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:	BAVENCIO® (avelumab), TALZENNA® (talazoparib)
Protocol Number:	B9991032 (Javelin BRCA/ATM)
Dates of Study:	18 June 2018 to 03 February 2023
Title of this Study:	Avelumab Plus Talazoparib in Patients With BRCA or ATM Mutant Solid Tumors [A Phase 2 Study to Evaluate Safety and Anti-Tumor Activity of Avelumab in Combination With Talazoparib in Patients With BRCA or ATM Mutant Tumors]
Date(s) of this Report:	28 August 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 BRCA 1, BRCA 2 and ATM mutations?

The participants in this study had advanced cancer that may have spread to other areas of the body. Their cancer also tested positive for specific changes in DNA (deoxyribonucleic acid). DNA is the set of instructions found within all cells that tells them how to behave. Changes in DNA are known as mutations and participants in this study had cancer with specific changes in DNA called BRCA 1, BRCA 2, and ATM mutations. Participants in this study had various different types of cancer but all of them had one or more of these mutations.

What is avelumab?

Avelumab (a-VEL-you-mab) 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's immune system fight the tumor cell. Avelumab is given as an infusion injection (drip) into a vein that lasts around an hour.

Avelumab was an investigational cancer drug that was not specifically approved for treating cancer with BRCA 1, BRCA 2, and ATM mutations at the time of this study. Avelumab has been approved for the treatment of different cancer types.

What is talazoparib?

Talazoparib (TAL-a-ZOE-parib) is another medication made to help patients fight cancer in a different way. Talazoparib stops the activity of a protein called "poly ADP-ribose polymerase" (PARP). Cancer cells rely on the PARP protein to keep on 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.

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 patients with BRCA 1, BRCA 2, and ATM mutated tumors.

In this study, researchers wanted to know the response of tumors to treatment, i.e., if any of the participant's 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 cancer disappeared ("Complete Response") or got smaller ("Partial Response") during treatment.

Researchers wanted to know:

- **What was the response of BRCA 1, BRCA 2, and ATM mutated tumors to treatment with avelumab plus 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.

Participants were then divided into 2 groups, depending on their type of tumors. The groups were called 'Group A' and 'Group B':

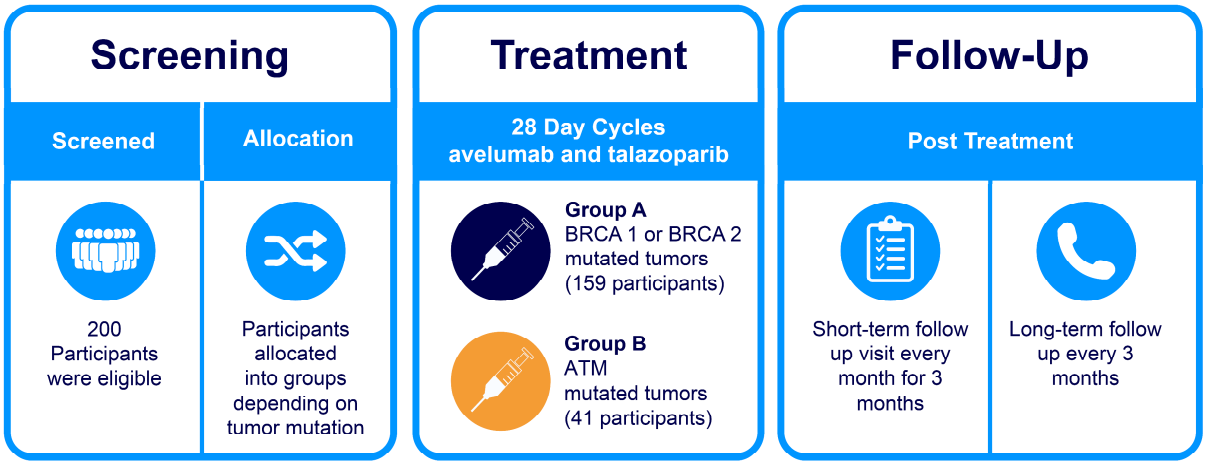
- Participants in Group A had BRCA 1 or BRCA 2 mutated tumors
- Participants in Group B had ATM mutated tumors

Participants took the same treatment in both groups. 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 took 1 mg talazoparib as a tablet once a day by mouth.

