Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis
Drug Studied: QBW251
Protocol: CQBW251X2201

Thank you!

Thank you for taking part in the clinical trial for the drug QBW251. You and all of the patients helped researchers learn more about how QBW251 works in people with chronic obstructive pulmonary disease, also called COPD.

Novartis sponsored this trial and thinks it is important to share the results of the trial with you and the public. An independent, non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your important role in medical research.

If you participated in the trial and have questions about the results, please speak with the doctor or staff at your trial site.

What has happened since the trial ended?

You were in this trial for about 3 months. But, the entire trial took almost 2 years to finish. This is because patients started and stopped at different times. The trial started in April 2015 and ended in January 2017. The trial included 92 patients from 16 trial sites in Poland and the United States.

The sponsor reviewed the data collected when the trial ended and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers are looking for a better way to treat COPD in people who smoke or used to smoke for at least 10 years. Before a drug can be approved for patients to take, researchers do many clinical trials to find out how well it works and how safe it is. This information is important to know before other trials can be done that help find out if QBW251 improves the health of people with COPD.

In this trial, the researchers wanted to find out if QBW251 works in a small number of patients with COPD and chronic bronchitis. Patients with COPD and chronic bronchitis have inflammation and extra mucus that builds up and traps air in the airways of their lungs. This “trapped air” cannot be breathed out. This makes it harder to breathe and can damage the lungs over time. Most people who develop COPD are current or former smokers.

Researchers think the mucus caused by COPD may be harder to clear out of the lungs because of a protein that does not work well. The protein is called cystic fibrosis transmembrane receptor, also called CFTR. Researchers think cigarette smoke causes this problem with CFTR. QBW251 may help CFTR work better and reduce the amount of mucus built up in the lungs so patients can breathe easier.

The researchers compared QBW251 to a placebo. A placebo looks like the trial drug but does not have any medicine in it. Using a placebo helps researchers better understand the actual effect of a trial drug. The main questions the researchers wanted to answer in this trial were:

- Did QBW251 help the patients’ lungs work more evenly?
- Did QBW251 help the patients’ lungs in other ways?
- How much QBW251 got into the blood?
- What medical problems did the patients have during the trial?

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of women and men like you. The patients in this trial were 46 to 75 years old. They were all current smokers or former smokers with COPD and chronic bronchitis.

This was a “double-blind” trial. This means none of the patients, trial staff, or sponsor staff knew what treatment each patient took. Some trials are done this way because knowing what treatment the patients are taking can affect the results of the trial. Doing a trial this way helps make sure the results are looked at fairly.

A computer program was used to randomly choose the treatment each patient took. Researchers do this so that comparing the results of each treatment is done as fairly as possible. When the trial ended, the research sponsor found out which treatment patients took so they could create a report of the trial results.

What happened during the trial?

Before the trial treatment started, the trial doctors did tests to make sure you could take part in the trial. This lasted up to 4 weeks. Then, you took a placebo twice a day for 2 weeks. This part of the trial was "single-blind". This means that you and the other patients did not know you were taking the placebo, but the trial doctors did. The trial doctors may have asked you to stop taking certain medicines. This part of the trial helped the researchers make sure any effects they saw during the treatment part of the trial were due to the trial drug and not due to other reasons.

During the trial:

- 64 patients took QBW251 twice a day for 4 weeks
- 28 patients took the placebo twice a day for 4 weeks
- All patients took pills of QBW251 or the placebo by mouth
- All patients visited the trial site about 8 times

The planned dose of QBW251 was 450 milligrams, also called mg. Shortly after the trial started, the researchers learned from other QBW251 trials that a lower dose can be used. So, the researchers lowered the dose from 450 mg to 300 mg.

