IATDMCT Honorary Member. Doc, as he was frequently called by his friends, was regarded as one of the founding fathers of modern-day toxicology. He was a leader in transforming toxicological analysis from relatively crude early methods using “wet chemistry” to the use of modern techniques such as gas chromatography-mass spectrometry (GC-MS). He died at age 90 on June 14, 2006, but Dr Sunshine’s life was shaped by his generosity in sharing his wealth of knowledge as an international teacher, scientist, mentor, scholar and orator. It is in the spirit of this outstanding person, that the award was created.

At the 2019 IATDMCT Congress in Foz do Iguacu, Brazil the winner of Irving Sunshine Award was Dr. Amadeo Pesce. His distinguished career has spanned well over 50 years. He has worked in laboratories in several states in the United States of America, and through this time he has published over 250 peer reviewed papers, over 35 books and book chapters, and mentored numerous fellows, residents and students.

As many are aware, the epicenter of the opioid crisis is the United States of America, and Dr. Pesce pioneered the use of LC-MS/MS assays to determine compliance in pain management patients. His presentation in Foz do Iguacu discussed a variety of strategies using urine drug assays to monitor patients on opioid medication for potential compliance to their prescribed regimens. He also discussed how anomalous findings in the urine of these patients, such as altered metabolic ratios and patterns, were indicative of aberrant behavior. Additionally, in certain cases these anomalous findings identified the presence of pharmaceutical impurities in the prescription medications and not illicit use of these other compounds. It also brought into question what are or should be appropriate detection limits or analytical cuts offs.

Dr. Pesce also commented on how we can use these large patient data sets. In 2016, the Center for Disease Control (CDC) in the United States of America released an Opioid Guideline for Prescribing Opioids for Chronic Pain. It recommends that “Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible” (recommendation category: A, evidence type: 3). Using the data from the opioid compliance monitoring of patients over a three year period 2016 to 2019 there was a decrease in the co-identification of opioids and benzodiazepines from ~14 to 8.5%, suggesting the potential influence of the effectiveness of the guideline.

While the majority of Dr. Pesce’s work probably had its initial impact because of the “opioid crisis” in the United States of America, the “opioid crisis” it is quickly becoming a global issue.

So once again, Congratulations to the 2019 IATDMCT Irving Sunshine Award winner Dr. Amadeo Pesce.

References:
http://clinchem.aaccjnls.org/content/53/2/373
https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm (accessed 10/26/2019)
It is a great honor for me to be awarded the Best Young Scientist Poster Presentation Prize at the 17th International Congress of Therapeutic Drug Monitoring and Clinical Toxicology. I am an Assistant Professor in the Clinical Pharmacy Laboratory of Ritsumeikan University, Japan. My research fields are (1) pharmaceutical research of inhalation medicine and (2) clinical research of personalized medicine based on therapeutic drug monitoring and pharmacogenomics.

In this work, entitled “Novel TDM of Inhaled Budesonide in Exhaled Breath for Confirmation of Adequate Inhalation” we conducted basic and clinical studies of inhalation medicine. In the basic study, we showed that pulmonary deposition of a dry powder inhaler (DPI), Symbicort® Turbuhaler®, increases depending on increased micronized drug particles, based on an increase in the inhalation flow rate. Conversely, pulmonary deposition of a pressurized metered-dose inhaler is independent of inhalation flow rate. In the clinical study of healthy subjects, drug amount in exhaled breath after inhalation of Symbicort® Turbuhaler® was determined quantitatively. Here, we showed that the amount of exhaled budesonide was significantly higher in the high inhalation flow rate group (>60 L/min) than in the low inhalation flow rate group (30 L/min).

More importantly, in DPIs, pulmonary deposition and exhaled drug amount increase owing to enhanced micronization of drug particles at a higher inhalation flow rate. Accordingly, drug amount in exhaled breath after inhalation was shown to be useful as a novel, alternative sampling strategy to predict the therapeutic effect of DPIs.

Despite intensive TDM, graft and patient survival do not improve anymore in liver transplantation. Some liver transplant recipients still exhibit rejection and/or adverse events while having tacrolimus whole-blood (TAC-WB) concentrations within the therapeutic range. Thus, new ways of immunosuppressive drugs (ISD) TDM should be explored. Measuring TAC intracellular concentrations (TAC-IC) (i.e measurement of TAC concentration in peripheral blood mononuclear cells for practical purpose) and calcineurin activity (CA) appear as promising methods, but there is few data on their practical relevance. Moreover, if their interest has been suggested in the early post-operative period, little is known at mid- and long-term. The aim of the OPTILTH study was to evaluate the feasibility of TAC-IC and of CA measurements and to assess their values as biomarkers of rejection during longitudinal follow-up in liver transplantation. The preliminary results have been presented during the 17th IATDMCT congress.

