Clinical Study Results

MedImmune
A member of the AstraZeneca Group

Research Sponsor: MedImmune

Drug Studied: MEDI4736 with tremelimumab

Study Title: A study to learn about the safety of MEDI4736 with tremelimumab in participants with advanced non-small cell lung cancer, also called NSCLC

Thank you!

Thank you for taking part in the clinical study for the study drugs MEDI4736 and tremelimumab.

MedImmune 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 for you.

If you participated in the study and 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 people with a type of lung cancer called non-small cell lung cancer, also called NSCLC. The participants in this study were 22 to 87 years old when they joined. Some of the participants may have already tried treatments for their cancer. All of the participants had “advanced” cancer. This usually means that the cancer keeps growing even with treatment.

The study included 457 participants in Australia, Belgium, France, Italy, South Korea, Spain, Taiwan, the United Kingdom, and the United States.

Why was the research needed?

Researchers are looking for a better way to treat advanced NSCLC. Before a drug can be approved for people to get, researchers do clinical studies to find out how safe it is and how it works.

In people with cancer, the body is not able to control the growth of cells. The extra cells can form tumors. Normally, the immune system fights infections or anything it does not recognize, and can help stop tumors from growing. But in people with advanced NSCLC, a protein on the tumor cells can interact with certain proteins on the immune cells. This stops the immune cells from recognizing tumor cells and being able to fight them.

The study drugs, MEDI4736 and tremelimumab, were each designed to stop the tumor cells from interacting with some of these proteins. This lets the immune cells recognize the tumor cells again and help stop the tumor from growing.

In this study, the researchers wanted to find out about the safety of MEDI4736 with tremelimumab in participants with advanced NSCLC.

What was the purpose of this study?

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

- What signs and symptoms did the participants have during the study?
- Did MEDI4736 with tremelimumab slow the growth of the participants’ tumors?
- What medical problems did the participants have during the study?

The answers to these questions are important to know before other studies can be done to find out if MEDI4736 with tremelimumab helps improve the health of people with advanced NSCLC.

What treatments did the participants take?

All of the participants in this study got MEDI4736 and tremelimumab through a needle into a vein, also known as an IV infusion.

The study happened in 2 parts. Both parts were “open-label”. This means the participants, researchers, study doctors, and other study staff knew what each participant was getting.

Part A was done so the researchers could find the dose to give to the participants in Part B. In Part A, there were 102 participants. There were 10 groups of participants, and the groups got different doses of MEDI4736 and tremelimumab. Each participant stayed on the same assigned dose throughout this part of the study.

- The participants in Groups 1 through 8 got 1 dose of MEDI4736 every 4 weeks.
- The participants in Groups 9 and 10 got 1 dose of MEDI4736 every 2 weeks.
- All of the participants got 1 dose of tremelimumab every 4 weeks for 24 weeks, then every 12 weeks for 36 weeks.

In **Part B** there were 355 participants. The participants in Part B were not the same participants that were in Part A. In this part, the participants were put into 1 of 3 groups based on the types of NSCLC treatments they had tried before the study.

All of the participants got MEDI4736 and tremelimumab every 4 weeks for 16 weeks. Then, they got only MEDI4736 every 4 weeks for 36 weeks.

The chart below shows the groups in Part B.

Group	Earlier NSCLC treatments	Number of participants (out of 355)
1 	No earlier treatments	45
2 	Had earlier treatments that were a different kind of treatment than the study drugs	232
3 	Had earlier treatments that were the same kind of treatment as the study drugs	78

What happened during the study?

The study started in October 2013 and ended in September 2019.

Before the participants got study treatment, they visited their study site 1 time. This happened about 4 weeks before the participants got study treatment. At this visit, the study doctors made sure that the participants could join the study. The study doctors:

- did a physical exam and asked about the participants' medications and any medical problems they were having
- checked the participants' heart health using an electrocardiogram, also called an ECG
- took pictures of each participant's tumor using an MRI scan
- if needed, did a procedure called a biopsy to take a sample of the participants' tumors
- took blood and urine samples

The study doctors also did these tests and measurements throughout the study.

While the participants were getting study treatment in Part A, the participants visited their study site up to about 35 times based on which group they were in.

At each of these visits, the participants got their IV infusions of MEDI4736. At some of these visits, they got IV infusions of tremelimumab.

While the participants were getting study treatment in Part B, they visited their study site up to about 23 times. At each of these visits, the participants got their IV infusions of MEDI4736. At some of these visits, they got IV infusions of tremelimumab.

After the participants got their last study treatment, they visited their study site 6 times over 12 months. At these visits, the study doctors checked the health of the participants. After that, the study doctors called the participants every 3 months until the study ended. If a participant's cancer got worse after their last treatment, he or she could keep getting the study treatments for up to 12 months.

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 change.

The websites listed at the end of this summary may have a full report of the study results.

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

To answer this question, the study doctors did tests and measurements before and after the participants got the study treatment. The study doctors did physical exams and tested the participants' blood and urine samples to check their overall health. They also did ECGs to check the participants' heart health.

Overall, the researchers found that there were some small changes in the results of these tests and measurements. But, the researchers did not consider these to be 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.

