Vepdegestrant (ARV-471), a PROTAC® ER degrader, in people with ER+/HER2- advanced breast cancer

This summary contains information from the scientific poster:

VERITAC update: phase 2 study of ARV-471, a PROteolysis TArgeting Chimera (PROTAC) estrogen receptor (ER) degrader in ER+/human epidermal growth factor receptor 2 (HER2)- advanced breast cancer

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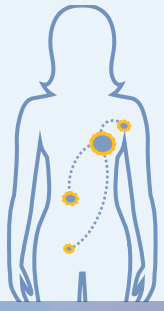
What is ER+/HER2- advanced breast cancer?

ER+/HER2- breast cancer is one type of breast cancer

- Certain types of breast cancer grow in response to **estrogen**, a hormone (or **chemical messenger**) in your body. This is called **estrogen receptor-positive** (**ER+**) breast cancer
- Some types of breast cancer have a lot 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?

Some treatments, called **endocrine therapies**, work by either blocking the body's ability to produce hormones, such as estrogen, or blocking the activity of these hormones 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 binds estrogen receptor leading to their degradation, which reduces estrogen's effects on tumors

Chemotherapy is a treatment that damages cancer cells. Sometimes people get chemotherapy prior to surgery to shrink the size of their tumor, after surgery to kill lingering cancer cells, or if their cancer has spread beyond the breast

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

What is vepdegestrant?

Vepdegestrant, also called **ARV-471**, is an investigational drug that is being evaluated as a treatment for ER+ breast cancer. It is a **PROteolysis TArgeting Chimera (PROTAC) protein degrader that binds to estrogen receptors**

- PROTAC protein degraders are designed to bind specific proteins of interest in cells, 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 could potentially stop ER+ breast cancer tumors from growing or cause the tumors to shrink

In the first part of a **clinical study that tested different doses of vepdegestrant** in people with ER+/HER2- advanced breast cancer:

- During the study, **40%** of the people who could be evaluated had tumors that remained stable (neither grew nor shrank) or **shrank following vepdegestrant treatment**
- The **side effects of vepdegestrant were mostly mild or moderate**

In the second part of the clinical study, researchers tested 2 doses of **vepdegestrant** in people with breast cancer

This summary describes results from the **35 participants who received the lower dose of vepdegestrant** (200 mg once per day)

The **main aims** of this study are to evaluate

- **If vepdegestrant can cause tumors to stop growing or shrink in people with ER+/HER2- advanced breast cancer**
- **The side effects people who take vepdegestrant may experience**

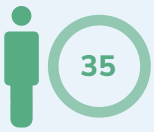
This summary describes

- **How well vepdegestrant caused tumors to stop growing or shrink in people with ER+/HER2- advanced breast cancer and the side effects they experienced while taking the lower dose of vepdegestrant**

Study Population

WHO PARTICIPATED IN THIS STUDY?

35 people with ER+/HER2- locally advanced or metastatic breast cancer enrolled in this study and were assigned to receive the lower dose of vepdegestrant



PEOPLE ASSIGNED TO THE LOWER DOSE IN THIS STUDY

Before the study

had received a CDK4/6 inhibitor

had received an aromatase inhibitor

had received fulvestrant

had received chemotherapy

During the study

Participants took vepdegestrant 200 mg as a pill by mouth once each day

Results

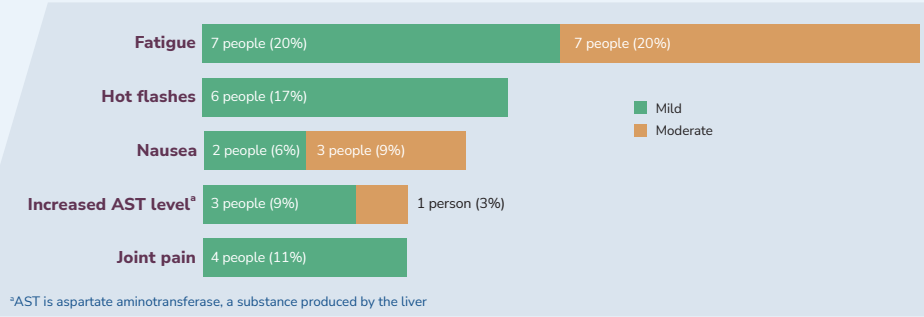
WHAT WERE THE RESULTS OF THE STUDY?

During the study, **tumors shrank or stopped growing in 37%** of people taking the lower dose of vepdegestrant

of those taking the **lower dose**

Half of the people who took the lower dose of vepdegestrant lived without their cancer getting worse for

People taking vepdegestrant experienced **mostly mild or moderate side effects**. The most common side effects were:



[a]AST is aspartate aminotransferase, a substance produced by the liver

TAKE-HOME MESSAGES

Treatment with the lower dose of vepdegestrant showed **clinical benefits for people with ER+/HER2- advanced breast cancer**

- Most of the side effects with vepdegestrant were **mild or moderate**
- A **larger study comparing vepdegestrant vs fulvestrant** in people with ER+/HER2- advanced breast cancer is ongoing
  - **The lower dose of vepdegestrant was selected** to use in the larger study based on the results from this study

Who sponsored this study?

This study is sponsored by **Arvinas Estrogen Receptor, Inc.**
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Arvinas thanks the **people who volunteered to participate in this study** and **their caregivers**, as well as the **investigators, researchers, and coordinators** who are contributing to this study

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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**, please visit

https://www.clinicaltrials.gov/ct2/about-studies/learn