Understanding Gene Therapy

FAQs for Individuals and Families

Q. What is gene therapy?

A. Gene therapies introduce new genetic material into a patient's body to treat or slow the progression of a genetic disease.

Q. How does gene therapy work?

A. The intention of gene therapy is to treat or prevent disease by administering new genetic material into affected cells using a delivery vehicle known as a vector. Genes provide instructions on how to make the proteins our bodies need. Gene therapies only target specific cells in the body. A person's basic genetic composition is not changed, just the cells targeted by the therapy.

Q. What does accelerated drug approval by the FDA mean?

A. Accelerated approval is an approval mechanism for FDA to determine whether a product is safe, effective, and ready to be marketed by the company. "Compassionate use" is a pathway for certain individuals to access a product before it is approved by FDA, and only in limited circumstances. Both are important but play very different roles in accessing innovative products.

Q. What is a vector?

A. A vector is a delivery vehicle used to introduce new genetic material into cells of the human body. Commonly used vehicles include viral vectors (such as adeno-associated virus, AAV), which carry new genetic material into cells. Nonviral vectors such as lipid nanoparticles and biopolymers are also in development.

Q. What will gene therapy do to my body?

A. Gene therapies introduce new genetic code that can restore critical functions that are missing in cells of a patient's body. Gene therapies only target specific cells in the body. A person's basic genetic composition is not changed, just the cells targeted by the therapy.

Q. Will gene therapy make matters worse?

A. Neither the response to gene therapy nor its side effects can be accurately predicted for any individual. Unexpected side effects or death can occur following gene therapy but are uncommon for patients whose course is closely monitored and managed for several months after treatment.

Q. Who is eligible for gene therapy?

A. Not everyone is eligible for gene therapy. Restrictions determined by age, mobility, mutation type, pre-existing antibodies, etc., can affect eligibility.

Benefits and risks

Q. What are the potential benefits of gene therapy?

A. The aim of gene therapy is to introduce a healthy copy of a gene that is otherwise missing or not functioning optimally in patients. Animal studies and human clinical trials have shown that gene therapies can restore physical function or stop or slow disease progression.

Q. What are the risks and side effects of gene therapy?

A. There are no guarantees that gene therapy will improve function or stop progression in any individual. In clinical trials of gene therapies, patients have responded differently in terms of benefits and side effects. Potential risks, side effects, and expectations of benefit must be thoroughly reviewed with your physician before receiving any gene therapy.

Q. I heard patients have died from gene therapy. Is this true?

A. Yes, there have been deaths associated with gene therapy treatments for Duchenne muscular dystrophy (DMD), spinal muscular atrophy (SMA), and myotubular myopathy.

Q. What is viral vector shedding?

A. Viral vector shedding occurs following virus-based gene therapy treatments in which a patient excretes or secretes virus byproducts (e.g., in feces, urine, sores, wounds, etc.) during a post-treatment period. Careful consideration is required during this "infectious" period if additional family members are planning to receive gene therapy.

Q. How long can I expect the gene therapy treatment to last?

A. Based on animal studies, gene therapy is expected to last at least several years, although the exact duration is unknown and may differ from person to person. Factors that determine how long gene therapy will last in the body include the type of cell being treated (nerve cells or muscle cells), age of the patient at dosing, dose level, disease progression, and patient-specific responses.

Q. If I am ineligible for gene therapy now, does this mean I am ineligible for any gene therapy in the future?

A. If you are ineligible now for gene therapy, that does not mean you would be ineligible for other forms of future gene therapy or other treatments. Advances in gene therapy methods will continue to evolve and hopefully provide access to all individuals affected by neuromuscular disease.

Q. If I receive gene therapy now, can I receive future gene therapy treatments?

A. Gene therapy delivered via viral vectors (AAV) is currently limited to a single treatment. Limitations of current technology and human biology will not allow patients to be re-dosed with AAV therapies. However, this may change in the future with improved technologies to overcome high AAV antibody levels in patients who have previously received gene therapy.

Q. Is gene therapy the best choice for me?

A. Review all associated risks and benefits of gene therapy with your physician. Determine if you are eligible for gene therapy and determine realistic expectations regarding likely benefits and possible risks. Establish a specific plan for post-administration monitoring and care.

Q. Can gene therapy be reversed and/or undone?

A. At this time, viral-based gene therapies cannot be reversed or undone.

Process and administration

Q. Can I get gene therapy outside of a clinical trial?

A. Yes, there are FDA-approved gene therapies available outside of clinical trials for specific diseases and patients.

Q. How can I find out about ongoing clinical trials for neuromuscular disease?

A. Check out **mda.org/research/clinical-trials** or **clinicaltrials.gov** to learn more about clinical trials.

Q. Where will I receive gene therapy?

A. Gene therapy is administered at medical facilities by healthcare providers. Please consult your administering healthcare provider to ensure their facility is adequately prepared to formulate, administer, and monitor gene therapy before considering whether or not to receive gene therapy.

