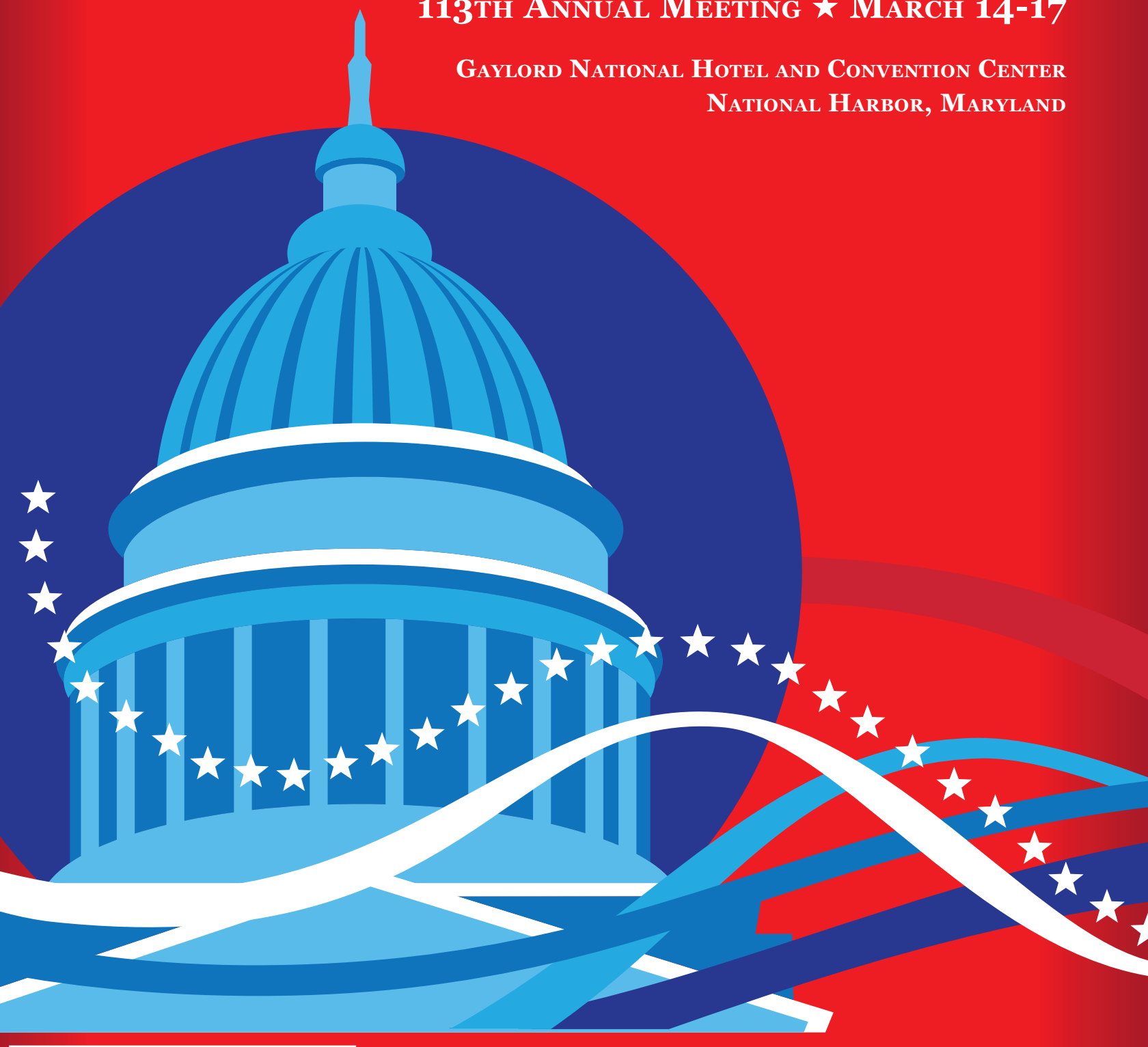
ASCPT 2012 ANNUAL MEETING
PROGRAM

American Society for Clinical Pharmacology and Therapeutics

113th Annual Meeting ★ March 14-17

Gaylord National Hotel and Convention Center
National Harbor, Maryland



ASCPT 2012 ANNUAL MEETING

March 14-17 ★ National Harbor, Maryland

WELCOME

to the ASCPT 2012 Annual Meeting

Dear Colleague:

Welcome to Maryland and to the 2012 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics (ASCPT). As the premier organization in the field of clinical pharmacology, ASCPT is proud to offer you an outstanding scientific program, a robust roster of internationally renowned speakers, and abundant networking opportunities.

Consistent with the Society's strategic plan, ASCPT seeks to increase our joint programming and coordinated scientific efforts with colleague organizations. We extend a warm welcome to our colleagues who attended the two preconference programs jointly sponsored by ASCPT. The second workshop of the International Transporter Consortium (ITC), and the American Society of Pharmacometrics (ASoP) Decision Making workshop. In addition, we also welcome our colleagues from the Food and Drug Administration who hosted their Clinical Pharmacology and Pharmaceutical Sciences Advisory Committee Meeting at the ASCPT meeting.

The 2012 scientific program includes three outstanding State of the Art lectures by Stephen Spielberg, MD, PhD, Deputy Commissioner, US Food and Drug Administration, discussing an interactive model for the future of therapeutics; Harvey Fineberg, MD, PhD, President of the Institute of Medicine, discussing the impact of the Institute of Medicine health policy; and Francis Collins, MD, PhD, Director, National Institutes of Health, discussing new partnerships to accelerate translation. This year's featured speakers include Mary Jeanne Kreek, MD, Rockefeller University and Alex Sparreboom, PhD, St. Jude Children's Research Hospital.

We are pleased to bring you new programming this year, including the Ask the Editors session on Thursday, March 15 from 2:45 pm - 3:45 pm. This is your opportunity to meet our new editor-in-chief of *CPT: Pharmacometrics & Systems Pharmacology* as well as Scott Waldman, MD, PhD, Editor-in-Chief of *Clinical Pharmacology & Therapeutics*. This highly interactive session will provide new information on both journals and answer any questions you may have on either journal. Also new this year is the Career Bootcamp, a half-day program providing career consultation and mentoring opportunities for trainees and junior faculty. You won't want to miss this outstanding program.

ASCPT will honor a number of outstanding individuals for their work in advancing clinical pharmacology, improving patient care, and their contributions to ASCPT. The 2012 honorees are D. Craig Brater, MD; Malcolm Rowland, DSc, PhD; Scott Waldman, MD, PhD; Peter Honig, MD, MPH; Carl Peck, MD; Michael Maitland, MD, PhD; and Janice Schwartz, MD.

Join us at the Town Hall Session which will feature a host of ASCPT members leading roundtable discussions. As a member of ASCPT, this is your opportunity to meet the leadership of ASCPT and discuss issues of interest. This year table facilitators will include members of the ASCPT Board of Directors, CPT Editorial Team, and Scientific Section and Committee Chairs. We hope you will take the opportunity to participate in this session.

Visit the poster and exhibit hall where more than 300 scientific posters will be presented and will be available for viewing, Thursday, March 15 through Saturday, March 17. In addition, a wide range of exhibitors will be in attendance, eager to share their clinical pharmacology related products and services with attendees.

This year, ASCPT is proud and pleased to have the largest number of attendees from outside of North America. We wish to offer a very warm welcome to all of our international attendees.

Let me take this opportunity to thank the chairperson of this year's Scientific Program Committee, John Wagner, MD, PhD, as well as the entire Committee for putting together an outstanding scientific program.

Finally, I encourage everyone to make the most of your time here and thank you for attending the 2012 ASCPT Annual Meeting!

Sincerely,

Richard L. Lalonde, PharmD
President

SCHEDULE AT A GLANCE

TUESDAY • MARCH 13

12n	12:30	1pm	1:30	2pm	2:30	3pm	3:30	4pm	4:30	5pm
ASCPT Annual Meeting Registration & ASCPT Central Open Maryland Foyer										

WEDNESDAY • MARCH 14 AM

6:30	7am	7:30	8am	8:30	9am	9:30	10am	10:30	11am	11:30	12n
	ASCPT Annual Meeting Registration & ASCPT Central Open Maryland Foyer										
		FDA Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting Maryland C									
			CPT Editorial Team Meeting *(by invitation only)* Maryland 1								

WEDNESDAY • MARCH 14 PM

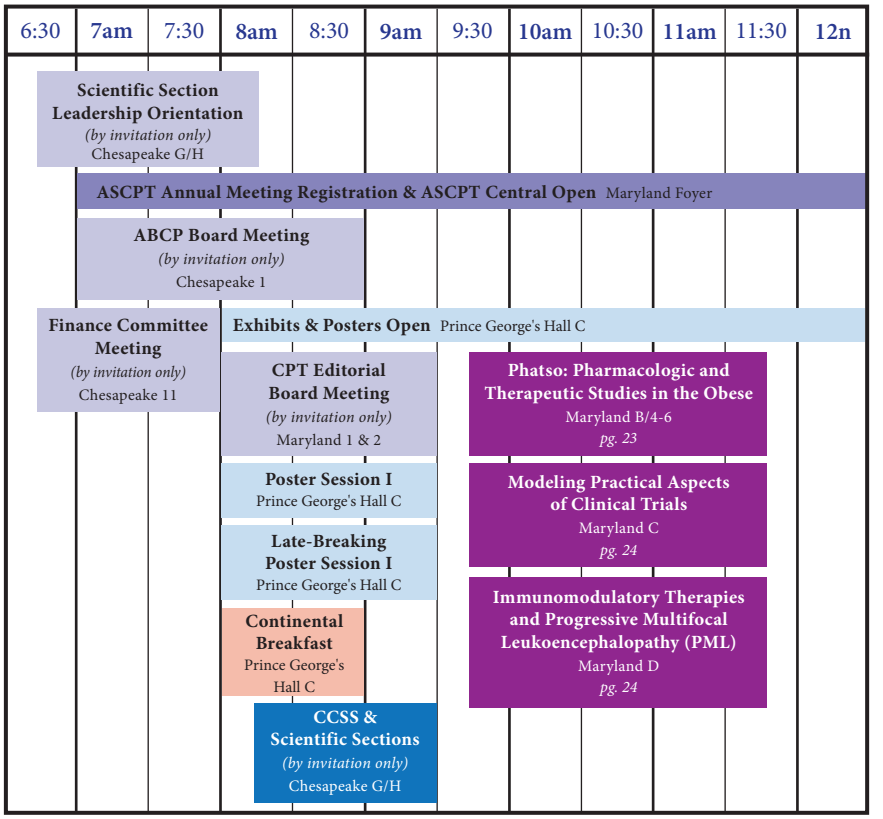
12n	12:30	1pm	1:30	2pm	2:30	3pm	3:30	4pm	4:30	5pm	5:30	6pm	6:30	7pm	7:30	8pm
ASCPT Annual Meeting Registration & ASCPT Central Open Maryland Foyer																
FDA Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting Maryland C																
ASCPT Board of Directors and CPT Editorial Team Lunch *(by invitation only)* Maryland 2			**New Member Welcome** Chesapeake D/E			**Opening Session** Maryland B/4-6 *pg. 20*		**State of the Art Lecture** Maryland B/4-6 *pg. 21*			**Showcase of Top Trainee Abstracts** Prince George's Hall C Foyer *pg. 22*	**Opening Reception** Prince George's Hall C				
				Award Reception *(by invitation only)* Maryland 3								**Exhibit Hall Opens** Prince George's Hall C				

Schedule at a Glance Key

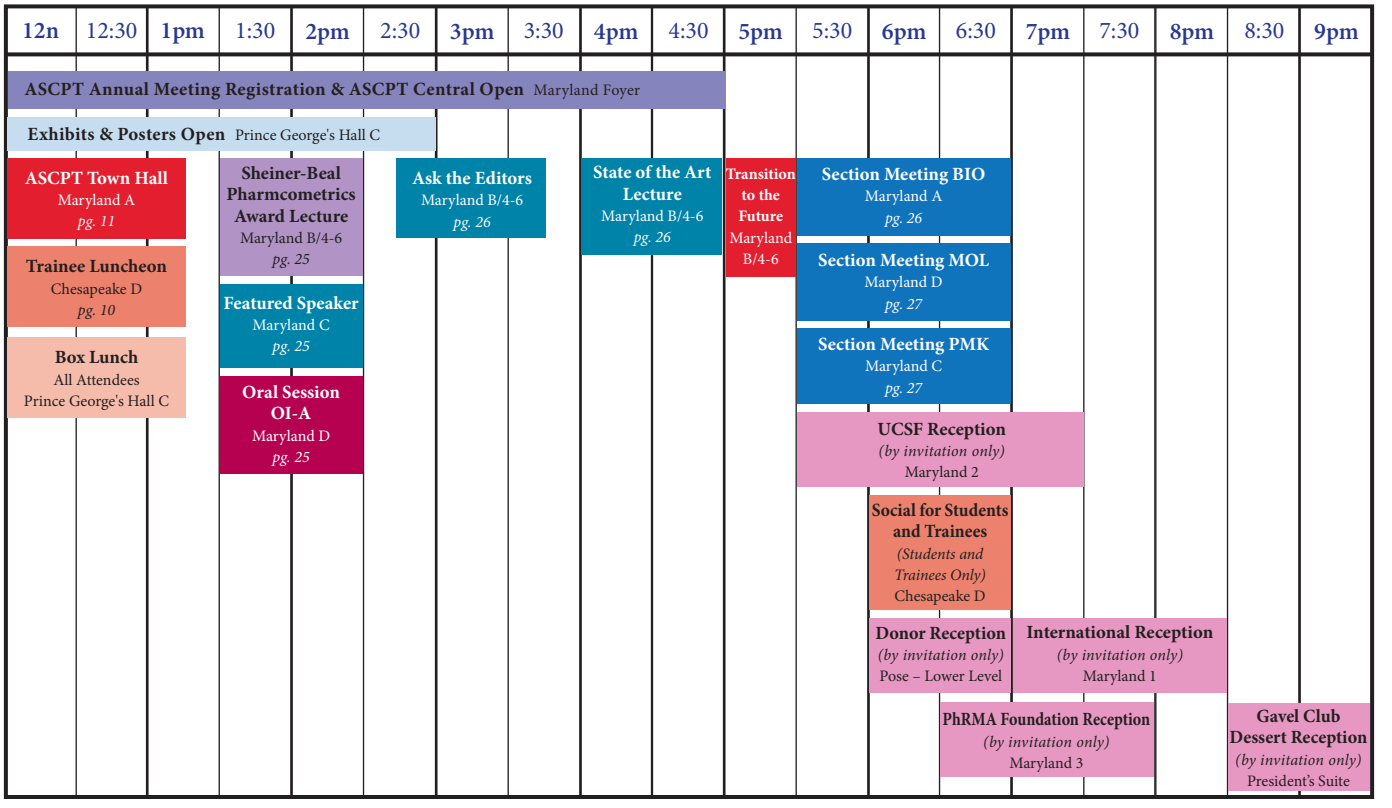
- ASCPT Central & Registration
- Award Lecture
- Committee Meeting
- Exhibits/Posters/Late-Breaking Posters
- Meal/Break
- Oral/Late-Breaking Session
- Reception
- Scientific Section
- Special Event
- State of the Art / Featured Speaker / Special Session
- Symposium
- Trainee & Student Event
- Workshop

SCHEDULE AT A GLANCE

THURSDAY • MARCH 15 AM

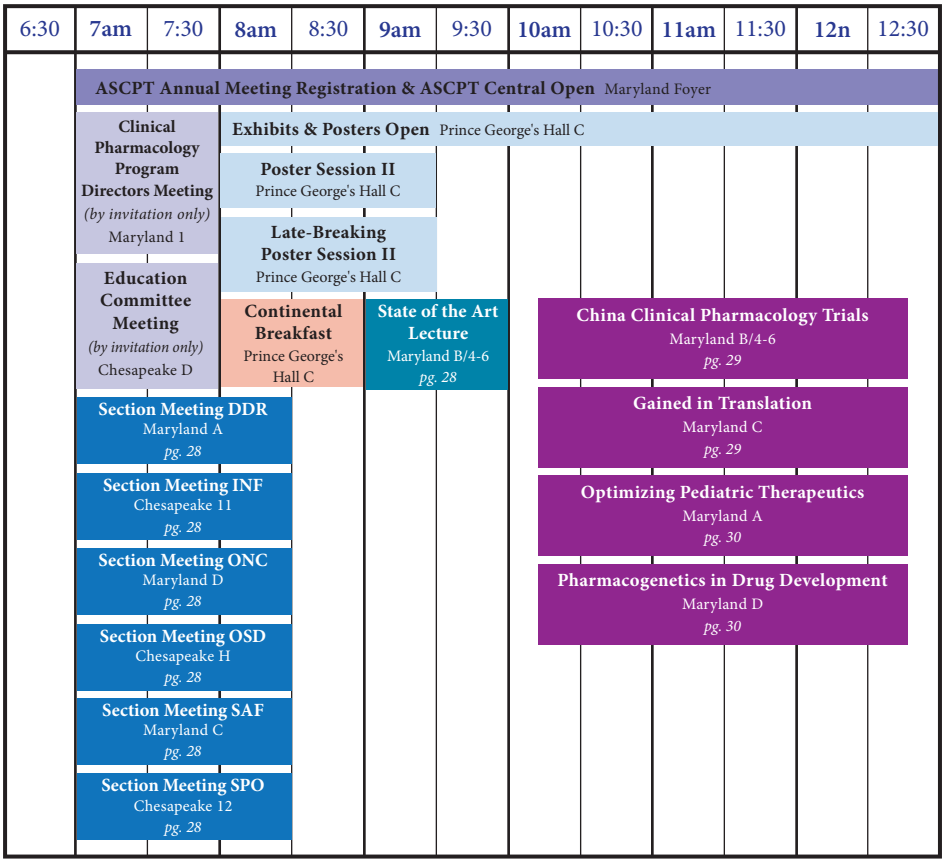


THURSDAY • MARCH 15 PM

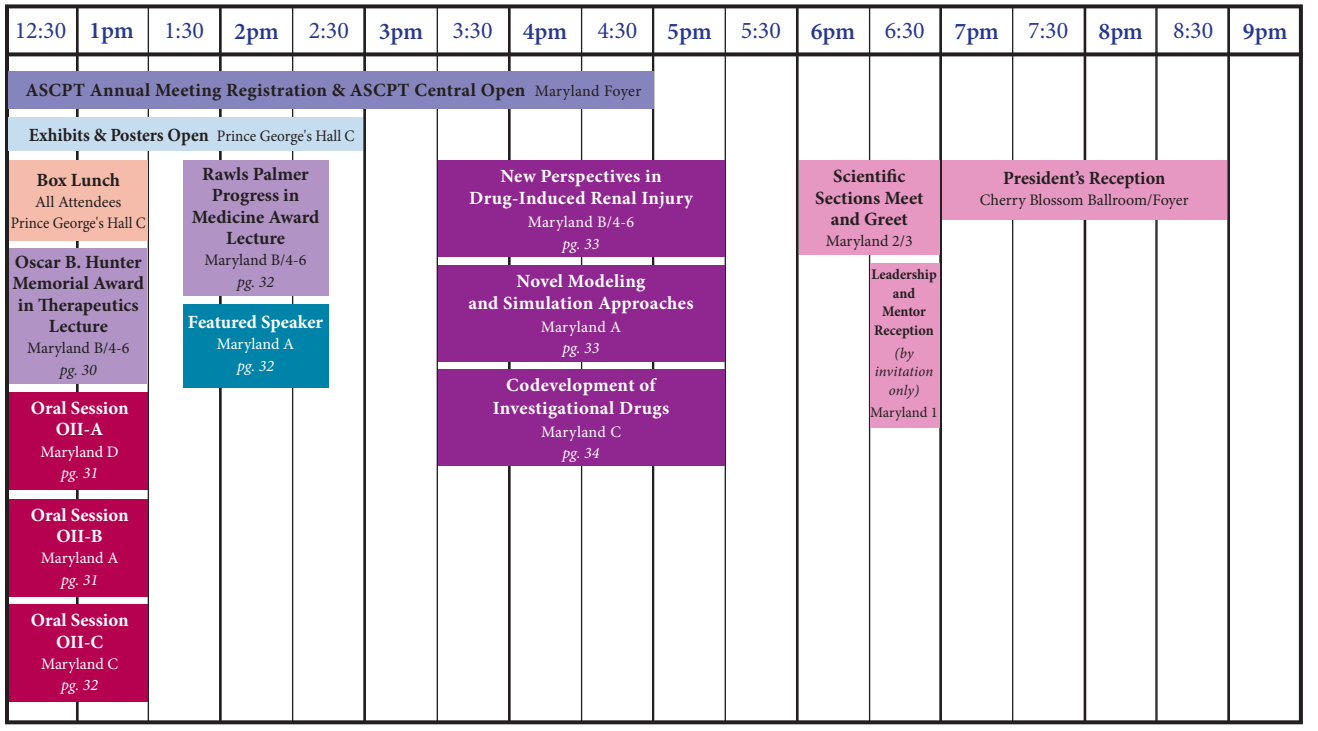


SCHEDULE AT A GLANCE

FRIDAY • MARCH 16 AM

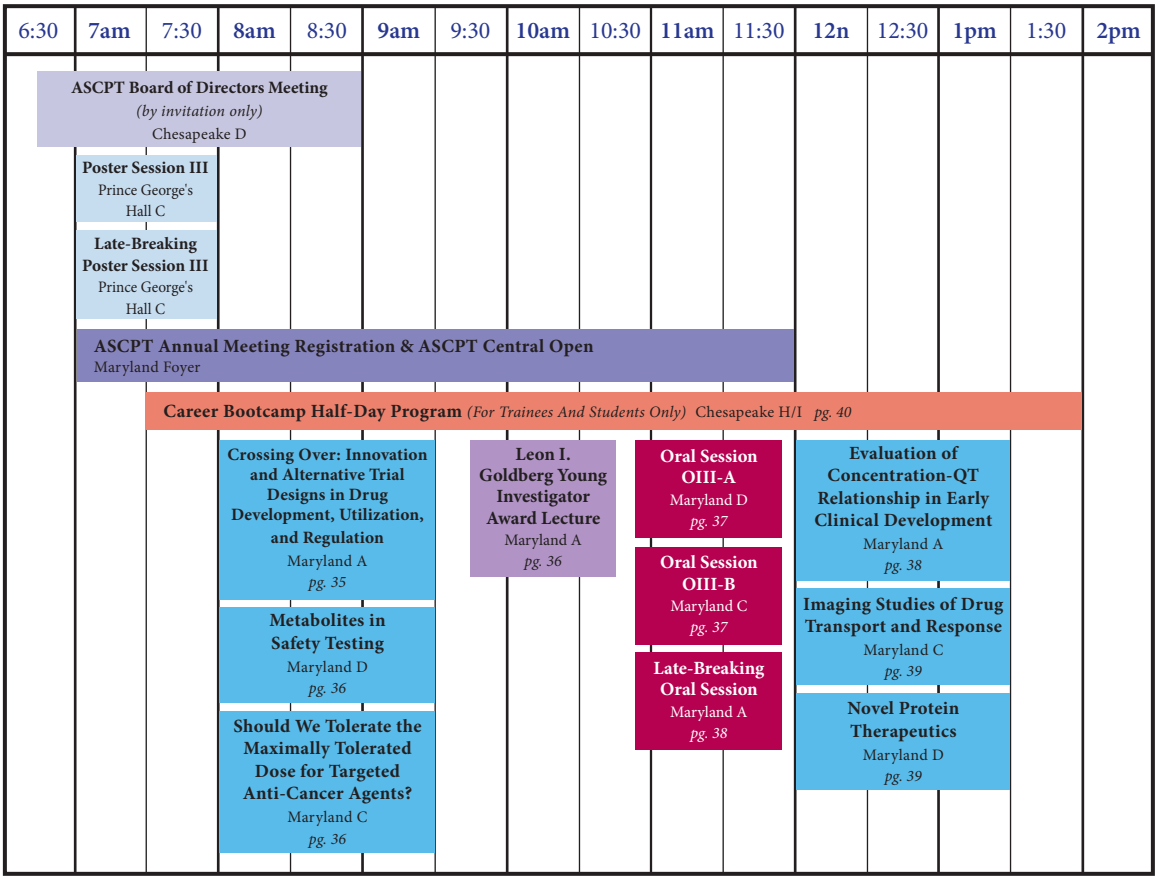


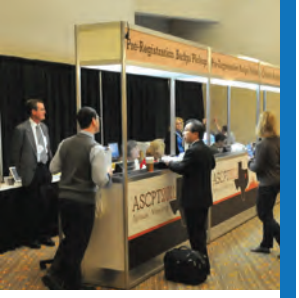
FRIDAY • MARCH 16 PM



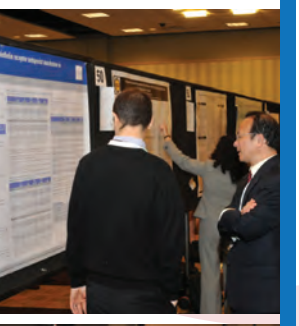
SCHEDULE AT A GLANCE

SATURDAY • MARCH 17










EVENTS & HIGHLIGHTS

@ASCPT_ClinPharm While at the meeting, stay up-to-date with session updates and schedule changes by following ASCPT on Twitter.

WEDNESDAY • MARCH 14

New Member Welcome

1:30 pm - 2:30 pm • Chesapeake D/E

This is a great opportunity to meet other new members and learn how to get involved in the Society. Find out more about your member benefits and how to get the most out of the ASCPT Annual Meeting.

David Goldstein and Jason Morrow Trainee Awards

3:00 pm • Maryland B/4-6


The David Goldstein and Jason Morrow Trainee Awards recognize top scoring trainee abstracts. The awards are named in honor of David J. Goldstein, MD, PhD, and Jason D. Morrow, MD, longtime ASCPT members who were committed to trainees and the future of the discipline of clinical pharmacology.

The 2012 recipients of the David Goldstein Trainee Award are Jason Sprowl, PhD, Cynthia S. Lancaster, PhD, and Xu Han. The 2012 recipient of the Jason Morrow Trainee Award is Qiping Feng, PhD. All recipients will be recognized during the Opening Session.

State of the Art Lecture

4:00 pm - 5:00 pm • Chesapeake D/E

Join us as Stephen P. Spielberg, MD, PhD, ASCPT Past President and newly named Deputy Commissioner for Medical Products and Tobacco of the US Food and Drug Administration, will be delivering the lead-off State of the Art Lecture at the opening of the 2012 Annual Meeting. Dr. Spielberg's presentation is entitled "Basic, Applied, Translational, and Regulatory Science: An Interactive Model for the Future of Therapeutics."

Showcase of Top Trainee Abstracts

5:30 pm - 6:00 pm • Prince George's Exhibit Hall C Foyer

View the top trainee abstracts submitted by the 2012 Presidential Trainee Award recipients while supporting your peers and networking with colleagues.

Opening Reception and Exhibits

6:00 pm - 8:00 pm • Prince George's Exhibit Hall C

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

Sponsored by Pfizer

THURSDAY • MARCH 15

ASCPT Town Hall

Noon - 1:15 pm • Maryland A

The Town Hall session has been reformatted to encourage open discussion on topics important to all members of the Society. All members are invited to participate in round table discussions led by the ASCPT Board of Directors, CPT Editors, and Section and Committee Chairs.

See page 11 for full details.

Trainee Luncheon: Careers in Clinical Pharmacology

Noon - 1:15 pm • Chesapeake D

Back by popular demand, the Trainee Luncheon allows trainees and students to connect with established clinical pharmacologists, colleagues, and peers in roundtable discussions. Trainees and students will have the opportunity to converse about their potential career paths and seek advice from leaders and experts in the academia, consulting, industry, and government sectors of clinical pharmacology. See page 10 for full details. *Advance registration required.*

Special Session

Ask the Editors

2:45 pm - 3:45 pm • Maryland B/4-6

All attendees are invited to participate in this special session where the latest information about *Clinical Pharmacology & Therapeutics* will be presented and ASCPT's new journal, *CPT: Pharmacometrics & Systems Pharmacology*, will be discussed. The Ask the Editors session will provide a forum for member interaction with the editorial leadership of ASCPT's journals to discuss the future of these two publications, and plans to showcase even more cutting-edge research.

Transition to the Future

5:00 pm - 5:15 pm • Maryland B/4-6

Please join us as Kathleen M. Giacomini, PhD, receives the Presidential Gavel as the incoming President of ASCPT.

Russ B. Altman, MD, PhD, will be introduced as the new President-Elect of ASCPT. Witness these two outstanding scientists take their place as the new vanguard of leadership for ASCPT.

FRIDAY • MARCH 16

Scientific Sections Meet and Greet

6:00 pm - 7:00 pm • Maryland 2/3

In a social setting, this is an ideal opportunity to network with the members of your Scientific Section. Sections will discuss goals for the coming year including reviewers for the 2013 Annual Meeting as well as ideas for symposia, workshops and abstract submissions. Scientific Sections are the primary forum for member exchange and communication. They facilitate growth within the field of interest by promoting interaction among members.

President's Reception

7:00 pm - 9:00 pm • Cherry Blossom Ballroom/Foyer

Join your colleagues and friends for an enjoyable evening of networking over food and beverages on the last night of the 2012 Annual Meeting. You won't want to miss this event as ASCPT expresses its appreciation of Richard L. Lalonde, PharmD, for his service as President of ASCPT.

Sponsored by CLINILABS www.clinilabs.com

SATURDAY • MARCH 17

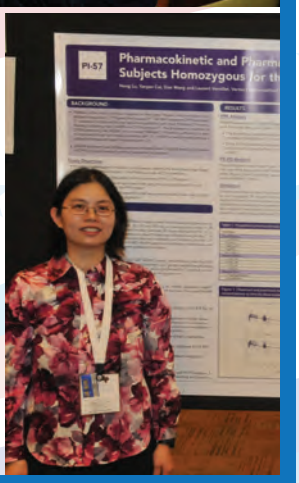
Trainees & Students: Career Bootcamp Half-Day Program

7:30 am - 2:00 pm • Chesapeake H/I

Get your early career in shape! ASCPT has developed a half-day session to provide take-home points and prompt questions that stimulate discussion and mentoring opportunities exclusively for trainees and junior faculty. Some of the session content will include how to find a mentor, a five-year plan to jump-start your career, negotiating a starting package, grants 101, and meet the NIH.

See page 40 for full program details. *Advance registration required.*



TRAINEE LUNCHEON

Thursday, March 15 | Noon-1:15pm | Chesapeake D

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

In support of ASCPT's initiative to build capacity through the development, promotion, recognition, and support of career development programs for junior and mid-career investigators, ASCPT is pleased to offer the highly successful Trainee Luncheon, again. This luncheon – open only to trainees – is a roundtable discussion for students and fellows to meet with established clinical pharmacologists to network and to discuss potential career paths. This Luncheon is a perfect complement to the **ASCPT Career Bootcamp** being offered on **Saturday March 17, 2012**.

Trainee participants will rotate between tables to allow for multiple facilitator discussions. Discussions are designed to center around aspects of a career in clinical pharmacology, but are informal and largely driven by trainees' questions. Faculty listed will be seated at tables bearing their names and type of employment sector they represent. A short summary of each facilitator's background and current position will be distributed to all trainees' signed up for the luncheon.

Trainee Luncheon Facilitators

Bridgette L. Jones, MD
and Kathleen A. Neville, MD, MS

Industry

Rebecca Blanchard, PhD • Merck & Co.
Ying-Jun Cao, MD, PhD • Astellas Pharmaceutical
Stephen D. Hall, PhD • Eli Lilly and Co.
Joan Korth-Bradley, PharmD • Pfizer
Masako Nakano, MD, PhD • Eli Lilly and Co.
Donald Stanski, MD • Novartis Pharma, AG
Aubrey Stoch, MD • Merck & Co.

Consulting

Joann L. Data, MD, PhD
Gary Novack, PhD

Government

Gilbert Burckart, PharmD
US Food and Drug Administration

Shiew-Mei Huang, PhD
US Food and Drug Administration

Kellie Reynolds, PhD
US Food and Drug Administration

Issam Zineh, PharmD, MPH
US Food and Drug Administration

Academia

Zeruesenay Desta, PhD
Indiana University School of Medicine

Jean D. Gray, MD, FRCPC
Dalhousie University

Patricia Slattum, PharmD, PhD, CGP
Virginia Commonwealth University

Michael Spigarelli, MD, PhD
University of Utah

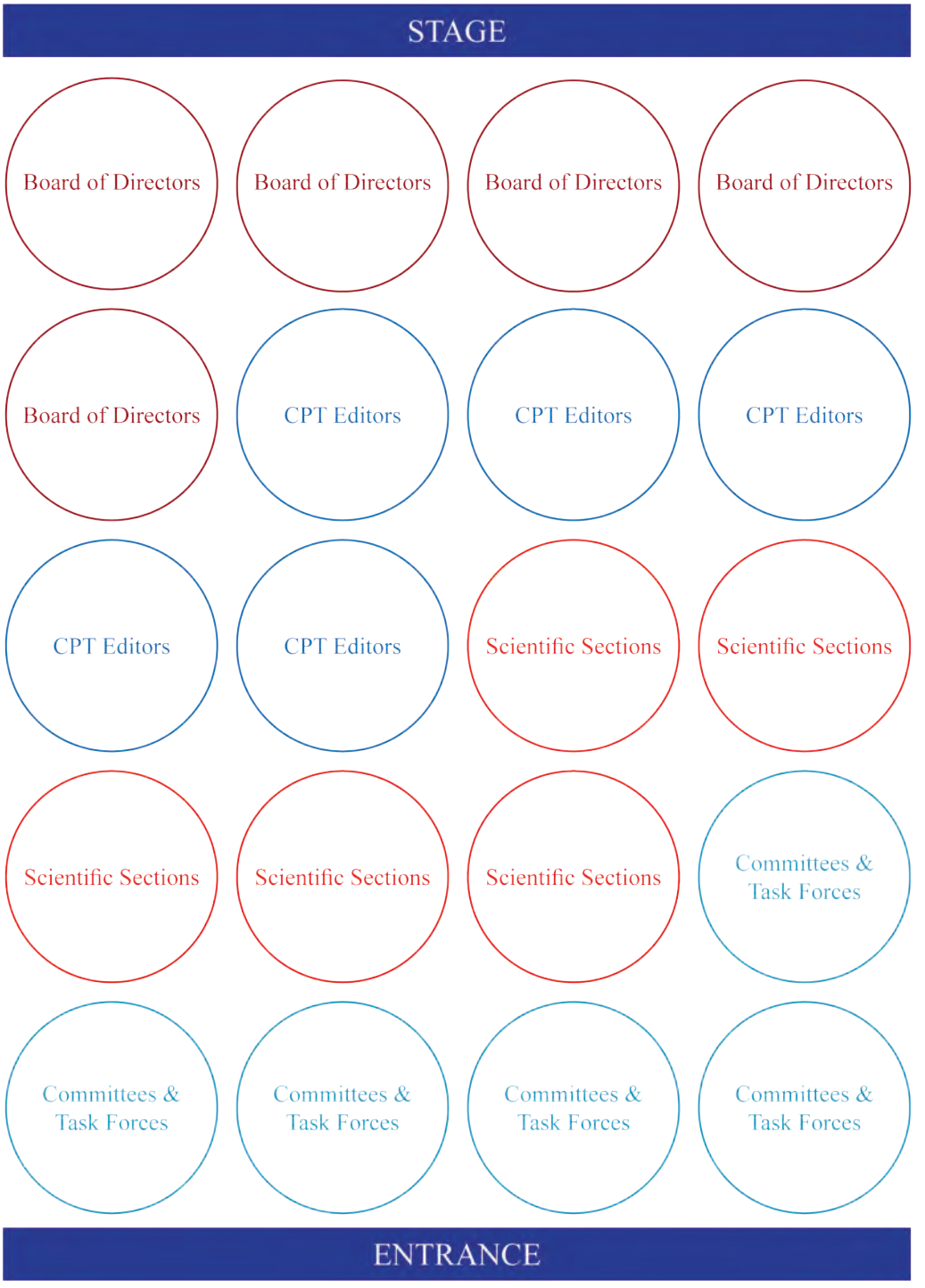
Janice Sullivan, MD
Kosair Children's Hospital-University of Louisville

John van den Anker, MD, PhD
Children's National Medical Center

TOWN HALL MEETING

Thursday, March 15 | Noon-1:15pm | Maryland A

The ASCPT Town Hall session has been reformatted to encourage open discussion on topics important to all members of the Society. All members are invited to participate in round table discussions led by ASCPT volunteer leaders. The room will be set up with at least two volunteer leaders representing the following at each table:



AWARD RECIPIENTS

2012 Henry W. Elliott Distinguished Service Award

Peter K. Honig, MD, MPH

Head of Global Regulatory Affairs
AstraZeneca
Wilmington, DE

2012 Gary Neil Prize for Innovation in Drug Development

Carl C. Peck, MD

Adjunct Professor
Center for Drug Development Science
University of California, San Francisco
San Francisco, CA

2012 Leon I. Goldberg Young Investigator Award

Michael L. Maitland, MD, PhD

Assistant Professor
Department of Medicine
University of Chicago Medical Center
Chicago, IL

2012 William B. Abrams Award for Geriatric Clinical Pharmacology

Janice B. Schwartz, MD

University of California,
San Francisco
San Francisco, CA

2012 Rawls-Palmer Progress in Medicine Award

Scott A. Waldman, MD, PhD

Samuel M.V. Hamilton Professor and Chair
Departments of Pharmacology and Experimental Therapeutics
Thomas Jefferson University
Philadelphia, PA

2012 Sheiner-Beal Pharmacometrics Award

Malcolm Rowland, DSc, PhD

University of Manchester
Manchester, United Kingdom

2012 Oscar B. Hunter Memorial Award in Therapeutics

D. Craig Brater, MD

Dean and Walter J. Daly Professor
Indiana University School of Medicine
Indianapolis, IN

2012 ASCPT Mentor Award

Arthur J. Atkinson, Jr., MD

Northwestern University
Evanston, IL

2011 ASCPT Young Investigator Award Top Junior Faculty

Landry Kamdem Kamdem, PharmD, PhD

Assistant Professor
Department of Pharmaceutical Sciences
Harding University College of Pharmacy
Searcy, AR

2011 ASCPT Young Investigator Award Top Fellow

Laura J. Wozniak, MD

Pediatric Gastroenterology Fellow
Department of Pediatrics
University of California, Los Angeles
Los Angeles, CA

2011 Top Membership Recruiter

Gregory L. Kearns, PharmD, PhD

Chairman
Children's Mercy Hospital and Clinics
Kansas City, MO

2011 Membership Recruiter Honorable Mention

Jason Karnes, PharmD

University of Florida
Gainesville, FL

2012 David J. Goldstein Trainee Award Recipient

Jason Sprowl, PhD

Postdoctoral Fellow
St. Jude Children's Research Hospital
Memphis, TN

2012 David J. Goldstein Trainee Award Recipient

Cynthia S. Lancaster, PhD

St. Jude Children's Research Hospital
Memphis, TN

2012 David J. Goldstein Trainee Award Recipient

Xu Han

Department of Pharmacology and Toxicology
Indiana University School of Medicine
Indianapolis, IN

2012 Jason Morrow Trainee Award Recipient

Qiping Feng, PhD

Vanderbilt University
Nashville, TN

ASCPT PRESIDENTIAL TRAINEE AWARD RECIPIENTS

Jason Sprowl, PhD
St. Jude Children's Research Hospital

Cynthia S. Lancaster, PhD
St. Jude Children's Research Hospital

Xu Han
Indiana University School of Medicine

Qiping Feng, PhD
Vanderbilt University

Daniela Conrado, MS
University of Florida

Manuela Vieira, PhD
US Food and Drug Administration

SeungHwan Lee, MD
Seoul National University College of Medicine and Hospital

J. Kevin Hicks, PharmD, PhD
St. Jude Children's Research Hospital

Jessica Lam, BSc
Hospital for Sick Children

Virginie Ancrenaz, PhD Student
Geneva University Hospitals

Hylke de Jonge, MD
University Hospitals Leuven

Teodora Pene Dumitrescu, PhD
University of North Carolina

Geert W. t' Jong, MD, PhD
Hospital for Sick Children

PHRMA FOUNDATION AWARDS

2012 Awards in Clinical Pharmacology

2012 Award in Excellence in Clinical Pharmacology

Andre Terzic, MD, PhD
Director,
Center for Regenerative Medicine
Mayo Clinic
Rochester, MN

2012 Paul Calabresi Medical Student Fellowship

Jenny Barker
University of Texas Southwestern Medical Center
Department of Internal Medicine
Dallas, TX

Elizabeth Dong
Vanderbilt University
Department of Pharmacology, Chemistry and Biomedical Informatics
Nashville, TN

2012 Faculty Development Award

Timothy J. Nelson, MD, PhD
Mayo Clinic
Rochester, MN

2011 DONORS

LEGACY SOCIETY

Arthur J. Atkinson, Jr., MD

Carl C. Peck, MD

Joann L. Data, MD, PhD & Herman Cantrell

Estate of Berenda Abrams

SOCIETY OF FOUNDERS

Lawrence J. Lesko, PhD

Michael H. Skinner, MD, PharmD

Louis R. Cantilena, Jr., MD, PhD

WILLIAM B. ABRAMS AWARD IN GERIATRIC CLINICAL PHARMACOLOGY

Patricia W. Slattum, PharmD, PhD, CGP

John F. Mullane, MD, PhD, JD

Edward A. Carr, Jr., MD

GARY NEIL PRIZE FOR INNOVATION IN DRUG DEVELOPMENT

Terrence F. Blaschke, MD

Michael H. Skinner, MD, PharmD

HENRY W. ELLIOTT DISTINGUISHED SERVICE AWARD

Edward A. Carr, Jr., MD

TRAINEE AND SCIENTIFIC AWARDS FUND

Raymond J. Hohl, MD, PhD

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

Jean D. Gray, MD, FRCPC

Jean T. Barbey, MD

Richard C. Brundage, PharmD, PhD

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John Mendelson, MD

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Richard M. Weinshilboum, MD

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Brian L. Strom, MD, MPH

Edward A. Carr, Jr., MD

ASCPT/FDA ABRAMS LECTURE

John F. Mullane, MD, PhD, JD

Carl C. Peck, MD

Lei Zhang, PhD

Sue-Chih H. Lee, PhD

SHEINER-BEAL AWARD

Kathleen M. Giacomini, PhD

Bing Wang, PhD

Helen S. Pentikis, PhD

BUILDING FUND

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

Shiew-Mei Huang, PhD

Kathleen Uhl, MD, FAAFP

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Joann L. Data, MD, PhD & Herman Cantrell

MATCHING GIFTS

Pfizer Foundation Matching Gifts Program

Amgen Foundation

Merck Partnership for Giving

UNRESTRICTED GIFT

Arthur J. Atkinson, Jr., MD

Joann L. Data, MD, PhD & Herman Cantrell

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Sang-Goo Shin, MD, PhD

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Nancy A. Lass, MD

John F. Mullane, MD, PhD, JD

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In-Jin Jang, MD, PhD

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Michelle A. Rudek, PharmD, PhD

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Addison A. Taylor, MD, PhD

Kathleen M. Tornatore, PharmD

Donald R. Bennett, MD, PhD, MPH

Shinya Ito, MD

John Mendelson, MD

Carl C. Peck, MD

Michael Spigarelli, MD, PhD

Sean Hennessy, PharmD, PhD

Akira Asada, MD

Joseph C. Veltri, PharmD

ACKNOWLEDGEMENTS

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

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James J. Keirns, PhD
John Wagner, MD, PhD
Keith D. Wilner, PhD
Anne Zajicek, MD, PharmD

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

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Vice Chair
Christine Haller, MD

Immediate Past Chair
Kellie S. Reynolds, PharmD

President
Richard L. Lalonde, PharmD

President-Elect
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Donald R. Stanski, MD
Pieter van der Graaf, PharmD, PhD
Karthik Venkatakrishnan, PhD
Lei Zhang, PhD
Issam Zineh, PharmD

ASCPT would like to give special thanks to the leadership of the Coordinating Committee on Scientific Sections (CCSS) and recognize the Scientific Section Chairs for their dedicated leadership in support of section symposia, workshops, and other scientific endeavors.

CCSS Chair
Craig W. Hendrix, MD
(INF, PMK)

CCSS Vice Chair
Andrea Gaedigk, MS, PhD
(MOL, SPO)

CCSS Members
Maurice Emery, PharmD, PhD
(OSD Chair, PMK)

Kellie S. Reynolds, PharmD
(DDR, PMK)

Michelle A. Rudek, PharmD, PhD
(ONC Chair, MOL)

Michael Spigarelli, MD, PhD
(SPO Chair, MOL)

Scientific Section Chairs
Adriana S. Andrade, MD, MPH (INF)
Uwe Christians, MD, PhD (BIO)
Sean Hennessy, PharmD, PhD (SAF)
Masako Nakano, MD, PhD (DDR)
Virginia Schmith, PhD, FCP (PMK)
Issam Zineh, PharmD (MOL)

ACKNOWLEDGEMENTS

ASCPT would like to recognize the Scientific Awards Nominations Task Force for securing nominations for the 2012 Scientific Awards.

Chair
Robert E. Vestal, MD

Members
Hartmut Derendorf, PhD
David A. Flockhart, MD, PhD
Howard E. Greenberg, MD, MS, MBA
Stephen D. Hall, PhD
Armen P. Melikian, PharmD, PhD
Jae-Gook Shin, MD, PhD
Julia Stingl, MD

Board Liaison
Dhanesh K. Gupta, MD

ASCPT would like to acknowledge the Scientific Awards Selection Task Force for selecting the 2012 Scientific Award recipients from a robust and highly competitive roster of exceptional nominees.

Chair
Julie A. Johnson, PharmD

Members
Jerry Collins, PhD
Deanna L. Kroetz, PhD
David S. Lee, PharmD, PhD
Steve Ryder, MD
Sang-Goo Shin, MD, PhD
John T. Sullivan, MB, ChB, FRACP
Andre Terzic, MD, PhD

Board Liaison
Glenn Gormley, MD, PhD

ASCPT wishes to thank the abstract reviewers for their contributions to the 2012 ASCPT Annual Meeting.

Prajakta Badri, PhD
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Raymond J. Hohl, MD, PhD
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John Wagner, MD, PhD
David L. Wesche, MD, PhD
Jim Xiao, PhD
Claire Xu
Lei Zhang, PhD
Issam Zineh, PharmD

ASCPT would like to recognize its members who have achieved ten year incremental membership anniversaries and thank them for their continued efforts on behalf of the Society and their contributions to the field of clinical pharmacology. These individuals exemplify ASCPT as an organization that provides valuable benefits throughout the careers of its members.

GENERAL INFORMATION

ASCPT Annual Meeting Sponsor

American Society for Clinical Pharmacology and Therapeutics
528 North Washington Street
Alexandria, VA 22314

Phone 703.836.6981 • Fax 703.836.5223
Web www.ascpt.org

Registration Hours

Maryland Lobby

Tuesday, March 13	Noon – 5:00 pm
Wednesday, March 14	7:00 am – 8:00 pm
Thursday, March 15	7:00 am – 5:00 pm
Friday, March 16	7:00 am – 5:00 pm
Saturday, March 17	7:00 am – Noon

Badges

For security reasons, all Annual Meeting attendees ***MUST*** wear their badges at all times for admission to sessions, the poster and exhibit hall, and social events.

Ribbons

Ribbons are available at the Registration kiosk located in the Maryland Lobby. Please pick up the appropriate ribbons at the registration area.

Target Audience

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

ADA Compliance

ASCPT makes every effort to comply with the Americans with Disabilities Act.

ASCPT Ethics Statement

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

ASCPT Disclaimer Statement

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

Gather Digital Mobile Application

We're excited to announce that this year ASCPT has collaborated with Gather Digital to provide a mobile application for this event. Get up-to-the-minute information for the agenda, updates from the conference planner, speaker information, maps, exhibitor and sponsor details, an attendee list, and more.

An iPhone and iPad app are available in the iTunes app store. Search ASCPT and download the ASCPT 2012 Annual Meeting app. You can also access the app with your BlackBerry, Android or other smart phone. Simply point your mobile browser and bookmark http://ascpt2012.gatherdigital.com.

A feature of the mobile app is that you and other attendees have the option to send messages to each other. It's a great way to network with fellow attendees up to and during the event. You can also create a profile of yourself that other event attendees can view. To enable these features simply create a password through the app.

We hope you use and enjoy the mobile application.

ASCPT Central

Maryland Lobby

ASCPT Central will be open during the following hours:

Tuesday, March 13	Noon – 5:00 pm
Wednesday, March 14	7:00 am – 8:00 pm
Thursday, March 15	7:00 am – 5:00 pm
Friday, March 16	7:00 am – 5:00 pm
Saturday, March 17	7:00 am – Noon

At ASCPT Central you'll have the opportunity to:

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

And much more!

Cyber Café

Maryland Lobby

ASCPT offers the complimentary use of computers with high speed internet access in one centralized location, thanks to the generous support of **Duck Flats Pharma**. In consideration of your fellow attendees, please limit your internet use to 10 minutes at a time.

