

Clinical research - an outlook



presentation to give precise and concise detail of clinical research and trials ..

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Clinical research-an outlook:

Clinical research basically deals with drugs, medical devices, other interventions and human subjects in order to identify and test toxicity, absorption, distribution, metabolism, route of administration, excretion, efficacy, safety and possible side effects of drugs and other interventions depending on trial.

It involves highly legally approved procedures, clinical research purely takes route of clinical trial in application.

Clinical trials:

The most commonly performed clinical trials evaluate new drugs, medical devices, biologics, or other interventions to patients in strictly scientifically controlled settings, and are required for regulatory authority (in the USA, the Food and Drugs Administration) approval of new therapies. Trials may be designed to assess the safety and efficacy of an experimental therapy, to assess whether the new intervention is better than standard therapy, or to compare the efficacy of two standard or marketed interventions. The trial objectives and design are usually documented in a Clinical trial protocol. In USA there is a 50% tax credit on clinical trials.

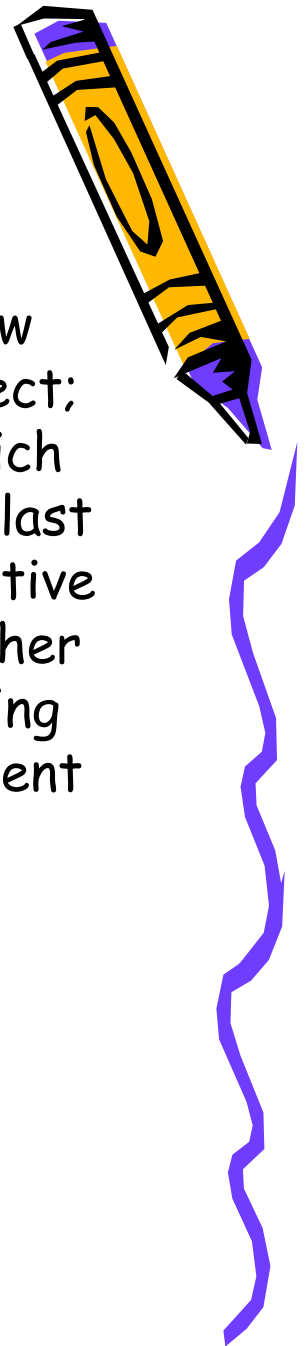


Further developments ahead:

- To be ethical, they must involve the full and informed consent of participating human subjects. They are closely supervised by appropriate regulatory authorities. All interventional studies must be approved by an ethics committee (in the USA, this body is the Institutional Review Board) before permission is granted to run the trial.
- The study design that provides the most compelling evidence of a causal relationship between the treatment and the effect, is the randomized controlled trial.
 - Currently some Phase II and most Phase III drug trials are designed to be randomized, double-blind, and placebo-controlled. This means that each study subject is randomly assigned to receive one of the treatments, which might be the placebo.



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Neither the subjects nor scientists involved in the study know which study treatment is being administered to any given subject; and, in particular, none of those involved in the study know which subjects are being administered a placebo. Of note, during the last ten years or so it has become a common practice to conduct "active comparator" trials (also known as "active control" trials) - in other words, when a treatment exists that is clearly better than doing nothing (*i.e.* the placebo) for the subject, the alternate treatment would be a standard-of-care therapy.



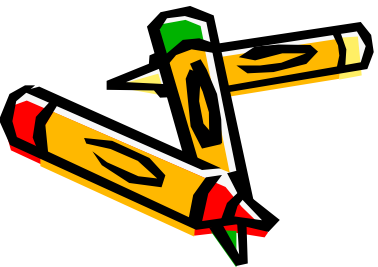
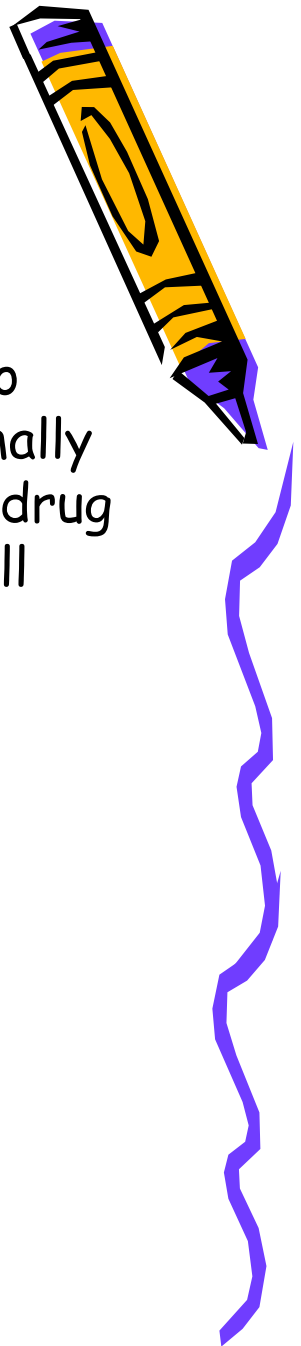
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- The number of patients enrolled in the study also has a large bearing on the ability of the trial to reliably detect an effect of a treatment. This is described as the "power" of the trial. It is usually expressed as the probability that, if the treatments differ in their effect on the outcome of interest, the statistical analysis of the trial data will detect that difference. The larger the sample size or number of participants, the greater the statistical power. However, in designing a clinical trial, this consideration must be balanced with the greater costs associated with larger studies. The power of a trial is not a single, unique value; it estimates the ability of a trial to detect a difference of a particular size (or larger) between the treated and control groups.



