Clinical Study 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 medication works, how it works, and if it is safe to prescribe to study participants. 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, formerly MDV3800)

Protocol Number: C3441020

Dates of Study: 27 August 2018 to 23 September 2020

Title of this Study: Talazoparib For Neoadjuvant Treatment Of Germline BRCA1/2 Mutation Patients With Early Human Epidermal Growth Factor Receptor 2 Negative Breast Cancer

[A Phase 2, Non-Randomized, Open-Label, Single-Arm, Multi-Center Study of Talazoparib for Neoadjuvant Treatment of Germline BRCA1/2 Mutation Patients With Early Human Epidermal Growth Factor Receptor 2 Negative Breast Cancer]

Date(s) of this Report: 25 June 2021

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is breast cancer?

Breast cancer is the most common cancer in women. In 2012, about 1.7 million women were diagnosed with breast cancer and over 522,000 women died due to the disease.

Some people carry changes or "mutations" in their DNA in genes called breast cancer susceptibility (BRCA) genes 1 and 2, or "BRCA1" and "BRCA2". BRCA gene mutations can be inherited by a child from one of their parents (germline). When a person's BRCA1 or BRCA2 genes contain mutations, it can cause breast cancer. Researchers are looking for treatments for breast cancer patients with BRCA mutations.

What is talazoparib?

Talazoparib (Talzenna®) is known as a PARP inhibitor. PARP inhibitors are drugs that are believed to inhibit (stop) the normal activity of certain proteins called "Poly (ADP-ribose) polymerases", also called "PARPs". PARPs are proteins (made from genes which are part of DNA) that are found in all normal and cancer cells that are involved in the repair of DNA. PARPs are needed to repair mistakes that can happen in DNA when cells divide. If the mistakes are not repaired, the cell will usually die and be replaced. Cells with mistakes in their DNA (like cells with BRCA1 and BRCA2 gene mutations) that do not die can become cancer cells.

Clinical trials have shown that the use of talazoparib, as well as other PARP inhibitors, may reduce tumor size and slow tumor growth in patients with certain types of cancer with BRCA1 or BRCA2 mutations. Talazoparib is given in a capsule and is taken by mouth once daily at around the same time every day.

What was the purpose of this study?

Talazoparib is now approved in the United States, the European Union, and other countries for the treatment of people with a certain type of breast cancer (human

epidermal growth factor receptor 2 [HER2]-negative), who have an abnormal inherited BRCA gene, and their cancer has spread beyond the original tumor ("locally advanced") or has spread to other parts of the body ("metastatic"). This study was done to see if talazoparib treatment followed by surgery could result in a "pathologic complete response" (complete disappearance of cancer in the breast or underarm lymph node tissues at surgery) in participants with early breast cancer (original location) who have inherited a BRCA1 or BRCA2 gene mutation in HER2 negative breast cancer.

Researchers also wanted to learn more about the safety of talazoparib. They monitored the participants for any medical problems that happened while they were in the study.

Researchers wanted to know:

How many participants had a pathologic complete response (complete disappearance of cancer at surgery) after 24 weeks of treatment with talazoparib followed by surgery?

What happened during the study?

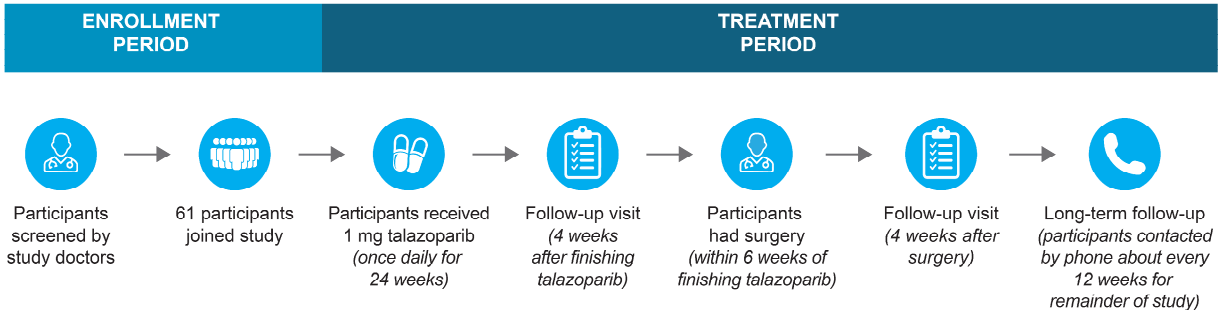
How was the study done?

