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), Inlyta® (Axitinib), Sutent® (Sunitinib)
Protocol Number:	B9991003 (JAVELIN Renal 101)
Dates of Study:	23 March 2016, ongoing
Title of this Study:	A study of Avelumab with Axitinib Versus Sunitinib in Advanced Renal Cell Cancer (JAVELIN Renal 101) [A Phase 3, Multinational, Randomized, Open-label, Parallel-Arm Study of Avelumab (MSB0010718C) in Combination With Axitinib (INLYTA®) Versus Sunitinib (SUTENT®) Monotherapy in the First-Line Treatment of Patients With Advanced Renal Cell Carcinoma]
Date(s) of this Report:	09 May 2024

– 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 advanced renal cell carcinoma?

Renal cell carcinoma (RCC) is a type of kidney cancer that starts in the small tubes of the kidney. Kidneys are organs in the body that help get rid of waste while also controlling the amount of water in the body by producing urine. Advanced RCC means that the cancer has grown or spread outside of the kidney.

What is avelumab?

Avelumab (a-VEL-yoo-mab) (Bavencio®) is a medicine that 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 cancer. Not all patients have the PD-L1 protein in their tumor or immune system. Patients who have the PD-L1 protein are called “PD-L1 positive”.

At the time this study started, avelumab was a new investigational drug. Avelumab is given through a needle into a vein in a treatment that lasts around an hour.

What is axitinib?

Axitinib (AK-sih-TIH-nib) (Inlyta®) is approved for treating patients with advanced RCC. Axitinib stops cancer cell growth by depriving the cancer cells of the nutrients and oxygen that they need. It does this by stopping the cancer from forming new blood vessels that would bring nutrients and oxygen to the cancer.

Axitinib is given as a tablet, by mouth.

Combination of avelumab and axitinib

At the time this study started, the combination of avelumab plus axitinib had not been approved for use outside of clinical trials and was being investigated. At the time of this report, avelumab in combination with axitinib is approved as an initial ("first-line") treatment of participants with advanced RCC.

What is sunitinib?

Sunitinib (soo-NIH-tih-nib) (Sutent®) is approved for the treatment of advanced RCC and is used as a first-line treatment for the disease. Sunitinib works in a similar way to axitinib.

Sunitinib is given as a tablet, by mouth.

What was the purpose of this study?

The purpose of this study, called the "**Javelin Renal 101**" study, was to investigate adding avelumab to axitinib for the treatment of advanced RCC. Because these medicines work in different ways, researchers believed that combining the different medicines might help participants' response to treatment. Treatment with avelumab plus axitinib was compared to treatment with sunitinib alone. Researchers particularly looked at the results for participants who had the PD-L1 protein, who were called "PD-L1 positive" participants.

Researchers wanted to know:

How long did PD-L1 positive participants live without their cancer getting worse when they took avelumab plus axitinib compared to participants who took sunitinib?

How long did PD-L1 positive participants live overall when they took avelumab plus axitinib compared to participants who took sunitinib?

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 assigned by chance (like the flip of a coin) to receive either avelumab in combination with axitinib, or to receive sunitinib alone. The study participants and researchers knew who took which treatment. This is known as a “open-label” study.

Each treatment cycle was 6 weeks (42 days) long. At first, participants visited the study site every 2 weeks. As the study progressed some participants only needed to visit the study site once per cycle, for example if they were in the sunitinib group.

