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-05280014

Protocol Number: B3271002

Dates of Trial: 24 February 2014 to 27 June 2020

Title of this Trial: A Study Of PF-05280014 [Trastuzumab-Pfizer] Or Herceptin® [Trastuzumab-EU] Plus Paclitaxel In HER2 Positive First Line Metastatic Breast Cancer Treatment (REFLECTIONS B327-02)

[A Phase 3 Randomized, Double-Blind Study of PF-05280014 Plus Paclitaxel Versus Trastuzumab Plus Paclitaxel for the First-Line Treatment of Patients with HER2-Positive Metastatic Breast Cancer]

Date of this Report: 29 January 2021

– 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?

Some women with breast cancer have high levels of a certain protein receptor on the surface on their cancer cells. This protein is called HER2 (human epidermal growth factor receptor 2). A cell with too many HER2 receptors is stimulated to grow and multiply too fast and can become a cancer tumor. When women with breast cancer have too much of this protein their cancer is called "HER2-positive".

Trastuzumab (Herceptin®) is an approved drug for the treatment of patients with HER2-positive breast cancer. PF-05280014 was the investigational drug in this study. An investigational drug is one that is not approved for sale.

Researchers think that PF-05280014 may work like Herceptin in the body. Herceptin is an antibody, which is a type of protein. Herceptin binds to the HER2 receptor on the surface of cells. By attaching to the HER2 receptor, this medicine can block the signals that cause the cells to grow and multiply.

Patients who were in this study received either PF-05280014 or Herceptin in combination with paclitaxel. Paclitaxel is a standard chemotherapy treatment for breast cancer. It was used in this study because it is commonly given to patients by doctors for the treatment of breast cancer.

The main purpose of this study was to find out if PF-05280014 worked similarly to Herceptin in patients with breast cancer. Researchers wanted to answer this question:

- What percentage of patients who received PF-05280014 and paclitaxel had a reduction in tumor size, compared to patients who received Herceptin and paclitaxel?

WHAT HAPPENED DURING THE STUDY?

This study compared 2 groups of patients. Researchers wanted to find out if PF-05280014 worked similarly to Herceptin in patients with breast cancer.

This study included adult women who:

- Had HER2-positive breast cancer
- Had breast cancer that had spread to another part of the body
- Had at least 1 breast cancer tumor that could be measured

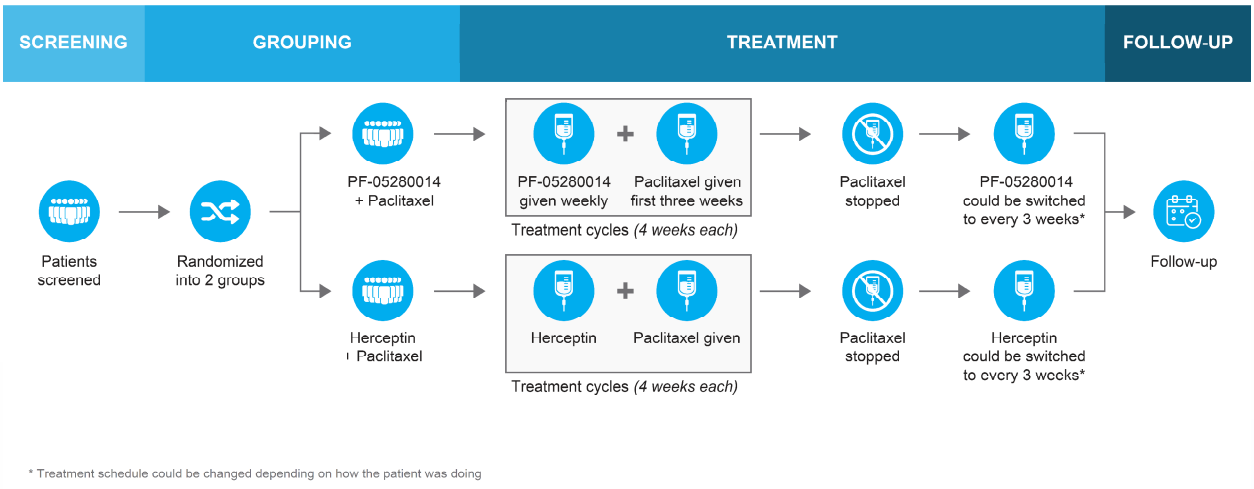
The patients and researchers did not know who received PF-05280014 and who received Herceptin. This is known as a "double-blinded" study. Researchers use "double-blinded" studies to make sure that the results of the study are not influenced in any way.

First, patients were checked (screened) to make sure they met all the requirements to be in the study. Then, 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 for things like age and race. Reducing differences between the groups makes the groups more even to compare. Patients had a 50% chance (1 in 2 chances, like the flip of a coin) of getting either treatment.

For at least the first 33 weeks of the study, patients were treated with PF-05280014 or Herceptin every week. Depending on how the patient was doing, the treatments were given in at least 6 "cycles", with a new cycle starting every 4 weeks. Paclitaxel was given weekly for the first 3 weeks of each cycle. After 33 weeks and treatment with paclitaxel had stopped, depending on how the patient was doing, the study doctor could change the PF-05280014 or Herceptin treatment schedule to every 3 weeks. After completing study treatment, patients were followed by researchers to see how they did after taking study medicines.

