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Clinical Trial Results Summary

A clinical trial to learn about the safety of GT005 in people with geographic atrophy due to macular degeneration

Thank you!

Thank you to the participants who took part in the clinical trial for **geographic atrophy due to dry, age-related macular degeneration**. Every participant helped the researchers learn about the trial drug **GT005**, also called **PPY988**.

Gyroscope Therapeutics Limited, a Novartis company, 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: CPPY988A12101 and GT005-01

Novartis drug studied: **GT005**, also called **PPY988**

Sponsor: Gyroscope Therapeutics Limited, a Novartis company

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.

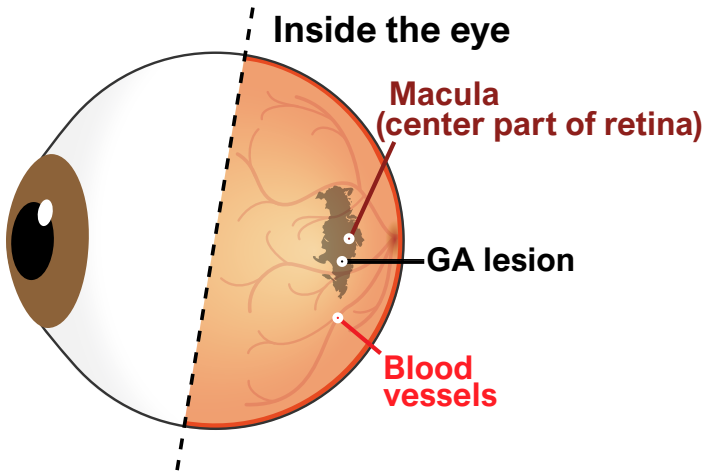
What was the main purpose of this trial?

The purpose of this trial was to learn about the safety of different doses of **GT005** for people with geographic atrophy due to dry, age-related macular degeneration. When this trial started, there were no approved treatments for people with this condition.

Geographic atrophy (GA) is late stage **dry, age-related macular degeneration (AMD)** that causes vision loss. AMD is an eye disease caused by damage to cells in the retina. The **retina** is the clear part at the back of the eye that is sensitive to light.

As AMD worsens and becomes GA, cells in the center of the retina, also called the **macula**, waste away and die. This is known as atrophy. This causes blind spots and vision loss. The patches of dead cells, called **GA lesions**, grow in size over time across the retina and look like islands on a map when doctors examine the eye.

Researchers think inflammation due to an overactive part of the immune system plays a role in causing GA.



GT005, also called **PPY988**, is a **gene therapy** designed to treat GA by adding a gene into the eye. The gene is designed to make cells in the eye produce more of a protein in the immune system called complement factor I (CFI).

People with GA often have low levels of CFI. Researchers think **GT005** could raise the levels of CFI in the eye, which could lessen inflammation and possibly slow the growth of GA lesions.

What is gene therapy?

Gene therapy is a treatment that works by replacing or adding a gene inside a person's cells to treat a disease or condition.
A **gene** is a section of DNA that can store instructions for making a protein.

This trial was the first time that **GT005** was given to people. Therefore, the researchers had to test different doses in small groups of participants to learn about the safety of different doses of **GT005**. The researchers also needed to carefully check all the medical problems that happened during the trial and identify any that could cause changes in dosing.

The trial's purpose was to answer this main question:

- What medical problems, also called adverse events, including those related to the eyes, 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 December 2018 and ended in June 2024. Each participant was in the trial for up to 5 years.

The sponsor decided to end the trial early because results from this and other trials that happened at the same time showed **GT005** did not affect GA lesion growth. The decision was not due to safety concerns.

Some participants who had received **GT005** were invited to join another trial, CPPY988A12203B, to learn about the safety and effects of **GT005** for about 5 years.

Who was in this trial?

56 participants with GA received treatment in this trial – 17 men and 39 women. Participants' ages ranged from 56 to 93 years. Their average age was 79 years.

The number of participants by race is shown below.

Race

55 White	1 Asian

The participants could take part in this trial if they:

- Had at least one GA lesion on their retina in at least one eye (called the **study eye**)
- Did not have certain other eye conditions in the study eye
- Had not had surgery on the study eye up to 3 months before joining the trial

56 participants from 2 countries received treatment in this trial. The participants took part in:

- United Kingdom | 27 participants
- United States | 29 participants

What treatments did the participants receive?

