The International Society for Biopharmaceutical Statistics

The 6th International Symposium on Biopharmaceutical Statistics

Statistical Innovation and Contribution in the Era of Precision Healthcare

Program Book

August 19, 2019

Kyoto International Conference Center, Kyoto, Japan
Short course: August 26 | Main Conference: August 27-29, 2019

SYMPOSIUM LEADERSHIP TEAM (CO-CHAIRS)

Jie Chen
Merck, Sharp & Dohme, Corp.

Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center

Satoshi Morita
Kyoto University

SCIENTIFIC PROGRAM COMMITTEE

Yuki Ando
Pharmaceuticals and Medical Devices Agency

Scott Berry
Berry Consulting

Ivan S. F. Chan
AbbVie

Alan Chiang
Celgene Corporation

Luyan Dai
Harbour Biomed

Jie Ding
MSD China

Scott R. Evans
George Washington University

Frank Fan
Novartis

Tony Guo
BeiGene

Susan Halabi
Duke University

Lisa Hampson
Novartis Pharma AG

Chin-Fu Hsiao
National Health Research Institutes

HM James Hung
Food and Drug Administration

Seung-Ho Kang
Yonsei University

Florian Klinglmüeller
Austrian Medicines & Medical Devices Agency

Franz König
Medical University of Vienna

Ying Lu
Stanford University

Olga Marchenko
Bayer

Sandeep Menon
Pfizer Inc.

Guo Tong
QVIA

Mey Wang
The Center for Drug Evaluation

William Wang
Merck, Sharp & Dohme, Corp.

Jiawei Wei
Novartis Institutes for BioMedical Research

Haiyan Xu
Johnson and Johnson

Guosheng Yin
The University of Hong Kong

Ying Yuan
University of Texas MD Anderson Cancer Center

Helen Zhang
University of Arizona

Sarah Zohar
Centre de Recherche des Cordeliers

SHORT COURSE COMMITTEE

Martin Posch
Medical University of Vienna

Wenjin Wang
Pfizer Inc.

FUNDRAISING COMMITTEE

Jie Chen
Merck, Sharp & Dohme, Corp.

Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center

Norisuke Kawai
Pfizer Japan Inc.

Akira Wakana
MSD K.K.

LOCAL ORGANIZING COMMITTEE

Hiroyasu Abe
Kyoto University

Koko Asakura
National Cerebral and Cardiovascular Center

Kimitoshi Ikeda
AbbVie GK

Naoki Isogawa
Pfizer Japan Inc.

Tomoyuki Kakizume
Novartis Pharma K.K

Shoichi Ohwada
Daiichi Sankyo Company

Kentaro Sakamaki
Yokohama City University

Masataka Taguri
Yokohama City University

Fumihiro Takahashi
Mitsubishi Tanabe Pharma Corporation

Ryuji Uozumi
Kyoto University

ADVISORY BOARD

Frank Bretz
Novartis Pharm AG

Yutaka Matsuyama
The University of Tokyo

Yasuo Ohashi
Chuo University

Thanks to Our Wonderful Sponsors

Platinum Sponsors

JMDC

PPD SNBL

abbvie

Gold Sponsors

Takumi Information Technology

NOVARTIS

DOT WORLD

Silver Sponsors

日本メディア株式会社 Japan Media Corporation

Cytel

A2 Healthcare

Eisai

SAS

DAY 1 | MONDAY, AUGUST 26, 2019

MORNING SHORT COURSES

9:00AM-4:30PM **REGISTRATION**
RECEPTION, MAIN ENTERANCE, 1F

9:30AM-12:45PM **SHORT COURSE A**
ROOM 663, 6F

MISSING DATA ANALYSIS IN CLINICAL TRIALS USING SAS®

PRE-REGISTRATION REQUIRED

Instructors **Frank Liu**, Merck, Sharp & Dohme, Corp.; **Fang Chen**, SAS Institute Inc.

Overview Missing data are inevitable and post many issues and challenge in analysis for clinical trials. Despite a great amount of research has been devoted to this topic, properly handling missing data in clinical trials remains complex. Conventionally, under the missing at random (MAR) assumption, we often use maximum likelihood or multiple imputation based methods for inferences. However, the MAR assumption is unverifiable. More critically, the estimand under MAR is hypothetical as indicated in the recent ICH E9 (R1) addendum and has been considered as overly-simplistic and unrealistic. Both regulatory agencies and industry sponsors have been seeking alternative approaches to handle missing data in clinical trials under missing not at random (MNAR) assumption.

This half-day tutorial is intended to cover issues of missing data in clinical trials including various methods and how to carry out the analyses using SAS software. The tutorial begins with an overview of missing data issues, and concepts and strategies as proposed by ICH E9 (R1) addendum. Then we will review traditional missing data handling methods such as maximum likelihood methods, multiple imputation, generalized estimation equation approaches, and Bayesian methods. The rest of the course is devoted to more recently-developed methods, such as sensitivity analysis to assess robustness, control-based imputation, control-based mean imputation, trimmed mean and tipping point analysis. Real clinical trial examples will be presented for illustration with implementation of the analysis using SAS/STAT software, including PROC MIXED, PROC MI, PROC MIANALYZE, PROC GEE, and PROC MCMC.

9:30AM-12:45PM **SHORT COURSE B**
ROOM 664, 6F

CONFIRMATORY ADAPTIVE DESIGNS WITH MULTIPLE OBJECTIVES: METHODS AND REGULATORY EXPERIENCES

PRE-REGISTRATION REQUIRED

Sponsored by 国立循環器病研究センター National Cerebral and Cardiovascular Center

Instructors **Franz König**, Medical University of Vienna; **Martin Posch**, Medical University of Vienna; **H.M. James Hung**, US Food and Drug Administration; **Sue-Jane Wang**, US Food and Drug Administration; **Frank Bretz**, Novartis Pharma AG

Overview Adaptive (flexible) designs allow for mid-course design adaptations based on interim data without compromising the overall type I error rate. Examples of design adaptations are the adjustment of sample sizes or the number and timing of interim analyses. These design parameters may be adapted depending on interim estimates of the variance, the treatment effect and safety parameters. An important field of application of the adaptive design methodology are clinical trials with several treatment arms, where promising treatments can be selected at an interim analysis. Using adaptive multiple test procedures the type I error rate can be controlled even if the selection rule, the number of selected treatments or the final sample sizes are not prefixed. Adaptive multiple testing procedures can also be used in adaptive designs with the option of population enrichment. In such designs a sub population may be selected in an interim analysis and further recruitment of patients is restricted to the selected subgroup. In the past few years adaptations proposed in regulatory applications may involve a hybrid or a complex form of various design features, such as reasonably likely surrogate or predictive biomarker, external control. This short course will share with some regulatory experiences in such adaptive designs in cardiovascular, renal, CNS and imaging drug trials.

9:30AM-12:45PM **SHORT COURSE C**
ROOM 665, 6F

ACCELERATING DRUG DISCOVERY THROUGH PRECISION MEDICINE AND INNOVATIVE DESIGNS: CONCEPTS, RATIONALE, AND CASE STUDIES

PRE-REGISTRATION REQUIRED

Instructors **Sandeep M Menon**, Pfizer Inc.; **Weidong Zhang**, Pfizer Inc.

Overview Precision medicine has paved the way for a new era of delivering tailored treatment options to patients according to their biological profiles. Advancement of the biotechnologies such as next generation sequencing technology (NGS) and other omics technologies have enabled us to interrogate a patient's many molecular biomarkers, and associate them with disease and drug responses. In addition, incorporation of biomarker information in the innovative clinical trial design has presented drug developers unprecedented opportunities to bring a successful drug to patients in needs.

The first part of this course will focus on the concept of precision medicine, biomarker discovery and its application in clinical trials. Comprehensive review of omics data and major technologies will be presented. Statistical considerations and challenges such as data normalization, dimension reduction and biomarker threshold development and using biomarker for decision making in clinical development will be discussed in details.

The second part of this course will focus on the strategy of the study design that is important to critically determine biomarker performance, reliability and eventually regulatory acceptance. A general overview of the concept and statistical methodologies and designs related to precision medicine will be presented. Specifically, we will discuss various designs including adaptive designs available at our disposal and its merits and limitations.

