AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drugs Studied: AZD9150 and durvalumab

Study Purpose: This study was done to learn about the safety of AZD9150 and durvalumab in participants with advanced solid tumors

Protocol Number: D5660C00016

Thank you

Thank you for taking part in the clinical study for the study drugs AZD9150 and durvalumab. AZD9150 is also called danvatirsen.

AstraZeneca AB 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 26 to 81 years old when they joined.

The study included 78 participants in 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. These extra cells can form tumors. When cancer reaches the "advanced" stage, it means that the cancer keeps growing, even with treatment.

At this stage, the cancer is often "metastatic". This means that the tumors have spread into other tissue near the organ where they started or to other parts of the body.

The study drugs, AZD9150 and durvalumab, were each designed to stop different proteins in the body from allowing tumors to grow.

In this study, the researchers wanted to find out about the safety of AZD9150 and durvalumab in participants with advanced solid tumors.

What was the purpose of this study?

There were 2 parts in this study. The main questions the researchers wanted to answer in this study were:

- What signs and symptoms did the participants have during Part 1 of the study?
- How much AZD9150 got into the participants' blood when given in different ways in Part 2?
- What medical problems did the participants have during Part 1 and Part 2 of the study?

The answers to these questions are important to know before other studies can be done to find out if AZD9150 and durvalumab help improve the health of people with advanced solid tumors.

What treatments did the participants get?

In this study, all of the participants got AZD9150 and durvalumab. Some participants also got chemotherapy. This was an "open-label" study. This means the participants, researchers, study doctors, and other study staff knew what each participant was getting.

This study happened in 2 parts. In **Part 1**, the participants got AZD9150 and durvalumab through a needle directly into the blood, also known as an intravenous or "IV" infusion.

Most of the participants in Part 1 also got different types and doses of chemotherapy, depending on what the study doctors thought was best for each participant.

In **Part 2**, the participants got durvalumab as an IV infusion, and AZD9150 either as an IV infusion or through a needle under the skin, also called an injection. A computer program was used to randomly choose whether a participant got AZD9150 as an IV infusion or injection. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each treatment is as accurate as possible.

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

	Part 1	Part 2
	36 participants	42 participants
	**AZD9150** as an IV infusion, every 1 to 2 weeks	**AZD9150** as an IV infusion or as an injection, once every week
	**Durvalumab** as an IV infusion, every 3 to 4 weeks	**Durvalumab** as an IV infusion, every 4 weeks
	Different types and doses of **chemotherapy**, depending on what the study doctors thought was best for each participant	No **chemotherapy**
	19 weeks of treatment in total	19 weeks of treatment in total

What happened during this study?

The study started in February 2018 and ended in March 2019.

Before the participants got study treatment, they visited their study site 1 time. This part of the study lasted for up to 3 weeks. At this visit, the study doctors made sure the participants could join the study.

They also:

- did physical exams and asked about the participants' medications and any medical problems they were having
- took blood, urine, and saliva samples
- checked the participants' heart health using an electrocardiogram, also known as an ECG
- took pictures of the participants' tumors using computed tomography scans, also known as CT scans, or magnetic resonance imaging scans, also known as MRI scans
- if needed, took a sample of the participants' tumors using surgery, also known as a biopsy

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

While the participants in Part 1 got study treatment, they visited their study site:

- 3 times in the first week, then
- once a week or once every 2 weeks, for 18 weeks

At these visits, the study doctors gave the participants their doses of study treatment and checked their health. If the doctors thought the study treatments were helping the participants, they could keep getting study treatment for longer.

While the participants in Part 2 got study treatment, they visited their study site:

- 3 times in the first week, then
- once a week for 6 weeks, then
- every 2 weeks for 12 weeks

At these visits, the study doctors gave the participants their doses of study treatment and checked their health. The participants in Part 2 also kept a diary and answered surveys about their symptoms and quality of life. If the doctors thought the study treatments were helping the participants, they could keep getting study treatment for longer.

After the participants stopped getting study treatment, they visited their study site 2 times in the first 3 months. The participants whose cancer had worsened at the time they had stopped getting study treatment ended their participation in the study after these 2 visits. The participants whose cancer had not gotten worse continued to visit their study site once every 3 months until their cancer did get worse. 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.

There were 4 participants in Part 1, and 2 participants in Part 2, who did not get any doses of study treatment. So, the results below are for 32 participants in Part 1 and 40 participants in Part 2.

What signs and symptoms did the participants have during Part 1 of the study?

To answer this question, the study doctors did tests and measurements throughout Part 1.

The 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 changes 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 treatment.

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 study 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 study. A lot of research is needed to know whether a treatment causes an adverse event.

	Part 1 (out of 32 participants)
How many participants had adverse events?	100% (32)
How many participants had serious adverse events?	31.3% (10)
How many participants stopped getting AZD9150 due to adverse events?	12.5% (4)
How many participants stopped getting durvalumab due to adverse events?	3.1% (1)

The most common serious adverse events in Part 1 were:

- Low levels of red blood cells
- Pneumonia

The most common adverse events in Part 1 were:

- Low levels of a type of white blood cell called neutrophils
- Low levels of blood cells that help form clots, known as platelets
- Low levels of red blood cells
- Nausea
- Vomiting
- High levels of liver proteins called AST and ALT
- Diarrhea
- Decreased appetite
- Fatigue
- Low levels of magnesium in the blood
- Dehydration

The study doctors also counted the number of "dose limiting toxicities" the participants had during the study. A dose limiting toxicity is an adverse event 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".

There were **9.4%** of participants in Part 1 who had a DLT. This was 3 out of 32 participants.

How much AZD9150 got into the participants' blood when given in different ways in Part 2?