The treatment in this trial was:

GT005, also called **PPY988**, which was given once as an injection into the study eye. The injection was given behind the retina during surgery. This trial looked at 3 doses of **GT005**:

- **Low dose GT005**
- **Medium dose GT005**
- **High dose GT005**

A surgeon injected **GT005** using 1 of 2 ways:

- **Standard procedure** called transvitreal procedure: a surgeon removed the vitreous fluid (gel-like substance inside the eye) and replaced it with another solution. Then, they injected **GT005** into the eye.
- **New procedure** called orbit subretinal delivery system: a surgeon used a device with a very small needle to inject **GT005** without removing the vitreous fluid.

Participants who received **GT005** also received steroids as an injection, and eye drops, to lower inflammation in their eyes during and after surgery.

The participants, researchers, and trial staff knew that all participants received **GT005**.

What happened during this trial?

Before treatment Up to 2 months

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

During treatment 1 day

Participants received **GT005** through the standard procedure or new procedure:

Standard procedure

Researchers started by giving the low dose of **GT005** through the **standard procedure** to a few participants. Researchers checked the safety of **GT005** after 5 weeks before giving the medium dose through the standard procedure to the next group of participants. This continued until the safety of the high dose had been checked through the standard procedure. Then, researchers gave a larger number of participants the low, medium, or high dose of **GT005** through the standard procedure.

31 participants received **GT005** through the **standard procedure**:

- **Low dose GT005** – 6 participants
- **Medium dose GT005** – 10 participants
- **High dose of GT005** – 15 participants

New procedure

After the safety of each dose had been checked through the standard procedure, researchers decided to start giving a few participants the medium dose of **GT005** using the **new procedure**. Researchers checked the safety of **GT005** after 5 weeks before giving the high dose through the new procedure to the next group of participants. Then, researchers gave a larger number of participants the medium or high dose of **GT005** through the new procedure.

25 participants received **GT005** through the **new procedure**:

- **Medium dose GT005** – 3 participants
- **High dose of GT005** – 22 participants

After treatment Up to about 5 years

Trial staff checked participants for any medical problems for up to 5 years after participants' received trial treatment.

At the end of this trial, participants who had not completed their last trial visit were invited to join another trial called CPPY988A12203B, so researchers could continue to check for any medical problems for at least 5 years.

Trial staff checked the participants' general health throughout the trial.

What were the main results of this trial?

What medical problems, also called adverse events, including those related to the eyes, 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 injection of trial treatment until about 5 years after 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.

In this trial, researchers kept track of adverse events that happened in the eye (eye-related, or ocular, adverse events) and in other parts of the body (non-eye related, or non-ocular, adverse events).

Out of 56 participants:

- 17 participants had serious adverse events
- 54 participants had other (not including serious) adverse events
- 48 participants had eye-related adverse events in the study eye
- No participants left the trial due to an adverse event
- 4 participants died due to any cause

Some participants had changes or damage to cells in the retina (retinal pigmentation or depigmentation), which was similar to safety results from other trials with **GT005**. There were no new safety concerns for **GT005** in this trial.

How many participants had adverse events during the trial?

	Standard procedure			New procedure	
	Low dose GT005 6 participants	Medium dose GT005 10 participants	High dose GT005 15 participants	Medium dose GT005 3 participants	High dose GT005 22 participants
Had at least 1 **serious adverse event**	2 of 6	6 of 10	4 of 15	0 of 3	5 of 22
Had at least 1 **other (not including serious) adverse event**	4 of 6	10 of 10	15 of 15	3 of 3	22 of 22
Had at least 1**eye-related adverse event in the study eye**	3 of 6	7 of 10	14 of 15	3 of 3	21 of 22
Died	1 of 6	3 of 10	0 of 15	0 of 3	0 of 22

What serious adverse events did the participants have?

17 participants had serious adverse events. None of the serious adverse events were eye-related.

The table below shows the most common serious adverse events that happened. Additional serious adverse events happened in fewer participants.

