Clinical Study Results

Research Sponsor: AstraZeneca AB

Drugs Studied: Tremelimumab

Study Title: A study to learn how tremelimumab works in participants with advanced solid tumors

Thank you!

Thank you to the participants who took part in the clinical study for the study drug tremelimumab. All of the participants helped researchers learn more about tremelimumab to help people with advanced cancer.

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

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?

The participants could be in the study for up to 36 months, but the entire study took about 30 months to finish. The study started in November 2015 and ended in February 2018.

The study included 64 participants in 5 countries: Belgium, the Netherlands, Poland, South Korea, and the United States.

The sponsor, AstraZeneca AB, 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 people with advanced solid tumors. 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 tremelimumab works in a small number of participants with advanced solid tumors. They also wanted to find out if the participants had any medical problems during the study.

A solid tumor is a type of cancer that starts in an organ of the body. An “advanced” solid tumor usually means that the cancer has spread to other parts of the body. Researchers have found that sometimes, the body’s own immune system may control tumor growth by killing cancer cells. Some treatments may help the immune system to slow down or stop tumor growth. The study drug, tremelimumab, was designed to work in this way.

In this study, the researchers wanted to learn how tremelimumab affected participants with advanced cancer of the bladder, breast, or pancreas. There are currently not many treatment options for people with these types of advanced solid tumors. A treatment called durvalumab is being developed to treat solid tumors that also works on the immune system, but in different way than tremelimumab.

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

- Did any participants have their tumors shrink enough after getting tremelimumab?
- What medical problems did the participants have during the study?

To answer the questions in this study, researchers asked for the help of men and women with advanced cancer of the bladder, breast, or pancreas. There were 32 participants who had bladder cancer and 20 participants who had pancreatic cancer. There were 12 participants who had a type of breast cancer known as “triple negative” breast cancer. The participants in this study were 41 to 85 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 taking. All participants in this study got tremelimumab through a needle into their vein, also called an intravenous infusion.

The study had 2 parts. All participants were in Part 1 of the study for up to 12 months. If a participant’s cancer got worse during Part 1, they had the option to be in Part 2 for up to 12 months. This decision was made by the doctor, in discussion with the participant. It also depended on if certain criteria were met. These options were all discussed with the participants before they got any treatment.

During Part 1, all 64 participants got up to 9 doses of 750 milligrams, known as “mg”, of tremelimumab for up to 12 months. The first 7 doses were given once every 4 weeks. The next 2 doses were given once every 12 weeks.

If a participant’s cancer got worse during or after Part 1, they stopped treatment with tremelimumab. If eligible, they had the option to go on to Part 2.

During Part 2, eligible participants got either an infusion of 1.5 g durvalumab, or 75 mg tremelimumab and 1.5 g durvalumab, for up to 12 months.

In Part 2:

- 5 participants got durvalumab once every 4 weeks, for up to a total of 13 doses.
- 16 participants got durvalumab and tremelimumab once every 4 weeks, for a total of 4 doses. Then, they got durvalumab once every 4 weeks, for up to a total of 9 doses.

What happened during the study?

Before the participants got any treatment, they visited their study site once. The doctors or study site staff checked the overall health of the participants to make sure that they could join the study. The doctors:

- asked questions about the participants’ health
- checked the participants’ heart health using an electrocardiogram, also called an ECG
- reviewed the results of a tumor sample, known as a biopsy, taken before or at the start of the study

The doctors also took pictures of the participants’ tumors using computed tomography or magnetic resonance imaging. Computed tomography is also known as “CT”. Magnetic resonance imaging is also known as “MRI”.

During the study, the participants visited their study site every 4 weeks. There were a total of 13 visits in each part. During Part 1, all of the participants got tremelimumab.

