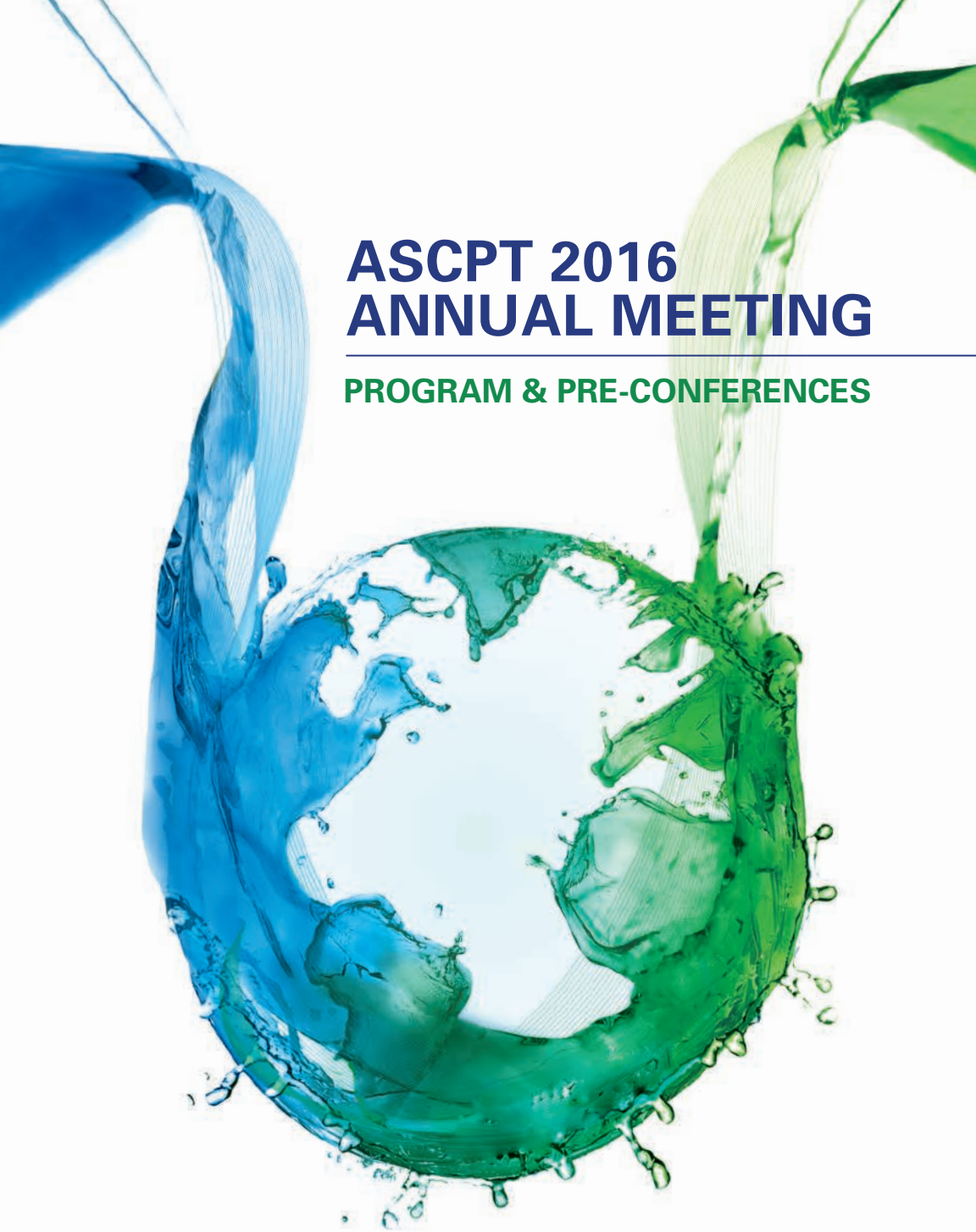

ASCPT 2016 ANNUAL MEETING

PROGRAM & PRE-CONFERENCES

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

ADVANCING THERAPEUTIC HORIZONS THROUGH GLOBAL COLLABORATIONS

ASCPT
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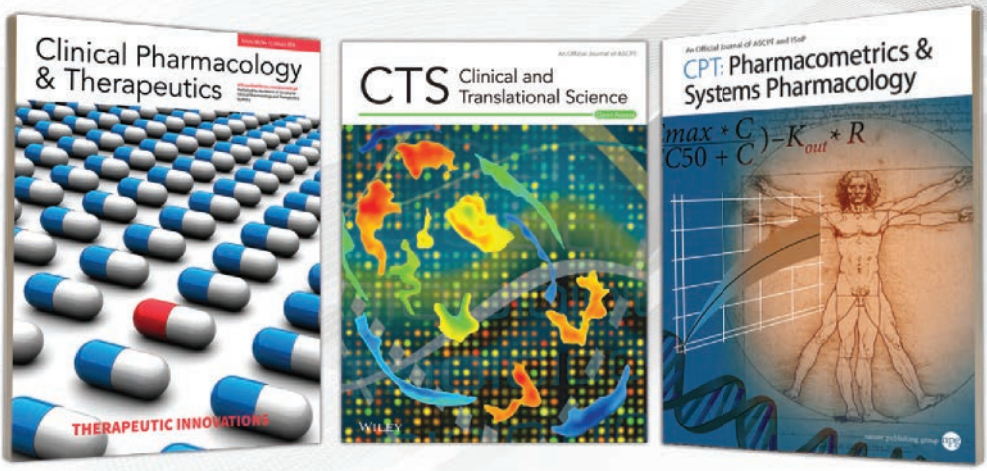
The ASCPT Journal Family is Growing



WILEY

ASCPT relaunched the new and improved *Clinical and Translational Science* as an **online-only, Open Access** journal in **January 2016**

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WELCOME MESSAGE

Dear Colleague,

Welcome to San Diego and to the 117th Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics (ASCPT), the premier scientific event for scientists in clinical pharmacology and translational medicine.

With a theme of *Advancing Therapeutic Horizons Through Global Collaborations,* ASCPT 2016 features two outstanding Pre-conference programs, along with two exciting partnership offerings: the Asia Pacific Symposium, *Racial and Ethnic Differences in Drug Response*, with colleagues from Japan and Korea and, in partnership with the Pharmacogenomics Research Network, a half-day program entitled *Scientific Horizons and Opportunities in Pharmacogenomics Research*.

ASCPT 2016 includes three excellent State of the Art lectures by Anne Wojcicki, 23andMe, Dan Hartman, MD, Bill and Melinda Gates Foundation, and Alice T. Shaw, MD, PhD, Harvard Medical School, Massachusetts General Hospital. Featured speakers include Micheline Piquette-Miller, PhD, University of Toronto, and Dan Roden, MD, Vanderbilt University.

ASCPT will honor those who have made remarkable contributions in the fields of clinical pharmacology and translational medicine. This year's award recipients are Peter K. Honig, MD, MPH; Minoli A. Perera, PharmD, PhD; Liewei Wang, MD, PhD; Brian L. Strom, MD, MPH; Kenneth Thummel, PhD; Joseph T. Hanlon, PharmD, Shiew-Mei Huang, PhD; and Scott A. Waldman, MD, PhD.

Special events are planned specifically for our student and trainee attendees, including the Career Bootcamp, Speed Mentoring, Trainee Luncheon, and a special session, "*Pursuing the Management Track in a Scientific Organization, Learn From the Experts.*"

We will feature more than 350 Scientific Posters, Symposia, Workshops, Roundtables, Science at Sunrise Sessions, and a Bioinnovation Forum. Our Exhibit Hall will showcase a wide range of products and services for our Annual Meeting attendees.

There will be a whole host of networking opportunities throughout the Annual Meeting, so I encourage you to take advantage of these sessions to meet new colleagues and connect with friends. We will be co-hosting the President's Networking Reception with the PhRMA Foundation as we join them in celebrating 50 years of supporting research and early career endeavors of scientists in drug discovery and development!

Please join me in thanking the people who have made this meeting possible, including the Scientific Program Committee, under the outstanding leadership of Mark J. Dresser, PhD, the leaders of the Networks, Anne C. Heatherington, PhD, Michelle Rudek, PharmD, PhD, and Lei Zhang, PhD, as well as our Community Leaders, who provided the scientific and creative energy for this Annual Meeting.

Finally, I encourage you to make the most of your time here in San Diego with the many learning and networking opportunities available and thank you for attending ASCPT 2016!

Sincerely,

Mario L. Rocci, Jr., 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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TUESDAY, MARCH 8, 2016

7:00 am – 3:00 pm	Pre-conference Registration	Indigo Foyer
8:00 am – 5:30 pm	PRE-CONFERENCES	
	Challenges in Global Drug Development and Regulation	Aqua A-C
	Quantitative Translational Approaches in Oncology	Aqua D-F
12:15 pm – 1:30 pm	Challenges in Global Drug Development Pre-conference Lunch	Aqua Foyer/Aqua ABC
12:15 pm – 1:45 pm	Quantitative Translational Approaches Pre-conference Lunch	Sapphire Foyer/Terrace
1:00 pm – 5:00 pm	*CPT* Associate Editors Meeting *(By Invitation Only)*	Indigo 202A
5:30 pm – 7:30 pm	PGRN Meeting *(By Invitation Only)*	Indigo 202B

WEDNESDAY, MARCH 9, 2016

7:00 am – 5:00 pm	ASCPT Central and Registration Open	Indigo Foyer
7:00 am – 9:00 am	Board of Directors Meeting (By Invitation Only)	Aqua Boardroom
8:00 am – 12:00 noon	*PSP* Associate Editors Meeting *(By Invitation Only)*	Indigo 202A
	CTS Associate Editors Meeting *(By Invitation Only)*	Indigo 202B
8:00 am – 2:00 pm	CAREER BOOTCAMP *(Ticket Required)*	Aqua A/B
	SPECIAL SESSION	Indigo A/E
	Scientific Horizons and Opportunities in Pharmacogenomics Research (PGRN) (Pre-registration Required)	
10:00 am – 12:00 noon	SPECIAL SESSION	Indigo D
	ASCPT/Asia Pacific Symposium: *Racial/Ethnic Differences in Drug Response*	
11:30 am – 1:00 pm	Network & Community Steering Committee Meeting *(By Invitation Only)*	Aqua 300

SCHEDULE-AT-A-GLANCE

WEDNESDAY, MARCH 9, 2016

1:00 pm – 2:00 pm	New Member Welcome	Aqua 310
2:00 pm – 2:30 pm	Awards Reception *(By Invitation Only)*	Indigo 202B
2:30 pm – 3:30 pm	Opening Session	Indigo BCFG
3:30 pm – 4:30 pm	STATE OF THE ART LECTURE *Anne Wojcicki*	Indigo BCFG
4:30 pm – 6:30 pm	Opening Reception *(Sponsored by Genentech)*	Sapphire Ballroom
	Exhibits, Late-breaking & Encore Posters	Sapphire Ballroom
4:45 pm – 5:45 pm	Showcase of Top Trainee Abstracts	Sapphire Ballroom/ ASCPT Theater
5:45 pm – 6:30 pm	POSTER WALK *Essential Tools for Precision Medicine*	Sapphire Foyer

THURSDAY, MARCH 10, 2016

7:00 am – 5:00 pm	ASCPT Central and Registration Open	Indigo Foyer
7:00 am – 8:00 am	Infectious Diseases (INF) Community Meeting	Aqua 300
7:00 am - 9:00 am	American Board of Clinical Pharmacology (ABCP) Board Meeting *(By Invitation Only)*	Elevation
7:30 am – 9:00 am	ROUNDTABLE *How Should Simulated DDI Results be Communicated in the Label?*	Indigo A/E
	CPT Editorial Board Meeting *(By Invitation Only)*	Indigo H
	PSP Editorial Board Meeting *(By Invitation Only)*	Aqua A/B
8:00 am – 9:00 am	BioTelemetry Research Product Theater	Aqua 310
9:15 am – 10:15 am	STATE OF THE ART LECTURE *Dan Hartman, MD*	Indigo BCFG
10:30 am – 11:30 am	RAWLS-PALMER PROGRESS IN MEDICINE AWARD LECTURE *Kenneth E. Thummel, PhD*	Indigo BCFG

THURSDAY, MARCH 10, 2016

10:30 am – 12:30 pm	SYMPOSIA	
	Characterizing Dose/Exposure Response of Biologics: Are We There Yet?	Indigo A/E
	Epigenetic Biomarkers and Modifications in Clinical Pharmacology	Indigo D
11:00 am – 12:00 noon	International Transporter Consortium (ITC) Community Meeting	Aqua 310
11:30 am – 6:30 pm	EXHIBIT AND POSTER HALL OPEN	Sapphire Ballroom
12:00 noon – 1:00 pm	Covance Hosted Event	Aqua 300
12:00 noon – 1:30 pm	Lunch Available for Purchase in the Poster and Exhibit Hall *(Ticket Required)*	Sapphire Ballroom
	Trainee Luncheon *(Ticket Required)*	Aqua A-F
	ASCPT Finance Committee Meeting *(By Invitation Only)*	Aqua Boardroom
1:00 pm – 2:00 pm	FEATURED SPEAKER	Indigo BCFG
	Dan Roden, MD	
1:00 pm – 2:30 pm	WORKSHOPS	
	Pediatric Dose Selection for Pediatric-Specific Diseases	Indigo A/E
	Discovery and Development of First-in-Class Drugs That Target Membrane Transporters	Indigo D
2:00 pm – 3:30 pm	SPECIAL SESSION	Indigo BCFG
	Bioinnovation Forum	
3:00 pm – 4:00 pm	Systems Pharmacology (SP) Community Meeting	Aqua 300
3:00 pm – 4:00 pm	Pharmacogenomics (PMG) Community Meeting	Aqua 310
3:00 pm – 5:00 pm	DEVELOPMENT, REGULATORY & OUTCOMES (DRO) NETWORK MEETING	Indigo H
3:30 pm – 4:30 pm	ORAL SESSION	Indigo A/E
	Old Players, New Game	

SCHEDULE-AT-A-GLANCE

THURSDAY, MARCH 10, 2016

4:00 pm – 5:30 pm	UCSF/Stanford/Genentech Reception *(By Invitation Only)*	Aqua ABC
4:30 pm – 6:30 pm	President's Networking Reception *(Co-Sponsored by the PhRMA Foundation)*	Sapphire Ballroom
	POSTER SESSION *Quantitative Pharmacology (QP)*	Sapphire Ballroom
4:45 pm – 5:30 pm	POSTER WALK *Mechanisms Behind Special Populations: What Makes Them So Special*	Sapphire Foyer
5:00 pm – 6:00 pm	Pharmacometabolomics (PM) Community Meeting	Aqua 300
5:30 pm – 6:15 pm	POSTER WALK *Novel Modeling Approaches to Solve Old Problems: PK, DDI, Toxicity*	Sapphire Foyer
6:00 pm – 7:30 pm	Donor Reception *(By Invitation Only)*	Elevation
8:00 pm – 9:00 pm	Gavel Club Dessert Reception *(By Invitation Only)*	President's Suite

FRIDAY, MARCH 11, 2016

7:00 am – 5:00 pm	ASCPT Central and Registration Open	Indigo Foyer
7:00 am – 2:00 pm	EXHIBIT AND POSTER HALL OPEN	Sapphire Ballroom
7:00 am – 8:00 am	Oncology (ONC) Community Meeting	Aqua 310
7:00 am – 9:00 am	Breakfast in Exhibit Hall	Sapphire Ballroom
7:00 am – 9:00 am	POSTER SESSION *Translational and Precision Medicine* (TPM) and *Development, Regulatory, and Outcomes* (DRO)	Sapphire Ballroom
	QUANTITATIVE PHARMACOLOGY (QP) NETWORK MEETING	Indigo H

FRIDAY, MARCH 11, 2016

7:15 am – 8:00 am	POSTER WALK *Translational Determinants of Toxicity*	Sapphire Foyer
7:30 am – 9:00 am	SCIENCE AT SUNRISE SESSION *Use of Medications During Pregnancy and Breastfeeding: Maternal, Fetal, and Neonatal*	Indigo A/E
	ROUNDTABLE SESSION *Food for Thought: Need, Timing, and Labelling Implications for Clinical Food Effect Studies*	Indigo D
	CTS Editorial Board Meeting *(By Invitation Only)*	Aqua A/B
8:00 am – 9:00 am	Quotient Clinical Product Theater	Aqua 300
9:15 am – 10:15 am	STATE OF THE ART LECTURE *Alice T. Shaw, MD, PhD*	Indigo BCFG
10:30 am – 11:30 am	OSCAR B. HUNTER MEMORIAL AWARD IN THERAPEUTICS LECTURE *Brian L. Strom, MD, MPH*	Indigo BCFG
10:30 am – 12:30 pm	SYMPOSIA	
	Don't Do Different Things… Do Things Differently! Drug Development in Rare Diseases	Indigo A/E
	The Path of Effective Treatments for Alzheimer's Disease: From the Bench to the Clinic	Indigo D
11:30 am – 1:00 pm	Clinical Pharmacology Program Directors Meeting *(By Invitation Only)*	Aqua E/F
11:45 am – 1:15 pm	Speed Mentoring *(Ticket Required)*	Aqua ABCD
12:00 noon – 1:00 pm	OmniComm Systems, Inc. Product Theater	Sapphire Ballroom Theater

SCHEDULE-AT-A-GLANCE

FRIDAY, MARCH 11, 2016

12:00 noon – 1:30 pm	Lunch Available for Purchase in the Poster and Exhibit Hall *(Ticket Required)*	Sapphire Ballroom
1:00 pm – 2:00 pm	FEATURED SPEAKER *Micheline Piquette-Miller, PhD*	Indigo BCFG
1:00 pm – 2:00 pm	Special Populations (SPO) Community Meeting	Aqua 310
1:00 pm – 2:30 pm	WORKSHOPS	
	Rationale Development of Combination Cancer Immunotherapy through Collaborations	Indigo A/E
	Quantitative Systems Pharmacology: A Case for Disease Models	Indigo D
2:15 pm – 3:15 pm	LEON I. GOLDBERG EARLY INVESTIGATOR AWARD LECTURE *Minoli A. Perera, PharmD, PhD* *Liewei Wang, MD, PhD*	Indigo BCFG
2:45 pm – 4:45 pm	SYMPOSIUM *Benefit/Risk Optimization in the Confirmatory Space and Beyond: Myths, Reality and Possibilities*	Indigo A/E
3:00 pm – 4:00 pm	Drug Utilization & Outcomes (DUO; formerly SAF) Community Meeting	Aqua 310
3:00 pm – 5:00 pm	TRANSLATIONAL & PRECISION MEDICINE (TPM) NETWORK MEETING	Indigo H
5:00 pm – 6:00 pm	Biologics Community Meeting	Aqua 300

SATURDAY, MARCH 12, 2016

7:00 am – 10:00 am	ASCPT Central and Registration Open	Indigo Foyer
7:00 am – 9:00 am	ASCPT Board of Directors Meeting *(By Invitation Only)*	Elevation
7:30 am – 9:00 am	SPECIAL EDUCATION SESSION	Aqua A/B
	Pursuing the Management Track in a Scientific Organization: Learn From the Experts	
	SCIENCE AT SUNRISE SESSION	Indigo A
	Genome Wide Association Studies Reveal Important Transporter Polymorphisms as Biomarkers for Pharmacokinetics and Pharmacodynamics	
9:00 am – 10:00 am	ORAL SESSIONS	
	Advances in Model Based Drug Development: Application to Translational Medicine	Indigo D
	Pharmacogenomics: From Discovery to Implementation	Indigo H
10:15 am – 11:45 am	WORKSHOPS	
	Dose Selection for Biologics Combination Therapies	Indigo D
	Lessons Learned from Failed Pediatric Trials	Indigo H
10:15 am – 12:15 pm	SYMPOSIA	
	Adherence: Assessing and Mitigating the Perpetual Fly in the Ointment in Drug Development and Utilization	Indigo A
	Clinical and Translational Pharmacology of Emerging Modalities of Therapeutics: RNA and Gene Therapies	Indigo E

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 Therapeutic Horizons Through Global Collaborations.**" This theme is incorporated in Symposia, Workshops, Roundtables, 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, Roundtables, 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 and translational medicine, including educators, regulatory officials, consultants, industry professionals, and students and fellows. Please see pages 23-30 for details on these sessions.

TUESDAY, MARCH 8
8:00 AM – 5:00 PM
AQUA A-C

Challenges in Global Drug Development and Regulation Pre-conference

TUESDAY, MARCH 8
8:00 AM – 5:30 PM
AQUA D-F

Quantitative Translational Approaches in Oncology Pre-conference

WEDNESDAY, MARCH 8

SPECIAL SESSION

Scientific Horizons and Opportunities in Pharmacogenomics Research
Organized by the Pharmacogenomics Research Network (PGRN)

PGRN

8:00 AM – 2:00 PM
INDIGO A/E

The field of pharmacogenomics received considerable attention when President Obama launched the Precision Medicine Initiative last year. The Pharmacogenomics Research Network (PGRN) is bringing together scientists who study the interactions between genes and drug responses. This session, organized by the PGRN and open to all ASCPT attendees, is intended to present new research horizons in pharmacogenomics and precision medicine. The session includes an interactive panel discussion with different stakeholders who will describe emerging opportunities for research partnerships in pharmacogenomics. This session is intended for a diverse range of scientists across multiple sectors who are interested in learning about the latest research in pharmacogenomics

and precision medicine. Importantly, the session is intended to present new opportunities for collaborative research and access to innovative resources to advance research in basicand translational pharmacogenomics.
(Pre-registration is required.)

SPECIAL SESSION
ASCPT-ASIA PACIFIC SYMPOSIUM
Racial/Ethnic Differences in Drug Response
10:00 AM – 12:00 NOON
INDIGO D

Providers, regulators and drug development scientists are increasingly interested in understanding racial and ethnic differences in drug response. The goal of this symposium is to provide a forum to review and discuss our current understanding of racial/ethnic differences in drug response. Racial/ethnic differences in physiology, pathophysiology, environment and genetics can all affect drug disposition, efficacy and toxicity. This symposium will illustrate these differences across drug classes and disease states.

NEW MEMBER WELCOME
1:00 PM – 2:00 PM
AQUA 310

If you've joined ASCPT in the past year, please join us for this special session dedicated to welcoming you to the Society. You will learn how to make the most of your ASCPT member benefits, how to navigate the Annual Meeting and network with ASCPT leaders and other new members.

There will also be a special awards presentation recognizing the top 2015 Membership Recruiters!

OPENING SESSION
2:30 PM – 3:30 PM
INDIGO BCFG

Join us as ASCPT President, Mario L. Rocci, Jr., PhD presents the State of the Society Address and recognizes the 2016 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
SAPPHIRE BALLROOM

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

ENCORE AND LATE-BREAKING POSTER SESSIONS
4:30 PM – 6:30 PM
SAPPHIRE BALLROOM

View the Encore and Late-breaking abstracts selected by the ASCPT Scientific Program Committee.

SHOWCASE OF TOP TRAINEE ABSTRACTS
4:45 PM – 5:45 PM
ASCPT THEATER/SAPPHIRE BALLROOM

View the top trainee abstracts submitted by the 2016 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.

POSTER WALK
Essential Tools for Precision Medicine
5:45 PM – 6:30 PM
SAPPHIRE FOYER

Led by John A. Wagner, MD, PhD, Takeda Pharmaceuticals

ASCPT is pleased to present videos of the 2016 Presidential Trainee Award recipients highlighting their own exceptional research. View them in the Exhibit Hall or online at www.ascpt.org.

SCHEDULE-AT-A-GLANCE

THURSDAY, MARCH 10

INFECTIOUS DISEASES (INF) COMMUNITY MEETING
7:00 AM – 8:00 AM
AQUA 300

BIOTELEMETRY RESEARCH PRODUCT THEATER
8:00 AM – 9:00 AM
AQUA 310

INTERNATIONAL TRANSPORTER CONSORTIUM (ITC) COMMUNITY MEETING
11:00 AM – 12:00 PM
AQUA 310

EXHIBITS
11:30 AM – 6:30 PM
SAPPHIRE BALLROOM

COVANCE HOSTED EVENT
12:00 PM – 1:00 PM
AQUA 300

TRAINEE LUNCHEON
12:00 NOON – 1:30 PM
AQUA A-F

The Trainee Luncheon is a roundtable discussion that allows trainees and young scientists to meet with established clinical pharmacologists and translational medicine scientists to discuss potential career paths and other topics driven by trainees' questions. Facilitators include top leaders from industry, academia, government, and consulting sectors of clinical pharmacology and translational medicine.
Registration is required.

TICKETED LUNCH
12:00 NOON – 1:30 PM
SAPPHIRE BALLROOM

BIOINNOVATION FORUM
2:00 PM – 3:30 PM
INDIGO BCFG

Chaired by Russ B. Altman, MD, PhD, the ASCPT 2016 Bioinnovation Forum will feature "rising stars" in the areas of clinical pharmacology, therapeutics, translational science, regulatory science, and global healthcare and will engage the audience with new ideas in emerging areas of science, healthcare, and policy. See page 57 for program details.

DEVELOPMENT, REGULATORY & OUTCOMES (DRO) NETWORK MEETING
3:00 PM – 5:00 PM
INDIGO H

SYSTEMS PHARMACOLOGY (SP) COMMUNITY MEETING
3:00 PM – 4:00 PM
AQUA 300

PHARMACOGENOMICS (PMG) COMMUNITY MEETING
3:00 PM – 4:00 PM
AQUA 310

PRESIDENT'S NETWORKING RECEPTION
4:30 PM – 6:30 PM
SAPPHIRE BALLROOM

Co-Sponsored by

PhRMA FOUNDATION

Join us for the President's Networking Reception, offering further opportunities to network and interact with your colleagues and the exhibitors and celebrate the 50th anniversary of the PhRMA Foundation.

UCSF/STANFORD/GENENTECH RECEPTION
4:30 PM – 5:30 PM
AQUA ABC
(By Invitation Only)

POSTER WALK
Mechanisms Behind Special Populations: What Makes Them So Special?
4:45 PM – 5:30 PM
SAPPHIRE FOYER

Led by Deanna L. Kroetz, PhD, University of California San Francisco

PHARMACOMETABOLOMICS (PM) COMMUNITY MEETING
5:00 PM – 6:00 PM
AQUA 300

POSTER WALK
Novel Modeling Approaches to Solve Old Problems: PK, DDI, Toxicity
5:30 PM – 6:15 PM
SAPPHIRE FOYER

Led by Kellie Schoolar Reynolds, PharmD

FRIDAY, MARCH 11

ONCOLOGY (ONC) COMMUNITY MEETING
7:00 AM – 8:00 AM
AQUA 310

QUANTITATIVE PHARMACOLOGY (QP) NETWORK MEETING
7:00 AM – 9:00 AM
INDIGO H

BREAKFAST
7:00 AM – 9:00 AM
SAPPHIRE BALLROOM

EXHIBITS
7:00 AM – 2:00 PM

POSTER WALK
Translational Determinants of Toxicity
7:15 AM – 8:00 AM
SAPPHIRE FOYER

Led by Kim L.R. Brouwer, PharmD, PhD, University of North Carolina

QUOTIENT CLINICAL PRODUCT THEATER
8:00 AM – 9:00 AM
AQUA 300

SPEED MENTORING
11:45 AM – 1:15 PM
AQUA ABCD

The Mentor Task Force is pleased to offer the Speed Mentoring event. Senior clinical pharmacologists and translational medicine scientists 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.)*

OMNICOMM SYSTEMS, INC. PRODUCT THEATER
12:00 NOON – 1:00 PM
SAPPHIRE BALLROOM THEATER

TICKETED LUNCH
12:00 NOON – 1:30 PM
SAPPHIRE BALLROOM

SPECIAL POPULATIONS (SPO) COMMUNITY MEETING
1:00 PM – 2:00 PM
AQUA 310

DRUG UTILIZATION & OUTCOMES (DUO; FORMERLY SAF) COMMUNITY MEETING
3:00 PM – 4:00 PM
AQUA 310

TRANSLATIONAL & PRECISION MEDICINE (TPM) NETWORK MEETING
3:00 PM – 5:00 PM
INDIGO H

BIOLOGICS COMMUNITY MEETING
5:00 PM – 6:00 PM
AQUA 300

SCHEDULE-AT-A-GLANCE

SATURDAY, MARCH 12

SPECIAL EDUCATION SESSION

Pursuing the Management Track in a Scientific Organization: Learn from the Experts

7:30 AM – 9:00 AM

AQUA A/B

The overall goal of this session is to provide guidance to ASCPT members on the important steps and preparation for getting promoted and moving thru the ranks of academia, industry, and government. There is a need for guidance for early to mid-career clinical pharmacologists on how to get promoted and become leaders within the major career paths in clinical pharmacology and translational medicine (academia, industry, and government). The speakers will provide advice on requirements and expectations for promotion within academia, industry, and government. The importance of mentors throughout the career trajectory will be highlighted. They will also discuss skills, experiences, and preparation needed to move into managerial and administrative roles. This topic addresses an important area for junior and mid-career clinical pharmacologists. Such career development topics are important to the future and continued success of our members and are not currently regularly covered in other venues.

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 9

3:30 PM – 4:30 PM
INDIGO BCFG

Anne Wojcicki, 23andMe
Accelerating Discovery Through Human Genetics

THURSDAY, MARCH 10

9:15 AM – 10:15 AM
INDIGO BCFG

Dan Hartman, MD, Bill and Melinda Gates Foundation
How Pharmacology and Quantitative Methodologies are Impacting Global Health: A Perspective from the Bill and Melinda Gates Foundation

FRIDAY, MARCH 11

9:15 AM – 10:15 AM
INDIGO BCFG

Alice T. Shaw, MD, PhD, Massachusetts General Hospital
Advances in Targeted Therapies for Lung Cancer

FEATURED SPEAKERS

JOIN US FOR THE TWO ASCPT 2016 ANNUAL MEETING FEATURED SPEAKER SESSIONS AND HEAR PRESENTATIONS FROM YOUR FELLOW ASCPT MEMBERS.

THURSDAY, MARCH 10

1:00 PM – 2:00 PM
INDIGO BCFG

Dan Roden, MD, Vanderbilt University School of Medicine
Understanding Variability in Drug Action: Big Data and Little Data

FRIDAY, MARCH 11

1:00 PM – 2:00 PM
INDIGO BCFG

Micheline Piquette-Miller, PhD, Leslie Dan Faculty of Pharmacy, University of Toronto
Inflammation as a Source of Variability in Drug Disposition and Response

STUDENT AND TRAINEE INFORMATION

The ASCPT 2016 Annual Meeting features several education sessions and networking events designed specifically for trainees and young scientists to guide them in their personal and professional developments.

CAREER BOOTCAMP

WEDNESDAY, MARCH 9

8:00 AM – 2:00 PM

This half-day program is designed to stimulate discussion and address the immediate needs of trainees and young scientists in the early years of their career. The session will allow attendees to get a first-hand account of a typical workday of a clinical pharmacologist and translational medicine scientists at various stages in their careers. Topics covered will include the role of the clinical pharmacologist and translational medicine scientists in their respective organization, position-specific responsibilities and duties, day-to-day activities, and career paths. The objective of the series is to provide information that will assist attendees in determining whether a career in industry, academia, or government is a good personal fit. Open only to Trainees/Students.
(Registration required.)

TRAINEE LUNCHEON

THURSDAY, MARCH 10

12:00 NOON – 1:30 PM

The Trainee Luncheon is a roundtable discussion for trainees and young scientists to meet with established clinical pharmacologists and translational medicine scientists to discuss potential career paths and other topics driven by trainees' questions. Facilitators include top leaders from the industry, academia, government, and consulting sectors of clinical pharmacology.
(Registration required.)

SPEED MENTORING

FRIDAY, MARCH 11

11:45 AM - 1:15 PM

Seasoned and mid-career 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. Based upon areas of expertise and interest, mentees will be notified of their ASCPT mentor within six weeks following the Annual Meeting.
(Registration required.)

PURSUING THE MANAGEMENT TRACK IN A SCIENTIFIC ORGANIZATION: LEARN FROM THE EXPERTS

SATURDAY, MARCH 12

7:30 AM - 9:00 AM

Developed by the ASCPT Education Committee and the Mentor Task Force

The overall goal of this session is to provide guidance to our ASCPT members on the important steps and preparation for getting promoted and moving thru the ranks of academia, industry, and government. There is a need for guidance for early to mid-career clinical pharmacologists and translational medicine scientists on how to get promoted and become leaders within the major career paths in clinical pharmacology (academia, industry, and government). The speakers will provide advice on requirements and expectations for promotion within academia, industry, and government. The importance of mentors throughout the career trajectory will be highlighted. They will also discuss skills, experiences, and preparation needed to move into managerial and administrative roles. This topic addresses an important area for junior and mid-career clinical pharmacologists and translational medicine scientists. Such career development topics are important to the future and continued success of our members and are not currently regularly covered in other venues.

TRAINEE LUNCHEON
THURSDAY, MARCH 10
12:00 NOON – 1:30 PM
AQUA A-F

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

In support of ASCPT's strategic initiative to build capacity through the development and support of career development and leadership programs for junior scientists and investigators, ASCPT is pleased to bring back the highly successful Trainee Luncheon to the 2016 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 and translational medicine scientists 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 and translational medicine scientists. 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.

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CHALLENGES IN GLOBAL DRUG DEVELOPMENT AND REGULATION PRE-CONFERENCE

TUESDAY, MARCH 8

8:00 AM – 5:30 PM
AQUA A-C

CHAIRS

Lei Zhang, PhD
US Food and Drug Administration, Silver Spring, MD

Mark C.Rogge, PhD
Biogen Idec, Cambridge, MA.

8:00 AM – 8:30 AM
CONTINENTAL BREAKFAST

8:30 AM – 8:45 AM
OPENING COMMENTS

SESSION 1: ENABLING PRECISION MEDICINE

8:45 AM – 9:15 AM
Optimizing Study Outcomes, Stratification & Enrichment Approaches in Oncology
Alice Chen, MD, National Cancer Institute, Silver Spring, MD

9:15 AM – 9:45 AM
Optimizing Study Outcomes, Stratification & Enrichment Approaches in Neurology
Roger Lane, MD, MPH, Isis Pharmaceuticals, Inc., Carlsbad, CA

9:45 AM – 10:15 AM
Opportunities & Challenges with Capturing Patient-Reported Outcome Data Electronically
Stephen Joel Coons, PhD, Critical Path Institute, Tucson, AZ

10:15 AM – 10:30 AM
QUESTION AND ANSWER

10:30 AM – 10:45 AM
COFFEE BREAK

10:45 AM – 11:15 AM
Use of Novel Data in Pursuit of Precision Medicine
Atul Butte, MD, University of California, San Francisco, San Francisco, CA

11:15 AM – 11:45 AM
Regulatory Perspectives in Precision Medicine
Michael Pacanowski, PharmD, MPH, Silver Spring, MD

11:45 AM – 12:15 PM
Q&A WITH ROUNDTABLE DISCUSSION

12:15 PM – 1:30 PM
LUNCH

SESSION 2: REGULATORY SCIENCE AND POLICY

1:30 PM – 2:15 PM
Pediatric Assessment in Drug Development and Regulatory Approval
TBD

Gilbert Burckart, PharmD, US Food and Drug Administration, Silver Spring, MD

Mayumi Shikano, PhD, Pharmaceuticals and Medical Devices Agency, Tokyo, Japan

2:15 PM – 2:45 PM
PANEL DISCUSSION

2:45 PM – 3:00 PM
BREAK

CHALLENGES IN GLOBAL DRUG DEVELOPMENT AND REGULATION PRE-CONFERENCE

3:00 PM – 4:15 PM
Drug Interaction Assessment in Drug Development and Regulatory Approval
TBD

Shiew-Mei Huang, PhD,
North Potomac, MD

Akihiro Ishiguro, PhD, Pharmaceuticals and Medical Devices Agency, Tokyo, Japan

4:15 PM – 4:45 PM
PANEL DISCUSSION

4:45 PM – 5:15 PM
OPEN PANEL AND EMERGING TOPICS IN GLOBAL DRUG DEVELOPMENT

5:15 PM – 5:30 PM
CLOSING REMARKS

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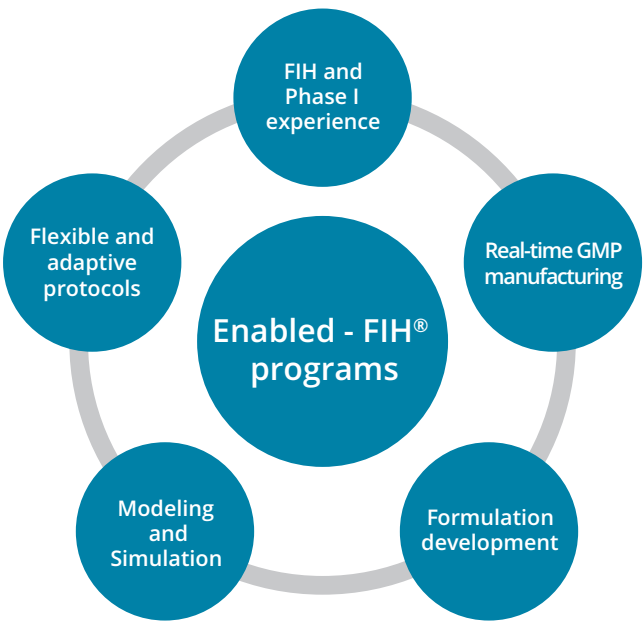

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QUANTITATIVE TRANSLATIONAL APPROACHES IN ONCOLOGY PRE-CONFERENCE

TUESDAY, MARCH 8

8:00 AM – 5:30 PM
AQUA D-F

CHAIRS
Karthik Venkatakrishnan, PhD, FCP, Takeda Pharmaceuticals, Cambridge, MA

Karen Rowland Yeo, PhD, Certera, Waterford, CT

8:00 AM – 8:30 AM
CONTINENTAL BREAKFAST

8:30 AM – 8:40 AM
WELCOME AND INTRODUCTION

8:40 AM – 9:25 AM
Personalized Medicine
Razelle Kurzrock, MD, University of California San Diego, San Diego, CA

9:25 AM – 9:50 AM
Systems Pharmacology and Modeling of Oncogene Signaling Networks for Rational Combinations
Daniel Kirouac, PhD, Merrimack Pharmaceuticals, Cambridge, MA

9:50 AM – 10:15 AM
PK/PD Efficacy Modeling of Combinations to Guide Scheduling and Sequencing
Sonya C. Tate, PhD, Eli Lilly & Company, Surrey, United Kingdom

10:15 AM – 10:35 AM
COFFEE BREAK

10:35 AM – 11:00 AM
Translational Safety Models in the Development of Oncology Compounds
Jay Mettetal, PhD, AstraZeneca, Waltham, MA

11:00 AM – 11:25 AM
Dose Optimization by Safety Guided Titration Approaches: Axitinib as a Case Example
Yazdi Pithavala, PhD, Pfizer Global R&D, San Diego, CA

11:25 AM – 11:50 AM
Model-Based Integration of Clinical Safety/Tolerability of Oncology Drugs to Optimize Dosing
Lena E. Friberg, PhD, Uppsala University, Uppsala, Sweden

11:50 AM – 12:15 PM
Therapeutic Drug Monitoring in Oncology Improves Patient Outcomes
Jeannine McCune, PharmD, University of Washington, Seattle, WA

12:15 PM – 1:45 PM
LUNCH/NETWORKING/POSTERS

POSTERS
For complete abstract content download the ASCPT Annual Meeting Mobile App.

PC-01
PHARMACOGENOMIC VARIANTS ASSOCIATED WITH CELLULAR SENSITIVITY TO IDELALISIB.
Presenter: Kristen Pettit, MD, University of Chicago

PC-02
CONCENTRATION-QTC ANALYSIS OF POLATUZUMAB VEDOTIN IN PATIENTS WITH B-CELL HEMATOLOGIC MALIGNANCIES.
Presenter: Dan Lu, PhD, Genentech

PC-03
PHARMACOKINETIC PREDICTION OF PACLITAXEL INDUCED PERIPHERAL NEUROPATHY.
Presenter: Dan L. Hertz, University of Michigan College of Pharmacy

PC-04
POPULATION PHARMACOKINETICS OF RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN ALFA IN PEDIATRIC HEMATOLOGIC MALIGNANCY PATIENTS WITH DISSEMINATED INTRAVASCULAR COAGULATION.
Presenter: Masanobu Takeuchi, MD, The Hospital for Sick Children

QUANTITATIVE TRANSLATIONAL APPROACHES IN ONCOLOGY PRE-CONFERENCE

PC-05
INTEGRATED NON-CLINICAL AND CLINICAL RISK ASSESSMENT TO OBVIATE THE NEED FOR A DEDICATED QTC STUDY OF IXAZOMIB IN CANCER PATIENTS.
Presenter: Neeraj Gupta, PhD, Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited

PC-06
POTENTIAL OF TARGETING WEE1 AS THERAPY IN THE MANAGEMENT OF TRIPLE NEGATIVE BREAST CANCER.
Presenter: Gladys Morrison, PhD, The University of Chicago

PC-07
ASSOCIATION OF SINGLE NUCLEOTIDE POLYMORPHISMS IN IL8 AND IL13 WITH SUNITINIB-INDUCED TOXICITY IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA.
Presenter: Jesse Swen, Leiden University Medical Center

PC-08
GENETIC PREDICTORS OF EXEMESTANE PHARMACOKINETICS AND PHARMACODYNAMICS IN HEALTHY HUMAN VOLUNTEERS.
Presenter: Bryana J. Gregory, Harding University

PC-09
APPLICATION OF PBPK MODELING TO ASSESS THE VICTIM DDI POTENTIAL OF PACLITAXEL IN ONCOLOGY COMBINATION THERAPIES.
Presenter: Alice Ke, PhD, Simcyp (a Certara Company)

PC-10
EXPOSURE-RESPONSE (E-R) ANALYSIS OF OVERALL SURVIVAL (OS) FOR NIVOLUMAB IN PATIENTS WITH PREVIOUSLY TREATED ADVANCED OR METASTATIC NON-SMALL-CELL LUNG CANCER (NSCLC).
Presenter: Yan Feng, PhD, Bristol-Myers Squibb

PC-11
ASSESSMENT OF PHARMACOKINETIC INTERACTION BETWEEN RILOTUMUMAB AND EPIRUBICIN, CISPLATIN, AND CAPECITABINE IN A PHASE III STUDY IN PATIENTS WITH MET-POSITIVE GASTRIC CANCER.
Presenter: Yilong Zhang, PhD, Amgen, Inc.

PC-12
A SYSTEMS BIOLOGY APPROACH TO PREDICTING CARDIOTOXICITY ASSOCIATED WITH TYROSINE KINASE INHIBITORS.
Presenter: Shadia Zaman, PhD, US Food and Drug Administration

PC-13
POPULATION PHARMACOKINETIC STUDY OF METHOTREXATE IN CHINESE PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND OSTEOSARCOMA.
Presenter: Tai Ning Lam, PharmD, PhD, Chinese University of Hong Kong

PC-14
STING PATHWAY ACTIVATION ENHANCES IMMUNE RESPONSE AND IMPROVES SURVIVAL IN MURINE MYELOID LEUKEMIA.
Presenter: Emily Curran, MD, University of Chicago

QUANTITATIVE TRANSLATIONAL APPROACHES IN ONCOLOGY PRE-CONFERENCE

PC-15
AMELIORATION OF CISPLATIN NEPHROTOXICITY BY NILOTINIB.
Presenter: Alix F. Leblanc, PhD, The Ohio State University

PC-16
MODEL-BASED ASSESSMENT OF DRUG-DRUG INTERACTION AND IMMUNOGENICITY ON THE PHARMACOKINETICS (PK) OF NIVOLUMAB AND IPILIMUMAB IN COMBINATION IN ADVANCED MELANOMA PATIENTS.
Presenter: Li Zhu, RPh, PhD, Bristol-Myers Squibb

PC-17
ASSESSMENT OF THE IMMUNOGENICITY OF NIVOLUMAB (NIVO) AND IPILIMUMAB (IPI) IN COMBINATION AND POTENTIAL IMPACT ON SAFETY AND EFFICACY IN PATIENTS WITH ADVANCED MELANOMA.
Presenter: Paul Statkevich, RPh, PhD, Bristol-Myers Squibb

PC-18
INTRINSIC AND EXTRINSIC DETERMINANTS OF PHARMACOKINETIC (PK) VARIABILITY OF CANCER THERAPEUTICS.
Presenter: Eric L. Reyner, Genentech

PC-19
PHASE I SINGLE AND MULTIPLE-DOSE PHARMACOKINETICS OF EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) INHIBITOR PF-06747775 IN ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS.
Presenter: Joanna C. Master, PharmD, Pfizer, Inc.

PC-20
NOVEL DELETERIOUS DIHYDROPYRIMIDINE DEHYDROGENASE VARIANTS MAY CONTRIBUTE TO 5-FLUOROURACIL SENSITIVITY IN AN EAST AFRICAN POPULATION.
Presenter: Tarig Elraiyah, Mayo Clinic

PC-21
POPULATION PHARMACOKINETIC (PK) ANALYSIS OF BORTEZOMIB (BTZ) IN PEDIATRIC LEUKEMIA PATIENTS (PTS): SUPPORT FOR BODY SURFACE AREA (BSA)-BASED DOSING IN PTS AGED 2-16 YRS.
Presenter: Michael J. Hanley, PharmD, PhD, Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited

PC-22
USE OF SUPPORTIVE CARE THERAPIES AMONG PEDIATRIC CANCER PATIENTS WITH HEMATOLOGIC MALIGNANCIES UNDERGOING CHEMOTHERAPY.
Presenter: Jonathan Constance, PhD, University of Utah

PC-23
IDENTIFICATION OF A NOVEL HIGH-AFFINITY CARRIER OF NUCLEOSIDE ANALOGUES.
Presenter: Christina D. Drenberg, PhD, The Ohio State University

PC-24
BIOMARKER OUTCOMES IN EARLY PHASE ONCOLOGY TRIALS INCLUDING NON-DIAGNOSTIC BIOPSIES.
Presenter: Randy F. Sweis, MD, University of Chicago

QUANTITATIVE TRANSLATIONAL APPROACHES IN ONCOLOGY PRE-CONFERENCE

PC-25
SUNITINIB-INDUCED HYPERTENSION IN CYP3A4 RS4646437 A-ALLELE CARRIERS WITH METASTATIC RENAL CELL CARCINOMA.
Presenter: Jesse J. Swen, PharmD, PhD, Leiden University Medical Center

PC-26
CHARACTERIZATION OF INOTUZUMAB OZOGAMICIN TIME-DEPENDENT CLEARANCE IN RELAPSED/REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS BY NONLINEAR MIXED-EFFECTS ANALYSIS.
Presenter: May Garrett, Pfizer, Inc.

PC-27
NONHOMOGENEOUS DRUG PENETRANCE OF VELIPARIB MEASURED IN TRIPLE NEGATIVE BREAST TUMORS.
Presenter: Imke H. Bartelink, PharmD, PhD, University of California, San Francisco

1:45 PM – 2:30 PM
Clinical Perspective: Immuno-Oncology
Suresh S. Ramalingam, MD, Emory University School of Medicine, Atlanta, GA

2:30 PM – 2:55 PM
M&S Approaches for Immuno-Oncology
Amit Roy, PhD, Bristol-Myers Squibb, Plainsboro, NJ

2:55 PM – 3:20 PM
Disease Models in Oncology: Optimizing Trial Designs to Maximize POS
Rene Bruno, PhD, Certara, Marseille, France

3:20 PM – 3:45 PM
Special Considerations for Modeling Exposure-Response for Biologics
Yaning Wang, PhD, US Food and Drug Administration, Silver Spring, MD

3:45 PM – 4:00 PM
BREAK

4:00 PM – 5:00 PM
ORAL SESSION FROM POSTERS
For complete abstract content download the ASCPT Annual Meeting Mobile App.

OPC-1
PBPK-PD MODELING TO PROVIDE A TRANSLATIONAL RATIONALE BETWEEN DRUGS AND BETWEEN SPECIES: EXAMPLE OF TRAIL FUSION PROTEINS.
Presenter: Michael Block, PhD, Bayer Technology Services GmbH

OPC-2
A JOINT MODEL RELATING CHANGES IN PROSTATE SPECIFIC ANTIGEN (PSA) TO SURVIVAL IN CASTRATE RESISTANT PROSTATE CANCER (CRPC).
Presenter: Tu Mai, PhD, University of Chicago

OPC-3
QUANTITATIVE ASSESSMENT OF THE EFFICACY OF TAK-385, AN INVESTIGATIONAL, ORAL GNRH ANTAGONIST IN PROSTATE CANCER PATIENTS (PTS) TO OPTIMIZE TRIAL DESIGN AND DOSE SELECTION.
Presenter: Hélène Faessel, PharmD, PhD, Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited

OPC-4
COMBINED POPULATION PK MODELING AND DISPROPORTIONALITY ANALYSES TO ASSESS THE ASSOCIATION BETWEEN KINASE INHIBITION AND ADVERSE EVENTS.
Presenter: Jinzhong Liu, PhD, Indiana University School of Medicine

5:00 PM – 5:30 PM
CLOSING REMARKS

GENERAL INFORMATION

ACKNOWLEDGMENTS

ASCPT WOULD LIKE TO GIVE SPECIAL THANKS TO THE LEADERSHIP OF THE NETWORKS & COMMUNITIES AND RECOGNIZE THE CHAIRS AND VICE CHAIRS FOR THEIR DEDICATED LEADERSHIP OF IMPORTANT SOCIETY ENDEAVORS.

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INDIGO FOYER

TUESDAY, MARCH 8
7:00 AM – 3:00 PM

WEDNESDAY, MARCH 9
7:00 AM – 5:00 PM

THURSDAY, MARCH 10
7:00 AM – 5:00 PM

FRIDAY, MARCH 11
7:00 AM – 5:00 PM

SATURDAY MARCH 12
7:00 AM – 10:00 AM

TARGET AUDIENCE

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

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

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

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GENERAL INFORMATION

ASCPT CENTRAL
INDIGO FOYER

ASCPT Central will be open during the following hours:

WEDNESDAY, MARCH 9
7:00 AM – 5:00 PM

THURSDAY, MARCH 10
7:00 AM – 5:00 PM

FRIDAY, MARCH 11
7:00 AM – 5:00 PM

SATURDAY, MARCH 12
7:00 AM – 10:00 AM

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- Join ASCPT or refer a colleague for membership

And much more!

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WEDNESDAY, MARCH 9
4:30 PM – 6:30 PM

THURSDAY, MARCH 10
11:30 AM – 6:30 PM

FRIDAY, MARCH 11
7:00 AM – 2:00 PM

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INDIGO FOYER

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ASCPT JOB BOARD
INDIGO 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 9 until Saturday, March 12. 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
INDIGO 204A

ASCPT provides technical support through the services available in the Speaker Ready Room, Indigo 204A. 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 8
7:00 AM – 5:00 PM

WEDNESDAY, MARCH 9
7:00 AM – 5:00 PM

THURSDAY, MARCH 10
7:00 AM – 5:00 PM

FRIDAY, MARCH 11
7:00 AM – 5:00 PM

SATURDAY, MARCH 12
7:00 AM – 10:00 AM

HOTEL SAFETY
Your safety while attending the Annual Meeting is important to ASCPT and the Hilton Bayfront San Diego. In case of an emergency please dial 911 from the nearest house phone. Should there be a hotel emergency please follow the directions provided on the public address system and by hotel staff.

DAILY LUNCH TICKET
Buy your daily lunch ticket in the Poster and Exhibit Hall on Thursday and Friday. For $20 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.

GENERAL INFORMATION

ASCPT NETWORK AND COMMUNITY DESIGNATIONS

Communities are categorized into three main Networks: Quantitative Pharmacology (QP), Translational & Precision Medicine (TPM), and Development, Regulatory & Outcomes (DRO). Each Symposia, Workshop, Roundtable and Science at Sunrise session is correlated with or reflective of a Community. See the Scientific Agenda for the sessions representing your field of interest.

QUANTITATIVE PHARMACOLOGY (QP)

	Biologics
PMK	Pharmacometrics & Pharmacokinetics
SP	Systems Pharmacology

TRANSLATIONAL & PRECISION MEDICINE

BTT	Biomarker & Translational Tools
INF	Infectious Diseases
ITC	International Transporter Consortium
ONC	Oncology
OSD	Organ Specific Diseases
PMG	Pharmacogenomics
PM	Pharmacometabolomics
SPO	Special Populations

DEVELOPMENT, REGULATORY & OUTCOMES (DRO)

DUO	Drug Utilization & Outcomes
EDDS	Early Development & Drug Safety
RS	Regulatory Science

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 a guest will accompany you to the Annual Meeting, please note that ASCPT does not offer spouse programs. However, the concierge at the Hilton Bayfront San Diego is adept at making arrangements for dining reservations, excursion reservations, providing shopping and transportation information, and answering general questions about local attractions.

