NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of dapagliflozin and metformin compared to metformin alone in participants with advanced breast cancer being treated with BYL719 and fulvestrant

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 **BYL719**, also called alpelisib.

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: CBYL719C2202

Drug studied: BYL719, also known as alpelisib

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 findings.

What was the main purpose of this trial?

The purpose of the trial was to learn if **dapagliflozin** and **metformin** could prevent episodes of high blood sugar levels better than **metformin** alone in people with advanced breast cancer treated with **BYL719**.

BYL719 in combination with **fulvestrant** is an approved treatment for advanced breast cancer in post–menopausal women as well as in men. Menopause is when women stop having monthly menstruation, also called period.

Breast cancer happens when cells in the breast start growing uncontrollably and form a lump, which is called a tumor. There are different types of breast cancer. Participants in this trial had the following type of breast cancer:

- **Advanced:** Breast cancer that has spread from the breast to areas around it and/or to other parts of the body.
- **Hormone receptor-positive, or HR-positive:** Breast cancer cells that respond to treatment with estrogen or progesterone hormones through the presence of receptors (proteins) that bind to these hormones.
- **Human epidermal growth factor receptor 2-negative or HER2-negative:** Breast cancer cells that have a normal number of **HER2** receptor (proteins). HER2 receptors help cancer grow faster. Treatments that target the **HER2** receptors do not work to treat this type of breast cancer.
- **PIK3CA mutation following progression on or after endocrine-based therapy:** Changes (a mutation) in the **PIK3CA** gene that cause the cancer cells to grow rapidly and spread even after receiving an anti-cancer hormone treatment.

BYL719, also called alpelisib, works by targeting the breast cancer cells that have a mutation in the PIK3CA gene.

Researchers are looking for ways to treat and prevent high blood sugar levels which often occur in people with advanced breast cancer who are treated with **BYL719** by giving **dapagliflozin** and **metformin** rather than **metformin** alone.

Trial drug
BYL719, also called alpelisib

Pronounced as
AL-PEL-i-sib

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

- How many participants experienced very high blood sugar levels for the first 8 weeks of treatment with **BYL719** and **fulvestrant** with a combination of **dapagliflozin** and **metformin** or **metformin** alone?
- What adverse events did the participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during the trial.

How long was this trial?

The trial began in April 2022 and ended in May 2023. It was planned for individual participants to be on the trial for about 1 year and 2 months.

Researchers planned to enroll approximately 132 participants in the trial. In December 2022, the researchers decided to stop the trial early after 2 participants were enrolled.

The sponsor made this decision based on new information suggesting that **metformin** alone helped in reducing high blood sugar levels in people treated with **BYL719** and **fulvestrant**. The decision to stop the trial early was also made because of slow enrollment of participants and not because of safety concerns.

Who was in this trial?

2 participants received treatment in this trial. Participants' average age was about 70 years. Both participants in the trial were women, one Asian from Malaysia and one Caucasian from the United States of America.

Both men and post-menopausal women could take part in this trial if they:

- were 18 years or above in age.
- had HR-positive and HER2-negative advanced breast cancer with a PIK3CA gene mutation and whose cancer had spread even after taking an anti cancer hormone treatment.
- were at risk of developing very high blood sugar levels.

What treatment did the participants receive?

Participants were to receive treatment with **BYL719** and **fulvestrant** in 12 **cycles*** of 28 days or for as long as the participants benefitted from the treatment.

*A cycle is the time period between the start of one round of cancer treatment to the start of the next.

The treatments in this trial were:

BYL719, 300 milligrams (mg) given as tablets by mouth once daily on Day 8 of each cycle.

Fulvestrant, 500 mg solution given as an injection into the muscle on Day 1 and Day 15 of the Cycle 1 and then on Day 1 of the remaining cycles.

Metformin 500 mg as tablets by mouth once daily on Day 1 of each cycle. In this trial, participants received **metformin** as extended-release tablets, which means the medicine is released in the body slowly and consistently over time.

Dapagliflozin 5 mg and **metformin** 500 mg as a single combination tablet taken by mouth once daily on Day 1 of each cycle.

