

Research Sponsor: AstraZeneca AB

Drug Studied: Durvalumab and tremelimumab

Study Title: A study to learn how durvalumab alone or together with tremelimumab, with chemotherapy, worked and about their safety in participants with advanced small-cell lung cancer

Thank you

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

You and all of the participants helped researchers learn more about how durvalumab alone or together with tremelimumab, with chemotherapy, worked to help people with advanced small-cell lung cancer, also called ES-SCLC.

AstraZeneca 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 talk to the study doctor or staff at your study site.

Overview



Why was the research needed?

Researchers are looking for a better way to treat advanced small-cell lung cancer, also called ES-SCLC. 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.



What treatments did the participants take?

The participants in this study got either:

- > durvalumab with chemotherapy
- > durvalumab and tremelimumab with chemotherapy
- > chemotherapy alone



What were the results of the study?

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

- > **Did durvalumab alone or together with tremelimumab, with chemotherapy, help the participants live longer than chemotherapy alone?**

Overall, the researchers found that the participants who got durvalumab with chemotherapy **did** live longer than those who got chemotherapy alone. However, the participants who got durvalumab and tremelimumab with chemotherapy **did not** live longer than those who got chemotherapy alone.

- > **Did the participants feel that durvalumab alone or together with tremelimumab, with chemotherapy, affected their symptoms and quality of life?**

Overall, the researchers found that the participants in all treatment groups felt that some specific symptoms got better after getting study treatment. The participants who got durvalumab with chemotherapy had a longer time before their quality of life got worse than the participants who got chemotherapy alone. The participants who got durvalumab and tremelimumab with chemotherapy had a similar quality of life to those who got chemotherapy alone.



What medical problems did the participants have during this study?

There were 89.8% of participants who had medical problems that the study doctors thought might be related to the study drugs during the study. The most common medical problem was having very low levels of a type of white blood cell called a neutrophil. This problem was seen in participants from all 3 treatment groups. 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 can also be found on those websites.



Who took part in this study?

The researchers asked for the help of men and women with ES-SCLC. The participants in this study were 28 to 88 years old when they joined. All of the participants had tumors that were large enough to measure using CT or MRI scans. Most of the participants were current or previous smokers.

Overall, the study included participants in Argentina, Austria, Brazil, Bulgaria, China, Czech Republic, France, Germany, Hungary, Israel, Italy, Japan, Netherlands, Poland, Romania, Russia, Slovakia, South Korea, Spain, Taiwan, Turkey, Ukraine, and the United States.

Most of the participants in the study from China and Taiwan joined the study later than the participants in the rest of the world. This group of participants is known as the China Part. The results for these participants are in a different summary.

The main report this summary is based on is for 805 participants in the rest of the world, including 6 participants in China and Taiwan. This group of participants is known as the Global Part.



Why was the research needed?

Researchers are looking for a better way to treat people with ES-SCLC. 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.

In this study, the researchers wanted to find out how durvalumab alone or together with tremelimumab, with chemotherapy, worked in a large number of participants with ES-SCLC. 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 cells. The extra cells can form tumors. When cancer progresses to a late stage, tumors spread to other parts of the body or grow beyond the organ where they started. Sometimes there are too many tumors or they are too difficult to remove by surgery.

Normally, the immune system can help stop tumors from growing. But, in people with ES-SCLC, proteins on the tumor cells can interact with certain proteins on the immune cells. This may stop the immune cells from recognizing the tumor cells and being able to attack them.

The study drugs, durvalumab and tremelimumab, were designed to stop the tumor cells from interacting with some of these proteins on the immune cells.

In this study, the researchers wanted to find out how durvalumab, alone or together with tremelimumab, worked in participants with ES-SCLC when given with chemotherapy.



What was the purpose of this study?

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

- > Did durvalumab, alone or together with tremelimumab, with chemotherapy help the participants live longer than chemotherapy alone?
- > Did the participants feel that durvalumab, alone or together with tremelimumab, with chemotherapy affected their symptoms and quality of life?
- > What medical problems did the participants have during this study?

