

An Adaptive Hierarchical Test Procedure after Selecting Safe and Efficient Treatments

Franz König, Peter Bauer, Werner Brannath

Dept of Medical Statistics and Informatics
Medical University Vienna, Austria
e-mail: franz.koenig@meduniwien.ac.at

We consider the situation where during a multiple treatment (dose) control comparison high doses are truncated because of lack of safety and low doses are truncated because of lack of efficacy, e.g., by decisions of a data safety monitoring committee in multiple interim looks. We investigate the properties of a hierarchical test procedure for the efficacy outcome in the set of treatments carried on until the end of the trial, starting with the highest selected treatment to be compared with the control at the full level α . Left truncation, i.e., dropping doses in a sequence starting with the lowest dose, does not inflate the type I error rate. It is shown that right truncation does not inflate the type I error if efficacy and toxicity are positively related and treatment selection is based on monotone functions of the safety data. A positive relation is given e.g. in the case where the efficacy and toxicity data are normally disturbed with a positive pairwise correlation. Two specific right truncation rules are considered, one based on the mean treatment-control differences, the other based on the absolute treatment means at the interim looks. The power is increased if sample sizes saved for the truncated treatment groups are reallocated to the remaining treatments and control at the following stages.