Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca

Drugs Studied: Durvalumab (MEDI4736) and tremelimumab (MEDI1123)

Study Title: A study to learn more about how durvalumab affects patients with non-small cell lung cancer when taken alone or with tremelimumab

Thank you

Thank you to the participants who took part in the clinical study for the study drugs durvalumab and tremelimumab, and to their families. All of the participants and their families helped researchers learn more about using these study drugs to help people who have non-small-cell lung cancer.

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

If you or a family member 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 study started in August 2015. At the time this summary was written, the study was still ongoing. As of October 2018, the participants who were in the study participated in the study for an average of about 1.5 years.

The study included 1,118 participants. The study was done in the following countries:

Australia, Belgium, Canada, France, Germany, Hungary, Italy, Japan, the Netherlands, the Republic of Korea, Russia, Spain, Switzerland, Taiwan, Thailand, Vietnam, and the United States.

The sponsor reviewed the data collected 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 patients who have advanced or metastatic non-small-cell lung cancer. 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.

Cancer is a disease that happens when the body cannot control the growth of cells. Many of these extra cells can form tumors, which can start in any part of the body. “Advanced” means that the tumor is unlikely to be removed completely by surgery. “Metastatic” means that the cancer has spread to other parts of the body to form new tumors, called metastases. “Non-small cell cancer”, the most common type of lung cancer, means that the cancer cells are large compared to another common type of lung cancer.

In this study, the researchers wanted to find out if durvalumab and tremelimumab work as treatments for a large number of participants who have advanced or metastatic non-small-cell lung cancer. They also wanted to find out if the participants had any medical problems with these treatments during the study.

There are treatments for advanced or metastatic non-small-cell lung cancer. But these treatments may not stop cancer cells from growing or spreading. They may also cause other medical problems. This is because these treatments sometimes attack healthy cells in addition to cancer cells. Researchers think that durvalumab and tremelimumab may be able to help the body’s immune system attack only the cancer cells.

In this study, researchers compared durvalumab and tremelimumab to a non-small-cell lung cancer treatment known as a “standard of care” treatment, or SOC treatment. A treatment is considered an SOC treatment if the medical community thinks it is an appropriate and widely used treatment for a disease.

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

- Did the participants who got durvalumab alone live longer compared to the participants who got SOC treatment?
- Did the participants who got durvalumab and tremelimumab together live longer compared to the participants who got SOC treatment?
- Did the participants who got durvalumab and tremelimumab together live longer without their cancer getting worse compared to the participants who got SOC treatment?
- Did the participants’ cancer symptoms and overall health change after getting durvalumab alone or durvalumab and tremelimumab together compared to SOC treatment?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women who had advanced or metastatic non-small-cell lung cancer. The participants in this study were 28 to 87 years old.

What kind of study was this?

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

In this study, the participants got their treatment during periods called “cycles.” The participants could take part in as many cycles as they wanted unless their cancer got worse. If their cancer got worse, the participants stopped the treatment cycles. If the study treatment was helping the participants’ cancer at the end of the study, the participants could choose to continue treatment.

There were 3 treatment groups during the study: Group 1, Group 2, and Group 3. The treatments are listed below:

- Group 1 - durvalumab alone
- Group 2 - durvalumab and tremelimumab
- Group 3 - SOC treatment

The study doctors chose the SOC treatment that the participants got. In this study, the doctors used different combinations of cancer drugs for the SOC treatment. These cancer drugs are listed below

- paclitaxel
- carboplatin
- gemcitabine
- cisplatin
- pemetrexed

Durvalumab, tremelimumab, and the SOC treatment were given through a needle into the vein. This is known as intravenous infusion, also called IV infusion. The doses were measured in milligrams per kilograms of body weight, also called mg/kg.

A computer program was used to randomly choose the treatment that 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.

