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 than the results of other studies that the researchers review.

Sponsor: Pfizer, Inc.

Medicine(s) Studied: PF-05280586 (Rituximab – Pfizer)

Protocol Number: B3281006

Dates of Trial: 30 September 2014 to 19 April 2018

Title of this Trial: A Phase 3, Randomized, Double-Blind Study of PF-05280586 Versus Rituximab for the First-Line Treatment of Patients With CD20-Positive, Low Tumor Burden, Follicular Lymphoma

Date of this Report: 15 March 2019

– 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.

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WHY WAS THIS STUDY DONE?

The purpose of this research study was to compare the safety and effectiveness of PF-05280586 to currently approved and marketed rituximab for treatment of low tumor burden follicular lymphoma (also called LTB-FL). LTB-FL is a type of non-Hodgkin's lymphoma (NHL). NHL is a type of cancer which starts in your lymphatic system (the disease fighting system). LTB-FL is not as aggressive and has a better prognosis (the likely outcome) than other types of NHL.

One of the most common treatments for LTB-FL is with a medication called rituximab (also called Rituxan® or MabThera®). Rituximab is given as a monotherapy for LTB-FL. Monotherapy means one medicine given without other medicines at the same time. Rituximab works by attaching to a protein called CD20. CD20 sits on the surface of B lymphocytes (a type of white blood cell). When rituximab binds to the CD20 protein it causes the B lymphocytes, including the cancerous ones, to die.

Rituximab is a biologic medicine. Biologics can be made up of sugars, proteins, genetic material, human or non-human cells, and tissues (or groups of cells). Rituximab is a good first-line treatment option for LTB-FL as per treatment guidelines like the National Comprehension Cancer Network (NCCN) guidelines.

PF-05280586 is another biologic medicine. PF-05280586 was made to be like Rituxan® or MabThera®. It was designed to have a similar structure and work in the same way that Rituxan® or MabThera® do. This type of medicine is known as a biosimilar. PF-05280586 was the investigational medicine in this study. An investigational medicine is one that is not approved for sale in any country.

The table on the next page shows the differences between rituximab (the "biologic") and PF-05280586, (the medicine tested to see if it was a "biosimilar" to rituximab) in this study.

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	Biologic Reference Product	Biosimilar to Reference Product
	**Rituxan® and MabThera® were the biologic reference products in this study.**	**PF-05280586 was the investigational medicine tested in this study to see if it was a biosimilar to Rituxan® and MabThera®.**
	**Made up of sugars, proteins, genetic material, human or non-human cells, and tissues (or groups of cells).**	**PF-05280586 was designed to have a similar structure and was tested to see if it works in the same way as the Rituxan® and MabThera®.**
	**Approved by a country's health authority for use.**	**PF-05280586 is not approved by a country's health authority for use. It must be similar to Rituxan® and MabThera® in structure, effectiveness, and safety to be approved for use.**
	**Information is known about safety and effectiveness.**	**PF-05280586 was tested to see if the safety and effectiveness of this investigational medicine is comparable to Rituxan® and MabThera®.**

WHAT HAPPENED DURING THE STUDY?

Researchers wanted to compare how safe and effective PF-05280586 was to that of currently approved and marketed rituximab for the treatment of LTB-FL. They wanted to see if PF-05280586 could be another treatment option for patients with LTB-FL.

The main criteria which patients had to have to be a part of this study were:

- Adult men and women who had Grade 1 to 3a (cancer that has not spread to distant parts of the body) CD20-positive LTB-FL;
- Who had not been previously treated with rituximab; and
- Who did not have certain symptoms such as fever higher than 38° C for 3 days in a row, recurring drenching night sweats, or unintentional weight loss (more than 10% of your body weight in 6 months).