The OPTILTH study (NCT02877628) was a prospective, monocentric, observational study. Beside of TAC-WB TDM, patients included in the study benefited from a TAC-IC measurement and CA evaluation at day-7, -14, -21 and -28, week-6, -8, -12 and -24. Among the 110 patients included, 95 were evaluable. Fifteen patients were excluded for: withdrawn of the transplantation, death, retransplantation or treatment discontinuation before day-7. Rejections were evaluated by clinicians based on biological parameters, the need for ISD treatment modification and clinical evaluation. These suspected rejections were validated by an external committee. TAC-WB, TAC-IC and CA measurements were compared between the group of patients with a suspected rejection and the group without suspicion of rejection. Relationships between TAC-WB, TAC-IC and CA were explored using Pearson’s correlation test and association with rejection with a Mann-Whitney test.

Around 760 triplets (TAC-WB, TAC-IC and CA) were analyzed showing a statistically significant but poor correlation between TAC-WB and TAC-IC (R2 = 0.21, p < 0.001). Most of the suspected rejections occurred at day-7 or before making it hard to evaluate the results beyond that time point. At day-7, patients with rejections showed lower TAC-IC than patients without rejection (median value 18.7 vs 25.5 pg/106 cells; p < 0.05) while TAC WB was not different between the groups (Figure 1). CA seemed to offer few advantages over TAC-WB or TAC-IC TDM.

In conclusion, measuring TAC-IC and CA appears to be feasible and measurements can be achieved within 3 hours. In the OPTILTH study, we confirmed the results obtained by Capron et al. that is liver transplant recipients with rejection in the early post-operative period have lower TAC-IC but not TAC-WB. However, due to insufficient events, we were not able to extend this conclusion beyond day-7. The main limitation of this work is the lack of an optimal endpoint (i.e biopsy proven rejection). Nevertheless, intracellular measurements of tacrolimus might be an additional tool to prevent rejection in the liver transplant era.
IATDMCT TRAVEL GRANTS

Paula Melipillán Figueroa

I am a Clinical Pharmacist from Concepción, Chile. First of all, I would like to thank the IATDMCT Awards Committee for awarding me the International Travel Grant to participate in the 2019 Congress in Iguazu. This Congress was a great opportunity to learn from experts in the field of TDM in oncology, pharmacometrics and pharmacogenetics, my main areas of interest. It was a chance to get to know scientists from different countries and exchange ideas and share research experiences. The program of scientific activities was excellent as well as the activities of camaraderie and the place chosen for the development of the congress. I also had the opportunity to present our research work on TDM of 5-Fluorouracil in patients with gastrointestinal cancers in the clinical practice of a public hospital, led by the team formed by Dr. Salvador Cabrera, Dr. Rodrigo Ascui and myself. Overall, it was a great experience that certainly contributes to the development of academic research and clinical implementation worldwide.

Brenda Marisol del Valle Monge

It was a dream to attend the IATDMCT Congress in Brazil! I am so thankful for receiving the travel grant. As a young scientist, this Congress gave me the great opportunity to meet wonderful people in a scientific environment with the same interests as me and to enable transmission of the newest findings in TDM. I strongly believe that such exchange of experiences improves my future scientific development and inspires me to encourage TDM in my home country. IATDMCT Congress also gave me the chance to share time with people outside the scientific environment, as visiting the amazing Foz do Iguacu, the city center, the Birds National Park and, of course, the party! It was indeed an amazing congress! Thanks IATDMCT!

Georgios Shoretsanitis

I am a psychiatrist currently working as a research fellow in the Zucker Hillside Hospital, Glen Oaks, NY, USA under the supervision of Prof. John M. Kane. As TDM comprises my major research interest I was always thrilled to join one of the IATDMCT congresses. Receiving the 2019 Travel Award made it possible for me to participate in the 17th IATDMCT Congress in Iguassu, Brazil gaining unique knowledge in the field. Further, it was an opportunity to meet well-established experts from all over the world and network with investigators with similar research interests. This experience was also a great stimulation for future research activity based upon the knowledge gained during the congress. Therefore, I am particularly grateful to the organization committee for having supported me.

