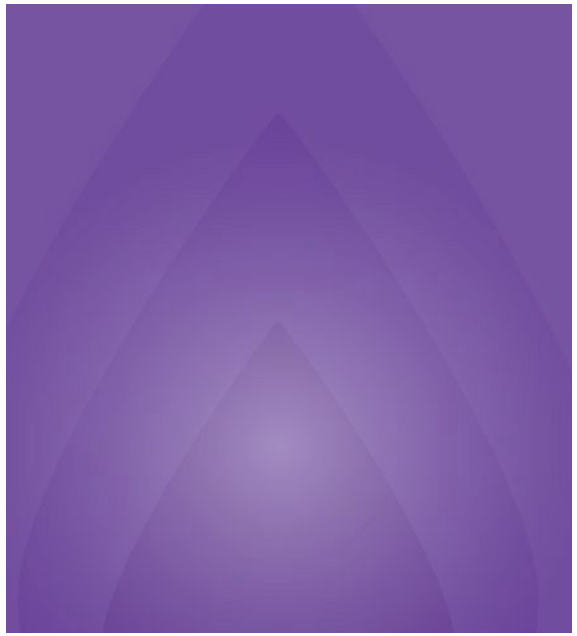
Innovative Hematology
Indiana Hemophilia & Thrombosis Center

Patient Education for HEMGENIX Gene Therapy

Live session with your Innovative Hematology/IHTC doctor

What is HEMGENIX gene therapy? How does it work?



HEMGENIX Hemophilia B Gene Therapy

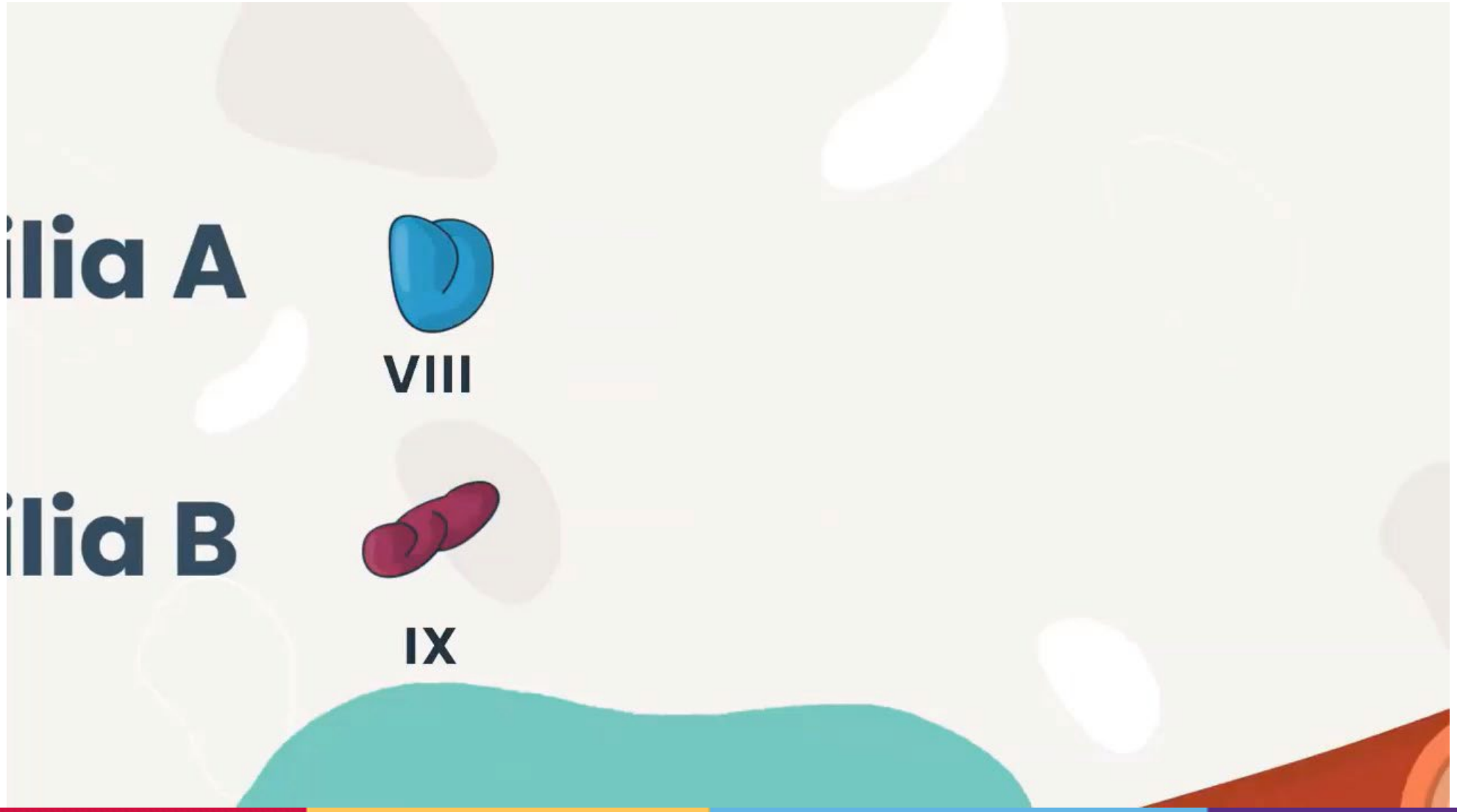
- In November, the FDA approved HEMGENIX for Factor IX (FIX) deficiency or Hemophilia B
- To take HEMGENIX, you must have Hemophilia B and meet one of these conditions:

Use Factor IX prophylaxis therapy	Have life-threatening bleeding, now or in the past	Have had repeated, serious bleeding episodes with no known cause

- Many people treated with HEMGENIX have fewer bleeding events and need fewer or no regular factor infusions[3,4,5], but results may be different between people
- Other gene therapy treatments for Hemophilia are still in review

