AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Treatment Studied: Durvalumab and tremelimumab

Study Purpose: This study was done to learn how durvalumab and tremelimumab work in participants with advanced or metastatic non-small cell lung cancer

Protocol Number: D419AC00003

Thank you

Thank you to the participants and their families for taking part in the clinical study for the study drugs durvalumab and tremelimumab. Durvalumab is also called MEDI4736, and tremelimumab is also called MEDI1123.

You and all of the participants helped researchers learn more about durvalumab and tremelimumab to help people with advanced or metastatic non-small cell lung cancer, also called NSCLC.

AstraZeneca AB sponsored this study and believes 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 study doctor or staff at your study site.

Overview of this study

Why was the research needed?

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

What treatments did the participants get?

The participants in this study got either:

- durvalumab together with tremelimumab
- standard treatment, which was chemotherapy

What were the results of this study?

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

- **Did durvalumab together with tremelimumab help the participants live longer compared with standard treatment?**

  In the Global group, which included participants from across the world: No. The researchers found that there were some differences in how long the participants lived when comparing the durvalumab and tremelimumab combined treatment with the standard treatment. But, the difference between the 2 groups was too small for the researchers to know if durvalumab together with tremelimumab affected how long the participants lived.

  In the China Group, which included participants from China who joined the study later than participants in the Global group: Overall, the researchers found that there were some differences in how long the participants lived after getting durvalumab with tremelimumab or standard treatment. But, the number of participants was too small for the researchers to know if durvalumab together with tremelimumab affected how long the participants lived.

What medical problems happened during the study?

In the Global group: There were 74.8% of participants who had medical problems that the study doctors thought might be related to the study drugs during the study. This was 605 out of 809 participants. The most common medical problem was low levels of red blood cells.

In the China group: There were 87.1% of participants who had medical problems that the study doctors thought might be related to the study drugs during the study. This was 135 out of 155 participants. The most common medical problem was low levels of red blood cells.

More details about the results of this study are included later in this summary.

Where can I learn more about this study?

You can find more information about this study on the websites listed on the last page. When a full report of the study results is available, it also can be found on these websites.

Who took part in this study?

The researchers asked for the help of men and women with advanced or metastatic non-small cell lung cancer, also called "NSCLC".

The participants also:

- had never received chemotherapy for this condition.
- had a life expectancy of at least 12 weeks at the start of the study.
- had no changes in genes called "epidermal growth factor receptor" and "anaplastic lymphoma kinase" in their tumors.

The participants in this study were 27 to 90 years old when they joined.

The study included participants in Argentina, Brazil, Bulgaria, Chile, China, Denmark, Finland, Greece, Hong Kong, India, Israel, Japan, Malaysia, Mexico, Peru, the Philippines, Poland, Portugal, Qatar, Romania, Russia, Saudi Arabia, Singapore, South Korea, Sweden, Turkey, Ukraine, the United Kingdom, and the United States.

The study had 2 groups:

- **The Global group** included 823 participants from across the world.
- **The China group** included 160 participants from China, who joined the study later than participants in the Global group.

Why was the research needed?

Researchers are looking for a better way to treat advanced or metastatic NSCLC. Before a drug can be approved for people to get, 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 together with tremelimumab works in a large number of participants with advanced or metastatic NSCLC. They also wanted to find out if the participants had any medical problems during the study.

In people with cancer, the body is not able to control the growth of some cells. These extra cells can form tumors in any part of the body. NSCLC is a type of lung cancer.

"Advanced" usually means that the cancer continues to grow even with treatment. When cancer cells spread to another part of the body, this is called "metastatic" cancer.

Normally, the immune system fights infections or anything it does not recognize, which can help stop tumors from growing. But in some people with advanced NSCLC, a protein on the tumor cells can interact with certain proteins on the immune cells. This stops the immune cells from recognizing the tumor cells and being able to fight them.

