סילבוס עקרונות בסיסיים בפיתוח תרופות; Fundamentals in Drug Development

מס קורס: 1501.1012

מרצים: ד"ר דנה בר-און, (ייעוץ אקדמי: פרופ׳ אורי אשרי)
נציג מרכז מטעם חברת טבע: ד"ר גיא רוזנטל.
תשע"ז, סמסטר א': יום ב' 14-12
מיקום: טרובוביץ' 101
היקף הקורס: 2 ש״ס

דרישות קדם לקורס ודרישות מיוחדות - אין
הקורס מיועד לתמידי תואר שני ושלישי. תלמידי תואר ראשון-שנה ג', רשאים להרשם ע"ב מקום פנוי בקורס.
מטלת הקורס: מבחן סופי

בחינה: מועד א' – 13.2.17
מועד ב' – 6.3.17

- The 'Fundamentals in Drug Development' course will cover the main aspects of the drug development process and will expose students to the essential activities in the pharmaceutical development
- Lectures will be given by Teva experts
- Annual course for MSc and PhD students (a possibility of opening for registration to last year undergraduate students – 3rd year students pending # of registered students)
- Academic year: 2016-2017
- 12 lectures (One includes a visit at the factory); each lecture 1.5hr – 2 academic points *
- Course prerequisites - none
- Course teaching method - lecture
- Course syllabus – see below
- End of course student evaluation - Exam
- Lecture order may change based on availability of presenters along the year

1. Overview to Drug Development

This session will provide an overview spanning new drug idea conception through Investigational New Drug (IND) Application to New Drug Application (NDA) submission and beyond. We will define and explore the various functions/teams involved in drug development, looking into their role at the stages of the drug development process. This will serve as a high level guide

and overview to the lectures that will follow where each lecture will revolve around a specific function/topic in the drug development process

Bibliography

- http://www.fda.gov/ForPatients/Approvals/Drugs/default.htm
- http://www.fdareview.org/index.shtml
- Guide to Drug Development: A Comprehensive Review & Assessment - Bert Spilker

Dr. Elyahu Berkovich, **Non-Clinical Pharmacology**

2. **Intellectual Property in Pharma**

Patents:

- This session will deal with introduction to patents in the pharmaceutical world - What is a patent, why do we need it and what is the philosophy behind it, the different type of patents in the pharmaceutical industry and specific basic concepts in the patent law.
- The session will also focus on patent infringement & patentability issues – what activities are defined as infringing, IP and R&D activities and ways to challenge validity of patents. In addition, we will have a brief discussion on the unique patent system in the US

Dr. Alon Shainberg – Patents

3. Clinical Pharmacology

- This session will discuss the role of pharmacokinetics and pharmacodynamics, the two fundamental disciplines of clinical pharmacology, for drug development. Some basic concepts will be presented, as well as the regulatory expectations from a clinical pharmacology program for a new drug application. Real examples of clinical pharmacology studies conducted by Teva will also be presented

Bibliography

- FDA Clinical Pharmacology guidance: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm064982.htm

Dr. Ofer Spiegelstein – Phase-1 & Clinical Pharmacology

4. Planning of a Clinical Trial

This session will focus on the Target Product Plan (TPP), the Clinical Development Plan (CDP), planning of a phase II, phase III and phase IIIb/IV study. Translating this plan into a study synopsis, protocol that is submitted and approved by regulatory authorities will be discussed .Examples of different study designs will be reviewed including: population, duration, arms, endpoints, Inclusion/exclusion criteria, procedures and ancillary studies.

Dr. Natalia Ashtamker/Dr. Yuval Dagon (MD, MBA) – Director, Global Clinical Development Multiple Sclerosis, Teva R&D Clinical

5. Chemistry Manufacturing and Control (CMC)

1. CMC main principles
2. How do the physico-chemical properties of a drug substance (DS) influence its formulation in drug product (DP)
3. Process development for DS and DP
4. Analytical method development and quality control

Dr. Adrian Gilbert/Dr. Muhammad Safadi

6. Pre Clinical Pharmacology

- This session will discuss the role of preclinical studies in discovery and development paradigms as employed in today's pharmaceutical industry. These assessments play an important role in the development of new drug candidates. They serve as a guide for clinical development and provide information required for regulatory authorities. Such systems can also be used to investigate novel candidates as well as approved drugs.

- The talk will focus on methods for understanding a drug candidates therapeutic potential by combining information of it’s efficacy , pharmacokinetic, metabolic and safety profiles.

- Examples of the use of *in vitro* system and *in vivo* studies at various stages of the drug development will be presented. This talk will emphasis models used for understanding a potential drugs efficacy in disease and elaborate on its mode of action.