The table below shows the treatments the participants got in this study, as well as the lowest and highest number of cycles the participants received. The table also includes the median number of cycles in each group. A median is the middle number in a set of numbers and is found between the lowest and highest numbers.

Group	Treatment given	Cycle length	Number of cycles
Group 1 (durvalumab alone) 369 participants	• 20 mg/kg of durvalumab 1 time each cycle	4 weeks	1 to 38 cycles (median of 4 cycles)
Group 2 (durvalumab and tremelimumab) 371 participants	• 20 mg/kg of durvalumab 1 time each cycle for 4 cycles • 1 mg/kg of tremelimumab 1 time each cycle for 4 cycles • after 4 cycles, 20 mg/kg of durvalumab 1 time each cycle	4 weeks	1 to 41 cycles (median of 4 cycles)
Group 3 (SOC treatment) 352 participants	• SOC treatment 1 time during each cycle	3 weeks	1 to 46 cycles (median of 6 cycles)

What happened during the study?

Before the study started, the participants visited their study site 1 time over the course of 4 weeks. At this visit, the doctors checked to make sure they could join the study. The doctors:

- did a physical examination
- asked the participants about their medical history and what medicines they were taking
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG
- measured the participants' tumors using computed tomography scans, also called CT scans, and magnetic resonance imaging scans, also called MRI scans
- took tissue samples and pictures of the tumors
- gave the participants surveys that asked them about their symptoms and how they were feeling

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

During the study, the participants could take part in as many cycles as they wanted unless their cancer got worse. If their cancer got worse, the participants stopped the treatment cycles. If the study treatment was helping the participants' cancer at the end of the study, the participants could choose to continue treatment.

All of the participants visited their study site 1 time during each cycle and got their treatment 1 time at each visit.

At the end of the study, the participants visited their study site 1 time each month for 4 months. Then, they visited their study site 1 time every 2 months until the study ended. At these visits, the study doctors gave the participants surveys and did tests and measurements to check their overall health.

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. A full list of the questions the 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.

At the time this summary was written, the study was still ongoing. The results presented below were collected from August 2015 to October 2018.

Some tumors have features that allow the immune system to strongly attack cancer cells when patients are given treatments like durvalumab and tremelimumab. So, the researchers in this study first focused on the results for the 488 participants whose tumors had these features. The results for these 488 participants are summarized below.

Did the participants who got durvalumab alone live longer compared to the participants who got SOC treatment?

Yes. Overall, the researchers found that the participants who got durvalumab alone lived longer after getting treatment than the participants who got SOC treatment.

To answer this question, the researchers compared:

- the "hazard ratio" between the 2 groups
- how likely it was that the participants would be alive 2 years after starting the study
- how long the participants lived after starting the study

To compare some of the study results, the researchers determined if the differences between the results were "statistically significant". If the difference between 2 numbers is considered to be statistically significant, it means the researchers believe that the difference is caused by the study drug. Researchers define what a statistically significant difference between numbers will be before the study starts. They choose this difference based on previous research and studies.

Hazard ratio

A hazard ratio is a mathematical formula presented as a percentage. It compares over time how likely it is for something to happen in one group of participants compared to another group.

For the hazard ratio, the researchers found that the participants who got durvalumab alone were 24% less likely to die during the study compared to the participants who got SOC treatment. But, the difference between the 2 groups was too small for the researchers to consider this difference to be statistically significant.