Participants took either:

Avelumab 10 mg/kg as a 1-hour infusion every 2 weeks, plus axitinib as a 5 mg tablet by mouth twice a day every day,

or:

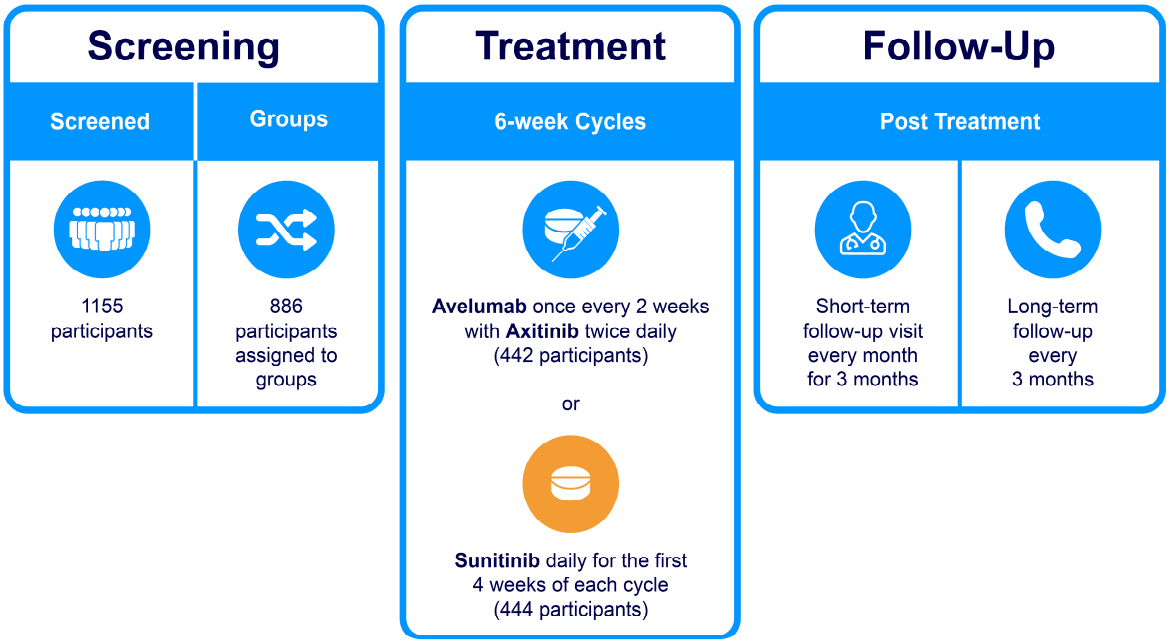
sunitinib as a 50 mg tablet every day for 4 weeks, followed by 2 weeks off.

Participants were to be treated in these continuous 6-week cycles until their cancer worsened, they developed side effects that could not be controlled, or they chose not to continue participating in the study.

After treatment ended, participants visited the site about every month for 3 months and were then contacted about every 3 months.

Figure 1 shows a diagram of what happened in the study.

Figure 1. Study Design



Researchers then compared the results of study participants taking avelumab plus axitinib to the results of study participants taking sunitinib.

Where did this study take place?

The Sponsor ran this study at 156 locations in 20 countries in North America, Latin America, Asia, Australasia, Eastern Europe, Western Europe, and the Middle East.

When did this study take place?

It began 23 March 2016 and is ongoing.

Who participated in this study?

The study included 886 adult participants with advanced RCC who had not previously been treated for their advanced RCC.

- A total of 660 men participated
- A total of 226 women participated
- All participants were between the ages of 27 and 88 years.

Of the 886 participants who started the study, 873 received at least one dose of study medication. Researchers counted participants separately for avelumab and axitinib. This is because a participant in the avelumab plus axitinib group may have stopped taking one study medication but not the other. At the time of this report,

- 24 (5.4%) out of 442 participants were still taking avelumab,
- 27 (6.1%) out of 442 participants were still taking axitinib, and
- 10 (2.3%) out of 444 participants were still taking sunitinib.

The most common reason for stopping study treatment was worsening of the cancer and the second most common reason was a medical problem. Other participants stopped taking study treatment by their own choice, or because a doctor decided it was best for the participant, or because the participant died. Medical problems and deaths are described later in this report.

How long did the study last?

Study participants were in the study for varying lengths of time. The entire study had been running for 7 years and 5 months by August 2023. The study was still ongoing at the time of this report.

The Sponsor reviewed the information collected up to June 2018 for a first study analysis and then up to August 2023 for a final analysis. The Sponsor then created reports of the results. This is a summary of those reports.

