Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca

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

Study Title: A study to compare how treatment with durvalumab alone or treatment with durvalumab combined with tremelimumab affect patients with cancer of the head and neck compared to chemotherapy treatment

Thank you

Thank you to the participants who took part in the clinical study for the study drugs durvalumab and tremelimumab. All of the participants and their family members helped researchers learn whether these study drugs could help people who have cancer of the head and neck.

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

If you or your 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 September 2015. At the time this summary was written, the study was still ongoing. As of September 2018, the participants who were in the study participated in the study for an average of about 2 years.

The study included 736 participants. The study was completed in the following countries: Argentina, Australia, Belgium, Brazil, Bulgaria, Chile, Croatia, the Czech Republic, France, Germany, Hungary, Israel, Italy, Japan, Poland, Romania, Russia, Serbia, South Korea, Spain, Taiwan, Ukraine, and the United States.

The sponsor reviewed the data collected throughout the study 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 recurrent or metastatic cancer of the head and neck. 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. These extra cells can come together to form tumors, which can start in any part of the body. “Recurrent” means that the cancer was treated, but later returned. “Metastatic” means that the cancer has spread to other parts of the body. There are treatments for recurrent and metastatic cancer of the head and neck. 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 instead of cancer cells.

In this study, the researchers wanted to find out more about using durvalumab alone and durvalumab and tremelimumab together as treatments for participants who had recurrent or metastatic cancer of the head and neck. The researchers wanted to compare these 2 treatments to a cancer treatment known as a “standard of care” chemotherapy 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 researchers also wanted to find out if the participants had any medical problems with these treatments during the study.

Durvalumab is also called MEDI4736, and tremelimumab is also called MEDI1123. Researchers think that these drugs may be able to help the body’s immune system attack cancer cells.

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

- Did the participants who received the study drugs live longer compared to the participants who received SOC treatment?
- Did the study drugs affect how the participants felt about their health?
- 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 recurrent or metastatic cancer of the head and neck. The participants in this study were 22 to 84 years old.

What kind of study was this?

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

A computer program was used to randomly choose the treatment that each participant got. This helps make sure that the treatment groups are chosen fairly and that the groups are comparable at the time treatment is started. Researchers do this so that comparing the results of each treatment is as fair as possible.

What happened during the study?

Before the study started, the participants visited their study site. At this visit, the study doctors checked to make sure they could join the study. The doctors:

- did a physical examination
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG
- measured the size of the participants' tumors using computerized tomography scans, also called CT scans, or using magnetic resonance imaging scans, also called MRI scans
- took new tumor samples or asked participants for tumor samples that had already been taken
- asked the participants about their medical history, how they were feeling, and what medicines they were taking

During the study, the participants got study treatment in 4-week periods called "cycles". The participants could take part in as many cycles as they wanted unless their cancer got worse or if they had medical problems that caused them to stop taking study treatment. 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.

Throughout the study, the researchers continued checking the participants' overall health and tumors. The researchers also gave the participants surveys throughout the study that asked them how they were feeling.

There were 3 treatment groups in the study: Group 1, Group 2, and Group 3.

The participants in Group 1 got durvalumab and tremelimumab. The participants in Group 2 got durvalumab alone. The participants in Group 3 got an SOC treatment that was chosen by the study doctors from a specific list of treatments for managing the participants' cancer.

Durvalumab and tremelimumab were given through a needle into a vein. This is known as intravenous treatment, also called IV treatment. The SOC treatment was given as IV treatment or taken as a tablet or capsule.

There were 13 of the 736 participants who left the study before getting any treatment. These participants left the study either because they did not meet the study requirements or because they chose to leave the study for personal reasons.

The table below shows the treatments for each group.

	Group 1	Group 2	Group 3
What treatments were given?	• 246 participants got durvalumab and tremelimumab	• 237 participants got durvalumab alone	• 240 participants got an SOC treatment
How were the treatments given?	• Durvalumab and tremelimumab were given by IV	• Durvalumab was given by IV	• SOC treatment was given by IV or as a tablet or capsule
When were the treatments given?	Participants got durvalumab and tremelimumab: • 1 time each cycle for 4 cycles until their cancer got worse After 4 cycles, participants could get: • durvalumab 2 times each cycle until their cancer got worse	Participants got durvalumab: • 2 times each cycle until their cancer got worse	Participants got an SOC treatment: • throughout each cycle until their cancer got worse

At the end of the study, the doctors checked the participants' overall health and tumors. The doctors also gave the participants surveys that asked them how they were feeling.

