NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of alpelisib when given with fulvestrant or letrozole in people with advanced breast cancer

Thank you!

Thank you to the participants who took part in the clinical trial for **advanced breast cancer**. Every participant helped the researchers learn more about the trial drug **alpelisib**, also called **BYL719**.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public. We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CBYL719X2402

Novartis drug studied: **Alpelisib**, also called **BYL719**

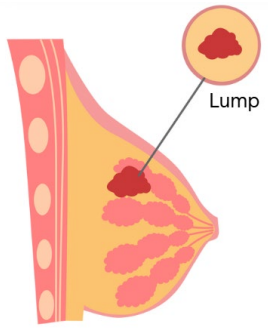
Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **alpelisib** when given with either **fulvestrant** or **letrozole** in people with advanced breast cancer that had worsened after prior treatment.



Breast cancer

Breast cancer happens when cells in the breast start growing uncontrollably and form a lump, which is called a tumor. In **advanced breast cancer**, the cancer cells have spread from the breast to nearby areas or other parts of the body. Breast cancer can cause a wide range of symptoms. Most frequent symptoms of **advanced breast cancer** include:

- change in the size, shape, or appearance of one or both breasts
- a lump or swelling in the breast, chest, or armpits
- shortness of breath
- bone pain

Participants in this trial had the following type of breast cancer:

- **Hormone receptor-positive, or HR-positive**: This is a type that uses the hormones estrogen and progesterone to help the breast cancer cells grow.
- **Human epidermal growth factor receptor 2-negative or HER2-negative**: Breast cancer cells do not have high levels of a protein called HER2, which normally helps the cancer cells to grow and divide. Treatments that target the HER2 protein do not work to treat this type of breast cancer.
- **PIK3CA mutation**: Changes (a mutation) in the PIK3CA gene that cause cancer cells to grow rapidly.

Alpelisib, also called **BYL719**, is an approved treatment for certain types of breast cancers. It works by targeting the cancer cells that have a mutation in the PIK3CA gene.

Alpelisib in combination with **fulvestrant** is an approved treatment for advanced breast cancer in postmenopausal women as well as in men. Menopause is when women stop having monthly menstruation, also called a period.

Trial drugs:

- **Alpelisib**
  Pronounced as
  AL-PEL-i-sib
- **Fulvestrant**
  Pronounced as
  Ful-VES-trant
- **Letrozole**
  Pronounced as
  LET-ro-zole

Fulvestrant and **letrozole** work by blocking estrogen receptors or lowering estrogen levels in the body, which stops breast cancer cells from growing. They are also called hormone therapy or endocrine therapy.

In this trial, researchers wanted to learn if adding **alpelisib** to **fulvestrant** or **letrozole**, helped to further reduce the growth of breast cancer cells. The decision to give either **fulvestrant** or **letrozole** was based on the previous anti-cancer treatment the participants had received.

The trial's purpose was to answer these main questions:

- How many participants were alive without worsening of their cancer after 6 months of trial treatment?
- What medical problems, also called adverse events, happened during this trial?

  An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in August 2017 and ended in November 2024.

This trial was designed to have 2 parts:

- **Part 1 (Core part) -** This part was done to assess the effects of using **alpelisib** with either **fulvestrant** or **letrozole**. Participants were divided into 3 groups (**Group 1**, **Group 2**, and **Group 3**) based on their previous anti-cancer treatment.
- **Part 2 (Extension part) -** This part was done to assess the safety of the treatment the participants were receiving in **Part 1**. Participants who were benefitting from the trial treatment and who could not access the treatment locally due to their country's regulations entered this part of the trial.

When the trial ended, the researchers collected information from participants and created a report of the trial results. This summary is based on that report.

Who was in this trial?

379 participants with advanced breast cancer received treatment in this trial: 1 man and 378 women. Participants' ages ranged from 31 to 84 years.
The number of participants by race is shown below.