MOVING BEYOND IMMUNOASSAYS FOR THE POISONED PATIENTS: ANALYTICAL APPROACHES AND INTERACTIVE CASE STUDIES

By Dr. Amitava Dasgupta, The University of Texas Health Science Center at Houston (UTHealth) and Dr. Kara Lynch, University of California, San Francisco

On behalf of the Clinical Toxicology and Drugs of Abuse Committee

This toxicology symposium was presented at AACC annual meeting on August 7th 2019 at Anaheim convention center. The session had two speakers. Amitava Dasgupta talked on “The Poisoned Patient: How to Communicate with Clinicians and Guide Further Testing” while Kara Lynch talked on “Moving beyond urine tox immunoassays: analytical testing strategies and case studies”.

In the first talk limitations of immunoassays in drug testing was discussed. Emphasis was placed on communicating with physicians when drug testing is negative in a poisoned patient. When a physician is sure that a patient is overdosed, then negative toxicology report indicates false negative result because immunoassays for a drug class may not detect all drugs in the class due to poor cross-reactivity (commonly benzodiazepines and opiate immunoassays). Sometimes clinicians order benzodiazepine screen and opiate screen in urine to ensure compliance of a patient with such drugs (benzodiazepines are often prescribed in a pain management along with opioids). However, urine benzodiazepine immunoassays at a cut-off of 200 ng/mL are inadequate to monitor patient compliance because several benzodiazepines (for example alprazolam) have poor cross reactivity with antibodies used in such assays. It has been accepted that LC-MS/MS at a cut-off of 40 ng/mL is more appropriate to monitor patient compliance with benzodiazepines. Similarly opiate immunoassays utilize antibodies that recognize morphine. Therefore, opiate immunoassays are inappropriate to detect keto- opiates such as oxycodone and oxymorphine as well as opioid used in pain medications
such as tramadol, buprenorphine, methadone, and fentanyl. In addition, hydrocodone and hydromorphone may also have poor cross-reactivity with opiate immunoassays. However, specific immunoassays are available for detecting oxycodone/oxymorphone, hydrocodone/hydromorphone, tramadol, methadone, buprenorphine and fentanyl. These assays are more appropriate for monitoring patient compliance with specific opioid medication. Patients poisoned with novel psychoactive substances including, bath salts (synthetic cathinone), spices (synthetic cannabinoids such as JWH-018, JWH-073 etc.) or date rape drugs (gamma-hydroxybutyric acid (GHB), ketamine and possibly Rohypnol due to poor cross-reactivity with benzodiazepine immunoassays) also show negative toxicity report. However, more recently Randox Corporation has marketed V biochip array assay capable of detecting synthetic cathinone and also some synthetic cannabinoids in urine. Other manufacturers also developed or are developing immunoassays for detecting these compounds in urine.

When a clinician complains about negative toxicology report, following scenarios are most common:

**Scenario A:**
The physician ordered a 9-11 drug panel but many drugs escape detection; most commonly certain benzodiazepines and opioids. Further testing recommendation should be benzodiazepine or opioid confirmation using LC-MS/MS.

**Scenario B:**
Patient admitted with suspected overdose which is reversed after naloxone therapy but morphine level is low (usually 500-1000 ng/mL) or not detected. Further testing approach includes ordering fentanyl screen using DRI assay or opioid confirmation using LC-MS/MS. We are seeing some overdose cases where heroin is laced with fentanyl.

**Scenario C:**
The clinician is convinced that the patient is overdosed but toxicology screen is negative along with benzodiazepines and opioid confirmation. Further testing: This is probably a case of designer drug abuse. If the patient is young (age 18-29) and male: suggest ordering bath salts and synthetic cannabinoid panel. If the patient is a young female and physical exam indicates recent sexual activity but no evidence of struggle, specimen must be sent to a forensic laboratory under chain of custody for testing of gamma-hydroxybutyric acid, ketamine and Rohypnol. In a rare case where the patient is a Native American it may indicate use of peyote cactus during religious ceremony. Mescaline is the active substance but only few laboratories test for mescaline.

