# 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:** Talazoparib (PF-06944076)

**Protocol Number:** Study 673-201 (C3441008; ABRAZO)

**Dates of Trial:** 13 December 2013 to 31 October 2018

**Title of this Trial:** A Study of Talazoparib in Patients with Breast Cancer That is Advanced or Has Spread [A Phase 2, 2-Stage, 2-Cohort Study of Talazoparib (BMN 673) Administered to Germline BRCA Mutation Subjects With Locally Advanced and/or Metastatic Breast Cancer]

**Date of this Report:** 19 December 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.

# WHY WAS THIS STUDY DONE?

Breast cancer is one of the most common causes of cancer in women. In 2012, around 1.7 million women were diagnosed with this disease around the world. Men can also get breast cancer, though this is quite rare.

Some breast cancers are caused by "mutations" in "DNA" in the BReast CAncer "genes" 1 and 2, which are more commonly known as BRCA1 and BRCA2. DNA is a material inside the cells of all living things that controls how cells in the body grow. Genes are parts of DNA that contain the code for a specific feature, like eye color. Mutations are changes in the DNA that can alter how a cell will behave.

If the BRCA1 and BRCA2 genes have mutations then this may cause breast cancer. These mutations can be inherited from a parent with this mutation or through chance, which is like the roll of a dice. Special proteins known as "poly (ADP-ribose) polymerase" or "PARP" are found in all cells, and these proteins can help damaged cells fix or repair themselves so that the cell survives. When PARP helps cancer cells fix or repair themselves, it means that the cancer cell (and the tumor it is part of) can continue to grow and spread.

Talazoparib is a "PARP inhibitor," which means it is a drug that can help stop the normal activity of PARP. At the time of this study, talazoparib was an "investigational drug". An investigational drug means that the treatment has not been approved by the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), or other regulatory agencies. This study was carried out to see if talazoparib could help reduce tumor size and slow growth in people with advanced breast cancer who have inherited mutations in the BRCA1 or BRCA2 genes from a parent.

On 16 October 2018, talazoparib received approval from the FDA for use in some people with breast cancer. While this study was taking place, the sponsor decided it was better to recruit patients into a Phase 3 study that compared talazoparib with usual treatment for breast cancer rather than enroll patients into this study. This study was stopped early on 31 October 2018, and the sponsor transferred patients who were still being treated with talazoparib into another study.

# WHAT HAPPENED DURING THE STUDY?

All patients in this study received talazoparib. The researchers wanted to find out if a patient's previous breast cancer treatment could change the way talazoparib was able to treat the tumor. Some patients with cancer are given chemotherapy with drugs containing platinum while others are given chemotherapy with drugs that do not contain platinum. This study included 2 different groups of patients previously treated for breast cancer as shown in the table below. The patients in both of these groups had breast cancer that was advanced and difficult to treat.