- 2 patients took 450 mg of QBW251
- 62 patients took 300 mg of QBW251

To check your overall health and your lungs, the trial staff:

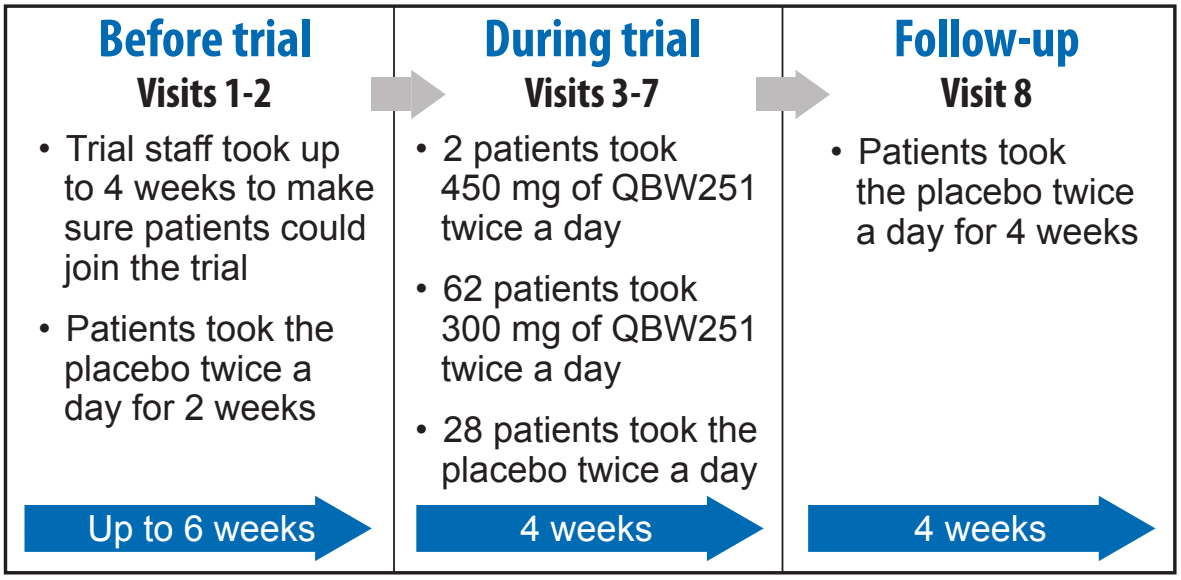
- checked your heart health and your COPD symptoms before and after taking the trial treatment
- checked how well your lungs were working
- took blood, saliva, and urine samples
- asked questions about how you felt and any other medicines you were taking

There was a follow-up period that lasted 4 weeks. All the patients took a placebo twice a day for 4 weeks. This way, the researchers would know if any long term effects they saw were due to the trial drug and not due to other reasons.

During the follow-up period, the trial staff:

- checked your COPD symptoms and how well your lungs were working
- checked how you were feeling and what medicines you were taking

The chart below shows how the trial was done.



What were the results of the trial?

This is a summary of the overall results from this trial. The individual results of each patient might be different and are not in this summary. The results from several trials are needed to decide which treatments work best and are safest. Other trials may provide new information or different results. Always talk to a doctor before making any treatment changes.

The results for some patients are not included in the results below. This is because:

- some patients did not complete 28 days of treatment
- for some patients, too much time passed between their last dose and their visit on Day 29

Did QBW251 help the patients' lungs work more evenly?

No. QBW251 did not help the patients' lungs work more evenly. The researchers used a test that measured how evenly air got in and out of the lungs. The test is called the lung clearance index. The test was done both before the patients took the first dose and 28 days after the patients started treatment. Each patient was given a score based on this test. Lower scores meant the patients' lungs worked more evenly.

