An Introduction of the Fourth Year Pharmacy Student to the Drug Development Process and Applied Translational Medicine, a Phase I Clinical Research Rotation.

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ABSTRACT

Objectives: To expose fourth year pharmacy students to the unique learning environment of clinical research and applied translational medicine to further their knowledge base of the drug development process and to generate interest in the field of clinical pharmacology and pharmaceutical development as a career choice.

Background: Understanding the drug development process and how applied translational medicine and clinical pharmacology are utilized in bringing drugs to market in an efficient and cost effective manner is an important aspect of a pharmacy student's education yet pharmacy school curriculums are typically limited and generalized regarding these topics.

Rotation Description: Projects and research focus on evaluation of preclinical data, subject and staff safety, study feasibility and protocol/investigator brochure review, study design (First-in-Human single ascending dose and multiple ascending dose, thorough QT, drug-drug interactions etc.), clinical pharmacology outcomes, interdisciplinary execution of study conduct, and regulatory affairs.

Conclusion: After completion of the Phase I Clinical Research Rotation, the pharmacy student will have been exposed to a variety of projects which are specific and unique to clinical research. This opportunity allows students to utilize clinical pharmacology skills in a distinctive manner as it relates to drug development and translational medicine.

BACKGROUND

The Accreditation Council for Pharmacy Education (ACPE) goals for curriculum are to prepare graduates to ensure optimal medication therapy outcomes and patient safety. The goals of the skills learned are meant to be integrated and applied not only to present pharmacy practice but also to the advancement of the profession. [1] The curriculum guidelines are heavily focused on areas such as pathophysiology, pharmacology, and pharmacotherapy. These areas along with many others are important in the development of new pharmaceuticals and are a leading reason as to why pharmacists can and should play an integral role in drug development.

Understanding the drug development process and how applied translational medicine and clinical pharmacology are utilized to bring drugs to market in an efficient and cost effective manner is an important aspect of a pharmacy student's education. Pharmacy school curriculums however, are typically limited and generalized regarding these topics.[2] In a small survey of pharmacy schools, it was noted that students are typically provided with approximately two to four hours of instruction regarding the drug approval process and are required to take one course covering topics related to the basics of drug literature and evaluation of such (L. Morin, R. Herrier, and S. Tennant, personal communication, Aug 2014). What is noticeably lacking is exposure to clinical research and the regulatory aspects related to this area. This phenomenon is not unique to the pharmacy profession and has been noted for other medical professionals as well including physicians and mid-level practitioners.[3]

Insufficient training in drug development means that it is difficult to identify applicants qualified, even with just basic clinical research training, when needed to work in a clinical research environment. Even rarer is a candidate with an understanding of regulations governing good clinical practice, good manufacturing practice or institutional review boards. Finding a candidate with appropriate clinical qualifications as well as industry knowledge can seem like searching for a needle in a haystack.

The lack of understanding of how clinical research is performed and regulated, can lead to additional challenges beyond staffing concerns. There is some reluctance in the medical community at large to participate in clinical research. This unwillingness can be due, at least in part, to a lack of understanding of clinical research. [4] Those familiar with clinical research understand that it can take a large number of people to collect the required data for a clinical study. This may include efforts for recruitment of sites and patients, then collection and analysis of the data. Unfortunately, it appears that involvement of investigators in clinical research in the United States (US) is declining. [5] This has ramifications not only for the forward progression of drug development programs but also a potentially negative impact on the applicability of the study results to the US population. An analysis of data available from 5809 studies from the Clinical Trial Transformation Initiative indicated a median of 20 sites are needed for each clinical study with a mean of 47 sites. Using a conservative assumption of 4 medical professionals for each site that is a range of 80 to 188 qualified medical professionals that are needed for each study; demonstrating the high demand for these uniquely qualified professionals.

This has led staff at Celerion, a Phase I and II focused clinical research organization, to collaborate with pharmacy schools to provide additional training in this area in order to increase interest in clinical research and drug development as a career but also to help increase the number of practitioners willing to participate in clinical research.

