DIA IN COOPERATION WITH FDA AND PhRMA

Progression-Free Survival Oncology Workshop

Tutorials October 7, 2009
Conference October 8-9, 2009

DoubleTree Hotel and Executive Meeting Center
Bethesda, MD, USA

Hear FDA, NCI, Academia, and PhRMA Perspectives on Clinical, Radiological, and Statistical Evaluation of Progression-Free Survival.

Progression Free Survival (PFS) endpoints are increasingly used for evaluation and approval of oncology drugs. This conference will discuss:

- Definition of PFS: combining radiological data and clinical assessments;
- Application of PFS in various cancers;
- Strategies for use of independent review with PFS endpoints;
- Approaches to the design and analysis of randomized trials with PFS as the primary end-point
- Increasing awareness among the oncology clinical trials community about the critical design and analysis issues with PFS outcome, and;
- Strategies for the evaluation of alternative approaches to the analysis of PFS data.

KEYNOTE SPEAKER

Richard Pazdur, MD, *Director, Office of Oncology Drug Products, CDER, FDA*

In addition to his experience as a regulatory expert at FDA, Dr. Pazdur has distinguished himself in clinical and academic oncology. He served as a fellow in oncology at Rush Presbyterian-St. Luke's Medical Center at the University of Chicago and as a practicing oncologist, researcher, and teacher at Wayne State University, where he directed the medical oncology fellowship program. Dr. Pazdur was also a tenured Professor of Medicine and Assistant Vice President for Academic Affairs at M.D. Anderson Cancer Center at the University of Texas. He joined FDA in 1999 as the Director of the Division of Oncology Drug Products and was named Director of the Office of Oncology Drug Products in April 2005. He has authored over 160 peer-reviewed papers in the field of oncology, has written chapters for over 30 oncology textbooks, and is the editor of two standard reference oncology texts.

PROGRAM COMMITTEE

RAJESHWARI SRIDHARA, PhD
Deputy Division Director, Office of Biostatistics
CDER, FDA

WILLIAM BUSHNELL, MS*
Group Director, Oncology Biometrics and Epidemiology
GlaxoSmithKline

ANDREW STONE, MSc*
Therapeutic Area Statistical Expert Oncology
AstraZeneca

LORI E. DODD, PhD
Mathematical Statistician
Biometric Research Branch
National Institute of Allergy and Infectious Diseases

BORIS FREIDLIN, PhD
Mathematical Statistician
Biometric Research Branch
Division of Cancer Treatment and Diagnosis
National Cancer Institute (NCI)

** Leader of the PhRMA PFS Working Group*

TARGET AUDIENCE This program will benefit Oncology professionals involved in:

- **Biostatistics**
- **Regulatory affairs**
- **Compliance**
- **Data analysis**
- **Quality assurance/Quality control**
- **Oncology**
- **Radiology**

CONTACT INFORMATION

Conference

Ben Zaitz, Phone +1-215-293-5803/
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Accreditation and Credit Designation

The Drug Information Association is accredited by the Accreditation Council for Pharmacy Education as a Provider of continuing pharmacy education. This program is designated for 12 contact hours or 1.2 continuing education units (CEUs).

The Drug Information Association (DIA) has been approved as an Authorized Provider by the International Association for Continuing Education and Training (IACET), 8405 Greensboro Drive, Suite 800, McLean, VA 22102. DIA is authorized by IACET to offer 1.2 CEUs for this program. Each tutorial from Wednesday, October 7th is authorized by IACET to offer .3 CEUs

The Drug Information Association will offer nursing credits for this program in collaboration with Corexcel. This program is designated a maximum of 12 nursing contact hours.

Corexcel is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

Continuing Education Credit Allocation for the Two-day Conference: 12 nursing contact hours.

Disclosure Policy: It is Drug Information Association policy that all faculty participating in continuing education activities must disclose to the program audience (1) any real or apparent conflict(s) of interest related to the content of their presentation and (2) discussions of unlabeled or unapproved uses of drugs or medical devices. Faculty disclosure will be included in the course materials.

Learning Objectives: At the conclusion of this meeting, participants should be able to:

- Describe the key issues with progression-free survival as an endpoint;
- Explain the latest techniques used in progression-free survival; and
- Evaluate and appraise alternative solutions.

