How pharmacometrics could significantly impact regulatory decision making process

Co-Chairs

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Description

Over the past decade, pharmacometrics has played an increasingly important role in driving drug development. Most of the efforts are focused on model-informed discovery and development, with an emphasis on dose optimization. However, pharmacometrics is not only limited to characterization of PK with population PK analyses and dose justification with exposure-efficacy/safety analyses. By leveraging prior knowledge and integrating different methodologies, pharmacometrics can be used strategically to have significant impacts on the regulatory decisions, so the treatment options would become available for patients much earlier than anticipated. Such pharmacometrics strategies have an increasing impact on the regulatory decision making process in recent years, and they are generally accepted by health authorities. As stated in the FDA PDUFA VI Performance Goals for 2018-2022, the role of pharmacometrics is expected to further influence drug development. This symposium is intended to highlight a few successful examples of leveraging pharmacometric strategies which had significant impacts on the regulatory decision. In addition, representatives from the FDA and EMA will also share their perspectives on this topic.

Learning Objectives

Understand development challenges and opportunities in reality to leverage pharmacometric strategies for significant impact on regulatory decisions. Review successful examples on the utilization of pharmacometric. Provide regulatory perspectives

Session Speakers and Presentations

Pascal Chanu - Modifying "Dosage and Administration" section of vismodegib label based on Modeling & Simulation

Vismodegib is approved for treatment of metastatic or locally advanced basal cell carcinoma as a 150mg daily regimen. Adverse events such as muscle spasm may lead to patients interrupting or discontinuing vismodegib therapy. Study MIKIE evaluated two intermittent treatment regimens using 8-week treatment interruptions in a different patient...
population. A model-based evaluation was used to show that using 8-weeks treatment interruptions would still preserve efficacy and therefore support USPI guidance on treatment interruptions to help manage individual tolerability in the labeled population of patients with metastatic or locally advanced basal cell carcinoma.

Amit Roy - Pharmacometric Driven Post-Approval Nivolumab Dose Optimization

This presentation will share the example on the utilization of model-based strategies to extrapolate efficacy and safety of Nivolumab following the Q2W regimen to the Q4W regimen.

Joy C. Hsu - First-line alectinib approval in the U.S. and E.U. for ALK-positive NSCLC one year ahead of global trial readout based on Japanese trial findings: a M&S story

Alecensa 300mg BID received approval for the treatment of ALK infusion gene-positive, unresectable, recurrent or advanced non-small cell lung cancer (NSCLC) in Japan in 2014. Subsequently, a global Phase 3 study in 1L NSCLC following 600mg BID was conducted. While the Phase 3 was on-going, pharmacometric strategies were utilized to bridge Alecensa from Japanese patients to NSCLC patients globally in 1L setting. This enabled approval of Alecensa 600mg BID for the treatment of 1L NSCLC from FDA EMA approximately 1 year ahead of the global Phase 3 readout.

Yaning Wang - A regulatory perspective on the application of model based analyses

This talk will focus on the FDA's perspective on what are the critical components or challenges for the utilization of pharmacometric strategies for significant impacts on regulatory decisions.

Efthymios Manolis - High Regulatory impact M&S: The EMA experience and outlook

This talk will focus on the EMA's perspective on what are the critical components or challenges for the utilization of pharmacometric strategies for significant impacts on regulatory decisions.