Introduction To Clinical Trials

A clinical trial or study is defined by the International Conference on Harmonisation Principles of Good Clinical Practice (ICH GCP) as being any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study ADME of an investigational product(s) with the object of ascertaining its safety and/or efficacy...

What are the different types of clinical trials?

- Treatment
- Prevention
- Early detection/ Screening
- Diagnostic
- Quality of life/Supportive care

Treatment Trials.

What new treatments can help people with a particular disease?

- what is the most effective treatment for people with that disease?

□ Prevention Trials:

Evaluate the effectiveness of ways to reduce the risk of a particular disease

- Enroll healthy people at high risk for developing that disease
- Unlike treatment trials, prevention clinical trials are studies involving healthy people who are at high risk for developing a particular disease.
- These studies try to answer specific questions about and evaluate the effectiveness of ways to reduce the risk of disease.

□ Randomized Trials:

Participants have an equal chance to be assigned to one of two or more groups:

- One gets the most widely accepted treatment (standard treatment)

oThe other gets the new treatment being tested, which researchers hope and have reason to believe will be better than the standard treatment.

- Phase 3 trials are randomized clinical trials, and some phase 2 trials may also be randomized.
- Randomization is a method used to prevent bias in research.
- Treatment assignments are generated by a computer, and each participant has an equal chance of being assigned to one of two or more groups, the control group and the treatment group.
- The control group is made up of the people who get the most widely accepted treatment (standard treatment) for the disease.

- Randomization in clinical Trial Studies

Randomization is of central importance in clinical trials. It prevents selection bias and insures against accidental bias. It produces comparable groups, and

eliminates the source of bias in treatment assignments. Finally, it permits the use of probability theory to express the likelihood of chance as a source for the difference btw outcomes.

Introduction:

-A good clinical trial minimizes variability of the evaluation and provides an unbiased evaluation of the intervention by avoiding confounding from other factors. Randomization insures that each patient have an equal chance of receiving any of the treatments under study, generate comparable intervention groups which are alike in all important aspects except for the intervention each group receives. It also provides a basis for the statistical methods used in analyzing data.

Criteria For Randomization:

1. Unpredictability

- Each participant has the same chance of

receiving any of the interventions.

- Allocation (تخصيص) is carried out using a chance mechanism so that neither the participant nor the investigator will know in advance which will be assigned.

2. Balance:

- Treatment groups are of a similar size and constitution, groups are alike in all important aspects and only differ in the intervention each group receives.

3. Simplicity:

- Easy for investigator / staff to implement

#Methods of Randomization:

The common types of randomization include 1-simple 2-block 3-Stratified and 4-unequal randomization. Some other methods such as biased coin, minimization and response-adaptive methods may be applied for specific purposes.

1. Simple Randomization:

This method is equivalent to tossing a coin for each subject that enters a trial, such as Heads = Active, Tails = Placebo. The random number generator is generally used. It is simple and easy to implement and treatment assignment is completely unpredictable. However, it can get imbalanced in treatment assignment, especially in smaller trials. Imbalanced randomization reduces statistical power.

2. Block Randomization:

The basic idea of block randomization is to divide potential patients into m blocks of size 2n, randomize each block such that n patients are allocated to A and n to B. then choose the blocks randomly. This method ensures equal treatment allocation within each block if the complete block is used. Example: Two treatments of A-B and Block size of 2x2 = 4 Possible treatment allocations within each block are (1) AABB

2) BBAA 3) AB AB 4) BABA 5) ABBA 6. BAAB

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3. Stratified Randomization:

Imbalance randomization in numbers of subjects reduces statistical power, but imbalance in prognostic factors is also more likely inefficient for estimating treatment effect. Trial may not be valid if it is not well balanced across prognostic factors. Stratification can balance subjects on baseline covariates. tend to produce comparable groups with regard to certain characteristics (e.g. gender, age, race, disease severity) thus produces valid statistical tests. The block size should be relative small to maintain balance in small strata.

4. Unequal Randomization:

Most randomized trials allocate equal numbers of patients to experimental and control groups. This is the most statistically efficient randomization ratio as it maximizes statistical power for a

Stratified randomization refers to the situation in which strata are constructed based on values of prognostic variables and a randomization scheme is performed separately within each stratum.

given total sample size. However this may not be the most economically efficient or ethically/practically feasible. When two or more treatments under evaluation have a cost difference it may be more economically efficient to randomize fewer patients to the expensive treatment and more to the cheaper one. The substatistical cost saving can be achieved by adopting a smaller randomization ratio such as a ratio of 2:1 with only a modest loss in statistical power. When one arm of the treatment saves lives and the other such as placebo/medical care only does not much to save them in the oncology trials. The subject survival time depends on which treatment they receive. More extreme allocation may be used in these trials to allocate fewer patients into the placebo group. Generally randomization ratio of 3:1 will lose considerable statistical power more extreme than ..... which leads to much longer sample size.

- The investigational group is made up of the people who get the new treatment being tested.
- Why is randomization important?

So all groups are as alike as possible

Provides the best way to prove the effectiveness of a new agent or intervention

- Clinical trial protocol:

→ A recipe or blueprint.

→ Strict scientific guidelines:

- Purpose of study
- How many people will participate
- Who is eligible to participate
- How the study will be carried out
- What information will be gathered about participants
- End points

- Clinical trials follow strict scientific guidelines. These guidelines clearly state the study's design and who will be able to participate in the study.

- Every trial has a head person in charge, usually a doctor, who is called the principal investigator.

- The principal investigator prepares a plan for the study, called a protocol, which acts like a "recipe" for conducting a clinical trial.

- Every doctor or research center that takes part in the trial uses the same protocol. This ensures that participants are treated identically no matter where they are receiving treatment, and that information from all the participating sites can be combined and compared.

- The case report form:

CRF is the document which collects all the data necessary for analysis is to be recorded.

CRF is to be filled by investigator or any person formally delegated to carry out the procedure in question.

- Finding suitable patients

They must pass the inclusion and exclusion criteria and the consent to the study.

- They must also be deemed likely to complete the study.