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: Gedatolisib (PF-05212384), Dacomitinib (PF-00299804)

Protocol Number: B2151002

Dates of Trial: 10 September 2013 to 08 January 2020

Title of this Trial: A Study Of PF-05212384 In Combination with Other Anti-Tumor Agents and in Combination with Cisplatin in Patients with Triple Negative Breast Cancer (TNBC) in an Expansion Arm

[A Phase 1b Open-Label Three-Arm Multi-Center Study to Assess the Safety and Tolerability of PF-05212384 (PI3K/mTOR Inhibitor) in Combination with Other Anti-Tumor Agents]

Date(s) of this Report: 12 April 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?

Cancer, in general, is one of the common causes of death for both men and women.

Drug PF-05212384 (gedatolisib) was the investigational drug in this study. An investigational drug is one that is not approved for sale in this country at the time of the study. Gedatolisib is still under development to control the growth of cancer cells. Researchers think that gedatolisib might help to stop or slow down certain types of proteins which cause cancer cells to grow. Gedatolisib stops cancer growth pathways.

This study was divided into 2 parts, or phases. The main purpose of this trial was to learn about the effects of gedatolisib and to find a correct dose for when it is given in combination with other drugs in adult patients with different types of advanced cancer. All the patients in this study received gedatolisib in addition to one other drug. There were 3 treatment combinations or groups called "arms" in this study:

- (Arm A) - Docetaxel kills fast dividing cells like cancer cells.
- (Arm B) - Cisplatin stops cancer cells from growing.
- (Arm C) - Dacomitinib inhibits cancer growth pathways.

Both docetaxel and cisplatin are regarded as standard treatment for these types of cancer.

In the first part of the study, several patients left the study early on due to their cancer getting worse or due to other medical problems. As a result, Arms A and C had to finish early. This means that only Arm B (gedatolisib in combination with cisplatin) was used to estimate the correct dose of gedatolisib for that combination.

In the second part of the study, researchers wanted to assess the effect of gedatolisib when taken in combination with cisplatin in patients with a certain type of breast cancer called Triple Negative Breast Cancer (TNBC).

WHAT HAPPENED DURING THIS STUDY?

The first part of this study was set up to determine the best dose of gedatolisib (the test medicine) when taken in combination with another drug. The first part of this study compared 3 groups of patients that were given gedatolisib at different doses in combination with 1 of 3 other treatments. Both the patients and researchers knew who took which medicine. The figure below shows the 3 groups in the study.

First Part of the Study – Description of Treatment Groups

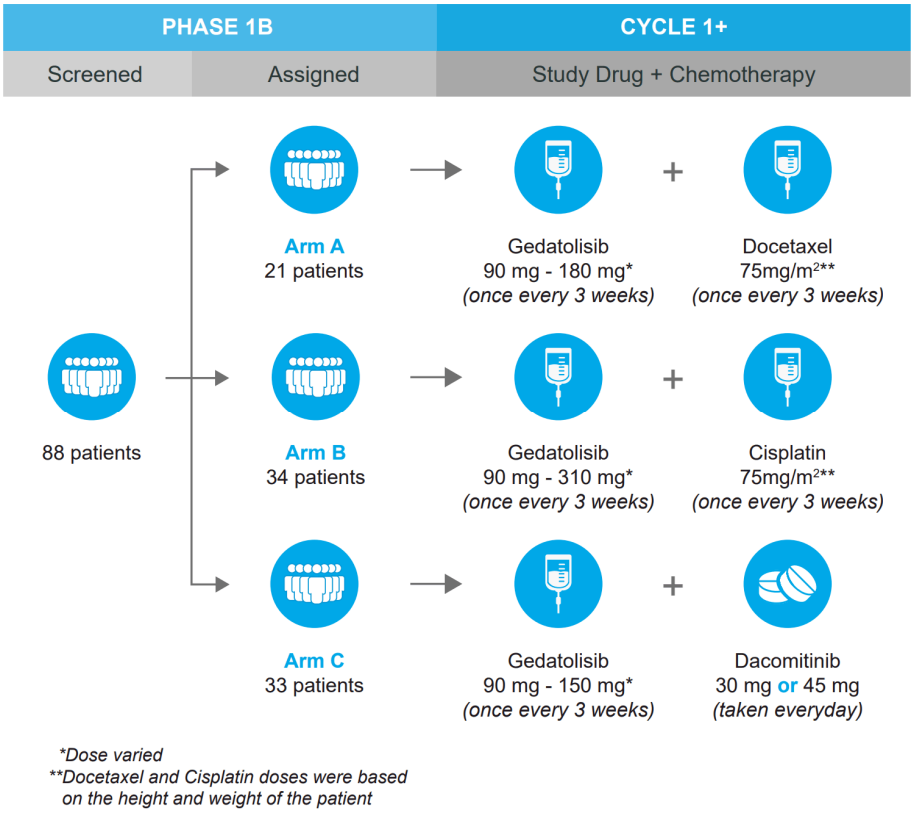
Group	Type of Cancer Treated	Treatment Given in the Study	Number of Patients		
			Assigned	Treated	Completed* the Study Treatment
A	Castrate-resistant prostate cancer, advanced breast cancer, or non-small cell lung cancer and were candidates for treatment.	Gedatolisib plus docetaxel	21	20	9
B	Urothelial transitional cell cancer, triple negative breast cancer, non-small cell lung cancer, or ovarian cancer.	Gedatolisib plus cisplatin	34	33	17
C	HER2+ breast cancer (that is cancer which is resistant to treatment with Herceptin or lapatinib), HER2+ esophago-gastric cancer, head and neck squamous cell cancer, or non-small cell lung cancer.	Gedatolisib plus dacomitinib	33	32	19

