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 (Talzenna®)

Protocol Number: 673-301 (C3441009)

Dates of Trial: 14 October 2013 to 05 March 2021

Title of this Trial: A Study Evaluating Talazoparib (BMN 673), a PARP Inhibitor, in Advanced and/or Metastatic Breast Cancer Patients With BRCA Mutation (EMBRACA)

[A Phase 3, Open-Label, Randomized, Parallel, 2-Arm, Multi-Center Study of Talazoparib (BMN 673) Versus Physician's Choice in Germline BRCA Mutation Subjects With Locally Advanced and/or Metastatic Breast Cancer, Who Have Received Prior Chemotherapy Regimens for Metastatic Disease]

Date of this Report: 09 November 2018; updated 24 April 2020 and 02 October 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?

Breast cancer is one of the most common causes of cancer deaths 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 that can help them have more time without their cancer getting worse.

Talazoparib (Talzenna®) is a drug that inhibits (stops) 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, can reduce tumor size or delay the cancer getting worse, and slow tumor growth in some cancer patients 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.

Talazoparib is now approved in the United States, the European Union, and other countries for the treatment of patients with a certain type of breast cancer that has spread beyond the original tumor ("advanced") or has spread to other parts of the body ("metastatic") and have an inherited BRCA1 or BRCA2 gene mutation. This study was done to see if talazoparib treatment could help patients with advanced or metastatic breast cancer, and have inherited a BRCA1 or BRCA2 gene mutation, have more time without their cancer getting worse when compared to commonly used chemotherapies.

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

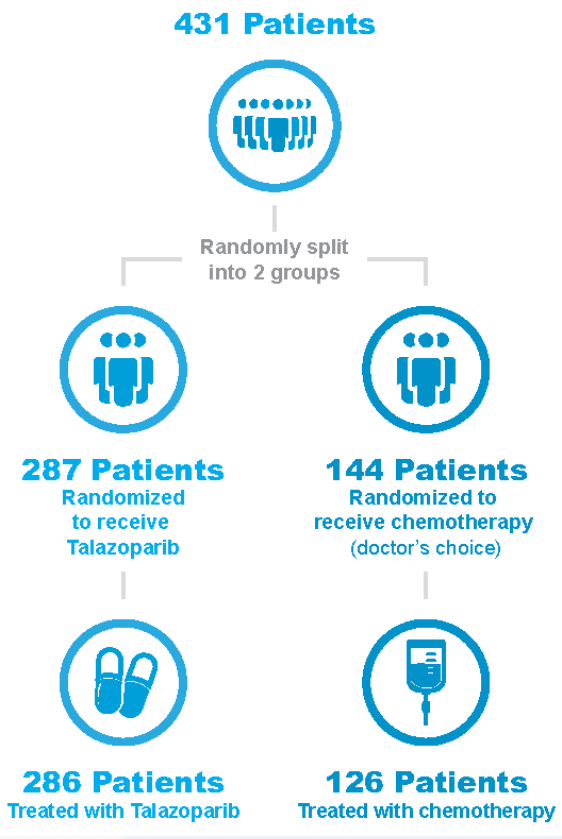
WHAT HAPPENED DURING THE STUDY?

This study compared 2 groups of patients to find out if patients taking talazoparib had more time without their cancer getting worse compared to patients taking other commonly used chemotherapies.

The study included patients who:

- Were at least 18 years old
- Had breast cancer that was advanced or had spread to other parts of the body (also called "metastatic cancer")
- Inherited the BRCA1 or BRCA2 gene mutation
- Did not have more than 3 chemotherapy treatments for their advanced cancer
- Had previously taken at least 1 of the commonly used cancer chemotherapies
- Had good organ function and adequate blood counts

This trial was an open-label study. This means that both the patient and the doctor knew whether the patient received talazoparib or chemotherapy.



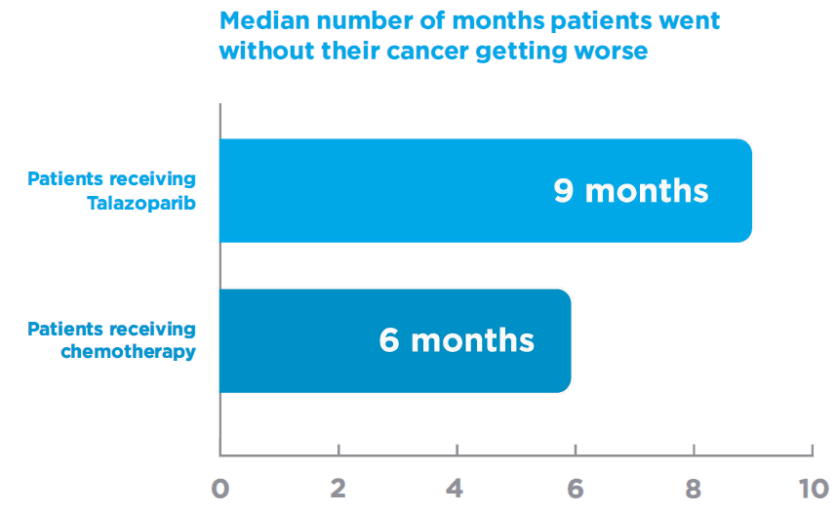
Patients joined the study at 1 of 145 locations in the US, Europe (Belgium, France, Germany, Ireland, Italy, Poland, Spain, UK, Israel, Russia, and Ukraine), Brazil, South Korea, Australia, and Taiwan. It began on 14 October 2013 and ended on 05 March 2021. A total of 7 men and 424 women participated in this study. All patients were between the ages of 24 and 88. Patients were to be treated until their doctor determined that their cancer was getting worse, the side effects were too severe, or until they chose to stop participation in the study. All of the 431 patients who started the study had stopped treatment by the end of the study, mostly due to the patient's cancer getting worse, the patient chose to stop, or a doctor decided it was best for a patient to stop their assigned treatment.