WEDNESDAY • OCTOBER 7

1:00-4:30 PM CONCURRENT TUTORIAL OFFERINGS

TUTORIAL #1: Time to Event Analysis for Non-Statisticians

TUTORIAL INSTRUCTOR

Daniel Sargent, PhD
Professor of Oncology and Biostatistics
Mayo Clinic Cancer Center

Time to event endpoints such as overall survival, disease free survival, or time to progression, dominate phase III oncology trials, and are becoming increasingly popular in phase II trials due to the increase in non-cytotoxic agents. This tutorial will cover the critical issues in the analysis of time to event data in oncology from a non-technical and clinically-oriented perspective. Specific topics that will be covered include 1) the need for special approaches for the analysis of such data, 2) the appropriate clinical interpretation of techniques such as Kaplan-Meier curves, log-rank tests, and Cox proportional hazards models (including critical assumptions made in such analyses), 3) the meaning of hazard functions and hazard ratios, 4) choice of the appropriate time to event endpoint for a given study, 5) the need for sensitivity analyses for endpoints such as progression-free survival, 6) methods for interim analyses for time to event endpoints, 7) methods to deal with competing risks (for example, death from other cause in a trial with a time to progression endpoint), and 8) sample size calculations. All concepts will be presented through a liberal use of examples.

TUTORIAL #2: Statistical Methods for Interval Censored Data Analyses

TUTORIAL INSTRUCTOR

Michael P. Fay, PhD
Mathematical Statistician
National Institute of Allergy and Infectious Diseases
NIH/NIAID

This tutorial is geared to statisticians. We will review tools for analyzing right-censored data then show how the tools need to be modified to be applied to interval censored data. Specifically, we discuss non-parametric maximum likelihood estimation (NPMLE) of the survival curve, generalizations of weighted logrank tests, and generalizations of survival regression models. The focus will be on theory necessary for the applied statistician, answering questions such as: What assumptions are necessary for each approach? Which test should be applied? An R package for calculating the NPMLE and weighted logrank tests will be demonstrated.

4:00-6:00 PM **CONFERENCE REGISTRATION**

THURSDAY • OCTOBER 8

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

8:30-8:45 AM WELCOME AND OPENING REMARKS

Rajeshwari Sridhara, PhD
Deputy Division Director, Office of Biostatistics
CDER, FDA

8:45-9:30 AM **PLENARY KEYNOTE SPEAKER**

Richard Pazdur, MD
Director, Office of Oncology Drug Products
CDER, FDA

9:30-11:00 AM SESSION 1

CLINICAL ASSESSMENT OF PROGRESSION-FREE SURVIVAL (PFS)

SESSION CHAIRPERSON

Amna Ibrahim, MD
Clinical Team Leader
Division of Drug Oncology Products (DODP)
CDER, FDA

Session Objectives:

1. Discussion of criteria for determining when prolongation of PFS or DFS may be regarded as a clinical benefit

2. Discussion of role of non-radiological components (symptoms, physical examination, and laboratory measurements) in the determination of progression in clinical practice vs. regulatory requirements.
3. Pros and cons of blinded vs. open-label studies; Mitigating bias in open-label studies
4. Pros and cons of audit and oversight of PFS assessments

Amna Ibrahim, MD
Clinical Team Leader
Division of Drug Oncology Products (DODP)
CDER, FDA

Vicki L. Goodman, MD
Director, Clinical Development
GSK Oncology

Deborah K. Armstrong, MD
Associate Professor Oncology
Sidney Kimmel Comprehensive Cancer Center
Associate Professor in Gynecology and Obstetrics
Johns Hopkins University School of Medicine

11:00–11:30 AM **REFRESHMENT BREAK**

11:30 AM–1:00 PM SESSION 2

Radiological Evaluation of Progression-Free Survival (PFS)

Session Chairperson

Lawrence H. Schwartz, MD
Professor of Radiology, Vice Chair, Technology Development
Memorial Sloan-Kettering Cancer Center, Department of Radiology

Session Objectives

1. Sources of variability in radiological assessments
2. Quality control – issues with adjudication
3. Anatomical sites/diseases that are not amenable for radiological assessment
4. Issues to consider when determining frequency of assessment, including when radiation exposure is a concern
5. Novel imaging techniques for evaluating progression and response

