do you OR SOMEONE YOU KNOW have hemophilia A

GENE TRANSFER STUDY

A clinical research study is recruiting **hemophilia A** males to understand a factor VIII (FVIII) gene transfer method

MUST BE:

- ✔ Male 18 years or older with hemophilia A
- ✔ Factor VIII deficiency (≤ 2%)
- ✔ On-demand therapy or prophylaxis with history of bleeding
- ✔ No history of inhibitor to factor VIII
- ✔ No history of allergic reaction to factor VIII products
- ✔ Available for study-related visits for about 12 months

ClinicalTrials.gov Identifier: [NCT03003533]

Have questions?

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This research study is being sponsored by Spark Therapeutics, Inc.

Recruitment-Flyer-A1-Version-3.0
of 06 January, 2017

GENE TRANSFER CLINICAL TRIAL FOR MALES WITH HEMOPHILIA A

WHAT IS IT?

Since the factor VIII gene was discovered, scientists have been working on a way to transfer the factor VIII gene into hemophilia patients' cells to produce factor VIII protein. In fact, the Sponsor of this study received "breakthrough therapy designation" of their hemophilia B gene transfer investigational study product from the regulator. In this research study, SPK-8011 (the study product) uses a modified recombinant AAV "vector" (adeno-associated virus) to transfer factor VIII gene into males with hemophilia A. The study product is injected into the blood-stream by an intravenous (IV) infusion, then travels to the liver where factor VIII protein is made. The factor VIII protein is then released into the blood-stream. If the production of factor VIII by the liver results in high enough levels in the bloodstream, the number of bleeding events may be reduced; however, there are also some risks associated with the study. This research study is to determine if factor VIII gene transfer is safe for the treatment of hemophilia A.

Please contact us to learn more about the benefits and risks related to this study.

CAN I TAKE PART? Yes, you may be eligible if you meet the following criteria:

- ✔ You are an 18 years or older male with hemophilia A (factor VIII level is 2% or less)
- ✔ You had a history of bleeding that requires prophylaxis or on-demand therapy
- ✔ You had no history of inhibitor or allergic reaction to factor VIII products
- ✔ Don't have active Hepatitis B or C (eligible if clear for at least 6 months)
- ✔ You are not on antiviral therapy for Hepatitis B or C
- ✔ HIV positive could be eligible when receiving effective treatment
- ✔ Don't have severe liver disease
- ✔ Available for study-related visits for about 12 months*

* It is recommended by the U.S. Food and Drug Administration that study volunteers be followed for up to 15 years after gene transfer. Study volunteers will be asked to take part in a long-term follow-up study for additional 14 years before the end of this study.

WHAT IS INVOLVED?

- ➤ A screening / baseline phase that may last up to several weeks.
- ➤ An outpatient infusion day may last up to 24 hours. On the infusion day, the study volunteer will have an intravenous (IV) infusion of his regular factor VIII concentrates for 10 minutes then the infusion of the gene transfer study product for about an hour.
- ➤ After the infusion,he will have follow-up visits** up to 52 weeks.
- ➤ Most visits will include physical exams, questionnaire, blood draws, and other tests (ranging from 1 hour to 2 hours per visit).

**There is flexibility regarding the location of the follow-up visits after the infusion of the study product and some visits can be arranged by mobile phlebotomists for your convenience (*please inquire for more details*).

HOW IS THIS STUDY DIFFERENT FROM OTHERS?

- This study uses a modified recombinant AAV "vector" which has a higher attraction to the liver and lower chance of inflammation
- This is the first AAV-mediated hemophilia A gene transfer study done in the United States.

PARTICIPATING CLINICAL CENTERS

Louisiana Center for Advanced Medicine
Slidell, LA
Mississippi Center for Advanced Medicine
Madison, MS
CLINICALTRIALS.GOV identifier: NCT03003533

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Recruitment-Flyer-A2-Version-3.0
of 06 January, 2017

DO YOU

OR SOMEONE YOU KNOW

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GENE TRANSFER STUDY

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MUST BE

- ✓Male 18 years or older with Hemophilia A
- ✓Factor VIII deficiency (≤ 2%)
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- ✓No history of inhibitor to FVIII
- ✓No history of allergic reaction to FVIII products
- ✓Available for study-related visits for about 12 months

Have questions?

