GMP

Groupe de Métabolisme et Pharmacocinétique

DMPK-centred approach to predict Drug Efficacy and Safety

2019 GMP Symposium

16th - 18th October 2019

Château de Montchat | Lyon | France

PROGRAMME

DMPK-centred approach to predict Drug Efficacy and Safety

Day 1: 16th October 2019

12.30 - 13:30 **Arrival and Registration – Welcome Coffee/tea**
13:30 - 13:40 **Welcome to 2019 GMP symposium**
13:40 - 15.10 **SESSION 1:**

Drug related transporter DDI: let's open the Pandora's box

Chairs: Y. Parmentier (Servier), O. Barberan (Elsevier) A. Sharma (Eurosafe)

If metabolizing enzymes are pretty well mastered in term of DDI prediction and clinical outputs, drug transporters remain more challenging. Where do we stand now with regard to assessing risk related to drug transporters starting from in silico predictions to clinical impacts and evaluation, **this is the time to open the Pandora's box.**

S1.1 *Gabriele Cruciani (Perugia University, Italy)*

In silico challenges in transport simulation and prediction

S1.2 *Pieter Annaert (Leuven University, Belgium)*

In vitro approaches to predict transporter related drug-drug interactions

S1.3 *Bruno Stieger (Zurich University, Switzerland)*

Transport proteins as a key component of drug disposition

15:10 - 15:40 **Coffee break and Poster session**

15:40 - 17:10 **SESSION 2:**

How to predict dermal absorption? What is new in this field?

Chairs: R. Barcham (Oroxcell), M Millet (Pierre Fabre), Y. Courbebaisse (Adocia)

Dermal route is a classical route of administration for many drugs, but a lot of questions are still to be addressed such as the role of skin transporters in the absorption, the building of PBPK models and how to use PK-PD data to select the good candidate. This session will try to answer to these questions!

S2.1 *Lionel Trottet (Galapagos, France)*
Dermal PK and PK/PD: Their role in the selection of a dermal drug candidate

S2.2 *Hanan Osman-Ponchet (PKDerm, France)*
Drug transporters in the skin: Role in dermal absorption

S2.3 *Laurence Del-Frari (Laboratoires Pierre Fabre, France)*

PBPK modelling strategy to predict skin and systemic exposure to support the development of cutaneous topical drugs

17:10 - 18:10 **Students Poster Blitz**
Chairs: A. Fahri (Citoxlab), S. Cartot-Cotton (Sanofi), M. Millet (Pierre Fabre)

18:10 - 20:30 **Poster Session & Cocktail**

Day 2: 17th October 2018

8:00 - 8:30 **Welcome Coffee/Tea**

8:30 - 10:00 **SESSION 3:**

Bioanalysis of endogenous and Xenobiotic macromolecules: LC-MS/MS and/or Immuno-methods?

Chairs: Y. Courbebaisse (Adocia), S. Cartot-Cotton (Sanofi), Y. Parmentier (Servier)

An insight in the progress done combining immunocapture with LC-MS/MS quantification to optimize specificity and sensitivity in the field of biologics. A new multiplexed quantitative space for drug and biomarkers in clinical studies? What are the next challenges?

S3.1 *François Becher (CEA, France)*
Bioanalysis of protein biomarkers by targeted high resolution LC-MS/MS

S3.2 *Michael Blackburn (Arcinova, UK)*
Hybrid immunoaffinity LC-MS methodology for the quantification of exogenous and endogenous insulins in human and animal plasma samples

S3.3 *Alexandra Tavernier (Sanofi, France)*
M-Protein semi-quantification in serum from Multiple Myeloma patients based on Immuno-Capture and Liquid Chromatography coupled to High Resolution Mass Spectrometry.

10:00 - 10:30 **Coffee break and Poster session**

10:30 - 12:00 **SESSION 4:**

PKPD modelling in oncology

Chairs: M. Tod (CHU Lyon), F. Hurbin (Sanofi), A. Coquerel (Caen University)

The rate of approval of anticancer drugs remains low compared to other therapeutic areas. Advances in Model Informed Drug Development may help to fill the gap: some illustrations are presented.

S4.1 *Marylore Chenel (Servier, France)*
Model Informed Drug Development of anticancer drugs: feedback from a pharmaceutical company.

