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Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of EMA401 in people with postherpetic neuralgia

Protocol number: CEMA401A2201

Thank You!

Novartis, the sponsor of this clinical trial, would like to thank you for taking part in this trial for the drug EMA401, also known as olodanrigan. You helped researchers learn more about how EMA401 works in people with postherpetic neuralgia.

As a clinical trial participant, you belong to a large community of people around the world. Your invaluable contribution to medicine and healthcare is greatly appreciated.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

How long was this trial?

This trial was designed so that an individual participant could take part for about 13 weeks. The participants began on different dates. The trial started in June 2017. The researchers did not complete this trial as planned. Novartis ended this trial early in February 2019.

Why did this trial end early?

This trial ended early because new results from an ongoing animal trial found that the trial drug EMA401 may be linked to possible liver damage in monkeys after 39 weeks of receiving doses of EMA401 twice a day. Earlier studies where monkeys received EMA401 for only 13 weeks did not show liver damage. 13 weeks is the same treatment period for this trial.

After receiving this information, Novartis stopped all treatment in this trial and asked participants who took EMA401 to return to the trial site 2 more times to check their liver health. When the last additional safety follow-up was completed, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

Why was the research needed?

Researchers are looking for a better way to treat different types of neuropathic pain. **Neuropathic pain** is long-term (chronic) pain caused by nerves that are damaged or do not work properly. Typical pain medicines, such as acetaminophen and ibuprofen, often do not work well to treat neuropathic pain and may cause unwanted side effects. The pain tends to get worse over time.

One type of neuropathic pain is called **postherpetic neuralgia (PHN)**. PHN happens to people whose nerves are damaged during shingles, a viral infection that causes a painful, blistering skin rash. When the pain caused by shingles doesn't go away after the rash clears up, it is called PHN. People with PHN often have severe burning, aching, or shooting pain in the areas where the shingles rash happened. This pain can come and go at random, and last over a year for some people.

EMA401 is a drug that researchers had suspected may be able treat neuropathic pain. Researchers wanted to learn if EMA401 could lower pain caused by PHN. To do this, they designed this clinical trial to learn about the effects and safety of EMA401 in people with PHN.

Trial treatments

The treatments taken in this trial were:

EMA401, also known as olodanrigan, taken by mouth as capsules

Placebo: looks like the trial drug, taken by mouth as capsules, but does not have any trial drug in it. Using a placebo helps researchers better understand the effect of a trial drug.

Trial purpose

This trial was done to learn more about the effects and safety of EMA401. The main questions the researchers wanted to answer in this trial were:

- What dose levels of EMA401 lowered participants' pain after 12 weeks?
- What medical problems did the participants have during the trial?

Researchers also checked participants' liver health during an additional safety follow-up period because of the results from the animal trial that showed EMA401 may be linked to possible liver damage in monkeys.

Who was in this trial?

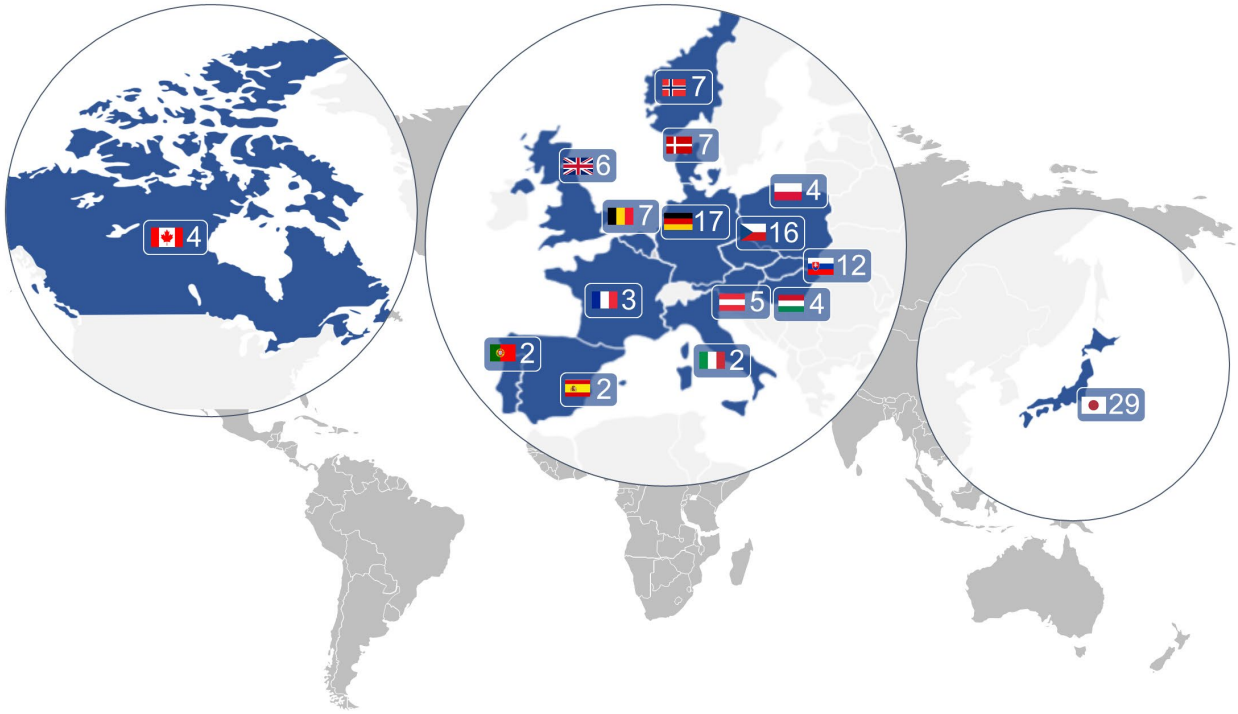
The researchers planned for 360 participants to take part in this trial. Since this trial ended early, only 129 participants began this trial – 65 women and 64 men. The participants could take part in this trial if they:

