EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

efpia
European Federation of Pharmaceutical Industries and Associations

25 November 2011
EMA/926027/2011

EMA-EFPIA Modelling and Simulation Workshop

Break Out Session 2 (BOS2)

Room 4B

Organisers/Panellists: L. Aarons, N. Benda, C. Benson, M. Maliepaard, F. Mentre, K. Prasad, A. Rostami, E. Rook, A. Staab, Prasad Krishna, Norbert Benda
Chairs: C. Benson, E. Rook, A. Staab
Framework: Use of M&S with existing information (data, physiological/ mechanistic knowledge) and reasonable assumptions will allow for improvements and efficiency in informed decision making to improve the outcomes for patient safety and efficacy in the clinical pharmacology arena
Theme 1 : Dose –exposure-response relationship What is the minimum data needed and on which set of assumptions would every stakeholder be comfortable to agree on to make decisons on M&S results for dosing decisions? How do we provide a risk versus benefit approach based on M&S that demonstrates a probabilistic assurance of minimizing risk while maximizing benefit, knowing that risk will not be zero? Differentiate into: - When should M&S be the primary analysis to establish the doses for phase 2/3 rather than traditional statistical analysis? - When and how should prior knowledge be used to establish the doses for phase 2/3? - When can the M&S results be used to interpolate and extraploate for doses to be tested in future trials?
Theme 2: The integration of data (e.g. across studies or clinical and in-vitro data) using M&S along with reasonable assumptions can provide evidence for evaluation of efficacy/safety risks without the need for a separate study. What is the minimum data needed (in-vitro/human/physiologic) and on which set of assumptions would every stakeholder be comfortable to agree on to derive dosing recommendations for untested scenarios (how to deal with scientifically unknown things: transporter activities in different species, impact of renal impairment on hepatic impairment) What is the minimum data needed (in-vitro/human/physiologic), that when combined with a M&S approach and reasonable assumptions, would stakeholders be comfortable to agree on the evaluation of TdP without a TQT study? How do we provide a risk versus benefit approach based on M&S that demonstrates a probabilistic assurance of minimizing risk while maximizing benefit, knowing that risk will not be zero?

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Theme 1: Dose–Exposure-Response relationship		08:30-10:15
Time	**Title**	**Presenter**
8:30-8:45	Industry perspective	M. Lobby / P. Miligan
8:45-9:00	Regulatory perspective	E. Rook
9:00-9:10	Dose finding under model uncertainty – A case study based on a multi-regional clinical trial	C.H. Hsu
9:10-9:20	Design of a model based dose finding study in diabetes	S. Friberg / M. Sandstrom
9:20-9:30	Improvement of clinical benefit for a sub-group of pediatric sJIA patients utilizing model-based dose adjustment optimization	N. Frey
9:30-10:15	Discussion	

~ Coffee Break ~

10:15-10:45

Theme 2: The integration of data (e.g. across studies or clinical and in-vitro data) using M&S along with reasonable assumptions can provide evidence for evaluation of efficacy/safety risks without the need for a separate study		10:45-12:30
Time	**Title**	**Presenter**
10:45-11:00	Industry perspective	C. Benson
11:00-11:15	Regulatory perspective	M. Maliepaard
11:15-11:25	M&S for dose adjustment in renally impaired patients	M. Edholm
11:25-11:35	Modelling of drug interaction mechanism and estimation of drug interaction in patients with renal impairment	M. Edholm
11:35-11:45	Assessment of QTc liability using First Time in Human data, based on PKPD modelling and a more quantitative evaluation of preclinical data	O. Della Pasqua
11:45-12:30	Discussion	