NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of INC424 when taken with steroids in children and adolescents with chronic graft vs. host disease after stem cell transplantation

Thank you!

Thank you to the participants who took part in the clinical trial for **chronic graft vs. host disease**. Every participant helped the researchers learn more about **INC424**, also called **ruxolitinib**.

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: CINC424G12201

Drug studied: **INC424,** also known as **ruxolitinib**

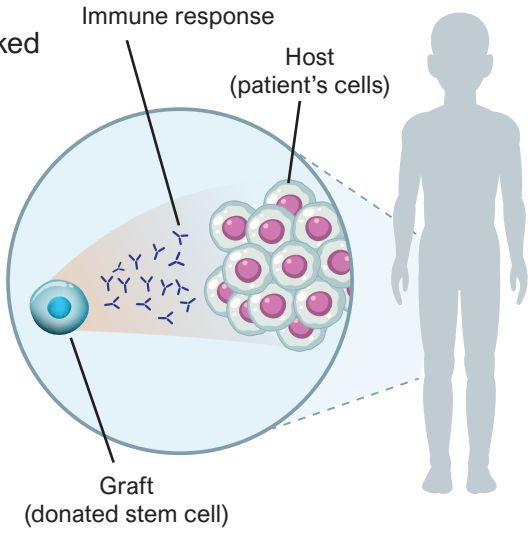
Sponsor: Novartis

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 findings.

What was the main purpose of this trial?

The purpose of this trial was to learn how well **INC424** worked when given along with steroids. It focused on children and adolescents with **chronic graft vs. host disease (cGvHD)** following stem cell transplant.



Graft vs. host disease (GvHD) is a serious condition that can happen after a stem cell transplant. A stem cell transplant is a medical procedure where unhealthy or damaged cells are replaced with healthy stem cells. These healthy cells are collected from a donor. In the case of **GvHD**, donated stem cells (the graft) may consider the patient's body (the host) as foreign and attack it, causing an immune response. This can cause cause inflammation, tissue damage, organ failure, or even death.

There are 2 types of **GvHD**:

- **Acute GvHD (aGvHD)** – In this type, the symptoms usually start within 100 days of the transplant, mainly affecting the skin, liver, and digestive system.
- **Chronic GvHD (cGvHD)** – This type develops over time, usually more than 100 days after the transplant. It is long-lasting and can affect various parts of the body, including the eyes, skin, liver, lungs, muscles, and joints.

Currently, steroids are the approved standard treatment for **cGvHD**. They work by reducing inflammation and lowering the immune response. However, they may stop working for some people over time. When steroids do not improve symptoms or organ function, the condition is called **steroid-refractory cGvHD (SR-cGvHD)**.

The trial drug, **INC424**, also known as **ruxolitinib**, blocks a set of proteins called Janus Kinase (JAK) which is involved in immune reactions and inflammation. **INC424** is approved in the EU and the US for the treatment of aGvHD and cGvHD in adults and children aged 12 years and above.

In this trial, researchers wanted to find out how well **INC424** worked to treat **cGVHD** in children and adolescents, including those under the age of 12.

The main questions that researchers wanted to answer were:

- How many participants had an improvement in their cGvHD symptoms without the need for any additional therapy after 24 weeks of INC424 treatment?
- 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 May 2020 and ended in August 2024. The participants could continue trial treatment as long as they were benefitting from it.

When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

46 participants with **cGvHD** received treatment in this trial. However, **45 participants** were included in the analyses, as 1 participant did not meet all of the trial requirements Participants' ages ranged from 2 to 17 years. Their average age was 11 years.

