Clinical Trial RESULTS

Roche

Research Sponsor: F. Hoffman-LaRoche, Ltd.
Drug Studied: Bitopertin (RO4917838)
National Clinical Trial #: NCT01192867
Protocol #: NN25310 [FlashLyte]
Study Date: October 2010 to May 2014

Thank you!

As a clinical study participant, you belong to a large community of people who take part in research around the world. You help researchers answer important health questions and discover new medical treatments.

Thank you for taking part in the clinical study for the study drug bitopertin (RO4917838). Your study began in October 2010 and finished in May 2014. Bitopertin was studied for use in people with schizophrenia. You and 625 other participants helped researchers find out how bitopertin works for people with negative symptoms of schizophrenia.

F. Hoffman-LaRoche, the sponsor of this study, thinks it is important for you to know the results. The sponsor asked an independent non-profit organization called CISCRP to prepare this summary of the results for you. We hope it helps you understand and feel proud of 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 study site.

WHAT'S HAPPENED SINCE MY STUDY ENDED?

You were in the study for up to 56 weeks, or longer if you chose to keep taking the study drug. The entire study took more than 3 years to finish and included participants from 14 countries around the world. The sponsor published the results from this study in an academic journal in April 2014. This is a summary of results from the study.

WHY WAS THE RESEARCH NEEDED?

Researchers were looking for a better way to treat symptoms of schizophrenia. The primary medicines for schizophrenia help treat "positive symptoms," such as believing things that are not true and seeing things that are not really there. But these medicines may not help "negative symptoms," such as losing interest in work or social activities, having trouble talking to other people or taking care of yourself, and having trouble enjoying life or expressing your feelings. So, researchers wanted to learn if the study drug could help with "negative symptoms" of schizophrenia.

Researchers wanted to know if taking bitopertin with antipsychotics could reduce negative symptoms. The main questions they wanted to answer were:

- Did bitopertin reduce negative symptoms of schizophrenia in the first 24 weeks of the study?
- Was bitopertin safe?

All of the participants in your study were at least 18 years old and had no major changes in their schizophrenia for at least 6 months. All participants were taking antipsychotics and had mainly negative symptoms that did not go away with antipsychotics.

WHAT KIND OF STUDY WAS THIS?

This was a "double-blind" study. This means none of the participants or study staff knew who was taking the study drug and who was taking a placebo. A placebo looks like the study drug, but does not contain any real medicine. Researchers use a placebo to learn if the study drug works better than no medicine at all.

WHAT HAPPENED DURING THE STUDY?

There were 3 groups of participants in the study:

Group 1 had 208 participants who took a 10 milligram (mg) pill of bitopertin.

Group 2 had 208 participants who took a 20 milligram (mg) pill of bitopertin.

Group 3 had 210 participants who took a placebo. The placebo was a pill that looked like bitopertin but contained no real medicine.

The list below tells you about the 3 parts of the study in the order they happened:

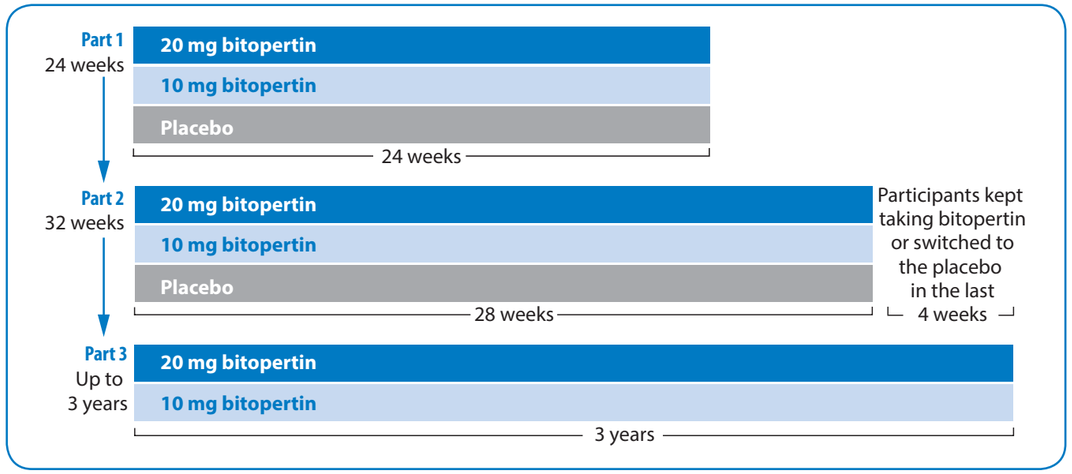
Part 1 lasted 24 weeks. Participants took a 10 mg or 20 mg dose of the study drug, biopertin, or a placebo.

