Basel Biometrics Society seminar
Basel, 26th June 2018

BBS Seminar:
RCTs, personalized medicine, and surrogacy

Date: Tuesday, June 26, 2018, 15:30-17.45
Venue: Auditorium Building 71, Roche Campus,
Grenzacherstrasse, Basel

The BBS would like to offer a half-day seminar on topics related to clinical trials and personalized medicine with three eminent speakers. All talks will be accessible to general biostatisticians and highlight the relevance of these topics for clinical research and drug development.

The seminar is free of charge. For registration however please send an informal e-mail to Laurence Guillier (laurence.guillier@roche.com) or Barbora Martinec (barbora.martinec@roche.com) until 19th June.

Note that on the next day there will be also a one day joint BBS / EFSPI seminar on small populations at Idorsia, Allschwil. program BBS / EFSPI seminar on small populations

Program:

15:30 - 15:45 **Evaluation of time-to-event surrogate endpoints using accelerated failure time models**
Tomasz Burzykowski
I-BioStat, University of Hasselt, Belgium and International Drug Development Institute (IDDI), Louvain-la-Neuve, Belgium

15:45 – 16:30 **Precision medicine needs randomized trials**
Everardo D. Saad
International Drug Development Institute (IDDI), Louvain-la-Neuve, Belgium

16:30 – 17:00 Coffee

17:00 - 17:45 **Generalized pairwise comparisons for personalized medicine**
Marc Buyse
International Drug Development Institute (IDDI), San Francisco, USA and I-BioStat, University of Hasselt, Belgium

We look forward to your participation!

Remark: Abstracts and map included below.

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Abstracts

Evaluation of time-to-event surrogate endpoints using accelerated failure time models
Tomasz Burzykowski

Currently, the only practical approach to validate surrogate endpoints is the so-called meta-analytic approach (Burzykowski et al., 2005; Alonso et al., 2017). It uses data on the clinical and surrogate endpoints collected in multiple clinical trials organized in the past. When the clinical and surrogate endpoints are time-to-event variables, the meta-analytic approach is most often applied to treatment effects estimated by using the proportional hazards model. In the presentation, an alternative based on semi-parametric accelerated-failure-time models will be presented.

Burzykowski T, Molenberghs G, Buyse M. (eds.) (2005). The Evaluation of Surrogate Endpoints. Springer, New York.

Alonso A, Bigirumurame T, Burzykowski T, Buyse M, Molenberghs G, Muchene L, Perualila NJ, Shkedy Z, Van der Elst W (2017). Applied Surrogate Endpoint Evaluation Methods with SAS and R. Chapman and Hall/CRC Press, New York.

Precision medicine needs randomized trials
Everardo D. Saad

Clinical cancer research is undergoing several changes brought about by precision medicine, which makes it appealing to move efficacy assessment to earlier phases of development and questions the need for randomized trials. Indeed, some remarkably efficacious drugs have even been approved based on uncontrolled phase I or II trials. We challenge the view that the expected benefits from new drugs are generally sufficient to forgo randomization to a standard-of-care arm. Apparently improved outcomes in a single-arm early trial may be due at least in part to the prognostic nature of the target and to selection bias, rather than result from a true effect of therapy. Moreover, the predictive role of biomarkers cannot be ascertained in a definitive way without randomization to a control arm.

Sharma MR and Schilsky RL. Role of randomized phase III trials in an era of effective targeted therapies. Nat Rev Clin Oncol 2012; 9:208–214.

Le Tourneau C, Delord JP, Goncalves A, et al: Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial. Lancet Oncol 2015; 16:1324-34.

Saad ED, Paoletti X, Burzykowski T, Buyse M. Precision medicine needs randomized clinical trials. Nat Rev Clin Oncol 2017; 14:317–23.

Generalized pairwise comparisons for personalized medicine
Marc Buyse

A novel statistical approach to the analysis of randomized clinical trials uses all pairwise comparisons between two patients, one in the treatment arm and one in the control arm. Each pair favors treatment, control, or neither. The “net treatment benefit” is the difference between the proportion of pairs in favor of treatment minus the proportion of pairs in favor of control. Pairwise comparisons can incorporate several outcomes of interest and several thresholds of clinical relevance in the analysis, and as such, they can be used flexibly to personalize treatment choices, and to assess the benefit / risk of randomized therapeutic interventions.

Buyse M. Generalized pairwise comparisons for prioritized outcomes in the two-sample problem. Stat Med 2010; 29: 3245-3257.

Pocock SJ, Ariti CA, Collier TJ, Wang D. The win ratio: a new approach to the analysis of composite endpoints in clinical trials based on clinical priorities. Eur Heart J 2012; 33: 176-82.

Péron J, Roy P, Ozenne B, Roche L, Buyse M. The net chance of a longer survival as a patient-oriented measure of benefit in randomized clinical trials. JAMA Oncology 2016; 2:901-5.

Péron J, Buyse M, Ozenne B, Roche L, Roy P. An extension of generalized pairwise comparisons of prioritized outcomes with censoring. Stat Meth Med Res 2016; doi 10.1177/0962280216658320.

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