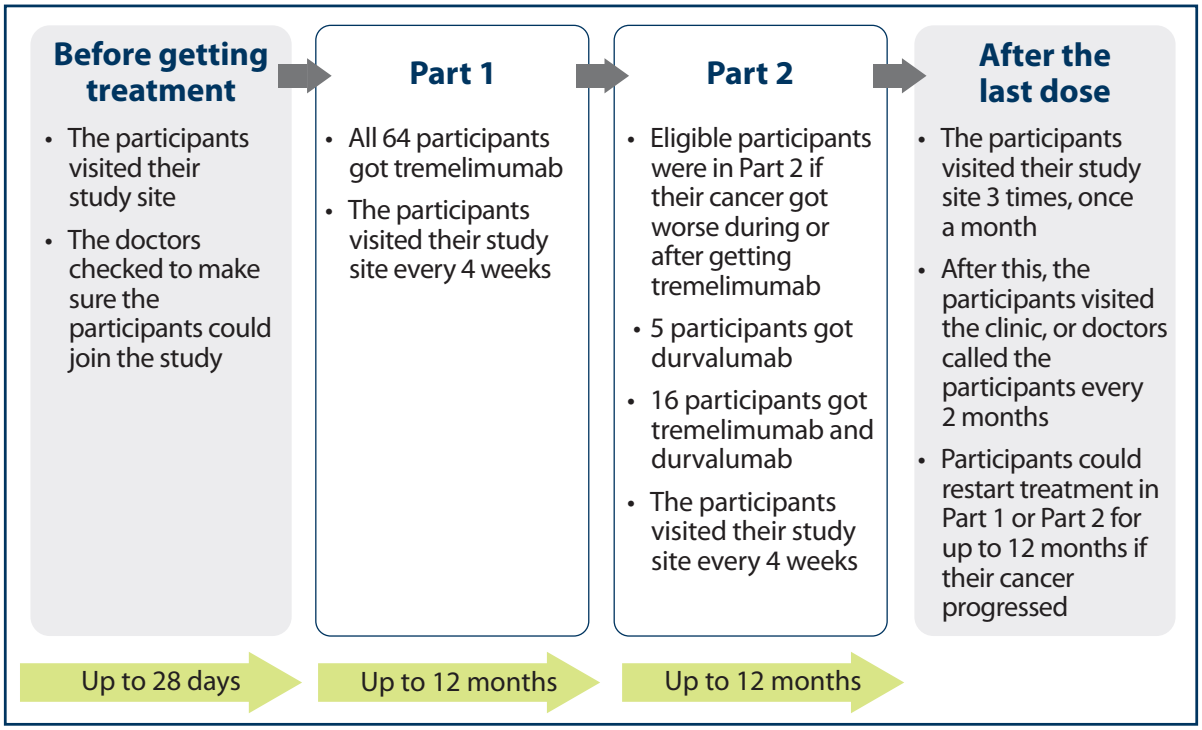
During Part 2, the eligible participants got either durvalumab, or tremelimumab and durvalumab.

At each visit, the doctors checked the health of the participants and took blood and urine samples.

At most visits, the doctors measured the participants' tumor size using CT or MRI.

After the participants got the last dose of treatment, they visited the clinic 3 times, once a month for up to 3 months. The doctors checked on the participants' health, measured the participants' tumors, and took blood and urine samples. After this, doctors checked on the health of participants every 2 months. This was done by a phone call or by a study visit. If the participant's cancer got worse, they could go on to receive another 12 months of study treatment in Part 1 or Part 2. This was done in discussion with the doctor and also depended on if certain criteria were met.

The figure below summarizes the study process.



What were the results of the study?

This is a summary of the main study results. 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.

Did any participants' have their tumors shrink enough after getting tremelimumab?