Participants visited the study center every 2 weeks, on Day 1 and Day 15 of every 28-day treatment cycle. They 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 42 locations in 9 countries in Europe, the United States, and Asia.

When did this study take place?

The study began 18 June 2018 and ended 03 February 2023.

Who participated in this study?

The study included participants with various types of advanced cancer that may have spread to other areas of the body. The different types of cancer all had BRCA 1, BRCA 2, or ATM mutation.

- A total of 68 men participated
- A total of 132 women participated
- All participants were between the ages of 26 and 89

Participants were 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 died (researchers do not believe any deaths were related to study medications)
- 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

There were 8 participants (4%) 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 approximately 4 years and 8 months to complete.

When the study ended in February 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 BRCA 1, BRCA 2 and ATM mutated tumors to treatment with avelumab plus talazoparib?

A “Complete Response” means that the cancer completely disappeared.

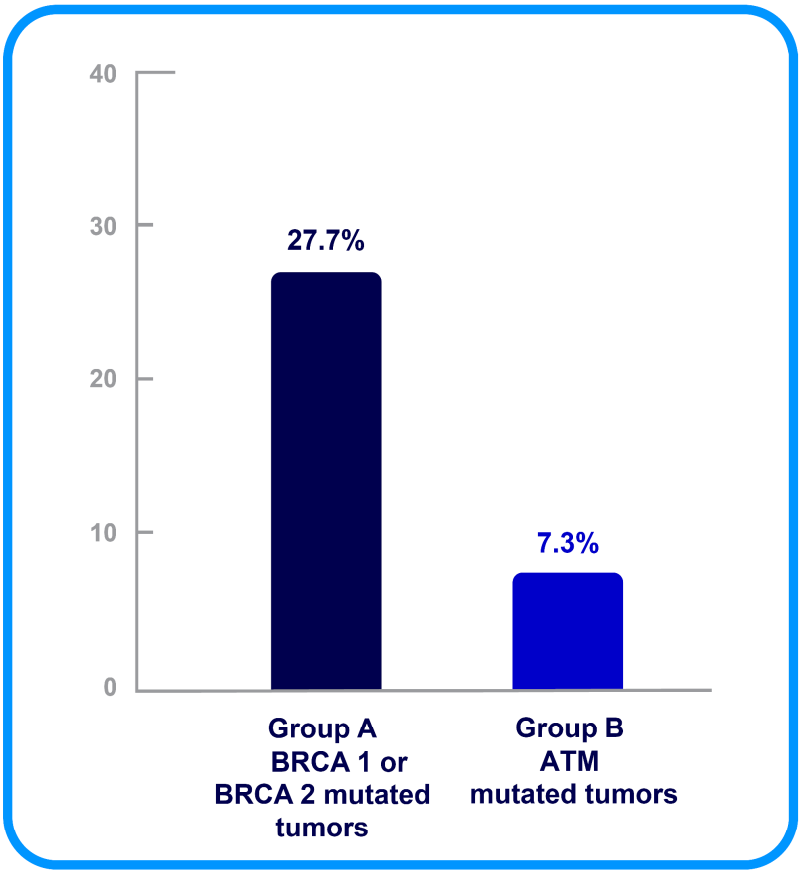
- A total of 11 participants (6.9%) with BRCA 1 or BRCA 2 mutated tumors (Group A) had a complete response
- No participants ATM mutated tumors (Group B) had a “Complete Response”.

A “Partial Response” means that the cancer got smaller but did not disappear.

- A total of 33 participants (20.8%) with BRCA 1 or BRCA 2 mutated tumors (Group A) had a Partial Response
- A total of 3 participants (7.3%) with ATM mutated tumors (Group B) had a Partial Response.

The “Objective Response Rate” of Complete Responses plus Partial Responses was 27.7% for participants in Group A with BRCA 1 or BRCA 2 mutated tumours, and 7.3% for participants in Group B with ATM mutated tumors (see Figure 2).

