Clinical Study Results

MedImmune
A member of the AstraZeneca Group

Research Sponsor: MedImmune, LLC

Drug Studied: Durvalumab, tremelimumab, and AZD9150

Study Title: A study to learn about the safety of durvalumab, tremelimumab, and AZD9150 in participants with relapsed or refractory lymphoma

Thank you!

Thank you to the participants who took part in the clinical study for the study drugs durvalumab, tremelimumab, and AZD9150, and to the participants' families. Medimmune, LLC sponsored this study and believes it is important to share the results. An independent non-profit organization called CISCRP helped prepare this summary of the study results.

If you or a family member participated in the study and you have questions about the results, please speak with the study doctor or staff at your study site.

Who took part in the study?

The researchers asked for the help of men and women who have relapsed or refractory lymphoma. The participants in this study were 41 to 87 years old when they joined.

The study included 32 participants in France, Ireland, the United Kingdom, and the United States.

Why was the research needed?

Researchers are looking for a better way to treat people who have relapsed or refractory lymphoma. Before a drug can be approved for people to take, researchers do clinical studies to find out how safe it is and how it works.

Cancer is a disease that happens when the body cannot control the growth of cells. Lymphoma is a type of cancer that starts in the lymphocytes, which are white blood cells. Lymphocytes help the body fight infection and disease and are stored in an area of the immune system called the lymph nodes. Lymphoma starts in the lymphocytes and can grow within the lymph nodes. “Relapsed” means that the cancer was treated and seemed to be gone, but then later returned. “Refractory” means that treatment did not affect the cancer at all.

There are treatments for lymphoma. But, these treatments may not stop the cancer from growing or spreading and may not stop the cancer from returning. These treatments may also cause medical problems.

In this study, the researchers wanted to learn about the safety of a current cancer treatment called durvalumab when given with the study drugs tremelimumab or AZD9150.

To do this, the researchers kept track of the “dose limiting toxicities” that the participants had during the study. A dose limiting toxicity is a medical problem that is severe enough to stop the study doctor from increasing the participant’s dose of study treatment. A dose limiting toxicity is also called DLT.

The researchers also wanted to find the “maximum tolerated dose” of the study drugs. The maximum tolerated dose is the highest dose of a drug that does not cause a DLT. The maximum tolerated dose is also called MTD.

What was the purpose of this study?

The main questions the researchers wanted to answer in this study were:

- Did the participants have any DLTs during the study?
- What were the MTDs of the study drugs?
- What signs and symptoms did the participants have during the study?
- What medical problems happened during the study?

The answers to these questions are important to know before other studies can be done that help find out if the study treatments help improve the health of people who have relapsed or refractory lymphoma.

What treatments did the participants get?

This was an “open-label” study. This means the participants, researchers, study doctors, and other study staff knew what each participant was getting.

This study had 2 parts, called Part A and Part B. Each participant could be in only 1 part.

The participants in Part A got durvalumab and either tremelimumab or AZD9150. Each of the study treatments was given through a needle into a vein. This is known as intravenous treatment, also called IV treatment.

The participants who got AZD9150 during Part A started out getting a low dose of AZD9150. The study doctors carefully reviewed the results for these participants. Then, they decided whether or not to increase the dose of AZD9150.

The participants in Part B got durvalumab and AZD9150 through IV treatment.

All of the doses were measured in milligrams per kilogram, also called mg/kg.

What happened during the study?

The study started in July 2016 and ended in February 2019.

The researchers ended the study early. This was because they found that the study treatments were only helping a small number of the participants with their cancer.

Before the participants got study treatment, they visited their study site 1 time during a 1 month period. During this visit, the study doctors checked to make sure the participants could join the study.

The study doctors:

- did a physical examination
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG
- asked the participants about their medical history, how they were feeling, and what medicines they were taking

During the study, the participants got treatment in 4-week periods called "cycles". The participants could start a new cycle until either their cancer got worse or they had medical problems that caused them to stop taking study treatment. If the study treatment was helping the participants' cancer at the end of the study, the participants could choose to continue treatment.

