Clinical Study Results

Research Sponsor: AstraZeneca AB

Drugs Studied: MEDI4736 (durvalumab) and AZD5069

Study Title: A study to learn more about the safety of durvalumab combined with other treatments and how these treatments work in patients with metastatic pancreatic cancer

Thank you

Thank you to the participants who took part in the clinical study for the study drugs durvalumab, also called MEDI4736, and AZD5069. Also, thank you to the families of the participants. All of the participants and their families helped researchers learn more about durvalumab combined with other treatments in order to help people with metastatic pancreatic cancer.

AstraZeneca AB sponsored this study and thinks it is important to share the results of the study with the participants, their families, and the public. An independent, non-profit organization called CISCRP helped prepare this summary of the study results. We hope it helps the participants and their families understand their important role in medical research.

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

What is happening with the study now?

The study started in March 2016 and ended in July 2018. The study included 23 participants in the United Kingdom and the United States.

There were 2 groups in the study, Group 1 and Group 2. The participants in Group 1 were in the United States and were in the study for up to about 1.5 years. The participants in Group 2 were in the United Kingdom and were in the study for up to about 1 year.

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 patients with metastatic pancreatic cancer. Before a drug can be approved for patients to take, researchers do clinical studies to find out how it works and how safe it is.

In this study, the researchers wanted to find out if durvalumab combined with other treatments works in a small number of participants with metastatic pancreatic cancer. They also wanted to find out if the participants had any medical problems during the study.

Cancer is a disease that happens when the body cannot control the growth of cells. These extra cells can come together to form tumors. Tumors can start in any part of the body. When a cancer is metastatic, it means that the cancer has spread to other parts of the body to form new tumors.

There are current treatments for metastatic pancreatic tumors. But, many of these treatments do not stop tumors from growing and can cause other medical problems. This is because these treatments sometimes attack healthy cells instead of pancreatic tumor cells. Researchers think that the study drug, durvalumab, may be able to attack only the tumor cells and stop pancreatic tumors from growing.

In this study, the participants got durvalumab with other cancer treatments.

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

- Did the tumors of the participants in Group 2 shrink after getting durvalumab and a drug called AZD5069?
- Did the participants' safety results change after they started study treatment?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women with metastatic pancreatic cancer. The participants in this study were 46 to 74 years old.

What kind of study was this?

This was an “open-label” study. This means the researchers and the participant knew what treatment the participant got.

The participants in Group 1 had not gotten any treatment for their metastatic pancreatic cancer before the study started. They got 2 cancer drugs during the study, called nab-paclitaxel and gemcitabine, as well as durvalumab.

The participants in Group 2 had tried 1 treatment for their metastatic pancreatic cancer before the study started, but it did not help them. They got durvalumab and another drug called AZD5069, which is being developed to treat cancer.

What happened during the study?

Before treatment, the study doctors used a computed tomography scan, also called a CT scan, and magnetic resonance imaging, also called an MRI, to scan participants’ tumors. They also:

- did physical examinations and checked participants’ vital signs
- took blood and urine samples
- checked participants’ heart health using an electrocardiogram, also called an ECG
- measured the size of participants’ tumors
- took tissue samples from the tumors

During treatment, the participants got study treatment in 4-week periods called “cycles”. The participants could take part in as many treatment 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.

There were 3 participants in Group 1. They got nab-paclitaxel, gemcitabine, and durvalumab. Nab-paclitaxel and gemcitabine were given through a needle under the skin. This is known as intravenous treatment, also called IV treatment. Durvalumab was given as an infusion through a needle under the skin, also called an IV infusion. An IV infusion is similar to an IV treatment, but an infusion gets medicine into the body more slowly and more steadily, and can be done at home.

There were 20 participants in Group 2. They got durvalumab and AZD5069. Durvalumab was given through an IV infusion. AZD5069 was taken as a pill by mouth.

Throughout the treatment period, the researchers continued checking the participants' overall health and tumors.

The table below shows the treatments for each group.

	Group 1	Group 2
What treatments were given?	• 3 participants got nab-paclitaxel, gemcitabine, and durvalumab	• 20 participants got durvalumab and AZD5069
How were the treatments given?	• Nab-paclitaxel and gemcitabine were given by IV • Durvalumab was given by IV infusion	• Durvalumab was given by IV infusion • AZD5069 was taken as a pill
When were the treatments given?	The participants got nab-paclitaxel and gemcitabine: • the 1st day of each cycle • the 8th day of each cycle • the 15th day of each cycle The participants got durvalumab on the 1st day of each cycle	• The participants got durvalumab on the 1st day of each cycle • The participants took AZD5069 twice a day during each cycle

After treatment, the study doctors checked the participants' overall health. They did this every 4 weeks for 4 months, then every 2 months until the end of the study. The study doctors also checked the participants' tumors every 8 weeks in Group 1, or every 6 weeks in Group 2, until their cancer got worse. After 48 weeks, if the participant was still in the study, tumor checks were only done every 12 weeks.