The Cyber Cafe will be available during the following hours:

Tuesday, March 13	Noon – 5:00 pm
Wednesday, March 14	7:00 am – 8:00 pm
Thursday, March 15	7:00 am – 5:00 pm
Friday, March 16	7:00 am – 5:00 pm
Saturday, March 17	7:00 am – Noon

Exhibit Hall and Poster Hours

Prince George's Exhibition Hall C

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

Wednesday, March 14	6:00 pm – 8:00 pm (Opening Reception)
Thursday, March 15	8:00 am – 3:00 pm
Friday, March 16	8:00 am – 3:00 pm
Saturday, March 17	7:00 am – 12:30 pm (Posters Only)

Speaker Ready Room

Chesapeake A

ASCPT provides technical support through the services available in the Speaker Ready Room, Chesapeake A. Speakers will 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.** Our AV 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 13	Noon – 5:00 pm
Wednesday, March 14	7:00 am – 8:00 pm
Thursday, March 15	7:00 am – 5:00 pm
Friday, March 16	7:00 am – 5:00 pm
Saturday, March 17	7:00 am – Noon

ASCPT Job Board

Maryland Lobby

Are you looking for a new job in industry, academia, or government? Or are you an employer looking for a prime candidate to fill a position? If so, the ASCPT Job and Volunteer Opportunities Board is the perfect opportunity to reach over 1,000 leading professionals in clinical pharmacology.

The Job Board is located near ASCPT Central and is open during registration hours, from Tuesday, March 13 until Saturday, March 17. Stop by to speak to an ASCPT staff member to post a position or for more information on the Job Board.

Annual Meeting Evaluations

ASCPT is proud to provide its members with the highest quality of care and service. We appreciate all attendees' feedback to continue to make the Annual Meeting a successful and enjoyable experience. Please take the time to evaluate the 2012 Annual Meeting and its daily sessions through the online evaluation website. All registrants will receive an email prior to the meeting with a link to the evaluation system. If you do not receive the email link, please visit www.ascpt.org.

The online evaluation system will be available from March 12, 2012 - April 30, 2012. Attendees will be able to complete session evaluations as they occur and will be able to save and return to the evaluation as needed. Upon completion of the evaluation, attendees will be able to print their certificate of attendance from their computer or send it directly to their email account.

Policy on Photography and Photo Release

Attendees at the ASCPT Annual Meeting are asked to refrain from taking photographs of posters and/or power point presentations during the meeting.

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

Policy on Children, Spouses, and Guests

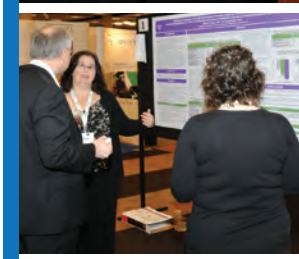
The ASCPT Annual Meeting is geared toward adult participation. For their safety, children under the age of 16 are not permitted in the exhibit hall, session rooms, or receptions for the duration of the meeting. Spouses and guests with a Social registration category are eligible to attend social functions only; admittance to educational programming is not permitted unless the registrant upgrades to a full conference or one-day registration. We appreciate your cooperation and understanding.

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

Should you need childcare during the ASCPT Annual Meeting we suggest you contact: SeekingSitters – an on-demand babysitting referral service. You can submit requests online for your last minute, one-time, part-time or full-time needs. A local SeekingSitters owner works to schedule a background screened Professional Sitter. SeekingSitters was founded by a licensed private investigator and mother of three young children making security their priority. Every SeekingSitters approved Professional Sitter undergoes an extensive interview process by a local owner and intense background screening before acceptance into the SeekingSitters Babysitting Team. SeekingSitters screen their members for their sitters safety! www.seekingsitters.com

ASCPT has not made any group arrangements or discounts and is not able to endorse the use of this firm; these are informational only.

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 Gaylord National Hotel is adept at making arrangements for dining reservations, excursion reservations, providing shopping and transportation information and answering general questions about local attractions.



PUBLISH YOUR NEXT CPT PAPER

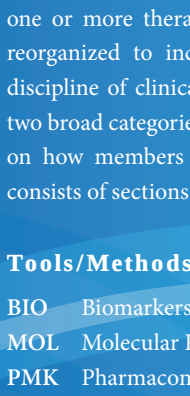
OPEN ACCESS

CPT offers authors the option to publish their articles with immediate open access upon publication. Authors of original research will have the option to pay a one-time fee for their accepted paper to be made freely available online immediately upon publication. Papers that publish online as open access content will be identified in the journal with an open access image. Open access articles will also be deposited in PubMed Central at the time of publication and will be freely available immediately. This means more exposure for your research!

Contact the Editorial Office staff at cpt@ascpt.org for additional information.

SCIENTIFIC AGENDA

SPEAKERS & SESSIONS



John Wagner, MD, PhD
Scientific Program Committee Chair

ASCPT SCIENTIFIC SECTION DESIGNATIONS

Consistent with the Society's Scientific Section structure, each session presented at the Annual Meeting must also correlate to one or more therapeutic areas. Scientific Sections have been reorganized to increase scientific interaction and reflect the discipline of clinical pharmacology. Sections are grouped into two broad categories: the tools group consists of sections focused on how members do their work, and the applications group consists of sections focused on areas where tools are employed.

Tools/Methods

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

Applications

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

Janice B. Schwartz, MD
Award Recipient

Peter K. Honig, MD
Award Recipient

Carl C. Peck, MD
Award Recipient

Landry Kamden Kamden, PharmD, PhD
Award Recipient

Laura Wozniak, MD
Award Recipient

Gregory L. Kearns, PharmD, PhD
Award Recipient

Jason Karnes, PharmD
Award Recipient

TUESDAY • MARCH 13

Noon - 5:00 pm

ASCPT Annual Meeting Registration Open Maryland Foyer

WEDNESDAY • MARCH 14

7:00 am - 8:00 pm

ASCPT Registration Open Maryland Foyer

ASCPT Central Open Maryland Foyer

7:30 am - 3:00 pm

FDA Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting Maryland C

8:00 am - Noon

CPT Editorial Team Meeting *(by invitation only)* Maryland 1

Noon - 1:30 pm

ASCPT Board of Directors and CPT Editorial Team Lunch *(by invitation only)* Maryland 2

1:30 pm - 2:30 pm

New Member Welcome Chesapeake D/E

2:00 pm - 2:45 pm

Award Reception *(by invitation only)* Maryland 3

3:00 pm - 4:00 pm

Opening Session Maryland B/4-6 *sponsored by* Genentech A Member of the Roche Group

State of the Society Address **President** Richard L. Lalonde, PharmD

Award Presentations

William B. Abrams Award for Geriatric Clinical Pharmacology

Presenter Darrell Abernethy, MD, PhD • US Food and Drug Administration
Recipient Janice B. Schwartz, MD • University of California

Henry E. Elliott Distinguished Service Award

Presenter Scott A. Waldman, MD, PhD • Thomas Jefferson University
Recipient Peter K. Honig, MD • AstraZeneca

Gary Neil Prize for Innovation in Drug Development

Presenter Terrence Blaschke, MD • Stanford University School of Medicine
Recipient Carl C. Peck, MD • University of California, San Francisco

ASCPT 2011 Young Investigator Awards

Presenter Richard L. Lalonde, PharmD
Recipients Landry Kamden Kamden, PharmD, PhD • Harding University School of Pharmacy
Laura Wozinak, MD • University of California, Los Angeles

2011-2012 Top Membership Recruiter

Presenter Nancy A. Lass, MD • University of Chicago
Recipient Gregory L. Kearns, PharmD, PhD • Children's Mercy Hospital and Clinics

2011-2012 Membership Recruiting Honorable Mention

Presenter Nancy A. Lass, MD • University of Chicago
Recipient Jason Karnes, PharmD • University of Florida

WEDNESDAY • MARCH 14

3:00 pm - 4:00 pm *(continued)*

Opening Session - Award Presentations *(continued)*

David J. Goldstein Trainee Award Winners

Presenter Richard L. Lalonde, PharmD
Recipients Jason Sprowl, PhD • St. Jude Children's Research Hospital
Cynthia S. Lancaster, PhD • St. Jude Children's Research Hospital
Xu Han • Indiana University School of Medicine

Jason Morrow Trainee Award Winner

Presenter Richard L. Lalonde, PharmD
Recipient Qiping Feng, PhD • Vanderbilt University

2012 ASCPT Mentor Award

Presenter Richard L. Lalonde, PharmD
Recipient Arthur J. Atkinson, Jr., MD • Northwestern University

Phrma Foundation Awards

Presenter Darrell Abernethy, MD, PhD • US Food and Drug Administration

2012 Award in Excellence in Clinical Pharmacology
Recipient Andre Terzic, MD, PhD • Mayo Clinic

2012 Paul Calabresi Medical Student Fellowship
Recipients Jenny Barker • University of Texas Southwestern Medical Center
Elizabeth Dong • Vanderbilt University

2012 Faculty Development Award
Recipient Timothy J. Nelson, MD, PhD • Mayo Clinic

CEO Remarks **Sharon J. Swan, FASAE, CAE**

4:00 pm - 5:00 pm

State of the Art Lecture Maryland B/4-6

Stephen P. Spielberg, MD, PhD • Deputy Commissioner for Medical Products and Tobacco, US Food and Drug Administration
Basic, Applied, Translational, and Regulatory Science: An Interactive Model for the Future of Therapeutics
Chair Richard L. Lalonde, PharmD

5:30 pm - 6:00 pm

Showcase of Top Trainee Abstracts Prince George's Hall C

ASCPT Presidential Trainee Award Winners **Presenter** Richard L. Lalonde, PharmD

Jason Sprowl, PhD
St. Jude Children's Research Hospital

Cynthia S. Lancaster, PhD
St. Jude Children's Research Hospital

Xu Han
Indiana University School of Medicine

Qiping Feng, PhD
Vanderbilt University

Daniela Conrado, MS
University of Florida

Manuela Vieira, PhD
US Food and Drug Administration

SeungHwan Lee, MD
Seoul National University College of Medicine and Hospital

J. Kevin Hicks, PharmD, PhD
St. Jude Children's Research Hospital

Jessica Lam, BSc
Hospital for Sick Children

Virginie Ancrenaz, PhD student
Geneva University Hospitals

Hylke de Jonge, MD
University Hospitals Leuven

Teodora Pene Dumitrescu, PhD
University of North Carolina

Geert W. t'Jong, MD, PhD
Hospital for Sick Children

6:00 pm - 8:00 pm

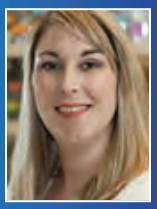
Opening Reception and Exhibit Hall Open Prince George's Exhibit Hall C

sponsored by Pfizer

Stephen P. Spielberg, MD, PhD
State of the Art Lecturer

Arthur J. Atkinson, Jr., MD
Award Recipient

Jason Sprowl, PhD
Award Recipient



Cynthia S. Lancaster, PhD
Award Recipient

Xu Han
Award Recipient

Qiping Feng, PhD
Award Recipient

SHOWCASE OF TOP TRAINEE ABSTRACTS

PT-1

OXALIPLATIN-INDUCED PERIPHERAL NEUROTOXICITY IS DEPENDENT ON OCT2-MEDIATED TRANSPORT

J.A. Sprowl, C. S. Lancaster, H. Giovinazzo, G. Du, L. Janke, A. Sparreboom; St Jude Children's Research Hospital, Memphis, TN

PT-2

OATP1B1 POLYMORPHISM AS A DETERMINANT OF ERYTHROMYCIN DISPOSITION

C. Lancaster,[1] G. Hoffman Bruun,[2] T. S. Mikkelsen,[2] R. H. Mathijssen,[3] A. Sparreboom[1]; [1]St Jude Children's Research Hospital, Memphis, TN, [2]Skejby Hospital, Aarhus University Hospital, Aarhus, Denmark, [3]Erasmus MC, Rotterdam, Netherlands

PT-3

NOVEL TRANSLATIONAL PARADIGM FOR DRUG-DRUG INTERACTION RESEARCH: A COMBINATION OF LITERATURE-BASED DISCOVERY, ELECTRONIC MEDICAL RECORDS AND *IN VITRO* DDI SCREENING ASSAYS

X. Han,[1] Z. Wang,[2] A. Subhadarshini,[2] S. Karnik,[2] R. M. Strother,[3] S. D. Hall,[4] Y. Jin,[4] D. A. Flockhart,[5] S. K. Quinney,[6] J. D. Duke,[7] L. Li[8]; [1]Department of Pharmacology and Toxicology, Indiana University School of Medicine, Indianapolis, IN, [2]Center for Computational Biology and Bioinformatics, Indiana University School of Medicine, Indianapolis, IN, [3]Division of Hematology/Oncology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, [4]Eli Lilly INC, Indianapolis, IN, [5]Division of Clinical Pharmacology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, [6]Department of Obstetrics/Gynecology, Indiana University School of Medicine, Indianapolis, IN, [7]Regenstrief Institute, Indiana University School of Medicine, Indianapolis, IN, [8]Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN

PT-4

DOSE-RESPONSE CURVES EXTRACTED FROM ELECTRONIC MEDICAL RECORDS IDENTIFY SORT-1 AS A NOVEL GENETIC PREDICTOR OF STATIN POTENCY (ED_{50}).

Q. Feng,[1] M. S. Waitara,[1] L. Jiang,[1] H. Xu, M. Jiang,[1] C. A. McCarty,[2] R. L. Davis,[3] D. M. Roden,[1] D. A. Nickerson,[4] J. Smith,[4] M. Rieder,[4] J. I. Rotter,[5] R. M. Krauss,[6] R. A. Wilke[1]; [1]Vanderbilt University, Nashville, TN, [2]Marshfield Clinic Research Foundation, Marshfield, WI, [3]Kaiser Permanente Southeast, Atlanta, GA, [4]University of Washington, Seattle, WA, [5]Cedars-Sinai Medical Center, Los Angeles, CA, [6]Children's Hospital Oakland Research Institute, Oakland, CA

PT-5

PHARMACOKINETIC-PHARMACODYNAMIC MODELING OF ARMODAFINIL: EFFECTS ON ALERTNESS AND ELECTROENCEPHALOGRAM OF SLEEP DEPRIVED ADULTS

D. J. Conrado, M. Bewernitz, M. Ding, J. Cibula, S. Eisenschenk, C. Seubert, H. Derendorf; University of Florida, Gainesville, FL

PT-6

EVALUATION OF FDA AND EMA MODELS' CUT-OFF VALUES FOR CYP3A INHIBITION PREDICTION: A COLLABORATIVE EFFORT AMONG ACADEMIC, REGULATORY AGENCIES, AND INNOVATION AND QUALITY CONSORTIUM (IQC) PHARMACEUTICAL SCIENTISTS

M. L. Vieira,[1] B. Kirby,[2] I. Ragueneau-Majlessi,[3] J. Y. Chien,[4] V. Fischer,[5] A. Fretland,[6] A. Galetin,[7] K. Grime,[8] S. D. Hall,[4] D. R. Plowchalk,[9] R. Riley,[10] E. Seibert,[11] K. Skordos,[12] J. Snoeys,[13] K. Venkatakrishnan,[14] H. J. Einolf,[15] R. S. Obach,[9] E. G. Berglund,[16] P. Zhao,[1] L. Zhang,[1] K. S. Reynolds,[1] S. Huang[1]; [1]FDA, Silver Spring, MD, [2]University of Washington, Seattle, WA, [3]University of Washington, Silver Spring, WA, [4]Eli-Lilly, Indianapolis, IN, [5]Abbott, Abbott Park, IL, [6]Hoffmann-LaRoche, Nutley, NJ, [7]University of Manchester, Manchester, United Kingdom, [8]AstraZeneca, Mindal, Sweden, [9]Pfizer, Groton, CT, [10]AstraZeneca, London, United Kingdom, [11]Boehringer Ingelheim, Ridgefield, CT, [12]GlaxoSmithKline, King of Prussia, PA, [13]Janssen Pharmaceutical Companies of Johnson & Johnson, Beerse, Belgium, [14]Millennium, Cambridge, MA, [15]Novartis, East Hanover, NJ, [16]MPA, Uppsala, Sweden

PT-7

INDUCTIVE EFFECT OF RIFAMPIN ON THE PHARMACOKINETICS OF VORICONAZOLE IN HEALTHY SUBJECTS

S. Lee, D. Shin, S. Kim, S. C. Ji, S. H. Yoon, J. Y. Cho, S. G. Shin, I. J. Jang, K. S. Yu; Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea

PT-8

AUTOMATED INCORPORATION OF PHARMACOGENETIC CONSULTS AND CLINICAL DECISION SUPPORT INTO AN ELECTRONIC MEDICAL RECORD

J. K. Hicks,[1] K. R. Crews,[1] J. M. Hoffman,[1] N. M. Kornegay,[1] M. R. Wilkinson,[1] R. Lorier,[2] W. Yang,[1] C. Smith,[1] C. Fernandez,[1] S. Cross,[1] C. Haidar,[1] D. K. Baker,[1] S. Howard,[1] W. E. Evans,[1] U. Broeckel,[2] M. V. Relling[1]; [1]St. Jude Children's Research Hospital, Memphis, TN, [2]Medical College of Wisconsin, Milwaukee, WI

PT-9

PHARMACOGENETIC INSIGHT INTO OXYCODONE: IMPLICATIONS TO BREASTFEEDING MOTHERS AND NEONATES DURING THE POSTPARTUM PERIOD

J. Lam,[1] P. Madadi,[1] I. Matok,[1] L. Kelly,[2] B. C. Carleton,[3] M. R. Hayden,[3] G. Koren[1]; [1]Division of Pharmacology and Toxicology, Hospital for Sick Children, Toronto, ON, Canada, [2]Department of Physiology and Pharmacology, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON, Canada, [3]Child and Family Research Institute, Children's and Women's Health Center of British Columbia, Vancouver, BC, Canada

PT-10

DUAL CYTOCHROME P450 3A AND CYP2B6 INHIBITION BY RITONAVIR AFFECTS PRASUGREL PHARMACOKINETICS IN HEALTHY VOLUNTEERS

V. Ancrenaz, Y. Daali, C. Samer, J. Deglon, C. Staub, P. Dayer, J. Desmeules; Geneva University Hospitals, Geneva, Switzerland

PT-11

IN VIVO CYP3A4-ACTIVITY AND *CYP3A5*-GENOTYPE PREDICT TACROLIMUS PHARMACOKINETICS IN RENAL TRANSPLANT RECIPIENTS

H. de Jonge,[1] H. de Loor,[1] K. Verbeke,[2] Y. Vanrenterghem,[1] D. R. Kuypers[1]; [1]Department of Nephrology and Renal Transplantation, University Hospitals Leuven, Leuven, Belgium, [2]Department of Gastrointestinal Research, Catholic University Leuven, Leuven, Belgium

PT-12

AZITHROMYCIN (AZI) MODEL TO DESCRIBE BLOOD AND PLASMA CONCENTRATIONS OVER TIME IN HEALTHY SUBJECTS

T. Pene Dumitrescu,[1] T. Anic-Milic,[2] K. Oreskovic,[2] J. Padovan,[2] K. L. R. Brouwer,[1] P. Zuo,[3] V. D. Schmith[3]; [1]Division of Pharmacotherapy and Experimental Therapeutics, UNC Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]GSK Research Center Zagreb Ltd, presently Galapagos istraivački centar d.o.o., Zagreb, Croatia, [3]Clinical Pharmacology Modeling and Simulation, GlaxoSmithKline, Research Triangle Park, NC

PT-13

PHENOBARBITAL CAN REVERSIBLY CONVERT TO ITS PRODRUG PRIMIDONE: A CASE REPORT AND ANIMAL MODEL

R. Tanoshima,[1] **G. W. Jong**,[1] D. Colantonio,[1] A. Merlocco,[1] J. Simpson,[2] J. N. Friedman,[1] G. Koren[1]; [1]Hospital for Sick Children, Toronto, ON, Canada, [2]Human Health and Nutritional Sciences, University of Guelph, Guelph, ON, Canada

THURSDAY • MARCH 15

6:45 am - 8:15 am

Scientific Section Leadership Orientation *(by invitation only)* Chesapeake G/H

6:45 am - 8:00 am

Finance Committee Meeting *(by invitation only)* Chesapeake 11

7:00 am - 5:00 pm

ASCPT Registration Open Maryland Foyer

ASCPT Central Open Maryland Foyer

7:00 am - 9:00 am

ABCP Board Meeting *(by invitation only)* Chesapeake 1

8:00 am - 3:00 pm

Exhibits and Posters Open Prince George's Hall C

8:00 am - 9:00 am

Continental Breakfast in Exhibit Hall (all attendees) Prince George's Hall C

8:00 am - 9:30 am

CPT Editorial Board Meeting *(by invitation only)* Maryland 1 & 2

Poster Session I Prince George's Hall C

Late-Breaking Poster Session I Prince George's Hall C

8:15 am - 9:30 am

CCSS & Scientific Sections *(by invitation only)* Chesapeake G/H

9:45 am - 11:45 am • *3 Concurrent Symposia*

PHATSO: Pharmacologic and Therapeutic Studies in the Obese

endorsed by DDR/SAF/ONC/SPO/PMK Maryland B/4-6

Chairs Geert W. 't Jong, MD, PhD • Hospital for Sick Children
Alex Sparreboom, PhD • St. Jude Children's Research Hospital

Speakers Darrell Abernethy, MD, PhD • US Food and Drug Administration
Pharmacokinetics and Obesity: Historic Perspective

Nicholas Holford, MBChB, FRACP • University of Auckland, New Zealand
Mechanistic Basis of Using Size Metrics to Predict Clearance in the Obese

Gary Rosner, ScD • John Hopkins University
Anticancer Drug Dosing in the Obese: ASCO Guidelines

Catherijne Knibbe, PharmD, PhD • Leiden/Amsterdam Center for Drug Research
Obesity in Children: Dose Considerations and the Role of Population PK-PD Modeling

Learning Objectives

1. To review the influence of obesity on all aspects of pharmacokinetics and dynamics of drugs.
2. To review the application of modeling for understanding alterations in body composition and influences on pharmacokinetic parameters such as clearance and volume of distribution.
3. To discuss the impact of obesity on drug dosing in critical therapeutics like oncology drugs and special populations such as infants and children.

Geert W. 't Jong, MD, PhD
Symposium Chair

Alex Sparreboom, PhD
Symposium Chair

THURSDAY • MARCH 15

9:45 am - 11:45 am • *3 Concurrent Symposia (continued)*

Modeling Practical Aspects of Clinical Trials

(Joint Symposium with ASCPT and Model Based Drug Development Consortium)

endorsed by DDR/SAF/PMK Maryland C

Chairs Virginia D. Schmith, PhD • GlaxoSmithKline
Joga Gobburu, PhD • University of Maryland

Speakers Diane Mould, PhD • Projections Research Inc.
Modeling Heterogeneity From International Trials

Huybert Groenendaal, MSc, PhD, MBA • EpiX Analytics LLC
When There are Differences in Opinions: Expert Modeling

Brendan Johnson, PhD • GlaxoSmithKline
Bayesian Model Averaging: Addressing Uncertainty in Final Model Selection, When More Than One Model May be Appropriate

Mats O. Karlsson, PhD • Uppsala University
The Impact of Decisions by Treating Physicians on Modeling and Simulation of Clinical Trials

Learning Objectives

1. To describe the practical aspects of conducting clinical trials that complicate interpretation of results and modeling solutions to these issues.
2. To describe how to handle modeling of heterogeneity in international clinical trials.
3. To describe solutions to incorporating differences in expert opinions using a quantitative approach.
4. To describe how Bayesian Modeling Averaging can be used when there is uncertainty in the final model when more than one model may be appropriate.
5. To describe the consequences of physicians or patients making decisions during clinical trials.

Immunomodulatory Therapies and Progressive Multifocal Leukoencephalopathy (PML): Novel Approaches to Risk Minimization and Treatment of JC Virus Infection

endorsed by INF/OSD/SPO Maryland D

Chairs Juan J.L. Lertora, MD, PhD • NIH Clinical Center
Dhanesh K. Gupta, MD • Northwestern University Feinberg School of Medicine

Speakers Eugene O. Major, PhD • National Institute of Neurologic Disorders and Stroke
PML as a Complication of Immunomodulatory Therapies: Clinical Impact and New Antiviral Agents for JC Virus

Russell R. Lonser, MD • National Institute of Neurologic Disorders and Stroke
The Challenge of Drug Delivery to the Brain: Convection Perfusion and Other Novel Approaches With Potential Application in the Therapy of PML

Petra Duda, MD, PhD • Biogen Idec
Clinical Strategies for PML Risk Stratification and Minimization

Russell Katz, MD • US Food and Drug Administration
Regulatory Perspectives on Serious Immunomodulatory Therapy: Related Complications

Learning Objectives

1. To inform the clinical significance of PML as a serious complication of effective immunomodulatory therapies and JC virus reactivation.
2. To discuss novel approaches to drug discovery and drug delivery to the CNS for the treatment of JC virus infection.
3. To address new strategies for PML risk minimization and related regulatory issues.

Virginia D. Schmith, PhD
Symposium Chair

Joga Gobburu, PhD
Symposium Chair

Juan J.L. Lertora, MD, PhD
Symposium Chair

Dhanesh K. Gupta, MD
Symposium Chair

THURSDAY • MARCH 15

Noon - 1:15 pm

ASCPT Town Hall (box lunch available for attendees) See page 11 for complete details. Maryland A

Trainee Luncheon *(ticketed event)* See page 10 for complete details. Chesapeake D

Box Lunch (all attendees) Prince George's Exhibit Hall C

1:30 pm - 2:30 pm • *3 Concurrent Sessions*

Sheiner-Beal Pharmacometrics Award Lecture Maryland B/4-6

This award is sponsored by the Department of Bioengineering and Therapeutic Sciences University of California, San Francisco

Malcolm Rowland, DSc, PhD • University of Manchester, United Kingdom

Ask Not What, But Why: A Modeler's Journey

Chair Leslie Benet, PhD • University of California, San Francisco

The *Sheiner-Beal Pharmacometrics Award* was established as an ASCPT award by the University of California, San Francisco (UCSF) to acknowledge the pioneering contributions of Drs. Lewis B. Sheiner and Stuart Beal to the field of Quantitative Pharmacology and Pharmacometrics.

The *Sheiner-Beal Pharmacometrics Award* recognizes an investigator or leader who is actively advancing the scientific discipline of pharmacometrics and/or its impact on research, development, regulatory evaluation, or utilization of therapeutic products.

Featured Speaker Maryland C

Alex Sparreboom, PhD • St. Jude Children's Research Hospital

Transporters and Chemotherapy Toxicity

Honorary Chair Mary V. Relling, PharmD • St. Jude Children's Research Hospital

Oral Session OI-A: Biomarker Strategies in Neuroscience Maryland D

Chairs Masako P. Nakano, MD, PhD • Eli Lilly and Company
Malle Jurima-Romet, PhD • Celerion Inc.

OI-A-1
TIME-ON-TARGET PET STUDY DEMONSTRATES EQUIVALENT BRAIN NK1-RECEPTOR OCCUPANCY FOLLOWING SINGLE DOSES OF I.V. FOSAPREPITANT AND P.O. APREPITANT

Presenter Craig R. Shadle, MS • Merck and Company

OI-A-2
BNA REVEALS FM-THETA NETWORK IN A WORKING MEMORY TASK PERFORMED UNDER DONEPEZIL AND PLACEBO CONDITIONS

Presenter Keren Ziv, BSc • ElMindA LTD

OI-A-3
EEG EFFECTS OF SCOPOLAMINE IN HEALTHY SUBJECTS: A QEEG AND A SOURCE LOCALISATION STUDY

Presenter Geoffrey Viardot, PhD • Forenap

OI-A-4
PHARMACOKINETIC-PHARMACODYNAMIC MODELING OF ARMODAFINIL: EFFECTS ON ALERTNESS AND ELECTROENCEPHALOGRAM OF SLEEP DEPRIVED ADULTS

Presenter Daniela A. Conrado, MS • University of Florida

Malcolm Rowland, DSc, PhD
Award Lecturer

Alex Sparreboom, PhD
Featured Speaker

Masako P. Nakano, MD, PhD
Oral Session Chair

Malle Jurima-Romet, PhD
Oral Session Chair

THURSDAY • MARCH 15

2:45 pm - 3:45 pm

Special Session **Ask the Editors** Maryland B/4-6

Chair Richard L. Lalonde, PharmD
Introduction and Overview

Speakers CPT:PSP Editor • to be announced
Welcome to the New Journal

Scott Waldman, MD, PhD, FCP • Thomas Jefferson University
CPT…What's New

Questions and Answers Interactive Q&A with the Audience

Summary and Next Steps

All attendees are invited to participate in this special session where the latest information about *Clinical Pharmacology & Therapeutics* will be presented and ASCPT's new journal, *CPT: Pharmacometrics & Systems Pharmacology*, will be discussed. The Ask the Editors session will provide a forum for member interaction with the editorial leadership of ASCPT's journals to discuss the future of these two publications and plans to showcase even more cutting-edge research.

4:00 pm - 5:00 pm

State of the Art Maryland B/4-6

Harvey V. Fineberg, MD, PhD • Institute of Medicine
Vaccines, Devices, Biomarkers, and Evaluation: The Impact of the Institute of Medicine Health Policy

Chair Richard L. Lalonde, PharmD

5:00 pm - 5:15 pm

Transition to the Future Maryland B/4-6

5:30 pm - 7:00 pm • *3 Concurrent Section Meetings*

Biomarkers and Imaging (BIO) Maryland A

Speakers Geoffrey Viardot, PhD • FORENAP, Rouffach, France
EEG Effects of Scopolamine in Healthy Subjects: A QEEG and a Source Localization Study

Kazuyoshi Arao • Oita, Japan
Mirtazapine Suppresses the Increases in Plasma Levels of Adrenocorticotropic Hormone and Neuropeptide Y Under Continual Stress Exposure

Ho-Sook Kim, PhD • Inje University College of Medicine, Busan, Republic of Korea
Both CYP2C19 and PON1 Genotypes are Associated with the Clinical Outcome of Clopidogrel in Patients with Acute Myocardial Infarction but not Angina

Jeremy Matlow, MSc Candidate • Hospital for Sick Children, Toronto, Canada
Ethyl Glucuronide as a Biomarker of Alcohol Consumption During Pregnancy

Aniket Natekar, MSc Candidate • Hospital for Sick Children, Toronto, Canada
Hair Cocaethylene as a Biomarker of Alcohol and Cocaine Co-Exposure

Craig Shadle, MS • Merck, North Wales, PA
Time-On-Target PET Study Demonstrates Equivalent Brain NK1-Receptor Occupancy Following Single Doses of I.V. Fosaprepitant and P.O. Aprepitant

Harvey V. Feinberg, MD, PhD
State of the Art Lecturer

Richard L. Lalonde, PharmD
Special Session Chair

THURSDAY • MARCH 15

5:30 pm - 7:00 pm • *3 Concurrent Section Meetings (continued)*

Molecular Pharmacology and Pharmacogenetics (MOL) Maryland D

Speakers Yubo Chai, MD, PhD and Richard M. Weinshilboum, MD • Mayo Clinic, Rochester, MN
Selective Serotonin Reuptake Inhibitor (SSRI) Pharmacogenomics: Identification of Riboflavin Kinase (RFK) as a Novel Candidate Gene for SSRI Response by Genome-Wide Association Study (GWAS) Combined with Functional Genomics

Mingta Michael Lee • Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan
A Prospective Study of Hla-B*5801 Genotyping for the Prevention of Allopurinol Induced Severe Cutaneous Adverse Reactions

Pharmacometrics and Pharmacokinetics (PMK) Maryland C

Speaker Ted Grasela, PharmD, PhD • President & CEO, Cognigen Corporation, Buffalo, NY
PMx Saves Pharma: Can It Be a Reality?

5:30 pm - 7:30 pm

UCSF Reception *(by invitation only)* Maryland 2

6:00 pm - 7:00 pm

Donor Reception *(by invitation only)* Pose – Lower Level

Social for Students and Trainees *(students and trainees only)* Chesapeake D

6:30 pm - 8:00 pm

PhRMA Foundation Reception *(by invitation only)* Maryland 3

7:00 pm - 8:30 pm

International Reception *(by invitation only)* Maryland 1

8:30 pm - 9:30 pm

Gavel Club Dessert Reception *(by invitation only)* President's Suite

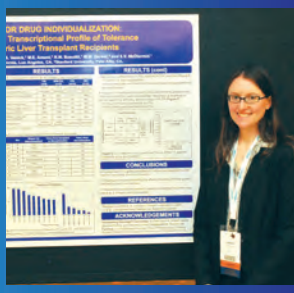
Gather Digital Mobile Application

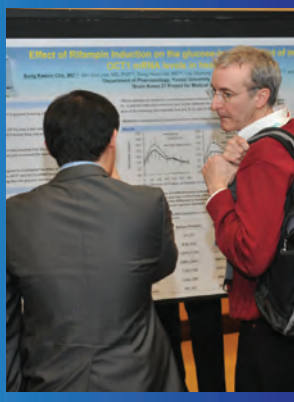
We're excited to announce that this year ASCPT has collaborated with Gather Digital to provide a mobile application for the event. You will get up-to-the-minute information such as the latest agenda, updates from the conference planner, speaker information, maps, exhibitor and sponsor details, an attendee list and more.

An iPhone and iPad app are available in the iTunes app store. Search ASCPT and download the ASCPT 2012 Annual Meeting app. You can also access the app with your BlackBerry, Android or other smart phone. Simply point your mobile browser to http://ascpt2012.gatherdigital.com (note: omit the www) and bookmark it.

One of the features of the mobile app is that you and other attendees will have the option to send messages to each other through the app. It's a great way to network with fellow attendees up to and during the event. You can also create a profile of yourself that other event attendees can view. To enable these features you must establish a password which you can do from the app.

We hope you use and enjoy the mobile application.





FRIDAY • MARCH 16

7:00 am - 5:00 pm

ASCPT Registration Open Maryland Foyer

ASCPT Central Open Maryland Foyer

7:00 am - 8:00 am

Clinical Pharmacology Program Directors Meeting *(by invitation only)* Maryland 1

Education Committee Meeting *(by invitation only)* Chesapeake D

7:00 am - 8:30 am • *6 Concurrent Section Meetings*

Drug Development and Regulatory Sciences (DDR) Maryland A

Infectious Diseases (INF) Chesapeake 11

Speaker Craig Hendrix, MD • Johns Hopkins University School of Medicine, Baltimore, MD
Pharmacology as an Influential Factor for Understanding Outcomes in HIV Pre-Exposure Prophylaxis Trials

Oncology (ONC) Maryland D

Speakers Steven J. Bowlin, DO, MPH, PhD • Medco Research Institute, Franklin Lakes, NJ
12-Month Rates of Potential Drug Metabolizing and Transporter Based Drug-Drug Interactions with Enzyme-Targeted Oral Neoplastic Drugs

Weiwei Tan, PhD • Pfizer, Inc., San Diego, CA
The Development of Crizotinib in the Treatment of ALK-positive Non-Small Cell Lung Cancer: A Perspective of Clinical Pharmacology

Organ Specific Diseases (OSD) Chesapeake H

Speaker Mariellen J. Moore, PharmD • University of Florida, College of Pharmacy, Gainesville, FL
Clinical Predictors of Dysglycemic Effects Associated with Use of Beta Blockers and Thiazide Diuretics

Mariellen J. Moore, PharmD • University of Florida, College of Pharmacy, Gainesville, FL
Antihypertensive Medication Exposure and Adverse Glycemic Effects: An Evaluation of Fasting and Stimulated Glucose

Drug Safety (SAF) Maryland C

Speaker Xu Han • Indiana University, School of Medicine, Division of Clinical Pharmacology, Indianapolis, IN
Novel Translational Paradigm for Drug-Drug Interaction Research: A Combination of Literature-Based Discovery, Electronic Medical Records and *In Vitro* DDI Screening Assays

Special Populations (SPO) Chesapeake 12

SPO Top Trainee Presentations: A Selection of the Best of ASCPT 2012 Abstracts

8:00 am - 3:00 pm

Exhibits and Posters Open Prince George's Hall C

8:00 am - 9:00 am

Continental Breakfast in Exhibit Hall (all attendees) Prince George's Hall C

8:00 am - 9:30 am

Poster Session II Prince George's Hall C

Late-Breaking Poster Session II Prince George's Hall C

9:00 am - 10:00 am

State of the Art Lecture Maryland B/4-6

Francis Collins, MD, PhD • Director, National Institutes of Health
New Partnerships to Accelerate Translation

Chair Kathleen M. Giacomini, PhD

Francis S. Collins, MD, PhD
State of the Art Lecturer

Kathleen M. Giacomini, PhD
State of the Art Lecture Chair

FRIDAY • MARCH 16

10:15 am - 12:15 pm • *4 Concurrent Symposia*

China Clinical Pharmacology Trials and Ethnic Differences in PK and PD/New Asian Strategies for Drug Development

endorsed by DDR/PMK/SPO Maryland B/4-6

Chairs Feng Guo, PhD • Pfizer China Research and Development Center
Shiew-Mei Huang, PhD • US Food and Drug Administration

Speakers Peng Wang, MD • Center for Drug Evaluation (CDE), State of Food & Drug Administration (SFDA), China
Phase I Trial Regulations in China and Extrapolation of Foreign Trial Data to the Chinese Population

Pei Hu, MD • Peking Union Medical College Hospital
Current Status of Phase I Trials in China

Robert Powell, PharmD • Roche (China) Holding Ltd.
Ethnicity Considerations on a New Bridging Strategy Driven by Patient Need and Science

Feng Guo, PhD • Pfizer China R&D Center
Ethnic Differences in Pharmacokinetics: Analysis of More Than 100 Phase I Studies

Learning Objectives

1. To introduce Phase I trial regulations, challenges, and opportunities for drug development in China and Chinese regulatory agency perspective on extrapolation of foreign trial data to the Chinese population.
2. To discuss mechanistic basis for differences in PK and PD in Chinese subjects, as well as ethnic differences in pharmacokinetics based on an analysis of more than 100 Phase I studies.
3. To provide ethnicity considerations on a new bridging strategy driven by patient need and science.

Gained in Translation: Quantitative Preclinical and Clinical Approaches to the Development of New Pain Medicines

endorsed by OSD/PMK Maryland C

Chairs John Roberts, PhD • Novartis Pharmaceuticals
Donald Mager, PharmD, PhD • University at Buffalo, SUNY

Speakers Jeffrey Mogil, PhD • McGill University
Animal Models of Pain as Pharmacodynamic Endpoints: Progress and Challenges

Anne Estrup Olesen, PhD • Center for Mech-Sense, Aalborg Hospital
Translational Pain Research: Case Studies in Evaluating PK/PD in Experimental Pain Studies

Jaap Mandema, PhD • Quantitative Solutions, Inc.
Model-Based Meta-Analyses for Development of Pain Medicines

Jianren Mao, MD, PhD • Harvard Medical School
Achievements and Challenges in Translational Pain Research

Learning Objectives

1. To define currently available preclinical pharmacodynamic models/endpoints for pain research and highlight key assumptions in translating drug pharmacology from the laboratory to the clinic based on these endpoints.
2. To gain an understanding of the current preclinical quantitative translatability of pain (PK/PD) models through several case studies and to convey experimental design implications that follow.
3. To review current clinical pain drugs as a means to understand the ultimate goal of translational PK/PD as related to clinical efficacy and adverse events.

Feng Guo, PhD
Symposium Chair

Shiew-Mei Huang, PhD
Symposium Chair

John Roberts, PhD
Symposium Chair

Donald Mager, PharmD, PhD
Symposium Chair

D. Craig Brater, MD
Award Lecturer

Walter K. Kraft, MD, MS
Symposium Chair

Issam Zineh, PharmD, MPH
Symposium Chair

Yan Jin, MS, MD
Symposium Chair

FRIDAY • MARCH 16

10:15 am - 12:15 pm • *4 Concurrent Symposia (continued)*

Optimizing Pediatric Therapeutics by Applying Lessons From Adult Drug Development

endorsed by DDR/SPO Maryland A

Chair Walter K. Kraft, MD, MS • Thomas Jefferson University

Speakers Gilbert J. Burckart, PharmD • US Food and Drug Administration
Regulatory Viewpoint of the Use of Adult Data in Pediatric Submissions

Theoklis E. Zaoutis, MD, MSCE • The Children's Hospital of Philadelphia
The Use of Epidemiology in Pediatric Drug Development

Daniel K. Benjamin, Jr., MD, PhD, MPH • Duke University Medical Center
Pediatric Trials Network: Optimizing Pediatric Clinical Trial Design

Walter K. Kraft, MD, MS • Thomas Jefferson University
Pediatric Drug Development When a Disease Exists in Both Adults and Children

Learning Objectives

1. To examine approaches to maximally leveraging adult data and methodologies to pediatric research.
2. To understand the FDA position on the use of adult data in pediatric drug development programs.
3. To identify research approaches for diseases common to adults and children.

Pharmacogenetics in Drug Development: At the Academic-Industry-Regulatory Crossroads

endorsed by BIO/DDR/MOL/ONC Maryland D

Chairs Issam Zineh, PharmD, MPH • US Food and Drug Administration
Yan Jin, MS, MD • Eli Lilly & Company

Speakers Issam Zineh, PharmD, MPH • US Food and Drug Administration
Pharmacogenetics in Drug Development and Regulation: The FDA Experience

Robert L. Becker, Jr., MD, PhD • US Food and Drug Administration
Development and Validation of Pharmacogenetic Tests During Drug Development: CDRH Points of View

Michelle Penny, PhD • Eli Lilly and Company
Genetics-Guided Drug Development: An Industry Perspective

Michael Bristow, MD, PhD • University of Colorado - Arca Biopharma
Academic-Based Research to Enhance Pharmacogenetics in Drug Development

Learning Objectives

1. To demonstrate enhanced understanding of regulatory guidance and experience in pharmacogenetics.
2. To outline prerequisites for successful development of pharmacogenetic markers to support personalized medicine.
3. To describe how academia based PGx research can inform development of drug therapy in target populations.

12:30 pm - 1:30 pm • *4 Concurrent Sessions*

Box Lunch (all attendees) Prince George's Hall C

Oscar B. Hunter Memorial Award in Therapeutics Lecture Maryland B/4-6

D. Craig Brater, MD • Indiana University School of Medicine
Making a Career Out of Urine

Presenter Terrence F. Blaschke, MD • Stanford University School of Medicine

The *Oscar B. Hunter Memorial Award in Therapeutics Lecture* recognizes an individual scientist for outstanding contributions to clinical pharmacology and therapeutics throughout his/her professional career.

FRIDAY • MARCH 16

12:30 pm - 1:30 pm • *4 Concurrent Sessions (continued)*

Oral Session OII-A
Next Generation Physiologically-Based Pharmacoinformatics Maryland D

Chairs Karthik Venkatakrishnan, PhD • Millennium Pharmaceuticals, Inc.
Lang Li, PhD • Indiana University

OII-A-1
NOVEL TRANSLATIONAL PARADIGM FOR DRUG-DRUG INTERACTION RESEARCH: A COMBINATION OF LITERATURE-BASED DISCOVERY, ELECTRONIC MEDICAL RECORDS AND *IN VITRO* DDI SCREENING ASSAYS

Presenter Xu Han • Indiana University School of Medicine

OII-A-2
APPLICATION OF PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELING FOR PREDICTION OF COMPLEX DRUG-DRUG INTERACTIONS (DDIs) INVOLVING OATP1B1-MEDIATED UPTAKE AND CYTOCHROME P450 (CYP) METABOLISM AND MULTIPLE INHIBITORS

Presenter Karen Rowland Yeo • Simcyp Ltd., Sheffield, United Kingdom

OII-A-3
EVALUATION OF FDA AND EMA MODELS' CUT-OFF VALUES FOR CYP3A INHIBITION PREDICTION: A COLLABORATIVE EFFORT AMONG ACADEMIC, REGULATORY AGENCIES, AND INNOVATION AND QUALITY CONSORTIUM (IQC) PHARMACEUTICAL SCIENTISTS

Presenter Manuela Vieira, PhD • US Food and Drug Administration

OII-A-4
DOSE-RESPONSE CURVES EXTRACTED FROM ELECTRONIC MEDICAL RECORDS IDENTIFY SORT-1 AS A NOVEL GENETIC PREDICTOR OF STATIN POTENCY (ED_{50})

Presenter Qiping Feng, PhD • Vanderbilt University

Oral Session OII-B
Emerging Genomic Data on CYP-3A4 Maryland A

Chairs Larisa Reyderman, PhD • Eisai Medical Research
Rebecca Blanchard, PhD • Merck & Co Inc.

OII-B-1
ASSOCIATION BETWEEN THE *CYP3A4*22* ALLELE AND THE PHARMACOKINETICS OF THE CYP3A4 PHENOTYPING PROBES MIDAZOLAM AND ERYTHROMYCIN IN CANCER PATIENTS

Presenter Laure Elens, PhD • Erasmus Medical Center

OII-B-2
GLOBAL ANALYSIS OF *CYP3A4* AND *CYP3A5* GENOTYPE ON *IN VIVO* CLEARANCE OF CYP3A4 SUBSTRATES

Presenter Sara K. Quinney, PharmD, PhD • Indiana University School of Medicine

OII-B-3
IN VIVO CYP3A4-ACTIVITY AND *CYP3A5*-GENOTYPE PREDICT TACROLIMUS PHARMACOKINETICS IN RENAL TRANSPLANT RECIPIENTS

Presenter Hylke de Jonge, MD • University Hospitals Leuven

OII-B-4
EXPRESSION OF DRUG METABOLIZING ENZYMES AND TRANSPORTER PROTEINS ALONG THE ENTIRE HUMAN GASTROINTESTINAL TRACT

Presenter Marek Drozdzik, MD • Pomeranian Medical University

Karthik Venkatakrishnan, PhD
Oral Session Chair

Lang Li, PhD
Oral Session Chair

Larisa Reyderman, PhD
Oral Session Chair

Rebecca Blanchard, PhD
Oral Session Chair

FRIDAY • MARCH 16

12:30 pm - 1:30 pm • *4 Concurrent Sessions (continued)*

Oral Session OII-C
Targeted Investigation in Vulnerable Populations Maryland C

Chairs Mara L. Becker, MD, MSCE • Children's Mercy Hospitals and Clinics
Raymond J. Hohl, MD, PhD • University of Iowa

OII-C-1
WITHDRAWN

OII-C-2
PHARMACOGENETIC INSIGHT INTO OXYCODONE: IMPLICATIONS TO BREASTFEEDING MOTHERS AND NEONATES DURING THE POSTPARTUM PERIOD

Presenter Jessica Lam, BSc • Hospital for Sick Children

OII-C-3
USING PBPK MODEL TO GAIN INSIGHT INTO CHANGES IN DISPOSITION OF CYP3A-METABOLIZED DRUGS IN PREGNANT WOMEN: DISCERNING CYP3A INDUCTION IN THE GUT VS. THE LIVER

Presenter Ban (Alice) Ke, MS • US Food and Drug Administration

OII-C-4
POPULATION PHARMACOKINETIC MODELING OF PROPOFOL IN OBESE CHILDREN AND ADOLESCENTS

Presenter Jeroen Diepstraten • St. Antonius Hospital

1:45 pm - 2:45 pm • *2 Concurrent Sessions*

Rawls Palmer Progress in Medicine Award Lecture Maryland B/4-6

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

Translational Medicine: From Knowledge Generation to Healthcare Delivery

Presenter Howard E. Greenberg, MD, MS, MBA • Thomas Jefferson University

The *Rawls Palmer Progress in Medicine Award Lecture* recognizes a clinical pharmacologist for significant contributions to drug investigation that incorporate the efforts of modern drug research in the care of patients.

Featured Speaker Maryland A

Mary Jeanne Kreek, MD • The Rockefeller University

Molecular, Neurobiological, and Genetics Studies of Specific Addictive Diseases: Bidirectional Translational Research

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

2:45 pm - 3:15 pm

Afternoon Refreshment Break Prince George's Hall C


Scott A. Waldman, MD, PhD
Award Lecturer


Mary Jeanne Kreek, MD
Featured Speaker


Mara L. Becker, MD, MSCE
Oral Session Chair


Raymond J. Hohl, MD, PhD
Oral Session Chair

FRIDAY • MARCH 16

3:30 pm - 5:30 pm • *3 Concurrent Symposia*

New Perspectives in Drug-Induced Renal Injury

endorsed by DDR/SAF/ONC/OSD/SPO Maryland B/4-6

Chair Michael Spigarelli, MD, PhD • University of Utah

Speakers Douglas Throckmorton, MD • US Food and Drug Administration
Drug-Induced Renal Injury: Implications for Drug Development and Regulation

John van den Anker, MD, PhD • Children's National Medical Center
Drug-Induced Renal Injury in Special Populations:
Focus on the Neonate as a Patient Population at Increased Risk for Drug-Induced Renal Injury

Gideon Koren, MD • Hospital for Sick Children
Novel Strategies to Prevent Drug-Induced Renal Injury:
Translation of *In Vitro* Protective Strategies to Animal Models and Clinical Trials

Learning Objectives

1. To appreciate the importance of drug-induced renal injury in drug development and drug regulation.
2. To appreciate the importance of drug-induced renal injury in special populations such as neonates.
3. To describe new mechanisms of drug-induced renal injury and potential new strategies to reduce the risk of drug-induced renal injury.

