GRÜNENTHAL

Summary of clinical trial results for the public

Trial Information

Simple trial name: A clinical trial to find out if neridronic acid given intravenously (into a vein) eases the pain felt by patients who have severe lasting pain in the hand, wrist, ankle or foot from complex regional pain syndrome (CRPS)

Protocol number: KF7013-04

Trial Sponsor: Grünenthal GmbH

Thank you to the trial patients

If you are a patient who took part in the clinical trial, thank you for your time and commitment.

You made the clinical trial possible.

You helped us on our way to bringing new medicines to patients.

Important note: You should not use this summary to make decisions about the medical treatment you use. You should always see your doctor for advice about medical treatment.

About this summary

This summary is written to share the results of this clinical trial with the public. It is written in a way that should be easy for most people to understand. It describes why the trial was needed, how it was done, and the results.

General information about the clinical trial

Why was this trial needed?

Complex regional pain syndrome (CRPS) is a condition that can develop after a minor injury such as a fracture or sprain, usually in the hand, wrist, ankle or foot. People with CRPS feel severe lasting pain in their affected hand, wrist, ankle or foot. The pain felt can be described as a “burning”, “electrical” or “shooting” pain.

Although CRPS treatment options are available, many patients are not treated adequately for their pain.

Researchers are looking for new ways to treat CRPS. In this trial, researchers studied the effect of a trial medicine called neridronic acid in participants with CRPS.

Which medicines were studied?

Neridronic acid

Neridronic acid belongs to a group of medicines already used to treat other conditions like osteoporosis (softening of the bones).

Placebo (Dummy medicine)

A placebo or dummy medicine looks like the trial medicine and is given in the same way, but does not have any medicine in it. Researchers sometimes use a placebo or dummy medicine to understand if the changes seen were due to the trial medicine or were caused by other factors.

What was the main objective of the trial?

The main objectives of the trial were to find out:

- if neridronic acid eased participants’ pain after 12 weeks of treatment.
- if neridronic acid is safe to be given to participants with severe lasting pain in the hand, wrist, ankle or foot from CRPS.

When was the trial?

This trial started on 31 May 2018 and ended on 01 August 2019.

As per plan, the sponsor measured the initial combined results from this trial and another neridronic acid trial, while they were both ongoing. The sponsor ended this trial early because the initial results indicated that neridronic acid only had a very small chance of providing pain relief to the participants by the end of the trial.

Where did this trial take place?

The clinical trial took place in the following countries:

European Union (EU) countries

- Czech Republic (9 participants)
- United Kingdom (7 participants)
- Slovakia (5 participants)
- Poland (1 participant)

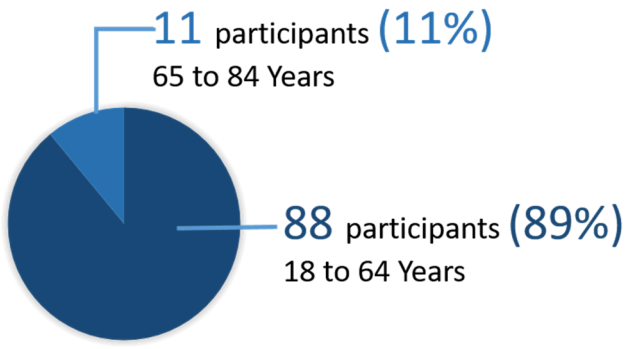
Non-EU countries

- United States (73 participants)
- Canada (5 participants)

Which participants were included in this trial?