Figure 2: Objective Response Rate (Complete Responses Plus Partial Responses)



What effect did treatment with avelumab and talazoparib have on participants' BRCA 1, BRCA 2, or ATM mutated tumors?

Some participants had a Complete Response or a Partial Response to treatment with the combination of avelumab and talazoparib. However, the researchers have decided that the "Objective Response Rate" to the combination of avelumab and talazoparib was not high enough in either Group A or Group B to be the only treatment a doctor could decide to use.

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 156 out of 159 (98.1%) participants in Group A and 40 out of 41 (97.6%) participants in Group B in this study had at least 1 medical problem. Most participants stopped treatment with the study medication because their cancer worsened, they had medical problems, or their doctor thought they should stop.

The most common medical problems – those reported by more than 20% of participants in either Group A or Group B – 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 20% of participants in either Group A or Group B are listed.

- The **2nd** column tells how many of the Group A participants taking the study medication reported each medical problem. Next to this number is the percentage of the 159 Group A participants who reported the medical problem.
- The **3rd** column tells how many of the Group B participants taking the study medication reported each medical problem. Next to this number is the percentage of the 41 Group B participants who reported the medical problem.
- Using these instructions, you can see that 82 out of the 159 (51.6%) Group A participants reported low red blood cell count. A total of 18 out of the 41 (43.9%) Group B participants reported low red blood cell count.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Group A BRCA 1 or BRCA 2 mutated tumors (159 Participants)	Group B ATM mutated tumors (41 Participants)
Low red blood cell count	82 out of 159 participants (51.6%)	18 out of 41 participants (43.9%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Group A** **BRCA 1 or BRCA 2 mutated tumors (159 Participants)**	**Group B** **ATM mutated tumors (41 Participants)**
Nausea (upset stomach)	73 out of 159 participants (45.9%)	21 out of 41 participants (51.2%)
Fatigue (feeling very tired)	50 out of 159 participants (31.4%)	19 out of 41 participants (46.3%)
Vomiting	39 out of 159 participants (24.5%)	11 out of 41 participants (26.8%)
Constipation	39 out of 159 participants (24.5%)	8 out of 41 participants (19.5%)
Diarrhoea (loose stools)	36 out of 159 participants (22.6%)	11 out of 41 participants (26.8%)
Decreased appetite	33 out of 159 participants (20.8%)	12 out of 41 participants (29.3%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Group A** **BRCA 1 or BRCA 2 mutated tumors (159 Participants)**	**Group B** **ATM mutated tumors (41 Participants)**
Difficulty breathing	37 out of 159 participants (23.3%)	8 out of 41 participants (19.5%)
Joint pain	30 out of 159 participants (18.9%)	11 out of 41 participants (26.8%)
Headache	35 out of 159 participants (22.0%)	6 out of 41 participants (14.6%)
Low levels of platelets	25 out of 159 participants (15.7%)	11 out of 41 participants (26.8%)
Back pain	21 out of 159 participants (13.2%)	10 out of 41 participants (24.4%)

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.

Overall, 50 participants (31.4%) in Group A and 7 participants (17.1%) in Group B had at least 1 serious medical problem.

Serious medical problems experienced by at least 2% (4 out of 200) of the participants in total (both Group A and Group B) were:

- Cancer getting worse: 8 out of 159 (5%) participants in Group A and 2 out of 41 (4.9%) participants in Group B.
- Low red blood cell count: 4 out of 159 (2.5%) participants in Group A and 2 out of 41 (4.9%) participants in Group B.
- Infection of the lung: 4 out of 159 (2.5%) participants in Group A and 1 out of 41 (2.4%) participants in Group B.

There were 123 out of 159 (77.4%) participants in Group A and 29 out of 41 (70.7%) participants in Group B that passed away during the study. Most of these deaths were due to the participant’s cancer getting worse. Researchers do not believe any of the deaths were related to study medications.

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 B9991032

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

www.clinicaltrials.gov	Use the study identifier **NCT03565991**
www.clinicaltrialsregister.eu	Use the study identifier EudraCT: 2018-000345-39

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!