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COMPLIMENTARY HEADSHOTS

Covance is proud to sponsor complimentary headshots for ASCPT Annual Meeting attendees. Take advantage of this opportunity to have a professional headshot taken by No appointment is necessary, and it will only take a few seconds of your time! Stop by the Exhibit Hall between 11:30 am – 6:30 pm on Thursday and 7:00 am – 2:00 pm on Friday for your professional headshot, which will be provided to you electronically.

AWARD RECIPIENTS

2016 GARY NEIL PRIZE FOR INNOVATION IN DRUG DEVELOPMENT

Peter K. Honig, MD, MPH
Senior Vice-President
Pfizer, Inc.

2016 HENRY W. ELLIOTT DISTINGUISHED SERVICE AWARD

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

2016 LEON I. GOLDBERG EARLY INVESTIGATOR AWARD

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

Liewei Wang, MD, PhD
Professor Mayo Clinic,
Mayo Foundation

2016 OSCAR B. HUNTER CAREER AWARD IN THERAPEUTICS

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

2016 RAWLS-PALMER PROGRESS IN MEDICINE AWARD

Kenneth Thummel, PhD
Associate Professor
University of Washington

2016 WILLIAM B. ABRAMS AWARD IN GERIATRIC CLINICAL PHARMACOLOGY

Joseph T. Hanlon, PharmD
Professor
University of Pittsburgh

2016 ASCPT MENTOR AWARD

Scott A. Waldman, MD, PhD

Samuel M.V. Hamilton Professor and Chair
Thomas Jefferson University

2015 TOP MEMBERSHIP RECRUITERS

Caroline Lee, PhD
Mayo Clinic

Liewei Wang, MD, PhD
Mayo Clinic

Seung Hwan Lee, MD, PhD
Seoul National University Hospital

GENERAL INFORMATION

2016 DAVID J. GOLDSTEIN TRAINEE AWARD

Tu H. Mai, PhD
University of Chicago

2016 JASON MORROW TRAINEE AWARD

Chia-Hsiang Hsueh, PhD
University of California, San Francisco

Tore B. Stage, MSc Pharm
University of Southern Denmark

ASCPT PRESIDENTIAL TRAINEE AWARD RECIPIENTS

Priya Bapat
University of Toronto

Laiyi Chua
Lilly-NUS Centre for Clinical Pharmacology

Tanima De, PhD
University of Chicago

Christina D. Drenberg, PhD
The Ohio State University College of Pharmacy

Tarig Elraiyah
Mayo Clinic

Hani M. Ghazarian
UC San Diego Skaggs School of Pharmacy

Sonja Hartmann, PhD
University of Florida

Chia-Hsiang Hsueh, PhD
University of California, San Francisco

Kawita Kanhai, MD
Centre for Human Drug Research

Johannes Kast
University of Florida

Lisa H. Lam, PharmD
University of California, San Diego

Alix F. Leblanc, PhD
The Ohio State University

Xiaomin Liang
University of California, San Francisco

Chay Ngee Lim
University of Minnesota

Duan Liu, PhD
Mayo Clinic

Marcelo R. Luizon, PhD
University of California, San Francisco

Oyunbileg Magvanjav
University of Florida

Tu H. Mai, PhD
University of Chicago

Ryan P. McKillip
University of Chicago

Kana Mizuno, PhD
Cincinnati Children's Hospital Medical Center

Kristen Pettit, MD
University of Chicago

Daniel Rotroff, PhD
North Carolina State University

Ana C. Sá
University of Florida

Mohamed H. Shahin
University of Florida

Valentina Shakhnovich, MD
Children's Mercy Hospital

Nithya Srinivas
University of North Carolina at Chapel Hill

Tore B. Stage, MSc Pharm
University of Southern Denmark

Marcus P.J. van Diemen, MD
Centre for Human Drug Research

Shadia Zaman, PhD
US Food and Drug Administration

Arik A. Zur, PhD
University of California, San Francisco

PHRMA FOUNDATION AWARDS

PRESENTER

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

2015 POST DOCTORAL FELLOWSHIPS IN TRANSLATIONAL MEDICINE

Jing Sun, PhD
Dana-Farber Cancer Institute

Adam Swick, PhD
University of Wisconsin School of Medicine

2015 RESEARCH STARTER GRANTS IN TRANSLATIONAL MEDICINE

Ritika Jaini, PhD
Cleveland Clinic

Georgios Paschos, PhD
University of Pennsylvania

2015 PAUL CALABRESI MEDICAL STUDENT FELLOWSHIP

Joyce Chen
University of California San Diego

2016 FACULTY DEVELOPMENT AWARD

Crystal Clark, MD
Northwestern Feinberg School of Medicine

2016 AWARD IN EXCELLENCE IN CLINICAL PHARMACOLOGY

David J. Greenblatt, MD
Tufts University School of Medicine

CPT: PHARMACOMETRICS & SYSTEMS PHARMACOLOGY AWARD

PRESENTER

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

RECIPIENT

Ron Keizer, PharmD, PhD
InsightRX/Pirana Software & Consulting

GENERAL INFORMATION

2015 DONORS

SOCIETY OF FOUNDERS
Michael H. Skinner, MD, PharmD
David W. Nierenberg, MD and
Joan Nierenberg

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

LEON I. GOLDBERG YOUNG INVESTIGATOR AWARD
Kim L. R. Brouwer, PharmD, PhD
Joann L. Data, MD, PhD &
Herman Cantrell
John T. Sullivan, MD, ChB, FRACP

WILLIAM B. ABRAMS AWARD IN GERIATRIC CLINICAL PHARMACOLOGY
John F. Mullane, MD, PhD, JD

SHEINER-BEAL PHARMACOMETRICS AWARD
Bing Wang, PhD
Lei Zhang, PhD
Peter J. Rix, DABT
Jiraganya Bhongsatiern, MSPharm

MALLE JURIMA-ROMET AWARD
Shiew-Mei Huang, PhD
Kellie Schoolar Reynolds, PharmD
Kim L. R. Brouwer, PharmD, PhD

SCIENTIFIC AWARDS
Gregory L. Kearns, PharmD, PhD &
Kathleen Neville, MD, MS

STUDENT/TRAINEE AWARDS & TRAVEL
Raymond J. Hohl, MD, PhD &
Nina Gannon, DVM
Gregory L. Kearns, PharmD, PhD &
Kathleen Neville, MD, MS
Kellie Schoolar Reynolds, PharmD
Kim L. R. Brouwer, PharmD, PhD
Julie A. Johnson, PharmD
Anne C. Heatherington, PhD
Anuradha Ramamoorthy, PhD
Joseph Alan Ware, PhD
Susan M. Abdel-Rahman, PharmD
Jing Liu, PhD

ASCPT/FDA ABRAMS LECTURE
Shiew-Mei Huang, PhD
Lei Zhang, PhD

BUILDING FUND
John F. Mullane, MD, PhD, JD

UNRESTRICTED GIFT
Shiew-Mei Huang, PhD
Mario L. Rocci, Jr., PhD
Mark J. Dresser, PhD
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Sharon J. Swan, FASAE, CAE
Anne Zajicek, PharmD, MD
Virginia (Ginny) D. Schmith, PhD, FCP
Kellie Schoolar Reynolds, PharmD
Kim L. R. Brouwer, PharmD, PhD
Anne Heatherington, PhD
Walter Kraft, MD, FACP
Andre Terzic, MD, PhD, FAHA
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D. Craig Brater, MD
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Maurice G. Emery, PharmD, PhD
Richard L. Lalonde, PharmD
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Robert E. Vestal, MD
Robert L. Roe, MD
Peter R. Bieck, MD, PhD
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MATCHING GIFTS

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GENERAL INFORMATION

OPENING SESSION

2:30 PM – 3:30 PM
INDIGO BCFG

Sponsored by:

STATE OF THE SOCIETY ADDRESS
Mario L. Rocci, Jr., PhD
ICON, President

AWARD PRESENTATIONS
William B. Abrams Award in Geriatric Clinical Pharmacology
PRESENTER
Patricia W. Slattum, PharmD,
Virginia Commonwealth University

RECIPIENT
Joseph T. Hanlon, PharmD
University of Pittsburgh

Henry W. Elliott Distinguished Service Award
PRESENTER
Lei Zhang, PhD
US Food and Drug Administration

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

Gary Neil Prize for Innovation in Drug Development
PRESENTER
Shiew-Mei Huang, PhD
US Food and Drug Administration

RECIPIENT
Peter K. Honig, MD, MPH
Pfizer, Inc.

2016 David J. Goldstein Trainee Award
PRESENTER
Mario L. Rocci, Jr., PhD
ICON

RECIPIENT
Tu H. Mai, PhD
University of Chicago

2016 Jason Morrow Trainee Award
PRESENTER
Mario L. Rocci, Jr., PhD
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RECIPIENTS
Chia-Hsiang Hsueh, PhD
University of California, San Francisco

Tore B. Stage, MSc Pharm
University of Southern Denmark

2016 ASCPT Mentor Award
PRESENTER
Walter Kraft, MD, FACP
Thomas Jefferson University

RECIPIENT
Scott A. Waldman, MD, PhD
Thomas Jefferson University

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

2015 Post Doctoral Fellowships in Translational Medicine
Jing Sun, PhD
Dana-Farber Cancer Institute

Adam Swick, PhD
University of Wisconsin School of Medicine

2015 Research Starter Grants in Translational Medicine
Ritika Jaini, PhD
Cleveland Clinic

Georgios Paschos, PhD
University of Pennsylvania

2015 Paul Calabresi Medical Student Fellowship
Joyce Chen
University of California San Diego

2016 Faculty Development Award
Crystal Clark, MD
Northwestern Feinberg School of Medicine

2016 Award in Excellence in Clinical Pharmacology
David J. Greenblatt, MD
Tufts University School of Medicine

CPT: Pharmacometrics & Systems Pharmacology Award
PRESENTER
Piet H. van der Graaf, PhD, PharmD
Leiden Academic Centre for Drug Research

RECIPIENT
Ron Keizer, PharmD, PhD
InsightRX/Pirana Software & Consulting

CEO REMARKS
Sharon J. Swan, FASAE, CAE

GENERAL INFORMATION

PRODUCT THEATERS & EXHIBITOR HOSTED EVENTS

Join our exhibitors as they host the following special events at this year's Annual Meeting:

BIOTELEMETRY RESEARCH PRODUCT THEATER

BioTelemetry inc
RESEARCH
Formerly Cardiocore

THURSDAY, MARCH, 10, 2016
8:00 – 9:00 AM
AQUA 310

Complimentary breakfast refreshments provided

Meet with BioTelemetry Research as Polina Voloshko, MD, presents an engaging morning session, "Definitive Assessment of Cardia Safety in Phase I."

COVANCE HOSTED EVENT

COVANCE
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THURSDAY, MARCH, 10, 2016
12:00 – 1:00 PM
AQUA 300

Complimentary afternoon refreshments provided

Join Covance and Karen Cornelissen for an exclusive luncheon seminar, "FIH Trial Design: Increase Flexibility, Decrease Time and Cost, and Add Value to Your Asset."

QUOTIENT CLINICAL PRODUCT THEATER

QUOTIENT CLINICAL
The Translational Pharmaceutics Company

FRIDAY, MARCH, 11, 2016
8:00 – 9:00 AM
AQUA 300

Complimentary breakfast refreshments provided

Quotient Clinical will present case studies on integrated and adaptive clinical protocols combining healthy volunteer and POC investigations in this special presentation, "Accelerating Timelines from Candidate Selection to Proof-of-Concept with Enabled-FIH® Programs."

OMNICOMM INC. PRODUCT THEATER

OmniComm
eClinical Solutions for Life™

FRIDAY, MARCH, 11, 2016
12:00 – 1:00 PM
SAPPHIRE BALLROOM

Complimentary snacks & refreshments provided

Join OmniComm in the Product Theater located in the center of the Exhibit Hall for their exclusive special presentation.

Space is limited in these special events so if you did not RSVP, please be sure to arrive early to secure your spot or stop by ASCPT Central to indicate your desired attendance.

NETWORK & COMMUNITY MEETINGS

THURSDAY, MARCH 10

INFECTIOUS DISEASES (INF) COMMUNITY MEETING
7:00 AM – 8:00 AM
AQUA 300

Led by INF Leadership

INTERNATIONAL TRANSPORTER CONSORTIUM (ITC) COMMUNITY MEETING
11:00 AM – 12:00 PM
AQUA 310

Led by ITC Leadership

SYSTEMS PHARMACOLOGY (SP) COMMUNITY MEETING
3:00 PM – 4:00 PM
AQUA 300

Led by SP Leadership

PHARMACOGENOMICS (PMG) COMMUNITY MEETING
3:00 PM – 4:00 PM
AQUA 310

Join PMG Leadership for this Community Planning Meeting

DEVELOPMENT, REGULATORY & OUTCOMES (DRO) NETWORK MEETING
3:00 PM – 5:00 PM
INDIGO H

The DRO Network Meeting will include network business and administrative updates and scientific presentation and discussion. There will be break outs to Community-level interactions to mingle with Community leadership and members, and to facilitate ideas for future Annual Meeting Programming, Webinars, White Papers, and Scientific Collaborations. Communities represented will include: DUO, EDDS & RS.

PHARMACOMETABOLOMICS (PM) COMMUNITY MEETING
5:00 PM – 6:00 PM
AQUA 300

Led by the PM Leadership

FRIDAY, MARCH 11

ONCOLOGY (ONC) COMMUNITY MEETING
7:00 AM – 8:00 AM
AQUA 310

Led by the ONC Leadership

QUANTITATIVE PHARMACOLOGY (QP) NETWORK MEETING
7:00 AM – 9:00 AM
INDIGO H

The Quantitative Pharmacology Network is comprised of 3 Communities – Pharmacometrics, Modeling and Kinetics (PMK), Biologics and Systems Pharmacology (SP). This meeting will have the following main areas of focus:
Science: Abstracts will be selected for short presentation around "dose optimization" from across the 3 Communities with the aim of generating discussion to fuel the 2017 Annual Meeting programming.
Grassroots programming for 2017: Fuel 2017 programming focused on QP by taking advantage of the ability to "match" and develop ideas together.
Networking: Meet other like-minded members who share your passion for the quantitative aspects of clinical pharmacology, including the Network and Community leadership.
Business: Hear how ASCPT is acting on its Strategic Plan, our new Webinar series and about our family of Journals.

SPECIAL POPULATIONS (SPO) COMMUNITY MEETING
1:00 PM – 2:00 PM
AQUA 310

Join this meeting to discuss Community goals, education and communication along with 2017 proposal ideas.

GENERAL INFORMATION

DRUG UTILIZATION & OUTCOMES (DUO; FORMERLY SAF) COMMUNITY MEETING
3:00 PM – 4:00 PM
AQUA 310

Led by DUO Leadership

TRANSLATIONAL & PRECISION MEDICINE (TPM) NETWORK MEETING
3:00 PM – 5:00 PM

Multiple presentations on the theme of Precision Medicine by TPM Communities followed by an interactive roundtable discussion. Communities represented will include: BTT, INF, ITC, ONC, OSD, PMG, PM, SPO.

BIOLOGICS COMMUNITY MEETING
5:00 PM – 6:00 PM
AQUA 300

Led by Biologics Leadership

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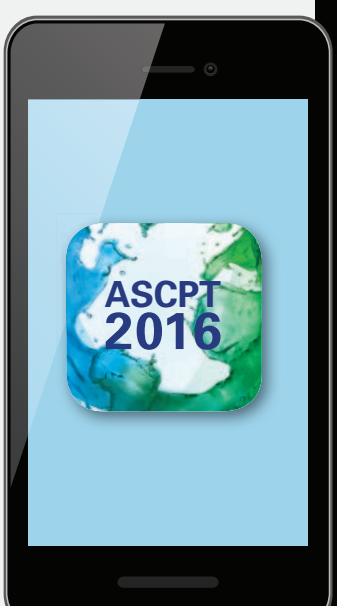
- The current program schedule
- Speaker information
- Exhibitor and sponsor details
- Live Twitter feeds
- Floor plans
- Attendee list and attendee-to-attendee communication
- Session Evaluations



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Search "ASCPT 2016" to download the app from the Apple App Store.

ANDROID USERS
Search "ASCPT 2016" to download the app from the Google Play Marketplace.

WINDOWS, BLACKBERRY, OTHER SMART PHONES/ MOBILE DEVICES, LAPTOPS AND DESKTOP USERS
Go to https://guidebook.com/app/ASCPT/ and bookmark it.

PROGRAM & SCIENTIFIC AGENDA

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Complete the ASCPT Annual Meeting online evaluation via the ASCPT 2016 Annual Meeting App to be entered in a drawing for **complimentary registration** to the **ASCPT 2017 Annual Meeting** at the **Washington Marriott Wardman Park, Washington, DC**.

VISIT **WWW.ASCPT.ORG** TO DOWNLOAD THE ASCPT 2016 ANNUAL MEETING APP AND CLICK ON THE EVALUATION LINK.

CONNECT WITH US

TUESDAY, MARCH 8, 2016

1:00 PM – 5:00 PM
CPT ASSOCIATE EDITOR MEETING
INDIGO 202A
(By Invitation Only)

5:30 PM – 7:30 PM
PGRN MEETING
INDIGO 202B
(By Invitation Only)

WEDNESDAY, MARCH 9, 2016

7:00 AM – 9:30 AM
BOARD OF DIRECTORS MEETING
AQUA BOARDROOM
(By Invitation Only)

8:00 AM – 12:00 PM
PSP ASSOCIATE EDITOR MEETING
INDIGO 202A
(By Invitation Only)

8:00 AM – 12:00 PM
CTS ASSOCIATE EDITOR MEETING
INDIGO 202B
(By Invitation Only)

8:00 AM – 2:00 PM
CAREER BOOTCAMP
AQUA A/B

CHAIRS
Anuradha Ramamoorthy, PhD, US Food and Drug Administration, Silver Spring, MD

Catherine M. T. Sherwin, BSc(Hons), PhD, University of Utah School of Medicine, Salt Lake City, UT

8:00 AM
BREAKFAST AND INTRODUCTION

8:20 AM
A Day in the Life of a Clinical Pharmacologist Series

CHAIR
Dionna Green, MD, US Food and Drug Administration, Silver Spring, MD

SPEAKERS
INTRODUCTION
Dionna Green, MD, US Food and Drug Administration, Silver Spring, MD

A Day in the Life of a Clinical Pharmacologist in the Industry
Aubrey Stoch, MD, Merck Inc., Rahway, NJ

A Day in the Life of a Clinical Pharmacologist in Academia
Craig W. Hendrix, MD, Johns Hopkins University, Baltimore, MD

A Day in the Life of a Clinical Pharmacologist in the FDA
Edward Dennis Bashaw, PharmD, US Food and Drug Administration, Silver Spring, MD

PANEL DISCUSSION

9:20 AM
BREAK

WEDNESDAY, MARCH 9, 2016

9:30 AM

Here is What You Need to Know About Clinical Pharmacology Internships in Government and Industry

CHAIR
Anuradha Ramamoorthy, PhD, US Food and Drug Administration, Silver Spring, MD

SPEAKERS
Introduction
Anuradha Ramamoorthy, PhD, US Food and Drug Administration, Silver Spring, MD

Why do an Internship?
Lawrence J. Lesko, PhD, FCP, University of Florida, Orlando, FL

Internship Opportunities in Clinical and Translational Research at the NIH
William D. Figg, PharmD, National Cancer Institute, Bethesda, MD

Internship Opportunities at the FDA
Gilbert J. Burckart, PharmD, US Food and Drug Administration, Silver Spring, MD

Internship Opportunities in the Industry
Bert L. Lum, PharmD, Genentech, South San Francisco, CA

PANEL DISCUSSION

10:45 AM

BREAK

11:00 AM

Clinical Pharmacology Postdoctoral Fellowships in the Academia, Government and Industry

CHAIR
Anuradha Ramamoorthy, PhD, US Food and Drug Administration, Silver Spring, MD

SPEAKERS
Introduction
Anuradha Ramamoorthy, PhD, US Food and Drug Administration, Silver Spring, MD

Fellowship Opportunities in Academia
Kathleen M. Giacomini, PhD, School of Pharmacy, University of California San Francisco, San Francisco, CA

Fellowship Opportunities at the NIH
Anne Zajicek, MD, PharmD, National Institutes of Health, Bethesda, MD

Fellowship Opportunities at the FDA
Anuradha Ramamoorthy, PhD, US Food and Drug Administration, Silver Spring, MD

Fellowship Opportunities in the Industry
Kathleen M. Hillgren, PhD, Eli Lilly and Company, Indianapolis, IN

PANEL DISCUSSION

12:30 PM

Lunch and Learn: Job Search Strategies for Clinical Pharmacologists

SPEAKER
Bill Lindstaedt, MS, University of California San Francisco, San Francisco, CA

1:15 PM

BEING MENTORED

CHAIR
Catherine M. T. Sherwin, BSc(Hons), PhD, University of Utah School of Medicine, Salt Lake City, UT

SPEAKERS
INTRODUCTION
Catherine M. T. Sherwin, BSc(Hons), PhD, University of Utah School of Medicine, Salt Lake City, UT

Why Do You Need to be Mentored?
Patricia W. Slattum, PharmD, PhD, Virginia Commonwealth University, Richmond, VA

What Have I Learned from Being a Mentor?
Myong Jin Kim, PharmD, US Food and Drug Administration, Silver Spring, MD

D Discovery
R Regulation
D Development
U Utilization

WEDNESDAY, MARCH 9, 2016

What are the Benefits of the ASCPT Mentoring Program and How do You Sign Up?
Mary Peace McRae, PharmD, PhD, Virginia Commonwealth University, Richmond, VA

PANEL DISCUSSION

8:00 AM – 2:00 PM
SPECIAL SESSION
Scientific Horizons and Opportunities in Pharmacogenomics Research
INDIGO A/E

Organized by the Pharmacogenomics Research Network (PGRN)

Breakfast available at 7:30 am to all registered attendees of this Special Session.

8:00 AM
SPEAKER
Overview of PGRN Transition
Rochelle M. Long, PhD, National Institutes of Health, Bethesda, MD

8:15 AM
EMERGING HORIZONS IN PHARMACOGENOMICS RESEARCH

CHAIR
Mary Relling, PharmD, St. Jude Children's Research Hospital, Memphis, TN

SPEAKERS
Center for Precision Medicine in Leukemia: Genome Variants Influencing de novo and Acquired Resistance to Antileukemic Agents
William E. Evans, PharmD, St. Jude Children's Research Hospital, Memphis, TN

The Vanderbilt P50 Center: New Approaches to Evaluating the Genetics of Adverse Drug Reactions
Elizabeth J. Phillips, MD, Vanderbilt University, Nashville, TN

System Pharmacogenomics of Statin Therapy
Ronald M. Krauss, MD, Children's Hospital Oakland Research Institute, Oakland, CA

Improving Clinical Outcomes Through Pharmacogenomics
Julie A. Johnson, PharmD, University of Florida, Gainesville, FL

10:15 AM
BREAK

10:30 AM
PHARMACOGENOMICS RESOURCES OF THE PGRN

CHAIR
Sook Wah Yee, PhD, University of California San Francisco, San Francisco, CA

SPEAKERS
Warfarin Pharmacogenomics in Alaskan Natives: Focus on Novel Pharmacogene Variant Function
Allan E. Rettie, PhD, University of Washington, Seattle, WA

Clinical Pharmacogenetics Implementation Consortium
Mary Relling, PharmD, St. Jude Children's Research Hospital, Memphis, TN

PharmGKB: Pharmacogenomics Knowledge for Precision Medicine
Teri E. Klein, PhD, Stanford University, Palo Alto, CA

11:45 AM
LUNCH

12:15 PM
PANEL DISCUSSION ON PARTNERSHIP OPPORTUNITIES

WEDNESDAY, MARCH 9, 2016

CHAIRS
Kathleen M. Giacomini, PhD, School of Pharmacy, University of California San Francisco, San Francisco, CA

Rachel F. Tyndale, PhD, Section Head, Pharmacogenetics, Centre for Addiction and Mental Health, University of Toronto, Toronto, ON, Canada

SPEAKERS
INTRODUCTION
Kathleen M. Giacomini, PhD, School of Pharmacy, University of California San Francisco, San Francisco, CA

PGRN WEBSITE
Megan Riel-Mehan, University of California San Francisco, San Francisco, CA

PANELIST
Alan R. Shuldiner, MD, Regeneron Genetics Center, Tarrytown, NY

PANELIST
Richard Weinshilboum, MD, Mayo Clinic, Rochester, MN

1:30 PM

Pharmacogenetic Implementation Initiatives in Europe
Ron H.N. van Schaik, PhD, Erasmus University, Rotterdam, Netherlands

Pharmacogenetic Implementation Initiatives in Europe
Jesse J. Swen, PharmD, PhD, Leiden University Medical Centre, Leiden, Netherlands

10:00 AM – 12:00 NOON

ASCPT-ASIA PACIFIC SYMPOSIUM: RACIAL/ETHNIC DIFFERENCES IN DRUG RESPONSE
INDIGO D

CHAIRS
Keith D. Wilner, PhD, Pfizer Global Research and Development, San Diego, CA

Masako P. Nakano, MD, PhD, Eli Lilly Japan K.K., Kobe, Japan

SPEAKERS
Factors Influencing Racial/Ethnic Differences in Drug Responses
Jae-Gook Shin, MD, PhD, Inje University College of Medicine, Busan Paik Hospital, Busan, Korea, Republic of

Genetic Admixture and Drug Response
Esteban Burchard, MD, MPH, University of California San Francisco, San Francisco, CA

Ethnic Differences in Pharmacokinetics and Pharmacodynamics: Review Experiences of New Drugs for Hepatitis C Virus Infection
Naomi Nagai, PhD, Pharmaceuticals and Medical Devices Agency, Tokyo, Japan

Green Tea Effects on Pharmacokinetics and Pharmacodynamics
Shingen Misaka, PhD, Fukushima Medical University School of Medicine, Fukushima, Japan

11:30 AM – 1:00 PM

NETWORK AND COMMUNITY STEERING COMMITTEE MEETING
AQUA 300
(By Invitation Only)

1:00 PM – 2:00 PM

NEW MEMBER WELCOME
AQUA 310

2:00 PM – 2:30 PM

AWARDS RECEPTION
INDIGO 202B
(By Invitation Only)

D Discovery R Regulation
D Development U Utilization

WEDNESDAY, MARCH 9, 2016

2:30 PM - 3:30 PM

OPENING SESSION
INDIGO BCFG

Sponsored by:

Genentech
A Member of the Roche Group

STATE OF THE SOCIETY ADDRESS
Mario L. Rocci, Jr., PhD
ICON, President

AWARD PRESENTATIONS
William B. Abrams Award in Geriatric Clinical Pharmacology
PRESENTER
Patricia W. Slattum, PharmD,
Virginia Commonwealth University

RECIPIENT
Joseph T. Hanlon, PharmD
University of Pittsburgh

Henry W. Elliott Distinguished Service Award
PRESENTER
Lei Zhang, PhD
US Food and Drug Administration

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

Gary Neil Prize for Innovation in Drug Development
PRESENTER
Shiew-Mei Huang, PhD
US Food and Drug Administration

RECIPIENT
Peter K. Honig, MD, MPH
Pfizer, Inc.

2016 David J. Goldstein Trainee Award
PRESENTER
Mario L. Rocci, Jr., PhD
ICON

RECIPIENT
Tu H. Mai, PhD
University of Chicago

2016 Jason Morrow Trainee Award
PRESENTER
Mario L. Rocci, Jr., PhD
ICON

RECIPIENTS
Chia-Hsiang Hsueh, PhD
University of California, San Francisco

Tore B. Stage, Msc Pharm
University of Southern Denmark

2016 ASCPT Mentor Award
PRESENTER
Walter Kraft, MD, FACP
Thomas Jefferson University

RECIPIENT
Scott A. Waldman, MD, PhD
Thomas Jefferson University

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

2015 Post Doctoral Fellowships in Translational Medicine
Jing Sun, PhD
Dana-Farber Cancer Institute

Adam Swick, PhD
University of Wisconsin School of Medicine

2015 Research Starter Grants in Translational Medicine
Ritika Jaini, PhD
Cleveland Clinic

Georgios Paschos, PhD
University of Pennsylvania

WEDNESDAY, MARCH 9, 2016

2015 Paul Calabresi Medical Student Fellowship
Joyce Chen
University of California San Diego

2016 Faculty Development Award
Crystal Clark, MD
Northwestern Feinberg School of Medicine

2016 Award in Excellence in Clinical Pharmacology
David J. Greenblatt, MD
Tufts University School of Medicine

CPT: Pharmacometrics & Systems Pharmacology Award
PRESENTER
Piet H. van der Graaf, PhD, PharmD
Leiden Academic Centre for Drug Research

RECIPIENT
Ron Keizer, PharmD, PhD
InsightRX/Pirana Software & Consulting

CEO REMARKS
Sharon J. Swan, FASAE, CAE

3:30 PM – 4:30 PM
STATE OF THE ART LECTURE
INDIGO BCFG

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

SPEAKER

Accelerating Discovery Through Human Genetics
Anne Wojcicki, 23andMe, Mountain View, CA

4:30 PM – 6:30 PM
OPENING RECEPTION
SAPPHIRE BALLROOM

Sponsored by:

Genentech
A Member of the Roche Group

4:30 PM – 6:30 PM
EXHIBIT HALL
SAPPHIRE BALLROOM

4:45 PM – 5:45 PM
SHOWCASE OF TOP TRAINEE ABSTRACTS
SAPPHIRE BALLROOM

For complete abstract content download the ASCPT Annual Meeting Mobile App.

PT-01
EVALUATING THE TRANSPLACENTAL TRANSFER OF APIXABAN USING A DUALLY PERFUSED ISOLATED HUMAN PLACENTAL LOBULE.
Presenter: Priya Bapat, University of Toronto

PT-02
MODELING ALZHEIMER'S DISEASE (AD) PROGRESSION ON A PATHOLOGICAL TIMELINE.
Presenter: Laiyi Chua, Lilly-NUS Centre for Clinical Pharmacology

PT-03
GENOME-WIDE ASSOCIATION STUDY TO IDENTIFY THE GENETIC DETERMINANTS OF WARFARIN INDUCED HEMORRHAGIC COMPLICATIONS IN AFRICAN AMERICANS (AAS).
Presenter: Tanima De, PhD, University of Chicago

D Discovery R Regulation
D Development U Utilization

WEDNESDAY, MARCH 9, 2016

PT-04
IDENTIFICATION OF A NOVEL HIGH-AFFINITY CARRIER OF NUCLEOSIDE ANALOGUES.
Presenter: Christina Drenberg, PhD, The Ohio State University College of Pharmacy

PT-05
NOVEL DELETERIOUS DIHYDROPYRIMIDINE DEHYDROGENASE VARIANTS MAY CONTRIBUTE TO 5-FLUOROURACIL SENSITIVITY IN AN EAST AFRICAN POPULATION.
Presenter: Tarig Elraiyah, Mayo Clinic

PT-06
PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELING TO PREDICT CLINICAL EFFECT OF PROTON PUMP INHIBITORS (PPI) ON EXPOSURE OF ANTICANCER PROTEIN KINASE INHIBITORS (PKI).
Presenter: Hani Ghazarian, UC San Diego Skaggs School of Pharmacy

PT-07
DEVELOPMENT OF A SYSTEMS PHARMACOLOGY MODEL TO PREDICT THE EFFECTS OF WARFARIN AND RIVAROXABAN ON THE HUMAN COAGULATION NETWORK.
Presenter: Sonja Hartmann, PhD, University of Florida

PT-08
THE ACTIVITIES OF ORGANIC ANION TRANSPORTERS, OATP1B1/1B3 AND OAT1/3 ARE MODULATED BY UREMIC TOXINS.
Presenter: Chia-Hsiang Hsueh, PhD, University of California, San Francisco

PT-09
QUANTIFYING MYELIN KINETICS IN HEALTHY SUBJECTS USING DEUTERIUM LABELING.
Presenter: Kawita Kanhai, MD, Centre for Human Drug Research

PT-10
ASSESSMENT OF COVARIATE EFFECT BASED ON INDIVIDUAL PATIENT DATA VS. MODEL-BASED META-ANALYSIS OF AGGREGATE DATA FOR DPP-4 INHIBITORS.
Presenter: Johannes Kast, University of Florida

PT-11
EXPOSURE-RESPONSE (ER) ANALYSIS OF AXITINIB IN PATIENTS WITH METASTATIC OR UNRESECTABLE LOCALLY ADVANCED THYROID CANCER (TC).
Presenter: Lisa Lam, PharmD, University of California, San Diego

PT-12
AMELIORATION OF CISPLATIN NEPHROTOXICITY BY NILOTINIB.
Presenter: Alix Leblanc, PhD, The Ohio State University

PT-13
METFORMIN IS A SUBSTRATE AND INHIBITOR OF THE HUMAN INTESTINAL THIAMINE TRANSPORTER 2 (THTR-2; SLC19A3).
Presenter: Xiaomin Liang, University of California, San Francisco

PT-14
IMPACT OF CORRELATION STRUCTURE ASSUMPTIONS ON MODEL-BASED META-ANALYSIS OF AGGREGATE LONGITUDINAL DATA.
Presenter: Chay Ngee Lim, PhD, University of Minnesota

PT-15
ERICH3 GENETIC VARIATION ASSOCIATED WITH PLASMA SEROTONIN AND CHANGE IN PLASMA SEROTONIN AFTER SSRI THERAPY: PHARMACOMETABOLOMICS-INFORMED PHARMACOGENOMICS.
Presenter: Duan Liu, PhD, Mayo Clinic

WEDNESDAY, MARCH 9, 2016

PT-16
GENOMIC IDENTIFICATION AND FUNCTIONAL CHARACTERIZATION OF METFORMIN-RESPONSIVE REGULATORY ELEMENTS.
Presenter: Marcelo Luizon, PhD, University of California San Francisco

PT-17
PHARMACOGENETIC ASSOCIATION OF SS1-ADRENERGIC RECEPTOR SER49GLY POLYMORPHISM WITH OUTCOMES IN THE SECONDARY PREVENTION OF SMALL SUBCORTICAL STROKES (SPS3) TRIAL.
Presenter: Oyunbileg Magvanjav, University of Florida

PT-18
A JOINT MODEL RELATING CHANGES IN PROSTATE SPECIFIC ANTIGEN (PSA) TO SURVIVAL IN CASTRATE RESISTANT PROSTATE CANCER (CRPC).
Presenter: Tu Mai, PhD, University of Chicago

PT-19
PATIENT (PT) PERCEPTIONS OF CARE AS INFLUENCED BY THE IMPLEMENTATION OF A LARGE INSTITUTIONAL PHARMACOGENOMIC TESTING PROGRAM.
Presenter: Ryan McKillip, University of Chicago

PT-20
ECULIZUMAB POPULATION PHARMACOKINETICS AND PHARMACODYNAMICS IN PATIENTS WITH HEMATOPOIETIC STEM CELL TRANSPLANT-ASSOCIATED THROMBOTIC MICROANGIOPATHY (HSCT-TMA).
Presenter: Kana Mizuno, PhD, Cincinnati Children's Hospital Medical Center

PT-21
PHARMACOGENOMIC VARIANTS ASSOCIATED WITH CELLULAR SENSITIVITY TO IDELALISIB.
Presenter: Kristen Pettit, MD, University of Chicago

PT-22
PHARMACOMETABOLOMICS SIGNATURES FROM WOMEN WITH PREMENSTRUAL DYSPHORIC DISORDER ADMINISTERED ESTRADIOL AND PROGESTERONE TREATMENT.
Presenter: Daniel Rotroff, PhD, North Carolina State University

PT-23
HYPERTENSION (HTN)/BLOOD PRESSURE (BP) SIGNATURE GENES AND BP RESPONSE TO THIAZIDE DIURETICS (TD): RESULTS FROM PEAR AND PEAR-2 STUDIES.
Presenter: Ana Sá, University of Florida

PT-24
FINDING A NEEDLE IN THE HAYSTACK FOR THIAZIDE DIURETIC RESPONSE USING GENOMICS/ TRANSCRIPTOMICS IN THE PHARMACOGENOMIC EVALUATION OF ANTIHYPERTENIVE RESPONSES (PEAR) STUDY.
Presenter: Mohamed Shahin, University of Florida

PT-25
EFFECT OF OBESITY ON CYP2C19 METABOLISM IN CHILDREN.
Presenter: Valentina Shakhnovich, MD, Children's Mercy Hospital

PT-26
ANTIRETROVIRAL DRUG EXPOSURE IN CEREBROSPINAL FLUID (CSF) AS A PREDICTOR OF NEUROCOGNITIVE OUTCOMES IN HIV INFECTED PATIENTS.
Presenter: Nithya Srinivas, University of North Carolina at Chapel Hill

D Discovery R Regulation
D Development U Utilization

WEDNESDAY, MARCH 9, 2016

PT-27
CHANGE IN INTERNATIONAL NORMALIZED RATIO AMONG PATIENTS TREATED WITH DICLOXACILLIN AND VITAMIN K ANTAGONISTS.
Presenter: Tore Stage, University of Southern Denmark

PT-28
NOVEL IN VIVO HUMAN MODEL FOR TRANSIENT MITOCHONDRIAL DYSFUNCTION: SIMVASTATIN-INDUCED MITOCHONDRIAL DYSFUNCTION IN HEALTHY SUBJECTS AND ITS REVERSIBILITY BY UBIQUINOL.
Presenter: Marcus van Diemen, MD, Centre for Human Drug Research

PT-29
A SYSTEMS BIOLOGY APPROACH TO PREDICTING CARDIOTOXICITY ASSOCIATED WITH TYROSINE KINASE INHIBITORS.
Presenter: Shadia Zaman, PhD, US Food and Drug Administration

PT-30
SCREENING A LIBRARY OF DRUGS WITH CNS ACTIVITY TO IDENTIFY SUBSTRATES OF ORGANIC CATION INFLUX TRANSPORTERS.
Presenter: Arik Zur, PhD, University of California, San Francisco

5:45 PM – 6:30 PM
POSTER WALK
Essential Tools for Precision Medicine
SAPPHIRE FOYER

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

For complete abstract content download the ASCPT Annual Meeting Mobile App.

PWI-1
PHARMACOMETABOLOMICS SIGNATURES FROM WOMEN WITH PREMENSTRUAL DYSPHORIC DISORDER ADMINISTERED ESTRADIOL AND PROGESTERONE TREATMENT.
Presenter: Daniel Rotroff, PhD, North Carolina State University

PWI-2
INVESTIGATING THE EPIGENETIC DYSREGULATION OF APOPTOSIS GENES IN PANCREATIC CANCER PATIENTS AND THEIR POTENTIAL IMPLICATION IN PREDICTING CHEMOTHERAPEUTIC OUTCOME.
Presenter: Lee Cheng Phua, PhD, Singapore General Hospital

PWI-3
A METFORMIN METABOLOMIC EXPRESSION PROFILE STUDY UTILIZING AN ELECTRONIC HEALTH RECORD (EHR)-LINKED BIOREPOSITORY AND INTEGRATIVE MOLECULAR EPIDEMIOLOGY APPROACHES.
Presenter: Matthew Breitenstein, PhD, Mayo Clinic

PWI-4
NOVEL IN VIVO HUMAN MODEL FOR TRANSIENT MITOCHONDRIAL DYSFUNCTION: SIMVASTATIN-INDUCED MITOCHONDRIAL DYSFUNCTION IN HEALTHY SUBJECTS AND ITS REVERSIBILITY BY UBIQUINOL.
Presenter: Marcus van Diemen, MD, Centre for Human Drug Research

PWI-5
EVALUATION OF HYPOXIA ADAPTATION IN NEUROBLASTOMA IDENTIFIES REPRODUCIBLE TRANSCRIPTIONAL AND PHENOTYPIC RESPONSES.
Presenter: Mark Applebaum, MD, University of Chicago

THURSDAY, MARCH 10, 2016

7:00 AM – 8:00 AM
INFECTIOUS DISEASES (INF) COMMUNITY MEETING
AQUA 300

Led by INF Chair and Vice Chair

7:00 AM - 9:00 AM
AMERICAN BOARD OF CLINICAL PHARMACOLOGY (ABCP) BOARD MEETING
(By Invitation Only)
ELEVATION

7:30 AM – 9:00 AM
ROUNDTABLE
How Should Simulated DDI Results be Communicated in the Label?
INDIGO A/E

COMMUNITIES
Regulatory Science (RS), Pharmacometrics & Pharmacokinetics (PMK)

D D R U

CHAIRS
Ping Zhao, PhD, US Food and Drug Administration, Silver Spring, MD

Vikram Sinha, PhD, Rockville, MD

PANELISTS
Lawrence J. Lesko, PhD, FCP, University of Florida, Orlando, FL

Joseph Grillo, PharmD, US Food and Drug Administration, Silver Spring, MD

TBD

Jack Cook, PhD, Pfizer Inc., Groton, CT

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

- Discuss recent regulatory experience in including PBPK simulation results in US labels and discuss challenges and heterogeneity of using simulated data for regulatory decision making; and
- Brainstorm solutions towards clarity and consistency of using PBPK information in product labels.

7:30 AM – 9:00 AM
PSP EDITORIAL BOARD MEETING
AQUA A/B
(By Invitation Only)

7:30 AM – 9:00 AM
CPT EDITORIAL BOARD MEETING
INDIGO H
(By Invitation Only)

8:00 AM – 9:00 AM
BIOTELEMETRY RESEARCH PRODUCT THEATER
AQUA 310

Join BioTelemetry for a free, exclusive seminar and breakfast bites. Seating is limited.

9:15 AM - 10:15 AM
STATE OF THE ART LECTURE
INDIGO BCFG

CHAIR
Mario L. Rocci, Jr., PhD, ICON, Whitesboro, NY

SPEAKER

How Pharmacology and Quantitative Methodologies are Impacting Global Health: A Perspective from the Bill and Melinda Gate Foundation
Dan Hartman, MD, Bill and Melinda Gates Foundation, Seattle, WA

D Discovery
D Development
R Regulation
U Utilization

THURSDAY, MARCH 10, 2016

10:30 AM – 11:30 AM

AWARD LECTURE

Rawls-Palmer Progress in Medicine Award Lecture

INDIGO BCFG

AWARD PRESENTER

Evan Kharasch, MD, PhD, Washington University, St Louis, MO

SPEAKER

Genes and the Environment: How they Affect Drug Metabolism and Response
Kenneth E. Thummel, PhD, University of Washington, Seattle, WA

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

- Discuss the contribution of intestinal CYP3A4 to first-pass drug metabolism and how variation in CYP3A4 and associated regulatory genes contribute to inter-individual differences in intestinal CYP3A4 function;
- Identify a clearer perspective of the role of vitamin D in regulating intestinal CYP3A4 and conversely how perturbation of CYP3A4 function can adversely modify vitamin D and mineral homeostasis; and
- Discuss the challenges and positive outcomes that can manifest in the conduct of pharmacogenomics research with indigenous US populations.

10:30 AM - 12:30 PM

SYMPOSIUM

Characterizing Dose/Exposure Response of Biologics: Are We There Yet?

INDIGO A/E

COMMUNITIES

Biologics, Pharmacometrics & Pharmacokinetics (PMK)

D D R U

CHAIRS

Anne Heatherington, PhD, Pfizer Inc., Cambridge, MA

Ganesh M. Mugundu, PhD, AstraZeneca Boston R&D, Waltham, MA

SPEAKERS

Model-Based Meta-Analysis of Clinical Dose-Response of Biologics
Joseph Wu, PhD, Pfizer Inc., Groton, CT

Dose Response: The Confluence of Disease, Endpoints, Pharmacology, Modality and Their Impact
Bernd Meibohm, PhD, FCP, University of Tennessee, Memphis, TN

The Challenges of Developing a Biologic with an Unclear/Non-Monotonic Dose Response
Lorin Roskos, PhD, Medimmune/AstraZeneca, Gaithersburg, MD

What are the Regulatory Expectations for Characterizing Dose-Response for Biologics
Yaning Wang, PhD, US Food and Drug Administration, Silver Spring, MD

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

- Identify core concepts and challenges in characterizing the exposure response relationship for biologics; and
- Understand the confluence of disease, endpoints, pharmacology, modality and their impact on dose response of biologics. Describe regulatory expectations on biologics dose/exposure response modeling and optimizing the dose/dosing regimen.

THURSDAY, MARCH 10, 2016

10:30 AM – 12:30 PM

Epigenetic Biomarkers and Modifications in Clinical Pharmacology
INDIGO D

COMMUNITIES
Pharmacogenomics (PMG), Biomarkers & Translational Tools (BTT)

D D R U

CHAIRS
Jeffrey Waring, PhD, AbbVie, North Chicago, IL

Richard B. Kim, MD, FRCP(C), Western University, London, ON, Canada

SPEAKERS
Growth Inhibition of SCLC Cell Lines by Treatment with LSD1 Inhibitor is Associated with Modulation of Neuroendocrine Pathways
Thomas Paul, PhD, Pfizer Inc., San Diego, CA

Overview of the State of Epigenetics
Jonathan Pevsner, PhD, Kennedy Krieger Institute and Johns Hopkins University, Baltimore, MD

Application of Epigenetics for Clinical Immunology
Robert Georgantas, PhD, AbbVie, North Chicago, IL

Histone Deacetylase Inhibitors: Assessing Their Potential for Clinical Use in Neurodegenerative Disorders
Elizabeth Thomas, PhD, Scripps Research Institute, La Jolla, CA

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

- Gain a broader understanding of the role that epigenetic modifications play in disease mechanisms and response to therapies;
- Discover how epigenetic analysis can be successfully applied in clinical trials to identify markers of response; and
- Gain a broader understanding of the interplay between epigenetic modifications and genomics in disease therapies and therapeutic response.

11:00 AM – 12:00 NOON

INTERNATIONAL TRANSPORTER CONSORTIUM (ITC) COMMUNITY MEETING
AQUA 310

Led by ITC Chair and Vice Chairs

11:30 AM – 6:30 PM

EXHIBITS AND POSTERS
SAPPHIRE BALLROOM

12:00 NOON – 1:00 PM

COVANCE HOSTED EVENT
AQUA 300

Join Covance for a free, exclusive seminar and refreshments. Seating is limited.

12:00 NOON - 1:30 PM

TRAINEE PROGRAMMING
TRAINEE LUNCHEON
AQUA A-F
(Ticket required)

12:00 NOON – 1:30 PM

FINANCE COMMITTEE MEETING
AQUA BOARDROOM
(By Invitation Only)

12:00 NOON – 1:30 PM

EXHIBIT HALL
Lunch Available for Purchase in the Poster and Exhibit Hall
SAPPHIRE BALLROOM
(Ticket required)

1:00 PM – 2:00 PM

FEATURED SPEAKER
Understanding Variability in Drug Action: Big Data and Little Data
INDIGO BCFG

D Discovery R Regulation
D Development U Utilization

THURSDAY, MARCH 10, 2016

CHAIR
Julie A. Johnson, PharmD, University of Florida, Gainesville, FL

SPEAKER

Dan Roden, MD, Vanderbilt University School of Medicine, Nashville, TN

1:00 PM – 2:30 PM

WORKSHOP
Discovery and Development of First-in-Class Drugs That Target Membrane Transporters
INDIGO D

COMMUNITIES
International Transporter Consortium (ITC), Pharmacogenomics (PMG)

D D R U

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

Teri E. Klein, PhD, Stanford University, Palo Alto, CA

SPEAKERS
Targeting SGLT2 Inhibitors for the Treatment of Type 2 Diabetes
Ernest M. Wright, PhD, DSc, University of California Los Angeles, Los Angeles, CA

Development of URAT1 Inhibitors for the Treatment of Gout: Challenges with First-in-Class Drugs
Jeffrey N. Miner, PhD, Ardea Biosciences, San Diego, CA

Transporters Potentiators and Correctors for the Treatment of Rare Diseases: Therapeutic Use of Ivacaftor in Cystic Fibrosis
John P. Clancy, MD, University of Cincinnati, Cincinnati, OH

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

- List three membrane transporters that represent targets for new drugs and describe the disease that is treated by the drugs that modulate function of the target; and
- Describe three major challenges for the discovery, development or use of new molecular entities that target membrane transporters.

1:00 PM – 2:30 PM

WORKSHOP
Pediatric Dose Selection for Pediatric-Specific Diseases
INDIGO A/E

COMMUNITIES
Special Populations (SPO), Pharmacometrics & Pharmacokinetics (PMK)

D D R U

CHAIRS
Paulien Ravenstijn, PhD, Janssen Research and Development, Beerse, Belgium

Dionna Green, MD, US Food and Drug Administration, Silver Spring, MD

SPEAKERS
How M&S Can Help in the Different Stages of Pediatric Drug Development for a Pediatric-Specific Sisease: RSV as a Case Study
Anne Brochot, Eng, MSc, Ablynx, Ghent, Belgium

Combining Benefit-Risk Assessment with M&S to Inform Pediatric Dose Selection
Oscar Della Pasqua, MD, PhD, GlaxoSmithKline and Clinical Pharmacology & Therapeutics, University College London, Stockley Park, United Kingdom

THURSDAY, MARCH 10, 2016

Regulatory Experience in Pediatric Dose Selection for Pediatric-Specific Diseases
Gilbert J. Burckart, PharmD, US Food and Drug Administration, Silver Spring, MD

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

- Understand some of the innovative modeling and simulation approaches applied for dose selection for pediatric-specific diseases;
- Understand the value of evidence synthesis and benefit-risk analysis in the selection of pediatric dosing regimens; and
- Review the regulatory experience available in dose selection for pediatric clinical trials for children with pediatric-specific diseases.

2:00 PM – 3:30 PM
SPECIAL SESSION
Bioinnovation Forum
INDIGO BCFG

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

SPEAKERS

Rob Knight, PhD
University of California San Diego

Hugh Rosen, MD, PhD
The Scripps Research Institute
La Jolla, CA

Craig H. Lipset, MBA
Pfizer Inc.
New York, NY

Geoffrey Kim, MD
US Food and Drug Administration
Silver Spring, MD

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

- Discuss important new and novel research in diverse fields related to therapeutic discovery and development such as translational science, translational medicine, clinical pharmacology, regulatory science, and global health care; and
- Discuss emerging topics in clinical pharmacology, health care, and policy.

3:00 PM – 5:00 PM
DEVELOPMENT, REGULATORY & OUTCOMES (DRO) NETWORK MEETING
INDIGO H

The DRO Network Meeting will include network business and administrative updates and scientific presentation and discussion. There will be break outs to Community-level interactions to mingle with Community leadership and members, and to facilitate ideas for future Annual Meeting Programming, Webinars, White Papers, and Scientific Collaborations.

3:00 PM – 4:00 PM
SYSTEMS PHARMACOLOGY (SP) COMMUNITY MEETING
AQUA 300

Led by SP Chair and Vice Chair

3:00 PM – 4:00 PM
PHARMACOGENOMICS (PMG) COMMUNITY MEETING
AQUA 310

Join the Chair and Vice Chair for this Community Planning Meeting.

D Discovery
R Regulation
D Development
U Utilization

THURSDAY, MARCH 10, 2016

3:30 PM – 4:30 PM
ORAL ABSTRACT SESSION
Old Players, New Game
INDIGO A/E

CHAIRS
Aubrey Stoch, MD, Merck Inc.

Akintunde Bello, MSc, PhD, Bristol-Myers Squibb

For complete abstract content download the ASCPT Annual Meeting Mobile App.

