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/PF-06834635/MSB0010718C

Protocol Number: B9991010

Dates of Trial: 19 May 2016 to 16 May 2019

Title of this Trial: Avelumab in Previously Untreated Patients with Epithelial Ovarian Cancer [Javelin Ovarian 100]

[A Randomized, Open-Label, Multicenter, Phase 3 Study to Evaluate the Efficacy and Safety of Avelumab (MSB0010718C) in Combination With and/or Following Chemotherapy in Patients With Previously Untreated Epithelial Ovarian Cancer]

Date of this Report: 06 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 originates in the ovary, which is the female reproductive organ that produces eggs and sex hormones. Ovarian cancer is a major cause of cancer death in women. Epithelial ovarian cancer is the most common type of ovarian cancer, and it originates in the cells that cover the outer surface of the ovary.

Researchers are looking for treatments for ovarian cancer. Avelumab is a medicine that may work by targeting a protein called "Programmed Death-Ligand 1" (PD-L1) found on the cancer cell. PD-L1 is involved in the body's immune system response to cancer.

When this study was started, avelumab was being tested for use in women with advanced ovarian cancer. Although avelumab is approved in other types of cancer, it is not approved for use in ovarian cancer.

For women with newly diagnosed advanced ovarian cancer, the standard treatment includes a combination of chemotherapy and surgery. Chemotherapy is often used after surgery to kill any cancer cells that might remain. It can also be used before surgery. This approach is usually effective, but in many cases the cancer comes back.

The main goal of this study was to determine if adding a new drug (avelumab) both during and/or after standard chemotherapy treatment would increase the amount of time it takes for ovarian cancer to worsen (progress). The study also evaluated the overall safety of avelumab alone or in combination with standard chemotherapy.

WHAT HAPPENED DURING THE STUDY?

This study included 3 groups of patients taking platinum-based chemotherapy with no maintenance treatment, platinum-based chemotherapy followed by avelumab maintenance treatment, or platinum-based chemotherapy given together with avelumab then followed by avelumab maintenance treatment. Maintenance treatment means a treatment that is given to stop cancer from coming back after it has disappeared following an initial treatment.

The study included adult women with advanced epithelial ovarian cancer that had spread beyond the pelvis or throughout the body who had not yet received treatment for their advanced cancer. Patients in this study must have had a surgery to remove as much cancer as possible. This was an "open-label" study, which means that both the patients and researchers knew which medicines were being given.

Potential patients were evaluated by the study doctor to make sure they met the criteria to participate in the study. This was known as the "screening period", which lasted up to 28 days. Next, eligible patients were assigned to 1 of 3 treatment groups:

- Group A (335 patients): Platinum-based chemotherapy with no maintenance treatment
- Group B (332 patients): Platinum-based chemotherapy followed by avelumab maintenance treatment
- Group C (331 patients): Platinum-based chemotherapy given together with avelumab, then followed by avelumab maintenance treatment

Patients were assigned to each group by chance. Putting people into groups by chance is called randomization. This helps make it more likely that the groups will be more even to compare.

The chemotherapy combination of medicines used in this study was paclitaxel and carboplatin. All study treatments were given by intravenous (IV) infusion (a needle into a vein).

During the chemotherapy phase, patients received carboplatin every 3 weeks and paclitaxel either every 1 week or every 3 weeks (patient's doctor allowed to choose). Patients in Group C also received avelumab every 3 weeks during the chemotherapy phase.

