# Clinical Study Results

MedImmune
A member of the AstraZeneca Group

**Research Sponsor:** MedImmune LLC

**Treatment Studied:** MEDI9197

**Study Title:** A study to learn how MEDI9197 worked and how safe it was in people with solid tumors or cutaneous T-cell lymphoma

## *Thank you*

Thank you for taking part in the clinical study for MEDI9197, also called telratolimod. You and all the other participants helped the researchers learn about using MEDI9197 to help people with solid tumors or cutaneous T-cell lymphoma, also called CTCL.

MedImmune sponsored this study and thinks it is important to share the results with the participants and the public. MedImmune reviewed the results of the study when it ended. An independent non-profit organization called CISCRP helped prepare this summary of the study results.

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

## What is happening with the study now?

The study included 53 participants in Canada, France, and the United States

Each participant was in the study for up to 12 months. The entire study took place for 36 months before it was stopped early. The study researchers found that the participants were having a lot of medical problems and the study results were not as expected. So, the study doctors and the researchers agreed to end the study early. The study started in November 2015 and ended in October 2018.

The sponsor reviewed the data collected when the study ended and created a report of the results. This is a summary of that report.

# Why was the research needed?

Researchers are looking for a better way to treat people who have different types of cancer. 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.

In this study, the researchers wanted to learn more about the safety of different doses of MEDI9197 in participants with advanced cancer that was no longer responding to standard treatment. The cancer could be either solid tumor cancers or a type of cancer that affects the skin called cutaneous T-cell lymphoma, also called CTCL. They also wanted to learn about the safety of MEDI9197 when it was taken together with other cancer treatments. The researchers also wanted to know if the participants had any medical problems during the trial.

When cells become abnormal, they can grow out of control and form tumors. This is also called cancer. MEDI9197 is designed to work by stimulating the immune system to identify and kill the abnormal tumor cells. There are other studies with similar drugs to MEDI9197, that suggest that advanced cancers may respond well to this type of treatment.

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

- Did the participants' safety results change after taking MEDI9197?
- 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 that help find out if MEDI9197 improves the health of people with advanced cancer that was no longer responding to standard treatment.

The researchers asked for the help of men and women with advanced cancer that is no longer responding to standard treatment. Everyone in the study was 25 to 85 years old when they joined. The participants had previously received treatment that did not work or was no longer working when they enrolled in this study.

# What kind of study was this?

There were 3 parts to this study. The participants in Parts 1 and 3 had advanced cancer that was no longer responding to standard treatment. The participant in Part 2 had CTCL. Each part was "open-label". This means the researchers and the participant knew which study treatment the participant was getting.

In each part, a group of participants started out getting a low, fixed dose of MEDI9197. The study doctors looked at the safety results for these participants. Depending on the safety results and general health of the participants, the researchers decided whether to increase or decrease the dose in the next group of participants.

There were 3 study treatments that could be given in this study: MEDI9197, radiation therapy, and durvalumab. Durvalumab is a cancer treatment that is approved to use for some types of cancer. Researchers are also studying how to use it alone, and with other treatments, for other types of cancer. Different combinations of treatments and doses were given to the participants.

The doses of MEDI9197 were given through a needle into the tumor. This is also called an intratumoral injection. The doses of durvalumab were given through a needle into a vein. This is also called an intravenous infusion or an IV infusion. MEDI9197 and durvalumab doses were measured in milligrams, also called mg.

Some participants had tumors that were easy for doctors to access called surface tumors. Others had tumors that were not easy for doctors to access called deep tumors.

The tables below show the different treatment groups in each part of the study. The researchers expected to include other groups with different doses in the study, but no participants joined these groups.

**Part 1**

| Group number | Treatment given |
|---|---|
| 1 (7 participants with surface tumors) | • 0.037 mg MEDI9197 every 28 days |
| 2 (5 participants with surface tumors) | • 0.037 mg MEDI9197 every 28 days<br>• Radiation therapy every 28 days |
| 3 (10 participants with surface tumors) | • 0.012 mg MEDI9197 every 28 days |
| 4 (4 participants with deep tumors) | • 0.012 mg MEDI9197 every 28 days |
| 5 (1 participant with surface tumors) | • 0.055 mg MEDI9197 every 28 days |
| 6 (8 participants with surface tumors) | • 0.005 mg MEDI9197 every 28 days |

| Part 2 | |
|---|---|
| **Group number** | **Treatment given** |
| 7 (1 participant with surface tumors) | • 0.005 mg MEDI9197 every 28 days |

| Part 3 | |
|---|---|
| **Group number** | **Treatment given** |
| 8 (3 participants with surface tumors) | • 0.012 mg MEDI9197 every 28 days<br>• 1500 mg durvalumab |
| 9 (6 participants with deep tumors) | • 0.012 mg MEDI9197 every 28 days<br>• 1500 mg durvalumab |
| 10 (2 participants with deep tumors) | • 0.012 mg MEDI9197 every 28 days<br>• 1500 mg durvalumab<br>• Radiation therapy |
| 11 (6 participants with surface tumors) | • 0.005 mg of MEDI9197 every 28 days<br>• 1500 mg durvalumab |

