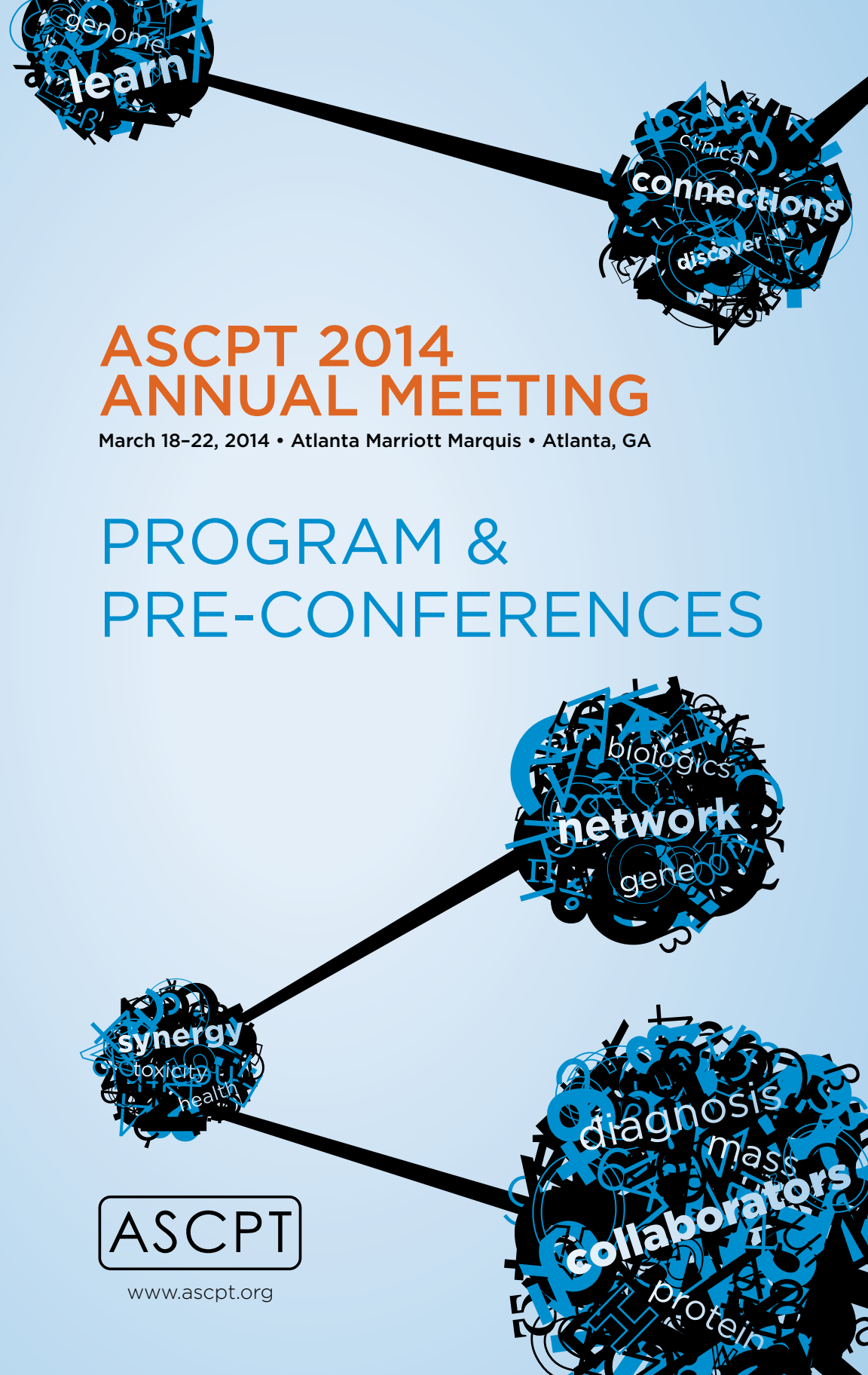

ASCPT 2014 ANNUAL MEETING

March 18–22, 2014 • Atlanta Marriott Marquis • Atlanta, GA

PROGRAM & PRE-CONFERENCES

ASCPT

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LEAD
INTRODUCE
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REVIEW
SHOWCASE
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GUIDE
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CULTIVATE
IMPROVE
INTEGRATE
DECIDE
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WELCOME MESSAGE

Dear Colleague:

As President of the American Society for Clinical Pharmacology and Therapeutics (ASCPT), it is my pleasure to welcome you to Atlanta and to the 115th Annual Meeting of ASCPT. ASCPT is the premier organization in the field of clinical pharmacology, and is proud to offer an outstanding scientific program, including a robust roster of internationally renowned speakers and an abundance of networking opportunities.

Consistent with the Society's Strategic Plan, ASCPT has expanded the content of this year's meeting by offering three outstanding Pre-conference programs, and one focused Post-conference session. We welcome our colleagues who attended the Pre-conferences and those who will attend the Post-conference. In addition, we extend a warm welcome to our colleagues from the US Food and Drug Administration.

Karthik Venkatakrishnan, PhD, has been a visionary and effective chairperson of this year's Scientific Program Committee (SPC), and we are grateful for his efforts and those of the entire SPC in developing a best-in-class scientific program.

The 2014 scientific program includes four exciting State of the Art lectures by Brian Kobilka, MD, Stanford University; Harold Jaffe, MD, MA, Centers for Disease Control and Prevention; Paula Stephan, PhD, Georgia State University; and Jeffrey Glenn, MD, PhD, Stanford University. This year's Featured Speakers include Virginia (Ginny) Schmith, PhD, FCP, GlaxoSmithKline, and Rachel Tyndale, PhD, University of Toronto.

ASCPT will honor a number of outstanding individuals for their work in advancing clinical pharmacology, improving patient care, and their contributions to ASCPT. The 2014 honorees are Edward Sellers, MD, PhD; Mats Karlsson, PhD; Bruce Pollock, MD, PhD; Shiew-Mei Huang, PhD; Nadav Ahituv, PhD; Yuichi Sugiyama, PhD; and Juan Lertora, MD, PhD.

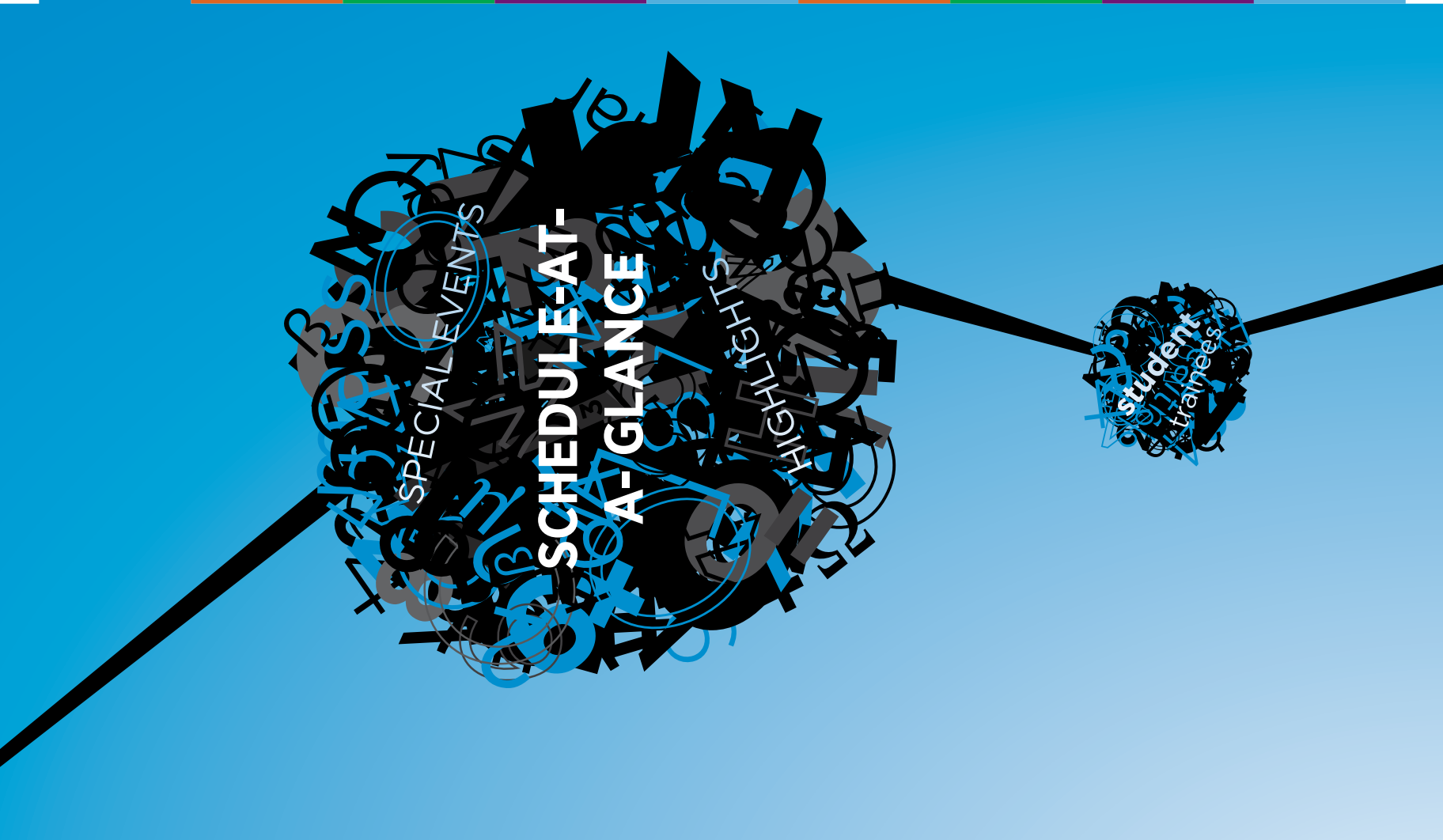
I urge you to stop by the Town Hall Session (even for 10 minutes!) and take the opportunity to engage with a host of ASCPT leaders, discuss issues important to you, and learn about opportunities for involvement in the Society.

Visit the poster and exhibit hall from Wednesday, March 19 through Friday, March 21. Not only will you see a host of cutting-edge science, you'll meet a wide range of exhibitors showcasing clinical pharmacology products and services relevant to you.

Finally, I encourage you to make the most of your time here and thank you for attending the ASCPT 2014 Annual Meeting!

Sincerely,

Russ B. Altman, MD, PhD
President


SPECIAL EVENTS
SCHEDULE-AT-A-GLANCE
HIGHLIGHTS
student trainees

ACKNOWLEDGMENT

Thank you to the ASCPT Board of Directors for their leadership and dedication in guiding the Society.

Russ B. Altman, MD, PhD
President

John A. Wagner, MD, PhD
President-Elect

Kathleen M. Giacomini, PhD
Immediate Past President

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Director

Mario L. Rocci, Jr., PhD
Director

Anne Zajicek, MD, PharmD
Director

TUESDAY, MARCH 18, 2014

7:00 am – 3:00 pm	Pre-conferences Registration	Marquis Foyer
8:00 am – 5:00 pm	**PRE-CONFERENCE** *Current Considerations in the Clinical Pharmacology of Biologics*	Marquis C
	PRE-CONFERENCE *Next-Generation Clinical Pharmacology: Integrating Systems Pharmacology, Data-Driven Therapeutics, and Personalized Medicine*	Marquis D
12:00 noon – 1:00 pm	Pre-conferences Joint Lunch	Skyline
1:00 pm – 5:00 pm	CPT Associate Editors Meeting *(By Invitation Only)*	M101

WEDNESDAY, MARCH 19, 2014

7:00 am – 8:30 am	CPT Editorial Board Meeting *(By Invitation Only)*	Marquis D
8:00 am – 10:00 am	Pre-conference Registration	Marquis Foyer
9:00 am – 1:00 pm	CPT:PSP Associate Editors Meeting *(By Invitation Only)*	M108
9:30 am – 2:00 pm	**PRE-CONFERENCE** *Using Big Data to Study Drug Effects in Populations*	Marquis C
11:00 am – 1:00 pm	CCSS & Section Orientation *(By Invitation Only)*	M103/ 104/105
11:30 am – 12:15 pm	Using Big Data Pre-conference Lunch *(Ticket Required)*	Marquis D
12:00 noon – 7:00 pm	ASCPT Central/Registration Open	Marquis Foyer
12:30 pm – 1:30 pm	New Member Welcome	M106/107
12:30 pm – 1:45 pm	Clinical Pharmacology Program Director's Meeting	L504/505
1:30 pm – 2:00 pm	Awards Reception *(By Invitation Only)*	M102
2:00 pm – 3:00 pm	Opening Session	Imperial Ballroom
3:00 pm – 4:00 pm	**STATE OF THE ART LECTURE** *Brian Kobilka, MD*	Imperial Ballroom
4:30 pm – 5:00 pm	Showcase of Top Trainee Abstracts	Marquis C
5:00 pm – 6:30 pm	Exhibits Open Opening Reception	International Hall
6:45 pm – 7:45 pm	Quiz Bowl	Marquis D
8:00 pm – 9:30 pm	Speed Mentoring	M103/ 104/105
8:00 pm – 9:00 pm	Board of Directors Dessert Reception *(By Invitation Only)*	President's Suite
8:00 pm – 9:30 pm	Dessert Reception Honoring Shiew-Mei Huang and Yuichi Sugiyama *(By Invitation Only)*	M106/107

THURSDAY, MARCH 20, 2014

7:00 am – 4:00 pm	ASCPT Central/ Registration Open	Marquis Foyer
7:00 am – 8:30 am	CPT:PSP Editorial Board Meeting *(By Invitation Only)*	M101
7:30 am – 2:00 pm	Posters and Exhibits Open	International Hall
7:30 am – 9:00 am	**SCIENCE AT SUNRISE SESSIONS** *Next Generation Sequencing 101: The Basics You Need to Know*	Marquis A
	Clinical and Regulatory Challenges in the Development of Oral Cancer Drugs	Marquis B
	Endogenous Biomarkers for the Assessment of CYP3A Activity	Marquis C
7:30 am – 9:00 am	Continental Breakfast in the Exhibit Hall Attended Posters*	International Hall
8:30 am – 10:15 am	**INTERNATIONAL SESSION** *Clinical Pharmacology in the Netherlands: Impact on Use of Medication and Teaching Health Professionals*	Marquis D
9:15 am – 10:15 am	**RAWLS-PALMER PROGRESS IN MEDICINE AWARD LECTURE** *Yuichi Sugiyama, PhD*	Imperial Ballroom
10:15 am – 10:45 am	Morning Break in the Exhibit Hall	International Hall
10:45 am – 11:45 am	**FEATURED SPEAKER** *Virginia (Ginny) Schmith, PhD, FCP*	Marquis A
10:45 am – 12:15 pm	**ASCPT DEBATE** *Debating About the Evidence for Clinical Utility of Pharmacogenetic Testing*	Imperial Ballroom
10:45 am – 12:00 noon	**ORAL SESSION** *Population-Based Advances in Pharmacotherapy*	Marquis C
12:00 noon – 1:30 pm	Lunch Available for Purchase in the Poster and Exhibit Hall *(Ticket Required)*	International Hall
	Trainee Luncheon *(Ticket Required)*	Marquis D
	ASCPT Board of Directors Luncheon *(By Invitation Only)*	M102

*Including Late-breaking and Encore Posters

THURSDAY, MARCH 20, 2014

1:30 pm – 3:30 pm	**SYMPOSIA**	
	Systems Pharmacology Approach to Defining and Predicting Tyrosine Kinase Inhibitor (TKI) Toxicity	Imperial Ballroom
	Challenging the Maximum Tolerated Dosing Paradigm in Oncology: Threading the Needle with Targeted Agents	Marquis A
	What is the Best Type of Data for POC Studies: Continuous, Categorical, or Count Data?	Marquis B
	Early Drug Development Challenges and Strategies for Orphan Indications	Marquis C
3:45 pm – 5:15 pm	**STATE OF THE ART LECTURE** *Harold W. Jaffe, MD, MA*	Imperial Ballroom
5:30 pm – 7:00 pm	**SECTION MEETINGS**	
	Molecular Pharmacology and Pharmacogenetics (MOL)	Marquis B
	Pharmacometrics and Pharmacokinetics (PMK)	Marquis C
	Biomarkers and Imaging (BIO)	M102

6:00 pm – 7:00 pm	Donor Reception *(By Invitation Only)*	Sear Private Dining Room
6:30 pm – 8:00 pm	UCSF–Stanford-Genentech Reception for Faculty and Staff, Trainees, Alumni and Friends *(By Invitation Only)*	M106/107
	PhRMA Foundation Reception *(By Invitation Only)*	M109
7:00 pm – 8:00 pm	Career Bootcamp Reception *(Ticket Required)*	M101
	International Reception *(By Invitation Only)*	M104/105
8:00 pm – 9:00 pm	Gavel Club Dessert Reception *(By Invitation Only)*	President's Suite

FRIDAY, MARCH 21, 2014

7:00 am – 4:00 pm	ASCPT Central/ Registration Open	Marquis Foyer
7:00 am – 8:00 am	ASCPT Finance Committee Meeting *(By Invitation Only)*	M102
7:00 am – 9:00 am	American Board of Clinical Pharmacology (ABCP) Board Meeting *(By Invitation Only)*	L504
7:30 am – 3:30 pm	Posters and Exhibits Open	International Hall
7:30 am – 9:00 am	Continental Breakfast in the Exhibit Hall	International Hall
7:30 am – 9:00 am	**SECTION MEETINGS** *Drug Development and Regulatory Sciences (DDR)*	Marquis C
	Drug Safety (SAF)	M108
	Infectious Diseases (INF)	M105
	Oncology (ONC)	M106/107
	Organ Specific Diseases (OSD)	M109
	Special Populations (SPO)	M104
9:15 am – 10:15 am	**STATE OF THE ART LECTURE** *Paula Stephan, PhD*	Imperial Ballroom
10:15 am – 10:25 am	Transition to the Future	Imperial Ballroom
10:30 am – 11:30 am	**OSCAR B. HUNTER MEMORIAL AWARD IN THERAPEUTICS LECTURE** *Edward M. Sellers, MD, PhD, FRCPC, FACP*	Imperial Ballroom
10:30 am – 11:45 am	**ORAL SESSIONS** *Transporters Across the Therapeutic Spectrum*	Marquis A
	Computational Drug Discovery and Development	Marquis B
	Having Your Drugs and Safety Too	Marquis C
11:45 am – 1:15 pm	Lunch Available for Purchase in the Poster and Exhibit Hall *(Ticket Required)* Attended Posters*	International Hall
12:00 noon – 1:00 pm	**INTERNATIONAL TRANSPORTER CONSORTIUM (ITC)** Special Interest Group Meeting *(By Invitation Only)*	M102

*Including Late-breaking and Encore Posters

FRIDAY, MARCH 21, 2014

12:00 noon – 1:00 pm	**PHARMACOMETABOLOMICS** Special Interest Group Meeting	M101
12:15 pm – 1:00 pm	**TOWN HALL SESSION**	International Level - Room B
1:15 pm – 2:15 pm	**FEATURED SPEAKER** *Rachel F. Tyndale, PhD*	Marquis A
1:15 pm – 2:15 pm	**SHEINER-BEAL PHARMACOMETRICS AWARD LECTURE** *Mats O. Karlsson, PhD*	Imperial Ballroom
1:15 pm – 2:45 pm	**SPECIAL SESSION** *Expanding Your Horizons: A Guide to Mid-Career Transitions*	Marquis C
1:15 pm – 2:45 pm	**WORKSHOP** *Next Generation Cancer Immunotherapy Coming of Age: Targeting Immune Checkpoints*	Marquis B
2:45 pm – 3:15 pm	Networking Break in the Poster and Exhibit Hall	International Hall
3:15 pm – 4:15 pm	**STATE OF THE ART LECTURE** *Jeffrey S. Glenn, MD, PhD*	Imperial Ballroom
4:30 pm – 6:30 pm	**SYMPOSIA** *New Applications of Quantitative Approaches in a Changing Health Care Environment: Incorporating Effectiveness and Cost in Our Models*	Imperial Ballroom
	Challenges and Opportunities for Physiologically-Based Pharmacokinetic (PBPK) Modeling in Pediatric Drug Development	Marquis A
	Next Generation Sequencing and Bioinformatics: The Driving Force of the New Era of Pharmacogenomics	Marquis B
	Trends in Oral Drug Exposure in Post-Bariatric Surgery Patients: Challenges in Pharmacotherapy of an Ever-Growing Population	Marquis C
7:00 pm – 8:30 pm	**PRESIDENT'S RECEPTION**	Atrium A

SATURDAY, MARCH 22, 2014

7:00 am – 10:00 am	ASCPT Central/ Registration Open	Marquis Foyer
7:00 am – 9:00 am	ASCPT Board of Directors Meeting *(By Invitation Only)*	M101
7:30 am – 9:00 am	**SCIENCE AT SUNRISE SESSIONS** *The Human Blood Brain Barrier in Drug Development*	Marquis A
	Study Participants and Social Media: Recruitment, Participation and Impact on Study Design	Marquis B
7:30 am – 9:00 am	Continental Breakfast	Marquis Foyer
8:00 am – 2:00 pm	**CAREER BOOTCAMP** *(Ticket Required)*	M103/104/ 105
8:30 am – 10:00 am	**WORKSHOPS** *The Rising Challenge of Polypharmacy: Considerations for Concurrent Therapies in Oncology with HIV/AIDS*	Marquis C
	Microdosing in Children: A Useful Tool for Pediatric Drug Development?	Marquis D
9:00 am – 10:00 am	**LEON I. GOLDBERG YOUNG INVESTIGATOR AWARD LECTURE** *Nadav Ahituv, PhD*	Marquis A
9:00 am – 10:00 am	**ORAL SESSION** *Innovation in Physiologically Based PK Applications*	Marquis B
10:15 am – 11:45 am	**WORKSHOPS** *Pharmacological Considerations of Fetal Therapy*	Marquis C
	Registries and Databases in Clinical Research	Marquis D
10:15 am – 12:15 pm	**SYMPOSIA** *Pharmacometabolomics: Biochemical Tools for Mapping Pathways Implicated in Drug Response Phenotypes*	Marquis A
	Quantitative and Systems Pharmacology Approaches for the Development of Oncology Drugs	Marquis B

SPECIAL EVENTS & HIGHLIGHTS

To achieve the goal of attaining a diverse, well-rounded, educational program, the Scientific Program Committee (SPC) has developed an overall Annual Meeting theme of "Advances in Therapeutics." This theme is incorporated in Symposia, Workshops, and Science at Sunrise sessions and throughout the entire program.

Additionally, the SPC has resumed the identification and branding of sessions according to the drug discovery, development, regulation, and utilization (DDRU) continuum to be consistent with ASCPT's Strategic Plan and the ongoing work of its members.

Component(s) of the DDRU continuum that apply to the particular Symposium, Workshop, and Science at Sunrise session have been identified and branded accordingly.

- D Discovery
- D Development
- R Regulation
- U Utilization

For example, this image indicates that the corresponding session includes the Discovery and Development components of the DDRU continuum.

Pre-conference Programs

ASCPT will offer three scientific Pre-conference programs designed for scientists and health professionals engaged in all aspects of clinical pharmacology, including educators, regulatory officials, consultants, industry professionals, and students and fellows. See pages 19-38 for details on these sessions.

Current Considerations in the Clinical Pharmacology of Biologics
Pre-conference
Tuesday, March 18, 2014
8:00 am – 5:00 pm, Marquis C

Next-Generation Clinical Pharmacology: Integrating Systems Pharmacology, Data-Driven Therapeutics, and Personalized Medicine Pre-conference
Tuesday, March 18, 2014
8:00 am – 5:00 pm, Marquis D

Wednesday, March 19, 2014

Using Big Data to Study Drug Effects in Populations
Pre-conference
9:30 am – 2:00 pm, Marquis C

This half-day Pre-conference on pharmacoepidemiology is supported by a grant from the Burroughs Wellcome Fund and endorsed by the Drug Safety Scientific Section.

The primary target audience for this course is pre-doctoral and post-doctoral students as well as junior faculty. All other ASCPT attendees are welcome to attend.

SHOWCASE OF TOP TRAINEE ABSTRACTS
4:30 pm – 5:00 pm, Marquis C

View the abstracts submitted by the 2014 Presidential Trainee Award recipients, while supporting your peers and networking with colleagues. Posters will be on display during the Opening Reception and poster session hours on Thursday and Friday.

The Showcase of Top Trainee Abstracts is sponsored by Janssen Research and Development.

OPENING RECEPTION AND EXHIBITS
5:00 pm – 6:30 pm
International Hall

ASCPT invites you to join your colleagues on Wednesday evening for the first networking event of the meeting. Interact with fellow scientists from all over the globe and exhibitors representing a wide range of services and products.

The Opening Reception is sponsored by Pfizer.

SPECIAL EVENTS & HIGHLIGHTS

QUIZ BOWL
6:45 pm – 7:45 pm, Marquis D

Back by popular demand! Teams representing academia, consulting, industry, government, and trainees/students (new this year!), are quizzed on clinical pharmacology and ASCPT history trivia in a highly interactive game of intelligence and strategy. Join host Gregory L. Kearns, PharmD, PhD, for this fun and interactive way to network and learn with your colleagues.

The Quiz Bowl is sponsored by Janssen Research and Development.

SPEED MENTORING
8:00 pm – 9:30 pm, M103/104/105

New in 2014! The Mentor Task Force will host a Speed Mentoring event where potential mentors and mentees can network and find potential matches. Attendees interested in participating in the ASCPT Mentoring Program are encouraged to join us to develop new partnerships that will prove to be beneficial to both parties.

Speed Mentoring is sponsored by Janssen Research and Development.

Thursday, March 20, 2014

INTERNATIONAL SESSION
Clinical Pharmacology in the Netherlands: Impact on Use of Medication and Teaching Health Professionals
8:30 am – 10:15 am, Marquis D

Recent position papers addressing the profession of clinical pharmacology have expressed concerns about the decline of interest in the field among clinicians and medical educators in the United Kingdom and other Western countries about whether clinical pharmacology is actually therapeutics. The Dutch Society for Clinical Pharmacology and Biopharmacy offers answers to these questions and presents a new model for clinical pharmacology.

ASCPT DEBATE
Debating about the Evidence for Clinical Utility of Pharmacogenetic Testing
10:45 am – 12:15 pm
Imperial Ballroom

New in 2014! A live point/counterpoint debate about the evidence for clinical utility of pharmacogenetic testing. This exciting new session will make available to attendees different opinions on the level of evidence in pharmacogenetic testing. The debate will focus audience attention on the scientific information that underlies the issues being presented by multiple debaters, inviting lively engagement of the audience through the exchange of ideas and contribution to definitions of a consensus on the topic.

SPECIAL EVENTS & HIGHLIGHTS

INTERNATIONAL RECEPTION
7:00 pm – 8:00 pm, M104/105

This special, invitation only reception is intended as an opportunity for our international attendees to interact with the ASCPT leadership, as well as meet colleagues from around the globe.

The International Reception is sponsored by PRA.

CAREER BOOTCAMP RECEPTION
7:00 pm – 8:00 pm, M101

ASCPT will host a Career Bootcamp Reception preceding the Bootcamp program, on Thursday, March 20, 7:00 pm – 8:00 pm. This special social event is designed to provide networking time for the registrants with the Bootcamp speakers. This reception is a ticketed event.

Friday, March 21, 2014

ASCPT TOWN HALL SESSION
12:15 pm – 1:00 pm
International Level–Room B

Led by ASCPT President, Russ B. Altman, MD, PhD, this is a unique opportunity for ASCPT members to talk with the Society's leadership, and discuss ways to engage with the Society. You'll have the opportunity to have one-on-one discussions with key leaders of ASCPT, learn about important Society initiatives and discuss how you can play a role in ASCPT's future. Whether you can stop by the Town Hall for 10 minutes, or stay for the duration of the event, you are encouraged to attend!

MID-CAREER TRANSITIONS
1:15 pm – 2:45 pm, Marquis C

New in 2014! This Special Session titled, "Expanding Your Horizons: A Guide to Mid-Career Transitions," will focus on mid-career transitions and the factors involved. This 90-minute session will begin with two 15-minute talks by mid-career scientists who transitioned between areas within clinical pharmacology. Speakers will describe their experiences and the factors that aided the transition, including a discussion on how mentorship (mentoring and being mentored) guided their decisions. Presentations will be followed by a moderated panel discussion.

PRESIDENT'S RECEPTION
7:00 pm – 8:30 pm, Atrium A

Join us as we honor and recognize the contributions of ASCPT President Russ B. Altman, MD, PhD, during the last evening of the meeting, and network with your colleagues over light fare and beverages.

The President's Reception is sponsored by Clinilabs.

Saturday, March 22, 2014

HALF-DAY POST-CONFERENCE PROGRAM
Career Bootcamp
8:00 am – 2:00 pm, M103/104/105
Separate registration is required and admission is by ticket only.

The ASCPT Career Bootcamp is a half-day Post-conference designed to address the immediate needs of trainees, junior faculty, and young scientists in the early years of their career. Discussion topics include Grants 101, Negotiating a Startup Package, and Interviewing for Industry. This Post-conference will conclude with a panel discussion driven by questions and topics brought forth by the attendees.

STATE OF THE ART LECTURES

Don't miss out! Plan to attend the State of the Art Lectures from four renowned professionals in their fields.

WEDNESDAY, MARCH 19

3:00 pm – 4:00 pm, Imperial Ballroom
Brian Kobilka, MD, Stanford University
Structural Insights into G Protein Coupled Receptor Signaling

THURSDAY, MARCH 20

3:45 pm – 5:15 pm, Imperial Ballroom
Harold W. Jaffe, MD, MA, Centers for Disease Control and Prevention
The Early Days of the AIDS Epidemic in the United States: Views from Hollywood and Atlanta

FRIDAY, MARCH 21

9:15 am – 10:15 am, Imperial Ballroom
Paula Stephan, PhD, Georgia State University
How Economics Shapes Science

3:15 pm – 4:15 pm, Imperial Ballroom
Jeffrey S. Glenn, MD, PhD, Stanford University School of Medicine
Taking Down Hepatitis C

FEATURED SPEAKERS

Join us for the two Featured Speaker sessions and hear presentations from your fellow ASCPT members.

THURSDAY, MARCH 20

10:45 am – 11:45 am, Marquis A
Virginia (Ginny) Schmith, PhD, FCP, GlaxoSmithKline
Pharmacometrics: Focus on the Patient

FRIDAY, MARCH 21

1:15 pm – 2:15 pm, Marquis A
Rachel F. Tyndale, PhD, University of Toronto
Smoking—It's in Your Genes

STUDENT & TRAINEE INFORMATION

The ASCPT 2014 Annual Meeting features several educational sessions and networking events designed specifically for trainees and young scientists to aid them in their personal and professional development.

PHARMACOEPIDEMIOLOGY PRE-CONFERENCE

Wednesday, March 19, 2014
9:30 am – 2:00 pm, Marquis C

ASCPT will host a half-day Pre-conference on pharmacoepidemiology titled "Using Big Data to Study Drug Effects in Populations." Chaired by Sean Hennessy, PharmD, PhD, this Pre-conference will feature key pharmacoepidemiology talks by four outstanding scientists. The primary target audience for this Pre-conference includes pre-doctoral students, post-doctoral fellows, and junior faculty.

This complimentary Pre-conference requires advance registration, and is funded by a grant from the Burroughs Wellcome Fund and endorsed by the Drug Safety Scientific Section.

SHOWCASE OF TOP TRAINEE ABSTRACTS

Wednesday, March 19, 2014
4:30 pm – 5:00 pm, Marquis C

View the abstracts submitted by the 2014 Presidential Trainee Award recipients, while supporting your peers as they present their latest high-quality research. Posters will be on display during the Opening Reception and Poster Session hours on Thursday and Friday.

The Showcase of Top Trainee Abstracts is sponsored by Janssen Research and Development.

ASCPT QUIZ BOWL

Wednesday, March 19, 2014
6:45 pm – 7:45 pm, Marquis D

The second annual ASCPT Quiz Bowl will feature an all new Trainee/Student team. Teams will be quizzed on clinical pharmacology topics and ASCPT history in this exciting and highly competitive game. Come out and support your peers as they fight for the grand prize and ultimate bragging rights.

The Quiz Bowl is sponsored by Janssen Research and Development.

SPEED MENTORING – NEW IN 2014!

Wednesday, March 19, 2014
8:00 pm – 9:30 pm, M103/104/105

The Mentor Task Force will host a Speed Mentoring event following the Quiz Bowl. Potential mentors and mentees are invited to this new networking event for the opportunity to meet and speak with numerous potential matches. Attendees of this new event will walk away with connections who may influence their personal and professional lives for years to come.

Speed Mentoring is sponsored by Janssen Research and Development.

TRAINEE LUNCHEON

Thursday, March 20, 2014
12:00 noon – 1:30 pm, Marquis D

Back by popular demand, the Trainee Luncheon offers roundtable discussions for trainees and young scientists to meet with established clinical pharmacologists to discuss potential career paths. Learn more about the facilitators by viewing their bios online at www.ascpt.org. This complimentary luncheon requires advance registration.

STUDENT & TRAINEE INFORMATION

MID-CAREER TRANSITIONS – NEW IN 2014!

Friday, March 21, 2014
1:15 pm – 2:45 pm, Marquis C

This Special Session titled, "Expanding Your Horizons: A Guide to Mid-Career Transitions," will focus on mid-career transitions and the factors involved. This 90-minute session will begin with two 15-minute talks by mid-career scientists who transitioned between areas within clinical pharmacology. Speakers will describe their experiences and the factors that aided the transition, including a discussion on how mentorship (mentoring and being mentored) guided their decisions. Presentations will be followed by a moderated panel discussion. Plan to attend this complimentary session and get insight from those who have successfully navigated across different career paths.

CAREER BOOTCAMP RECEPTION

Thursday, March 20, 2014
7:00 pm – 8:00 pm, M101

ASCPT will host a Career Bootcamp Reception, preceding the Bootcamp program, designed to provide networking time for the registrants with the Bootcamp speakers. Meet the speakers and fellow registrants ahead of the Career Bootcamp and discuss what you look forward to most about the upcoming program. This reception is a ticketed event. You must register for the Career Bootcamp in order to receive a ticket to attend this event.

CAREER BOOTCAMP

Saturday, March 22, 2014
8:00 am – 2:00 pm, M103/104/105

This half-day Post-conference program addresses common questions and concerns among trainees and young scientists as they navigate through the early years of their career development. This interactive session will include a panel discussion where you can ask your questions directly of the facilitators. View the speakers' bios online at www.ascpt.org. Separate registration is required.

ASCPT MENTORING PROGRAM

The ASCPT Mentoring Program pairs young scientists with esteemed professionals in the field to establish mutually beneficial relationships. Network with your mentoring partner at the Annual Meeting and experience the meeting through their eyes. To be paired up with a mentor or mentee, visit ASCPT Central and complete the participation form.

SOCIAL MEDIA FEEDBACK

On-site, share your thoughts and comments about the ASCPT Annual Meeting with your peers on Facebook, Twitter (#ASCPT2014), or LinkedIn. Post a message about a session or event that resonated with you and be entered to win a $100 American Express gift card. Follow us on Facebook at www.facebook.com/clinpharm, on Twitter @ascpt_clinpharm, or connect to the American Society for Clinical Pharmacology and Therapeutics on LinkedIn.

TRAINEE LUNCHEON

THURSDAY, MARCH 20, 2014
12:00 noon – 1:30 pm, Marquis D
This is a ticketed event; you must have registered and received a ticket with your registration materials to attend this luncheon.

In support of ASCPT's strategic initiative to build capacity through the development and support of career development and leadership programs for junior scientists and investigators, ASCPT is pleased to bring back the highly successful Trainee Luncheon to the 2014 Annual Meeting. This luncheon—open only to trainees and students—is a roundtable discussion for trainees and young scientists to meet with established clinical pharmacologists to discuss potential career paths and other topics driven by trainees' questions.

Participants will rotate between tables to allow for multiple facilitator discussions. Facilitators include top leaders from the academia, consulting, government, and industry sectors of clinical pharmacology. Facilitators will be seated at tables bearing their names and the employment sector that they represent. A short summary of each facilitator's background and current position is available on the ASCPT website at www.ascpt.org.

This luncheon is a perfect complement to the ASCPT Career Bootcamp being offered on Saturday, March 22, 2014.

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Dionna J. Green, MD, US Food and Drug Administration

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Issam Zineh, PharmD, MPH, US Food and Drug Administration

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Megan A. Gibbs, BscPharm, PhD, FCP, Amgen

Christine Haller, MD, BioMarin Pharmaceutical Inc.

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CURRENT CONSIDERATIONS IN THE CLINICAL PHARMACOLOGY OF BIOLOGICS PRE-CONFERENCE

Tuesday, March 18, 8:00 am – 5:00 pm, Marquis C
UAN: 0708-9999-14-209-L04-P

Upon completion of this Pre-conference, the attendee will be able to:

- Apply novel strategies in the application of clinical pharmacology in the development of biotherapeutics;
- Discuss unique differences in regulatory strategy and drug development decision making for biosimilars;
- Discuss perspectives on when PBPK models are useful for the internal industry decision making and regulatory submissions of biologics; and
- Explain the use of pharmacometrics applied to biologics to inform trial design.

7:00 AM – 3:00 PM
PRE-CONFERENCE REGISTRATION OPEN
Marquis Foyer

8:00 AM – 8:30 AM
CONTINENTAL BREAKFAST

8:30 AM – 8:50 AM
INTRODUCTIONS AND MEETING OVERVIEW

Megan Gibbs, PhD, BscPharm, FCP, Amgen

8:50 AM – 10:15 AM
SESSION I: CLINICAL PHARMACOLOGY
SPEAKERS
The PCSK9 Translational Story: Modeling and Simulation in the Preclinical and Early Development Stages
John Gibbs, MD, PhD, Amgen

Can the Immunogenicity Risk of Monoclonal Antibody Drugs Be Predicted?

Liang Zhao, PhD, US Food and Drug Administration

Special Populations

Honghui Zhou, PhD, FCP, Janssen Research and Development

10:15 AM – 10:30 AM
BREAK

10:30 AM – 11:55 AM
SESSION II: MODELING AND SIMULATION
SPEAKERS
Applications of Physiologically Based Models to Predict the Human Pharmacokinetics and Target Binding of Therapeutic Proteins

Iain Gardner, BPharm, PhD, Simcyp

Translational Modeling for Cancer Vaccines

Iñaki F. Trocóniz, PhD, University of Navarra

Model-Based Meta-Analysis to Facilitate Development of Biologics

Marc Pfister, MD, FCP, Quantitative Solutions

CURRENT CONSIDERATIONS IN THE CLINICAL PHARMACOLOGY OF BIOLOGICS PRE-CONFERENCE

Tuesday, March 18, 8:00 am – 5:00 pm, Marquis C
UAN: 0708-9999-14-209-L04-P

SESSION III: LUNCH AND POSTERS

12:00 NOON – 12:45 PM
LUNCH BREAK
Skyline

12:45 PM – 1:30 PM
ATTENDED POSTERS
Skyline

1:30 PM – 3:00 PM
SESSION IV: BIOSIMILARS
SPEAKERS
Overview of Clinical Pharmcology Data to Support a Demonstration of Biosimilarity

Yow-Ming Wang, PhD, US Food and Drug Administration

Pharmacokinetic Considerations for Biosimilars Development

Primal Kaur, MD, Amgen

The Potential for Modeling and Simulation in the Development of Biosimilar Products: A European Regulator's View

Jacob Brogren, MSc, PharmD, Medical Products Agency

3:00 PM – 3:15 PM
BREAK

3:15 PM – 4:45 PM
SESSION V: SPECIAL TOPICS
SPEAKERS
Overview of Antibody Drug Conjugate Development and Clinical Pharmacology Strategy

Chunze Li, PhD, Genentech

Dual Action Antibodies

Amit Garg, PhD, Amgen

4:45 PM – 5:00 PM
CLOSING REMARKS

Megan Gibbs, PhD, BscPharm, FCP, Amgen

BIOLOGICS PRE-CONFERENCE POSTER PRESENTATIONS

BP-001
EVALUATION OF THE EFFECTS OF BLINATUMOMAB-MEDIATED CYTOKINE ELEVATIONS ON CYTOCHROME P450 ENZYMES USING A PHYSIOLOGY-BASED PHARMACOKINETIC (PBPK) MODEL.
Y. Xu,[1] Y. Hijazi,[2] A. Wolf,[2] B. Wu,[1] Y. Sun,[1] M. Zhu[1]; [1]Amgen Inc., Thousand Oaks, CA, [2]Amgen Research (Munich) GmbH, Munich, Germany.

BP-002
A MODEL-BASED APPROACH TO PREDICT PLASMA/BRAIN COCAINE LEVELS FOLLOWING RBP-8000, A DOUBLE MUTANT BACTERIAL COCAINE ESTERASE; ADMINISTRATION IN HUMANS.
B. Zheng, Y. Liu, C. Heidbreder, P. J. Fudala, A. Nasser; Reckitt Benckiser Pharmaceuticals Inc., Richmond, VA.

BP-003
CLINICAL DOSE PREDICTION FOR ALBUMIN-BINDING DOMAIN ANTIBODY WITH LONG-DURATION GLP-1 ACTION, GSK2374697, INTENDED FOR USE IN T2DM AND OBESITY.
R. L. O'Connor-Semmes, M. A. Paulik, A. E. Acker; GlaxoSmithKline, Research Triangle Park, NC.

BP-004
MODELING AND SIMULATIONS OF ECULIZUMAB IN PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH) AND ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS) PATIENTS.
C. Lathia,[1] N. Kassir,[2] M. S. Mouksassi,[2] B. Jayaraman,[2] J. F. Marier,[2] C. L. Bedrosian[2]; [1]Alexion Pharmaceuticals, Cheshire, CT, [2]Pharsight, Montreal, QC, Canada.

BP-005
PK/PD MODELING OF ECULIZUMAB AND FREE COMPLEMENT COMPONENT PROTEIN C5 IN PEDIATRIC AND ADULT PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS).
C. Lathia,[1] N. Kassir,[2] M. S. Mouksassi,[2] B. Jayaraman,[2] J. F. Marier,[2] C. L. Bedrosian[1]; [1]Alexion Pharmaceuticals, Cheshire, CT, [2]Pharsight, Montreal, QC, Canada.

BP-006
SELECTION OF DOSING REGIMEN USING A PKPD MODEL INCORPORATING TARGET MEDIATED DRUG DISPOSITION (TMDD) OF LAMPALIZUMAB (LPZ) IN GEOGRAPHIC ATROPHY (GA) PATIENTS.
K. N. Le,[1] L. Gibiansky,[2] J. Good,[1] T. Davancaze,[1] A. Morimoto,[1] K. Loyet,[1] M. van Lookeren Campagne,[1] E. Strauss,[1] R. Graham,[1] J. Jin,[1] J. Visich[1]; [1]Genentech, South San Francisco, CA, [2]Quantpharm LLC, North Potomac, CA.

BP-007
A SYSTEMS PHARMACOLOGY MODEL TO CHARACTERIZE THE EFFECT OF BLINATUMOMAB IN PATIENTS WITH ADULT B-PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL).
I. Singh,[1] T. Yuraszeck,[1] M. Klinger,[2] M. Reed,[3] C. Friedrich,[3] R. Kumar,[3] S. Pagano,[3] M. Zhu[1]; [1]Amgen Inc., Thousand Oaks, CA, [2]Amgen Research (Munich) GmbH, Munich, Germany, [3]Rosa & Co., San Carlos, CA.

BP-008
POPULATION PHARMACOKINETICS OF MAVRILIMUMAB IN RHEUMATOID ARTHRITIS PATIENTS.
C. Wu,[1] B. Wang,[1] B. Yang,[2] K. Kowalski,[2] P. Ryan,[3] A. Godwood,[4] D. Saurigny,[4] D. Close,[4] L. Roskos[3]; [1]Medimmune, Hayward, CA, [2]Ann Arbor Pharmacometrics Group, Ann Arbor, MI, [3]Medimmune, Gaithersburg, MD, [4]MedImmune, Cambridge, United Kingdom.

BP-009
REPEATED TIME TO EVENT MODELING OF THE RELATIONSHIP BETWEEN rFVIIIFc ACTIVITY AND SPONTANEOUS BLEEDING IN HEMOPHILIA A.
Y. Hang, I. Nestorov; Biogen Idec, Cambridge, MA.

BIOLOGICS PRE-CONFERENCE POSTER PRESENTATIONS

BP-010
A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFECTS OF RBP-8000 ON COCAINE PK AND COCAINE-INDUCED PHYSIOLOGICAL EFFECTS IN COCAINE USERS.
Y. Chen, B. Zheng, Y. Liu, C. Heidbreder, P. J. Fudala, A. Nasser; Reckitt Benckiser Pharmaceuticals Inc., Richmond, VA.

BP-011
DEVELOPMENT AND APPLICATION OF SYSTEMS PHARMACOLOGY MODEL TO PREDICT NAUSEA RESULTED FROM ADMINISTRATION OF GLP-1 AGONISTS.
V. Voronova, O. Demin Jr, S. Smirnov, O. Demin; Institute for Systems Biology SPb, Moscow, Russian Federation.

BP-012
CLINICAL PHARMACOKINETICS OF INTRATHECALLY ADMINISTERED HGT-1410 IN PATIENTS WITH SANFILIPPO SYNDROME TYPE A (MPS IIIA).
J. Chung, R. Pfeifer, P. Haslett, M. Mascelli, T. G. McCauley; Shire, Lexington, MA.

BP-013
LBEC0101, AN ETANERCEPT BIOSIMILAR, SHOWED COMPARABLE TOLERABILITY AND PHARMACOKINETIC PROFILES TO THOSE OF ETANERCEPT IN HEALTHY MALE VOLUNTEERS.
H. Chung, L. Ahn, Y. Choi, S. Shin, I. Jang, K. Yu, H. Lee; Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

BP-014
PHARMACOKINETICS OF MOXETUMOMAB PASUDOTOX, AN INVESTIGATIONAL IMMUNOTOXIN TARGETING CD22, IN PATIENTS WITH RELAPSED OR REFRACTORY HAIRY CELL LEUKEMIA.
B. Wang,[1] **L. Chang,[1]** R. J. Kreitman,[2] R. Ibrahim,[3] T. Goswami,[3] I. Pastan,[2] M. Liang,[1] L. Roskos[1]; [1]MedImmune, Hayward, CA, [2]National Cancer Institute/National Institutes of Health, Bethesda, MD, [3]MedImmune, Gaithersburg, MD.

BP-015
PHARMACOKINETICS OF PEGINTERFERON BETA-1A DELIVERED BY SINGLE-USE AUTOINJECTOR AND PRE-FILLED SYRINGE.
X. Hu, Y. Cui, A. Ali Seddighzadeh, S. Hung; Biogen Idec, Cambridge, MA.

BP-016
PHARMACOKINETIC AND EXPOSURE-RESPONSE ANALYSES OF PERTUZUMAB PLUS TRASTUZUMAB AND DOCETAXEL DURING NEOADJUVANT TREATMENT OF HER2+ EARLY BREAST CANCER.
A. L. Quartino,[1] H. Li,[2] J. Y. Jin,[1] D. Wada,[2] G. Ross,[3] L. Gianni,[4] J. Visich,[1] B. Lum,[1] **A. Garg[1];** [1]Genentech Inc., South San Francisco, CA, [2]Quantitative Solutions Inc., Menlo Park, CA, [3]Roche Products Ltd, Welwyn Garden City, United Kingdom, [4]Oncologia Medica, San Raffaele Cancer Centre, Milan, Italy.

BP-017
POPULATION PHARMACOKINETICS AND EVALUATION OF FIXED DOSING FOR PERTUZUMAB, A HER2 TARGETED MONOCLONAL ANTIBODY, IN CANCER PATIENTS.
A. Garg,[1] J. Li,[1] A. Quartino,[1] J. Jin,[1] D. R. Wada,[2] H. Li,[2] J. Cortes,[3] V. McNally,[4] J. Visich,[1] B. Lum[1]; [1]Genentech, Inc., South San Francisco, CA, [2]Quantitative Solutions Inc., Menlo Park, CA, [3]Department of Oncology, Vall d'Hebron University Hospital, Barcelona, Spain, [4]Roche Products, Welwyn Garden City, United Kingdom.

BP-018
C-REACTIVE PROTEIN ANTISENSE SELECTIVELY AND POTENTLY INHIBITS CRP INCREASE FOLLOWING ENDOTOXIN CHALLENGE IN HUMANS.
R. J. Noveck; Duke University School of Medicine, Durham, NC.

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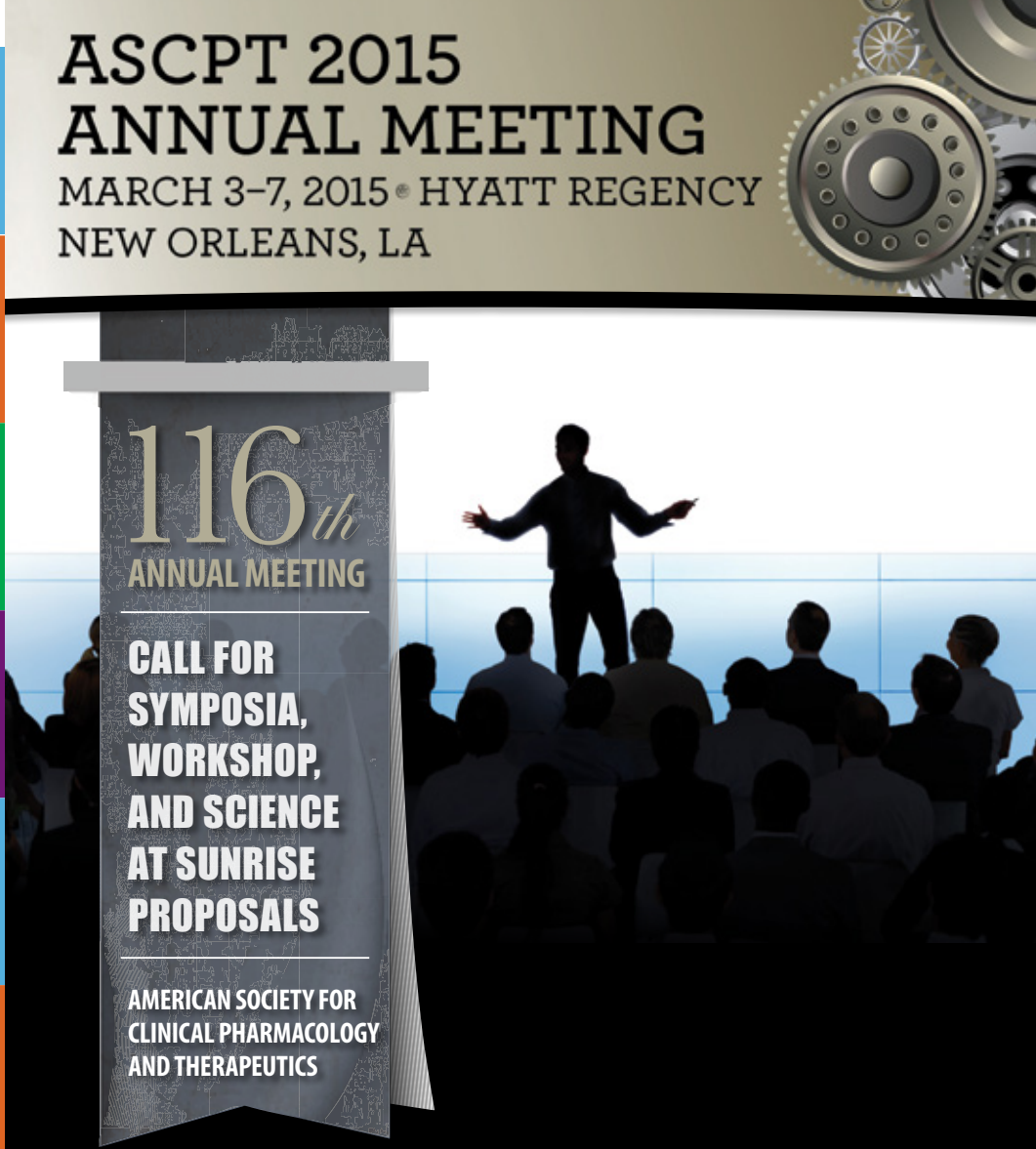

116th ANNUAL MEETING

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THURSDAY, JUNE 5, 2014

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NEXT-GENERATION CLINICAL PHARMACOLOGY

Integrating Systems Pharmacology, Data-Driven Therapeutics, and Personalized Medicine Pre-Conference

Tuesday, March 18, 8:00 am – 5:00 pm, Marquis D
UAN: 0708-9999-14-210-L04-P

Upon completion of this Pre-conference, the participant should be able to:

- Define large-scale data analysis and its use in clinical pharmacology;
- Evaluate studies using high-throughput data for the study of disease pharmacology; and
- Illustrate the new pharmaco-informatics approaches and their applications in clinical pharmacology.

7:00 AM – 3:00 PM
PRE-CONFERENCE REGISTRATION OPEN
Marquis Foyer

8:00 AM – 8:30 AM
CONTINENTAL BREAKFAST

8:30 AM – 8:45 AM
OPENING REMARKS

Nicholas P. Tatonetti, PhD, Columbia University

Pankaj Agarwal, PhD, GlaxoSmithKline

Lang Li, PhD, Indiana University

8:45 AM – 10:30 AM
SYSTEMS PHARMACOLOGY
Systems Pharmacology Approaches to Pharmacogenomics Discovery

Russ B. Altman, MD, PhD, Stanford University

Integrating Systems Pharmacology, Data Driven Therapeutics and Personalized Medicine

Amin Rostami-Hodjegan, PharmD, PhD, University of Manchester

Library-Scale Gene-Expression Profiling and Digital Open Innovation

Justin Lamb, PhD, Genometry

10:30 AM – 11:00 AM
BREAK

11:00 AM – 12:15 PM
DATA DRIVEN THERAPEUTICS
Learning from Observational Healthcare Data: Lessons from the Observational Medical Outcomes Partnership

Patrick Ryan, PhD, Janssen Research and Development Observational Medical Outcomes Partnership

NEXT-GENERATION CLINICAL PHARMACOLOGY

Integrating Systems Pharmacology, Data-Driven Therapeutics, and Personalized Medicine Pre-Conference

Tuesday, March 18, 8:00 am – 5:00 pm, Marquis D
UAN: 0708-9999-14-210-L04-P

Cancer Genomics Informs Therapeutic Options

Elaine Mardis, PhD, Washington University in St. Louis

12:15 PM – 1:00 PM

LUNCH BREAK
Skyline

1:00 PM – 3:00 PM

PERSONALIZED MEDICINE WORKSHOP
Moving from Big Data to Better Models of Disease and Drug Response

Joel T. Dudley, PhD, Mount Sinai School of Medicine

Exploring Personal Genomics

Konrad J. Karczewski, PhD, MGH/The Broad Institute

3:00 PM – 3:30 PM

BREAK

3:30 PM – 4:00 PM

NEXT GENERATION DATA AND OPPORTUNITIES FOR CLINICAL PHARMACOLOGISTS

Philip E. Bourne, PhD, Associate Director for Data Science, National Institutes of Health

4:00 PM – 5:00 PM

PANEL BATTLE
All speakers will be included in a dynamic panel discussion. Attendees are encouraged to participate.

5:00 PM

CLOSING REMARKS

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Nagi Abdalla • Inje University, College of Medicine
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Vanessa Fontana • University of Campinas
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Varun Garg • Vertex Pharmaceuticals, Inc.
Kathleen M. Giacomini • University of California, San Francisco
Valeria Gomes • FMRP-USP
Srijib Goswami • University of California, San Francisco
Gopichand Gottipati • Virginia Commonwealth University
Yingying Guo • Eli Lilly and Company
Meenal Gupta • Mayo Clinic
Donald Heald • Johnson & Johnson PRD
Anne Heatherington • Pfizer
Craig Hendrix • Johns Hopkins University School of Medicine
Kathleen Hillgren • Lilly Research Labs
Nicolas Hohmann • University Medical Hospital
Nan Huang • Capital One
Yeamin Huh • Ann Arbor Pharmacometrics Group
In-Jin Jang • Seoul National University College of Medicine and Hospital
Amita Joshi • Genentech, Inc
Konrad Karczewski • Massachusetts General Hospital
Jason Karnes • Vanderbilt University
Primal Kaur • Amgen
Marina Kawaguchi-Suzuki • University of Florida
Shinicni Kijima • Pharmaceuticals and Medical Devices Agecy
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As of February 11, 2014

NEXT-GENERATION CLINICAL PHARMACOLOGY REGISTRATION LIST

J. Steven Leeder • Children's Mercy Hospitals and Clinics
Lang Li • Indiana University
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Lawrence Lin • University of California, San Francisco
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Lichuan Liu • Genentech, Inc.
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Maryann Mazer-Amirshahi • Children's National Medical Center
Caitrin McDonough • University of Florida
Tsuyoshi Morishita • Kyowa Hakko Kirin Co., Ltd.
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Yaa Oppong • Thomas Jefferson University
Ying Ou • Onyx Pharmaceuticals
Min Soo Park • Severance Hospital, Yonsei University College of Medicine
Sang-In Park • Seoul National University
Jeffrey Paul • Astellas
Minoli Perera • University of Chicago
Anuradha Ramamoorthy • US Food and Drug Administration
Philip Ross • Bristol-Myers Squibb
Amin Rostami-Hodjegan • University of Manchester
Patrick Ryan • Janssen Research and Development
Sirarat Sarntivijai • US Food and Drug Administration
Stephan Schmidt • University of Florida
Bharti Shah • Asubio Pharmaceuticals, Inc
Jinshan Shen • Vertex Pharmaceuticals
Todd Skaar • Indiana University
Wayne Snodgrass • University of Texas Medical Branch
Boyd Steere • Eli Lilly and Company
Takatoshi Takubo • Takeda Bio Development Center Limited
Nicholas Tatonetti • Columbia University
Piet H. van der Graaf • Leiden Academic Centre for Drug Research (LACDR)
Raja Venkatasubramanian • Cincinnati Childrens Hospital
Christopher Wen • University of California, San Francisco
Seonghae Yoon • Seoul National University
Liming Zhang • Takeda Pharmaceuticals
Xiaoyan Zhang • CPSP Center
Yuan Zhao • Ohio State University
Min Zhu • Amgen
Arik Zur • University of California, San Francisco

As of February 11, 2014

USING BIG DATA TO STUDY DRUG EFFECTS IN POPULATIONS PRE-CONFERENCE

ACKNOWLEDGMENT

ASCPT wishes to acknowledge the outstanding efforts of the Scientific Program Committee in developing an exceptional educational offering.