- The advantage and limitations of such models as well as the measures currently used to increase predictability and "translation" of preclinical finding to clinical relevance will be discussed

Dr. Aric Orbach – Non-Clinical Pharmacology

7. Pharmacovigilance

- This session will describe the PhV activities relevant for clinical trials. It will start with a definition of PhV and PhV in Teva. It will explain the importance of managing one global data base and the concept of signal detection. We will introduce the process of collection of serious adverse events from clinical trials.
- The second part of the session will describe the safety management of a product during development phases: starting on the transition from pre-clinical to clinical phases, going through the assessment of clinical safety data during the clinical development phases, the development of a risk management plan preparation for submission and meta-analysis of data, and post marketing safety studies and signal detection process. Also, the session will describe the various levels of safety assessment leaded by PhV: product safety group, medical scientific group and corporate safety board

Bibliography:

- Pharmacovigilance from A to Z, Barton L. Cobert, MD; Pierre Biron, MD.
- Detection of New Adverse Drug Reactions, 4th ed. M.D.B. Stephens, J.C.C. Talbot and P.A. Routledge
- MHRA – Good Pharmacovigilance Practice Guide
- FDA – Guide to FDA Drug Safety Regulation, FDAnews.

Dr. Orit Neudorfer - Global Pharmacovigilance

8. Generics and NTEs

1. Generic drug development – what are the main challenges? comparison to brand drug development, differences, requirements (safety, budget, etc.), patent applications, process of manufacturing.

2. NTE – New Therapeutic Entity – definition, development and examples

Dr. Sharon Fireman / Dr. Dafna Arieli, Director, GxR&D Biopharmaceutics TEVA Pharmaceutical Ind.

9. Personalized medicine and pharmacogenomics

- This session will discuss the definitions of personalized medicine, how it can affect individual healthcare through prevention, monitoring, and treatment tailoring. We will go over high level concepts of pharmacogenomics and present some key examples of implementation of pharmacogenomics and personalized medicine to date, as well as discuss the integration of personalized medicine within the drug development process, from drug discovery, to population selection, to clinical trial design, and application in the clinic. Finally, we will discuss the future of healthcare with technological advancement in a patient-focused approach

Dr. Daphna Laifenfeld - Personalized Medicine & Pharmacogenomics

10. Biostatistics

This session will describe the role of the biostatistician prior, during and in closure of clinical trial. The planning of a clinical trial will be discusses: Choosing the model, randomization, power, sample size, drop outs, sequential and adaptive methods for clinical trials, the statistical challenges that arise due to their use and the advantages and disadvantages of utilizing a sequential or adaptive design compared to a standard, fixed-sample design. The process of the Statistical Analysis Plan (SAP), interim analysis, retrospective analysis, meta-analysis and the Database lock will be described.

Dr. Anat Sakov – Statistics - Global Biometrics

11. Technology Transfer and IP Commercialization

1. What is the meaning of Tech Transfer?
2. TTOs – what is their role, including examples and models
3. Bayh Dole Act – definition and implications
4. License agreement – key license terms
5. Academic start ups

Ms. Efrat Shalom Berensohn, LLM - Executive Counsel, Global R&D Teva Pharmaceutical Industries

12. Academia-Industry partnership + Visit at Teva Factory – Kfar Saba

Visiting and observing different stages of the manufacturing process of drug development.

Dr. Neta zach, Director, Head of Academic Affairs & Networks Discovery and Product Development Global R&D

Extra Reading for the Course:

Operational activities of the Clinical Trials/Data Management and Clinical Programming

http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/Step4/E9_Guideline.pdf

Medical Monitoring during clinical study

- FDA Guidance for Industry - Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring, August 2013
- FDA Guidance for Industry - Establishment and Operation of Clinical Trial Data Monitoring Committees, March 2006

Regulatory Affairs

- Communication from the Commission 2010/C 82/01 — Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1), March 2010
- United States Code Title 21, Part 312, Investigational New Drug Application, April 2012
- FDA Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants, May 2009
- European Commission: Notice to Applicants Vol. 2A: Procedures for marketing authorisation, June 2013
- European Commission. (2008, May). Volume 2B: Notice to Applicants: Medicinal products for human use. Presentation and format of the dossier: Common Technical Document (CTD).
- U.S. Food and Drug Administration: New Drug Application, May 2012
- The CDER Handbook, produced by the Department of Health and Human Services, Food and Drug Administration, March 1998
- CDER 21st Century Review Process, Desk Reference Guide, produced by the Department of Health and Human Services, Food and Drug Administration, September 2014
- Beishon M., Approval rating: how do the EMA and FDA compare?, 12 I CancerWorld I January-February 2014
- Navigating the Regulatory Landscape for Healthcare Product Development: Key principles and best practices, MaRS Discovery District, October 2012

Introduction to nonclinical safety testing

- ICH M3(R2) guideline. 11 June 2009.
- Principles of Toxicology by David L. Eaton and Curtis D. Klaassen. In: Casarett & Doull's Toxicology: The Basic Science of Poisons, Eighth Edition. Unit 1: Editor: Curtis D. Klaassen. Chapter 2, pages 13-48. Publisher: McGraw-Hill Professional Publishing, 2013.

CFR - Code of Federal Regulations Title 21 PART 58: GOOD LABORATORY PRACTICE FOR NONCLINICAL LABORATORY STUDIES In: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=58