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: Avelumab and talazoparib

Protocol Number: B9991025 (JAVELIN PARP MEDLEY)

Dates of Study: 19 October 2017 to 04 January 2023

Title of this Study: Study on the Use of Avelumab Plus Talazoparib in Patients With Locally Advanced or Metastatic Solid Tumors

[A Phase 1b/2 Study to Evaluate Safety and Anti-Tumor Activity of Avelumab in Combination With the Poly (Adenosine Diphosphate (ADP)-Ribose) Polymerase (PARP) Inhibitor Talazoparib in Patients With Locally Advanced or Metastatic Solid Tumors]

Date(s) of this Report: 14 September 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 are locally advanced or metastatic solid tumors?

Cancer occurs when cells in the body divide without control. Sometimes these cells form masses called tumors. Locally advanced and metastatic solid tumors are tumors made up of cancer cells.

A locally advanced tumor is a tumor that has grown outside the body part it started in. It has spread only to nearby organs or lymph nodes. A metastatic solid tumor is a tumor that started in one part of the body and spread to other distant parts of the body.

Participants in this study had locally advanced or metastatic solid tumors. These tumors could have affected the lungs, breasts, ovaries, bladder, urinary tract, prostate, or a different body part.

What is avelumab?

Avelumab (a-VEL-you-mab) was a new cancer medicine. At the time of this study, avelumab had been approved for different types of cancers, but it was not approved for locally advanced or metastatic solid tumors. It works by allowing the immune system to fight against cancer cells. It does this by stopping or preventing the action of a protein known as programmed death receptor ligand-1 (PD-L1). This helps the body fight the tumor. Avelumab is given through a needle into a vein in a treatment that lasts around an hour.

What is talazoparib?

Talazoparib (tal-a-ZOE-parib) is another medicine that helps the body fight against cancer cells. Talazoparib stops the activity of a protein called “poly ADP-ribose polymerase” (PARP). Cancer cells rely on the PARP protein to keep growing and dividing. Talazoparib is known as a “PARP inhibitor”

medication. By blocking the PARP protein, talazoparib may help to slow down the growth or spread of cancer. Talazoparib is given as a tablet and is taken by mouth.

At the time of this study, talazoparib had been approved for different types of cancers, but it was not approved for the treatment of locally advanced or metastatic solid tumors.

What was the purpose of this study?

The purpose of this study was to investigate the combination of avelumab and talazoparib for the treatment of locally advanced or metastatic solid tumors. Some patients have cancer that does not get better with one sort of treatment. Other patients get better with one treatment at first and then the treatment stops working. Combining treatments may mean that a patient still gets the benefit of another treatment if one treatment in the combination stops working for them.

In this study, researchers wanted to know the response of the tumors to treatment. In other words, they looked to see if the patients' tumors got smaller during the study. To do this, they measured many things, including the "Objective Response Rate". This is the percentage of participants whose tumors disappeared or got smaller during treatment.

Researchers wanted to know:

- **What was the response of locally advanced or metastatic solid tumors to treatment with the combination of avelumab and talazoparib?**
- **What medical problems, if any, did the participants have during the study?**

What happened during the study?

How was the study done?

First, a study doctor checked each participant to make sure they were able to join the study. This is known as a screening period. There were 223 screened participants in this study.

The first 12 participants were put into a specific group to choose the best dose of talazoparib, regardless of the cancer they had. The other 211 participants were divided into cohorts depending on the type of cancer they had. There were 10 cohorts. Table 1 shows the cohort name, the cancer type, and number of participants in that cohort. For example, participants in Cohort A1 had non-small cell lung cancer (NSCLC) and 42 participants were enrolled in this cohort.

Table 1. Cohorts in this Study

Cohort Name	Cancer Type	Number of Participants in Cohort
Cohort A1	NSCLC.	42
Cohort A2	DNA damage repair (DDR+) NSCLC. This is a specific type of NSCLC.	5
Cohort B1	Triple negative breast cancer	22

Table 1. Cohorts in this Study		
Cohort Name	**Cancer Type**	**Number of Participants in Cohort**
Cohort B2	Hormone receptor-positive (HR+) human epidermal growth factor receptor 2-negative (HER2-) DDR+ breast cancer	23
Cohort C1	Ovarian cancer	20
Cohort C2	Breast cancer susceptibility gene (BRCA)-mutated ovarian cancer. This is a specific type of ovarian cancer.	11
Cohort D	Bladder or urinary tract cancer	40
Cohort E1	Prostate cancer	21
Cohort E2	DDR+ prostate cancer. This is a specific type of prostate cancer.	18
Cohort F	Other types of cancer called BRCA/ataxia-telangiectasia mutated (ATM) cancer.	9

