Phase I/II Clinical Trials Research and Design

Autumn Semester 2018
(Tentative Schedule and course syllabus)

I. Course Information
PHDD8050
3 Credit Hours
Pre-requisites: Preclinical/Non-Clinical Studies for IND Approval (PHDD8030)
Course Times: Thursdays, 6:00 PM to 8:45 PM

Location: MSB E155

II. Course Director
Pankaj B. Desai, Ph.D.
Professor of Pharmacokinetics and Biopharmaceutics
Ph. No: (513) 558-3870 (Office)
Email: pankaj.desai@uc.edu

III. Course Catalog Description
This course will provide an understanding of the early clinical drug development activities for new chemical entities that have received IND approval. Concepts of early clinical pharmacology studies, typically conducted in a Phase I setting, such as single and multiple dose pharmacokinetics, dose escalation studies to determine the safety and tolerability of drugs, mass balance and drug metabolism studies, and bioavailability studies, will be taught. Emphasis will then be placed on Phase II clinical trials as key proof-of-concept studies, and on the dose-ranging requirements for Phase II. Trial designs, including cross-over and parallel group, will be discussed. The importance of Phase I/II trials for making dose selections for Phase III studies will be explored, as will the use of Phase II trials as a go/no-go decision point. The importance of exposure-response (PK/PD) information in guiding the go/no-go decision will also be discussed. The use of biomarkers and pharmacogenomic information in decision making will be addressed.

IV. Student Learning Outcomes
- Understand the goals and objectives of Phase I and Phase II clinical trials
- Learn about different strategies for deriving the first-in-human dose and the pharmacokinetic basis for dose escalation
- Acquire an understanding of various non-therapeutic goals of Phase I trials (e.g., safety/tolerability, mass balance, drug metabolism)
• Gain an understanding of the design of bioavailability and bioequivalence trials and analyze the findings from bioavailability and bioequivalence trials
• Learn about logistics of the clinical research site, trial monitoring activities, blood sample collection, drug inventory control, screening and patient recruitment
• Understand “proof of concept” and “proof of activity” studies and their role in go/no-go decisions
• Understand the importance of exposure-response information in guiding go/no-go decisions
• Comprehend novel approaches for accelerating drug development such as the Phase 0 trials and exploratory IND studies.
• State the purpose of Phase II trials and the differences between Phase IIa and IIb studies
• Identify the different study designs that are commonly used for Phase II studies
• Acquire an understanding of endpoints and biomarkers discussed in class that can be used for Phase II studies
• Understand the role of pharmacogenetics and pharmacogenomics in Phase I/II study designs and the differences between these two terms
• Able to design a Phase II study protocol with the appropriate level of detail and know the pros and cons of various study designs
• Understand the importance of drug-drug interaction studies and other special studies, such as organ impairment studies
• Identify the appropriate controls, patient populations, sample sizes, and randomization schemes for Phase I and Phase II trials
• Learn the role of pharmacokinetics (PK) and pharmacodynamics (PD) in Phase I and Phase II study designs
• Know the information from Phase II studies required prior to the design of Phase III trials

V. College Educational Outcomes
This course will provide the student with the necessary tools to understand and design clinical trials for new chemical entities involved in the early phases of a drug development programs (i.e., Phase I and Phase II clinical trials).

VI. Teaching Methods
In addition to conventional teaching methodologies, active learning techniques, which will include case studies, problem-based learning and group discussion/assignments, will be employed. As part of this course, students will design both Phase I and Phase II clinical trials in study outline format and present their designs to fellow students and the instructors. Students will pair up for these design workshops and will select a disease indication for which an FDA or EMEA guidance document has been issued. Students will also be assigned homework and reading from the literature.

VII. Assessment
The mid-term and final exams will be take home exams and will not be cumulative. Students will have one week to complete each take home exam. No make-ups will be scheduled. Students are allowed to use the internet, class notes, or other sources of information to complete the take home exams. Students are not permitted to consult with anyone else in completing their
take home exams. Periodic homework will also be assigned to help the student master the concepts.

