CLINICAL TRIAL RESULTS

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different from the results of other studies that the researchers review.

Sponsor: Pfizer, Inc.

Medicine(s) Studied: Bococizumab

Protocol Number: B1481045

Dates of Trial: 28 October 2014 to 15 July 2016

Title of this Trial: A Randomized Clinical Trial of Bococizumab (PF-04950615; RN316) in Patients at High Risk for Heart Disease (SPIRE-LL Study)

[A 52-Week Phase 3 Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study to Assess the Efficacy, Safety and Tolerability of PF-04950615 in Subjects With Primary Hyperlipidemia or Mixed Dyslipidemia at Risk of Cardiovascular Events]

Date of this Report: 01 August 2018

– 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 results, please contact the doctor or staff at your study site.

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 disease.

Doctors prescribe medicines called 'statins' to patients with high LDL cholesterol to lower the LDL cholesterol in the blood. For some people, statins may not lower LDL cholesterol enough.

Researchers did this study to look for a new way to treat patients who are taking a statin and who still have LDL cholesterol that is higher than what their doctors consider ideal. Bococizumab was the medicine tested in this study. It is not a statin. Bococizumab is a medicine that is given as an injection under the skin (subcutaneous) that may help to further lower LDL cholesterol. For this study, researchers wanted to answer the question: Does bococizumab help to lower LDL cholesterol in patients who take statins but are still at high risk for heart problems?

After the primary study had started, the Food and Drug Administration (FDA) asked Pfizer to do a follow-up study (a substudy). For this substudy, Pfizer followed patients for up to 1 year after the first part of the study ended to monitor for medical problems and to see how long it took for certain antibodies to disappear or lower in amount after patients stopped taking bococizumab. Antibodies are proteins that fight foreign "invaders". In some cases, antibodies can fight against medicines, which make them not work.

WHAT HAPPENED DURING THE STUDY?

Researchers wanted to know if patients taking a statin who took 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.

This study included adult men and women who:

- Had high cholesterol that required medicine to treat
- Were already taking a statin treatment for at least 6 weeks, and did not plan to change or stop taking their statin
- Had a high or very high risk of heart disease because of other health problems, like smoking, diabetes, or damage to their blood vessels

Patients were assigned either bococizumab or placebo treatment 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. Reducing differences between the groups makes the groups more even to compare.

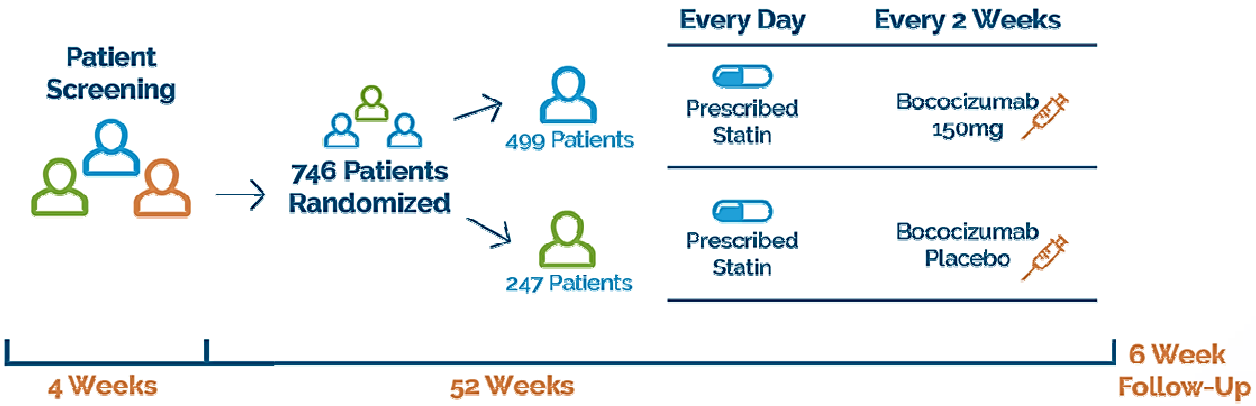
The patients, study doctors, and Sponsor did not know who took what medicine during the study. This is known as a "double-blinded" study. Researchers use "double-blinded" studies to make sure that the results are not influenced in any way.

Descriptions of Medicines Given in Each Group

Group	Medicines Given	Why the Group Was Used in this Study
1	Bococizumab 150 mg	To see if bococizumab lowered LDL cholesterol
2	Bococizumab placebo	To compare bococizumab with taking no other medicine besides their statin

For 4 weeks, patients were checked (screened) to make sure they met all the needs to be in the study. Next, patients were put into 1 of the 2 treatment groups and were treated for 1 year. Twice as many patients were assigned bococizumab as placebo (a

2:1 ratio). At the end of 1 year, patients were followed by researchers for 6 weeks (follow-up phase) to see how they did after taking the study medicines.



