Clinical Study Results

Research Sponsor: AstraZeneca

Drugs Studied: Selumetinib and durvalumab

Study Title: A study to learn about the safety of selumetinib given with durvalumab in patients with advanced solid tumors

Thank you

Thank you to the participants who took part in the clinical study that studied the drugs selumetinib and durvalumab, and thank you to the families of the participants. AstraZeneca sponsored this study and thinks 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 have questions about the results, please speak with the doctor or staff at your study site.

What is happening with the study now?

The study started in December 2015 and ended in July 2018.

There were 2 parts in the study, Part 1 and Part 2. The participants in Part 1 had advanced solid tumors of different types of cancer and were in the study for up to about 2 years. The participants in Part 2 had advanced cancer of the colon and were in the study for up to about 1 year. The entire study took about 2 and a half years to finish.

The researchers planned for this study to have 3 parts, but they found that the participants' cancer was not responding to the study drugs as expected. The researchers ended the study after Part 2 and did not start Part 3.

Part 1 of the study included 28 participants in the United States. Part 2 included 30 participants in the United States.

AstraZeneca 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 patients who have advanced cancer. Before a drug or drug combination can be approved for patients to receive, researchers do clinical studies to find out how safe the drug or drug combination is and if the drug or drug combination helps patients.

Cancer is a disease that happens when the body cannot control the growth of cells. These extra cells can come together to form solid tumors. Solid tumors can start in any part of the body. “Advanced” means that the tumor cannot be completely or safely removed by surgery. In this study, the researchers wanted to learn about the safety of selumetinib and durvalumab when given together to patients who have advanced solid tumors.

There are treatments for advanced cancer. But these treatments may not stop cancer cells from growing or spreading. They may also cause other medical problems. This is because these treatments can cause side effects by negatively affecting normal cells and tissue in the body instead of cancer cells.

One way that cancer can occur is when a protein in the body does not work normally. When it works correctly, this protein creates new healthy cells. But when the protein does not work correctly, it can create abnormal cells. This can lead to cancer. Researchers think that one of the study drugs, selumetinib, may be able to block this protein from creating new cells.

The second study drug, durvalumab, is an immunotherapy that is currently used in several countries to treat certain types of bladder and lung cancers. An immunotherapy uses the body’s own immune system to help attack cancer cells without negatively affecting normal cells or tissues. Durvalumab was previously called MEDI4736.

In this study, the researchers wanted to find out if selumetinib given with durvalumab would help stop cancer cells from growing or spreading without causing medical problems.

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

- Did the participants have significant changes in their health tests and measurements 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 that help find out if selumetinib given with durvalumab improves the health of people who have advanced solid tumors.

The researchers asked for the help of men and women who have advanced solid tumors. The men and women had received other cancer treatments before the study, but those treatments had not helped their cancer. The participants in this study were 30 to 79 years old when they joined.

What kind of study was this?

This study was designed to have 3 parts. Part 1 was designed to learn if the different study doses of selumetinib were safe to take with durvalumab. This would then help the researchers choose the highest dose that would be safe to use for Part 2. The researchers would only begin Part 2 if a dose from Part 1 was shown to be safe.

Part 1 was the “dose escalation” part of the study. This means that the first group of participants started out by getting a low dose of selumetinib. The study doctors carefully looked at the results for these participants. Then, the researchers decided whether to increase the dose in the next group of participants in Part 1. Researchers use dose escalation to learn about the safety of a specific dose before participants are given a higher dose.

Part 2 was designed to learn more about selumetinib when taken with durvalumab, and if the dose chosen from Part 1 was able to help the participants’ cancer without causing medical problems. If this dose was shown to be effective at helping participants’ cancer, the researchers would begin Part 3.

Part 3 was designed to learn more about the Part 2 study dose. Part 3 was designed to include this dose, as well as another cancer drug called tremelimumab. But in Part 2, the study dose was not effective at helping the participants’ cancer. So, the researchers stopped the study after Part 2.

