MAY 2025

Vepdegestrant (vep-DEG-eh-strent), a PROTAC ER degrader, vs fulvestrant in people living with ER+/HER2- advanced breast cancer

This summary contains information from the scientific presentation:

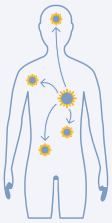
Vepdegestrant, a PROTAC ER Degrader, vs Fulvestrant in ER+/HER2- Advanced Breast Cancer: Results of the Global, Randomized, Phase 3 VERITAC-2 Study

CLICK HERE TO VIEW THE PRESENTATION SLIDES

What is ER+/HER2- advanced breast cancer?

ER+/HER2- breast cancer is a specific type of breast cancer

- Certain types of breast cancer grow in response to **estrogen**, a hormone in the body. This is called **estrogen receptor–positive (ER+)** breast cancer
- Some types of breast cancer have high levels of a protein called **human epidermal growth factor receptor 2 (HER2)** and are called **HER2-positive (HER2+)**. Other breast cancer types have low levels or no HER2 and are called **HER2-negative (HER2-)**



Advanced breast cancer is cancer that has spread from the breast to nearby tissue **(locally advanced cancer)** or from the breast to more distant parts of the body **(metastatic cancer)**

What are some common treatments for ER+/HER2- advanced breast cancer?

Doctors often use hormone therapy (also called **endocrine therapy**), which works by either blocking the body's ability to produce estrogen or blocking the activity of estrogen in cancer cells. This may slow or stop cancer growth

- **Aromatase inhibitors**, such as letrozole, anastrozole, or exemestane, are endocrine therapies that reduce the production of estrogen
- **Fulvestrant** is an endocrine therapy that attaches to estrogen receptors and blocks their activity, which reduces estrogen's effects on tumors

CDK4/6 inhibitors are another type of treatment and work by blocking certain proteins that cause cancer cells to grow

Some people have tumors that develop mutations, or changes in the tumor's DNA, in a gene called the **estrogen receptor 1 gene (*ESR1*)**. These mutations can make certain endocrine therapies not work as well

- Some new medicines specifically aim to treat people with ER+/HER2- advanced breast cancer whose tumors have developed *ESR1* mutations

What is vepdegestrant?

Vepdegestrant, also called **ARV-471**, is an investigational drug taken by mouth as a pill that researchers are testing for the treatment of ER+/HER2- breast cancer. It is a **PROteolysis TArgeting Chimera (PROTAC) estrogen receptor degrader**

- PROTACs are designed to attach to specific proteins in cells that can cause disease, which causes those proteins to be **marked for elimination** by a natural protein disposal system in the body
- Vepdegestrant works by causing **estrogen receptors to be eliminated**, which blocks the activity of estrogen and may stop ER+ breast cancer tumors from growing or cause the tumors to shrink

Why is vepdegestrant being compared to fulvestrant in this study?

Fulvestrant is an endocrine therapy given to people with ER+/HER2- breast cancer whose tumors grow or spread after treatment with a different endocrine therapy

In laboratory research studies, vepdegestrant **eliminated more estrogen receptors** and had **stronger effects at preventing tumor growth** than fulvestrant

This summary describes results from a clinical study comparing vepdegestrant to fulvestrant in people with ER+/HER2- advanced breast cancer who had prior treatment with endocrine therapy and a CDK4/6 inhibitor

The **main aim** of the study was to find out

- **How long people live without their cancer growing or spreading when taking vepdegestrant vs fulvestrant**

This summary describes

- **How long people lived without their cancer growing or spreading when taking vepdegestrant vs fulvestrant**
- **How well vepdegestrant caused tumors to stop growing or shrink compared to fulvestrant**
- **The side effects people experienced while taking vepdegestrant or fulvestrant**

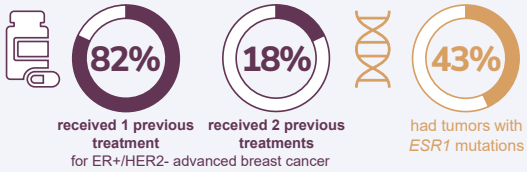
Analysis Population

WHO PARTICIPATED IN THIS STUDY?