S4.2 *Benjamin Ribba (Roche, Switzerland)*
Optimal Dosing Regimen Using a Mathematical Model of Tumor Uptake for Immunocytokine-Based Cancer Immunotherapy

S4.3 *Wenyuan Xiong (Merck-Serono, Switzerland)*
A model for the mutual interaction between PK and PD of the check-point inhibitor avelumab

12:00 - 12:45 **GMP Assemblée Générale 2019**

12:45 - 14:00 **Lunch and Posters**

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Day 2: 17th October 2019 (Continued)

14:00 - 15:00 **Keynote speaker:** Marc Pallardy (Paris-Sud University)

Chair: A. Coquerel (Caen University)

State-of-the-art and recent evolution in safety assessment of new drugs (small and large molecules)

15:00 - 16:00 **SESSION 5:**

Estimating the clinical starting dose in human from preclinical data: theory and practice

Chairs: C. Amara (Sanofi), L. Penard (Charles River), C. Khaldi-Serdjebi (Genoscience Pharma), M. Fonsi (Citoxlab)

Decisions on strategies for development of a new medicine and the experimental approaches used to assemble information relevant to the safety (and efficacy) of clinical trials must be science-based, made and justified on a case-by-case basis. In particular, pre-clinical safety assessment may raise specific difficulties because the nature of the target is more specific to humans. Attention should be given to the calculation of the first-in-man dose and to the subsequent dose escalations approach. This session will try to address these questions, presenting some real-life case studies.

S5.1 *Darren Bentley (Certara, UK)*

How to use preclinical data for the selection of the first dose in humans?

S5.2 *Madani Rachid (Genoscience Pharma, France)*

Use of PK and safety data for the selection of the first dose in humans: case study for a small molecule

16:00 - 16:30 **Coffee break and Poster session**

16:30 - 17:30 **SESSION 5 (continued):**

S5.3 *Philippe Ancian (Citoxlab, France)*

Use of pharmacological data (Rc occupancy / biomarker) for selecting the first dose in humans: case study

S5.4 *Céline Amara (Sanofi, France)*

Different approaches for First in human dose selection of Antibodies: case study in autoimmune disease

17:30 – 17:35 **SPONSOR TALK**

Maxime Le Merdy (Simulation plus)

Prediction of the First-in-human Oral Dose for Poorly Soluble Compound using Mechanistic Absorption and Physiologically Based Pharmacokinetic Modeling"

17:35 - 18:20 **SESSION ONE STEP ASIDE:**

Chairs: F. Gattacceca (Smartc, CRCM, Aix-Marseille Université)

Emilie Berland (Institut National de la Police Scientifique, Marseille, France)

Contribution de la pharmacocinétique dans la toxicologie médico-légale

19:30 **Gala Dinner at Victoria Hall**

Day 3: 18th October 2019

8:30 - 9:00 **Welcome coffee/Tea**

9:00 - 10:30 **SESSION 6:**

PK in renal and hepatic impaired subjects: Regulatory aspects and implications in clinical development

Chairs: S. Goutelle (CHU Lyon), Q. Nguyen (IPSEN), F. Hurbin (Sanofi)

Most of small molecules are eliminated either through renal and/or hepatic pathways. Clinical studies in special populations such as patients with hepatic or renal impairment or hemodialysed patients are then requested to support New Drug Application (NDA). Case studies illustrating the specific features and requirements of those studies will be presented in this session.

S6.1 *Vincent Launay-Vacher (AP-HP, France)*

Regulatory aspects for the conduct of clinical studies in renal impaired populations

S6.2 *Annie St-Pierre (Novartis, Switzerland)*

Clinical Pharmacology studies in subjects with hepatic impairment: case studies and impact on the label

S6.3 *Henri Merdjan (Certara, France)*

Pharmacokinetics in hemodialysed patients – from theory to practice

10:30 - 11:00 **Coffee break**

11:00 - 12:00 **SESSION 7:**

Future of modelling: case studies

Chairs: F. Mazuir (Poxelpharma), J. Henri (ANSES), F. Gattacceca (Smartc, CRCM, Aix-Marseille Université)

In the current scientific literature, few papers address the question of the future of modeling. The aim of this session is to show, **with real case examples** applied to drugs and pathologies, that this future is already there. Examples from academia or industry will illustrate how systems biology and artificial intelligence can be implemented to enhance population and physiologically-based PK modeling.

S7.1 *Kerstin Bunte (University of Groningen, NL)*

Learning pharmacokinetic models: combining the predictive power of machine learning with the explanatory power of modelling

S7.2 *Dave Duverle (Novadiscovery, France)*

Building a knowledge-driven modelling & simulation platform for in silico clinical trials

12:00 - 12:15 **POSTER AWARDS**

12:15 - 12:25 **Closing Remarks**

12:25 - 14:00 **Farewell Lunch**