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

This summary contains information from the scientific poster:

TACTIVE-E: phase 1b study of ARV-471, a PROteolysis TArgeting Chimera (PROTAC) estrogen receptor (ER) degrader, in combination with everolimus in ER+/human epidermal growth factor receptor 2 (HER2)-advanced breast cancer

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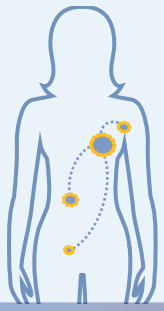
What is ER+/HER2- advanced breast cancer?

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 receptors 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 including abemaciclib, palbociclib, and ribociclib, or **mTOR inhibitors**, such as everolimus, 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 laboratory research studies, vepdegestrant plus everolimus **had stronger effects at preventing tumor growth** than vepdegestrant or everolimus alone

In a **clinical study that tested 2 doses of vepdegestrant** alone in people with ER+/HER2- advanced breast cancer:

- During the study, **tumors shrank or stopped growing in 38% of people** taking vepdegestrant
- People taking either the **lower or higher dose** of vepdegestrant most commonly experienced **fatigue**, **nausea**, and **joint pain**; these side effects were **mostly mild or moderate**

This summary describes a clinical study to test the combination of **vepdegestrant plus everolimus** in people with ER+/HER2- advanced breast cancer

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

- **The side effects people who take vepdegestrant plus everolimus may experience**
- **The best doses of vepdegestrant plus everolimus to use, and the best timing of the doses for future clinical studies**

This study also will look at

- **If vepdegestrant plus everolimus can cause tumors to stop growing or shrink**
- **How well vepdegestrant and everolimus are absorbed by the body and how long they last in the body**

Study Design

WHO CAN PARTICIPATE IN THE STUDY?

Women or men with **ER+/HER2- advanced or metastatic breast cancer** who also

- For women only: are **postmenopausal or receiving estrogen-suppressing therapy**
- Were previously treated with **1–3 anticancer therapies**, including
  - A **CDK4/6 inhibitor** that either failed to stop tumor growth or was discontinued due to side effects
  - **1 or more endocrine therapy**
  - Up to **1 chemotherapy**
- Are **physically healthy** and able to do regular daily activities

WHO CANNOT PARTICIPATE IN THE STUDY?

- People with **cancer that has spread to the brain** that has **not been treated** or that requires **high doses of steroids**
- People previously treated with **vepdegestrant or an mTOR inhibitor**
- People treated with **fulvestrant within 4 weeks of starting their study treatment**
- People treated with **tamoxifen**, an **aromatase inhibitor**, or a **CDK4/6 inhibitor within 2 weeks of starting their study treatment**

WHAT IS THE TREATMENT?

People will receive a combination of **vepdegestrant plus everolimus**

Vepdegestrant and everolimus will be taken as **pills by mouth every day**

WHAT WILL BE MEASURED IN THE STUDY?

- The **side effects** experienced by people taking vepdegestrant plus everolimus
  - This includes any **symptoms** felt by the participants in the study, **signs** observed in the participants by the investigators, or **abnormalities** that are detected in the participants' blood samples
- In the first dosing cycle, any **side effects that prevent continuing at the current dose or increasing the dose** (also called **dose-limiting toxicity**)
- **Tumor size will be measured** by scans to evaluate if vepdegestrant plus everolimus treatment has any effect on slowing tumor growth or shrinking tumors
- Levels of **vepdegestrant and everolimus in the blood** will be measured

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