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Issam Zineh, PharmD, MPH

USING BIG DATA TO STUDY DRUG EFFECTS IN POPULATIONS PRE-CONFERENCE

Wednesday, March 19, 9:30 am – 2:00 pm, Marquis C
UAN: 0708-9999-14-221-L05-P
Supported by a grant from the Burroughs Wellcome Fund and endorsed by the Drug Safety Scientific Section.

Upon completion of this Pre-conference, the participant should be able to:

- Describe the role of pharmacoepidemiology in generating new knowledge concerning the effects of drugs in humans;
- Describe the most commonly used research designs in pharmacoepidemiologic research;
- Discuss the advantages and limitations of using pre-existing healthcare data for pharmacoepidemiologic research.

8:00 AM – 10:00 AM
PRE-CONFERENCE REGISTRATION OPEN
Marquis Foyer

9:30 AM – 9:35 AM
WELCOME
Sean Hennessy, PharmD, PhD, Perelman School of Medicine, University of Pennsylvania

9:35 AM – 10:00 AM
THE ROLE OF BIG DATA IN STUDYING DRUG EFFECTS IN POPULATIONS

Brian Strom, MD, MPH, Rutgers, The State University of New Jersey

10:00 AM – 10:45 AM
RESEARCH DESIGNS FOR POPULATION STUDIES OF DRUG EFFECTS

Sean Hennessy, PharmD, PhD, Perelman School of Medicine, University of Pennsylvania

10:45 AM – 11:30 AM
SPONTANEOUS REPORTS TO IDENTIFY DRUG SAFETY SIGNALS

Joshua Gagne, PharmD, ScD, Brigham and Women's Hospital

11:30 AM – 12:15 PM
LUNCH BREAK

12:15 PM – 1:00 PM
USE OF HEALTHCARE DATA IN PHARMACOEPIDEMIOLOGY

Daniel Mines, MD, MSCE, Perelman School of Medicine, University of Pennsylvania

1:00 PM – 1:45 PM
TOOLS TO REDUCE CONFOUNDING AND BIAS

Tobias Gerhard, PhD, Rutgers, The State University of New Jersey

1:45 PM – 2:00 PM
CLOSING REMARKS AND ADJOURNMENT

Brian Strom, MD, MPH, Rutgers, The State University of New Jersey

USING BIG DATA TO STUDY DRUG EFFECTS IN POPULATIONS REGISTRATION LIST

Nagi Abdalla • Inje University, College of Medicine
Susan Abdel-Rahman • Children's Mercy Hospitals and Clinics
Abiodun Adefurin • Vanderbilt University Medical Center
Antoinette Ajavon • Bayer Pharmaceuticals
Houda Alachkar • University of Chicago
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Inbum Chung • Seoul National University
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Daniela Conrado • Pfizer
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Paul Deutsch • Sanofi U.S.
Sheetal Dharia • University of South Florida College of Pharmacy
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Nihal El Rouby • University of Florida
Daryl Fediuk • University of North Carolina/GlaxoSmithKline
Brian Ferslew • University of North Carolina at Chapel Hill
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Ryan Funk • Children's Mercy Hospitals and Clinics
Puneet Gaitonde • University of Florida
Tara Gangadhar • Abramson Cancer Center of the University of Pennsylvania
Yue Gao • Celgene Corporation
Marilyn Giacomini • University of California, San Francisco
Gopichand Gottipati • Virginia Commonwealth University
Joseph Grippo • Roche TCRC Inc
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Neeraj Gupta • Millennium Pharmaceuticals
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As of February 11, 2014

USING BIG DATA TO STUDY DRUG EFFECTS IN POPULATIONS REGISTRATION LIST

Kristin Karlsson • Uppsala University
Jason Karnes • Vanderbilt University
Priska Kaufmann • Actelion Pharmaceuticals Ltd.
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Choon Ok Kim • Severance Hospital
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Gezim Lahu • Takeda Pharmaceuticals International
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Nancy Lass • NL Specialty Consulting, Inc. & University of Chicago
Jieon Lee • Seoul National University College of Medicine
Donghwan Lee • Yonsei University College of Medicine
Lawrence Lee • National University of Singapore
Zhaoyang Li • Sanofi
Mengyao Li • Virginia Commonwealth University
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Zheng Lu • Astellas
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Jialin Mao • Genentech Inc.
Elizabeth Marek • Thomas Jefferson University
Meret Martin-Facklam • F. Hoffmann-La Roche Ltd
Joanna Masters • Pfizer La Jolla
Maryann Mazer-Amirshahi • Children's National Medical Center
Caitrin McDonough • University of Florida
Calvin Meaney • University at Buffalo School of Pharmacy and Pharmaceutical Sciences
Anisha Mendonza • Novartis
Georgina Meneses-Lorente • Roche Products Ltd
Kana Mizuno • Cincinnati Children's Hospital Medical Center
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Huy Nguyen • Upsher-Smith Laboratories, Inc.
Elizabeth Nguyen • Vanderbilt University
Jing Niu • Cincinnati Children's Hospital Medical Center
Julie Oestreich • University of Nebraska Medical Center
Aram Oganesian • Astex Pharmaceuticals, Inc.
Kyung Hoon Oh • Inje University, PharmacoGenomics Research Center
Jaeseong Oh • Seoul National University Hospital
Yaa Oppong • Thomas Jefferson University
Stefan Oswald • University of Greifswald
Anne Paccaly • Amgen
Paul Panorchan •Vertex Pharmaceuticals
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Dany Patoine • IUCPQ Research Center
Jeffrey Paul • Astellas
Vidya Perera • University at Buffalo/Novartis
Minoli Perera • University of Chicago
Itay Perlstein • Bristol-Myers Squibb
Diane Plotkin • Activx Biosciences
Baralee Punyawudho • Chulalongkorn University
Andrew Ralya • Mayo Clinic

As of February 11, 2014

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Anuradha Ramamoorthy • US Food and Drug Administration
Josephine F. Reyes • Celgene Corporation
Jessica Roberts • University of Utah
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Snehal Samant • University of Florida
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Ravi Shankar Singh • University of Florida
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As of February 11, 2014


sponsors
exhibit
quiz bowl
ASCPT CENTRAL
GENERAL INFORMATION
SCIENTIFIC SECTION DESIGNATIONS

ACKNOWLEDGMENT

ASCPT would like to give special thanks to the leadership of the Coordinating Committee on Scientific Sections (CCSS) and recognize the Scientific Section Chairs and Vice Chairs for their dedicated leadership of Scientific Section endeavors.

Andrea Gaedigk, MS, PhD
Chair, CCSS

Maurice Emery, PharmD, PhD
Vice Chair, CCSS

Section Chairs and Vice Chairs

BIOMARKERS AND IMAGING SECTION (BIO)

Dhanesh K. Gupta, MD, Chair
Barry Mangum, PharmD, Vice Chair

DRUG DEVELOPMENT AND REGULATORY SCIENCES SECTION (DDR)

Kellie Schoolar Reynolds, PharmD, Chair
Megan A. Gibbs, PhD, BscPharm, FCP, Vice Chair

DRUG SAFETY SECTION (SAF)

Tobias Gerhard, PhD, Chair
Geert W. 't Jong, MD, PhD, Vice Chair

INFECTIOUS DISEASES SECTION (INF)

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MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS SECTION (MOL)

Bert L. Lum, PharmD, Chair
Kathryn Momary, PharmD, BCPS, Vice Chair

ONCOLOGY SECTION (ONC)

Federico Innocenti, MD, PhD, Chair
Alex Sparreboom, PhD, Vice Chair

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Shirley M. Tsunoda, PharmD, Chair
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Satsuki Yamada, MD, PhD, Vice Chair

PHARMACOMETRICS AND PHARMACOKINETICS SECTION (PMK)

Virginia (Ginny) Schmith, PhD, FCP, Chair
Jogarao Gobburu, PhD, FCP, MBA, Vice Chair

SPECIAL POPULATIONS SECTION (SPO)

Saskia N. de Wildt, MD, PhD, Chair
Parvaz Madadi, PhD, Vice Chair
Scott Oglesby, PhD, Vice Chair

GENERAL INFORMATION

ASCPT Annual Meeting Sponsor

American Society for Clinical Pharmacology and Therapeutics (ASCPT)
528 North Washington Street
Alexandria, VA 22314
Phone (703) 836-6981
Fax (703) 836-5223
Web www.ascpt.org

Registration Hours

Marriott Marquis Foyer

WEDNESDAY, MARCH 19
12:00 noon – 7:00 pm

THURSDAY, MARCH 20
7:00 am – 4:00 pm

FRIDAY, MARCH 21
7:00 am – 4:00 pm

SATURDAY, MARCH 22
7:00 am – 10:00 am

Target Audience

Clinical pharmacologists, including physicians, pharmacists, scientists, and others interested in learning about the most current advances in drug discovery, development, regulation and safe utilization of drugs in humans.

Badges

For security reasons, all attendees and exhibitors MUST wear their badge at all times for admission to sessions, the poster and exhibit hall, and social events.

To provide a safe and secure meeting experience for all attendees, badge polices are in effect for the ASCPT Annual Meeting. Please have your picture ID ready to present when you pick up your badge materials. Once issued, badges are non-transferable.

If you need to have a badge reprinted, a photo ID is required.

Ribbons

Ribbons are available at the Registration kiosk located in the Marriott Marquis Foyer. Please pick up the appropriate ribbons at the registration area.

ADA Compliance

ASCPT makes every effort to comply with the Americans with Disabilities Act. For additional information, please contact the ASCPT office at (703) 836-6981 or via email at meetings@ascpt.org.

ASCPT Ethics Statement

All scientific presentations at the ASCPT-sponsored events must adhere to the highest standards of scientific ethics, including acknowledgments or references to sources (both scientific and financial), and the absence of promotional content or endorsement of commercial products. Any conflict of interest must be disclosed prior to the meeting.

ASCPT Disclaimer Statement

Speakers are responsible for the content and ideas shared in their oral and written presentations. ASCPT is not responsible for, nor do we endorse, any oral statements or written information given by presenters at this meeting.

ASCPT Continuing Education Information

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Pharmaceutical Education and Research Institute, Inc. (PERI) and the American Society for Clinical Pharmacology and Therapeutics. The Pharmaceutical Education and Research Institute, Inc. (PERI) is accredited by the ACCME to provide continuing medical education for physicians.

GENERAL INFORMATION

The Pharmaceutical Education and Research Institute, Inc. (PERI) designates this live activity for a maximum of *25 AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This activity has been planned and implemented in accordance with the standards and policies of the Accreditation Council for Pharmacy Education through the joint sponsorship of the Pharmaceutical Education and Research Institute, Inc. (PERI) and the American Society for Clinical Pharmacology and Therapeutics.

The Pharmaceutical Education and Research Institute, Inc. (PERI) is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

The assigned universal program numbers for this meeting begin with 0708-9999-14-201-L04-P and end with 0708-9999-14-221-L05-P. Topic designations and descriptions for the 2014 ASCPT Annual Meeting are L01 – Disease State Management/Drug Therapy, L02 – AIDS Therapy, L03 – Law Related to Pharmacy Practice, L04 – General Pharmacy and L05 – Patient Safety. Total available credit for pharmacists is 25 hours or 2.5 CEUs. These activities have been designated as knowledge-based CPE.

The CME/CPE fee for the 2014 ASCPT Annual Meeting is $50 for ASCPT members and $100 for non-members. Please visit ASCPT Central located in the Marquis Foyer to purchase.

ANNUAL MEETING MOBILE APP

The Annual Meeting Program can be in the palm of your hands! Download the ASCPT 2014 Annual Meeting Mobile App today.

Get up-to-the-minute information including:

- The current program schedule
- Speaker information
- Exhibitor and sponsor details
- Live Twitter feeds
- Floor plans
- Attendee list and attendee-to-attendee communication

iPhone, iPad, iPod Touch users
Search “ASCPT 2014” to download the app from the Apple App Store.

Android users
Search “ASCPT 2014” to download the app from the Google Play Marketplace.

Windows, BlackBerry, other smart phones/ mobile devices, laptops and desktop users
Go to **https://ascpt2014.gatherdigital.com** and bookmark it.

GENERAL INFORMATION

Wi-Fi Access

ASCPT is pleased to provide complimentary Wi-Fi access to our meeting attendees.

Meeting Evaluations

Please take the time to evaluate the Annual Meeting and its daily sessions through the online evaluation. Your feedback is important to us and is used to improve future meetings. We encourage all who attend the Annual Meeting and the Pre- and Post-conferences to complete the evaluation. Attendees will be provided with a certificate of attendance upon completion of the evaluation. The online evaluation will be available from March 19, 2014 – April 19, 2014.

ASCPT Central

Marriott Marquis Foyer

ASCPT Central will be open during the following hours:

WEDNESDAY, MARCH 19
12:00 noon – 7:00 pm

THURSDAY, MARCH 20
7:00 am – 4:00 pm

FRIDAY, MARCH 21
7:00 am – 4:00 pm

SATURDAY, MARCH 22
7:00 am – 10:00 am

At ASCPT Central, you'll have the opportunity to:

- Update your membership record
- Speak with a member of the CPT or CPT:PSP Editorial Staff
- Update your Scientific Section designations
- Sign up to participate on various ASCPT Committees
- Volunteer as a CPT or CPT:PSP manuscript or ASCPT abstract reviewer
- Join ASCPT or refer a colleague for membership

And much more!

Cyber Café

ASCPT is proud to offer the complimentary use of computers with high speed internet access during the Annual Meeting.

The Cyber Café is sponsored by DUCK FLATS Pharma.

Poster and Exhibit Hall Hours

International Hall

The Exhibit Hall and Posters will be open during the following hours:

WEDNESDAY, MARCH 19
5:00 pm – 6:30 pm (Exhibits only)

THURSDAY, MARCH 20
7:30 am – 2:00 pm

FRIDAY, MARCH 21
7:30 am – 3:30 pm

NO PHOTOGRAPHY

Use of camera or digital recording devices by attendees is not permitted.

POLICY ON PHOTOGRAPHY AND PHOTO RELEASE

Registrants of the ASCPT Annual Meeting agree to allow ASCPT and its official photographer and/or videographer to photograph or videotape them in the context of the meeting setting. Footage captured by the official ASCPT photographer/videographer may be used in future print and electronic promotional and archival materials.

GENERAL INFORMATION

ASCPT Literature Display

Marquis Foyer

ASCPT members are invited to display flyers featuring scientific courses you are offering, recently published books, and other scientific events. The Literature Display is located near ASCPT Central and is open during registration hours, from Wednesday, March 19 until Saturday, March 22. Stop by ASCPT Central to speak to an ASCPT staff member to post a flyer or for more information on the Literature Display.

ASCPT Job Board

Marquis Foyer

Looking for a new job? Recruiting for open positions? Stop by the ASCPT Job Board while you are at the Annual Meeting. The Job Board is located near ASCPT Central and is open during registration hours, from Wednesday, March 19 until Saturday, March 22. Stop by ASCPT Central to speak to an ASCPT staff member to post a position or for more information on the Job Board.

Speaker Ready Room

Room M302

ASCPT provides technical support through the services available in the Speaker Ready Room, Room M302. Speakers have the opportunity to review and revise their upcoming presentations. Speakers are strongly encouraged to check in to the Speaker Ready Room a minimum of 90 minutes in advance of their scheduled presentation. The A/V support staff will be available to make changes to presentations received in advance and assist with technical issues.

The Speaker Ready Room will be available during the following hours:

TUESDAY, MARCH 18
7:00 am – 5:00 pm

WEDNESDAY, MARCH 19
7:00 am – 5:00 pm

THURSDAY, MARCH 20
7:00 am – 5:00 pm

FRIDAY, MARCH 21
7:00 am – 5:00 pm

SATURDAY, MARCH 22
7:00 am – 10:00 am

HOTEL SAFETY

Your safety while attending the Annual Meeting is important to ASCPT and the Atlanta Marriott Marquis. In case of an emergency please dial 911 from the nearest house phone. Should there be a hotel emergency, please follow the directions provided on the public address system and by hotel staff.

DAILY LUNCH TICKET

Buy your daily lunch ticket in the Poster and Exhibit Hall on Thursday and Friday. For $25 you may select from a salad or sandwich package. Enjoy lunch in the Poster and Exhibit Hall while networking with exhibitors and viewing the posters.

GENERAL INFORMATION

ASCPT Scientific Section Designations

Sections are categorized into two main groups: Tools (or Methods) and Applications. As the primary forum for member exchange and networking, ASCPT's Scientific Sections promote interaction among members who share a common field of interest. Each Symposium, Workshop, and Science at Sunrise session must also correlate to one Scientific Section. See the Schedule for the sessions representing your field of interest.

TOOLS/METHODS

BIO	Biomarkers and Imaging
MOL	Molecular Pharmacology and Pharmacogenetics
PMK	Pharmacometrics and Pharmacokinetics

APPLICATIONS

DDR	Drug Development and Regulatory Sciences
INF	Infectious Diseases
ONC	Oncology
OSD	Organ Specific Diseases
SAF	Drug Safety
SPO	Special Populations

SPECIAL INTEREST GROUPS

International Transporter Consortium (ITC)
Pharmacometabolomics

Policy on Children, Spouses, and Guests

The ASCPT Annual Meeting is geared toward adult participation. For their safety, children under the age of 16 are not permitted to attend any portion of the Annual Meeting, including but not limited to, educational sessions, networking and social events, and the exhibit hall.

If your child(ren) will accompany you to the conference and another adult will not be traveling with you, please make arrangements for care while you are attending conference functions.

Childcare

Professional childcare services are available during the ASCPT 2014 Annual Meeting. Arrangements can be made by contacting TLC Sitters of Atlanta (http://tlcsittersofatlanta.com) directly at (770) 410-4774. ASCPT has not made any group arrangements or discounts and is not able to endorse the use of this firm; this is informational only.

If your spouse or guest will accompany you to the Annual Meeting, please note that ASCPT does not offer spouse programs. However, the concierge at the Atlanta Marriott Marquis is adept at making arrangements for dining reservations, excursion reservations, providing shopping and transportation information, and answering general questions about local attractions.

NEW MEMBER WELCOME

If you joined ASCPT in the last year and would like to learn more about getting involved in your Society, or how to make the most of your Annual Meeting experience, join us at the New Member Welcome on Wednesday, March 19 from 12:30 pm – 1:30 pm. We will have a new member gift for you.

TOWN HALL

ASCPT TOWN HALL SESSION

The Town Hall Session has been reformatted to encourage open discussion on topics important to all members of the Society.

All members are invited to participate in discussions with ASCPT Volunteer Leaders.

Stop by for 5 to 10 minutes and engage!

QUIZ BOWL

Wednesday, March 19, 6:45 pm – 7:45 pm, Marquis D

The Quiz Bowl is sponsored by Janssen Research and Development.

Gregory L. Kearns, PharmD, PhD

Back by popular demand! Teams representing academia, consulting, industry, government, and new this year, trainees/students, are quizzed on clinical pharmacology and ASCPT history trivia in a highly interactive game of intelligence and strategy. Join host Gregory L. Kearns, PharmD, PhD, for this fun and interactive way to network and learn with your colleagues.

ACADEMIA TEAM

Saskia N. de Wildt, MD, PhD

Lawrence Lesko, PhD

Howard McLeod, PharmD

Mark Ratain, MD

CONSULTING TEAM

Kevin Dykstra, PhD

Nancy A. Lass, MD

Diane Mould, PhD

Gary D. Novack, PhD

GOVERNMENT TEAM

Darrell R. Abernethy, MD, PhD

Jerry Collins, PhD

Kellie Schoolar Reynolds, PharmD

Anne Zajicek, MD, PharmD

INDUSTRY TEAM

Maurice Emery, PharmD, PhD

Mark Hovde, MBA

Virginia (Ginny) Schmith, PhD, FCP

Joseph Ware, PhD

STUDENT/TRAINEE TEAM

Brian Ferslew, PharmD

Puneet Gaitonde, PhD

Jason Karnes, PharmD, PhD, BCPS

Snehal Samant, BPharm, MS

Brandon T. Gufford, PharmD (alternate)

INTERNATIONAL SESSION AND RECEPTION

International Session

THURSDAY, MARCH 20
8:30 am – 10:15 am, Marquis D

Clinical Pharmacology in the Netherlands: Impact on Use of Medication and Teaching Health Professionals
Recent position papers addressing the profession of clinical pharmacology have expressed concerns about the decline of interest in the field among clinicians and medical educators in the United Kingdom and other Western countries about whether clinical pharmacology is actually therapeutics, and whether the profession should be limited to physicians. The Dutch Society for Clinical Pharmacology and Biopharmacy offers answers to these questions and presents a new model for clinical pharmacology.

CHAIRS

Hendrik Jan Guchelaar, PharmD, PhD, Leiden University Medical Center

Teun van Gelder, MD, PhD, Erasmus Medical Center

SPEAKERS
The Dutch Vision on Clinical Pharmacology

Teun van Gelder, MD, PhD, Erasmus Medical Center

Training and Education in Clinical Pharmacology

Kees Kramers, MD, PhD, Radboud Medical Center, University of Nijmegen

Reception

THURSDAY, MARCH 20
7:00 pm - 8:00 pm
M104/105
Sponsored by PRA.

ASCPT invites all international colleagues to join the Society's leadership for refreshments and conversation about international events taking place around the world.

(By invitation only)

AWARD RECIPIENTS

2014 GARY NEIL PRIZE FOR INNOVATION IN DRUG DEVELOPMENT

Shiew-Mei Huang, PhD
Deputy Director, Office of Clinical Pharmacology
Center for Drug Evaluation and Research, US Food and Drug Administration

2014 HENRY W. ELLIOTT DISTINGUISHED SERVICE AWARD

Juan J. L. Lertora, MD, PhD

2014 LEON I. GOLDBERG YOUNG INVESTIGATOR AWARD

Nadav Ahituv, PhD
Assistant Professor, University of California, San Francisco

2014 OSCAR B. HUNTER MEMORIAL AWARD IN THERAPEUTICS

Edward M. Sellers, MD, PhD, FRCPC, FACP
President
DL Global Partners Inc.

2014 RAWLS-PALMER PROGRESS IN MEDICINE AWARD

Yuichi Sugiyama, PhD
Head of Sugiyama Laboratory
Sugiyama Laboratory
Riken Innovation Center

2014 SHEINER-BEAL PHARMACOMETRICS AWARD

Mats O. Karlsson, PhD
Faculty of Pharmacy
Uppsala University

2014 WILLIAM B. ABRAMS AWARD IN GERIATRIC CLINICAL PHARMACOLOGY

Bruce G. Pollock, MD, PhD, FRCPC
Vice President, Research, Centre for Addiction and Mental Health,
Professor and Head, Division of Geriatric Psychiatry, University of Toronto

2014 ASCPT MENTOR AWARD

Gregory L. Kearns, PharmD, PhD
Chief Scientific Officer and Chairman Children's Mercy Hospitals and Clinics Professor of Pediatrics and Pharmacology, University of Missouri, Kansas City

2013 TOP MEMBERSHIP RECRUITERS

Gideon Koren, MD
The Hospital for Sick Children

Jin Yan Jin, MD
Genentech

2014 DAVID J. GOLDSTEIN TRAINEE AWARD

Chie Emoto, PhD
Cincinnati Children's Hospital Medical Center

AWARD RECIPIENTS

2014 JASON MORROW TRAINEE AWARD

Vicky Hsu, PhD
US Food and Drug Administration

2014 JASON MORROW TRAINEE AWARD

Bin Chen, PhD
Stanford University

2013-2014 ASCPT YOUNG INVESTIGATOR AWARD

Eun Kyoung (Christina) Chung, PharmD
Purdue University

ASCPT PRESIDENTIAL TRAINEE AWARD RECIPIENTS

Chie Emoto, PhD
Cincinnati Children's Hospital Medical Center

Vicky Hsu, PhD
US Food and Drug Administration

Bin Chen, PhD
Stanford University

Masaaki Komatsu, MD, PhD
University of Chicago

Jennifer E. Hibma, PharmD
University of California, San Francisco

Sook Wah Yee, PhD
University of California, San Francisco

Meenal Gupta, PhD
Mayo Clinic

Joseph C. Maranville, PhD
University of Chicago

Wenndy Hernandez, PhD
University of Chicago

Srijib Goswami, BS
University of California, San Francisco

Yun Chen, PhD
Reckitt Benckiser Pharmaceuticals Inc.

Katarzyna Drozda, PharmD
University of Illinois

Brandon T. Gufford, PharmD
Washington State University

Shin-Wen Chang, BPharm
University of Florida

Gopichand Gottipati, BPharm
Virginia Commonwealth University

Ahmed M. Abdelhady, MS
Purdue University

Valentina Shakhnovich, MD
Children's Mercy Hospitals and Clinics

Shailly Mehrotra, BPharm
University of Maryland

Henry M. Dunnenberger, PharmD
St Jude Children's Research Hospital

Christopher C. Wen, BS
University of California, San Francisco

Nisha Wadhwa
University of Chicago, Pritzker School of Medicine

Priya Bapat, BMSc
University of Toronto, The Hospital for Sick Children

Ming-Fen Ho, PhD
Mayo Clinic

Ashraf G. Madian, PhD
University of Chicago

AWARD RECIPIENTS

PhRMA FOUNDATION AWARDS

2013 PAUL CALABRESI MEDICAL STUDENT FELLOWSHIPS

Maria Vivienne Boboila
Weill Cornell Medical College

Isha Gupta
Univesity of Utah, School of Medicine

2013 FACULTY DEVELOPMENT AWARD

Sara Lynn Van Driest, MD, PhD
Vanderbilt University

2014 AWARD IN CLINICAL EXCELLENCE IN CLINICAL PHARMACOLOGY

Terrence F. Blaschke, MD
Professor of Medicine and of Molecular Pharmacology (Emeritus)
Stanford University, Senior Program Officer, Bill and Melinda Gates Foundation

CPT: PHARMACOMETRICS & SYSTEMS PHARMACOLOGY AWARD

Diane R. Mould, PhD
Projections Research Inc.

2013 DONORS

SOCIETY OF FOUNDERS
Michael H. Skinner, MD, PharmD
Louis R. Cantilena, Jr., MD, PhD

HENRY W. ELLIOTT DISTINGUISHED SERVICE AWARD
Jean D. Gray, MD, FRCPC

GARY NEIL PRIZE FOR INNOVATION IN DRUG DEVELOPMENT
Terrence F. Blaschke, MD and Jeannette Blaschke, MD
Gregory L. Kearns, PharmD, PhD and Kathleen A. Neville, MD, MS
Malle Jurima-Romet, PhD
Michael H. Skinner, MD, PharmD
John F. Mullane, MD, PhD, JD

LEON I. GOLDBERG YOUNG INVESTIGATOR AWARD
Raymond J. Hohl, MD, PhD and Nina Gannon, DVM
Joann L. Data, MD, PhD and Herman Cantrell
Richard M. Weinshilboum, MD
Juan J. L. Lertora, MD, PhD
Michael J. Rieder, MD, PhD, FRCPC

WILLIAM B. ABRAMS AWARD IN GERIATRIC CLINICAL PHARMACOLOGY
Joann L. Data, MD, PhD and Herman Cantrell
John F. Mullane, MD, PhD, JD
Patricia W. Slattum, PharmD, PhD, CGP

RAWLS-PALMER PROGRESS IN MEDICINE AWARD
Joann L. Data, MD, PhD and Herman Cantrell

SHEINER-BEAL PHARMACOMETRICS AWARD
Terrence F. Blaschke, MD and Jeannette Blaschke, MD
Richard C. Brundage, PharmD, PhD
Bing Wang, PhD
Joann L. Data, MD, PhD and Herman Cantrell
Kathleen M. Giacomini, PhD
Lei Zhang, PhD
John Urquhart, MD
Helen S. Pentikis, PhD

OSCAR B. HUNTER MEMORIAL AWARD IN THERAPEUTICS
Joann L. Data, MD, PhD and Herman Cantrell

TRAINEE AND SCIENTIFIC AWARDS
Scott A. Waldman, MD, PhD, FCP
Russ B. Altman, MD, PhD
Shiew-Mei Huang, PhD
Susan M. Abdel-Rahman, PharmD
Gregory L. Kearns, PharmD, PhD and Kathleen A. Neville, MD, MS
Alexander M.M. Shepherd, MD, PhD
Bridgette L. Jones, MD
Joann L. Data, MD, PhD and Herman Cantrell
Saskia N. de Wildt, MD, PhD
Steven J. Ryder, MD
Jean T. Barbey, MD
Joseph Alan Ware, PhD
Peter R. Bieck, MD, PhD

ASCPT/FDA ABRAMS LECTURE
Lei Zhang, PhD
John F. Mullane, MD, PhD, JD

BUILDING FUND
Joann L. Data, MD, PhD and Herman Cantrell
Gregory L. Kearns, PharmD, PhD and Kathleen A. Neville, MD, MS
Shiew-Mei Huang, PhD
John F. Mullane, MD, PhD, JD
Michael H. Skinner, MD, PharmD

2013 DONORS

UNRESTRICTED GIFT

Arthur J. Atkinson, Jr., MD
Joann L. Data, MD, PhD and Herman Cantrell
Shiew-Mei Huang, PhD
Dhanesh K. Gupta, MD
Barbara A. Levey, MD and Gerald S. Levey, MD
Bert L. Lum, PharmD
Russ B. Altman, MD, PhD
Sharon J. Swan, FASAE, CAE
Steve Ryder, MD
John Sullivan, MB, ChB
Anne Zajicek, MD, PharmD
Saskia N. de Wildt, MD, PhD
Kathleen M. Giacomini, PhD
Shinya Ito, MD, FRCPC
James J. Keirns, PhD
Mario L. Rocci Jr., PhD
Donald R. Stanski, MD
John Vincent, MD, PhD
Kellie Schoolar Reynolds, PharmD
Michael J. Avram, PhD
Edward A. Carr, Jr., MD
Mark Dresser, PhD
Malle Jurima-Romet, PhD
Walter Kraft, MC, FACP
Nancy A. Lass, MD
David W. Nierenberg, MD
Sang-Goo Shin, MD, PhD
Susan E. Shoaf, PhD
Raymond L. Woosley, MD, PhD
Leslie Z. Benet, PhD
John T. Callaghan, MD, PhD
Barbara Ameer, PharmD, MBA, BCPS, FCP
O'Neill Barrett, Jr., MD
Neal L. Benowitz, MD
Julie A. Johnson, PharmD
Judith K. Jones, MD, PhD
J. Steven Leeder, PharmD, PhD
German Navarro, MD, PhD
J. Frederick Pritchard, PhD
Marcus M. Reidenberg, MD
Michelle A. Rudek, PharmD, PhD
Jae-Gook Shin, MD, PhD
Wayne R. Snodgrass, MD, PhD
Brian L. Strom, MD, MPH
Pavur R. Sundaresan, MD, PhD
Geert W. 't Jong, MD, PhD
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Robert E. Vestal, MD
Arnold G. Vulto, PhD, PharmD
Satsuki Yamada, MD, PhD
Lei Zhang, PhD
Donald R. Bennett, MD, PhD, MPH
Sean Hennessy, PharmD, PhD
John Mendelson, MD
Gene D. Morse, PharmD
Kathleen M. Tornatore, PharmD
Robert W. Buckman, PhD
Leon Darghosian, MD

MATCHING GIFTS

Pfizer Foundation Matching Gifts Program
Amgen Foundation - Matching Gifts and Staff Volunteer Program
Genentech, Inc.
Merck Partnership for Giving

OPENING SESSION

2:00 pm - 3:00 pm, Imperial Ballroom
Sponsored by Genentech.

State of the Society Address

Russ B. Altman, MD, PhD, Stanford University, President

Karthik Venkatakrishnan, PhD, Takeda Pharmaceuticals International Company, Scientific Program Committee Chair

Award Presentations

WILLIAM B. ABRAMS IN GERIATRIC CLINICAL PHARMACOLOGY

Presenter: Edward M. Sellers, MD, PhD, FRCPC, FACP, DL Global Partners Inc.
Recipient: Bruce G. Pollock, MD, PhD, FRCPC, Vice President, Research Centre for Addiction and Mental Health, Professor and Head, Division of Genatric Psychiatry, University of Toronto

HENRY W. ELLIOTT DISTINGUISHED SERVICE AWARD

Presenter: Arthur J. Atkinson, Jr., MD, Northwestern University
Recipient: Juan J. L. Lertora, MD, PhD

GARY NEIL PRIZE FOR INNOVATION IN DRUG DEVELOPMENT

Presenter: Kellie Schoolar Reynolds, PharmD, US Food and Drug Administration
Recipient: Shiew-Mei Huang, PhD, US Food and Drug Administration

2013-2014 TOP MEMBERSHIP RECRUITERS

Presenter: Nancy A. Lass, MD, University of Chicago
Recipients: Jin Yan Jin, PhD, Genentech

Gideon Koren, MD, Hospital for Sick Children

2013-2014 ASCPT YOUNG INVESTIGATOR AWARD

Presenter: Russ B. Altman, MD, PhD, Stanford University
Recipient: Eun Kyoung (Christina) Chung, PharmD, Purdue University

2014 DAVID J. GOLDSTEIN TRAINEE AWARD

Presenter: Russ B. Altman, MD, PhD, Stanford University
Recipient: Chie Emoto, PhD, Cincinnati Children's Hospital Medical Center

2014 JASON MORROW TRAINEE AWARD

Presenter: Russ B. Altman, MD, PhD, Stanford University
Recipients: Vicky Hsu, PhD, US Food and Drug Administration

Bin Chen, PhD, Stanford University

2014 ASCPT MENTOR AWARD

Presenter: Kathleen A. Neville, MD, MS, Children's Mercy Hospitals and Clinics
Recipient: Gregory L. Kearns, PharmD, PhD, Chief Scientific Officer and Chairman, Children's Mercy Hospitals and Clinics Professor of Pediatrics and Pharmacology, University of Missouri, Kansas City

PhRMA Foundation Awards

Presenter: Darrell R. Abernethy, MD, PhD, US Food and Drug Administration

2013 PAUL CALABRESI MEDICAL STUDENT FELLOWSHIPS

Maria Vivienne Boboila, Weill Cornell Medical College
Isha Gupta, University of Utah School of Medicine

2013 FACULTY DEVELOPMENT AWARD

Sara Lynn Van Driest, MD, PhD, Vanderbilt University

2014 AWARD IN EXCELLENCE IN CLINICAL PHARMACOLOGY

Terrence F. Blaschke, MD, Professor of Medicine and Molecular Pharmacology (Emeritus) Stanford University, Senior Program Officer, Bill and Melinda Gates Foundation

CPT: PHARMACOMETRICS & SYSTEMS PHARMACOLOGY AWARD

Presenter: Piet H. van der Graaf, PhD, PharmD, Leiden Academic Centre for Drug Research
Recipient: Diane R. Mould, PhD, Projections Research Inc.

CEO Remarks

Sharon J. Swan, FASAE, CAE

SCIENTIFIC SECTION MEETINGS

Thursday, March 20
5:30 pm – 7:00 pm

BIOMARKERS & IMAGING (BIO)
M102

Joseph C. Fleishaker, PhD, FAAPS, Chair
Jerry M. Collins, PhD, Vice Chair
Ronda K. Ripley, PhD, Vice Chair

Welcome and Introductions of New Leadership

Discuss New Vision Statement and Section Name, Brainstorm Ideas for Symposia, Workshops and Science at Sunrise Sessions for 2015

MOLECULAR PHARMACOLOGY & PHARMACOGENETICS (MOL)
Marquis B

Bert L. Lum, PharmD, Chair
Kathryn Momary, PharmD, BCPS, Vice Chair

PRESENTATIONS

A Pharmacogenomic Genome-Wide Association Study for Adverse Cardiovascular Outcomes in the International Verapamil SR-Trandolapril Study (INVEST)
Caitrin W. McDonough, PhD, University of Florida

Genome-Wide Significant Association of TSPAN 5 SNPS with Plasma Serotonin and Change in Plasma Serotonin After SSRI Therapy
Meenal Gupta, PhD, Mayo Clinic

Follow up commentary by Richard Weinshilboum, MD, Mayo Clinic

Business meeting/section discussion

PHARMACOMETRICS & PHARMACOKINETICS (PMK): PMX IN SUBMISSION: WHERE ARE WE NOW? WHERE SHOULD WE GO?
Marquis C

Virginia (Ginny) Schmith, PhD, FCP, Chair
Jogarao Gobburu, PhD, FCP, MBA, Vice Chair

SPEAKERS

Christoffer Tornoe, PhD
Director, Quantitative Clinical Pharmacology, Novo Nordisk

Brian Corrigan, PhD
Senior Director, Clinical Pharmacology, Pfizer

Vikram Sinha, PhD
Director, Division of Pharmacometrics, CDER/US Food and Drug Administration

Business meeting/section discussion

Friday, March 21
7:30 am – 9:00 am

DRUG DEVELOPMENT & REGULATORY SCIENCES (DDR)
Marquis C

Kellie Schoolar Reynolds, PharmD, Chair
Megan A. Gibbs, PhD, BscPharm, FCP, Vice Chair

PRESENTATIONS

PK and PD Assessments of Hormonal Contraceptive Drug-Drug Interactions
Chongwoo Yu, PhD, US Food and Drug Administration

Lithium Treatment and Risk for Dementia Among Patients with Bipolar Disorder
Tobias Gerhard, PhD, Rutgers, The State University of New Jersey

Business meeting/section discussion

DRUG SAFETY (SAF)
M108

Tobias Gerhard, PhD, Chair
Geert W. 't Jong, MD, PhD, Vice Chair

Welcome and Introductions

SPEAKER

Studying Drug-Drug Interactions in Administrative Data
Joshua Gagne, PharmD, ScD, Harvard Medical School

SAF Symposia and Workshops for ASCPT 2015

SCIENTIFIC SECTION MEETINGS

Improving Visibility and Impact of SAF

Business meeting/section discussion

INFECTIOUS DISEASES (INF)
M105

Steven M. Belknap, MD, Chair
David L. Wesche, MD, PhD, Vice Chair

PRESENTATIONS
Some Observations on PK/PD of the Second Generation Hepatitis C NS3/NS4 Protease Inhibitor, Faldaprevir
Fenglei Huang, PhD, Boehringer Ingelheim Pharmaceuticals, Inc.

Vancomycin AUC24H/MIC Does Not Predict Clinical Outcomes in Children with MRSA Bacteremia
Andrea Hahn, MD, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Business meeting/section discussion

ONCOLOGY (ONC): NEWS, UPDATES, AND INTRODUCTIONS OF THE NEW CHAIR AND VICE-CHAIR
M106/107

Federico Innocenti, MD, PhD, Chair
Alex Sparreboom, PhD, Vice Chair

PRESENTATIONS
Updates on New ONC Section Leadership
Federico Innocenti, MD, PhD, University of North Carolina at Chapel Hill

A Modeling and Simulation Framework to Support Early Clinical Drug Development in Oncology with Application to Multiple Myeloma
Fredrik Jonsson, PhD, Pharsight, a Certara Company

MEET-THE-EXPERT
Phase I and the Cancer Genome
Patricia LoRusso, DO, Karmanos Cancer Institute

Business meeting/section discussion

ORGAN SPECIFIC DISEASES (OSD)
M109

Shirley M. Tsunoda, PharmD, Chair
Dean K. Naritoku, MD, Vice Chair
Sony Tuteja, PharmD, MS, Vice Chair
Satsuki Yamada, MD, PhD, Vice Chair

PRESENTATIONS
Citalopram and Escitalopram Plasma Drug and Metabolite Concentrations: Genome-Wide Associations.
Yuan Ji, PhD, Mayo Clinic

Mechanisms of Neuraminidase Inhibitor Transport Across the Blood-Brain Barrier.
Lawrence Lin, University of California, San Francisco

Business meeting/section discussion

SPECIAL POPULATIONS (SPO)
M104

Saskia N. de Wildt, MD, PhD, Chair
Parvaz Madadi, PhD, Vice Chair
Scott Oglesby, PhD, Vice Chair

PRESENTATIONS
Benzodiazepine Prescribing Among Older Adults in Emergency Departments and Ambulatory Clinics
Maryann E. Mazer-Amirshahi, PharmD, MD, George Washington University

The Transfer of Dabigatran Across a Dually Perfused Isolated Human Placental Cotyledon: Implications for Therapy in Pregnancy
Priya Bapat, BMSc, University of Toronto

Population Pharmacokinetic Analysis of Temsirolimus in Children
Tomoyuki Mizuno, PhD, Cincinnati Children's Hospital Medical Center

Business meeting/section discussion


PROGRAM &
SCIENTIFIC AGENDA
SCIENCE AT SUNRISE
TRAINEE
debate
bootcamp
symposium

SCIENTIFIC AGENDA

Speakers And Sessions

KARTHIK VENKATAKRISHNAN, PHD
Scientific Program Committee Chair

TUESDAY, MARCH 18, 2014

1:00 PM – 5:00 PM
CPT ASSOCIATE EDITORS MEETING (BY INVITATION ONLY)
M101

WEDNESDAY, MARCH 19, 2014

7:00 AM – 8:30 AM
CPT EDITORIAL BOARD MEETING (BY INVITATION ONLY)
Marquis D

9:00 AM – 1:00 PM
CPT:PSP ASSOCIATE EDITORS MEETING (BY INVITATION ONLY)
M108

9:30 AM – 2:00 PM
PHARMACOEPIDEMIOLOGY PRE-CONFERENCE
Using Big Data to Study Drug Effects in Populations
Marquis C
UAN: 0708-9999-14-221-L05-P
Supported by a grant from the Burroughs Wellcome Fund and endorsed by the Drug Safety Scientific Section

CHAIR
Sean Hennessy, PharmD, PhD, Perelman School of Medicine, University of Pennsylvania

See page 33 for complete session details.

11:00 AM – 1:00 PM
CCSS & SECTION ORIENTATION
M103/104/105

12:00 NOON – 7:00 PM
ASCPT REGISTRATION OPEN
ASCPT CENTRAL OPEN

12:30 PM – 1:30 PM
NEW MEMBER WELCOME
M106/107

12:30 PM – 1:45 PM
CLINICAL PHARMACOLOGY PROGRAM DIRECTORS MEETING
L504

1:30 PM – 2:00 PM
AWARDS RECEPTION (BY INVITATION ONLY)
M102

2:00 PM – 3:00 PM
OPENING SESSION
Imperial Ballroom

Genentech A Member of the Roche Group *Sponsored by Genentech.*

State of the Society Address
Russ B. Altman, MD, PhD, Stanford University, President

Karthik Venkatakrishnan, PhD, Takeda Pharmaceuticals International Company, Scientific Program Committee Chair

AWARD PRESENTATIONS

William B. Abrams Award in Geriatric Clinical Pharmacology
Presenter: Edward M. Sellers, MD, PhD, FRCPC, FACP, DL Global Partners Inc.
Recipient: Bruce G. Pollock, MD, PhD, FRCPC, Centre for Addiction and Mental Health, University of Toronto

Henry W. Elliott Distinguished Service Award
Presenter: Arthur J. Atkinson, Jr., MD, Northwestern University
Recipient: Juan J. L. Lertora, MD, PhD

Gary Neil Prize for Innovation in Drug Development
Presenter: Kellie Schoolar Reynolds, PharmD, US Food and Drug Administration
Recipient: Shiew-Mei Huang, PhD, US Food and Drug Administration

2013-2014 Top Membership Recruiter
Presenter: Nancy A. Lass, MD University of Chicago
Recipients: Jin Yan Jin, PhD, Genentech

Gideon Koren, MD, Hospital for Sick Children

D Discovery D Development R Regulation U Utilization

WEDNESDAY, MARCH 19, 2014

2013-2014 ASCPT Young Investigator Award
Presenter: Russ B. Altman, MD, PhD, Stanford University
Recipient: Eun Kyoung (Christina) Chung, PharmD, Purdue University

2014 David J. Goldstein Trainee Award
Presenter: Russ B. Altman, MD, PhD, Stanford University
Recipient: Chie Emoto, PhD, Cincinnati Children's Hospital Medical Center

2014 Jason Morrow Trainee Award
Presenter: Russ B. Altman, MD, PhD, Stanford University
Recipients: Vicky Hsu, PhD, US Food and Drug Administration
Bin Chen, PhD, Stanford University

2014 ASCPT Mentor Award
Presenter: Kathleen A. Neville, MD, MS, Children's Mercy Hospitals and Clinics
Recipient: Gregory L. Kearns, PharmD, PhD, Chief Scientific Officer and Chairman, Children's Mercy Hospitals and Clinics Professor of Pediatrics and Pharmacology, University of Missouri, Kansas City

PhRMA Foundation Awards
Presenter: Darrell R. Abernethy, MD, PhD, US Food and Drug Administration

2013 Paul Calabresi Medical Student Fellowships
Maria Vivienne Boboila, Weill Cornell Medical College
Isha Gupta, University of Utah School of Medicine

2013 Faculty Development Award
Sara Lynn Van Driest, MD, PhD, Vanderbilt University

2014 Award in Excellence in Clinical Pharmacology
Terrence F. Blaschke, MD, Professor of Medicine and of Molecular Pharmacology (Emeritus) Stanford University, Senior Program Manager, Bill and Melinda Gates Foundation

CPT: Pharmacometrics & Systems Pharmacology Award
Presenter: Piet H. van der Graaf, PhD, PharmD, Leiden Academic Centre for Drug Research
Recipient: Diane R. Mould, PhD, Projections Research Inc.

CEO Remarks
Sharon J. Swan, FASAE, CAE

3:00 PM – 4:00 PM

STATE OF THE ART LECTURE
Structural Insights into G Protein Coupled Receptor Signaling
Imperial Ballroom

CHAIR
Russ B. Altman, MD, PhD, Stanford University

Brian Kobilka, MD, Stanford University

4:30 PM – 5:00 PM

SHOWCASE OF TOP TRAINEE ABSTRACTS (SEE PAGES 62-64)
Marquis C

ASCPT PRESIDENTIAL TRAINEE AWARD RECIPIENTS
Presenter Russ B. Altman, MD, PhD

Chie Emoto, PhD, Cincinnati Children's Hospital Medical Center
Vicky Hsu, PhD, US Food and Drug Administration
Bin Chen, PhD, Stanford University
Masaaki Komatsu, MD, PhD, University of Chicago
Jennifer E. Hibma, PharmD, University of California, San Francisco
Sook Wah Yee, PhD, University of California, San Francisco
Meenal Gupta, PhD, Mayo Clinic
Joseph C. Maranville, PhD, University of Chicago
Wenndy Hernandez, PhD, University of Chicago

D Discovery D Development R Regulation U Utilization

WEDNESDAY, MARCH 19, 2014

ASCPT PRESIDENTIAL TRAINEE AWARD RECIPIENTS CONTINUED

Srijib Goswami, BS, University of California, San Francisco

Yun Chen, PhD, Reckitt Benckiser Pharmaceuticals Inc.

Katarzyna Drozda, PharmD, University of Illinois

Brandon T. Gufford, PharmD, Washington State University

Shin-Wen Chang, BPharm, University of Florida

Gopichand Gottipati, BPharm, Virginia Commonwealth University

Ahmed M. Abdelhady, MS, Purdue University

Valentina Shakhnovich, MD, Children's Mercy Hospitals and Clinics

Shailly Mehrotra, BPharm, University of Maryland

Henry M. Dunnenberger, PharmD, St Jude Children's Research Hospital

Christopher C. Wen, BS, University of California, San Francisco

Nisha Wadhwa, University of Chicago, Pritzker School of Medicine

Priya Bapat, BMSc, University of Toronto, The Hospital for Sick Children

Ming-Fen Ho, PhD, Mayo Clinic

Ashraf G. Madian, PhD, University of Chicago

5:00 PM – 6:30 PM

OPENING RECEPTION AND EXHIBIT HALL OPEN

International Hall

6:45 PM – 7:45 PM

QUIZ BOWL

Marquis D

Host

Gregory L. Kearns, PharmD, PhD

ACADEMIA TEAM

Saskia N. de Wildt, MD, PhD
Lawrence Lesko, PhD
Howard McLeod, PharmD
Mark Ratain, MD

CONSULTING TEAM

Kevin Dykstra, PhD
Nancy A. Lass, MD
Diane Mould, PhD
Gary D. Novack, PhD

GOVERNMENT TEAM

Darrell R. Abernethy, MD, PhD
Jerry Collins, PhD
Kellie Schoolar Reynolds, PharmD
Anne Zajicek, MD, PharmD

INDUSTRY TEAM

Maurice Emery, PharmD, PhD
Mark Hovde, MBA
Virginia (Ginny) Schmith, PhD, FCP
Joseph Ware, PhD

STUDENT/TRAINEE TEAM

Brian Ferslew, PharmD
Puneet Gaitonde, PhD
Jason Karnes, PharmD, PhD, BCPS
Snehal Samant, BPharm, MS
Brandon T. Gufford, PharmD (alternate)

8:00 PM – 9:00 PM

BOARD OF DIRECTORS DESSERT RECEPTION (BY INVITATION ONLY)

President's Suite

8:00 PM – 9:30 PM

SPEED MENTORING

M103/104/105

CHAIRS

Kathleen A. Neville, MD, MS, Children's Mercy Hospitals and Clinics
Gary D. Novack, PhD, Pharmalogic Development Inc.

8:00 PM – 9:30 PM

DESSERT RECEPTION HONORING SHIEW-MEI HUANG AND YUICHI SUGIYAMA (BY INVITATION ONLY)

M106/107

SHOWCASE OF TOP TRAINEE ABSTRACTS

PT-001
DEVELOPMENT OF A PEDIATRIC PBPK MODEL FOR SIROLIMUS: APPLING PRINCIPLES OF GROWTH AND MATURATION IN NEONATES AND INFANTS.
C. Emoto,[1] T. Fukuda,[1] T. N. Johnson,[2] D. M. Adams,[3] A. A. Vinks[1]; [1]Division of Clinical Pharmacology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Simcyp Limited, Sheffield, United Kingdom, [3]Cancer and Blood Diseases Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PT-002
PBPK MODELS OF RENALLY ELIMINATED DRUGS AND THEIR APPLICATION IN EVALUATING THE EFFECT OF PATIENT FACTORS.
V. Hsu,[1] M. de L T Vieira,[1] P. Zhao,[1] L. Zhang,[1] J. Zheng,[1] A. Nordmark,[2] E. Gil Berglund,[2] K. M. Giacomini,[3] S.-M. Huang[1]; [1]US Food and Drug Administration, Silver Spring, MD, [2]Swedish MPA, Uppsala, Sweden, [3]University of California, San Francisco, CA.

PT-003
AN INTEGRATIVE BIOINFORMATICS APPROACH TO IDENTIFY TRANSCRIPTION FACTOR MODULATORS FROM A CLINICAL DRUG LIBRARY.
B. Chen, R. Auerbach, H. Fan-Minogue, W. Sikora-Wohlfeld, A. J. Butte; Stanford University, Stanford, CA.

PT-004
A NOVEL HUMAN NEURONAL MODEL OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY.
M. Komatsu, H. E. Wheeler, C. Wing, S. Delaney, M. E. Dolan; Section of Hematology/Oncology, Department of Medicine, University of Chicago, Chicago, IL.

PT-005
CLINICAL VALIDATION OF A SELECTIVE INHIBITOR OF MULTIDRUG AND TOXIN EXTRUSION PROTEIN, MATE1 (SLC47A1) IN HEALTHY VOLUNTEERS.
J. E. Hibma, A. A. Zur, M. B. Wittwer, R. A. Castro, S. L. Stocker, K. M. Morrissey, S. Goswami, S. Yee, R. M. Savic, C. M. Brett, K. M. Giacomini; University of California, San Francisco, San Francisco, CA.

PT-006
TRANSPORTEROME-WIDE ANALYSIS OF GENETIC VARIANTS IN SLC TRANSPORTERS AND THEIR EFFECTS ON METFORMIN RESPONSE.
S. Yee,[1] C. Wen,[1] J. A. Mefford,[1] K. Chua,[1] J. D. Mosley,[2] S. Goswami,[1] A. Takahashi,[3] M. Kubo,[3] S. Maeda,[3] M. D. Simpson,[4] R. L. Davis,[5] D. M. Roden,[2] K. M. Giacomini1; [1]University of California San Francisco, San Francisco, CA, [2]Vanderbilt University, Nashville, TN, [3]Center for Genomic Medicine, The Institute of Physical and Chemical Research (RIKEN), Tokyo, Japan, [4]Center for Human Genetics, Marshfield Clinical Research Foundation, Marshfield, WI, [5]Kaiser Permanente Georgia, Atlanta, GA.

PT-007
GENOME-WIDE SIGNIFICANT ASSOCIATION OF TSPAN5 SNPS WITH PLASMA SEROTONIN AND CHANGE IN PLASMA SEROTONIN AFTER SSRI THERAPY.
M. Gupta,[1] H. Zhu,[2] Y. Ji,[1] Y. Chai,[1] J. Biernacka,[1] D. Hall-Flavin,[1] M. Skime,[1] G. D. Jenkins,[1] A. Batzler,[1] W. Matson,[3] M. Kubo,[4] T. Mushiroda,[4] Y. Nakamura,[5] R. Kaddurah-Daouk,[2] R. Weinshilboum[1]; [1]Mayo Clinic, Rochester, MN, [2]Duke University, Durham, NC, [3]Bedford VA Medical Center, Bedford, MA, [4]RIKEN Center for Integrative Medicinal Sciences, Yokohama, Japan, [5]University of Chicago, Chicago, IL.

PT-008
IN VITRO SENSITIVITY ASSAYS AND CLINICAL RESPONSE TO GLUCOCORTICOIDS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE.
J. C. Maranville, S. B. Hanauer, A. Di Rienzo, S. S. Kupfer; University of Chicago, Chicago, IL.

SHOWCASE OF TOP TRAINEE ABSTRACTS

PT-009

LIVER EQTLS FOR WARFARIN DOSE RESPONSE GENES REVEAL SUSCEPTIBILITY TO VENOUS THROMBOEMBOLISM AMONG AFRICAN AMERICANS.

W. Hernandez,[1] E. R. Gamazon,[1] K. Aquino-Michaels,[1] S. Patel,[2] T. J. O'Brien,[3] A. F. Harralson,[3] R. A. Kittles,[2] A. Barbour,[3] M. Tuck,[4] S. D. McIntosh,[4] J. N. Douglas,[4] D. Nicolae,[1] L. H. Cavallari,[2] M. A. Perera[1]; [1]The University of Chicago, Chicago, IL, [2]The University of Illinois, Chicago, IL, [3]The George Washington University, Washington, DC, [4]Uniformed Services University of the Health Sciences, Washington, DC.

PT-010

GENETIC VARIANTS IN TRANSCRIPTION FACTORS ARE LINKED TO THE PHARMACOKINETICS AND PHARMACODYNAMICS OF METFORMIN.

S. Goswami,[1] S. Yee,[1] S. L. Stocker,[1] J. D. Mosley,[2] M. Kubo,[3] S. Maeda,[3] M. D. Simpson,[4] R. L. Davis,[5] D. M. Roden,[2] R. Savic,[1] K. M. Giacomini[1]; [1]University of California, San Francisco, San Francisco, CA, [2]Vanderbilt, Nashville, TN, [3]RIKEN Center for Genomic Medicine, Yokohama City, Japan, [4]Marshfield Clinical Research Foundation, Marshfield, WI, [5]Kaiser Permanente Georgia, Atlanta, GA.

PT-011

A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFECTS OF RBP-8000 ON COCAINE PK AND COCAINE-INDUCED PHYSIOLOGICAL EFFECTS IN COCAINE USERS.

Y. Chen, B. Zheng, Y. Liu, C. Heidbreder, P. J. Fudala, A. Nasser; Reckitt Benckiser Pharmaceuticals Inc., Richmond, VA.

PT-012

EFFECTS OF AFRICAN-SPECIFIC GENETIC VARIATION ON PERFORMANCE OF WARFARIN PHARMACOGENETIC DOSING ALGORITHMS.

K. Drozda, S. Wong, S. Patel, E. Nutescu, L. H. Cavallari; University of Illinois, Chicago, IL.

PT-013

AN INTEGRATED *IN VITRO / IN SILICO / IN VIVO* FRAMEWORK FOR QUANTITATIVE PREDICTION OF AN HERB-DRUG INTERACTION IN HEALTHY VOLUNTEERS.

B. T. Gufford,[1] S. J. Brantley,[2] R. Dua,[2] D. J. Fediuk,[2] T. N. Graf,[3] Y. V. Scarlett,[4] K. S. Frederick,[5] M. B. Fisher,[6] N. H. Oberlies,[3] M. F. Paine[1]; [1]College of Pharmacy, Washington State University, Spokane, WA, [2]Eshelman School of Pharmacy, The University of North Carolina at Chapel Hill, Chapel Hill, NC, [3]Department of Chemistry and Biochemistry, The University of North Carolina at Greensboro, Greensboro, NC, [4]School of Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, [5]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, [6]ProPharma Services, LLC, Oxford, CT.

