A REVIEW ON CLINICAL TRIALS AND ROLE OF PHARMACIST

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ABSTRACT

A clinical trials is a research study in human volunteers to answer specific health questions. Investigational trails determine whether experimental treatment or new ways of using known therapies are safe and effective under controlled environment. Clinical trials aims to measure therapies effectiveness and constitute an important and highly specialized form of biological assay. In phase I pharmacokinetics, safety, gross effects are studied on human volunteers by clinical pharmacologists. If the drug passes the test, it enters phase II testing, where pharmacokinetics safety, therapeutic efficiency are studied on selected patients by clinical pharmacologists, if passes hundreds of selected patients are now studied, primarily for safety and therapeutic effectiveness by clinical investigator in phase III. If this is passed the drug is now approved and marketed.

KEYWORDS: Clinical trials, Preclinical Studies, Clinical studies, NDA.

INTRODUCTION

A clinical trial is a research study that tests a new medical treatment or a new way of using an existing treatment to see if it will be a better way to prevent and screen for diagnose or treat a disease.\cite{1} For any new drug to enter in clinical trial, it must pass preclinical studies. Preclinical studies involve in vitro (i.e. test-tube or Laboratory) studies and trials on animal populations. Wide range of dosages of the study drug is given to animal subjects or to an in-vitro substrate in order to obtain preliminary efficacy, toxicity and pharmacokinetic information.\cite{2} A clinical trials (also called clinical research) is a research study using human volunteers designed to determine the safety and effectiveness of a drug. Biologic (such as vaccine), device (such as prosthesis) or other treatment or behavioral intervention, carefully conducted clinical trials are the fastest and safety way to find out treatments that work in people and methods to improve health. Interventional trails determine whether experimental
treatments or new ways of using known therapies are safe and effective under controlled environments.

Table 1. Phases of clinical trails

<table>
<thead>
<tr>
<th>Phases</th>
<th>Dosing</th>
<th>Number of subjects</th>
<th>Main goal of clinical trail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinical</td>
<td>Unrestricted</td>
<td>Not applicable</td>
<td>Testing in nonhumans</td>
</tr>
<tr>
<td>0</td>
<td>Sub therapeutic</td>
<td>About 10</td>
<td>pharmacokinetics</td>
</tr>
<tr>
<td>IA/IB</td>
<td>Ascending doses</td>
<td>20-100</td>
<td>Dose-ranging</td>
</tr>
<tr>
<td>IIA/IIB</td>
<td>Therapeutic dose</td>
<td>100-300</td>
<td>Drug efficacy</td>
</tr>
<tr>
<td>IIIA/IIIB</td>
<td>Therapeutic dose</td>
<td>1000-3000</td>
<td>Therapeutic effect</td>
</tr>
</tbody>
</table>

Pre-clinical studies

Pre-clinical studies involve in vitro studies and trails on animal population. Wide-ranging dosages of the study drug are given to the animal subjects or to an in-vitro substrate in order to obtain preliminary efficacy, toxicity and pharmacokinetic information and to assist pharmaceutical companies in deciding whether it is worthwhile to go ahead with further testing.

Phase 0

Phase 0 trails are the first clinical trials done among people. They aim to learn how a drug is processed in the body and how it effects the body. In these trials, a very small dose of a drug is given to about 10 to 15 people.

Phase I

Phase I trials aim to find out the best dose of a new drug with the fewest side effects. The drug will be tested in a small group of 15 to 30 patients. Doctors start by giving very low doses of the drug to few patients. Higher doses are given to other patients until side effects become too severe or the desired effect is seen. The drug may help patients, but phase I trials are to test a drug safety. If a drug is found to work, it can be tested in a phase II Clinical trial.

Phase II

Phase II trials further assess safety as well as if a drug works. The drug is often test among patients with a specific type of cancer. Often new combinations of drugs are tested. Patients are closely watched to see if the drug works. However the new drug is rarely compared to the current drug that is used. If a drug is found to work, it can be tested in a phase III clinical trial.

Phase III
Phase III trials compare a new drug to the standard-of-care drug. These trails assess the side effects of each drug and which drug works better. Phase III trial enroll 100 or more patients often these trails are randomized. This means that patients are put in to a treatment group called trail arms by chance. Randomization is needed to make sure that the people in all trial arms are alike. This lets scientists know that the results of the clinical trial are due to the treatment and not differences between the groups. Every patient in a phase III study is watched closely. The study will be stopped early if the side effects of the new drug are too severe.