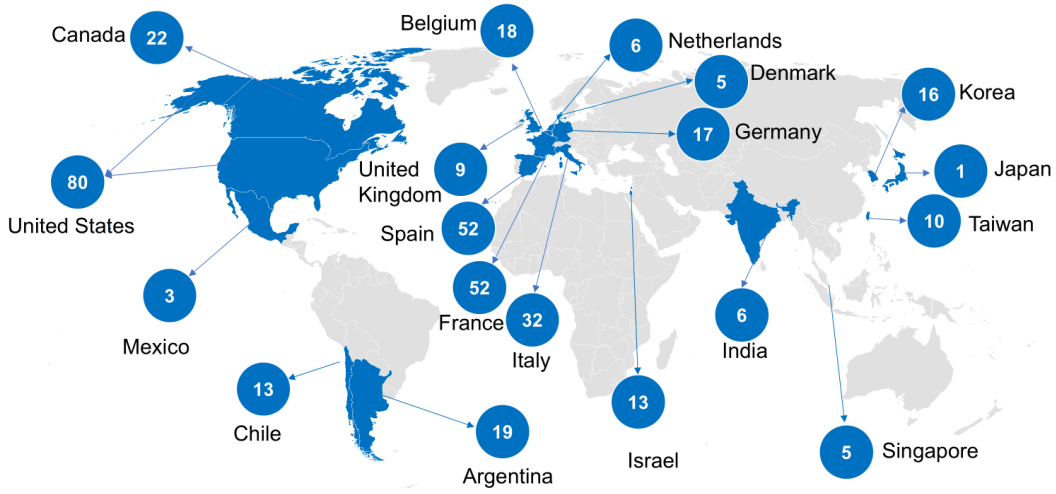
Race

48	Asian	8	Black	1	Pacific islander
249	Caucasian	13	Other	58	Unknown
2	Not reported				

The participants could take part in this trial if they:

- were 18 years or above
- had HR-positive and HER2-negative advanced breast cancer that got worse after a maximum of 2 prior therapies
- had a confirmed PIK3CA gene mutation and did not receive a PI3K inhibitor treatment before
- were able to walk and do light work

379 participants from 19 countries with advanced breast cancer received treatment in this trial. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatments in this trial were given as **28-day cycles**. A cycle is a treatment period that is repeated.

The treatments in this trial were:

Alpelisib, 300 milligrams (mg), was taken by mouth as tablets, once daily.

Fulvestrant: 500 mg, which was given as an injection into the muscle, on Days 1 and 15 of the first cycle and then on Day 1 of the remaining cycles.

Letrozole: 2.5 mg, which was taken by mouth as tablets, once daily.

Apart from the above-mentioned drugs, the man in **Group 2** and premenopausal women also received the following drugs to suppress estrogen and progesterone further, so that **fulvestrant** and **letrozole** could work appropriately:

Goserelin: 3.6 mg, which was given as a small implant placed under the skin with a needle, every 28 days. The implant slowly releases the medicine into the body over time.

Leuprolide: 7.5 mg, which was given as an injection into the muscle once every 28 days.

The participants, researchers, and trial staff knew what treatment the participants were receiving.

What happened during the trial?

Before treatment

Up to 21 days

The trial staff checked participants' health and took their tumor sample to confirm for PIK3CA gene mutation. This was done to make sure the participants could be in this trial.

During treatment

Up to 4.5 years

The trial was done in 2 parts:

Part 1 (core part): (up to 1 year and 6 months)

A total of 379 participants received **alpelisib** with either **fulvestrant** or **letrozole** in this part. Researchers divided participants into 3 groups depending on the previous anti-cancer treatment they had received.

Participants in **Group 1** and **Group 2** had previously been treated with a type of medicine that helps slow down the growth of cancer cells (an inhibitor) along with hormone therapy. Participants in **Group 3** had previously received either chemotherapy or hormone therapy that was different from what the **Groups 1** and **2** participants had received.

Core part (379 participants)		
Group 1: Alpelisib + Fulvestrant (127 participants)	**Group 2: Alpelisib + Letrozole** (126 participants)	**Group 3: Alpelisib + Fulvestrant** (126 participants)

At the end of **Part 1**, participants who were still benefiting from the trial treatment but could not access the treatment locally due to their country's regulations, entered **Part 2** of the trial.