# What happened during the study?

**Before the participants received study treatment,** they visited their study site one time. At this visit, the study doctors checked their overall health and medical history to make sure they could join the study. The study doctors:

- took blood and urine samples
- checked participants' heart health using an electrocardiogram, also called an ECG
- used a needle to take a sample of the tumor tissue, also called a tumor biopsy
- did a physical exam and checked vital signs
- did imaging scans, including CT and MRI

**During the study,** the participants visited their study site at least 4 times. They received study treatment based on what group they were in.

The study doctors checked the participants' overall health, heart health, and vital signs and took blood and urine samples throughout the study. They did this again after the last dose.

At the visit during week 4 of the study, the study doctors took a tumor biopsy.

**After receiving the last dose,** the participants visited their study site at least another 3 times for at least 2 months.

At these visits, the study doctors checked the participants' health and measured the size of their tumors using a CT scan of the chest.

For the participants in Part 1, these visits continued every month until the participant started a different treatment, their cancer got worse, or they left the study. For the participant in Part 2, there was one more visit that happened after 6 months. For the participants in Part 3, these visits continued every 12 weeks until the participant started a different treatment, their cancer got worse, or they left the study.

# 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 a full report of the study results.

### Did the participants' safety results change after taking MEDI9197?

To help answer this question, the researchers compared the results of the tests and measurements that the study doctors took before and after the participants received study treatment. They found that there were no significant changes in the results of the participants' blood and urine tests or ECGs. They found that there was not enough information about the participants' changes in vital signs to make a conclusion.

The researchers also collected information about the "adverse events" 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 treatment. This section is a summary of all the adverse events, whether they might be related to the trial 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 trial. A lot of research is needed to know whether a treatment causes an adverse event.

The table below shows a summary of the adverse events that happened during the study.

| | Part 1 (out of 35 participants) | Part 2 (out of 1 participant) | Part 3 (out of 17 participants) | Overall (out of 53 participants) |
|---|---|---|---|---|
| How many participants in this study had adverse events? | 97.1% (34) | 100% (1) | 100% (17) | 98.1% (52) |
| How many participants in this study had serious adverse events? | 54.3% (19) | 0% (0) | 35.3% (6) | 47.2% (25) |
| How many participants left this study because of adverse events? | 2.9% (1) | 0% (0) | 0% (0) | 1.9% (1) |

The most common serious adverse events were a high fever and severe inflammation because of an infection, also called cytokine release syndrome.

The most common adverse events were high fever and fatigue.

## Dose-limiting toxicities

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

There were 3 participants who had a DLT during this study:

- 1 participant who received 0.037 mg MEDI9197 had a DLT. This happened in Group 1 in Part 1 of the study. This DLT was due to high fever and severe inflammation because of an infection called cytokine release syndrome.
- 1 participant who received 0.055 mg MEDI9197 had a DLT. This happened in Group 5 in Part 1 of the study. This DLT was due to cytokine release syndrome, which resulted in severe inflammation because of an infection. Because of this DLT, the researchers decided not to give this dose to any more participants in Part 1.
- 1 participant who received 0.012 mg MEDI9197 and 1500 mg of durvalumab had a DLT. This happened in Group 9 in Part 3 of the study. This DLT was due to heavy bleeding and caused the body to shut down due to a lack of oxygen. This participant died as a result of this DLT.

### Deaths

Overall, 39.6% of participants died during the study due to their cancer getting worse. This was 21 out of 53 participants.

In Part 1, 25.7% of participants died. This was 9 out of 35 participants. These deaths were due to the participants' cancer getting worse and not thought to be related to MEDI9197.

In Part 2, none of the participants died.

In Part 3, 70.6% of participants died. This was 12 out of 17 participants.

- There was 1 death that the study doctors thought was related to MEDI9197. This was the participant in Group 9 who had a DLT.
- There were 11 deaths that were due to the participants' cancer getting worse.

## 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 drug. These medical problems are called "adverse reactions". An adverse reaction is considered "serious" when it is life-threatening, cause 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.

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.

The study doctors, in agreement with the study researchers, stopped the study early because MEDI9197 did not help the participants and was causing a lot of adverse reactions. The researchers only included in their final report the results that would be most important for people to understand more about the study drug. So, the results below do not include information from the 5 groups who did not have participants included in the study.

