CLINICAL TRIAL 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 medicine 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 (MSB0010718C)

Protocol Number: B9991009

Dates of Trial: 21 December 2015 to 19 September 2018

Title of this Trial: A Phase 3, Multicenter, Randomized, Open-Label Study of Avelumab (MSB0010718C) Alone or in Combination With Pegylated Liposomal Doxorubicin Versus Pegylated Liposomal Doxorubicin Alone in Patients With Platinum-Resistant/Refractory Ovarian Cancer

Date of this Report: 12 May 2020

– Thank You –

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your study site.

WHY WAS THIS STUDY DONE?

Ovarian cancer is the name for cancer that starts in the ovaries, which are the female reproductive organs that produce eggs. Ovarian cancer is a major cause of cancer death in women.

Researchers are looking for treatments for ovarian cancer. Avelumab is a medicine that is currently used to treat different types of cancer, which may work by targeting a protein called PD-L1. PD-L1 is involved in the body's immune system response to cancer.

When this study was started, avelumab was still being tested for use in women with ovarian cancer. Avelumab is not approved for use in women with ovarian cancer.

Medicines containing platinum are commonly used to treat ovarian cancer, but these medicines may not work well for all patients. The main goal of this study was to learn more about the use of avelumab in patients with ovarian cancer, particularly those who did not have satisfactory improvement in ovarian cancer symptoms from medicines containing platinum. These patients are said to have ovarian cancer that is "platinum resistant" or "platinum refractory". Patients in this study may have also received another medicine for ovarian cancer, called pegylated liposomal doxyrubicin (PLD). Researchers wanted to answer 2 main questions:

- How long did patients who were assigned to receive either avelumab alone or avelumab plus PLD survive, compared to patients who were assigned to receive PLD alone?
- How long did patients who were assigned to receive either avelumab alone or avelumab plus PLD survive without ovarian cancer getting worse, compared to patients who were assigned to receive PLD alone?

WHAT HAPPENED DURING THE STUDY?

This study compared 3 groups of patients taking either avelumab alone, avelumab plus PLD, or PLD alone. The study included adult patients with platinum-resistant or platinum-refractory ovarian cancer. Patients in this study could have received up to 3 prior rounds of platinum-containing medicines, and must have received a platinum-

containing medicine as their most recent ovarian cancer treatment. However, patients in this study could not have received prior treatment for platinum-resistant or platinum-refractory ovarian cancer. This was an "open-label" study, which means that both the patients and researchers knew which medicines were being given.

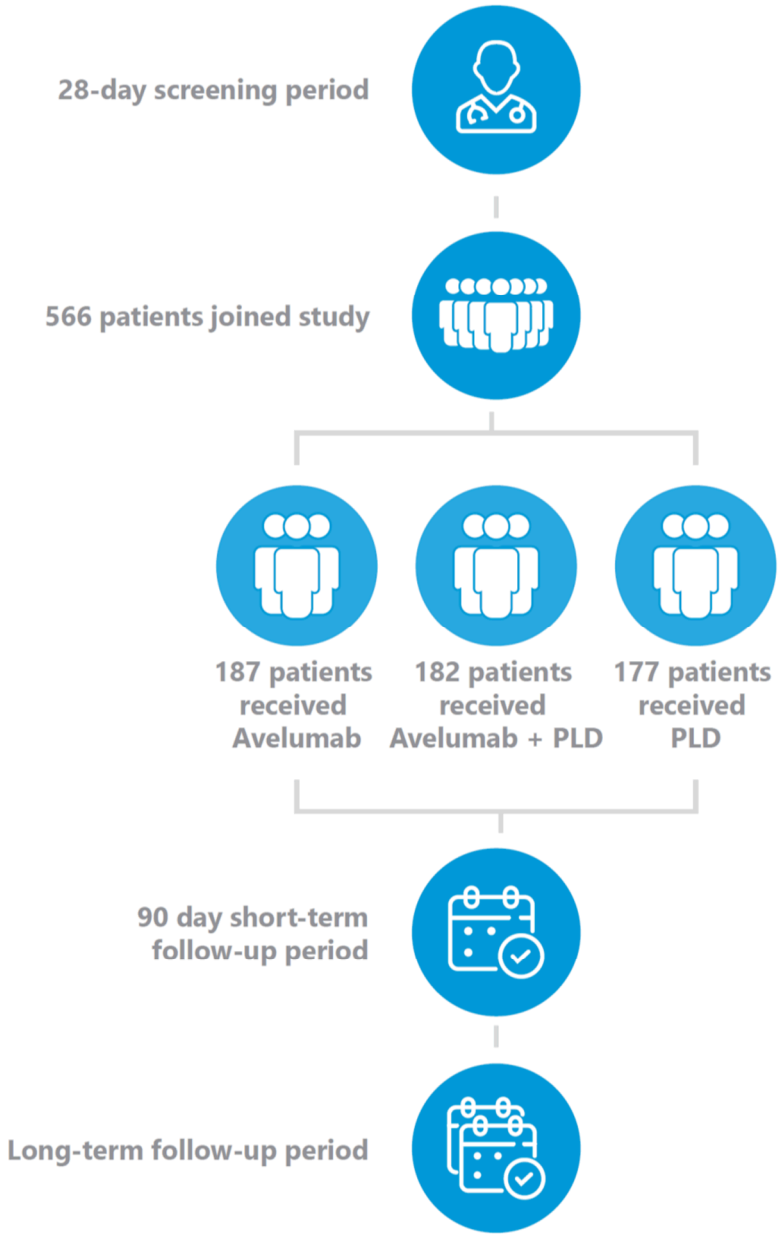
Patients were screened by the study doctor to make sure they were a good fit to join the study. This was known as the "screening period", which lasted up to 28 days. Next, patients were assigned to receive either avelumab alone, avelumab plus PLD, or PLD alone. Patients were assigned to each group by chance alone. Putting people into groups by chance helps make the groups more even to compare.