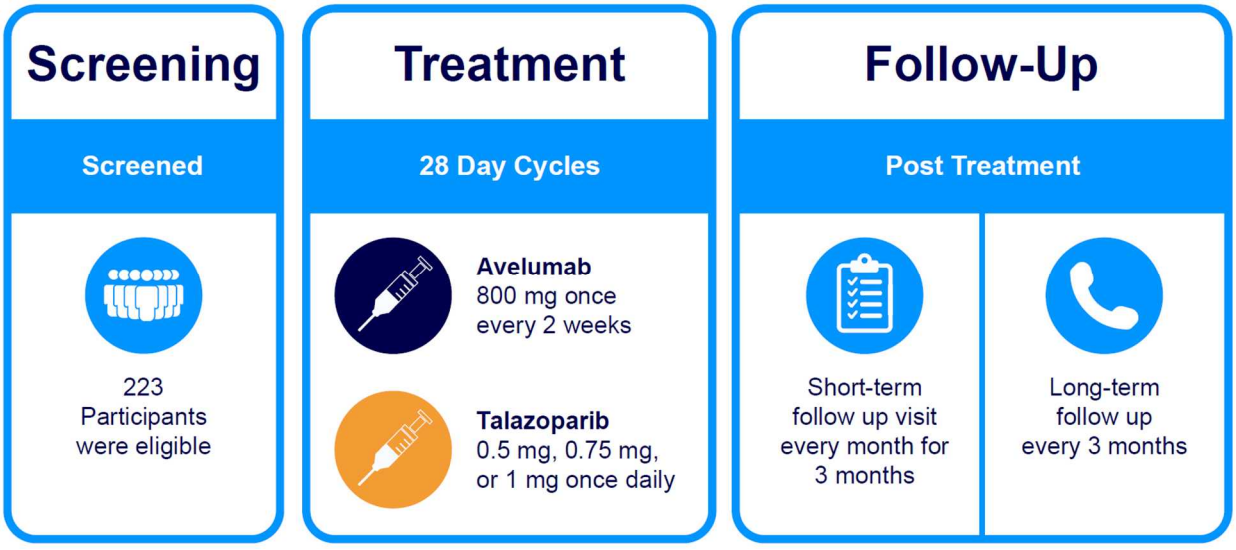
Participants visited the study center every 2 weeks, on Day 1 and Day 15 of every 28-day treatment cycle. All participants took the same treatment in this study. Participants took 800 mg avelumab given as an infusion injection (drip) at the study center on Day 1 and Day 15 of every 28-day treatment cycle. Participants also took 1 mg talazoparib (or reduced dose

0.75 or 0.5 mg if participant had medical problems) as a tablet one time a day by mouth.

Participants also attended an end of the study visit. Follow-up visits were done monthly for the first 3 months (90 days) after stopping the study medication. After that, participants were contacted by phone every 3 months to check on their health.

Figure 1 shows what happened during the study.

Figure 1. Study Design



Where did this study take place?

The Sponsor ran this study at 33 locations in 9 countries.

When did this study take place?

It began 19 October 2017 and ended 04 January 2023.

Who participated in this study?

The study included participants who had locally advanced or metastatic solid tumors. Participants in this study had tumors that affected the lungs, breasts, ovaries, bladder, urinary tract, prostate, or a different body part.

- A total of 117 men participated
- A total of 106 women participated
- All participants were between the ages of 30 and 89

Participants were to be treated until one of the following occurred:

- The participant's cancer got worse (this was the most common reason for stopping the treatment)
- The participant experienced medical problems
- The participant left before the study was over by their own choice or a doctor decided it was best for a participant to stop being in the study
- The participant passed away

There were 8 participants who stopped their treatment in this study and continued the same treatment in another study.

How long did the study last?

The amount of time that each participant was in the study varied. The entire study took 5 years and 3 months to complete.

