
Princeton-Trenton Chapter



The Princeton-Trenton Chapter of the American Statistical Association is pleased to present:

Fall Seminar
Wednesday, November 30, 2011
Holiday Inn
100 Independence Way, Princeton, NJ 08540

Schedule

8:30 – 9:00 AM	Registration and networking	
9:00 – 9:45 AM	Probability of Success Assessment Based on Efficacy and Safety Data	Weili He, Merck & Co., Inc.
9:45 - 10:30 AM	Assessing Consistency of Treatment Effect in Multi-Regional Clinical Trials	Josh Chen, Merck & Co., Inc.
10:30 – 11:00 AM	Break and networking	
11:00 –11:45 PM	The TIMP-4 Biomarker and Small Tumors in Breast Cancer	Michael Chernick,
11:45 –1:00 PM	Lunch and end of seminar	

1. Dr. Weili He

Abstract: A Framework for Joint Modeling and Joint Assessment of Efficacy and Safety Endpoints for Probability of Success Evaluation and Optimal Dose Selection

Evaluation of clinical proof of concept (POC), optimal dose selection, and phase III probability of success (POS) has traditionally been conducted by subjective and qualitative assessment of efficacy and safety data. This, in part, was responsible for the numerous failed phase III programs in the past. The need to utilize more quantitative approaches to assess efficacy and safety profiles has never been greater. In this paper, we propose a framework that incorporates efficacy and safety data simultaneously for joint evaluation of clinical POC, optimal dose selection, and phase III POS. Simulation studies were conducted to evaluate the properties of our proposed methods. The proposed approach was applied to two real clinical studies. Based on the true outcome of the two clinical studies, the assessment based on our proposed approach suggested reasonable path forward for both clinical programs. This research work was recently accepted for publication by *Statistics in Medicine*.

Bio: Dr. Weili He is Associate Director of Clinical Biostatistics at Merck & Co., Inc. Dr. He has a Ph.D. degree in biostatistics. She has over 16 years of experience in pharmaceutical industry and over 20 years of experience conducting clinical trial design and analysis. Her research interests include survival and longitudinal data modeling, cancer phase I & II designs, repeated categorical data modeling, surrogate marker evaluations, adaptive design methodologies and implementations, and probability of success assessment for clinical development programs. Dr He's collaborative experience with colleagues and medical researchers in various disciplines has led to over 30 publications in statistical and medical journals.

2. Dr. Josh Chen

Abstract: Assessing Consistency of Treatment Effect in Multi-Regional Clinical Trials

Multi-regional clinical trials (MRCTs), with participation from relatively new regions/countries such as Asia, Russia, South America and Eastern Europe, have become a common practice. Such MRCTs can accelerate the availability of important medical products and increase efficiency in clinical development. However, they also present many statistical, clinical, operational, regulatory and ethical challenges. Among them, one key issue is to assess the consistency of treatment effects across regions. The Japanese health authority issued a guidance document in 2007 with one Q&A specifically to address this in Japanese patients. The importance of this issue is further highlighted in recent MRCTs where the experimental drug was shown to be superior to comparator but the treatment effect was not apparent in the US patients. To address the challenges and fully realize the opportunities MRCTs present, a PhRMA MRCT Limited Duration Key Issue Team (LDKIT) was formed in 2008, with one workstream specifically to address the issue of consistency assessment. Points to consider recommended by this Consistency Workstream are summarized in two white papers (1 for design and 1 for execution/interpretation) and published in the September, 2011 issue of *Drug Information Journal*. In this talk, I will provide an overview of recommendations on assessing consistency in MRCTs from this cross-industry collaboration.

Bio: Dr. Joshua Chen has been working on late stage clinical trials for over 12 years. He has been project lead statistician for multiple clinical programs including antiviral drugs and vaccines. Josh is active in statistical research and has published extensively covering group sequential methods, adaptive designs, survival analysis, and other statistical applications in clinical trials. He is a member of the PhRMA Multi-Regional Clinical Trial Limited Duration Key Issue Team, and a co-lead of the Consistency Workstream to assess consistency of treatment effect across regions.

3. Dr. Michael Chernick

Abstract: The TIMP-4 Biomarker and Small Tumors in Breast Cancer

An increasing number of breast cancer patients are diagnosed with small, localized, early-stage tumors. These patients are typically thought to have a good prognosis for long-term disease-free survival, but epidemiological studies indicate that up to 30% may suffer a recurrence within 3-5 years of diagnosis. Identifying patients with a high risk of recurrence and/or progression is important, because they could be more aggressively treated at diagnosis to improve their chances for disease-free survival. Recent evidence suggests that elevated levels of matrix metalloproteinase inhibitor TIMP-4 are associated with malignant progression of ductal carcinoma in situ (DCIS), a pre-cancerous lesion. To examine the association of TIMP-4 with survival outcomes, we conducted a retrospective immunohistochemical analysis of 314 cases from patients with early-stage disease, defined by tumors smaller than 2cm and no spread to lymph nodes (T1N0MX). We found that tumors with elevated levels of TIMP-4 were correlated with a reduced probability of long-term disease-free survival, especially in patients with estrogen receptor-negative tumors. Our findings prompt further evaluation of TIMP-4 as a simple prognostic marker that may help identify early-stage breast cancer patients who could benefit from more aggressive treatment at diagnosis. These results were published in the article titled “Tissue inhibitor of metalloproteinase-4 (TIMP-4) is elevated in early-stage breast cancers with accelerated progression and poor clinical course” that I coauthored.

Bio: Michael Chernick is the Director of Biostatistical Services at the Lankenau Institute for Medical Research. He has a PhD in statistics from Stanford University and is a Fellow of the American Statistical Association. He has over 30 years of industrial experience applying statistical methods in several industries including the aerospace, insurance, medical device and pharmaceutical industries. He has published over 40 articles in statistics, mathematics and medical journals. He also is the author of “Bootstrap Methods” now in its second edition and “The Essentials of Biostatistics for Physicians, Nurses, and Clinicians” and has coauthored an introductory text in biostatistics for the health sciences and most recently “An Introduction to Bootstrap with Applications to R”. He has also given numerous short courses and lectures on bootstrap and currently teaches bootstrap methods online at statistics.com and biostatistics courses at Thomas Jefferson University School of Population Health. Dr. Chernick is also a former President of the Princeton-Trenton Chapter of ASA (2009-2010) and the Southern California Chapter of ASA (1991-1992). He is also an Associate Editor of the Journal of Biopharmaceutical Statistics and Statistics in Biopharmaceutical Research and an Editorial Board member for the Pakistan Journal of Statistics and Operations Research.