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DIA Adaptive Designs in Clinical Trials: Overcoming Persistent Barriers

November 29-30, 2012

Hyatt Regency Washington • Washington, DC

Co-located with:
Data Monitoring Committees: Best Practices and Future Directions

PROGRAM CHAIRPERSONS

Brenda L. Gaydos, PhD
Research Fellow, Advanced Analytics
Head of Clinical Trial Optimization
Eli Lilly and Company

Lisa M. LaVange, PhD
Director, Office of Biostatistics
Office of Translational Sciences
CDER, FDA

PROGRAM COMMITTEE

Frank Bretz, PhD
Global Head of Statistical Methodology
Novartis Pharma AG, Switzerland

Gregory Campbell, PhD
Director, Division of Biostatistics
CDRH, FDA

David L. DeMets, PhD
Professor, Department of Biostatistics &
Medical Informatics
University of Wisconsin

José C. Pinheiro, PhD
Senior Director, Quantitative Decision Strategies
Janssen Research & Development, LLC

Estelle Russek-Cohen, PhD
Acting Division Director, Division of Biostatistics
CBER, FDA

CONFERENCE OVERVIEW

Clinical trials designed with adaptive features have great potential to result in more efficient decision making within a drug development program, and these potential benefits have been recognized by FDA, as expressed in the 2010 draft guidance on Adaptive Design Clinical Trials for Drugs and Biologics. Surveys of adaptive trials designed or conducted in 2008 and again in 2011 with medium to large pharmaceutical companies and CROs have identified barriers to the implementation of these designs. Some barriers have been reduced over time, such as availability of statistical tools and flexible randomization and drug supply systems. Others persist, such as education, change management, pre-planning and simulation, and perceptions of regulatory acceptance.

The goal of this conference is to provide a forum to examine persistent barriers to the use of adaptive design approaches in clinical trials. Recommendations to address these and other barriers will be discussed in an interactive format and within the framework of practical approaches and best practices for conducting AD trials.

FEATURED TOPICS

- Industry experience to date: review of 2008 and 2011 surveys
- FDA, CDER experience to date, pre and post guidance
- Learning from FDA, Center for Devices
- Considerations for DMCs when adaptive designs are utilized
- Adaptive design approaches for confirmatory trials
- Case studies in the confirmatory setting
- Adaptive design approaches in the exploratory setting
- Case studies in the exploratory setting
- Importance of trial simulation
- Learning from the ADAPT-IT grant *(Adaptive Designs Accelerating Promising Trials Into Treatments)*

Featuring joint sessions with the co-located *Data Monitoring Committees: Best Practices and Future Directions*

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WHO SHOULD ATTEND

Pharmaceutical, academic and government senior-level professionals and decision-makers involved in drug development:

- Academic health centers/Investigator sites
- Clinical research & development
- Data Management
- Modeling & Simulation
- Pharmacometrics
- Project management
- Regulatory affairs/operations
- Statistics

LEARNING OBJECTIVES

At the conclusion of this conference, participants should be able to:

- Recognize the benefits and issues with the use of adaptive trials
- Discuss the industry experience to date relative to designing and implementing adaptive trials
- Recognize the progress that has been made in adaptive designs
- Identify persistent barriers to the use of AD approaches in clinical trials
- Gain answers for solutions to barriers they may be encountering

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DAY 1, NOVEMBER 29

7:00-8:30 AM REGISTRATION AND CONTINENTAL BREAKFAST

8:30-9:00 AM WELCOME AND OPENING REMARKS

Brenda L. Gaydos, PhD
Research Fellow, Advanced Analytics
Head of Clinical Trial Optimization
Eli Lilly and Company

Gregory Campbell, PhD
Director, Division of Biostatistics
CDRH, FDA

9:00-10:30 AM SESSION 1

Where Are We Today With Adaptive Designs?

Session Chairpersons

Alex Dmitrienko, PhD
Executive Director, Center for Statistics in Drug Development Innovation
Quintiles

Telba Irony, PhD
Chief, Biostatistics: General Surgical Devices Branch
CDRH, FDA

An overview of the experiences gained to date with adaptive designs will be provided from the prospective of industry and FDA across CDER, DBER, and CDRH. The results of a recent survey conducted by the DIA ADSWG will be shared and compared to a similar survey conducted in 2008. The survey assessed the perception and use of adaptive designs, and identified persistent barriers.