To answer this question, the study doctors took blood samples at different times during the study from the participants in Part 2 and measured how much AZD9150 was in the participants' blood.

The researchers looked at 2 different measurements of AZD9150 in the blood:

- The average **lowest** amount of AZD9150 in the blood just before getting another dose.
- The average **total** amount of AZD9150 in the blood over time.

Then, the researchers compared the results between the participants in Part 2 who got AZD9150 as an IV infusion and the participants who got AZD9150 as an injection.

The results shown below are for the participants in Part 2 who got study treatment and had data that could be calculated. This was:

- **12** participants who got AZD9150 as an **injection**
- **14** participants who got AZD9150 as an **IV infusion**

The researchers found that:

- The average **lowest** amount of AZD9150 in the blood just before getting another dose was **17% lower** for the participants who got AZD9150 as an injection, compared with the participants who got AZD9150 as an IV infusion.
- The average **total** amount of AZD9150 in the blood over time was **26% lower** for the participants who got AZD9150 as an injection, compared with the participants who got AZD9150 as an IV infusion.

What medical problems happened during Part 1 and Part 2 of 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 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. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for AZD9150 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.

	Part 1 (out of 32 participants)	**Part 2 (out of 40 participants)**
How many participants had adverse reactions related to AZD9150?	93.8% (30)	75.0% (30)
How many participants had adverse reactions related to durvalumab?	59.4% (19)	62.5% (25)
How many participants had serious adverse reactions related to AZD9150?	6.3% (2)	5.0% (2)
How many participants had serious adverse reactions related to durvalumab?	6.3% (2)	5.0% (2)
How many participants stopped getting AZD9150 due to adverse reactions related to AZD9150?	12.5% (4)	15.0% (6)
How many participants stopped getting durvalumab due to adverse reactions related to durvalumab?	3.1% (1)	10.0% (4)

What serious adverse reactions happened during this study?

The tables below show the serious adverse reactions that the study doctors thought might be related to the study drugs that happened during the study.

Serious adverse reactions related to AZD9150

Serious adverse reaction to AZD9150	Part 1 (out of 32 participants)	Part 2 (out of 40 participants)
Breakdown of red blood cells	3.1% (1)	none
Low levels of blood cells that help form clots, known as platelets	3.1% (1)	none
Low levels of a type of white blood cell called neutrophils	3.1% (1)	none
Fever with low levels of a type of white blood cell called neutrophils	none	2.5% (1)
High levels of a liver protein called ALT	none	2.5% (1)
High levels of a liver protein called AST	none	2.5% (1)

Serious adverse reactions related to durvalumab

Serious adverse reaction to durvalumab	Part 1 (out of 32 participants)	Part 2 (out of 40 participants)
Breakdown of red blood cells	3.1% (1)	none
Low levels of red blood cells	3.1% (1)	none
Liver injury	none	2.5% (1)
Low levels of hormones made by the adrenal glands	none	2.5% (1)
High levels of a liver protein called ALT	none	2.5% (1)
High levels of a liver protein called AST	none	2.5% (1)

None of the participants died because of serious adverse reactions that the study doctors thought might be related to the study drugs.

What adverse reactions happened during this study?

The tables below show the adverse reactions that happened in 10.0% or more of participants in either treatment group during the study. There were other adverse reactions but these happened in fewer participants.

Most common adverse reactions to AZD9150

Adverse reaction to AZD9150	Part 1 (out of 32 participants)	Part 2 (out of 40 participants)
Low levels of blood cells that help form clots, known as platelets	53.1% (17)	37.5% (15)
Low levels of red blood cells	40.6% (13)	30.0% (12)
Low levels of a type of white blood cell called neutrophils	40.6% (13)	15.0% (6)
Increased levels of a liver protein called ALT	31.3% (10)	30.0% (12)
Increased levels of a liver protein called AST	21.9% (7)	22.5% (9)
Fatigue	18.8% (6)	10.0% (4)
Decreased levels of blood cells that help form clots, known as platelets	18.8% (6)	5.0% (2)
Decreased levels of a type of white blood cell called neutrophils	18.8% (6)	2.5% (1)
Nausea	15.6% (5)	15.0% (6)
Diarrhea	15.6% (5)	2.5% (1)
Low appetite	12.5% (4)	7.5% (3)
Low levels of all types of white blood cells	9.4% (3)	12.5% (5)
Vomiting	9.4% (3)	12.5% (5)
Reaction at the injection site	none	17.5% (7)

Most common adverse reactions to durvalumab

Adverse reaction to durvalumab	Part 1 (out of 32 participants)	Part 2 (out of 40 participants)
Increased levels of a liver protein called ALT	18.8% (6)	30.0% (12)
Increased levels of a liver protein called AST	12.5% (4)	25.0% (10)
Low levels of blood cells that help form clots, known as platelets	12.5% (4)	20.0% (8)
Fatigue	12.5% (4)	15.0% (6)
Low levels of red blood cells	12.5% (4)	15.0% (6)
Low levels of all types of white blood cells	6.3% (2)	12.5% (5)
Rash	3.1% (1)	10.0% (4)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of AZD9150 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 AZD9150 and durvalumab 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 **"D5660C00016"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"NCT03421353"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase Ib/II, Open-Label, Multicentre Study to Assess Safety, Tolerability, Pharmacokinetics, and Preliminary Anti-tumour Activity of AZD9150 plus Durvalumab alone or in Combination with Chemotherapy in Patients with Advanced, Solid Tumours and Subsequently in Patients with Non-Small-Cell Lung Cancer

AstraZeneca AB Protocol Number: D5660C00016

National Clinical Trials Number: NCT03421353

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.

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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