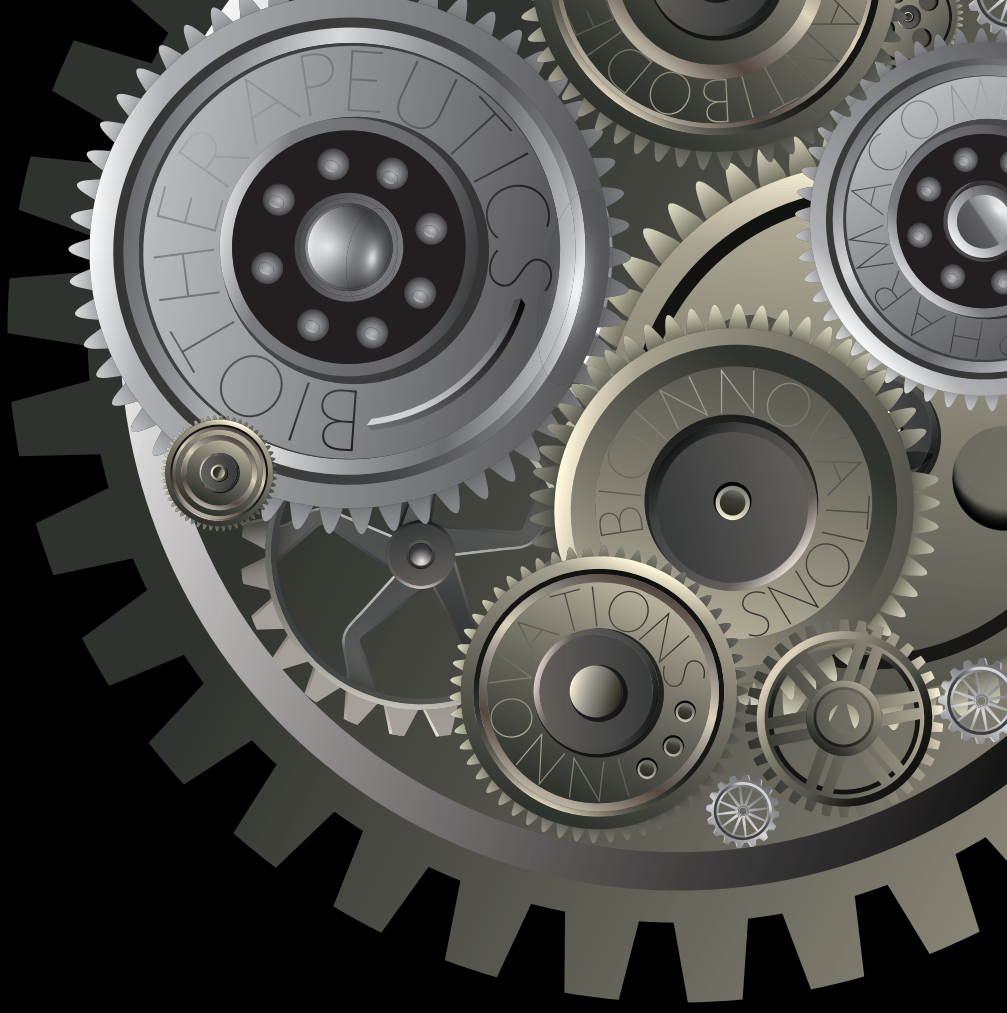

ASCPT 2015 ANNUAL MEETING

March 3–7, 2015 ❁ Hyatt Regency ❁ New Orleans, LA

PROGRAM & PRE-CONFERENCES

ASCPT

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ASCPT

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WELCOME MESSAGE

GREETINGS COLLEAGUE!

Welcome to New Orleans and to the 116th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics (ASCPT)! This Meeting is the highlight of the year for our Society, providing the perfect opportunity to network and engage in a world-class scientific program featuring Nobel laureates, as well as scientific leaders from academia, government, and industry.

With a theme of "Advancing the Bioinnovation Engine," ASCPT 2015 features two outstanding pre-conference programs, the post-conference Clinical Pharmacology Curriculum Review Course, and, interposed between these signature educational offerings, a "best-in-class" roster of outstanding scientific speakers. Students and trainees will enjoy great programming including Speed Mentoring and the Trainee Luncheon.

New in 2015, we will showcase the new 2015-2020 Strategic Plan, a Bioinnovation Forum with TED-Style talks, an asparagus population kinetics member volunteer study, and guided poster walks; and, based on attendee feedback, addition of considerable networking time in the Exhibit and Poster hall. Our ground-breaking Strategic Plan promises to impact the science and practice of translational medicine, building on our strong foundation of clinical pharmacology and therapeutics.

Join me in celebrating the success and growth of our family of journals. Besides our flourishing existing portfolio of *Clinical Pharmacology & Therapeutics* and *CPT: Pharmacometrics & Systems Pharmacology,* please welcome *Clinical and Translational Science* as the new addition to our family.

ASCPT 2015 includes State of the Art lectures by Michael Levitt, PhD, Stanford University; John Brownstein, PhD, Children's Hospital, and Suzanne L. Topalian, MD, Johns Hopkins University. Our Featured Speakers highlight two outstanding member scientists, Julie A. Johnson, PharmD, University of Florida, and Kim L. R. Brouwer, PharmD, PhD, University of North Carolina, Chapel Hill.

This year's outstanding ASCPT awardees are: Michel Eichelbaum, MD; Thomas Ludden, PhD; Mikko Niemi, MD, PhD; Kenneth Rockwood, MD, FRCPC, FRCP; Patricia Slattum, PharmD, PhD; Robert Temple, MD; and Paul Watkins, MD.

Finally, join me in thanking the many people who have made this meeting possible, including the Scientific Program Committee, under the fantastic leadership of Lei Zhang, PhD, the members and leadership of the Scientific Sections, who provided the creative energy to the program, Sharon Swan and the excellent staff at ASCPT, and each and every ASCPT member because your engagement will make this meeting spectacular.

I encourage you to make the most of the many learning and networking opportunities available and thank you for attending ASCPT 2015!

Sincerely,

John A. Wagner, MD, PhD
President

SCHEDULE-AT-A-GLANCE

ACKNOWLEDGMENTS

ASCPT BOARD OF DIRECTORS

THANK YOU TO THE ASCPT BOARD OF DIRECTORS FOR THEIR LEADERSHIP AND DEDICATION IN GUIDING THE SOCIETY.

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Malle Jurima-Romet, PhD
In Memoriam

TUESDAY, MARCH 3, 2015

7:00 am – 3:00 pm	Pre-conference Registration	EMPIRE FOYER
8:30 am - 5:00 pm	**PRE-CONFERENCES**	
	Clinical Pharmacology: Toward a Global Agenda	EMPIRE A
	Quantitative Systems Pharmacology: Multiscale Model-Based Drug Development Through Integrating Systems Biology and Pharmacometrics	EMPIRE B
12:00 noon – 1:00 pm	Pre-conferences Lunch	EMPIRE FOYER
1:00 pm – 5:00 pm	CPT Editorial Team Meeting *(By Invitation Only)*	STRAND 10

WEDNESDAY, MARCH 4, 2015

7:00 am – 5:00 pm	ASCPT Central and Registration Open	EMPIRE FOYER
7:00 am – 8:30 am	Board of Directors Meeting *(By Invitation Only)*	STRAND 10
8:00 am – 12:00 noon	PSP Editorial Team Meeting *(By Invitation Only)*	STRAND 14
8:30 am – 11:00 am	**SPECIAL SESSION** Evidence of Effectiveness: What is the Role of Clinical Pharmacology in Providing Confirmatory or Supportive Evidence?	EMPIRE C
10:00 am – 12:00 noon	**SPECIAL SESSION** The Other EBM: Evidence-Based Monitoring	EMPIRE D
11:30 am – 2:00 pm	Bioinnovation Fieldtrip *(Ticket Required)*	
12:00 noon – 1:00 pm	New Member Welcome	STRAND 11
12:00 noon – 1:30 pm	CCSS Meeting *(By Invitation Only)*	STRAND 12
1:00 pm – 2:30 pm	**SPECIAL EDUCATION SESSION** Effectively Presenting Your Work	EMPIRE D
1:00 pm – 2:30 pm	Clinical Pharmacology Training Program Directors Meeting *(By Invitation Only)*	STRAND 13
2:00 pm – 2:30 pm	Awards Reception *(By Invitation Only)*	EMPIRE C

SCHEDULE-AT-A-GLANCE

WEDNESDAY, MARCH 4, 2015

2:30 pm – 3:30 pm	Opening Session	EMPIRE A/B
3:30 pm – 4:30 pm	**STATE OF THE ART LECTURE** *Michael Levitt, PhD*	EMPIRE A/B
4:00 pm – 5:00 pm	PhRMA Foundation Meeting	STRAND 2
4:30 pm – 6:30 pm	Opening Reception/Exhibit Hall Open	ELITE HALL
	Asparagus Population Kinetic Project	
5:00 pm – 5:30 pm	Showcase of Top Trainee Abstracts	ELITE HALL

THURSDAY, MARCH 5, 2015

7:00 am – 5:00 pm	ASCPT Central and Registration Open	EMPIRE FOYER
7:00 am – 9:00 am	American Board of Clinical Pharmacology (ABCP) Board Meeting *(By Invitation Only)*	STRAND 10
7:30 am – 9:00 am	**SECTION MEETINGS**	
	Pharmacometrics & Pharmacokinetics (PMK)	EMPIRE B
	Biomarkers & Translational Tools (BTT)	STRAND 12
	SCIENCE AT SUNRISE	
	Clinical Pharmacology for Biologics 101: Key Differences From Small Molecules	EMPIRE C/D
	Informal Gathering of Pediatric Pharmacology Research Unit Members (PPRU) *(By Invitation Only)*	STRAND 7
	PSP Editorial Board Meeting *(By Invitation Only)*	STRAND 14
9:15 am – 10:15 am	**STATE OF THE ART LECTURE** *John Brownstein, PhD*	EMPIRE A
10:30 am – 11:30 am	**RAWLS-PALMER PROGRESS IN MEDICINE AWARD LECTURE** *Paul Watkins, MD*	EMPIRE A
10:30 am – 12:30 pm	**SYMPOSIA**	
	Little Data, Big Decisions in Drug Development and Therapeutics	EMPIRE B
	Breakthrough Therapy Designation: Advancing the Bioinnovation Engine in Oncology and Infectious Diseases	EMPIRE C/D
11:30 am – 6:30 pm	**EXHIBIT AND POSTER HALL OPEN**	ELITE HALL

THURSDAY, MARCH 5, 2015

12:00 noon – 1:30 pm	Lunch Available for Purchase in the Poster and Exhibit Hall *(Ticket Required)*	ELITE HALL
	Covance Product Theater *(By Invitation Only)*	ELITE HALL
	Trainee Luncheon *(Ticket Required)*	STORYVILLE
1:00 pm – 2:00 pm	**FEATURED SPEAKER** *Julie A. Johnson, PharmD*	EMPIRE A
1:00 pm – 2:30 pm	**WORKSHOPS**	
	Translating In Vitro Transporter Data into Clinical Predictions: What We Know and Where We Are Going	EMPIRE B
	Bioequivalence Standards for Narrow Therapeutic Index (NTI) Drugs: Are They Stringent Enough to Ensure Safety and Efficacy?	EMPIRE C/D
2:30 pm – 4:00 pm	**SPECIAL SESSION** *Bioinnovation Forum*	EMPIRE A
3:00 pm – 4:30 pm	**SECTION MEETINGS**	
	Drug Development & Regulatory Sciences (DDR)	STRAND 11
	Molecular Pharmacology & Pharmacogenetics (MOL)	STRAND 12
	Organ Specific Diseases (OSD)	STRAND 13
3:30 pm – 4:30 pm	**ORAL ABSTRACT SESSION** *High Impact Application of Modeling and Simulation*	EMPIRE B
4:30 pm – 6:30 pm	Wines Around the World Networking Reception	ELITE HALL
	Attended Posters and Poster Walks	
4:45 pm – 5:30 pm	**POSTER WALK I**	
	Innovations Across the Drug Development Spectrum in Oncology	ELITE FOYER
5:00 pm – 6:00 pm	Donor Reception *(By Invitation Only)*	ELITE HALL ASCPT THEATER
5:30 pm – 6:15 pm	**POSTER WALK II**	
	Late-breaking/Encore Abstracts	ELITE FOYER

SCHEDULE-AT-A-GLANCE

THURSDAY, MARCH 5, 2015

6:00 pm – 7:00 pm	UCSF-Stanford-Genentech Reception for Faculty, Trainees, Staff, Alumni and Friends *(By Invitation Only)*	STRAND 10
	Metrum Research Reception *(By Invitation Only)*	STRAND 8
6:00 pm – 7:30 pm	PhRMA Foundation Reception *(By Invitation Only)*	STRAND 2

FRIDAY, MARCH 6, 2015

7:00 am – 5:00 pm	ASCPT Central and Registration Open	EMPIRE FOYER
7:30 am – 9:00 am	**SCIENCE AT SUNRISE SESSION**	
	Biomarkers: Enhancing Success in Drug Development	EMPIRE C/D
	SECTION MEETINGS	
	Oncology (ONC)	STRAND 11
	Special Populations (SPO)	STRAND 12
	CPT Editorial Board Meeting *(By Invitation Only)*	CELESTIN A/B/C
9:15 am – 10:15 am	**STATE OF THE ART LECTURE** *Suzanne L. Topalian, MD*	EMPIRE A
10:30 am – 11:30 am	**OSCAR B. HUNTER MEMORIAL AWARD IN THERAPEUTICS LECTURE** *Michael Eichelbaum, MD*	EMPIRE A
10:30 am – 12:30 pm	**SYMPOSIA**	
	Development of PCSK9 Inhibitors: A Paradigm Shift in the Treatment of Hypercholestrolemia	EMPIRE B
	Sex is the Most Important Polymorphism to Be Considered in Personalized Medicine: Or is It?	EMPIRE C/D
11:30 am – 6:30 pm	**EXHIBIT AND POSTER HALL OPEN**	ELITE HALL
11:45 am – 12:45 pm	Speed Mentoring	STORYVILLE
11:45 am – 1:00 pm	Finance Committee Meeting	STRAND 6
12:00 noon – 1:00 pm	Pharmacometabolomics Special Interest Group	STRAND 7

FRIDAY, MARCH 6, 2015

12:00 noon – 1:30 pm	OmniComm Product Theater *(By Invitation Only)* Lunch Available for purchase in the Poster and Exhibit Hall *(Ticket Required)*	ELITE HALL
1:00 pm – 2:00 pm	**FEATURED SPEAKER** *Kim L. R. Brouwer, PharmD, PhD*	EMPIRE A
1:00 pm – 2:30 pm	**WORKSHOPS**	
	Emerging Approaches to Assess Pro-Arrhythmia Risk in Drug Development: Moving Beyond hERG and QTc	EMPIRE B
	The ABC's of Antibody Drug Conjugate (ADC)	EMPIRE C/D
2:15 pm – 2:30 pm	Transition to the Future	EMPIRE A
2:30 pm – 4:30 pm	**SYMPOSIUM**	
	Personalized Medicines Using Genome-Wide Approaches	EMPIRE A
2:45 pm – 3:45 pm	**SHEINER-BEAL PHARMACOMETRICS AWARD LECTURE** *Thomas M. Ludden, PhD*	EMPIRE B
3:00 pm – 4:30 pm	**SECTION MEETINGS**	
	Infectious Diseases (INF)	STRAND 11
	Biologics	STRAND 12
	Drug Safety (SAF)	STRAND 13
4:30 pm – 5:30 pm	International Transporter Consortium (ITC) Special Interest Group Meeting *(By Invitation Only)*	STRAND 10
4:30 pm – 6:30 pm	**PRESIDENT'S RECEPTION**	ELITE HALL
	Attended Posters and Poster Walks	
4:45 pm – 5:30 pm	**POSTER WALK III**	
	Practical Approaches for Optimizing Pediatrics Dosage or Delivery	ELITE FOYER
	POSTER WALK IV	
5:30 pm – 6:15 pm	Utility of Real Life Data to Answer Clinical Questions	ELITE FOYER
6:30 pm – 8:30 pm	Gavel Club Dessert Reception *(By Invitation Only)*	PRESIDENT'S SUITE

SCHEDULE-AT-A-GLANCE

SATURDAY, MARCH 7, 2015

7:00 am – 10:00 am	ASCPT Central and Registration Open	EMPIRE FOYER
7:00 am – 9:00 am	Board of Directors Meeting *(By Invitation Only)*	STRAND 14
7:00 am – 4:00 pm	**CLINICAL PHARMACOLOGY CURRICULUM REVIEW COURSE**	
	Clinical Track	CELESTIN A
	Drug Development Track	CELESTIN B/C
7:30 am – 9:00 am	**SCIENCE AT SUNRISE**	
	New Insights and Novel Biomarkers for Predicting Transporter-Mediated Drug-Drug Interactions: A Multi-Sector Perspective	EMPIRE D
9:00 am – 10:00 am	**LEON I. GOLDBERG YOUNG INVESTIGATOR AWARD LECTURE** *Mikko Niemi, MD, PhD*	EMPIRE A
	ORAL ABSTRACT SESSIONS	
	Translating 'Omics' for Clinical Discovery and Delivery	EMPIRE C
	Ongoing Challenges in Regulatory Sciences: Emerging Perspectives	EMPIRE B
10:15 am – 12:15 pm	**SYMPOSIA**	
	New Perspectives on Drug-Target Interactions: Implications for Systems Pharmacology and Clinical Practice	EMPIRE A
	Tackling the Big 3: Using Quantitative Pharmacology Tools to Develop Better Treatments for HIV, Tuberculosis and Malaria	EMPIRE B
10:15 am – 11:45 am	**WORKSHOPS**	
	Impact of the Gut Microbiome on Disease Pathogenesis and Drug Response	EMPIRE C
	Patient Reported Outcomes: Bringing Your Patient's Feelings to Center Stage of the Clinically Relevant Dose Equation	EMPIRE D

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 "**Advancing the Bioinnovation Engine**". 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
R Regulation
D Development
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 offers two 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. Please pages 19-30 for details on these sessions.

TUESDAY, MARCH 3
8:30 am – 5:00 pm
EMPIRE A

Clinical Pharmacology: Toward a Global Agenda Pre-conference
Co-Sponsored by the International Consortium for Innovation and Quality in Pharmaceutical Development

TUESDAY, MARCH 3
8:30 am – 5:00 pm
EMPIRE B

Quantitative Systems Pharmacology: Multiscale Model-Based Drug Development Through Integrating Systems Biology and Pharmacometrics Pre-conference
Co-Sponsored by the International Society of Pharmacometrics

ASCPT would like to thank the International Consortium for Innovation and Quality in Pharmaceutical Development and the International Society of Pharmacometrics for their sponsorship of the 2015 Pre-conference programs.

SCHEDULE-AT-A-GLANCE

WEDNESDAY, MARCH 4

SPECIAL SESSION

Evidence of Effectiveness: What is the Role of Clinical Pharmacology in Providing Confirmatory or Supportive Evidence?
8:30 am – 11:00 am
EMPIRE C

The US FDA is currently updating the 1998 clinical "effectiveness" guidance, a key document for all stakeholders involved in research, development and regulatory approval of new medicines. A very significant issue is the approval of new drugs based on a single pivotal clinical trial plus confirmatory evidence. This will be a great opportunity for ASCPT meeting attendees to hear the latest thinking on the proposed revisions and influence what should be considered confirmatory evidence based on clinical pharmacology approaches. The revised guidance is expected to have a broad impact on drug development and regulation.

SPECIAL SESSION

The Other EBM: Evidence-Based Mentoring
10:00 am – 12:00 noon
EMPIRE D

Sharon E. Straus, author of *Mentorship in Academic Medicine*, will facilitate an interactive discussion of the evidence base for mentoring and best practices contributing to productive mentoring relationships. In small groups facilitated by ASCPT members, participants will discuss case studies illustrating common issues in mentoring and share mentoring experiences. Common themes will be discussed among the larger group, including tips for mentors, tips for mentees, distance mentoring, team mentoring, and managing conflict in mentoring relationships. Resources available to enhance mentoring relationships, including personal development planning tools, will be explored.

SPECIAL EDUCATION SESSION

Effectively Presenting Your Work
1:00 pm – 2:30 pm
EMPIRE D

This session will provide attendees with important instruction and guidance on how to compose and present effective oral/poster presentations and abstracts. It is important that scientific discoveries are communicated effectively in order to disseminate new knowledge, engage potential collaborators, and receive important feedback from fellow scientists. Attendees will learn how to present their work with focus on use of figures, conveying concise and clear messages, organizations and structure, and how to keep the audience engaged.

OPENING SESSION

2:30 pm – 3:30 pm
EMPIRE A/B

Join us as ASCPT President, John A. Wagner, MD, PhD presents the State of the Society Address and recognizes the 2015 ASCPT Award recipients.

The Opening Session is sponsored by:

Genentech
A Member of the Roche Group

OPENING RECEPTION AND EXHIBITS

4:30 pm – 6:30 pm
ELITE 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:

CLINiLABS

SHOWCASE OF TOP TRAINEE ABSTRACTS
5:00 pm – 5:30 pm
ELITE HALL

View the top trainee abstracts submitted by the 2015 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 Thursday and Friday.

THURSDAY, MARCH 5

PRODUCT THEATER
(By Invitation Only)
12:00 noon – 1:30 pm
ELITE HALL

Hear the latest advancements at Covance during this special presentation in the Exhibit Hall.

The Thursday Product Theater is sponsored by:

BIOINNOVATION FORUM
2:30 pm – 4:00 pm
EMPIRE A

New Interactive Session Format! Chaired by ASCPT President John A. Wagner, MD, PhD, five speakers from different sectors emphasizing bioinnovation in their respective sectors will each present 10-15 minute TED-Style talks. This special *Bioinnovation Forum* session will conclude with a moderated discussion roundtable with the speakers and the audience. See page 61 for program details.

WINES AROUND THE WORLD NETWORKING RECEPTION
4:30 pm – 6:30 pm
ELITE HALL

Join us for the new Networking Reception, offering further opportunities to network and interact with your colleagues and the exhibitors.

POSTER WALKS INNOVATIONS ACROSS THE DRUG DEVELOPMENT SPECTRUM
4:45 pm – 5:30 pm
ELITE FOYER

Led by Raymond J. Hohl, MD, PhD, Penn State, Milton S. Hershey Medical Center

5:30 pm – 6:15 pm
LATE-BREAKING/ENCORE POSTER WALK

Led by Russ B. Altman, MD, PhD, Stanford University

SCHEDULE-AT-A-GLANCE

FRIDAY, MARCH 6

SPEED MENTORING
11:45 am – 12:45 pm
STORYVILLE

For the second year, ASCPT is pleased to offer the Speed Mentoring event. Senior clinical pharmacologists will be available for a series of one-on-one discussions that will ultimately result in mentoring partnerships that are valuable to both parties.
Registration is required.

PRODUCT THEATER
(By Invitation Only)
12:00 noon – 1:30 pm
ELITE HALL

Hear the latest advancement at OmniComm during this special presentation in the Exhibit Hall.

The Friday Product Theater is sponsored by:

OmniComm®
eClinical Solutions for Life™

POSTER WALKS
ELITE FOYER

PRACTICAL APPROACHES FOR OPTIMIZING PEDIATRICS DOSAGE OR DELIVERY
4:45 pm – 5:30 pm

Led by Gregory L. Kearns, PharmD, PhD, Children's Mercy Hospitals and Clinics

UTILITY OF REAL LIFE DATA TO ANSWER CLINICAL QUESTIONS
5:30 pm – 6:15 pm

Led by Anne C. Heatherington, PhD, Pfizer

PRESIDENT'S RECEPTION
4:30 pm – 6:30 pm
ELITE HALL

Join us as we honor and recognize the contributions of ASCPT President John A. Wagner, MD, PhD, during the last evening of the meeting, and network with your colleagues over light food and beverage.

SATURDAY, MARCH 7

POST-CONFERENCE PROGRAM
Clinical Pharmacology Curriculum Review Course
7:00 am – 4:00 pm
CELESTIN D/E
(Separate registration is required and admission is by ticket only.)

The CRC is a full day program divided into two separate tracks. The Drug Development track will discuss key approaches to drug development in the areas of clinical trials, drug interactions, biologics, modeling, pediatrics, and pharmacokinetics. The Clinical Track will identify core concepts in clinical pharmacology in the areas of pharmacokinetics, aging, pediatrics, drug safety, and drug interactions as well as pharmacogenetics. See pages 75 & 76 for program details.

Don't Miss the All-New Poster Walks! On Thursday, March 5 and Friday, March 6 top experts will lead Poster Walks highlighting significant and thought-provoking research submitted by your colleagues. These Poster Walks provide an opportunity for convivial scientific discussions and exchange. Poster Walks will take place in the Elite Hall Foyer.

STATE OF THE ART LECTURES

DON'T MISS OUT! PLAN TO ATTEND THE STATE OF THE ART LECTURES FROM THESE RENOWNED PROFESSIONALS IN THEIR FIELDS.

WEDNESDAY, MARCH 4

3:30 pm – 4:30 pm

EMPIRE A/B

Michael Levitt, PhD, Stanford University

Birth and Future of Multi-Scale Modeling of Macromolecules

THURSDAY, MARCH 5

9:15 am – 10:15 am

EMPIRE A

John Brownstein, PhD, Children's Hospital Boston

Digital Disease Detection: Current Capabilities and Future Directions in the Use of the Non-Traditional Data Sources for Public Health Surveillance and Rapid Detection of Emerging Infectious Diseases

FRIDAY, MARCH 6

9:15 am – 10:15 am

EMPIRE A

Suzanne L. Topalian, MD, Johns Hopkins University

Harnessing the Immune System to Treat Cancer

FEATURED SPEAKERS

JOIN US FOR THE TWO ASCPT 2015 ANNUAL MEETING FEATURED SPEAKER SESSIONS AND HEAR PRESENTATIONS FROM YOUR FELLOW ASCPT MEMBERS.

THURSDAY, MARCH 6

1:00 pm – 2:00 pm

EMPIRE A

Julie A. Johnson, PharmD, University of Florida

Pharmacogenomics: Discovery Through Clinical Implementation

FRIDAY, MARCH 7

1:00 pm – 2:00 pm

EMPIRE A

Kim L. R. Brouwer, PharmD, PhD, University of North Carolina, Chapel Hill

Altered Hepatobiliary Drug Transport in Disease: Clinical Impact and Innovative Approaches for Measurement and Prediction

STUDENT/TRAINEE INFORMATION

The ASCPT 2015 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.

NEW! THE OTHER EBM: EVIDENCE-BASED MENTORING

WEDNESDAY, MARCH 4
10:00 am – 12:00 noon
EMPIRE D

Sharon E. Straus, author of *Mentorship in Academic Medicine*, will facilitate an interactive discussion of the evidence base for mentoring and best practices contributing to productive mentoring relationships. In small group discussions, you will discuss case studies illustrating common issues in mentoring. Those interested in becoming a Mentor or Mentee are encouraged to attend.

NEW! EFFECTIVELY PRESENTING YOUR WORK

WEDNESDAY, MARCH 4
1:00 pm – 2:30 pm
EMPIRE D

In this special education session established specifically for trainees and students, you will learn how to compose and present effective oral/poster presentations and abstracts.

SHOWCASE OF TOP TRAINEE ABSTRACTS

WEDNESDAY, MARCH 4
5:00 pm – 5:30 pm
ELITE HALL

The Showcase will take place in the Exhibit Hall unopposed giving you dedicated time to view the top trainee abstracts that have been awarded the Presidential Trainee Award. You can also take part in the all-new Poster Walks and let an expert lead you through select abstracts being presented.

TRAINEE LUNCHEON

THURSDAY, MARCH 5
12:00 noon – 1:30 pm
STORYVILLE

A fan favorite, the Trainee Luncheon is back again and will offer roundtable discussions with established clinical pharmacologists from academia, consulting, government, and industry. Engage with these top leaders in the field and get insight to help you with your next career move. See page 17 for program details.
Registration is required.

SPEED MENTORING

FRIDAY, MARCH 6
11:45 am – 12:45 pm
STORYVILLE

For the second year, ASCPT is pleased to offer the Speed Mentoring event. Senior clinical pharmacologists will be available for a series of one-on-one discussions that will ultimately result in mentoring partnerships that are valuable to both parties.
Registration is required.

SOCIAL MEDIA DRAWING

On-site, share your thoughts and comments about the ASCPT Annual Meeting with your peers on Facebook, Twitter (#ASCPT2015), or LinkedIn. Post a message about a session or event that resonated with you and be entered into a drawing for 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 5, 2015

12:00 pm – 1:30 pm

STORYVILLE

This is a ticketed event; you must have registered and have received a ticket with your registration materials to attend this luncheon.

In support of ASCPT's new Strategic Plan, ASCPT provides programming to help members develop their careers inclujding through mentorship, and ASCPT develops leaders prepared to represent the organization and the field of clinical pharmacology. ASCPT is pleased to bring back the highly successful Trainee Luncheon to the 2015 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.

Bridgette L. Jones, MD, Children's Mercy Hospitals and Clinics
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Catherine M. T. Sherwin, PhD, University of Utah School of Medicine
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Russ B. Altman, MD, PhD, Stanford University

Sara VanDriest, MD, PhD, Vanderbilt University

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Myong Jin Kim, PharmD, US Food and Drug Administration

Lilly Mulugeta, PharmD, US Food and Drug Administration

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Christine Haller, MD, BioMarin Pharmaceutical Inc.

Richard L. Lalonde, PharmD, FCP, FAAPS, FCCP, Pfizer

Ashley Milton, BSc, PhD, Takeda Pharmaceuticals

Masako Nakano, MD, PhD, Eli Lilly, Japan

Virginia (Ginny) Schmith, PhD, FCP, Nuventra Pharma Sciences

ASCPT 2016 ANNUAL MEETING

MARCH 8–12, 2016
HILTON BAYFRONT, SAN DIEGO, CA

2016 ASCPT CALL FOR AWARD NOMINATIONS

Each year ASCPT's **Scientific Awards** program seeks to recognize outstanding science in clinical pharmacology. ASCPT's awards span the continuum of clinical pharmacology and recognize every turning point in the career path from young investigator to seasoned scientist.

- Gary Neil Prize for Innovation in Drug Development
- Henry W. Elliott Distinguished Service Award
- Leon I. Goldberg Young Investigator Award
- Oscar B. Hunter Memorial Award in Therapeutics
- Rawls-Palmer Progress in Medicine Award
- Sheiner-Beal Pharmacometrics Award
- William B. Abrams Award in Geriatric Clinical Pharmacology
- ASCPT Mentor Award

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NOMINATION DEADLINE:
THURSDAY, JUNE 11, 2015

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CLINICAL PHARMACOLOGY PRE-CONFERENCE

ACKNOWLEDGMENTS

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TUESDAY, MARCH 3

8:30 AM – 5:00 PM

EMPIRE A

CLINICAL PHARMACOLOGY: TOWARD A GLOBAL AGENDA

UAN: 0708-9999-15-201-L03-P

Co-Sponsored by the International Consortium for Innovation and Quality in Pharmaceutical Development

7:00 AM – 3:00 PM

PRE-CONFERENCE REGISTRATION OPEN

EMPIRE FOYER

8:00 AM – 8:30 AM

CONTINENTAL BREAKFAST

8:30 AM – 8:40 AM

INTRODUCTION AND MEETING OVERVIEW

Aubrey Stoch, MD, Merck Inc.

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

8:40 AM – 10:15 AM

SESSION I: THE GREAT DEBATE: CLINICAL PHARMACOLOGY AT A CROSSROADS

SPEAKERS

Arthur J. Atkinson, Jr., MD, Northwestern University

Jeffrey Aronson, DPhil, FRCP, University of Oxford

Peter K. Honig, MD, MPH, Pfizer

10:15 AM – 10:30 AM

BREAK

10:30 AM – 12:30 PM

SESSION II: KEYS TO SUCCESS FOR CLINICAL PHARMACOLOGY AND THERAPEUTICS: A FOCUS ON ORGANIZATIONAL DEVELOPMENT

SPEAKERS

Julie A. Johnson, PharmD, University of Florida

Caroline Pike, PhD, Ascension

Ted Grasela, PharmD, PhD, Cognigen Corporation

12:30 PM – 1:30 PM

SESSION III: LUNCH AND OPEN FORUM

PANELISTS

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

Caroline Pike, PhD, Ascension

Peter K. Honig, MD, MPH, Pfizer

1:30 PM – 2:45 PM

SESSION IV: GLOBAL VIEWS ON CLINICAL PHARMACOLOGY: CURRENT REALITIES AND FUTURE STATE

SPEAKERS

Malcolm Rowland, DSc, PhD, University of Manchester

Matthias Schwab, MD, Dr Margarete Fisher-Bosch Institute of Clinical Pharmacology and the European Association of Clinical Pharmacology and Therapeutics

Edmund Lee, MD, PhD, National University of Singapore

CLINICAL PHARMACOLOGY PRE-CONFERENCE

2:45 PM – 3:00 PM
BREAK

3:00 PM – 4:50 PM
SESSION V: FRAMEWORKS FOR ADVANCING SCIENCE AND PUBLIC HEALTH

SPEAKERS
William E. Evans, PharmD, St. Jude Children's Research Hospital

Russ B. Altman, MD, PhD, Stanford University

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

4:50 PM – 5:00 PM
CLOSING REMARKS

Aubrey Stoch, MD, Merck Inc.

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

QUANTITATIVE SYSTEMS PHARMACOLOGY PRE-CONFERENCE

ASCPT 2016 ANNUAL MEETING

MARCH 8–12, 2016
HILTON BAYFRONT, SAN DIEGO, CA

QUANTITATIVE SYSTEMS PHARMACOLOGY PRE-CONFERENCE

117th ANNUAL MEETING

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THURSDAY, JUNE 4, 2015

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Mario L. Rocci, Jr., PhD President | **Mark J. Dresser, PhD** Scientific Program Committee Chair

TUESDAY, MARCH 3

8:30 AM – 5:00 PM

EMPIRE B

QUANTITATIVE SYSTEMS PHARMACOLOGY: MULTISCALE MODEL-BASED DRUG DEVELOPMENT THROUGH INTEGRATING SYSTEMS BIOLOGY AND PHARMACOMETRICS

UAN: 0708-9999-15-202-L01-P

Co-Sponsored by the International Society of Pharmacometrics

8:00 AM – 8:30 AM

CONTINENTAL BREAKFAST

8:30 AM – 8:45 AM

OPENING REMARKS

CHAIRS

Donald E. Mager, PharmD, PhD, State University of New York at Buffalo

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

8:45 AM – 10:15 AM

NEXT GENERATION PHYSIOLOGICALLY-BASED PKPD MODELING

Beyond Small Molecules: PBPK of Biological Therapeutics
Stephan Schaller, PhD, Bayer

Physiological-Based Cardiomyocyte Model: Predicting QT Changes in Humans
Sebastian Polak, PhD, Certara

Integrating Systems Pharmacology and PBPK: Application to Oncology
James M. Gallo, PharmD, PhD, Mount Sinai School of Medicine

10:15 AM – 10:30 AM

BREAK

10:30 AM – 12:00 NOON

PHARMACOMETABOLOMICS

Integrative Systems Biology Based Drug Development and Assessment of Detoxification Capacity
Hans V. Westerhoff, PhD, University of Amsterdam

Enabling Tools for Systems Pharmacology
Rima Kaddurah-Daouk, PhD, Duke University

Systems Biology of the RBC
Aarash Bordbar, PhD, University of California, San Diego

12:00 NOON – 12:45 PM

LUNCH

12:45 PM – 1:45 PM

ELITE FOYER

POSTER SESSION ON MULTI-SCALE PHARMACODYNAMIC MODELING

QUANTITATIVE STYSTEMS PHARMACOLOGY PRE-CONFERENCE

1:45 PM – 2:45 PM
SYSTEMS PHARMACOLOGY MODEL OBSERVABILITY AND VALIDATION

Observability of Complex Systems
Yang-Yu Liu, PhD, Harvard University

Identifying and Validating Systems Pharmacology Models
Juergen Hahn, PhD, Rensselaer Polytechnic Institute

2:45 PM – 3:00 PM
BREAK

3:00 PM – 4:30 PM
TOP-DOWN AND BOTTOM-UP MODELING

Pharmacometrics of Tyrosine Kinase Inhibitor Adverse Drug Reactions
Mats O. Karlsson, PhD, Uppsala University

Systems Pharmacology Approach to Tyrosine Kinase Inhibitor Toxicity
Hiroshi Suzuki, PhD, University of Tokyo

Requisite Hybrid Modeling: Mathematical Theory Applied to Systems Pharmacological Modeling
Angelean O. Hendrix, PhD, GlaxoSmithKline

4:30 PM – 5:00 PM
MODERATED PANEL DISCUSSION

Top-Down and Bottom-Up: Answering Similar or Different Questions?

PANELISTS
Piet H. van der Graaf, PhD, PharmD, Leiden Academic Centre for Drug Research

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

Virginia (Ginny) D. Schmith, PhD, FCP, Nuventra Pharma Sciences

Gianluca Nucci, PhD, Pfizer

QUANTITATIVE STYSTEMS PHARMACOLOGY PRE-CONFERENCE

QP-01

MODELING AND SIMULATION-GUIDED RATIONAL DRUG DISCOVERY AND DEVELOPMENT: A CASE STUDY OF MAVRILIMUMAB.

B. Wang,[1] C. Wu,[1] L. Roskos[2]; [1]AstraZeneca/MedImmune, Mountain View, CA, [2]AstraZeneca/MedImmune, Gaithersburg, MD

QP-02

ASSESSING SYNERGY OF DRUG AGONISTS USING A SURFACE RESPONSE ANALYSIS IN R.

G. Vlasakakis,[1] R. L. O'Connor-Semmes,[2] M. A. Young[2]; [1]GlaxoSmithKline, London, United Kingdom, [2]GlaxoSmithKline, Research Triangle Park, NC

QP-03

APPLICATION OF PBPK AND BAYESIAN MODELING FOR PREDICTION OF THE LIKELIHOOD OF INDIVIDUAL PATIENTS EXPERIENCING SERIOUS ADVERSE REACTIONS TO A STANDARD DOSE OF EFAVIRENZ.

M. Chetty, T. Cain, M. Jamei, A. Rostami; Simcyp, Sheffield, United Kingdom

QP-04

INTEGRATING METABOLOMICS AND GENOMICS REVEALS NOVEL BIOMARKERS OF HYDROCHLOROTHIAZIDE RESPONSE IN PHARMACOGENOMIC EVALUATION OF ANTIHYPERTENSIVE RESPONSES (PEAR) STUDY.

M. H. Shahin,[1] D. M. Rotroff,[2] Y. Gong,[1] T. Langaee,[1] C. W. McDonough,[1] A. L. Beitelshees,[3] T. J. Garrett,[4] A. B. Chapman,[5] J. G. Gums,[1] S. T. Turner,[6] A. Motsinger-Reif,[2] R. F. Frye,[1] S. E. Scherer,[7] W. Sadee,[8] O. Fiehn,[9] R. M. Cooper-DeHoff,[1] R. Kaddurah-Daouk,[10] J. A. Johnson[1]; [1]Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville, FL, [2]Bioinformatics Research Center, North Carolina State University, Raleigh, NC, [3]Department of Medicine, University of Maryland, Baltimore, MD, [4]Department of Pathology, Immunology, and Laboratory Medicine, College of Medicine, University of Florida, Gainesville, FL, [5]Department of Medicine, Emory University, Atlanta, GA, [6]College of Medicine, Mayo Clinic, Rochester, MN, [7]Human Genome Sequencing Center, Baylor College of Medicine, Houston, TX, [8]Program in Pharmacogenomics, Department of Pharmacology, The Ohio State University, Columbus, OH, [9]Genome Center, University of California at Davis, Davis, CA, [10]Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC

QP-05

SYSTEMS PHARMACOLOGY MODELING OF HYPOMETHYLATING AGENTS DECITABINE & SGI-^{11}0 FOR EVALUATION OF AML TREATMENT BY TARGETING S-PHASE WITH PROLONGED PHARMACOKINETIC EXPOSURES.

A. Oganesian,[1] O. Demin, Jr.,[2] A. Nikitich,[2] O. Demin,[2] M. Azab[1]; [1]Astex Pharmaceuticals, Dublin, CA, [2]Institute for Systems Biology, Moscow, Russian Federation

QP-06

PHARMACOKINETIC/PHARMACODYNAMIC MODELING OF HUMAN ANTI-FGF^{23} ANTIBODY (KRN^{23}) AND SERUM PHOSPHORUS IN ADULTS WITH X-LINKED HYPOPHOSPHATEMIA.

X. Zhang,[1] N. H. Gosselin,[2] J. Marier,[2] T. Peyret,[2] T. Ito,[1] E. Imel,[3] T. O. Carpenter[4]; [1]Kyowa Hakko Kirin Pharma Inc., Princeton, NJ, [2]Pharsight-A Certara Company, Montreal, QC, Canada, [3]Indiana University School of Medicine, Indianapolis, IN, [4]Yale University School of Medicine, New Haven, CT

QUANTITATIVE STYSTEMS PHARMACOLOGY PRE-CONFERENCE

QP-07

PHARMACOMETABOLOMICS STUDY: REVEALS THAT METFORMIN TREATMENT IMPACTS THE UREA CYCLE.

X. Liang,[1] N. Oki,[2] S. Yee,[1] D. Rotroff,[3] M. Meisner,[3] O. Fiehn,[4] K. Giacomini,[1] R. Kaddurah-Daouk,[2] Pharmacometabolomics Research Network; [1]University of California, San Francisco, San Francisco, CA, [2]Duke University Medical Center, Durham, NC, [3]North Carolina State University, Raleigh, NC, [4]West Coast Metabolomics Center, University of California, Davis, Davis, CA

QP-08

A PHARMACOMETRICS APPROACH COMBINED WITH VARIOUS GENETIC ANALYSES UNCOVERS GENES LINKED TO THE DYNAMICS OF HBA1C.

S. Goswami,[1] S. Yee,[1] J. Mosley,[2] M. Hedderson,[3] M. Kabu,[4] S. Maeda,[5] D. M. Roden,[2] M. D. Simpson,[6] K. M. Giacomini,[1] R. M. Savic[1]; [1]University of California, San Francisco, CA, [2]Vanderbilt University, Nashville, TN, [3]Kaiser Permanente Division of Research, Oakland, CA, [4]RIKEN Yokohama Institute, Yokohama City, Japan, [5]RIKEN Yokohama Institute, Yokohama City, CA, [6]Marshfield Clinic Research Foundation, Marshfield, WI

QP-09

OXYLIPID PROFILE OF LOW-DOSE ASPIRIN EXPOSURE- A PHARMACOMETABOLOMICS STUDY.

S. Ellero-Simatos,[1] A. L. Beitelshees,[2] J. P. Lewis,[2] L. M. Yerges-Armstrong,[2] A. Georgiades,[3] A. Dane,[1] A. C. Harms,[1] K. Strassburg,[1] F. Guled,[1] M. M. Hendriks,[1] R. B. Horenstein,[2] A. R. Shuldiner,[2] T. Hankemeier,[1] **R. Kaddurah-Daouk**[3]; [1]Leiden Academic Centre for Drug Research, Leiden, Netherlands, [2]University of Maryland School of Medicine, Baltimore, MD, [3]Duke University Medical Center, Durham, NC

QP-10

USING PBPK MODELING TO EXPLORE THE IMPACT OF ROUTE OF ADMINISTRATION ON THE METABOLIC DRUG-DRUG INTERACTION (DDI) BETWEEN MIDAZOLAM (MDZ) AND FLUCONAZOLE (FLZ).

M. Li, J. Venitz; Virginia Commonwealth University, Richmond, VA

QP-11

METABOLOMICS, GENOMICS AND LIPIDOMICS REVEAL NOVEL SIGNATURES OF HYDROCHLOROTHIAZIDE RESPONSE IN PHARMACOGENOMIC EVALUATION OF ANTIHYPERTENSIVE RESPONSES (PEAR) STUDY.

M. H. Shahin,[1] Y. Gong,[2] T. Langaee,[2] A. L. Beitelshees,[3] D. M. Rotroff,[4] A. B. Chapman,[5] J. G. Gums,[2] S. T. Turner,[6] A. Motsinger-Reif,[4] R. F. Frye,[2] O. Fiehn,[7] J. A. Johnson,[2] R. Cooper-DeHoff,[2] X. Han,[8] R. Kaddurah-Daouk[9]; [1]University of Florida, Gainesville, FL, [2]Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville, FL, [3]Department of Medicine, University of Maryland, Baltimore, MD, [4]Bioinformatics Research Center, North Carolina State University, Raleigh, NC, [5]Department of Medicine, Emory University, Atlanta, GA, [6]College of Medicine, Mayo Clinic, Rochester, MN, [7]Genome Center, University of California at Davis, Davis, CA, [8]Sanford-Burnham Medical Research Institute, Orlando, FL, [9]Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC

QP-12

UNDERSTANDING OF GFR (GLOMERULAR FILTRATION RATE) CHANGES IN RESPONSE TO ARB ADMINISTRATION USING QUANTITATIVE SYSTEMS PHARMACOLOGY APPROACH.