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. A full list of the questions researchers wanted to answer can be found on the websites listed at the end of this summary. If a full report of the study results is available, it can also be found on these websites.

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.

For Group 1, the researchers were not able to get as many participants to join the study as they had originally planned for. Because of this, the researchers did not think there were enough participants in Group 1 to determine if the study results for this group were meaningful. So, for the first question below, the researchers only studied the results from Group 2.

For Group 2, the researchers were not able to gather all of the study results for 2 of the 20 participants. So, the researchers could only study some of the results below for 18 out of the 20 participants in Group 2.

Did the tumors of the participants in Group 2 shrink after getting durvalumab and AZD5069?

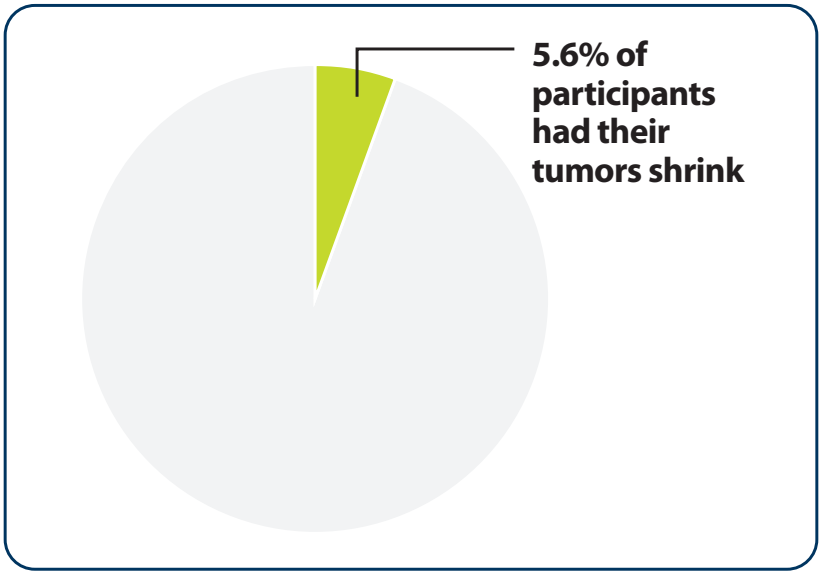
No. Overall, the participants in Group 2 did not have their tumors shrink after getting durvalumab and AZD5069.

To answer this question, the researchers studied participants' tumors throughout the study. They did this by measuring the size of the tumors, using CT scans and MRIs to scan the tumors, and taking tissue samples from the tumors.

For Group 2, the researchers found that 5.6% of the participants had their tumors shrink. This was 1 out of 18 participants. After about 18 weeks, this participant's tumor started to grow again.

The figure below shows these results.

Participants in Group 2 whose tumors shrunk during the study



Did the participants' safety results change after they started study treatment?

No. Overall, the participants' safety results did not change throughout the study.

To answer this question, the researchers did the following throughout the study:

- performed physical examinations and checked participants' vital signs
- took blood and urine samples
- checked participants' heart health using an ECG

There were some changes in the results of these tests throughout the study, but these changes were too small for the researchers to consider them meaningful.

The study doctors also counted the number of dose-limiting toxicities, also called DLTs, that the participants had during the study. A DLT is a medical problem that is serious enough to stop the study doctor from increasing the participant's study treatment dose.

Overall, the researchers found that:

- None of the participants in Group 1 had DLTs during the study.
- 20.0% of the participants in Group 2 had DLTs during the study. This was 4 out of 20 participants.

The number of DLTs was too small for the researchers to know if the DLTs were related to the study treatment.

In this study, the researchers also collected information about how many adverse events the participants had. An adverse event is any medical problem that happens during the study. Adverse events are considered "serious" when they are life-threatening, cause lasting problems, or require hospital care. Adverse events may or may not be caused by the study drugs.

What serious adverse events did the participants have?

There were 73.9% of participants who had serious adverse events during the study. This was 17 out of 23 participants.

The only serious adverse events that happened in more than 1 participant overall were serious vomiting and serious constipation:

- None of the participants in Group 1 had serious vomiting.
- 10.0% of the participants in Group 2 had serious vomiting. This was 2 out of 20 participants.
- 33.3% of the participants in Group 1 had serious constipation. This was 1 out of 3 participants.
- 5.0% of the participants in Group 2 had serious constipation. This was 1 out of 20 participants.

There were 21.7% of participants who died during the study because of adverse events. This was 5 out of 23 participants:

- 33.3% of the participants in Group 1 died during the study from the serious adverse event of liver failure. This was 1 out of 3 participants.
- 20.0% of the participants in Group 2 died during the study from serious adverse events. This was 4 out of 20 participants. These serious adverse events were bleeding in the stomach, fluid build-up in the lungs, general worsening of health, and swelling near the liver from an infection.

How many participants had adverse events?

There were 100.0% of participants who had adverse events during the study. This was 23 out of 23 participants.

There were 21.7% of participants who stopped treatment because of adverse events. This was 5 out of 23 participants.