The study drugs, durvalumab and tremelimumab, were designed to stop the tumor cells from interacting with certain proteins on the immune cells. This lets the immune cells recognize the tumor cells and help stop the tumor from growing.

What was the purpose of this study?

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

- Did durvalumab together with tremelimumab help the participants live longer compared with standard treatment?
- What medical problems happened during the study?

The answers to these questions are important to know before other studies can be done to find out if durvalumab together with tremelimumab helps improve the health of people with advanced or metastatic NSCLC.

What treatments did the participants get?

The participants either got durvalumab together with tremelimumab, or they got standard treatment. "Standard treatment" means the treatment that the medical community thinks is appropriate for a condition. In this study, the standard treatment was chemotherapy.

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

A computer program was used to randomly choose the treatment each participant got. 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.

Each treatment was given through a needle into a vein. This is known as an intravenous infusion, also called an IV infusion.

The participants who received standard treatment of chemotherapy got it in periods called "cycles". Each cycle was 3 weeks long. The participants got chemotherapy on Day 1 of each cycle. Some participants also got chemotherapy on Day 8 of each cycle.

The participants got treatment until their condition got worse, they changed their treatment, or they left the study.

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

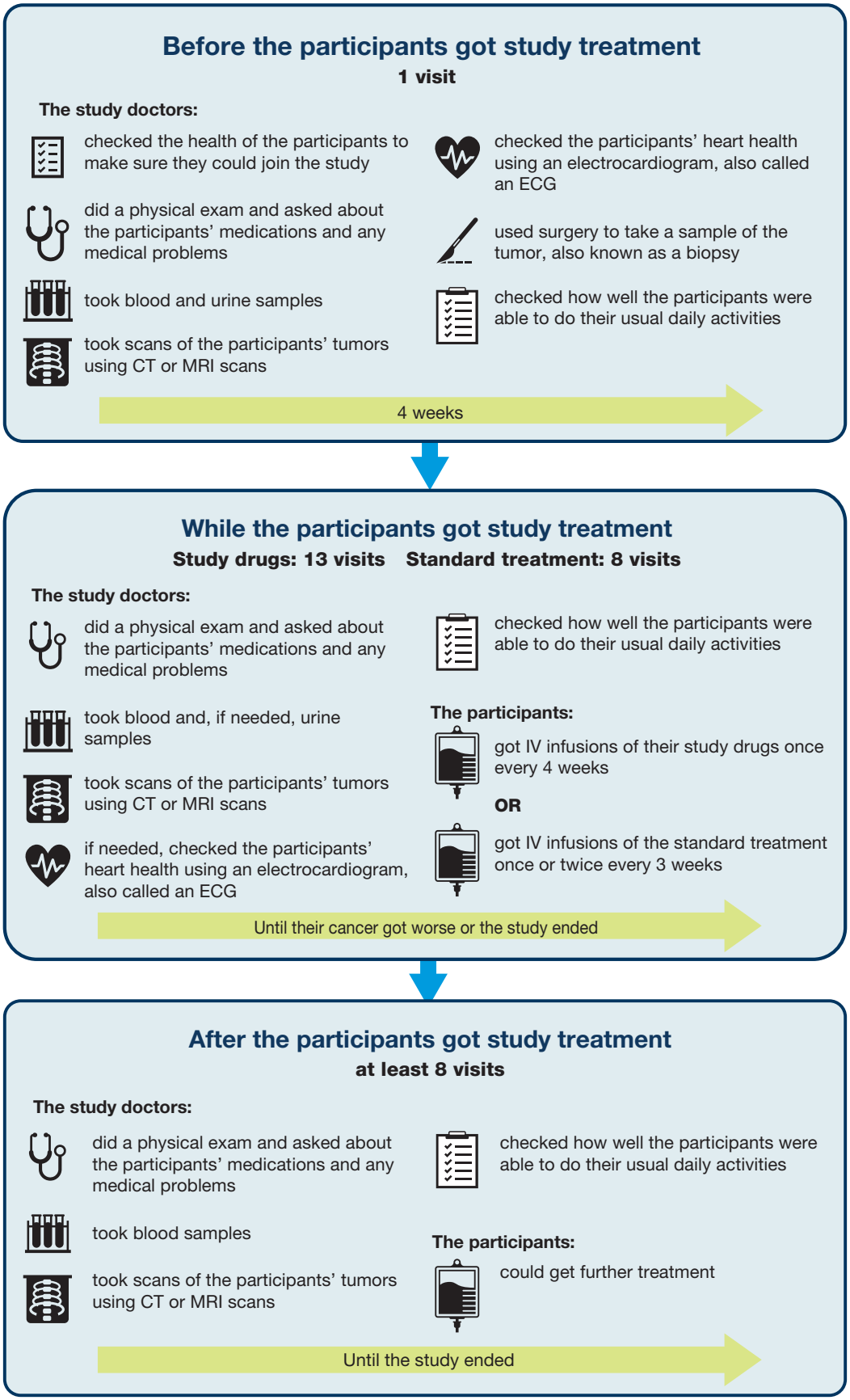
	Durvalumab with tremelimumab		Standard treatment	
	Global group	China group	Global group	China group
	410 participants	78 participants	413 participants	82 participants
	• Durvalumab as an IV infusion • Tremelimumab as an IV infusion		• Chemotherapy as an IV infusion	
	• Durvalumab with tremelimumab once every 4 weeks for 12 weeks **THEN** • Durvalumab alone every 4 weeks for 8 months • If their condition got worse, the participants could get durvalumab with tremelimumab again		• 1 to 2 times every 3 weeks • 4 to 6 cycles, which was about 3 months	

