ABSTRACT ISCB45:

Title Basket trials in very rare diseases: are they feasible?

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Background In recent years, innovative designs have been proposed in the context of personalized medicine to study the effect of single/multiple drugs on multiple/single sub-populations simultaneously. Specifically, basket trials are used to study a single targeted therapy in multiple diseases or disease types sharing common genetic characteristics. This approach is very useful in rare diseases, where basket trials allow for a more efficient analysis due to borrowing of information across sub-trials. Explicitly, the treatment effect in each sub-trial may provide information on the treatment effect in other sub-trials. Our aim is to assess the feasibility and robustness of a basket design in the setting of very rare diseases, an even more challenging situation.

Methods The clinical setting of interest involves a few trials, each one using the same therapy on very small numbers of patients with different diseases. We evaluated the standard Bayesian approaches on a binary and a continuous endpoint. To achieve concurrent borrowing of information, several methods for a binary outcome have been considered: i) the standard Bayesian hierarchical model (1), ii) the exchangeability nonexchangeability model by Neuenschwander (2) and iii) its recent improvement given by Daniells (3). The case of a continuous endpoint, which might be very informative when the innovative treatment is highly effective, has been addressed with the strategy proposed by Ouma (4). Our simulation study considered various scenarios characterised by the treatment effects of about five sub-trials, each involving a maximum of 15 subjects.
Results The results of the simulation study suggest that basket trials are feasible even in the context of very rare diseases, especially when the effect size is large and consistent across sub-trials.

Conclusions Operating characteristics of the different approaches showed promising results. This encourages our further work to investigate leveraging external information both on controls and on trials conducted with the same treatment on different diseases.

References:

1. Berry SM, Broglio KR, Groshen S, Berry DA. Bayesian hierarchical modeling of patient subpopulations: Efficient designs of Phase II oncology clinical trials. *Clinical Trials*. 2013;10(5):720-734. doi:10.1177/1740774513497539

2. Neuenschwander B, Wandel S, Roychoudhury S, Bailey S. Robust exchangeability designs for early phase clinical trials with multiple strata. Pharm Stat. 2016 Mar-Apr;15(2):123-34. doi: 10.1002/pst.1730.

3. Daniells L, Mozgunov P, Bedding A, Jaki T. A comparison of Bayesian information borrowing methods in basket trials and a novel proposal of modified exchangeability-nonexchangeability method. Statistics in Medicine. 2023;42(24):4392-4417. doi: 10.1002/sim.9867

4. Ouma, L.O., Grayling, M.J., Wason, J.M.S. & Zheng, H. (2022) Bayesian modelling strategies for borrowing of information in randomised basket trials. Journal of the Royal Statistical Society: Series C (Applied Statistics), 71(5), 2014–2037. Available from: https://doi.org/10.1111/rssc.12602