Part 2 lasted 32 weeks. Participants kept taking bitopertin or a placebo until week 28. Then, for 4 weeks, participants taking bitopertin kept taking it or were switched to a placebo.

Part 3 lasted up to 3 years. Participants who completed both Part 1 and Part 2 and wanted to stay in the study kept taking 10 or 20 mg of bitopertin, depending on what they took earlier. Participants who took a placebo in Part 1 and 2 took a 10 mg dose of bitopertin in Part 3.

After you stopped taking the study drug or placebo, researchers stayed in contact with you for 4 weeks to check for any medical problems.

During the study, participants saw the study doctor and staff 18 times.



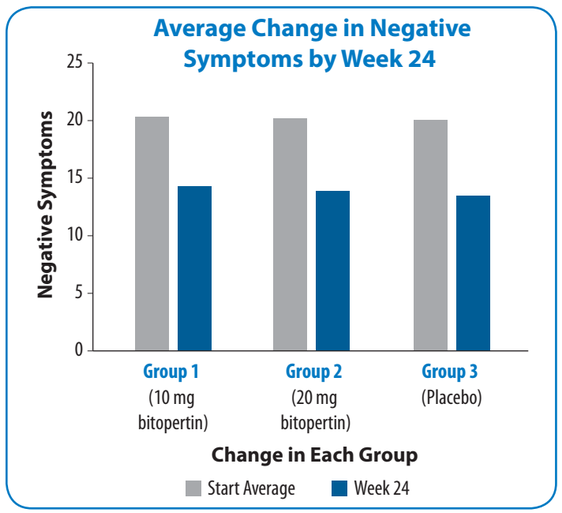
At study visits, participants answered questions about their condition, completed tests, and gave blood and urine samples.

WHAT WERE THE STUDY RESULTS?

Below is a summary of the main questions researchers asked in this study, and the study results.

Did bitopertin reduce negative symptoms of schizophrenia in the study?

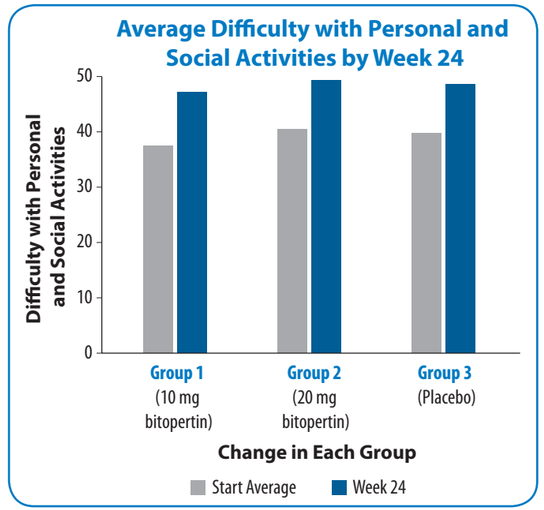
Participants in all 3 groups had fewer negative symptoms. Participants in Group 1 (10 mg bitopertin) and Group 2 (20 mg bitopertin) scored lower on a test of negative symptoms after 24 weeks than they did at the beginning of the study. But participants in Group 3 (placebo) also scored lower after 24 weeks.



