NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of OAV101 in babies with spinal muscular atrophy

Thank you!

Thank you to the parents and babies who took part in the clinical trial for **spinal muscular atrophy (SMA)**. All of the parents and babies helped the researchers learn more about the trial drug **OAV101**, also called AVXS-101 or onasemnogene abeparvovec.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public. We hope this helps the parents and babies understand their important role in medical research.

Trial information

Trial number: COAV101A1IC01

Drug studied: OAV101, also called onasemnogene abeparvovec

Sponsor: Novartis

If your child was a participant and you have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings.

What was the main purpose of this trial?

The purpose of this trial was to learn more about the effects of OAV101 given to babies up to 2 years old with **spinal muscular atrophy (SMA)**.

SMA is a group of conditions that cause the body to lose motor neurons. **Motor neurons** are the nerve cells in the spinal cord that control muscle movement in the arms, legs, chest, face, throat, and tongue. In SMA, the motor neurons die and can't tell the muscles how to work. The muscles become weak and cause problems with:

- Moving parts of the body
- Breathing
- Swallowing

SMA is caused by a missing or nonworking **survival motor neuron 1 (*SMN1*) gene**. *SMN1* is needed for motor neurons to live. When the *SMN1* gene isn't working, motor neurons die and can't control muscles. Without treatment, many babies with SMA are never able to walk and have problems with breathing and swallowing.

OAV101, also called onasemnogene abeparvovec or AVXS-101, is a gene therapy designed to treat SMA by giving a working *SMN1* gene.

When this trial started, OAV101 was approved to treat babies with certain types of SMA in Argentina, Brazil, and other countries.

Trial drug
OAV101, also called onasemnogene abeparvovec

Pronounced as
ON-a-SEM-noe-jeen A-be-PAR-voe-vek

The trial purpose was to answer these main questions:

- What adverse events of special interest did babies have after receiving OAV101?
  - ↳ An **adverse event of special interest** is a medical problem that the researchers expect to happen based on other trials.
- What adverse events did the babies have?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in November 2021 and ended in August 2023. It was planned for the babies to be in the trial for about 18 months after receiving the trial treatment.

Who was in this trial?

16 babies with SMA received treatment in this trial. Their ages ranged from 3 to 23 months when they joined the trial. Their average age when they received trial treatment with OAV101 was 16 months. The number of babies by gender is shown below.

Gender

11 Girls	5 Boys

The babies could take part in this trial if they had SMA and:

- Weighed up to 17 kilograms (about 37 pounds)
- Had not previously received gene therapy for SMA

10 babies had SMA type 1, and 6 babies had SMA type 2.

16 babies from 2 countries received treatment. The babies took part in:

- Argentina | 6 babies
- Brazil | 10 babies

What treatments did the babies receive?

The treatment in this trial was:

OAV101, also known as onasemnogene abeparvovec, which was given once through a vein as a one-hour intravenous (IV) infusion.

In this trial, the parents and clinical trial team knew what treatment each baby received. All babies received OAV101.

What happened during this trial?

Before treatment **20 days**

After the babies' parents gave their written consent, trial doctors checked the babies' health and SMA to make sure they could be in this clinical trial.

During treatment **1 dose**

The babies received OAV101 as one IV infusion, which lasted about 1 hour.

After receiving the IV infusion, they stayed with their family at the hospital site for 12 to 48 hours so the researchers could closely check their health.

After treatment **About 18 months**

The babies had follow-up visits after receiving their dose of treatment. The researchers checked the babies' health and ability to do certain movements.

What were the main results of this trial?

What adverse events of special interest did babies have after receiving OAV101?

The researchers found that 12 of 16 babies (75%) had adverse events of special interest within 18 months of receiving OAV101. The most common adverse event of special interest was possible signs of liver damage based on blood test results.

To learn this, researchers kept track of how many babies had **adverse events of special interest** within 18 months after receiving OAV101.

What were adverse events of special interest in this trial?

The types of adverse events of special interest in this trial included:

- **Thrombotic microangiopathy (TMA)**, which is damage caused by blood clots in the smallest blood vessels of many organs, often in the kidneys and brain. This can damage the organs and cause serious medical problems, such as kidney failure and stroke.
- **Liver damage or failure** based on blood test results
- **Low blood levels of platelets** (cells that help blood to clot)

The types of adverse events of special interest that babies had after receiving OAV101

The table below shows the types of adverse events of special interest that happened during this trial.

	Babies who had adverse events of special interest 16 babies
Possible signs of liver damage in the blood Hepatotoxicity	**11 of 16** 69%
Low platelet levels in the blood Thrombocytopenia	**5 of 16** 31%
Blood clots in small blood vessels of organs Thrombotic microangiopathy (TMA)	**2 of 16** 13%

What adverse events did the babies have?

