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

Protocol Number: MDV3800-02 (C3441002)

Dates of Study: 30 September 2016 to 12 February 2020

Title of this Study: A Study Evaluating Talazoparib (MDV3800) in Patients with Advanced Solid Tumors and a Normal or Decreased Liver Function

[A Phase 1 Open-Label Pharmacokinetics and Safety Study of Talazoparib (MDV3800) in Patients With Advanced Solid Tumors and Normal or Varying Degrees of Hepatic Impairment]

Date(s) of this Report: 20 May 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.

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Why was this study done?

What is meant by liver function or decreased liver function?

The liver processes medicines in the body into substances the body can use and converts toxins into harmless substances or makes sure they are removed from the body. Decreased liver function or damage to the liver may change the way a medicine is processed by the liver in comparison to a liver that is functioning normally and make it difficult for a patient to tolerate this medicine.

What is talazoparib?

Talazoparib is a medicine approved in the United States (US) and the European Union to treat patients with a certain type of breast cancer. Previous studies showed that talazoparib did not have an effect on patients with mildly decreased liver function. Talazoparib had not been studied in patients with moderately or severely decreased liver function.

Talazoparib may stop the normal activity of certain proteins called "poly ADP-ribose polymerases" also called "PARPs". PARPs are proteins that are found in all cells, normal and cancer, and are involved in the repair of mistakes in the DNA (the molecule that provides the blueprint for structure and function of every individual cell) that may happen when cells divide. Some people have inherited or acquired defects (mutations) in particular DNA damage repair proteins (eg, BRCA1 or BRCA2, ATM, and/or PALB2). When such patients are given a PARP inhibitor the cancer cells cannot repair DNA and die. This may lead to an effective treatment for such patients.

All participants in this study received the same treatment which was talazoparib alone at the daily dose of 0.5 mg, by mouth, for 22 calendar days (from Day 1 to Day 22).

What was the purpose of this study?

- The purpose of this study was to learn how participants with advanced solid tumors with normal liver function and those with decreased liver function handled and tolerated talazoparib.

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- This study did not test if the talazoparib helps to improve advanced solid tumors.

Researchers wanted to know:

- **How did the body metabolize talazoparib?**

  - Researchers wanted to understand better how much talazoparib remained in the blood over the study period in participants with different liver functioning. This is important to understand as decreased liver function can either increase or decrease the amount of medication in the bloodstream.

- **What medical problems did participants have during the study?**

  - 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.

What happened during the study?

How was the study done?

This study compared 4 groups of participants to find out how well participants with advanced solid tumors and varying degrees of liver function impairment tolerated talazoparib. A description of the how the study was done can be seen in Figure 1 below.

The 4 groups included:

- Group A - Participants with normal liver function
- Group B - Participants with mildly decreased liver function
- Group C - Participants with moderately decreased liver function
- Group D - Participants with severely decreased liver function

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Participants were to take talazoparib at a dose of 0.5 mg every day for 22 days.

Researchers took samples of blood and urine from participants during the study and measured the amount of talazoparib that remained in the blood or was metabolized to the urine. Researchers also checked the participants' health during the study and asked them how they were feeling.

This was an open-label study, which means that both the participant and the study doctor knew which treatment the participants received.