V. Voronova,[1] T. Karelina,[1] O. Demin,[1] D. Chen[2]; [1]Institute for Systems Biology SPb, Moscow, Russian Federation, [2]Pfizer Inc., Cambridge, MA

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QP-13
PBPK MODELLING AND SIMULATION IN CHILDREN FOR TAPENTADOL METABOLIZED THROUGH GLUCURONIDATION.
P. G. Ravenstijn; Janssen Research & Development, Beerse, Belgium

QP-14
QUANTITATIVE MECHANISTIC STATIC MODEL FOR THE PREDICTION OF HUMAN RENAL ORGANIC ANION TRANSPORTER (OAT)-MEDIATED DRUG INTERACTIONS.
M. M. Posada, K. M. Hillgren, S. D. Hall; Eli Lilly and Company, Indianapolis, IN

QP-15
SIMULATING CARDIAC CONSEQUENCES OF THE GENETIC VARIABILITY AT THE METABOLISM LEVEL WITH USE OF MIDDLE-OUT APPROACH AND FLECAINIDE AS AN EXAMPLE COMPOUND.
S. Polak; Simcyp, Sheffield, United Kingdom

QP-16
CHARACTERIZING THE CHANGES IN DRUG CLEARANCE FROM NEONATES TO ADULTS BY PHYSIOLOGICALLY BASED PHARMACOKINETIC MODELING USING GASTROPLUS.
T. S. Samant,[1] V. Lukacova,[2] L. J. Lesko,[1] S. Schmidt[1]; [1]University of Florida, Orlando, FL, [2]Simulations Plus, Inc., Lancaster, CA

QP-17
SYSTEMS PHARMACOLOGY MODELING OF ACUTE LYMPHOBLASTIC LEUKEMIA PROGRESSION AND TREATMENT.
A. Nikitich, O. Demin Jr., O. Demin; Institute for Systems Biology Moscow, Moscow, Russian Federation

QP-18
THE SYSTEMS PHARMACOLOGY MODEL OF HEPATITIS C PROGRESSION AND TREATMENT.
T. Yakovleva, O. Demin Jr., O. Demin; Institute for Systems Biology Moscow, Moscow, Russian Federation

QP-19
NIVOLUMAB EXPOSURE-RESPONSE (E-R) ANALYSIS FOR CLINICAL DEVELOPMENT OF NIVOLUMAB IN ADVANCED REFRACTORY SQUAMOUS NON-SMALL CELL LUNG CANCER.
Y. Feng, X. Wang, S. Agrawal, B. Lestini, J. Park, A. Roy; Bristol-Myers Squibb, Princeton, NJ

QP-20
GENOME WIDE ASSOCIATION ANALYSIS WITH AMINE METABOLITES REVEALS NOVEL LOCI IMPACTING HUMAN METABOLOMIC PROFILES.
D. Rotroff,[1] L. Yerges-Armstrong,[2] J. Lewis,[2] A. Beitleshees,[2] R. Horenstein,[2] A. Shuldiner,[2] A. Motsinger-Reif,[1] R. Kaddurah-Daouk[3]; [1]North Carolina State University, Raleigh, NC, [2]University of Maryland School of Medicine, Baltimore, MD, [3]Duke University Medical Center, Durham, NC

QP-21
MARS (META-ANALYSIS USING R SHINY): A BROWSER BASED META-ANALYSIS MODELING VISUALIZATION APPLICATION.
J. Liu,[1] B. Corrigan,[2] T. Nicholas,[2] K. Ito,[2] L. Zhao,[3] D. A. Flockhart[1]; [1]Division of Clinical Pharmacology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, [2]Global Clinical Pharmacology, Global Innovative Pharma at Pfizer Inc., Groton, CT, [3]Office of Clinical Pharmacology, Office of Translational Sciences, Center for Drug Evaluation and Research, US Food and Drug Administration, Silver Spring, MD

QP-22
IMPACT OF ALTERED *IN VITRO* DISSOLUTION PROFILE ON WARFARIN *IN VIVO* PHARMACOKINETICS PERFORMANCE- POPULATION PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) SIMULATION.
J. Fan, X. Zhang, R. Lionberger; US Food and Drug Administration, Silver Spring, MD

QUANTITATIVE STYSTEMS PHARMACOLOGY PRE-CONFERENCE

QP-23
PHYSIOLOGICALLY-BASED ABSORPTION MODELING AND SIMULATION FOR ASSESSING BIOAVAILABILITY IN ELDERLY, CHILDREN AND GASTROINTESTINAL DISEASES.
J. P. Bai,[1] A. Babiskin,[1] **X. Zhang,[1]** R. A. Lionberger,[1] G. Burckart,[1] A. E. Mulberg,[1] V. Sinha,[1] T. Uno[2]; [1]US Food and Drug Administration, Silver Spring, MD, [2]Zikeikai-Aoimori Hospital, Aomori City, Japan

QP-24
SEARCHING FOR OPTIMAL THERAPY OF THE AMYLOID PATHOLOGY USING MECHANISM-BASED MODEL.
T. Karelina,[1] O. Demin,[1] S. Divvuri,[2] T. Nicholas[3]; [1]Institute for Systems Biology, Moscow, Russian Federation, [2]Pfizer R&D, Groton, CT, [3]Pfizer Global R&D, Groton, CT

QP-25
P-MAP: NETWORK BIOLOGY APPLIED TO DETERMINE CELLULAR SENSITIVITY OF DRUG RESPONSE IN TRIPLE NEGATIVE BREAST CANCER CELL LINES.
J. Cairns, H. Li, C. Ung, L. Wang; Mayo Clinic, Rochester, MN

QP-26
DEVELOPMENT OF A HUMAN WHOLE-BODY PHYSIOLOGICALLY-BASED PHARMACOKINETIC (WB-PBPK) MODEL OF LOVASTATIN LACTONE AND CARBOXYLATE (ACID) TO PREDICT HEPATIC CONCENTRATIONS.
E. Tsakalozou,[1] M. Sampson,[1] M. Z. Wang,[2] K. L. Brouwer[1]; [1]University of North Carolina, Chapel Hill, NC, [2]University of Kansas, Lawrence, KS

QP-27
REVIEW: WORKFLOW AND TECHNICAL METHODOLOGIES FOR ROBUST APPLICATION OF QUANTITATIVE SYSTEMS PHARMACOLOGY APPROACHES IN MODEL-BASED DRUG DEVELOPMENT.
K. Gadkar, S. Ramanujan; Genentech, South San Francisco, CA

QP-28
A CLINICAL-DATA DRIVEN MECHANISTIC SYSTEMS MODEL OF ASTHMA DISEASE AND TREATMENT.
K. Gadkar, S. Sukumaran, M. Rodrigo, C. Stokes, H. Scheerens, S. Ramanujan; Genentech, South San Francisco, CA

QP-29
NETWORK-BASED SYSTEMS PHARMACOLOGY APPROACH FOR TARGET IDENTIFICATION IN HETEROGENEOUS NON-HODGKIN'S LYMPHOMA.
X. Zhao, D. E. Mager; University at Buffalo, Buffalo, NY

QP-30
VIRTUAL SYSTEMS PHARMACOLOGY (VISP) FLEXIBLE WEB-BASED ENVIRONMENT FOR RUNNING LARGE MULTI-SCALE MODELS.
S. Ermakov,[1] P. Forster,[2] J. Pagidala,[1] M. Miladinov,[1] A. Wang,[1] D. Bartlett,[3] R. Baillie,[3] M. Reed,[3] **T. Leil[1]**; [1]Bristol-Myers Squibb, Princeton, NJ, [2]Forster Solutions, LLC, Wilmington, DE, [3]Rosa & Co LLC, San Carlos, CA

QP-31
REVIEW AND APPLICATION OF A THEORETICAL FRAMEWORK TO ASSESS PARAMETER IDENTIFIABILITY AND SUBSET SELECTION IN SYSTEMS PHARMACOLOGY MODELS.
W. C. Thompson, Y. Zhou, S. Talukdar, C. Musante; Pfizer, Cambridge, MA

QP-32
DEVELOPMENT OF A QUANTITATIVE SYSTEMS PHARMACOLOGY PLATFORM TO SUPPORT TRANSLATIONAL RESEARCH AND CLINICAL DEVELOPMENT IN IMMUNO-ONCOLOGY.
B. J. Schmidt,[1] D. W. Bartlett,[2] S. Agrawal,[1] M. Reed,[2] M. Jure-Kunkel,[1] A. A. Gutierrez,[1] R. A. Clynes,[1] B. S. Fischer,[1] A. Kadambi,[2] C. Friedrich,[2] K. Kudrycki,[2] A. Roy,[1] T. A. Leil[1]; [1]Bristol-Myers Squibb, Princeton, NJ, [2]Rosa & Co., San Carlos, CA

GENERAL INFORMATION

ACKNOWLEDGMENTS

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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.

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EMPIRE FOYER

TUESDAY, MARCH 3
7:00 am – 3:00 pm

WEDNESDAY, MARCH 4
7:00 am – 5:00 pm

THURSDAY, MARCH 5
7:00 am – 5:00 pm

FRIDAY, MARCH 6
7:00 am – 5:00 pm

SATURDAY MARCH 7
7:00 am – 10:00 am

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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.

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All scientific presentations at the ASCPT-sponsored events must adhere to the highest standards of scientific ethics, including acknowledgements 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.

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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.

GENERAL INFORMATION

ASCPT CONTINUING EDUCATION CREDIT

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.
The Pharmaceutical Education and Research Institute, Inc. (PERI) designates this live activity for a maximum of 31 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Your credits will be submitted electronically to the CPE Monitor. Pharmacists or pharmacy technicians with questions regarding their NABP e-profile or CPE Monitor should refer to the FAQ section on the NAPBP Web site (www.nabp.net/programs/cpe-monitor/cpe-monitor-service/) or contact the NABP Customer Service (custserv@nabp.net) or telephone 847-391-4406.

The assigned universal program numbers for this meeting begin with 0708-9999-15-201-L03-P and end with 0708-9999-15-220-L01-P. Topic designations and descriptions for the ASCPT 2015 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 31 hours or 3.1 CEUs. These activities have been designated as knowledge-based CPE.

The CME/CPE fee for the 2015 ASCPT Annual Meeting is $50 for ASCPT members and $100 for non-members. Please visit the Registration Desk located in the Empire Foyer to purchase.

WI-FI ACCESS

ASCPT is pleased to provide complimentary Wi-Fi access to our meeting attendees. Use access code ASCPT2015.

MEETING EVALUATIONS

Please take the time to evaluate the Annual Meeting and its daily sessions through the Annual Meeting App. 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 3, 2015 – April 3, 2015.

ASCPT CENTRAL
EMPIRE FOYER

ASCPT Central will be open during the following hours:

WEDNESDAY, MARCH 4
7:00 am – 5:00 pm

THURSDAY, MARCH 5
7:00 am – 5:00 pm

FRIDAY, MARCH 6
7:00 am – 5:00 pm

SATURDAY, MARCH 7
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, CTS or CPT:PSP Editorial Staff
- Update your member profile
- Sign up to participate on various ASCPT Committees and Task Forces
- Volunteer as a CPT, CTS or CPT:PSP manuscript or abstract reviewer
- Join ASCPT or refer a colleague for membership

And much more!

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

The Cyber Café is sponsored by:

POSTER AND EXHIBIT HALL HOURS
ELITE HALL

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

WEDNESDAY, MARCH 4
4:30 pm – 6:30 pm
Exhibits, Reception, and Showcase of Top Trainee Abstracts

THURSDAY, MARCH 5
11:30 am – 6:30 pm
Posters, Exhibits, Poster Walks, and Reception

FRIDAY, MARCH 6
11:30 am – 6:30 pm
Posters, Exhibits, Poster Walks, and Reception

NO PHOTOGRAPHY

Use of cameras 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
EMPIRE FOYER

ASCPT members offer their latest publication flyers featuring scientific courses they 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 4 until Saturday, March 7. Stop by ASCPT Central to speak to an ASCPT staff member for information on posting a flyer or for more information on the Literature Display.

ASCPT JOB BOARD
EMPIRE 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 4 until Saturday, March 7. Stop by to speak to an ASCPT staff member to post a position, access resumes and learn about member discounts applicable to the online Career Center.

SPEAKER READY ROOM
STRAND 1

ASCPT provides technical support through the services available in the Speaker Ready Room, located in Strand 1. 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 3
7:00 am – 5:00 pm

WEDNESDAY, MARCH 4
7:00 am – 5:00 pm

THURSDAY, MARCH 5
7:00 am – 5:00 pm

FRIDAY, MARCH 6
7:00 am – 5:00 pm

SATURDAY, MARCH 7
7:00 am – 10:00 am

HOTEL SAFETY

Your safety while attending the Annual Meeting is important to ASCPT and the Hyatt Regency New Orleans. 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 or the Registration Desk on Thursday and Friday. For $10 you may select from a salad or other healthy option. Enjoy lunch in the Poster and Exhibit Hall while networking with exhibitors and viewing the posters.

JOIN US FOR THE ASPARAGUS POPULATION KINETIC PROJECT!

One of the many exciting events planned for the ASCPT 2015 Annual Meeting is the Asparagus Population Kinetic Project, to be held in the Exhibit Hall during the Opening Reception. The Asparagus Experiment will be a fun and productive activity for meeting attendees. Study participants will eat prepared asparagus spears at the Opening Reception and report their perception of the odor in urine the next few days by completing a questionnaire. Both dose-response relationship (between asparagus consumption and the perception of odorous urine) and time-course of odor perception will be investigated.

See Real Time Data Analysis on the Asparagus Project
Visit the ICON Booth #111

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 is correlated with or reflective of a section(s). See the Scientific Agenda for the sessions representing your field of interest.

TOOLS/METHODS

Biologics	Biologics
BTT	Biomarkers and Translational Tools
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

Pharmacometabolomics (PMSIG)
International Transporter Consortium (ITC)

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 Poster and 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.

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 Hyatt Regency New Orleans is adept at making arrangements for dining reservations, excursion reservations, providing shopping and transportation information, and answering general questions about local attractions.

GENERAL INFORMATION

AWARD RECIPIENTS

2015 Gary Neil Prize for Innovation in Drug Development

Robert Temple, MD
Deputy Director for Clinical Science
US Food and Drug Administration

2015 Henry W. Elliott Distinguished Service Award

Patricia W. Slattum, PharmD, PhD
Professor of Pharmacotherapy and Outcomes Science
Virginia Commonwealth University

2015 Leon I. Goldberg Young Investigator Award

Mikko Niemi, MD, PhD
Professor
University of Helsinki

2015 Oscar B. Hunter Memorial Award in Therapeutics

Michel Eichelbaum, MD
Director
Margarete Fischer-Bosch Institute of Clinical Pharmacology

2015 Rawls-Palmer Progress in Medicine Award

Paul Watkins, MD
Director
the Hamner-University of North Carolina Institute for Drug Safety Sciences

2015 Sheiner-Beal Pharmacometrics Award

Thomas M. Ludden, PhD
Vice President, Pharmacometric Research & Development
ICON Development Solutions

2014 William B. Abrams Award in Geriatric Clinical Pharmacology

Kenneth Rockwood, MD, FRCPC, BA, MPA, BMS
Professor of Medicine, Kathryn Allen Weldon Professor of Alzheimer Research
Dalhousie University

2015 ASCPT Mentor Award

Myong Jin Kim, PharmD
US Food and Drug Administration

2014 Top Membership Recruiter

Howard Lee, MD, PhD
Seoul National University Hospital

2015 David J. Goldstein Trainee Award

Mohamed Hossam A. Shahin
University of Florida

Matthew K. Breitenstein, PhD
Mayo Clinic

Jinzhong Liu
Indiana University School of Medicine

2015 Jason Morrow Trainee Award

Kimberly Burgess
Indiana University School of Medicine

Christian Wagner, PhD
US Food and Drug Administration

ASCPT Presidential Trainee Award Recipients

Meta Diekstra, PharmD
Leiden University Medical Center

Akinyemi Oni-Orisan, PharmD
UNC Eshelman School of Pharmacy

Ming-Fen Ho, PhD
Mayo Clinic

Brandon T. Gufford, PharmD
Washington State University

Anuradha Ramamoorthy, PhD
US Food and Drug Administration

Kana Mizuno, PhD
Cincinnati Children's Hospital Medical Center

Drew Neavin
Mayo Clinic

Navaz Karimian Pour
University of Toronto

Jaeseong Oh, MD
Seoul National University College of Medicine and Hospital

Mengyao Li
Virginia Commonwealth University

Kevin Watt, MD
Duke University Medical Center

Peng Duan, PhD
US Food and Drug Administration

Jieon Lee
National University College of Medicine and Hospital

Tomoyuki Mizuno, PhD
Cincinnati Children's Hospital Medical Center

Shin-Wen Chang
University of Florida

Balmiki Ray, MD
Mayo Clinic

Victoria C. Ziesenitz, MD
Heidelberg University and Children's National Medical Center

PHRMA FOUNDATION AWARDS

2014 Paul Calabresi Medical Student Fellowships

Ranjodh Singh
Weill Cornell Medical Center

2014 Faculty Development Award

Michael T. Eadon, MD
Indiana University School of Medicine

2015 Award in Clinical Excellence in Clinical Pharmacology

Mark J. Ratain, MD
University of Chicago

***CPT: Pharmacometrics & Systems Pharmacology* Award**

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Piet H. van der Graaf, PhD, PharmD
Leiden University Medical Center

RECIPIENT
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Mount Sinai School of Medicine

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Gregory L. Kearns, PharmD, PhD &
Kathleen Neville, MD, MS
Kim L. R. Brouwer, PharmD, PhD
Jeannine McCune, PharmD
German Navarro, MD, PhD
Marc Anthony Ramos Yago, BS

GARY NEIL PRIZE FOR INNOVATION IN DRUG DEVELOPMENT
Terrence F. Blaschke, MD & Jeannette Blaschke, MD
Michael H. Skinner, MD, PharmD

LEON I. GOLDBERG YOUNG INVESTIGATOR AWARD
Joann L. Data, MD, PhD & Herman Cantrell
John T. Sullivan, MD, ChB, FRACP
Juan J. L. Lertora, MD, PhD
Michael J. Rieder, MD, PhD, FRCPC
Addison A. Taylor, MD, PhD
Daniel L. Azarnoff, MD

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

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

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

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

TRAINEE AND SCIENTIFIC AWARDS
Raymond J. Hohl, MD, PhD & Nina Gannon, DVM
Gregory L. Kearns, PharmD, PhD &
Kathleen Neville, MD, MS
Shiew-Mei Huang, PhD
Susan M. Abdel-Rahman, PharmD
Kim L. R. Brouwer, PharmD, PhD
Geert W. 't Jong, MD, PhD
Addison A. Taylor, MD, PhD
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ASCPT/FDA ABRAMS LECTURE
Lei Zhang, PhD
John F. Mullane, MD, PhD, JD

BUILDING FUND
Joann L. Data, MD, PhD & Herman Cantrell
Joop van Gerven, MD, PhD
Kathleen Uhl, MD
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UNRESTRICTED GIFT

Arthur J. Atkinson, Jr., MD
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Barbara A. Levey, MD, FACP & Gerald S. Levey, MD
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Scott A. Waldman, MD, PhD, FCP
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John A. Wagner, MD, PhD
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Steve Ryder, MD
Lei Zhang, PhD
Joann L. Data, MD, PhD & Herman Cantrell
Donald Mattison, MD
David W. Nierenberg, MD and Joan Nierenberg
Susan E. Shoaf, PhD
Donald R. Bennett, MD, PhD, MPH
Rosina B. Dixon, MD
Michelle A. Rudek, PharmD, PhD
Leslie Z. Benet, PhD
John T. Callaghan, MD, PhD
Kim L. R. Brouwer, PharmD, PhD
Maurice G. Emery, PharmD, PhD
Jean D. Gray, MD, FRCPC
William M. Heller, PhD
Shinya Ito, MD, FRCPC
Marcus M. Reidenberg, MD
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Wayne R. Snodgrass, MD, PhD
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Michael H. Skinner, MD, PharmD
P. Timothy Pollak, MD, PhD, FACP
Lucien Joubert, MD

MATCHING GIFTS

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

OPENING SESSION

2:30 pm – 3:30 pm
EMPIRE A/B
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STATE OF THE SOCIETY ADDRESS

John A. Wagner, MD, PhD
Takeda Pharmaceuticals
ASCPT President

AWARD PRESENTATIONS

William B. Abrams Award in Geriatric Clinical Pharmacology

PRESENTER
Jean D. Gray, MD, FRCPC
Dalhousie University

RECIPIENT
Kenneth Rockwood, MD, FRCPC, BA, MPA, BMS
Dalhousie University & Center for Health Care of the Elderly

Henry W. Elliott Distinguished Service Award

PRESENTER
Vijay A. Ramchandani, PhD
National Institute on Alcohol Abuse and Alcoholism

RECIPIENT
Patricia W. Slattum, PharmD, PhD
Virginia Commonwealth University

Gary Neil Prize for Innovation in Drug Development

PRESENTER
Carl C. Peck, MD
University of California, San Francisco

RECIPIENT
Robert Temple, MD
US Food and Drug Administration

2014 Top Membership Recruiter

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John A. Wagner, MD, PhD
Takeda Pharmaceuticals

RECIPIENT
Howard Lee, MD, PhD
Seoul National University Hospital

David J. Goldstein Trainee Award

PRESENTER
John A. Wagner, MD, PhD
Takeda Pharmaceuticals

RECIPIENTS
Mohamed Hossam A. Shahin
University of Florida

Matthew K. Breitenstein, PhD
Mayo Clinic

Jinzhong Liu
Indiana University School of Medicine

2015 Jason Morrow Trainee Award

PRESENTER
John A. Wagner, MD, PhD
Takeda Pharmaceuticals

RECIPIENTS
Kimberly Burgess
Indiana University School of Medicine

Christian Wagner, PhD
US Food and Drug Administration

2015 ASCPT Mentor Award

PRESENTER
John A. Wagner, MD, PhD
Takeda Pharmaceuticals

RECIPIENT
Myong Jin Kim, PharmD
US Food and Drug Administration

GENERAL INFORMATION

PHRMA FOUNDATION AWARDS

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

2014 Paul Calabresi Medical Student Fellowships

Ranjodh Singh
Weill Cornell Medical Center

2014 Faculty Development Award

Michael T. Eadon, MD
Indiana University School of Medicine

2015 Award in Clinical Excellence in Clinical Pharmacology

Mark J. Ratain, MD
University of Chicago

***CPT: Pharmacometrics & Systems Pharmacology* Award**

PRESENTER
Piet H. van der Graaf, PhD, PharmD
Leiden Academic Centre for Drug Research

RECIPIENT
James M. Gallo, PharmD, PhD
Mount Sinai School of Medicine

CEO REMARKS

Sharon J. Swan, FASAE, CAE

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SCIENTIFIC SECTION MEETINGS

THURSDAY, MARCH 5

7:30 am – 9:00 am

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

EMPIRE B

CHAIR
Jogarao Gobburu, PhD, FCP, MBA

VICE CHAIRS
Sriram Krishnaswami, PhD
Yu-Nien (Tom) Sun, PhD

Business meeting/section discussion including call for topics and section updates.

BIOMARKERS AND TRANSLATIONAL TOOLS (BTT)

STRAND 12

CHAIR
Joseph C. Fleishaker, PhD

VICE CHAIRS
Ronda K. Rippley, PhD
Jerry M. Collins, PhD

Business meeting/section discussion including call for topics and section updates.

3:00 pm – 4:30 pm

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

STRAND 12

CHAIR
Kathryn Momary, PharmD, BCPS

VICE CHAIR
Joseph Ware, PhD

PRESENTATIONS
Aromatase Inhibitor-Induced Arthralgia Associated with tcl1a snp and Estrogen-Dependent Variation in Cytokine Expression: Possible Links Between Estrogen and Arthritis
Ming-Fen Ho, PhD, Mayo Clinic

A Pharmacometrics Approach Combined with Various Genetic Analyses Uncovers Genes Linked to the Dynamics of HBALC
Srijib Goswami, University of California, San Francisco

Follow up commentary by Kathleen M. Giacomini, PhD, University of California, San Francisco

DRUG DEVELOPMENT AND REGULATORY SCIENCES (DDR)

STRAND 11

CHAIR
Megan Gibbs, PhD

VICE CHAIR
Robin O'Connor-Semmes, RPh, PhD

PRESENTATION
Landscape of Pharmacokinetic Studies in Subjects with Hepatic Impairment
Islam Younis, PhD

Business meeting/section discussion including call for topics and section updates.

ORGAN SPECIFIC DISEASES (OSD)

STRAND 13

CHAIR
Sony Tuteja, PharmD, MS

VICE CHAIRS
Kathleen M. Tornatore, PharmD
Richard Graham, PhD

WELCOME

PRESENTATIONS
Altered Vitamin A Homeostasis in Chronic Kidney Disease
Jing Jing, MS, University of Washington

Biomarkers in Chronic Kidney Disease
Michael Eadon, MD, Indiana University School of Medicine

Business meeting/section discussion including call for topics and section updates.

FRIDAY, MARCH 6
7:30 am – 9:00 am

ONCOLOGY (ONC)
STRAND 11

CHAIR
R. Donald Harvey, PharmD, FCCP, BCOP

VICE CHAIR
Stacy Shord, PharmD, FCCP, BCOP

PRESENTATIONS
Model-Based Analysis to Influence Posology Decisions in Oncology Drug Development
Neeraj Gupta, PhD
Takeda Pharmaceuticals International Co.

First Do No Harm: An Evaluation of Tools Used in Early Phase Anticancer Drug Development
Mark Ratain, MD, The University of Chicago

Business meeting, section updates and presentations.

SPECIAL POPULATIONS (SPO)
STRAND 12

CHAIR
Parvaz Madadi, PhD, Clinical Pharmacology & Toxicology and The Motherisk Program

VICE CHAIRS
Erica L. Woodahl, PhD, University of Montana
Catherine M.T. Sherwin, PhD, University of Utah School of Medicine

PRESENTATIONS
Prevalence of Heavy Fetal Alcohol Exposure in Canada: A Population-Based Meconium Study.
Kaitlyn Delano, MSc, The Hospital for Sick Children

Maybe We Just Need to Ask: Knowledge and Beliefs About Clinical and Genetic Research Among African American Community Members.
Dr. Bridgette L. Jones, MD, Children's Mercy Hospital

Trends in U.S. Childhood Vaccination Practices and Outbreaks of Vaccine-Preventable diseases, 2006-2010.
Victoria Ziesenitz, MD, University of Heidelberg

Business meeting/section discussion.

3:00 pm – 4:30 pm

BIOLOGICS
STRAND 12

CHAIR
Anne C. Heatherington, PhD

VICE CHAIR
Amita S. Joshi, PhD

Come to the Biologics Section Meeting to participate in discussions on selected posters pertaining to Biologics.

INFECTIOUS DISEASES (INF)
STRAND 11

CHAIR
Radojka Savic, PhD

VICE CHAIRS
Larissa Wenning, PhD
Kelly E. Dooley, MD, PhD

Business meeting/section discussion including call for topics and section updates.

DRUG SAFTY (SAF)
STRAND 13

CHAIR
Tobias Gerhard, PhD

VICE CHAIR
Geert W. 't Jong, MD, PhD

Welcome and introductions.

PRESENTATION
Pioglitazone and Bladder Cancer
Brian L. Strom, MD, MPH, Rutgers University

Business meeting/section discussion.

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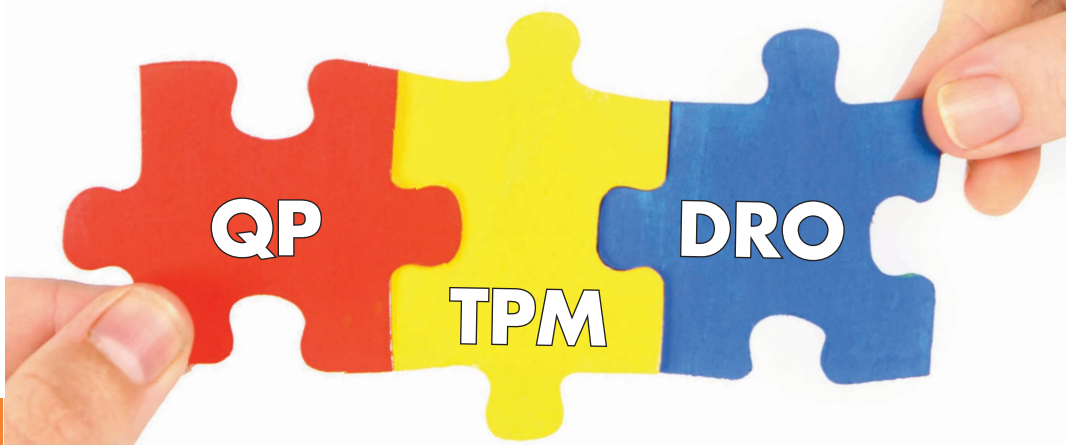
PROGRAM & SCIENTIFIC AGENDA

ASCPT is Evolving!

In order to best serve members and keep the focus on important scientific developments, ASCPT is transforming Scientific Sections into three larger NETWORKS and smaller, more focused COMMUNITIES.



Quantitative Pharmacology (QP)

- PMK
- Biologics
- Systems Pharmacology

Translational and Precision Medicine (TPM)

- INF
- OSD
- Special Populations
- BTT
- PGx
- Pharmacometabolomics
- ONC
- ITC

Development, Regulatory and Outcomes (DRO)

- Drug Safety
- Regulatory Science
- Drug Utilization and Outcomes

Why the Change?

- Member Engagement
- Energized Education
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- And more!

ASCPT

Visit www.ascpt.org or email members@ascpt.org to learn more about all of the new and exciting Network and Community options for ASCPT members!

TUESDAY, MARCH 3, 2015

1:00 PM – 5:00 PM
CPT EDITORIAL TEAM MEETING
(By Invitation Only)
STRAND 10

WEDNESDAY, MARCH 4, 2015

7:00 AM – 5:00 PM
REGISTRATION/ASCPT CENTRAL OPEN
EMPIRE FOYER

7:00 AM – 8:30 AM
BOARD OF DIRECTORS MEETING
(By Invitation Only)
STRAND 10

8:00 AM – 12:00 NOON
PSP EDITORIAL TEAM MEETING
(By Invitation Only)
STRAND 14

8:30 AM – 11:00 AM
SPECIAL SESSION
Evidence of Effectiveness: What is the Role of Clinical Pharmacology in Providing Confirmatory or Supportive Evidence?
EMPIRE C
UAN: 0708-9999-15-203-L01-P

Scientific Sections: Pharmacometrics & Pharmacokinetics (PMK), Drug Development & Regulatory Sciences (DDR)

D D R U

CHAIRS
Richard L. Lalonde, PharmD, Pfizer

Vikram Sinha, PhD, US Food and Drug Administration

SPEAKERS
A Single Trial as Evidence of Effectiveness: History and Implementation
Carl C. Peck, MD, University of California, San Francisco

Statistical Considerations for Evidence Effectiveness:
Donald Rubin, PhD, Harvard University

Role of Clinical Pharmacology in Developing Evidence of Effectiveness
Vikram Sinha, PhD, US Food and Drug Administration

Where Are We Headed with Evidence of Effectiveness: A Regulatory Perspective
Robert Temple, MD, US Food and Drug Administration

Where are we Headed with Evidence of Effectiveness: A European Regulatory Perspective
Robert Hemmings, PhD, MHRA

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

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

- Describe examples of confirmatory evidence that have been used to support approval with a single adequate and well-controlled clinical trial; and
- Discuss the relative merit of different types of causal evidence of effectiveness based on clinical pharmacology principles.

PROGRAM & SCIENTIFIC AGENDA

WEDNESDAY, MARCH 4, 2015

10:00 AM – 12:00 NOON
SPECIAL SESSION
The Other EBM: Evidence-Based Mentoring
EMPIRE D

CHAIR
Patricia W. Slattum, PharmD, PhD, Virginia Commonwealth University

SPEAKER
Sharon E. Straus, MD, MSc, FRCPC, Li Ka Shing Knowledge Institute of St. Michael's and the University of Toronto

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

- Identify characteristics of successful mentor-mentee partnerships;
- Discuss issues that arise in mentoring relationships using case studies;
- Develop a personal plan for your role as a mentor and/or a mentee; and
- Network with other clinical pharmacologists exploring mentorship.

11:30 AM – 2:00 PM
BIOINNOVATION FIELD TRIP
(Ticket Required)

12:00 NOON – 1:00 PM
NEW MEMBER WELCOME
STRAND 11

12:00 NOON – 1:30 PM
CCSS MEETING
(By Invitation Only)
STRAND 12

1:00 PM – 2:30 PM
CLINICAL PHARMACOLOGY TRAINING PROGRAM DIRECTORS MEETING
(By Invitation Only)
EMPIRE D

1:00 PM – 2:30 PM
SPECIAL EDUCATION SESSION
Effectively Presenting Your Work
EMPIRE D
Scientific Sections: Molecular Pharmacology & Pharmacogenetics (MOL), Pharmacometrics & Pharmacokinetics (PMK)

D D R U

CHAIRS
Bridgette Jones, MD, Children's Mercy Hospitals and Clinics

Catherine Sherwin, BSc(Hons), PhD, University of Utah School of Medicine

SPEAKERS
Effective Oral Presentations
Kathleen Uhl, MD, Silver Spring, US Food and Drug Administration

Presenting Your Work So That People Remember It
Russ B. Altman, MD, PhD, Stanford University

Successful Abstracts
Scott A. Waldman, MD, PhD, Thomas Jefferson University

DISCUSSION ROUNDTABLE

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

- Provide instruction on how to convey your work visually via figures and tables with abstracts, poster presentations, and oral presentations; and
- Provide instruction of basic oral presentation skills which allow engagement of the audience and convey your message clearly and concisely.

WEDNESDAY, MARCH 4, 2015

2:00 PM – 2:30 PM
AWARDS RECEPTION
(By Invitation Only)
EMPIRE C

2:30 PM – 3:30 PM
OPENING SESSION
EMPIRE A/B

Sponsored by:

Genentech
A Member of the Roche Group

STATE OF THE SOCIETY ADDRESS
John A. Wagner, MD, PhD
Takeda Pharmaceuticals
ASCPT President

Lei Zhang, PhD
US Food and Drug Administration,
Scientific Program Committee Chair

AWARD PRESENTATIONS

William B. Abrams Award in Geriatric Clinical Pharmacology

PRESENTER
Jean D. Gray, MD, FRCPC
Dalhousie University

RECIPIENT
Kenneth Rockwood, MD, FRCPC, BA, MPA, BMS
Dalhousie University & Center for Health Care of the Elderly

Henry W. Elliott Distinguished Service Award

PRESENTER
Vijay A. Ramchandani, PhD
National Institute on Alcohol Abuse and Alcoholism

RECIPIENT
Patricia W. Slattum, PharmD, PhD
Virginia Commonwealth University

Gary Neil Prize for Innovation in Drug Development

PRESENTER
Carl C. Peck, MD
University of California, San Francisco

RECIPIENT
Robert Temple, MD
US Food and Drug Administration

2014 Top Membership Recruiter

PRESENTER
John A. Wagner, MD, PhD
Takeda Pharmaceuticals

RECIPIENT
Howard Lee, MD, PhD
Seoul National University Hospital

David J. Goldstein Trainee Award

PRESENTER
John A. Wagner, MD, PhD
Takeda Pharmaceuticals

RECIPIENTS
Mohamed Hossam A. Shahin
University of Florida

Matthew K. Breitenstein, PhD
Mayo Clinic

Jinzhong Liu
Indiana University School of Medicine

2015 Jason Morrow Trainee Award

PRESENTER
John A. Wagner, MD, PhD
Takeda Pharmaceuticals

RECIPIENTS
Kimberly Burgess
Indiana University School of Medicine

Christian Wagner, PhD
US Food and Drug Administration

WEDNESDAY, MARCH 4, 2015

2015 ASCPT Mentor Award

PRESENTER
John A. Wagner, MD, PhD
Takeda Pharmaceuticals

RECIPIENT
Myong Jin Kim, PharmD
US Food and Drug Administration

PhRMA Foundation Awards

PRESENTER
Darrell R. Abernthy, MD, PhD
US Food and Drug Administration

2014 Paul Calabresi Medical Student Fellowships
Ranjodh Singh
Weill Cornell Medical Center

2014 Faculty Development Award
Michael T. Eadon, MD
Indiana University School of Medicine

2015 Award in Clinical Excellence in Clinical Pharmacology
Mark J. Ratain, MD
University of Chicago

CPT: Pharmacometrics & Systems Pharmacology Award

PRESENTER
Piet H. van der Graaf, PhD, PharmD
Leiden Academic Centre for Drug Research

RECIPIENT
James M. Gallo, PharmD, PhD
Mount Sinai School of Medicine

CEO REMARKS
Sharon J. Swan, FASAE, CAE

3:30PM – 4:30PM
STATE OF THE ART LECTURE
Birth and Future of Multi-Scale Modeling of Macromolecules
EMPIRE A/B
UAN: 0708-9999-15-204-L01-P

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

SPEAKER

Michael Levitt, PhD,
Stanford University

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

- Describe the genesis of computational structural biology; and
- Indicate current and future applications of multi-scale modeling of macromolecules to human health.

4:00 PM – 5:00 PM
PHRMA FOUNDATION MEETING
STRAND 2

4:30 PM – 6:30 PM
OPENING RECEPTION
ELITE HALL

Sponsored by:

CLINILABS

5:00PM – 5:30PM
SHOWCASE OF TOP TRAINEE ABSTRACTS
ELITE HALL

SHOWCASE OF TOP TRAINEE ABSTRACTS

PT-01

INTEGRATING METABOLOMICS AND GENOMICS REVEALS NOVEL BIOMARKERS OF HYDROCHLOROTHIAZIDE RESPONSE IN PHARMACOGENOMIC EVALUATION OF ANTIHYPERTENSIVE RESPONSES (PEAR) STUDY.

M. H. Shahin,[1] D. M. Rotroff,[2] Y. Gong,[1] T. Langaee,[1] C. W. McDonough,[1] A. L. Beitelshees,[3] T. J. Garrett,[4] A. B. Chapman,[5] J. G. Gums,[1] S. T. Turner,[6] A. Motsinger-Reif,[2] R. F. Frye,1 S. E. Scherer,[7] W. Sadee,[8] O. Fiehn,[9] R. M. Cooper-DeHoff,1 R. Kaddurah-Daouk,[10] J. A. Johnson[1]; [1]Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville, FL, [2]Bioinformatics Research Center, North Carolina State University, Raleigh, NC, [3]Department of Medicine, University of Maryland, Baltimore, MD, [4]Department of Pathology, Immunology, and Laboratory Medicine, College of Medicine, University of Florida, Gainesville, FL, [5]Department of Medicine, Emory University, Atlanta, GA, [6]College of Medicine, Mayo Clinic, Rochester, MN, [7]Human Genome Sequencing Center, Baylor College of Medicine, Houston, TX, [8]Program in Pharmacogenomics, Department of Pharmacology, The Ohio State University, Columbus, OH, [9]Genome Center, University of California at Davis, Davis, CA, [10]Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC.

PT-02

USING ELECTRONIC HEALTH RECORDS TO IDENTIFY DISEASE-SPECIFIC EFFECTS OF METFORMIN IN BREAST CANCER PATIENTS WITH TYPE II DIABETES MELLITUS.

M. K. Breitenstein,[1] L. Wang,[1] R. M. Weinshilboum,[1] G. J. Simon,[2] J. Pathak1; [1]Mayo Clinic, Rochester, MN, [2]University of Minnesota, Minneapolis, MN.

PT-03

MARS (META-ANALYSIS USING R SHINY): A BROWSER BASED META-ANALYSIS MODELING VISUALIZATION APPLICATION.

J. Liu,[1] B. Corrigan,[2] T. Nicholas,2 K. Ito,[2] L. Zhao,[3] D. A. Flockhart[1]; [1]Division of Clinical Pharmacology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, [2]Global Clinical Pharmacology, Global Innovative Pharma at Pfizer Inc., Groton, CT, [3]Office of Clinical Pharmacology, Office of Translational Sciences, Center for Drug Evaluation and Research, US Food and Drug Administration, Silver Spring, MD.

PT-04

USE OF TRANSCRIPTION ACTIVATOR LIKE EFFECTOR-TRANSCRIPTION FACTORS (TALE-TFS) AS A NEW TECHNIQUE TO INDUCE CYP GENE EXPRESSION AND VALIDATE MIRNA PREDICTIONS.

K. Burgess,[1] E. Benson,[1] Z. Desta,[1] A. Gaedigk,[2] Y. Liu,[1] T. Skaar[1]; [1]Indiana University School of Medicine, Indianapolis, IN, [2]Children's Mercy Hospital and Clinics, Kansas City, MO.

PT-05

PREDICTIVE PERFORMANCE OF PHYSIOLOGICALLY BASED PHARMACOKINETC (PBPK) MODELS FOR THE EFFECT OF CYP 3A INDUCERS ON SUBSTRATE DRUGS: ANALYSIS OF SUBMISSIONS TO THE FDA.

C. Wagner,[1] Y. Pan,[2] V. Hsu,[1] V. Sinha,[1] P. Zhao[1]; [1]Office of Clinical Pharmacology, US Food and Drug Administration, Silver Spring, MD, [2]Office of Generic Drugs, US Food and Drug Administration, Silver Spring, MD.

PROGRAM & SCIENTIFIC AGENDA

SHOWCASE OF TOP TRAINEE ABSTRACTS

PT-06

A MULTICENTER VALIDATION STUDY OF GENETIC POLYMORPHISMS ASSOCIATED WITH TOXICITY AND EFFICACY OF SUNITINIB IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA.

M. Diekstra,[1] J. J. Swen,[1] E. Boven,[2] D. Castellano,[3] R. Ganapathi,[4] H. Gelderblom,1 R. H. Mathijssen,[5] C. Rodríguez-Antona,[6] J. García-Donas,[7] B. Rini,[8] H. Guchelaar[1]; [1]Leiden University Medical Center, Leiden, Netherlands, [2]VU University Medical Center, Department of Medical Oncology, Amsterdam, Netherlands, [3]Hospital Universitario 12 de Octubre, Oncology Department, Madrid, Spain, [4]Cleveland Clinic Taussig Cancer Institute (CCF), Department of Solid Tumor Oncology, Cleveland, OH, [5]Erasmus MC Cancer Institute, Department of Medical Oncology, Rotterdam, Netherlands, [6]Spanish National Cancer Research Centre (CNIO), Hereditary Endocrine Cancer Group, Madrid, Spain, [7]Clara Campal Comprehensive Cancer Center, Oncology Unit, Madrid, Netherlands, [8]Cleveland Clinic Taussig Cancer Institute, Department of Solid Tumor Oncology, Cleveland, OH.

PT-07

CHARACTERIZATION OF THE RELATIONSHIP BETWEEN BIOMARKERS OF CYTOCHROME P450-MEDIATED EICOSANOID METABOLISM AND CORONARY ARTERY DISEASE SEVERITY IN HUMANS.

A. Oni-Orisan,[1] M. L. Edin,[2] J. Lee,[1] G. A. Stouffer,[3] D. C. Zeldin,[2] C. R. Lee1; [1]UNC Eshelman School of Pharmacy, Chapel Hill, NC, [2]National Institute of Environmental Health Sciences, Research Triangle Park, NC, [3]UNC School of Medicine, Chapel Hill, NC.

PT-08

AROMATASE INHIBITOR-INDUCED ARTHRALGIA ASSOCIATED WITH TCL1A SNP AND ESTROGEN-DEPENDENT VARIATION IN CYTOKINE EXPRESSION: POSSIBLE LINKS BETWEEN ESTROGEN AND ARTHRITIS.

M. Ho,[1] L. Wang,[1] J. Ingle,[1] P. Goss,[2] T. Mushiroda,[3] M. Kubo,[3] Y. Nakamura,[4] L. Shepherd,[5] R. Weinshilboum,[1] T. Bongartz1; [1]Mayo Clinic, Rochester, MN, [2]Massachusetts General Hospital, Boston, MA, [3]Riken Center, Yokohama City, Japan, [4]The University of Chicago Knapp Center for Biomedical Discovery, Chicago, IL, [5]NCIC Clinical Trials Group, Kingston, ON, Canada.

PT-09

A NOVEL HUMAN MODEL TO ASSESS REVERSAL OF OPIOID EFFECTS.

B. T. Gufford,[1] G. R. Ainslie,[2] J. M. Padowski,[3] M. E. Layton,[3] J. R. White,[1] M. F. Paine[1]; [1]College of Pharmacy, Washington State University, Spokane, WA, [2]Curriculum in Toxicology, School of Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, [3]College of Medical Sciences, Washington State University, Spokane, WA.

PT-10

PHARMACOGENETICS AND RACIAL COMPOSITION IN CLINICAL TRIALS FOR NON-SMALL CELL LUNG CANCER AND CHRONIC HEPATITIS C INFECTION.

A. Ramamoorthy, J. Bull, L. Zhang, M. A. Pacanowski; US Food and Drug Administration, Silver Spring, MD.

SHOWCASE OF TOP TRAINEE ABSTRACTS

PT-11

THE PHARMACOKINETIC-PHARMACODYNAMIC RELATIONSHIP OF ETHOSUXIMIDE IN CHILDREN WITH CHILDHOOD ABSENCE EPILEPSY.

K. Mizuno,[1] E. V. Capparelli,[2] T. Fukuda,[1] M. Dong,[1] A. A. Vinks,[1] T. A. Glauser[3]; [1]Division of Clinical Pharmacology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Department of Pediatrics, University of California San Diego, La Jolla, CA, [3]Division of Pediatric Neurology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PT-12

TRYPTOPHAN METABOLITE RATIO PHARMACOGENOMICS AND PHARMACOMETABOLOMICS: SOD2 AS A MARKER FOR SSRI RESPONSE IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER (MDD).

D. Neavin,[1] A. Taddei,[1] B. Ray,[1] J. Biernacka,[1] H. Zhu,2 G. Jenkins,[1] K. Kalari,[1] T. Mushiroda,[3] Y. Nakamura,4 M. Kubo,[3] W. Matson,[5] L. Wang,[1] R. Kaddurah-Daouk,[2] R. Weinshilboum[1]; [1]Mayo Clinic, Rochester, MN, [2]Pharmacometabolomics Research Network, Duke University School of Medicine, Durham, NC, [3]RIKEN Center for Integrative Medicinal Sciences, Yokohama City, Japan, [4]The University of Chicago, Chicago, IL, [5]Bedford VA Medical Center, Bedford, MA.

PT-13

ENDOTOXIN MODULATES THE RENAL EXPRESSION OF DRUG TRANSPORTERS IN A HIV-1 TRANSGENIC RAT MODEL.

N. Karimian Pour, M. Piquette-Miller; Leslie Dan Faculty of Pharmacy, Toronto, ON, Canada.

PT-14

PYRIMETHAMINE, A MATE TRANSPORTER INHIBITOR, INCREASES THE SYSTEMIC EXPOSURE TO METFORMIN BUT DOES NOT INCREASE ITS BLOOD GLUCOSE LOWERING ACTION.

J. Oh,[1] S. Yi,[1] A. Kim,[1] S. Lee,[1] J. Cho,[1] S. Yoon,[1] I. Jang,[1] J. Chung[2]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Bundang Hospital, Seongnam, Korea, Republic of.

PT-15

USING PBPK MODELING TO EXPLORE THE IMPACT OF ROUTE OF ADMINISTRATION ON THE METABOLIC DRUG-DRUG INTERACTION (DDI) BETWEEN MIDAZOLAM (MDZ) AND FLUCONAZOLE (FLZ).

M. Li, J. Venitz; Virginia Commonwealth University, Richmond, VA.

PT-16

ANTIFUNGAL EXTRACTION BY THE EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) CIRCUIT EX VIVO.

K. Watt,[1] M. Cohen-Wolkowiez,[1] D. Williams,2 D. Bonadonna,[1] I. Cheifetz,[1] D. K. Benjamin, Jr,[1] K. L. Brouwer[3]; [1]Duke University Medical Center, Durham, NC, [2]Children's Hospital of Richmond, Richmond, VA, [3]University of North Carolina Eshelman School of Pharmacy, Chapel Hill, NC.

SHOWCASE OF TOP TRAINEE ABSTRACTS

PT-17

PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODELING (PBPK) OF PITAVASTATIN AND ATORVASTATIN TO PREDICT DRUG-DRUG INTERACTIONS (DDIS).

P. Duan,[1] P. Zhao,[2] L. Zhang[2]; [1]Commissioner's Fellow, US Food and Drug Administration, Silver Spring, MD, [2]Office of Clinical Pharmacology, Office of Translational Sciences, CDER, US Food and Drug Administration, Silver Spring, MD.

PT-18

ASSESSMENT OF NEW GENOMIC BIOMARKERS OF DRUG-INDUCED LIVER INJURY AFTER ADMINISTRATION OF AMOXICILLIN/CLAVULANIC ACID IN HUMAN SUBJECTS.

J. Lee,[1] S. Ji,[1] S. Kim,[2] K. Shin,[3] S. Yi,[1] K. Lim,[1] S. Lee,[1] J. Cho,[1] K. Yu,[1] I. Jang[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Department of Allergy & Clinical Immunology, Ajou University School of Medicine, Suwon, Korea, Republic of, [3]College of Pharmacy, Research Institute of Pharmaceutical Science, Kyungpook National University, Daegu, Korea, Republic of.

PT-19

DEVELOPMENTAL TRAJECTORY OF INDIVIDUAL SIROLIMUS CLEARANCE IN NEONATES AND INFANTS WITH VASCULAR ANOMALIES.

T. Mizuno, C. Emoto, T. Fukuda, D. M. Adams, A. A. Vinks; Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PT-20

CORRELATING THE MELATONIN (MT) PATHWAY WITH ATENOLOL ASSOCIATED GLUCOSE DYSREGULATION IN THE PHARMACOGENOMIC EVALUATION OF ANTIHYPERTENSIVE RESPONSES (PEAR) STUDY.

