Symposium on Dose Selection for Cancer Treatment Drugs

Event Organizers:
Stanford Cancer Institute (SCI), Stanford Center for Innovative Study Design (CISD), UCSF-Stanford Center of Excellence in Regulatory Science and Innovation (CERSI), University of Chicago Comprehensive Cancer Center

Symposium Objective: The goal of this workshop is to exchange research progress and discuss challenges in appropriate dosage for cancer treatments.

Both academic institutions and pharmaceutical industry have conducted early phase trials to select appropriate doses for later development of cancer treatments. The increasing need for the development of combination therapy due to resistance to monotherapy and poor tolerance of approved dose regimens underscores the need for a more efficient process of dose selection in the early stages of study design and refinement through the whole cycle of drug development and post-marketing research. Furthermore, with gaining insights of pharmacology and pharmacogenomics, multidisciplinary approaches are necessary to understand the exposure-response relationships, genomic modifications, modeling and simulation for dose findings, and new design for dose-optimization studies. This symposium will bring together researchers from academia and pharmaceutical industry to exchange research progress and discuss common challenges in appropriate dosage for cancer treatments.

Program, Date and Location (searchable Stanford map: https://campus-map.stanford.edu):

May 11, 2017. Short course on "Phase I/II Clinical Trial Design and Dose Finding"
***8:30am-4:00pm*, Alway Building M106, 300 Pasteur Drive, Stanford, CA, United States**
Instructors: Naitee Ting, Ph.D., and Qiqi Deng, Ph.D., Beohringer-Ingelheim, Inc., Editor of the book published by Springer, 2006.

May 12, 2017. Symposium Program on Dose Selection for Cancer Treatments
***8:20am-12:00pm*, *Munzer Auditorium*,** *Beckmann Center, 279 Campus Drive West, Ground Floor, Stanford, CA 94305*
***1:00pm-6:00pm*, *LK 130*,** *Li Ka Shing Center for Learning and Knowledge (LKSC), 291 Campus Drive, 1st Floor, Stanford, CA 94305*

Keynote Speakers:

- Dr. Rajeshwari Sridhara, Ph.D., Director of Division of Biometrics V, CDER, US FDA
- Dr. Shivaani Kummar, MD, FACP, Professor and Director, Phase I Clinical Research Program, Division of Oncology, Stanford Cancer Institute, Stanford University
- Dr. Peter Mueller, Ph.D., Professor, Division of Statistics and Scientific Computation, Department of Mathematics, University of Texas, Austin

Organization Committee: Ying Lu, Ph.D. (Co-Chair, Stanford University); Yuan Ji, Ph.D. (Co-Chair, University of Chicago); Philip Lavori, Ph.D. (Stanford University), Tze L. Lai Ph.D. (Stanford University), Shivaani Kummar, MD (Stanford University)

Registration and more detailed information about this Symposium:
http://med.stanford.edu/cisd/events/symposium-May2017.html

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PROGRAM

May 11, 2017. Short Course on Phase I/II Clinical Trial Design and Dose Finding

(searchable Stanford map: https://campus-map.stanford.edu)

8:30am-4:00pm, Alway Building M106, 300 Pasteur Drive, Stanford, CA, United States

In the process of drug discovery and drug development, understanding the dose-response relationship is one of the most challenging tasks. It is also critical to identify the right range of doses in early stages of clinical development so that Phase III trials can be designed to confirm some doses within this dose range. Usually at the beginning of Phase II, there is not a lot of available information to help guiding the study design. At this stage, Phase II clinical studies are needed to establish proof of concept (PoC), to identify a set of potentially effective and safe doses, and to estimate dose-response relationships.

Challenges in designing these studies include: selection of the dose frequency and the dose range, choice of clinical endpoints or biomarkers, and use of control(s), among others. Consequences of bad Phase II study designs may lead to the delay of the entire clinical development program or the waste of R&D investment. Misleading results obtained from poor designs could cause a Phase III program to confirm a wrong set of doses, or to stop developing a potentially useful drug. Therefore, it is critical to consider an entire drug development plan, to make best use of all the available information, and to include all relevant experts in designing Phase II dose response clinical trials. This presentation discusses some of these considerations.

