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MODULE 3

Place: Semmelweis University, Department of Pharmacology and Pharmacotherapy
Floor 4, Issekutz Room
1089 Budapest, Nagyárad tér 4.

Date: March 1-4, 2018

MODULE 3: CLINICAL DEVELOPMENT OF MEDICINES: EXPLORATORY AND CONFIRMATORY

Module Leaders: Sandor Kerpel-Fronius, Romaldas Maciulaitis and Detlef Niese

PHARMATRAIN BASE COURSE **MODULE 3: CLINICAL DEVELOPMENT OF MEDICINES: EXPLORATORY AND CONFIRMATORY**
LEARNING OUTCOMES
At the end of this Module the student should be able to demonstrate an understanding of:
1. Early studies in patients: dose-finding / proof of concept studies and their impact on drug development plan
2. Clinical trial design (including legal, regulatory, ethical and practical aspects): international differences. Orphan drugs
3. Principles and application of statistics in clinical trials
4. Procedures for clinical trial data collection (paper and electronic) and data management (including validation processes) to ensure optimal quality data
5. Key strategic issues in the clinical trial process, in terms of legislative requirements and Good Clinical Practice (GCP)
6. The role of the investigator drug brochure (IDB)
7. Principles and practical relevance of ethical issues in biomedical research
8. Legal and ethical provisions for protection of clinical trial subjects

PharmaTrain MASTERING MEDICINES DEVELOPMENT

CEMDC Cooperative European Medicines Development Course

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Day 1 - March 1, 2018 – Thursday

Time	Lecturer	Titles and topics of the lectures	Learning Outcomes	Syllabus topics
9:00-9:10	S. Kerpel-Fronius	Welcome and introductory remarks		
9:10-10:00	D. Niese	General concept of a development plan. Ethics general, ethics of research questions and clinical drug trials. Equipoise and Conflict of Interest, vulnerable populations CS 1: "The Willowbrook Studies": Clinical Research in mentally disabled children Case discussion	3.2, 3.7, 3.8	7.1, 7.2, 7.4, 7.6, 7,11,8.1, 8.2, 8.3, 8.5, 8.9; 8,13
10:00-10:45	I. Peták	Development and validation of biomarkers. Their role in clinical drug development	3.1	5.1
11:00-11:50	J. Borvendég	Trial regulations, GCP, relevance of the Investigators' Brochure for planning and conduct of clinical trials. Documents needed for starting a clinical trial	3.5, 3.6	7.4, 7.5, 7.6, 10.10
12:00-12:50	R. Maciulaitis	Early clinical development: build clinical objectives out of non-clinical result, PK/PD data and phase objectives throughout pre- and post-authorization phases.	3.1, 3.2	5.1, 5.2, 5.4, 5.5, 5.9, 5.12, 5.13, 5.14, 8.4
13:00-14:30	**Lunch**			
14:30-15:15 15:15 16:00	L. Tóthfalusi	The role & responsibility of the statistician, statistical considerations of study design, hypothesis testing (Null hypothesis,, type 1 and 2 error, significance, power), randomization, sample size calculation, analysis plan, interim analysis, paired and non-paired tests, parametric and non-parametric tests, confidence limits	3.3	9.6, 9.7, 9.8, 9.9, 9.10, 9.11, 9,12, 9.15, 9.16,
16:15-17:00 17:15-18:00	S. Kerpel-Fronius	The changing paradigm of early clinical development of medicines. Clinical pharmacological basis for selecting the starting dose and phase I dose escalation program The Proof of Concept.	3.1, 3.2	5.1, 5.2, 5.3, 5.4, 5.9, 5.12, 5.13, 5.14, 8.4

Day 2 - March 2, 2018 – Friday

Time	Lecturer	Titles and topics of the lectures	Learning Outcomes	Syllabus topics
9:00-9:50 10:00-10:50	L. Tóthfalusi	Efficacy endpoints, Appropriate Master Analysis Plan, Statistical interpretation of the results and reporting.	3.3, 3.4	9.1, 9.2, 9.3,9.7, 9.13, 9.14, 9.18, 9.15, 9.20, 9.21, 9.22, 9.23, 9.24
11:00-11:50 12:00-12:50	D. Niese	Writing the Protocol: Short introduction to the strategy of hypertension treatment. Clinical trial objective, purpose and endpoint, deciding on trial design, trial population, comparators, bias reduction, interim analysis, choice of locations, literature review for a writing a protocol.	3.2, 3.3, 3.4, 3.5, 3.6, 3.8	7.1, 7.2, 7.4, 7.6, 7.7, 7.10, 7.11, 7.10.10, 9,26
13:00-14:30	**Lunch**			
14:30-15:15	Szakolczai Sándor Norbert	Data collection and related quality assurance, types of data and standardization of measurements, patient reported outcomes Risk based monitoring Case Report Form (CRF). View of the investigators	3, 4	9.1, 9.2, 9.3, 9.4, 9.5, 9.12, 9.13, 9.14
15:30 - 16:15	R. Maciulaitis	Innovative techniques to speed up clinical part of product development (Biomarkers, surrogate endpoints, adaptive design, etc.)	3.1, 3.2	5.1, 7.1, 7.2, 9.9, 9.24
16:30-17:15	R. Maciulaitis	Clinical development of biological and target oriented medicinal products. Therapy related companion diagnostics. Personalized medicine. Ethical aspects of taking trial samples for genomic and molecular analyses and handling biological samples. Protection of the personal rights	3.1, 3.5, 3.7, 3.8, 5	8.9, 8.10, 8.14, 14.4
17:15-18:00	M. Sobor	Rare diseases. Scientific and regulatory principles of orphan drug development	3.1, 3.2	2.4

Day 3 - March 3, 2018 – Saturday

Time	Lecturer	Titles and topics of the lectures	Learning Outcomes	Syllabus topics
9:00-9:50	D. Niese	The choice of the control group. Use of placebo, impact of selection of comparator on label	3.2,3.3, 3.8	5.1, 6.3, 6.7, 7.1
10:00-10:50 11:00-11:50 12:00-12:50	R. Maciulaitis D. Niese	CS3: Joint discussion of a drug trial protocol using a real word example Difficulties / failures in R&D developments, fraud in clinical trials; what can we learn	3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8	7.1, 7.6, 8.16, , 9.9, 9.11, 9.19, 9.22, 9,24, 9.25, 9.26, 10.10
13:00-14:30	**Lunch**			
14:30-15:15 15:15-16:00	A. Cseh-Pálos	Drug supply in clinical trials. „Quality by Design" in Drug Development Process	2.4, 3.2	4.1, 4.2, 4.3, 4.4,
16:15-17:00 17:15-18:00	S. Kerpel-Fronius	Ethics: principles, history including Declaration of Helsinki, EU Regulation, Risks, benefits and burden of study participation. Ethical review process, safety and human dignity of research subjects. Informed consent. Ethical aspects of biomedical research, drug trial conduct. The use of placebo	3.8	7.4, 8.1, 8.3, 8.4, 8.6, 8,7, 8.8, 8.9, 8.10, 8, 11, 8.13, 8.14, 8.15

Day 4 - March 4, 2018 – Sunday

Time	Lecturer	Titles and topics of the lectures	Learning Outcomes	Syllabus topics
9:00-9:50 10:00-10:50		**MCQ EXAMINATION**		
11:00-11:50	D. Niese	Good Science is not enough: How to enhance the credibility of research data		