S. Chang,[1] Y. Gong,[1] C. W. McDonough,[1] N. Nasiri Kenari,[1] T. Langaee,1 A. L. Beitelshees,[2] J. G. Gums,[1] A. B. Chapman,[3] S. T. Turner,[4] J. A. Johnson,[1] R. M. Cooper-DeHoff[1]; [1]University of Florida, Gainesville, FL, [2]University of Maryland, Baltimore, MD, [3]Emory University, Atlanta, GA, [4]Mayo Clinic, Rochester, MN.

PT-21

ARYL HYDROCARBON RECEPTOR (AHR) GENETIC VARIATION ASSOCIATED WITH KYNURENINE LEVELS IN MAJOR DEPRESSIVE DISORDER: PHARMACOMETABOLOMICS-INFORMED PHARMACOGENOMICS.

B. Ray,[1] F. Boakye-Agyeman,[1] H. Zhu,[2] J. Biernacka,[1] D. Liu,[1] A. Taddei,[1] G. Jenkins,[1] K. Kalari,[1] T. Mushiroda,[3] M. Kubo,[3] Y. Nakamura,[4] W. Matson,[5] L. Wang,[1] R. Kaddurah-Daouk,[2] R. M. Weinshilboum[1]; [1]Mayo Clinic, Rochester, MN, [2]Pharmacometabolomics Research Network, Duke University School of Medicine, Durham, NC, [3]RIKEN Center for Integrative Medical Sciences, Yokohama, Japan, [4]The University of Chicago, Chicago, IL, [5]Bedford VA Research Corporation, Inc., Bedford, MA.

PT-22

TRENDS IN US CHILDHOOD VACCINATION PRACTICES AND OUTBREAKS OF VACCINE-PREVENTABLE DISEASES, 2006-2010.

V. C. Ziesenitz,[1] P. M. Mullins,[2] J. N. van den Anker,[3] M. E. Amirshahi4; [1]Department of Pediatric Cardiology, Heidelberg University, Heidelberg, Germany and Division of Pediatric Clinical Pharmacology, Children's National Medical Center, Washington, DC, [2]George Washington University School of Medicine and Health Sciences, Washington, DC, [3]Division of Pediatric Clinical Pharmacology, Children's National Medical Center, Washington DC, and Department of Pediatric Pharmacology, University Children's Hospital, Basel, Switzerland, [4]Department of Emergency Medicine, MedStar Washington Hospital Center, Washington, DC.

THURSDAY, MARCH 5, 2014

7:00 AM – 5:00 PM
ASCPT CENTRAL AND REGISTRATION OPEN
EMPIRE FOYER

7:00 AM – 9:00 AM
AMERICAN BOARD OF CLINICAL PHARMACOLOGY (ABCP) BOARD MEETING
(By Invitation Only)
STRAND 10

7:00 AM – 9:00 AM
PSP EDITORIAL BOARD MEETING
(By Invitation Only)
STRAND 14

7:30 AM – 9:00 AM
SCIENTIFIC SECTION MEETINGS
Pharmacometrics & Pharmacokinetics (PMK)
EMPIRE B

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

VICE CHAIRS
Sriram Krishnaswami, PhD, Pfizer Global Research and Development

Yu-Nien (Tom) Sun, PhD, Amgen Inc.

Biomarkers and Translational Tools (BTT)
STRAND 12

CHAIR
Joseph C. Fleishaker, PhD, Astellas

VICE CHAIRS
Ronda K. Rippley, PhD, Merck & Co., Inc.

Jerry M. Collins, PhD, National Cancer Institute

7:30 AM – 9:00 AM
SCIENCE AT SUNRISE
Clinical Pharmacology for Biologics 101: Key Differences From Small Molecules
EMPIRE C/D

Scientific Section: Biologics

D D R U

CHAIRS
Anne Heatherington, PhD, Pfizer
Megan Gibbs, PhD, BSC Pharm, FCP, Amgen

SPEAKERS
What Clinical Pharmacology Aspects are "Simpler" with a Biologic?
Meina Tang, PhD, Genentech Inc.

What Clinical Pharmacology Aspects are "More Complex" with a Biologic?
Indranil Bhattacharya, PhD, Pfizer

What are the Regulatory Expectations for Dose Selection of Biologics
Hong Zhao, PhD, US Food and Drug Administration

PANEL DISCUSSION

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

- Appreciate the breadth of different types of biologics, their different properties and subsequent impact on clinical pharmacology characteristics; and
- Understand which aspects of development, from a clinical pharmacology perspective, are simplified for a biologics project.

7:30 AM – 9:00 AM
INFORMAL GATHERING OF PEDIATRIC PHARMACOLOGY RESEARCH UNIT MEMBERS (PPRU)

9:15 AM – 10:15 AM
STATE OF THE ART LECTURE
Digital Disease Detection: Current Capabilities and Future Directions in the Use of the Non-Traditional Data Sources for Public Health Surveillance and Rapid Detection of Emerging Infectious Diseases
EMPIRE A
UAN: 0708-9999-15-205-L01-P

THURSDAY, MARCH 5, 2014

PRESENTER
John A. Wagner, MD, PhD
Takeda Pharmaceuticals

SPEAKER

John Brownstein, PhD,
Children's Hospital Boston

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

- Discuss how various new digital technologies can be used to augment traditional disease surveillance; and
- Describe the current capabilities and future directions in the use of the non-traditional data sources for the purposes of public health surveillance and rapid detection of emerging diseases.

10:30 AM – 11:30 AM
RAWLS-PALMER PROGRESS IN MEDICINE AWARD LECTURE
EMPIRE A
UAN: 0708-9999-15-208-L05-P

AWARD PRESENTER
Kim L. R. Brouwer, PharmD, PhD,
University of North Carolina at Chapel Hill

SPEAKER
Why Good Drugs are Sometimes Bad for the Liver

Paul Watkins, MD,
Institute for Drug Safety Sciences, The Hamner-University of North Carolina

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

- Describe the challenges of drug-induced liver injury from the perspectives of the patient, the physician and the pharmaceutical industry; and
- Discuss the potential of new biomarkers to manage the risk of drug-induced liver injury, and the role of the clinical pharmacologist in the application of these biomarkers to patients.

10:30 AM – 12:30 PM
SYMPOSIUM
Little Data, Big Decisions in Drug Development and Therapeutics
EMPIRE B
UAN: 0708-9999-15-206-L01-P

Scientific Sections: Pharmacometrics & Pharmacokinetics (PMK), Drug Development & Regulatory Sciences (DDR)

D D R U

CHAIRS
Virginia (Ginny) Schmith, PhD, FCP,
Nuventra Pharma Sciences

Vivek Purohit, PhD, Pfizer

SPEAKERS
When the (Data) Glass is Half Full: Using Probabilistic Risk Analysis to Make Better Decisions
Cathrine Leonowens, PhD, Parexel

Little Data, Big Decisions in Regulatory Review
Kevin Krudys, PhD, US Food and Drug Administration

Quantitative Approach for Study Design and Establishing Decision Criteria for High Uncertainty Scenarios
Matthew M. Hutmacher, MS, A2PG

Little Data, Big Decisions in Drug Development
Pravin Jadhav, PhD, MPH, Merck

THURSDAY, MARCH 5, 2014

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

- Discuss how decision making in drug development and therapeutics can be enhanced using quantitative framework despite limited data with effective communication;
- Explain how Bayesian concepts can help to assess the probability of success based on competitor data; and
- Outline how scenario planning using preclinical and theoretical data can be useful in cases where there is not enough data to make a decision.

SYMPOSIUM

Breakthrough Therapy Designation: Advancing the Bioinnovation Engine in Oncology and Infectious Diseases
EMPIRE C/D
UAN: 0708-9999-15-207-L03-P

Scientific Sections: Drug Development & Regulatory Sciences (DDR), Oncology (ONC)

CHAIRS
Stacy Shord, PharmD, FCCP, BCOP, US Food and Drug Administration

Larissa Wenning, PhD, Merck & Co., Inc.

SPEAKERS
Breakthrough Therapy Designation Driving Medical Innovation
Issam Zineh, PharmD, MPH,
US Food and Drug Administration

Certinib: Breakthrough Treatment for Non-Small Cell Lung Cancer
Yvonne Lau, PhD, Novartis Pharmaceuticals Corporation

Sofosbuvir Initiates New Era in Treatment of Hepatitis C: A Cure for Hepatitis C on the Horizon
Brian J. Kirby, PhD, Gilead Sciences

Placing the Fulcrum: Balancing the Benefits and Risks of Breakthrough Therapy Designation?
Michael L. Maitland, MD, PhD, University of Chicago

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

- Describe the expedited program authorized under the US Food and Drug Administration Safety and Innovation Act (FDASIA), including the additional burden placed on industry and FDA;
- Articulate the challenges of developing new molecular entities under the expedited programs, including dose selection and clinical pharmacology characterization; and
- Illustrate the potential safety concerns identified for new drug products identified as breakthrough therapy upon approval in contrast to the potential benefits in a population with limited or no treatment alternatives.

11:30 AM – 6:30 PM
EXHIBIT HALL AND POSTER HALL OPEN
ELITE HALL

12:00 NOON – 1:30 PM
LUNCH AVAILABLE FOR PURCHASE IN THE POSTER AND EXHIBIT HALL
(Ticket Required)
ELITE HALL

COVANCE PRODUCT THEATER
(By Invitation Only)
ELITE HALL

TRAINEE LUNCHEON
(Ticket Required)
STORYVILLE

PROGRAM & SCIENTIFIC AGENDA

THURSDAY, MARCH 5, 2014

1:00 PM – 2:00 PM
FEATURED SPEAKER
Pharmacogenomics: Discovery through Clinical Implementation
EMPIRE A

CHAIR
Richard L. Lalonde, PharmD, Pfizer

SPEAKER

Julie A. Johnson, PharmD, University of Florida

1:00 PM – 2:30 PM
WORKSHOP
Translating *In Vitro* Transporter Data into Clinical Predictions: What We Know and Where We Are Going
EMPIRE B

Scientific Sections: Molecular Pharmacology & Pharmacogenetics (MOL), Drug Development & Regulatory Sciences (DDR)

D D R U

CHAIRS
Yong Huang, PhD, Optivia Biotechnology Inc.

Xin-Ning Yang, PhD, US Food and Drug Administration

In Vitro Models and Methodologies for Evaluating Drug Transport: Advantages, Limitations and Current Challenges
Harma Ellens, PhD, GlaxoSmithKline

Putting it All Together: Transporter Function in the Context of Organ Systems
Adrian S. Ray, PhD, Gilead Sciences Inc.

Translating In Vitro Transporter Studies into In Vivo Predictions: Successes, Challenges and Future Directions
Leslie Benet, PhD, University of California, San Francisco

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

- Understand the major advantages and limitations of different *in vitro* transporter assay models and methodologies and learn important factors to be considered to minimize variability in *in vitro* transporter study results; and
- Learn the coordinated and synergistic interplays among transporters and enzymes in organ systems, and the impact of such dynamic interactions on *in vitro* and *in vivo* drug disposition and DDI, thus develop better understanding on the meaning of transporter data and further devise more informed strategies for correlating *in vitro* data with clinical DMPK and DDI study results.

WORKSHOP
Bioequivalence Standards for Narrow Therapeutic Index (NTI) Drugs: Are They Stringent Enough to Ensure Safety and Efficacy?
EMPIRE C/D

Scientific Sections: Pharmacometrics & Pharmacokinetics (PMK), Drug Development & Regulatory Sciences (DDR)

D D R U

CHAIRS
Jogarao Gobburu, PhD, MBA, University of Maryland

Robert Lionberger, PhD, US Food and Drug Administration

SPEAKERS
Industrial Perspective: NTI Considerations in Ongoing Product Quality
Jack Cook, PhD, Pfizer

Use of PK/PD Modeling to Aid in Classification of NTI Drugs
Michael Cohen-Walkowiez, MD, PhD, Duke University School of Medicine

THURSDAY, MARCH 5, 2014

Bioequivalence Standards for Narrow Therapeutic Index (NTI) Drugs: Are They Stringent Enough to Ensure Safety and Efficacy?
Lanyan (Lucy) Fang, PhD, US Food and Drug Administration

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

- Appreciate the challenges in BE assessment for generic NTI products such as NTI classification, within-subject variability of clinical response of generic substitution and patient perception; and
- Understand quantitative assessment of the BE standards using modeling and simulation approaches incorporating therapeutic range, within-subject variability, PK and PD information.

2:30 PM – 4:00 PM
SPECIAL SESSION
BioInnovation Forum
EMPIRE A
UAN: 0708-9999-15-209-L03-P

CHAIR
John A. Wagner, MD, PhD, Takeda Pharmaceuticals

PANELISTS
Martha A. Brumfield, PhD, Critical Path Institute

Keith M. Gottesdiener, MD, FACP, Rhythm Pharmaceuticals

Jon R. Lorsch, PhD, National Institutes of Health

Steve Ryder, MD, FACP, Alexion Pharmaceuticals

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

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

- Outline the spectrum of bio-innovation across FDA, NIH, industry, and non-profit organizations; and
- Discuss examples, themes, future trends, and collaborative approaches of bio-innovation.

3:00 PM – 4:30 PM
SCIENTIFIC SECTION MEETINGS
Drug Development & Regulatory Sciences (DDR)
STRAND 11

CHAIR
Megan Gibbs, PhD, Amgen

VICE CHAIR
Robin O'Conner-Semmes, PharmD, PhD, GlaxoSmithKline

Molecular Pharmacology and Pharmacogenetics (MOL)
STRAND 12

CHAIR
Kathryn Momary, PharmD, BCPS, Mercer University

VICE CHAIR
Joseph Ware, PhD, Genentech

Organ Specific Diseases (OSD)
STRAND 13

CHAIR
Sony Tuteja, PharmD, MS, University of Pennsylvania School of Medicine

VICE CHAIRS
Kathleen M. Tornatore, PharmD, University of Buffalo

Richard Graham, PhD, Onyx Pharmaceuticals

PROGRAM & SCIENTIFIC AGENDA

THURSDAY, MARCH 5, 2014

3:30 PM – 4:30 PM
ORAL SESSION
High Impact Application of Modeling and Simulation
EMPIRE B

CHAIRS
Donald Heald, PhD, Johnson & Johnson PRD

Jing Liu, PhD, Pfizer

OI-1
EXPOSURE RESPONSE ANALYSIS AS EVIDENCE FOR APPROVAL OF CANAGLIFLOZIN-METFORMIN IMMEDIATE RELEASE FIXED-DOSE COMBINATION PRODUCT: A REGULATORY PERSPECTIVE.
Presenter: Anshu Marathe, PhD, US Food and Drug Administration

OI-2
MARS (META-ANALYSIS USING R SHINY): A BROWSER BASED META-ANALYSIS MODELING VISUALIZATION APPLICATION.
Presenter: Jinzhong Liu, Indiana University School of Medicine

OI-3
USE OF MODELING AND SIMULATION TO SUPPORT NALOXEGOL CLINICAL DEVELOPMENT AND SUBMISSION.
Presenter: Khanh H. Bui, PhD, AstraZeneca

OI-4
IPX066 DOSE-RESPONSE IN PATIENTS WITH EARLY PARKINSON'S DISEASE USING A DELAYED START STUDY DESIGN.
Presenter: Nishit B. Modi, PhD, Impax Labs

4:30 PM – 6:30 PM
WINES AROUND THE WORLD NETWORKING RECEPTION
ELITE HALL

ATTENDED POSTERS
ELITE HALL

4:45 PM – 5:30 PM
POSTER WALK I
Innovations Across the Drug Development Spectrum in Oncology
ELITE FOYER

5:30 PM – 6:15 PM
POSTER WALK II
Late-breaking/Encore Abstracts
ELITE FOYER

DONOR RECEPTION
ELITE HALL–ASCPT THEATER

6:00 PM – 7:00 PM
UCSF-STANFORD-GENENTECH RECEPTION FOR FACULTY, TRAINEES, STAFF, ALUMNI AND FRIENDS
(By Invitation Only)
STRAND 10

6:00 PM – 7:00 PM
METRUM RESEARCH RECEPTION
(By Invitation Only)
STRAND 8

6:00 PM – 7:30 PM
PhRMA FOUNDATION RECEPTION
(By Invitation Only)
STRAND 2

FRIDAY, MARCH 6, 2015

7:00 AM – 5:00 PM
ASCPT CENTRAL AND REGISTRATION OPEN
EMPIRE FOYER

7:30 AM – 9:00 AM
SCIENCE AT SUNRISE
Biomarkers: Enhancing Success in Drug Development?
EMPIRE C/D

Scientific Sections: Pharmacometrics & Pharmacokinetics (PMK), Biomarkers and Translational Tools (BTT)

D D R U

CHAIRS
Joseph Fleishaker, PhD, Astellas

Wendy Comisar, PhD, Merck & Co., Inc.

SPEAKERS
Proof of Pharmacology: The Three Pillars of Survival Underpinning POC Success
Piet H. van der Graaf, PhD, PharmD, Leiden Academic Centre for Drug Research (LACDR)

Biomarkers and Beyond: Translating from the Clinic to the Lab and Back Again
Wendy (Ankrom) Comisar, PhD, Merck & Co. Inc.

Biomarkers and Pharmacometrics in Drug Development: A Regulatory Perspective
Dhananjay Marathe, PhD, US Food and Drug Administration

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

- Understand the "three pillars" concept for assuring that the concept is tested in a POC study; and
- Learn the use of biomarkers and quantitative translational approaches to PK/PD analyses for guiding discovery and development.

SCIENTIFIC SECTION MEETINGS

Oncology (ONC)
STRAND 11

CHAIR
R. Donald Harvey, PharmD, FCCP, BCOP

VICE-CHAIR
Stacy Shord, PharmD, FCCP, BCOP

Special Populations (SPO)
STRAND 12

CHAIR
Parvaz Madadi, PhD, Clinical Pharmacology & Toxicology and The Mothersick Program

VICE-CHAIRS
Erica L. Woodahl, PhD, University of Montana

Catherine M. T. Sherwin, PhD, University of Utah School of Medicine

PROGRAM & SCIENTIFIC AGENDA

FRIDAY, MARCH 6, 2015

PRESENTATIONS

Prevalence of Heavy Fetal Alcohol Exposure in Canada: A Population-Based Meconium Study
Kaitlyn Delano, MSc, The Hospital for Sick Children

Maybe we Just Need to Ask: Knowledge and Beliefs About Clinical and Genetic Research Among African American Community Members
Bridgette L. Jones, MD, Children's Mercy Hospital

Trends in US Childhood Vaccination Practices and Outbreaks of Vaccine-Preventable Diseases, 2006-2010.
Victoria C. Ziesenitz, MD, University of Heidelberg

CPT EDITORIAL BOARD MEETING
(By Invitation Only)
CELESTIN A/B/C

CPT EDITORIAL BOARD MEETING
(By Invitation Only)
CELESTIN A/B/C

9:15 AM – 10:15 AM
STATE OF THE ART LECTURE
Harnessing the Immune System to Treat Cancer
EMPIRE A
UAN: 0708-9999-15-210-L01-P

CHAIR
Michelle A. Rudek, PharmD, PhD, Johns Hopkins University

SPEAKER

Suzanne L. Topalian, MD, Johns Hopkins University

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

- Outline the principles of tumor immunology and cancer immunotherapies; and
- Identify clinical strategies and biomarkers in the development of immunotherapies to optimize immune checkpoint modulation for the treatment of cancer.

10:30 AM – 11:30 AM
OSCAR B. HUNTER MEMORIAL AWARD IN THERAPEUTICS LECTURE
EMPIRE A
UAN: 0708-9999-15-213-L01-P

AWARD PRESENTER
William E. Evans, PharmD, St. Jude Children's Research Hospital

Of Broom, CYPs, SNPs and Other Things
Michel Eichelbaum, MD, University of Tübingen

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

- Discuss the contribution of pharmacogenetics of drug metabolizing enzymes and transporter proteins to the variability in drug disposition and action; and
- Discuss the pitfalls and shortcomings of pharmacogenomic association studies.

10:30 AM – 12:30 PM
SYMPOSIUM
Sex is the Most Important Polymorphism to Be Considered in Personalized Medicine: Or is It?!
EMPIRE C/D
UAN: 0708-9999-15-212-L05-P

Scientific Section: Drug Development & Regulatory Sciences (DDR), Special Populations (SPO)

D D R U

FRIDAY, MARCH 6, 2015

CHAIR
Dhanesh Gupta, MD, Duke University Medical School

Kellie S. Reynolds, PharmD, US Food and Drug Administration

SPEAKERS
Porgy & Bess: Sex-Related Disparities in Basic and Translational Research
Melina Kibbe, MD, Chicago, Northwestern University and the Jesse Brown VA Medical Center

Birth of the Cool: Sex, Pain, Analgesics and Pregnancy
Pamela Flood, MD, Stanford University

Decoy: Sex is NOT the Most Important Polymorphism Determining Drug Exposure or Drug Response
Lisa von Moltke, MD, FCP, Genzyme

Milestones: Sex-Related Insights from Post-Marketing Data
Myong-Jin Kim, PharmD, US Food and Drug Administration

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

- Describe sex-related differences in the development of disease and response to therapy, using the therapeutic areas of pain and mood-disorders as paradigms; and
- Explain how post-marketing surveillance data can provide insight into what sex-specific data could be acquired pre-approval to improve drug efficacy and safety in women and men.

SYMPOSIUM
Development of PCSK9 Inhibitors: A Paradigm Shift in the Treatment of Hypercholesterolemia
EMPIRE B
UAN: 0708-9999-15-211-L01-P

Scientific Sections: Pharmacometrics & Pharmacokinetics (PMK), Biologics

D D R U

CHAIRS
Sreeneeranj Kasichayanula, PhD, Amgen

John Davis, PhD, Regeneron Pharmaceuticals

SPEAKERS
Novel Lipid Lowering Strategies and the Role of PCSK9
Evan A. Stein, MD, PhD, Cincinatti Metabolic and Atherosclerosis Research Center

Translational and Clinical Pharmacology Development of Anti-PCSK9 Therapy: From Bench to Bedside
John Gibbs, MD, PhD, Amgen

Utilizing Model Based Meta-Analysis to Inform Clinical Impact of PCSK9 Inhibitors
Jaap Mandema, PhD, Quantitative Solutions

Use of Anti-PCSK9 Therapies in Pediatric Patients
Frederick J. Raal, FRCP, FRCPC, PhD, University of the Witwatersrand

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

- Define the role of PCSK9 in hypercholesterolemia;
- Describe the development of clinical pharmacology package for regulatory filing of a novel biologics in the treatment of hypercholesterolemia; and
- Explain the role of model based meta-analysis in prediction of long term clinical outcomes and identify opportunities in developing pediatric indications for novel therapies in hyperlipidemia.

11:30 AM – 6:30 PM
EXHIBIT HALL AND POSTER HALL OPEN
ELITE HALL

11:45 AM – 12:45 PM
SPEED MENTORING
STORYVILLE

FRIDAY, MARCH 6, 2015

11:45 AM – 1:00 PM
FINANCE COMMITTEE MEETING
STRAND 1
(By Invitation Only)

12:00 NOON – 1:30 PM
LUNCH AVAILABLE FOR PURCHASE IN THE POSTER AND EXHIBIT HALL
(By Invitation Only)

OMNICOMM PRODUCT THEATER
(By Invitation Only)
ELITE HALL

1:00 PM – 2:00 PM
FEATURED SPEAKER
Altered Hepatobiliary Drug Transport in Disease: Clinical Impact and Innovative Approaches for Measurement and Prediction
EMPIRE A

CHAIR
Lei Zhang, PhD, US Food and Drug Administration

SPEAKER

Kim L. R. Brouwer, PharmD, PhD, University of North Carolina at Chapel Hill

1:00 PM – 2:30 PM
WORKSHOP
Emerging Approaches to Assess Pro-Arrhythmia Risk in Drug Development: Moving Beyond hERG and QTc
EMPIRE B

D D R U

CHAIRS
Neeraj Gupta, PhD, Cambridge, Takeda Pharmaceuticals

Rameshraja Palaparthy, PhD, Amgen, Inc.

SPEAKERS
Mechanistic-Based In Vitro/In Silico Approaches to Assess Proarrhythmic Risk
Gary Gintant, PhD, Abbvie

Exploiting Mathematical Models to Understand and Predict Individualized Arrhythmia Risk
Eric A. Sobie, PhD, Icahn School of Medicine at Mount Sinai

Regulatory Perspectives on TQT Studies and Alternative Approaches to Assess TdP Risk
Norman Stockbridge, MD, PhD, US Food and Drug Administration

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

- Demonstrate the utility of *in vitro* assays, and innovative quantitative systems pharmacology approaches for the assessment of proarrhythmia risk of therapeutics in development;
- Encourage discussion on the challenges associated with integrating multiple types of preclinical and clinical data into mechanistic models that allow translation to clinical decision making on proarrhythmia risk; and
- Understand the regulatory perspective on the current status of TQT studies and the importance for alternative approaches in regulatory submissions.

FRIDAY, MARCH 6, 2015

WORKSHOP
The ABC's of Antibody Drug Conjugate (ADC)
EMPIRE C/D

Scientific Section: Biologics

CHAIR
Ganesh Mugundu, MPharm, PhD, Pfizer

Sandhya Girish, PhD, Genentech

SPEAKER
Overview of Clinical Pharmacology Plan for ADCs
Tae Han, PhD, Stem CentRx, Inc.

Translational PK/PD and Dose Optimization for ADCs
Jin Jin, PhD, Genentech

Regulatory Experience on Approval of ADCs
Sarah Schrieber, PharmD, US Food and Drug Administration

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

- Describe the overall clinical pharmacology plan for antibody drug conjugates including strategies for population PK/PD, DDI, organ impairment, immunogenicity and QTc studies;
- Describe the approaches and challenges in optimization of dose and schedule using quantitative modeling; and
- Discuss regulatory perspectives on review and approval of ADCs.

2:15 PM – 2:30 PM
TRANSITION TO THE FUTURE
EMPIRE A

2:30 PM – 4:30 PM
SYMPOSIUM
Personalized Medicines Using Genome-Wide Approaches
EMPIRE A
UAN: 0708-9999-15-220-L01-P

CHAIRS
Munir Pirmohamed, MD, PhD, University of Liverpool

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

SPEAKERS
Genomewide Approaches to the Discovery of Drug Safety Biomarkers
Munir Pirmohamed, MD, PhD, University of Liverpool

Personalizing Medicines through Drug Sequencing
Mark Caulfield, MD, William Harvey Research Institute, Barts and The London School of Medicine and Dentistry

Personalized Medicines Using Genomewide Approaches
Mary Relling, PharmD, St. Jude Children's Research Hospital

Phenomewide Association Studies, PheWAS, in Furthering Pharmacogenomic Discoveries
Dan Roden, MD, Vanderbilt University School of Medicine

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

- Describe key challenges in implementing genetic testing in patient care;
- Define a phenomewide association study and differentiate it from a genomewide association study of drug response; and
- Discuss how sequencing a gene is different from genotyping.

PROGRAM & SCIENTIFIC AGENDA

FRIDAY, MARCH 6, 2015

2:45 PM – 3:45 PM
SHEINER-BEAL PHARMACOMETRICS AWARD LECTURE
EMPIRE B
UAN: 0708-9999-15-214-L01-P

PRESENTER
Steve Riley, PharmD, PhD, Pfizer

SPEAKER

Contributions to Applied Pharmacometrics
Thomas M. Ludden, PhD, ICON Development Solutions

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

- Describe the value of using multiple estimation methods when performing nonlinear mixed-effects analyses; and
- State how the "multimode" problem in empirical Bayes estimation can be detected and addressed.

3:00 PM – 4:30 PM
SCIENTIFIC SECTION MEETINGS

Infectious Diseases (INF)
STRAND 11

CHAIR
Radojka Savic, PhD, University of California, San Francisco

VICE CHAIRS
Larissa Wenning, PhD, Merck & Co., Inc.

Kelly E. Dooley, MD, PhD, Johns Hopkins University School of Medicine

Biologics
STRAND 12

CHAIR
Anne C. Heatherington, PhD, Pfizer

VICE CHAIR
Amita S. Joshi, PhD, Genentech, Inc.

Drug Safety (SAF)
STRAND 13

CHAIR
Tobias Gerhard, PhD, Rutgers University

VICE CHAIR
Geert W. 't Jong, MD, PhD, Children's Hospital

4:30 PM – 5:30 PM
INTERNATIONAL TRANSPORTER CONSORTIUM (ITC) SPECIAL INTEREST GROUP MEETING
(Ticket Required)
STRAND 10

4:30 PM – 6:30 PM
PRESIDENT'S RECEPTION
ELITE HALL

ATTENDED POSTERS
ELITE HALL

4:45 PM – 5:30 PM
POSTER WALK III
Practical Approaches for Optimizing Pediatric Dosage or Delivery

5:30 PM – 6:15 PM
POSTER WALK IV
Utility of Real Life Data to Answer Clinical Questions

6:30 PM – 8:30 PM
GAVEL CLUB DESSERT RECEPTION
(By Invitation Only)
PRESIDENT'S SUITE

SATURDAY, MARCH 7, 2015

7:00 AM – 10:00 AM
ASCPT CENTRAL AND REGISTRATION OPEN
EMPIRE FOYER

7:00 AM – 9:00 AM
BOARD OF DIRECTORS MEETING
(By Invitation Only)
STRAND 14

7:00 AM – 4:00 PM
CLINICAL PHARMACOLOGY CURRICULUM REVIEW COURSE
CELESTIN D/E
See page 75 & 76 for program details.

7:30 AM – 9:00 AM
SCIENCE AT SUNRISE
New Insights and Novel Biomarkers for Predicting Transporter-Mediated Drug-Drug Interactions: A Multi-Sector Perspective
EMPIRE C/D

Scientific Sections: Molecular Pharmacology & Pharmacogenetics (MOL), Drug Development & Regulatory Sciences (DDR)

D D R U

CHAIRS
Sook Wah Yee, PhD, University of California, San Francisco

Kathleen M. Hillgren, PhD, Eli Lilly and Company

SPEAKERS
Interactions of Drug Metabolites with Transporters: Perspectives and Issues for Drug Development

Maciej Zamek-Gliszczynski, PhD, GlaxoSmithKline, Inc.

When Should In Vivo Transporter-Mediated Drug-Drug Interaction Studies be Conducted? A Regulatory Perspective
Lei Zhang, PhD, US Food and Drug Administration

Discovery of Endogenous Biomarkers for Transporters
Kathleen Giacomini, PhD, University of California, San Francisco

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

- Discuss and provide examples of drug metabolites that cause drug-drug interactions and toxicities;
- Describe new transporters in regulatory decision trees for transporter-mediated drug-drug interactions (DDI) and describe creatinine as a biomarker for renal drug interactions; and
- Describe the design of clinical studies to identify and to validate transporters biomarkers and list two challenges for using transporter biomarkers as part of the drug development process.

9:00 AM – 10:00 AM
LEON I. GOLDBERG YOUNG INVESTIGATOR AWARD LECTURE
EMPIRE A
UAN: 0708-9999-15-217-L01-P

AWARD PRESENTER
Kathleen M. Giacomini, PhD, University of California, San Francisco

SPEAKER
Studies on the Pharmacogenetics of Drug Transporters

Mikko Niemi, MD, PhD, University of Helsinki

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

- Discuss the role of drug transporter pharmacogenetics as a determinant of interindividual variability in drug response; and
- Identify the clinically most relevant drug transporters and their genetic variants.

PROGRAM & SCIENTIFIC AGENDA

SATURDAY, MARCH 7, 2015

9:00 AM – 10:00 AM

ORAL SESSION

Ongoing Challenges in Regulatory Sciences: Emerging Perspectives

EMPIRE B

CHAIRS

Karthik Venkatakrishnan, PhD, Takeda Pharmaceuticals

Karen Rowland-Yeo, PhD, Certara

OII-1

PREDICTIVE PERFORMANCE OF PHYSIOLOGICALLY BASED PHARMACOKINETC (PBPK) MODELS FOR THE EFFECT OF CYP 3A INDUCERS ON SUBSTRATE DRUGS: ANALYSIS OF SUBMISSIONS TO THE FDA.

Presenter: Christian Wagner, PhD; US Food and Drug Administration

OII-2

QUANTITATIVE MECHANISTIC STATIC MODEL FOR THE PREDICTION OF HUMAN RENAL ORGANIC ANION TRANSPORTER (OAT)-MEDIATED DRUG INTERACTIONS.

Presenter: Maria M. Posada, PhD; Eli Lilly and Company

OII-3

EXPERIENCES WITH CONCENTRATION-EFFECT MODELING OF QT PROLONGATION.

Presenter: Jorg Taubel, MD; Richmond Pharmacology, Ltd.

OII-4

RITONAVIR IS THE BEST ALTERNATIVE TO KETOCONAZOLE AS AN INDEX CYP3A INHIBITOR.

Presenter: David J. Greenblatt, MD; Tufts University School of Medicine

ORAL SESSION

Translating 'Omics' for Clinical Discovery and Delivery

EMPIRE C

CHAIRS

Liewei Wang, MD, PhD, Mayo Clinic

Hendrik Jan Guchelaar, PharmD, PhD, Leids Universitair Medisch Centrum

OIII-1

INTEGRATING METABOLOMICS AND GENOMICS REVEALS NOVEL BIOMARKERS OF HYDROCHLOROTHIAZIDE RESPONSE IN PHARMACOGENOMIC EVALUATION OF ANTIHYPERTENSIVE RESPONSES (PEAR) STUDY.

Presenter: Mohamed H. Shahin, PhD; University of Florida

OIII-2

PERSONALIZED THERAPY FOR H. PYLORI INFECTION.

Presenter: Takahisa Furuta, PhD; Hamamatsu University School of Medicine

OIII-3

PERSONALIZED THIOPURINE DOSING BASED ON TPMT GENOTYPING REDUCES LEUCOPENIA OCCURRENCE AND RESULTS IN COST-SAVINGS IN IBD PATIENTS; A RANDOMIZED TRIAL IN THE NETHERLANDS.

Presenter: Marieke J. Coenen, PhD; Radboud University Medical Center

OIII-4

CHARACTERIZATION OF THE RELATIONSHIP BETWEEN BIOMARKERS OF CYTOCHROME P450-MEDIATED EICOSANOID METABOLISM AND CORONARY ARTERY DISEASE SEVERITY IN HUMANS.

Presenter: Akinyemi Oni-Orisan, PharmD; UNC Eshelman School of Pharmacy

10:15 AM – 12:15 PM

SYMPOSIUM

New Perspectives on Drug-Target Interactions: Implications for Systems Pharmacology and Clinical Practice

EMPIRE A

UAN: 0708-9999-15-219-L01-P

SATURDAY, MARCH 7, 2015

Scientific Sections: Molecular Pharmacology & Pharmacogenetics (MOL), Drug Development & Regulatory Sciences (DDR)

D D R U

CHAIRS

Thaddeus Grasela, PhD, Simulations Plus, Inc./Cognigen Corporation

Malcolm Rowland, PhD, University of Manchester

SPEAKERS

The Expanding Universe of Receptors and Receptor Signaling: Hierarchical Complexity in a Reductionist World
Michael Williams, PhD, DSc, Feinberg School of Medicine

Biochemical Mechanisms of Successful Drugs with Emphasis on Drug Characteristics
David Swinney, PhD, Institute for Rare and Neglected Diseases

Systems Pharmacology Approaches to Knowledge Integration
Donald Mager, PhD, University at Buffalo

How Can We Use Mechanism-Based Receptor Models for Designing First in Human Studies
Richard W. Peck, MD, Roche

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

- Describe the processes and tools used to identify and select lead candidates during discovery;
- Define the drug characteristics, such as potency, affinity, and residence time and their impact on the time course of drug effect; and
- Describe the data requirements for systems pharmacology models and the importance of interdisciplinary definitions of concepts and terminology.

SYMPOSIUM

Tackling the Big 3: Using Quantitative Pharmacology Tools to Develop Better Treatments for HIV, Tuberculosis and Malaria

EMPIRE B

UAN: 0708-9999-15-218-L01-P

Scientific Sections: Pharmacometrics & Pharmacokinetics (PMK), Infectious Diseases (INF)

D D R U

CHAIRS

Kelly Dooley, MD, PhD, Johns Hopkins University School of Medicine

David Hermann, PhD, Certera

SPEAKERS

The Big 3: Using Clinical Pharmacology and Epidemiologic Modeling as Tools to Achieve Global Control or Eradication of TB, HIV and Malaria
Steven Kern, MD, Bill & Melinda Gates Foundation

Systems Pharmacology Modeling to Predict Tuberculosis Treatment Response: Bug, Drug, Gene and Host Interactions
Rada Savic, PharmD, PhD, University of California

In Vitro System to Evaluate Pharmacokinetic/Pharmacodynamic Relationships for Anti-Malarial Drugs
Rahul P. Bakshi, PhD, Johns Hopkins University

HIV Cure: How Can We Get There? Modeling Viral Dynamics, Drug Effects, and the Latent Reservoir to Devise Curative Strategies
Daniel Rosenbloom, PhD, Columbia University

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

- Indicate how innovative modeling and simulation methods, including multiscale modeling, are being used to advance malaria and tuberculosis therapeutics and HIV cure strategies; and

SATURDAY, MARCH 7, 2015

- Recognize the role of *in vitro* pharmacodynamics systems (hollow fiber models with dynamic drug delivery) in assessing the pharmacokinetic-pharmacodynamic relationships for combination drug treatments.

10:15 AM – 11:45 AM

WORKSHOP

Impact of the Gut Microbiome on Disease Pathogenesis and Drug Response

EMPIRE C

Scientific Section: Organ Specific Diseases (OSD)

D D R U

CHAIRS

Sony Tuteja, PharmD, University of Pennsylvania

Rima Kaddurah-Daouk, PhD, Duke University

SPEAKERS

The Role of the Gut Microbiota in the Pathogenesis of Disease and Drug Response
Rob Knight, PhD, University of Colorado

Gut Microbiome and Drug Response Phenotypes
Rima Kaddurah-Daouk, PhD, Duke University Medical Center

Drugs from the Microbiome: SER-109, an Oral Microbial Therapeutic, Repairs the Dysbiosis Underlying Susceptibility to Clostridium difficile Infection
David Cook, PhD, Seres Health

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

- Understand how the gut microbiome can contribute to the pathogenesis of diseases and impact the pharmacokinetics/pharmacodynamics of drugs; and
- Discuss regulatory issues surrounding fecal microbial transplantation.

WORKSHOP

Patient Reported Outcomes: Bringing Your Patient's Feelings to Center Stage of the Clinically Relevant Dose Equation

EMPIRE D

Scientific Sections: Pharmacometrics & Pharmacokinetics (PMK), Oncology (ONC)

D D R U

CHAIRS

Bert L. Lum, PharmD, Genentech

Michelle Rudek, PharmD, PhD, Sidney Kimmel Cancer Center at Johns Hopkins

SPEAKERS

The Development and Utility of PRO Tools: The PRO-CTCAE Measurement System
Lori Minasian, MD, National Cancer Institute

Pro Endpoints in Oncology Trials: A Regulatory Perspective
Ashley Slagle, MS, PhD, US Food and Drug Administration

PRO Data in Clinical Trials as a New Opportunity for Modeling and Simulation of Optimal Dose and Improve Patient Benefit
Mats O. Karlsson, PhD, Uppsala University

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

- Discuss the development and utility of Patient Reported Outcomes (PRO) methods systems, the PRO- Common Terminology Criteria for Adverse Events (CTCAE) and contrast to the commonly used National Cancer Institute-CTCAE system of adverse event report in oncology clinical trials; and
- Review the use of Patient Reported Outcomes (PRO) data in oncology drug approvals and labeling.

CURRICULUM REVIEW COURSE

ACKNOWLEDGMENTS

AWARD NOMINATIONS TASK FORCE AND SCIENTIFIC AWARDS SELECTION TASK FORCE

ASCPT WOULD LIKE TO RECOGNIZE THE SCIENTIFIC AWARDS NOMINATIONS TASK FORCE FOR SECURING NOMINATIONS FOR THE 2015 SCIENTIFIC AWARDS.

Virginia (Ginny) D. Schmith, PhD, FCP,
Chair

Michael J. Avram, PhD
Neal L. Benowitz, MD
Jean D. Gray, MD, FRCPC
Nancy A. Lass, MD
Jing Liu, PhD
Min Soo Park, MD, PhD
Dan M. Roden, MD
Lei Zhang, PhD

ASCPT WOULD LIKE TO ACKNOWLEDGE THE SCIENTIFIC AWARDS SELECTION TASK FORCE FOR SELECTING THE 2015 SCIENTIFIC AWARD RECIPIENTS FROM A ROBUST AND HIGHLY COMPETITIVE ROSTER OF EXCEPTIONAL NOMINEES.

Deanna L. Kroetz, PhD,
Chair

Darrell R. Abernethy, MD, PhD
Richard F. Bergstrom, PhD
M. Eileen Dolan, PhD
William E. Evans, PharmD
Mary Jayne Kennedy, PharmD
Richard L. Lalonde, PharmD
Lawrence J. Lesko, PhD
Mary V. Relling, PharmD

Malle Jurima-Romet, PhD
In Memoriam

CURRICULUM REVIEW COURSE

8:00 AM – 4:00 PM
CLINICAL PHARMACOLOGY CURRICULUM REVIEW COURSE
Drug Development Track
CELESTIN D
UAN: 0708-9999-15-215-L03-P

SPEAKERS

8:00 AM – 8:45 AM
Clinical Pharmacology in Drug Development
David W. Feigal, Jr., MD, MPH, NDA Partners LLC

8:45 AM – 9:30 AM
Clinical Trials in Drug Development: Thinking Quantitatively
David W. Feigal, Jr., MD, MPH, NDA Partners LLC

9:30 AM – 10:15 AM
Biological Therapies in Oncology
Michael L. Maitland, MD, PhD, University of Chicago Medical Center

10:15 AM – 10:30 AM
BREAK

10:30 AM – 11:15 AM
Noncompartmental Pharmacokinetics
David J. Greenblatt, MD, Tufts University School of Medicine
David W. Feigal, Jr., MD, MPH, NDA Partners LLC

11:15 AM – 1200 NOON
Hepatitis Therapy
Raj K. Vuppalanchi, MD, IU Health University Hospital

12:00 NOON – 12:45 PM
LUNCH

12:45 PM – 1:30 PM
Physiologically Based Pharmacokinetic Modeling (PBPK)
Amin Rostami-Hodjegan, PharmD, PhD, University of Manchester

1:30 PM – 2:15 PM
Population Pharmacokinetics/ Pharmacodynamics: Bayesian Approaches to Pharmacologic Data Analysis
Robert Bies, PharmD, PhD, Indiana University

2:15 PM – 2:30 PM
BREAK

2:30 PM – 3:15 PM
Mechanistic Pharmacokinetic/ Pharmacodynamic Models
Donald E. Mager, PharmD, PhD, State University of New York at Buffalo

3:15 PM – 4:00 PM
Drug Interactions: An Evolution in Drug Development
Shiew-Mei Huang, PhD, US Food and Drug Administration

Upon completion of this Curriculum Review Course, the participant should be able to describe the key approaches to drug development in the areas of clinical trials, drug interactions, biologics, modeling, pediatrics and pharmacokinetics.

8:00 AM – 4:00 PM
CLINICAL PHARMACOLOGY CURRICULUM REVIEW COURSE
Clinical Track
CELESTIN E
UAN: 0708-9999-15-216-L01-P

SPEAKERS

8:00 AM – 8:45 AM
Electronic Medical Records to Evaluate Drug Effects
Joshua C. Denny, MD, Vanderbilt University

8:45 AM – 9:30 AM
Clinical Pharmacogenomics
David A. Flockhart, MD, PhD, Indiana University School of Medicine

CURRICULUM REVIEW COURSE

9:30 AM – 10:15 AM
Effects of Aging Pathophysiology on Drug Disposition and Effect
Darrell R. Abernethy, MD, PhD, US Food and Drug Administration,

10:15 AM – 10:30 AM
BREAK

10:30 AM – 11:15 AM
Pediatric Clinical Pharmacology
Dionna J. Green, MD, US Food and Drug Administration

11:15 AM – 12:00 NOON
Drugs in Pregnancy: Treating the Mother, Protecting the Unborn
Gideon Koren, MD, FRCPC, The Hospital for Sick Children

12:00 NOON – 12:45 PM
LUNCH

12:45 PM – 1:30 PM
Principles of Antiretroviral Therapy
Craig W. Hendrix, MD, Johns Hopkins University School of Medicine

1:30 PM – 2:15 PM
Pharmacoepidemiology: The Study of Drugs in Populations
Sean Hennessy, PharmD, PhD, University of Pennsylvania

2:15 PM – 2:30 PM
BREAK

2:30 PM – 3:15 PM
Psychiatry: Clinical Pharmacology of Antipsychotics and Antidepressants
Sheldon H. Preskorn, MD, University of Kansas Medical Center

3:15 PM – 4:00 PM
Drugs Used for Phenotyping in Clinical Pharmacology
Michelle A. Rudek, PharmD, PhD, Johns Hopkins University

Upon completion of this Curriculum Review Course, the participant should be able to identify course concepts in clinical pharmacology in the areas of pharmacokinetics, aging, pediatrics, drug safety and drug interactions as well as pharmacogenetics.

