Testing Superiority And Non-Inferiority Hypotheses In Active Controlled Clinical Trials

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Switching between testing for the hypotheses of superiority and non-inferiority has been an important statistical issue in the design and analysis of active controlled clinical trials. In practice, it is often conducted with a two-stage procedure. It has been shown with δ-margin approach that there is no type I error rate adjustment required to switch to testing non-inferiority hypothesis once the data fail to support the superiority claim. Neither is the adjustment required to switch to testing superiority hypothesis once the null hypothesis of non-inferiority is rejected when the non-inferiority margin is properly pre-specified. However, when using a λ-margin approach for non-inferiority testing, controlling the type I error rate may become an issue with two-stage procedure. We proposed to adopt a single-stage simultaneous test based on Fieller's confidence interval for testing both hypotheses of non-inferiority and superiority simultaneously. Impact on type I error rate of superiority test is evaluated.

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