PT-014

A PHARMACOGENOMIC GENOME-WIDE ASSOCIATION STUDY (GWAS) FOR NEW ONSET DIABETES (NOD) IN THE INTERNATIONAL VERAPAMIL SR-TRANDOLAPRIL STUDY (INVEST).

S. Chang, C. W. McDonough, Y. Gong, C. J. Pepine, J. A. Johnson, R. M. Cooper-DeHoff; University of Florida, Gainesville, FL.

PT-015

MODEL-BASED META-ANALYSIS (MBMA) OF EFFICACY AT END-OF-TRIAL AND EFFICACY-TIME COURSE FOR DRUGS EVALUATED FOR THE TREATMENT OF FIBROMYALGIA PAIN (FMP).

G. Gottipati,[1] M. N. Trame,[2] C. Lin,[3] J. Venitz,[1] L. J. Lesko,[2] G. An[2]; [1]Virginia Commonwealth University, Richmond, VA, [2]Center for Pharmacometrics and Systems Pharmacology, University of Florida at Lake Nona, Orlando, FL, [3]Department of Clinical Pharmacology and Pharmacometrics, Abbvie, Chicago, IL.

SHOWCASE OF TOP TRAINEE ABSTRACTS

PT-016
EFAVIRENZ INHIBITS hERG-RELATED POTASSIUM CURRENT IN A CONCENTRATION-DEPENDENT MANNER.
A. M. Abdelhady,[1] T. A. Shugg,[1] M. Shao,[1] J. E. Tisdale,[1] Z. Desta,[2] B. R. Overholser[1]; [1]Purdue University, West Lafayette, IN, [2]Indiana University, Indianapolis, IN.

PT-017
DECREASED PREGNANE X RECEPTOR (PXR) EXPRESSION IN CHILDREN WITH CROHN'S DISEASE.
V. Shakhnovich, C. A. Vyhlidal, C. Friesen, A. Hildreth, J. Daniel, V. Singh, G. L. Kearns, S. J. Leeder; Children's Mercy Hospitals and Clinics, Kansas City, MO.

PT-018
LONGITUDINAL DOSE-RESPONSE MODELING FOR TOPICAL GLYCOPYRROLATE, AN ANTI-HYPERHIDROSIS AGENT.
S. Mehrotra,[1] V. D. Schmith,[2] T. Pene Dumitrescu,[2] J. Gobburu[1]; [1]Center for Translational Medicine, University of Maryland, Baltimore, MD, [2]Clinical Pharmacology Modeling and Simulation, GlaxoSmithKline, Research Triangle Park, NC.

PT-019
IMPLEMENTING PREEMPTIVE CLINICAL PHARMACOGENETICS: REPORTING ON 2 YEARS OF EXPERIENCE.
H. M. Dunnenberger,[1] K. R. Crews,[1] J. M. Hoffman,[1] C. E. Haidar,[1] M. R. Wilkinson,[1] K. E. Caudle,[1] U. Broeckel,[2] W. E. Evans,[1] S. C. Howard,[1] M. V. Relling[1]; [1]St Jude Children's Research Hospital, Memphis, TN, [2]Medical College of Wisconsin, Milwaukee, WI.

PT-020
GENOMEWIDE ANALYSIS OF URIC ACID LEVELS AND ALLOPURINOL RESPONSE IN THE KAISER GENETIC EPIDEMIOLOGY RESEARCH ON AGING COHORT.
C. C. Wen,[1] S. Yee,[1] C. Schaefer,[2] R. Neil,[1] K. M. Giacomini[1]; [1]University of California, San Francisco, San Francisco, CA, [2]Kaiser Permanente, Oakland, CA.

PT-021
CLINICAL IMPACT OF AN ON-DEMAND GENOMIC PRESCRIBING SYSTEM (GPS) FOR PHARMACOGENOMIC (PGx) RESULTS DELIVERY.
N. Wadhwa,[1] K. Danahey,[2] H. Cao,[3] D. Saner,[3] M. Ratain,[4] P. O'Donnell[4]; [1]The University of Chicago, Pritzker School of Medicine, Chicago, IL, [2]Center for Research Informatics, The University of Chicago, Chicago, IL, [3]Department for Health Studies, The University of Chicago, Chicago, IL, [4]Committee on Clinical Pharmacology and Pharmacogenomics, The University of Chicago, Chicago, IL.

PT-022
THE TRANSFER OF DABIGATRAN ACROSS A DUALLY PERFUSED ISOLATED HUMAN PLACENTAL COTYLEDON–IMPLICATIONS FOR THERAPY IN PREGNANCY.
P. Bapat,[1] R. Kedar,[2] A. Lubetsky,[2] K. Aleksa,[2] J. Matlow,[1] H. Berger,[3] G. Koren[2]; [1]University of Toronto, Toronto, ON, Canada, [2]The Hospital for Sick Children, Toronto, ON, Canada, [3]St. Michael's Hospital, Toronto, ON, Canada.

PT-023
AROMATASE INHIBITOR TREATMENT AND MUSCULOSKELETAL ADVERSE EVENTS: SNP MODULATED, ESTROGEN-DEPENDENT VARIATION IN CCR6/CCL20 EXPRESSION.
M. Ho, M. Liu, L. Wang, J. Ingle, R. Weinshilboum, T. Bongartz; Mayo Clinic, Rochester, MN.

PT-024
TARGETED PHARMACOPROTEOMIC PROFILING OF CHEMOTHERAPEUTIC RESISTANCE MECHANISM.
A. G. Madian,[1] A. L. Stark,[1] V. Chen,[1] A. To,[1] R. J. Hause Jr,[1] A. Gill,[1] J. Myers,[1] L. Gorsic,[1] M. F. Ciaccio,[2] K. P. White,[1] M. E. Dolan,[1] R. B. Jones[1]; [1]The University of Chicago, Chicago, IL, [2]Northwestern University, Evanston, IL.

THURSDAY, MARCH 20, 2014

7:00 AM – 4:00 PM
ASCPT REGISTRATION OPEN
ASCPT CENTRAL OPEN

7:00 AM – 8:30 AM
CPT:PSP EDITORIAL BOARD MEETING (BY INVITATION ONLY)
M101

7:30 AM – 9:00 AM
SCIENCE AT SUNRISE
Next Generation Sequencing 101: The Basics You Need to Know
Marquis A
Scientific Section: Molecular Pharmacology and Pharmacogenetics (MOL)
D D R U

CHAIRS
Andrea Gaedigk, MS, PhD, Children's Mercy Hospitals and Clinics
Todd C. Skaar, PhD, Indiana University

SPEAKERS
Next Generation Sequencing 101
Pui-Yan Kwok, MD, PhD, University of California San Francisco School of Medicine

CYP2D6 Gene Locus Characterization by NGS
Andrea Gaedigk, MS, PhD, Children's Mercy Hospitals and Clinics

Upon completion of this Science at Sunrise session, the participant should be able to:
- Discuss the basic concept of Next Generation Sequencing (NGS) platforms; and
- Describe the challenges and limitations of NGS in the research and clinical settings.

7:30 AM – 9:00 AM
SCIENCE AT SUNRISE
Clinical and Regulatory Challenges in the Development of Oral Cancer Drugs
Marquis B
Scientific Section: Oncology (ONC)
D D R U

CHAIRS
R. Donald Harvey, PharmD, FCCP, BCOP, Winship Cancer Institute of Emory University
Stacy S. Shord, PharmD, FCCP, BCOP, US Food and Drug Administration
Joseph Ware, PhD, Genentech

SPEAKERS
Academic Perspective on the Clinical Pharmacology Characterization of Oral Targeted Anticancer Drugs
Mark J. Ratain, MD, The University of Chicago

Industry Perspective on the Clinical Pharmacology Characterization of Oral Targeted Anticancer Drugs
Richard A. Graham, PhD, Genentech

Regulatory Perspective on the Clinical Pharmacology Characterization of Oral Targeted Anticancer Drugs
Nam Atiqur Rahman, PhD, US Food and Drug Administration

Upon completion of this Science at Sunrise Session, the participant should be able to:
- Describe the challenges oral anticancer agent development presents to clinician-investigators, industry, and regulatory agencies;
- Review sources of variability in exposure for oral targeted anticancer drugs; and
- Discuss the role clinical pharmacology data may have on decisions for subsequent efficacy trials and development of novel oral agents.

D Discovery D Development R Regulation U Utilization

THURSDAY, MARCH 20, 2014

7:30 AM – 9:00 AM

SCIENCE AT SUNRISE

Endogenous Biomarkers for the Assessment of CYP3A Activity

Marquis C

Scientific Section: Drug Development and Regulatory Sciences (DDR)

D D R U

CHAIRS

Sreeneeranj Kasichayanula, PhD, Bristol-Myers Squibb

Jialin Mao, PhD, Genentech

SPEAKERS

Current Status of Endogenous CYP3A Biomarkers

Yvonne Lin, PhD, University of Washington

Clinical Validation and Utility of 4β-Hydroxycholesterol for the Assessment of CYP3A Activity

Craig Lambert, BSC, PhD, AstraZeneca

Pharmacometric Approach to Assess CYP3A Activity Using 4β -Hydroxycholesterol

Tarek Leil, PhD, Bristol-Myers Squibb

Upon completion of this Science at Sunrise Session, the participant should be able to:

- Highlight current status of endogenous biomarkers for assessment of clinical drug-drug interactions involving CYP3A4/5 pathway, and showcase regulatory perspective of currently used endogenous biomarkers;
- Provide examples of widely used endogenous biomarkers along with some pros and cons of each biomarker. Highlight challenges in gaining wider acknowledgement in the Clinical Pharmacology community; and
- Discuss the current status of 4β-hydroxycholesterol (4βHC) and its potential utility in assessing CYP3A activity in clinical studies. Provide case-study of validating 4βHC compared to commonly used markers such as midazolam pharmacokinetics. Learn how mechanistic modeling approach can integrate *in vitro* and *in vivo* parameters to predict 4βHC changes during a clinical study.

7:30 AM – 9:00 AM

CONTINENTAL BREAKFAST IN THE POSTER AND EXHIBIT HALL

International Hall

POSTER SESSION I, LATE-BREAKING AND ENCORE ABSTRACT POSTER SESSION I ATTENDED

(See page 103 for poster presentation titles being presented this morning)

7:30 AM – 2:00 PM

POSTERS AND EXHIBITS OPEN

8:30 AM – 10:15 AM

INTERNATIONAL SESSION

Clinical Pharmacology in the Netherlands: Impact on Use of Medication and Teaching Health Professionals

Marquis D

CHAIRS

Hendrik Jan Guchelaar, PharmD, PhD, Leiden University Medical Center

Teun van Gelder, MD, PhD, Erasmus Medical Center

SPEAKERS

The Dutch Vision on Clinical Pharmacology

Teun van Gelder, MD, PhD, Erasmus Medical Center

Training and Education in Clinical Pharmacology

Kees Kramers, MD, PhD, Radboud Medical Center, University of Nijmegen

D Discovery D Development R Regulation U Utilization

THURSDAY, MARCH 20, 2014

9:15 AM – 10:15 AM

RAWLS-PALMER PROGRESS IN MEDICINE AWARD LECTURE

Clinical Significance of Drug Transporters in Pharmacokinetics, Efficacy and Toxicity

Imperial Ballroom

UAN: 0708-9999-14-205-L04-P

Presenter: Shiew-Mei Huang, PhD, US Food and Drug Administration

Yuichi Sugiyama, PhD, Riken Innovation Center

Upon completion of this Award Lecture, the participant should be able to:

- Discuss the development of drugs that have wide therapeutic ranges; and
- Identify drugs that can be less affected by drug-drug interactions, inter-individual variation and disease states.

10:15 AM – 10:45 AM

MORNING BREAK IN THE POSTER AND EXHIBIT HALL

International Hall

10:45 AM – 11:45 AM

FEATURED SPEAKER

Pharmacometrics: Focus on the Patient

Marquis A

CHAIR

Richard L. Lalonde, PharmD, Pfizer

Virginia (Ginny) Schmith, PhD, FCP, GlaxoSmithKline

10:45 AM – 12:00 NOON

ORAL SESSION

Population-Based Advances in Pharmacotherapy

Marquis C

CHAIRS

Issam Zineh, PharmD, MPH, US Food and Drug Administration

Minoli A. Perera, PharmD, PhD, University of Chicago

OI-1

Risk of Ischemic Stroke Among Users of Clopidogrel and Five Different Proton Pump Inhibitors.

Presenter: Sean Hennessy, PharmD, PhD, Perelman School of Medicine at the University of Pennsylvania

OI-2

Transporterome-Wide Analysis of Genetic Variants in SLC Transporters and their Effects on Metformin Response.

Presenter: Sook Wah Yee, PhD, University of California, San Francisco

OI-3

Genomewide Analysis of Uric Acid Levels and Allopurinol Response in the Kaiser Genetic Epidemiology Research on Aging Cohort.

Presenter: Christopher C. Wen, University of California, San Francisco

OI-4

Genome-Wide Association Analysis (GWAS) of Blood Pressure Response to Atenolol-Results From the Pharmacogenomic Evalution of Antihypertensive Responses (PEAR) Study.

Presenter: Yan Gong, PhD, University of Florida

OI-5 [ENCORE PRESENTATION]

Clinically Actionable Genotypes Among 10,000 Patients with Preemptive Pharmacogenomic Testing.

Presenter: Sara L. Van Driest, MD, PhD, Vanderbilt University

10:45 AM – 12:15 PM

ASCPT DEBATE

Debating About the Evidence for Clinical Utility of Pharmacogenetic Testing

Marquis A

MODERATOR

Federico Innocenti, MD, PhD, University of North Carolina Institute for Pharmacogenomics and Individualized Therapy

THURSDAY, MARCH 20, 2014

DEBATERS

Inclusive: Lower Level of Evidence, Without Harm

Randomized Clinical Trials of Individual Pharmacogenetic Diagnostics: Reductio Ad Absurdum

Mark J. Ratain, MD, The University of Chicago Medical Center

Julie Johnson, PharmD, University of Florida

Selective: Higher Evidence, Outcome Measures, etc.

Cecile Janssens, MA, MSc, PhD, Emory University

Patricia Deverka, MD, MS, MBE, Center for Medical Technology Policy

David F. Ransohoff, MD, University of North Carolina School of Medicine

12:00 NOON – 1:15 PM

ASCPT BOARD OF DIRECTORS LUNCH MEETING (BY INVITATION ONLY)

12:00 NOON – 1:30 PM

LUNCH AVAILABLE FOR PURCHASE IN THE POSTER AND EXHIBIT HALL

International Hall

12:00 NOON – 1:30 PM

TRAINEE LUNCHEON (TICKETED EVENT)

Marquis D

1:30 PM – 3:30 PM

SYMPOSIUM

Systems Pharmacology Approach to Defining and Predicting Tyrosine Kinase Inhibitor (TKI) Toxicity

Imperial Ballroom

UAN: 0708-9999-14-211-L01-P

Scientific Section: Drug Safety (SAF)

D D R U

CHAIRS

Darrell R. Abernethy, MD, PhD, US Food and Drug Administration

Lori Minasian, MD, MPH, National Cancer Institute/Reagan-Udall Foundation

SPEAKERS

Proposed Mechanisms for TKI Cardiotoxicity

Thomas Force, MD, Temple University School of Medicine

Ontological Framework for Systems Analysis of TKI Cardiotoxicity: Extension of the Ontology of Adverse Events (OAE)

Sirarat Sarntivijai, PhD, US Food and Drug Administration

Systems Drug Design and Software Platform for Adverse Drug Effects: Application to TKI Cardiotoxicity

Hiroaki Kitano, PhD, Okinawa Institute of Science and Technology Graduate University/ The Systems Biology Institute

Application of High Performance Computing to Systems Biology: Whole Heart Bioenergetics and Electrophysiology

Fred Streitz, PhD, Lawrence Livermore National Laboratories

D Discovery D Development R Regulation U Utilization

THURSDAY, MARCH 20, 2014

Upon completion of this Symposium Session, the participant should be able to:

- Present methodology for the tools of systems pharmacology as applied to a case study of drug toxicity;
- Demonstrate the critical input of diverse disciplines to effectively address systems pharmacology-based drug toxicity prediction; and
- Discuss the approach to integration of diverse data sources that is required for predictive analysis of TKI cardiotoxicity.

1:30 PM – 3:30 PM

SYMPOSIUM

Challenging the Maximum Tolerated Dosing Paradigm in Oncology: Threading the Needle with Targeted Agents

Marquis A

UAN: 0708-9999-14-212-L01-P

Scientific Section: Oncology (ONC)

CHAIRS

Mark Stroh, PhD, Genentech

Bert L. Lum, PharmD, Genentech

SPEAKERS

Surveying Dosing Paradigm in Oncology: A Review of the Labeled Dose Recommendation for New Drugs Approved by FDA Between 2010 and 2013

Dan Lu, PhD, Genentech

Selection of Recommended Phase II and Phase III Dose in Oncology Drug Development

Patricia LoRusso, DO, Karmanos Cancer Center

Discuss Regulatory Expectations for Clinical Pharmacology Support of Dose Optimization of Targeted Oncology Agents

Stacy S. Shord, PharmD, FCCP, BCOP, US Food and Drug Administration

Discuss Regulatory Expectations for Pharmacometrics Support of Dose Optimization of Targeted Oncology Agents

Nitin Mehrotra, PhD, US Food and Drug Administration

Upon completion of this Symposium Session, the participant should be able to:

- Review historical approaches for selection of marketed dose in oncology;
- Illustrate use of optimal biological dosing in oncology drug development; and
- Discuss regulatory expectations for dose optimization of targeted oncology drugs.

1:30 PM – 3:30 PM

SYMPOSIUM

What is the Best Type of Data for POC Studies: Continuous, Categorical, or Count Data?

Marquis B

UAN: 0708-9999-14-213-L03-P

Scientific Section: Pharmacometrics and Pharmacokinetics (PMK)

CHAIRS

Virginia (Ginny) Schmith, PhD, FCP, GlaxoSmithKline

Mats O. Karlsson, PhD, Uppsala University

SPEAKERS

Impact of Choice of Endpoint and Analysis for the Design of Proof of Concepts Studies in Hot Flash

Brian P. Smith, PhD, Amgen

How Inferences from Continuous and Discontinuous Endpoints Can Be Integrated to Decision Making?

Jogarao Gobburu, PhD, FCP, MBA, University of Maryland

Comparisons of Analysis Methods and Variables for Proof-of-Concept Trials

Mats O. Karlsson, PhD, Uppsala University

THURSDAY, MARCH 20, 2014

Balancing the Statistical Efficiency of Continuous Endpoints with the Attractiveness of Clinical Interpretability of Categorical Endpoints
Sriram Krishnaswami, PhD, Pfizer

Upon completion of this Symposium Session, the participant should be able to:

- Demonstrate that choice of how an endpoint is analyzed will have a large impact on the amount of information that can be extracted from a clinical trial;
- Discuss how to determine probability of technical success based on continuous and discontinuous data, along with the potential sources of differences between them; and
- Discuss how to combine these two types of endpoints to support drug development decisions.

1:30 PM – 3:30 PM

SYMPOSIUM

Early Drug Development Challenges and Strategies for Orphan Indications
Marquis C
UAN: 0708-9999-14-214-L01-P
Scientific Section: Drug Development and Regulatory Sciences (DDR)
D D R U

CHAIRS
Mary Ann Mascelli, PhD, Shire HGT
JF Marier, PhD, FCP, Pharsight Consulting Services, A Division of Certara

SPEAKERS
Exendin-(9-39) for Treating Children with Congenital Hyperinsulinism
Jeffrey Barrett, PhD, FCP, Sanofi Pharmaceuticals

The Use of Quantitative Clinical Pharmacology to Guide Orphan Drug Development: A Regulatory Perspective
Kevin Krudys, PhD, US Food and Drug Administration

Biomarker-Disease Models as Innovative Tools for Trial Enrichment and Trade-Offs in Orphan Disease Programs
JF Marier, PhD, FCP, Pharsight Consulting Services, A Division of Certara

Early Clinical Drug Development in Rare Diseases: A Big Pharma Perspective and Experience
Paul N. Mudd, Jr., PharmD, MBA, GlaxoSmithKline

Upon completion of this Symposium Session, the attendee should be able to:

- Provide a detailed overview of preclinical, clinical and regulatory challenges related to the development of small and large molecules for orphan indications; and
- Present test cases of successful preclinical/early clinical development technologies and strategies which facilitated drug development for orphan indications, including: Modeling and simulations (bottom-up, top-down and middle-out), Biochemical and imaging biomarkers, Trial simulations, study design optimization and trial enrichment.

3:45 PM – 5:15 PM

STATE OF THE ART LECTURE

The Early Days of the AIDS Epidemic in the United States: Views from Hollywood and Atlanta
Imperial Ballroom
UAN: 0708-9999-14-202-L02-P

CHAIR
Russ B. Altman, MD, PhD, Stanford University

Harold W. Jaffe, MD, MA, Associate Director for Science, Centers for Disease Control and Prevention

D Discovery D Development R Regulation U Utilization

THURSDAY, MARCH 20, 2014

5:30 PM – 7:00 PM

SCIENTIFIC SECTION MEETINGS
BIOMARKERS & IMAGING (BIO)
M102

Joseph C. Fleishaker, PhD, FAAPS, Chair
Jerry M. Collins, PhD, Vice Chair
Ronda K. Ripley, PhD, Vice Chair

Welcome and Introductions of New Leadership

Discuss New Vision Statement and Section Name, Brainstorm Ideas for Symposia, Workshops and Science at Sunrise Sessions for 2015

MOLECULAR PHARMACOLOGY & PHARMACOGENETICS (MOL)
Marquis B

Bert L. Lum, PharmD, Chair
Kathryn Momary, PharmD, BCPS, Vice Chair

PRESENTATIONS

A Pharmacogenomic Genome-Wide Association Study for Adverse Cardiovascular Outcomes in the International Verapamil SR-Trandolapril Study (INVEST)
Caitrin W. McDonough, PhD, University of Florida

Genome-Wide Significant Association of TSPAN 5 SNPS with Plasma Serotonin and Change in Plasma Serotonin After SSRI Therapy
Meenal Gupta, PhD, Mayo Clinic

Follow up commentary by Richard Weinshilboum, MD, Mayo Clinic

PHARMACOMETRICS & PHARMACOKINETICS (PMK)
PMX in Submission: Where are We Now? Where Should We Go?
Marquis C

Virginia (Ginny) Schmith, PhD, FCP, Chair
Jogarao Gobburu, PhD, FCP, MBA, Vice Chair

SPEAKERS
Christoffer Tornoe, PhD
Director, Quantitative Clinical Pharmacology, Novo Nordisk
Brian Corrigan, PhD
Senior Director, Clinical Pharmacology, Pfizer
Vikram Sinha, PhD
Director, Division of Pharmacometrics, CDER/ US Food and Drug Administration

6:00 PM – 7:00 PM

DONOR RECEPTION
(BY INVITATION ONLY)
Sear Private Dining Room

6:30 PM – 8:00 PM

PhRMA FOUNDATION RECEPTION
(BY INVITATION ONLY)
M109

6:30 PM – 8:00 PM

UCSF—STANFORD–GENENTECH RECEPTION FOR FACULTY AND STAFF, TRAINEES, ALUMNI AND FRIENDS
(BY INVITATION ONLY)
M106/107

7:00 PM – 8:00 PM

CAREER BOOTCAMP RECEPTION
(REGISTERED CAREER BOOTCAMP ATTENDEES AND SPEAKERS ONLY)
M101

7:00 PM – 8:00 PM

INTERNATIONAL RECEPTION
(BY INVITATION ONLY)
Sponsored by PRA.
M104/105

8:00 PM – 9:00 PM

GAVEL CLUB DESSERT RECEPTION
(BY INVITATION ONLY)
President's Suite

FRIDAY, MARCH 21, 2014

7:00 AM – 4:00 PM

ASCPT REGISTRATION OPEN
ASCPT CENTRAL OPEN

7:00 AM – 8:00 AM

ASCPT FINANCE COMMITTEE MEETING (BY INVITATION ONLY)
M102

7:00 AM – 9:00 AM

AMERICAN BOARD OF CLINICAL PHARMACOLOGY (ABCP) BOARD MEETING (BY INVITATION ONLY)
L504

7:30 AM – 9:00 AM

SCIENTIFIC SECTION MEETINGS

DRUG DEVELOPMENT & REGULATORY SCIENCES (DDR)
Marquis A

Kellie Schoolar Reynolds, PharmD, Chair
Megan A. Gibbs, PhD, BscPharm, FCP, Vice Chair

PRESENTATIONS

PK and PD Assessments of Hormonal Contraceptive Drug-Drug Interactions
Chongwoo Yu, PhD, US Food and Drug Administration

Lithium Treatment and Risk for Dementia Among Patients with Bipolar Disorder
Tobias Gerhard, PhD, Rutgers, The State University of New Jersey

Business meeting/section discussion

DRUG SAFETY (SAF)
M108

Tobias Gerhard, PhD, Chair
Geert W. 't Jong, MD, PhD, Vice Chair

Welcome and Introductions

SPEAKER

Studying Drug-Drug Interactions in Administrative Data
Joshua Gagne, Harvard Medical School

SAF Symposia and Workshops for ASCPT 2015

Improving Visibility and Impact of SAF

INFECTIOUS DISEASES (INF)
M105

Steven M. Belknap, MD, Chair
David L. Wesche, MD, PhD, Vice Chair

PRESENTATIONS

Some Observations on PK/PD of the Second Generation Hepatitis C NS3/NS4 Protease Inhibitor, Faldaprevir
Fenglei Huang, PhD, Boehringer Ingelheim Pharmaceuticals, Inc.

Vancomycin AUC24H/MIC Does Not Predict Clinical Outcomes in Children with MRSA Bacteremia
Andrea Hahn, MD, Cincinnati Children's Hospital Medical Center

ONCOLOGY (ONC): NEWS, UPDATES, AND INTRODUCTIONS OF THE NEW CHAIR AND VICE-CHAIR
M106/107

Federico Innocenti, MD, PhD, Chair
Alex Sparreboom, PhD, Vice Chair

PRESENTATIONS

Updates on New ONC Section Leadership
Federico Innocenti, MD, PhD, University of North Carolina at Chapel Hill

A Modeling and Simulation Framework to Support Early Clinical Drug Development in Oncology with Application to Multiple Myeloma
Fredrik Jonsson, PhD, Pharsight, a Certara Company

MEET-THE-EXPERT

Phase I and the Cancer Genome
Patricia LoRusso, DO, Karmanos Cancer Institute

Business meeting/section discussion

D Discovery D Development R Regulation U Utilization

FRIDAY, MARCH 21, 2014

ORGAN SPECIFIC DISEASES (OSD)
M109

Shirley M. Tsunoda, PharmD, Chair
Dean K. Naritoku, MD, Vice Chair
Sony Tuteja, PharmD, MS, Vice Chair
Satsuki Yamada, MD, PhD, Vice Chair

PRESENTATIONS

Citalopram and Escitalopram Plasma Drug and Metabolite Concentrations: Genome-Wide Associations.
Yuan Ji, PhD, Mayo Clinic

Mechanisms of Neuraminidase Inhibitor Transport Across the Blood-Brain Barrier.
Lawrence Lin, University of California, San Francisco

Business meeting/section discussion

SPECIAL POPULATIONS (SPO)
M104

Saskia N. de Wildt, MD, PhD, Chair
Parvaz Madadi, PhD, Vice Chair
Scott Oglesby, PhD, Vice Chair

PRESENTATIONS

Benzodiazepine Prescribing Among Older Adults in Emergency Departments and Ambulatory Clinics
Maryann E. Mazer-Amirshahi, PharmD, MD, George Washington University

The Transfer of Dabigatran Across a Dually Perfused Isolated Human Placental Cotyledon: Implications for Therapy in Pregnancy
Priya Bapat, BMSc, University of Toronto

Population Pharmacokinetic Analysis of Temsirolimus in Children
Tomoyuki Mizuno, PhD, Cincinnati Children's Hospital Medical Center

7:30 AM – 9:00 AM
CONTINENTAL BREAKFAST IN THE POSTER AND EXHIBIT HALL
International Hall

7:30 AM – 3:30 PM
POSTERS AND EXHIBITS OPEN
International Hall

9:15 AM – 10:15 AM
STATE OF THE ART LECTURE
How Economics Shapes Science
Imperial Ballroom
UAN: 0708-9999-14-203-L03-P

CHAIR
Kathleen M. Giacomini, PhD, University of California, San Francisco

Paula Stephan, PhD, Georgia State University

Upon completion of this State of the Art Lecture, the attendee should be able to:

- Describe how costs and incentives affect the behavior of individuals and institutions as they compete for funding;
- Discuss the imbalance between biomedical science and physics/engineering; and
- Discuss how costs and incentives affect the training of graduate students and postdocs.

10:15 AM – 10:25 AM
TRANSITION TO THE FUTURE
Imperial Ballroom

John A. Wagner, MD, PhD, Takeda Pharmaceuticals

FRIDAY, MARCH 21, 2014

10:30 AM – 11:30 AM

OSCAR B. HUNTER MEMORIAL AWARD IN THERAPEUTICS LECTURE

The Dance of Therapeutics

Imperial Ballroom

UAN: 0708-9999-14-206-L04-P

Presenter: Rachel F. Tyndale, PhD, University of Toronto

Edward M. Sellers, MD, PhD, FRCPC, FACP, DL Global Partners Inc.

Upon completion of this Award Lecture, the attendee should be able to discuss research, teaching, and clinical care strategies as they relate to clinical pharmacology.

10:30 AM – 11:45 AM

ORAL SESSION

Transporters Across the Therapeutic Spectrum

Marquis A

CHAIRS

Lei Zhang, PhD, US Food and Drug Administration

Aubrey Stoch, MD, Merck, Inc.

OII-A-1

PBPK Models of Renally Eliminated Drugs and Their Application in Evaluating the Effect of Patient Factors.

Presenter: Vicky Hsu, PhD, US Food and Drug Administration

OII-A-2

Assessment of Ritonavir and Efavirenz Effects on Blood-Brain Barrier P-Glycoprotein Activity in Humans Using Positron Emission Tomography.

Presenter: Evan D. Kharasch, MD, PhD, Washington University in St. Louis

OII-A-3

Clinical Validation of a Selective Inhibitor of Multidrug and Toxin Extrusion Protein Mate1 (SLC47A1) in Health Volunteers.

Presenter: Jennifer E. Hibma, PharmD, University of California, San Francisco

OII-A-4

Genetic Variants in Transcription Factors are Linked to the Pharmacokinetics and Pharmacodynamics of Metformin.

Presenter: Srijib Goswami, BS, University of California, San Francisco

OII-A-5 [LATE-BREAKING ABSTRACT]

Ontogeny of Human Drug Transporter Expression in the Pediatric Kidney.

Presenter: Saskia N. de Wildt, MD, PhD, Erasmus MC-Sophia Children's Hospital

10:30 AM – 11:45 AM

ORAL SESSION

Computational Drug Discovery and Development

Marquis B

CHAIRS

Piet H. van der Graaf, PhD, PharmD, Leiden Academic Centre for Drug Research (LACDR)

Mark Dresser, PhD, Genentech

OII-B-1

Use of Predictive Models to Implement Prognostic Enrichment Study Design Strategies.

Presenter: Roberto Gomeni, PhD, Pharmacometrica

OII-B-2

An Integrative Bioinformatics Approach to Identify Transcription Factor Modulators from a Clinical Drug Library.

Presenter: Bin Chen, PhD, Stanford University

D Discovery D Development R Regulation U Utilization

FRIDAY, MARCH 21, 2014

OII-B-3
An Assessment of the Operating Characteristics (OCS) of Time-to-Event (TTE) Exposure-Response (ER) Analyses of Adverse Events (AES).
Presenter: Cecilia Fosser, PhD, Pfizer

OII-B-4
The Use of Tumor Growth Parameters as Early Clinical Endpoints in Oncology: A Retrospective Analysis Across GSK Compounds.
Presenter: Daniele Ouellet, PhD, GlaxoSmithKline

OII-B-5 [ENCORE PRESENTATION]
Application of Physiologically-Based Pharmacokinetic (PBPK) Model in Predicting Acetaminophen Metabolism and Pharmacokinetics in Children.
Presenter: Xiling Jiang, PhD, University of Florida

10:30 AM – 11:45 AM
ORAL SESSION
Having Your Drugs and Safety Too
Marquis C

CHAIRS
Kathleen Butler, MD, MS, Teva Pharmaceuticals
Susan M. Abdel-Rahman, PharmD, Children's Mercy Hospitals and Clinics

OII-C-1
Predicting Adverse Events Based Upon a Drug's Molecular Target Profile.
Presenter: Darrell R. Abernethy, MD, PhD, US Food and Drug Administration

OII-C-2
A Pharmacogenomic Genome-Wide Association Study (GWAS) for New Onset Diabetes (NOD) in the International Verapamil SR-Trandolapril Study (INVEST)
Presenter: Shin-Wen Chang, BPharm, University of Florida

OII-C-3
Aromatase Inhibitor Treatment and Musculoskeletal Adverse Events: SNP Modulated, Estrogen-Dependent Variation in CCR6/CCL20 Expression.
Presenter: Ming-Fen Ho, PhD, Mayo Clinic

OII-C-4
Liver EQTLS for Warfarin Dose Response Genes Reveal Susceptibility to Venous Thromboembolism Among African Americans.
Presenter: Wenndy Hernandez, PhD, University of Chicago

OII-C-5 [LATE-BREAKING ABSTRACT]
Mechanistic Modeling of Drug-Induced Liver Injury (DILI) Predicts Species Differences in Bile Acid (BA)-Mediated Troglitazone (TGZ) Hepatotoxicity.
Presenter: Kyunghee Yang, MS, University of North Carolina at Chapel Hill

11:45 AM – 1:15 PM
LUNCH AVAILABLE FOR PURCHASE IN THE POSTER AND EXHIBIT HALL
International Hall

POSTER SESSION II LATE-BREAKING AND ENCORE ABSTRACT POSTER SESSION II ATTENDED

12:00 NOON – 1:00 PM
INTERNATIONAL TRANSPORTER CONSORTIUM SPECIAL INTEREST GROUP MEETING (BY INVITATION ONLY)
M102

12:00 NOON – 1:00 PM
PHARMACOMETABOLOMICS SPECIAL INTEREST GROUP MEETING
M101

12:15 PM – 1:00 PM
TOWN HALL
International A/B

1:15 PM – 2:15 PM
FEATURED SPEAKER
Smoking – It's in Your Genes
Marquis A

CHAIR
Edward M. Sellers, MD, PhD, FRCPC, FACP, DL Global Partners Inc.

Rachel F. Tyndale, PhD, University of Toronto

FRIDAY, MARCH 21, 2014

1:15 PM – 2:15 PM

SHEINER-BEAL PHARMACOMETRICS AWARD LECTURE

Two Sides of a Coin

Imperial Ballroom

UAN: 0708-9999-14-207-L04-P

Presenter: Virginia (Ginny) Schmith, PhD, FCP, GlaxoSmithKline

Mats O. Karlsson, PhD, Uppsala University

Upon completion of this Award Lecture, the participant should be able to:

- Discuss methodological aspects of non-linear mixed effects model building; and
- Discuss the application of PKPD modeling to problems in drug development and routine drug therapy.

1:15 PM – 2:45 PM

SPECIAL SESSION

Expanding Your Horizons: A Guide to Mid-Career Transitions

Marquis C

CHAIR

Kellie Schoolar Reynolds, PharmD, US Food and Drug Administration

SPEAKERS

Transitioning from Industry to Academia

Jeffrey Barrett, PhD, FCP, Sanofi Pharmaceuticals

Transitioning from Government to Industry

Lisa Mathis, MD, Amgen

Mentorship During Mid-Career

Phillip D. Byrne, EdD, Children's Mercy Hospitals and Clinics

PANELISTS

Darrell R. Abernethy, MD, PhD, US Food and Drug Administration

Gregory L. Kearns, PharmD, PhD, Chief Scientific Officer and Chairman Children's Mercy Hospitals and Clinics Professor of Pediatrics and Pharmacology, University of Missouri, Kansas City

1:15 PM – 2:45 PM

WORKSHOP

Next Generation Cancer Immunotherapy Coming of Age: Targeting Immune Checkpoints

Marquis B

Scientific Section: Oncology (ONC)

D D R U

CHAIRS

Lucy Lee, PharmD, Eisai Inc.

Srikumar Sahasranaman, PhD, Genentech

SPEAKERS

Introduction to Tumor Immunology and Cancer Immunotherapies

Mark Stroh, PhD, Genentech

Clinical Pharmacology Strategies and Considerations in Development of Immunotherapies

Manish Gupta, PhD, Bristol-Myers Squibb

Early Clinical Results and Biomarkers for Combination Immunotherapies Demonstrating Enhanced Anti-Tumor Activities

Margaret Callahan, MD, PhD, Memorial Sloan-Kettering Cancer Center

Upon completion of this Workshop, the participant should be able to:

- Review tumor immunology and cancer immunotherapies;
- Discuss clinical pharmacology strategies in development of immunotherapies; and
- Present early clinical results and biomarkers for combination immunotherapies.

2:45 PM – 3:15 PM

AFTERNOON BREAK IN THE POSTER AND EXHIBIT HALL

International Hall

D Discovery D Development R Regulation U Utilization

FRIDAY, MARCH 21, 2014

3:15 PM – 4:15 PM

STATE OF THE ART LECTURE

Taking Down Hepatitis C

Imperial Ballroom

UAN: 0708-9999-14-204-L01-P

CHAIR

John A. Wagner, MD, PhD, Takeda Pharmaceuticals

Jeffrey S. Glenn, MD, PhD, Stanford University School of Medicine

Upon completion of this State of the Art Lecture, the participant should be able to:

- Identify key determinants of pathogenesis; and
- Analyze novel antiviral strategies.

4:30 PM – 6:30 PM

SYMPOSIUM

New Applications of Quantitative Approaches in a Changing Health Care Environment: Incorporating Effectiveness and Cost in Our Models

Imperial Ballroom

UAN: 0708-9999-14-215-L03-P

Scientific Section: Pharmacometrics and Pharmacokinetics (PMK)

D D R U

CHAIRS

Michael A. Tortorici, PharmD, PhD, Pfizer

Ganesh Mugundu, MPharm, PhD, Pfizer

SPEAKERS

Comparative Effectiveness of Newly Marketed Medications

Sebastian Schneeweiss, MD, ScD, Brigham & Women's Hospital, Harvard Medical School

Quantitative Approaches to Economic Evaluations of Health Care Decisions

J. Jaime Caro, MD, McGill University/Evidera

Potential Impact of Clinical Pharmacology/Pharmacometrics on Clinical and Cost Effectiveness and Vice Versa

Brian P. Smith, PhD, Amgen

Case Studies: Quantitative Approaches to Evaluate Comparative Efficacy and Safety of Anticoagulants

Rebecca Boyd, PhD, Pfizer

Upon completion of this Symposium Session, the participant should be able to:

- Report the key concepts and quantitative approaches of comparative effectiveness research (CER) and the importance of why they matter in the current changing health care environment;
- Describe an overview of pharmacoeconomics and the current quantitative methodologies to assess value;
- Describe how clinical pharmacology/pharmacometrics can impact CER and pharmacoeconomics in the next decade; and
- Review a case study of quantitative approaches used to assess effectiveness and economics of various drug choices.

FRIDAY, MARCH 21, 2014

4:30 PM – 6:30 PM

SYMPOSIUM

Challenges and Opportunities for Physiologically-Based Pharmacokinetic (PBPK) Modeling in Pediatric Drug Development

Marquis A

UAN: 0708-9999-14-216-L03-P

Scientific Section: Drug Development and Regulatory Sciences (DDR)

D D R U

CHAIRS

Megan Gibbs, PhD, BscPharm, FCP, Amgen

Stephan Schmidt, PhD, University of Florida

SPEAKERS

Perspective on Pediatric Development and Use of PBPK

Ping Zhao, PhD, US Food and Drug Administration

Pros and Cons of Model Based Development Applied to Pediatric Population

Jeffrey Barrett, PhD, FCP, Sanofi Pharmaceuticals

Model Application to Pediatrics for mABs

Joseph Balthasar, PhD, The State University of New York at Buffalo

Industrial Perspective on Applying PBPK in Pediatric Drug Development Decision Making for Biologics

Marliee Andrew, PhD, Amgen

Upon completion of this Symposium Session, the participant should be able to:

- Identify how, from a regulators point of view, acceptable approaches in pediatric drug development would look like and outline what role PBPK can play;
- Compare and contrast strengths and limitations of currently employed PBPK models in pediatric drug development relative to conventional PK/PD approaches; and
- Discuss the challenges and opportunities of PBPK/PD models for large molecules in pediatric drug development.

4:30 PM – 6:30 PM

SYMPOSIUM

Next Generation Sequencing and Bioinformatics: The Driving Force of the New Era of Pharmacogenomics

Marquis B

UAN: 0708-9999-14-217-L03-P

Scientific Section: Pharmacometrics and Pharmacokinetics (PMK)

D D R U

CHAIR

Lang Li, PhD, Indiana University

SPEAKERS

New Technologies, New Approaches to their Analysis, and Resulting Discoveries in Pharmacogenomics

Nancy Cox, PhD, University of Chicago

The Rare Variants in the Pharmacogenomics Studies

Marylyn D. Ritchie, PhD, Penn State University

FRIDAY, MARCH 21, 2014

Roles of Regulatory Variants in Pharmacogenomics
Yunlong Liu, PhD, Indiana University

Examining Coding Variation in the Context of Protein Structure
William S. Bush, PhD,
Vanderbilt University

Upon completion of this Symposium Session, the participant should be able to:

- Illustrate how pharmacogenomics hypotheses from clinical studies and pharmacology experiments can be answered by the next generation sequencing technologies;
- Examine bioinformatic methods and public domain genomic databases that answer significant pharmacogenomics questions; and
- Demonstrate how the next generation sequencing technology and bioinformatics methods drive the pharmacogenomics research.

4:30 PM – 6:30 PM

SYMPOSIUM
Trends in Oral Drug Exposure in Post Bariatric Surgery Patients: Challenges in Pharmacotherapy of an Ever-Growing Population
Marquis C
UAN: 0708-9999-14-218-L01-P
Scientific Section: Special Populations (SPO)
D D R U

CHAIRS
Amin Rostami-Hodjegan, PharmD, PhD, University of Manchester
Alexander A. Vinks, PharmD, PhD, University of Cincinnati College of Medicine and Pharmacy

SPEAKERS
Bariatric Surgery: Procedures and Outcomes
Bruce M. Wolfe, MD, Oregon Health and Science University

Systemic Exposure of Immunosuppressants Following Roux-en-Y Gastric Bypass
Rita R. Alloway, PharmD, University of Cincinnati

Pharmacokinetic and Pharmacodynamic Alterations Following Roux-en-Y Gastric Bypass
Raj K. Vuppalanchi, MD, Indiana University School of Medicine, Indiana University Health

Development and Application of a Mechanistic Physiologically Based Pharmacokinetic Model to Assess Oral Drug Bioavailability Post Bariatric Surgery
Adam S. Darwich, MSc, University of Manchester

Upon completion of this Symposium Session, the participant should be able to:

- Describe existing challenges regarding pharmacotherapy by most commonly prescribed drugs in a post bariatric surgery population;
- Discuss the mechanistic approaches to describe the altered oral drug bioavailability post-bariatric surgery; and
- Debate the labeling requirements in the absence of pharmacokinetic or pharmacodynamic data.

7:00 PM – 8:30 PM

PRESIDENT'S RECEPTION
Atrium A

SATURDAY, MARCH 22, 2014

7:00 AM – 9:00 AM
ASCPT BOARD OF DIRECTORS MEETING (BY INVITATION ONLY)
M101

7:00 AM – 10:00 AM
ASCPT REGISTRATION OPEN
ASCPT CENTRAL OPEN

7:30 AM – 9:00 AM
CONTINENTAL BREAKFAST
Marquis Foyer

7:30 AM – 9:00 AM
SCIENCE AT SUNRISE
The Human Blood Brain Barrier in Drug Development
Marquis A
Scientific Section: Molecular Pharmcology and Pharmacogenetics (MOL)
D D R U

CHAIRS
Sook Wah Yee, PhD, University of California, San Francisco
Lei Zhang, PhD, US Food and Drug Administration

SPEAKERS
Overview of Transporters in the Human Brain Barrier
Kathleen M. Giacomini, PhD, University of California, San Francisco

Targeting the Brain: Issues in Drug Discovery and Development
Jennifer Liras, PhD, Pfizer Inc.

Efflux Transporters in the Blood Brain Barrier: Why Clinically Relevent Drug Interactions are Unlikely
Joseph W. Polli, PhD, GlaxoSmithKline

Upon completion of this Science at Sunrise Session, the participant should be able to:
- List three transporters in the human blood brain barrier and their association with drug disposition, response or toxicity;
- Describe cellular components and proteins that comprise the barrier function of the blood brain barrier; and
- Describe the methods that are used to enhance the delivery of therapeutic agents to treat diseases in the central nervous system.

7:30 AM – 9:00 AM
SCIENCE AT SUNRISE
Study Participants and Social Media: Recruitment, Participation and Impact on Study Design
Marquis B
Scientific Section: Drug Development and Regulatory Science (DDR)
D D R U

CHAIRS
Geert W. 't Jong, MD, PhD, Manitoba Institute of Child Health
Kathryn Momary, PharmD, BCPS, Mercer University, College of Pharmacy and Health Sciences

SPEAKERS
Use of Social Media for Study Recruitment: An Academic Perspective
Michael Spigarelli, MD, PhD, University of Utah

Use of Social Media for Social Recruitment: An CRO Perspective
Jim Kremidas, BS, inVentiv Health

Upon completion of this Science at Sunrise Session, the participant should be able to:
- Discuss the potential role of social media in subject recruitment; and
- Learn from the experiences of other researchers using social media.

8:00 AM – 2:00 PM
CAREER BOOTCAMP
M103/104/105
See page 85 for complete program.

EDUCATION COMMITTEE CHAIR
Bridgette L. Jones, MD, Children's Mercy Hospitals and Clinics

D Discovery D Development R Regulation U Utilization

SATURDAY, MARCH 22, 2014

EDUCATION COMMITTEE VICE CHAIR
Jun J. Yang, PhD, St. Jude Children's Research Hospital

8:30 AM – 10:00 AM

WORKSHOP

The Rising Challenge of Polypharmacy: Considerations for Concurrent Therapies in Oncology with HIV/AIDS

Marquis C

Scientific Section: Oncology (ONC)

D D R U

CHAIRS

Michelle A. Rudek, PharmD, PhD, The SKCCC at Johns Hopkins

Adriana Andrade, MD, MPH, FACP, Johns Hopkins University

SPEAKERS

The Evolution of Cancer and Challenges in Drug Development in AIDS Patients
Richard F. Little, MPH, MD, National Cancer Institute

In vitro-In vivo Correlations for Drug Interaction Potential in Cancer Patients
Jan H. Beumer, PharmD, PhD, University of Pittsburgh Cancer Institute

From Translation to Trials and Dosing Recommendations in Cancer Patients with Polypharmacy
Michelle A. Rudek, PharmD, PhD, The SKCCC at Johns Hopkins

Upon completion of this Workshop, the participant should be able to:

- Discuss the evolution of cancer and understand the controversies surrounding the optimal design of therapeutic regimens in special populations prone to drug interactions including AIDS;
- Discuss the utility of hepatocytes and animal studies to ascertain information about the magnitude of drug interactions in clinical trial design and patient treatment; and
- Illustrate how clinical pharmacology principles apply when designing clinical trials in patients with cancer and HIV/AIDS.

8:30 AM – 10:00 AM

WORKSHOP

Microdosing in Children: A Useful Tool for Pediatric Drug Development?

Marquis D

Scientific Section: Special Populations (SPO)

D D R U

CHAIRS

L. Steven Leeder, PharmD, PhD, Children's Mercy Hospitals and Clinics

Parvaz Madadi, PhD, The Hospital for Sick Children

SPEAKERS

Microdosing in Children: A Tool to Study Maturation of Pharmacokinetics?
Saskia N. de Wildt, MD, PhD, FCP, Erasmus MC Sophia Children's Hospital

Microdosing in Children, Fundamental Concepts and Practical Considerations
Le Thuy Vuong, MBA, PhD, Vitalea Science, Inc

Ethics of Non-Therapeutic Research in Children: Focus on Microdosing
John Lantos, MD, Children's Mercy Hospitals and Clinics

Upon completion of this Workshop, the participant should be able to:

- Review the technical and practical aspects of microdosing in children, as well as the potential use of microdosing to study ontogeny of drug disposition;
- Review the ethics of enrolling children in non-therapeutic research, with a focus on microdosing; and
- Discuss the challenges and potential uses of microdosing in pediatric drug development.

SATURDAY, MARCH 22, 2014

9:00 AM – 10:00 AM

LEON I. GOLDBERG YOUNG INVESTIGATOR AWARD LECTURE

Pharmacogene Regulatory Elements: From Discovery to Applications

Marquis A

UAN: 0708-9999-14-208-L01-P

Presenter: Kathleen M. Giacomini, PhD, University of California, San Francisco

Nadav Ahituv, PhD, University of California, San Francisco

Upon completion of this Award Lecture, the participant should be able to:

- Describe the importance of regulatory variants in pharmacogenomics; and
- Describe the prevention of adverse effects and the optimization of therapies for individual patients.

9:00 AM – 10:00 AM

ORAL SESSION

Innovation in Physiologically Based PK Applications

Marquis B

CHAIRS

Karen Rowland-Yeo, PhD, Simcyp Limited

Donald Heald, PhD, Johnson & Johnson PRD

OIII-1

Alternatives to Ketoconazole for Estimating the Fraction Metabolized of CYP3A Substrates.

Presenter: Alice Ban Ke, PhD, Eli Lilly and Company

OIII-2

Modeling Cerebrospinal Fluid and Plasma Exposure Profiles from Healthy Obese/Overweight Subjects Administered Lorcaserin Hydrochloride to Estimate Human Brain Exposure.

Presenter: Michael Morgan, PhD, Arena Pharmaceuticals, Inc.

OIII-3

A Semi-Physiological Population Pharmacokinetic/Pharmacodynamic Model for the Development of Bedside-Ready Dosing Algorithm for Clopidogrel.

Presenter: Snehal Samant, MS, University of Florida

OIII-4

Application of the FDA PBPK Knowledgebase in Evaluating Model Predictability for Drug-Drug Interactions.

Presenter: Yuzhuo Pan, MD, PhD, US Food and Drug Administration

10:15 AM – 11:45 AM

WORKSHOP

Pharmacological Considerations of Fetal Therapy

Marquis C

Scientific Section: Special Populations (SPO)

D D R U

CHAIR

Gideon Koren, MD, FRCPC, FACMT, The Hospital for Sick Children

SPEAKERS

Overview: Pharmacokinetics and Pharmacodynamics of the Maternal-Placental-Fetal Unit

Robert Ward, MD, FAAP, FCP, University of Utah School of Medicine

Maternal Drug Therapy: When the Fetus is the Patient!

Mark Mirochnick, MD, Boston University School of Medicine

D Discovery D Development R Regulation U Utilization

SATURDAY, MARCH 22, 2014

Ethics and Regulatory Aspects of Fetal Therapy: Unique Problems Facing Clinical Studies in Fetal Pharmacology
Gilbert J. Burckart, PharmD, US Food and Drug Administration

Upon completion of this Workshop, the participant should be able to:

- Identify and define the core pharmacokinetic (PK) and pharmacodynamic (PD) concepts for the treatment of the fetus;
- Describe the PK/PD and safety of drug treatment in pregnant women when the fetus is the patient and intended target; and
- Identify the ethical and regulatory challenges in the pharmacological treatment of the fetus.

10:15 AM – 11:45 AM

WORKSHOP
Registries and Databases in Clinical Research
Marquis D
Scientific Section: Drug Safety (SAF)

CHAIRS
Katarina Ilic, MD, PhD, MPH, Exelixis
Mitchell A. H. Levine, MD, MSc, FRCPC, FISPE, Center for Evaluation of Medicines

SPEAKERS
Registry Design, Data Collection and Quality Assurance
Katarina Ilic, MD, PhD, MPH, Exelixis

Cancer Registries in Clinical Research
Leah Sansbury, PhD, MSP, GlaxoSmithKline

Evaluating Registries
Judith Jones, MD, PhD, The Degge Group, Ltd.

Upon completion of this Workshop, the participant should be able to:

- Set up registries;
- Evaluate registries; and
- Combine data from different sources in order to predict or explain safety issues.

10:15 AM – 12:15 PM

SYMPOSIUM
Pharmacometabolomics: Biochemical Tools for Mapping Pathways Implicated in Drug Response Phenotypes
Marquis A
UAN: 0708-9999-14-219-L04-P
Scientific Section: Molecular Pharmacology and Pharmacogenetics (MOL)

CHAIRS
Rima Kaddurah-Daouk, PhD, Duke University Medical Center
Liewei Wang, MD, PhD, Mayo Clinic – Mayo Foundation

SPEAKERS
Pharmacometabolomics – Enabling Tools for Clinical Pharmacology, Drug Discovery and Drug Development
Rima Kaddurah-Daouk, PhD, Duke University Medical Center

Pharmacometabolomics of the SSRI Therapy of Major Depressive Disorder
Richard M. Weinshilboum, MD, Mayo Clinic Rochester

Pharmacometabolomics of Antiplatelet Therapies and Personalized Approaches to Antiplatelet Treatment
Amber Beitelshees, PharmD, MPH, University of Maryland

Identification of Panel of Blood Biomarkers in Rats for Prediction of Acute and Idiosyncratic Hepatotoxicity
Richard Beger, PhD, US Food and Drug Administration

SATURDAY, MARCH 22, 2014

Upon completion of this Symposium Session, the participant should be able to:

- Explain developments in pharmacometabolomics;
- Describe how to use enabling tools for studying the effects of drugs on metabolism to make it possible to map pathways implicated in mechanism of action of drugs and mechanisms involved in variation in response;
- Cite national and international initiatives in the creation of pharmacometabolomics as a new field that compliments pharmacogenomics and enables a systems pharmacology approach;
- Exemplify how pharmacometabolomics is being applied to define novel pathways implicated in mechanisms of action of antidepressants and drugs used in the prevention and treatment of cardiovascular disease; and
- Illustrate the potential impact of metabolomics on clinical pharmacology as well as the drug discovery and drug development processes.

10:15 AM – 12:15 PM

SYMPOSIUM

Quantitative and Systems Pharmacology Approaches for the Development of Oncology Drugs

Marquis B

UAN: 0708-9999-14-220-L04-P

Scientific Section: Pharmacometrics and Pharmacokinetics (PMK)

D D R U

CHAIRS

Jay Mettetal, PhD, AstraZeneca
Karen Rowland-Yeo, PhD, Simcyp Limited

SPEAKERS

Application of Physiologically Based Pharmacokinetic Modeling to the Development of Oncology Drugs
Karen Rowland-Yeo, PhD, Simcyp Limited

Multiscale Mechanistic Modeling for Development of Liposomal Formulations in Oncology
Bart Hendriks, PhD, Merrimack Pharmaceuticals

Bench to Bedside Translation of Antibody Drug Conjugates Using a Multiscale Mechanistic PK/PD Model
Dhaval Shah, PhD, State University of New York at Buffalo

Combined Evolutionary and Pharmacokinetic Modeling for Optimizing Erlotinib Dosing
Jasmine Foo, PhD, University of Minnesota

Upon completion of this Symposium Session, the participant should be able to:

- Demonstrate utility of quantitative and systems pharmacology in oncology where a deeper understanding of compound efficacy has been gained by linking pharmacokinetics with a mechanism-based model of patient and/or tumor physiology;
- Discuss the challenges associated with integrating multiple types of preclinical and clinical data into mechanistic models that allow translation to clinical decision making and understanding; and
- Describe recent advances in oncology which have been supported heavily by modeling and simulation.

D Discovery D Development R Regulation U Utilization

CAREER BOOTCAMP
SATURDAY, MARCH 22, 2014

HALF-DAY POST-CONFERENCE FOR TRAINEES & STUDENTS
M103/104/105

Bridgette L. Jones, MD
Education Committee Chair

Jun J. Yang, PhD
Education Committee Vice Chair

7:30 AM – 7:55 AM
CONTINENTAL BREAKFAST

7:55 AM – 8:00 AM
INTRODUCTION

8:00 AM – 8:30 AM
A FIVE YEAR PLAN TO JUMP START A CAREER IN ACADEMIA
Daniel K. Benjamin, Jr., MD, PhD, MPH, Duke University

This session will provide trainees and those who are early in their career instruction regarding how to develop a five-year strategy for starting a successful career. Topics covered will include: obtaining and maintaining funding, considerations regarding tenure/promotion, and how to develop and stay on track with career goals including how to choose high yield projects and how/when to skillfully say no.

8:30 AM – 9:00 AM
SUCCESSFUL INTERVIEWING FOR INDUSTRY
Steve Ryder, MD, Alexion Pharmaceuticals

This session will cover how to showcase your skills (technical, research, general talents) and ambitions when applying for a position. It will also discuss types of positions available (small vs. large pharma, biotech vs. pharma).

9:00 AM – 9:45 AM
CAREER OPPORTUNITIES AT THE FDA
Yeruk "Lily" Mulugeta, PharmD, US Food and Drug Administration, and Dionna Jeter Green, MD, US Food and Drug Administration

This session will describe potential career opportunities at the FDA from the perspective of a pharmacy/PharmD background and from an MD background. The session will focus on entry-level opportunities at the FDA and how to move up within the system.