Trial doctors keep track of all **adverse events** that happen in trials, even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the day of treatment until 18 months after treatment.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

All 16 babies had adverse events. 11 babies had adverse events that were considered serious, and 2 babies died.

How many babies had adverse events?

Babies who:	All babies 16 babies
Had at least 1 **serious adverse event**	11 of 16
Had at least 1 **other adverse event**	16 of 16
Left the trial due to an adverse event	0 of 16
Died during the trial	2 of 16

What serious adverse events did the babies have?

11 babies had serious adverse events, and 2 babies died. The causes of death were reported as:

- **Blood clots in small blood vessels of organs** (thrombotic microangiography, or TMA)
- **Infection in the sinuses, throat, airways, or lungs** (respiratory tract infection)

The table below shows the most common serious adverse events that happened in **2 or more** babies.

	All babies 16 babies
A type of lung infection Bronchiolitis	**3 of 16** 27%
Infection in the sinuses, throat, airways, or lungs Respiratory tract infection	**3 of 16** 27%
COVID-19	**2 of 16** 18%
Blood clots in small blood vessels of organs Thrombotic microangiopathy (TMA)	**2 of 16** 18%

What other adverse events did the babies have?

All 16 babies had other adverse events.

The table below shows the other adverse events that happened in **5 or more** babies.

	All babies 16 babies
Fever Pyrexia	**7 of 16** 44%
Throwing up Vomiting	**7 of 16** 44%
Possible sign of liver damage or other health conditions Alanine aminotransferase increased	**5 of 16** 31%
Possible sign of liver damage or other health conditions Aspartate aminotransferase increased	**5 of 16** 31%
Possible sign of liver damage or other health conditions Gamma-glutamyltransferase increased	**5 of 16** 31%

Could more babies do certain movements up to 18 months after treatment?

More babies could do certain movements up 18 months after receiving OAV101 compared to before treatment.

To learn this, researchers counted how many babies could do certain movements before treatment and up to 18 months after treatment. The table below shows how many babies could do certain movements 6 and 18 months after treatment compared to before treatment.

Movements	Before treatment Babies who could do a movement	6 months after treatment Babies who could do a movement	18 months after treatment Babies who could do a movement
Sit up without support	6 of 16 38%	12 of 14 86%	10 of 12 83%
Crawl	2 of 16 13%	2 of 14 14%	3 of 12 25%
Stand up with help	1 of 16 6%	2 of 14 14%	7 of 12 58%
Walk with help	0 of 16 0%	2 of 14 14%	2 of 12 17%
Stand up alone	0 of 16 0%	1 of 14 7%	3 of 12 25%
Walk alone	0 of 16 0%	0 of 14 0%	1 of 12 8%

What was learned from this trial?

This trial helped researchers learn more about the effects of OAV101 given to babies up to 2 years old with SMA.

During this trial, babies had these adverse events of special interest that could be related to OAV101:

- Possible signs of liver damage in the blood
- Low platelet levels in the blood
- Blood clots in small blood vessels of organs (thrombotic microangiopathy, or TMA)

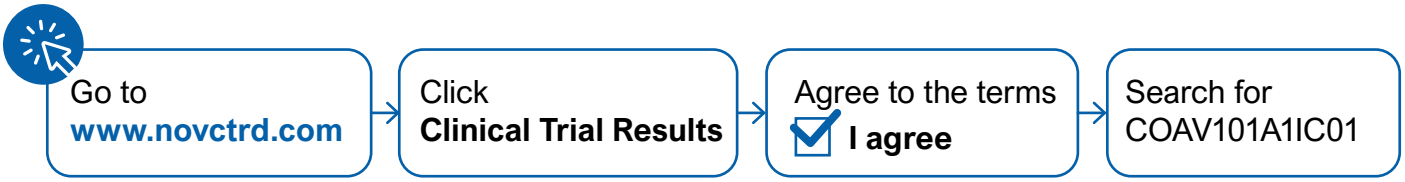
The researchers also learned that more babies could do certain movements, like sitting or standing up, 18 months after receiving OAV101 compared to before treatment.

When this summary was written, there were other ongoing trials to learn about the long-term safety of OAV101 in children with SMA.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website **www.novctrd.com**

Follow these steps to find the scientific summary:



For more information about this trial, go to this website:

- clinicaltrials.gov – search using the number **NCT05073133**

If more trials are planned, they will appear on the public websites above. When there, search for **OAV101, onasemnogene abeparvovec, AVXS-101, spinal muscular atrophy,** or **SMA.**

Full clinical trial title: A Phase IV Open-label, single-arm, single-dose, multicenter study to evaluate the saFEty, toLerability and effIcacy of gene replacement therapy with intravenous OAV101(AVXS101) in pediatric patients from Latin America with spinal muscular atrophy (SMA) – OFELIA

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