

## Trial Information

**Simple trial name:** A clinical trial to test how different doses of GRT6018 are tolerated and how GRT6018 is processed in healthy people

**Protocol number:** HP6018-01

**Trial Sponsor:** Grünenthal GmbH

### Thank you to the trial participants



If you 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 treatments you use. You should always see your doctor for advice about medical treatments.

## 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?

**GRT6018** is an experimental medicine being developed to treat chronic (long-lasting) nerve pain. Nerve pain occurs when an injury or illness affects the pain-conducting fibers of the nervous system. In people with diabetes, damage to the nerves results in nerve pain in some body regions, such as the limbs. This condition is called diabetic neuropathy. Currently, there are only a few medicines approved for the treatment of pain caused by diabetic neuropathy. These medicines only lead to adequate pain reduction for some of the patients and can cause unwanted side effects, so there is a need to develop better medicines. **GRT6018** binds to certain proteins in the nerve cells (known as NOP receptors), blocking the pain signals.

In this trial, researchers wanted to know how different doses of **GRT6018** are tolerated in healthy people. To understand this, researchers recorded the number and type of medical events that occurred at different levels of single and multiple doses of **GRT6018** compared to **placebo**. Researchers also wanted to know how much **GRT6018** is taken up by the body and what happens to **GRT6018** blood levels over time, the effect of food on the blood levels of **GRT6018** in healthy participants and if the blood levels of **midazolam**, an approved drug, change when **GRT6018** is taken. To understand this, they tested the participants blood at multiple times during the trial.

## Which medicines were studied?



**GRT6018** is an experimental medicine that is being developed to treat chronic nerve pain. It is taken as capsules. **GRT6018** has not been approved for use in humans.



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



**Midazolam** is an approved medicine and it is used in trials to measure the interaction between drugs. **Midazolam** is taken as tablets. Researchers wanted to understand the effect of multiple doses of **GRT6018** on the blood levels of **midazolam**.

## What was the main objective of the trial?

The main objective of the trial was:

How are different doses of **GRT6018** tolerated in healthy participants when given as a single dose or multiple doses?

Researchers also wanted to know:

- how much **GRT6018** is taken up by the body and what happens to **GRT6018** blood levels over time,
- how **GRT6018** blood levels are affected when **GRT6018** is taken with or without food, and
- how **midazolam** blood levels are affected when **midazolam** is taken with or without **GRT6018**.

## When and where did this trial take place?



This trial started on 02 November 2020 and ended on 27 October 2022.



The trial took place in one trial centre in Germany.

## Which participants were included in this trial?

The trial consisted of 3 parts: Part A, Part B and Part C.

In Part A, the participants received a single dose of **GRT6018** or **placebo**. There were 64 participants.

In Part B, the participants received multiple doses of **GRT6018** or **placebo**. There were 32 participants.

In Part C, the participants received multiple doses of **GRT6018** and single doses of **midazolam**. There were 14 participants.

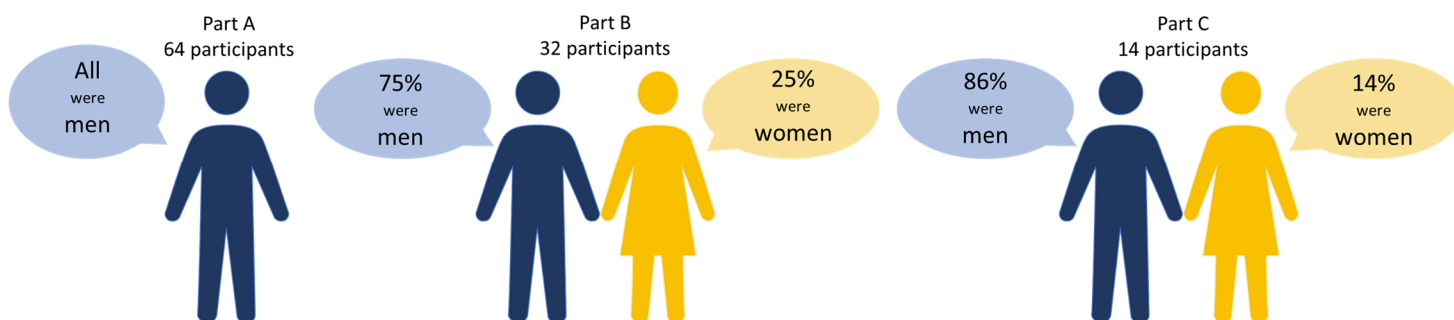
## How old were the participants?