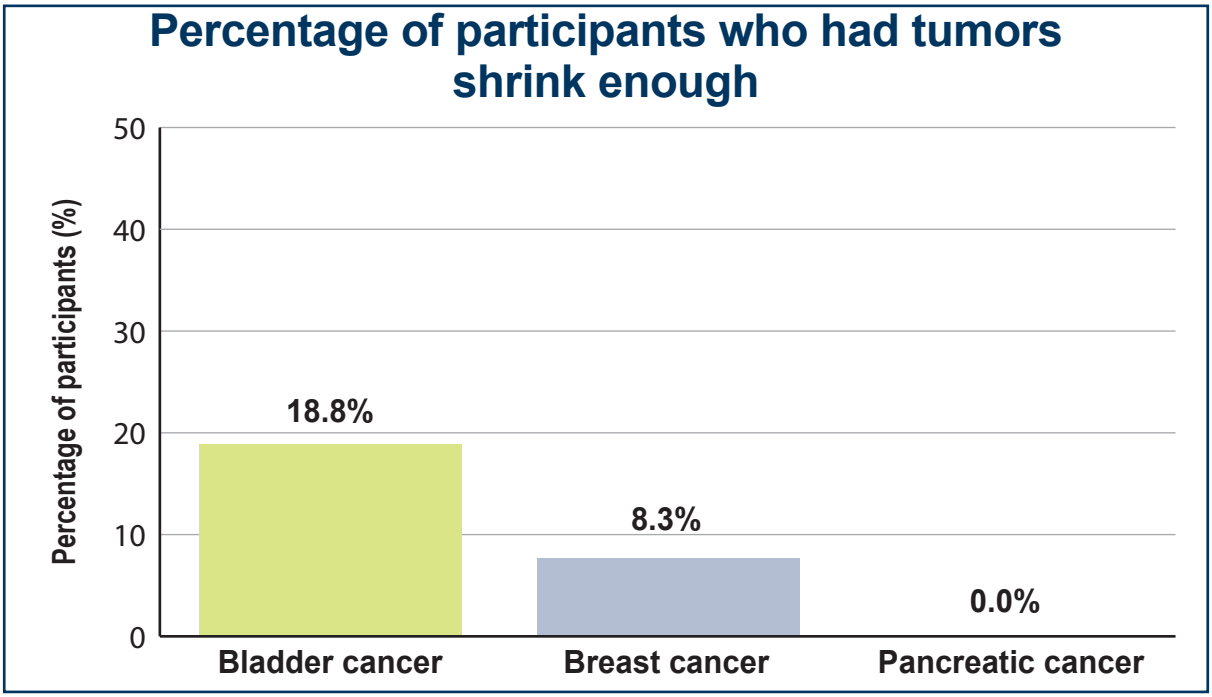
Yes. Overall, researchers found that for some participants their tumors shrank enough after getting tremelimumab. This did not happen for every participant.

To answer this question, the doctors took pictures of the participants' tumors using MRI or CT before and after Part 1. The doctors measured the change in the participants' tumors after 12 months of treatment with tremelimumab. To do this, they used a set of rules called Response Evaluation Criteria in Solid Tumors, also called RECIST. This was done to find out how much the tumor shrank or grew. It was also used to check if other new tumors were growing.

Overall, the researchers found that a small number of participants had their tumors shrink enough after getting tremelimumab:

- 18.8% of participants with bladder cancer had their tumors shrink enough. This was 6 out of 32 participants.
- 8.3% of participants with triple negative breast cancer had their tumors shrink enough. This was 1 out of 12 participants.
- None of the 20 participants with pancreatic cancer had their tumors shrink enough.

The graph below shows these results.



What medical problems did 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 treatment. 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.

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

How many participants had serious adverse reactions?

In Part 1, 23.4% of participants who got tremelimumab had serious adverse reactions. This was 15 out of 64 participants.

- 28.1% of participants with bladder cancer had a serious adverse reaction. This was 9 out of 32 participants.
- 8.3% of participants with triple negative breast cancer had a serious adverse reaction. This was 1 out of 12 participants.
- 25.0% of participants with pancreatic cancer had a serious adverse reaction. This was 5 out of 20 participants.

The table below shows the serious adverse reactions during Part 1.

Serious adverse reactions in Part 1

	Bladder cancer (out of 32 participants)	Breast cancer (out of 12 participants)	Pancreatic cancer (out of 20 participants)
Diarrhea	6.3% (2)	0% (0)	10.0% (2)
Inflammation of the colon	9.4% (3)	0% (0)	5.0% (1)
Vomiting	3.1% (1)	8.3% (1)	0% (0)
Inflammation of the colon caused by the immune system	6.3% (2)	0% (0)	0% (0)
Inflammation of the liver caused by the immune system	0% (0)	0% (0)	5.0% (1)
Inflammation of the lung	0% (0)	0% (0)	5.0% (1)
Hepatotoxicity, also known as liver toxicity	3.1% (1)	0% (0)	0% (0)
Inflammation of the brain's pituitary gland	3.1% (1)	0% (0)	0% (0)
Meningitis	3.1% (1)	0% (0)	0% (0)

In Part 2:

- None of the participants who got only durvalumab had a serious adverse reaction.
- 12.5% of participants who got tremelimumab and durvalumab had serious adverse reactions. This was 2 out of 16 participants. Of the 2 participants who had serious adverse reactions, 1 participant with breast cancer had diarrhea with bleeding, and 1 participant with pancreatic cancer had diarrhea.