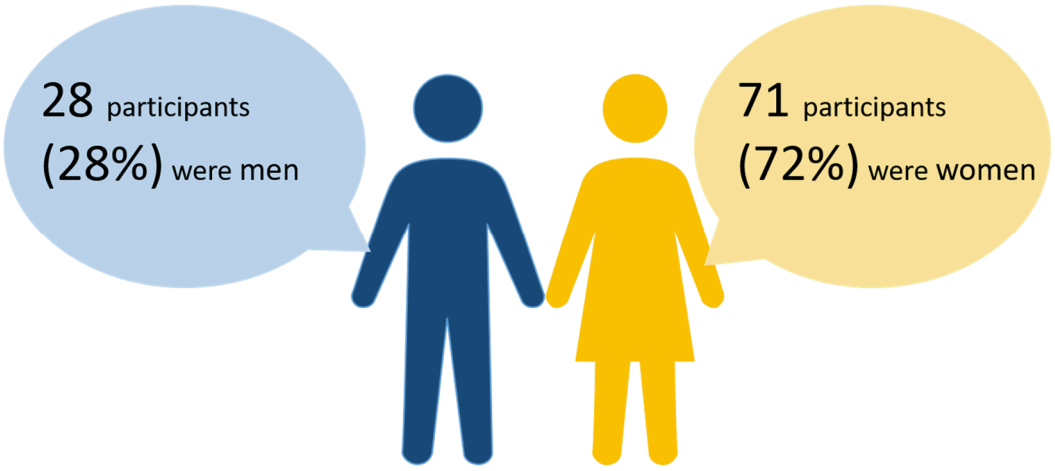
A total of 99 participants were treated with neridronic acid or dummy medicine in this clinical trial.

How old were the participants?



The average age of the participants was 50 years. The youngest participant was 18 years old and the oldest participant was 84 years old.

Were the participants' men or women?



Which participants were able to take part in the trial?

Participants were only able to take part in the clinical trial if they met certain criteria. This was important to make sure that it was safe for each participant to take part in the clinical trial, that the results of the clinical trial were valid, and that the laws and regulations were followed.

People could take part in this trial if they:

- ☑ were at least 18 years of age.
- ☑ had severe lasting pain in the hand, wrist, ankle or foot from CRPS for 2 years or less.
- ☑ had a pain score of at least 4 on a scale of 0=no pain to 10=worst pain.
- ☑ must have failed at least 2 available treatments for severe lasting pain, 1 of which must have been a pain medication.
- ☑ must have been on stable treatment for severe lasting pain for at least 1 month before entering the trial.

What happened during this trial?

This was a Phase 3 trial that compared neridronic acid with a dummy medicine. In Phase 3 trials, the trial medicine is given to a large number of participants with the disease condition to learn more about the effects of the trial medicine and its safety.

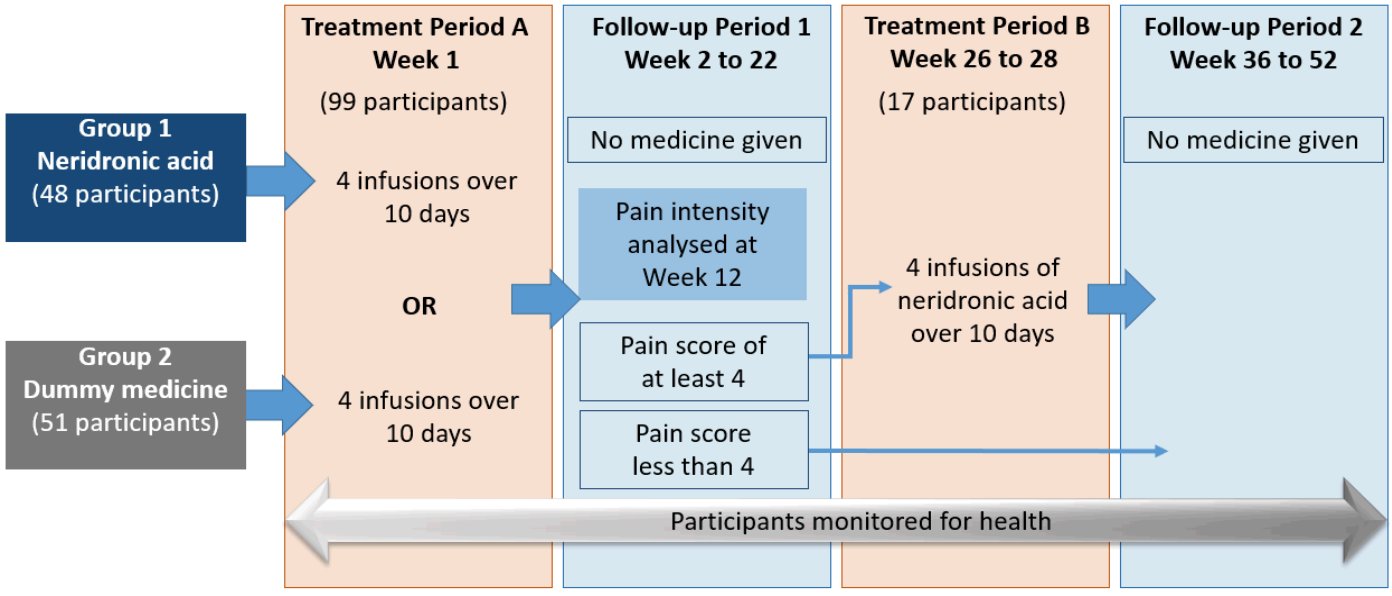
This trial had Treatment Period A with Follow-up Period 1, and Treatment Period B with Follow-up Period 2.