The study treatments were given by IV infusion (a needle into the vein), as follows:

- Group 1 (187 patients): Avelumab 10 milligrams (mg) per kilogram (kg) of weight, every 2 weeks
- Group 2 (182 patients): Avelumab 10 milligrams (mg) per kilogram (kg) of weight, every 2 weeks plus PLD 40 mg per square meter of body surface area, every 4 weeks
- Group 3 (177 patients): PLD 40 mg per square meter of body surface area, every 4 weeks

After patients completed study treatment, there was a short-term follow-up period that lasted for 90 days. Finally, there was a long-term follow-up period, which lasted until patients left the study or the study ended.

The figure on the following page shows what happened during this study.



The amount of time that patients were in the study varied, and the study is still ongoing. The sponsor ran this study at 300 locations in 25 countries in Asia, Australia, Europe, and North America. It began 21 December 2015. 566 women participated. All patients were between the ages of 26 and 86.

Patients were to complete study treatment and a 90-day short-term follow-up period, then enter the long-term follow-up period. Of the 566 patients who started the study,

389 patients (69%) entered the short-term follow-up period. Of these 389 patients, 205 patients (53%) either completed or remain in the follow-period. 184 patients (46%) left the study and did not complete the follow-up period by their choice, because a doctor decided it was best for a patient to stop the study, or because they passed away.

In September 2018, the Sponsor began reviewing the information collected thus far. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

How long did patients who were assigned to receive avelumab alone or avelumab plus PLD survive without ovarian cancer getting worse, compared to patients who were assigned to receive PLD alone?