**Description of Treatment Groups**

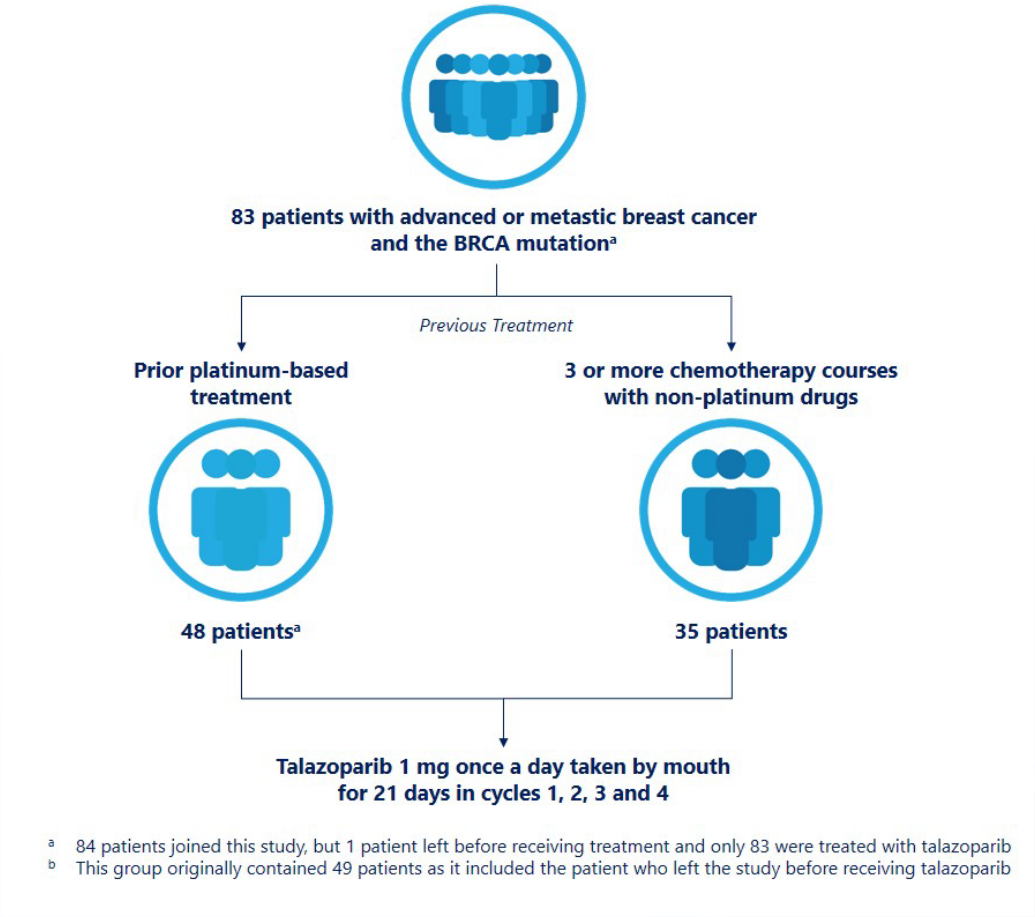
| Group | Previous Treatment for Breast Cancer | Number of Patients Treated[a] |
|---|---|---|
| 1 | Prior chemotherapy with drugs containing platinum (platinum-based therapy) like cisplatin or carboplatin. Patients initially responded to treatment, and while the cancer came back, this occurred more than 8 weeks after last dose of platinum-therapy | 48[b] |
| 2 | Prior chemotherapy with 3 or more courses of treatment with drugs like docetaxel, paclitaxel, doxorubicin, capecitabine, vinorelbine, or eribulin that are not based on a platinum drug. Note: Use of a platinum-based therapy before or after surgery was allowed providing the cancer did not return within 6 months of the last platinum dose | 35 |

[a] 84 patients originally joined this study, but 1 patient left before receiving treatment and only 83 patients were treated with talazoparib

[b] This group originally contained 49 patients as it included the patient who left the study before receiving talazoparib.

The study included patients who:

- Were 18 years or older
- Had breast cancer that was advanced and not suitable for radiotherapy or surgery or had "metastatic disease", which is when the cancer has spread to other parts of the body
- Inherited the BRCA1 or BRCA2 gene mutation




Patients joined the study at 1 of 34 sites in the United States (US), United Kingdom (UK), France, Germany, and Spain. The study began on 13 December 2013 when the first patient had their first visit. All patients were aged between 31 years and 75 years, and nearly all were women. There were 2 men treated in the study, with 1 in each group. There were originally 84 patients who joined the study, but 1 patient left before receiving treatment with talazoparib. A total of 83 patients were treated with talazoparib in this study until their doctor determined their cancer was getting worse, the side effects were too severe, the patient decided they wanted to leave the study, or the study was closed by the Sponsor. The main reason patients treated with talazoparib left the study was because they passed away (81%, or 67 out of the 83 treated patients).

