8th Data Science Round Table Discussion

Points to consider to use the Bayesian approaches based on the CID cases

*This English translation of the Japanese presentation file is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Discussion points for the Bayesian theme

Based on discussions in each case,

① What are the characteristics behind adoption of Bayesian study design?

② What are the points to consider when using the Bayesian method?

- Design characteristics, bias/probability of type I error
- Pros and cons/scope of evaluating operating characteristics by simulation

③ How the industry, government, and academia should discuss when planning and implementing Bayesian study designs in the future

Discussion Points (1)

- What are the characteristics behind adoption of Bayesian study design?
  - Reduce sample size by borrowing across doses
  - Reduce sample size by borrowing across diseases and compounds
  - Shorter study duration to ensure minimum sample size
  - Is it appropriate to use Bayesian for the purpose of reducing the sample size? → Conducting a study efficiently such as reducing the sample size may be an incentive to use Bayesian, but it needs to be supported by disease or pharmacological background.
  - It is considered good that efficient conduct of the study may benefit patients, but it is necessary to explain the clinical/pharmacological validity of using Bayesian, and therefore it is necessary to discuss not only with statistics but also with the entire development team.

Discussion Points (2)

- Considerations for using the Bayesian approach (Design characteristics, bias, probability of type I error, etc.)
  - Bayesian hierarchy introduces bias, but it is difficult to determine to what extent it is acceptable.
  - It is also important to estimate how much ESS becomes.
  - Attention also needs to be paid to the misspecification of the model and the impact of parameter setting (so as not to favor the sponsor)
  - Since the simulation takes time, it is necessary to consider the man-hours required at the time of planning.
  - It should also be noted that there may be discrepancies between the simulation and actual operation (e.g., length of time it takes to make a study design change).

- Pros and cons/scope of evaluating operating characteristics by simulation
  - Controlling the type I error rate is important but trying to it too much could make the use of Bayesian less useful. Taking into account that there is a possibility that the application will not be submitted if a large discrepancy with external data is suggested, it is questionable whether it is necessary to conduct a simulation in all settings and control the probability of type I error by considering even the worst cases.
  - From the regulatory perspective, the probability of type I error should be controlled in all situations, but it may not be necessary to confirm it even in clinically unlikely situations. However, it may deviate from the actual study.

Discussion Points (3)

- How the industry, government, and academia should discuss when planning and implementing Bayesian study designs in the future
  - From the regulatory authority's point of view, should first consult with PMDA in the preliminary meeting.
  - From the perspective of academia, there are times that we want to take on the challenge of Bayesian study design, but due to the sponsor's thinking, we cannot freely do it and often become conservative.
  - Is it possible to use Bayesian in a confirmatory study? → Discussion using actual cases is needed.
  - CID may be adopted if it is possible to explain that the use of Bayesian is more appropriate, but it will take effort on the sponsor side and the regulatory authority side to consult. → It would be good if there is a place where we can freely discuss.
  - It would be good to have a framework of consultation with a lower hurdle, instead of formal consultation such as preliminary meeting.