Novel Modeling and Simulation Approaches Applied to the Development of Biologics

endorsed by DDR/OSD/PMK Maryland A

Chairs Megan Gibbs, PhD • Amgen, Inc.
Manish Gupta, PhD, FCP • Bristol-Myers Squibb

Speakers Jeroen Jansen, PhD • Mapi Values, Inc.
Network Meta-Analysis to Evaluate the Value of Biologics

David Salinger, PhD • Amgen, Inc.
Modeling of Early Biomarker Data in P1a to Inform P2b for a Novel Treatment for Psoriasis

Jing Yu, PhD • Novartis Institutes for Biomedical Research, Inc.
Mechanism Based Drug-Target Binding Models for Dose Selection of Biologics:
From Target Feasibility to Market Support

Jaap Mandema, PhD • Quantitative Solutions, Inc.
Relative Effectiveness of Biologics in Rheumatoid Arthritis: A Dose-Response Meta-Analysis

Learning Objectives

1. To identify and evaluate the role of quantitative clinical pharmacology, modeling and simulation in the research and development of new biologics.
2. To appreciate the unique challenges and limitations of model based drug development for biologics.
3. To understand the value of advanced modeling and simulation in evidence-based drug development for therapeutics applied throughout the continuum for biologic drug development.
4. To understand the application of modeling and simulations to impact dose selection, study design, and endpoint selection.
5. To appreciate the application of meta-analysis to inform biologic drug development.

Megan Gibbs, PhD
Symposium Chair

Manish Gupta, PhD, FCP
Symposium Chair

Mark Dresser, PhD
Symposium Chair

Lei Zhang, PhD
Symposium Chair

FRIDAY • MARCH 16

3:30 pm - 5:30 pm • *3 Concurrent Symposia (continued)*

Codevelopment of Investigational Drugs for Use in Combination to Treat Cancer and Infectious Diseases

endorsed by DDR/INF/MOL/ONC Maryland C

Chairs Mark Dresser, PhD • Genentech, Inc.
Lei Zhang, PhD • US Food and Drug Administration

Speakers Helen Chen, MD • National Cancer Institute
Codevelopment of Investigational Drugs to Treat Cancer: Overview, Background, and Scientific Rationale

Iris T. Chan, MD, PhD • Genentech, Inc.
Novel Combination Drug Development in Oncology: First-In-Human Phase 1b Study of the MEK Inhibitor GDC-0973 and Pan-PI3K Inhibitor GDC-0941

Patrick Smith, PharmD • Roche, Inc.
Addressing Unmet Medical Needs Through Multiple Combination Development: The Infectious Disease Perspective

Jeffrey Murray, MD • US Food and Drug Administration
Regulatory Considerations for the Codevelopment of Unmarketed Investigational Drugs

Learning Objectives

1. To describe the scientific rationale and historical context of combining multiple NMEs to maximize cancer and infectious disease treatment outcomes.
2. To understand the potential risks and benefits associated with combining two or more NMEs in drug development, including the relative merits of various clinical development and clinical trial approaches for optimizing combination regimens through presentation of oncology and virology case studies.
3. To understand the regulatory perspective on the codevelopment of investigational agents for use in combination.

6:00 pm - 7:00 pm

Scientific Sections Meet and Greet Maryland 2/3

6:30 pm - 7:00 pm

Leadership and Mentor Reception *(by invitation only)* Maryland 1

7:00 pm - 9:00 pm

President's Reception Cherry Blossom Ballroom/Foyer

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Gather Digital Mobile Application

We're excited to announce that this year ASCPT has collaborated with Gather Digital to provide a mobile application for the event. You will get up-to-the-minute information such as the latest agenda, updates from the conference planner, speaker information, maps, exhibitor and sponsor details, an attendee list and more.

An iPhone and iPad app are available in the iTunes app store. Search ASCPT and download the ASCPT 2012 Annual Meeting app. You can also access the app with your BlackBerry, Android or other smart phone. Simply point your mobile browser to http://ascpt2012.gatherdigital.com (note: omit the www) and bookmark it.

One of the features of the mobile app is that you and other attendees will have the option to send messages to each other through the app. It's a great way to network with fellow attendees up to and during the event. You can also create a profile of yourself that other event attendees can view. To enable these features you must establish a password which you can do from the app.

We hope you use and enjoy the mobile application.

SATURDAY • MARCH 17

6:45 am - 9:00 am

ASCPT Board of Directors Meeting *(by invitation only)* Chesapeake D

7:00 am - Noon

ASCPT Registration Open Maryland Foyer

ASCPT Central Open Maryland Foyer

7:00 am - 8:00 am

Continental Breakfast in Exhibit Hall (all attendees) Prince George's Hall C
Posters Open Prince George's Hall C
Poster Session III Prince George's Hall C
Late-Breaking Poster Session III Prince George's Hall C

7:30 am - 2:00 pm

Career Bootcamp Half-Day Program *(Trainees and students only.)*
Chesapeake H/I • See page 40 for program details. *(Registration is required.)*

Chairs Kathleen Neville, MD, MS • Children's Mercy Hospitals and Clinics
Bridgette Jones, MD • Children's Mercy Hospitals and Clinics

8:00 am - 9:30 am • *3 Concurrent Workshops*

Crossing Over: Innovation and Alternative Trial Designs in Drug Development, Utilization, and Regulation
endorsed by BIO/DDR/MOL/ONC Maryland A

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

Speakers Nicholas Schork, PhD • Scripps Research Institute
Marker-Based Enrichment and N-of-1 Clinical Trial

Robert Temple, MD • US Food and Drug Administration
Crossover Trials: A Regulatory History and Perspective on Future Utility

Robert Schmouder, MD, MPH • Novartis
Innovations in Early Clinical Trial Designs: Application to New Drug Development

Learning Objectives

1. To provide an overview of and rationale for biomarker-restricted clinical trials and discuss the "N-of-1" clinical trial as the "ultimate study design for personalizing medicine."
2. To outline FDA regulatory precedents related to crossover studies.
3. To describe current and future clinical and drug development contexts for innovations in clinical trial designs and discuss innovative ways to conduct trials required to prove that a new medicine is safe, effective, and of superior value to patients.

Kathleen Neville, MD
Career Bootcamp Chair

Bridgette Jones, MD
Career Bootcamp Chair

Issam Zineh, PharmD, MPH
Workshop Chair

SATURDAY • MARCH 17

8:00 am - 9:30 am • *3 Concurrent Workshops (continued)*

Metabolites in Safety Testing: What Have Clinical Pharmacologists MIST?

endorsed by DDR/PMK Maryland D

Chair Malle Jurima-Romet, PhD • Celerion, Inc.

Speakers Mark W. Powley, PhD • US Food and Drug Administration
FDA MIST and ICH M3(R2) Guidance-Interpretation and Considerations

R. Scott Obach, PhD • Pfizer, Inc.
MIST for Clinical Pharmacologist

Graham Lappin, PhD • University of Lincoln and Xceleron
Analytical Technologies for Metabolite Identification and Quantitation

Learning Objectives

1. To discuss the rationale for the FDA and ICH regulatory guidances pertaining to MIST, areas in common and differences between these guidances, present an update on regulatory perspectives, and review some recent examples of regulatory application of the guidance documents.
2. To discuss the concerns underlying MIST: how can metabolites cause or contribute to toxicity, and the scientific issues involved and strategies for addressing the requirement for profiling of circulating human metabolites early in clinical development.
3. To discuss analytical technologies and strategies to obtain qualitative and quantitative metabolite data from early clinical studies to address MIST issues.

Should We Tolerate the Maximally Tolerated Dose for Targeted Anti-Cancer Agents?

endorsed by DDR/ONC/PMK Maryland C

Chairs Keith Orford, MD, PhD • GlaxoSmithKline
Mark Stroh, PhD • Amgen Inc.

Speakers Christopher Carpenter, MD, PhD • GlaxoSmithKline
The Maximally Tolerated Dosing Paradigm: History and Defense

Michael Maitland, MD, PhD • University of Chicago Medical Center
Being PC (Pharmacologically and Politically Correct) in Current Cancer Drug Development

René Bruno, PhD • Pharsight
The Use of Clinical Endpoints for Dose Selection

Learning Objectives

1. To review the rationale for use of maximally-tolerated dosing (MTD) in oncology.
2. To review the rationale for selection of the optimal dose (or dose range) based upon biomarker readout and/or clinical endpoints.
3. To encourage discussion regarding selection of the most appropriate dosing paradigm for targeted anti-cancer agents.

9:45 am - 10:45 am

Leon I. Goldberg Young Investigator Award Lecture Maryland A

Michael Maitland, MD, PhD • University of Chicago Medical Center

Next Phase, New Wave, Drug Craze, Anyways…

Presenter Mark J. Ratain, MD • University of Chicago Medical Center

The *Leon I. Goldberg Young Investigator Award Lecture* recognizes a young scientist for accomplishments in the field of clinical pharmacology early in his/her career.

Michael Maitland, MD, PhD
Award Lecturer

Malle Jurima-Romet, PhD
Workshop Chair

Keith Orford, MD, PhD
Workshop Chair

Mark Stroh, PhD
Workshop Chair

SATURDAY • MARCH 17

10:50 am - 11:50 am • *3 Concurrent Abstract Sessions*

Oral Session OIII-A

Innovative Quantitative Approaches in Drug Development and Trial Design

Maryland D

Chair Amita Joshi, PhD • Genentech, Inc.

OIII-A-1

UNDERSTANDING PLACEBO RESPONSES IN ALZHEIMER'S DISEASE CLINICAL TRIALS FROM THE LITERATURE META-DATA AND CAMD DATABASE

Presenter Kaori Ito, PhD • Pfizer, Inc.

OIII-A-2

DEVELOPMENT AND APPLICATION OF A MODEL-BASED DECISION CRITERION FOR A LABORATORY ENDPOINT TO FACILITATE TOFACITINIB (CP-690,550) PHASE 3 DOSE SELECTION

Presenter Pankaj Gupta, BPharm, PhD • Pfizer, Inc.

OIII-A-3

A SYSTEMS MODELING APPROACH TO UNDERSTANDING THE MECHANISMS OF RENAL PROTECTION WITH THE DIRECT RENIN INHIBITOR ALISKIREN (ALI)

Presenter K. Melissa Hallow, PhD • Novartis, Inc.

OIII-A-4

USE OF THE TARGET-MEDIATED DRUG DISPOSITION (TMDD) MODEL TO SUPPORT DOSE SELECTION OF AN OPTIMAL DOSING REGIMEN IN PHASE III TRIALS FOR GA101, THE FIRST TYPE II GLYCOENGINEERED, HUMANIZED MONOCLONAL ANTI-CD20 ANTIBODY

Presenter Florence Hourcade-Potelleret, PharmD • F. Hoffman-LaRoche, LTD

Oral Session OIII-B

Application of Biomarkers in Oncology: from Discovery to Utilization

Maryland C

Chairs Jerry Collins, PhD • National Cancer Institute, NIH
Sarah Holstein, MD, PhD • University of Iowa

OIII-B-1

A GENOME WIDE APPROACH FOR DISCOVERING POTENTIAL BIOMARKERS OF CHEMOTHERAPEUTIC AGENTS SUSCEPTIBILITY

Presenter Yujia Wen, PhD • The University of Chicago

OIII-B-2

IDENTIFICATION OF TRANSPORTERS AND KINASE TARGETS INVOLVED IN SORAFENIB SKIN TOXICITY

Presenter Sharyn D. Baker, PharmD, PhD • St. Jude Children's Research Hospital

OIII-B-3

PHARMACOGENOMICS OF BREAST CANCER ENDOCRINE THERAPY: TSPLY5 SNPS ARE ASSOCIATED WITH PLASMA ESTRADIOL (E2) CONCENTRATIONS AND THE REGULATION OF AROMATASE

Presenter Mohan Liu, PharmD • Mayo Clinic

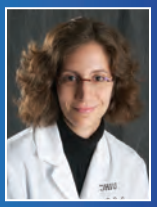
OIII-B-4

ASSOCIATION BETWEEN TUMOR SIZE DYNAMICS AND TREATMENTS, PROGNOSTIC FACTORS AND CLINICAL OUTCOMES IN 2ND LINE NSCLC

Presenter Kelong Han • Genentech, Inc.

Amita Joshi, PhD
Oral Session Chair

Jerry Collins, PhD
Oral Session Chair



Sarah Holstein, MD, PhD
Oral Session Chair

SATURDAY • MARCH 17

10:50 am - 11:50 am • *3 Concurrent Abstract Sessions (continued)*

Late-Breaking Oral Session Maryland A

These late-breaking abstracts will be presented as oral and poster presentations.
See page 74 for complete abstract information.

Chairs Kellie S. Reynolds, PharmD • US Food and Drug Administration
Susan Shoaf, PhD • Otsuka Pharmaceutical Development and Commercialization

LB-A-1
AGE-RELATED DIFFERENCES IN PLASMA AND INTRACELLULAR (IC) TENOFOVIR (TFV) CONCENTRATIONS
Presenter Gautam Baheti, MSc • University of Nebraska Medical Center

LB-A-2
PHARMACOKINETICS AND SAFETY OF METRONIDAZOLE IN PRETERM INFANTS: VALIDATION OF DRIED BLOOD SPOT SAMPLING
Presenter Mario Sampson • Duke Clinical Research Institute

LB-A-3
EFFECT OF THE NOVEL CYP3A4 INTRON 6 POLYMORPHISM (CYP3A4*22) AND CYP3A COMBINED GENOTYPES ON TACROLIMUS DOSING REQUIREMENTS AND BLOOD CONCENTRATIONS IN PEDIATRIC HEART TRANSPLANT RECIPIENTS
Presenter Violette M. Gijsen, MSc • Erasmus MC-Sophia Children's Hospital

LB-A-4
INTRAVENOUS PARACETAMOL REDUCES MORPHINE REQUIREMENTS IN NEONATES AND YOUNG INFANTS UNDERGOING MAJOR NON-CARDIAC SURGERY: RESULTS OF A RANDOMIZED CONTROLLED TRIAL
Presenter Saskia N. de Wildt, MD, PhD • Erasmus MC-Sophia Children's Hospital

Noon - 1:30 pm • *3 Concurrent Workshops*

Evaluation of Concentration-QT Relationship in Early Clinical Development: Is a Thorough QT Study Necessary?

endorsed by SAF/PMK Maryland A

Chairs Venkat Jarugula, PhD • Novartis Institutes for Biomedical Research
Joga Gobburu, PhD • University of Maryland

Speakers Venkat Jarugula, PhD • Novartis Institutes for Biomedical Research
QT Evaluation in Early Clinical Development and Impact on Thorough QT Study

Brian Smith, PhD • Amgen, Inc.
Statistical Considerations in Characterizing Exposure: QTc Relationship in Drug Development

Christine Garnett, PharmD • US Food and Drug Administration
Value of Evaluation Concentration: QTc Relationship in Regulatory Decision Making

Learning Objectives

1. To review and understand the role of concentration-QT relationship evaluation in drug development and its impact on regulatory decision making.
2. To discuss if a well characterized concentration-QT relationship during early clinical development can obviate the need to conduct a thorough QT study.

Kellie S. Reynolds, PharmD
Late-Breaking Oral Chair

Susan Shoaf, PhD
Late-Breaking Oral Chair

Venkat Jarugula, PhD
Workshop Chair

Noon - 1:30 pm • *3 Concurrent Workshops (continued)*

Imaging Studies of Drug Transport and Response

endorsed by BIO/MOL Maryland C

Chairs John Mendelson, MD • California Pacific Medical Center Research Institute
Kim L. R. Brouwer, PharmD, PhD • University of North Carolina

Speakers J. James Frost, MD, PhD, MBA • BioMolecular Imaging, LLC
Imaging CNS Drug Transporters: From Early Development to Novel Market Opportunities

Bertha Madras, PhD • Harvard Medical School
Imaging Drug Occupancy of the Dopamine Transporter

Kim L.R. Brouwer, PharmD, PhD • University of North Carolina at Chapel Hill
Technetium-Labeled Probes to Assess Hepatic Transporter Activity and Drug-Drug Interactions in Humans

Learning Objectives

1. To be able to describe the use of imaging probes in the measurement of transport activity in the brain and liver, and in cocaine addiction.
2. To list potential sites of drug-drug interactions (DDIs) in hepatobiliary transport and describe how imaging agents can be used to assess hepatic transport-mediated DDIs.

Novel Protein Therapeutics: Delivering Toxins to Tumors and mAbs to Patients to Improve Therapeutic Benefit

endorsed by ONC Maryland D

Chairs Richard Graham, PhD • Genentech, Inc.
Stacy Shord, PharmD • US Food and Drug Administration

Speakers Christine McIntyre, PhD • F. Hoffman-La Roche AG
Enhancing Therapeutic Benefit of Monoclonal Antibodies Through Subcutaneous Administration

Manish Gupta, PhD, FCP • Bristol-Myers Squibb
Clinical Pharmacology of Antibody Drug Conjugates

Stacy Shord, PharmD • US Food and Drug Administration
Regulatory Commentary on Clinical Pharmacology of Novel Protein Therapeutics

Learning Objectives

1. To understand how delivery of monoclonal antibodies by subcutaneous administration may improve patient convenience and therapeutic benefit.
2. To diagram how each of the structural components of an ADC, including the monoclonal antibody or fragment, the linker, and the small molecule (payload), influence the nonclinical/preclinical and clinical pharmacology development study of a proposed drug product using examples of currently approved ADCs or those undergoing development.
3. To illustrate approaches within the US FDA to support the development of drug products in which the benefits outweigh the risks.

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John Mendelson, MD
Workshop Chair

Kim L. R. Brouwer, PharmD, PhD
Workshop Chair

Richard Graham, PhD
Workshop Chair

Stacy Shord, PharmD
Workshop Chair

CAREER BOOTCAMP

HALF-DAY PROGRAM FOR TRAINEES & STUDENTS

SATURDAY, MARCH 17 • Chesapeake H/I

CHAIRS

Kathleen Neville, MD, MS

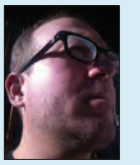
Bridgette Jones, MD

SPEAKERS

Gregory L. Kearns, PharmD, PhD

Jun Yang, PhD

Bert L. Lum, PharmD



David Katz, PhD

Deanna Kroetz, PhD

Anne Zajicek, MD, PharmD

7:30 am - 8:00 am **Continental Breakfast**

8:00 am - 8:30 am

How to Find a Mentor

Kathleen Neville, MD, MS

This session will instruct trainees and those who are early in their career on how to find an appropriate mentor. Included will be expectations of a mentor/mentee relationship and how to foster highly productive lifelong mentor relationships.

8:30 am - 9:00 am

A Five Year Plan to Jump Start a Career in Academia

Gregory L. Kearns, PharmD, PhD

This session will provide trainees and those who are early in their career with instructions on how to develop a five year strategy for starting a successful career. Topics covered will include: 1) obtaining and maintaining funding; 2) considerations regarding tenure/promotion; and 3) how to develop and stay on track with career goals, including how to choose high yield projects and how/when to skillfully say no.

9:00 am - 9:30 am

Negotiating a Starting Package

Jun Yang, PhD

This session will provide valuable instructions on negotiating salary, lab/office space, faculty development and educational support, as well as other support infrastructure to ensure a successful start to a career.

9:30 am - 10:00 am

Practical Points in Finding/Evaluating/Applying for Biotech/Pharma Positions

Bert L. Lum, PharmD

This session will cover integrating the biotech revolution and clinical pharmacology into a career path that makes a difference. It will also cover how to showcase your skills (technical, research, general talents) and ambitions when applying for a position. Types of positions available (small vs. large pharma, biotech vs. pharma) will also be discussed.

10:00 am - 10:30 am

Considerations Unique to Early Career Decisions in the Biotech/Pharma Industry

David Katz, PhD

This session will cover the how/when/why to move within a company/between companies/between subspecialties in the biotech/pharma industry.

10:30 am - 10:45 am **Break**

10:45 am - 11:45 am

Ask the Experts: Getting Real Answers to Your Most Difficult Questions

Kathleen Neville, MD, MS, Gregory L. Kearns, PharmD, PhD, and Jun Yang, PhD

This panel discussion will more fully elaborate on topics covered in the previous sessions, specifically in the areas of Academia and Industry. This session is designed to be an interactive discussion with attendees and between panelists and is intended to stimulate discourse around topics not routinely covered during training.

11:45 am - Noon **Working Lunch Grab-n-Go**

Noon - 12:45 pm

Grants 101/Non-NIH Funding

Deanna Kroetz, PhD

This session will cover the basic components of every grant application and will briefly discuss resources in addition to NIH that are available for extramural funding.

12:45 pm - 1:45 pm

Meet the NIH

Anne Zajicek, MD, PharmD

This session will provide insight into navigating the NIH. A representative from the NIH will discuss award mechanisms through the NIH (K awards, R awards, early investigator status), organization structure, what do the acronyms mean, and how to navigate through the system.

1:45 pm - 2:00 pm

Questions/Wrap-up

HOTEL & MEETING ROOM FLOOR PLAN

GAYLORD NATIONAL HOTEL AND CONVENTION CENTER

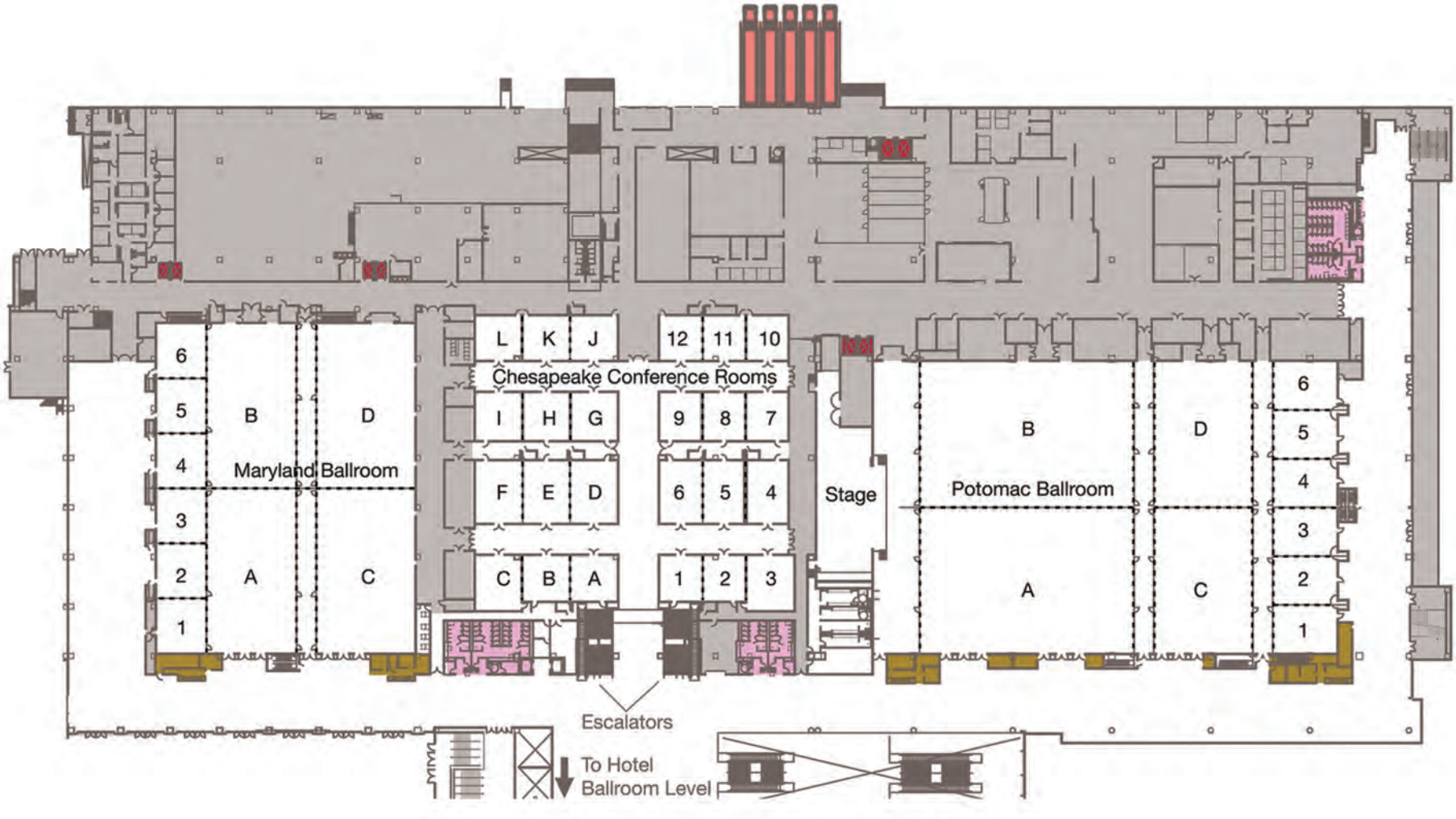
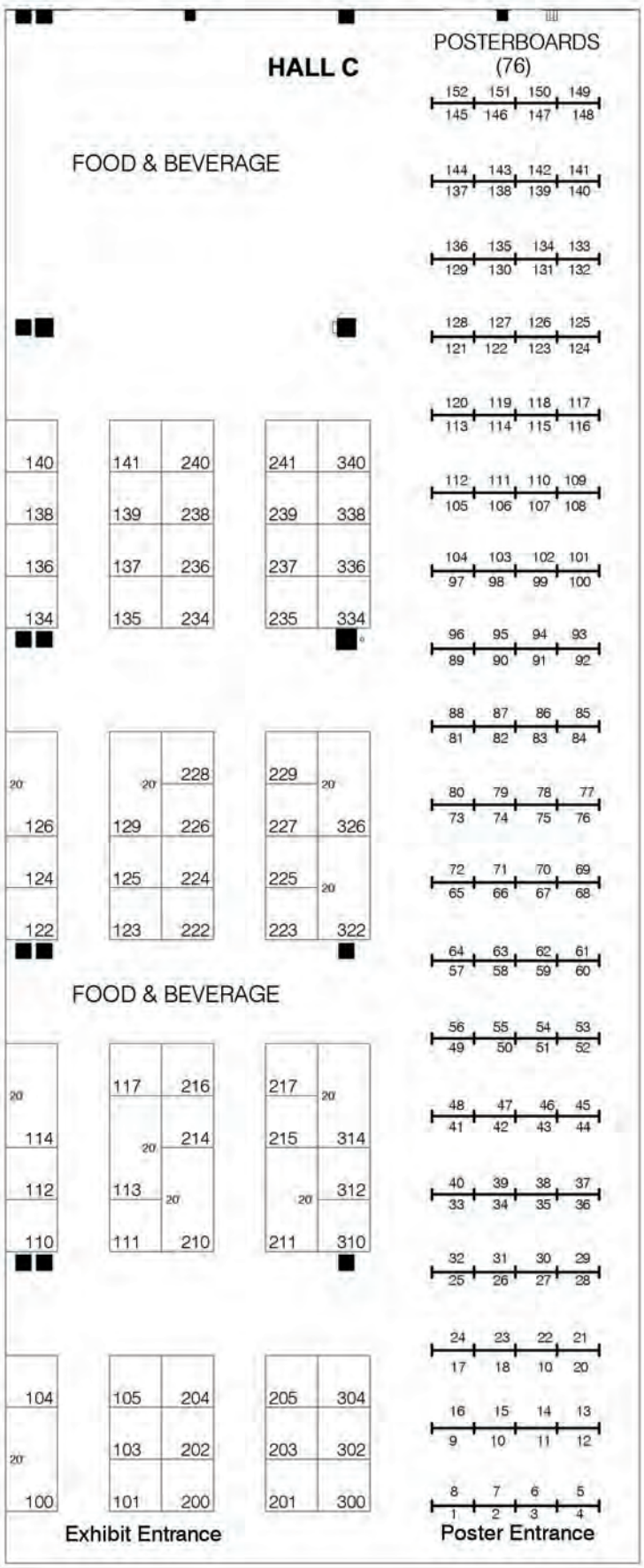


EXHIBIT HALL/POSTER FLOOR PLAN

GAYLORD NATIONAL HOTEL AND CONVENTION CENTER

PRINCE GEORGE'S EXHIBIT HALL C



EXHIBITORS BY COMPANY NAME

PRINCE GEORGE'S EXHIBIT HALL C
Wednesday, March 14 | 6:00pm-8:00pm ★ Thursday, March 15 | 8:00am-3:00pm ★ Friday, March 16 | 8:00am-3:00pm

112 Accel Research Sites
103 Advanced Pharma CR, LLC
140 Algorithme Pharma
235 American College of Clinical Pharmacology
105 Anaheim Clinical Trials (formerly ACRI-Phase, LLC)
200 ARENSIA Exploratory Medicine (formerly ASCENT Clinical Research Solutions)
134 Aspire*irb*
111 Bayer Technology Services GmbH
241 Bio Pharma Services Inc.
203 Biotrial
141 Ce3, Inc.
224 CMAX, a division of IDT Australia, Limited
334 CNS Network, Inc.
227 CPR Pharma Services Pty. Ltd.
122 CRI Lifetree (formerly CRI Worldwide LLC)
340 CRS - Clinical Research Services
210 Celerion
322 Cetero Research (i.e. CRS Management, Inc.)
304 Clinical Pharmacology of Miami, Inc.
135 clinicalRSVP
110 Clinigene International
223 Clinilabs
237 Community Research
338 Compass Research Inc.
101 Comprehensive Clinical Development (formerly Comprehensive NeuroScience)
222 CoreLab Partners, Inc.
326 Covance, Inc.
113 DaVita Clinical Research
104 Duke Clinical Research
336 ERT, Inc.
124 EUROFINS OPTIMED
314 ICON Development Solutions LLC
228 INC Research
236 Johnson & Johnson
137 LMC Endocrinology Centres
117 Logos Technologies, Inc.
226 MD Clinical
239 Microconstants China, Inc.
214 Mortara Instrument
125 NIH/Obstetric and Pediatric Pharmacology Branch (OPPB)
215 Nature Publishing Group
205 New Orleans Center for Clinical Research
225 Nuvisan GmbH
302 OmniComm
238 Oracle Health Sciences
204 Orlando Clinical Research Center
114 PRA International
129 PAREXEL International
217 PharmaNet/i3 (formerly PharmaNet Development Group)
202 Prism Research
310 Profil Institute for Clinical Research
123 ProMedica CRC, Inc.
300 QPS Bio-Kinetic
216 Quintiles
234 Quotient Clinical
211 SGS Life Science Services
240 SNBL Clinical Pharmacology Center
229 Simcyp Limited
312 Simulations Plus, Inc.
126 Spaulding Clinical Research
100 Vince and Associates Clinical Research
201 WCCT Global, LLC

EXHIBITORS BY BOOTH NUMBER

Wednesday, March 14 | 6:00pm-8:00pm ★ Thursday, March 15 | 8:00am-3:00pm ★ Friday, March 16 | 8:00am-3:00pm

100 Vince and Associates Clinical Research
101 Comprehensive Clinical Development (formerly Comprehensive NeuroScience)
103 Advanced Pharma CR, LLC
104 Duke Clinical Research
105 Anaheim Clinical Trials (formerly ACRI-Phase, LLC)
110 Clinigene International
111 Bayer Technology Services GmbH
112 Accel Research Sites
113 DaVita Clinical Research
114 PRA International
117 Logos Technologies, Inc.
122 CRI Lifetree (formerly CRI Worldwide LLC)
123 ProMedica CRC, Inc.
124 EUROFINS OPTIMED
125 NIH/Obstetric and Pediatric Pharmacology Branch (OPPB)
126 Spaulding Clinical Research
129 PAREXEL International
134 Aspire*irb*
135 clinicalRSVP
137 LMC Endocrinology Centres
140 Algorithme Pharma
141 Ce3, Inc.
200 ARENSIA Exploratory Medicine (formerly ASCENT Clinical Research Solutions)
201 WCCT Global, LLC
202 Prism Research
203 Biotrial
204 Orlando Clinical Research Center
205 New Orleans Center for Clinical Research
210 Celerion
211 SGS Life Sciences Services
214 Mortara Instrument
215 Nature Publishing Group
216 Quintiles
217 PharmaNet/i3 (formerly PharmaNet Development Group)
222 CoreLab Partners, Inc.
223 Clinilabs
224 CMAX, a division of IDT Australia, Limited
225 Nuvisan GmbH
226 MD Clinical
227 CPR Pharma Services Pty. Ltd.
228 INC Research
229 Simcyp Limited
234 Quotient Clinical
235 American College of Clinical Pharmacology
236 Johnson & Johnson
237 Community Research
238 Oracle Health Sciences
239 Microconstants China, Inc.
240 SNBL Clinical Pharmacology Center
241 Bio Pharma Services, Inc.
300 QPS Bio-Kinetic
302 OmniComm
304 Clinical Pharmacology of Miami, Inc.
310 Profil Institute for Clinical Research
312 Simulations Plus, Inc.
314 ICON Development Solutions LLC
322 Cetero Research (i.e. CRS Management, Inc.)
326 Covance, Inc.
334 CNS Network, Inc.
336 ERT
338 Compass Research, Inc.
340 CRS - Clinical Research Services

EXHIBITS

PRINCE GEORGE'S EXHIBIT HALL C

Wednesday, March 14 | 6:00pm-8:00pm ★ Thursday, March 15 | 8:00am-3:00pm ★ Friday, March 16 | 8:00am-3:00pm

Accel Research Sites — Booth 112

860 Peachwood Drive
DeLand, FL 32720
USA

Phone 919.342.6512
Email scalandra@accelclinical.com
Web www.accelclinical.com

Accel Research Sites are industry-leading clinical research sites with the clinical expertise, therapeutic experience and capabilities to successfully fulfill clinical trials in a wide range of therapeutic indications. We pride ourselves on delivering high quality work to our customers, which include major Pharmaceutical, Biotechnology, and Clinical Research Organizations. **We conduct Phase I, In-Hospital, Oncology, Vaccine and Outpatient Phase II-IV trials.**

Speed to delivery, a dedicated in-house patient recruitment team, disciplined process management and quality data collection ensure our sponsors receive the highest value for their clinical research investments.

Advanced Pharma CR, LLC — Booth 103

University of Miami
Life Science & Technology Park
1951 NW 7th Avenue
Suite 13133
Miami, FL 33136 USA

Phone 305.220.2727
Fax 305.220.2730
Email samaba@advancedpharmacr.com
Web www.advancedpharmacr.com

Advanced Pharma CR is a dedicated Phase I-IV Clinical Research Facility located in the densely populated South Florida area at the state-of-the-art University of Miami Life Science & Technology Park. Our facility includes a 24-bed dedicated Phase I Unit, which will soon expand to a dedicated 125-bed Phase I Unit. APCR conducts clinical trials in ALL Specialties and ALL Indications.

Algorithme Pharma — Booth 140

575, Armand-Frappier Blvd.
Laval, Quebec Canada
H7V 4B3

Phone 450.973.6077
1.888.267.7449
Email contact@algopharm.com
Web www.algopharm.com

Algorithme Pharma, a member of Altasciences, is an early stage clinical CRO with a full service offering, from study design to study conduct, PK/PD analysis and bioanalysis. Working along with their sister company, Simbec Research in the UK, they have been servicing international pharmaceutical, biotechnology and generic drug companies for over 35 years.

Algorithme Pharma's GLP-compliant bioanalytical facilities perform large and small molecule bioanalysis on samples from preclinical to Phase IV studies.

The team is made up of almost 500 professionals from the medical and scientific fields who work together to conduct Phase I/IIa, Bioequivalence and 505(b)(2) studies, involving over 5,000 participants including patient populations.

American College of Clinical Pharmacology — Booth 235

PO Box 1637
Rockville, MD 20849
USA

Phone 240.399.9070 / 240.399.9076
Fax 240.399.9071
Email TStevens@ACCP1.org
Web www.ACCP1.org

American College of Clinical Pharmacology (ACCP) is a non-profit organization comprised of a wide spectrum of health care professionals devoted to improving health by optimizing therapeutics and providing innovative leadership and interdisciplinary education that will enable the generation, integration and translation of scientific knowledge to optimize research, development and utilization of medication for the benefit of all.

Anaheim Clinical Trials — Booth 105

1085 N. Harbor Boulevard
Anaheim, CA 92801
USA

Phone 714.774.7777
Fax 714.399.4135
Email pm@act-trials.com
Web www.act-trials.com

Anaheim Clinical Trials (ACT) is a research center of excellence for the administration of PHASE I clinical trials.

ACT is one of the largest independently owned Research Sites in the United States. It is an organization committed to exceeding the needs and expectations of our clients by providing innovative, professional and superior quality service with integrity and reliability. Our mission is to advance science and ensure the protection and safety of all patients who choose to participate in our clinical trials, ensure compliance with government regulations, recognize the value of our client, subject, and employee partnerships, exceed customer expectations through a combination of dedication, hard work and perseverance without compromise, and champion solutions through innovative thinking.

ARENSIA Exploratory Medicine — Booth 200

Moskauer Str. 25
40227 Duesseldorf
Germany

Phone + 49 211 15 77 89 0
Fax + 49 211 15 77 89 10
Email info@arensia-em.com
Web www.arensia-em.com

ARENSIA EXPLORATORY MEDICINE is expert in performing EARLY PATIENT STUDIES in various therapeutic areas. We run modern Phase I units located in Eastern European university clinics.

Our projects imply a high degree of scientific and logistical features (e.g. sophisticated designs, biomarkers), within a fast regulatory approval environment.

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Aspire*irb* — Booth 134

11491 Woodside Avenue
Santee, CA 92104
USA

Phone 619.469.0108
Fax 619.469.4108
Email john@aspire-irb.com
Web www.aspire-irb.com

Aspire IRB is a fully AAHRPP accredited Independent Review Board (IRB), based in San Diego, CA, providing full IRB review and approval services for clinical trials in all therapeutic areas and Phases I-IV.

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EXHIBITS

PRINCE GEORGE'S EXHIBIT HALL C

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Bayer Technology Services GmbH — Booth 111

Building K-9
D-51368 Leverkusen
Germany

Phone +49 (0) 214 30-1
Email info@bayertechnology.com
Web www.bayertechnology.com

Bayer Technology Services GmbH, a Bayer AG company, is a capable supplier of technology solutions for the chemical and pharmaceutical industries. With the aim of supporting decision making along the pharma research and development process, our Systems Pharmacology Group offers software products for predictive simulation of drug behavior and modeling of cellular pathways (Computational Systems Biology Software Suite with PK-Sim® and MoBi®) as well as professional application and consulting services, integrating many years of in-house and external market experience.

Bio Pharma Services Inc. — Booth 241

4000 Weston Road
Toronto Ontario
Canada M9L3A2

Phone 416.747.8484
Fax 416.747.8480
Email tfoster@biopharmaservices.ca
Web www.biopharmaservices.ca

BioPharma Services Inc. is an FDA-inspected, physician-owned, Contract Research specializing in Phase I/IIa clinical trials in healthy volunteers, special populations, and patient populations. Founded in 2006, we currently work with over 40 pharmaceutical companies to conduct clinical trials for US, Canadian, and European submission. Bio Pharma's modern Toronto-based Clinical Facility and Headquarters has 50,000 square feet in space and a174-bed capacity comprised of three 48-64 bed BA/BE study clinics and one 14 bed ICU unit for first-in-man and first-in-patient clinical trials. This facility has also been inspected by Health Canada and UK MHRA.

Biotrial — Booth 203

7-9 rue Jean-Louis Bertrand
35000 Rennes
France

Phone +33 0 2 99 599 191
Fax +33 0 2 99 599 197
Email smarin@biotrial.com
Web www.biotrial.com

Founded in 1989, Biotrial is a leading CRO specialized in Early Development with a large range of services from Non-Clinical Pharmacology, Phase I studies, Phase II-IV Trial Management, Oncology, Data Management, Biostatistics, Core Lab (ECG, Imaging, cognitive assessments…), Regulatory Affairs to Medical Writing.

Based in France, the UK, and Belgium, Biotrial performs hundreds of studies a year and offers tailor-made solutions to Pharma and Biotech companies. In the past year Biotrial expanded its Paris Unit, has opened a new 50,000 sq. ft. extension in Rennes and has announced the location of the new 100-bed Phase I Clinic in Newark, NJ, USA. In 2012 Biotrial continues to develop new partnerships in India as well as will be increasing bed capacity in the Rennes Phase I Clinic.

Ce3 Inc. — Booth 141

246 Goose Lane
Suite 202
Guilford, CT 06437
USA

Phone 203.252.7594
Fax 203.646.9919
Email mforgione@ce3inc.com
Web www.ce3inc.com

Ce3 is a full service contract research organization focused on providing biotechnology companies with Phase 1 – 3 clinical trial execution and regulatory submission services. Our seasoned staff works across a broad range of therapeutic areas, with particular expertise in oncology and infectious disease indications. CE3 stands for Collaborative, Experience, Efficiency & Excellence which are qualities that represent our core values and serve as the foundation for all that we do. Clients benefit from our flexibility, process efficiency, value pricing, and our collaborative relationships with state-of-the-art niche providers; a competitive edge that amplifies value in this highly regulated environment.

CMAX, a Division of IDT Australia Limited — Booth 224

Level 5 East Wing
Royal Adelaide Hospital
North Terrace
Adelaide, SA, 5000
Australia

Phone +61 8 82222 3923
Fax +61 8 8223 3475
Email jane.kelly@cmax.com.au
Web www.cmax.com.au

CMAX, a Division of IDT Australia Limited, has been established as a Phase I clinical research facility since December 1993, making it the longest-running in Australia. The facility has 50 beds, housed within a self-contained unit co-located within the Royal Adelaide Hospital, which is the largest public, teaching hospital in South Australia.

CMAX specializes in the conduct of Phase I studies including first-time-in-man studies, as well as participating in Phase II-IV studies as an investigative site. CMAX provides services to both local and international clients. We pride ourselves on the provision of high quality data and responsiveness to our clients.

CNS Network, Inc. — Booth 334

12772 Valley View Street
Suite #3
Garden Grove, CA 92845
USA

Phone 714.799.7799
Fax 714.799.1633
Email clinicaltrials@cnstrial.com
Web www.cnstrial.com

CNS Network, Inc. is a leading research institution specializing in disease specific early phase studies. Our 25,000 square foot facility is located in Long Beach, California with 45 beds on our Phase I/II unit and 14 in our licensed psychiatric facility. Our area of expertise is in recruiting challenging patient populations for complex research protocols including schizophrenia, Alzheimer's disease, Parkinson's disease, migraine and depression. Additionally, CNS Network has outpatient clinics for later phase research in Garden Grove, Long Beach, Torrance and Oakland, CA. For more information please access our web-site at www.cnstrial.com or contact Bobbie Theodore at 916-939-6696.

CPR Pharma Services Pty Ltd. — Booth 227

Suite C
32 West Thebarton Road
Thebarton, South Australia
5031

Phone 1 514 441 2313 (NA)
+61 8 8125 1900 (AUS)
Fax +61 8 8354 3146
Email jeanmarie.houle@cprservices.com.au
Web www.cprservices.com.au

Australia and Singapore have very efficient and dependable regulatory/ethics paths facilitating faster transition into Phase 1 studies and POC trials in patients, with globally recognized quality. Join other Biotech and Pharma companies that are already benefiting from this opportunity.

CPR is the only Australia and Singapore-based full-service CRO with a focus on early-stage clinical research, due to its unique combination of clinical trial, data management and accredited GLP bioanalytical services.

CPR expertise is recognized globally. CPR's experienced staff and quality processes are confirmed by a successful FDA audit in 2011 and >85% rate of repeat business.

CRI Lifetree — Booth 122

16000 Horizon Way
Suite 100
Mount Laurel, NJ 08054
USA

Phone 865.533.5020
Fax 856.235.0048
Email jsacco@criww.com
Web www.criwwcom

CRI Lifetree is a leader in specialized, multi-therapeutic early stage research. The company has significant expertise in psychiatry, pain, neurology, pediatrics, and patient population trials, as well as widely recognized clinical trial expertise in Phase I-III pain management and abuse liability studies. CRI Lifetree offers a broad range of Phase I-IV services and rapid access to specific patient populations to meet the requirements of complex clinical research programs. With sites in Philadelphia, New Jersey, and Salt Lake City, the company conducts inpatient and outpatient clinical research in special populations and healthy volunteers.

CRS - Clinical Research Services — Booth 340

Lohmannstraße 2
56626 Andernach
Germany

Phone +49 2632 992784
Fax +49 2632 992401
Email david.surjo@crs-group.de
Web www.crs-group.de

CRS is a leading European full-service CRO (Phase I-IIa, Phase IIb-IV, Bioanalytics, CDM/Statistics and CTSM services) with more than three decades experience in clinical trials. We have 200 beds amongst our three own clinical pharmacology units all of which function under a centralized common SOP system maintaining rigorous adherence to GCP, GLP, and GMP guidelines. These units are located in metropolitan areas providing facilitated recruitment of either healthy volunteers or patients. CRS offers the conduct of a complete range of high-quality clinical trials including FIM, POC, interaction trials, patient trials, and specialities like TQT, skin safety, respiratory research and renal/hepatic insufficiency studies.

Celerion — Booth 210

621 Rose Street
Lincoln, Nebraska 68502
USA

Phone 1.402.476.2811
Fax 1.866.358.7993
Email info@celerion.com
Web www.celerion.com

Celerion is the premier provider of innovative early stage clinical research solutions. From facilities strategically located around the world, advanced scientific and technological expertise is applied to global clinical research (over 730 beds (24 in-hospital) in Phases 0, I and IIa, NDA-enabling clinical pharmacology, ADME), clinical pharmacology sciences, global bioanalytical services (discovery through late stage), and drug development services. Celerion has a full spectrum of resources to meet the needs of the pharmaceutical, biotechnology and generic industries for Phase 0 through IIa proof-of-concept studies.

Cetero Research (i.e. CRS Management, Inc.) — Booth 322

2000 Regency Parkway
Suite 255
Cary, NC 27518
USA

Phone 877.7CETERO
Fax 919.468.6850
Email info@cetero.com
Web www.cetero.com

Cetero is the industry's leading early-phase CRO, specializing in full-service clinical pharmacology, bioanalytical and scientific affairs services. With nearly 30 years of experience, we have conducted more than 20,000 clinical pharmacology studies – more than any other CRO.

Cetero's proven track record allows us to provide flexible and high-quality, drug-development services, and our time-tested systems produce consistent and reliable data you can trust.

With five clinical sites across North America, Cetero is the leader in early-stage development. Our repertoire of clinical-pharmacology study experience includes first-in-human, accelerated proof-of-concept, interaction, bioavailability, PK/PD and Thorough QT studies.

Clinical Pharmacology of Miami, Inc. — Booth 304

550 West 84 Street
Miami, Florida 33014
USA

Phone 305.817.2900
Fax 305.817.2900
Email klasseter@clinpharmmiami.com
Web www.clinpharmmiami.com

Clinical Pharmacology of Miami, Inc. is a private pharmaceutical research organization dedicated to the conduct of clinical trials (Phase I-IV) in the South Florida area. Kenneth C. Lasseter, MD, Stacy C. Dilzer, RN, BSN, and E Cooper Shamblen are the principals who make up our experienced management team. We have the experience, expertise and facility to conduct safe, well controlled clinical research with new and existing drugs. Our research facility is state of the art and fully equipped with 120 beds. Our local subject population includes healthy males and females, Hepatically Impaired, Renal insufficiency, Hypertensive, Geriatric, Diabetic and Obese volunteers.

clinicalRSVP — Booth 135

401 E. Las Olas Boulevard
Suite 130-395
Ft. Lauderdale, FL 33301
USA

Phone 954.727.5785
Fax 888.308.7787
Email contact@clinicalRSVP.com
Web www.clinicalrsvp.com

Clinical Research Subject Verification Program, or ClinicalRSVP, is an online registry for clinical trial investigators to securely check subject wash-out criteria prior to enrollment in clinical trials. The results for investigators are improved enrollment accuracy, increased data integrity, and higher levels of participant safety.

Clinigene International — Booth 110

Tower-I, Semicon Park
Phase-2
Electronic City, Bangalore
INDIA-560100

Phone +91 802 808 2732
Fax + 91 802 852 2989
Email bd@clinigeneintl.com
Web www.clinigeneintl.com

Clinigene is an India-based CRO specializing in end-to-end clinical development solutions for biologics. They are a full-service CRO for Phase 1-3 trials (including Central Lab and Data Management Services), and also offer cGLP Bioanalytical and Immunoassay Services. Clinigene's FDA-inspected, 96 bed Human Pharmacology Unit offers full SAD, MAD, DDI, and PK study capability in male and female subjects and patients. Their Phase 2-3 trial data, Phase 1 clinic, and Bioanalytical Lab were inspected by US-FDA and EMA with no major findings. Clinigene has a decade of experience working with American Pharma and Biotech Companies.

EXHIBITS

PRINCE GEORGE'S EXHIBIT HALL C

Wednesday, March 14 | 6:00pm-8:00pm ★ Thursday, March 15 | 8:00am-3:00pm ★ Friday, March 16 | 8:00am-3:00pm

Clinilabs — Booth 223

423 West 55th Street
4th Floor
New York, NY 10019
USA

Phone 646.215.6400
Fax 646.215.6401
Email info@clinilabs.com
Web www.clinilabs.com

Clinilabs is a full-service contract research organization (CRO) that provides early-phase and specialty clinical drug development services to industry. We offer teams, processes, and technology solutions designed to serve single center and multicenter early-phase or specialty patient studies – these services can be scaled as needed to meet the requirements of any clinical development program. Clinilabs is recognized globally as a leading specialty CRO, and has made important contributions to eleven successful new drug applications (NDAs) since 2001.