Part A: The average age of the participants was 36 years. The youngest participant was 19 years old, and the oldest participant was 55 years old.

Part B: The average age of the participants was 43 years. The youngest participant was 21 years old, and the oldest participant was 60 years old.

Part C: The average age of the participants was 45 years. The youngest participant was 28 years old, and the oldest participant was 60 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 requirements. This was important to make sure that it was safe for each participant to take part in the clinical trial. Also, to make sure 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:

- Part A: were male between 18-55 years of age.  
Part B and C: were male or female between 18-60 years of age.
- had a body mass index (a measure of body weight based on height) between 18.5 and 29.9 kg/m<sup>2</sup>,
- had a body weight of at least 60 kg, and
- were healthy and did not take prohibited/not allowed medications.

## What happened during this trial?

This was a Phase 1 trial that looked at how different doses of **GRT6018** are tolerated in healthy people compared with **placebo**. Phase 1 trials are done to find out how a new test medicine works in a small number of healthy participants. This helps researchers understand what happens to the test medicine in the body, and if there are any side effects.

Participants could enroll in 1 of 3 parts of the trial.

The parts were:

- **Part A (64 participants):** Researchers assigned 64 healthy male participants to 8 groups, each group receiving a different **GRT6018** dose. Within each group, 8 participants were randomly assigned to receive a **single dose** of **GRT6018** or **placebo**, in a 6:2 ratio using a computer system.