Video: Hemophilia Gene Therapy Basics

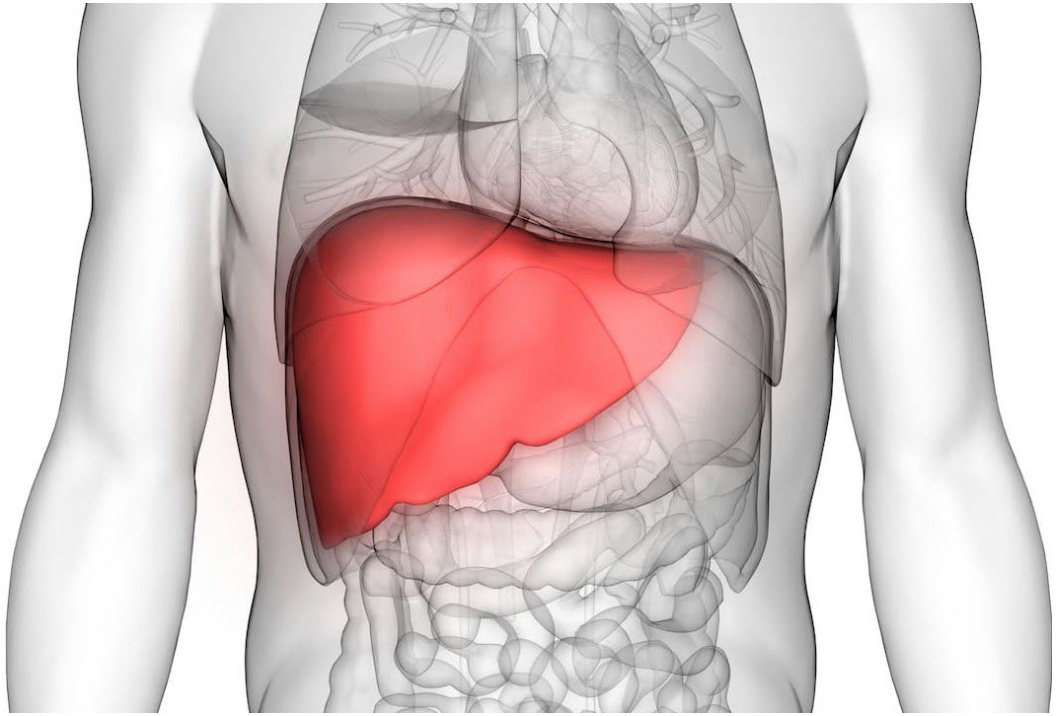
https://youtube.com/clip/UgkxYO_RottT8pAfqwNnVMAoSJXaeGYcvUQm



How is HEMGENIX given?

- Given as a one-time infusion
- Best given at a hemophilia treatment center
- Infused into a vein with a needle, like factor
- The infusion takes a few hours
- Patients must be watched for a few hours after the infusion for safety

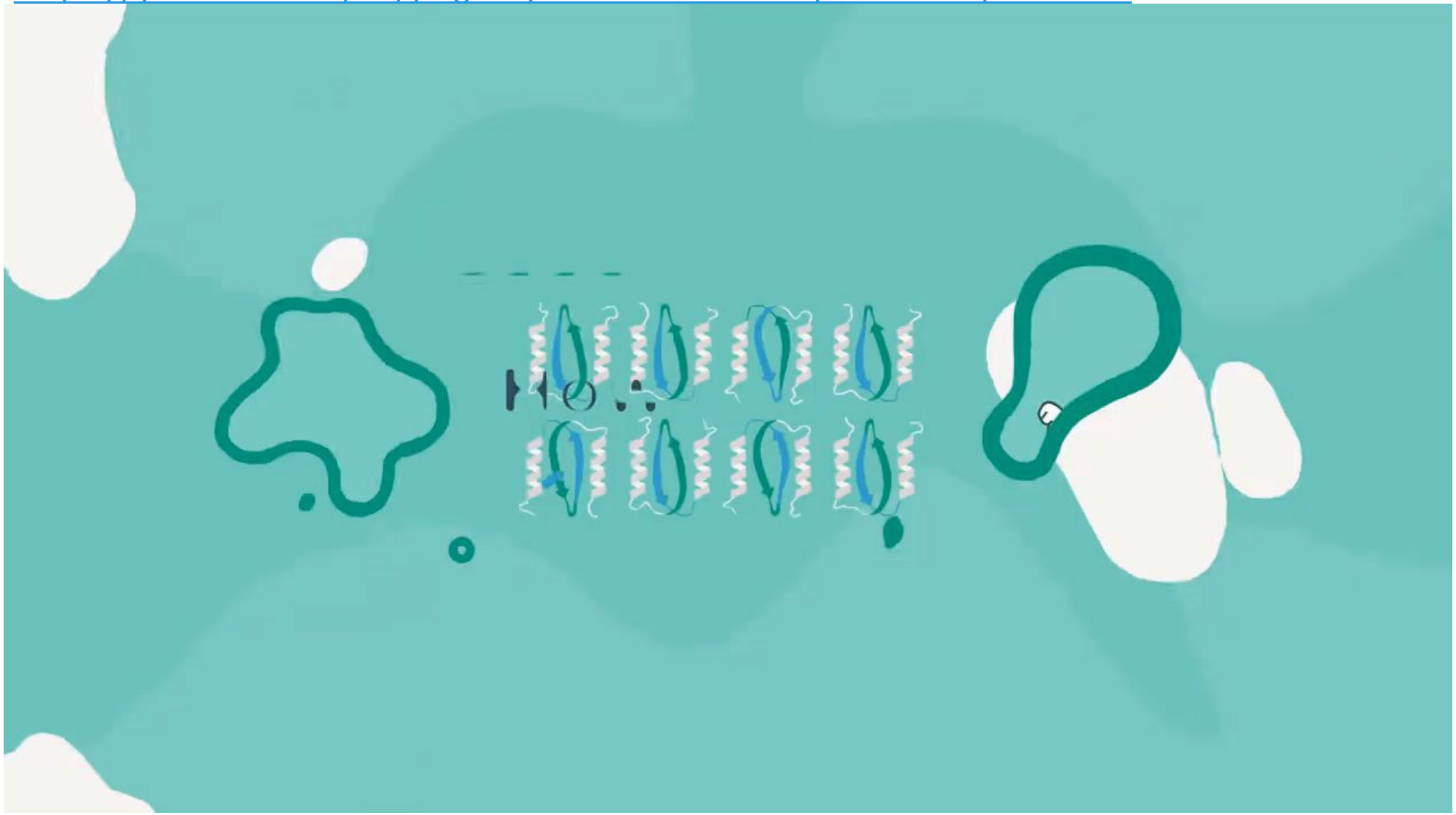
What is the target body tissue?



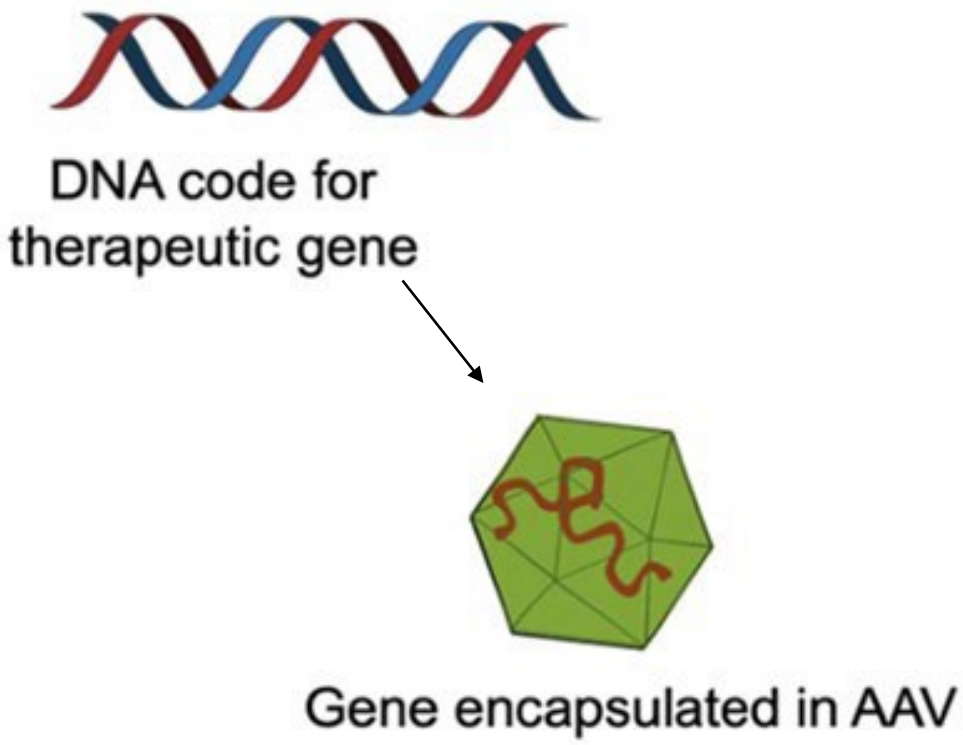
- In Hemophilia B, your liver does not make enough FIX
- HEMGENIX targets cells in the liver
- This ensures that the FIX made by your body after gene therapy will work properly