Community Research — Booth 237

4460 Red Bank Expressway
Cincinnati, OH 45227
USA

Phone 513.721.3868
Fax 513.639.7343
Email mmetzner@communityresearch.com
Web www.communityresearch.com

Compass Research, Inc. — Booth 338

100 W. Gore Street
2nd Floor
Orlando, FL 32806
USA

Phone 407.590.9400
Fax 407.426.9290
Email sstanton@compassresearch.com
Web www.compassresearch.com

Comprehensive Clinical Development — Booth 101

3100 SW 145th Avenue
Suite 340
Miramar, FL 33027
USA

Phone 954.266.2620
Fax 754.201.3956
Email info@comprehensivecd.com
Web www.ComprehensiveCD.com

Comprehensive Clinical Development is a leading provider of premium early phase pharmacology and specialty trials. Concentrating in Phase 0-4 studies in three clinical pharmacology units and coast to coast patient-focused research centers, our expertise spans standard through complex studies, including radiolabelled and cardiac safety.

With access to healthy volunteers and special populations nationwide, we deliver a full range of clinical development services across an array of therapeutic areas, consistently delivering on time and within budget.

CoreLab Partners Inc. — Booth 222

100 Overlook Center
Princeton, NJ 08540
USA

Phone 1.877.632.9432
Fax 1.609.936.2602
Email info@corelabpartners.com
Web www.corelabpartners.com

CoreLab Partners is a leading, independent core lab providing best-in-class centralized cardiac safety services and medical imaging assessment solutions for pharmaceutical, biotechnology, and medical device sponsors of Phase I-V studies. Our commitment to service quality and scientific excellence is focused on expediting our clients' drug development programs.

By combining proven operational processes, experienced project teams and full-time, board-certified, sub-specialty trained radiologists, cardiologists, nuclear medicine physicians and oncologists, we deliver accurate, credible trial data on-time and on-budget.

CoreLab Partners boasts a truly global footprint with more than 325 employees and operational offices in North America, Europe and Asia.

Covance, Inc. — Booth 326

210 Carnegie Center
Princeton, NJ 08540
USA

Phone 1.888.268.2623
Email info@covance.com
Web www.covance.com

Covance, with headquarters in Princeton, New Jersey, is one of the world's largest and most comprehensive drug development services companies with more than 10,500 employees in over 60 countries.

Covance has the people, processes, client service, and global resource capabilities to respond to biotechnology and pharmaceutical clients' toughest drug development challenges.

With the most comprehensive portfolio of preclinical, clinical development and commercialization services, Covance provides industry-leading services, the world's largest central laboratory network, and a global team of clinical trial and commercialization experts.

DaVita Clinical Research — Booth 113

825 South 8th Street
Suite 300
Minneapolis, MN 55404
USA

Phone 888.345.2567
Fax 866.852.3241
Email contactdcr@davita.com
Web www.davitaclinicalreseach.com

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

Duke Clinical Research — Booth 104

300 W Morgan Street
Suite 800
Durham, NC 27701
USA

Phone 919.668.8700 / 877.693.DUKE
Fax 919.668.7150
Email kelly.mehrer@duke.edu
Web www.dcru.org

The Duke Clinical Research Unit combines the clinical expertise and academic leadership of one of the most prestigious university medical centers in the world with the operational capabilities of a full-service contract research organization, giving us the resources to conduct truly science driven global proof-of-concept studies in both adults and children. We offer rapid start-up, experienced thought leadership, direct access to patients, cutting-edge technologies, and first rate facilities. Combined with extensive operational capabilities, we offer a unique model for conducting early phase global clinical research that accelerates the development of new medical therapies and their translation into patient care.

ERT, Inc.

Booth 336

1818 Market Street
Suite 1000
Philadelphia, PA 19103
USA

Phone 215.972.0420
Fax 215.972.0414
Email eresearch@ert.com
Web www.ert.com

ERT is a global technology-driven provider of customizable medical devices and health outcomes research services. ERT harnesses internet and telecommunications technology to provide stakeholders with multiple modes of available technology for collecting health outcomes data, including Patient (PRO), Clinician (ClinRO) and Observer (ObsRO) reported outcomes.

ERT is the industry leader in centralized cardiac safety and respiratory efficacy services and also provides electronic patient reported outcomes (ePRO) for multiple modalities across all phases.

EUROFINS OPTIMED

Booth 124

1 rue des Essarts
38610 Gières
France

Phone +33 4 38 37 27 40
Fax +33 4 38 37 27 41
Email contact@optimed.fr
Web www.optimed.fr

A French company founded in 1990, EUROFINS OPTIMED provides services for Early Clinical Development (First into Human and First into Patient studies, PK/PD studies, Proof of concept etc).

Eurofins OPTIMED has its own facilities on 2 sites with a full capacity of 100 beds including a hospital based unit. Thanks to its position within the Lyon Sud Hospital, Eurofins OPTIMED has access to various types of patients, and to a large network of experts.

In addition to its services in pharmacology, Eurofins OPTIMED offers all services needed to achieve your study: regulatory services, medical writing, monitoring, data management, and statistics.

ICON Development Solutions LLC

Booth 314

7740 Milestone Parkway
Hanover, MD 21076
USA

Phone 410.696.3000
Fax 410.480.0776
Email IDSinfo@iconplc.com
Web www.iconplc.com

ICON Development Solutions specializes in the strategy and delivery of early-phase clinical development services to enable informed, timely decision making for our clients. With global, industry-leading capabilities in early-phase clinical research, bioanalytical, PK/PD modeling & simulation and the full range of supporting scientific services, we have the operational flexibility to provide stand-alone development services or an integrated full-service solution.

Our clinical pharmacology team has extensive experience in the design, conduct and interpretation of studies in all major therapeutic areas, with a strong reputation for incorporating high science approaches and operational excellence across all elements of your clinical pharmacology program.

INC Research

Booth 228

3201 Beechleaf Court
Suite 600
Raleigh, NC 27604
USA

Phone 919.876.9300
Fax 919.876.9360
Email info@incresearch.com
Web www.incresearch.com

INC Research is a leading global CRO providing the full range of Phase I to IV clinical development services across six continents through our global scale and scope, broad therapeutic expertise and commitment to operational excellence using our proven Trusted Process®.

Johnson & Johnson

Booth 236

501 George Street
New Brunswick, NJ 08933
USA

Phone 732.524.2577
Email ncummin1@its.jnj.com
Web www.jnj.com

Johnson & Johnson, through its operating companies, is the world's most comprehensive and broadly-based manufacturer of health care products, as well as a provider of related services for the consumer, pharmaceutical, and medical devices and diagnostics markets. The more than 200 Johnson & Johnson operating companies employ approximately 114,000 men and women in 60 countries and sell products throughout the world.

LMC Endocrinology Centres

Booth 137

107 – 1929 Bayview Avenue
Toronto, Ontario M4G 3E8
Canada

Phone 647.274.4133
Fax 416.645.2931
Web www.lmc.ca

Logos Technologies, Inc.

Booth 117

91 Peterborough Road
London, SW6 3BU
UK

Phone +44 (0)845 8385900
Fax +44 (0) 8707 478600
Email contact@logostechnologies.com
Web www.logostechnologies.com

ALPHADAS®, from Logos Technologies, is the market leading e-Source, pro-active EDC and site automation system for Early Phase clinical trials which addresses the needs of investigators and sponsors alike. It is a world class, proven product used by small to large early phase CRO's and top 10 pharmaceuticals, globally. ALPHADAS is a mobile, schedule-driven event based system which provides real-time pro-active EDC at the bedside, station, or remote location. Its ability to integrate with medical devices, central ECG systems and central laboratories means minimum human data entry is required, simultaneously reducing human error and increasing efficiency, yielding immediate significant ROI.

MD Clinical

Booth 226

911 E Hallandale Beach Blvd.
Hallandale Beach, Fl 33009
USA

Phone 954.455.5757 ext 126
Fax 954.455.5859
Email bsafirstein@mdclinical.org
Web www.mdclinical.org

We conduct Healthy Phase 1, Disease Specific Phase 1, Alzheimer's Disease, MCI, Insomnia, RLS, Apnea, Depression, Anxiety, ADHD, ADD, Migraine, Diabetes Mellitus, Hypertension, Osteoarthritis, Neuropathy, and other neurological and psychiatric trials. Co-President/PI's Drs. Wilks and Safirstein have participated in 300+ studies.

Phase 1 capabilities
- PK/PD, Proof of concept, Bioequivalence/Bioavailability, Dose-Response & Escalation, Food Effect, Genotyping, Drug interaction, Drug metabolism, Safety & Efficacy.

Facilities and Operations
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- Drug room
- Refrigerators, freezers, refrigerated centrifuges, ECG machines, holter monitor, telemetry, crash cart, and an AED.

Microconstants China, Inc. — Booth 239

Suite 1-201, Bldg. 18
99 Kechuangshisi Street
BDA, Beijing 101111
Republic of China

Phone 86-010-59776728
Email jhou@microconstants.com
Web www.microconstants.com

MicroConstants China is a Contract Research Organization (CRO) that provides premier quality bioanalytical services, integrated clinical trial management services, IND-enabling drug metabolism (DMPK) assays, pharmacokinetic analysis, ELISA immunoassay, biomarker analysis, and quality system consulting to pharmaceutical/biotech companies and research institutes worldwide. Our in-house OECD GLP compliant bioanalytical laboratory specializes in method development, method validation, and sample analysis of small molecules, proteins, and peptides using LC/MS/MS, HPLC/UV, and ELISA for preclinical and clinical PK samples. MicroConstants China also serves as a site management organization (SMO) to implement ICH GCP quality system in clinical trial centers in China.

Mortara Instrument — Booth 214

7865 N. 86th Street
Milwaukee, WI 53224
USA

Phone 414.354.1600
Fax 414.354.4760
Email sales@mortara.com
Web www.mortara.com

Founded in 1982 by David W. Mortara, PhD, Mortara Instrument was born with a guiding philosophy: design to a need, keep it simple, and make it economically accessible. Building on this philosophy, Mortara Instrument has created a complete line of electrocardiography products that are well suited to today's health care market.

The company is headquartered in Milwaukee, Wisconsin and has grown since 1982 to include offices in Australia, Italy, Germany, and the Netherlands. Products are marketed worldwide through subsidiaries and distribution partners.

NIH/Obstetric and Pediatric Pharmacology Branch (OPPB) — Booth 125

6100 Executive Boulevard
Room 4A01, MSC 7510
Bethesda, MD 20892-7510
USA

Phone 301.402.7357
Web www.nichd.nih.gov/oppb

The Obstetric and Pediatric Pharmacology Branch (OPPB), part of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, offers research funding to improve the safety and efficacy of drugs for children and pregnant women. OPPB has funding opportunities in basic, translational and clinical obstetric and pediatric pharmacology research and training.

Nature Publishing Group — Booth 215

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New Orleans Center for Clinical Research — Booth 205

1928 Alcoa Highway
Suite G50
Knoxville, TN 37920
USA

Phone 865.305.9100 x 246
Fax 865.305.9393
Email brichardson@noccr.com
jlacey@noccr.com
aaskew@noccr.com
Web www.NOCCR.com

Located within the University of Tennessee Medical Center, NOCCR and VRG are privately owned multispecialty facilities providing expertise in all areas of Phase I – IV clinical research. The 52 bed Phase I unit is located in a level I trauma center offering 24 hour critical care coverage, affording an environment well suited for First In Man trials. This Unit is known for its ability to perform procedurally difficult trials and to recruit special populations. Our primary missions are to help develop safe, advanced medical options in an ethical manner and to deliver high-quality, clean data to our sponsors.

Nuvisan GmbH — Booth 225

Wegenerstrasse 13
89231 Neu-Ulm
Germany

Phone +49 731 9840 0
Fax +49 731 9840 280
Email bdinfo@nuvisan.com
Web www.nuvisan.com

NUVISAN Pharma Services is a global provider of product development and support services to the pharmaceutical, biotechnology and medical device industries. We deliver services ranging from a single test to fully integrated drug development programs.

The Headquarter of NUVISAN GmbH is based in Neu-Ulm. In addition to this there are affiliates in several European countries.

Through the combined experience and expertise offered by both NUVISAN and FOCUS Clinical Drug Development, we are pleased to offer the sponsor the complete spectrum of drug development services.

While NUVISAN is one of the industry's most favored partners in the field of Clinical Development, Bioanalytics, pharmaceutical analytics and clinical trial supplies. FOCUS has in turn earned a top-rank position in the field of Early Clinical Drug Development.

OmniComm — Booth 302

2101 West Commercial Blvd.
3500
Ft. Lauderdale, FL 33309
USA

Phone 1.877-Go-To-EDC
Fax 1.954.473.1256
Email info@omnicomm.com
Web www.omnicomm.com

OmniComm provides web-based electronic data capture (EDC), and eClinical solutions to pharmaceutical, biotechnology, medical device, and other sponsor and contract research organizations that conduct life-changing clinical trial research. OmniComm's solutions have been used in over 3,000 clinical trials, from phases I – IV, in over 50 countries around the globe. Our growing base of satisfied customers is a direct result of a continued focus on customer needs and service. OmniComm has U.S. headquarters in Fort Lauderdale, FL and European headquarters in Bonn, Germany, with satellite offices in New Jersey and the United Kingdom, as well as sales offices throughout the U.S. and Europe.

Oracle Health Sciences — Booth 238

10 Twin Dolphin
Redwood Shores, CA 94065
USA

Phone 408.595.3077
Email peggy.taylor@oracle.com
Web www.oracle.com/healthsciences

Oracle is a leading strategic software solutions provider to the health sciences industry. Oracle Health Sciences helps pharmaceutical, biotechnology, medical device, and healthcare organizations become the most successful in the world by offering innovative products and services that deliver the highest customer and shareholder value. Addressing industry requirements, Oracle provides comprehensive solutions including clinical trial management and analysis, electronic data capture, adverse event reporting and pharmacovigilance, healthcare interoperability , and analytics for translational research and enterprise management. Oracle partners with health sciences industry leaders – including 20 of the top 20 life sciences companies and 10 of the top 12 Fortune Global 500 healthcare organizations – to prevent and cure disease, enhance quality of life and accelerate insights for better health.

Orlando Clinical Research Center — Booth 204

5055 S. Orange Avenue
Orlando, FL 32809
USA

Phone 407.240.7878
Fax 407.240.9846
Email tmarbury@ocrc.net
Web www.ocrc.net

Located in the heart of Central Florida, OCRC is a cutting edge independent Phase I – IV custom-built 35,000 sq. ft. research site. Designed specifically for Phase 1 clinical trials, OCRC includes 110 in-house volunteer beds, dual lead digital telemetry, CCTV security system, and cardkey access. A special treatment/observation area has 12 hospital beds (6 used for onsite Hemodialysis studies). OCRC is specialized in Phase I trials with an emphasis in pharmacokinetic, QTc, and SAD/MAD studies in healthy, hepatic, hemodialysis, renal, diabetes, elderly, and post-menopausal populations.

PRA International — Booth 114

Glen Lake 6
4130 ParkLake Avenue
Raleigh, NC
USA

Phone 919.786.8200
Fax 919.786.8201
Email endpoints@praintl.com
Web www.clearlypra.com

PRA's Early Development Service group conducts Phase I-IIa studies in our clinics in Europe and the U.S. with bioanalytical laboratories in close proximity to each, facilitating analysis of time-critical patient samples. Additionally, we operate our Unit on Demand model in Central and Eastern Europe for early phase patient studies.

PRA operates two bioanalytical laboratories with a choice of GLP and GLP-like services, providing clients with the flexibility to customize analysis to meet regulatory requirements and timelines. The strategic locations of the laboratories close to our Phase I units facilitate an innovative working collaboration, enabling rapid turnaround of time-critical samples.

PAREXEL International — Booth 129

195 West Street
Waltham, MA 02451
USA

Phone 781.487.9900
Fax 781.768.5512
Email earlyphase@parexel.com
Web www.PAREXEL.com

For nearly 30 years, PAREXEL has developed significant expertise to assist clients in the worldwide pharmaceutical, biotechnology and medical device industries with the development and launch of their projects in order to bring safe and effective treatments to the global marketplace for the patients who need them. We are a leading global bio/pharmaceutical services organization that helps clients expedite time-to-market through our development and launch services. These include a broad range of clinical development capabilities including a global network of early phase clinics, integrated advanced technologies, regulatory affairs consulting and commercialization services.

PharmaNet/i3 — Booth 217

504 Carnegie Center
Princeton, NJ 08540
USA

Phone 609.951.6800
Fax 609.514.0390
Email pni@pharmanet.com
Web www.pharmanet-i3.com

PharmaNet/i3, the inVentiv Health clinical segment, is recognized as a leading provider of global drug development services to pharmaceutical, biotechnology, generic drug, and medical device companies, including therapeutically-specialized capabilities for Phase I-IV clinical development, bioanalytical services, and staffing from a single clinical professional to an entire functional team. For intelligent solutions needed to accelerate high quality drug development programs of all sizes around the world, ***PharmaNet/i3 works for you***.

Prism Research — Booth 202

1000 Westgate Drive
Suite #149
St. Paul, MN 55114
USA

Phone 651.641.2914
Fax 651.641.2901
Email jcosgrove@prismresearchinc.com
Web www.prismresearchinc.com

Prism Research is a 52 bed phase I-IV clinical research facility located in the epicenter of the Minneapolis/St. Paul Metropolitan Area. Prism Research has an extensive history of performing complex, early phase research studies in healthy volunteers and numerous patient populations including;

- Healthy Volunteer (FIM, DDI, QT interval, BA/BE)
- Renal PK
- T2DM
- HTN
- Hyperlipidemia
- Asthma & Allergy
- COPD
- GI
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525 S. Silverbrook Drive
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USA

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Fax 262.334.6067
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Web www.spauldingclinical.com

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Email lrusch@vinceandassociates.com
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PRINCE GEORGE'S EXHIBIT HALL C ★ Thursday, March 15 | 8:00am-3:00pm | Attended Poster 8:00am-9:30am

BIOMARKERS AND IMAGING (BIO)

PI-1

MIRTAZAPINE SUPPRESSES THE INCREASES IN PLASMA LEVELS OF ADRENOCORTICOTROPIC HORMONE AND NEUROPEPTIDE Y UNDER CONTINUAL STRESS EXPOSURE

K. Arao, Y. Makihara, Y. Suzuki, T. Abe, Y. Sato, M. Takeyama; Oita University Hospital, Oita, Japan.

PI-2

BOTH CYP2C19 AND PON1 GENOTYPES ARE ASSOCIATED WITH THE CLINICAL OUTCOME OF CLOPIDOGREL IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION BUT NOT ANGINA

H. Kim,[1] K. Chang,[2] Y. Koh,[3] M. Park,[4] Y. Choi,[5] C. Park,[5] S. Lee,[6] M. Oh,[6] S. Lee,[6] E. Kim,[1] J. Shon,[1] E. Chu,[2] H. Park,[2] P. Kim,[2] S. Her,[4] D. Kim,[7] J. Lee,[3] H. Kim,[8] K. Yoo,[9] D. Jeon,[10] W. Chung,[2] K. Seung,[2] J. Shin[1]; [1]Department of Pharmacology and Clinical Pharmacology, Inje University College of Medicine and Busan Paik Hospital, Busan, Korea, Republic of, [2]Cardiovascular Center and Cardiology Division, Seoul St. Mary's Hospital and College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of, [3]Department of Cardiology, Catholic University Uijeongbu St. Mary's Hospital, Uijeongbu, Korea, Republic of, [4]Department of Cardiology, Catholic University Daejeon St. Mary's Hospital, Daejeon, Korea, Republic of, [5]Department of Cardiology, Catholic University Yeouido St. Mary's Hospital, Seoul, Korea, Republic of, [6]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of, [7]Department of Cardiology, Catholic University St. Pauls Hospital, Seoul, Korea, Republic of, [8]Department of Cardiology, Catholic University Bucheon St. Mary's Hospital, Bucheon, Korea, Republic of, [9]Department of Cardiology, Catholic University St. Vincent's Hospital, Suwon, Korea, Republic of, [10]Department of Cardiology, Catholic University Incheon St. Mary's Hospital, Incheon, Republic of Korea.

PI-3

ETHYL GLUCURONIDE AS A BIOMARKER OF ALCOHOL CONSUMPTION DURING PREGNANCY

J. Matlow, K. Aleksa, A. Lubetsky, G. Koren; The Hospital For Sick Children, Toronto, ON, Canada.

PI-4

HAIR COCAETHYLENE AS A BIOMARKER OF ALCOHOL AND COCAINE CO-EXPOSURE

A. Natekar, K. Aleksa, G. Koren; The Hospital for Sick Children, Toronto, ON, Canada.

DRUG DEVELOPMENT AND REGULATORY SCIENCES (DDR)

PI-5

PHARMACODYNAMICS OF THE NOVEL RHO KINASE INHIBITOR SAR407899 IN COMBINATION WITH A CALCIUM CHANNEL BLOCKER IN HEALTHY ELDERLY SUBJECTS AS ASSESSED BY 24 HOURS ABPM

J. Tillner,[1] A. Lehmann,[2] C. Frosio,[1] G. Golor,[3] J. Pinquier[4]; [1]Clinical Exploratory Pharmacology, Sanofi, Frankfurt, Germany, [2]Biostatistics, Sanofi, Frankfurt, Germany, [3]Parexel, Berlin, Germany, [4]Clinical Exploratory Pharmacology, Sanofi, Chilly Mazarin, France.

DRUG DEVELOPMENT AND REGULATORY SCIENCES (DDR)

PI-6

IDENTIFYING DIGOXIN DRUG INTERACTION POTENTIAL BY RECEIVER OPERATING CHARACTERISTIC ANALYSIS

H. Ellens,[1] C. A. Lee,[2] J. Bentz,[3] J. Palm,[4] K. Herdi-Szab,[5] M. E. Taub,[6] D. Bednarczyk,[7] E. Perloff,[8] C. Funk,[9] P. Balimane,[10] L. Salphati,[11] A. Guo,[12] I. Hanna,[13] C. Xia,[14] L. Li,[15] G. Xiao,[16] H. Wortelboer,[17] D. Weitz,[18] A. Pak,[19] E. Reyner,[2] J. Taur,[20] X. Chu,[21] T. Yamagata,[22] S. Deng,[23] G. Rajaraman[24]; [1]GlaxoSmithKline, Philadelphia, PA, [2]Consultant, Carlsbad, CA, [3]Drexel University, Philadelphia, PA, [4]AstraZeneca, Molndal, Sweden, [5]Solvo, Szeged, Hungary, [6]Boehringer Ingelheim, Ridgefield, CT, [7]Novartis, Boston, MA, [8]BD Biosciences, Boston, MA, [9]Roche, Basel, Switzerland, [10]Bristol-Myers Squibb, Princeton, NJ, [11]Genentech, San Francisco, CA, [12]Roche, Nutley, NJ, [13]Novartis, East Hanover, NJ, [14]Millenium, Boston, MA, [15]Absorption Systems, Exton, PA, [16]BiogenIdec, Boston, MA, [17]TNO Quality of Life, Utrecht Area, Netherlands, [18]Sanofi-Aventis, Frankfurt, Germany, [19]Eli Lilly, Indianapolis, IN, [20]Eisai, Boston, MA, [21]Merck, Rahway, NJ, [22]Merck Serono, Grafing, Germany, [23]Pfizer, La Jolla, CA, [24]CellzDirect, Austin, TX.

PI-7

NO EFFECT OF PAR-1 RECEPTOR ANTAGONIST VORAPAXAR ON QT/QTC INTERVAL IN HEALTHY VOLUNTEERS

T. Kosoglou,[1] T. L. Hunt,[2] F. Xuan,[1] B. Kumar,[1] P. Statkevich,[1] S. Young,[1] R. Hoffman,[1] A. G. Meehan,[1] D. L. Cutler[1]; [1]Merck Sharp & Dohme Corp., Whitehouse Station, NJ, [2]PPD Development LP, Austin, TX.

PI-8

PHARMACOKINETICS AND PHARMACODYNAMICS OF MDCO-216 (APOA-I MILANO/POPC COMPLEX), A REVERSE CHOLESTEROL TRANSPORT (RCT) INDUCER IN CYNOMOLGUS MONKEYS AFTER SINGLE DOSE AND 6 WEEKS OF TREATMENT

S. E. Bellibas, B. Zerler, H. Kempen, D. Goundis, P. Wijngaard; The Medicines Company, Parsippany, NJ.

PI-9

DRUG INTERACTION STUDY OF IPRAGLIFLOZIN AND MIGITOL IN HEALTHY JAPANESE SUBJECTS

I. Nakajo,[1] Y. Taniuchi,[1] S. Yoshida,[1] T. Kadokura,[1] S. Kageyama[2]; [1]Astellas Pharma Inc, Tokyo, Japan, [2]Jikei University School of Medicine, Tokyo, Japan.

PI-10

LACK OF PHARMACOKINETIC AND PHARMACODYNAMIC INTERACTION BETWEEN IPRAGLIFLOZIN, A SELECTIVE SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITOR, AND GLIMEPIRIDE IN HEALTHY SUBJECTS

S. A. Veltkamp, J. van Dijk, W. J. Krauwinkel, R. A. Smulders; Astellas Pharma Europe BV, Leiderdorp, Netherlands.

PI-11

ETHNIC SENSITIVITY ASSESSMENT DURING DRUG DEVELOPMENT: PAST, PRESENT AND FUTURE IN A LARGE PHARMACEUTICAL COMPANY

C. S. Weber,[1] Y. Fukushima,[1] A. Guenther,[1] Q. Jiang,[2] S. Kim,[3] R. Li,[2] Y. Lim,[3] P. Lu,[4] R. Peck,[5] C. Rayner,[6] S. Zhai,[2] J. Zhi[4]; [1]Fa. Hoffmann-La Roche Ltd, Basel, Switzerland, [2]Roche R&D Center, Shanghai, China, [3]Roche Korea Company Ltd, Seoul, Korea, Republic of, [4]Hoffmann-La Roche Inc, Nutley, NJ, [5]Roche Products Ltd, Welwyn Garden City, United Kingdom, [6]Roche Products Pty. Ltd, Dee Why, Australia.

DRUG DEVELOPMENT AND REGULATORY SCIENCES (DDR)

PI-12

APPLICATIONS OF EXPLORATORY CLINICAL TRIALS IN DRUG DEVELOPMENT- REVIEW OF EXPLORATORY TRIAL USER GROUP MEETING, WASHINGTON, JUNE 2011

I. Shaw,[1] L. Stevens,[1] P. Mudd,[2] M. Young,[2] P. Y. Muller,[3] D. Boulton,[4] D. Spracklin,[5] C. Lambert,[6] E. Helmer,[7] M. Rizk[8]; [1]Quotient Clinical Ltd, Ruddington, United Kingdom, [2]GlaxoSmithKline, Research Triangle Park, NC, [3]Novartis Institutes for BioMedical Research, Cambridge, MA, [4]Bristol-Myers Squibb Co, Princeton, NJ, [5]Pfizer, Groton, CT, [6]AstraZeneca R&D, Alderley Park, United Kingdom, [7]Takeda Global Research & Development Centre (Europe), London, United Kingdom, [8]Merck Research Laboratories, West Point, PA.

PI-13

LACK OF EFFECT OF IPRAGLIFLOZIN, A SELECTIVE SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITOR, ON CARDIAC REPOLARIZATION IN HEALTHY MALE AND FEMALE SUBJECTS

W. Zhang,[1] R. Smulders,[2] A. Abeyratne,[1] A. Dietz,[3] J. Keirns[1]; [1]Astellas Pharma Global Development, Inc, Deerfield, IL, [2]Astellas Pharma Global Development, Leiderdorp, Netherlands, [3]Spaulding Clinical Research, West Bend, WI.

PI-14

EFFECT OF HEPATIC IMPAIRMENT ON THE PHARMACOKINETICS OF IPRAGLIFLOZIN, A NOVEL SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITOR

W. Zhang,[1] W. Krauwinkel,[2] J. Keirns,[1] R. Townsend,[1] K. C. Lasseter,[3] L. Plumb,[1] R. Smulders[2]; [1]Astellas Pharma Global Development, Inc, Deerfield, IL, [2]Astellas Pharma Europe BV, Leiderdorp, Netherlands, [3]Clinical Pharmacology of Miami, Inc., Miami, FL.

DRUG SAFETY (SAF)

PI-15

FOLIC ACID AND COLORECTAL ADENOMA RECURRENCE: A SYSTEMATIC REVIEW OF RANDOMIZED CONTROL TRIALS

D. A. Kennedy, S. J. Stern, I. Matok, M. Moretti, M. Sarkar, T. Adams-Webber, G. Koren; The Hospital for Sick Children, Toronto, ON, Canada.

PI-16

HIGH RISK PRESCRIBING AND INCIDENCE OF FRAILTY AMONG OLDER COMMUNITY-DWELLING MEN

D. Gnjidic,[1] S. N. Hilmer,[1] D. G. Le Couteur,[2] D. R. Abernethy[3]; [1]Royal North Shore Hospital and University of Sydney, Sydney, Australia, [2]Centre for Education and Research on Ageing (CERA) and University of Sydney, Sydney, Australia, [3]Food and Drug Administration, Silver Spring, MD.

PI-17

POLYPHARMACY AND ADVERSE OUTCOMES: DETERMINING THE BEST CUT-OFF FOR POLYPHARMACY ASSOCIATED WITH GERIATRIC SYNDROMES, FUNCTIONAL OUTCOMES AND MORTALITY IN OLDER ADULTS

D. Gnjidic,[1] D. G. Le Couteur,[2] S. N. Hilmer[1]; [1]Royal North Shore Hospital and University of Sydney, Sydney, Australia, [2]Centre for Education and Research on Ageing (CERA) and University of Sydney, Sydney, Australia.

PI-18

A REVIEW OF FOOD AND DRUG ADMINISTRATION (FDA) LABELING FOR OVERDOSE TREATMENT AND TOXICITY DATA

M. E. Mazer,[1] G. Sokol,[2] L. Cantilena[2]; [1]George Washington University, Washington, DC, [2]Uniformed Services University of the Health Sciences, Division of Clinical Pharmacology, Bethesda, MD.

DRUG SAFETY (SAF)

PI-19

AN *IN VIVO* HUMAN TIME-EXPOSURE INVESTIGATION OF A COMMERCIAL SILVER NANO-PARTICLE SOLUTION

M. A. Munger, P. Radwanski, G. J. Stoddard, A. Shaaban, D. Grainger, G. Yost; Univ of Utah, SLC, UT.

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PI-20

CAPILLARY ELECTROPHORESIS-LASER INDUCED FLUORESCENCE (CE-LIF) ASSAY FOR MEASUREMENT OF INTRA-CELLULAR D-SERINE AND SERINE RACEMASE ACTIVITY

N. S. Singh, R. K. Paul, M. Sichler, R. Moaddel, M. Bernier, I. W. Wainer, A. Ramamoorthy; National Institute on Aging/NIH, Baltimore, MD.

PI-21

KETAMINE AND METABOLITES SUBTYPE SELECTIVITY IN THE NICOTINIC RECEPTOR FAMILY

R. Moaddel,[1] A. Rosenberg,[1] G. Abdrakhmanova,[2] K. Jozwiak,[3] A. Ramamoorthy,[1] I. W. Wainer[1]; [1]NIA/NIH, Baltimore, MD, [2]Virginia Commonwealth University, Richmond, VA, [3]Medical University of Lublin, Lublin, Poland.

PI-22

HYPERTENSION SUSCEPTIBILITY LOCI ASSOCIATED WITH BLOOD PRESSURE RESPONSE TO ANTIHYPERTENSIVES- RESULTS FROM THE PHARMACOGENOMIC EVALUATION OF ANTIHYPERTENSIVE RESPONSES (PEAR) STUDY

Y. Gong,[1] C. W. McDonough,[1] Z. Wang,[2] R. M. Cooper-DeHoff,[1] T. Y. Langaee,[1] A. L. Beitelshee,[3] S. T. Turner,[4] A. B. Chapman,[5] J. G. Gums,[1] K. R. Bailey,[4] E. Boerwinkle,[2] J. A. Johnson[1]; [1]University of Florida, Gainesville, FL, [2]University of Texas, Houston, TX, [3]University of Maryland, Baltimore, MD, [4]Mayo Clinic, Rochester, MN, [5]Emory University, Atlanta, GA.

PI-23

N-ISOPROPYL-*P*-IODOAMPHETAMINE HYDROCHLORIDE (IMP) IS PREDOMINANTLY METABOLIZED BY CYP2C19

K. Fujita,[1] M. Sugiyama,[1] Y. Akiyama,[1] K. Hioki,[2] M. Kunishima,[3] M. Kobayashi,[3] K. Kawai,[3] Y. Sasaki[1]; [1]Saitama Medical University, Hidaka, Japan, [2]Kobe Gakuin University, Kobe, Japan, [3]Kanazawa University, Kanazawa, Japan.

PI-24

HEME OXYGENASE-1 (HO-1) IS A POSSIBLE MEDIATOR OF CYTOPROTECTIVE EFFECTS BY N-ACETYLCYSTEINE (NAC) IN CHILDHOOD CEREBRAL ADRENOLEUKODYSTROPHY (CCALD) PATIENTS

J. Zhou, R. V. Kartha, L. Basso, P. J. Orchard, H. Schroder, J. C. Cloyd; University of Minnesota, Minneapolis, MN.

PI-25

THE INTERACTIVE EFFECTS OF *PREGNANE X RECEPTOR* AND *HEPATOCYTE NUCLEAR FACTOR 4A* POLYMORPHISMS ON THE DURATION TO REACH THE MAINTENANCE DOSE OF CARBAMAZEPINE DURING MONOTHERAPY

J. Saruwatari,[1] S. Yoshida,[1] N. Ogusu,[1] Y. Okada,[1] Y. Tsuda,[1] K. Oniki,[1] N. Yasui-Furukori,[2] S. Kaneko,[2] T. Ishitsu,[3] K. Nakagawa[4]; [1]Graduate School of Pharmaceutical Sciences, Kumamoto University, Kumamoto, Japan, [2]Department of Neuropsychiatry, Hirosaki University School of Medicine, Hirosaki, Japan, [3]Kumamoto Saishunso National Hospital, Kumamoto, Japan, [4]Division of Pharmacology and Therapeutics, Graduate School of Pharmaceutical Sciences, and Center for Clinical Pharmaceutical Sciences, Kumamoto University, Kumamoto, Japan.

POSTER SESSION I

PRINCE GEORGE'S EXHIBIT HALL C ★ Thursday, March 15 | 8:00am-3:00pm | Attended Poster 8:00am-9:30am

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PI-26

THE ASSOCIATION BETWEEN THE *CYP2C19* GENOTYPE AND CLOBAZAM DOSE REQUIREMENTS IN JAPANESE PATIENTS WITH EPILEPSY

J. Saruwatari,[1] N. Ogusu,[1] M. Shimomasuda,[1] T. Seo,[1] R. Nagata,[1] S. Yoshida,[1] K. Oniki,[1] N. Yasui-Furukori,[2] S. Kaneko,[2] T. Ishitsu,[3] K. Nakagawa[4]; [1]Division of Pharmacology and Therapeutics, Graduate School of Pharmaceutical Sciences, Kumamoto University, Kumamoto, Japan, [2]Department of Neuropsychiatry, Hirosaki University School of Medicine, Hirosaki, Japan, [3]Kumamoto Saishunso National Hospital, Kumamoto, Japan, [4]Division of Pharmacology and Therapeutics, Graduate School of Pharmaceutical Sciences, and Center for Clinical Pharmaceutical Sciences, Kumamoto University, Kumamoto, Japan.

PI-27

PROGRESSIVE DECLINE IN *IN VIVO* CYP3A4-ACTIVITY EXPLAINS TIME-RELATED INCREASE IN DOSE CORRECTED TACROLIMUS EXPOSURE AFTER RENAL TRANSPLANTATION

H. de Jonge,[1] H. de Loor,[1] K. Verbeke,[2] Y. Vanrenterghem,[1] D. R. Kuypers[1]; [1]Department of Nephrology and Renal Transplantation, University Hospitals Leuven, Leuven, Belgium, [2]Department of Gastrointestinal Research, Catholic University Leuven, Leuven, Belgium.

PI-28

SYSTEMATIC EVALUATION OF PHARMACOGENETIC ASSOCIATED ADVERSE EVENTS IN THE LITERATURE AND THE LABELING

S. S. Shord, P. Mummaneni, J. Vaidyanathan, G. Gieser, S. Amur, A. Adebowale; U.S. Food and Drug Administration, Silver Spring, MD.

PI-29

THE CONTRIBUTION OF GENETIC VARIATIONS ASSOCIATED WITH *FKBP5* EXPRESSION IN PREDICTION OF CLINICAL OUTCOMES IN DEPRESSION PATIENTS

K. A. Ellsworth,[1] I. Moon,[1] L. L. Pelleymounter,[1] B. W. Eckloff,[1] B. L. Fridley,[1] G. D. Jenkins,[1] A. Batzler,[1] J. Biernacka,[1] E. D. Wieben,[1] T. Mushiroda,[2] M. Kubo,[2] Y. Nakamura,[2] N. Kamatani,[2] D. A. Mrazek,[1] R. M. Weinshilboum,[1] L. Wang[1]; [1]Mayo Clinic, Rochester, MN, [2]RIKEN Center for Genomic Medicine, Yokohama, Japan.

PI-30

FUNCTIONAL ACTIVITY OF HUMAN HEART MICROSOMES EXPRESSING CYP2E1

J. Huguet,[1] E. Chehade,[1] V. Michaud,[2] F. Gaudette,[1] J. Turgeon[1]; [1]University of Montreal - CRCHUM, Montreal, QC, Canada, [2]University of Indianapolis, Indianapolis, IN.

PI-31

CYP450 FUNCTIONAL ACTIVITIES IN HUMAN HEART MICROSOMES

J. Huguet,[1] V. Michaud,[2] F. Gaudette,[3] J. Turgeon[4]; [1]University of Montreal - CRCHUIM, Montreal, QC, Canada, [2]University of Indianapolis, Indianapolis, IN, [3]CRCHUM, Montreal, QC, Canada, [4]University of Montreal - CRCHUM, Montreal, QC, Canada.

PI-32

STEREOSELECTIVE CONJUGATION OF 4'-METHOXYFENOTEROL STEREOISOMERS BY SULFOTRANSFERASES

L. V. Iyer,[1] **A. Ramamoorthy**,[2] A. M. Furimsky,[1] L. Tang,[1] P. Catz,[1] C. E. Green,[1] I. W. Wainer[2]; [1]SRI International, Menlo Park, CA, [2]National Institute on Aging, Baltimore, MD.

PI-33

DEXMEDETOMIDINE DECREASES SERUM INSULIN CONCENTRATIONS AND THIS RESPONSE IS INFLUENCED BY ALPHA2A ADRENOCEPTOR GENETIC VARIATION

L. V. Ghimire,[1] D. Kurnik,[1] M. Muszkat,[1] G. G. Sofowora,[1] M. Scheinin,[2] A. J. Wood,[1] C. Stein[1]; [1]Vanderbilt University, Nashville, TN, [2]University of Turku, Turku, Finland.

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PI-34

IN VITRO METABOLISM STUDY OF EBASTINE AND 7-ETHOXYRESORUFIN IN BREAST CANCER CELL LINES

C. Armstrong,[1] J. Huguet,[1] F. Gaudette,[2] F. Belanger,[2] D. Balicki,[3] J. Turgeon[1]; [1]University of Montreal-CRCHUM, Montreal, QC, Canada, [2]CRCHUM, Montreal, QC, Canada, [3]University of Montreal, Montreal, QC, Canada.

PI-35

NON-SYNONYMOUS SNPS IN *SELE, SELP,* AND *SIGLEC12* ASSOCIATE WITH CARDIOVASCULAR (CV) OUTCOMES IN THE INTERNATIONAL VERAPAMIL SR-TRANDOLAPRIL STUDY GENETIC SUBSTUDY (INVEST-GENES)

C. W. McDonough,[1] B. Burkley,[1] Y. Gong,[1] T. Y. Langaee,[1] C. J. Pepine,[2] R. M. Cooper-DeHoff,[1] J. A. Johnson[1]; [1]University of Florida College of Pharmacy, Gainesville, FL, [2]University of Florida College of Medicine, Gainesville, FL.

PI-36

ALPHA ADDUCIN-1 (*ADD1*) SINGLE NUCLEOTIDE POLYMORPHISM (SNP) ASSOCIATED WITH NEW ONSET DIABETES RISK WITH HYDROCHLOROTHIAZIDE (HCTZ) THERAPY IN THE INTERNATIONAL VERAPAMIL SR TRANDOLAPRIL GENETIC SUBSTUDY (INVEST-GENES)

J. H. Karnes, C. W. McDonough, Y. Gong, T. Y. Langaee, C. J. Pepine, J. A. Johnson, R. M. Cooper-DeHoff; University of Florida, Gainesville, FL.

PI-37

SULFONYLUREA RECEPTOR POLYMORPHISMS IN ABCC8 AFFECT THE RESPONSE TO SULFONYLUREA TREATMENT IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

J. A. Wessels, **J. J. Swen**, T. Van der Straaten, T. El Hajoui, W. J. Assendelft, H. J. Guchelaar; Leiden University Medical Centre, Leiden, Netherlands.

PI-38

PON-1 IS NOT THE MAJOR BIOACTIVATION PATHWAY OF CLOPIDOGREL *IN-VITRO*

V. Ancrenaz,[1] J. Desmeules,[1] R. James,[2] P. Dayer,[1] Y. Daali[1]; [1]Clinical Pharmacology Service, Geneva University Hospitals, Geneva, Switzerland, [2]Geneva University Hospitals, Geneva, Switzerland.

ONCOLOGY (ONC)

PI-39

MULTIPLE DOSES (MD) OF RIDAFOROLIMUS (RIDA) DO NOT HAVE A CLINICALLY IMPORTANT IMPACT ON THE SINGLE DOSE (SD) PHARMACOKINETICS (PK) OF MIDAZOLAM (MDZ)

A. Patnaik,[1] A. Tolcher,[1] **J. E. Talaty**,[2] M. A. Stroh,[3] J. B. McCrea,[2] M. Trucksis,[4] J. Palcza,[5] K. Orford,[6] K. Cerchio,[2] S. Breidinger,[7] D. Panebianco,[5] J. A. Wagner,[8] N. Agrawal,[7] G. Carrizales,[1] R. Lush,[9] K. Papadopoulos[1]; [1]South Texas Accelerated Research Therapeutics, San Antonio, TX, [2]Clinical Pharmacology, Merck & Co., Inc., North Wales, PA, [3]At the time of the study, Dr. Stroh was in Clinical PK/PD, Merck & Co., Inc., West Point, PA, [4]Clinical Pharmacology, Merck & Co., Inc., Boston, PA, [5]BARDS, Merck & Co., Inc., North Wales, PA, [6]At the time of the study, Dr. Orford was in Clinical Pharmacology, Merck & Co., Inc., North Wales, PA, [7]Clinical PK/PD, Merck & Co., Inc., West Point, PA, [8]Clinical Pharmacology, Merck & Co., Inc., Rahway, NJ, [9]H. Lee Moffit Cancer Center and Research Institute, Tampa, FL.

ONCOLOGY (ONC)

PI-40

THE BIOAVAILABILITY OF AN ORAL LIQUID FORMULATION (OLF) RELATIVE TO A FORMULATED CAPSULE (FC) OF CRIZOTINIB, A DUAL ALK/MET INHIBITOR, IN HEALTHY SUBJECTS

H. Xu,[1] M. O'Gorman,[1] W. Tan,[2] C. Leister,[3] M. Monajati,[2] N. Brega,[4] G. Ni,[1] S. Phillips,[1] L. Mendes da Costa,[5] A. Bello[6]; [1]Pfizer Inc, Groton, CT, [2]Pfizer Inc, La Jolla, CA, [3]Pfizer Inc, Collegeville, PA, [4]Pfizer Inc, Milan, Italy, [5]Pfizer Inc, Brussels, Belgium, [6]Pfizer Inc, New York, NY.

PI-41

ASSOCIATION OF ABCC2 POLYMORPHISMS WITH CISPLATIN DISPOSITION AND EFFICACY

J. A. Sprowl,[1] V. Gregorc,[2] C. Lazzari,[2] R. H. Mathijssen,[3] W. J. Loos,[3] A. Sparreboom[1]; [1]St Jude Children's Research Hospital, Memphis, TN, [2]Scientific Institute University Hospital San Raffaele, Milan, Italy, [3]Erasmus MC, Rotterdam, Netherlands.

PI-42

CONTRIBUTION OF P53 SIGNALING TO CISPLATIN NEPHROTOXICITY IN OCT1/2-DEFICIENT MICE

C. S. Lancaster, J. A. Sprowl, R. M. Franke, A. A. Gibson, L. Li, D. Finkelstein, L. Janke, A. Sparreboom; St Jude Children's Research Hospital, Memphis, TN.

PI-43

CONTRIBUTION OF METABOLISM TO SORAFENIB PHARMACOKINETIC VARIABILITY

E. I. Zimmerman, J. L. Roberts, L. Li, A. Gibson, J. E. Rubnitz, H. Inaba, S. D. Baker; St. Jude Children's Research Hospital, Memphis, TN.

ORGAN SPECIFIC DISEASES (OSD)

PI-44

MANAGING ACUTE DEXMEDETOMIDINE WITHDRAWAL SYNDROME: A NOVEL MECHANISM BASED USE OF ORAL CLONIDINE

A. T. Kukoyi,[1] **S. A. Coker**,[2] L. D. Lewis,[2] D. W. Nierenberg[2]; [1]Albert Einstein Hospital, Philadelphia, PA, [2]Dartmouth Hitchcock Medical Center, Lebanon, NH.

PI-45

CLINICAL PREDICTORS OF DYSGLYCEMIC EFFECTS ASSOCIATED WITH USE OF BETA BLOCKERS AND THIAZIDE DIURETICS

M. Moore,[1] G. Yan,[1] W. Hou,[1] A. B. Chapman,[2] T. Langaee,[1] G. L. Schwartz,[3] S. T. Turner,[4] J. G. Gums,[5] K. Bailey,[4] E. Boerwinkle,[6] A. L. Beitelshees,[7] R. M. Cooper-DeHoff,[5] J. A. Johnson[5]; [1]University of Florida, College of Pharmacy, Gainesville, FL, [2]Emory University School of Medicine, Atlanta, GA, [3]Mayo Clinic College of Medicine, Rochester, MN, [4]Mayo Clinic College of Medicine, Rochester, GA, [5]University of Florida, Colleges of Pharmacy and Medicine, Gainesville, FL, [6]University of Texas at Houston Center for Human Genetics, Houston, TX, [7]University of Maryland College of Medicine, Baltimore, MD.

PI-46

ANTIHYPERTENSIVE MEDICATION EXPOSURE AND ADVERSE GLYCEMIC EFFECTS: AN EVALUATION OF FASTING AND STIMULATED GLUCOSE

M. J. Moore,[1] Y. Gong,[1] S. Schmidt,[2] K. Hall,[2] T. Langaee,[1] J. G. Gums,[3] R. M. Cooper-DeHoff,[3] J. A. Johnson[3]; [1]University of Florida, College of Pharmacy, Gainesville, FL, [2]University of Florida, College of Medicine, Gainesville, FL, [3]University of Florida, Colleges of Pharmacy and Medicine, Gainesville, FL.

PI-47

WITHDRAWN

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PI-48

NONLINEAR MIXED-EFFECTS MODELING OF THE DISTRIBUTION KINETICS OF PEPT2 SUBSTRATE, GLYCYLSARCOSINE, AT THE BLOOD-CEREBROSPINAL FLUID BARRIER

Y. Huh, D. E. Smith, M. R. Feng; University of Michigan, Ann Arbor, MI.

PI-49

WITHDRAWN

PI-50

NO EFFECTS OF GENDER, AGE AND FOOD ON THE PHARMACOKINETICS OF CC-930 IN HEALTHY SUBJECTS

M. E. Thomas, Jr, A. Wu, L. Liu, L. Kong, S. Choudhury, Y. Ye, M. Palmisano, O. L. Laskin; Celgene Corporation, Summit, NJ.

PI-51

SAFETY/TOLERABILITY AND PHARMACOKINETICS OF MULTIPLE ORAL DOSES OF APREMILAST IN HEALTHY MALE SUBJECTS

A. Wu,[1] P. Rohane,[1] J. Ng,[2] B. DeGroot,[2] B. Colgan,[2] O. L. Laskin[1]; [1]Celgene Corp., Summit, NJ, [2]Celerion, Inc., Lincoln, NE.

PI-52

POPULATION PHARMACOKINETIC ANALYSIS OF (R)- AND (S)-KETAMINE AND NORKETAMINE IN RATS ON AD LIB AND CALORIE RESTRICTED DIETS

A. Ramamoorthy,[1] S. Van Wart,[2] R. de Cabo,[1] D. Mager,[2] I. Wainer[1]; [1]National Institute on Aging (NIA/NIH), Baltimore, MD, [2]University at Buffalo, Buffalo, NY.

PI-53

DETERMINATION OF KETAMINE AND ITS DOWNSTREAM METABOLITES IN PLASMA AND BRAIN OF WISTAR RATS

M. Sanghvi,[1] R. Moaddel,[1] K. OLoughlin,[2] C. Green,[2] A. Ramamoorthy,[1] I. Wainer[1]; [1]NIA/NIH, Baltimore, MD, [2]SRI International, Menlo Park, CA.

