Please join the Biometric Colloquium

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INCREASED EFFICIENCY OF FREQUENTIST BASKET TRIALS THROUGH ADAPTIVE CLUSTERING METHODS

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Seminarraum Center for Medical Data Science (previously CeMSIIS),
Spitalgasse 23, Room 88.03.513
Medical University of Vienna, 1090 Wien
Host: Franz König

Abstract:

Traditionally, cancer treatments were based on the location of the primary tumor. However, advances in precision medicine shifted this paradigm towards molecular-targeted drugs, which can be efficacious in multiple tumor sides. By this, treatments become more patient-individualized, resulting in novel statistical challenges like stratification, small sample sizes, and adaptive decision making. One way of incorporating molecular profiling into drug development is using basket designs. In oncologic basket trials, a single drug is simultaneously tested in various tumor locations, where each location defines a substudy, the so-called "basket". These baskets share a common study protocol, streamlining logistic, legal, clinical, and statistical aspects as much as possible. Besides the common infrastructure, the gain in efficiency is partly due to the exchange of data between the substudies. While numerous Bayesian designs with borrowing across baskets have been proposed and compared, substantially fewer frequentist designs were developed and methodological comparisons between those are still lacking.

We compare, develop and improve frequentist approaches addressing clustering in basket trials, including the very recently published methods by Hattori and Morita (2023), and Kanapka and Ivanova (2023). We evaluate these methods using various performance indicators, including marginal power, familywise error rate, and correctness of clusters, to provide recommendations on the best-suited method for specific applications. Furthermore, we modify these methods by e.g. incorporating optimal futility stopping rules in the clustering process.

This comprehensive analysis aims to advance the understanding and application of frequentist approaches in oncologic basket trials, ultimately contributing to more effective and individualized cancer treatments.