Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca AB

Drugs Studied: Durvalumab and tremelimumab

Study Title: A study to learn how durvalumab or durvalumab in combination with tremelimumab acts in the blood of Chinese patients with advanced solid tumors

Thank you

Thank you to the participants who took part in the clinical trial for the study drugs durvalumab and durvalumab in combination with tremelimumab.

AstraZeneca AB 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 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?

This study started in December 2016. There are 2 parts in this study, called Part A and Part B. Part A of the study is still ongoing. Part B of the study was canceled before it started. Part A of the study included 26 participants in China.

The sponsor reviewed the data collected during Part A 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 with advanced solid tumors, which is a form of cancer that grows as lumps. Before a drug can be approved for patients to take, researchers do clinical studies to find out how safe it is and how it works.

When cancer develops in the body, the body's immune system can sometimes control cancer growth. But in some patients with cancer, cancer cells and other cells send signals that stop the immune system from doing this. Durvalumab is a drug that blocks one of these signals. Tremelimumab is a drug that blocks another one of these signals. Researchers are testing these treatments to see if blocking the signals will help the patient's immune system to control cancer growth.

In this study, the researchers wanted to learn more about how durvalumab acts in the blood. The main questions the researchers wanted to answer in this study were:

- How did durvalumab act in the blood when given alone?
- How did durvalumab act in the blood when given with tremelimumab?
- How did tremelimumab act in the blood when given with durvalumab?
- 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 durvalumab and tremelimumab improve the health of patients with advanced solid tumors.

The researchers asked native Chinese men and women with advanced solid tumors whose cancer had not gotten better with other treatment to participate in this study. Everyone in the study was 33 to 76 years old when they joined.

What kind of study was this?

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

In Part A, the participants were given 1 of 2 treatments:

- 20 milligrams of durvalumab per kilogram of body weight, or mg/kg
- 20 mg/kg of durvalumab and 1 mg/kg of tremelimumab

What happened during the study?

The participants got either durvalumab alone, or durvalumab and tremelimumab. Both of these treatments were given through a needle placed into a vein. This is called an intravenous infusion, also called an IV.

- 13 participants got durvalumab once every 4 weeks until their tumor grew.
- 13 participants got durvalumab and tremelimumab once every 4 weeks for up to 16 weeks. After that, they kept getting durvalumab once every 4 weeks until their tumor grew.

Before treatment, the doctors:

- checked the overall health of the participants
- checked the heart health of the participants using an electrocardiogram, also called an ECG
- took blood samples
- looked at the participants' tumors using computed tomography scans or magnetic resonance imaging
- asked questions about the participants' medical history and what medicines they were taking

This part of the study lasted up to 4 weeks.

During treatment, the doctors:

- checked the health of the participants
- took blood samples
- looked at the participants' tumors using computed tomography scans or magnetic resonance imaging
- asked the participants how they were feeling and what medicines they were taking

This part of the study lasted until the participant's tumor grew.

After treatment, the doctors:

- checked the health of the participants
- took blood samples
- asked the participants how they were feeling and what medicines they were taking

During this part of the study, the participants visited the site once a month for 4 months. After that, they visited the site every 2 months.

What were the results of the study?

This is a summary of the main results from Part A of this study. 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.

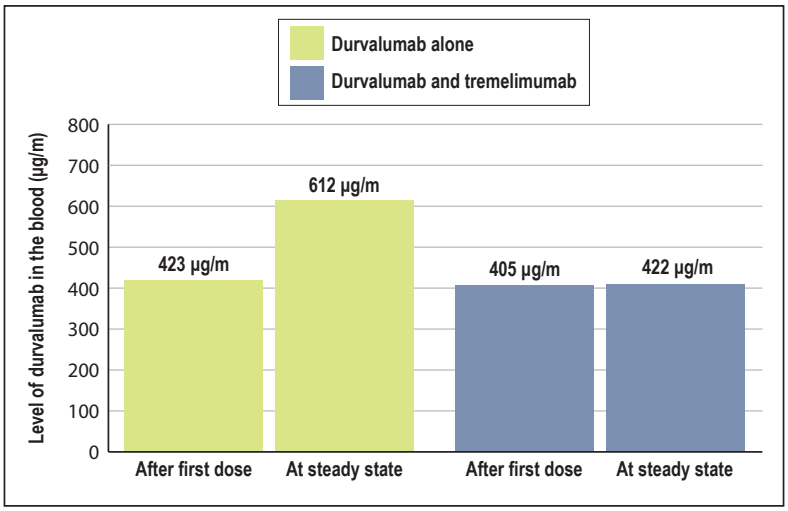
The websites listed at the end of this summary may have a full report of the study results.