Both Part 1 and Part 2 were “open-label”. This means the researchers and the participant knew which treatment the participant was getting. Each participant was in only 1 part of the study.

In this study, the treatments given were selumetinib and durvalumab. Selumetinib was taken as a pill by mouth. Durvalumab was given through a needle into a vein. This is known as intravenous treatment, also called IV treatment. The selumetinib and durvalumab doses were measured in milligrams, also called mg.

What happened during the study?

Before getting any study treatment, the participants in Part 1 and in Part 2 visited their study site 2 times over the course of about 6 weeks. At these visits, the study doctors checked to make sure the participants could join the study. The study doctors performed several tests and measurements. They:

- did a physical examination
- took blood and urine samples
- checked the participants’ heart health using an electrocardiogram, also called an ECG
- measured the size of the participants’ tumors using computed tomography scans, also called CT scans, and magnetic resonance imaging scans, also called MRI scans
- took tissue samples from the participants’ tumors
- asked the participants about their medical history, how they were feeling, and what medicines they were taking

During both parts of the study, treatments were given during 4-week periods called “cycles”. The participants could take part in as many cycles as they wanted unless their cancer got worse. If their cancer got worse, the participants stopped the treatment cycles. If the study treatment was helping the participants’ cancer at the end of the study, the participants could choose to continue treatment.

Throughout both Part 1 and Part 2, the study doctors continued checking the participants’ tumors and overall health and asking the participants how they were feeling.

Part 1

The participants visited their study site 2 times during the first week of Part 1. Then, they visited their study site up to 5 times during each cycle. Each cycle lasted 4 weeks.

In Part 1, there were 28 participants. There were 4 treatment groups. The chart below shows the treatments for each group.

Participants	First week	After the first week
Group 1 (6 participants)	• 50 mg of selumetinib each day • did not get any durvalumab during this time	• 1,500 mg of durvalumab 1 time each cycle • 50 mg of selumetinib each day during the second and fourth week of each cycle
Group 2 (10 participants)	• 75 mg of selumetinib each day • did not get any durvalumab during this time	• 1,500 mg of durvalumab 1 time each cycle • 75 mg of selumetinib each day during the second and fourth week of each cycle
Group 3 (6 participants)	• 100 mg of selumetinib each day • did not get any durvalumab during this time	• 1,500 mg of durvalumab 1 time each cycle • 100 mg of selumetinib each day during second and fourth week of each cycle
Group 4 (6 participants)	• 125 mg of selumetinib each day • did not get any durvalumab during this time	• 1,500 mg of durvalumab 1 time each cycle • 125 mg of selumetinib each day during the second and fourth week of each cycle

Part 2

The participants visited their study site 2 times during the first week of Part 2. Then, they visited their study site up to 5 times during each cycle. Each cycle lasted 4 weeks.

In Part 2, there were 30 participants. There was 1 treatment group. The chart below shows the treatments in Part 2.

First week	After the first week
All participants: • took 100 mg of selumetinib each day • did not get any durvalumab during this time	All participants: • took 100 mg of selumetinib each day during the second and fourth week of each cycle • got 1,500 mg of durvalumab 1 time each cycle

After getting their last dose, the participants in Part 1 and Part 2 visited their study site up to 2 times over the course of about 3 months. At these visits, the study doctors checked the participants' tumors and overall health, and asked them how they were feeling.

What were the results of the study?

This is a summary of the main results from this study overall. Each participant's results may have been 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.

Did the participants have significant changes in their health tests and measurements during the study?

No. To answer this question, the researchers compared the results of the tests and measurements that were done before the study to the results throughout the study.

The researchers studied the results from the below tests and measurements:

- physical examinations
- blood and urine samples
- heart health, by using ECGs

Overall, there were some changes in the results of these tests and measurements. But these changes were too small for the researchers to consider the participants' overall health to have changed after taking the study treatments together.

What medical problems did the participants have during the study?

To answer this question, the researchers recorded any medical problems the participants had during the study. These medical problems are called “adverse events”. An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or requires hospital care. Adverse events may or may not be caused by the study drugs.

