DMDG past Open and Joint meeting programmes

Joint Meeting 2021
- in partnership with the SPS (Swedish Academy of Pharmaceutical Sciences)

19 - 21 January 2021 - ONLINE MEETING

Tuesday 19th January 2021

08.30 - 08.45 **Chairs' Opening Address**
Johanna Haglund, SPS Section Chair and Mark Seymour, DMDG Chair

08.45 - 10.15 **Session 1. Oral delivery beyond rule of 5**
Chair. Stephen Buckley, NovoNordisk
Scope.
Historically, Lipinski's rule-of-five (Ro5) has served as guide for the design of drug compounds amenable to delivery via the oral route. Importantly, its implementation in the traditional druggable target space has resulted in a reduction of attrition originating from poor PK. However, the on-going transition in drug discovery towards alternative means for binding and modulating (often challenging) biological targets has necessitated a rethinking of the approach towards the design, formulation and oral delivery of new modalities. These so-called beyond the Ro5 (bRo5) small molecules (e.g., PROTACs), peptide/peptidomimetics and nucleic acid-based modalities provide new challenges (and opportunities) with respect to their amenability towards oral dosing. This session will highlight the strategies – both chemistry and formulation – being harnessed to overcome the inherent complexity associated with the oral administration of bRo5 and new modalities.
Speakers.
1.1 Intramolecular hydrogen bonding and chameleonicity to design new oral drugs in the bRo5 chemical space
Giulia Caron, University of Torino
1.2 Design of oral drugs beyond the rule of 5 - Opportunities, some guidelines and challenges
Jan Kihlberg, Uppsala University
1.3 Oral antisense oligonucleotides and PKPD considerations
Peter Gennemark, AstraZeneca

10.15 - 10.45 **Bring-Your-Own-Coffee, Posters, Trade Exhibition**

10.45 - 11.10 **Session 2a. Student Poster Blitz**
Chairs. Sarah Armstrong, DMDG Apprentice Committee member
Scope.
Student poster blitz. This is a chance for students who are presenting posters during the open meeting to promote their research through an "elevator-pitch" 2-minute oral presentation in a quick-fire format.

11.15 - 12.00 **Session 2b. Rosenön award**
Chairs. Suzanne Iverson Hemberg, SPS Committee
Scope.
The second part of this session will be the Rosenön award organised by the Swedish Pharmaceutical Society, Pharmacokinetic and drug metabolism section. To stimulate research within the areas drug metabolism, pharmacokinetics and/or pharmacodynamics AstraZeneca, Admescope Sweden and Pharmetheus sponsor the Rosenön Award with 30 000 SEK, to be awarded to the best doctoral thesis of the year, defended at a Swedish university. See details here.
https.//www.apotekarsocieteten.se/stipendier-och-priser/vara-priser/the-rosenon-award/

12.00 - 13.00 **Bring-Your-Own-Lunch, Posters, Trade Exhibition**

13.00 - 14.45 **Session 3. Organ-on-a-chip. hype or revolution?**
Chair. Reiner Class, UCB and *Graeme Scarfe, AstraZeneca*
Scope.
The use of traditional cell culture and animal models in preclinical drug screening did not significantly reduce high drug attrition rates in clinical trials. There is general agreement in the scientific community that this is largely due to their inability to accurately predict the human

response. Microphysiological systems (MPS) are currently considered the most promising alternative and a milestone in preclinical drug testing. MPS interconnect human organoids with a flow thus mimicking the human body in a physiologically relevant manner. MPS have the potential to recapitulate the in vivo drug processes of ADMET, simulate PK/PD and drug-drug interactions, and ultimately guide drug candidate screening and dose selection for clinical trials. The session will highlight the various technological approaches in the MPS field, showcase selected platforms, present data and their clinical correlation. Representatives from leading organizations will share their experience and data, discuss regulatory acceptance, and provide an outlook.

Speakers.

3.1 Microphysiological Systems for Human Focused Drug Discovery
Tomasz Kostrzewski, CN Bio Innovations Limited, Cambridge, UK

3.2 Multi-organ Microphysiological Systems with Physiological Amounts of Blood Surrogate
Mandy B. Esch, National Institute of Standards and Technology, Gaithersburg, USA

3.3 Multi-organ microphysiological system coupled with mechanistic mathematical modelling for studying cardio-metabolic disorders
Liisa Vilén, AstraZeneca

3.4 ADME Requirements for Microphysiological System Adoption
Stephen Fowler, Roche Innovation Centre, Basel, Switzerland

14.45 - 15.30 **Bring-Your-Own-Tea, Posters, Trade Exhibition**

15.30 - 17.00 **Session 4. Novel approaches for studying hepatobiliary elimination and transporter inhibition**

Chairs. Laurent Salphati, Genentech and Carina Cantrill, Roche

Scope.