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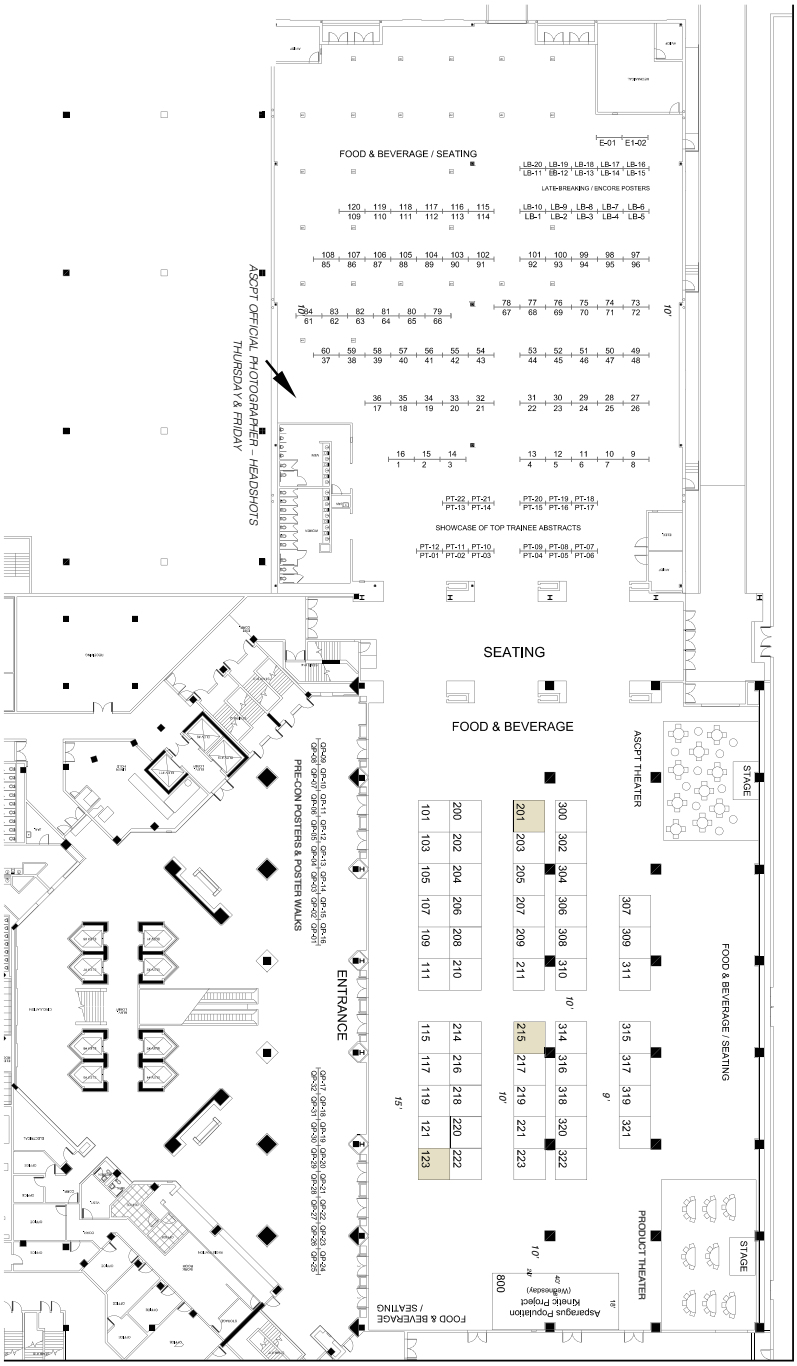

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Ashburn, VA 20146
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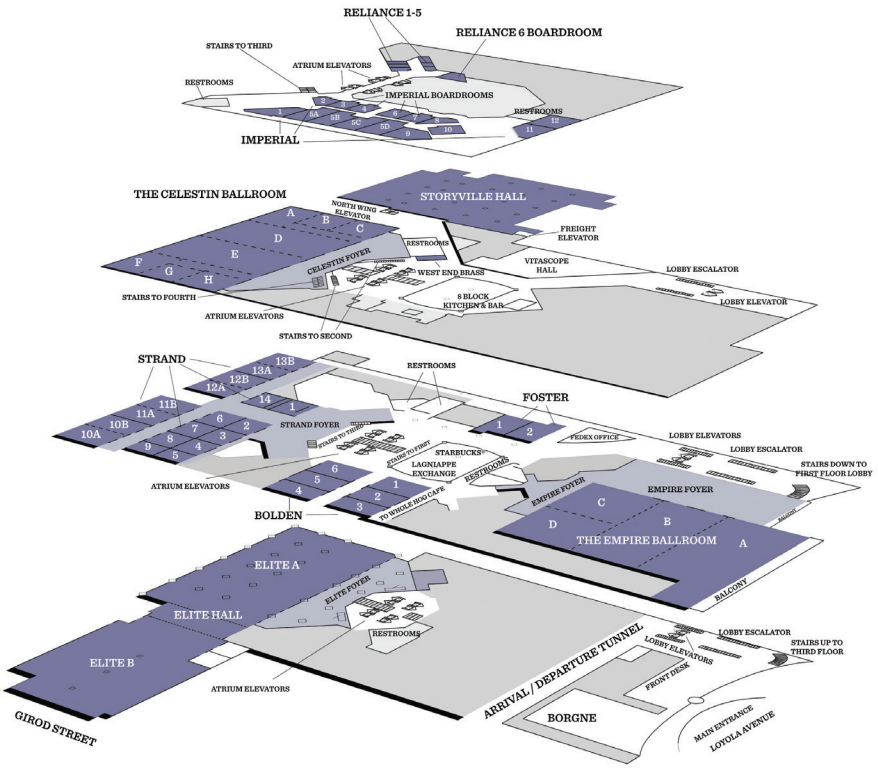

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ACKNOWLEDGMENTS

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ASCPT WISHES TO THANK THE ABSTRACT REVIEWERS FOR THEIR TIME AND EFFORT REVIEWING ABSTRACTS SUBMITTED FOR THE ASCPT 2015 ANNUAL MEETING.

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THURSDAY, MARCH 5, 2015
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BIOMARKERS AND TRANSLATIONAL TOOLS (BTT)

PI-001
5HT2A RECEPTOR OCCUPANCY (RO) IN HEALTHY SUBJECTS DETERMINED BY POSITRON EMISSION TOMOGRAPHY (PET) FOLLOWING SINGLE-DOSE ADMINISTRATION OF SAM760 (PF-05212377).
P. Lockwood,[1] J. Bell,[1] L. Chen,[1] J. Miceli,[1] K. Macci,[2] J. Van Winkle,[2] B. Planeta,[3] S. Henry[3] N. Nabulsi,[3] R. Carson[3]; [1]Pfizer Inc., Groton, CT, [2]Pfizer Inc., New Haven, CT, [3]Yale University, New Haven, CT.

PI-002
VARIABILITY OF TRIMETHOPRIM BIOACTIVATION IN CHILDREN.
J. L. Goldman, L. Van Haandel, J. Leeder; Children's Mercy Hospital, Kansas City, MO.

PI-003
EFFECTS OF VARENICLINE IN HUMAN LABORATORY MODELS FOR SCREENING OF PHARMACOTHERAPEUTICS FOR ALCOHOL USE DISORDER.
V. Vatsalya,[1] J. L. Gowin,[1] M. L. Schwandt,[1] R. Momenan,[1] M. Heilig,[1] S. E. Bartlett,[2] **V. A. Ramchandani[1];** [1]National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD, [2]Queensland University of Technology, Brisbane, Australia.

PI-004
OXYLIPID PROFILE OF LOW-DOSE ASPIRIN EXPOSURE- A PHARMACOMETABOLOMICS STUDY.
S. Ellero-Simatos,[1] A. L. Beitelshees,[2] J. P. Lewis,[2] L. M. Yerges-Armstrong,[2] A. Georgiades,[3] A. Dane,[1] A. C. Harms,[1] K. Strassburg,[1] F. Guled,[1] M. M. Hendriks,[1] R. B. Horenstein,[2] A. R. Shuldiner,[2] T. Hankemeier,[1] **R. Kaddurah-Daouk[3];** [1]Leiden Academic Centre for Drug Research, Leiden, Netherlands, [2]University of Maryland School of Medicine, Baltimore, MD, [3]Duke University Medical Center, Durham, NC.

PI-005
MATERNAL HAIR AS A BIOMARKER TO ASSESS POLYBROMINATED DIPHENYL ETHER (PBDE) EXPOSURE IN MALE INFANTS WITH HYPOSPADIAS.
S. Poon,[1] A. Carnevale,[1] K. Aleksa,[2] B. Kapur,[3] D. Bagli,[1] G. Koren[1]; [1]University of Toronto, Toronto, ON, Canada, [2]University of Waterloo, Waterloo, ON, Canada, [3]Sunnybrook Health Sciences Centre, Toronto, ON, Canada.

PI-006
COST-EFFECTIVENESS OF GENOTYPE-GUIDED WARFARIN DOSING IN KOREAN PATIENTS WITH MECHANICAL HEART VALVE REPLACEMENT UNDER FEE-FOR-SERVICE SYSTEM.
D. Kim,[1] M. Oh,[1] H. Kim,[1] J. Shin[2]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of, [2]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine; Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Korea, Republic of.

POSTERS, POSTER WALKS AND LATE-BREAKING AND ENCORE ABSTRACT POSTERS

DRUG DEVELOPMENT AND REGULATORY SCIENCES (DDR)

PI-007

EVALUATION OF THE SAFETY, TOLERABILITY, PHARMACOKINETICS (PK), AND PHARMACODYNAMICS (PD) OF MULTIPLE ORAL DOSES OF CC-220 IN HEALTHY SUBJECTS.

M. E. Thomas,[1] Y. Ye,[1] D. Weiss,[1] A. Gaudy,[1] N. Chen,[1] Z. Yang,[1] L. Liu,[1] P. H. Schafer,[1] D. Mandarino,[2] M. Palmisano,[1] E. O'Mara[1]; [1]Celgene Corporation, Summit, NJ, [2]Covance Clinical Research Unit Inc., Madison, WI.

PI-008

WHAT IS THE IMPACT OF "PROFESSIONAL SUBJECTS" ON MEDICATION EFFICACY TRIALS?

D. J. McCann; National Institute of Health/ National Institute of Allergy and Infectious Diseases, Bethesda, MD.

PI-009

INVERTED U-SHAPED (UMBRELLA OR BELL-SHAPED) DOSE RESPONSE RELATIONSHIP: DOES IT OCCUR AND WHAT ARE THE LIKELY LEAD CANDIDATES TO CONSIDER IN DRUG DEVELOPMENT?

C. Oo,[1] Y. Cao,[1] L. Lee,[1] **L. S. Lee[2];** [1]Gatheringhill Court, Morris Plains, NJ, [2]National University of Singapore, Singapore, Singapore.

PI-010

SAFETY, PHARMACOKINETIC AND PHARMACODYNAMIC EVALUATION OF LC23-1306 IN SINGLE OR MULTIPLE ADMINISTRATIONS.

S. Moon, D. Shin, I. Chung, S. Yi, H. Lee, I. Jang, K. Yu; Department of Clinical Pharmacology and Therapeutics, Seoul National University Hospital, Seoul, Korea, Republic of.

INFECTIOUS DISEASES (INF)

PI-011

DRUG-DRUG INTERACTIONS OF CARBAMAZEPINE WITH THE HCV DIRECT ACTING ANTIVIRAL (DAA) COMBINATION OF ABT-450/R, OMBITASVIR AND DASABUVIR.

P. Badri, S. Dutta, A. Asatryan, H. Wang, T. Podsadecki, W. Awni, R. Menon; AbbVie Inc., North Chicago, IL.

PI-012

DRUG-DRUG INTERACTIONS OF PRAVASTATIN AND ROSUVASTATIN WITH THE DIRECT ACTING ANTIVIRAL COMBINATION OF ABT-450/R, OMBITASVIR ± DASABUVIR IN HEALTHY VOLUNTEERS.

A. Khatri, S. Dutta, U. Das, E. Coakley, T. Podsadecki, W. Awni, R. Menon; AbbVie, North Chicago, IL

PI-013

PHARMACOKINETIC INTERACTION OF HCV NS3/4A PROTEASE INHIBITOR VANIPREVIR AND ROSUVASTATIN.

Y. Orito,[1] T. Iwasa,[1] N. Uemura,[2] G. Fujimoto,[1] S. Yama,[1] W. Gao,[3] L. Caro,[3] C. Fandozzi,[3] T. Prueksaritanont,[3] M. Anderson,[3] J. Butterton,[3] S. Hasegawa[4]; [1]MSD K.K., Tokyo, Japan, [2]Oita University, Oita, Japan, [3]Merck Sharp & Dohme Corp., Whitehouse Station, NJ, [4]Pharmaspur Inc., Tokyo, Japan.

PI-014

PHARMACOKINETICS, SAFETY AND TOLERABILITY OF THE COADMINISTRATION OF KETOCONAZOLE WITH ABT-450/R, OMBITASVIR AND DASABUVIR IN HEALTHY ADULT SUBJECTS.

T. Wang, S. Dutta, E. Coakley, U. Das, T. J. Podsadecki, W. Awni, R. Menon; AbbVie Inc., North Chicago, IL.

PI-015
DRUG-DRUG INTERACTIONS OF DIGOXIN WITH THE HCV DIRECT ACTING ANTIVIRAL (DAA) COMBINATION OF ABT-450/R, OMBITASVIR AND DASABUVIR.
P. Badri, S. Dutta, L. Rodrigues, Jr, B. Ding, T. Podsadecki, W. Awni, R. Menon; AbbVie Inc., North Chicago, IL.

PI-016
EXPOSURE-SAFETY RESPONSE RELATIONSHIP FOR ABT-450/ RITONAVIR, OMBITASVIR, DASABUVIR AND RIBAVIRIN IN HEPATITIS C GENOTYPE 1 VIRUS-INFECTED SUBJECTS IN PHASE III STUDIES.
C. Lin,[1] R. Menon,[1] W. Liu,[1] S. Mensing,[2] T. Podsadecki,[1] N. Shulman,[1] B. DaSilva-Tillmann,[1] W. Awni,[1] S. Dutta[1]; [1]Abbvie, North Chicago, IL, [2]Abbvie, Ludwigshafen, Germany.

PI-017
EXPLORING *IN VITRO* ANTIPSEUDOMONAL ACTIVITY OF SYNERGISTIC TIGECYCLINE-TETRACYCLINE COMBINATIONS.
A. N. Deitchman, R. P. Singh, J. K. Mukker, S. K. Sy, A. Zoehner, H. Derendorf; University of Florida, Gainesville, FL.

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PI-018
GENETIC ASSOCIATIONS WITH WARFARIN RESPONSE IN PATIENTS RECEIVING GENOTYPE-GUIDED DOSING.
K. Drozda,[1] Y. Lee,[1] S. R. Patel,[1] J. Lee,[1] O. Pugach,[1] J. D. Duarte,[1] E. A. Nutescu,[1] L. H. Cavallari[2]; [1]University of Illinois, Chicago, IL, [2]University of Florida, Gainesville, FL.

PI-019
OATP1B1 T521C POLYMORPHISM (RS4149056) DOES NOT AFFECT THE PHARMACOKINETICS OF EDOXABAN.
A. Vandell, J. Lee, M. Shi, K. Brown, J. R. Walker; Daiichi Sankyo Pharma Development, Edison, NJ.

PI-020
INFLUENCE OF CARBOXYLESTERASE 1 (CES1) GENETIC POLYMORPHISM ON PHARMACOKINETIC CHARACTERISTICS OF OSELTAMIVIR IN HEALTHY KOREAN SUBJECTS.
K. Park,[1] J. Oh,[1] J. Lee,[1] S. Yoon,[1] J. Cho,[1] I. Jang,[1] K. Lim[2]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Department of Clinical Pharmacology and Therapeutics, CHA University School of Medicine and Bundang CHA Medical Center, Seongnam, Korea, Republic of.

PI-021
EFFECTS OF UGT1A1 GENETIC VARIANTS ON PHARMACOKINETICS AND TOXICITIES OF BELINOSTAT ADMINSTERED BY CONTINUOUS INFUSION IN COMBINATION WITH CISPLATIN AND ETOPOSIDE.
A. K. Goey, T. M. Sissung, C. J. Peer, S. Ehrlich, S. Balasubramaniam, C. Bryla, S. E. Bates, W. D. Figg; National Cancer Institute, Bethesda, MD.

PI-022
GENOME-WIDE ASSOCIATION STUDY OF PLATELET FACTOR 4/ HEPARIN ANTIBODY FORMATION.
J. H. Karnes, J. C. Denny, E. A. Bowton, C. M. Shaffer, J. D. Mosley, S. Van Driest, P. E. Weeke, Q. S. Wells, D. M. Roden; Vanderbilt University, Nashville, TN.

PI-023
MULTIDRUG RESISTANCE-ASSOCIATED PROTEIN 4 MAY CONTRIBUTE TO BETA-LACTAM INDUCED NEUTROPENIA.
A. Hahn, T. Fukuda, T. Mizuno, D. Hahn, R. W. Frenck, A. A. Vinks; Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

POSTERS, POSTER WALKS AND LATE-BREAKING AND ENCORE ABSTRACT POSTERS

PI-024
EVALUATION OF THE IMPACT OF UGT1A1 PROMOTER VARIANTS ON BILIRUBIN LEVELS IN HYPERBILIRUBINEMIC PATIENTS.
A. M. Moyer, J. M. Skierka, L. M. Baudhuin; Mayo Clinic College of Medicine, Rochester, MN.

PI-025
EFFECTS OF TRICYCLIC COMPOUNDS ON NARATRIPTAN TRANSPORT THROUGH OATP1A2.
J. Lu,[1] A. Grangeon,[1] F. Gaudette,[2] M. Keiser,[3] V. Michaud,[2] J. Turgeon[2]; [1]Montreal University, Montreal, QC, Canada, [2]CRCHUM, Montreal, QC, Canada, [3]University Medicine of Greifswald, Greifswald, Germany.

PI-026
CHARACTERIZATION OF P450 ENZYME INVOLVEMENT IN THE FORMATION OF TRIMETHOPRIM PRIMARY METABOLITES.
J. L. Goldman, L. Van Haandel, J. Leeder, R. Pearce; Children's Mercy Hospital, Kansas City, MO.

PI-027
PHARMACOMETABOLOMICS STUDY: REVEALS THAT METFORMIN TREATMENT IMPACTS THE UREA CYCLE.
X. Liang,[1] N. Oki,[2] S. Yee,[1] D. Rotroff,[3] M. Meisner,[3] O. Fiehn,[4] K. Giacomini,[1] R. Kaddurah-Daouk,[2] Pharmacometabolomics Research Network; [1]University of California, San Francisco, San Francisco, CA, [2]Duke University Medical Center, Durham, NC, [3]North Carolina State University, Raleigh, NC, 4West Coast Metabolomics Center, University of California, Davis, Davis, CA.

PI-028
A PHARMACOGENOMIC STUDY ON THE PHARMACOKINETICS OF TACROLIMUS IN HEALTHY VOLUNTEERS USING THE AFFYMETRIX DMET PLUS PLATFORM.
Y. Choi, F. Jiang, H. Lee; Department of Clinical Pharmacology and Therapeutics, Seoul National University Hospital, Seoul, Korea, Republic of.

PI-029
ANTI-HIV PROTEASE INHIBITORS MAY AGGRAVATE RIFAMPICIN INDUCED LIVER INJURY THROUGH MULTIFACETED INTERACTIONS ON HEPATIC TRANSPORTERS.
M. S. Warren, C. Li, J. Baik, **Y. Huang;** Optivia Biotechnology Inc., Menlo Park, CA.

PI-030
A PHARMACOMETRICS APPROACH COMBINED WITH VARIOUS GENETIC ANALYSES UNCOVERS GENES LINKED TO THE DYNAMICS OF HBA1C.
S. Goswami,[1] S. Yee,[1] J. Mosley,[2] M. Hedderson,[3] M. Kabu,[4] S. Maeda,[5] D. M. Roden,[2] M. D. Simpson,[6] K. M. Giacomini,[1] R. M. Savic[1]; [1]University of California, San Francisco, CA, [2]Vanderbilt University, Nashville, TN, [3]Kaiser Permanente Division of Research, Oakland, CA, [4]RIKEN Yokohama Institute, Yokohama City, Japan, [5]RIKEN Yokohama Institute, Yokohama City, CA, [6]Marshfield Clinic Research Foundation, Marshfield, WI.

PI-031
COMPARISON OF DRUG-TRANSPORTER MRNA EXPRESSION LEVELS IN PBMC FROM HIV-INFECTED PATIENTS WITH AND WITHOUT DIABETES.
N. Ghazal,[1] Y. Yeung,[2] Z. Ngan,[2] H. Wang,[2] M. El-Sakkary,[2] F. Belanger,[1] N. Sheehan,3 B. Lebouche,[3] L. Labbe,[2] J. Turgeon,[1] **V. Michaud[1];** [1]CHUM Research Centre, Montreal, QC, Canada, [2]Faculty of Pharmacy, University of Montreal, Montreal, QC, Canada, [3]McGill University Health Center, Montréal, QC, Canada.

PI-032
METABOLOMICS, GENOMICS AND LIPIDOMICS REVEAL NOVEL SIGNATURES OF HYDROCHLOROTHIAZIDE RESPONSE IN PHARMACOGENOMIC EVALUATION OF ANTIHYPERTENSIVE RESPONSES (PEAR) STUDY.
M. H. Shahin,[1] Y. Gong,[2] T. Langaee,[2] A. L. Beitelshees,[3] D. M. Rotroff,[4] A. B. Chapman,[5] J. G. Gums,[2] S. T. Turner,[6] A. Motsinger-Reif,[4] R. F. Frye,[2] O. Fiehn,[7] J. A. Johnson,[2] R. Cooper-DeHoff,[2] X. Han,[8] R. Kaddurah-Daouk[9]; [1]University of Florida, Gainesville, FL, [2]Department of Pharmacotherapy and Translational Research, College of Pharmacy, University of Florida, Gainesville, FL, [3]Department of Medicine, University of Maryland, Baltimore, MD, [4]Bioinformatics Research Center, North Carolina State University, Raleigh, NC, [5]Department of Medicine, Emory University, Atlanta, GA, [6]College of Medicine, Mayo Clinic, Rochester, MN, [7]Genome Center, University of California at Davis, Davis, CA, [8]Sanford-Burnham Medical Research Institute, Orlando, FL, [9]Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC.

ONCOLOGY (ONC)

PI-033
ORANGE JUICE AND APPLE JUICE INGREDIENTS INHIBIT DASATINIB EFFLUX VIA P-GLYCOPROTEIN AND BREAST CANCER RESISTANCE PROTEIN: A NEW TYPE OF BEVERAGE-DRUG INTERACTION.
J. D. Unum,[1] B. Fleisher,[1] J. Shao,[2] G. An[2]; [1]College of Pharmacy, University of Florida, Orlando, FL, [2]Center for Pharmacometrics & Systems Pharmacology, Department of Pharmaceutics, College of Pharmacy, University of Florida, Orlando, FL.

PI-034
IDENTIFICATION OF CONSERVED HYPOXIA-INDUCED GENOMIC PATHWAYS THAT DRIVE AGGRESSIVE NEUROBLASTOMA PHENOTYPES.
M. A. Applebaum, A. R. Jha, K. Hernandez, C. J. Mariani, B. E. Stranger, S. L. Cohn; University of Chicago, Chicago, IL.

PI-035
OPTIMIZATION OF THE DOSE OF IRINOTECAN IN CANCER PATIENTS WITH SEVERE RENAL FAILURE (SRF) BASED ON PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODEL.
K. Fujita,[1] Y. Masuo,[2] H. Okumura,[2] Y. Sasaki,[1] Y. Kato[2]; [1]Showa University, Tokyo, Japan, [2]Kanazawa University, Kanazawa, Japan.

PI-036
GRAPEFRUIT JUICE INGREDIENTS INTERACT WITH DASATINIB THROUGH INHIBITION OF BREAST CANCER RESISTANCE PROTEIN: A NEW TYPE OF BEVERAGE-DRUG INTERACTION.
B. Fleisher,[1] J. Unum,[1] J. Shao,[2] G. An[2]; [1]College of Pharmacy, University of Florida, Orlando, FL, [2]Center for Pharmacometrics & Systems Pharmacology, Department of Pharmaceutics, College of Pharmacy, University of Florida, Orlando, FL.

PI-037
EFFECT OF RENAL IMPAIRMENT ON THE PHARMACOKINETICS AND SAFETY OF AXITINIB.
Y. Chen,[1] M. Garrett,[1] B. I. Rini,[2] R. J. Motzer,[3] J. P. Dutcher,[4] O. Rixe,[5] G. Wilding,[6] W. Stadler,[7] J. Tarazi,[1] **Y. K. Pithavala[1];** [1]Pfizer, San Diego, CA, [2]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, [3]Memorial Sloan Kettering Cancer Center, New York, NY, [4]Our Lady of Mercy Cancer Center, Bronx, NY, [5]University of New Mexico Cancer Center, Albuquerque, NM, [6]University of Wisconsin, Madison, WI, [7]University of Chicago, Chicago, IL.

PI-038

IN VITRO MOLECULAR IMAGING OF UNLABELED DRUGS IN HUMAN TUMOR SPECIMENS USING IMAGING MASS SPECTROMETRY.

A. Hamada, K. Yonemori, T. Shimoi, S. Shimma, S. Osawa, Y. Tanabe, J. Hashimoto, M. Kodaira, H. Yamamoto, M. Yunokawa, C. Shimizu, Y. Fujiwara, K. Tamura; National Cancer Center, Tokyo, Japan.

PI-039

ANALYZING THE CLINICAL ACTIONABILITY OF GERMLINE PHARMACOGENOMIC (PGX) DATA IN ONCOLOGY (ONC).

R. Wellmann, K. Danahey, S. Hussain, M. J. Ratain, P. H. O'Donnell; The University of Chicago, Chicago, IL.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PI-040

PHARMACOKINETICS OF ANTIBODY-DRUG CONJUGATE (ADC) - DNIB0600A IN A PHASE I STUDY IN PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER (OC)/ NON-SMALL CELL LUNG CANCER (NSCLC).

J. Xu,[1] H. Burris III,[2] M. Gordon,[3] D. Gerber,[4] Y. Choi,[1] K. Lin,[1] D. Maslyar,[1] S. Girish[1]; [1]Genentech, A member of the Roche Group, South San Francisco, CA, [2]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, [3]Pinnacle Oncology Hematology, Scottsdale, AZ, [4]Harold C. Simmons Cancer Center, UT Southwestern Medical Center, Dallas, TX.

PI-041

EVALUATION OF THE EFFECT OF MOMELOTINIB ON THE QT/QTC INTERVAL IN HEALTHY SUBJECTS.

Y. Xin, S. Jun, L. Moorehead, E. Kwan, M. Hepner, S. Ramanathan; Gilead Sciences, Inc., Foster City, CA.

PI-042

DRUG INTERACTION PROFILE OF MOMELOTINIB.

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PI-043

EFFECT OF HIGH SODIUM INTAKE ON PHARMACOKINETICS OF FIMASARTAN, AN ANGIOTENSIN RECEPTOR TYPE I BLOCKER, IN HEALTHY SUBJECTS.

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PI-044

MODEL-BASED META-ANALYSIS (MBMA) OF THE HBA1C LOWERING EFFECT OF SGLT-2 INHIBITORS (SGLT2I): IMPACT OF BASELINE HBA1C, RENAL FUNCTION AND BACKGROUND TREATMENT.

J. Mandema,[1] S. Terra,[2] K. Sweeney,[3] **V. Sahasrabudhe[3];** [1]Quantitative Solutions, Inc., Menlo Park, CA, [2]Pfizer, Inc., Andover, MA, [3]Pfizer, Inc., Groton, CT.

PI-045

STRATEGY TO EVALUATE AMG 853 1-β-O-ACYL GLUCURONIDE EARLY IN CLINICAL DEVELOPMENT.

B. Amore,[1] V. Chow,[1] M. Gibbs,[2] L. Wienkers[1]; [1]Amgen, Inc., Seattle, WA, [2]Amgen, Inc., Thousand Oaks, CA.

PI-046
COLLECTION OF FLUIDS FROM THE UPPER SMALL INTESTINE OF HEALTHY SUBJECTS IN FASTED AND FED CONDITION FOR THE *EX VIVO* ASSESSMENT OF SOLUBILITY AND DISSOLUTION OF DRUG PRODUCTS.
M. van den Boer,[1] A. Van Peer,[2] J. Vandenbossche,[2] J. Biewenga,[2] J. Bevernage,[3] J. Lenz,[4] S. Mesens,[1] J. Van hove,[1] M. Raghoebar[1]; [1]Clinical Pharmacology Unit Janssen R&D, Merksem, Belgium, [2]Clinical Pharmacology, Janssen R&D, Beerse, Belgium, [3]Pharmaceutical and Material Sciences, Janssen R&D, Beerse, Belgium, [4]Department Gastro-enterology, ZNA Hospital Jan Palfijn, Merksem, Belgium.

PI-047
USING INNOVATIVE COMPUTATIONAL TOOLS TO IDENTIFY THE CLINICALLY IMPORTANT DRIVERS OF VARIABILITY IN CLOPIDOGREL ANTIPLATELET THERAPY.
S. Samant,[1] X. Jiang,[1] R. B. Horenstein,[2] A. R. Shuldiner,[2] L. M. Yerges-Armstrong,[2] L. A. Peletier,[3] X. Zhang,[1] M. N. Trame,[1] L. J. Lesko,[1] S. Schmidt[1]; [1]Center for Pharmacometrics & Systems Pharmacology, University of Florida, Orlando, FL, [2]Division of Endocrinology, Diabetes and Nutrition, University of Maryland School of Medicine, Baltimore, MD, [3]Mathematical Institute, Leiden University, Leiden, Netherlands.

PI-048
PHARMACOKINETICS OF AN ANTIBODY-DRUG CONJUGATE (ADC) - DMUC5754A IN A PHASE I STUDY WITH PLATINUM-RESISTANT OVARIAN CANCER (PROC) OR UNRESECTABLE PANCREATIC CANCER (PANC).
J. Xu,[1] R. Zhang,[1] O. Saad,[1] J. F. Liu,[2] K. N. Moore,[3] H. A. Burris, III,[4] E. Humke,[1] K. Achilles Poon,[1] S. Girish[1]; [1]Genentech, A member of the Roche Group, South San Francisco, CA, [2]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, [3]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [4]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN.

PI-049
SYSTEMATIC ASSESSMENT OF INTESTINAL METABOLISM AND DEGREE OF INHIBITION IN DRUG-DRUG INTERACTIONS CAUSED BY INHIBITION OF CYP3A.
M. Nakamura,[1] S. Koh,[2] A. Hisaka,[3] H. Suzuki[4]; [1]Chugai Pharmaceutical Co, Ltd., Tokyo, Japan, [2]Asahi Kasei Pharma Corporation, Izunokuni, Japan, [3]Chiba University, Chiba, Japan, [4]University of Tokyo, Tokyo, Japan.

PI-050
OBSERVED LONG PLASMA TERMINAL HALF-LIFE OF ANACETRAPIB IS ASSOCIATED WITH ADIPOSE DEPOSITION: PLASMA AND ADIPOSE PHARMACOKINETICS IN MICE AND HUMANS.
D. E. Gutstein, R. Krishna, D. Johns, K. Mitra, G. Hartmann, V. Hamilton, J. Cote, F. Gheyas, S. Shah, Y. Mitchel; Merck & Co., Rahway, NJ.

PI-051
DEVELOPMENT OF A HUMAN WHOLE-BODY PHYSIOLOGICALLY-BASED PHARMACOKINETIC (WB-PBPK) MODEL OF LOVASTATIN LACTONE AND CARBOXYLATE (ACID) TO PREDICT HEPATIC CONCENTRATIONS.
E. Tsakalozou,[1] M. Sampson,[1] M. Z. Wang,[2] K. L. Brouwer[1]; [1]University of North Carolina, Chapel Hill, NC, [2]University of Kansas, Lawrence, KS.

PI-052
TENOFOVIR (TFV) ALAFENAMIDE (TAF) DOSE IN THE FIRST PI-BASED SINGLE TABLET REGIMEN (STR) DARUNAVIR/COBICISTAT/EMTRICITABINE/TAF (DRV/COBI/FTC/TAF; D/C/F/TAF).
J. M. Custodio, X. Wei, H. Wang, M. Hepner, J. Z. Zack, C. Callebaut, S. McCallister, M. Miller, B. P. Kearney, S. Ramanathan; Gilead Sciences, Foster City, CA.

POSTERS, POSTER WALKS AND LATE-BREAKING AND ENCORE ABSTRACT POSTERS

PI-053
THE ROLE OF MRP3 IN THE GENERATION OF CLOPIDOGREL ACTIVE METABOLITE.
T. Tai, Q. Y. Mi, Y. Q. Pan, Q. Yin, **H. G. Xie;** Nanjing First Hospital, Nanjing Medical University, Nanjing, China.

PI-054
EFFECT OF GRAPEFRUIT JUICE ON THE BIOACTIVATION OF PRASUGREL.
M. Holmberg, **A. Tornio,** H. Hyvärinen, M. Neuvonen, P. J. Neuvonen, J. T. Backman, M. Niemi; University of Helsinki and HUSLAB, Helsinki, Finland.

PI-055
ABSOLUTE ORAL BIOAVAILABILITY OF FIMASARTAN IN HEALTHY KOREAN ADULT MALE VOLUNTEERS.
Y. Choi,[1] J. Ghim,[2] E. Sim,[1] S. Park,[1] S. Baek,[3] J. Shin[2]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of, [2]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine; Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Korea, Republic of, [3]Boryung Pharmaceutical Corp, Ltd. Republic of Korea., Seoul, Korea, Republic of.

PI-056
PBPK MODELLING AND SIMULATION IN CHILDREN FOR TAPENTADOL METABOLIZED THROUGH GLUCURONIDATION.
P. G. Ravenstijn; Janssen Research & Development, Beerse, Belgium.

PI-057
UNDERSTANDING OF GFR (GLOMERULAR FILTRATION RATE) CHANGES IN RESPONSE TO ARB ADMINISTRATION USING QUANTITATIVE SYSTEMS PHARMACOLOGY APPROACH.
V. Voronova,[1] T. Karelina,[1] O. Demin,[1] D. Chen[2]; [1]Institute for Systems Biology SPb, Moscow, Russian Federation, [2]Pfizer Inc., Cambridge, MA.

PI-058
LONGITUDINAL ANALYSIS OF HAM-A FOR EFFICACY IN MONOTHERAPY AND ADJUNCTIVE GAD STUDIES.
T. Nicholas,[1] B. Binneman[2]; [1]Pfizer, Groton, CT, [2]Pfizer, Cambridge, MA.

PI-059
PARAMETER ESTIMATION PERFORMANCE FOR SIGMOID EMAX MODELS IN EXPOSURE-RESPONSE RELATIONSHIP.
H. Choi, H. MD, Y. Jarrar, M. Song, D. Lee; Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of.

PI-060
SYSTEMS PHARMACOLOGY MODELING OF ACUTE LYMPHOBLASTIC LEUKEMIA PROGRESSION AND TREATMENT.
A. Nikitich, O. Demin Jr., O. Demin; Institute for Systems Biology Moscow, Moscow, Russian Federation.

PI-061
MODELING AND SIMULATION TO EVALUATE AZTREONAM DOSE RECOMMENDATION FOR PATIENTS WITH RENAL IMPAIRMENT.
H. Xu, D. Zhou, J. Li, N. Al-Huniti; AstraZeneca, Waltham, MA.

PI-062
THE SYSTEMS PHARMACOLOGY MODEL OF HEPATITIS C PROGRESSION AND TREATMENT.
T. Yakovleva, O. Demin Jr., O. Demin; Institute for Systems Biology Moscow, Moscow, Russian Federation.

PI-063
QUANTITATIVE STRUCTURE-PHARMACOKINETIC (PK) PROPERTIES-RELATIONSHIPS (QSPKR) FOR TRIPTANS (TRP) IN HUMANS.
G. Gottipati, J. Venitz; Virginia Commonwealth University, Richmond, VA.

PI-064
A FIRST IN HUMAN TOPICAL STUDY TO CHARACTERIZE THE PHARMACOKINETICS (PK) FOLLOWING ADMINISTRATION OF [14C]UMECLIDINIUM (UMEC) TO THE AXILLA OR PALM OF HEALTHY MALE SUBJECTS.
T. Pene Dumitrescu,[1] L. Santos,[2] S. Hughes,[3] A. Pereira,[3] G. Young,[3] E. Hussey,[2] P. Charlton,[2] S. Baptiste-Brown,[4] J. S. Stuart,[2] V. D. Schmith[1]; [1]Clinical Pharmacology Modeling and Simulation, GlaxoSmithKline, Research Triangle Park, NC, [2]Stiefel, a GlaxoSmithKline Company, Research Triangle Park, NC, [3]Drug Metabolism and Pharmacokinetics, GlaxoSmithKline, Ware, United Kingdom, [4]Clinical Pharmacology Sciences & Study Operations, GlaxoSmithKline, King of Prussia, PA.

PI-065
PROBIOTICS FOR INFANTILE COLIC: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL INVESTIGATING LACTOBACILLUS REUTERI DSM 17938.
K. Chau,[1] E. Lau,[2] S. Greenberg,[2] S. Jacobson,[2] P. Yazdani-Brojeni,[2] N. Verma,[2] G. Koren[2]; [1]University of Toronto, Toronto, ON, Canada, [2]The Hospital for Sick Children, Toronto, ON, Canada.

PI-066
QUANTITATIVE STRUCTURE-PHARMACOKINETIC (PK) PROPERTIES-RELATIONSHIPS (QSPKR) FOR CLASS III ANTI-ARRHYTHMIC AGENTS (AAR) IN HUMANS.
G. Gottipati, J. Venitz; Virginia Commonwealth University, Richmond, VA.

PI-067
PHARMACOKINETIC INTERACTION BETWEEN ATORVASTATIN AND METFORMIN AT STEADY-STATE IN HEALTHY KOREAN VOLUNTEERS.
H. Choi,[1] D. Kim,[1] J. Seo,[1] J. Ghim,[2] Y. Koo,[1] J. Shin,[1] E. Kim,[2] E. Kim[3]; [1]Inje University College of Medicine, Busan, Korea, Republic of, [2]Inje University Busan Paik Hospital, Busan, Korea, Republic of, [3]CJ HealthCare Crop., Seoul, Korea, Republic of.

PI-068
DRUG-SYSTEMS-DISEASE MODEL TO PREDICT TREATMENT-OUTCOME IN TYPE 2 DIABETES MELLITUS.
P. Gaitonde,[1] P. Garhyan,[2] J. Y. Chien,[2] S. Schmidt[1]; [1]University of Florida, Orlando, FL, [2]Eli Lilly and Co., Indianapolis, IN.

PI-069
EFFECTS OF A HIGH-FAT MEAL ON THE RELATIVE ORAL BIOAVAILABILITY OF A FIXED-DOSE COMBINATION OF ATORVASTATIN AND METFORMIN IN HEALTHY KOREAN VOLUNTEERS.
D. Kim,[1] S. Lee,[1] J. Choi,[1] J. Ha,[1] Y. Noh,[2] J. Shin,[2] J. Ghim[2]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of, [2]Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine; Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Korea, Republic of.

PI-070
MODELING, SIMULATIONS AND EXTERNAL VALIDATION OF AN OPTIMAL DOSING STRATEGY OF TESTOSTERONE UNDECANOATE IN HYPOGONADAL MEN.
N. Kassir,[1] R. Dudley,[2] J. Longstreth,[3] S. Mouksassi,[1] J. F. Marier,[1] T. Danoff[2]; [1]Pharsight, a Certara Company, Montreal, QC, Canada, [2]Clarus Therapeutics, Northbrook, IL, [3]Longstreth & Associates, Mundelein, IL.

PI-071
MODEL-BASED ANALYSIS OF NIVOLUMAB TO SUPPORT CLINICAL PHARMACOLOGY PROFILING IN SUBJECTS WITH SOLID TUMORS.
Y. Feng, G. Bajaj, X. Wang, S. Agrawal, M. Gupta, A. Roy; Bristol-Myers Squibb, Princeton, NJ.

PI-072
RELATIVE BIOAVAILABILITY OF CRUSHED APIXABAN TABLETS ADMINISTERED WITH WATER OR APPLESAUCE IN HEALTHY SUBJECTS.
Y. Song,[1] M. Chang,[2] R. Frost,[1] A. Kelly,[3] F. LaCreta,[1] C. Frost[1]; [1]Bristol-Myers Squibb, Princeton, NJ, [2]Bristol-Myers Squibb, Pennington, NJ, [3]Bristol-Myers Squibb, New Brunswick, NJ.

PI-073
CHARACTERIZATION OF EXPOSURE-RESPONSE (E-R) RELATIONSHIP FOR NIVOLUMAB IN SUBJECTS WITH ADVANCED MELANOMA PROGRESSING POST ANTI-CTLA4.
X. Wang, G. Bajaj, Y. Feng, M. Gupta, S. Agrawal, A. Yang, J. Park, A. Roy; Bristol-Myers Squibb, Princeton, NJ.

PI-074
CLOPIDOGREL DOES NOT SIGNIFICANTLY AFFECT THE PHARMACOKINETICS OF SIMVASTATIN: A CROSSOVER STUDY IN HEALTHY VOLUNTEERS.
M. K. Itkonen, A. Tornio, P. J. Neuvonen, M. Niemi, J. T. Backman; University of Helsinki, Helsinki, Finland.

PI-075
PHARMACOKINETICS/ PHARMACODYNAMICS/ PHARMACOGENETICS OF DINACICLIB AND DINACICLIB GLUCURONIDE IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA.
Y. Zhao, Y. Ling, M. Poi, L. J. Schaaf, A. J. Johnson, J. C. Byrd, J. A. Jones, M. A. Phelps; Ohio State University, Columbus, OH.

PI-076
USE OF PARTIAL AUC TO DEMONSTRATE BIOEQUIVALENCE OF GENERIC METHYLPHENIDATE EXTENDED-RELEASE PRODUCTS USING PHYSIOLOGICALLY BASED ABSORPTION MODELING AND SIMULATION.
A. Babiskin, H. Kim, L. Fang, L. Lapteva, W. Jiang, R. Lionberger; Food and Drug Administration, Silver Spring, MD.

PI-077
***IN VITRO* METABOLISM OF MONTELUKAST BY CYTOCHROME P450S (CYPS) AND UDP-GLUCURONOSYLTRANSFERASES (UGTS): IMPLICATIONS FOR CYP2C8 PHENOTYPING.**
J. O. Cardoso,[1] R. V. Oliveira,[2] J. Lu,[1] Z. Desta[1]; [1]Indiana University, Indianapolis, IN, [2]Federal University of São Carlos, São Carlos, Brazil.

PI-078
A SNAPSHOT OF PRESCRIBING PRACTICE FOR THE CO-PRESCRIPTION OF CLOPIDOGREL AND ESOMEPRAZOLE IN A UNIVERSITY HOSPITAL.
V. Rollason, N. Vernaz, L. Adlere, P. Bonnabry, J. A. Desmeules; Geneva University Hospitals, Geneva, Switzerland.

PI-079
PROBABILITY OF PK/PD TARGET ATTAINMENT (PTA) FOR ASIAN PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA (CAP) TREATED WITH CEFTAROLINE FOSAMIL (CPT-F).
J. Li,[1] D. A. Melnick,[2] J. Ambler[1]; [1]AstraZeneca LP, Waltham, MA, [2]AstraZeneca LP, Wilmington, DE.

PI-080
PK/PD ANALYSES AND CLINICAL DOSE SELECTION FOR ZILEUTON IN SICKLE CELL DISEASE PATIENTS.
M. Dong, M. E. Mpollo, P. Malik, A. A. Vinks; Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PI-081
IMPACT OF ALTERED *IN VITRO* DISSOLUTION PROFILE ON WARFARIN *IN VIVO* PHARMACOKINETICS PERFORMANCE- POPULATION PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) SIMULATION.
J. Fan, X. Zhang, R. Lionberger; US Food and Drug Administration, Silver Spring, MD.

PI-082
ALTERED HEPATIC PROTEIN EXPRESSION OF CYP2C AND CYP4A IN MOUSE MODELS OF TYPE I AND TYPE II DIABETES.
S. Pilote, A. Kamaliza, A. Blais-Boilard, D. Patoine, B. Drolet, C. Simard; Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Quebec City, QC, Canada.

PI-083
MODELING AND SIMULATION TO EVALUATE POSSIBLE CONSEQUENCES OF DOSE DUMPING FOR RBP-7000, A NEW SUSTAINED RELEASE FORMULATION OF RISPERIDONE (RIS).
J. P. Jones, P. J. Fudala, C. Heidbreder, A. F. Nasser; Reckitt Benckiser Pharmaceuticals, Inc., Richmond, VA.

PI-084
PHYSIOLOGICALLY-BASED ABSORPTION MODELING AND SIMULATION FOR ASSESSING BIOAVAILABILITY.
J. P. Bai,[1] A. Babiskin,[1] X. Zhang,[1] R. A. Lionberger,[1] G. Burckart,[1] A. E. Mulberg,[1] V. Sinha,[1] T. Uno[2]; [1]US Food and Drug Administration, Silver Spring, MD, [2]Zikeikai-Aoimori Hospital, Aomori City, Japan.

PI-085
A GASTRIC PH MODIFIER PANTOPRAZOLE DID NOT SIGNIFICANTLY AFFECT THE ON PHARMACOKINETICS OF FEDRATINIB IN HEALTHY MALE SUBJECTS.
C. Xu,[1] E. Shamiyeh,[1] V. Kanamaluru,[1] L. von Moltke,[2] B. Vince,[3] M. Zhang[1]; [1]Sanofi, Bridgewater, NJ, [2]Sanofi, Cambridge, MA, [3]Vince & Associates Clinical Research, Overland Park, KS.

PI-086
EXPLORATORY EXPOSURE-SAFETY ANALYSES OF INX-08032 IN SUBJECTS WITH HEPATITIS C VIRUS INFECTION RECEIVING BMS-986094 (INX-08189).
P. H. Chan,[1] M. AbuTarif,[1] T. Eley,[1] B. He,[2] P. Yin,[3] P. Sukumar,[2] H. Kandoussi,[1] J. Wang,[1] R. Bertz[1]; [1]Bristol-Myers Squibb, Lawrenceville, NJ, [2]Bristol-Myers Squibb, Hopewell, NJ, [3]Bristol-Myers Squibb, Wallingford, CT.

PI-087
OPTIMIZING THE OPERATING CHARACTERISTICS OF DOSE RESPONSE TRIALS BY COMBINING TRADITIONAL AND MODEL-BASED ANALYTICAL APPROACHES.
V. S. Purohit,[1] M. M. Hutmacher[2]; [1]Pfizer, Groton, CT, [2]Ann Arbor Pharmacometrics Group, Ann Arbor, MI.

PI-088
PHARMACOKINETICS (PK) OF ANTI-MSLN ANTIBODY DRUG CONJUGATE (ADC) IN PATIENTS WITH UNRESECTABLE PANCREATIC OR PLATINUM-RESISTANT OVARIAN CANCER IN A PHASE I STUDY.
D. Samineni, C. Li, D. Nazzal, D. Maslyar, D. Li, S. Girish; Genentech, South San Francisco, CA.

PI-089
A POPULATION PHARMACOKINETIC MODEL FOR OPTIMIZED BELINOSTAT DOSING BY CONTINUOUS INFUSION BASED ON UGT1A1 GENOTYPE.
C. J. Peer, A. Goey, T. M. Sissung, S. Ehrlich, C. Bryla, S. E. Bates, W. D. Figg; National Cancer Institute, Bethesda, MD.

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PI-090
FED AND FASTED COMPARATIVE BIOAVAILABILITY STUDY OF RHB-102 (ONCE-DAILY ONDANSETRON 24 MG EXTENDED-RELEASE TABLETS) IN HEALTHY VOLUNTEERS.
L. Sayegh,[1] R. Essalihi,[1] E. Sicard,[1] M. Noumeir,[1] J. Massicotte,[1] M. Lefebvre,[1] R. Fathi,[2] T. F. Plasse,[2] G. Raday[2]; [1]Algorithme Pharma, Laval, QC, Canada, [2]RedHill Biopharma Ltd., Tel-Aviv, Israel.

PI-091
ANALYSIS OF THE IMPACT OF DIFFERENCES IN DOSING ADHERENCE ON THE EXPOSURE PROFILES OF APIXABAN AND RIVAROXABAN.
M. Green,[1] **T. Leil,**[2] C. Frost,[2] X. Wang,[2] R. Wada[1]; [1]Quantitative Solutions, Menlo Park, CA, [2]Bristol-Myers Squibb, Princeton, NJ.

PI-092
COMPARATIVE BIOAVAILABILITY STUDY OF RHB-102 (ONDANSETRON 24 MG ER TABLETS QD) VS. ONDANSETRON 8 MG TABLETS BID AND A SINGLE DOSE OF ONDANSETRON 24 MG IN HEALTHY VOLUNTEERS.
L. Sayegh,[1] J. M. Paquette,[1] R. Essalihi,[1] E. Sicard,[1] M. Noumeir,[1] J. Massicotte,[1] M. Lefebvre,[1] R. Fathi,[2] T. F. Plasse,[2] G. Raday[2]; [1]Algorithme Pharma, Laval, QC, Canada, [2]RedHill Biopharma Ltd., Tel-Aviv, Israel.

PI-093
PHARMACOKINETIC AND SAFETY EVALUATION OF GS-6637, A PRODRUG OF THE ALDEHYDE DEHYDROGENASE 2 (ALDH2) INHIBITOR GS-548351, IN HEALTHY NON-SMOKERS AND SMOKERS.
C. H. Nelson, D. Gossage, S. West, A. Zari, S. Ramanathan; Gilead Sciences, Foster City, CA.

