Clinical Study Results

MedImmune
A member of the AstraZeneca Group

Research Sponsor: MedImmune LLC, a wholly owned subsidiary of AstraZeneca

Drug Studied: MEDI0562, durvalumab, and tremelimumab

Study Title: A study to learn about the safety of MEDI0562 and durvalumab or MEDI0562 and tremelimumab in participants with advanced solid tumors

Thank you

Thank you for taking part in the clinical study for the study drugs MEDI0562, durvalumab, 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 advanced solid tumors. The participants in this study were 31 to 90 years old when they joined.

The study included 58 participants in France, the Netherlands, and the United States.

Why was the research needed?

Researchers are looking for a better way to treat advanced solid tumors. 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.

A solid tumor is a type of cancer that starts in an organ of the body. “Advanced” usually means that the cancer keeps growing even with treatment. The cancer may also be “metastatic”. This means that it has spread to other parts of the body or has grown beyond the organ where it started. In people with advanced solid tumors, certain proteins cause the tumor to grow.

MEDI0562, durvalumab, and tremelimumab were each designed to stop some of these proteins from letting the tumor grow and to cause tumor cells to die.

In this study, the researchers wanted to find out about the safety of MEDI0562 and durvalumab or MEDI0562 and tremelimumab in participants with advanced solid tumors.

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?
- 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 the study drugs help improve the health of people with advanced solid tumors.

What treatments did the participants take?

All of the participants got MEDI0562 and durvalumab or MEDI0562 and tremelimumab through a needle into a vein, also known as an IV infusion.

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

At the beginning of the study, several groups of participants started out taking a low dose of the study treatments. The study doctors looked at the results for these participants. Then, the researchers decided whether to increase the dose of study treatments in the next groups of participants.

The participants kept getting their study treatment until any of the these happened:

- they had a serious medical problem that the study doctors thought might be related to the study treatment
- their tumors grew
- they decided to stop taking study treatment for any other reason

The sponsor planned to include 19 treatment groups in the study, but they ended the study early. So, there were 8 treatment groups.

The doses were measured in milligrams, also known as mg. The doses of each study drug depended on what group the participants were in.

These treatment groups are shown in the table below.

Group	Dose of MEDI0562	Dose of durvalumab	Dose of tremelimumab
Group 1 (3 participants)	• 2.25 mg • Every 2 weeks	• 1500 mg • Every 4 weeks	None
Group 2 (16 participants)	• 7.5 mg • Every 2 weeks	• 1500 mg • Every 4 weeks	None
Group 3 (8 participants)	• 22.5 mg • Every 2 weeks	• 1500 mg • Every 4 weeks	None
Group 4 (5 participants)	• 2.25 mg • Every 2 weeks	None	• 75 mg • Every 4 weeks, up to 4 doses
Group 5 (11 participants)	• 2.25 mg • Every 2 weeks	None	• 225 mg • Every 4 weeks, up to 4 doses
Group 6 (3 participants)	• 7.5 mg • Every 2 weeks	None	• 225 mg • Every 4 weeks, up to 4 doses
Group 7 (7 participants)	• 22.5 mg • Every 2 weeks	None	• 225 mg • Every 4 weeks, up to 4 doses
Group 8 (5 participants)	• 22.5 mg • Every 2 weeks	None	• 75 mg • Every 4 weeks, up to 4 doses

What happened during the study?

The study started in March 2016 and ended in August 2019. The researchers planned to have 2 parts to this study. In Part 2 of the study, a larger number of participants with different tumor types were planned to be included. But, the sponsor ended the study early. This was because they decided not to keep researching MEDI0562 in people with advanced solid tumors. This decision was not because of any safety worries about the study treatments.

Before the participants got study treatment, they visited their study site 1 time. At this visit, the study doctors checked the health of the participants to make sure they could join the study. This part of the study lasted up to 4 weeks. 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 tumors and their brain using CT or MRI scans
- used surgery to take a sample of the tumor called a biopsy for some participants
- took blood and urine samples

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

While the participants got study treatment, they visited their study site at least 11 times during the first 12 weeks. After that, participants visited their study site every 2 weeks for as long as they got study treatment. At each visit the doctors checked the health of the participants.

After the participants got study treatment, they visited their study site 1 time, up to 4 weeks after their last dose. After that, the participants visited their study site every 3 months until the study ended. The study doctors checked the health of the participants at these visits.

