

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 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: C3441037

Dates of Study: 21 December 2020 to 22 July 2022

Title of this Study: A Phase 1 Bioequivalence Study Between the Current Commercial Capsule and the Proposed Soft Gel Capsule of Talazoparib, and Food Effect Study for the Proposed Talazoparib Soft Gel Capsule in Participants With Advanced Solid Tumors
[A Phase 1, Open Label, Crossover Study to Establish Bioequivalence Between the Proposed Soft Gel Talazoparib Capsule Formulation and the Current Talazoparib Commercial Formulation and to Estimate the Food Effect on Pharmacokinetics of the Proposed Talazoparib Soft Gel Capsule Formulation in Participants With Advanced Solid Tumors.]

Date(s) of this Report: 09 February 2023



— 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 cancer?

Cancer is the name for a group of diseases in which abnormal cells divide without control. Most types of cancer cause solid tumors to form, which are masses of these abnormal cells. Advanced solid tumors are cancers that have spread to other areas of the body and do not respond to many treatments.

What is talazoparib?

Talazoparib (Talzenna[®]) is a PARP inhibitor. PARP inhibitors are drugs that inhibit (stop) the normal activity of certain proteins called “Poly (ADP-ribose) polymerases”, also called “PARPs”. PARPs can be found in all normal and cancer cells and are involved in the repair of DNA. Mistakes in the DNA can happen when cells divide. PARPs can keep cancer cells alive. Talazoparib can stop PARPs from working and prevent cancer cells from repairing their DNA. If the mistakes are not repaired, the cell will usually die.

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. 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 approved in the United States, the European Union, and other countries for the treatment of people with a type of cancer known as metastatic breast cancer with BRCA mutations. The purpose of this study was to see if the new soft-gel capsule of talazoparib acted similarly in the body to the current hard capsule of talazoparib. In addition, researchers wanted to see how the new talazoparib soft-gel capsules acted when taken on an empty stomach compared to when taken with a meal.

Researchers wanted to know:

- How did the new soft-gel capsule of talazoparib compare to the current hard capsule for the highest amount and total amount of talazoparib that entered the blood?
 - How did the amount of talazoparib that entered the blood when the new soft-gel capsules were taken on an empty stomach compared to when the new soft-gel capsules were taken with a meal?
 - What medical problems did participants have during the study?
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What happened during the study?

How was the study done?

Researchers gave the 2 different capsule types of talazoparib to adult participants with advanced solid tumors and compared the levels of talazoparib in the blood of participants after receiving either the soft-gel capsule or the hard capsule. Researchers also compared the amount of talazoparib in the blood of participants who took the soft-gel capsule with a meal (“fed”) or on an empty stomach (“fasted”) to see if food affected the levels of talazoparib in the blood.

Participants received both the soft-gel capsules and hard capsules of talazoparib in random order during this study. Researchers used a computer program to place each participant into Treatment Sequence #1 or Treatment Sequence #2 in a random way, a process called “randomization”. This means that each participant had an equal chance of ending up in either treatment sequence. This is similar to flipping a coin.

The participants and researchers knew who was in each dosing sequence. This is known as a “open-label” study.

Treatment Phase

During the treatment phase:

- Participants in Treatment Sequence #1 were given:
 - 1) Talazoparib soft-gel capsule once a day for the first 28 days (“Period 1”)
 - 2) Talazoparib hard capsule once a day for the next 21 days (“Period 2”)
- Participants in Treatment Sequence #2 were given:
 - 1) Talazoparib hard capsule once for the first 28 days (“Period 1”)
 - 2) Talazoparib soft-gel capsule once a day for the next 21 days (“Period 2”)
- During Period 1 and Period 2, participants in both treatment sequences took talazoparib on an empty stomach.
- During the last 21 days of the treatment phase (“Period 3”), all participants took talazoparib soft-gel capsule once a day with a meal.

All participants visited the study clinic once before the study started to make sure they were qualified to participate in the study. During the treatment phase, participants made approximately 9 visits to the study clinic. At these visits, researchers took samples of blood from participants to measure the amount of talazoparib in their blood. Researchers also checked the participants’ health at some of these visits.