The Sponsor reviewed the study results in September 2017, September 2019, and March 2021. The Sponsor then created reports of the results collected up to those time points. This is a summary of those reports.

WHAT WERE THE RESULTS OF THE STUDY?

Did taking talazoparib help patients in this study have more time without their cancer getting worse than those treated with chemotherapy?

Researchers measured the "median time" between starting the study and the patients' cancer getting worse, or dying of any cause. The median time was the time point where half (50%) of the patients taking talazoparib or chemotherapy had their cancer get worse, or they had passed away from any cause. For patients taking talazoparib, the median number of months patients went without their cancer getting worse was about 9 months. For patients taking chemotherapy, it was about 6 months.



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 over time, doctors may be able to understand what the side effects of an experimental drug might be.

A total of 405 out of 412 patients in this study who received at least 1 dose of study medication had at least 1 medical problem (282 out of 286 on talazoparib and 123 out of 126 on chemotherapy). Most medical problems were manageable by lowering the dose of talazoparib or chemotherapy medications.

The most common medical problems reported by patients in this study are listed below.

Number of Patients With Most Common Medical Problems (Reported by At Least 10% of Patients in Either Group)

Medical Problem	Talazoparib (286 Patients Treated)	Chemotherapy (126 Patients Treated)
Low blood count (red blood cell, hemoglobin)	155 (54%)	24 (19%)
Tiredness (fatigue)	147 (51%)	54 (43%)
Nausea	142 (50%)	60 (48%)
Headache	97 (34%)	29 (23%)
Low white blood cell count (neutropenia)	78 (27%)	38 (30%)
Hair loss	78 (27%)	35 (28%)
Vomiting	76 (27%)	30 (24%)
Back pain	69 (24%)	20 (16%)
Diarrhea	68 (24%)	34 (27%)
Constipation	67 (23%)	28 (22%)
Cough	65 (23%)	20 (16%)
Decreased appetite	62 (22%)	28 (22%)
Joint pain	55 (19%)	15 (12%)
Difficulty breathing	54 (19%)	19 (15%)
Dizziness	53 (19%)	13 (10%)

Low platelet count	50 (18%)	7 (6%)
Arm or leg pain	45 (16%)	14 (11%)
Weakness	45 (16%)	12 (10%)
Nose and throat infection	41 (14%)	13 (10%)
Stomach pain	38 (13%)	20 (16%)
Lack of sleep	38 (13%)	10 (8%)
Nose and throat infection (viral)	36 (13%)	8 (6%)
Decreased platelet count	36 (13%)	4 (3%)
Fever	35 (12%)	22 (18%)
Indigestion	33 (12%)	10 (8%)
Decreased white blood cells	32 (11%)	5 (4%)
Urinary tract infection	31 (11%)	3 (2%)
Low white blood cell count (neutrophils)	30 (11%)	18 (14%)
Altered taste	30 (11%)	11 (9%)
Rash	29 (10%)	12 (10%)
Pain related to the muscles or bones	29 (10%)	9 (7%)
Muscle pain	25 (9%)	14 (11%)
Weight loss	23 (8%)	15 (12%)
Abnormal lab test results that could indicate liver damage (Aspartate aminotransferase increased)	16 (6%)	15 (12%)

Damage to nerves that can cause tingling, numbness, pain, or loss of feeling	**13 (5%)**	**15 (12%)**
Abnormal lab test results that could indicate liver damage (Alanine aminotransferase increased)	**12 (4%)**	**15 (12%)**
Swelling or pain in the hands or feet (hand-foot syndrome)	**4 (1%)**	**28 (22%)**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

A total of 142 patients out of 412 (34%, or approximately 1 out of 3 patients) had serious medical problems (103 out of 286 on talazoparib and 39 out of 126 on chemotherapy). Most of these problems were not thought to be related to the study drug. A total of 320 out of 412 patients who had received at least 1 dose of talazoparib or chemotherapy medication died during the study (220 out of 286 on talazoparib and 100 out of 126 on chemotherapy). Most deaths were due to the patient's cancer getting worse. Two (2) serious medical problems that occurred in patients who died (veno-occlusive liver disease in a patient receiving talazoparib and sepsis in a patient receiving chemotherapy) may have been related to study treatment.

In addition, 2 patients who received talazoparib developed blood cancer (acute myeloid leukemia) after they finished participating in the study that may have been related to the study treatment. These patients also received other cancer treatments which could have helped cause their acute myeloid leukemia.

Number of Patients With Serious Medical Problems (Reported by ≥2% of Patients in Either Group)		
Serious Medical Problem	**Talazoparib (286 Patients Treated)**	**Chemotherapy (126 Patients Treated)**
Low blood count (red blood cell, hemoglobin)	18 (6%)	0 (0%)
Fever	8 (3%)	2 (2%)
Blood clots in the lungs	6 (2%)	0 (0%)
Buildup of fluid in the lungs	4 (1%)	7 (6%)
Low white blood cell count (neutropenia)	3 (1%)	4 (3%)
Diarrhea	0 (0%)	3 (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.

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT01945775**
www.clinicaltrialsregister.eu	Use the study identifier **2013-002716-28**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C3441009**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients. Clinical trials with talazoparib are ongoing and further trials are planned.

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!