OI-1
EVALUATING THE TRANSPLACENTAL TRANSFER OF APIXABAN USING A DUALLY PERFUSED ISOLATED HUMAN PLACENTAL LOBULE.
Presenter: Priya Bapat, University of Toronto

OI-2
CALMING THE ROLLER-COASTER RIDE, BIPOLAR DISEASE: A DOUBLE-BLIND, ACTIVE CONTROLLED TRIAL DEMONSTRATES ANTI-MANIC EFFICACY OF A NEW PROTEIN KINASE C INHIBITOR ENDOXIFEN.
Presenter: Ateeq Ahmad, PhD, Jina Pharmaceuticals

OI-3
PHARMACOGENETIC PROFILING WITHIN A PEDIATRIC COHORT OF ADHD PATIENTS FOR PREDICTING RESPONSE TO ATOMOXETINE.
Presenter: David Hahn, PhD, Cincinnati Children's Hospital Medical Center

OI-4
HYPERTENSION (HTN)/BLOOD PRESSURE (BP) SIGNATURE GENES AND BP RESPONSE TO THIAZIDE DIURETICS (TD): RESULTS FROM PEAR AND PEAR-2 STUDIES.
Presenter: Ana Sá, University of Florida

4:30 PM – 5:30 PM
UCSF/STANFORD/GENENTECH RECEPTION
AQUA A-C
(By Invitation Only)

4:30 PM – 6:30 PM
PRESIDENT'S NETWORKING RECEPTION
SAPPHIRE BALLROOM
Co-Sponsored by:

PhRMA FOUNDATION

4:45 PM – 5:30 PM
POSTER WALK
Mechanisms Behind Special Populations: What Makes Them So Special?
SAPPHIRE FOYER

CHAIR
Deanna Kroetz, PhD, University of California San Francisco

For complete abstract content download the ASCPT Annual Meeting Mobile App.

PWII-1
THE ACTIVITIES OF ORGANIC ANION TRANSPORTERS, OATP1B1/1B3 AND OAT1/3 ARE MODULATED BY UREMIC TOXINS.
Presenter: Chia-Hsiang Hsueh, PhD, University of California, San Francisco

PWII-2
GENOME-WIDE ASSOCIATION STUDY TO IDENTIFY THE GENETIC DETERMINANTS OF WARFARIN INDUCED HEMORRHAGIC COMPLICATIONS IN AFRICAN AMERICANS (AAS).
Presenter: Tanima De, PhD, University of Chicago

THURSDAY, MARCH 12, 2016

PWII-3
IMPACT OF PREECLAMPSIA ON THE EXPRESSION OF ABC AND SLC TRANSPORTERS IN HUMAN PLACENTA.
Presenter: Dea Kojovic, University of Toronto

PWII-4
NOVEL DELETERIOUS DIHYDROPYRIMIDINE DEHYDROGENASE VARIANTS MAY CONTRIBUTE TO 5-FLUOROURACIL SENSITIVITY IN AN EAST AFRICAN POPULATION.
Presenter: Tarig Elraiyah, Mayo Clinic

5:00 PM – 6:00 PM
PHARMACOMETABOLOMICS (PM) COMMUNITY MEETING
AQUA 300

Led by the PM Chair and Vice Chair

5:30 PM – 6:15 PM
Novel Modeling Approaches to Solve Old Problems: PK, DDI, Toxicity
SAPPHIRE FOYER

CHAIR
Kellie Reynolds, PharmD

For complete abstract content download the ASCPT Annual Meeting Mobile App.

PWIII-1
IN SILICO PREDICTION OF ORAL BIOAVAILABILITY.
Presenter: Michael Lawless, PhD, Simulations Plus, Inc.

PWIII-2
DEVELOPMENT OF A SYSTEMS PHARMACOLOGY MODEL TO PREDICT THE EFFECTS OF WARFARIN AND RIVAROXABAN ON THE HUMAN COAGULATION NETWORK.
Presenter: Sonja Hartmann, PhD, University of Florida

PWIII-3
PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELING TO PREDICT CLINICAL EFFECT OF PROTON PUMP INHIBITORS (PPI) ON EXPOSURE OF ANTICANCER PROTEIN KINASE INHIBITORS (PKI).
Presenter: Hani Ghazarian, UC San Diego Skaggs School of Pharmacy

PWIII-4
A SYSTEMS BIOLOGY APPROACH TO PREDICTING CARDIOTOXICITY ASSOCIATED WITH TYROSINE KINASE INHIBITORS.
Presenter: Shadia Zaman, PhD, US Food and Drug Administration

PWIII-5
THE UTILITY OF LINEAR QUANTILE MIXED MODELING (LQMM) APPROACH IN PREDICTING THROUGH-QT (TQT) STUDY OUTCOME USING PHASE I SINGLE ASCENDING DOSE STUDIES (SAD).
Presenter: Nidal Al-Huniti, PhD, AstraZeneca

6:00 PM – 7:30 PM
DONOR RECEPTION
ELEVATION
(By Invitation Only)

8:00 PM – 9:00 PM
GAVEL CLUB DESSERT RECEPTION
PRESIDENT'S SUITE
(By Invitation Only)

D Discovery
R Regulation
D Development
U Utilization

FRIDAY, MARCH 11, 2016

7:00 AM – 2:00 PM
EXHIBIT HALL AND POSTERS
SAPPHIRE BALLROOM

7:00 AM – 8:00 AM
ONCOLOGY (ONC) COMMUNITY MEETING
AQUA 310

Led by the ONC Chair and Vice Chair

7:00 AM – 9:00 AM
EXHIBIT HALL – NETWORKING BREAKFAST
SAPPHIRE BALLROOM

Take advantage of this special morning networking time during breakfast in the Exhibit Hall.

7:00 AM – 9:00 AM
QUANTITATIVE PHARMACOLOGY (QP) NETWORK MEETING
INDIGO H

The Quantitative Pharmacology Network is comprised of 3 Communities – Pharmacometrics, Modeling and Kinetics (PMK), Biologics and Systems Pharmacology (SP). This meeting will have the following main areas of focus:

- Science: Abstracts will be selected for short presentation around "dose optimization" from across the 3 Communities with the aim of generating discussion to fuel the 2017 Annual Meeting programming.
- Grassroots programming for 2017: Fuel 2017 programming focused on QP by taking advantage of the ability to "match" and develop ideas together.
- Networking: Meet other like-minded members who share your passion for the quantitative aspects of clinical pharmacology, including the Network and Community leadership.
- Business: Hear how ASCPT is acting on its Strategic Plan, our new Webinar series and about our family of Journals.

7:15 AM – 8:00 AM
POSTER WALK
Translational Determinants of Toxicity
SAPPHIRE FOYER

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

For complete abstract content download the ASCPT Annual Meeting Mobile App.

PWIV-1
STUDYING INDIVIDUAL DIFFERENCES IN CANCER DRUG EFFICACY USING CELL LINES DERIVED FROM PATIENTS.
Presenter: Thomas Hankemeier, PhD, Leiden/Amsterdam Centre for Drug Research

PWIV-2
ANTIVIRAL DRUGS INTERACT MORE POTENTLY WITH THE HUMAN ORGANIC ANION TRANSPORTER 1, OAT1 THAN WITH RODENT AND NON-RODENT SPECIES ORTHOLOGS.
Presenter: Ling Zou, PhD, University of California, San Francisco

PWIV-3
METFORMIN IS A SUBSTRATE AND INHIBITOR OF THE HUMAN INTESTINAL THIAMINE TRANSPORTER 2 (THTR-2; SLC19A3).
Presenter: Xiaomin Liang, University of California, San Francisco

PWIV-4
AMELIORATION OF CISPLATIN NEPHROTOXICITY BY NILOTINIB.
Presenter: Alix Leblanc, PhD, The Ohio State University

FRIDAY, MARCH 11, 2016

PWIV-5

ANTIRETROVIRAL DRUG EXPOSURE IN CEREBROSPINAL FLUID (CSF) AS A PREDICTOR OF NEUROCOGNITIVE OUTCOMES IN HIV INFECTED PATIENTS.

Presenter: Nithya Srinivas, University of North Carolina at Chapel Hill

7:30 AM – 9:00 AM

ROUNDTABLE

Food for Thought: Need, Timing and Labelling Implications for Clinical Food Effect Studies

INDIGO D

COMMUNITIES

Regulatory Science (RS), Drug Safety (DS)

D D R U

CHAIRS

Neeraj Gupta, PhD, Takeda Pharmaceuticals, Cambridge, MA

Sreeneeranj Kasichayanula, PhD, Amgen, Thousand Oaks, CA

SPEAKERS

Design, Need and Timing of Food Effect Studies, an Industry Experience
Joan Korth-Bradley, PharmD, PhD, Pfizer Inc., Collegeville, PA

Can Model Based Approaches Used to Make Reliable Predictions of Clinical Food Effects and Obviate Need for a Clinical Study?
Tycho Heimbach, PhD, Novartis Institutes for Biomedical Research, East Hanover, NJ

Regulatory Perspective on the Need and Timing of Food Effect Studies
Mehul Mehta, PhD, US Food and Drug Administration, Silver Spring, MD

7:30 AM – 9:00 AM

SCIENCE AT SUNRISE

Use of Medications During Pregnancy and Breastfeeding: Maternal, Fetal, and Neonatal Impact

INDIGO A/E

COMMUNITIES

Special Populations (SPO), Pharmacometrics & Pharmacokinetics (PMK)

D D R U

CHAIRS

Anne Zajicek, MD, PharmD, National Institutes of Health, Bethesda, MD

Catherine M. T. Sherwin, BSc(Hons), PhD, University of Utah School of Medicine, Salt Lake City, UT

SPEAKERS

Clinical Pharmacology During Pregnancy: Efforts of the MFM and OPRU to Expand Understanding
Maged Costantine, MD, University of Texas Medical Branch, Galverston, TX

Application of Pharmacometrics in Pregnancy
Kevin Krudys, PhD, US Food and Drug Administration, Silver Spring, MD

Generating Meaningful Information for Use in Pregnant Women during Program Development
Christina Bucci-Rechtweg, MD, Novartis Pharmaceuticals, East Hanover, NJ

7:30 AM – 9:00 AM

CTS EDITORIAL BOARD MEETING

AQUA A/B

(By Invitation Only)

D Discovery R Regulation
D Development U Utilization

FRIDAY, MARCH 11, 2016

8:00 AM – 9:00 AM
QUOTIENT CLINICAL PRODUCT THEATER
AQUA 300

Join Quotient Clinical for a free, exclusive seminar and breakfast bites. Seating is limited

9:15 AM – 10:15 AM
STATE OF THE ART LECTURE
INDIGO BCFG

CHAIR
Keith D. Wilner, PhD, Pfizer Global Research and Development, San Diego, CA

SPEAKER

Advances in Targeted Therapies for Lung Cancer
Alice T. Shaw, MD, PhD, Massachusetts General Hospital, Boston, MA

10:30 AM – 11:30 AM
AWARD LECTURE
Oscar B. Hunter Career Award in Therapeutics Lecture
INDIGO BCFG

AWARD PRESENTER
Sean Hennessy, PharmD, PhD, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

SPEAKER

What are Our Drugs Truly Doing to Our Patients? Lessons from Pharmacoepidemiology
Brian L. Strom, MD, MPH, Rutgers the State University of New Jersey, Newark, NJ

10:30 AM – 12:30 PM
SYMPOSIUM
Don't Do Different Things…Do Things Differently! Drug Development in Rare Diseases
INDIGO A/E

COMMUNITIES
Biologics, Regulatory Science (RS)

D D R U

CHAIRS
Joan Korth-Bradley, PharmD, PhD, Pfizer Inc., Collegeville, PA

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

SPEAKERS
Challenges and Hurdles to Business as Usual in Drug Development for Treatment of Rare Diseases
David Swinney, PhD, Institute for Rare and Neglected Diseases Drug Discovery, Mountain View, CA

Making Every Subject Count: Case Study of Drug Development Path for Medication in a Pediatric Rare Disease
Indranil Bhattacharya, PhD, Pfizer Inc., Cambridge, MA

Regulatory Perspectives on the Approval of Rare Diseases
Edward Dennis Bashaw, PharmD, US Food and Drug Administration, Silver Spring, MD

The Patient's Perspective
Lorna Speid, PhD, Putting Rare Diseases Patients First!, San Diego, CA

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

- Discuss the importance of new drug therapy to patients with rare disease and the fact that despite very small patient populations, standards of efficacy and safety of drug therapy cannot be compromised; and

FRIDAY, MARCH 11, 2016

- Discuss innovative clinical pharmacology methods that can be used to mitigate some of the challenges of small patient populations, whose characteristics are poorly predicted from healthy volunteers.

10:30 AM – 12:30 PM

The Path to Effective Treatments for Alzheimer's Disease: From the Bench to the Clinic
INDIGO D

COMMUNITIES
Pharmacometrics & Pharmacokinetics (PMK)

D D R U

CHAIRS
Theresa Yuraszeck, PhD, Amgen, Thousand Oaks, CA

Julie A. Stone, PhD, Merck Research Laboratories, North Wales, PA

SPEAKERS
Clinical Candidates for the Treatment of Alzheimer's Disease
William Potter, MD, PhD, National Institute of Mental Health, National Institutes of Health, Bethesda, MD

Building Whole Brain Models of Alzheimer's Disease to Advance Our Understanding of Disease Pathophysiology, Aid Target Identification, and Improve Translational Research
Julie Harris, PhD, Allen Institute for Brain Science, Seattle, WA

Identifying and Overcoming Clinical Pharmacology Challenges during Development of Alzheimer's Disease Interventions: From Discovery to the Clinic
Mark Forman, MD, PhD, Merck & Co., Inc., Whitehouse Station, NJ

Increasing the Probability of Success for Alzheimer's Disease Interventions through Modeling and Simulation
Stephen P. Arneric, PhD, Coalition Against Major Diseases, Critical Path Institute, Tucson, AZ

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

- Describe the pathophysiology of Alzheimer's diseases and the progress in research and development of treatment options in AD;
- Appreciate the potential for the Allen Institute's efforts to develop brain connectome's in healthy and diseased mice to transform our understanding of Alzheimer's disease pathophysiology, improve preclinical models in Alzheimer's disease, and enhance their predictive capabilities;
- Discuss the challenges related to conducting clinical trials for drugs indicated for cognitive disorders like Alzheimer's disease, with an emphasis on issues like biomarker identification and dose selection and appreciate unique considerations for development in emerging markets and;
- Describe the role of modeling and simulation in the development of therapeutics for Alzheimer's disease, including the target selection and validation and the design and interpretation of clinical trials.

11:30 AM – 1:00 PM

CLINICAL PHARMACOLOGY PROGRAM DIRECTORS MEETING
AQUA C/D
(By Invitation Only)

11:45 AM – 1:15 PM

TRAINEE PROGRAMMING
SPEED MENTORING
AQUA A-D
(Ticketed Event)

D Discovery R Regulation
D Development U Utilization

FRIDAY, MARCH 11, 2016

12:00 NOON – 1:00 PM
OMNICOMM SYSTEMS, INC.
PRODUCT THEATER
SAPPHIRE BALLROOM THEATER

Join OmniComm Systems as they present a free, exclusive seminar with complimentary refreshments. Seating is limited.

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

1:00 PM – 2:00 PM
FEATURED SPEAKER
Inflammation as a Source of Variability in Drug Disposition and Response
INDIGO BCFG

CHAIR
Scott A. Waldman, MD, PhD, Thomas Jefferson University, Philadelphia, PA

SPEAKER

Inflammation as a Source of Variability in Drug Disposition and Response

Micheline Piquette-Miller, PhD, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

1:00 PM – 2:00 PM
SPECIAL POPULATIONS (SPO) COMMUNITY MEETING
AQUA 310

Join this meeting to discuss Community goals, education and communication along with 2017 proposal ideas.

1:00 PM – 2:30 PM
WORKSHOP
Quantitative Systems Pharmacology: A Case for Disease Models ISoP SIG on QSP
INDIGO D

COMMUNITIES
Systems Pharmacology (SP), Pharmacometrics & Pharmacokinetics (PMK)

D D R U

CHAIRS
Cynthia Musante, PhD, Pfizer Inc., Cambridge, MA

Saroja Ramanujan, PhD, Genentech, South San Francisco, CA

SPEAKERS
Development of a Quantitative Systems Pharmacology Platform to Support Translational Research and Clinical Development in Immuno-Oncology
Brian Schmidt, PhD, Bristol-Myers Squibb, Princeton, NJ

Strategy and Applications in Psoriasis Drug Discovery and Clinical Development Using AbbVie's Dermatology QSP Platform
Oliver Ghobrial, PhD, AbbVie, North Chicago, IL

A Mechanistic Model of Lipoprotein Metabolism and Kinetics for Cardiovascular Disease Targets
James Lu, PhD, AstraZeneca, Cambridge, United Kingdom

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

- Understand the differences between "fit-for-purpose" and "disease platform" QSP models, and when and where each are best applied; and
- Explore case study examples of disease modeling platforms currently being applied in drug discovery and development.

FRIDAY, MARCH 11, 2016

1:00 PM – 2:30 PM

Rationale Development of Combination Cancer Immunotherapy through Collaborations
INDIGO A/E

COMMUNITIES
Oncology (ONC)

D D R U

CHAIRS
Eric Masson, PharmD, AstraZeneca, Waltham, MA

Paul Statkevich, PhD, Bristol-Myers Squibb, Lawrenceville, NJ

SPEAKERS
Role of Biomarkers in Immuno-Oncology Combination Development
John Kurland, PhD, MedImmune, Gaithersburg, MD

Quantitative Clinical Pharmacology for Early Decision Making During Combination Immunotherapy Development
Shruti Agrawal, PhD, Bristol-Myers Squibb, Lawrenceville, NJ

Regulatory Considerations for Immuno-Oncology Combination Drug Development
Atiqur Rahman, PhD, US Food and Drug Administration, Silver Spring, MD

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

- Highlight the current challenges in development of immunotherapy in combination with other treatment modalities in oncology such as combination selection based on biomarker strategies, clinical trial design initial dosing scenarios, evaluation of safety and efficacy, and potential solutions for overcoming challenges and faster clinical development; and
- Describe case studies where immune check point inhibitors in combination have resulted in benefit to patients in terms of response and elaborate onto challenges and issue resolution in combination drug development, integrated quantitative exposure-response analyses of combination immunotherapy, and case control analysis to guide decision making.

2:15 PM – 3:15 PM

AWARD LECTURE
Leon I. Goldberg Early Investigator Award Lecture
INDIGO BCFG

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

SPEAKER
African American Pharmacogenomics: Challenge Accepted
Minoli A. Perera, PharmD, PhD, University of Chicago, Chicago, IL

AWARD PRESENTER
Richard Weinshilboum, MD, Mayo Clinic, Rochester, MN

SPEAKER
Pharmacogenomics: Science and Promise
Liewei Wang, MD, PhD, Mayo Clinic, Rochester, MN

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

- Describe common mechanisms by which nonsynonymous cSNPs affect function is through regulation of protein stability;
- Describe the concept of patient derived xenograft and their application in cancer research;
- Describe the unique aspects of the African American genome and how they can be used to elucidate novel genetics findings;

D Discovery R Regulation
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- Discuss the use of secondary phenotypes and eQTLs in GWAS studies; and
- Place in context the findings of pharmacogenomic clinical trials and how they may apply to African American populations.

2:45 PM – 4:45 PM

SYMPOSIUM

Benefit/Risk Optimization in the Confirmatory Space and Beyond: Myths, Reality and Possibilities

INDIGO A/E

COMMUNITIES

Pharmacometrics & Pharmacokinetics (PMK), Regulatory Science (RS)

D D R U

CHAIRS

Rajanikanth Madabushi, PhD, US Food and Drug Administration, Silver Spring, MD

Pankaj Gupta, PhD, Pfizer Inc., Groton, CT

SPEAKERS

Scientific, Strategic and Organizational Challenges and Opportunities: An Industry Perspective
Sriram Krishnaswami, PhD, Pfizer Inc., Groton, CT

Registration Trials: Are They Meant to be Confirmatory or is Learning Allowed?
Joga Gobburu, PhD, FCP, MBA, University of Maryland, Baltimore, MD

Does Pharmacometric Modeling Reliably Predict Efficacy and Safety Outcomes in Registration Trials and Can it be Utilized to Optimize Benefit-Risk?
Sanjay Kaul, MD, MPH, FACC, FAHA, Cedars-Sinai Medical Center, Los Angeles, CA

Integration of Knowledge from Late Phase Trials to Support Regulatory Decisions
Yaning Wang, PhD, US Food and Drug Administration, Silver Spring, MD

The following questions will be discussed:

- Should findings of post-hoc exercises be considered only as hypothesis generating and require confirmatory evidence for regulatory review? When should post-hoc approaches be considered and what are the risks?
- Can pharmacometric analyses based on totality of available data be used to inform labeling and dosing? What constitutes adequate evidence in registration and post marketing studies that can allow optimization of benefit/risk and dosing?
- Case studies across different therapeutic areas will highlight the following scenarios to answer the above mentioned questions: Learning analyses using data from confirmatory trials to facilitate regulatory decision making and inform clinical practice.
- Approval of a different dose/dosing regimen than that studied in the registration trial.
- Deriving titration based dosing from fixed dose confirmatory trials.

3:00 PM – 4:00 PM

DRUG UTILIZATION & OUTCOMES (DUO; FORMERLY SAF) COMMUNITY MEETING

AQUA 310

Led by the Chair and Vice Chair

3:00 PM – 5:00 PM

TRANSLATIONAL & PRECISION MEDICINE (TPM) NETWORK MEETING

INDIGO H

Multiple presentations on the theme of Precision Medicine by TPM Communities followed by an interactive roundtable discussion.

5:00 PM – 6:00 PM

BIOLOGICS COMMUNITY MEETING

AQUA 300

Led by the Chair and Vice Chair

SATURDAY, MARCH 12, 2016

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

7:30 AM – 9:00 AM
SCIENCE AT SUNRISE
Genome Wide Association Studies Reveal Important Transporter Polymorphisms as Biomarkers for Pharmacokinetics and Pharmacodynamics
INDIGO A

COMMUNITIES
International Transporter Consortium (ITC), Pharmacogenomics (PMG)

D D R U

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

Shiew-Mei Huang, PhD, North Potomac, MD

SPEAKERS
In Vitro and In Vivo Methodologies for Studying Transporter Polymorphisms
Kathleen M. Hillgren, PhD, Eli Lilly and Company, Indianapolis, IN

Discovery of ABCG2 (BCRP) as a Determinant of Allopurinol Response through Genomewide Association Studies
Kathleen M. Giacomini, PhD, University of California San Francisco, San Francisco, CA

PANEL DISCUSSION

7:30 AM – 9:00 AM
SPECIAL SESSION
Pursuing the Management Track in a Scientific Organization: Learn From the Experts
AQUA A/B

COMMUNITIES
Special Populations (SPO)
Developed by the ASCPT Education Committee and Mentor Task Force

CHAIRS
Catherine M. T. Sherwin, BSc(Hons), PhD, University of Utah School of Medicine, Salt Lake City, UT

Patricia Slattum, PharmD, PhD, Virginia Commonwealth University, Richmond, VA

SPEAKERS
Moving Up, Promotion and Tenure in the Academic Setting
Stephen Spielberg, MD, PhD, DIA, Washington, DC

Guidance in Moving Through the Ranks of Industry
Raafat Bishai, MD, AstraZeneca R&D, Gaithersburg, MD

The Hard Truth About Soft Skills: Leadership and Promotion at the US Food and Drug Administration
Issam Zineh, PharmD, MPH, US Food and Drug Administration, Silver Spring, MD

Opportunities for the Management Track at NIH
Anne Zajicek, MD, PharmD, National Institutes of Health, Bethesda, MD

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

- Provide guidance in how to move through promotion and tenure in the academic setting as well as moving up into administrative roles;
- Provide guidance in moving through the ranks of industry from entry level positions to managerial positions to administrative roles;

D Discovery R Regulation
D Development U Utilization

SATURDAY, MARCH 12, 2016

- Provide guidance in getting promoted through the Food and Drug Administration;
- Provide guidance in getting promoted through the NIH; and
- Discuss key points that can be applied in all settings such as the importance of finding mentors for different aspects of your career

9:00 AM – 10:00 AM

ORAL ABSTRACT SESSION

Advances in Model Based Drug Development: Application to Translational Medicine

INDIGO D

CHAIRS

Virginia (Ginny) Schmith, PhD, FCP, Nuventra, Inc.

Donald Heald, PhD, Johnson & Johnson PRD

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OII-1

A JOINT MODEL RELATING CHANGES IN PROSTATE SPECIFIC ANTIGEN (PSA) TO SURVIVAL IN CASTRATE RESISTANT PROSTATE CANCER (CRPC).

Presenter: Tu Mai, PhD, University of Chicago

OII-2

DEVELOPMENT OF A MECHANISM-BASED DRUG-DISEASE MODEL TO QUANTIFY POSTMENOPAUSAL OSTEOPOROSIS.

Presenter: Li Li, PhD, US Food and Drug Administration

OII-3

ASSESSMENT OF COVARIATE EFFECT BASED ON INDIVIDUAL PATIENT DATA VS. MODEL-BASED META-ANALYSIS OF AGGREGATE DATA FOR DPP-4 INHIBITORS.

Presenter: Johannes Kast, University of Florida

OII-4

IMPACT OF CORRELATION STRUCTURE ASSUMPTIONS ON MODEL-BASED META-ANALYSIS OF AGGREGATE LONGITUDINAL DATA.

Presenter: Chay Ngee Lim, PhD, University of Minnesota

9:00 AM – 10:00 AM

Pharmacogenomics: From Discovery to Implementation

INDIGO H

CHAIRS

Susan Abdel-Rahman, PharmD, Children's Mercy Hospitals and Clinics

Sarah Robertson, PharmD, Vertex Pharmaceuticals, Inc.

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OIII-1

GENOMIC IDENTIFICATION AND FUNCTIONAL CHARACTERIZATION OF METFORMIN-RESPONSIVE REGULATORY ELEMENTS.

Presenter: Marcelo Luizon, PhD, University of California San Francisco

OIII-2

ERICH3 GENETIC VARIATION ASSOCIATED WITH PLASMA SEROTONIN AND CHANGE IN PLASMA SEROTONIN AFTER SSRI THERAPY: PHARMACOMETABOLOMICS-INFORMED PHARMACOGENOMICS.

Presenter: Duan Liu, PhD, Mayo Clinic

SATURDAY, MARCH 12, 2016

OIII-3
PHARMACOGENETIC ASSOCIATION OF SS1-ADRENERGIC RECEPTOR SER49GLY POLYMORPHISM WITH OUTCOMES IN THE SECONDARY PREVENTION OF SMALL SUBCORTICAL STROKES (SPS3) TRIAL.
Presenter: Oyunbileg Magvanjav, University of Florida

OIII-4
ANALYSIS OF CLINICALLY ACTIONABLE PREEMPTIVE PHARMACOGENOMIC (PGX) INFORMATION TO IMPACT IN-HOSPITAL PRESCRIBING.
Presenter: Yee Ming Lee, PharmD, The University of Chicago

10:15 AM – 11:45 AM

WORKSHOP
Dose Selection for Biologics Combination Therapies
INDIGO D

COMMUNITIES
Biologics

D D R U

CHAIRS
Chaitali Passey, PhD, Bristol-Myers Squibb, Princeton, NJ

Li Yan, PhD, MedImmune, LLC, Mountain View, CA

SPEAKERS
Dose Selection Approaches for Combination Oncology/ImmunoOncology Agents
Manish Gupta, PhD, Bristol-Myers Squibb, Princeton, NJ

Strategies for Combining Novel Anti-Cancer Therapies in Hematological Malignancies: Clinical Pharmacology Impact on Drug Evaluation, Dose Finding, and Study Design
Dale Miles, PhD, Genentech, South San Francisco, CA

Two Birds with One Stone: Promises and Challenges for Bispecific Molecules
Bing Wang, PhD, MedImmune, Gaithersburg, MD

Regulatory Perspectives on Developing Biologic Combinations Therapies
Sarah Schrieber, PharmD, US Food and Drug Administration, Silver Spring, MD

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

- Discuss dose-finding strategies for biologics-based combination therapies; and
- Describe bispecific large molecule development strategies and challenges

10:15 AM – 11:45 AM

Lessons Learned from Failed Pediatric Trials
INDIGO H

COMMUNITIES
Special Populations (SPO), Regulatory Science (RS)

D D R U

CHAIRS
Jeffrey Barrett, PhD, Sanofi, Bridgewater, NJ

Lily (Yeruk) Mulugeta, PharmD, US Food and Drug Administration, Silver Spring, MD

SPEAKERS
Guanfacine for ADHD in Adolescents: Utility of Clinical Trial Simulation
Marc Gastonguay, PhD, Metrum Research Group, Tariffville, CT

Challenges in Developing Biologics for Pediatric Diseases: Approaches to Dose Selection
Sameer Doshi, MS, Amgen, Thousand Oaks, CA

D Discovery R Regulation
D Development U Utilization

SATURDAY, MARCH 12, 2016

Failed Trials and Design Considerations in Pediatric Oncology
Brenda Weigel, MD, University of Minnesota, Minneapolis, MN

Failed Trials and Design considerations in Pediatric Type 2 Diabetes
William Tamborlane, MD, Yale University, New Haven, CT

PANELISTS
Gilbert J. Burckart, PharmD, US Food and Drug Administration, Silver Spring, MD

Yaning Wang, PhD, US Food and Drug Administration, Silver Spring, MD

Kevin Krudys, PhD, US Food and Drug Administration, Silver Spring, MD

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

- Review factors contributing to failure of pediatric efficacy trials; and
- Present approaches to optimize pediatric trial design.

10:15 AM – 12:15 PM

SYMPOSIA
Clinical and Translational Pharmacology of Emerging Modalities of Therapeutics: RNA and Gene Therapies
INDIGO E

COMMUNITIES
Pharmacogenomics (PMG), Biomarkers & Translational Tools (BTT)

D D R U

CHAIRS
Sandeep Dutta, PhD, AbbVie, North Chicago, IL

Richard J. Bertz, PhD, Bristol-Myers Squibb, Princeton, NJ

SPEAKERS
Nucleic Acid-Based Drug Modalities: Developing New Classes of Drugs
Jeffrey Waring, PhD, AbbVie, North Chicago, IL

Targeting microRNAs for Disease Therapy: Overview of Progress and Pharmacological Challenges
Tariq Rana, PhD, University of California San Francisco, San Diego, CA

Preclinical and Early Development for RNA-Based Therapy
Jian-Ping Tang, PhD, Alexion Pharmaceuticals, Cheshire, CT

Translational Pharmacology and Biology of Gene Therapy
David Gordon, PhD, Bristol-Myers Squibb, Princeton, NJ

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

- Describe the biology and appreciate the broader issues and challenges of clinical and translational pharmacology of these break-through products; and
- Articulate and contribute to the design of early clinical pharmacology studies of RNA based therapies (micro RNA, mRNA) and gene therapies that establish optimal dose, treatment durations and safety for further exploration in larger confirmatory Phase 2/3 trials.

10:15 AM – 12:15 PM

Adherence: Assessing and Mitigating the Perpetual Fly in the Ointment in Drug Development and Utilization
INDIGO A

COMMUNITIES
Infectious Diseases (INF), Drug Utilization & Outcomes (DUO)

D D R U

PROGRAM & SCIENTIFIC AGENDA

CHAIRS

Craig W. Hendrix, MD, Johns Hopkins University, Baltimore, MD

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

SPEAKERS

Impact of Non-Adherence on Drug Development & Therapeutics
Terrence Blaschke, MD, Bill and Melinda Gates Foundation, Seattle, WA

Pharmacometric Approaches to Adherence Assessment
Michael Fossler, PharmD, PhD, Trevena, Inc., King of Prussia, PA

New Technologies for Assessing Adherence
John Mendelson, MD, California Pacific Medical Center Research Institute, San Francisco, CA

Interventions for Adherence Enhancement
Ariane van der Straten, PhD, MPH, RTI International, San Francisco, CA

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

- Discuss the impact of poor adherence on clinical care, clinical drug development, and introducing bias in estimates of pharmacokinetic and pharmacodynamic parameters critical to rational drug development; and
- Discuss current and developmental methods to objectively and quantitatively assess adherence in the clinical trial setting as well as interventions for ongoing, real-time enhancement of adherence within the clinical trial context.

D Discovery R Regulation
D Development U Utilization

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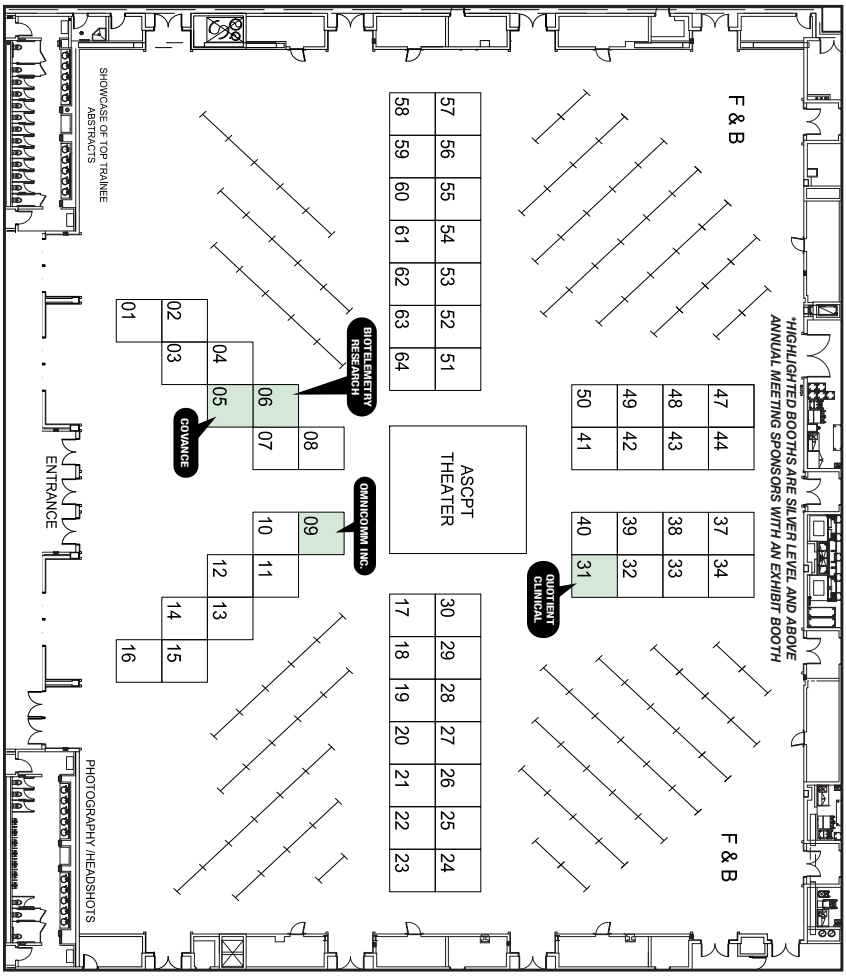

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EXHIBITOR DESCRIPTIONS

49
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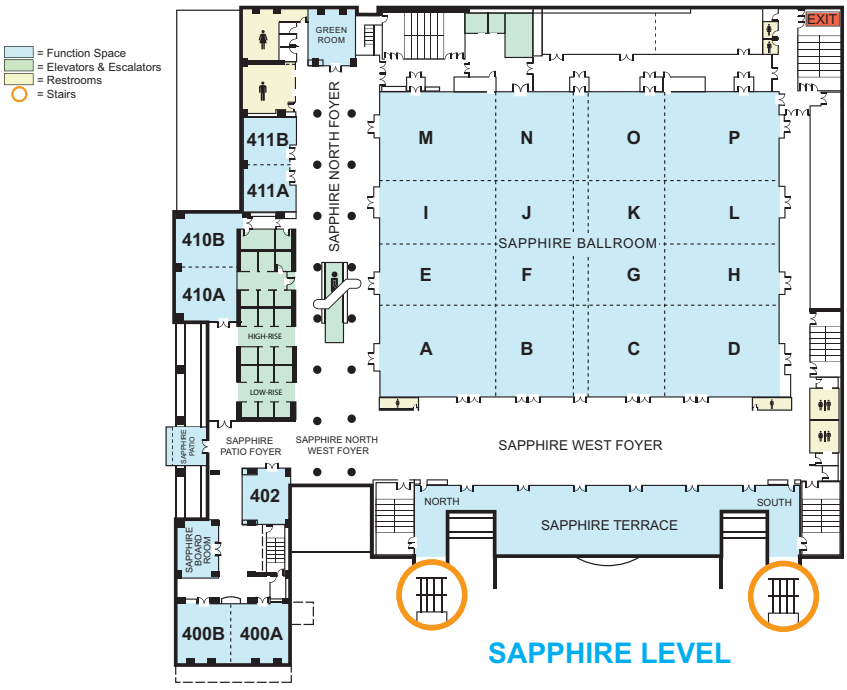

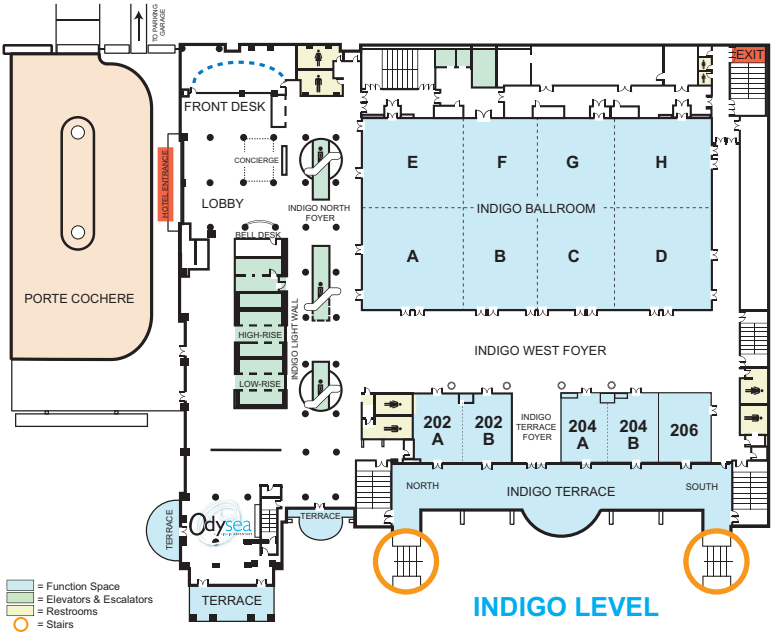

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ACKNOWLEDGMENTS

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4:30 PM – 6:30 PM

SAPPHIRE BALLROOM

E-001

PHARMACOKINETICS, SAFETY AND TOLERABILITY OF TEDIZOLID PHOSPHATE AFTER SINGLE-DOSE ADMINISTRATION IN HEALTHY KOREAN SUBJECTS.

Y. Kim, A. Kim, S. Rhee, S. Yoon, H. Lee, I. Jang, K. Yu; Seoul National University Hospital, Clinical Pharmacology and Therapeutics, Seoul, Korea, Republic of Korea.

E-002

PHASE I STUDY OF TRASTUZUMAB EMTANSINE (T-DM1) IN HER2-POSITIVE METASTATIC BREAST CANCER (MBC) PATIENTS WITH NORMAL OR REDUCED HEPATIC FUNCTION.

P. Agarwal[1], C. Li1, L. Gibiansky[1], S. Dent[2], A. Goncalves[3], I. Nijem[1], A. Strasak[4], P. Lorusso[5], S. Girish[1]; [1]Genentech, South San Francisco, CA, [2]The Ottawa Hospital Cancer Center, Department of Medicine, University of Ottawa, South San Francisco, ON, Canada, [3]Marseille, Marseille, France, [4]Roche, Basel, Switzerland, [5]Yale Cancer Center Administration, New Haven, CT.

E-003

META-ANALYTIC APPROACH TO EVALUATE ALTERNATIVE MODELS FOR CHARACTERIZING THE PK PROFILES OF EXTENDED RELEASE FORMULATIONS OF MPH.

R. Gomeni[1], F. Bressolle[1], T. J. Spencer[2], S. V. Faraone[3]; [1]Pharmacometrica, La Fouillade, France, [2]Massachusetts General Hospital, Boston, MA, [3]SUNY Upstate Medical University, Syracuse, NY.

E-004

USE OF A CLINICAL RESPONSE INDEX DERIVED FROM A PK/PD MODEL TO ESTIMATE THE OPTIMAL *IN VIVO* RELEASE RATE OF EXTENDED RELEASE FORMULATIONS OF MPH.

R. Gomeni[1], F. Bressolle[1], T. J. Spencer[2], S. V. Faraone[3]; [1]Pharmacometrica, La Fouillade, France, [2]Massachusetts General Hospital, Boston, MA, [3]SUNY Upstate Medical University, Syracuse, NY.

E-005

OPTIMAL STUDY DESIGN TO EVALUATE THE CLINICAL RESPONSE OF EXTENDED RELEASE FORMULATIONS OF METHYLPHENIDATE (MPH) IN A PEDIATRIC POPULATION.

R. Gomeni[1], F. Bressolle[1], T. J. Spencer[2], S. V. Faraone[3]; [1]Pharmacometrica, La Fouillade, France, [2]Massachusetts General Hospital, Boston, MA, [3]SUNY Upstate Medical University, Syracuse, NY.

E-006

IDENTIFICATION OF NPC1L1 AS A PHYSIOLOGICAL VITAMIN K TRANSPORTER IN THE SMALL INTESTINE.

T. Takada, Y. Yamanashi, T. Yamamoto, Y. Toyoda, H. Yamamoto, H. Suzuki; Department of Pharmacy, The University of Tokyo Hospital, Tokyo, Japan.

E-007

AN AUTOMATED MODELING TOOL FOR CLINICAL PHARMACOLOGISTS.

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

E-008

POPULATION PHARMACOKINETIC MODELING AND SIMULATION OF MOXIFLOXACIN IN HUMAN AQUEOUS HUMOR AFTER TOPICAL OCULAR APPLICATION.

J. Lee[1], B. Ohk[1], S. Seong[1], W. Kang[1], M. Gwon[1], H. Lee[1], S. Han[2], Y. Yoon[1]; [1]Kyungpook National University Hospital Clinical Trial Center, Daegu, Korea, Republic of, [2]Catholic University Clinical Pharmacology, Seoul, Korea, Republic of.

E-009

INTEGRATED NON-CLINICAL AND CLINICAL RISK ASSESSMENT TO OBVIATE THE NEED FOR A DEDICATED QTC STUDY OF IXAZOMIB IN CANCER PATIENTS.

N. Gupta[1], Y. Huh[2], M. M. Hutmacher[2], S. Ottinger[1], A. Hui[1], K. Venkatakrishnan[1]; [1]Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, [2]Ann Arbor Pharmacometrics Group (A2PG), Ann Arbor, MI.

E-010

EFFECT OF RIFAMPIN ON THE STEADY-STATE PHARMACOKINETICS (PK) OF CRIZOTINIB AFTER REPEATED DOSING IN CANCER PATIENTS.

W. Tan[1], U. Conte[2], M. O'Gorman[3], K. Monti[4], K. Wilner[1]; [1]Pfizer, Inc., San Diego, CA, [2]Pfizer, Inc., New York, NY, [3]Pfizer, Inc., Groton, CT, [4]Rho, Chapel Hill, NC.

E-011

PHARMACOKINETIC INTERACTION BETWEEN CLEVUDINE AND ADEFOVIR DIPIVOXIL AFTER A SINGLE ORAL ADMINISTRATION IN HEALTHY MALE SUBJECTS.

S. Moon[1], S. Kim[1], S. Park[1], Y. Kim[1], H. Hwang[2], S. Yoon[1], I. Jang[1], K. Yu[1], S. Lee[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University Hospital, Seoul, Korea, Republic of, [2]Bukwang Pharm. Co., Ltd., Seoul, Korea, Republic of.

E-012

SUNITINIB-INDUCED HYPERTENSION IN CYP3A4 RS4646437 A-ALLELE CARRIERS WITH METASTATIC RENAL CELL CARCINOMA.

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

E-013

A STUDY OF GASTRIC PH MODULATION ON THE PHARMACOKINETICS OF CC-292 IN HEALTHY SUBJECTS.

J. Nissel, D. Weiss, Y. Li, J. Liu, L. Liu, M. Palmisano; Celgene Corporation, Summit, NJ.

E-014

POTENTIAL FOR RACE-GENOTYPE INTERACTIONS IN EVALUATION OF CYP2C19 GENOTYPE EFFECTS ON PHARMACOKINETICS: AN IN SILICO PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PB-PK) STUDY.

C. Patel[1], C. Rathi[2], K. Venkatakrishnan[1]; [1]Takeda Pharmaceuticals International Co., Cambridge, MA, [2]University of Tennessee Health Sciences Center, Memphis, TN.

E-015

EFFECT OF FOOD INTAKE ON THE PHARMACOKINETICS OF YH4808, A NOVEL K+-COMPETITIVE ACID BLOCKER, AFTER MULTIPLE ORAL ADMINISTRATION IN HEALTHY SUBJECTS.

H. Lee[1], A. Kim[1], S. Yoon[1], S. Yi[1], S. Nam[2], S. Jang[2], S. Yoon[1], J. Cho[1], K. Yu[1], H. Lee[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Yuhan Research Institute, Yuhan Corporation, Seoul, Korea, Republic of.

E-016

EFFECT OF FOOD ON THE PHARMACOKINETICS AND SAFETY OF YH4808, A NOVEL K+-COMPETITIVE ACID BLOCKER, AFTER SINGLE ORAL ADMINISTRATION IN HEALTHY SUBJECTS.

H. Lee[1], A. Kim[1], Y. Kim[1], S. Yi[1], S. Lee[1], S. Nam[2], S. Jang[2], S. Yoon[1], J. Cho[1], K. Yu[1], H. Lee[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Yuhan Research Institute, Yuhan Corporation, Seoul, Korea, Republic of.

E-017

EFFECT OF GENETIC POLYMORPHISMS ON ERLOTINIB PHARMACOKINETICS AND ADVERSE EVENTS JAPANESE PATIENTS WITH NON-SMALL-CELL LUNG CANCER (NSCLC).

A. Hamada[1], J. Sasaki[2], S. Saeki[3], M. Inaba[4], S. Ushijima[4], H. Kishi[5], S. Fujii[6], H. Semba[6], K. Kashiwabara[7], Y. Tsubata[8], C. E. Tsukude[3], Y. K. Shimizu[3], T. Isobe[8], H. Kohrog[3], H. Saito[3]; [1]National Cancer Center, Tokyo, Japan, [2]Kitasato University Hospital, Kanagawa, Japan, [3]Kumamoto University, Kumamoto, Japan, [4]Kumamoto Central Hospital, Kumamoto, Japan, [5]Kumamoto City Hospital, Kumamoto, Japan, [6]Kumamoto Regional Medical Center, Kumamoto, Japan, [7]Kumamoto Medical Center, Kumamoto, Japan, [8]Shimane University Hospital, Shimane, Japan.

E-018

INFLUENCE OF 6-DAY CO-ADMINISTRATION OF DEXAMETHASONE ON THE PHARMACOKINETICS OF OSELTAMIVIR IN HEALTHY VOLUNTEERS.

K. Jang[1], J. Oh[1], M. Kim[2], S. Lee[1], J. Cho[1], I. Jang[1], K. Yu[1], T. Choi[2], S. Shin[3], K. Lim[4]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul, Korea, Republic of, [2]Department of Psychiatry, Seongnam, Korea, Republic of, [3]CHA Health Systems, Seongnam, Korea, Republic of, [4]Department of Clinical Pharmacology and Therapeutics, Seongnam, Korea, Republic of.

E-019

POPULATION MODELING STUDY FOR EVALUATION OF EFFECTIVE AND SAFE DOSE OF RPH-104 FOR THE TREATMENT OF BEHÇET'S SYNDROME AND FMF.

E. Metelkin[1], T. Petukhova[1], O. Demin[1], E. Shipaeva[2], M. Samsonov[2], A. Krotkova[2], Y. Lavrovsky[3]; [1]Institute for Systems Biology, Moscow, Russian Federation, [2]CJSC R-Pharm, Moscow, Russian Federation, [3]R-Pharm Overseas, Inc., San Diego, CA.

E-020

ASSESSMENT OF PHARMACOKINETIC INTERACTION BETWEEN RILOTUMUMAB AND EPIRUBICIN, CISPLATIN, AND CAPECITABINE IN A PHASE III STUDY IN PATIENTS WITH MET-POSITIVE GASTRIC CANCER.

Y. Zhang, M. Kuchimanchi, M. Zhu, S. Doshi, T. Hoang, S. Kasichayanula; Amgen, Inc., Thousand Oaks, CA.

E-021
PHARMACOKINETCS, PHARMACODYNAMICS AND TOLERABILITY OF DWP05195, A NOVEL TRPV1 ANTAGONIST, AFTER MULTIPLE ORAL DOSES IN HEALTHY VOLUNTEERS.

J. Lee[1], S. Lee[1], N. Gu[2], B. Kim[3], Y. Choi[1], J. Kim[4], H. Kim[4], S. Park[1], H. Lee[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 Clinical Pharmacology and Therapeutics and Clinical Trial Center, Dongguk University College of Medicine and Ilsan Hospital, Ilsan, Korea, Republic of, [3]Department of Clinical Pharmacology and Therapeutics, Kyung Hee University College of Medicine and Hospital, Seoul, Korea, Republic of, [4]Daewoong Pharmaceutical Co., Ltd., Seoul, Korea, Republic of.

E-022
PREDICTING THE EFFECT OF CYP3A INDUCERS ON THE PHARMACOKINETICS OF SUBSTRATE DRUGS USING PBPK MODELING - AN ANALYSIS OF PBPK SUBMISSIONS TO THE FDA.

C. Wagner, Y. Pan, **V. Hsu**, V. Sinha, P. Zhao; US Food and Drug Administration, Silver Spring, MD.

E-023
SAMPLE SIZE AND INTRASUBJECT COEFFICIENT OF VARIATION OF BIOEQUIVALENCE STUDIES: A POST-HOC ANALYSIS.

I. Chung[1], S. Lee[1], S. Yoon[1], K. Yu[1], H. Lee[1], I. Jang[1], J. Chung[2]; [1]Seoul National University Hospital, Seoul, Korea, Republic of, [2]Department of Clinical Pharmacology and Therapeutics, Seoul National University Bundang Hospital and College of Medicine, Seongnam, Korea, Republic of.

E-024
REPRODUCIBILITY OF A BATTERY OF HUMAN EVOKED PAIN MODEL TO DETECT PHARMACOLOGICAL EFFECTS OF ANALGESIC DRUGS.

P. S. Siebenga[1], G. van Amerongen[1], P. Okkerse[1], R. Butt[2], J. Hay[1], G. Groeneveld[1]; [1]Centre for Human Drug Research, Leiden, Netherlands, [2]Pfizer, Inc., Cambridge, United Kingdom.

E-027
INTRINSIC AND EXTRINSIC DETERMINANTS OF PHARMACOKINETIC (PK) VARIABILITY OF CANCER THERAPEUTICS.

E. L. Reyner[1], L. J. Dickmann[1], B. Lum[1], N. R. Budha[1], P. Morcos[2], A. Phipps[3], K. M. Morrissey[1], **J. A. Ware[1]**; [1]Genentech, South San Francisco, CA, [2]Roche, New York, NY, [3]Roche, Welwyn Garden City, United Kingdom.

E-028
ACCELERATING TREATMENTS FOR ALZHEIMER DISEASE: A METABOLOMICS APPROACH FOR PRECISION MEDICINE.

R. Kaddurah-Daouk; Duke University Medical Center, Durham, NC.

E-029
PHARMACOMETABOLOMIC SIGNATURES OF SUBJECTS WITH REFRACTORY MAJOR DEPRESSIVE DISORDER TREATED WITH ESKETAMINE OR KETAMINE.

D. M. Rotroff[1], D. G. Corum[2], A. A. Motsinger-Reif[1], O. Fiehn[3], N. Bottrel[4], W. C. Drevets[4], J. Singh[4], G. Salvadore[4], R. Kaddurah-Daouk[5]; [1]Bioinformatics Research Center, North Carolina State University, Raleigh, NC, [2]Department of Drug Discovery and Biomedical Sciences, Medical University of South Carolina, Charleston, SC, [3]UC Davis Genome Center, University of California Davis, Davis, CA, [4]Janssen Research & Development, LLC, Titusville, NJ, [5]Department of Psychiatry, Duke University Medical Center, Durham, NC.

E-030

INFLUENCE OF SEX AND RACE ON MYCOPHENOLIC ACID PHARMACOKINETICS IN STABLE AFRICAN AMERICAN AND CAUCASIAN RENAL TRANSPLANT RECIPIENTS.

K. M. Tornatore[1], C. J. Meaney[1], G. E. Wilding[2], S. S. Chang[3], A. Gundroo[4], L. M. Cooper[1], V. Gray[5], K. N. Shin[1], G. J. Fetterly[6], J. J. Prey[7], K. Clark[7], R. C. Venuto[3]; [1]School of Pharmacy & Pharmaceutical Sciences, NYS Center of Excellence Bioinformatics & Life Sciences, University at Buffalo, Buffalo, NY, [2]School of Public Health & Health Professions, CBLS, University at Buffalo, Buffalo, NY, [3]School of Medicine and Biomedical Sciences University at Buffalo, Buffalo, NY, [4]School of Medicine & Biomedical Sciences; University at Buffalo, Buffalo, NY, [5]Erie County Medical Center, Buffalo, NY, [6]Pharmacokinetics Analytical Core; Roswell Park Cancer Institute Pharmaceutical Sciences; CBLS; University at Buffalo, Buffalo, NY, [7]Pharmacokinetics Analytical Core; Roswell Park Cancer Institute, Buffalo, NY.