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

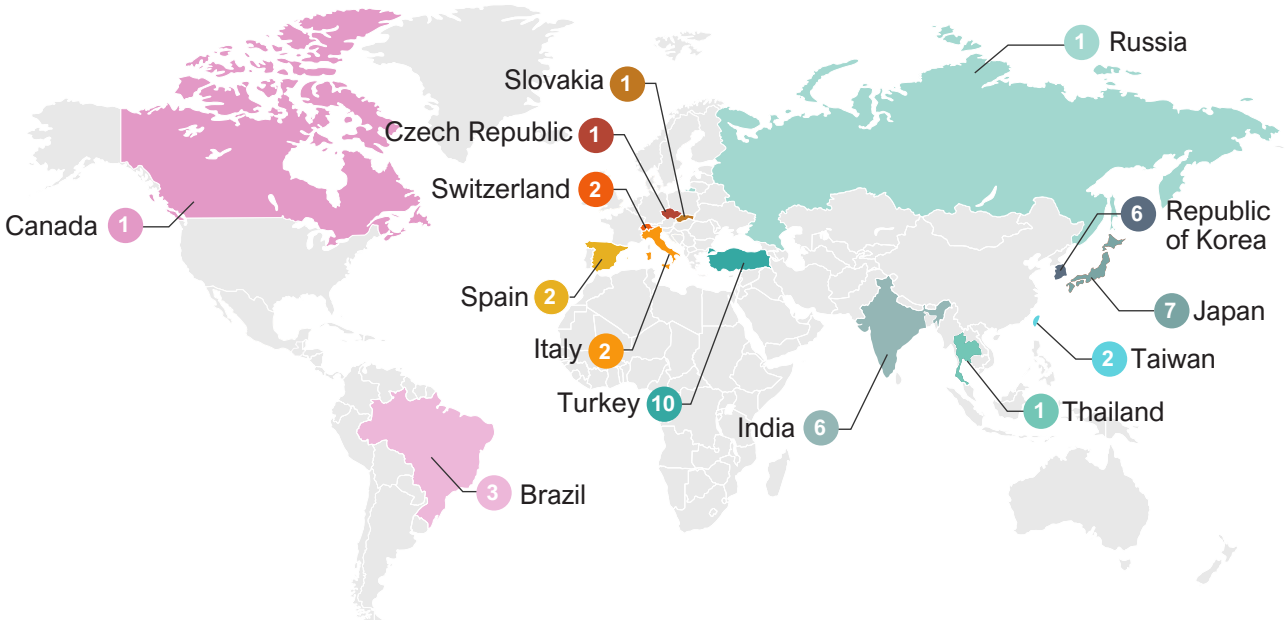
Gender

- 29 Boys
- 16 Girls

Race

- 23 Asian
- 21 White or Caucasian
- 1 Black or African American

45 participants from **14 countries** received treatment. The map below shows the number of participants who took part in each country.



Participants **could take part** in this trial if they:

- Were under 18 years old and over 28 days old
- Had a stem cell transplant from a donor
- Had moderate to severe **cGvHD**
- Did not receive any prior treatments for **cGvHD** or were resistant to steroid treatments

What treatments did the participants receive?

Researchers studied the following treatments.

INC424: 4 milligrams per square meter (mg/m^2), as an oral solution for younger children, or **5 or 10 milligrams (mg)**, as tablets or an oral solution for older children, both taken twice a day.

The 4 mg/m^2 dose was calculated based on the weight and height of each child.

All participants either started or continued receiving steroids along with **INC424**. Participants were allowed to take medications to prevent infections and also receive blood transfusions, if they needed them.

The participants, researchers, and trial staff knew what treatment the participants were receiving. The participants received **INC424**.

What happened during this trial?

Before treatment

Up to 1 month

Trial doctors checked the participants' health to make sure they could be in this clinical trial.

During treatment

Up to 38 months

A total of 45 participants received treatment with **INC424** during this trial. They continued treatment for up to 3 years unless their condition got worse and they had to stop.

Participants were divided into 3 groups based on their ages:

Group 1 22 participants	**INC424**, 10 mg twice a day	12 to 17 years old
Group 2 16 participants	**INC424**, 5 mg twice a day	6 to 11 years old
Group 3 7 participants	**INC424**, 4 mg/m^2 twice a day	2 to 5 years old

INC424 was given along with regular doses of steroids.

