Promoting Statistical Insight

Webinar: MCP-Mod – Theory, Implementation and Extensions

Cytel sponsored webinar in association with the PSI

8 May 2019, 14:00 – 15:30 UK

Pantelis Vlachos (Cytel Inc.)

MCP-Mod in East®: Early development dose-finding design and analysis

Selection of a dose (or doses) to carry into a confirmatory phase III study is among the most difficult decisions in drug development. A prerequisite for informed decision making and dose selection at the end of phase II is a solid characterization of the dose-response relationship(s).The MCP-Mod method combines principles of multiple comparisons with modelling techniques to provide an efficient alternative to traditional dose-finding studies which are either designed and analyzed based on multiple comparisons of active doses vs placebo within an ANOVA framework, of assume a functional relationship between response and dose according to a certain parametric model. We illustrate MCP-Mod design and analysis capabilities with East®.

Pantelis is Director/Strategic Consultant for Cytel, Inc. based in Geneva. He joined the company in January 2013. Before that, he was a Principal Biostatistician at Merck Serono as well as a Professor of Statistics at Carnegie Mellon University for 12 years. His research interests lie in the area of adaptive designs, mainly from a Bayesian perspective, as well as hierarchical model testing and checking although his secret passion is Text Mining. He has served as Managing Editor of the journal “Bayesian Analysis” as well as editorial boards of several other journals and online statistical data and software archives.

Register at: http://psiweb.org/events/psi-events

Please contact the PSI secretariat on psi@mci-group.com if you have any queries.

Promoting Statistical Insight

Neal Thomas
(Pfizer Inc.)

Understanding MCP-Mod dose finding as a method based on linear regression

MCP-MOD is a testing and model selection approach utilizing contrast-based test statistics and p-values adjusted for multiple comparisons. The MCP-Mod procedure can be alternatively represented as a method based on simple linear regression, where 'simple' refers to the inclusion of an intercept and a single predictor variable, which is a transformation of dose. It is shown that the contrasts are equal to least squares linear regression slope estimates. The test for each contrast is the usual t-statistic for a null slope parameter, except that a variance estimate with fewer degrees of freedom is used in the standard error. Selecting the model corresponding to the most significant contrast p-value is equivalent to selecting the predictor variable yielding the smallest residual sum of squares. Many of the properties of MCP-Mod procedure can be understood and quantified using results from least squares linear model theory.

Neal received a PhD in Statistics from the University of Chicago. He is the leader of the Statistical Research and Innovation center at Pfizer working on clinical and non-clinical applications in several therapeutic areas. Previous work experience includes sample surveys, educational statistics (ETS), and health policy applications. Statistical research interests include design of observational studies, dose response, missing data methods, matrix sampling, psychometric models, and Bayesian statistics.

Register at: http://psiweb.org/events/psi-events
Please contact the PSI secretariat on psi@mci-group.com if you have any queries.

Saswati Saha (Inserm, Aix-Marseille University)

Model based dose-finding methods in Phase II clinical trials

The primary objective of this presentation is to discuss dose-finding methods in Phase II clinical trials that can simultaneously establish the dose-response relationship and identify the right dose. MCP-Mod is one of the pioneer approaches developed within the last 10 years. Though MCP-Mod is identified as an efficient statistical methodology for model-based design and analysis of Phase II dose finding studies under model uncertainty, a major disadvantage of MCP-Mod is that the parameter values of the candidate models need to be pre-specified a priori for the PoC testing step. This may lead to loss in power and unreliable model selection. Off late several new variations and alternatives to MCP-Mod are explored where the parameter values need not be pre-specified in the PoC testing step and can be estimated after the model selection step. We will briefly introduce four such state-of-art dose-finding methods, show how to implement the methods in R software and present a numerical comparison between the different new methods and the MCP-Mod approach.

Saswati completed her Ph.D as a part of IDEAS network on December 2018 from the Competence Center for Clinical Trials (KKSB) at University of Bremen under the supervision of Professor Werner Brannath. Her primary areas of research during her PhD were dose response modelling, multiple testing, drug combination studies, dose finding and confidence interval estimation for target doses in drug development.

Saswati studied at the Indian Statistical Institute, where she completed her Bachelor's degree (2011) and Master's degree (2013) in Statistics. After her masters she worked on credit risk modelling in two renowned financial institutions, Ernst & Young and Genpact, for two years and dealt with time series modelling for stress testing and logistic regression modelling for building scorecards.