Session Presenters

Li Chen, PhD, ScD
Director, Biostatistics
Amgen

Sue-Jane Wang, PhD
Associate Director, Pharmacogenomics and Adaptive Design
Office of Biostatistics
Office of Translational Sciences
CDER, FDA

Yonghong Gao, PhD
Mathematical Statistcian, Division of Biostatistics
CDRH, FDA

Estelle Russek-Cohen, PhD
Acting Division Director, Division of Biostatistics
Office of Biostatistics and Epidemiology
CBER, FDA

10:30-11:00 AM MORNING BREAK

11:00-12:30 PM SESSION 2

Overcoming Persistent Barriers

Session Chairpersons

Michael Krams, PhD
Vice President, Neurology and Franchise Head for CNS
Johnson & Johnson

Amelia Dale Horne, DrPH
Chief, Vaccine Evaluation Branch
Division of Biostatistics
Office of Biostatistics and Epidemiology
CBER, FDA

Four persistent barriers were identified from the DIA ADSWG survey: education, change management, planning, and risk of regulatory acceptance. This session will address potential solutions to these barriers. Two industry speakers will address education, change management and planning. To address the risk of regulatory acceptance, a FDA panel will follow with representatives from different offices and divisions. Each panel member will briefly present on experiences within their division prior to taking questions from the audience.

Session Presenters

Vladimir Dragalin, PhD
Senior Vice President
Aptiv Solutions

Brenda Gaydos, PhD
Research Fellow, Advanced Analytics
Head of Clinical Trial Optimization
Eli Lilly and Company

Regulatory Panel Discussion

Session Panelists

Gregory Campbell, PhD
Director, Division of Biostatistics
CDRH, FDA

Daphne Lin, PhD
Deputy Director, Division of Biometrics IV
Office of Biostatistics
Office of Translational Sciences
CDER, FDA

Rajeshwari Sridhara, PhD
Director, Division of Biometrics V
Office of Biostatistics
Office of Translational Sciences
CDER, FDA

John Scott, PhD
Acting Deputy Director, Division of Biostatistics
Office of Biostatistics and Epidemiology
CBER, FDA

12:30-1:30 PM NETWORKING LUNCH

1:30-3:00 PM SESSION 3

Sample Size Re-estimation in the Confirmatory Setting

Session Co-Chairpersons

Inna Perevozkaya, PhD
Senior Director
Pfizer

Annie Lin, PhD
Visiting Scientist, Division of Biostatistics
Office of Biostatistics and Epidemiology
CBER, FDA

This session will discuss the use of sample-size re-estimation (SSR) in the confirmatory setting from a strategy, operational and regulatory perspective. Representatives from industry will present motivating examples to illustrate why SSR is preferable in some cases to a group sequential design, provide operational issues and solutions, and raise the discussion on whether SSR should be considered as a well understood method. The session will conclude with a presentation on the regulatory experience.

Session Presenters

William Prucka, PhD
Senior Research Scientist
Eli Lilly and Company

Olga V. Marchenko, PhD
Vice President, Center for Statistics in Drug Development Innovation
Quintiles

Keaven Anderson, PhD
Executive Director, Statistics: Late Stage Development
Merck

Peiling Yang, PhD
Team Lead, Division of Biometrics I
Office of Biostatisitcs
Office of Translational Sciences
CDER, FDA

Thomas Laughren, MD
Director, Division of Psychiatry Products
Office of Drug Evaluation I
CDER, FDA

3:00-3:30 PM AFTERNOON BREAK

3:30-5:30 PM JOINT SESSION 4

Role of DMC in Adaptive Designs

Session Chairperson

Lisa M. LaVange, PhD
Director, Office of Biostatistics
Office of Translational Sciences
CDER, FDA

Adaptive designs present additional challenges to the role of a DMC The primary role of a DMC is patient safety. Yet some interim decisions in an adaptive design, such as dose selection, may lie in a domain which is traditionally a sponsor responsibility. Concerns about restricting access to interim results need to be addressed, and operational bias needs to be minimized. In this session, views will be presented from the sponsor and DMC member perspective. Case studies will be discussed followed by a panel discussion.