PI-54

POPULATION PHARMACODYNAMICS OF NADROPARIN IN MORBIDLY OBESE PATIENTS USING ANTI-XA LEVELS AS PHARMACODYNAMIC ENDPOINT

J. Diepstraten, E. J. Janssen, C. M. Hacking, S. van Kralingen, M. Y. Peeters, E. P. van Dongen, R. J. Wiezer, B. van Ramshorst, C. A. Knibbe; St. Antonius Hospital, Nieuwegein, Netherlands.

PI-55

DEVELOPMENTAL PHARMACOKINETICS OF PROPYLENE GLYCOL IN PRETERM AND TERM NEONATES

R. F. De Cock,[1] K. Allegaert,[2] A. Kulo,[3] J. de Hoon,[2] R. Verbesselt,[2] M. Danhof,[1] C. A. Knibbe[4]; [1]Leiden University (LACDR), Leiden, Netherlands, [2]University Hospital Leuven, Leuven, Belgium, [3]University of Sarajevo, Sarajevo, Bosnia Herzegovina and University Hospital Leuven, Leuven, Belgium, [4]Leiden University (LACDR), Leiden, Netherlands and St. Antonius Hospital, Nieuwegein, Netherlands.

PI-56

EXTRAPOLATION OF THE DEVELOPMENTAL GLOMERULAR FILTRATION RATE MODEL DERIVED FROM AMIKACIN CLEARANCE TO NETILMICIN AND VANCOMYCIN IN PRETERM AND TERM NEONATES

R. F. De Cock,[1] K. Allegaert,[2] C. M. Sherwin,[3] M. de Hoog,[4] J. N. van den Anker,[5] M. Danhof,[1] C. A. Knibbe[6]; [1]Leiden University (LACDR), Leiden, Netherlands, [2]University Hospital Leuven, Leuven, Belgium, [3]University of Utah School of Medicine, Salt Lake City, UT, [4]Erasmus MC - Sophia Children's Hospital, Rotterdam, Netherlands, [5]Erasmus MC - Sophia Children's Hospital, Rotterdam, Netherlands and Children's National Medical Center, Washington, WA, [6]Leiden University (LACDR), Leiden, Netherlands and St. Antonius Hospital, Nieuwegein, Netherlands.

POSTER SESSION I

PRINCE GEORGE'S EXHIBIT HALL C ★ Thursday, March 15 | 8:00am-3:00pm | Attended Poster 8:00am-9:30am

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PI-57

MODEL-BASED LITERATURE META-ANALYSIS OF LONGITUDINAL MATRICS CONSENSUS COGNITIVE BATTERY (MCCB) IN COGNITIVE IMPAIRMENT ASSOCIATED WITH SCHIZOPHRENIA (CIAS)

B. Tan, S. Ahadieh, D. Palumbo, A. Banerjee, N. DeMartinis, **J. Liu**; Pfizer, Groton, CT.

PI-58

PHARMACOKINETICS AND PHARMACODYNAMICS OF MLTA3698A, A NOVEL ANTI-LYMPHOTOXIN-α MONOCLONAL ANTIBODY, IN A PHASE I STUDY WITH RHEUMATOID ARTHRITIS PATIENTS

Y. Zheng, J. Xiao, M. Williams, C. Woods, F. Fuh, B. Emu, M. Tang, J. F. Visich; Genentech Inc., South San Francisco, CA.

PI-59

THE SINGLE DOSE PHARMACOKINETIC (PK) AND PHARMACODYNAMIC (PD) PROFILES OF SUVOREXANT (MK-4305), A DUAL OREXIN RECEPTOR ANTAGONIST, IN HEALTHY MALE SUBJECTS

H. Sun,[1] D. Kennedy,[2] N. Lewis,[1] T. Laethem,[3] K. Yee,[4] X. Li,[1] J. Hoon,[5] L. Van Bortel,[6] L. Rosen,[1] J. Chodakewitz,[1] J. Wagner,[7] G. Murphy[1]; [1]Merck, North Wales, PA, [2]Genentech, South San Francisco, CA, [3]Merck, Brussels, Belgium, [4]Merck, West Point, PA, [5]U.Z. Gasthuisberg, Center for Clinical Pharmacology, Leuven, Belgium, [6]U.Z. Gent, Drug Research Unit Gent, Gent, Belgium, [7]Merck, Rahway, NJ.

PI-60

NO ADVERSE IMPACT OF REPEATED ORAL DOSES OF TERIFLUNOMIDE ON THE PHARMACOKINETICS OF ORAL CONTRACEPTIVE STEROIDS (ETHINYLESTRADIOL AND LEVONORGESTREL) IN YOUNG HEALTHY FEMALE SUBJECTS

S. Turpault,[1] B. Miller,[1] F. Menguy-Vacheron[2]; [1]Sanofi-Aventis, Bridgewater, NJ, [2]Sanofi-Aventis, Chilly-Mazarin, France.

PI-61

GENOTYPE-BASED *IN VITRO-IN VIVO* EXTRAPOLATION (IVIVE) OF EFAVIRENZ PHARMACOKINETICS USING A PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODEL

C. Xu,[1] S. Quinney,[2] Y. Guo,[3] Z. Desta[1]; [1]Division of Clinical Pharmacology, Indiana University School of Medicine, Indianapolis, IN, [2]Department of Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, IN, [3]Drug Disposition, Lilly Research Laboratories, Indianapolis, IN.

PI-62

POPULATION PHARMACOKINETICS OF SM-26000, LIPOSOMAL AMPHOTERICIN B, IN JAPANESE PEDIATRIC PATIENTS WITH INVASIVE FUNGAL INFECTION

Y. Ohata,[1] Y. Tomita,[1] K. Suzuki,[1] T. Maniwa,[1] Y. Yano,[2] K. Sunakawa[3]; [1]Dainippon Sumitomo Pharma Co., Ltd., Osaka, Japan, [2]Kyoto Pharmaceutical University, Kyoto, Japan, [3]Kitasato University, Tokyo, Japan.

PI-63

LOW DENSITY LIPOPROTEIN (LDL-C) EXPOSURE-RESPONSE ANALYSIS FOR TOFACITINIB (CP-690,550) IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. P. Riley, M. G. Boy, R. Riese, S. Krishnaswami; Pfizer, Inc, Groton, CT.

PI-64

A PHASE 1 STUDY TO ESTIMATE THE EFFECT OF KETOCONAZOLE ON THE PHARMACOKINETICS OF TOFACITINIB (CP-690,550) IN HEALTHY VOLUNTEERS

P. Gupta,[1] R. Wang,[1] I. Kaplan,[1] C. W. Alvey,[1] M. Ndongo,[2] S. Krishnaswami[1]; [1]Pfizer Inc, Groton, CT, [2]Pfizer Clinical Research Unit, Brussels, Belgium.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PI-65

NONLINEAR MIXED-EFFECTS MODELING OF THE INTERSPECIES PHARMACOKINETIC SCALING OF CEFADROXIL AFTER ORAL AND INTRAVENOUS BOLUS ADMINISTRATION

M. M. Posada, D. Smith, M. Feng; University of Michigan, Ann Arbor, MI.

PI-66

SIMULTANEOUS PHARMACOKINETIC MODELING OF WR-1065 IN BLOOD AND TISSUES USING NONLINEAR MIXED EFFECTS MODELING AND EXTRAPOLATION FROM RATS TO HUMANS WITH BODY WEIGHT AS A COVARIATE

M. R. Feng,[1] **X. Chen**,[1] M. Hutchmatt,[2] Z. Lu,[3] B. Yang,[1] D. Smith[1]; [1]University of Michigan, Ann Arbor, MI, [2]The Ann Arbor Pharmacometrics Group, Ann Arbor, MI, [3]AstraZeneca Pharmaceuticals, Wilmington, DE.

PI-67

CHARACTERIZATION OF THE RELATIONSHIP BETWEEN IPILIMUMAB EXPOSURE, TUMOR SIZE, AND SURVIVAL IN PREVIOUSLY UNTREATED NON-SMALL CELL LUNG CANCER PATIENTS

Y. Feng,[1] E. Masson,[1] D. Williams,[1] J. Song,[2] J. Cuillerot,[2] A. Roy[1]; [1]Bristol-Myers Squibb Co., Princeton, NJ, [2]Bristol-Myers Squibb Co., Wallingford, CT.

PI-68

INVESTIGATION OF THE ELIMINATION OF DABIGATRAN BY HAEMODIALYSIS IN PATIENTS WITH END STAGE RENAL DISEASE (ESRD)

S. Haertter,[1] M. Trenmmel,[1] G. Nehmiz,[2] K. Liesenfeld,[1] V. Moschetti,[1] H. Peters,[3] F. Wagner,[4] S. Formella[5]; [1]Boehringer Ingelheim Pharma, Translational Medicine, Germany, [2]Boehringer Ingelheim Pharma, Biberach, Germany, [3]Department of Nephrology, Charite, Berlin, Germany, [4]Charite Research Organization, Berlin, Germany, [5]Boehringer Ingelheim Pharma, Ingelheim, Germany.

PI-69

PHARMACOKINETIC (PK) ANALYSIS OF COADMINISTRATION OF AXITINIB AND PEMETREXED/CISPLATIN (PEM/CIS) IN PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC)

M. A. Tortorici,[1] L. Iglesias,[2] M. F. Kozloff,[3] Y. K. Pithavala,[1] A. Ingrosso,[4] C. P. Belani[5]; [1]Pfizer Oncology, San Diego, CA, [2]Hospital Doce de Octubre, Madrid, Spain, [3]Ingalls Hospital, Harvey, IL, [4]Pfizer Italia Srl, Milano, Italy, [5]Penn State Hershey Cancer Institute, Hershey, PA.

PI-70

SINGLE AND MULTIPLE-DOSE PHARMACOKINETICS OF TOFACITINIB (CP-690,550) FROM A DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-ESCALATION STUDY IN MEDICALLY STABLE SUBJECTS WITH PSORIASIS

S. Menon, M. G. Boy, C. Wang, B. E. Wilkinson, S. H. Zwillich, G. Chan, S. Krishnaswami; Pfizer Inc, Specialty Care Business Unit, Groton, CT.

PI-71

THE EFFECT OF TOFACITINIB (CP-690,550) ON THE PHARMACOKINETICS OF ORAL CONTRACEPTIVE STEROIDS IN HEALTHY FEMALE VOLUNTEERS

S. Menon,[1] R. Riese,[1] R. Wang,[1] C. W. Alvey,[1] W. Petit,[2] S. Krishnaswami[1]; [1]Pfizer Inc, Groton, CT, [2]Pfizer Clinical Research Unit, Brussels, Belgium.

PI-72

EFFECTS OF QUINIDINE ON PHARMACOKINETICS (PK) OF ORAL (PO) AND INTRAVENOUSLY (IV) ADMINISTERED EDOXABAN

N. Matsushima,[1] J. Mendell,[1] H. Zahir,[1] F. Lee,[2] T. Sato,[1] J. Jin,[1] D. Weiss[2]; [1]Daiichi Sankyo, Co, Ltd, Parsippany, NJ, [2]Celerion, Inc, Neptune, NJ.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PI-73

THE EFFECT OF RIFAMPIN ON THE PHARMACOKINETICS OF TOFACITINIB (CP-690,550) IN HEALTHY VOLUNTEERS

M. Lamba,[1] R. Wang,[1] I. Kaplan,[1] J. Salageanu,[1] S. Tarabar,[2] S. Krishnaswami[1]; [1]Pfizer, Groton, CT, [2]Pfizer Clinical Research Unit, New Haven, CT.

PI-74

THE EFFECT OF FOOD ON THE PHARMACOKINETICS OF TOFACITINIB (CP-690,550)

M. Lamba,[1] R. Wang,[1] T. Stock,[2] M. O'Gorman,[1] S. Krishnaswami[1]; [1]Pfizer Inc, Groton, CT, [2]Pfizer Inc, Collegeville, PA.

PI-75

A PHARMACOKINETIC STUDY OF ORAL PACLITAXEL IN COMBINATION WITH HM30181 IN SOLID CANCER PATIENTS

S. E. Kim, N. Gu, D. Shin, S. H. Yoon, J. Y. Cho, S. G. Shin, K. S. Yu, I. J. Jang; Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PI-76

DIFFERENCES IN ACUTE PAIN, HYPERALGESIA, ALLODYNIA AND NEUROGENIC FLARE IN RESPONSE TO TOPICAL AND INTRADERMAL CAPSAICIN

K. Francke,[1] E. Neuhoff,[1] W. Heber,[2] J. Lambert,[1] M. Grossmann[3]; [1]PAREXEL, London, United Kingdom, [2]PAREXEL, Baltimore, MD, [3]PAREXEL, Berlin, Germany.

PI-77

PROPOFOL PHARMACOKINETICS IN CHILDREN IN EGYPTIEN POPULATION

A. A. Guemei,[1] R. S. Saleh,[2] A. M. El-Attar,[3] O. T. Fahmy[4]; [1]Faculty of Medicine at King Fahad Medical City, Riyadh, Saudi Arabia, [2]Faculty of Medicine, Alexandria University, Alexandria, Egypt, [3]Faculty of Medicine, Alexandria University, Alexandria, Egypt, [4]Faculty of Pharmacy, Alexandria University, Alexandria, Egypt.

PI-78

POPULATION MODELING OF THE PHARMACOKINETICS AND PHARMACODYNAMICS OF PONESIMOD, A SELECTIVE S1P1 RECEPTOR AGONIST

A. Krause, P. Brossard, D. D'Ambrosio, J. Dingemanse; Actelion Pharmaceuticals, Allschwil, Switzerland.

PI-79

MODEL-BASED META-ANALYSIS (MBMA) OF TOTAL MOTOR SCORE, CHOREA SCORE, AND TOTAL FUNCTIONAL CAPACITY FOR PATIENTS WITH HUNTINGTON'S DISEASE (HD)

Y. Jin, S. Ahadieh, E. Pickering, R. Evans, J. Liu; Pfizer Inc, Groton, CT.

PI-80

IMPORTANCE OF PK VARIABILITY ON DOSE SELECTION FOR COMPOUNDS WITH POTENTIAL INVERTED U SHAPE DOSE RESPONSE

Y. Jin,[1] J. Liu,[1] D. Nichols[2]; [1]Pfizer Inc, Groton, CT, [2]Pfizer Inc, Sandwich, United Kingdom.

PI-81

CHARACTERIZATION OF GUINEA PIG MDR1/P-GP FUNCTION

I. Hasibu, D. Patoine, S. Pilote, B. Drolet, **C. Simard**; Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Quebec, QC, Canada.

PI-82

CHARACTERIZATION OF GUINEA PIG CYP2C FUNCTION

I. Hasibu, S. Pilote, D. Patoine, B. Drolet, **C. Simard**; Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Quebec, QC, Canada.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PI-83

A NEWLY DEVELOPED PEDIATRIC FORMULATION OF REVATIO FOR PEDIATRIC PULMONARY ARTERIAL HYPERTENSION PATIENTS IS BIOEQUIVALENT TO THE 1X20 MG REVATIO COMMERCIAL TABLET AND TO THE 2X10 MG SILDENAFIL CITRATE CLINICAL TRIAL TABLETS IN HEALTHY ADULT VOLUNTEERS

X. Gao, L. Robert, M. O'Gorman, J. Cook; Pfizer, Inc, Groton, CT.

PI-84

A PHASE 1 STUDY TO ASSESS THE EFFECT OF LU AA21004 ON THE STEADY-STATE PHARMACOKINETICS OF LITHIUM IN HEALTHY MALE SUBJECTS

G. Chen, R. Lee, Z. Zhao, M. Serenko; Takeda Global Research and Development Center, Deerfield, IL.

PI-85

A POPULATION ANALYSIS OF UNBOUND MYCOPHENOLIC ACID PHARMACOKINETICS AND PHARMACOGENETICS IN ADULT ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

A. Frymoyer,[1] D. Verotta,[1] P. A. Jacobson,[2] J. Long-Boyle[1]; [1]University of California, San Francisco, San Francisco, CA, [2]University of Minnesota, Minneapolis, MN.

PI-86

EFFECT OF CHRONIC CONSUMPTION OF GREEN TEA ON THE PHARMACOKINETICS AND PHARMCODYNAMICS OF NADOLOL IN HEALTHY VOLUNTEERS

S. Misaka,[1] N. Miyazaki,[1] J. Yatabe,[1] K. Kawabe,[2] K. Takano,[1] T. Ono,[1] S. Onoue,[2] T. Fukushima,[1] H. Watanabe,[3] S. Yamada,[2] J. Kimura[1]; [1]Fukushima Medical University, Fukushima, Japan, [2]University of Shizuoka School of Pharmaceutical Sciences, Shizuoka, Japan, [3]Hamamatsu University School of Medicine, Hamamatsu, Japan.

PI-87

WITHDRAWN

PI-88

PHARMACOKINETIC AND PHARMACODYNAMIC EVALUATION OF A NOVEL K+-COMPETITIVE ACID PUMP ANTAGONIST, YH4808, IN HEALTHY VOLUNTEERS

S. J. Yi,[1] S. Y. Nam,[2] H. M. Byun,[2] S. B. Jang,[2] H. Jeon,[1] S. E. Kim,[1] S. H. Yoon,[1] K. S. Lim,[1] J. Y. Cho,[1] S. G. Shin,[1] I. J. Jang,[1] K. S. Yu[1]; [1]Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]R&D, Yuhan Corporation, Seoul, Republic of Korea.

PI-89

EXPOSURE-RESPONSE MODELING OF LY2439821 (AN ANTI-IL-17 MONOCLONAL ANTIBODY) IN PATIENTS WITH MODERATE-TO-SEVERE PSORIASIS

C. Tang,[1] S. Choi,[1] J. Satterwhite,[2] G. Cameron,[2] S. Banerjee,[2] **L. Tham**[1]; [1]Lilly-NUS Centre for Clinical Pharmacology Pte Ltd, Singapore, Singapore, [2]Eli Lilly and Company, Indianapolis, IN.

PI-90

EFFECT OF ACTIVATED CHARCOAL ON THE PHARMACOKINETICS OF APIXABAN IN HEALTHY SUBJECTS

X. Wang, G. Tirucherai, N. Pannacciulli, J. Wang, A. Elsrougy, V. Teslenko, M. Chang, D. Zhang, C. Frost; Bristol-Myers Squibb, Princeton, NJ.

POSTER SESSION I

PRINCE GEORGE'S EXHIBIT HALL C ★ Thursday, March 15 | 8:00am-3:00pm | Attended Poster 8:00am-9:30am

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PI-91

A CLINICAL STUDY TO ASSESS EFFECT OF RIFAMPIN ON THE PHARMACOKINETICS (PK) OF NERATINIB (HKI-272), A PAN-ERBB RECEPTOR TYROSINE KINASE INHIBITOR, WHEN ADMINISTERED CONCOMITANTLY IN HEALTHY SUBJECTS

R. Abbas, B. Hug, C. Leister, D. Sonnichsen; Pfizer, Collegeville, PA.

PI-92

USE OF A PHARMACOKINETIC-PHARMACODYNAMIC (PKPD) MODEL FRAMEWORK IN THE DESIGN OF A DOSING REGIMEN FOCUSED ON RESPONSE

A. Grover, L. Z. Benet; University of California, San Francisco, San Francisco, CA.

PI-93

ORAL MIDAZOLAM (MDZ) PARTIAL AREA-UNDER CURVE (AUC) DOES NOT RELIABLY PREDICT CYTOCHROME P450 (CYP) 3A BASELINE ACTIVITY IN HEALTHY SUBJECTS

W. Tai,[1] S. L. Gong,[1] **S. M. Tsunoda**,[1] H. E. Greenberg,[2] J. C. Gorski,[3] S. R. Penzak,[4] S. A. Stoch,[5] J. D. Ma[1]; [1]UCSD, Skaggs School of Pharmacy & Pharmaceutical Sciences, La Jolla, CA, [2]Department of Pharmacology and Experimental Therapeutics, Thomas Jefferson University, Philadelphia, PA, [3]Mylan Pharmaceuticals, Morgantown, WV, [4]Pharmacy Department, National Institutes of Health, Bethesda, MD, [5]Merck, Rahway, NJ.

PI-94

ORAL MIDAZOLAM (MDZ) PARTIAL AREA-UNDER CURVE (AUC) DOES NOT RELIABLY PREDICT CYTOCHROME P450 (CYP) 3A INHIBITION AND INDUCTION/ACTIVATION IN HEALTHY SUBJECTS

S. L. Gong,[1] W. Tai,[1] **S. M. Tsunoda**,[1] H. E. Greenberg,[2] J. C. Gorski,[3] S. R. Penzak,[4] S. A. Stoch,[5] J. D. Ma[1]; [1]UCSD, Skaggs School of Pharmacy & Pharmaceutical Sciences, La Jolla, CA, [2]Department of Pharmacology and Experimental Therapeutics, Thomas Jefferson University, Philadelphia, PA, [3]Mylan Pharmaceuticals, Morgantown, WV, [4]Pharmacy Department, National Institutes of Health, Bethesda, MD, [5]Merck, Rahway, NJ.

PI-95

POPULATION PHARMACOKINETIC ANALYSIS OF DAPAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Y. Hong,[1] A. Roy,[1] D. Boulton,[1] F. LaCreta,[1] S. Parikh,[2] J. List[1]; [1]Bristol-Myers Squibb, Princeton, NJ, [2]AstraZeneca, Wilmington, DE.

PI-96

PHARMACOKINETICS AND PHARMACODYNAMICS OF PT302, A LONG ACTING EXENATIDE, IN HEALTHY VOLUNTEERS

D. Shin,[1] N. Gu,[1] S. Yoon,[1] E. Seol,[2] H. Lee,[2] K. Lim,[1] I. Jang,[1] S. Shin,[1] K. Yu[1]; [1]Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Peptron, Inc., Daejeon, Republic of Korea.

PI-97

POPULATION PHARMACOKINETIC ANALYSIS OF RUXOLITINIB IN SUBJECTS WITH MYELOFIBROSIS

X. Chen, X. Liu, S. Peng, W. V. Williams, V. Sandor, S. Yeleswaram; Incyte Corp., Wilmington, DE.

PI-98

POPULATION PK/PD ANALYSIS OF SPLEEN VOLUME IN SUBJECTS WITH MYELOFIBROSIS (MF) ADMINISTERED WITH RUXOLITINIB

X. Chen, X. Liu, S. Peng, W. V. Williams, V. Sandor, S. Yeleswaram; Incyte Corp., Wilmington, DE.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PI-99

POPULATION PK/PD ANALYSIS OF TOTAL SYMPTOM SCORE (MFSAF) IN SUBJECTS WITH MYELOFIBROSIS (MF) TREATED WITH RUXOLITINIB

X. Chen, X. Liu, S. Peng, W. V. Williams, V. Sandor, S. Yeleswaram; Incyte Corp., Wilmington, DE.

PI-100

TOLVAPTAN PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) IN HEALTHY CAUCASIAN AND JAPANESE MEN FOLLOWING 30 MG IN EITHER THE FASTED STATE OR FOLLOWING A HIGH FAT MEAL OR JAPANESE STANDARD MEAL

S. E. Shoaf,[1] S. Kim,[2] P. Bricmont,[1] S. Mallikaarjun[1]; [1]Otsuka Pharmaceutical Development & Commercialization, Inc, Rockville, MD, [2]Otsuka Pharmaceutical Co., Ltd., Osaka, Japan.

PI-101

ASSEMBLING OF A MULTICENTER AND MULTINATIONAL DATA BASE TO DEVELOP AND VALIDATE A PHYSIOLOGICALLY BASED PHARMACOKINETIC SOTALOL MODEL FOR PEDIATRIC EXTRAPOLATION

F. Khalil, S. Laeer; Department of Clinical Pharmacy and Pharmacotherapy, Heinrich-Heine-University of Duesseldorf, Duesseldorf, Germany.

PI-102

POPULATION PHARMACOKINETICS OF VORICONAZOLE IN HUMAN PLASMA AND AQUEOUS HUMOUR AFTER ORAL ADMINISTRATION

Y. Daali, L. Cottet, M. Gex-Fabry, P. Dayer, E. Baglivo, J. Desmeules; Geneva University Hospitals, Geneva, Switzerland.

SPECIAL POPULATIONS (SPO)

PI-103

PAIN PERCEPTION AND PROCESSING IN A MEDICATED STATE: A PILOT STUDY IN AN ELDERLY COHORT

A. Edginton,[1] K. Schaffler[2]; [1]University of Waterloo, Waterloo, ON, Canada, [2]HPR Dr. Schaffler GmbH, Munich, Germany.

PI-104

A PROBABILISTIC RISK ASSESSMENT OF BREAST CANCER TREATMENT FAILURE DURING CO-ADMINISTRATION OF TAMOXIFEN AND PAROXETINE AS IT RELATES TO CYP2D6 GENOTYPE

A. Edginton,[1] M. Sevestre,[2] J. Stingl[3]; [1]University of Waterloo, Waterloo, ON, Canada, [2]Design2Code, Waterloo, ON, Canada, [3]Univerity of Ulm, Ulm, Germany.

PI-105

THE UTILITY OF PROBABILISTIC SIMULATION IN DRUG RISK-BENEFIT ASSESSMENT IN OLDER ADULTS

J. Lee, V. Crentsil; U.S. Food and Drug Administration, Silver Spring, MD.

PI-106

USING MODELING AND SIMULATION TO OPTIMIZE DRUG RISK-BENEFIT IN OLDER ADULTS

V. Crentsil, **J. Lee**, A. Jackson; U.S. Food and Drug Administration, Silver Spring, MD.

POSTER SESSION II

PRINCE GEORGE'S EXHIBIT HALL C ★ Friday, March 16 | 8:00am-3:00pm | Attended Poster 8:00am-9:30am

DRUG DEVELOPMENT AND REGULATORY SCIENCES (DDR)

PII-1

THE PHARMACOKINETICS OF BRENTUXIMAB VEDOTIN (SGN-35), AN ANTIBODY-DRUG CONJUGATE (ADC)

T. H. Han,[1] D. Kennedy,[1] S. Hayes,[2] C. M. Lynch[1]; [1]Seattle Genetics, Inc., Bothell, WA, [2]ICON Development Solutions, Ellicott City, MD.

PII-2

BRENTUXIMAB VEDOTIN (SGN-35), AN ANTIBODY-DRUG CONJUGATE, DOES NOT AFFECT MIDAZOLAM PHARMACOKINETICS

T. H. Han, L. E. Grove, C. M. Lynch; Seattle Genetics, Inc., Bothell, WA.

PII-3

EFFECT OF DISCONTINUING ORAL ANTI-DIABETIC DRUGS (OAD) PRIOR TO ENROLLMENT IN A PHASE I TRIAL

R. J. Schott,[1] J. E. Angeles,[2] H. Larrabee,[2] C. Humphreys,[2] K. M. Schott,[2] L. A. Morrow,[2] **M. Hompesch**[2]; [1]Profil Institute for Clinical Research, Chula Vista, CA, [2]Profil Institute for Clinical Research, Chula Vist, CA.

PII-4

ANEMIA SUBSEQUENT TO REPEATED PHLEBOTOMY IN TYPE 2 DIABETICS (T2D) PARTICIPATING IN A PHASE I TRIAL

R. J. Schott, J. E. Angeles, H. Larrabee, C. Humphreys, K. M. Schott, L. A. Morrow, **M. Hompesch**; Profil Institute for Clinical Research, Chula Vista, CA.

PII-5

ALTERNATIVE TRIAL DESIGNS USED IN ONCOLOGY PHASE I CLINICAL TRIALS: A LITERATURE SURVEY (2008-2011)

S. Rajan, N. Budha, M. Dresser; Genentech, South San Francisco, CA.

PII-6

PREDICTING CYP3A4 INHIBITION IN CYP2D6 POOR METABOLIZERS USING PBPK MODELING AND SIMULATION: FESOTERODINE AS AN EXAMPLE

M. L. Vieira, P. Zhao, M. Kim, S. Apparaju, S. Huang; Food and Drug Administration, Silver Spring, MD.

PII-7

WHAT CRITERIA MAY BE APPROPRIATE IN DETERMINING THE NEED FOR *IN VIVO* EVALUATION OF A NEW MOLECULAR ENTITY'S (NME'S) POTENTIAL TO INHIBIT OATP1B1 (ORGANIC ANION TRANSPORTING POLYPEPTIDE 1B1)

J. Vaidyanathan, V. Arya, S. Agarwal, M. de L T Vieira, P. Zhao, S. Huang, L. Zhang; FDA, Silver Spring, MD.

PII-8

COMPARISON OF PAYMENT ESTIMATES BETWEEN HEALTHY VOLUNTEERS AND CLINICAL INVESTIGATORS IN KOREA CLINICAL TRIAL SITES

J. Cho,[1] **H. Kim**,[1] S. Back,[2] J. Choi,[1] I. Jang,[3] G. Bae,[4] J. Shin[1]; [1]Department of Pharmacology and Clinical Pharmacology, Inje University College of Medicine and Busan Paik Hospital, Busan, Korea, Republic of, [2]Clinical Trial Center, Busan Paik Hospital, Busan, Korea, Republic of, [3]Department of Clinical Pharmacology & Therapeutics, Seoul National University Hospital, Seoul, Korea, Republic of, [4]Department of Clinical Pharmacology and Therapeutics, Asan Medical Center, Seoul, Republic of Korea.

PII-9

PHARMACOKINETICS OF VORAPAXAR AND ITS METABOLITE SCH 2046273 (M20) FOLLOWING ORAL ADMINISTRATION IN HEALTHY CHINESE AND US SUBJECTS

P. Statkevich, T. Kosoglou, B. Kumar, J. Li, F. Xuan, Z. Wang, A. G. Meehan, D. L. Cutler; Merck Sharp & Dohme Corp., Whitehouse Station, NJ.

DRUG DEVELOPMENT AND REGULATORY SCIENCES (DDR)

PII-10

LEARN-APPLY APPROACH FOR ESTABLISHING DOSING RECOMMENDATIONS: PALIPERIDONE FOR THE TREATMENT OF ADOLESCENT SCHIZOPHRENIA

I. R. Younis, T. P. Laughren, Y. Wang, M. Mathis, J. V. Gobburu; FDA, Silver Spring, MD.

PII-11

THE PHARMACOKINETIC PARAMETERS OF A NOVEL, NANO-FORMULATED LOWER DOSE ORAL DICLOFENAC

G. Manvelian,[1] S. Daniels,[2] A. Gibofsky[3]; [1]Iroko Pharmaceuticals, LLC, Philadelphia, PA, [2]Premier Research Group, Austin, TX, [3]Hospital for Special Surgery, New York, NY.

PII-12

ACUTE PAIN RELIEF BY A PROPRIETARY, NANO-FORMULATED LOWER DOSE ORAL DICLOFENAC

G. Manvelian,[1] S. Daniels,[2] A. Gibofsky[3]; [1]Iroko Pharmaceuticals, LLC, Philadelphia, PA, [2]Premier Research Group, Austin, TX, [3]Hospital for Special Surgery, New York, NY.

PII-13

CHARACTERIZATION OF OPERANT INTRAVENOUS (IV) ETHANOL SELF-ADMINISTRATION IN HUMANS: OPEN-BAR AND PROGRESSIVE-RATIO PARADIGMS

B. L. Stangl, M. Zametkin, V. Vatsalya, V. A. Ramchandani; NIAAA, Bethesda, MD.

DRUG SAFETY (SAF)

PII-14

OCULAR TOLERABILITY AND SAFETY ASSESSMENT OF DA-6034 OPHTHALMIC SOLUTION IN HEALTHY SUBJECTS

S. Yoon, N. Gu, S. Kim, K. S. Lim, K. S. Yu, I. J. Jang, S. G. Shin; Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PII-15

RG1678, A NOVEL GLYCINE REUPTAKE INHIBITOR, DOES NOT CAUSE QTcF PROLONGATION IN HEALTHY MALE VOLUNTEERS AT THERAPEUTIC AND SUPRATHERAPEUTIC EXPOSURE

C. Hofmann,[1] L. Banken,[1] M. Hahn,[2] D. Swearingen,[3] S. Nagel,[4] M. Martin-Facklam[1]; [1]F. Hoffmann-La Roche Ltd., Basel, Switzerland, [2]Roche Products Ltd., Welwyn Garden City, United Kingdom, [3]Celerion, Phoenix, AZ, [4]Roche Ltd., Strasbourg, France.

PII-16

SAFETY, TOLERABILITY AND PHARMACOKINETICS OF RG1678, A NOVEL GLYCINE REUPTAKE INHIBITOR: A SINGLE ASCENDING DOSE STUDY IN HEALTHY VOLUNTEERS

M. Martin-Facklam,[1] C. Hofmann,[1] L. Banken,[1] D. Alberati,[1] G. Schmitt,[1] N. Parrott,[1] D. Hainzl,[1] R. Robson,[2] S. Nave,[1] B. Boutouyrie[1]; [1]F. Hoffmann-La Roche Ltd., Basel, Switzerland, [2]CCST, Christchurch, New Zealand.

PII-17

SAFETY, TOLERABILITY AND PHARMACOKINETICS OF RG1678, A NOVEL GLYCINE REUPTAKE INHIBITOR: A MULTIPLE ASCENDING DOSE STUDY IN HEALTHY VOLUNTEERS

C. Boetsch,[1] C. Hofmann,[1] M. Martin-Facklam,[1] L. Banken,[1] U. Biedinger,[2] A. Patat,[2] B. Boutouyrie[1]; [1]F. Hoffmann-La Roche Ltd., Basel, Switzerland, [2]Biotrial, Rennes, France.

PII-18

SURVEILLANCE OF DRUG METABOLIZING ENZYME AND TRANSPORTER-BASED DRUG-DRUG INTERACTION POTENTIAL IN PATIENTS RECEIVING ORAL ANTINEOPLASTIC AGENTS

S. J. Bowlin, F. Xia, W. Wang, K. D. Robinson, E. J. Stanek; Medco Research Institute, Bethesda, MD.

POSTER SESSION II

PRINCE GEORGE'S EXHIBIT HALL C ★ Friday, March 16 | 8:00am-3:00pm | Attended Poster 8:00am-9:30am

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PII-19

EFFECT OF CYP3A4*1G POLYMORPHISM ON THE PHARMACOKINETICS AND PHARMACODYNAMICS OF ZOLPIDEM IN HEALTHY CHINESE

Z. Jiao, P. Sun, X. Qiu, M. Zhong; Huashan Hospital, Fudan University, Shanghai, China.

PII-20

UGT2B17 GENETIC POLYMORPHISM DRAMATICALLY AFFECTS THE PHARMACOKINETICS OF MK-7246 IN HEALTHY SUBJECTS IN A FIRST-IN-MAN STUDY

Y. Wang,[1] M. Trucksis,[1] J. McElwee,[1] P. Wong,[1] C. Maciolek,[1] C. Thompson,[1] T. Prueksaritanont,[1] C. Gibson,[1] G. Garrett,[1] R. Delercq,[1] E. Vets,[2] K. Willson,[1] R. Smith,[1] J. Klappenbach,[1] G. Opiteck,[1] J. Tsou,[1] T. Laethem,[1] P. Panorchan,[1] L. Maganti,[1] M. Iwamoto,[1] R. Rippley,[1] P. Shaw,[1] J. Wagner,[1] J. Harrelson[1]; [1]Merck & Co., Inc., Whitehouse Station, NJ, [2]SGS Life Science. Services, Antwerp, Belgium.

PII-21

ASSOCIATION OF FTO WITH HYDROCHLOROTHIAZIDE (HCTZ)-INDUCED ELEVATION IN URIC ACID (UA) IN AFRICAN AMERICAN (AA) HYPERTENSIVES IN THE PHARMACOGENOMIC EVALUATION OF ANTIHYPERTENSIVE RESPONSE (PEAR) STUDY

A. G. Vandell,[1] C. W. McDonough,[1] T. Y. Langaee,[1] B. Burkley,[1] Y. Gong,[1] S. T. Turner,[2] J. G. Gums,[1] A. B. Chapman,[3] A. L. Beitelshees,[4] K. R. Bailey,[2] E. Boerwinkle,[5] R. M. Cooper-DeHoff,[1] J. A. Johnson[1]; [1]University of Florida, Gainesville, FL, [2]Mayo Clinic, Rochester, MN, [3]Emory University, Atlanta, GA, [4]University of Maryland, Baltimore, MD, [5]University of Texas, Houston, TX.

PII-22

A TRANSLATIONAL APPROACH TO LINK CLINICAL OBSERVATIONS WITH MECHANISMS OF ACTION FOR FENOFIBRATE

R. A. Farris, C. A. Wiley, **E. T. Price**; University of Arkansas for Medical Sciences, Little Rock, AR.

PII-23

DRUG-DRUG INTERACTIONS BETWEEN ROSUVASTATIN AND β-BLOCKERS THROUGH THE OATP1A2 TRANSPORTER

J. Lu,[1] F. Gaudette,[2] Y. Leung,[1] J. Turgeon[2]; [1]Montreal University, Montreal, QC, Canada, [2]CRCHUM, Centre de Recherche du Centre Hospitalier de l'Universite de Montreal, Montreal, QC, Canada.

PII-24

DRUG-TRANSPORTER INTERACTIONS: INHIBITION OF MCT1 AND MCT4 BY STATINS

Y. Leung,[1] F. Blanger,[2] C. Armstrong,[1] J. Lu,[1] J. Turgeon[2]; [1]University of Montreal (CRCHUM), Montreal, QC, Canada, [2]CRCHUM, Montreal, QC, Canada.

PII-25

GENOME-WIDE GENETIC ASSOCIATION STUDIES OF SSRI SIDE EFFECTS

C. C. Wen,[1] L. Shen,[2] K. M. Giacomini,[1] N. Risch,[3] C. Schaefer[2]; [1]Department of Bioengineering and Therapeutic Sciences, University of California, San Francisco, San Francisco, CA, [2]Kaiser Permanente Northern California Division of Research, Oakland, CA, [3]Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA.

PII-26

MIDAZOLAM PHARMACOKINETICS ARE NOT INFLUENCED BY POLYMORPHISMS OF HEPATIC OATP 1B1 IN HEALTHY VOLUNTEERS

V. C. Ziesenitz,[1] S. K. Koenig,[2] J. Weiss,[2] J. Burhenne,[2] W. E. Haefeli,[2] G. Mikus[2]; [1]Department of Clinical Pharmacology and Pharmacoepidemiology, University Hospital Heidelberg, Heidelberg, Germany and Center for Clinical and Community Research, Children's National Medical Center, Washington, DC, [2]Department of Clinical Pharmacology and Pharmacoepidemiology, University Hospital Heidelberg, Heidelberg, Germany.

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PII-27

EFFECT OF OATP INHIBITION BY RIFAMPICIN ON THE PHARMACOKINETICS OF FENTANYL IN HEALTHY VOLUNTEERS GENOTYPED FOR ORGANIC ANION-TRANSPORTING POLYPEPTIDE 1B1

V. C. Ziesenitz,[1] N. Mahlke,[2] S. K. Koenig,[3] G. Skopp,[2] J. Weiss,[3] J. Burhenne,[3] W. E. Haefeli,[3] G. Mikus[3]; [1]Department of Clinical Pharmacology and Pharmacoepidemiology, University Hospital Heidelberg, Heidelberg, Germany and Center for Clinical and Community Research, Children's National Medical Center, Washington, DC, [2]Institute of Legal Medicine, University Hospital Heidelberg, Heidelberg, Germany, [3]Department of Clinical Pharmacology and Pharmacoepidemiology, University Hospital Heidelberg, Heidelberg, Germany.

PII-28

CYP1A2 GENETIC POLYMORPHISMS ASSOCIATED WITH ANTIDEPRESSANT ESCITALOPRAM METABOLISM AND ADVERSE REACTIONS AT EARLY STAGE

Y. Liu,[1] J. Tian,[1] H. Kuo,[1] H. Tsou,[1] S. Liu,[1] S. Lu,[2] K. Lin,[1] Y. Chen[1]; [1]National Health Research Institutes, Miaoli County, Taiwan, [2]College of Medicine, National Taiwan University, Taipei, Taiwan.

PII-29

IDENTIFICATION OF CLINICALLY RELEVANT AND SELECTIVE INHIBITORS OF RENAL ORGANIC CATION TRANSPORT

K. M. Morrissey, K. M. Giacomini; UC San Francisco, San Francisco, CA.

PII-30

RESPONSIVENESS OF VERY LOW-DOSE WARFARIN ASSOCIATED WITH GENETIC VARIANTS OF VKORC1, CYP2C9, CYP4F2 AND CYP2C19 IN INDONESIAN PATIENTS

T. Rusdiana,[1] T. Araki,[1] T. Nakamura,[1] A. Subarnas,[2] K. Yamamoto[1]; [1]Department of Clinical Pharmacology, Gunma University Graduate School of Medicine, Maebashi, Japan, [2]Faculty of Pharmacy, Padjadjaran University, Jl. Raya Bandung-Sumedang km 21 Jatinangor, Indonesia.

PII-31

INFLUENCE OF OATP1B2 DEFICIENCY ON THE DISPOSITION OF METHOTREXATE

G. H. Bruun,[1] L. Li,[2] T. J. Corydon,[1] M. V. Relling,[2] A. Sparreboom,[2] T. S. Mikkelsen[3]; [1]Department of Biomedicine, Aarhus University, Aarhus, Denmark, [2]Department of Pharmaceutical Sciences, St. Jude Children's Research Hospital, Memphis, TN, [3]Department of Pediatric Oncology and Hematology, Aarhus University Hospital, Skejby, Denmark.

PII-32

THE *ARG389GLY ADRB1* POLYMORPHISM AFFECTS THE HEART RATE RESPONSE TO ESMOLOL AMONG HEALTHY SUBJECTS

M. Muszkat, A. Hoofien, E. Orlanski-Meyer, H. Makhoul, E. Porat, E. Davidson, S. Blotnick, **Y. Caraco**; Hadassah University Hospital, Jerusalem, Israel.

PII-33

EFFECTS OF OCT2 AND MATE1 POLYMORPHISMS AND INHIBITION BY TRIMETHOPRIM ON METFORMIN PHARMACOKINETICS

D. Czock,[1] B. Grun,[1] M. Kiessling,[1] J. Burhenne,[1] K. Riedel,[1] J. Weiss,[1] G. Rauch,[2] W. E. Haefeli[1]; [1]University Hospital Heidelberg, Heidelberg, Germany, [2]University Heidelberg, Heidelberg, Germany.

PII-34

GENOTYPE-BASED ESTIMATION OF CYP2C19 CONTRIBUTION TO THE ELIMINATION OF OMEPRAZOLE IN HEALTHY SUBJECTS

V. Michaud, Y. Kreutz, T. Skaar, E. Ogburn, N. Thong, D. A. Flockhart, Z. Desta; Indiana University School of Medicine, Department of Clinical Pharmacology, Indianapolis, IN.

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PII-35

EVALUATION OF THE USE OF SINGLE PLASMA SAMPLES FOR DETERMINATION OF OMEPRAZOLE HYDROXYLATION AND SULFOXIDATION INDICES TO PHENOTYPE CYP2C19 AND CYP3A UNDER INDUCTION DRUG INTERACTIONS

V. Michaud, E. Ogburn, N. Thong, Z. Desta; Indiana University School of Medicine, Department of Clinical Pharmacology, Indianapolis, IN.

PII-36

EFFECTS OF PROGESTERONE ON THE EXPRESSION AND ACTIVITIES OF CYTOCHROME P450 (CYP) IN PRIMARY HUMAN HEPATOCYTES

S. Choi, H. Jeong; University of Illinois at Chicago, Chicago, IL.

PII-37

SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI) PHARMACOGENOMICS: IDENTIFICATION OF RIBOFLAVIN KINASE(RFK) AS A NOVEL CANDIDATE GENE FOR SSRI RESPONSE BY GENOME-WIDE ASSOCIATION STUDY (GWAS) COMBINED WITH FUNCTIONAL GENOMICS

Y. Chai,[1] Y. Ji,[1] J. M. Biernacka,[1] K. A. Snyder,[1] T. Mushiroda,[2] M. Kubo,[2] Y. Nakamura,[2] N. Kamatani,[2] D. Schaid,[1] D. A. Mrazek,[1] R. M. Weinshilboum[1]; [1]Mayo Clinic, Rochester, MN, [2]RIKEN Center for Genomic Medicine, Yokohama, Japan.

ONCOLOGY (ONC)

PII-38

CONTRIBUTION OF ABCC4 (MRP4)-MEDIATED GASTRIC ABSORPTION TO THE ORAL BIOAVAILABILITY OF DASATINIB

B. Furmanski,[1] K. Fujita,[2] M. Adachi,[1] L. Li,[1] S. Hu,[1] A. Gibson,[1] M. Leggas,[3] J. Schuetz,[1] S. D. Baker,[1] **A. Sparreboom**[1]; [1]St. Jude Children's Research Hospital, Memphis, TN, [2]Saitama Medical University, Saitama, Japan, [3]University of Kentucky, Lexington, KY.

PII-39

ABCC4 IS A DETERMINANT OF CYTARABINE-INDUCED CYTOTOXICITY AND MYELOSUPPRESSION

S. Hu, S. Orwick, D. Nachagari, J. Schuetz, A. Sparreboom, S. D. Baker; St. Jude Children's Research Hospital, Memphis, TN.

PII-40

PHARMACOKINETIC (PK) AND PHARMACODYNAMIC (PD) ANALYSIS OF TRASTUZUMAB EMTANSINE (T-DM1) IN JAPANESE PATIENTS WITH ADVANCED OR RECURRENT HER2-POSITIVE BREAST CANCER (JO22591): COMPARISON WITH WESTERN PATIENTS

Y. Igawa,[1] M. Matsubara,[1] K. Matsunaga,[1] K. Aogi,[2] Y. Fujiwara,[3] H. Iwata,[4] S. Girish,[5] S. Olsen,[5] J. Yi,[5] O. Saad,[5] M. Gupta[5]; [1]Chugai Pharmaceutical Co., Ltd., Tokyo, Japan, [2]National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan, [3]National Cancer Center Central Hospital, Tokyo, Japan, [4]Chuo Hospital Aichi Cancer Center, Nagoya, Japan, [5]Genentech, Inc, South San Francisco, CA.

ORGAN SPECIFIC DISEASES (OSD)

PII-41

MDMA-INDUCED INCREASES IN BLOOD PRESSURE AND NOT MEDIATED BY A-ADRENERGIC MECHANISMS AND ARE NOT DUE TO ELEVATED PERIPHERAL VASCULAR RESISTANCE

J. Mendelson, M. J. Baggott, L. Li, J. Coyle, G. P. Galloway; CPMCRI, San Francisco, CA.

PII-42

EFFECT OF SIROLIMUS ON IMMUNE CELL FUNCTION ASSAY IN LIVER TRANSPLANT RECIPIENTS

C. Tu, R. G. Gish, A. Kuo, C. Collins, S. M. Tsunoda; University of California, San Diego, La Jolla, CA.

PII-43

A SYSTEM MODELING APPROACH TO UNDERSTANDING THE MECHANISMS OF SALT SENSITIVITY IN ESSENTIAL HYPERTENSIVE PATIENTS AND THE EFFECT ON BLOOD PRESSURE RESPONSE TO ANTIHYPERTENSIVE AGENTS

Y. Xiong,[1] D. A. James,[1] A. Soubret,[2] R. Sarangapani,[1] A. Georgieva,[1] R. Webb,[1] K. M. Hallow[1]; [1]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [2]Novartis Pharma AG, Basel, Switzerland.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PII-44

SIMULTANEOUS MODELING OF PNU-100480 AND ITS ACTIVE METABOLITE PNU-101603 PHARMACOKINETICS IN HEALTHY VOLUNTEERS AFTER REPEATED DOSING

T. Zhu, B. Tan, G. Nucci; Pfizer Inc, Groton, CT.

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PHARMACOKINETIC ANALYSIS OF TWO FLAVORANTS USED IN A NOVEL BREATH-BASED SYSTEM (SMART™) DESIGNED TO ASSESS USE OF VAGINALLY APPLIED PRODUCTS

D. Gonzalez,[1] A. van der Straten,[2] T. E. Morey,[3] S. Wasdo,[3] J. Wishin,[3] B. Quinn,[4] M. Booth,[3] R. J. Melker,[5] H. Derendorf,[6] D. M. Dennis[5]; [1]Department of Pharmaceutics, University of Florida College of Pharmacy, Gainesville, FL, [2]Center for AIDS Prevention Studies, Department of Medicine, University of California San Francisco and Women's Global Health Imperative, RTI International, San Francisco, CA, [3]Department of Anesthesiology, University of Florida College of Medicine, Gainesville, FL, [4]Xhale, Inc., Gainesville, FL, [5]Department of Anesthesiology, University of Florida College of Medicine and Xhale, Inc., Gainesville, FL, [6]Department of Pharmaceutics, University of Florida College of Pharmacy and Xhale, Inc., Gainesville, FL.

PII-46

COMPARATIVE BIOAVAILABILITY STUDY OF A 10-MG CAPSULE AND A 10-MG TABLET OF LENVATINIB (E7080) IN HEALTHY SUBJECTS

R. Shumaker, J. Fan, G. Martinez, K. Chen; Eisai Product Creation Systems, Woodcliff Lake, NJ.

PII-47

DAILY DOSING OF VISOMODEGIB TO STEADY-STATE DOES NOT PROLONG THE QTc INTERVAL IN HEALTHY VOLUNTEERS

R. A. Graham,[1] I. Y. Chang,[1] J. Y. Jin,[1] B. Wang,[1] M. B. Dufek,[1] J. Abou-Ayache,[2] F. Ezzet,[3] K. Zerivitz,[1] J. Low,[1] M. J. Dresser[1]; [1]Genentech, South San Francisco, CA, [2]Roche, Basel, Switzerland, [3]Pharsight, Sunnyvale, CA.