The answers to these questions are important to find out if durvalumab alone or together with tremelimumab, with chemotherapy, works to help improve the lifespan of people with ES-SCLC.



What treatments did the participants take?

In the Global Part of this study:

- > 268 participants got durvalumab with chemotherapy
- > 268 participants got durvalumab and tremelimumab with chemotherapy
- > 269 participants got chemotherapy alone




This was an “open-label” study. This means the participants, 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.

For the first 12 weeks of the study, the participants got their treatment once every 3 weeks. Each of the study treatments were given through a needle in a vein, also known as an IV infusion.

After about 12 weeks:

- > All of the participants who were getting durvalumab stopped getting chemotherapy and continued getting durvalumab once every 4 weeks until they left the study or the study doctors thought the treatments were no longer helping them.
- > The participants who were also getting tremelimumab got 1 more dose of tremelimumab and then continued getting durvalumab once every 4 weeks until they left the study or the study doctors thought the treatments were no longer helping them.
- > The participants who were getting chemotherapy alone could get an additional 2 rounds of chemotherapy and also brain radiation therapy if the study doctors thought they needed it. Doctors sometimes give brain radiation therapy to people with lung cancer just in case the tumors have spread to the brain but are still too small to see.

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

	First 12 weeks of the study	After 12 weeks of study treatment
Group 1 (268 participants) 	<ul style="list-style-type: none">• Durvalumab with chemotherapy by IV infusions once every 3 weeks	<ul style="list-style-type: none">• Durvalumab by IV infusion once every 4 weeks
Group 2 (268 participants) 	<ul style="list-style-type: none">• Durvalumab and tremelimumab with chemotherapy by IV infusions once every 3 weeks	<ul style="list-style-type: none">• Durvalumab by IV infusion once every 4 weeks and• 1 more dose of tremelimumab
Group 3 (269 participants) 	<ul style="list-style-type: none">• Chemotherapy alone by IV infusions once every 3 weeks	<ul style="list-style-type: none">• 2 more rounds of chemotherapy and brain radiation therapy if the study doctors thought the participants needed it