*Completed the study means those patients that stayed in the study and did not leave early due to either the cancer getting worse or because of medical problems.

The first part of the study included patients who were:

- Aged 18 years or over
- Had a diagnosis of specific types of advanced cancer as described in the table above.

Patients were unable to take part in the first part of the study if they had active brain cancer, severe heart disease, or had experienced a heart attack in the previous 12 months.



The time that patients spent in the overall study varied depending on the individual. There was no maximum to the number of cycles of treatment that a patient could undergo. The entire study took over 6 years to complete.

Patients were to be treated until their cancer got worse, until they had unacceptable medical problems or until they chose to stop. Of the 85 patients who were treated and who started the first part of the study to find the best dose, 45 finished the study. Forty (40) patients did not finish the first part of the study because they left before the study was over by their choice or a doctor decided it was best for a patient to stop being in the study.

The second part of the study was an extension of Arm B and was made up of patients with Triple Negative Breast Cancer taking gedatolisib plus cisplatin. All the patients in this second part of the study were aged 18 years or over and were selected because their cancer had spread.

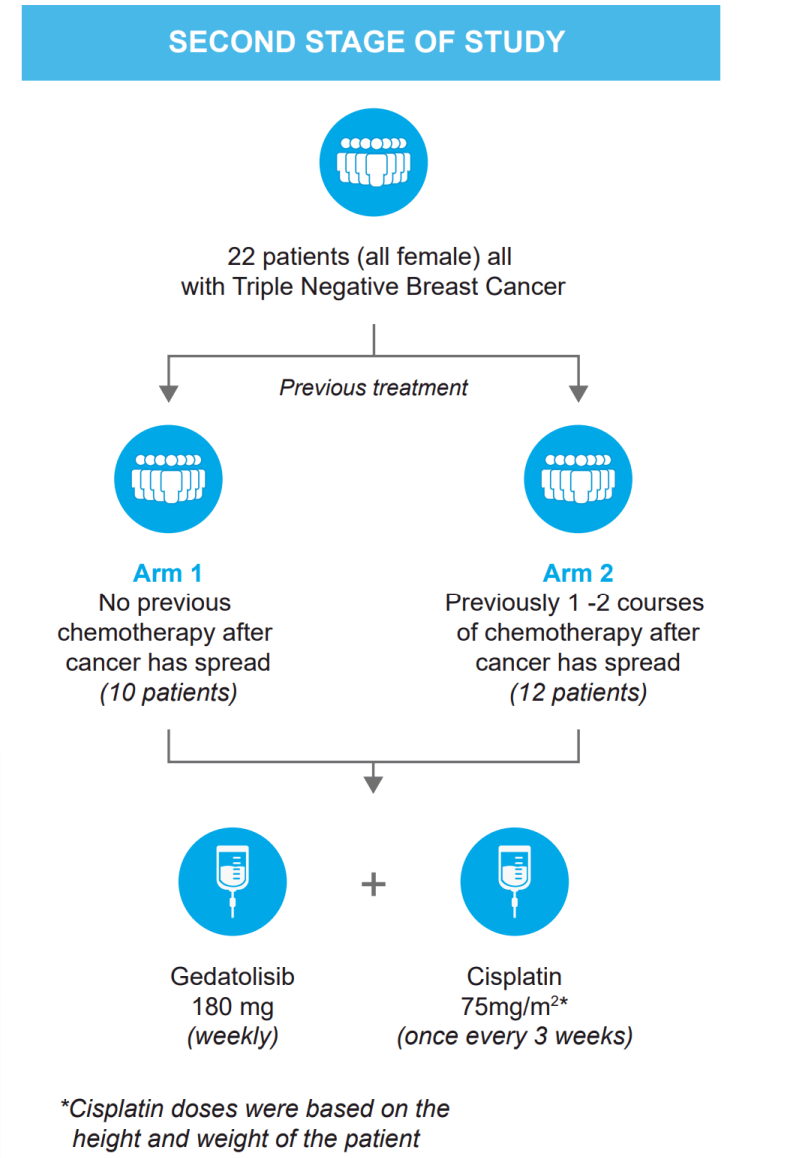
This group was spilt into 2 further groups as shown in the table below:

