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 (Bavencio®)

Utomilumab (PF-05082566)

Protocol Number: B9991011

Dates of Trial: 16 December 2016 to 02 December 2019

Title of this Trial: Avelumab In Combination Treatments in Patients With Relapsed or Refractory Diffuse Large B-cell Lymphoma (Javelin DLBCL)

[Phase 1b/Phase 3 Multicenter Study of Avelumab (MSB0010718C) in Combination Regimens That Include an Immune Agonist, Epigenetic Modulator, CD20 Antagonist and/or Conventional Chemotherapy in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL)]

Date(s) of this Report: 02 November 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?

Diffuse Large B-Cell Lymphoma (or "DLBCL") is a kind of non-Hodgkin lymphoma. It is the most common type of blood cancer. DLBCL happens when cells of the immune system, known as B-cells, grow and multiply uncontrollably. DLBCL occurs mostly in adults and is a fast-growing (aggressive) lymphoma. While there are treatments available for DLBCL, some patients' cancer does not get better or gets worse over time. Researchers are looking for new and better treatments that can be combined with other medicines to help keep patients' DLBCL from getting worse over time.

Avelumab and utomilumab were investigational treatments for DLBCL when this study began. Both of these treatments are a type of protein called "monoclonal antibodies", and they are thought to work by helping the cells of the immune system fight cancer cells. Although avelumab is approved for use in other types of cancer under the brand name Bavencio®, it is not approved for use in DLBCL.

The medicines rituximab, azacitidine, and bendamustine are commonly used to treat DLBCL, but these medicines may not work well for all patients. Patients who's DLBCL did not get better with approved cancer treatments are said to have "refractory" DLBCL. Patients whose DLBCL got better after treatment but later got worse are said to have "relapsed" DLBCL.

This study was divided into 2 parts, or "phases". The main purpose of the first phase of the study (Phase 1) was to learn about the effects of avelumab when given with other investigational or approved cancer therapies. This information would determine the best treatment combination to use in the second phase of the study (Phase 3). To do this, the researchers asked:

- **How many dose-limiting toxicities, or "DLTs", did patients have when taking avelumab with other therapies?**

  DLTs are certain medical problems caused by taking avelumab which require the patient to lower the dose or stop taking the medicine temporarily or permanently.

- **How many patients had their DLBCL get better when taking avelumab with other therapies?**

  To do this, the researchers looked to see if the patients' tumors got smaller after taking the study medications.

WHAT HAPPENED DURING THE STUDY?

This study compared 3 groups of patients taking avelumab with other investigational and approved cancer medications to see what DLTs the patients had, and to see if their DLBCL improved.

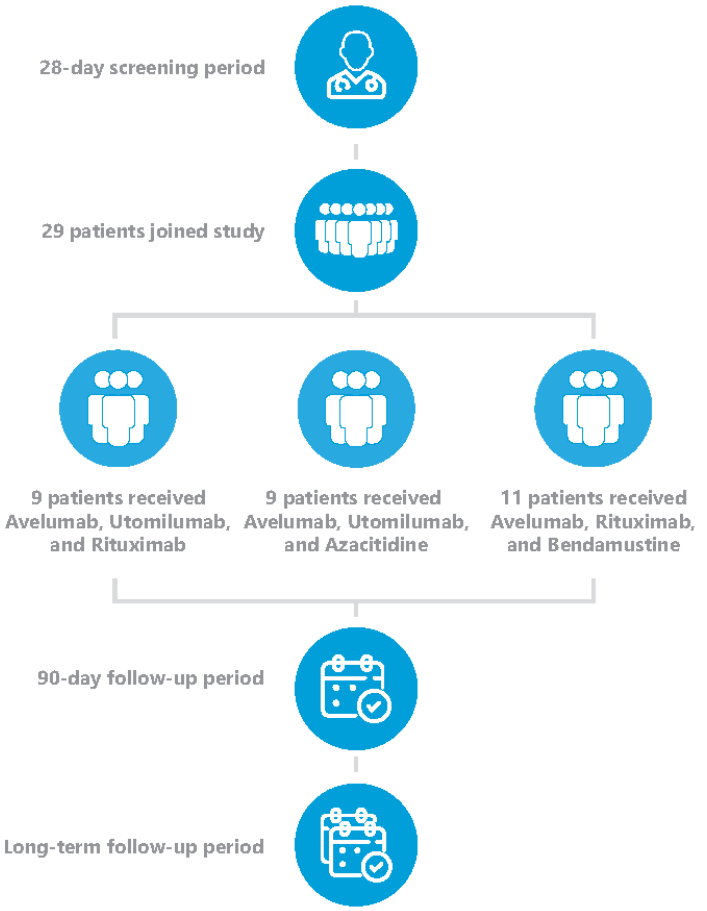
The study included adult patients with relapsed or refractory DLBCL who met the following conditions:

- They had completed at least 2 (but no more than 4) cycles of treatment with rituximab and chemotherapy, with or without a stem cell transplant. If they were not eligible to be treated with a stem cell transplant and/or intensive chemotherapy (for example, due to medical problems), they must have completed 1 cycle of treatment with rituximab and chemotherapy.
- They did not have evidence of cancer in the brain or spinal cord.
- They had not received an organ transplant.
- They had not been treated before with certain monoclonal antibody medications or non-drug anti-cancer therapies.
- They had not received any anti-cancer therapy in the 2 weeks before starting the study medications.