	Part A (out of 102 participants)	Part B (out of 355 participants)
How many participants had adverse events?	99.0% (101)	98.3% (349)
How many participants had serious adverse events?	66.7% (68)	56.1% (199)
How many participants stopped taking study treatment because of adverse events?	32.4% (33)	10.1% (36)

The most common serious adverse events were:

Part A:

- Worsening of NSCLC
- Inflammation of the large intestine
- Diarrhea
- Difficulty breathing
- Inflammation of the lungs
- Dehydration
- Fatigue
- Fever
- Increased levels of a liver protein called AST

Part B:

- Worsening of NSCLC
- Pneumonia
- New lung tumors
- Inflammation of the large intestine
- Blood clot in the lung

The most common adverse events were:

Part A:

- Diarrhea
- Fatigue
- Nausea
- Difficulty breathing
- Itchiness
- Rash
- Decreased appetite
- Fever
- Anemia
- Increased levels of the digestive protein called amylase
- Cough
- Vomiting

Part B:

- Fatigue
- Difficulty breathing
- Diarrhea
- Decreased appetite
- Constipation
- Nausea
- Worsening of NSCLC
- Cough
- Itchiness
- Anemia
- Joint pain

The study doctors also counted the number of dose-limiting toxicities the participants had during the study. A dose-limiting toxicity is an adverse event that is severe enough to stop the study doctor from increasing the participant's dose of study treatment. A dose-limiting toxicity is also known as a DLT.

- 2.0% of participants had a DLT during **Part A** of the study. This was 2 out of 102 participants.
- None of the participants had DLTs during **Part B** of the study.

Did MEDI4736 with tremelimumab slow the growth of the participants' tumors?

To answer this question, the study doctors took pictures of the participants' tumors using MRI scans. They measured the size of the participants' tumors before they got study treatment and throughout the study. To do this, they used a set of rules called Response Evaluation Criteria in Solid Tumors, also called RECIST.

The researchers looked at these results only for the participants in Part B. This is because the main purpose of Part A was to learn about different doses. In Part B, the researchers compared groups of participants who had received different types of treatment before the study.

The results below include information for Groups 2 and 3 in Part B:

- Group 2: Participants who had earlier treatments that were a different kind of treatment than the study drugs. The results in this section do not include information from 19 participants who got their MEDI4736 and tremelimumab infusions at the same time.
- Group 3: Participants who had earlier treatments that were the same kind of treatment as the study drugs. In this group, there were some participants whose cancer had not got better after earlier treatments. There were also some participants whose cancer had got better but had come back again.

The researchers found that tumor growth slowed in:

- 16.9% of participants in Group 2. This was 36 out of 213 participants.
- 5.3% of the participants in Group 3 whose cancer had not gotten better after earlier treatments. This was 2 out of 38 participants.
- None of the 40 participants in Group 3 whose cancer had gotten better after earlier treatments but had come back again.

What medical problems happened 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 drug. 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 drug. A lot of research is needed to know whether a drug causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for drug.

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?

	Part A (out of 102 participants)	Part B (out of 355 participants)
How many participants had adverse reactions?	84.3% (86)	74.9% (266)
How many participants had serious adverse reactions?	38.2% (39)	16.1% (57)
How many participants stopped taking a study treatment because of adverse reactions?	30.4% (31)	7.6% (27)

What serious adverse reactions happened during this study?

The most common serious adverse reaction was inflammation of the large intestine.

The table below shows the most common serious adverse reactions that happened in more than 1 participant. There were other serious adverse reactions, but these happened in fewer participants. None of the participants died due to serious adverse reactions.

Most common serious adverse reactions

Serious adverse reaction	Part A (out of 102 participants)	Part B (out of 355 participants)
Large intestine inflammation	9.8% (10)	3.7% (13)
Diarrhea	8.8% (9)	2.5% (9)
Inflammation of the lungs	4.9% (5)	2.3% (8)
Dehydration	2.0% (2)	0.3% (1)
Increased levels of a liver protein called AST	2.0% (2)	0.3% (1)
Fatigue	2.0% (2)	0.0% (0)
Nausea	1.0% (1)	0.8% (3)
Kidney damage	1.0% (1)	0.8% (3)
Vomiting	1.0% (1)	0.6% (2)
Low numbers of blood cells that help clotting	1.0% (1)	0.3% (1)
Inflammation of the colon caused by the immune system	1.0% (1)	0.3% (1)
Weakness or lack of energy	1.0% (1)	0.3% (1)
Increased levels of a liver protein called ALT	1.0% (1)	0.3% (1)
Increased levels of a protein called amylase	1.0% (1)	0.3% (1)
Increased levels of a protein called lipase	1.0% (1)	0.3% (1)
Low levels of oxygen in the body	1.0% (1)	0.3% (1)

What adverse reactions happened during this study?

The most common adverse reaction was diarrhea.

The adverse reactions below happened in 10% or more of participants in each part. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

Adverse reaction	Part A (out of 102 participants)	Part B (out of 355 participants)
Diarrhea	36.3% (37)	18.9% (67)
Fatigue	23.5% (24)	20.3% (72)
Itchiness	21.6% (22)	14.6% (52)
Increased levels of a digestive protein called amylase	16.7% (17)	7.3% (26)
Rash	13.7% (14)	9.6% (34)
Nausea	12.7% (13)	11.3% (40)
Increased levels of a digestive enzyme called lipase	12.7% (13)	6.8% (24)
Inflammation of the large intestine	11.8% (12)	4.5% (16)
Decreased appetite	10.8% (11)	11.5% (41)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of MEDI4736 with tremelimumab in participants with NSCLC.

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 MEDI4736 are planned.

Where can I learn more about this study?

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

- www.clinicaltrials.gov. Once you are on this website, type **"NCT02000947"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click "Home and Search", then type **"2015-003715-38"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D4190C00006"** into the search box, and click **"Find a Study**".

Full Study Title: A Phase 1b Open-label Study to Evaluate the Safety and Tolerability of MEDI4736 in Combination With Tremelimumab in Subjects With Advanced Non-small Cell Lung Cancer

AstraZeneca Protocol Number: D4190C00006

EudraCT Number: 2015-003715-38

National Clinical Trials number: NCT02000947

MedImmune sponsored this study and has its headquarters in Gaithersburg, MD, USA.

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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