Lawrence H. Schwartz, MD
Professor of Radiology, Vice Chair, Technology Development
Memorial Sloan-Kettering Cancer Center, Department of Radiology

Daniel C. Sullivan, MD
Director, Imaging Program
Duke Comprehensive Cancer Center
Duke University

Constantine Gatsonis, PhD
Professor of Medical Science (Biostatistics)
Director, Center for Statistical Sciences
Acting Head, Biostatistics Section
Department of Community Health
Brown University

1:00-2:00 PM **NETWORKING LUNCHEON**

2:00-3:30 PM SESSION 3

Criteria for Determination of Progression

Session Chairperson

Patrick Therasse, MD, PhD
Vice President
Head of Global Clinical Development, Immunotherapeutics
GlaxoSmithKline Biologicals

Session Objectives:

1. Update on RECIST criteria and evaluation of novel imaging techniques
2. Progression in hematological malignancies
3. Pros and cons of RECIST criteria

Grant Williams, MD
Williams Cancer Drug Consulting, LLC

Janet Dancey, MD, FRCPC
Program Leader, High Impact Clinical Trials at Ontario Institute for Clinical Research (OICR), Director of Clinical Translational Research, National Cancer Institute of Canada Clinical Trials Group (NCIC CTG)

Ann Farrell, MD
Deputy Division Director
Division of Drug Oncology in the Office of Oncology Drug Products, CDER, FDA.

3:30-4:00 PM **REFRESHMENT BREAK**

4:00-5:30 PM SESSION 4

Statistical Evaluation of Progression-Free Survival (PFS) Part 1 – Role and Design of Independent Review

Lori E. Dodd, PhD
Mathematical Statistician, Biometric Research Branch
National Institute of Allergy and Infectious Diseases

Session Objectives:

1. Limitations of centralized independent review
2. Review of differences between independent and investigator reviews
   a. Determinants of discordances and strategies for minimizing them
3. Discuss whether an audit is a feasible alternative to complete-case independent central review
4. Measurement variability versus bias in the assessment of treatment effect

Suman Bhattacharya, PhD
Clinical Biostatistics
Genentech Bio-oncology

Ohad Amit, PhD
Director, Oncology
GlaxoSmithKline

Boris Friedlin, PhD
Mathematical Statistician, Biometric Research Branch
Division of Cancer Treatment and Diagnosis
National Cancer Institute (NCI)

Panel Discussant

Daniel Sargent, PhD
Professor of Oncology and Biostatistics
Mayo Clinic Center

5:30-6:30 PM **NETWORKING RECEPTION**

FRIDAY • OCTOBER 9

7:30-9:00 AM CONFERENCE REGISTRATION AND CONTINENTAL BREAKFAST

9:00-10:00AM SESSION 5

INVITED LECTURE

Thomas Fleming, PhD
Professor of Biostatistics and Statistics
University of Washington

10:00-11:00 AM SESSION 6

STATISTICAL EVALUATION OF PROGRESSION-FREE SURVIVAL
PART 2 – HANDLING MISSING/CENSORED OBSERVATIONS

SESSION CHAIRPERSON

Thomas Fleming, PhD
Professor of Biostatistics and Statistics
University of Washington

Session Objectives:

1. Right censoring vs. interval censoring: Different censoring rules used in practice
2. Results of PhRMA survey comparing different approaches to endpoint definition in terms of when to censor
3. Assumptions on censoring – how serious are the deviations
4. Use of sensitivity analyses

Renee Iacona, MD, MPH
Associate Director-Biostatistics
AstraZeneca Pharmaceuticals LP

Jonathan S. Denne, PhD
Director, Statistics
Eli Lilly and Company

Weishi (Vivian) Yuan, PhD
Mathematical Statistician
OB/CDER/FDA

11:00-11:30 AM REFRESHMENT BREAK

11:30 AM-1:00PM SESSION 7

STATISTICAL EVALUATION OF PROGRESSION-FREE SURVIVAL
PART 3 – ANALYSIS OF PROGRESSION-FREE SURVIVAL

SESSION CHAIRPERSON

Andrew Stone, MSc
Therapeutic Area Statistical Expert Oncology
AstraZeneca

Session Objectives:

1. Optimum visit frequency of assessment relative to rate of progression
2. Discussion of alternative analysis approaches, which could include
   a. Interval censored approaches and properties;
   b. Whether to move unscheduled visits to nominal time and implications on tie handling

Dianne Finkelstein, PhD
Professor, Harvard Medical School and Harvard School of Public Health Biostatistics Center
Massachusetts General Hospital

Cong Chen, PhD
Merck & Co., Inc.