E-031

LACK OF EFFECT OF ROLAPITANT, A CANCER SUPPORTIVE CARE ANTIEMETIC, ON QTC INTERVALS IN HEALTHY SUBJECTS.

X. Wang, Z. Zhang, D. Powers, J. Christensen, V. Kansra; TESARO, Waltham, MA.

E-032

PREDICTED ANTI-CRYPTOCOCCAL EFFICACY OF SERTRALINE IN HIV-INFECTED UGANDANS.

A. A. Alhadab, R. C. Brundage, ASTRO-CM GROUP; University of Minnesota, Minneapolis, MN.

E-033

PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELING OF AZD4017 TO SUPPORT DOSE SELECTION IN PHASE II TRIAL.

H. Xu, W. Zhou, C. Wegner, D. Zhou, N. Al-Huniti; AstraZeneca, Waltham, MA.

E-034

NALOXEGOL CONCENTRATION-QT ANALYSIS FROM THOROUGH QT STUDY TO PREDICT QTCF INTERVAL PROLONGATION WITH PRESENCE OF DRUG-DRUG INTERACTION.

H. Xu, J. Li, N. Al-Huniti; AstraZeneca, Waltham, MA.

E-035

EFFECT OF MILD HEPATIC IMPAIREMENT (CHILD PUGH CLASS A) ON PHARMACOKINETICS OF ISTRADEFYLLINE.

X. Zhang[1], M. Mukai[1], T. Uchimura[2], M. Vergeire[1], M. Cantillon[1]; [1]Kyowa Hakko Kirin Pharma, Inc., Princeton, NJ, [2]Kyowa Hakko Kirin Co., Tokyo, Japan.

E-036

EFFECT OF RIFAMPIN ON PHARMAOCKINETICS OF ISTRADEFYLLLINE IN HEALTHY SUBJECTS.

X. Zhang[1], M. Mukai[1], T. Uchimura[2], M. Vergeire2[1], M. Cantillon[1]; [1]Kyowa Hakko Kirin Pharma, Inc., Princeton, NJ, [2]Kyowa Hakko Kirin Co., Tokyo, Japan.

Abstracts E-001 – E-036

HAVE BEEN INCLUDED IN THE SUPPLEMENT ISSUE OF CPT: *CLINICAL PHARMACOLOGY & THERAPEUTICS.*

E-037

GLUCOCORTICOID RECEPTOR ANTAGONISM DECREASES ALCOHOL SEEKING IN ALCOHOL-DEPENDENT SUBJECTS.

M. H. Skinner, D. Estey, B. Mason; The Scripps Research Institute, La Jolla, CA.

E-038

PHYSIOLOGICALLY BASED AND POPULATION PK MODELING IN OPTIMIZING DRUG DEVELOPMENT: A PREDICT-LEARN-CONFIRM ANALYSIS.

A. Suri[1], S. Chapel[2], C. Lu[1], K. Venkatakrishnan[1]; [1]Millennium Pharmaceuticals Inc., Cambridge, MA, USA, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, [2]Ann Arbor Pharmacometrics Group, Ann Arbor, MO.

E-039

NOVEL MODEL-BASED DOSING GUIDELINES FOR GENTAMICIN AND TOBRAMYCIN IN PRETERM AND TERM NEONATES.

P. A. Valitalo[1], J. N. van der Anker[2], K. Allegaert[3], R. F. de Cock[1], M. de Hoog[4], S. H. Simons[4], J. W. Mouton[4], C. A. Knibbe[5]; [1]Leiden University, Leiden, Netherlands, [2]Children's National Medical Center, Washington, WA, [3]KU Leuven, Leuven, Belgium, [4]Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands, [5]St Antonius Hospital, Nieuwegein, Netherlands.

E-040

CYP2C19 METABOLIZER STATUS AND CLOPIDOGREL EFFICACY IN THE SECONDARY PREVENTION OF SMALL SUBCORTICAL STROKES (SPS3) STUDY.

C. W. McDonough[1], L. A. McClure[2], B. D. Mitchell[3], Y. Gong[1], R. B. Horenstein[3], J. P. Lewis[3], T. S. Field[4], R. L. Talbert[5], O. R. Benavente[4], J. A. Johnson[1], A. R. Shuldiner[3]; [1]University of Florida, Gainesville, FL, [2]Drexel University, Philadelphia, PA, [3]University of Maryland School of Medicine, Baltimore, MD, [4]University of British Columbia, Vancouver, BC, Canada, [5]University of Texas at Austin, Austin, TX.

E-041

SUBCLINICAL HYPOTHYROIDISM IS A RISK FACTOR FOR STATIN-ASSOCIATED DIABETES MELLITUS.

N. Gronich[1], S. N. Deftereos[2], I. Lavi[1], A. S. Persidis[2], D. R. Abernethy[3], G. Rennert[4]; [1]Pharmacoepidemiology unit, Department of Community Medicine and Epidemiology, Carmel Medical Center, Clalit health Services, Haifa, Israel, [2]Biovista Inc., Charlottesville, VA, [3]Drug Safety Group, Office of Clinical Pharmacology, U.S. Food and Drug Administration, Silver Spring, MD, [4]Carmel Medical Center, and Bruce Rappaport Faculty of Medicine, Technion – Israel Institute of Technology and Office of Chief Physician, Clalit Health Services, Haifa, Israel.

E-042

MOXIFLOXACIN-INDUCED QTC PROLONGATION IN HEALTHY JAPANESE AND CAUCASIAN VOLUNTEERS: A DIRECT COMPARISON OF ETHNIC DIFFERENCES IN A THOROUGH QTC STUDY.

R. Kleiman[1], J. Morganroth[1], Y. Wang[2]; [1]ERT, Philadelphia, PA, [2]Food and Drug Administration, Silver Spring, MD.

E-043

BENEFITS OF CENTRALIZED ECG ANALYSIS IN CLINICAL ONCOLOGY STUDIES.

R. Kleiman, J. Litwin, J. Morganroth; ERT, Philadelphia, PA.

E-044

SAFE LONG-TERM SORAFENIB THERAPY IN HEPATOCELLULAR CARCINOMA PATIENTS REQUIRES MONITORING OF SERUM LEVELS OF SORAFENIB AND ITS *N-OXIDE:* A PILOT STUDY.

M. Shimada[1], H. Okawa[2], Y. Kondo[3], T. Maejima[4], Y. Kataoka[4], K. Hisamichi[4], M. Maekawa[4], M. Matsuura[4], Y. Jin[5], T. Shimosegawa[3], N. Mano[4]; [1]Tottori university hospital, Yonago, Japan, [2]Department of Clinical Pharmacy, Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, Japan, [3]Department of Gastroenterology, Graduate School of Medicine, Tohoku University, Sendai, Japan, [4]Department of Pharmaceutical Sciences, Tohoku University Hospital, Sendai, Japan, [5]Division of Nursing, Tohoku University Hospital, Sendai, Japan.

E-045

THE EFFECTS OF A MEAL ON QTC TO DEMONSTRATE ECG ASSAY SENSITIVITY.

J. Taubel[1], G. Ferber[2], U. Lorch[1], D. Wang[3], M. Sust[4], A. Camm[1]; [1]Richmond Pharmacology Ltd, London, United Kingdom, [2]Statistik Georg Ferber GmbH, Riehen, Switzerland, [3]Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [4]ESTEVE Research & Development, Barcelona, Spain.

QUANTITATIVE PHARMACOLOGY (QP) POSTER SESSION

THURSDAY, MARCH 10, 2016

4:30 PM – 6:30 PM

SAPPHIRE BALLROOM

PI-001

BIOEQUIVALENCE OF FIXED DOSE COMBINATION (FDC) TABLETS OF LINAGLIPTIN / METFORMIN EXTENDED RELEASE COMPARED WITH THE FREE COMBINATIONS IN HEALTHY VOLUNTEERS.

C. Lippert[1], R. Sennewald[1], J. Bell[2], S. Wiebe[1], S. Hüttner[1]; [1]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany, [2]Boehringer Ingelheim Ltd., Bracknell, United Kingdom.

PI-002

MODEL-BASED ASSESSMENT OF DRUG-DRUG INTERACTION AND IMMUNOGENICITY ON THE PHARMACOKINETICS (PK) OF NIVOLUMAB AND IPILIMUMAB IN COMBINATION IN ADVANCED MELANOMA PATIENTS.

L. Zhu, P. Chan, H. Vezina, X. Wang, Y. Feng, P. Statkevich, A. Roy; Bristol-Myers Squibb, Princeton, NJ.

PI-003

REPEATED TIME-TO-EVENT MODELING TO CHARACTERIZE THE BLEEDING-PROPHYLACTIC EFFICACY OF ACE910, A BISPECIFIC ANTIBODY TO FACTORS IXA AND X, IN PATIENTS WITH HEMOPHILIA A.

K. Yoneyama[1], C. Schmitt[2], N. Kotani[1], N. Fukazawa[1], G. G. Levy[3], S. Iida[1], M. Shima[4], T. Kawanishi[1]; [1]Chugai Pharmaceutical Co., Ltd., Tokyo, Japan, [2]F. Hoffmann-La Roche AG, Basel, Switzerland, [3]Genentech, South San Francisco, CA, [4]Nara Medical University, Nara, Japan.

PI-004

CLINICAL EVALUATION OF LY2944876 MODEL-BASED DOSING REGIMENS TO ACHIEVE SUPRATHERAPEUTIC EXPOSURES FOR A THOROUGH QTC ASSESSMENT STUDY.

L. Tham[1]**,** C. Loghin[2], C. Cai Tang[1], E. Chen Quin Lam[1]; [1]Lilly-NUS Center for Clinical Pharmacology, Singapore, Singapore, [2]Eli Lilly and Company, Indianapolis, IN.

PI-005

DIFFERENT IMPACT OF CYP INHIBITOR AND INDUCER AMONG SUBJECTS WITH DIFFERENT BASAL CYP ACTIVITIES.

K. Odagiri[1], S. Miyakawa[1], A. Hakamata[1], N. Katayama[1], N. Inui[1], S. Tanaka[2], S. Uchida[2], N. Namiki[2], H. Watanabe[1]; [1]Hamamatsu University School of Medicine, Hamamatsu, Japan, [2]University of Shizuoka, Shizuoka, Japan.

PI-008

FIRST-IN-HUMAN (FIH) STUDY OF E6011, A NOVEL HUMANIZED ANTI-FRACTALKINE (CX3CL1) MONOCLONAL ANTIBODY.

H. Tabuchi[1], K. Oketani[1], T. Katsurabara[1], M. Mori[1], T. Muraishi[1], M. Aoyama[1], T. Obara[1], N. Yasuda[1], H. Akama[1], T. Kawano[2], T. Imai[2], I. Ieiri[3], Y. Kumagai[4]; [1]Eisai Co., Ltd., Tokyo, Japan, [2]KAN Research Institute, Inc., Kobe, Japan, [3]Kyushu University, Fukuoka, Japan, [4]Kitasato University Hospital, Sagamihara, Japan.

PI-009

DRUG-DRUG INTERACTION OF LY2623091 WITH CYP3A INHIBITORS ITRACONAZOLE (ITR) AND DILTIAZEM (DIL) AND THE STEADY STATE PHARMACOKINETICS OF ITRACONAZOLE.

G. L. Dickinson, D. L. Phillips, M. M. Posada, A. Chaudhary, S. D. Hall; Eli Lilly and Company, Indianapolis, IN.

PI-010
DISTRIBUTION, METABOLISM, AND EXCRETION OF GEDATOLISIB IN HEALTHY MALE VOLUNTEERS AFTER A SINGLE [^{14}C]-LABELED IV INFUSION.
B. E. Houk, C. Alvey, L. Kirkovsky, K. Matschke, T. Ryder, R. Obach; Pfizer, Inc., San Diego, CA.

PI-011
DRUG-DRUG INTERACTION RISK ASSESSMENT OF SIROLIMUS THERAPY DURING CO-ADMINISTRATION OF CALCINEURIN INHIBITORS IN RENAL TRANSPLANT PATIENTS.
C. Emoto, A. A. Vinks, T. Fukuda; Division of Clinical Pharmacology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PI-012
POPULATION PHARMACOKINETIC MODELING OF AXITINIB IN PATIENTS WITH ADVANCED HEPATOCELLULAR CANCER.
Y. Chen[1], Y. Kang[2], O. Valota[3], Y. Pithavala[4]; [1]Pfizer, Inc., San Diego, CA, [2]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of, [3]Pfizer, Inc., Milan, Italy, [4]Pfizer, Inc., San Diego, CA.

PI-013
EFFECT OF AGE AND ADMINISTRATION WITH FOOD ON THE SINGLE-DOSE PHARMACOKINETICS OF HT-3951, A SELECTIVE AND REVERSIBLE INHIBITOR OF MAO-B, IN NORMAL HEALTHY SUBJECTS.
D. J. Carpenter, J. J. Anderson, T. Dewitt, J. Djan, C. Mason, J. Parsons, J. Ruckle, P. Perera; Dart NeuroScience, San Diego, CA.

PI-014
EFFECT OF MODERATE AND STRONG CYP3A INHIBITORS ON THE PHARMACOKINETICS OF PF-00489791, A SELECTIVE PDE5 INHIBITOR.
S. Raje[1], S. Ripp[2], R. LaBadie[2], C. Alvey[2], W. Scheele[3]; [1]Pfizer, Inc., Collegeville, PA, [2]Pfizer, Inc., Groton, CT, [3]Pfizer, Inc., Cambridge, MA.

PI-015
DETERMINATION OF ABSOLUTE ORAL BIOAVAILABILITY AND FRACTION ABSORBED OF ERTUGLIFLOZIN USING A NOVEL MICROTRACER APPROACH.
S. Raje[1], E. Callegari[2], V. Sahasrabudhe[2], A. Vaz[2], H. Shi[2], E. Fluhler[3], E. Woolf[4], K. Schildknegt[2], K. Matschke[1], C. Alvey[2], S. Zhou[5], D. Papadopoulos[6], R. Fountaine[2], D. Saur[7], S. Terra[8], L. Stevens[9], D. Cutler[5]; [1]Pfizer, Inc., Collegeville, PA, [2]Pfizer, Inc., Groton, CT, [3]Pfizer, Inc., Pearl River, NY, [4]Merck & Co., Inc., West Point, PA, [5]Merck & Co., Inc., Rahway, NJ, [6]Pfizer, Inc., Sandwich, United Kingdom, [7]Pfizer, Inc., Paris, France, [8]Pfizer, Inc., Andover, MA, [9]Quotient Clinical Limited, Nottingham, United Kingdom.

PI-016
PHARMACOKINETIC PREDICTION OF PACLITAXEL INDUCED PERIPHERAL NEUROPATHY.
H. V. Nguyen[1], D. Sun[1], N. Henry[2], **D. L. Hertz**[1]; [1]University of Michigan College of Pharmacy, Ann Arbor, MI, [2]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI.

PI-017
APPLICATION OF A HAZARD-BASED VISUAL PREDICTIVE CHECK TO EVALUATE PARAMETRIC HAZARD MODELS.
Y. Huh, M. M. Hutmacher; Ann Arbor Pharmacometrics Group (A2PG), Ann Arbor, MI.

PI-018
CONCENTRATION-QTC ANALYSIS OF POLATUZUMAB VEDOTIN IN PATIENTS WITH B-CELL HEMATOLOGIC MALIGNANCIES.
D. Lu[1], S. Girish[1], M. Marchand[2], M. Mouksassi[3], C. Garnett[4], C. Li[1], P. Agarwal[1], J. Essig[5], C. Jones[1], J. Hirata[1], Y. Chu[1], J. Jin[1]; [1]Genentech, South San Francisco, CA, [2]Pharsight Consulting Services, Pharsight, part of Certara™, Marseille, France, [3]Pharsight Consulting Services, Pharsight, part of Certara™, Montreal, QC, Canada, [4]Pharsight Consulting Services, Pharsight, part of Certara™, Princeton, NJ, [5]Roche, Basel, Switzerland.

PI-019

PHARMACOKINETIC ANALYSIS OF THE ORAL CYP17 INHIBITOR VT464 TO DESCRIBE TIME-DEPENDENT CHANGES IN CLEARANCE IN MEN WITH METASTATIC CASTRATE-RESISTANT PROSTATE CANCER.

C. J. Peer[1], K. T. Schmidt[1], M. F. Nogueira Filho[1], J. Eisner[2], W. Moore[2], W. D. Figg[1]; [1]National Cancer Institute, Bethesda, MD, [2]Innocrin Pharmaceuticals, Inc., Durham, NC.

PI-020

RIFAMPIN MODULATION OF XENO- AND ENDO-BIOTIC CONJUGATING ENZYME MRNA EXPRESSION IN HUMAN HEPATOCYTES.

B. T. Gufford[1], H. Gao[2], H. Lin[2], Y. Liu[2], Z. Desta[1], T. C. Skaar[1]; [1]Department of Medicine, Division of Clinical Pharmacology, Indiana University School of Medicine, Indianapolis, IN, [2]Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN.

PI-021

MANY ANSWERS FROM A FIRST IN HUMAN (FIH) STUDY: SAFETY, TOLERABILITY, PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) OF PF-06260414 IN HEALTHY WESTERN AND JAPANESE MALES.

I. Bhattacharya[1], S. Tarabar[2], Y. Liang[3], V. Pradhan[1], J. Owens[1], B. Oemar[1]; [1]Pfizer, Inc., Cambridge, MA, [2]Pfizer, Inc., New Haven, CT, [3]Pfizer, Inc., Groton, CT.

PI-022

COMPARISON OF MODEL PERFORMANCES IN CHARACTERIZING THE PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) OF AN ANTI-MYOSTATIN MONOCLONAL ANTIBODY.

I. Bhattacharya[1], L. Harnisch[2], P. Chan[2], S. Marraffino[1], A. Heatherington[1]; [1]Pfizer, Inc., Cambridge, MA, [2]Pfizer, Inc., Sandwich, United Kingdom.

PI-023

EFFECT OF HEPATIC IMPAIRMENT ON ELUXADOLINE PHARMACOKINETICS.

J. M. Davenport[1], **T. Marbury**[2], J. Berg[3], L. S. Dove[1], P. S. Covington[1]; [1]Former employee of Furiex Pharmaceuticals, Inc., a subsidiary of Allergan plc., Jersey City, NJ, [2]Orlando Clinical Research Center, Orlando, FL, [3]DaVita Clinical Research, Minneapolis, MN.

PI-024

DEVELOPMENT OF A MECHANISM-BASED DRUG-DISEASE MODELING PLATFORM FOR TYPE 2 DIABETES MELLITUS.

F. K. Hurtado[1], P. Gaitonde[1], P. Garhyan[2], J. Y. Chien[2], S. Schmidt[1]; [1]University of Florida, Orlando, FL, [2]Eli Lilly and Company, Indianapolis, IN.

PI-025

LACK OF EFFECT OF RIVIPANSEL ON QT_C INTERVAL IN HEALTHY ADULT MALE AFRICAN AMERICAN SUBJECTS.

B. Tammara[1], A. Plotka[1], F. Shafer[1], D. Readett[2], S. Riley[2], J. Korth-Bradley[1]; [1]Pfizer, Inc., Collegeville, PA, [2]Pfizer, Inc., Groton, CT.

PI-026

MODEL-BASED EVALUATION OF THE EFFECT OF KETOCONAZOLE ON PARITAPREVIR HARMACOKINETICS.

M. Ahmed, A. Khatri; AbbVie, North Chicago, IL.

PI-027

RECOMMENDATION OF AN ALTERNATIVE DOSING REGIMEN FOR RILPIVIRINE DURING CO-ADMINISTRATION WITH HCV 3D REGIMEN: MODEL-BASED APPROACH.

M. Ahmed, A. Polepally, R. Menon, A. Khatri; AbbVie, North Chicago, IL.

PI-028

EFFECT OF A STRONG INDUCER ON THE PLASMA PHARMACOKINETICS (PK) OF THE SMOOTHENED (SMO) INHIBITOR GLASDEGIB (PF-04449913).

M. Shaik[1], B. Hee[1], H. Wei[2], R. LaBadie[3]; [1]Pfizer, Inc., San Diego, CA, [2]Pfizer, Inc., Shanghai, China, [3]Pfizer, Inc., Groton, CT.

PI-029

A PHASE IB CLINICAL STUDY TO EVALUATE THE ANALGESIC EFFECT OF GIC-1001 AND GIC-1002 ON VISCERAL PAIN UNDER RECTAL DISTENSION USING THE BAROSTAT METHOD IN HEALTHY VOLUNTEERS.

J. Paquette[1], M. Iovu Niculita[1], M. Rufiange[1], S. Boily[1], E. Sicard[1], J. Massicotte[1], M. Lefebvre[1], O. Uresandi[2], P. Colin[2], M. Ranger[2]; [1]Algorithme Pharma Inc., Montreal, QC, Canada, [2]glcare Pharma Inc., Montreal, QC, Canada.

PI-030

PAIN THRESHOLDS OBSERVED FOLLOWING THE ADMINISTRATION OF PLACEBO, GIC-1001 AND GIC-1002 IN HEALTHY VOLUNTEERS UNDERGOING RECTAL DISTENSIONS USING THE BAROSTAT METHOD.

J. Paquette[1], M. Iovu Niculita[1], M. Rufiange[1], S. Boily[1], E. Sicard[1], J. Massicotte[1], M. Lefebvre[1], O. Uresandi[2], P. Colin[2], M. Ranger[2]; [1]Algorithme Pharma Inc., Montreal, QC, Canada, [2]glcare Pharma Inc., Montreal, QC, Canada.

PI-031

POPULATION PHARMACOKINETICS OF RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN ALFA IN PEDIATRIC HEMATOLOGIC MALIGNANCY PATIENTS WITH DISSEMINATED INTRAVASCULAR COAGULATION.

M. Takeuchi[1], R. Tanoshima[2], K. Sasaki[2], H. Kato[2], M. Yanagimachi[2], S. Ito[2], S. Yokota[2], N. Miyagawa[3], T. Sarashina[3], T. Yokosuka[3], S. Ito[1], H. Goto[3]; [1]Division of Clinical Pharmacology and Toxicology, The Hospital for Sick Children, Toronto, ON, Canada, [2]Department of Pediatrics, Yokohama City University Hospital, Yokohama, Japan, [3]Division of Hemato-Oncology/Regenerative Medicine, Kanagawa Children's Medical Center, Yokohama, Japan.

PI-032

USING PBPK MODELING TO PREDICT HEPATIC AND GUT WALL CONCENTRATIONS OF ERYTHROMYCIN (ERY) AFTER P.O. ADMINISTRATION AS ENTERIC-COATED (EC) OR STEARATE SALT (SS) FORMULATIONS.

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

PI-033

SAFETY, TOLERABILITY, PHARMACOKINETICS (PK), AND PHARMACODYNAMICS (PD) OF AZD7594 AFTER SINGLE AND MULTIPLE ASCENDING INHALED DOSES IN HEALTHY MALE VOLUNTEERS.

Y. Chen[1], S. Prothon[2], M. Aurivillius[2], U. G. Eriksson[2], A. Aggarwal[1]; [1]AstraZeneca, Waltham, MA, [2]AstraZeneca, Molndal, Sweden.

PI-034
CLINICAL PHARMACOKINETICS (PK) OF AZD4901, THE NEUROKININ B RECEPTOR ANTAGONIST.
Y. Chen[1], N. Al-Huniti[1], L. Webber[2], E. Masson[1]; [1]AstraZeneca, Waltham, MA, [2]AstraZeneca, Alderley Park, United Kingdom.

PI-035
EFFECTS OF THE CYP3A PERPETRATORS VORICONAZOLE, EFAVIRENZ AND RIFAMPIN ON MIDAZOLAM PLASMA CONCENTRATIONS DURING CONTINUOUS MICRODOSE INFUSION IN HEALTHY VOLUNTEERS.
N. Hohmann, K. Gottwald, D. Czock, J. Burhenne, W. E. Haefeli, G. Mikus; Department of Clinical Pharmacology, Heidelberg, Germany.

PI-036
QUANTITATIVE ASSESSMENT OF THE EFFICACY OF TAK-385, AN INVESTIGATIONAL, ORAL GNRH ANTAGONIST IN PROSTATE CANCER PATIENTS (PTS) TO OPTIMIZE TRIAL DESIGN AND DOSE SELECTION.
H. M. Faessel[1], N. Snelder[2], M. Ahsman[2], D. B. MacLean[1], F. Saad[3], N. D. Shore[4], H. Shi[1], K. Venkatakrishnan[1], P. Vis[2]; [1]Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, [2]LAP&P Consultants BV, Leiden, Netherlands, [3]University of Montreal Hospital Center, Montreal, QC, Canada, [4]Carolina Urologic Research Center, Myrtle Beach, SC.

PI-037
A MODEL-BASED COMPARISON OF RESPONSE TO IXEKIZUMAB IN PATIENTS WITH MODERATE TO SEVERE PLAQUE PSORIASIS AFTER 12 AND 60 WEEKS OF TREATMENT.
E. Chigutsa[1], N. V. de Mendizabal[1], L. Chua[2], S. L. Choi[2], L. Hu[1], S. Friedrich[1], K. Jackson[3]; [1]Eli Lilly and Company, Indianapolis, IN, [2]Eli Lilly and Company, Singapore, Singapore, [3]Eli Lilly and Company, Windlesham, United Kingdom.

PI-038
PBPK MODELING AND SIMULATION OF RECTAL/COLON ABSORPTION FOR SUPPOSITORY DRUGS.
Y. Pan, M. Cui, X. Jiang, D. Conner, L. Zhao, E. Stier; US Food and Drug Administration, Silver Spring, MD.

PI-039
POPULATION PHARMACOKINETIC-PHARMACOGENETIC ANALYSIS OF TACROLIMUS IN RENAL TRANSPLANT PATIENTS PARTICIPATING IN A PROSPECTIVE BIOEQUIVALENCE STUDY.
T. Mizuno[1], T. Fukuda[1], C. Emoto[1], U. Christians[2], W. Jiang[3], R. R. Alloway[4], A. A. Vinks[1]; [1]Division of Clinical Pharmacology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]iC42 Clinical Research and Development, University of Colorado, Aurora, CO, [3]Office of Generic Drugs, US Food and Drug Administration, Silver Spring, MD, [4]Division of Nephrology, Department of Internal Medicine, University of Cincinnati College of Medicine, Cincinnati, OH.

I-040
CLINICAL TOXICITY PROFILES OF ANTIBODY DRUG CONJUGATES (ADCS): A META-ANALYSIS ACROSS PAYLOAD CLASSES.
J. C. Masters, D. J. Nickens, D. Xuan, R. Shazer, M. Amantea; Pfizer, Inc., San Diego, CA.

PI-041
POPULATION PHARMACOKINETICS OF BRENTUXIMAB VEDOTIN, AN ANTIBODY-DRUG CONJUGATE (ADC), IN PATIENTS WITH CD30-POSITIVE HEMATOLOGIC MALIGNANCIES.
H. Li[1], T. H. Han[2], N. Hunder[1], G. Jang[1], B. Zhao[1]; [1]Seattle Genetics, Bothell, WA, [2]Stemcentrx, Inc., South San Francisco, CA.

PI-042
4-FACTOR PROTHROMBIN CONCENTRATE REVERSES APIXABAN INHIBITION OF THROMBIN GENERATION IN HEALTHY VOLUNTEERS.
W. K. Kraft, L. Thompson, Y. Oppong, B. Bachman, I. Chervoneva, S. Nagalla; Thomas Jefferson University, Philadelphia, PA.

PI-043
A MODEL-BASED APPROACH FOR THE RESOLUTION OF FREQUENT DISCONTINUATION OF TACROLIMUS ADMINISTRATION IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS.
M. Kim[1], J. Kim[1], H. Yun[2], H. Kang[3], J. Oh[1]; [1]Seoul National University, College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul, Korea, Republic of, [2]College of Pharmacy, Chungnam National University, Daejeon, Korea, Republic of, [3]Department of Pediatrics, Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea, Republic of.

PI-044
APPLICATION OF PBPK MODELING TO ASSESS THE VICTIM DDI POTENTIAL OF PACLITAXEL IN ONCOLOGY COMBINATION THERAPIES.
A. Ke, K. R. Yeo; Simcyp (a Certara Company), Sheffield, United Kingdom.

PI-045
ASSESSMENT OF THE CONTRIBUTION OF CYP2D6 TO THE ELIMINATION OF IDALOPIRDINE AS WELL AS THE ABSOLUTE BIOAVAILABILITY FOLLOWING MULTIPLE ORAL DOSING.
E. Schmidt[1], J. Areberg[1], P. Evans[2], V. Zann[2], B. Søgaard[1]; [1]Lundbeck A/S, Copenhagen, Denmark, [2]Quotient Clinical, Nottingham, United Kingdom.

PI-046
PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELING OF DRUG-DRUG INTERACTION (DDI) FOLLOWING COADMINISTRATION OF ERTUGLIFLOZIN AND UGT INHIBITOR MEFENAMIC ACID.
E. Callegari, J. Lin, S. Tse, T. C. Goosen, V. Sahasrabudhe; Pfizer, Inc., Groton, CT.

PI-047
PUTTING THE "AND" BACK IN QUANTITATIVE AND SYSTEMS PHARMACOLOGY.
M. L. Rizk, B. Topp, A. Cabal, K. Mehta, S. Visser, M. Trujillo, D. Tatosian, M. Cicmil, M. Caniga, J. Wu, J. Mu, P. Kothare, L. Wenning, J. Stone, S. R. Allerheiligen; Merck & Co., Inc., Kenilworth, NJ.

PI-048
APPLICATION OF PHARMACOMETRICS IN DOSE SELECTION OF DRUGS AND BIOLOGICS DEVELOPED UNDER THE ANIMAL RULE.
L. Zhuang, X. Wang, L. Ma, A. Bhattaram, Y. Mulugeta, J. Yu, N. Mehrotra, Y. Wang; US Food and Drug Administration, Silver Spring, MD.

PI-049

EXPOSURE-RESPONSE ANALYSIS TO ASSESS THE EFFECT OF GSK1278863 ON CARDIAC REPOLARIZATION.

J. W. Collins[1], P. Zuo[2], D. A. Smith[2], B. Johnson[2], R. Ravindranath[3], G. Serbest[1], A. Cobitz[4], S. Caltabiano[4]; [1]GlaxoSmithKline, Research Triangle Park, NC, [2]PAREXEL International, Research Triangle Park, NC, [3]GlaxoSmithKline, Bangalore, India, [4]GlaxoSmithKline, King of Prussia, PA.

PI-050

EFFECT OF FOOD AND ACID REDUCING AGENTS ON THE RELATIVE BIOAVAILABILITY AND PHARMACOKINETICS OF SOFOSBUVIR/VELPATASVIR FIXED-DOSE COMBINATION TABLET.

E. Mogalian, OsinusiAnu, Gong Shen , Karim Sajwani , McNallyJohn, LingJohn, MathiasAnita; Gilead Sciences, Inc., Foster City, CA.

PI-051

DOSE INDIVIDUALIZATION TO MANAGE CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY (CIPN): SHIFT FROM AN EMPIRICAL APPROACH TO BAYESIAN FORECASTING.

S. Mehrotra[1], M. Gopalakrishnan[1], M. Sharma[2], E. Gray[2], J. Gobburu[1]; [1]University of Maryland, Baltimore, MD, [2]The University of Chicago Medicine, Chicago, IL.

PI-052

SAFETY, TOLERABILITY AND PHARMACOKINETIC CHARACTERISTICS OF VVZ-149 INJECTIONS IN HEALTHY ELDERLY SUBJECTS.

Y. Kim[1], J. Oh[1], K. Park[1], J. Yoon[1], K. Jang[1], H. Lee[1], I. Jang[1], S. Cho[2], D. Lee[2], J. Chung[3]; [1]Seoul National University Hospital, Clinical Pharmacology and Therapeutics, Seoul, Korea, Republic of, [2]Vivozon, Inc., Seoul, Korea, Republic of, [3]Seoul National University College of Medicine and Bundang Hospital, Clinical Pharmacology and Therapeutics, Seongnam, Korea, Republic of.

PI-053

POPULATION PHARMACOKINETIC STUDY OF METHOTREXATE IN CHINESE PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND OSTEOSARCOMA.

H. Chu, P. Fong, W. F. Cheng, **T. Lam;** Chinese University of Hong Kong, Hong Kong, Hong Kong.

PI-054

A MODEL BASED META-ANALYSIS (MBMA) FOR COMPARATIVE EFFICACY OF PSORIASIS TREATMENTS: DOSE-RESPONSE MODEL FOR PSORIASIS AREA AND SEVERITY INDEX (PASI) RESPONSES.

T. Checchio[1], K. Ito[1], J. Mandema[2], R. Wolk[1], H. Valdez[3], H. Tan[1], S. Krishnaswami[1], A. Tallman[3], **P. Gupta[1]**; [1]Pfizer, Inc., Groton, CT, [2]Quantitative Solutions, Menlo Park, CA, [3]Pfizer, Inc., New York, NY.

PI-055

EVALUATION OF PHARMACOKINETICS AND TOLERABILITY OF TAUROURSODEOXYCHOLIC ACID (T-UDCA) AND ITS METABOLITES AFTER A SINGLE ORAL ADMINISTRATION IN HEALTHY SUBJECTS.

K. Park, S. Lee, Y. Kim, H. Chung, H. Lee, S. Yoon, J. Cho, K. Yu, I. Jang; Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of.

PI-056

PHARMACOKINETICS/ PHARMACODYNAMICS, SAFETY AND TOLERABILITY OF GX-E2, A HYBRID FC FUSION ERYTHROPOIETIN, AFTER SINGLE INTRAVENOUS ADMINISTRATION.

S. LEE, A. Kim, H. Lee, H. Lee, S. Yoon, J. Cho, H. Lee, K. Yu; Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of.

PI-057

COMPARISON OF PHARMACOKINETIC CHARACTERISTICS AND SAFETY BETWEEN BK-C-0701 320MG, 480MG AND THIOCTIC ACID 600MG IN HEALTHY MALE SUBJECTS.

J. Yoon[1], S. Kim[1], H. Chung[1], Y. Choi[1], H. Hwang[2], S. Yoon[1], I. Jang[1], K. Yu[1], S. Lee[1]; [1]Seoul National University Hospital, Seoul, Korea, Republic of, [2]Bukwang Pharm. Co., Ltd., Seoul, Korea, Republic of.

PI-058

PHARMACOKINETICS OF FIXED DOSE COMBINATION (FDC) TABLETS OF LINAGLIPTIN/METFORMIN EXTENDED RELEASE COMPARED WITH THE FREE COMBINATIONS IN HEALTHY VOLUNTEERS.

P. Norman[1], C. Lippert[2], N. Hummel[2], T. Hunt[3], S. Hüttner[2]; [1]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, [2]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany, [3]Pharmaceutical Product Development Phase I Clinic, Austin, TX.

PI-059

POPULATION PHARMACOKINETIC (PK) ANALYSIS OF BORTEZOMIB (BTZ) IN PEDIATRIC LEUKEMIA PATIENTS (PTS): SUPPORT FOR BODY SURFACE AREA (BSA)-BASED DOSING IN PTS AGED 2-16 YRS.

M. J. Hanley[1], N. Gupta[1], K. Suryanarayan[1], R. Neuwirth[1], D. Esseltine[1], T. Horton[2], R. Aplenc[3], T. A. Alonzo[4], X. Lu[5], A. Milton[1], D. R. Mould[6], K. Venkatakrishnan[1]; [1]Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, [2]Baylor College of Medicine, Texas Children's Hospital, Houston, TX, [3]Children's Hospital of Philadelphia, Philadelphia, PA, [4]University of Southern California, Los Angeles, CA, [5]Children's Oncology Group, Gainesville, FL, [6]Projections Research, Inc., Phoenixville, PA.

PI-060

PHARMACOKINETICS, PHARMACODYNAMICS, AND TOLERABILITY OF CKD-712 AFTER A SINGLE INTRAVENOUS ADMINISTRATION IN HEALTHY VOLUNTEERS.

S. Park, S. Lee, S. Moon, K. Park, J. Chung, I. Jang; Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of.

PI-061

LACK OF A CLINICALLY MEANINGFUL PHARMACOKINETIC INTERACTION BETWEEN ERTUGLIFLOZIN AND GLIMEPIRIDE OR SIMVASTATIN IN HEALTHY SUBJECTS.

V. Sahasrabudhe[1], V. Kumar[1], K. Matschke[2], H. Shi[1], C. Alvey[1], Y. Liang[1], R. J. Fountaine[1], A. Hickman[1], D. Saur[3], S. G. Terra[4], S. Zhou[5], D. L. Cutler[5]; [1]Pfizer, Inc., Groton, CT, [2]Pfizer, Inc., Collegeville, PA, [3]Pfizer, Inc., Paris, France, [4]Pfizer, Inc., Andover, MA, [5]Merck & Co., Inc., Kenilworth, NJ.

PI-062

ALTERED CARDIAC PROTEIN EXPRESSION OF CYP2J IN MOUSE MODELS OF TYPE I AND TYPE II DIABETES.

S. Pilote[1], C. Gélinas[2], D. Patoine[1], B. Drolet[3], C. Simard[3]; [1]CRIUCPQ, Québec, QC, Canada, [2]Faculté de Pharmacie, Université Laval, Québec, QC, Canada, [3]CRIUCPQ, Faculté de Pharmacie, Université Laval, Québec, QC, Canada.

PI-063

EFFECT OF RIFAMPIN ON THE PHARMACOKINETICS OF ERTUGLIFLOZIN IN HEALTHY SUBJECTS.

V. Kumar[1], V. Sahasrabudhe[1], Y. Liang[1], K. Matschke[2], H. Shi[1], R. J. Fountaine[1], A. Hickman[1], D. Saur[3], S. G. Terra[4], D. L. Cutler[5]; [1]Pfizer, Inc., Groton, CT, [2]Pfizer, Inc., Collegeville, PA, [3]Pfizer, Inc., Paris, France, [4]Pfizer, Inc., Andover, MA, [5]Merck & Co., Inc., Kenilworth, NJ.

PI-064
LACK OF A PHARMACOKINETIC INTERACTION BETWEEN ERTUGLIFLOZIN AND SITAGLIPTIN OR METFORMIN IN HEALTHY SUBJECTS.
V. Kumar[1], V. Sahasrabudhe[1], K. Matschke[2], H. Shi[1], C. Alvey[1], R. J. Fountaine[1], A. Hickman[1], D. Saur[3], S. G. Terra[4], S. Zhou[5], R. Krishna[5], D. L. Cutler[5]; [1]Pfizer, Inc., Groton, CT, [2]Pfizer, Inc., Collegeville, PA, [3]Pfizer, Inc., Paris, France, [4]Pfizer, Inc., Andover, MA, [5]Merck & Co., Inc., Kenilworth, NJ.

PI-065
HYDROXYCHLOROQUINE INHIBITS THE CELLULAR CATABOLISM OF HUMAN IMMUNOGLOBULIN.
R. Singh, **R. S. Funk**; University of Kansas Medical Center, Kansas City, KS.

PI-066
THE EFFECTS OF FOOD AND GASTRIC ACID REDUCING AGENTS ON THE PHARMACOKINETICS OF THE ASK1 INHIBITOR GS-4997.
C. H. Nelson, K. Etchevers, L. Wang, J. Lin, M. Hepner, T. Tarnowski, S. Ramanathan; Gilead Sciences, Inc., Foster City, CA.

PI-067
IMPACT OF FORMULATION AND FOOD ON TASELISIB (GDC-0032) BIOAVAILABILITY: POWDER-IN-CAPSULE FORMULATION REPRESENTS UNIQUE DRUG DEVELOPMENT CHALLENGE.
K. P. Faber[1], M. T. Borin[1], S. Cheeti[1], G. Fraczkiewicz[2], E. Nelson[1], Y. Ran[1], M. J. Dresser[1], R. A. Graham[1], S. Sahasranaman[1], J. Hsu[1], J. A. Ware[1], K. M. Morrissey[1]; [1]Genentech, South San Francisco, CA, [2]Simulations Plus, Lancaster, CA.

PI-068
PARAMETRIC MODELS OF THE VARIABILITY AND CIRCADIAN RHYTHM IN HEART RATE, BLOOD PRESSURE AND QT INTERVAL IN HEALTHY VOLUNTEERS WHO RECEIVED PLACEBO IN ABBVIE PHASE I TRIALS.
A. A. Othman, M. Minocha, H. Li, Y. Chiu; AbbVie, North Chicago, IL.

PI-069
LACK OF EFFECT OF SMOKING ON AXITINIB PHARMACOKINETICS (PK) IN NON SMALL CELL LUNG CANCER (NSCLC) PATIENTS (PTS).
M. Garrett[1], T. Taylor[2], D. Mould[3], M. A. Amantea[1], Y. Chen[1], A. Ingrosso[4], **Y. K. Pithavala[1]**; [1]Pfizer, Inc., San Diego, CA, [2]Projections Research, Inc., Niantic, CT, [3]Projections Research, Inc., Phoenixville, PA, [4]Pfizer, Inc., Milan, Italy.

PI-070
PREDICTION OF LONG-TERM EFFICACY OF ANTIDIABETIC DRUGS ON HBA1C USING LONGITUDINAL MODEL-BASED META-ANALYSIS (MBMA) OF LITERATURE DATA.
J. Liu[1], R. Boyd[1], W. Denney[2], K. Sweeney[1], B. Tan[2], C. Buckeridge[1], G. Nucci[2], J. Mandema[3]; [1]Pfizer, Inc., Groton, CT, [2]Pfizer, Inc., Cambridge, MA, [3]Quantitative Solutions, Menlo Park, CA.

PI-071
A GENERALIZED ADDITIVE MIXED MODEL (GAMM) TO CHARACTERIZE AMBULATORY SYSTOLIC BLOOD PRESSURE (SBP) DIFFERENCES BETWEEN ALTERNATE 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]Memorial University, St. John's, NL, Canada.

PI-072
BIOACTIVATION OF TRIMETHOPRIM TO PROTEIN-REACTIVE METABOLITES IN HUMAN LIVER MICROSOMES.
J. L. Goldman[1], Y. Koen[2], S. Rogers[2], K. Li[2], J. S. Leeder[1], R. Hanzlik[2]; [1]Children's Mercy Hospital, Kansas City, MO, [2]University of Kansas, Department of Medicinal Chemistry, Lawrence, KS.

PI-073
PATIENTS WITH HEMATOPOIETIC SYNDROME OF ACUTE RADIATION SYNDROME (HS-ARS): CONSIDERATIONS ON THE DOSE SELECTION FOR FILGRASTIM UNDER THE ANIMAL RULE.
L. Ma[1], G. M. Williams[1], Y. Ouyang[1], W. Dickerson[1], L. Huang[1], M. Melhem[2], A. T. Chow[2], B. Yang[2], J. M. Harrold[2], A. Laniyonu[1], J. Zalkikar[1], A. Gorovets[1], L. Marzella[1], N. Mehrotra[1]; [1]US Food and Drug Administration, Silver Spring, MD, [2]Amgen, Inc., Thousand Oaks, CA.

PI-074
OPTIMIZING THE DOSE OF PLERIXAFOR IN LOW BODY WEIGHT PATIENTS WITH NON-HODGKIN'S LYMPHOMA.
L. Ma[1], B. Habtemariam[1], P. Dinndorf[1], M. S. Mercado[2], T. Lin[2], Y. Wang[1]; [1]US Food and Drug Administration, Silver Spring, MD, [2]Sanofi, Cambridge, MA.

PI-075
PHARMACOKINETIC AND PHARMACODYNAMIC INTERACTIONS BETWEEN EVOGLIPTIN AND METFORMIN AFTER ORAL ADMINISTRATION IN HEALTHY SUBJECTS.
S. Rhee, K. Jang, J. Lee, Y. Cho, Y. Choi, S. Yoon, J. Cho, H. Lee, K. Yu; Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of.

PI-076
A COMPARISON OF THE PHARMACOKINETICS, SAFETY, AND TOLERABILITY OF A FIXED DOSE COMBINATION OF GEMIGLIPTIN AND METFORMIN VERSUS CO-ADMINISTERED GEMIGLIPTIN AND METFORMIN.
C. Yoosang; Seoul National University Hospital, Seoul, Korea, Republic of.

PI-077
HOW QUANTITATIVE CLINICAL PHARMACOLOGY PROVIDED IMPORTANT INSIGHTS INTO THE GANTENERUMAB PHASE III ALZHEIMER'S PROGRAM USING DISEASE PROGRESSION MODELING.
S. Retout[1], R. Gieschke[1], N. Frey[1], C. Weber[1], J. E. Charoin[1], D. Volz[2], R. Lasser[2], C. Hofmann[1]; [1]Roche Pharma Research and Early Development, Clinical Pharmacology, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland, [2]F. Hoffmann-La Roche Ltd., Basel, Switzerland.

PI-078
QUANTITATIVE PHARMACOLOGY SUPPORTING PHASE III TRIAL CONTINUATION OF THE ANTI-ASS ANTIBODY GANTENERUMAB - MODEL-BASED META-ANALYSIS GUIDED INCREASED DOSAGE REGIMENS.
R. Gieschke, S. Retout, N. Frey, C. Weber, J. E. Charoin, J. Laurent, D. Serafin, C. Hofmann; Roche Pharma Research and Early Development, Clinical Pharmacology, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd., Basel, Switzerland.

PI-079

MODEL-BASED META-ANALYSIS (MBMA) FOR EVALUATING TIME COURSE OF CLINICAL RESPONSE ACROSS PSORIASIS TREATMENTS.

S. Ahadieh[1], K. Ito[1], R. Wolk[1], H. Valdez[2], A. Tallman[2], S. Krishnaswami[1], P. Gupta[1]; [1]Pfizer, Inc., Groton, CT, [2]Pfizer, Inc., New York, NY.

PI-080

PREDICTION OF MIDAZOLAM PHARMACOKINETICS IN PREGNANT WOMEN WITH COELIAC DISEASE USING A PREGNANCY PBPK MODEL.

K. Abduljalil, T. Johnson, M. Jamei; Simcyp (a Certara Company), Sheffield, United Kingdom.

PI-081

PREDICTION OF ENFUVERTIDE CONCENTRATION-TIME PROFILE IN A PEDIATRIC POPULATION AFTER PARENTERAL ADMINISTRATION USING A PHYSIOLOGICALLY BASED PHARMACOKINETIC MODEL.

K. Abduljalil, K. Gill, F. Stader, T. Johnson, I. Gardner; Simcyp (a Certara Company), Sheffield, United Kingdom.

PI-082

EXPOSURE-RESPONSE CHARACTERISTICS AND PREDICTORS OF EFFICACY IN MODERATE TO SEVERE CHRONIC PLAQUE PSORIASIS PATIENTS RECEIVING TOFACITINIB.

M. M. Hutmacher[1], K. A. Papp[2], M. Lebwohl[3], K. Ito[4], H. Tan[4], R. Wolk[4], C. Mebus[4], S. Rottinghaus[4], H. Valdez[5], S. Krishnaswami[4], P. Gupta[4]; [1]Ann Arbor Pharmacometrics Group (A2PG), Ann Arbor, MI, [2]Probity Medical Research and K Papp Clinical Research Inc., Waterloo, ON, Canada, [3]Kimberly and Eric J. Waldman Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, [4]Pfizer, Inc., Groton, CT, [5]Pfizer, Inc., New York, NY.

PI-083

THE PROOF IS IN THE PEE: WHAT HAVE WE LEARNED ABOUT POPULATION ASPARAGUS URINARY ODOR KINETICS?

A. Ramamoorthy[1], B. M. Sadler[2], J. van Hasselt[3], J. Elassaiss-Schaap[3] S. Kasichayanula[4], Y. Edwards[2], P. H. van der Graaf[3], L. Zhang[1], J. A. Wagner[5]; [1]US Food and Drug Administration, Silver Spring, MD, [2]ICON, Raleigh-Durham, NC, [3]Leiden University, Leiden, Netherlands, [4]Amgen, Inc., Thousand Oaks, CA, [5]Takeda Pharmaceuticals International Co., Cambridge, MA.

PI-084

INFLAMMATION AND CYTOCHROME P450 MEDIATED METABOLISM OF TOFACITINIB.

X. Wang[1], S. Krishnaswami[2], S. Tse[2], J. Lin[2], M. Dowty[3], S. Menon[2], A. Tallman[4], P. Gupta[2]; [1]College of Pharmacy, University of Michigan, Ann Arbor, MI, [2]Pfizer, Inc., Groton, CT, [3]Pfizer, Inc., Cambridge, MA, [4]Pfizer, Inc., New York, NY.

PI-085

PHARMACOKINETIC/ PHARMACODYNAMIC RELATIONSHIP FOR AN ANTI-CD28 ANTAGONISTIC DOMAIN ANTIBODY, LULIZUMAB PEGOL, IS WELL TRANSLATED FROM CYNO MONKEYS TO HUMANS.

R. Shi, H. Wang, Z. Yang, S. Lee, B. Murthy; Bristol-Myers Squibb, Princeton, NJ.

PI-086

BIOEQUIVALENCE EVALUATION OF TWO AMLODIPINE SALTS, BESYLATE AND CAMSYLATE, EACH IN FIXED-DOSE COMBINATION WITH LOSARTAN IN HEALTHY SUBJECTS.

S. Yoon; Seoul National University, Seoul, Korea, Republic of.

PI-087
ANALYSIS OF THE BRAIN PHARMACODYNAMICS OF GAMMA SECRETASE INHIBITORS USING QUANTITATIVE TRANSLATIONAL SYSTEMS PHARMACOLOGY MODEL.
T. Karelina[1], O. Demin[1], T. Nicholas[2], S. Duvvuri[2]; [1]Institute for Systems Biology, Moscow, Russian Federation, [2]Pfizer Worldwide Research and Development, Groton, CT.

PI-088
SIMULATION OF LONGITUDINAL TAU SPECIE BEHAVIOUR DURING DIFFERENT THERAPIES USING QUANTITATIVE SYSTEMS PHARMACOLOGY MODEL.
T. Karelina[1], O. Demin[1], A. Stepanov[1], N. Markevich[1], S. Duvvuri[2], T. Nicholas[2]; [1]Institute for Systems Biology, Moscow, Russian Federation, [2]Pfizer Worldwide Research and Development, Groton, CT.

PI-089
EFFECTS OF THE COADMINISTRATION OF SINGLE AND MULTIPLE DOSES OF RIFAMPIN ON THE PHARMACOKINETICS AND SAFETY OF ELAGOLIX IN HEALTHY PREMENOPAUSAL FEMALES.
J. Ng, A. Salem, D. Carter, L. A. Williams, C. E. Klein; AbbVie, North Chicago, IL.

PI-090
EFFECT OF THE COADMINISTRATION OF KETOCONAZOLE ON THE PHARMACOKINETICS AND SAFETY OF ELAGOLIX IN HEALTHY PREMENOPAUSAL FEMALES.
J. Ng, A. Salem, D. Carter, L. A. Williams, C. E. Klein; AbbVie, North Chicago, IL.

PI-091
POPULATION PHARMACOKINETICS/ PHARMACODYNAMICS OF 3,4-DIAMINOPYRIDINE FREE BASE IN PATIENTS WITH LAMBERT-EATON MYASTHENIC SYNDROME (LEMS).
N. Thakkar[1], C. Peloquin[2], K. Aleš[3], D. Jacobus[3], L. Jacobus[3], M. Cohen-Wolkowiez[4], J. T. Guptill[5], D. Gonzalez[1], for the DAPPER Study Group; [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]University of Florida, Gainesville, FL, [3]Jacobus Pharmaceutical Company, Inc., Plainsboro, NJ, [4]Duke Clinical Research Institute, Durham, NC, [5]Duke University, Department of Neurology, Durham, NC.

PI-092
PHYSIOLOGICALLY BASED PHARMACOKINETICS (PBPK) MODEL TO ASSESS CYP1A2 AND CYP3A4 INDUCTION EFFECT OF AZD7325.
W. Zhou, K. Bui, H. Xu, J. Li, N. Al-Huniti, **D. Zhou**; AstraZeneca, Waltham, MA.