9:45 AM – 10:00 AM
BREAK

10:00 AM – 10:45 AM
NEGOTIATING A STARTUP PACKAGE
D. Craig Brater, MD, Indiana University School of Medicine, and Kathryn Momary, PharmD, BCPS, Mercer University

This session will provide trainees and those who are early in their career instruction regarding negotiating salary, lab/office space, faculty development and educational support, as well as other support infrastructure to ensure a successful start to a career. The session will provide perspectives both from a junior/mid-career faculty person and upper administration.

10:45 AM – 11:30 AM
GRANTS 101/NON-NIH FUNDING
Kathleen M. Giacomini, PhD, University of California, San Francisco

This session will cover the basic components of every grant application and will briefly discuss non-NIH extramural funding.

CAREER BOOTCAMP SATURDAY, MARCH 22, 2014

11:30 AM – 12:15 PM

MEET THE NIH

Richard Okita, PhD, National Institute of General Medical Sciences

This session will provide insights from NIH staff to discuss award mechanisms through NIH (K awards, R awards, early investigator status), organization structure, what do the acronyms mean, and how to navigate through the system (communication with the Program Officer).

12:15 PM – 12:30 PM

LUNCH

12:30 PM – 1:45 PM

ASK THE EXPERTS PANEL DISCUSSION: GETTING REAL ANSWERS FOR YOUR MOST DIFFICULT QUESTIONS

Moderated by Gregory L. Kearns, PharmD, PhD, Chief Scientific Officer and Chairman Children's Mercy Hospitals and Clinics Professor of Pediatrics and Pharmacology, University of Missouri, Kansas City and Kathleen A. Neville, MD, MS, Children's Mercy Hospitals and Clinics

Includes all of the Career Bootcamp Speakers

This panel discussion will more fully elaborate on topics covered in the previous sessions and will allow the speakers to specifically address the needs of the attendees. This session will be an interactive discussion between attendees and panelists and will allow the attendees to have all of their "real world" questions answered by the experts.

1:45 PM – 2:00 PM

QUESTIONS

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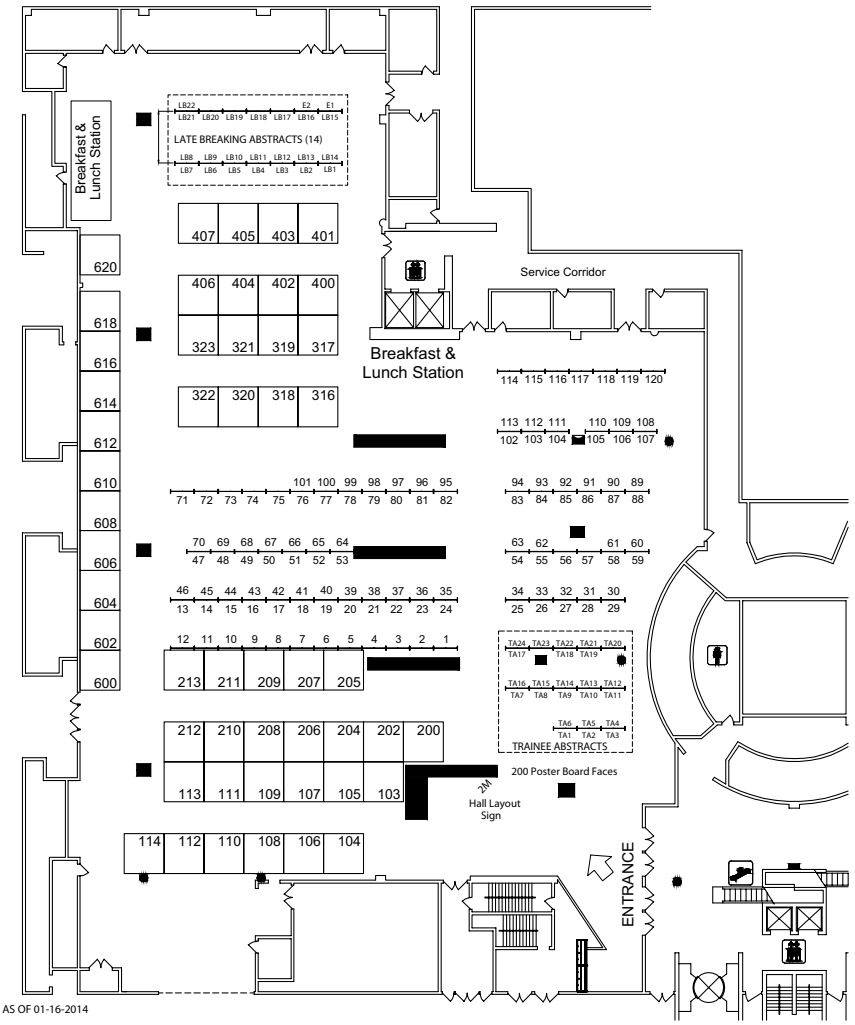

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618	CRCHUM (Centre de recherche du Centre hospitalier de l'Université de Montréal)
620	Wake Research Associates

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ACCEL RESEARCH SITES
860 Peachwood Dr.
Deland, FL 32720
www.accelresearch.com

Avail Clinical Research, an Accel Research Site renovated to a larger 18,500 sq. ft., 50 bed facility with a 270 on-site laboratory. Our expanded site continues to provide stellar clinical services for Phase I – IV trials and Vaccines. Our facility supports healthy volunteer study and multiple therapeutic areas for special populations.

614
AMERICAN COLLEGE OF CLINICAL PHARMACOLOGY
PO Box 1637
Rockville, MD 20849
www.accp1.org

American College of Clinical Pharmacology (ACCP) is a non-profit membership association with a 40+ year history of providing exceptional interdisciplinary, accredited Continuing Education programs, publications, networking and other career-enhancing opportunities to a wide spectrum of healthcare professionals using clinical pharmacology in disciplines from research to patient care.

604
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AnovaFill provides cGMP contract sterile filling services of investigative new drugs, biologics, and commercial injectable pharmaceuticals. Capabilities to batch, sterilize, fill, label, and package. We specialize in small batch clinical and commercial runs. AnovaFill is a part of Afton Scientific.

204
ARENSIA EXPLORATORY MEDICINE
Moskauer Str. 25
Duesseldorf, 40227
Germany
www.arensia-em.com

ARENSIA EXPLORATORY MEDICINE is a private research organization with German ownership, specialized in conducting Phase I/II and PROOF OF CONCEPT studies in various PATIENT populations. ARENSIA's corporate office is located in Dusseldorf, Germany. Phase I units are based in large university hospitals in Bucharest, Romania, Chisinau, Moldova and Vilnius, Lithuania. We serve the following therapeutic areas: immuno-inflammatory, cardiovascular, diabetes/metabolic, respiratory, hepatology, nephrology, gastroenterology, infectious diseases HCV/HIV, urology, oncology, dermatology, neurology, psychiatry. ARENSIA's unique strengths are: 1. The ability to perform highly complex Phase I/II PATIENT studies, in our Phase I units (intensive PK/PD schedules, long hospitalization, imaging, etc.) 2. Extraordinary fast recruitment speed (incl. treatment/biological naïve patients).

606
ASPIRE IRB
11491 Woodside Avenue
Santee, CA 92071
www.aspire-irb.com

Aspire IRB is committed to Protecting People and Empowering Research. We are Focused on Accuracy, Driven by Integrity, and the Difference is Service. Aspire's Simple Automated Portal, ASAP, is very intuitive, easy to navigate, and powerful in its search, save, and print functions.

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BIOPHARMA SERVICES INC.
4000 Weston Road
Toronto, ON M9L3A2
Canada
www.biopharmaservices.ca

BioPharma Services Inc. is a physician-owned, US FDA-inspected Phase I CRO, with a 174 bed clinical facility and onsite bioanalytical laboratory in Toronto, Canada, and access to >18,000 healthy volunteers, patients and special populations such as renally impaired patients.

318
BIOTRIAL
7-9 Rue Jean-Louis Bertrand
35000
Rennes, EC4Y 0HP
France
www.biotrial.com

Founded in 1989, Biotrial is a leading CRO specialized in Early Development with a wide range of services from Non-Clinical Pharmacology, Phase I studies, Phase II-IV Trial Management, Bioanalysis, Oncology, Data Management, Biostatistics, ECG & Imaging Core Lab (QT/QTc Trials, Psychometric Testing, Imaging, EEG/PSG Assessment), Regulatory Affairs to Medical Writing. Based in France, Belgium, the United Kingdom, Canada and the United States, Biotrial performs hundreds of studies a year and offers tailor-made solutions to Biotech and Pharmaceutical companies. Recent developments in Biotrial's growth include the strengthening of CNS services, the addition of an in-house Bioanalytical Lab as well as the opening of the US Phase I Unit.

106
CE3 INC.
246 Goose Lane Suite 202
Guilford, CT 06437
www.ce3inc.com

Ce3 is a full service contract research organization focused on providing biotechnology companies with Early Phase clinical trial execution and regulatory submission services. Our seasoned staff works across a broad range of therapeutic areas, with particular expertise in oncology and infectious disease indications. CE3 stands for Collaborative, Experience, Efficiency & Excellence which are qualities that represent our core values and serve as the foundation for all that we do. Clients benefit from our flexibility, process efficiency, value pricing, and our collaborative relationships with state-of-the-art niche providers; a competitive edge that amplifies value in this highly regulated environment.

208
CNS NETWORK, INC.
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CNS has extensive experience performing Phase I-IV trials in special patient populations and Healthy Volunteers. In addition to a dedicated Phase I Clinical Pharmacology Unit in Long Beach, CA – CNS runs a licensed psychiatric unit and four outpatient locations.

618
CRCHUM (CENTRE DE RECHERCHE DU CENTRE HOSPITALIER DE L'UNIVERSITÉ DE MONTRÉAL)
3850, Saint-Urbain Pavillon
Jeanne-Mance, 7-322
Montreal, QC H2W 1T7
Canada
www.chumtl.qc.ca/crchum.fr.html

The University of Montreal Hospital Research Centre (CRCHUM) is the research arm of the University of Montreal Hospitals. Its 6,500 m^2 facilities include a fully equipped

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Phase I and II unit of 15 beds. Home to more than 360 researchers and 450 graduate students, its research activities are carried out in an integrated continuum of basic science, clinical studies and population health research. It has Quebec's largest Centre in cancer treatment, neuroscience clinics, solid organ treatment with expertise in diabetes and cardiovascular disorders.

202
CRS CLINICAL RESEARCH SERVICES
Lohmannstrasse 3
Andernach 56626
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CRS offers full-service in phases I - IV to pharma and biotech industries worldwide conducting the complete range from FIM to POC trials plus trial specialities like TQT, skin safety, respiratory research, renal/hepatic insufficiency and women's and men's health.

213
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621 Rose Street
Lincoln, NE 68502
www.celerion.com

Celerion is the premier provider of innovative early stage clinical research solutions. A full spectrum of resources is available for Phase I and IIa proof-of-concept studies. With six locations and over 750 beds, our experience and expertise is applied to provide solutions to pharmaceutical, biotechnology and generic clients.

407
CERTERA
Blades Enterprise Center
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United Kingdom
www.certera.com

Certara is dedicated to improving human health by offering a broad spectrum of software products and services from early drug discovery through clinical drug development, with special focus on model based approaches to drug development. Formed from the blending of Tripos, Pharsight, and Simcyp, to bring together world-class scientific consulting services and software, Certara provides unique expertise in modeling, analysis, and simulation methods including molecular modeling, PK/PD modeling and simulation, PBPK modeling and simulation, prediction of drug-drug interactions, and clinical trial simulation, to accelerate decision making and enable the cross-disciplinary approaches necessary for translational science.

108
CLINICAL PHARMACOLOGY OF MIAMI, INC.
550 West 84 Street
Hialeah, FL 33014
www.clinpharmmiami.com

Clinical Pharmacology of Miami, Inc. (CPMI) is a private and independent pharmaceutical research organization dedicated to the development and implementation of clinical trials (Phase I-IV) in the South Florida Miami metropolitan area. This unit was opened in December 2007. Clinical Pharmacology of Miami, Inc. (CPMI) is a Florida Corporation founded by three principals: Stacy C Dilzer, RN, BSN (President), Kenneth C Lasseter, MD (Vice President & Medical Director) and E Cooper Shamblen (Chief Executive Officer). They have all worked together in

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academia and previous clinical research units as well as part of a large multinational research group, and now as the principals of our experienced management team of CPMI. Dr. Lasseter is certified by the American Board of Clinical Pharmacology but also had residency training and is board qualified in cardiology. His career started on the faculty of the University of Miami School of Medicine where he developed a clinical pharmacology research unit and was joined by E. Cooper Shamblen. In 1977 they founded a clinical pharmacology research unit in the private sector and became one of the first such units in the now burgeoning CRO industry. Stacy Dilzer, RN, BSN, joined them and became the operational head of that organization.

200
CLINILABS, INC.
423 West 55th Street 4th Floor
New York, NY 10019
www.clinilabs.com

Clinilabs is a full-service contract research organization (CRO) that provides early-phase and specialty clinical drug development services. Clinilabs is recognized globally as a leading speciality CRO, and has made important contributions to twelve successful new drug applications.

616
COMPASS RESEARCH, LLC
100 W. Gore St. 2nd floor
Orlando, FL 32806
www.compassresearch.com

Compass Research is a Phase I-IV clinical trials site in Orlando, FL. Compass has 78 total beds, including a 10-bed intensive treatment room. Compass focuses on delivering high-quality data in specialty patient populations, including Alzheimer's disease, Parkinson's disease, hepatic, renal, healthy elderly, chemical dependent, and psychiatry. Compass is known for its proven capabilities in lumbar punctures and continuous CSF sampling.

107
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825 South 8th Street Suite 300
Minneapolis, MN 55404
www.davitaclinicalresearch.com

DCR is committed to advancing the knowledge and practice of kidney care. Through our experience and pursuit of innovation, we continue to lead the charge. Our extensive array of patients, data points, and clinics is unparalleled. We remain focused on our services and uphold our duty as premier specialists in the field.

323
DUKE CLINICAL RESEARCH INSTITUTE
300 W. Morgan Street Suite 800
Durham, NC 27701
www.dcri.org

The Duke Clinical Research Institute's early phase unit, the Duke Clinical Research Unit, combines the clinical expertise and scientific leadership of one of the most prestigious university medical centers with the operational capabilities of a full-service contract research organization.

206
EUROFINS OPTIMED
1, rue des Essarts
Gieres, 38610
France
www.optimed.fr
Eurofins.com

Since 1990, Eurofins OPTIMED has been providing services in clinical research and biometry, from Phase I to Phase II-IV clinical trials and clinical studies in Nutrition and Medical Devices. Eurofins Optimed operates two ClinPharm Units, in Grenoble and Lyon and offers a partnership with several sites in Eastern European countries and in the US. With the experience of more than 800 clinical studies, Eurofins Optimed is a reliable partner for pharmaceutical and biotechnology companies and the agro-food industry.

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113
ICON DEVELOPMENT SERVICES
7740 Milestone Parkway, Suite 150
Hanover, MD 21076
www.iconclinical.com
ICON is a global provider of outsourced development services to the pharmaceutical, biotechnology and medical device industries, specializing in the strategic development, management and analysis of programs that support clinical development from compound selection to Phase I-IV. ICON currently has approximately 10,170 employees, operating from 78 locations in 37 countries.

317
IDEM TRANSLATIONS INC.
550 S. California Ave. Suite 310
Palo Alto, CA 94306
www.idemtranslations.com

Idem, your trusted translation partner for 30 years, supporting certified medical translation neeeds from clinical trial stages to product launch and manintenance. Idem's ISO9001/13485 and EN15038 certified quality system focuses on the unique requirements of the life sciences industry ensuring consistant quality translation.

316
INC RESEARCH
Riverview The Meadows
Business Park
Surrey, Camberley G417 9AB
United Kingdom
www.incresearch.com

INC Research is a full-service CRO, delivering Phase I-IV clinical research programs to schedule and budget worldwide. We do this by incorporating our proprietary therapeutic and operational expertise into everything we do.

406
INSTEM CLINICAL
91 Peterborough Rd.
London, SW6 3BU
United Kingdom
www.instemclinical.co.uk

The ALPHADAS® software solution suite is a proactive, eSource clinical trials system that is mobile, schedule-driven, and provides real-time bedside or station based direct data capture that virtually eliminates paper-based data. It accelerates data throughput, and enhances data integrity.

401
INVENTIV HEALTH CLINICAL
504 Carnegie Center
Princeton, NJ 08540
www.inventivhealthclinical.com

inVentiv Health Clinical is a leading provider of global drug development services to pharmaceutical, biotechnology, generic drug, and medical device companies, offering therapeutically specialized capabilities for Phase I-IV clinical development, bioanalytical services, and strategic resourcing from a single clinical professional to an entire functional team. With 6,500 passionate employees operating in 70 countries, inVentiv Health Clinical works to accelerate high quality drug development programs of all sizes around the world.

109
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Shawnee, KS 66216
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For the past 35 years we have provided our clients with a full range of high-quality bioanalytical services for small molecule, large molecule PK and immunogenicity and biomarker analysis. We are capable of supporting your GLP and non-GLP preclinical and clinical programs – even global trials. If you would like to learn more about KCAS and the bioanalytical services we provide, please visit www.kcasbio.com.

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111
NEW ORLEANS CENTER FOR CLINICAL RESEARCH/ VOLUNTEER RESEARCH GROUP
1928 Alcoa Hwy Ste G50
Knoxville, TN 37920
www.noccr.com

NOCCR and VRG are privately owned multispecialty clinical research centers which together have conducted 2000+ clinical trials. Staffing includes full-time MDs, Nurse Practitioner, Nurse/Coordinators, EMTs, nursing assistants, with separate regulatory, data and recruiting departments. NOCCR-Knoxville is a fully equipped Phase I Unit with 50 beds and 24,500+ sq. ft. of space located within the University of Tennessee Medical Center. This Unit excels at FIH, procedurally complex trials and special populations. VRG and NOCCR New Orleans are focused on conducting later phase studies in a broad array of therapeutic areas.

205
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2525 Meridian Pkwy 280
Durham, NC 27713
www.nuventra.com

Nuventra is the pharmaceutical industry's go-to resource for clinical pharmacology, pharmacokinetic, and pharmacometric consulting services. We conduct all types of analyses from noncompartmental PK, PK/PD, TK, Population PK, Modeling & Simulation, and Model-based drug development. Nuventra gives pharmaceutical companies and CROs rare access to a hands-on team of industry-leading consultants experienced in complex studies and analyses. We make complex pharmacokinetic and pharmacometric principals understandable and usable for common sense drug development. Nuventra's flexible business structure enables us to integrate with our clients and help them maximize the potential of clinical pharmacology studies and pharmacokinetic analyses to pave the way toward marketing approval.

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OBS MEDICAL LIMITED
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Milton Park Abingdon
Oxon, OX14 4SD
United Kingdom
www.obsmedical.com

BioQT, the fully automated ECG analysis service for cardiac safety. OBS Medical, the provider of choice, for quality and performance where knowledge, time and cost are essential in today's challenging environment. Delivering cardiac safety with confidence.

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Suite 3500
Fort Lauderdale, FL 33309
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OmniComm is dedicated to helping pharmaceutical, biotechnology, CROs, device and research organizations maximize the value of clinical research investments through use of innovative technologies. Our Electronic Data Capture (EDC) and eClinical solutions have been utilized in over 3,800 trials worldwide.

321
OPTIVIA BIOTECHNOLOGY
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Optivia Biotechnology, Inc. is an award-winning and innovative contract research organization (CRO), offering drug transporter research services and solutions to biotechnology, pharmaceutical and academic organizations.

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110
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www.ocrc.net

OCRC is a cutting edge independent Phase I – IV custom-built 36,000 sq. ft. research site. Designed specifically for Phase I clinical trials, OCRC includes 110 in-house volunteer beds, dual lead digital telemetry, CCTV security system, and cardkey access.

114
PRA
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As a leading CRO, PRA is transforming clinical trials through our people, innovation and transparency. We combine therapeutic and operational expertise with local knowledge to serve clients across all phases of drug development. PRA's dynamic services and forward-thinking approach are making a difference to healthcare patients worldwide.

402
PHASE ONE SOLUTIONS
1405 NW 167 Street
Miami Gardens, FL 33169
www.phase1solutions.com

Phase One Solutions is a privately owned Clinical Research Organization focused on providing quality Phase 1 through Phase 4 services. Our dedicated research unit is located in Miami Gardens, Florida. Our facility is 25,000 square feet and has 140 dormitory style beds.

612
PRISM RESEARCH
1000 Westgate Drive Suite 149
Saint Paul, MN 55114
www.prismresearchinc.com

Prism Research is a 52-bed inpatient facility in the center of the Minneapolis/St. Paul metro area. Prism Research specializes in first-in-man and patient-based inpatient trials.

608
PROFIL INSTITUTE FOR CLINICAL RESEARCH, INC.
855 3rd Avenue Suite 4400
Chula Vista, CA 91911
www.profilinstitute.com

Profil Institute for Clinical Research has expertise in design and conduct of early phase clinical studies for therapies and devices in diabetes, and other metabolic disorders. We handle first dose in human, glucose clamp, PK and PD projects.

319
QPS
3 Innovation Way Suite 240
Newark, DE 19711
www.qps.com

QPS is a GCP/GLP – CRO that supports discovery, preclinical, and clinical drug development. Our regional laboratories and/or clinics are located in Newark, DE, USA; Springfield, MO, USA; Miami, FL, USA; Groningen, The Netherlands; Graz, Austria; Hyderabad, India; and Taipei, Taiwan.

212
SGS LIFE SCIENCE SERVICES
820 West Diamond Avenue #100
Gaithersburg, MD 20878
www.sgs.com

SGS is a leading contract service organization providing clinical research, quality control and biopharmaceutical characterization services. SGS provides Phase I-IV clinical trial management and services encompassing clinical pharmacology studies, bioanalytical services, data management, regulatory and drug safety consultancy. Our quality control services consist of analytical chemistry, microbiology, stability and protein analysis. SGS Life Science Services is a truly global organization with approximately 1,500 employees, located in 28 facilities, in 15 countries.

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Lancaster, CA 93534
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Simulations Plus gold-standard simulation & modeling software is used worldwide in drug discovery and development – GastroPlus™, DDDPlus™, MembranePlus™, ADMET Predictor™, MedChem Studio™ & MedChem Designer™ – for simulation of oral absorption/PK/PD/PBPK, *in vitro* dissolution & permeability experiments, and accurate ADMET property prediction, fast ADMET/QSAR model-building and classification of molecules.

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SPAULDING CLINICAL RESEARCH
525 S. Silverbrook Drive
West Bend, WI 53095
www.spauldingclinical.com

Spaulding Clinical Research, LLC provides Clinical Pharmacology, Cardiac Safety Core Lab clinical research services, and is a medical device manufacturer. Spaulding Clinical operates a paperless, 155-bed clinical pharmacology unit with 96-beds of telemetry in West Bend, Wisconsin.

209
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10103 Metcalf Avenue
Overland Park, KS 66212
www.vinceandassociates.com

Our state-of-the-art 90 bed early development unit combines the ultimate in subject safety and luxury while positively impacting subject recruitment and retention. Vince and Associates Clinical Research has been providing clinical research services to the global biopharmaceutical industry for over a decade. We have become one of the premier US clinical research sites by utilizing the Physician Research Model® of operation where study teams are led by highly experienced Principal Investigators intricately involved in all aspects of the clinical trial process. Our quality is demonstrated through our FDA audit record of no 483 findings in over 10 years of operation and over 70 sponsor audits.

620
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3100 Duraleigh Road Suite 304
Raleigh, NC 27612
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Located in Raleigh, Wake Research is North Carolina's premier clinical research site, featuring a 34-bed Phase I unit, and focusing on special patient population studies. Expertise includes Dermatology, GI, Vaccines, CNS & Pain, Obesity, and Metabolic disorders including Diabetes.

600
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5630 Cerritos Avenue
Cypress, CA 90630
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WCCT Global is a multi-site, full service global Contract Research Organization (CRO) of outsourced early drug development and late phase services to the pharmaceutical, biotechnology and medical device industries.

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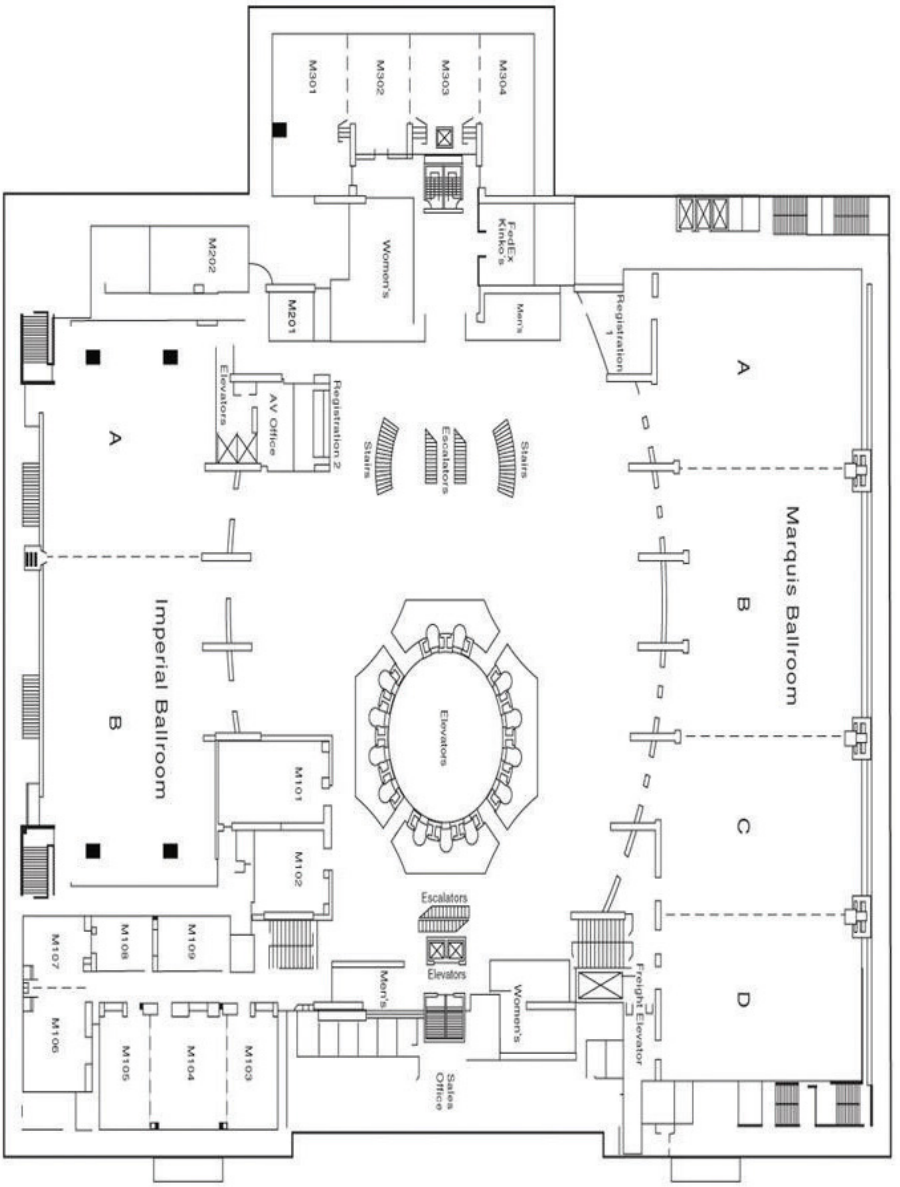


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POSTER SESSION I
THURSDAY, MARCH 20, 2014

International Hall 7:30 am – 2:00 pm • Attended Posters 7:30 am – 9:00 am

Biomarkers and Imaging (BIO)

PI-001
C-REACTIVE PROTEIN ANTISENSE SELECTIVELY AND POTENTLY INHIBITS CRP INCREASE FOLLOWING ENDOTOXIN CHALLENGE IN HUMANS.
R. J. Noveck; Duke University School of Medicine, Durham, NC.

PI-002
UTILITY OF HAIR AS A BIOMARKER OF SYSTEMIC DEPOSITION TO POLYBROMINATED DIPHENYL ETHERS (PBDES) IN A RAT MODEL.
S. Poon,[1] K. Aleksa,[1] D. Rawn,[2] A. Carnevale,[1] D. Pirrello,[1] D. Gaertner,[2] M. Wade,[3] S. Ernest,[4] G. Koren,[1] B. Hales[4]; [1]Hospital for Sick Children, Toronto, ON, Canada, [2]Food Research Directorate, Health Canada, Ottawa, ON, Canada, [3]Environmental Health Science & Research Bureau, Health Canada, Ottawa, ON, Canada, [4]McGill University, Montreal, QC, Canada.

Drug Development and Regulatory Sciences (DDR)

PI-003
PHASE I DOSE-ESCALATION AND DRUG INTERACTION STUDY OF ABT-888 (PARP1 INHIBITOR) AND TOPOTECAN (TOPOISOMERASE I INHIBITOR) IN PATIENTS WITH ADVANCED CANCER.
F. Boakye-Agyeman,[1] J. Reid,[1] M. Menefee,[2] S. Buhrow,[1] C. Walden,[1] J. Piens,[1] O. Kayode,[2] C. Erlichman,[1] P. Haluska,[1] D. W. Northfelt,[3] S. H. Kaufmann,[1] M. Ames,[1] D. V. Satele,[1] H. Tang,[1] P. P. Peethambaram,[1] A. H. Chen,[2] L. Hartmann,[1] H. J. Long[1]; [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Jacksonville, FL, [3]Mayo Clinic, Scottsdale, AZ.

PI-004
EVALUATION OF THE EFFECTS OF SEQUENTIAL MULTIPLE-DOSE REGIMENS OF LEVOMILNACIPRAN ER ON CARDIAC REPOLARIZATION IN HEALTHY SUBJECTS.
L. Chen, C. Chen, T. J. Carrothers, W. M. Greenberg, A. Periclou, P. Ghahramani; Forest Research Institute, Jersey City, NJ.

PI-005
CARDIOVASCULAR SAFETY PREDICTION FOR EARLY DRUG DEVELOPMENT: A META-ANALYTICAL COMPARISON OF MODELING METHODS.
D. J. Conrado, D. Chen, W. S. Denney; Pfizer, Cambridge, MA.

PI-006
LITHIUM TREATMENT AND RISK FOR DEMENTIA AMONG PATIENTS WITH BIPOLAR DISORDER.
T. Gerhard,[1] D. P. Devanand,[2] C. Huang,[1] S. Crystal,[1] M. Olfson[2]; [1]Rutgers University, New Brunswick, NJ, [2]Columbia University, New York, NY.

PI-007
EVALUATING THE EFFECT OF SUBJECT DEMOGRAPHICS ON RIVAROXABAN EXPOSURE USING PBPK MODELING.
V. Hsu, J. Grillo, Y. Pan, P. Zhao, J. Bullock; US Food and Drug Administration, Silver Spring, MD.

PI-008
DAPAGLIFLOZIN, A SELECTIVE SGLT2 INHIBITOR, IMPROVED GLYCEMIC CONTROL OVER 2 WEEKS IN PATIENTS WITH TYPE 1 DIABETES MELLITUS.
S. Kasichayanula, S. C. Griffen, A. Chalamandaris, F. LaCreta, D. W. Boulton; Bristol-Myers Squibb, Princeton, NJ.

PI-009
PHARMACOKINETIC AND PHARMACODYNAMIC ASSESSMENTS FOR HORMONAL CONTRACEPTIVE DRUG-DRUG INTERACTIONS.
N. Kim, L. Li, M. Kim, D. Davis, S.-M. Huang, L. Zhang, P. Zhao, L. Soule, G. Willett, **C. Yu;** US Food and Drug Administration, Silver Spring, MD.

PI-010
AMOUNT OF RADIOACTIVITY & ESTIMATED EFFECTIVE DOSE EQUIVALENTS FOR RESEARCH SUBJECTS GIVEN 14C/3H DRUGS IN ABSORPTION, METABOLISM & EXCRETION STUDIES.
R. G. Kochan, L. A. Joas, R. J. Hammes, E. Smith, S. D. Flach, C. L.

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Hale, D. A. Mandarino, I. R. Mirkin, N. M. Siebers, L. Leonard, D. C. Bronson; Covance Clinical Pharmacology Services, Madison, WI.

PI-011
EVALUATION OF DRUG-DRUG INTERACTION BETWEEN THE NOVEL cPLA2 INHIBITOR AK106-001616 AND METHOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS.
T. Kozaki,[1] M. Tagashira,[1] K. Yamanishi,[2] Y. Osawa,[3] B. Ellis,[2] T. Kayanoki,[2] R. Ooishi,[2] K. Sugiyama,[2] K. Tsuruta,[3] T. Kohira,[2] K. Tsurui[1]; 1Asahi Kasei Pharma Corporation, Izunokuni-shi, Japan, [2]Asahi Kasei Pharma Corporation, Tokyo, Japan, [3]Asahi Kasei Pharma America Corporation, Waltham, MA.

PI-012
HYDROXYNORENDOXIFEN, AN ACTIVE TAMOXIFEN METABOLITE, POSSESSES DUAL AROMATASE INHIBITORY AND ESTROGEN RECEPTOR MODULATORY ACTIVITIES.
J. Liu,[1] D. Lu,[1] J. Lu,[1] W. Lv,[2] M. Cushman,[2] Z. Desta,[1] D. A. Flockhart[1]; [1]Division of Clinical Pharmacology, IUSM, Indianapolis, IN, [2]College of Pharmacy, Purdue University, West Lafayette, IN.

PI-013
PHARMACOKINETIC COMPARISON OF AMLODIPINE ADIPATE VALSARTAN FIXED DOSE COMBINATION WITH AMLODIPINE BESYLATE VALSARTAN COMBINATION IN HEALTHY VOLUNTEERS.
J. Nam,[1] M. Oh,[1] H. Kim,[2] S. Han,[2] E. Kim,[2] G. Song,[2] E. Kim,[3] J. Shin,[3] J. Ghim,[3] H. Kim[3]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Busan, Republic of Korea, [2]Pharmaceutical BU, CJ Cheiljedang Corp., Seoul, Republic of Korea, [3]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Republic of Korea.

PI-014
AN IMPLEMENTATION OF CDISC STANDARDS FOR NON-STANDARDS PHARMACODYNAMIC DATA ON CDISC SDTM.
J. Nam,[1] M. Oh,[1] J. Shin[2]; [1]Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Republic of Korea, [2]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Republic of Korea.

PI-015
QUANTITATIVE STRUCTURE-PHARMACOKINETIC/PHARMACODYNAMIC (PK/PD) PROPERTIES-RELATIONSHIPS (QSPR) FOR NEUROMUSCULAR BLOCKERS (NMB).
G. Gottipati, J. Venitz; Virginia Commonwealth University, Richmond, VA.

PI-016
MODEL-BASED META-ANALYSIS (MBMA) OF ADVERSE EVENTS (AE) AND DROPOUTS (DO) FOR DRUGS EVALUATED FOR THE TREATMENT OF FIBROMYALGIA PAIN (FMP).
G. Gottipati,[1] C. Lin,[2] J. Venitz,[1] L. J. Lesko,[3] G. An[3]; [1]Virginia Commonwealth University, Richmond, VA, [2]Department of Clinical Pharmacology and Pharmacometrics, Abbvie, Chicago, IL, [3]Center for Pharmacometrics and Systems Pharmacology, University of Florida at Lake Nona, Orlando, FL.

Drug Safety (SAF)

PI-017
EFFECT OF DICLOFENAC ON URINARY CONCENTRATION AND EXCRETION OF REBAMIPIDE.
D. L. Cooper, P. C. Panus, **S. Harirforoosh;** East Tennessee State University, Johnson City, TN.

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PI-018
BETWEEN A ROCK AND A HARD PLACE; LIFE THREATENING ECHIS COLORATUS ENVENOMATION -EVIDENCE BASED USE OF ANTIVENOM.
T. Leibson,[1] A. Broides,[2] M. Lifshitz,[2] G. Koren[1]; [1]Hospital for Sick Children, Toronto, ON, Canada, [2]Soroka University Medical Center, Beer Sheva, Israel.

PI-019
THE SECOND GENERATION ANTISENSE OLIGONUCLEOTIDE (ASO) MIPOMERSEN DOES NOT PROLONG QT INTERVAL IN A THOROUGH QT/QTC STUDY IN HEALTHY SUBJECTS.
Z. Li,[1] R. Yu,[2] M. Hard,[1] R. Mittleman,[1] W. Chin,[1] A. Mahmood,[1] J. Middleton,[1] R. Geary,[2] W. Singleton,[2] J. Grundy[2]; [1]Sanofi, Cambridge, MA, [2]ISIS Pharmaceuticals, Carlsbad, CA.

Infectious Diseases (INF)

PI-020
STEADY-STATE DISPOSITION OF THE SECOND GENERATION HEPATITIS C NS3/NS4 PROTEASE INHIBITOR, FALDAPREVIR.
L. Chen,[1] P. Rose,[2] Y. Mao,[1] C. Yong,[1] R. St. George,[1] F. Huang,[1] B. Latli,[1] D. Mandarino,[3] Y. Li[1]; [1]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, [2]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany, [3]Covance Clinical Research Unit Inc., Madison, WI.

PI-021
POPULATION PHARMACOKINETICS AND PHARMACODYNAMICS OF CEFEPIME IN HOSPITALIZED OBESE AND NON-OBESE PATIENTS.
E. Chung,[1] S. Cheatham,[2] M. R. Fleming,[3] D. P. Healy,[4] M. B. Kays[1]; [1]Purdue University, College of Pharmacy, Indianapolis, IN, [2]St. Francis Hospital, Indianapolis, IN, [3]Methodist Dallas Medical Center, Dallas, TX, [4]University of Cincinnati, The James L. Winkle College of Pharmacy, Cincinnati, OH.

PI-022
PHARMACOKINETICS OF FALDAPREVIR FOLLOWING MULTIPLE ORAL RISING DOSES IN HEALTHY VOLUNTEERS AND SUBJECTS WITH GILBERT'S SYNDROME.
M. Elgadi,[1] C. Yong,[2] J. Wruck,[2] C. Cooper,[3] **F. Huang,**[2] J. Stern[2]; [1]Boehringer Ingelheim Canada Ltd/Ltee, Burlington, ON, Canada, [2]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, [3]University of Ottawa, Ottawa, ON, Canada.

PI-023
VANCOMYCIN AUC24H/MIC DOES NOT PREDICT CLINICAL OUTCOMES IN CHILDREN WITH MRSA BACTEREMIA.
A. Hahn, R. W. Frenck, Jr., M. A. Staat, A. A. Vinks; Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

Molecular Pharmacology and Pharmacogenetics (MOL)

PI-024
GENETIC VARIATION IN THE α1A-ADRENERGIC RECEPTOR AND VASCULAR RESPONSE TO AGONIST.
A. Adefurin, L. V. Ghimire, U. Kohli, M. Muszkat, G. G. Sofowora, C. Li, S. Y. Paranjape, M. Stein, D. Kurnik; Vanderbilt University Medical Center, Nashville, TN.

PI-025
A NOVEL DEFECT CYP3A4 GENOTYPE IDENTIFIED IN A KIDNEY TRANSPLANT PATIENT WITH SEVERELY DIMINISHED TACROLIMUS CLEARANCE.
I. Cascorbi,[1] A. N. Werk,[1] S. Lefeldt,[2] H. Bruckmueller,[1] G. Hemmrich-Stanisak,[1] A. Franke,[1] M. Roos,[2] C. Küchle,[2] D. Steubl,[2] C. Schmaderer,[2] U. Heemann,[2] L. Renders[2]; [1]University of Kiel, Kiel, Germany, [2]Technical University of Munich, Munich, Germany.

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PI-026

METHYLATION PHARMACOGENOMICS: METHIONINE CYCLE ENZYME GENES, AHCY, CBS AND ADA, GENOTYPE-PHENOTYPE CORRELATIONS AND FUNCTIONAL GENOMICS.

Y. Chai,[1] Y. Ji,[1] G. D. Jenkins,[1] J. Zhang,[2] I. Moon,[1] L. Wang,[1] R. M. Weinshilboum[1]; [1]Mayo Clinic, Rochester, MN, [2]Jinan University, Guangzhou, China.

PI-027

ESTABLISHMENT OF CYP2D6 REFERENCE SAMPLES BY MULTIPLE VALIDATED GENOTYPING PLATFORMS.

H. Fang, X. Liu, J. Ramírez, N. Choudhury, H. Im, A. Konkashbaev, N. Cox, M. Ratain, Y. Nakamura, P. O'Donnell; University of Chicago, Chicago, IL.

PI-028

ATP2B1 LOCUS IS ASSOCIATED WITH RESISTANT HYPERTENSION IN THE INTERNATIONAL VERAPAMIL SR TANDOLAPRIL STUDY-GENETIC SUBSTUDY (INVEST-GENES).

V. Fontana,[1] C. W. McDonough,[2] Y. Gong,[2] N. M. El Rouby,[2] A. C. Sá,[2] C. J. Pepine,[2] R. M. Cooper-DeHoff,[2] J. A. Johnson[2]; [1]University of Campinas, Campinas, Brazil, [2]University of Florida, Gainesville, FL.

PI-029

IMPLEMENTATION OF PHARMACO-GENETICS IN EARLY STAGE CLINICAL TRIALS: AN EMERGING TREND FOR ACCELERATED CHARACTERIZATION OF NEW ENTITIES.

M. Francis, C. Dussault, J. Massicotte, E. Sicard, M. Lefebvre; Algorithme Pharma, Laval, QC, Canada.

PI-030

IMPACT OF CYP2C19 POLYMORPHISM ON THE PHARMACOKINETICS OF TACROLIMUS WHEN CO-ADMINISTERED WITH VORICONAZOLE.

K. Furihata,[1] C. K. Imamura,[2] H. Kojima,[1] S. Kusayama,[1] K. Ogoe,[1] N. Hashimoto,[3] S. Okamoto,[3] Y. Tanigawara[2]; [1]Keikokai Medical Corporation, P-One Clinic, Hachioji, Japan, [2]Department of Clinical Pharmacokinetics and Pharmaco-dynamics, School of Medicine, Keio University, Tokyo, Japan, [3]Division of Hematology, Department of Internal Medicine, School of Medicine, Keio University, Tokyo, Japan.

PI-031

A NOVEL SIMPLE METHOD FOR DETERMINING CYP2D6 GENE COPY NUMBER AND IDENTIFYING ALLELE(S) WITH DUPLICATION/MULTIPLICATION.

I. S. Hamadeh,[1] T. Langaee,[1] A. Chapman,[2] S. Turner,[3] J. Gums,[1] J. A. Johnson[1]; [1]University of Florida, Gainesville, FL, [2]Emory University, Atlanta, GA, [3]Mayo Clinic, Rochester, MN.

PI-032

METABOLISM OF MEGESTROL ACETATE *IN VITRO* AND THE ROLE OF OXIDATIVE METABOLITES.

M. J. Seminerio, **L. House,** S. Mirkov, J. Ramirez, J. Sachleben, M. Isikbay, H. Singhal, G. Greene, D. Vander Griend, M. Ratain; University of Chicago, Chicago, IL.

PI-033

UGT1A POLYMORPHISMS AND SIMVASTATIN EFFICACY IN ROUTINE CLINICAL CARE.

O. F. Iwuchukwu,[1] Q. Feng,[1] W. Wei,[2] L. Jiang,[3] J. C. Denny,[2] D. M. Roden,[1] R. A. Wilke,[4] M. C. Stein[1]; [1]Division of Clinical Pharmacology, Vanderbilt University, Nashville, TN, [2]Department of Biomedical Informatics, Vanderbilt University, Nashville, TN, [3]Department of Molecular Physiology and Biophysics, Vanderbilt University, Nashville, TN, [4]Department of Internal Medicine, Sanford Healthcare, Fargo, ND.

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PI-034

CITALOPRAM AND ESCITALOPRAM PLASMA DRUG AND METABOLITE CONCENTRATIONS: GENOME-WIDE ASSOCIATIONS.

Y. Ji,[1] D. J. Schaid,[1] Z. Desta,[2] M. Kubo,[3] A. J. Batzler,[1] K. Snyder,[1] T. Mushiroda,[3] N. Kamatani,[3] E. Ogburn,[2] D. Hall-Flavin,[1] D. A. Flockhart,[2] Y. Nakamura,[4] D. A. Mrazek,[1] R. M. Weinshilboum[1]; [1]Mayo Clinic, Rochester, MN, [2]Indiana University, Indianapolis, IN, [3]RIKEN Center for Genomic Medicine, Yokohama, Japan, [4]Chicago University, Chicago, IL.

PI-035

GENETIC VARIANTS OF CYP4F2 EXHIBITING DECREASED ENZYME ACTIVITY IN THE METABOLISM OF ARACHIDONIC ACID AND THEIR POTENTIAL ROLES IN WARFARIN SENSITIVITY.

W. Kim,[1] S. Cho,[1] **H. Kim,**[1] K. Oh,[1] D. Kim,[1] S. Lee,[1] J. Shin[2]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Busan, Republic of Korea, [2]Department of Pharmacology and PharmacoGenomics Research Center, Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Republic of Korea.

PI-036

PROTEIN KINASE CK2 MEDIATED HSP90B PHOSPHORYLATION AS A NOVEL MECHANISM OF RIFAMPIN INDUCED MDR1 GENE EXPRESSION.

S. Kim,[1] M. Cho,[2] Y. Heo,[2] M. Hasanuzzaman,[2] M. Ryu,[2] N. Ha,[2] O. C. Erkin,[2] J. Shin[1]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Republic of Korea, [2]Department of Pharmacology and PharmacoGenomics Research Center, Busan, Republic of Korea.

PI-037

GENETIC FINDINGS AND COMPARATIVE ANALYSIS OF UDP-GLUCURONOSYLTRANSFERASE 2B15 POLYMORPHISMS IN A KOREAN POPULATION.

W. Kim,[1] M. Hwang,[1] H. Jeong,[1] **S. Lee,**[1] J. Shin[2]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Busan, Republic of Korea, [2]Department of Pharmacology and PharmacoGenomics Research Center, Department of Clinical Pharmacology, Inje University College of Medicine, Inje University Busan Paik Hospital, Busan, Republic of Korea.

PI-038

STATIN-SPECIFIC TRANSPORT BY MCT1 AND MCT4.

Y. Leung,[1] M. Papillon,[2] J. Turgeon,[1] V. Michaud[1]; [1]Université de Montréal/CRCHUM, Montreal, QC, Canada, [2]Université de Montréal, Montreal, QC, Canada.

PI-039

DECIPHERING ADME GENETIC DATA WITH AN AUTOMATED HAPLOTYPE APPROACH.

Y. Guo,[1] M. Farmen,[2] Y. Jin,[3] H. Lee,[2] M. Penny,[4] K. Hillgren,[1] S. Fossceco[2]; [1]Drug Disposition, Eli Lilly and Company, Indianapolis, IN, [2]Discovery and Development Statistics, Eli Lilly and Company, Indianapolis, IN, [3]Clinical Pharmacology, Eli Lilly and Company, Indianapolis, IN, [4]Tailored Therapeutics, Eli Lilly and Company, Indianapolis, IN.

PI-040

A SIMCYP MODELING APPROACH TO EVALUATE CYP3A5 PHARMACOGENETIC (PGX) EFFECTS ON PHARMACOKINETICS (PK) VARIABILITY.

Y. Guo,[1] J. Baker,[2] G. Dickinson,[1] L. Shen,[3] P. Turner,[1] Z. Wang,[4] K. Hillgren,[1] S. Hall1; [1]Drug Disposition, Eli Lilly and Company, Indianapolis, IN, [2]Clinical Diagnostic Laboratory, Eli Lilly and Company, Indianapolis, IN, [3]Advanced Analytics, Eli Lilly

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and Company, Indianapolis, IN, [4]Department of Pharmaceutical Chemistry, School of Pharmacy, the University of Kansas, Lawrence, KS.

PI-041

INTERSUBJECT VARIABILITY CYP2J2 ACTIVITY IN HUMAN HEART MICROSOMES.

J. Huguet,[1] F. Gaudette,[2] F. Bélanger,[2] V. Michaud,[1] J. Turgeon[1]; [1]University of Montreal, Montreal, QC, Canada, [2]CRCHUM, Montreal, QC, Canada.

PI-042

CYP450 MEDIATED METABOLISM IN EXTRA-HEPATIC TISSUES.

J. Huguet,[1] S. Sharma,[1] F. Gaudette,[2] F. Bélanger,[2] S. Fulton,[1] J. Turgeon,[1] V. Michaud[1]; [1]University of Montreal, Montreal, QC, Canada, [2]CRCHUM, Montreal, QC, Canada.

Oncology (ONC)

PI-043

NANOSOMAL PACLITAXEL LIPID SUSPENSION (NPLS) DEMONSTRATES HIGHER RESPONSE RATES COMPARED TO PACLITAXEL IN PATIENTS WITH METASTATIC BREAST CANCER (MBC).

A. Ahmad,[1] S. Sheikh,[1] A. Mehta,[2] R. Nagarkar,[3] S. Krishnan,[4] A. Majumdar,[5] K. Mukerjee,[6] J. K. Singh,[7] S. P. Shrivastav,[8] C. T. Satheesh,[9] T. Maksud,[10] S. Pawar,[11] S. Sonawane,[12] S. Kamath,[13] M. Sharma,[14] R. C. Rane,[15] I. Ahmad[1]; [1]Jina Pharmaceuticals, Libertyville, IL, [2]Central India Cancer Research Institute, Nagpur, India, [3]Curie Manavta Cancer Centre, Nashik, India, [4]Dr. Rai Memorial Medical Centre, Chennai, India, [5]IPGME & R and SSKM Hospital, Kolkatta, India, [6]Chittaranjan National cancer Institute, Kolkatta, India, [7]Mahavir Cancer Sansthan, Patna, India, [8]Lions Cancer Research Centre, Surat, India, [9]Sri Venkateswara Hospital, Bangalore, India, [10]Bharat Cancer Hospital & Research Institute, Surat, India, [11]Kolhapur Cancer Centre, Kolhapur, India, [12]Anandrishiji Hospital & Medical Research Centre, Ahmednagar, India, [13]Asha Cancer Center, Thane, India, [14]Lambda Ther. Research Ltd., Ahmedabad, India, [15]Intas Pharmaceuticals Ltd., Ahmedabad, India.

PI-044

POPULATION PHARMACOKINETIC/ PHARMACODYNAMIC MODELING OF TUMOR SHRINKAGE BY AXITINIB IN PATIENTS WITH RENAL CELL CARCINOMA.

Y. Chen, B. A. Houk, A. Ruiz, A. A. Bair, **Y. K. Pithavala;** Pfizer, San Diego, CA.

PI-045

EFFECT OF CYP3A PERPETRATORS ON IBRUTINIB EXPOSURE IN NORMAL HEALTHY SUBJECTS.

J. de Jong,[1] D. Skee,[1] J. Murphy,[1] J. Sukbuntherng,[2] P. Hellemans,[3] J. Smit,[3] R. de Vries,[3] J. Jiao,[1] E. Mannaert[3]; [1]Janssen Research and Development, Raritan, NJ, [2]Pharmacyclics, Inc., Sunnyvale, CA, [3]Janssen Research and Development, Beerse, Belgium.

PI-046

MODELING AND SIMULATIONS OF β-GLUCAN AFTER ADMINISTRATION OF PGG-GLUCAN ALONE OR IN COMBINATION WITH CETUXIMAB, WITH AND WITHOUT IRINOTECAN, IN COLORECTAL CANCER PATIENTS.

J. F. Marier,[1] A. L. Menard,[1] M. Beliveau,[1] M. A. Gargano,[2] R. Walsh,[2] M. L. Patchen[2]; [1]Pharsight Consulting Services, A Division of Certara, Montreal, QC, Canada, [2]Biothera, Eagan, MN.

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PI-047
PHARMACOKINETIC ANALYSIS OF β-GLUCAN FOLLOWING ADMINISTRATION OF PGG-GLUCAN, A NOVEL IMMUNOMODULATOR BEING DEVELOPED FOR THE TREATMENT OF NON-SMALL CELL LUNG CANCER.
J. F. Marier,[1] C. Jomphe,[1] M. Beliveau,[1] J. Lowe,[2] P. Mattson,[2] R. Walsh,[2] M. L. Patchen[2]; [1]Pharsight Consulting Services, A Division of Certara, Montreal, QC, Canada, [2]Biothera, Eagan, MN.

Organ Specific Diseases (OSD)

PI-048
FENOFIBRATE EXHIBITS DIFFERENTIAL EFFECTS ON THE KIDNEY UNDER EXPERIMENTAL CONDITIONS OF DIABETES VS CHRONIC KIDNEY DISEASE.
R. A. Farris, T. Alexander, C. Wiley, E. T. Price; University of Arkansas for Medical Sciences, Little Rock, AR.

PI-049
PHARMACOMETABOLOMIC ANALYSIS FOLLOWING ACUTE NIACIN ADMINISTRATION.
S. Tuteja, A. Weljie, J. Millar, R. Dunbar, L. Qu, M. Li, D. Rader; University of Pennsylvania School of Medicine, Philadelphia, PA.

Pharmacometrics and Pharmacokinetics (PMK)

PI-050
EFFECT OF PTEROSTILBENE ON *IN VITRO* DRUG-METABOLIZING ENZYME ACTIVITY.
A. A. Albassam, C. Libema, R. F. Frye; Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville, FL.

PI-051
SYSTEMS PHARMACOLOGY MODELING OF CALCIUM AND PHOSPHATE METABOLISM IN CHRONIC KIDNEY DISEASE.
A. Bakhmutova, O. Demin Jr, O. Demin; Institute for Systems Biology, Moscow, Russian Federation.

PI-052
A NEW REVERSIBLE AND POTENT $P2Y_{12}$ RECEPTOR ANTAGONIST: TOLERABILITY, PHARMACODYNAMICS, AND PHARMACOKINETICS IN A FIRST-IN-MAN TRIAL.
D. Baldoni,[1] A. Krause,[1] S. Bruderer,[1] B. Astruc,[2] J. Dingemanse[1]; [1]Actelion Pharmaceuticals Ltd., Allschwil, Switzerland, [2]Biotrial, Rennes, France.

PI-053
SAMPLE SIZE DETERMINATION FOR A POPULATION PHARMACOKINETIC SUB-STUDY BASED ON THE POWER TO DETECT AN EXPOSURE/RESPONSE (ADVERSE EVENT) RELATIONSHIP.
A. M. Barbour, M. H. Magee, N. Goyal, M. J. Fossler; GlaxoSmithKline, King of Prussia, PA.

PI-054
COCKTAIL APPROACH FOR CYTOCHROME P450 AND P-GLYCOPROTEIN ACTIVITY ASSESSMENT USING DRIED BLOOD SPOT.
M. Bosilkovska,[1] C. Samer,[1] J. Deglon,[2] C. Staub,[2] P. Dayer,[1] B. Walder,[3] J. A. Desmeules,[1] Y. Daali[1]; [1]Clinical Pharmacology and Toxicology, Geneva University Hospitals, Geneva, Switzerland, [2]Toxicology Unit, Geneva University Hospitals, Geneva, Switzerland, [3]Anesthesiology Service, Geneva University Hospitals, Geneva, Switzerland.

PI-055
DEVELOPMENT OF A PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODEL OF CANAGLIFLOZIN IN HUMANS.
M. K. Courtois, **J. E. Rower,** E. L. Bradshaw-Pierce; University of Colorado Denver, Anschutz Medical Campus, Aurora, CO.

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PI-056
PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PK) MODELS FOR THE PREDICTION OF CYP DDIS FOR THE LIVER TARGETED GLUCOKINASE ACTIVATOR PF-04991532.
E. Callegari, M. Varma, J. Litchfield, A. Bergman, D. J. Kazierad; Pfizer, Inc., Groton, CT.

PI-057
A STUDY OF THE EFFECT OF DABRAFENIB (D) AS AN INDUCER OF CYTOCHROME P450 (CYP) USING WARFARIN (W) AS A PROBE.
S. W. Carson,[1] K. Grossmann,[2] L. E. Richards-Peterson,[3] D. Ouellet,[1] G. Aktan,[3] K. Kendra,[4] P. LoRusso,[5] S. Sharma,[2] M. R. Middleton,[6] S. C. Blackman,[7] B. Suttle[1]; [1]GlaxoSmithKline, Research Triangle Park, NC, [2]Huntsman Cancer Institute University of Utah, Salt Lake City, UT, [3]GlaxoSmithKline, Collegeville, PA, [4]Ohio State University, Columbus, OH, [5]Karmanos Cancer Institute Wayne State University, Detroit, MI, [6]NHS Dept of Oncology, Oxford, United Kingdom, [7]Seattle Genetics, Seattle, WA.

PI-058
PHARMACODYNAMIC EFFECTS OF A COMBINATION TABLET OF AMLODIPINE/VALSARTAN IN HEALTHY MALE KOREANS.
D. Chae, Y. Kim, M. Son, D. Lee, H. Roh, K. Park; Yonsei University College of Medicine, Seoul, Republic of Korea.

PI-059
PHARMACOKINETICS OF MOXETUMOMAB PASUDOTOX, AN INVESTIGATIONAL IMMUNOTOXIN TARGETING CD22, IN PATIENTS WITH RELAPSED OR REFRACTORY HAIRY CELL LEUKEMIA.
B. Wang,[1] **L. Chang,**[1] R. J. Kreitman,[2] R. Ibrahim,[3] T. Goswami,[3] I. Pastan,[2] M. Liang,[1] L. Roskos[1]; [1]MedImmune, Hayward, CA, [2]National Cancer Institute/National Institutes of Health, Bethesda, MD, [3]MedImmune, Gaithersburg, MD.