- Had PHN for at least 6 months after having a shingles rash
- Had moderate to severe neuropathic pain that was not relieved by typical PHN treatments
- Had no medical history of serious liver, heart, or kidney problems
- Were in otherwise good mental and physical health

Participants' ages ranged from 43 to 92 years. They were 71 years old on average.

Participants took part at 45 trial sites in Austria, Belgium, Canada, Czech Republic, Denmark, France, Germany, Hungary, Italy, Japan, Norway, Poland, Portugal, Slovakia, Spain, and the United Kingdom.

Number of participants who took part in each country



What kind of trial was this?

This was a double-blind trial. This means that none of the participants, trial doctors, or trial staff knew what treatment the participants were taking. Some trials are done this way because knowing what treatment each participant is getting can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

What happened during this trial?

Screening period

Up to 5 weeks before taking either EMA401 or placebo, trial doctors checked participants' health and PHN symptoms to make sure they could be in this clinical trial. 129 participants could take part in this trial. Researchers checked the participants' general health throughout the trial.

Treatment period
At the start of the trial, the participants were randomly assigned to take one of these treatments:

- **High dose of EMA401,** 100 milligrams (mg) taken by mouth as capsules twice a day
- **Low dose of EMA401,** 25 mg taken by mouth as capsules twice a day
- **Placebo,** taken by mouth as capsules twice a day

Participants took their assigned treatment for 12 weeks.

In addition to their assigned treatment, participants were able to continue taking their regular treatments for PHN – either pregabalin or duloxetine.

Treatment withdrawal period
After 12 weeks of treatment, researchers randomly assigned participants to stop taking EMA401 (treatment withdrawal) for week 13. The purpose was to check the effects and safety when participants stop taking EMA401. Participants who had been assigned the high or low dose of EMA401 during the treatment period were randomly assigned to take either:

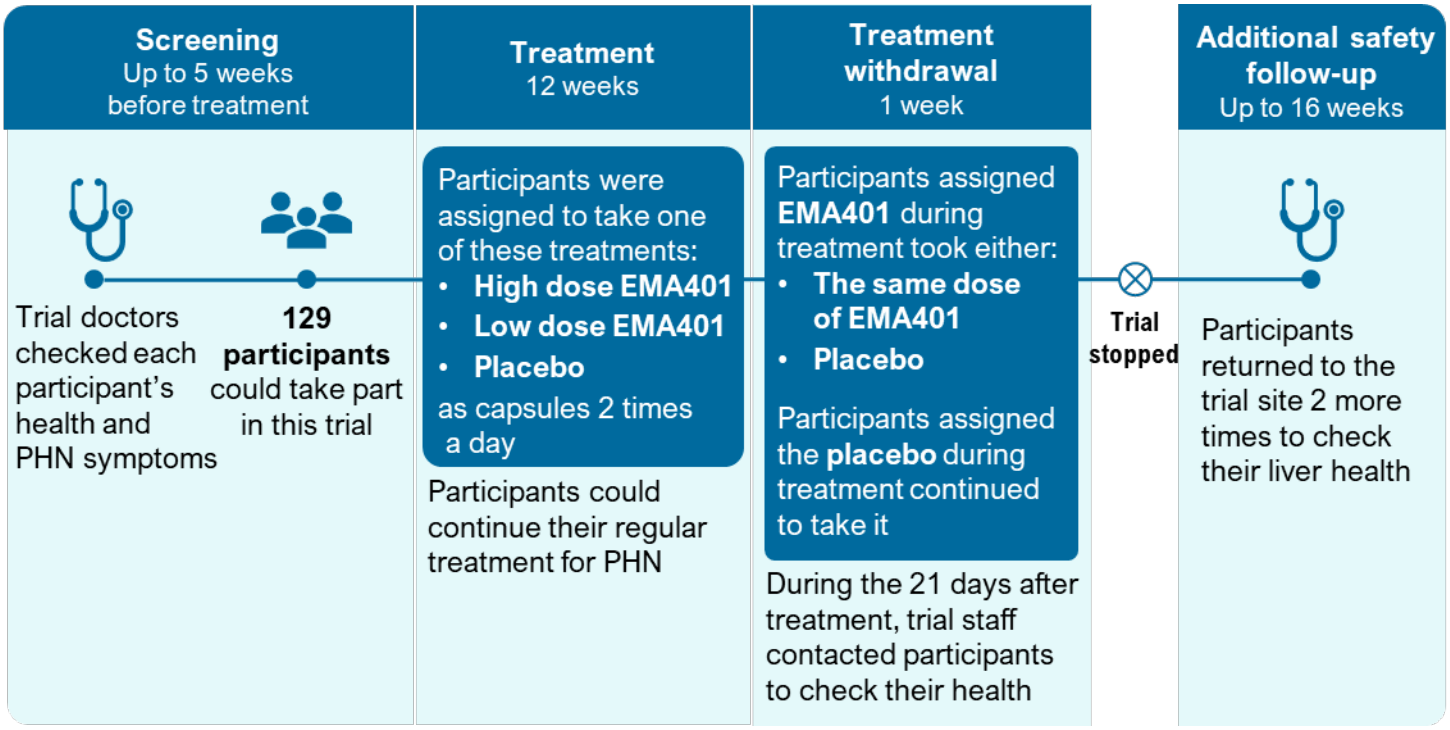
- The same dose of EMA401 from the treatment period (about half of participants)
- Placebo (about half of participants)

Participants who had been assigned placebo during the treatment period continued taking placebo for week 13.

After Novartis stopped the trial

Additional safety follow-up period
After receiving new safety information about EMA401, Novartis stopped all treatment in this trial and asked participants who took EMA401 to return to the trial site 2 more times to check their liver health and take blood samples. The additional safety follow-up period lasted up to 16 weeks.

How researchers designed this trial:



What were the main results of this trial?

This is a summary of the overall results for all participants in both treatment groups. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. More details on the results can be found on the websites listed at the end of this summary.

What dose levels of EMA401 lowered participants' pain after 12 weeks?

During the screening, treatment, and treatment withdrawal periods, participants rated their pain daily on a scale from 0 (no pain) to 10 (worst pain you can imagine). Researchers had planned to compare the change in pain scores of participants who took different doses of EMA401 to those who took the placebo.

Because the trial ended early, the clinical trial team could not conclude if a dose level of EMA401 lowered pain in participants with PHN after 12 weeks.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event is an unwanted sign or symptom that participants have during a trial. An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. So, when new drugs are being studied, researchers keep track of all adverse events the participants have.

This section is a summary of the adverse events that happened during the treatment period, during the 21 days after treatment, and during the additional safety follow-up that lasted up to 16 weeks. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 5% of participants in any group are listed below.

Most common non-serious adverse events

Treatment assigned during treatment period	High dose EMA401	Low dose EMA401	Placebo
	Percent % (out of 43 participants)	**Percent %** (out of 43 participants)	**Percent %** (out of 43 participants)
Diarrhea	**5%** (2)	**7%** (3)	**7%** (3)
Stomach pain Dyspepsia	**7%** (3)	**0%** (0)	**2%** (1)
Common cold Nasopharyngitis	**5%** (2)	**7%** (3)	**9%** (4)
UTI Urinary Tract Infection	**5%** (2)	**0%** (0)	**7%** (3)
Possible sign of pancreas injury Lipase increased	**7%** (3)	**2%** (1)	**0%** (0)
Dizziness	**2%** (1)	**2%** (1)	**7%** (3)
Headache	**5%** (2)	**0%** (0)	**7%** (3)

What were the serious adverse events?