The table below shows how many participants had adverse events during the study.

Adverse events during the study

	Part 1 (out of 28 participants)				
	Group 1 (out of 6 participants)	Group 2 (out of 10 participants)	Group 3 (out of 6 participants)	Group 4 (out of 6 participants)	Part 2 (out of 30 participants)
How many participants had adverse events during the study?	100.0% (6)	100.0% (10)	100.0% (6)	100.0% (6)	100.0% (30)
How many participants had serious adverse events during the study?	50.0% (3)	20.0% (2)	33.3% (2)	33.3% (2)	33.3% (10)
How many participants stopped selumetinib treatment because of adverse events?	33.3% (2)	10.0% (1)	16.7% (1)	0.0% (0)	3.3% (1)
How many participants stopped durvalumab treatment because of adverse events?	33.3% (2)	10.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)

Serious adverse events

There were 32.8% of participants who had serious adverse events during the study. This was 19 out of 58 participants.

None of the participants died from serious adverse events during the study.

The table below shows the serious adverse events that happened in at least 2 participants during the study. There were other serious adverse events that happened during the study, but those happened in fewer participants.

Most common serious adverse events during the study

	Part 1 (out of 28 participants)				
Serious adverse event	Group 1 (out of 6 participants)	Group 2 (out of 10 participants)	Group 3 (out of 6 participants)	Group 4 (out of 6 participants)	Part 2 (out of 30 participants)
Fever	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)	6.7% (2)
Stomach pain	16.7% (1)	10.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Diarrhea	16.7% (1)	0.0% (0)	16.7% (1)	0.0% (0)	0.0% (0)
Vomiting	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)	3.3% (1)

Most common adverse events

The most common adverse event during the study was diarrhea.

The table below shows the adverse events that happened in at least 10 participants during the study. There were other adverse events that happened during the study, but those happened in fewer participants.

Most common adverse events during the study

Adverse event	Part 1 (out of 28 participants)				Part 2 (out of 30 participants)
	Group 1 (out of 6 participants)	Group 2 (out of 10 participants)	Group 3 (out of 6 participants)	Group 4 (out of 6 participants)	
Diarrhea	66.7% (4)	30.0% (3)	50.0% (3)	83.3% (5)	40.0% (12)
Tiredness	50.0% (3)	40.0% (4)	50.0% (3)	0.0% (0)	53.3% (16)
Nausea	50.0% (3)	20.0% (2)	33.3% (2)	50.0% (3)	46.7% (14)
Constipation	33.3% (2)	30.0% (3)	33.3% (2)	16.7% (1)	43.3% (13)
Skin reaction causing acne	0.0% (0)	0.0% (0)	16.7% (1)	16.7% (1)	56.7% (17)
Increase in blood pressure	0.0% (0)	50.0% (5)	66.7% (4)	16.7% (1)	23.3% (7)
Vomiting	33.3% (2)	0.0% (0)	33.3% (2)	50.0% (3)	33.3% (10)
Decrease in amount of blood in the body	33.3% (2)	30.0% (3)	50.0% (3)	33.3% (2)	16.7% (5)
Decrease in appetite	16.7% (1)	30.0% (3)	16.7% (1)	33.3% (2)	26.7% (8)
Stomach pain	33.3% (2)	30.0% (3)	0.0% (0)	33.3% (2)	23.3% (7)
Skin rash	16.7% (1)	50.0% (5)	33.3% (2)	16.7% (1)	16.7% (5)
Increase in amount of aspartate aminotransferase in the body (a sign of liver damage)	50.0% (3)	20.0% (2)	16.7% (1)	0.0% (0)	23.3% (7)
Fever	16.7% (1)	0.0% (0)	50.0% (3)	33.3% (2)	23.3% (7)
Cough	16.7% (1)	10.0% (1)	0.0% (0)	33.3% (2)	26.7% (8)
Increase in amount of alanine aminotransferase in the body (a sign of liver damage)	33.3% (2)	30.0% (3)	16.7% (1)	0.0% (0)	16.7% (5)
Headache	33.3% (2)	10.0% (1)	16.7% (1)	16.7% (1)	16.7% (5)

Adverse reactions

This section is a summary of the adverse events the participants had during the study that the study doctors thought might be related to the study drugs. These adverse events 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.

