Clinical Trials for Gene Therapy

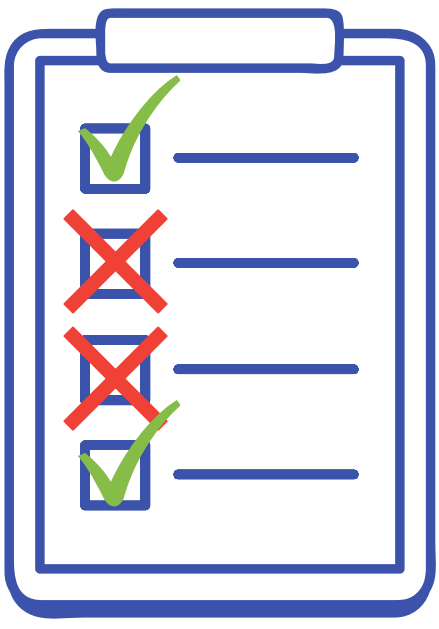
What is a clinical trial?

A clinical trial is a research study that tests a medical, surgical, or behavioral intervention on patient volunteers. Clinical trials can also be observational, when patients are carefully monitored but don't receive an intervention.

Does everyone get a treatment?

Clinical trials have different protocols based on what they are testing. Protocols can also vary by what phase the clinical trial is in. A few options for treatment protocols are:

- Everyone gets the intervention
- Some people get the intervention, some people get standard of care
- Some people get the intervention, some people get a placebo



Placebo

A placebo is an inactive substance that is used so that patients don't know if they got the intervention or not. This helps researchers see if the intervention itself is providing therapeutic benefit, or if people just think it is.

Placebo studies can be either be single-blind studies, where the patient does not know what they are getting but the researcher does, or double-blind studies, where neither the patient nor the researchers working directly with patients know who got the intervention.

Pros: Efficient at transferring therapeutic material to the intended cell

Cons: Potential to cause an unwanted immune response in the body or damage cells

Standard of Care

Standard of care is the current best practice for treating a condition. This standard care has already been approved by the FDA and is the typical care that patients with this condition receive.

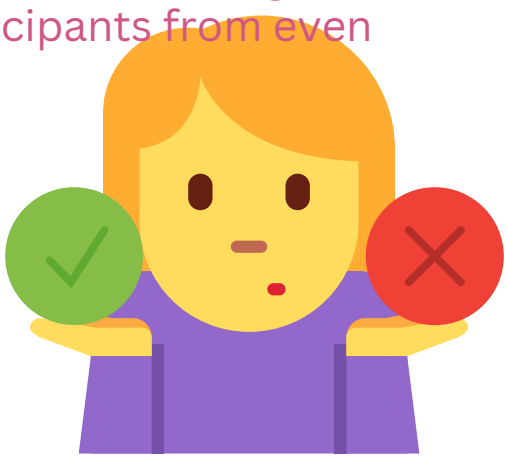
Standard of care varies based on the condition, but could include things like taking medications, following a strict diet, or other medical care.

Pros: Everyone gets some form of treatment

Cons: May be more difficult for researchers to test effectiveness; standard of care in one country may be different or better than in other countries

Are placebos going to be used in gene therapy clinical trials?

We aren't really sure. While this can vary by trial, there are many reasons not to use placebos for gene therapy trials, particularly for rare diseases. First, for some rare diseases, there are no other treatments, so it may be unethical to withhold the therapy. Second, the procedures for getting gene therapy can be taxing and require risks, calling in to question whether using a placebo is ethical. Third, for rare diseases there is only a small patient population. If trials use a placebo, patients may be less likely to join, therefore making the already small population to find participants from even smaller.



So if researchers don't use placebos, what can they use instead to test effectiveness? Researchers and governing bodies are still learning how to do this. One option is looking at biomarkers or patient's status before, during, and after the trial. Another option could be comparing the therapy to current standard of care, or creating a "placebo group" using real-world data from others who have or have had the disease.

What are the phases of a clinical trial?

Phase 1

In phase 1, researchers want to test if the treatment is safe, whether people can tolerate it, what dose people can tolerate, and what the side effects are. This is usually done with a very small group.

Phase 2

In phase 2, researchers still look at safety and short-term side effects. However, they are also testing to see if the treatment is doing what it is supposed to do. This is done with a slightly larger group than phase 1 trials.

Phase 3

In phase 3, researchers compare effectiveness and side effects of the intervention to the current standard of care or a placebo. They also test how the intervention does on a broader, more diverse group of people. This phase has many more participants.

Phase 4

If a trial passes through phase 3, then the FDA approves the drug. Phase 4 trials look at long-term safety and effectiveness for the treatment.

Are clincal trials safe?

Clinical trials involve risk, which is why it's important to have a good understanding of the trial before agreeing to participate.

Informed Consent

Informed consent is the process of learning about a trial, including learning its' purpose, how long it lasts, what procedures or tests are done, risks, and benefits. Participants are given an informed consent document that they need to sign that says they understand the trial and agree to participate.

For children under 18 years old, a parent or guardian almost always has to consent to the trial. In addition, children over 7 years old are often asked if they agree to participate.

While the informed consent document is signed before a person starts partaking in a clinical trial, researchers should continue to provide information to participants throughout the entire study.

Scientific Overview

Different groups oversee clinical trials. Some examples are listed below.

Institutional Review Board: Approves and monitors trials to see that the potential benefits outweigh potential risks; ensures clinical trials are ethical and protects patient rights

Office for Human Research Protections (OHRP): Helps protect the rights, welfare, and well-being of study participants

Data and Safety Monitoring Board: Reviews data to look at differences between groups, safety issues, etc.

FDA: Makes sure makes studies are following their protocols, provides guidance to researchers

Who pays for people to join a clinical trial?

Costs for clinical trials can be covered by the research team, health insurance, or out-of-pocket by patients. Before joining a clinical trial, it's important to ask about different costs and determine who is responsible for what.

Costs could include (but are not limited to):

- Pre-intervention visits with researchers
- Pre-intervention care or preparation
- The intervention itself
- Post-intervention and follow-up care
- Travel to research or care facilities
- Lodging

How do people find clinical trials?

People can look for US clinical trials by going to https://clinicaltrials.gov/

You can also utilize ResearchMatch, a nonprofit funded by the NIH (National Institutes of Health) that connects people interested in research studies with researchers at top medical centers across the US.

https://www.nhlbi.nih.gov/research/clinical-trials/safety-benefits-risks
https://www.nhlbi.nih.gov/research/clinical-trials/how-studies-work
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