PI-060
A NOVEL "RESPONSE LAG" METHOD IN NONMEM FOR IMPLEMENTING DELAYED RESPONSES WITHOUT DELAYED DIFFERENTIAL EQUATIONS (DDE).
A. Chaturvedula,[1] A. Boeckmann,[2] M. Sale[3]; [1]Mercer University, Atlanta, GA, [2]Icon Development Solutions, Hanover, MD, [3]Next Level Solutions Inc, Raleigh, NC.

PI-061
PHARMACOKINETIC RATIONALE FOR THE SAME-DAILY-DOSE CONVERSION FROM IMMEDIATE-RELEASE- TO GASTRORETENTIVE-GABAPENTIN FOR POSTHERPETIC NEURALGIA.
C. Chen, V. E. Cowles, K. Patel, M. Sweeney; Depomed, Newark, CA.

PI-062
POPULATION PHARMACOKINETIC ANALYSIS OF PREGABALIN IN PEDIATRIC PATIENTS WITH PARTIAL ONSET SEIZURES.
M. L. Chew,[1] H. N. Bockbrader,[2] S. Chapel,[2] V. W. Pitman,[3] D. Mann,[3] J. Liu[1]; [1]Pfizer Global Clinical Pharmacology, Groton, CT, [2]Ann Arbor Pharmacometrics Group, Ann Arbor, MI, [3]Pfizer Clinical Sciences, Groton, CT.

PI-063
PHARMACOKINETICS AND PHARMACODYNAMICS OF HIGH DOSE MELPHALAN IN MULTIPLE MYELOMA PATIENTS UNDERGOING AUTOLOGOUS STEM CELL TRANSPLANT.
Y. Cho,[1] J. Wang,[2] Y. Gao,[1] J. Li,[3] M. Lamprecht,[2] M. Jukich,[2] L. J. Schaaf,[1] M. Poi,[2] C. C. Hofmeister,[4] M. A. Phelps[1]; [1]Division of Pharmaceutics and Pharmaceutical Chemistry, College of Pharmacy, The Ohio State University, Columbus, OH, [2]Comprehensive Cancer Center, The Ohio State University, Columbus, OH, [3]College of Public Health, The Ohio State University, Columbus, OH, [4]Division of Hematology, College of Medicine, The Ohio State University, Columbus, OH.

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PI-064
COMPARATIVE PHARMACOKINETICS AND TOLERABILITY OF HCP1004 (A FIXED-DOSE COMBINATION OF NAPROXEN AND ESOMEPRAZOLE STRONTIUM) IN HEALTHY VOLUNTEERS.
Y. Choi,[1] H. Han,[1] D. Shin,[1] J. Yoon,[1] K. Park,[2] S. Kim,[2] S. Shin,[1] K. Yu,[1] S. Yoon,[1] K. Lim,[1] I. Jang[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University Hospital, Seoul, Republic of Korea, [2]Clinical Research Team, Hanmi Pharmaceutical Co., Ltd., Seoul, Republic of Korea.

PI-065
NO PHARMACOKINETIC DRUG INTERACTION BETWEEN GEMIGLIPTIN AND GLIMEPIRIDE.
H. Choi,[1] Y. Kim,[1] M. Kim,[1] H. Jeon,[1] S. Lee,[1] J. Kim,[2] P. Kim,[2] H. Lim,[1] K. Bae[1]; [1]Asan Medical Center, Seoul, Republic of Korea, [2]LG Life Science, Seoul, Republic of Korea.

PI-066
SINGLE AND MULTIPLE-DOSE PHARMACOKINETICS AND TOLERABILITY OF LORCASERIN HYDROCHLORIDE, A NOVEL 5HT2C SELECTIVE AGONIST, IN HEALTHY ADULT SUBJECTS.
R. J. Christopher, M. Morgan, Y. Tang, W. Shanahan; Arena Pharmaceuticals, Inc, San Diego, CA.

PI-067
LBEC0101, AN ETANERCEPT BIOSIMILAR, SHOWED COMPARABLE TOLERABILITY AND PHARMACOKINETIC PROFILES TO THOSE OF ETANERCEPT IN HEALTHY MALE VOLUNTEERS.
H. Chung, L. Ahn, Y. Choi, S. Shin, I. Jang, K. Yu, H. Lee; Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PI-068
OPEN-LABEL, SINGLE-SEQUENCE STUDY OF THE EFFECTS OF KETOCONAZOLE ON THE PHARMACOKINETICS OF BMS-754807 IN HEALTHY SUBJECTS.
P. L. Clemens, J. Park, A. Woolfson, J. Wang; Bristol-Myers Squibb, Princeton, NJ.

PI-069
APPLICATION OF TRANSLATIONAL PHARMACOKINETIC/PHARMACODYNAMIC (TPK/PD) PRINCIPLES TO DEFINE STANDARD OF CARE TO GUIDE DISCOVERY AND EARLY DEVELOPMENT.
W. Comisar,[1] J. E. Talaty,[1] M. Chatterjee,[2] R. Ogert,[2] L. Caro,[1] R. Kong,[2] R. Ripley[1]; [1]Merck, Sharp, & Dohme, Corp., West Point, PA, [2]Merck, Sharp, & Dohme, Corp., Kenilworth, NJ.

PI-070
BRINGING MODELS AND SIMULATIONS INTO THE LIGHT: SHINY.
B. W. Corrigan; Pfizer Global Research and Development, Groton, CT.

PI-071
SEMI-PHYSIOLOGICAL PK MODEL FOR ELUXADOLINE (ELX)—INTEGRATION OF EFFECTS OF DRUG TRANSPORTER (DT) INHIBITION AND HEPATIC IMPAIRMENT (HI).
J. Venitz,[1] **J. Davenport,[2]** P. S. Covington[3]; [1]Medical College of Virginia Campus of Virginia Commonwealth University, Richmond, VA, [2]Furiex Pharmaceuticals, Richmond, VA, [3]Furiex Pharmaceuticals, Wilminton, NC.

PI-072
EFFECT OF MULTIPLE DOSES OF ISAVUCONAZOLE ON THE PHARMACOKINETICS OF METFORMIN IN HEALTHY SUBJECTS.
A. Desai,[1] T. Yamazaki,[1] D. Kowalski,[1] C. Lademacher,[1] H. Pearlman,[1] D. Rammelsberg,[2] **R. Townsend[1];** [1]Astellas, Northbrook, IL, [2]Ranstad Pharma, Deerfield, IL.

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PI-073

POPULATION PHARMACOKINETIC MODEL OF VALPORIC ACID IN CHILDREN WITH EPILEPSY: A NONLINEAR PHARMACOKINETIC MODEL BASED ON PROTEIN-BINDING SATURATION.

J. Ding,[1] W. Lin,[2] Y. Wang,[1] Z. Jiao[3]; [1]Children's Hospital of Fudan University, Shanghai, China, [2]First Hospital Affiliated to Fujian Medical University, Fuzhou, China, [3]Huashan Hospital, Fudan University, Shanghai, China.

PI-074

THE EFFECT OF FOOD ON THE POSACONAZOLE PHARMACOKINETICS INVESTIGATED DURING THE DEVELOPMENT OF A NEW TABLET FORMULATION.

P. Dogterom,[1] M. van Iersel,[1] J. Xu,[2] H. Waskin,[3] W. Kersemaekers[1]; [1]MSD, Oss, Netherlands, [2]Merck & Co., Inc., Upper Gwynedd, PA, [3]Merck & Co., Inc., Kenilworth, NJ.

PI-075

PHARMACOKINETICS OF EXENDIN-(9-39) (E39) IN NEONATES WITH CONGENITAL HYPERINSULISM (HI).

E. Dombrowsky, D. De Leon-Crutchlow, J. Barrett; Children's Hospital of Philadelphia, Philadelphia, PA.

PI-076

POPULATION PHARMACOKINETIC MODELING OF D3-CREATINE IN HEALTHY SUBJECTS WITH VARYING MUSCLE MASS.

D. J. Fediuk, X. Gong, B. M. Johnson, R. L. O'Connor-Semmes; GlaxoSmithKline, Research Triangle Park, NC.

PI-077

MECHANISM-BASED EVALUATION OF CODEINE TOXICITY IN CHILDREN.

P. Gaitonde,[1] M. N. Trame,[1] S. Syvanen,[2] L. J. Lesko,[1] S. Schmidt[1]; [1]University of Florida, Orlando, FL, [2]Uppsala Universitet, Uppsala, Sweden.

PI-078

NONLINEAR MIXED EFFECTS MODELING AND SIMULATION FOR MELPHALAN PHARMACOKINETIC SAMPLING SCHEME OPTIMIZATION IN PATIENTS WITH MULTIPLE MYELOMA.

Y. Gao,[1] J. Li,[2] J. Wang,[3] M. Poi,[4] X. Li,[5] M. Lamprecht,[6] M. Jukich,[3] K. Petrovskis,[1] D. Jarjoura,[5] W. Falk,[7] L. Schaaf,[7] C. Hofmeister,[8] M. Phelps[1]; [1]The College of Pharmacy, The Ohio State University, Columbus, OH, [2]College of Public Health, The Ohio State University, Columbus, OH, [3]Comprehensive Cancer Center, The Ohio State University, Columbus, OH, [4]The College of Pharmacy, Comprehensive Cancer Center, Arthur G. James Cancer Hospital, The Ohio State University, Columbus, OH, [5]Center for Biostatistics, The Ohio State University, Columbus, OH, [6]Arthur G. James Cancer Hospital, The Ohio State University, Columbus, OH, [7]Comprehensive Cancer Center, Arthur G. James Cancer Hospital, The Ohio State University, Columbus, OH, [8]Comprehensive Cancer Center, Arthur G. James Cancer Hospital, Division of Hematology, The Ohio State University, Columbus, OH.

PI-079

PHARMACOKINETIC AND EXPOSURE-RESPONSE ANALYSES OF PERTUZUMAB PLUS TRASTUZUMAB AND DOCETAXEL DURING NEOADJUVANT TREATMENT OF HER2+ EARLY BREAST CANCER.

A. L. Quartino,[1] H. Li,[2] J. Y. Jin,[1] D. Wada,[2] G. Ross,[3] L. Gianni,[4] J. Visich,[1] B. Lum,[1] **A. Garg[1];** [1]Genentech Inc., South San Francisco, CA, [2]Quantitative Solutions Inc., Menlo Park, CA, [3]Roche Products Ltd, Welwyn Garden City, United Kingdom, [4]Oncologia Medica, San Raffaele Cancer Centre, Milan, Italy.

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PI-080
POPULATION PHARMACOKINETICS AND EVALUATION OF FIXED DOSING FOR PERTUZUMAB, A HER2 TARGETED MONOCLONAL ANTIBODY, IN CANCER PATIENTS.
A. Garg,[1] J. Li,[1] A. Quartino,[1] J. Jin,[1] D. R. Wada,[2] H. Li,[2] J. Cortes,[3] V. McNally,[4] J. Visich,[1] B. Lum[1]; [1]Genentech, Inc., South San Francisco, CA, [2]Quantitative Solutions Inc., Menlo Park, CA, [3]Department of Oncology, Vall d'Hebron University Hospital, Barcelona, Spain, [4]Roche Products, Welwyn Garden City, United Kingdom.

PI-081
POPULATION PHARMACOKINETIC MODELING OF ISONIAZID, RIFAMPIN, AND ETHAMBUTOL IN KOREAN TUBERCULOSIS PATIENTS.
S. Lyu,[1] Y. Noh,[2] H. Kim,[1] Y. Lee,[2] J. Shin,[1] D. Kim,[1] **J. Ghim[2];** [1]Inje University College of Medicine, Busan, Republic of Korea, [2]Inje University Busan Paik Hospital, Busan, Republic of Korea

PI-082
A DOSE SWITCHING SIMULATION ANALYSES FROM INVEGA® SUSTENNA® OR RISPERDAL® CONSTA® TO RBP-7000, A NEW SUSTAINED-RELEASE FORMULATION OF RISPERIDONE.
R. Gomeni,[1] C. M. Laffont,[2] B. Zheng,[3] C. Heidbreder,[3] P. Fudala,[3] A. Nasser[3]; [1]Alleantis, Research Triangle Park, NC, [2]Pharmacometrica, La Fouillade, France, [3]Reckitt Benckiser Pharmaceuticals Inc., Richmond, VA.

PI-083
INFLUENCE OF ROSUVASTATIN ON THE BLOOD PRESSURE LOWERING EFFECT OF TELMISARTAN IN HEALTHY KOREANS.
J. Gug,[1] M. Son,[1] Y. Kim,[1] H. Roh,[1] D. Lee,[2] H. Son,[2] K. Park[2]; [1]Yonsei University College of Medicine, Brain Korea 21 Project for Medical Science, Seoul, Republic of Korea, [2]Department of Pharmacology, Yonsei University College of Medicine, Seoul, Republic of Korea

PI-084
REPEATED TIME TO EVENT MODELING OF THE RELATIONSHIP BETWEEN rFVIIIFc ACTIVITY AND SPONTANEOUS BLEEDING IN HEMOPHILIA A.
Y. Hang, I. Nestorov; Biogen Idec, Cambridge, MA.

PI-085
PHARMACOKINETICS OF AN INTRAVENOUS MICROGRAM DOSE OF MIDAZOLAM.
N. Hohmann, F. Kocheise, A. Carls, J. Burhenne, W. E. Haefeli, G. Mikus; Department of Clinical Pharmacology and Pharmacoepidemiology, Heidelberg, Germany.

PI-086
ASSESSMENT OF PHARMACOKINETIC DRUG-DRUG INTERACTION BETWEEN LCZ696 AND AMLODIPINE.
H. Hsiao,[1] M. Greeley,[1] P. Pal,[2] T. Langenickel,[3] I. Rajman,[4] G. Sunkara,[1] P. Chandra[1]; [1]Novartis Institutes for Biomedical Research, East Hanover, NJ, [2]Novartis Healthcare Pvt. Ltd, Hyderabad, India, [3]Novartis Institutes for Biomedical Research, Basel, Switzerland, [4]Novartis Institute for Biomedical Research, Basel, Switzerland.

PI-087
PHARMACOKINETICS OF PEGINTERFERON BETA-1A DELIVERED BY SINGLE-USE AUTOINJECTOR AND PRE-FILLED SYRINGE.
X. Hu, Y. Cui, A. Ali Seddighzadeh, S. Hung; Biogen Idec, Cambridge, MA.

PI-088
EVALUATING THE USE OF LINEAR MIXED-EFFECT MODELS FOR INFERENCE OF THE CONCENTRATION-QTC SLOPE ESTIMATE AS A SURROGATE FOR A BIOLOGICAL QTC MODEL.
Y. Huh, M. M. Hutmacher; Ann Arbor Pharmacometrics Group, Ann Arbor, MI.

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PI-089

PHARMACOKINETIC AND SAFETY EVALUATION OF LC28-0126, A NECROSIS INHIBITOR, IN HEALTHY VOLUNTEERS.

K. Jang,[1] S. Kim,[1] J. Oh,[1] I. Chung,[1] I. Jang,[1] S. Shin,[1] H. Cho,[2] K. Yu[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea, [2]Department of Internal Medicine, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PI-090

PHARMACODYNAMIC ASSOCIATION OF PIOGLITAZONE AND ITS ACTIVE METABOLITES WITH LIVER OUTCOMES AMONG PATIENTS DIAGNOSED WITH NONALCOHOLIC STEATOHEPATITIS.

M. Kawaguchi-Suzuki, F. Bril, R. Lomonaco, S. Subbarayan, K. Cusi, R. F. Frye; University of Florida, Gainesville, FL.

PI-091

EFFECT OF HEPATIC IMPAIRMENT ON THE PHARMACOKINETICS OF UDENAFIL, A SELECTIVE PDE-5 INHIBITOR IN MALE SUBJECTS.

A. Kim,[1] **J. Lee,**[1] H. Lee,[2] S. Jeong,[3] Y. Jung,[4] H. Kim,[4] Y. Lim,[5] S. Rhee,[1] K. Yu,[1] J. Cho,[1] S. Shin,[1] M. Bahng,[6] K. Lim,[1] I. Jang[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea, [2]Department of Internal Medicine and Liver Research Institute, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea, [3]Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea, [4]Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul National University College of Medicine, Seoul, Republic of Korea, [5]Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [6]Department of Clinical Development, Dong-A ST Co., Ltd., Seoul, Republic of Korea.

PI-092

SUSTAINED RELEASE NITRATE AGENT IS A DETERMINANT OF CLOPIDOGREL LOWER RESPONSIVENESS IN PATIENTS WITH DUAL ANTIPLATELET MAINTENANCE THERAPY.

M. Kim,[1] D. Lee,[1] S. Yi,[2] M. Park,[2] L. Guo,[3] T. Park,[1] J. Park,[1] K. Park,[1] Y. Cho[1]; [1]Department of Cardiology, Dong-A University Hospital, Busan, Republic of Korea, [2]Department of Clinical Pharmacology, Dong-A University Hospital, Busan, Republic of Korea, [3]Clinical Trial Center, Dong-A University Hospital, Busan, Republic of Korea.

PI-093

PHARMACOKINETICS, PHARMACODYNAMICS, AND SAFETY OF CTB-001 AFTER SINGLE INTRAVENOUS DOSES IN HEALTHY MALE VOLUNTEERS.

Y. Kim,[1] H. Choi,[1] Y. Noh,[2] M. Kim,[1] H. Jeon,[1] H. Lim,[1] K. Bae[1]; [1]Asan Medical Center, University of Ulsan, Department of Clinical Pharmacology and Therapeutics, Seoul, Republic of Korea, [2]Department of Clinical Pharmacology, Busan Paik Hospital, Busan, Republic of Korea.

PI-094

PHARMACOKINETIC-PHARMACODYNAMIC (PK-PD) MODELING FOR METFORMIN IN HEALTHY VOLUNTEERS.

Y. Kim, S. Cho, D. Lee, H. Son, H. Roh, M. Son, Y. Heo, K. Park; Yonsei University, Seoul, Republic of Korea.

PI-095

ASSESSMENT OF PHARMACOKINETIC INTERACTION BETWEEN PRADIGASTAT AND EFAVIRENZ OR REPAGLINIDE IN HEALTHY SUBJECTS.

K. M. Kulmatycki,[1] D. Meyers,[1] K. Danis,[1] S. Neelakantham,[2] Z. Su,[3] T. Majumdar,[4] R. Sam,[4] G. Sunkara,[4]

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J. Chen[4]; [1]Novartis Biomedical Research Institute, Cambridge, MA, [2]Novartis Biomedical Research Institute, Hyberdad, India, [3]Novartis Biomedical Research Institute, Shanghai, China, [4]Novartis Biomedical Research Institute, East Hanover, NJ.

PI-096

HUMANIZATION OF SOLITHROMYCIN (SOL) NON-HUMAN PRIMATE (NHP) PK PROFILES TO IMPROVE PK-PD CLINICAL TRANSLATION.

E. A. Lakota,[1] O. O. Okusanya,[2] S. M. Bhavnani,[2] K. Keedy,[3] A. Sheets,[3] P. Fernandes,[3] P. G. Ambrose,[2] A. Forrest[2]; [1]University at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY, [2]Institute for Clinical Pharmacodynamics, Latham, NY, [3]Cempra Pharmaceuticals, Chapel Hill, NC.

PI-097

SELECTION OF DOSING REGIMEN USING A PKPD MODEL INCORPORATING TARGET MEDIATED DRUG DISPOSITION (TMDD) OF LAMPALIZUMAB (LPZ) IN GEOGRAPHIC ATROPHY (GA) PATIENTS.

K. N. Le,[1] L. Gibiansky,[2] J. Good,[1] T. Davancaze,[1] A. Morimoto,[1] K. Loyet,[1] M. van Lookeren Campagne,[1] E. Strauss,[1] R. Graham,[1] J. Jin,[1] J. Visich[1]; [1]Genentech, South San Francisco, CA, [2]QuantPharm LLC, North Potomac, CA.

PI-098

COMPARATIVE PHARMACODYNAMIC MODELING OF ORIGINAL AND GENERIC FORMULATIONS OF SEVOFLURANE USING BISPECTRAL INDEX IN GENERAL ANESTHESIA.

S. Lee, S. Jeong; Anesthesiology and Pain Medicine, Chonnam National University Medical School, Gwangju, Republic of Korea.

PI-099

COMPARISON OF THE PHARMACOKINETICS BETWEEN TWO VORICONAZOLE FORMULATIONS AND THE EFFECT OF CYP2C19 POLYMORPHISMS ON VORICONAZOLE EXPOSURE.

J. Lee, H. Han, D. Shin, J. Cho, I. Jang, K. Lim, K. Yu, S. Shin; Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PI-100

A POPULATION PHARMACOKINETIC EVALUATION OF RALTEGRAVIR AND RALTEGRAVIR GLUCURONIDE FOLLOWING TREATMENT WITH KETOCONAZOLE, RITONAVIR OR RIFAMPIN.

K. Seng, K. Hee, **L. S. Lee;** National University of Singapore, Singapore, Singapore.

PI-101

PHARMACOKINETICS OF CARIPRAZINE IN HEALTHY SUBJECTS AND PATIENTS WITH IMPAIRED HEPATIC FUNCTION.

Y. Lee,[1] A. Periclou,[1] M. Kapás,[2] I. Laszlovszky,[2] P. Ghahramani[1]; [1]Forest Research Institute, Jersey City, NJ, [2]Gedeon Richter Plc, Budapest, Hungary.

PI-102

PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELING TO PREDICT THE IMPACT OF CYP2D6 POLYMORPHISMS ON VELIPARIB PHARMACOKINETICS FROM *IN VITRO* DATA.

J. Li, J. Wu, P. LoRusso; Karmanos Cancer Institute, Detroit, MI.

PI-103

PHARMACOKINETICS (PK) OF MIDAZOLAM (MDZ) AFTER I.V. AND P.O. ADMINISTRATION WITHOUT AND WITH CYP3A INHIBITORS (INH) – A QUANTITATIVE META ANALYSIS.

M. Li, J. Venitz; Virginia Commonwealth University, Richmond, VA.

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PI-104
WITHDRAWN

PI-105
PHARMACOKINETICS, SAFETY, AND TOLERABILITY OF MB12066 AFTER MULTIPLE ORAL ADMINISTRATIONS IN HEALTHY VOLUNTEERS.
S. Park, S. Kim, I. Chung, S. Shin, I. Jang, S. Yoon, K. Lim, K. Yu; Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PI-106
A PHYSIOLOGICALLY BASED PHARMACOKINETIC MODEL OF GEFITINIB DISPOSITION: FROM RAT TO MAN.
J. Deng, L. J. Lesko, G. An; Center for Pharmacometrics & Systems Pharmacology, Department of Pharmaceutics, University of Florida College of Pharmacy, Orlando, FL.

PI-107
PREDICTION OF GEFITINIB HUMAN PHARMACOKINETICS FROM ANIMAL DATA – COMPARATIVE ASSESSMENT OF DIFFERENT ALLOMETRIC SCALING APPROACHES.
J. Deng, L. J. Lesko, G. An; Center for Pharmacometrics & Systems Pharmacology, Department of Pharmaceutics, University of Florida College of Pharmacy, Orlando, FL.

PI-108
EFFECTS OF CYP3A MODULATORS ON THE PK OF NALOXEGOL.
K. Bui, D. Zhou, M. Sostek, F. She, N. Al-Huniti; AstraZeneca, Wilmington, DE.

PI-109
A PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODEL FOR SIMULATION OF NALOXEGOL PHARMACOKINETICS AND DRUG-DRUG INTERACTION (DDI) POTENTIAL.
D. Zhou, **K. Bui,** M. Sostek, N. Al-Huniti; AstraZeneca, Wilmington, DE.

TPI-110
METHADONE ENANTIOMERS METABOLISM AND CLEARANCE ARE IMPAIRED IN INDIVIDUALS WITH CYP2B6*6 GENOTYPE.
E. D. Kharasch, J. Parchomski, K. Regina, J. Blood, Y. Yang; Washington University in St. Louis, St Louis, MO.

PI-111
INFLUENCE OF CYP2B6*6 GENOTYPE ON BUPROPION ENANTIOMERS METABOLISM AND CLEARANCE.
E. D. Kharasch, A. Crafford, J. Parchomski, J. Blood, K. Regina; Washington University in St. Louis, St Louis, MO.

PI-112
USE OF LONGITUDINAL DOSE-RESPONSE (DR) MODELING TO SUPPORT THE EFFICACY AND SAFETY OF ALITRETINOIN (BAL4079) IN SEVERE REFRACTORY CHRONIC HAND ECZEMA (CHE).
V. D. Schmith,[1] R. Singh,[2] R. Gomeni,[3] X. Li,[1] O. Graff,[1] A. Hamedani,[1] J. Troughton,[1] S. Learned[1]; [1]GlaxoSmithKline, Research Triangle Park, NC, [2]GlaxoSmithKline, Upper Merion, PA, [3]Alleantis, Research Triangle Park, NC.

Special Populations (SPO)

PI-113
FACTORS INFLUENCING VANCOMYCIN DOSE REDUCTION IN NEONATAL AND PEDIATRIC PATIENTS.
A. H. Balch,[1] C. R. Stockmann,[1] E. A. Thorell,[1] J. E. Constance,[1] M. G. Spigarelli,[1] C. M. Sherwin,[1] K. Korgenski[2]; [1]University of Utah, Salt Lake City, UT, [2]Intermountain Health, Salt Lake City, UT.

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PI-114
CIRCULATING MMP-9 AND VISFATIN LEVELS CORRELATE NEGATIVELY IN CHILDREN AND ADOLESCENTS.
V. A. Belo,[1] J. A. Miranda,[2] R. Lacchini,[1] C. M. Lanna,[1] J. A. Tanus-Santos[1]; [1]FMRP-USP, Ribeirao Preto, Brazil, [2]UNICAMP, Campinas, Brazil.

PI-115
PHARMACOKINETICS OF MIDAZOLAM IN MORBIDLY OBESE PATIENTS FOLLOWING ORAL AND INTRAVENOUS ADMINISTRATION.
M. J. Brill,[1] A. van Rongen,[1] A. P. Houwink,[1] J. Burggraaf,[2] B. van Ramshorst,[1] R. J. Wiezer,[1] E. P. van Dongen,[1] C. A. Knibbe[1]; [1]St. Antonius Hospital, Nieuwegein, Netherlands, [2]Centre for Human Drug Research, Leiden, Netherlands.

PI-116
CHARACTERISTICS OF PEDIATRIC CANCER PATIENTS RECEIVING VANCOMYCIN.
J. E. Constance, A. Balch, C. Stockmann, K. Korgenski, C. M. Sherwin, M. G. Spigarelli; University of Utah, Salt Lake City, UT.

PI-117
PREVALENCE OF HEAVY ALCOHOL USE DURING PREGNANCY IN CANADA.
K. E. Delano,[1] E. Pope,[2] G. Koren[1]; [1]Hospital for Sick Children, Toronto, ON, Canada, [2]McMaster University, Hamilton, ON, Canada.

PI-118
A SEMI-MECHANISTIC MODEL TO DESCRIBE MATERNAL-FETAL PROPOFOL PHARMACOKINETICS.
M. Dong, P. Ngamprasertwong, J. Niu, S. Sadhasivam, T. Fukuda, A. A. Vinks; Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PI-119
THERAPEUTIC MONITORING OF VANCOMYCIN IN CHILDREN: IS THERE A COST TO NON-ADHERENCE OF GUIDELINES?.
S. D. Firth, S. Y. Yakub, C. M. Sherwin, K. Korgenski, J. E. Constance, C. Stockmann, A. Balch, M. G. Spigarelli; University of Utah, Salt Lake City, UT.

PI-120
CODEINE-RELATED DEATHS IN ONTARIO, CANADA: THE ROLE OF PHARMACOGENETICS AND DRUG INTERACTIONS.
J. Lam,[1] K. Woodall,[2] P. Solbeck,[2] C. J. Ross,[3] B. C. Carleton,[4] M. R. Hayden,[3] G. Koren,[1] P. Madadi[2]; [1]Hospital for Sick Children, Toronto, ON, Canada, [2]Center of Forensic Sciences, Toronto, ON, Canada, [3]University of British Columbia, Vancouver, BC, Canada, [4]Children's and Women's Health Centre of British Columbia, Vancouver, BC, Canada.

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POSTER SESSION II
FRIDAY, MARCH 21, 2014

International Hall 7:30 am – 3:30 pm • Attended Posters 11:45 am – 1:15 pm

Drug Development and Regulatory Sciences (DDR)

PII-001
THE SAFETY AND PHARMACOKINETICS OF MELOXICAM IN COMBINATION WITH OMEPRAZOLE COMPARED TO RESPECTIVE MONOTHERAPIES IN HEALTHY VOLUNTEERS.

J. Massicotte,[1] A. Fortier,[1] S. Boily,[1] J. M. Paquette,[1] L. Sayegh,[1] E. Sicard,[1] M. Lefebvre,[1] J. Hofmann[2]; [1]Algorithme Pharma, Laval, QC, Canada, [2]Zentiva, K.S., Prague, Czech Republic.

PII-002
SAFETY, TOLERABILITY AND PHARMACOKINETIC OF GIC-1001 FOLLOWING MULTIPLE ASCENDING DOSES ADMINISTRATIONS THROUGH AN ADAPTIVE FIRST IN HUMAN STUDY IN HEALTHY VOLUNTEERS.

J. M. Paquette,[1] M. Rufiange,[1] A. Ait Sadoune,[1] E. Sicard,[1] J. Massicotte,[1] M. Lefebvre,[1] P. Colin,[2] M. Ranger[2]; [1]Algorithme Pharma, Laval, QC, Canada, [2]glcare Pharma Inc., Montréal, QC, Canada.

PII-003
A FIRST-IN-HUMAN (FIH) STUDY OF BCX4161, AN ORAL KALLIKREIN INHIBITOR, USING A TRANSLATIONAL PHARMACEUTICS PLATFORM.

S. Sweet,[1] J. Collier,[1] A. Connor,[1] **M. Paterson,**[1] P. Collis,[2] W. Sheridan,[2] Y. El-Kattan[2]; [1]Quotient Clinical, Nottingham, United Kingdom, [2]BioCryst Pharmaceuticals, Inc., Durham, NC.

PII-004
MULTIPLE-DOSE STUDY TO EVALUATE APIXABAN PHARMACOKINETICS, PHARMACODYNAMICS, SAFETY, AND TOLERABILITY IN PEDIATRIC SUBJECTS WITH AN INDWELLING CENTRAL VENOUS CATHETER.

I. Perlstein,[1] S. Suryawanshi,[1] E. Elefant,[1] Z. Wang,[1] L. Cohen,[1] M. AbuTarif,[1] S. Calderwood,[2] C. Frost[1]; [1]Bristol-Myers Squibb, Princeton, NJ, [2]Saint Peter's University Children's Hospital, New Brunswick, NJ.

PII-005
RACE/ETHNICITY BASED PRESCRIBING RECOMMENDATIONS FOR NEW MOLECULAR ENTITIES: SURVEY OF RECENT APPROVALS.

A. Ramamoorthy, M. A. Pacanowski, J. Bull, L. Zhang; US Food and Drug Administration, Silver Spring, MD.

PII-006
A STANDARDIZED APPROACH TO ADVERSE EVENT TERMINOLOGY IN ABUSE POTENTIAL EVALUATION: THE NEXT ITERATION.

M. Romach, E. Sellers; DL Global Partners; University of Toronto, Toronto, ON, Canada.

PII-007
EFFECT OF FOOD AND ANTACID TREATMENT ON BIOAVAILABILITY OF 45 MG TABLET OF DACOMITINIB RELATIVE TO DACOMITINIB ADMINISTRATION UNDER FASTED CONDITIONS.

A. Ruiz-Garcia,[1] **J. C. Masters,**[2] R. R. LaBadie,[3] Y. Liang,[3] T. Boutros,[1] L. Mendes da Costa,[4] C. L. Bello[5]; [1]Pfizer Inc., San Diego, CA, [2]University of California, San Diego, San Diego, CA, [3]Pfizer Inc., Groton, CT, [4]Pfizer CRU, Brussels, Belgium, [5]Pfizer Inc., New York, NY.

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POSTER SESSION II
FRIDAY, MARCH 21, 2014

International Hall 7:30 am – 3:30 pm • Attended Posters 11:45 am – 1:15 pm

PII-008

A PHASE 1 ADAPTIVE DESIGN STUDY TO ASSESS SAFETY, TOLERABILITY AND PHARMACOKINETICS OF SINGLE ASCENDING ORAL DOSES OF GIC-1001 IN HEALTHY VOLUNTEERS.

L. Sayegh,[1] M. Rufiange,[1] A. Ait Sadoune,[1] E. Sicard,[1] J. Massicotte,[1] M. Lefebvre,[1] P. Colin,[2] M. Ranger[2]; [1]Algorithme Pharma Inc., Laval, QC, Canada, [2]glcare Pharma Inc., Montreal, QC, Canada.

PII-009

CURRENT INDUSTRY PRACTICES IN THE *IN VIVO* ASSESSMENT OF HUMAN DRUG METABOLISM: A SURVEY BY THE DRUG METABOLISM AND CLINICAL PHARMACOLOGY LEADERSHIP GROUPS OF THE IQ CONSORTIUM.

J. G. Slatter,[1] N. G. Agrawal,[2] S. K. Chowdhury,[3] L. J. Christopher,[4] T. Edeki,[5] P. D. Gorycki,[6] C. E. Hop,[7] J. Keirns,[8] R. D. Lee,[9] M. L. Marshall,[10] S. D. Oliver,[11] C. Prakash,[12] D. K. Spracklin,[13] R. Subramanian,[14] Z. Zeng[15]; [1]Amgen, Seattle, WA, [2]Merck, West Point, PA, [3]Takeda, Cambridge, MA, [4]Bristol-Myers Squibb, Princeton, NJ, [5]AstraZeneca, Wilmington, DE, [6]GlaxoSmithKline, King of Prussia, PA, [7]Genentech, South San Francisco, CA, [8]Astellas, Northbrook, IL, [9]Takeda, Deerfield, IL, [10]Drinker Biddle & Reath LLP, Washington, DC, [11]AstraZeneca, Macclesfield, United Kingdom, [12]Biogen Idec, Cambridge, MA, [13]Pfizer, Groton, CT, [14]Amgen, Thousand Oaks, CA, [15]Sanofi, Bridgewater, NJ.

PII-010

USING DILISYM® AND MITOSYM™ TO INVESTIGATE *IN VIVO* ETOMOXIR-INDUCED DILI BASED ON *IN VITRO* DATA.

Y. Yang, J. W. Woodhead, P. B. Watkins, B. A. Howell, S. Q. Siler; The Hamner Institutes for Health Sciences, Research Triangle Park, NC

PII-011

RETURN ON INVESTMENT OF PHARMACOKINETIC STUDIES IN SUBJECTS WITH MILD RENAL IMPAIRMENT.

I. R. Younis; US Food and Drug Administration, Silver Spring, MD.

PII-012

CREATININE AS AN ENDOGENOUS MARKER FOR RENAL FUNCTION—EMERGING ROLE OF TRANSPORTERS IN THE OVERALL ASSESSMENT OF RENAL TOXICITY.

V. Arya,[1] X. Yang,[1] P. Balimane,[2] L. Chinn,[2] P. Hinderling,[2] J. Vaidyanathan,[2] A. A. Zur,[3] M. B. Wittwer,[3] **L. Zhang[2];** [1]Co-First Author, Office of Clinical Pharmacology, Office of Translational Sciences, CDER, FDA, Silver Spring, MD, [2]Office of Clinical Pharmacology, Office of Translational Sciences, CDER, FDA, Silver Spring, MD, [3]ORISE Fellow, Department of Bioengineering and Therapeutic Sciences, University of California, San Francisco, CA.

PII-013

PH-DEPENDENT DRUG-DRUG INTERACTIONS: POTENTIAL IMPLICATIONS FOR NEW DRUG DEVELOPMENT.

L. Zhang,[1] F. Wu,[2] S. Lee,[1] H. Zhao,[1] L. Zhang[1]; [1]Office of Clinical Pharmacology, Office of Translational Sciences, CDER, US Food and Drug Administration, Silver Spring, MD, [2]ORISE Fellow, Oak Ridge Institute for Science and Education & Office of Clinical Pharmacology, Office of Translational Sciences, CDER, US Food and Drug Administration, Silver Spring, MD.

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POSTER SESSION II
FRIDAY, MARCH 21, 2014

International Hall 7:30 am – 3:30 pm • Attended Posters 11:45 am – 1:15 pm

Drug Safety (SAF)

PII-014
IMPLICATIONS OF SERUM CREATININE MEASUREMENTS ON GFR ESTIMATION AND VANCOMYCIN DOSING IN CHILDREN.

G. Neuman,[1] I. Nulman,[1] K. Adeli,[2] G. Koren,[1] D. A. Colantonio,[2] A. Helldén[1]; [1]Division of Clinical Pharmacology and Toxicology, The Hospital for Sick Children, Toronto, ON, Canada, [2]Division of Clinical Biochemistry, The Hospital for Sick Children, Toronto, ON, Canada.

PII-015
PHARMACOKINETIC INTERACTION BETWEEN TELMISARTAN AND CHLORTHALIDONE AT STEADY-STATE IN HEALTHY KOREAN MALE VOLUNTEERS.

S. Seong,[1] M. Lim,[2] J. Park,[1] **J. Lee,**[1] S. Park,[1] J. Seo,[1] M. Gwon,[1] H. Lee,[1] Y. Yoon[1]; [1]Kyungpook National University Hospital Clinical Trial Center, Daegu, Republic of Korea, [2]College of Pharmacy, Yeungnam University, Kyungpook, Republic of Korea.

PII-016
AN EVIDENCE-BASED PROCESS TO ASSESS CAUSALITY AND CATEGORIZE QT-PROLONGING DRUGS FOR THEIR RISK OF TORSADES DE POINTES.

R. L. Woosley,[1] K. Black,[1] K. Romero[2]; [1]AZCERT, Oro Valley, AZ, [2]Critical Path Institute, Tucson, AZ.

PII-017
BENZODIAZEPINE PRESCRIBING AMONG OLDER ADULTS IN EMERGENCY DEPARTMENTS AND AMBULATORY CLINICS.

M. E. Mazer-Amirshahi,[1] G. Brooks,[1] E. Marra,[1] J. M. Pines,[1] J. van den Anker,[2] L. May[1]; [1]George Washington University, Washington, DC, [2]Children's National Medical Center, Washington, DC.

PII-018
CHARACTERIZING DRUG SHORTAGES IN THE EMERGENCY DEPARTMENT.

M. E. Mazer-Amirshahi, A. Pourmand, J. M. Pines, J. van den Anker; George Washington University, Washington, DC.

PII-019
RISING RATES OF PROTON PUMP INHIBITOR PRESCRIBING IN US EMERGENCY DEPARTMENTS.

M. E. Mazer-Amirshahi,[1] P. M. Mullins,[1] A. Meltzer,[1] J. van den Anker,[2] J. M. Pines[1]; [1]George Washington University, Washington, DC, [2]Children's National Medical Center, Washington, DC.

PII-020
THE ONTOLOGICAL REPRESENTATION OF ADVERSE EVENTS WITH COMPOSITE SYMPTOMS: EXPANDING ONTOLOGY OF ADVERSE EVENTS TO DESCRIBE DRUG-INDUCED CARDIOTOXICITY.

S. Sarntivijai,[1] Y. Lin,[2] E. Blair,[3] K. Burkhart,[1] Y. He,[2] G. S. Omenn,[4] B. D. Athey,[4] D. R. Abernethy[1]; [1]US Food and Drug Administration, Silver Spring, MD, [2]Unit of Laboratory Animal Medicine, Department of Microbiology and Immunology, University of Michigan, Ann Arbor, MI, [3]The University of North Carolina at Chapel Hill, Eshelman School of Pharmacy, Chapel Hill, NC, [4]Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI.

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FRIDAY, MARCH 21, 2014

International Hall 7:30 am – 3:30 pm • Attended Posters 11:45 am – 1:15 pm

PII-021

PREDICTING GENE INTERACTIONS OF TYROSINE KINASE INHIBITORS INDUCED CARDIOTOXICITY WITH THE ONTOLOGY OF ADVERSE EVENTS-ASSISTED BIOINFORMATICS APPROACH.

S. Sarntivijai,[1] J. Hur,[2] A. Ozgur,[3] K. Burkhart,[1] Y. He,[4] G. S. Omenn,[5] B. D. Athey,[5] D. R. Abernethy[1]; [1]US Food and Drug Administration, Silver Spring, MD, [2]Department of Neurology, Medical School, University of Michigan, Ann Arbor, MI, [3]Department of Computer Science, Bogazici University, Istanbul, Turkey, [4]Unit of Laboratory Animal Medicine, Medical School, University of Michigan, Ann Arbor, MI, [5]Department of Computational Medicine and Bioinformatics, Medical School, University of Michigan, Ann Arbor, MI.

PII-022

SAFETY, TOLERABILITY AND PHARMACOKINETICS OF SINGLE DOESES OF THE TRPV1 ANTAGONIST SAF312 IN HEALTHY SUBJECTS.

M. El Mouelhi,[1] M. Bartlett,[2] J. Roberts,[3] **S. Vaidya[4];** [1]Novartis Institutes for BioMedical Research, Inc., East Hanover, NJ, [2]Novartis Institutes for BioMedical Research, Inc., Basel, Switzerland, [3]Novartis, East Hanover, NJ, [4]Novartis Institutes for BioMedical Research, Inc., Cambridge, MA.

PII-023

SAFETY, TOLBERABILITY AND PHARMACOKINETICS OF MULTIPLE DOSES OF THE TRPV1 ANTAGONIST SAF312 IN HEALTHY SUBJECTS.

U. Schramm,[1] **S. Vaidya,[2]** G. Tavares,[3] J. Roberts,[4] K. Francke,[5] M. El Mouelhi[6]; [1]Novartis Institutes for BioMedical Research, Inc., Basel, Switzerland, [2]Novartis Institutes for BioMedical Research, Inc., Cambridge, MA, [3]Novartis, Basel, Switzerland, [4]Novartis, East Hanover, NJ, [5]Parexel, Harrow, United Kingdom, [6]Novartis Institutes for BioMedical Research, Inc., East Hanover, NJ.

Infectious Diseases (INF)

PII-024

EFFECT OF MDR1 GENOTYPE ON THE INTRACELLULAR CONCENTRATION AND THE CLINICAL EFFICACY OF DARUNAVIR IN HIV PATIENTS.

D. Nagano,[1] T. Araki,[1] K. Yanagisawa,[2] T. Hayashi,[2] Y. Ogawa,[2] Y. Nojima,[2] T. Nakamura,[1] K. Yamamoto[1]; [1]Department of Clinical Pharmacology, Gunma University Graduate School of Medicine, Maebashi, Japan, [2]Department of Medicine and Clinical Science, Gunma University Graduate School of Medicine, Maebashi, Japan.

PII-025

SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF FALDAPREVIR AFTER SINGLE RISING DOSES IN HEALTHY SUBJECTS.

R. Sennewald,[1] H. Narjes,[1] C. Yong,[2] G. Nehmiz,[1] **F. Huang,[2]** J. Stern[2]; [1]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany, [2]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT.

PII-026

INVESTIGATION OF THE EFFECT OF FOOD AND INCREASED GASTRIC pH ON THE RELATIVE BIOAVAILABILITY OF FALDAPREVIR IN HEALTHY SUBJECTS.

J. Wu,[1] T. Giessmann,[2] N. Hummel,[2] M. Elgadi,[3] **F. Huang[1];** [1]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, [2]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany, [3]Boehringer Ingelheim Canada Ltd/Ltee, Burlington, ON, Canada.

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POSTER SESSION II
FRIDAY, MARCH 21, 2014

International Hall 7:30 am – 3:30 pm • Attended Posters 11:45 am – 1:15 pm

Molecular Pharmacology and Pharmacogenetics (MOL)

PII-027
MECHANISMS OF NEURAMINIDASE INHIBITOR TRANSPORT ACROSS THE BLOOD-BRAIN BARRIER.

L. Lin,[1] E. C. Chen,[1] V. Hsu,[2] P. Zhao,[2] L. Zhang,[2] S.-M. Huang,[2] K. M. Giacomini[1]; [1]University of California San Francisco, San Francisco, CA, [2]US Food and Drug Administration, Silver Spring, MD.

PII-028
INHIBITION OF THE OATP1A2 TRANSPORTER BY TRICYCLIC COMPOUNDS.

J. Lu,[1] L. Guilarte Moya,[1] Y. Leung,[1] F. Gaudette,[2] M. Keiser,[3] V. Michaud,[2] J. Turgeon[2]; [1]Montreal University, Montreal, QC, Canada, [2]CRCHUM/ Hotel Dieu, Montreal, QC, Canada, [3]University of Greifswald, Greifswald, Germany.

PII-029
FUNCTIONAL CHARACTERIZATION OF MRP2 CODING POLYMORPHISMS PREVALENT IN AFRICAN AMERICANS.

S. Markova, A. Forsman, F. Franek, J. Bjorck, T. D. Nguyen, D. L. Kroetz; University of California San Francisco, San Francisco, CA.

PII-030
A PHARMACOGENOMIC GENOME-WIDE ASSOCIATION STUDY FOR ADVERSE CARDIOVASCULAR OUTCOMES IN THE INTERNATIONAL VERAPAMIL SR-TRANDOLAPRIL STUDY (INVEST).

C. W. McDonough, Y. Gong, T. Y. Langaee, C. J. Pepine, R. M. Cooper-DeHoff, J. A. Johnson; University of Florida, Gainesville, FL.

PII-031
MEGESTROL ACETATE GLUCURONIDATION.

S. Mirkov, M. Seminerio, J. Ramírez, L. House, M. J. Ratain; University of Chicago, Chicago, IL.

PII-032
PATIENT AWARENESS OF THE EFFECT OF GENOTYPE ON CLOPIDOGREL RESPONSIVENESS AFTER THE RELEASE OF THE BLACK BOX WARNING.

K. M. Momary,[1] L. P. Kimble[2]; [1]Mercer University, College of Pharmacy, Atlanta, GA, [2]Mercer University, Georgia Baptist College of Nursing, Atlanta, GA.

PII-033
LIGAND-RECEPTOR INTERACTIONS GOVERNING THE BINDING AND COOPERATIVITY OF DIVERSE MODULATORS TO THE METABOTROPIC GLUTAMATE RECEPTOR 5 ALLOSTERIC SITE.

E. D. Nguyen,[1] K. J. Gregory,[2] C. Malosh,[1] J. L. Mendenhall,[1] J. Z. Zic,[3] B. S. Bates,[1] M. J. Noetzel,[1] E. F. Squire,[1] E. M. Turner,[1] K. A. Emmitte,[1] S. R. Stauffer,[1] C. W. Lindsley,[1] J. Meiler,[1] J. Conn[1]; [1]Vanderbilt University, Nashville, TN, [2]Monash University, Parkville, Australia, [3]University of Notre Dame, South Bend, IN.

PII-034
WITHDRAWN

PII-035
EFFECT OF PLASMA MEMBRANE MONOAMINE TRANSPORTER GENOTYPES ON PHARMACOKINETICS OF METFORMIN.

J. Oh, J. Lee, H. Chung, J. Cho, S. Yoon, S. Shin, J. Chung; Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine, Seoul, Republic of Korea.

PII-036
FUNCTIONAL CHARACTERIZATION OF GENETIC VARIANTS IN THE *OCTN1* PROMOTER IN KOREANS.

H. Park, J. Choi; Ewha Womans University, Seoul, Republic of Korea.

Presenting author in bold.

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FRIDAY, MARCH 21, 2014

International Hall 7:30 am – 3:30 pm • Attended Posters 11:45 am – 1:15 pm

PII-037
IN VITRO GLUCURONIDATION OF OTS167.
J. Ramirez,[1] S. Mirkov,[1] Y. Matsuo,[2] M. J. Ratain[1]; [1]University of Chicago, Chicago, IL, [2]OncoTherapy Science, Inc., Kawasaki City, Kanagawa, Japan.

PII-038
CYTOCHROME P450S INVOLVED IN THE METABOLISM OF ARACHIDONIC ACID IN HUMAN PLATELETS AND THEIR POSSIBLE INFLUENCES ON BLOOD HOMEOSTASIS.
Y. B. Jarrar,[1] S. Cho,[1] K. Oh,[1] D. Kim,[1] **J. Shin,**[2] S. Lee[1]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Busan, Republic of Korea, [2]Department of Pharmacology and PharmacoGenomics Research Center, Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Republic of Korea.

PII-039
IDENTIFICATION OF BCRP, URAT1, GLUT9, AND NPT4 RESPONSIBLE FOR TRANSPORT OF ALLOPURINOL AND OXYPURINOL USING *X. LAEVIS* OOCYTES.
H. Shin, M. Kim, K. Oh, S. Lim, J. Kim, K. Oh, N. Abdalla, D. Kim, J. Shin; Inje University, Busan, Republic of Korea.

PII-040
AN INTEGRATED APPROACH TO ASSESS THE IMPACT OF GASTRIC PH ON GDC-0941 AND GDC-0980 PHARMACOKINETICS.
G. S. Smelick, G. Dalziel, L. Salphati, J. Pellett, J. Li, B. Dean, X. Ding, S. Holden, J. Lauchle, J. Pang, J. Jin, T. Lu, N. Budha, M. Dresser, J. A. Ware; Genentech, South San Francisco, CA.

PII-041
LACK OF AN EFFECT OF THE ABCB1 C3435T (RS1045642) POLYMORPHISM ON THE PHARMACOKINETICS OF EDOXABAN, A NOVEL FACTOR XA INHIBITOR.
A. Vandell,[1] J. Lee,[1] M. Shi,[1] I. Rubets,[2] K. Brown,[1] J. R. Walker[1]; [1]Daiichi Sankyo Pharma Development, Edison, NJ, [2]Pharsight Consulting Services, Montreal, QC, Canada.

PII-042
ASSOCIATION BETWEEN GENETIC VARIATIONS OF MERTK AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE.
J. Choi; Ewha Womans University, Seoul, Republic of Korea.

Oncology (ONC)

PII-043
POPULATION PHARMACOKINETIC ANALYSIS OF CARFILZOMIB IN PATIENTS WITH RELAPSED OR RELAPSED AND REFRACTORY MULTIPLE MYELOMA OR ADVANCED SOLID TUMORS.
R. Gunawan,[1] A. Badros,[2] K. Papadopoulos,[3] D. Siegel,[4] S. Jagannath,[5] R. Vij,[6] R. Niesvizky,[7] Y. Ou,[8] Z. Wang,[8] K. Rajangam,[8] C. Garnett[1]; [1]Pharsight Consulting Services, Cary, NC, [2]University of Maryland, Baltimore, MD, [3]South Texas Accelerated Research Therapeutics (START), San Antonio, TX, [4]John Theurer Cancer Center, Hackensack, NJ, [5]Mt. Sinai Medical Center, New York, NY, [6]Washington University School of Medicine, St. Louis, MO, [7]Weill Cornell Medical College, New York, NY, [8]Onyx Pharmaceuticals, Inc., South San Francisco, CA.

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POSTER SESSION II
FRIDAY, MARCH 21, 2014

International Hall 7:30 am – 3:30 pm • Attended Posters 11:45 am – 1:15 pm

PII-044
A TUMOR GROWTH INHIBITION MODEL BASED ON M-PROTEIN LEVELS IN PATIENTS WITH RELAPSED/ REFRACTORY MULTIPLE MYELOMA FOLLOWING SINGLE-AGENT CARFILZOMIB USE.
F. Jonsson,[1] D. Siegel,[2] S. Jagannath,[3] R. Vij,[4] A. Badros,[5] Y. Ou,[6] L. Claret,[1] E. Kavalerchik,[6] R. Bruno[1]; [1]Pharsight, a Certara Company, St. Louis, MO, [2]John Theurer Cancer Center, Hackensack, NJ, [3]Mount Sinai Medical Center, New York, NY, [4]Washington University School of Medicine, St. Louis, MO, [5]Greenebaum Cancer Center, University of Maryland, Baltimore, MD, [6]Onyx Pharmaceuticals, Inc., South San Francisco, CA.

PII-045
ETHNIC SENSITIVITY ASSESSMENT FOR AN ADC, TRASTUZUMAB EMTANSINE (KADCYLA®).
C. Li,[1] B. Wang,[1] D. Lu,[1] J. Y. Jin,[1] C. Gao,[2] K. Matsunaga,[3] Y. Igawa,[3] S. Girish[1]; [1]Genentech, South San Francisco, CA, [2]Quantitative Solutions, Menlo Park, CA, [3]Chugai Pharmaceutical Co, Tokyo, Japan.

PII-046
THE ROLE OF THE GLUCOCORTICOID RECEPTOR (GR) IN INHIBITING CHEMOTHERAPY-INDUCED APOPTOSIS IN HIGH-GRADE SEROUS OVARIAN CARCINOMA (HGS-OvCa).
E. Stringer, M. Skor, L. Zhao, K. Gwin, E. Lengyel, G. Fleming, S. Conzen; University of Chicago, Chicago, IL.

PII-047
POPULATION PHARMACOKINETIC MODELING OF SUNITINIB (SU) AND SU012662 IN GASTROINTESTINAL STROMAL TUMOR (GIST) AND RENAL CELL CARCINOMA (RCC) PATIENTS.
R. Khosravan,[1] G. M. Mugundu,[1] P. G. Casali,[2] B. I. Rini[3]; [1]Pfizer Inc., San Diego, CA, [2]Istituto Nazionale dei Tumori, Milan, Italy, [3]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH.

PII-048
POPULATION PHARMACOKINETIC-PHARMACODYNAMIC MODELING OF SUNITINIB (SU) IN GASTROINTESTINAL STROMAL TUMOR (GIST) AND RENAL CELL CARCINOMA (RCC) PATIENTS.
R. Khosravan,[1] G. M. Mugundu,[1] P. G. Casali,[2] B. I. Rini[3]; [1]Pfizer Inc., San Diego, CA, [2]Istituto Nazionale dei Tumori, Milan, Italy, [3]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH.

Pharmacometrics and Pharmacokinetics (PMK)

PII-049
A MODEL-BASED APPROACH TO CHARACTERIZE RISPERIDONE RELEASE, ABSORPTION, AND DISPOSITION AFTER ADMINISTRATION OF RBP-7000 IN SCHIZOPHRENIC PATIENTS.
M. Li,[1] C. Heidbreder,[2] P. Fudala,[2] A. Nasser[2]; [1]Virginia Commonwealth University, Richmond, VA, [2]Reckitt Benckiser Pharmaceuticals Inc., Richmond, VA.

PII-050
APPLICATION OF PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODEL IN PREDICTING PREGABALIN PHARMACOKINETICS (PK) IN PEDIATRIC POPULATIONS.
J. Liu, C. W. Alvey, M. L. Chew, D. Mann, V. Pitman, B. Corrigan; Pfizer, Groton, CT.

PII-051
WHERE TOP-DOWN MEETS BOTTOM-UP: COMBINED POPULATION (POPPK) AND PBPK APPROACHES TO EVALUATE THE IMPACT OF FOOD AND GASTRIC PH ON THE PHARMACOKINETICS OF GDC-0941.
T. Lu,[1] G. Fraczkiewicz,[2] L. Salphati,[1] N. Budha,[1] G. Dalziel,[1] G. S. Smelick,[1] J. D. Davis,[1] M. J. Dresser,[1] J. A. Ware,[1] J. Y. Jin[1]; [1]Genentech, South San Francisco, CA, [2]Simulations Plus, Lancaster, CA.

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PII-052
ESTIMATION OF PROTON-PUMP INHIBITIOR (PPI) EFFECT ON DACOMITINIB ABSORPTION AND RELATIVE BIOAVAILABILITY USING NON-LINEAR MIXED EFFECTS MODELING.
J. C. Masters,[1] N. Giri,[2] C. L. Bello,[2] T. Boutros,[2] Z. Goldberg,[2] A. Ruiz-Garcia[2]; [1]University of California, San Diego, San Diego, CA, [2]Pfizer Inc., San Diego, CA.

PII-053
PHARMACOMETRICS GUIDED DESIGN OF A PROOF OF CONCEPT (POC) STUDY FOR TOPICAL GLYCOPYRROLATE, AN ANTI-HYPERHIDROSIS AGENT.
S. Mehrotra,[1] V. D. Schmith,[2] T. Pene Dumitrescu,[2] J. Gobburu[1]; [1]Center for Translational Medicine, University of Maryland, Baltimore, MD, [2]Clinical Pharmacology Modeling and Simulation, GlaxoSmithKline, Research Triangle Park, NC.

PII-054
ASSESSMENT OF PHARMACOKINETIC INTERACTION BETWEEN PRADIGASTAT AND ATAZANAVIR OR PROBENECID IN HEALTHY SUBJECTS.
A. Mendonza,[1] D. Meyers,[1] P. Koo,[2] S. Neelakantham,[3] T. Majumdar,[2] S. Rebello,[2] G. Sunkara,[2] J. Chen[2]; [1]Novartis Institutes for BioMedical Research, Cambridge, MA, [2]Novartis Institutes for BioMedical Research, East Hanover, NJ, [3]Novartis Healthcare Pvt. Ltd., Hyderabad, India.

PII-055
POPULATION PHARMACOKINETICS AND OPTIMAL SAMPLING STRATEGIES FOR INDIVIDUALIZED MELPHALAN EXPOSURE PREDICTION IN MULTIPLE MYELOMA PATIENTS.
K. Mizuno,[1] M. Dong,[1] T. Fukuda,[1] A. J. Elias,[2] A. A. Vinks[1]; [1]Division of Clinical Pharmacology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]University of Cincinnati Cancer Institute, College of Medicine, University of Cincinnati, Cincinnati, OH.

PII-056
PHARMACOKINETICS AND PHARMACODYNAMICS OF GEMIGLIPTIN/METFORMIN SUSTAINED RELEASE FIXED-DOSE COMBINATION VERSUS SEPARATE FORMULATION.
S. Moon,[1] L. Ahn,[1] J. Oh,[1] J. Lee,[1] I. Jang,[1] H. Lee,[1] K. Yu,[1] J. Kim,[2] J. Jung,[2] J. Chung[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea, [2]LG Life Sciences, Ltd., Seoul, Republic of Korea.