In the second talk Kara Lynch commented that it is important to move beyond immunoassay for proper identification of toxins in poisoned patients. She talked about importance of mass spectrometry especially high resolution mass spectrometry (HRMS) in identifying such toxins and presented very interesting cases from San Francisco General Hospital (SFGH) where she practices. Identifying toxin is very important because in many cases accurate history of exposure is unknown. In addition, newer drugs including designer drugs are constantly entering the clandestine market. In HRMS, data collection could be untargeted or targeted. A 27 y/o male and 37 y/o female were transported by ambulance to the emergency department with complaints of extremity weakness and paresthesias. Drug analysis indicated that the alprazolam tablets they consumed were contaminated with 3.4 µg of fentanyl and 10.6 µg of etizolam causing severe toxicity. These fake Xanax tablets were purchased from clandestine market. In the next two months additional nine cases were reported with four deaths. Another severely overdosed patient admitted that he purchased both U-47700 and phenazepam over the darknet using decentralized digital money. Another case of severe overdose due to designer drug 2,5-dimethoxy-4-chloro-amphetamine (DOC) was also discussed where HRMS was used for confirming DOC in urine. A total of five interesting cases from SFGH was presented by Dr. Lynch in the final presentation of the symposium.

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**A NEW SCIENTIFIC COMMITTEE HAS BEEN CREATED WITHIN IATDMCT**

**THE COMMITTEE IS DEDICATED TO PROMOTING THE USE OF THERAPEUTIC DRUG MONITORING OF BIOLOGICS**

Biologic therapy has revolutionized the treatment of immune mediated inflammatory diseases (IMID), cancer and infectious diseases (1,2). However, there is a considerable variation in clinical response to biologic therapy. Primary non-response and loss of therapeutic response to biologics have been attributed to pharmacokinetics (e.g. inadequate trough concentrations) and inflammatory processes (mechanistic failure) (1). In addition, this lack or loss of response may originate from several little-known epigenetic mechanisms (2). Factors that influence the pharmacokinetics (PK) of a biologic should be taken into account (antidrug antibodies, serum albumin, serum levels of C-reactive protein, disease mediated clearance, body weight, and gender among others) (3). Hence, to optimize the efficacy of biologic treatment, there is a need to implement personalized medicine in IMID and oncology. This can be guided by therapeutic drug monitoring (TDM).

Different assays exist to measure drug and antidrug antibody (ADA). PK assays are mostly affected by ADA presence, which results in a fair reflection of bio-active drug. ADA assays are divided into drug tolerant or drug sensitive; drug-sensitive assays can only detect anti-drug antibodies...
in the absence of free drug. Differences in assays must be taken into account when assessing PK or ADA data (2). Inter-assay reliability assessments for drug and ADA levels are needed to guarantee reproducible clinical decision making across the different diagnostic platforms.

There is now general agreement that TDM can guide clinical decisions in inflammatory bowel disease (IBD) or rheumatoid arthritis (RA) patients which is mostly used when a clinician sees a loss of response. In addition, current data show a clear correlation between biologic drug concentrations and favourable clinical outcomes in RA, IBD and psoriasis (4). Furthermore, some monoclonal antibodies (mAbs) used in oncology therapy show a positive exposure-response relationship for efficacy and safety (2). Although its utility is still debated, recent studies of proactive TDM of infliximab and adalimumab showed promising results for IBD management and better therapeutic outcomes than empirical dose optimization or reactive TDM alone (4). From an economic point of view, different studies have compared the cost-effectiveness of empirical dose adjustment to that of the TDM-based strategy, and all have shown that TDM is more cost-effective in IBD and RA patients (5,6). A recent meta-analysis found that TDM was associated with cost benefits and favourable outcomes related to the durability of anti-TNF response in IBD patients (7). There are data on the exposure-response relationship of biologics other than anti-TNF although the majority of papers describe anti-TNFs. More studies comparing exposure-based dosing vs fixed dosing are required.

Furthermore, mAbs clearance (CL) changes over time because their PK can be affected by the pharmacodynamic response (3,8,9). Time-dependent changes in the catabolism of endogenous and exogenous proteins can be produced by the natural progression of the disease or by the pharmacodynamic and therapeutic effect of the administered mAb. Patients’ drug exposure could increase significantly over time due to decreased CL as a consequence of improved inflammatory status. Bayesian-based dosing should allow us to modulate drug exposure based on patient response (8). However, to date there have been only a few prospective intervention studies in real-world population cohorts to determine the usefulness of individualized Bayes-based dosing in IMID, cancer or infectious diseases patients treated with biologics.

