

A PROPOSAL OF APPROXIMATE ONE-SIDED TEST IN CLINICAL TRIALS WITH MULTIPLE ENDPOINTS

Y. Nakazuru^{†1,2}, T. Sozu², C. Hamada², I. Yoshimura²

¹*Japan Tobacco Inc., Tokyo, Japan;* ²*Tokyo University of Science, Tokyo, Japan*

[†] E-mail: *email.yoshiomi.nakazuru@ims.jti.co.jp*

In this paper we consider one-sided testing problem with multiple endpoints in clinical trials to demonstrate the superiority of new treatment for at least one of the endpoints and the non-inferiority for the other endpoints. Bloch et al. (2001, Biometrics) proposed an intersection-union test (IUT) for this testing problem, and Perlman (2004, Biometrics) modified their IUT by replacing the T^2 -type statistic with an one-sided likelihood-ratio test (LRT). However, the test statistic in LRT with unknown variance-covariance matrix is too complicated to be applied to real cases as was pointed out by Tamhane (2002, Biometrics) and Tang (1989, Biometrika).

We, therefore, modified the IUT by applying the principle of an approximate likelihood ratio test proposed by Glimm et al. (2002, Commun. Stat.), and compared the performance of the proposed test with Perlman's IUT using a Monte Carlo simulation with a normality assumption. The simulation results suggested that powers of the proposed test were generally higher than those of Perlman's IUT, keeping type I error rates nearly within the nominal significance level. The inferiority of LRT in Perlman's IUT in power seems to come from the conservativeness due to the nuisance effect of the unknown variance-covariance matrix. The easy-to-use property without performance decrease of the proposed modification should be appreciated.