PII-057
POPULATION PHARMACOKINETICS OF BETAHISTINE IN PATIENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).
G. Moorthy,[1] F. Sallee,[1] F. Zemlan,[2] L. Sallans,[1] P. Desai[1]; [1]University of Cincinnati, Cincinnati, OH, [2]P2D Biosciences, Cincinnati, OH.

PII-058
METAL ION CHELATION BY TIGECYCLINE EXPLAINS ATYPICAL NONLINEAR PLASMA PROTEIN BINDING BEHAVIOR.
J. K. Mukker, R. S. Singh, H. Derendorf; University of Florida, Gainesville, FL.

PII-059
POPULATION PHARMACOKINETIC/PHARMACODYNAMIC (PK/PD) MODELING OF DEPOT TESTOSTERONE CYPIONATE IN HEALTHY MALE SUBJECTS.
Y. Bi,[1] **D. Murry,**[1] M. Ellerby,[2] P. J. Perry[2]; [1]University of Iowa, Iowa City, IA, [2]Touro University, Vallejo, CA.

PII-060
USEFULNESS OF COVARIATE-BASED PK MODELS OF ENOXAPARIN (ENX) IN PROVIDING DOSING RECOMMENDATIONS IN OBESE AND RENALLY IMPAIRED (RI) PATIENTS (PTS.).
A. M. Nader; Qatar University, Doha, Qatar.

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PII-061
A MODEL-BASED APPROACH TO EVALUATE THE PK AND μ-OPIOID RECEPTOR OCCUPANCY OF RBP-6000, A ONCE MONTHLY DEPOT FORMULATION OF BUPRENORPHINE.
A. Nasser,[1] C. Heidbreder,[1] P. J. Fudala,[1] H. Sutton,[1] B. Zheng,[1] M. K. Greenwald[2]; [1]Reckitt Benckiser Pharmaceuticals, Richmond, VA, [2]Wayne State University, Detroit, MI.

PII-062
ADDITIVITY VS. SYNERGISM: UNDERSTANDING THE CONTRIBUTION OF DABRAFENIB AND TRAMETINIB COMBINATION IN MELANOMA.
N. Nebot,[1] K. Patel,[2] D. Ouellet[1]; [1]GlaxoSmithKline, Research Triangle Park, NC, [2]GlaxoSmithKline, Upper Providence, PA.

PII-063
POPULATION PHARMACOKINETICS OF DESVENLAFAXINE: PHARMACOKINETICS IN KOREAN VS. US POPULATIONS.
A. Nichols,[1] S. Liao[2]; [1]Pfizer, Collegeville, PA, [2]PharMax Research, Newport Beach, CA.

PII-064
INTERACTION STUDY BETWEEN SELEXIPAG, A PROSTACYCLIN RECEPTOR AGONIST, AND LOPINAVIR/RITONAVIR IN HEALTHY MALE SUBJECTS.
S. Niglis,[1] S. Bruderer,[1] **P. Kaufmann,**[1] A. Halabi,[2] J. Dingemanse[1]; [1]Actelion Pharmaceuticals Ltd., Allschwil, Switzerland, [2]Clinical Research Services GmbH, Kiel, Germany.

PII-065
POPULATION PHARMACOKINETICS AND PHARMACODYNAMICS OF ETOMIDATE IN CHINESE ADULTS.
J. Niu,[1] S. Ren,[2] S. Wang,[2] M. Dong,[3] R. Venkatasubramanian,[3] S. Sadhasivam,[3] A. A. Vinks,[3] M. Zhang[1]; [1]Shanghai Children's Medical Centre, Shanghai, China, [2]Renji Hospital, Shanghai, China, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PII-066
CLINICAL DOSE PREDICTION FOR ALBUMIN-BINDING DOMAIN ANTIBODY WITH LONG-DURATION GLP-1 ACTION, GSK2374697, INTENDED FOR USE IN T2DM AND OBESITY.
R. L. O'Connor-Semmes, M. A. Paulik, A. E. Acker; GlaxoSmithKline, Research Triangle Park, NC.

PII-067
PHARMACOKINETICS (PK) OF EDOXABAN, A NOVEL ORAL ANTICOAGULANT (NOAC), WHEN DOSED ALONE OR FOLLOWING SWITCHING FROM DABIGATRAN OR RIVAROXABAN.
D. Parasrampuria,[1] D. Weilert,[2] J. Maa,[3] L. He,[1] M. Shi,[1] K. Brown[1]; [1]Daiichi Sankyo Pharma Development, Edison, NJ, [2]Quintiles, Overland Park, KS, [3]Daiichi Sankyo, Inc., Parsippany, NJ.

PII-068
NOVEL *IN VITRO* TARGET-SITE DRUG DISPOSITION (TSDD)/PHARMACODYNAMIC (PD) MODEL FOR 5-HYDROXYMETHYL FURFURAL (5-HMF) IN HUMAN WHOLE BLOOD.
A. Parikh, J. Venitz; Virginia Commonwealth University, Richmond, VA.

PII-069
COMPARATIVE PHARMACOKINETICS OF FDC TABLET VERSUS CO-ADMINISTRATION OF TELMISARTAN/S-AMLODIPINE IN HEALTHY ADULT SUBJECTS.
S. Park,[1] J. Ghim,[1] M. Oh,[1] E. Shim,[1] Y. Sun,[2] J. Shon,[1] J. Lim,[3] J. Shin,[1] **E. Kim[2];** [1]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Busan, Republic of Korea, [2]Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Republic of Korea, [3]Chong Kun Dang Pharmaceutical Corp., Seoul, Republic of Korea.

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PII-070
PHARMACOKINETIC AND BIOEQUIVALENCE STUDY OF TWO DIFFERENT FILM-COATED IMATINIB TABLET FORMULATIONS OF TWO DIFFERENT STRENGTHS IN HEALTHY VOLUNTEERS.
J. Park, H. Lee, S. Seong, J. Lee, S. Park, M. Gwon, Y. Yoon; Clinical Trial Center, Kyungpook National University Hospital, Daegu, Republic of Korea.

PII-071
TYPE II DIABETES INCREASES HEPATIC CYP2C29 ACTIVITY AND EXPRESSION IN MOUSE.
D. Patoine,[1] S. Pilote,[1] M. Petit,[1] B. Drolet,[2] C. Simard[2]; [1]CRIUCPQ, Quebec, QC, Canada, [2]Faculté de Pharmacie, Université Laval, Quebec, QC, Canada.

PII-072
SIMULATIONS TO HARNESS THE POWER OF [14C] TRACING BY ACCELERATOR MASS SPECTROMETRY (AMS) TO DETECT [14C]UMECLIDINIUM FOLLOWING DERMAL DOSING TO HUMANS.
T. Pene Dumitrescu,[1] L. Santos,[1] S. Hughes,[2] A. Pereira,[2] E. Hussey,[1] P. Charlton,[1] V. D. Schmith[1]; [1]GlaxoSmithKline, Research Triangle Park, NC, [2]GlaxoSmithKline, Ware, United Kingdom.

PII-073
POPULATION PHARMACOKINETICS OF TENOFOVIR IN HIV-HBV COINFECTED PATIENTS.
B. Punyawudho,[1] A. Avihingsanon,[2] N. Thammajaruk,[2] P. Thongpeang,[2] D. Burger,[3] K. Ruxrungtham[4]; [1]Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand, [2]HIV-NAT Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [3]Radboud University Nijmegen Medical Center & Nijmegen Institute for Infection, Inflammation, Nijmegen, Netherlands, [4]HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand.

PII-074
INVESTIGATION OF CLINICAL AME CHARACTERISTICS OF THE PI3K INHIBITORS, GDC-0941(PICTILISIB) AND GDC-0980: A TALE OF TWO ANTI-CANCER DRUG CANDIDATES.
E. L. Reyner,[1] S. Ma,[1] S. Holden,[1] L. Salphati,[1] T. Lu,[1] J. Jin,[1] G. Dalziel,[1] J. Pellett,[1] M. Regalado-Dell,[1] D. Amin,[1] J. Huang,[1] X. Ding,[1] A. Kim,[1] H. Shimizu,[1] N. Siebers,[2] L. Joas,[2] S. Wills,[2] J. McKnight,[2] Y. Chen,[1] G. Smelick,[1] M. Dresser,[1] J. Ware[1]; [1]Genentech, Inc., South San Francisco, CA, [2]Covance, Madison, WI.

PII-075
SAFETY AND PHARMACOKINETIC EVALUATION OF MB12066 AFTER SINGLE ORAL ADMINISTRATION IN HEALTY MALE VOLUNTEERS.
S. Rhee, S. Yoon, S. Park, I. Jang, K. Yu, S. Yoon, J. Chung, S. Shin; Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PII-076
INFLUENCE OF SIMVASTATIN ON AMLODIPINE'S PHARMACODYNAMICS EFFECTS IN HEALTHY MALE KOREANS.
H. Roh,[1] H. Son,[2] D. Lee,[2] K. Park[2]; [1]Yonsei University College of Medicine, Department of Pharmacology, Supported by Brain Korea 21 Project for Medical Science, Yonsei University, Seoul, Republic of Korea, [2]Yonsei University College of Medicine, Department of Pharmacology, Seoul, Republic of Korea.

PII-077
A WINDOWS POPULATION PK/PD MODELING ENVIRONMENT FOR NONMEM.
M. Ruppert, S. Zeiser, P. van den Berg, K. Bol, E. Spaans; Kinesis Pharma, Breda, Netherlands.

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PII-078

POPULATION PHARMACOKINETICS OF FLUDARABINE (F-ARA-A) IN NON-MYELOABLATIVE HEMATOPOIETIC STEM CELL TRANSPLANT (HCT) PATIENTS.

K. Sanghavi,[1] P. Jacobson,[1] J. Long-Boyle,[2] R. Brundage,[1] M. Kirsten[1]; [1]University of Minnesota, Minneapolis, MN, [2]Univerisity of California, San Fransico, CA.

PII-079

STEADY-STATE RED BLOOD CELL AND PLASMA FOLATE LEVELS ACHIEVED WITH 5 MG VS. 1.1 MG FOLIC ACID IN PRENATAL MULTIVITAMINS AMONG PREGNANT WOMEN.

M. Shere, B. Kapur, D. O'Connor, G. Koren; Hospital for Sick Children, Toronto, ON, Canada.

PII-080

MONTE CARLO SIMULATION TO DETERMINE THE EFFECT OF ATYPICAL NONLINEAR PLASMA PROTEIN BINDING ON CLINICAL BREAKPOINT OF TIGECYCLINE.

R. S. Singh, J. K. Mukker, H. Derendorf; University of Florida, Gainesville, FL.

PII-081

A SYSTEMS PHARMACOLOGY MODEL TO CHARACTERIZE THE EFFECT OF BLINATUMOMAB IN PATIENTS WITH ADULT B-PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL).

I. Singh,[1] T. Yuraszeck,[1] M. Klinger,[2] M. Reed,[3] C. Friedrich,[3] R. Kumar,[3] S. Pagano,[3] M. Zhu[1]; [1]Amgen Inc., Thousand Oaks, CA, [2]Amgen Research (Munich) GmbH, Munich, Germany, [3]Rosa & Co., San Carlos, CA.

PII-082

PHARMACOKINETICS OF LOWER-DOSE INDOMETHACIN SUBMICRON PARTICLE CAPSULES 20 AND 40 MG COMPARED WITH INDOMETHACIN 50 MG CAPSULES IN HEALTHY VOLUNTEERS.

K. Olugemo,[1] **D. Solorio,**[2] C. Sheridan,[2] C. Young[2]; [1]Questcor Pharmaceuticals.Inc, Ellicott City, MD, [2]Iroko Pharmaceuticals, Philadelphia, PA.

PII-083

ABSENCE OF A CLINICALLY SIGNIFICANT PHARMACOKINETIC INTERACTION BETWEEN TELMISARTAN AND ROSUVASTATIN, AND DEVELOPMENT OF A BIOEQUIVALENT FIXED-DOSE COMBINATION.

M. Son,[1] Y. Kim,[1] D. Chae,[1] D. Lee,[2] J. Gug,[1] S. Jang,[3] J. Seo,[4] Y. Park,[4] S. Nam,[4] M. Kim,[5] K. Park[2]; [1]Yonsei University College of Medicine, Brain Korea 21 Plus Project for Medical Science, Seoul, Republic of Korea, [2]Yonsei University College of Medicine, Seoul, Republic of Korea, [3]Department of Clinical Research and Pharmacovigilance, Seoul, Republic of Korea, [4]Yuhan Research Institute, Yuhan Corporation, Seoul, Republic of Korea, [5]Clinical Pharmacology Unit, Chonbuk National University Hospital, Jeonju-si, Jeollabuk-do, Republic of Korea.

PII-084

PHARMACOKINETICS OF COLISTIMETHATE SODIUM (CMS) AND COLISTIN AFTER REPEATED INHALATION OF CMS IN ADULTS, ADOLESCENTS AND CHILDREN WITH CYSTIC FIBROSIS.

S. Su,[1] C. Chen,[1] P. Ghahramani,[1] T. Riccobene,[1] P. Turay[2]; [1]Forest Research Institute, Jersey City, NJ, [2]Forest Laboratories UK Ltd, Dartford, United Kingdom.

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PII-085
A STUDY OF THE EFFECTS OF INHIBITION OF CYP3A4 BY KETOCONAZOLE (K) AND CYP2C8 BY GEMFIBROZIL (G) ON THE PHARMACOKINETICS DABRAFENIB (D).
B. Suttle,[1] K. Grossmann,[2] L. Richards-Peterson,[3] D. Ouellet,[1] G. Aktan,[3] M. Gordon,[4] P. LoRusso,[5] J. R. Infante,[6] S. Sharma,[2] K. Kendra,[7] M. Patel,[8] S. Pant,[9] H. Arkenau,[10] M. R. Middleton,[11] S. C. Blackman,[12] S. W. Carson[1]; [1]GlaxoSmithKline, Research Triangle Park, NC, [2]Huntsman Cancer Institute University of Utah, Salt Lake City, UT, [3]GlaxoSmithKline, Collegeville, PA, [4]Pinnacle Oncology, Scottsdale, AZ, [5]Karmanos Cancer Institute, Wayne State University, Detroit, MI, [6]Tennessee Oncology, Nashville, TN, [7]The Ohio State University, Columbus, OH, [8]Sarah Cannon Research Institute, Sarasota, FL, [9]Sarah Cannon Research Institute, Oklahoma City, OK, [10]Sarah Cannon Research Institute, London, United Kingdom, [11]NHS Department of Oncology, Headington, Oxford, United Kingdom, [12]Seattle Genetics, Seattle, WA.

PII-086
DAPAGLIFLOZIN TWICE DAILY OR ONCE DAILY: EFFECT ON PHARMACOKINETICS AND URINARY GLUCOSE EXCRETION IN HEALTHY SUBJECTS.
W. Tang,[1] S. Reele,[2] J. E. Hamer-Maansson,[1] S. Parikh,[1] T. W. de Bruin[1]; [1]AstraZeneca Pharmaceuticals, Wilmington, DE, [2]Reele Consulting, LLC, Scottsville, VA.

PII-087
PHARMACOKINETICS OF OMARIGLIPTIN (MK-3102), A ONCE-WEEKLY DIPEPTIDYL PEPTIDASE-IV (DPP-4) INHIBITOR, IN PATIENTS WITH RENAL IMPAIRMENT.
D. A. Tatosian,[1] S. Glasgow,[1] M. Caceres,[1] J. Grenier,[2] B. DeGroot,[2] T. Ward,[2] A. Johnson-Levonas,[1] L. George,[1] K. C. Lasseter,[3] T. C. Marbury,[4] E. Kauh[1]; [1]Merck Sharp & Dohme Corp., Whitehouse Station, NJ, [2]Celerion, Lincoln, NE, [3]Clinical Pharmacology of Miami, Inc., Miami, FL, [4]Orlando Clinical Research Center, Orlando, FL.

PII-088
EFFECT OF MULTIPLE DOSES OF ISAVUCONAZOLE ON THE PHARMACOKINETICS OF ORAL CONTRACEPTIVE WITH ETHINYL ESTRADIOL AND NORETHINDRONE IN HEALTHY SUBJECTS.
R. Townsend,[1] T. Yamazaki,[1] D. Kowalski,[1] C. Lademacher,[1] H. Pearlman,[1] D. Rammelsberg,[2] A. Desai[1]; [1]Astellas, Northbrook, IL, [2]Ranstad Pharma, Deerfield, IL.

PII-089
COMPARISON OF INHIBITORY DURATION OF GRAPEFRUIT JUICE ON ORGANIC ANION-TRANSPORTING POLYPEPTIDE AND CYTOCHROME P450 3A4.
S. Uchida,[1] S. Tanaka,[1] S. Miyakawa,[2] N. Inui,[2] K. Takeuchi,[2] N. Namiki,[1] H. Watanabe; [1]University of Shizuoka, Shizuoka, Japan, [2]Hamamatsu University School of Medicine, Hamamatsu, Japan.

PII-090
NOVEL BAYESIAN MODEL BASED DETERMINATION OF DELAYED GASTRIC EMPTYING.
G. Vlasakakis,[1] L. S. Vasist Johnson,[2] M. A. Young,[2] G. E. Dukes[2]; [1]GlaxoSmithKline, London, United Kingdom, [2]GlaxoSmithKline, Research Triangle Park, NC.

PII-091
DEVELOPMENT AND APPLICATION OF SYSTEMS PHARMACOLOGY MODEL TO PREDICT NAUSEA RESULTED FROM ADMINISTRATION OF GLP-1 AGONISTS.
V. Voronova, O. Demin Jr, S. Smirnov, O. Demin; Institute for Systems Biology SPb, Moscow, Russian Federation.

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PII-092
POPULATION PHARMACOKINETICS OF MAVRILIMUMAB IN RHEUMATOID ARTHRITIS PATIENTS.
C. Wu,[1] B. Wang,[1] B. Yang,[2] K. Kowalski,[2] P. Ryan,[3] A. Godwood,[4] D. Saurigny,[4] D. Close,[4] L. Roskos[3]; [1]MedImmune, Hayward, CA, [2]Ann Arbor Pharmacometrics Group, Ann Arbor, MI, [3]MedImmune, Gaithersburg, MD, [4]MedImmune, Cambridge, United Kingdom.

PII-093
EVALUATION OF THE EFFECTS OF BLINATUMOMAB-MEDIATED CYTOKINE ELEVATIONS ON CYTOCHROME P450 ENZYMES USING A PHYSIOLOGY-BASED PHARMACOKINETIC (PBPK) MODEL.
Y. Xu,[1] Y. Hijazi,[2] A. Wolf,[2] B. Wu,[1] Y. Sun,[1] M. Zhu[1]; [1]Amgen Inc., Thousand Oaks, CA, [2]Amgen Research (Munich) GmbH, Munich, Germany.

PII-094
INVESTIGATION OF DAPAGLIFLOZIN INHIBITION EFFECT ON GLUCOSE REABSORPTION USING SYSTEMS PHARMACOLOGY APPROACH.
T. Yakovleva, O. Demin Jr, O. Demin; Institute for Systems Biology SPb, Moscow, Russian Federation.

PII-095
EFFECT OF MULTIPLE DOSES OF ISAVUCONAZOLE ON THE PHARMACOKINETICS OF METHOTREXATE IN HEALTHY SUBJECTS.
T. Yamazaki,[1] A. Desai,[1] D. Kowalski,[1] C. Lademacher,[1] H. Pearlman,[1] D. Rammelsberg,[2] R. Townsend[1]; [1]Astellas, Northbrook, IL, [2]Ranstad Pharma, Deerfield, IL

PII-096
PHARMACOKINETIC, PHARMACODYNAMIC AND TOLERABILITY ASSESSMENTS OF GC1113 AFTER SINGLE INTRAVENOUS OR SUBCUTANEOUS ADMINISTRATION IN HEALTHY VOLUNTEERS.
J. Yoon, H. Han, A. Kim, J. Lee, K. Yu, I. Jang, **H. Lee;** Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PII-097
PHARMACOKINETICS, PHARMACODYNAMICS AND TOLERABILITY OF LC350189, A NOVEL XANTHINE OXIDASE INHIBITOR, IN HEALTHY SUBJECTS.
S. Yoon, S. Moon, K. Jang, I. Jang, K. Lim, K. Yu; Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PII-098
POPULATION PHARMACOKINETICS OF CAFFEINE AND ITS METABOLITES IN PREGNANT WOMEN.
T. Yu, K. Schoen, C. Tak, E. A. Clark, M. W. Varner, M. G. Spigarelli, C. M. Sherwin; University of Utah, Salt Lake City, UT.

PII-099
SAFETY, TOLERABILITY, PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) OF SINGLE DOSE OF ASP4058 IN HEALTHY MALES AND FEMALES.
W. Zhang,[1] J. Keirns,[1] C. Howieson,[1] U. Valluri,[1] K. Lasseter,[2] R. Stoltz,[3] G. Nomikos[1]; [1]Astellas Pharma Global Development, Inc., Northbrook, IL, [2]Clinical Pharmacology of Miami, Inc., Miami, FL, [3]Covance Evansville CRU, Evansville, IN.

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PII-100

DINACICLIB AND DINACICLIB GLUCURONIDE PHARMACOKINETICS IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA.

Y. Zhao,[1] Y. Ling,[2] S. Kolli,[1] M. Poi,[3] L. J. Schaaf,[3] A. J. Johnson,[4] J. C. Byrd,[4] J. A. Jones,[5] M. A. Phelps[6]; [1]Division of Pharmaceutics, College of Pharmacy, The Ohio State University, Columbus, OH, [2]Pharmacoanalytical Shared Resources, The Ohio State University, Columbus, OH, [3]Comprehensive Cancer Center, The Ohio State University, Columbus, OH, [4]Division of Medicinal Chemistry, College of Pharmacy, Comprehensive Cancer Center and Division of Hematology, Department of Internal Medicine, The Ohio State University, Columbus, OH, [5]Division of Hematology, Department of Internal Medicine, The Ohio State University, Columbus, OH, [6]Division of Pharmaceutics, College of Pharmacy and Comprehensive Cancer Center, The Ohio State University, Columbus, OH.

PII-101

INHIBITOR MODELS IN PREDICTING DRUG-DRUG INTERACTIONS USING PBPK: A CASE STUDY WITH FLUVOXAMINE .

S. Zheng,[1] J. Snoeys,[2] S. Schmidt,[1] L. J. Lesko,[1] P. Zhao[3]; [1]Center for Pharmacometrics and Systems Pharmacology, University of Florida, Orlando, FL, [2]Janssen Pharmaceutical Companies of Johnson & Johnson, Beerse, Belgium, [3]Division of Pharmacometrics, Office of Clinical Pharmacology at US Food and Drug Administration, Silver Spring, MD.

PII-102

A MODEL-BASED APPROACH TO PREDICT PLASMA/BRAIN COCAINE LEVELS FOLLOWING RBP-8000, A DOUBLE MUTANT BACTERIAL COCAINE ESTERASE; ADMINISTRATION IN HUMANS.

B. Zheng, Y. Liu, C. Heidbreder, P. J. Fudala, A. Nasser; Reckitt Benckiser Pharmaceuticals Inc., Richmond, VA.

PII-103

MULTIPLE POLYMORPHISM EFFECTS IDENTIFIED ON THE PHARMACOKINETICS OF SIMVASTATIN AND SIMVASTATIN ACID USING A POPULATION MODELLING APPROACH.

N. Tsamandouras,[1] G. Dickninson,[2] Y. Guo,[2] S. Hall,[2] A. Rostami-Hodjegan,[1] A. Galetin,[1] L. Aarons[1]; [1]Centre for Applied Pharmacokinetic Research, University of Manchester, Manchester, United Kingdom, [2]Eli Lilly and Company, Indianapolis, IN.

PII-104

REDUCED PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODEL OF REPAGLINIDE: IMPACT OF OATP1B1 AND CYP2C8 GENOTYPE ON THE PREDICTION OF DDI RISK.

M. Gertz,[1] **N. Tsamandouras,**[2] L. Aarons,[2] A. Galetin[2]; [1]F. Hoffmann-La Roche, Basel, Switzerland, [2]Centre for Applied Pharmacokinetic Research, University of Manchester, Manchester, United Kingdom.

PII-105

DIFFERENCES IN NOCTURNAL BLOOD PRESSURE DIPPING OBSERVED IN PATIENTS SWITCHED BETWEEN AVAILABLE NIFEDIPINE OSMOTIC DELIVERY FORMULATIONS.

P. Pollak, R. J. Herman, K. B. Zarnke; University of Calgary, Calgary, AB, Canada.

Presenting author in bold.

POSTER SESSION II
FRIDAY, MARCH 21, 2014

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PII-106
LARGE GEOGRAPHIC DIFFERENCES IN PREVALENCE OF HYPERTHYROIDISM OBSERVED IN PATIENTS EXPOSED TO AMIODARONE.
P. Pollak,[1] N. Vijayaratnam[2]; [1]University of Calgary, Calgary, AB, Canada, [2]University of Alberta, Edmonton, AB, Canada.

PII-107
MODELING AND SIMULATIONS OF ECULIZUMAB IN PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH) AND ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS) PATIENTS.
C. Lathia,[1] N. Kassir,[2] M. S. Mouksassi,[2] B. Jayaraman,[2] J. F. Marier,[2] C. L. Bedrosian[2]; [1]Alexion Pharmaceuticals, Cheshire, CT, [2]Pharsight, Montreal, QC, Canada.

PII-108
PK/PD MODELING OF ECULIZUMAB AND FREE COMPLEMENT COMPONENT PROTEIN C5 IN PEDIATRIC AND ADULT PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS).
C. Lathia,[1] N. Kassir,[2] M. S. Mouksassi,[2] B. Jayaraman,[2] J. F. Marier,[2] C. L. Bedrosian[1]; [1]Alexion Pharmaceuticals, Cheshire, CT, [2]Pharsight, Montreal, QC, Canada.

Special Populations (SPO)

PII-109
SAFETY, TOLERABILITY AND PHARMACOKINETICS (PK) OF SINGLE DOSE INTRAVENOUS MOXIFLOXACIN IN PEDIATRIC PATIENTS.
J. Lettieri,[1] K. Vanevski,[1] H. Stass,[2] C. Rotolo,[1] J. S. Bradley,[3] L. James,[4] J. Sullivan,[5] A. Arrieta[6]; [1]Bayer HealthCare, Whippany, NJ, [2]Bayer HealthCare, Wuppertal, Germany, [3]Rady Children's Hospital San Diego, San Diego, CA, [4]Department of Pediatrics, University of Arkansas for Medical Science, Little Rock, AR, [5]University of Louisville/Kosair Children's Hospital, Louisville, KY, [6]Children's Hospital of Orange County, Orange, CA.

PII-110
POPULATION PHARMACOKINETIC ANALYSIS OF TEMSIROLIMUS IN CHILDREN.
T. Mizuno,[1] T. Fukuda,[1] M. Fouladi,[1] S. M. Blaney,[2] J. P. Perentesis,[1] A. A. Vinks[1]; [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Baylor College of Medicine, Houston, TX.

PII-111
DECREASED ACTIVITY OF CYP1A2 ENZYME IN CHILDREN WITH KWASHIORKOR USING THE CAFFEINE BREATH TEST.
K. A. Oshikoya,[1] K. Smith[2]; [1]Academic Division of Child Health, University of Nottingham in Derby, Derby, United Kingdom, [2]Clinical Physiology Department, University of Nottingham in Derby, Derby, United Kingdom.

PII-112
A PHARMACOMETRIC APPROACH TO INVESTIGATE OPTIMAL SAMPLING OF ANTIPSYCHOTIC MEDICINES.
V. Perera,[1] G. Mo,[1] M. J. Dolton,[2] V. J. Carr,[3] J. Xu,[4] A. Forrest[1]; [1]Faculty of Pharmacy and Pharmaceutical Sciences, State University of New York at Buffalo, Buffalo, NY, [2]Faculty of Pharmacy, The University of Sydney, Sydney, Australia, [3]School of Psychiatry, University of New South Wales, Sydney, Australia, [4]Department of Psychiatry, Western New York Veteran Affairs Hospital, Buffalo, NY.

PII-113
PHARMACOKINETICS OF DARBEPOETIN ALFA IN THE TREATMENT OF NEONATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY.
J. K. Roberts, C. M. Sherwin, J. Beachy, R. M. Ward, M. Baserga, M. G. Spigarelli; University of Utah, Salt Lake CIty, UT.

Presenting author in bold.

POSTER SESSION II
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PII-114
ASSESSMENT OF CYP2C19 PHENOTYPE IN CHILDREN USING THE 13C-PANTOPRAZOLE BREATH TEST.
V. Shakhnovich,[1] S. Abdel-Rahman,[1] M. Buri,[2] J. Weigel,[1] R. E. Pearce,[1] A. Gaedigk,[1] G. L. Kearns[1]; [1]Children's Mercy Hospitals and Clinics, Kansas City, MO, [2]Creighton University School of Medicine, Omaha, NE.

PII-115
OPTIMAL VANCOMYCIN DOSE IN NEONATES AND INFANTS WITH CONGENITAL HEART DISEASE: DEVELOPMENTAL TRAJECTORY WITHIN INDIVIDUALS.
Y. Shimamoto,[1] T. Fukuda,[2] C. Moon,[1] A. A. Vinks,[2] H. Ichikawa[1]; [1]National Cerebral and Cardiovascular Center, Osaka, Japan, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PII-116
APPLICATION OF MODELING AND SIMULATION IN DESIGNING A PEDIATRIC CLINICAL OXYCODONE TRIAL WITH D-OPTIMAL SAMPLING STRATEGY.
R. Venkatasubramanian,[1] M. Dong,[1] T. Fukuda,[1] M. L. Goodhead,[2] A. A. Vinks[1]; [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Pharmaceutical Project Solutions, Inc., Riverview, FL.

PII-117
THE ROLE OF GENETIC VARIANTS GSTA1 AND CYP39A1 AND ONTOGENESIS ON BUSULFAN CLEARANCE IN PEDIATRIC PATIENTS UNDERGOING HEMATOPOIETIC SCT.
M. ten Brink, T. van Bavel, J. J. Swen, T. van der Straaten, R. G. Bredius, A. C. Lankester, J. Zwaveling, H. Guchelaar; Leiden University Medical Center, Leiden, Netherlands.

PII-118
PHARMACOKINETICS OF TREOSULFAN IN PEDIATRIC PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION.
M. ten Brink,[1] O. Ackaert,[2] J. Zwaveling,[1] R. G. Bredius,[1] F. J. Smiers,[1] J. den Hartigh,[1] A. C. Lankester,[1] H. Guchelaar[1]; [1]Leiden University Medical Center, Leiden, Netherlands, [2]LAP&P Consultants, Leiden, Netherlands.

PII-119
PRESCRIBING PATTERNS IN OBESE PEDIATRIC PATIENTS IN AMBULATORY CARE IN THE UNITED STATES.
V. C. Ziesenitz,[1] J. D. Vaughns,[2] J. N. van den Anker,[3] M. E. Mazer-Amirshahi[3]; [1]Pediatric Cardiology, University Children's Hospital, Heidelberg, Germany and Division of Pediatric Clinical Pharmacology, Children's National Medical Center, Washington, DC, [2]Department of Anesthesia and Pain Medicine, Children's National Medical Center, Washington, DC, [3]Division of Pediatric Clinical Pharmacology, Children's National Medical Center, Washington, DC.

PII-120
OFF-LABEL USE OF CARDIOVASCULAR AGENTS IN PEDIATRIC AMBULATORY CARE IN THE UNITED STATES.
V. C. Ziesenitz,[1] M. Gorenflo,[2] J. N. van den Anker,[3] M. E. Mazer-Amirshahi[3]; [1]Department of Pediatric Cardiology, University Children's Hospital, Heidelberg, Germany and Division of Pediatric Clinical Pharmacology, Washington, DC, [2]Department of Pediatric Cardiology, University Children's Hospital, Heidelberg, Germany, [3]Division of Pediatric Clinical Pharmacology, Children's National Medical Center, Washington, DC.

Presenting author in bold.

LATE-BREAKING AND ENCORE ABSTRACT SESSION I

Thursday, March 20, 2014 • International Hall 7:30 am – 2:00 pm
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EI-001

GENETIC VARIANTS ASSOCIATED WITH WARFARIN DOSE IN AFRICAN-AMERICAN INDIVIDUALS: A GENOME-WIDE ASSOCIATION STUDY.

M. A. Perera,[1] L. H. Cavallari,[2] N. A. Limdi,[3] E. R. Gamazon,[1] A. Konkashbaev,[1] R. Daneshjou,[4] A. Pluzhnikov,[1] D. C. Crawford,[5] J. Wang,[3] N. Liu,[3] N. Tatonetti,[4] S. Bourgeois,[6] H. Takahashi,[7] Y. Bradford,[5] B. M. Burkley,[8] R. J. Desnick,[9] J. L. Halperin,[9] S. I. Khalifa,[10] T. Y. Langaee,[8] S. A. Lubitz,[11] E. A. Nutescu,[2] M. Oetjens,[5] M. H. Shahin,[8] S. R. Patel,[2] H. Sagreiya,[4] M. Tector,[12] K. E. Weck,[13] M. J. Rieder,[14] S. A. Scott,[15] A. H. Wu,[16] J. K. Burmester,[17] M. Wadelius,[18] P. Deloukas,[6] M. J. Wagner,[13] T. Mushiroda,[19] M. Kubo,[19] D. M. Roden,[5] N. J. Cox,[1] R. B. Altman,[4] T. E. Klein,[4] Y. Nakamura,[19] J. A. Johnson[8]; [1]University of Chicago, Chicago, IL, [2]University of Illinois, Chicago, Chicago, IL, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Stanford University, Stanford, CA, [5]Vanderbilt University, Nashville, TN, [6]Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Cambridge, United Kingdom, [7]Department of Biopharmaceutics, Meiji Pharmaceutical University, Tokyo, Japan, [8]University of Florida, Gainesville, FL, [9]Mount Sinai School of Medicine, New York, NY, [10]Qatar University, Doha, Qatar, [11]Massachusetts General Hospital, Boston, MA, [12]Aurora St Luke's Medical Center, Milwaukee, WI, [13]University of North Carolina at Chapel Hill, Chapel Hill, NC, [14]University of Washington, Seattle, WA, [15]Mount Sinai School of Medicine,, New York, NY, [16]University of California, San Francisco, San Francisco, CA, [17]Marshfield Clinic Research Foundation, Marshfield, WI, [18]Uppsala University, Uppsala, Sweden, [19]RIKEN Center for Genomic Medicine, Yokohama, Japan.
M.A. Perera: None. **L.H. Cavallari:** None. **N.A. Limdi:** None. **E.R. Gamazon:** None. **A. Konkashbaev:** None. **R. Daneshjou:** None. **A. Pluzhnikov:** None. **D.C. Crawford:** None. **J. Wang:** None. **N. Liu:** None. **N. Tatonetti:** None. **S. Bourgeois:** None. **H. Takahashi:** None. **Y. Bradford:** None. **B.M. Burkley:** None. **R.J. Desnick:** None. **J.L. Halperin:** None. **S.I. Khalifa:** None. **T.Y. Langaee:** None. **S.A. Lubitz:** None. **E.A. Nutescu:** None. **M. Oetjens:** None. **M.H. Shahin:** None. **S.R. Patel:** None. **H. Sagreiya:** None. **M. Tector:** None. **K.E. Weck:** 2. I am a paid consultant/employee for Gentris Corporation. **M.J. Rieder:** None. **S.A. Scott:** None. **A.H. Wu:** None. **J.K. Burmester:** 4. I hold a patent for CYP4F2 use for warfarin dosing. **M. Wadelius:** None. **P. Deloukas:** None. **M.J. Wagner:** None. **T. Mushiroda:** None. **M. Kubo:** None. **D.M. Roden:** None. **N.J. Cox:** None. **R.B. Altman:** 2. I am a paid consultant/employee for Personalis. 5. I am a significant stockholder for Personalis. **T.E. Klein:** None. **Y. Nakamura:** None. **J.A. Johnson:** None.

BACKGROUND

VKORC1 and CYP2C9 are important contributors to warfarin dose variability, but explain less variability for individuals of African descent than for those of European or Asian descent. We aimed to identify additional variants contributing to warfarin dose requirements in African Americans via a genome-wide association study.

METHODS

Samples from African-American adults on a stable warfarin maintenance dose were obtained at International Warfarin Pharmacogenetics Consortium (IWPC) sites and the University of Alabama at Birmingham. An independent replication cohort was also obtained through the IWPC. We did a stepwise conditional analysis, conditioning first for VKORC1 -1639G→A, followed by the composite genotype of CYP2C9*2 and CYP2C9*3.

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RESULTS

The discovery cohort contained 533 participants and the replication cohort 432 participants. After the prespecified conditioning in the discovery cohort, we identified a novel association at a single nucleotide polymorphism (SNP) in the CYP2C cluster on chromosome 10 (rs12777823) that reached genome-wide significance ($p=1.51\times10^{-8}$). This association was confirmed in the replication cohort ($p=5.04\times10^{-5}$); with a combined p value of 4.5×10^{-12}. Individuals heterozygous for the rs12777823 A allele need a dose reduction of 6.92 mg/week and those homozygous required 9.34 mg/week reduction. Regression analysis showed that the addition of rs12777823 significantly improves warfarin dose variability explained by the IWPC dosing algorithm (21% relative improvement).

CONCLUSION

A novel CYP2C SNP exerts a clinically relevant effect on warfarin dose in African Americans, independent of CYP2C9*2 and CYP2C9*3. Incorporation of this SNP into pharmacogenetic dosing algorithms may improve warfarin dose prediction in this population.

EI-002

PHARMACOGENOMIC ASSOCIATION OF NON-SYNONYMOUS SNPS IN SIGLEC12, A1BG AND THE SELECTIN REGION AND CARDIOVASCULAR OUTCOMES.

C. W. McDonough,[1] Y. Gong,[1] S. Padmanabhan,[2] B. Burkley,[1] T. Y. Langaee,[1] O. Melander,[3] C. J. Pepine,[1] A. F. Dominiczak,[2] R. M. Cooper-DeHoff,[1] J. A. Johnson[1]; [1]University of Florida, Gainesville, FL, [2]University of Glasgow, Glasgow, United Kingdom, [3]Lund University, Malmo, Sweden. **C.W. McDonough:** None. **Y. Gong:** None. **S. Padmanabhan:** 1. This research was sponsored by the British Heart Foundation. **B. Burkley:** None. **T.Y. Langaee:** None. **O. Melander:** None. **C.J. Pepine:** 1. This research was sponsored by Abbott. 2. I am a paid consultant/employee for NHLBI Study Section for Progenitor Cell Biology Consortium, NHLBI DSMB Chair for Freedom Trial, MedTelligence, Lilly/Cleveland Clinic DSMB for Phase 2 Efficacy and Safety study of Ly2484595. **A.F. Dominiczak:** 1. This research was sponsored by the British Heart Foundation. **R.M. Cooper-DeHoff:** 1. This research was sponsored by Abbott. 4. I hold a patent for University of Florida. **J.A. Johnson:** 1. This research was sponsored by NIH.

BACKGROUND

We sought to identify novel pharmacogenetic markers associated with cardiovascular (CV) outcomes in patients with hypertension on antihypertensive therapy.

METHODS

We genotyped a 1:4 case:control cohort (n=1345) on the Illumina HumanCVD Beadchip from the International Verapamil SR-Trandolapril Study (INVEST), where participants were randomized to a β-blocker strategy (BB) or a calcium channel blocker strategy (CCB). Genome-spanning SNP x treatment interaction analyses of non-synonymous SNPs were conducted in white and Hispanic race/ethnic groups. Top hits from whites were tested in Hispanics for consistency. A genetic risk score was constructed from the top three signals and tested in the Nordic Diltiazem study (NORDIL).

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RESULTS

SIGLEC12 rs16982743 and *A1BG* rs893184 had a significant interaction with treatment strategy for adverse CV outcomes (INVEST whites and Hispanics combined interaction *P*=0.0038, and 0.0036, respectively). A genetic risk score including rs16982743, rs893184 and rs4525 in *F5*, was significantly associated with treatment-related adverse CV outcomes in whites and Hispanics from INVEST and in NORDIL (meta-analysis interaction $P=2.39\times10^{-5}$). In patients with a genetic risk score of zero or 1, CCB treatment was associated with lower risk (OR (95% CI) = 0.60 (0.42-0.86)), and in those with a genetic risk score of 2-3, CCB treatment was associated with higher risk, OR (95% CI) = 1.31 (1.08-1.59)).

CONCLUSION

These results suggest CV outcomes may differ based on *SIGLEC12, A1BG, F5* genotypes and antihypertensive treatment strategy. These specific genetic associations and our risk score provide insight into a potential approach to personalized antihypertensive treatment selection.

McDonough *et al. Hypertension*. 2013; 62(1):48-54.

LBI-001

SEIZURES AND VOMITING IN AN INFANT EXPOSED TO BUPROPION AND ESCITALOPRAM IN LACTATION: A CASE REPORT.

G. Neuman, D. Colantonio, S. Delaney, M. Szynkaruk, S. Ito; The Hospital for Sick Children, Toronto, ON, Canada. **G. Neuman:** None. **D. Colantonio:** None. **S. Delaney:** None. **M. Szynkaruk:** None. **S. Ito:** None.

BACKGROUND

A 6.5 months old previously healthy infant presented to our hospital with vomiting and seizures. She was exclusively breastfed; her mother was taking bupropion 150 mg and escitalopram 10 mg once daily for several months. The infant's urine tested positive for bupropion and escitalopram. Investigation for seizure etiology was negative. Discharge diagnosis was bupropion induced seizures.

METHODS

Bupropion (BUP) and its major metabolite, hydroxybuproion (HB), were analyzed in breast milk and in the infant's serum using HPLC-MS/MS. BUP steady state concentration ($[BUP]_{ss}$, ng/mL) in the infant was calculated.

RESULTS

The Table provides the different levels of BUP and HB. Calculated $[BUP]_{ss}$ in the infant around the time of the event was 0.12 ng/mL (1 nmol/L).

CONCLUSION

This is a case of seizures and vomiting in an infant, probably associated with exposure to bupropion in lactation. Combined use with escitalopram may have increased the risk for these adverse events. Existing data only describes the safety of each of these drugs separately in lactation. This is the first report of combined escitalopram and bupropion in lactation. Given the increasing use of combined antidepressants, there is a need to investigate the safety of combined antidepressants in lactating women.

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LBI-001. Table. Measured levels of bupropion and hydroxybupropion in samples of breast milk in infant's serum, from different times.

Infant's age (months)	Time of day	Milk levels ng/mL (nmol/L)		Infant Serum levels ng/mL (nmol/L)	
		BUP	HB	BUP	HB
6.0	Morning	16 (66)	87 (340)	N/A	N/A
6.0	Evening	19 (78)	77 (300)	N/A	N/A
6.25	Morning	23 (94)	46 (178)	N/A	N/A
6.25	Evening	23 (102)	61 (240)	N/A	N/A
6.5	Evening (at the time of the event)	N/A *	N/A *	Detected but not quantified++	11.25 (44)
6.5	Morning	N/A+	N/A+	Detected but not quantified++	17.13 (67)

* The infant was breastfed during this day, but no sample was kept.
+ From this point futher, the mother was not breastfeeding her infant.
++ Level of quantification: 4.8 ng/mL (20 nmol/L)

LBI-002

EXPOSURE-RESPONSE OF IDELALISIB, A NOVEL PI3Kδ INHIBITOR, IN THE TREATMENT OF HEMATOLOGIC MALIGNANCIES.

F. Jin,[1] H. Zhou,[2] L. Fang,[1] L. Holes,[2] X. Li,[2] T. Newcomb,[2] R. Dansey,[1] S. Ramanathan[1]; [1]Gilead Sciences, Foster City, CA, [2]Gilead Sciences, Seattle, WA. **F. Jin:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **H. Zhou:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **L. Fang:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **L. Holes:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **X. Li:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **T. Newcomb:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **R. Dansey:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **S. Ramanathan:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib.

BACKGROUND

Idelalisib (IDELA) is a potent PI3Kδ inhibitor that demonstrated efficacy in monotherapy and combination-therapy clinical studies in hematologic malignancies (eg. iNHL, CLL). The relationships between IDELA and GS-563117 (inactive metabolite) plasma exposures vs. efficacy/safety were evaluated.

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METHODS

The relationships between IDELA and GS-563117 exposures from population pharmacokinetics (PK) and efficacy/safety from a dose ranging and a Phase II studies were determined. Efficacy endpoints included best overall response rate (BOR), duration of response (DOR), progression free survival (PFS), sum of products of the greatest perpendicular diameters (SPD) of index lesions, and lymph node response rate (LNR) and safety endpoints included neutropenia, diarrhea, skin rash, infection, and aspartate aminotransferase (AST) or alanine aminotransferase (ALT) elevation.

RESULTS

Over a wide dose/exposure range, median SPD response increased with IDELA exposure (C_{trough}) quartiles, reaching a plateau at the third quartile (Q3: range ~280-405 ng/mL), which encompassed the mean 150 mg BID C_{trough} (381 [56%] ng/mL). No relationship with exposure was observed for incidence rate or severity of AST or ALT elevation. At 150 mg BID, no relevant association was observed between IDELA/GS-563117 exposure vs. any of the efficacy or safety endpoints evaluated.

CONCLUSION

There were no exposure-response relationships observed for efficacy or safety endpoints at IDELA 150 mg BID supporting this dose in the treatment of patients with hematologic malignancies.

LBI-003

EVALUATION OF THE EFFECT OF IDELALISIB ON THE QT/QTC INTERVAL IN HEALTHY SUBJECTS.

F. Jin,[1] M. Robeson,[2] H. Zhou,[2] A. Nichols,[1] S. Ramanathan[1]; [1]Gilead Sciences, Foster City, CA, [2]Gilead Sciences, Seattle, WA. **F. Jin:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **M. Robeson:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **H. Zhou:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **A. Nichols:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib. **S. Ramanathan:** 1. This research was sponsored by Gilead Sciences. 6. The following product discussed is not labeled for the use under discussion or is still investigational Idelalisib.

BACKGROUND

Idelalisib (IDELA) is a potent inhibitor of PI3Kδ and displayed no significant inhibition of hERG channel activity *in vitro* (IC50 ≥ 50 μM). The effects of IDELA 150 mg (therapeutic) and 400 mg (supratherapeutic) on QTc interval were evaluated in healthy subjects.

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METHODS

Healthy subjects (N=48) were enrolled into one of two cohorts (each a 4x4 Williams square) to receive IDELA 150 or 400 mg single dose, placebo, or moxifloxacin (positive control) with a 10-day washout between treatments. Time-matched ECGs were collected in triplicate over 24 hours after each treatment. Blood samples were collected to determine IDELA and GS-563117 (major metabolite) levels. Change from baseline in QTc for IDELA or moxifloxacin vs placebo was determined. PK and exposure-QT relationships were evaluated after 9/19/2013. Safety was monitored throughout the study.

RESULTS

Subjects (N = 48) were mainly Black/African-American (58.3%) or White (33.3%), with roughly even distribution by gender. Adverse events and laboratory abnormalities were generally Grade 1 in severity. The lower bound of the 2-sided 90% CI for the mean difference in QTcF for moxifloxacin vs. placebo was >5 msec at 3 and 4 hours post-dose, establishing assay sensitivity. Following IDELA dosing, the upper bound of the 2-sided 90% CIs for the mean difference in QTcF between 150 or 400 mg dose vs. placebo were below 10 msec at all time points post-dose. Analyses with QTcB, QTcN, and QTcI provided similar results. IDELA and GS-563117 peak plasma levels were 70-80% higher at 400 mg vs. 150 mg. There were no relevant relationships between change from baseline in QTcF and IDELA/GS-563117 plasma levels.

CONCLUSION

IDELA does not affect QTc interval in healthy adults and met the definition of a negative thorough QT study per ICH E14 guidance.

LBI-004

POPULATION PHARMACOKINETICS OF ENTERAL MORPHINE TO AID DOSING STRATEGY IN NEONATAL ABSTINENCE SYNDROME (NAS).

T. R. Lewis,[1] T. Liu,[2] E. B. Gauda,[1] D. A. Sartori,[3] T. Ezell,[1] C. W. Hendrix,[4] J. Gobburu,[2] V. D. Ivaturi[2]; [1]Department of Pediatrics, Johns Hopkins Medical Institutions, Baltimore, MD, [2]Center for Translational Medicine, School of Pharmacy, University of Maryland, Baltimore, MD, [3]Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, [4]Division of Clinical Pharmacology, Department of Medicine, Johns Hopkins School of Medicine, Baltimore, MD. **T.R. Lewis:** 6. The following product discussed is not labeled for the use under discussion or is still investigational morphine. **T. Liu:** None. **E.B. Gauda:** None. **D.A. Sartori:** None. **T. Ezell:** None. **C.W. Hendrix:** None. **J. Gobburu:** None. **V.D. Ivaturi:** None.

BACKGROUND

NAS is a set of physiologic signs of withdrawal resulting from opiate exposure, either *in utero* or as part of medical care. Although enteral morphine is used to treat NAS, the pharmacokinetics (PK) is unknown. A better understanding of the PK and clinical covariates will allow for future simulations and links to pharmacodynamic (PD) endpoints, allowing for individualized dosing and improved symptom control. The objective of this analysis was to develop a population PK (PopPK) model on interim data, the first on enteral morphine in NAS, which can be used to develop an integrated PKPD model after trial completion.

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METHODS

Infants >35 weeks gestational age exposed to heroin or methadone *in utero,* morphine or fentanyl in the ICU, and at risk for treatment or currently being treated with enteral morphine were enrolled. Previously published PopPK model of morphine and its two metabolites, M3G and M6G, after IV administration was used to fit the observed concentrations from 19 infants with an add-on absorption compartment allowing estimation of bioavailability (BA) of morphine and formation of metabolites using Phoenix NLME V_1.3. (data 11/20/13, analyzed 12/3/13).

RESULTS

In accordance with literature, results from this model indicate extensive first pass metabolism, approximately 60% of enteral morphine in this neonatal population. About 49% is converted into inactive metabolite M3G, and only 11% into the active metabolite M6G.

CONCLUSION

The add-on absorption compartment morphine PopPK model fit the interim observed morphine, M3G and M6G concentration data in neonates with NAS well with reasonable parameter estimates. The BA estimated from this model will allow optimized dosing strategy to reduce the duration and exposure to morphine in infants being treated for NAS.

LBI-005

ALTERED HEPATIC TRANSPORT IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS (NASH) INCREASES MORPHINE-GLUCURONIDE SYSTEMIC CONCENTRATIONS.

B. C. Ferslew, C. K. Johnston, K. L. Brouwer, A. S. Barritt; University of North Carolina at Chapel Hill, Chapel Hill, NC. **B.C. Ferslew:** None. **C.K. Johnston:** None. **K.L. Brouwer:** None. **A.S. Barritt:** None.

BACKGROUND

Expression of the hepatic efflux transporters multidrug resistance-associated protein (MRP)2, MRP3 and MRP4 is increased in patients with NASH. These changes may decrease hepatic exposure to anionic drugs/metabolites with a corresponding increase in systemic concentrations.

METHODS

Healthy volunteers and biopsy-proven NASH patients were recruited from November 2012-October 2013; data were analyzed in November 2013. Morphine (M; 5 mg [6.6 µmoles] IV bolus) was administered and blood/urine samples were collected pre-dose and at specified times for 8 hr. M and M-glucuronides (M-3&6-glucuronides=MG) serum and urine concentrations were quantified by LC-MS/MS. Pharmacokinetic (PK) parameters were obtained by non-compartmental analysis. The study was powered to detect a difference in serum MG C_{max}, which was hypothesized to increase in NASH patients.

RESULTS

Demographic and PK parameters from study subjects are presented in the Table below.

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CONCLUSION

MG serum C_{max} was significantly increased in NASH patients presumably due to increased MRP3-mediated hepatic basolateral efflux. No significant difference in MG recovery was noted. These changes may explain increased systemic toxicities or decreased hepatic efficacy of drugs transported in a similar manner in patients with NASH. *Supported in part by NIH 1UL1TR001111.*

LBI-005 Table

Demographics	Healthy (n=8)	NASH (n=7)	PK Parameters		Healthy (n=8)	NASH (n=7)
Gender	5 Males 3 Females	3 Males 4 Females	Morphine	C_{max} (nM)	250 (194 – 322)	312 (188 – 518)
Age	35 ± 10	48 ± 10 *		AUC_{last} (min*µM)	4.8 (3.4 – 6.8)	4.6 (3.3 – 6.3)
Race	6 Caucasian 2 African-American	7 Caucasian		Half-life (min)	96 (64 – 145)	81 (55 – 121)
Ethnicity	1 Hispanic 7 Non-Hispanic	1 Hispanic 6 Non-Hispanic	Morphine Glucuronides	C_{max} (nM)	245 (204 – 294)	323 * (268 – 389)
BMI (kg/m²)	25 ± 2	32 ± 5 *		T_{max} (min)	38 (10 – 60)	15 (5 – 90)
Total Bilirubin (mg/dL)	0.56 ± 0.21	0.81 ± 0.29		AUC_{last} (min*µM)	41 (34 – 49)	55 (39 – 77)
Serum Triglycerides (mg/dL)	96 ± 57	253 ± 98 *		Half-life (min)	172 (146 – 201)	162 (120 – 219)
Insulin Resistance (HOMA-IR)	1.5 ± 0.5	11 ± 9 *		Xurine 0-8 hr (µmoles)	4.7 (3.5 – 6.2)	5.9 (4.0 – 8.6)

Demographics (Mean ± SD); PK Parameters (geometric mean [95% CI of the geometric mean point estimate]), T_{max} (median [min-max]); Xurine 0-8 hr: Total mass excreted in urine over 8-hr PK sampling period; * p<0.05, NASH vs. Healthy using two-sample, two-sided t-test or Wilcoxon Mann-Whitney Rank Sum test (T_{max})

LBI-006

THE PHARMACOKINETICS OF PREGABALIN (Pgb) IN BREAST MILK, PLASMA AND URINE OF HEALTHY POSTPARTUM WOMEN.

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P. Lockwood: 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. 5. I am a significant stockholder for Pfizer. **L. Pauer:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. 5. I am a significant stockholder for Pfizer. **J. Scavone:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. 5. I am a significant stockholder for Pfizer. **C. Alvey:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. 5. I am a significant stockholder for Pfizer. **M. Allard:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. **N. Varvenne:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. **L. Mendes da Costa:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. **C. Constandt:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer.

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M. Spiliers: 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. **T. Alebic-Kolbah:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. 5. I am a significant stockholder for Pfizer. **A. Plotka:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. 5. I am a significant stockholder for Pfizer. **P. Furcolo:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer. **P. Garnick:** 1. This research was sponsored by Pfizer. 2. I am a paid consultant/employee for Pfizer.

BACKGROUND

A study was conducted to determine Pgb drug concentrations in human breast milk, estimate the infant daily dose resulting from Pgb secretion in breast milk and to characterize the safety and tolerability of Pgb in lactating women.

METHODS

Pgb 150 mg was administered q 12 hrs to 10 healthy lactating women who were at least 12 weeks post partum. No dietary restrictions were associated with dosing. Plasma, breast milk and urine samples were collected for up to 48 hours after the last dose. Database lock occurred on October 21st and the PK analysis was completed by October 25th.

RESULTS

The plasma PK profile in healthy lactating women was similar to that reported for healthy volunteers. The mean (%CV) peak plasma concentration of 4.67 (18) µgr/mL occurred 2 hours after dosing. The mean (%CV) plasma $AUC12_{ss}$ was 32.5 (24) µg•hr/mL. Pregabalin distribution into milk was slower than its absorption from the GI tract into plasma. The mean (%CV) milk to plasma ratio was 0.53 (22) based on C_{max} and 0.76 (18) based on AUC. Over 24 hours, the mean (%CV) amount of Pgb secreted into breast milk was 574 (60) µg. The mean absolute daily dose that an infant would receive based on the standard infant breast milk consumption of 150 mL/kg/day is approximately 308 µg/kg/day. Elimination of Pgb via breast milk expression was <0.2% of total Pgb oral clearance. The safety profile was consistent with the known profile for Pgb.

CONCLUSION

Pgb distributes into breast milk. Approximately 0.2% of the daily maternal dose was secreted into breast milk. An infant of a nursing mother taking Pgb would receive approximately 7% of the body weight normalized maternal dose (23% CV). An infant dose of less than 10% of the weight adjusted maternal dose is commonly cited as an acceptable level of infant exposure. Pgb was well tolerated in lactating women.

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LBI-007

GENOMIC CHARACTERIZATION OF METFORMIN RESPONSE.

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BACKGROUND

Metformin, the first-line therapy for Type 2 Diabetes, decreases hepatic glucose production but its mechanisms of action are not well known. We set out to identify novel molecular pathways and transcription regulators related to metformin response by carrying out RNA-seq and ChIP-seq on human hepatocytes treated with metformin.

METHODS

Human primary hepatocytes were treated with 2.5 mM metformin or vehicle control for 8 hours, followed by RNA-seq and ChIP-seq. Differentially expressed genes were analyzed using the Ingenuity Pathway Analysis (IPA). ChIP-seq was carried out using antibodies against differentially expressed transcription factors discovered through RNA-seq, H3K27ac, and H3K27me3. Analysis of ChIP-seq data was only possible from November 20, 2013.

