Phases of Clinical Trials

Phases of Clinical Trials

When testing a new treatment or disease preventive regimen, phase III confirmatory studies are typically preceded by several phase I and II screening studies

- Phase I: Initial safety / dose finding
- Phase II: Preliminary efficacy / further safety
- Phase III: Establishment of efficacy
- Phase IV:
  - Therapeutics: Post-marketing surveillance
  - Prevention: Effectiveness

Phase I Clinical Trials

Phase I: Initial safety / dose finding in humans

Goals:

- Pharmacokinetics / pharmacodynamics
- Incidence of major adverse effects
- Decide whether it is ethical to continue testing in humans

Methods

- Relatively small number of participants
- Participants often not true target population
- Sometimes dose escalation
- Sometimes no comparison group

Phase II Clinical Trials

Phase II: Preliminary evidence of efficacy

Goals:

- Screening trial to look for any evidence of treatment efficacy
- Incidence of major adverse effects
- Decide if treatment is worth studying in larger samples

Methods

- Relatively small number of participants
- Participants closer to true target population
- Outcome often a surrogate
- Sometimes no comparison group (especially in cancer)

Phase III Clinical Trials

Phase III: Establishment of efficacy

Goals:

- Obtain measure of treatment's efficacy on disease process
- Incidence of major adverse effects
- Therapeutic index
- Modify clinical practice (obtain regulatory approval)

Methods

- Relatively large number of participants from true target population (almost)
- Clinically relevant outcome

Phase III Clinical Trials: Settings

Phase III: Common scenarios

Establish efficacy of new treatment

- superiority over no intervention
- superiority over existing treatment

Establish equivalence with current treatment

- Two-sided equivalence: bioequivalence
- One-sided equivalence: noninferiority
  - perhaps superior on secondary endpoint

Establish harm of existing treatment

Phase IV Clinical Trials

Therapeutic Phase IV: Post-marketing surveillance

Goals:

- Monitor for rare serious events

(Some "Phase IV" trials are of more interest for marketing than for science)

Prevention Phase IV: Effectiveness

Impact on Study Design

The stage of clinical investigation is a major factor to consider in choosing a particular clinical trial design

Scientific issues

- Strength of evidence required at the end of the trial

Ethical issues

- Potential for benefit (or harm) to patients