PI-094
POPULATION PHARMACOKINETICS OF THE PARP INHIBITOR VELIPARIB IN WOMEN WITH OVARIAN CANCER.
F. Boakye-Agyeman,[1] M. Menefee,[2] C. Erlichman,[1] D. Northfelt,[3] S. H. Kaufmann,[1] D. Satele,[1] B. C. Brundage,[4] J. M. Reid[1]; [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, FL, [3]Mayo Clinic, Scotsdale, AZ, [4]University of Minnesota, Minneapolis, MN.

PI-095
PROTON PUMP INHIBITORS DO NOT IMPAIR THE EFFECTIVENESS OF METFORMIN IN DIABETIC PATIENTS.
J. H. Flory,[1] C. Leonard,[2] K. Haynes,[2] S. Hennessy[2]; [1]Weill Cornell Medical College, New York, NY, [2]University of Pennsylvania, Philadelphia, PA.

PI-096
POPULATION PHARMACOKINETICS OF INTRADERMAL VS. SUBCUTANEOUS INSULIN DELIVERY IN PATIENTS WITH TYPE 1 DIABETES.
T. Yu,[1] M. Sinha,[2] M. Hillard,[2] C. Sherwin,[1] S. Russell,[2] M. Spigarelli[1]; [1]University of Utah, Salt Lake City, UT, [2]Massachusetts General Hospital, Boston, MA.

PI-097
PANOBINOSTAT PK/PD IN COMBINATION WITH BORTEZOMIB AND DEXAMETHASONE IN PATIENTS WITHRELAPSED AND RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM).
S. Mu,[1] T. Tajima,[2] C. Corrado,[3] K. Sunami,[4] K. Suzuki,[5] M. Hino,[6] Y. Kuroda,[7] H. Shibayama,[8] R. Lin,[1] E. Waldron,[1] F. Binlich[9]; [1]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [2]Novartis Pharmaceuticals Corporation, Tokyo, Japan, [3]Novartis Pharmaceuticals Corporation, Basel, Switzerland, [4]National Hospital Organization, Okayama, Japan, [5]Japanese Red Cross Medical Center, Tokyo, Japan, [6]Osaka City University Hospital, Okayama, Japan, [7]Hiroshima University Hospital, Hiroshima, Japan, [8]Osaka University, Osaka, Japan, [9]Novartis Pharma S.A.S, Rueil-Malmaison, France.

PI-098
RE-EVALUATION OF NEVIRAPINE METABOLISM BY HUMAN CYTOCHROME P450S (CYPS) *IN VITRO*.
J. O. Cardoso, E. T. Ogburn, Z. Desta; Indiana University, Indianapolis, IN.

PI-099
GENETIC AND DRUG RESPONSE: STUDY ON THE INFLUENCES OF GENETICS IN VARIATION TO MORPHINE RESPONSE.
T. Onojighofia,[1] D. Holman,[2] B. Akindele,[1] B. Meshkin,[2] R. Alexander,[2] D. Schwarz,[1] J. Hubbard[2]; [1]Proove Biosciences, Columbia, MD, [2]Proove Biosciences, Irvine, CA.

DRUG SAFETY (SAF)

PI-100
A TQT STUDY CONFIRMS EARLY PK/PD MODELING THAT A SUPRATHERAPEUTIC DOSE OF OMARIGLIPTIN, A ONCE-WEEKLY DPP 4 INHIBITOR, DOES NOT PROLONG THE QTC INTERVAL.
D. A. Tatosian,[1] N. Cardillo Marricco,[2] X. Glasgow,[1] B. DeGroot,[3] K. Dunnington,[3] L. George,[1] I. Gendrano,[1] A. O. Johnson-Levonas,[1] D. Swearingen,[4] E. Kauh[1]; [1]Merck, Whitehouse Station, NJ, [2]Celerion, Montreal, QC, Canada, [3]Celerion, Lincoln, NE, [4]Celerion, Tempe, AZ.

PI-101
POLYPHARMACY IN CANCER PATIENTS RECEIVING RADIATION THERAPY.
G. H. Sokol,[1] L. S. Loftus,[1] G. Wright,[2] L. R. Cantilena[3]; [1]Moffitt Cancer Center, Tampa, FL, [2]Florida Cancer Specialists, Hudson, FL, [3]Uniformed Services University, Bethesda, MD.

PI-102
NATURAL HISTORY OF PULMONARY FUNCTION IN PATIENTS RECEIVING AMIODARONE THERAPY FOR MORE THAN TWO YEARS.
P. T. Pollak,[1] P. A. Tourin[2]; [1]University of Calgary, Calgary, AB, Canada, [2]University of Alberta, Edmonton, AB, Canada.

PI-103
AMBULATORY MONITORING DEMONSTRATES STATISTICALLY DIFFERENT 24-HOUR AND NOCTURNAL BP IN PATIENTS SWITCHING BETWEEN DIFFERING NIFEDIPINE OSMOTIC DELIVERY FORMULATIONS.
P. T. Pollak,[1] N. Dehar,[1] R. J. Herman,[1] K. B. Zarnke,[1] R. D. Feldman[2]; [1]University of Calgary, Calgary, AB, Canada, [2]Western University, London, ON, Canada.

PI-104
NOMOGRAM GUIDED MAINTENANCE DOSE SELECTION AS A TOOL FOR TEACHING BETTER UNDERSTANDING OF THE PHARMACOKINETICS OF AMIODARONE MANAGEMENT.
P. T. Pollak,[1] V. Frenkel[2]; [1]University of Calgary, Calgary, AB, Canada, [2]Soroka University Medical Center of the Negev, Beer Sheva, Israel.

PI-105
SIMULATING CARDIAC CONSEQUENCES OF THE GENETIC VARIABILITY AT THE METABOLISM LEVEL WITH USE OF MIDDLE-OUT APPROACH AND FLECAINIDE AS AN EXAMPLE COMPOUND.
S. Polak; Simcyp, Sheffield, United Kingdom.

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SPECIAL POPULATIONS (SPO)

PI-106
COMPARATIVE EFFECTIVENESS AND SAFETY OF CLOZAPINE VERSUS STANDARD ANTIPSYCHOTIC TREATMENT IN ADULTS WITH SCHIZOPHRENIA.
T. S. Stroup,[1] **T. Gerhard,**[2] C. Huang,[2] S. Crystal,[2] M. Olfson[1]; [1]Columbia University, New York, NY, [2]Rutgers University, New Brunswick, NJ.

PI-107
HIGH SYSTEMIC EXPOSURE OF METFORMIN WITH COMPARABLE GLUCOSE LOWERING EFFECT IN HEALTHY ELDERLY SUBJECTS COMPARED TO HEALTHY YOUNGER SUBJECTS.
K. Jang,[1] H. Chung,[1] J. Yoon,[1] S. Moon,[1] S. Yoon,[1] K. Kim,[2] J. Chung[3]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul, Korea, Republic of, [2]Department of Internal Medicine, Seongnam, Korea, Republic of, [3]Department of Clinical Pharmacology and Therapeutics, Seongnam, Korea, Republic of.

PI-108
MAYBE WE JUST NEED TO ASK: KNOWLEDGE AND BELIEFS ABOUT CLINICAL AND GENETIC RESEARCH AMONG AFRICAN AMERICAN COMMUNITY MEMBERS.
B. L. Jones,[1] C. A. Vyhlidal,[1] M. Brooks,[2] M. Robinson,[3] K. J. Goggin[1]; [1]Children's Mercy Hospitals and Clinics, Kansas City, MO, [2]Zion Grove Missionary Baptist Church, Kansas City, MO, [3]Black Healthcare Coalition, Inc., Kansas City, MO.

PI-109
PLACENTAL TRANSFER OF INSULIN DETEMIR *IN VIVO*.
P. Bapat,[1] K. Suffecool,[2] B. Rosenn,[3] U. Kiernan,[4] E. E. Niederkofler,[4] D. Daneman,[1] G. Koren[1]; [1]Hospital for Sick Children, Toronto, ON, Canada, [2]St. Luke's–Roosevelt Hospital Center, New York, NY, [3]Icahn School of Medicine at Mount Sinai, New York, NY, [4]Thermo Fisher Scientific, Tempe, AZ.

PI-110
PREVALENCE OF HEAVY FETAL ALCOHOL EXPOSURE IN CANADA: A POPULATION BASED MECONIUM STUDY.
K. Delano, E. Pope, B. Kapur, G. Koren; Hospital for Sick Children, Toronto, ON, Canada.

PI-111
CHARACTERIZING THE CHANGES IN DRUG CLEARANCE FROM NEONATES TO ADULTS BY PHYSIOLOGICALLY BASED PHARMACOKINETIC MODELING USING GASTROPLUS.
T. S. Samant,[1] V. Lukacova,[2] L. J. Lesko,[1] S. Schmidt[1]; [1]University of Florida, Orlando, FL, [2]Simulations Plus, Inc., Lancaster, CA.

PI-112
MDR1, MRP2, OATP2B1 AND PEPT1 TRANSPORTER PROTEIN IS PRESENT IN HUMAN NEONATAL AND INFANT SMALL INTESTINE.
M. G. Mooij,[1] B. A. De Koning,[1] J. N. Samsom,[2] D. J. Lindenbergh-Kortleve,[2] D. Tibboel,[1] S. N. De Wildt[1]; [1]Erasmus MC - Sophia Children's Hospital, Rotterdam, Netherlands, [2]Erasmus MC, Rotterdam, Netherlands.

PI-113
EXTENDED INTERVAL GENTAMICIN DOSING IN PRETERM INFANTS LESS THAN 35 WEEKS CORRECTED GESTATIONAL AGE.
G. W. 't Jong,[1] J. McKitrick,[2] B. Bewick,[3] R. Ariano,[3] M. Narvey[4]; [1]Manitoba Institute for Child Health (MICH), Winnipeg, MB, Canada, [2]Health Sciences Centre, Winnipeg, MB, Canada, [3]St. Boniface General Hospital, Winnipeg, MB, Canada, [4]Manitoba Institute for Child Health (MICH), Health Sciences Centre, MB, Canada.

PI-114
THE EFFECTS OF BODY WEIGHT/BODY MASS INDEX ON THE DISPOSITION OF LEVONORGESTREL AFTER A SINGLE DOSE ADMINISTRATION OF LEVONORGESTREL CONTAINING EMERGENCY CONTRACTIVES.
J. Shon, L. Li, **M. Kim;** US Food and Drug Administration, Silver Spring, MD.

BIOLOGICS

PI-115
PHARMACOKINETICS, PHARMACODYNAMICS AND TOLERABILITY OF DA-3091 AFTER SUBCUTANEOUS INJECTION IN HEALTHY SUBJECTS.
S. Rhee,[1] K. Shin,[2] S. Yi,[1] Y. Choi,[1] F. Jiang,[1] S. Yoon,[1] J. Cho,[1] K. Yu[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Kyungpook National University College of Pharmacy, Daegu, Korea, Republic of.

PI-116
TIME TO EVENT MODELING OF CODRITUZUMAB(GC33) ON OVERALL SURVIVAL IN PATIENTS WITH HEPATOCELLULAR CARCINOMA.
M. Nakamura,[1] C. Diack,[2] N. Ohishi,[1] C. Xu,[3] A. Phipps,[4] C. Rossin,[3] A. Muehlig,[3] T. Kawanishi,[1] T. Ohtomo,[1] R. Lee,[3] Y. Chen[3]; [1]Chugai, Tokyo, Japan, [2]F. Hoffmann-La Roche, Basel, Switzerland, [3]Roche TCRC, New York, NY, [4]F. Hoffmann-La Roche, Welwyn Garden City, United Kingdom.

PI-117
AN OPEN-LABEL STUDY IN HEALTHY MEN TO EVALUATE THE CONCENTRATION OF DENOSUMAB IN SEMINAL FLUID.
W. Y. Sohn,[1] E. Lee,[1] M. K. Kankam,[2] O. Egbuna,[1] G. Moffat,[1] J. Bussiere,[1] D. Padhi,[1] E. W. Ng,[1] S. Kumar,[1] J. G. Slatter[1]; [1]Amgen, Thousand Oaks, CA, [2]Vince & Associates, Overland Park, KS.

PI-118
DACLIZUMAB HIGH YIELD PROCESS HAS NO EFFECT ON ACTIVITY OF THE CYTOCHROME P450 ENZYMES: RESULTS OF A DRUG COCKTAIL INTERACTION STUDY IN SUBJECTS WITH MULTIPLE SCLEROSIS.
J. Q. Tran,[1] A. A. Othman,[2] A. Mikulskis,[1] Y. Wu,[1] P. Wolstencroft,[1] J. Elkins[1]; [1]Biogen Idec, Cambridge, MA, [2]AbbVie, Chicago, IL.

PI-119
MODEL-BASED MINIMUM ANTICIPATED BIOLOGICAL EFFECT LEVEL (MABEL) APPROACH LED TO SAFE HUMAN STARTING DOSE OF THREE DOMAIN ANTIBODIES FOR AUTOIMMUNE DISEASES.
R. Shi, H. Wang, S. Suchard, S. Nadler, M. Honczarenko, S. Zhang, T. Salcedo, K. Price, C. Fleener, B. Ganguly, J. Mora, J. Haulenbeek, R. Liu, B. Murthy, Z. Yang; Bristol-Meyers Squibb, Princeton, NJ.

PI-120
MODEL-BASED META-ANALYSIS OF THE CLINICAL EFFICACY OF ANTI-PCSK9 (PROPROTEIN CONVERTASE SUBTILISIN KEXIN TYPE 9) MONOCLONAL ANTIBODIES.
N. Kaila, E. Wang, K. Sweeney, D. Plowchalk; Pfizer Inc., Groton, CT.

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INNOVATIONS ACROSS THE DRUG DEVELOPMENT SPECTRUM IN ONCOLOGY

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ELITE HALL ATRIUM

CHAIR
Raymond J. Hohl, MD, PhD, Penn State

PW-01
SYSTEMS PHARMACOLOGY MODELING OF HYPOMETHYLATING AGENTS DECITABINE & SGI-110 FOR EVALUATION OF AML TREATMENT BY TARGETING S-PHASE WITH PROLONGED PHARMACOKINETIC EXPOSURES.
A. Oganesian,[1] O. Demin, Jr.,[2] A. Nikitich,[2] O. Demin,[2] M. Azab[1]; [1]Astex Pharmaceuticals, Dublin, CA, [2]Institute for Systems Biology, Moscow, Russian Federation.

PW-02
PK/PD MEDIATED DOSE OPTIMIZATION OF RG7155, A CSF1R INHIBITOR, IN PATIENTS WITH ADVANCED SOLID TUMORS AND PVNS (PIGMENTED VILLONODULAR SYNOVITIS).
G. Meneses-Lorente,[1] K. Smart,[1] A. Broeske,[2] D. Rüttinger,[2] C. Mueller,[2] A. Phipps,[1] A. Walz,[3] C. Ries,[2] M. Baehner,[2] M. Cannarile[2]; [1]Roche Products Limited, Welwyn Garden City, United Kingdom, [2]Roche Diagnostics GmbH, Penzberg, Germany, [3]F. Hoffmann-La Roche Ltd., Basel, Switzerland.

PW-03
NIVOLUMAB EXPOSURE-RESPONSE (E-R) ANALYSIS FOR CLINICAL DEVELOPMENT OF NIVOLUMAB IN ADVANCED REFRACTORY SQUAMOUS NON-SMALL CELL LUNG CANCER.
Y. Feng, X. Wang, S. Agrawal, B. Lestini, J. Park, A. Roy; Bristol-Myers Squibb, Princeton, NJ.

PW-04
A MULTICENTER VALIDATION STUDY OF GENETIC POLYMORPHISMS ASSOCIATED WITH TOXICITY AND EFFICACY OF SUNITINIB IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA.
M. Diekstra,[1] J. J. Swen,[1] E. Boven,[2] D. Castellano,[3] R. Ganapathi,[4] H. Gelderblom,[1] R. H. Mathijssen,[5] C. Rodríguez-Antona,[6] J. García-Donas,[7] B. Rini,[8] H. Guchelaar[1]; [1]Leiden University Medical Center, Leiden, Netherlands, [2]VU University Medical Center, Department of Medical Oncology, Amsterdam, Netherlands, [3]Hospital Universitario 12 de Octubre, Oncology Department, Madrid, Spain, [4]Cleveland Clinic Taussig Cancer Institute (CCF), Department of Solid Tumor Oncology, Cleveland, OH, [5]Erasmus MC Cancer Institute, Department of Medical Oncology, Rotterdam, Netherlands, [6]Spanish National Cancer Research Centre (CNIO), Hereditary Endocrine Cancer Group, Madrid, Spain, [7]Clara Campal Comprehensive Cancer Center, Oncology Unit, Madrid, Netherlands, [8]Cleveland Clinic Taussig Cancer Institute, Department of Solid Tumor Oncology, Cleveland, OH.

PW-05
PHARMACOGENETICS AND RACIAL COMPOSITION IN CLINICAL TRIALS FOR NON-SMALL CELL LUNG CANCER AND CHRONIC HEPATITIS C INFECTION.
A. Ramamoorthy, J. Bull, L. Zhang, M. A. Pacanowski; US Food and Drug Administration, Silver Spring, MD.

POSTER WALK II

LATE-BREAKING/ENCORE ABSTRACTS

THURSDAY, MARCH 5, 2015
5:30 pm - 6:15 pm
ELITE HALL ATRIUM

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

LBPW-1
RESULTS FROM THE IQ-CSRC PROSPECTIVE STUDY SUPPORT REPLACEMENT OF THE THOROUGH QT STUDY BY QT ASSESSMENT IN THE EARLY CLINICAL PHASE.
J. Keirns,[1] N. Sarapa,[2] C. Benson,[3] C. Dota,[4] G. Ferber,[5] C. Garnett,[6] C. L. Green,[7] V. Jarugula,[8] L. Johannesen,[9] K. Krudys,[9] J. Liu,[9] C. Ortemann-Renon,[10] S. Riley,[11] B. Smith,[12] R. R. Stolz,[13] M. Zhou,[12] N. Stockbridge,[9] B. Darpo[14]; [1]Astellas Pharma Global Development, Northbrook, IL, [2]Bayer Healthcare, Inc, Whippany, NJ, [3]Eli Lilly & Co., Indianapolis, IN, [4]AstraZeneca R&D, Mölndal, Sweden, [5]Statistik.Georg.Ferber GmbH, Riehen, Switzerland, [6]Certara, St. Louis, MO, [7]Duke Clinical Research Institute, Durham, NC, [8]Novartis Institute for Biomedical Research, East Hanover, NJ, [9]US FDA, Silver Spring, MD, [10]Sanofi, Bridgewater, NJ, [11]Pfizer Inc., Groton, CT, [12]iCardiac Technologies, Inc., Rochester, NY, [13]Covance Clinical Research Unit, Evansville, IN, [14]Karolinska Institutet, Stockholm, Sweden

LBPW-2
GENETIC VARIANT IN FOLATE HOMEOSTASIS IS ASSOCIATED WITH LOWER WARFARIN DOSE IN AFRICAN AMERICANS.
R. Daneshjou,[1] E. R. Gamazon,[2] B. Burkley,[3] L. H. Cavallari,[3] J. A. Johnson,[3] T. E. Klein,[1] N. Limdi,[4] S. Hillenmeyer,[1] B. Percha,[1] K. J. Karczewski,[1] T. Langaee,[3] S. R. Patel,[5] C. D. Bustamante,[1] R. B. Altman,[1] M. A. Perera[2]; [1]Stanford University, Stanford, CA, [2]University of Chicago, Chicago, IL, [3]University of Florida, Gainesville, FL, [4]University of Alabama, Birmingham, AL, [5]University of Illinois, Chicago, IL

LBPW-3
CARBOXYLESTERASE 1 C.428G>A SINGLE NUCLEOTIDE VARIATION INCREASES THE ANTIPLATELET EFFECTS OF CLOPIDOGREL BY REDUCING ITS HYDROLYSIS IN HUMANS.
K. Tarkiainen, M. T. Holmberg, A. Tornio, M. Neuvonen, P. J. Neuvonen, J. T. Backman, M. Niemi; University of Helsinki, Helsinki, Finland

LBPW-4
FEWER CARDIOVASCULAR EVENTS AFTER PERCUTANEOUS CORONARY INTERVENTION WITH GENOTYPE-GUIDED ANTIPLATELET THERAPY: RESULTS FROM THE UF HEALTH PERSONALIZED MEDICINE PROGRAM.
L. H. Cavallari, O. Magvanjav, R. David Anderson, A. Owusu-Obeng, B. Kong, T. Vo, J. N. Ashton, B. J. Staley, A. R. Elsey, R. M. Cooper-Dehoff, K. W. Weitzel, M. J. Clare-Salzler, D. R. Nelson, J. A. Johnson; University of Florida, Gainesville, FL

LBPW-5
GLUCURONIDATION CONVERTS CLOPIDOGREL TO A STRONG METABOLISM-DEPENDENT INHIBITOR OF CYP2C8: A PHASE II METABOLITE AS A CAUSE OF DRUG-DRUG INTERACTIONS.
A. Tornio, A. M. Filppula, O. Kailari, M. Neuvonen, T. H. Nyrönen, T. Tapaninen, P. J. Neuvonen, M. Niemi, **J. T. Backman**; University of Helsinki, Department of Clinical Pharmacology, Helsinki, Finland

POSTERS, POSTER WALKS AND LATE-BREAKING AND ENCORE ABSTRACT POSTERS

POSTER SESSION II

FRIDAY, MARCH 6, 2015
11:30 am - 6:30 pm
Attended Posters: 4:30 pm - 6:30 pm
ELITE HALL

BIOMARKERS AND TRANSLATIONAL TOOLS (BTT)

PII-001
THE COMPLEXITY AND DYNAMICS OF TUMOR RESPONSE TO VORINOSTAT CAN BE ELUCIDATED BY INTEGRATING MULTIPLE LARGE HIGH-THROUGHPUT DATASETS.
P. Geeleher,[1] A. Loboda,[2] D. Lenkala,[1] F. Wang,[1] J. Wang,[1] M. Nebozhyn,[2] M. Chisamore,[2] J. Hardwick,[2] M. L. Maitland,[1] **R. Huang[1];** [1]University of Chicago, Chicago, IL, [2]Merck Research Laboratories, North Wales, PA.

PII-002
***IN VITRO-IN VIVO* CORRELATION (IVIVC) OF DRUG INDUCED INHIBITION OF CREATININE TUBULAR SECRETION USING MDCK CELLS EXPRESSING OCT2/OAT2/OCT3/MATE1/MATE2K TRANSPORTERS.**
X. Zhang, W. Jiang, C. Li, J. Huang, Y. Huang; Optivia Biotechnology Inc., Menlo Park, CA.

PII-003
ENDOGENOUS BILE ACIDS ARE POTENTIAL BIOMARKERS FOR OATP1B3 ACTIVITY.
S. N. Gupta,[1] C. Hsueh,[1] S. Yee,[1] D. Weitz,[2] K. Mertsch,[2] W. Brain,[3] K. Giacomini[1]; [1]UCSF, Department of Bioengineering and Therapeutic Sciences, Schools of Pharmacy and Medicine, San Francisco, CA, [2]Sanofi-Aventis Deutschland GmbH, Frankfurt am Main, Germany, [3]R&D DSAR/Drug Disposition FFSciences, Schools of Pharmacy and Medicine, Frankfurt, Germany.

PII-004
GENOME WIDE ASSOCIATION ANALYSIS WITH AMINE METABOLITES REVEALS NOVEL LOCI IMPACTING HUMAN METABOLOMIC PROFILES.
D. Rotroff,[1] L. Yerges-Armstrong,[2] J. Lewis,[2] A. Beitleshees,[2] R. Horenstein,[2] A. Shuldiner,[2] A. Motsinger-Reif,[1] R. Kaddurah-Daouk[3]; [1]North Carolina State University, Raleigh, NC, [2]University of Maryland School of Medicine, Baltimore, MD, [3]Duke University Medical Center, Durham, NC.

PII-005
EFFECTS OF CC-220, AN ORAL IMMUNOMODULATOR, ON IMMUNE RESPONSES.
Y. Ye, P. Schafer, M. Thomas, D. Weiss, A. Gaudy, Z. Yang, L. Liu, E. O'Mara, M. Palmisano; Celgene, Summit, NJ.

PII-006
INTERACTIVE GENOTYPE-BASED DOSING GUIDELINES.
M. Whirl-Carrillo,[1] R. M. Whaley,[1] K. E. Caudle,[2] M. V. Relling,[2] R. B. Altman,[1] T. E. Klein[1]; [1]Stanford University, Palo Alto, CA, [2]St. Jude Children's Research Hospital, Memphis, TN.

DRUG DEVELOPMENT AND REGULATORY SCIENCES (DDR)

PII-007
PRECLINICAL EFFICACY OF T-LAK CELL-ORIGINATED PROTEIN KINASE INHIBITOR IN FLT3-ITD MUTANT ACUTE MYELOID LEUKEMIA.
H. Alachkar,[1] M. Mutonga,[1] G. Malnassy,[1] J. Park,[1] A. Woods,[1] G. Raca,[1] O. M. Odenike,[1] Y. Matsuo,[2] W. Stock,[1] Y. Nakamura[1]; [1]University of Chicago, Chicago, IL, [2]OncoTherapy Science, Inc., Kanagawa, Japan.

PII-008
PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODEL PREDICTIONS OF CYP MEDIATED DDIS: POTENTIAL INTERACTIONS BETWEEN ICA-105665 AND CYP ENZYME INDUCERS.
E. Callegari,[1] P. Dua,[2] G. Rigdon,[3] S. Werness,[4] J. Lin,[1] S. Tse[1]; [1]Pfizer, Groton, CT, [2]Pfizer, Cambridge, United Kingdom, [3]Salix Pharmaceuticals, Raleigh, NC, [4]Pfizer, Durham, NC.

PII-009
INTRA-ARTERIAL MICRODOSING (IAM), A NOVEL DRUG DEVELOPMENT APPROACH, PROOF OF CONCEPT IN RATS.
T. Burt, D. C. Rouse, B. B. Chin, S. Chow, D. H. Weitzel, H. Wu, T. C. Hawk, M. Cohen-Wolkowiez, R. J. Noveck; Duke University, Durham, NC.

PII-010
PHARMACOKINETIC INTERACTION BETWEEN ROSUVASTATIN AND FENOFIBRATE IN HEALTHY VOLUNTEERS.
S. Yi,[1] M. Kim,[2] S. Han,[3] **M. Park**[1]; [1]Department of Clinical Pharmacology & Therapeutics, Dong-A University College of Medicine and Hospital, Busan, Korea, Republic of, [2]Department of Cardiology, College of Medicine, Dong-A University, Busan, Korea, Republic of, [3]Department of Family Medicine, College of Medicine, Dong-A University, Busan, Korea, Republic of.

PII-011
EXPLORATORY HUMAN ABUSE POTENTIAL ASSESSMENT OF CENTANAFADINE, A NOVEL TRIPLE REUPTAKE INHIBITOR.
M. Shram,[1] K. Schoedel,[1] N. Chen,[2] D. Kelsh,[3] C. O'Brien,[4] B. Robertson,[4] T. Hsu[4]; [1]Altreos Research Partners Inc., Toronto, ON, Canada, [2]Alstat, Toronto, ON, Canada, [3]Vince & Associates Clinical Research, Overland Park, KS, [4]Neurovance, Inc., Cambridge, MA.

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PII-012
STATIN INHIBITION OF LACTIC ACID TRANSPORT IN HUMAN SKELETAL MUSCLE.
Y. Leung, J. Turgeon, V. Michaud; CRCHUM/Université de Montréal, Montreal, QC, Canada.

PII-013
IDENTIFICATION AND FUNCTIONAL STUDIES OF CYP4V2 VARIANTS AMONG KOREAN POPULATION.
Y. Jarrar,[1] S. Cho,[1] J. Park,[1] M. Lee,[1] W. Kim,[1] **D. Kim,**[1] S. Lee,[1] J. Shin[2]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of, [2]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine; Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Korea, Republic of.

PII-014
THE EFFECT OF INTRACELLULAR METHADONE ON HERG CURRENT IS MODULATED BY THE COEXPRESSION OF THE CYP450 ISOZYME 2B6.
S. Pilote,[1] A. Kamaliza,[1] J. Turgeon,[2] V. Michaud,[2] C. Simard,[1] B. Drolet[1]; [1]Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Quebec City, QC, Canada, [2]CHUM, Montreal, QC, Canada.

PII-015
ILOPERIDONE METABOLISM IN HUMAN HEART.
S. Gravel,[1] J. Huguet,[1] F. Gaudette,[2] J. Turgeon,[1] V. Michaud[1]; [1]CRCHUM/Université de Montréal, Montreal, QC, Canada, [2]CRCHUM, Montreal, QC, Canada.

POSTERS, POSTER WALKS AND LATE-BREAKING AND ENCORE ABSTRACT POSTERS

PII-016
THE EFFECT OF CIGARETTE SMOKING ON THE PLASMA AND URINE EICOSANOID METABOLIC PROFILE IN A HEALTHY MALE POPULATION.
N. Abdalla,[1] M. Parvez,[1] Y. Yu,[1] M. Yi,[1] H. Shin,[1] D. Kim,[1] D. Kim,[1] J. Shin[2]; [1]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of, [2]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine; Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Korea, Republic of.

PII-017
CYP2D6 GENE COPY NUMBER VARIATION (CNV): HOW ACCURATE IS THE AFFYMETRIX CYTOSCAN HD?
A. Gaedigk, E. Repnikova, L. Cooley, J. S. Leeder; Children's Mercy Hospital, Kansas City, MO.

PII-018
METABOLISM OF OLANZAPINE IN HUMAN HEART MICROSOMES.
R. Pelletier,[1] **S. Gravel,**[2] J. Huguet,[2] F. Gaudette,[3] J. Turgeon,[2] V. Michaud[2]; [1]Université de Montréal, Montreal, QC, Canada, [2]CRCHUM/Université de Montréal, Montreal, QC, Canada, [3]CRCHUM, Montreal, QC, Canada.

PII-019
PHARMACOGENOMICS OF MITHRAMYCIN-INDUCED HEPTATOTOXICITY.
T. M. Sissung, C. J. Peer, D. S. Schrump, W. D. Figg; National Cancer Institute, Bethesda, MD.

PII-020
RHEIN ELICITS *IN VITRO* CYTOTOXICITY IN PRIMARY HUMAN LIVER L-02 (HL-7702) CELLS BY INDUCING APOPTOSIS VIA MITOCHONDRIA-MEDIATED PATHWAY.
G. Bounda, F. Yu, W. Zhou, D. Wang; China Pharmaceutical University, Nanjing, China.

PII-021
RIFAMPIN REGULATION OF DRUG TRANSPORTERS AND THE ROLE OF MICRORNA IN HUMAN HEPATOCYTES.
E. A. Benson,[1] Z. Desta,[1] Y. Liu,[1] M. Eadon,[1] A. Gaedigk,[2] **T. C. Skaar**[1]; [1]Indiana University School of Medicine, Indianapolis, IN, [2]Children's Mercy Hospital, Kansas City, MO.

PII-022
ABC TRANSPORTER POLYMORPHISMS ARE ASSOCIATED WITH IRINOTECAN EXPOSURE AND NEUTROPENIA.
M. Li,[1] E. L. Seiser,[2] R. M. Baldwin,[1] J. Ramirez,[3] M. J. Ratain,[3] F. Innocenti[2] D. L. Kroetz[1]; [1]University of California, San Francisco, San Francisco, CA, [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, [3]The University of Chicago, Chicago, IL.

PII-023
INTERINDIVIDUAL VARIABILITY IN CYP2D6 ACTIVITY IN HUMAN LIVER MICROSOMES TO CHARACTERIZE RARE GENETIC VARIATION.
R. Dalton,[1] B. Phillips,[2] L. Risler,[2] D. D. Shen,[2] E. L. Woodahl[1]; [1]University of Montana, Missoula, MT, [2]University of Washington, Seattle, WA.

PII-024
P-MAP: NETWORK BIOLOGY APPLIED TO DETERMINE CELLULAR SENSITIVITY OF DRUG RESPONSE IN TRIPLE NEGATIVE BREAST CANCER CELL LINES.
J. Cairns, H. Li, C. Ung, L. Wang; Mayo Clinic, Rochester, MN.

PII-025
INTENSIVE STATINS EXHIBIT VARIABLE PARADOXICAL EFFECTS WHEN COMBINED WITH FIBRATES IN A MODEL OF CARDIOVASCULAR DISEASE.
R. A. Farris, C. Wiley, E. T. Price; University of Arkansas for Medical Sciences, Little Rock, AR.

PII-026
GENOME-WIDE ASSOCIATION STUDY TO IDENTIFY SUSCEPTIBILITY LOCI ASSOCIATED WITH HEMORRHAGIC COMPLICATIONS AMONG AFRICAN AMERICAN PATIENTS ON STABLE WARFARIN DOSE.
N. Nwanze,[1] W. Hernandez,[1] M. Tuck,[2] T. O'Brien,[3] R. Kittles,[4] J. Duarte,[5] S. Bourgeois,[6] L. Cavallari,[7] M. Perera[1]; [1]The University of Chicago, Chicago, IL, [2]Veterans Affairs Medical Center, District of Columbia, DC, [3]The George Washington University Medical Center, District of Columbia, DC, [4]University of Arizona, Tucson, AZ, [5]University of Illinois, Chicago, IL, [6]Queen Mary University of London, London, United Kingdom, [7]University of Florida, Gainesville, FL.

ONCOLOGY (ONC)

PII-027
ASSESSMENT OF THE POTENTIAL FOR DRUG-DRUG INTERACTIONS BETWEEN TRASTUZUMAB EMTANSINE (T-DM1) AND CYP3A INHIBITORS OR INDUCERS AND THE IMPACT ON ITS PK AND SAFETY.
P. Agarwal, B. Wang, C. Li, M. Lu, B. Kang, N. Chernyukhin, S. Girish; Genentech Inc., South San Francisco, CA.

PII-028
POPULATION PHARMACOKINETIC (PPK) MODELING OF AXITINIB IN PATIENTS WITH METASTATIC OR UNRESECTABLE LOCALLY ADVANCED THYROID CANCER.
A. Chang,[1] Y. K. Pithavala,[2] P. Bycott,[2] A. Ingrosso,[3] A. Ruiz[2]; [1]University of California, San Diego, La Jolla, CA, [2]Pfizer La Jolla, San Diego, CA, [3]Pfizer Milan, Milan, Italy.

PII-029
POPULATION PHARMACOKINETIC AND PHARMACODYNAMIC ANALYSIS OF VORINOSTAT IN PATIENTS WITH ADVANCED SOLID TUMORS WITH VARYING DEGREES OF HEPATIC FUNCTION.
H. Yang,[1] S. Ramalingam,[2] S. Kummar,[3] R. Harvey,[2] P. Ivy,[4] J. Beumer[1]; [1]University of Pittsburgh, Pittsburgh, PA, [2]Winship Cancer Institute of Emory University, Atlanta, GA, [3]National Institutes of Health Clinical Center Maryland, Bethesda, MD, [4]Investigational Drug Branch, National Institutes of Health, Pittsburgh, PA.

POSTERS, POSTER WALKS AND LATE-BREAKING AND ENCORE ABSTRACT POSTERS

PII-030
TARGETING TUMOR-ASSOCIATED HYPOXIA TO OVERCOME CHEMORESISTANCE IN PANCREATIC DUCTAL ADENOCARCINOMA (PDA).
F. Blanco,[1] M. Jimbo,[1] N. Meisner Kober,[2] E. Londin,[1] I. Rigoutsos,[1] M. V. Risbud,[1] C. Yeo,[1] J. Winter,[1] P. McCue,[1] J. Brody[1]; [1]Thomas Jefferson University, Philadelphia, PA, [2]Novartis Institutes for Biomedical Research, Basel, Switzerland.

PII-031
A PHARMACOKINETIC AND PHARMACOGENETIC STUDY OF ALISERTIB COMBINED WITH IRINOTECAN AND TEMOZOLOMIDE IN CHILDREN AND ADOLESCENTS WITH RELAPSED OR REFRACTORY NEUROBLASTOMA.
R. A. Kudgus,[1] E. Fox,[2] R. M. McGovern,[1] G. Moorthy,[2] A. Marachelian,[3] S. G. DuBois,[4] J. M. Reid[1]; [1]Mayo Clinic, Rochester, MN, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]Children's Hospital Los Angeles, Los Angeles, CA, [4]University of California, San Francisco, San Francisco, CA.

PII-032
A MODEL RELATING OVERALL SURVIVAL RELATED TO TUMOR GROWTH INHIBITION IN RENAL CELL CARCINOMA PATIENTS TREATED WITH SUNITINIB, AXITINIB OR TEMSIROLIMUS.
F. Mercier, **L. Claret;** Pharsight, Wintzenheim, France.

PII-033
POPULATION PHARMACOKINETICS OF BEVACIZUMAB: ANALYSIS OF INDIVIDUAL DATA FROM 1,792 PATIENTS WITH SOLID TUMORS FROM 15 STUDIES.
K. Han,[1] T. Peyret,[2] A. Quartino,[1] N. H. Gosselin,[2] M. Mouksassi,[2] S. Girish,[1] D. E. Allison,[1] J. Jin[1]; [1]Genentech, South San Francisco, CA, [2]Pharsight, Montreal, QC, Canada.

ORGAN SPECIFIC DISEASES (OSD)

PII-034
EVOLOCUMAB PHARMACOKINETICS AND ITS EFFECTS ON LDL-C AND PCSK9 LOWERING IN SUBJECTS WITH MILD OR MODERATE HEPATIC IMPAIRMENT.
M. G. Emery,[1] J. P. Gibbs,[1] J. G. Slatter,[2] L. Hamilton,[3] S. M. Wasserman,[1] M. Geller,[1] C. Dias[1]; [1]Amgen Inc., Thousand Oaks, CA, [2]Amgen Inc., Seattle, WA, [3]Amgen Ltd., Uxbridge, United Kingdom.

PII-035
DIFFERENCES IN MYCOPHENOLIC ACID AND METABOLITE, MYCOPHENOLIC ACID GLUCURONIDE EXPOSURES BETWEEN CALCINEURIN INHIBITOR REGIMENS POST-RENAL TRANSPLANT.
C. Meaney,[1] P. Sudchada,[1] J. Consiglio,[2] G. Wilding,[2] R. Venuto,[3] K. Tornatore[1]; [1]School of Pharmacy and Pharmaceutical Sciences, Immunosuppressive Pharmacology Research Program, CBLS, University at Buffalo, Buffalo, NY, [2]School of Public Health and Health Professions, University at Buffalo, Buffalo, NY, [3]School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY.

PII-036
ALTERED VITAMIN A HOMEOSTASIS IN CHRONIC KIDNEY DISEASE.
J. Jing, N. Isoherranen, C. Yeung, B. Kestenbaum; University of Washington, Seattle, WA.

PII-037
SEARCHING FOR OPTIMAL THERAPY OF THE AMYLOID PATHOLOGY USING MECHANISM-BASED MODEL.
T. Karelina,[1] O. Demin,[1] S. Divvuri,[2] T. Nicholas[3]; [1]Institute for Systems Biology, Moscow, Russian Federation, [2]Pfizer R&D, Groton, CT, [3]Pfizer Global R&D, Groton, CT.

PII-038
GENOME-WIDE ASSOCIATION STUDY IDENTIFIES NOVEL SUSCEPTIBILITY LOCI FOR VENOUS THROMBOEMBOLISM IN AFRICAN AMERICANS.
W. Hernandez,[1] E. R. Gamazon,[1] A. Konkashbaev,[1] A. Konkashbaev,[1] R. A. Kittles,[2] L. H. Cavallari,[3] M. A. Perera[1]; [1]The University of Chicago, Chicago, IL, [2]University of Arizona College of Medicine, Tucson, AZ, [3]University of Florida, Gainesville, FL.

PII-039
A TWO-WEEK COURSE OF HIGH-DOSE INTEGRASE INHIBITORS DOES NOT LEAD TO NEPHROTOXICITY IN MICE.
M. T. Eadon, H. Zhang, T. C. Skaar, S. Gupta, Z. Desta; Indiana University, Indianapolis, IN.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PII-040
NOVEL METHODOLOGY FOR ESTIMATING THE TREATMENT EFFECT IN PRESENCE OF HIGHLY VARIABLE PLACEBO RESPONSE.
R. Gomeni,[1] N. Goyal,[2] F. Bressolle,[1] M. Fava[3]; [1]Pharmacometrica, La Fouillade, France, [2]GlaxoSmithKline, King of Prussia, PA, [3]Massachusetts General Hospital, Boston, MA.

PII-041
INVESTIGATION INTO THE INTERCHANGEABILITY OF GENERIC FORMULATIONS USING A RANDOM SELECTION OF MEDICINES AND IMMUNOSUPPRESSANTS.
Y. Yu,[1] S. Teerenstra,[2] C. Neef,[3] D. Burger,[4] M. Maliepaard[2]; [1]CARIM, Maastricht University Medical Centre, Maastricht, Netherlands, [2]Medicines Evaluation Board (CBG-MEB), Utrecht, Netherlands, [3]CAPHRI, Maastricht University Medical Centre, Maastricht, Netherlands, [4]Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands.

PII-042
A PHASE I STUDY TO DETERMINE THE SINGLE DOSE SAFETY AND PHARMACOKINETICS OF SYM-1219 (SECNIDAZOLE) IN HEALTHY FEMALE VOLUNTEERS.
H. S. Pentikis,[1] N. Adetoro,[2] C. J. Braun[1]; [1]Symbiomix Therapeutics, SAJE Consulting, Baltimore, MD, [2]Symbiomix Therapeutics, Baltimore, MD.

PII-043
EFFECT OF FOOD ON THE PHARMACOKINETICS OF ANAPLASTIC LYMPHOMA KINASE (ALK) INHIBITOR CERITINIB IN HEALTHY SUBJECTS.
Y. Lau, T. Lin, D. Song, J. Gu, R. Yu, A. Joe; Novartis Pharmaceuticals Corporation, East Hanover, NJ.

PII-044
DRUG INTERACTION POTENTIAL OF EMTRICITABINE (F; FTC)/TENOFOVIR (TFV) ALAFENAMIDE (TAF) (F/TAF) FIXED DOSE COMBINATION AND COBICISTAT (COBI)-BOOSTED DARUNAVIR (DRV).
J. M. Custodio, H. Wang, A. Silva, L. Zhong, J. Z. Zack, C. Callebaut, S. McCallister, B. P. Kearney, S. Ramanathan; Gilead Sciences, Foster City, CA.

PII-045
SAFETY, TOLERABILITY AND PHARMACOKINETIC CHARACTERISITCS OF VVZ-149 INJECTION IN HEALTHY SUBJECTS.
J. Yoon,[1] J. Oh,[1] Y. Kim,[1] S. Cho,[2] D. Lee,[2] S. Shin,[1] I. Jang,[1] K. Yu,[1] J. Chung[3]; [1]Seoul National University Hospital, Jongno-gu, Seoul, Korea, Republic of, [2]Vivozon, Inc., Sungbuk-gu, Seoul, Korea, Republic of, [3]Seoul National University Bundang Hospital, Seongnam, Gyeonggi-do, Korea, Republic of.

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NO DOSE ADJUSTMENT IS NEEDED WHEN COADMINISTERING DULAGLUTIDE WITH A COMBINATION ORAL CONTRACEPTIVE.
C. Loghin, A. de la Peña, X. Cui; Eli Lilly and Company, Indianapolis, IN.

PII-047
SITE OF INJECTION DOES NOT AFFECT DULAGLUTIDE PHARMACOKINETICS.
B. A. Moser, X. Cui, **C. Loghin,** A. Chaudhary, A. de la Peña, J. Y. Chien; Eli Lilly and Company, Indianapolis, IN.

PII-048
POPULATION PHARMACODYNAMIC MODELING OF LANREOTIDE AUTOGEL IN JAPANESE ACROMEGALIC PATIENTS.
K. Saito,[1] T. Mochizuki,[1] A. Shimatsu,[2] Y. Kasahara[1]; [1]Teijin Pharma Limited, Tokyo, Japan, [2]Clinical Research Institute, National Hospital Organization Kyoto Medical Center, Kyoto, Japan.

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A TARGET MEDIATED DRUG DISPOSITION (TMDD) DOSE OPTIMIZATION OF RG7116, A HER3 MONOCLONAL ANTIBODY, IN PATIENTS WITH ADVANCED OR METASTATIC SOLID TUMORS EXPRESSING HER3.
G. Meneses-Lorente,[1] C. McIntyre,[1] W. Jacob,[2] M. Zajac,[1] I. James,[2] M. Thomas,[3] M. Weisser,[2] J. Hsu[4]; [1]Roche Products Limited, Welwyn Garden City, United Kingdom, [2]Roche Diagnostics GmbH, Penzberg, Germany, [3]Roche Pharma AG, Grenzach-Wyhlen, Germany, [4]Roche TCRC, Inc., New York, NY.

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EFFECTS OF ETHANOL ON ASPIRIN HYDROLYSIS BY CARBOXYLESTERASE-2 IN HUMANS.
R. B. Parker, Z. Hu, S. C. Laizure; University of Tennessee College of Pharmacy, Memphis, TN.

PII-051
APPLICATION OF PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODELING TO BOSUTINIB PHARMACOKINETICS: PREDICTION OF DRUG-DRUG INTERACTIONS AS CYP3A SUBSTRATE.
C. Ono,[1] P. Hsyu,[2] R. Abbas,[3] C. Loi,[2] S. Yamazaki[2]; [1]Pfizer Japan Inc., Tokyo, Japan, [2]Pfizer Inc., San Diego, CA, [3]Pfizer Inc., Collegeville, PA.

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APPLICATION OF PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODELING TO BOSUTINIB PHARMACOKINETICS: PREDICTION OF DRUG-DISEASE INTERACTION IN ORGAN DYSFUNCTION PATIENTS.
C. Ono,[1] P. Hsyu,[2] R. Abbas,[3] C. Loi,[2] S. Yamazaki[2]; [1]Pfizer Japan Inc., Tokyo, Japan, [2]Pfizer Inc., San Diego, CA, [3]Pfizer Inc., Collegeville, PA.

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PHARMACOKINETICS AND TOLERABILITY OF IDP-73152 MESYLATE AFTER A SINGLE ORAL ADMINISTRATION UNDER FASTING AND FED CONDITIONS IN HEALTHY VOLUNTEERS.
S. Park,[1] D. Shin,[2] Y. Choi,[1] J. Kang,[3] S. Park,[3] J. Won,[3] F. Jiang,[1] H. Lee,[1] I. Jiang,[1] K. Yu[1]; [1]Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Clinical Trials Center, Gachon University Gil Medical Center, Incheon, Korea, Republic of, [3]Ildong Pharmaceutical Co., Ltd., Korea, Seoul, Korea, Republic of.

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A MULTIPLE-DOSE STUDY OF BLOCKADE OF OPIOID SUBJECTIVE EFFECTS BY SUBCUTANEOUS INJECTIONS OF DEPOT BUPRENORPHINE IN SUBJECTS WITH OPIOID USE DISORDER.
H. Jia,[1] M. K. Greenwald,[2] B. D. Vince,[3] P. J. Fudala,[1] C. Heidbreder,[1] A. F. Nasser[1]; [1]Reckitt Benckiser Pharmaceuticals, Inc., Richmond, VA, [2]Substance Abuse Research Division, Department of Psychiatry and Behavioral Neurosciences and Addiction Research Institute, Wayne State University, Detroit, MI, [3]Vince & Associates Clinical Research, Inc., Overland Park, KS.