How did durvalumab act in the blood?

To answer this question, the researchers measured the level of durvalumab in the participants' blood after the first dose and after multiple doses at "steady state". Steady state means the body is absorbing the drug at the same rate the body is removing it. This was measured in micrograms per milliliter of blood, also called µg/mL.

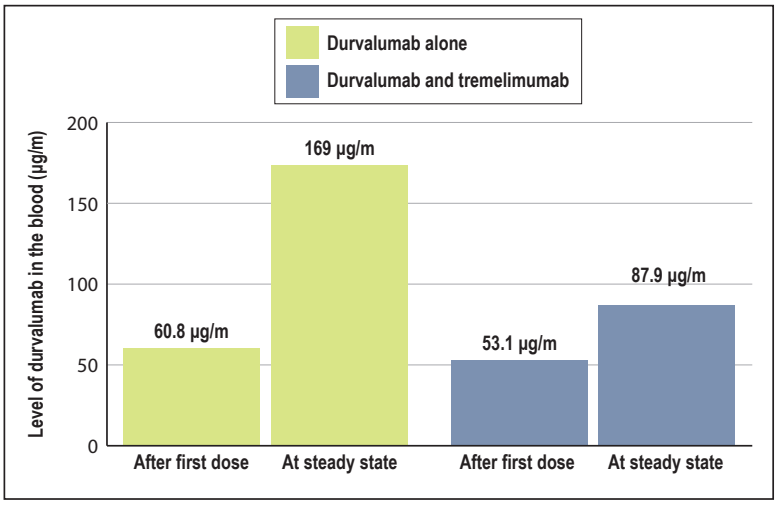
In general, the researchers found that steady state was reached after about 4 doses in a row. The highest level of durvalumab in the blood after the first dose was about the same whether it was given alone or with tremelimumab. At steady state, the highest level of durvalumab in the blood was higher when it was given alone than when it was given with tremelimumab.

Highest level of durvalumab in the blood



After the first dose, the researchers found that the level of durvalumab in the blood just before the next dose was about the same whether it was given alone or with tremelimumab. At steady state, the level of durvalumab in the blood just before the next dose was higher when it was given alone than when it was given with tremelimumab.

Level of durvalumab in the blood just before the next dose

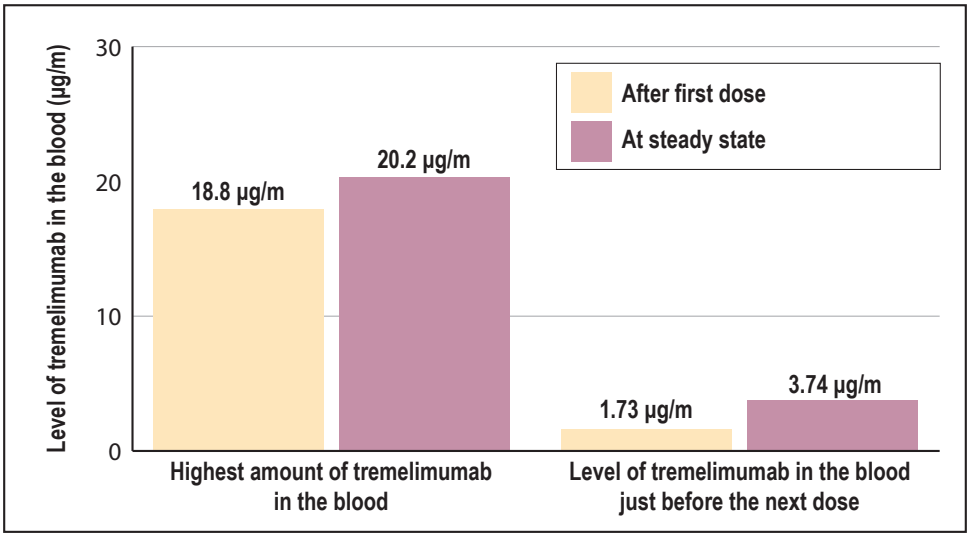


The researchers also measured the overall amount of durvalumab in the participants' blood over the 4 weeks after their first dose. This was measured in days multiplied by µg/mL, also called day•µg/mL. The amounts of durvalumab in the blood were about the same whether durvalumab was given alone or with tremelimumab. For durvalumab alone, the amount was 4,250 day•µg/mL. For durvalumab given with tremelimumab, the amount was 4,060 day•µg/mL.