Part 2 (extension part): (up to 3 years)

Participants in **Part 2** continued to receive the same treatment as in **Part 1**. A total of 11 participants entered **Part 2**.

Extension part (11 participants)		
Group 1: Alpelisib + Fulvestrant (1 participant)	**Group 2: Alpelisib + Letrozole** (0 participants)	**Group 3: Alpelisib + Fulvestrant** (10 participants)

After treatment

Up to 1 month

Trial staff checked participants' general health and for any medical problems for 1 month after participants' last dose of the trial treatment. They also checked how long participants lived until the end of the trial.

What were the main results of this trial?

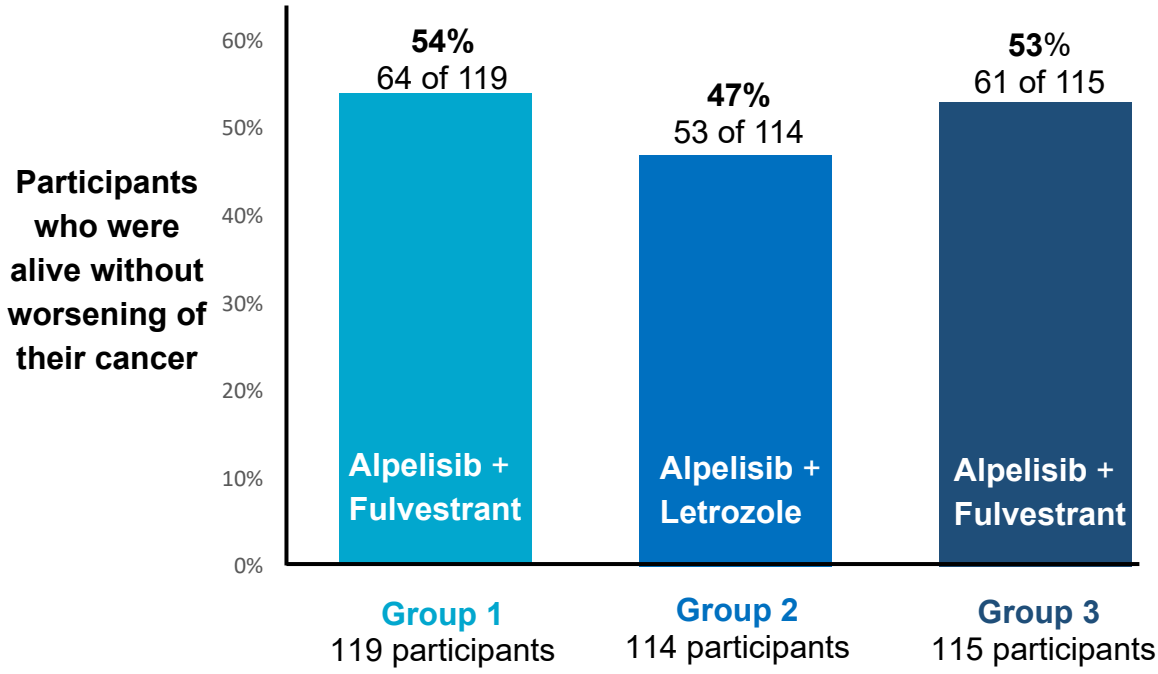
How many participants were alive without worsening of their cancer after 6 months of trial treatment?

About half of participants in all 3 groups were alive without worsening of their cancer after 6 months of trial treatment.

To answer this question, researchers assessed participants' cancer using different imaging scans at different time points during the trial. They then calculated the number of participants in each group who were alive without worsening of their cancer after 6 months of trial treatment.

The results are available for 348 participants who received at least one dose of the trial treatment and whose PIK3CA gene mutation was confirmed by a designated laboratory.

Number of participants (percentage) who were alive without worsening of their cancer after 6 months of trial treatment



What were the other results of this trial?

How long did the participants live with their cancer before it worsened or they died due to any cause?