Video: How is the gene transferred?

https://youtube.com/clip/UgkxZy4dt8UOX3a6MLvq80Pt86HGp9PL_ET2



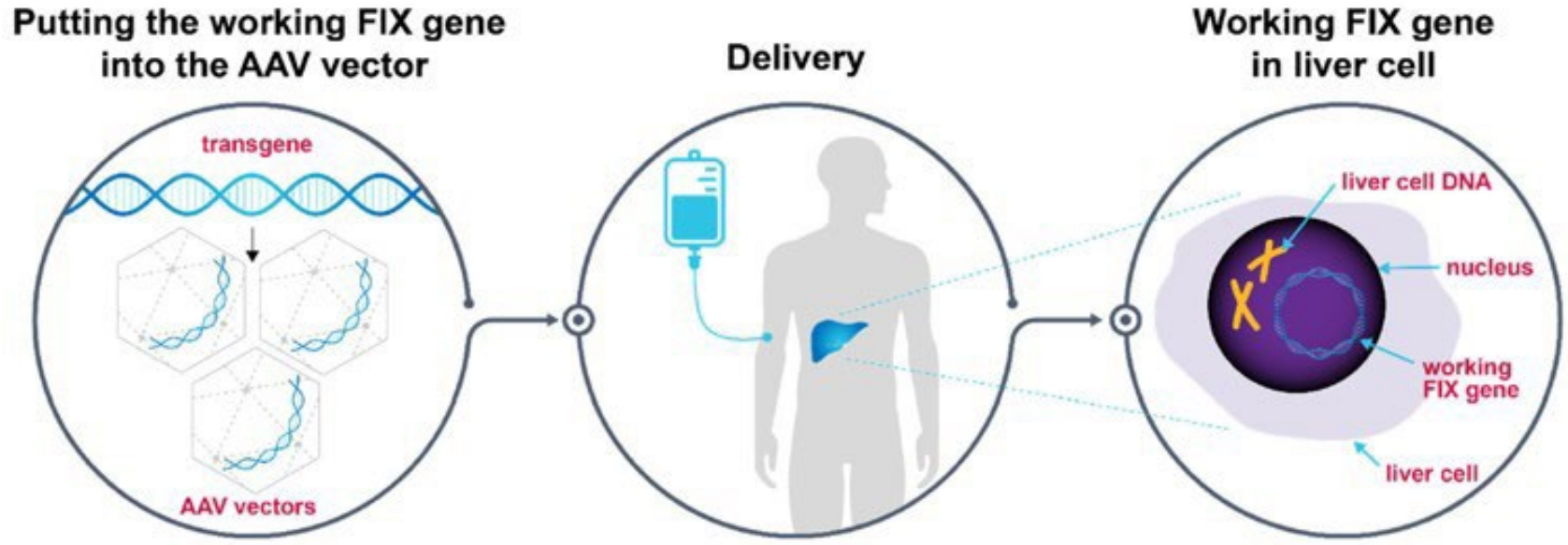
How is the gene packaged and what is inside?



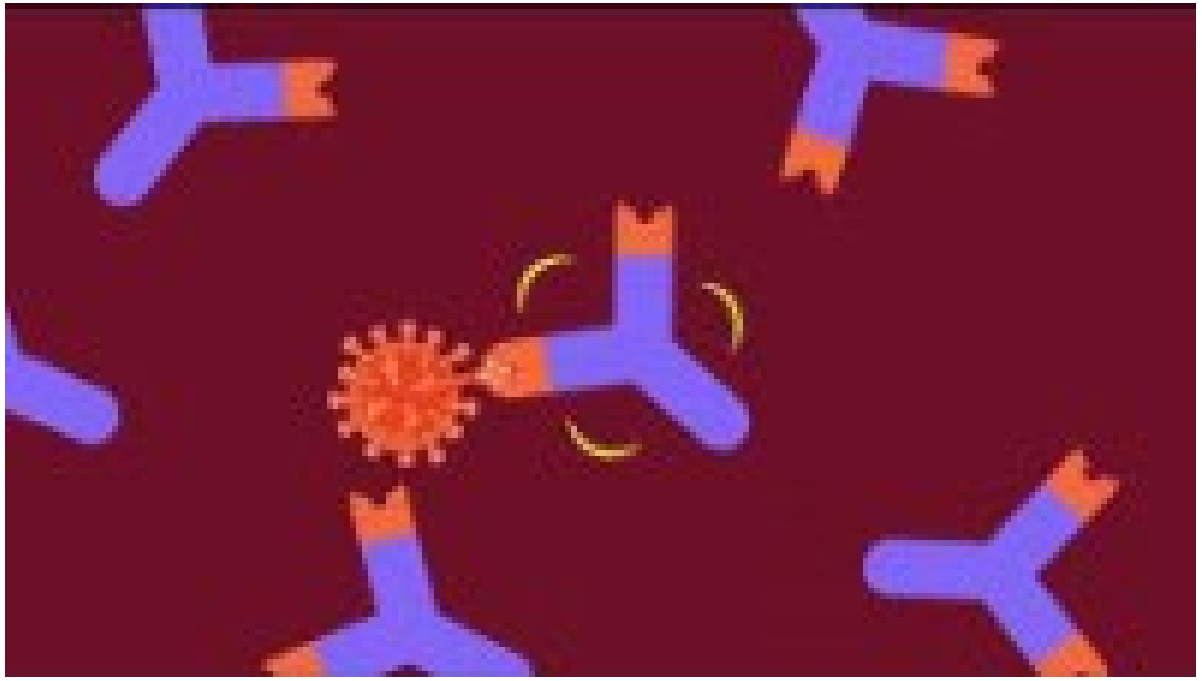
- The gene used is packaged inside a **vector**
- Think of the vector as a suitcase carrying the gene to its destination
- The vector can then enter certain cells in your body – in this case, cells in the liver – and deliver the gene
- Hemophilia gene therapy uses a modified virus as the vector
- HEMGENIX uses **adeno-associated virus 5, or AAV5**, as its vector, a virus that is not dangerous to humans

How is the gene packaged and what is inside?

