AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Treatments Studied:
- AZD4635 with durvalumab
- AZD4635 with oleclumab

Study Purpose: This study was done to learn if AZD4635, with durvalumab or with oleclumab, is safe and works in participants with prostate cancer

Protocol Number: D8731C00001

Thank you

Thank you for taking part in the clinical study for the study treatments AZD4635 with durvalumab and AZD4635 with oleclumab.

You and all of the participants helped researchers learn more about AZD4635 with durvalumab or with oleclumab to help people with prostate cancer.

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 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 prostate cancer. Before a treatment can be approved for people to receive, researchers do clinical studies to find out if it works and how safe it is.

What treatments did the participants get?

The participants in this study received 1 of the following treatments:

- **AZD4635 with durvalumab**
- **AZD4635 with oleclumab**

What were the results of this study?

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

- **How many participants' tumors disappeared or shrank after receiving AZD4635 with durvalumab or with oleclumab?**

  Overall, the researchers found that after receiving **AZD4635 with durvalumab**:

  - 1 out of 20 participants had their tumors disappear. This was 5.0% of participants.
  - None of the participants' tumors shrank.

  Overall, the researchers found that after receiving **AZD4635 with oleclumab**:

  - None of the participants' tumors disappeared.
  - None of the participants' tumors shrank.

  Only some of the participants from each group were able to be included in this calculation.

- **How many participants' prostate-specific antigen levels decreased significantly after receiving AZD4635 with durvalumab or with oleclumab?**

  Prostate-specific antigen, also called "PSA", is a protein made by the prostate that is related to prostate cancer.

  Overall, the researchers found that after receiving **AZD4635 with durvalumab**:

  - 1 out of 28 participants had their PSA levels decrease significantly. This was 3.6% of participants.

  Overall, the researchers found that after receiving **AZD4635 with oleclumab**:

  - 1 out of 30 participants had their PSA levels decrease significantly. This was 3.3% of participants.

- **What medical problems happened during this study?**

  There were 49 out of 59 participants who had medical problems during the study that the study doctors thought might be related to the study treatments. This was 83.1% of the participants. The most common medical problem was nausea.

  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 those websites.

Who took part in this study?

The researchers asked for the help of men with prostate cancer.

The participants in this study were 53 to 90 years old when they joined. The study included 59 men in the United States.

Why was the research needed?

Researchers are looking for a better way to treat prostate cancer. Before a treatment can be approved for people to receive, researchers do clinical studies to find out if it works and how safe it is.

In people with prostate cancer, the body is not able to control the growth of abnormal prostate cells. These extra cells can form tumors in the prostate gland that can spread to other parts of the body.

The participants in this study had received other standard types of treatments for prostate cancer before the study started. But, these treatments were no longer working for them, and other treatment options that work in different ways were needed.

The body's immune system can help attack cancer cells. But, sometimes tumors decrease the immune system's activity. This is called "immune suppression". Stopping immune suppression can allow the immune system to help attack tumor cells again. AZD4635 was designed to stop the immune suppression caused by tumors.

AZD4635 may work better when it is combined with other types of treatments like durvalumab and oleclumab. Both durvalumab and oleclumab were designed to boost the immune system's activity and ability to attack cancer cells.

In this study, the researchers wanted to find out if AZD4635 with durvalumab or oleclumab worked in a small number of participants with prostate cancer. They also wanted to find out if the participants had any medical problems during the study.

What was the purpose of this study?

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

- How many participants' tumors disappeared or shrank after receiving AZD4635 with durvalumab or with oleclumab?
- How many participants' prostate-specific antigen levels decreased significantly after receiving AZD4635 with durvalumab or with oleclumab?
- What medical problems happened during this study

The answers to these questions are important to know before other studies can be done to find out if AZD4635 with durvalumab or with oleclumab helps improve the health of people with prostate cancer.

What treatments did the participants receive?

In this study, the participants received 1 of the following treatments:

- **AZD4635 with durvalumab**
- **AZD4635 with oleclumab**

The participants took AZD4635 as capsules by mouth. Both durvalumab and oleclumab were given through a needle into a vein. This is known as an intravenous infusion, also called an "IV infusion". The doses of AZD4635, durvalumab, and oleclumab were measured in milligrams, also known as "mg".

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

If a participant met the requirements for only 1 treatment group, they were assigned to that group. For participants who met the requirements for more than 1 group, a computer program was used to randomly choose the treatment each participant received. 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.