Participants were checked (screened) to make sure they were a good fit for the study. Participants received 1 milligram (mg) talazoparib once per day by mouth, for 24 weeks (participants with kidney disease received a lower dose, 0.75 mg talazoparib). Within 6 weeks of finishing talazoparib treatment, participants had surgery and study doctors took tissue samples to evaluate and remove breast cancer.

This was an "open-label" study, which means that the participants and doctors knew which treatment and dose they received.

Participants joined the study and received talazoparib for 24 weeks and were expected to attend a follow-up visit about 4 weeks later. Within 6 weeks of completing talazoparib treatment, participants had surgery (if appropriate) followed by another follow-up visit 4 weeks later. Participants were thereafter contacted by phone about every 12 weeks for the remainder of the study.

The figure below shows what happened during this study.



Where did this study take place?

The Sponsor ran this study at 18 locations in the United States.

When did this study take place?

It began on 27 August 2018 and ended 23 September 2020.

Who participated in this study?

This study included adult participants who:

- Had HER2 negative (HER2 is a type of protein receptor that may be on the surface of cancer cells) or early invasive triple-negative breast cancer
- Had a BRCA 1 or BRCA 2 gene mutation
- Were appropriate to receive treatment prior to surgery
- Had breast cancer which had not spread to parts of the body that are far away from the breast
- Had a measurable tumor and lymph nodes which were less than 2 inches in size

- Had not received other cancer treatment within the past 3 years (with the exception of treatments for breast cancer of the milk ducts only)
- Had adequate kidney, liver, and bone marrow function

- A total of 61 women participated
- No men participated
- All participants were between the ages of 26 and 75 years

Participants received talazoparib treatment for 24 weeks. Of the 61 participants who started the study, 45 participants (74%) completed talazoparib treatment.

A total of 16 participants (26%) stopped taking talazoparib early

- by their choice,
- because their breast cancer was worsening,
- because they had a medical problem, or
- because a doctor decided it was best for them to stop talazoparib

How long did the study last?

The amount of time that each participant was in this study varied. The entire study took about 2 years to complete.

After the last participant's surgical safety follow-up was completed, the study ended in September 2020, and 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?

How many participants had a pathologic complete response (complete disappearance of cancer at surgery) after 24 weeks of treatment with talazoparib followed by surgery?

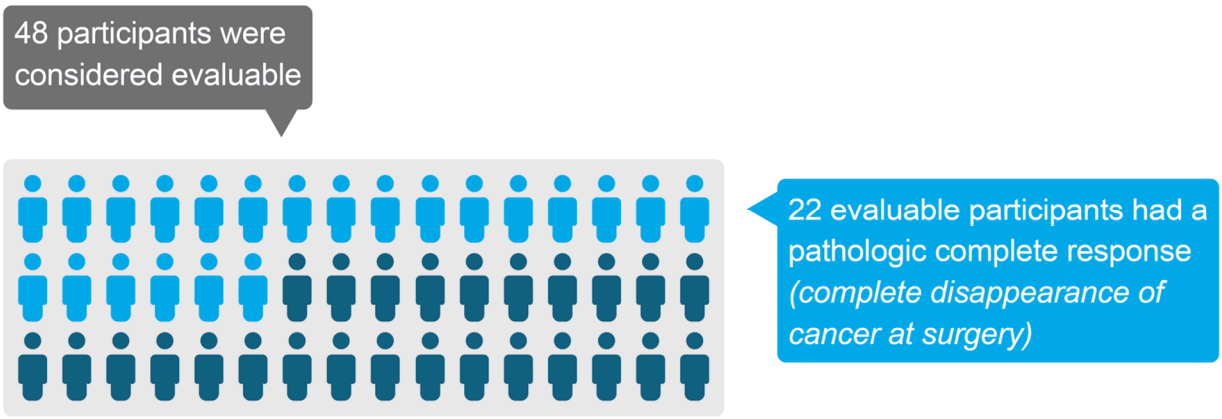
To answer this question, the researchers looked at the number of "evaluable participants" who had a complete disappearance of cancer at surgery. Evaluable participants are participants that the researchers collected enough information from to get a good idea of how well the study treatments worked. There were 48 evaluable participants in this study.

