The Probability of Being in Response Function and Its Applications

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Abstract

Cancer clinical trials usually have two or more types of related clinical events (i.e. response, progression, relapse and death). Patients with solid tumors may experience a response (shrinkage of the tumor by a defined amount) after treatment, or instead a progression of disease (enlargement of the tumor). Patients in response may also eventually progress. Hence, to compare treatments, efficacy is often measured using multiple outcome variables. Many clinical trials use a primary composite endpoint such as disease free survival, progression free survival or overall survival for measuring treatment efficacy. Although the use of the primary composite endpoint causes no difficulty, it is not uncommon for different endpoints to indicate different results. Two summary measure the probability of being in response as a function of time (PBRF) and the expected duration of response (EDOR), was proposed and was studied about 35 years ago. It can be easily seen that the area under the PBRF, if available to infinity, is identical to EDOR. Hence, EDOR and PBRF can both be used to compare treatment efficacy in cancer clinical trials. The PBRF and EDOR are excellent measures which consider the response rate and the duration of response simultaneously. In particular, other composite endpoints may give contradictory results. The biggest challenge for multiple endpoints analysis is censoring. Analysis of multiple endpoints is complicated by the fact that fatal endpoints (e.g. death) can censor non-fatal endpoints, potentially resulting in informative censoring. Data consisting of a non-fatal endpoint (e.g. response) and a fatal endpoint are called semi-competing risk data. It is unrealistic to assume that response time and death time are independent. However we will assume that censoring time are independent of death times and response time.

This talk will discuss statistical methods to analyze the multiple endpoints in the presence of semicompeting risk censoring. We will study the properties of some existing nonparametric and semiparametric estimators of PBRF. We will also develop, study and proposed estimators of some functionals based on multi-state survival data.