- A vector may contain different genes, depending on the disorder being treated
- In HEMGENIX, the AAV5 vector contains a working FIX gene
- This gene teaches your liver cells to make FIX

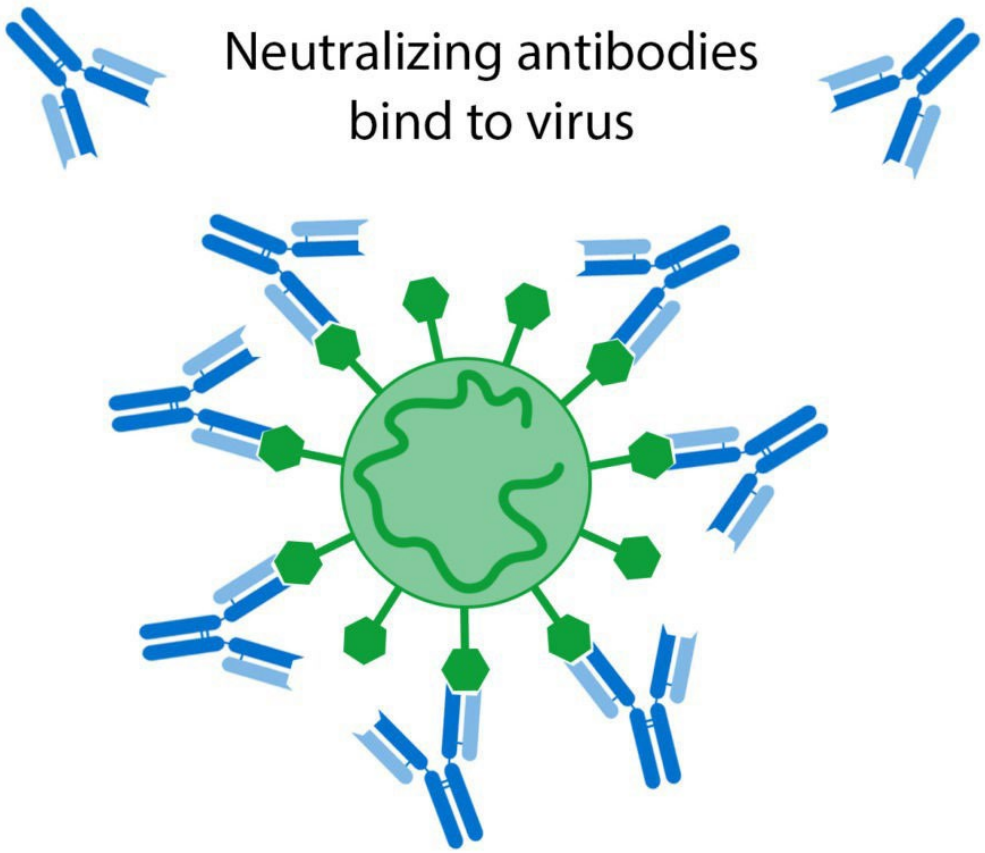


Why do I need to be tested for AAV5 first?



- When you are exposed to a virus, your body responds by forming proteins called antibodies
- Antibodies let your body remember the virus and try to protect you from a future infection
- We can test if a person has antibodies to a virus by checking their blood

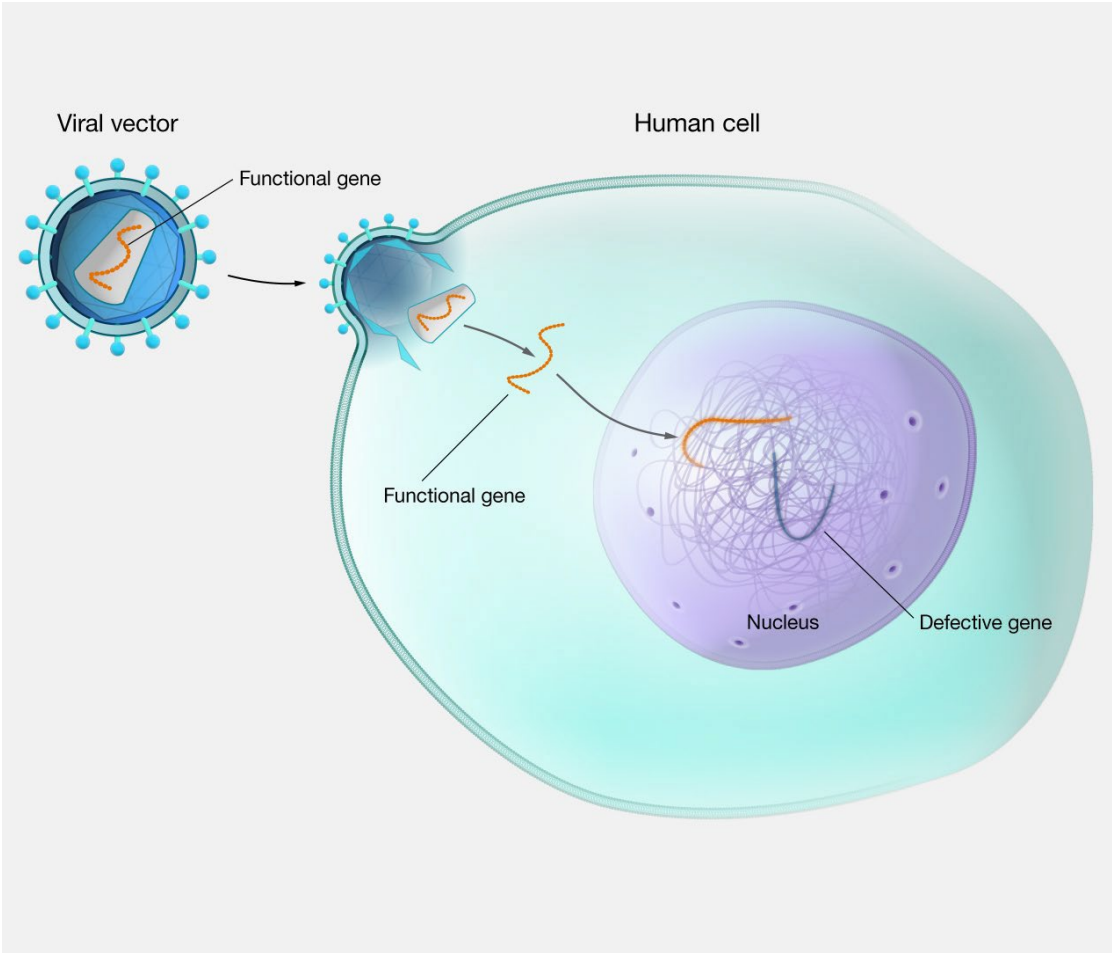
Why do I need to be tested for AAV5 first?