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A PHASE 1 STUDY TO ASSESS THE EFFECT OF AGE, GENDER AND RACE ON THE PHARMACOKINETICS OF SINGLE AND MULTIPLE DOSES OF LU AA21004 IN HEALTHY SUBJECTS

C. Dudkowski, R. Lee, R. Wu, Z. Zhao, M. Serenko; Takeda Global Research and Development Center, Deerfield, IL.

POSTER SESSION II

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EFFECT OF FORMULATION AND FOOD ON THE PHARMACOKINETICS OF LU AA21004 IN HEALTHY SUBJECTS

M. Mayer, J. Xie, M. Serenko; Takeda Global Research and Development Center, Deerfield, IL.

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QUANTITATIVE STRUCTURE-PHARMACOKINETIC (PK) PROPERTIES-RELATIONSHIPS (QSPKR) FOR BENZODIAZEPINES (BZD)

G. Gottipati, J. Venitz; Virginia Commonwealth University, Richmond, VA.

PII-51

SAFETY, PHARMACOKINETIC AND PHARMACODYNAMIC EVALUATION OF HM10460A WHEN ADMINISTERED SUBCUTANEOUSLY TO HEALTHY KOREAN VOLUNTEERS

L. Ahn, K. H. Shin, S. Lee, K. S. Lim, K. S. Yu, I. J. Jang, S. G. Shin; Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

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PHARMACOKINETICS AND TOLERABILITY OF ELETRIPTAN IN KOREAN HEALTHY MALE VOLUNTEERS

K. H. Shin, Y. J. Cha, L. Ahn, K. S. Lim, S. G. Shin, K. S. Yu, I. J. Jang; Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

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MECHANISM-BASED POPULATION PHARMACOKINETIC META-ANALYSIS OF HEDGEHOG PATHWAY INHIBITOR VISMODEGIB, A NOVEL MOLECULE WITH UNIQUE PK NONLINEARITY IN HUMANS

J. Y. Jin,[1] B. Wang,[1] Y. Gao,[2] J. A. Low,[1] A. Joshi,[1] R. A. Graham,[1] M. Dresser[1]; [1]Roche/Genentech, South San Francisco, CA, [2]Quantitative Solutions, Menlo Park, CA.

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PHARMACOKINETICS AND TOLERABILITY OF A NEW TRPV1 ANTAGONIST AFTER MULTIPLE ADMINISTRATIONS IN HEALTHY VOLUNTEERS

Y. J. Cha, N. Gu, D. Shin, K. S. Lim, S. G. Shin, K. S. Yu, I. J. Jang; Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PII-55

EFFICACY OF ORAL AND SUBCUTANEOUS METHYLNALTREXONE TO PREVENT LOPERAMIDE-INDUCED CONSTIPATION IN HEALTHY SUBJECTS

A. Nassif,[1] S. Oswald,[1] J. Kuehn,[2] C. Modess,[1] J. Penski,[1] M. Zimmer,[3] F. Balzer,[3] **W. Siegmund**[1]; [1]University of Greifswald, Department of Clinical Pharmacology, Greifswald, Germany, [2]University of Greifswald, Center of Radiology, Greifswald, Germany, [3]YES Pharmaceutical Development Services, Friedrichsdorf, Germany.

PII-56

POPULATION PHARMACOKINETICS OF IXABEPILONE IN PEDIATRIC CANCER PATIENTS

S. Suryawanshi,[1] L. Iacono,[1] J. Rosenberg,[2] A. Roy[1]; [1]Clinical Pharmacology & Pharmacometrics, Bristol-Myers Squibb, Princeton, NJ, [2]Global Clinical Research, Bristol-Myers Squibb, Princeton, NJ.

PII-57

INFLUENCE OF THE DOSING SCHEDULE OF RABEPRAZOLE ON THE ANTI-PLATELET FUNCTION OF CLOPIDOGREL

T. Furuta, M. Sugimoto, M. Nishino, M. Yamade, T. Uotani, S. Sahara, S. Kachi, H. Watanabe, K. Umemura; Hamamatsu University School of Medicine, Hamamatsu, Japan.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

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SEVERE ADVERSE EVENTS OBSERVED IN PHASE III CLINICAL TRIALS CONDUCTED AT HAMAMATSU UNIVERSITY SCHOOL OF MEDICINE

S. Kachi, H. Tachibana, E. Otobe, N. Eguchi, M. Katsumata, K. Goto, M. Tanaka, F. Kino, M. Yokohara, A. Ito, M. Tateishi, M. Kawai, **T. Furuta**, K. Umemura, H. Watanabe; Hamamatsu University School of Medicine, Hamamatsu, Japan.

PII-59

A SEMI-PHYSIOLOGIC ADME MODEL FOR SIMULATION OF APIXABAN PHARMACOKINETICS AND DRUG-DRUG INTERACTION POTENTIAL

D. R. Plowchalk,[1] T. C. Goosen,[1] D. Zhang,[2] C. Frost,[3] R. Boyd[1]; [1]Pfizer Inc., Groton, CT, [2]Bristol-Myers Squibb, Lawrenceville, NJ, [3]Bristol-Myers Squibb, Lawrenceville, CT.

PII-60

THE EFFECT OF ALCOHOL ON THE *IN VIVO* DISPOSITION OF TWO CYCLOBENZAPRINE EXTENDED-RELEASE FORMULATIONS IN ALCOHOL TOLERANT VOLUNTEERS

J. C. Gorski, T. D. Reynolds, S. Liu, M. Danna, B. A. Duty, B. Li; Mylan Pharmaceuticals, Inc, Morgantown, WV.

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EFFECT OF HEPATIC INSUFFICIENCY ON THE PHARMACOKINETICS OF AVANAFIL, A NEW, POTENT, SELECTIVE PDE-5 INHIBITOR, IN MALE SUBJECTS

M. Obaidi,[1] T. M. Grant,[1] P. Chai,[1] D. J. Katzer,[1] C. M. Brandquist,[1] E. Offman,[2] A. Spivack,[3] S. Yee[3]; [1]Celerion, Lincoln, NE, [2]Celerion, Montreal, QC, Canada, [3]Vivus Inc., Mountain View, CA.

PII-62

DOSING RATIONALE OF BELATACEPT IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS SWITCHING FROM CALCINEURIN INHIBITOR- BASED REGIMEN

S. Lee, Z. Zhou, A. Roy, C. Jones-Burton, M. Harler, J. Shen; Bristol-Myers Squibb, Princeton, NJ.

PII-63

SINGLE AND MULTIPLE DOSE PHARMACOKINETICS OF TOFACITINIB (CP-690,550) IN HEALTHY CHINESE VOLUNTEERS

S. Krishnaswami,[1] T. Wang,[2] Y. Yuan,[1] C. W. Alvey,[1] T. Checchio,[1] M. Peterson,[3] R. Riese[1]; [1]Pfizer Inc, Groton, CT, [2]Pfizer, Shanghai, China, [3]Pfizer Inc, Cambridge, MA.

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DOSE RESPONSE MODELING OF TOFACITINIB (CP-690,550) FOR THE TREATMENT OF SIGNS AND SYMPTOMS OF RHEUMATOID ARTHRITIS

M. Suzuki,[1] S. Neelakantan,[2] M. Peterson,[3] M. Hutmacher,[4] **S. Krishnaswami**[2]; [1]Pfizer Inc, Tokyo, Japan, [2]Pfizer Inc, Groton, CT, [3]Pfizer Inc, Cambridge, MA, [4]Arbor Pharmacometrics Group (A2PG), Ann Arbor, MI.

PII-65

MIDAZOLAM *N*-GLUCURONIDATION INCREASES IN THE PRESENCE OF A CYP3A INHIBITOR IN HEALTHY VOLUNTEERS

C. L. Denton,[1] K. S. Frederick,[2] Y. V. Scarlett,[1] M. B. Fisher,[3] M. F. Paine[1]; [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, CT, [3]ProPharma Services, Oxford, CT.

PII-66

IN VITRO CHARACTERIZATION OF HEPATIC OXIDATIVE METABOLISM OF KNOWN, SYNTHETIC ALLOSTERIC EFFECTORS OF HEMOGLOBIN (AEH)

A. Parikh, J. Venitz; Virginia Commonwealth University, Richmond, VA.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

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TYPE II DIABETES DECREASES HEPATIC CYP3A EXPRESSION IN MOUSE

D. Patoine, P. Mercier, S. Pilote, M. Petit, B. Drolet, C. Simard; Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Quebec, QC, Canada.

PII-68

CYP3A IS EXPRESSED IN MOUSE HEART VENTRICLES AND IS DOWN REGULATED IN TYPE I AND TYPE II DIABETES

D. Patoine, P. Mercier, S. Pilote, M. Petit, B. Drolet, C. Simard; Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Quebec, QC, Canada.

PII-69

EFFECTS OF AGE, GENDER, AND RACE ON THE SAFETY AND PHARMACOKINETICS OF SINGLE AND MULTIPLE DOSES OF AZILSARTAN MEDOXOMIL IN HEALTHY SUBJECTS

R. Harrell, Jr.,[1] A. Karim,[2] W. Zhang,[3] **C. Dudkowski**[3]; [1]Arkansas Research Medical Testing, Little Rock, AR, [2]AzK Consulting, Skokie, IL, [3]Takeda Global Research and Development, Deerfield, IL.

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AZILSARTAN MEDOXOMIL DOES NOT AFFECT THE QTC INTERVAL IN HEALTHY SUBJECTS: RANDOMIZED, DOUBLE-BLIND, PLACEBO- AND POSITIVE-CONTROLLED CROSSOVER STUDY

T. Hunt,[1] A. Karim,[2] Z. Ye,[3] **C. Dudkowski**,[3] B. Barger[3]; [1]PPD Development, Austin, TX, [2]AzK Consulting, Skokie, IL, [3]Takeda Global Research and Development, Deerfield, IL.

PII-71

UTILIZING ACCELERATOR MASS SPECTROMETRY (AMS) FOR THE METABOLIC PROFILING IN A HUMAN ADME STUDY OF [14C]-SAM-531 (PF-05212365)

S. Tse,[1] S. Raje,[2] M. Seymour,[3] Y. Shishikura,[3] R. S. Obach[1]; [1]Pfizer Inc, Groton, CT, [2]Pfizer Inc, Collegeville, PA, [3]Xceleron, LLC, Heslington, York, United Kingdom.

PII-72

SKIN PERMEABILITY AND TISSUE CONCENTRATIONS OF DICLOFENAC ADMINISTERED BY THE FLECTOR® PATCH IN YORKSHIRE-LANDRACE PIGS

S. Tse,[1] K. Powell,[2] S. Fournier,[3] S. J. MacLennan,[4] A. R. Moorman,[5] C. Paterson,[6] R. Bell[7]; [1]Pfizer Inc., Groton, CT, [2]Tandem Lab., Durham, NC, [3]CiTox LAB Research, N.A., Laval, QC, Canada, [4]Pfizer Inc., Cary, NC. Currently BioCryst Pharmaceuticals, Inc., Durham, NC, [5]Pfizer Inc., Cary, NC. Currently Alta Vetta Pharmaceutical Consulting LLC, Durham, NC, [6]Pfizer Inc., Cary, NC. Currently Salix Pharmaceuticals Inc., Raleigh, NC, [7]Pfizer Inc, Groton, CT.

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PHARMACOKINETICS AND PHARMACODYNAMICS OF MEDI-573, A HUMAN MONOCLONAL ANTIBODY AGAINST INSULIN-LIKE GROWTH FACTOR (IGF)-I/II, IN CANCER PATIENTS

X. Chen,[1] B. Wang,[1] J. Viner,[2] B. Lam,[1] M. Liang,[1] F. Jin,[1] L. Roskos[1]; [1]MedImmune, Hayward, CA, [2]MedImmune, Gaithersburg, MD.

PII-74

PHARMACOKINETIC AND PHARMACODYNAMIC MODELING OF THE RELATIONSHIP BETWEEN SERUM RHUMAB BETA7 LEVELS AND β7 RECEPTOR OCCUPANCY IN PHASE I PATIENTS WITH ULCERATIVE COLITIS

X. Wei, Y. Wang, F. Fuh, D. Sinclair, C. Looney, K. Pham, D. Danilenko, W. Mathews, S. O'Byrne, J. Visich, A. Joshi, M. Williams, M. Tang; Genentech, South San Francisco, CA.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

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A MICROTRACER STUDY OF GSK962040, A MOTILIN RECEPTOR AGONIST, TO SUPPORT DOSING REGIMENS IN THE CRITICAL CARE SETTING

L. S. Vasist Johnson,[1] M. A. Young,[1] L. A. Stevens,[2] S. J. Cozens,[3] J. Collier,[4] D. C. Robertson,[5] G. E. Dukes[1]; [1]GlaxoSmithKline, RTP, NC, [2]Quotient Bioresearch, Nottingham, United Kingdom, [3]GlaxoSmithKline, Ware, United Kingdom, [4]Quotient Bioresearch, Canterbury, United Kingdom, [5]GlaxoSmithKline, Cambridge, United Kingdom.

PII-76

IMPROVED SUCCESS IN CANDIDATE SELECTION BY EARLY ASSESSMENT OF CONCENTRATION-QTC RELATIONSHIP

P. Zuo, **L. S. Vasist Johnson**, L. J. Haberer, M. A. Young; GlaxoSmithKline, RTP, NC.

PII-77

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) IN NORMAL SUBJECTS REVEALS DIFFERENCES IN NOCTURNAL DIPPING WHEN SWITCHED BETWEEN DIFFERING NIFEDIPINE OSMOTIC DELIVERY SYSTEMS

P. T. Pollak, R. J. Herman, K. B. Zarnke; University of Calgary, Calgary, AB, Canada.

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APPLE JUICE GREATLY REDUCES PLASMA CONCENTRATIONS OF ATENOLOL

H. Jeon,[1] K. S. Lim,[1] K. Ohashi,[2] T. Kotegawa,[2] I. Ieiri,[3] J. Y. Cho,[1] S. H. Yoon,[1] S. G. Shin,[1] K. S. Yu,[1] I. J. Jang[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Departments of Clinical Pharmacology and Therapeutics, Oita University Faculty of Medicine, Oita, Japan, [3]Department of Clinical Pharmacokinetics, Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan.

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PHARMACOKINETICS AND PHARMACODYNAMICS OF A SINGLE INTRAVENOUS DOSE of HM10760A IN HEALTHY KOREAN SUBJECTS

S. Kim, S. Lee, S. Yoon, K. S. Lim, S. G. Shin, K. S. Yu, I. J. Jang; Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PII-80

PREDICTION OF LONG-TERM (48 WEEKS) HCV TREATMENT OUTCOMES, USING POPULATION PHARMACOKINETIC-PHARMACODYNAMIC/VIRAL DYNAMIC MODEL DEVELOPED FROM A TWO WEEK CLINICAL DATA

T. Kim,[1] J. Kim[2]; [1]University of North Carolina-Chapel Hill, Chapel Hill, NC, [2]Clinical Pharmacology Modeling and Simulation, GlaxoSmithKline, Research Triangle Park, NC.

PII-81

NONLINEAR PHARMACOKINETICS AND CLINICAL IMPLICATIONS OF BLOOD-BRAIN EQUILIBRATION HALF-TIME OF PROPOFOL

Y. Kim,[1] H. Yoon,[2] B. Choi,[3] G. Noh[4]; [1]Department of Clinical Pharmacology and Therapeutics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of, [2]Department of Anesthesiology and Pain Medicine, Chungnam National University College of Medicine, Daejeon, Korea, Republic of, [3]Department of Anesthesiology and Pain Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of, [4]Department of Clinical Pharmacology and Therapeutics, Department of Anesthesiology and Pain Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea.

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DISEASE PROGRESSION MODELING OF INFLAMMATORY LESION COUNTS (LES) IN ACNE VULGARIS

R. P. Singh,[1] M. D. Sahre,[2] H. Derendorf,[1] V. D. Schmith[3]; [1]University of Florida, Gainesville, FL, [2]Food and Drug Administration, Silver Spring, MD, [3]GlaxoSmithKline, RTP, NC.

POSTER SESSION II

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PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

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MODELING OF INVESTIGATIVE STATIC GLOBAL ASSESSMENT SCORE (ISGA) IN ACNE VULGARIS

R. P. Singh,[1] M. D. Sahre,[2] H. Derendorf,[1] V. D. Schmith[3]; [1]University of Florida, Gainesville, FL, [2]Food and Drug Administration, Silver Spring, MD, [3]GlaxoSmithKline, RTP, NC.

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POPULATION PHARMACOKINETIC MODELING OF S-AMLODIPINE IN HEALTHY MALE SUBJECTS

J. Lee,[1] S. Park,[1] S. Seong,[1] S. Han,[2] M. Lim,[3] J. Park,[1] J. Seo,[1] H. Lee,[1] Y. Yoon[1]; [1]Kyungpook National University Hospital Clinical Trial Center, DAEGU, Korea, Republic of, [2]Department of Pharmacology, College of Medicine, the Catholic University of Korea, Seoul, Korea, Republic of, [3]Kyungpook National University Hospital Clinical Trial Center, DAEGU, Republic of Korea.

PII-85

THE SAFETY AND PHARMACOKINETICS OF REVAPRAZAN IN COMBINATION WITH ITOPRIDE COMPARED TO RESPECTIVE MONOTHERAPIES IN HEALTHY VOLUNTEERS

H. Choi,[1] Y. Kim,[1] S. Jin,[1] Y. Noh,[1] M. Kim,[1] H. Sung,[1] S. Nam,[2] S. Jang,[2] K. Bae[1]; [1]Department of Clinical Pharmacology and Therapeutics, Asan Medical Center and University of Ulsan College of Medicine, Seoul, Korea, Republic of, [2]Yuhan Corporation, Seoul, Republic of Korea.

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THE SAFETY AND THE PHARMACOKINETIC EFFECT OF TELMISARTAN ON S-AMLODIPINE IN HEALTHY VOLUNTEERS

H. Sung, Y. Kim, S. Jin, Y. Noh, H. Choi, M. Kim, K. Bae; Department of Clinical Pharmacology and Therapeutics, Asan Medical Center and University of Ulsan College of Medicine, Seoul, Republic of Korea.

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PHARMACOKINETICS OF LACOSAMIDE IN KOREAN HEALTHY SUBJECTS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, SINGLE AND REPEATED DOSE STUDY

N. Gu,[1] B. H. Kim,[1] S. Lee,[1] T. E. Kim,[1] A. Fichtner,[2] J. Elshoff,[2] K. S. Yu,[1] I. J. Jang,[1] S. G. Shin[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine, Seoul, Korea, Republic of, [2]SCHWARZ BIOSCIENCES GmbH, UCB Group, Monheim am Rhein, Germany.

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PHARMACOKINETICS AND PHARMAODYNAMICS OF TOLVAPTAN FOLLOWING 15 MG TO 60 MG SINGLE ORAL DOSES IN HEALTHY KOREANS

H. Han, S. J. Yi, H. Jeon, K. S. Lim, K. S. Yu, I. J. Jang, S. G. Shin; Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

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INVESTIGATION OF THE ABSORPTION, METABOLISM, AND EXCRETION OF 14C-SELEXIPAG FOLLOWING ORAL ADMINISTRATION TO HEALTHY MALE SUBJECTS

P. Kaufmann,[1] K. Okubo,[2] P. N. Sidharta,[1] T. Yamada,[2] J. Dingemanse,[1] H. Mukai[2]; [1]Actelion Pharmaceuticals Ltd, Allschwil, Switzerland, [2]Nippon Shinyaku, Kyoto, Japan.

PII-90

DRUG-DRUG INTERACTION (DDI) RISK MANAGEMENT IN CLINICAL DEVELOPMENT OF THE INVESTIGATIONAL AGENT IXAZOMIB CITRATE (IC) AND DESIGN OF A DDI STUDY WITH KETOCONAZOLE (KC): APPLICATION OF PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PB-PK) MODEL BASED SIMULATIONS

N. Gupta, C. Lu, K. Venkatakrishnan; Millennium Pharmaceuticals, Inc., Cambridge, MA.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

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A PHASE 1 STUDY OF SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF TAK-701, AN INVESTIGATIONAL HUMANIZED ANTI-HEPATOCYTE GROWTH FACTOR (HGF) MONOCLONAL ANTIBODY, IN PATIENTS WITH ADVANCED NONHEMATOLOGIC MALIGNANCIES

N. Gupta, D. Noe, Y. Liu, T. Wyant, J. Gomez Navarro; Millennium Pharmaceuticals, Inc., Cambridge, MA.

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SWITCH FROM BSA-BASED DOSING TO FIXED DOSING FOR THE INVESTIGATIONAL DRUG IXAZOMIB CITRATE (IC): APPLICATION OF MODELING AND SIMULATION TO INFLUENCE POSOLOGY DECISIONS IN ONCOLOGY DRUG DEVELOPMENT

N. Gupta, M. Saleh, K. Venkatakrishnan; Millennium Pharmaceuticals, Inc., Cambridge, MA.

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MIXED-EFFECT CIRCADIAN RHYTHM MODEL FOR HUMAN ERYTHROCYTE ACETYLCHOLINESTERASE ACTIVITY - APPLICATION TO THE PROOF OF CONCEPT OF CHOLINESTERASE INHIBITION BY ACORN EXTRACT IN HEALTHY SUBJECTS WITH GALANTAMINE AS POSITIVE CONTROL

S. Han, J. Lee, S. Jeon, T. Hong, D. Yim; The Catholic University of Korea, Seoul, Republic of Korea.

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POPULATION PHARMACOKINETICS OF PROTHIONAMIDE IN KOREAN PATIENTS

S. Seong, J. Lee, S. Park, M. Lim, J. Park, J. Seo, H. Lee, Y. Yoon; Kyungpook National University Hospital Clinical Trial Center, Daegu, Republic of Korea.

SPECIAL POPULATIONS (SPO)

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INOSINE MONOPHOSPHATE DEHYDROGENASE (IMPDH) GENE AND PROTEIN EXPRESSION AND ACTIVITY IS MARKEDLY LOWER IN KIDNEY TRANSPLANT RECIPIENTS WITH DIABETES MELLITUS

M. Dostalek,[1] R. Y. Gohh,[2] **F. Akhlaghi**[1]; [1]University of Rhode Island, Kingston, RI, [2]Brown University Medical School, Rhode Island Hospital, Providence, RI.

PII-96

DIABETES MELLITUS REDUCES THE CLEARANCE OF ATORVASTATIN-LACTONE: THE RESULTS OF A POPULATION PHARMACOKINETIC ANALYSIS AND *EX VIVO* STUDIES USING LIVERS FROM DIABETIC DONORS

M. Dostalek, W. Sam, **F. Akhlaghi**; University of Rhode Island, Kingston, RI.

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QUALITY OF REPORTING IN STUDIES OF DRUG EXCRETION INTO HUMAN MILK.

W. Chandranipapongse, S. Ito; The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada.

SPECIAL POPULATIONS (SPO)

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ACETAMINOPHEN PROTEIN ADDUCTS IN HOSPITALIZED CHILDREN RECEIVING ACETAMINOPHEN

L. P. James,[1] L. Letzig,[1] D. W. Roberts,[1] J. E. Sullivan,[1] K. Yan,[2] P. M. Simpson[2]; [1]Arkansas Children's Hospital Research Institute, Little Rock, AR, [2]Medical College of Wisconsin, Milwaukee, WI.

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SINGLE-CENTER PHASE I STUDY OF THE SINGLE- AND MULTIPLE-DOSE PHARMACOKINETICS AND SAFETY OF AZILSARTAN MEDOXOMIL (AZL-M) IN HEPATIC IMPAIRMENT

R. Preston,[1] A. Karim,[2] D. Garg,[3] Z. Zhao,[4] C. Dudkowski[4]; [1]Miller School of Medicine, University of Miami, Miami, FL, [2]AzK Consulting, Skokie, IL, [3]Clinical Research Services, Boynton Beach, FL, [4]Takeda Global Research and Development, Deerfield, IL.

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A COMPARISON OF THE COCKCROFT-GAULT AND THE MODIFICATION OF DIET IN RENAL DISEASE STUDY EQUATIONS AS PREDICTIVE MODELS OF CLINICAL OUTCOMES WITH EPTIFIBATIDE

E. Park, T. Dong, V. Crentsil, J. Zhang, **N. N. Xu**; FDA/CDER, Silver Spring, MD.

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IMATINIB FOR PULMONARY HYPERTENSION IN NEONATES WITH CONGENITAL DIAPHRAGMATIC HERNIA - DOES IT MAKE SENSE?

S. N. de Wildt, M. Koninckx, U. Kraemer, E. A. Buijs, I. Reiss, D. Tibboel; Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands.

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WITHDRAWN

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PHYSIOLOGICALLY BASED PHARMACOKINETIC EXPOSURE MODELING OF SELECTED DRUGS IN PREGNANT VS. NON-PREGNANT POPULATION

C. Nanavati,[1] B. Xia,[2] T. Heimbach,[2] H. He[2]; [1]Department of Pharmaceutical Sciences, University at Buffalo, State University of New York, Buffalo, NY, [2]Novartis Institute for Biomedical Research, East Hanover, NJ.

PII-104

MALARIA INFECTION AND ITS IMPACT ON DRUG-DISPOSITION MECHANISMS IN PREGNANCY

A. M. Cressman,[1] K. L. Silver,[2] K. C. Kain,[2] M. Piquette-Miller[3]; [1]University of Toronto, Department of Pharmacology and Toxicology, Toronto, ON, Canada, [2]University of Toronto, McLaughlin-Rotman Centre for Global Health, Toronto, ON, Canada, [3]University of Toronto, Leslie Dan Faculty of Pharmacy, Toronto, ON, Canada.

PII-105

MODEL-BASED ANALYSIS AND SIMULATION OF IMATINIB (GLEEVEC/GLIVEC) PEDIATRIC DATA (2-18 YEARS OF AGE) TO SUPPORT BSA NORMALIZED DOSING REGIMEN

G. D. Dai, T. Sing, W. Sallas, O. Chiparus, K. Gillis, S. Novick, Y. Wang; Novartis Oncology, East Hanover, NJ.

SPECIAL POPULATIONS (SPO)

PII-106

REPEATED-DOSE PHARMACOKINETICS OF INTRAVENOUS ITRACONAZOLE IN PEDIATRIC CANCER PATIENTS

D. Shin,[1] H. Kim,[2] H. Kang,[2] S. H. Yoon,[1] J. Y. Cho,[1] S. G. Shin,[1] K. S. Yu,[1] I. J. Jang[1]; [1]Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of, [2]Department of Pediatrics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PII-107

EFFECT OF VARIOUS DEGREES OF RENAL IMPAIRMENT (RI) ON THE PHARMACOKINETICS OF RG3487 AFTER ORAL ADMINISTRATION, AND COMPARISON OF DIFFERENT METHODS TO ASSESS RENAL FUNCTION

B. Ricci,[1] C. Reid,[2] X. Liogier d'Ardhuy,[1] M. Hahn,[2] R. Robson,[3] C. Boetsch[1]; [1]F. Hoffmann-LaRoche AG, Basel, Switzerland, [2]Roche Products Limited, Welwyn Garden City, United Kingdom, [3]CCST, Christchurch, New Zealand.

PII-108

COMPARISON OF CLINICAL CHARACTERISTICS AND OUTCOMES OF PATIENTS ON CLOZAPINE AND LONG ACTING ANTIPSYCHOTICS

D. Durand, R. Caceda; University of Miami School of Medicine, Miami, FL.

TEACHING CLINICAL PHARMACOLOGY (TEA)

PII-109

EFFECTS OF THREE DIFFERENT UP-TITRATION REGIMENS OF PONESIMOD, A SELECTIVE S1P1 RECEPTOR AGONIST, ON HEART RATE

P. Brossard,[1] D. D'Ambrosio,[1] I. Murat,[2] J. Dingemanse[1]; [1]Actelion Pharmaceuticals Ltd, Allschwil, Switzerland, [2]Parexel International, Berlin, Germany.

PII-110

ASCENDING MULTIPLE-DOSE STUDY WITH PONESIMOD, A SELECTIVE S1P1 RECEPTOR AGONIST: TOLERABILITY, SAFETY, PHARMACOKINETICS, AND PHARMACODYNAMICS

P. Brossard,[1] H. Maatouk,[2] A. Halabi,[3] J. Dingemanse[1]; [1]Actelion Pharmaceuticals Ltd, Allschwil, Switzerland, [2]CRS Clinical Research Services Kiel GmbH, Kiel, Germany, [3]CRS Clinical Research Services Kiel GmbH, Kiel, Germany.

PII-111

ASCENDING SINGLE-DOSE STUDY WITH PONESIMOD, A SELECTIVE S1P1 RECEPTOR AGONIST: SAFETY, PHARMACOKINETICS, PHARMACODYNAMICS, AND MODELING

P. Brossard,[1] A. Halabi,[2] H. Derendorf,[3] J. Dingemanse[1]; [1]Actelion Pharmaceuticals Ltd, Allschwil, Switzerland, [2]CRS Clinical Research Services Kiel GmbH, Kiel, Germany, [3]University of Florida, Gainesville, FL.

POSTER SESSION III

PRINCE GEORGE'S EXHIBIT HALL C ★ Saturday, March 17 | 7:00am-12:30pm | Attended Poster 7:00am-8:00am

DRUG DEVELOPMENT AND REGULATORY SCIENCES (DDR)

PIII-1

PHARMACOKINETICS AND EXPOSURE-EFFICACY RELATIONSHIP OF TRASTUZUMAB EMTANSINE (T-DM1) IN PATIENTS WITH HER2-POSITIVE METASTATIC BREAST CANCER WHO HAVE NOT RECEIVED PRIOR CHEMOTHERAPY FOR METASTATIC DISEASE

B. Wang,[1] G. Bianchi,[2] S. Hurvitz,[3] J. Kocsis,[4] O. Saad,[1] J. Yi,[1] M. Gupta,[1] E. Guardino,[1] C. Song,[1] S. Girish[1]; [1]Genentech, Inc, South San Francisco, CA, [2]Istituto Nazionale, Milan, Italy, [3]UCLA Jonsson Comprehensive Cancer Center and Translational Oncology Research International, Los Angeles, CA, [4]Semmelweis University Hospital, Budapest, Hungary.

PIII-2

COMPARISON OF INCLUSION OF WOMEN IN EARLY VERSUS LATE PHASE CLINICAL TRIALS IN NEW DRUG AND BIOLOGICS APPLICATIONS RECENTLY APPROVED BY THE US FDA

L. W. Chinn, R. Poon, E. O. Fadiran, A. Parekh, S. Huang, L. Zhang; FDA, Silver Spring, MD.

PIII-3

EXPLORING ADDITIONAL CUT-OFF CRITERIA IN THE P-GP DECISION TREE: THE I_{GUT} CONCEPT

S. Agarwal, V. Arya, L. Zhang; FDA, Silver Spring, MD.

PIII-4

SURVEY OF THE PRESENTATION OF SEX ANALYSIS IN THE FDA REVIEW OF EFFICACY AND SAFETY CLINICAL DATA OF NEW MOLECULAR ENTITY DRUGS AND BIOLOGICS APPROVED FROM 2007 TO 2009

O. Otugo, R. Poon, V. Copeland, K. Khanijow, S. Umarjee, L. Chinn, **E. O. Fadiran**, L. Zhang, A. Parekh; FDA, Silver Spring, MD.

PIII-5

CANAGLIFLOZIN, A SODIUM GLUCOSE CO-TRANSPORTER 2 [SGLT2] INHIBITOR: PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) IN SUBJECTS WITH TYPE 2 DIABETES MELLITUS (T2DM)

D. Devineni, C. R. Curtin, D. Polidori, J. Murphy, S. Rusch, P. L. Rothenberg; Johnson & Johnson Pharmaceutical Research and Development, Raritan, NJ.

PIII-6

QUALIFICATION OF DRUG-DISEASE TRIAL MODELS UNDER THE DRUG DEVELOPMENT TOOL (DDT) DRAFT GUIDANCE: CAMD EXPERIENCE

K. Romero,[1] D. Stephenson,[1] L. Hudson,[1] J. Rogers,[2] D. Polhamus,[2] K. Ito,[3] R. Qiu,[3] B. Corrigan[3]; [1]Critical Path Institute, Tucson, AZ, [2]Metrum Research Group, Tarrifville, CT, [3]Pfizer, Groton, CT.

PIII-7

POINTS TO CONSIDER IN A DRUG-DRUG INTERACTION (DDI) STUDY WITH ORAL CONTRACEPTIVES (OC)

C. Yu,[1] S. Choi,[2] L. Li,[1] D. Dave,[3] M. Kim[1]; [1]Office of Clinical Pharmacology, OTS, CDER, US Food and Drug Administration, Silver Spring, MD, [2]College of Pharmacy, University of Illinois at Chicago, Chicago, IL, [3]Office of Women's Health, OC, US Food and Drug Administration, Silver Spring, MD.

PIII-8

SAFETY, PHARMACOKINETICS (PK), AND ANTIVIRAL ACTIVITY OF RG7348, A NOVEL HEPDIRECT™ LIVER-TARGETED DOUBLE PRODRUG HEPATITIS C VIRUS (HCV) NUCLEOTIDE POLMERASE INHIBITOR

K. A. Nieforth, **P. N. Morcos**, L. Chang, B. Davies, R. Li, P. F. Smith; Roche, Nutley, NJ.

PIII-9

COMPARISON OF AN AUTOMATED QTCF ANALYSIS PLATFORM WITH SEMI-AUTOMATED QTCF ANALYSIS IN A PROBE QTCF STUDY

D. E. Gutstein, R. Liu, **D. Harris**, J. A. Wagner; Merck Research Laboratories, Rahway, NJ.

DRUG SAFETY (SAF)

PIII-10

SIX CASES OF DECREASED VALPROIC ACID SERUM CONCENTRATIONS BY INTERACTION WITH CARBAPENEM ANTIBIOTICS

M. Park, D. Shin, H. K. Han, K. S. Lim, I. J. Jang, S. G. Shin, K. S. Yu; Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea.

PIII-11

RISK FACTORS OF SEVERE THROMBOCYTOPENIA FOLLOWING INITIATION OF INTERFERON-BASED THERAPY FOR THE TREATMENT OF HEPATITIS-C AMONG PATIENTS WITH DIAGNOSED CHRONIC LIVER DISEASE

E. Lawler,[1] **A. Altincatal**,[2] K. Cho,[2] K. Grotzinger,[3] P. Wang,[4] J. Hermos,[2] D. Gagnon[2]; [1]MAVERIC, VA Cooperative Studies Program, VA Boston Healthcare System, Jamaica Plain, MA, [2]VA Boston Healthcare System, Jamaica Plain, MA, [3]GlaxoSmithKline, Philadelphia, PA, [4]GlaxoSmithKline, Philadelphia, PA.

PIII-12

SECOND GENERATION ANTIPSYCHOTICS AND RISK OF TYPE 2 DIABETES IN PUBLICLY INSURED CHILDREN AND ADOLESCENTS

T. Gerhard,[1] W. V. Bobo,[2] M. Olfson,[3] S. Crystal[1]; [1]Rutgers University, New Brunswick, NJ, [2]Vanderbilt University, Nashville, TN, [3]Columbia University, New York, NY.

PIII-13

MANY DRUGS HIGHLY ASSOCIATED WITH ANGIOEDEMA ENHANCE NITRIC OXIDE SIGNALING

K. Burkhart; FDA, Silver Spring, MD.

PIII-14

RISK OF PPHN IN NEWBORNS WITH MOTHERS EXPOSED TO SSRIS IN PREGNANCY: A META-ANALYSIS

G. W. Jong,[1] A. Einarson,[1] G. Koren,[1] T. Einarson[2]; [1]Hospital for Sick Children, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada.

PIII-15

LONG-TERM NEURODEVELOPMENT OF CHILDREN EXPOSED TO ABOVE MANUFACTURER RECOMMENDED DOSES OF DOXYLAMINE/PYRIDOXINE IN UTERO

N. Carey, G. Koren, I. Nulman; Hospital for Sick Children, Toronto, ON, Canada.

PIII-16

NITROUS OXIDE ANESTHESIA AND PLASMA HOMOCYSTEINE IN CHILDREN

P. Nagele, D. Tallchief, J. Blood, A. Sharma, E. D. Kharasch; Washington University, St. Louis, MO.

PIII-17

ACQUIRED LONG QT SYNDROME IN THE PERIOPERATIVE PERIOD

P. Nagele, J. Johnston, F. Brown; Washington University, St. Louis, MO.

INFECTIOUS DISEASES (INF)

PIII-18

INTRAPULMONARY PHARMACOKINETICS OF LANINAMIVIR AFTER A SINGLE INHALED ADMINISTRATION OF LANINAMIVIR OCTANOATE IN HEALTHY VOLUNTEERS

H. Ishizuka,[1] K. Toyama,[1] S. Yoshiba,[1] H. Okabe,[1] H. Furuie[2]; [1]DaiichiSankyo Co., Ltd., Tokyo, Japan, [2]Osaka Pharmacology Clinical Research Hospital, Osaka, Japan.

PIII-19

US UTILIZATION PATTERNS OF INFLUENZA ANTIVIRAL MEDICATIONS DURING THE 2009 H1N1 INFLUENZA PANDEMIC

V. Borders-Hemphill, A. D. Mosholder; FDA, Silver Spring, MD.

PIII-20

PHARMACOKINETIC AND PHARMACODYNAMIC ANALYSIS OF EFAVIRENZ DOSE REDUCTION USING A PHYSIOLOGICALLY-BASED DYNAMIC MODEL

M. Siccardi,[1] L. Almond,[2] A. Schipani,[1] C. Csajka,[3] C. Marzolini,[4] D. Edwards,[2] S. Khoo,[1] A. Owen,[1] D. Back[1]; [1]University of Liverpool, Liverpool, United Kingdom, [2]Simcyp Limited, Sheffield, United Kingdom, [3]University Hospital and University of Lausanne, Department of Clinical Pharmacology and Toxicology, Lausanne, Switzerland, [4]Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, Basel, Switzerland.

PIII-21

INTRAVENOUS INFUSIONS OF TIGECYCLINE (TIG) DO NOT PROLONG QTC INTERVALS IN HEALTHY SUBJECTS

J. M. Korth-Bradley,[1] P. C. McGovern,[1] J. Salageanu,[2] K. Matschke,[1] A. Plotka,[1] S. Pawlak[3]; [1]Pfizer Inc., Collegeville, PA, [2]Pfizer Inc., Groton, CT, [3]Pfizer Inc., New Haven, CT.

PIII-22

FENOFIBRATE MODULATES THE EXPRESSION OF THE CCR5 RECEPTOR IN CD4+T CELLS: POTENTIAL IMPLICATIONS FOR HIV

B. K. Odeniyi, R. A. Farris, A. J. Stolarz, C. A. Wiley, E. T. Price; University of Arkansas for Medical Sciences, Little Rock, AR.

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PIII-23

CAN THE OLD DRUG DEBRISOQUINE HELP US LEARN NEW PHARMACOGENETICS TRICKS?: DEBRISOQUINE AS A SUBSTRATE OF THE ORGANIC CATION TRANSPORTER OCT1

A. R. Saadatmand, S. Tadjerpisheh, J. Brockmller, **M. V. Tzvetkov**; University of Goettingen, Goettingen, Germany.

PIII-24

MORPHINE IS A SUBSTRATE OF THE ORGANIC CATION TRANSPORTER OCT1 AND POLYMORPHISMS IN THE OCT1 GENE AFFECT MORPHINE PHARMACOKINETICS

M. V. Tzvetkov,[1] J. C. Stingl,[2] J. Brockmoller[1]; [1]University of Goettingen, Goettingen, Germany, [2]University of Ulm, Ulm, Germany.

PIII-25

INFLUENCE OF THE CYP2C8*3 POLYMORPHISM ON THE DRUG-DRUG INTERACTION BETWEEN GEMFIBROZIL AND PIOGLITAZONE

C. Aquilante,[1] L. Kosmiski,[1] D. Bourne,[2] E. Daily,[1] C. Hopley,[1] R. Kadam,[1] A. Kanack,[1] U. Kompella,[1] M. Le,[1] J. Predhomme,[1] J. Rower,[1] M. Sidhom[1]; [1]University of Colorado Denver, Aurora, CO, [2]University of Oklahoma, Oklahoma City, OK.

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PIII-26

EFFECTS OF TESTOSTERONE AND 17β-OESTRADIOL ON EXPRESSION OF THE G PROTEIN-COUPLED RECEPTOR P2Y12 IN HUMAN MEGAKARYOCYTES

E. Kim,[1] S. Lee,[2] J. Kwon,[2] S. Cho,[2] Y. B. Jarrar,[2] J. Shin[3]; [1]Department of Clinical Pharmacology Busanpaik Hospital, Busan, Korea, Republic of, [2]Department of Pharmacology and Pharmacogenomics Research Center, Busan, Korea, Republic of, [3]Inje University College of Medicine, Busan, Republic of Korea.

PIII-27

WITHDRAWN

PIII-28

THE EFFECT OF *UGT1A1* POLYMORPHISM ON ATORVASTAIN PHARMACOKINECTICS AND RESPONSE OF TOTAL CHOLESTEROL AND LDL CHOLESTEROL

S. Cho, K. Park, J. Chung; Brain Korea 21 Project Medical Science, Yonsei University; Department of Pharmacology, Yonsei University, Seoul, Republic of Korea.

PIII-29

A PROSPECTIVE STUDY OF HLA-B*5801 GENOTYPING FOR THE PREVENTION OF ALLOPURINOL INDUCED SEVERE CUTANEOUS ADVERSE REACTIONS

M. Lee, Y. Chen, C. Shen; Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan.

PIII-30

A NEW FUNCTIONAL *CYP3A4* POLYMORPHISM (*CYP3A4*22*) IS ASSOCIATED WITH INCREASED RISK OF DELAYED GRAFT FUNCTION AND WORSE RENAL FUNCTION IN CYCLOSPORIN-TREATED KIDNEY TRANSPLANT RECIPIENTS

L. Elens,[1] R. Bouarmar,[2] D. A. Hesselink,[3] V. Haufroid,[4] T. van Gelder,[3] R. H. van Schaik[1]; [1]Erasmus Medical Center, Department of Clinical Chemistry, Rotterdam, Netherlands, [2]Erasmus Medical Center, Department of Hospital Pharmacy, Rotterdam, Netherlands, [3]Erasmus Medical Center, Department of Internal Medicine, Rotterdam, Netherlands, [4]Louvain Centre for Toxicology and Applied Pharmacology, Universit Catholique de Louvain, Brussels, Belgium.

PIII-31

THE NEW *CYP3A4* INTRON 6 POLYMORPHISM (*CYP3A4*22*) IS SIGNIFICANTLY ASSOCIATED WITH DECREASED TACROLIMUS METABOLISM

R. H. van Schaik,[1] L. Elens,[1] R. Bouamar,[1] D. A. Hesselink,[1] V. Haufroid,[2] T. van Gelder[1]; [1]Erasmus University Medical Center, Rotterdam, Netherlands, [2]Cliniques Universitaires Saint-Luc, Bruxelles, Belgium.

PIII-32

WITHDRAWN

PIII-33

ABCB1 GENE EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS IN AFRICAN AMERICAN AND CAUCASIAN RENAL TRANSPLANT RECIPIENTS

K. M. Tornatore,[1] D. Brazeau,[1] A. Gundroo,[2] V. Gray,[3] R. C. Venuto[4]; [1]School of Pharmacy, Buffalo, NY, [2]School of Medicine, Buffalo, NY, [3]Erie County Medical Center, Buffalo, NY, [4]School of Medicine, University at Buffalo; Buffalo, NY.

POSTER SESSION III

PRINCE GEORGE'S EXHIBIT HALL C ★ Saturday, March 17 | 7:00am-12:30pm | Attended Poster 7:00am-8:00am

MOLECULAR PHARMACOLOGY AND PHARMACOGENETICS (MOL)

PIII-34

BIOINFORMATIC DISCOVERY AND LABORATORY VALIDATION OF THE ANTIESTROGENIC PROPERTIES OF PHENAZOPYRIDINE IN BREAST CANCER CELLS

S. Philips, N. Mokraoui, L. Li, **T. C. Skaar**; Indiana University, Indianapolis, IN.

PIII-35

GLOBAL ANALYSIS OF RIFAMPIN-REGULATED MRNA AND MIRNA GENE EXPRESSION IN PRIMARY HUMAN HEPATOCYTES

A. Ramamoorthy,[1] Y. Liu,[1] C. Goswami,[1] S. Philips,[1] A. Gaedigk,[2] D. A. Flockhart,[1] Z. Desta,[1] **T. C. Skaar**[1]; [1]Indiana University, Indianapolis, IN, [2]Children's Mercy Hospital, Kansas City, MO.

PIII-36

IMPLICATIONS OF PLASMA PROTEIN BINDING FOR PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) OF THE γ-SECRETASE INHIBITOR RO4929097 (RO)

J. Wu, P. LoRusso, L. H. Matherly, **J. Li**; Karmanos Cancer Institute, Detroit, MI.

PIII-37

INHIBITION ACTIVITY OF WARFARIN ENANTIOMER ON VITAMIN K1 AND K2 EPOXIDES METABOLISM

T. Araki, M. Kawano, T. Nakamura, K. Yamamoto; Department of Clinical Pharmacology, Gunma University Graduate School of Medicine, Maebashi, Japan.

PIII-38

THE EFFECTS OF *OPRM1* c.118A>G POLYMORPHISM ON THE PHARMACODYAMICS OF BUPRENORPHINE IN HUMANS

H. Imai, M. Morita, T. Morimoto, Y. Suzaki, T. Oyama, T. Kotegawa, K. Ohashi; Oita University, Yufu-city, Oita, Japan.

PIII-39

MIRNA EXPRESSION IN FOCAL AND NON-FOCAL BRAIN TISSUE OF THERAPY-RESISTANT EPILEPSY PATIENTS

S. Haenisch,[1] A. Chhibber,[2] I. Cascorbi,[1] D. L. Kroetz[2]; [1]University Hospital Schleswig-Holstein, Kiel, Institute of Experimental and Clinical Pharmacology, Kiel, Germany, [2]School of Pharmacy, Department of Bioengineering and Therapeutic Sciences, University of California, San Francisco, San Francisco, CA.

PIII-40

GENETIC VARIATIONS OF *SLC28A1* GENE IN A KOREAN POPULATION AND HAPLOTYOE-BASED FUNCTIONAL CHARACTERIZATION OF *SLC28A1* VARIANTS

H. Shin,[1] **J. Ghim**,[2] I. Song,[1] H. Jung,[1] M. Kim,[1] S. Lee,[1] J. Shin[1]; [1]Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of, [2]Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Republic of Korea.

ONCOLOGY (ONC)

PIII-41

BUDESONIDE DOES NOT AFFECT THE PLASMA EXPOSURE OF CABAZITAXEL IN CASTRATE RESISTANT PROSTATE CANCER PATIENTS

A. M. de Graan,[1] A. J. Nieuweboer,[1] W. J. Loos,[1] H. J. Meulenbeld,[1] F. A. Eskens,[1] M. P. Huls,[2] J. Verweij,[1] E. A. Wiemer,[1] R. de Wit,[1] R. H. Mathijssen[1]; [1]Erasmus Medical Center Rotterdam, Rotterdam, Netherlands, [2]Sanofi The Netherlands, Gouda, Rotterdam, Netherlands.

PIII-42

PREVALENCE OF ACID-REDUCING AGENTS IN CANCER (CA) POPULATIONS: AN EPIDEMIOLOGICAL PERSPECTIVE TO PREDICT DRUG-DRUG INTERACTION (DDI) POTENTIAL OF ORALLY ADMINISTERED pH-DEPENDENT CANCER THERAPEUTICS

G. S. Smelick,[1] D. A. West,[1] L. K. Chu,[1] S. L. DuVall,[2] S. N. Holden,[1] A. R. Frymoyer,[3] L. Z. Benet,[3] M. J. Dresser,[1] J. A. Ware[1]; [1]Genentech, South San Francisco, CA, [2]University of Utah, Salt Lake City, UT, [3]UCSF, San Francisco, CA.

PIII-43

GENETIC VARIATION AND CHEMOTHERAPY RESPONSE IN LYMPHOMA PATIENTS

R. Al Ejielat, E. A. Chrischilles, N. L. Denburg, B. K. Link, B. Smith, M. M. West, S. Eddy, N. J. Rudzianski, D. J. Murry; University of Iowa, Iowa City, IA.

PIII-44

ASSESSMENT OF DRUG INTERACTION POTENTIAL OF AN ANTIBODY DRUG CONJUGATE WITH OTHER THERAPEUTIC AGENTS: CASE STUDIES OF TRASTUZUMAB EMTANSINE (T-DM1) IN COMBINATION WITH PERTUZUMAB OR TAXANES

D. Lu,[1] A. Joshi,[1] P. Agarwal,[1] B. Wang,[1] P. LoRusso,[2] M. Martin,[3] F. Branle,[4] B. Althaus,[1] T. Shih,[1] S. Girish[1]; [1]Genentech, Inc, South San Francisco, CA, [2]Karmanos Cancer Institute, Detroit, MI, [3]Hospital General Universitario Gregorio Maran, Madrid, Spain, [4]F. Hoffmann-La Roche, Basel, Switzerland.

