Clinical Trial Results

NOVARTIS

Research Sponsor:	Novartis
Location of Headquarters:	Basel, Switzerland
Drug Studied:	QBW251
Protocol #:	CQBW251X2101
Full Trial Title:	A Randomized, Double-blind, Placebo-controlled Study to Assess the Safety, Tolerability, Pharmacokinetics, and Preliminary Pharmacodynamics of Single and Multiple Ascending Doses of QBW251 in Healthy Subjects, and Multiple Doses in Cystic Fibrosis Patients
Full Scientific Summary:	www.novctrd.com
Trial Date:	July 2012 to November 2015

Thank you!

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

Thank you for taking part in the clinical trial for the drug QBW251. You helped researchers learn more about how QBW251 works in both healthy people and people with cystic fibrosis. This trial started in July 2012 and ended in November 2015.

Novartis, the sponsor of this trial, thanks you for your help and thinks it is important for you to know the results of your trial. 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 have questions about the results, please speak with the doctor, research nurse, or other team member at your trial site.

What's happened since the trial ended?

You were in this trial for up to 6 weeks, but the trial took close to 3.5 years to complete. The trial included 153 participants from 28 sites in Europe and the United States. When the trial ended in November 2015, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers were looking for a better way to treat cystic fibrosis, or CF. This is a disease that causes thick, sticky mucus to build up in the lungs, digestive tract, and other areas of the body. This can result in life-threatening lung infections and other serious problems.

People with CF have a protein in the body called the cystic fibrosis transmembrane conductance regulator, or CFTR, that does not work well. When CFTR does not work well, the amount of salt and water in the lungs and other parts of the body are not balanced, which can lead to serious health problems. In this trial, researchers wanted to study a drug called QBW251, which is thought to help CFTR work better. Researchers compared QBW251 with a placebo. A placebo looks like medicine, but does not have any real medicine in it.

In your trial, researchers wanted to know:

- What medical problems did participants have during the trial?
- Did QBW251 increase participants' lung function more than the placebo?
- How much QBW251 got into the blood, and did food affect this amount?
- Did QBW251 help in any other ways?

To answer these questions, researchers asked for the help of men and women like you. The participants in this trial were 18 to 56 years old. This trial included both healthy volunteers as well as volunteers with CF, also known as patients, who had tested positive for a CFTR mutation. Many trials include both healthy volunteers and patients so that researchers can compare the results between the 2 groups.

What kind of trial was this?

In this trial, participants took either QBW251 or a placebo. This trial was "double-blind". This means that none of the participants, trial doctors, or staff knew what treatment each participant received.

Some trials are done this way because knowing what treatment each participant is getting can affect the results of the trial. This way, it ensures that the results are looked at fairly. When the trial ended, the research sponsor found out which treatment participants received so they could create a report of the trial results.