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INFORMATIVE DROPOUT MODELING AND EXPOSURE-RESPONSE ANALYSIS FOR MAVRILIMUMAB PHASE IIB STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS.
C. Wu,[1] C. D. Jin,[1] L. Roskos,[2] B. Wang[1]; [1]AstraZeneca/MedImmune, Mountain View, CA, [2]AstraZeneca/MedImmune, Gaithersburg, MD.

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MODELING AND SIMULATION-GUIDED RATIONAL DRUG DISCOVERY AND DEVELOPMENT: A CASE STUDY OF MAVRILIMUMAB.
B. Wang,[1] C. Wu,[1] L. Roskos[2]; [1]AstraZeneca/MedImmune, Mountain View, CA, [2]AstraZeneca/MedImmune, Gaithersburg, MD.

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ASSESSING SYNERGY OF DRUG AGONISTS USING A SURFACE RESPONSE ANALYSIS IN R.
G. Vlasakakis,[1] R. L. O'Connor-Semmes,[2] M. A. Young[2]; [1]GlaxoSmithKline, London, United Kingdom, [2]GlaxoSmithKline, Research Triangle Park, NC.

PII-058
EFFECT OF NEOMYCIN (N) ON THE PHARMACOKINETICS (PK) OF REGORAFENIB (REG).
J. Lettieri,[1] A. Ajavon,[1] Z. Jirakova,[2] I. Sturm,[2] M. Gerisch[3]; [1]Bayer HealthCare, Whippany, NJ, [2]Bayer Pharma AG, Berlin, Germany, [3]Bayer Pharma AG, Wuppertal, Germany.

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POPULATION PHARMACOKINETIC ANALYSIS OF SUMATRIPTAN IN HEALTHY KOREAN MALE SUBJECTS.
J. Lee,[1] S. Seong,[1] S. Park,[1] M. Gwon,[1] Y. Jang,[1] H. Lee,[1] H. Yoo,[2] Y. Yoon[1]; [1]Kyungpook National University Hospital Clinical Trial Center, Daegu, Korea, Republic of, [2]College of Pharmacy and Institute of Bioequivalence and Bridging Study, Chonnam National University Republic of Korea, Kwangju, Korea, Republic of.

PII-060
EVALUATION OF THE TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF ORALLY ADMINISTERED DWP05195, A NEW TRPV1 ANTAGONIST IN HEALTHY ADULT MALE VOLUNTEERS.
S. Lee,[1] F. Jiang,[1] J. Lee,[1] J. Chung,[2] I. Jang,[1] H. Lee,[1] K. Yu,[1] K. Jang[1]; [1]Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Seoul National University College of Medicine and Bundang Hospital, Sungnam, Korea, Republic of.

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POPULATION PHARMACOKINETICS OF CIPROFLOXACIN AND DOSING RECOMMENDATION IN NEONATES AND INFANTS LESS THAN 3 MONTHS OF AGE.
C. Barin-Le Guellec,[1] W. Zhao,[2] B. Kassai,[3] M. A. Turner,[4] E. Jacqz-Aigrain,[2] on behalf of the TINN Consortium; [1]Pharmacogenetics Unit, Department of Biochemistry, Tours, France, [2]Department of Paediatric Pharmacology and Pharmacogenetics, Paris, France, [3]EPICIME-CIC 1407, Lyon, France, [4]Neonatal Unit, Liverpool Women's Hospital, Liverpool, United Kingdom.

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A. R. Polepally, S. Dutta, T. Baykal, B. Hu, T. J. Podsadecki, W. M. Awni, R. M. Menon; AbbVie Inc., North Chicago, IL.

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C. H. Nelson, L. Fang, F. Cheng, L. Wang, M. Hepner, J. Lin, S. Ramanathan; Gilead Sciences, Foster City, CA.

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K. Yamaguchi, M. Watanabe, T. Motoki, H. Tanaka, M. Asakura, T. Tai, K. Takahashi, T. Nozaki, S. Kosaka, H. Houchi; Department of Pharmacy, Kagawa University Hospital, Miki-cho, Kita-gun, Japan.

PII-065
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B. Wang,[1] L. Yan,[1] M. Hutmacher,[2] L. Roskos[3]; [1]MedImmune, Mountain View, CA, [2]Ann Arbor Pharmacometrics Group, Ann Arbor, MI, [3]MedImmune, Gaithersburg, MD.

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THE PAN-PHOSPHOINOSITIDE-3 KINASE INHIBITOR PICTILISIB (GDC-0941), AN *IN VITRO* CYP2C8 INHIBITOR, DOES NOT IMPACT THE PHARMACOKINETICS OF PACLITAXEL, A CYP2C8 SUBSTRATE.
K. Morrissey, T. Lu, K. Faber, D. Apt, J. Lauchle, J. Schutzman, G. Shankar, S. Singel, M. Dresser, J. Jin, J. Ware; Genentech, Inc., South San Francisco, CA.

PII-067
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S. Seong, J. Lee, S. Park, M. Gwon, H. Kim, H. Lee, Y. Yoon; Kyungpook National University Hospital Clinical Trial Center, Daegu, Korea, Republic of.

PII-068
POPULATION PHARMACOKINETIC-PHARMACODYNAMIC (PKPD) MODELING OF AMG 747, A GLYCINE TRANSPORTER TYPE 1 (GLYT 1) INHIBITOR, IN HEALTHY SUBJECTS.
J. Chen, C. Dias, M. Bragasin, S. F. Wilson, N. Narayanan, G. Jang, P. Ma, T. Vu; Amgen Inc., Newbury Park, CA.

PII-069
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Y. Choi,[1] S. Yoon,[1] E. Ismatova,[1] Y. Kumagai,[2] H. Lee,[1] K. Yu,[1] J. Chung,[3] I. Jang[1]; [1]Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Clinical Trial Center, Kitasato University Hospital, Kitamoto, Japan, [3]Seoul National University Bundang Hospital, Seongnam, Korea, Republic of.

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BIOEQUIVALENCE AND PHARMACOKINETIC EVALUATION OF TWO FORMULATIONS OF ULTRACET® ER TABLET.
E. Ismatova, K. Jang, J. Lee, H. Lee, S. Shin, K. Yu, I. Jang; Seoul National University Hospital, Clinical Pharmacology and Therapeutics, Seoul, Korea, Republic of.

PII-071
APPLICATION OF PBPK AND BAYESIAN MODELING FOR PREDICTION OF THE LIKELIHOOD OF INDIVIDUAL PATIENTS EXPERIENCING SERIOUS ADVERSE REACTIONS TO A STANDARD DOSE OF EFAVIRENZ.
M. Chetty, T. Cain, M. Jamei, A. Rostami; Simcyp, Sheffield, United Kingdom.

PII-072
SERUM HEMOGLOBIN IS A PREDICTOR OF TACROLIMUS WHOLE BLOOD CONCENTRATION IN HEMATOPOEITIC STEM CELL TRANSPLANT PATIENTS.
T. A. Miano, A. Ganetsky, D. L. Porter, R. Reshef; University of Pennsylvania, Philadelphia, PA.

PII-073
ASSESSMENT OF PHARMACOKINETIC INTERACTION BETWEEN THE PI3K INHIBITOR TASELISIB (GDC-0032) AND A STRONG CYP3A4 INDUCER OR INHIBITOR.
S. Sahasranaman, R. A. Graham, L. Salphati, J. Hsu, X. Lu, M. Gates, D. Amin, D. Bradford, M. Dresser, J. Ware; Genentech, Inc., South San Francisco, CA.

PII-074
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E. Laille,[1] Z. Xiao,[2] X. Du,[3] Q. Dong,[1] S. Songer,[1] C. Beach[1]; [1]Celgene Corporation, Summit, NJ, [2]Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China, [3]Guangdong General Hospital, Guangzhou, China.

PII-075
ASSESSMENT OF ABSOLUTE BIOAVAILABILITY AND MASS BALANCE OF THE PI3K INHIBITOR TASELISIB (GDC-0032) IN HEALTHY SUBJECTS.
S. Sahasranaman, S. Ma, J. Hsu, M. Gates, Y. Ran, K. Zhang, P. Yehl, L. Salphati, X. Ding, D. Bradford, M. Dresser, J. Ware; Genentech, Inc., South San Francisco, CA.

PII-076
POPULATION PHARMACOKINETIC/ PHARMACODYNAMIC (PK/PD) MODELING FOR AN ANTISENSE OLIGONUCLEOTIDE (ISIS-FXIRX), TARGETING FACTOR XI, IN HEALTHY SUBJECTS.
R. Yu,[1] K. Luu,[1] C. Bethune,[1] S. Bhanot,[1] Q. Liu,[2] Y. Wang[1]; [1]Isis Pharmaceuticals, Inc., Carlsbad, CA, [2]Takeda Pharmaceuticals, Deerfield, IL.

PII-077
PHARMACOKINETIC, PHARMACODYNAMIC AND TOLERBILITY PROFILES OF CKD-11101, A BIOSIMILAR TO NESP®, AFTER A SINGLE SUBCUTANEOUS ADMINISTRATION IN HEALTHY VOLUNTEERS.
J. Park,[1] S. Rhee,[1] S. Kim,[1] Y. Koh,[2] T. Koo,[2] J. Sohn,[2] J. Kim,[2] I. Jang,[1] S. Shin,[1] K. Yu,[1] H. Lee[1]; [1]Seoul National University, Seoul, Korea, Republic of, [2]Chong Kun Dang Pharmaceutical Corp. Yongin, Seoul, Korea, Republic of.

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POPULATION PHARMACOKINETICS OF KRN23, A HUMAN ANTI-FGF23 ANTIBODY DEVELOPED FOR THE TREATMENT OF ADULTS WITH X-LINKED HYPOPHOSPHATEMIA.
X. Zhang,[1] T. Peyret,[2] N. H. Gosselin,[2] J. Marier,[2] T. Ito,[1] E. Imel,[3] T. O. Carpenter[4]; [1]Kyowa Hakko Kirin Pharma Inc., Princeton, NJ, [2]Pharsight-A Certara Company, Montreal, QC, Canada, [3]Indiana University School of Medicine, Indianapolis, IN, [4]Yale University School of Medicine, New Haven, CT.

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IMMUNOGENICITY AND TOLERABILITY OF NOVEL HUMAN PAPILLOMAVIRUS-16/18 VACCINE IN HEALTHY MALE VOLUNTEERS.
Y. Kim,[1] D. Shin,[1] S. Lee,[1] J. Oh,[1] J. Han,[2] N. Lee,[2] H. Lee,[1] K. Yu,[1] J. Chung,[1] I. Jang[1]; [1]Department of Clinical Pharmacology and Therapeutics Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Department of Bioscience & Biotechnology, Sejong University, Seoul, Korea, Republic of.

PII-080
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I. Choi,[1] S. Rhee,[1] S. Kim,[1] I. Jang,[1] S. Shin,[1] H. Lee,[1] K. Yu,[1] Y. Koh,[2] T. Koo,[2] J. Sohn,[2] J. Kim[2]; [1]Seoul National University Hospital, Seoul, Korea, Republic of, [2]Chong Kun Dang Phamaceutical Corp., Republic of Korea, Gyeonggi-do, Korea, Republic of.

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EFFECT OF ACID REDUCING AGENTS ON THE PHARMACOKINETICS OF IDELALISIB, A NOVEL PI3K INHIBITOR, IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES.
F. Jin,[1] S. Sharma,[1] H. Zhou,[2] Y. Gao,[3] X. Li,[4] T. Newcomb,[4] S. Ramanathan[1]; [1]Gilead Sciences, Foster City, CA, [2]Cell Therapeutics INC., Seattle, WA, [3]Quantitative Solutions, Menlo Park, CA, [4]Gilead Sciences, Seattle, WA.

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S. Lee, A. Minnich, D. D. Desai, Y. Shen, H. Tang, J. Postelnek, W. L. Trigona, R. Townsend, B. Murthy, R. L. Parsons; Bristol-Myers Squibb, Princeton, NJ.

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R. Zheng,[1] B. Kim,[1] K. Lee,[2] S. Yim[3]; [1]Clinical Pharmacology and Therapeutics, Seoul, Korea, Republic of, [2]Department of Pharmaceutical Biochemistry, Seoul, Korea, Republic of, [3]Department of Clinical Pharmacology, Seoul, Korea, Republic of.

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F. Jin,[1] H. Zhou,[2] Y. Gao,[3] X. Li,[4] T. Newcomb,[4] S. Ramanathan[1]; [1]Gilead Sciences, Foster City, CA, [2]CTI BioPharma Corp, Seattle, WA, [3]Quantitative Solutions, Menlo Park, CA, [4]Gilead Sciences, Seattle, WA.

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J. Yang, M. C. Palanca-Wessels, Y. Wang, N. Josephson, S. L. Peng; Seattle Genetics, Inc., Bothell, WA.

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A. Lo,[1] S. Kshirsagar,[2] S. Patil,[1] S. Dubé,[1] D. L. Bourdet[1]; [1]Theravance Biopharma, South San Francisco, CA, [2]Consultant, Mountain View, CA.

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POPULATION PHARMACOKINETICS OF BELIMUMAB IN HEALTHY AMERICAN AND JAPANESE SUBJECTS FOLLOWING SUBCUTANEOUS ADMINISTRATION.
S. W.S. Yapa, H. Struemper; GlaxoSmithKline, Research Triangle Park, NC.

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S. Ciric,[1] R. Preston,[2] D. M. Heuman,[3] T. C. Marbury,[4] J. Holland,[5] R. D. Mamelok,[6] N. Benrimoh,1 D. A. Ramies,[5] E. Gavis,[7] S. Lacy,[5] L. T. Nguyen[5]; [1]Celerion, Saint-Laurent (Montreal), QC, Canada, [2]University of Miami, Miami, FL, [3]Virginia Commonwealth University, Richmond, VA, [4]Orlando Clinical Research Center, Orlando, FL, [5]Exelixis, Inc., South San Francisco, CA, [6]Mamelok Consulting, Palo Alto, CA, [7]McGuire VAMC, Richmond, VA.

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PHARMACOKINETIC/ PHARMACODYNAMIC (PK/ PD) ANALYSES OF ARGININE VASOPRESSIN TYPE-1B (V1B) RECEPTOR ANTAGONIST EFFECT ON CORTISOL.
I. Singh,[1] **W. Liu,[2]** D. A. Katz,[1] W. M. Awni,[2] S. Dutta[2]; [1]Former AbbVie Employee, North Chicago, IL, [2]AbbVie, North Chicago, IL.

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POTENTIAL PRASUGREL DRUG INTERACTIONS BASED ON INHIBITION OF CARBOXYLESTERASE-2.
S. C. Laizure, **Z. Hu**, R. B. Parker; University of Tennessee Health Science Center, Memphis, TN.

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POPULATION PHARMACOKINETIC AND PHARMACODYNAMIC ANALYSIS OF ECULIZUMAB TO SUPPORT PHASE III DOSING REGIMEN IN PATIENTS WITH REFRACTORY GENERALIZED MYASTHENIA GRAVIS.
C. Lathia,[1] X. Gao,[1] N. Kassir,[2] S. M. Mouksassi,[2] B. Jayaraman,[2] J. Marier,[2] J. Wang,[1] C. Bedrosian[1]; [1]Alexion Pharmaceuticals Inc., Cheshire, CT, [2]Pharsight, a Certara Company, Montreal, QC, Canada.

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A PHASE I, OPEN-LABEL STUDY TO DETERMINE THE EFFECT OF SYM-1219 ON THE PHARMACOKINETICS OF ETHINYL ESTRADIOL (EE2) AND NORETHINDRONE (NET) IN HEALTHY FEMALE VOLUNTEERS.
H. S. Pentikis,[1] N. Adetoro,[2] C. J. Braun[1]; [1]Symbiomix Therapeutics, SAJE Consulting, Baltimore, MD, [2]Symbiomix Therapeutics, Baltimore, MD.

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ATAZANAVIR ABSORPTION IN HEALTHY VOLUNTEERS WITH PHARMACOLOGICALLY-INDUCED HYPOCHLORHYDRIA USING BETAINE HCL.
K. P. Faber,[1] H. F. Wu,[2] M. R. Yago,[2] L. Frassetto,[2] **L. Z. Benet[2]; [1]**Genentech, South San Francisco, CA, [2]University of California, San Francisco, San Francisco, CA.

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A PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODEL FOR PREDICTION OF PLASMA AND LUNG CONCENTRATIONS AFTER ADMINISTRATION OF CEFTAZIDIME.
D. Zhou, J. Li, H. Xu, N. Al-Huniti; AstraZeneca, Waltham, MA.

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POPULATION PHARMACOKINETICS AND EXPOSURE-RESPONSE ASSESSMENT OF ANTI-CD79B ANTIBODY DRUG CONJUGATE IN PATIENTS: INTERIM ANALYSIS RESULTS.
D. Lu,[1] J. Y. Jin,[1] L. Gibiansky,[2] P. Agarwal,[1] R. Dere,[1] C. Jones,[1] C. Li,[1] M. Wenger,[1] Y. Chu,[1] R. Kahn,[1] A. Joshi,[1] S. Girish[1]; [1]Genentech, South San Francisco, CA, [2]QuantPharm, North Potomac, MD.

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PHARMACOKINETICS AND SAFETY OF SINGLE ASCENDING DOSES, FOOD EFFECT AND KETOCONAZOLE (KTZ) INTERACTION OF ARGININE VASOPRESSIN TYPE-1B (V1B) RECEPTOR ANTAGONIST ABT-436.
W. Liu,[1] D. A. Katz,[2] K. Tracy,[2] C. Locke,[1] W. M. Awni,[1] S. Dutta[1]; [1]AbbVie, North Chicago, IL, [2]Former AbbVie Employee, North Chicago, IL.

PII-097
PHARMACOKINETIC/ PHARMACODYNAMIC MODELING OF HUMAN ANTI-FGF23 ANTIBODY (KRN23) AND SERUM PHOSPHORUS IN ADULTS WITH X-LINKED HYPOPHOSPHATEMIA.
X. Zhang,[1] N. H. Gosselin,[2] J. Marier,[2] T. Peyret,[2] T. Ito,[1] E. Imel,[3] T. O. Carpenter[4]; [1]Kyowa Hakko Kirin Pharma Inc., Princeton, NJ, [2]Pharsight-A Certara Company, Montreal, QC, Canada, [3]Indiana University School of Medicine, Indianapolis, IN, [4]Yale University School of Medicine, New Haven, CT.

PII-098
PHARMACOKINETICS (PK) AND SAFETY OF ARGININE VASOPRESSIN TYPE-1B (V1B) RECEPTOR ANTAGONIST ABT-436 IN HEALTHY VOLUNTEERS FOLLOWING MULTIPLE DOSES.
W. Liu,[1] D. A. Katz,[2] K. Tracy,[2] C. Locke,[1] W. M. Awni,[1] S. Dutta[1]; [1]AbbVie, North Chicago, IL, [2]Former AbbVie Employee, North Chicago, IL.

DRUG SAFETY (SAF)

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A CONCENTRATION-QTC ANALYSIS IN PATIENTS WITH NON-SMALL CELL LUNG CANCER RECEIVING CRIZOTINIB: ACCOUNTING FOR BIAS IN CORRECTION METHODS.
M. L. Zierhut, D. J. Nickens, W. Tan; Pfizer, San Diego, CA.

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N. Hohmann, A. Maus, A. Carls, A. Blank, W. E. Haefeli, G. Mikus; Department of Clinical Pharmacology, Heidelberg, Germany.

PII-101
AZITHROMYCIN IS NOT ASSOCIATED WITH QT PROLONGATION IN HOSPITALIZED PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA.
A. Gabin, A. Fawaz, N. A. Freedberg, N. Schwartz, M. Elias, W. Saliba, **L. H. Goldstein**; Haemek Medical Center, Afula, Israel.

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THE CATASTROPHIC FIRST-IN-HUMAN TGN1412 TRIAL: A SYSTEMATIC REVIEW OF PUBLICATION PATTERNS AND LESSONS LEARNED SINCE THE 2006 INCIDENT.
T. Leibson, G. Koren; Hospital for Sick Children, Toronto, ON, Canada.

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A. Kim,[1] F. Jiang,[1] S. Yoon,[1] S. Yi,[1] K. Yu,[1] I. Jang,[1] J. Chung[2]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Bundang Hospital, Seongnam-si, Korea, Republic of.

SPECIAL POPULATIONS (SPO)

PII-104
ASSOCIATION OF MEGALIN GENETIC POLYMORPHISMS WITH ACUTE KIDNEY INJURY (AKI) IN AMINOGLYCOSIDE (AG)-TREATED NEWBORNS.
M. J. Kennedy, H. J. Rozycki; Virginia Commonwealth University, Richmond, VA.

PII-105
THE PHARMACOGENETICS OF CODEINE PAIN RELIEF IN THE POSTPARTUM PERIOD.
M. Baber,[1] S. Chaudhry,[1] L. Kelly,[1] C. Ross,[2] B. Carleton,[3] H. Berger,[4] G. Koren[1]; [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]University of British Columbia, Vancouver, BC, Canada, [3]Child and Family Research Institute, Vancouver, BC, Canada, [4]St. Michael's Hospital, Toronto, ON, Canada.

PII-106
STEADY-STATE PHARMACOKINETICS OF GSK1278863 AND METABOLITES IN SUBJECTS WITH NORMAL AND IMPAIRED RENAL FUNCTION.
S. W.S. Yapa,[1] B. M. Johnson,[1] R. Ravindranath,[2] S. Caltabiano,[3] A. R. Cobitz[3]; [1]GlaxoSmithKline, Research Triangle Park, NC, [2]GlaxoSmithKline, Bangalore, India, [3]GlaxoSmithKline, King of Prussia, PA.

PII-107
ANALYSIS OF THE EFFECT OF VARIOUS DEGREES OF RENAL IMPAIRMENT ON THE PHARMACOKINETICS OF NONRENALLY ELIMINATED DRUGS.
K. Yoshida,[1] C. K. Yeung,[2] M. Kusama,[3] H. Zhang,[1] I. Ragueneau-Majlessi,[2] S. Argon,[2] P. Zhao,[1] L. Zhang,[1] I. Zineh,[1] Y. Sugiyama,[4] S. Huang[1]; [1]US Food and Drug Administration, Silver Spring, MD, [2]University of Washington, Seattle, WA, [3]The University of Tokyo, Tokyo, Japan, [4]The Institute of Physical and Chemical Research (RIKEN), Yokohama, Japan.

PII-108
AGE-DEPENDENT CHANGES IN CYP3A METABOLIC CAPACITY DETERMINE SIROLIMUS CLEARANCE IN PEDIATRIC PATIENTS.
C. Emoto,[1] T. Fukuda,[1] T. Mizuno,[1] B. Schniedewind,[2] U. Christians,[2] D. M. Adams,[3] B. C. Widemann,[4] M. J. Fisher,[5] J. Perentesis,[3] B. Weiss,[3] A. A. Vinks[1]; [1]Division of Clinical Pharmacology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]iC42 Integrated Solutions in Clinical Research and Development, University of Colorado, Aurora, CO, [3]Cancer & Blood Disease Institute, Division of Oncology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [4]Pediatric Oncology Branch, National Cancer Institute, Bethesda, MD, [5]Division of Oncology, The Children's Hospital of Philadelphia, Philadelphia, PA.

PII-109
THE EFFECT OF HEPATIC IMPAIRMENT (HI) OR HCV INFECTION ON THE PHARMACOKINETICS (PK) OF BUPRENORPHINE AND NALOXONE.
J. P. Jones, Y. Liu, P. J. Fudala, C. Heidbreder, A. F. Nasser; Reckitt Benckiser Pharmaceuticals, Inc., Richmond, VA.

PII-110
PHARMACOKINETICS OF ELAGOLIX, A NOVEL ORAL GONADOTROPIN-RELEASING HORMONE (GNRH) ANTAGONIST ADMINISTERED TO FEMALE SUBJECTS WITH HEPATIC IMPAIRMENT.
J. Ng, C. E. Klein, W. R. Duan, J. Yan, L. A. Williams; AbbVie Inc., North Chicago, IL.

PII-111
PHARMACOKINETICS OF ELAGOLIX, A NOVEL ORAL GONADOTROPIN-RELEASING HORMONE (GNRH) ANTAGONIST, ADMINISTERED TO FEMALE SUBJECTS WITH RENAL IMPAIRMENT.
J. Ng, C. E. Klein, W. R. Duan, J. Yan, A. Kaefer, L. A. Williams; AbbVie Inc., North Chicago, IL.

PII-112
PHARMACOKINETICS OF SINGLE DOSE ESCITALOPRAM IN THE HEALTHY ELDERLY COMPARED WITH THE YOUNG.
H. Chung,[1] S. Yi,[1] S. Moon,[1] J. Park,[1] S. Yoon,[1] J. Cho,[1] K. Yu,[1] J. Chung[2]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Bundang Hospital, Seongnam, Korea, Republic of.

PII-113
PHARMACOKINETICS (PK) OF TWO 6-MERCAPTOPURINE (6-MP) LIQUID FORMULATIONS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL).
J. A. Tolbert,[1] G. L. Kearns,[1] S. M. Abdel-Rahman,[1] S. J. Weir,[2] J. S. Leeder,[1] K. A. Neville[1]; [1]Division of Clinical Pharmacology, Children's Mercy Hospital and the Department of Pediatrics, University of Missouri-Kansas City, Kansas City, MO, [2]Department of Pharmacology, Toxicology and Therapeutics, University of Kansas Medical Center, Kansas City, KS.

BIOLOGICS

PII-114
ELUCIDATION OF THE MECHANISM OF THERAPEUTIC PROTEIN-DRUG INTERACTION (TPDI) BETWEEN METHOTREXATE (MTX) AND AN ANTI-TNFα MONOCLONAL ANTIBODY (MAB), GOLIMUMAB.
W. Wang, J. Leu, H. Zhou; Janssen R&D, Spring House, PA.

PII-115
IMMUNOGENICITY OF NIVOLUMAB AND ITS IMPACT ON PHARMACOKINETICS (PK) AND SAFETY IN SUBJECTS WITH METASTATIC SOLID TUMORS.
S. Agrawal, A. Roy, Y. Feng, G. Bajaj, S. Saeger, J. Park, I. Waxman, M. Gupta; Bristol-Myers Squibb, Princeton, NJ.

PII-116
PHARMACOKINETICS AND PHARMACODYNAMICS OF BENRALIZUMAB IN SUBJECTS WITH MODERATE-TO-SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE.
L. Yan,[1] L. Roskos,[2] C. K. Ward,[2] D. She,[2] R. Merwe,[3] B. Wang[1]; [1]MedImmune, Mountain View, CA, [2]MedImmune, Gaithersburg, MD, [3]MedImmune, Cambridge, United Kingdom.

PII-117
ABSENCE OF QT PROLONGATION (QTP) EFFECT BY NIVOLUMAB (NIVO) OR IPILIMUMAB (IPI) IN SUBJECTS WITH SOLID TUMORS.
S. Agrawal, D. Williams, I. Waxman, D. Liu, A. Lambert, A. Roy, R. Darbenzio; Bristol-Myers Squibb, Princeton, NJ.

PII-118
ASSESSMENT OF DRUG INTERACTION POTENTIAL BY NIVOLUMAB USING CYTOKINE MODULATION DATA.
C. Passey, J. Simon, Q. Hong, A. Roy, S. Agrawal; Bristol-Myers Squibb, Princeton, NJ.

PII-119
ASSESSMENT OF CLINICAL RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) BETWEEN PF-05280586, A PROPOSED BIOSIMILAR TO RITUXIMAB AND TWO RITUXIMAB PRODUCTS.
J. Williams,[1] M. H. Hutmacher,[2] M. Zierhut,[1] J. Becker,[1] B. Gumbiner,[1] G. Spencer-Green,[1] L. Melia,[1] D. Yin,[1] R. Li,[1] X. Meng[1]; [1]Pfizer, San Diego, CA, [2]Ann Arbor Pharmacometrics Group, Ann Arbor, MI.

POSTERS, POSTER WALKS AND LATE-BREAKING AND ENCORE ABSTRACT POSTERS

POSTER WALK III

PRACTICAL APPROACHES FOR OPTIMIZING PEDIATRICS DOSAGE OR DELIVERY

FRIDAY, MARCH 6, 2015
4:45 pm - 5:30 pm
ELITE HALL ATRIUM

CHAIR
Gregory L. Kearns, PharmD, PhD, Children's Mercy Hospitals and Clinics

PW-06
APPLICATION OF PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELING FOR PREDICTION OF BUPRENORPHINE EXPOSURE IN NEONATES: INC.ORPORATION OF CYP3A4 AND UGT1A1 ONTOGENIES.
K. Rowland-Yeo,[1] T. Johnson,[1] M. Dickins,[1] A. Rostami-Hodjegan[2]; [1]Simcyp Ltd., Sheffield, United Kingdom, [2]University of Manchester, Manchester, United Kingdom.

PW-07
SINGLE DOSE PHARMACOKINETICS OF ATOMOXETINE IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) STRATIFIED BY THEIR CYP2D6 ACTIVITY SCORE (AS).
J. T. Brown,[1] S. M. Abdel-Rahman,[2] L. Van Haandel,[2] A. Gaedigk,[2] J. S. Leeder[2]; [1]University of Minnesota College of Pharmacy, Duluth, MN, [2]Children's Mercy Kansas City, Kansas City, MO.

PW-08
PEDIATRIC MICRODOSE STUDY OF [14C]PARACETAMOL TO STUDY DRUG METABOLISM USING ACCELERATED MASS SPECTROMETRY: PROOF OF CONCEPT.
M. G. Mooij,[1] E. Van Duijn,[2] C. A. Knibbe,[3] A. D. Windhorst,[4] N. H. Hendrikse,[4] W. H. Vaes,[2] E. Spaans,[1] B. O. Fabriek,[2] H. Sandman,[2] D. Grossouw,[2] L. M. Hanff,[5] P. J. Janssen,[5] B. C. Koch,[5] D. Tibboel,[1] S. N. De Wildt[1]; [1]Erasmus MC - Sophia Children's Hospital, Rotterdam, Netherlands, [2]TNO, Zeist, Netherlands, [3]Leiden University, Leiden, Netherlands, [4]VU University Medical Center, Amsterdam, Netherlands, [5]Erasmus MC - Hospital Pharmacy, Rotterdam, Netherlands.

PW-09
THE PHARMACOKINETIC-PHARMACODYNAMIC RELATIONSHIP OF ETHOSUXIMIDE IN CHILDREN WITH CHILDHOOD ABSENCE EPILEPSY.
K. Mizuno,[1] E. V. Capparelli,[2] T. Fukuda,[1] M. Dong,[1] A. A. Vinks,[1] T. A. Glauser[3]; [1]Division of Clinical Pharmacology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Department of Pediatrics, University of California San Diego, La Jolla, CA, [3]Division of Pediatric Neurology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PW-10
PHARMACOKINETICS OF MICAFUNGIN IN INFANTS SUPPORTED WITH EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO).
J. Autmizguine,[1] M. Cohen-Wolkowiez,[2] K. L. Brouwer,[3] D. K. Benjamin, Jr,[2] K. M. Watt[2]; [1]University of Montreal, Montreal, QC, Canada, [2]Duke University Medical Center, Durham, NC, [3]The University of North Carolina, School of Pharmacy, Chapel Hill, NC.

POSTER WALK IV

UTILITY OF REAL LIFE DATA TO ANSWER CLINICAL QUESTIONS

FRIDAY, MARCH 6, 2015
5:30 pm - 6:15 pm
ELITE HALL ATRIUM

CHAIR
Anne C. Heatherington, PhD, Pfizer

PW-11
MEASURING THE QUALITY OF ORAL ANTICOAGULATION AMONG HOSPITALIZED PATIENTS: A ONE-YEAR RETROSPECTIVE ANALYSIS.
V. Rollason, I. Welle, J. Iavindrasana, R. Meyer, P. Chopard, J. A. Desmeules; Geneva University Hospitals, Geneva, Switzerland.

PW-12
USING ELECTRONIC HEALTH RECORDS TO IDENTIFY DISEASE-SPECIFIC EFFECTS OF METFORMIN IN BREAST CANCER PATIENTS WITH TYPE II DIABETES MELLITUS.
M. K. Breitenstein,[1] L. Wang,[1] R. M. Weinshilboum,[1] G. J. Simon,[2] J. Pathak[1]; [1]Mayo Clinic, Rochester, MN, [2]University of Minnesota, Minneapolis, MN.

PW-13
TYROSINE KINASE TARGETING DRUGS-ASSOCIATED CONGESTIVE HEART FAILURE: TRASTUZUMAB, CETUXIMAB, PANITUMUMAB AND SUNITINIB ARE ASSOCIATED WITH INC.REASED RISK.
N. Gronich,[1] I. Lavi,[1] O. Barnett,[1] D. R. Abernethy,[2] G. Rennert[1]; [1]Carmel Medical Center, Haifa, Israel, [2]US Food and Drug Administration, Silver Spring, MD.

PW-14
RISKS OF CONGENITAL MALFORMATIONS IN OFFSPRING EXPOSED TO VALPROIC ACID IN UTERO: A SYSTEMATIC REVIEW AND CUMULATIVE META-ANALYSIS.
T. Kobayashi,[1] M. Tanoshima,[1] R. Tanoshima,[1] J. Beyene,[2] G. Koren,[1] S. Ito[1]; [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]McMaster University, Hamilton, ON, Canada.

PW-15
APIXABAN FOR TREATMENT OF VENOUS THROMBOEMBOLISM (VTETX): USE OF MODEL-BASED META-ANALYSES (MBMA) TO SUPPORT PHASE III DOSE SELECTION.
R. Boyd,[1] W. Byon,[1] J. Thompson,[1] M. Johnson,[1] J. Mandema[2]; [1]Pfizer, Groton, CT, [2]Quantitative Solutions Inc., Menlo Park, CA.

POSTERS, POSTER WALKS AND LATE-BREAKING AND ENCORE ABSTRACT POSTERS

LATE-BREAKING AND ENCORE POSTER SESSION I

THURSDAY, MARCH 5, 2015
11:30 am - 6:30 pm
Attended Posters 4:30 pm – 6:30 pm
ELITE HALL

EI-1

MODEL-BASED ASSESSMENT OF DOSING STRATEGIES IN CHILDREN FOR MONOCLONAL ANTIBODIES EXHIBITING TARGET-MEDIATED DRUG DISPOSITION.

S. Zheng,[1] P. Gaitonde,[1] M. Andrew,[2] M. Gibbs,[3] L. Lesko,[1] S. Schmidt[1]; [1]Center for Pharmacometrics and Systems Pharmacology, University of Florida, Orlando, FL, [2]Department of Pharmacokinetics and Drug Metabolism, Amgen, Seattle, WA, [3]Department of Pharmacokinetics and Drug Metabolism, Amgen, Thousand Oaks, CA
S. Zheng: None. **P. Gaitonde:** None. **M. Andrew:** None. **M. Gibbs:** None. **L. Lesko:** None. **S. Schmidt:** None.

BACKGROUND:
Body weight (BW)-based and/or tiered fixed dosing is widely utilized to scale adult clinical doses to children for monoclonal antibodies (mAbs) that exhibit linear clearance. Whether these scaling strategies are also applicable to mAbs that exhibit target-mediated drug disposition (TMDD) is unclear.
METHODS:
A published TMDD model for an anti-ALK1 receptor mAb was adopted and its linear clearance and volume of distribution were scaled from adults to children using a BW-based allometric function with fixed exponents of 0.75 and 1, respectively. A set of hierarchical simulations was performed to compare BW-based vs. fixed dosing and full TMDD vs. Michaelis-Menten approximation for the same target concentration vs. same target amount in adults and children. Sensitivity analysis was performed for target concentrations and amounts to determine their impact on free drug concentrations and target occupancy.
RESULTS:
For the same target concentrations, drug exposure becomes increasingly similar between adults and children with increasing target concentrations and decreasing doses following BW-based dosing, whereas the opposite holds true if the target amount is the same. In comparison, fixed dosing results in increased mAb exposure in children of young age, at low doses and high amounts of target. Despite different systemic mAb concentrations, target occupancy is quite similar between adults and children. Michaelis-Menten approximation yielded similar profiles compared to the full TMDD model and may be used to guide the selection of pediatric dosing regimen.
CONCLUSION:
The PK of mAbs exhibiting TMDD has to be interpreted in a PK/PD context because similar drug exposure may not reflect similar target occupancy. Our simulations suggest that BW-based dosing is superior to fixed dosing for the same target concentration, whereas the opposite is observed for the same target amount in adults and children.

EI-2

VIRTUAL SYSTEMS PHARMACOLOGY (VISP) FLEXIBLE WEB-BASED ENVIRONMENT FOR RUNNING LARGE MULTI-SCALE MODELS.

S. Ermakov,[1] P. Forster,[2] J. Pagidala,[1] M. Miladinov,[1] A. Wang,[1] D. Bartlett,[3] R. Baillie,[3] M. Reed,[3] **T. Leil**[1]; [1]Bristol-Myers Squibb, Princeton, NJ, [2]Forster Solutions, LLC, Wilmington, DE, [3]Rosa & Co LLC, San Carlos, CA. **S. Ermakov:** None. **P. Forster:** 2. I am a paid consultant/employee for; **Company/Drug**; Bristol-Myers Squibb. **J. Pagidala:** None. **M. Miladinov:** None. **A. Wang:** None. **D. Bartlett:** None. **R. Baillie:** None. **M. Reed:** None. **T. Leil:** None.

BACKGROUND:
Currently there is no single systems-level modeling software that ranks favorably against multiple criteria, e.g. model development capabilities, friendly user interface, export-import options, cost of ownership, etc. We developed Virtual Systems Pharmacology (ViSP) platform designed to easily set up and run multiple simulations in a flexible hardware/software environment.
METHODS:
ViSP separates the instance of a simulation from the software that sets up the simulation. It relies on an executable file produced by compiling the model code into a binary file. The executable is initialized with a number of parameters, some are model specific, e.g. disease characteristics, properties of a particular patient or a drug, while others define simulation time, output frequency etc. Multiple executable files with different initial conditions can be initiated and run in parallel on separate processors, or in a cloud environment. This process was implemented in ViSP to handle executable files originating from different modeling software packages initialized with appropriate data. ViSP relies on web-based UI designed to be configurable by a user to accommodate the specifics of a particular model. It is capable of handling multiple models and large number of parameters presenting them in tree-like structure.
RESULTS:
ViSP was used with a mechanistic metabolic diseases model to simulate the effects of metformin and a GPR40 agonist on glycemic biomarkers in type 2 diabetes patients. ViSP permitted easy set up of the clinical study design and simulations for a high dimensional model (> 100 ODEs, > 800 parameters) with multiple virtual patients.
CONCLUSION:
Web-based user-friendly software was developed for running multiple simulations in a flexible hardware/software environment that is neither model nor software specific.

LBI-1

INFLUENCE OF CYP2D6 ACTIVITY ON THE PHARMACOKINETICS AND PHARMACODYNAMICS OF SINGLE DOSE IBOGAINE IN HEALTHY VOLUNTEERS.

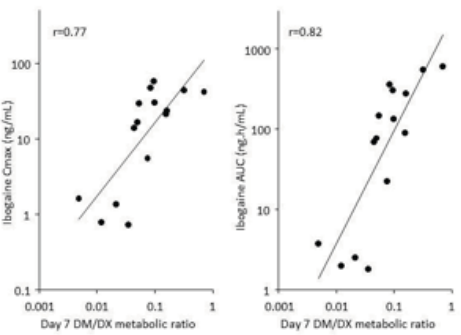
P. Glue,[1] H. Winter,[2] K. Garbe,[1] H. Jakobi[1]; [1]University of Otago, Dunedin, New Zealand, [2]Genentech, South San Francisco, CA. **P. Glue:** 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; ibogaine. **H. Winter:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech. **K. Garbe:** None. **H. Jakobi:** None.

BACKGROUND:
The naturally occurring psychoactive ibogaine (IBO) may reduce symptoms of opioid withdrawal. Conversion of IBO to its active metabolite noribogaine (NI) is mainly via CYP2D6.

METHODS:
We compared 168h PK/PD profiles of IBO and NI after single 20mg IBO doses in 21 healthy subjects, pretreated for 6 days with blinded placebo (PBO) or the CYP2D6 inhibitor paroxetine (PAR) 20mg/day.

RESULTS:
All data analysed 10/1/14. In PBO-pretreated subjects, IBO was rapidly converted to NI, with undetectable IBO levels by 4 hours post dose. PAR-pretreated subjects had rapid (median T_{max} = 1.5h) and substantial absorption of IBO, with detectable levels out to 72 h, and an elimination half-life of 10.2 h. In PAR-pretreated subjects, IBO was also rapidly converted to NI (median T_{max} 3h). Extent of NI exposure was similar in both groups. CYP2D6 phenotype correlated with IBO AUC0-t (r=0.82) and C_{max} (r=0.77; Figure). Active moiety (IBO+NI) exposure was ~2-fold higher in PAR-pretreated subjects. Single 20mg IBO doses were safe and well tolerated. No between-group differences were seen in mu-opioid PD measures (pupil miosis).

CONCLUSION:
Doubling of exposure to active moiety in subjects with reduced CYP2D6 activity suggests it may be prudent to genotype patients awaiting IBO treatment, and to at least halve the intended dose of IBO in CYP2D6 PMs.



LBI-2

A STRUCTURAL MODEL CHARACTERIZING PLACEBO EFFECT FOR THE CHILDREN'S DEPRESSION RATING SCALE (CDRS) IN A PEDIATRIC MAJOR DEPRESSIVE DISORDER POPULATION.

J. Liu,[1] B. Corrigan,[2] K. Ito,[2] K. Sweeney,[2] J. Liu,[2] D. Flockhart,[1] T. Nicholas[2]; [1]Division of Clinical Pharmacology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, [2]Global Clinical Pharmacology, Global Innovative Pharma at Pfizer Inc., Groton, CT. **J. Liu:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. **B. Corrigan:** 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **K. Ito:** 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **K. Sweeney:** 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **J. Liu:** 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **D. Flockhart:** None. **T. Nicholas:** 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc.

BACKGROUND:
Designing and evaluating clinical trials for major depressive disorder (MDD) is challenging as the placebo response is poorly understood and affected by trial design. Variation in placebo response within and among clinical trials can substantially affect the interpretation of the trial. Prevalence of MDD in a pediatric population was estimated at 5%, however, there have been few quantitative clinical analyses reported. The Children's Depression Rating Scale (CDRS) is a clinician-rated, semi-structured interview for assessing current depressive symptoms in the pediatric population. A longitudinal model was developed to characterize the placebo effect for CDRS.

METHODS:
4 randomized, double-blinded, placebo-controlled, 12-week clinical trials in MDD were assessed. CDRS change from baseline (CFB) was obtained from 324 subjects, (191 were children (6 to 12 years); 133 were adolescents (13 to 17 years)). A nonlinear mixed effects model was used to characterize the disease progression. Age, gender, weight, and baseline CDRS status were tested as potential covariates.

RESULTS:
The placebo effect was characterized using an exponential model with a rate constant: CDRS_change = PE*[1-exp(-k*t)]*(CDRS_baselinei/60)^θ+ε, where CDRS_change is the CDRS CFB, PE describes the magnitude of the placebo effect, k is the rate constant characterizing severity, t is time (unit: week), CDRS_baselinei is the CDRS at baseline for each individual, θ describes the effect of baseline CDRS status and ε is the residual error term. Between subject variability (BSV) was included on the PE and k as exponential. CDRS baseline status was found to be significant for describing the placebo effect. Age, gender, and weight were not found to be significant.

CONCLUSION:
The final model provides a good understanding of placebo effect in pediatric MDD and offers a useful tool to aid both clinical trial design and interpretation.

LBI-3

RELIABLE MEASUREMENTS OF INTRACELLULAR METFORMIN CONCENTRATIONS FOR *IN VITRO/IN VIVO* CORRELATION ANALYSES.

H. Chien,[1] A. A. Zur,[1] T. S. Maurer,[2] D. O. Scott,[2] J. Enogieru,[1] K. M. Giacomini[1]; [1]University of California, San Francisco, San Francisco, CA, [2]Pfizer, Cambridge, MA. **H. Chien:** None. **A.A. Zur:** None. **T.S. Maurer:** 1. This research was sponsored by; **Company/Drug**; Pfizer. **D.O. Scott:** 1. This research was sponsored by; **Company/Drug**; Pfizer. **J. Enogieru:** None. **K.M. Giacomini:** None.

BACKGROUND:
Anti-diabetic drug, Metformin, requires membrane transporters such as organic cation transporter 1, OCT1, to gain access to intracellular targets. However, considerable controversy exists about the subcellular compartments through which the drug acts, with many studies claiming that metformin acts in the mitochondria and other studies disputing those claims and suggesting that the drug has cytosolic targets. The goal of the current study was to develop a method to measure the intracellular concentrations of metformin *in vitro* to assess whether the drug accumulates in subcellular compartments.
METHODS:
Intracellular space (ICS) for HEK cells was calculated by subtracting [3H]-inulin distribution volume (ECS) from [14C]-Urea distribution volume (TWS). Unbound drug fraction measurement was performed using RED device. [14C]-metformin, [14C]-aminoguanidine and [14C]-guanidine were used to measure intracellular concentration.
RESULTS:
Values obtained for ICS (mean±SE; uL/106 cells) of HEK-EV and HEK-OCT1 cells were 1.21±0.1 and 1.25±0.1, respectively. The intracellular metformin concentration in HEK-EV and HEK-OCT1 cells were 26.4±7.8 uM and 267.7 ± 11.0 uM, respectively. Based on the Nernst equation, the observed accumulation ratio of unbound metformin was much higher than predicted (53.6-fold vs. 10-fold), suggesting that the positively charged metformin accumulates in subcellular compartments (e.g. mitochondria).
CONCLUSION:
The data indicate that intracellular concentrations of metformin in cells expressing OCT1 greatly exceed predicted steady-state concentrations. These results suggest that metformin accumulates highly in subcellular compartments, which may act as storage depots for metformin to sustain and enhance its pharmacologic action. This method can be applied to *in vitro/in vivo* modeling to predict intracellular drug levels and pharmacologic response.

LBI-4

EFFECT OF SEVERE RENAL IMPAIRMENT ON THE PHARMACOKINETICS (PK) OF CRIZOTINIB (XALKORI®).

W. Tan,[1] S. Yamazaki,[1] R. Wang,[2] T. R. Johnson,[1] M. T. O'Gorman,[2] L. Kirkovsky,[1] T. Boutros,[1] A. Bello[3]; [1]Pfizer, San Diego, CA, [2]Pfizer, Groton, CT, [3]Pfizer, New York, NY**W. Tan:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **S. Yamazaki:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **R. Wang:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **T.R. Johnson:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **M.T. O'Gorman:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **L. Kirkovsky:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **T. Boutros:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. **A. Bello:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc.