AFTERNOON SHORT COURSES

1:45-5:00PM **SHORT COURSE D**
ROOM 663, 6F

NOVEL ADAPTIVE CLINICAL TRIAL DESIGNS FOR IMMUNOTHERAPY AND MODERN DRUG DEVELOPMENT

PRE-REGISTRATION REQUIRED

Instructors **Cong Chen,** Merck Sharp & Dohme Corp.; **Guosheng Yin**; The University of Hong Kong; **Ying Yuan**, University of Texas MD Anderson Cancer Center

Overview Following the success of PD-1 (or PD-L1) inhibitors, a flood of next generation immunotherapies with different mechanisms of action are being developed. While the

expectation is high for these new immunotherapies, it is unrealistic to expect all of them to have the same success as their predecessors, especially given the improved standard-of-care. Innovative adaptive clinical trial designs provide a cost-effective and flexible way to improve the success rate of drug development. In this short course, we will present novel Bayesian designs for phase I and II clinical trials (including both single-agent and drug-combination trials), statistical strategies on phase 1 efficacy screening, adaptive 2-in-1 design for seamless Phase 2/3, Phase 3 adaptive designs for population expansion. We will introduce the freely available software and illustrate the application of the designs using real-world examples. This short course is suitable for statisticians and clinicians from industry, regulatory agencies and academia. Students of this short course are expected to not only apply the new methods learned to their studies but also think out of box when facing unique situations.

1:45-5:00PM **SHORT COURSE E**
ROOM 664, 6F

ARTIFICIAL INTELLIGENCE FOR MEDICINE AND HEALTH CANCELLED

Instructor **Mark Chang,** Boston University

Overview Artificial intelligence (AI) or machine learning (ML) has been used in drug discovery for many years under name of bioinformatics, such as sequencing, annotating genomes, analysis of gene and protein expression and regulation, linking the biological and disease network to the symptoms and adverse events, identifying structure-activity relationships in discovery and designing new drugable molecules. AI has also been used for the prediction of cancer susceptibility (risk assessment), cancer recurrence/local control, and cancer survival. In analysis of clinical trial data, predicted individual patient outcomes for precision medicine, similarity-based machine learning (SBML) has recently been used in clinical trials for oncology and rare disease without the requirement of big data as most ML methods do. The introductory course will cover supervised, unsupervised, semi-supervised, and reinforcement learning methods, and swarm and evolutionary intelligences. It aims at conceptual clarity and mathematical simplicity. Provide R code for some of the supervised learning methods and discussion case studies.

1:45-5:00PM **SHORT COURSE F**
ROOM 665, 6F

HOT TOPICS IN CLINICAL TRIALS: MULTIPLE OUTCOMES AND BENEFIT:RISK

PRE-REGISTRATION REQUIRED

Sponsored by 国立循環器病研究センター National Cerebral and Cardiovascular Center

Instructors **Scott R. Evans**, George Washington University; **Toshimitsu Hamasaki**, National Cerebral and Cardiovascular Center

Overview We discuss two hot topics in clinical trials. In Part I we discuss the design and analysis of clinical trials with multiple outcomes. In Part II, we discuss benefit:risk evaluation in clinical trials by using outcomes to analyze patient rather than patients to analyze outcomes.

PART I: The effects of interventions are multidimensional. Use of more than one outcome offers an attractive design feature in clinical trials as they capture more complete characterization of the benefit and risk of an intervention and provide more informative intervention comparisons. The tutorial will focus on design and analysis of clinical trials with such multiple outcomes. The first part of the tutorial will focus on methods for clinical trial designs evaluating efficacy of two interventions with multiple primary endpoints, especially co-primary endpoints. “Co-primary” means that a trial is designed to evaluate if the test intervention is superior (or noninferior) to the control on all primary endpoints. We describe methods for power and sample size calculations in clinical trials with multiple endpoints including recently developed approaches. We include real clinical trial examples to illustrate the concepts and to help participants apply the methods in practice, and illustrate how to implement the methods using standard statistical software including R and SAS.

PART 2: In the future, clinical trials will have an increased emphasis on pragmatism, providing a practical description of the effects of new treatments in realistic clinical settings. Accomplishing pragmatism requires better summaries of the totality of the evidence that allow for informed benefit:risk decision-making and in a way that clinical trials consumers—patients, physicians, insurers—find transparent. The current approach to the analysis of clinical trials is to analyze efficacy and safety separately and then combine these analyses into a benefit:risk assessment. Many assume that this will effectively describe the impact on patients. But this approach is suboptimal for evaluating the totality of effects on patients. In part II of the tutorial, we will describe a broad vision for the future of clinical trials consistent with increased pragmatism. Greater focus on using outcomes to analyze patients rather than patients to analyze outcomes particularly in late-phase/stage clinical trials is an important part of this vision. We discuss the desirability of outcome ranking (DOOR) and the partial credit strategy for design and analysis of clinical trials based on benefit:risk assessment. These strategies involve utilizing composite benefit:risk endpoints with a goal of understanding how to analyze one patient before trying to figure out how to analyze many. With a desire to measure and weigh outcomes that are most important from the patient’s perspective, we discuss using patients as a resource to inform analyses.

DAY 2 | TUESDAY, AUGUST 27, 2019

MAIN CONFERENCE

8:30AM-4:30PM **REGISTRATION**
RECEPTION, MAIN ENTERANCE, 1F

8:45-9:30AM **OPENING SESSION**
SAKURA, 1F

WELCOME REMARKS

Jie Chen
Merck Sharp & Dohme Corp.

Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center

Satoshi Morita
Kyoto University

OPENING REMARKS

Yasuhiro Fujiwara
Pharmaceutical and Medical Devices Agency

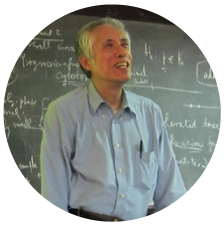
Yasuo Ohashi
Chuo University

9:30-10:15AM **PLENARY SESSION I**
SAKURA, 1F

Chair

Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center

Keynote Speaker



Adaptive Design of Confirmatory Clinical Trials: Regulatory Perspectives and Recent Advances

Tze Leung Lai
Stanford University

10:15-10:45AM **REFRESHMENT BREAK**

10:45AM -12:15PM **INVITED SESSION IS01**
SAKURA, 1F

ENHANCING REGULATORY DECISION MAKING TO SUPPORT DRUG DEVELOPMENT: US FDA PILOT PROGRAMS ON COMPLEX INNOVATIVE DESIGNS AND MODEL-INFORMED DRUG DEVELOPMENT

Organizers

Olga V. Marchenko
Bayer

José Pinheiro
Janssen Research & Development

Chair

Jeff Maca
Bayer

Speakers

Promoting the Use of Complex Innovative Trial Designs: An Overview

Dionne L. Price
US Food and Drug Administration

Model-Informed Drug Development at the US Food and Drug Administration: A Perspective on Progress

Issam Zineh
US Food and Drug Administration

Panelists

Frank Bretz
Novartis Pharma AG

Norisuke Kawai
Pfizer Japan Inc.

Olga V. Marchenko
Bayer

José Pinheiro
Janssen Research & Development

Martin Posch
Medical University of Vienna

Dionne L. Price
US Food and Drug Administration

Issam Zineh
US Food and Drug Administration

10:45AM-12:15PM **INVITED SESSION IS03**
ROOM 510, 5F

RECENT DEVELOPMENT AND CHALLENGES IN BIOEQUIVALENT OR BIOSIMILAR ASSESSMENT

Organizers

Hsiao-Hui Tsou
National Health Research Institutes

Seung-Ho Kang
Yonsei University

Chair

Victoria Chang
BeiGene

Speakers

Statistical Considerations for Demonstration of Analytical Similarity

Harry Yang
Astra Zeneca

Recent Development Strategies and Challenges in Biosimilarity Assessment

Heike Woehling
Sandoz Biopharmaceuticals

Effects of Between-Batch Variability on the Type I Error Rate in Biosimilar Development

Seung-Ho Kang
Yonsei University

Statistical Quality Control for Biosimilar Assessment

Hsiao-Hui Tsou
National Health Research Institutes

10:45AM-12:15PM **TOPIC-CONTRIBUTED SESSION TC16**
ROOM 554, 5F

THE IMPLEMENTATION OF ICH E17 IN ASIAN REGIONS

Organizers

Chin-Fu Hsiao
National Health Research Institutes

Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center

Chair

Chin-Fu Hsiao
National Health Research Institutes

Speakers

Taiwan CDE's Experience to Review MRCT Results

I-Chun Lai
Taiwan Center for Drug Evaluation

Key Principles of the ICH E17 and Their Implementation

William W. Wang
Merck Sharp & Dohme Corp.

Panelists

Tony Guo
BeiGene Ltd.

I-Chun Lai
Taiwan Center for Drug Evaluation

Nobushige Matsuoka
Pfizer Japan Inc.

Mey Wang
Taiwan Center for Drug Evaluation

William W. Wang
Merck Sharp & Dohme Corp.