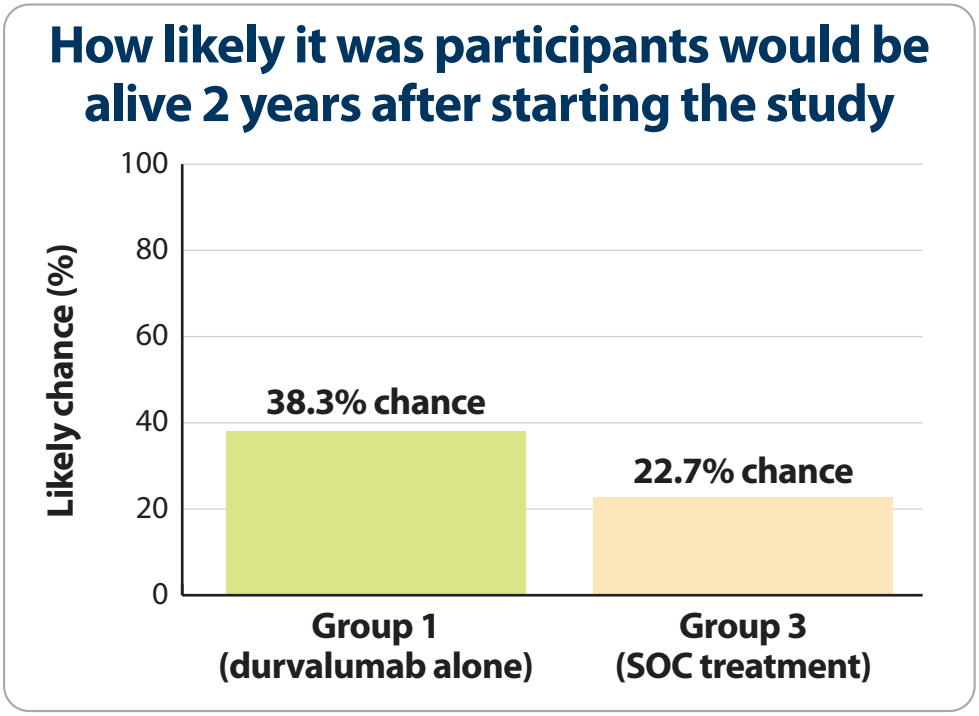
How likely it was that the participants would be alive 2 years after starting the study

The researchers used a percentage to determine how likely it was that the participants would be alive 2 years after starting the study.

The researchers found that:

- There was a 38.3% chance that the participants who got durvalumab alone would still be alive 2 years after starting the study.
- There was a 22.7% chance that the participants who got SOC treatment would still be alive 2 years after starting the study.

The figure below shows these results.



How long the participants lived after starting the study

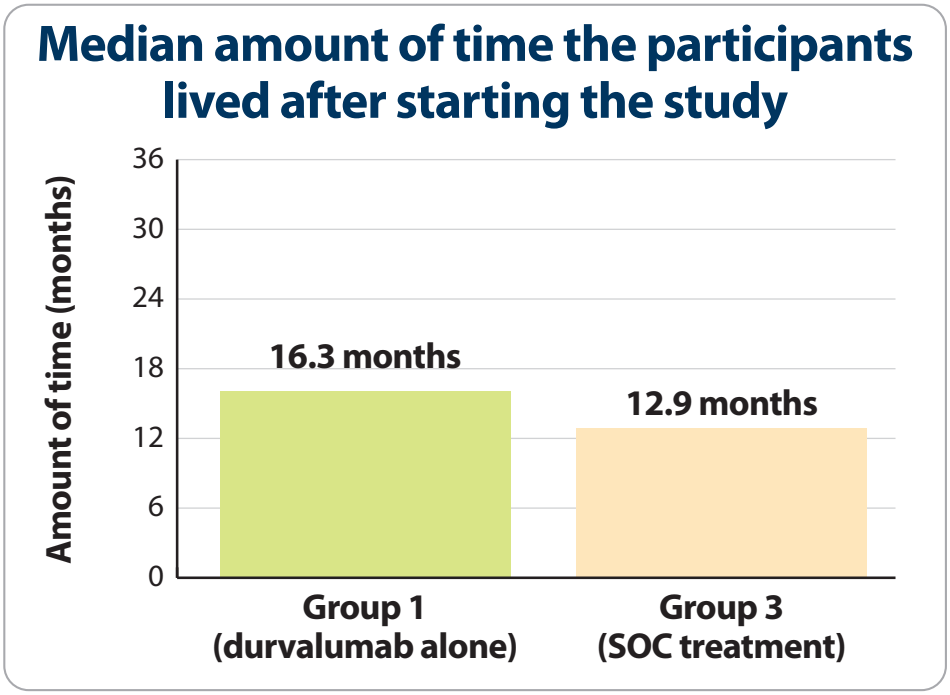
To find out how long the participants lived after starting the study, the researchers used the median length of time they lived.