## Did any adverse reactions happen in this study?

The adverse reactions that the participant had during Part 2 of the study are not in this summary. Because there was only 1 participant in Part 2, leaving this information out helps protect their identity.

| | Part 1 (out of 35 participants) | Part 3 (out of 17 participants) | Overall (out of 52 participants) |
|---|---|---|---|
| How many participants had adverse reactions in this study? | 80.0% (28) | 94.1% (16) | 84.6% (44) |
| How many participants had serious adverse reactions in this study? | 28.6% (10) | 17.6% (3) | 25.0% (13) |
| How many participants left the study because of adverse reactions? | 2.9% (1) | 0% (0) | 1.9% (1) |

## What serious adverse reactions happened during this study?

Overall, the most common serious adverse reaction was high fever. This happened in 15.4% of participants. This was 8 out of 52 participants.

There were 1.9% of participants who died during the study, which the study doctors thought might be related to the treatment. This was 1 out of 53 participants. This was the participant from Group 9 in Part 3 who had a DLT.

### Part 1

There were 28.6% participants who had at least 1 serious adverse reaction. This was 10 out of 35 participants.

- 22.9% of participants had a high fever. This was 8 out of 35 participants. This happened in Groups 1, 2, 3, and 6.
- 2.9% of participants had a fast heart rate. This was 1 out of 35 participants. This happened in Group 1.
- 2.9% of participants had vomiting. This was 1 out of 35 participants. This happened in Group 1.
- 2.9% of participants had chills. This was 1 out of 35 participants. This happened in Group 6.
- 2.9% of participants had a flu-like illness. This was 1 out of 35 participants. This happened in Group 6.
- 2.9% of participants had a nodule. This was 1 out of 35 participants. This happened in Group 6.
- 8.6% of participants had a strong inflammatory reaction in the whole body due to an infection or disease. This was 3 out of 35 participants. This happened in Groups 1, 2, and 5.
- 2.9% of participants had a seizure. This was 1 out of 35 participants. This happened in Group 1.
- 2.9% of participants had difficulty breathing. This was 1 out of 35 participants. This happened in Group 6.

### Part 2

The serious adverse reactions that the participant had during Part 2 of the study are not in this summary. Because there was only 1 participant in Part 2, leaving this information out helps protect their identity.

### Part 3

There were 17.6% participants who had at least 1 serious adverse reaction. This was 3 out of 17 participants.

- 11.8% of participants had a flu-like illness. This was 2 out of 17 participants. This happened in Group 9.
- 5.9% of participants had a decreased amount of oxygen in the blood, meaning organs cannot function properly. This was 1 out of 17 participants. This was the participant in Group 9 who had a DLT.

## What adverse reactions happened during this study?

Overall, the most common adverse reaction was a high fever. This happened in 36.5% of participants. This was 19 out of 52 participants.

### Part 1

There were 80.0% participants who had at least 1 adverse reaction during the study. This was 28 out of 35 participants. The most common adverse reactions that happened in at least 20% of groups are listed below.

- 54.3% of participants had a high temperature. This was 19 out of 35 participants. This happened in Groups 1, 2, 3, 4, 5, and 6.
- 28.6% of participants had fatigue, also called extreme tiredness. This was 10 out of 35 participants. This happened in Groups 1, 2, 3, 4, and 6.
- 20.0% of participants had chills. This was 7 out of 35 participants. This happened in Groups 1, 3, 4, 5, and 6.
- 20.0% of participants had a low number of lymphocytes, which are white blood cells and are needed for the immune system to recover from illnesses. This was 7 out of 35 participants. This happened in Groups 1, 3, and 6.

### Part 2

The adverse reactions that the participant had during Part 2 of the study are not in this summary. Because there was only 1 participant in Part 2, leaving this information out helps protect their identity.

### Part 3

There were 94.1% participants who had at least 1 adverse reaction that the study doctors thought might be related to the study drug. This was 16 out of 17 participants. The most common adverse reactions that occurred in at least 20% of groups are listed below.

- 58.8% of participants had a high temperature. This was 10 out of 17 participants. This happened in Groups 9, 10, and 11.
- 35.3% of participants had fatigue. This was 6 out of 17 participants. This happened in Groups 8, 9, and 11.
- 29.4% of participants had nausea. This was 5 out of 17 participants. This happened in Groups 9, 10, and 11.
- 23.5% of participants had a headache. This was 4 out of 17 participants. This happened in Groups 8, 9, and 11.

## How has this study helped patients and researchers?

This study helped researchers learn about the safety of MEDI9197 and if the drug could help participants with advanced cancer that was no longer responding to standard treatment.

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 MEDI9197 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 **"NCT02556463"** into the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D6410C00001"** into the search box, and click **"Find a Study"**.

**Full study title:** A Phase 1, First-Time-in-Human Study of MEDI9197, a TLR 7/8 Agonist, Administered Intratumorally as a Single Agent in Subjects with Solid Tumors or CTCL and in Combination with Durvalumab and/or Palliative Radiation in Subjects with Solid Tumors

**National Clinical Trials number:** NCT02556463

**AstraZeneca Protocol Number:** D6410C0001

**MedImmune Ltd.,** an AstraZeneca company, sponsored this study and has its headquarters in Mölndal, Sweden.

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