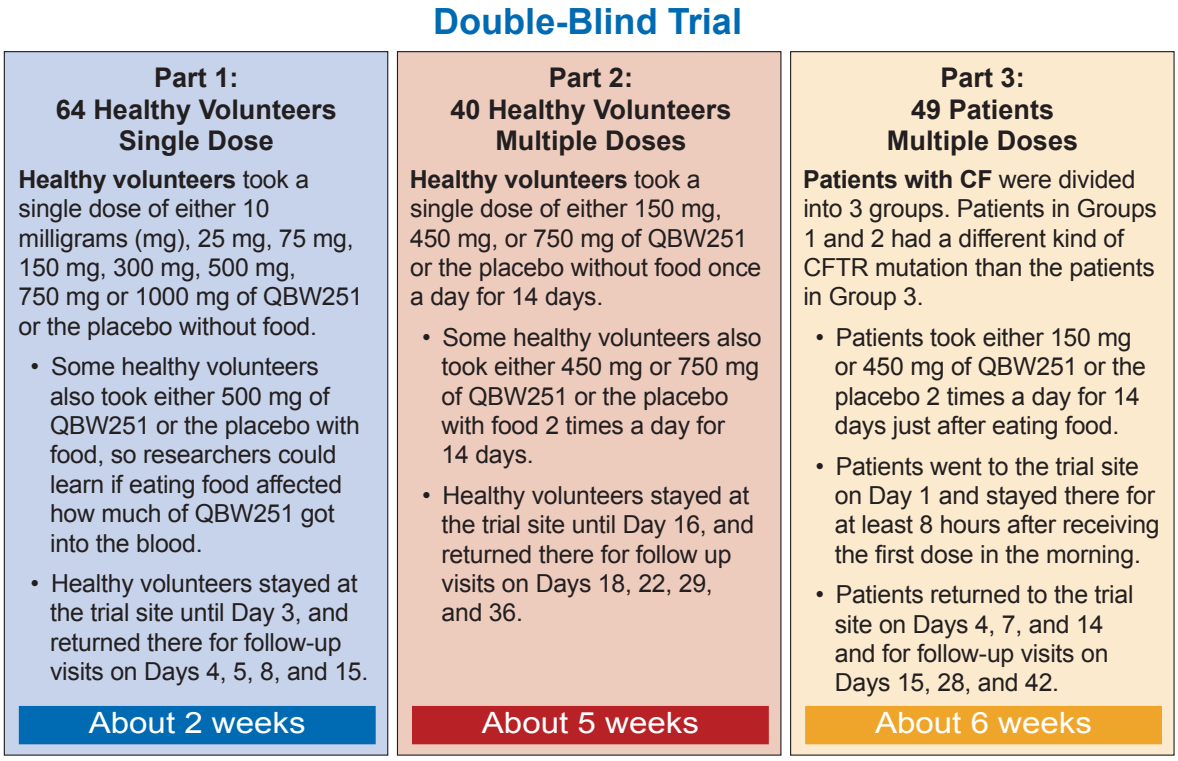
What happened during the trial?

Trial doctors first did a full checkup of all participants to make sure they could join the trial.

Participants were randomly assigned, like flipping a coin, to take either QBW251 or the placebo.

This trial took place in 3 parts. Each trial participant was enrolled in only 1 part of the trial.

The figure below shows the 3 parts of the trial.



Throughout the trial, the doctors checked the blood pressure, pulse rate, and breathing rate of each participant. They also collected blood and urine samples from each participant. During Part 3, trial doctors also collected mucus and sweat samples from each patient. They also checked each patient's lung function, and asked about their CF symptoms.

Part 3 patients were divided into 3 groups. All Part 3 patients had CF-causing mutations. Group 1 and 2 patients had 2 different CF-causing mutations. Group 3 patients had 2 specific CF-causing mutations that were the same.

What were the results of the trial?

This is a summary of the overall results of your trial, not your individual results. The results presented here are for a single trial. Researchers look at the results of many studies to decide which drugs work best and are safest for patients. Other trials may provide new information or different results. You should not make changes to your treatment based on the results of a single trial without first talking to your doctor.

What medical problems did participants have during the trial?

A lot of research is needed to know whether a drug causes a medical problem. So, when new drugs are being studied, researchers keep track of all medical problems that patients have. These medical problems are called "adverse events". An adverse event is any sign or symptom that may or may not be caused by the trial drug.

How many participants had adverse events during the trial?

The tables below show how many participants had adverse events during this trial.

The tables below include all participants who took QBW251 and all participants who took the placebo.