10:45AM-12:15PM **TOPIC-CONTRIBUTED SESSION TC02**
ROOM 555, 5F

NEW DEVELOPMENTS FOR STATISTICAL METHODS IN PERSONALIZED MEDICINE

Organizer

Menggang Yu
University of Wisconsin – Madison

Chair

Takashi Sozu
Tokyo University of Science

Speakers

Diagnosis-Group-Specific Translational Care Program Recommendation for Thirty-Day Rehospitalization Reduction

Menggang Yu
University of Wisconsin – Madison

Comparative Intervention Scoring for Assessing Heterogeneity of Long-term Health System Intervention Effects

Jared Huling
Ohio State University

Change-Point Detection for Infinite Horizon Dynamic Treatment Regimes

Yair Goldberg
Technion

Multi-Category Individualized Treatment Regime Using Outcome Weighted Learning

Jin Xu
East China Normal University

10:45AM-12:15PM **CONTRIBUTED SESSION CS01**
ROOM 509, 5F

Chair

Taro Amagasaki
Novartis Pharma K.K.

Speakers

Integration of Elicited Expert Information via a Power Prior in Bayesian Variable Selection: Application to Colon Cancer Data

Sandrine Boulet
INSERM

Assessing Overall Treatment Effect Based on Robust Estimation in Multi-Regional Clinical Trials

Shuhei Kaneko
Novartis Pharma K.K.

Robust Estimates of Regional Treatment Effects in Multiregional Randomized Clinical Trial with Ordinal Response

Chongyang Duan
Southern Medical University

Using Cure Rate Models to Characterize Survival Data in Oncology

Kohinoor Dasgupta
Novartis Healthcare Pvt. Lmt.

Design and Analysis of Biosimilarity with an Estimated Margin on Interval Estimations

Chieh Chiang
National Health Research Institutes

Introducing the BGLIMM Procedure for Bayesian Generalized Linear Mixed Models

Fang Chen
SAS Institute

12:15-1:30PM **LUNCH BREAK**
ROOM E, 1F

1:30 -3:00PM **INVITED SESSION IS06**
SAKURA, 1F

USE OF MACHINE LEARNING AND AI FOR PRECISION MEDICINE IN DRUG DEVELOPMENT

Organizer

Ivan SF Chan
AbbVie Inc.

Chair

Ivan SF Chan
AbbVie Inc.

Speakers

Subgroup Identification in Precision Medicine

Xin Huang
AbbVie Inc.

Ivan SF Chan
AbbVie Inc.

How to Use Machine Learning Algorithms in Clinical Development

Yoshitake Kitanishi
Shionogi & Co., LTD.

Masakazu Fujiwara
Shionogi & Co., LTD.

The Future Is Now, but Where We Should Focus

Haoda Fu
Eli Lilly & Co.

Estimation and Validation of Regressions for Precision Medicine using Real World Data

Lu Tian
Stanford University

1:30 -3:00PM **INVITED SESSION IS02**
ROOM 510, 5F

STATISTICAL DESIGNS AND CONSIDERATIONS IN EARLY CLINICAL DEVELOPMENT

Organizer

Chin-Fu Hsiao
National Health Research Institutes

Chair

Tong Gao
IQVIA

Speakers

An Adaptive Phase I/II Design

Chin-Fu Hsiao
National Health Research Institutes

Two-stage Phase I/II Designs

Yuh-Ing Chen
National Central University

The Win Ratio: On Interpretation and Handling of Ties

Victoria Chang
BeiGene

Statistical Design and Analysis of Rare Diseases Clinical Trials

Shein-Chung Chow
Duke University

1:30 -3:00PM **TOPIC-CONTRIBTUED SESSION TC07**
ROOM 554, 5F

MULTIPLICITY ISSUES IN COMPLEX CLINICAL TRIALS

Organizers

Dong Xi
Novartis

Kentaro Sakamaki
Yokohama City University

Chair

Ying Lu
Stanford University

Speakers

An Enhanced Mixture Method for Constructing Gatekeeping Procedures in Clinical Trials

Thomas Brechenmacher
IQVIA Japan

Group Sequential Designs for Clinical Trials with Multiple Survival Endpoints

Kentaro Sakamaki
Yokohama City University

Practical Strategies for Testing Co-primary Endpoints in Group-sequential Clinical Trials

Koko Asakura
National Cerebral and Cardiovascular Center

A Case Study of Refining Testing Strategy Using Graphical Approach

Naoko Kataoka
Novartis Japan K.K.

1:30-3:00PM **TOPIC-CONTRIBTUED SESSION TC01**
ROOM 555, 5F

BIOSTATISTICIAN ROLE IN INNOVATIVE TRIAL DESIGN IN THE NEW ERA OF DRUG DEVELOPMENT

Organizer

Summer Xia
Novartis

Chair

Valerie L. Durkalski-Mauldin
Medical University of South Carolina

Speakers

Improving the Assessment of Probability of Success in Late Stage Drug Development

Lisa Hampson
Novartis

A Statistical Framework for Quantitative Decision Making in Early Clinical Development

Weidong Zhang
Pfizer Inc.

Comparison of Frameworks for Tipping Point Analyses

Summer Xia
Novartis

Dynamic Bayesian Decision Making in Early Phase Trials Using Historical Information

Fan Xia
BeiGene Ltd.

1:30 -5:00PM **IN-CONFERENCE WORKSHOP I**
ROOM 509, 5F

INNOVATIVE AND FLEXIBLE DESIGNS FOR CLINICAL TRIALS IN THE ERA OF PRECISION MEDICINE

Sponsored by 国立循環器病研究センター National Cerebral and Cardiovascular Center

Organizer

Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center

Moderator

H.M. James Hung
US Food and Drug Administration

Instructors

James Wason
Newcastle University

Florian Klinglmüeller
Austrian Medicines & Medical Devices Agency

3:00-3:30AM **REFRESHMENT BREAK**

3:30 -5:00PM **INVITED SESSION IS19**
SAKURA, 1F

INDUSTRY LEADERSHIP PANEL DISCUSSION

Organizers

Jie Chen
Merck Sharp & Dohme Corp

Haiyan Xu
Janssen Research & Development

Chair

Jie Chen
Merck Sharp & Dohme Corp

Panelists

Francois Beckers
Merck Serono

Ivan SF Chan
AbbVie Inc.

Pandu Kulkarni
Eli Lilly & Co.

Kannan Natarajan
Pfizer Inc.

Akiko Okamoto
Janssen Research & Development

Susan Wang
Boehringer-Ingelheim Pharmaceuticals, Inc.

William W. Wang
Merck Sharp & Dohme Corp.

Sherry Zhao
Allergan

3:30-5:00PM **INVITED SESSION IS14**
ROOM 510, 5F

INNOVATIVE APPROACHES FOR TRIAL DESIGN AND ANALYSIS

Organizer

Jie Chen
Merck Sharp & Dohme Corp.

Chair

Frank Fan
Novartis

Speakers

BMA-Mod: A Bayesian Model Averaging Strategy for Determining Dose-Response Relationships in the Presence of Model Uncertainty

A. Lawrence Gould
Merck Sharp & Dohme Corp.

Practical Considerations of Sequential Analysis of the Restricted Mean Survival Time for Immuno-Oncology Trials

Ying Lu
Stanford University

BOP2: Bayesian Optimal Design for Phase II Clinical Trials with Binary, Co-primary and Other Complex Endpoints

Ying Yan
University of Texas MD Anderson Cancer Center

Estimand - An Alternative Implementation of the While on Treatment Strategy

Naitee Ting
Boehringer-Ingelheim Pharmaceuticals, Inc.

3:30 -5:00PM **TOPIC-CONTRIBUTED SESSION TC11**
ROOM 554, 5F

ADVANCES IN DESIGN AND ANALYSIS OF CLINICAL STUDIES THAT INCORPORATE INTERNAL AND EXTERNAL DATA SOURCES

Organizer

Yang Song
Vertex Pharmaceuticals Incorporated

Chair

Tony Guo
BeiGene Ltd.

Speakers

Target Population Statistical Inference with Data Integration across Multiple Sources: An Approach to Mitigate Information Shortage in Rare Disease Clinical Trials

Yang Song
Vertex Pharmaceuticals Inc.

Estimation of the Effect of the NSAID Celecoxib on the Risk of Cancer using Electronic Healthcare Record Data

Tasuku Okui
Kyushu University Hospital

Biomarker-integrated Clinical Trials with Threshold Selection and Enrichment

Xiaofei Wang
Duke University

Discussant

Jie Ding
MSD R&D (China) Ltd.

3:30 -5:00PM **TOPIC-CONTRIBUTED SESSION TC09**
ROOM 555, 5F

ADVERSE EVENTS IN CLINICAL TRIALS AND POST-MARKETING PHARMACOVIGILANCE

Organizers

Tim Friede
University Medical Center Göttingen

Brenda Crowe
Eli Lilly & Co.

