Wiener Biometrische Sektion
der Internationalen Biometrischen Gesellschaft
Region Österreich – Schweiz
http://www.meduniwien.ac.at/wbs/

Einladung zum

BIOMETRISCHEN KOLLOQUIUM

am **Donnerstag, 11. Juni 2015** um **16:00 Uhr** (s.t.)

Im Schulungsraum 512 des
Zentrums für Medizinische Statistik, Informatik und Intelligente Systeme (CeMSIIS)
der Medizinischen Universität Wien, Spitalgasse 23, 1090 Wien
(Plan siehe http://www.muw.ac.at/cemsiis/allgemeines/anschrift/)

Vortragender:

XAVIER PAOLETTI

Biostatistics and epidemiology dpt / INSERM U1018
Gustave Roussy Hospital, Vielljuif, France

DOSE FINDING ON REPEATED MEASUREMENTS IN ONCOLOGY PHASE I CLINICAL TRIALS

Wir freuen uns auf zahlreichen Besuch.

Franz König
Präsident

Stephan Lehr
Sekretär

DOSE FINDING ON REPEATED MEASUREMENTS IN ONCOLOGY PHASE I CLINICAL TRIALS

XAVIER PAOLETTI

Biostatistics and epidemiology dpt / INSERM U1018
Gustave Roussy Hospital, Vielljuif, France

Abstract:

Phase I oncology clinical trials are designed to evaluate the toxicity profile of several doses of a new treatment and to identify a dose that can be safely recommended for phase II trials (RP2D). The recommended for phase II is defined as the maximum tolerated dose (MTD). The main endpoint is toxicity. Severity of toxicity is graded from 1 (mild adverse event) to 5 (death). Classically, the MTD is a dose associated with a predefined probability of severe grade 3 or 4 toxicity, called dose-limiting toxicity (DLT) evaluated on the first cycle of treatment. O'Quigley et al. (1990) proposed a continual reassessment method, an adaptive design based on continuous re-estimation of the dose-DLT probability using Bayesian or likelihood inference. The performances of these trials including small sample sizes are limited by the elementary binomial variability of the main outcome. Moderate toxic side events, repeated measurements of toxicity throughout the trial, activity endpoints are not considered. Furthermore the assumption that the RP2D is the MTD is repeatedly challenged and a formal evaluation of the risk of toxicity together with the chance of benefit is increasingly requested.
Recently, it was recommended that all cycles of treatment be analyzed to determine the RP2D. In this communication, we focus on the incorporation of time in the conduct and analysis of phase I trials. Extensions of the CRM for time to event as well as for repeated measurement will be presented. The issue of the impact of dose modification during the course of the trial on the estimated of the probability of toxicity will be illustrated. Finally an approach for the joint modeling of toxicity and activity endpoints at two cycles will be introduced (IDEAS project).