Adverse Events in Part 1 (Healthy Volunteers)

	QBW251 10 mg (out of 6 healthy volunteers)	QBW251 25 mg (out of 6 healthy volunteers)	QBW251 75 mg (out of 6 healthy volunteers)	QBW251 150 mg (out of 6 healthy volunteers)	QBW251 300 mg (out of 6 healthy volunteers)	QBW251 500 mg (out of 6 healthy volunteers)
How many healthy volunteers had adverse events?	3 (50.0%)	2 (33.3%)	0 (0%)	1 (16.7%)	2 (33.3%)	2 (33.3%)
	QBW251 500 mg with food (out of 5 healthy volunteers)	QBW251 750 mg (out of 6 healthy volunteers)	QBW251 1000 mg (out of 6 healthy volunteers)	Placebo (out of 16 healthy volunteers)	All groups combined (out of 64 healthy volunteers)	
How many healthy volunteers had adverse events?	1 (20.0%)	1 (16.7%)	4 (66.7%)	8 (50.0%)	24 (37.5%)	

Adverse Events in Part 2 (Healthy Volunteers)

	QBW251 150 mg (out of 6 healthy volunteers)	QBW251 400 mg (out of 6 healthy volunteers)	QBW251 750 mg (out of 6 healthy volunteers)	QBW251 450 mg twice daily (out of 6 healthy volunteers)	QBW251 750 mg twice daily (out of 6 healthy volunteers)	Placebo (out of 10 healthy volunteers)	All groups combined (out of 40 healthy volunteers)
How many healthy volunteers had adverse events?	3 (50.0%)	6 (100.0%)	3 (50.0%)	6 (100.0%)	4 (66.7%)	7 (70.0%)	29 (72.5%)

Adverse Events in Part 3 (Patients with CF)

	QBW251 150 mg twice daily (out of 6 patients) (Group 1)	QBW251 450 mg twice daily (out of 12 patients) (Group 2)	QBW251 450 mg twice daily (out of 19 patients) (Group 3)	Placebo (out of 12 patients) (Groups 1, 2 and 3)	All groups combined (out of 49 patients)
How many patients had adverse events?	6 (100.0%)	8 (66.7%)	18 (94.7%)	8 (66.7%)	40 (81.6%)

Did any participants have serious adverse events?

An adverse event is called “serious” when it is life-threatening, causes lasting problems, or leads to hospitalization. No deaths occurred during this trial. Some participants experienced serious adverse events in Part 3 of the trial.

Three patients in Part 3 experienced a serious adverse event - 1 patient each in Groups 1, 2, and 3. The serious adverse events were sinus infection in 1 patient and increased difficulty in breathing in 2 patients. But the trial doctors did not think that any of the serious adverse events were related to the trial drug.

What were the most common non-serious adverse events?

In Part 1, headache and dizziness were the only non-serious adverse events that happened in at least 7% of all healthy volunteers in the trial. This happened in:

- In the QBW251 1000 mg group, 2 out of 6 (33.3%) healthy volunteers each had headache and dizziness.
- In the QBW251 300 mg group, 1 out of 6 (16.7%) healthy volunteers had headache.
- In the placebo group, 2 out of 16 (12.5%) healthy volunteers had headache, and 3 out of 16 (18.8%) healthy volunteers had dizziness.

The tables below show the most common non-serious adverse events (in at least 7% of all participants) in Parts 2 and 3 of this trial.

Most Common Non-serious Adverse Events in Part 2 (Healthy Volunteers)

Non-serious Adverse Event	QBW251 150 mg (out of 6 healthy volunteers)	QBW251 400 mg (out of 6 healthy volunteers)	QBW251 750 mg (out of 6 healthy volunteers)	QBW251 450 mg twice daily (out of 6 healthy volunteers)	QBW251 750 mg twice daily (out of 6 healthy volunteers)	Placebo (out of 10 healthy volunteers)	All groups combined (out of 40 healthy volunteers)
Headache	0 (0%)	1 (16.7%)	0 (0%)	1 (16.7%)	2 (33.3%)	4 (40.0%)	8 (20.0%)
Passing gas	0 (0%)	0 (0%)	0 (0%)	4 (66.7%)	0 (0%)	2 (20.0%)	6 (15.0%)
Cough	0 (0%)	1 (16.7%)	0 (0%)	4 (66.7%)	0 (0%)	0 (0%)	5 (12.5%)
Dizziness	0 (0%)	0 (0%)	0 (0%)	1 (16.7%)	0 (0%)	2 (20.0%)	3 (7.5%)

