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Vepdegestrant (vep-DEG-eh-strent), a PROTAC ER degrader, vs fulvestrant in people living with *ESR1*-mutated ER+/HER2- advanced breast cancer who had different characteristics

This summary contains information from the scientific presentation:

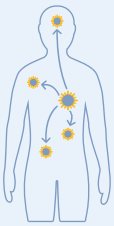
Subgroup Analyses of VERITAC-2: A Phase 3 Trial of Vepdegestrant, a PROTAC ER Degrader, Versus Fulvestrant in ER+/HER2- Advanced Breast Cancer

CLICK HERE TO VIEW THE PRESENTATION

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

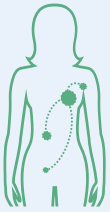
- Some new medicines specifically aim to treat people with ER+/HER2- advanced breast cancer whose tumors have developed *ESR1* mutations

What is vepdegestrant?

Vepdegestrant 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**

- PROTAC protein degraders 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

The phase 3 VERITAC-2 clinical study compared vepdegestrant with fulvestrant in people with ER+/HER2- advanced breast cancer who had prior treatment with endocrine therapy and a CDK4/6 inhibitor:



624 people with ER+/HER2- advanced breast cancer, **including 270 with *ESR1* mutations**

Randomize 1:1

Vepdegestrant
200 mg by mouth once daily

Fulvestrant
500 mg as an injection into muscle every 2 weeks during the first month and every 4 weeks after the first month

Treatment with **vepdegestrant extended the time people lived without their cancer growing or spreading compared with treatment with fulvestrant (5.0 months vs 2.1 months)** 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**

The **main aim** of this analysis of the VERITAC-2 clinical study was to find out

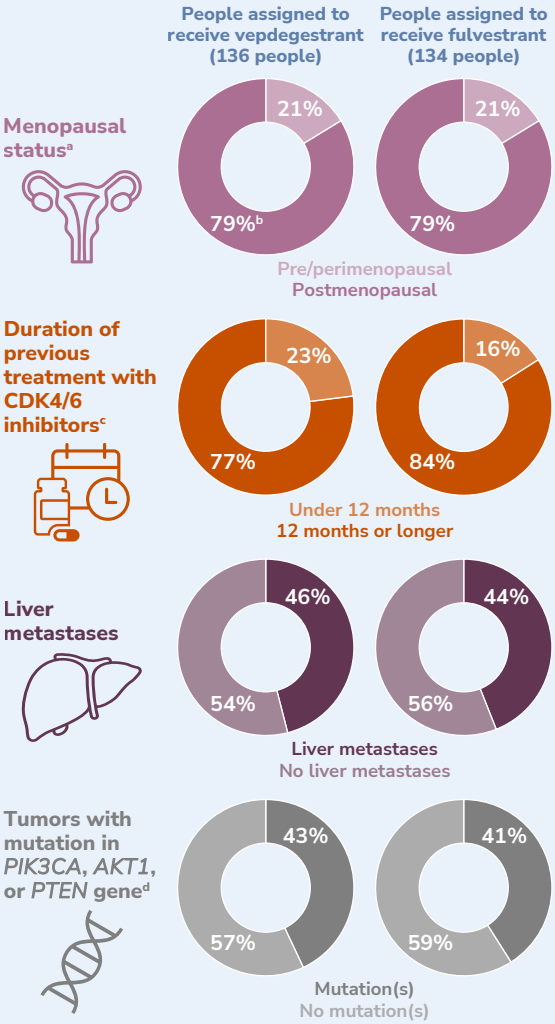
- **How long people with tumors that have *ESR1* mutations and with specific clinical characteristics lived without their cancer growing or spreading when taking vepdegestrant vs fulvestrant**
  - **Specific characteristics evaluated were**
    - **People who have not undergone or are close to menopause (pre/perimenopausal) and those who are postmenopausal**
    - **How long people had previously taken a CDK4/6 inhibitor**
    - **Whether the cancer had spread to the liver (liver metastases)**
    - **People with or without certain other gene mutations in their tumors**

Analysis Population

WHO PARTICIPATED IN THIS ANALYSIS?

