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 Studied: Bavencio® (avelumab)

Protocol Number: B9991001 (JAVELIN Bladder 100)

Dates of Study: 25 April 2016 to 28 March 2023

Title of this Study: A Study of Avelumab Maintenance Treatment in Patients With Locally Advanced or Metastatic Urothelial Cancer (JAVELIN Bladder 100)

[A Phase 3, Multicenter, Multinational, Randomized, Open-Label, Parallel-Arm Study of Avelumab (MSB0010718C) Plus Best Supportive Care Versus Best Supportive Care Alone as a Maintenance Treatment in Patients With Locally Advanced or Metastatic Urothelial Cancer Whose Disease Did Not Progress After Completion of First-Line Platinum-Containing Chemotherapy]

Date of this Report: 17 November 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 locally advanced or metastatic urothelial cancer?

Cancer occurs when cells in the body divide without control. Urothelial cancer is a type of cancer that began from cells lining the bladder or urinary tract. The participants in this study had locally "advanced or metastatic" urothelial cancer. This means that the cancer has spread beyond the urinary tract into nearby tissues (locally advanced) and other organs in the body (metastatic) and cannot be removed by surgery.

Chemotherapy is often the first main treatment given to people with advanced urothelial cancer. This is called the 'first-line' treatment. Although the cancer might get better with chemotherapy at first, it sometimes starts growing again. If a person's cancer stops growing or shrinks with first-line chemotherapy, they may receive a different treatment with an aim to stop the cancer from getting worse or growing back. This is called 'maintenance treatment'.

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 patients with locally advanced or metastatic urothelial cancer that had not received previous lines of therapy. Avelumab 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 once every 2 weeks.

JAVELIN Bladder 100 Study

This study, called the JAVELIN Bladder 100 study, looked at avelumab as a maintenance treatment for people with advanced urothelial cancer, following initial chemotherapy. All participants who took part in the study

had finished first-line chemotherapy within 10 weeks before entering the study, and their cancer had stayed the same or shrunk. Participants were divided into 2 groups:

- Group A: Participants received avelumab maintenance treatment plus best supportive care. Best supportive care is care that the study doctor feels is appropriate for a participant's condition and may have included antibiotics, nutritional support, correction of any metabolic issues, and care to control symptoms and pain. Best supportive care did not include any treatment that affect the cancer.
- Group B: Participants received only best supportive care.

What was the purpose of this study?

The main purpose of this study was to compare avelumab maintenance treatment plus best supportive care with best supportive care alone to see if avelumab helped increase overall participant survival. Researchers wanted to find out if maintenance treatment with avelumab would help participants with advanced urothelial cancer live longer.

Researchers wanted to know:

- **Did participants receiving avelumab maintenance treatment plus best supportive care survive longer than participants receiving best supportive care alone?**
- **What medical problems, if any, did the participants have during the study?**

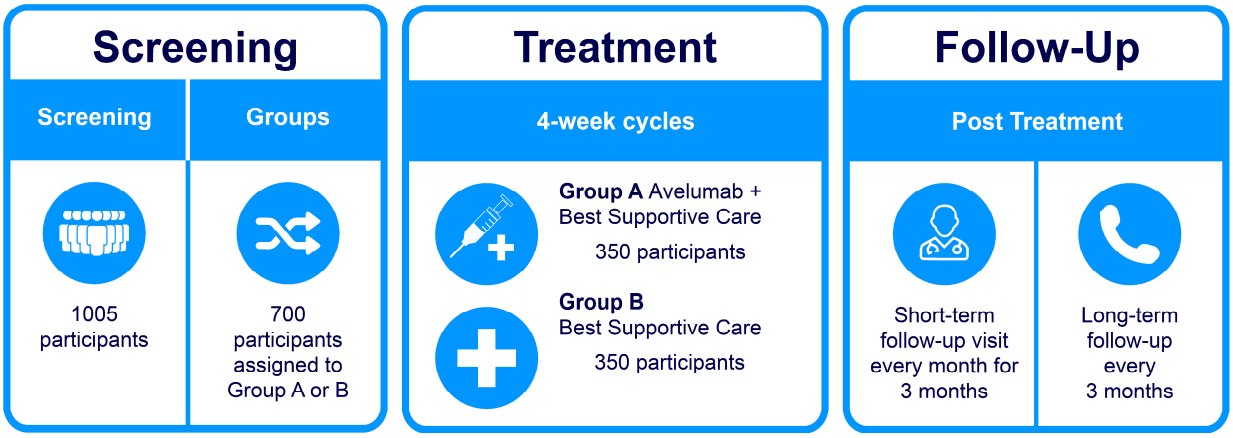
What happened during the study?

