Conduct of Clinical Trials

Clinical trials are pivotal to making progress against cancer. There are many ways researchers can design a clinical trial.

A clinical trial can be **nonrandomized**, which means that participants are not assigned by chance to different treatment groups, and may choose which group they want to be in, or they may be assigned to the groups by the researchers.

A clinical trial can be **randomized**, which means that participants are divided by chance into separate groups that compare different treatments or other interventions.

Highlighted below are major designs of traditional and modern clinical trials:

TRADITIONAL CLINICAL TRIALS

Conducted in successive phases to test an investigational anticancer therapeutic in humans. Traditional clinical trials remain an integral part of clinical research:

Phase I

Studies involve tens of patients and determine safety and dosage.*

Phase II

Studies involve hundreds of patients and determine safety and initial efficacy.*

Phase III

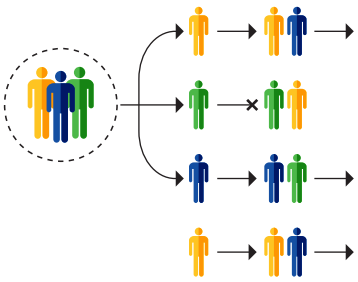
Studies involve thousands of patients and determine efficacy of the new drug in comparison to standard of care.†

Phase IV

Studies are conducted after a therapy is provisionally approved by FDA and provide additional effectiveness or "real-world" data on the therapy.

MODERN CLINICAL TRIALS

Conducted as parallel substudies or experimental arms and driven by genomics to test multiple drugs against the same cancer type or a single drug against multiple cancer types. Parallel experimental arms within modern clinical trials typically include different phases of conventional clinical trial design, and are typically randomized:



Adaptive Design

Allows for making prespecified planned changes to one or more aspects of the study based on accumulating data from participants in the trial. Because of the complexity of the design, adaptive clinical trials may require a large number of participants and a well-established clinical infrastructure to support the study.

Main Protocol (Also called Master Protocol)

Answers multiple questions within a single overall clinical trial. Following are examples of clinical trials that use the main protocol:

- **Basket trials** test one drug against multiple cancer types that have the same genetic characteristic. This trial design requires fewer participants before safety and efficacy of the drug are determined, and/or decreases the time it takes for the drug to be tested and made available to patients.
- **Umbrella trials**‡ test multiple drugs against a single cancer type. This trial design allows participants to be assigned to different treatment arms based on the molecular characteristics of their cancer.
- **Platform trials**‡ provide an infrastructure for evaluating multiple targeted therapies for one or more cancer types through ongoing changes in experimental arms. They are typically randomized. These trials contain a control arm and multiple experimental arms that undergo adaptive changes based on accumulating data from participants in the trial. A shared control arm allows researchers to assign more participants in the experimental arms, and the adaptive nature allows researchers to efficiently incorporate newly available therapeutics.

*In some cases, researchers combine different phases into one clinical trial, also called phase I/II or phase III/IV clinical trials depending upon the phases combined, which allows research questions to be answered more quickly or with fewer patients.

†When successful, the results of phase III trials can be used by the U.S. Food and Drug Administration (FDA) to approve new therapeutics or new use of existing therapeutics.

‡Umbrella and basket trials that allow adding experimental arms (for example, if a new targeted therapeutic becomes available against a cancer type being tested in the trial), or removing existing ones (for example if a targeted therapeutic being tested does not prove to be safe and/or efficacious) are also considered platform trials.