Chair

Tim Friede
University Medical Center Göttingen

Speakers

Rationale and First Results from the SAVVY Project

Regina Stegherr
University of Ulm

A Bayesian Meta-analytic Approach for Safety Signal Detection in Randomized Clinical Trials

Motoi Odani
Ono Pharmaceutical Co., Ltd.

Modified Bayesian Confidence Propagation Neural Network for Signal Detection Analysis

Keisuke Tada
Sanofi. K.K.

Discussant

Yuki Ando
Pharmaceutical and Medical Devices Agency

Satoshi Hattori
Osaka University Graduate School of Medicine

6:00-8:00PM	**RECEPTION AND POSTER SESSION** **SWAN, 1F**

DAY 3 | WEDNESDAY, AUGUST 28, 2019

MAIN CONFERENCE

8:30AM-4:30PM REGISTRATION
RECEPTION, MAIN ENTERANCE, 1F

8:45-10:15AM PLENARY SESSION II
SAKURA, 1F

Chair
Satoshi Morita
Kyoto University

Keynote Speakers

Open Science, Data Sharing, and Reproducibility: What's All the Fuss About and Why Should Statisticians Care and Engage in the Journey?
Frank W. Rockhold
Duke University

Recent Advances in Regulatory Statistics in Imaging Diagnostics and Imaging Precision Medicine
Sue-Jane Wang
US Food and Drug Administration

10:15-10:45AM REFRESHMENT BREAK

10:45AM -12:15PM INVITED SESSION IS12
SAKURA, 1F

SOME INNOVATIVE APPROACHES TO TRIALS DESIGNS AND MEDICAL PRODUCT DEVELOPMENT

Organizers
Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center
H.M. James Hung
US Food and Drug Administration

Chair
Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center

Speakers

Master Protocol Design Considerations in Settings Where Randomized Controlled Trials Are Not Feasible
Sue-Jane Wang
US Food and Drug Administration

Sequential, Multiple-Assignment, Randomized Trials for COMparing Personalized Antibiotic StrategieS (SMART-COMPASS)
Scott R. Evans
George Washington University

Missing data treatment in Sequential Parallel Comparison Design Studies
Gheorghe Doros
Boston University

Discussant
H.M. James Hung
US Food and Drug Administration

10:45AM -12:15PM INVITED SESSION IS09
ROOM 510, 5F

STATISTICAL ISSUES AND METHODS FOR VACCINE DEVELOPMENT

Organizers
Frank Liu
Merck Sharp & Dohme Corp.
Jie Chen
Merck Sharp & Dohme Corp.

Chair
Frank Liu
Merck Sharp & Dohme Corp.

Speakers

Potential Study Designs for HIV Vaccine Efficacy Trials in the Era of an Expanding Portfolio of Non-Vaccine HIV Prevention Strategies
Holly Janes
Fred Hutchinson Cancer Research Center

Assessment of Correlate of Risk and Protection in Tetravalent Dengue Vaccine Efficacy Trials
Jing Jin
Sanofi R&D Beijing

Quantitative Decision-Making Framework for Phase III Vaccine Efficacy Trial
Wenji Pu
GlaxoSmithKline Plc.

Statistical Challenges of an Immunobridging Approach to Assess Clinical Benefit as the Basis for Licensure of a Prophylactic Ebola Vaccine
Bart Spiessens
Janssen Research & Development

Discussant
Wenquan Wang
Sanofi Pasteur

10:45AM -12:15PM TOPIC-CONTRIBUTED SESSION TC17
ROOM 554, 5F

INNOVATIVE AND STRATEGIC THINKING IN PEDIATRIC TRIAL AND EARLY DRUG DEVELOPMENT BASED ON BAYESIAN HIERARCHICAL MODEL

Organizer
Binqi Ye
Boehringer Ingelheim, China

Chair
Binqi Ye
Boehringer Ingelheim, China

Speakers

Leveraging Available Information in Pediatric Trial Designs and Analyses using Bayesian Modeling
Susan Wang

Boehringer-Ingelheim Pharmaceuticals, Inc.

A Robust Bayesian Approach for Using Co-data in Phase I Oncology Trials: An Application to Bridging Studies

Haiyan Zheng
Newcastle University

Introduction to the Bayesian Early-Phase Seamless Transformation (BEST) Platform Design

Jiaying Lyu
Fudan University

A Case study: A Bayesian Type Adaptive Dose Finding in a Clinical Trial with Multiple Agents

Wenxiao Zhou
Beigene, Ltd.

10:45AM -12:15PM **TOPIC-CONTRIBUTED SESSION TC08**
ROOM 555, 5F

INNOVATIVE METHODS TO SUPPORT THE DEVELOPMENT OF NEW PEDIATRIC MEDICINES

Organizer

Lisa Hampson
Novartis Pharma AG

Chair

Lisa Hampson
Novartis Pharma AG

Speakers

A Clinician's View of the Importance of Pediatric Extrapolation

Robert M. Nelson
Johnson & Johnson

Extrapolating Information from Adult to Paediatric Studies: a Comparison of Methods

Juan Jose Abellan-Andres
GlaxoSmithKline

Current Situation of Pediatric Drug Development and Evolving Discussion on Extrapolation in Japan

Hidefumi Nakamura
National Center for Child Health and Development

The Challenge of Implementing Bayesian Methods in Paediatric Studies: Our Experience at UCB

Rosalind J. Walley
UCB Pharma

10:45AM -12:15PM **TOPIC-CONTRIBUTED SESSION TC14**
ROOM 555, 5F

OTHER WAY FORWARD FOR DESIGN, SUMMARY MEASURES, AND ESTIMANDS IN SURVIVAL CLINICAL TRIALS

Organizers

Shogo Nomura
National Cancer Center

Tomohiro Shinozaki
Tokyo University of Science

Chair

Yuko Y. Palesch
Medical University of South Caronia

Speakers

Hazards of Proportional Hazards Assumption and Small Number of Events: Actual Clinical Problems in Oncology and Alternative Ideas

Shogo Nomura
National Cancer Center

Using Restricted Mean Survival Time in a Non-Inferiority Trial

Isao Yokota
Hokkaido University

Pairwise Pseudolikelihood Estimation of an Average Hazard Ratio under Nonproportional Hazards

Tomohiro Shinozaki
Tokyo University of Science

A Design Consideration on RCTs Assessing Superiority of Immuno-oncology Agents: Sample Size Determination and Monitoring

Takahiro Hasegawa
Shionogi & Co., Ltd.

12:15-1:30PM **LUNCH BREAK**
ROOM E, 1F

1:30 -3:00PM **INVITED SESSION IS04**
SAKURA, 1F

RETHINKING ESTIMATORS WITHIN THE ESTIMAND FRAMEWORK

Organizer

Dong Xi
Novartis

Chair

Frank Bretz
Novartis Pharma AG

Speakers

Semiparametric Copula-based Analysis for Treatment Effects in the Presence of Treatment Switching

Chia-Hui Huang
National Taipei University

What Estimands Do Recurrent Event Data Approaches Estimate When Terminal Event Exists?

Jiawei Wei
Novartis Pharma AG

Mixture of Multivariate t Linear Mixed Models with Missing Information

Tzy-Chy Lin
Taiwan Center for Drug Evaluation

Estimands and Estimation of Population-Averaged Parameters in Randomized Clinical Trials

Tosiya Sato
Kyoto University School of Public Health

1:30 -3:00PM **INVITED SESSION IS07**
ROOM 510, 5F

ADAPTIVE DESIGNS FOR SMALL POPULATION CLINICAL TRIALS

Organizer

Frank Bretz
Novartis Pharma AG

Chair

Chin-Fu Hsiao
National Health Research Institutes

Speakers

A Bayesian Nonparametric Utility-Based Design for Comparing Treatments to Resolve Air Leaks After Lung Surgery

Peter Müller
University of Texas at Austin

Clinical Trial Designs with Data-Driven Selection of Subgroups

Franz König
Medical University of Vienna

Increasing Evidence Designs in Small Population Clinical Trials

Andreas Faldum
University of Münster

Experiences with Adaptive Design Clinical Trials for Medical Device Development

Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center

Discussant

Yuki Ando
Pharmaceuticals and Medical Devices Agency

1:30 -3:00PM **TOPIC-CONTRIBUTED SESSION TC05**
ROOM 554, 5F

MACHINE LEARNING METHODS FOR IMPROVING CLINICAL DECISION MAKING AND PRECISION HEALTH CARE

Organizer

Yuanjia Wang
Columbia University

Chair

Haoda Fu
Eli Lilly & Co.