Q. Is gene therapy only offered at MDA Care Center locations?

A. Gene therapy is available at some healthcare institutions outside the MDA Care Center Network.

Q. What factors should I consider when selecting where to receive treatment?

A. Consider whether your administering healthcare institution has the following in place:

1. A team of providers on staff that includes physicians, nurse practitioners, or physician assistants prepared to monitor benefits and side effects; nurses or other coordinators who can help schedule and monitor treatment and follow-up appointments; a pharmacist trained in the preparation of gene therapy products; and waste service and biosafety personnel.
2. Standard operation procedure (SOP) for the formulation, infusion, and subsequent monitoring of the gene therapy treatment.
   - The institutional pharmacy should have policies and experience required for pharmacy/specialty pharmacy access; freezer and refrigeration storage; preparation hoods; disinfection and decontamination processes; and waste disposal and infection control.
   - The institutional infusion center should be equipped with established policies and experience required for baseline laboratory testing and analysis. The center should have adequate means and personnel for monitoring patient response and vital signs post-administration for the appropriate period of time as defined by the institution. The center should also have a process for:
     > Verifying that all required pre-infusion medications have been administered.
     > Monitoring vital signs at baseline, throughout the infusion, and in the immediate post-infusion period.
     > Placing one or two IV (into the vein) catheters for secure rapid IV infusion without tissue infiltration or infusion reaction, or be able to obtain access for a secure intrathecal injection (into the spinal canal).
     > Administering and monitoring the infusion over the precise time stipulated for the product.
   - Care and monitoring center with dedicated personnel and established protocols for laboratory and clinical testing at predetermined intervals post-infusion; methods to secure patient access for required testing over the institutionally established period of months post-infusion; established protocol for adjusting immunomodulatory (modulating the immune system) treatment during the defined monitoring period.

Q. Will my health insurance company pay for gene therapy?

A. Pre-authorization and approval are required from your health insurance company before receiving gene therapy. The preauthorization process can take days, weeks, or months depending on patient, disease, and insurance company specifics, in addition to the experience of the treating institution.

Q. How long will the gene therapy process take?

A. Administration of gene therapy depends on your healthcare provider and medical facility. Although the injection or infusion lasts up to a few hours at most, that is only a small portion of the overall treatment process. The treatment starts by establishing the genetic diagnosis and counseling the family and patient about treatment options, followed by specific laboratory testing for those interested in gene therapy. For those eligible and interested, establishing prior authorization can take days or weeks. Although days of delay are meaningful in terms of disease progression for some disorders (e.g., in neonates with SMA and two copies of SMN2), even a few weeks of delay might not have measurable effects on other disorders (e.g., older boys with DMD). Preparing a patient's immune system for gene therapy infusion can take days or weeks, depending on the recommended regimen to modulate the immune system. Following the infusion, a prescribed period of blood tests and clinical follow-up is necessary for at least three (3) months, and potentially longer, before the patient's infusion-related treatments can be tapered to baseline. Afterward, the patient requires long-term management of the underlying genetic disorder to determine any functional changes and appropriately adjust management, while also monitoring for potential long-term effects of the gene therapy.

Q. Will I have to stay overnight at the hospital?

A. Overnight stays will be determined by your healthcare provider. Overnight hospital stays are common during clinical trials of gene therapy approaches to capture detailed measures of acute gene therapy effects that can help determine optimal dosing or other aspects of treatment. However, institutions are strongly encouraged to administer commercial gene therapy infusions in outpatient facilities, with close monitoring during and immediately after the infusion. In general, patients receiving systemic gene therapy treatments will remain near the treatment center for weeks after the infusion so they can be closely monitored for negative reactions. Whether occurring hours, days, or weeks after a gene therapy infusion, patients must be able to immediately contact the gene therapy center to adjust their care, including hospitalization if necessary.

MDA's involvement in gene therapy

MDA has invested over $125M in the development of gene therapy (GTx) for neuromuscular diseases over the past 20 years. With new gene therapy drug approvals in the pipeline, MDA is here to help facilitate access and provide support and education to the neuromuscular disease community.

Call: 1-833-ASK-MDA1 (1-833-275-6321)
Email: ResourceCenter@mdausa.org

Gene therapy support from MDA

MDA Gene Therapy Support staff are available Monday through Friday, 9 a.m. to 5 p.m. CT. Answers to inquiries can be expected within one to two business days. MDA services are available only in the US. If you live outside the US, we may be able to connect you to muscular dystrophy groups in your area.

REFERENCES:
Gene Therapy Network **genetherapynetwork.com**
Mayo Clinic **mayoclinic.org/tests-procedures/gene-therapy/about/pac-20384619**
American Society of Gene and Cell Therapy **patienteducation.asgct.org/gene-therapy-101**

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