RESULTS

Analysis of RNA-seq using IPA revealed 84 metformin responsive genes, some of which are implicated in gluconeogenesis (ATF3, DUSP1, FOXO1, NR0B2 and PPARGC1A), and others represent novel transcriptional regulators not previously associated with metformin response (KLF6 and AJUBA). ChIP-seq for H3K27ac, an active enhancer mark, identified 7,969 metformin induced peaks. Analysis of these peaks found them to be near genes associated with increased insulin secretion (FDR = 3.501e-2) and positive regulation of glucose metabolic process (FDR = 1.441e-2). We also found several of them to be near differentially expressed genes identified in our RNA-seq.

CONCLUSION

Using RNA-seq and ChIP-seq, we identified novel genes and regulatory elements associated with metformin exposure, suggesting potential genes that may be involved in metformin's mechanism of action. These genes and regulatory sequences provide prime candidates to screen for genetic variability associated with metformin efficacy and toxicity.

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LBI-008

INFLUENCE OF ABCC2 HAPLOTYPE AND CALCINEURIN INHIBITORS ON MYCOPHENOLIC ACID PHARMACOKINETICS IN STABLE RENAL TRANSPLANT RECIPIENTS.

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BACKGROUND

Mycophenolic acid (MPA) exhibits interpatient pharmacokinetic (PK) variability in renal transplant recipients (RTR). A component of this PK variability includes ABCC2 polymorphisms which encodes for multidrug resistance protein 2 (MRP2) and mediates enterohepatic recycling of mycophenolic acid glucuronide (MPAG) to MPA. This analysis evaluated the association of ABCC2 haplotypes with MPA PK in stable RTR receiving either cyclosporine (CYA) or tacrolimus (TAC).

METHODS

Intensive PK of MPA and MPAG at steady-state was determined in 147 stable RTR on CYA + MPA (n=80) or TAC + MPA (n=67). Non-compartmental analysis was used to determine area under the concentration-time curve (AUC_{0-12}) and clearance (CL). ABCC2 polymorphisms that were assayed included: -24C>T (rs717620), 1249G>A (rs2273697), and 3972C>T (rs3740066) with haplotype computation using THESIAS (completed 11/26/13) for MPA AUC_{0-12} and CL phenotypic means (PM).

RESULTS

RTR were 51±11 yrs old with eGFR 52±17ml/min/1.73m2. MPA AUC_{0-12} was lower in RTR with the CGT haplotype (PM: 18.0 hr•mg/L; 95% confidence interval [CI]: 8.4-27.7) compared to wild-type CGC (PM: 31.1 hr• mg/L; CI: 27.8-34.3; p=0.018) and at the lower therapeutic MPA AUC range. This haplotype association to AUC_{0-12} was maintained in RTR on MPA+TAC (p=0.032) only. Oral MPA clearance was higher with CGT (PM: 11.0 L/hr; CI: 8.8-13.3) compared to CGC (PM: 7.1 L/hr; CI: 5.7-8.5; p=0.013) and maintained in RTR on MPA+TAC (p=0.014).

CONCLUSION

MPA exposure is reduced in stable RTR with the ABCC2 haplotype variant CGT and varies in relation to the calcineurin inhibitor therapy that is included in these combination regimens.

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LBI-009

POPULATION PHARMACOKINETICS AND PHARMACOGENETICS OF ONCE DAILY TACROLIMUS FORMULATION IN STABLE LIVER TRANSPLANT RECIPIENTS.

D. J. Moes, S. A. van der Bent, **J. J. Swen,** T. van der Straaten, H. W. Verspaget, H. Guchelaar, J. den Hartigh, B. van Hoek; Leiden University Medical Centre, Leiden, Netherlands. **D.J. Moes:** None. **S.A. van der Bent:** None. **J.J. Swen:** None. **T. van der Straaten:** None. **H.W. Verspaget:** None. **H. Guchelaar:** None. **J. den Hartigh:** None. **B. van Hoek:** None.

BACKGROUND

The once daily formulation of tacrolimus is an important immunosuppressive drug metabolized by CYP3A enzymes. Inter-patient variability in tacrolimus metabolism has been related to both the *CYP3A4* and *CYP3A5* genotype. However, in liver transplants, both donor and recipient genotypes may affect pharmacokinetics. The aim of this study was to investigate the effect of *CYP3A4*22* and *CYP3A5*3* of both donor and recipient on once daily tacrolimus pharmacokinetics in liver transplant recipients.

METHODS

Stable liver transplant patients receiving once daily tacrolimus (N=49) were included. Blood concentrations were determined with LC-MS/MS. Population pharmacokinetic analysis was performed and demographic factors *CYP3A4*22* and *CYP3A5*3* were tested as covariates. Moreover, a limited sampling model was developed.

RESULTS

Tacrolimus once daily formulation pharmacokinetics was best described by a two-compartment disposition model with delayed absorption. *CYP3A5*1* carrying recipients engrafted with a *CYP3A5*1* carrying liver had a 1.65-fold higher clearance compared to non-carriers. *CYP3A5*1* carrying recipients engrafted with a *CYP3A5*1* non-carrying liver or vice versa showed a 1.13-fold higher clearance compared to non-carriers. *CYP3A4*22* was not associated with once daily tacrolimus pharmacokinetics. A limited sampling model using 0, 1 and 3 hours postdose resulted in a significantly improved prediction of tacrolimus exposure.

CONCLUSION

Dose adjustments based on *CYP3A5* genotype of both donor and recipient are indicated. In contrast, *CYP3A4*22* appears not suitable as biomarker for tacrolimus pharmacokinetics. 0, 1 and 3 hours postdose as limited sampling model can be used to accurately estimate tacrolimus once daily formulation exposure in liver transplantation.

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LBI-010

NOVEL REGULATORY SCIENCE RESEARCH FOR DEVELOPING A GUIDELINE ON THE CLINICAL EVALUATION OF DRUGS FOR ALZHEIMER'S DISEASE IN JAPAN.

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BACKGROUND

Japan's Ministry of Health, Labor and Welfare launched the project "Accelerating Regulatory Science Initiative" in 2012 to establish guidelines for development of innovative drugs. This is the first project in Japan to promote regulatory science through interaction between academia and regulatory agency. As a significant and groundbreaking result of this project, we show the result of our research to develop a guideline on the clinical evaluation of drugs for Alzheimer's disease (AD).

METHODS

We established a research system in this project in collaboration with Pharmaceuticals and Medical Devices Agency (PMDA) to develop a guideline of new drugs for AD in Japan and two research grups: (1) the Biomarker and Clinical Evaluation Group to establish biomarker-based criteria for clinical evaluation of drugs for AD, and (2) the Modeling and Simulation (M&S) Group to create a disease model of AD by using M&S techniques. An interim report of this research mentioned below was finalized and opened to public on our website on November 8, 2013.

RESULTS

In this report, we summarized the issues to consider for the clinical evaluation and development, such as issues of inclusion criteria, endpoint and clinical data package required for application in Japan, including early stage of AD. Additionally, we made the questionnaire to collect comments from industry and academia in Japan to refine the report and to create the final guideline.

CONCLUSION

This is the first document that summarized perspectives on the development of drugs for AD in Japan while incorporating the viewpoint of PMDA. At this time, however, there are still many issues to consider, such as usage of appropriate biomarkers and ethnic differences. We will continue this research and establish the final guideline at the next step.

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LBI-011

THE COMMON ADRB1 389 POLYMORPHISM AFFECTS THE HEMODYNAMIC RESPONSE TO DOBUTAMINE IN HEALTHY MALES AND FEMALES.

D. Yogev, Y. Caraco, **M. Muszkat;** Hadassah University Hospital, Jerusalem, Israel. **D. Yogev:** None. **Y. Caraco:** None. **M. Muszkat:** None.

BACKGROUND

The beta adrenergic receptor (ADRB) agonist dobutamine (DA) is widely used in diagnostic testing for coronary disease, however gender differences have been suggested in DA stress testing. The common *ADRB1* 389 polymorphism affects ADRB1-mediated responses. However, the combined effect of gender and the *ADRB1* 389 polymorphism on DA hemodynamic responses has not been previously studied.

METHODS

Healthy subjects (n=35) were recruited according to their *ADRB1* 49 and 389 positions genotype, in 3 gender-balanced groups [15 Arg389Arg, 10 Gly389Arg, and 10 Gly389Gly subjects (all Ser49Ser), including 21 men and 14 women]. DA was infused in incremental doses of 2, 4, 6 µg/kg/min (15 minute each). Heart Rate (HR) and blood pressure (BP) were monitored and blood samples were obtained for active renin 2 min before the end of each phase. During the last minute of each phase a standardized exercise was performed. Differences between end of infusion and baseline values were calculated for rest and exercise (ΔHR, ΔBP, ΔRenin).

RESULTS

Resting HR response to DA (ΔHR) varied significantly among genotypes (p ANOVA= 0.012), and was approximately 3-fold larger in Arg389Arg than in Gly389Gly subjects (12.95 ± 6.99 bpm, 2.75 ± 1.65 bpm, respectively, p = 0.016 *post hoc* test), with an intermediate value in heterozygotes (6.51 ± 11.40 bpm). Similarly, resting ΔRenin was more than 3-fold larger in Arg389Arg than in Gly389Gly subjects (14.11 ± 10.85 pg/mL, 3.93 ± 3.62 pg/mL, respectively, p ANOVA = 0.032; p= 0.031, *post hoc* test), and was 7.72 ± 9.28 pg/mL in heterozygotes. There were no gender differences in ΔHR, ΔBP or ΔRenin responses to DA.

CONCLUSION

The *ADRB1* Arg389Gly polymorphism contributes to the variability in HR and renin responses to DA in healthy subjects. There were no gender differences in DA responses.

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LBI-012

LC-MS/MS-BASED TARGETED PROTEOMICS ASSAY TO DETERMINE THE ABSOLUTE PROTEIN EXPRESSION OF CLINICALLY RELEVANT PHASE I and II ENZYMES.

C. Gröer,[1] M. Drozdzik,[2] W. Siegmund,[1] **S. Oswald[1];** [1]University of Greifswald, Department of Clinical Pharmacology, Greifswald, Germany, [2]Department of Experimental and Clinical Pharmacology, Pomeranian Medical University, Szczecin, Poland. **C. Gröer:** None. **M. Drozdzik:** None. **W. Siegmund:** None. **S. Oswald:** None.

BACKGROUND

The pharmacokinetics of many drugs is markedly influenced by biotransformation enzymes such as cytochrome P450 (CYP450) enzymes and UDP-glucuronosyltransferases (UGT). In order to predict their impact on drug disposition, data on their absolute intestinal and hepatic abundance are required. Therefore, it was the aim of this study to develop and validate LC-MS/MS methods for the absolute quantification of clinically relevant CYP and UGT enzymes.

METHODS

LC-MS/MS methods were developed for CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4, CYP3A5, UGT1A1, UGT1A3, UGT2B7 and UGT2B15. Proteins were quantified by measuring proteospecific tryptic peptides using stable isotope labeled standards. The assays were validated with respect to specificity, linearity, within-day and between-day accuracy and precision, stability as well as digestion efficiency.

RESULTS

For the aforementioned 13 proteins, two LC-MS/MS assays were developed. All methods were shown to be selective for the respective enzyme and the analytical range was in each case 0.25-50 nmol/l. Within-day (intra-day) as well as between-day (inter-day) accuracy (relative error) was between -13.1-12.5% and precision 1.1-14.8%. All peptides were shown to be stable during preparation, storage in the autosampler (24 h at 4°C) and during overnight digestion (16 h at 37 °C). The method was successfully applied to measure CYP and UGT expression in human intestinal and liver samples.

CONCLUSION

The developed methods were shown to possess sufficient specificity, sensitivity, accuracy, precision and stability to measure clinically relevant metabolizing enzymes in human tissues. These absolute expression data may allow more precise prediction of drug disposition using PBPK modeling-based approaches.

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LBI-013

ALCOHOL EFFECT ON EFAVIRENZ (EFV) PHARMACOKINETICS: *IN SILICO* EVALUATION AND PRELIMINARY FINDINGS FROM BOTSWANA CLINICAL TRIAL.

D. Patel, G. Moorthy, R. Gross, H. Xiaoyan, J. Barrett; The Children's Hospital of Philadelphia, Philadelphia, PA. **D. Patel:** None. **G. Moorthy:** None. **R. Gross:** None. **H. Xiaoyan:** None. **J. Barrett:** None.

BACKGROUND

Alcohol has been associated with poor response to HIV treatment. The objective of this study was to evaluate whether alcohol consumption is likely to impact efavirenz (EFV) PK in HIV-infected patients based on *in silico* modeling techniques while comparing simulation results with observations from a recent prospective trial in Botswana.

METHODS

EFV exposure after multiple 600 mg oral dose administration (180 days) in CYP2B6*1/*6 genotype population consuming alcohol were simulated using a PBPK model implemented in Simcyp™ V13. Input parameters of physicochemical and ADME were obtained from the literature. The effect of multiple doses of alcohol (7 drinks/day, 98 g) was tested under various alcohol consumption scenarios in 1 trial and 100 virtual patients for 7 days. PK parameters from the simulated results were compared with literature data to confirm the validity of SimCyp model.

RESULTS

Sparse observed EFV plasma concentrations of Botswana patients (n=346) across sampling windows were collected between 0-12 h (7.8 %), 12-16 h (77.2%) and >16 h (16.8%). The mean ± std dev of observed data for three alcohol consumption groups were 3274 ± 3273 (0 drinks, 59.4%), 3207 ± 3210 (≤ 20 drinks, 25.5%) and 2584 ± 1849 (>20 drinks, 15.1%). The simulated PK parameters (C_{max}, T_{max}, $AUC_{0-\infty}$ and CL_{po}) for EFV alone were 4.71 mg/L, 1.07 h, 60.2 mg/L.hr, and 8.23 L/hr, respectively, and EFV with alcohol (7 drinks/day, 98 g) were 4.71 mg/L, 1.07 hr, 60.2 mg/L.hr, and 8.23 L/hr, respectively. Similar PK parameters were observed for all other alcohol consumption scenarios that were tested.

CONCLUSION

EFV exposure and simulated PK parameters were similar across all 3 alcohol consumption groups. Hence, alcohol-related effects on HIV-treatment with EFV is unlikely to be PK-mediated.

LBI-014

USE OF A BIOINFORMATICS TOOL, MASE (MOLECULAR ANALYSIS OF SIDE EFFECTS), GENERATES THE HYPOTHESIS OF AN ASSOCIATION BETWEEN FGFR2 AND BONE FRACTURES.

P. Schotland,[1] K. Burkhart,[1] D. R. Abernethy,[1] D. Jackson[2]; [1]Food and Drug Administration, Silver Spring, MD, [2]Molecular Health, Inc, Heidelberg, Germany. **P. Schotland:** None. **K. Burkhart:** None. **D. Abernethy:** None. **D. Jackson:** 2. I am a paid consultant/employee for Molecular Health, Inc.

BACKGROUND

MASE integrates Adverse Event (AE) data from FAERS with drug, target, and pathway data to analyze AE mechanisms. Two pilot AEs, Supraventricular Tachycardia (SVT) and Urinary Retention (UR), were used to assess MASE's ability to replicate known pathophysiology.

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METHODS

For SVT, MASE was queried for AE reports containing MedDRA Preferred Terms (PTs) supraventricular tachycardia, atrial tachycardia, and sinus tachycardia. For UR, the PT urinary retention was queried. MASE was then queried to identify molecular targets for bone fractures using PTs bone infection, spinal cord compression, aseptic necrosis bone, pathological fracture, compression fracture, osteomyelitis, osteonecrosis, osteonecrosis of jaw, and hip fracture. Query results were assessed for significantly associated drug targets using Proportional Reporting Ratio (PRR), lower CI ≥ 2. The analysis is ongoing from 10/21/2013.

RESULTS

For SVT, the most frequent targets/receptor families are muscarinic acetylcholine, histamine, α and β-adrenergic, and serotonin. For UR, the receptors are muscarinic acetylcholine, α-adrenergic, and GABA-A. These targets are consistent with the known physiology of SVT and UR. For bone fracture, hydroxyapatite; PRR 23.28, CI (23 - 23.57), pyrophosphate synthetase; PRR 23.57, CI (23.29 - 23.87), and tyrosine-protein phosphatase; PRR 17.86, CI (17.37 - 18.37) are highly associated targets. A potential association was found with fibroblast growth factor receptor 2 (FGFR2): PRR 5.70, CI (5.32 - 6.10). A literature review does not associate FGFR2 with bone fractures.

CONCLUSION

MASE can correctly assess the mechanistic molecular targets of drug-AE pairs. The relationship between FRFR2 and bone fractures warrants experimental investigation.

LBI-015

5-FLUOROURACIL DOWNREGULATES CYP2C ENZYMES IN RATS.

M. J. Seminerio, S. Mirkov, L. House, J. Ramirez, M. J. Ratain; University of Chicago, Chicago, IL. **M.J. Seminerio:** None. **S. Mirkov:** None. **L. House:** None. **J. Ramirez:** None. **M.J. Ratain:** None.

BACKGROUND

There is a Black Box Warning regarding the potentiation of warfarin's effects by capecitabine, and a similar effect has been observed with 5-fluorouracil (5-FU). However, the mechanistic basis remains to be elucidated, as 5-FU does not inhibit CYP2C9 at clinically achievable concentrations. The purpose of this study was to demonstrate an interaction between 5-FU and warfarin *in vivo* and to assess the effect of 5-FU on hepatic expression of P450 isozymes in rats.

METHODS

S- and R-warfarin blood serum levels were measured via LC/MS/MS following oral administration of 1.5 mg/kg racemic warfarin to Male Sprague-Dawley rats during an 8-day intraperitoneal dose (i.p.) regimen of 5-FU (13.3 mg/kg). Inhibition studies in rat supersomes evaluated the effects of 5-FU on CYP450 activity. Gene expression studies were conducted using liver tissue extracted from rats receiving an 8-day regimen of 5-FU (13.3 mg/kg, i.p.) (this data was analyzed after September 19, 2013).

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RESULTS

A significant increase in $AUC_{(0\text{-}96hr)}$ of S-warfarin was observed with animals receiving 5-FU/warfarin compared with animals receiving saline/warfarin. Eight-day treatment of 5-FU (13.3 mg/kg) resulted in significant downregulation of CYP2C6 and CYP2C11 (the rat homologs of CYP2C9) gene expression, while having no effect on controls (CYP3A2, CYP2D2).

CONCLUSION

A pharmacological interaction between 5-FU and warfarin was demonstrated *in vivo*. This interaction likely involves an indirect downregulation of CYP450s involved in warfarin metabolism. Additional studies are currently underway evaluating transcriptional coactivators involved in CYP2C9 regulation.

LBI-016

A NOVEL SNP IN TNFRSF1B IS ASSOCIATED WITH RESPONSE TO ANTI-TNF THERAPY IN INFLAMMATORY BOWEL DISEASE PATIENTS.

E. Smithberger, S. Kwan, W. Hernandez, E. Gamazon, L. Shen, J. H. Kwon, M. A. Perera; University of Chicago, Chicago, IL. **E. Smithberger:** None. **S. Kwan:** None. **W. Hernandez:** None. **E. Gamazon:** None. **L. Shen:** None. **J.H. Kwon:** None. **M.A. Perera:** None.

BACKGROUND

Inflammatory bowel disease (IBD) is a chronic and debilitating gastrointestinal disease estimated to affect 1.4 million individuals in the US. While anti-TNF antibodies have led to a dramatic improvement in IBD treatment, over 20% of patients fail to respond to these therapies. Identifying predictors of response to anti-TNF drugs is essential to determine which patients will benefit from this class of therapy. In a retrospective candidate gene study of 167 IBD patients, we identified a SNP in *TNFRSF1B* (rs1061628) that was associated with response to anti-TNF agents (OR= 1.8; p=0.048). In this study, we aimed to validate our findings in an independent cohort of IBD patients.

METHODS

We genotyped rs1061628 in 84 IBD patients for our validation cohort. Patients were classified as primary non-responders or responders to anti-TNF therapy. Collection of clinical data and genotypes for allelic analysis were obtained after September 19, 2013.

RESULTS

We found the presence of the minor allele (T) to be associated with an increased risk of being a primary non-responder to anti-TNF agents (OR=4.3, p=0.03). Furthermore, *in vitro* studies revealed an increase in gene expression with the T allele by qPCR analysis ($p<0.002$) and by luciferase assay ($p<0.05$) in colon cells.

CONCLUSION

The *TNFRSF1B* SNP rs1061628 is predictive of response to anti-TNF therapy and *TNFRSF1B* has differential gene expression in IBD patients. This SNP is located in the 3' UTR of *TNFRSF1B* and may modulate gene expression, potentially as a miRNA binding site. Increased receptor expression may lead to decreased sensitivity to anti-TNF drugs, as shown by the association with anti-TNF drug response.

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LBI-017

EARLY-STAGE COMPARATIVE EFFECTIVENESS: RANDOMIZED CONTROLLED TRIAL WITH HISTAMINE INVERSE AGONIST MK-7288 IN EXCESSIVE DAYTIME SLEEPINESS PATIENTS.

H. Sun,[1] C. Macleod,[2] K. Mostoller,[2] C. Mahon,[2] L. Han,[3] J. Renger,[2] J. Ma,[2] K. Brown,[2] V. Schulz,[2] G. Kay,[4] W. Herring,[2] C. Lines,[2] L. Rosen,[5] G. Murphy,[2] J. Wagner[2]; [1]Amgen, Thousand Oaks, CA, [2]Merck, North Wales, PA, [3]Gilead, San Francisco, CA, [4]Cognitive Research Corp., Petersburg, FL, [5]Shire, Wayne, PA. **H. Sun:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **C. Macleod:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **K. Mostoller:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **C. Mahon:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **L. Han:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **J. Renger:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **J. Ma:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **K. Brown:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **V. Schulz:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **G. Kay:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **W. Herring:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **C. Lines:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **L. Rosen:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **G. Murphy:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck. **J. Wagner:** 1. This research was sponsored by Merck. 2. I am a paid consultant/employee for Merck.

BACKGROUND

Histaminergic neurons are regulators of the sleep-wake cycle. MK-7288 is a novel histamine-3 receptor inverse agonist (H3RIA). In this early comparative effectiveness study, we evaluated the alerting effects of MK-7288 in comparison with modafinil, a standard treatment of excessive daytime sleepiness (EDS).

METHODS

A randomized, double-blind, placebo controlled, crossover study was conducted in 56 sleep apnea patients with EDS. Each patient received four treatments in randomized order: MK-7288 10 and 20 mg, modafinil 200 mg, and placebo. Efficacy was assessed using maintenance of wakefulness tests (MWT) and a novel functional test, driving simulation tests. Safety and tolerability were assessed through adverse effects reporting, vital sign and lab safety evaluations. This work was published online in the *Journal of Clinical Pharmacology* in Oct 2013.

RESULTS

Both MK-7288 and modafinil demonstrated alerting effects by improving MWT sleep latency and driving performance as assessed by standard deviation of lane position (SDLP). The effect of modafinil on sleep latency was significantly greater than MK-7288 (difference for MK-7288 20 mg vs modafinil = -2.1 minutes [90% CI: -3.8, -0.4]). But there was no difference between modafinil and MK-7288 on driving performance

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(SDLP difference for MK-7288 20 mg vs modafinil =-0.0 meters [90% CI: -0.0, 0.0]). MK-7288 and modafinil were generally well tolerated. MK-7288 was associated with more insomnia (29%) than modafinil (9%) and placebo (6%).

CONCLUSION

The study demonstrated the potential of an H3RIA for treating EDS, but did not show efficacy and/or tolerability differentiation from modafinil. Early-stage comparative effectiveness can help prevent late-stage failure and increase the cost-effectiveness of drug development.

LBI-018

THE STABILITY AND HYDROLYSIS OF NOVEL GLUTARIC ACID ESTER PRODRUG OF LOPINAVIR IN HUMAN TISSUE FRACTIONS.

M. Wang, A. Joshi, Z. Hassan, P. M. Gerk; Virginia Commonwealth University, Richmond, VA. **M. Wang:** None. **A. Joshi:** None. **Z. Hassan:** None. **P.M. Gerk:** None.

BACKGROUND

Lopinavir (LPV) is a potent protease inhibitor specific for HIV-1. However, LPV has poor placental penetration. Therefore, to increase fetal exposure of LPV, a series of fatty acid monoester prodrugs of LPV have been synthesized putatively targeting fatty acid transporters. The glutaric acid monoester prodrug of lopinavir (GLPV) was demonstrated as the leading compound, which showed 16-fold higher uptake than LPV in human syncytiophoblast cells. The purpose of this study was to determine presystemic and systemic stability of GLPV and also to determine whether GLPV can be hydrolyzed in the human placenta.

METHODS

GLPV (140 μM) was incubated with 100 μL of human intestinal cytosol (HIC, 0.25 mg/mL), human liver cytosol (HLC, 0.25 mg/mL), and human placenta homogenates (HPH, 10 mg tissue/mL) for 8 hours, and incubated with recombinant human carboxylesterase I (CES I, 0.25 mg/mL) and caboxylesterase II (CES II, 0.25 mg/mL) for 1 hour. GLPV (0.7 μM) was incubated with human albumin solution (0.05%) for 1 hour. Acetonitrile and methanol (1:1, 100 μL) containing ritonavir (internal standard, 70 μM) was used to quench the reaction. 4-nitrophenol acetate hydrolysis was monitored by UV detection. GLPV was measured by LC-MS/MS or HPLC.

RESULTS

The results showed that GLPV disappearance was undetectable in HIC, human albumin and HPH, CES I and CES II. However, GLPV disappearance was 9.1 nmol/hr/mg protein in HLC.

CONCLUSION

GLPV is relatively stable in intestine, hepatic cytosol and human plasma before it reaches placenta. However, its hydrolysis in placental homogenate is required to reveal the active LPV. Therefore, further study will need to balance between the hydrolysis and uptake in prodrugs design. Also, it is worth knowing whether GLPV itself has antiretroviral activity.

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LBI-019

LUNG CANCER RISK IN TWO AFRICAN AMERICAN SMOKING POPULATIONS IS ASSOCIATED WITH VARIATION IN CYP2A6, A NICOTINE/NITROSAMINE METABOLISM GENE.

C. A. Wassenaar,[1] Q. Cai,[2] Y. Ye,[3] M. Aldrich,[2] J. Knight,[4] M. R. Spitz,[5] W. J. Blot,[2] X. Wu,[3] R. F. Tyndale[1]; [1]University of Toronto, Toronto, ON, Canada, [2]Vanderbilt University, Nashville, TN, [3]MD Anderson, Houston, TX, [4]CAMH, Toronto, ON, Canada, [5]Baylor College of Medicine, Houston, TX. **C.A. Wassenaar:** None. **Q. Cai:** None. **Y. Ye:** None. **M. Aldrich:** None. **J. Knight:** None. **M.R. Spitz:** None. **W.J. Blot:** None. **X. Wu:** None. **R.F. Tyndale:** 2. I am a paid consultant/employee for McNeil.

BACKGROUND

We investigated CYP2A6 and lung cancer risk among African American smokers. CYP2A6 gene variants are hypothesized to contribute to the risk of smoking-related lung cancer through the bioactivation of carcinogenic nitrosamines and/or by influencing cigarette use, through nicotine inactivation.

METHODS

Participants were smokers from a case-control study nested within the Southern Community Cohort Study, Nashville, TN with 1-2 controls matched to each lung cancer case by age, sex and recruitment site (SCCS: n = 494), and from a case-control study from MD Anderson Cancer Center, Houston, TX with controls frequency matched to cases by smoking history in addition to age and sex (MDA: n = 407). CYP2A6 genotyping for 12 reduced/null activity alleles was completed October 2013. Participants with genotypes previously associated with a 25% or more reduction in CYP2A6 activity were considered reduced metabolizers. Lung cancer risk was estimated through logistic regression.

RESULTS

CYP2A6 reduced vs. normal metabolizer genotypes were associated with a reduction in lung cancer risk in SCCS, MDA, and the pooled data (SCCS: OR 0.62, 95% CI 0.43-0.90; MDA: OR 0.66, 95% 0.44-0.98; Pooled: OR 0.64, 95% CI 0.49-0.84; ORs adjusted for age and sex). The association remained following additional adjustments for cigarettes/day and years of smoking (SCCS: OR 0.58, 95% CI 0.39-0.87; MDA: OR 0.66, 95% CI 0.44-0.99; Pooled: OR 0.62, 95% CI 0.47-0.83). We observed an interaction between genotype and sex (SCCS: P=.03; MDA: P=.03; Pooled: P=.003), with a greater effect in men. Additional analyses are underway to explore this interaction.

CONCLUSION

CYP2A6 genetics contribute to lung cancer risk among African American smokers furthering our understanding of carcinogenesis within this high-risk population.

LATE-BREAKING AND ENCORE ABSTRACT SESSION I

Thursday, March 20, 2014 • International Hall 7:30 am – 2:00 pm
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LBI-020

QUANTITATIVE SYSTEMS PHARMACOLOGY MODELING TO EVALUATE CLINICAL RESPONSE OF AN ANTI-TNFα/ANTI-ANG2 BISPECIFIC ANTIBODY IN RHEUMATOID ARTHRITIS.

L. Yan,[1] C. Friedrich,[2] K. Balic,[1] N. Ageyeva,[1] S. Nicholson,[3] J. Connor,[3] N. Dimasi,[3] R. Baillie,[2] C. Wu,[1] R. Faggioni[1]; [1]MedImmune, LLC, Mountain View, CA, [2]Rosa & Co, San Carlos, CA, [3]MedImmune, LLC, Gaithersburg, MD. **L. Yan:** 1. This research was sponsored by MedImmune. **C. Friedrich:** 2. I am a paid consultant/employee for MedImmune. **K. Balic:** 1. This research was sponsored by MedImmune. **N. Ageyeva:** 1. This research was sponsored by MedImmune. **S. Nicholson:** 1. This research was sponsored by MedImmune. **J. Connor:** 1. This research was sponsored by MedImmune. **N. Dimasi:** 1. This research was sponsored by MedImmune. **R. Baillie:** 2. I am a paid consultant/employee for MedImmune. **C. Wu:** 1. This research was sponsored by MedImmune. **R. Faggioni:** 1. This research was sponsored by MedImmune.

BACKGROUND

Neovascularization in rheumatoid arthritis (RA) patients has been shown to associate with progression of disease. Increased expression of Angiopoietin-2 (Ang2) may contribute to disease maintenance and progression. An anti-TNFα/anti-Ang2 bispecific antibody (BsAb) was designed to provide the clinical effect of anti-TNF therapies with the additional benefit of neutralizing Ang2 in one single agent.

METHODS

Nonclinical pharmacokinetics (PK) and pharmacodynamics (PD) data following single or repeat-dose were collected from non-GLP and GLP studies in cynomolgus monkeys. PK and PD data were analyzed using Non-Compartmental Analysis (NCA) and a Target-Mediated Drug Disposition (TMDD) model. A quantitative systems pharmacology model (PhysioPD™ model) was constructed to integrate key features of RA pathophysiology with the pharmacological properties of an anti-TNFα approved in RA and the BsAb. The model was used to simulate the effects of the BsAb in virtual patients (VPs) representing relevant biology and explore different hypotheses about TNFα and Ang2 effects in the RA joint.

RESULTS

In cynomolgus monkeys, the BsAb exhibited TMDD due to an Ang2 sink at doses lower than 3 mg/kg. The RA PhysioPD model predicted that the BsAb has superior clinical response to anti-TNFα alone in all VPs. VPs with the least anti-angiogenic response to anti-TNFα alone had the greatest additional clinical response from the addition of anti-Ang2.

CONCLUSION

Using the RA PhysioPD model, the anti-TNFα/anti-Ang2 bispecific antibody was predicted to provide greater clinical response compared to anti-TNFα alone. The RA PhysioPD model is a useful tool for understanding the dynamic interactions between different disease pathways and the effect on clinical outcome.

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Thursday, March 20, 2014 • International Hall 7:30 am – 2:00 pm
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LBI-021

EVALUATION OF CYP3A4 ENDOGENOUS BIOMARKERS IN A SONIDEGIB DRUG–DRUG INTERACTION STUDY WITH RIFAMPICIN AND KETOCONAZOLE IN HEALTHY SUBJECTS.

J. Zhou,[1] E. Hurh,[2] C. Emotte,[3] S. Winter,[3] M. Quinlan,[1] T. Austin,[1] S. Kalambakas,[1] Y. Wang[1]; [1]Novartis Pharmaceutical Corporation, East Hanover, NJ, [2]Novartis Institutes for Biomedical Research, Cambridge, MA, [3]Novartis Pharma AG, Basel, Switzerland. **J. Zhou:** 1. This research was sponsored by Novartis. 2. I am a paid consultant/employee for Novartis. 6. The following product discussed is not labeled for the use under discussion or is still investigational. **E. Hurh:** 2. I am a paid consultant/employee for Novartis. **C. Emotte:** 2. I am a paid consultant/employee for Novartis. **S. Winter:** 2. I am a paid consultant/employee for Novartis. **M. Quinlan:** 2. I am a paid consultant/employee for Novartis. **T. Austin:** 2. I am a paid consultant/employee for Novartis. **S. Kalambakas:** 2. I am a paid consultant/employee for Novartis. **Y. Wang:** 2. I am a paid consultant/employee for Novartis.

BACKGROUND

Sonidegib, a selective Smoothened inhibitor, is a substrate of CYP3A4. This drug–drug interaction study between sonidegib and rifampicin (RIF) or ketoconazole (KETO) evaluated the changes of 2 endogenous CYP3A4 biomarkers, 4β-OHcholesterol (4βHC) in plasma and 6β-OHcortisol/cortisol ratio (6βCR) in urine, in healthy volunteers (HVs).

METHODS

50 HVs were randomized to 1 of 3 arms: 1) sonidegib 800 mg single dose alone, 2) 14 days of KETO 200 mg bid + sonidegib 800 mg dosed on Day 5, 3)14 days of RIF 600 mg qd + sonidegib 800 mg dosed on Day 5. Plasma 4βHC and urinary 6βCR were monitored for 19 days in Arms 2 and 3. Sonidegib C_{max} and AUC in the combination arms were compared with those in the sonidegib alone arm. Data were available from September 23, 2013.

RESULTS

In the sonidegib alone arm, both biomarkers remained stable. In the RIF arm, the 4βHC increased 2.1, 3.1, 3.8, 3.9, 3.7, and 3.0-fold on Days 5, 8, 12, 15, 17 (3 days post RIF dose), and 19 (5 days post RIF dose), respectively, vs baseline (BL) while 6βCR increased 4.8, 4.8, 5.2, 5.5, 5.9, and 2.8-fold on these days. In the KETO arm, 4βHC ratios (vs BL) were 0.80, 0.76, 0.80, 0.76, 0.83, and 0.88 on these days while 6βCR ratios (vs BL) were 0.033, 0.080, 0.12, 0.28, 0.95, and 1.1. The overall inter- and intra-individual CV% for 4βHC was 36.3% and 8.6%, and for 6βCR was 58.4% and 25.1%, respectively. RIF reduced the Geo-mean of C_{max} and AUC of sonidegib by 54% and 72%, and KETO increased these parameters 1.5- and 2.3-fold, respectively.

CONCLUSION

Both biomarkers showed good response to induction, 4βHC showed less variability but slower response, while 6βCR was more sensitive to inhibition but with higher variability. Sonidegib exposure was sensitive to CYP3A4 activity and correlated with biomarker levels.

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Thursday, March 20, 2014 • International Hall 7:30 am – 2:00 pm
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LBI-022

ASSESSMENT OF THE EFFECT OF 5-HT2A RECEPTORS ON BRAIN SEROTONIN (5-HT) VIA A MECHANISM-BASED MATHEMATICAL INDIRECT MODEL.

Z. Zhou, J. Sun, J. A. Uchizono; University of the Pacific, Stockton, CA.
Z. Zhou: None. **J. Sun:** None. **J.A. Uchizono:** 1. This research was sponsored by Formurex, Inc.

BACKGROUND

Although major ethical challenges make it nearly impossible to invasively and directly measure 5-HT brain levels in humans, neuroimaging technologies have shown macroscopic structural and functional abnormalities in the prefrontal cortex (PFC) and dorsal raphe nucleus (DRN) in depressed patients. Characterization of these two key areas can lead to new strategies in the treatment of depression. A mechanism-based mathematical model has been developed to predict 5-HT levels in the DRN and PFC in response to different infusion concentrations of DOI (5-HT2A agonist) given into the PFC.

METHODS

Extracellular 5-HT levels in the PFC and DRN of rats (n=3-5) were measured by intracerebral microdialysis. A modified indirect model was used to capture the effects at the 5-HT2A receptor. Six model parameters were obtained from model estimation and three were fixed from experimental data. Phoenix WinNonlin® and Berkeley MadonnaTM were used for model estimation, external validation with secondary data set, and simulation. (Model validated on 10/23/2013).

RESULTS

The time-course profiles of 5-HT in both DRN and PFC was well modeled with different dosing schemes of DOI. Model parameters were estimated with reasonable precision (CV% ranged from 1.37% to 35.03%), AIC was -72.81149 and SBC was -59.61987. The R2 values were 0.9475 and 0.913 for the DRN and PFC models, respectively. Simulations from this model suggested the modulation of the 5-HT2A receptor located in PFC was predictably controlling the 5-HT in DRN and PFC.

CONCLUSION

A mechanism based model was developed to identify the neurotransmitter mechanisms, and quantitatively estimate various key parameters of the disease related receptor system. Simulations using this model supports a hypothesized mechanism of 5-HT2A effect on 5-HT.

LATE-BREAKING AND ENCORE ABSTRACT SESSION I

Thursday, March 20, 2014 • Marquis C • 10:45 am - 12:00 noon

OI-5

CLINICALLY ACTIONABLE GENOTYPES AMONG 10,000 PATIENTS WITH PREEMPTIVE PHARMACOGENOMIC TESTING.

S. L. Van Driest, Y. Shi, E. A. Bowton, J. S. Schildcrout, J. F. Peterson, J. Pulley, J. C. Denny, D. M. Roden; Vanderbilt University, Nashville, TN.
S.L. Van Driest: None. **Y. Shi:** None. **E.A. Bowton:** None. **J.S. Schildcrout:** None. **J.F. Peterson:** None. **J. Pulley:** None. **J.C. Denny:** None. **D.M. Roden:** None.

BACKGROUND

The Vanderbilt Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment (PREDICT) program was initiated in September 2010. Over 10,000 patients have now undergone preemptive, panel-based pharmacogenomic testing as part of this program.

METHODS

In this study published in *Clinical Pharmacology & Therapeutics* in November 2013, genetic and clinical data from the first 9,589 individuals were analyzed to determine frequency of actionable genotypes and drug exposures relevant to five currently implemented drug-genome interactions (clopidogrel with *CYP2C19*, simvastatin with *SLCO1B1*, warfarin with *CYP2C9* and *VKORC1*, thiopurines with *TPMT*, and tacrolimus with *CYP3A5*). The pre-emptive, multiplexed genotyping approach was compared to a theoretical "reactive," prescription-triggered, serial single-gene testing strategy.

RESULTS

The frequency of genetic variants in the patient population is concordant with published allele frequencies. Based on the five drug-genome interactions, one or more actionable variants were identified in 8,760 (91%) of the genotyped patients and in 913/953 (96%) African-American patients. Among those with one or more actionable genotypes, 4,018 (42% of the entire cohort) had evidence of exposure to the risk-associated drug or drug class. Reactive genotyping would have generated 14,656 genetic tests, compared to the 9,589 preemptive tests performed.

CONCLUSION

These data highlight three advantages of preemptive genotyping: i) the vast majority of patients carry at least one pharmacogene variant; ii) data are available at the point of care; and iii) there is a substantial reduction in testing burden compared to a reactive strategy.

Friday, March 21, 2014 • Marquis A • 10:30 am - 11:45 am

OII-A-5

ONTOGENY OF HUMAN DRUG TRANSPORTER EXPRESSION IN THE PEDIATRIC KIDNEY.

E. Spaans, B. A. de Koning, M. G. Mooij, J. N. Samsom, D. Tibboel, **S. N. de Wildt;** Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands.
E. Spaans: None. **B.A. de Koning:** None. **M.G. Mooij:** None. **J.N. Samsom:** None. **D. Tibboel:** None. **S.N. de Wildt:** None.

BACKGROUND

Transporters involved in absorption, disposition and clearance of drugs account for a significant part of the variability in pharmacokinetics. However, little is known about developmental changes of transporter

LATE-BREAKING AND ENCORE ABSTRACT SESSION I

expression during childhood. Transporters in the proximal tubules of the kidney influence renal clearance of drugs. Therefore, ontogeny of transporters in the kidney is likely to result in age-related effects on renal clearance of drugs. We aimed to evaluate the expression of the transporters: MDR1, MRP2, OAT1, OAT3 and OCT2 in kidney tissue in relation to age.

METHODS

Thirty-eight post mortem tissue samples without renal abnormalities on pathology, evenly distributed across the pediatric age-range, were analyzed and compared with 14 adult samples. Samples with RNA Integrity Number RINs < 5 were excluded to ensure RNA quality. Target gene expression was determined using real time RT-PCR using delta CT with GAPDH as household gene.

RESULTS

For MDR1 (PgP) expression, a sigmoidal developmental pattern was observed with minimal expression (Eo: dCT=0.002 95% CI: -0.024 - 0.028) within the first 2 months of age being roughly a factor 20 lower than the maximum expression (E_{max}: dCT=0.043 95% CI: 0.03 - 0.05) occurring at 12 months and older. The halfway increase (E_{50}) was at 4.3 months. For OAT1, OAT3, MRP2, OCT2 and MATE1 no developmental pattern was observed and expression across the different ages remained within the adult variability.

CONCLUSION

These results suggest that kidney MDR1 expression, but not MRP2, OAT1, OAT3, OCT2, shows a maturation pattern, putatively resulting in age-related changes in the clearance of drugs. Studies on protein expression and *in vivo* activity to determine the clinical relevance of our findings are needed.

Friday, March 21, 2014 • Marquis B • 10:30 am - 11:45 am

OII-B-5

APPLICATION OF PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODEL IN PREDICTING ACETAMINOPHEN METABOLISM AND PHARMACOKINETICS IN CHILDREN.

X. Jiang,[1] P. Zhao,[2] J. S. Barrett,[3] L. J. Lesko,[1] S. Schmidt[1]; [1]University of Florida, Orlando, FL, [2]US Food and Drug Administration, Silver Spring, MD, [3]The Children's Hospital of Philadelphia, Philadelphia, PA. **X. Jiang:** None. **P. Zhao:** None. **J.S. Barrett:** None. **L.J. Lesko:** None. **S. Schmidt:** None.

BACKGROUND

Maturational changes in Phase I and II drug metabolizing enzymes from birth greatly affect elimination and bioactivation of acetaminophen (APAP), which cause uncertainties when predicting dosing recommendations for children based on adult efficacy and safety data. The objective of our study was to develop a PBPK model that allows for a mechanistic understanding of age-dependent changes in the clearance, systemic exposure, and bioactivation of APAP in children.

METHODS

The PBPK model was developed by integrating *in vitro* enzyme kinetic and adult PK data into a single model using a population-based simulator. Once externally qualified, it was expanded for application in kids by accounting for maturational changes from birth.

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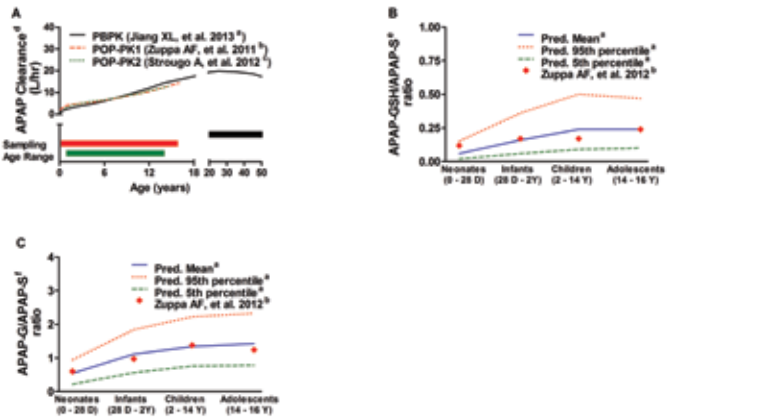
RESULTS

Our PBPK model allowed predicting APAP plasma profiles in children (0-17 years) as well as maturation in systemic clearance (Fig. A). Its mechanistic nature further allowed characterizing age-dependent changes in bioactivation (Fig. B) and major metabolic pathways (Fig. C).

CONCLUSION

This approach represents a general strategy for predicting drug exposure and dosing in children, in the absence of age-specific PK data, using prior drug- and system-specific information in adults. It will further allow identifying subgroups which are most susceptible to APAP-induced liver injury.



[a]Jiang XL, et al. CPT Pharmacometrics Syst Pharmacol. 2013 Oct 16;2:e80.
[b]Zuppa AF, et al. J Pediatr Pharmacol Ther. 2011 Oct; 16(4):246-61.
[c]Strougo A, et al. J Pharmacokinet Pharmacodyn. 2012 Apr;39(2):195-203.
[d]Comparison of the simulated systemic clearance values of APAP using the developed PBPK model[a] and two independent population PK (pop-PK) analyses[b,c] in children of different age ranges. Black line represents the APAP clearance vs. age profile in children predicted from the current PBPK model, whereas the red and green lines represent the clearance vs. age profiles estimated from the pop-PK analyses. The corresponding bars with respective colors represent the age ranges of APAP PK data used for the development of the APAP clearance vs. age curves with either the PBPK or pop-PK approach.
[e]Values are calculated based on observed 4 hr urinary recovered APAP-GSH (sum of 3'-[S-cysteinyl]-APAP, APAP mercapturate and 3'-[S-methyl] -APAP) and APAP-sulfate (APAP-S) data and simulated 4 hr urinary recovered APAP-GSH and APAP-S data after first APAP dose.
[f]Values are calculated based on observed or simulated 4 hr urinary recovered APAP-glucuronide (APAP-G) and APAP-S data at steady states after multiple APAP doses.

Friday, March 21, 2014 • Marquis C • 10:30 am - 11:45 am

OII-C-5

MECHANISTIC MODELING OF DRUG-INDUCED LIVER INJURY (DILI) PREDICTS SPECIES DIFFERENCES IN BILE ACID (BA)-MEDIATED TROGLITAZONE (TGZ) HEPATOTOXICITY.

K. Yang,[1] J. L. Woodhead,[2] P. B. Watkins,[2] B. A. Howell,[2] K. L. Brouwer[1]; [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]The Hamner Institutes for Health Sciences, Research Triangle Park, NC. **K. Yang:** None. **J.L. Woodhead:** None. **P.B. Watkins:** None. **B.A. Howell:** None. **K.L. Brouwer:** None.

BACKGROUND

TGZ elevated ALT>3X ULN in 2% of patients and was withdrawn due to severe DILI. The hepatotoxic potential of TGZ mediated by bile salt export pump (BSEP) inhibition and hepatic accumulation of toxic BAs was evaluated.

LATE-BREAKING AND ENCORE ABSTRACT SESSION I

METHODS

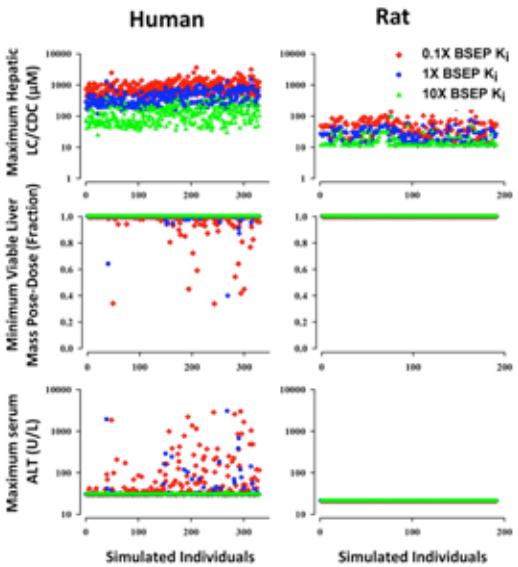
A PBPK model of TGZ was developed. BA physiology and pathophysiology [hepatotoxicity induced by lithocholate (LC) and chenodeoxycholate (CDC)] were incorporated in DILIsym®, a mechanistic DILI model (model development completed on October 19). Using BA transporter inhibition constants from *in vitro* studies, TGZ (600 mg human; 5 mg/kg rat)-mediated perturbation of BA disposition and DILI responses (e.g, ↓viable liver mass, ↑serum ALT) were simulated in rat and human populations that included variability in key model parameters.

RESULTS

Hepatotoxicity was sensitive to BSEP inhibition K_i in humans. With 1X BSEP K_i, 12/331 simulated individuals (3.6%) showed serum ALT elevation>3X baseline; 2 Hy's law cases were identified. No hepatotoxicity was observed in rats, consistent with preclinical data. TGZ-induced hepatic accumulation of toxic BA was lower in rats than humans due to more hydrophilic BA pool and LC detoxification by hydroxylation.

CONCLUSION

Mechanistic modeling incorporating physiology and pathophysiology of BAs in rats and humans correctly predicted differential TGZ hepatotoxicity.



LATE-BREAKING AND ENCORE ABSTRACT SESSION II

Friday, March 21, 2014 • International Hall 7:30 am – 3:30 pm
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EII-001

THOROUGH QT STUDY OF THE EFFECT OF ORAL MOXIFLOXACIN ON QTC INTERVAL IN THE FED AND FASTED STATE IN HEALTHY JAPANESE AND CAUCASIAN SUBJECTS.

J. Taubel,[1] G. Ferber,[2] U. Lorch,[1] V. Batchvarov,[3] I. Savelieva,[3] A. J. Camm[3]; [1]Richmond Pharmacology Ltd., St George's University of London, London, United Kingdom, [2]Statistik Georg Ferber GmbH, Riehen, Switzerland, [3]Department of Cardiological Sciences, St George's University of London, London, United Kingdom. **J. Taubel:** None. **G. Ferber:** None. **U. Lorch:** None. **V. Batchvarov:** None. **I. Savelieva:** None. **A.J. Camm:** None.

BACKGROUND

Moxifloxacin is used as a probe to confirm assay sensitivity in thorough electrocardiogram (ECG) studies. A meal shortens the QT interval and in some instances it is desirable to use moxifloxacin after a meal which may affect PK or PD or both; however there is no published data.

METHODS

The study consisted of 32 healthy Caucasian (n = 13) and Japanese (n = 19) subjects, aged between 20-45 years. ECGs were recorded in triplicate with subsequent blinded manual adjudication of the automated interval measurements. The comparisons of treatment effects were made intra-individually.

RESULTS

The effect on ΔΔQTc in the fed state, led to a significant delay and a modest reduction compared to the fasted state. The largest QTcF change from baseline was observed at 4 hours (11.6 ms, two-sided 90% CI: 9.1, 14.1) in the fed state, and at 2.5 hours post-dose (14.4 ms, 90% CI 11.9, 16.8 ms) in the fasted state. The PK of moxifloxacin was altered by food what was consistent with the observed QTcF change. In the fed state drug concentrations in plasma were considerably and consistently lower in comparison to the fasted state for both ethnicities. The concentration effect analysis revealed no change in slope and confirmed that the difference in the response was caused predominantly by a change in the PK profile.

CONCLUSION

The typical moxifloxacin PK profile is altered by food prior to dosing which reduces the C_{max} and delays the peak effects of QTc prolongation up to several hours resulting in reduced overall magnitude of the effect. There was no significant difference between Japanese and Caucasian subjects in PK-PD relationship in both the fed and fasted conditions, thereby providing further evidence that the sensitivity to the QTc prolonging effects of fluoroquinolones are likely to be independent of ethnicity.

LATE-BREAKING AND ENCORE ABSTRACT SESSION II

Friday, March 21, 2014 • International Hall 7:30 am – 3:30 pm
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EII-002

REDUCED SUBCUTANEOUS TISSUE DISTRIBUTION OF CEFAZOLIN IN MORBIDLY OBESE VERSUS NON-OBESE PATIENTS DETERMINED USING CLINICAL MICRODIALYSIS.

M. J. Brill,[1] A. P. Houwink,[2] S. Schmidt,[3] E. P. van Dongen,[2] E. J. Hazebroek,[4] B. van Ramshorst,[4] V. H. Deneer,[1] J. W. Mouton,[5] C. A. Knibbe[1]; [1]Department of Clinical Pharmacy, St. Antonius Hospital, Nieuwegein, Netherlands, [2]Department of Anaesthesiology and Intensive Care, St Antonius Hospital, Nieuwegein, Nieuwegein, Netherlands, [3]College of Pharmacy, Department of Pharmaceutics, Center for Pharmacometrics and Systems Pharmacology, University of Florida, Orlando, FL, [4]Department of Surgery, St Antonius Hospital, Nieuwegein, Netherlands, [5]Department of Medical Microbiology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands. **M.J. Brill:** 1. This research was sponsored by Fonds Nuts OHRA. **A.P. Houwink:** None. **S. Schmidt:** None. **E.P. van Dongen:** None. **E.J. Hazebroek:** None. **B. van Ramshorst:** None. **V.H. Deneer:** None. **J.W. Mouton:** None. **C.A. Knibbe:** None.

BACKGROUND

As morbidly obese patients are prone to surgical site infections, adequate blood and subcutaneous tissue concentrations of prophylactic antibiotic agents during surgery are imperative. Using microdialysis, we evaluated cefazolin subcutaneous adipose tissue distribution in morbidly obese and non-obese patients, thereby quantifying the influence of morbid obesity on cefazolin pharmacokinetics and enabling Monte Carlo simulations for dose adjustments.

METHODS

Nine morbidly obese patients [body mass index (BMI) 47±6 kg/m^2], of whom eight were evaluable, and seven non-obese patients (BMI 28±3 kg/m^2) received cefazolin 2 g intravenously before surgery. Using microdialysis, interstitial space fluid (ISF) samples of the subcutaneous adipose tissue were collected together with total and unbound plasma cefazolin samples until 240 min after dosing. Using NONMEM, pharmacokinetic modeling, covariate analysis and Monte Carlo simulations were performed.

RESULTS

The median unbound (free) cefazolin ISF penetration ratio ($fAUC_{tissue}$/$fAUC_{plasma}$) was 0.70 (range 0.68-0.83) in morbidly obese patients versus 1.02 (range 0.85-1.41) in non-obese patients ($P<0.05$). A two-compartment model with saturable protein binding was identified in which the central volume of distribution and cefazolin distribution from the central compartment to the ISF compartment proved dependent on bodyweight ($P<0.001$ and $P<0.01$, respectively). Monte Carlo simulations showed reduced probability of target attainment for morbidly obese versus non-obese patients for MIC values of 2 and 4 mg/L.

CONCLUSION

This study shows that cefazolin tissue distribution is lower in morbidly obese patients and reduces with increasing body weight, and that dose adjustments are required in this patient group.

LATE-BREAKING AND ENCORE ABSTRACT SESSION II

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LBII-001

MIDAZOLAM PHARMACOKINETICS FOLLOWING ORAL AND INTRAVENOUS ADMINISTRATION IN MORBIDLY OBESE PATIENTS BEFORE AND 1 YEAR POST GASTRIC BYPASS/SLEEVE SURGERY.

M. J. Brill,[1] A. van Rongen,[1] A. P. Houwink,[2] B. van Ramshorst,[3] E. J. Hazebroek,[3] E. P. van Dongen,[2] C. A. Knibbe[1]; [1]Department of Clinical Pharmacy, St. Antonius Hospital, Nieuwegein, Netherlands, [2]Department of Anaesthesiology and Intensive Care, St. Antonius Hospital, Nieuwegein, Netherlands, [3]Department of Surgery, St. Antonius Hospital, Nieuwegein, Netherlands. **M.J. Brill:** 1. This research was sponsored by The Netherlands Organisation for Health Research and Development (ZonMw). **A. van Rongen:** None. **A.P. Houwink:** None. **B. van Ramshorst:** None. **E.J. Hazebroek:** None. **E.P. van Dongen:** None. **C.A. Knibbe:** None.

BACKGROUND

Gastric bypass/sleeve surgery is considered the most successful treatment for morbid obesity (body mass index, BMI >40 kg/m^2). As both surgery induced weight loss and gastro-intestinal alterations may influence a drug's pharmacokinetics, we aimed to quantify the influence of bariatric surgery on oral and intravenous pharmacokinetics of CYP3A substrate midazolam in patients before and 1 year post bariatric surgery.

METHODS

Twenty morbidly obese patients [144.4 kg (112-186 kg) and BMI 47.1 kg/m2 (40-68 kg/m^2)] participated before gastric bypass/sleeve surgery and 18 patients [-44.5 kg (21-58 kg)] returned 52 ± 2 weeks post surgery. On both occasions, patients received 7.5 mg oral and 5 mg IV midazolam separated by 160 ± 50 minutes and 21-23 blood samples were collected until 9-11 h post oral dose. Part of the concentrations collected on the second occasion were not released before November 6, 2013. Population pharmacokinetic modeling was performed using NONMEM.

RESULTS

Midazolam concentrations of both groups were best described by a three-compartment model with equalized peripheral volumes and a transit compartment model for absorption with transit rates set equal to the absorption rate. Post bariatric surgery, mean (RSE) midazolam absorption rate and clearance were higher compared to before bariatric surgery [0.30 (13%) vs. 0.11 (10%) min-1 ($P<0.01$) and 0.64 (8%) vs. 0.50 (9%) L/min ($P<0.01$), respectively]. Bioavailability, central and peripheral volume of distribution were similar to before surgery (0.56 (9%), 55 (13%) L and 74 (12%) L, respectively).

CONCLUSION

Oral and IV midazolam pharmacokinetics in post gastric bypass/sleeve patients revealed higher oral absorption rate and clearance compared to before bariatric surgery, while bioavailablility was unaltered.

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LBII-002

FOUR YEARS AND 314 CASES OF CLINICAL PHARMACOLOGY IMPACT: GSK EXPERIENCE FROM 2009 TO 2013.

