USE OF AN ADAPTIVE APPROACH ON MULTI-REGIONAL CLINICAL TRIALS WITH DIFFERENT CONTINUOUS PRIMARY ENDPOINTS ACROSS REGIONS

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Multi-regional clinical trials (MRCTs) have been considered widely to accelerate the development of new drugs and to shorten their approval time. This study focuses on the scenario that the primary endpoints between regions are different and the authority agencies concentrate only on their own endpoints as mentioned in the draft guidance of International Conference on Harmonisation E17. A two-stage adaptive design based on interval estimators is developed for early stopping due to futility and for the final decision of each endpoint. Under the proposed adaptive MRCT, each endpoint can be evaluated at the interim analysis to decide “GO” or “NO GO.” Consequently, the required sample size and criteria at the final analysis may need to be modified. We show that the interval estimators at the interim and final analyses are asymptotically binormally distributed. Therefore, sample size can be determined. Simulation studies exhibit that the proposed adaptive MRCT is able to control type I error rate and provide sufficient power.