	Standard procedure			New procedure	
	Low dose GT005 6 participants	Medium dose GT005 10 participants	High dose GT005 15 participants	Medium dose GT005 3 participants	High dose GT005 22 participants
Skin infection Cellulitis	0 of 6 0%	1 of 10 10%	1 of 15 7%	0 of 3 0%	0 of 22 0%
Infection in airways and lungs Lower respiratory tract infection	1 of 6 17%	1 of 10 10%	0 of 15 0%	0 of 3 0%	0 of 22 0%
Fall	0 of 6 0%	0 of 10 0%	2 of 15 13%	0 of 3 0%	0 of 22 0%
Broken hip Femoral neck fracture	1 of 6 17%	1 of 10 10%	0 of 15 0%	0 of 3 0%	0 of 22 0%
Stroke Cerebrovascular accident	1 of 6 17%	0 of 10 0%	0 of 15 0%	0 of 3 0%	1 of 22 5%

What other (not including serious) adverse events did the participants have?

54 participants had other adverse events.

The table below shows the most common other adverse events that happened.

	Standard procedure			New procedure	
	Low dose GT005 6 participants	Medium dose GT005 10 participants	High dose GT005 15 participants	Medium dose GT005 3 participants	High dose GT005 22 participants
Eye-related					
Changes to cells in retina – study eye Retinal pigmentation – study eye	0 of 6 0%	4 of 10 40%	10 of 15 67%	0 of 3 0%	8 of 22 36%
Broken blood vessel in study eye Conjunctival hemorrhage – study eye	0 of 6 0%	0 of 10 0%	0 of 15 0%	3 of 3 100%	15 of 22 68%
Cloudy lens of study eye Cataract – study eye	1 of 6 17%	3 of 10 30%	7 of 15 47%	0 of 3 0%	2 of 22 9%
Broken blood vessel in retina in study eye Retinal hemorrhage – study eye	0 of 6 0%	2 of 10 20%	1 of 15 7%	3 of 3 100%	5 of 22 23%
Dry eye – study eye	1 of 6 17%	2 of 10 20%	2 of 15 13%	0 of 3 0%	2 of 22 9%
Non-eye related					
COVID-19	0 of 6 0%	2 of 10 20%	2 of 15 13%	0 of 3 0%	5 of 22 23%
Fall	3 of 6 50%	2 of 10 20%	2 of 15 13%	0 of 3 0%	0 of 22 0%

What was learned from this trial?

Researchers learned about the safety of different doses of **GT005** for people with geographic atrophy due to dry, age-related macular degeneration.

The sponsor ended this trial early because results from this and other trials showed that GA lesions continued to grow larger after treatment with **GT005**. Researchers concluded that **GT005** did not affect GA lesion growth. The decision to end the trial early was not due to safety concerns.

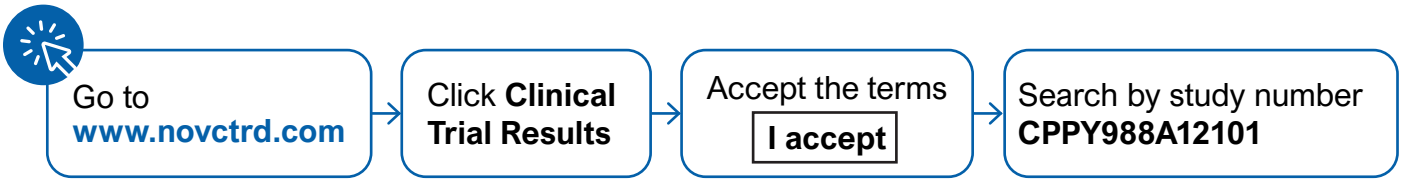
Some participants had changes or damage to cells in the retina (retinal pigmentation or depigmentation), which was similar to safety results from other trials with **GT005**. There were no new safety concerns for **GT005** in this trial.

When this summary was written, an extension trial CPPY988A12203B was ongoing for certain participants who received **GT005** in this and other trials.

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:

- **clinicaltrials.gov** – search using the number **NCT03846193**
- **clinicaltrialsregister.eu** – search using the number **2017-003712-39**

Other trials of **GT005** may appear on the public websites above. When there, search for **GT005** or **PPY988**, including CPPY988A12201 and CPPY988A12202.

Full clinical trial title: FOCUS: An open label first in human Phase I/II multicentre study to evaluate the safety, dose response and efficacy of GT005 administered as a single subretinal injection in subjects with Macular Atrophy due to AMD

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

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