Plain Language Study Summary

SRP-9001-101: A Gene Transfer Therapy Study to Evaluate the Safety of Delandistrogene Moxeparvovec (SRP-9001) in Participants with Duchenne Muscular Dystrophy (DMD)

Sarepta would like to thank the study participants and their families for their participation in this study. Their contribution helped researchers learn more about delandistrogene moxeparvovec as a treatment for Duchenne muscular dystrophy.

Sarepta created this summary to share the results of the study with the participants, their family members, and the general public.

This summary only shows the results from this study. Other studies with delandistrogene moxeparvovec could have different results. Researchers evaluate results of many studies to understand which treatments work, how well they work, and how safe they are for patients.

This summary shows the overall results of this study. Results for each participant may have been different and are not part of this summary.

If you have questions about these results, please feel free to email Sarepta (advocacy@sarepta.com) or, if you were a participant, talk to your study doctor.

Here are the key parts of this summary:

If you are reading this on a computer, you can click on a topic below to skip to that section.

- **Why was this study done?**
- **Who took part?**
- **What treatment was studied?**
- **What happened during the study?**
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- **What were the other results of the study?**
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Why was this study done?

Researchers are looking for better ways to treat **Duchenne muscular dystrophy**, or **Duchenne** for short. Duchenne is a rare disease that affects mostly males. People with Duchenne have a **genetic mutation** that limits their ability to make a protein called **dystrophin**. Dystrophin plays an important role in protecting and strengthening muscles. Without the ability to make dystrophin, people with Duchenne have muscle weakness in many parts of the body that gets worse with time. Duchenne is an irreversible, progressive disease.

What are genetic mutations?
Genes are like tiny instruction manuals contained in the body's cells. Genes tell the cells how to make different kinds of proteins. Proteins play lots of different roles in keeping the body healthy and strong. If someone has a genetic mutation, it means there is a problem with the instructions for making a protein.

Delandistrogene moxeparvovec (also known as SRP-9001) is a type of treatment called **gene therapy**. It is given as a one-time **intravenous (IV) infusion** (through a needle in the vein).

Each infusion of delandistrogene moxeparvovec contains many copies of a gene that have instructions for how to make a shorter form of dystrophin called **delandistrogene moxeparvovec dystrophin**. Each copy of the gene is packaged in a special carrier called a **vector**. The vector acts like a delivery vehicle that helps get the gene to the right place inside the body's cells. Once the new gene is inside the cell, the body can use it as an instruction manual to help make delandistrogene moxeparvovec dystrophin.

Not all gene therapies have the same components. The vector (rAAVrh74) and the gene (delandistrogene moxeparvovec) in the treatment for this study are different from those used in other gene therapies.

This study was done to learn about delandistrogene moxeparvovec as a possible treatment for Duchenne.

Who took part?

Researchers asked for the help of males with Duchenne. Everyone in this study was between 4 and 6 years old when they joined. There were 4 participants. This study took place in the United States.

What treatment was studied?

The treatment studied was delandistrogene moxeparvovec. All 4 participants got delandistrogene moxeparvovec, which is a one-time infusion.

What happened during the study?

First, the study team discussed the study with potential participants.

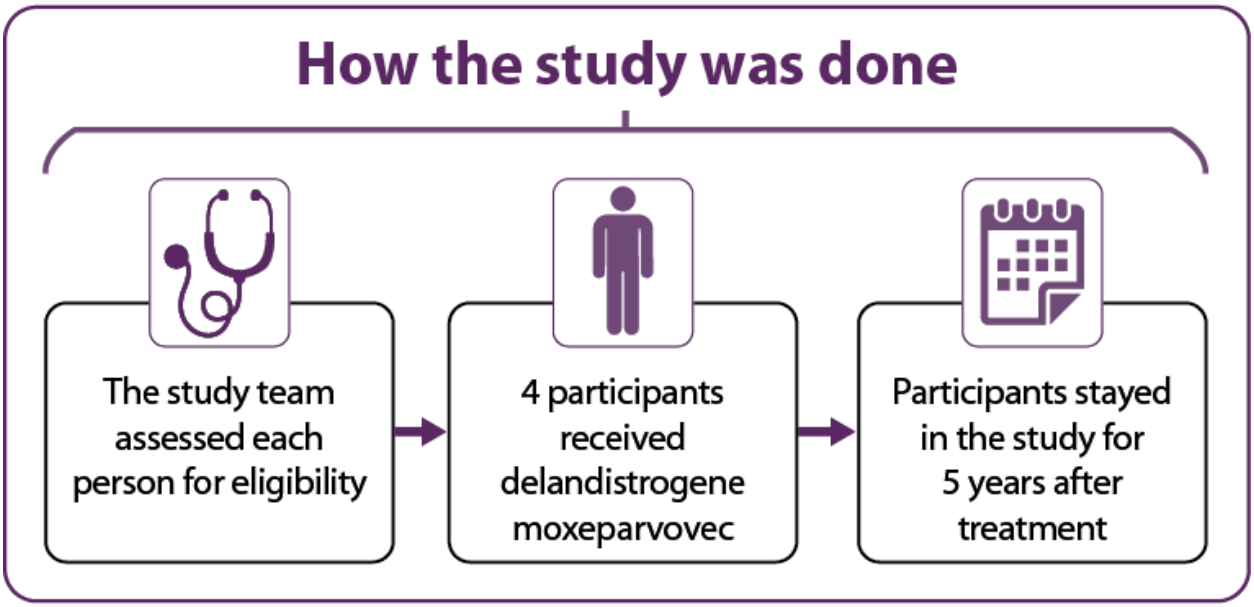
The study team checked to make sure everyone who joined the study had Duchenne caused by certain genetic mutations.