- Arm 1 – Patients who had not received chemotherapy to try to kill their cancer cells after the cancer had spread.

- Arm 2 – Patients who had received 1 or 2 rounds of chemotherapy to try and kill their cancer cells after their cancer had spread.

Patients were unable to take part in the second part of the study if they had active brain cancer or if they had received 3 or more rounds of chemotherapy to try to kill their cancer cells after it had spread.

This part of the study only included people with Triple Negative Breast Cancer, 22 patients started the study and 12 patients finished the study. Ten (10) patients left this part of the study before the end.



The Sponsor ran this whole study at 16 locations in 5 countries including the United States (US), Canada, United Kingdom (UK), Italy and Spain. It began 10 September 2013 and ended 8 January 2020. In total 34 men and 73 women took part in the overall study including both part 1 and 2 of the study. All patients were between the ages of 22 and 74.

When the overall study ended in January 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 THIS STUDY?

During the first part of the study, what dose-limiting toxicities (DLT) were reported?

In the first part of the study, researchers wanted to find out what was the correct dose of gedatolisib for treating patients with cancer.

To find the correct maximum dose that patients can take without causing unwanted medical problems, the researchers needed to know how many patients in each group had a dose-limiting toxicity (DLT) during their treatment.

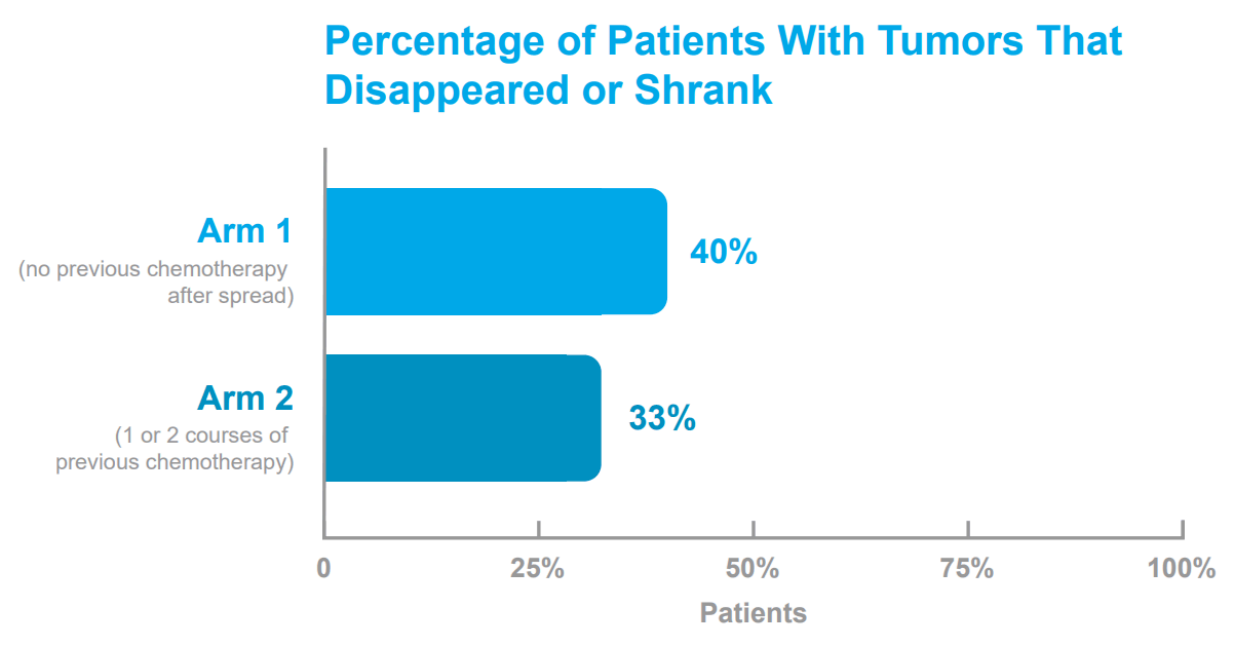
Arm A (gedatolisib together with docetaxel) and Arm C (gedatolisib together with dacomitinib) were both closed early so it was not possible to calculate the correct dose in these two groups.