After treatment

Up to 3 years

Participants were checked for their overall health and well-being for up to 1 month after their last dose of trial treatment.

Researchers continued monitoring the participants' overall health every 6 months for up to 3 years after the first dose.

Trial doctors checked participants for their overall health throughout the trial.

What were the main results of this trial?

How many participants had an improvement in their cGvHD symptoms without the need for any additional therapy after 24 weeks of INC424 treatment?

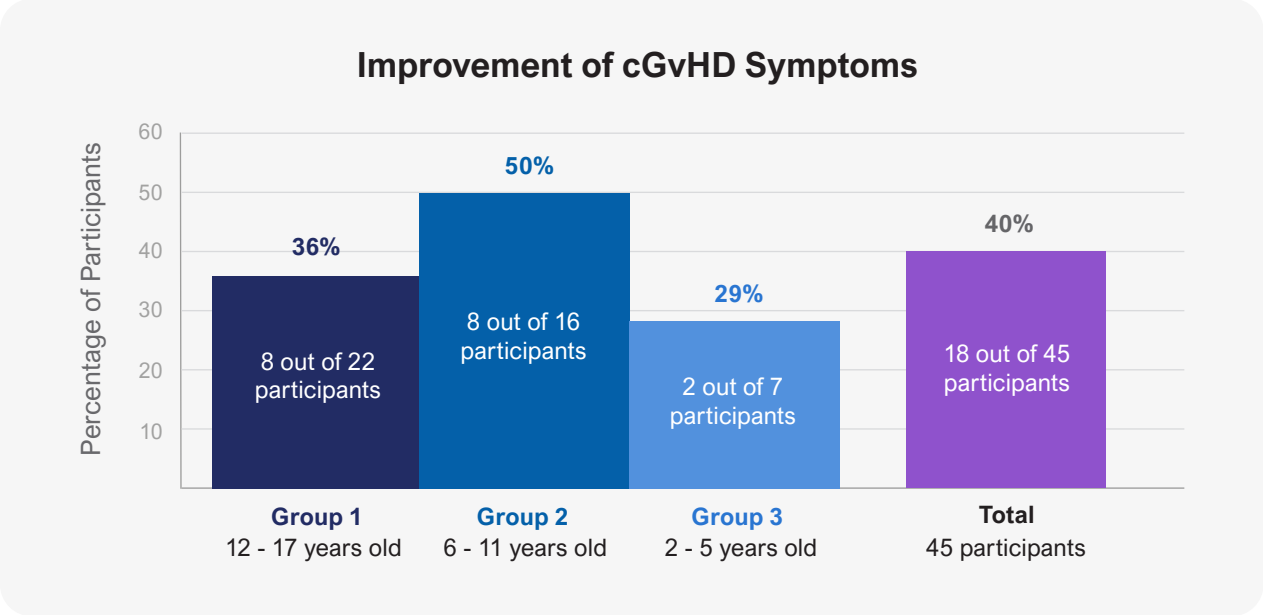
Researchers found that a total of **18 out of 45 participants (40%)** had an improvement in their **cGvHD** symptoms.

At the start of the study, researchers checked the children's health and noted what problems and symptoms existed in each part of the body. This included the mouth, stomach, intestines, lungs, eyes, joints, liver, and skin.

Throughout the study, doctors monitored these symptoms and noted if there was an improvement in specific organs or areas of the body. They reported if the children were responding to the treatment.

After 24 weeks of treatment, study doctors checked the participants for any improvement in their **cGvHD** symptoms to find out how well the treatment worked. Improvement could mean either some relief from symptoms or no symptoms at all.

The graph below shows the participants who had their **cGvHD** symptoms improve 24 weeks after starting treatment.



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 during the treatment period, and up to 30 days after the last 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.

A total of **44 out of 45** participants had adverse events.