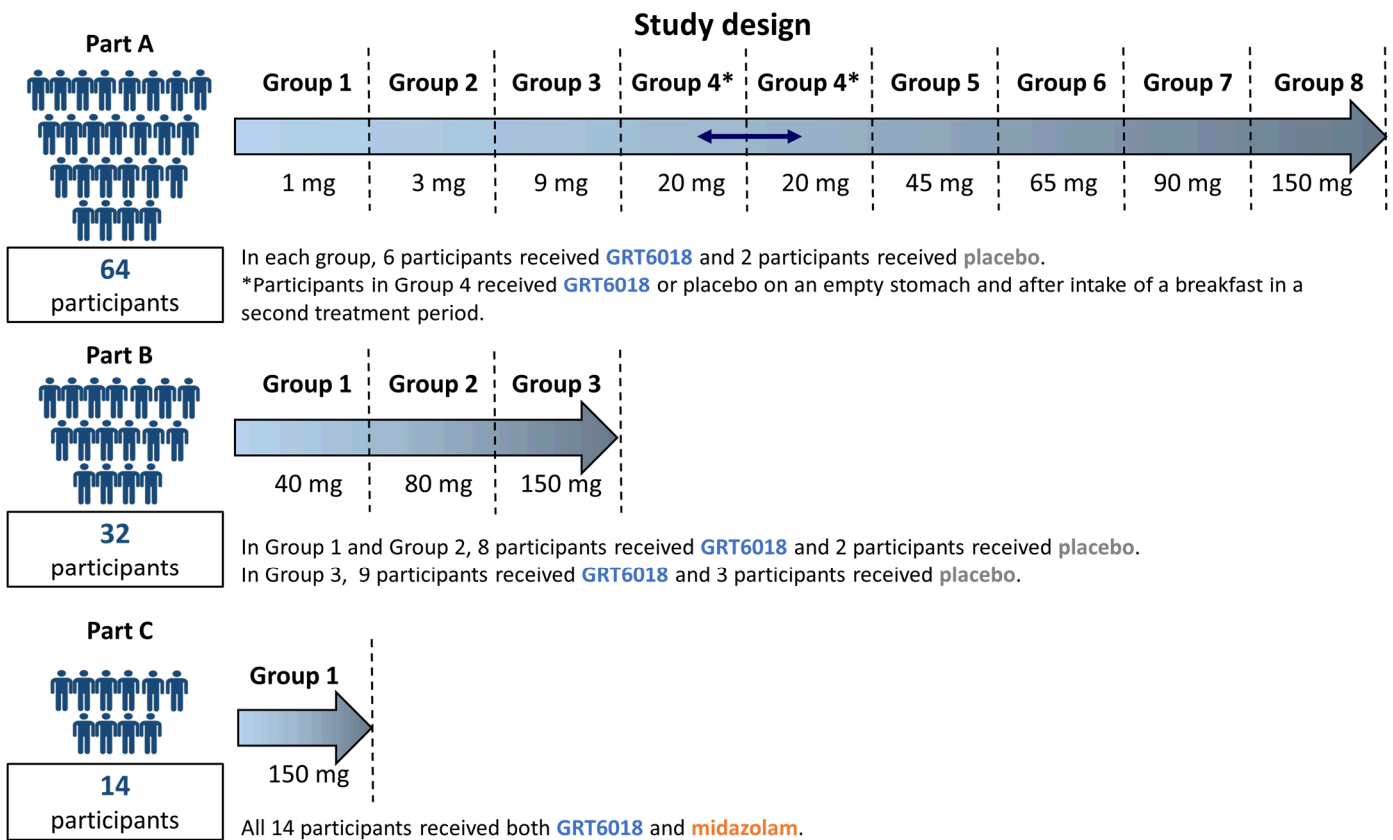
This process is called randomization. It means that within each group, a participant could be assigned to receive either **GRT6018** or **placebo**. This helps to make sure the groups are distributed fairly. The dose of **GRT6018** was between 1mg and 150mg.

Participants in Group 4 took 20mg **GRT6018** or **placebo** as capsules, both on an empty stomach and after food in a second treatment period. In all the other groups, participants took **GRT6018** or **placebo** on an empty stomach. The dose of **GRT6018** was increased from treatment group to treatment group as long as each dose was well tolerated and a certain blood level was not exceeded.

- **Part B (32 participants):** Researchers assigned 32 healthy male and female participants to 3 treatment groups. Within each treatment group, participants were randomly assigned to receive **multiple doses** of **GRT6018** or **placebo**, in an 8:2 ratio using a computer system. Participants took either 40mg, 80mg, or 150mg **GRT6018** or **placebo** in the form of capsules. Participants received an initial single-dose on Day 1, and then after 48 hours started receiving multiple-doses twice a day over 13 days. Participants received a single dose-dose in the morning of the last day (Day 16).

Neither the participants nor the researchers in Part A and Part B of the trial knew who was given which treatment. This is called a double-blind trial. Trials are sometimes done this way to make sure that trial results are not biased by this information.

