Wiener Biometrische Sektion
der Internationalen Biometrischen Gesellschaft
Region Österreich – Schweiz

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Einladung zum

Biometrischen Kolloquium

am Montag den 13.03.06 um 14:00 Uhr

im Seminarraum (3.Stock, Raum 88.03.513) der
Besonderen Einrichtung für Medizinische Statistik und Informatik
(MSI) der Medizinischen Universität Wien
Spitalgasse 23, 1090 Wien

Es spricht Doz. Dr. Frank Bretz (Biostatistics, Novartis Pharma AG, Basel, Switzerland) zum Thema:

Combining Multiple Comparisons and Modeling Techniques in Dose Response Studies

Wir ersuchen um zahlreichen Besuch für diesen sehr interessanten und aktuellen Vortrag.

Karl Moder
Präsident

Werner Brannath
Sekretär

Combining Multiple Comparisons and Modeling Techniques in Dose Response Studies

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Abstract

The search for an adequate dose involves some of the most complex series of decisions to be made in developing a clinically viable product. Typically, decisions based on such dose-finding studies reside in two domains: the first being one of "proof" that the treatment provides evidence of effectiveness. The second concerns the need to choose dose(s) for further development.

In this talk we consider a unified strategy for designing and analyzing dose-finding studies, including the testing of proof-of-concept and the selection of one or more doses to take into further development. The methodology combines the advantages of multiple comparisons and modeling approaches, consisting of a multi-stage procedure. Proof-of-concept is tested in the first stage, using multiple comparison methods to identify statistically significant contrasts corresponding to a set of candidate models. If proof-of-concept is established in the first stage, the best model is then used for dose selection in subsequent stages. In particular, we describe and illustrate practical considerations related to the implementation of this methodology. We discuss how to determine sample sizes and perform power calculations based on the proof-of-concept step. A relevant topic in this context is how to

obtain good prior values for the model parameters; different methods to translate prior clinical knowledge into parameter values are presented and discussed. In addition, different possibilities of performing sensitivity analyses to assess the consequences of mis-specifying the true parameter values are introduced. All methods are illustrated by real dose-response phase II studies.

References

- Bretz, F., Pinheiro, J.C., and Branson, M. (2004) On a hybrid method in dose finding studies. *Methods of Information in Medicine*, **43**(5), 457-461.

- Bretz, F., Pinheiro, J.C., and Branson, M. (2005) Combining multiple comparisons and modeling techniques in dose-response studies. *Biometrics*, **61**(3), 738-748.

- Pinheiro, J., Bretz, F., and Branson, M. (2006) Analysis of dose-response studies: Modeling approaches. In: *Dose Finding in Drug Development*. Ting, N. (ed.), Springer, New York, p. 146-171.

- Pinheiro, J., Bornkamp, B., and Bretz, F. (2006) Design and analysis of dose finding studies combining multiple comparisons and modeling procedures. (submitted)

Information about the authors

Both authors work in the Statistical Methodology group of the Biostatistics Department at Novartis. Frank Bretz is an expert on multiple comparison procedures and dose-response analyses. José Pinheiro is an expert on non-linear / mixed models and co-author of the Springer book "Mixed-Effects Models in S and S-PLUS".