



CLINICAL TRIAL RESULTS

Sponsor: Pfizer, Inc.

Medicine Studied: Bococizumab

Protocol Number: B1481030

Dates of Trial: 04 June 2014 to 03 November 2015

Title of this Trial: A Randomized Clinical Trial of Bococizumab (PF-04950615; RN316) in Patients Who Cannot Take Statins (SPIRE-SI)

[A Phase 3, Double-Blind, Double-Dummy, Randomized, Placebo and Active Controlled, Parallel-Group Study to Assess the Efficacy, Safety and Tolerability of PF-04950615 in Subjects With Dyslipidemia Who Are Intolerant to Statins]

Date of this Report: 01 June 2017

– *Thank You* –

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or its results please contact the doctor or staff at your study site. This summary of results represents a single trial only.

WHY WAS THIS STUDY DONE?

Heart disease is a leading cause of death in both men and women. One of the biggest risks for getting heart disease is having high “bad” cholesterol (called LDL, or low-density lipoprotein cholesterol). Having high LDL cholesterol can lead to heart problems.

Doctors prescribe medicines called “statins” to patients with high LDL cholesterol to lower the LDL cholesterol in the blood. Some people have muscle-related medical problems when taking statins. These medical problems include muscle spasms and pain in the muscles (myalgia), which may be severe. This may prevent them from being able to take their prescribed statin medications.

Researchers did this study to look for a new way to treat patients with high LDL cholesterol who are unable to take a statin because of muscle-related medical problems. Bococizumab was the medicine tested in this study. It is not a statin. Bococizumab is a medicine that was given in this study as an injection under the skin (subcutaneous) which may help to lower LDL cholesterol. For this study, researchers wanted to answer the question: Does bococizumab help to lower LDL cholesterol in patients who cannot take statin medications?

WHAT HAPPENED DURING THE STUDY?

This study compared 3 groups of patients. Researchers wanted to find out if patients taking bococizumab had lower LDL cholesterol than patients who took a placebo. A placebo does not have any medicine in it, but looks just like the medicine being tested. One group got a statin medicine (atorvastatin). The statin medicine was used to see if people taking it had the same medical problems as when they had used statins before (re-challenge).

This study included adult men and women who:

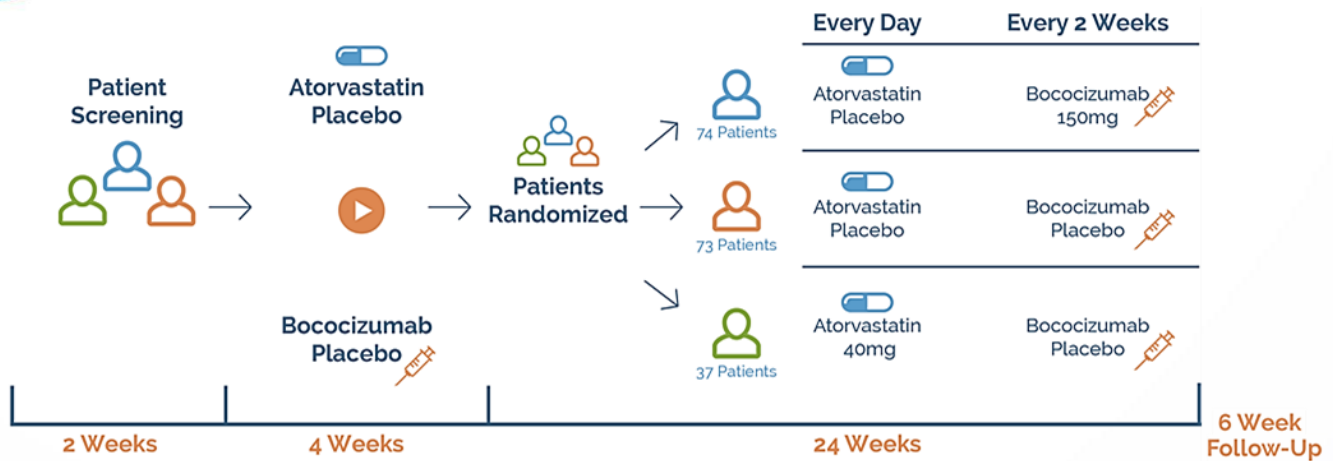
- Had high cholesterol that requires medicine to treat
- Tried taking at least 2 different statins in the past
- Stopped taking their statins because of muscle problems (like pain, or muscle spasms)

Patients were put into 1 of 3 treatment groups by chance alone. This is known as a “randomized” study. This is done to make the groups more similar for things like age and the number of men and women. Making the groups more similar makes comparing the groups more fair.

The patients and researchers did not know who took what medicine during the study. This is known as a “double-blinded” study. Researchers use “double-blinded” studies to make sure that the results of the study are not influenced in any way.

Descriptions of Medicines Given in Each Group		
Group	Medicines Given	Why the Group Was Used in this Study
1	Bococizumab 150 mg AND atorvastatin placebo	To see if bococizumab lowered LDL cholesterol
2	Bococizumab placebo AND atorvastatin placebo	To see if bococizumab worked better than no medicine
3	Bococizumab placebo AND 40 mg atorvastatin	To confirm that the enrolled patients were, in fact, unable to take a statin

For 2 weeks, patients were checked (screened) to make sure they met all the requirements to be in the study. Next, all patients took the same placebo treatments for 4 weeks. Then, patients were put into 1 of 3 groups and were treated for 24 weeks. After taking the study medicines, patients were followed by researchers for 6 weeks (follow-up phase) to see how they did after taking study medicines.