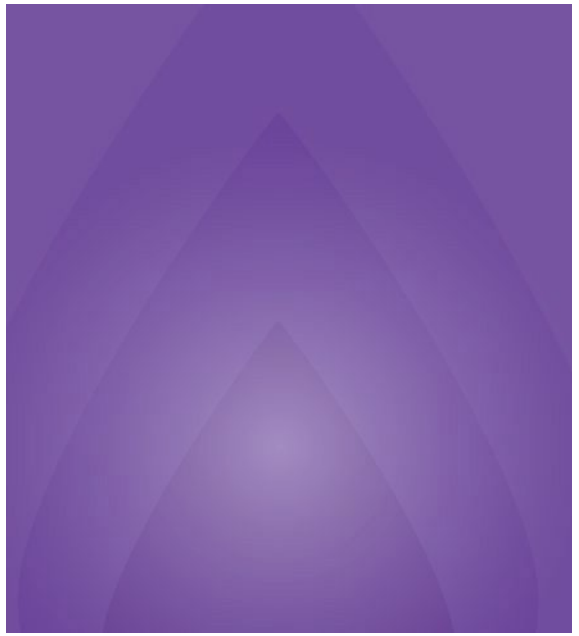
- About 1 in 4 (25%) people in the US have been exposed to AAV5 and have antibodies to it[1]
- If your blood contains too many antibodies to AAV5, your immune system will try to “protect” you from it
- This might keep the AAV5 from being able to work in your cells, which means HEMGENIX would not work for you
- Before you can take HEMGENIX, we need to check your blood to make sure you don’t have too many AAV5 antibodies

Where does the new gene stay in the target tissue?

- The new gene contains instructions that will help the liver cells make FIX
- Current gene therapy for hemophilia delivers a healthy copy of a gene, but does not insert it into your DNA
- That means it does not edit your own genes
- You will still have the genes for hemophilia. It will still be passed on to your daughters



How long does the new gene last?



How long does the new gene last?

- Some gene therapies might be long-term or life-long and others might last for a few years
- It's different for each patient and each kind of gene therapy
- We cannot predict how long your gene therapy results will last, but we can show you results from other patients
- The early follow-up period is critical for gene therapy to work. This period includes labs, check-ups, and medicines
- Gene therapy might not work on every patient

Research data for HEMGENIX

- We have information from 3 HEMGENIX research studies beginning in 2015
- Researchers have not seen any new safety concerns after 5 years of follow-up

First study:
Looked at safety only in 10 patients receiving a low dose[2]

FIX activity levels remained stable in all patients 5 years after dosing.

Second study:
Looked at 3 patients that took HEMGENIX 3 years ago[3]

Average FIX levels are now 36.9%.

Third study:
Looked at 54 patients that took HEMGENIX 2 years ago[4]

Average FIX levels are now 36.7%.

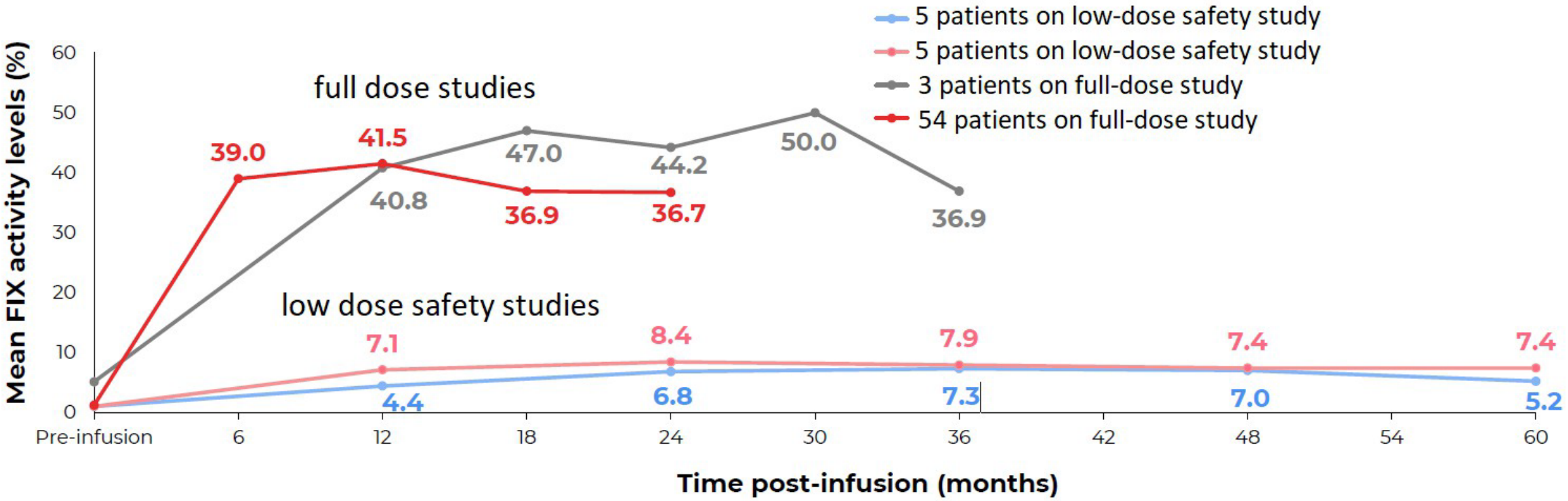
2 of 54 the patients did not respond to treatment.

One patient had a high level of AAV5 immunity. This probably neutralized the gene therapy (stopped it from working)

The other patient received a partial dose because the infusion was stopped early

Research data for HEMGENIX [5]

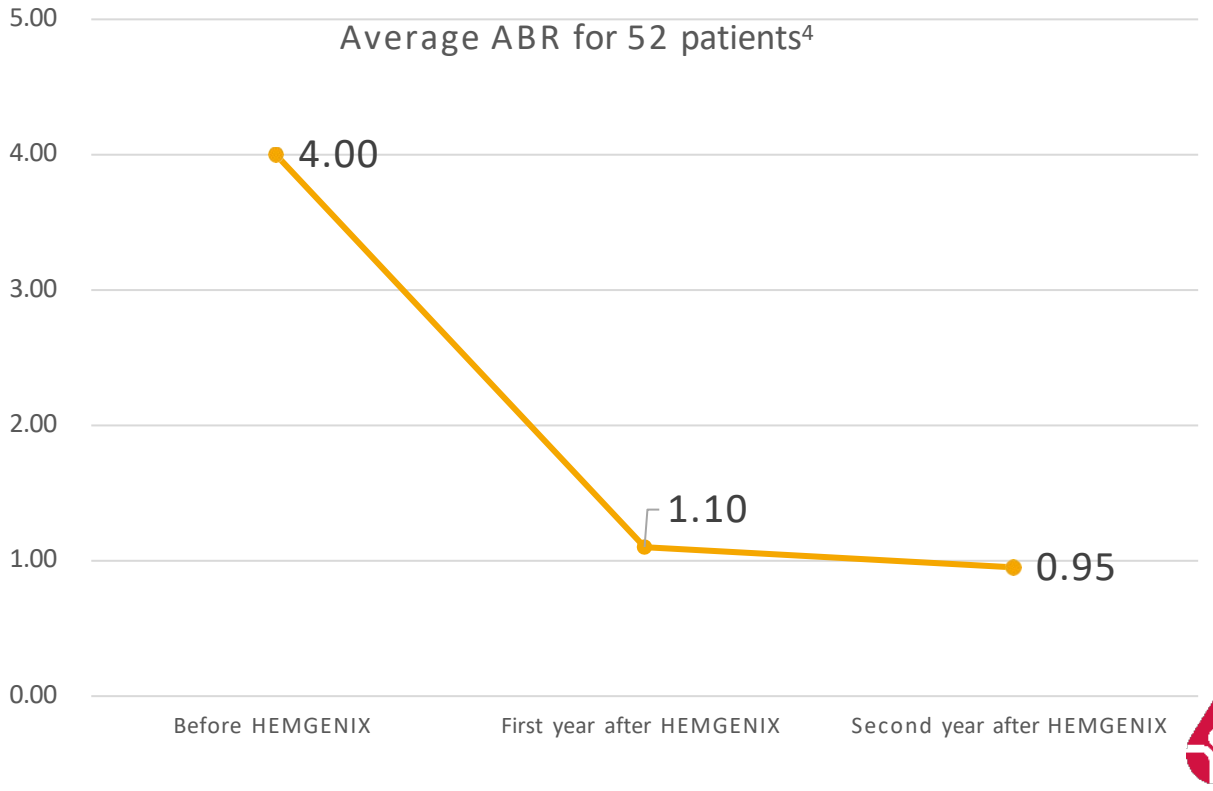
Figure 2. Mean FIX activity levels over time in the clinical trials of AMT-060 and etranacogene dezaparvovec[a]