People were not allowed to take part in this study if:

- they had received prior gene therapy, a stem cell transplant, or a gene editing treatment
- they had certain medical conditions that, in the opinion of the study doctor, would make it unsafe for them to take part or difficult for them to complete the study assessments
- they had elevated levels of antibodies to the vector component of delandistrogene moxeparvovec

Participants received 1 dose of delandistrogene moxeparvovec.

After treatment, participants were asked to stay in the study for 5 years. During this time, the participants and their families visited the study hospital regularly so that the study team could keep track of the participants' long-term health outcomes.



During the study:

The participants:

- Got check-ups
- Gave blood and urine samples
- Had 2 muscle **biopsies** (one before treatment and one about 3 months after treatment)
- Completed different activities, such as walking or running 100 meters (about 330 feet), which allowed doctors to measure their physical function

What is a biopsy?

A biopsy is a procedure in which doctors collect a small amount of tissue. In this study, doctors collected samples of muscle tissue so they could measure how delandistrogene moxeparvovec dystrophin levels changed after treatment.

The participants and their families told study doctors about:

- How the participant was feeling
- Any new or worsening medical issues the participant might be having
- Any medications the participant was taking

What was the main goal of the study?

The main goal of the study was to learn about the side effects of delandistrogene moxeparvovec. Study doctors kept close track of the participants' health after treatment to help understand the long-term effects of treatment.

What were the results?

What side effects did the participants have?

These results describe the side effects that participants had during the 5-year study. These are new or worsening medical events that happened to participants during the study that the study doctors thought might be related to delandistrogene moxeparvovec.

None of the participants had a serious side effect. Serious side effects are those that are life threatening, need hospital care for treatment, or cause long-term medical problems or death.

None of the participants left the study because of a side effect.

There were 3 participants (75%) who had non-serious side effects. The table below shows the non-serious side effects that happened during the study.

Side Effect	Out of 4 participants
Vomiting	3 (75%)
Increased levels of liver enzymes Liver enzymes are proteins that are made in the liver. High levels of these enzymes in the blood might be a sign of a problem in the liver.	3 (75%)
Decreased appetite	2 (50%)
Nausea	1 (25%)
Feeling weak	1 (25%)
Fatigue	1 (25%)

What were the other results of the study?

The main goal of the study was to learn about the side effects of delandistrogene moxeparvovec. But in an effort to learn as much as possible about delandistrogene moxeparvovec as a possible treatment for Duchenne, the researchers also set other (secondary) goals.

These included checking to see:

- if participants started to make delandistrogene moxeparvovec dystrophin in their muscle cells after treatment
- how the participants' physical function changed after treatment