- 26 participants had adverse events that were considered serious.
- None of the participants left the trial due to an adverse event.
- 3 participants died.

How many participants had adverse events?

The table below shows how many participants had adverse events during the treatment and the 30-day follow-up period.

Summary of adverse events

	Group 1 22 participants	**Group 2** 16 participants	**Group 3** 7 participants
Had at least **1 adverse event**, which includes **serious and non-serious**	**22 of 22 (100%)**	**15 of 16 (94%)**	**7 of 7 (100%)**
Had at least 1 **serious adverse event**	**15 of 22 (68%)**	**7 of 16 (44%)**	**4 of 7 (57%)**
Died	**0 of 22 (0%)**	**2 of 16 (13%)**	**1 of 7 (14%)**

What serious adverse events did the participants have?

The table below shows the top 6 most common serious adverse events that happened during the treatment and the 30-day follow-up period. All of these serious adverse events happened in 2 or more participants.

Serious adverse events

	Group 1 22 participants	Group 2 16 participants	Group 3 7 participants
Fever Pyrexia	2 of 22 (9%)	0 of 16 (0%)	1 of 7 (14%)
COVID-19	2 of 22 (9%)	0 of 16 (0%)	0 of 7 (0%)
Painful rash (shingles) Herpes zoster	2 of 22 (9%)	0 of 16 (0%)	0 of 7 (0%)
Low blood sodium levels Hyponatraemia	2 of 22 (9%)	0 of 16 (0%)	0 of 7 (0%)
Muscular weakness	2 of 22 (9%)	0 of 16 (0%)	0 of 7 (0%)
Lung infection Pneumonia	1 of 22 (5%)	1 of 16 (6%)	0 of 7 (0%)

What other, non-serious adverse events did the participants have?

The table below shows the top 5 most common other, non-serious adverse events that happened during the treatment and the 30-day follow-up period.

Other, non-serious adverse events

	Group 1 22 participants	Group 2 16 participants	Group 3 7 participants
Low red blood cells Anaemia	7 of 22 (32%)	2 of 16 (13%)	2 of 7 (29%)
Neutrophil count decreased (a type of white blood cell)	5 of 22 (23%)	2 of 16 (13%)	2 of 7 (29%)
Infection of the nose, sinuses, and the upper throat Upper respiratory tract infection	1 of 22 (5%)	4 of 16 (25%)	4 of 7 (57%)
COVID-19	4 of 22 (18%)	3 of 16 (19%)	2 of 7 (29%)
Low levels of neutrophils Neutropenia	2 of 22 (9%)	4 of 16 (25%)	2 of 7 (29%)

What was learned from this trial?

This trial helped researchers learn about the effects of **INC424** when given along with steroids in participants with **chronic GvHD**.

The researchers concluded that:

- Almost half of the children in this trial responded to treatment. 40% of the children had their symptoms improve after 24 weeks of treatment.
- There were no new or unexpected safety concerns with **INC424**.

The results from this and other **INC424** clinical trials are being used to obtain approvals in different parts of the world.

When this summary was written, the sponsor had no plans for future trials of **INC424** in people with **chronic GvHD**.

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** → Agree to the terms ☑ **I agree** → Search for **CINC424G12201**

For information about the other clinical trials used to obtain approval of **INC424**, search for: **CINC424F12201**, **CINC424C2301**, and **CINC424D2301**.

For more information about this trial go to any of the following websites:

- clinicaltrials.gov – search using the number **NCT03774082**
- clinicaltrialsregister.eu – search using the number **2018-003296-35**

Other studies with INC424 appear on the public websites above. When there, search for INC424 or ruxolitinib.

Full clinical trial title: A Phase II Open-label, Single-arm, Multi-center Study of Ruxolitinib Added to Corticosteroids in Pediatric Subjects With Moderate and Severe Chronic Graft vs. Host Disease After Allogeneic Stem Cell Transplantation

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