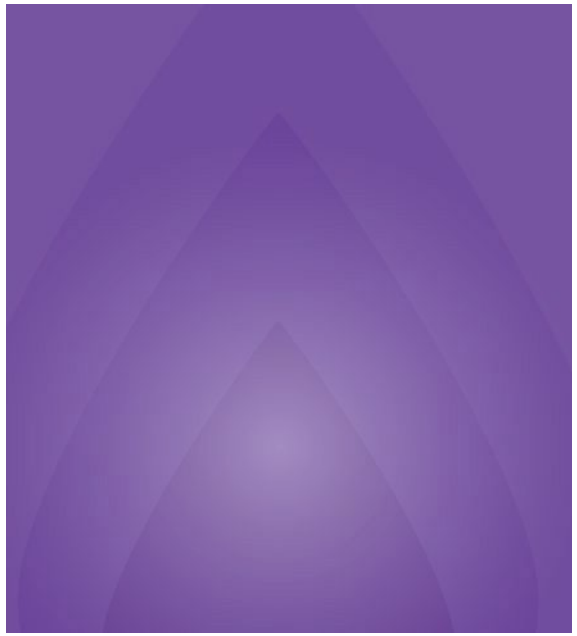
[a] Phase 1/2 AMT-060 and Phase 2b had no lead-in period; Phase 3 HOPE-B had a ≥6-month lead-in period where participants received FIX prophylaxis. For Phase 2b, baseline FIX expression was 0–2%, but no washout of infused FIX was required prior to Day 1; n=3 for all timepoints except pre-infusion (n=1), 18 months (n=2), and 36 months (n=2). For HOPE-B Phase 3, n=54 at pre-infusion, n=51 at 6 months, and n=50 at 12, 18 and 24 months.
FIX, factor IX.

Research data for HEMGENIX

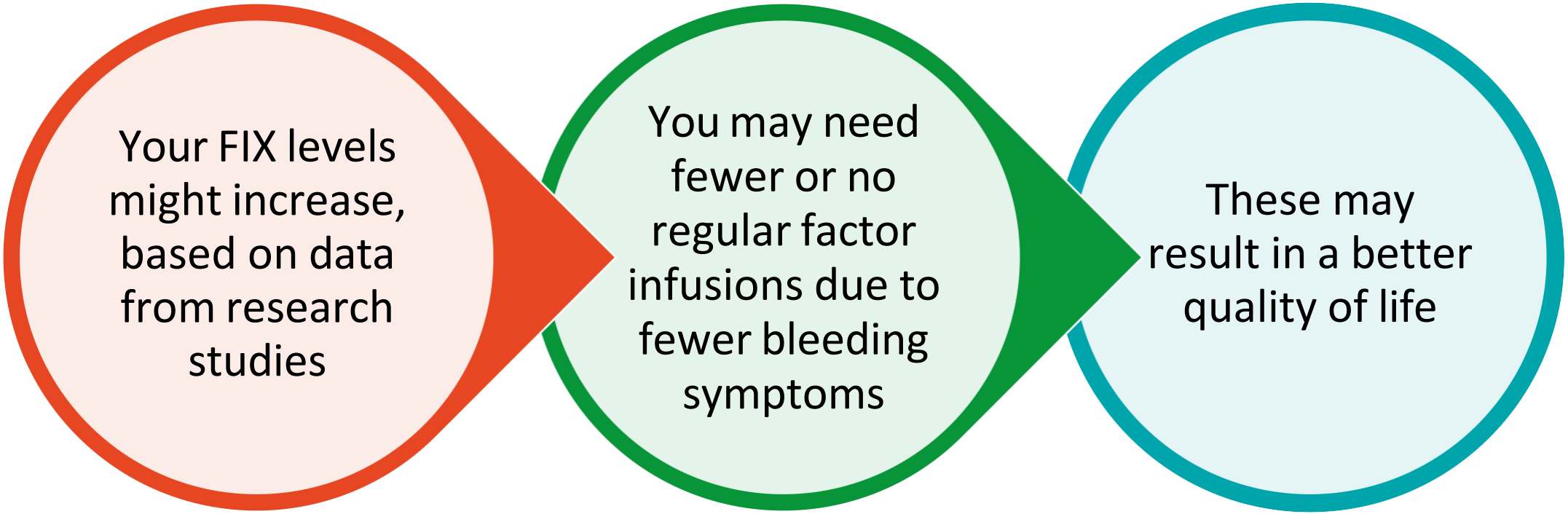
- Annual bleed rate, also called ABR, is the average number of bleeding events a patient has in one year
- 52 patients received a full dose and responded to HEMGENIX[4]:
  - Before HEMGENIX, they had an average ABR of 4 bleeds
  - In the first year after HEMGENIX, they had an average ABR of of 1.1 bleeds
  - In the second year, they had an average ABR of 0.95 bleeds



What are the possible benefits and risks of HEMGENIX?