How did tremelimumab act in the blood when given with durvalumab?

To answer this question, the researchers measured the level of tremelimumab in the participants' blood after their first dose and at steady state. The researchers found that the highest level of tremelimumab in the blood after the first dose was about the same as the amount at steady state. The level of tremelimumab in the blood just before the next dose was higher at steady state than after the first dose.

Level of tremelimumab in the blood



The researchers also measured the overall amount of tremelimumab in the participants' blood over the 4 weeks after their first dose, which was 174 day•µg/mL.

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 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 adverse reactions or other medical problems that happened during this study.

How many participants had serious adverse reactions?

Overall, there were 4 out of 26 participants who had serious adverse reactions during Part A of the study. This was 15.4% of participants.

- There was 1 out of the 13 participants who got durvalumab alone who had at least 1 serious adverse reaction. This was 7.7% of participants. This serious adverse reaction led to the death of this participant.
- There were 3 out of the 13 participants who got durvalumab and tremelimumab who had at least 1 serious adverse reaction. This was 23.1% of participants.

Serious adverse reactions

	Durvalumab alone (out of 13 participants)	Durvalumab and tremelimumab (out of 13 participants)
Abnormal liver function	0.0% (0)	15.4% (2)
Decreased number of platelets, cells that help blood to clot	0.0% (0)	15.4% (2)
Increased bilirubin, a yellow substance made by the liver after breakdown of old red blood cells	0.0% (0)	7.7% (1)
Cell damage causing muscle weakness and pain	7.7% (1)	0.0% (0)

How many participants had adverse reactions?

There were 21 out of 26 participants who had at least 1 adverse reaction. This was 80.8% of participants.

- There were 9 out of the 13 participants who got durvalumab alone who had adverse reactions during the study. This was 69.2% of participants.
- There were 12 out of the 13 participants who got durvalumab and tremelimumab who had adverse reactions during the study. This was 92.3% of participants.

Overall, there were 4 out of 26 participants who had at least 1 adverse reaction that led to stopping treatment. This was 15.4% of participants.

What adverse reactions did the participants have?

The adverse reactions below happened in 3 or more of participants in either treatment group.

The table below shows which adverse reactions the participants had most often.

Most common adverse reactions

Adverse reaction	Durvalumab alone (out of 13 participants)	Durvalumab and tremelimumab (out of 13 participants)
Increased alanine aminotransferase, a liver enzyme	30.8% (4)	30.8% (4)
Increased aspartate aminotransferase, a liver enzyme	30.8% (4)	30.8% (4)
Increased gamma-glutamyl transferase, a liver enzyme	23.1% (3)	15.4% (2)
Decreased appetite	15.4% (2)	30.8% (4)
Diarrhea	15.4% (2)	30.8% (4)
Decreased number of red blood cells	15.4% (2)	23.1% (3)
Nausea	0.0% (0)	23.1% (3)
Decreased hemoglobin, a protein in red blood cells	7.7% (1)	23.1% (3)
Low count of neutrophils, a type of white blood cell	0.0% (0)	23.1% (3)
Decreased number of platelets, cells that help blood to clot	0.0% (0)	23.1% (3)
Decreased number of white blood cells	0.0% (0)	23.1% (3)

How has this study helped participants and researchers?

These results helped the researchers learn more about using durvalumab or durvalumab in combination with tremelimumab in Chinese 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.

Where can I learn more about this study?

You can find more information about this study on the websites listed below, once made available. If a full report of the study results is available, it also can be found here.

- www.clinicaltrials.gov. Once you are on the website, type "**NCT02978482**" into the search box and click "**Search**".
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type "**D419AC00006**" into the search box and click "**Find a Study**".
- http://www.chinadrugtrials.org.cn/. Once you are on the website, type **"CTR20160926"** into the search box and click **"Search"**.

Full Trial Title: A Phase 1/2 Open-label, Multi-center Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of Durvalumab (MEDI4736) in combination with tremelimumab in Chinese Patients with Advanced Malignancies

AstraZeneca Protocol Number: D419AC00006

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

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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