The characterization of the mechanisms driving the hepatic elimination of drugs and the assessment of transporter inhibition are essential activities during drug development. These investigations are critical for the prediction of human pharmacokinetic parameters and the evaluation of the potential for drug-drug interactions (DDI). However, the processes involved in hepatobiliary elimination are often studied in independent experiments or systems, leading to challenges in data integration. Similarly, models for transporter inhibition studies and DDI predictions are still being tested and optimized. This session will highlight novel in vitro models/approaches that attempt to assess simultaneously the combined effects of hepatic transporters and enzymes, and their use in predicting drug disposition. Recent developments in the study of transporter inhibition will also be presented.

Speakers.

4.1 Insights on hepatobiliary transporter kinetics and DDIs from imaging. Lessons from PBPK modelling of gadoxetate
Dr Daniel Scotcher, Centre for Applied Pharmacokinetic Research (CAPkR) University of Manchester, UK

4.2 Impact of preincubation time on transporter inhibition potency
Dr Birk Poller, Novartis Basel, CH

4.3 Transporter/enzyme activities and interactions in a novel long-term hepatocytes culture system
Eugene Chen, Genentech

17.00 - 18.00 **Session 5. Candlelight Keynote Speaker**

Tommy B. Andersson, PhD, Prof. Emeritus

Scope.

The Candlelight Keynote lecture is a recurring feature from the Swedish Pharmaceutical Society and started as a serendipity. A number of symposiums back (called Rosenön meeting) there was a big snowstorm and the power was shut down. To continue with the show, the conference moved to the cafeteria where candles were lightened and the lecture was continued. Ever since, there has been a so-called Candle light lecture where an important contributor in the field of PK and Drug metabolism has been invited to make a presentation supported by candle lights, chalks and a board. We are now in a Pandemic and never so dependent on the electronic and digital tools. However, switch off the spot lights, bring a candle light and enjoy the streamed version of the Candle light lecture of this year´s meeting.

Chair. Rasmus Jansson Löfmark, SPS committee

Wednesday 20th January 2021

08.15 - 10.00 **Session 6. Free Communications**

Chair. Jamie Henshall, DMDG Committee

Scope.

This is an open session for hot topics or informative case studies which may not fit into the themes of any of the other sessions but were too good to leave out!

Speakers.

6.1 Update from the IQ Commenting Group on FDA Guidance Draft for DDI Assessment of Therapeutic Proteins

Kevin Brady, UCB

6.2 Case studies from mechanistic DILI investigations in 3D liver micro-tissues

Armin Wolf, InSphero

6.3 Predicting food effect through identifying solubility-limited absorption *in vivo*

Sheila-Annie Peters, Merck Group

6.4 Radiolabeling and ADME strategies for nucleic acid based therapeutics

Stephen Harris, Pharmaron

10.10 - 10.30 **Bring-Your-Own-Coffee, Posters, Trade Exhibition**

10.30 - 12.15 **Session 7. DMPK of oligonucleotide-based therapies**

Chair. Shalini Andersson, AstraZeneca

Scope.

Oligonucleotide-based therapies, with their characteristic mode-of-action, shows a great potential to treat diseases that have previously been challenging to treat and are also expanding from rare diseases to broader patient populations. Currently there are 10 approved oligonucleotide drugs and several more in clinical trials. Natural oligonucleotides have poor DMPK properties with poor cell penetration and are readily degraded by nucleases. Chemical modifications, of both the nucleotide backbone and the sugar moiety, have improved the "drug-like" properties of oligonucleotide drugs. Additionally, the use of enhanced delivery to specific cell types and conjugation of oligonucleotides to multivalent N-acetylgalactosamine (GalNAc) has also enabled low clinical dose and infrequently subcutaneous dosing. Furthermore, there are promising pre-clinical data suggesting that the use of targeted drug delivery has the potential to target specific cell types beyond hepatocytes in the human body at low therapeutic doses.

However, there are challenges in terms of driving oligonucleotide-based therapy projects forward in the drug discovery, development and clinical phases. These challenges are experimentally based (e.g. drug quantification, metabolite characterization), experimental design based (e.g. drug-drug interaction assessment, duration of in vitro/in vivo studies) as well as regulatory considerations. This session will focus on the DMPK pitfalls, tactical considerations, challenges and recent advancements in this highly expanding field.

Speakers.

7.1 Key lessons learned in designing potent and safe therapeutic oligonucleotides

Marie W Lindholm, Silence Therapeutics

7.2 Comparison of clinical oligonucleotides against HBV - what are crucial PK/PD features?

Ben-Fillippo Krippendorff, Roche

7.3 Exploring the ADME Properties of a GalNAc ASO during non-clinical and early Clinical Development

Steve Hood, GlaxoSmithKline

7.4 Oligonucleotide therapy for kidney targets

Christine Ahlström, AstraZeneca

12.30 - 13.30 **Bring-Your-Own-Lunch, Posters, Trade Exhibition**

13.30 - 15.00 **Session 8. PKPD of New Therapeutic modalities. learnings from clinical successes and remaining challenges**

Chairs. Karelle Menochet, UCB

Scope.