The researchers found that the participants who got durvalumab alone lived longer after starting the study compared to the participants who got SOC treatment. But, the difference between the 2 groups was too small for the researchers to consider this difference to be statistically significant.

Overall, the researchers found that after starting the study:

- The participants who got durvalumab alone lived for a median of about 16.3 months.
- The participants who got SOC treatment lived for a median of about 12.9 months.

The figure below shows these results.



Did the participants who got durvalumab and tremelimumab together live longer compared to the participants who got SOC treatment?

No. Overall, the researchers found that the participants who got durvalumab and tremelimumab together did not live significantly longer than the participants who got SOC treatment.

To answer this question, the researchers compared:

- the “hazard ratio” between the 2 groups
- how likely it was that the participants would be alive 2 years after starting the study
- how long the participants lived after starting the study

Hazard ratio

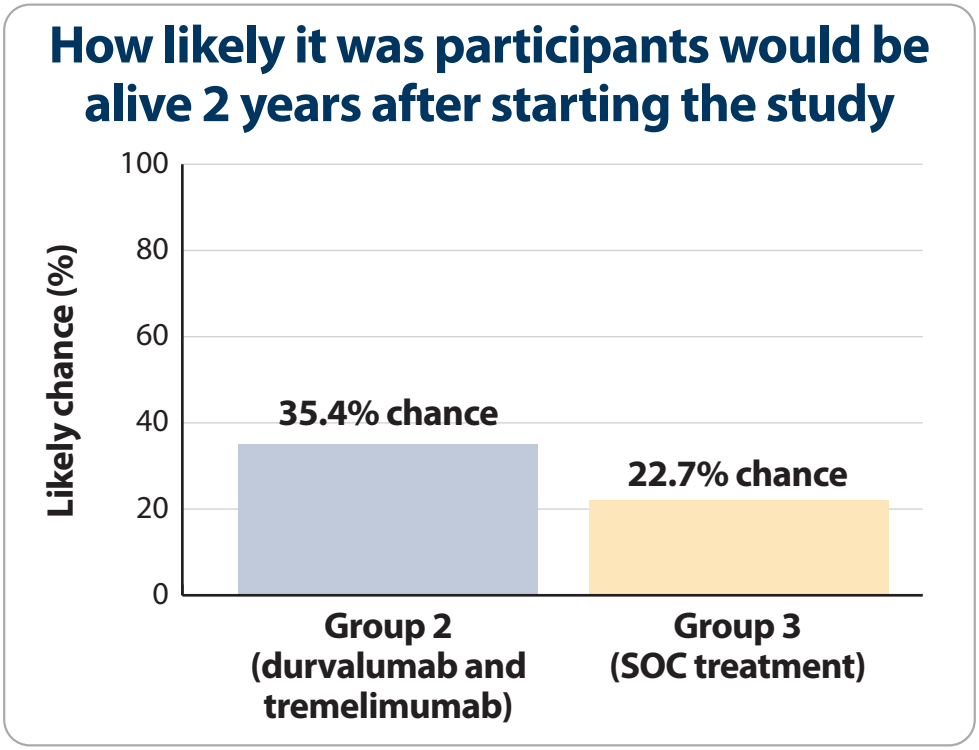
For the hazard ratio, the researchers found that the participants who got durvalumab and tremelimumab together were 15% less likely to die during the study compared to the participants who got SOC treatment. But, the researchers did not consider this 15% difference between the 2 groups to be statistically significant.