Treatment Period A was "double blind". This means that neither the participants nor the researchers knew who was given which trial medicine. Trials are sometimes done this way to make sure that the trial results are not biased by this information.

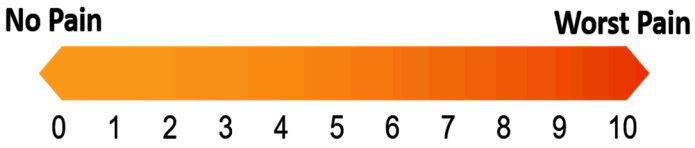
Researchers randomly assigned participants to one of 2 treatment groups using a computer system. This process is called randomisation. It means that each participant could be assigned to any group and it helps to make sure the groups are distributed fairly.

Treatment Period A consisted of 4 infusions of trial medicine over 10 days. Participants in Group 1 received a total dose of 400 milligrams (mg) of neridronic acid intravenously (into a vein) and participants in Group 2 received dummy medicine intravenously. Participants who rated their pain score as at least 4 on a scale of 0=no pain and 10=worst pain could enter **Treatment Period B** which was "open label". This means that both the researchers and the participants knew which medicine they took. All participants who entered Treatment Period B received 4 additional infusions of neridronic acid over 10 days.

Participants who did not enter Treatment Period B continued to Follow-up Period 2. Researchers monitored the health of the participants throughout the trial.



What were the overall results of the trial?



From 1 week before receiving the first dose of trial medicine up until 12 weeks after treatment, participants recorded every day how much pain they felt. Participants measured how strong their pain was using a numerical rating scale from 0=no pain to 10=worst pain.

For this trial, the average pain scores at the end of Week 12 were compared to the average pain scores before the start of the trial treatment. There was a reduction in pain in both neridronic acid and placebo groups. However, researchers could not conclude the effect of neridronic acid on easing participants' pain in this trial.

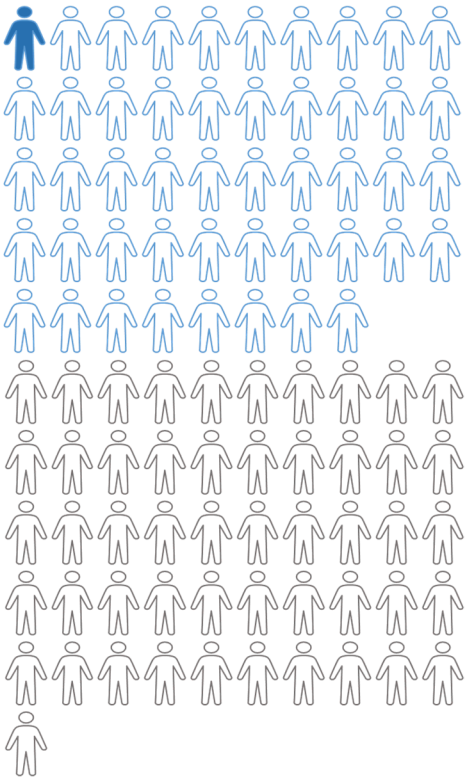
During this trial, some participants experienced medical problems which the trial doctor thought could be side effects of the medicine they had taken.