The adverse reactions shown in the sections below are also included in the adverse events sections above. The websites listed at the end of this summary may have other information about the adverse events and adverse reactions that happened during this study.

The table below shows how many participants had adverse reactions during the study.

Adverse reactions during the study

	Part 1 (out of 28 participants)				
	Group 1 (out of 6 participants)	Group 2 (out of 10 participants)	Group 3 (out of 6 participants)	Group 4 (out of 6 participants)	Part 2 (out of 30 participants)
How many participants had adverse reactions during the study considered related to selumetinib?	66.7% (4)	100.0% (10)	100.0% (6)	100.0% (6)	96.7% (29)
How many participants had adverse reactions during the study considered related to durvalumab?	83.3% (5)	90.0% (9)	83.3% (5)	33.3% (2)	73.3% (22)
How many participants had serious adverse reactions during the study considered related to selumetinib?	16.7% (1)	10.0% (1)	16.7% (1)	0.0% (0)	3.3% (1)
How many participants had serious adverse reactions during the study considered related to durvalumab?	16.7% (1)	20.0% (2)	16.7% (1)	0.0% (0)	3.3% (1)
How many participants stopped treatment during the study because of adverse reactions considered related to selumetinib?	33.3% (2)	10.0% (1)	16.7% (1)	0.0% (0)	3.3% (1)
How many participants stopped treatment during the study because of adverse reactions considered related to durvalumab?	33.3% (2)	10.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)

Serious adverse reactions

There were 8.6% of participants who had serious adverse reactions during the study. This was 5 out of 58 participants.

The 2 tables below and on the next page show the serious adverse reactions that happened during the study. Some of the participants had more than 1 serious adverse reaction. The study doctors considered some of the serious adverse reactions to be related to both selumetinib and durvalumab. So, some of the serious adverse reactions are listed in both tables below.

Serious adverse reactions during the study considered related to selumetinib

	Part 1 (out of 28 participants)				
Serious adverse reaction	Group 1 (out of 6 participants)	Group 2 (out of 10 participants)	Group 3 (out of 6 participants)	Group 4 (out of 6 participants)	Part 2 (out of 30 participants)
Diarrhea	16.7% (1)	0.0% (0)	16.7% (1)	0.0% (0)	0.0% (0)
Fever	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)	3.3% (1)
Rapid heartbeat	0.0% (0)	10.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Swelling in the digestive tract	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)	0.0% (0)
Vomiting	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)	0.0% (0)

Serious adverse reactions during the study considered related to durvalumab

	Part 1 (out of 28 participants)				
Serious adverse reaction	Group 1 (out of 6 participants)	Group 2 (out of 10 participants)	Group 3 (out of 6 participants)	Group 4 (out of 6 participants)	Part 2 (out of 30 participants)
Diarrhea	16.7% (1)	0.0% (0)	16.7% (1)	0.0% (0)	0.0% (0)
Fever	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)	3.3% (1)
Increase in amount of alanine aminotransferase in the body (a sign of liver damage)	0.0% (0)	10.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Increase in amount of alkaline phosphatase in the body (a possible sign of bone cancer)	0.0% (0)	10.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Increase in amount of aspartate aminotransferase in the body (a sign of liver damage)	0.0% (0)	10.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Rapid heartbeat	0.0% (0)	10.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Swelling in the digestive tract	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)	0.0% (0)
Vomiting	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)	0.0% (0)

Most common adverse reactions

The most common adverse reaction during the study was participants reporting that they felt tired. Some of the participants had more than 1 adverse reaction. The study doctors considered some of the adverse reactions to be related to both selumetinib and durvalumab. So, some of the adverse reactions are listed in both tables below.