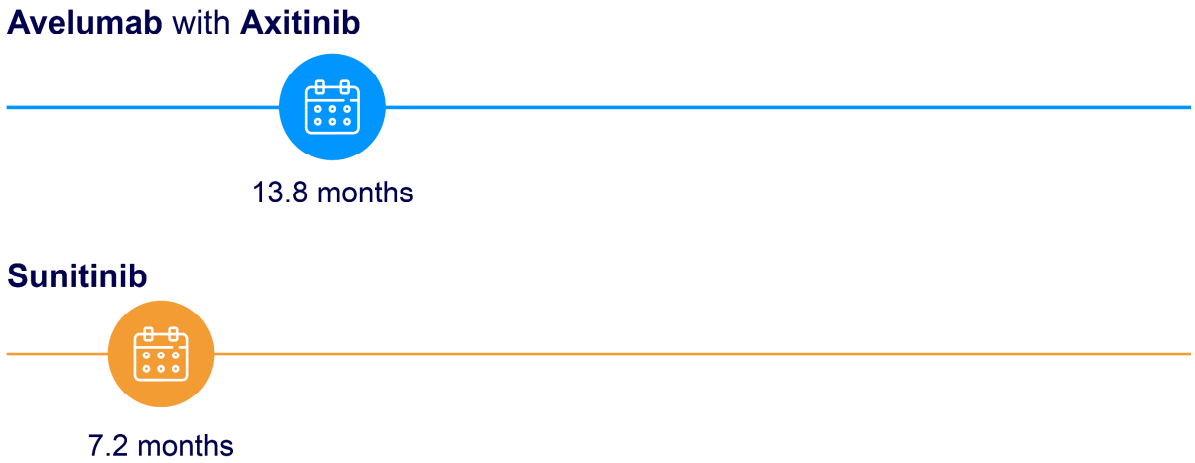
What were the results of the study?

How long did PD-L1 positive participants live without their cancer getting worse when they took avelumab with axitinib compared to participants who took sunitinib?

To answer this question, the researchers looked at "progression-free survival" during the study. Progression-free survival measures how long a participant lives without their cancer getting worse. The researchers looked at the time from the start of the study treatment until the time half of the participants were still alive without their cancer getting worse. This is known as the "median" progression-free survival time.

Researchers used the information collected up to June 2018, for the 270 participants who took avelumab plus axitinib and the 290 participants who took sunitinib, who were PD-L1 positive. The results are shown in Figure 2.

Figure 2. Median Progression-Free Survival for PD-L1 Positive Participants



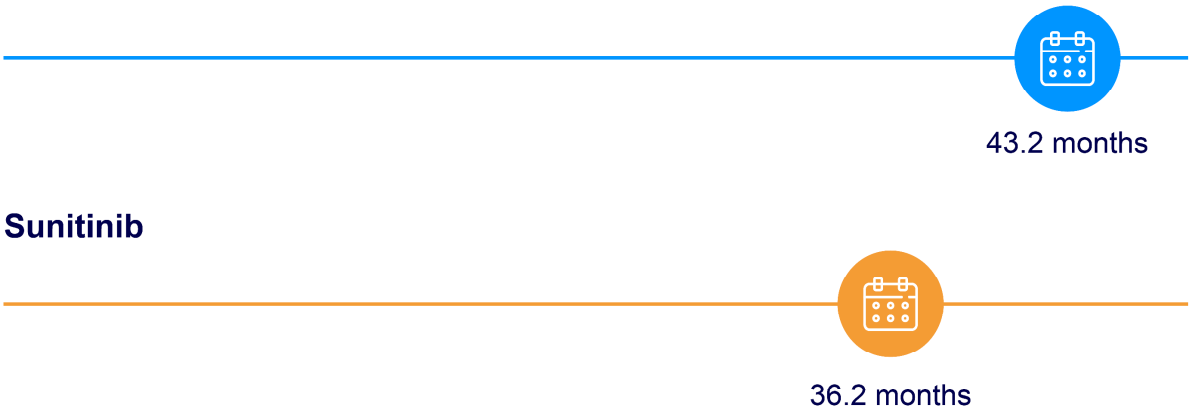
- Researchers also looked at the results for all participants, whether they were PD-L1 positive or not. They used the information collected up to June 2018. For these participants, median progression-free survival was 13.8 months for the 442 participants who took avelumab with axitinib and 8.4 months for the 444 participants who took sunitinib.