Speakers

Learning Optimal Individualized Treatment Strategies from Randomized Trials and Electronic Health Records

Yuanjia Wang
Columbia University

Application of Machine Learning to Real World Data

Shintaro Hiro
Pfizer R&D Japan

Joint Variable Screening in Accelerated Failure Time Models

Jinfeng Xu
The University of Hong Kong

Discussant

Ying Lu
Stanford University

1:30 -3:00PM **TOPIC-CONTRIBUTED SESSION TC04**
ROOM 555, 5F

BAYESIAN APPROACHES FOR THE UTILIZATION OF CO-DATA FOR EFFICIENT DRUG DEVELOPMENT

Organizer

Tomoyuki Kakizume
Novartis Pharma K.K.

Chair

Lisa Hampson
Novartis Pharma AG

Speakers

Bayesian Dose- Finding Phase I Trial Design Incorporating Historical Data from a Preceding Trial

Kentaro Takeda
Astellas Global Development Inc.

Selection of Robust Meta-Analytic-Predictive Priors based on the Evaluation of Operating Characteristics for Proof-of-Concept Studies

Yi Cheng
China Novartis Institutes for Biomedical Research Co., Ltd

Utility of Bayesian Single-Arm Design in New Drug Application for Rare Cancers in Japan

Akihiro Hirakawa
The University of Tokyo

Use of Co-data for Interim Analysis in Clinical Trials

Tomoyuki Kakizume
Novartis Pharma K.K.

1:30 -5:00PM **IN-CONFERENCE WORKSHOP II**
ROOM 509, 5F

ADAPTIVE MULTI-ARM MULTI-STAGE (MAMS) DESIGNS IN CONFIRMATORY CLINICAL TRIALS: A PRACTICAL INTRODUCTION TO THE STATISTICAL METHODOLOGY AND ITS APPLICATION

Sponsored by 国立循環器病研究センター National Cerebral and Cardiovascular Center

Organizer

Yannis Jemiai
Cytel Inc.

Instructors

Yannis Jemiai
Cytel Inc.

Lingyun Liu
Cytel Inc.

Hrishikesh Kulkarni
Cytel Inc.

3:00-3:30PM **REFRESHMENT BREAK**

3:30 -5:00PM **INVITED SESSION IS18**
SAKURA, 1F

INFERENCE AND DECISION MAKING FOR CONTEMPORARY DRUG DEVELOPMENT AND APPROVAL

Organizer

Satoshi Morita
Kyoto University

Chair

Satoshi Morita
Kyoto University

Speakers

Journey of Bayesian Inference and Decision Making on Drug Development and Approval

J. Jack Lee
University of Texas MD Anderson Cancer Center

Update Your Prior: Use of Bayesian Methods in Drug Development

Martin Posch
Medical University of Vienna

Panelists

Andy Grieve
UCB Pharma

J. Jack Lee
University of Texas MD Anderson Cancer Center

Martin Posch
Medical University of Vienna

Susan Wang
Boehringer-Ingelheim Pharmaceuticals, Inc.

3:30 -5:00PM **INVITED SESSION IS10**
ROOM 510, 5F

RECENT DEVELOPMENT ON MISSING DATA ISSUES UNDER ICH E9 (R1) ESTIMAND FRAMEWORK

Organizers

Frank Liu
Merck Sharp & Dohme Corp.

Jie Chen
Merck Sharp & Dohme Corp.

Chair

Jie Chen
Merck Sharp & Dohme Corp.

Speakers

Principal Stratification: A Strategy for Intercurrent Events that Lead to Unascertainable Outcomes or Confounding

Bohdana Ratitch
Eli Lilly & Co.

Post E9 (R1) World: Points to Consider from Industry's Point of View

Satoru Tsuchiya
Sumitomo Dainippon Pharma, Co., Ltd.

Implementation of Estimand Concept in Immunology Disease Area

Na Hu
Boehringer-Ingelheim Inc., Shanghai, China.

On Statistical Methods for Some Common Hypothetical Estimands in Clinical Trials

Frank Liu
Merck Sharp & Dohme Corp.

3:30 -5:00PM **TOPIC-CONTRIBUTED SESSION TC13**
ROOM 554, 5F

DATA SCIENCE FOR MEDICINE

Organizer

Lisa Hampson
Novartis Pharma AG

Chair

Lisa Hampson
Novartis Pharma AG

Speakers

Integrative Analysis of Genetic, Transcriptomic and Functional Data in Identification of Potential Driver Genes in Tumors

Chen Suo
Fudan University

A Bivariate Shared Parameter Model for Intensive Longitudinal Data Subject to Informative Missing

Xiaolei Lin
University of Chicago

Data Processing and Data Analysis with Real World Big Data

Kazuo Ishii
Kurume University

Sequential Adaptive Subject and Variable Selection for Generalized Estimating Equation Methods

Yuan-Chin Chang
Institute of Statistical Science, Academia Sinica

3:30 -5:00PM **TOPIC-CONTRIBUTED SESSION TC10**
ROOM 555, 5F

DESIGNING CLINICAL TRIALS WITH RECURRENT EVENTS

Organizers

Tim Friede
University Medical Center Göttingen

Satoshi Hattori
Osaka University

Chair

Satoshi Hattori
Osaka University

Speakers

Designing a Trial in Multiple Sclerosis with Relapses as Endpoint

Isao Tsumiyama
Novartis Pharma K.K.

Introducing a Clinical Trial Sample Size Calculation: Experiences in Hemophilia A using recurrent events

Wataru Ohtsuka
Chugai Pharmaceutical Co., Ltd.

Incorporating Variance Miss-Specification in Designing Comparative Clinical Trials with Over-Dispersed Count Data

Masataka Igeta
Hyogo College of Medicine

Adaptive Designs for Clinical Trials with Recurrent Events

Tim Friede
University Medical Center Göttingen

Discussant

Tzy-Chy Lin
Taiwan Center for Drug Evaluation

DAY 4 | THURSDAY, AUGUST 29, 2019

MAIN CONFERENCE

8:30AM-4:30PM **REGISTRATION**
RECEPTION, MAIN ENTERANCE, 1F

8:45-10:15AM **PLENARY SESSION III**
SAKURA, 1F

Chair
Jie Chen
Merck Sharp & Dohme Corp.

Keynote Speakers

Statistical Innovation and Contribution Today. Will We Need Statisticians Tomorrow?
Robert J. Hemmings
Consilium Salmonson and Hemmings

Regulatory Reform and Challenges of the Japanese Pharmaceutical Regulations
Daisaku Sato
Pharmaceuticals and Medical Devices Agency

10:15-10:45AM **REFRESHMENT BREAK**

10:45AM -12:15PM **INVITED SESSION IS05**
SAKURA, 1F

DEMYSTIFYING ESTIMANDS FOR LIFE HISTORY PROCESSES

Organizer
Jiawei Wei
Novartis

Chair
Jiawei Wei
Novartis

Speakers

Recurrent Event Analysis Yielding Estimands with a Causal Interpretation
Richard J. Cook
University of Waterloo

Assessment of a Treatment Effect for Recurrent Event Data in the Presence of a Terminal Event
Philip Hougaard
Lundbeck

Efficiency Comparison of Time-To-First and Recurrent Event Analyses with A Focus on Heart Failure Trials
Arno Fritsch
Bayer

Causal Mediation of Semi-competing Risks
Yen-Tsung Huang
Institute of Statistical Science, Academia Sinica

Discussant
Mey Wang
Taiwan Center for Drug Evaluation

10:45AM -12:15PM **INVITED SESSION IS11**
ROOM 510, 5F

METHODOLOGY RESEARCH FOR BIOPHARMACEUTICAL INDUSTRY

Organizers
Frank Liu
Merck Sharp & Dohme Corp.
Jie Chen
Merck Sharp & Dohme Corp.

Chair
Frank Liu
Merck Sharp & Dohme Corp.

Panelists
Frank Bretz
Novartis Pharma AG
Ivan SF Chan
AbbVie Inc.
José Pinheiro
Janssen Research & Development
A. Lawrence Gould
Merck Sharp & Dohme Corp.

10:45AM -12:15PM **INVITED SESSION IS15**
ROOM 554, 5F

ISSUES IN ADAPTIVE AND COMPLEX CLINICAL TRIAL DESIGNS

Organizer
Franz König
Medical University of Vienna

Chairs
Franz König
Medical University of Vienna
Martin Posch
Medical University of Vienna

Speakers

Patient-Centred Clinical Trial Designs to Support Precision Healthcare
Andrew P. Grieve
UCB Pharma

Bias and Type I Error of Promising Zone Designs Testing One or More Hypotheses
Florian Klinglmüeller
Austrian Medicines & Medical Devices Agency

Adapting Study Designs Based on All Available Information from Baseline up to the Primary Endpoint: Is It Worth the Effort?

An Vandebosch
Janssen Research and Development

From Adaptive Designs to Complex Innovative Trials: What Has Changed?

Yannis Jemiai
Cytel

When and How Should Precision Medicine Trials Be Adaptive?