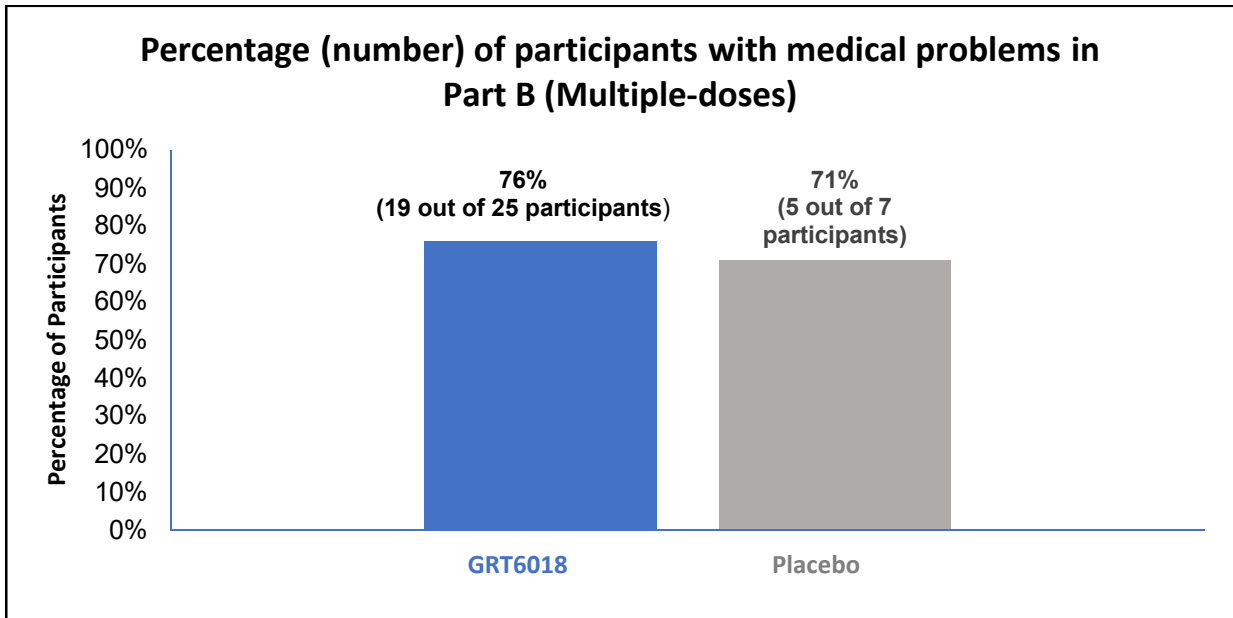
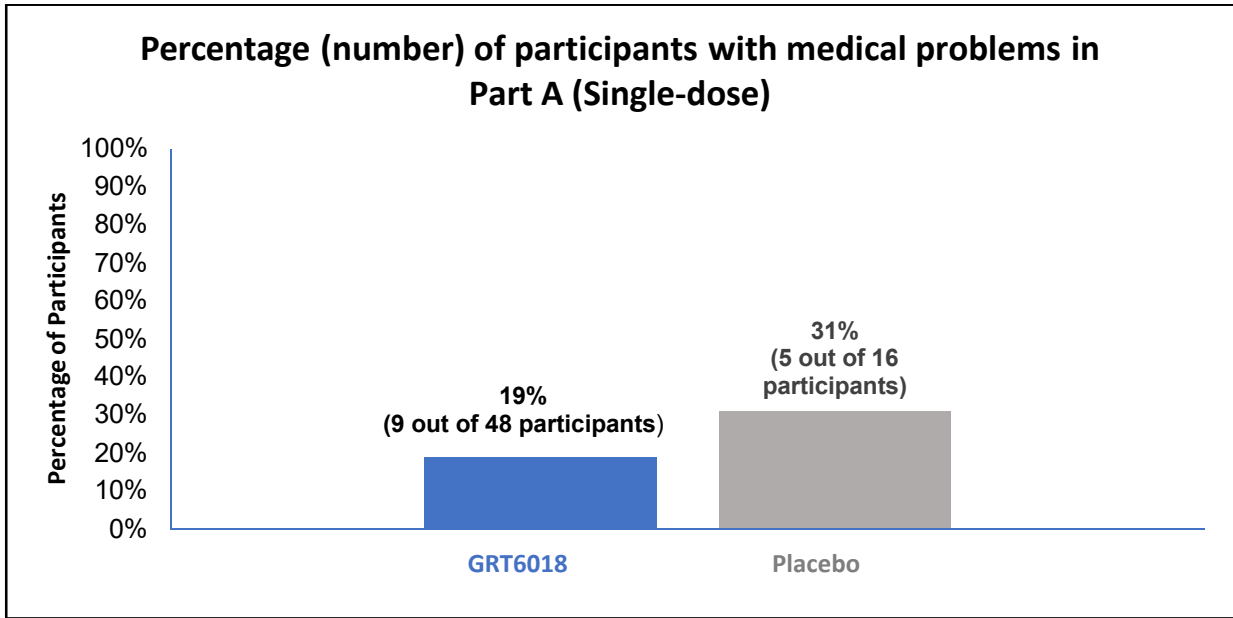
- **Part C (14 participants):** Participants received treatment for 14 days. All participants took a single dose of **midazolam** (7.5mg) on 2 days and multiple doses of **GRT6018** (150mg) on all 14 days.