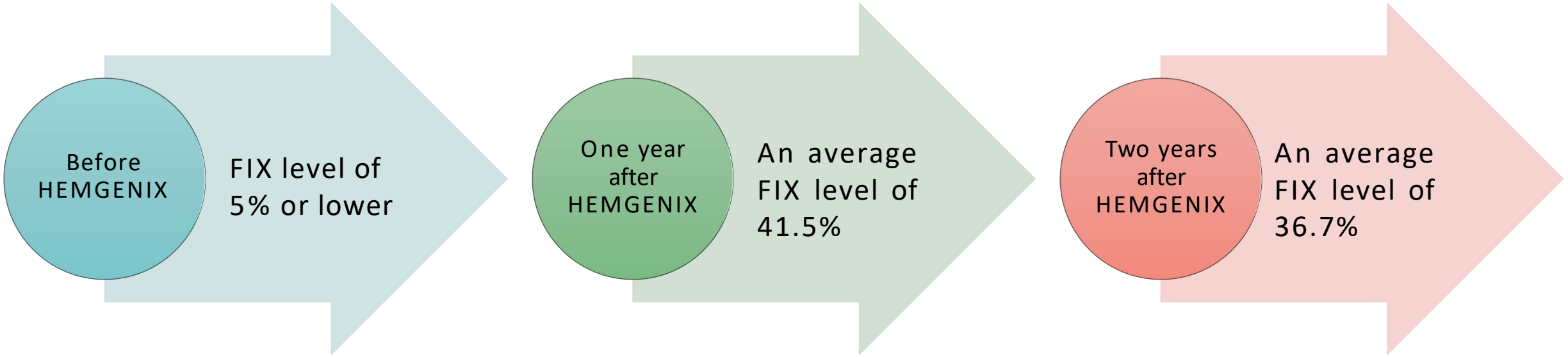


Possible benefits after taking HEMGENIX [3,4,5]



FIX levels after HEMGENIX [4,5]

A study that looked at 54 people who took HEMGENIX showed these FIX levels:



Most common side effects: Infusion reactions [2,3,4,5]

- These can include the following:
  - Facial flushing (face getting red and hot)
  - Feeling cold
  - Shivering
  - Rise in blood pressure
  - Stomach pain
  - Tight feeling in throat
  - Itching
  - Headache
  - Feeling dizzy
  - Tight feeling in chest

Possible serious side effects [2,3,4,5]

Liver inflammation

- HEMGENIX targets cells in your liver which can cause liver inflammation (your liver can become swollen and irritated)
- This is an expected response to these cells from your immune system
- Some people may need to take a medicine called a corticosteroid (like Prednisone) for some time to reverse the liver inflammation
- In clinical trials, liver function test results got worse for 24 out of 54 (44%) people
  - Nine (9) out of 54 (17%) people needed treatment with steroids as a result
  - These 9 people needed steroid treatment for an average of 80 days

Possible serious side effects [2,3,4,5]

Treatment failure

- HEMGENIX may not work for you—meaning your FIX levels may not improve
- If it does not work for you, you will not be able to take HEMGENIX again because your immune system will reject the vector
- You may also not be able to take other gene therapy products in the future

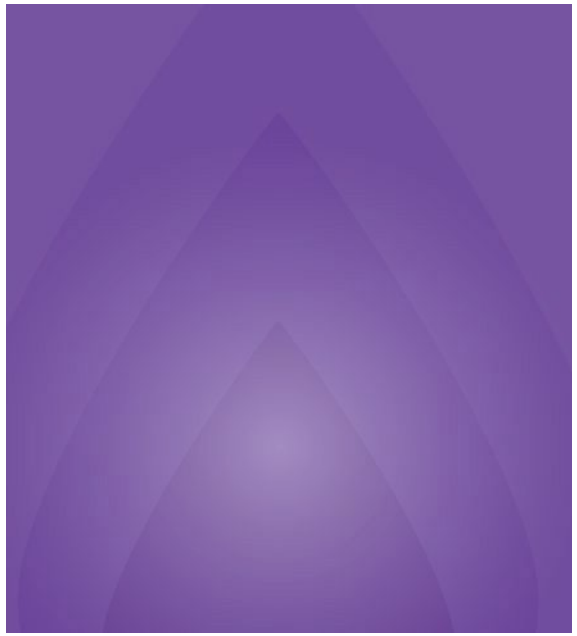
Increased risk of cancer

- Gene therapy could increase your risk for cancer
- We think this risk is very low

Unknown benefits or risks

HEMGENIX is a new treatment. There may be other benefits and risks of HEMGENIX that we do not know about at this time.

What is expected of me if I take HEMGENIX?



Your commitment: Screening

- You need an in-depth screening to make sure you can safely take HEMGENIX
- You will have or have already had:
  - Discussions with your doctor
  - Bloodwork
  - Mental health assessment
  - Evaluation of your liver and heart health
  - Possible scans of your liver and heart if there are concerns

Your commitment: Safety at a glance

Your commitment: Safety at a glance

Safety Expectation	How long
Use a condom during sexual activity	At least 6 months after your infusion
Do not drink any alcohol	At least 1 year after your infusion
Do not donate blood, organs, tissues, or transplant cells	Never again after your infusion
Follow your steroid treatment plan (if needed)	Every day for weeks to months

Your commitment: Safety

- **Not drinking alcohol**
  - Alcohol is not good for your liver and can cause or worsen inflammation
  - After the gene therapy infusion, you must not drink alcohol for 1 year
  - This is to protect your liver and increase your chance that the gene therapy will work, since it targets liver cells
  - After 1 year, we recommend no more than 3 drinks total in a week, with no more than 1 drink on a given day

Your commitment: Safety

- **Sexual precautions**
  - The gene therapy vector can stay in semen for some time after the infusion
  - After the gene therapy infusion, you must wear a condom during sexual activity for at least 6 months
  - This is not only to prevent pregnancy but to protect your sexual partners from exposure to the gene therapy vector
  - If you have sex with a partner who can get pregnant, we recommend they also use birth control like the pill or an IUD

Your commitment: Safety

- After gene therapy, you can **no longer donate any blood, organs, tissues, or cells for transplant** for life
- After gene therapy, **you will still have the hemophilia gene** and will pass it on to daughters you may have after treatment
- **Staying well and keeping your liver healthy** will increase the chance that the gene therapy will work for you
  - Eat a healthy diet
  - Be physically active
  - Avoid any alcohol
  - Follow health and safety guidelines that keep you well

Your commitment: Follow-up at a glance

Time period	Activity	How often
First 2 weeks after infusion	Physical exam and blood test	1 time a week
3 weeks to 3 months after infusion	Blood test	1 time a week
Months 4 through 12 after infusion	Blood test	1 time a month. You might need blood tests more often if you have liver inflammation.
1 year after infusion	Physical exam and blood test	2 times a year

Your commitment: Blood draws

- In the first year after your infusion, you need regular blood draws to check:
  - Your liver health
  - Your FIX levels
- These blood draws will be at least weekly for the first 3 months
- They may be more frequent if you need extra monitoring
- After that, they will be at least monthly through the first year

Your commitment: Communication

For your safety and for the best chance for the gene therapy to work, your doctor needs to know everything going on with your health before and during the follow-up period.