When the study ended in January 2023, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

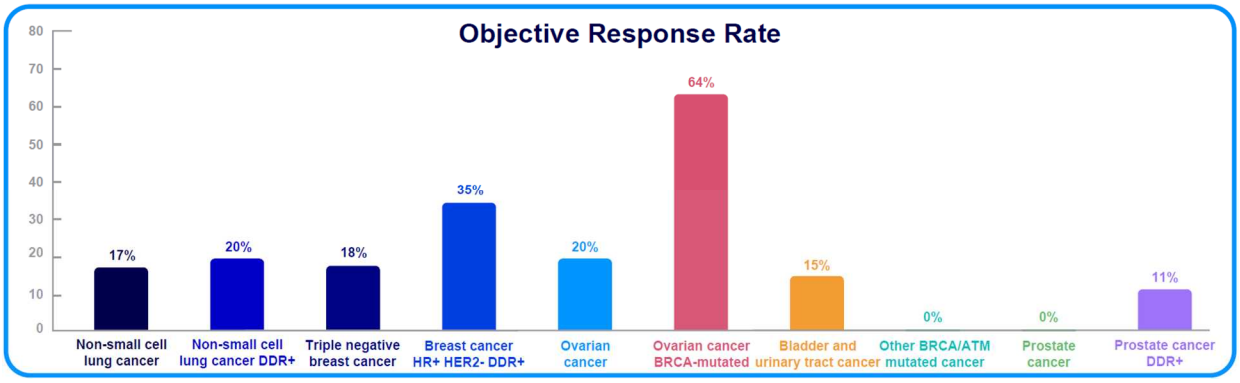
What were the results of the study?

What was the response of locally advanced or metastatic solid tumors to treatment with avelumab and talazoparib?

The “Objective Response Rate” is the percentage of participants whose tumors disappeared or got smaller during treatment (See Figure 2).

Figure 2 shows the Objective Response Rate. The number above each bar shows the percentage of participants whose tumors disappeared or got smaller during treatment. For example, 17% of participants who had non-small cell lung cancer (NSCLC) had tumors that disappeared or got smaller during treatment.

Figure 1



What effect did treatment with combination of avelumab and talazoparib have on participants with locally advanced or metastatic solid tumors?

The researchers found that treatment with avelumab and talazoparib had different effects depending on the type of cancer the participant had.

The researchers have decided that combination treatment had an effect in participants with BRCA-mutated ovarian cancer (Cohort C2) and HR+ HER2- DDR+ breast cancer (Cohort B2).

The researchers have decided that combination treatment had little effect in participants with ovarian cancer (Cohort C1) or breast cancer (Cohort B1).

The researchers have decided that combination treatment did not reduce tumor size more than avelumab or talazoparib alone in participants with prostate cancer (Cohort E1 and E2), NSCLC (Cohort A1 and A2), and bladder or urinary tract cancer (Cohort D).

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.

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.

A total of 219 out of 223 (98%) participants in this study had at least one medical problem. A total of 21 participants left the study because of medical problems. The most common medical problems – those reported by more than 20% of participants – are described below.

Instructions on how to read Table 2.

- The **1st** column of Table 2 lists medical problems that were commonly reported during the study. Only medical problems reported by more than 20% of participants are listed.
- The **2nd** column tells how many of the 223 participants taking the study medication reported each medical problem. Next to this number is the percentage of the 223 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 148 out of the 223 (66%) participants taking the study medication reported low red blood cell count.

Table 2. Commonly reported medical problems by study participants

Medical Problem	Participants Treated With Avelumab and Talazoparib Who Had a Medical Problem
Low red blood cell count	148 out of 223 participants (66%)
Feeling tired	96 out of 223 participants (43%)
Nausea (upset stomach)	83 out of 223 participants (37%)

Table 2. Commonly reported medical problems by study participants	
Medical Problem	**Participants Treated With Avelumab and Talazoparib Who Had a Medical Problem**
Low blood platelets	73 out of 223 participants (33%)
Shortness of breath	55 out of 223 participants (25%)
Decreased appetite	54 out of 223 participants (24.2%)
Decreased blood platelets	49 out of 223 participants (22.0%)
Low white blood cell count	46 out of 223 participants (21%)
Diarrhea (loose stools)	45 out of 223 participants (20%)

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.

A total of 26 participants (12%) had at least one serious medical problem.

Serious medical problems experienced by two or more participants were:

- Low red blood cell count: 11 out of the 223 participants (5%)
- Low blood platelets: 3 out of the 223 participants (1%)
- Reaction to receiving the medicine through a needle: 3 out of the 223 participants (1%)
- Blood platelet count decreased: 2 out of the 223 participants (1%)

There were 154 of the 223 participants (69%) who passed away during the study. Of these deaths, 114 were due to the participant's cancer getting worse. There was 1 out of the 154 deaths that researchers believed was related to the study treatment.

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.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number B9991025

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

www.clinicaltrials.gov	Use the study identifier NCT03330405
www.clinicaltrialsregister.eu	Use the study identifier 2017-001509-33

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!