P. N. Mudd Jr, F. Hoke; GlaxoSmithKline, Research Triangle Park, NC.
P. N. Mudd Jr: 1. This research was sponsored by GlaxoSmithKline. 2. I am a paid consultant/employee for GlaxoSmithKline. 4. I hold a patent for GlaxoSmithKline. 5. I am a significant stockholder for GlaxoSmithKline.
F. Hoke: 1. This research was sponsored by GlaxoSmithKline. 2. I am a paid consultant/employee for GlaxoSmithKline. 5. I am a significant stockholder for GlaxoSmithKline.

BACKGROUND

Impact case studies were used to determine key value drivers of a Clinical Pharmacology Modeling/Simulation (CPMS) department. Our group is responsible for clinical PK/PD, population PK/PD and Pharmacometrics. This unique body of work deepens our understanding and communicates our perspective on the value of Clinical Pharmacology in a global R&D organization.

METHODS

Impact cases were collected from December 2009 to December 2013 by CPMS (70 people). The case study approach (problem/solution/impact) provides the needed context for assessing value in a matrix environment, with shared input/ownership of decisions. Other metrics collected per case: tools/approaches, time/effort, business partners, customers and benefits.

RESULTS

Presented as % of total cases (n=314). Seven key value drivers were identified that provided benefit to "customers" (e.g. project teams, regulatory agencies, external partners): 1. Selected/defended human dose/regimen (27%); 2. Informed team decision (terminating, pausing or progressing a program, candidate selection, due diligence, milestone criteria) (20%); 3. Optimized clinical study design (18%); 4. Addressed a regulatory issue, question, or need (16%); 5. Improved scientific understanding of a candidate molecule or product (10%); 6. Created clinical development strategy (clinical pharmacology plan, pediatric plan, formulation strategy, new indication) (6%); 7. Departmental process improvement/efficiency (3%) The most frequent customers, business partners, and tool used were: project teams (67%), clinical statistics (21%) and population PK/PD (41%), respectively.

CONCLUSION

Key value drivers and metrics of a Clinical Pharmacology department have been identified with a wide range of beneficial impact on a global R&D organization.

LBII-003

PREVENTION OF BACLOFEN WITHDRAWAL SYNDROME: PHARMACOKINETICS AND TOLERABILITY OF ORAL AND INTRAVENOUS BACLOFEN IN HEALTHY ADULT VOLUNTEERS.

S. K. Agarwal, R. L. Kriel, J. C. Cloyd, L. D. Coles, M. H. Tobin, L. E. Krach; University of Minnesota, Minneapolis, MN. **S.K. Agarwal:** 1. This research was sponsored by Medtronic Inc., and Paralyzed Veterans of America. 2. I am a paid consultant/employee for University of Minnesota. 6. The following product discussed is not labeled for the use under discussion or is still investigational Lioresal Intrathecal, 2 mg/mL.

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R.L. Kriel: 1. This research was sponsored by Medtronic Inc. and Paralyzed Veterans of America Research Foundation. 2. I am a paid consultant/employee for University of Minnesota. 6. The following product discussed is not labeled for the use under discussion or is still investigational Lioresal Intrathecal, 2 mg/mL. **J.C. Cloyd:** 1. This research was sponsored by Medtronic Inc., and Paralyzed Veterans of America. 2. I am a paid consultant/employee for the University of Minnesota. 6. The following product discussed is not labeled for the use under discussion or is still investigational Lioresal Intrathecal, 2 mg/mL. **L.D. Coles:** 1. This research was sponsored by Medtronic and Paralyzed Veterans of America. 2. I am a paid consultant/employee for University of Minnesota. 6. The following product discussed is not labeled for the use under discussion or is still investigational Lioresal Intrathecal, 2 mg/mL. **M.H. Tobin:** None. **L.E. Krach:** 1. This research was sponsored by Medtronic Inc., and Paralyzed Veterans of America. 2. I am a paid consultant/employee for Medtronic Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational Lioresal Intrathecal, 2 mg/mL.

BACKGROUND

Patients treated with oral or intrathecal baclofen (ITB) may experience a withdrawal syndrome when therapy is acutely interrupted. The management of baclofen withdrawal is inadequate with slow response and frequent adverse effects secondary to therapy. Intravenous (IV) baclofen could help prevent or minimize withdrawal symptoms; however, there is no IV formulation. Study aims were to characterize pharmacokinetics (PK) and safety of baclofen given orally and IV in healthy subjects.

METHODS

Twelve subjects were enrolled in a randomized, open-label, crossover study. Subjects received single doses of baclofen: 3 or 5 mg given IV and 5 or 10 mg taken orally with a 48-hr washout. Blood samples for baclofen analysis were collected pre-dose and at regular intervals up to 24 hours post-dose. Plasma baclofen concentration-time data were analyzed using a non-compartmental PK approach (Drug assays completed in Nov 2013 and data analyzed by 12/06/13). Descriptive statistics were used to summarize PK parameters and a paired t-test was used to test for significant difference in IV vs. oral area under the curve (AUC).

RESULTS

The mean absolute bioavailability of oral baclofen was 74% (95% CI: 61%, 86%). There was a significant difference in dose-adjusted AUCs ($p = 0.0024$). AUC variability was similar (CV:18-24%) in both oral and IV arms. Most common adverse effects were somnolence, mild ataxia and nystagmus, all of which were resolved within six hours after drug administration.

CONCLUSION

Three and 5 mg doses of IV baclofen were well tolerated, and incomplete absorption of baclofen indicates that smaller doses of IV baclofen are needed to attain comparable plasma concentrations. The PK data from this study will guide design of future trials that are required for commercial development of IV baclofen.

LBII-004
WITHDRAWN

LATE-BREAKING AND ENCORE ABSTRACT SESSION II

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LBII-005

INVESTIGATING THE RELATIONSHIP BETWEEN CODEINE ANALGESIA AND GENETIC POLYMORPHISMS IN POST-PARTUM PAIN MANAGEMENT.

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BACKGROUND

Codeine is an opioid analgesic commonly prescribed in North America to treat post-partum pain resulting from C-sections. Considerable portion of such patients do not achieve optimal analgesia, raising doubt in the efficacy of codeine for the above purpose. The objective of this study was to investigate interindividual variability to codeine based management of post-partum pain caused by C-sections and optimal dosage requirements by examining genetic polymorphisms relevant to codeine analgesia.

METHODS

The study recruited a total of 235 women that were prescribed codeine following a C-section and a saliva sample was collected. Women were instructed to report on levels of pain using the Visual Analog Scale (VAS) one hour after each dose of codeine for the entire duration of the medication's use. Women were genotyped for selected polymorphisms of the *COMT, ABCB1, CYP2D6* and *OPRM1* genes. Data analysis began on October 15, 2013.

RESULTS

Mean length of codeine therapy following caesarean section was 1.99 0.8 days. On day 1, poor metabolizers (PM) of the CYP2D6 gene consumed a greater cumulative dose/kg compared to intermediate metabolizers (IM) (p=0.022) or extensive metabolizers (EM) (p=0.023). On day 2, patients homozygous (A/A) for the OPRM1 118 A>G polymorphism consumed a lower average dose/kg compared to heterozygous (A/G) (p=0.001) or homozygous (G/G) (p=0.049) patients.

CONCLUSION

Analysis revealed significant association between maternal polymorphisms and dosage requirement. Differences in dosage intake seen across certain genetic polymorphisms suggests there may be a need for dose adjustments or alternative forms of therapy in managing post-partum pain resulting from C-sections.

LBII-006

AN IMPROVED VANCOMYCIN DOSING STRATEGY IN NEONATES USING POPULATION PHARMACOKINETICS AND SIMULATIONS TO ACHIEVE PHARMACODYNAMIC TARGET ATTAINMENT.

J. Bhongsatiern,[1] C. M. Sherwin,[2] C. Stockmann,[2] T. Yu,[2] D. M. Reith,[3] P. B. Desai,[1] M. G. Spigarelli[2]; [1]The James L. Winkle College of Pharmacy, University of Cincinnati, Cincinnati, OH, [2]Department of Pediatrics, University of Utah, Salt Lake City, UT, [3]Department of Women's and Children's Health, University of Otago, Dunedin, New Zealand.

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J. Bhongsatiern: None. **C.M. Sherwin:** None. **C. Stockmann:** None. **T. Yu:** None. **D.M. Reith:** None. **P.B. Desai:** None. **M.G. Spigarelli:** None.

BACKGROUND

Vancomycin is a first-line therapy for neonatal MRSA. Two dosing strategies, postmenstrual age (PMA)-based and serum creatinine (SCR)-based are currently used. This study aimed to evaluate pharmacodynamic (PD) target attainment rates using current dosing regimens, and derive an optimal vancomycin dosing strategy for neonates.

METHODS

Data were collected for neonates with ≥1 vancomycin serum concentrations. Completed data were not available before September 19, 2013. A population PK model was constructed using NONMEM 7.2. Dosing simulations were performed in MATLAB R2010a. The PD target that best predicts clinical success was defined as a ratio of the area under the curve to the minimum inhibitory concentration (AUC/MIC) ≥400.

RESULTS

A one-compartment model with first-order elimination was developed. Overall, 1,458 serum concentrations were obtained from 515 patients. The final model established clearance (CL) = 0.042 • (CWT/1.5)^0.72 • (1/SCR) • (PMA/33) and volume of distribution (V) = 1.04 • (CWT/1.5)^1.06. In simulations, >90% of patients achieved the AUC/MIC target for both current dosing regimens at an MIC 0.5 mg/L. At MICs of 1 and 2, 72% and 12% of the simulated SCR-based dosing profiles achieved the AUC/MIC target, which was higher than the rates achieved with PMA-based dosing. An improved dosing strategy was developed that featured increased SCR-based doses and dosing intervals from 7.5-30 to 10-40 mg/kg/day. This strategy achieved the AUC/MIC target in 98%, 86%, and 25% of simulations at MICs of 0.5, 1, and 2, respectively.

CONCLUSION

For neonates, a dosing strategy that incorporates weight and SCR is predicted to achieve the PD target that is predictive of successful therapy in >80% of patients at MICs ≤1 mg/L. Vancomycin is not recommended for isolates with MICs ≥2 mg/L.

LBII-007

EXAMINATION OF GENTAMICIN AND MAGNESIUM SULFATE DRUG-DRUG INTERACTIONS IN NEONATES.

S. C. Campbell, C. Stockmann, C. M. Sherwin, M. G. Spigarelli; University of Utah, Salt Lake City, UT. **S.C. Campbell:** None. **C. Stockmann:** None. **C.M. Sherwin:** None. **M.G. Spigarelli:** None.

BACKGROUND

Neonates maternally exposed to magnesium sulfate ($MgSO_4$) can develop hypermagnesemia, which may mimic the symptoms of sepsis. Consequently, empiric treatment with antibiotics including gentamicin is often initiated. Concurrent use of gentamicin and $MgSO_4$ is contraindicated owing to the potential for serious drug-drug interactions, including cardiac and respiratory arrest. This project sought to determine the risk concordance between hypermagnesemia and gentamicin use in neonates.

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METHODS

Neonates maternally exposed to $MgSO_4$ who subsequently received gentamicin were studied from 1/2009-10/2011. A weight and gestational age matched control cohort (n=2407) was identified from neonates who received gentamicin but were not exposed to $MgSO_4$. Mann-Whitney U tests were performed to compare NICU treatment between cohorts and relative risk (RR), and 95% confidence intervals (95% CI) were calculated for cardiac arrest and respiratory failure using ICD-9 discharge diagnosis codes (data available 12/2013).

RESULTS

Overall, 38% of 677 neonates who were maternally exposed to $MgSO_4$ were subsequently treated with gentamicin. Of these, 61% had magnesium concentrations measured and 74% were hypermagnesemic. Maternally $MgSO_4$ exposed neonates who received gentamicin were more likely to require NICU care (79% vs. 3%; P<0.0001), and experience cardiac arrest (RR 9.4; 95% CI 1.3-66.5). These neonates also tended towards respiratory failure (RR 1.5; 95% CI 0.8-2.9). In a comparison group of 470 neonates maternally exposed to $MgSO_4$ but not gentamicin, the incidence of these events was zero.

CONCLUSION

Neonates maternally exposed to $MgSO_4$ are often treated with gentamicin which was associated with a heightened risk of life-threatening adverse events and should be monitored closely.

LBII-008

APPLICATION OF NON-LINEAR POPPK WITH TARGET MEDIATED DRUG DISPOSITION (TMDD) IN OPTIMIZATION OF AN ONCOLOGY DOSING REGIMEN.

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BACKGROUND

GC33 is a first-in-class recombinant, humanized mAb that binds to glypican-3 (GPC3), an oncofetal protein highly expressed in hepatocellular carcinoma (HCC). A PopPK covariate model composed of TMDD was developed from Phase II study data to estimate individual target saturation and provide a rational basis for model guided dose selection.

METHODS

GC33 PK data were obtained from 119 patients (768 observations) with advanced HCC who had previously failed at least one systemic agent treatment. The dosing regimen was 1600 mg every 2 weeks with loading doses 1600 mg on days 1 and 7. Intensive PK sampling occurred on cycles 1 and 6; 6 sparse PK samples were taken prior to infusion of cycles. Additional samples were taken at the final visit, follow-up, and progression of disease. A PopPK model was used to estimate GC33

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Cycle 3 Day 1 (C3D1) C_{trough}. The target saturation was derived from Michaelis-Menten constant (K_m). The relationship between exposure and progression free survival (PFS) was explored.

RESULTS

GC33 PK was described by a two-compartment disposition with linear and saturable (Michaelis-Menten) elimination. Linear CL and V was dependent on weight and the TMDD parameter (V_{max}) was influenced by log-transformed sum of lesion diameter times serum GPC3 level. An exposure-response analysis showed that increased exposure (C3D1 C_{trough}) was associated with prolonged PFS, suggesting that high target saturation may be needed for a beneficial effect of GC33. Simulations of alternative dosing regimens suggest that GC33 1600 mg every week will provide targeted C_{trough} in > 90% of patients.

CONCLUSION

GC33 PK exhibits TMDD with GPC3 as the only known specific target. TMDD can be used to assess target saturation and serve as a surrogate marker for efficacy to guide dose selection.

LBII-009

UTILITY OF CYP3A4 TRANSGENIC MOUSE MODEL TO DETERMINE THE CONTRIBUTION OF INTESTINAL METABOLISM ON THE DISPOSITION OF COBIMETINIB, A MEK INHIBITOR.

E. F. Choo, S. Woolsey, J. Ly, R. Takahashi, K. Messick, A. Qin; Genentech Inc, South San Francisco, CA. **E.F. Choo:** 2. I am a paid consultant/employee for Genentech Inc. 5. I am a significant stockholder for Roche. **S. Woolsey:** 2. I am a paid consultant/employee for Genentech Inc. **J. Ly:** 2. I am a paid consultant/employee for Genentech Inc. 5. I am a significant stockholder for Roche. **R. Takahashi:** 2. I am a paid consultant/employee for Genentech Inc. 5. I am a significant stockholder for Roche. **K. Messick:** 2. I am a paid consultant/employee for Genentech Inc. 5. I am a significant stockholder for Roche. **A. Qin:** 2. I am a paid consultant/employee for Genentech Inc. 5. I am a significant stockholder for Roche.

BACKGROUND

Cobimetinib is a MEK inhibitor currently being tested in multiple combinations, including a Phase III clinical trial in combination with vemurafenib, in patients with metastatic melanoma. Data from the absolute bioavailability (F) study suggested that the F of cobimetinib was lower than predicted based on its low hepatic extraction and good absorption.

METHODS

The CYP3A4 transgenic mouse model with differential expression of CYP3A4 in the liver, gut or liver and gut, was used to study the contribution of intestinal metabolism to the F of cobimetinib.

RESULTS

After IV administration of 1 mg/kg cobimetinib to wild-type (WT; FVBn), CYP3A4 transgenic mice with liver, gut or liver and gut CYP3A4 expression, CL (26-35 mL/min/kg) was similar in the CYP3A4 transgenic and WT mice. After oral administration of 5 mg/kg cobimetinib, the AUC of cobimetinib in WT and transgenic mice with liver, gut or liver and gut CYP3A4 expression were 1.35, 3.39, 1.04 and 0.701 uM.h, respectively.

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The ~3-fold lower AUC of cobimetinib in transgenic mice when gut CYP3A4 was present suggested that intestinal first pass contributed to the oral CL of cobimetinib. The oxidative metabolites in human plasma were observed in the transgenic mice, with up to ~10-fold higher metabolite to parent ratios observed after oral vs. IV administration.

CONCLUSION

Collectively, this data along with clinical observations, suggested that CYP3A4 intestinal metabolism contributed to the oral disposition of cobimetinib. This model was further evaluated for its potential to predict CYP3A4 mediated clinical drug-drug interactions.

LBII-010

ELUCIDATING PITAVASTATIN AS A MORE SENSITIVE AND SELECTIVE OATP1B CLINICAL PROBE THAN ROSUVASTATIN USING SINGLE INTRAVENOUS AND ORAL DOSES OF RIFAMPIN IN HEALTHY SUBJECTS.

T. Prueksaritanont,[1] X. Chu,[2] R. Evers,[2] S. O. Klopfer,[3] L. Caro,[1] P. Kothare,[1] C. Dempsey,[2] R. Houle,[2] G. H. Chan,[2] X. Cai,[2] R. J. Valesky,[1] I. P. Fraser,[2] **A. Stoch[2];** [1]Merck & Co., Inc, West Point, PA, [2]Merck & Co., Inc, Rahway, NJ, [3]Merck & Co., Inc, Upper Gwynned, PA. **T. Prueksaritanont:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **X. Chu:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **R. Evers:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **S.O. Klopfer:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **L. Caro:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **P. Kothare:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **C. Dempsey:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **R. Houle:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **G.H. Chan:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **X. Cai:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **R.J. Valesky:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **I.P. Fraser:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc. **A. Stoch:** 1. This research was sponsored by Merck & Co., Inc. 2. I am a paid consultant/employee for Merck & Co., Inc.

BACKGROUND

OATP1B are major hepatic uptake transporters. Inhibition of these transporters may cause clinically significant DDIs.

METHODS

The effects of single intravenous (IV) and oral (PO) doses of rifampin (600 mg) on single oral dose of pitavastatin (1 mg) and rosuvastatin (5 mg) pharmacokinetics were investigated in healthy volunteers. *In vitro* inhibition studies were conducted in hepatocytes and transporter recombinant systems.

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RESULTS

Marked, but differential increases in the exposure of pitavastatin and rosuvastatin were observed with both PO (GMR for $AUC_{0-\alpha}$ = 5.7 and 4.4, respectively) and IV rifampin (GMR for $AUC_{0-\alpha}$ = 7.6 and 3.3, respectively). *In vitro*, rifampin was an inhibitor of OATP1B1, OATP1B3, BCRP, and MRP2, but not OAT3.

CONCLUSION

Our results suggest that i) pitavastatin is a more sensitive and selective and thus preferred clinical OATP1B probe substrate than rosuvastatin, and ii) a single IV dose of rifampin is a more selective OATP1B inhibitor than a PO dose.

LBII-011

QTVIE: COMPARISON OF THE QTC INTERVAL BETWEEN AN OUTPATIENT HIV-INFECTED POPULATION ON ANTIRETROVIRAL THERAPY AND TWO LARGE HIV-NEGATIVE COHORTS.

B. Crevier,[1] J. Yee,[1] S. Jouni,[1] R. Therrien,[2] S. Mansour,[2] J. Nam Nguyen,[2] C. Tremblay,[1] J. Turgeon,[1] V. Michaud[1]; [1]CHUM Research Center, Université de Montreal, Montréal, QC, Canada, [2]CHUM, Montréal, QC, Canada.
B. Crevier: None. **J. Yee:** None. **S. Jouni:** None. **R. Therrien:** None. **S. Mansour:** None. **J. Nam Nguyen:** None. **C.**

BACKGROUND

HIV drugs, especially protease inhibitors (PI), have been associated with QTc interval prolongation. However, studies have shown conflicting results. The objective of this study was to compare QTc interval between an outpatient HIV-infected population on antiretroviral regimen (PI vs no PI based-regimen) and outpatient HIV-negative populations.

METHODS

The QTVIE study was a single-center observational study comparing the QTc interval between a prospective HIV-infected population on antiretrovirals and two retrospective HIV-negative control cohorts: HIV-infected cohort (n=160), surgical pre-admission cohort (n=1,761) and ECG-ViEW database (n=60,023) were included in the study analysis. The HIV-infected subjects were enrolled at the CHUM's HIV/AIDS outpatient clinic from March to October 2013. MANOVA were performed to compare the QTc interval between the HIV-infected outpatients and the HIV-negative cohorts. Prevalence of QTc interval prolongation was compared with the $\chi 2$ test.

RESULTS

Mean adjusted Fridericia rate-corrected QT (QTc-F) was of 392 ±25 ms in HIV-infected subjects, 409 ±19 ms in the surgical pre-admission subjects and 411 ±24 ms in the ECG-ViEW population ($p< 0.01$). Overall, age, sex, heart rate, hypertension, arrhythmia, myocardial infarction history and cirrhosis were associated with an increased risk of QTc interval prolongation ($p<0.01$). Our study showed no difference in the prevalence of QTc interval prolongation between HIV-infected subjects treated with a PI-based antiretroviral regimen and those treated with a non-PI based regimen (5.7% vs 0%, respectively).

CONCLUSION

Our results suggest that HIV-infected patients should not be viewed as a population at increased risk of QTc interval prolongation.

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LBII-012

DISEASE-, GENE-, AND DRUG-DRUG INTERACTIONS: IMPACT OF RENAL IMPAIRMENT, CYP2D6 DEFICIENCY, AND OCT2 INHIBITOR ON VALIPARIB (V) PHARMACOKINETICS (PK).

J. Li, S. Kim, P. LoRusso; Karmanos Cancer Institute, Detroit, MI.
J. Li: None. **S. Kim:** None. **P. LoRusso:** None.

BACKGROUND

V, a poly(ADP-ribose) polymerase inhibitor, acts as chemotherapy and radiation sensitizers. ~ 70% of V dose is cleared by renal and ~30% is metabolized mainly via CYP2D6. V is a substrate of organic cation transporter 2 (OCT2). This study aimed to evaluate the effects of complex disease-, gene-, and drug-drug interactions on V PK.

METHODS

V PK was evaluated in 20 cancer patients treated with V (20, 40, or 50 mg orally twice daily) with irinotecan in a Phase I trial. A physiologically-based PK (PBPK) model was developed to predict the individual and combined effects of renal impairment, CYP2D6 deficiency, and inhibitor of OCT2 (cimetidine) or CYP2D6 (quinidine) on V PK. Since the last treated patient PK samples were not analyzed before 9/19, the PK modeling was not finalized until 11/25/2013.

RESULTS

Population PK analysis identified creatinine clearance (CL_{Cr}) as a significant covariate explaining 30% of the interindividual variability on V CL/F in 20 patients. The PBPK modeling predicted changes in V systemic exposure under various clinical scenarios are shown in the Table.

CONCLUSION

Renal function is a major determinant of V PK. Combined factors significantly increase V exposure. This study underscores the importance of evaluating complex disease-, gene-, and drug-drug interactions in clinical drug development.

	CL_{Cr} >3.6 L/h	CL_{Cr} 1.8–3.6 L/h	CL_{Cr} <1.8 L/h	CL_{Cr} >3.6 L/h	CL_{Cr} 1.8–3.6 L/h	CL_{Cr} <1.8 L/h
	CYP2D6 Extensive Metabolizer (EM)			CYP2D6 Poor Metabolizer (PM)		
AUCτ ratio following Single-dose of V						
No inhibitor	1.00	1.73	2.59	1.17	1.94	2.83
+Cimetidine	1.17	2.06	2.98	1.37	2.31	3.27
+Quinidine	1.00	1.73	2.59	1.17	1.94	2.83
AUCτ ratio at steady-state following 7-day V treatment						
No inhibitor	1.00	1.81	2.75	1.18	2.07	3.09
+Cimetidine	1.27	2.59	3.83	1.55	3.08	4.52
+Quinidine	1.00	1.81	2.75	1.18	2.07	3.09

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LBII-013

PLASMA CYTOKINE LEVELS CORRELATE WITH SIX MONTH RESPONSE AND ERYTHROCYTE METHOTREXATE DISPOSITION IN JUVENILE IDIOPATHIC ARTHRITIS.

R. S. Funk, L. van Haandel, M. Chan, L. Rosenwasser, A. Lasky, M. Ibarra, M. Hoeltzel, J. S. Leeder, M. L. Becker; Children's Mercy Hospitals and Clinics, Kansas City, MO. **R.S. Funk:** None. **L. van Haandel:** None. **M. Chan:** None. **L. Rosenwasser:** None. **A. Lasky:** None. **M. Ibarra:** None. **M. Hoeltzel:** None. **J.S. Leeder:** None. **M.L. Becker:** None.

BACKGROUND

Cytokines are important in the pathogenesis of juvenile idiopathic arthritis (JIA). However, little is known in regard to their relationship with therapeutic response to methotrexate (MTX) therapy. Therefore, this study evaluates the relationship between MTX therapy and plasma cytokines in JIA over a 6 month treatment period.

METHODS

Blood samples collected prior to and 6 months into therapy (n=19) were evaluated. Plasma levels of IL-1α, IL-1β, IL-1Ra, IL-6, IL-17a, IL-23, IL-33, IL-37, TNFα and NAMPT were measured by immunoassay. Erythrocyte levels of MTX were measured by UPLC/MS/MS. Therapeutic response was determined by the Juvenile Arthritis Disease Activity Score (JADAS) and Peds ACR criteria. Statistical analyses were conducted by linear regression and Wilcoxon signed rank tests following the abstract submission deadline.

RESULTS

JADAS scores positively correlate with IL-1β ($p<0.05$), IL-1Ra ($p<0.05$), IL-6 ($p<0.0001$), IL-17a ($p<0.05$), TNFα ($p<0.05$) and IL-23 ($p<0.05$). Reductions in JADAS from 0-6 months correlated with reductions in IL-1α ($p<0.01$), IL-1β ($p<0.05$), IL-1Ra ($p<0.01$), IL-6 ($p<0.001$), IL-17a ($p<0.01$), IL-23 ($p<0.01$) and IL-33 ($p<0.01$). Significant reductions in IL-6 from baseline were found in ACR Ped 30 responders compared to non-responders ($p<0.01$). Erythrocyte levels of long chain MTX polyglutamates (MTXGlu3-5) at 6 months on therapy were found to correlate with reductions in IL-1α ($p<0.05$), IL-1Ra ($p<0.05$), IL-6 ($p<0.01$), IL-17a ($p<0.05$), IL-23 ($p<0.05$), IL-33 ($p<0.05$) and IL-37 ($p<0.05$).

CONCLUSION

JIA disease activity correlates directly with plasma concentrations of several cytokine markers, and reductions in these cytokines after initiation of MTX were correlated with both therapeutic response and erythrocyte disposition of MTX.

LBII-014

EFFECT OF DOSING SCHEME OF AMOXICILLIN ON ERADICATION RATES OF H. PYLORI BY THERAPY WITH PPI, AMOXICILLIN AND CLARITHROMYCIN OR METRONIDAZOLE.

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BACKGROUND

Usually, drugs used in standard regimens for H. pylori infection are dosed twice daily. However, the bactericidal effect of amoxicillin depends on the time-above-MIC, not C_{max} or AUC. Then, we aimed to examine the influence of different dosing schedules of amoxicillin on eradication rates of H. pylori by triple therapies.

METHODS

Patients infected with clarithromycin-sensitive strains of H. pylori were treated with a PPI, clarithromycin 200 mg bid and amoxicillin 750 mg bid, 500 mg tid or 500 mg qid for 1 week and those infected with clarithromycin-resistant strains were treated with a PPI, metronidazole 250 mg bid and amoxicillin 750 mg bid, 500 mg tid or 500 mg qid for 1 week. In the rapid metabolizers of CYP2C19, a PPI was dosed 4 times daily, whereas in the intermediate and poor metabolizers, a PPI was dosed twice daily.

RESULTS

Ten patients were excluded from the analysis. The eradication rates (PP) of the triple PPI/amoxicillin/clarithromycin therapy with bid, tid and qid dosings of amoxicillin were 80.3% (49/61), 96.7% (58/60) and 95.0% (57/60), respectively. Those of the triple PPI/amoxicillin/metronidazole therapy were 82.5% (33/40), 95.0% (38/40) and 97.6% (40/41), respectively. The eradication rates in the regimens with tid and qid dosings of amoxicillin were higher than that of the regimen with the bid dosing of amoxicillin.

CONCLUSION

The dosing schedule of amoxicillin significantly influenced the eradication rates of the standard triple therapies. Although amoxicillin is empirically dosed twice daily, 3 or 4 times daily dosing is appropriate for amoxicillin in H. pylori eradication therapy.

LBII-015

GENOME-WIDE ANALYSIS OF THE VARIATION IN HEPATIC PROTEIN EXPRESSION OF 22 KEY DRUG METABOLIZING ENZYMES.

N. K. Gillis, E. L. Seiser, J. K. Fallon, P. C. Smith, F. Innocenti; University of North Carolina, Chapel Hill, NC. **N.K. Gillis:** None. **E.L. Seiser:** None. **J.K. Fallon:** None. **P.C. Smith:** None. **F. Innocenti:** None.

BACKGROUND

A high degree of interindividual variability exists in the activity of ADME genes in the liver; the genetic basis of which has yet to be fully elucidated. We aimed to identify novel genetic variations in key drug metabolizing enzymes that associate with hepatic protein levels and, therefore, might alter enzyme activity.

METHODS

Human liver microsomes (HLMs) were prepared from 145 non-diseased livers. Protein levels of 22 metabolizing enzymes (8 CYPs, 14 UGTs) were measured with targeted quantitative analysis using a validated nanoUPLC-MS/MS method (Fallon *et al. J Proteome Res*. 2013; 12:4402-4413). Due to the time-intensive nature of this method, collection of protein levels was not completed until 11/8/13, at which point data

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analyses began. Available GWAS data (530,920 SNPs) (Innocenti *et al. PLoS* Genet. 2011) was used to identify quantitative trait loci (QTLs) associated with protein levels using regression analysis with covariates including ancestry (among others) and an FDR-corrected p-value (q<0.05).

RESULTS

The majority of samples were from white (90%) adult (mean age 42 years) males (67%). We identified previously published and novel *cis* (n=54) and *trans* QTLs associated with protein levels (p<6.0x10-3, q<0.05). We also identified haplotype blocks (range 1-3) that explain variability within proteins (n=6). Within class, the most variable protein levels were CYP3A5 (191 %CV), CYP3A4 (145 %CV), UGT2B17 (131 %CV), and UGT1A3 (88 %CV).

CONCLUSION

Using genomics and targeted proteomic analysis, we identified novel genetic determinants of the interindividual variability in liver protein levels of CYPs and UGTs. These findings may have important clinical implications for variable response to drugs metabolized by these enzymes.

LBII-016

DECREASED LEVELS OF TISSUE INHIBITOR OF MATRIX METALLOPROTEINASE- 2 IN NON-OBESE WOMEN WITH POLYCYSTIC OVARY SYNDROME.

V. A. Gomes, C. S. Vieira, R. A. Ferriani; FMRP-USP, Ribeirão Preto, Brazil. **V.A. Gomes:** None. **C.S. Vieira:** None. **R.A. Ferriani:** None.

BACKGROUND

Polycystic ovary syndrome (PCOS) has been associated with some cardiovascular risk factors. Matrix metalloproteinase-9 and tissue inhibitor of MMP-1 (TIMP) are implicated in cardiovascular disease. The objective of this study was to compare the plasma levels of MMP-9 and TIMP-2 in young and non-obese PCOS women with those found in healthy ovulatory controls (controls).

METHODS

A cross-sectional study was conducted at the University Hospital of the Faculty of Medicine of Ribeirao Preto, University of Sao Paulo (HC-FMRP-USP), Brazil. Included were 30 PCOS women and 19 controls, matched for age and body mass index. Plasma MMP-9 and TIMP-2 levels were measured using enzyme-linked immunoassays. These data were analyzed on December 1, 2013.

RESULTS

Patients with PCOS had significantly lower plasma TIMP-2 concentrations when compared with those found in controls (145.13 ± 7.92 vs. 173.68 ± 9.73 ng/ml; P=0.02), while MMP-9 levels did not differ significantly between PCOS and controls (p>0.05). In addition, MMP-9 was positively correlated with systolic arterial pressure, (r=0.41 P=0.01), and diastolic arterial pressure (r=0.33, P=0.01) of all participants in both groups.

CONCLUSION

The present study demonstrated that the level of TIMP-2 was reduced in non-obese PCOS women. This finding may help to explain the increased cardiovascular risk usually found in this group of patients. Support: FAPESP. There are no conflicts of interest.

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LBII-017

DEVELOPMENTAL PHARMACOKINETICS OF CLINDAMYCIN FROM PREMATURE INFANTS TO ADOLESCENTS.

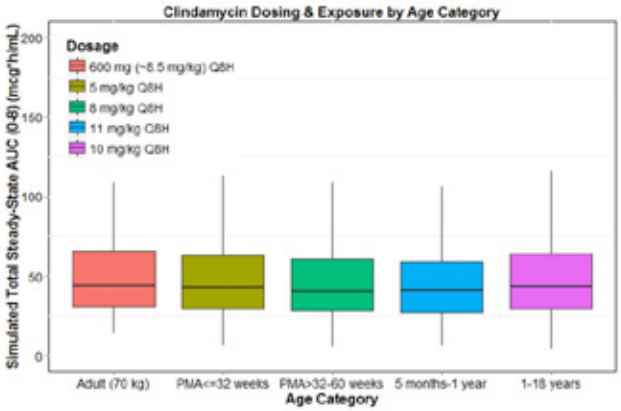
D. Gonzalez,[1] C. Melloni,[2] R. Yogev,[3] K. Watt,[2] B. Poindexter,[4] S. Mendley,[5] P. Delmore,[6] J. Autmizguine,[2] A. Lewandowski,[7] B. Harper,[2] E. Capparelli,[8] D. K. Benjamin Jr,[2] M. Cohen-Wolkowiez,[2] Best Pharmaceuticals for Children Act-Pediatric Trials Network; [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]Duke Clinical Research Institute, Durham, NC, [3]Ann and Robert Laurie Children's Hospital of Chicago, Chicago, IL, [4]Riley Hospital for Children at Indiana University, Indianapolis, IN, [5]University of Maryland, Baltimore, MD, [6]Wesley Medical Center, Wichita, KS, [7]EMMES Corporation, Rockville, MD, [8]University of California, San Diego, San Diego, CA. **D. Gonzalez:** None. **C. Melloni:** None. **R. Yogev:** None. **K. Watt:** None. **B. Poindexter:** None. **S. Mendley:** None. **P. Delmore:** None. **J. Autmizguine:** None. **A. Lewandowski:** None. **B. Harper:** None. **E. Capparelli:** 2. I am a paid consultant/employee for consultant for Trius Pharmaceuticals (< $10,000) and a DSMB member for Cempra Pharmaceuticals (**D.K. Benjamin Jr:** 2. I am a paid consultant/employee for Astellas Pharma US, Cempra, Cubist Pharmaceuticals,Johnson & Johnson Pharmaceutical Research & Development, Merck & Co., Pfizer, and The Medicines Company) **M. Cohen-Wolkowiez:** 2. I am a paid consultant/employee for Cempra Pharmaceuticals, GlaxoSmithKlein, Janssen Research and Development, Special Products Ltd., Tetraphase Pharmaceuticals, and The Medicines Company (<$25,000).

BACKGROUND

Clindamycin is commonly given to treat children with methicillin-resistant *Staphylococcus aureus* (MRSA), yet little is known about the PK across pediatric age groups.

METHODS

A population PK analysis was performed in NONMEM using sparse samples collected from children receiving intravenous clindamycin per standard of care. PK data included in this analysis were available October 11, 2013. Covariates were selected using a forward inclusion-backward elimination approach. The final model was used to optimize pediatric dosing to match adult exposure proven effective against MRSA.



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RESULTS

A total of 191 plasma PK samples collected from 123 children were included in the analysis. Median age (range) was 3.3 (0-20) years and postmenstrual age (PMA) was 212 (23.6-1081) weeks. Median clindamycin dosing was 9.9 (3.8-15.1) mg/kg. A one-compartment PK model described the data well. The final model included body weight and a sigmoidal maturation relationship between PMA and CL: CL (L/h)=13.5*(weight/70)$^{0.75}$*(PMA$^{3.1}$/(43.5$^{3.1}$+PMA$^{3.1}$)); V (L)=61.5*(weight/70). Maturation reached 50% adult CL values at ~44 weeks PMA. Dosing simulations support age-based dosing (Figure).

CONCLUSION

Clindamycin dosing should be age-adjusted to match exposure proven effective in adults with MRSA.

LBII-018

QUANTITATIVE PREDICTION OF *IN VIVO* CYP2C19 ACTIVITY AND INTER-INDIVIDUAL VARIABILITY IN DIFFERENT CYP2C19 GENOTYPES.

B. Steere, J. Baker, J. Rehmel, S. Hall, **Y. Guo;** Eli Lilly and Company, Indianapolis, IN. **B. Steere:** 2. I am a paid consultant/employee for Eli Lilly and Company. **J. Baker:** 2. I am a paid consultant/employee for Eli Lilly and Company. **J. Rehmel:** 2. I am a paid consultant/employee for Eli Lilly and Company. **S. Hall:** 2. I am a paid consultant/employee for Eli Lilly and Company. **Y. Guo:** 2. I am a paid consultant/employee for Eli Lilly and Company.

BACKGROUND

The design of clinical trials intended to elucidate the role of CYP2C19 genetics in drug disposition requires estimates of CYP2C19 genetic effects and their variabilities. However, methods lack that predict these two critical parameters. This study aimed to examine the utility of a hybrid approach of top-down and bottom-up IVIVE methods to estimate them in each CYP2C19 genotype.

METHODS

Simcyp Population-based Simulator® (v.12.2) was used to simulate PK profiles of CYP2C19 substrates. The hepatic CYP2C19 abundance and its variability in each genotype were derived from the metabolic activity as measured by S-mephenytoin in genotyped human liver microsomal samples (N=128), tested by simulation using S-mephenytoin and then validated with citalopram (CT). The activity ratio between each non-wild type (WT) and the WT were used as a scaling factor to estimate CYP2C19 abundance relative to the WT default value. The CV of activity was used as the abundance CV within each genotype. Clinical data of S/R-mephenytoin metabolic ratio (MR) and IV systemic clearance of CT was used to calculate respective total hepatic $Cl_{int,u}$ by the Simcyp retrograde model. The simulation of S/R-mephenytoin MR and CT Cl_{po} was conducted for 14 and 3 published studies, respectively.

RESULTS

Relative to the WT, the CYP2C19 abundance (CV values) in genotypes *1/*1, *1/null, *1/*17, *17/null, *17/*17 and null/null was determined to be 1.00 (138%), 0.38 (130%), 1.79 (155%), 0.83 (80%), 1.85 (117%), and 0 (55%), respectively. All of the point estimates and variability of S/*R*-mephenytoin MR or CT Cl_{po} within each genotype were predicted within 2-fold of the observed.

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CONCLUSION

CYP2C19 hepatic abundance and variability in different genotypes were validated to facilitate PK variability prediction and clinical trial design for CYP2C19-metabolized drugs.

LBII-019

A PHARMACOKINETIC COMPARISON OF IMA-638, AN ANTI- IL-13 MONOCLONAL ANTIBODY, AMONG HEALTHY VOLUNTEERS AND PATIENTS WITH ASTHMA OR ULCERATIVE COLITIS.

F. Hua,[1] J. Ribbing,[2] S. Martin,[1] A. Heatherington[1]; [1]Pfizer Inc., Cambridge, MA, [2]Pfizer Inc., Sollentuna, Sweden. **F. Hua:** 2. I am a paid consultant/employee for Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational: IMA-638.
J. Ribbing: 2. I am a paid consultant/employee for Pfizer Inc. **S. Martin:** 2. I am a paid consultant/employee for Pfizer Inc. **A. Heatherington:** 2. I am a paid consultant/employee for Pfizer Inc.

BACKGROUND

IMA-638 (Anrukinzumab) is a humanized antibody (IgG1) that binds and inhibits human IL-13. It has been evaluated in both asthma and ulcerative colitis (UC) patients, as well as healthy volunteers. Since differences in drug exposure in different patient populations could lead to different treatment regimens, the objective of the current analysis was to compare PK properties for IMA-638 in different populations.

METHODS

IMA-638 has been tested in a total of 5 Phase I and II trials with subcutaneous (SC) and intravenous (IV) administration and doses ranging from 10 mg to 600 mg across the 3 populations. Serum concentration of IMA-638 was analyzed using the same validated enzyme-linked immunosorbent assay (ELISA) for all the studies. A population pharmacokinetic analysis was performed using nonlinear mixed-effects modeling (NONMEM) with all PK data. A two-compartment model with first-order absorption and elimination was found to best describe the data. The final dataset for this analysis was available after September 19, 2013.

RESULTS

The preliminary model included an allometric model on volume and clearance parameters. Subjects with mild asthma have similar clearance to healthy volunteers (0.007 L/h, with 32% CV). However, the clearance was 17% higher in moderate-severe asthma patients and 91% higher in UC patients. There was no indication on target mediated drug disposition contributing to the increased CL.

CONCLUSION

The popPK modeling indicates that IMA-638 has a faster clearance in UC vs asthma or healthy volunteers. Consequently, for any given dose of IMA-638, the exposure in UC patients would be lower.

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LBII-020

STEREOSELECTIVE AND INTERINDIVIDUAL DIFFERENCES IN METHADONE METABOLISM IN HUMAN HEART MICROSOMES.

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J. Huguet: None. **F. Gaudette:** None. **F. Bélanger:** None. **V. Michaud:** None. **J. Turgeon:** None.

BACKGROUND

The CYP450-mediated metabolism in the heart can modulate the intracellular drug concentration, and therefore its cardiac drug action locally in the organ. Drugs known to prolong the QT interval are candidate drug, for this approach. We therefore tested the stereoselective metabolism of methadone in the human heart ventricle.

METHODS

Human heart microsomes were prepared by differential centrifugation among a large cohort (n=70) of human hearts transplanted patients. S- and R-methadone was incubated (150 µM). EDDP and EMDP, metabolites of methadone were analyzed by LC-MSMS. Patient's cohort was divided in 5 groups: Group 1 (n=13); Men (M), left ventricle (LV), non-ischemic (NI), Group 2 (n=18); M, LV, ischemic (I), Group 3 (n=18); M, right ventricle (RV), Group 4 (n=13); women, LV and Group 5 (n=9); normal hearts. Comparison among all groups was performed using the Kruskal-Wallis test.

RESULTS

(These data could not be analyzed before September 19, 2013, and were analyzed on November 1, 2013): First, there was a stereoselective metabolism toward the S-methadone. The mean metabolic activity of S-methadone, which was expressed in pmoles of EDD formed / min / mg of protein was for group 1 to 5 : 0,37 ± 0,3, 0,19 ± 0,09, 0,13 ± 0,12, 0,12 ± 0,1 and 0,71 ± 1,64. There was a statistical significant difference between M-LV-NI and M-RV ($p<0,01$). Moreover, there was a significant difference between M-LV-NI and W-LV ($p<0,01$).

CONCLUSION

Our results suggest that the heart is capable of stereoselective metabolism toward the S-methadone. Moreover, groups with covariates such as RV and gender compared to NI heart had lower metabolism. This suggests that a lower metabolism of methadone would increase S-methadone concentration within the cell and favor methadone known cardiotoxic effect, such as QT prolongation.

LATE-BREAKING AND ENCORE ABSTRACT SESSION II

Friday, March 21, 2014 • International Hall 7:30 am – 3:30 pm
Attended Posters 11:45 am – 1:15 pm

LBII-021

GENE VARIANTS IN CYP2C19, IN ADDITION TO CYP2B6, ARE ASSOCIATED WITH ALTERED *IN VIVO* BUPROPION PHARMACOKINETICS.

A. Zhu, N. Benowitz, R. F. Tyndale; University of Toronto, Toronto, ON, Canada. **A. Zhu:** None. **N. Benowitz:** 2. I am a paid consultant/employee for Pfizer, McNeil and GlaxoSmithKline. **R.F. Tyndale:** 2. I am a paid consultant/employee for McNeil.

BACKGROUND

Bupropion (BUP) is used to treat depression and promote smoking cessation. Urinary recovery of BUP, and its metabolites hydroxybupropion (OH-BUP, an active metabolite made by CYP2B6), threohydrobupropion (TB), and erythrohydrobupropion (EB) only account for ~10% of an administered BUP dose, suggesting the existence of novel primary and secondary metabolites. *In vitro* data suggested CYP2C19 may mediate the formation of these novel metabolites. Following our evaluation of *CYP2B6*, we recently investigated the additional impact of *CYP2C19* on *in vivo* BUP pharmacokinetics (PK).

METHODS

Steady state BUP PK was investigated in 42 health volunteers. Subjects were given 150 mg BUP per day for 7 days and then their plasma BUP and metabolites levels were monitored for 24 h. The impact of *CYP2C19*2* (a decreased activity allele) and **17* (an increased activity allele) on BUP PK, with and without controlling for *CYP2B6* genotype, were analyzed using regression in November.

RESULTS

*CYP2C19*2* was associated with higher BUP AUC. The mean (95%CI) BUP AUC were 637(568,706) and 771(694,848) h.ng/mL in individuals without and with *CYP2C19*2,* respectively (P=0.01, accounting for ~14% of the variation). *CYP2C19*2* was also associated with significantly higher EB and TB AUC (P<0.001). Those with *CYP2C19*17* had 5~10% lower BUP, EB and TB AUC (non-significant, P=0.25-0.27). However, neither *CYP2C19*2* nor **17* altered OH-BUP AUC. Adjusting for CYP2B6 genotype did not alter these associations.

CONCLUSION

These data suggest that CYP2C19 is involved in the metabolism of BUP, EB and TB, but not OH-BUP. *CYP2C19* variants may not alter BUP's smoking treatment outcomes, which are determined by OH-BUP levels (unaffected by CYP2C19). However, *CYP2C19* variants may alter the side effects mediated by BUP, EB and TB, such as seizure.

LATE-BREAKING AND ENCORE ABSTRACT SESSION II

Friday, March 21, 2014 • International Hall 7:30 am – 3:30 pm
Attended Posters 11:45 am – 1:15 pm

LBII-022

ASSOCIATION OF CHRNA5-A3-B4 SNPS RS2036527 WITH SMOKING CESSATION THERAPY RESPONSE IN AFRICAN AMERICAN SMOKERS.

A. Zhu,[1] Q. Zhou,[1] L. Sanderson Cox,[2] S. P. David,[3] J. S. Ahluwalia,[4] N. L. Benowitz,[5] R. F. Tyndale[1]; [1]University of Toronto, Toronto, ON, Canada, [2]University of Kansas School of Medicine, Kansas City, KS, [3]Stanford University School of Medicine, Stanford, CA, [4]University of Minnesota Medical School, Minneapolis, MN, [5]University of California, San Francisco, San Francisco, CA. **A. Zhu:** None. **Q. Zhou:** None. **L. Sanderson Cox:** None. **S.P. David:** 2. I am a paid consultant/employee for Genophen. **J.S. Ahluwalia:** None. **N.L. Benowitz:** None. **R.F. Tyndale:** 2. I am a paid consultant/employee for McNeil.

BACKGROUND

Robust associations between *CHRNA5-A3-B4* variants and smoking behaviors exist, however, the association with smoking abstinence is less understood, particularly among African Americans. It is unclear whether *CHRNA5-A3-B4* variants have an overall effect on abstinence (i.e. all treatment arms including placebo) or whether they interact with specific pharmacotherapy(s) to influence cessation.

METHODS

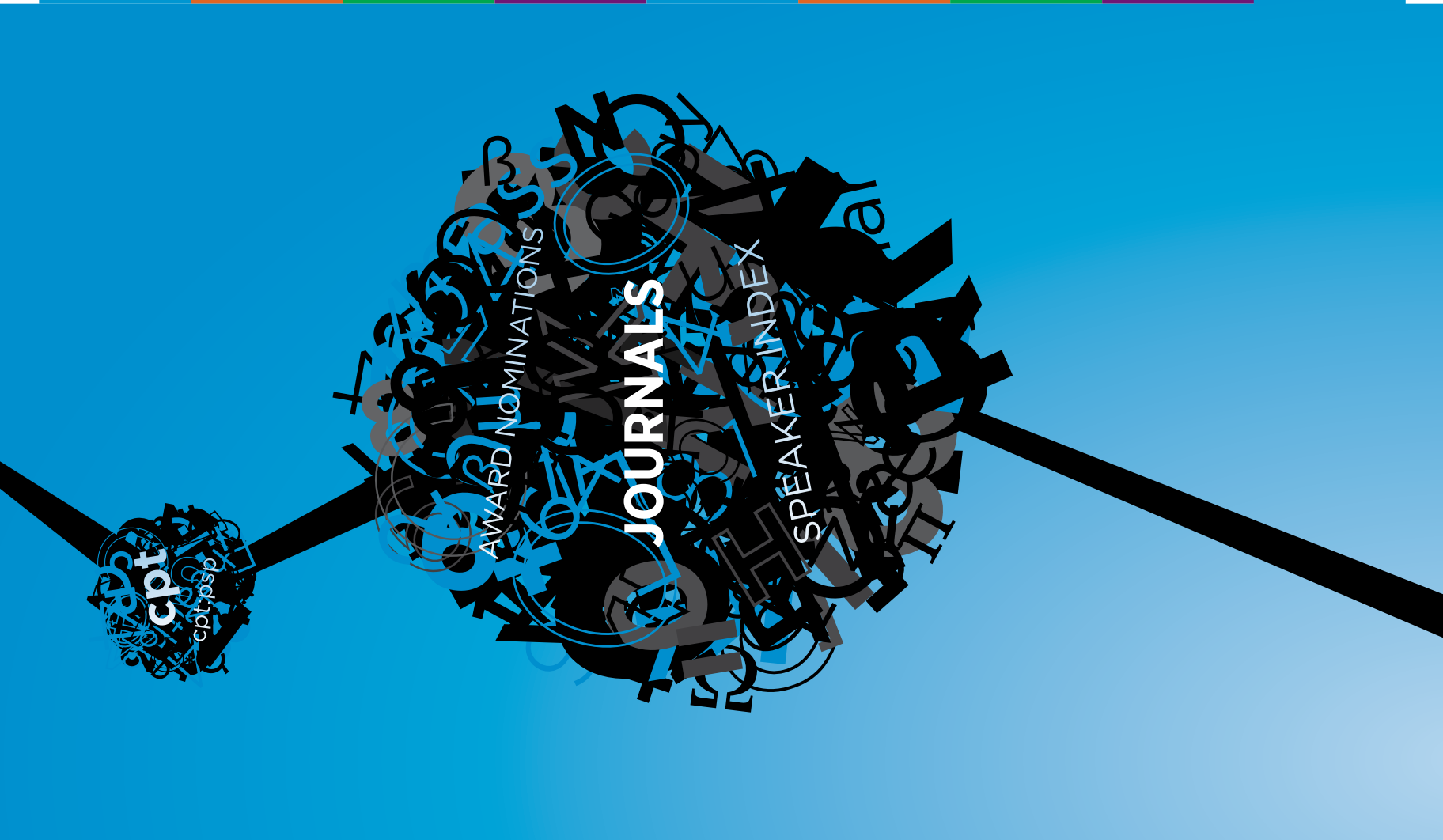
We investigated the association of four independent *CHRNA5-A3-B4* SNPs with tobacco consumption and smoking abstinence in two independent smoking cessation trials of 1,295 African American smokers. The effects of rs2036527 after adjusting for other genetic variants and smoking behaviors were tested after September 19.

RESULTS

A consistent association between rs2036527[A] and lower abstinence during active pharmacotherapy was observed. Rs2056527[A] was associated with lower abstinence with nicotine gum (during-treatment: OR=0.31&P<0.001; end of treatment (EOT): OR=0.51&P=0.02), bupropion (during-treatment: OR=0.54&P=0.05; EOT: OR=0.59&P=0.08) and both together (during-treatment: OR=0.42&P<0.001; EOT: OR=0.55&P=0.004). Additionally, rs588765[T] was associated with abstinence with nicotine gum (OR=2.31&P<0.01). Rs16969968 occurred at a low frequency and was not consistently associated with abstinence. *CHRNA5-A3-B4* variants were not associated with tobacco consumption and adjustments for smoking behaviors and other *CHRNA5-A3-B4* variants did not alter the associations between rs2036527 with smoking abstinence.

CONCLUSION

CHRNA5-A3-B4 gene variants were not associated with baseline smoking, but did alter smoking abstinence during active pharmacotherapy in African Americans, even after adjusting for smoking behaviors and other *CHRNA5-A3-B4* SNPs.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ACKNOWLEDGMENT

ASCPT would like to recognize the Scientific Awards Nominations Task Force for securing nominations for the 2014 Scientific Awards.

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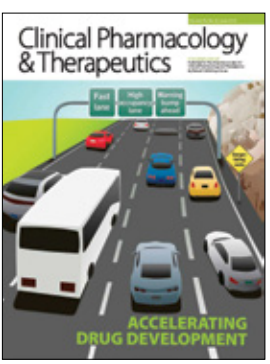

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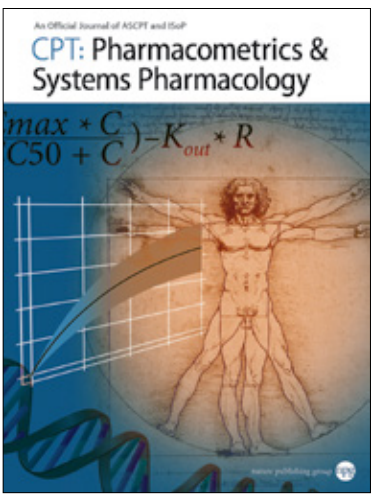

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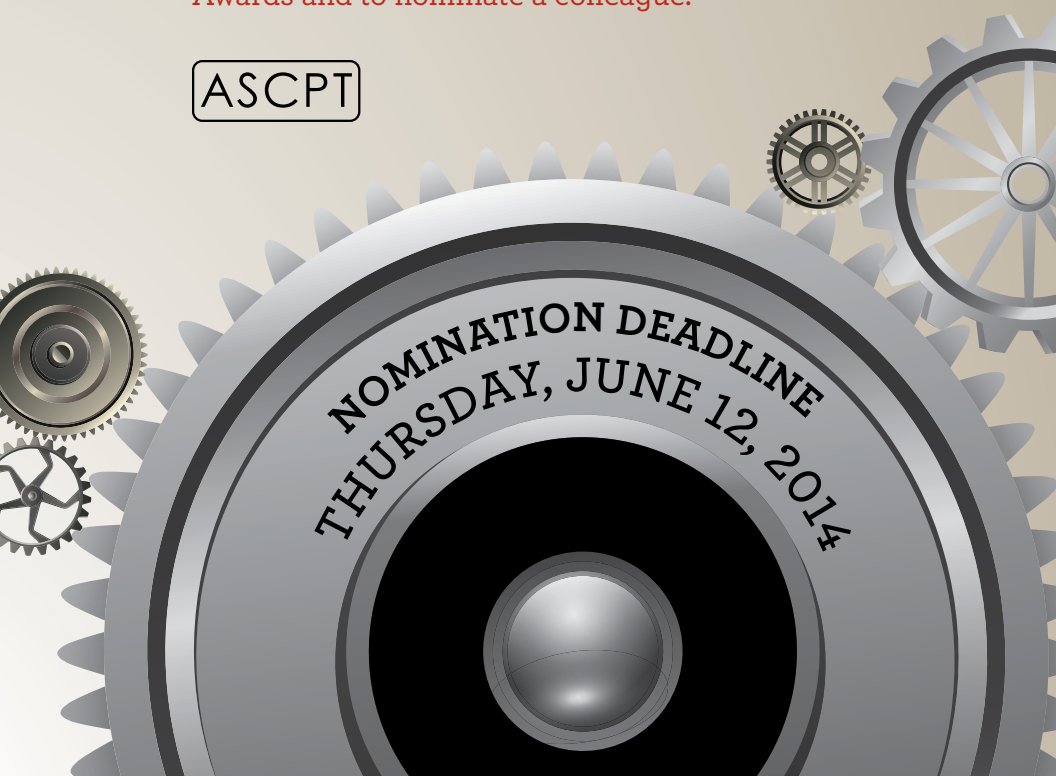

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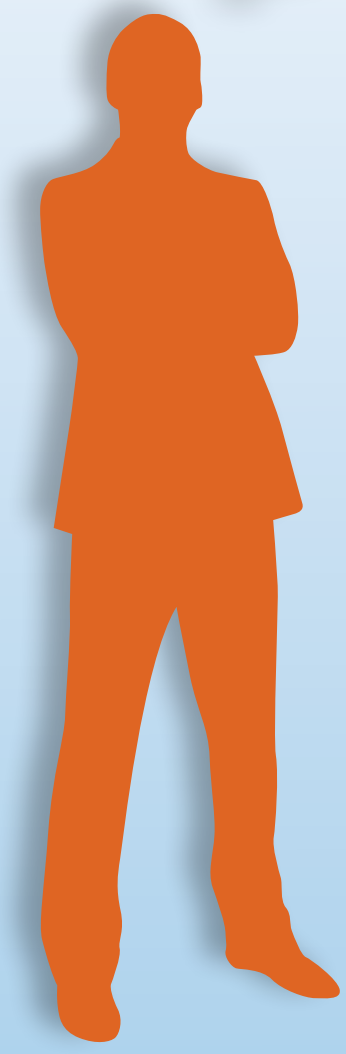

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