What happened during this study?

The participants were in the study until their condition got worse or they decided to leave the study. The entire study took almost 5 years to finish.

The study started in November 2015 and ended in September 2020.

The chart below shows what happened during the study.



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. A full list of the questions that researchers wanted to answer can be found on the websites listed at the end of this summary. When 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 durvalumab together with tremelimumab help the participants live longer compared with standard treatment?

The researchers tried to answer this question by studying both the Global group and the China group.

In the Global group:

No. The researchers found that there were some differences in how long the participants lived when comparing the durvalumab and tremelimumab combined treatment with the standard treatment. But, the difference between the 2 treatment groups was too small for the researchers to know if durvalumab together with tremelimumab helped the participants live longer.

To answer this question, the researchers measured how long the participants lived after they started the study. The researchers looked at data collected until June 2019. Then, they calculated the average number of months the participants lived during this period.

The researchers were most interested in studying treatment in a group of **participants who had a specific type of tumor.** The researchers thought that participants with this type of tumor might benefit from treatment more than others. There were 129 participants with this type of tumor. The results below are for 69 participants who got durvalumab together with tremelimumab and 60 participants who got the standard treatment.

The researchers found that these participants lived an average of:

- **11.7 months** after getting durvalumab together with tremelimumab
- **9.1 months** after getting the standard treatment

The researchers also studied how long **all of the participants from the Global group** lived after getting durvalumab with tremelimumab or the standard treatment. They studied this in 410 participants who got durvalumab together with tremelimumab and 413 participants who got the standard treatment.

The researchers found that these participants lived an average of:

- **10.9 months** after getting durvalumab together with tremelimumab
- **12.1 months** after getting the standard treatment

In the China Group:

Overall, the researchers found that there were some differences in how long the participants lived after getting durvalumab with tremelimumab or the standard treatment. But, the number of participants was too small for the researchers to know if durvalumab together with tremelimumab helped the participants live longer.

To answer this question, the researchers counted the number of months the participants lived from the start of treatment. The researchers looked at the data collected until September 2020 to calculate the average number of months the participants lived.