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

Adverse events during the study

	Group 1 (out of 3 participants)	Group 2 (out of 20 participants)
How many participants had adverse events during the study?	100.0% (3)	100.0% (20)
How many participants had serious adverse events during the study?	33.3% (1)	80.0% (16)
How many participants stopped treatment because of adverse events?	66.7% (2)	15.0% (3)

What adverse events did the participants have?

The most common adverse event during the study was tiredness.

The table below shows the adverse events that happened in 4 or more participants overall during the study. There were other adverse events that happened during the study, but these happened in fewer participants. The websites listed at the end of this summary may have other information about the adverse events that happened during this study.

Most common adverse events during the study

	Group 1 (out of 3 participants)	Group 2 (out of 20 participants)
Tiredness	66.7% (2)	50.0% (10)
Nausea	33.3% (1)	45.0% (9)
Vomiting	33.3% (1)	45.0% (9)
Diarrhea	66.7% (2)	25.0% (5)
Decreased appetite	0.0% (0)	35.0% (7)
Constipation	0.0% (0)	25.0% (5)
Low amount of white blood cells, which can make it difficult for the body to fight infections	100.0% (3)	10.0% (2)
Mouth infection	0.0% (0)	25.0% (5)
Swelling of the mouth and lips	0.0% (0)	25.0% (5)
Muscle pain	33.3% (1)	15.0% (3)
Blood cells grouping together and blocking lung arteries	0.0% (0)	20.0% (4)

What medical problems did the 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 drugs. 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.

The websites listed at the end of this summary may have other information about the adverse reactions that happened during this study.

How many participants had serious adverse reactions?

There were 39.1% of participants who had serious adverse reactions during the study. This was 9 out of 23 participants.

There were 4.3% of participants who died during the study because of adverse reactions. This was 1 out of 23 participants. This participant was in Group 1 and died from the serious adverse reaction of liver failure.

The table below shows the serious adverse reactions that happened during the study.

Serious adverse reactions during the study

	Group 1 (out of 3 participants)	Group 2 (out of 20 participants)
Swelling in the lungs	33.3% (1)	0.0% (0)
Serious pain in the legs	33.3% (1)	0.0% (0)
Liver failure	33.3% (1)	0.0% (0)
High risk of developing a fatal liver injury	33.3% (1)	0.0% (0)
Blockage in the arteries	0.0% (0)	5.0% (1)
Large decrease in amount of white blood cells, which can make it difficult for the body to fight infections	0.0% (0)	5.0% (1)
Negative reaction in the body when infusion was given	0.0% (0)	5.0% (1)
Serious constipation	0.0% (0)	5.0% (1)
Serious diarrhea	0.0% (0)	5.0% (1)
Serious difficulty in breathing	0.0% (0)	5.0% (1)
Serious fever	0.0% (0)	5.0% (1)
Serious vomiting	0.0% (0)	5.0% (1)
Swelling from a low amount of white blood cells	0.0% (0)	5.0% (1)
Swelling in the digestive system	0.0% (0)	5.0% (1)
Swelling in the liver	0.0% (0)	5.0% (1)
Swelling in the throat from an infection	0.0% (0)	5.0% (1)

How many participants had adverse reactions?

There were 73.9% of participants who had adverse reactions during the study. This was 17 out of 23 participants.

There were 8.7% of participants who stopped treatment because of adverse reactions. This was 2 out of 23 participants.

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

Adverse reactions during the study

	Group 1 (out of 3 participants)	Group 2 (out of 20 participants)
How many participants had adverse reactions during the study?	100.0% (3)	70.0% (14)
How many participants had serious adverse reactions during the study?	33.3% (1)	40.0% (8)
How many participants stopped treatment because of adverse reactions?	33.3% (1)	5.0% (1)

What adverse reactions did the participants have?

The most common adverse reaction during the study was tiredness.

The table below shows the adverse reactions that happened in 4 or more participants overall during the study. There were other adverse reactions that happened during the study, but these happened in fewer participants.

Most common adverse reactions

	Group 1 (out of 3 participants)	Group 2 (out of 20 participants)
Tiredness	66.7% (2)	25.0% (5)
Diarrhea	66.7% (2)	20.0% (4)
Mouth infection	0.0% (0)	25.0% (5)
Decrease in amount of white blood cells, which can make it difficult for the body to fight infections	66.7% (2)	10.0% (2)
Nausea	33.3% (1)	15.0% (3)
Vomiting	33.3% (1)	10.0% (2)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of durvalumab combined with other treatments and how durvalumab combined with AZD5069 works in patients with metastatic pancreatic cancer.

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 treatments of durvalumab and AZD5069 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 **"NCT02583477"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2015-003639-37"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D4198C00003"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase Ib and II Open-Label, Multi-Center Study of MEDI4736 Evaluated in Different Combinations in Patients with Metastatic Pancreatic Ductal Adenocarcinoma

AstraZeneca Protocol Number: D4198C00003

AstraZeneca AB sponsored this study and has its headquarters in Södertälje, 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.