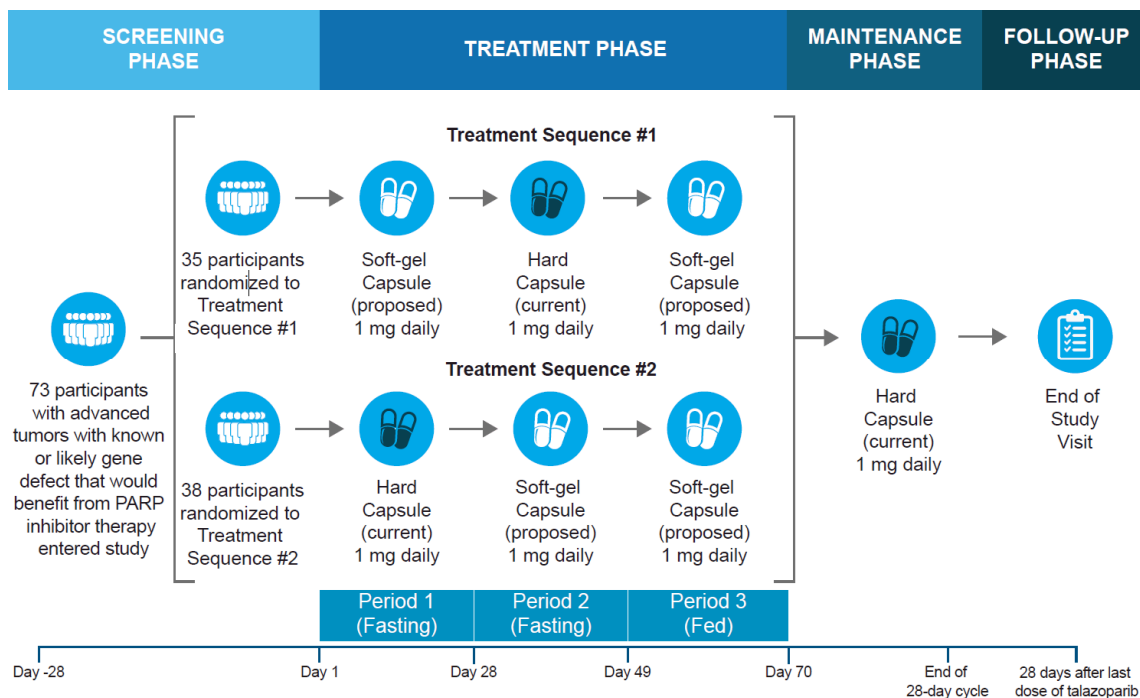
Optional Maintenance Phase

After completing the treatment phase, participants could continue taking talazoparib hard capsules as part of an optional maintenance phase. During the maintenance phase, participants took talazoparib once a day for 28 days (called a “cycle”). On the first day of the next 28-day cycle, participants visited the study clinic so that a study doctor could check the participant’s health. If the doctor determined that a participant’s cancer was not getting worse and that the participant was still benefitting from treatment, the participant was allowed to start another 28-day cycle of treatment.

Safety Follow-Up Phase

After a participant’s last dose of talazoparib, they entered a 28-day safety follow-up phase. At the end of the 28-day safety follow-up phase, participants underwent an End of Study visit. The End of Study visit was conducted by phone or by visiting the study clinic.

Participants who completed the treatment phase and the End of Study visit were counted as completing the study.



Where did this study take place?

The Sponsor ran this study at 20 locations in 2 countries, the United States and Australia.

When did this study take place?

It began 21 December 2020 and ended 22 July 2022.

Who participated in this study?

The study included adult participants with advanced solid tumors who had a known or likely gene defect that was expected to respond to PARP inhibitors.

- A total of 30 men participated
- A total of 43 women participated
- All participants were between the ages of 25 and 70 years

Of the 73 participants who entered the study, 46 (63%) participants completed the study.

How long did the study last?

Study participants were to be in the study for about 3 months (treatment phase and safety follow-up). The entire study took 19 months to complete.

