Vepdegestrant (ARV-471), a PROTAC® ER degrader, combined with other anticancer treatments in people with ER+ advanced breast cancer

This summary contains information from the scientific poster:

TACTIVE-U: Phase 1b/2 Umbrella Study of Vepdegestrant, a Proteolysis Targeting Chimera (PROTAC) Estrogen Receptor (ER) Degrader, Combined With Other Anticancer Treatments in ER-Positive Advanced or Metastatic Breast Cancer

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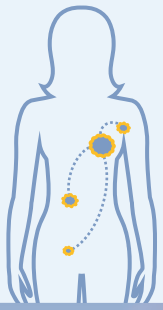
What is ER+ advanced breast cancer?

ER+ 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+ 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
- **SERDs**, such as fulvestrant, are endocrine therapies that bind 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, and **CDK7 inhibitors**, including samuraciclib, are treatments that work by blocking certain proteins that cause cancer cells to grow

What is vepdegestrant?

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

- 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, the combination of vepdegestrant with abemaciclib or ribociclib had **stronger effects in ER+ breast cancer cells** than each treatment alone

In a **clinical study that tested vepdegestrant** alone in people with ER+/HER2- advanced breast cancer who had received prior therapy for their cancer:

- During the study, **tumors shrank or stopped growing for at least 24 weeks in 37% of people** taking vepdegestrant
- People taking vepdegestrant experienced **mostly mild or moderate** side effects; most common side effects were **fatigue**, **hot flush**, and **joint pain**

This study is called an umbrella study, where multiple therapies can be tested on a single disease - in this case, we will be testing vepdegestrant in combination with several other anticancer therapies in people with ER+ advanced breast cancer

The first three sub-studies will be evaluating vepdegestrant plus abemaciclib, vepdegestrant plus ribociclib, or vepdegestrant plus samuraciclib

Additional combinations will be investigated in the future

The **main aims** of the study are to

- **Identify the best doses of vepdegestrant plus other anticancer treatments to use for future clinical studies**
- **Evaluate if the treatments can cause tumors to stop growing or shrink**

The study also will look at

- **How long people receiving these treatments live without their cancer getting worse**
- **The side effects people may experience with these treatments**
- **How well the treatments are absorbed by the body and how long they last in the body**

Study Design

WHO CAN PARTICIPATE IN THE STUDY?

- People with **ER+/HER2- advanced or metastatic breast cancer** who also
  - Were previously treated with **1 CDK4/6 inhibitor**
  - Were treated with **up to 1 more anticancer treatment** (in addition to CDK4/6 inhibitor)
  - Are able to do most of their **regular daily activities**

WHO CANNOT PARTICIPATE IN THE STUDY?

- People whose cancer **has spread to the brain**
- People who have **inflammatory breast cancer**
- People who are **at risk of life-threatening complications in the short term** due to their cancer

WHAT IS THE TREATMENT?

In the first three sub-studies, people will take a combination of vepdegestrant plus abemaciclib, a combination of vepdegestrant plus ribociclib, or a combination of vepdegestrant plus samuraciclib

- Vepdegestrant will be taken as **pills by mouth once daily**
- Abemaciclib will be taken as **pills by mouth twice daily**
- Ribociclib will be given as **pills once daily for 3 weeks followed by 1 week without ribociclib**
- Samuraciclib will be taken as **pills by mouth once daily**

WHAT WILL BE MEASURED IN THE STUDY?

- The **side effects** experienced by people in each of the sub-studies
  - This includes any **symptoms** felt by the participants in the studies, **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 the effect of vepdegestrant plus other anticancer therapies on slowing tumor growth or shrinking tumors
- The amount of time that people **survive without their cancer getting worse** during each of the sub-studies
- Levels of **vepdegestrant and other anticancer therapies in the blood** will be measured and evaluated to assess how the different treatments may **influence each other**

Who sponsored the study?

This study is sponsored in the United States by **Arvinas Estrogen Receptor, Inc.**

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and outside of the United States by **Pfizer Inc.**

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Where can I find more information?

For more information on the study testing the combination of **vepdegestrant plus abemaciclib**

VIEW CLINICAL TRIAL RECORD

For more information on the study testing the combination of **vepdegestrant plus ribociclib**

VIEW CLINICAL TRIAL RECORD

For more information on the study testing the combination of **vepdegestrant plus samuraciclib**

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