The participants in Part A received up to 4 treatment cycles for up to 4 months.

The participants in Part B received up to 4 treatment cycles for up to 4 months.

Throughout the study, the researchers continued checking the participants' health.

After the participants got their last treatment, they visited their study site about once a month for 3 months. Then, they visited their study site:

- once every 3 months for about 9 months
- once every 6 months for up to about another 12 months

At these visits, the study doctors checked the participants' health and asked them how they were feeling. If the participants were not healthy enough to visit their study site, the study doctors called to ask the participants how they were feeling.

What were the results of the study?

This is a summary of the main results from this study overall. The results each participant had might be different and are not in this summary.

Researchers look at the results of many studies to decide which treatments work best and are safest. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

The websites listed at the end of this summary may have more information about the study results.

Did the participants have any DLTs during the study?

No. None of the participants in either part of the study had a medical problem severe enough to stop the study doctor from increasing their dose.

What were the MTDs of the study drugs?

To answer this question, the researchers kept track of the medical problems the participants had during the study to determine if any participants had a DLT. None of the participants who got the highest doses of the study drugs had a DLT. So, the researchers could not determine the MTD for any of the study drugs.

The highest doses of the study drugs were:

- 20 mg/kg of durvalumab given with 1 mg/kg of tremelimumab
- 20 mg/kg of durvalumab given with 3 mg/kg of AZD9150

What signs and symptoms did the participants have during the study?

To answer this question, the researchers compared the results of the tests and measurements that were done before and during the study.

Overall, the researchers found that there were some changes in the results of these tests and measurements during the study. But, in both parts of the study, there were too few participants for the researchers to determine if these changes were significant.

The study doctors also kept track of the “adverse events” that the participants had. An adverse event is any sign or symptom that participants have during a study.

Doctors keep track of all the adverse events that happen in studies, even if they do not think the adverse events might be related to the study treatment.

Later in this document, there will be a summary of the adverse events that the study doctors thought might be related to the study treatment. This section is a summary of all the adverse events, whether they might be related to the study treatment or not. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.

Adverse events may or may not be caused by the treatments in the study. A lot of research is needed to know whether a treatment causes an adverse event.

How many participants had adverse events?

During this study:

- There were 100% of participants who had adverse events. This was 32 out of 32 participants.
- There were 65.6% of participants who had serious adverse events. This was 21 out of 32 participants.
- There were 18.8% of participants who left the study due to adverse events. This was 6 out of 32 participants.
- There were 6.3% of participants who died due to serious adverse events during the study. This was 2 out of 32 participants. These deaths were not thought to be related to the study treatments.

What medical problems did participants have during the study?

This section is a summary of the medical problems the participants had during the study that the study doctors thought might be related to the study treatments. These medical problems are called “adverse reactions”. An adverse reaction is considered “serious” when it is life threatening, causes lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the study treatments. A lot of research is needed to know whether a treatment causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for treatment.

The websites listed at the end of this summary may have other information about adverse reactions or other medical problems that happened during this study.

Did any adverse reactions happen during this study?

There were 65.6% of participants who had adverse reactions during the study. This was 21 out of 32 participants.

The table below shows how many participants had adverse reactions.

Adverse reactions during the study

	Part A			Part B
	20 mg/kg of durvalumab and 1 mg/kg of tremelimumab (out of 3 participants)	**20 mg/kg of durvalumab and 2 mg/kg of AZD9150 (out of 5 participants)**	**20 mg/kg of durvalumab and 3 mg/kg of AZD9150 (out of 9 participants)**	**20 mg/kg of durvalumab and 3 mg/kg of AZD9150 (out of 15 participants)**
How many participants had adverse reactions?	66.7% (2)	20.0% (1)	77.8% (7)	73.3% (11)
How many participants had serious adverse reactions?	33.3% (1)	0.0% (0)	0.0% (0)	6.7% (1)
How many participants left the study due to adverse reactions?	33.3% (1)	0.0% (0)	33.3% (3)	6.7% (1)

What serious adverse reactions happened during the study?