Somesh Chattopadhyay
Mathematical Statistician
OB, CDER, FDA

1:00-2:00 PM NETWORKING LUNCHEON

2:00-3:30 PM SESSION 8

REGULATORY CONSIDERATIONS

Aloka Chakravarty, PhD
Director, Division of Biometrics
CDER, FDA

Session Objectives:

1. FDA's current approach in considering PFS as primary endpoint
2. EU's current approach in considering PFS as primary endpoint

Aloka Chakravarty, PhD
Director, Division of Biometrics, CDER, FDA

Michael R. Langley DVM, RAC
Lilly US Regulatory Affairs

TRAVEL AND HOTEL

The most convenient airport is Reagan National Airport and attendees should make airline reservations as early as possible to ensure availability. The DoubleTree Hotel and Executive Meeting Center, Bethesda was holding a block of rooms for the DIA event attendees. That block is now full.

The DIA has contracted an additional block of rooms at the nearby Hyatt Regency Bethesda at reduced rates until September 16, 2009 for the DIA event attendees. Room availability at this rate is guaranteed only until that date or until the block is filled. The Hyatt Regency Bethesda can be reached by telephone at +1-301-657-1234. Please mention the DIA event to receive the reduced rates below. The hotel is located at One Bethesda Metro Center (7400 Wisconsin Avenue), Bethesda, MD 20814, USA.

Single $229 **Double $254**

Participants with Disabilities: *DIA event facilities and overnight accommodations are accessible to persons with disabilities. Services will be made available to sensory-impaired persons attending the event if requested at least 15 days prior to event. Contact the DIA office to indicate your needs.*

Robert Hemmings
Statistics Unit Manager
Medicine and Healthcare Products Regulatory Agency
MHRA

Panel Discussion Speakers and Health Canada Representative

3:30-4:30 PM SESSION 9

Panel Discussion – Lessons Learned and Path Forward

Session Chairperson

Rajeshwari Sridhara, PhD
Deputy Division Director
DBV/OB/CDER/FDA

Panelists

William Bushnell, MS
Group Director, Oncology Biometrics and Epidemiology
GlaxoSmithKline

Richard Pazdur, MD
Director, Office of Oncology Drug Products
CDER, FDA

Robert Hemmings
Statistics Unit Manager
Medicine and Healthcare Products Regulatory Agency
MHRA

Rajeshwari Sridhara, PhD
Deputy Division Director
DBV/OB/CDER/FDA

Andrew Stone, MSc
Therapeutic Area Statistical Expert Oncology
AstraZeneca

4:30 PM CONFERENCE ADJOURNED

Unless otherwise disclosed, DIA acknowledges that the statements made by speakers are their own opinion and not necessarily that of the organization they represent, or that of the Drug Information Association. Speakers and agenda are subject to change without notice. Recording of any DIA tutorial/workshop information in any type of media, is prohibited without prior written consent from DIA.

Upcoming DIA Conferences, Training Courses, and Webinars

CONFERENCES

SEPTEMBER 23-24, 2009
Cardiovascular Safety and Development of Type 2 Diabetes Mellitus Medications: Current State of the Art and Opportunities to Advance the Science
Washington, DC

SEPTEMBER 23-25, 2009
DIA's 6th Latin American Congress of Clinical Research
Mexico City, Mexico

OCTOBER 7-8, 2009
DIA's 3rd Clinical Trial Disclosure Workshop: Recipes for Success
National Harbor, MD

OCTOBER 15-16, 2009
Personalized Medicine: Biomarkers and Diagnostics in Drug Development, Regulatory Approval, and Access to Patients
Toronto, Ontario, Canada

OCTOBER 26-27, 2009
Measuring Study Endpoints in Multinational Clinical Trials: Outcomes Reported from the Viewpoint of the Clinician, Patient, and Caregiver
New Orleans, LA