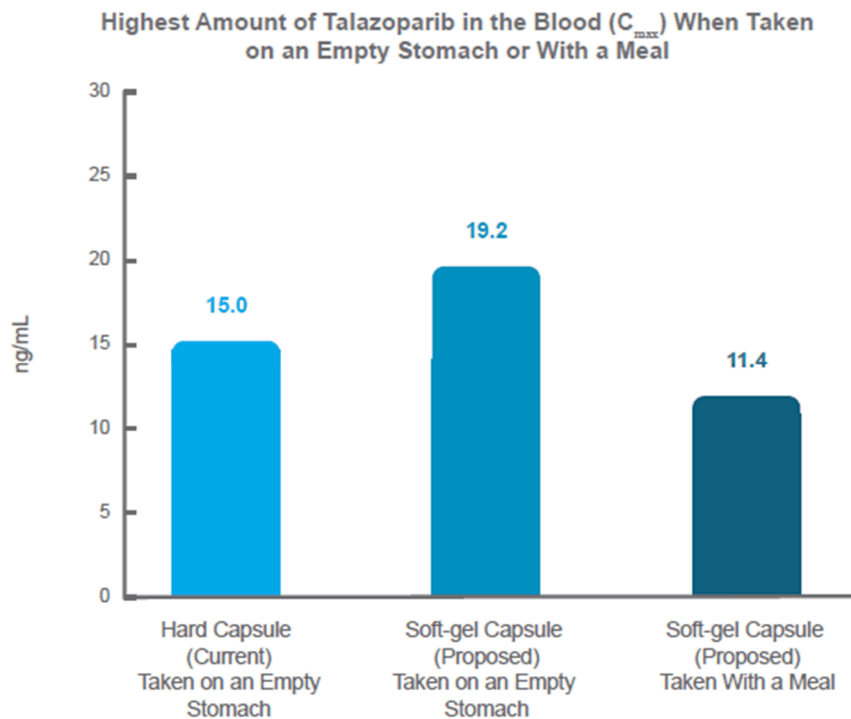
When the study ended in July 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How did the new soft-gel capsule of talazoparib compare to the current hard capsule for the highest amount and total amount of talazoparib that entered the blood?

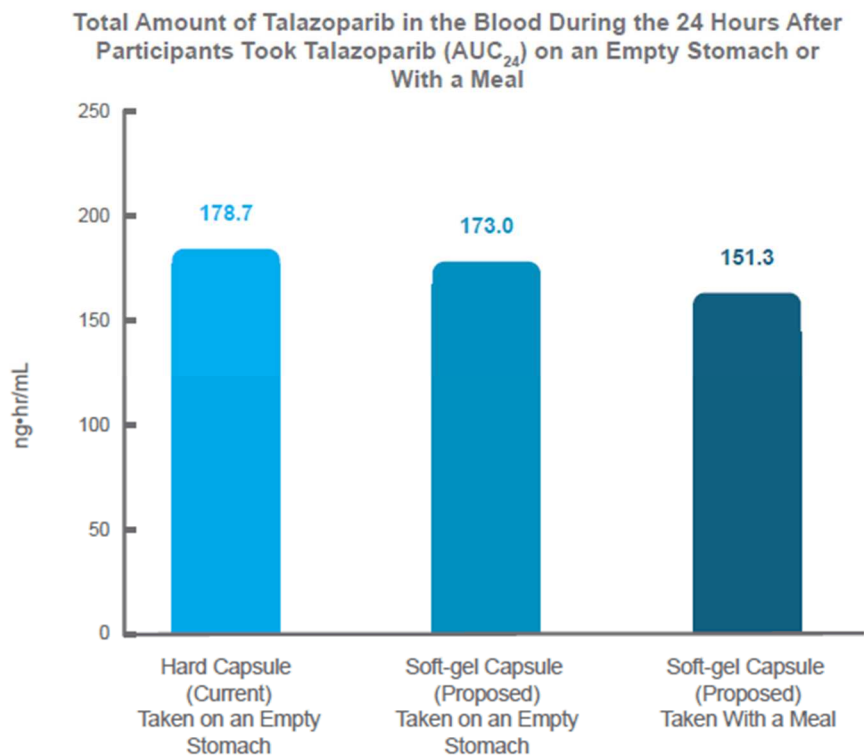
What was the highest amount of talazoparib in the blood after participants took a 1 mg hard capsule or a 1 mg soft-gel capsule on an empty stomach? What was the highest amount of talazoparib in the blood after participants took a 1 mg soft-gel capsule with a meal?