ORGAN SPECIFIC DISEASES (OSD)

PIII-45

FENOFIBRATE ATTENUATES INTERLEUKIN-1B-STIMULATED INFLAMMATORY CHEMOKINE PRODUCTION IN SMALL AIRWAY EPITHELIAL CELLS

A. J. Stolarz, R. A. Farris, C. Obrien, E. T. Price; University of Arkansas for Medical Sciences, Little Rock, AR.

PIII-46

WHAT HAPPENS TO LEVELS OF ONCE-DAILY ANTIEPILEPTIC (AED) FORMULATIONS FOLLOWING A MISSED DOSE?

D. K. Naritoku,[1] S. M. Belknap[2]; [1]Departments of Neurology and Pharmacology, University of South Alabama, Mobile, AL, [2]Departments of Dermatology and Internal Medicine, Northwestern University, Chicago, IL.

PIII-47

VERAPAMIL AND ATENOLOL HAVE DISPARATE EFFECTS ON ENA-78 PRODUCTION IN HUMAN MICROVASCULAR ENDOTHELIAL CELLS OF CARDIAC ORIGIN (HMVEC-C)

R. A. Farris, C. A. Wiley, E. T. Price; University of Arkansas for Medical Sciences, Little Rock, AR.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PIII-48

EFFECT OF FOOD ON VX-809 PHARMACOKINETICS IN HEALTHY AND CYSTIC FIBROSIS SUBJECTS AFTER SINGLE ORAL DOSING OF VX-809

H. Lu,[1] J. Zha,[1] Y. Cui,[1] K. Yen,[1] E. Rietschel,[2] R. Fischer,[3] **L. Vernillet**[1]; [1]Vertex Pharmaceuticals Incorporated, Cambridge, MA, [2]CF Center Cologne, Universitatskinderklinik, Koln, Germany, [3]Klinikum der Universitat Munchen, Munchen, Germany.

PIII-49

POPULATION PHARMACOKINETICS OF GENTAMICIN: THE IMPACT OF FRAILTY AND IMPLICATIONS FOR DOSING

C. F. Johnston,[1] S. N. Hilmer,[1] A. J. McLachlan,[2] C. M. Kirkpatrick[3]; [1]University of Sydney/Royal North Shore Hospital, Sydney, Australia, [2]University of Sydney/Centre for Education and Research on Aging, Sydney, Australia, [3]Centre for Medicine Use and Safety, Monash University, Melbourne, Australia.

PIII-50

PHARMACOKINETICS OF SINGLE AND MULTIPLE DOSES OF MOGUISTEINE IN HEALTHY CHINESE VOLUNTEERS

Z. Gou, J. Xiang, P. Feng; Institute of Drug Clinical Trial, West China Hospital, Sichuan University, Chengdu, Sichuan, P.R. Ch, Chengdu, China.

PIII-51

AFFINITY OF THE BLADDER SPASMOLYTIC TROSPIUM CHLORIDE TO DRUG TRANSPORT PROTEINS

M. Keiser,[1] T. Graf,[1] U. Schwantes,[2] W. Siegmund[1]; [1]Ernst-Moritz-Arndt-University of Greifswald, Greifswald, Germany, [2]Dr. R. Pfleger GmbH, Bamberg, Germany.

PIII-52

EFFECT OF CILOSTAZOL ON THE PHARMACOKINETICS OF SIMVASTATIN IN HEALTHY VOLUNTEERS

J. Ko,[1] J. Jung,[1] T. Kim,[1] D. Kim,[2] S. Kim,[1] J. Kim,[1] J. Ha,[2] M. Kim,[2] S. Lee,[1] W. Huh,[1] J. Shin[3]; [1]Department of Clinical Pharmacolgy and Therapeutics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of, [2]Department of Pharmacology and Pharmacogenomics Research Center, Inje University College of Medicine, Busan, Korea, Republic of, [3]Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Republic of Korea.

PIII-53

PHARMACOKINETIC COMPARISON OF THE MALEATE AND FREEBASE FORMULATIONS OF LB80380 IN HEALTHY MALE VOLUNTEERS

J. Kim, J. Jung, S. Kim, T. Kim, S. Lee, W. Huh, J. Ko; Department of Clinical Pharmacology and Therapeutics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea.

PIII-54

IMPACT OF UGT1A9 AND CYP2B6 POLYMORPHISM ON PHARMACOKINETICS OF PROPOFOL IN KOREAN PATIENTS

M. Kim,[1] S. Jin,[1] G. Noh[2]; [1]Department of Clinical Pharmacology and Therapeutics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of, [2]Department of Clinical Pharmacology and Therapeutics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Department of Anesthesiology and Pain Medicine, Asan Medical Center and University of Ulsan College of Medicine, Seoul, Republic of Korea.

PIII-55

EFFECTS OF AN ACUTE FLUID RESTRICTION ON COGNITION, MOOD, AND PHYSIOLOGICAL MARKERS OF HYDRATION

N. Pross,[1] A. Demazieres,[1] R. Barnouin,[1] A. Klein,[2] I. Guelinckx,[2] L. Le Bellego[2]; [1]Forenap, Rouffach, France, [2]Danone Research, Palaiseau, France.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PIII-56

PHARMACOKINETICS AND TOLERABILITY OF MITIGLINIDE/METFORMIN FIXED-DOSE COMBINATION TABLET COMPARED WITH CONCOMITANT ADMINISTRATION OF MITIGLINIDE AND METFORMIN IN HEALTHY MALE VOLUNTEERS

J. Jung, S. Kim, T. Kim, J. Kim, S. Lee, J. Ko, W. Huh; Department of Clinical Pharmacology and Therapeutics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea.

PIII-57

A PHARMACOKINETIC INTERACTION ASSESSMENT BETWEEN A NOVEL CYCLOPHILIN INHIBITOR ALISPORIVIR (ALV) AND A MACROLIDE ANTIBIOTIC AZITHROMYCIN (AZI) IN HEALTHY SUBJECTS

J. Ke, **A. Barve**, S. Kovacs, K. Dabovic, J. Praestgaard, J. Zhang, D. Stein, G. Sunkara; Novartis, East Hanover, NJ.

PIII-58

PHARMACOKINETICS OF SINGLE AND MULTIPLE DOSES OF PITAVASTATIN CALCIUM IN CHINESE HEALTHY VOLUNTEERS

P. Feng,[1] J. Gu,[2] Z. Luo,[1] Y. Zhang,[2] Z. Gou[1]; [1]Institute of Drug Clinical Trial, West China Hospital, Sichuan University, Chengdu, Sichuan, China, [2]Research Center for Drug Metabolism, Jilin University, Changchun, Jilin, China.

PIII-59

ASSESSMENT OF THE INDUCTION OF SYSTEMIC CLEARANCE VS. FIRST-PASS EFFECT OF MIDAZOLAM (MDZ) USING A PHYSIOLOGICALLY-BASED DYNAMIC MODEL

L. Almond,[1] K. Okialda,[2] S. Mukadam,[2] K. Rowland-Yeo,[1] I. Gardener,[1] A. Rostami-Hodjegan,[1] J. Kenny[2]; [1]Simcyp Limited, Sheffield, United Kingdom, [2]Genentech, San Francisco, CA.

PIII-60

A CLINICAL STUDY TO INVESTIGATE PHARMACOKINETICS (PK), PHARMACODYNAMICS (PD), EFFICACY, AND SAFETY OF TOCILIZUMAB (TCZ) AFTER SUBCUTANEOUS (SC) ADMINISTRATION WEEKLY (QW) OR EVERY TWO WEEKS (Q2W) IN PATIENTS (pts) WITH RHEUMATOID ARTHRITIS (RA)

X. Zhang,[1] Y. Chen,[1] S. Fettner,[1] J. Anzures-Cabrera,[2] T. Gott,[1] P. Grimsey,[2] A. Unsworth[2]; [1]Hoffmann-La Roche Inc., Nutley, NJ, [2]Roche Products Ltd., Welwyn Garden City, United Kingdom.

PIII-61

NEW aQTL SNPs FOR THE CYP2D6 IDENTIFIED BY A NOVEL MEDIATION ANALYSIS OF GENOME-WIDE SNP ARRAYS, GENE EXPRESSION ARRAYS, AND CYP2D6 ACTIVITY

G. Jiang,[1] B. Zhang,[2] Z. Desta,[3] Y. Liu,[1] A. Gaedigk,[4] T. Skaar,[3] L. Li[1]; [1]Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN, [2]Sage Bionetworks, Seattle, WA, [3]Division of Clinical Pharmacology, Indiana University School of Medicine, Indianapolis, IN, [4]University of Missouri-Kansas City, Clinical Pharmacology & Medical Toxicology, Children's Mercy Hospital and Clinics Kansas City, Kansas, MO.

PIII-62

POPULATION PHARMACOGENETIC-BASED PHARMACOKINETIC MODELING OF EFAVIRENZ AND ITS METABOLITES, 7-HYDROXY- AND 8-HYDROXYEFAVIRENZ

A. M. Abdelhady,[1] Z. Desta,[2] F. Jiang,[3] C. W. Yeo,[3] J. Shin,[3] B. R. Overholser[1]; [1]Purdue University College of Pharmacy, West Lafayette, IN, [2]Indiana University School of Medicine, Indianapolis, IN, [3]Inje University College of Medicine, Busan, Republic of Korea.

POSTER SESSION III

PRINCE GEORGE'S EXHIBIT HALL C ★ Saturday, March 17 | 7:00am-12:30pm | Attended Poster 7:00am-8:00am

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PIII-63

A COMPARATIVE, RANDOMIZED, SINGLE-DOSE, 2-WAY CROSSOVER BIOAVAILABILITY STUDY OF A CLONAZEPAM ORAL SOLUTION VS. TABLETS IN HEALTHY ADULT VOLUNTEERS

N. Cardillo Marricco,[1] M. C. Bonhomme,[1] M. Di Spirito,[1] E. M. Offman,[1] K. Cassidy[2]; [1]Celerion Inc, Montreal, QC, Canada, [2]Rosemont Pharmaceuticals Ltd., Leeds, United Kingdom.

PIII-64

EFFECT OF RENAL INSUFFICIENCY ON THE PHARMACOKINETICS OF AVANAFIL, A NEW, POTENT, SELECTIVE PDE-5 INHIBITOR, IN MALE SUBJECTS

T. M. Grant,[1] M. Obaidi,[1] P. Chai,[1] D. J. Katzer,[1] E. M. Offman,[2] A. Spivack,[3] S. Yee[3]; [1]Celerion, Lincoln, NE, [2]Celerion, Montreal, QC, Canada, [3]Vivus, Inc., Mountain View, CA.

PIII-65

PREDICTION OF THE IMPACT OF P-GP-MEDIATED EFFLUX ON THE DOSE PROPORTIONALITY OF DIGOXIN BIOAVAILABILITY

S. Neuhoff,[1] **K. Rowland Yeo**,[1] M. Jamei,[1] A. Rostami Hodjegan[2]; [1]Simcyp Ltd, Sheffield, United Kingdom, [2]Centre for Applied Pharmacokinetic Research, The School of Pharmacy and Pharmaceutical Sciences, The University of Manchester, Manchester, United Kingdom.

PIII-66

THE VALUE OF EVIDENCE SYNTHESIS: MODEL-BASED META-ANALYSIS BASED ON THE CAMD DATABASE, THE ADNI AD COHORT, AND LITERATURE META-DATA

J. A. Rogers,[1] D. Polhamus,[1] K. Ito,[2] K. Romero,[3] R. Qiu,[2] B. Gillespie,[1] B. Corrigan[2]; [1]Metrum Research Group, Tariffville, CT, [2]Pfizer, Groton, CT, [3]Critical Path Institute, Tucson, AZ.

PIII-67

DEVELOPMENT OF POPULATION PHARMACOKINETIC MODEL OF VANCOMYCIN USING SINGLE TROUGH COLLECTED DURING ROUTINE THERAPEUTIC DRUG MONITORING

A. Chaturvedula, N. Metzger, M. Fossler, M. Jann; Mercer University, Atlanta, GA.

PIII-68

COMPARISON OF PHARMACOKINETICS OF SARPOGRELATE AND ITS METABOLITE BETWEEN CONTROLLED-RELEASE FORMULATION AND IMMEDIATE-RELEASE FORMULATION

T. Kim,[1] J. Kim,[1] S. Kim,[1] J. Jung,[1] J. Lee,[2] H. Jun,[2] S. Lee,[1] W. Huh,[1] J. Ko[1]; [1]Department of Clinical Pharmacology and Therapeutics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of, [2]Business Development Division, DreamPharma, Seoul, Republic of Korea.

PIII-69

LACK OF EFFECT OF ABCB1 GENOTYPE ON THE DRUG-DRUG INTERACTIONS BETWEEN INDINAVIR AND VENLAFAXINE EXTENDED-RELEASE OR DESVENLAFAXINE EXTENDED-RELEASE

K. M. Momary,[1] M. Jann,[1] V. Spratlin,[1] H. Zhang,[1] D. Turner,[1] S. Penzak,[2] A. Wright,[1] C. VanDenBerg[1]; [1]Mercer University, College of Pharmacy and Health Sciences, Atlanta, GA, [2]Clinical Pharmacokinetics Laboratory, NIH, Bethesda, MD.

PIII-70

CLINICAL PHARMACOKINETICS, PHARMACODYNAMICS AND DURATION OF ACTION OF ICATIBANT

T. G. McCauley,[1] W. G. Kramer,[2] L. Fahy,[1] B. J. Bloom[1]; [1]Shire HGT, Lexington, MA, [2]Kramer Consulting LLC, North Potomac, MD.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PIII-71

A DECISION TREE FOR TISSUE: PLASMA PARTITION COEFFICIENT ALGORITHM SELECTION BASED ON PHYSICO-CHEMICAL SPACE

E. Yun, A. Edginton; University of Waterloo, Waterloo, ON, Canada.

PIII-72

WITHDRAWN

PIII-73

CHRONOTHERAPEUTIC DOSE OPTIMIZATION OF ANTI-CANCER AGENTS

C. DiLea; Bristol-Myers Squibb, Princeton, NJ.

PIII-74

A COMPARATIVE, RANDOMIZED, SINGLE-DOSE, 2-WAY CROSSOVER BIOAVAILABILITY STUDY OF A RAMIPRIL ORAL SOLUTION VS. TABLET IN HEALTHY ADULT VOLUNTEERS

M. C. Bonhomme,[1] N. Cardillo Marricco,[1] M. Di Spirito,[1] E. M. Offman,[1] S. P. Smith,[2] K. Cassidy[3]; [1]Celerion Inc, Montreal, QC, Canada, [2]Celerion Inc, Belfast, United Kingdom, [3]Rosemont Pharmaceuticals Ltd., Leeds, United Kingdom.

PIII-75

BIOAVAILABILITY OF VALSARTAN LIQUID ORAL DOSAGE FORMS

G. Sunkara,[1] G. Bende,[2] **A. Mendonza**,[3] S. Solar-Yohay,[4] S. Biswal,[2] S. Neelakantham,[5] R. Wagner,[4] M. Calder,[4] H. Smith,[1] Y. Zhang,[4] V. Jarugula[1]; [1]Novartis Institutes for Biomedical Research, East Hanover, NJ, [2]Novartis Institutes for Biomedical Research, Hyderabad, India, [3]Novartis Institutes for Biomedical Research, Cambridge, MA, [4]Novartis Pharma, East Hanover, NJ, [5]Novartis Pharma, Hyderabad, India.

PIII-76

A POPULATION PHARMACOKINETIC (PK)-PHARMACODYNAMIC (PD) MODEL DESCRIBING THE TIME COURSE OF PLATELET CHANGES IN ADVANCED SOLID TUMOR PATIENTS TREATED WITH PD 0332991

M. Shaik,[1] A. Ruiz-Garcia,[1] P. O'Dwyer,[2] P. M. LoRusso,[3] G. Schwartz,[4] S. Randolph[1]; [1]Pfizer, San Diego, CA, [2]University of Pennsylvania, Philadelphia, PA, [3]Barbara Ann Karmanos Cancer Center, Detroit, MI, [4]Memorial Sloan Kettering Cancer Center, New York, NY.

PIII-77

POPULATION PK MODELING OF IMMEDIATE-RELEASE PHENTERMINE AND MODIFIED-RELEASE TOPIRAMATE ADMINISTERED AS A FIXED-DOSE COMBINATION PRODUCT (VI-0521)

J. F. Marier,[1] N. Kassir,[1] M. S. Mouksassi,[1] N. H. Gosselin,[1] S. Yee,[2] C. Peterson,[3] W. Day[3]; [1]Pharsight, Montreal, QC, Canada, [2]Independent Consultant, Mountain View, CA, [3]Vivus, Mountain View, CA.

PIII-78

POPULATION PK/PD MODELING OF VI-0521, A FIXED-DOSE COMBINATION PRODUCT OF IMMEDIATE-RELEASE PHENTERMINE AND CONTROLLED-RELEASE TOPIRAMATE FOR THE TREATMENT OF OBESITY

J. F. Marier,[1] N. G. Gosselin,[1] M. S. Mouksassi,[1] N. Kassir,[1] S. Yee,[2] C. Peterson,[3] W. Day[3]; [1]Pharsight, Montreal, QC, Canada, [2]Independent Consultant, Mountain View, CA, [3]Vivus, Mountain View, CA.

PIII-79

EFFECT OF GEMFIBROZIL ON THE METABOLISM OF BRIVARACETAM IN HUMAN LIVER MICROSOMAL ASSAYS AND IN HUMAN SUBJECTS

A. Stockis, H. Chanteux, M. Rosa, S. Watanabe, J. Nicolas; UCB Pharma, Braine-l'Alleud, Belgium.

PIII-80

IN-VITRO CHARACTERIZATION AND INTER-SPECIES COMPARISON OF ALDEHYDE DEHYDROGENASE (ALDH) ENZYME KINETICS IN HEPATIC CYTOSOL

M. Bruce, A. Parikh, J. Venitz; Virginia Commonwealth University, Richmond, VA.

PIII-81

POPULATION PHARMACOKINETICS AND PHARMACODYNAMICS OF SALMON CALCITONIN AFTER ORAL ADMINISTRATION OF SMC021 IN HEALTHY SUBJECTS

E. Chigutsa,[1] E. Ngaimisi-Kitabi,[1] G. Sunkara,[2] L. Choi,[2] T. Bouillon,[1] **X. Jiang**[2]; [1]Novartis, Basel, Switzerland, [2]Novartis, East Hanover, NJ.

PIII-82

EFFECT OF ESOMEPRAZOLE ON THE PHARMACOKINETICS AND PHARMACODYNAMICS OF SMC021 IN HEALTHY VOLUNTEERS

L. Choi,[1] R. Sivasubramanian,[2] P. Bhad,[2] U. Junker,[3] J. Jones,[3] M. Azria[3]; [1]Novartis Institutes for Biomedical Research, East Hanover, NJ, [2]Novartis Institutes for Biomedical Research, Hyderabad, India, [3]Novartis Institutes for Biomedical Research, Basel, Switzerland.

PIII-83

PHARMACOKINETIC INTERACTION ASSESSMENT BETWEEN SMC021 AND ROSIGLITAZONE

L. Choi,[1] R. Sivasubramanian,[2] U. Junker,[3] S. Biswal,[2] J. Jones,[3] S. Machineni[2]; [1]Novartis Institutes for Biomedical Research, East Hanover, NJ, [2]Novartis Institutes for Biomedical Research, Hyderabad, India, [3]Novartis Institutes for Biomedical Research, Basel, Switzerland.

PIII-84

PHARMACOKINETIC INTERACTION ASSESSMENT BETWEEN SMC021 AND IBUPROFEN AND BETWEEN SMC021 AND ACETAMINOPHEN

L. Choi,[1] R. Sivasubramanian,[2] U. Junker,[3] S. Kamireddy,[2] J. Jones,[3] M. Azria[3]; [1]Novartis Institutes for Biomedical Research, East Hanover, NJ, [2]Novartis Institutes for Biomedical Research, Hyderabad, India, [3]Novartis Institutes for Biomedical Research, Basel, Switzerland.

PIII-85

POPULATION PHARMACOKINETIC-PHARMACODYNAMIC MODEL OF MYCOPHENOLIC ACID WITH INOSINE MONOPHOSPHATE DEHYDROGENASE ACTIVITY FOLLOWING ADMINISTRATION OF MYCOPHENOLATE MOFETIL IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

T. Fukuda, M. Dong, M. T. de Vries, S. Cox, J. Goebel, A. A. Vinks; Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

PIII-86

ETHNIC SENSITIVITY ASSESSMENT OF CANAKINUMAB PHARMACOKINETICS AND PHARMACODYNAMICS IN GOUTY ARTHRITIS PATIENTS

J. Roberts, S. Tannenbaum, G. Sunkara, A. Chakraborty; Novartis Pharmaceuticals, East Hanover, NJ.

PIII-87

CLINICAL TRIAL SIMULATIONS IN ALZHEIMER'S DISEASE: EXAMPLE APPLICATIONS OF A MODELING AND SIMULATION TOOL IN DRUG DEVELOPMENT

R. Qiu,[1] J. Rogers,[2] D. Polhamus,[2] K. Romero,[3] K. Ito,[1] B. Corrigan[1]; [1]Pfizer, Inc, Groton, CT, [2]Metrum Research Group, Tarrifville, CT, [3]Critical Path Institute, Tucson, AZ.

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PIII-88

THE EFFECT OF EVEROLIMUS (EVE) ON THE PHARMACOKINETICS (PK) OF MIDAZOLAM (MID) IN HEALTHY SUBJECTS

S. Urva,[1] E. Bouillaud,[2] R. Delaney,[3] A. Jappe,[2] W. Cheung[3]; [1]Novartis Pharmaceuticals, Florham Park, NJ, [2]Novartis Pharma AG, Basel, Switzerland, [3]Novartis Pharmaceuticals, Florham Park, NJ.

PIII-89

SKIN BLOOD FLOW (SBF) RESPONSE FOLLOWING ACUTE INTRAVENOUS (IV) ETHANOL AND ASSOCIATION WITH SUBJECTIVE RESPONSES IN SOCIAL DRINKERS

V. Vatsalya, B. Stangl, M. Zametkin, V. A. Ramchandani; NIAAA NIH, Bethesda, MD.

PIII-90

POPULATION PHARMACOKINETIC ANALYSIS OF HYDROCHLOROTHIAZIDE IN PATIENTS WITH HYPERTENSION FOLLOWING ADMINISTRATION OF HYDROCHLOROTHIAZIDE IN COMBINATION WITH VALSARTAN, OR AMLODIPINE, OR BOTH

J. Chen, X. Jiang, R. Parasrampuria, G. Sunkara, V. Jarugula; Novartis, East Hanover, NJ.

PIII-91

POPULATION MODEL BASED PREDICTIONS OF PHARMACOKINETICS FROM ALTERNATIVE FORMULATION

S. Upadhyay, J. Zack; Gilead Sciences, Foster City, CA.

PIII-92

POPULATION PHARMACOKINETICS OF DACOMITINIB (PF-00299804) IN HEALTHY VOLUNTEERS

A. Ruiz-Garcia,[1] N. Giri,[1] J. O'Connell,[2] C. L. Bello,[1] J. L. French[2]; [1]Pfizer Global R&D, San Diego, CA, [2]Pfizer Global R&D, Groton, CT.

PIII-93

POPULATION PK: SINGLE DOSE MIDAZOLAM IN OBESE CHILDREN

J. D. Vaughns,[1] A. V. Rongen,[2] J. Finkel,[1] E. Dombrowsky,[3] G. Moorthy,[3] J. Barrett,[3] J. N. van den Anker[1]; [1]Children's National Medical Center, Washington, DC, [2]University of Utrecht, Netherlands, Netherlands, [3]Children's Hospital of Philadelphia, Philadelphia, PA.

PIII-94

COMPARISON OF LAMOTRIGINE POPULATION PHARMACOKINETICS IN PREGNANT WOMEN BY TWO NON-LINEAR MIXED EFFECT MODELING SOFTWARE PRODUCTS: NONMEM® AND PHOENIXTM NLME

A. R. Polepally,[1] J. Chittenden,[2] B. J. Matzuka,[2] R. C. Brundage,[1] P. B. Pennell,[3] A. K. Birnbaum[1]; [1]Experimental and Clinical Pharmacology, University of Minnesota, Minneapolis, MN, [2]Pharsight Corporation, Cary, NC, [3]Department of Neurology at Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

PIII-95

PHARMACOKINETICS OF BENDAMUSTINE IN PATIENTS WITH BRAIN METASTASES FROM SOLID TUMORS: EVALUATION OF BENDAMUSTINE BLOOD-BRAIN BARRIER PENETRATION

L. He, J. Grecula, Y. Ling, X. Yang, M. Enzerra, J. Cotrill, M. Ammirati, K. Kendra, R. Cavaliere, E. Mrozek, B. McCracken-Bussa, L. Mayer, N. Mayr, L. Wei, M. Phelps; The Ohio State University, Columbus, OH.

PIII-96

MODEL BASED META-ANALYSIS (MBMA) OF EFFICACY ENDPOINTS FROM RANDOMIZED PHASE 2 OR PHASE 3 TRIALS FOR ADVANCED OR METASTATIC BREAST CANCER

D. Kang,[1] J. French,[2] S. Ahadieh,[2] D. Wang[1]; [1]Pfizer, San Diego, CA, [2]Pfizer, Groton, CT.

POSTER SESSION III

PRINCE GEORGE'S EXHIBIT HALL C ★ Saturday, March 17 | 7:00am-12:30pm | Attended Poster 7:00am-8:00am

PHARMACOMETRICS AND PHARMACOKINETICS (PMK)

PIII-97

ROLE OF MYOSTATIN PATHWAY IN MUSCLE GROWTH: KEY LEARNINGS FROM RETROSPECTIVE ANALYSIS OF MYO-029 PRECLINICAL AND CLINICAL DATA THRU PK/PD MODELING

P. Singh,[1] T. Gordi,[2] J. Bosley,[2] H. Rong[1]; [1]Pfizer, Andover, MA, [2]ROSA and Co. LLC, Philadelphia, PA.

PIII-98

COMPARISON OF DOSE PREDICTIONS FOR TACROLIMUS BY NON-LINEAR MIXED EFFECTS MODELING WITH NONMEN AND PHOENIX NLME

C. Passey,[1] J. Chittenden,[2] B. J. Matzuka,[2] R. C. Brundage,[1] P. A. Jacobson,[1] A. K. Birnbaum[1]; [1]Experimental and Clinical Pharmacology, University of Minnesota, Minneapolis, MN, [2]Pharsight Corporation, Cary, NC.

PIII-99

META ANALYSIS OF DAPAGLIFLOZIN PHARMACOKINETICS AND DOSE/EXPOSURE-URINARY GLUCOSE PHARMACODYNAMIC RELATIONSHIPS

S. Kasichayanula, X. Liu, M. Hesney, S. Griffen, F. LaCreta, D. Boulton; Bristol-Myers Squibb, Princeton, NJ.

PIII-100

PRELIMINARY EXPOSURE RESPONSE (ER) ANALYSIS OF CRIZOTINIB IN PATIENTS WITH ALK-POSITIVE ADVANCED NON-SMALL CELL LUNG CANCER

J. French,[1] **W. Tan**,[2] D. Kang,[2] A. Bello,[3] P. Selaru,[2] K. Wilner[2]; [1]Pfizer, Groton, CT, [2]Pfizer, San Diego, CA, [3]Pfizer, New York, NY.

PIII-101

APPLICATION OF A POPULATION PHARMACOKINETIC MODEL IN ESTIMATING ILLICIT DRUG EXPOSURE

L. Li,[1] G. P. Galloway,[1] D. Verotta,[2] T. E. Everhart,[3] M. J. Baggott,[1] J. Mendelson[1]; [1]CPMCRI, San Francisco, CA, [2]Departments of Bioengineering and Therapeutic Sciences and Epidemiology and Biostatistics, UCSF, San Francisco, CA, [3]Langley Porter Psychiatric Inst, UCSF, San Francisco, CA.

PIII-102

PHARMACOKINETIC-PHARMACODYNAMIC ANALYSIS OF PF-04995274, 5HT4 PARTIAL AGONIST, FOLLOWING SINGLE AND MULTIPLE ORAL DOSES IN HEALTHY HUMAN VOLUNTEERS

S. Duvvuri, T. Nicholas, C. Leurent, D. Raunig, A. Plotka, E. Schwam, S. Grimwood, J. Park, C. Rowinski, T. Rapp; Pfizer, Groton, CT.

SPECIAL POPULATIONS (SPO)

PIII-103

URINARY NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (UNGAL) AS A BIOMARKER FOR RENAL FUNCTION IN PEDIATRIC LIVER AND KIDNEY TRANSPLANTATION RECIPIENTS: A PILOT STUDY

V. M. Gijsen,[1] R. H. van Schaik,[2] O. P. Soldin,[3] S. J. Soldin,[3] I. Nulman,[4] G. Koren,[4] S. N. de Wildt[1]; [1]Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands, [2]Erasmus MC, Rotterdam, Netherlands, [3]Georgetown University Medical Center, Washington, DC, [4]Hospital for Sick Children, Toronto, ON, Canada.

SPECIAL POPULATIONS (SPO)

PIII-104

P450 OXIDOREDUCTASE *28 (POR*28) GENOTYPE AND TACROLIMUS DOSING REQUIREMENTS IN PEDIATRIC KIDNEY RECIPIENTS EARLY AFTER TRANSPLANTATION

V. M. Gijsen,[1] R. H. van Schaik,[2] O. P. Soldin,[3] S. J. Soldin,[3] I. Nulman,[4] G. Koren,[4] S. N. de Wildt[1]; [1]Erasmus MC Children's Hospital, Rotterdam, Netherlands, [2]Erasmus MC, Rotterdam, Netherlands, [3]Georgetown University Medical Center, Washington, DC, [4]Hospital for Sick Children, Toronto, ON, Canada.

PIII-105

ANTIPSYCHOTIC USE IN MEDICAID-INSURED YOUTH: SAFETY AND POLICY IMPLICATIONS

M. Burcu,[1] A. Ibe,[2] D. J. Safer,[3] J. M. Zito[4]; [1]Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore, MD, [2]Morgan State University, Baltimore, MD, [3]Departments of Psychiatry and Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD, [4]Departments of Pharmaceutical Health Services Research and Psychiatry, University of Maryland, Baltimore, MD.

PIII-106

WARFARIN-ANTIBIOTIC INTERACTIONS IN OLDER ADULTS OF AN OUTPATIENT ANTICOAGULATION CLINIC

P. K. Ghaswalla,[1] P. W. Slattum,[1] S. E. Harpe,[1] D. Tassone[2]; [1]Virginia Commonwealth University, Richmond, VA, [2]McGuire Veterans Affairs Medical Center, Richmond, VA.

PIII-107

CONCURRENT USE OF ALCOHOL AND CENTRAL NERVOUS SYSTEM (CNS)-ACTING MEDICATIONS AMONG OLDER ADULTS

M. Mohanty, S. E. Harpe, P. W. Slattum; Virginia Commonwealth University, Richmond, VA.

PIII-108

QUANTITATIVE ASSESSMENT OF VITAMIN D SUPPLEMENTATION ON 25-OH VITAMIN D LEVELS IN NURSING HOME RESIDENTS

S. Kshirsagar,[1] L. Kane,[2] K. Moore,[2] D. Verotta,[1] J. Schwartz[2]; [1]University of California, San Francisco, San Francisco, CA, [2]Jewish Home of San Francisco Center for Research on Aging, San Francisco, CA.

PIII-109

COMPARTMENTAL PHARMACOKINETICS (PK) OF IMMEDIATE RELEASE NIFEDIPINE (NIF) IN PREGNANCY: VARIABILITY IN ABSORPTION

A. M. Nader,[1] S. N. Caritis,[2] M. F. Hebert,[3] S. M. Clark,[4] D. A. Flockhart,[5] **S. K. Quinney**,[5] for the NICHD Obstetrical-Fetal Pharmacology Research Units (OPRU) Network; [1]Purdue University School of Pharmacy, Indianapolis, IN, [2]University of Pittsburgh School of Medicine, Pittsburgh, PA, [3]University of Washington Departments of Pharmacy and OBGYN, Seattle, WA, [4]University of Texas Medical Branch - Galveston, Galveston, TX, [5]Indiana University School of Medicine, Indianapolis, IN.

PIII-110

PHARMACOKINETICS OF ORAL 3,4-METHYLENEDIOXYAMPHETAMINE IN HUMANS

M. J. Baggott,[1] L. Li,[1] G. P. Galloway,[1] K. B. Scheidweiler,[2] A. J. Barnes,[2] M. A. Huestis,[2] J. Mendelson[1]; [1]CPMCRI, San Francisco, CA, [2]Clinical Pharmacology and Therapeutic Research Branch, NIDA Intramural, Baltimore, MD.

American Society for Clinical Pharmacology and Therapeutics (ASCPT)
and the Food and Drug Administration/Center for Drug Evaluation and Research (FDA/CDER)

DR. WILLIAM B. ABRAMS LECTURE

INTEGRATING MULTIPLE SOURCES OF INFORMATION TO UNDERSTAND DRUG ACTION:

FROM MOLECULAR STRUCTURE TO CLINICAL POPULATION DATA

DATE

MAY 23, 2012

1:30 pm – 2:30 pm

LECTURER

RUSS B. ALTMAN, MD, PHD

Professor of Bioengineering,
Genetics and Medicine
Stanford University

LOCATION

FOOD AND DRUG ADMINISTRATION

White Oak Campus
Shared Use Facility / Room 2047
10903 New Hampshire Avenue
Silver Spring, MD

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LATE-BREAKING ORAL SESSION

Saturday, March 17 | 10:50am-11:50am
MARYLAND A | Refer to page 38 for Chair information

LB-A-1

AGE-RELATED DIFFERENCES IN PLASMA AND INTRACELLULAR (IC) TENOFOVIR (TFV) CONCENTRATIONS

G. Baheti,[1] J. King,[2] E. P. Acosta,[2] C. V. Fletcher[1]; [1]University of Nebraska Medical Center, Omaha, NE, [2]The University of Alabama at Birmingham, Birmingham, AL

BACKGROUND

To use population pharmacokinetic (PK) modeling to investigate apparent differences in plasma TFV and IC TFV-diphosphate (TFV-DP) concentrations (conc) in children and adolescents compared with adults following tenofovir disoproxil fumarate (TDF) dosing.

METHODS

Data were pooled from 3 different studies in HIV-infected children, adolescents, and adults receiving TDF 300 mg daily. TFV plasma conc were measured 6-8 times and IC TFV-DP 2-3 times in each subject. Data analysis began in October, 2011. A 2-compartment model (NONMEM® 7.2) subdivided by age, allometrically scaled for children and adolescents and partitioned for slow and fast absorbers (Tmax either <2 or >2 hrs, respectively) was utilized for plasma TFV. IC conc were modeled using an indirect response model: EC50 (plasma conc producing 50% of maximum effect [Emax]); kin (0 order rate constant for TFV-DP production); kout (IC elimination rate constant); partitioned by age (>25 or <25 years). kout for adults was fixed to a previous estimate. Covariates included age, sex, weight, race, creatinine clearance (CRCL), Tanner stage (adolescents), total bilirubin, and concomitant protease inhibitor.

RESULTS

Subjects: N=102 (61 male/41 female), 88 with IC conc. Median (range) age and CRCL were: 21 (9-60) years and 128 (43.3-267.6) ml/min, respectively. In final plasma model (FOCEI), oral clearance (CL/F) was significantly faster in those < vs. > 25 years. CRCL was the most significant covariate on CL/F and central distribution volume. IC TFV-DP EC50 was 69 vs 116 ng/mL, and t1/2 (= to 0.693/kout) was 70 h vs 86 hrs for those < vs > 25 yrs; Emax was fixed at 1200 fmol/106 cells.

CONCLUSION

Children and adolescents achieve higher IC TFV-DP conc than adults despite lower plasma conc. This analysis suggests a mechanism of greater phosphorylation sensitivity (quantified as lower EC50) vs. slower IC elimination. Additional mechanistic studies are needed to understand fully the clinical pharmacology of IC TFV.

LB-A-2

PHARMACOKINETICS AND SAFETY OF METRONIDAZOLE IN PRETERM INFANTS: VALIDATION OF DRIED BLOOD SPOT SAMPLING

M. Sampson,[1] B. Bloom,[2] P. B. Smith,[1] D. K. Benjamin Jr.,[1] G. L. Kearns,[3] E. V. Capparelli,[4] M. Cohen-Wolkowiez,[1] Pediatric Trials Network; [1]Duke Clinical Research Institute, Durham, NC, [2]University of Kansas School of Medicine, Wichita, KS, [3]University of Missouri–Kansas City School of Medicine, Kansas City, MO, [4]University of California, San Diego, San Diego, CA

BACKGROUND

Metronidazole is routinely used to treat intra-abdominal infections in preterm infants. Pharmacokinetic (PK) data for this drug in this population are virtually absent. Dried blood spot (DBS) technology has the potential to enable appropriate PK studies in this population necessary to define age-appropriate dose.

METHODS

A prospective, open-label, multicenter study of 24 infants (<32 weeks gestation and 15 days postnatal age) was performed. Sparse plasma and DBS samples were obtained around the first dose, at doses 3-5, and with the last dose. Concentrations were determined by HPLC/MS/MS (LLOQ 50 ng/mL). Population nonlinear mixed effect modeling was used to analyze the PK data, and plasma vs. DBS concentration association was evaluated using linear regression techniques. Last infant was enrolled November 1, 2011, and data were subsequently analyzed.

RESULTS

24 infants (median [range] gestational age at birth 25 [23-31] weeks, postnatal age 27 [1-82] days) provided 101 plasma and 50 DBS samples for analysis. Metronidazole population PK was described by a 1-compartment model: mean clearance (CL, liter/kg/h) = 0.042 x (postnatal age/27)$^{0.45}$. Apparent volume of distribution (V) was 0.95 L/kg. The relative standard errors around CL and V estimates were 10% and 3%, respectively. The median (range) ratio of metronidazole DBS to plasma concentrations was 88% (39-112%). DBS and plasma concentrations were highly correlated (r^2 0.85, P<0.001), and no significant differences were found when metronidazole PK were calculated from plasma vs. DBS concentrations.

CONCLUSION

Metronidazole CL increased as a function of postnatal age as expected with development. DBS sampling offers an avenue to critically evaluate the PK of metronidazole and potentially other drugs in neonates and young infants.

LB-A-3

EFFECT OF THE NOVEL CYP3A4 INTRON 6 POLYMORPHISM (CYP3A4*22) AND CYP3A COMBINED GENOTYPES ON TACROLIMUS DOSING REQUIREMENTS AND BLOOD CONCENTRATIONS IN PEDIATRIC HEART TRANSPLANT RECIPIENTS

V. M. Gijsen,[1] R. H. van Schaik,[2] L. Elens,[2] S. Mital,[3] O. P. Soldin,[4] S. J. Soldin,[4] G. Koren,[3] S. N. de Wildt[1]; [1]Erasmus MC- Sophia Children's Hospital, Rotterdam, Netherlands, [2]Erasmus MC, Rotterdam, Netherlands, [3]Hospital for Sick Children, Toronto, ON, Canada, [4]Georgetown University Medical Center, Washington, DC

BACKGROUND

Both CYP3A4 and CYP3A5 are involved in the metabolism of tacrolimus, an immunosuppressant. We aimed to determine the influence of the newly recognized CYP3A4*22 polymorphism, and the CYP3A5*3 polymorphism. In addition, we clustered CYP3A4 and CYP3A5 genotypes to study the effect of clustered CYP3A genotype on tacrolimus dosing requirements in pediatric heart transplant recipients.

METHODS

Thirty-nine pediatric heart transplant recipients (median age 6.0 [IQR: 13.75] years) were included. Tacrolimus doses and trough concentrations collected in the first 14 days post-transplantation were compared between patients and correlated with CYP3A4*22 and CYP3A5*3 genotype. Clustered CYP3A genotypes were extensive metabolizers (CYP3A5*1 carriers + CYP3A4*1/*1), intermediate metabolizers (CYP3A5*3/*3 + CYP3A4*1/*1), and poor metabolizers (CYP3A5*3/*3 + CYP3A4*22 carriers). All analyses were done in November 2011.

RESULTS

CYP3A poor metabolizers had significantly lower median (day4-14) dosing requirements (0.040 [range: 0.018-0.053] mg/kg/day) compared to intermediate metabolizers (0.062 [IQR: 0.047] mg/kg/day) and extensive metabolizers (0.123 [IQR: 0.086] mg/kg/day), P = 0.001. Age and CYP3A genotype clusters were independently associated with median tacrolimus dosing requirements ($R2 = 0.507$, $p<0.0001$) and concentration/dose ratio ($R2 = 0.415$, $p<0.0001$). No significant differences in tacrolimus dosing requirements ($p = 0.062$) or trough concentrations ($p = 0.128$), and concentration/dose ratio ($p = 0.057$) were found between patients carrying at least one CYP3A4*22 allele carriers compared to CYP3A4*1/*1 patients. No relationship was found between the genetic variability and estimated glomerular filtration rate.

CONCLUSION

Despite the small sample size, this novel report shows that clustered CYP3A genotypes show promising results for further individualization of tacrolimus therapy in pediatric heart transplant patients.

LB-A-4

INTRAVENOUS PARACETAMOL REDUCES MORPHINE REQUIREMENTS IN NEONATES AND YOUNG INFANTS UNDERGOING MAJOR NON-CARDIAC SURGERY: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

I. Ceelie,[1] **S. N. de Wildt**,[1] M. van Dijk,[1] M. M. van den Berg,[1] G. E. van den Bosch,[1] H. J. Duivenvoorden,[1] T. G. de Leeuw,[1] R. A. Mathôt,[2] C. A. Knibbe,[3] D. Tibboel[1]; [1]Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands, [2]Academic Medical Center, Rotterdam, Netherlands, [3]Leiden University, Leiden, Netherlands

BACKGROUND

Continuous morphine infusion as standard postoperative analgesic therapy in neonates and infants is associated with side effects such as respiratory depression. We aimed to assess whether intermittent intravenous paracetamol administration would significantly (>30%) reduce morphine requirements.

METHODS

In this single-center prospective, randomized double-blind study, infants under the age of 1 year were randomized to receive either continuous morphine or intermittent intravenous paracetamol after major surgery. Infants in both study groups received morphine (boluses and/or continuous infusion) as rescue medication on the guidance of the validated pain assessment instruments. Endpoints in the first 48 hours post-operatively were: 1) cumulative morphine dose (study and rescue dose) (mcg/kg); 2) morphine rescue dose (mcg/kg); 3) morphine-related side effects. Analysis was by intention to treat. www.trialregister.nl: number NTR1438. Final data analyses were performed after September 20, 2011.

RESULTS

Between March 2008 and July 2010, 71 of 74 patients were included in the primary analysis (paracetamol (P), n=33 vs. morphine (M), n=38). Patients in the paracetamol group received 66% less morphine than patients in the morphine group [121 (IQR 99-264) vs. 357 (IQR 220-605) mcg/kg, $p< 0.001$]. The median rescue dose of morphine (P; 25 (0-164) mcg/kg vs. M; 20 (IQR 0-226), $p=0.99$), incidences of morphine-related side effects (P; 27.3 % vs. M; 34.2 %), RR 1.4, 95% CI 0.5-3.8) and levels of pain scores did not differ between study groups.

CONCLUSION

Intravenous paracetamol reduces morphine requirements in neonates and young infants after major surgery, thereby potentially reducing the risk for opioid-related side effects with similar validated pain scores demonstrating identical pain levels.

LBI-1

PHARMACOKINETIC/PHARMACODYNAMIC (PK/PD) MODELING OF INTRAVENOUS AND ORAL TOPIRAMATE (TPM) AND ITS EFFECTS ON PHONEMIC FLUENCY (PF) IN ADULT HEALTHY VOLUNTEERS

G. F. Ahmed, S. E. Marino, R. C. Brundage, S. V. Pakhomov, I. E. Leppik, J. C. Cloyd, A. Clark, A. K. Birnbaum; University of Minnesota, Minneapolis, MN

BACKGROUND

TPM affects PF as measured by the controlled oral word association test (COWA), but the relationship to drug exposure has not been evaluated. Objectives were to: 1) characterize TPM PK; 2) develop a PK/PD model to quantify effects of TPM on PF; 3) simulate effects of TPM at higher doses.

METHODS

Subjects were healthy volunteers (n=32, 18- 65 yrs) not taking interacting medications. Three randomized crossover studies were conducted: I) 50 and 100 mg TPM given orally and intravenously; II&III) 100 mg oral TPM versus placebo. COWA was assessed pre and post-treatment baselines (BL), at 0.25, 2.5, 6 h (study I), or at 2.5 h after dose (studies II&III). Blood was collected until 120 h after dose (study I) or immediately after COWA (studies II&III). Linear and nonlinear PK/PD links of TPM concentration (Cp) to COWA under 3 distributions (normal, negative binomial, and Poisson) were explored. The final model was used to simulate the effect of a 200 mg daily dose of TPM on COWA. PK/PD data were available for analysis 9/26/2011. Data analysis was finalized 11/30/2011.

RESULTS

A 2-compartment model first order absorption and elimination described TPM PK. Estimates (95% CI) were: CL, 1.3 L/h (1.2, 1.5); Vc, 58.8 L (50.6, 67); Vp, 12.8 L (10.2, 15.4); Q, 1.27 L/h (0.3, 2.3); Ka, 2.9 h-1 (1.9, 3.9); and oral bioavailability, 1.08 (1.03, 1.13). Interindividual variances (IIV) were estimated for CL (19.6% CV), and Vc (23.3% CV). Body weight was a predictor of Vc. PD model estimates and intervals were similar for all distributions. Mean COWA-Cp profiles fit an exponential decline function. Estimate (95% CI) for BL was 42.7 words/3 min (39.9, 45.5); learning effect on repeated testing was 10% (5%, 15%) of BL. TPM at 4.47 mg/L (3.9, 5.2) reduced BL COWA by half. The IIV for BL was 16.7% CV. The median simulated COWA score after a daily dose of 200 mg of TPM was ~15 words/3 min.

CONCLUSION

PF declined exponentially with rise in TPM Cp. Simulations showed an increased effect of TPM on PF after a daily dose of 200 mg.

LBI-2

MODEL-BASED META-ANALYSIS FOR COMPARATIVE EFFICACY OF OSTEOPOROSIS AGENTS: DENOSUMAB VS. OTHER TREATMENT OPTIONS

J. Zheng,[1] J. W. Mandema,[2] J. Perez Ruixo[1]; [1]Amgen, Thousand Oaks, CA, [2]Quantitative Solutions, Menlo Park, CA

BACKGROUND

Bone mineral density (BMD) changes are critical for evaluating the efficacy of osteoporosis agents. Many osteoporosis agents are clinically available but comparisons in BMD response among those agents are lacking. This model-based meta-analysis allows the comparisons of BMD changes at both lumbar spine and total hip after various treatment durations of different osteoporosis agents at different doses.

METHODS

Data were obtained from randomized controlled clinical trials in postmenopausal women available in the public domain. The longitudinal BMD changes from baseline at lumbar spine and total hip were analyzed using a nonlinear least square random effect regression analysis in October 2011.

RESULTS

Data from 72 trials, representing over 96,000 patients and 13 drugs including denosumab, bisphosphonates, selective estrogen receptor modulators, and parathyroid hormone, were analyzed. The dose response relationship of BMD changes was well characterized by an E_{max} model with a different E_{max} for lumbar spine and total hip for each drug class. The ratio of lumbar spine and total hip BMD changes was significantly different across the different drug classes. The potency, dose achieving 50% E_{max}, was different for each drug. The time course of BMD changes was well characterized by an exponential onset with different rate constant for lumbar spine and total hip for each class. Difference in baseline BMD was an important factor explaining between trial variability in treatment effect.

CONCLUSION

Denosumab at 60 mg Q6M SC administration provided the greater improvement in total hip and lumbar spine BMD throughout 36 months of treatment when compared with 10 mg/day oral alendronate, 5 mg/year iv zoledronic acid, 5 mg/day oral risedronate, 150 mg/month oral ibandronate, 3 mg Q3M iv ibandronate, and 60 mg/day oral raloxifene. The dose response relationship of denosumab indicated that dose greater than the current registered dose would provide limited additional benefit.

LBI-3

A POPULATION (POP) PHARMACOKINETIC (PK)/ PHARMACODYNAMIC (PD) ANALYSIS OF MIPOMERSEN (MIPO)

Z. Li,[1] D. Mould,[2] M. Hard,[1] **L. von Moltke**[1]; [1]Genzyme, A Sanofi Company, Cambridge, MA, [2]Projection Research, Phoenixville, PA

BACKGROUND

Mipo, an antisense oligonucleotide, is an apoB 100 synthesis inhibitor and has completed Phase 3 trials in hypercholesterolemia. ApoB 100 is the structural core of all atherogenic lipoproteins and required for hepatic secretion of VLDL. The objective was to develop pop PK and PD models for Mipo and to identify any influential covariates for PK or PD.

METHODS

NONMEM 7.2 was used to describe data from 17 clinical trials. Most patients had > 4 plasma samples taken; and most were taken 120-240 hours post last dose. The log transform both sides approach and evaluated using FOCE method were used. Model building and covariate assessments were conducted using standard methods. Final models were evaluated with several tests, including evaluation of an internal validation database, and visual predictive checks. The data analyses were complete on September 28, 2011.