BACKGROUND:
Crizotinib (CRZ) is an oral tyrosine kinase inhibitor approved for the treatment of ALK-positive non-small cell lung cancer (NSCLC) at a dose of 250 mg BID. CRZ is primarily metabolized by and is a moderate inhibitor of CYP3A. Renal excretion of unchanged CRZ is negligible (2.3%). The purpose of this study was to evaluate the effect of severe renal impairment (SRI) on single-dose PK of CRZ and to predict the magnitude of the effect on multiple-dose PK using a modeling approach.
METHODS:
A single 250 mg oral dose of CRZ was administered to 8 SRI subjects not requiring dialysis (creatinine clearance [CLcr]<30 mL/min) and 1-to-1 matched healthy subjects with normal renal function (NRF) (CLcr ≥90 mL/min) as for age, body weight , race and gender. Plasma and urine concentrations of CRZ and its metabolite PF-06260182 were determined using validated LC/MS/MS methods. CRZ plasma protein binding was determined by equilibrium dialysis. An ANOVA model was used to compare the differences in CRZ AUC_{inf} and C_{max} between groups. CRZ multiple-dose PK was predicted using a physiologically-based pharmacokinetic (PBPK) model, Simcyp population-based simulator.
RESULTS:
Single CRZ 250 mg doses were safe and well tolerated for all subjects in NRF and SRI groups. CRZ AUC and C_{max} were 79% and 34% higher in SRI subjects than in NRF subjects, respectively. Similarly, PF-026260182 exposure was higher in the SRI group. Unbound fractions of CRZ were comparable in SRI and NRF groups (0.0914 vs. 0.0980). Unchanged CRZ in urine accounted for <2% of the dose in both groups. The PBPK simulation suggests that SRI would result in a 50-70% higher steady-state CRZ AUC following 250 mg QD or BID dosing.
CONCLUSION:
An adjustment in the CRZ dose to 250 mg QD is recommended for ALK-positive NSCLC patients with SRI not requiring dialysis.

LBI-5

MULTIPLE DOSE PHARMACOKINETICS (PK), IMMUNOGENICITY AND SAFETY OF AN INTERLEUKIN-1 DUAL VARIABLE DOMAIN IMMUNOGLOBULIN (DVD-IG) IN KNEE OSTEOARTHRITIS (OA) PATIENTS.

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BACKGROUND:
OA is a degenerative joint disease characterized by focal and progressive loss of the hyaline cartilage in the joints. ABT-981 is a novel DVD-Ig capable of simultaneously neutralizing pro-inflammatory cytokines IL-1α and IL-1β, both of which are thought to play a central role in OA pathogenesis.
METHODS:
PK, immunogenicity and safety of ABT-981 in OA patients were evaluated in a randomized, double-blind, placebo-controlled, multiple ascending dose study to assess SC injections of ABT-981 in 36 patients with OA of the knee (9 subjects/group; 7 active + 2 placebo). PK samples were collected following ABT-981 administration of 0.3, 1, or 3 mg/kg every other week (EOW) for 6 weeks or 3 mg/kg every four weeks (E4W) for 8 weeks. Immunogenicity, safety and tolerability were assessed throughout the study. Legal approval for release of results was received September 9, 2014, and data was finalized on September 13, 2014.
RESULTS:
ABT-981 reached T_{max} from 3 to 7 days after dosing with mean terminal half-life of 10 to 13 days. After 4 EOW doses mean C_{max} and AUCτ were 2.59 - 22.6 μg/mL and 30.7 - 248 μg·day/mL at 0.3 - 3.0 mg/kg; exposures increased approximately linearly between 0.3 and 3 mg/kg and accumulation was approximately two-fold. The magnitude of anti-drug antibody response was low and did not impact ABT-981 PK. Laboratory data suggest a dose-response relationship for declines in absolute neutrophil count. Most common adverse events were injection site erythema and headache. Severity of all the adverse events was Grade 1 or 2 with the exception of one serious adverse event of bronchitis/viral syndrome in a subject receiving ABT-981.
CONCLUSION:
ABT-981 exhibited behavior similar to a conventional antibody with linear pharmacokinetics. ABT-981 PK profile supports EOW or E4W dosing. PK, immunogenicity and safety profile support further evaluation of ABT-981 as an OA disease modifying agent in phase II studies.

LBI-6

SOLITHROMYCIN CONCENTRATIONS MEASURED IN DRIED BLOOD SPOTS COLLECTED FROM ADOLESCENTS.

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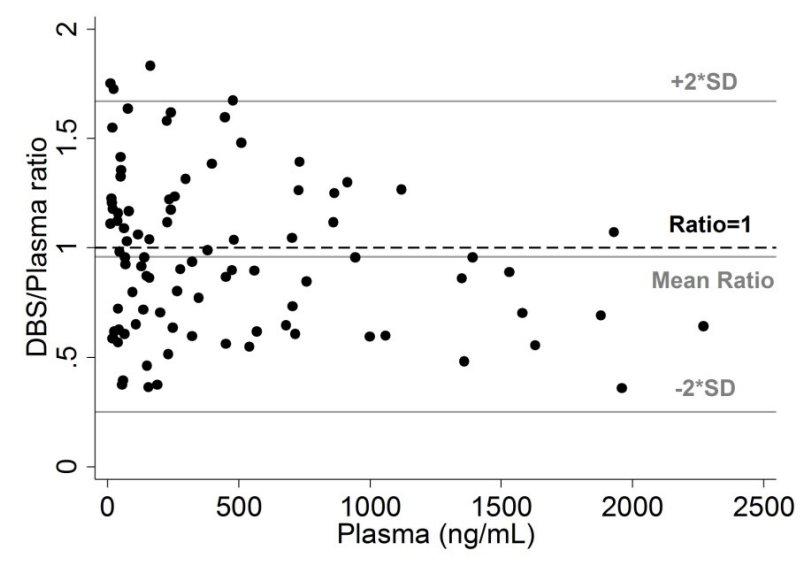
by; **Company/Drug**; Cempra. 3. I received honoraria from; **Company/Drug**; Research support from Astellas, Medical Advisory Board for Raptor, Medical Advisory Board for Alexion. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin not labeled for use in pediatrics. **L. James:** 1. This research was sponsored by; **Company/Drug**; Cempra. 3. I received honoraria from; **Company/Drug**; Partially paid by an NIH STTR grant for Acetaminophen Toxicity Diagnostics. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **J. Bradley:** 1. This research was sponsored by; **Company/Drug**; Cempra. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **N. Neu:** 1. This research was sponsored by; **Company/Drug**; Cempra. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **T. Jasion:** 1. This research was sponsored by; **Company/Drug**; Cempra. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **C. Hornik:** 1. This research was sponsored by; **Company/Drug**; Cempra. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **P.B. Smith:** 1. This research was sponsored by; **Company/Drug**; Cempra. 2. I am a paid consultant/employee for; **Company/Drug**; Mission Pharma, Abbvie, GlaxoSmithKline. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin not labeled for use in pediatrics. **D.K. Benjamin Jr.:** 1. This research was sponsored by; **Company/Drug**; Cempra. 2. I am a paid consultant/employee for; **Company/Drug**; Astellas Pharma, Cempra, Cubist Pharmaceuticals, Johnson and Johnson, Merck & Co., Pfizer and The Medicines Co. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **C. Rosiak:** 1. This research was sponsored by; **Company/Drug**; Cempra. 2. I am a paid consultant/employee for; **Company/Drug**; Cempra. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **R. Oh:** 1. This research was sponsored by; **Company/Drug**; Cempra. 2. I am a paid consultant/employee for; **Company/Drug**; Cempra. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **K. Keedy:** 1. This research was sponsored by; **Company/Drug**; Cempra. 2. I am a paid consultant/employee for; **Company/Drug**; Cempra. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **P. Fernandes:** 1. This research was sponsored by; **Company/Drug**; Cempra. 2. I am a paid consultant/employee for; **Company/Drug**; Cempra. 5. I am a significant stockholder for; **Company/Drug**; Cempra. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics. **M. Cohen-Wolkowiez:** 1. This research was sponsored by; **Company/Drug**; Cempra. 2. I am a paid consultant/employee for; **Company/Drug**; Cempra, GlaxoSmithKline, Janssen Research & Development, Special Products Ltd., Tetraphase, the Medicines Company. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Solithromycin is not labeled for use in pediatrics.

BACKGROUND:
Solithromycin is a new fourth-generation macrolide fluoroketolide antibiotic undergoing phase III trials in adults. Phase I studies in children and infants are planned, and dried blood spot (DBS) samples can minimize blood sample volumes.
METHODS:
We enrolled adolescents with suspected or confirmed bacterial infections who received solithromycin capsules (12 mg/kg on Day 1 [up to 800 mg], 6 mg/kg daily on Days 2-5 [up to 400 mg]). We collected paired DBS-plasma samples at pre-specified sampling points. Data for this analysis were available September 30, 2014. We used weighted linear regression (WLR) and DBS/plasma concentration ratio to perform a comparability analysis.
RESULTS:
12 adolescents (median age 16 years [range; 12-17]; weight 64 kg [30-84]; 75% male) had 92 paired DBS-plasma samples available for analysis. We observed a linear relationship between DBS and plasma concentrations, slope=0.91 (95% CI; 0.82, 0.99). The mean DBS/plasma concentration ratio was 0.96 (95% CI; 0.89, 1.04) and was conserved throughout the concentration range, ratio slope=-0.0006 (95% CI:-0.0002, 0.0001).
CONCLUSION:
DBS and plasma solithromycin concentrations were comparable in a small cohort of adolescents. The results are promising and further validation of this method is warranted.



LBI-7

A TRANSLATIONAL PLATFORM TO EVALUATE THE EFFECTS OF RIVAROXABAN, IBUPROFEN, AND PLACEBO ON GASTROINTESTINAL MICROBLEEDING IN NORMAL HEALTHY SUBJECTS.

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BACKGROUND:
The ideal anti-thrombotic agent effectively reduces thrombosis with minimal bleeding risk, and can only be assessed in large outcome trials. We present a study designed to validate the ability of a gastrointestinal (GI) microbleeding platform to evaluate bleeding for novel anticoagulants, in order to facilitate early decision making and enable dose focusing of novel anti-thrombotic pathways.
METHODS:
This was a randomized, single-blind, parallel group, placebo- and active- controlled study of the effect of two weeks of treatment with rivaroxaban (10 mg or 30 mg) and ibuprofen, ibuprofen, or placebo on fecal blood loss (FBL) in 60 healthy subjects. Red blood cells from each subject were labeled with chromium-51 (51Cr) and re-injected into the same subject. Weekly averages of daily FBL were estimated over three consecutive weeks using 51Cr measured in blood and stool samples.
RESULTS:
Comparison Geometric Mean Ratio at Week 2 Confidence Interval (CI) Percent CI 1-Sided P-valueRivaroxaban 30 mg + IBU vs. IBU Alone 1.45 (1.07, 1.96) 0.90 0.024*Rivaroxaban 10 mg + IBU vs. IBU Alone 1.37 (1.08, 1.72) 0.80 0.044*
Riva 30 mg + IBU vs. Riva 10 mg + IBU 1.06 (0.84, 1.33) 0.80 0.373
Ibuprofen vs. Placebo 2.41 (1.79, 3.24) 0.90 <0.001**statistically significant
CONCLUSION:
The human GI microbleeding platform effectively detected increased bleeding between rivaroxaban co-dosed with ibuprofen vs. ibuprofen alone, as well as ibuprofen vs. placebo, however, it could not discriminate between two doses of rivaroxaban with ibuprofen. This approach may enable dose focusing for novel anti-thrombotics, although it may not be sufficiently sensitive to discriminate levels of microbleeding over a narrow range of drug concentration.

LBI-8

DEVELOPMENT OF PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODEL FOR ITRACONAZOLE PHARMACOKINETC (PK) AND DRUG-DRUG INTERACTION (DDI) PREDICTION.

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BACKGROUND:
PBPK modeling for itraconazole (ITZ) has been challenging due to highly variable ***in vitro*** data and the complex CYP3A4 inhibition mechanism. Inaccurate prediction of PK and DDI using the current PBPK model has lowered the confidence of using model simulation to optimize clinical DDI study design. The aim of this work was to develop and validate an ITZ PBPK model to enable a more accurate DDI prediction.
METHODS:
The PBPK model was constructed in Simcyp®. The intravenous dose clinic PK data for ITZ and ***in vitro*** and preclinical PK data for metabolite OH-ITZ were used in model development. The distribution model was justified to best describe the shape of ITZ and OH-ITZ PK profiles from 12 single oral solution dose ITZ studies. The model's predictive performance was verified using all available clinical study data from multiple dose ITZ in solution and as capsule. The verified model was used to simulate clinical DDIs between ITZ and midazolam.
RESULTS:
Our PBPK model significantly improved accuracy in simulating ITZ and OH-ITZ PK profiles, especially in capturing their accumulation after multiple doses. The model is able to describe PK profiles of ITZ and OH-ITZ from solution dose, as well as from capsule with modification of absorption parameters known to be different from solution. The model with improved PK predictability provided more accurate prediction of DDI between ITZ and midazolam (9/10 predicted within 1.5 fold of observed).
CONCLUSION:
A PBPK model was developed and validated to successfully simulate the PK of ITZ and OH-ITZ after multiple dose of ITZ in solution and as capsule. The improved PK and DDI predictability will enable dose/regimen simulations to provide mechanistic rationale for the recommended clinical ITZ DDI study design.

LBI-9

PHARMACOKINETICS OF MIGALASTAT HYDROCHLORIDE, A NOVEL PHARMACOLOGICAL CHAPERONE, IN PATIENTS WITH FABRY DISEASE.

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BACKGROUND:
Migalastat hydrochloride (HCl) is in clinical development for treatment of Fabry disease. The objectives of this analysis were to develop a population pharmacokinetic (PPK) model of plasma migalastat after oral dosing, to assess potential covariate effects, and to estimate individual PK exposures in phase III Fabry patients.
METHODS:
Pooled from 13 (phase I, II and III) clinical studies funded by Amicus Therapeutics Inc. and/or GlaxoSmithKline, a total of 4,447 pharmacokinetic (PK) samples (~90% were serial PK samples) from 260 subjects (179 healthy and 81 Fabry patients) who received single (~64%) or repeat (~36%) oral doses of migalastat HCl between 25 mg and 675 mg were analyzed using FOCE-I in NONMEM v7. Model selection and evaluation were based on change in objective function value (αOFV), precision of parameter estimates, diagnostic plots, bootstrap procedures, and dose-normalized visual predictive checks.
RESULTS:
A first-order two-compartment model with time-varying absorption was developed, with good model diagnostics, to characterize the plasma PK of migalastat. Disease status (healthy or Fabry patient) and body weight were significant covariates of central volume. Body weight and renal function were significant covariates of central clearance. The estimated individual PK exposures (AUC, C_{max} and C48h) in Fabry patients from the phase III study (NCT00925301) were consistent with phase I and II historical data.
CONCLUSION:
A two-compartment PPK model with linear time-dependent absorption adequately characterized the plasma PK of migalastat after oral administration. Disease status, body weight, and renal function were identified as significant covariates in the PPK model. A summary of post-hoc PK exposure parameters from phase III Fabry patients will be presented.

LBI-10
ASSESSMENT OF THE USE OF PBPK MODELING: A SYSTEMATIC REVIEW OF THE RECENT LITERATURE.

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J. Sager: None. **I. Ragueneau-Majlessi:** None. **N. Isoherranen:** None.

BACKGROUND:
Modeling and simulation of the pharmacokinetics and disposition of drugs has emerged as an important utility in pre-clinical risk assessment and clinical study design. Thus, a growing number of publications incorporate physiologically based pharmacokinetic (PBPK) modeling. However, there is limited information available as to what PBPK models are used for and how published models are validated. The goal of this literature review was to provide information about the applications of PBPK modeling as well as highlight common validation criteria.
METHODS:
PubMed searches were conducted using the search terms PBPK, physiologically based pharmacokinetic model and Simcyp. Publications were selected for analysis if they were published after 2008, and they contained one or more PBPK models of pharmaceutical drugs in humans. The model application, names of compounds modeled, and validation criteria were extracted from each article.

RESULTS:
330 publications that included human PBPK models of pharmaceutical agents were identified. Of these, 250 were original research papers and 80 were reviews, commentaries or introductions to new prediction tools. The most common applications of PBPK modeling were drug-drug interaction predictions (20%), general clinical PK predictions (20%), age related changes in PK (8%), and absorption modeling (7%). Validation criteria, when used, ranged from assuring the predicted PK in absence of a perpetrator was within 2 fold of the observed to cross validating the model in multiple populations.
CONCLUSION:
No uniform trend in model validation criteria emerged from this systematic analysis of recent publications, highlighting the need for the development of validation guidelines that would minimize subjectivity during the model verification process.

LBI-11
A PLACEBO-CONTROLLED, ASCENDING-DOSE STUDY OF THE SAFETY AND TOLERABILITY, PK AND PD, OF DS-7309 IN PATIENTS WITH TYPE 2 DIABETES MELLITUS.

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BACKGROUND:
DS-7309 is a relatively liver selective glucokinase activator (GKA) under development for Type 2 diabetes mellitus (T2DM). In healthy volunteers, dose escalation was halted at 20 mg due to hypoglycemia. The objectives of this study were to examine the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of higher and repeated doses of DS-7309 in T2DM patients.
METHODS:
This was a randomized, placebo-controlled, single-blind study in six cohorts of eight patients with T2DM (6 active / 2 placebo per cohort) given DS-7309 doses ranging from 10 mg BID to 112.5 mg BID. In the first five cohorts, patients received a one day regimen of DS-7309 or placebo, followed by a 4 day washout, then a 14 day BID regimen. The last cohort (75mg BID) also received metformin during the 14 day treatment period. PK was assessed following the single and 14 day regimens. Plasma glucose excursions following a meal tolerance test and 24 h weighted mean glucose were the primary PD measures. The hypoglycemic risk of DS-7309 was evaluated on day 13 when the morning dose was followed by a four hour fasting.
RESULTS:
48 DM patients, aged 18 to 65, completed the study. DS-7309 was rapidly absorbed (T_{max}-30 min) and eliminated with a T1/2 of 3-4 h and exposures increased dose-proportionally with minimal accumulation by Day 14. Except for hypoglycemia, all doses of DS-7309 were relatively safe and well tolerated. Three patients on the metformin combination cohort experienced repeated events of postprandial hypoglycemia which led to early discontinuation of that cohort. By day 14, DS-7309 treatment resulted in a non-dose dependent decrease in plasma glucose compared to placebo.
CONCLUSION:
DS-7309 showed evidence for glucose lowering effects in T2DM, but lacks dose dependency and carries a risk of hypoglycemia.

LBI-12

ESTIMATION OF MMAE DELIVERY TO TUMOR FOLLOWING ANTI-STEAP1 ADC (DSTP3086S) ADMINISTRATION USING 89ZR-DFO-MSTP2109A CLINICAL IMMUNO-PET IMAGING.

S. Sukumaran,[1] S. Sanabria,[1] S. Williams,[1] S. Ramanujan,[1] K. Lin,[1] B. Wang,[1] D. Samineni,[1] J. Carrasquillo,[2] D. Danila,[2] J. O'Donoghue,[2] S. Cheal,[2] P. Zanzonico,[2] S. Larson,[2] M. Morris,[2] A. De Crespigny,[1] B. Fine[1]; [1]Genentech Inc., South San Francisco, CA, [2]Memorial Sloan-Kettering Cancer Center, New York City, NY. **S. Sukumaran:** 1. This research was sponsored by; **Company/Drug**; Genentech and Memorial Sloan-Kettering Cancer Center. 2. I am a paid consultant/employee for; **Company/Drug**; Genentech. **S. Sanabria:** 1. This research was sponsored by; **Company/Drug**; Genentech and Memorial Sloan-Kettering Cancer Center. 2. I am a paid consultant/employee for; **Company/Drug**; Genentech. **S. Williams:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech. **S. Ramanujan:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech. **K. Lin:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech. **B. Wang:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech. **D. Samineni:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech. **J. Carrasquillo:** 2. I am a paid consultant/employee for; **Company/Drug**; Memorial Sloan-Kettering Cancer Center. **D. Danila:** 2. I am a paid consultant/employee for; **Company/Drug**; Memorial Sloan-Kettering Cancer Center. **J. O'Donoghue:** 2. I am a paid consultant/employee for; **Company/Drug**; Memorial Sloan-Kettering Cancer Center. **S. Cheal:** 2. I am a paid consultant/employee for; **Company/Drug**; Memorial Sloan-Kettering Cancer Center. **P. Zanzonico:** 2. I am a paid consultant/employee for; **Company/Drug**; Memorial Sloan-Kettering Cancer Center. **S. Larson:** 2. I am a paid consultant/employee for; **Company/Drug**; Memorial Sloan-Kettering Cancer Center. **M. Morris:** 2. I am a paid consultant/employee for; **Company/Drug**; Memorial Sloan-Kettering Cancer Center. **A. De Crespigny:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech. **B. Fine:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech.

BACKGROUND:
ADCs combine the high target specificity and favorable pharmacokinetics (PK) of mAbs with the potent tumor killing properties of cytotoxic agents. Attaining required accumulation of the cytotoxic agent inside tumor cells is critical for efficient killing. Clinical immune-PET (iPET) imaging (Carrasquillo et al AACR 2014) along with PK data for anti-STEAP1 ADC (Danila et al ASCO 2014) was used to develop a semi-mechanistic model to characterize tumor delivery for MMAE (cytotoxic agent) in prostate cancer patients.
METHODS:
Time series iPET imaging for tumor lesions and normal tissues were performed with the administration of 10 mg of residualizing Zirconium labeled Ab (89Zr-DFO-MSTP2109A) against STEAP1 in prostate cancer patients. Anti-STEAP1-vc-MMAE (DSTP3086S) PK was assessed for the dose ranging Phase I study in patients. Total Ab and Ab-conjugated MMAE (AcMMAE) were measured. Integrated modeling analysis of the data from the studies was performed (Completed in Oct).
RESULTS:
Quantification of iPET data showed a cumulative increase in the standardized uptake values over time in tumor lesions and a decline in normal tissues confirming STEAP1 specific uptake of the imaging Ab by tumor. A two-compartment model with linear elimination and a linear first order uptake into tumor was able to capture the mean data for 89Zr-DFO-MSTP2109A in circulation and tumor. Total Ab PK for DSTP3086S was captured with a two-compartment model with linear elimination and an additional deconjugation elimination process was added to the model to capture AcMMAE profile. Total MMAE delivery to the tumor was projected for various dose levels based on the parameter estimates obtained from the previous steps.
CONCLUSION:
Model-aided approaches were used to project MMAE delivery and instantaneous MMAE levels in the tumor providing a better understanding of the drug kinetics in the tumor.

LBI-13
PHARMACOGENETIC ANALYSIS OF VARIABLE RESPONSE TO ATOMOXETINE TREATMENT IN A PEDIATRIC COHORT OF ADHD PATIENTS.

D. R. Hahn,[1] T. Fukuda,[1] D. L. Gilbert,[1] F. R. Sallee[2]; [1]CCHMC, Cincinnati, OH, [2]University of Cincinnati, Cincinnati, OH. **D.R. Hahn:** None. **T. Fukuda:** None. **D.L. Gilbert:** None. **F.R. Sallee:** None.

BACKGROUND:
Atomoxetine (ATX) is a norepinephrine reuptake inhibitor approved for managing symptoms of attention deficit hyperactivity disorder (ADHD). Although attractive for ADHD pharmacotherapy due to a lack of abuse potential, individual response to ATX treatment is highly variable. We hypothesize that variability in ATX response can be explained by genetic variation at gene loci involved in regulation of neuronal dopamine and norepinephrine signaling.

METHODS:
77 subjects between 7-12 years with positive diagnoses of ADHD were recruited for study. Subject ADHD symptom severity was assessed both before and following four weeks therapy with 0.5-1.8 mg/kg/day of ATX. Genomic DNA isolated from subject whole blood samples was genotyped for multiple SNPs at genes DAT1, NET, and DRD2 (TaqMan, Applied Biosystems) and the 3'-UTR VNTR region of DAT1. Data mining and statistical analyses were performed in JMP to correlate genetic variants to ATX response (% of final/baseline score).
RESULTS:
Univariate analyses showed correlations between ATX response and DAT1-VNTR genotype as well as SNP variants at DAT1 and DRD2. Further pathway-directed data mining of candidate SNPs revealed stronger gene-response associations in combination with VNTR genotype (10/10 vs 10/9) which produced distinct patient subpopulations with divergent gene-ATX response relationships. In subjects with VNTR 10/10 genotype, one or more "beneficial" SNP variants at the DAT1 locus significantly improved ATX response (p=0.0021). "10/9" subject response appeared to depend upon the presence of SNPs at the DRD2 locus (p=0.0123).
CONCLUSION:
This study suggests that the efficacy of Atomoxetine for treatment of ADHD depend in part upon individual genetic setting at DAT1 and DRD2.

LBI-14
ALTERED METHADONE PHARMACOKINETICS IN OBESE PATIENTS.
P. K. Lala, B. M. Kapur; Hospital for Sick Children, Toronto, ON, Canada
P.K. Lala: None. **B.M. Kapur:** None.

BACKGROUND:
Rising trends in obesity worldwide have led to increases in related conditions, such as cardiovascular disease and type 2 diabetes, in a progressively younger demographic. While obesity is known to alter the pharmacokinetics of some drugs, published clinical studies are sparse. We studied pharmacokinetic data of methadone, a highly lipophilic drug, in obese patients and show that both loading and maintenance doses may be inadequate if current recommended dosing guidelines are followed.
METHODS:
As part of our methadone kinetics service, we obtain patients' pre- and post-dose blood samples, methadone dosing data, height, weight, and medication list. Assays for methadone and its metabolite, EDDP, were done by immunoassay, previously validated against both HPLC and GC. We calculated $t_{½}$, clearance (CL), and volume of distribution (Vd) for both methadone and EDDP. All assays were performed as part of clinical care requests from attending physicians.
RESULTS:
From June 2002 to November 2014, 268 patient samples were analysed; all patients were long-term enrollees of an MMT program. Height and weight data were available to calculate BMI for 67 of 268 patients; we report here results from these 67 patients. Mean methadone dose was 1.31 mg/kg (0.64-3.61 mg/kg); mean BMI 30.9 (19.6-58.5); mean methadone $t_{½}$ 29.1 h (11.8-74.6 h); and mean EDDP $t_{½}$ 28.7 h (7.4-97.2 h). BMI was significantly correlated with methadone $t_{½}$ ($r^2 = 0.21$, $p < 0.001$) and Vd ($r^2 = 0.20$, $p < 0.001$). There was no correlation between BMI and CL ($p = 0.35$) or number of medications received ($p = 0.40$).

CONCLUSION:
We show, for the first time, a significant correlation between obesity (BMI) and methadone $t_{½}$. We suggest that this phenomenon may play a broader significant role in the management of patients who are obese and receiving lipophilic medications. Furthermore, we strongly recommend that obese subject be included in all future clinical drug trials.

LBI-15
IV TOPIRAMATE IN CANINE EPILEPSY: USE OF PHARMACOKINETIC MODELING AND SIMULATION TO SELECT THE LOADING DOSE FOR A CLINICAL TRIAL OF CANINE STATUS EPILEPTICUS.

I. Vuu,[1] L. Coles,[1] I. Leppik,[1] E. E. Patterson,[2] K. M. Johnson,[1] U. Mishra,[1] J. C. Cloyd[1]; [1]University of Minnesota, College of Pharmacy, Minneapolis, MN, [2]University of Minnesota, College of Veterinary Medicine, Minneapolis, MN. **I. Vuu:** None. **L. Coles:** None. **I. Leppik:** 2. I am a paid consultant/employee for; **Company/Drug**; CuRx. **E.E. Patterson:** None. **K.M. Johnson:** None. **U. Mishra:** None. **J.C. Cloyd:** 2. I am a paid consultant/employee for; **Company/Drug**; CuRx. 4. I hold a patent for; **Company/Drug**; IV Topiramate and receive royalty payments under a licensing agreement between the University of Minnesota and Ligand. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; IV Topiramate.

BACKGROUND:
The development of new therapies for human status epilepticus (HSE) is challenged by the limitations of translating from experimental models to human clinical trials. Canine status epilepticus (CSE) provides a clinically relevant tool to study the safety and efficacy of potential HSE therapies. The objective of this study was to use pharmacokinetic (PK) modeling and simulations to select a loading dose of intravenous (IV) topiramate (TPM) that will produce TPM concentrations in dogs that have been reported in case reports of HSE.
METHODS:
Four dogs were used in this study. Two of the four dogs remained on an antiepileptic maintenance regimen of levetiracetam, zonisamide, and phenobarbital (PB) throughout the study. Each dog received a 10 mg/kg dose of IV TPM infused over five minutes. Blood samples were collected and plasma TPM concentrations were measured using HPLC-MS. PK modeling and simulations were used to select a dose predicted to attain a target concentration of 30-60 μg/mL TPM at 30 minutes post-dose. These data were analyzed 9/15/14.
RESULTS:
A two-compartment model best fit the data. TPM clearance was greater and elimination half-life was shorter in the dogs on PB. The central clearance was 0.6-0.9 L/hr/kg vs 0.1 L/hr/kg and elimination half-life 0.1-0.3 hrs vs 0.6-1.3 hrs in dogs with and without PB, respectively. Based on our analyses, doses of 20 mg/kg for unmedicated dogs and 25 mg/kg for dogs on PB infused over 10 minutes are predicted to produce, on average, a 30 μg/mL TPM concentration 30 minutes post infusion.
CONCLUSION:
We estimated TPM doses and infusion rates predicted to attain target plasma concentrations of 30-60 μg/mL. The goal of this study was to demonstrate that using a small group of dogs can be informative in optimizing therapy for clinical trials of CSE. If effective in dogs, we have also obtained information that can guide the selection of dosage regiments for HSE.

LBI-16

OPTIMIZATION DOSING OF PIPERACILLIN-TAZOBACTAM FOR THE TREATMENT OF PSEUDOMONAS AERUGINOSA INFECTION IN FOUR AGE-GROUPS BASED ON MONTE CARLO SIMULATION.

M. Takeuchi,[1] R. Tanoshima,[1] K. Timberlake,[2] S. Boodhan,[2] S. Ito[1]; [1]Division of Clinical Pharmacology and Toxicology, The Hospital for Sick Children, Toronto, ON, Canada, [2]Division of Pharmacy, The Hospital for Sick Children, Toronto, ON, Canada

M. Takeuchi: None. **R. Tanoshima:** None. **K. Timberlake:** None. **S. Boodhan:** None. **S. Ito:** None.

BACKGROUND:

Piperacillin / Tazobactam (PIP/TAZ) is a widely used antimicrobial for systemic bacterial infection, especially for febrile neutropenia. The minimum inhibitory concentration (MIC) against ***pseudomonas aeruginosa*** in the Hospital for Sick Children has increased for a decade, and more patients have possibly encountered insufficient effectiveness of PIP/TAZ. In order to assess the optimal dosing strategy of PIP/TAZ, we performed Monte Carlo simulation.

METHODS:

A 10,000-patient Monte Carlo simulation was performed for the following PIP/TAZ dosing regimens in populations of four age groups: 80 mg/kg q6h (of the piperacillin component), 80 mg/kg q8h, 100 mg/kg q6h, and 100 mg/kg q8h as 0.5- hour infusions. Infusions with longer time i.e. 1-, 2-, 3-, and 4- hour infusions, were also simulated. Age groups were defined as follows: 2-5 months old, 6-23 months old, 2-5 years old, and 6-12 years old. Pharmacokinetic parameters were derived from the previous paper. MIC data were extracted from our hospital data from 2007 to 2013. The percent of the dosing interval of the free drug above MIC (%T>MIC) was calculated. The bactericidal target attainment was defined as more than 50% %T>MIC for PIP/TAZ. Cumulative Fraction of Response (CFR) > 90% was defined as optimal.

RESULTS:

Current dosing regimen, 80 mg/kg q8h as 0.5-hours infusion, did not achieve sufficient bactericidal target attainment and CFR>90% in any age groups. Even in high dose regimens CFR>90% were not attained. CFR in younger age group was higher than in older age group. Longer infusion time achieved higher CFR than standard infusion. We decided to increase dose of PIP/TAZ based on these results.

CONCLUSION:

Our study revealed that the dose should be increased to achieve the optimal dosing in all the age groups. Our study also revealed longer infusion time was better than standard infusion. Future studies need to be conducted to confirm this result.

LBI-17

PK-PD BINDING MODEL OF IDARUCIZUMAB-MEDIATED REVERSAL OF DABIGATRAN ANTICOAGULATION FROM THREE STUDIES IN HEALTHY VOLUNTEERS AND RENALLY IMPAIRED PATIENTS.

B. Lalovic,[1] R. Niebecker,[2] C. Doege,[2] S. Glund,[2] S. Olson,[1] P. Reilly[3]; [1]Translational Medicine Clinical Pharmacology, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, [2]Translational Medicine Clinical Pharmacology, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany, [3]Clinical Development, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT

B. Lalovic: 1. This research was sponsored by; **Company/Drug**; Boehringer Ingelheim. 2. I am a paid consultant/employee for; **Company/Drug**; Boehringer Ingelheim. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Boehringer Ingelheim/Idarucizumab. **R. Niebecker:** 1. This research was sponsored by; **Company/Drug**; Boehringer Ingelheim. 2. I am a paid consultant/employee for; **Company/Drug**; Boehringer Ingelheim. 6. The following product discussed is

not labeled for the use under discussion or is still investigational; **Company/Drug**; Boehringer Ingelheim/Idarucizumab. **C. Doege:** 1. This research was sponsored by; **Company/Drug**; Boehringer Ingelheim. 2. I am a paid consultant/employee for; **Company/Drug**; Boehringer Ingelheim. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Boehringer Ingelheim/Idarucizumab. **S. Glund:** 1. This research was sponsored by; **Company/Drug**; Boehringer Ingelheim. 2. I am a paid consultant/employee for; **Company/Drug**; Boehringer Ingelheim. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Boehringer Ingelheim/Idarucizumab. **S. Olson:** 1. This research was sponsored by; **Company/Drug**; Boehringer Ingelheim. 2. I am a paid consultant/employee for; **Company/Drug**; Boehringer Ingelheim. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Boehringer Ingelheim/Idarucizumab. **P. Reilly:** 1. This research was sponsored by; **Company/Drug**; Boehringer Ingelheim. 2. I am a paid consultant/employee for; **Company/Drug**; Boehringer Ingelheim. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Boehringer Ingelheim/Idarucizumab.

BACKGROUND:
Idarucizumab (BI 655075) is a monoclonal humanized antigen-binding fragment engineered to bind dabigatran. Dabigatran etexilate (DE) is a direct thrombin inhibitor approved for prevention of stroke and systemic embolism in patients with atrial fibrillation and the treatment and prevention of recurrent deep vein thrombosis and pulmonary embolism. In rare emergencies, a specific, fast acting dabigatran anticoagulation reversal agent could provide a treatment alternative to already existing measures of bleeding management.
METHODS:
PK-PD data from three placebo-controlled, randomized clinical studies in healthy volunteers and renally impaired subjects (n=283) available after September 8, 2014, were used to develop this dabigatran-idarucizumab pharmacokinetic binding model. The model describes the time course of dabigatran and idarucizumab binding kinetics and the impact of demographic covariates on the parameters of the two interactants. Model predictions were used in the assessment of the dabigatran concentration-coagulation marker relationships.
RESULTS:
The model quantifies idarucizumab-mediated reversal of dabigatran anticoagulation across a range of doses and dosing regimens of both interactants. This population, binding model of free and total dabigatran and total idarucizumab proposes the formation of dabigatran-idarucizumab complex from central dabigatran and central and peripheral idarucizumab compartments with estimates of ***in vivo*** binding affinity in the presence of dabigatran plasma protein binding.
CONCLUSION:
This model predicted reversal of anticoagulant activity of dabigatran in the presence of rapid, practically irreversible binding by idarucizumab, free dabigatran concentrations below the quantification limit and redistribution of dabigatran from peripheral spaces in typical patients in ongoing clinical trials.

LBI-18

TYROSINE KINASE IN PEDIATRIC GROWTH.

A. Balch, J. Constance, C. Sherwin, M. Spigarelli; University of Utah, Salt Lake City, UT **A. Balch:** None. **J. Constance:** None. **C. Sherwin:** None. **M. Spigarelli:** None.

BACKGROUND:
The use of tyrosine kinase inhibitor (TKI) therapy has become more common in pediatric patients in the last few years. This trend is likely to continue as more TKIs are approved and the list of conditions for which TKIs have clinical utility expands. Imatinib (Gleevec™) is a tyrosine kinase inhibitor that is specifically indicated for Philadelphia positive chronic myelogenous leukemia (PH+CML). Dasatinib (Sprycel™) and nilotinib (Tasigna™) are TKIs indicated for CML patients who are no longer benefitting from, or did not tolerate, other treatments including imatinib.
OBJECTIVE:
The objective of this study was to determine whether there is evidence of growth retardation as an adverse drug experience for TKIs.
METHODS:
The FDA Adverse Event Reporting System (FAERS) was reviewed for currently posted data from 4th quarter 2012 until 1st quarter 2014 for individuals ≤ 18 years of age. The most recent update of the FAERs data was in October of 2014. These are sponsor, patient and physician reported events. A search for approximate matches to the drug names using the generalized Levenshtein edit distance using the R and SAS™ 9.3 was used to search for patterns in the adverse experiences. These AEs were grouped by Preferred Term(PT), and the ranking of growth related AEs was conducted relative to other PTs.
RESULTS:
Of 574 self-reported adverse experiences reported for imatinib from 2012-2014, there were 12 (2.1%) cases of growth retardation. Growth retardation was the 5th most commonly occurring AE. Of 594 self-reported adverse experiences for dasatinib from 2012-2014, no cases of growth retardation occurred. Likewise, of 25 self-reported AEs for nilotinib, none were growth related.
CONCLUSION:
There appears to be some evidence of growth retardation in imatinib patients, and none for dasatinib patients. Not enough AEs have yet been reported for nilotinib to judge whether growth is also retarded in these patients.

POSTERS, POSTER WALKS AND LATE-BREAKING AND ENCORE ABSTRACT POSTERS

LATE-BREAKING AND ENCORE POSTER SESSION II

FRIDAY, MARCH 6, 2015
11:30 am - 6:30 pm
Attended Posters 4:30 pm – 6:30 pm
ELITE HALL

LBII-1

PREDICTING THE PROBABILITY OF SUCCESSFUL EFFICACY OF A DISSOCIATED AGONIST OF THE GLUCOCORTICOID RECEPTOR FROM DOSE- RESPONSE ANALYSIS.

D. J. Conrado,[1] S. Krishnaswami,[1] S. Shoji,[2] N. Thomas,[1] S. Kolluri,[3] J. Hey-Hadavi,[3] D. McCabe,[3] R. Rojo,[1] B. K. Tammara[4]; [1]Pfizer Inc., Groton, CT, [2]Pfizer Inc., Shibuya-ku, Tokyo, Japan, [3]Pfizer Inc., New York, NY, [4]Pfizer Inc., Collegeville, PA

D.J. Conrado: 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **S. Krishnaswami:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **S. Shoji:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **N. Thomas:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **S. Kolluri:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **J. Hey-Hadavi:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **D. McCabe:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **R. Rojo:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **B.K. Tammara:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327.

BACKGROUND:
PF-04171327 is a dissociated agonist of the glucocorticoid receptor (DAGR) being developed to retain anti-inflammatory efficacy while reducing unwanted effects. Our aim was to conduct a longitudinal dose-response (D-R) analysis to inform the DAGR doses at which there was sufficient efficacy compared with prednisone 10 mg once daily (QD).
METHODS:
This was a phase II, randomized, double-blind, parallel-group study in 323 subjects with active rheumatoid arthritis on a background of methotrexate. Subjects received DAGR 1, 5, 10 or 15 mg, prednisone 5 or 10 mg, or placebo QD for eight weeks followed by a 4-week taper. The Disease Activity Score 28-4 C-Reactive Protein (DAS28-4 CRP) was the efficacy endpoint utilized in this D-R model. The time course of placebo effect was described using an exponential plus a linear process. Prednisone effect was estimated for the two dose levels, and DAGR effect was characterized by an inhibitory E_{max} model. NONMEM 7.2 and R 2.15.2 were used for modeling and simulation (data was analyzed from September 30 to November 10, 2014).
RESULTS:
For DAGR, the maximum DAS28-4 CRP reduction (E_{max}) was estimated to be 1.2 points (95% CI: -1.7, -0.84), and the evaluated dose range provided 31% to 87% of the E_{max}; for 10 mg prednisone, the estimated reduction was 0.94 points (95% CI: -1.3, -0.59). The drug effect portion of the model indicated near maximal responses by week 2 for both agents, with improvement post week two attributed to placebo effect. Stochastic simulations suggested that DAGR 1, 5, 10 and 15 mg have probabilities of 0.9%, 29%, 54% and 62%, respectively, to achieve efficacy greater than prednisone 10 mg at week eight.
CONCLUSION:
D-R in DAS28-4 CRP was observed for DAGR and prednisone. DAGR ≥ 9 mg has an effect on DAS28-4 CRP comparable to or greater than prednisone 10 mg.

LBII-2

A KINETIC-PHARMACODYNAMIC (K-PD) MODEL OF P1NP RESPONSE TO PF-04171327 AND PREDNISONE IN SUBJECTS WITH RHEUMATOID ARTHRITIS (RA).

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6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **S. Kolluri:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **J. Hey-Hadavi:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **D. McCabe:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **R. Rojo:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327. **B.K. Tammara:** 1. This research was sponsored by; **Company/Drug**; Pfizer Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Pfizer Inc. 5. I am a significant stockholder for; **Company/Drug**; Pfizer Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; PF-04171327.

BACKGROUND:
PF-04171327 is a dissociated agonist of the glucocorticoid receptor (DAGR) being developed as a treatment in patients with RA. Since osteoporosis is an adverse effect of chronic glucocorticoid use, we assessed amino-terminal propeptide of type I collagen (P1NP) changes as a marker of bone formation by DAGR compared to prednisone, as an initial differential indicator of impact on bone homeostasis.
METHODS:
This was a phase II, randomized, parallel-group, double-blind study in RA subjects (n = 323) with DAGR 1, 5, 10, or 15 mg , prednisone 5 or 10 mg, or placebo daily for eight weeks (methotrexate background) followed by a four week taper. A mixed effects longitudinal K-PD model was fit using 13 weeks of trough P1NP concentrations using NONMEM 7.2 and R 2.15.2 (data was analyzed from September 16 to November 11, 2014). Simulations were performed to obtain prediction intervals for median % change from baseline in P1NP at Week 8, to evaluate DAGR comparability to prednisone 5 mg.
RESULTS:
Visual predictive check suggested P1NP-time course was well described by the K-PD model. Estimates (%RSE) for baseline P1NP and degradation rate constant were 47.4 ng/ml (3.0%) and 0.286 /week (9.7%), respectively. Placebo response showed slight increase in P1NP over time (0.384 ng/ml/week). The 50% inhibition of P1NP by DAGR and prednisone was estimated to be 68.3 mg/week (17%) and 76.5 mg/week (16%), respectively. Simulations showed that DAGR 1, 5, and 10 mg were comparable to 5 mg prednisone.
CONCLUSION:
The developed K-PD model adequately characterizes P1NP-time course following administration of DAGR, prednisone, and placebo and is a quantitative tool for finding an optimal dose of DAGR with less effects on bone formation.

LBII-3

TARGETING VANCOMYCIN AUC IN NEONATES - A MODEL BASED BAYESIAN APPROACH FOR PERSONALIZED THERAPEUTIC DRUG MONITORING.

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BACKGROUND:
When treating methicillin-resistant Staphylococcus aureus (MRSA) infections with vancomycin, national guidelines recommend targeting an AUC24/MIC ≥400 to ensure adequate drug exposure. To optimize neonatal vancomycin dosing, accurate AUC24 estimates are needed. The objective of this study was to assess the utility of a model based Bayesian approach for estimating vancomycin AUC24 in neonates.
METHODS:
Neonates who received vancomycin and had ≥1 'peak' and ≥1 'trough' concentrations at two healthcare systems (2006-2013) were studied. Bayesian estimates of clearance were calculated for each neonate using a published, externally validated population pharmacokinetic model in NONMEM (external validation was not completed until October 2014). AUC24 was calculated as the daily dose ÷ clearance. The percent prediction error (PE) and the percent absolute prediction error (APE) of the AUC24 estimates were compared for: 1) the full dataset, 2) a dataset with only the first peak and trough concentrations, and 3) a dataset with only the first trough concentration.
RESULTS:
A total of 427 neonates were studied (median [IQR] postmenstrual age 36 [29-41] weeks and weight 2.3 [1.0-3.4] kg). Compared with the full dataset, Bayesian estimates of AUC24 using only the first trough concentration had a median PE of -0.7% (95% CI: -1.3% to 0.0%) and a median APE of 4.1% (95% CI: 3.5% to 4.8%). AUC24 predictions were within 15% of the full dataset for 90% of neonates. The addition of a peak concentration provided no substantial predictive benefit.
CONCLUSION:
A model based therapeutic monitoring strategy using only a single trough concentration can adequately predict vancomycin AUC24 in neonates. Application of this approach can help clinicians personalize vancomycin therapy and warrants further study.

LBII-4

POPULATION-BASED META-ANALYSIS OF ROXITHROMYCIN PHARMACOKINETICS: SIGNIFICANT EFFECT OF SATURABLE ABSORPTION AND PROTEIN BINDING.

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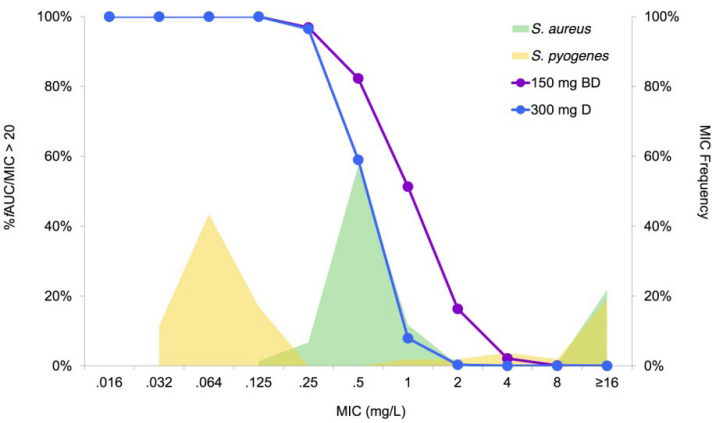
BACKGROUND:
Roxithromycin has seen widespread use for several decades, however, no population pharmacokinetic (PK) analysis has been published. Early studies indicated saturation of protein binding and absorption at doses within the approved range, which may impact pharmacodynamic target attainment since regimens of 150 mg twice daily (BD) and 300 mg once daily (D) are used interchangeably in clinical practice. This study aimed to develop a population-based meta-analysis of roxithromycin PK, and utilize this model to inform optimal dosing.

METHODS:
Roxithromycin PK data was collected or digitized from literature publications. 25% of data was not received until 9/23 (analyzed 9/26). Population modeling was undertaken with ADAPT 5.
RESULTS:
A two-compartment model with saturable absorption and protein binding described the dataset (n=63). Simulations indicated that a 300 mg D regimen achieves a 46% lower free AUC (fAUC) compared to 150 mg BD. Target attainment (fAUC/MIC ratio >20) was significantly lower with a 300 mg D regimen at MICs of 0.5 and 1 mg/L (59% and 8%) compared to patients receiving 150 mg BD (82% and 51%), overlapping the MIC distribution for S. aureus (Figure).
CONCLUSION:
Roxithromycin displays saturable absorption and protein binding leading to lower target attainment at MICs ≥0.5 mg/L with widely used once daily dosing regimens, indicating that twice daily regimens may be preferable for certain important pathogens (S. aureus).



LBII-5
A CLINICAL-DATA DRIVEN MECHANISTIC SYSTEMS MODEL OF ASTHMA DISEASE AND TREATMENT.

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BACKGROUND:
Asthma is a chronic inflammatory disease of the airways involving numerous underlying immunological and stromal pathways. Various treatments in development target activities or proteins in these pathways, and show differential impact on clinical outcomes and pathway biomarkers. Although specific molecular pathways are being characterized more thoroughly, the understanding of the linkage between the different pathways as well as the functional clinical outcomes is still very limited.