Number of participants with side effects by treatment group Before Week 26

Serious side effects: Serious side effects are those that may cause death, disability, lasting problems, life-threatening conditions or hospitalisation.

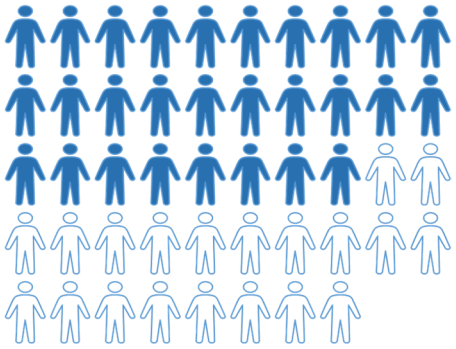
Neridronic acid: 1 out of 48 (2%)

Dummy medicine: 0 out of 51 (0%)

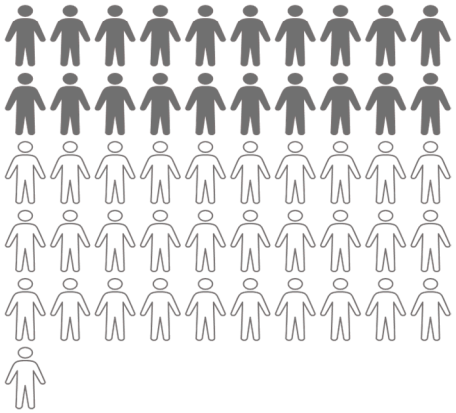


Most common side effects:

Neridronic acid: 28 out of 48 (58%)



Dummy medicine: 20 out of 51 (39%)



The most common side effects in participants before Week 26 were non-specific diseases at the infusion site, diseases of muscles and connective tissues, nerve problems and stomach problems.

After Week 26

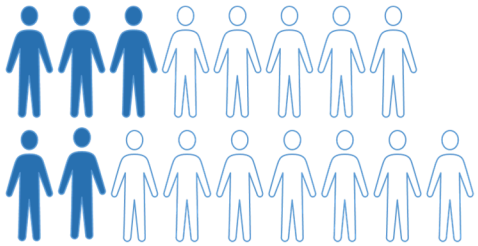
Serious side effects:

Serious side effects were not reported.

Most common side effects:

Placebo (Treatment Period A) + Neridronic acid (Treatment Period B): 3 out of 8 (38%)

Neridronic acid (Treatment Period A) + Neridronic acid (Treatment Period B): 2 out of 9 (22%)



The most common side effects in participants after Week 26 were stomach problems, diseases of muscles and connective tissues, skin problems, non-specific diseases at the infusion site, and kidney and urinary problems. The remaining 43 participants in the placebo group and the 39 participants in the neridronic acid group who did not receive neridronic acid in Treatment Period B did not report any side effects after Week 26.

How was this trial useful for patients and researchers?

This trial was planned to help researchers learn more about the effects of neridronic acid in participants with severe pain in the hand, wrist, ankle or foot from CRPS lasting for 2 years or less.

The sponsor ended this trial early because the combined initial results from this trial and another neridronic acid trial indicated that neridronic acid only had a very small chance of providing pain relief to the participants by the end of the trial. Because the trial ended early, researchers could not conclude the effect of neridronic acid on easing participants' pain in this trial.

Findings from this trial may be used in other trials with neridronic acid. There are no ongoing trials for neridronic acid as of 23-June-2020 and the sponsor does not plan to conduct any more trials for neridronic acid in the future.

The results described in this report are for one trial. The findings of other trials might be different. How neridronic acid works and how safe it is to use must not be judged on the results of one clinical trial alone.

If you have questions, please contact your trial doctor.

Where can I learn more about this trial?

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

www.clinicaltrials.gov Use the NCT identifier NCT03560986 in the search field.	https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2017-004244-37 in the search field.

Full trial name: Placebo-controlled efficacy and safety trial of intravenous neridronic acid in subjects with complex regional pain syndrome (CRPS)

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