NOVARTIS

Clinical Trial Results Summary

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

Thank you!

Thank you to the participants who took part in the clinical trial for spinal muscular atrophy (SMA). Every participant helped the researchers learn more about the trial drug **OAV101**, also called 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 participants understand their important role in medical research.

Trial information

Trial number: COAV101A12306

Drug studied: OAV101, also known as 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 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 in children with **spinal muscular atrophy (SMA)**, who weighed between 19 and 46 pounds.

SMA is a group of conditions that cause the body to lose motor neurons. 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

Motor neurons are nerve cells in the spinal cord that control muscle movement in the arms, legs, chest, face, throat, and tongue.

SMA is caused by a missing or non working ***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 are unable to control muscle movement.

Copies of a similar gene called *SMN2* can help make up for a non working SMN1 gene. People can have up to 5 copies of the *SMN2* gene. Those who have more copies of the *SMN2* gene often have milder symptoms that start later in life.

OAV101, also called **onasemnogene abeparvovec**, (pronounced on-a-SEM-noe jeen a-be-PAR-voe-vek) is a **gene therapy** designed to treat children with SMA by correcting the missing or non-working *SMN1* gene.

When this trial started, OAV101 was approved in the United States and other countries to treat children with SMA type 1.

Gene therapy is a treatment that corrects or replaces a missing or non working gene to treat disease.

The main question the researchers wanted to answer in this trial was:

- How many children had adverse events and serious adverse events during this trial?
  - An **adverse event** is any sign or symptom that participants have during a trial. An adverse event is considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death.

How long was this trial?

The trial began in September 2021 and ended in June 2023. It was planned for the children to be in the trial for about 13 months.

Who was in this trial?

24 children with SMA received treatment in this trial. Children's ages ranged from 1.5 to 9 years. The average age was 5 years.

The number of children by gender and race are shown below.