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 1005 participants screened for this study.

A total of 700 participants with advanced urothelial cancer, who had received first-line chemotherapy and whose cancer had not gotten worse, finished screening and took part in this study. As shown in Figure 1, 350 participants received avelumab plus best supportive care (Group A) and 350 participants received best supportive care only (Group B). Study participants were randomly assigned (similar to flipping a coin) to either Group A or Group B. The chance a participant was assigned to one group or the other was 1 in 2, or 50%.

Figure 1. Study Design



Of the 350 participants in each group, 189 participants in Group A and 169 participants in Group B had PD-L1 positive cancer.

This was an open-label study. This means that both the participants and researchers knew which study treatment was given to participants.

Each 4-week period during the treatment part of the study was called a cycle. Participants in Group A visited the study center every 2 weeks on Day 1 and Day 15 of each cycle. Avelumab was given to study participants in Group A through a needle into a vein every 2 weeks over 1-2 hours. Participants in Group B visited the study center every 4 weeks on Day 1 of each cycle.

All participants attended an End-of-Treatment visit. Follow-up visits were also done 30, 60, and 90 days after stopping study treatment. Participants were then contacted by telephone every 3 months after the 90-day follow-up visit to ask about health and any cancer treatments being received.

Where did this study take place?

The Sponsor ran this study at 231 locations in 35 countries.

When did this study take place?

It began 25 April 2016 and ended 28 March 2023.

Who participated in this study?

The study included participants with locally advanced or metastatic urothelial cancer whose disease did not get worse on or following completion of first-line platinum-based chemotherapy.

- A total of 541 men participated
- A total of 159 women participated
- All participants were between the ages of 32 and 90

Participants were treated until one of the following occurred:

- The participant's cancer got worse
- The participant left before the study was over by their own choice
- The participant experienced unacceptable medical problems

This study has been completed and all study participants have left the study. The most common reason for stopping the study treatment was cancer getting worse (60.9%, or 213 out of 350 participants in Group A and 78.6%, or 275 out of 350 participants in Group B).

In Group A, 28 participants (8.0%) stopped the study treatment by their own choice, and 15 participants (4.3%) stopped the study treatment because a doctor decided it was best for them.

In Group B, 31 participants (8.9%) stopped the study treatment by their own choice, and 7 participants (2.0%) stopped the study treatment because a doctor decided it was best for them.

How long did the study last?

The amount of time that each participant was in the study varied. The entire study took about 6 years and 11 months to complete.

Researchers collected the initial results of this study in October 2019. This was called the 'interim analysis'. Researchers then collected the long-term results of this study after all the participants had been studied for at least 2 years after receiving the treatment. These updated results were collected in June 2021. When the study ended in March 2023, the Sponsor reviewed the information collected to create a report of these results. This is a summary of that report.

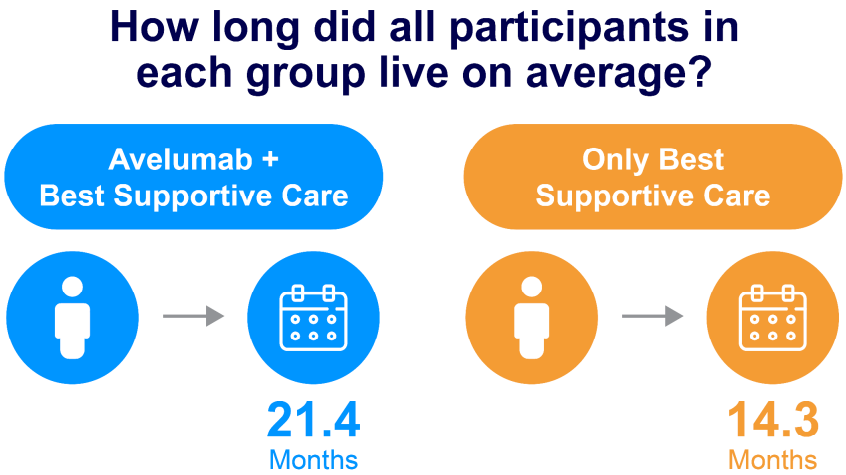
What were the results of the study?