VIII. Course Communication
The course syllabus will be published on Blackboard under the Course Documents section. The published syllabus will define the dates of the take-home exams and reading assignments, in addition to the lecture topics and instructor. There will be a 10 minute break provided at approximately the middle of each class period. Updates or communications to the class will be made using the email function on Blackboard. Students are responsible for maintaining the approved University email address in Blackboard and are responsible for insuring that their mailbox is able to receive email notices. All communications for weather related changes will take place on Blackboard. It is the student’s responsibility to check Blackboard on a regular basis to keep up to date on class assignments and exams.

IX. Course and Grading Policies

Competency will be assessed using the following:

1. Mid-term Exam (Phase I) 35%
2. Assignments 30%
3. Final Exam 35%

Total 100%

Grading is based on the following scale:

90-100 A
85-90 B+
80-85 B
75 - 80 C+
70-75 C
<70 F

Examinations: Students will be provided with an examination schedule for this course during the first week of the semester. Scheduled examinations will not be changed once they have been posted unless the University is closed due to weather. Examinations postponed due to University closure will be rescheduled once the University reopens.

Students are expected to participate in all scheduled examinations and to notify the instructor, in advance, when they will be absent for an examination.
Students are expected to be present for the scheduled study design presentations.

**Course Withdrawal:** The university policy on withdrawal from this course will be followed. The process for withdrawal and the policies that govern grading are available at: http://www.uc.edu/registrar/withdraw_reg.htm

**Student Code of Conduct:** The Student Code of Conduct is intended to provide broad guidance in identifying and discouraging behavior that conflicts with the idea of building a strong and just community that respects and protects the diverse interests and goals of all students, all student organizations, and the University of Cincinnati’s mission. The Student Code of Conduct defines prohibited conduct for all University of Cincinnati students and organizations. The revised code approved by the Board of Trustees is available online at: http://www.uc.edu/studentlife/conduct.

X. Special Accommodations

**Professional Meeting Attendance:** Students participating in or traveling to professional organizations or scientific meetings should make requests for accommodation during the first week of the semester. Whenever possible, faculty will work with the students to allow for their participation in these activities.

XI. Texts

No required text needs to be purchased from the bookstore, but recommended texts are *Strategic Clinical Development Planning* by Dr. William Sietsema and *Fundamentals of Clinical Trials* by Friedman, Furberg and Demets.

XII. Tentative Class Schedule

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<thead>
<tr>
<th>Date</th>
<th>Faculty</th>
<th>Lecture Topic</th>
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<tbody>
<tr>
<td>8/30</td>
<td>Desai</td>
<td>Course Overview – Goals of Phase I/II/Clinical Pharmacology Key Single Dose and Steady State Pharmacokinetics Concepts</td>
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<tr>
<td>9/6</td>
<td>Desai</td>
<td>Concepts in PK/PD/Clinical Pharmacology and Common Phase I Designs</td>
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<tr>
<td>9/13</td>
<td>Heller</td>
<td>Radiolabeled studies and mass balance</td>
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<tr>
<td>9/20</td>
<td>Stevens</td>
<td>Food Effect/BA/Bioequivalence Studies</td>
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<tr>
<td>9/27</td>
<td>Desai</td>
<td>Workshop on First in Human Dose Calculations</td>
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<tr>
<td>10/4</td>
<td>Dave</td>
<td>Phase I Oncology Trials</td>
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10/11 FALL BREAK

10/18 Perentesis Drug development in pediatric oncology

10/25 Carey: Phase I trials of biotherapeutics

11/1 Djuric: QT prolongation & Phase I Development of Cardiovascular Drugs
Carey: Introduction to Phase II Studies: Purpose and Design; Basics of Phase II Designs (parallel, x-over, etc.)

11/08 Fichtenbaum: Development of HIV Drugs and Phase II Studies
Carey: Proof of Concept Studies; Regulatory Guidance Documents
Selection of Appropriate Controls and Study Objective

11/15 Privitera: Development of AEDs and Epilepsy Trial Designs
Carey: Choosing Endpoints, Surrogate Markers, and Biomarkers

11/22 THANKSGIVING BREAK

11/29 Ajayi: Pharmacogenetics and Pharmacogenomics in Phase II Studies
Ajayi: Data from Phase II Trials Needed Prior to Phase III

12/6 Carey: Development of Diabetes Drugs and Phase II Studies
Development of Drugs for Rare Diseases