While each patient was only in the study for about 14 months, the whole study took almost 2 years to finish. Of the 746 patients who started the study, 643 finished the whole study. 103 patients left before the study was over by their choice or a doctor decided it was best for a patient to stop the study. 2 patients died in the bococizumab group, and 2 patients died in the placebo group. Study doctors and the Sponsor determined that study medicines did not cause their deaths.

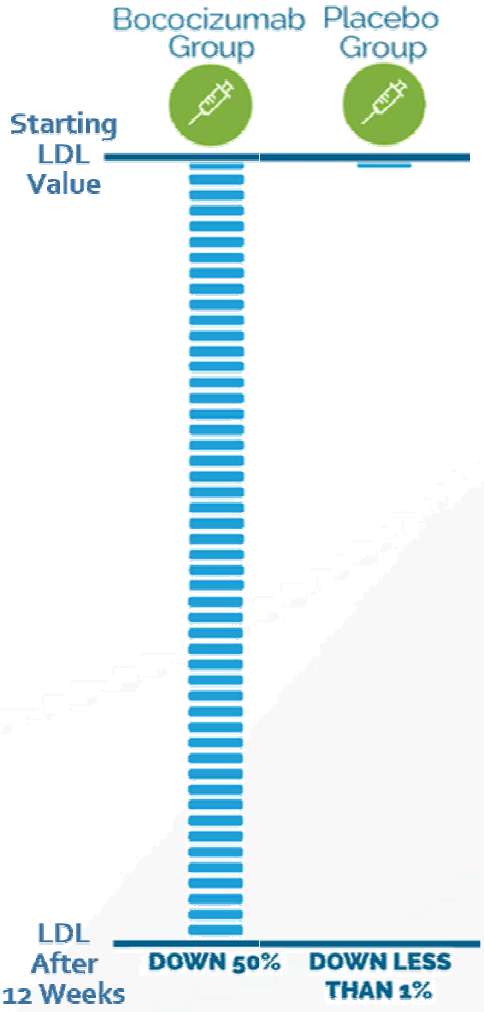
The study took place at 170 locations in 12 countries in North America and Western Europe, Eastern Europe, and Asia. It began on 28 October 2014 and ended 15 July 2016. 746 patients started this study. 416 patients were men and 330 patients were women. All patients were between the ages of 26 and 86.

As soon as the study ended in July 2016, the Sponsor began looking at the study results. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

ORIGINAL STUDY RESULTS

Did bococizumab help to lower LDL cholesterol in patients who are still at high risk for heart disease while taking statins?



Yes, bococizumab lowered LDL cholesterol more than the placebo did for the patients in this study.

The main goal (or primary objective) was to see if bococizumab was working after 12 weeks of treatment. Researchers compared the changes in patient's LDL cholesterol from the start of the study to after 12 weeks of taking the study medicines.

In this study, on average, patients who took bococizumab for 12 weeks had their LDL cholesterol drop by about 50% from their starting value. The patients who took placebo had their LDL cholesterol lowered less than 1% from their starting value.

Patients continued their treatment for 1 year, and doctors continued to monitor them for 6 weeks after finishing treatment. Based on the careful studying of all trial details and results, researchers determined that these results are not likely due to chance, and that bococizumab worked better than a placebo to lower LDL cholesterol.

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. These are just some of the main findings of the study. More information may be available at the websites listed at the end of this summary.

SUBSTUDY RESULTS

How long did it take for antibodies against bococizumab present at the end of the original study to disappear or lower in amount after patients stopped taking bococizumab during the substudy?

