NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of QBW251 in people with bronchiectasis

Thank you!

Thank you to the participants who took part in the clinical trial for **bronchiectasis**. Every participant helped the researchers learn more about the trial drug **QBW251**, also called icenticaftor.

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: CQBW251C12201

Novartis drug studied: QBW251, also known as icenticaftor

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 about the effects and safety of trial drug QBW251 in people with bronchiectasis.

Bronchiectasis is a long-term condition in which the lung's airways are permanently damaged. The damaged airways can't clear mucus out of the lungs as well as they should. This causes mucus to build up in the airways. Harmful bacteria grow in the mucus, raising the chance of infections and inflammation. Inflammation is part of the body's response to infection. Too much inflammation can be harmful.

Why is mucus in the airways?
The airways create a thick fluid called mucus to trap and get rid of germs from air that's breathed in. Then, the airways move the mucus out of the lungs to remove germs from the body by coughing.

QBW251 is a trial drug designed to lower inflammation and thin mucus in the airways. Researchers think it may help people with bronchiectasis.

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

- Did QBW251 lower the amount of harmful bacteria in the participants' lungs?
- What medical problems, also called adverse events, did the participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in February 2021 and ended in June 2023.

In June 2023, the trial ended early because the sponsor decided to stop all research on QBW251 in people with bronchiectasis. This was a business decision and not related to the safety of the trial drug.

Who was in this trial?

42 participants with bronchiectasis received treatment in this trial – 21 men and 21 women. Participants' ages ranged from 25 to 78 years. Their average age was 55 years.

The number of participants by race is shown below.

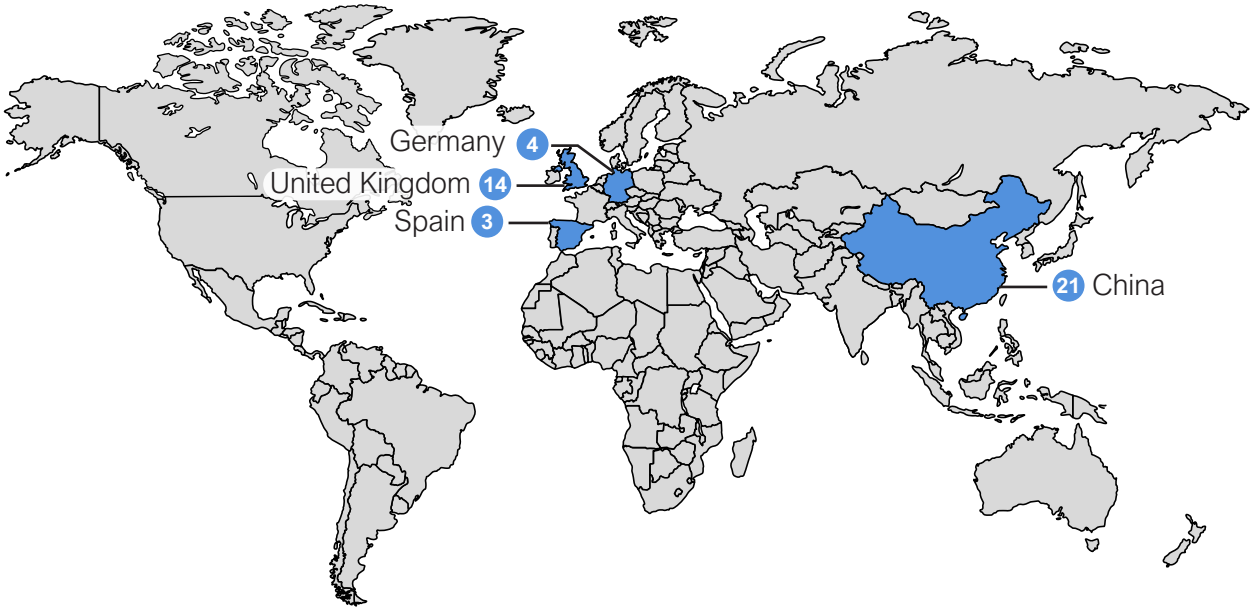
Race

21 Asian	21 White

The participants could take part in this trial if they:

- Did not have a history of liver disease
- Did not have certain cancers or a lung transplant within 5 years before they joined the trial
- Did not have certain heart problems

42 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?

The treatments in this trial were:

QBW251 – 300 milligrams (mg) taken by mouth as capsules twice a day.

Placebo – Taken by mouth as capsules twice a day. A placebo looks like the trial drug but does not have any trial drug in it. Using a placebo helps researchers better understand the effect of a trial drug.

Researchers randomly assigned participants to treatment groups using a computer.

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.

All participants could continue taking certain medicines for bronchiectasis.

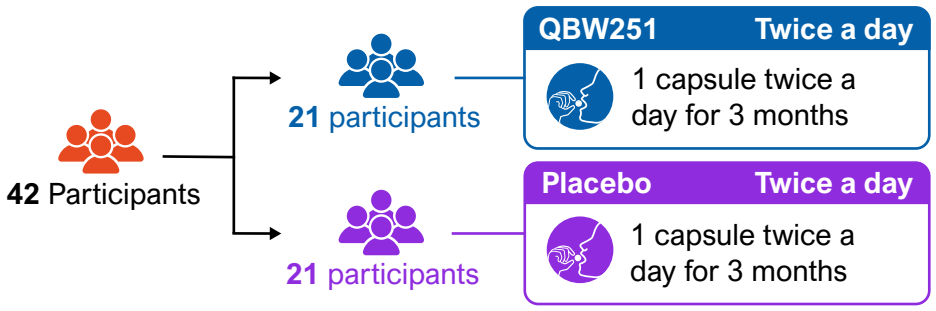
What happened during this trial?