22 out of 48 evaluable participants (46%) had a pathologic complete response (complete disappearance of cancer at surgery) after 24 weeks of treatment with talazoparib followed by surgery.

The researchers also calculated the "confidence intervals", which are used to show what the uncertainty is for a particular result. The 95% and 80% confidence intervals showed:

- a 95% confidence interval was between 32% and 61%
- an 80% confidence interval was between 36% and 55%

This does not mean that everyone in this study had these results. These are just some of the main findings of this study. Other studies may have different results.



What medical problems did participants 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 also 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 effects a study medication might have on a participant.

60 out of 61 (98%) participants in this study had at least 1 medical problem. A total of 3 out of 61 (5%) participants discontinued talazoparib because of a medical problem. Medical problems were managed by holding talazoparib doses (33%), providing blood transfusions (33%), and reducing talazoparib doses (39%).

The most common medical problems – those reported by at least 10% of participants – are described below.

Below are instructions on how to read Table 1 and Table 2.

Instructions for Understanding Table 1 and Table 2.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by at least 10% of participants are listed.
- The **2nd** column tells how many of the 61 participants taking talazoparib reported each medical problem. Next to this number is the percentage of the 61 participants taking talazoparib who reported the medical problem.
- Using these instructions, you can see that 48 out of the 61 (79%) participants taking talazoparib reported feeling tired.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Talazoparib (61 Participants Treated)
Feeling tired	48 out of 61 participants (79%)
Nausea	42 out of 61 participants (69%)
Hair loss	35 out of 61 participants (57%)
Low red blood cell count	30 out of 61 participants (49%)
Headache	26 out of 61 participants (43%)
Dizziness	20 out of 61 participants (33%)
Constipation	19 out of 61 participants (31%)
Loose stools	13 out of 61 participants (21%)

Table 1. Commonly reported medical problems by study participants

Medical Problem	Talazoparib (61 Participants Treated)
Nose, sinus, or throat infection	12 out of 61 participants (20%)
Anxiety	11 out of 61 participants (18%)
Joint pain	11 out of 61 participants (18%)
Difficulty sleeping	11 out of 61 participants (18%)
Difficulty breathing	10 out of 61 participants (16%)
Cough	9 out of 61 participants (15%)
Muscle pain	9 out of 61 participants (15%)
Low levels of white blood cells (neutrophils)	9 out of 61 participants (15%)
White blood cells count decreased	9 out of 61 participants (15%)
Low appetite	8 out of 61 participants (13%)
ALT liver test result increased	7 out of 61 participants (12%)
Breast pain	7 out of 61 participants (12%)
Hot flush	7 out of 61 participants (12%)
Throat pain	7 out of 61 participants (12%)
Rash	7 out of 61 participants (12%)
Vomiting	7 out of 61 participants (12%)

Did study participants have any serious medical problems?

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

11 out of 61 (18%) participants in this study had at least 1 serious medical problem.

No deaths occurred during the safety reporting period. A total of 2 participants died during the long-term follow-up period due to progression of their breast cancer. These deaths were not considered to be related to talazoparib.

The serious medical problems are described below.

Table 2. Serious medical problems reported by study participants

Medical Problem	Talazoparib (61 Participants Treated)
Low red blood cell count	9 out of 61 participants (15%)
Low white blood cell count	1 out of 61 participants (2%)
Blockage in bowel	1 out of 61 participants (2%)
Flu-like illness	1 out of 61 participants (2%)

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 **NCT03499353**

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

Again, if you participated in this study,
thank you for volunteering.
We do research to try to find the
best ways to help study participants, and you
helped us to do that!