Contact Innovative Hematology/IHTC right away:

About any changes in your health: New problems, symptoms, or medicines including herbal supplements	If you have trouble doing your follow-up blood draws	If you are not able to follow the expectations for alcohol use or safe sex

This will help us decide:

- If we need to change your treatment plan, like starting steroids
- If we should monitor your sexual partner for pregnancy or other problems

Your commitment: Steroid treatment (if needed)

- If your liver health gets worse or FIX levels go down, you may need to take corticosteroids (also just called steroids) for some time
- Steroids (like Prednisone) can lower inflammation in the body
- Taking them can help lower the inflammation in your liver
- If you need steroids, you will have to take them every day until your liver inflammation gets better
- In a HEMGENIX study, 9 out of 54 patients (17%) needed steroids for an average time of 80 days[4]

Your commitment: Steroid treatment (if needed)

You must take steroids at the same time every day

Your dose will get smaller over time until you are done

It is important for you to follow the exact schedule and instructions for your steroid treatment

You cannot skip doses, change the dose or schedule, or stop taking them all the sudden

Your commitment: Steroid treatment (if needed)

There are many possible side effects while taking corticosteroids:

- Increased hunger
- Weight gain
- Feeling sick to your stomach (nausea)
- Acne and skin changes
- Having a weakened immune system (immunosuppression)
- Mood changes and mood swings (feeling irritable, angry, or very anxious and excited)
- Mental health problems (feeling depressed or anxious, thinking about suicide)
- High blood sugar (this is usually short-term, but you may need treatment)
- If you have a seizure disorder, steroids can make it worse
- Acid reflux, ulcers, or bleeding from your stomach or small intestine
- Increased blood pressure
- Nerve damage to your eyes (glaucoma) or cloudy vision (cataracts)
- Higher risk of infection
- Having trouble sleeping

Your commitment: Steroid treatment (if needed)

- You will need extra monitoring while you're on steroids if you have:
  - Diabetes or pre-diabetes
  - High blood pressure
  - Glaucoma
  - Mental health or mood disorders

Your commitment: Public health

- Hemophilia gene therapy is a brand-new treatment. We need information about how it works for each person who gets it to help understand how it will work for everyone
- Innovative Hematology/IHTC can enroll you in these public health studies that add to national data about people with hemophilia:

ATHN Transcends National History Study	ATHN Dataset National Database for Hemophilia Treatment Centers	Community Counts: Public Health Surveillance Project for Bleeding Disorders

- If you enroll in these studies, information about your gene therapy treatment can be used for the greater good of hemophilia care

Considering your commitment

Gene therapy is a big commitment.

You should reconsider if you cannot commit to any of these:

- You cannot commit to the lifestyle and safety requirements (no alcohol for 1 year, condom use for at least 6 months)
- You cannot commit to the follow-up blood draws and visits (at least weekly for 3 months, then monthly for a year)
- You cannot take steroids using the instructions given to you

Are you ready for gene therapy?

- Do you understand how gene therapy works?
- Do you understand the possible risks?
- What is your goal for taking gene therapy?
- Does your goal line up with the information you've learned?
- Can you stick to the follow-up and safety requirements?

“The journey of a thousand miles begins with a single step.”

Lao Tzu

Checking your understanding

- Before taking HEMGENIX, you must understand how it works, the possible benefits and risks, and the expectations of you as the patient.
- We will now ask you to fill out a questionnaire to check your understanding of the information we've talked about.
- Do you prefer to do this on a tablet or paper?

Links for more learning

Videos:

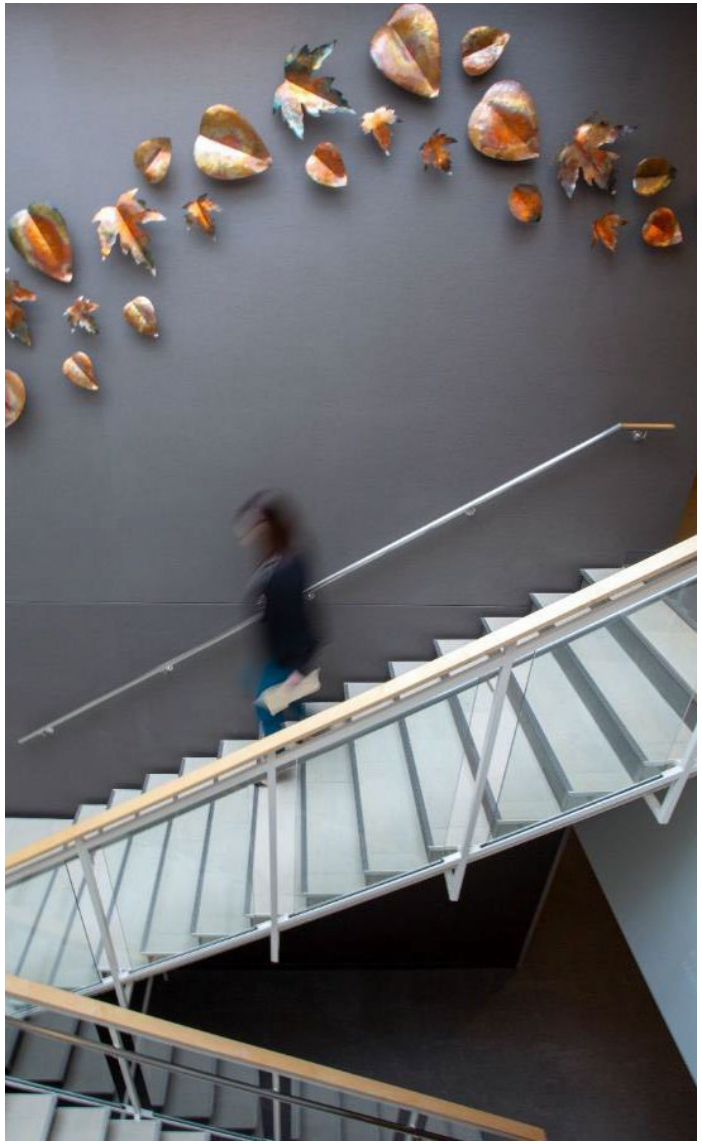
- Gene Therapy Basics (ASGCT)
- Hemophilia and Gene Therapy (ASGCT)
- Viral Vectors Overview (ASGCT)
- How the Gene Therapy for Hemophilia B Got FDA Approval

Websites:

- https://patienteducation.asgct.org/
- https://edhad.org
- https://www.ehc.edu
- https://haemophilia.org.uk
- https://isth.org
- https://www.hemophilia.org
- https://www.wfh.org/en/resourceseducation/educational-materials

References

1. Klamroth R. et al. (2022). Global Seroprevalence of Pre-existing Immunity Against AAV5 and Other AAV Serotypes in People with Hemophilia A. *Hum Gene Ther, 33*(7-8), 432-441. doi:10.1089/hum.2021.287
2. Miesbach W. et al. (2018). Gene therapy with adeno-associated virus vector 5-human factor IX in adults with hemophilia B. *Blood, 131*(9), 1022–1031. https://doi.org/10.1182/blood-2017-09-804419
3. Von Drygalski A, et al. Etranacogene dezaparvovec (AMT-061 phase 2b): normal/near normal FIX activity and bleed cessation in hemophilia B. *Blood Adv 2019; 3*(21):3241
4. Pipe, S. W. et al. (2023). Gene therapy with Etranacogene Dezaparvovec for hemophilia B. *New England Journal of Medicine, 388*(8), 706–718. doi.org/10.1056/nejmoa2211644
5. Miesbach W. et al. (2023, February 7-10). Durability of response after long term follow up in the Phase 1/2 study of AMT 060, and Phase 2b and 3 studies of etranacogene dezaparvovec in haemophilia B [Poster Abstract]. 2023 Congress for European Association for Haemophilia and Allied Disorder, Brussels, Belgium.



Thank you!

Carter Cox, PA-C

1-877-CLOTTER

www.innovativehematology.org