NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the safety of OAV101 in children with spinal muscular atrophy who stopped other treatments

Thank you!

Thank you to the children and families who took part in the clinical trial for **spinal muscular atrophy (SMA)**. All the children 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: COAV101B12302

Novartis drug studied: OAV101, also called onasemnogene abeparvovec

Sponsor: Novartis

If you were a participant and 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 results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the safety of **OAV101** for children with spinal muscular atrophy who stopped taking certain standard treatments. The trial also learned about the effects of **OAV101** for children with spinal muscular atrophy.

Spinal muscular atrophy (SMA) is a group of conditions that cause the body to lose motor neurons. Motor neurons are the nerve cells that control muscle movement in the body, including the arms, legs, chest, face, throat, and tongue. In SMA, motor neurons die and can't tell the muscles 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. The children in this trial had 2 copies of the SMN1 gene that did not work.

What is a gene?

A **gene** is a section of DNA that stores the instructions for a cell. **DNA** is like a special code inside cells that tells cells what to do and how to grow. Each gene has a job, like telling a muscle how to move or hair how to grow.

OAV101, also called onasemnogene abeparvovec, is a gene therapy designed to treat SMA by correcting the missing or nonworking SMN1 gene. **Gene therapy** is a treatment that works by replacing or adding a gene inside a person's cells to treat a disease or condition.

Trial drug

OAV101 also called onasemnogene abeparvovec

Pronounced as

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

The trial's purpose was to answer this main question:

- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in January 2023 and ended in November 2024. Each child was in the trial for about 1 year.

Who was in this trial?

27 children with SMA received treatment in this trial – 15 boys and 12 girls. Children's ages ranged from 2 to 17 years. Their average age was 7 years.

The number of children by race is shown below.

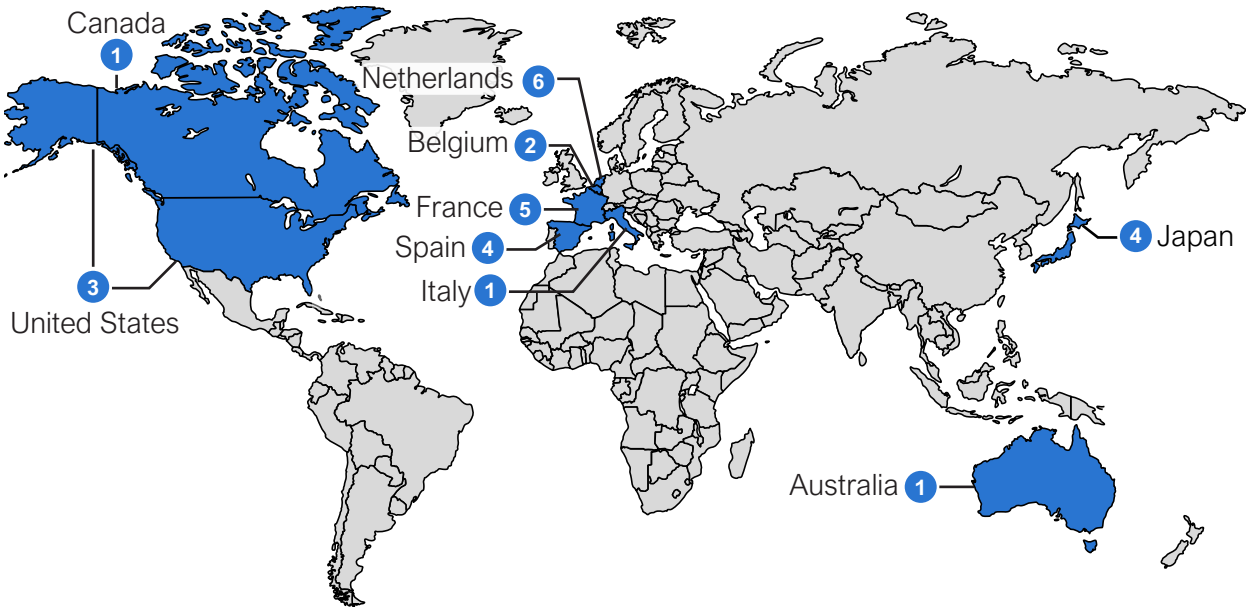
Race

- 13 White
- 7 Unknown or Not reported
- 6 Asian
- 1 More than one race

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

- Had taken one of these standard treatments:
  - Nusinersen for at least 2 months, and stopped taking it at least 4 months before receiving trial treatment
  - Risdiplam for at least 3 months, and stopped taking it at least 15 days before receiving trial treatment
- Could sit by themselves but had never walked by themselves
- Had certain blood test results

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



What treatment did the children receive?

The treatment in this trial was:

OAV101, which was given one time as an intrathecal (IT) injection. An **IT injection** is given through the lower back and into the fluid around the spinal cord.

The children and their families, researchers, and trial staff knew that each child received **OAV101**.

What happened during this trial?

Before treatment — **Up to 6 weeks**

The trial staff checked to make sure the children could be in this trial. For example, trial staff checked that the children had SMA and that they had stopped taking certain standard treatments within the required timeframe.

During treatment — **At least 2 days**

27 children received **OAV101** as one IT injection.

After receiving the injection, they stayed at the hospital for at least 2 days so the researchers could closely check their health. Their families could stay with them.

