



GENE THERAPY FREQUENTLY ASKED QUESTIONS (FAQ)

GENERAL INFORMATION

What is gene therapy?

Gene therapy is a treatment where new working genes are introduced into a person's cells to fight disease. In the case of hemophilia, the new genes give the body instructions on how to make factor. There are different kinds of gene therapy, including gene transfer, gene editing, and cell therapy. The FDA approved gene therapy treatments involve gene transfer. There is one clinical trial for gene editing that is in the follow-up phase until 2030. There are no current trials for gene therapy using cell therapy.

How does gene therapy work for hemophilia?

A working gene has clear instructions that tell the cell how to make factor. In gene therapy, a working gene is carried into the liver cells of a person with hemophilia. Once the working gene reaches the cells, they should begin producing factor.

What is a vector?

At this time, gene therapy focused on treating hemophilia uses viral vectors. A vector is a virus that has been changed to remove the illness-causing (viral) material. It is used to bring the new, working genes into a person's cells. Viral vectors are used in gene therapy because they are very effective at getting into cells.

What vectors are being used in gene therapy for hemophilia?

The most commonly used vectors in hemophilia are called adeno-associated viruses, or AAV. These vectors do not carry any infectious material, meaning they do not cause viral infections. They are used to deliver working genes into liver cells in the body so that they can start producing clotting factor.

What are the differences between gene editing and gene transfer?

Gene transfer puts genetic information into a vector, which then carries the working copy of a gene to a person's cells. Once inside the cell, the new, working gene allows the cell to start making factor.

Gene editing tries to "fix" the part of a gene that isn't working. By editing the genetic directions, the cell can then start to make factor.

Where will I receive gene therapy?

Gene therapy is given at an approved healthcare facility, usually an HTC.^{2,7}

Which tests do I need before taking gene therapy?

Blood and imaging tests are used before gene therapy treatment. Speak with your health care provider about the specific tests you will need.

How is gene therapy administered?

Gene therapy is administered at an approved medical site using a one-time infusion that takes approximately 2 hours. You will also remain at the medical site for at least 3 hours after infusion for observation.^{3,4,5,6}

Who should I speak with if I have questions about gene therapy?

It is important to speak with the health care providers at your HTC or your hematologist to learn more about gene therapy.

WHO IS ELIGIBLE FOR GENE THERAPY?

Can women with hemophilia receive gene therapy?

At this time, gene therapy is not being studied in women with hemophilia.

Who is eligible for gene therapy to treat hemophilia A or B?

Males assigned at birth who are 18 years or older with hemophilia A or B should speak with their health care providers about all eligibility requirements if they are interested in gene therapy.

Can my child undergo gene therapy?

At this time, gene therapy for hemophilia is not available for people under 18 years of age. Gene therapy for hemophilia targets the liver cells. Children's livers continue to grow until, at least, age 12. As the liver grows, the effects of gene therapy are reduced. As we learn more about gene therapy safety, there may be opportunities for people under 18 in the future.

WHAT CAN I EXPECT FROM GENE THERAPY?

Is gene therapy a cure for hemophilia?

Current studies have shown that patients with hemophilia who undergo gene therapy may see their factor levels increase – sometimes to normal levels. They may also be able to avoid some factor infusions for a long period of time. However, the effectiveness of gene therapy will continue to be studied for many years to determine how long these benefits will last. Each patient that receives gene therapy may have different results, meaning some patients may reach higher factor levels than others.

Will gene therapy heal my existing joint damage?

No, gene therapy may enable your body to produce its own factor, but it will not heal previous joint damage.

When will gene therapy for hemophilia be available to everyone without enrolling in a clinical trial?

FDA approved gene therapy for hemophilia A has been available since June 2023. FDA approved gene therapy for hemophilia B has been available since November 2022.

If I undergo gene therapy and it stops working, can I try again in the future?