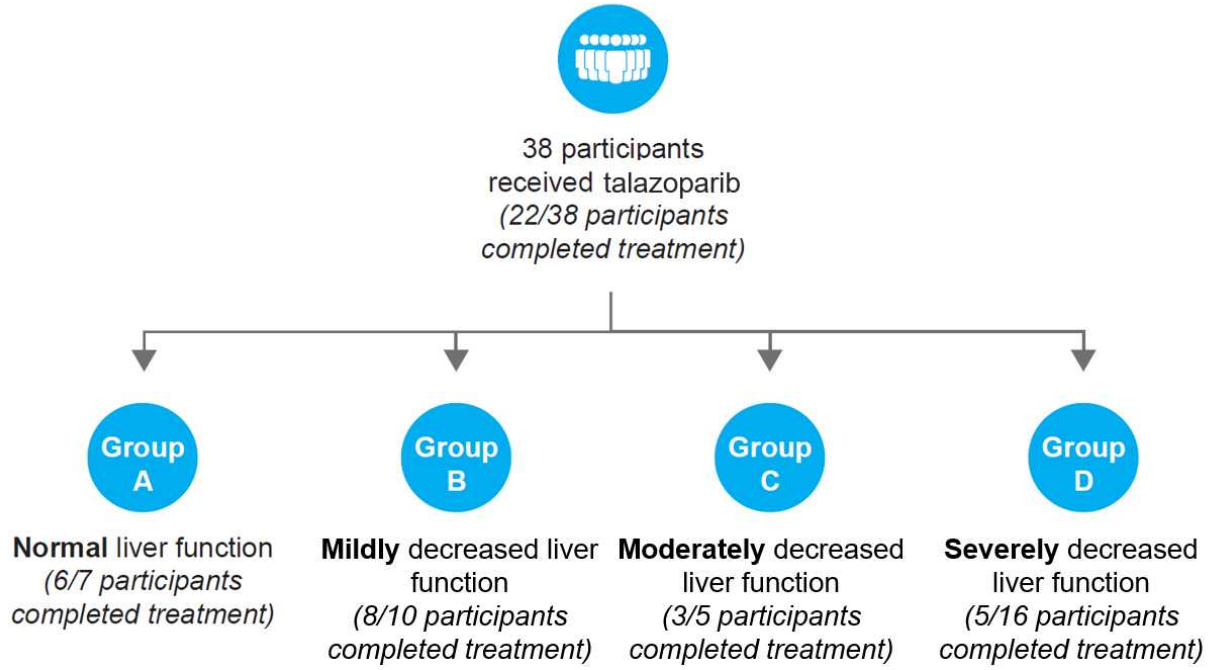

Figure 1. The description of the study design

Where did this study take place?

The Sponsor ran this study at 5 locations in the United States.

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When did this study take place?

It began on 30 September 2016 and ended 12 February 2020.

Who participated in this study?

The study included male and female participants over the age of 18 years with advanced solid tumors that had no standard treatment available and who were expected to live longer than 3 months.

- A total of 12 men participated
- A total of 26 women participated
- All participants were between the ages of 33 and 84 years

Of the 38 participants who started the study, 22 finished the study treatment.

Thirteen participants did not finish the study because:

- they experienced a side effect,
- their disease got worse, or
- they passed away

Three participants left before the study was over by their choice or a doctor decided it was best for a participant to stop being in the study.

How long did the study last?

The entire study took 3.4 years to complete, but study participants were only in the trial and received study treatment for approximately 22 days. This helps researchers understand how much talazoparib accumulates in the blood when taken repeatedly every day for multiple days in a row.

After the study ended in February 2020, the Sponsor created a report of the results. This is a summary of that report.

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What were the results of the study?

How well did participants with advanced solid tumors who had either normal liver function or mildly, moderately, or severely decreased liver function process talazoparib in their bodies?

- Researchers measured the total amount of talazoparib in the blood within 24 hours at steady state on Day 22 (Figure 2). Steady state is when the amount of talazoparib in the body stays the same when study participants take talazoparib at scheduled times.
- Study participants took talazoparib for 22 days because talazoparib took this many days to reach a steady state in earlier studies. This helps researchers understand how much talazoparib accumulates in the blood when taken repeatedly every day for multiple days in a row.