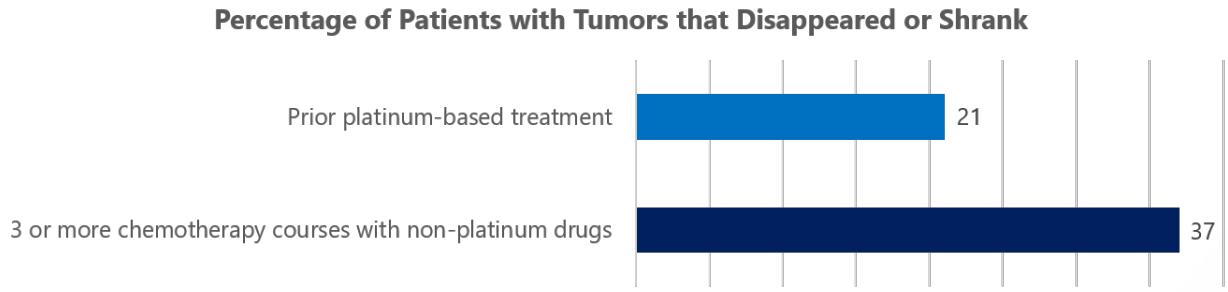
As of 01 September 2016 (the data cutoff date for the full report), 10 patients from the group previously treated with platinum-based treatment (21%, or 10 out of the 48 treated patients) and 16 patients from the group previously treated with 3 or more chemotherapy courses with non-platinum drugs (46%, or 16 out of the 35 treated patients) were still in the study but were "off-treatment" and not taking talazoparib. In addition, 5 patients from the group previously treated with platinum-based treatment (10%, or 5 out of 48 treated patients) and 4 patients from the group previously treated with 3 or more chemotherapy courses with non-platinum drugs (11%, or 4 out of 35 treated patients) were "on-treatment" and taking talazoparib. These on-treatment patients were followed until 31 October 2018, when the study was closed early by the Sponsor. At the time the study ended, 2 out of these 9 patients were continuing to receive talazoparib treatment. As these 2 patients were benefitting from talazoparib, the Sponsor transferred them into another study so they could continue this treatment.

Data collected up to 01 September 2017 were reviewed by the Sponsor and used to write a report. This is a summary of the information included in the report on how talazoparib was able to treat breast cancer. Data collected up until 31 October 2018, when the Sponsor closed the study, were analyzed in a supplementary safety report. The main findings of the safety report are summarized in this document.

# WHAT WERE THE RESULTS OF THE STUDY?

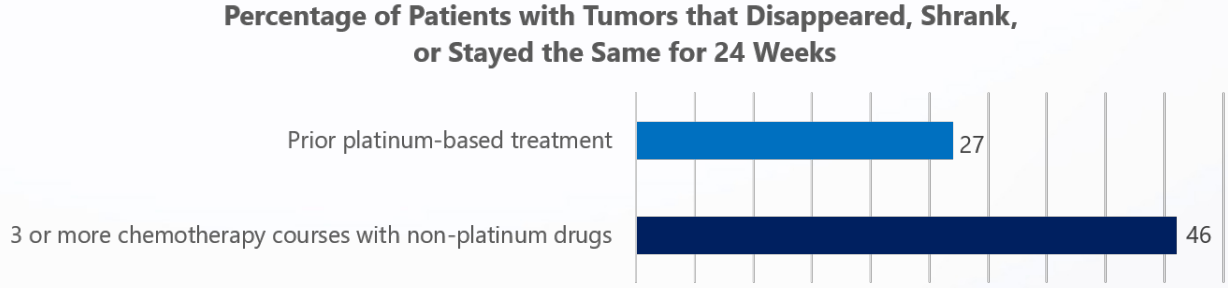
## Did taking talazoparib help tumors disappear or shrink?

Researchers looked at the "objective response rate," which is whether tumors disappeared (eg, "complete response") or shrunk (eg, "partial response") after taking talazoparib. Overall, 23 patients had a tumor that disappeared or shrunk (28%, or 23 out of the 83 treated patients). This included patients from the group previously treated with platinum-based treatment (21%, or 10 out of the 48 treated patients) and also from the group previously treated with 3 or more chemotherapy courses with non-platinum drugs (37%, or 13 out of the 35 treated patients).




## Did taking talazoparib help tumors disappear, shrink or stay the same for 24 weeks?

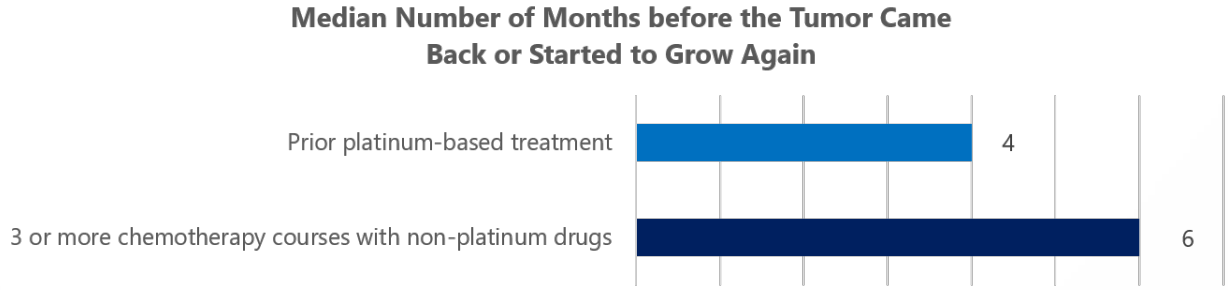
Researcher looked at whether tumors disappeared, shrunk or stayed the same (eg, "stable disease") for 24 weeks, as this gives researchers an idea of the clinical benefit of talazoparib. Overall, 29 patients had clinical benefit from treatment at 24 weeks (35%, or 29 out of the 83 treated patients). This included patients from the group previously treated with platinum-based treatment (27%, or 13 out of the 48 treated patients) and patients from the group previously treated with 3 or more chemotherapy courses with non-platinum drugs (46%, or 16 out of the 35 treated patients).




