Translational ADMET for Drug Therapy

Principles, Methods and Pharmaceutical Applications

Course Scope:

Drug disposition, implicated by absorption, distribution, metabolism, excretion (ADME) and toxicity (T) are two of the most critical issues pharmaceutical scientists and regulatory authorities are focussing on during discovery and development of a new medicine of any target disease among all human population. Pharmaceutical companies spend 20-30% of R&D budget to assess compound behaviour with respect to ADMET, the factor that subsequently affecting the pharmacological response and safety of any given drug in target patient populations. Advancements in developing preclinical and clinical tools and technologies that predict pharmacokinetic (PK), Pharmacodynamic (PD) in relation to Toxicokinetics (TK) and Toxicodynamics (TD) have proven the capabilities to reduce the cost and increase the precision in developing a new medicine that ensures efficacy and safety of target human populations.

Because human population can vary depending on age, race, gender, disease, environment, etc, drug dose has to be adjusted. Updated *in vitro* and *in vivo* tools that generate data from bench to bedside to be used in improving drug design and the design of clinical studies towards the individualized medicine and ensure a quality of drug therapy to every patient. The regulatory organizations like FDA and EMA through updated guidance are outreaching pharmaceutical companies, biotech, and CROs in order to support the research and development efforts by listing the most acceptable tools, methodologies, and approaches that scientists can be employed to strategically design preclinical and clinical investigations. These efforts can aid in distinguishing the drug candidates that might be developed to become a new therapeutic agent or those that are not and fail fast, fail cheap.

Predictive ADMET tools that have the potential to enhance the selections of lead compounds and evaluate the drug candidates that facilitate the understanding of mechanisms underlying the disposition of drugs and determine pharmacokinetic parameters, and lastly to select a safe and effective drug dose for First-in-human (FIH) investigation are the focus of the **"Translational ADMET Training"**. *In vitro* and *in vivo* that could translate data generated from bench to bed side or from bed side to bench have now frequently used approach to reveal hidden adverse events, adverse drug reaction, drug-drug interactions, and elucidate the mechanism of drug disposition, selection of animal model by extrapolate across species, ensure the selection of preclinical toxicity species, thus minimize variability among human populations and optimize drug therapy regardless of age, gender, race, or disease.

This state-of-the-art training will provide a broad and current coverage of translational ADMET from drug discovery to drug development and will serve as an extensive classroom training for broad levels of scientists and managers from multidisciplinary functions within biotechnology and pharmaceutical companies as well as CROs. The course will offer an insight to the problems that bench scientists and mangers may face during preclinical and clinical drug development, trouble shooting, and approaches to overcome technical, scientific, and business challenges towards better design studies and ADMET programs. Open classroom discussions will have an emphasis on translational ADMET, mapping of the most effective approaches and technologies that are currently used in the industry to investigate ADME, Pharmacokinetics, and toxicology prior to the setup of clinical studies.

Several case studies from drug discovery and drug development of drug candidates from various therapeutic areas including, study design, possible data interpretations, decision-making, and tactics will be illustrated. The integration of *in vitro* and *in vivo* and *in silico* data to address human PK/PD/TK/TD hence to select the safe and therapeutic dose in human, and support the design of clinical studies, IND, and NDA submissions will be demonstrated. The strategy in translating ADME properties retrospectively from bedside to bench and from bench to bedside towards the design of a safe and effective medicine in special human populations, e.g. paediatrics will be discussed. Such training will be beneficial for business development leaders, sr. graduate pharmaceutical sciences students, and medical students. The training should set the stage for pharmaceutical professionals who are interested to become pharmaceutical managers and leaders for ADMET programs by increasing their knowledge on a scope of tools, resources, staff and budgets needed to develop a successful translational ADMET program.

Day One

09:00-10:15 Absorption: The role of drug intestinal drug Transporters, Physiological, and Physiochemical factors as well as DDI on drug Disposition and PK in clinical: Preclinical tools to predict human data

10:15-10:30 Coffee Break

10:30-12:15 Drug Metabolism and Mechanisms: Role of hepatic drug metabolizing enzymes and hepatobiliary drug transporters and other physiological factors and DDI on drug safety and efficacy in clinic: Preclinical tools to predict human data. Metabolite ID, species difference, and meeting "MIST" regulation

12:15-13:30 Lunch

13:30-15:00 Hands on Exercise (retrospective clinical to be improved by Preclinical investigation on Absorption and Metabolism)

15:00-15:15 Coffee Break

15:15-17:00 Drug Distribution and Excretion: Their impact on drug exposure in body organs, efficacy and safety. Hepatic and renal elimination using preclinical predicting approaches to assess human data

Day Two

09:00-10:30 Preclinical Pharmacokinetic and Toxicokinetics Studies Towards IND Submission

10:30-10:45 Coffee Break

10:45- 12:15 Clinical studies and NDA Submission

12:15-13:30 Lunch

13:30-15:00 The use of translational medicine tools to support the Clinical study design

15:00-15:15 Coffee Break

15:15-17:00 Class Exercise with case studies from bench to bedside: blind practice on efficacious and safe and drugs or those that failed in early clinical investigations or after launch