How long did PD-L1 positive participants live overall when they took avelumab with axitinib compared to participants who took sunitinib?

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.

Researchers used the information collected up to August 2023, for the 270 participants who took avelumab plus axitinib and the 290 participants who took sunitinib, who were PD-L1 positive. The results are shown in Figure 3.

Figure 3. Median Overall Survival for PD-L1 Positive Participants



- Researchers also looked at the results for all participants, whether they were PD-L1 positive or not. They used the information collected up to August 2023. For these participants, median overall survival was 44.8 months for the 442 participants who took avelumab with axitinib and 38.9 months for the 444 participants who took sunitinib.

Based on all these results:

The researchers have decided that the combination of avelumab and axitinib may help to extend progression-free survival more than treatment with sunitinib. The researchers have decided that these results were not likely due to chance.

The median overall survival was longer for participants who took avelumab with axitinib than for participants who took sunitinib. However, the researchers believe that this difference could have been the result of chance. This means that the results did not show that avelumab plus axitinib was any better than sunitinib at extending overall survival.

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.

Researchers looked at medical problems for the 873 participants who received at least one dose of study medication (434 participants in the avelumab plus axitinib group and 439 participants in the sunitinib group).

- A total of 870 out of 873 (99.7%) participants in this study had at least 1 medical problem.
- A total of 149 out of 434 (34.3%) participants who took avelumab plus axitinib and 77 out of 439 participants (17.5%) who took sunitinib stopped taking a study medicine because of medical problems.

The most common medical problems – those reported by more than 20% of participants in any treatment group – are described below.

Below are instructions on how to read Table 1. Table 2 and Table 3 can be read in a similar way.

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 any treatment group are listed.
- The **2nd** column tells how many of the 434 participants taking avelumab plus axitinib reported each medical problem. Next to this number is the percentage of the 434 participants taking avelumab plus axitinib who reported the medical problem.
- The **3rd** column tells how many of the 439 participants taking sunitinib reported each medical problem. Next to this number is the percentage of the 439 participants taking sunitinib who reported the medical problem.
- Using these instructions, you can see that 305 out of the 434 (70.3%) participants taking avelumab plus axitinib reported loose stools (diarrhea). A total of 230 out of the 439 (52.4%) participants taking sunitinib reported loose stools.