Gender

- 12 **Men**
- 12 **Women**

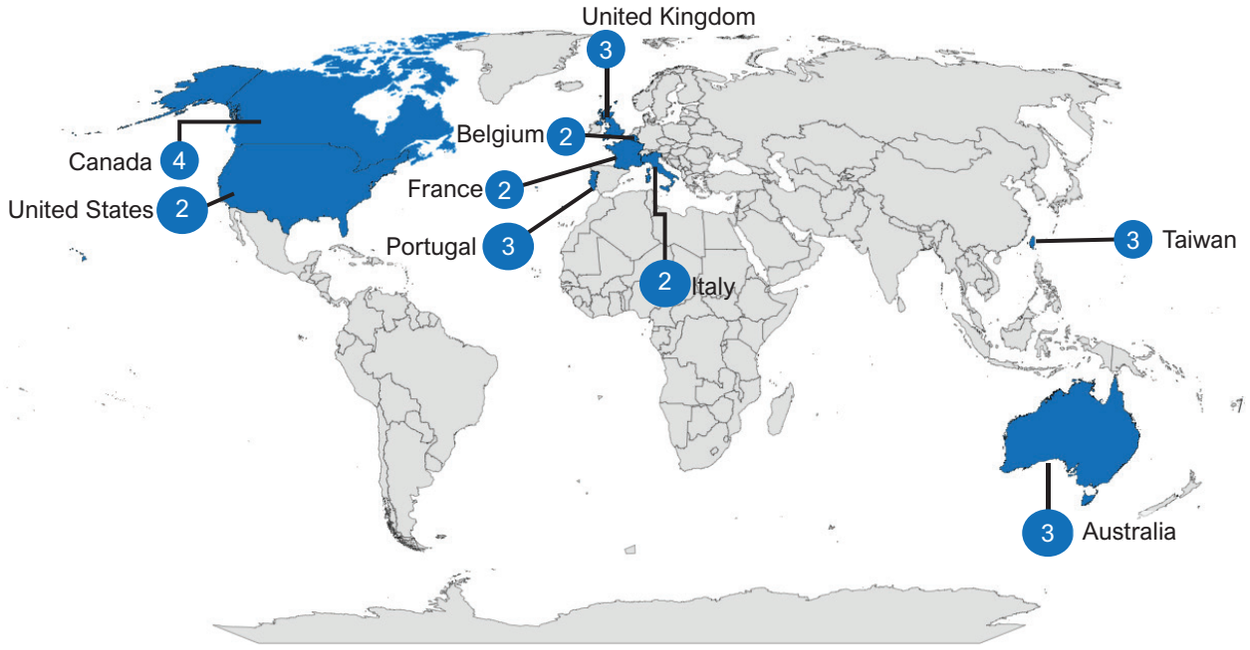
Race

- 13 **White**
- 9 **Asian**
- 2 **Not reported**

The children could take part in this trial if they:

- had SMA with a mutation in the *SMN1* gene
- weighed between 19 and 46 pounds (8.5 and 21 kg) at the start of the trial
- had not received any treatment or stopped taking treatment for SMA

24 children from 9 countries received treatment during this trial. The map below shows the number of children who took part in each country.



What treatments did the children receive?

The treatment given in this trial was:

OAV101, also known as **onasemnogene abeparvovec**, given once as an infusion directly into a vein which lasted for an hour.

This was an open-label trial, which means that the parents, trial doctors, and trial staff knew what treatment the children received.

What happened during this trial?

Before treatment **45 days**

Trial doctors checked the children's health and measured their weight to ensure they could take part in this clinical trial.

During treatment **3 days**

Children received a single dose of OAV101 as an infusion directly into a vein which lasted about an hour.

After receiving the infusion, children and their families stayed at the hospital for 2 days so trial doctors could closely check children's health.

After treatment **12 months**

The children visited the hospital regularly for 12 months after their treatment. During the visits, the study doctors performed health check-ups on the children.

After this trial, the parents were given an option to enroll their child in a separate, long-term follow-up trial COAV101A12308.

What were the main results of this trial?

How many children had adverse events and serious adverse events during this trial?

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 up to 12 months after receiving **OAV101**.

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 the children (24 of 24) had adverse events. 15 children had adverse events that were considered serious. None of the children left the trial due to an adverse event. The researchers concluded there were no new safety concerns for OAV101 for this trial. The safety results for the children were similar to the safety results from previous trials with OAV101.

The table below shows the overall adverse events and serious adverse events that happened in children during this trial.

	OAV101		
Children with bodyweight of:	**19 to 29 pounds (8.5 to 13 kg) (7 children)**	**More than 29 to 37 pounds (13 to 17 kg) (8 children)**	**More than 37 to 46 pounds (17 to 21 kg) (9 children)**
Had at least 1 serious adverse event	**3 of 7** 43%	**7 of 8** 88%	**5 of 9** 56%
Had at least 1 other adverse event	**7 of 7** 100%	**8 of 8** 100%	**9 of 9** 100%
Died during this trial	**0**	**0**	**0**

What serious adverse events did the children have?

Most of the serious adverse events that were reported during the trial happened in 1 child except for **decreased levels of platelets in the blood** (thrombocytopenia), and vomiting reported in 3 out of 24 (13%) children each, and **COVID-19 infection, stomach infection** (gastroenteritis viral), **and lung infection** (pneumonia) reported in 2 out of 24 (8%) children each.

What other adverse events did the children have?

The table below shows the other adverse events that happened in **40% or more** children.