Here we would like to give an example from the IBD clinic. Combining TDM with a Bayesian approach using a population pharmacokinetic model (model-informed precision dosing) allows one to calculate a more accurate individualized exposure-targeted regimen. However, to adopt model-informed precision dosing, it is essential to provide proof of improved efficacy, reduced toxicity, and/or reduced costs (10). In a recent prospective randomized clinical trial of one-year duration, the proportion of IBD patients with clinical remission was significantly higher in the dashboard-guided dosing group than in the group who continued treatment without proactive adjustments (PRECISION trial) (11). Eser et al reported no differences between a group of patients with a recommendation to maintain the infliximab regimen and another group treated with a Bayesian dashboard intensified dose of infliximab. However, in their study, patients treated with infliximab dosing according to dashboard retained treatment for a longer period of time than those with no dose intensification despite recommendation (12). In line with this, Dreesen et al (13) found that 78% of patients with an early clinical response to treatment intensification were still on infliximab therapy one year after intervention.

The TDM of Biologics Scientific Committee was officially installed in the 2019 IATDMCT Congress. The committee’s objectives are:

- To develop guidelines for the use of TDM of biologics.
- To encourage the use of TDM of biologics with the aim of optimizing clinical drug use.
- To promote development of PK and PKPD models that can be used for dose adjustment in clinical practice.
- To provide knowledge of PK and the PK-response interaction.
- To promote best practice in relation to laboratory analysis of biologics.
- To enhance collaboration between groups working in the field and disseminate research in this area.
- To provide information on the measurement and clinical relevance of antibodies to biologics.
- To focus on harmonization and standardization of assays for TDM.

The TDM of Biologics Committee is chaired by Núria Padullés-Zamora and its vice-chair is Murray Barclay. The current members of the scientific committee are: Adam Cheifetz, Anne Strik, Annick de Vries, Bella Ungar, Catherine Smith, David Foster, David Ternant, Debby Thomas, Gertjan Wolbink, Helena Colom Codina, Jordi Guardiola, Konstantinos Papamichail, Lisa Stamp, Maya Imbrechts, Murray Barclay, Niels Vande Casteele, Núria Padullés-Zamora, Satohiro Masuda, Tomoyuki Mizuno, Zoe van Kempen.

If you are wishing to become involved in this field, you are welcome to join the new scientific committee. We also welcome you to submit abstracts on TDM of biologics for the 18th IATDMCT Congress in Banff (Canada).

References

The 36th annual meeting of the Japanese Society of Therapeutic Drug Monitoring (JSTDM) was held in Tokyo in May 2019. During the meeting, the young scientist committee (YSC) of the JSTDM held the third JSTDM-IATDMCT young scientist (YS) joint symposium with YSC of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology (IATDMCT). The JSTDM-IATDMCT YS joint symposium was held twice before with great success. The joint symposium was designed to share the recent research topics of TDM and Clinical Toxicology and improve the relationship between YS of the JSTDM and IATDMCT.

The symposium consisted of four presentations and it was managed by two chairs: Dr. Yosuke Suzuki (Department of Medication Use Analysis and Clinical Research, Meiji Pharmaceutical University, Japan) and Dr. Jyoti Nehra (Canadian Cancer Trial Group, Queens University, Kingston, Canada). Four YS speakers presented their recent research. The first presentation was “Strategy for TDM and its implications on response and tolerability of sunitinib in patients with metastatic renal cell cancer” by Dr. Jyoti Nehra. Her study was designed to develop a TDM strategy for sunitinib and showed that sunitinib exhibits high pharmacokinetic variability and the trough levels were highly predictive of response and toxicity. TDM of sunitinib is a hot topic in Japan because it is covered by insurance in Japan since 2018. There were many questions and comments after her presentation. The second presentation was “PK and PD study of mycophenolic acid in kidney transplant recipients” by Dr. Yasuaki Mino (Department of Hospital Pharmacy, Hamamatsu University School of Medicine, Japan). He demonstrated that large pharmacokinetic variability of mycophenolic acid and inosine 5’-monophosphate dehydrogenase (IMPDH) is a useful indicator of immunosuppression by mycophenolic acid. The third presentation was “Interaction between phenytoin and enteral nutrients” by Dr. Yoko Urashima (Laboratory of Clinical Pharmaceutics, Osaka Ohtani University, Japan). She introduced a clinical case that showed decreased plasma phenytoin concentrations and suggested the interaction between phenytoin and enteral nutrients. The final presentation was “From Data Monitoring to Dosage Optimization Clinical application of voriconazole PopPK in patients with liver dysfunction” by Dr. Miao Yan (Department of Pharmacy, The Second Xiangya Hospital of Central South University, China). His study focused on the pharmacokinetics of voriconazole and showed a significant decrease in total clearance in patients with liver dysfunction and total bilirubin, but not CYP2C19 polymorphisms, as the significant factors involved in voriconazole clearance. In his presentation, he briefly introduced his experiences at the 15th and 16th IATDMCT in Kyoto and Brisbane with some pictures and brightened up the atmosphere.