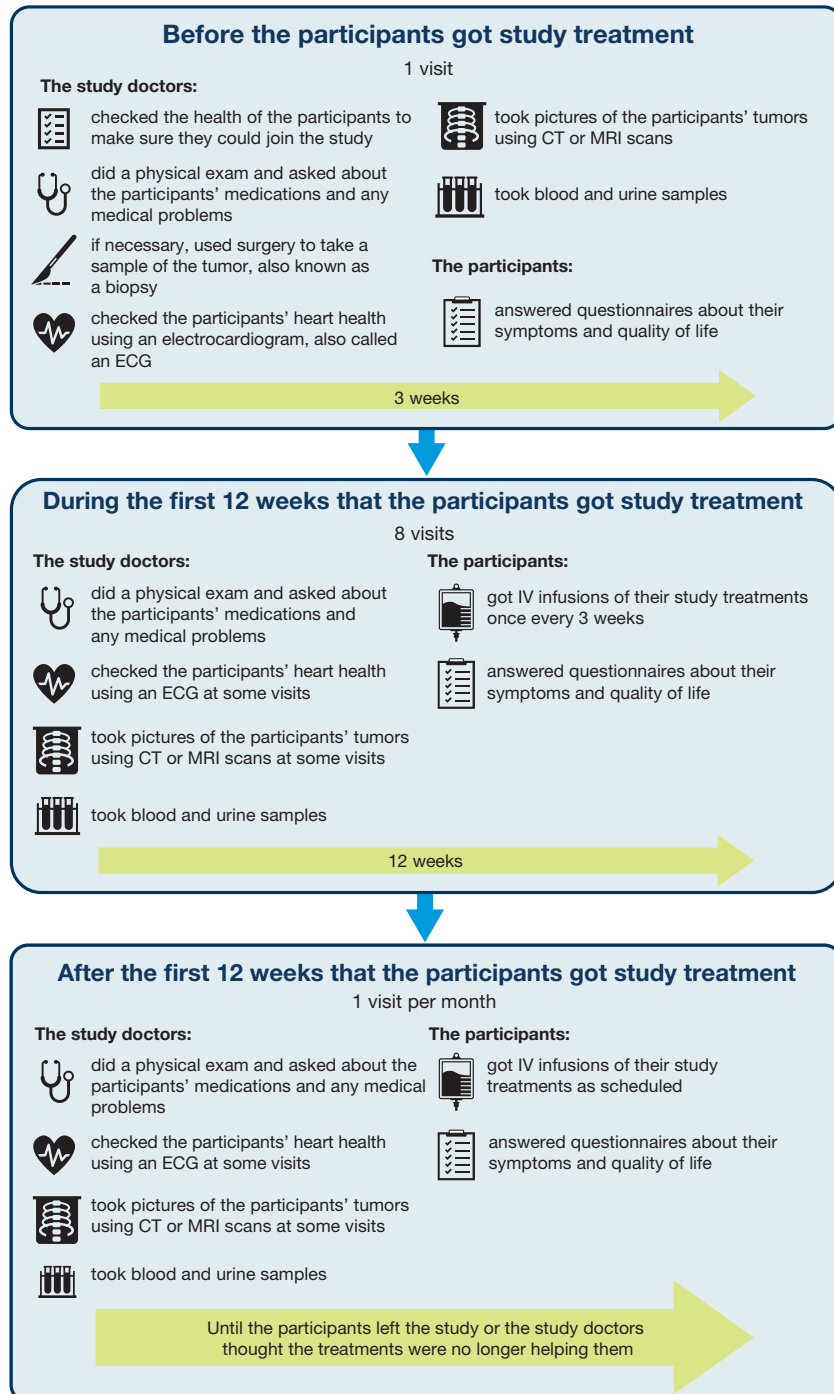


What happened during this study?

The entire study has taken nearly 3 years to finish.

The Global Part of this study started in April 2017 and is expected to end in March 2021.

The chart below shows what happened during this study.





What were the results of this study?

This is a summary of the main results from the Global Part of this study overall. The results from the China Part can be found in a different summary. 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. 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 alone or together with tremelimumab, with chemotherapy, help the participants live longer than chemotherapy alone?

Overall, the researchers found that the participants who got durvalumab with chemotherapy **did** live longer than those who got chemotherapy alone. The participants who got durvalumab and tremelimumab with chemotherapy **did not** live longer than those who got chemotherapy alone.

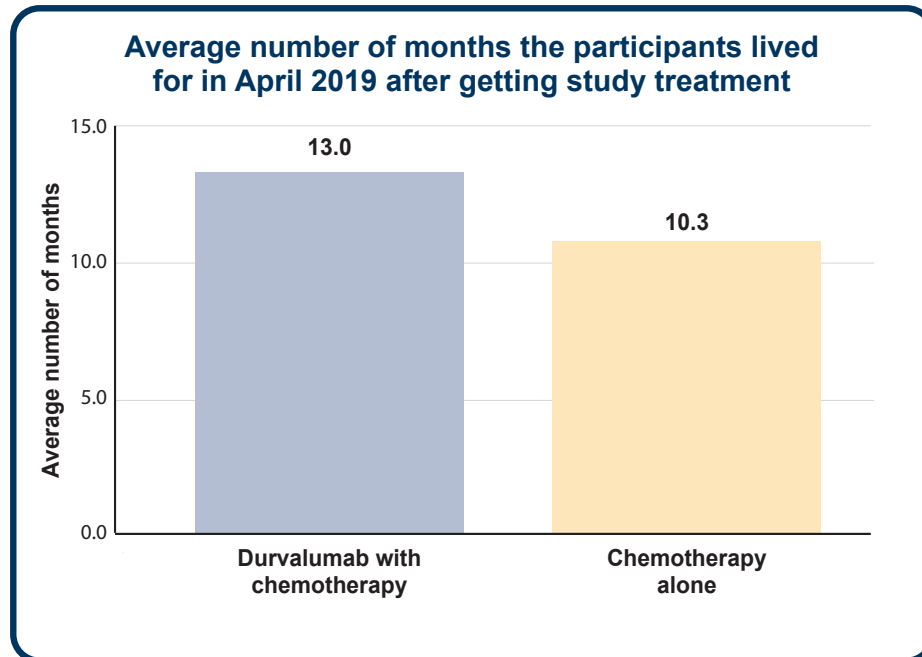
To answer this question, the researchers counted the average number of months the participants lived during and after the study. They did this at 2 different times to get 2 different sets of results. The first time was in April 2019 and the second time was in March 2020.