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 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 treatments.

Later in this document, there will be a summary of the adverse events that the study doctors thought might be related to the study treatments. This section is a summary of all the adverse events, whether they might be related to the study treatments 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.

	Groups 1 to 3 MEDI0562 and durvalumab (out of 27 participants)	Groups 4 to 8 MEDI0562 and tremelimumab (out of 31 participants)
How many participants had adverse events?	96.3% (26)	100.0% (31)
How many participants had serious adverse events?	51.9% (14)	51.6% (16)
How many participants stopped taking any study treatment because of adverse events?	22.2% (6)	19.4% (6)

The most common serious adverse events are shown in the table below.

Most common serious adverse events in the study
Serious adverse event
Water on the lungs
Inflammation of large bowel
Tumor pain
Stomach pain
Constipation
Blockage in the small intestine
Reaction related to the IV infusion

The most common adverse events are shown in the table below.

Most common adverse events in the study
Adverse event
Tiredness
Nausea
Fever
Itchy skin
Diarrhea
Vomiting
Decreased appetite
Constipation
Chills
Stomach pain

The study doctors also counted the number of dose-limiting toxicities 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 known as a DLT.

Counting the number of DLTs helps researchers determine the safety of different doses of a treatment. This helps them find the highest dose that the participants can take.

The study doctors were not able to measure DLTs for 7 of the participants. So, the DLT information collected was for 51 participants.

In this study, 9.8% of the participants had a DLT. This was 5 out of 51 participants.

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 MEDI0562. 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 drugs. 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 MEDI0562.

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?

	Groups 1 to 3 MEDI0562 and durvalumab (out of 27 participants)	Groups 4 to 8 MEDI0562 and tremelimumab (out of 31 participants)
How many participants had adverse reactions?	74.1% (20)	77.4% (24)
How many participants had serious adverse reactions?	11.1% (3)	16.1% (5)
How many participants stopped taking study treatment because of adverse reactions?	22.2% (6)	19.4% (6)

What serious adverse reactions happened during this study?

The most common serious adverse reaction that the study doctors thought was related to MEDI0562 and that happened in 2 or more participants was a reaction related to the IV infusion.

- 3.4% of participants who got MEDI0562 had a serious adverse reaction related to the IV infusion. This was 2 out of 58 participants.

There were other serious adverse reactions but these happened in fewer participants. There was 1 participant who died from a serious adverse reaction of kidney failure. The study doctors thought that this death might be related to MEDI0562 and durvalumab.

What adverse reactions happened during this study?

The most common adverse reaction that the study doctors thought might be related to MEDI0562 was tiredness.

The table below shows the most common adverse reactions that the study doctors thought might be related to MEDI0562 and that happened in 10% or more of participants. There were other adverse reactions that the study doctors thought might be related to MEDI0562, but these happened in fewer participants.

Most common adverse reactions during the study

Adverse reaction to MEDI0562	Groups 1 to 3 MEDI0562 and durvalumab (out of 27 participants)	Groups 4 to 8 MEDI0562 and tremelimumab (out of 31 participants)
Tiredness	40.7% (11)	12.9% (4)
Fever	18.5% (5)	22.6% (7)
Itchy skin	7.4% (2)	32.3% (10)
Diarrhea	7.4% (2)	25.8% (8)
Nausea	14.8% (4)	12.9% (4)
Chills	14.8% (4)	12.9% (4)
Reaction to IV infusion	7.4% (2)	19.4% (6)
Rash	7.4% (2)	12.9% (4)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of MEDI0562 and durvalumab or MEDI0562 and tremelimumab for participants with advanced solid tumors.

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 MEDI0562, durvalumab, and tremelimumab 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 more information about the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02705482"** into the **"Other Terms"** search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D6060C00002"** into the search box, and click **"Find a Study"**.

Full study title: A Phase 1 Multicenter, Open-label, Study to Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, Immunogenicity, and Antitumor Activity of MEDI0562 in Combination With Immune Therapeutic Agents in Adult Subjects With Advanced Solid Tumors

MedImmune Protocol Number: D6060C00002

National Clinical Trials number: NCT02705482

MedImmune LLC, a wholly owned subsidiary of AstraZeneca, sponsored this study and has its headquarters in Gaithersburg, Maryland, USA

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.

CISCRP
One Liberty Square, Suite 1100
Boston, MA 02109

1-877-MED-HERO

www.ciscrp.org