Approximately 60 YS members attended the symposium and the symposium was a great success. I would like to express my sincere appreciation to Presidents Prof. Toshiyuki Sakaeda and Prof. Teun van Gelder, Prof. Tsuyoshi Shiga, Prof. Yusuke Tanigawara, Prof. Satohiro Masuda, Dr. Ryuji Kato, and the respective Executive Boards for their support.

Group photo of the joint symposium speakers. From left to right, Dr. Yoko Urashima (Laboratory of Clinical Pharmaceutics, Osaka Ohtani University, Japan), Dr. Miao Yan (Department of Pharmacy, The Second Xiangya Hospital of Central South University, China), Dr. Jyoti Nehra (Canadian Cancer Trial Group, Queens University, Kingston, Canada), Dr. Yasuaki Mino (Department of Hospital Pharmacy, Hamamatsu University School of Medicine, Japan), and Dr. Yosuke Suzuki (Department of Medication Use Analysis and Clinical Research, Meiji Pharmaceutical University, Japan).
THE 1ST CHINATDM-IATDMCT YOUNG SCIENTIST JOINT SYMPOSIUM AT THE 9TH INTERNATIONAL XIANGYA CLINICAL PHARMACY FORUM

The 9th International Xiangya Clinical Pharmacy Forum was held in Changsha, China, from 5th to 7th September, 2019. As a special session for young scientists who are working in the fields of Therapeutic Drug Monitoring and Clinical Toxicology (TDM&CT), the 1st CHINATDM-IATDMCT Young Scientist Joint Symposium was successfully held by the Youth Committee, Division of TDM, Chinese Pharmacological Society (CHINA-TDM). The theme was “International Perspectives on Individualized Precision Medicine”.

The symposium consisted of two sections with nine presentations, which are monitored by two chairs, Prof. Vivian WY Lee and Prof. Yan Cheng. Prof. Xianglin Zhang (China-Japan Friendship Hospital) and Prof. Liyan Miao (The First Affiliated Hospital of Soochow University) were conducted as the consultants of the symposium. The executive chair of the symposium was Dr. Miao Yan, the secretary-general was Dr. Hualin Cai. The activities were mediated and presented by international young scientists and professionals from Netherlands, Canada, Japan, America and China.

In the first section, Dr. Wenqian Chen briefly introduced the history, annual conference, work prospects of CHINA-TDM and the youth committee on the topic of “TDM in China—Present, Past and Future”. Dr. Brenda de Winter gave her presentation- “Optimizing tacrolimus therapy using population pharmacokinetics”. She proposed a way to predict the starting dose of tacrolimus using the population pharmacokinetic (PopPK) models in pediatric and adult renal transplant recipients. Dr. Miao Yan is actively involved in the area of individualized application of voriconazole and he showed us how to tailor the voriconazole dosage in patients with liver dysfunction using TDM data and PopPK strategy. Dr. Jyoti Nehra’s presentation introduced a prospective study in 42 patients with metastatic renal cell cancer and showed that sunitinib trough concentration within 66~80 ng/ml is the target range to obtain a good efficacy and low adverse effects.

In the second section, Dr. Yosuke Suzuki showed a validated UPLC-MS/MS method for ultra-sensitive quantification of CYP2E1 probe drug chlorzoxazone and the application to a clinical PK study after microdosing of chlorzoxazone and midazolam. Dr. Hunlin Cai discussed
the “Correlation and interaction between clozapine concentration and therapeutic biomarkers in blood of schizophrenia patients”, which found that the biomarkers could be categorized into “fast-responsive” and “slow-responsive” types. Dr. Xuebin Wang showed us ‘Why and How to Switch Cyclosporine to Tacrolimus for Kidney Transplant Recipients?’. Dr. Wang suggested that the use of CYP3A5 genotyping to guide the initial dosage of tacrolimus is necessary when converting the immunosuppression therapy from cyclosporine to tacrolimus. Dr. Feng Chen’s study proposed that tailoring the dosage of tacrolimus individually for pediatric nephrotic syndrome patients at different developmental stages should be based on the CYP3A maturation, integrate ontogeny and genetics together. The final presentation was “Overview: Pharmacy Residency Training” by Dr. Diane Erdman (St Joseph Hospital, USA). Dr. Erdman explained the types, benefits, the accreditation and process of a pharmacy residency program.