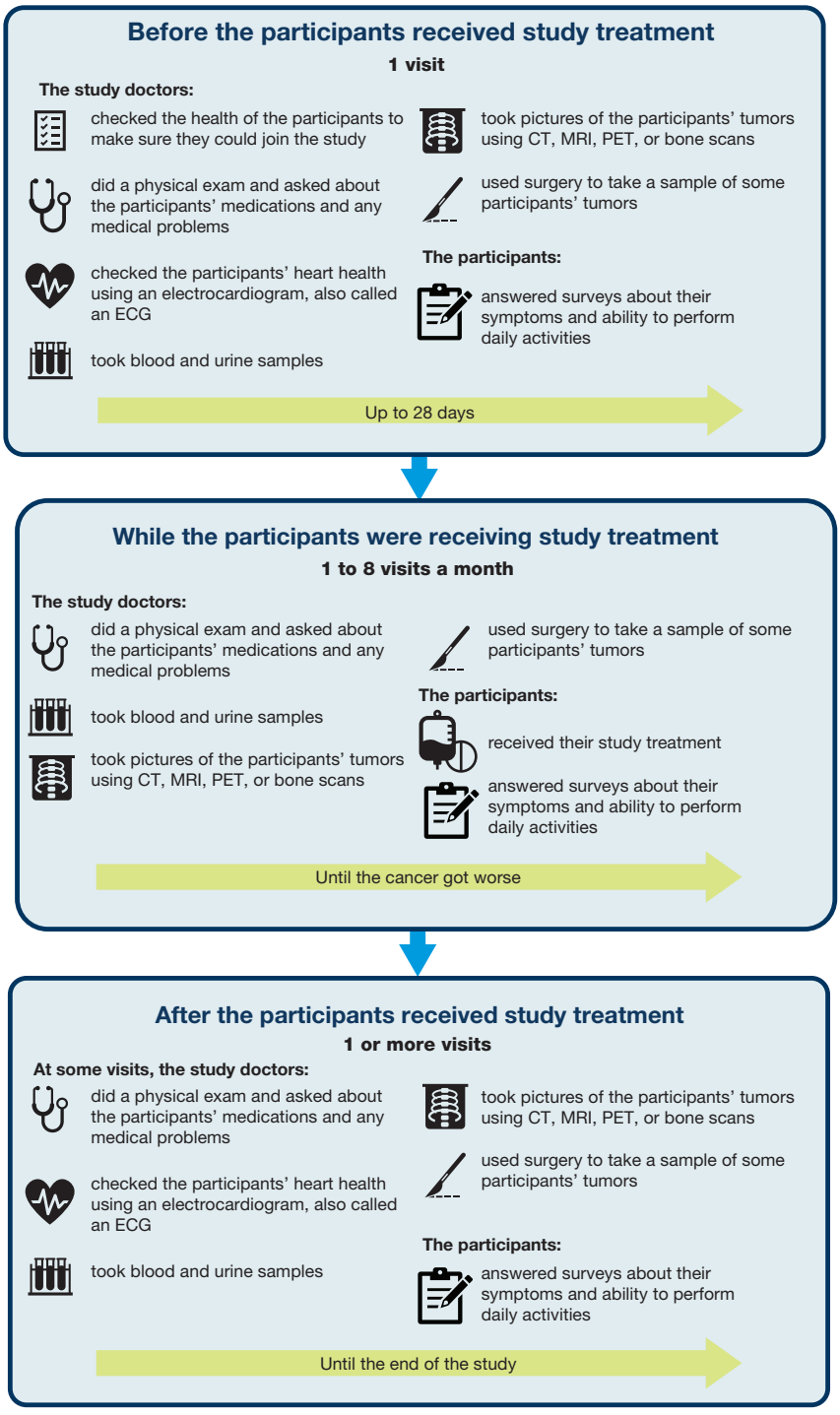
The chart below shows the treatments the participants received.

Group	Treatments and doses
AZD4635 with durvalumab (29 participants) 	• 75 mg of AZD4635 once a day for the first 2 weeks **then** • 75 mg of AZD4635 once a day • 1,500 mg of durvalumab once every 4 weeks
AZD4635 with oleclumab (30 participants) 	• 50 mg or 75 mg of AZD4635 once a day • 1,500 mg of oleclumab once every 2 weeks for the first 4 doses, then once every 4 weeks

What happened during this study?

The participants were in the study until their cancer got worse, the study doctors thought they should stop study treatment, or they left for another reason. The entire study took about 2 years to finish. The study started in August 2019 and ended in June 2021.

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.

How many participants' tumors disappeared or shrank after receiving AZD4635 with durvalumab or with oleclumab?

Overall, the researchers found that after receiving **AZD4635 with durvalumab**:

- 1 out of 20 participants had their tumors disappear. This was **5.0%** of participants.
- None of the other participants' tumors shrank.

Overall, the researchers found that after receiving **AZD4635 with oleclumab**:

- None of the participants' tumors disappeared.
- None of the participants' tumors shrank.