James Wason
Newcastle University

10:45AM -12:15PM **TOPIC-CONTRIBUTED SESSION TC03**
ROOM 555, 5F

REGULATORY SUBMISSIONS IN ELECTRONIC FORMAT

Organizer

Hong Qi
Merck Sharp & Dohme Corp.

Chair

Mary N. Varughese
Merck Sharp & Dohme Corp.

Speakers

Study Data Technical Rejection Criteria, Validation, and Self-Check Worksheet

Ethan Chen
US Food and Drug Administration

Differences between FDA and PMDA for E-data Submission

Masato Suzuki
MSD K.K.

NMPA Reform and Keytruda Filing in China

Jing Zhang
Merck Sharp & Dohme Corp.

Information Requests during an FDA Review

Hong Qi
Merck Sharp & Dohme Corp.

10:45AM -12:15PM **TOPIC-CONTRIBUTED SESSION TC15**
ROOM 509, 5F

REAL-WORLD DATA: IMPLICATIONS AND CHALLENGES FOR MEDICAL PRODUCT DEVELOPMENT

Sponsored by AMED-funded Project “Regulatory Science Research to Achieve Efficiency of Clinical Research and Development with Utilization of Patient Registry”

Organizers

Shogo Nomura
National Cancer Center

Taro Shibata
National Cancer Center

Hisateru Tachimori
National Center of Neurology and Psychiatry

Chair

Toshimitsu Hamasaki
National Cerebral and Cardiovascular Center

Speakers

Validity and Reliability of Real-World Data for Medical Product Development

Taro Shibata
National Cancer Center

Statistical Methods in Use of Real-world Data in Medical Product Development: Propensity-Based Methods

Hisateru Tachimori
National Center of Neurology and Psychiatry

Instrumental Variable Analysis in Clinical Trials Incorporating Patient Registry Databases as Controls

Yukari Uemura
The University of Tokyo

Discussants

Scott R. Evans
George Washington University

Kit C.B. Roes
Radboud University Medical Centre

12:15-1:30AM **LUNCH BREAK**
ROOM E, 1F

1:30-3:00PM **INVITED SESSION IS16**
SAKURA, 1F

ONCOLOGY TRIALS WITH NON-PROPORTIONAL HAZARDS

Organizers

Franz König
Medical University of Vienna

Martin Posch
Medical University of Vienna

Chairs

Franz König
Medical University of Vienna

Martin Posch
Medical University of Vienna

Speakers

A Modestly Weighted Logrank Test
Carl-Fredrik Burman
AstraZeneca R&D Gothenburg

Design Challenges in the Era beyond Proportional Hazard Assumptions
Armin Schueler
Merck KGaA

The Consideration of Non-Proportional Hazards when Choosing a Randomization Procedure in Survival Studies
Viviane Rückbeil
RWTH Aachen University
Ralf-Dieter Hilgers
RWTH Aachen University

Evaluating the Impact of Delayed Effects in Oncology Confirmatory Clinical Trials
Jose Luis Jimenez
Novartis Pharma AG

1:30 -3:00PM **INVITED SESSION IS13**
ROOM 510, 5F

STATISTICAL METHODS IN DRUG DEVELOPMENT

Organizer

Hongyuan Cao
Florida State University

Chair

Jiawei Wei
Novartis Institutes for BioMedical Research

Speakers

Accounting for Pilot Study Uncertainty in Sample Size Determination of Randomized Controlled Trials
Jie Chen
Merck Sharp & Dohme Corp.

When Convention Meets Practicality: Pooled Analysis Testing under the Two-Study Paradigm
Frank Bretz
Novartis Pharma AG

Roles of Frailty in Modelling Competing-Risks Data: Assessing Treatment Effect
Il Do Ha
Pukyong National University

Accelerating Clinical Development by Incorporating Historical Controls in Proof of Concept Studies
Ivan SF Chan
AbbVie Inc.

1:30 -3:00PM **INVITED SESSION IS17**
ROOM 554, 5F

STATISTICAL METHODOLOGY FOR THE COMPARATIVE ASSESSMENT OF QUALITY ATTRIBUTES

Organizer

Florian Klinglmüeller
Austrian Medicines & Medical Devices Agency

Chair

Florian Klinglmüeller
Austrian Medicines & Medical Devices Agency

Speakers

Can Statistical Inference Improve the (Bio-) Similarity Exercise?
Kit C.B. Roes
Radboud University Medical Centre

Similarity Assessment of Quality Attributes: The Calculation of Operating Characteristics to Compare Different Statistical Approaches
Thomas Stangler
Novartis Pharma AG.

Analytical Similarity and Comparability: What is the Question?
Bruno E. Boulanger
PharmaLex Belgium

Discussant

Shein-Chung Chow
Duke University

1:30 -3:00PM **TOPIC-CONTRIBUTED SESSION TC12**
ROOM 555, 5F

OPPORTUNITIES AND CHALLENGES FOR THE USE OF PARAMETRIC LONGITUDINAL MODELLING IN DRUG DEVELOPMENT

Organizer

Tobias Mielke
Janssen-Cilag GmbH

Chair

José Pinheiro
Janssen Research & Development

Speakers

Opportunities and Pitfalls in the use of Nonlinear Mixed-Effects Models for Leveraging Longitudinal Information in Drug Development
Andrew C. Hooker
Uppsala University

Quantifying and Addressing Model Uncertainty on Longitudinal Data in the Design and Analysis of Clinical Studies
Tobias Mielke
Janssen Pharmaceuticals

Leveraging Parametric Longitudinal Modeling to Improve Drug Development Efficiency

Olga V. Marchenko
Bayer

Calibrated Predictions of Survival based on Tumor Size Dynamics and New Lesions in Lung Cancer via Joint Modeling Approach

Katsuomi Ichikawa
AstraZeneca K.K.

Discussant

Dionne L. Price
US Food and Drug Administration

1:30 -3:00PM **TOPIC-CONTRIBUTED SESSION TC06**
ROOM 509, 5F

UTILIZATION OF SUBGROUP AND CAUSAL INFERENCE TOWARDS PERSONALIZED MEDICINE

Organizer

Ming Tan
Georgetown University

Chair

Chiung-Yu Huang
University of California San Francisco

Speakers

Identifying Targeted Patients Population in Major Depressive Disorder by Enhanced Enrichment Design

Peter Zhang
Otsuka Development & Commercialization Inc.

Double-Robust Inference for Differences in Restricted Mean Lifetimes Using Pseudo-Observations

Sangbum Choi
Korea University

Fortified Robust Estimate of Rx Effects in Nonrandomized External Control Trial, Subgroup and RWD Analysis

Ming Tan
Georgetown University

3:00-3:30PM **REFRESHMENT BREAK**

REGULATORY SYMPOSIUM

3:30 -5:00PM **REGULATORY SESSION RS03**
SAKURA, 1F

ICH-E17: HOW TO IMPLEMENT MULTI-REGIONAL CLINICAL TRIALS BASED ON THE GUIDANCE?

Organizer

Yuki Ando
Pharmaceutical and Medical Devices Agency

Chair

Hideharu Yamamoto
Chugai Pharmaceutical Co., Ltd.

Speakers

TBD

Osamu Komiyama
Pfizer Japan Inc.

TBD

William W. Wang
Merck, Sharp & Dohme, Corp.

TBD

Hiroyuki Sato
Pharmaceutical and Medical Devices Agency

3:30 -5:00PM **REGULATORY SESSION RS01**
ROOM 510, 5F

HARMONIZATION OF MODEL-INFORMED DRUG DEVELOPMENT APPROACHES IN REGULATORY REVIEW AND DECISIONS

Organizers

Olga V. Marchenko
Bayer

José Pinheiro
Janssen Research & Development

Chair

Olga V. Marchenko
Bayer

Speaker

Model Informed Drug Development Good Practices: An Industry Perspective

Scott F. Marshall
Pfizer R&D LTD

Panelists

Yuki Ando
Pharmaceutical and Medical Devices Agency

Robert J. Hemmings
Consilium Salmonson and Hemmings

Scott F. Marshall
Pfizer R&D LTD

José Pinheiro
Janssen Research & Development

Hiromi Tanii
Janssen

Issam Zineh
US Food and Drug Administration

7:00 -9:00PM **CONFERENCE DINNER**
FUNATSURU KYOTO KAMOGAWA RESORT

DAY 5 | FRIDAY, AUGUST 30, 2019

8:30AM-11:30PM **REGISTRATION**
RECEPTION, MAIN ENTERANCE, 1F

REGULATORY SYMPOSIUM

8:45-10:15AM **REGULATORY SESSION RS04**
SAKURA, 1F

ICH-E9(R1)- GUIDANCE CONCEPT AND IMPLEMENTATION

Organizer

Yuki Ando
Pharmaceutical and Medical Devices Agency

Chair

Satoru Tsuchiya
Sumitomo Dainippon Pharma Co., Ltd

Speakers

TBD
Robert J. Hemmings
Consilium Salmonson and Hemmings

TBD
Hideki Suganami
Kowa Pharmaceutical Co.