How long did participants receiving avelumab plus best supportive care survive compared to participants receiving best supportive care alone?

To answer this question, the researchers looked at “overall survival” during the study. Overall survival measures how long a participant lives. The researchers looked at the time from the start of the study treatment until the time half of the participants were still alive. This is known as the “median” overall survival time.

The initial results collected during the interim analysis for overall survival are shown in Figure 2. The median overall survival for all participants was 21.4 months in Group A and 14.3 months in Group B. For all participants in Group A, there was a 31% reduction in the risk of death compared to participants in Group B.

Figure 2: Median Overall Survival For All Participants At the Interim Analysis

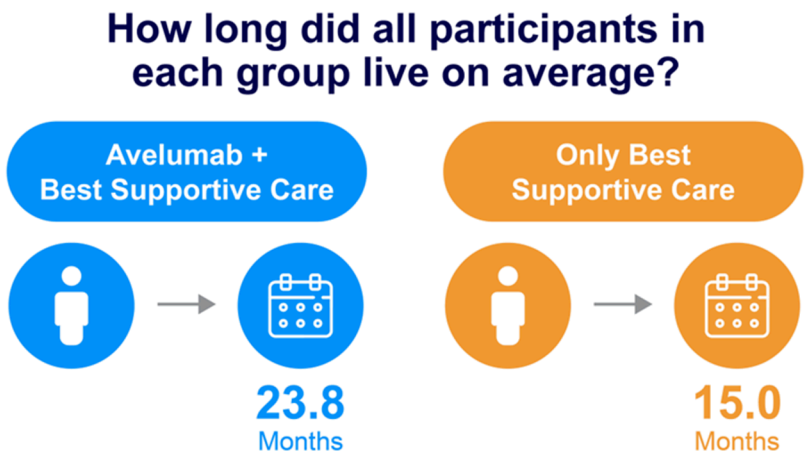


For participants with PD-L1 positive tumors receiving avelumab maintenance treatment plus best supportive care, there was a 44% reduction in the risk of death compared to participants with PD-L1 positive tumors receiving best supportive care alone.

The median overall survival for participants with PD-L1 positive tumors in Group A was not reached yet. For participants in Group B the median overall survival was found to be 17.1 months.

The updated overall survival results are presented in Figure 3 and 4. The median overall survival for all participants was 23.8 months in Group A and 15.0 months in Group B (Figure 3). Researchers found that there was a 24% reduction in the risk of death for participants in Group A compared to participants in Group B.

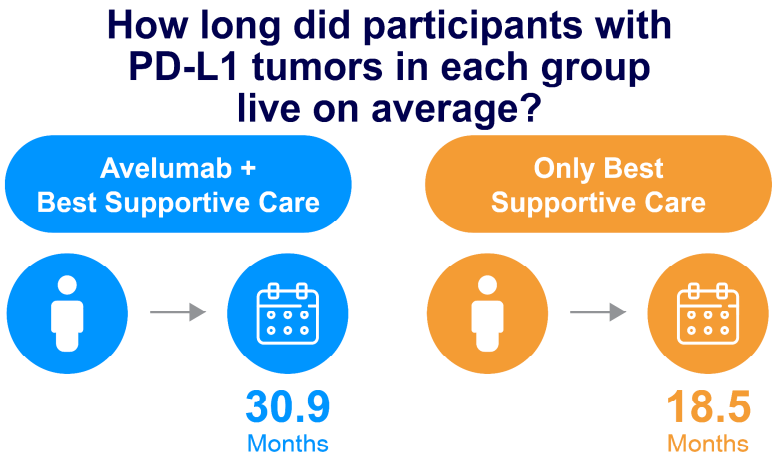
Figure 3: The Median Overall Survival For All Participants



The median overall survival for participants with PD-L1 positive tumors was 30.9 months in Group A and 18.5 months in Group B as shown below in Figure 4. For participants with PD-L1 positive tumors receiving avelumab plus best supportive care, there was a 31% reduction in the

risk of death compared to participants with PD-L1 positive tumors receiving best supportive care alone.

Figure 4. Median Overall Survival For Participants With PD-L1 Tumors



Based on the initial and the updated overall survival results, researchers found that avelumab may be used as a maintenance treatment for participants with advanced urothelial cancer whose cancer has shrunk or not grown with first-line chemotherapy. The study results showed that avelumab maintenance treatment plus best supportive care may help participants live longer than best supportive care alone.