To answer this question, researchers recorded the period from the start of the treatment to the worsening of the cancer or death from any cause, also called **progression-free survival**.

About half the participants lived for at least the following duration without their cancer getting worse:

- **Group 1** (**Alpelisib** + **Fulvestrant**): 8 months
- **Group 2** (**Alpelisib** + **Letrozole**): 6 months
- **Group 3** (**Alpelisib** + **Fulvestrant**): 6 months

How long did the participants live after starting the trial treatment?

To answer this question, researchers recorded the period for which the participants lived after starting treatment during the trial, also called **overall survival**.

About half the participants lived for at least the following duration after starting the treatment in the trial:

- **Group 1** (**Alpelisib** + **Fulvestrant**): 2 years and 3 months
- **Group 2** (**Alpelisib** + **Letrozole**): 2 years and 5 months
- **Group 3** (**Alpelisib** + **Fulvestrant**): 1 year and 9 months

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment until 1 month after the last dose of trial treatment.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

Core part:

- A total of 126 of 127 participants in **Group 1**, all 126 participants in **Group 2**, and 125 of 126 participants in **Group 3** had adverse events**.**
- 37 participants in **Group 1**, 48 in **Group 2**, and 38 in **Group 3** had adverse events that were considered serious.
- 78 participants in **Group 1**, 76 in **Group 2**, and 67 in **Group 3** died.
- 20 participants in **Group 1**, 14 in **Group 2**, and 13 in **Group 3** left the trial due to an adverse event.

Extension part:

- All participants had adverse events**.**
- 3 participants in **Group 3** had adverse events that were considered serious.
- 1 participant in **Group 3** died.
- 1 participant in **Group 3** left the trial due to an adverse event.

The researchers concluded there were no new safety concerns for **alpelisib** when combined with either **fulvestrant** or **letrozole** in this trial.

What serious adverse events did the participants have?

Core part

37 participants in **Group 1**, 48 in **Group 2**, and 38 in **Group 3** had serious adverse events in the **core part**.

The table below shows the most common serious adverse events in the **core part**. Additional serious adverse events happened in fewer participants.

	Core part		
	Group 1 **Alpelisib + Fulvestrant** 127 participants	**Group 2** **Alpelisib + Letrozole** 126 participants	**Group 3** **Alpelisib + Fulvestrant** 126 participants
High blood glucose levels Hyperglycaemia	**7 of 127** 6%	**3 of 126** 2%	**2 of 126** 2%
Difficult breathing Dyspnea	**3 of 127** 2%	**2 of 126** 2%	**2 of 126** 2%
Flat and raised red spots on the skin Rash maculo-papular	**3 of 127** 2%	**2 of 126** 2%	**1 of 126** Less than 1%
Fluid in the lungs Pleural effusion	**3 of 127** 2%	**2 of 126** 2%	**2 of 126** 2%
Stomach pain Abdominal Pain	**2 of 127** 2%	**4 of 126** 3%	**0**
Joint Pain Arthralgia	**1 of 127** Less than 1%	**3 of 126** 2%	**1 of 126** Less than 1%
Lung infection Pneumonia	**1 of 127** Less than 1%	**4 of 126** 3%	**2 of 126** 2%
Sudden decrease in kidney function Acute kidney injury	**0**	**3 of 126** 2%	**1 of 126** Less than 1%
Back pain	**0**	**0**	**3 of 126** 2%

Extension part

3 participants had serious adverse events in the **extension part**.

The table below shows all the serious adverse events that happened in the participants in the **extension part**.

	Extension part		
	Group 1 **Alpelisib + Fulvestrant** 1 participant	**Group 2** **Alpelisib + Letrozole** 0 participants	**Group 3** **Alpelisib + Fulvestrant** 10 participants
Large intestine inflammation Colitis ulcerative	**0**	**0**	**1 of 10** 10%
Broken ankle Ankle fracture	**0**	**0**	**1 of 10** 10%
Migraine with warning signs Migraine with aura	**0**	**0**	**1 of 10** 10%

What other adverse events did the participants have?