Who should attend?

Who wants to gain knowledge in dose finding process in clinical development, including but not limited to statisticians, pharmacometricians, clinicians and clinical pharmacologists, etc.

Agenda:

Part I: Introduction and general considerations in DF (by Naitee Ting, Ph.D.)

- Overview of dose finding in clinical development
- FIH (First-time in humans), PK/PD and dosing Frequency
- Phase I non-life-threatening disease
- Phase I oncology
- Phase II proof of concept and Go/NoGo decision
- Dose range, number of doses and dose ranging.

Part II: Statistical methods in Dose-Finding (by Qiqi Deng, Ph.D.)

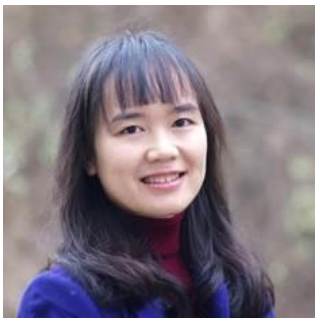
- BLRM and EWOC
- General concept of contrast test
- Ordinal Linear Logistics regression (OLCT)
- Multiple comparison procedure and modeling approach (MCPMod)
- Emax models
- Modeling and estimation, target dose, effective dose
- Optimal design in dose finding study
- Dose finding study for non-normal endpoint

Course materials: Slides, and "Dose Finding in Drug Development", published by Springer, Edited by Ting, N (2006).

Biography of Short Course Instructors

Dr. Naitee Ting, Ph.D., is a Fellow of American Statistical Association (ASA). He is currently a Director in the Department of Biostatistics and Data Sciences at Boehringer-Ingelheim Pharmaceuticals Inc. (BI). He joined BI in September of 2009, and before joining BI, he was at Pfizer Inc. for 22 years (1987-2009). Naitee received his Ph.D. in 1987 from Colorado State University (major in Statistics). He has an M.S. degree from Mississippi State University (1979, Statistics) and a B.S. degree from College of Chinese Culture (1976, Forestry) at Taipei, Taiwan.

Dr. Ting published articles in Technometrics, Statistics in Medicine, Drug Information Journal, Journal of Statistical Planning and Inference, Journal of Biopharmaceutical Statistics, Biometrical Journal, Statistics and Probability Letters, and Journal of Statistical Computation and Simulation. His book "Dose Finding in Drug Development" was published in 2006 by Springer, and is considered as the leading reference in the field of dose response clinical trials. The book "Fundamental Concepts for New Clinical Trialists", co-authored with Scott Evans, was published by CRC in 2015. Naitee is an adjunct professor of Columbia University, University of Connecticut and University of Rhode Island. Naitee has been an active member of both the ASA and the International Chinese Statistical Association (ICSA).



Dr. Qiqi Deng, Ph.D., is a Senior Principle Biostatistician at Boehringer Ingelheim Pharmaceutical. She is currently a member of the Methodology Expert team within global statistics, which focuses on statistical methodology innovation. Her research area includes hypothesis and modeling in dose finding, pragmatic considerations in designing dose finding trials, including adaptive design aspects. Before she joined the methodology group, she has served as leading statistician for multiple projects, across different clinical development phases and therapeutic areas. Dr. Deng received her bachelor's degree in Mathematics from Peking University in China, and obtained her Ph. D. in Statistics from University of Minnesota.