There were no deaths reported during this trial. A total of 7 participants (5% of all participants) had serious adverse events.

High dose EMA401	Low dose EMA401	Placebo
3 participants who took the high dose of EMA401 had a total of 3 serious adverse events:	1 participant who took the low dose of EMA401 had 1 serious adverse event:	3 participants who took placebo had a total of 5 serious adverse events:
• **Abnormal heartbeat** Electrocardiogram ST segment elevation • **Infection in the airways of the lungs** Lower respiratory tract infection • **Severe bruising** Traumatic hematoma	• **Chest pain related to heart disease** Angina pectoris	• **Arthritis in the joints** Osteoarthritis • **Cancerous brain tumor** Central nervous system lymphoma • **Chest pain not related to the heart** Non-cardiac chest pain • **Lower spine pain** Lumbar radiculopathy • **Back pain**

What were the adverse events during the safety follow-up period?

During the additional safety follow-up period, researchers looked for any adverse events, and focused on specific adverse events that could be from serious liver damage.

A total of 5 participants (4% of all participants) had adverse events during the safety follow-up period. They are all listed in the table on the next page. None of the adverse events were considered to be from serious liver damage. 1 participant had a possible sign of liver damage that was not considered serious. Researchers believe it was due to a non-trial pain medicine that the participant took.

Adverse events found during the safety follow-up period

Treatment assigned during treatment period	High dose EMA401	Low dose EMA401	Placebo
	Percent % (out of 43 participants)	**Percent %** (out of 43 participants)	**Percent %** (out of 43 participants)
Possible sign of diabetes			
Blood glucose increased	**2%** (1)	**0%** (0)	**0%** (0)
Possible sign of kidney damage			
Blood creatinine increased	**0%** (0)	**2%** (1)	**0%** (0)
Blood potassium increased	**0%** (0)	**2%** (1)	**0%** (0)
Glomerular filtration rate decreased	**2%** (1)	**2%** (1)	**0%** (0)
Possible sign of liver damage			
Alanine aminotransferase increased	**2%** (1)	**0%** (0)	**0%** (0)
Possible sign of muscle damage			
Blood creatine phosphokinase increased	**2%** (1)	**0%** (0)	**0%** (0)

How has this trial helped?

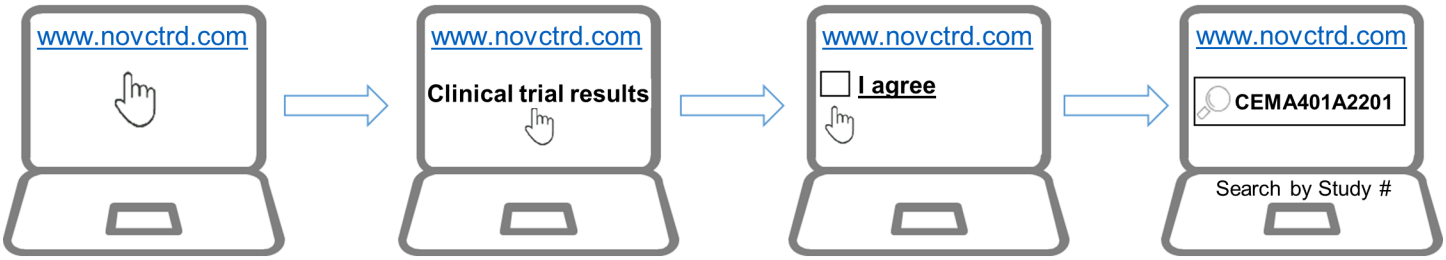
This trial helped researchers learn if EMA401 is safe to use in people with PHN. Novartis stopped this trial early after receiving new safety information about EMA401 from ongoing monkey trials. After the participants completed 2 additional safety follow-up visits, the researchers concluded that EMA401 was generally safe for the participants in this trial. None of the participants who took EMA401 had signs of serious liver damage.

Because the trial ended early, the clinical trial team could not conclude if a dose level of EMA401 lowered pain in participants with PHN after 12 weeks.

Please remember, this summary only shows the results of one clinical trial. Other clinical trials may have different results. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

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).



You can find more information about this trial on the following websites:

- www.clinicaltrials.gov. Use the NCT identifier 03094195 in the search field.
- www.clinicaltrialsregister.eu. Use the EudraCT identifier 2016-000280-16 in the search field.

Full clinical trial title: A double-blind, placebo-controlled, randomized dose ranging trial to determine the safety and efficacy of three dose levels of EMA401 in reducing 24-hour average pain intensity score in patients with post-herpetic neuralgia

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

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

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