Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Durvalumab and tremelimumab

Study Title: A study to learn about durvalumab and tremelimumab for participants with advanced solid tumors who are getting chemotherapy

Thank you!

Thank you for taking part in this clinical study for the study drugs durvalumab and tremelimumab.

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 this study and have questions about the results, please speak with the study doctor or staff at your study site.

Who took part in the study?

The researchers asked for the help of people with advanced solid tumors. The participants in this study were 31 to 81 years old when they joined.

The study included 32 participants in Japan and South Korea.

Why was the research needed?

Researchers are looking for a better way to treat advanced solid tumors. Before a drug can be approved for people to get, researchers do clinical studies to find out how safe it is and how it works.

A solid tumor is a type of cancer that starts in a solid organ of the body. “Advanced” usually means that the cancer keeps growing and is hard to treat. Normally, immune cells help stop tumors from growing. But in people with advanced solid tumors, the tumor cells can interact with certain proteins on the immune cells and stop the immune cells from recognizing tumor cells.

The study drugs, durvalumab and tremelimumab, were each designed to stop the tumor cells from interacting with some of these proteins. This lets the immune cells recognize the tumor cells again and help stop the tumor from growing.

In this study, the researchers wanted to find out about the safety of durvalumab and tremelimumab with chemotherapy in participants with advanced solid tumors. They also wanted to find out if taking the study drugs with chemotherapy affected the size of the participants’ tumors.

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?
- Did durvalumab and tremelimumab with chemotherapy slow the growth of the participants’ tumors?
- 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 durvalumab and tremelimumab help improve the health of people with advanced solid tumors.

What treatments did the participants get?

This was an “open-label” study. This means the participants, researchers, study doctors, and other study staff knew what each participant was getting.

All of the participants got durvalumab and tremelimumab through a needle into a vein, also known as an IV infusion. They also got standard chemotherapy treatments by IV infusion throughout the study.

The researchers planned to study 7 different treatment groups, but participants only joined 6 of the groups. The groups were chosen based on the types of tumors the participants had, and the type of chemotherapy they received.

The doses of durvalumab and tremelimumab were based on which group the participants were in. They were measured in milligrams, also known as mg.

The participants got treatment in periods called cycles. The participants got 1 dose of durvalumab and tremelimumab in each cycle. The participants in Group 4 got 2 doses of chemotherapy in each cycle and the other groups got 1 dose in each cycle.

Most participants were planned to be in the study for up to 4 cycles. The participants in Group 6 were planned to be in the study for up to 6 cycles.

The table below shows the different treatment groups.

Group	Types of cancer	Length of each cycle	Dose of durvalumab	Dose of tremelimumab	Chemotherapy
Group 1 (6 participants)	Lung cancer	3 weeks	1120 mg	75 mg	Carboplatin with etoposide
Group 2 (2 participants)	Breast cancer	3 weeks	1120 mg	75 mg	Carboplatin with gemcitabine
Group 3 (1 participant)	Breast cancer	3 weeks	1120 mg	75 mg	Carboplatin with nab-paclitaxel
Group 4 (1 participant)	Stomach cancers	4 weeks	1500 mg	75 mg	Oxaliplatin with 5FU and leucovorin (2 doses per cycle)
Group 5 (6 participants)	Pancreas cancer	4 weeks	1500 mg	75 mg	Nab-paclitaxel with gemcitabine
Group 6 (16 participants)	Esophagus cancer	4 weeks	1500 mg	75 mg	Cisplatin with 5FU

In Group 6, treatment happened in 2 parts. There were 6 participants in Part A and 10 participants in Part B. The participants in Part B started the study after the participants in Part A finished the study. The participants in Part B only got tremelimumab in the first and last cycles.

What happened during the study?

The study started in April 2016 and ended in November 2019.

Before the participants got study treatment, they visited their study site at least 1 time. Some participants may have had more than 1 visit. At these visits, the study doctors checked the health of the participants to make sure they could join the study. This part of the study lasted up to 4 weeks. The study doctors:

- did a physical exam and asked about the participants' medications and any medical problems they were having
- checked the participants' heart health using an electrocardiogram, also called an ECG
- took pictures of each participant's tumors using CT or MRI scans
- used surgery to take a sample of the tumor called a biopsy for some participants
- took blood and urine samples

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

While the participants got study treatment, they visited their study site 1 time at the beginning of each cycle.