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.

Six (6) out of 350 participants in Group A and 5 out of 350 participants in Group B were not evaluated for medical problems. In Group A, 338 out of 344 (98.3%) participants had at least 1 medical problem. In Group B, 270 out of 345 (78.3%) participants had at least 1 medical problem. A total of 50 out of 344 (14.5%) participants in Group A discontinued avelumab because of medical problems. The most common medical problems – those reported by at least 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 at least 10% of participants are listed.

- The **2nd** column tells how many of the 344 participants receiving avelumab plus best supportive care reported each medical problem. Next to this number is the percentage of the 344 participants receiving avelumab plus best supportive care who reported the medical problem.
- The **3rd** column tells how many of the 345 participants receiving best supportive care alone reported each medical problem. Next to this number is the percentage of the 345 participants receiving best supportive care alone who reported the medical problem.
- Using these instructions, you can see that 68 out of the 344 participants receiving avelumab plus best supportive care reported pain in a joint. A total of 29 out of the 345 participants receiving best supportive care alone reported pain in a joint.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Group A (344 Participants)	Group B (345 Participants)
Pain in a joint	68 out of 344 participants (19.8%)	29 out of 345 participants (8.4%)
Very tired	66 out of 344 participants (19.2%)	24 out of 345 participants (7.0%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Group A (344 Participants)**	**Group B (345 Participants)**
Loss of strength or energy	64 out of 344 participants (18.6%)	19 out of 345 participants (5.5%)
Itching	64 out of 344 participants (18.6%)	6 out of 345 participants (1.7%)
Loose stools	63 out of 344 participants (18.3%)	18 out of 345 participants (5.2%)
Constipation	62 out of 344 participants (18.0%)	34 out of 345 participants (9.9%)
Urinary tract infection	62 out of 344 participants (18.0%)	38 out of 345 participants (11.0%)
Back pain	58 out of 344 participants (16.9%)	35 out of 345 participants (10.1%)
Fever	58 out of 344 participants (16.9%)	13 out of 345 participants (3.8%)
Nausea	55 out of 344 participants (16.0%)	22 out of 345 participants (6.4%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Group A (344 Participants)**	**Group B (345 Participants)**
Cough	49 out of 344 participants (14.2%)	18 out of 345 participants (5.2%)
Low red blood cell count	48 out of 344 participants (14.0%)	24 out of 345 participants (7.0%)
Decreased appetite	48 out of 344 participants (14.0%)	24 out of 345 participants (7.0%)
Vomiting	47 out of 344 participants (13.7%)	12 out of 345 participants (3.5%)
Low levels of thyroid hormone	44 out of 344 participants (12.8%)	2 out of 345 participants (0.6%)
Rash	43 out of 344 participants (12.5%)	5 out of 345 participants (1.4%)
Blood in the urine	39 out of 344 participants (11.3%)	37 out of 345 participants (10.7%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Group A (344 Participants)**	**Group B (345 Participants)**
Abdominal pain	35 out of 344 participants (10.2%)	26 out of 345 participants (7.5%)

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.

In Group A, 111 participants (32.3%, or 111 out of 344 participants) had serious medical problems. The most common serious medical problem in this group was infection of the kidneys, bladder, or urethra (4.9%, or 17 out of 344 participants).

In Group B, 73 participants (21.2%, or 73 out of 345 participants) had serious medical problems. The most common serious medical problem in this group was disease getting worse (4.6%, or 16 out of 345 participants).

In Group A, 7 participants (2.0%, or 7 out of 344 participants) had medical problems leading to death. Researchers believe that for 2 of these participants, the medical problems that led to death were related to study treatment.

In Group B, 24 participants (7.0%, or 24 out of 345 participants) had medical problems leading to death. None of these medical problems that led to death were believed to be related to the study treatment.

A total of 225 participants (65.4%, or 225 out of 344) in Group A and 242 participants (70.1%, or 242 out of 345) in Group B died during this study. The most common cause of death was cancer getting worse in both the groups (58.1% in Group A and 62.6% in Group B respectively). A total of 3 deaths were believed to be because the study treatment was too toxic for the participant.

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 B9991001

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

www.clinicaltrials.gov	Use the study identifier **NCT02603432**
www.clinicaltrialsregister.eu	Use the study identifier **2015-003262-86**

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!