Not currently. Right now, gene therapy for hemophilia can only be done once. It is possible that this could change in the future.

Are there gene therapy treatments for both hemophilia A and hemophilia B?

Yes, there are now approved treatments for both hemophilia A and B.

If I undergo gene therapy and it stops working, can I go back to my previous hemophilia therapy?

Yes, you will be able to return to your previous prophylaxis or on demand treatment if gene therapy does not work for you.

Once I undergo gene therapy will I still need annual checkups at my HTC?

Yes. It is very important that you continue seeing your health care team after undergoing gene therapy. They will need to monitor the effects of gene therapy long term to make sure that it works as expected and to monitor any problems that may arise.

How long does gene therapy take to work in the body?

Gene therapy works differently for everyone. Gene therapy for hemophilia A or B can take from weeks to months to begin working. Speak with your doctor about which treatment option you may need to take while you are waiting to see if gene therapy works for you.^{3,7}

What is the likelihood gene therapy will work for me?

Unlike other available treatments for hemophilia A or B, gene therapy seems to work differently in everyone and there is no way to know before receiving the treatment if gene therapy will work for you. It's best to speak with your health care provider to determine if this treatment is right for you.^{1,3,6,7,8}

Can I stop or turn off gene therapy?

No. Once you undergo gene therapy the changes made to your cells cannot be undone. It cannot be reversed or stopped.

Can I drink alcohol after receiving gene therapy?

Since gene therapy works in the liver to create factor, you will need to speak with your doctor about how much alcohol you may drink if you receive gene therapy.¹

Am I able to donate blood or organs after receiving gene therapy?

You should not donate blood, organs, tissues, or cells for transplant after receiving gene therapy for hemophilia A or hemophilia B.^{1,6}

What are short-term monitoring requirements after receiving gene therapy?

Short term monitoring requirements after receiving gene therapy include weekly blood tests. How often testing is needed and which tests are needed will be determined by your health care provider.^{1,5,6,7}

What are long term monitoring requirements after receiving gene therapy?

Long-term monitoring may be different for each person but typically includes blood tests every few months. How often testing is needed and which tests are needed will be determined by your health care provider.^{1,6}

Will I still need factor if I receive gene therapy? What if I have an accident, injury or need surgery?

The need for factor after undergoing gene therapy will depend on how much factor your body makes and how long it lasts. Each person's response to gene therapy will be different and will require an approach that is specific to them. This is a topic you should discuss with your health care provider.

RISKS ASSOCIATED WITH GENE THERAPY

What is vector shedding?

It is the way the viral vector leaves the body once it is no longer needed. The virus is released through urine, feces, blood, saliva and semen.

What happens if I undergo gene therapy and my factor levels get really high?

In some cases, gene therapy has led to factor levels above the normal range. If this happens, you will need to be closely monitored by your hemophilia treatment center. High factor levels may be linked to the development of dangerous clots.

What are short-term safety risks of taking gene therapy?

Some short-term side effects that have been seen in patients include nausea, tiredness, headache, and vomiting. Some individuals may need to take steroids for a period of weeks to months due to a reaction to the gene therapy. Speak with your health care provider about all the possible short-term safety risks.^{1,5,6,8}

What are long-term safety risks of taking gene therapy?

Some long-term safety risks include unwanted blood clots if factor levels get too high, DNA from the gene therapy going into cells in the body it was not meant to go into, the potential to develop liver cancer, and the potential to develop an inhibitor. Speak with your health care provider about all the possible long-term safety risks.^{1,3,7}

GENE THERAPY AND REPRODUCTION

Can I pass the effects of gene therapy to my children?

No. Gene therapy to treat hemophilia corrects the non-working gene only in the person who receives it. The viral vector carries a working copy of the factor VIII (8) or factor IX (9) gene to the liver cells, providing them with the instructions of how to produce the missing factor. Gene therapy does not correct genes passed on to children.

Will gene therapy impact my ability to have children?