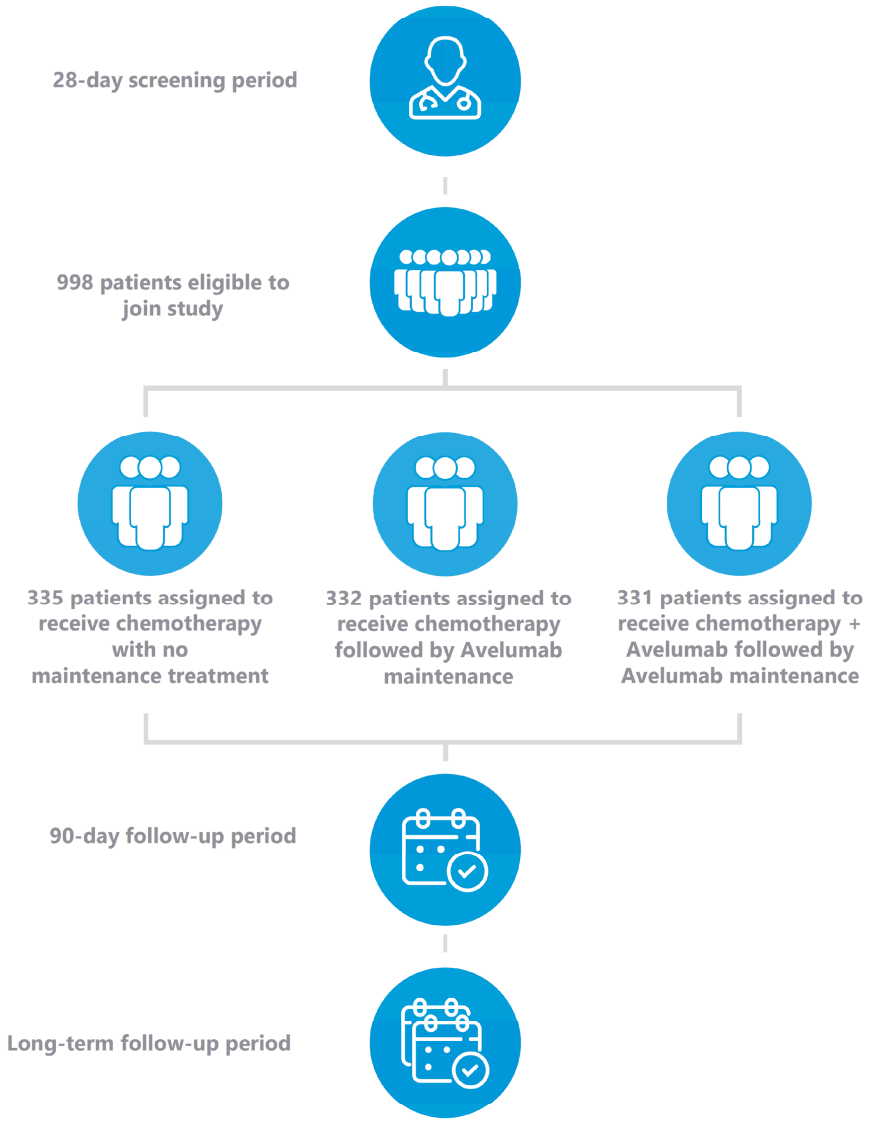
During the maintenance phase, patients in Groups B and C received avelumab every 2 weeks, and patients in Group A received observation only (no study treatments) during this time.

The main goal of this study was to determine if adding a new drug (avelumab) both during and/or after standard chemotherapy treatment would increase the amount of

time it takes for ovarian cancer to worsen (progress). The study also evaluated the overall safety of avelumab alone or in combination with standard chemotherapy.

After the last dose of study treatment, there was a 90-day follow-up period that included a monthly safety follow-up. There was a long-term follow-up period, which lasted until patients left the study or the study ended.

The figure below shows what happened during this study.



The amount of time that patients were in the study varied, but the entire study lasted about 3 years. The sponsor ran this study at 182 locations in 25 countries in Asia, Europe, and North America. It began on 19 May 2016. 998 women joined the study, and 991 women received study treatment. Patients in the study were between the ages of 26 and 86.

Patients were expected to complete study treatment and a 90-day follow-up period, then enter the long-term follow-up period. The tables below show how many patients completed study treatment, and how many patients did not complete study treatment either by their choice or because a doctor decided it was best for a patient to stop being in the study.