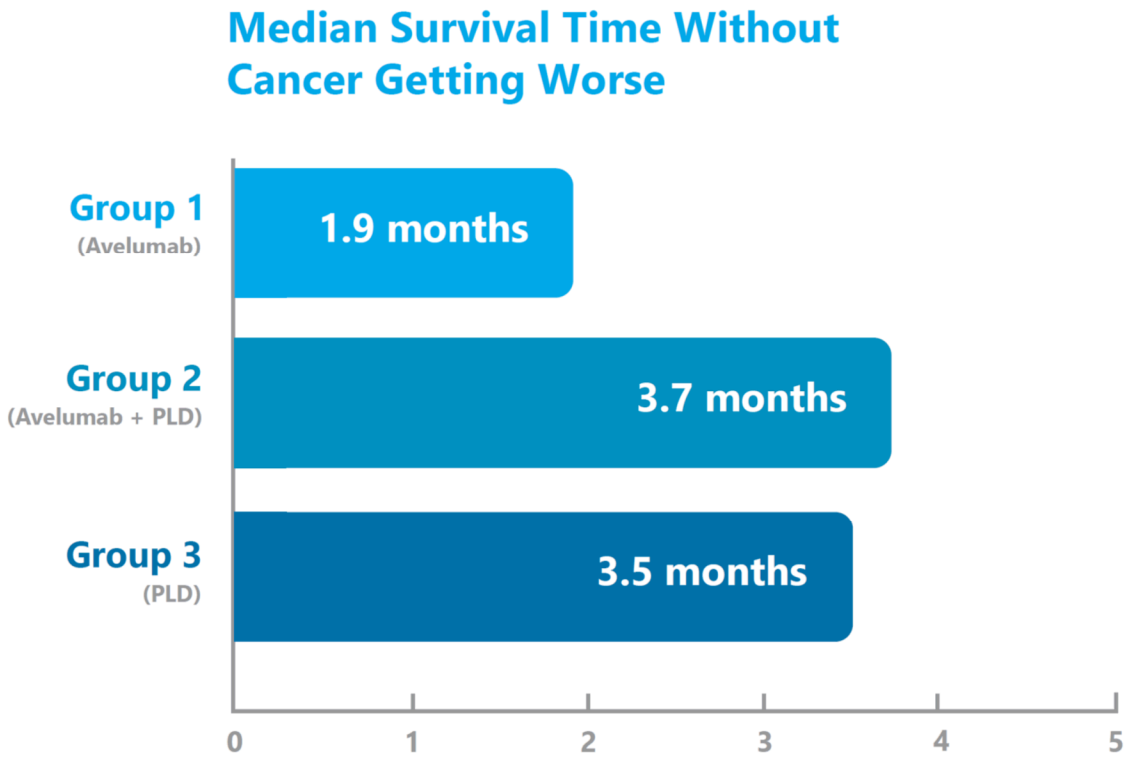
To answer this question, the researchers looked at the median length of time that patients survived without ovarian cancer getting worse. The median is the time by which half of the patients are expected to survive without their cancer getting worse. So, patients would have the same chance of surviving without their cancer getting worse a longer time or a shorter time than this number.

In this study, the median length of time that patients survived without cancer getting worse was as follows:

- Group 1 (avelumab alone): 1.9 months
- Group 2 (avelumab plus PLD): 3.7 months
- Group 3 (PLD alone): 3.5 months

The researchers have decided that these results are not likely based on chance.

The figure on the following page shows the results of the study.



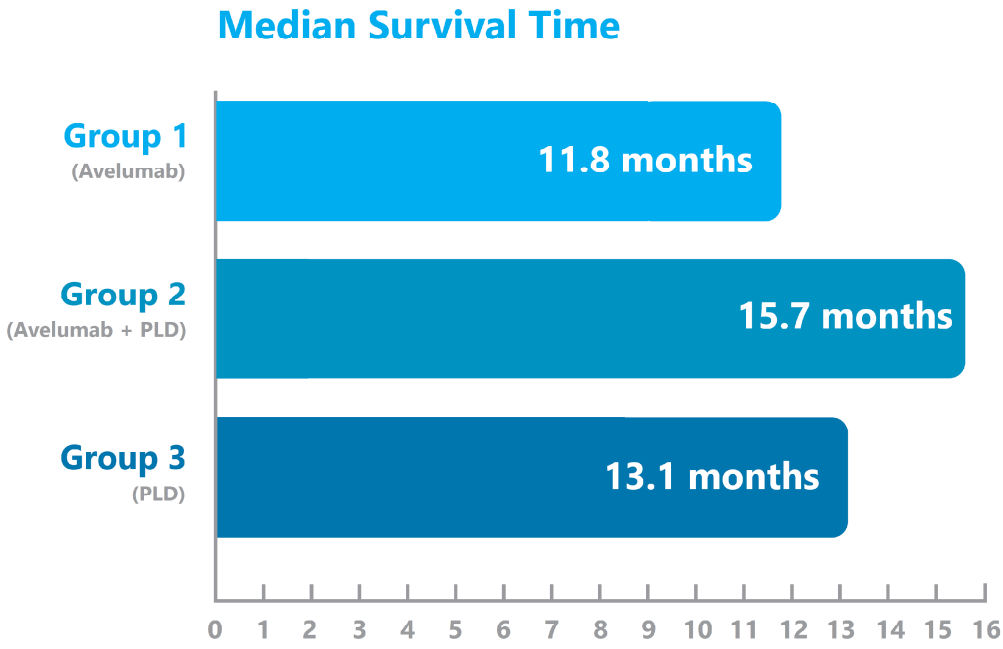
How long did patients who were assigned to receive avelumab alone or avelumab plus PLD survive, compared to patients who were assigned to receive PLD alone?

