Tutorial on Adaptive Designs for Confirmatory Clinical Trials

On behalf of the IDEAL consortium Franz König will give an invited tutorial on „Adaptive Designs for Confirmatory Clinical Trials" at the ENAR 2016 Spring Meeting in Austin, Texas, on March 8. The meeting is organized by **Eastern North American Region (ENAR)** of the **International Biometric Society (IBS)**. A recent review by Elsaeßer et al (2014) showed that about 59% of adaptive designs evaluated by the scientific advice working party of the European Medicines Agency related to trials in rare diseases and about 36% applied for orphan designation.

Since the first methodological papers on adaptive designs, some published more than 25 years ago (see Bauer et al 2016) , adaptive designs have gained increasing attention in drug development. Especially in pivotal phase III trials, their use is subject to enhanced scrutiny by regulators as the increased complexity of flexible study designs also increases the risk of operational and statistical biases and hidden fallacies. Broad enthusiasm about potential applications of such designs faced critical positions regarding their statistical efficiency. Despite, or possibly because of, this controversy, the methodology and its areas of applications grew steadily over the years, with significant contributions from statisticians working in academia, industry and agencies around the world. In the meantime, such types of adaptive designs have become the subject of three major regulatory guidance documents in the US and Europe and the field is still evolving. The main goal of this tutorial is to give an introduction to the key principles and statistical methodologies of adaptive designs for confirmatory clinical trials. Important applications of adaptive designs include sample size reassessment, treatment selection procedures, and population enrichment designs. The change of design parameters at an adaptive interim analysis may depend on any internal and external data available. Using adaptive multiple test procedures the type I error rate can be controlled even if the selection rule, the number of selected treatments or the final sample sizes are not prefixed. The tutorial shall provide an overview of methods from the published literature including the most recent developments. Special emphasis is put on sample size reassessment and multiple hypotheses testing with adaptive designs. Regulatory issues and case studies will be discussed.

Resources: **https://www.enar.org/meetings/spring2016/index.cfm**

References:

P. Bauer, F. Bretz, V. Dragalin, F. Koenig, and G. Wassmer
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