Chemotherapy Phase
Group A: Out of 335 patients, 279 (83%) completed paclitaxel and 290 patients (87%) completed carboplatin. 56 patients (17%) stopped taking paclitaxel early and 45 patients (13%) stopped taking carboplatin early. The most common reasons for stopping study treatment were medical problems, worsening ovarian cancer, or patient choice.
Group B: Out of 332 patients, 275 (83%) completed paclitaxel and 280 patients (84%) completed carboplatin. 57 patients (17%) stopped taking paclitaxel early and 52 patients (16%) stopped taking carboplatin early. The most common reasons for stopping study treatment were medical problems, worsening cancer, or patient choice.
Group C: Out of 331 patients, 284 (86%) completed avelumab, 281 (85%) completed paclitaxel, and 290 patients (88%) completed carboplatin. 47 patients (14%) stopped taking avelumab early, 50 patients (15%) stopped taking paclitaxel early, and 41 patients (12%) stopped taking carboplatin early. The most common reasons for stopping study treatment were medical problems, worsening cancer, or patient choice.

Maintenance Phase
Group A: Out of 335 patients, 114 patients (34%) stopped the observation early, and 172 patients (51%) were still under observation at the time of the data cutoff. The most common reasons for stopping the observation were medical problems, worsening cancer, or patient choice.
Group B: Out of 332 patients, 112 patients (34%) stopped the maintenance therapy early, and 155 patients (47%) were continuing maintenance therapy at the time of the data cutoff. The most common reasons for stopping maintenance therapy were medical problems, worsening cancer, or patient choice.
Group C: Out of 331 patients, 107 patients (32%) stopped the maintenance therapy early, and 180 patients (54%) were continuing maintenance therapy at the time of the data cutoff. The most common reasons for stopping maintenance therapy were medical problems, worsening cancer, or patient choice.

In September 2018, 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?

Did adding avelumab both during and after standard chemotherapy treatment increase the amount of time it takes for ovarian cancer to worsen (progress)?

To answer this question, the researchers compared the progression free survival (PFS), which is the time patients survived without their cancer getting worse. A more easily understood measure is the median PFS, or the estimated time by which half (50%) of the patients would have survived without their cancer getting worse. It is equally likely for a patient to have survived longer than this time without their cancer getting worse as it is that they survived less time without their cancer getting worse.

In this study, the estimated median time of survival (PFS) without cancer getting worse for each group was as follows:

- Group A (platinum-based chemotherapy with no maintenance treatment): At the time that the researchers analyzed the study results, the median time of survival without cancer getting worse in this group could not be estimated because there were too few patients with worsening cancer to make an accurate estimation.
- Group B (platinum-based chemotherapy followed by avelumab maintenance treatment): 16.8 months
- Group C (platinum-based chemotherapy given together with avelumab, followed by avelumab maintenance treatment): 18.1 months

The study data was reviewed by an independent Data and Safety Monitoring Board (DSMB). DSMBs are used to ensure the safety of study participants and to determine if it is appropriate for a study to continue. There were no new or unexpected safety issues identified with avelumab alone, or with the combination of avelumab plus paclitaxel and carboplatin. However, the DSMB concluded that there was little to no chance that the trial would demonstrate any benefit when adding avelumab to the standard chemotherapy treatment. The addition of avelumab did not increase the amount of time it takes for ovarian cancer to worsen, and consequently the study was stopped early to give patients an opportunity to seek other treatments.

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.

In this report, all medical problems that occurred during the study are discussed, regardless of whether or not the study doctors thought that the medical problems were related to taking the study treatment.

Of the 991 patients who received study treatment, 970 (98%) patients had at least 1 medical problem. A total of 125 (13%) patients stopped taking study treatment 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 A Chemotherapy With No Maintenance Treatment (334 Patients treated)	Group B Chemotherapy Followed by Avelumab (328 Patients treated)	Group C Chemotherapy + Avelumab Followed by Avelumab (329 Patients treated)
Hair loss	177 (53%)	166 (51%)	169 (51%)
Nausea	152 (46%)	151 (46%)	150 (46%)
Low number of red blood cells (anemia)	143 (43%)	150 (46%)	155 (47%)
Low number of a type of white blood cells	113 (34%)	114 (35%)	124 (38%)
Feeling tired	109 (33%)	121 (37%)	114 (35%)
Constipation	94 (28%)	114 (35%)	98 (30%)