The table below shows the adverse reactions that happened in at least 4 participants in any treatment group during the study that were considered related to selumetinib. There were other adverse reactions that happened during the study that were considered related to selumetinib, but those happened in fewer participants.

Most common adverse reactions during the study considered related to selumetinib

Adverse reaction	Part 1 (out of 28 participants)				Part 2 (out of 30 participants)
	Group 1 (out of 6 participants)	Group 2 (out of 10 participants)	Group 3 (out of 6 participants)	Group 4 (out of 6 participants)	
Diarrhea	16.7% (1)	20.0% (2)	50.0% (3)	66.7% (4)	36.7% (11)
Feeling tired	33.3% (2)	20.0% (2)	16.7% (1)	0.0% (0)	43.3% (13)
Skin reaction causing acne	0.0% (0)	0.0% (0)	16.7% (1)	16.7% (1)	53.3% (16)
Nausea	0.0% (0)	20.0% (2)	33.3% (2)	33.3% (2)	26.7% (8)
Vomiting	16.7% (1)	0.0% (0)	33.3% (2)	33.3% (2)	16.7% (5)
Rash	16.7% (1)	10.0% (1)	16.7% (1)	16.7% (1)	16.7% (5)
Decreased appetite	16.7% (1)	0.0% (0)	16.7% (1)	0.0% (0)	20.0% (6)
Decrease in the number of red blood cells	0.0% (0)	10.0% (1)	0.0% (0)	16.7% (1)	16.7% (5)
Dry mouth	16.7% (1)	0.0% (0)	0.0% (0)	16.7% (1)	13.3% (4)
Increase in amount of alkaline phosphatase in the body (a possible sign of bone cancer)	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)	16.7% (5)
Decrease in amount of thyroid hormone produced by the body, which can lead to medical problems	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	13.3% (4)
Dry skin	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	13.3% (4)

The table below shows the adverse reactions that happened in at least 4 participants in any treatment group during the study that were considered related to durvalumab. There were other adverse reactions that happened during the study that were considered related to durvalumab, but those happened in fewer participants.

Most common adverse reactions during the study considered related to durvalumab

Adverse reaction	Part 1 (out of 28 participants)				Part 2 (out of 30 participants)
	Group 1 (out of 6 participants)	Group 2 (out of 10 participants)	Group 3 (out of 6 participants)	Group 4 (out of 6 participants)	
Feeling tired	33.3% (2)	10.0% (1)	33.3% (2)	0.0% (0)	30.0% (9)
Diarrhea	16.7% (1)	0.0% (0)	16.7% (1)	0.0% (0)	20.0% (6)
Nausea	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)	20.0% (6)
Vomiting	16.7% (1)	0.0% (0)	16.7% (1)	0.0% (0)	13.3% (4)
Decreased appetite	0.0% (0)	10.0% (1)	16.7% (1)	0.0% (0)	13.3% (4)
Decrease in the number of red blood cells	0.0% 0)	10.0% (1)	16.7% (1)	0.0% (0)	13.3% (4)
Skin reaction causing acne	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	20.0% (6)

How has this study helped patients and researchers?

This study helped researchers learn more about using selumetinib and durvalumab together in patients who have advanced solid tumors. The researchers plan to compare the information collected in this study to the results of other studies that used the study drugs separately.

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 combined selumetinib and durvalumab treatments 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 this website, type **"NCT02586987"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2016-003780-19"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D1345C00003"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase I, Open-Label, Multi-Centre Study to Assess the Safety, Tolerability and Preliminary Anti-tumour Activity of Ascending Doses of Selumetinib (AZD6244 Hyd-sulfate) in Combination with MEDI4736 and Selumetinib in Combination with MEDI4736 and Tremelimumab in Patients with Advanced Solid Tumours

AstraZeneca Protocol Number: D1345C00003

AstraZeneca sponsored this study and has its headquarters at 1800 Concord Pike in Wilmington, Delaware.

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

Thank you

Clinical study participants and their families 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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