Researchers monitored the health of the participants in all groups throughout the trial and 3 to 7 days after discharge.

## What were the overall results of this trial?

To find out how different doses of **GRT6018** are tolerated, researchers looked at the number of participants with medical events in Parts A and B. Researchers keep track of all medical events, no matter how big or small, that participants have when a new treatment is tested. A medical event may or may not be related to the treatments given in the trial.



## What were other results of this trial?

Researchers also wanted to know what happens to blood levels of **GRT6018** when it is taken with or without food and if the blood levels of **midazolam** changed when **GRT6018** is taken.

To understand the effect of food, they measured the blood levels of **GRT6018** in participants on the 20 mg dose during Part A of the trial. They found that levels of **GRT6018** in participants' blood were slightly higher when **GRT6018** was taken with food as compared to when taken without food.

To understand the effect of **GRT6018** on **midazolam**, they measured the levels of **midazolam** in the participants' blood during Part C of the trial. They found that levels of **midazolam** in participants' blood were lower when **GRT6018** 150 mg was taken.

## What side effects did participants have in this trial?

Side effects are medical events that happened during the trial which the trial doctor considered related to the trial treatment. Researchers need to compare the results of many trials to know whether a medical event is related to a treatment.

### What serious side effects did the participants have?

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

No serious side effects or deaths were reported during any part of this trial.

### How many participants had non-serious side effects?

**Part A:** In Part A, 6 out of 64 participants had non-serious side effects. Non-serious side effects that happened in more than 1 participant who took **GRT6018** were headache in 2 out of 48 participants.

**Part B:** In Part B, 13 out of 32 participants had non-serious side effects. Non-serious side effects that happened in more than 1 participant who took **GRT6018** were hard stools (faeces hard) and headache, each in 4 out of 25 participants, loose stools (diarrhoea) in 3 out of 25 participants, and swelling of hands and feet (oedema peripheral) in 2 out of 25 participants.

**Part C:** In Part C, 9 out of 14 participants had non-serious side effects. Non-serious side effects that happened in more than 1 participant who took **GRT6018** were hard stools (faeces hard) in 8 out of 14 participants, stomach discomfort (abdominal discomfort) and stomach pain (abdominal pain), each in 2 out of 14 participants.

## How many participants stopped treatment because of side effects?

No participants stopped trial treatment due to side effects in this trial.

The trial was completed as planned. When the trial ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report. The results of an individual participant might be different and may not be in this summary

## How was this trial useful for patients and researchers?

The researchers found that **GRT6018** was tolerated by all trial participants. The researchers found no new safety concerns with **GRT6018**.

Findings from this trial may be used in other trials to learn whether patients with diabetic neuropathy are helped by this treatment.

The results described in this report are for one trial. The findings of other trials might be different. How **GRT6018** works and how safe it is to use must not be judged based 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?

**EudraCT identifier:** 2020-002573-10

**Full trial name:** A randomized, single-center, double-blind, placebo-controlled, first-in-human trial with single and multiple ascending doses to determine safety, tolerability, and pharmacokinetics of GRT6018 in healthy subjects

**Sponsor's contact information:** Grünenthal GmbH, 52099 Aachen, Germany

**Email ID:** [clinical-trials@grunenthal.com](mailto:clinical-trials@grunenthal.com)

**Date of summary:** 27-March-2025