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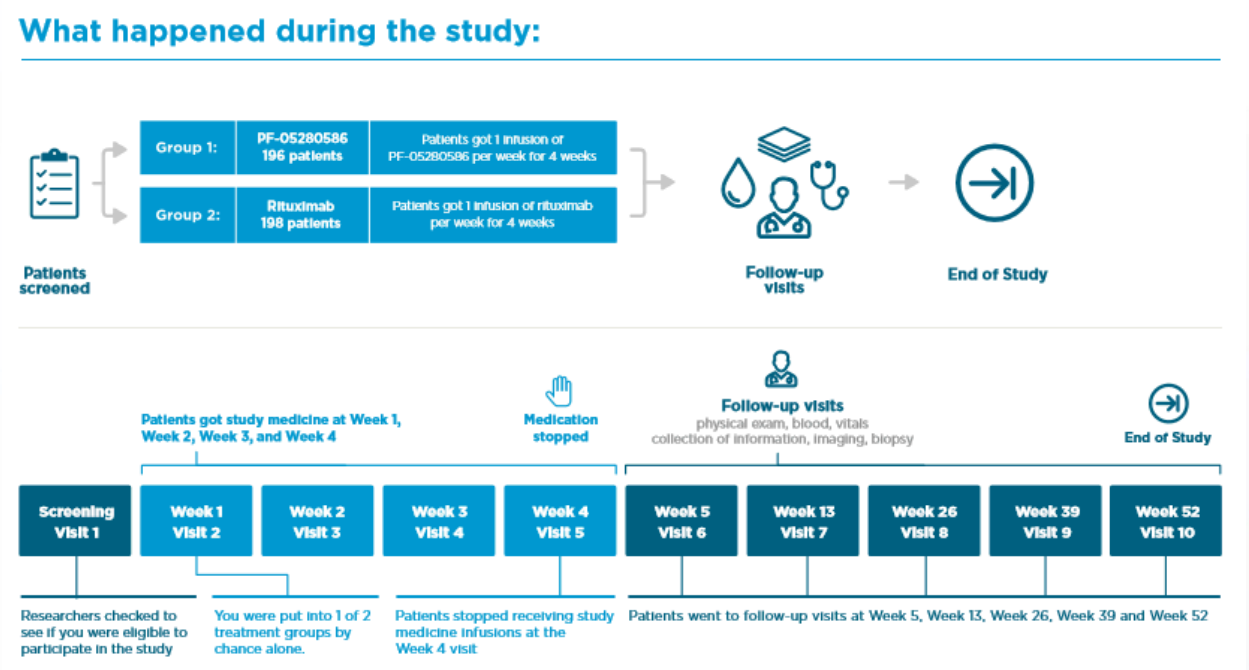
There were other criteria patients had to have to be a part of the study in addition to the ones listed above. These were just some of the main criteria patients had to have.

This study compared 2 groups of patients. One group was treated with PF-05280586. The other group was treated with rituximab.

The patients and researchers did not know who took PF-05280586 and who took rituximab. This is known as a "blinded" study. This was done to make sure the trial results were not influenced in any way.

Patients were put into 1 of 2 treatment groups by chance alone. This is known as a "randomized" study. This is done to make the groups more similar, which makes comparing the groups more fair.

The figure below shows a summary of what happened during the study.



While patients were in the study for a year, the entire study took about 3 ½ years to complete. Patients joined the study at 1 of 160 locations in 29 countries in Europe, Asia, North America, and South America. It began 30 September 2014 and ended 19 April 2018. 178 men and 216 women participated. All patients were between the ages of 21 and 93 years old.

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Patients were supposed to be treated until they got 4 weekly treatments with either PF-05280586 or rituximab. Of the 394 patients who started the study, 393 patients got at least 1 dose of either study medicine. 1 patient left the study before getting any study medicine. 390 patients finished the 4 weekly cycles of study medicine. 340 patients completed the entire study. This means that they completed all of the visits in the study including the Week 52 visit. 54 patients did not finish the Week 52 visit. They left before the study was over by their choice, or a doctor decided it was best for a patient to stop the study.

When the study ended in April 2018, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

