EMA-EFPIA Modelling and Simulation Workshop

Current position and expectation for use of M&S in drug development and regulatory decision making

The PMDA Viewpoint

Yuki Ando

Senior Scientist for Biostatistics

Biostatistics Group/Center for Product Evaluation

Pharmaceuticals and Medical Devices Agency

Outline

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- Role of M&S in regulatory decision
- New project team for innovative methods
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Introduction

- Several approaches are expected to be key for efficient drug development.
  - Multi-regional clinical trials
  - Modeling and simulation
  - Adaptive design
  - Bayesian statistics
  - Etc.
- Global use of the clinical data with understanding ethnic difference, and appropriate use of innovative methods in the drug development will be key to providing effective drugs to the patients in the world with sufficient information.

Role of M&S

- Planning /optimizing the design of future trials
  - Appropriate integration of prior/existing data is useful especially for dose selection
  - M&S might prove to be efficient way to plan the future trials
- Providing additional information in special population
  - The limitation of the population included in the pre-approval clinical trials should be considered
  - M&S can provide additional information for special population such as pediatrics, elderly, and patients with renal/lever impairment.
- There is also possibility of using M&S for consideration of ethnic difference.

M&S for decision making

- M&S has an aspect of “black-box”, because of its complexity and ambiguity of reason for selecting the method.
- When the simulation results will be a certain part of the information in the submission package, the characteristics of the selected methods and implementation should be clearly stated.
  - Details of the modeling and simulation settings
  - Possibility of alternative analysis
  - Analysis plan and implementation
  - Limitation of the interpretation

Interaction with the PMDA review team

- M&S may be a good communication tool for reviewers in several areas such as clinical pharmacology, medical, and statistics.
  - By showing visualized and quantitative results of consideration
- Active discussion of M&S between pharmaceutical industry and the PMDA is encouraged both in the clinical trial consultation meetings and new drug review.

Interaction with the PMDA review team

- Delivery and receipt of written inquiries and answers will form a certain part of our review and preparation, for clinical trial consultation and new drug review
  - Instead of asking sponsors to submit raw data, we usually ask sponsors to re-analyze the trial data
- Regarding active discussion for M&S, submitting detailed explanations of the design and results of M&S is encouraged

New project team: Background

- Innovative approaches for efficient and successful new drug development are actively discussed in Japan.
  - Modeling and simulation (Model-based drug development)
  - Adaptive design
- The PMDA is expected to play an important role in promoting and supporting the appropriate use of such methods based on the experience reviewing study protocols and new drug applications.
  - Providing useful information by investigating submitted information across these drugs
  - Explaining acceptability of the methods in various situations

New project team

- A new project team for innovative methods for drug development was recently established.
- The members are selected from several areas.
  - Clinical pharmacologists
  - Clinicians
  - Biostatisticians
  - (Review management, regulatory science, and standards)
- The Immediate objective of the PT is the use of modeling and simulation.
  - Effects of ethnic factors in multi-regional clinical trials
  - Use of PK/PD and M&S for pediatric dose
  - (Additional topics are under consideration)

Effects of ethnic factors in MRCTs

- With experience in evaluating trial designs and results of MRCTs, the need of further scientific investigation has been discussed.
- Several points should be reviewed across drugs in the PMDA, based on the experience
  - Effects of the ethnic factors on efficacy and safety
  - Relationship among results for global, east Asian, and Japanese population
  - Ethnic factors that should be considered even among east Asian countries
- Since providing useful information is also expected in the context of global simultaneous drug development, this topic may be covered by the PT.

PK/PD and M&S for pediatric dose

- There are several drugs approved for both adults and pediatric patients with specific doses respectively.
- Investigation of several points across such drugs in the PMDA may be useful for deciding pediatric dose.
  - Relationship between PK/PD profiles for adults and children
  - Possibility and limitation of the use of M&S for deciding pediatric dose
- Since promoting appropriate use of the PK/PD and M&S for the population who have difficulty being regularly included in the clinical trial is basically expected, this topic should be covered by the PT.
- Collaborative activity with pediatric project team is also expected.

Other expected topic

- There are additional topics that the PMDA is expected to investigate.
  - e.g. Natural course of disease or placebo effect in some disease areas
- The PT would like to cover such topics as much as possible, considering the importance, urgency, and feasibility.

Summary

- In the environment of active discussion and use of M&S for drug development, we expect further accumulation of experience via consultation meetings, new drug review, and activity of the new project team in the PMDA.
- We are excited about the potential of M&S in providing effective and safe drugs to patients faster, and we are glad to discuss appropriate and efficient use of M&S in drug development with industry, academia and also other regulatory agencies.

Thank you for your attention.

- Information
  - Email: ando-yuki@pmda.go.jp
  - PMDA Homepage (English)
    - http://www.pmda.go.jp/english/index.html
  - PMDA Drug Information (Japanese)
    - http://www.info.pmda.go.jp/