Most Common Medical Problems (Reported by More Than 10% of Patients)			
Medical Problem	Group A Chemotherapy With No Maintenance Treatment (334 Patients treated)	Group B Chemotherapy Followed by Avelumab (328 Patients treated)	Group C Chemotherapy + Avelumab Followed by Avelumab (329 Patients treated)
Numbness or pain from damage to sensory nerves	82 (25%)	91 (28%)	75 (23%)
Vomiting	68 (20%)	87 (27%)	77 (23%)
Numbness or pain from damage to peripheral nerves	64 (19%)	63 (19%)	77 (23%)
Diarrhea	63 (19%)	83 (25%)	97 (29%)
Low number of platelets	59 (18%)	47 (14%)	62 (19%)
Abdominal pain	58 (17%)	64 (20%)	64 (19%)
Joint pain	54 (16%)	72 (22%)	77 (23%)
Muscle pain	43 (13%)	67 (20%)	53 (16%)
Low appetite	38 (11%)	63 (19%)	53 (16%)
Pain in hands and feet	37 (11%)	27 (8%)	30 (9%)
Trouble sleeping	32 (10%)	50 (15%)	39 (12%)
Trouble breathing	30 (9%)	39 (12%)	48 (15%)

Most Common Medical Problems (Reported by More Than 10% of Patients)			
Medical Problem	Group A Chemotherapy With No Maintenance Treatment (334 Patients treated)	Group B Chemotherapy Followed by Avelumab (328 Patients treated)	Group C Chemotherapy + Avelumab Followed by Avelumab (329 Patients treated)
Urinary tract infection	29 (9%)	36 (11%)	47 (14%)
Headache	28 (8%)	51 (16%)	48 (15%)
Dizziness	28 (8%)	43 (13%)	37 (11%)
Rash	25 (7%)	55 (17%)	63 (19%)
Fever	23 (7%)	37 (11%)	43 (13%)
Feeling weak	22 (7%)	34 (10%)	46 (14%)
Upper abdominal pain	21 (6%)	28 (9%)	35 (11%)
Cough	20 (6%)	35 (11%)	51 (16%)
Itching	19 (6%)	36 (11%)	34 (10%)
Reaction to IV infusion	19 (6%)	26 (8%)	34 (10%)
Underactive thyroid	4 (1%)	28 (9%)	33 (10%)

Most Common Abnormal Lab Test Results (Reported by More Than 10% of Patients)			
Abnormal Lab Test Result	Group A Chemotherapy With No Maintenance Treatment (334 Patients treated)	Group B Chemotherapy Followed by Avelumab (328 Patients treated)	Group C Chemotherapy + Avelumab Followed by Avelumab (329 Patients treated)
Neutrophil count decreased	75 (22%)	60 (18%)	54 (16%)
Platelet count decreased	44 (13%)	25 (8%)	39 (12%)
White blood cell count decreased	34 (10%)	32 (10%)	31 (9%)
Low magnesium level	27 (8%)	32 (10%)	42 (13%)

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 267 out of 991 patients (27%) who received study treatment had serious medical problems. 63 patients (19%) in Group A, 89 patients (27%) in Group B, and 115 patients (35%) in Group C had serious medical problems. The most common serious medical problems are listed below.

Most Common Serious Medical Problems (Reported by More Than 2% of Patients)			
Serious Medical Problem	Group A Chemotherapy With No Maintenance Treatment (334 Patients treated)	Group B Chemotherapy Followed by Avelumab (328 Patients treated)	Group C Chemotherapy + Avelumab Followed by Avelumab (329 Patients treated)
Inability of intestines to contract normally	9 (3%)	3 (1%)	3 (1%)
Low number of red blood cells (anemia)	6(2%)	6 (2%)	8 (2%)
Fever with low number of a type of white blood cell	7 (2%)	10 (3%)	8 (2%)
Fever	2 (1%)	6 (2%)	10 (3%)
Urinary tract infection	2 (1%)	7 (2%)	7 (2%)

A total of 53 (5%) patients died during the study, including 13 patients (4%) in Group A, 19 patients (6%) in Group B, and 21 patients (6%) in Group C. Most of these deaths were due to ovarian cancer, including 11 patients (3%) in Group A, 15 patients (5%) in Group B, and 17 patients (5%) in Group C.

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 **NCT02718417**
www.clinicaltrialsregister.eu	Use the study identifier **2015-003239-36**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **B9991010**

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!