After treatment — **1 year**

Trial staff checked children for any medical problems for up to **1 year** after they received trial treatment.

At the end of this trial, children were invited to join another trial called **COAV101A12308** to learn about the long-term safety and effects of **OAV101**.

Trial staff checked the children's general health throughout the trial.

What were the main results of this trial?

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events 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 injection of trial treatment until 1 year after receiving trial 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 27 children had at least 1 adverse event, including serious and other adverse events.

- 4 children had adverse events that were considered serious
- 13 children had **adverse events of special interest**, which are adverse events that researchers expect could happen based on other trials
- 13 children had adverse events that researchers thought could be related to the trial treatment, including throwing up, headache, and fever
- No children left the trial due to an adverse event
- No children died

The researchers concluded there were no new safety concerns for **OAV101** in this trial.

How many children had adverse events?

	OAV101 27 children
Had **any adverse event**	**27 of 27** 100%
Had at least 1 **serious adverse event**	**4 of 27** 15%
Had an **adverse event** **of special interest**	**13 of 27** 48%
Had an **adverse event** **related to trial treatment**	**13 of 27** 48%

What serious adverse events did the children have?

4 children had serious adverse events. No children died.

The table below shows the most common type of serious adverse events during this trial, which were viral or bacterial infections.

	OAV101 27 children
Infection in the airways of the lungs from a virus Bronchitis viral	**1 of 27** 4%
COVID-19	**1 of 27** 4%
Stomach flu Gastroenteritis	**1 of 27** 4%
Lung infection Pneumonia	**1 of 27** 4%
Lung infection from breathing food or liquid into lungs Pneumonia aspiration	**1 of 27** 4%

What other (not including serious) adverse events did the children have?

The table below shows the most common other adverse events that happened during this trial.

	OAV101 27 children
Common cold Nasopharyngitis	**15 of 27** 56%
Fever Pyrexia	**13 of 27** 48%
Throwing up Vomiting	**13 of 27** 48%
Headache	**8 of 27** 30%
Upper belly pain Abdominal pain upper	**6 of 27** 22%

What were the adverse events of special interest?

13 children had **adverse events of special interest**, which are adverse events that researchers expect could happen based on other trials. In this trial, examples included liver problems and low number of blood cells that help blood to clot (platelets).

The table below shows the adverse events of special interest that researchers looked for during this trial.

	OAV101 27 children
Possible signs of liver damage based on blood tests Hepatotoxicity	**4 of 27** 15%
Lower number of cells that help blood to clot Transient thrombocytopenia	**8 of 27** 30%
Signs and symptoms of possible damage to nerve cells that branch out from the spine Signs of dorsal root ganglia toxicity	**2 of 27** 7%
Blood clots in small blood vessels of organs Thrombotic microangiopathy	**0 of 27** 0%
Heart problems Cardiac adverse events	**0 of 27** 0%
New cancers New malignancies	**0 of 27** 0%

What were the other results of this trial?

Did children's ability to move stay the same 1 year after receiving OAV101?

Although SMA causes the body to lose muscle movement over time, children's ability to move stayed about the same from before treatment to 1 year after receiving **OAV101**. This means that children's ability to move did not get worse after treatment.

To learn this, the researchers checked children's ability to:

- Sit, push themselves up, move their body, and stand for short periods of time without help
- Move their hands and arms to do certain tasks, such as pick up a cup or open a lid

Did quality of life for the children's caregivers change 1 year after receiving OAV101?

There may not have been a meaningful change in quality of life for the children's caregivers from before treatment to 1 year after receiving **OAV101**.

To learn this, each child's caregiver answered questions about their:

- Child's need for physical help from them, such as to eat, get dressed, and move
- Emotional well-being as caregivers
- Time spent giving care to their child
- Costs of living

What was learned from this trial?

Researchers learned about the safety and effects of **OAV101** for children with spinal muscular atrophy (SMA) who stopped taking certain standard treatments.

The researchers concluded that:

- There were no new safety concerns for **OAV101** in this trial
- Children's ability to move stayed about the same from before treatment to 1 year after receiving **OAV101**
- There may not have been a meaningful change in quality of life for the children's caregivers from before treatment to 1 year after receiving **OAV101**

When this summary was written, a long-term follow-up trial COAV101A12308 was ongoing for children and adults with SMA who completed this and other trials of **OAV101**.

The follow-up trial accepts participants up to 100 years old.
https://clinicaltrials.gov/study/NCT05335876

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:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Accept the terms **I accept** → Search by study number **COAV101B12302**

For more information about this trial, go to any of these websites:

- **clinicaltrials.gov** – search using the number **NCT05386680**
- **clinicaltrialsregister.eu** – search using the number **2021-006709-31**

Other trials of **OAV101** may appear on the public websites above. When there, search for **OAV101** or onasemnogene abeparvovec.

Full clinical trial title: Phase IIIb, open-label, single-arm, multi-center study to evaluate the safety, tolerability and efficacy of OAV101 administered intrathecally (1.2 x 10^14 vector genomes) to participants 2 to < 18 years of age with spinal muscular atrophy (SMA) who have discontinued treatment with nusinersen (Spinraza®) or risdiplam (Evrysdi®)

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

1-888-669-6682 (US) | +41-61-324 1111 (EU)

www.novartis.com/clinicaltrials