To answer this question, the study doctors took pictures of the participants' tumors using different types of scans. Then, the study doctors measured the size of the participants' tumors before they received study treatment and throughout the study. To do this, they used a set of rules commonly used in cancer clinical studies called Response Evaluation Criteria in Solid Tumors, also called "RECIST".

The researchers calculated the percentage of participants whose tumors disappeared or shrank. This percentage of participants needed to be at least 25.0% for the researchers to decide that AZD4635 with durvalumab or with oleclumab worked in a meaningful way.

Only some of the participants from each group met the RECIST rules and were able to be included in this calculation. There were 20 out of 29 participants who received AZD4635 with durvalumab that were included, and 21 out of 30 participants who received AZD4635 with oleclumab that were included.

How many participants' prostate-specific antigen levels decreased significantly after receiving AZD4635 with durvalumab or with oleclumab?

To answer this question, the study doctors measured the levels of prostate-specific antigen, also called "PSA", in the participants' blood before they received treatment and throughout the study. When PSA levels are high or increasing, it can mean that tumors are growing. When PSA levels are low or decreasing, it can mean that tumors are shrinking.

The researchers calculated the percentage of participants whose PSA levels decreased significantly. This means that a participant's PSA level had decreased by more than half of what it was before they received treatment. This percentage of participants needed to be at least 30.0% for the researchers to decide that AZD4635 with durvalumab or with oleclumab worked in a meaningful way. There was 1 participant in the AZD4635 with durvalumab group that was not included in this calculation because they did not have an abnormal PSA level.

Overall, the researchers found that after receiving **AZD4635 with durvalumab**:

- 1 out of 28 participants had their PSA levels decrease significantly. This was **3.6%** of participants.

Overall, the researchers found that after receiving **AZD4635 with oleclumab**:

- 1 out of 30 participants had their PSA levels decrease significantly. This was **3.3%** of participants.

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 treatments. These medical problems are called "adverse reactions". An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the study treatments. A lot of research is needed to know whether a treatment causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for AZD4635, durvalumab, and oleclumab.

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.

Did any adverse reactions happen during this study?

	AZD4635 with durvalumab (out of 29 participants)	AZD4635 with oleclumab (out of 30 participants)
How many participants had adverse reactions?	82.8% (24)	83.3% (25)
How many participants had serious adverse reactions?	0.0% (0)	0.0% (0)
How many participants stopped taking AZD4635 due to adverse reactions?	0.0% (0)	3.3% (1)

What serious adverse reactions happened during this study?

There were no serious adverse reactions during this study.

What adverse reactions happened during this study?

There were 83.1% of participants who had adverse reactions during this study. The most common adverse reaction was nausea.

The table below shows the adverse reactions that happened in more than 1 participant. There were other adverse reactions, but these happened in only 1 participant.

Most common adverse reactions

Adverse reaction	AZD4635 with durvalumab (out of 29 participants)	AZD4635 with oleclumab (out of 30 participants)
Nausea	37.9% (11)	53.3% (16)
Feeling tired	20.7% (6)	30.0% (9)
Decreased appetite	17.2% (5)	16.7% (5)
Vomiting	10.3% (3)	23.3% (7)
Diarrhea	13.8% (4)	10.0% (3)
Feeling dizzy	13.8% (4)	6.7% (2)
Constipation	10.3% (3)	3.3% (1)
Low amount of a type of blood cell called platelets, which help blood to clot	0.0% (0)	6.7% (2)
Difficulty sleeping	6.9% (2)	0.0% (0)
High blood pressure	0.0% (0)	6.7% (2)
Pain in the stomach	6.9% (2)	0.0% (0)
Disease where stomach acid often goes upwards into the tube connecting the mouth and stomach	3.4% (1)	3.3% (1)
Itching	3.4% (1)	3.3% (1)
Rash	3.4% (1)	3.3% (1)
Swelling of lower legs or hands	6.9% (2)	0.0% (0)
Increased amounts in the blood of a type of protein called amylase that helps digest food	3.4% (1)	3.3% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about how AZD4635 with durvalumab or with oleclumab worked in participants with prostate 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 AZD4635 with durvalumab and with oleclumab are not planned by the sponsor at this time.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. When 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 **"NCT04089553"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D8731C00001"** into the search box, and click **"Find a Study"**.

Full Study Title: An Open-label, Multi-drug, Multi-center Phase II Combination Study of AZD4635 in Patients with Prostate Cancer

AstraZeneca Protocol Number: D8731C00001

National Clinical Trials Number: NCT04089553

AstraZeneca sponsored this study and has its headquarters in Cambridge, UK.

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

Version 1.0 2022_03_30