Clinical Trial Insights: An Overview

Mansi Kushwah

Anand College of Pharmacy, keetham, Agra, U. P. India

*Corresponding Author**
Mansi Kushwah
Anand College of Pharmacy, keetham, Agra, U.P, India
mansikushwah192000@gmail.com

Received: 8-July-2024, Manuscript No. cep-24-140963; **Editor assigned:** 10-July-2024, PreQC No. cep-24-140963(PQ); **Reviewed:** 12-July-2024, QC No. cep-24-140963(Q); **Revised:** 18-July-2024, Manuscript No. cep-24-140963(R); **Published:** 21-July-2024, doi: 10.35248/ 2471-2701.24.10(1).340

Abstract

A clinical trial is a research study involving human volunteers to answer specific health questions. These trials are the quickest and safest way to find treatments that work and improve health. There are two main types of clinical trials: investigational trials and observational trials. Investigational trials test whether new treatments or new ways of using existing treatments are safe and effective in controlled settings. Observational trials study health issues in large groups of people in their natural environments. Clinical trials measure how well treatments work and are a crucial and specialized form of biological testing. The process involves several phases. In Phase I, clinical pharmacologists study the drug's safety, effects, and how it moves through the body in a small group of healthy volunteers. If the drug passes this phase, it moves to Phase II, where it is tested on a larger group of selected patients to study its safety and effectiveness. In Phase III, hundreds of patients are studied, focusing primarily on safety and therapeutic effectiveness. Once a drug passes Phase III, it is approved and marketed. Even after marketing, doctors from various hospitals and clinics continue to report on the drug's safety and effectiveness in Phase IV. This thorough process ensures that new treatments are both safe and effective before they become widely available.

Keywords: Clinical trials • Preclinical studies • Clinical studies • Nda

Introduction

A clinical trial is a research study that evaluates a new medical treatment or a new application of an existing treatment to determine if it is a better way to prevent, screen for, diagnose, or treat a disease. Before a new drug can enter clinical trials, it must pass preclinical studies. These preclinical studies involve laboratory (*in vitro*) tests and trials on animal populations. Various dosages of the study drug are administered to animal subjects or tested in vitro to gather preliminary information on efficacy, toxicity, and pharmacokinetics.

Literature Review

Phases of clinical trial

Before pharmaceutical companies begin clinical trials on a drug, they conduct extensive pre-clinical studies [1]. These pre-clinical studies include in vitro (test tube or laboratory) tests and trials on animal populations. A range of dosages of the study drug is administered to animal subjects or tested in vitro to gather preliminary information on efficacy, toxicity, and pharmacokinetics. This data helps pharmaceutical companies determine whether it is worthwhile to proceed with further testing.

Phase 0: Is a recent classification for exploratory, first-in-human trials conducted according to the U.S. Food and Drug Administration's (FDA) 2006 Guidance on Exploratory Investigational New Drug (IND) Studies [2]. These trials are designed to accelerate the development of promising drugs or imaging agents by determining early on whether the drug or agent behaves in human subjects as expected based on preclinical studies. Key features of Phase 0 trials include administering single subtherapeutic doses of the study drug to a small group of subjects to collect preliminary data on the drug's pharmacokinetics (how the body processes the drug) and pharmacodynamics (how the drug works in the body) [3].

Phase I: Trials are the initial stage of testing in human subjects, typically involving a small group of 20-80 healthy volunteers. The primary goals of this phase are to assess the safety, tolerability, pharmacokinetics (how the drug is processed in the body), and pharmacodynamics (how the drug affects the body) of a drug. These trials are often conducted in inpatient clinics where subjects can be closely monitored by full-time staff. Participants are usually observed until the drug has been processed and cleared from their system, as determined by several half-lives of the drug [4].