While patients were only in the study for 36 weeks (about 9 months), the entire study took 17 months to complete. The study took place at 26 sites in the US and 6 sites in Canada. It began on 04 June 2014 and ended on 03 November 2015. 184 patients started this study. 85 patients were men and 99 patients were women. All patients were between the ages of 33 and 83.

Of the 184 patients who started the study, 183 took at least one dose of the study medicine. 172 finished the study. 11 patients left before the study was over by their choice or because a doctor decided it was best for a patient to stop the study. 1 patient died. Study medicines did not cause the patient’s death.

When the study ended in November 2015, the Sponsor began to look at the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

Does bococizumab help to lower LDL cholesterol in patients who cannot take statins?

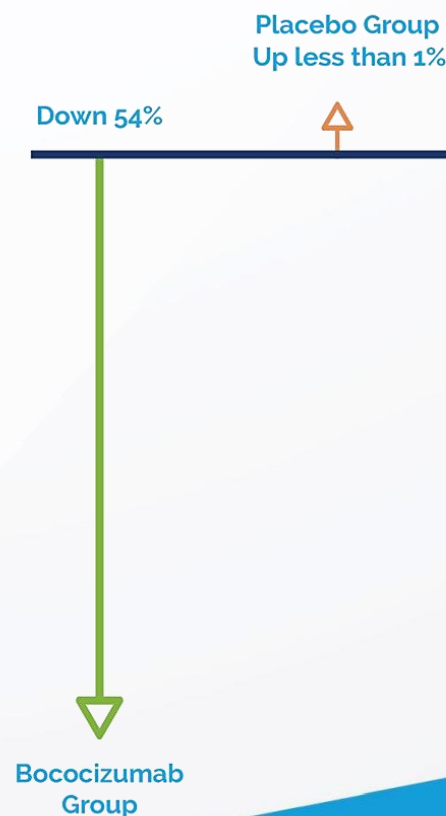
Yes, bococizumab worked better than placebo to lower LDL cholesterol.

Researchers looked at the average change in patient's LDL cholesterol from the start of the study compared to the patient's average LDL cholesterol after 12 weeks of taking the study medicines. On average, patients who took bococizumab had their LDL cholesterol drop by about 54% from their starting value. The patients taking a placebo had their LDL cholesterol go up a little bit, less than 1%, from their starting value.

The group who took a statin had their LDL cholesterol go down by about 25% from their starting value. Based on these results, the researchers have concluded that the results are not likely the result of chance.

This does not mean that everyone in this study had these results. Each patient's result could be better or worse than the overall group. Other studies may find different results. This is just one of the main findings of the study. More information may be available at the website listed at the end of this summary.

WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?



The researchers recorded any medical problems the patients had during the study. Patients could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could have been caused by a study treatment, or by another drug the patient was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what the side effects of an experimental drug might be.

A total of 6 patients left the study due to medical problems. 105 out of 183 patients in this study had at least 1 non-serious medical problem. The most common are listed in the table on the next page.

Patients taking bococizumab had a similar rate of muscular medical problems (muscle pain and muscle spasms) as patients in the atorvastatin and placebo group. Patients taking bococizumab had a higher amount of injection site reactions than patients did in the other groups. 14 patients (19%, or 14 out of 74 patients) taking bococizumab had a non-serious injection site reaction. 2 patients (3%, or 2 out of 73 patients) in the placebo group had a non-serious injection site reaction. No one in the atorvastatin group had an injection site reaction.

Most Common Non-Serious Medical Problems (Reported by More Than 5% of Patients)

Medical Problem	Bococizumab (74 Patients Treated)	Atorvastatin (36 Patients Treated)	Placebo (73 Patients Treated)
Muscle pain	13 (18%)	7 (19%)	13 (18%)
Muscle spasms	7 (9%)	3 (8%)	8 (11%)
Injection site reaction	14 (19%)	0 (0%)	2 (3%)
Tiredness	3 (4%)	4 (11%)	6 (8%)
Pain in a joint	5 (7%)	1 (3%)	6 (8%)
Pain in arms or legs	4 (5%)	1 (3%)	7 (10%)
Infection (any kind)	2 (3%)	3 (8%)	6 (8%)
Nausea	4 (5%)	2 (6%)	2 (3%)
Back pain	2 (3%)	0 (0%)	6 (8%)
Diarrhea	4 (5%)	1 (3%)	4 (5%)
Dizziness	2 (3%)	3 (8%)	3 (4%)
Headache	4 (5%)	1 (3%)	2 (3%)
Stomach pain	1 (1%)	0 (0%)	4 (5%)
Constipation	0 (0%)	1 (3%)	4 (5%)
Cough	1 (1%)	2 (6%)	0 (0%)
Rash	0 (0%)	2 (6%)	1 (1%)
Seasonal allergy	0 (0%)	2 (6%)	1 (1%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered “serious” when it is life-threatening, causes lasting problems, or needs hospital care.

16 patients (9%, or 16 out of 183 patients) had serious medical problems. 8 patients in the bococizumab group, 7 patients in the placebo group, and 1 patient in the atorvastatin group had a serious medical problem. All serious medical problems were considered by the study doctors and Sponsor as not related to study medicines. One patient died during the study. The patient had stopped taking the study medications about 1 month before he died. The study doctor and Sponsor considered that the death was not related to the study medicines.

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on this study protocol, please visit www.clinicaltrials.gov (use the study identifier NCT02135029).

Please remember that researchers look at the results of many studies to find out which medicines work best and are safest for patients. No further clinical trials with bococizumab are planned at this time.

Again, thank you for volunteering.
We do research to try to find the best ways to help patients, and you helped us to do that!