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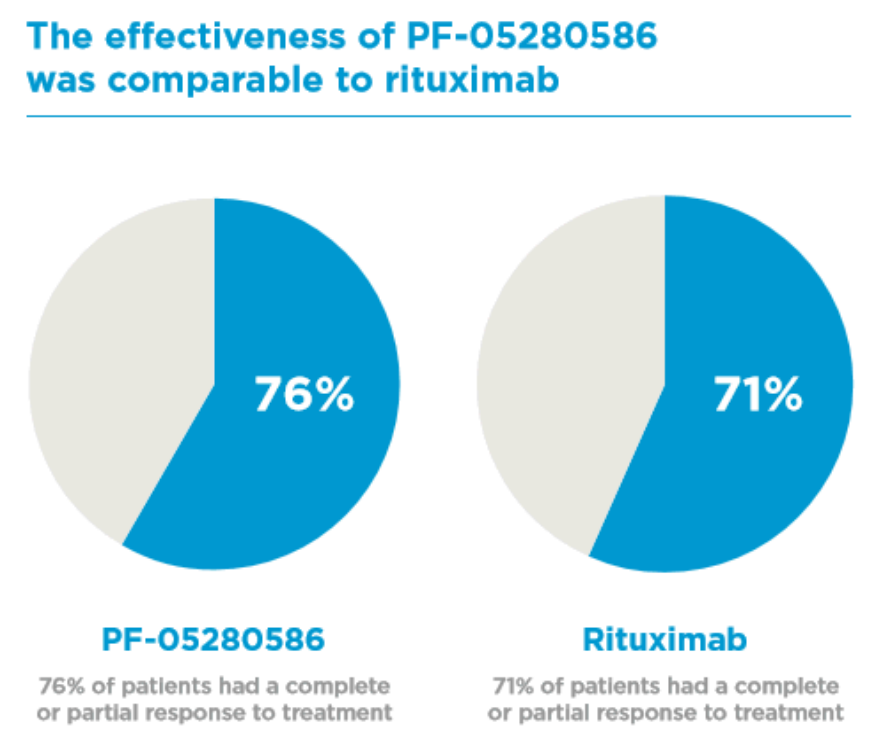
WHAT WERE THE RESULTS OF THE STUDY?

Was PF-05280586 as effective as rituximab?

Researchers wanted to compare whether PF-05280586 was as effective as rituximab for patients with LTB-FL. In this study, patients received either PF-05280586 or rituximab in an infusion once per week for 4 weeks. Patients were checked to see if they had a complete response or a partial response to the treatment. A complete response is when there is no evidence of cancer after treatment. A partial response is when the cancer has improved after treatment. At the Week 26 visit, 148 patients (76%, or 148 of 196 patients) who were in the PF-05280586 group had a complete or partial response to treatment. 140 patients (71%, or 140 of 198 patients) who were in the rituximab group had a complete or partial response to treatment at the Week 26 visit. The amount of patients who had a complete or partial response at Week 26 was comparable between the 2 groups.



Based on these results, the researchers have concluded that the results are not likely the result of chance.

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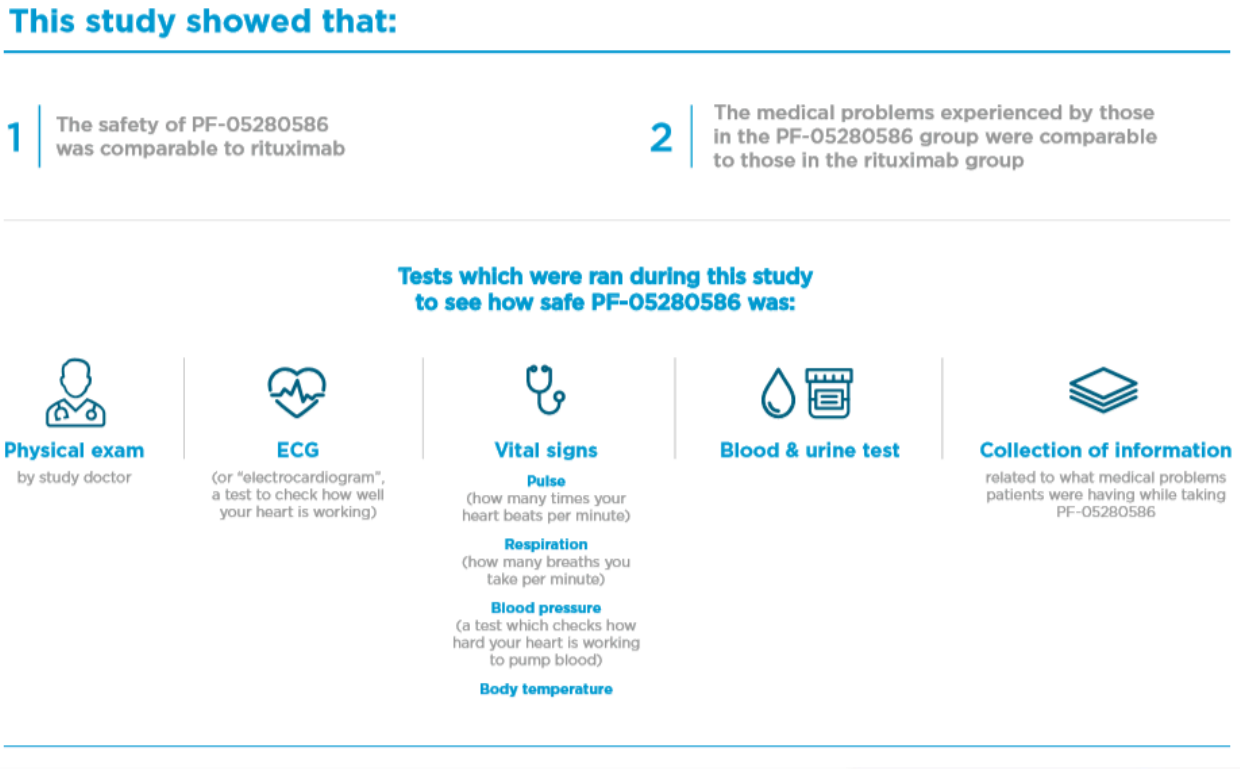
Was the safety of taking PF-05280586 comparable to rituximab?

