Announcement

Please take note of the agenda for the upcoming

BBS Seminar talks on Biomarker analyses

➔ **Monday, March 13, 2017 from 15:00-16:30**
Roche ITC learning center located at
Aeschenvorstadt 56, Basel

The Seminar free of charge.

Agenda

15:00 – 15:05	**Welcome**
15:05-15:35	**Statistical perspectives on umbrella trials** Werner Vach, Universitätsspital Basel
15:35 – 16:00	**Comparison of clinical development plans for a confirmatory trial with subpopulation selection** Kaspar Rufibach, Hoffmann-La Roche
16:00-16:30	**Discussion**

Abstracts:

Statistical perspectives on umbrella trials

Werner Vach [12], Nikolaus von Bubnoff [3], Hong Sun [2]
[1] Department of Orthopaedics & Traumatology, University Hospital Basel
[2] Institute of Medical Biometry and Statistics, University of Freiburg
[3] Comprehensive Cancer Center Freiburg, Medical Center, University of Freiburg

The emergence of more and more (rare) molecular markers for targeted therapies in cancer patients is changing the culture of clinical trials. Umbrella trials, aiming to investigate a set of targeted therapies simultaneously in one (wide) patient population constitute one promising approach. However, until now such trials are merely seen as an organisational frame to conduct single sub-studies on each therapy. In my talk I discuss potential advantages when interpreting and conducting such trials as one study. First, based on previous work by Vach & Christensen (Biometrical Journal, 2006) I discuss potential benefits from randomizing patients with multiple markers in a clever way, in particular when allowing to give a combination of treatments. Second I discuss potential benefits from using a model based analysis allowing to borrow information across sub-studies. Finally, I will point to challenges arising from using rapid response evaluation as a tool to allow patients to move to another therapy.

Comparison of clinical development plans for a confirmatory trial with subpopulation selection

Kaspar Rufibach
Methods, Collaboration & Outreach Group, Department of Biostatistics, F. Hoffmann-La Roche, Basel
Joint work with Hoa Nguyen (Genentech, South San Francisco) and Meng Chen (F. Hoffmann-La Roche, Shanghai)

Given ever increasing costs to develop a new drug and intense competition, population enrichment designs should be considered during the planning phase of a pivotal trial with potential subgroup defined by a binary biomarker. Population enrichment designs explicitly factor in the possibility that the new drug might differentially benefit distinct biomarker subgroups. We have compared three clinical development plans for a time-to-event endpoint, such as overall survival, that all lead to a final decision in a pivotal trial either in allcomers only, in allcomers and biomarker positive, in the biomarker positive only, or to declare the drug futile. The decision about which hypothesis to test at the final analysis is made based on a quick time-to-event endpoint, such as progression-free survival, at an interim analysis. We quantify the time gain when using a seamless Phase II/III adaptive design versus alternative development approaches. Furthermore, we discuss operational requirements and considerations when implementing such designs and conclude with an outlook on ongoing work on what information to best combine to make an interim decision.

Rufibach, K, Chen, M, Nguyen, H (2016). Comparison of different clinical development plans for confirmatory subpopulation selection. Contemp Clin Trials, 47:78-84.

Brückner, M, Brannath, W., Rufibach, K. (2017). Interim decisions in adaptive enrichment designs with progression-free and overall survival. Preprint.