RESULTS

Mipo PK was best described by a 2-compartment model with a time dependent clearance (TDCL), described via exponential asymptotic decrease. A mixture model found two TDCL groups: SLOW (88.6% patients) and FAST (11.4% patients) with 25% and 86% decrease in CL, respectively, after 1 year of dosing. Creatinine CL was found to be a covariate for CL. The significance of this finding is limited by the small number of patients with low CrCL (<60 mL/min). Route of administration was predictive of central volume of distribution (Vc), with Vc for IV 25% lower than SC. ApoB PD was described with an indirect effect model with Mipo nearly completely inhibiting ApoB formation. The SLOW group had a 10-fold lower IC50 for ApoB production (91 vs 1080 ug/L, respectively).

CONCLUSION

The PK and PD of Mipo have been well described by the models. Model based simulation has indicated TDCL occurs within first 6 months of dosing and plateaus thereafter. A 200 mg Mipo weekly SC dose for 1 year would reduce ApoB 46% for SLOW and 27% for FAST subpopulation with commensurate reduction in LDL-C. Underlying etiology of the two populations is not yet understood.

LBI-4

FIRST APPLICATION OF A DIFFERENTIAL ORDERED CATEGORICAL MODEL FOR ORDERED EFFICACY ENDPOINTS OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

B. Yang,[1] S. Krishnaswami,[2] M. Hutmacher,[3] M. Lamba[2]; [1]College of Pharmacy, University of Michigan, Ann Arbor, MI, [2]Specialty Care Clinical Pharmacology, Pfizer Inc, Groton, CT, [3]The Ann Arbor Pharmacometrics Group, Inc., Ann Arbor, MI

BACKGROUND

Tofacitinib (CP-690,550) is a novel oral Janus kinase inhibitor being investigated as a targeted immunomodulator for the treatment of RA. Objective was to jointly characterize the dose-time-response (efficacy) of tofacitinib across the American College of Rheumatology (ACR) response thresholds of 20, 50, and 70% improvements (ACR20/50/70).

METHODS

Data were pooled from two randomized, double-blind, monotherapy, dose-ranging studies (N=642) in RA patients. Treatments included placebo, 1, 3, 5, 10, and 15 mg BID doses of tofacitinib for 12 or 24 weeks. Binary ACR responses were combined into a 4-level ordered categorical endpoint. Pharmacologically-based logistic longitudinal models with proportional odds (PO) and differential odds (DO) assumptions were evaluated (analysis completed October 2011).

RESULTS

A DO model with an effect compartment provided the best description of the data with statistically significant and clinically important improvements over the PO model, particularly in predicting the magnitude and time course of ACR70. The DO model predicted that steady state response was achieved by 10, 11, and 24 weeks for ACR20, ACR50, and ACR70 respectively. Common estimates of E_{max} and ED50 for all categories resulted in improved precision of the dose-response (D-R) curves (90% confidence interval width 7-9%). Important differences were noted in the estimation of the probability of exceeding clinically meaningful response rates between the DO and PO models and between week 12 and 24 for ACR70, while results were similar when compared to binary models for each endpoint.

CONCLUSION

This first application of a semi-mechanistic DO model for tofacitinib provides potential for increased accuracy and precision of the D-R relationship. By allowing for different rate-constants with common drug parameter estimates, the DO model provides an integrated estimation of probability of success for all ACR endpoints to inform dose-selection decisions.

LBI-5

POPULATION PHARMACOKINETIC MODELING OF BUPRENORPHINE IN NEWBORNS WITH NEONATAL ABSTINENCE SYNDROME

D. Wu,[1] W. K. Kraft,[2] M. E. Ehrlich,[3] E. Dombrowsky,[1] J. S. Barrett[1]; [1]The Children's Hospital of Philadelphia, Philadelphia, PA, [2]Thomas Jefferson University, Philadelphia, PA, [3]Mount Sinai School of Medicine, New York, NY

BACKGROUND

About 55 to 94% of infants born to opioid dependent mothers have neonatal abstinence syndrome (NAS). Buprenorphine (BUP) is currently used in clinics as a detoxification and maintenance treatment for opioid dependence. No pharmacokinetic (PK) data of BUP is available to newborns following sublingual administration of BUP.

METHODS

Population PK were estimated using NONMEM in 25 newborns in NAS sublingually administered with BUP in an open labeled study, with 4 co-treated with phenobarbital within a certain period of time after treatment started. PK parameters, obtained using published 3-CMT model in adults administered with BUP intravenously and 2-CMT model constructed using published plasma concentrations -time data in adult using sublingual administration, were extrapolated to those in neonate using allometric scaling. The predicted plasma concentration-time data obtained by extrapolation under-predicted our BUP-Norbuprenorphine (NorBUP) data profile. 1-CMT model with1st- order absorption and 1st order elimination was used to describe data. (Half data were analyzed on December 15).

RESULTS

The population mean of total CL of BUP including metabolism is approximately 12.0 L/hr. The volume of distribution of BUP is approximately 145 L. The estimated metabolism of BUP to NorBUP accounts for approximately 23% of the total CL of BUP. A 56% of increase in metabolism and total CL for patients co-treated with phenorbarbital was observed.

CONCLUSION

The population PK 1-CMT model with 1st-order absorption, metabolism, and elimination developed on sparse data was adequate in describing the PK of BUP and NorBUP in neonates. Difference in PK between neonates and adults were demonstrated, suggesting that special attention should be paid if allometric scaling is adopted to apply PK results from adults to neonates. The results would be used to guide the dose selection and titration in the ongoing larger trials of buprenorphine in newborns.

LBI-6

PREDICTION OF CYP3A4-MEDIATED DRUG-DRUG INTERACTION POTENTIAL BETWEEN PI3K INHIBITOR GDC-0941 AND KETOCONAZOLE THROUGH PHYSIOLOGICALLY-BASED PHARMACOKINETIC (PBPK) MODELING

J. Y. Jin,[1] I. Gong,[2] Y. Chen,[1] L. Salphati,[1] N. Budha,[1] D. A. West,[1] S. Mukadam,[1] S. Holden,[1] J. A. Ware,[1] M. J. Dresser[1]; [1]Genentech, South San Francisco, CA, [2]University of Western Ontario, London, ON, Canada

BACKGROUND

GDC-0941 is a potent, selective pan-inhibitor of class I PI3K which has good activity in xenograft models and is being investigated for oncology. Human liver microsomes and recombinant cytochrome P450s (CYPs) studies identified CYP3A4 as the major enzyme contributing to GDC-0941 oxidative metabolism. The aim of this study was to assess the effect of ketoconazole (KTZ) co-administration on GDC-0941 pharmacokinetics (PK), and to evaluate the ability of Simcyp to predict the drug-drug interaction (DDI) potential.

METHODS

This was a single center, open label, randomized study conducted in healthy volunteers (n=20). All subjects received 60 mg GDC-0941 alone or with 200 mg KTZ twice daily. Simcyp was used prospectively to assess the CYP3A4-mediated DDI potential, and the predictions were retrospectively evaluated and refined en light of the observed results (not available until after abstract deadline).

RESULTS

The geometric mean ratios (90% CI) of C_{max} and $AUC_{0\text{-}inf}$ were 1.04 (0.88, 1.24; P = 0.67) and 1.43 (1.24, 1.64; P < 0.0005), when comparing GDC-0941 alone to KTZ co-administration, respectively. Increased GDC-0941 half-life in the presence of KTZ suggested that the impact of KTZ was on GDC 0941 elimination. Prospective Simcyp simulations reasonably predicted the DDI risk (1.8-fold AUC change), assuming 50% CYP3A4 metabolic contribution (fm). Evaluation of CYP3A4 fm based on the clinical DDI result using Simcyp suggested fm of 40%. Overall, retrospective refinement of Simcyp simulations allowed for more accurate prediction of PK attributes and DDI risk.

CONCLUSION

Concomitant administration of the CYP3A4 inhibitor KTZ with GDC-0941 resulted in a mean exposure increase of 43%, and was well-predicted by Simcyp simulation assuming 40% CYP3A4 contribution. Simcyp simulations can be used prospectively to assess DDI risk and assist clinical study design, and should be iteratively refined to optimize predictability.

LBI-7

LONGITUDINAL POPULATION PHARMACOKINETIC/ PHARMACODYNAMIC (PK/PD) ANALYSIS FOR PF-02545920 EXPOSURE AND POSITIVE AND NEGATIVE SYNDROME SCALE (PANSS) TOTAL RESPONSE IN PATIENTS WITH ACUTE EXACERBATION OF SCHIZOPHRENIA

J. Ahn, Y. Jin, J. Liu, V. Kumar; Pfizer, Inc., Groton, CT

BACKGROUND

PF-02545920 is a highly selective phosphodiesterase 10A inhibitor (PDE10Ai) that has been evaluated for the treatment of acute schizophrenia. Presented here is the result of modeling and simulation activity (final data delivered on September 27, 2011) that aimed to: 1) develop a model that characterizes the time course of placebo response and the effect of PF-02545920 on PANSS total scores (PANSS hereafter); and 2) assess the probability of achieving the target value (PTV) of -10 points on PANSS for PF-02545920 vs. placebo at week 4.

METHODS

A total of 1263 observations from 222 patients were obtained from a 4-week double-blind, placebo & positive-controlled, randomized, inpatient phase 2a study investigating 5 and 15 mg BID of PF-02545920, placebo, and 3 mg risperidone (risperidone data was excluded from the analysis). The model development consisted of describing placebo response, characterizing treatment effects, evaluating the model, and assessing the PTV. NONMEM 7.1.2 and R 2.10.1 were the main analysis tools.

RESULTS

An exponential model was used to describe placebo response that tended to asymptotically decrease over time. Typical maximum placebo response (P_{max}) was estimated to be a decrease in PANSS by 12.2 (17.5% RSE) points (9.56 points drop at week 4), with a half life of ~11 days to reach P_{max}. A slight and time-dependent trend of improvement in PANSS with increase in average steady-state concentration (C_{avg}) was also characterized. The slope estimate of C_{avg} dependency in PANSS was 0.0476 points per ng/mL (66.6% RSE) at week 4, which corresponds to ~2 points drop in PANSS at the median Cavg of 42.5 ng/mL. The model predicted 90% CI for placebo adjusted mean was [-4.2, 0.13], which was not significantly different from 0.

CONCLUSION

Longitudinal exposure response analysis on PANSS was performed to characterize placebo and treatment effect of PF-02545920. The model concluded a minimal treatment effect on PANSS and near 0% PTV at either dose of PF-02545920.

LBI-8

META-ANALYSES OF VIRAL LOAD DECLINE, DOSE RESPONSE AND CLINICAL OUTCOMES IN TREATMENT-NAÏVE GENOTYPE-1 HEPATITIS C VIRUS (HCV) INFECTED SUBJECTS RECEIVING PEGYLATED

A. Polepally,[1] R. Menon,[2] S. Dutta[2]; [1]University of Minnesota, Minneapolis, MN, [2]Abbott Laboratories, Abbott Park, IL

BACKGROUND

Hepatitis C viral infection is treated with Pegylated Interferon (pegIFN) and Ribavirin (RBV). A clinical outcomes hepatitis C virus (HCV) database was used to: summarize viral load (VL) decline and VL responses (rapid virological response (RVR), early virological response (EVR), end of the treatment response (ETR), and sustained virological response (SVR))*; characterize SVR by pegIFN +/- RBV therapies; predict SVR from short term virologic end points (RVR/EVR/ETR).

**VL below HCV RNA detection limit at 4 wks (RVR), 12 wks (EVR) during the treatment, at end of the treatment (ETR) and at 24 wks after completion of the treatment (SVR)*

METHODS

Criteria used for meta-analyses: treatment naïve subjects; HCV Genotype-1 infection; pegIFN +/- RBV therapies. Dose response models were fit to SVR in NONMEM® 7 by implementing RBV dose as categorical or continuous covariate. Linear regression was performed in R to evaluate predictability of SVR by short term virologic end points. The data analyses and review was completed after September 23.

RESULTS

The final dataset included 44 arms, 2150 subjects for VL and 51 arms, 8293 subjects for SVR. Median VL decline across trial arms were 2.3 (range: 0.3, 3.6) and 3.5 (range: 1.9, 4.4) $\log_{10}$ IU/mL at 4 and 12 weeks, respectively. By week 12, 49% (range: 19, 94) of subjects had an undetectable viral load when treated with pegIFN + RBV compared to 15% (range: 10, 60) with pegIFN alone. SVR is increased by ~2.4 (95% CI: 2, 2.8) fold in the presence of RBV (categorical) and increased by ~2.75% with every 100 mg of RBV (continuous) when co-dosed with 180 µg/wk of pegIFN. Rank order of SVR prediction : adj. R^2 For ETR (0.66) ≥ EVR (0.64) > RVR (0.37).

CONCLUSION

RBV has a significant effect on SVR. For the recommended clinical doses (180 µg/wk pegIFN / 800-1200 mg/day RBV) predicted SVR is between 41% and 52%. SVR predictability by both EVR and ETR was similar. Thus, a prediction of SVR can be made as early as 12 wks into treatment rather than at 48 wks (ETR).

LATE-BREAKING POSTER SESSION II

Friday, March 16 | 8:00am-3:00pm | Attended Poster 8:00am-9:30am
PRINCE GEORGE'S EXHIBIT HALL C

LBII-1

THE EFFECT OF MATE2K GENOTYPE ON METFORMIN DISPOSITION AND RESPONSE IN ASIANS AND CAUCASIANS

S. Stocker, R. Castro, J. Hibma, K. Morrissey, K. Giacomini; University of California, San Francisco, CA

BACKGROUND

Metformin is the first line therapy for the treatment of type II diabetes. The disposition and response to metformin varies significantly. The aims of this study were to examine the effect of genotype of the kidney transporter, MATE2K, on the pharmacokinetics and pharmacodynamics of metformin in Asian and Caucasian healthy volunteers. A gain of function variant of MATE2K, -130G>A, identified in previous studies was the focus of the study.

METHODS

Healthy Asian (n=18) and Caucasian (n=6) volunteers with known MATE2K (-130G>A) genotype were recruited into an open label study. A 3-hour oral glucose tolerance test, OGTT (75g glucose), was conducted in the morning on Day 1 and Day 2. Metformin was administered in the evening of Day 1 (850 mg) and the morning of day 2 (1000 mg). Blood and urine were collected for determination of metformin, glucose and creatinine. Data were analyzed using WinNonLin (12/9/11) and unpaired t-test.

RESULTS

The metformin half-life was significantly greater in Asians (3.9±0.8h) compared to Caucasians (3.0±0.3h; $p<0.01$). Consistent with the shorter half-life, Caucasians had a higher metformin renal clearance (1056±301 versus 663±310 mL/min, respectively; $p<0.01$) and renal secretion (967±281 versus 554±301 mL/min, respectively; $p<0.001$) compared to Asians. The Vd and AUC were similar for Asians and Caucasians. However, the glucose lowering effect of metformin was greater in Caucasians compared to Asians (pA, Asian subjects homozygous for the MATE2K variant, -130A, (n=4) had a significantly greater renal clearance (973±422 versus 510±148mL/min; $p<0.01$) and renal secretion (512±356 versus 452±228mL/min; $p<0.05$) than those carrying one reference allele of MATE2K (n=8).

CONCLUSION

Our data indicate that ethnicity and genetic variation in MATE2K influence the pharmacokinetics of metformin. Furthermore, metformin response was greater in Caucasians compared to Asians.

LBII-2

METABOLIC RATIO OF OPIOIDS IN HAIR: A NOVEL METHOD TO STUDY POPULATION GENETIC POLYMORPHISMS

K. Delano, P. Walasek, K. Aleksa, G. Koren; Hospital for Sick Children, Toronto, ON, Canada

BACKGROUND

Codeine, still widely prescribed for its analgesic effects, is subject to CYP2D6 polymorphisms affecting its metabolism. Metabolic ratio (MR) of morphine to codeine represents the extent of codeine metabolism to its active metabolite. MR has previously been studied in blood, and urine. However, these compounds can be found in hair, which has never been used as a matrix to study MR. Studying MR in hair can provide a simple method to evaluate population variability obviating the need for blood..

METHODS

Hair samples were collected from the Motherisk Laboratory for testing as per request by social workers, lawyers and other agencies. Since July 2010, 1468 samples were tested for codeine and morphine through GC-MS analysis. All codeine positive samples (n=214) and respective morphine results were used to calculate metabolite-to-parent MR. Frequencies of MR were graphed to assess population distribution. Data was analyzed on October 4th because trainee began graduate program on September 6th.

RESULTS

The distribution of MR frequency illustrated in Figure 1 shows similarities to distributions using blood samples. Similar to blood, hair appears to exhibit large inter-individual variability of MR.

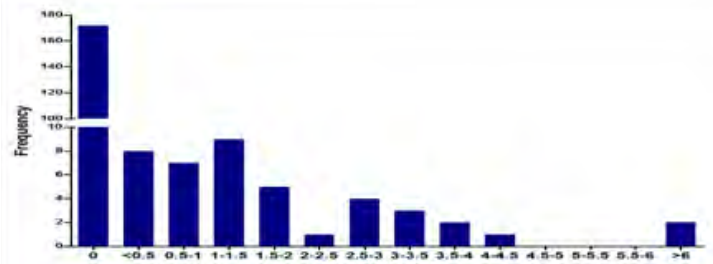


Figure 1 | Metabolic ratio of morphine to codeine in human hair.

CONCLUSION

With better understanding of codeine and morphine incorporation into human hair, polymorphisms can be studied in hair using MR. Unlike blood, hair collection is non-invasive and shows previous use. This is the first study to assess the use of human hair as a matrix to study CYP2D6 polymorphisms.

LBII-3

A SEMI-MECHANISTIC PHARMACOKINETIC/ PHARMACODYNAMIC (PK/PD) MODEL FOR IMIPENEM (IMP)/MK-7655 COMBINATION THERAPY AGAINST RESISTANT PSEUDOMONAS AERUGINOSA (PA)

G. F. Ahmed,[1] M. L. Rizk,[2] K. Young,[2] M. Motyl,[2] C. Li,[2] L. Wenning[2];
[1]University of Minnesota, Minneapolis, MN, [2]Merck Research Laboratories, Merck & Co., West Point, PA

BACKGROUND

MK-7655 (beta-lactamase inhibitor) is under development as a combination therapy to restore IMP's activity against resistant PA. Objectives of this study were to: (1) build a PK/PD model that describes time-kill (TK) curves of resistant PA after treatment, and (2) translate the model to an *in vivo* species.

METHODS

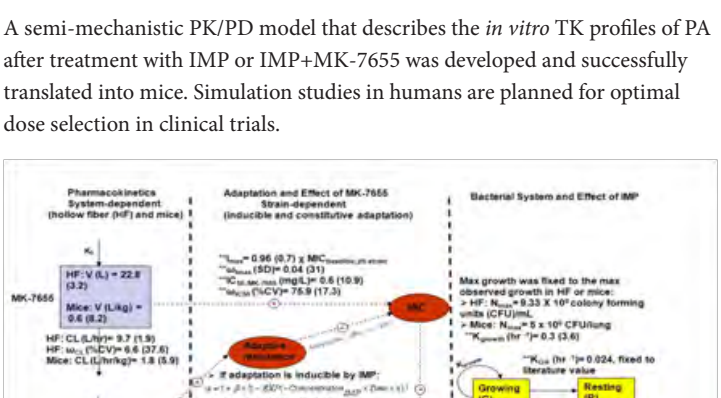
Three studies were conducted: (I) a TK and PK study in an *in vitro* hollow fiber, (II) an *in vitro* study of minimum inhibitory concentration (MIC) of IMP against PA at varying concentrations of MK-7655 (C of MK-7655) and (III) an *in vivo* TK and PK study in a mouse model of lung infection. Model fitting and simulations were performed in NONMEM 7. Precision of parameter estimates was evaluated using bootstrapping. The model was tested in mice and evaluated by simulations. All data were available for analysis 9/25/2011. Data analysis was finalized 11/22/2011.

RESULTS

PK (n=32)/TK (n=16), and MIC-C of MK-7655 (n=93) profiles were collected from studies I and II, respectively. PK (n=17) and TK curves (n=9) were generated from study III. The PK/PD model and assumptions for the mouse model are shown in the figure. Simulations in mice showed that 94% of the observed CFU/lung fell within the 5th, 95th percentiles of the simulated profiles.

CONCLUSION

A semi-mechanistic PK/PD model that describes the *in vitro* TK profiles of PA after treatment with IMP or IMP+MK-7655 was developed and successfully translated into mice. Simulation studies in humans are planned for optimal dose selection in clinical trials.



LBII-4

GENETIC POLYMORPHISM OF CYTOCHROME P450 2D6 AND PAROXETINE INFLUENCE FORMATION OF THE ACTIVE METABOLITES OF THE 1ST LINE INFERTILITY DRUG CLOMIPHENE

R. Kerb,[1] T. E. Mürdter,[2] M. Turpeinen,[3] W. Schroth,[2] B. Ganchev,[2] G. M. Böhmer,[4] S. Igel,[1] E. Schaeffeler,[1] U. Zanger,[1] H. Brauch,[1] M. Schwab[1];
[1]Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology and University Tübingen, Stuttgart, Germany, [2]IKP-Stuttgart, Stuttgart, Germany, [3]Department of Pharmacology and Toxicology, University of Oulu, Oulu, Finland, [4]Department of Clinical Pharmacology, University Hospital Tübingen, Tübingen, Germany

BACKGROUND

Ovulation induction with clomiphene (CLOM) is the first-line treatment in women with polycystic ovarian syndrome and unexplained infertility. While CLOM provides safe and effective medication, up to 30% of women fail to respond despite dose triplication.

CLOM is structurally similar to tamoxifen, which is predominantly bio-activated by the polymorphic cytochrome P450 (CYP) 2D6 suggesting that *CYP2D6* poor (PM) or extensive metabolism (EM) may predict individual success of CLOM.

METHODS

Incubations with pooled human liver microsomes from 150 donators of known CYP geno- and phenotype, from 8 PM donators, and from recombinant CYP (supersomes). The capacity of CLOM and its metabolites to inhibit oestrogen at its receptor was tested using an oestrogen response element reporter assay. CLOM and metabolites were quantified by *LC-MS*/MS.

An *in vivo* metabolic drug-drug interaction study was performed in 7 healthy female volunteers selected according to their *CYP2D6* genotype. Two single doses of 100 mg CLOM were applied with and without co-administration of 2-days paroxetine 40 mg qd (analysis from December 2011).

RESULTS

Incubation experiments identified CYP2D6 as major enzyme to form (E)-4-hydroxyclomiphene (OHCLOM) and (E)-4-hydroxy-N-desethylclomiphene (OHDECLOM). Formation rate of hydroxyl-metabolites in 30 human liver donors correlated with *CYP2D6* genotype showing a distinct gene-dose effect. OHCLOM and OHDECLOM were identified as active metabolites with strongest inhibition of the oestrogen receptor activity.

In the clinical study C_{max} of OHCLOM and OHDECLOM showed 8- and 12-times lower concentrations in PM. Co-administration of paroxetine significantly decreased formation of hydroxyl-metabolites in EM, while metabolic profile in PM remained unaffected.

CONCLUSION

Data provide proof-of-concept that polymorphic CYP2D6 influences bio-activation of CLOM and that response to CLOM may be prone to drug-drug interaction by CYP2D6 inhibitors.

LBII-5

WITHDRAWN

LBII-6

CLINICAL PHARMACOLOGY STUDY INVESTIGATING THE PRESSOR RESPONSE TO ORAL TYRAMINE DURING CO-ADMINISTRATION WITH SAFINAMIDE IN HEALTHY VOLUNTEERS

A. Marquet,[1] A. Johne,[2] K. Kupas,[2] S. Krösser,[2] B. Astruc,[3] A. Patat,[3] A. Kovar[2]; [1]Merck Serono SA, Geneva, Switzerland, [2]Merck KGaA, Darmstadt, Germany, [3]Biotrial, Rennes, France

BACKGROUND

Safinamide is an alpha-aminoamide with dopaminergic (potent, selective, reversible MAO-B inhibition) and non-dopaminergic activities in phase 3 development for Parkinson's disease. This controlled study investigated pressor response to oral tyramine during co-administration with safinamide to assess need for dietary restrictions.

METHODS

Design was a randomized, double-blind, placebo-, comparator (selegiline 10 mg/day)- and active (phenelzine 30 mg/day)-controlled multiple-dose study in 90 healthy subjects aged 18 to 70 years, evaluating safinamide at therapeutic (100 mg/day) and supratherapeutic (350 mg/day) doses. Response was characterized by Tyr30, defined as dose of oral tyramine producing a sustained increase of Systolic Blood Pressure (SBP) ≥30 mmHg compared to a daily-defined baseline SBP. During the treatment period, daily tyramine pressor tests (with escalating tyramine doses) were conducted on Days 7 through 16 or until Tyr30 was reached. Primary endpoint was Tyramine Sensitivity Factor (TSF), defined as subject-specific Tyr30 at screening divided by subject-specific Tyr30 under treatment. Complete analyses were not released before October.

RESULTS

TSF geometric means were: placebo: 1.52, safinamide 100 mg: 2.15, safinamide 350 mg: 2.74, selegiline 10 mg: 3.12, phenelzine 30 mg: 9.98. ANOVA analysis of log-transformed TSF showed consistent results, with treatment ratios versus placebo (90% CI) of: safinamide 100 mg: 1.6 (1-2.4), safinamide 350 mg: 1.8 (1.1-2.7), selegiline 10 mg: 2.2 (1.4-3.3), phenelzine 30 mg: 6 (3.9-9.1).

CONCLUSION

Safinamide induced a mild increase in TSF. However, its pressor effect at both doses remained lower than that of selegiline, which is devoid of a label warning for tyramine at the tested dose level. This study confirms that safinamide is a highly selective MAO-B inhibitor, even at supratherapeutic doses, and supports its administration without tyramine-related dietary restrictions.

LBII-7

D-LIMONENE MODULATES T LYMPHOCYTE ACTIVITY AND VIABILITY

C. M. Lappas,[1] N. T. Lappas[2]; [1]Lebanon Valley College, Annville, PA, [2]The George Washington University, Washington, DC

BACKGROUND

d-limonene is a cyclic terpene that possesses chemopreventative and chemotherapeutic activity. Treatment with d-limonene and related monoterpenes inhibits the development of mammary carcinomas, lung neoplasms, pancreatic tumors, liver cancer, pulmonary adenomas and forestomach tumors in rodent models. Phase I and II human clinical trials of d-limonene and d-limonene metabolites indicate that these agents show promise in the treatment of breast and colorectal cancers. Given the integral role the immune system plays in tumor surveillance, it is surprising that only a limited number of studies have been conducted investigating the effects of d-limonene on immune system function.

METHODS

$CD3^+$ T lymphocytes (>94% pure) were purified from the spleens of C57BL/6 mice and activated by incubation in 96-well plates coated with 2-10 μg/ml immobilized anti-CD3 mAb for 24 hours at 37°C in 5% CO_2. Cells were co-cultured with 0.5-8 mM d-limonene or vehicle control. TH1 and TH2 cytokine production was measured by ELISA, cell proliferation was measured by CFSE staining, activation marker expression was measured by flow cytometry and cell viability was measured via annexin V and propidium idodide staining.

RESULTS

Exposure to d-limonene inhibited the production by activated T lymphocytes of IFN-γ (EC_{50} = 2.03 ± 0.35 mM); IL-2 (EC_{50} = 2.62 ± 0.52 mM); TNF-α (EC50 = 4.22 ± 0.85 mM); IL-4 (EC_{50} = 2.30 ± 0.29 mM); and IL-13 (EC_{50} = 1.26 ± 0.30 mM). The expression of CD40L was inhibited by up to 44.13 ± 8.42% as a result of exposure to 2-8 mM d-limonene, while no significant effect on T cell proliferation was observed. An approximate 14 fold increase in T cell death was induced by treatment with 8 mM d-limonene, with lower doses having no significant effect on cell viability. (analyzed 10/11-12/11)

CONCLUSION

d-limonene possesses immunosuppressant and cytotoxic potential. These immunomodulatory activities must be considered when evaluating therapeutic applications of the compound.

LBII-8

NO CLINICALLY RELEVANT INTERACTION BETWEEN SUGAMMADEX AND ACETYLSALICYLIC ACID ON PLATELET AGGREGATION

P. J. de Kam,[1] R. El Galta,[2] J. Burggraaf,[3] H. Fennema,[2] K. Mihara,[2] A. C. Kruithof,[3] M. Moerland,[3] M. Jagt-Smook,[2] J. A. Wagner,[1] P. Peeters,[3] M. D. Troyer[1]; [1]Merck, Whitehouse Station, NJ, [2]MSD, Oss, Netherlands, [3]Centre for Human Drug Research, Leiden, Netherlands

BACKGROUND

This study evaluated a potential interaction between sugammadex and acetylsalicylic acid (ASA) on whole blood platelet aggregation.

METHODS

A randomized, double-blind, placebo-controlled, 4-way crossover study in 26 healthy males (18-45 yr). Subjects received intravenous (IV) placebo or sugammadex 4 mg/kg in the absence (periods 1 and 2) or presence (periods 3 and 4) of background daily oral ASA 75 mg. Primary assessment: potential interaction between sugammadex and ASA on whole blood collagen-induced platelet aggregation. Secondary assessments: activated partial thromboplastin time (APTT); bleeding time; safety. Platelet aggregation and APTT were evaluated by geometric mean ratios, using area under effect curves from 3-30 min after dosing. Non-inferiority margins were determined via thorough literature review. Type I error was controlled using a hierarchical strategy. Data became available for analysis on October 17, 2011.

RESULTS

There was no clinically relevant interaction between sugammadex and ASA on platelet aggregation. Interactions and/or effects on APTT and bleeding time did not exceed pre-specified non-inferiority margins (Table). Sugammadex (alone or with ASA) was generally well tolerated.

Parameter	Treatment comparison	Geometric mean ratio	One-sided 95% confidence limit	Non-inferiority margin
Whole blood platelet aggregation	ASA + sugammadex vs ASA alone	1.01	0.91	>0.75
Bleeding time (test at t=5 min)	ASA + sugammadex vs ASA alone	1.20	1.45	<1.5
APTT	Statistical interaction ASA by sugammadex	1.01	1.04	<1.5
	Sugammadex alone vs placebo alone	1.06	1.07	<1.5

CONCLUSION

There was no clinically relevant reduction in platelet aggregation with the addition of sugammadex to ASA treatment. Furthermore, the pre-specified non-inferiority margins were not exceeded for bleeding time and APTT.

LBIII-1

AGE-RELATED DIFFERENCES IN PLASMA AND INTRACELLULAR (IC) TENOFOVIR (TFV) CONCENTRATIONS

G. Baheti,[1] J. King,[2] E. P. Acosta,[2] C. V. Fletcher[1]; [1]University of Nebraska Medical Center, Omaha, NE, [2]The University of Alabama at Birmingham, Birmingham, AL

BACKGROUND

To use population pharmacokinetic (PK) modeling to investigate apparent differences in plasma TFV and IC TFV-diphosphate (TFV-DP) concentrations (conc) in children and adolescents compared with adults following tenofovir disoproxil fumarate (TDF) dosing.

METHODS

Data were pooled from 3 different studies in HIV-infected children, adolescents, and adults receiving TDF 300 mg daily. TFV plasma conc were measured 6-8 times and IC TFV-DP 2-3 times in each subject. Data analysis began in October, 2011. A 2-compartment model (NONMEM® 7.2) subdivided by age, allometrically scaled for children and adolescents and partitioned for slow and fast absorbers (T_{max} either <2 or >2 hrs, respectively) was utilized for plasma TFV. IC conc were modeled using an indirect response model: EC_{50} (plasma conc producing 50% of maximum effect [E_{max}]); kin (0 order rate constant for TFV-DP production); k_{out} (IC elimination rate constant); partitioned by age (>25 or <25 years). k_{out} for adults was fixed to a previous estimate. Covariates included age, sex, weight, race, creatinine clearance (CRCL), Tanner stage (adolescents), total bilirubin, and concomitant protease inhibitor.

RESULTS

Subjects: N=102 (61 male/41 female), 88 with IC conc. Median (range) age and CRCL were: 21 (9-60) years and 128 (43.3-267.6) ml/min, respectively. In final plasma model (FOCEI), oral clearance (CL/F) was significantly faster in those < vs. > 25 years. CRCL was the most significant covariate on CL/F and central distribution volume. IC TFV-DP EC_{50} was 69 vs 116 ng/mL, and $t_{1/2}$ (= to 0.693/k_{out}) was 70 h vs 86 hrs for those < vs > 25 yrs; E_{max} was fixed at 1200 fmol/10^6 cells.

CONCLUSION

Children and adolescents achieve higher IC TFV-DP conc than adults despite lower plasma conc. This analysis suggests a mechanism of greater phosphorylation sensitivity (quantified as lower EC_{50}) vs. slower IC elimination. Additional mechanistic studies are needed to fully understand the clinical pharmacology of IC TFV.

LBIII-2

PHARMACOKINETICS AND SAFETY OF METRONIDAZOLE IN PRETERM INFANTS: VALIDATION OF DRIED BLOOD SPOT SAMPLING

M. Sampson,[1] B. Bloom,[2] P. B. Smith,[1] D. K. Benjamin Jr.,[1] G. L. Kearns,[3] E. V. Capparelli,[4] M. Cohen-Wolkowiez,[1] Pediatric Trials Network; [1]Duke Clinical Research Institute, Durham, NC, [2]University of Kansas School of Medicine, Wichita, KS, [3]University of Missouri–Kansas City School of Medicine, Kansas City, MO, [4]University of California, San Diego, San Diego, CA

BACKGROUND

Metronidazole is routinely used to treat intra-abdominal infections in preterm infants. Pharmacokinetic (PK) data for this drug in this population are virtually absent. Dried blood spot (DBS) technology has the potential to enable appropriate PK studies in this population necessary to define age-appropriate dose.

METHODS

A prospective, open-label, multicenter study of 24 infants (<32 weeks gestation and 15 days postnatal age) was performed. Sparse plasma and DBS samples were obtained around the first dose, at doses 3-5, and with the last dose. Concentrations were determined by HPLC/MS/MS (LLOQ 50 ng/mL). Population nonlinear mixed effect modeling was used to analyze the PK data, and plasma vs. DBS concentration association was evaluated using linear regression techniques. Last infant was enrolled November 1, 2011, and data were subsequently analyzed.

RESULTS

24 infants (median [range] gestational age at birth 25 [23-31] weeks, postnatal age 27 [1-82] days) provided 101 plasma and 50 DBS samples for analysis. Metronidazole population PK was described by a 1-compartment model: mean clearance (CL, liter/kg/h) = 0.042 x (postnatal age/27)$^{0.45}$. Apparent volume of distribution (V) was 0.95 L/kg. The relative standard errors around CL and V estimates were 10% and 3%, respectively. The median (range) ratio of metronidazole DBS to plasma concentrations was 88% (39-112%). DBS and plasma concentrations were highly correlated (r^2 0.85, P<0.001), and no significant differences were found when metronidazole PK were calculated from plasma vs. DBS concentrations.

CONCLUSION

Metronidazole CL increased as a function of postnatal age as expected with development. DBS sampling offers an avenue to critically evaluate the PK of metronidazole and potentially other drugs in neonates and young infants.

LBIII-3

EFFECT OF THE NOVEL CYP3A4 INTRON 6 POLYMORPHISM (CYP3A4*22) AND CYP3A COMBINED GENOTYPES ON TACROLIMUS DOSING REQUIREMENTS AND BLOOD CONCENTRATIONS IN PEDIATRIC HEART TRANSPLANT RECIPIENTS

V. M. Gijsen,[1] R. H. van Schaik,[2] L. Elens,[2] S. Mital,[3] O. P. Soldin,[4] S. J. Soldin,[4] G. Koren,[3] S. N. de Wildt[1]; [1]Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands, [2]Erasmus MC, Rotterdam, Netherlands, [3]Hospital for Sick Children, Toronto, ON, Canada, [4]Georgetown University Medical Center, Washington, DC

BACKGROUND

Both CYP3A4 and CYP3A5 are involved in the metabolism of tacrolimus, an immunosuppressant. We aimed to determine the influence of the newly recognized CYP3A4*22 polymorphism, and the CYP3A5*3 polymorphism. In addition, we clustered CYP3A4 and CYP3A5 genotypes to study the effect of clustered CYP3A genotype on tacrolimus dosing requirements in pediatric heart transplant recipients.

METHODS

Thirty-nine pediatric heart transplant recipients (median age 6.0 [IQR: 13.75] years) were included. Tacrolimus doses and trough concentrations collected in the first 14 days post-transplantation were compared between patients and correlated with CYP3A4*22 and CYP3A5*3 genotype. Clustered CYP3A genotypes were extensive metabolizers (CYP3A5*1 carriers + CYP3A4*1/*1), intermediate metabolizers (CYP3A5*3/*3 + CYP3A4*1/*1), and poor metabolizers (CYP3A5*3/*3 + CYP3A4*22 carriers). All analyses were done in November 2011.

RESULTS

CYP3A poor metabolizers had significantly lower median (day4-14) dosing requirements (0.040 [range: 0.018-0.053] mg/kg/day) compared to intermediate metabolizers (0.062 [IQR: 0.047] mg/kg/day) and extensive metabolizers (0.123 [IQR: 0.086] mg/kg/day), P = 0.001. Age and CYP3A genotype clusters were independently associated with median tacrolimus dosing requirements ($R2 = 0.507$, $p<0.0001$) and concentration/dose ratio ($R2 = 0.415$, $p<0.0001$). No significant differences in tacrolimus dosing requirements ($p = 0.062$) or trough concentrations ($p = 0.128$), and concentration/dose ratio ($p = 0.057$) were found between patients carrying at least one CYP3A4*22 allele carriers compared to CYP3A4*1/*1 patients. No relationship was found between the genetic variability and estimated glomerular filtration rate.

CONCLUSION

Despite the small sample size, this novel report shows that clustered CYP3A genotypes show promising results for further individualization of tacrolimus therapy in pediatric heart transplant patients.

LBIII-4

INTRAVENOUS PARACETAMOL REDUCES MORPHINE REQUIREMENTS IN NEONATES AND YOUNG INFANTS UNDERGOING MAJOR NON-CARDIAC SURGERY: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

I. Ceelie,[1] **S. N. de Wildt**,[1] M. van Dijk,[1] M. M. van den Berg,[1] G. E. van den Bosch,[1] H. J. Duivenvoorden,[1] T. G. de Leeuw,[1] R. A. Mathôt,[2] C. A. Knibbe,[3] D. Tibboel[1]; [1]Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands, [2]Academic Medical Center, Rotterdam, Netherlands, [3]Leiden University, Leiden, Netherlands

BACKGROUND

Continuous morphine infusion as standard postoperative analgesic therapy in neonates and infants is associated with side effects such as respiratory depression. We aimed to assess whether intermittent intravenous paracetamol administration would significantly (>30%) reduce morphine requirements.

METHODS

In this single-center prospective, randomized double-blind study, infants under the age of 1 year were randomized to receive either continuous morphine or intermittent intravenous paracetamol after major surgery. Infants in both study groups received morphine (boluses and/or continuous infusion) as rescue medication on the guidance of the validated pain assessment instruments. Endpoints in the first 48 hours post-operatively were: 1) cumulative morphine dose (study and rescue dose) (mcg/kg); 2) morphine rescue dose (mcg/kg); 3) morphine-related side effects. Analysis was by intention to treat. www.trialregister.nl: number NTR1438. Final data analyses were performed after September 20, 2011.

RESULTS

Between March 2008 and July 2010, 71 of 74 patients were included in the primary analysis (paracetamol (P), n=33 vs. morphine (M), n=38). Patients in the paracetamol group received 66% less morphine than patients in the morphine group [121 (IQR 99-264) vs. 357 (IQR 220-605) mcg/kg, $p< 0.001$]. The median rescue dose of morphine (P; 25 (0-164) mcg/kg vs. M; 20 (IQR 0-226), $p=0.99$), incidences of morphine-related side effects (P; 27.3 % vs. M; 34.2 %), RR 1.4, 95% CI 0.5-3.8) and levels of pain scores did not differ between study groups.

CONCLUSION

Intravenous paracetamol reduces morphine requirements in neonates and young infants after major surgery, thereby potentially reducing the risk for opioid-related side effects with similar validated pain scores demonstrating identical pain levels.

LBIII-5

EVIDENCE OF DISTINCT HISTAMINE PHARMACODYNAMIC PHENOTYPES IN CHILDREN

B. L. Jones,[1] C. M. Sherwin,[2] K. A. Neville,[1] M. G. Spigarelli,[2] G. L. Kearns,[1] J. S. Leeder[1]; [1]Children's Mercy Hospital and Clinics, Kansas City, MO, [2]University of Utah, Salt Lake City, UT

BACKGROUND

Histamine iontophoresis with laser Doppler monitoring (HILD) provides a surrogate endpoint of histamine microvasculature response which is more dynamic and robust than classical epicutaneous histamine challenge. The purpose of this study was to characterize the pharmacodynamics (PD) of histamine in children using HILD.

METHODS

HILD was performed in children with allergic rhinitis (n=54). PD data were analyzed with a non-linear mixed-effects model (NONMEM v7.2). Effect data (relative maximal response over baseline; Eff_{maxNt}) and time of Eff_{maxNt}; T_{max}) were initially evaluated by visualization of time vs. response relationships which revealed apparent sub-groups within the cohort. Differences in model parameters between groups were determined using ANOVA and post-hoc analysis using Tukey's HSD. Linear regression was used to explore associations between parameters to validate apparent sub-group differences in PD. Data analysis was completed 12/15/11.

RESULTS

Evaluable data were obtained for N=43 participants 7-17 years of age (mean 12.2 yr). Three distinct histamine response phenotypes were identified; one group (n=7) demonstrated a pattern consistent with an apparent hyper-responsive phenotype that was characterized by significantly higher T_{max}, Eff_{maxNt} , and AUEC with respect to microvascular blood flow as a function of time ($p<.007$). There were no significant differences observed for E_{50}, and Ke0. Identification of the hyper-responsive subgroup was further validated by a stronger association between AUEC and Eff_{maxNt} ($r^2 =0.86$) when compared to the entire cohort ($r^2 = 0.005$).

CONCLUSION

Our data demonstrate the presence of an apparent hyper-responsive phenotype for histamine effect as reflected by HILD monitoring. This "effect phenotype" must be considered in future pediatric studies which are designed to assess the PK-PD relationship for antihistamines, either as a function of age or disease state.

LBIII-6

ANALYSIS OF FAILED PEDIATRIC STUDIES CONDUCTED UNDER THE FDA AMENDMENTS ACT (FDAAA) OF 2007

J. D. Momper,[1] Y. Mulugeta,[1] C. S. Lee,[2] G. J. Burckart[1]; [1]Office of Clinical Pharmacology, Center for Drug Evaluation and Research, US Food and Drug Administration, Silver Spring, MD, [2]Office of Pediatric Therapeutics, Office of the Commissioner, US Food and Drug Administration, Silver Spring, MD

BACKGROUND

Since 2007, over 130 drugs and biologics have been studied in pediatric patients under the renewed PREA and BPCA sections of FDAAA. The goal of these studies is to achieve labeling for an approved indication in the pediatric population. The objective of this study was to analyze all pediatric drug trials under FDAAA, and to determine the causes of the failed or incomplete trials.

METHODS

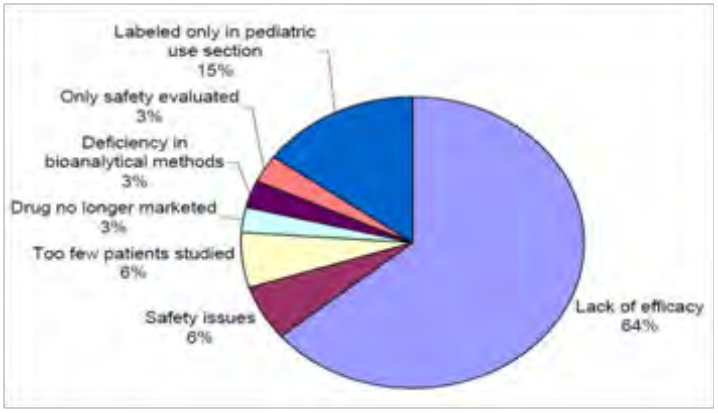
Design: Retrospective analysis of all products studied under FDAAA since the 2007 reauthorization. *Data collection*: The FDA labels and medical, statistical, and clinical pharmacology reviews were evaluated, and the principal reason for failure or lack of completion was identified. These data were analyzed in December 2011 in preparation for the FDA Advisory Committee meeting in March 2012.

RESULTS

: A total of 137 products were reviewed. Overall, 25% of BPCA and PREA studies did not achieve a new pediatric indication. Of the 89 products studied under PREA, 76 (85%) obtained a new pediatric indication. Of the 21 products studied under BPCA, 8 (38%) were given a new pediatric indication. For products studied under both PREA and BPCA (n=27), a new pediatric indication was achieved in 19 cases (70%). The reasons that pediatric studies did not achieve a labeled indication are shown in the Figure.

CONCLUSION

We conclude that (1) pediatric trial failures or delays in completion are still common, and (2) improved methods of selecting drug doses and outcome measures for pediatric drug approval trials are critically needed.



LBIII-7

IMMUNOPHENOTYPING PEDIATRIC LIVER TRANSPLANT RECIPIENTS TO ASSESS THE PHARMACODYNAMICS OF TACROLIMUS

L. J. Wozniak, Y. Korin, T. Smith, G. Lopez, R. Venick, S. V. McDiarmid, E. F. Reed; University of California, Los Angeles, CA

BACKGROUND

In liver transplantation, therapeutic drug monitoring is based on serum trough tacrolimus levels which can be variable, may not reflect cellular concentration, and have not been established to correlate with inhibition of immune cells involved in rejection. Few studies have correlated pharmacodynamic marker assay results with immunosuppressive efficacy. Our objective was to characterize peripheral blood mononuclear cell (PBMC) immunophenotypes associated with tacrolimus use in pediatric liver transplant recipients.

METHODS

100 peripheral blood samples were collected in CPT tubes from 58 pediatric liver transplant recipients and 3 normal healthy controls. Starting December 2011, immunophenotyping of T, B, NK, and dendritic cells was performed with multi-color monoclonal antibody panels. Cell fluorescence was acquired on an LSR Fortessa, and population measurements were determined using FCS Express V3 analysis software.

RESULTS

6 samples from 4 stable recipients on tacrolimus monotherapy and 2 control samples have been analyzed to date. Compared to controls, the liver recipients have a higher percentage of CD4 and CD8 memory effector cells, as determined by CD45RA-/CD27- surface markers (40% vs 20%). The liver recipients also have an increased ratio of monocytoid to plasmacytoid dendritic cells (2.1 vs 0.7), a pattern that has previously been associated with non-tolerogenic states. The remaining samples are currently being analyzed, including those from liver transplant recipients on no immunosuppression versus dual or triple immunosuppression.

CONCLUSION

This is the first study to assess variations in PBMC immunophenotypes associated with tacrolimus use in pediatric liver transplant recipients. By comparing these immunophenotypes to allograft function, we hope to develop a pharmacodynamic assay that can better assess the therapeutic effects of tacrolimus and ultimately enable clinicians to individualize immunosuppression.

LBIII-8

ENDOMYOCARDIAL, INTRALYMPHOCYTE AND WHOLE BLOOD CONCENTRATIONS OF CYCLOSPORINE A IN HEART TRANSPLANT RECIPIENTS

I. Robertsen,[1] P. Falck,[1] N. Næss,[1] A. Andreassen,[2] L. Gullestad,[2] H. Christensen,[1] A. Åsberg[1]; [1]School of Pharmacy, University of Oslo, Oslo, Norway, [2]Department of Cardiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway

BACKGROUND

Previous studies indicate that intracellular cyclosporine A (CsA) concentration may be a more sensitive monitoring tool for acute rejections in renal transplant recipients. In the present study we investigated CsA concentrations in isolated T-lymphocytes from heart transplant recipients. In addition, concentration of CsA and its metabolites were measured in endomyocardial biopsies to elucidate its association with rejections and side effects.

METHODS

Ten heart transplant recipients (8 men, 2 women) on CsA-based immunosuppression were enrolled in this prospective single-center pilot study. Blood samples were obtained twice weekly initially, and thereafter weekly for up to 12 weeks after transplantation. One of the weekly routine biopsies was allocated to this study. Whole blood, intralymphocyte and biopsy CsA concentrations were determined with a validated high-performance liquid chromatography-tandem mass spectrometry method. Due to analytical challenges, the analysis of CsA concentrations in endomyocardial biopsies was delayed and finalized mid-November 2011.

RESULTS

The average (range) intralymphocyte CsA trough concentrations were 10.6 (1.5-39.3) and 7.4 (1.3-25.2) ng/10^6 cells in the rejection and non-rejection group, respectively (P=0.70). The corresponding whole blood CsA concentrations were 321 (153-941) and 308 (152-847) ng/mL, respectively (P=0.26). There were no correlation between whole blood and intralymphocyte CsA concentration (r^2=0.03) and no correlations were found between endomyocardial CsA concentrations and whole blood (r^2=0.065) or intralymphocyte concentrations (r^2=0.072).

CONCLUSION

The present study did not reveal any correlation between CsA concentrations in whole blood, T-lymphocytes or endomyocardial tissue. The study could not support previous findings, as no association between intralymphocyte CsA concentrations and acute rejections was present.

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