After this visit, the doctors continued checking the participants' overall health and tumors every 4 weeks until the study finished.

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.

Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

Even though 13 of the 736 participants did not get study treatment, the researchers were still able to study their overall results. So, the below results are for all 736 participants.

Did the participants who received the study drugs live longer compared to the participants who received SOC treatment?

No. Overall, the participants in Group 1 and Group 2 did not live longer after starting treatment compared to the participants in Group 3.

To answer this question, the researchers studied the percentage of participants who were still alive at different time points throughout the study. They also studied the number of participants who died. The researchers recorded these results until about 2 years after the participants started treatment.

The researchers found that:

6 months after starting treatment

- 52.9% of participants in Group 1 were still alive
- 58.0% of participants in Group 2 were still alive
- 66.1% of participants in Group 3 were still alive

12 months after starting treatment

- 30.4% of participants in Group 1 were still alive
- 37.0% of participants in Group 2 were still alive
- 30.5% of participants in Group 3 were still alive

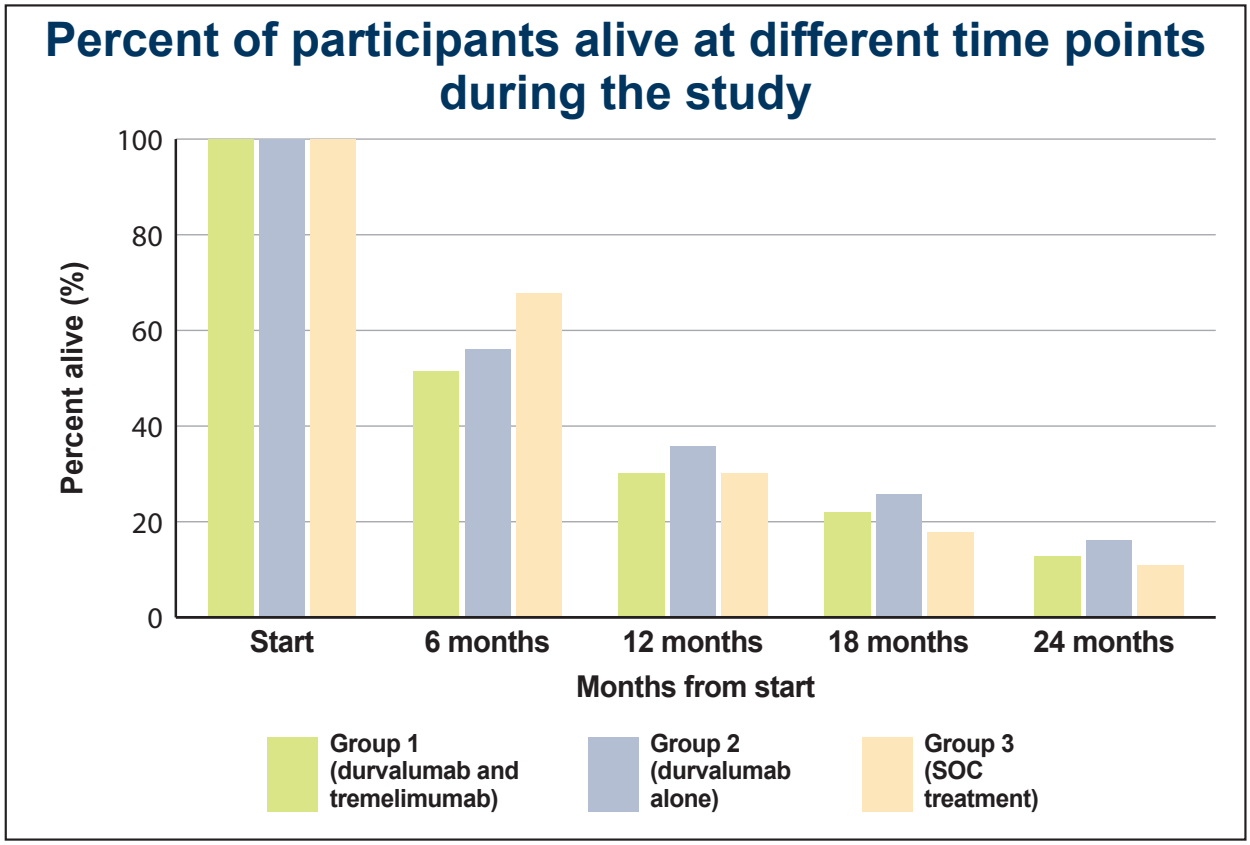
18 months after starting treatment

- 21.0% of participants in Group 1 were still alive
- 25.4% of participants in Group 2 were still alive
- 17.8% of participants in Group 3 were still alive