Phase I trials also include dose-ranging, or dose-escalation studies, to determine the appropriate dose for therapeutic use. The range of doses tested is typically a fraction of the dose that caused harm in animal studies. While Phase I trials usually involve healthy volunteers, there are exceptions where patients with end-stage diseases who have no other treatment options participate, especially in oncology (cancer) and HIV drug trials. Volunteers are compensated for their time, with payments ranging from a small amount for short stays to up to approximately £4000 for longer participation periods [5].

Phase II: Once the initial safety of the study drug has been confirmed in Phase I trials, Phase II trials are conducted on larger groups (20-300 participants). These trials aim to evaluate the drug's effectiveness and continue safety assessments in a broader group of volunteers and patients. The development process for a new drug often fails during Phase II trials, as this is when the drug may be found to be ineffective or to have toxic effects.

Phase II studies are sometimes divided into Phase IIA and Phase IIB. Phase IIA focuses on determining the appropriate dosing (how much of the drug should be given), while Phase IIB focuses on studying the drug's efficacy (how well the drug works at the prescribed doses). Some trials combine Phase I and Phase II to test both efficacy and toxicity simultaneously.

Phase III: Studies are randomized controlled multicenter trials conducted on large patient groups, ranging from 300 to over 3,000 participants, depending on the disease or medical condition being studied. These trials aim to definitively assess the drug's effectiveness compared to the current 'gold standard' treatment. Due to their size and length, Phase III trials are the most expensive, time-consuming, and challenging to design and execute, especially for therapies targeting chronic medical conditions.

It is common for certain Phase III trials to continue while the regulatory submission is pending with the appropriate agency. Although not always

required, it is generally expected that at least two successful Phase III trials demonstrate the drug's safety and efficacy to gain approval from regulatory agencies such as the FDA in the USA, the TGA in Australia, and the EMEA in the European Union.

Phase IV: Trials, also known as Post-Marketing Surveillance Trials, involve monitoring the safety (pharmacovigilance) and providing ongoing technical support for a drug after it has been approved for sale. These studies may be required by regulatory authorities or initiated by the sponsoring company for various reasons, such as finding new markets for the drug or testing interactions with other medications and specific population groups, like pregnant women, who were not included in earlier trials.

The primary goal of safety surveillance in Phase IV is to detect any rare or long-term adverse effects across a larger patient population and over a longer time period than was possible during Phases I-III. If harmful effects are discovered during Phase IV, the drug may be withdrawn from the market or have its usage restricted. Recent examples of drugs affected by Phase IV findings include cerivastatin (Baycol and Lipobay), troglitazone (Rezulin), and rofecoxib (Vioxx) [6].

Investigational New Drug (IND)/Clinical Trial Exception (CTX) / Clinical Trial Authorization (CTA) application

INDs (in the U.S.), CTXs (in the U.K.), and CTAs (in Australia) are examples of requests submitted to the appropriate regulatory authorities seeking permission to conduct investigational research. This research may involve testing a new dosage form or a new use of a drug already approved for marketing. Alongside regulatory approval, Institutional or Independent Review Boards (IRBs) or Ethical Advisory Boards must also approve the testing protocol and the informed consent documents signed by volunteers before participating in a clinical study. An IRB, comprising independent physicians, community advocates, and others, ensures the ethical conduct of clinical trials and safeguards the rights of study participants [7].

New Drug Applications (NDAs) in the U.S. or Marketing Authorization Applications (MAAs) in the U.K. are examples of applications submitted to market a new drug. These applications document the safety and efficacy of the investigational drug and include all information collected during the drug development process. Upon successful completion of preclinical and clinical testing, this comprehensive documentation is submitted to the FDA in the U.S. or relevant regulatory authorities in other countries. The application must provide substantial evidence that the drug will produce the intended effects as represented, prescribed, recommended, or suggested in the labeling. Obtaining approval to market a new drug typically requires between six months and two years [8].

Types of cinical trial

- **Treatment trials:** Test experimental treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.
- **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, vaccines, minerals, or lifestyle changes.
- **Diagnostic trials:** Conducted to find better tests or procedures for diagnosing a particular disease or condition.
- **Screening trials:** Test the best way to detect certain diseases or health conditions.
- **Quality of Life:** Trials (or Supportive Care trials) explore ways to improve comfort and the quality of life for individuals with a chronic illness.