Core part

The following table shows the most common other adverse events in the **core part**. Additional adverse events happened in fewer participants.

	Core part		
	Group 1 **Alpelisib + Fulvestrant** 127 participants	**Group 2** **Alpelisib + Letrozole** 126 participants	**Group 3** **Alpelisib + Fulvestrant** 126 participants
Diarrhea	**82 of 127** 65%	**86 of 126** 68%	**68 of 126** 54%
High blood sugar Hyperglycaemia	**76 of 127** 60%	**81 of 126** 64%	**85 of 126** 67%
Feeling sick to your stomach Nausea	**59 of 127** 46%	**68 of 126** 54%	**51 of 126** 40%
Skin rash Rash	**39 of 127** 31%	**39 of 126** 31%	**51 of 126** 40%
Decreased appetite	**37 of 127** 29%	**56 of 126** 44%	**42 of 126** 33%

Extension part

The table below shows the most common other adverse events in the **extension part**. Additional adverse events happened in fewer participants.

	Extension part		
	Group 1 **Alpelisib + Fulvestrant** 1 participant	**Group 2** **Alpelisib + Letrozole** 0 participants	**Group 3** **Alpelisib + Fulvestrant** 10 participants
Diarrhea	**1 of 1** 100%	**0**	**7 of 10** 70%
High blood sugar Hyperglycemia	**1 of 1** 100%	**0**	**6 of 10** 60%
Dry Skin	**1 of 1** 100%	**0**	**4 of 10** 40%
Skin rash Rash	**1 of 1** 100%	**0**	**4 of 10** 40%
Tiredness Fatigue	**0**	**0**	**5 of 10** 50%

What was learned from this trial?

Researchers learned about the effects of **alpelisib** when given in combination with either **fulvestrant** or **letrozole** in people with HR-positive, HER2-negative advanced breast cancer with a PIK3CA mutation that had worsened after a previous anti-cancer treatment.

Researchers concluded that:

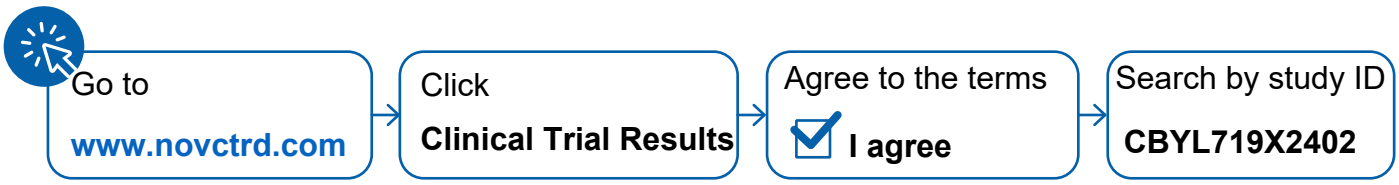
- after 6 months of treatment, about half of the participants in all 3 treatment groups were alive without their cancer getting worse
- the combination treatment of **alpelisib** with **fulvestrant** or **letrozole** showed an effect on breast cancer that had worsened after receiving previous anti-cancer treatment
- there were no new safety concerns with the use of **alpelisib** in combination with **fulvestrant** or **letrozole** in this trial

When this summary was written, the sponsor was considering the next steps for **alpelisib**.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website,

Follow these steps to find the scientific summary:



For more information about this trial, go to any of the following websites:

- www.clinicaltrials.gov– search using the number **NCT03056755**
- clinicaltrialsregister.eu/ctr-search/search - search using the number **2016-004586-67**

Other trials of **alpelisib** may appear on the public websites above. When there, search for **BYL719** or **alpelisib**.

Full clinical trial title: A phase II, multicenter, open-label, three-cohort, non-comparative study to assess the efficacy and safety of alpelisib plus fulvestrant or letrozole in patients with PIK3CA mutant, hormone receptor (HR) positive, HER2-negative advanced breast cancer(aBC), who have progressed on or after prior treatments

NOVARTIS

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

1-888-669-6682 (US) | +41-61-324 1111 (EU)

www.novartis.com/clinicaltrials