The amount of drug in the blood was measured in nanograms per milliliter, also called ng/mL. The highest amount of talazoparib in the blood after participants took 1 mg of talazoparib (known as C_{max}) on an empty stomach was 15.0 ng/mL for the hard capsule and 19.2 ng/mL for the soft-gel capsule (see figure below). When the 1 mg soft-gel capsule was taken with a meal, the highest amount of talazoparib in the blood was 11.4 ng/mL.



What was the total amount of talazoparib in the blood during the 24 hours after participants took a 1 mg hard capsule or a 1 mg soft-gel capsule on an empty stomach? What was the total amount of talazoparib in the blood during the 24 hours after participants took a 1 mg soft-gel capsule with a meal?

- The estimated total amount of talazoparib in the blood during the 24 hours after participants took 1 mg of talazoparib (known as AUC_{24}) is measured in nanogram hours per milliliter, also called $ng \cdot hr/mL$. The $ng \cdot hr/mL$ is a unit used to measure total amount of drug over time in the blood. The AUC_{24} was 178.7 $ng \cdot hr/mL$ for the hard capsule and 173.0 $ng \cdot hr/mL$ for the soft-gel capsule when taken on an empty stomach (see figure below). When the soft-gel capsule was taken with a meal, the total amount of talazoparib in the blood during the 24 hours after participants took talazoparib was 151.3 $ng \cdot hr/mL$.



How did the new soft-gel capsule of talazoparib compare to the current hard capsule for the highest amount (C_{max}) and total amount after 24 hours (AUC_{24}) of talazoparib that entered the blood when taken on an empty stomach?

- The C_{max} of the soft-gel capsule was higher than the C_{max} of the hard capsule.
- The AUC_{24} of the soft-gel capsule was similar to the AUC_{24} of the hard capsule.

How did the amount of talazoparib that entered the blood when the new soft-gel capsule were taken on an empty stomach compare to when the new soft-gel capsule were taken with a meal?

How did the highest amount (C_{max}) of talazoparib that entered the blood compare when soft-gel capsule were taken on an empty stomach or when taken with a meal?

- The C_{max} of the soft-gel capsule taken with a meal (11.4 ng/mL) was lower than the C_{max} of the soft-gel capsule taken on an empty stomach (19.2 ng/mL).
- This means that the highest amount of talazoparib that entered the blood after taking a soft-gel capsule with a meal was about 58% of the amount compared to when the soft-gel capsule was taken on an empty stomach.

How did the total amount of talazoparib that entered the blood in the 24 hours after taking talazoparib (AUC_{24}) compare when soft-gel capsules were taken on an empty stomach or taken with food?

- The AUC_{24} of the soft-gel capsule taken with a meal (151.3 ng•hr/mL) was similar to the AUC_{24} of the soft-gel capsule taken without food (173.0 ng•hr/mL).
- This means that the total amount of talazoparib that entered the blood in the 24 hours after taking a soft-gel capsule with a meal was about 88% of the amount compared to when the soft-gel capsule was taken on an empty stomach.

Researchers considered the differences in the results as minor. This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study.

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 solid cancers or 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.