PI-093
USE OF A POPULATION PHARMACOKINETIC APPROACH AND TIME-TO-EVENT ANALYSIS TO SUPPORT THE CLINICAL RECOMMENDATION OF A FLAT DOSING OF COPANLISIB IN CANCER PATIENTS.
S. Reif[1], M. Ahsman[2], G. Jentsch[3], E. Wiegert[1], J. Grevel[3], C. Granvil[4]; [1]Bayer Pharma AG, Berlin, Germany, [2]LAP&P Consultants BV, Leiden, Netherlands, [3]BAST Inc. Ltd., Loughborough, United Kingdom, [4]Bayer HealthCare Pharmaceuticals, Whippany, NJ.

PI-094
MOVING TO NONCLINICAL TRIAL SIMULATIONS: REPURPOSING OF DRUGS.
V. D. Schmith[1], L. E. Poag[2], R. Williams[2], S. Brantley[2], J. Herman[3]; [1]Nuventra, Inc., Wrightsville Beach, NC, [2]Nuventra, Inc., Durham, NC, [3]Intergrated Nonclinical Development Solutions, Inc., Ann Arbor, MI.

PI-095
ROLE OF CYP3A4 IN ORAL CONTRACEPTIVE CLEARANCE.
N. Zhang, J. Shon, M. Kim, **L. Li;** US Food and Drug Administration, Silver Spring, MD.

PI-096
PHARMACOKINETIC MODELING AND SIMULATION OF NALTREXONE FOR EXTENDED-RELEASE INTRAMUSCULAR INJECTABLE SUSPENSION TO DERIVE ALTERNATIVE BIOEQUIVALENCE METRICS.
A. Babiskin, L. Fang, S. Choi, L. Zhao; US Food and Drug Administration, Silver Spring, MD.

PI-097
MOVING FROM PEDIATRICS TO ADULTS: REPURPOSING OF DRUGS.
S. Brantley[1], R. Kavoussi[2], V. Schmith[3]; [1]Nuventra, Inc., Durham, NC, [2]Neurite Consulting, Raleigh, NC, [3]Nuventra, Inc., Wrightsville Beach, NC.

PI-098
EXPOSURE-RESPONSE (E-R) ANALYSIS OF OVERALL SURVIVAL (OS) FOR NIVOLUMAB IN PATIENTS WITH PREVIOUSLY TREATED ADVANCED OR METASTATIC NON-SMALL-CELL LUNG CANCER (NSCLC).
Y. Feng, G. Bajaj, S. Agrawal, X. Wang, A. Bello, A. Roy; Bristol-Myers Squibb, Princeton, NJ.

PI-099
POPULATION PHARMACOKINETICS OF VANCOMYCIN IN INFANT LIVER TRANSPLANT RECIPIENTS.
K. Shoji[1], J. D. Momper[1], H. Nakagawa[2], T. Funaki[2], M. Kasahara[2], A. Fukuda[2], I. Miyairi[2], E. V. Capparelli[1], Research in Pediatric Developmental Pharmacology; [1]University of California, San Diego, San Diego, CA, [2]National Center for Child Health and Development, Tokyo, Japan.

PI-100
LEVERAGING POTENTIAL CHANGES IN RENAL TRANSPORTER ACTIVITY TO PREDICT DRUG PHARMACOKINETICS DURING PREGNANCY USING PBPK MODELING.
V. Hsu, M. Grimstein, P. Zhao; US Food and Drug Administration, Silver Spring, MD.

PI-101
PBPK MODELING OF CIPROFLOXACIN - KNOWLEDGE EXTENSION BY CONFIRMING THE EFFECT OF INTRINSIC AND EXTRINSIC PATIENT FACTORS ON RENAL OAT ACTIVITIES.
M. Grimstein, V. Hsu, P. Zhao; US Food and Drug Administration, Silver Spring, MD.

PI-102
HEPATIC AND RENAL FUNCTION OF PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS EXPLAINS THE VARIABILITY IN CYCLOSPORINE PHARMACOKINETICS.
J. Kim[1], M. Kim[1], H. Yun[2], H. Kang[3], J. Oh[1]; [1]Seoul National University, College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul, Korea, Republic of, [2]College of Pharmacy, Chungnam National University, Daejeon, Korea, Republic of, [3]Department of Pediatrics, Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea, Republic of.

PI-103
EFFECT OF RENAL IMPAIRMENT ON THE PHARMACOKINETICS OF THE LOBEGLITAZONE.
H. Choi, **J. Jung,** Y. Choi, J. Seo, J. Ghim, E. Kim, J. Shin; Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of.

PI-104
POPULATION PHARMACOKINETICS OF CYCLOSERINE IN KOREAN PATIENTS WITH MULTIDRUG-RESISTANT TUBERCULOSIS.
Y. Choi[1], D. Kim[2], H. Choi[1], Y. Yoon[1], J. Ghim[1], **J. Jung[1]**, D. Kim[1], J. Shin[1]; [1]Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of, [2]Department of Thoracic Surgery, Mokpo National Hospital, Mokpo, Korea, Republic of.

PI-105
PHARMACOKINETIC-PHARMACODYNAMIC RELATIONSHIP AND PHARMACOGENETICS OF METFORMIN IN HEALTHY VOLUNTEERS.
H. Chung[1], J. Oh[1], I. Chung[1], Y. Kim[1], S. Yoon[1], J. Cho[1], J. Chung[2]; [1]Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Seoul National University College of Medicine and Bundang Hospital, Seongnam, Korea, Republic of.

PI-106
DRUG INTERACTION PROFILE OF ENTOSPLETINIB USING PROBE INHIBITORS, INDUCERS, OR SUBSTRATES OF METABOLIZING ENZYMES AND TRANSPORTERS.
S. Sharma, M. Dolton, F. Cheng, M. Robeson, A. Worth, T. Tarnowski, J. Silverman, S. Ramanathan; Gilead Sciences, Inc., Foster City, CA.

PI-107
PHARMACOKINETICS, SAFETY, PHARMACODYNAMICS, AND FOOD AND ACID REDUCING AGENT INTERACTION OF ENTOSPLETINIB SPRAY DRIED FORMULATION.
F. Jin, **S. Sharma**, L. Moorehead, D. Stefanidis, M. Hepner, J. Ling, S. Abella, S. Ramanathan; Gilead Sciences, Inc., Foster City, CA.

PI-108
ANALYSIS AND FUNCTIONAL CHARACTERIZATION OF CYTOCHROME 4V2 GENETIC VARIANTS AMONG KOREAN POPULATION.
Y. Jarrar, M. Yi, S. Yoo, S. Cho, W. Kim, H. Choi, **E. Kim,** D. Kim, S. Lee, J. Shin; Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of.

PI-109
PHARMCOKINETIC COMPARISON BETWEEN ATORVASTATIN/METFORMIN EXTENDED RELEASE FIXED-DOSE COMBINATION AND CO-ADMINISTRATION OF INDIVIDUAL FORMULATIONS UNDER FED CONDITION.
D. Kim, S. Park, J. Jung, **E. Kim**, J. Shin; College of Medicine, INJE University, Busan, Korea, Republic of.

PI-110
APPLICATION OF PBPK (SIMCYP®) MODELING FOR THE PREDICTION OF TOFACITINIB CLINICAL DRUG-DRUG INTERACTIONS.
S. Tse[1], M. Dowty[2], S. Menon[1], P. Gupta[1], S. Krishnaswami[1]; [1]Pfizer, Inc., Groton, CT, [2]Pfizer, Inc., Cambridge, MA.

PI-111
PREDICTION OF SOFOSBUVIR ACTIVE COMPOUND DYNAMICS IN HUMAN LIVER *IN VIVO* DURING TREATMENT.
O. Demin, Jr., O. Demin; Institute for Systems Biology, Moscow, Russian Federation.

PI-112
DEVELOPMENT OF IMMUNE RESPONSE TEMPLATE FOR SYSTEMS PHARMACOLOGY MODELING OF IMMUNOTHERAPY IN ONCOLOGY.
A. Nikitich, **O. Demin, Jr.**, O. Demin; Institute for Systems Biology, Moscow, Russian Federation.

PI-113
SYSTEMS PHARMACOLOGY MODEL OF HEPATITIS C: IMPLEMENTATION OF IMMUNE RESPONSE SUPPRESSION BY HEPATITIS C VIRUS.
O. Demin, Jr., O. Demin; Institute for Systems Biology, Moscow, Russian Federation.

PI-114
SYSTEMS PHARMACOLOGY MODEL OF HEPATITIS C: EXPLORATION OF EFFECT OF COMBINATIONS OF DIRECT ANTIVIRAL AGENTS ON HCV PRODUCTION DURING TREATMENT OF HCV PATIENTS.
O. Demin, Jr., O. Demin; Institute for Systems Biology, Moscow, Russian Federation.

PI-115
SYSTEMS PHARMACOLOGY MODEL OF HEPATITIS C: PREDICTION OF RESULTS OF ONGOING CLINICAL TRIALS OF DIRECT ANTIVARAL AGENTS COMBINATION THERAPIES.
O. Demin, Jr., O. Demin; Institute for Systems Biology, Moscow, Russian Federation.

PI-116
METFORMIN ALONE OR IN COMBINATION WITH VITAMIN E ATTENUATES ISOPROTERENOL-INDUCED CARDIAC INJURY: POSSIBLE MECHANISMS?
N. M. Alrasheed[1], D. A. Al-Rabeeah[1], H. S. Al-Barrak[1], S. A. Al-Salman[1], S. A. Ibrahim[1], S. A. Al-Hassab[1], M. A. Ali[1], I. H. Hasan[1], H. N. Al-Ajmi[1], N. Alrasheed[2]; King Saud University, Riyadh, Saudi Arabia, [2]Princess Nora Bint Abdulrahman university, Riyadh, Saudi Arabia.

PI-117
APPLICATION OF PHARMACOKINETIC/ PHARMACODYNAMIC MODELING TO SIMULATE POTENTIAL DIFFERENCES IN BIOEQUIVALENCE BETWEEN GENERIC AND BRAND NAME GABAPENTIN PRODUCTS.
Z. Meng[1], M. N. Trame[1], S. Schmidt[1], L. Fang[2], L. Lesko[1]; [1]University of Florida, Orlando, FL, [2]US Food and Drug Administration, Silver Spring, MD.

PI-118
ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION (ADME) OF THE ALK INHIBITOR ALECTINIB: RESULTS FROM AN ABSOLUTE BIOAVAILABILITY/ MASS BALANCE STUDY IN HEALTHY SUBJECTS.
P. N. Morcos[1], L. Yu[1], K. A. Nieforth[2], M. Sato[3], H. Katsuki[3], K. Kawashima[3], D. J. Moore[1], M. Whayman[4], K. Bogman[5], E. Guerini[5], M. Martin-Facklam[5], A. Phipps[4]; [1]Roche Innovation Center, New York City, NY, [2]d3 Medicine, Parsippany, NJ, [3]Chugai Pharmaceuticals Co., Ltd., Gotemba, Japan, [4]Roche Innovation Center, Welwyn, United Kingdom, [5]Roche Innovation Center, Basel, Switzerland.

PI-119
CLINICAL DRUG-DRUG INTERACTIONS (DDIS) THROUGH CYTOCHROME P450 3A (CYP3A) FOR ALECTINIB, A HIGHLY SELECTIVE ALK INHIBITOR.
P. N. Morcos[1], Y. Cleary[2], G. Dall[3], E. Guerini[2], K. Bogman[2], L. De Petris[4], S. Viteri Ramirez[5], W. Bordogna[2], L. Yu[1], M. Martin-Facklam[2], A. Phipps[6]; [1]Roche Innovation Center, NYC, NY, [2]F. Hoffmann-La Roche Ltd., Basel, Switzerland, [3]d3 Medicine, Parsippany, NJ, [4]Karolinska Institutet, Stockholm, Sweden, [5]Instituto Oncologico Dr Rosell, Barcelona, Spain, [6]F. Hoffmann-La Roche Ltd., Welwyn Garden City, United Kingdom.

PI-120

EFFECT OF FOOD AND THE PROTON PUMP INHIBITOR (PPI) ESOMEPRAZOLE ON THE PHARMACOKINETICS (PK) OF ALECTINIB, A HIGHLY SELECTIVE ALK INHIBITOR, IN HEALTHY SUBJECTS.

P. N. Morcos[1], G. C. Dall[2], N. J. Parrott[3], K. Bogman[3], E. Guerini[3], A. Zeaiter[4], M. Martin-Facklam[3], A. Phipps[5]; [1]Roche Innovation Center, New York City, NY, [2]d3 Medicine, Parsippany, NJ, [3]Roche Innovation Center, Basel, Switzerland, [4]F. Hoffmann-La Roche Ltd., Basel, Switzerland, [5]Roche, Welwyn, United Kingdom.

PI-121

EFFECT OF THE WETTING AGENT SODIUM LAURYL SULFATE (SLS) ON THE PHARMACOKINETICS (PK) OF ALECTINIB: RESULTS FROM A BIOEQUIVALENCE (BE) STUDY IN HEALTHY SUBJECTS.

P. N. Morcos[1], N. Parrott[2], G. Dall[3], L. Banken[2], C. Timpe[2], M. Lindenberg[2], E. Guerini[2], K. Bogman[2], M. Martin-Facklam[2], A. Zeaiter[4], A. Phipps[5]; [1]Roche Innovation Center, New York City, NY, [2]Roche Innovation Center, Basel, Switzerland, [3]d3 Medicine, Parsippany, NJ, [4]F. Hoffmann-La Roche Ltd., Basel, Switzerland, [5]Roche Innovation Center, Welwyn Garden City, United Kingdom.

PI-122

DISEASE MAPPING WITH EXPERIMENTAL FACTOR ONTOLOGY LINKS RARE TO COMMON DISEASES VIA SHARED ETIOLOGICAL PHENOTYPES.

S. Sarntivijai[1], C. Leroy[1], D. Vasant[1], G. Saunders[1], P. Bento[1], D. Gonzalez[1], J. Betts[2], S. Hasan[2], G. Koscielny[2], I. Dunham[1], H. Parkinson[1], J. Malone[1]; [1]European Bioinformatics Institute (EMBL-EBI), Cambridge, United Kingdom, [2]GlaxoSmithKline, Stevenage, United Kingdom.

PI-123

INITIAL ASSESSMENT OF THE EFFECT OF BMS-986142 ON THE QT INTERVAL IN EXPLORATORY CLINICAL DEVELOPMENT.

S. Lee, J. Xing, B. Murthy, B. Cirincione, I. G. Girgis; Bristol-Myers Squibb, Princeton, NJ.

PI-124

CARDIOVASCULAR CIRCULATORY MECHANISM-BASED MODEL ANALYSIS OF CHRONIC HEART FAILURE: ESTIMATED MYOCARDIAL OXYGEN CONSUMPTION AS A PREDICTIVE MARKER OF FATAL EVENT RISK.

A. Hisaka[1], R. Takaoka[2], H. Suzuki[2]; [1]Chiba University, Chiba, Japan, [2]The University of Tokyo Hospital, Tokyo, Japan.

PI-125

POPULATION-DEPENDENT LONG-TERM BIOMARKER CHANGES IN PATIENTS OF SPORADIC ALZHEIMER'S DISEASE ANALYZED BY SREFT.

A. Hisaka[1], T. Ishida[2], K. Tokuda[2], M. Honma[2], K. Motohashi[2], T. Moritoyo[2], T. Iwatsubo[1], H. Suzuki[2], Alzheimer's Disease Neuroimaging Initiative; [1]The University of Tokyo, Tokyo, Japan, [2]The University of Tokyo Hospital, Tokyo, Japan.

PI-126

ASSESSMENT OF THE IMMUNOGENICITY OF NIVOLUMAB (NIVO) AND IPILIMUMAB (IPI) IN COMBINATION AND POTENTIAL IMPACT ON SAFETY AND EFFICACY IN PATIENTS WITH ADVANCED MELANOMA.

P. Statkevich, C. Passey, J. Park, S. Saeger, A. Bello, A. Roy, S. Agrawal, M. Gupta; Bristol-Myers Squibb, Princeton, NJ.

PI-127

A NOVEL CLINICAL UTILITY ANALYSIS COMBINING MULTIPLE EFFICACY AND SAFETY ENDPOINTS TO SUPPORT DOSE SELECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS.

J. Huang[1], B. Balasubrahmanyam[1], M. M. Riggs[2], K. T. Baron[2], M. R. Gastonguay[2], B. J. Bloom[3], N. Kinnman[1], Y. Zhang[1], T. Hoock[1], **J. Shen[1]**; [1]Vertex Pharmaceutical, Inc., Boston, MA, [2]Metrum Research Group LLC, Tariffville, CT, [3]Covance, Inc., Princeton, NJ.

PI-128

CHARACTERIZATION OF INOTUZUMAB OZOGAMICIN TIME-DEPENDENT CLEARANCE IN RELAPSED/REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS BY NONLINEAR MIXED-EFFECTS ANALYSIS.

M. Garrett[1], A. Ruiz-Garcia[1], K. Parivar[1], J. Boni[2]; [1]Pfizer, Inc., San Diego, CA, [2]Pfizer, Inc., Collegeville, PA.

PI-129

EXPOSURE-RESPONSE MODELING TO PREDICT QTCF INTERVAL PROLONGATION FOR SELUMETINIB.

D. Zhou[1], P. Martin[2], N. Al-Huniti[1]; [1]AstraZeneca, Waltham, MA, [2]AstraZeneca, Alderley Park, United Kingdom.

PI-130

DRUG-DRUG INTERACTIONS BETWEEN NEXT GENERATION DIRECT ACTING ANTIVIRALS ABT-493 AND ABT-530 WITH DIGOXIN.

M. P. Kosloski, S. Dutta, B. Ding, A. Astryan, J. Kort, W. Liu; AbbVie, North Chicago, IL.

PI-131

DRUG-DRUG INTERACTIONS BETWEEN NEXT GENERATION DIRECT ACTING ANTIVIRALS ABT-493 AND ABT-530 WITH SOFOSBUVIR.

M. P. Kosloski, S. Dutta, B. Ding, S. Wang, J. Kort, W. Liu; AbbVie, North Chicago, IL.

PI-132

DOSE-RESPONSE AND EXPOSURE-RESPONSE MODELING OF ALPHA1-PROTEINASE INHIBITOR (A1-PI) IN PATIENTS WITH A1-PI DEFICIENCY BASED ON RAPID AND RAPID EXTENSION TRIALS.

J. A. Rogers[1], **M. A. Tortorici[2]**, O. Vit[3], M. Bexon[3], R. A. Sandhaus[4], J. Burdon[5], E. Piitulainen[6], N. Seersholm[7], J. Stocks[8], N. G. McElvaney[9], K. R. Chapman[10], J. Edelman[2]; [1]Metrum Research Group LLC, Tariffville, CT, [2]CSL Behring, King of Prussia, PA, [3]CSL Behring, Bern, Switzerland, [4]Division of Pulmonary Critical Care and Sleep Medicine, National Jewish Health, Denver, CO, [5]Department of Respiratory Medicine, St. Vincent's Hospital, Melbourne, Australia, [6]Faculty of Medicine, Lund University, Malmo, Sweden, [7]Department of Respiratory Medicine Gentofte Hospital, Hellerup, Denmark, [8]Pulmonary and Critical Care University of Texas Science Center at Tyler, Tyler, TX, [9]Department of Respiratory Medicine Beaumont Hospital, Royal College of Surgeons in Ireland, Dublin, Ireland, [10]Department of Medicine, University of Toronto, Toronto, ON, Canada.

PI-133

DEVELOPMENT AND VALIDATION OF A SEMI-PHYSIOLOGICAL PULMONARY DEPOSITION AND ABSORPTION MODEL FOR INHALED BUDESONIDE (BUD) IN HEALTHY SUBJECTS.

B. Hanna, J. Venitz; Virginia Common Wealth University, Richmond, VA.

PI-134

ASSESSMENT OF DRUG-DRUG INTERACTION POTENTIAL BETWEEN DASABUVIR AND CLOPIDOGREL USING PBPK MODELING AND SIMULATIONS: A CASE OF SUCCESSFUL REGULATORY SUBMISSION USING PBPK.

M. Shebley, W. Fu, Y. Pang, D. Bow, V. Fischer; AbbVie, North Chicago, IL.

PI-135
PHARMACOKINETICS AND PHARMACODYNAMICS OF A CHEMOKINE CCR2/5 RECEPTOR ANTAGONIST (PF-04634817) ADMINISTERED DAILY IN ADULTS WITH TYPE 2 DIABETES AND OVERT NEPHROPATHY.
K. Goteti, S. Martin, R. Webster, S. Gilbert, K. Page, C. Banfield, J. Gale; Pfizer, Inc., Cambridge, MA.

PI-136
MODELING DOSE NON-PROPORTIONAL INCREASE OF AZD5672 EXPOSURE IN PHASE I SINGLE AND MULTIPLE ASCENDING DOSE (SAD/MAD) STUDIES.
A. S. Ayyoub, N. Al-Huniti, J. Li; AstraZeneca, Waltham, MA.

PI-137
A RELATIVE BIOAVAILABILITY STUDY OF THE GRAZOPREVIR/ELBASVIR FIXED-DOSE COMBINATION IN HEALTHY SUBJECTS.
B. M. Davit[1], A. Alon[1], L. Caro[2], H. Feng[2], Z. Guo[2], F. Kesisoglou[2]; [1]Merck Research Laboratories, Rahway, NJ, [2]Merck Research Laboratories, North Wales, PA.

PI-138
EVALUATION OF CYP3A4 INDUCTION USING ENDOGENOUS PROBE 4SS-HYDROXYCHOLESTEROL IN A FIRST-IN-HUMAN STUDY.
X. Luo, S. Karan, P. Panorchan, W. Chen, J. Lekstrom, **J. Shen**; Vertex Pharmaceutical, Inc., Boston, MA.

PI-139
A SEMI-MECHANISTIC COMPARATOR PKPD MODEL FOR INTRAVENOUS IMMUNOGLOBULIN (IVIG) PROVIDED MECHANISTIC INSIGHTS AND SUPPORTED A GO/NO-GO DECISION FOR NOVEL IVIG.
A. Hussain[1], J. Lommerse[2], J. Elassaiss-Schaap[2], P. Jadhav[3], S. Khalilieh[4], A. Sitlani[4]; [1]Merck & Co., Inc., West Point, PA, [2]Quantitative Solutions, Oss, Netherlands, [3]Merck & Co., Inc., Upper Gwynedd, PA, [4]Merck & Co., Inc., Kenilworth, NJ.

PI-140
EXPOSURE-RESPONSE ANALYSES IN THE RISK-BENEFIT EVALUATION OF SECUKINUMAB FOR PLAQUE PSORIASIS.
J. Lee, J. Wang, J. Florian, Y. Wang, D. Kettl, K. Marcus, A. Woitach; US Food and Drug Administration, Silver Spring, MD.

PI-141
SAFETY, TOLERABILITY AND PHARMACOKINETICS OF SINGLE AND MULTIPLE DOSES OF ABT-493 IN HEALTHY SUBJECTS.
C. Lin, S. Dutta, J. Clifton II, A. Asatryan, A. Campbell, W. Liu; AbbVie, North Chicago, IL.

PI-142
PHARMACOKINETICS, TOLERABILITY AND SAFETY OF ABT-530 FOLLOWING SINGLE AND MULTIPLE DOSES IN HEALTHY SUBJECTS.
C. Lin, S. Dutta, J. Clifton II, A. Asatryan, A. Campbell, W. Liu; AbbVie, North Chicago, IL.

PI-143
SHINY_NCAPPC, A SHINY APP FOR NON-COMPARTMENTAL ANALYSIS (NCA).
J. Hibma, L. Fostvedt, C. Acharya, A. Ruiz-Garcia; Pfizer, Inc., La Jolla, CA.

PI-144
ALLOMETRY IS AN EFFICIENT APPROACH TO PROJECT DOSING FOR PEDIATRIC TRIALS.
T. Liu, P. Ghafoori, J. Gobburu; University of Maryland Baltimore, Baltimore, MD.

PI-145
BRINCIDOFOVIR (CMX001, BCV) DOES NOT INHIBIT THE P-GLYCOPROTEIN (P-GP) PROBE SUBSTRATE DABIGATRAN ETEXILATE (DAB).
K. Van Sickle, T. Tippin, M. Anderson, M. Morrison, O. Naderer; Chimerix, Durham, NC.

PI-146
PBPK-PD MODELING TO PROVIDE A TRANSLATIONAL RATIONALE BETWEEN DRUGS AND BETWEEN SPECIES: EXAMPLE OF TRAIL FUSION PROTEINS.

M. Block[1], J. Jäger[1], P. Mavroudis[1], M. Hutt[2], N. Pollak[2], M. Siegemund[2], O. Seifert[2], R. Kontermann[2], K. Pfizenmaier[2], K. Dickschen[1]; [1]Bayer Technology Services GmbH, Leverkusen, Germany, [2]Institute of Cell Biology and Immunology, University of Stuttgart, Stuttgart, Germany.

PI-147
POPULATION PHARMACOKINETIC MODELING AFTER REPEATED ADMINISTRATIONS OF RBP-6000, A NEW, SUBCUTANEOUS FORMULATION OF BUPRENORPHINE FOR THE TREATMENT OF OPIOID USE DISORDER.

C. M. Laffont[1], R. Gomeni[2], C. Heidbreder[1], N. Buzin[1], **J. Jones**[1], A. Nasser[1]; [1]Indivior, Inc., Richmond, VA, [2]Pharmacometrica, La Fouillade, France.

PI-148
PHARMACOKINETICS AND SAFETY OF GUSELKUMAB, AN ANTI-IL-23 MONOCLONAL ANTIBODY, IN HEALTHY SUBJECTS AND PATIENTS WITH MODERATE TO SEVERE PSORIASIS IN A FIRST-IN-HUMAN STUDY.

Y. Zhuang, C. Calderon, S. J. Marciniak, Jr., E. Bouman-Thio, Y. Wasfi, P. Szapary, T. Yang, A. Schantz, H. M. Davis, H. Zhou, Z. Xu; Janssen Research & Development, LLC, Spring House, PA.

PI-149
BIOAVAILABILITY AND PHARMACOKINETIC COMPARABILITY OF SIRUKUMAB FOLLOWING SUBCUTANEOUS ADMINISTRATION BY A PREFILLED SYRINGE OR AN AUTOINJECTOR.

Y. Zhuang[1], D. de Vries[2], S. J. Marciniak[1], H. Liu[1], H. Zhou[1], H. M. Davis[1], F. Leon[1], D. Raible[1], Z. Xu[1]; [1]Janssen Research & Development, LLC, Spring House, PA, [2]Janssen Biologics B.V., Leiden, Netherlands.

PI-150
EXPOSURE RESPONSE ANALYSIS FOR A NEW ONCE A MONTH LONG ACTING RISPERIDONE FOR SCHIZOPHRENIA.

C. M. Laffont[1], V. Ivaturi[2], J. Gobburu[2], M. Gopalakrishnan[2], W. Zhang[1], **J. Jones, III**[1], P. Twumasi-Ankrah[1], C. Heidbreder[1], A. F. Nasser[1]; [1]Indivior, Inc., Richmond, VA, [2]University of Maryland, Baltimore, MD.

PI-151
DEVELOPMENT OF A PHYSIOLOGICALLY BASED PHARMACOKINETIC MODEL OF TACROLIMUS IN ADULT ORGAN TRANSPLANT PATIENTS.

T. Yu[1], J. E. Rower[1], X. Liu[1], A. H. Balch[1], Z. Halford[2], E. K. Korgenski[2], C. M. Sherwin[1]; [1]University of Utah, Salt Lake City, UT, [2]Intermountain Healthcare, Salt Lake City, UT.

PI-152
MEDICATION CO-PRESCRIPTION (COP) INTERACTIONS WITH TYROSINE KINASE INHIBITORS (TKI) IN PRECISION GENOMICS CLINIC FOR PATIENTS WITH REFRACTORY CANCERS.

M. A. Hyder[1], J. T. Callaghan[1], M. Radovich[2], B. P. Schneider[2], P. J. Kiel[2], S. M. Nance[2], T. C. Skaar[1]; [1]Division of Clinical Pharmacology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, [2]Indiana University Health Precision Genomics Program, Melvin and Bren Simon Cancer Center, Indianapolis, IN.

PI-153
EFFECT OF ALDEHYDE DEHYDROGENASE 2 ON THE BIOTRANSFORMATION OF NITROGLYCERIN.

K. Zhou, J. Parker; University of Toronto, Toronto, ON, Canada.

PI-154

POPULATION PHARMACOKINETICS AND EXPOSURE-RESPONSE ANALYSIS OF AMG 333, A TRPM8 INHIBITOR FOR MIGRAINE PROPHYLAXIS.

T. Yuraszeck[1], C. Davis[2], K. Gabriel[3], S. Kasichayanula[4], R. Palaparthy[4]; [1]Clinical Pharmacology, Modeling and Simulation, Amgen, Thousand Oaks, CA, [2]Pharmacokinetics and Drug Metabolism, Amgen, Thousand Oaks, CA, [3]Medical Sciences, Early Development, Amgen, Thousand Oaks, CA, [4]Clinical Pharmacology, Modeling, and Simulation, Amgen, Thousand Oaks, CA.

PI-155

A POPULATION-BASED APPROACH TO SYSTEMS PHARMACOLOGY MODELING OF THE EFFECT OF BLINATUMOMAB (BLIN) IN ADULT B-PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) PATIENTS.

T. Yuraszeck[1], I. Singh[2], M. Klinger[3], M. Reed[4], C. Friedrich[4], R. Kumar[4], S. Pagano[4], S. Kasichayanula[1], M. Zhu[1]; [1]Clinical Pharmacology, Modeling and Simulation, Amgen, Thousand Oaks, CA, [2]Clinical Pharmacology, Modeling, and Simulation, Amgen, Thousand Oaks, CA, [3]Amgen Research Munich GmbH, Munich, Germany, [4]Rosa & Co LLC, San Carlos, CA.

TRANSLATIONAL AND PRECISION MEDICINE (TPM) AND DEVELOPMENT, REGULATORY, AND OUTCOMES (DRO) POSTER SESSION

FRIDAY, MARCH 11, 2016

7:00 AM – 9:00 AM

SAPPHIRE BALLROOM

PII-001

UTILIZATION OF ANTIPSYCHOTIC MEDICATIONS IN THE TREATMENT OF NEW DEPRESSIVE EPISODES IN THE NATIONAL MEDICAID POPULATION.

T. Gerhard[1], T. Stroup[2], C. Correll[3], C. Huang[1], Z. Tan[1], S. Crystal[1], M. Olfson[2]; [1]Rutgers University, New Brunswick, NJ, [2]Columbia University, New York, NY, [3]The Zucker Hillside Hospital, Glen Oaks, NY.

PII-002

METABOLISM AND DISPOSITION OF THE PAN-CLASS I PHOSPHATIDYLINOSITOL-3-KINASE (PI3K) INHIBITOR COPANLISIB IN HEALTHY VOLUNTEERS.

M. Gerisch[1], T. Schwarz[1], D. Lang[1], J. Lemmen[1], S. Reif[2], I. Genvresse[2], S. Reschke[2], **C. Granvil**[3]; [1]Bayer Pharma AG, Wuppertal, Germany, [2]Bayer Pharma AG, Berlin, Germany, [3]Bayer HealthCare Pharmaceuticals, Whippany, NJ.

PII-003

CLINICAL DECISION SUPPORTS (CDS) TO INCORPORATE PHARMACOGENOMICS (PGX) INTO DECISION MAKING IN PERIOPERATIVE CARE.

K. Hikino, K. Danahey, J. L. Apfelbaum, M. J. Ratain, P. H. O'Donnell; University of Chicago, Chicago, IL.

PII-004

COMPARISON OF THE EFFECT OF CHRONIC KIDNEY DISEASE (CKD) ON PHARMACOKINETICS OF OATP, CYP2D6, AND CYP3A SUBSTRATES.

K. Yoshida, B. Sun, P. Zhao, L. Zhang, S. Huang; US Food and Drug Administration, Silver Spring, MD.

PII-005

MARINE PYRROLOIMINOQUINONE ALKALOIDS: A PROMISING NOVEL CLASS OF HIF-1A/P300 INHIBITORS IN ONCOLOGY.

A. K. Goey[1], C. H. Chau[1], T. M. Sissung[1], K. M. Cook[1], D. J. Venzon[1], A. Castro[2], T. R. Ransom[2], C. J. Henrich[2], T. C. McKee[2], J. B. McMahon[2], T. Grkovic[3], M. M. Cadelis[3], B. R. Copp[3], K. R. Gustafson[2], W. D. Figg[1]; [1]National Cancer Institute, Bethesda, MD, [2]National Cancer Institute, Frederick, MD, [3]University of Auckland, Auckland, New Zealand.

PII-006

A RANDOMIZED DOUBLE-BLIND DOSE ESCALATION STUDY TO EVALUATE THE SAFETY AND DOSE RESPONSE OF SUBCUTANEOUS ADMINISTRATION OF COVERSIN IN HEALTHY SUBJECTS.

A. Connor[1], W. Weston-Davies[2], V. Zann[1], S. Mair[1]; [1]Quotient Clinical, Nottingham, United Kingdom, [2]Volution Immuno Pharmaceuticals, London, United Kingdom.

PII-007

PEDIATRIC MORPHINE PBPK MODEL INCORPORATING OCT1 TRANSPORTER PHARMACOGENETICS.

C. Emoto, A. A. Vinks, T. Fukuda; Division of Clinical Pharmacology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PII-008

PHARMACODYNAMIC EFFECTS OF HT-3951, A SELECTIVE AND REVERSIBLE INHIBITOR OF MAO-B, AFTER SINGLE DOSING IN NORMAL HEALTHY SUBJECTS.

J. J. Anderson, D. J. Carpenter, R. Rojas, J. Djan, T. Dewitt, C. Mason, J. Parsons, J. Ruckle, P. Perera; Dart NeuroScience, San Diego, CA.

PII-009

ANALYSIS OF SELECT SAFETY PARAMETERS IN THE BRISTOL-MYERS SQUIBB PHASE I DATABASE FOR NORMAL HEALTHY VOLUNTEERS RECEIVING PLACEBO.

T. C. Young[1], M. L. Vetter[1], V. Sethuraman[1], Z. Bhagwagar[2], S. Srinivasan[3], **B. J. Smyth[4]**; [1]Bristol-Myers Squibb, Lawrenceville, NJ, [2]Yale University, New Haven, CT, [3]Bristol-Myers Squibb, Wallingford, CT, [4]Bristol-Myers Squibb, Hopewell, NJ.

PII-010

FTY720 MITIGATES ORGAN DYSFUNCTION AND INFLAMMATION IN A TWO-HIT MODEL OF HEMORRHAGE/RESUSCITATION AND ENDOTOXEMIA IN RAT.

C. Huang[1], P. Tsai[2]; [1]Taipei Tzu Chi Hospital, New Taipei City, Taiwan, [2]Taipei Medical University, Taipei, Taiwan.

PII-011

SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF SINGLE RISING ORAL DOSES OF BI 1021958, A NOVEL CRTH$_2$ ANTAGONIST, IN HEALTHY MALE VOLUNTEERS.

R. Koenen[1], **A. Fowler[2]**, A. Gupta[1], J. Hilbert[3]; [1]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany, [2]Boehringer Ingelheim Ltd., Bracknell, United Kingdom, [3]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT.

PII-012

THE IMPACT OF HYPNOTICS USE ON THE RISK OF DEMENTIA IN TRAUMATIC BRAIN INJURY PATIENTS: A MATCHED COHORT STUDY.

P. Tsai[1], H. Chiu[1], C. Huang[2]; [1]Taipei Medical University, Taipei, Taiwan, [2]Taipei Tzu Chi Hospital, New Taipei City, Taiwan.

PII-015

AROMATASE INHIBITOR-INDUCED MUSCULOSKELETAL SYMPTOMS AND TCL1A-TLR-MYD88-DEPENDENT NF-KB ACTIVATION: MOLECULAR MECHANISMS INVOLVING A CRUCIAL ADAPTOR PROTEIN MYD88.

M. Ho[1], J. Ingle[1], P. Goss[2], T. Mushiroda[3], M. Kubo[4], L. Shepherd[5], L. Wang[1], R. Weinshilboum[1]; [1]Mayo Clinic, Rochester, MN, [2]Harvard University, Boston, MA, [3]RIKEN Center for Integrative Medical Sciences, Yokohama City, Japan, [4]RIKEN Center for Genomic Medicine, Yokohama City, Japan, [5]NCIC Clinical Trials Group, Kingston, ON, Canada.

PII-016

HUMAN ABUSE LIABILITY (HAL) STUDY OF AN EXPERIMENTAL TRIPLE MONOAMINE REUPTAKE INHIBITOR IN RECREATIONAL DRUG ABUSERS.

L. Webster, M. Smith; PRA Health Sciences, Salt Lake City, UT.

PII-018

PLASMA EXPOSURE TO METABOLITES OF MONOMETHYL AURISTATIN E (MMAE) IN PATIENTS WITH RELAPSED / REFRACTORY HODGKIN LYMPHOMA (HL) TREATED WITH BRENTUXIMAB VEDOTIN (BV).

A. Fasanmade[1], J. Kinley[2], M. Bargfrede[1], T. Wyant[1], K. Venkatakrishnan[1], M. Qian[1], M. Cwik[3], M. Paton[1], S. K. Balani[1], I. Purevjal[1], D. Huebner[1], L. Griskevicius[4], F. Offner[5]; [1]Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, [2]Takeda Development Centre Europe Ltd., London, United Kingdom, [3]Takeda Development Center Americas, Inc., Deerfield, IL, [4]Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania, [5]University of Gent, Gent, Belgium.

PII-019

USE OF TRANSCRIPTION ACTIVATOR LIKE EFFECTOR-TRANSCRIPTION FACTORS (TALE-TFS) TO INDUCE CYP1A2 GENE EXPRESSION AND VALIDATE MICRORNA 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, Kansas City, KS.

PII-020

LACK OF SUBJECTIVE ABUSE-RELATED EFFECTS OF ORAL ELUXADOLINE: A NOVEL MU-DELTA OPIATE MODULATOR FOR ORAL USE IN IBS-D.

N. Levy-Cooperman[1], G. McIntyre[2], L. Bonifacio[3], J. M. Davenport[2], P. S. Covington[2], L. S. Dove[2], E. M. Sellers[4]; [1]Altreos Research Partners, Inc., Toronto, ON, Canada, [2]Former employee of Furiex Pharmaceuticals, Inc., a subsidiary of Allergan plc., Jersey City, NJ, [3]Lodestar Pharma Consulting, LLC, Durham, NC, [4]University of Toronto and DL Global Partners, Inc., Toronto, ON, Canada.

PII-021

EFFECTS OF ITRACONAZOLE, A STRONG CYP3A INHIBITORS, ON THE PHARMACOKINETICS (PK) OF ALISERTIB IN PATIENTS (PTS) WITH ADVANCED SOLID TUMORS OR RELAPSED/REFRACTORY LYMPHOMA.

X. Zhou[1], G. Falchook[2], S. Pant[3], A. Lockhart[4], J. Nemunaitis[5], M. Bargfrede[1], A. Muehler[1], L. Rangachari[1], K. Venkatakrishnan[1]; [1]Takeda Pharmaceuticals International Co., Cambridge, MA, [2]Sarah Cannon Research Institute at HealthONE, Denver, CO, [3]Oklahoma Health Science Center – Stephenson Cancer Center, Oklahoma City, OK, [4]Washington University, St. Louis, MO, [5]Mary Crowley Cancer Research Centers, Dallas, TX.

PII-022

IN VIVO DIGOXIN KINETICS IN TWO DIFFERENT MDR1 GENOTYPES.

E. Sparve, E. Akillu, L. Bertilsson, G. Panagiotidis; Division of Clinical Pharmacology, Stockholm, Sweden.

PII-023

PHASE I STUDY TO ASSESS THE RELATIVE BIOAVAILABILITY OF TWO CAPSULE FORMULATIONS OF IXAZOMIB, AN ORAL PROTEASOME INHIBITOR, IN PATIENTS WITH ADVANCED SOLID TUMORS OR LYMPHOMA.

M. J. Hanley[1], N. Gupta[1], K. Venkatakrishnan[1], A. Bessudo[2], S. Sharma[3], B. O'Neil[4], B. Wang[1], A. Hui[1], J. Nemunaitis[5]; [1]Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, [2]California Cancer Associates for Research and Excellence, San Diego, CA, [3]Huntsman Cancer Institute, Salt Lake City, UT, [4]Indiana University Simon Cancer Center, Indianapolis, IN, [5]Mary Crowley Cancer Research Centers, Dallas, TX.

PII-024

PHASE I SINGLE AND MULTIPLE-DOSE PHARMACOKINETICS OF EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) INHIBITOR PF-06747775 IN ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS.

J. C. Masters, M. A. Zientek, L. Kirkovsky, Z. Goldberg; Pfizer, Inc., La Jolla, CA.

PII-025

CORRELATION OF DACOMITINIB AND ITS METABOLITE (PF-05199265) EXPOSURE WITH KEY ADVERSE EVENTS.

N. Giri[1], R. N. Upton[2], D. R. Mould[2], C. L. Bello[3], M. A. Amantea[1]; [1]Pfizer, Inc., San Diego, CA, [2]Projections Research, Inc., Phoenixville, PA, [3]Pfizer, Inc., New York, NY.

PII-026
TRANSLATIONAL EVALUATION OF THE RELATIONSHIP BETWEEN BIOMARKERS OF CYTOCHROME P450-MEDIATED EICOSANOID METABOLISM AND NON-ALCOHOLIC STEATOHEPATITIS (NASH).
M. A. Wells[1], K. C. Vendrov[1], M. L. Edin[2], B. C. Ferslew[1], K. L. Brouwer[1], A. S. Barritt[3], D. C. Zeldin[2], C. R. Lee[1]; [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.

PII-027
CLINICAL TRIAL OF CHRONO-CHEMOTHERAPY WITH DOCETAXEL, CISPLATIN AND 5-FLUOROURACIL: INFLUENCE OF DOSING-SCHEDULE ON CHEMOTHERAPY-INDUCED TOXICITIES.
K. Ushijima, T. Noguchi, Y. Tsuchiya, J. Hayasaka, Y. Arakawa, Y. Mori, A. Fujimura; Jichi Medical University, Shimotsuke, Japan.

PII-028
LONGITUDINAL TRENDS IN US VACCINE SHORTAGES, 2001-2014.
V. C. Ziesenitz[1], E. R. Fox[2], M. Zocchi[3], J. M. Pines[3], L. S. May[4], M. Mazer-Amirshahi[5]; [1]Children's National Health System, Washington, DC, and Heidelberg University, Heidelberg, Germany, [2]University of Utah, Salt Lake City, UT, [3]George Washington University, Washington, DC, [4]UC Davis Medical Center, Sacramento, CA, [5]MedStar Washington Hospital Center, Washington, DC.

PII-029
OPTIMIZATION AND SIMPLIFICATION OF IMIPENEM DOSING TO REMOVE WEIGHT-BASED DOSING ADJUSTMENTS.
M. Lala, M. Brown, B. Kantesaria, B. Walker, A. Paschke, **M. L. Rizk;** Merck & Co., Inc., Kenilworth, NJ.

PII-030
EFFECTS OF ITRACONAZOLE AND GEMFIBROZIL ON ARN-509 PHARMACOKINETICS (PK): COMPARISON OF *IN SILICO* PREDICTIONS BY PHYSIOLOGIC-BASED PK (PBPK) MODELING AND *IN VIVO* RESULTS.
C. Chien[1], A. Van Den Bergh[2], F. Saad[2], P. Ward[3], J. Snoeys[2], H. Stieltjes[2], J. Jiao[4], P. Hellemans[2]; [1]Janssen R&D, Titusville, NJ, [2]Janssen R&D, Beerse, Belgium, [3]Janssen R&D, La Jolla, CA, [4]Janssen R&D, Raritan, NJ.

PII-031
BIOMARKER OUTCOMES IN EARLY PHASE ONCOLOGY TRIALS INCLUDING NON-DIAGNOSTIC BIOPSIES.
R. F. Sweis, M. W. Drazer, M. J. Ratain; University of Chicago, Chicago, IL.

PII-032
PLACEBO AS GOLD STANDARD IN ANTIPSYCHOTIC RANDOMIZED CONTROLLED TRIALS, BASED ON LITERATURE SEARCH.
L. S. Lee[1], Y. J. Cao[2], C. Oo[3]; [1]National University of Singapore, Singapore, Singapore, [2]Astellas, Northbrook, IL, [3]Asubio Pharmaceuticals, Paramus, NJ.

PII-033
POTENTIAL OF TARGETING WEE1 AS THERAPY IN THE MANAGEMENT OF TRIPLE NEGATIVE BREAST CANCER.
G. Morrison, J. Wang, F. Wang, P. Geeleher, R. Huang; The University of Chicago, Chicago, IL.

PII-034
THEOPHYLLINE POPULATION PHARMACOKINETICS AND DOSING IN CHILDREN FOLLOWING CONGENITAL HEART SURGERY WITH CARDIOPULMONARY BYPASS.
A. Frymoyer, F. Su, P. C. Grimm, S. M. Sutherland, D. M. Axelrod; Stanford University, Palo Alto, CA.

PII-035

OCT1 GENOTYPE AND O-DESMETHYLTRAMADOL EXPOSURE IN NEWBORN INFANTS.

M. Matic; Erasmus University Medical Center - Sophia Children Hospital, Rotterdam, Netherlands.

PII-036

ASSOCIATION OF SINGLE NUCLEOTIDE POLYMORPHISMS IN IL8 AND IL13 WITH SUNITINIB-INDUCED TOXICITY IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA.

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

PII-038

AROMATASE INHIBITOR-INDUCED HORMONE LEVEL CHANGE ASSOCIATED WITH CSMD1 SNP AND ANDROSTENEDIONE-DEPENDENT VARIATION IN AROMATASE EXPRESSION.

J. Cairns[1], J. Ingle[1], T. Dudenkov[1], K. Kalari[1], A. Buzdar[2], M. Kubo[3], M. Robson[4], M. Ellis[5], P. Goss[6], L. Shepherd[7], R. Weinshilboum[1], L. Wang[1]; [1]Mayo Clinic, Rochester, MN, [2]The University of Texas MD Anderson Cancer Center, Houston, TX, [3]RIKEN Center for Integrative Medical Science, Yokohama City, Japan, [4]Memorial Sloan Kettering Cancer Center, New York, NY, [5]Baylor Cancer Center, Houston, TX, [6]Massachusetts General Hospital, Boston, MA, [7]NCIC Clinical Trials Group, Kingston, ON, Canada.

PII-039

IMPLEMENTATION OF HIGHLY CHARACTERIZED CYP2D6 GENOTYPES WITH COPY NUMBER ASSESSMENT: RESULTS OF A PREEMPTIVE INSTITUTIONAL PHARMACOGENOMIC (PGX) TESTING PROGRAM.

E. Agolini[1], K. T. Yeo[1], E. K. Leung[1], P. N. Friedman[1], P. Peterson[2], K. Danahey[1], Y. M. Lee[1], M. J. Ratain[1], P. O'Donnell[1]; [1]The University of Chicago, Chicago, IL, [2]Hologic, Inc., San Diego, CA.

PII-040

PHARMACODYNAMICS OF MULTIPLE RISING ORAL DOSES OF BI 1021958, A NOVEL $CRTH_2$ ANTAGONIST, IN CONTROLLED ASTHMATIC PATIENTS.

A. Fowler[1], J. Hilbert[2], R. Koenen[3], D. Kappeler[4], C. Wood[2], **A. Gupta[3]**; [1]Boehringer Ingelheim Ltd., Bracknell, United Kingdom, [2]Boehringer Ingelheim Inc., Ridgefield, CT, [3]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany, [4]Inamed GmbH, Gauting, Germany.

PII-041

SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF SINGLE RISING ORAL DOSES OF BI 1021958, A NOVEL CRTH2 ANTAGONIST, IN HEALTHY CHINESE AND JAPANESE MALES.

I. Jang[1], J. Kim[2], R. Koenen[3], A. Gupta[3], **A. Fowler[4]**, Y. Tadayasu[5]; [1]Department of Clinical Pharmacology & Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Genzyme Korea, Seocho-Gu, Seoul, Korea, Republic of, [3]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany, [4]Boehringer Ingelheim Ltd., Bracknell, United Kingdom, [5]Nippon Boehringer Ingelheim Co. Ltd., Kobe, Japan.

PII-042

DOSE INDIVIDUALIZATION FOR HYDROXYUREA USING BAYESIAN ADAPTIVE CONTROL IN CHILDREN WITH SICKLE CELL ANEMIA.

M. Dong, P. T. McGann, T. Mizuno, R. E. Ware, A. A. Vinks; Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PII-043

EFFECT OF DEXAMETHASONE CO-ADMINISTRATION ON THE PHARMACOKINETICS AND IMMUNOGENICITY OF ELOTUZUMAB.

C. Passey[1], L. Gibiansky[2], J. Mora[1], A. Roy[1], A. Bello[1], M. Gupta[1]; [1]Bristol-Myers Squibb, Princeton, NJ, [2]QuantPharm LLC, North Potomac, MD.

PII-044

COMBINED POPULATION PK MODELING AND DISPROPORTIONALITY ANALYSES TO ASSESS THE ASSOCIATION BETWEEN KINASE INHIBITION AND ADVERSE EVENTS.

J. Liu[1], G. Kim[2], J. Xu[2], A. McKee[2], M. Hu[3], T. Palmby[2], L. Zhuang[4], L. Zhao[3]; [1]Division of Clinical Pharmacology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, [2]Office of Hematology and Oncology Products, Office of New Drugs, CDER, US Food and Drug Administration, Silver Spring, MD, [3]Division of Quantitative Methods and Modeling, Office of Research and Standards, Office of Generic Drugs, CDER, US Food and Drug Administration, Silver Spring, MD, [4]Division of Pharmacometrics, Office of Clinical Pharmacology, Office of Translational Sciences, CDER, US Food and Drug Administration, Silver Spring, MD.

PII-045

CLINICAL PHARMACOKINETICS AND BRAIN PENETRATION OF GDC-0084, AN ORAL PI3K/MTOR INHIBITOR, IN PATIENTS WITH HIGH-GRADE GLIOMA.

K. Morrissey[1], B. Vora[1], R. Zhu[1], D. Apt[1], A. Olivero[1], J. Ware[1], L. Mueller[1], T. Cloughesy[2], E. Gerstner[3], J. Rodon[4], P. Wen[5], L. Salphati[1]; [1]Genentech, South San Francisco, CA, [2]University of California, Los Angeles, Los Angeles, CA, [3]Massachusetts General Hospital Cancer Center, Boston, MA, [4]Vall d'Hebron Institute of Oncology, Barcelona, Spain, [5]Dana-Farber Cancer Institute, Boston, MA.

PII-046

A1B-ADRENERGIC RECEPTOR GENETIC VARIATION AFFECTS VASCULAR RESPONSE TO ADRENERGIC STIMULATION.

A. Adefurin, L. Ghimire, U. Kohli, M. Muszkat, G. Sofowora, C. Li, R. Levinson, S. Paranjape, C. Stein, D. Kurnik; Vanderbilt University Medical Center, Nashville, TN.

PII-047
TRIPLICATE ECGS ARE SUFFICIENT IN OBTAINING PRECISE ESTIMATES OF QTCF.
R. M. Lester[1], **S. M. Azzam[2]**, C. Erskine[3], J. Olbertz[1]; [1]Celerion, Tempe, AZ, [2]Celerion, Lincoln, NE, [3]Celerion, Belfast, United Kingdom.

PII-048
EVALUATION OF THE EFFECT OF GS-5806 ON THE QT/QTC INTERVAL IN HEALTHY ADULTS.
Y. Xin[1], S. Toback[2], Y. Guo[2], P. Costales[1], J. Weston[1], J. W. Chien[2], J. A. Silverman[1], S. Ramanathan[1]; [1]Gilead Sciences, Inc., Foster City, CA, [2]Gilead Sciences, Inc., Seattle, WA.

PII-049
THE PHARMACOKINETICS AND SAFETY OF MOMELOTINIB IN SUBJECTS WITH MODERATE OR SEVERE RENAL IMPAIRMENT.
Y. Xin, H. Collins, F. Cheng, E. Kwan, S. Ramanathan, J. A. Silverman; Gilead Sciences, Inc., Foster City, CA.

PII-050
THE PHARMACOKINETICS AND SAFETY OF MOMELOTINIB IN SUBJECTS WITH MODERATE OR SEVERE HEPATIC IMPAIRMENT.
Y. Xin, H. Collins, F. Cheng, E. Kwan, S. Ramanathan, J. A. Silverman; Gilead Sciences, Inc., Foster City, CA.