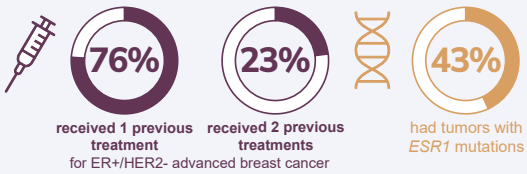
624 people living with ER+/HER2- advanced or metastatic breast cancer **who received previous treatment for their cancer with endocrine therapy plus a CDK4/6 inhibitor**

Before the study

Among the 313 people assigned to receive vepdegestrant:



Among the 311 people assigned to receive fulvestrant:



During the study

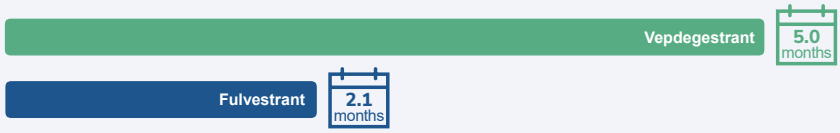
Participants took vepdegestrant (200 mg) as pills by mouth once daily or fulvestrant (500 mg) as an injection into muscle every 2 weeks during the first month and every 4 weeks after the first month

Results

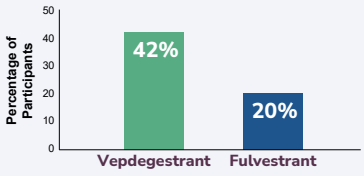
WHAT WERE THE RESULTS OF THIS PHASE 3 STUDY?

Participants who had tumors with *ESR1* mutations:

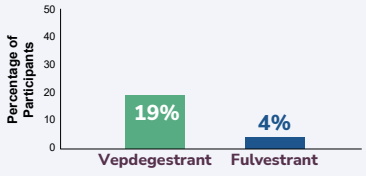
The time that half of the people in each group lived without their cancer growing or spreading was longer in those taking vepdegestrant than those taking fulvestrant



Tumors shrank or stopped growing for at least 24 weeks in 42% of people taking vepdegestrant and **20%** of people taking fulvestrant

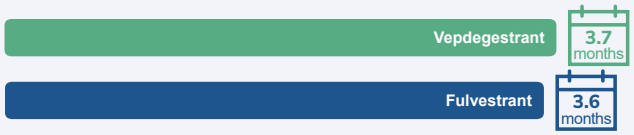


Tumors shrank in 19% of people taking vepdegestrant and in **4%** of people taking fulvestrant



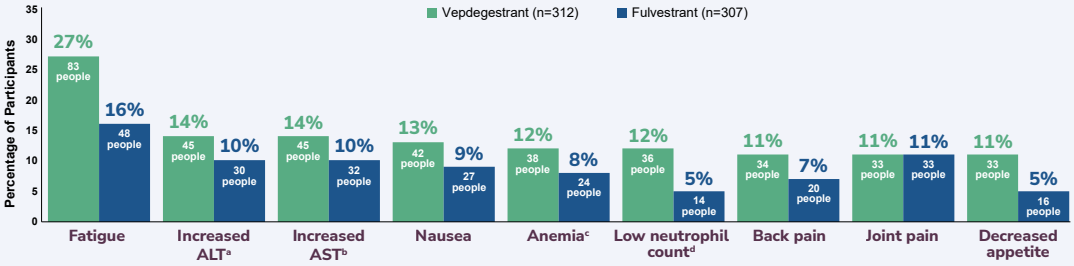
All participants (who had tumors with or without *ESR1* mutations):

The time that half of the people in each group lived without their cancer growing or spreading was not different between those taking vepdegestrant and those taking fulvestrant



People taking either vepdegestrant or fulvestrant experienced some side effects (also known as adverse events), which are health problems that occurred during the study (these may or may not have been caused by the treatment)

- 57% of people experienced side effects related to vepdegestrant, and 40% of people experienced side effects related to fulvestrant
- Most people experienced side effects that were mild or moderate
- 3% of people stopped taking vepdegestrant because of side effects, and 1% of people stopped taking fulvestrant because of side effects



[a]ALT, or alanine aminotransferase, is an enzyme found mainly in the liver. Increased ALT can indicate damage to the liver.
[b]AST, or aspartate aminotransferase, is an enzyme found in the liver as well as other organs. Increased AST can indicate damage to the liver or other organs, including the heart, muscles, or kidneys.
[c]Anemia is a condition that occurs when the body produces a lower-than-normal amount of healthy red blood cells.
[d]Neutrophils are a type of white blood cell that helps the body fight infections and heal wounds.

TAKE-HOME MESSAGES

Treatment with **vepdegestrant extended the time people lived without their cancer growing or spreading compared to treatment with fulvestrant** in people living with ER+/HER2- advanced breast cancer who had tumors with ***ESR1* mutations**

Most people had side effects with vepdegestrant that were **mild or moderate**

Who sponsored the study?

This study is sponsored by **Pfizer, Inc., in collaboration with Arvinas Estrogen Receptor, Inc.**

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Where can I find more information?

For more information on **this study** VIEW CLINICAL TRIAL RECORD

For more information on **clinical studies in general** VIEW INFORMATION