

Bayesian Predictive Approach for the Decision-making in Clinical Trials

Background: To improve the probability of success in the development of new chemical entities, evidence-based decision-making is essential in every phase, in particular, in the proof of concept phase. Conventionally, such decision-making has been done mainly based on a p-value or statistical significance of the primary endpoint of a clinical trial. However, as stated in the ASA's statement on p-values, scientific decisions should be based on a more quantitative method instead of a p-value or statistical significance alone. Against this background, several methods for decision-making have been introduced based on the three-outcome approach originally proposed by Lalonde et al. This study aimed to assess the existing approaches and to propose new approach for the interim decision-making.

Methods: Operation characteristics of three types of methods for decision-making in a clinical trial, a traditional hypothesis testing approach, a frequentist approach, and a Bayesian-based three-outcome approach were assessed by numerical simulation with some scenarios with respect to the effect size and sample size. In addition, the approach for decision-making at an interim time point was proposed using the Bayesian predictive probability and its operation characteristics of the proposed approach was also assessed by numerical simulation.

Results: The three-outcome approach was more efficient than the hypothesis testing approach in that it enabled us to reach conclusion with a smaller sample size, and to rule out ineffective drugs with ease. In our simulation settings, the Bayesian-based approach was comparable to the frequentist approach in terms of the operation characteristics and is straightforward due to its interpretation of credible interval. The proposed Bayesian predictive approach for interim decision-making was more beneficial in that it can be regarded as the generalized form of the existing approach and can flexibly be applied at any time during a trial. In this study, the decision-making in a single or two-arm clinical trial with a binary endpoint was assumed, but the setting can potentially be extended to the trials with other types of endpoint.

Conclusion: It is recommended to use the Bayesian-based method to facilitate the decision-making based on the three-outcome approach. The proposed approach can be one of the choices for the interim decision-making in a clinical trial.

Reference:

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