PII-051
USE OF MOLECULAR IMAGING IN CLINICAL DRUG DEVELOPMENT*: A SYSTEMATIC REVIEW*.
H. Son, K. Jang, H. Lee, H. Lee; Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of Korea.

PII-052
A SYSTEMATIC REVIEW ON THE ROLE OF OPIOID PHARMACOGENETICS IN THE POSTPARTUM PERIOD.
M. Baber[1], P. Bapat[1], G. Nichol[2], G. Koren[2]; [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada.

PII-053
SAFETY, TOLERABILITY AND PHARMACOKINETICS OF MULTIPLE ORAL ADMINISTRATION OF LCB01-0371, A NEW OXAZOLIDINONE ANTIBIOTICS, IN HEALTHY MALE SUBJECTS.
Y. Choi[1], J. Yoon[1], S. Lee[1], S. Moon[1], I. Chung[1], H. Nam[2], Y. Cho[2], J. Chung[3]; [1]Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Development Center, LegoChem Biosciences, Inc., Daejeon, Korea, Republic of, [3]Seoul National University College of Medicine and Bundang Hospital, Seongnam, Korea, Republic of.

PII-054
VANCOMYCIN DOSAGE REQUIRED FOR NEONATES AND INFANTS WITH SEVERE CONGENITAL HEART DISEASE IN THE INTENSIVE CARE UNIT.
Y. Shimamoto[1], T. Fukuda[2], K. Mizuno[2], H. Ichikawa[1]; [1]National Cerebral and Cardiovascular Center, Osaka, Japan, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PII-055
PHARMACOKINETIC CHARACTERISTICS AND SAFETY OF SS-LAPACHONE IN HEALTHY MALE VOLUNTEERS.
S. Seong[1], W. Kang[1], J. Lee[1], B. Ohk[1], B. Kim[1], M. Gwon[1], H. Kim[1], H. Lee[1], I. Lee[2], Y. Yoon[1]; [1]Kyungpook National University Hospital Clinical Trial Center, Daegu, Korea, Republic of, [2]Kyungpook National University School of Medicine, Daegu, Korea, Republic of.

PII-056
AN EVALUATION OF DUTCH PHARMACISTS' KNOWLEDGE, EXPERIENCE, AND ATTITUDES TOWARDS PHARMACOGENETIC TESTING: RESULTS OF A NATIONWIDE SURVEY.
P. Bank, **J. Swen**, H. Guchelaar; Leiden University Medical Center, Leiden, Netherlands.

PII-057
COMPARING VARIOUS *IN VITRO* PREDICTION CRITERIA TO ASSESS THE POTENTIAL OF A NEW MOLECULAR ENTITY (NME) TO INHIBIT P-GLYCOPROTEIN (P-GP) *IN VIVO*.
T. Zhou[1], **V. Arya[2]**, L. Zhang[2]; [1]ORISE Fellow, Office of Clinical Pharmacology, Office of Translational Sciences, CDER, 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.

PII-058
GENETIC PREDICTORS OF EXEMESTANE PHARMACOKINETICS AND PHARMACODYNAMICS IN HEALTHY HUMAN VOLUNTEERS.
B. J. Gregory, N. M. Hussein, J. D. Simpson, M. A. Plunk, M. A. Murphy, L. K. Kamdem; Harding University, Searcy, AR.

PII-059
USE OF SUPPORTIVE CARE THERAPIES AMONG PEDIATRIC CANCER PATIENTS WITH HEMATOLOGIC MALIGNANCIES UNDERGOING CHEMOTHERAPY.
J. Constance[1], C. Stockmann[1], M. Linakis[1], A. Balch[1], K. Korgenski[2], H. Spraker-Perlman[1], R. Lemons[1], C. Sherwin[1]; [1]University of Utah, Salt Lake City, UT, [2]Intermountain Healthcare, Pediatric Clinical Program, Salt Lake City, UT.

PII-060
IN VIVO ADMINISTRATION OF SHRNA TARGETED TO THE HEPATIC TRANSPORTER OCT1 RESULTS IN PHOSPHORYLATION OF KEY PROTEINS INVOLVED IN FATTY ACID OXIDATION.
H. Chien, S. Yee, X. Liang, Y. Zhang, K. M. Giacomini; University of California, San Francisco, San Francisco, CA.

PII-061
ABSOLUTE BIOAVAILABILITY OF BOSUTINIB IN HEALTHY SUBJECTS FROM AN OPEN-LABEL, RANDOMIZED, 2-PERIOD CROSSOVER STUDY.
P. Hsyu[1], D. Soriano Pignataro[2], K. Matschke[3]; [1]Pfizer, Inc., La Jolla, CA, [2]Pfizer, Inc., Surrey, United Kingdom, [3]Pfizer, Inc., Collegeville, PA.

PII-062
ACQUISITION OF CONDITIONED RESPONSES BETWEEN METHAMPHETAMINE AND ASSOCIATED CUES IN HEALTHY HUMANS.
J. S. Cavallo, N. Ruiz, A. Lee, F. Enger, H. de Wit; University of Chicago, Chicago, IL.

PII-063
PHARMACOGENETICS GUIDED PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODELING OF OXYCODONE AND ITS METABOLITES FOR CHRONIC PAIN MANAGEMENT (CPM).
T. S. Samant[1], S. Schmidt[1], A. M. Trescot[2], S. Norton[2], M. Palmer[2], L. J. Lesko[1]; [1]University of Florida, Orlando, FL, [2]Pinnacle Laboratory Services, Ocala, FL.

PII-064
PHARMACOKINETICS AND EXPOSURE-RESPONSE ANALYSIS OF RG7667, A COMBINATION MONOCLONAL ANTIBODY THERAPY, IN KIDNEY TRANSPLANT RECIPIENTS AT HIGH RISK OF CMV INFECTION.
Y. Wang, M. Maia, T. Burgess, X. Liao, J. Tavel, **R. Deng;** Genentech, South San Francisco, CA.

PII-065
ESTROGEN RECEPTOR COREGULATOR CALML3 REGULATES GENE EXPRESSION AND DRUG RESPONSE IN A SNP AND ESTROGEN OR SERM DEPENDENT FASHION.
S. Qin, M. Liu, R. M. Weinshilboum, J. N. Ingle, L. Wang; Mayo Clinic, Rochester, MN.

PII-066
QUANTITATIVE ANALYSIS AND CLONAL CHARACTERIZATION OF T-CELL RECEPTOR BETA REPERTOIRES IN NON-SMALL-CELL LUNG CANCER PATIENTS IN A PHASE II VACCINE CLINICAL TRIAL.
T. H. Mai[1], Y. Daigo[2], K. Kiyotani[1], Y. Nakamura[1]; [1]University of Chicago, Chicago, IL, [2]Shiga University, Shiga, Japan.

PII-067
POPULATION PHARMACOKINETIC MODELING OF MAGNESIUM SULFATE FOR TREATMENT OF SEVERE ACUTE ASTHMA IN CHILDREN IN AN EMERGENCY ROOM SETTING.
J. E. Rower, X. Liu, T. Yu, M. Mundorff, C. Sherwin, M. Johnson; University of Utah, Salt Lake City, UT.

PII-068
DUAL THERAPY WITH VONOPRAZAN AND AMOXICILLIN IS AS EFFECTIVE AS THOSE WITH STANDARD PPI-BASED TRIPLE THERAPY WITH AMOXICILLIN AND CLARITHROMYCIN OR METRONIDAZOLE IN JAPAN.
T. Furuta, S. Sahara, H. Ichikawa, T. Kagami, E. Nagata, K. Odagiri, K. Umemura, H. Watanabe; Hamamatsu University School of Medicine, Hamamatsu, Japan.

PII-069
PHARMACOTHERAPY OF OBESE PATIENTS: TREATMENT AS N-OF-1 TRIALS.
P. K. Lala, B. M. Kapur; Hospital for Sick Children, Toronto, ON, Canada.

PII-070
LEARNINGS FROM FDA CLINICAL PHARMACOLOGY (CP) REVIEWS OF ONCOLOGY (ONC) NEW MOLECULAR ENTITIES (NMES) APPROVED FROM 2011 TO 2015.
S. Faucette[1], A. Trivedi[2], N. Gupta[1]; [1]Takeda Pharmaceuticals International Co., Cambridge, MA, [2]University of Tennessee Health Science Center, Memphis, TN.

PII-071
CHARACTERIZATION OF ATOMOXETINE METABOLISM AND POTENTIAL CLINICAL IMPLICATIONS FOR A BOTTOM-UP PBPK MODEL FOR DOSE INDIVIDUALIZATION IN CHILDREN.
J. C. Dinh, L. Van Haandel, K. T. Gibson, R. E. Pearce, A. Gaedigk, J. S. Leeder; Children's Mercy Hospital, Kansas City, MO.

PII-072
LAMOTRIGINE PHARMACOKINETICS ACROSS PREGNANCY: IMPLICATIONS FOR TREATMENT OF BIPOLAR DISORDER IN PREGNANCY.
C. T. Clark, K. L. Wisner, C. Stika, S. Schuette, M. J. Avram; Northwestern University, Chicago, IL.

PII-073
MODULATION OF SIRT7-FKBP51 INTERACTION AS A THERAPEUTIC STRATEGY FOR CANCER TREATMENT.
J. Yu[1], B. Qin[1], H. Pei[2], Z. Lou[1], L. Wang[1]; [1]Mayo Clinic, Rochester, MN, [2]Beijing Institute of Radiation Medicine, Beijing, China.

PII-074

ROLE OF FATTY ACID AMIDE HYDROLASE (FAAH) GENETIC POLYMORPHISM IN EXPOSURE-RESPONSE RELATIONSHIPS DURING IV ALCOHOL SELF-ADMINISTRATION (IV-ASA) IN SOCIAL DRINKERS.

J. Yan, B. L. Stangl, J. G. Westman, M. L. Schwandt, P. Spagnolo, R. Momenan, C. Hodgkinson, D. Goldman, **V. A. Ramchandani**; National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD.

PII-075

COMPARING VARIOUS *IN VITRO* PREDICTION CRITERIA TO ASSESS THE POTENTIAL OF A NEW MOLECULAR ENTITY (NME) TO INHIBIT ORGANIC ANION TRANSPORTER 1 AND 3 (OAT1 AND OAT3) *IN VIVO*.

Z. Dong[1], **X. Yang[2]**, V. Arya[2], L. Zhang[2]; [1]ORISE Fellow, Office of Clinical Pharmacology, Office of Translational Sciences, CDER, 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.

PII-076

COMPARING VARIOUS *IN VITRO* PREDICTION CRITERIA TO ASSESS THE POTENTIAL OF A NEW MOLECULAR ENTITY (NME) TO INHIBIT OCT2 AND MATE TRANSPORTERS *IN VIVO.*

Z. Dong[1], **X. Yang[2]**, V. Arya[2], L. Zhang[2]; [1]ORISE Fellow, Office of Clinical Pharmacology, Office of Translational Sciences, CDER, 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.

PII-077

THE RS662 POLYMORPHISM OF PARAOXONASE 1 (PON1) AFFECTS THE DIFFERENCE IN THE INHIBITION OF BUTYRYLCHOLINESTERASE ACTIVITY BY ORGANOPHOSPHORUS PESTICIDES IN HUMAN BLOOD.

Y. Ha[1], S. Kim[2], S. Cho[3], S. Lee[4], M. Park[5]; [1]Department of Clinical Pharmacology, Dong-A University Medical Center, Pusan, Korea, Republic of, [2]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [3]Armed Forces Medical Research Institute, Daejeon, Korea, Republic of, [4]Department of Rehabilitation Medicine, Dong-A University Hospital, Pusan, Korea, Republic of, [5]Department of Clinical Pharmacology, Dong-A University Medical Center & Department of Pharmacology, College of Medicine, Dong-A University, Pusan, Korea, Republic of.

PII-078

THEORETICAL CONSIDERATION ON SREFT FOR RECONSTRUCTION OF LONG-TERM BIORMARKER CHANGES FROM TEMPORALLY FRAGMENTED DATA.

K. Tokuda[1], T. Ishida[1], A. Hisaka[2], M. Honma[3], T. Moritoyo[4], T. Iwatsubo[5], H. Suzuki[1]; [1]Department of Pharmacy, The University of Tokyo Hospital, Tokyo, Japan, [2]Faculty of Pharmaceutical Sciences, The University of Tokyo (Current affiliation: Chiba University, Chiba, Japan), Tokyo, Japan, [3]Pharmacology and Pharmacokinetics, The University of Tokyo Hospital, Tokyo, Japan, [4]Department of Clinical Research Governance, The University of Tokyo Hospital, Tokyo, Japan, [5]Department of Neuropathology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan.

PII-079

FUNCTIONAL CHARACTERIZATION OF ETHAMBUTOL BY ORGANIC CATION TRANSPORTER 2 (OCT2), *IN VITRO.*

H. Shin, Y. Lee, H. Choi, S. Lim, M. Cho, Y. Yoon, D. Lee, P. Md. Masud, **J. Jung,** J. Shin; Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of.

PII-080

CHARACTERIZATION OF 22 ANTI-TUBERCULOSIS DRUGS FOR THE INHIBITORY EFFECT ON OATPS TRANSPORTERS MEDIATED UPTAKE; POSSIBILITY OF DRUG-DRUG INTERACTIONS.

P. Md. Masud, **J. Jung,** J. Kim, H. Choi, H. Shin, D. Kim, J. Shin; Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of.

PII-081

PARA-AMINOSALYCYLIC ACID (PAS) CHARACTERIZED AS A SUBSTRATE OF OCT1 AND OCT2 AND OAT1 AND OAT3 TRANSPORTER, *IN VITRO.*

P. Masud, **J. Jung,** H. Choi, H. Shin, D. Kim, J. Shin; Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of.

PII-082

INHIBITORY EFFECTS OF RIFAMYCINS ON SIX UDP-GLUCURONOSYLTRANSFERASE ACTIVITIES IN HUMAN LIVER MICROSOMES.

M. Kim, J. Ha, P. Masud, H. Choi, **E. Kim,** D. Kim, J. Shin; Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of.

PII-083

DIFFERENTIAL MIRNA INTERACTION OF ABCB1 (P-GLYCOPROTEIN) THROUGH 3′-UTR LENGTH VARIANTS.

O. Bruhn[1], K. Drerup[1], M. Kaehler[1], S. Haenisch[1], C. Röder[2], **I. Cascorbi[1]**; [1]Institute of Experimental and Clinical Pharmacology, University of Kiel, Kiel, Germany, [2]Institute for Experimental Cancer Research, University of Kiel, Kiel, Germany.

PII-084

DRUG-DRUG INTERACTION (DDI) STUDY BETWEEN THE INVESTIGATIONAL NAE INHIBITOR PEVONEDISTAT (TAK-924) AND FLUCONAZOLE OR ITRACONAZOLE IN PATIENTS WITH ADVANCED SOLID TUMORS.

H. M. Faessel[1], R. D. Harvey[2], A. C. Lockhart[3], T. M. Bauer[4], L. Wang[1], F. Sedarati[1], S. Santillana[1], J. J. Nemunaitis[5]; [1]Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, [2]Winship Cancer Institute of Emory University, Atlanta, GA, [3]Washington University School of Medicine/Siteman Cancer Center, St. Louis, MO, [4]Sarah Cannon Research Institute/Tennessee Oncology PLLC, Nashville, TN, [5]Mary Crowley Cancer Research Centers, Dallas, TX.

PII-085

THE SURVEY OF FDA APPROVED NEW MOLECULAR ENTITIES THAT ARE TERATOGENIC AND THEIR DRUG INTERACTION POTENTIALS WITH HORMONAL CONTRACEPTIVES.

M. Ahn, L. Li, **M. Kim;** US Food and Drug Administration, Silver Spring, MD.

PII-087
STING PATHWAY ACTIVATION ENHANCES IMMUNE RESPONSE AND IMPROVES SURVIVAL IN MURINE MYELOID LEUKEMIA.
E. Curran, X. Chen, L. Corrales, J. Kline; University of Chicago, Chicago, IL.

PII-088
PHARMACOKINETICS OF MEDICATIONS IN PREGNANCY - A COMPREHENSIVE SYSTEMATIC REVIEW OF THE LITERATURE.
T. Leibson[1], G. Pariente[1], G. Koren[2], S. Ito[1]; [1]Hospital for Sick Children, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada.

PII-089
ALCOHOL AND ALDEHYDE DEHYDROGENASES CONTRIBUTE TO SEXUAL DIMORPHISM OF ZOLPIDEM.
C. J. Peer[1], J. D. Strope[1], S. Beedie[1], A. M. Ley[1], W. H. Theodore[2], W. D. Figg[1], **T. Sissung[1]**; [1]National Cancer Institute, Bethesda, MD, [2]National Institute of Neurological Disorders and Stroke, Bethesda, MD.

PII-090
A PHASE I STUDY TO ASSESS FOOD EFFECT ON OPROZOMIB IN PATIENTS WITH ADVANCED MALIGNANCIES.
R. D. Harvey[1], L. Gore[2], D. Wang[3], A. Mita[4], S. Sharma[5], J. Nemunaitis[6], K. Papadopoulos[7], D. Pinchasik[8], Y. Ou[8], E. Demirhan[8], R. E. Cutler, Jr.[8], A. M. Tsimberidou[9]; [1]Winship Cancer Institute of Emory University, Atlanta, GA, [2]University of Colorado Cancer Center, Aurora, CO, [3]Henry Ford Health System, Detroit, MI, [4]Cedars-Sinai Medical Center, Los Angeles, CA, [5]University of Utah Health Sciences Center, Huntsman Cancer Institute, Salt Lake City, UT, [6]Mary Crowley Cancer Research Centers, Dallas, TX, [7]South Texas Accelerated Research Therapeutics, San Antonio, TX, [8]Onyx Pharmaceuticals, Inc., South San Francisco, CA, [9]University of Texas MD Anderson Cancer Center, Houston, TX.

PII-091
EXPLORING THE HYPOTHESIS THAT AGE RELATED DIFFERENCES IN THE RESPONSE TO TRIAZOLAM ARE DUE TO ALTERED PHARMACOKINETICS AND INCREASED SENSITIVITY TO THE DRUG IN THE ELDERLY.
M. Chetty, M. Jamei, A. Rostami; Simcyp (a Certara Company), Sheffield, United Kingdom.

PII-092
PREDICTING THE IMPACT OF CYP3A5 POLYMORPHISM ON TACROLIMUS TROUGH CONCENTRATIONS IN BLACK AFRICAN TRANSPLANT RECIPIENTS.
K. Machavaram[1], L. Almond[1], B. Small[1], Z. Barter[1], M. Jamei[1], A. Rostami-Hodjegan[2], I. Gardner[1]; [1]Simcyp (a Certara Company), Sheffield, United Kingdom, [2]University of Manchester, Manchester, United Kingdom.

PII-093
DRUG-INDUCED NEUROCOGNITIVE CHANGES ON CHOICE REACTION TIME IN CNS POLYDRUG USERS.
T. Hopyan, B. Setnik; INC Research Toronto, Inc., Toronto, ON, Canada.

PII-094
BIOMEDICAL INFORMATICS APPROACHES TO IDENTIFYING DRUG-DRUG INTERACTIONS (DDIS): APPLICATION TO INSULIN SECRETAGOGUES (SGS).
X. Han[1], C. Chiang[2], C. E. Leonard[1], W. B. Bilker[1], C. M. Brensinger[1], L. Li[2], S. Hennessy[1]; [1]University of Pennsylvania, Philadelphia, PA, [2]Indiana University, Indianapolis, IN.

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CHANGES IN PEDIATRIC PRESCRIBING PATTERNS DURING THERAPEUTIC DRUG MONITORING OF TACROLIMUS.

S. Abdelaziz[1], T. Yu[1], C. Stockmann[2], C. T. Sherwin[1], J. E. Constance[1], **A. Balch[1];** [1]Department of Pediatrics, Division of Clinical Pharmacology, University of Utah, Salt Lake City, UT, [2]Department of Pediatrics, University of Utah, Salt Lake City, UT.

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A PHASE I STUDY OF OPROZOMIB TO ASSESS DRUG-DRUG INTERACTION WITH MIDAZOLAM IN PATIENTS WITH ADVANCED MALIGNANCIES.

A. M. Tsimberidou[1], Y. Ou[2], Y. Xu[3], Z. Wang[2], R. D. Harvey[4], A. Mita[5], S. Sharma[6], K. Papadopoulos[7], D. Wang[8], D. Pinchasik[2], E. Demirhan[2], R. E. Cutler, Jr.[2], L. Gore[9]; [1]University of Texas MD Anderson Cancer Center, Houston, TX, [2]Onyx Pharmaceuticals, Inc., South San Francisco, CA, [3]Amgen, Inc., Thousand Oaks, CA, [4]Winship Cancer Institute, Atlanta, GA, [5]Cedars-Sinai Medical Center, Los Angeles, CA, [6]University of Utah Health Sciences Center, Huntsman Cancer Institute, Salt Lake City, UT, [7]South Texas Accelerated Research Therapeutics, San Antonio, TX, [8]Henry Ford Health System, Detroit, MI, [9]University of Colorado Cancer Center, Aurora, CO.

PII-097

GENETIC VARIANTS INFLUENCING INR VARIABILITY IN WARFARIN TREATED PATIENTS AFTER THE DOSE-TITRATION PHASE.

O. F. Iwuchukwu, R. Andrea, Y. Shi, E. A. Bowton, V. K. Kawai, J. Schildcrout, J. C. Denny, D. M. Roden, M. C. Stein; Vanderbilt University, Nashville, TN.

PII-098

MODULATON OF SORAFENIB-MEDIATED KERATINOCYTE INJURY BY PROBENECID.

S. Hu[1], E. I. Zimmerman[2], A. A. Gibson[1], A. Vasilyeva[2], L. Li[2], A. Sparreboom[1], S. D. Baker[1]; [1]The Ohio State University, Columbus, OH, [2]St. Jude Children's Research Hospital, Memphis, TN.

PII-099

OATP1B2-DEFICIENCY PROTECTS AGAINST PACLITAXEL-INDUCED NEUROTOXICITY.

S. Hu[1], T. Florea[2], G. Du[3], A. A. Gibson[1], A. Sparreboom[1], J. A. Sprowl[2]; [1]The Ohio State University, Columbus, OH, [2]D'Youville College, Buffalo, NY, [3]St. Jude Children's Research Hospital, Memphis, TN.

PII-100

NONHOMOGENEOUS DRUG PENETRANCE OF VELIPARIB MEASURED IN TRIPLE NEGATIVE BREAST TUMORS.

I. H. Bartelink[1], B. Prideaux[2], G. Krings[1], L. Wilmes[1], P. R. Lee[1], B. Hann[1], J. Coppé[1], D. Heditsian[1], L. Swigart-Brown[1], E. F. Jones[1], S. Magnitsky[1], R. Keizer[1], L. Esserman[1], W. Ruan[1], A. Wu[1], D. Yee[1], V. Dartois[1], D. Wolf[1], R. Savic[1], L. vantVeer[1]; [1]University of California, San Francisco, San Francisco, CA, [2]The State University of New Jersey, New Jersey, NJ.

PII-101

YES1-MEDIATED REGULATION OF OCT2 FUNCTION IN THE KIDNEY.

N. Pabla[1], S. Hu[1], A. A. Gibson[1], L. Li[2], A. Sparreboom[1]; [1]The Ohio State University, Columbus, OH, [2]St. Jude Children's Research Hospital, Memphis, TN.

PII-102

PRELIMINARY EXPERIENCE WITH INTRAVENOUS INFUSION OF TREHALOSE (CABALETTA) FOR OPMD: THE EFFECT ON PLASMA GLUCOSE AND THE PRESENCE OF GLYCOSURIA.

Y. Caraco[1], H. Vornovizki[1], S. Blotnick[1], I. Gliko-Kabir[2], Z. Argov[2]; [1]Hadassah University Hospital, Jerusalem, Israel, [2]Bioblast Pharma, Tel-Aviv, Israel.

PII-103
EFFECT OF HEPATIC IMPAIRMENT ON COBIMETINIB PHARMACOKINETICS: AN OPEN-LABEL, SINGLE-DOSE, PARALLEL GROUP STUDY.
I. Templeton, S. Kshirsagar, Y. Deng, N. Choong, I. Chang, I. Georgescu, L. Musib; Genentech, South San Francisco, CA.

PII-104
INTEGRATION OF PK-PD AND HEALTH ECONOMIC MODELING TO ASSESS COST-EFFECTIVENESS OF IMPROVING ADHERENCE IN REAL WORLD SETTING.
L. Jain[1], K. Tunceli[2], J. Chen[2], M. Lala[1], C. Davis[1], J. Liu[2], A. Chain[1], D. Tatosian[1], Y. Lu[1], S. Visser[1], P. Mavros[2], P. Jadhav[1]; [1]Quantitative Pharmacology and Pharmacometrics (QP2), Pharmacokinetics Pharmacodynamics and Drug Metabolism (PPDM), Merck Research Laboratories, Upper Gywnedd, PA, [2]Center for Observational and Real-world Evidence, Merck Research Laboratories, Upper Gywnedd, PA.

PII-105
ASSOCIATION OF GENETIC POLYMORPHISMS AND RESPONSE TO RBP-7000 IN PATIENTS WITH SCHIZOPHRENIA.
Z. Konsoula, C. Heidbreder, P. Twumasi-Ankrah, S. Agarwal, J. Jones, III, A. Nasser; Indivior, Inc., Richmond, VA.

PII-106
THE ROLE OF POPULATION PK IN INFORMING DOSING RECOMMENDATIONS FOR PATIENTS WITH HEPATIC AND RENAL IMPAIRMENT.
I. R. Younis, V. Sinha; US Food and Drug Administration, Silver Spring, MD.

PII-107
INCREASING PLACEBO RESPONSE AND DECREASING TREATMENT EFFECTS IN SCHIZOPHRENIA TRIALS -THE TREND CONTINUES: AN UPDATE FROM US FOOD AND DRUG ADMINISTRATION.
M. Gopalakrishnan, M. Mehta, R. Uppoor, M. Mathis, T. Farchione, L. Kempf, J. Zhang, **I. Younis;** US Food and Drug Administration, Silver Spring, MD.

POSTER WALKS

ESSENTIAL TOOLS FOR PRECISION MEDICINE

WEDNESDAY, MARCH 9, 2016
5:45 PM – 6:30 PM
SAPPHIRE FOYER

PWI-1
PHARMACOMETABOLOMICS SIGNATURES FROM WOMEN WITH PREMENSTRUAL DYSPHORIC DISORDER ADMINISTERED ESTRADIOL AND PROGESTERONE TREATMENT.
D. Rotroff[1], N. W. Gaikwad[2], J. M. Reuter[3], C. Smith[1], H. R. Kucera[2], T. Vi Nguyen[4], D. R. Rubinow[5], A. A. Motsinger-Reif[1], P. J. Schmidt[3], R. Kaddurah-Daouk[6]; [1]Bioinformatics Research Center, North Carolina State University, Raleigh, NC, [2]Departments of Nutrition and Environmental Toxicology, University of California at Davis, Davis, CA, [3]Behavioral Endocrinology Branch, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, [4]Departments of Psychiatry and Obstetrics-Gynecology, McGill University Health Center, Montreal, QC, Canada, [5]Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC, [6]Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, NC.

PWI-2

INVESTIGATING THE EPIGENETIC DYSREGULATION OF APOPTOSIS GENES IN PANCREATIC CANCER PATIENTS AND THEIR POTENTIAL IMPLICATION IN PREDICTING CHEMOTHERAPEUTIC OUTCOME.

L. Phua[1], D. Tai[2], T. Lim[1]; [1]Singapore General Hospital, Singapore, Singapore, [2]National Cancer Centre Singapore, Singapore, Singapore.

PWI-3

A METFORMIN METABOLOMIC EXPRESSION PROFILE STUDY UTILIZING AN ELECTRONIC HEALTH RECORD (EHR)-LINKED BIOREPOSITORY AND INTEGRATIVE MOLECULAR EPIDEMIOLOGY APPROACHES.

M. K. Breitenstein[1], R. Berger[2], S. Bos[3], M. Cascante[3], T. Hankemeier[2], A. C. Harms[2], R. F. Kaddurah-Daouk[4], K. R. Kalari[1], V. V. Koval[2], S. Marin[3], I. Moon[1], K. S. Nair[1], M. Persson[1], R. M. Weinshilboum[1], L. Wang[1]; [1]Mayo Clinic, Rochester, MN, [2]Leiden Academic Centre for Drug Research, Leiden University, Leiden, Netherlands, [3]Department of Biochemistry and molecular Biology, University of Barcelona, Barcelona, Spain, [4]Duke University, Durham, NC.

PWI-4

NOVEL *IN VIVO* HUMAN MODEL FOR TRANSIENT MITOCHONDRIAL DYSFUNCTION: SIMVASTATIN-INDUCED MITOCHONDRIAL DYSFUNCTION IN HEALTHY SUBJECTS AND ITS REVERSIBILITY BY UBIQUINOL.

M. P. van Diemen[1], C. Berends[1], N. Akram[1], J. Wezel[2], J. L. Hay[1], W. M. Teeuwisse[2], K. E. Malone[3], E. G. Mik[4], H. Kan[2], A. Webb[2], G. Groeneveld[1]; [1]Centre for Human Drug Research, Leiden, Netherlands, [2]Leiden University Medical Center, Leiden, Netherlands, [3]Good Biomarker Sciences, Leiden, Netherlands, [4]Erasmus Medical Center, Rotterdam, Netherlands.

PWI-5

EVALUATION OF HYPOXIA ADAPTATION IN NEUROBLASTOMA IDENTIFIES REPRODUCIBLE TRANSCRIPTIONAL AND PHENOTYPIC RESPONSES.

M. A. Applebaum, A. Jha, C. Mariani, K. White, B. Stranger, S. Cohn; University of Chicago, Chicago, IL.

MECHANISMS BEHIND SPECIAL POPULATIONS: WHAT MAKES THEM SO SPECIAL?

THURSDAY, MARCH 10, 2016

4:45 PM – 5:30 PM

SAPPHIRE FOYER

PWII-1

THE ACTIVITIES OF ORGANIC ANION TRANSPORTERS, OATP1B1/1B3 AND OAT1/3 ARE MODULATED BY UREMIC TOXINS.

C. Hsueh[1], K. Yoshida[2], T. Meyer[3], L. Zhang[2], S. Huang[2], K. Giacomini[1]; [1]University of California, San Francisco, San Francisco, CA, [2]US Food and Drug Administration, Silver Spring, MD, [3]Stanford University, Stanford, CA.

PWII-2

GENOME-WIDE ASSOCIATION STUDY TO IDENTIFY THE GENETIC DETERMINANTS OF WARFARIN INDUCED HEMORRHAGIC COMPLICATIONS IN AFRICAN AMERICANS (AAS).

T. De[1], N. Nwanze[1], W. Hernandez[1], E. Smithberger[1], M. Tuck[2], T. O'Brien[3], R. Kittles[4], J. Duarte[5], S. Bourgeois[6], L. Cavallari[7], M. Perera[1]; [1]University of Chicago, Chicago, IL, [2]Veterans Affairs Medical Center, Washington, DC, [3]The George Washington University, Washington, DC, [4]University of Arizona College of Medicine, Tucson, AZ, [5]University of Illinois, Chicago, IL, [6]Queen Mary University of London, London, United Kingdom, [7]University of Florida, Gainesville, FL.

PWII-3
IMPACT OF PREECLAMPSIA ON THE EXPRESSION OF ABC AND SLC TRANSPORTERS IN HUMAN PLACENTA.
D. Kojovic, M. Piquette-Miller; University of Toronto, Toronto, ON, Canada.

PWII-4
NOVEL DELETERIOUS DIHYDROPYRIMIDINE DEHYDROGENASE VARIANTS MAY CONTRIBUTE TO 5-FLUOROURACIL SENSITIVITY IN AN EAST AFRICAN POPULATION.
T. Elraiyah, S. Shrestha, L. R. Roberts, S. M. Offer, R. B. Diasio; Mayo Clinic, Rochester, MN.

NOVEL MODELING APPROACHES TO SOLVE OLD PROBLEMS: PK, DDI, TOXICITY

THURSDAY, MARCH 10, 2016
5:30 PM – 6:15 PM
SAPPHIRE FOYER

PWIII-1
IN SILICO PREDICTION OF ORAL BIOAVAILABILITY.
M. Lawless, J. DiBella, M. B. Bolger, **R. D. Clark**, M. Waldman, V. Lukacova; Simulations Plus, Inc., Lancaster, CA.

PWIII-2
DEVELOPMENT OF A SYSTEMS PHARMACOLOGY MODEL TO PREDICT THE EFFECTS OF WARFARIN AND RIVAROXABAN ON THE HUMAN COAGULATION NETWORK.
S. Hartmann[1], K. Biliouris[1], L. J. Lesko[1], U. Nowak-Goettl[2], M. N. Trame[1]; [1]Center for Pharmacometrics and Systems Pharmacology, Department of Pharmaceutics, College of Pharmacy, University of Florida, Orlando, FL, [2]University Hospital Schleswig-Holstein, Institute of Clinical Chemistry, Thrombosis & Hemostasis Treatment Center, Campus Kiel & Lubbeck, Kiel, Germany.

PWIII-3
PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELING TO PREDICT CLINICAL EFFECT OF PROTON PUMP INHIBITORS (PPI) ON EXPOSURE OF ANTICANCER PROTEIN KINASE INHIBITORS (PKI).
H. M. Ghazarian[1], L. H. Lam[1], S. Yamazaki[2], M. A. Zientek[2], A. Ruiz-Garcia[2], Y. K. Pithavala[2], J. C. Masters[2]; [1]UC San Diego Skaggs School of Pharmacy, La Jolla, CA, [2]Pfizer, Inc., San Diego, CA.

PWIII-4
A SYSTEMS BIOLOGY APPROACH TO PREDICTING CARDIOTOXICITY ASSOCIATED WITH TYROSINE KINASE INHIBITORS.
S. Zaman[1], C. Gao[2], D. R. Abernethy[1]; [1]US Food and Drug Administration, Silver Spring, MD, [2]Rutgers University, New Brunswick, NJ.

PWIII-5
THE UTILITY OF LINEAR QUANTILE MIXED MODELING (LQMM) APPROACH IN PREDICTING THROUGH-QT (TQT) STUDY OUTCOME USING PHASE I SINGLE ASCENDING DOSE STUDIES (SAD).
N. Al-Huniti, A. S. Ayyoub, J. Li; AstraZeneca, Waltham, MA.

TRANSLATIONAL DETERMINANTS OF TOXICITY

FRIDAY, MARCH 11, 2016
7:15 AM – 8:00 AM
SAPPHIRE FOYER

PWIV-1
STUDYING INDIVIDUAL DIFFERENCES IN CANCER DRUG EFFICACY USING CELL LINES DERIVED FROM PATIENTS.
T. Hankemeier[1], R. Kaddurah-Daouk[2], V. V. Koval[1], A. C. Harms[1], I. Moon[3], H. Kuwahara[4], S. Bos[5], S. Marin[5], M. Cascante[5], R. Weinshilboum[3], L. Wang[3]; [1]Leiden/Amsterdam Centre for Drug Research, Leiden, Netherlands, [2]Duke

University, Durham, NC, [3]Division of Clinical Pharmacology, Mayo Clinic, Rochester, MN, [4]Sumitomo Dainippon Pharma, Tokyo, Japan, [5]University of Barcelona, Barcelona, Spain.

PWIV-2

ANTIVIRAL DRUGS INTERACT MORE POTENTLY WITH THE HUMAN ORGANIC ANION TRANSPORTER 1, OAT1 THAN WITH RODENT AND NON-RODENT SPECIES ORTHOLOGS.

L. Zou[1], A. Gupta[2], S. Stahl[3], K. Fenner[3], K. Giacomini[1]; [1]University of California, San Francisco, San Francisco, CA, [2]AstraZeneca Pharmaceuticals, Waltham, MA, [3]AstraZeneca Pharmaceuticals, Cambridge, United Kingdom.

PWIV-3

METFORMIN IS A SUBSTRATE AND INHIBITOR OF THE HUMAN INTESTINAL THIAMINE TRANSPORTER 2 (THTR-2; SLC19A3).

X. Liang[1], H. Chien[1], S. Yee[1], M. Giacomini[2], E. Chen[1], M. Piao[1], J. Hao[2], J. Twelves[2], E. Lepist[2], A. Ray[2], K. Giacomini[1]; [1]University of California, San Francisco, San Francisco, CA, [2]Gilead Sciences, Inc., Foster City, CA.

PWIV-4

AMELIORATION OF CISPLATIN NEPHROTOXICITY BY NILOTINIB.

A. F. Leblanc, S. Hu, N. Pabla, A. A. Gibson, A. Sparreboom; The Ohio State University, Columbus, OH.

PWIV-5

ANTIRETROVIRAL DRUG EXPOSURE IN CEREBROSPINAL FLUID (CSF) AS A PREDICTOR OF NEUROCOGNITIVE OUTCOMES IN HIV INFECTED PATIENTS.

N. Srinivas, K. H. Yang, J. W. Collins, C. Sykes, S. B. Joseph, K. Robertson, J. J. Eron, R. Swanstrom, A. D. Kashuba; University of North Carolina at Chapel Hill, Chapel Hill, NC.

LATE-BREAKING POSTER SESSION

WEDNESDAY, MARCH 9, 2016

4:30 PM – 6:30 PM

SAPPHIRE BALLROOM

LB-001

POPULATION PK/PD MODELING OF A FIRST-IN-CLASS PORCUPINE INHIBITOR WNT974 IN ADVANCED CANCER PATIENTS TO SUPPORT DOSE SELECTION FOR PHASE I EXPANSION.

Y. Ji, J. Morawiak, A. Mignault, S. Dolan, P. Huang, C. Mahajan, A. Myers; Novartis, East Hanover, NJ.

BACKGROUND: Aberrant Wnt pathway activation is critical for initiation and maintenance of multiple tumor types. WNT974 is a first-in-class oral investigational agent that potently and selectively inhibits Porcupine, a membrane-bound O-acyltransferase required for Wnt secretion.
METHODS: A Phase I clinical trial is being conducted in advanced cancer patients to evaluate the safety, tolerability, PK, PD and antitumor activity of WNT974. Pre- and on-treatment blood, skin and tumor specimens were collected to evaluate PK/PD. Population PK modeling was performed using NONMEM 7. Exposure-response analysis was conducted for skin AXIN2 (a Wnt target gene) using S-PLUS 8.1.1. Logistic regression was conducted for dysgeusia (most frequent adverse event) using R 3.0.2. Analysis was completed in Oct. 2015 based on a full dose escalation dataset.
RESULTS: As of March 2, 2015 data cut-off, 66 patients were treated in the dose escalation at dose ranges and schedules of 5-30 mg QD; 30-45 mg QD 4 days on, 3 days off; and 5 mg BID. A 2-compartment model adequately described WNT974 PK. Exposure-response analysis of skin AXIN2 demonstrated that maintaining WNT974 Cmin,ss >2.6 ng/mL would provide >50% maximal inhibition with 95% probability. Logistic regression analysis for dysgeusia demonstrated that WNT974 Cmax,ss <118 ng/mL and AUC24h,ss <762 ng*h/mL would assure 50% probability of <25% patients to have Grade 2 dysgeusia. PK simulation revealed that 10 mg QD maintains exposure within the desired window for the majority of patients.
CONCLUSION: This first population PK/PD modeling for the first-in-class Porcupine inhibitor WNT974 estimated the therapeutic window and guided dose selection for Phase I expansion. The approach can be applied to dose selection in early oncology development.

LB-002

POPULATION PHARMACOKINETIC AND PHARMACODYNAMIC (PK/PD) ANALYSIS OF HUMANIZED MONOCLONAL ANTIBODY (MAB) TO HUMAN INTERLEUKIN-3 RECEPTOR ALPHA CHAIN (CD123).

Y. Zhang[1], J. Roberts[1], S. Dasen[1], S. Ghosh[2], B. Sedgmen[2], R. Davis[2], S. Hosback[2], B. Majcen[2], J. Sidhu[2]; [1]CSL Behring, King of Prussia, PA, [2]CSL, Parkville, Australia.

BACKGROUND: CSL362 is a humanized mAb targeting CD123+ cells and may benefit Acute Myeloid Leukemia (AML) patients by maintaining complete remission (CR) after standard induction and consolidation therapy. As part of the clinical development of CSL362, a population (pop) PK/PD analysis was performed, utilizing data from a phase 1 study in patients with CD123+ AML in CR or CRp at high risk for early relapse, with the objectives of characterizing the pop PK of CSL362 in AML patients and describing the pop PK/PD relationship using Receptor Occupancy (RO).

METHODS: The pop PK and RO datasets for 27 patients receiving up to six biweekly CSL362 intravenous (IV) infusions of 0.3, 0.75, 1, 3, or 9 mg/kg. PK samples of CSL362 serum concentrations were collected over 35 days. RO was quantified as the ratio of 7G3-IgG2a and 9F5-IgG1 of monocyte CD123 occupancy by CSL362. Pop PK models were developed separately for PK and RO. A visual predictive check (VPC) was used for model validation. The final pop PK and RO models were used to conduct the simulations for target trough concentration identification and RO outcomes for different dose regimens.
RESULTS: A Target-Mediated Drug Disposition model (TMDD) described the CSL362 PK data with good parameter precision. The identification of a target CSL362 trough concentration via simulation indicated with a CSL362 concentration of 1.9 µg/mL, 90% of patients would have 90% of CD123 receptors occupied.
CONCLUSION: The PK of CSL362 was best described by a TMDD pop PK model, with a separate PK/PD model characterizing the relationship between CSL362 concentration and free binding receptors. PK/PD simulations indicated target CSL362 trough concentration of 1.9 µg/mL and doses ≥3 mg/kg every two weeks were sufficient to achieve >90% RO in >90% of patients at steady state.

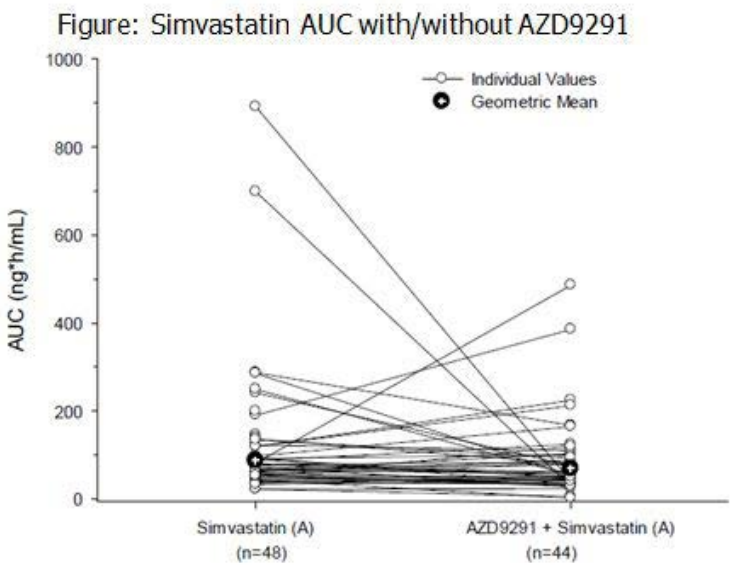
LB-003

IMPACT OF DISEASE AND TREATMENT RESPONSE IN DDI STUDIES: AZD9291 AND SIMVASTATIN IN ADVANCED NON-SMALL CELL LUNG CANCER (ANSCLC).

K. Vishwanathan[1], M. Cantarini[2], K. So[2], E. Masson[1], J. Fetterolf[3], H. Patel[4], E. Morgan[4], S. Ramalingam[4], D. Harvey[4]; [1]AstraZeneca, Waltham, MA, [2]AstraZeneca, Alderley Park, United Kingdom, [3]AstraZeneca, Gaithersburg, MD, [4]Emory University, Atlanta, GA.

BACKGROUND: AZD9291 is a potent, irreversible, T790M directed EGFR-TKI in development for aNSCLC. In a study (NCT02197234) of the potential effect of AZD9291 on simvastatin (SMV) PK, two outliers were noted.
METHODS: SMV 40mg PO was given on Day (D) 1, then AZD9291 80mg PO daily D3-34. AZD9291 was co-dosed with SMV on D31. PK was conducted on D1 and 31 for SMV and simvastatin acid (SVA) and D31 for AZD9291. Two patients (pts) had significantly higher SMV/SVA exposures on D1 (Fig). By D31, values returned to the mean.
RESULTS: At entry, 2 pts with aNSCLC had radiographic and laboratory evidence of significant liver metastases (elevated LFTs, hypoalbuminemia). High SMV/SVA D1 AUCs were likely due to substantial infiltrative cancer impairing hepatic clearance. By D31, SMV exposures had normalized, possibly due to AZD9291 treatment normalizing CYP activity via efficacy rather than influencing CYP3A4 activity via DDI. By D42, LFT resolution and >50% tumor reductions were seen. Two other pts from this site without liver metastases showed no differences in SMV exposure; other etiologies of increased exposure were ruled out.

CONCLUSION: In cancer patients with a heavy hepatic tumor burden receiving an efficacious drug, clinical efficacy may confound assessment of DDI, especially in sensitive CYP substrates.



LB-004

USABILITY TESTING A CLINICIAN-DRIVEN, EHR-EMBEDDED, BUSULFAN PHARMACOKINETIC DECISION SUPPORT TOOL (DST) DESIGNED FOR POINT-OF-CARE CLINICIANS.

S. M. Abdel-Rahman; Children's Mercy Hospitals & Clinics, Kansas City, MO.

BACKGROUND: Busulfan demonstrates a narrow therapeutic index for which clinicians employ therapeutic drug monitoring (TDM). However, operationalizing TDM can be inefficient. We developed software encoding a clinical DST that is embedded into our electronic health record (EHR) and designed to streamline the TDM process for our oncology partners. This study examined the usability, usefulness and satisfaction of providers with our DST.
METHODS: 12 content experts (CE) and 12 end-users (EU) participated in traditional usability testing. Information collected included; demographics, task success, time to complete tasks, steps to complete tasks, frequency of errors, perceived usability, and overall user satisfaction. Audio and video were captured using Morae software. All participants were enrolled with informed consent under an IRB approved protocol.
RESULTS: Participants ranged in age from 26-59 yrs, spent between 5 to >26 hr per week on a computer, and demonstrated variable proficiency with TDM. Greater than 97% of tasks were completed with no difficulty. Task time significantly decreased (65%) with repetition ($p<0.01$). On average, EU completed tasks faster than CE (0.28 vs. 0.32 min) with fewer number of clicks (144 vs. 176); however, these differences were not statistically significant. Overall satisfaction on a 7-point Likert scale was 1.6; with scores of 1.5 for system quality, 1.8 for information quality, and 1.4 for interface quality.

CONCLUSION: Participants were highly satisfied, and quickly became proficient, with our software. Our DST, designed for the non-pharmacologist, was well accepted and should afford our clinicians the ability to seamlessly transition from patient assessment, directly to pharmacokinetic modeling and simulation, and prescription order entry.

LB-005

SINGLE-DOSE PHARMACOKINETICS OF VORTIOXETINE IN SUBJECTS WITH MILD, MODERATE, OR SEVERE HEPATIC IMPAIRMENT.

G. Chen, G. G. Nomikos, J. Affinito, W. Jacobson, Z. Zhao, S. Wang, J. Xie; Takeda Development Center Americas, Inc., Deerfield, IL.

BACKGROUND: Vortioxetine is a novel antidepressant approved by FDA and EMA for the treatment of major depression. Pharmacokinetics (PK) of vortioxetine and its metabolites (Lu AA34443 and Lu AA39835) were evaluated in subjects with mild, moderate, or severe hepatic impairment and in healthy matched control (HMC) subjects in 2 open-label, parallel-group, single-dose studies.
METHODS: The first study, conducted Sep-Dec 2008, was a PK study of vortioxetine 10 mg in subjects with mild or moderate hepatic impairment and HMCs (dosing guidance provided in the label). The second study, an FDA post-marketing commitment PK study to provide further dosing guidance, was conducted Jul-Nov 2014 in subjects with severe hepatic impairment and in HMCs. All subjects received a single oral dose of vortioxetine 5 mg. Serial PK blood samples were collected up to 240 h postdose. Adverse events were monitored throughout these studies.
RESULTS: These studies enrolled 22 hepatically impaired subjects (8 mild, 8 moderate, 6 severe) and 23 HMCs. Exposure to vortioxetine was similar in subjects with mild, moderate, or severe hepatic impairment and in HMCs following a single dose of vortioxetine, with LS mean ratios of 0.91, 0.98, and 1.10, respectively, for AUC_{tlqc} and 0.86, 0.84, and 0.76 for C_{max}. No apparent differences in PK were observed for Lu AA34443 or Lu AA39835. Based on preliminary regression analysis, the PK of vortioxetine is independent of hepatic function as measured by Child-Pugh scores. Vortioxetine was well tolerated by subjects with hepatic impairment in both studies.
CONCLUSION: Mild, moderate, or severe hepatic impairment had no clinically meaningful impact on the single-dose PK of vortioxetine or its metabolites.

LB-006

MORBIDLY OBESE PATIENTS EXHIBIT AN INCREASED CYP2E1-MEDIATED OXIDATION OF ACETAMINOPHEN.

A. van Rongen[1], P. A. Valitalo[2], M. Y. Peeters[1], D. Boerma[1], F. W. Huisman[1], B. van Ramshorst[1], E. P. van Dongen[1], J. N. van den Anker[3], **C. A. Knibbe[1]**; [1]St. Antonius Hospital, Nieuwegein, Netherlands, [2]Leiden Acadamic Centre for Drug Research, Leiden University, Leiden, Netherlands, [3]Children's National Medical Center, Washington, DC.

BACKGROUND: Acetaminophen is mainly metabolized via glucuronidation and sulphation, with the minor pathway through CYP2E1 being responsible for hepatotoxicity. While in obese patients CYP2E1 activity is reported to be induced, the aim of this study was to determine the pharmacokinetics of acetaminophen and its metabolites (glucuronide, sulphate, cysteine and mercapturate) in morbidly obese and non-obese patients.
METHODS: In this prospective observational study 20 morbidly obese (median total body weight (TBW) of 140.1 kg (range 106-193.1) and BMI of 45.1 kg/m^2) and 8 non-obese patients (TBW of 69.4 kg (53.4-91.7) and BMI of 21.8 kg/m^2) received 2 grams of intravenous acetaminophen. Fifteen blood samples were collected per patient. A full validated population PK model was developed using NONMEM on September 18, 2015.

RESULTS: In morbidly obese patients, median $AUC_{0\text{-}8h}$ of acetaminophen was lower (p=0.009), while the $AUC_{0\text{-}8h}$ ratio of the glucuronide, sulphate and cysteine metabolite to acetaminophen were higher (p=0.043, 0.004 and 0.010, respectively). In the model, acetaminophen CYP2E1-mediated clearance (cysteine & mercapturate) increased with lean body weight (LBW) (population mean (RSE%) of 0.0185 L/min (15%), p<0.01). Moreover, an accelerated formation of the cysteine & mercapturate metabolites was found with increasing LBW (p<0.001). Glucuronidation clearance (0.219 L/min (5%)) and sulphation clearance (0.0646 L/min (6%)) also increased with LBW (p<0.001).
CONCLUSION: Obesity leads to lower acetaminophen concentrations and earlier and higher peak concentrations of acetaminophen-cysteine and mercapturate. While a higher dose may be anticipated to achieve adequate acetaminophen concentrations, the increased CYP2E1 mediated pathway may preclude this dose adjustment.

LB-007

PERSONALIZED MELPHALAN THERAPY FOR AUTOLOGOUS STEM CELL TRANSPLANT: G-CSF REGIMEN SIGNIFICANTLY INFLUENCES DURATION OF NEUTROPENIA.

Y. Cho, D. Sborov, J. Li, J. Wang, Y. Gao, M. Lamprecht, M. Jukich, W. Falk, L. J. Schaaf, M. Poi, C. C. Hofmeister, M. A. Phelps; The Ohio State University, Columbus, OH.