Approximately 200 young scientists and pharmacists attended in the symposium. Questions were discussed further between each speaker and the audience.

The organizing committee of CHINATDM-IATDMCT YS Joint Symposium scheduled a “Young Scientists Night Out”. About 50 young scientists who came from America, Canada, Cape Verde, China, Ghana, Iraq, Japan, Netherlands and Pakistan expressed their opinions about their future development and dreams in TDM, while enjoying the beautiful night scenery and yummy cuisines. Although the conference course has finished, our international friendship, correspondence and cooperation will go on.
Dr. Maurice Ahsmann

I received my Pharm.D. from Utrecht University in 2005. After a brief stint in hospital pharmacy I investigated the pharmacokinetics of a multitude of drugs in neonatal and pediatric intensive care patients treated with Extracorporeal Membrane Oxygenation (ECMO), at the Erasmus University Medical Center in Rotterdam the Netherlands (under the supervision of Prof. D. Tibboel and Prof. R.A.A. Mathôt), resulting in my PhD in 2010. For the past nine years I have been working as a pharmacometrics consultant at LAP&P Consultants BV (Leiden, the Netherlands), providing model-based support of clinical development (phase I to III) and registration of novel drugs for major industrial players. In addition to my commercial activities, I am involved in non-commercial modeling efforts for dose-optimization with academic partners. My population PK/PD work experience encompasses multiple clinical areas, including reproductive health, hematology, oncology and auto-immune diseases. I aim to encourage IATDMCT members to incorporate pharmacometrics as an integral part of their clinical and research practice. I currently reside in Sao Paulo (Brazil).

Dr. Sara Baldelli

is a wife and mother of two adorable kids of 6 and 11 years old. She has been involved in the development and validation of biochemical methods for the quantification of different drugs in several biological matrix by HPLC and LC-MS-MS for routine clinical drug monitoring since 2001, after obtaining her degree in analytical chemistry in 2000 at the University of Milan. Dr. Baldelli started her career at the Mario Negri Institute for Pharmacological Research (Bergamo, Italy), where she met Dr. Cattaneo, dealing with the TDM of immunosuppressants. In 2002-2003, thanks to a fellowship, she worked at the College of Pharmacy of the University of Texas in Austin under the direction of Professor Brunner. In 2009, she moved from the Mario Negri Institute to the Luigi Sacco Hospital together with Dr. Cattaneo where they began working with anti-infecting agents and psychotropic drugs. In 2015, Dr. Baldelli received her degree in Pharmacology at the Medical Pharmacology Postgraduate School, at the University of Milan. She authored more than 60 papers in high-rank scientific journals, and presented the results of her researches at several national and international conferences.

Professor Elza Kimura (BS in Pharmaceutical Sciences – UNESP – Araraquara and PhD in São Paulo University in Clinical Pharmacokinetics, Brazil). Dr. Kimura was a research fellow at the Japanese Science, Technology and Education Ministry in the Clinical Biochemistry Laboratory at Chiba University and for 1 year at Prof. Paul Beringer’s laboratory at the University of Southern California (USC). Currently, she is a Professor of Clinical Pharmacy and Pharmacokinetics at Universidade Estadual de Maringá and Head of the Bioequivalence Laboratory at Clinical Research Center at University Hospital. Dr. Kimura is trained in HPLC-DAD-MS/MS and clinical trials for pharmacokinetics studies. She contributes with some microbial and cell culture experiments for Photodynamic Therapy using new photosensitizers, but her main research interest focus is on the clinical pharmacokinetics of drugs in ICU patients, obese and bariatric patients.

Dr. Amélie Marsot is an Assistant Professor and Head of STP2 Laboratory at the Faculty of Pharmacy at the Montreal University. She is an Associate Research at the Research Center of the Sainte Justine Hospital in the Infectious Disease and Acute Care axis in the Clinical pharmacology team. Recently, she joined the extended Pharmacometrics expert group of Conect4children, a collaborative network for European clinical trials for children. In May 2019 she received the “Prix de la Francophonie pour Jeunes Chercheurs – Agence Universitaire de la Francophonie” for all her research. Dr. Marsot is an expert in pharmacokinetics/pharmacodynamics modeling, TDM and clinical pharmacology. Patients with special conditions have been at the center of Dr. Marsot’s research since her first research project. Since obtaining her PhD, she developed many population pharmacokinetic models in infectious diseases in vulnerable populations such as neonates, onco-pediatrics and critically ill patients. These models allowed to increase the knowledge of pharmacokinetics of various drugs in specific populations and to identify factors of variability. Currently, Dr. Marsot is leading a research program on personalized antibiotic pharmacotherapy in pediatric, cystic fibrosis and critically ill patients.