How likely it was that the participants would be alive 2 years after starting the study

The researchers found that:

- There was a 35.4% chance that the participants who got durvalumab and tremelimumab together would still be alive 2 years after starting the study.
- There was a 22.7% chance that the participants who got SOC treatment would still be alive 2 years after starting the study.

The figure below shows these results.



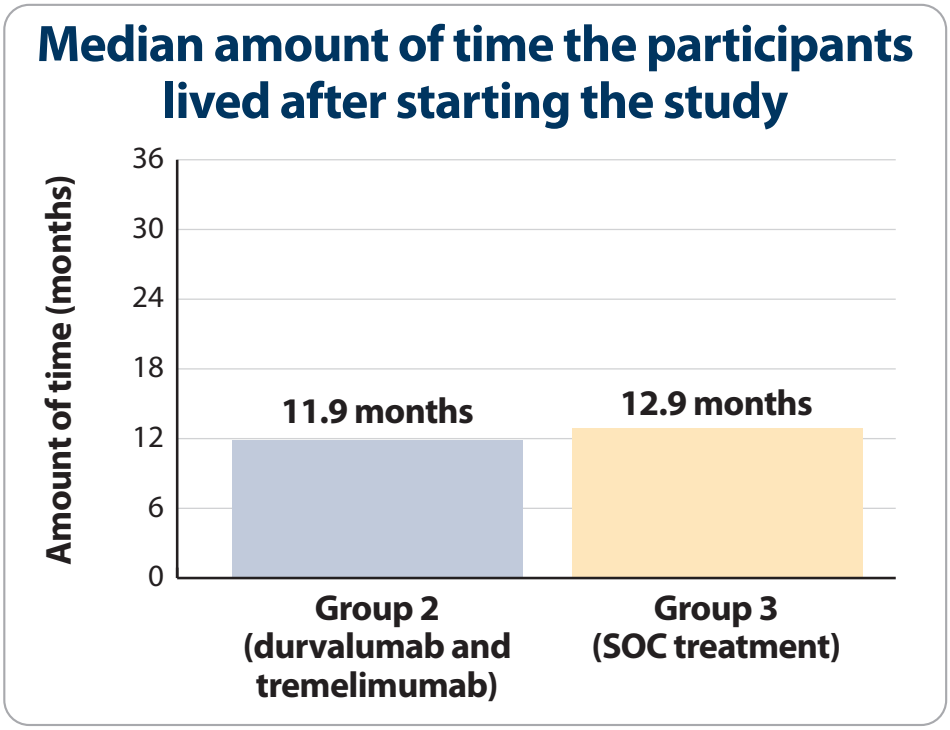
How long the participants lived after starting the study

The researchers found that the participants who got durvalumab and tremelimumab together did not live longer compared to the participants who got SOC treatment.

Overall, the researchers found that after starting the study:

- The participants who got durvalumab and tremelimumab together lived for a median of about 11.9 months.
- The participants who got SOC treatment lived for a median of about 12.9 months.

The figure below shows these results.



Did the participants who got durvalumab and tremelimumab together live longer without their cancer getting worse compared to the participants who got SOC treatment?

No. The researchers found that the participants who got durvalumab and tremelimumab together did not live longer without their cancer getting worse compared to the participants who got SOC treatment.

To answer this question, the researchers compared:

- the “hazard ratio” between the 2 groups
- how long the participants lived before their cancer got worse
- the percentage of participants likely to be alive without their cancer getting worse 1 year after starting treatment

Hazard ratio

For the hazard ratio, the researchers found that the participants who got durvalumab and tremelimumab together were 5.0% more likely to have their cancer get worse during the study compared to the participants who got SOC treatment. But, the researchers did not consider this 5.0% difference between the 2 groups to be statistically significant.