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Avelumab plus Axitinib (434 Participants)**	**Sunitinib (439 Participants)**
Loose stools (diarrhea)	305 out of 434 participants (70.3%)	230 out of 439 participants (52.4%)
High blood pressure	237 out of 434 participants (54.6%)	169 out of 439 participants (38.5%)
Feeling very tired	206 out of 434 participants (47.5%)	195 out of 439 participants (44.4%)
Nausea	188 out of 434 participants (43.3%)	185 out of 439 participants (42.1%)
Hand-foot syndrome	160 out of 434 participants (36.9%)	162 out of 439 participants (36.9%)
Joint pain	157 out of 434 participants (36.2%)	83 out of 439 participants (18.9%)
Difficulty speaking	148 out of 434 participants (34.1%)	20 out of 439 participants (4.6%)
Cough	147 out of 434 participants (33.9%)	103 out of 439 participants (23.5%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Avelumab plus Axitinib (434 Participants)**	**Sunitinib (439 Participants)**
Decreased appetite	141 out of 434 participants (32.5%)	144 out of 439 participants (32.8%)
Low levels of thyroid hormone	137 out of 434 participants (31.6%)	89 out of 439 participants (20.3%)
Headache	122 out of 434 participants (28.1%)	86 out of 439 participants (19.6%)
Back pain	119 out of 434 participants (27.4%)	82 out of 439 participants (18.7%)
Mouth pain and sores	117 out of 434 participants (27.0%)	113 out of 439 participants (25.7%)
Weight loss	112 out of 434 participants (25.8%)	46 out of 439 participants (10.5%)
Difficulty breathing	108 out of 434 participants (24.9%)	70 out of 439 participants (15.9%)
Vomiting	103 out of 434 participants (23.7%)	100 out of 439 participants (22.8%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Avelumab plus Axitinib (434 Participants)**	**Sunitinib (439 Participants)**
Hard or dry stool (constipation)	98 out of 434 participants (22.6%)	74 out of 439 participants (16.9%)
Itching	96 out of 434 participants (22.1%)	29 out of 439 participants (6.6%)
“ALT” liver test levels increased	95 out of 434 participants (21.9%)	50 out of 439 participants (11.4%)
Abdominal pain	91 out of 434 participants (21.0%)	62 out of 439 participants (14.1%)
Arm or leg pain	88 out of 434 participants (20.3%)	62 out of 439 participants (14.1%)
Bad taste in mouth	48 out of 434 participants (11.1%)	107 out of 439 participants (24.4%)
Low red blood cell count	41 out of 434 participants (9.4%)	120 out of 439 participants (27.3%)
Low blood platelets	17 out of 434 participants (3.9%)	90 out of 439 participants (20.5%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Avelumab plus Axitinib (434 Participants)**	**Sunitinib (439 Participants)**
Low white blood cell count	9 out of 434 participants (2.1%)	90 out of 439 participants (20.5%)

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.

A total of 397 out of 873 participants (45.5%) had serious medical problems:

- 231 out of 434 (53.2%) participants who took avelumab plus axitinib had serious medical problems.
- 166 out of 439 (37.8%) participants who took sunitinib had serious medical problems.

The most common serious medical problems – those reported by more than 2% of participants in any group – are shown in Table 2 below.

Table 2. Commonly reported serious medical problems by study participants		
Medical Problem	**Avelumab plus Axitinib (434 Participants)**	**Sunitinib (439 Participants)**
Loose stools (diarrhea)	12 out of 434 participants (2.8%)	3 out of 439 participants (0.7%)
Heart attack	11 out of 434 participants (2.5%)	0 participants
Worsening cancer	10 out of 434 participants (2.3%)	7 out of 439 participants (1.6%)
Kidney injury	9 out of 434 participants (2.1%)	9 out of 439 participants (2.1%)
Abdominal pain	2 out of 434 participants (0.5%)	12 out of 439 participants (2.7%)
Low red blood cell count	1 out of 434 participants (0.2%)	10 out of 439 participants (2.3%)

A total of 97 out of 434 (22.4%) participants who took avelumab plus axitinib and 68 out of 439 (15.5%) participants who took sunitinib had serious medical problems that researchers believed were related to the study treatment.

A total of 574 out of 873 (65.8%) participants had died during the study at the time of this report.

The categories of reasons for participant deaths are shown in Table 3.

Table 3. Reasons for deaths of study participants

Medical Problem	Avelumab plus Axitinib (434 Participants)	Sunitinib (439 Participants)
Worsening cancer	201 out of 434 participants (46.3%)	222 out of 439 participants (50.6%)
Side effect related to treatment	4 out of 434 participants (0.9%)	1 out of 439 participants (0.2%)
A medical problem that was not related to the study treatment	17 out of 434 participants (3.9%)	18 out of 439 participants (4.1%)
“Other” or “Unknown”	62 out of 434 participants (14.3%)	54 out of 439 participants (12.3%)

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 B9991003

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

www.clinicaltrials.gov	Use the study identifier **NCT02684006**
www.clinicaltrialsregister.eu	Use the study identifier 2015 002429 20

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!