When the researchers looked at the results in April 2019, they compared the participants who got durvalumab with chemotherapy with those who got chemotherapy alone.

In April 2019, the researchers found that the participants lived for an average of:

- > 13.0 months after getting durvalumab with chemotherapy
- > 10.3 months after getting chemotherapy alone

The results for April 2019 are shown in the chart below.



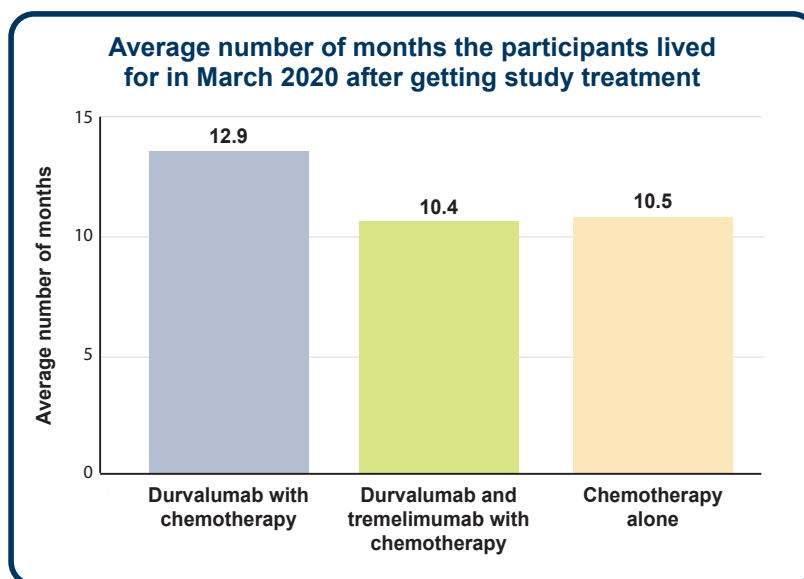
When the researchers looked at the results in March 2020, they did 2 comparisons:

- the participants who got durvalumab with chemotherapy compared with those who got chemotherapy alone
- the participants who got durvalumab and tremelimumab with chemotherapy compared with those who got chemotherapy alone

In March 2020, the researchers found that the participants lived for an average of:

- 12.9 months after getting durvalumab with chemotherapy
- 10.4 months after getting durvalumab and tremelimumab with chemotherapy
- 10.5 months after getting chemotherapy alone

The results for March 2020 are shown in the chart below.



Did the participants feel that durvalumab alone or together with tremelimumab, with chemotherapy, affected their symptoms and quality of life?

Overall, the researchers found that the participants in all treatment groups felt that some specific symptoms improved after getting study treatment. The researchers also found that the participants felt that their quality of life did not get worse during the study.

To answer this question, the study doctors asked the participants to complete 2 different questionnaires. These were:

- > The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30, also known as EORTC QLQ-C30
- > The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Lung Cancer 13, also known as EORTC QLQ-LC13

The answers to each questionnaire received a “score” based on the severity of their symptoms or the quality of life. The main answers the researchers wanted to compare were about fatigue, shortness of breath, cough, low appetite, and chest pain. The researchers measured how much the participants’ scores changed over 1 year. A bigger change in score means that the symptoms got better.

The researchers also did these measurements at 2 different times, in April 2019 and in March 2020. When the researchers looked at the results in April 2019, they compared the participants who got durvalumab with chemotherapy with those who got chemotherapy alone.