The difference was too small to tell if bitopertin really worked better than the placebo for negative symptoms of schizophrenia. So researchers stopped the study early. This sometimes happens in clinical studies. But the study can still give researchers important information that they can use to help patients in the future, so your participation was very important.

Did bitopertin help participants with personal and social activities?

Researchers measured general behavior and personal and social activities, including work or school, relationships, and taking care of themselves. A higher score meant participants had less difficulty. Participants in Groups 1 and 2 had less difficulty with these activities after 24 weeks, but so did participants in Group 3. There was not much difference between participants in all 3 groups. The chart below shows the average scores for each group after 24 weeks.



Was bitopertin safe?

Bitopertin was safe for most participants in the study. A few participants stopped taking bitopertin because of medical problems.

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 participants have. These medical problems are called “adverse events”, and may or may not be caused by the study drug.

WHAT ADVERSE EVENTS DID PARTICIPANTS HAVE?

Participants in all 3 groups had about the same number of adverse events at different times in the study. The table below shows how many participants in each group had at least 1 adverse event.

Adverse Events in the Study

	GROUP 1 10 mg of bitopertin	GROUP 2 20 mg of bitopertin	GROUP 3 Placebo (10 mg of bitopertin after week 56)
Up to week 52	124 out of 208 participants (59.6%)	108 out of 208 participants (51.9%)	123 out of 210 participants (58.6%)
After week 56 (participants who chose to keep taking bitopertin)	41 out of 116 participants (35.3%)	41 out of 120 participants (34.2%)	34 out of 102 participants (33.3 %)

What serious adverse events did participants have?

An adverse event is considered "serious" when it is life threatening, causes lasting problems, or needs hospital care. Most of the adverse events in your study were not serious.

Participants in Group 1 (10 mg bitopertin) and Group 3 (placebo) had more serious adverse events than participants in Group 2 (20 mg bitopertin) did. In this study, serious adverse events were mostly related to a participant's schizophrenia. The table below shows how many participants had at least 1 serious adverse event at different times in the study.

Serious Adverse Events in the Study

	GROUP 1 10 mg of bitopertin	GROUP 2 20 mg of bitopertin	GROUP 3 Placebo (10 mg of bitopertin after week 56)
Up to week 52	13 out of 208 participants (6.3%)	7 out of 208 participants (3.4%)	123 out of 210 participants (58.6%)
After week 56 (participants who chose to keep aking bitopertin)	7 out of 116 participants (6.0%)	5 out of 120 participants (4.2%)	1 out of 102 participants (1.0 %)

The study lasted more than 3 years, and 5 participants died during this time. Study doctors thought 2 of these deaths, 1 suicide and 1 heart attack, were related to the study drug but the other 3 were not.

What were the most common adverse events in the study?

Up to week 52, the most common adverse events were headaches, anxiety, and insomnia (trouble falling asleep or staying asleep). The most common serious adverse events up to week 52 were mental health problems and injuries.
The most common adverse events after week 56 were colds, flu, and sore throat, and the most common serious adverse events were mental health problems.

Did any participants leave the study because of adverse events?

Yes. Up to week 52, most of the participants who left were in Group 3 (placebo). Mental health problems were the most common reason for leaving.

Participants Left Study Because of Adverse Events

	GROUP 1 10 mg of bitopertin	GROUP 2 20 mg of bitopertin	GROUP 3 Placebo (10 mg of bitopertin after week 56)
Up to week 52	10 out of 208 participants (4.8%)	8 out of 208 participants (3.8%)	26 out of 210 participants (12.4%)
After week 56 (participants who chose to keep taking bitopertin)	3 out of 116 participants (2.6%)	3 out of 120 participants (2.5%)	4 out of 102 participants (3.9%)

* The full list of adverse events for your trial can be found on the U.S. government's clinical trial website at http://clinicaltrials.gov/ct2/show/study/NCT01192867

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

This summary of the clinical study results is available online at www.ciscrp.org/NCT01192867. At that webpage, you will also find links to more information about the scientific results. If you have questions about the results, please speak with the doctor, research nurse, or other team member at your study site.

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

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

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.