NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of MIJ821 in people with treatment-resistant depression

Thank you!

Thank you to the participants who took part in the clinical trial for **treatment-resistant depression**. Every participant helped the researchers learn more about the trial drug **MIJ821**.

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: CMIJ821B12201

Novartis drug studied: MIJ821

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 more about the effects of **MIJ821** in people with **treatment-resistant depression (TRD)**. To find this out, researchers compared the effects of different doses of **MIJ821** with a **placebo** when given along with other standard anti-depressant medicines.

Treatment-resistant depression (TRD) is depression that has not been well managed with at least two different prescribed anti-depressants. People with **TRD** often have severe symptoms, including suicidal thoughts, and face significant challenges in their daily lives.

MIJ821 is the trial drug that works by blocking a specific part of a receptor called N-methyl-D-aspartate, present on the nerve cells and is thought to play a role in depression. Researchers wanted to see if **MIJ821** could rapidly decrease the symptoms of **TRD** in comparison with the **placebo**.

A **placebo** looks like the trial drug but does not have any drug in it. Using a **placebo** helps researchers better understand the effect of a trial drug.

The trial's purpose was to answer these main questions:

- Did **MIJ821** reduce depression symptoms more than the **placebo** 24 hours after a single injection?
- 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.

The researchers measured the severity of the participants' depression symptoms using the **MADRS**, also called the **Montgomery Asberg Depression Rating Scale**. MADRS is a set of questions that a doctor asks a person to rate the severity of their depression symptoms. It includes 10 questions that look at different symptoms of depression including visible sadness, feelings of sadness, inner tension or stress, trouble sleeping, loss of appetite, difficulty concentrating, extreme tiredness, lack of emotions, pessimistic thoughts, and suicidal thoughts.

How long was this trial?

The trial began in March 2023 and ended in November 2023. Individual participants were in this trial for 28 days. The entire trial lasted for up to 8 months.

Who was in this trial?

60 participants with **treatment-resistant depression (TRD)** received treatment in this trial – 23 men and 37 women. Participants' ages ranged from 18 to 64 years. Their average age was 47 years.

The number of participants by race is shown below.

Race

57	White
3	Asian/Japanese

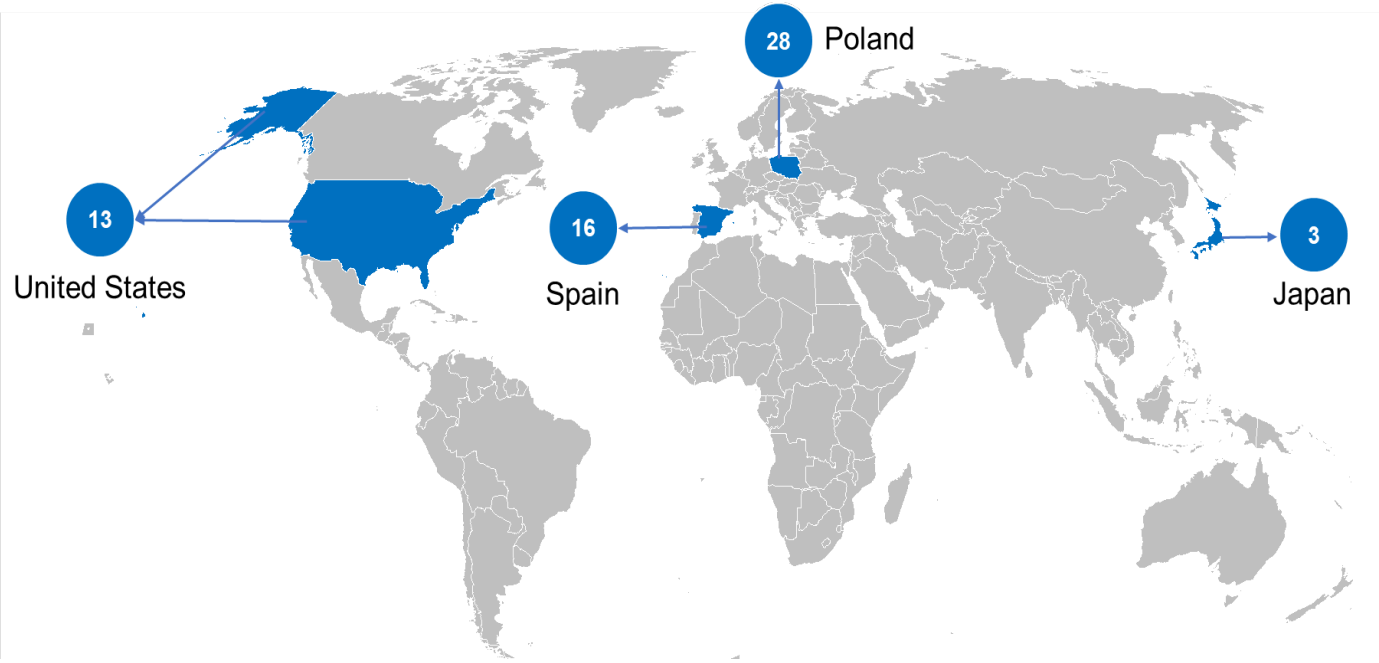
The participants could take part in this trial if they:

- were between 18 and 65 years of age
- were diagnosed with moderate to severe depression and were already on a stable dose of anti-depressants before the trial. Participants were required to continue their prescribed anti-depressant medications throughout the trial
- were diagnosed with **major depressive disorder** that failed at least 2 different prescribed anti-depressants, and had experienced a major depressive episode that lasted for at least 8 weeks
- had not started any new antidepressants within 6 weeks or begun **psychotherapy** within 4 weeks prior to joining the trial

Major depressive disorder is a condition that causes people to feel consistently sad or hopeless, making it difficult for them to manage daily activities.

Psychotherapy is a type of talk therapy where a person works with a trained therapist to address and manage mental health issues.

60 participants from 4 countries received treatment. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

Researchers used a computer to randomly assign participants to one of the following trial treatments:

MIJ821, which was received as a single injection under the skin.
The 3 different doses of **MIJ821** were:

- **high dose:** 10 milligrams (mg)
- **medium dose:** 4 mg
- **low dose:** 1 mg

Placebo, which was received as a single injection under the skin.

In addition to receiving **MIJ821** or **placebo**, all participants also received their regular anti-depressant medicines.

The participants, researchers, and trial staff did not know what treatment the participants were receiving. Some trials are done this way because knowing what treatment the participants receive can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

What happened during the trial?

Before the injection — Up to 28 days

The trial staff checked to make sure the participants could be in this trial.

Day of the injection — 24 hours

60 participants were divided into the following 4 treatment groups:

High dose MIJ821 — 15 participants

Medium dose MIJ821 — 14 participants

Low dose MIJ821 — 14 participants

Placebo — 17 participants

All participants received treatment as an injection under the skin once on Day 1. Participants were then monitored at the clinic for at least 4 hours for any medical problems. Participants' depression symptoms were assessed 24 hours after the injection.

After the injection — 28 days

Trial staff checked participants' symptoms of depression and any medical problems for 28 days after the injection.

What was the main result of this trial?

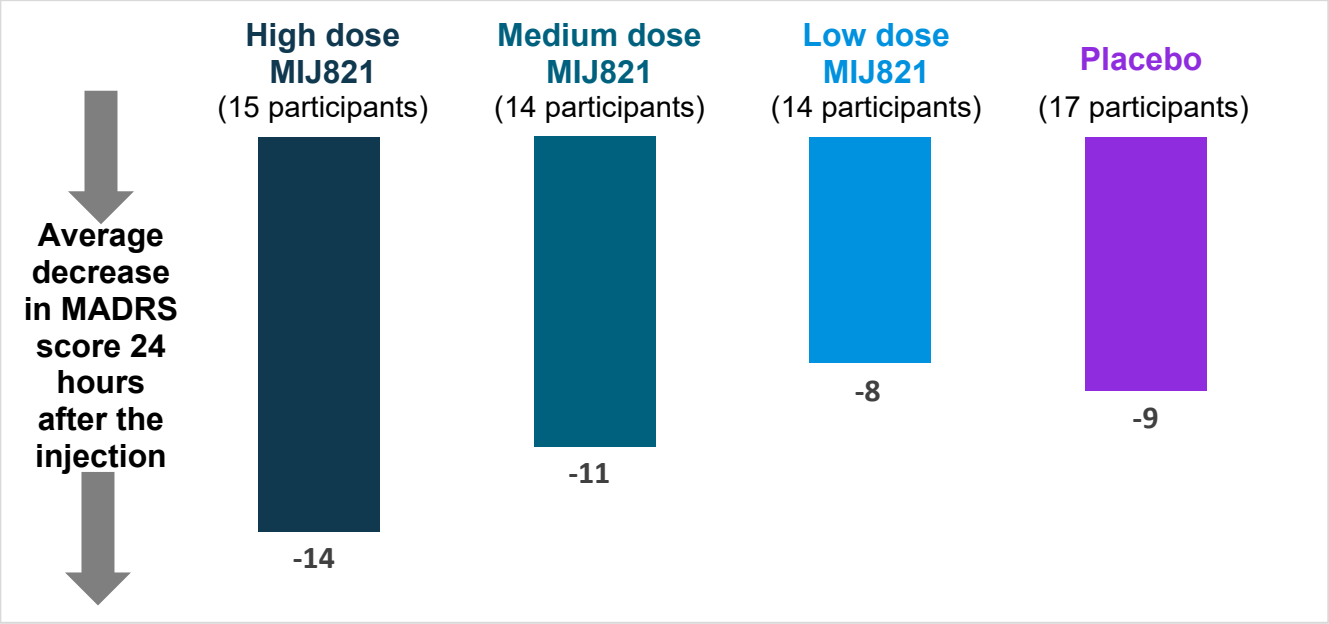
Did MIJ821 reduce depression symptoms more than the placebo 24 hours after a single injection?