Dr. Andrew W. Lyon

is a general clinical biochemist in Saskatoon hospitals and community practices. He has served leadership roles with the Canadian Society of Clinical Chemists, in provincial societies, the Canadian Academy of Clinical Biochemistry and was the IFCC website editor 2009-2011. Dr. Lyon has a variety of research interests including point-of-care testing, cannabinoids, cardiac and diabetes biomarkers and lab utilization.

(continued on page 14)
He is a returning member of IATDMCT. Recently he is involved in collaborations and clinical trials of cannabinoids with the Cannabinoid Research Initiative of Saskatchewan

Dr. Preeti Kulkarni is an academician currently working as Associate Professor and Head, Department of Quality Assurance, Gahlot Institute of Pharmacy, Navi Mumbai, India. Dr. Kulkarni has an industrial experience of six years in Quality Assurance and Regulatory Affairs. She completed her B. Pharmacy from Shivaji University Kolhapur (2002), M. Pharmacy with Quality Assurance specialization from SNDT Women’s University (2004), Mumbai and PhD in Pharmaceutical Sciences from Singhania University, Rajasthan (2016). Dr. Kulkarni has guided eleven M Pharmacy students so far. She has presented and published a number of research articles in National and International Journals and has received several research and travel grants from the Government of India and Pharmaceutical industries. Her research area, apart from Quality Assurance and Regulatory affairs, is biopharmaceutics, pharmacokinetics, bioanalysis and clinical trials. Dr. Kulkarni believes that learning process is eternal. It gives her immense happiness if students/ researcher scholars benefit from her knowledge and expertise. She is always excited about sharing her knowledge and experience with them and help them in any small way to scale greater heights.

Dr. Yanting Wang is a clinical pharmacist at National Cancer Center/Cancer Hospital Chinese Academy of Medical Sciences, Beijing China. She received her PhD degree of Pharmacology from Peking University, China. After graduation she completed a clinical pharmacy training in Western New England University and Yale New Haven Hospital in the United States. Dr. Wang now works in gynecologic oncology units, and her main responsibilities include participating in daily medical rounds with doctors, and performing routine clinical pharmacy services such as order verification, patient education, medication reconciliation, ADR reporting and management, pharmacy consultation, follow-up for patients in the Physician-Pharmacist Joint Clinic for Pain Management, pharmacy in-service education, oncology MDT, and TDM for some antibiotics and oncology medications, etc. Her focus of research interest includes TDM in oncology, rational use of opioids in cancer patients, molecular mechanisms underlying opioid addiction, etc. She is now hosting a grant from National Natural Science Foundation of China and a grant from Beijing Hope Run Foundation. Her story with IATDMCT began last year, when her abstract was accepted and she gave oral presentation at the “2018 IATDMCT Congress”. She got to know lots of great people in the conference and it is a precious memory of hers. Dr. Wang is also very interested in science communication and participated in several national and international competitions, here are a few examples of her awards: The First Prize of EURAXESS Science Slam China 2014, hosted by EURAXESS Links China, European Union Delegation to China and Mongolia, Think in China and Understanding Science; The Second Prize of the”National Competition for Science Communication Micro-videos in Oncology Pharmacy”, hosted by Chinese Pharmaceutical Association.

Wait to meet more new members at the Next Issue of COMPASS!!
The IATDMCT Council and the IATDMCT Office would like to extend their gratitude to Dr Paula Schaiquevich and Dr Edgar Spencer, the outgoing Editors of Compass, for their exemplary work during the past four years.

The Editors, IATDMCT Council and the IATDMCT Office would like to extend a very warm welcome to Dr Natalia Riva the new Editor-in-Chief and Dr Louise Andrews the new Associate Editor.

Wishing our readers, their colleagues and all the IATDMCT family a very joyous, peaceful and memorable holiday season. All the very best for 2020!
EXPLORING NEW FRONTEIRS IN TDM AND TOXICOLOGY

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