More pharmaceutical companies are moving beyond traditional small molecules and monoclonal antibodies to become modality agnostic. Understanding of the mechanism of action and the dynamics of novel targets is therefore critical to choose the appropriate modality to prosecute targets that were thought undruggable with traditional approaches. The

aim of this session is to review the PKPD understanding of new modalities that have recently gained market approval (gene and cell therapy) and to highlight the impact that early PKPD understanding can have on drug design (PROTACs, peptides).
Speakers.

8.1 RIP'ing up the 'small' molecule drug discovery book!
Paul Scott-Stevens, GlaxoSmithKline

8.2 DMPK/PD consideration for cellular therapies
Wouter Driessen, Roche

8.3 Modelling and simulation in Viral Gene Therapies. Applicability and Feasibility
Nagendra Chemuturi, Takeda

15.00 - 15.45 **Bring-Your-Own-Tea, Posters, Trade Exhibition**

15.45 - 17.15 **Session 9. PBPK and PD models of biologics & new modalities – An integrated approach**
Chair. Kunal Taskar, GSK

Scope.
There have been several recent advances and improvements in understanding the ADME of biologics and within this area PBPK models has played, and will play, an important role. This session aims to cover basics to advanced information on PBPK modeling of biologics and it's various applications including PD of biologics. The PBPK-PD applications aims to not only include target identification to FTIH, but also the use of PBPK to address the immune reaction mediated DDIs and in addition regulatory aspects. The cytokine mediated drug metabolizing enzymes-transporter changes and their modelling strategies for clinical perspective as well as retrospective predictions is gaining popularity in recent times. This session will primarily focus on biologics but applications of PBPK modelling to other new modalities is also encouraged.
Speakers.

9.1 Key concepts in building a PBPK model for therapeutic proteins
Rachel Rose, Certara

9.2 Industry Case Study for PBPK/PD for Biologics
Zhiyi Cui, GSK

9.3 PBPK for biologics. regulatory challenges & expectations
Fabienne Gaugazová, Swedish MPA

17.15 - 18.00 **Bring-Your-Own-Tea, Posters, Trade Exhibition**

Thursday 21st January 2021

08.30 - 10.00 **Session 10. Clinical Pharmacokinetics**
Chair. Anna Nordmark, SDS Life Science

Scope.
Clinical pharmacokinetics is a central aspect in clinical development. The type of clinical studies designed to describe PK varies in type (e.g. human ADME, DDI studies, food interaction, PKPD, healthy versus diseased, pediatrics) and in size. Accurate characterization of PK in clinics is often challenging, depending on the route of administration or the patient population. The aim of this session is to focus on innovative approaches, emerging topics and new regulatory considerations within this field. We invite speakers from the pharma industry to provide experiences, case examples and approaches used.
Speakers.

10.1 The human mass balance study - A clinical pharmacology centrepiece in regulatory submissions
Anita Andersson, Swedish MPA/EMA

10.2 Quantitative approach to support pediatric drug development
Amy Cheung, Certara

10.3 Lung Pharmacokinetics and Regional Targeting of Inhaled and Systemic Drugs. A Clinical Evaluation
Waqas Sadiq, AstraZeneca

10.00 - 10.30 **Bring-Your-Own-Coffee, Posters, Trade Exhibition**

10.30 - 12.00 **Session 11. Debate. "The DMDG/SPS believe that in 2021, CROs are the new champions of DMPK innovation"**
Ringmaster. Steve Hood, GSK

Scope.

The legendary DMDG debate returns for another round. There will be someone proposing for and someone proposing against, and we have the audience. Let the battle(s) begin....

A modern verse for a post-COVID Pharma...
In the beginning was there was the need for an assay
"I will build, validate and run the assay" said DMPK
And it was so.
Soon there was the need for another assay
"I will build and validate it" said DMPK, "but perhaps those nice CRO folks could run it".
And it was done.
Then there was need for yet another assay
"I will build it but my ex colleagues at the CRO will validate and run it" said the DMPK Rep
And it was reported.
Now there is a new need
"Which CRO should I use for this assay?" said the Biology Rep.
And it was budgeted.
Soon there will be a different need
"Which CRO did the biotech use?" said the Business Development rep
And the pdf was found in the data room.
Finally there will be another prompt
"10011101100100100010101010101" said the search BOT
"1010010P4501001001" said Skynet
And it was coded

- Proposing - *Richard Weaver (Sygnature Discovery) and Stephen Madden (Charles River)*
- Against - *Kevin Read (University of Dundee) and Tim Miles (GSK DDW)*

12.00 - 12.15 **Closing Remarks**

- DMDG - *Jo Goodman & Sherri Dudal*
- SPS - *Rasmus Jansson Löfmark*

12.15 - 13.15 **Bring-Your-Own-Lunch and delegates depart**