Designing Studies to Evaluate Biomarkers for Selecting Patient Treatment

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Abstract

Biomarkers associated with patient response to treatment have the potential to improve clinical outcomes by restricting treatments to the patients most likely to benefit. The ideal setting for evaluating a treatment selection biomarker is a randomized controlled trial. The biomarker may be measured at baseline on the entire trial population, or on a subset of participants potentially selected on the basis of treatment response. Existing study design methodology is limited, and focuses on evaluating biomarkers by testing for a statistical interaction between biomarker and treatment assignment. We propose an approach which powers the biomarker study to evaluate the impact of a marker-based treatment policy on the population response rate. We provide methods for determining the required number of patients and optimal treatment allocation and for sub-sampling from the trial population based on treatment response. We compare these designs with those powered to test for statistical interactions and illustrate the approach using a study to evaluate the Oncotype DX marker for selecting adjuvant chemotherapy to treat estrogen-receptor positive breast cancer.

Keywords: Biomarker; Treatment selection; Clinical trial; Interaction.

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