ROTATION DESCRIPTION

A two arm approach has been taken in designing the pharmacy clinical research rotation. The rotation begins with an overview of the basics of clinical research; focusing initially on introductory information on the traditional four phases of drug development, the Code of Federal Regulations, Good Clinical Practice, and International Conference on Harmonisation (ICH) guidelines. Time is spent with different members of the clinical team, giving students a hands-on view of the role of physicians, nurses and pharmacists in preparing and executing Phase I and II clinical studies as well as their role in helping to ensure participant and staff safety. The pharmacy student also assists with drug information questions or related concerns that are raised by sponsors or staff during the rotation.

At the conclusion of this introductory period, the focus of the rotation shifts to putting the student in the role of the drug developer. The goal is to provide the student with a glimpse of some of the challenges and difficult decisions that must be made every day when developing a new chemical entity. The scope of projects was designed to be broad enough for students to get a glimpse of several challenges encountered during drug development. From recruiting challenges, dealing with unexpected and sometimes unclear study results, to how to best navigate changing regulations governing clinical research. Further detail is provided below on some of these projects.

Informed Consent

The students research the history and reasoning behind obtaining participant consent. They are then provided with an investigator's brochure and study protocol and asked to develop an informed consent form based on these documents in compliance with applicable guidelines and federal regulations. Going through the exercise of developing the informed consent exposes the student to the intricacies involved with appropriately describing the study and associated risks in language that is clear for the general population.

First-in-Human (FIH) Study

The student is provided with an investigator's brochure and asked to complete the human equivalent dose (HED) calculations by identifying the no observable adverse effects level (NOAEL) in the appropriate animal species and utilizing the correct conversion formula, as applicable, in accordance with FDA guidance for industry. They are then given the study protocol and evaluate whether the proposed starting dose is appropriate based upon their calculations. The student is asked to identify what risks may be anticipated with the new chemical entity and what can be done to mitigate these risks. The student is then given the safety data results for a dose level and provide justification for moving forward with the next dose level or alternatively stopping the study. Finally the discussion focuses on what the next steps for development of the particular compound should be given the results of the FIH study. This project gives the student a greater appreciation for some of the risks inherent in clinical research and what is done to mitigate these risks and ensure participant safety.

Thorough QT Study

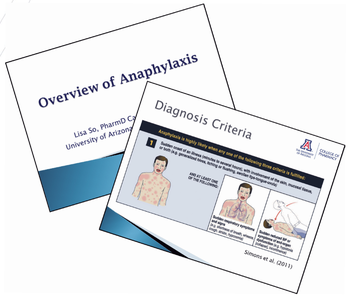
The student is provided with the ICH E14 guidance and basic pharmacokinetic information on a compound and then asked to design a Thorough QT study that meets FDA regulatory requirements. The student produces a synopsis and then must provide justification for many of the decision points in the design such as dose level, choice of crossover or parallel design, use of positive control and timing for pharmacokinetic and QT data collection. This project introduces the student to some of the challenges that come with trying to appropriately interpret regulatory requirements especially amid a changing regulatory landscape.

Bioavailability/Bioequivalence (BA/BE) Study

The student is asked to research the history and approval process for generic drugs. Then given basic pharmacokinetic information on a compound, they are asked to design a BA/BE study which complies with FDA regulations. This project gives students an awareness of the regulatory history and reasons behind performing these studies as well as introduces the student to basic concepts and principles of study design.

Translational Medicine Review

Students are asked to create and present a review paper on the topic of translational medicine. The review papers typically cover topics such as the importance of adaptive study design, common examples of how translational medicine is applied in the clinical research setting, and the impact of translational medicine on clinical research and drug development. Students are then asked to identify examples of translational medicine, within the ongoing studies being conducted at Celerion, and to critically evaluate whether the approaches being utilized will yield the desired information and improve the drug development process.