Session Presenters

Paul Gallo, PhD
Biometrical Fellow
Novartis

Dave DeMets, PhD
Professor, Department of Biostatistics & Medical Informatics
University of Wisconsin

Case Study 1: A seamless 2/3 design

Case Studies Presenters

Brenda L. Gaydos, PhD
Research Fellow, Advanced Analytics
Head of Clinical Trial Optimization
Eli Lilly and Company

Ray Carroll, PhD (via teleconference)
Distinguished Professor
Texas A&M University

Panel Discussion

Moderator

Lisa M. LaVange, PhD
Director, Office of Biostatistics
Office of Translational Sciences
CDER, FDA

Panelists

Gregory Campbell, PhD
Director, Division of Biostatistics
CDRH, FDA

Bram Zuckerman, MD
Director, Cardiovascular Devices
CDRH, FDA

John Orloff, MD
Senior Vice President
Chief Medical Officer
Novartis Pharmaceuticals Corporation

Dave DeMets, PhD
Professor, Department of Biostatistics and Medical Informatics
University of Wisconsin

Janet Wittes, PhD
President
Statistics Collaborative

Marc K. Walton, MD, PhD
Associate Director for Translational Medicine Office of Translational Sciences
CDER, FDA

5:30-6:30 PM NETWORKING RECEPTION WITH AD AND DMC JOINT SESSION

DAY 2, NOVEMBER 30

8:30-10:00 AM SESSION 5

Importance of Trial Simulation

Session Co-Chairpersons

Gerry Gray, PhD
Deputy Director, Division of Biostatistics
CDRH, FDA

Nitin Patel, PhD
Founder, Chairman and Chief Technology Officer
Cytel Inc

Trial simulation can improve design by providing quantitative estimates of a study's operating characteristics under a more realistic set of a therapies performance and trial conduct scenarios. If an adaptive design is one of the alternatives under consideration, simulations are typically required to understand the impact of interim decision on trial conduct and on the final analysis. In this session, the importance of using trial simulation in traditional fixed designs as well as in adaptive designs will be demonstrated. The issue of utilizing simulation to justify control of the type 1 error rate will be discussed. The session will conclude with a perspective on the use of simulation and Bayesian methods in CDRH.

Session Presenters

J. Kyle Wathen, PhD
Director
Janssen Research & Development

Scott Berry, PhD
Statistical Scientist
Berry Consultants

Andy Grieve, PhD
Senior Vice President Clinical Trial Methodology
Bayesic Statistical Solutions
Aptiv Solutions

Xuefeng Li, PhD
Senior Biostatistician
Mathematical Statistician
Division of Biostatistics
CDRH, FDA

10:00-10:15 AM MORNING BREAK

10:15 - 11:45 AM SESSION 6

Use of Biomarkers in Adaptive Designs

Session Co-Chairpersons

Todd Sahlroot, PhD
Deputy Director, Division of Biometrics II
Office of Biostatistics
Office of Translational Sciences
CDER, FDA

Eva Miller, PhD
Director, Biostatistics
ICON Clinical Research

This session will focus on ways in which biomarkers are incorporated into adaptive designs. Confirmatory clinical trials that incorporate biomarker analyses at interim for purposes of sample size re-estimation, while data on the clinical endpoint remains masked, will be discussed. Other topics include adaptive designs in group sequential trials with futility analyses conducted at interim time points that incorporate the correlation between biomarkers and clinical endpoints, comparisons between fixed and adaptive randomization, and Bayesian tools for adaptive enrichment based on biomarkers. The session closes with a regulatory perspective on the use of biomarkers in adaptive designs.