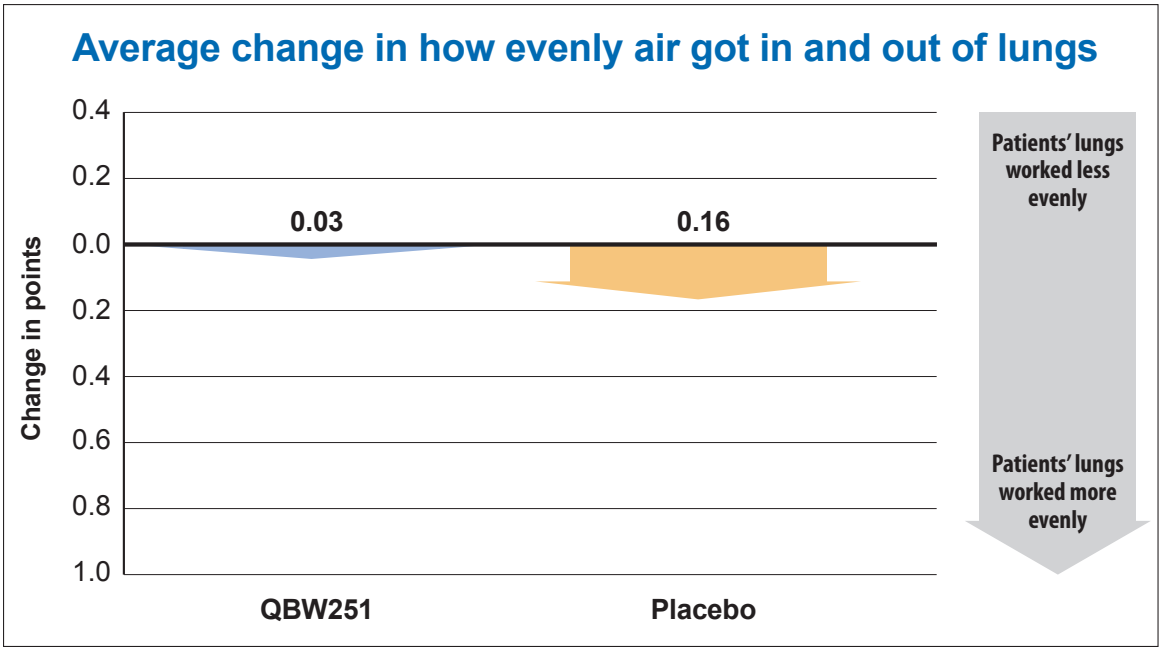
The difference between the patients who took QBW251 and the patients who took the placebo was too small for the researchers to know if QBW251 helped patients' lungs work more evenly than the placebo. The difference seen could have been due to chance.

After 28 days of treatment, the researchers found that:

- Patients who took QBW251 had an average decrease in points of 0.03.
- Patients who took the placebo had an average decrease in points of 0.16.

Overall, the researchers found that the lungs of the patients who took QBW251 did not work more evenly after 28 days of treatment compared to patients who took the placebo.

The figure below shows the changes in how evenly air got in and out of the lungs after 28 days of treatment.



Did QBW251 help the patients' lungs in other ways?

During the treatment period, the researchers learned if QBW251 helped patients with COPD and chronic bronchitis more than the placebo did.

The researchers measured 5 main things after 28 days of treatment to learn:

1. how much air the patients breathed out in 1 second
2. the total amount of air the patients could breathe out
3. the total amount of air the patients' lungs could hold
4. how much air got trapped in the lungs after the patients breathed out
5. how well the patients' lungs moved a gas called carbon monoxide from the air into the blood

1. How much air the patients breathed out in 1 second

The researchers found that QBW251 increased how much air the patients could breathe out in 1 second. Before and after treatment, the researchers measured how much air the patients could breathe out in 1 second. If the average change in this amount had increased after 28 days of treatment, this meant that the patients could breathe out more air in 1 second. This difference was measured in liters, also called L. The researchers tested this before and after patients used an inhaler to make sure the changes were due to the trial drug.

The researchers found that:

Average change in the amount of air patients breathed out in 1 second

	QBW251 (51 patients)	Placebo (23 patients)
Before the inhaler	0.04 L	-0.02 L

	QBW251 (51 patients)	Placebo (24 patients)
After the inhaler	0.05 L	-0.02 L

2. The total amount of air the patients could breathe out

The researchers found that QBW251 increased the total amount of air that the patients could breathe out. Before and after treatment, the researchers measured how much air the patients could breathe out after taking a deep breath. If the average change in this amount had increased after 28 days of treatment, this meant that the patients could breathe out more air. The researchers also tested this before and after the patients used an inhaler to make sure the changes were due to the trial drug.