At each visit, they got durvalumab, tremelimumab, and chemotherapy by IV infusion. The participants in Part B of Group 6 only got tremelimumab during their first and last cycle of the study.

After the participants got study treatment, they visited their study site once a month for the first 3 months. At these visits, the study doctors checked the health of the participants. After the first 3 months, the study doctors called the participants every 3 months until the study ended.

For participants who left the study early, the study doctors checked the participants' tumors regularly until their cancer got worse.

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 change.

The websites listed at the end of this summary may have a full report of 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 before and after the participants got durvalumab and tremelimumab with chemotherapy. 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 to be important.

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.

How many participants had adverse events?	100.0% (32 out of 32 participants)
How many participants had serious adverse events?	43.8% (14 out of 32 participants)
How many participants stopped taking any study treatment because of adverse events?	18.8% (6 out of 32 participants)

The most common serious adverse events were:

- pneumonia
- fever
- diarrhea
- a decreased count of white blood cells called neutrophils

The most common adverse events were:

- nausea
- a decreased count of white blood cells called neutrophils
- decreased appetite
- constipation
- an increase in a liver enzyme called ALT

Did durvalumab and tremelimumab with chemotherapy slow the growth of the participants' tumors?

To answer this question, the study doctors took pictures of the participants' tumors using CT or MRI scans. They measured the size of the participants' tumors before they got study treatment and throughout the study. To do this, they used a set of rules called Response Evaluation Criteria in Solid Tumors, also called RECIST.

The researchers only looked at these results for the participants in Group 5 with pancreas cancer because they could compare it to a previous study in pancreas cancer.

The researchers found that tumor growth slowed in some of the 6 participants in Group 5 after they got durvalumab and tremelimumab with nab-paclitaxel and gemcitabine. But, the number of participants in Group 5 was too small for the researchers to know if durvalumab and tremelimumab with nab-paclitaxel and gemcitabine slowed the growth of the participants' tumors compared to the previous study.

What medical problems happened 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 any of 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 the study treatments.

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.

Did any adverse reactions happen during this study?	
How many participants had adverse reactions to any study treatment?	100.0% (32 out of 32 participants)
How many participants had serious adverse reactions to any study treatment?	25.0% (8 out of 32 participants)
How many participants stopped taking study treatment because of adverse reactions to any study treatment?	12.5% (4 out of 32 participants)

What serious adverse reactions happened during this study?

The most common serious adverse reactions were diarrhea and a decreased count of white blood cells called neutrophils. The table on the next page shows the serious adverse reactions that happened during the study.

None of the participants died from serious adverse reactions.

Serious adverse reactions during the study	
Serious adverse reactions	**Durvalumab and tremelimumab with chemotherapy (out of 32 participants)**
Diarrhea	6.3% (2)
Decreased count of white blood cells called neutrophils	6.3% (2)
Pneumonia	3.2% (1)
A fever with low numbers of white blood cells called neutrophils	3.2% (1)
Dehydration	3.2% (1)
Inflammation of the colon	3.2% (1)
Abnormal liver function	3.2% (1)
Inflammation of the liver caused by the immune system	3.2% (1)
Inflammation of the muscles	3.2% (1)
Fever	3.2% (1)
Increase in a liver enzyme called AST	3.2% (1)
Reaction at the site of the IV infusion	3.2% (1)

What adverse reactions happened during this study?

The most common adverse reaction was a decreased count of white blood cells called neutrophils.

The table below shows the most common adverse reactions that happened in 8 or more participants. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during the study

Adverse reactions	Durvalumab and tremelimumab with chemotherapy (out of 32 participants)
Decreased count of white blood cells called neutrophils	56.3% (18)
Decreased appetite	34.4% (11)
Nausea	31.3% (10)
Itchiness	25.0% (8)
Decreased count of blood clotting fragments called platelets	25.0% (8)

How has this study helped patients and researchers?

This study helped researchers learn more about durvalumab and tremelimumab with chemotherapy for 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 durvalumab and tremelimumab are planned or ongoing.

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 **"NCT02658214"** into the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D419SC00001"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase Ib Study to Evaluate the Safety and Tolerability of Durvalumab and Tremelimumab in Combination With First-Line Chemotherapy in Patients With Advanced Solid Tumors

AstraZeneca AB Protocol Number: D419SC00001

National Clinical Trials number: NCT02658214

AstraZeneca AB sponsored this study and has its headquarters at 151 85 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.

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