The participants who received the **high** and **medium** doses of **MIJ821** showed greater improvement in their depression symptoms compared to those who received the **placebo** 24 hours after the injection. The effect of **low** dose of **MIJ821** was found to be similar to the **placebo**. Overall, the trial results showed that the higher doses led to better responses.

The researchers measured the severity of the participants' depression symptoms at the beginning of the trial until 24 hours after the injection. To do this, they used the **MADRS**. MADRS is a set of questions that a doctor asks a person to rate the severity of their depression symptoms. A person's MADRS score can range from 0 to 60.

A lower score means a person's depression symptoms are less severe. A negative change from baseline (before treatment) indicates improvement in depression symptoms.

Change in the level of depression symptoms after 24 hours



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 start of treatment until 28 days after the injection.

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.

20 participants in the **MIJ821** groups and 7 participants in the **placebo** group had adverse events. None of the participants had adverse events that were considered serious. None of the participants died or left the trial due to an adverse event. The researchers concluded there were no unexpected safety concerns with any of the doses of **MIJ821** in this trial.

How many participants had adverse events?

	High dose MIJ821 (15 participants)	Medium dose MIJ821 (14 participants)	Low dose MIJ821 (14 participants)	Placebo (17 participants)
Had at least 1 **adverse event**	10 of 15 67%	6 of 14 43%	4 of 14 29%	7 of 17 41%

What serious adverse events did the participants have?

None of the participants had serious adverse events or died during this trial.

What adverse events did the participants have?

The table below shows the adverse events that happened in **10% or more** participants in any group. Additional adverse events happened in fewer participants.

	High dose MIJ821 (15 participants)	Medium dose MIJ821 (14 participants)	Low dose MIJ821 (14 participants)	Placebo (17 participants)
Feeling disconnected from reality Dissociation	5 of 15 33% 	2 of 14 14% 	0	2 of 17 12% 
Feeling sick to the stomach Nausea	0	0	0	2 of 17 12% 
Headache	3 of 15 20% 	0	1 of 14 7%	3 of 17 18% 
Redness at the injection site Injection site erythema	3 of 15 20% 	0	0	0
Sleepiness Somnolence	4 of 15 27% 	1 of 14 7%	0	1 of 17 6%

What was learned from this trial?

Researchers learned about the effects of **MIJ821** in people with **treatment-resistant depression (TRD).**

The researchers concluded that the participants who received the **high** and **medium** doses of **MIJ821** showed greater improvement in their depression symptoms compared to those who received the **placebo** 24 hours after the injection. The effect of the **low** dose of **MIJ821** was found to be similar to the **placebo**. Overall, the trial results showed that the higher doses led to better responses.

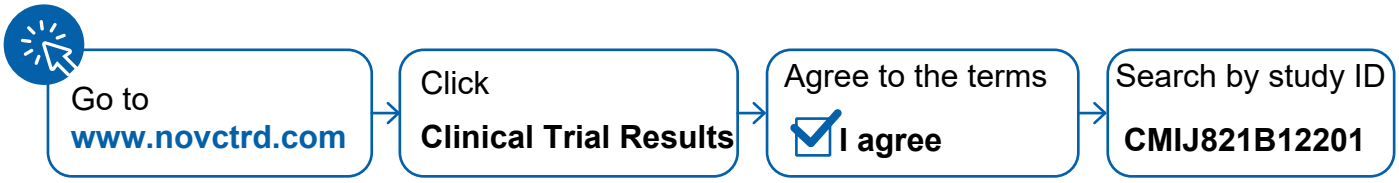
There were no new safety concerns with any of the 3 doses of **MIJ821** in this trial.

When this summary was written, the sponsor was considering the next steps for **MIJ821** in people with **TRD**.

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 these websites:

- www.clinicaltrials.gov – search using the number **NCT05454410**
- clinicaltrialsregister.eu– search using the number **2021-005992-38**

Other trials of **MIJ821** may appear on the public websites above. When there, search for **MIJ821.**

Full clinical trial title: A randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the efficacy, safety, tolerability, and pharmacokinetics of single subcutaneous MIJ821 injection in addition to standard of care in participants with treatment-resistant depression

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

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