The researchers were most interested in studying treatment in a group of **participants who had a specific type of tumor.** The researchers thought that the participants with this type of tumor might benefit from treatment more than others. There were 55 participants with this type of tumor. The results below are for 26 of the participants who got durvalumab together with tremelimumab, and 29 of the participants who got the standard treatment.

The researchers found that the participants lived an average of:

- **15.0 months** after getting durvalumab together with tremelimumab
- **11.7 months** after getting the standard treatment

The researchers also studied how long **all of the participants from the China group** lived after getting durvalumab with tremelimumab or the standard treatment. They studied this in 78 participants who got durvalumab together with tremelimumab and 82 participants who got the standard treatment.

The researchers found that these participants lived an average of:

- **20.0 months** after getting durvalumab together with tremelimumab
- **14.1 months** after getting the standard treatment

In summary, the researchers found that:

- **In the Global group,** taking durvalumab together with tremelimumab did not help the participants live longer compared with standard treatment. The researchers found that the differences between the 2 treatment groups were too small to know if durvalumab together with tremelimumab affected how long the participants lived.
- **In the China group,** the researchers found that there were some differences in how long the participants lived after getting durvalumab with tremelimumab or standard treatment. But, the number of participants was too small for the researchers to know if durvalumab together with tremelimumab affected how long the participants lived.

What medical problems happened during 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 durvalumab and tremelimumab.

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.

In the standard treatment group, there were 14 participants in the Global group and 4 participants in the China group who did not get any study treatment. So, the results for the standard treatment below are for 399 out of 413 participants from the Global group and 78 out of 82 participants from the China group.

In the durvalumab with tremelimumab group, there was 1 participant in the China group who did not get study treatment. So, the results below are for 77 out of 78 participants in the China group and for all 410 participants in the Global group.

Did any adverse reactions happen during this study?

	Durvalumab with tremelimumab		Standard treatment	
	Global group (out of 410 participants)	**China group** (out of 77 participants)	**Global group** (out of 399 participants)	**China group** (out of 78 participants)
How many participants had adverse reactions?	68.3% (280)	79.2% (61)	81.5% (325)	94.9% (74)
How many participants had serious adverse reactions?	19.8% (81)	22.1% (17)	15.5% (62)	19.2% (15)
How many participants stopped getting study treatment due to adverse reactions?	14.6% (60)	3.9% (3)	11.3% (45)	10.3% (8)

What serious adverse reactions happened during this study?

In the Global group:

The most common serious adverse reaction in the Global group was inflammation in the lungs. The table below shows the serious adverse reactions that happened in at least 1.0% of participants during the study. There were other serious adverse reactions, but these happened in fewer participants.

Most common serious adverse reactions in the Global group

Serious adverse reaction	Durvalumab with tremelimumab (out of 410 participants)	Standard treatment (out of 399 participants)
Inflammation in the lungs	3.9% (16)	none
Low levels of red blood cells	none	2.3% (9)
Diarrhea	2.0% (8)	none
Blood infection with low levels of a type of white blood cell called a neutrophil	none	1.5% (6)
Low levels of white blood cells with fever	none	1.3% (5)
Fever	1.2% (5)	none
Low levels of all types of blood cells	none	1.0% (4)
Infection of the lungs	0.7% (3)	1.0% (4)

There were 2.0% of participants who died because of serious adverse reactions. This was 16 out of 809 participants.

- 2.4% of participants who got durvalumab together with tremelimumab died because of serious adverse reactions. This was 10 out of 410 participants.
- 1.5% of participants who got the standard treatment died because of serious adverse reactions. This was 6 out of 399 participants.

In the China group:

The most common serious adverse reaction in the China group was the bone marrow producing fewer blood cells than the body needed. The table below shows the serious adverse reactions that happened in more than 1 participant in at least 1 treatment group. There were other serious adverse reactions, but these happened in fewer participants.