Out of the 33 patients that started Arm B (gedatolisib together with cisplatin), 28 stayed in the study long enough to measure whether a dose-limiting toxicity had taken place during their treatment. Patients in this part of the trial were given different doses of gedatolisib together with 75 mg/m^2 of cisplatin. Two (2) people out of the 28 experienced a dose-limiting toxicity. Using this information, the researchers decided that 180 mg weekly was the correct maximum dose of gedatolisib to be used in combination with cisplatin 75 mg/m^2 every 3 weeks in the second part of the study.

During the second part of the study, did taking gedatolisib together with cisplatin help tumors disappear or shrink in patients with Triple Negative Breast Cancer?

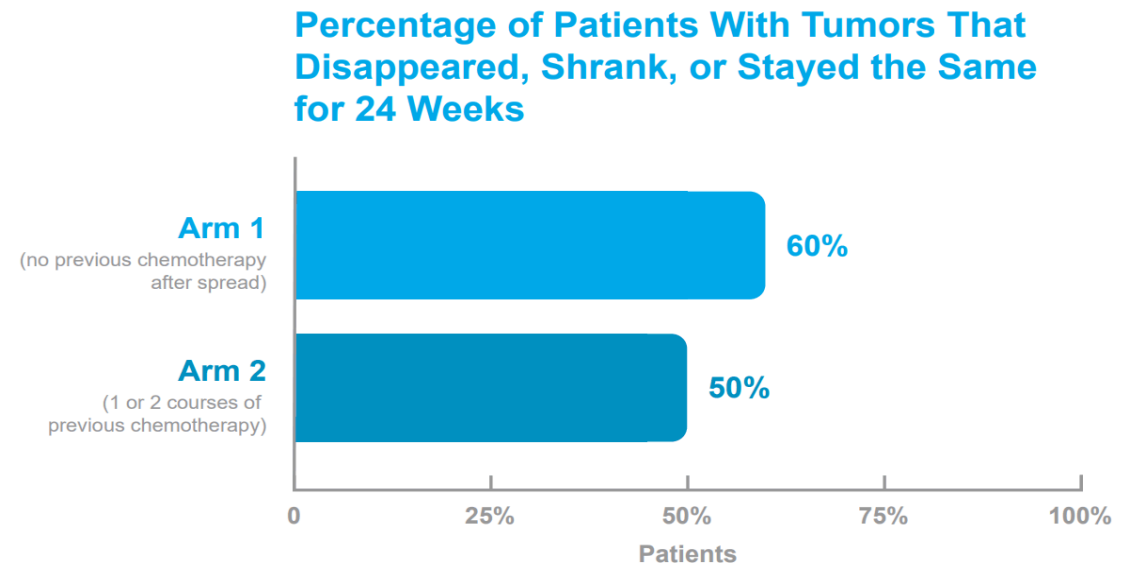
Researchers looked at the "overall response rate", which is whether tumors completely disappeared (known as a "complete response") or shrunk (known as a "partial response") after taking gedatolisib together with cisplatin. In Arm 1 (those patients who had not previously had chemotherapy to kill their cancer cells after their cancer had spread) the overall response rate was 40%. This means that 4 out of the 10 treated people had either a complete or partial response to the study drug.