May 12: *Symposium on Dose Selection for Cancer Treatment Drugs*

(searchable Stanford map: https://campus-map.stanford.edu)

Morning Program (8:25am-12:00pm)
Location: Munzer Auditorium, Beckmann Center, 279 Campus Drive West, Ground Floor, Stanford, CA 94305

Registration starts from 7:45am

Time	Topic	Speaker
8:25-8:30am	**Welcome**	**Beverly Mitchell, MD** Director, Stanford Cancer Institute (SCI) George E. Becker Professor in Medicine
Session 1.	***Dose Selection in the Development of Cancer Treatment Drugs***	**Chair: Ying Lu, Ph.D.** Co-Director, Biostatistics Core, SCI Professor of Biomedical Data Science
8:30-9:20am	**TBD**	**Rajeshwari Srihdara, Ph.D.** Director of Division of Biometrics V, CDER, US FDA
9:20-10:10am	**TBD**	**Shivaani Kummar, MD, FACP** Director, Phase I Clinical Research Program, Professor of Medicine, Stanford
10:10-10:20am	***Break***	
Session 2.	***Innovations in Design for Dose Selection Trials***	**Chair: Manisha Desai, Ph.D.** Co-Director, Biostatistics Core, SCI Professor of Medicine
10:20-10:40am	**TBD**	**Tze L. Lai, Ph.D.** Co-Director, CISD and Professor of Statistics, Stanford
10:40-11:00am	**TBD**	**Ray Liu, Ph.D.** Fellow, Takeda California
11:00-11:20am	**Clinical Challenges in Dose Selection for Combination Therapy**	**Mark D. Pegram, MD** Associate Director for Clinical Research, SCI, Susy Yuan-Huey Hung Professor
11:20-11:40pm	**Simulation Studies of Two Dose Escalation Methods for Oncology Drug Combination Therapies**	**Jing Hu, Ph.D** Associate Director, Biostatistics, Gilead
11:40-12:00pm	**Combination dose finding studies in Oncology: an industry perspective**	**Ling Wang, Ph.D.** Associate Director Statistics, Takeda Pharmaceuticals
12:00-1:10pm	***Lunch***	

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Afternoon Program (1:00-6:00pm)
Location: LKSC130, Li Ka Shing Center for Learning and Knowledge (LKSC), 291 Campus Drive, 1st Floor, Stanford, CA 94305

Time	Topic	Speaker
Session 3.	***Novel clinical trial designs for cancer treatments***	**Chair, Lei Nie, Ph.D.** Team Leader, Division of Biometrics V, CDER, US FDA
1:10-2:00pm	**Keynote: The future of Bayesian clinical trial design**	**Peter Mueller, Ph.D.** Professor of Statistics, UT Austin
2:00-2:20pm	**Collaboration of pharmacometrics and statistics: concentration-response MCPMod**	**Qi-Qi Deng, Ph.D.** Senior Principle Biostatistician, Boehringer Ingelheim Pharmaceutical
2:20-2:40pm	**TBD**	**Michel Friesenhahn, MS.** Principal Statistical Scientist, Genentech
2:40-3:00pm	**Addressing tumor molecular heterogeneity using a novel clinical trial design - PANGEA**	**Daniel Catenacci, MD** Associate Director, Gastrointestinal Oncology Program, Assistant Professor of Medicine, University of Chicago
3:00-3:20pm		**Eric C. Polley, Ph.D.** Assistant Professor of Biostatistics, Mayo Clinic
3:20-3:30pm	***Break***	
3:30-5:00pm	***Panel Discussions:*** ***Importance, Challenges, and Innovations in Dose Selection in Cancer Drug Development*** **Moderator: Yuan Ji, Ph.D.** Professor of Biostatistics University of Chicago	**Panel Members:** **Neby Bekele, Ph.D.,** Senior VP, Gilead **Lei Nie, Ph.D.,** Team Leader, Division of Biometrics V, CDER, US FDA **Kevin Grimes, MD,** Associate Professor, SPARK, Stanford University **Steve Goodman, MD, PhD,** Associate Dean of Clinical and Translational Research, Stanford University **Naitee Ting, Ph.D.,** Director, Biostatistics and Data Sciences, Boehringer-Ingelheim Pharmaceuticals Inc.
5:00-6:00pm	***Reception and Mix***	