270 people living with ER+/HER2- metastatic breast cancer **who had *ESR1*-mutated tumors after treatment with endocrine therapy and a CDK4/6 inhibitor**

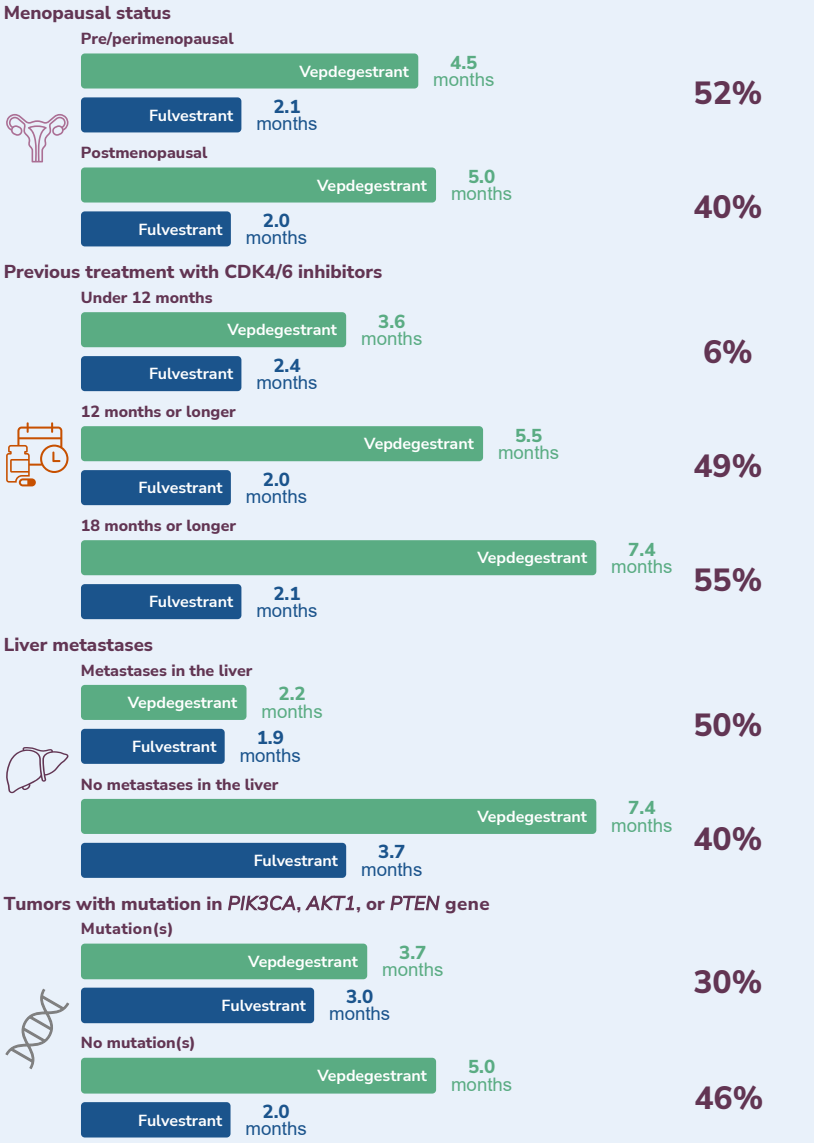
We looked at outcomes in people with different characteristics, including:



[a]Before/during the end of menstrual cycles (pre/perimenopausal) or after menstrual cycles have stopped for ≥12 months (postmenopausal).
[b]1 male in the vepdegestrant group was assigned a status of "pre/perimenopausal."
[c]57% of people assigned to receive vepdegestrant and 65% of people assigned to receive fulvestrant received previous treatment for 18 months or longer.
[d]*PIK3CA*=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha gene; *AKT1*=AKT serine/threonine kinase 1 gene; *PTEN*=phosphatase and tensin homolog gene.

Results

WHAT WERE THE RESULTS OF THIS ANALYSIS?



The amount of time that half of the people lived without their cancer growing or spreading was longer for those taking vepdegestrant than those taking fulvestrant in all subgroups

TAKE-HOME MESSAGES

People living with ***ESR1*-mutated** ER+/HER2– advanced breast cancer **who took vepdegestrant lived longer without their cancer growing or spreading** than those who took fulvestrant, **regardless of whether they had certain characteristics** that can influence the growth of the tumor and the tumor response to treatment

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 **the phase 3 VERITAC-2 study** VIEW CLINICAL TRIAL RECORD

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