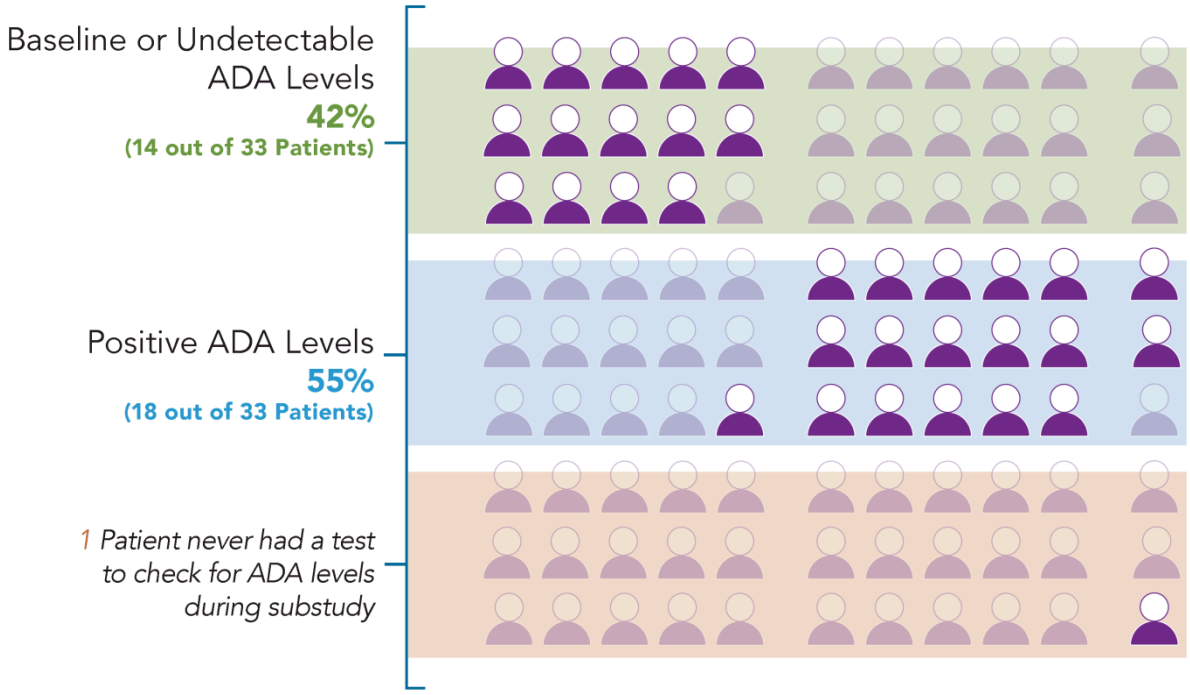
Anti-drug antibodies (ADAs) can sometimes be made by a patient's body when taking a biologic medicine, like bococizumab. ADAs can be neutralizing ADAs (or nAb) and non-neutralizing ADAs. When nAbs are formed, they can make the medicine become less effective. In the main study, patients with ADAs in general, had the same types of medical problems as patients without ADAs. However, some patients with ADAs did have more reactions at the site of injection. In addition, about twice as many patients with nAbs had injection site reactions than patients without nAbs.

In this study, 25% of the patients who participated (33 out of 133) had detectable ADAs at the last study visit of the original study. Of note, 2 of these patients had detectable ADAs at the start of the original study (before taking any study medicine at all). Pfizer wanted to see if the ADA level either went down to a certain baseline level, or was not detectable in these patients after they stopped taking bococizumab. They also wanted to see how long it took to get to this level after patients stopped taking bococizumab. The substudy went for up to 1 year after the last visit in the original study.

By the end of the substudy, 42% of patients (or 14 of 33) had ADA levels that returned to a baseline value or were undetectable. It took on average 170 days for these patients' ADA levels to go to baseline or to be undetectable. 55% of patients (or 18 of 33) still had a positive ADA level at the end of the substudy. 1 patient never had a test to check for ADA levels during the substudy.

See the next page for a summary of the substudy results.

ADA Levels at the End of the Substudy



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 21 patients left the study due to medical problems (16 in the bococizumab group and 5 in the placebo group). More than half of all patients in this study had at least 1 non-serious medical problem (62% in the bococizumab group and 56% in the placebo group). A non-serious medical problem means a medical problem that is not life-threatening, does not cause lasting problems, or needs hospital care. The most common are listed below.

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

Medical Problem	Bococizumab (499 Patients Treated)	Placebo (247 Patients Treated)
Injection site reaction	67 (13%)	2 (Less than 1%)
Common cold	17 (3%)	14 (6%)
Nose and throat infection	18 (4%)	14 (6%)

13% of patients in the bococizumab group (67 out of 499) had a non-serious injection site reaction (pain, stinging, redness, or swelling where the shot was given). Less than 1% in the placebo group (2 out of 247) had a non-serious injection site reaction.

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

Serious medical problems during the original study

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

44 patients in the bococizumab group (9%, or 44 out of 499 patients) and 32 patients in the placebo group (13%, or 32 out of 247 patients) had serious medical problems.

The most common serious medical problems were related to heart disease:

- Bococizumab group = 2% (12 out of 499 patients)
- Placebo group = 4% (11 out of 247 patients)

2% or less of patients had other serious medical problems. Most of the serious medical problems were only reported by 1 patient. These included serious infections, some cancers, brain or spine problems, problems with their kidneys, liver or digestive organs, low blood sugar, muscle or joint pain, eye or ear issues, blood or vessel problems, breathing trouble, and chest pain not caused by the heart.

A total of 4 patients out of 746 died during the study, 2 were in the placebo group and 2 were in the bococizumab group. The study doctors and Sponsor determined that none of the deaths were caused by study treatments.

What else is important to know?

Your body makes proteins (called antibodies) to fight foreign "invaders", like a virus that can cause an infection. Sometimes, the body makes antibodies that attack anything not made by your own body, including some medicines.

Researchers tested the blood of patients taking bococizumab in 3 different studies, including this one. More than half of all patients tested (55%, or 269 out of 491 patients) were making antibodies against bococizumab. There is the possibility

that if you have these antibodies, bococizumab or similar drugs will not work for you in the future.

Serious medical problems during the substudy

3 patients in the substudy (2%, or 3 of 133 patients) had a total of 5 serious medical problems. None were considered by researchers to be caused by taking the study medicines during the original study.

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.

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT02100514**
www.clinicaltrialsregister.eu	Use the study identifier **2014-000478-20**

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!