How long participants lived before their cancer got worse

To find out how long the participants lived before their cancer got worse, the doctors measured the change in tumor size throughout the study by using MRI and CT scans and taking pictures of the tumors. The doctors measured the change in tumor size using a set of rules called Response Evaluation Criteria in Solid Tumors, also called RECIST. They also used these and other tests and measurements to determine how long the participants lived before their cancer got worse. Then, they compared these results from the participants who got durvalumab and tremelimumab together with the results from the participants who got SOC treatment using a median.

The researchers found that:

- The participants who got durvalumab and tremelimumab together lived a median of about 3.9 months before their cancer got worse.
- The participants who got SOC treatment lived a median of about 5.4 months before their cancer got worse.

Percentage of participants likely to be alive without their cancer getting worse 1 year after starting treatment

The researchers found that the participants who got durvalumab and tremelimumab together were more likely to be alive 1 year after starting treatment compared to the participants who got SOC treatment. But, the difference between the 2 groups was too small for the researchers to think that durvalumab and tremelimumab given together increased the chance of participants being alive 1 year after starting treatment without their cancer getting worse.

The researchers found that:

- 25.8% of the participants who got durvalumab and tremelimumab together were likely to be alive 1 year after starting treatment without their cancer getting worse.
- 14.3% of the participants who got SOC treatment were likely to be alive 1 year after starting treatment without their cancer getting worse.

Did the participants' cancer symptoms and overall health change after getting durvalumab alone or durvalumab and tremelimumab together compared to SOC treatment?

Yes. Overall, the researchers found that the participants who got durvalumab alone or durvalumab and tremelimumab together had a change in their symptoms or overall health compared to the participants who got SOC treatment.

To answer this question, the doctors gave the participants surveys before they got any study treatment and throughout the study. These surveys asked the participants about their cancer symptoms and how they were feeling. The researchers compared the results from before the first study treatment with the results from the study treatment visits to see if there were changes.

The researchers found that compared to the participants who got SOC treatment:

- The participants who got durvalumab alone had fewer overall cancer symptoms over time.
- The participants who got durvalumab and tremelimumab together had fewer overall cancer symptoms over time.
- The participants who got durvalumab alone had a longer time until their cancer symptoms got worse.
- The participants who got durvalumab and tremelimumab together had a longer time until their cancer symptoms got worse.
- The participants who got durvalumab alone were more likely to have an increase in appetite and a decrease in nausea, vomiting, diarrhea, and feeling tired. They showed an improved ability to engage in social activities and create or maintain relationships with other people.
- The participants who got durvalumab and tremelimumab together were less likely to feel tired. They showed an improved ability to perform everyday tasks, engage in social activities, and create or maintain relationships with other people.

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 study doctors thought might be related to the study treatments. These medical problems are called "adverse reactions". An adverse reaction is considered "serious" when it is life threatening, causes lasting problems, requires hospital care, or leads to death.

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

Out of the 1,118 participants in the study, 1,092 participants got at least 1 dose of study treatment. So, the results below include information for only 1,092 of the 1,118 participants.

How many participants had serious adverse reactions?

The table below shows the serious adverse reactions that happened in at least 1.0% of participants in any treatment group during the study. There were other serious adverse reactions that happened during the study, but those happened in fewer participants.

Most common serious adverse reactions during the study

	Group 1 Durvalumab alone (out of 369 participants)	Group 2 Durvalumab and tremelimumab (out of 371 participants)	Group 3 SOC (out of 352 participants)
Inflammation in the lung	1.4% (5)	2.2% (8)	0.0% (0)
Diarrhea	0.5% (2)	3.0% (11)	0.6% (2)
Scarring of tissue in the lungs	0.3% (1)	1.9% (7)	0.0% (0)
Inflammation of the large bowel	0.3% (1)	1.6% (6)	0.0% (0)
Liver damage from study treatment	0.0% (0)	1.3% (5)	0.0% (0)
Feeling tired	0.0% (0)	1.1% (4)	0.0% (0)
Decreased number of red blood cells	0.0% (0)	0.0% (0)	3.1% (11)
Decreased number of white blood cells, red blood cells, and platelets in the blood	0.0% (0)	0.0% (0)	1.7% (6)

