Use of external information for assessing efficacy equivalence in biosimilar clinical trials

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Recently, numerous pharmaceutical sponsors have expressed a great deal of interest in the development of biosimilars in anticipation of the impending expiration of a number of patents for biological medicinal products. In this study, we focus on the clinical trial phase in the setting in which the equivalence of both pharmacokinetic (PK) and efficacy parameters should be demonstrated. In this context, Uozumi and Hamada (2017) have developed an adaptive seamless design for establishing PK and efficacy equivalence [1].

This talk discusses a multi-regional clinical trial (MRCT) in the aforementioned setting. Although the MRCT is usually performed in developing biosimilars, the Japanese region does not often participate in the MRCT. In consequence, clinical trials are required only in Japan owing to the requirement by the regulatory agency. In this work, we propose a statistical procedure for evaluating the efficacy equivalence in Japan by utilizing information from the MRCT. In the proposed procedure, the Bayesian inference is performed to evaluate the efficacy equivalence by incorporating the power prior [2] in accordance with the congruence of the PK parameters between two trials. Let $\gamma \in [0, 1]$ denote the power parameter that reflects the degree of information from the MRCT. For instance, we fully utilize information from the MRCT when $\gamma = 1$. However, it is difficult to specify γ at the planning stage in practice since the degree of congruence between trials is usually unknown. To address this issue, we have developed the conditional overlapping power prior to help the degree of discounting of information from the MRCT. This idea is based on the extrapolation method in bridging trials [3]. The method will be discussed and illustrated with clinical trial examples.

References

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