OCTOBER 28-29, 2009
***DIA/FDA/PhRMA:* Modeling and Simulation in Drug Development – Quantitative Approaches for Decision Making**
Bethesda, MD

NOVEMBER 3-4, 2009
DIA's 7th Canadian Annual Meeting: "Time to Act"
Ottawa, Ontario, Canada

NOVEMBER 4-5, 2009
Assessing Benefits and Risks of Medicinal Products in Regulatory Decisions
Bethesda, MD

NOVEMBER 3-4, 2009
Global Vaccine Development for World Health Symposium: FDA, EMEA, Emerging Regions, NGO, and Industry Perspectives
Bethesda, MD

TRAINING COURSES

SEPTEMBER 10-11, 2009
Statistics for Nonstatisticians
Baltimore, MD

SEPTEMBER 14-16, 2009
Regulatory Affairs – Part I: The IND Phase
Philadelphia, PA

SEPTEMBER 21-24, 2009
The Leadership Experience
Philadelphia, PA

SEPTEMBER 22-24, 2009
Fundamentals of Clinical Research
Baltimore, MD

SEPTEMBER 22-23, 2009
High-performance Biopharm Teams
Horsham, PA

SEPTEMBER 22-24, 2009
Fundamentals of Clinical Research
Baltimore, MD

SEPTEMBER 22-24, 2009
Drug Safety Surveillance and Epidemiology
Baltimore, MD

SEPTEMBER 24-25, 2009
New Drug Product Development and Lifecycle Management
Horsham, PA

ONLINE TRAINING COURSES

Three-part Training Series: Developing Standard Operating Procedures (SOPs)
SEPTEMBER 15 & 16, 2009 11:30 AM-2:00 pm
SEPTEMBER 17, 2009 11:30 AM-1:30 pm

Three-part Training Series: Development of a Clinical Study Report
SEPTEMBER 29, OCTOBER 6 & OCTOBER 13, 2009 10:00 AM-12:00 pm

Progression-free Survival Oncology Workshop

Event ID #09028
DoubleTree Hotel and Executive Meeting Center
Bethesda, MD, USA
OCTOBER 8-9, 2009

Register online or fax this page to +1-215-442-6199

DRUG INFORMATION ASSOCIATION
800 Enterprise Road, Suite 200
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Progression-Free Survival Oncology Workshop

Meeting I.D. # 09028 – October 7-9, 2009
DoubleTree Hotel and Executive Meeting Center Bethesda, Bethesda, MD, USA

Registration Fees *Registration fee includes refreshment breaks, luncheons, and reception (if applicable), and will be accepted by mail, fax, or online.*

Industry Fee	US $1275 ❑

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TUTORIALS

#1 1:00-4:30 pm	**Time to Event Analysis for Non-Statisticians**	US $ 405 ❑
#2 1:00-4:30 pm	**Statistical Methods for Interval Censored Data Analyses**	US $ 405 ❑

CANCELLATION POLICY: On or before OCTOBER 1, 2009

Administrative fee that will be withheld from refund amount:

Member or Nonmember = $200
Government or Academia or Nonprofit (Member or Nonmember) = $100
Tutorial (if applicable) = $50

Cancellations must be in writing and be received by the cancellation date above. Registrants who do not cancel by that date and do not attend will be responsible for the full registration fee paid. Registrants are responsible for cancelling their own hotel and airline reservations. You may transfer your registration to a colleague at any time but membership is not transferable. Please notify DIA of any such substitutions as soon as possible. Substitute registrants will be responsible for nonmember fee, if applicable.

DIA reserves the right to alter the venue, if necessary. If an event is cancelled, DIA is not responsible for any airfare, hotel or other costs incurred by registrants.

❑ **I cannot attend but please keep me informed of DIA's future events.**
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REGISTRATION FORM

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❑ **CHECK** drawn on a US bank payable to and mailed along with this form to: Drug Information Association Inc, P.O. Box 95000-1240, Philadelphia, PA 19195-1240, USA. Please include a copy of this registration form to facilitate identification of attendee.

❑ **BANK TRANSFER** When DIA completes your registration, an email will be sent to the address on the registration form with instructions on how to complete the Bank Transfer. Payment should be made in US dollars. Your name and company, as well as the Event I.D. # must be included on the transfer document to ensure payment to your account.