TBD
Yuki Ando
Pharmaceutical and Medical Devices Agency

10:15-10:30AM **STRETCH BREAK**

10:30AM-12:00PM **REGULATORY SESSION RS02**
SAKURA, 1F

ESTIMAND, MISSING DATA, AND SENSITIVITY ANALYSIS

Organizer

Mey Wang
Taiwan Center for Drug Evaluation

Chairs

Frank Bretz
Novartis Pharma AG

Panelists

Yuki Ando
Pharmaceutical and Medical Devices Agency

Robert J. Hemmings
Consilium Salmonson and Hemmings

Yen-Tsung Huang
Institute of Statistical Science, Academia Sinica

H.M. James Hung
US Food and Drug Administration

Hideki Suganami
Kowa Pharmaceutical Co.

Mey Wang
Taiwan Center for Drug Evaluation

MAIN CONFERENCE

8:45-10:15AM **CONTRIBUTED SESSION CS02**
ROOM 510, 5F

Chair

Tomokazu Inomata
IQVIA

Speakers

Multiple Imputation with Auxiliary Variables in Longitudinal Clinical Trials: Imputation Models Using Bayesian Lasso and Tree-Based Approaches
Yusuke Yamaguchi
Astellas Pharma Inc.

Efficient, Doubly Robust Estimation of the Effect of Dose Switching for Switchers in a Randomised Clinical Trial
Kelly Van Lancker
Ghent University

A Variable Selection Criterion for Competing Risk Data with Pseudo-Observations
Kenichi Hayashi
Keio University

The Impact of Heterogeneity and Outliers on Flexible Shrinkage Estimators for Local Treatment Effects in Multi-Regional Clinical Trials
Naoki Isogawa
Pfizer R&D Japan

Meta-Analysis and Matrix Decomposition for Pattern Extraction and Patient-Level Prediction of Adverse Events
Kentaro Matsuura
Johnson & Johnson

Adaptive Power Prior for Sequential Clinical Trials - Application to Bringing Studies
Adrien Nigel Ollier
INSERM

10:15-10:30AM **STRETCH BREAK**

10:30AM-12:00PM **CONTRIBUTED SESSION CS03**
ROOM 510, 5F

Chair

Akira Wakana
MSD K.K.

Speakers

A Novel Bayesian Analysis of Dose-Response Relationship with Dynamic Generalized Linear Models in Oncology Phase I Study Using Power Priors to Incorporate Historical Data
Joji Mori
Eli Lilly Japan K.K.

Adaptive Study Design using Model Based Dose Escalation with Two Pharmacodynamical Endpoints
Dion Chen
Janssen Research and Development

Sample Size and Power Calculations for Reference-Based Imputation

Kimitoshi Ikeda
AbbVie GK

Bayesian Random-Effects Meta-Analysis of Phase I Dose-Finding Studies

Moreno Ursino
INSERM

Blinded Sample Size Re-estimation with Survival Data

Ryuji Uozumi
Kyoto University

12:00-12:15PM	**CLOSING** **SAKURA, 1F**

POSTER PRESENTATIONS

#50005: A Powerful Method to Meta-Analysis for Testing no Treatment Effects CANCELLED

Kuang FuCheng
Asia University

#50029: Concentration-QTc Analysis for Phase 1 Studies without a Placebo Arm

Yasushi Orihashi
Tokai University School of Medicine

#50030: Model Selection for Semiparametric Marginal Mean Regression Accounting for Within-Cluster Subsampling Variability and Informative Cluster Size

Chung Wei Shen
National Chung Cheng University

#50031: Bayesian Flexible Modeling the Odds under Case II Interval-Censored Data

Li-Chu Chien
Kaohsiung Medical University

#50032: Role of Baseline Covariates in ex-Vivo Bioassay for the Assessment of Intrasubject Parallelism

Hideaki Uehara
Tsumura & Co.

#50042: Log-rank Test and Its Handicap Procedure Using Computational Algebraic Statistics

Kotaro Mizuma
Osaka University

#50047: Adaptive Randomization for Multiarm Survival Clinical Trials Using Short-Term Response Information

Yu Mei Chang
Tunghai University

#50049: A Robust Association Test with Multiple Genetic Variants and Covariates

Jen-Yu Lee
Feng Chia University

#50055: Bayesian Model Selection on the Structural Equation Model: An Application to a Longitudinal Myopia Trial

Yi-Fu Wang
National Chung Cheng University

#50056: Statistical Approach with Right-Censored Survival Data for Design and Evaluation in the Multiregional Clinical Trial

Yu-Chieh Zheng
National Health Research Institutes

#50065: Using PMDA Drug Adverse Event Report Database, Study on Collective Background of Adverse Events

Shoko Kamiya
Keio Research Institute at SFC

#50071: The Use of Maximum a Posteriori Estimation for Selecting Dose in Phase I Clinical Trials

Wen-Jin Guo
National Health Research Institutes

#50075: Bioequivalence Assessment between Sugar-coated and Film-coated Eperisone Tablets using Reference Replicated Crossover Study for Highly Variable Drug

In-Hwan Baek
Kyungsung University

#50081: Clustering-based Basket Trial Design for Assessing Heterogeneity of Treatment Effect among Strata

Ryo Sadachi
The University of Tokyo

#50087: A Joint Modeling Approach for Predictions of Survival Based on Tumor Dynamics and New Lesions in EGFR Mutation-Positive Non-Small Cell Lung Cancer Patients Treated with Gefitinib or Carboplatin and Paclitaxel

Mario Nagase
AstraZeneca

#50091: Non-Asymptotic Properties and Behaviors for Random-Effects Meta-Analyses When the Number of Studies Is Small

Keisuke Hanada
Kagoshima University

#50098: Comparison of Hazards in Two-Arm Trials with Exponential Distributed Outcomes from the Bayesian Viewpoint

Masaaki Doi
Kyoto University

#50110: Comparison of Bayesian Equivalency Methods for Two Binomial Outcomes Using Bayesian Index

Yohei Kawasaki
Chiba University

#50137: G-estimation of Structural Nested Mean Models for Interval-Censored Data Using Pseudo-Observations

Shiro Tanaka
Kyoto University

#50138: Bayesian Evidence Synthesis and Assessment Techniques across Longitudinal Time Points

Airi Takagi
Tohoku University

#50146: Patient Subtypes Associated with Medication Persistence Using Latent Class Analysis

Shiori Nishimura
Keio University

#50150: A Robust Covariate Selection Method for the Limited Sampling Design in Population Pharmacokinetic Analysis

Asuka Nemoto
Teikyo University Graduate School of Public Health

#50163: Mediation and interaction of age, follicle stimulating hormone(FSH) and anti-müllerian hormone (AMH) on in vitro fertilization pregnancy

Han-Chih Hsieh
Institute of Statistical Science, Academia Sinica

#50164: Semiparametric Causal Mediation Modeling of Semi-Competing Risks

Ju-Sheng Hong
Institute of Statistical Science, Academia Sinica

#50165: A Novel Extension of Keyboard Design: MT-Keyboard with Multiple Toxicity Constraints