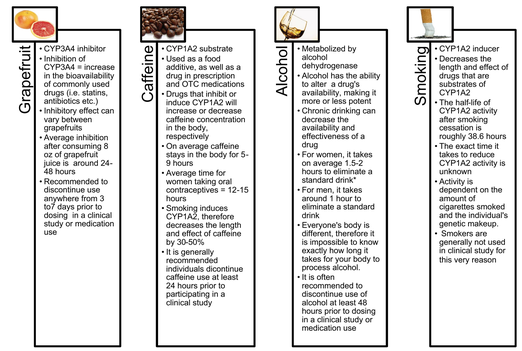
Introduction

JL-954 is an investigational antibiotic designed to treat staphylococcus infections. According to previous data, JL-954 has a half-life of 7 hours, time to maximum concentration of 2 hours, is 12% protein bound and about 90% of the compound is excreted in the urine as unchanged drug. Food has not been found to alter the pharmacokinetics of JL-954. The only known serious adverse event of JL-954 is rhabdomyolysis.

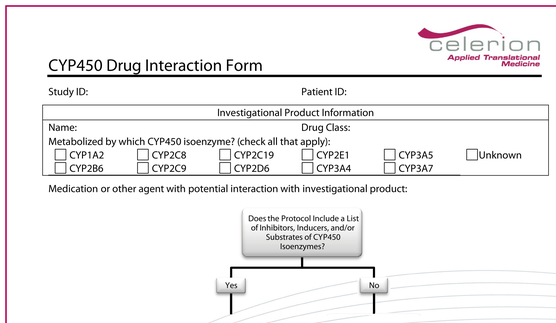
Methods

Study Design

The following study is a randomized, double blind, placebo/positive controlled, nested crossover/parallel trial. Moxifloxacin 400 mg will be utilized as the positive control to establish assay sensitivity. In order to avoid compromising the blinding procedure, identical dosage forms of JL-954, placebo and moxifloxicin will be utilized. Subjects will be evaluated for 16 days and randomized into the following treatment groups:



*Standard drink = 12 oz regular beer, 5 oz table wine, and 1.5 oz of 80 proof alcohol (keep in mind this is just a guide, it is always a good idea to check the label for the exact number of standard drinks).



"One big advantage was being exposed to working with pharmacists outside the traditional retail/hospital setting. As far as the influence of the rotation on my career, I think it did have a good influence: I decided to join the US Public Health Service and accepted a position at FDA, which I definitely learned a lot about while working in the clinical trial setting." – Ben Bishop

"I was always interested in research and most of my background is in in vivo preclinical trials. So this rotation was an opportunity for me to get a look at clinical trials.
I was pretty set on going to grad school before that rotation and most likely sticking with academia. However, I am now thinking about the potential of working for a pharmaceutical company. I got a better understanding of the role of a pharmacist in a company like Celerion. I realized even more that grad school is the right choice for me because I would want to be involved more in the science and research aspect. I enjoyed seeing the other side of research because I was so used to being in a lab. "– Lisa So

"It was interesting to see how industry pharmacy works and the role that a pharmacist can play. It was rewarding to see how our field can impact not just the general community but the medical field as well."– Karen Peat

CONCLUSION

After completion of the Phase I Clinical Research Rotation, the pharmacy student will have been exposed to a variety of projects and experiences which are specific and unique to clinical research. This opportunity allows students to see firsthand how pharmacists can apply clinical pharmacology skills learned during pharmacy school in a distinctive manner to contribute to drug development. Although preceptors recognize that not everyone who completes this rotation will decide to pursue a career in clinical research, others have shown that additional training in this area increases students' interest in clinical research careers.6 At a minimum, students go away with a better understanding of what is involved in collecting the information that they will ultimately utilize to counsel patients on how to best use prescribed medication.

The ultimate goal of providing more in-depth education to medical professionals in the area of drug development is to increase the number of qualified practitioners participating in drug development and clinical research by removing some of the preconceived fears associated with working on a clinical study and spurring interest in drug development as a career path. It takes an immense amount of manpower to bring a new compound to market. Getting more medical professionals involved and willing to assist in clinical research and drug development helps those in industry as well as patients in getting safe, effective medications approved and available for use as soon as possible.

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