Medical problems regardless of the cause were reported for participants who took hard capsules or soft-gel capsules. During the treatment phase:

- 42 out of 65 (65%) participants who took talazoparib hard capsules on an empty stomach reported at least 1 medical problem
- 36 out of 60 (60%) participants who took talazoparib soft-gel capsule on an empty stomach reported at least 1 medical problem
- 15 out of 30 (50%) participants who took talazoparib soft-gel capsule with a meal reported at least 1 medical problem

During the maintenance phase:

- 31 out of 41 (76%) participants who took talazoparib hard capsules reported at least 1 medical problem

A total of 11 participants left the study because of medical problems. The most common medical problems – those reported by more than 10% of participants – are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The 1st column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by more than 10% of participants in any group are listed.
- The 2nd column tells how many of the 65 participants taking the talazoparib hard capsule on an empty stomach reported each medical problem. Next to this number is the percentage of the 65 participants taking the talazoparib hard capsule on an empty stomach who reported the medical problem.
- The 3rd column tells how many of the 60 participants taking the talazoparib soft-gel capsule on an empty stomach reported each medical problem. Next to this number is the percentage of the 60 participants taking the talazoparib soft-gel capsule on an empty stomach who reported the medical problem.
- The 4th column tells how many of the 30 participants taking the talazoparib soft-gel capsule with a meal reported each medical problem. Next to this number is the percentage of the 30 participants taking the talazoparib soft-gel capsule with a meal who reported the medical problem.
- The 5th column tells how many of the 41 participants in the maintenance phase taking the talazoparib hard capsule reported each medical problem. Next to this number is the percentage of the 41 participants taking the talazoparib hard capsule on an empty stomach who reported the medical problem.
- Using these instructions, you can see that 8 out of the 65 (12%) participants taking talazoparib hard capsules on an empty stomach reported low red blood cell count. A total of 8 out of the 60 (13%)

participants taking talazoparib soft-gel capsule on an empty stomach reported low red blood cell count. A total of 5 out of the 30 (17%) participants taking talazoparib soft-gel capsule with a meal reported low red blood cell count. A total of 11 out of the 41 (27%) participants taking talazoparib hard capsules during the maintenance phase reported low red blood cell count.

Table 1. Commonly reported medical problems by $\geq 10\%$ of study participants in any group

| Medical Problem | Treatment Phase | | | Maintenance Phase |
|--------------------------|--|--|--|-----------------------------------|
| | Hard capsule (taken on an empty stomach) (65 Participants) | Soft-gel capsule (taken on an empty stomach) (60 Participants) | Soft-gel capsule (taken with a meal) (30 Participants) | Hard capsule (41 Participants) |
| Low red blood cell count | 8 out of 65 participants (12%) | 8 out of 60 participants (13%) | 5 out of 30 participants (17%) | 11 out of 41 participants (27%) |
| Nausea | 7 out of 65 participants (11%) | 5 out of 60 participants (8%) | 1 out of 30 participants (3%) | 2 out of 41 participants (5%) |
| Feeling tired | 4 out of 65 participants (6%) | 11 out of 60 participants (18%) | 2 out of 30 participants (7%) | 8 out of 41 participants (20%) |
| Hair loss | 2 out of 65 participants (3%) | 1 out of 60 participants (2%) | 2 out of 30 participants (7%) | 5 out of 41 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.

During the treatment phase:

- 9 out of 65 (14%) participants who took talazoparib hard capsules on an empty stomach reported at least 1 serious medical problem. Of these, 2 participants reported serious medical problems that researchers considered were related to the study medication.
- 7 out of 60 (12%) participants who took talazoparib soft-gel capsules on an empty stomach reported at least 1 serious medical problem. No participants reported serious medical problems that researchers considered were related to the study medication.
- 1 out of 30 (3%) participants who took talazoparib soft-gel capsules with a meal reported at least 1 serious medical problem. No participants reported serious medical problems that researchers considered were related to the study medication.

During the maintenance phase:

- 7 out of 41 (17%) participants who took talazoparib hard capsules reported at least 1 serious medical problem. Of these, 3 participants reported serious medical problems that researchers considered were related to the study medication.

10 participants died while taking study medication or within 28 days after the last dose of treatment, mostly from their cancer getting worse. The researchers did not consider any of the deaths to be related to the study medication.

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
www.clinicaltrialsregister.eu

Use the study identifier NCT04672460
Use the study identifier 2020-006101-35

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

[www.pfizer.com/research/
research_clinical_trials/trial_results](http://www.pfizer.com/research/research_clinical_trials/trial_results)

Use the protocol number C3441037

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

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