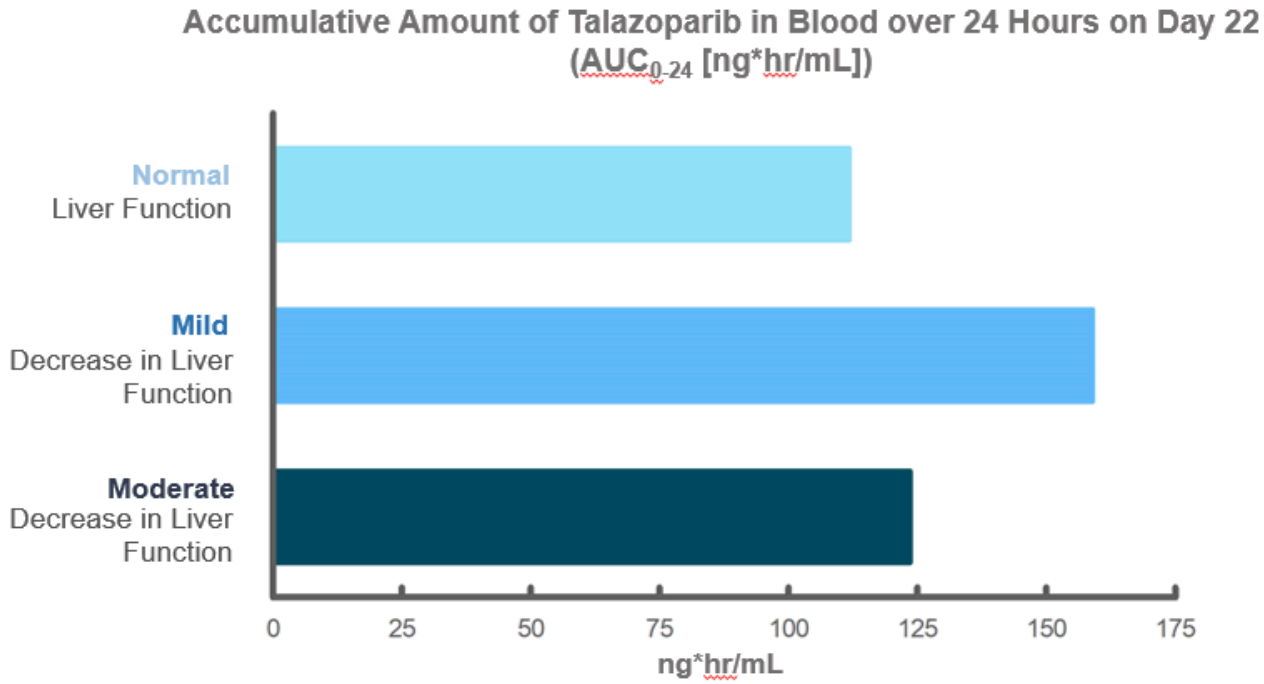

Figure 2. Accumulative amount of talazoparib in blood over 24 hours on Day 22

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How much talazoparib was bound to protein in the blood on Day 22?

- Researchers measured the total amount of unbound/free talazoparib in the blood over time from taking talazoparib until talazoparib is removed from the body. A drug is called 'free' or 'unbound' when it is not attached to anything (for example, protein) in the blood.
- The percentage of talazoparib not bound to protein in the blood (f_u) after participants with normal liver function took 0.5 mg of talazoparib was 27%.
- The percentage of talazoparib not bound to protein in the blood after participants with mildly decreased liver function took 0.5 mg of talazoparib was 28%.
- The percentage of talazoparib not bound to protein in the blood after participants with moderately decreased liver function took 0.5 mg of talazoparib was 27%.
- The percentage of talazoparib not bound to protein in the blood after participants with severely decreased liver function took 0.5 mg of talazoparib was 34%.
- Researchers considered the difference in the results as minor.

Based on these results, researchers have decided that there is not a clear trend for the accumulation of talazoparib in the blood of participants as a result of an impaired liver.

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. Other studies may have different results.

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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 medicine (for example, caused by an unknown underlying disease or by chance). Or, medical problems could also have been caused by a study medicine 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.

Thirty one out of 38 (82%) participants in this study had at least 1 medical problem. A total of 8 participants left the study because of medical problems. The most common medical problems recorded by more than 10% of participants – are described below.

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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 are listed.
- The **2nd** column tells how many of the 38 participants taking the study medication reported each medical problem. Next to this number is the percentage of the 38 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 6 out of the 38 participants taking the study medication reported feeling tired (fatigue).
- This section only shows the most commonly reported medical problems that happened during the study. The table below shows all grades or ranges of severity including mild, moderate, and severe medical problems).

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Table 1. Commonly reported medical problems in greater than 10% of study participants	
Medical Problem	**Study Medication (38 Participants)**
Feeling tired	6 out of 38 participants (16%)
Too much bilirubin (blood breakdown product) in the blood (Hyperbilirubinaemia)	5 out of 38 participants (13%)
Low blood sodium	5 out of 38 participants (13%)
Nausea	5 out of 38 participants (13%)
Low blood platelets	5 out of 38 participants (13%)
Abdominal pain	4 out of 38 participants (11%)
Loose stools	4 out of 38 participants (11%)
Disease worsening	4 out of 38 participants (11%)

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.

Nineteen out of 38 participants (50%) had serious medical problems.

- Four participants in the severely decreased liver function group had their disease worsen or progress further. This is considered a serious medical problem because the participant may experience a steadier decline in their health.

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- Three participants in the severely decreased liver function group had low blood sodium. This is considered serious because low blood sodium may lead to seizures, coma, or even death.

Researchers do not believe any of the serious medical problems reported by participants were caused by the study medication.

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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 **NCT02997176**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **MDV3800-02 (C3441002)**

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!

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