**Phase IV**

Phase IV trials test new drugs approved by the FDA. The drug is tested in several hundreds or thousands of patients. This allows for better research on short-lived and long-lasting side effects and safety. For instance, some rare side effects may only be found in large groups of people. Doctors can also learn more about how well he drug works and its helpful when used with other treatments.\[^3\]

**TYPES OF CLINICAL TRIALS**

1. Treatment trials
   Test experimental treatments, new combinations of drugs, or new approaches to surgery or radiation therapy
2. Prevention trials
   Look for better ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vitamins, minerals, or life style changes.
3. Diagnostic trials
   Conducted to find better tests or procedures for diagnosing a particular disease or in a particular condition
4. Screening trials
   Test the best way to detect certain diseases or health conditions.
5. Quality of life trials
   Trials explore ways to improve comfort and quality of life for individuals with a chronic illness.

**MONITORING CLINICAL TRAILS**
The purpose of trial monitoring are to verify that:
1. The rights and wellbeing of human subjects are protected.
2. The reported trial data are protected
3. The conduct of the trial is in compliance with the currently approved protocol/amendment with GCP

**METHODS OF COLLECTING ADVERSE EVENTS IN CLINICAL TRIAL**

Volunteer reporting by the patient
Investigator observation
Standard open question
Check list
Subject diaries
Laboratory/clinical values

**ICH GCP GUIDELINES**

The principals of ICH GCP—
1. Clinical trial should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement
2. Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject.
3. The rights, safety and wellbeing of the trial subjects are the most important considerations and should prevail over interests of science and society
4. Clinical trials should be scientifically sound and described in a clear, detailed protocol
5. A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB) Independent ethics committee (IEC) approval/favorable opinion
6. Freely given informed consent form should be obtained from every subject prior to clinical trial participation
7. All clinical trial information should be recorded, handled and stored in a way that allows its accurate reporting, interpretation and verification
8. Investigational products should be manufactured, handled, stored in accordance with applicable good manufacturing practice.[4]

**ETHICAL CONSIDERATION**
An independent body (a review board or a committee, institutional, or supra national) constituted of medical professionals and non-medical members, whose responsibility it is to ensure the protection of the rights and wellbeing of human subjects involved in a trial and to provide public assurance of that protection, by among other things, reviewing and approving favorable opinion on the trial protocol.

The legal status, composition, function, operations and regulatory requirements pertaining to independent ethics committees may differ among countries, but should allow the independent ethics Committees to act in agreement with GCP as described in this guide line.\[^5\]

**ROLE OF PHARMACISTS IN CLINICAL TRIALS**

Pharmacist plays an active role in research and clinical trials first of all, we provide the necessary facilities required for proper storage of investigational medicinal products, either in fridge or controlled room temperature.

Pharmacists are also conduct observational surveys that are aimed at investigating patients or physicians perspectives and attitudes towards medication.\[^6\]

It is also the duty of pharmacists to ensure there is constant supply of IMPs at all times and that they are dispensed to patients accordingly. Patients are counselled on the correct use of IMPs in addition to any written information that is provided, such as informed consent form or the patient information leaflet. IMPs return from patients are counted and documented to determine compliance to the treatment. For injectable IMPs pharmacists will also ensure that they are prepared in accordance with specifications stipulated in the trial and they are administered appropriately.\[^7\]

Besides managing the clinical trials, oncology pharmacists often run research projects that are aimed at improving outcomes in patients who receive medications, such as chemotherapy or other supportive drugs like anti-emetics, blood growth factor injections etc.

Drug utilization Evaluation (DUEs) are research projects that are commonly conducted by pharmacists. These projects aims to facilitate rational use of drugs within our patients. DUEs are sometimes considered as drug audits because pharmacists are ensuring the use of medication is appropriate.

Pharmacists are aimed at investigating patients use of complementary and alternative medications and on patients’ perspective of safe handling of oral-anti cancer drug.\[^8\]
CONCLUSION

A clinical trial for any new drug follows under the guidelines of ICH and GCP clinical trial are conducted in human volunteers for confirmation of useful properties of new drug. After pre-clinical development investigational new drug passes through clinical phases I, II, III, IV. These phases provide in detail explanation of pharmacokinetic, pharmacodynamics profile and side effect which may be harmful or beneficial, adverse effect and post marketing surveillance.

REFERENCES