The table below shows the average change in the participants' scores for each main symptom in April 2019. A bigger change in score means that the symptoms got better.

Average change in score over 1 year for each main symptom in April 2019

Average change in score over 1 year	Durvalumab with chemotherapy	Chemotherapy alone
Fatigue	7.4	5.6
Shortness of breath	8.6	8.0
Cough	17.1	17.1
Low appetite	12.7	8.2
Chest pain	8.1	9.4

When the researchers looked at the results in March 2020, they compared the participants who got durvalumab and tremelimumab with chemotherapy with those who got chemotherapy alone. A bigger change in score means that the symptoms got better.

The table below shows the average change in the participants' scores for each main symptom in March 2020.

Average change in score over 1 year for each main symptom in March 2020

Average change in score	Durvalumab and tremelimumab with chemotherapy	Chemotherapy alone
Fatigue	6.1	6.3
Shortness of breath	6.8	6.6
Cough	15.1	14.6
Low appetite	8.7	9.5
Chest pain	7.4	7.0



What medical problems happened during this study?

This section is a summary of the medical problems the participants had during the Global Part of this study that the study doctors thought might be related to the study drugs. The medical problems that the participants had during the China Part of this study are in a different summary. 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 the study drugs.

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.

There were 8 participants who left the study before getting any study treatment. So, the results below are for 797 out of 805 participants who got at least 1 dose of study treatment.

Did any adverse reactions happen during this study?

	Durvalumab with chemotherapy (out of 265 participants)	Durvalumab and tremelimumab with chemotherapy (out of 266 participants)	Chemotherapy alone (out of 266 participants)
How many participants had adverse reactions?	89.4% (237)	90.2% (240)	89.8% (239)
How many participants had serious adverse reactions?	13.2% (35)	25.2% (67)	18.8% (50)
How many participants stopped taking study treatment due to adverse reactions?	6.0% (16)	16.2% (43)	4.9% (13)

What serious adverse reactions happened during this study?

The most common serious adverse reaction was a fever with very low levels of a type of white blood cell called a neutrophil.

The table below shows the serious adverse reactions that happened in more than 1 participant in total during the study. There were other serious adverse reactions, but these happened in fewer participants.

Most common serious adverse reactions

Serious adverse reaction	Durvalumab with chemotherapy (out of 265 participants)	Durvalumab and tremelimumab with chemotherapy (out of 266 participants)	Chemotherapy alone (out of 266 participants)
Fever with very low levels of a type of white blood cell called a neutrophil	3.8% (10)	3.8% (10)	4.5% (12)
Low levels of red blood cells	1.5% (4)	3.0% (8)	4.5% (12)
Diarrhea	0.4% (1)	2.3% (6)	1.1% (3)
Low levels of blood cells that help form blood clots	0.0% (0)	2.3% (6)	3.0% (8)
Low levels of a white blood cell called a neutrophil	0.8% (2)	1.9% (5)	2.6% (7)
Lung infection with inflammation, also called pneumonia	0.4% (1)	1.5% (4)	0.4% (1)
Blood clot in the lungs	0.0% (0)	1.5% (4)	0.0% (0)
Inflammation of the large intestine	0.0% (0)	1.5% (4)	0.0% (0)
Inflammation of the large and small intestine	0.0% (0)	1.5% (4)	0.0% (0)
Inflammation of the lungs	0.8% (2)	1.1% (3)	0.0% (0)
Inflammation of the liver	0.0% (0)	1.1% (3)	0.0% (0)
Low levels of all types of blood cells	1.5% (4)	0.8% (2)	1.1% (3)
Scarring and stiffness in the lungs	0.5% (1)	0.8% (2)	0.0% (0)
Low levels of adrenal hormones	0.0% (0)	0.8% (2)	0.0% (0)
High levels of thyroid hormones	0.0% (0)	0.8% (2)	0.0% (0)
Low levels of thyroid hormones	0.0% (0)	0.8% (2)	0.0% (0)
Inflammation of the brain	0.0% (0)	0.8% (2)	0.0% (0)
Inflammation of the liver caused by immune cells	0.0% (0)	0.8% (2)	0.0% (0)
Rash	0.0% (0)	0.8% (2)	0.0% (0)
Kidney failure	0.0% (0)	0.8% (2)	0.0% (0)
Unexplained death	0.0% (0)	0.8% (2)	0.0% (0)