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GENE TRANSFER CLINICAL TRIAL FOR MALES WITH HEMOPHILIA A

PARTICIPATING CLINICAL CENTER

Louisiana Center for Advanced Medicine

Slidell, LA

ClinicalTrials.Gov Identifier:

NCT03003533

Description

Since the factor VIII gene was discovered, scientists have been working on a way to transfer the factor VIII gene into hemophilia patients' cells to produce factor VIII protein. In this study, the study product (SPK-8011) uses a modified recombinant AAV "vector" (adeno-associated virus) to transfer factor VIII gene into males with hemophilia A. The study product is injected into the bloodstream by an intravenous (IV) infusion, then travels to the liver where factor VIII protein is made. The factor VIII protein is then released into the bloodstream. If the production of factor VIII by the liver results in high enough levels in the bloodstream, the number of bleeding events may be reduced; however, there are also some risks associated with the study. This research study is to determine if factor VIII gene transfer is safe for the treatment of hemophilia A.

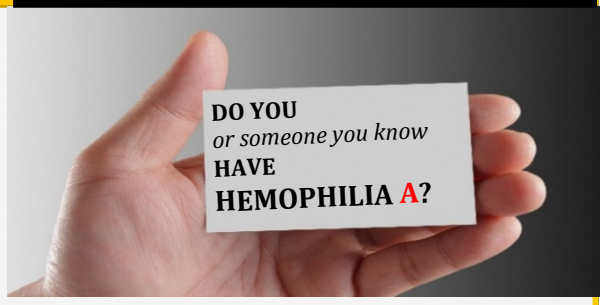
Please contact us to learn more about the benefits and risks related to this study.

Can I participate?

Yes, you may be eligible if you meet the following criteria:

- ☐ Male 18 years or older with hemophilia A
- ☐ Factor VIII deficiency (≤ 2%)
- ☐ Is on-demand therapy or on prophylaxis with history of bleeding
- ☐ No history of inhibitor to factor VIII
- ☐ No history of allergic reaction to factor VIII products
- ☐ Don't have active Hepatitis B or C (eligible if clear for at least 6 months)
- ☐ Not on antiviral therapy for Hepatitis B or C
- ☐ HIV positive could be eligible when receiving effective treatment
- ☐ Available for study-related visits for about 12 months*

** It is recommended by the U.S. Food and Drug Administration that study volunteer be followed for up to 15 years after gene transfer. Study volunteer will be asked to take part in a long term follow-up study for up to an additional 14 years*



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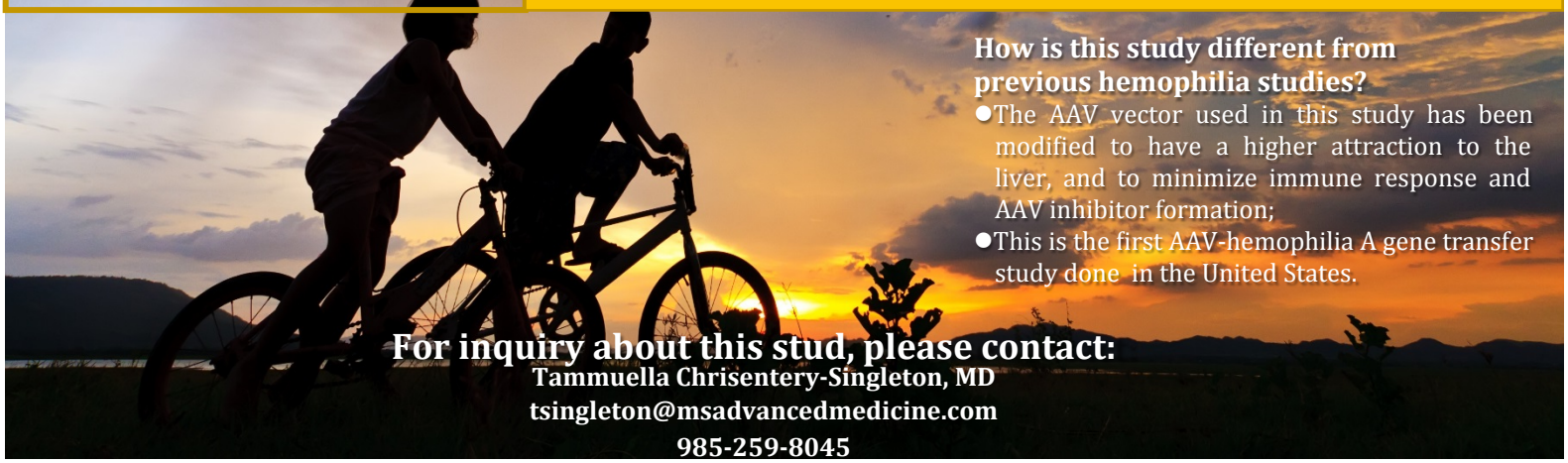

How is this study different from previous hemophilia studies?

- The AAV vector used in this study has been modified to have a higher attraction to the liver, and to minimize immune response and AAV inhibitor formation;
- This is the first AAV-hemophilia A gene transfer study done in the United States.

For inquiry about this stud, please contact:

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