Phases of clinical trial:

- Pharmaceutical clinical trials are commonly classified into four phases, and the drug-development process will normally proceed through all four stages over many years. If the drug successfully passes through the first three phases, it will usually be successfully approved for use in the general population.
- Before pharmaceutical companies start clinical trials on drugs, extensive pre-clinical studies are conducted.



Phases:

- Phase I
- Phase I trials are the first-stage of testing in human subjects. Normally a small (20-80) group of healthy volunteers will be selected. This phase includes trials designed to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of a therapy. These trials are almost always conducted in an inpatient clinic, where the subject can be observed by full-time medical staff. Phase I trials most often include healthy volunteers, however there are some circumstances when patients are used, such as with oncology (cancer) and HIV drug trials. In Phase I trials of new cancer drugs, for example, patients with advanced (metastatic) cancer are used. These trials are usually offered to patients who have had other types of therapy and who have few, if any, other treatment choices.



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Phase II

Once the initial safety of the therapy has been confirmed in Phase I trials, Phase II trials are performed on larger groups (100-300) and are designed to assess clinical efficacy of the therapy; as well as to continue Phase I assessments in a larger group of volunteers and patients. Phase II studies are sometimes divided into Phase IIA and Phase IIB. Phase IIA is specifically designed to assess dosing requirements, whereas Phase IIB is specifically designed to study efficacy.

Some trials combine Phase I and Phase II into a single trial, monitoring both efficacy and toxicity.



Phase-III:

Phase III studies are on large patient groups (1000-3000 or more) and are aimed at being the definitive assessment of the efficacy of the new therapy, especially in comparison with currently available alternatives. Phase III trials are the most expensive, time-consuming and difficult trials to design and run; especially in therapies for chronic conditions. Once a drug has proven satisfactory over Phase III trials, the trial results are usually combined into a large document containing a comprehensive description of the methods and results of human and animal studies, manufacturing procedures, formulation details, and shelf life. This collection of information makes up the "regulatory submission" that is provided for review to various regulatory authorities in different countries, such as the Therapeutic Goods Administration (TGA) in Australia, the European Medicines Agency (EMA) or the Food and Drug Administration (FDA) in the United States for marketing approval.



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- Phase IV:

Phase IV trials involve the post-launch safety surveillance and ongoing technical support of a drug. Phase IV studies may be mandated by regulatory authorities or may be undertaken by the sponsoring company for competitive or other reasons. Post-launch safety surveillance is designed to detect any rare or long-term adverse effects over a much larger patient population and timescale than was possible during the initial clinical trials. Such adverse effects detected by Phase IV trials may result in the withdrawal or restriction of a drug - recent examples include cerivastatin (brand names Baycol and Lipobay), troglitazone (Rezulin) and rofecoxib (Vioxx).



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- In this way clinical research revolves around 4 phases of clinical trial with all consideration of legal aspects, regulatory authorities and documentation at each step.
- Key persons involved:
- Ethics committee- for approval of trial
- Sponsor- financial support
- Investigator- a physician who conducts trial
- Human subjects- with which trial is incomplete
- Monitor- assess trial at each step
- Clinical research associate- link between sponsor and investigator.
- Statistician- to design trial, patient no, sample size
- Auditor- who audits the trial at the end
- Data manager- to handle, archive and reproduce data at anytime.