Most Common Non-serious Adverse Events in Part 3 (Patients with CF)

Non-serious Adverse Event	QBW251 150 mg BID twice daily (out of 6 patients) (Group 1)	QBW251 450 mg BID twice daily (out of 12 patients) (Group 2)	QBW251 450 mg BID twice daily (out of 19 patients) (Group 3)	Placebo (out of 12 patients) (Groups 1, 2 and 3)	All groups combined (out of 49 patients)
Increased mucus	3 (50.0%)	0 (0%)	5 (26.3%)	2 (16.7%)	10 (20.4%)
Cough	1 (16.7%)	1 (8.3%)	4 (21.1%)	2 (16.7%)	8 (16.3%)
Headache	1 (16.7%)	3 (25.0%)	4 (21.1%)	0 (0%)	8 (16.3%)
Worsening of CF with infection in the lungs	1 (16.7%)	1 (8.3%)	3 (15.8%)	3 (25.0%)	8 (16.3%)
Nausea	1 (16.7%)	4 (33.3%)	2 (10.5%)	0 (0%)	7 (14.3%)
Tiredness	0 (0%)	3 (25.0%)	2 (10.5%)	0 (0%)	5 (10.2%)

For a full list of the adverse events that occurred in this trial, please refer to the full scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

Did QBW251 increase participants' lung function more than the placebo?

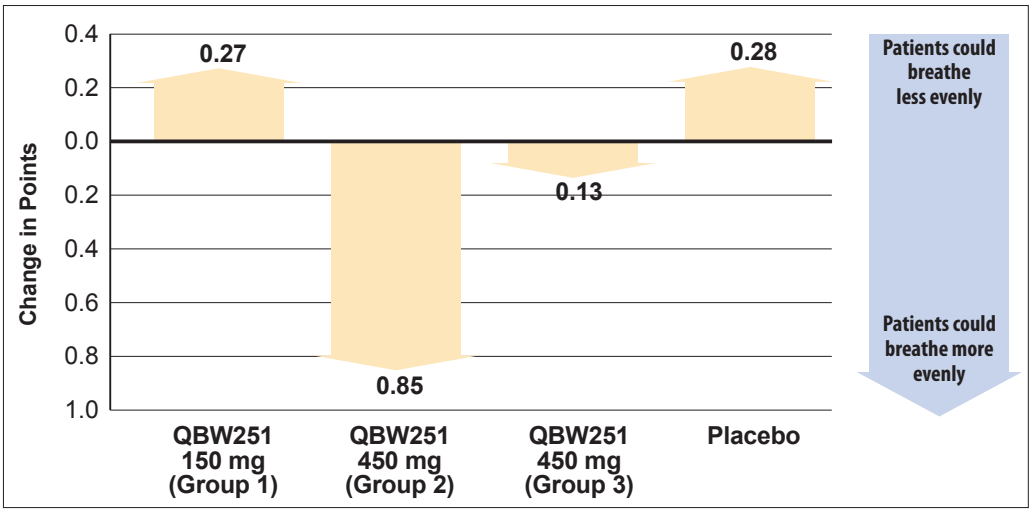
During Part 3, researchers learned if QBW251 increased lung function more than the placebo in patients with CF. They measured 2 things to learn this:

- How evenly air got in and out of the lungs
- How much air patients exhaled in 1 second

How evenly air got in and out of the lungs

Researchers used a test called the lung clearance index that measured how well the lungs could clear air. Each patient was given a score based on this test, which was done both before treatment started, and again on Day 15 after treatment started. The lower the score, the more evenly patients could breathe. The figure below shows the changes in how evenly air got in and out of the lungs by Day 15.