BACKGROUND: Melphalan combined with G-CSF is effective in multiple myeloma (MM) patients receiving autologous stem cell transplantation (ASCT). High inter-patient variability and individual sensitivity to melphalan cause severe toxicities, including potentially life-threatening prolonged severe neutropenia. Therefore, we aimed to personalize melphalan+G-CSF therapy to maximize efficacy and minimize prolonged neutropenia.
METHODS: Patients received melphalan followed by transplant then daily G-CSF beginning day +1 or day +7 after transplant. Plasma and peripheral blood mononuclear cells (PBMCs) were collected prior to and during melphalan treatment. Plasma melphalan was quantified using a validated LC-MS/MS assay. PBMCs were treated *ex vivo* with melphalan to measure potential biomarkers. Modeling was performed using a nonlinear mixed effects approach evaluating the impact of melphalan exposure on absolute neutrophil count (ANC). The influence of different G-CSF regimens on duration of severe neutropenia was fully analyzed in October 2015.
RESULTS: Four covariates (creatinine clearance, hematocrit, SLC7A5, fat free mass) were chosen for the final PK model. While melphalan exposure significantly impacted duration of severe neutropenia, G-CSF regimen was also a significant factor. Duration of severe neutropenia was 50.82 hours shorter (p<0.001) when G-CSF regimen was started day +1 (n=41) compared to starting day +7 (n=77).
CONCLUSION: The PK/PD model enables prediction of the ANC time course and individualized adjustment of melphalan dosing to minimize prolonged neutropenia. G-CSF regimen was found to significantly influence duration of severe neutropenia, and it was therefore incorporated into the model.

LB-008

UGT1A3*2 AFFECTS PHARMACOKINETICS OF RALIMETINIB (LY2228820 DIMESYLATE) IN CANCER PATIENTS: A RETROSPECTIVE GENETIC ANALYSIS GUIDED BY *IN VITRO* UGT PHENOTYPING ASSAYS.

Y. Guo, X. Zhang, R. Bell, D. L. Farrington, A. Kolur, M. Mohutsky, C. Pitou, P. Kulanthaivel; Eli Lilly and Company, Indianapolis, IN.

BACKGROUND: Ralimetinib, a selective inhibitor of the α and αisoforms of p38 MAPK, is an investigational agent under evaluation for cancer treatment. *In vitro* studies in human hepatocytes indicated N-glucuronidation as the major human metabolic pathway of ralimetinib. *In vitro* uridine diphosphate glucuronosyltransferase (UGT) phenotyping assays using a panel of human tissue microsomes and recombinant UGTs found UGT1A4 and UGT1A3 as major contributors to the N-glucuronidation.
METHODS: The role of clinically relevant variants of UGTs in ralimetinib PK variability was evaluated within 40 patients of a phase 1 study (NCT01393990) (N=89). Sanger sequencing was used to interrogate UGT1A4*2 and *3, UGT1A3*2 and UGT1A1*28, which revealed low frequencies of UGT1A4*2 (minor allele frequency, MAF=0.025) and UGT1A4*3 (MAF=0) in the present study.
RESULTS: In all patients (N=40) or Caucasians (N=36), UGT1A3*2 was significantly associated with ralimetinib individual apparent clearance (based on a population PK model) ($p<0.05$), with UGT1A3*2/*2 clearance being 1.7-fold relative to the non-UGT1A3*2/*2. Moreover, within a cohort of 26 patients, the dose-normalized $AUC_{0\text{-}24}$ at steady-state (cycle 1 day 14) was reduced in patients with UGT1A3*2/*2 variant compared to that of non-UGT1A3*2/*2 ($p=0.059$). Interestingly, UGT1A1*28 was also significantly associated with increased ralimetinib apparent clearance, probably due to its linkage disequilibrium with UGT1A3*2.
CONCLUSION: Collectively, our data suggest UGT1A3 as an important determinant in ralimetinib disposition. In this study, the impact of UGT1A4 variants could not be addressed due to a small sample size. This study demonstrates the utility of in vitro UGT phenotyping assays for identifying candidate genes to guide clinical genetic investigations.

LB-009

OCT1 IS A NOVEL TRANSPORTER FOR PARAQUAT AND ENHANCES ITS CYTOTOXICITY.

M. PIAO[1], X. LIANG[2], S. YEE[2], Q. Luo[1], K. M. GIACOMINI[2]; [1]Tsinghua University, Beijing, CHINA, [2]University of California San Francisco, San Francisco, CA.

BACKGROUND: Paraquat(PQ) is a herbicide, but is commonly used in developing countries to commit suicide. PQ can be transformed between its oxidative form (PQ^{2+}) and reduced form (PQ^{+}) in the body, which generates oxidative stress, thus causing toxicity. Hepatotoxicity is one of the significant morbidities associated with PQ ingestion. However, it is unclear how PQ accumulates in the liver. The goal of our study was to test the hypothesis that the hepatic organic cation transporter, OCT1, mediates the uptake of PQ.
METHODS: Uptake of PQ was measured in HEK293 cells overexpressing OCT1 (OCT1 cells) or transfected with empty vector (EV cells). PQ was converted to PQ^{+} by inclusion of sodium dithionite (SDT) (5 mM) in the uptake buffer. Cell viability of OCT1 and EV cells was measured using Promega CellTiter-Glo system after 6-hour incubation of different concentrations of PQ with SDT.
RESULTS: OCT1 transported the reduced but not the oxidized form of PQ. In the presence of SDT, PQ^{+} significantly accumulated in cells overexpressing OCT1 (15 folds higher than in EV cells) and yielded Km = 20.09±3.49 uM; Vmax = 2.87±0.10 nmol/ug protein/min. The accumulation of PQ was abolished by addition of the OCT1 inhibitor, tacrine (100 μM). In comparison to EV cells, OCT1 cells were more sensitive to PQ (IC_{50} in OCT1 cells was 2.2 μM compared with 8.4 μM in EV cells) suggesting that OCT1 plays a role in the cytotoxicity of PQ.

CONCLUSION: This is the first study to identify OCT1 as a transporter of the reduced form of PQ. Our data suggest that by mediating transmembrane influx of PQ, OCT1 may play a critical role in its hepatotoxicity. Though speculative, our data suggest that inhibitors of OCT1 may serve as potential antidotes to the hepatotoxicity associated with PQ poisoning.

LB-010

BUSULFAN EXPOSURE PREDICTS EVENT FREE SURVIVAL AND TOXICITY AFTER HEMATOPOIETIC CELL TRANSPLANTATION IN CHILDREN AND YOUNG ADULTS: A MULTICENTER RETROSPECTIVE ANALYSIS.

I. H. Bartelink[1], A. Lalmohamed[2], E. M. van Reij[2], C. C. Dvorak[1], R. M. Savic[1], J. Zwaveling[3], R. G. Bredius[3], A. C. Egberts[2], M. Bierings[2], M. Kletzel[4], P. J. Shaw[5], C. E. Nath[5], G. Hempel[6], M. Ansari[7], M. Krajinovic[8], Y. Theoret[8], M. Duval[9], R. Keizer[1], H. Bittencourt[9], M. Hassan[10], T. Guengoer[10], R. F. Wynn[11], P. Veys[12], G. Cuvelier[13], S. Marktel[14], R. Chiesa[15], M. J. Cowan[1], M. A. Slatter[16], M. Stricherz[17], C. Jennissen[17], J. R. Long-Boyle[1], J. J. Boelens[2]; [1]University of California, San Francisco, San Francisco, CA, [2]University Medical Center Utrecht, Utrecht, Netherlands, [3]Leiden University Medical Center, Leiden, Netherlands, [4]Children's Hospital of Chicago, Chicago, CA, [5]Children's Hospital at Westmead, Sydney, Australia, [6]Universitätsklinikum at Münster, Münster, Germany, [7]Hôpital des enfants (HUG), Genève, Switzerland, [8]Hôpital Sainte-Justine Montréal, Montréal, QC, Canada, [9]University of Montreal, Montréal, QC, Canada, [10]University Children`s hospital Zürich, Zürich, Switzerland, [11]The Royal Manchester Children's Hospital, Manchester, United Kingdom, [12]Great Ormond Street, Hospital for Children London, London, United Kingdom, [13]The CancerCare Manitoba, Winnipeg, Winnipeg, QC, Canada, [14]San Raffaele Scientific Institute, Milan, Italy, [15]IRCCS San Raffaele Scientific Institute, Milan, Italy, [16]The Institute of Cellular Medicine, Newcastle University, Newcastle, United Kingdom, [17]University of Minnesota, Masonic Children's Hospital, Minnesota, MN.

BACKGROUND: Intravenous-busulfan (IV-Bu) combined with therapeutic drug monitoring to guide dosing improves outcomes after hematopoietic cell transplantation (HCT). The best method to estimate Bu exposure and optimal exposure in children/young adults remains unclear. We therefore evaluated three approaches to estimate IV-Bu exposure and associated Bu-AUC with clinical outcomes in children/young adults undergoing HCT.

METHODS: Patients (0.1-30.4 years) who had received an IV-Bu conditioning regimen from 15 centers were included. Cumulative AUC was calculated by numerical integration using NONMEM (AUC_{NONMEM}), non-compartmental analysis ($AUC_{0\text{-}infinity}$ and $AUC_{0\text{-}tau}$) and by individual centers using a variety of approaches (AUC_{center}). Primary outcome event-free survival (EFS) and other outcomes were modeled using propensity score adjusted cox hazard, Weibull, and Fine-Gray competing risk regression models.

RESULTS: 706 patients were included (45% malignant,55% non-malignant). Median Bu AUC_{NONMEM} was 74.4 mg*h/L (CI95% 31.1-104.6 mg*h/L). Median AUC_{NONMEM} correlated poorly with AUC_{center} ($R^2 = 0.254$). Patients with optimal IV-Bu AUC of 78-101 mg*h/L showed 81% EFS at 2 years compared to 66.1% in low (<78 mg*h/L) and 49.5% in the high (>101 mg*h/L) Bu AUC group (P=0.024). Graft-failure/relapse occurred more frequently in the low AUC group (HR=1.75 P<0.001). Acute toxicity (VOD & aGvHD), chronic graft versus-host disease and transplantation related mortality was higher in the high AUC group (HR 1.69, 2.99 and 1.30), independent of indication.

CONCLUSION: These results demonstrate that improved clinical outcomes may be achieved by targeting Bu-AUC to 78-101mg*h/L using a validated pharmacokinetic-model for all indications.

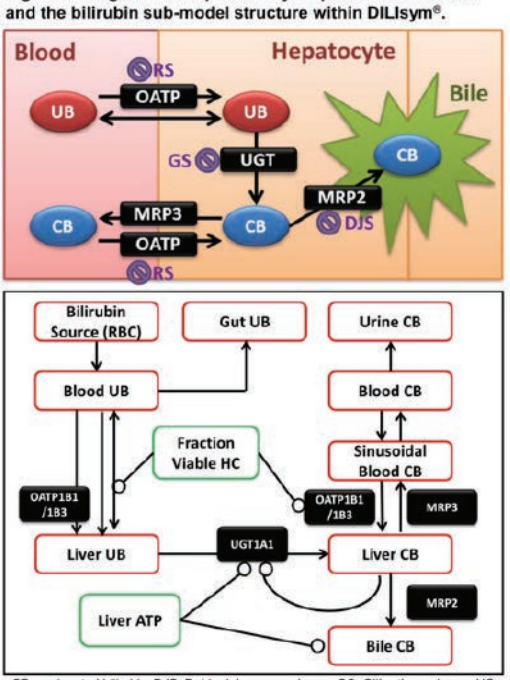
LB-011

MECHANISTIC MODELING PREDICTS DRUG-INDUCED HYPERBILIRUBINEMIA THAT INVOLVES INHIBITION OF ENZYMES AND TRANSPORTERS.

K. Yang, J. L. Woodhead, P. B. Watkins, S. Q. Siler, B. A. Howell; The Hamner-UNC Institute for Drug Safety Sciences, Research Triangle Park, NC.

BACKGROUND: Elevated serum ALT and bilirubin indicates high risk of fatal drug-induced liver injury. However, drugs also can increase serum bilirubin in the absence of hepatic injury by inhibiting enzymes/transporters. The bilirubin sub-model within DILIsym® (the product of a public-private partnership involving scientists from industry, academia, and the FDA) was updated to predict drug-induced hyperbilirubinemia (HB).
METHODS: The bilirubin sub-model was optimized to bilirubin levels in patients with inherited disorders of bilirubin disposition: Rotor syndrome (RS), Gilbert syndrome (GS), and Dubin-Johnson syndrome (DJS) (Fig 1; completed on Oct 15). Indinavir (INV)-mediated HB was simulated using an INV PBPK model and its inhibition constants for UGT1A1 (6.8 μM) and OATP1B1 (4.1 μM).
RESULTS: Simulations recapitulated conjugated HB in RS/DJS and unconjugated HB in GS [serum total bilirubin (TB): 2-7, 5-12, and 2-13 mg/dL, respectively]. After administration of 800 mg INV TID for 1 month, simulations predicted unconjugated HB (pre- and post-treatment serum TB: 0.55 and 0.70 mg/dL), which is consistent with reported clinical data (pre- and post-treatment serum TB: 0.5±0.28 and 0.84±0.36 mg/dL).
CONCLUSION: Mechanistic modeling of bilirubin can be used to predict drug-induced HB, which is not related to liver injury.

Figure 1. Diagrams of hepatobiliary disposition of bilirubin and the bilirubin sub-model structure within DILIsym®.



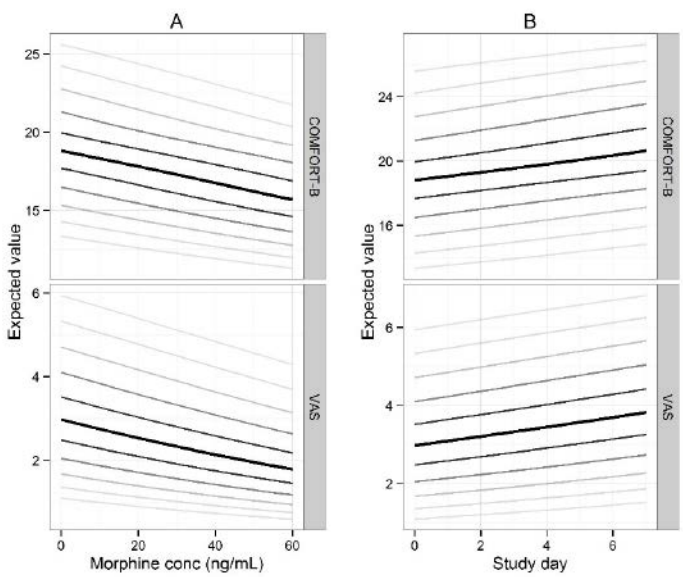
CB, conjugated bilirubin; DJS, Dubin-Johnson syndrome; GS, Gilbert's syndrome; HC, hepatocytes; MRP, multidrug resistance-associated protein; OATP, organic anion transporting polypeptide; RBC, red blood cell; RS, Rotor syndrome; UB, unconjugated bilirubin; UGT, UDP glucuronosyltransferase.

LB-012

MORPHINE PHARMACODYNAMICS IN MECHANICALLY VENTILATED PRETERM NEONATES.

P. A. Valitalo[1], E. H. Krekels[1], M. van Dijk[2], S. H. Simons[2], D. Tibboel[2], C. A. Knibbe[3];
[1]Leiden University, Leiden, Netherlands, [2]Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands, [3]St Antonius Hospital, Nieuwegein, Netherlands.

BACKGROUND: To date, data about morphine efficacy in newborns are ambiguous. The aim of this work was to quantify morphine pharmacodynamics in mechanically ventilated preterm neonates.
METHODS: Pain scores and morphine concentration-time data were obtained from 140 mechanically ventilated preterms who participated in an RCT comparing morphine and placebo for the treatment of pain caused by endotracheal and nasal suctioning. An item response theory model was developed to quantify pain as a latent variable, upon which the effects of morphine concentrations and demographic covariates were tested. The model was validated in Oct 2015.
RESULTS: Morphine was found to reduce pain ($p<0.001$), and time after study start was associated with increased pain ($p<0.001$). Figure 1 shows median pain (bold lines) and representative individual estimates within 95% CI (thin lines) expressed as COMFORT-B or VAS over morphine concentration and time after surgery in days.
CONCLUSION: Morphine causes a small concentration-dependent reduction of pain in preterm infants undergoing mechanical ventilation. Repeated suctioning may cause abrasion and thus lead to increasing pain when performed multiple times.



LB-013

GENOTYPED-GUIDED ROSUVASTATIN DOSING MITIGATES INTERETHNIC DRUG EXPOSURE DIFFERENCE BETWEEN ASIANS AND WHITES.

H. Wu, N. Hristeva, L. Benet; University of California, San Francisco, San Francisco, CA.

BACKGROUND: The US Food and Drug Administration approved label for rosuvastatin states "Pharmacokinetic studies have demonstrated an approximate 2-fold increase in median exposure to rosuvastatin in Asian subjects when compared to Caucasian controls" and recommends dosage adjustments in Asian patients. Prior studies have demonstrated that interethnic variation in rosuvastatin drug exposure cannot be explained by *SLCO1B1* genotype alone. Here we show that the 2-fold difference in rosuvastatin exposure is mitigated in Asian and White subjects controlled for *SLCO1B1* and *ABCG2* wildtype, and that both genes should be considered in rosuvastatin dosing rather than ethnicity.
METHODS: Asian and White (8 each) healthy volunteers were enrolled in a randomized, 2 period cross over study, where they received: 1) single oral 20mg rosuvastain and 2) 600mg rifampin I.V infusion for 30 min followed by single oral 20mg rosuvastatin. Rosuvastatin plasma samples, up to 48 hr, were measured by a validated HPLC-tandem mass spectrometry method.
RESULTS: For rosuvastatin alone, $AUC_{0\text{-}48}$ were 92.4(±34.0) and 83.4(±29.9) ng/mL*hr and Cmax were 10.0(±3.8) and 7.3(±2.7) ng/mL for Asians and Whites, respectively. Rosuvastatin $AUC_{0\text{-}48}$ in the presence of rifampin were 298(±97) and 285(±71) ng/mL*hr and Cmax were 78.1(±39.4)and 60.0(±24.5) ng/mL.
CONCLUSION: Our study shows that *SLCO1B1* and *ABCG2* are important for rosuvastatin disposition. By controlling for wildtype for both transporters, interethnic differences in rosuvastatin drug exposure were mitigated. We believe that the 39.6% of Asians carrying wildtype *SLCO1B1* and *ABCG2* would be under dosed based on the FDA label recommendations and they should receive the same dose as Whites. Our study suggests that both *SLCO1B1* and *ABCG2* polymorphisms should be considered before rosuvastatin dosing.

LB-014

A SEMI-PHYSIOLOGICALLY BASED PHARMACOKINETIC MODEL FOR MIDAZOLAM AND 1-OH-MIDAZOLAM IN MORBIDLY OBESE AND WEIGHT LOSS SURGERY PATIENTS.

M. J. Brill[1], P. A. Välitalo[2], A. S. Darwich[3], B. van Ramshorst[1], E. P. van Dongen[1], A. Rostami-Hodjegan[3], M. Danhof[2], **C. A. Knibbe[1]**; [1]St. Antonius Hospital, Nieuwegein, Netherlands, [2]Leiden Academic Centre for Drug Research, Leiden, Netherlands, [3]University of Manchester, Manchester, United Kingdom.

BACKGROUND: Morbid obesity and weight loss surgery may affect the activity of intestinal and hepatic CYP3A. This study aimed to describe the pharmacokinetics of midazolam and its CYP3A mediated metabolite 1-OH-midazolam in morbidly obese patients receiving oral and intravenous midazolam before and 1 year after weight loss surgery using semi-physiologically based pharmacokinetic modeling (semi-PBPK), thereby providing insight into the influence of weight loss surgery on CYP3A activity in both the gut wall and liver.

METHODS: Midazolam and 1-OH-midazolam concentrations were simultaneously analyzed using population pharmacokinetic modeling in NONMEM 7.2 (model validated on Sept. 8 2015). Data were from a published study [Brill et al. Pharm Res DOI 0.1007/s11095-015-1752-9] in which 20 morbidly obese patients undergoing weight loss surgery participated in a prospective observational study and of which 18 patients returned 1 year after surgery. At both occasions, patients received 7.5 mg oral and 5 mg intravenous midazolam separated by 160 ± 48 min. Per patient and occasion, a mean of 22 blood samples were collected.
RESULTS: In a semi-PBPK model in which different blood flow scenarios were evaluated, intrinsic hepatic clearance of midazolam ($CL_{int\,H}$) was 1.52 (95% CI 1.40 - 1.64) times higher compared to morbidly obese patients before surgery ($p<0.01$). Midazolam gut wall clearance ($CL_{int\,G}$) was slightly lower in patients after surgery ($p>0.05$), with low values for both groups.
CONCLUSION: The results of the semi-PBPK model suggest that in patients after weight loss surgery CYP3A hepatic metabolizing capacity seems to recover compared to morbidly obese patients, while CYP3A mediated intrinsic gut wall clearance was low for both populations and showed large inter-individual variability.

LB-015

EFFECT OF ABCB1 HAPLOTYPE ON TACROLIMUS DISPOSITION IN RENAL RECIPIENTS DEPENDS ON CYP3A5 AND CYP3A4 GENOTYPE.

T. Vanhove[1], P. Annaert[2], D. Lambrechts[2], D. R. Kuypers[1]; [1]University Hospitals Leuven, Leuven, Belgium, [2]University of Leuven, Leuven, Belgium.

BACKGROUND: Several clinical and genetic determinants of tacrolimus disposition have been identified. Tacrolimus exposure is decreased in patients possessing the *CYP3A5*1* allele (CYP3A5 expressers) and increased in patients possessing the *CYP3A4*22* polymorphism. The effect of polymorphisms in other genes such as *ABCB1*, *PPARA* and *NR1I2* has varied between studies.
METHODS: A linear mixed model was constructed for tacrolimus dose-corrected trough level (C/D ratio) at months 3, 12 and 24 after transplantation in a retrospective cohort of 766 predominantly causasian renal recipients. All patients were genotyped for 32 single nucleotide polymorphisms with a proven or possible relevance to tacrolimus disposition (genotyping complete 10/2015; analysis 11/01/2015). *ABCB1*, *MRP2*, *OATP1B1*, *COMT*, *FMO*, *PPARA* and *APOA5* were analyzed as (functional) haplotype groups.
RESULTS: Predictors of C/D ratio were presence of the *CYP3A5*1* allele (n=118), hematocrit, age, presence of *CYP3A4*22* (n=83), use of a CYP3A4 inhibitor or inducer, serum ALT and albumin, eGFR, tacrolimus formulation (OD vs. BID), *ABCB1* haplotype and time after transplantation. The final model explained 42.9% of interindividual variability in C/D. *ABCB1* haplotype had no effect in CYP3A5 expressers. In *CYP3A4* wild type patients, estimated C/D ratio was 1.46 (1.14-1.87), 1.47 (1.15-1.87) and 1.62 (1.28-2.07) for ABCB1 CGC-CGC, CGC-TTT and TTT-TTT diplotypes, respectively, compared with 1.57 (1.13-2.17), 1.83 (1.35-2.49) and 2.55 (1.85-3.52) in *CYP3A4*22* carriers ($p=0.017$).
CONCLUSION: The effect of loss-of-function haplotypes of *ABCB1* on tacrolimus disposition was strongly accentuated in *CYP3A4*22* carriers but non-existent in CYP3A5 expressers, likely because high CYP3A activity reduces the importance of the ABCB1 transporter.

LB-016

ALPHA$_{2A}$ ADRENERGIC RECEPTOR GENETIC VARIATION CONTRIBUTES TO HYPERGLYCEMIA AFTER MYOCARDIAL INFARCTION.

A. Adefurin[1], L. Darghosian[1], C. Okafor[1], V. Kawai[1], C. Li[2], A. Shah[1], W. Wei[1], D. Kurnik[1], C. Stein[1]; [1]Vanderbilt University Medical center, Nashville, TN, [2]Case Western Reserve University, Cleveland, OH.

BACKGROUND: Acute myocardial infarction (AMI) is frequently associated with transient hyperglycemia even in patients without pre-existing diabetes. Acute stress can lead to increased blood glucose through the effect of catecholamines on alpha2A-adrenergic receptors (α2A-ARs) present in pancreatic islet αcells. Variation in the gene (*ADRA2A*) that encodes the α2A-AR affects insulin release and glucose control and may play a particularly important role during times of stress.
METHODS: We performed a retrospective cohort study using de-identified electronic medical records linked to a DNA repository in 521 Caucasians and 55 African-American non-diabetic patients with AMI. We examined the association between admission blood glucose concentrations and ten selected *ADRA2A* SNPs in Caucasians.
RESULTS: Three *ADRA2A* SNPS were associated with stress-induced hyperglycemia in Caucasians. Individuals homozygous for the rs10885122 variant (n=9) had a 23% lower admission glucose (geometric mean [95% CI], 99 [83 - 118] mg/dl) compared with non-carriers (121 [118-125] mg/dl; n=401; P = 0.001). Admission glucose was 14% higher in rs1800544 variant homozygotes (134 [119-150] mg/dl; n=36) compared to non-carriers (118 [115-121] mg/dl; n=290, P=0.046). Furthermore, homozygotes of the rs553668 variant (n = 13) had a 13% higher glucose (133 [110-160] mg/dl) compared to non-carriers (118 [115-122] mg/dl; n=366; P = 0.056). Haplotypes including these *ADRA2A* SNPs were associated with higher admission glucose levels.
CONCLUSIONS: Three *ADRA2A* genetic variants are associated with blood glucose and stress-induced hyperglycemia after AMI in Caucasians.

LB-017

EFFECTS OF CYP2C19 GENETIC POLYMORPHISMS ON THE PHARMACOKINETICS/PHARMACODYNAMICS OF OMEPRAZOLE IN HEALTHY KOREAN.

Y. HYUN[1], J. Lee[1], Y. Kim[1], **S. Ryu**[1], I. Jang[2], H. Na[1], J. Kim[1]; [1]NIFDS, Ceongju City, Korea, Republic of Korea, [2]Seoul National University College of Medicine and Hospital, Seoul City, Korea, Republic of Korea.

BACKGROUND: Omeprazole, a proton pump inhibitor, is used to treat acid-realated diseases. It is metabolized by the CYP isoenzymes into 5-hydroxy omeprazole and omeprazole sulfone. The genetic polymorphism of CYP2C19 enzyme is known to affect the pharmacokinetic(PK) and pharmacodynamic(PD) characteristics of omepraozle, and thereby to affect the efficacy of it. This study is to compare the PK and PD of omeprazole between different CYP2C19 genotype groups in healthy Korean.
METHODS: An open label, multiple dose clinical study was performed. A total of 24 *H. pylori* sero-negative healthy Korean subjects were enrolled according to 3 genotypes by CYP2C19 polymorphism (*1/*1: EMs, *1/*2 and *1/*3: IMs, *2/*2, *2/*3 and *3/*3: PMs). Subjects received multiple oral dose of 20 mg omeprazole for 8 days. The plasma levels of omeprazole and its two metabolites were determined using LC-MS/MS and PK parameters were calculated by noncompartmental method. Intragastric pH was monitored and serum concentration of gastrin were calculated to evaluate the PD of omepraozle.

RESULTS: After multiple administrations, the systemic exposure of omeprazole was 3668±929, 2087±1045 and 1715±1199 in PM, IM and EM respectively. Geometric mean ratio and its 90% confidence intervals of metabolic ratio ($AUC_{0\text{-}12h,\ 5\text{-hydroxy omeprazole}}$/ $_{omeprazole}$) was 2.58 (1.41-4.72) for IMs to PMs and 5.59 (3.06-10.23) for EMs to PMs. The percentage of time with intragastric pH > 4 were significantly higher in PM group than in other groups (P = 0.001).
CONCLUSION: These finding indicate the systemic exposure of omeprazole and its pharmacologic effect is increased by CYP2C19 loss of function polymorphism. The result implies that the dose adjustment between different genotype groups in Korean may be necessary to show same efficacy of omeprazole.

LB-018

ALLOMETRIC SCALING IN PEDIATRICS: WHEN DOES THE MAGIC OF 0.75 FADE?

E. A. Calvier[1], E. H. Krekels[1], P. A. Välitalo[1], A. Rostami-Hodjegan[2], D. Tibboel[3], M. Danhof[1], C. A. Knibbe[1]; [1]Division of pharmacology, Leiden Academic Centre for Drug Research, Leiden University, Leiden, Netherlands, [2]Manchester Pharmacy School, University of Manchester, Manchester, United Kingdom, [3]Intensive Care and Department of Pediatric Surgery, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands.

BACKGROUND: Allometric scaling (AS) is frequently used to scale size-related changes in plasma clearance (CLp) from adults to children, using bodyweight normalized to an adult value and raised to the power of 0.75. A systematic assessment of its general applicability is however lacking and therefore undertaken in this study for drugs cleared through hepatic metabolism or glomerular filtration (GF).
METHODS: A physiologically-based pharmacokinetic (PBPK) simulation workflow was developed in R. In one scenario, only size related changes in liver weight, hepatic blood flow and GF were included in simulations of adult and pediatric 'true' CLp. Based on these 'true' CLp, an allometric exponent was estimated. In a second scenario, maturation in intrinsic clearance (CLint) with values ranging between 0.02% and 200% of the adult value, maturation in plasma protein concentration and in hematocrit were also included in the simulations. In both scenarios, the prediction error (PE) of AS-based pediatric CLp predictions compared to the 'true' PBPK-based CLp was assessed for a total of 6310 different hypothetical drugs (final results Oct 2015).
RESULTS: In the first scenario, PEs were close to 0% for children older than 5 years while for younger children, the PE increased with decreasing age, reaching up to 253% in neonates. The estimated allometric exponent ranged from 0.45 to 1.17, increased with decreasing age, and varied with drug properties. In the second scenario, AS led to systematic accurate CLp predictions above 5 years of age both for GF cleared drugs and for hepatically cleared drugs with CLint around maturity.
CONCLUSION: Using PBPK principles, AS was found to lead to biased CLp predictions in children younger than 5 years, where the PE is sensitive to the allometric exponent. This applies even to scenarios where only size-related changes apply.

LB-019

INFLAMMATION AND ORGAN FAILURE AFFECT MIDAZOLAM CLEARANCE IN CRITICALLY ILL CHILDREN.

J. M. Brussee[1], N. J. Vet[2], M. de Hoog[2], M. G. Mooij[2], C. W. Verlaat[3], I. S. Jerchel[2], R. H. van Schaik[2], B. C. Koch[2], D. Tibboel[2], C. A. Knibbe[1], S. N. de Wildt[2]; [1]Division of Pharmacology, Leiden Academic Centre for Drug Research (LACDR), Universiteit Leiden, Leiden, Netherlands, [2]Erasmus MC - Sophia Children's Hospital, Rotterdam, Netherlands, [3]Intensive Care, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands.

BACKGROUND: Studies suggest that inflammation and critical illness may alter the pharmacokinetics of midazolam. However, the magnitude of this impact is unknown. Our aim is to study the effect of inflammation and organ failure on midazolam clearance in critically ill children, using population pharmacokinetic modeling.
METHODS: A total of 83 critically ill children (median age 5 months (range 1 day-17 years), n=523 samples) receiving intravenous midazolam for continuous sedation during mechanical ventilation were included. Cytokines (IL-6, TNF-a) and C-reactive protein (CRP) were used as markers for inflammation. Organ dysfunction scores (PELOD, PRISM II, PIM2), as well as number of failing organs were markers for severity of organ failure. A population pharmacokinetic model for midazolam was recently (October 2015) developed using NONMEM 7.3. Body weight, age, inflammatory markers and severity of organ failure were considered as potential covariates.
RESULTS: In a two-compartmental PK model, body weight was found as most significant covariate for clearance and volume of distribution. Moreover, both CRP and organ failure were significantly associated with clearance ($p<0.01$), explaining both inter-individual and inter-occasional variability. With increasing CRP concentrations from 10 to 300 mg/L, clearance decreased with 65% and with an increasing number of organ failures from 1 to 3 clearance decreased with 35%.
CONCLUSION: Midazolam clearance is significantly reduced by inflammation and organ failure in critically ill children. Both CRP concentration and organ failure should be considered when dosing midazolam and potentially other CYP3A substrates in critically ill children.

LB-020

A BIG DATA APPROACH IDENTIFIES NICLOSAMIDE ETHANOLAMINE AS A POTENTIAL THERAPEUTIC FOR HEPATOCELLULAR CARCINOMA.

B. Chen[1], W. Wei[2], L. Ma[2], M. Chua[2], A. Butte[1], S. So[2]; [1]UCSF, San Francisco, CA, [2]Stanford University, Stanford, CA.

BACKGROUND: The pilot projects in molecularly characterizing cancer patient samples, cancer cell lines, and cellular drug responses have led to the generation of multi-layer big databases such as The Cancer Genome Atlas (TCGA), the Cancer Cell Line Encyclopedia (CCLE), and the Library of Integrated Network-Based Cellular Signatures (LINCS). Effectively translating these data points into actionable therapeutics becomes an exciting opportunity in cancer drug discovery. We leveraged these data to identify drug candidates for Hepatocellular carcinoma (HCC), one common deadly cancer.
METHODS: We first downloaded RNA-Seq profiles of 200 HCC tumors and 50 adjacent non-tumors from TCGA and identified HCC tumors that can be appropriately modeled by HCC cell lines using CCLE data. We created one HCC gene expression signature by comparing tumors and non-tumors, and validated it using 1624 patient samples from five independent studies. We identified drug candidates that can reverse the HCC disease gene expression from LINCS and Connectivity Map.

RESULTS: We identified niclosamide as the top candidate for HCC and demonstrated that niclosamide and niclosamide ethanolamine (NEN, a water soluble niclosamide salt) are equally effective at inhibiting the proliferation of HCC cells *in vitro* (IC50s ranging from 0.51 to 1.77 uM). NEN decreased the growth of three PDX models after oral administration (1,5000 ppm in food) for 4-6 weeks ($P<0.05$). Expression profiling demonstrated that niclosamide and NEN induced similar gene expression changes in HepG2 cells and in PDX models, and that both compounds significantly reversed HCC gene expression *in vitro* and *in vivo* ($P<1E-4$).
CONCLUSION: We successfully used a big data approach to identify niclosamide and its salt NEN as potential therapeutics for the treatment of HCC.

LB-021

PHARMACOGENOMIC VARIATION IN A LONG NON-CODING RNA AFFECTS AROMATASE INHIBITOR EFFICACY IN EARLY BREAST CANCER.

F. Xie[1], J. N. Ingle[2], M. J. Ellis[3], P. E. Goss[4], L. E. Shepherd[5], J. Chapman[5], B. E. Chen[5], M. Kubo[6], Y. Furukawa[6], V. Stearns[7], K. I. Pritchard[8], P. Barman[9], E. E. Carlson[9], M. P. Goetz[2], R. M. Weinshilboum[1], K. R. Kalari[9], L. Wang[1]; [1]Division of Clinical Pharmacology, Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic, Rochester, MN, [2]Division of Medical Oncology, Mayo Clinic, Rochester, MN, [3]Baylor Breast Center, Houston, TX, [4]Massachusetts General Hospital Cancer Center, Harvard University, Boston, MA, [5]NCIC Clinical Trials Group, Kingston, ON, Canada, [6]RIKEN Center for Integrative Medical Science, Tokyo, JAPAN, [7]Johns Hopkins School of Medicine, Baltimore, MD, [8]Sunnybrook Odette Regional Cancer Centre, University of Toronto, Toronto, ON, Canada, [9]Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, MN.

BACKGROUND: Aromatase inhibitors (AIs) are used for adjuvant endocrine therapy of early breast cancer in postmenopausal women. We used a GWAS to identify germline variants associated with breast cancer recurrence in women treated with anastrozole or exemestane in the MA.27 trial.
METHODS: The GWAS used breast cancer free interval as a phenotype, followed by functional genomic studies using ChIP, cell proliferation, colony formation and Western blot assays with breast cancer cell lines.
RESULTS: 4,665 patients, 254 having recurrence, were included in the GWAS. SNPs with the lowest p-values (6.0E-07) were located on chromosome 8 in or near FLJ39080, which encodes a longnon-coding RNA (lncRNA). FLJ39080 is expressed in many estrogen receptor positive (ER+) breast cancer cell lines and its expression is correlated with ER expression in TCGA breast cancer data. Two SNPs (rs4476990 and rs3802201) were in or near estrogen response elements. Functional genomic studies in lymphoblastoid cell lines showed that FLJ39080 expression was induced by estradiol and by AIs in a SNP-dependent fashion. Variant SNPs displayed increased binding to ER by ChIP assay. Knockdown (KD) of FLJ39080 in ER+ breast cancer cell lines decreased ER at both mRNA and protein levels. FLJ39080 regulation of FOXO3, an ER transcription factor, and regulation of ER proteasome-mediated degradation were identified as possible mechanisms for these effects on the ER. KD of FLJ39080 also reduced cell proliferation and colony formation, while overexpression increased both.
CONCLUSION: We have identified SNPs associated with risk for ER+ breast cancer recurrence in women treated with AIs. These SNPs were associated with the expression of a lncRNA that regulated ER levels as a possible mechanism for altering response to AI therapy.

LB-022

THE P-GLYCOPROTEIN PROBE FEXOFENADINE DOES NOT PREDICT TACROLIMUS DISPOSITION IN RENAL RECIPIENTS.

T. Vanhove[1], P. Annaert[2], D. R. Kuypers[1]; [1]University Hospitals Leuven, Leuven, Belgium, [2]University of Leuven, Leuven, Belgium.

BACKGROUND: Disposition of tacrolimus (Tac) can be accurately predicted in renal recipients by a combination of *CYP3A5* genotype, *in vivo* CYP3A4 activity assessed by apparent oral midazolam clearance (MDZ Cl/F) and hematocrit. Because Tac is a dual substrate for CYP3A and P-glycoprotein (P-gp, ABCB1), we explored whether quantifying P-gp activity using the probe drug fexofenadine (FEX) could further refine prediction of tacrolimus disposition.
METHODS: A cohort of 70 renal recipients > 1 year after transplantation underwent simultaneous 8-hour pharmacokinetic profiles for Tac, MDZ and FEX (LC-MS quantifications completed 10/2015; analysis 11/01/2015). Patients were genotyped for 32 polymorphisms in genes relevant to Tac or FEX disposition including *CYP3A5, CYP3A4, ABCB1, POR, COMT, FMO, PPARA, APOA5, MRP2, SIM1, GAN, OATP2B1, -1B1* and *-1B3*.
RESULTS: FEX Cl/F0-24 did not correlate with Tac Cl/F0-24 (correlation coefficient 0.057, p=0.642). In CYP3A5 non-expressers (n=54), independent predictors of Tac Cl/F0-24 were MDZ Cl/F0-inf, hematocrit and the *NR1I2 8055C>T* polymorphism (semipartial R^2 0.368, 0.153 and 0.063, respectively; p<0.01 for all), which together explained 58.4% of interpatient variability in Tac Cl/F0-24. In CYP3A5 expressers (n=16), no predictors of Tac Cl/F0-24 were identified. FEX Cl/F0-24 was not predicted by any genetic polymorphism.
CONCLUSION: The probe drug FEX did not predict tacrolimus disposition in renal recipients, which could be related to intrinsic limitations of the probe's specificity for P-gp and/or lack of a significant effect of variability in P-gp activity on interindividual differences in tacrolimus disposition. In renal recipients, none of the previously described genetic polymorphisms affecting FEX disposition could be confirmed.

LB-023

UNCOVERING DRUG INTERACTIONS VIA DATA SCIENCE: CEFTRIAXONE AND LANSOPRAZOLE ARE ASSOCIATED WITH ACQUIRED LONG QT SYNDROME.

N. P. Tatonetti, K. J. Sampson, R. Kass, T. Lorberbaum, J. Chang, R. Woosley; Columbia University, New York, NY.

BACKGROUND: Torsades de Pointes is a dangerous ventricular tachycardia that occurs as an adverse effect of over 40 medications that prolong the QT interval. Especially concerning is the potential for unexpected QT prolonging drug interactions (QT-DDIs). Despite FDA requirements, QT-DDIs can go undiscovered for years. Large clinical databases, such as electronic health records, represent an opportunity to rapidly detect QT-DDIs and save lives. Analyses of these data are complicated by biases and confounding effects.
METHODS: We used integrative statistical analysis to mine 4 million adverse event reports and 300,000 patient medical records for potential QT-DDIs. We used laboratory patch-clamp experiments of cells stably expressing hERG channels to validate our top prediction.

RESULTS: After multiplicity correction and confounder analysis we identified 26 unexpected interactions. The strongest signal was between ceftriaxone and lansoprazole. Patients on this combination have QTc intervals 15ms longer than patients on either drug alone and are 1.5X more likely to have a dangerously prolonged QTc. In the lab, we found no significant hERG block for either drug alone. However, in combination these drugs caused a dose-dependent hERG block of up to 58% ($p<0.001$).
CONCLUSION: Co-medication with ceftriaxone and lansoprazole is associated with acquired LQTS in clinical records, and corroborated by experiments. We discovered this interaction through data mining of millions of patient health records and validated using laboratory experiments. Our study represents the first step toward a rapid and comprehensive evaluation strategy of QT-DDIs.

LB-024

INVESTIGATING THE IMPACT OF THE CYP2C19 ULTRARAPID METABOLIZER PHENOTYPE ON VORICONAZOLE EXPOSURE IN PATIENTS WITH INVASIVE FUNGAL INFECTIONS.

I. S. Hamadeh, K. P. Klinker, S. J. Borgert, A. M. Richards, W. Li, M. Ramos, N. Mangal, J. W. Hiemenz, S. Schmidt, C. A. Peloquin, L. H. Cavallari, J. A. Johnson; University of Florida, Gainesville, FL.

BACKGROUND: Voriconazole is a first line agent for treatment of invasive fungal infections (IFIs). Approximately 40% of patients fail to achieve therapeutic trough concentrations (2-5.5mg/L) with standard weight-based dosing, placing them at increased risk for treatment failure that can be life threatening. We sought to test association between CYP2C19 ultrarapid metabolizer (UM) phenotype (defined by *CYP2C19* genotype) and subtherapeutic voriconazole plasma concentrations (Cp).
METHODS: Adult patients receiving weight-based voriconazole for treatment of IFIs were genotyped for *CYP2C19*2, *3,* and **17* polymorphisms. Steady state trough Cp, measured on days 5-7, and prevalence of subtherapeutic trough Cp (< 2 mg/L) were compared between patients with the **1/*17* or **17/*17* genotype (UMs) versus other genotypes. Logistic regression, adjusting for proton pump inhibitor use and age, was performed to estimate odds of subtherapeutic Cp. Analysis was performed after September 3, 2015 when the study reached its target accrual.
RESULTS: A total of 62 patients were included (mean age: 53±16 years, 35% UMs). Mean steady state trough Cp was significantly lower in UMs vs other CYP2C19 phenotypes (2.86±2.03 vs. 4.07±2.03, p=0.04). UMs had a higher prevalence of subtherapeutic trough Cp (50% vs. 18.9%, p=0.02) and increased odds of subtherapeutic Cp on regression analysis (OR: 3.8, 95%:1.15-12.52, p=0.02) compared to patients with other CYP2C19 phenotypes.
CONCLUSION: Our findings indicate that CYP2C19 UMs are more likely to have a subtherapeutic concentration with weight-based voriconazole dosing. These results corroborate previous findings in younger patients, and support the potential clinical utility of *CYP2C19* genotype-guided voriconazole therapy to avoid subtherapeutic dosing in UMs.

LB-025

PHARMACOKINETICS AND RENAL CLEARANCE OF BETA-HYDROXY-BETA-METHYLBUTYRATE IN HEALTHY ADULTS.

M. W. Linakis, S. F. Cook, J. E. Rower, D. E. Rollins, C. M. Sherwin, D. G. Wilkins; University of Utah, Salt Lake City, UT.

BACKGROUND: αhydroxy-αmethylbutyrate (HMB) is produced endogenously at low levels via metabolism from leucine. HMB supplementation has shown utility in treatment of AIDS and cancer cachexia, but little is known about its pharmacokinetics (PK). The purpose of this study was to describe the PK profile of HMB.
METHODS: The entirety of this PK dataset (plasma/urine concentrations) was obtained and analyzed on 11/11/15 after IRB and administrative approval had been granted. Eight healthy adult subjects received a 1g oral dose of HMB in the form of calcium-HMB capsules. Plasma was collected prior to HMB administration to establish a baseline HMB concentration, and at multiple times up to 6 h post-dose. All urine voided from 0-4 h was also analyzed. Non-compartmental analysis of plasma and urine concentrations (determined by gas chromatography/mass spectrometry) was performed using Phoenix WinNonlin v. 6.3.
RESULTS: Baseline HMB plasma concentrations were less than the lower limit of quantification in all subjects. Mean ± SD $AUC_{0\text{-}Last}$ was 118.1 ± 36.6 h*mg/L with $t_{1/2}$ of 2.6 ± 0.8 h and T_{max} of 1.9 ± 0.4 h. There was a non-significant tendency toward a longer $t_{1/2}$ in men (mean 3.1 h, n = 5) than in women (1.9 h, n = 3; p = 0.06, t-test). Mean renal clearance was 1.1 ± 0.7 L/h compared to an overall apparent clearance of 7.6 ± 4.7 L/h.
CONCLUSIONS: Half-life and T_{max} values were similar to those previously described in literature. This is the first study to describe average renal clearance of HMB. Relatively high variability of several PK parameters was shown. Future research will focus on compartmental modeling of available data and elucidation of covariate effects on HMB PK that may help explain this variability.

LB-026

RAPID SUBLINGUAL ABSORPTION OF CYCLOBENZAPRINE (CBP) WITH BASIFYING AGENTS: PROSPECT FOR BEDTIME TREATMENT OF FIBROMYALGIA SYNDROME (FM).

B. Daugherty[1], L. Gershell[1], N. Ceppi Monti[2], V. Panzeri[2], R. Marelli[2], E. Magnocavallo[2], G. Reiner[2], S. Lederman[1]; [1]Tonix Pharmaceuticals, Inc., New York, NY, [2]APR Applied Pharma Research s.a., Balerna, Switzerland.

BACKGROUND: Cyclobenzaprine (CBP) exposure during sleep improves daytime fibromyalgia (FM) symptoms and sleep quality. CBP absorption into plasma is delayed after ingesting immediate release (IR) tablets. To speed absorption, TNX-102 SL, a sublingual (SL) formulation of CBP was developed for transmucosal absorption.
METHODS: Plasma CBP was measured in healthy subjects (n=24) after a single tablet of TNX-102 SL 2.8 mg or CBP IR 5 mg, and PK parameters were calculated.

RESULTS: TNX-102 SL is a eutectic CBP formulation containing a basifying agent that disintegrates in saliva and rapidly dissolves. For TNX-102 SL 2.8 mg v. ingested CBP IR 5 mg, plasma CBP levels were: at 10 min 338 pg/ml v. below limit of detection (BLD); at 20 min 739 pg/mL v. BLD; at 30 min 988 pg/mL v. BLD; at 45 min 1209 v. 280 pg/mL (p=0.001); at 60 min 1545 v. 913 pg/mL (p=0.062); and at 120 min 2296 v. 1737 pg/mL (p=0.043). For TNX-102 SL 2.8 mg v. CBP IR 5 mg tablets, the mean exposure was 338% (p=0.009) higher at 1h, and 83% (p=0.034) higher at 2h. TNX-102 SL 2.8 mg had Cmax = 3.4 ng/mL and AUC0-8 = 79 ng hr/mL while CBP IR 5 mg had Cmax = 4.3 ng/mL and AUC0-8= 92 ng hr/mL showing more efficient dose-adjusted absorption for TNX-102 SL. The plasma levels of norcyclobenzaprine, the major metabolite of CBP, were lower with TNX-102 SL consistent with bypassing first pass hepatic metabolism. TNX-102 SL was well tolerated and side effects were similar to those of oral CBP although some subjects experienced numbness in the mouth that was transient and self-limited.
CONCLUSION: TNX-102 SL delivers CBP rapidly across the SL mucosal membrane into plasma and provides significantly increased plasma CBP levels during the first 1-2 hr. TNX-102 SL appears well suited for its development as a potential bedtime medication for FM in a long-term treatment regimen.

LB-027

POPULATION MODELING AND SIMULATION OF RPH-203 EFFECTS IN THE CONTEXT OF PREVENTION OF SKELETAL-RELATED EVENTS IN PATIENTS WITH BONE METASTASES.

E. Metelkin[1], T. Petukhova[1], O. Demin[1], S. Archuadze[2], G. Konopleva[2], D. Koloda[2], M. Samsonov[2]; [1]Institute for Systems Biology (Moscow), Moscow, Russian Federation, [2]CJSC R-Pharm, Moscow, Russian Federation.

BACKGROUND: Bone metastases are common complications of tumors. RANK/RANKL pathway promotes osteoclastogenesis and growth of bone metastases. RPH-203 (CJSC R-Pharm), a novel RANKL inhibitor, is a recombinant fusion protein for the treatment of solid tumor related bone lesions. The objective of this study was to develop population PKPD model of RPH-203 and to simulate treatment effect of RPH-203 in patients with breast cancer related bone metastases compared to denosumab.
METHODS: Healthy volunteers' data from phase I study were used. RPH-203 was given as single subcutaneous injection at 0 (buffer), 10, 30, 40, 60 mg doses. RPH-203 plasma concentrations and levels of bone resorption markers (uNTX, sCTX, etc.) were measured during clinical trial. Preclinical data of RPH-203 - RANKL binding affinity were used to develop the drug effect model. Population data were analyzed using NONMEM 7.3. Model-based simulations were done to assess RPH-203 treatment effect.
RESULTS: RPH-203 pharmacokinetics was characterized by two-compartment model with firstorder elimination. uNTX and sCTX time courses were described using sigmoid Imax model of effect. Under the model, suppression of biomarkers by RPH-203 treatment was statistically significant ($P < 0.05$).Based on simulations, RPH-203 40 mg weekly dosing provided stronger RANKL inhibition than denosumab and RPH-203 at 30 mg dose resulted in RANKL inhibition similar to that by denosumab. After 12 weeks of RPH-203 treatment at 40 mg and 30 mg doses (or denosumab) free RANKL level was reduced about 10000 times and 2000–5000 times, respectively. Suppression of uNTX was similar for all treatment regimens.
CONCLUSION: RPH-203 is an advanced drug for the treatment of bone metastases. Predicted effectiveness of RPH-203 is similar or exceeds that of denosumab.

LB-028

A DRUG-DRUG INTERACTION STUDY OF IBRUTINIB WITH MODERATE/ STRONG CYP3A INHIBITORS IN PATIENTS WITH B-CELL MALIGNANCY.

J. de Jong[1], P. Hellemans[2], T. Masterson[3], D. Skee[4], G. Manikhas[5], A. Myasnikov[6], D. Osmanov[7], R. Córdoba[8], C. Panizo[9], L. De Zwart[2], J. Snoeys[2], V. Chauhan[4], J. Jiao[4], D. Ouellet[3], J. Sukbuntherng[10]; [1]Janssen Research & Development, San Diego, CA, [2]Janssen Research & Development, Beerse, Belgium, [3]Janssen Research & Development, Spring House, PA, [4]Janssen Research & Development, Raritan, NJ, [5]St. Petersburg City Oncology Hospital, St-Petersburg, Russian Federation, [6]Baranov Republican Hospital, Petrozavodsk, Russian Federation, [7]N. N. Blokhin Russian Academy of Medical Sciences, Moscow, Russian Federation, [8]University Hospital Fundacion Jimenez Diaz, Health Research Institute IIS-FJD, Madrid, Spain, [9]University Clinic of Navarra, Pamplona, Spain, [10]Pharmacyclics LLC, Sunnyvale, CA.

BACKGROUND: Ibrutinib (IBR), metabolized predominantly during first-pass by CYP3A, displays strong interaction when coadministered with CYP3A perpetrators. However, CYP3A inhibitor data in uncontrolled Phase 2 studies suggested lower drug-drug interaction (DDI) magnitude than studies in healthy participants and in silico simulations. A dedicated DDI study in patients with B-cell malignancies was designed to understand the clinical implication of interaction and confirm recommended dose adjustments.
METHODS: Patients (n= 26 planned) received 560 mg IBR QD from days 1-4 (to steady-state) and 14-18. On days 5-13 and 19-27, dose was reduced to 140 mg, first combined with moderate inhibitor erythromycin (ERY, 500 mg TID-days 5-11), then with moderate/ strong inhibitor voriconazole (VOR, 200 mg BID-days 19-25; 60 min before IBR). IBR intake was to occur 30 min prior to breakfast. On days 4 (IBR alone), 11 (IBR+ERY) and 25 (IBR+VOR), PK samples were taken pre- and up to 24h postdose. Early stopping was allowed if DDI at interim (6/6 or 10/12 patients) exceeded 6-fold.
RESULTS: Patients (n=13) were enrolled at 5 clinical sites since 21 May 2015. Geometric mean ratios (GMR; 90% CI) on dose-normalized Cmax and AUC$_{0\text{-}\infty}$ respectively, were 4.7 (2.8-7.9) and 4.2 (2.3-7.7) for ERY (n=13), and 6.9 (4.2-11.4) and 6.3 (4.0-10.1) for VOR (n=12). PBPK model-predicted GMRs were 5.5 and 7.1 [ERY]; 6.3 and 7.6 [VOR]. Coadministration of IBR with ERY/VOR (1 week) was well-tolerated and consistent with IBR safety profile at therapeutic doses. As stopping rule was not met, enrollment is ongoing.
CONCLUSION: Preliminary PK data indicate that IBR 140 mg when combined with a moderate CYP3A inhibitor achieves exposures in line with those after 560 mg given alone and support recommended dose reduction to 140 mg/day in IBR label.

