

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

This summary contains information from the scientific poster:

Vepdegestrant, a PROteolysis Targeting Chimera (PROTAC) Estrogen Receptor Degradar, Plus Palbociclib in Estrogen Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer: Phase 1b Cohort

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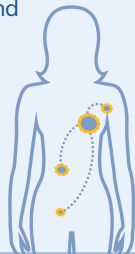
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What is ER+/HER2- advanced breast cancer?

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 degradation, which reduces estrogen's effects on tumors

Chemotherapy is a treatment that damages cancer cells. Sometimes people get it 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, such as palbociclib, 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 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

Why is the combination of vepdegestrant plus palbociclib being used in this study?

- Palbociclib plus fulvestrant is a **standard treatment option** for people with ER+/HER2- breast cancer whose tumors grow after treatment with an endocrine therapy
- In laboratory research studies, vepdegestrant plus palbociclib had **stronger effects at preventing tumor growth** than palbociclib plus fulvestrant

This summary describes results for one part of a clinical study that evaluated **different doses of vepdegestrant plus standard doses of palbociclib**

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

- The **best doses of vepdegestrant plus palbociclib to use for future clinical studies**
- The **side effects people who take vepdegestrant plus palbociclib may experience**

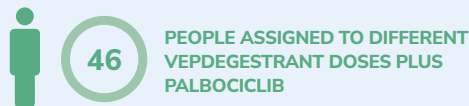
This summary describes

- The **side effects people experienced while taking vepdegestrant plus palbociclib**
- How well vepdegestrant plus palbociclib caused tumors to **stop growing or shrink** in people with ER+/HER2- advanced breast cancer
- How long people taking vepdegestrant plus palbociclib live without their cancer getting worse
- How well vepdegestrant and palbociclib are absorbed by the body and how long they last in the body

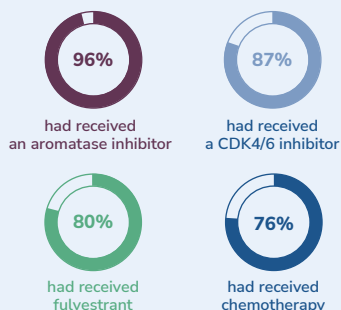
Analysis Population

WHO PARTICIPATED IN THIS STUDY?

46 people with ER+/HER2- locally advanced or metastatic breast cancer who have received previous treatment for their cancer enrolled in this study and were assigned to receive different doses of vepdegestrant plus palbociclib



Before the study



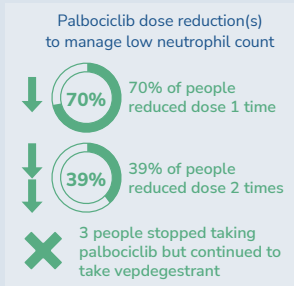
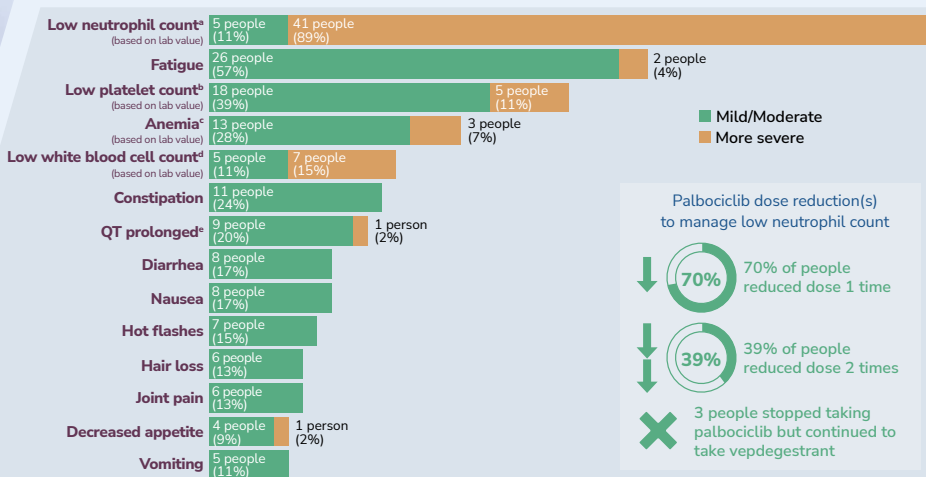
During the study

Participants took different doses of vepdegestrant (ranging from 180 mg to 500 mg) as pills by mouth once daily; palbociclib (125 mg) was taken as pills by mouth once daily for 3 weeks followed by 1 week without treatment

Results

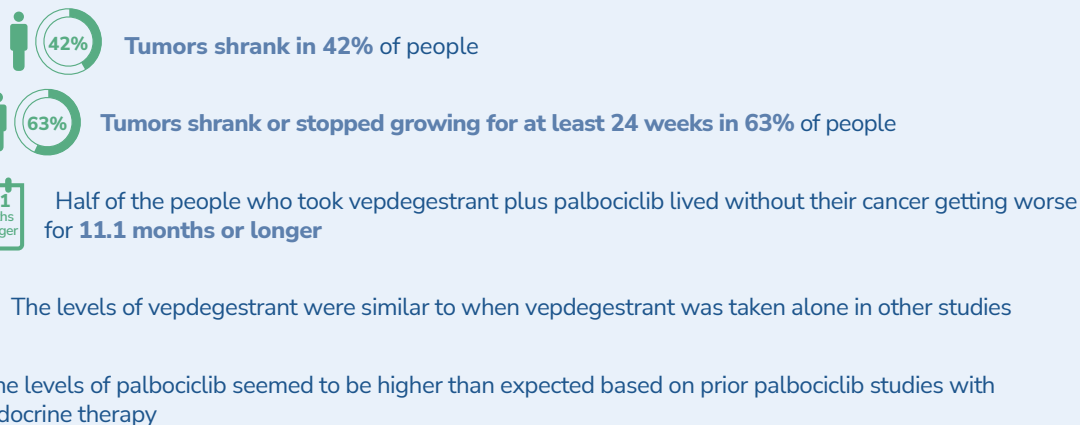
WHAT WERE THE RESULTS OF THE STUDY?

People taking vepdegestrant plus palbociclib experienced **some side effects**. The most common side effects were:



^aNeutrophils are a type of white blood cell that helps the body fight infections and heal wounds. ^bPlatelets are a type of blood cell that form clots and stop bleeding. ^cAnemia is a condition that occurs when your body produces a lower-than-normal amount of healthy red blood cells. ^dWhite blood cells contain types of immune cells that help protect against infections. ^eQT prolonged is when there is an extended interval between the heart contracting and relaxing.

DURING THE STUDY, IN PEOPLE TAKING VEPDEGESTRANT PLUS PALBOCICLIB



Treatment with vepdegestrant plus palbociclib showed **clinical benefit for people with ER+/HER2- advanced breast cancer**

- Most of the side effects with vepdegestrant plus palbociclib were **mild or moderate** with the exception of low neutrophil counts. **Low neutrophil counts were managed** in most people by reducing the dose of palbociclib
- A larger study will compare vepdegestrant plus palbociclib vs letrozole plus palbociclib in people with ER+/HER2- advanced breast cancer
 - A dose of vepdegestrant 200 mg was selected to use in the larger study based on the results of this study
 - An early portion of the larger study will first evaluate lower doses of palbociclib (100 mg and 75 mg) in combination with vepdegestrant

TAKE-HOME MESSAGES

Who sponsored the study?

This study is sponsored by 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](#)