METHODS:
We have developed a mechanism-based systems model representing different cellular and soluble contributors to asthma, including (1) innate immune, adaptive immune, and airway resident cells (2) soluble proteins such as IL5, IL13, IL4, and IgE and (3) other measurements such as FeNO and FEV1. Mechanistic pathways in the model were identified based on ***in vitro*** and ***in vivo*** literature, and parameters were calibrated based on clinical data. Measurements from a total of 50 clinical studies ranging from large randomized controlled trials to small observational studies were methodically catalogued into a data-repository.
RESULTS:
The model was calibrated to and was found to successfully describe the clinical measurements for different patient severities and for interventions such as anti-IgE, anti-IL5, and anti-IL13.
CONCLUSION:
The model will be useful to elucidate biological pathways underlying observed effects of the different interventions as well as to explore and predict the impact of additional interventional strategies for which little to no clinical data is available.

LBII-6
NETWORK-BASED SYSTEMS PHARMACOLOGY APPROACH FOR TARGET IDENTIFICATION IN HETEROGENEOUS NON-HODGKIN'S LYMPHOMA.
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BACKGROUND:
Non-Hodgkin's lymphoma (NHL) represents a heterogeneous B-cell neoplasm and the most common hematological cancer in adults. A diverse range of oncogenic mechanisms exists in lymphomagenesis creating challenges for developing NHL therapies. Discrete dynamic modeling is an excellent tool to analyze large regulatory networks and enhance understanding of complex biological systems. This study aimed to test the feasibility of using a network-based systems pharmacology analysis to identify intervention strategies based on molecular dysregulation in NHL.
METHODS:
A Boolean model of B-NHL was constructed that incorporates B-cell receptor signaling, toll-like receptor and cytokine receptor pathways, intrinsic and extrinsic apoptosis, cell cycle arrest and DNA damage. In order to increase model predictability, we have been continuously updating the nodes and edges in the network based on most recent publications. Network visualization and centrality measures were performed in yEd graph editor. The network was further implemented into CellNetAnalyzer (CNA) for dynamic simulations. Logical steady states (LSS) and minimal intervention sets (MIS) were assessed.
RESULTS:
The final B-NHL regulatory model contains 102 nodes and 180 edges. Common recurrent genetic alterations were considered by fixing nodes to either an "activated" or "inhibited" state. Centrality measures identified IKK/NFκB, PI3K/AKT, p53/p21, Lyn/Syk/Btk and c-Myc/Bcl-6 as critical network hubs. LSS also predicted CD79B mutation as a proliferative marker in B-NHL. Based on MIS analysis, several combination interventions, including inhibitors of mTOR and Bcl-2, were suggested for further experimental evaluation.
CONCLUSION:
A network-based systems pharmacology approach can be used to query key pharmacological targets in B-NHL and might provide a rational approach to design novel targeted combination therapies.

LBII-7

GENETIC POLYMORPHISM OF MATRIX METALLOPROTEINASE (MMP)-9 IN POLYCYSTIC OVARY SYNDROME.

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BACKGROUND:
Plasma matrix metalloproteinase-9 (MMP-9) levels have been considered predicts of cardiovascular risk, and functional polymorphism in the MMP-9 gene may modulate its expression and consequently its plasma concentration. However, no study has tested if functional MMP-9 polymorphisms could affect MMP-9 levels in patients with polycystic ovary syndrome (PCOS). We compared the MMP-9 plasma levels in PCOS women with those found in healthy ovulatory controls (controls). In addition, we examined if two polymorphisms (Q279R (rs17576) and 90(CA) (rs2234681)) affect MMP-9 levels in PCOS women.
METHODS:
A cross-sectional study was conducted at the University Hospital of the Faculty of Medicine of Ribeirão Preto, University of São Paulo, Brazil. We studied 64 PCOS women and 33 controls. Plasma MMP-9 levels were measured by ELISA. Genotypes were determined by RFLP-PCR and by Taqman allele discrimination assay. These data were analyzed on October 1, 2014.
RESULTS:
The distribution of genotype showed no deviation from Hardy-Weinberg equilibrium. MMP-9 levels did not differ significantly between PCOS and controls ($p>0.05$). We found similar MMP-9 genotypes and allelic frequency distribution when the two groups were compared ($P<0.05$). To examine the possible effects of MMP-9 genotype on plasma MMP-9 levels, we compared the MMP-9 genotype distributions in two extreme groups of subjects: the Lower group, which included subjects in the lower half of plasma MMP-9 distribution, and the Higher group, which included subjects in the upper half of plasma MMP-9 distribution. The genotype distribution was similar in both groups.
CONCLUSION:
In conclusion, our results suggest no association between MMP-9 genotypes and MMP-9 levels in PCOS women, but studies with larger samples are needed to confirm this finding.
SUPPORT:
FAPESP

LBII-8

COMPARATIVE SAFETY OF NSAIDS FOR GASTROINTESTINAL EVENTS IN ASIA-PACIFIC POPULATION.

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E. Lai: None. **C. Chen:** None. **K. Kubota:** 1. This research was sponsored by;

Company/Drug; Dr. Kubota was supported by a grant from Pfizer Health Research Foundation (Grant No. 11-2-021, http://www.pfizer-zaidan.jp). The funder had no role in study design, data collection and analysis, dec. **K. Man:** None. **B. Park:** None. **N. Pratt:** None. **E. Roughead:** None. **J. Shin:** None. **I. Wong:** None. **Y. Kao Yang:** None. **S. Setoguch:** None.

BACKGROUND:
The safety of non-steroidal anti-inflammatory drugs (NSAIDs) that are solely used in Asia/Pacific regions including loxoprofen and mefenamic acid is not well studied. This study aimed to assess comparative risk of hospitalized gastrointestinal (GI) events of loxoprofen and mefenamic acid to other well-studied NSAIDs.
METHODS:
We conducted a multi-database cohort study using databases from Taiwan, Japan, Korea, Hong Kong and Australia by distributed network approach. We selected diclofenac, loxoprofen, mefenamic acid or celecoxib initiators and followed the patients until hospitalized GI events, medication switching or discontinuation, disenrollment or the end date of the databases. We used Cox proportional hazards models with high-dimensional propensity score (HdPS) adjustment to assess the risks of hospitalized GI events among NSAIDs. We used inverse probability weighting (IPW) with HdPS to pool the results without sharing individual data from countries. We analyzed the aggregated weighted data by three month intervals by pooled logistic regression model.
RESULTS:
Compared with diclofenac users, we found the risk of GI events of loxoprofen was lower in Korea (hazard ratio, 0.35; 95% CI, 0.25-0.49) but not in Japan (1.67; 0.56-4.92); the risk of mefenamic acid was lower in Taiwan (0.54; 0.33-0.88) and Korea (0.13; 0.06-0.29). We found that celecoxib initiators had lower risk in Korea and Australia. The pooled results indicated the risk as lower in loxoprofen (odds ratio, 0.59; 95% CI, 0.41-0.85) mefenamic acid (0.27; 0.17-0.43) when compared with diclofenac users.
CONCLUSION:
This international study indicated that loxoprofen and mefenamic acid users had lower risk of GI events than diclofenac users. Compared with Cox-2 inhibitors, loxoprofen and mefenamic acid could be a cheaper option when the risk of GI events is concerned.

LBII-9

VACCINATION PATTERNS AMONG PEDIATRIC CANCER PATIENTS TREATED WITH VANCOMYCIN.

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E.Y. Enioutina: None. **A.H. Balch:** None. **J.E. Constance:** None. **C.M. Sherwin:** None. **M.G. Spigarelli:** None.

BACKGROUND:
The improvement in survival among children diagnosed with malignancy over the past two decades has been a remarkable achievement. As a consequence of therapy most of these patients are immunocompromised and therefore at high risk of infections. Vaccination is important to prevent infectious diseases, especially for patients who will become vulnerable to infections.
METHODS:
A multicenter retrospective study of patients from birth to 18 years who received ≥2 doses of IV vancomycin between 01/2006 and 12/2012 was performed using an EMR database. Cancer diagnoses were identified via validated hospital registry. These data could not be analyzed prior to September 8 due to time constraints for consultation with the data architect. Statistical analysis was performed in SAS™ version 9.3 and R.

RESULTS:
There were 259 cancer and 4,727 cancer-free patients who received vancomycin over the study period. Of these, there were a total of 19 vaccinations among 9 patients with cancer and 3,070 vaccinations for 1,169 cancer-free patients. Patients with cancer were vaccinated less frequently than cancer-free patients (3.4% vs. 24.7%, $p<0.001$). Cancer patients were vaccinated with viral inactivated vaccines (68.4% of all vaccines), while cancer-free patients received more bacterial vaccines (55.1%). The median number of vaccinations per hospitalization in cancer patients was lower than in cancer-free patients (1 vs. 3). Additionally, IV immunoglobulins were given to cancer patients almost at the same rate as to cancer-free patients (10.2% vs. 15.3%, $p<0.07$).
CONCLUSION:
Vaccinations are performed less frequently in pediatric patients with cancer, compared with their cancer-free peers, who are being treated with the IV antibiotic vancomycin. Medical professionals are extremely cautious with vaccination of pediatric cancer patient, while being less restrictive in the use of immunoglobulins for passive protection.

LBII-10
EVALUATION OF PHARMACOKINETIC (PK) DRUG-DRUG INTERACTION (DDI) STUDIES INFORMATION FOR FDA APPROVED NEW MOLECULAR ENTITIES (NMES) FROM THE YEARS 2004, 2012 & 2013.

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A.A. Somani: None. **C. Lagishetty:** None. **L. Bartolome:** None. **L.J. Lesko:** None.

BACKGROUND:
PK-DDI studies are conducted for NMEs as both victim and perpetrator drug to evaluate if concomitant administration of drugs alters their PK necessitating label recommendations. The objective of this study was to evaluate the rate of "positive" and "negative" PK-DDI studies for NMEs approved in the years 2004, 2012 and 2013 and their impact on drug labels.
METHODS:
The ratio of PK exposure parameters [maximum systemic concentration (C_{max}), area under the curve (AUC)] for the victim and perpetrator drug to that of victim drug alone from PK-DDI studies were collected from drugs@FDA2 for approved NMEs. A DDI study was considered "positive" if both AUC and C_{max} ratios were not completely within the 90% confidence interval of 80-125%. The % yield for each year was calculated as % ratio of number of positive DDI studies to the total number of DDI studies. The label recommendations contraindication (C), warning and precaution (WP), dose adjustment (DA), monitoring (M), and no action/ interaction (NA) were identified for all the DDI studies.

RESULTS:
A total of 116, 155 and 253 DDI studies were conducted for the approved NMEs in the years 2004, 2012 and 2013, resulting in 28, 70 and 144 positive DDI studies, respectively. The percent yield was 24%, 45% and 43% for the years 2004, 2012 and 2013, respectively. The label recommendations identified were 2 C, 8 WP, 10 DA, 3 M and 88NA for the year 2004; 21 C, 18 WP, 17 DA, 12 M and 85 NA for the year 2012; and 8 C, 21 WP, 27 DA, 15 M and 144 NA for the year 2013.
CONCLUSION:
The study results represent a benchmark for assessing the rate of positive and negative DDI studies in new drug development. Our results suggest that there may be a room for improvement in assessing why DDI studies are conducted, and whether or not ***in vitro*** DDI studies are responsible for false positive clinical DDI studies.
REFERENCES:
1. FDA guidance for industry on Drug Interaction Studies - Study Design, Data Analysis, Implications for Dosing, and Labeling Recommendations.
2. Drugs@FDA

LBII-11
DEVELOPMENT OF A QUANTITATIVE SYSTEMS PHARMACOLOGY PLATFORM TO SUPPORT TRANSLATIONAL RESEARCH AND CLINICAL DEVELOPMENT IN IMMUNO-ONCOLOGY.

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BACKGROUND:
Mechanistic models capable of integrating datasets from the molecular, cellular, and tissue level to provide research predictions of tumor response are well-positioned to play a central role in translational research and clinical development for the emerging immuno-oncology therapeutic paradigm. The availability of calibration and validation data from clinical trials from the first successful immuno-oncology therapies such as ipilimumab and nivolumab (including CA184004, MDX1106-03, CA209004, CA209009) facilitates comparison of the simulated outcomes with clinical data.
METHODS:
A multidisciplinary team developed the biological scope of a mechanistic, ODE-based simulation platform. The initial platform focuses on the interactions of multiple immune cell types, cancer cells, soluble mediators, cell-cell contact effects, as well as ipilimumab and nivolumab therapies within the microenvironment of a prototypical simulated lesion and effect on tumor shrinkage.
RESULTS:
The platform was calibrated, taking into account nivolumab and ipilimumab plasma concentrations, circulating absolute lymphocyte counts, trends in tumor cytokines, an IFNγ gene expression signal, changes in tumor infiltrating lymphocytes, and lesion size data. In agreement with clinical observations, an enhancement in lesion response was observed with the combination therapy.
CONCLUSION:
The platform recapitulates essential immune response pathways in a simulated lesion and exhibits qualitative agreement with patient response phenotypes to immuno-oncology agents. Having demonstrated proof-of-principle with a preliminary calibration, the platform will serve as a framework to facilitate biomarker identification, integrate additional therapeutic mechanisms, propose new combination strategies, and serve as a sub-model within a broader simulation framework for the cancer-immunity cycle.

LBII-12
INDEPENDENT VALIDATION OF THE EFFECT OF ABCC3 -211C>T GENOTYPE ON MORPHINE PHARMACOKINETICS.

R. Venkatasubramanian, J. Niu, T. Mizuno, K. Spruance, T. Fukuda, S. Sadhasivam, A. A. Vinks, C. Vidya; Cincinnati Childrens Hospital, Cincinnati, OH. **R. Venkatasubramanian:** None. **J. Niu:** None. **T. Mizuno:** None. **K. Spruance:** None. **T. Fukuda:** None. **S. Sadhasivam:** None. **A.A. Vinks:** None. **C. Vidya:** None.

BACKGROUND:
Morphine pharmacokinetics (PK) is a potential contributor to interindividual variability in morphine analgesia and adverse events. We recently showed that the C/C genotype of the -211C>T polymorphism of the hepatic metabolite transporter gene ATP-binding cassette ABCC3 had 40% higher Morphine-6-Glucuronide formation (M6G) than C/T+T/T genotypes [1]. In this study we aimed to validate the association between ABCC3 genotype and morphine PK.
METHODS:
After institutional IRB approval and informed consents, we enrolled 66 children aged 10-18 years, ASA 1-2, undergoing spine fusion in a prospective, genotype blinded study. All received morphine after surgery. Serial blood samples up to 100 min post morphine dose were obtained (n=250). Morphine, morphine-3-glucuronide (M3G) and M6G were recently quantified using liquid chromatography tandem mass spectrometry (after 9/8/14). Morphine, M3G and M6G PK were described by an allometric model using NONMEM.

RESULTS:
Morphine and metabolite PK was described using a five compartmental model with a distribution compartment for morphine and a hypothetical delay compartment to capture the lag in metabolite formation. Subjects with ABCC3 -211C>T polymorphism C/C+C/T genotype had significantly higher levels of M6G formation (~32%) than T/T genotypes (p T polymorphism C/C genotype had significantly higher M3G formation (~40%) than C/T+T/T genotypes ($p < 0.05$).
CONCLUSION:
Results from this study offer further independent validation that ABCC3 genotype significantly affects M3G and M6G formation clearance. Further studies are needed to evaluate the impact of altered PK of M6G which is known to be a more potent analgesic than morphine.
REFERENCES:
1) Pharmacogenomics 15 (10), 1297-1309 (2014)

LBII-13
HOW INFORMATIVE ARE DRUG-DRUG INTERACTIONS OF GENE-DRUG INTERACTIONS AND VICE VERSA?

C. Lagishetty,[1] J. Deng,[1] S. Schmidt,[1] L. J. Lesko,[1] H. Rogers[2]; [1]Center for Pharmacometrics and Systems Pharmacology, University of Florida, Orlando, FL, [2]US Food and Drug Administration Genomics and Targeted Therapy Group, Office of Clinical Pharmacology, Office of Translational Sciences, CDER, Silver Spring, MD, **C. Lagishetty:** 1. This research was sponsored by; **Company/Drug**; FDA ORISE Fellowship. **J. Deng:** None. **S. Schmidt:** None. **L. J. Lesko:** None. **H. Rogers:** 2. I am a paid consultant/employee for; **Company/Drug**; FDA.

BACKGROUND:
For US Food and Drug Administration-approved drugs, prescribing recommendations to manage CYP2D6-, CYP2C19- and CYP2C9-mediated drug-drug interactions (DDI) and gene-drug (GDI) interactions are typically similar. However, DDIs may not always reliably predict GDIs because the victim drug may have multiple metabolic pathways and the perpetrator drug may affect multiple enzymes or transporters. The objective of this study was to further investigate the circumstances under which DDIs can be used to confidently predict GDIs for prototypical victim drugs using physiologically based pharmacokinetic modeling (PBPK).
METHODS:
We investigated model substrates for CYP2D6 (metoprolol, dextromethorphan, atomoxetine, vortioxetine, eluglistat), CYP2C9 (warfarin, flurbiprofen, celecoxib) and CYP2C19 (omeprazole, clopidogrel). PK data were obtained for variant homozygotes (poor metabolism [PM] status) for GDIs and strong inhibitor studies for DDIs. In the first step, ratios of AUC and C_{max} of substrate drugs in the presence of DDI and GDI were calculated relative to normal, extensive metabolizers ([EMs]). The ratio, R, and 90% CI of 80-125% were used to evaluate concordance. Secondly, ***in vitro*** to ***in vivo*** extrapolation (***IVIVE***) in a PBPK framework using ***in vitro*** DDI or GDI information was used to predict clinical GDI and/or DDI (late analysis).
RESULTS:
R was within the 90% CI range for CYP2D6 substrates. However, CYP2C9 and CYP2C19 substrates showed an R outside this range. IVIVE using PBPK models for 2D6 substrates was able to predict GDI from DDI and vice versa.
CONCLUSION:
DDI for CYP2D6 generally predicts GDI and vice versa. However, CYP2C9 and 2C19 have discrepancies which are believed to be substrate, inhibitor or study related. PBPK models with IVIVE served as a powerful tool for making inference for 2D6 clinical DDI or GDI.

LBII-14

INTERPATIENT VARIATION IN OBSERVED PLASMA LEVEL OF NEW ORAL ANTICOAGULANTS RIVAROXABAN AND APIXABAN.

M. Gulilat, U. Schwarz, S. Morgan, C. Ross, S. LeMay, H. Vosper, G. Dresser, S. E. Gryn, R. B. Kim; Western University, London, ON, Canada. **M. Gulilat:** None. **U. Schwarz:** None. **S. Morgan:** None. **C. Ross:** None. **S. LeMay:** None. **H. Vosper:** None. **G. Dresser:** None. **S.E. Gryn:** None. **R.B. Kim:** None.

BACKGROUND:
Factor Xa Inhibitors (FXI), rivaroxaban and apixaban have become widely available for oral anticoagulant (OAC) therapy. Outside of clinical trials, the interpatient variation in drug response have not been assessed. Our study objectives were to examine the extent of interpatient variability in the plasma rivaroxaban and apixaban concentrations of patients with AF, for better identifying patients at risk for extreme drug response to FXIs.
METHODS :
In this cohort study we prospectively enrolled and collected a single blood sample from AF patients prescribed rivaroxaban and apixaban who are followed by our oral anticoagulation clinic. Interim analysis of enrolled subjects to date (rivaroxaban N=26, and apixaban N=33*) were carried out by measuring FXIs plasma levels using liquid chromatography-tandem mass spectrometry.
RESULTS:
In contrast to published rivaroxaban levels, in our patient cohort, we observed near 30-fold interpatient variation in rivaroxaban levels with nearly 50% of patients attaining a level greater than predicted 95th percentile. Apixaban plasma concentrations ranged from 57 to 443 ng/ml (7-fold variation) with a mean of 218 ng/ml (SD, 97).
CONCLUSION:
There is far greater variation in observed rivaroxaban plasma levels than currently reported, with a significant proportion of patients attaining higher than predicted plasma level. Observed apixaban plasma concentration appear to be less variable. We are currently enrolling additional patients with a goal of better delineating clinical as well as pharmacogenomic predictors of FXI response. Therapeutic monitoring of FXIs may prove to be an important strategy for OAC selection and dosing. Our findings have major clinical relevance to safe and effective utilization of newer OACs.
*2014/11/16

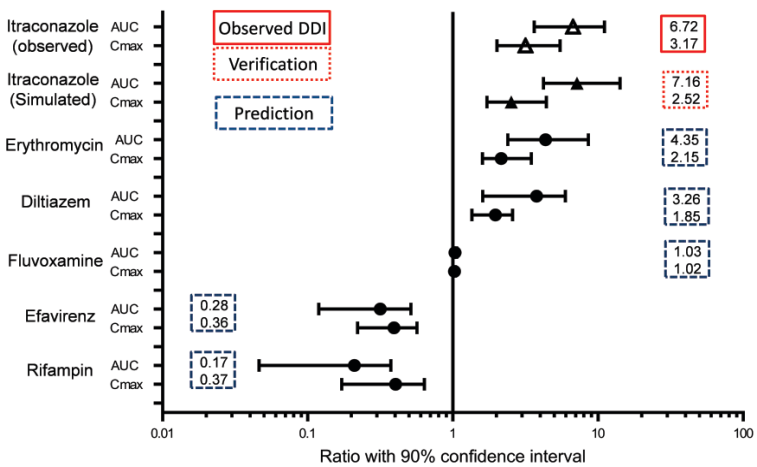
LBII-15

EVALUATION OF COBIMETINIB CYP3A MEDIATED DRUG INTERACTION POTENTIAL USING PHYSIOLOGICALLY-BASED PHARMACOKINETIC APPROACH.

N. Budha, T. Ji, L. Musib, S. Eppler, M. Dresser, Y. Chen, J. Jin; Genentech Inc., South San Francisco, CA. **N. Budha:** 1. This research was sponsored by; **Company/Drug**; Genentech Inc. 2. I am a paid consultant/employee for; **Company/Drug**; Genentech Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Cobimetinib. **T. Ji:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Cobimetinib. **L. Musib:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Cobimetinib. **S. Eppler:** 2. I am a paid consultant/employee for;

Company/Drug; Genentech Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Cobimetinib. **M. Dresser:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Cobimetinib. **Y. Chen:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Cobimetinib. **J. Jin:** 2. I am a paid consultant/employee for; **Company/Drug**; Genentech Inc. 6. The following product discussed is not labeled for the use under discussion or is still investigational; **Company/Drug**; Cobimetinib.

BACKGROUND:
The aim of this work was i) to develop a PBPK model for Cobimetinib (Cobi) that can accurately describe clinical PK and the effect of strong CYP3A inhibitor, itraconazole (ITZ) on cobi PK and ii) to predict the effect of other CYP3A inhibitors (moderate, weak) and inducers (strong, moderate) on Cobi PK.
METHODS:
The Simcyp Simulator with healthy volunteer population was used in all model development and application. ITZ, hydroxy-ITZ (ITZ metabolite) and Cobi PBPK models were optimized by matching simulated PK profiles to the PK profiles observed in clinical DDI Study. The verified PBPK model was then used to predict the effect of CYP3A inhibitors/inducers on Cobi PK.
RESULTS:
The verified Cobi and ITZ PBPK models were able to accurately capture the ITZ-Cobi DDI. The fraction of Cobi metabolized by CYP3A was estimated to be 78%. Simulations indicated that weak CYP3A inhibitors do not significantly affect Cobi PK. Moderate inhibitors increased Cobi AUC by 3 to 4-fold. Conversely, Cobi AUC is decreased by 72% and 83% in the presence of moderate and strong CYP3A inducers, respectively (Figure 1).
CONCLUSION:
The PBPK model accurately simulated DDI between Cobi and ITZ in healthy subjects. The verified PBPK model can be used to simulate the effect of other inducers and inhibitors of CYP3A on Cobi PK with higher confidence.



LBII-16

EXPECTED PERFORMANCE OF MODEL-BASED BAYESIAN DOSE OPTIMIZATION OF BUSULFAN IN PEDIATRIC CONDITIONING REGIMENS.

R. J. Keizer, J. Long-Boyle, R. Savic; University of California, San Francisco, San Francisco, CA
R.J. Keizer: 5. I am a significant stockholder for; **Company/Drug**; InsightRX. **J. Long-Boyle:** None. **R. Savic:** 5. I am a significant stockholder for; **Company/Drug**; InsightRX.

BACKGROUND:
Busulfan is used in conditioning regimens of hematopoietic cell transplantation (HCT) for various pediatric disorders. Because of large within- and between-patient variability and narrow therapeutic window, therapeutic drug monitoring (TDM) of busulfan is routinely performed. Dose personalization is commonly performed based on Css or AUC from non-compartmental pharmacokinetic (PK) analysis (NCA), but rarely using Bayesian model-based approaches (BMA). BMA could provide greater dose precision, attain target levels sooner than NCA, and require less sampling. Using simulations based on new clinical data, we compared BMA- to NCA-based optimization.
METHODS:
Busulfan dose advices were based on algorithms implemented on the InsightRX platform (www.insight-rx.com) and aimed to obtain Css levels of 750 ng/mL (=AUC of 1098 uM*min q6 hr). For both BMA and NCA, a target Css average over the treatment course ("A"), or for the next dose ("N") was defined. The population PK model was obtained from previous studies, while the dataset (Nov-2014) included new patients not included in the training dataset.
RESULTS:
MBA-A resulted in the lowest spread in average Css over the full treatment course, with a median average Css of 698 ng/mL (range 626-854), while NCA-A resulted in a Css of 775 ng/mL (range 584-1066). BMA-N reached an average Css of 732 ng/mL (range 506-948) and NCA-N 762 ng/ML (range 550-980).
CONCLUSION:
For busulfan dosing, particularly in young children, BMA are expected to improve targeted exposure and provide safer regimens. BMA-A provided the highest accuracy in dosing to achieve goal exposure, although on average Css in patients was slightly below target. More elaborate dose advice algorithms are currently being investigated.

LBII-17

POLYPHARMACY AMONG HOSPITALIZED PEDIATRIC CANCER PATIENTS.

J. E. Constance, A. Balch, E. Enioutina, C. Stockmann, M. Linakis, C. Sherwin, M. Spigarelli; University of Utah, Salt Lake City, UT. **J.E. Constance:** None. **A. Balch:** None. **E. Enioutina:** None. **C. Stockmann:** None. **M. Linakis:** None. **C. Sherwin:** None. **M. Spigarelli:** None.

BACKGROUND:
Very little information exists on the degree of polypharmacy among hospitalized children. Pediatric patients being treated for suspected or confirmed bacterial infections with IV antibiotics represent a complex patient population where drug exposure from multiple agents is known to be high and the risk of drug-drug interactions poorly understood. The objective of this study was to determine the drug exposure per hospitalization among pediatric cancer patients receiving IV vancomycin or meropenem antibiotic therapy.

METHODS:
Complete co-medication data was not available until after September 8, 2014, and were analyzed in November 2014. Patients ≤18 years of age hospitalized at one or more of 22 hospitals located in the Intermountain West receiving ≥2 doses of IV vancomycin or meropenem for the complete years of 2006 to 2012 were retrospectively evaluated using an EMR database. IV fluids, parenteral nutrition, vitamins, and heparin were excluded. Cancer diagnoses were derived from a validated hospital registry. Statistical analyses were performed in Prism 6 (GraphPad) and R.
RESULTS:
There were 294 patients with cancer and 5,834 patients without cancer representing 7,749 total hospitalizations over the study period. Patients with cancer received more drugs per hospitalization (median, IQR; 20, 10-37) compared to non-cancer patients (16, 8-29; $p<0.0001$). The overall top ten ranked medications used in patients with cancer (which differed from those without cancer) by dose volume, experienced a year-to-year trend ($p<0.0001$) toward fewer doses per patient.
CONCLUSION:
Over the study period, cancer patients were exposed to more drugs per hospitalization than their counterparts without cancer. However, among the most frequently used agents in cancer patients, there was a consistent pattern of fewer doses being administered over time.

LBII-18
RENAL FUNCTION DESCRIPTORS IN NEONATES: WHICH CREATININE-BASED EQUATION BEST DESCRIBES VANCOMYCIN CLEARANCE?

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BACKGROUND:
Glomerular function develops rapidly in the first month of life. Several estimated glomerular filtration rate (eGFR) equations have been applied to estimate the rate of clearance (CL) of renally-excreted drugs. This study aimed to compare eGFR with reference values and analyze their influence on vancomycin CL.
METHODS:
Data were collected for neonates (3-30 days postnatal age; PNA) with ≥1 vancomycin serum concentration(s). Complete data could not be analyzed before September 8, 2014. A population PK model was constructed using NONMEM 7.2. eGFR was calculated using creatinine (Cr)-based equations from modified Schwartz (1), Leger (2), Pottel (3), and British Columbia's Children's Hospital (4) equations. Reference eGFR values were derived from Cr.

RESULTS:
A total of 528 neonates contributed vancomycin 6,121 concentrations. The median gestational age (GA) was 29 (IQR 25-36) weeks. Schwartz equation provided comparable results with reference values in preterm neonates, i.e. 24.4 (20.6-26.6) mL/min/1.73 m2 at 14 days PNA in 29 weeks GA infants. In contrast, elevated eGFR were obtained: 46.7±18.2 (2), 52.8±21.5 (3), and 44.9± 17.6 (4) mL/min/1.73 m2. These were close to the values using equations based on cystatin C. Vancomycin PK was analyzed using a one-compartment model with first-order elimination. Weight, postmenstrual age, and eGFR were significant covariates for CL. Between-subject variability decreased by 38.3% with the inclusion of eGFR alone. Although Schwartz equation contributed the best fit, estimated CL (0.13 ± 0.1 L/hr/kg) across the eGFR equations were in reasonable agreement with literature values.
CONCLUSION:
Inclusion of eGFR can be used to estimate vancomycin CL. The modified Schwartz equation was the best predictor of vancomycin CL in this neonatal population.

LBII-19
SEMIMECHANISTIC PHARMACOKINETIC-ENZYME TURNOVER MODEL FOR RIFAPENTINE AUTOINDUCTION.

J. E. Hibma,[1] K. Dooley,[2] R. M. Savic[1]; [1]UCSF, San Francisco, CA, [2]Johns Hopkins University, Baltimore, MD, **J.E. Hibma:** None. **K. Dooley:** None. **R.M. Savic:** None.

BACKGROUND:
Rifapentine (RPT) is a longer-acting and more potent rifamycin compared to the first-line anti-tuberculosis (TB) agent, rifampin. A quantitative understanding of RPT's autoinduction properties is required to optimally design RPT-containing TB regimens. In this study, we pool data and information from several clinical studies to establish the link between RPT plasma concentrations and the magnitude and duration of autoinduction, with the ultimate goal to improve cure rates and reduce drug resistance.
METHODS:
Population analysis and nonlinear-mixed effect modeling were used to integrate and analyze pharmacokinetic data from patients and healthy volunteers receiving daily, weekly or intermittent RPT, e.g., RIFAQUIN trial (Jindani, A., N Engl J Med. 2014 Oct 23;371(17):1599-608). Basic model structure and various absorption models were fit to parent-drug and metabolite data. Linear and nonlinear models were evaluated to test the effect of time and concentrations on RPT pharmacokinetics.
RESULTS:
Using a semi-mechanistic enzyme turnover model, a nonlinear relationship was demonstrated for RPT plasma concentration and the rate of enzyme producton. The typical (%R.S.E) E_{max} and EC50 were estimated to be 205% (18%) and 3.5 mg/L (20%), respectively. The turnover half-life, estimated as 25 days, predicts approximately 2.8 months to reach 90% of the maximally induced state in a typical patient.
CONCLUSION:
A RPT integrated model is developed that represents a tool for evaluation of alternative dosing schedules and regimens, as well as simulation of future clinical trials and evaluation of clinical trial designs. Further optimization of the model using all available data, including the effect of covariates on RPT autoinduction, is ongoing.

LBII-20

MODEL-BASED NEUTROPHIL-GUIDED DOSE SELECTION OF SGI-110, A SECOND GENERATION HYPOMETHYLATING AGENT (HMA), IN THE TREATMENT OF ACUTE MYELOID LEUKEMIA (AML) PATIENTS.

C. Xu,[1] X. Su,[2] J. Issa,[3] H. Kantarjian,[4] G. Roboz,[5] T. Goggin[1]; [1]Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, [2]Astex Pharmaceuticals Inc., Dublin, CA, [3]Temple University, Philadelphia, PA, [4]MD Anderson Cancer Center, Houston, TX, [5]Weill Cornell Medical College, New York, NY, **C. Xu:** 2. I am a paid consultant/employee for; **Company/Drug**; Otsuka Pharmaceutical Development & Commercialization, Inc. **X. Su:** 2. I am a paid consultant/employee for; **Company/Drug**; Astex Pharmaceuticals Inc. **J. Issa:** None. **H. Kantarjian:** None. **G. Roboz:** None. **T. Goggin:** 2. I am a paid consultant/employee for; **Company/Drug**; Otsuka Pharmaceutical Development & Commercialization, Inc.

BACKGROUND:
SGI-110 is a dinucleotide of decitabine (DAC) and deoxyguanosine delivered as a subcutaneous (SC) injection that yields longer half-life and more extended DAC exposure than DAC IV infusion. Neutropenia is the major dose limiting toxicity, but difficult to evaluate due to the pancytopenia associated with the disease. A population kinetic-pharmacodynamic (K-PD) model that describes the relationship between SGI-110 dose and neutrophil counts was developed to aid dose selection.

METHODS:
Serial absolute blood neutrophil counts (ANC) were obtained from 121 Myelodysplastic Syndrome (MDS) and 248 AML patients given four different 28 day schedules of SC SGI-110 at doses of 3-125 mg/m2 per day. K-PD models with an inhibition of synthesis rate or a stimulation of degradation rate were tested. Simulations of ANC following 3 cycles of 60 and 90 mg/m2 5-day (Daily×5) or 10-day (Days 1-5 and 8-12) regimens in a typical patient were performed. Data analysis was completed on October 31, 2014.

RESULTS:
An inhibitory E_{max} model described the dataset. The lag time estimated to ~7 days was applied accounting for the delay in the onset of drug effect indicating that SGI-110 is impacting on pre-cursors of mature neutrophils probably in the bone marrow. The EKD50 was estimated to 14.7 mg/m2. Hill coefficient was estimated to 2.47 and fixed in the final model. Empirical Bayesian Estimations of EKD50 were not different in different disease populations. Simulated ANC following 60 mg/m2 on days 1-5 of a cycle were between 200 to 500/μl with partial recovery before the next cycle. The nadir of 90 mg/m2 on the same schedule was below 200/μl. Neutrophil counts following 60 mg/m2 10-day regimen were completely suppressed below 200/μl throughout all subsequent treatment.

CONCLUSION:
Simulations support 5-day regimen of 60 mg/m2 for phase III trial in treatment naive AML not candidate for intensive induction chemotherapy.

LATE-BREAKING/ENCORE ABSTRACTS POSTER WALK

THURSDAY, MARCH 5
5:30 pm – 6:15 pm
ELITE ATRIUM

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

LBPW-1

RESULTS FROM THE IQ-CSRC PROSPECTIVE STUDY SUPPORT REPLACEMENT OF THE THOROUGH QT STUDY BY QT ASSESSMENT IN THE EARLY CLINICAL PHASE.

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BACKGROUND:
As recommended by the ICH E14 guideline, new drugs with systemic availability typically are assessed in a so-called thorough QT study in healthy subjects. If an alternative way of QT assessment could be incorporated into a routinely performed early phase clinical pharmacology study, this would present not only a more efficient approach, but also allow improved understanding of a drug's QT liability early in clinical development.
METHODS:
The QT effects of 5 'QT positive' and one negative drug were tested to evaluate whether exposure-response analysis can detect and exclude QT effects in a small study with healthy subjects. Each drug was given to nine subjects (six for placebo) in two dose levels; for the positive drugs chosen to cause 10 to 12 ms and 15 to 20 ms QTcF prolongation.

RESULTS:
The slope of the concentration/ΔQTc effect was significantly positive for ondansetron, quinine, dolasetron, moxifloxacin and dofetilide and an effect above 10 ms could not be excluded for the lower dose, i.e., the upper bound of the confidence interval for the predicted mean ΔΔQTcF effect was above 10 ms. For the negative drug, levocetirizine, a ΔΔQTcF effect above 10 ms was excluded at six-fold the therapeutic dose.
CONCLUSION:
The study provides evidence that robust QT assessment in early phase clinical studies can replace the thorough QT study.

LBPW-2

GENETIC VARIANT IN FOLATE HOMEOSTASIS IS ASSOCIATED WITH LOWER WARFARIN DOSE IN AFRICAN AMERICANS.

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BACKGROUND:
The anticoagulant warfarin has >30 million prescriptions per year in the United States. Doses can vary 20-fold between patients, and incorrect dosing can result in serious adverse events. Variation in warfarin pharmacokinetic and pharmacodynamic genes, such as *CYP2C9* and *VKORC1*, do not fully explain the dose variability in African Americans. In this study, we sought to discover novel associations between genetic factors in African Americans and warfarin dose.
METHODS:
To identify additional genetic contributors to warfarin dose, we exome sequenced 103 African Americans on stable doses of warfarin at extremes (≤35 and ≥49 mg/week). We replicated our findings in an independent cohort of 372 African American subjects whose stable warfarin doses represented the full dosing spectrum.
RESULTS:
We found an association between lower warfarin dose and a population-specific regulatory variant, rs7856096 ($P = 1.82 \times 10^{-8}$, minor allele frequency = 20.4%), in the folate homeostasis gene folylpolyglutamate synthase (*FPGS*) and replicated this association in ($P = .046$). In a combined cohort, adding rs7856096 to the International Warfarin Pharmacogenetic Consortium pharmacogenetic dosing algorithm resulted in a 5.8 mg/week ($P = 3.93 \times 10^{-5}$) decrease in warfarin dose for each allele carried. The variant overlaps functional elements and was associated ($P = .01$) with *FPGS* gene expression in lymphoblastoid cell lines derived from combined HapMap African populations (N = 326).
CONCLUSION:
Our results provide the first evidence linking genetic variation in folate homeostasis to warfarin response.

LBPW-3

CARBOXYLESTERASE 1 C.428G>A SINGLE NUCLEOTIDE VARIATION INCREASES THE ANTIPLATELET EFFECTS OF CLOPIDOGREL BY REDUCING ITS HYDROLYSIS IN HUMANS.

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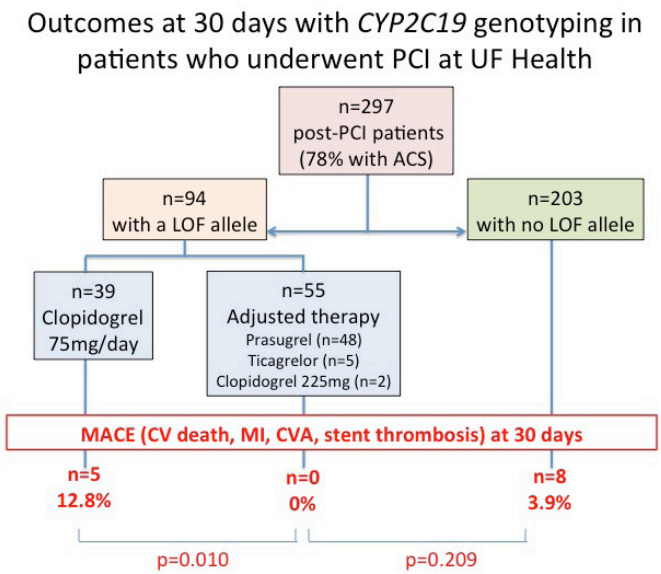
BACKGROUND:
Carboxylesterase 1 (CES1) hydrolyses about 90% of the prodrug clopidogrel to an inactive carboxylic acid metabolite. ***In vitro*** studies have shown that ***CES1*** single nucleotide variations (SNV), such as c.428G>A (p.Gly143Glu, rs71647871), can markedly affect clopidogrel metabolism.
METHODS:
We studied the pharmacokinetics and pharmacodynamics of a 600 mg oral dose of clopidogrel in 10 carriers and 12 noncarriers of the ***CES1*** c.428G>A SNV. Clopidogrel and its carboxylic acid, acyl-β-D-glucuronide, and active ***cis*** 5-thiol metabolite plasma concentrations and platelet aggregation were measured for up to 12 hours.
RESULTS:
The clopidogrel carboxylic acid to clopidogrel area under the plasma concentration-time curve from 0 h to infinity ($AUC_{0-\infty}$) ratio was 53% smaller in ***CES1*** c.428G/A carriers than in noncarriers (***P***=0.009), indicating impaired hydrolysis of clopidogrel. Consequently, the $AUC_{0-\infty}$ of clopidogrel and its active ***cis*** 5-thiol metabolite were 123% (***P***=0.004) and 67% (***P***=0.009) larger in the c.428G/A carriers than in noncarriers. Consistent with the pharmacokinetic findings, both the average inhibition of $P2Y_{12}$-mediated platelet aggregation 0-12 h after clopidogrel intake and the maximum observed platelet inhibition were 19 percentage points higher in the c.428G/A carriers than in noncarriers (***P***=0.036 and ***P***=0.041, respectively).
CONCLUSION:
Clopidogrel pharmacokinetics is highly sensitive to genetic variation in CES1 activity, indicating that clopidogrel can be used as a CES1 probe substrate in humans. The ***CES1*** c.428G>A SNV increases clopidogrel active ***cis*** 5-thiol metabolite concentrations and antiplatelet effects by reducing the hydrolysis of parent clopidogrel to inactive metabolites. Therefore, the ***CES1*** c.428A allele may increase clopidogrel efficacy and bleeding risk.

LBPW-4

FEWER CARDIOVASCULAR EVENTS AFTER PERCUTANEOUS CORONARY INTERVENTION WITH GENOTYPE-GUIDED ANTIPLATELET THERAPY: RESULTS FROM THE UF HEALTH PERSONALIZED MEDICINE PROGRAM.

L. H. Cavallari, O. Magvanjav, R. David Anderson, A. Owusu-Obeng, B. Kong, T. Vo, J. N. Ashton, B. J. Staley, A. R. Elsey, R. M. Cooper-Dehoff, K. W. Weitzel, M. J. Clare-Salzler, D. R. Nelson, J. A. Johnson; University of Florida, Gainesville, FL
L.H. Cavallari: None. **O. Magvanjav:** None. **R. David Anderson:** None. **A. Owusu-Obeng:** None. **B. Kong:** None. **T. Vo:** None. **J.N. Ashton:** None. **B.J. Staley:** None. **A.R. Elsey:** None. **R.M. Cooper-Dehoff:** None. **K.W. Weitzel:** None. **M.J. Clare-Salzler:** None. **D.R. Nelson:** None. **J.A. Johnson:** None.

BACKGROUND:
Clopidogrel is bioactivated by CYP2C19, and data show reduced clopidogrel effectiveness with the *CYP2C19* loss-of-function (LOF) genotype, especially after percutaneous coronary intervention (PCI) and stent placement. We examined whether clinical implementation of CYP2C19 genotype-guided antiplatelet therapy (APT) reduces the risk for major adverse cardiovascular events (MACE) after PCI.
METHODS:
CYP2C19 genotyping post-PCI was implemented at University of Florida Health Shands Hospital in July 2012, with alternative APT recommended for LOF allele carriers. Patient characteristics and MACE at 30 days per medical record review were compared between LOF allele carriers switched or not switched to alternative APT and between LOF allele carriers switched to alternative APT and non-LOF allele carriers using the Student's unpaired t-test or Fisher's exact test. Collection of 30-day outcomes was completed in September 2014.
RESULTS:
A total of 297 patients genotyped through August 2014 had follow-up data. Baseline characteristics were similar between LOF allele carriers with or without an APT change. In LOF allele carriers, switching to alternative APT resulted in less MACE (figure).
CONCLUSION:
Clinical implementation of CYP2C19-guided APT for patients undergoing PCI is associated with reduced occurrence of MACE at 30 days.



LBPW-5

GLUCURONIDATION CONVERTS CLOPIDOGREL TO A STRONG METABOLISM-DEPENDENT INHIBITOR OF CYP2C8: A PHASE II METABOLITE AS A CAUSE OF DRUG-DRUG INTERACTIONS.

A. Tornio, A. M. Filppula, O. Kailari, M. Neuvonen, T. H. Nyrönen, T. Tapaninen, P. J. Neuvonen, M. Niemi, **J. T. Backman**; University of Helsinki, Department of Clinical Pharmacology, Helsinki, Finland. **A. Tornio:** None. **A.M. Filppula:** None. **O. Kailari:** None. **M. Neuvonen:** None. **T.H. Nyrönen:** None. **T. Tapaninen:** None. **P.J. Neuvonen:** None. **M. Niemi:** None. **J.T. Backman:** None.

BACKGROUND:
Cerivastatin and repaglinide are substrates of CYP2C8, CYP3A4, and OATP1B1. An increased risk of rhabdomyolysis in patients using cerivastatin with clopidogrel has been reported, warranting further studies on clopidogrel interactions.
METHODS:
Nine healthy volunteers received clopidogrel 300 mg on day one, followed by 75 mg daily for two days or placebo in a cross-over study. Repaglinide was given 1 h after clopidogrel intake on days one and three, and after placebo. The effects of clopidogrel and its metabolites on CYP2C8 and CYP3A4 were studied ***in vitro***. A physiologically-based pharmacokinetic model was constructed in Simcyp and computational docking simulations were performed.
RESULTS:
In humans, the $AUC_{(0-\infty)}$ of repaglinide was increased 5.1- and 3.9-fold compared to control on days one and three of the clopidogrel treatment ($P<0.001$). *In vitro,* clopidogrel acyl-β-D-glucuronide was as a potent time-dependent inhibitor of CYP2C8. A physiologically based pharmacokinetic model indicated that inactivation of CYP2C8 by clopidogrel glucuronide leads to uninterrupted 60-85% inhibition of CYP2C8 during daily clopidogrel treatment. Computational modeling resulted in docking of clopidogrel acyl-β-D-glucuronide at the CYP2C8 active site with its thiophene moiety close to heme.
CONCLUSION:
Clopidogrel markedly increases the plasma concentrations of repaglinide due to strong inhibition of CYP2C8 by its acyl-β-D-glucuronide. Glucuronide metabolites should be considered potential inhibitors of CYP enzymes.

JOURNALS

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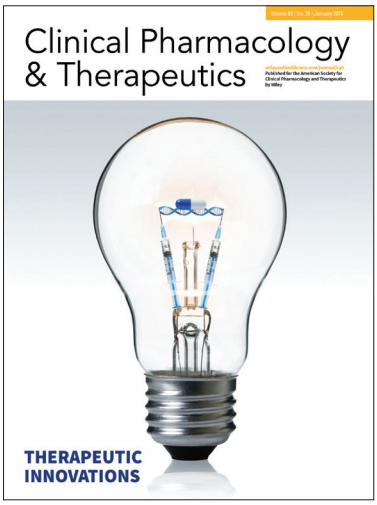

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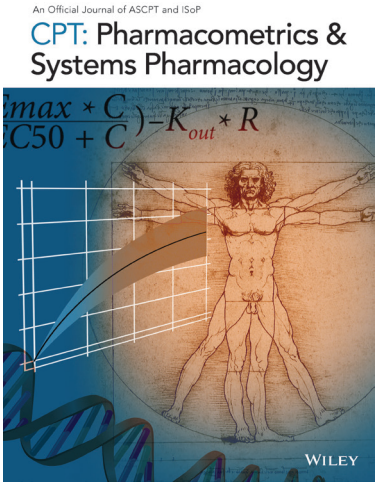

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