In this trial, each participant, the trial doctors, and the trial staff, all knew which treatments the participants were receiving.

What happened during this trial?

Before treatment — Up to 28 days

Trial doctors checked the participants' health to ensure they could take part in this clinical trial.

During treatment — 1 year

Researchers planned to randomly assign participants equally into the following 2 treatment groups:

Group 1: BYL719 + fulvestrant + dapagliflozin + metformin

Group 2: BYL719 + fulvestrant + metformin

- Researchers planned to enroll 66 participants in each treatment group. However, only 2 participants joined this trial.
- Both participants were placed in **Group 1**. No participants were enrolled in **Group 2**.
- The planned duration of treatment with **BYL719** and fulvestrant was 12 cycles of 28 days or for as long as the participants benefitted from the treatment.

After treatment — 30 days

After treatment, it was planned that all participants would enter the safety follow-up which would end 30 days after treatment.

One participant discontinued the treatment early and entered the safety follow-up. The other participant chose to take the commercially available **BYL719**.

What was the main result of this trial?

How many participants experienced very high blood sugar levels for the first 8 weeks of treatment with BYL719 and fulvestrant with a combination of dapaglifozin and metformin or metformin alone?

One of the 2 participants in Group 1 had very high blood sugar levels for the first 8 weeks of treatment. However, researchers were unable to reach any meaningful conclusions because there was small number of participants.

What adverse events did the participants have?

Trial doctors keep track of all **adverse events** that happen in trials, 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 up to 30 days after the participants discontinued the 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.

Both participants had adverse events. None of the participants had adverse events that were considered serious. No participant died due to an adverse event. No new safety concerns were identified with the use of **BYL719** in this trial.

How many participants had adverse events?

Participants who:	BYL719+Fulvestrant+ Dapaglifozin+Metformin (2 participants)
Had at least 1 serious adverse event	0
Had at least 1 other adverse event	2
Died during the trial	0

What other adverse events did the participants have?

Most of the adverse events reported during the trial happened in 1 participant each, except for **constipation**, **decreased appetite**, **tiredness** (fatigue), and **feeling sick** (nausea), that were reported by both participants.

What was learned from this trial?

No meaningful conclusions could be drawn because the trial was stopped early with only 2 participants.

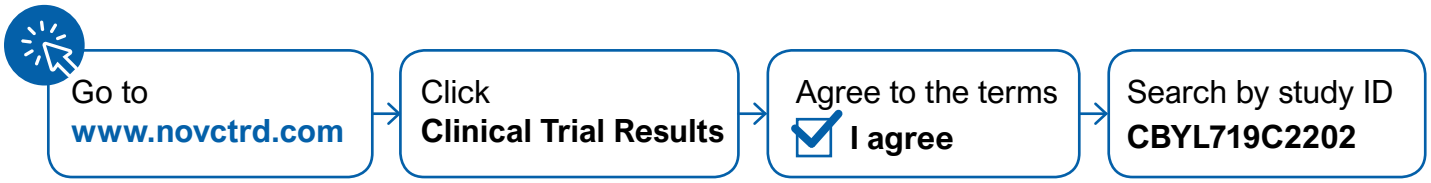
- 1 out of the 2 participants experienced very high blood sugar levels
- There were no new safety concerns with the use of **BYL719**

Currently, there are no new trials ongoing with **BYL719** on advanced breast cancer.

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, **www.novctrd.com**

Follow these steps to find the scientific summary:



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

- **www.clinicaltrials.gov** and-search using the number **NCT04899349**

Full clinical trial title: EPIK-B4: A Phase II, Multicenter, Randomized, Open-label, Active-controlled Study to Assess the Safety and Efficacy of dapagliflozin + Metformin XR versus Metformin XR During Treatment with Alpelisib (BYL719) in Combination with Fulvestrant in Participants with HR+, HER2-, Advanced Breast Cancer with a PIK3CA Mutation Following Progression on/after Endocrine-based Therapy

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.novartisclinicaltrials.com