Yale SCHOOL OF PUBLIC HEALTH
Biostatistics

SEMINAR

Bayesian adaptive designs for biomarker selection and adaptive randomization – from theory to practice

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ABSTRACT

Advances in biomedicine have fueled the development of targeted agents in cancer therapy with companion diagnostics. The main challenges are to evaluate the treatment efficacy as well as to identify prognostic and predictive markers among a large number of candidate markers. In addition, upon ascertaining each patient's marker profile, it is desirable to treat patients with best available treatments in clinical trials accordingly. We have developed Bayesian adaptive designs to (1) test the treatment efficacy, (2) identify prognostic and predictive markers, and (3) provide better treatments for patients enrolled in the trial. A two-step Bayesian Lasso with group Lasso followed by adaptive Lasso is used for selecting important markers. The outcome-adaptive randomization (AR) is implemented to assign more patients to more effective treatments based on patients' biomarker profile and the available data accumulated in the trial. Through simulations, design parameters can be chosen to yield the desirable operating characteristics in terms of high probability of selecting important markers, accurately assessing the treatment effect, and yielding an overall better patient outcomes. Compared with the traditional designs, the proposed adaptive designs can be more efficient, more ethical, and also more flexible in the study conduct. To move from theory to practice, additional infrastructure such as the Web-based database application, e-mail notification, adaptive randomization program, and clinical trial monitoring system, etc. must be set up to allow timely and frequent monitoring of interim results. Bayesian adaptive designs are distinctively suitable for the development of multiple targeted agents. Examples and lessons learned from the recently completed BATTLE-1 trial and the ongoing BATTLE-2 trial in non-small cell lung cancer will be given.

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