	OAV101		
Children with bodyweight of:	**19 to 29 pounds (8.5 to 13 kg) (7 children)**	**More than 29 to 37 pounds (13 to 17 kg) (8 children)**	**More than 37 to 46 pounds (17 to 21 kg) (9 children)**
Common cold (Upper respiratory tract infection)	**4 of 7** 57%	**2 of 8** 25%	**2 of 9** 22%
Cough	**3 of 7** 43%	**0**	**0**
COVID-19 infection	**1 of 7** 14%	**4 of 8** 50%	**2 of 9** 22%
Feeling sick (Nausea)	**3 of 7** 43%	**2 of 8** 25%	**3 of 9** 33%
Fever (Pyrexia)	**4 of 7** 57%	**1 of 8** 13%	**5 of 9** 56%
Increase in the liver test value called transaminases* (Hypertransaminasaemia)	**1 of 7** 14%	**1 of 8** 13%	**5 of 9** 56%
Vomiting	**5 of 7** 71%	**5 of 8** 63%	**7 of 9** 78%
Increase in the liver test value of alanine aminotransferase and aspartate aminotransferase enzyme (Transaminases increased)	**3 of 7** 43%	**2 of 8** 25%	**1 of 9** 11%
Lower number of platelets in the blood (platelet count decreased)	**3 of 7** 43%	**2 of 8** 25%	**2 of 9** 22%

**transaminases are liver enzymes that are used to check liver health.*

What adverse events of special interest (AESI) did children have after receiving OAV101?

To learn this, researchers kept track of how many children had AESI up to 12 months after receiving OAV101. An AESI is a medical problem that the researchers expect to happen based on other trials.

The table below shows all the AESI that happened in children during the trial.

	OAV101		
Children with bodyweight of:	**19 to 29 pounds (8.5 to 13 kg) (7 children)**	**More than 29 to 37 pounds (13 to 17 kg) (8 children)**	**More than 37 to 46 pounds (17 to 21 kg) (9 children)**
Damage to the liver (hepatotoxicity)	**6 of 7** 86% 	**5 of 8** 63% 	**9 of 9** 100% 
Decreased levels of platelets in the blood (transient thrombocytopenia)	**4 of 7** 57% 	**6 of 8** 75% 	**7 of 9** 78% 
Heart-related medical problems (cardiac adverse events)	**0**	**2 of 8** 25% 	**1 of 9** 11%
A condition which causes clots in the small blood vessels in the body (thrombotic microangiopathy)	**0**	**0**	**0**
Damage to the dorsal root ganglia* (dorsal root ganglia cell inflammation)	**0**	**0**	**0**

**dorsal root ganglia are clusters of nerve cell bodies located along the spinal cord.*

What was the other result of this trial?

How many children were able to sit, stand, and walk after treatment?

To answer this question, researchers used different scales to measure the ability of children with SMA to sit, stand, and walk after treatment.

Researchers compared the ability of all the 24 children to sit, stand, and walk, before treatment and up to 12 months after treatment.

Most of the children kept their ability to sit, stand, and walk. A few children showed improvement in their ability to sit, stand, and walk compared to the start of the trial.

What was learned from this trial?

Researchers learned about the safety and effects of **OAV101** in children with SMA, who weighed between 19 and 46 pounds (8.5 and 21 kg).

Researchers found that:

- there were no new safety concerns with the use of **OAV101**. The safety results for the children were similar to the safety results from previous trials with **OAV101**.
- all 24 (100%) children had adverse events and 15 (63%) children had adverse events that were considered serious.
- 20 (83%) children had **damage to the liver cells** (hepatotoxicity), 17 (71%) children had **decreased levels of platelets in the blood** (transient thrombocytopenia), and 3 (13%) children had **heart-related medical problems** (cardiac adverse events).
- most of the children kept their ability to sit, stand, and walk. A few children showed improvement in their ability to sit, stand, and walk compared to the start of the trial.

When this summary was written, the sponsor planned to conduct more trials with **OAV101** in children with SMA. Other trials with **OAV101** are ongoing.

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 any of the following websites:

- **clinicaltrials.gov** - search using the number **NCT04851873**
- **clinicaltrialsregister.eu/ctr-search/search** - search using the number **2020-005995-37**
- **www.novartis.com/clinicaltrials**

If more trials are planned, they will appear on the public websites above. When there, search for OAV101, onasemnogene abeparvovec.

Full clinical trial title: A Phase IIIb, open-label, single-arm, single-dose, multicenter study to evaluate the safety, tolerability and efficacy of gene replacement therapy with intravenous OAV101 (AVXS-101) in pediatric patients with spinal muscular atrophy (SMA)

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