Before treatment — About 6 weeks

Trial doctors checked the participants' health and bronchiectasis to make sure they could be in this trial.

During treatment — About 3 months

The graphic below shows how many participants were assigned each treatment.



Trial staff checked the participants' health and bronchiectasis throughout the trial.

After treatment — About 5 weeks

Participants returned to their trial site about 1 week after receiving their last dose of treatment for trial doctors to check their health and bronchiectasis.

Trial staff also called participants about 1 month after their last dose of treatment to check on their health.

What were the main results of this trial?

Did QBW251 lower the amount of harmful bacteria in the participants' lungs?

Because the trial ended early, researchers could not conclude if QBW251 lowered the amount of harmful bacteria in the participants' lungs compared to the placebo.

To learn this, trial staff took samples of the participants' **sputum**, which is mucus or thick fluid coughed up by the lungs.

The researchers measured the amount of harmful bacteria in the participants' sputum before treatment and after 3 months of treatment. Then, they compared these measures for participants who took QBW251 to those who took the placebo.

First, the researchers compared the amount of bacteria: **from** **Before** treatment **to** **After 3 months** of treatment

Then, they compared these measures: **from** Participants who took **QBW251** **to** Participants who took the **placebo**

The participants who took QBW251 had a little less bacteria in their sputum than those who took placebo after 3 months of treatment. However, because the trial ended early, the researchers could not conclude if this result was meaningful.

What were the other results of this trial?

Did QBW251 change other measures of bronchiectasis?

Because the trial ended early, researchers could not conclude if QBW251 changed other measures of bronchiectasis compared to the placebo.

The researchers also looked at these other measures of bronchiectasis before and after 3 months of trial treatment:

- How many participants had no harmful bacteria in their sputum
- Participants' answers to questions about their bronchiectasis symptoms and quality of life
- A sign of inflammation in the blood
- How many participants had to use a rescue inhaler less often
- How easily participants could breathe
- Imaging tests of the participants' airways

What medical problems, also called adverse events, did the participants have during this trial?

Trial doctors keep track of all **adverse events** that happen in trials, 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 until 30 days after the last dose of trial 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.

Most of the participants (32 of 42) had adverse events. 2 participants had adverse events that were considered serious. No participants died during the trial. 1 participant left the trial due to an adverse event. The researchers concluded there were no new safety concerns for QBW251 for this trial.

How many participants had adverse events?

Participants who:	QBW251 21 participants	Placebo 21 participants
Had at least 1 **serious adverse event**	**2 of 21** 10%	**0 of 21** 0%
Had at least 1 **other adverse event**	**14 of 21** 67%	**13 of 21** 62%
Left the trial due to an adverse event	**1 of 21** 5%	**0 of 21** 0%
Died during the trial	**0 of 21** 0%	**0 of 21** 0%

What serious adverse events did the participants have?

2 participants had serious adverse events. No participants died.

In the QBW251 group, these serious adverse events happened in 1 participant each:

- **Infection from bronchiectasis** | Infective exacerbation of bronchiectasis
- **A type of kidney disease** | Tubulointerstitial nephritis

What other adverse events did the participants have?

27 participants had other adverse events.

The table below shows the other adverse events that happened in 5% or more of the participants. This is **4 or more** participants across both groups. Additional adverse events happened in fewer participants.

	QBW251 21 participants	**Placebo** 21 participants
Bronchiectasis that got worse Bronchiectasis	8 of 21 38%	4 of 21 19%
Feeling weak and tired Fatigue	3 of 21 14%	5 of 21 24%
COVID-19	3 of 21 14%	1 of 21 5%
Fever Pyrexia	3 of 21 14%	1 of 21 5%
Headache	2 of 21 10%	2 of 21 10%
Infection in the ear, nose, throat, or airways Upper respiratory tract infection	2 of 21 10%	2 of 21 10%

What was learned from this trial?

Researchers learned about the effects and safety of QBW251 in people with bronchiectasis. The trial ended early because the sponsor decided to stop all research on QBW251 in people with bronchiectasis. This was a business decision and not related to the safety of the trial drug.

Because the trial ended early, researchers were unable to conclude if QBW251:

- Lowered harmful bacteria in the participants' lungs compared to the placebo
- Changed other measures of bronchiectasis compared to the placebo

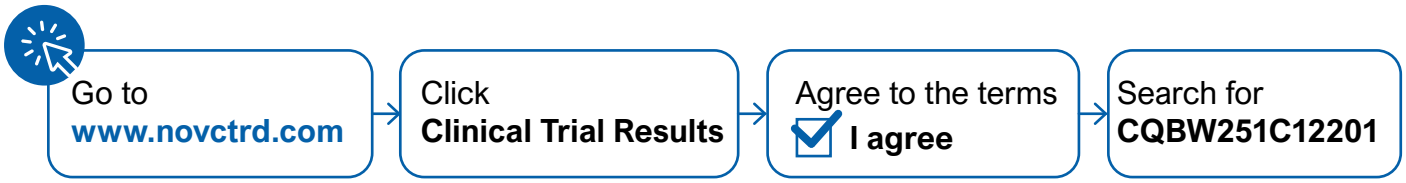
The researchers concluded that there were no new safety concerns for QBW251 for this trial.

When this summary was written, the sponsor had no plans for future trials of QBW251 in people with bronchiectasis.

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 **NCT04396366**
- clinicaltrialsregister.eu/ctr-search/search – search using the number **2019-002840-26**

Full clinical trial title: A randomized, subject- and investigator-blinded, placebo-controlled, parallel group study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of QBW251 in patients with bronchiectasis.

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

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www.novartis.com/clinicaltrials