There were 0.5% of participants who got durvalumab alone who died from serious adverse reactions. This was 2 out of 369 participants. These serious adverse reactions were:

- pneumonia caused by a virus
- inflammation in the lung

There were 1.6% of participants who got durvalumab and tremelimumab together who died from serious adverse reactions. This was 6 out of 371 participants. These serious adverse reactions were:

- scarring of the tissue in the lung, which happened in 2 participants
- blockage in the small bowel
- inflammation of the pancreas
- liver failure
- sudden death from unknown cause

There were 0.9% of participants who got SOC treatment who died from serious adverse reactions. This was 3 out of 352 participants. These serious adverse reactions were:

- pus around the lungs
- low number of platelets in the blood, which can make it difficult for the body to stop bleeding
- inflammation in the lung

How many participants had adverse reactions?

The table below shows how many participants had adverse reactions during the study.

Adverse reactions during the study

	Group 1 Durvalumab alone (out of 369 participants)	Group 2 Durvalumab and tremelimumab (out of 371 participants)	Group 3 SOC (out of 352 participants)
How many participants had adverse reactions during the study?	54.2% (200)	60.1% (223)	83.0% (292)
How many participants had serious adverse reactions during the study?	8.7% (32)	20.5% (76)	14.5% (51)
How many participants stopped treatment because of adverse reactions?	5.4% (20)	13.2% (49)	9.4% (33)

What adverse reactions did the participants have?

The most common adverse reaction during the study was nausea.

The table below shows the adverse reactions that happened in at least 10.0% of participants in any treatment group during the study. There were other adverse reactions that happened during the study, but those happened in fewer participants.

Adverse reactions during the study

	Group 1 Durvalumab alone (out of 369 participants)	Group 2 Durvalumab and tremelimumab (out of 371 participants)	Group 3 SOC (out of 352 participants)
Nausea	3.5% (13)	7.5% (28)	35.8% (126)
Feeling tired	7.3% (27)	12.7% (47)	18.2% (64)
Decreased number of red blood cells	2.2% (8)	1.3% (5)	31.3% (110)
Decreased appetite	5.1% (19)	8.6% (32)	16.5% (58)
Diarrhea	8.4% (31)	12.7% (47)	6.8% (24)
Rash	7.0% (26)	10.5% (39)	8.8% (31)
Irritated, itchy skin	8.7% (32)	12.7% (47)	3.7% (13)
Feeling weak	5.4% (20)	4.9% (18)	10.5% (37)
Vomiting	1.4% (5)	2.7% (10)	16.8% (59)
Decreased number of white blood cells, which can increase the risk of infection	0.5% (2)	0.3% (1)	18.2% (64)
Decreased number of platelets in the blood, which can make it difficult for the body to stop bleeding	0.3% (1)	0.8% (3)	12.2% (43)
Constipation	1.6% (6)	0.8% (3)	10.2% (36)
Hair loss	0.0% (0)	0.8% (3)	11.1% (39)

How has this study helped patients and researchers?

This study helped researchers learn more about using durvalumab alone and durvalumab together with tremelimumab to help patients who have advanced or metastatic non-small-cell lung 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.

Further clinical studies with durvalumab and tremelimumab are ongoing and planned.

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 this website, type **"NCT02453282"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2015-001279-39"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D419AC00001"** into the search box, and click **"Find a Study"**.

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

AstraZeneca Protocol Number: D419AC00001

AstraZeneca sponsored this study and has its headquarters at 1800 Concord Pike in Wilmington, Delaware.

The phone number for the AstraZeneca Information Center is +1-877-240-9479.

Thank you

Clinical study participants and their families 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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