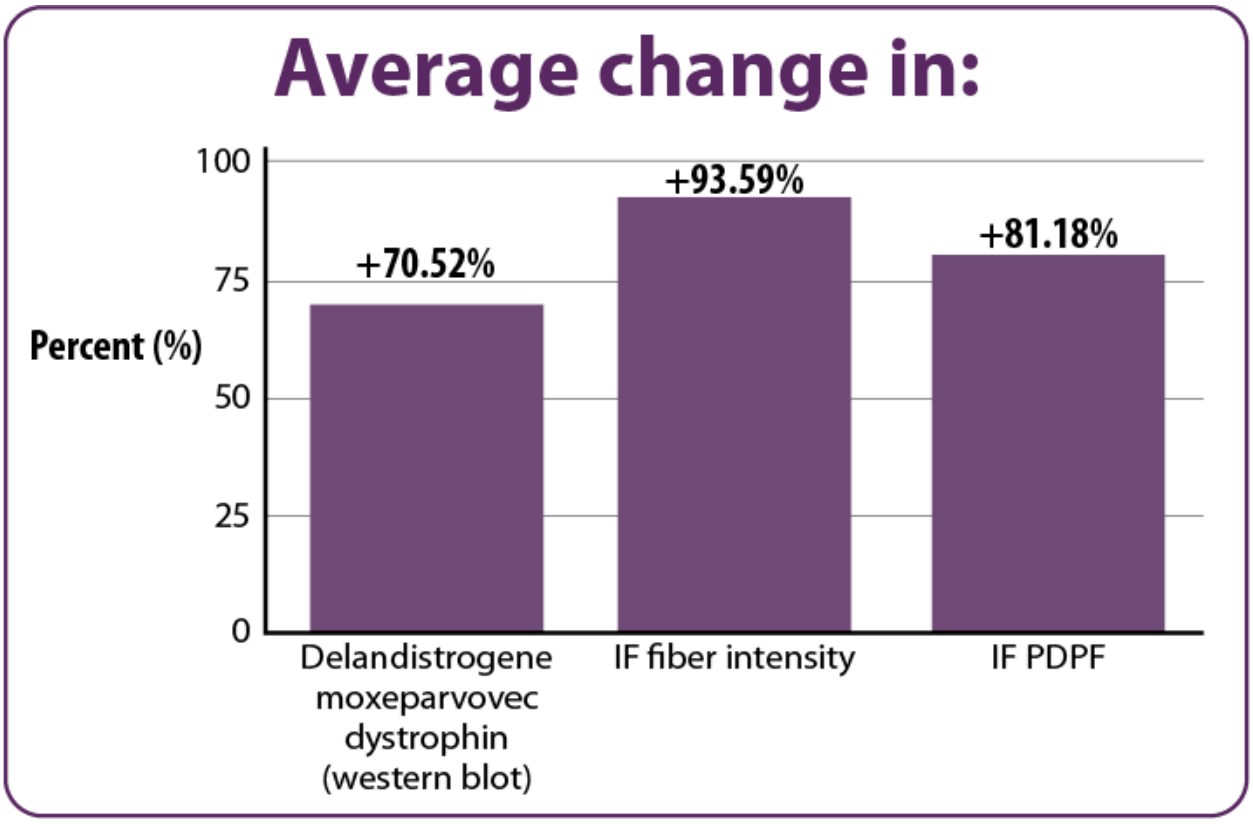
Did participants start to make delandistrogene moxeparvovec dystrophin in their muscle cells?

To answer this question, researchers looked at the biopsy samples that participants gave before and after treatment. They measured levels of delandistrogene moxeparvovec dystrophin in different ways:

- **with a lab test called a western blot**. The result is shown as a percentage (fraction) of how much dystrophin researchers would expect to see in a muscle tissue sample from someone who does not have Duchenne.
- **with a technique called immunofluorescence (IF)**. IF involves tagging a specific protein with a fluorescent dye. In this study, the tagged protein was delandistrogene moxeparvovec dystrophin. This lets researchers look at the biopsy samples under a microscope and see the muscle fibers that contain the protein. IF allowed researchers to measure delandistrogene moxeparvovec dystrophin in the biopsy samples in 2 different ways:
    - **IF fiber intensity**: IF fiber intensity tells researchers how much of the protein is present and if it is where it is supposed to be. Like the western blot test, the result is shown as a percentage (fraction) of how much dystrophin researchers would expect to see in a muscle tissue sample from someone who does not have Duchenne.

- **IF percent dystrophin-positive fibers (PDPF)**: IF PDPF tells researchers how the protein is distributed throughout the muscle cells. The results are shown as a percentage, which represents the proportion of muscle fibers that test positive for delandistrogene moxeparvovec dystrophin.