In Arm 2 (those patients who had been given chemotherapy to kill their cancer cells after their cancer had spread) the overall response rate was 33%. This means that 4 out of the 12 treated people had a complete or partial response to the study drug. Overall, 36% of patients (8 out of 22 treated patients) in this study who took the test medicine saw their condition improve.



Did taking gedatolisib in combination with cisplatin help tumors disappear, shrink or stay the same for 24 weeks?

Researchers looked at whether tumors disappeared, shrunk or stayed the same (e.g. "stable disease") for 24 weeks, as this gives researchers an idea of the clinical benefit of gedatolisib when used in combination with cisplatin. Overall, 12 patients had clinical benefit from treatment at 24 weeks (55%, or 12 out of the 22 treated patients). This included patients from Arm 1 (60%, or 6 out of the 10 treated patients) and patients from Arm 2 (50%, or 6 out of the 12 treated patients).



Based on these results, the researchers have decided gedatolisib in combination with cisplatin was generally tolerated by patients in the study.

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.

During the first part of this study, all the patients had at least 1 medical problem. A total of 18 out of 85 patients left this part of the study because of medical problems.

The most common medical problems across the whole first part of the study are listed below.

Most Common Medical Problems – First Part of Study (Reported by More Than 30% of All Patients across All 3 Arms)			
Medical Problem	**Arm A Gedatolisib + Docetaxel** (20 Patients Treated)	**Arm B Gedatolisib + Cisplatin** (33 Patients Treated)	**Arm C Gedatolisib + Dacomitinib** (32 Patients Treated)
Irritation of the moist linings of the mouth, throat and airways etc.	12 (60%)	19 (58%)	27 (84%)
Feeling sick	9 (45%)	26 (79%)	20 (63%)
Diarrhea	8 (40%)	11 (33%)	23 (72%)
Tiredness	8 (40%)	17 (52%)	15 (47%)
Vomiting or being sick	5 (25%)	20 (61%)	14 (44%)
Constipation	9 (45%)	14 (42%)	8 (25%)
Reduced appetite	5 (25%)	12 (36%)	12 (38%)
Low white blood cell count	18 (90%)	11 (33%)	Less than 10%
Low red cell count (anemia)	5 (25%)	20 (61%)	Less than 10%

During the second part of this study, all the patients had at least 1 medical problem. A total of 9 out of 22 patients left the study because of medical problems. The most common medical problems are listed below.

Most Common Medical Problems – Second Part of Study Treating Patients with Triple Negative Breast Cancer (Reported by 50% or More of Patients)

Medical Problem	Gedatolisib + Cisplatin (22 Patients Treated)
Low red cell count (anemia)	19 (86%)
Tiredness	16 (73%)
Feeling sick	16 (73%)
Vomiting	14 (64%)
Constipation	13 (59%)
Irritation of the moist linings of the mouth, throat and airways etc.	13 (59%)
Low white blood cell count	11 (50%)
Fever	11 (50%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

Of the 107 patients who received treatment in this study, 37 (35%) had a serious medical problem including 11 patients who died.

In the first part of this study to find the correct dose, 31 patients out of the 85 treated patients had serious medical problems. These included the cancer coming back or getting worse, irritation of the moist linings of the mouth, throat and airways, and low white blood cell count with a fever, shortness of breath and dehydration.

In addition, a total of 11 patients passed away during Part A of this study (4 in Arm A, 4 in Arm B, and 3 in Arm C) and the main cause of deaths was cancer. None of the deaths were related to the study drug.

In the second part of the study, 6 patients out of 22 had serious medical problems. This included irritation of the moist linings of the mouth, throat and airways. Four (4) patients died during Part B of the study and the main cause of deaths was cancer. None of the deaths were related to the study drug.

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 your study protocol, please visit:

www.clinicaltrials.gov	Use the study identifier **NCT01920061**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **B2151002**

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!