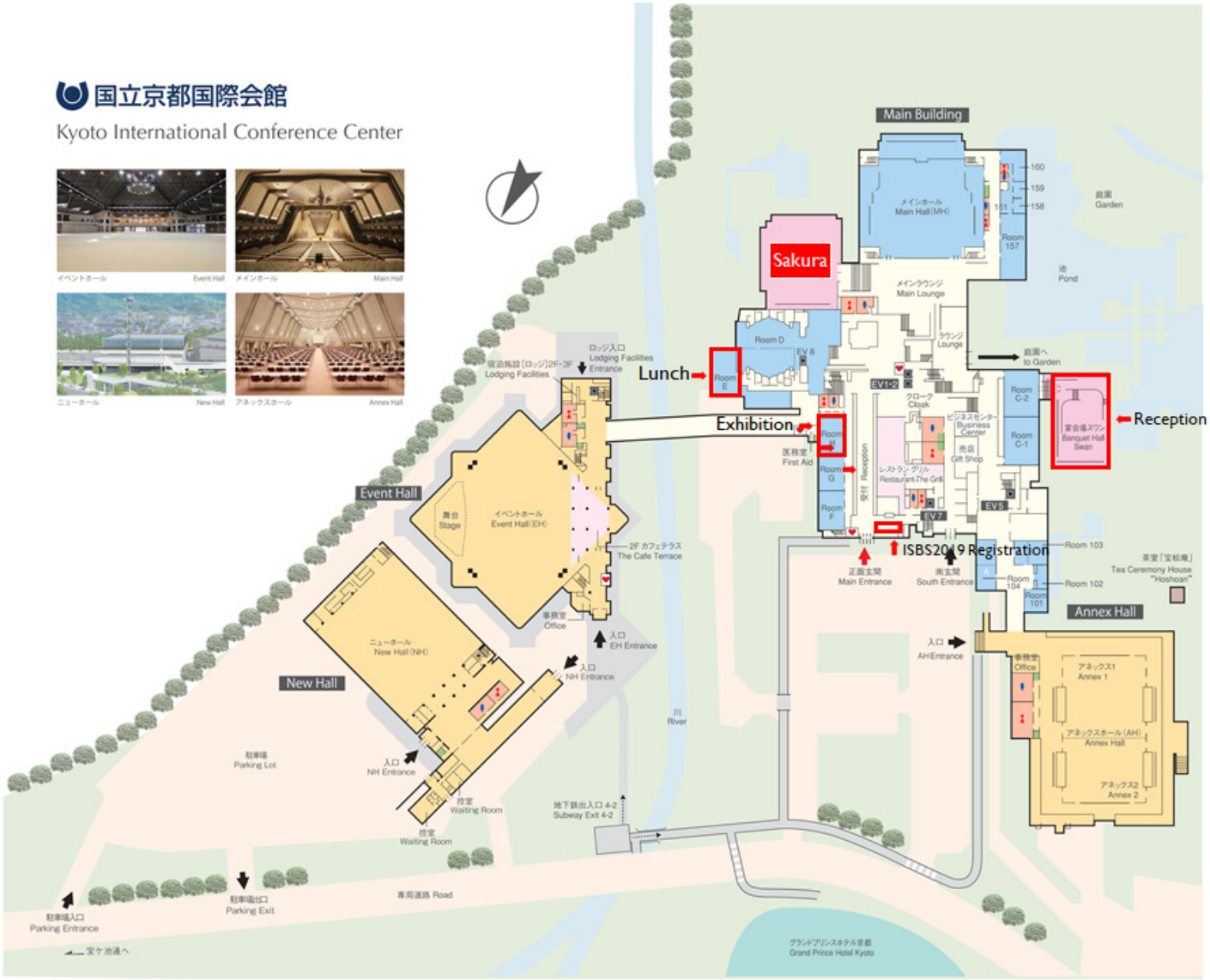
Fangrong Yan
China Pharmaceutical University

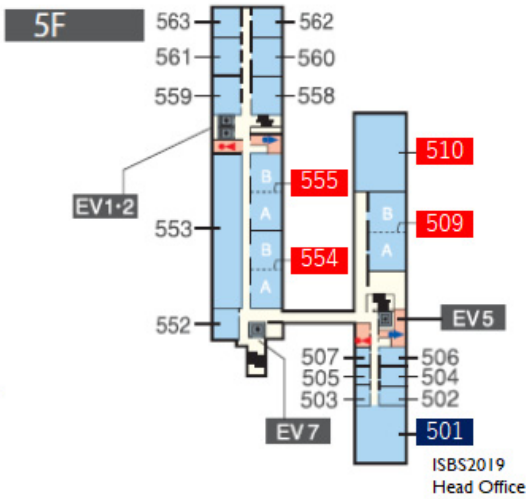
#50166: Causal Mediation of Chronic Hepatitis B or C on Mortality through Liver Cancer Incidence

Yi-Ting Huang
Institute of Statistical Science, Academia Sinica

#50167: Enterprise Investment Selection for the Kickstarter Projects

Yu-Jie, Huang
National Sun Yat-sen University


国立京都国際会館
Kyoto International Conference Center
Main Building
Sakura
Lunch
Exhibition
Reception
ISBS2019 Registration
Event Hall
New Hall
Annex Hall
Main Entrance
South Entrance
Parking Entrance
Parking Exit
Grand Prince Hotel Kyoto


5F
563
562
561
560
559
558
EV1·2
555
510
553
554
509
552
EV5
507
506
505
504
503
502
EV7
501
ISBS2019
Head Office

JMDC

Japan's Largest Claims Database.

☐ Payer-based DB

Data source : claim, enrollment information and health checkup from 130 + payers
Data period : January 2005 – the latest
Data volume : about 7 million enrollments

☐ Hospital-based DB

Data source : claim + DPC survey data from 190 + hospitals
Data period : April 2014 – the latest
Data volume : about 8 million patients

Our service

Data Provision service	Data Analysis service

JMDC Inc.

https://www.jmdc.co.jp/
pbmadmin@jmdc.co.jp
+81-3-5733-8614

Founded upon principles of excellence and innovation, PPD shares our clients' passion for delivering life-changing therapies to help people live healthier lives.

PPD SNBL

HELPING DELIVER LIFE CHANGING THERAPIES

St Luke's Tower 12F | 8-1 Akashi-cho, Chuo-ku
Tokyo 104-0044 Japan

www.ppdsnbl.co.jp

SOLVING THE WORLD'S TOUGHEST HEALTH CHALLENGES TAKES ALL OF US.

AbbVie starts with research and innovation to develop and deliver new treatments to manage some of the world's most difficult diseases.

Our global biopharmaceutical company builds our pipeline to provide solutions in therapeutic areas served by our proven expertise.

To make new solutions available to patients, we team with our scientific peers, physicians, governments and advocacy groups.

When we work together, the result is a remarkable impact on patients' lives and the healthcare systems which serve them.

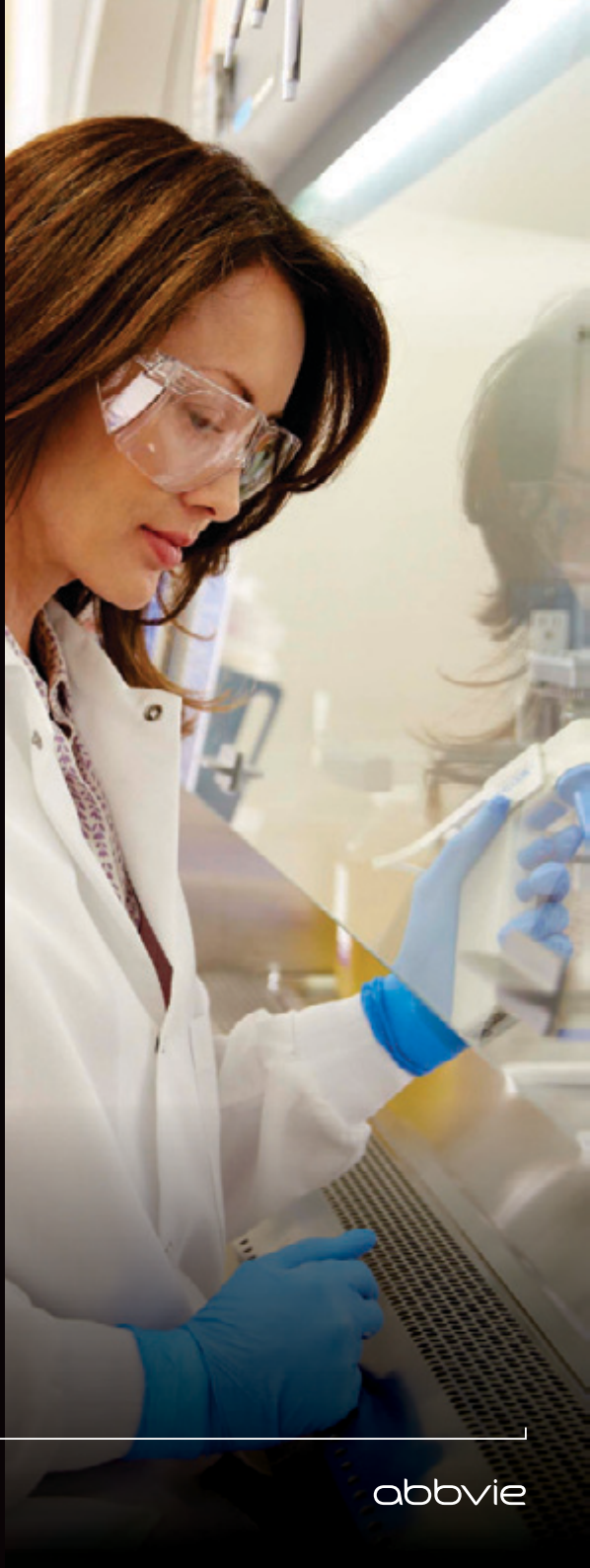
abbvie.com

170+ Countries

28,000+ Employees

21 R&D and Manufacturing Sites

ONE Priority: Our Patients



PEOPLE. PASSION.
POSSIBILITIES.

abbvie