MODULE 2

Place: University of Ljubljana, Faculty of Pharmacy
Aškerčeva 7, 1000 Ljubljana

Date: November 30 – December 3, 2017

MODULE 2: NON-CLINICAL, PHARMACEUTICAL AND EARLY CLINICAL DEVELOPMENT

Module Leaders: Prof. dr. Irena Mlinarič-Raščan and Prof. dr. Beatriz Silva Lima

PHARMATRAIN BASE COURSE **MODULE 2: NON-CLINICAL, PHARMACEUTICAL AND EARLY CLINICAL DEVELOPMENT**
LEARNING OUTCOMES
At the end of this Module the student should be able to demonstrate an understanding of the:
1. Choice and predictive value of the non-clinical testing programme as part of the overall drug development plan for chemical and biological compounds.
2. Integration of non-clinical tests into the overall drug development plan (including scheduling of toxicology tests with respect to clinical trials).
3. Steps in the pharmaceutical development of a drug substance and final drug product (including chemical and biological compounds).
4. Planning of clinical trial supplies for test substance and comparators (active and placebo).
5. Overview of non-clinical study requirements prior to First-into-Man studies.
6. Molecular and cellular basis of toxic reactions.
7. Principles and practical application of pharmacokinetics and toxicokinetics.
8. Early exploratory development in man.
9. Principles of clinical pharmacology and their application to clinical development.
10. Influence of genetic factors in drug development and drug response.

Day 1 – November 30, 2017 – Thursday

Time	Lecturer	Titles and topics of the lectures and cases	Syllabus	Learning outcomes
8:30-9:00	I. Mlinarič-Raščan S. Kerpel-Fronius	Welcome and introduction		
9:00-9:45	D. Ferčej-Temeljotov	Pharmaceutical industry. The overview of the development of drug substance and drug product for various stages of drug development	4.1, 4.2, 4.3, 4.4	3, 4, 5
9.45-10:30	B. Silva-Lima	Scheduling of general toxicological studies: Mechanism of toxicities, detection & elucidation. Importance of plasma level measurements in toxicological studies	3.2, 3.3 3.6, 3.7, 3.8	1, 2, 6
10.30-11.00		*Break*		
11:00-11:45 11:45-12:30	I. Grabnar	Importance and practical application of metabolic (ADME), pharmacokinetics (PhK) and toxicokinetics (TK) studies in non-clinical studies. In vitro/in silico modelling of human pharmacokinetics	3.3, 3.11, 5.5, 5.6	1, 7
12:30-13:45		*Lunch*		
13:45-14:30	B. Doljak	Principles and significance of GLP in non-clinical studies	3, 3.9, 10.5	1, 2
14:30-15:15	B. Silva-Lima	Safety Pharmacology, hypersensitivity	3.10	2, 5
15:15-16:00	R. Bass	Introduction. Principles of non-clinical (NC) safety testing: ICH guidelines M3 (ICHM3)	3.6, 3.7, 3..8	2, 5
16:00-16.30		*Break*		
16:30-17:15 17.15-18:00	B. Silva-Lima, S. Kerpel-Fronius	Case discussions: Species & model selection	3	1

Day 2 – December 1, 2017 – Friday

Time	Lecturer	Titles and topics of the lectures and cases	Syllabus	Learning outcomes
9:00-9:45	I. Mlinarič-Raščan	Choice of systems; species for NC testing; 3Rs ethical framework for conducting scientific experiments using animals humanely. Influence of genetic factors on drug response and development	1.7, 3.4, 3.5	1, 10
9.45-10:30	I. Mlinarič-Raščan	Introduction to biological medicinal products	1.7, 3.4, 3.5	1
10.30-11.00		*Break*		
11:00-11:45	J.Rozman-Pungečar	Biosimilar medicinal products development	1.7, 3.4, 3.5	1
11:45-12:30	B. Silva-Lima	Non-clinical evaluation of biological medicinal products	4.1	1, 2
12:30-13:45		*Lunch*		
13:45-14:30	B. Podobnik	Non-clinical and clinical pharmacologic aspects of biosimilar development	3.10	8, 9
14:30-15:15	R. Bass	Investigation Brochure: assess of NC data before First in Human (FIH) application; go/no-go decision; the role of biomarkers	3.7, 3.9, 5.1, 5.2	2, 5
15:15-15:45		*Break*		
15:45-16.30	B. Silva-Lima	Identifying and mitigating risks of investigational medicinal products for FIH clinical trials. Conventional and high risk medicinal products	5.1, 5.2	6, 8
16:30-17:15	S. Kerpel-Fronius	Clinical pharmacology of the transition from non-clinical to human development of medicinal products. The significance of microdose (phase 0) studies. Conventional and high risk medicinal products. Influence of genetic factors on drug response and development	5.3, 5.4	8, 9, 10
17:15-18:00	B. Silva-Lima	Introduction to group work. Estimation of FIH dose for conventional, small molecular weight agents. Estimation of FIH dose for high risk agents	5.3, 5.4	8

Day 3 – December 2, 2017 – Saturday

Time	Lecturer	Titles and topics of the lectures and cases	Syllabus	Learning outcomes
9:00-9:45	M. Černe	Genotoxicity and carcinogenicity testing. Scheduling and data interpretation	3.7, 3.9	1
9.45-10:30	R. Bass	Reproductive and developmental toxicology for CT in women of child bearing potential (WCB), pregnant women	3.5, 3.9	2
10.30-11.00		*Break*		
11:00-11:45	R. Bass	NC studies for clinical trials in pediatric population	3.5, 3.9, 14.6	2
11:45-12:30	F. De Bock	Toxicological Risk Assessment	10.20	
12:30-13:45		*Lunch*		
13:45-14:30	S. Srčič	Choice of formulation, pediatric formulations. Pharmacopoeias	4.3, 4.4, 10.19	3, 4
14:30-15:15	S. Kerpel-Fronius	Non-clinical evaluation of cytotoxic anticancer agents.	3.9	1, 2, 9
15:15-15:45		*Break*		
15:45-16:30	All	Presentations by the students on FIH		
16:30-17:15	B. Silva-Lima	Introduction to group work: the glitazone case		
17:15-18:00	All	Presentations by the students		

Day 4 – December 3, 2017 – Sunday

Time	Lecturer	Titles and topics of the lectures and cases	Syllabus	Learning outcomes
9:00-10.45		*MCQ Examination of module 2*		
10.45-11:15		*Break*		
11:15-12:15	Each 15 min I. Mlinarič-R B. Silva-L R. Bass S. Kerpel-F	New challenges of medicines development • Advanced Therapy Medicinal products • Non-clinical aspects • Safety evaluation aspects • Clinical pharmacological aspects	1.7, 3.4, 3.5, 3.10	1, 2, 5, 7, 8, 9
12:15-13:00	S. Kerpel-Fronius I. Mlinarič-Raščan	Discussion of the right answers to the MCQs. Closing of module 2		
13:00-14:00		*Lunch*		