There were 6.3% of participants who had serious adverse reactions during the study. This was 2 out of 32 participants.

The serious adverse reactions that happened during the study were:

- Diarrhea. This happened in 1 participant in Part A who got 20 mg/kg of durvalumab and 1 mg/kg of tremelimumab.
- Increase in amount of aspartate aminotransferase in the body, which is a sign of liver damage. This happened in 1 participant in Part B who got 20 mg/kg of durvalumab and 3 mg/kg of AZD9150.

None of the participants died due to serious adverse reactions during the study.

What adverse reactions happened during the study?

The most common adverse reaction during the study was:

- Increase in amount of alanine aminotransferase in the body, which is a sign of liver damage.

The table below shows the adverse reactions that happened in at least 3 participants during the study. There were other adverse reactions, but those happened in fewer participants.

Most common adverse reactions during the study

	Part A			Part B
Adverse reaction	**20 mg/kg of durvalumab and 1 mg/kg of tremelimumab (out of 3 participants)**	**20 mg/kg of durvalumab and 2 mg/kg of AZD9150 (out of 5 participants)**	**20 mg/kg of durvalumab and 3 mg/kg of AZD9150 (out of 9 participants)**	**20 mg/kg of durvalumab and 3 mg/kg of AZD9150 (out of 15 participants)**
Increase in amount of alanine aminotransferase in the body (a sign of liver damage)	0.0% (0)	20.0% (1)	44.4% (4)	26.7% (4)
Increase in amount of aspartate aminotransferase in the body (a sign of liver damage)	0.0% (0)	20.0% (1)	33.3% (3)	26.7% (4)
Decrease in number of red blood cells in the body	33.3% (1)	0.0% (0)	11.1% (1)	26.7% (4)
Feeling tired	0.0% (0)	0.0% (0)	33.3% (3)	6.7% (1)
Diarrhea	33.3% (1)	0.0% (0)	11.1% (1)	6.7% (1)
Increase in amount of gamma glutamyltransferase in the body (a sign of liver damage)	0.0% (0)	0.0% (0)	22.2% (2)	6.7% (1)
Nausea	0.0% (0)	0.0% (0)	22.2% (2)	6.7% (1)
Decrease in blood platelet count (the body cannot stop bleeding as well as it should)	0.0% (0)	0.0% (0)	11.1% (1)	13.3% (2)
Decrease in number of neutrophils (a type of white blood that helps the body fight infection)	0.0% (0)	0.0% (0)	11.1% (1)	13.3% (2)

How has this study helped patients and researchers?

This study helped researchers learn about the safety of durvalumab given with tremelimumab or AZD9150 in participants who have relapsed or refractory lymphoma.

Researchers look at the results of many studies to decide which treatments work best and are safest. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Further clinical studies with the combination of durvalumab, tremelimumab, and AZD9150 are not planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If a full report of the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02549651"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D4190C00023"** into the search box, and click **"Find a Study"**.

Full study title: A Phase 1b Study to Evaluate the Safety and Efficacy of MEDI4736 as Monotherapy and in Combination with Tremelimumab or AZD9150 in Subjects with Relapsed or Refractory Diffuse Large B-cell Lymphoma

AstraZeneca Protocol Number: D4190C00023

MedImmune, LLC, a member of the AstraZeneca Group, sponsored this study and has its headquarters at 1 Medimmune Way, Gaithersburg, MD 20878.

The phone number for the AstraZeneca Information Center is +1-877-240-9479.

Thank you!

Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical studies, nor is it involved in conducting clinical studies.

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