AstraZeneca

Clinical Study Results

Research Sponsor: MedImmune LLC

Treatments Studied: MEDI5083 and durvalumab

Study Purpose: This study was done to learn about the safety of MEDI5083 and durvalumab in participants with advanced solid tumors

Protocol Number: D6840C00001

Thank you

Thank you for taking part in the clinical study for the study treatments MEDI5083 and durvalumab.

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 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 this study?

The researchers asked for the help of men and women with advanced solid tumors. The participants in this study were 21 to 78 years old when they joined.

The study included 38 participants in Australia and the United States.

Why was the research needed?

Researchers are looking for a better way to treat advanced solid tumors. Before a treatment 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 some cells. The extra cells can form tumors. 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.

Normally, the immune system fights infections or anything it does not recognize, and can help stop tumors from growing or surviving. But in some people with solid tumors, proteins on the tumor cells can interact with certain proteins on the immune cells. This stops the immune cells from attacking the tumor cells.

The study treatments, MEDI5083 and durvalumab, were designed to stop the tumor cells from interacting with some of these immune cell proteins. This would help the immune cells stop the tumor from growing.

In this study, the researchers wanted to find out about the safety of MEDI5083 and durvalumab in participants with advanced solid tumors. This was the first time MEDI5083 was studied in people.

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 MEDI5083 and durvalumab help improve the health of people with advanced solid tumors.

What treatments did the participants get?

This study happened in 2 parts. The researchers planned for there to be 3 parts, but they stopped the study early because the participants were having medical problems.

In **Part 1,** all of the participants got MEDI5083. After getting up to 4 doses of MEDI5083, some of the participants started getting durvalumab. The results of Part 1 were used to decide which doses to give in Part 2.

In **Part 2,** all of the participants got both MEDI5083 and durvalumab at the same time. After receiving 4 doses of each, the participants continued to receive durvalumab alone.

The participants got MEDI5083 through a needle under the skin, also known as a "subcutaneous injection". They got durvalumab 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.

The chart below shows the treatments the researchers planned to study.

	Part 1	Part 2
	• 29 participants	• 9 participants
	All the participants got: • 1 of 4 different doses of MEDI5083 as an injection • Then, some participants also got durvalumab as an IV infusion	All the participants got: • 1 of 2 different doses of MEDI5083 as an injection • And durvalumab as an IV infusion
	For 6 weeks, the participants got: • MEDI5083 every 2 weeks • Then, there was a 4-week period without treatment to allow the drug to "wash-out" of the participants' bodies • Then, some of the participants started getting durvalumab every 4 weeks	For 6 weeks, the participants got: • MEDI5083 every 2 weeks • durvalumab every 4 weeks Then, the participants continued getting durvalumab every 4 weeks

What happened during this study?

The study started in March 2017 and ended in June 2020.

Before the participants got study treatment, they visited their study site 1 time. This part of the study lasted for 4 weeks. At this visit, the study doctors made sure the participants could join the study. They also:

- did a physical exam and asked about the participants' medications and any medical problems they were having
- did an eye exam
- checked the participants' heart health using an electrocardiogram, also known as an "ECG"
- took blood and urine samples
- took pictures of the participants' tumors using CT or MRI scans
- if needed, used surgery to take a sample of the participants' tumors, also known as a "biopsy"
- asked the participants about how well they were able to carry out their daily activities

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

While the participants got study treatment, they visited their study site:

- once every 2 weeks for the first 8 weeks
- then, once every 4 weeks until their cancer got worse or the study ended

At these visits, the study doctors gave the participants their study treatment.

After the participants got study treatment, they visited their study site once every month for 5 months. At these visits, the study doctors checked the health of the participants.

What were the results of this 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.

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

To answer this question, the study doctors did tests and measurements throughout the study.

The doctors did physical exams and tested the participants' blood and urine samples to check their overall health. They also used 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 meaningful.

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.

	Part 1 (out of 29 participants)	Part 2 (out of 9 participants)
How many participants had adverse events?	100.0% (29)	100.0% (9)
How many participants had serious adverse events?	41.4% (12)	44.4% (4)
How many participants stopped getting MEDI5083 due to adverse events?	24.1% (7)	22.2% (2)
How many participants stopped getting durvalumab due to adverse events?	10.3% (3)	11.1% (1)

The most common serious adverse event was sudden kidney injury.