LB-029

CLINICAL PHARMACOKINETICS, PHARMACODYNAMICS, SAFETY AND TOLERABILITY OF MLN3126, A HIGHLY SELECTIVE ORALLY BIOAVAILABLE, CCR9 ANTAGONIST.

A. Agyemang[1], S. Roepcke[2], G. Smithson[3], M. Chen[3], M. Helmick[3]; [1]Takeda Development Centre, London, United Kingdom, [2]Takeda Pharmaceuticals International AG, Zurich, Switzerland, [3]Takeda Development Center, Deerfield, IL.

BACKGROUND: MLN3126 is an oral, small molecule, highly selective chemokine C-C motif receptor 9 (CCR9) antagonist with the potential for the treatment of inflammatory and immunological diseases.

METHODS: The single rising dose study randomized 39 healthy male and female subjects who received single doses of MLN3126 or placebo up to 2000 mg. The multiple dose study randomized 23 healthy male and female non-Japanese and Japanese subjects who received single doses (100 mg and 300 mg) of MLN3126 or placebo for 7 days. Safety/tolerability, PK (plasma concentrations) and PD (CCR9 binding assay) were assessed throughout the dosing period.
RESULTS: MLN3126 was well absorbed with a median T_{max} of approximately 4 hours following both single and multiple dose regimens. $AUC_{(0\text{-}t)}$ and C_{max} increased in a less than dose proportional manner. Mean elimination $t_{1/2}$ was between approximately 12 and 14 hours. Mean accumulation ratios were less than 1 suggesting no relevant accumulation. Following once daily dosing for 7 days, systemic exposure (AUC) between the first and the last day of dosing was reduced by approximately 1.7-fold suggesting a degree of autoinduction. Single oral dose administration of MLN3126 with a high-fat breakfast delayed MLN3126 absorption by approximately 3 hours, increased systemic exposure by approximately 3-fold and decreased mean $t_{1/2}$ by 1 hour. Single dose treatment with MLN3126 resulted in a dose- and concentration-dependent reduction in the percentage of specific CCL25+ memory T cells and specific CCL25 binding by memory T cells. Once daily administration of MLN3126 for up to 7 days was well tolerated.
CONCLUSION: MLN3126 is a specific CCR9 antagonist that has been shown to be safe and well tolerated at the doses studied and reaches concentrations indicative of effective PD activity.

LB-030

HISTONE DEACETYLASE INHIBITORS ATTENUATE NEOINTIMAL HYPERPLASIA IN ANASTOMOTIC SITES OF ARTERIOVENOUS FISTULAS FOR HEMODIALYSIS.

J. Chiu, T. Yang; National Health Research Institutes, Taipei, Taiwan.

BACKGROUND: Chronic kidney disease is a major health problem in the world. End-stage renal disease (ESRD) patients receive hemodialysis, with the creation of arteriovenous fistula (AVF), which remains significant problems, such as thrombosis and stenosis. The relationship between hemodynamic forces and AVF failure remains unclear. Moreover, the therapeutic strategies for AVF stenosis and thrombosis remain to be determined.
METHODS: *In vitro* cell culture studies on effects of blood flows on molecular signaling to in vivo investigations on rats with AVF and clinical specimens from patients with AVF were performed.
RESULTS: Disturbed flow with high and oscillatory shear stress (HOSS, ~30±100 dynes/cm^2) is generated in the anastomotic site of AVF in patients and rat AVF models. Venous endothelial cells (ECs) in regions of anastomosis show higher expression of class I histone deacetylases (HDAC-1/2/3) and lower expression of thrombomodulin (TM) in both patients and rat AVF models. HOSS induces association of HDAC-3 with krüppel-like factor 2 (KLF2) to deacetylate KLF2 and down-regulate TM in ECs. Intraperitoneal administration of valproic acid (VPA), which is a specific inhibitor of class I HDACs, into AVF rats inhibits the increased formation of stenosis and intimal hyperplasia at anastomotic sites.
CONCLUSION: Disturbed flow with HOSS induces HDAC-3 to contribute to AVF intimal hyperplasia and failure. HDAC inhibitor attenuates neointimal hyperplasia of AVF in rats. Such information may help to generate new approaches for therapeutic interventions against AVF failure in patients.

LB-031

META-ANALYSIS OF *ABCG2* (BCRP) VARIANTS IN MULTIPLE COHORTS REVEALS AN ASSOCIATION BETWEEN THE MISSENSE VARIANT, Q141K, AND ALLOPURINOL RESPONSE.

D. Brackman[1], C. Wen[1], E. Jorgenson[2], S. Yee[1], W. Wei[3], C. Shaffer[3], C. Ingram[3], J. Denny[3], E. Chen[1], K. Cheung[1], D. Roden[3], C. Schaefer[2], N. Risch[1], K. Giacomini[1]; [1]University of California San Francisco, San Francisco, CA, [2]Kaiser Permanente Northern California, Oakland, CA, [3]Vanderbilt University, Nashville, TN.

BACKGROUND: Allopurinol (ALLO) is the first-line treatment for chronic gout, a debilitating disease caused by high levels of serum uric acid (SUA). Response to ALLO is highly variable, and many patients never achieve normal SUA levels. We previously published a GWAS identifying genetic variants in *ABCG2* that encodes Breast Cancer Resistance Protein (BCRP) as potential modifiers of ALLO pharmacodynamics. Using three separate, multi-ethnic cohorts, we aimed to expand our findings of BCRP's role in ALLO response.
METHODS: A retrospective study was performed using EMR data from Kaiser Permanente, BioVU at Vanderbilt and Marshfield. Data from 2,969 subjects, 2,332 of European descent, were collected for analysis. Subjects were all prescribed ALLO and had SUA readings both before and during treatment. Raw data for the BioVU and Marshfield cohorts was received on August 25, 2015, but quality control procedures were not completed until September 14. Linear regression models were used to determine the effects of 15 genetic variants in *ABCG2* on change in SUA in each cohort and combined via meta-analysis.
RESULTS: We found the BCRP Q141K variant (rs2231142) was associated with a reduced effect of ALLO on SUA (0.32 + 0.05 mg/dL), with a final p-value of 5.2 x 10-9 in our European subjects using both a fixed and random effects model. One variant in the noncoding region of *ABCG2*, rs10011796, also associated with ALLO response at genomewide level significance (p = 9.3 x 10-9).
CONCLUSION: Variants in *ABCG2* are associated with poor response to ALLO in a large meta-analysis of data from 2,332 individuals of European ancestry. Further studies are ongoing to determine the validity of these findings in other ethnic groups. Risk models of ALLO response should aid clinicians in more precise selection of anti-gout medications.

LB-032

LOGISTIC MODELING OF CORD BLOOD MAGNESIUM LEVEL AND CEREBRAL PALSY INCIDENCE IN CHILDREN WITH MATERNAL MAGNESIUM SULFATE DOSING.

X. Liu[1], A. Balch[1], C. L. Dixon[2], M. Costantine[2], C. M. Sherwin[1]; [1]University of Utah, Salt Lake City, UT, [2]University of Texas Medical Branch, Galveston, TX.

BACKGROUND: There is a paucity of data regarding the appropriate dosing of magnesium sulfate for fetal neuroprotection in women at risk of immediate delivery prior to 32 weeks gestation. Our goal is to associate cord blood magnesium levels at time of birth with cerebral palsy (CP) and neonatal death.
METHODS: This is a secondary analysis of a randomized controlled trial conducted by the Maternal-Fetal Medicine Units Network. The original trial randomized women at imminent risk of delivery between 24 and 32 weeks to receive magnesium sulfate or placebo. The study's primary outcome was a composite of either moderate to severe CP or death. Secondary outcomes were moderate to severe CP and neonatal death. We used logistic regression modeling to evaluate the relation between concentration of magnesium in cord blood and study outcomes.

RESULTS: 732 women were included in this analysis. The mean magnesium concentration in the cord blood was 2.98 mg/dL. We did not find an association between cord blood magnesium concentrations and the primary outcome of moderate to severe CP or death, or any of the secondary outcomes. The odds ratio fold change (95% confidence interval) of primary outcome, moderate to severe CP and neonatal death was 0.99 (0.69 - 1.43), 0.88 (0.38 - 2.03) and 1.03 (0.69 - 1.54) respectively with the increase of one unit of magnesium level in cord blood.
CONCLUSION: Cord blood magnesium concentrations were not associated with moderate to severe CP or death. Further research should involve pharmacodynamic modeling to evaluate the relationship between magnesium doses, cord blood levels and child outcomes.

LB-033

POPULATION PHARMACOKINETIC MODELING OF MORPHINE AND METABOLITES IN 3-18 YEAR-OLD CHILDREN FOLLOWING SURGERY.

X. Liu[1], M. W. Lieh-Lai[2], R. E. Kauffman[3], R. M. Ward[1], C. M. Sherwin[1]; [1]University of Utah, Salt Lake City, UT, [2]Wayne State University of Michigan, Detroit, MI, [3]University of Missouri, Kansas City, MO.

BACKGROUND: Morphine is the most widely used medication for postoperative pain management in pediatric intensive care unit. The dosing guide of morphine in children has been traditionally extrapolated from adults, assuming slower elimination and higher sensitivity in children. Evidence from various studies have challenged the validity of this assumption, especially in 3-18 year-old children. This study aims to assess the pharmacokinetics (PK) and pharmacodynamics (PD) of morphine and metabolites (morphine-3-glucuronid, M3G and morphine-6-glucuronid, M6G) in 3-18 year-old children following surgery using advanced pharmacometric approaches.
METHODS: Children of age 3-18 years old receiving intravenous morphine infusion immediately after surgery at Detroit Children's Hospital were included in this study. Blood samples were drawn before, and 0.25 to 12 hours after the dosing and analyzed for the concentrations of morphine and its metabolites. The population PK model was developed using NONMEM 7.3.
RESULTS: A total of 36 patients were included with average (range) age of 10.2 years (3.5 - 18.9 years) and weight of 37.9 kg (10.9 - 117.6 kg). Morphine and metabolites PK was simultaneously described by a three-compartment metabolite model with a combined additive and proportional error model. All PK parameters (clearance and volume of distribution of morphine, M3G and M6G) were estimated with high confidence.
CONCLUSION: Morphine and metabolites PK in 3-18 year-old children after surgery was best described by a three-compartment metabolite model. Future studies will evaluate the significance of potential covariates in the PK model and develop a PD model to describe the pain degree measurements.

LB-034

EFFECT OF GREEN TEA ON THE PHARMACOKINETICS OF ROSUVASTATIN.

T. Kim[1], H. Y. Kwak[1], S. Kim[2], J. Jeon[2], M. Kim[2]; [1]Konkuk University Medical Center, Seoul, Korea, Republic of Korea, [2]Chonbuk National University Hospital, Jeonju, Korea, Republic of Korea.

BACKGROUND: Rosuvastatin is an HMG-CoA reductase inhibitor used for the treatment of hypercholesterolemia. The aim of this study was to investigate effect of green tea on the pharmacokinetics of rosuvastatin in healthy volunteers.

METHODS: An open-label, 2-period, fixed-sequence study was conducted in healthy volunteers. Subjects were administered 20 mg of rosuvastatin alone. After 4 day-washout period, subject received 20 mg of rosuvastatin combined with epigallocatechin gallate (EGCG) 300 mg which is the extract of green tea. Blood samples for the pharmacokinetic assessments were collected at predose and at 0.5, 1, 2, 4, 6 and 8 hours after dosing. Pharmacokinetic parameters were obtained by noncompartmental analysis. The comparisons of Pharmacokinetic parameters between rosuvastatin alone and rosuvastatin plus EGCG were performed by mixed effect model.
RESULTS: A total of 13 healthy volunteers aged 20 to 33 were participated in this study. The plasma concentration reached a peak at 2-4 hours after the administration of rosuvastatin alone and at 1-4 hours after the coadministration of rosuvastatin and EGCG. The geometric mean ratios (Rosuvastatin+EGCG/Rosuvastatin) for rosuvastatin area under the plasma concentration-time curve (AUC) and C_{max} were 0.81 (90% confidence interval, 0.71-0.92), and 0.85 (0.73-1.00), respectively.
CONCLUSION: After the coadministration of the green tea extract, EGCG, the systemic exposure of rosuvastatin was decreased in healthy volunteers.

LB-035

EXPLORATORY POPULATION PK ANALYSIS OF DUPILUMAB, A FULLY HUMAN MONOCLONAL ANTIBODY AGAINST INTERLEUKIN RECEPTOR IL-4RA

P. Kovalenko, T. Dicioccio, J. Davis, R. Soltys; Regeneron Pharmaceuticals, Inc., Tarrytown, NY.

BACKGROUND: An exploratory population pharmacokinetic (PK) model for functional dupilumab was developed. The model was used to predict concentrations of functional dupilumab in future human studies, support regulatory responses, better understand PK profile of competitor drugs, and develop population pharmacodynamic model.
METHODS: The first human model was based on allometric scaling and was developed to predict PK profile in the first-in-human study. Data were integrated from two populations: healthy volunteers (HV) and patients with atopic dermatitis (AD). The final exploratory model included data for 509 subjects and 7829 dupilumab plasma concentrations from seven Phase 1 and Phase 2 studies. The data were analyzed using sequentially implemented SAEM and importance sampling.
RESULTS: The best structural model was a two-compartment model with parallel linear and Michaelis-Menten elimination from central compartment. Model based on single-dose first-in-human data and the later models based on integrated data predicted the subsequent single- and multiple-dose studies with high accuracy. The population PK estimate of elimination rate was 0.0460 day^{-1}, central-to-peripheral rate was 0.0910 day^{-1}, peripheral-to-central rate was 0.166 day^{-1}, SC bioavailability was 59.4%, maximal target-mediated elimination rate was 1.04 mg/L/day, and Michaelis-Menten constant was 0.01 mg/L. Body weight was a significant covariate of the central volume. When controlling for weight, no meaningful or statistically significant gender effect was observed. No meaningful or statistically significant differences between HV and patients with AD were identified.
CONCLUSION: The population PK model adequately described dupilumab PK in HV and patients with AD for IV and SC routes of administration.

LB-036

DOSE-FINDING STUDY OF THE MONOCLONAL ANTIBODY COCKTAIL ZMAPP™ AGAINST ZAIRE EBOLA VIRUS INFECTION IN A RHESUS MACAQUE MODEL.

J. Froude[1], A. Herbert[2], S. Zak[2], R. Ortiz[2], W. Pratt[2], S. Stonier[2], J. Brannan[2], L. Prugar[2], A. Kuehne[2], L. Zeitlin[3], J. Dye[2]; [1]Walter Reed Army Institute of Research, Silver Spring, MD, [2]United States Army Medical Research Institute of Infectious Disease, Fort Detrick, MD, [3]Mapp Biopharmaceutical, Inc., San Diego, CA.

BACKGROUND: The monoclonal antibody cocktail ZMapp™ (13C6, 2G4 and 4G7) has been previously evaluated in non-human primate models and is currently being assessed in Phase I and II clinical trials in Africa. The current ZMapp™ treatment regimen for Ebola virus infected non-human primates or human patients, is administration in three doses at 50 mg/kg every third day, initiating on Day 5 for NHPs under experimental studies or within 24-hrs of clinical enrollment for human cases.
METHODS: In this paper an initial dose-finding study was performed to assess the efficacy of a reduced dose frequency or dose quantity compared to the level of protection offered with the previous three dose regimen. Experimental groups were compared to the established three dose regimen of 50 mg/kg; either a single dose or two-dose regimen initiating on day 5, or a triple dose regimen at a reduced dose of 25 mg/kg on day 5,
8 and 11.
RESULTS: Each experimental group exhibited protection above controls; however, the two dose treatment cohort at 50 mg/kg had comparable survival to the group receiving the three dose regimen and was able to maintain equivalent anti-GP titers. An analysis of the antibody titers showed a dose response increase following treatments provided on days 5, 8, and 11 and was roughly equal between all groups after day 17, suggesting an adaptive immune response was generated.
CONCLUSION: These results indicate that ZMapp™ is able to provide equivalent protection and anti-GP titers utilizing a two dose treatment regimen and continued development should be pursued for clinical use utilizing this dosage evidence.

LB-037

TYPE 2 DIABETES MODULATES CYP450 METABOLIC ACTIVITIES; AN IMPORTANT VARIABILITY FACTOR IN DRUG RESPONSE.

S. Gravel[1], A. Grangeon[1], F. Gaudette[1], J. Chiasson[2], S. Dallaire[1], H. Langelier[1], J. Turgeon[1], V. Michaud[3]; [1]CRCHUM, Montreal, QC, Canada, [2]CHUM, Montreal, QC, Canada, [3]Université de Montréal, Montreal, QC, Canada.

BACKGROUND: Type 2 diabetes (T2D) patients show highly variable responses to different drugs; some T2D patients appear resistant to certain drugs while being more sensitive to other drugs. Therefore, we hypothesized that T2D and related inflammatory processes may alter CYP450 expression and activities involved in drug disposition.

METHODS: CYP450 activities were assessed in T2D patients and healthy subjects after one oral administration of a cocktail of CYP450 probe drugs consisting of 100mg caffeine (CAF; 1A2), 100mg bupropion (BUP; 2B6), 250mg tolbutamide (TOL; 2C9), 20mg omeprazole (OME; 2C19), 30mg dextromethorphan (DM; 2D6) and 2mg midazolam (MDZ; 3A4/5). Participants were ≥18 years old, BMI≤35 and did not receive CYP450 inhibitor or inducer drugs. Mann-Whitney test analysis was performed to compare plasma metabolic ratios (MR) of $AUC_{0\text{-}8h}$ drug/metabolite(s) between T2D vs non-T2D groups. At this time (09/2015), 38 subjects are recruited and preliminary analysis performed on 20 subjects (11/2015).
RESULTS: Plasma MR were obtained from 11 patients with T2D (mean A1C 6.9%) and 9 healthy subjects. Mean MR [95% CI] for CYP3As, and 2C19 activities were increased in T2D group: 3.9 [2.5, 5.3] vs 1.7 [1.4, 2.0] for MDZ and 7.1 [3.7, 10.5] vs 2.1 [1.2, 3.0] for OME ($p<0.005$). A decrease in TOL MR was observed in T2D vs non-T2D groups: 16.8 [13.6, 20.0] vs 28.7 [21.6, 35.8] ($p<0.002$). No significant difference was observed for CYP2B6 or 2D6 activities.
CONCLUSIONS: Our preliminary analyses indicate that T2D affects CYP activities in an isoform specific manner. Our results show that decreased metabolic activity of CYP3As and 2C19 may lead to unintentional overdosing in T2D patients treated with substrates of these isoforms or lack of efficacy for certain pro-drugs such as clopidogrel.
CIHR #299309
NTC02291666

LB-038

QUANTIFYING THE PHARMACOKINETICS OF AN OXIME ACETYCHOLINESTERASE REACTIVATOR USING ACCELERATOR MASS SPECTROMETRY IN GUINEA PIGS.

M. A. Malfatti, H. A. Enright, E. A. Kuhn, F. C. Lightstone, C. A. Valdez; Lawrence Livermore National Laboratory, Livermore, CA.

BACKGROUND: Organophosphorus (OP) nerve agents represent some of the most toxic substances known to mankind. The current standard of care for exposure has changed very little in the past decades, and relies on a combination of atropine to block receptor activity and oxime-type acetylcholinesterase (AChE) reactivators to reverse OP binding to AChE. Although these oximes are capable of eliminating the effects of nerve agents, their overall efficacy is reduced by their limited capacity to cross the blood-brain barrier (BBB). A new oxime developed by Radic et al. (*J. Biol. Chem, 287, 2012*) has shown promise for enhanced capabilities for crossing the BBB.
METHODS: To fully assess the potential of this compound as an effective treatment for OP poisoning, a comprehensive assessment of its pharmacokinetics (PK) and biodistribution is needed. We have used the ultra-sensitive technique of accelerator mass spectrometry to quantify the PK profile and tissue distribution, as well as, the brain/ plasma ratio of the oxime in guinea pigs.
RESULTS: PK analysis revealed a rapid distribution of oxime with a plasma $T_{1/2}$ of ~ 1.3 hr. Over a 20-fold dose range (10-200 mg/kg) the $AUC_{0\text{-}inf.}$ and the C_{max} had a 28 and 31–fold increase, respectively. The kidney and liver had the highest concentration of oxime with the brain having the least. The brain to plasma ratio ranged from 0.096 at the 10 mg/kg dose to 0.43 at the 200 mg/kg dose indicating dose dependent differences in brain and plasma clearance rates.

CONCLUSIONS: These results indicate that the PK profile of this oxime reactivator is conducive for further development as a potential treatment or OP poisoning.
This work was performed under the auspices of the U.S. DOE by LLNL under Contract DE-AC52-07NA27344 and supported by DTRA (CBS-03-2-004) and NIH/NIGMS (2P41GM103483-16).

LB-039

TRANSPORTER INDUCED PROTEIN BINDING SHIFT (TIPBS): IMPACT ON OATP1B1/1B3 MEDIATED DRUG TRANSPORT AND DRUG-DRUG INTERACTIONS.

X. Zhang, J. Baik, M. Jahic, W. Jiang, Y. Huang; Optivia Biotechnology Inc., Menlo Park, CA.

BACKGROUND: We recently proposed a Transporter-Induced Protein Binding Shift (TIPBS) hypothesis to describe the effects of serum proteins on transporter-mediated drug transport. This work substantiates our previous findings and theory by demonstrating drug-dependent discrepancies between predicted and measured OATP1B1/1B3 mediated transport and inhibition in human serum.
METHODS: OATP1B1 and OATP1B3 mediated substrate transport and inhibitor IC50s were measured in protein-free HBSS and human serum, using CHO cells stably expressing the transporters. Serum unbound fraction (fu) was used to calculate substrate transport or inhibitor IC50s in serum from the constants measured in HBSS. The predicted values were contrasted to that measured from assays conducted in human serum.
RESULTS: The fu adjustment method generally under-estimated substrate uptake and inhibitor potency in serum. For examples, actual OATP1B1 mediated uptake of 5uM atorvastatin in serum (fu=2%) is 5.8x higher than that of HBSS with the same unbound drug; rifampicin (fu=10%) OATP1B1 IC50 in serum was 1.6uM, which is 6x lower than the predicted value. Our data on various substrates and inhibitors with different fu indicated that the extent of underestimation were drug AND transporter dependent, possibly due to difference in drug binding affinities to serum proteins and transporters as predicted by our TIPBS models.
CONCLUSION: Our work suggests that drug transport and inhibition in serum may not be described by the simple unbound drug model, raising the question on whether/when is appropriate to use the conventional fu adjustment method for predicting in vivo drug clearance and DDIs.

LB-040

AN INVESTIGATION INTO KETAMINE AND NORKETAMINE STABILITY IN WHOLE BLOOD AT ROOM TEMPERATURE.

B. D. Tran[1], J. Sima[2], G. S. Moorthy[2], J. Healy[1], W. K. Kraft[1], A. F. Zuppa[2]; [1]Department of Pharmacology and Experimental Therapeutics, Jefferson Medical College, Philadelphia, PA, [2]Center for Clinical Pharmacology, The Children's Hospital of Philadelphia, Philadelphia, PA.

BACKGROUND: Critically ill extracorporeal membrane oxygenation (ECMO) patients may receive ketamine for sedation/analgesia. An ongoing pharmacokinetic (PK) study seeks to describe the PK of ketamine and its metabolite norketamine in adult ECMO patients. The conduct of PK studies in critically ill populations is hindered by the immediate need to process samples obtained in a busy intensive care setting, as resources are limited. The ability to store unprocessed samples at room temperature for an extended time period would overcome this barrier, and make PK studies in critically ill patients more feasible. Demonstration of ketamine and norketamine stability in unprocessed blood samples at room temperature would allow for this approach.
METHODS: Blank blood samples were spiked with ketamine and norketamine at 20, 60, 800, and 4000 ng/mL. Samples were left at room temperature, and aliquots were taken at times 0, 24, 48, and 72 hours. The samples were extracted and analyzed using a validated high-performance liquid chromatography tandem mass spectrometry assay.
RESULTS: Benchtop stability in blood was demonstrated up to 72 hours without chemical degradation for ketamine and norketamine. At all-time points, the coefficient of variation was <15%, indicating high precision, and accuracies were within 85 to 115% for all blood samples.
CONCLUSION: Due to the stability of ketamine in whole blood at room temperature for up to 72 hours, PK studies of ketamine in the clinical setting do not require immediate processing of blood. The lack of access to immediate processing and freezing should not serve as a barrier to performing pharmacology studies in this setting.

LB-041

VARIANTS ASSOCIATED WITH HIGH GRADE BEVACIZUMAB-INDUCED HYPERTENSION IDENTIFIED BY EXOME SEQUENCING: CALGB 80405 (ALLIANCE).

M. Li[1], F. Mulkey[2], C. Jiang[2], B. H. O'Neil[3], D. Niedzwiecki[2], P. N. Friedman[4], H. S. Hochster[5], H. Lenz[6], J. Atkins[7], A. P. Venook[1], K. Owzar[2], D. L. Kroetz[1]; [1]University of California, San Francisco, San Francisco, CA, [2]Alliance Statistics and Data Center, Durham, NC, [3]Indiana University Simon Cancer Center, Indianapolis, IN, [4]The University of Chicago, Chicago, IL, [5]Yale University, New Haven, CT, [6]University of Southern California, Los Angeles, CA, [7]Southeast Clinical Oncology Research Consortium, Winston Salem, NC.

BACKGROUND: Development of high-grade hypertension (HTN) is a dose-limiting toxicity in 5-18% of patients treated with bevacizumab (bev). Previous clinical studies implicated several common VEGF pathway and HTN-susceptibility variants in this adverse reaction. Additional genetic risk of bev-induced HTN remains to be discovered.
METHODS: Whole-exome sequencing was performed at a mean coverage of 65X on 62 Caucasian bev-treated patients from CALGB 80405 (Alliance); 19 cases developed Grade 3-4 HTN within the first 3 cycles and 43 controls had no reported HTN in the first year of treatment. Variant calling of sequencing data was completed on Sep 23, 2015, followed by quality control analyses, variant annotation and filtering, and association testing.
RESULTS: A total of 327,184 variants, including 103,762 of MAF<0.01, were identified. A candidate gene analysis (92,886 variants in 174 genes) identified two associated variants (P = 1.7 x 10-4, 7.5 x 10-4) in a transcriptionally active region upstream of *HSP90AB1*, which encodes a regulatory protein of VEGF-induced nitric oxide synthesis. Preliminary results of a gene-based analysis show enrichment of MAF<0.01 variants in endothelin-1 signaling and blood pressure regulation genes. An exome-wide exploratory analysis focusing on the most deleterious variants identified a weakly associated missense variant in *GTPBP4*, which has been implicated in renal function.

CONCLUSION: These findings will be extended to an analysis of all grade HTN in the full CALGB 80405 cohort and replicated in additional Alliance studies. Our results may inform the understanding of the pathogenesis of bev-induced HTN and how genetic variability influences the risk of developing this toxicity.
Support: U10CA180821; Alliance Foundation, GM61390, GM61393

LB-042

IN VIVO OPTIMIZATION OF A TIME SEQUENCE COMBINATION CHEMOTHERAPY OF PACLITAXEL WITH TRASTUZUMAB IN HER2-POSITIVE BREAST CANCER.

M. Le Merdy, S. Ait-Oudhia; University of Florida, Orlando, FL.

BACKGROUND: HER_2-positive (HER_2+) breast cancer (BC) is more fast-growing and aggressive than other types of BC. Trastuzumab (TZM) is a humanized monoclonal antibody directed against HER_2 receptor. It is clinically used for BC in combination with paclitaxel (PAC) in a 24 h sequence treatment during the first week of therapy followed by a simultaneous administration during the subsequent weeks. There is no scientific rationale for such therapeutic regimen. We propose to optimize the sequential combination of PAC+TZM to enhance their anti-tumoral activity and hence HER_2+ BC patients' outcome.
METHODS: Six therapeutic regimens were investigated on BALB/c nude mice xenografted with BT474 cells, a human BC cell line that overexpresses HER_2 receptor, including single agents PAC and TZM at 10 and 3mg/kg, a tumor priming regimen (TPR) with PAC given 24 h prior to TZM, a reverse-TPR with TZM given 24 h prior to PAC, a concurrent regimen, and a vehicle as a control. The anti-tumoral activity was monitored over time for all regimens through the measurement of tumor volumes as well as animals survival.
RESULTS: *In vivo* studies revealed that animals in the TPR was superior to all the other therapeutic schemes and showed: 1) a greater tumor volume shrinkage response, 2) a longer time to regrowth: 100 days versus 40 days for the reverse-TPR, and 3) a longer survival time: 80% versus 20% in the reverse-TPR after 4 months from the start of the study.
CONCLUSION: The *in vivo* anti-tumor results for TPR regimen are promising. A quantitative systems pharmacology model linking our *in vitro* and *in vivo* data is in progress. The model will be translated to human in order to optimize the dosing regimen for the association (PAC+TZM) in HER2+ BC and improve patients' outcome.

LB-043

IVIG USE AMONG CHILDREN IN FREESTANDING CHILDREN'S HOSPITALS IN THE UNITED STATES.

E. Y. Enioutina[1], A. H. Balch[1], J. Wilkes[2], J. Olsen[1], E. Thorell[1], A. T. Pavia[1], C. M. Sherwin[1];
[1]University of Utah, Salt Lake City, UT, [2]Intermountain Health, Salt Lake City, UT.

BACKGROUND: Intravenous immunoglobulin (IVIG) is primarily indicated as a replacement therapy for patients with primary immune deficiency (PID). However, IVIG is also prescribed for a variety of on- and off -label indications, only some of which are supported by clinical trials. IVIG is actively prescribed to children.

METHODS: This retrospective study analyzed IVIG use in children's hospitals between Jan 1, 2007 and Dec 31, 2014. We queried the Pediatric Hospital Information System database for all inpatients age <18 discharged with a pharmacy charge for IVIG. The primary diagnosis ICD9 codes were used to determine the indications for IVIG use. Statistical analysis was performed in SAS™ version 9.4.
RESULTS: We identified 66,135 admissions with IVIG administrations. The number of overall IVIG admissions rose 19.1% (8.6% per 10,000 admissions) from 2007 to 2014. IVIG use in grams/hospital/year increased from 1,741 in 2007 to 2,892 in 2014. One third of IVIG prescriptions were made to a group with on-label non-PIP conditions, which included Kawasaki disease (18.3%), idiopathic thrombocytopenic purpura (10.0%). Children with PID were 1.4% of all IVIG treated patients, infections - 13.7%, malignancies - 9.1%, neonatal conditions - 5.4%. A steady increase in IVIG use was observed for most conditions during 2007-2014. There was a drop (12.6%) in the use of IVIG for prophylaxis of infections in neonates and treatment of neonatal autoimmune diseases. IVIG use for treatment of neonatal confirmed infections decreased ~45% during 2010-2011, then recovered to 2007 levels.
CONCLUSIONS: The use of IVIG increased significantly from 2007 to 2014, for both on-label and off-label conditions. Improved stewardship could help restrict use to indications supported by adequate evidence.

ENCORE POSTER SESSION

WEDNESDAY, MARCH 9, 2016

4:30 PM – 6:30 PM

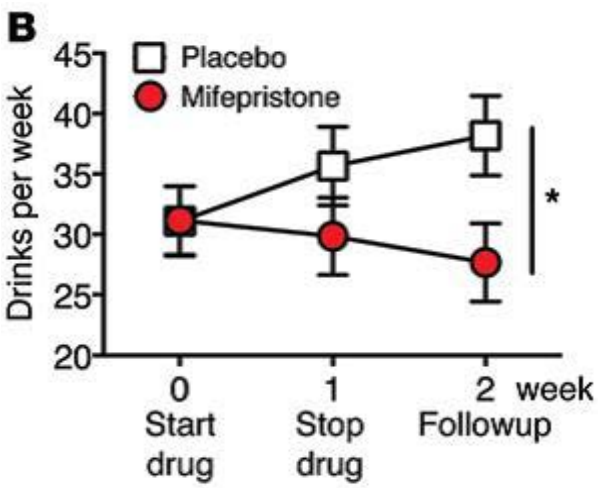
SAPPHIRE BALLROOM

E-037

GLUCOCORTICOID RECEPTOR ANTAGONISM DECREASES ALCOHOL SEEKING IN ALCOHOL-DEPENDENT SUBJECTS.

M. H. Skinner, D. Estey, B. Mason; The Scripps Research Institute, La Jolla, CA.

BACKGROUND: Alcoholism is characterized by overuse, craving and compulsive alcohol seeking. Alterations in brain glucocorticoid receptor (GR) expression accompany compulsive alcohol intake in rats, which is reduced by administering mifepristone, a GR antagonist. We examined the hypothesis that mifepristone would decrease craving in response to *in vivo* alcohol exposure, and reduce alcohol intake under actual life conditions in alcohol-dependent human subjects.
METHODS: Subjects (N = 56) were randomly treated with mifepristone 600 mg orally, or placebo for 7 days and were required to be abstinent the last 3 days. Alcohol craving was assessed at the end of treatment. Self-reported drinking was collected during and 7 days after treatment. Data were analyzed using Mixed Effects Models. Significance level was
-$P < 0.05$.
RESULTS: Mifepristone treatment was associated with a significantly greater reduction in alcohol-cued craving relative to placebo (sum of 4 VAS craving items, P = 0.0003) as well as a reduction in number of drinks per week during and post-treatment (P < 0.05, figure*). Mifepristone was well tolerated.
CONCLUSION: These results support further exploration of GR antagonism via mifepristone as a therapeutic strategy for treatment of alcoholism.



E-038

PHYSIOLOGICALLY BASED AND POPULATION PK MODELING IN OPTIMIZING DRUG DEVELOPMENT: A PREDICT-LEARN-CONFIRM ANALYSIS.

A. Suri[1], S. Chapel[2], C. Lu[1], K. Venkatakrishnan[1]; [1]Millennium Pharmaceuticals Inc., Cambridge, MA, USA, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, [2]Ann Arbor Pharmacometrics Group, Ann Arbor, MO.

BACKGROUND: Physiologically based pharmacokinetic (PBPK) modeling and classical population pharmacokinetic (PK) model-based simulations are increasingly used to answer various drug development questions. In this study, we propose a methodology to optimize the development of drugs, primarily cleared by the kidney, using model-based approaches to determine the need for a dedicated renal impairment (RI) study.
METHODS: The impact of RI on drug exposure is simulated via PBPK modeling and confirmed using classical population PK modeling of phase 2/3 data. This methodology was successfully evaluated and applied to an investigational agent, orteronel (nonsteroidal, reversible, selective 17,20-lyase inhibitor). A phase 1 RI study confirmed the accuracy of model-based predictions.
RESULTS: Orteronel is predominantly cleared through renal excretion based on a human radioactive carbon (^{14}C) mass balance study (78% recovered in urine). The prospective PBPK predictions of increases in orteronel exposure in subjects with RI were close to actual observed clinical values: 52% predicted vs. 38% observed in moderate RI; and 83% predicted vs. 87% observed in severe RI. Consistently, classical population PK modeling of data from patients with mCRPC also predicted an increase in orteronel plasma concentrations with increasing severity of RI (by approximately 20%, 50%, and 100% compared with controls at 400 mg BID in patients with mild, moderate, and severe RI, respectively).
CONCLUSION: Hence, for drugs eliminated primarily via renal clearance, this modeling approach can enable inclusion of patients with RI in phase 3 trials at appropriate doses, which may be an alternative to a dedicated RI study, or suggest that only a reduced-size study in severe RI may be sufficient.

E-039

NOVEL MODEL-BASED DOSING GUIDELINES FOR GENTAMICIN AND TOBRAMYCIN IN PRETERM AND TERM NEONATES.

P. A. Valitalo[1], J. N. van der Anker[2], K. Allegaert[3], R. F. de Cock[1], M. de Hoog[4], S. H. Simons[4], J. W. Mouton[4], C. A. Knibbe[5]; [1]Leiden University, Leiden, Netherlands, [2]Children's National Medical Center, Washington, WA, [3]KU Leuven, Leuven, Belgium, [4]Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands, [5]St Antonius Hospital, Nieuwegein, Netherlands.

BACKGROUND: In the heterogeneous group of preterm and term neonates, gentamicin and tobramycin are mainly dosed according to empirical guidelines, after which therapeutic drug monitoring and subsequent dose adaptation are applied. In view of the variety of neonatal guidelines available, the purpose of this study was to evaluate target concentration attainment of these guidelines, and to propose a new model-based dosing guideline for these drugs in neonates.

METHODS: Demographic characteristics of 1854 neonates (birth weight 390-5200 g, post-natal age 0-27 days) were extracted from earlier studies and sampled to obtain a test dataset of 5000 virtual patients. Monte Carlo simulations on the basis of validated models were undertaken to evaluate the attainment of target peak (5-12 mg/L) and trough (<0.5 mg/L) concentrations, and cumulative AUC, with the existing and proposed guidelines.
RESULTS: Across the entire neonatal age and weight range, the Dutch National Formulary for Children, the British National Formulary for Children, Neofax and the Red Book resulted in adequate peak but elevated trough concentrations (63%-90% above target). The proposed dosing guideline (4.5 mg/kg gentamicin or 5.5 mg/kg tobramycin) with a dosing interval based on birth weight and post-natal age leads to adequate peak concentrations with only 33%-38% of the trough concentrations above target, and a constant AUC across weight and post-natal age.
CONCLUSION: The proposed neonatal dosing guideline for gentamicin and tobramycin results in improved attainment of target concentrations and should be prospectively evaluated in clinical studies to evaluate the efficacy and safety of this treatment.

E-040

CYP2C19 METABOLIZER STATUS AND CLOPIDOGREL EFFICACY IN THE SECONDARY PREVENTION OF SMALL SUBCORTICAL STROKES (SPS3) STUDY.

C. W. McDonough[1], L. A. McClure[2], B. D. Mitchell[3], Y. Gong[1], R. B. Horenstein[3], J. P. Lewis[3], T. S. Field[4], R. L. Talbert[5], O. R. Benavente[4], J. A. Johnson[1], A. R. Shuldiner[3]; [1]University of Florida, Gainesville, FL, [2]Drexel University, Philadelphia, PA, [3]University of Maryland School of Medicine, Baltimore, MD, [4]University of British Columbia, Vancouver, BC, Canada, [5]University of Texas at Austin, Austin, TX.

BACKGROUND: The role of *CYP2C19* genotype on clopidogrel efficacy has been widely studied, with data suggesting reduced clopidogrel efficacy in loss-of-function variant carriers taking clopidogrel post-percutaneous coronary intervention. However, data are limited regarding the association between *CYP2C19* variants and outcomes in stroke patients. We investigated whether *CYP2C19* metabolizer status affects the risk of recurrent stroke or major bleeding in subcortical stroke patients taking dual antiplatelet therapy (DAPT) with aspirin and clopidogrel.
METHODS: *CYP2C19*2* and *CYP2C19*17* were genotyped in 522 DAPT-treated patients from the SPS3 study. *CYP2C19* metabolizer status was inferred from genotype, and associations with the risk of recurrent stroke and major bleeding were assessed in the overall cohort, and by race group, with logistic regression.
RESULTS: In the overall cohort, there were no differences in outcomes by *CYP2C19* metabolizer status (recurrent stroke OR (95% CI) = 1.81 (0.76-4.30); major bleeding OR (95% CI)= 0.67 (0.22-2.03)). In Caucasian patients (n=191), *CYP2C19* IM/PMs had a higher odds of recurrent stroke (OR (95% CI) = 5.19 (1.08-24.90)) than EM/UM individuals; there were no differences in major bleeding.
CONCLUSION: Significant differences in recurrent stroke by *CYP2C19* metabolizer status were found in Caucasian subcortical stroke patients receiving DAPT, consistent with cardiovascular studies on *CYP2C19* and clopidogrel. However, the bleeding risk that led to early termination of the antiplatelet arm of the SPS3 trial does not appear to be explained by *CYP2C19* genotype. This study was relatively underpowered; therefore these findings should be interpreted with caution and warrant replication. McDonough et al. *J Am Heart Assoc.* 2015 May 27;4(6):e001652.

E-041

SUBCLINICAL HYPOTHYROIDISM IS A RISK FACTOR FOR STATIN-ASSOCIATED DIABETES MELLITUS.

N. Gronich[1], S. N. Deftereos[2], I. Lavi[1], A. S. Persidis[2], D. R. Abernethy[3], G. Rennert[4]; [1]Pharmacoepidemiology Unit, Department of Community Medicine and Epidemiology, Carmel Medical Center, Clalit health Services, Haifa, Israel, [2]Biovista Inc., Charlottesville, VA, [3]Drug Safety Group, Office of Clinical Pharmacology, US Food and Drug Administration, Silver Spring, MD, [4]Carmel Medical Center, and Bruce Rappaport Faculty of Medicine, Technion – Israel Institute of Technology and Office of Chief Physician, Clalit Health Services, Haifa, Israel.

BACKGROUND: Statins may lead to the development of de novo diabetes mellitus (DM). Our objective was to identify risk factors for the development of statin-associated DM.
METHODS: Risk factor identification, by high-throughput in-silico processing of large biomedical data using COSS™, was followed by a cohort study in Clalit, the largest healthcare provider in Israel. All highly-compliant, diabetes-free, statin initiators in Clalit were matched with randomly selected cohort of diabetes-free non-statin users, using propensity score matching. Time-dependent Poisson regression multivariable models were used to assess rate ratios (RRs) with 95% CIs for DM occurrence.
RESULTS: The risk of developing DM was 2.57 (95% CI 2.45-2.70) in highly-compliant statin users. COSS™ analysis pointed out subclinical hypothyroidism as a prominent risk factor for statin-associated DM. In an analysis in a selected subpopulation following exclusion of patients with variables carrying high standardized mean difference between groups, that included 14,856 statin nonusers and 5,264 statin users, subclinical hypothyroidism was found to be a significant risk factor for DM within the statin users (RR 1.94 [95% CI 1.13-3.34]) and not within the statin nonusers (RR 1.20 [0.52-2.75]). Hypothyroidism carried an increased risk for new-onset DM in both cohorts. Patients with hypothyroidism treated with thyroid hormone replacement were not at increased risk for new onset DM.
CONCLUSION: Subclinical hypothyroidism is a risk factor for statin-associated DM. Clinicians might consider treating subclinical hypothyroid patients with thyroid hormone replacement therapy prior to starting statin treatment to reduce the risk of developing DM.Diabetes Care September 2015;38: 1657-1664

E-042

MOXIFLOXACIN-INDUCED QTC PROLONGATION IN HEALTHY JAPANESE AND CAUCASIAN VOLUNTEERS: A DIRECT COMPARISON OF ETHNIC DIFFERENCES IN A THOROUGH QTC STUDY.

R. Kleiman[1], J. Morganroth[1], Y. Wang[2]; [1]ERT, Philadelphia, PA, [2]US Food and Drug Administration, Silver Spring, MD.

BACKGROUND: This study investigated whether moxifloxacin-induced QTc prolongations in Japanese and Caucasian healthy male volunteers differed significantly.

METHODS: A two period, randomized, crossover study using ICH-E14-compliant thorough QT study methods compared QTcF placebo-corrected changes from baseline (ΔΔQTcF) and concentration-effect relationships following administration of placebo and 400 mg moxifloxacin in 40 subjects from each ethnic group. The point estimates of ΔΔQTcF for each population were calculated at a geometric mean Cmax of moxifloxacin using a linear mixed effects model. The concentration-effect slopes of the two populations were also compared. Equivalence was concluded if the 2-sided 90% confidence interval of the difference in ΔΔQTcF was contained within -5 ms to +5 ms limits and the ratio of the slopes was between 0.5 and 2.RESULTS: There were no statistically significant differences between the two populations studied for moxifloxacin Cmax (3.27 ± 0.6 vs 2.98 ± 0.7 µg/mL), ΔΔQTcF (9.63 ± 1.15 vs 11.46 ± 1.19 ms at Cmax of 3.07 µg/mL) and concentration-response slopes (2.58 ± 0.62 vs 2.34 ± 0.64 ms/µg/mL). The difference inΔQTcF of -1.8 (90% CI -4.6, 0.9) and the ratio of the slopes (1.1) were within pre-specified equivalence limits.
CONCLUSION: Moxifloxacin-induced QTc prolongation did not differ significantly between Japanese and Caucasian subjects.

E-043

BENEFITS OF CENTRALIZED ECG ANALYSIS IN CLINICAL ONCOLOGY STUDIES.

R. Kleiman, J. Litwin, J. Morganroth; ERT, Philadelphia, PA.

BACKGROUND: Many clinical trials of investigational oncologic agents utilize electrocardiogram (ECG) machine measurements of QTc for inclusion/exclusion and dosing decisions, though their reliability in this setting has not been established.
METHODS: We compared the digital ECG machine QTc measurements with those obtained by a centralized ECG core lab on more than 270,000 consecutive ECGs collected from 299 clinical oncology trials.
RESULTS: The mean difference between the ECG machine measurements and the central measured QTcF was 1.8 + 15.7 milliseconds. In addition, 29.7% of ECGs with an ECG machine-measured QTcF #gt 450 milliseconds had a centrally measured QTcF #lt 450 milliseconds, 44.6% of ECGs with an ECG machine-measured QTcF #gt 470 milliseconds had a centrally measured QTcF #lt 470 milliseconds, and 77.2% of ECGs with an ECG machine-measured QTcF #gt 500 milliseconds had a centrally measured QTcF #lt 500 milliseconds. The likelihood of a large discrepancy between the ECG machine and centrally measured value for QTcF increased at both the high and low ends of the range of ECG machine QTcF measurements.
CONCLUSION: While on average ECG machine-measured QTcF values were very similar to the central core lab measurements, there were very significant discrepancies which will have important implications for patient recruitment for clinical oncology trials as well as for patient safety during dosing with new oncologic agents. Reliance on ECG machine QTc measurements during clinical oncology trials may lead to unnecessary exclusion of patients as well as unneeded treatment interruptions.

E-044

SAFE LONG-TERM SORAFENIB THERAPY IN HEPATOCELLULAR CARCINOMA PATIENTS REQUIRES MONITORING OF SERUM LEVELS OF SORAFENIB AND ITS N-OXIDE: A PILOT STUDY.

M. Shimada[1], H. Okawa[2], Y. Kondo[3], T. Maejima[4], Y. Kataoka[4], K. Hisamichi[4], M. Maekawa[4], M. Matsuura[4], Y. Jin[5], T. Shimosegawa[3], N. Mano[4]; [1]Tottori University Hospital, Yonago, Japan, [2]Department of Clinical Pharmacy, Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, Japan, [3]Department of Gastroenterology, Graduate School of Medicine, Tohoku University, Sendai, Japan, [4]Department of Pharmaceutical Sciences, Tohoku University Hospital, Sendai, Japan, [5]Division of Nursing, Tohoku University Hospital, Sendai, Japan.

BACKGROUND: The oral multi-kinase inhibitor sorafenib is offered before palliative care to patients with advanced hepatocellular carcinoma (HCC). Due to adverse effects, 20% of patients discontinue sorafenib within 1 month. A safety information letter by the Ministry of Health, Labour and Welfare of Japan states that signs of serious adverse effects were observed within 1 week of initial administration in HCC patients. Pharmacokinetic data for sorafenib early in treatment might help prevent adverse effects.
Our aim is to identify pharmacokinetic predictors of sorafenib discontinuation due to adverse effects, and to administer sorafenib longer.
METHODS: Twenty-five patients with hepatocellular carcinoma (HCC) taking sorafenib fell into two groups: patients with dosage reduction or discontinuation versus maintained dosage for 1 month after initial administration (n=8 vs. 17). We evaluated early sorafenib accumulation as the area under the curve for sorafenib and its *N*-oxide during days 1–7 (AUCsorafenib and AUC*N*-oxide) and compared these values between groups.
RESULTS: AUC*N*-oxide and AUC*N*-oxide/AUCsorafenib (AUC ratio) were significantly higher in the dosage reduction/discontinuation group (P=0.03, P=0.002). Receiver operating characteristics analysis showed that AUC*N*-oxide and AUC ratio were reliable predictors of adverse effects. Based on cut-offs of 2.0 μg·day/mL for AUC*N*-oxide and 0.13 for AUC ratio, progression-free survival was significantly longer in patients with AUC*N*-oxide ≤2.0 μg·day/mL (P=0.005, log-rank test).
CONCLUSION: Controlling AUC*N*-oxide values to ≤ 2.0 μg·day/mL and AUC ratio to ≤ 0.13 may prevent early serious adverse effects with sorafenib and allow for longer therapy duration.

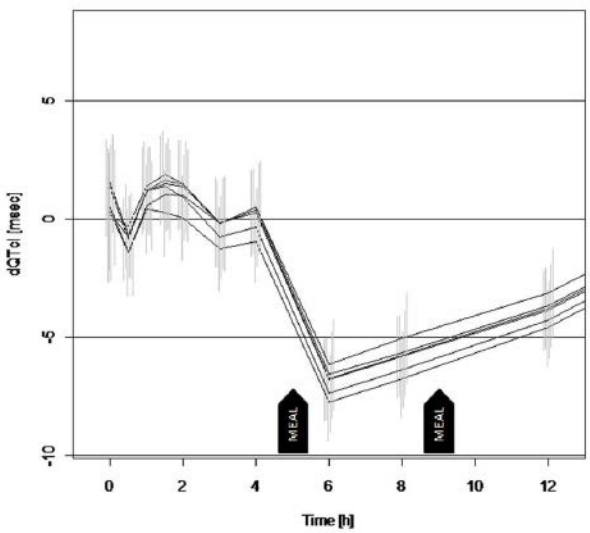
E-045

THE EFFECTS OF A MEAL ON QTC TO DEMONSTRATE ECG ASSAY SENSITIVITY.

J. Taubel[1], G. Ferber[2], U. Lorch[1], D. Wang[3], M. Sust[4], A. Camm[1]; [1]Richmond Pharmacology Ltd, London, United Kingdom, [2]Statistik Georg Ferber GmbH, Riehen, Switzerland, [3]Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [4]ESTEVE Research & Development, Barcelona, Spain.

BACKGROUND: iQT studies are not solely designed to assess QTc changes. The small sample size and their ability to show small QTc changes still raises concerns. To reduce the likelihood of false negatives, moxifloxacin been used to confirm assay sensitivity in an iQT study, thus showing a greater variability in the effect when compared with TQT studies. The effect of a standardised meal on QTc has been considered as an alternative method.

METHODS: A concentration effect analysis was applied to a 4-way crossover Phase I study in order to investigate the effect of escalating single doses of E-52862. Each period consisted of a placebo baseline ECG day and treatment day. Standardised meals were served and ECGs were recorded.
RESULTS: All slopes were negative for E-52862. The sensitivity was confirmed by a shortening of QTcF of 8.1 ms (90%CI 10.4, 5.9) 1 h and 7.2 ms (90%CI 9.4, 5.0) 3 h after food intake.
CONCLUSION: This study shows that E-52862 has no QTc prolonging effects. The food effects on QTc confirmed assay sensitivity and reproducibility of the method. Similarly to moxifloxacin, an iQT setting also increased variability in the effect indicating that the robustness of the 2 methods is comparable.



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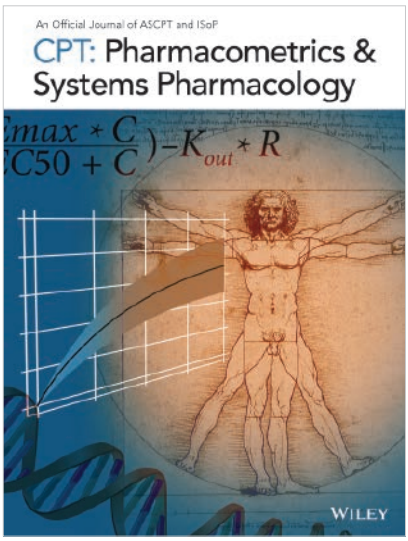

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