An analytical approach to assess the predictive value of biomarkers in Phase II decision making

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Abstract

In drug development programs, early phase II clinical trials typically have a biomarker as a primary outcome. Decision on whether to proceed with further development is then based on frequentist analysis of the biomarker data. We suggest an additional rule based on Bayesian predictive probabilities. We adopt the methodology suggested by for evaluating the probability of success of a subsequent phase III study. We estimate this probability based on phase II results on the biomarker. For a dichotomous clinical endpoint of interest to be measured in phase III, a Beta prior distribution is suggested. This distribution quantifies information from both the data observed on the biomarker and its predictive accuracy, which provides insight on how much information from the biomarker is passed on to inform decision-making. We quantify the substantial impact of the predictive ability of biomarkers, aiding decisions concerning both the choice of the biomarker and also further clinical development through a phase III trial. The approach is illustrated with a practical example where a biomarker has to be chosen as a primary endpoint for the phase II trial. A more extensive simulation study is also presented.