24 months after starting treatment

- 13.3% of participants in Group 1 were still alive
- 18.4% of participants in Group 2 were still alive
- 10.3% of participants in Group 3 were still alive

The figure below shows these results:

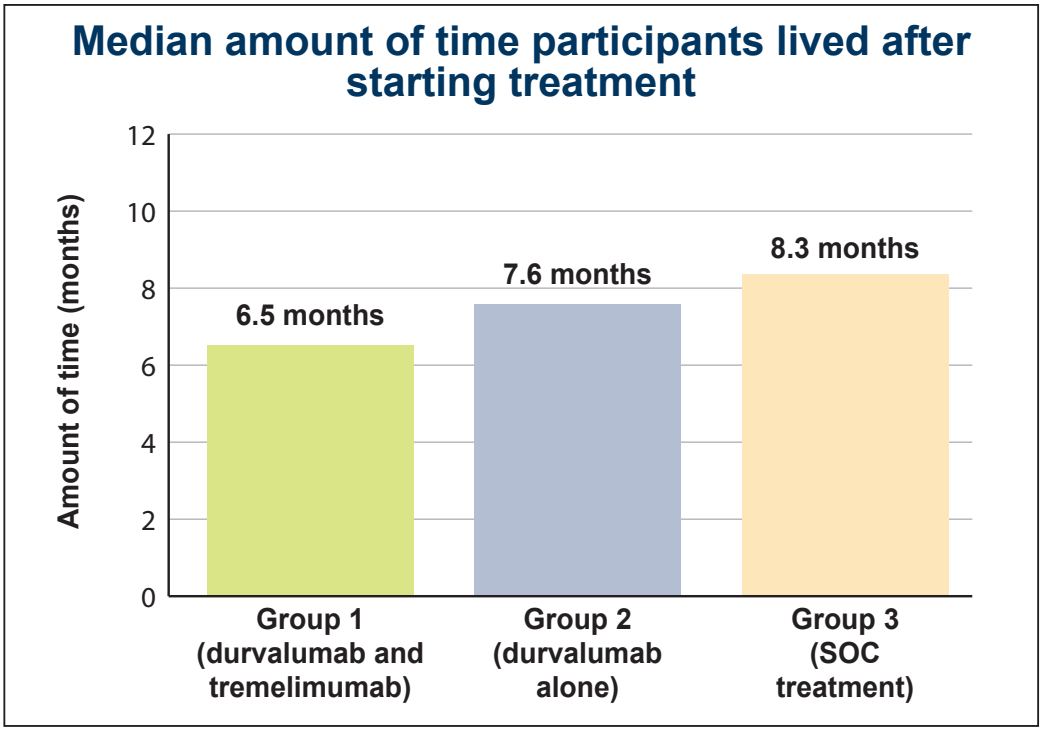


The researchers also studied the amount of time the participants lived after they started treatment. The researchers measured this by using the “median” number of months the participants lived after starting the study. A median is the middle number in a set of numbers. It is between the lowest and highest numbers.

The researchers found that overall:

- The participants in Group 1 lived for a median of 6.5 months after starting the study.
- The participants in Group 2 lived for a median of 7.6 months after starting the study.
- The participants in Group 3 lived for a median of 8.3 months after starting the study.

The figure below shows these results.



Did the study drugs affect how the participants felt about their health?

No. In all 3 treatment groups, the participants had very little change in how they felt about their health.

To answer this question, the researchers gave the participants surveys throughout the study that asked them how they were feeling. Each time the participants took a survey, they got a score based on their responses. Overall, the participants' survey scores did not change very much throughout the study. The survey scores were similar between participants in the 3 treatment groups. This meant that the participants had very little change in how they felt about their health.

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 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 be related to cancer, the study drugs, or neither. 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.

There were 13 of the 736 participants who did not get study treatment. So, the below adverse reaction information is for the 723 participants who did get study treatment.

How many participants had serious adverse reactions?

There were 11.8% of participants in Group 1 who had serious adverse reactions during the study. This was 29 out of 246 participants.

There were 7.2% of participants in Group 2 who had serious adverse reactions during the study. This was 17 out of 237 participants.

There were 6.3% of participants in Group 3 who had serious adverse reactions during the study. This was 15 out of 240 participants.