Average Change in How Evenly Air Got In and Out of Lungs



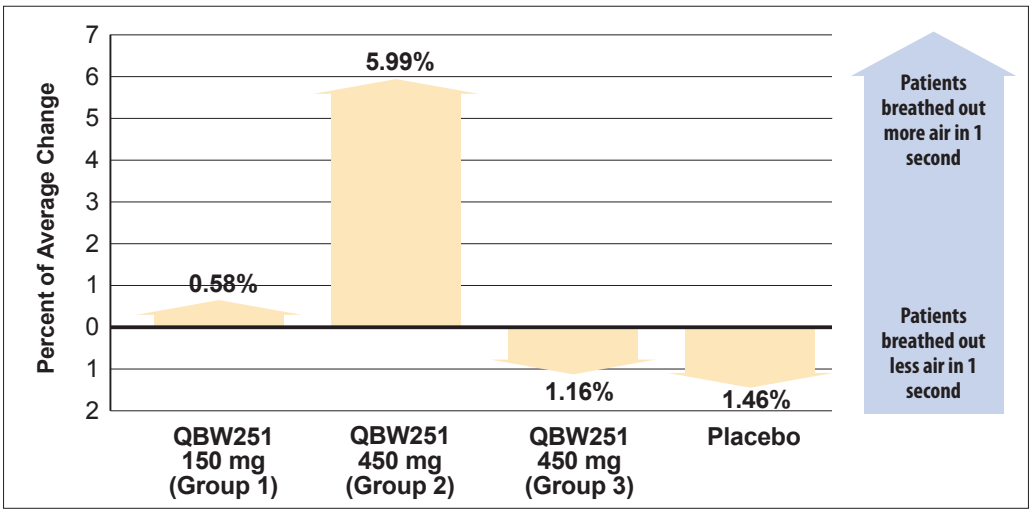
Overall, researchers found that patients in Group 2 who took 450 mg QBW251 could breathe more evenly after Day 15. For the other treatment groups, the results did not show that one treatment was better than the other.

How much air patients exhaled in 1 second

Researchers also tested how much air patients could breathe out in 1 second. They tested this both before treatment started, and again on Day 15 after treatment started. If the average change in this amount had increased by Day 15, this meant that patients could breathe out more air in 1 second.

The figure below shows the changes in how much air patients breathed out in 1 second by Day 15.

Average Change in How Much Air Patients Breathed Out in 1 Second



Overall, researchers found that patients in Group 2 had increases in the amount of air they could breathe out by Day 15. For the other treatment groups, the results did not show that one treatment was better than the other.

How much QBW251 got into the blood, and did food affect this amount?

Researchers wanted to know if patients who took higher doses of QBW251 had more QBW251 stay in the blood. The amount of QBW251 in the blood was higher for patients who took more QBW251. This was true for all parts of the trial. When healthy volunteers in Part 1 took QBW251 with a high-fat meal, the total amount of QBW251 in the blood was reduced by about 20%.

Did QBW251 help in other ways?

Quality of Life Scores

In Part 3 of the trial, researchers also used a survey to ask patients how they were feeling and how the trial drugs affected their CF symptoms. An increase in the survey score after taking treatment meant that a patient had a better quality of life than he or she had before treatment started. After 2 weeks of treatment, researchers found that:

- Patients in Groups 1 and 2 had bigger increases in their survey scores than patients in the placebo group.
- Patients in Group 3 had similar decreases in their survey scores as patients in the placebo group.

Where can I learn more about this trial?

Researchers look at the results of many trials to decide which drugs work best and are safest for patients. It takes many volunteers in many trials all around the world to advance medical science.

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). Once on the site, click **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **CQBW251X2101** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the doctor or staff at your trial site.

This trial was also registered on the following websites:

- Clinicaltrials.gov - **National Clinical Trial #** NCT02190604
- https://www.clinicaltrialsregister.eu/ctr-search - **EU Clinical Trial #** 2011-005085-37

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health.

Thank you for the gift of your participation in clinical research.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical trials, nor is it involved in conducting clinical trials.

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