The researchers found that:

Average change in the total amount of air patients could breathe out

	QBW251 (51 patients)	Placebo (23 patients)
Before the inhaler	0.07 L	0.01 L

	QBW251 (51 patients)	Placebo (24 patients)
After the inhaler	0.03 L	0.01 L

3. The total amount of air the patients' lungs could hold

Overall, the researchers learned that the patients who took QBW251 could take a deeper breath compared to the patients who took the placebo. The researchers measured the total amount of air the patients could breathe in. If the average change in this amount had increased after 28 days of treatment, this meant that the patients could take a deeper breath.

After 28 days of treatment, the researchers found that:

- The lungs of the patients who took QBW251 could hold 0.01 L more air on average.
- The lungs of the patients who took the placebo could hold 0.07 L less air on average.

4. How much air got trapped in the lungs after the patients breathed out

Overall, the researchers learned that the patients who took QBW251 had more trapped air in their lungs after breathing out compared to the patients who took the placebo.

This happened when the patients breathed out as much air as they could, and when they breathed out normally. But, the differences between the treatment groups were too small for the researchers to know if QBW251 caused these differences. These differences may have been due to chance.

The researchers measured how much air was trapped in the patients' lungs after the patients breathed out. They measured this when the patients breathed out as much air as they could and when the patients breathed out normally. If the average change in this amount increased after 28 days of treatment, this meant that more air got trapped in the patients' lungs after breathing out.

The researchers found that when the patients breathed out as much air as they could after 28 days of treatment:

- On average, 0.03 L more air got trapped in the lungs of the patients who took QBW251.
- On average, 0.02 L less air got trapped in the lungs of the patients who took the placebo.

The researchers found out that when patients breathed out normally after 28 days of treatment:

- On average, 0.01L more air got trapped in the lungs of patients who took QBW251.
- On average, 0.02L less air got trapped in the lungs of patients who took the placebo.

5. How well the patients' lungs moved a gas called carbon monoxide from the air into the blood

Overall, the researchers learned that the patients who took QBW251 could not move more carbon monoxide into the blood than the patients who took the placebo. But, the difference between the treatment groups was too small for the researchers to know if QBW251 decreased the movement of carbon monoxide into the blood. This difference may have been due to chance.

The researchers measured how much carbon monoxide was moved from the lungs into the blood. This measurement gives researchers an idea of how well the lungs can move oxygen from the lungs into the blood. If the average change in this amount had increased after 28 days of treatment, this meant that the patients' lungs could move more oxygen into their blood. This difference was measured in milliliters per minute per millimeter of mercury, also called mL/min/mmHg.

The researchers found that:

- The patients who took QBW251 decreased the amount of carbon monoxide that moved from their lungs into their blood by 0.9 mL/min/mmHg on average.
- The patients who took the placebo decreased the amount of carbon monoxide that moved from their lungs into their blood by 0.3 mL/min/mmHg on average.

How much QBW251 got into the blood?

The researchers wanted to know how much QBW251 got into the blood. This information is important because it helps the researchers decide when a dose should be given to patients and what dose is safe and effective for patients.

After 28 days of treatment, the researchers found that:

- The amount of QBW251 in the blood was higher in the 2 patients who took 450 mg compared to the patients who took 300 mg.
- On average, QBW251 reached expected and steady levels in the blood.
- After a single dose of QBW251, it took about 1.3 hours for QBW251 to reach its highest amount in the blood.
- After multiple doses of QBW251, it took about 2.0 hours for QBW251 to reach its highest amount in the blood.

What medical problems did patients have during the trial?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or the patients need 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 a medical problem. During a trial, all medical problems are reported and written down, whether or not they are caused by the trial drug. So, when new drugs are being studied, researchers keep track of all medical problems that patients have.

This section is a summary of the adverse events that happened during this trial.

How many patients had adverse events?