To answer this question, the researchers looked at the median length of time that patients survived. In this study, the median length of time that patients survived was as follows:

- Group 1 (avelumab alone): 11.8 months
- Group 2 (avelumab plus PLD): 15.7 months
- Group 3 (PLD alone): 13.1 months.

The researchers have decided that these results are not likely based on chance.

The figure on the following page shows the results of the study.



This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?

The researchers recorded any medical problems the patients had during the study. Patients 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 patient 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 the side effects of an experimental drug might be.

Of the 546 patients who received study treatment, 533 (98%) patients had at least 1 medical problem. A total of 51 (14%) patients stopped taking avelumab because of medical problems. A total of 55 (15%) patients stopped taking PLD because of medical problems. The most common medical problems are listed below.

Most Common Medical Problems (Reported by More Than 10% of Patients)			
Medical Problem	**Group 1 Avelumab (187 Patients treated)**	**Group 2 Avelumab + PLD (182 Patients treated)**	**Group 3 PLD (177 Patients treated)**
Feeling tired	**63 (34%)**	**77 (42%)**	**55 (31%)**
Abdominal pain	**57 (31%)**	**48 (26%)**	**41 (23%)**
Nausea	**57 (31%)**	**89 (49%)**	**77 (44%)**
Vomiting	**47 (25%)**	**44 (24%)**	**45 (25%)**
Diarrhea	**43 (23%)**	**37 (20%)**	**32 (18%)**
Low appetite	**38 (20%)**	**51 (28%)**	**37 (21%)**
Constipation	**37 (20%)**	**48 (26%)**	**45 (25%)**

Most Common Medical Problems (Reported by More Than 10% of Patients)			
Medical Problem	Group 1 Avelumab (187 Patients treated)	Group 2 Avelumab + PLD (182 Patients treated)	Group 3 PLD (177 Patients treated)
Trouble breathing	36 (19%)	33 (18%)	25 (14%)
Low number of red blood cells	32 (17%)	55 (30%)	42 (24%)
Fever	32 (17%)	37 (20%)	17 (10%)
Back pain	22 (12%)	17 (9%)	23 (13%)
Chills	19 (10%)	14 (8%)	3 (2%)
Feeling weak	18 (10%)	30 (17%)	14 (8%)
Cough	17 (9%)	28 (15%)	24 (14%)
Headache	15 (8%)	27 (15%)	11 (6%)
Bloating	15 (8%)	18 (10%)	18 (10%)
Urinary tract infection	15 (8%)	20 (11%)	14 (8%)
Reaction to IV infusion	13 (7%)	19 (10%)	16 (9%)
Swelling caused by fluid build-up in arms or legs	13 (7%)	25 (14%)	14 (8%)
Itching	13 (7%)	21 (12%)	8 (5%)
Rash	11 (6%)	51 (28%)	19 (11%)
Underactive thyroid	8 (4%)	19 (10%)	2 (1%)

Most Common Medical Problems (Reported by More Than 10% of Patients)			
Medical Problem	Group 1 Avelumab (187 Patients treated)	Group 2 Avelumab + PLD (182 Patients treated)	Group 3 PLD (177 Patients treated)
Swelling and sores in mouth	8 (4%)	53 (29%)	36 (20%)
Dry skin	5 (3%)	22 (12%)	8 (5%)
Swelling of mucus membranes	4 (2%)	25 (14%)	19 (11%)
Low number of white blood cells	1 (1%)	26 (14%)	26 (15%)
Redness, swelling, and pain on hands and feet	1 (1%)	61 (34%)	40 (23%)

WERE THERE 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 197 out of 546 patients (36%) who received study treatment had serious medical problems, including 71 patients (38%) in Group 1, 75 patients (41%) in Group 2, and 51 patients (29%) in Group 3.

A total of 309 (57%) out of 546 patients died during the study, including 108 patients (58%) in Group 1, 98 patients (54%) in Group 2, and 103 patients (58%) in Group 3. Most of these deaths were due to ovarian cancer, but study doctors determined that 29 of these deaths were related to 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 this study protocol, please visit:

www.clinicaltrials.gov	Use the study identifier **NCT02580058**
www.clinicaltrialsregister.eu	Use the study identifier **2015-003091-77**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients. No further studies with avelumab in patients with ovarian cancer are planned.

Again, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!