Most common serious adverse reactions in the China group

Serious adverse reaction	**Durvalumab with tremelimumab** (out of 77 participants)	**Standard treatment** (out of 78 participants)
Bone marrow producing fewer blood cells than the body needed. Bone marrow is the spongy tissue inside large bones where blood cells are produced.	none	3.8% (3)
Low levels of red blood cells	none	2.6% (2)
Rash	2.6% (2)	none
Reduced levels of a type of white blood cell called a neutrophil	none	2.6% (2)
Reduced levels of platelets, a type of blood cell that can help form clots	none	2.6% (2)

There were 1.3% of participants who died because of serious adverse reactions. This was 1 out of 77 participants. This participant got durvalumab together with tremelimumab.

What adverse reactions happened during this study?

In the Global group:

The most common adverse reaction in the Global group was low levels of red blood cells. The table below shows the adverse reactions that happened in more than 10.0% of participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions in the Global group

Adverse reaction	**Durvalumab with tremelimumab** (out of 410 participants)	**Standard treatment** (out of 399 participants)
Low levels of red blood cells	5.1% (21)	31.8% (127)
Nausea	8.3% (34)	28.8% (115)
Low levels of a type of white blood cell called a neutrophil	0.7% (3)	17.5% (70)
Feeling tired	7.1% (29)	14.0% (56)
Decreased appetite	6.6% (27)	13.0% (52)
Diarrhea	12.4% (51)	7.3% (29)
Rash	12.4% (51)	5.3% (21)
Vomiting	3.4% (14)	12.0% (48)
Hair loss	0.5% (2)	11.5% (46)
Reduced levels of platelets, a type of blood cell that can help form clots	0.7% (3)	11.3% (45)
An underactive thyroid gland	11.2% (46)	none
Itching	10.2% (42)	1.8% (7)

In the China group:

The most common adverse reaction in the China group was low levels of red blood cells. The table below shows the adverse reactions that happened in more than 15.0% of participants in at least 1 treatment group during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions in the China group

Adverse reaction	**Durvalumab with tremelimumab** (out of 77 participants)	**Standard treatment** (out of 78 participants)
Low levels of red blood cells	3.9% (3)	60.3% (47)
Reduced levels of neutrophils	3.9% (3)	44.9% (35)
Reduced levels of white blood cells	1.3% (1)	44.9% (35)
Nausea	2.6% (2)	42.3% (33)
Reduced levels of platelets, a type of blood cell that can help form clots	1.3% (1)	21.8% (17)
Vomiting	2.6% (2)	24.4% (19)
Increased levels of alanine aminotransferase, a sign of possible liver damage	22.1% (17)	24.4% (19)
Increased levels of amylase, a protein the body makes	23.4% (18)	2.6% (2)
Increased levels of aspartate aminotransferase, a sign of possible liver damage	23.4% (18)	21.8% (17)
Reduced appetite	7.8% (6)	19.2% (15)
Increased levels of lipase, a protein the body makes	16.9% (13)	1.3% (1)
Low levels of white blood cells	none	15.4% (12)
Weakness or lack of energy	6.5% (5)	15.4% (12)

How has this study helped patients and researchers?

This study helped researchers learn more about how durvalumab together with tremelimumab works in participants with advanced or metastatic NSCLC.

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. 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 **"NCT02542293"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2015-002197-21"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D419AC00003"** into the search box and click **"Find a Study"**.

Full Study Title: A Phase III Randomized, Open-Label, Multi-Center, Global Study of MEDI4736 in Combination with Tremelimumab Therapy Versus Standard of Care Platinum-Based Chemotherapy in First Line Treatment of Patients with Advanced or Metastatic Non Small-Cell Lung Cancer (NSCLC) (NEPTUNE)

AstraZeneca AB Protocol Number: D419AC00003

National Clinical Trials Number: NCT02542293

EudraCT Number: 2015-002197-21

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.

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