Adverse events happened about as often in the patients who took QBW251 compared to the patients who took the placebo. Five patients who took QBW251 left the trial due to adverse events compared to 1 patient who took the placebo.

The table below shows how many patients had adverse events during the trial.

Adverse events during this trial

	QBW251 (Out of 64 patients)	Placebo (Out of 28 patients)	Total (Out of 92 patients)
How many patients had adverse events?	40.6% (26)	39.3% (11)	40.2% (37)
How many patients had serious adverse events?	6.3% (4)	0.0% (0)	4.3% (4)
How many patients left the trial because of adverse events?	7.8% (5)	3.6% (1)	6.5% (6)

What were the most common serious adverse events?

Overall, only the patients taking QBW251 had serious adverse events.

The serious adverse event of a stroke happened during the follow-up period. All other serious adverse events happened during the treatment period. The doctors thought the vomiting and low potassium in the blood might have been related to QBW251.

The table below shows how many patients had serious adverse events during the trial.

Serious adverse events during this trial

Serious adverse event	QBW251 (Out of 64 patients)	Placebo (Out of 28 patients)	Total (Out of 92 patients)
Fluid in the lungs preventing oxygen from entering the blood	1.6% (1)	0.0% (0)	1.1% (1)
Low potassium in the blood	1.6% (1)	0.0% (0)	1.1% (1)
Pneumonia (lung infection)	1.6% (1)	0.0% (0)	1.1% (1)
Stroke	1.6% (1)	0.0% (0)	1.1% (1)
Vomiting	1.6% (1)	0.0% (0)	1.1% (1)
Worsening of COPD	1.6% (1)	0.0% (0)	1.1% (1)

What were the most common adverse events?

Worsening of COPD was the most common adverse event in both treatment groups. The table below shows the most common adverse events that happened in 2 or more patients total. Other adverse events happened in fewer patients.

Most common adverse events during this trial

Adverse event	QBW251 (Out of 64 patients)	Placebo (Out of 28 patients)	Total (Out of 92 patients)
Worsening of COPD	6.3% (4)	7.1% (2)	6.5% (6)
Diarrhea	3.1% (2)	7.1% (2)	4.3% (4)
Common cold	3.1% (2)	3.6% (1)	3.3% (3)
Difficulty breathing	3.1% (2)	3.6% (1)	3.3% (3)
Nausea	1.6% (1)	7.1% (2)	3.3% (3)
Chest pain not related to the heart	3.1% (2)	0.0% (0)	2.2% (2)
Cough	3.1% (2)	0.0% (0)	2.2% (2)
Cough with mucus	3.1% (2)	0.0% (0)	2.2% (2)
Vomiting	3.1% (2)	0.0% (0)	2.2% (2)
Constipation	1.6% (1)	3.6% (1)	2.2% (2)

For more information about the adverse events in this trial, please see the scientific summary that can be found on the websites noted at the end of the summary.

How has this trial helped patients and researchers?

This trial helped researchers better understand if QBW251 works in patients with COPD who also have chronic bronchitis. The results presented here are for a single trial. Researchers look at the results of many trials to decide which treatments work best and are safest. This summary shows only the main results from this 1 trial. Other trials may provide new information or different results. It takes volunteers in many trials all around the world to advance medical science.

Where can I learn more about this trial and future trials?

More information about the results of this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website (www.novctrd.com). Once on the site, click **"Read more"** under **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **"CQBW251X2201"** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the trial doctor or staff at your trial site.

You can find more information about this trial on websites listed below.

- www.clinicaltrials.gov Once you are on the website, type **"NCT02449018"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2014-001530-28"** in the search box and click **"Search"**.

If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com. Search for **"QBW251"**.

Short Trial Title: A Safety, Tolerability, and Efficacy Study with QBW251 in COPD Patients with QBW251

Full Trial Title: A randomized, double blind, placebo controlled study to assess the safety, tolerability, pharmacokinetics, and efficacy of multiple doses of QBW251 in patients with COPD

Thank you

As a clinical trial patient, you belong to a large community of patients around the world. You helped researchers answer important health questions and test new medical treatments.

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