Patients were put into 1 of the 3 treatment groups by chance alone. This is known as a "randomized" study. This is done to make the groups more similar and more even to compare. The patients and researchers knew which medications the patients were taking. This is known as an "open-label" study. The medications given to each treatment group are shown in the table below. All medications were given through a needle into a vein (intravenous) except for azacitidine, which was given by injection under the skin (subcutaneous).

Group A	Group B	Group C
Avelumab 10 mg/kg	**Avelumab 10 mg/kg**	**Avelumab 10 mg/kg**
Utomilumab 100 mg	**Utomilumab 100 mg**	**Bendamustine 90 mg/m^2**
Rituximab 375 mg/m^2	**Azacitidine 40 mg/m^2**	**Rituximab 375 mg/m^2**

A diagram of the study is shown below.



This study took 3 years to complete. The Sponsor ran this study at 15 locations in 5 countries in Europe, the United States, and Australia. It began 16 December 2016 and ended on 02 December 2019. A total of 24 men and 5 women participated. Ten (10) patients were under the age of 65 and 19 patients were 65 years of age or older.

Patients were to be treated until the patient or their doctor decided it was best for them to stop treatment. Of the 29 patients who started the study, no patients finished the first phase of the study. The most common reason for patients leaving the study was because their DLBCL got worse. Two (2) patients left before the study was over by their choice or a doctor decided it was best for a patient to stop being in the study.

The study was stopped before the second phase (Phase 3) began. Group A and Group B were closed to enrollment in May 2018, due to less than 2 patients in these groups having their DLBCL get better. Enrollment in Group C was closed in September 2018 due to lack of new patients enrolling in the study.

When the study ended in December 2019, the Sponsor reviewed 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?

How many DLTs did patients have when taking avelumab with other therapies?

There was 1 patient in Group A (taking avelumab, utomilumab, and rituximab) who had DLTs. This patient developed a herpes infection that involved the eyes, which the researchers think was related to taking rituximab. No DLTs were reported in Group B or Group C.

How many patients had their DLBCL get better when taking avelumab with other therapies?

One (1) of the 9 patients in Group A, none of the patients in Group B, and 3 of the 11 patients in Group C had their DLBCL get better. These results did not show that one treatment was better than another, and could have been due to chance.

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 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 the side effects of an experimental drug might be.

All patients in this study had at least 1 medical problem. A total of 4 patients stopped taking at least 1 study medicine because of medical problems. The most common medical problems are listed below.

Most Common Medical Problems (Reported by More Than 30% of Patients in Any Group)

Medical Problem	Group A Avelumab 10 mg/kg Utomilumab 100 mg Rituximab 375 mg/m^2 8 patients treated	Group B Avelumab 10 mg/kg Utomilumab 100 mg Azacitidine 40 mg/m^2 9 patients treated	Group C Avelumab 10 mg/kg Bendamustine 90 mg/m^2 Rituximab 375 mg/m^2 11 patients treated
Tiredness	1 (13%)	1 (11%)	5 (46%)
Low white blood cells (neutropenia)	2 (25%)	1 (11%)	5 (46%)
Low red blood cells (anemia)	2 (25%)	2 (22%)	4 (36%)
Constipation	1 (13%)	5 (56%)	4 (36%)
Nausea	2 (25%)	2 (22%)	4 (36%)
Low appetite	3 (38%)	1 (11%)	3 (27%)

Fever	**3 (38%)**	**1 (11%)**	**3 (27%)**
Chills	**3 (38%)**	**1 (11%)**	**1 (9%)**
Back pain	**2 (25%)**	**3 (33%)**	**0**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

Sixteen (16) patients (57%) had serious medical problems. When broken down by group, 3 patients in Group A (38%), 6 patients in Group B (67%), and 7 patients in Group C (64%) had serious medical problems. Most serious medical problems happened in 1 patient and were not thought to be related to avelumab treatment. The only serious medical problem reported by 2 or more patients was their DLBCL getting worse. A total of 18 patients died during the study, mostly due to their DLBCL getting worse.

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.

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

www.clinicaltrials.gov	Use the study identifier **NCT02951156**
www.clinicaltrialsregister.eu	Use the study identifier **2016-002904-15**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **B9991011**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

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!