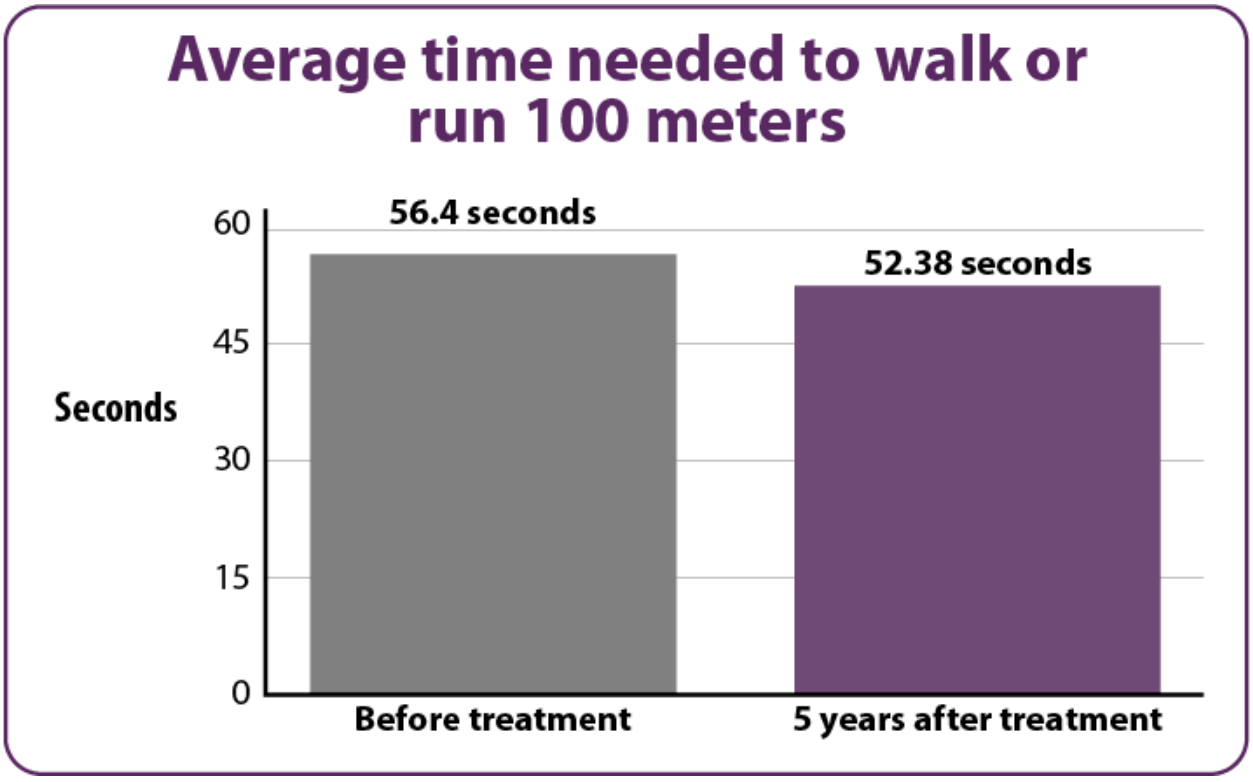
All 3 measurements showed that, on average, levels of delandistrogene moxeparvovec dystrophin increased after treatment with delandistrogene moxeparvovec.



How did participants' physical function change after treatment with delandistrogene moxeparvovec?

To answer this question, researchers looked at how long it took participants to walk or run 100 meters (about 330 feet). This timed test can serve as a sensitive measure of disease progression. A reduction in the time (fewer seconds) needed to walk or run 100 meters indicates an improvement in the skill.

On average, the time needed to walk or run 100 meters dropped from 56.4 seconds before treatment to 52.38 seconds 5 years after treatment, **a drop (improvement) of 4.02 seconds**.



What has happened since the study ended?

The study took about 5 years and 5 months to finish. It started in December 2017 and ended in April 2023.

When the study ended, Sarepta reviewed the data and created a report of the results. This is a summary of that report.

How has this study helped?

The results of this study helped doctors, researchers, and health authorities learn more about delandistrogene moxeparvovec as a possible treatment for Duchenne. The results also helped inform the designs of future studies. Clinical studies like this are important to help researchers understand which treatments work and how well they work.

At this time, additional clinical studies with delandistrogene moxeparvovec are ongoing, including long-term follow-up studies.

Where can I learn more about this study?

You can find more information about this study on the websites listed below.

http://www.clinicaltrials.gov → On this website, type **NCT03375164** into one of the search boxes and click "Search".

http://www.clinicaltrialsregister.eu → On this website, click "Home and Search". Then type **2021-000077-83** in the search box and click "Search".

Full study title: Systemic Gene Delivery Phase I/IIa Clinical Trial for Duchenne Muscular Dystrophy Using rAAVrh74.MHCK7.micro-dystrophin (microDys-IV-001)

Protocol number: SRP-9001-101

Sponsor: Sarepta Therapeutics, Inc.
Email: advocacy@sarepta.com
Phone: 1-888-SAREPTA (1-888-727-3782), For clinical study information, select option 4

Thank you!

Sarepta is grateful for the participants who helped make this study happen. Clinical study participants help researchers and health authorities find answers to important health questions and discover new treatments for disease.