What's New for People Living With HoFH

(Homozygous Familial Hypercholesterolemia)?

An innovative experimental gene therapy treatment for HoFH

Learn about the ongoing gene therapy clinical trial in HoFH

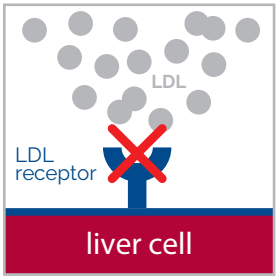
What Is HoFH?

Familial hypercholesterolemia (FH) is a life-threatening genetic disorder. In people with FH, a genetic mutation impairs the liver's ability to capture and remove low-density lipoprotein cholesterol (LDL-C), the "bad" cholesterol, from the blood. High levels of LDL-C result in a buildup of cholesterol and plaque in the arteries, known as atherosclerosis, which may lead to heart disease and stroke.

In FH, one genetic mutation is inherited. Homozygous familial hypercholesterolemia (HoFH) is a rare and severe form of FH, where two genetic mutations are inherited. People with HoFH have extremely high levels of LDL-C in their blood and can suffer serious cardiac events before the age of 30.

Normal

LDL receptors (LDLRs) capture and remove LDL-C from the blood, keeping LDL-C at a safe level.



HoFH

People with HoFH have defective or missing LDL receptors in their liver; as a result, LDL-C builds up in their blood.

Patients with HoFH need lifelong therapy (often combination therapy) to lower their LDL-C levels and prevent or delay serious health problems, such as heart disease and stroke.

Gene Therapy for HoFH

A new experimental treatment that has the potential to deliver functional copies of the human LDLR gene to the liver

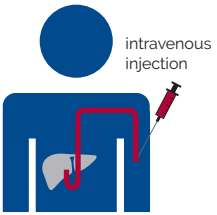
Genetic disorders are often caused by a defective gene. The defective gene may then produce a protein that does not function properly.

In people with HoFH, the LDLR gene is defective, meaning the LDLRs that the gene produces are missing or do not function properly. Gene therapy is an experimental treatment that has the potential to deliver to the cells a healthy LDLR gene using a modified virus, called AAV8, as a delivery vehicle. In people with HoFH the modified virus transports copies of the healthy LDLR gene to the liver. Once in the liver, the healthy gene is expected to make functional LDLRs.

How It Works:

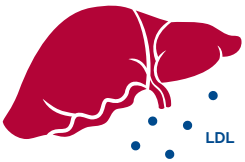
1 A functional copy of the LDLR gene is packaged in a modified virus called AAV8,* which acts like an envelope to carry the gene to the cells. This delivery vehicle is called a viral vector.

*The virus used is not known to cause disease in humans.



2 The AAV8 vector is given by a single intravenous injection into the bloodstream, where it is expected to travel to the liver.

3 Once the AAV8 vector reaches the liver, it is intended to deliver the functional gene to the liver cells, enabling the cells to make the LDLR protein it needs. The viral envelope leaves the body and the LDLR remains.



4 The liver is then expected to capture and remove LDL-C from the blood to prevent the buildup of “bad” cholesterol.

Why Consider Gene Therapy?

Current treatments for HoFH may not lower cholesterol to optimal levels.

- Medications are taken for life and may not be well tolerated and/or have limited results
- Lipoprotein apheresis, a procedure that removes LDL-C from the blood, needs to be administered every 1 to 2 weeks
- Liver transplants are high risk and rare

Gene therapy is an experimental treatment requiring a single administration that may have a long-lasting effect on LDL-C levels.

The HoFH Gene Therapy Clinical Trial

The University of Pennsylvania is recruiting adults for a Phase I/II clinical trial in people with HoFH. Genetic testing will be done to confirm if patients are eligible. The goal of this clinical trial is to show the safety of and potential long-lasting results from a single intravenous injection.

Safety

Gene therapy has shown promise in people living with another genetic disorder called hemophilia.

Learn More

Screening for this clinical trial is now in progress. For more information, contact: Marina Cuchel, MD, PhD at mcuchel@mail.med.upenn.edu or (215) 662-7188; Canita Brent at cbrent@mail.med.upenn.edu or (215) 615-4740; or visit https://clinicaltrials.gov/show/NCT02651675.

Participation

Ask your doctor if you or a loved one is eligible for this trial. Contact the University of Pennsylvania and visit https://clinicaltrials.gov/show/NCT02651675

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