How many participants had adverse reactions?

In Part 1, 59.4% of participants who got tremelimumab had at least 1 adverse reaction. This was 38 out of 64 participants.

- 56.3% of participants with bladder cancer had adverse reactions. This was 18 out of 32 participants.
- 50.0% of participants with triple negative breast cancer had adverse reactions. This was 6 out of 12 participants.
- 70.0% of participants with pancreatic cancer had adverse reactions. This was 14 out of 20 participants.

There were 18.8% of participants in Part 1 who stopped study treatment because of adverse reactions. This was 12 out of 64 participants.

In Part 2:

- 20.0% of participants who got only durvalumab had at least 1 adverse reaction. This was 1 out of 5 participants.
- None of the participants who got only durvalumab stopped study treatment because of adverse reactions.
- 31.3% of participants who got tremelimumab and durvalumab had at least 1 adverse reaction. This was 5 out of 16 participants.
- 6.3% of participants who got tremelimumab and durvalumab stopped study treatment because of adverse reactions. This was 1 out of 16 participants.

What adverse reactions did the participants have?

In Part 1, the most common adverse reaction in participants who got tremelimumab was itching of the skin.

The table below shows the most common adverse reactions that happened in more than 3 participants with each cancer type in Part 1. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during Part 1

Adverse reaction	Bladder cancer (out of 32 participants)	Breast cancer (out of 12 participants)	Pancreatic cancer (out of 20 participants)
Skin itching	21.9% (7)	16.7% (2)	30.0% (6)
Tiredness	28.1% (9)	0% (0)	10.0% (2)
Diarrhea	18.8% (6)	16.7% (2)	20.0% (4)
Nausea	18.8% (6)	8.3% (1)	0% (0)
Inflammation of the colon	18.8% (6)	0% (0)	5.0% (1)
Blood test showing raised liver enzyme (ALT)	0% (0)	0% (0)	15.0% (3)
Dry skin	12.5% (4)	0% (0)	5.0% (1)
Vomiting	9.4% (3)	8.3% (1)	0% (0)
Decreased appetite	9.4% (3)	8.3% (1)	5.0% (1)
Headache	9.4% (3)	0% (0)	0% (0)
Blood test showing raised enzyme (lipase)	9.4% (3)	0% (0)	0% (0)
Low levels of thyroid hormone	9.4% (3)	0% (0)	0% (0)

In Part 2:

- The adverse reactions in participants who got only durvalumab were hot flash, back pain, and high levels of calcium in the blood. These happened in 1 participant with bladder cancer.
- The most common adverse reaction in participants who got tremelimumab and durvalumab were diarrhea and low levels of thyroid hormone.

The table below shows the adverse reactions that happened. These adverse reactions may have occurred in more than one participant.

Adverse reactions during Part 2 with tremelimumab and durvalumab

Adverse reaction	Bladder cancer (out of 7 participants)	Breast cancer (out of 5 participants)	Pancreatic cancer (out of 4 participants)
Low levels of thyroid hormone	0% (0)	20.0% (1)	25.0% (1)
Diarrhea	0% (0)	20.0% (1)	25.0% (1)
Skin itching	0% (0)	0% (0)	25.0% (1)
Diarrhea with bleeding	0% (0)	20.0% (1)	0% (0)
Blood test showing raised enzyme (amylase)	0% (0)	20.0% (1)	0% (0)
Rash	14.3% (1)	0% (0)	25.0% (1)
Tiredness	14.3% (1)	0% (0)	0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about using tremelimumab to treat patients with advanced 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.

Other clinical studies with tremelimumab are 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 there.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02527434"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2015-002934-32"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D4884C00001"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase 2, Multi-Center, Open-Label Study of Tremelimumab Monotherapy in Patients with Advanced Solid Tumors

National Clinical Trials number: NCT02527434

AstraZeneca Protocol Number: D4884C00001

AstraZeneca AB sponsored this study and has its headquarters in Mölndal, 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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