Session Presenters

Emmanuel Zuber, PhD (via teleconference)
Global Head, Full Development, Biostatistics
Oncology Business Unit
Novartis Pharma AG, Switzerland

Dave DeMets, PhD
Professor, Department of Biostatistics & Medical Informatics
University of Wisconsin

Robert Temple, MD
Deputy Center Director for Clinical Science
CDER, FDA

Mei-Chiung Shih, PhD
VA Cooperative Studies Program Coordinating Center and
Department of Health Research and Policy
Stanford University

Sue-Jane Wang, PhD
Associate Director, Pharmacogenomics and Adaptive Design
Office of Biostatistics
Office of Translational Sciences
CDER, FDA

11:45 AM-12:45 PM LUNCH

12:45-2:15 PM SESSION 7

Adaptive Design Approaches in the Exploratory Setting

Session Co-Chairpersons

Weili He, PhD
Director, Biostatistics
Merck and Company

Kun He, PhD
Team Lead, Division of Biometrics V
Office of Biostatistics
Office of Translational Sciences
CDER, FDA

Adaptive designs have a great potential to improve the information value of studies in the exploratory phase of development. In particular, adaptive dose-finding designs provide opportunities to improve the characterization of the dose response more efficiently than a traditional fixed design. In this session, methods and examples of the use of adaptive designs in the exploratory setting will be presented. The session will conclude with a regulatory perspective.

Session Presenters

José C. Pinheiro, PhD
Senior Director, Quantitative Decision Strategies
Janssen Research & Development, LLC

Björn Bornkamp, MSc, PhD
Expert Statistical Methodologist
Integrated Information Sciences
Novartis Pharma AG

Yili L. Pritchett, PhD
Research Fellow
Director, Clinical Statistics
Data and Statistics Sciences
Abbott Laboratories

Greg Soon, PhD
Team Leader, Division of Biometrics IV
Office of Biostatistics
Office of Translational Sciences
CDER, FDA

Shiowjen Lee, PhD
Team Lead, Therapeutics Evaluation Branch
Division of Biostatistics
Office of Biostatistics and Epidemiology
CBER, FDA

2:15-2:30 PM AFTERNOON BREAK

2:30-4:30 PM SESSION 8

Adaptive Treatment or Population Selection in Confirmatory Setting

Session Co-Chairpersons

Jeff Maca, PhD
Senior Director, Center for Statistics in Drug Development Innovation
Quintiles

Boguang Zhen, PhD
Branch Chief, Therapeutics Evaluation Branch
Division of Biostatistics
CBER, FDA

Even with a robust phase 2 data package, too much uncertainty may exist at the end of Phase 2 to determine the best dose(s) or patient population to study further in phase 3. Adaptive dose selection and population selection designs enables the investigation of a broader range of variables in Phase 3 while also allowing for a reduction in the time and resources that would be necessary with a fixed design. In this session, statistical methods and case studies will be presented to illustrate the benefits and cautions for these approaches in the confirmatory setting. This session will conclude with a summary wrap-up and panel discussion of next steps based on the 2-day workshop.

Session Presenters

Martin Posch, PhD
Professor of Medical Statistics
Center for Medical Statistics, Informatics and Intelligent Systems
Medical University of Vienna, Austria

Case Study 1:

Case Study Presenter

Cyrus Mehta, PhD
Founder and President
Cytel Inc

Case Study 2:

Case Study Presenter

Caroline Morgan, PhD
Director, Business Development
Cytel Inc

Regulatory Perspective

H.M. James Hung, PhD
Director, Division of Biometrics I
Office of Biostatistics
Office of Translational Sciences
CDER, FDA

Session Panelists

Brenda L. Gaydos, PhD
Research Fellow, Advanced Analytics
Head of Clinical Trial Optimization
Eli Lilly and Company

Lisa M. LaVange, PhD
Director, Office of Biostatistics
Office of Translational Sciences
CDER, FDA

Robert Temple, MD
Deputy Center Director for Clinical Science
CDER, FDA

Dave DeMets, PhD
Professor, Department of Biostatistics & Medical Informatics
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Estelle Russek-Cohen, PhD
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Gregory Campbell, PhD
Director, Division of Biostatistics
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DIA Adaptive Designs in Clinical Trials: Overcoming Persistant Barriers

Event #12020 • November 29-30, 2012

Hyatt Regency Washington, Washington, DC, USA

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Fax **+1.215.442.6199,** email **Marilyn.Ginsberg@diahome.org**

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