## How long did patients taking talazoparib continue to respond to this treatment?

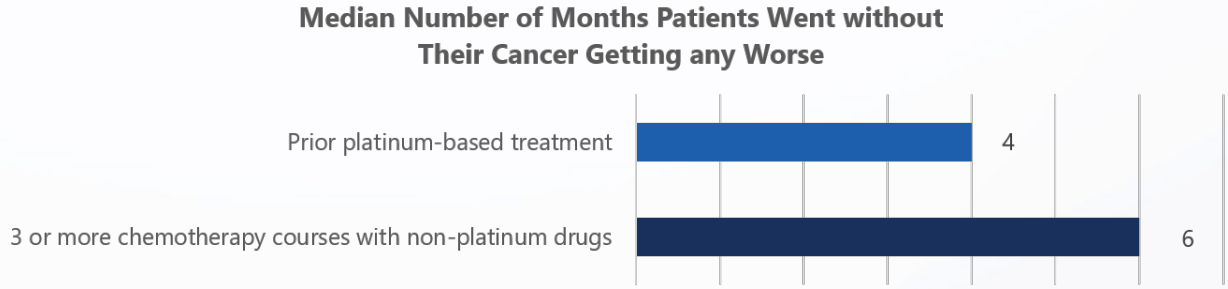
Researchers measured how long it took for the tumor to come back after it had disappeared and the time it took for the tumor to start to grow again after it had shrunk. The researchers took the results (in the number of months) and put them in order from the smallest to the largest. They then looked at the middle number, or the "median", to help them answer this question. There was a median of almost 4 months for patients in the group previously treated with platinum-based

chemotherapy and a median of almost 6 months for patients in the group previously treated with 3 or more chemotherapy courses with non-platinum drugs.



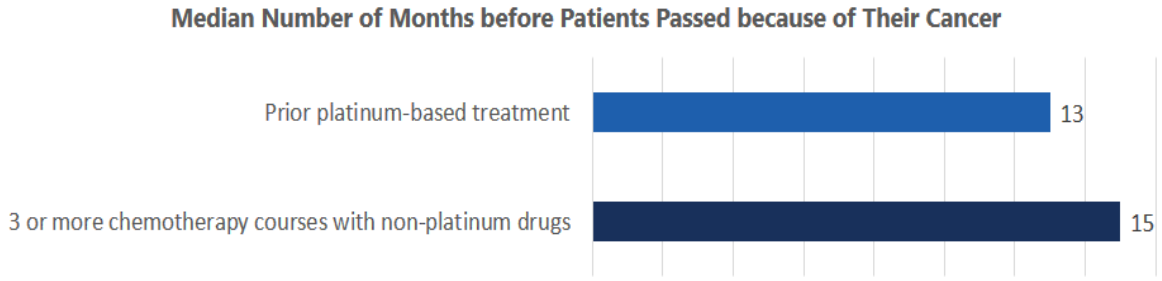

## How long did patients go without their cancer getting any worse after taking talazoparib?

Researchers measured how long patients went without their cancer getting any worse after taking talazoparib. There was a median of 4 months for patients in the group previously treated with platinum-based treatment and a median of 6 months for patients in the group previously treated with 3 or more chemotherapy courses with non-platinum drugs.