Monitoring clinical trials

- The rights and well being of human subjects are protected.
- The reported trial data are protected.
- The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s)

ICH GCP guidelines

- Clinical trial should be conducted in accordance with the ethical principals that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement.
- Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
- The rights, safety, and well being of the trial subjects are the most important considerations and should prevail over interests of science and society.
- The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
- Clinical trials should be scientifically sound, and described in a clear, detailed protocol.
- 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
- The medical care given to and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician, or when appropriate, of a qualified dentist.
- Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective tasks.
- Freely given informed consent should be obtained from every subject prior to clinical trial participation.
- All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.

Role of pharmacists in clinical trials

Pharmacists have an active role to play in research and clinical trials first of all, we provide the necessary facilities required for proper storage of the Investigational Medicinal Products (IMPs), either in the fridge or at controlled room temperature. Regular temperature monitoring is ensured and recorded.

It is also the pharmacist's duty 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 the IMPs in addition to any written information that is provided, such as, Informed Consent Form or the Patient Information Leaflet. IMPs returns from patients are counted and documented to determine compliance to the treatment. For inject able IMPs, pharmacists will also ensure that they are prepared in accordance to the specifications stipulated in the trial, and that they are administered appropriately. Besides managing 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 [9].

Drug Utilization Evaluations (DUEs) are research projects that are commonly conducted by pharmacists. These projects aim to facilitate rational use of drugs within our patients. Essentially, providing insights on how drugs are used in patients and observing prescribing patterns by

our physicians. DUEs are sometimes considered as drug audits because pharmacists are ensuring the use of medication is appropriate.

In addition, pharmacists also conduct observational surveys that are aimed at investigating patients' or physicians' perspectives and attitudes towards medications. Results obtained from surveys are used to improve the services that we provide to our patients. Currently, NCC's oncology pharmacy is conducting two surveys. They are aimed at investigating patients' use of complementary and alternative medications and on patients' perspective on safe handling of oral anti-cancer drugs. Very often, pharmacy students who are adequately trained to conduct research are assigned to survey the patients. We would like to take this opportunity to thank all our patients who have consented to participate in the survey [10].

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 preclinical development, investigational new drug passes through clinical phases I, II, III and IV. These phases provide in detail explanation of pharmacokinetic, pharmacodynamic profile and side effect which may be harmful or beneficial, adverse effect and post marketing surveillance.

References

1. Kulkarni, SK. "Hand book of experimental pharmacology". *Vallabh prakashan*. 1987: 27.
2. Barar, FSK. "Essentials of pharmacotherapeutics". *S Chand Publ.* 2000: 57-59.
3. Allen, LV. "Pharmaceutical Dosage Forms and Drug Delivery Systems." (1990): 2150-2150.
4. Mosteller, F. "Medical uses of statistics". *NEJM Books* 1992.
5. Colton, T. "Statistics in medicine. Boston: Little." *oxf acad.* (1974).
6. Ayala, F., et al. "On being a scientist. Committee on the Conduct of Science, National Academy of Sciences of the United States of America." *Proc Natl Acad Sci. U. S. A.* 86.23 (1989): 9053-9074.
7. Duncan, RC. et al. "Introductory biostatistics for the health sciences." *cinni* (1983).
8. Edwards, AL. "Multiple regression and the analysis of variance and covariance". *WH Freeman/Times Books/Henry Holt Co.* 1985.
9. Krauth, J. "Distribution-free statistics: An application-oriented approach." *cinii* (1988).
10. Sokal, RR. "The principles and practice of statistics in biological research." *Biometry* (1995): 451-554.

Cite this article: Kushwah, M. Clinical Trial Insights: An Overview**.** *Clin Exp Psychol.* 2024, 10(01), 001-003