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Meeting Abstract

Clinical Trial Designs for Predictive Marker Validation and Targeted Cancer Therapies

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Text

Background: Cancer is a major cause of death with an increasing incidence worldwide. Targeted therapies in combination with predictive markers can increase treatment success and reduce adverse events in cancer patients. There are several ways to design trials to evaluate these test-treatment combinations (i.e. companion diagnostics).

Research Question: To perform a systematic review on study designs that can be applied to validate test-treatment strategies in a single trial. Thereby, randomized controlled trial (RCT) subtypes for phase III clinical cancer trials are to be identified, characterized and assessed for their ability to provide valid results.

Methods: A systematic literature search of the databases MEDLINE, EMBASE and The Cochrane Library was performed (up to June 2011). A standardized extraction form was used to extract the following data for each identified RCT subtype: questions the design can answer; ethical considerations; influence of marker prevalence, test and treatment properties; internal validity; external validity; and precision

Results: Overall, 22 methodological papers were included. In addition to a retrospective design, four different prospective RCT subtypes were identified: the Enrichment Design, Biomarker-Stratified Design, and two marker-based approaches. These RCT subtypes differed in their research objective, prerequisites concerning test and treatment properties, generalizability, feasibility according to ethical demands, and required sample size. Furthermore, various design-specific sources of bias and analysis strategies were explored.

Conclusions: This review provides a detailed overview of existing RCT designs and can be used as a basis for further application in terms of evidence-based research in the field of companion diagnostics. Additionally, these findings provide valuable input for future research in terms of trial design and will serve as an input to an HTA framework on personalized cancer medicine.