No, gene therapy will not affect your ability to have children. However, because the vector is present in semen for a long period of time after receiving gene therapy, it is recommended that men use a barrier contraceptive method, such as condoms, to prevent pregnancies until the vector is no longer there.

Should patients who undergo gene therapy bank sperm?

After undergoing gene therapy, the body can take up to several months to get rid of the vector used. This process is called viral shedding. The vector leaves the body through different bodily fluids such as semen, blood, urine, feces and saliva. Although the risk for the vector to affect sperm is low, men who undergo gene therapy are asked to use a barrier contraceptive method such as condoms to prevent pregnancies for an extended period of time after receiving gene therapy. If you are considering having a child soon after receiving gene therapy, you should discuss banking sperm with your doctor before doing so.

GENE THERAPY AND CLINICAL TRIALS

How can I find out about on-going gene therapy clinical trials for hemophilia?

You can find information on clinical trials at www.ClinicalTrials.gov. Enter “hemophilia” in the text box labeled “condition/disease” and “gene therapy” in the one labeled “Other terms”. If you want to only find trials available in the United States, then select that option in the text box labeled “Location”. And then select the blue button that says “Search”. Once you get presented with the options you can use the filters on the left to select trials based on recruitment status, age, and sex. In addition, your HTC provider can also direct you to current clinical trials and answer specific questions you may have.

GENE THERAPY AND HEALTH INSURANCE

Will insurance still pay for factor replacement therapy or nonfactor replacement therapy if I receive gene therapy?

Different insurance companies have different benefits. It is important to contact your health insurance to determine whether they will pay for factor or nonfactor replacement therapy if you undergo gene therapy.

Will my insurance company pay for gene therapy?

NBDF supports access to all FDA approved treatments and therapies, and has been engaged from early on with payers, developers and other interested organizations, to be a voice for consumers who wish to receive these novel therapies. NBDF strives to assure payers recognize these treatments should be delivered by expert providers found within HTCs, the only recognized center of excellence model purposely established to care for patients with bleeding and clotting disorders.

GENE THERAPY AND INHIBITORS

Will gene therapy cause me to develop an inhibitor to my factor?

Probably not, but this is not yet known. Although current gene therapy trials have not studied persons with a higher risk of getting an inhibitor, they have not shown a higher risk for those who have.

Can I receive gene therapy if I have an inhibitor?

It depends on the gene therapy treatment. Talk with your health care provider to determine if you are eligible for gene therapy and if it is right for you.



PSYCHOSOCIAL ISSUES AND GENE THERAPY

What are the psychosocial issues to be expected if I undergo gene therapy?

You may have conflicting feelings after you undergo gene therapy or any other major life change. Examples could include guilt, feeling of not belonging to the community, or fear of how the therapy might impact you in the future. This is completely normal. It is important that you speak with your HTC or primary care provider who can help you understand these feelings. Your HTC may also be able to put you in touch with another patient who is enrolled in a gene therapy trial or who has taken one of the FDA approved gene therapy treatments.

Will I still have hemophilia if I have normal factor levels?

Yes. Because gene therapy is relatively new, it is not known how high your factor levels will be and how long they will last. Factor levels may end up in the mild, moderate, or normal range and could change over time. While you may rarely need infusions of factor, you may still need it for surgeries, procedures, or after an accident. For that reason, you will need to stay in touch with your hemophilia treatment center and your community.

Will I still be able to go to the HTC?

Yes, please do! It is very important to be monitored for changes in overall physical health, including laboratory tests, as well as emotional health. Also, any issues you had prior to gene therapy (ex. joint issues) will need to be monitored as well. Your hemophilia treatment center will always be an important partner before and after gene therapy.

Will I still be part of the bleeding disorders community?

The bleeding disorders community is warm and welcoming, regardless of a change in your health status. You will always be a member of the community. You have much to offer, and your experience and knowledge can be very helpful to others.

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