Serious adverse reaction	Durvalumab with chemotherapy (out of 265 participants)	Durvalumab and tremelimumab with chemotherapy (out of 266 participants)	Chemotherapy alone (out of 266 participants)
Type 1 diabetes	0.8% (2)	0.4% (1)	0.0% (0)
General worsening health	0.8% (2)	0.4% (1)	0.0% (0)
Low levels of sodium in the blood	0.0% (0)	0.4% (1)	0.8% (2)
Nausea	0.0% (0)	0.4% (1)	0.8% (2)
Vomiting	0.0% (0)	0.4% (1)	0.8% (2)
Lung infection	0.0% (0)	0.4% (1)	0.4% (1)
Kidney injury	0.8% (2)	0.0% (0)	0.8% (2)
Blood infection	0.4% (1)	0.0% (0)	0.4% (1)
General weakness	0.4% (1)	0.0% (0)	0.4% (1)
Low levels of potassium in the blood	0.0% (0)	0.0% (0)	0.8% (2)

There were 2.5% of participants who died because of serious adverse reactions. This was 20 out of 797 participants.

- > 2.3% of participants who got durvalumab with chemotherapy died because of serious adverse reactions. This was 6 out of 265 participants.
- > 4.5% of participants who got durvalumab and tremelimumab with chemotherapy died because of serious adverse reactions. This was 12 out of 266 participants.
- > 0.8% of participants who got chemotherapy alone died because of serious adverse reactions. This was 2 out of 266 participants.

What adverse reactions happened during this study?

The most common adverse reaction was having very low levels of a type of white blood cell called a neutrophil.

The table below shows the adverse reactions that happened in 15.0% or more participants in any group during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

Adverse reaction	Durvalumab with chemotherapy (out of 265 participants)	Durvalumab and tremelimumab with chemotherapy (out of 266 participants)	Chemotherapy alone (out of 266 participants)
Very low levels of a type of white blood cell called a neutrophil	39.2% (104)	41.4% (110)	43.6% (116)
Low levels of red blood cells	32.1% (85)	31.6% (84)	38.7% (103)
Hair loss	28.3% (75)	27.1% (72)	32.0% (85)
Nausea	27.9% (74)	24.8% (66)	27.8% (74)
Low levels of a blood cell that helps form blood clots	14.0% (37)	18.4% (49)	18.0% (48)
Fatigue	11.3% (30)	15.4% (41)	13.5% (36)



How has this study helped patients and researchers?

This study helped the researchers learn that durvalumab with chemotherapy helped participants with ES-SCLC live longer without lowering their quality of life. The researchers learned that adding tremelimumab as well did not help the participants. This study also helped the researchers understand about the safety of these treatments.

The results of this study were used to seek approval for using durvalumab with chemotherapy in people who have ES-SCLC.

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 1 study. Other studies may provide new information or different results.

Further clinical studies with durvalumab alone or together with tremelimumab in ES-SCLC and other types of cancer are ongoing.



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 **"NCT03043872"** into the search box and click **"Search"**.
- > <http://www.clinicaltrialsregister.eu> Once you are on the website, click **"Home and Search"**, then type **"2016-001203-23"** in the search box and click **"Search"**.
- > www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D419QC00001"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase III, Randomized, Multicenter, Open-Label, Comparative Study to Determine the Efficacy of Durvalumab or Durvalumab and Tremelimumab in Combination With Platinum-Based Chemotherapy for the First-Line Treatment in Patients with Extensive Disease Small-Cell Lung Cancer (SCLC) (CASPIAN)

AstraZeneca Protocol Number: D419QC00001

National Clinical Trials number: NCT03043872

EudraCT number: 2016-001203-23

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 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.



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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