The most common adverse events were:

- injection site reaction
- fatigue
- low appetite
- constipation

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 dose of study treatment in the next group of participants. A dose limiting toxicity is also known as a "DLT".

In Part 1, 23 out of 29 participants could be checked for DLTs. This is because only 23 participants got MEDI5083 as planned and completed the safety follow-up. Of these participants, 8.7% had a DLT. This was 2 out of 23 participants.

None of the participants in Part 2 had a DLT.

What medical problems happened during this 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 MEDI5083 and durvalumab.

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.

This study was stopped early because of some of the adverse reactions that happened during the study.

Did any adverse reactions happen during this study?

	Part 1 (out of 29 participants)	**Part 2** (out of 9 participants)
How many participants had adverse reactions related to **MEDI5083**?	96.6% (28)	100.0% (9)
How many participants had adverse reactions related to **durvalumab**?	27.6% (8)	44.4% (4)
How many participants had serious adverse reactions related to **MEDI5083**?	10.3% (3)	11.1% (1)
How many participants had serious adverse reactions related to **durvalumab**?	6.9% (2)	0.0% (0)
How many participants stopped getting **MEDI5083** due to adverse reactions?	13.8% (4)	22.2% (2)
How many participants stopped getting **durvalumab** due to adverse reactions?	3.4% (1)	11.1% (1)

What serious adverse reactions happened during this study?

The tables below show the serious adverse reactions that happened during the study.

Serious adverse reactions related to MEDI5083

	Part 1 (out of 29 participants)	Part 2 (out of 9 participants)
Sudden kidney injury	3.4% (1)	0.0% (0)
Fever	3.4% (1)	0.0% (0)
Injection site reaction	3.4% (1)	0.0% (0)
Unexplained death	0.0% (0)	11.1% (1)

Serious adverse reactions related to durvalumab

There were 11 participants in Part 1 who did not get any durvalumab. So, the results below are for 18 out of 29 participants in Part 1 and all 9 participants in Part 2.

	Part 1 (out of 18 participants)	Part 2 (out of 9 participants)
Sudden kidney injury	5.6% (1)	0.0% (0)
Diarrhea	5.6% (1)	0.0% (0)

In Part 1, none of the participants died because of serious adverse reactions.

In Part 2, 11.1% of the participants died because of serious adverse reactions related to **MEDI5083**. This was 1 out of 9 participants. The serious adverse reaction was unexplained death. None of the participants in Part 2 died because of serious adverse reactions related to **durvalumab**.

What adverse reactions happened during this study?

The most common adverse reaction was an injection site reaction.

The tables below show the adverse reactions that happened in more than 1 participant during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions related to MEDI5083

	Part 1 (out of 29 participants)	Part 2 (out of 9 participants)
Injection site reaction	86.2% (25)	100.0% (9)
Fatigue	13.8% (4)	11.1% (1)
Fever	10.3% (3)	11.1% (1)
Injection site pain	10.3% (3)	0.0% (0)
Injection site redness	6.9% (2)	0.0% (0)

Most common adverse reactions related to durvalumab

Only 18 of the 29 participants in Part 1 received any durvalumab. So, the results below are for those 18 participants.

	Part 1 (out of 18 participants)	Part 2 (out of 9 participants)
Fatigue	11.1% (2)	22.2% (2)
Diarrhea	11.1% (2)	11.1% (1)
Low levels of thyroid hormones	11.1% (2)	0.0% (0)
Joint pain	11.1% (2)	0.0% (0)
Itchiness	11.1% (2)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of MEDI5083 and durvalumab in 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 MEDI5083 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 **"NCT03089645"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D6840C00001"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase 1 First Time in Human Study to Evaluate the Safety, Pharmacokinetics and Immunogenicity of MEDI5083 Alone and in Combination with Durvalumab in Selected Advanced Solid Tumors

MedImmune LLC Protocol Number: D6840C00001

National Clinical Trials Number: NCT03089645

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

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