Patients were expected to receive study treatment until their breast cancer worsened. The entire study took more than 6 years to complete. The Sponsor ran this study at 168 locations in 25 countries in North America, South America, Europe, and Asia. It began 24 February 2014 and ended 27 June 2020. All patients were women between the ages of 19 and 85 years.

The figure below shows what happened in the study.



A total of 707 patients joined the study, but 5 patients (1%) did not receive any study treatment. 451 patients (64%) finished the study. 251 patients (35%) left before the study was over by their choice, because a doctor decided it was best for a patient to stop the study, because they passed away, or because the Sponsor stopped the study.

When the study ended in June 2020, the Sponsor began reviewing 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?

What percentage of patients who received PF-05280014 and paclitaxel had a reduction in tumor size, compared to patients who received Herceptin and paclitaxel?

Throughout the study, the researchers did imaging tests (such as MRI or CT scans) to see if tumors were changing in size. At Week 33 of the study:

- 63% of patients who were randomized to receive PF-05280014 and paclitaxel (220 out of 352 patients) had a reduction in tumor size (tumor got smaller or disappeared)

- 67% of patients who were randomized to receive Herceptin and paclitaxel (236 out of 355 patients) had a reduction in tumor size (tumor got smaller or disappeared)

In this study, PF-05280014 worked similarly to Herceptin in patients with breast cancer. 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. 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.

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 also have been caused by a study treatment or by another medicine 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.

685 out of 702 patients (98%) had at least 1 medical problem, including 344 out of 349 patients (99%) in the PF-05280014 group and 341 out of 353 patients (97%) in the Herceptin group. A total of 109 patients (16%) stopped study treatment due to medical problems, including 57 out of 349 patients (16%) in the PF-05280014 group and 52 out of 353 patients (15%) in the Herceptin group. The most common medical problems are listed in the table below.

Most Common Medical Problems (Reported by At Least 10% of Patients in Either Group)		
Medical Problem	PF-05280014 + Paclitaxel (349 Patients Treated)	Herceptin + Paclitaxel (353 Patients Treated)
Hair loss	189 (54%)	186 (53%)
Low red blood cell count	124 (36%)	136 (39%)
Low neutrophil count (a type of white blood cell)	100 (29%)	95 (27%)
Damage to the nerves that control feeling	93 (27%)	85 (24%)
Diarrhea	61 (17%)	66 (19%)
Nausea	57 (16%)	70 (20%)
Weakness	53 (15%)	46 (13%)
Headache	53 (15%)	70 (20%)
Decreased amount of blood pumped out of the heart	49 (14%)	47 (13%)
Tiredness	47 (13%)	51 (14%)
Joint pain	44 (13%)	38 (11%)
Increased liver enzyme in the blood, which may indicate liver problems (alanine aminotransferase)	42 (12%)	45 (13%)
Dizziness	38 (11%)	30 (8%)

Most Common Medical Problems (Reported by At Least 10% of Patients in Either Group)		
Medical Problem	**PF-05280014 + Paclitaxel (349 Patients Treated)**	**Herceptin + Paclitaxel (353 Patients Treated)**
Low white blood cell count	37 (11%)	46 (13%)
Increased liver enzyme in the blood, which may indicate liver problems (aspartate aminotransferase)	36 (10%)	31 (9%)
Infection in the nose, throat, and upper airways	36 (10%)	46 (13%)
High blood pressure	36 (10%)	31 (9%)
Nerve damage	35 (10%)	34 (10%)
Swelling in arms or legs	27 (8%)	45 (13%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

187 patients (27%) had serious medical problems, including 91 patients (26%) in the PF-05280014 group and 96 patients (27%) in the Herceptin group. The table below shows the most common serious medical problems.

Most Common Serious Medical Problems (Reported by At Least 1% of Patients in Either Group)		
Serious Medical Problem	**PF-05280014 + Paclitaxel (349 Patients Treated)**	**Herceptin + Paclitaxel (353 Patients Treated)**
Breast cancer worsening	**42 (12%)**	**42 (12%)**
Lung infection	**6 (2%)**	**4 (1%)**
Blockage in lung caused by blood clot	**5 (1%)**	**3 (less than 1%)**
Low red blood cell count	**4 (1%)**	**2 (less than 1%)**
Low potassium in the blood	**4 (1%)**	**0 (0%)**
Infection of skin and soft tissues	**2 (less than 1%)**	**4 (1%)**
Heart failure	**0 (0%)**	**4 (1%)**
Fever	**0 (0%)**	**4 (1%)**

128 out of 702 patients (18%) died during the study, including 61 patients (17%) in the PF-05280014 group and 67 patients (19%) in the Herceptin group. Most of these deaths were due to breast cancer. 3 patients (less than 1%) in the Herceptin group died due to medical problems related to the 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 **NCT01989676**
www.clinicaltrialsregister.eu	Use the study identifier **2013-001352-34**

Additional clinical trials with PF-05280014 are ongoing.

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

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!