

PRACTICAL BAYESIAN DESIGN AND ANALYSIS OF NON-INFERIORITY TRIAL WITH SURVIVAL RESPONSE

Debajyoti Sinha

Department of Statistics, Florida State University, FL, USA

Resumen

In bio-pharmaceutical industry, the clinical trials for determining the non-inferiority of a new treatment compared to an existing treatment of proven efficacy are becoming important tools for approving alternative treatment that may have other crucial advantages such as easier administration, lower cost, better tolerance (e.g., less toxicity than the cytotoxic drugs for solid tumors), better local resistance to cancer, and protection against drug resistance (for combination therapy). Such trials will also play prominent roles for evaluating immunotherapy agents including cancer vaccines and for assessing most modern-day antibiotics (e.g., quinolones, macrolides, linezolid, tigecycline, daptomycin). However, we show that the popular non-inferiority testing procedure for survival response suffers from higher than nominal type I error rate when survival responses from two treatment arms do not satisfy the underlying strict modeling assumption. We present a formulation of the hypothesis of non-inferiority of two treatments as a statistical hypothesis involving only the survival odds-ratio parameter. We further show that our new Bayesian non-inferiority test has the correct type I and type-II error rates under a wide class of models. These results show that use of our Bayesian test based on utility function is a safer and more statistical practice for non-inferiority trials of survival responses than the commonly used log-rank based tests.