When researchers looked at the time before patients passed away, this was a median of 12 months for patients in the group previously treated with platinum-based treatment and a median of 17 months for patients in the group previously treated with 3 or more chemotherapy courses with non-platinum drugs. This included data collected up until 01 September 2016. As the sponsor had access to data up to 07 April 2017, they used this to look again at the time before patients passed away. This date of 07 April 2017 is likely to give a more accurate result. This was a median of 13 months for patients in the group previously treated with platinum-based

treatment and a median of 15 months for patients in the group previously treated with 3 or more chemotherapy courses with non-platinum drugs.




Based on these results, the researchers thought talazoparib may be 1 of the options available to doctors who are treating patients with breast cancer who have the BRCA1 or BRCA2 mutation. This includes patients previously treated with platinum-based treatment as well as patients previously treated with 3 or more chemotherapy courses with non-platinum drugs. 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 investigational drug might be.

A total of 81 out of the 83 treated patients in this study had at least 1 "non-serious" medical problem. A "serious" medical problem is a medical problem that is life threatening, needs hospital care, or cause lasting problems. Overall, 5 patients left the study because of medical problems (6%, or 5 out of the 83 treated patients). This included 4 patients from the group previously treated with platinum-based treatment (8%, 4 out of the 48 treated patients) and 1 patient from the group previously treated with 3 or more chemotherapy courses with non-platinum drugs (3%, 1 out of the 35 treated patients). The most common medical problems experienced by patients in this study are listed in the following table, and these were most often in the digestive system (stomach and intestines), were general like tiredness, or were seen in blood test results. Medical problems were also seen in other areas of the body and affected the heart, eyes, brain, or blood system. While overall more than 1 in 10 patients had some type of problem that affected these areas of the body, none of the individual medical problems in these areas were seen in more than 1 in 10 patients.

**Most Common Medical Problems (Reported by at Least 10% of Patients in Either Group)**

| Medical Problem | Prior Platinum-based Chemotherapy (48 Patients Treated) | Previously Treated with 3 or More Chemotherapy Courses with Non-platinum Drugs (35 Patients Treated) |
|---|---|---|
| Feeling tired | 29 (60%) | 8 (23%) |
| Low red blood cell count (anemia) | 24 (50%) | 19 (54%) |
| Upset stomach or feeling sick | 20 (42%) | 15 (43%) |
| Diarrhea or loose stools | 18 (38%) | 10 (29%) |
| Low platelets (or small bits of cells in the blood) | 18 (38%) | 9 (26%) |
| Low numbers of neutrophils (a type of white blood cell) | 10 (21%) | 12 (34%) |

| Medical Problem | Prior Platinum-based Chemotherapy (48 Patients Treated) | Previously Treated with 3 or More Chemotherapy Courses with Non-platinum Drugs (35 Patients Treated) |
|---|---|---|
| Headache | 9 (19%) | 11 (31%) |
| Feeling weak | 3 (6%) | 10 (29%) |
| Not feeling hungry | 12 (25%) | 10 (29%) |
| Joint pains | 8 (17%) | 9 (26%) |
| Being out of breath | 11 (23%) | 9 (26%) |
| Back pain | 12 (25%) | 8 (23%) |
| Viral chest infection | 11 (23%) | 3 (9%) |
| Hair loss (baldness) | 11 (23%) | 6 (17%) |
| Vomiting or being sick | 10 (21%) | 8 (23%) |
| Stomach pain | 7 (15%) | 7 (20%) |
| Cough | 9 (19%) | 7 (20%) |
| Constipation | 9 (19%) | 6 (17%) |
| Low numbers of leukocytes (a type of white blood cell) | 7 (15%) | 6 (17%) |
| Low platelet count (from blood test) | 7 (15%) | 5 (14%) |
| Low neutrophil count (from blood test) | 5 (10%) | 5 (14%) |
| Muscle spasms | 4 (8%) | 5 (14%) |

## WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A total of 69 patients (83%, or 69 out of the 83 treated patients) passed away while in this study, and almost all of these deaths were due to the cancer coming back or getting worse. Other serious medical problems were seen in 16 patients in the group previously treated with prior platinum-based treatment (33%, or 16 out of the 48 treated patients) and 7 patients in the group previously treated with 3 or more chemotherapy courses with non-platinum drugs (20%, or 7 out of the 35 treated patients). These serious medical problems mainly affected the blood (eg, low levels of red blood cells or "platelets" or small bits of cells), the lungs or were because of the cancer.

## 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: **NCT02034916** |
| www.clinicaltrialsregister.eu | Use the EudraCT number: **2013-003076-12** |

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!