Patients were given a variety of different tests, such as physical exams by doctors, ECGs (a test to see how well your heart is working), collection of information (such as medical problems the patient was experiencing during the study), vital signs, and blood and urine tests (see below picture). Based on the data collected from these tests, getting infusions of PF-05280586 once per week for 4 weeks had comparable safety to rituximab for patients with LTB-FL.



This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

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WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the participants had during the study. Participants 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 medicine the participant 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.

190 out of 393 patients who received at least one dose of study medicine (either PF-05280586, or rituximab) in this study had at least 1 non-serious medical problem. A non-serious medical problem means that it is not life-threatening, does not cause lasting problems, or does not need hospital care. 97 patients (49%, or 97 out of 197 patients) in the rituximab treatment group had at least 1 non-serious medical problem. 93 patients (47%, or 93 out of 196 patients) in the PF-5280586 treatment group had at least 1 non-serious medical problem.

Between the 2 treatment groups, the medical problems were comparable in type and how often they occurred. They were also comparable to the known medical problems which can be caused by rituximab. The most common non-serious medical problems reported by participants in this study are listed on the next page.

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Most Common Non-Serious Medical Problems (Reported by More Than 5% of Patients)		
Medical Problem	**PF-05280586 (196 Patients)**	**Rituximab (197 Patients)**
Infusion-related reaction	49 (25%)	58 (29%)
Headache	16 (8%)	19 (10%)
Itchy skin	13 (7%)	22 (11%)
Nausea	15 (8%)	17 (9%)
Diarrhea	14 (7%)	12 (6%)
Tiredness	12 (6%)	13 (7%)
Throat irritation	14 (7%)	10 (5%)
Weakness	9 (5%)	13 (7%)
Fever	11 (6%)	11 (6%)
Cough	11 (6%)	11 (6%)
Back pain	8 (4%)	10 (5%)
Rash	10 (5%)	8 (4%)
Mouth and throat pain	2 (1%)	10 (5%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is either life-threatening or causes death, causes lasting problems, is considered medically important by the study doctor, or needs hospital care.

32 patients (8%, or 32 out of 393 patients) had serious medical problems. A total of 15 patients in the rituximab group had a serious medical problem. 17 patients in the PF-05280586 group had a serious medical problem. The most common serious medical problem experienced in both treatment groups was infection. 4 patients (2%, or 4 out of 196 patients) in the PF-05280586 group and 3 patients (2%, or 3 out of 197 patients) had an infection.

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2 patients died during the study because their cancer got worse (known as disease progression). 1 patient was in the PF-05280586 group and 1 patient was in the rituximab group. Both deaths occurred more than 4 weeks after the study ended. The deaths were considered by researchers to not be related to study treatment.

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 **NCT02213263**
www.clinicaltrialsregister.eu	Use the study identifier **2014-000132-41**

Findings from this trial and other studies will be used to seek approval for using the treatment for patients with the following conditions:

- Non-Hodgkin's lymphoma (NHL)
- Chronic lymphocytic leukemia
    - A type of cancer that starts in the B cells (a type of white blood cell) of the bone marrow and extends into the blood.
- Rheumatoid arthritis
    - A type of arthritis where the immune system attacks and causes damage to the joints and tissue.
- Granulomatosis with polyangiitis, and microscopic polyangiitis
    - These diseases both cause inflammation of the blood vessels which mainly affects the lungs and kidneys.
- Pemphigus vulgaris
    - A disease where the immune system attacks and causes painful blisters on the skin and mucus membranes (including but not limited to the mouth, throat, nose, eyes, and genitals).

Please remember that researchers look at the results of many studies to find out which medicines work best and are safest for patients.

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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!

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