In Group 1, 0.8% of participants died from serious adverse reactions they had during the study. This was 2 out of 246 participants. These serious adverse reactions were:

- swelling in the throat from a medical tube used to help a person breathe
- an unknown serious adverse reaction. This serious adverse reaction was unknown because the participant died at home, and the doctors could not determine the exact cause of death.

In Group 2, 1.7% of participants died from serious adverse reactions they had during the study. This was 4 out of 237 participants. These serious adverse reactions were:

- change in mental state
- bleeding
- increase in the level of the antidiuretic hormone, also known as ADH, in the body. An increase in ADH lowers the body's ability to get rid of water.
- an unknown serious adverse reaction. This serious adverse reaction was unknown because the participant died at home, and the doctors could not determine the exact cause of death.

In Group 3, none of the participants died from serious adverse reactions they had during the study.

The table below shows the serious adverse reactions that happened in at least 2 participants during the study. There were other serious adverse reactions that happened during the study, but these happened in fewer participants.

Most common serious adverse reactions during the study

	Group 1 (durvalumab and tremelimumab) out of 246 participants	Group 2 (durvalumab alone) out of 237 participants	Group 3 (SOC treatment) out of 240 participants
Swelling in the lungs	0.8% (2)	1.3% (3)	0.0% (0)
Pneumonia	0.8% (2)	0.0% (0)	0.8% (2)
Anemia (decrease in the amount of red blood cells in the blood)	1.2% (3)	0.0% (0)	0.0% (0)
Diarrhea	0.8% (2)	0.0% (0)	0.4% (1)
An unknown serious adverse reaction	0.4% (1)	0.4% (1)	0.0% (0)
Increase in level of ADH	0.0% (0)	0.8% (2)	0.0% (0)
Decrease in neutrophils, which are a type of white blood cell (may increase the risk of infection)	0.0% (0)	0.0% (0)	0.8% (2)

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 and tremelimumab) out of 246 participants	Group 2 (durvalumab alone) out of 237 participants	Group 3 (SOC treatment) out of 240 participants
How many participants had adverse reactions during the study?	61.0% (150)	57.4% (136)	82.1% (197)
How many participants had serious adverse reactions during the study?	11.8% (29)	7.2% (17)	6.3% (15)
How many participants stopped treatment because of adverse reactions?	4.1% (10)	3.8% (9)	4.2% (10)

What adverse reactions did the participants have?

The most common adverse reaction during the study was anemia, which is a decrease in the amount of red blood cells in the blood. The table below shows the adverse reactions that happened in at least 6.0% of participants in any treatment group during the study. There were other adverse reactions that happened during the study, but these happened in fewer participants.

Most common adverse reactions during the study

	Group 1 (durvalumab and tremelimumab) out of 246 participants	Group 2 (durvalumab alone) out of 237 participants	Group 3 (SOC treatment) out of 240 participants
Anemia (decrease in the amount of red blood cells in the blood)	8.1% (20)	5.1% (12)	17.5% (42)
Feeling weak	8.1% (20)	6.3% (15)	13.3% (32)
Feeling tired	7.3% (18)	6.8% (16)	10.8% (26)
Rash	4.5% (11)	6.3% (15)	13.8% (33)
Thyroid works less than it should	12.2% (30)	11.4% (27)	0.0% (0)
Nausea	8.1% (20)	5.9% (14)	7.1% (17)
Decreased appetite	5.7% (14)	5.1% (12)	11.7% (28)
Diarrhea	8.1% (20)	5.9% (14)	7.1% (17)
Itching sensation	8.1% (20)	3.4% (8)	2.5% (6)
Decrease in blood platelet count (the body cannot stop bleeding as well as it should)	4.5% (11)	2.1% (5)	6.7% (16)
Swelling in the mouth	1.2% (3)	1.7% (4)	9.6% (23)
Weakness and pain caused by nerve damage	1.2% (3)	1.3% (3)	8.3% (20)

How has this study helped patients and researchers?

This study helped researchers learn more about using durvalumab and tremelimumab to treat patients who have cancer of the head and neck.

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 both durvalumab and tremelimumab are planned.

Where can I learn more about this study?

More information about this study is available 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 the website, type **"NCT02369874"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2014-003863-40"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D4193C00002"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase III Randomized, Open-Label, Multi-Center, Global Study of MEDI4736 Monotherapy and MEDI4736 in Combination with Tremelimumab Versus Standard of Care Therapy in Patients with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN) (EAGLE)

AstraZeneca Protocol Number: D4193C00002

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 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.

CISCRP
One Liberty Square, Suite 1100 • Boston, MA 02109
1-877-MED-HERO • www.ciscrp.org