Vepdegestrant (vep-DEG-eh-strent), a PROTAC ER degrader, or anastrozole in postmenopausal women living with ER+/HER2- early breast cancer

This summary contains information from the scientific presentation:

TACTIVE-N: Phase 2 Study of Neoadjuvant Vepdegestrant, a PROTAC Estrogen Receptor (ER) Degrader, or Anastrozole in Postmenopausal ER+/Human Epidermal Growth Factor Receptor 2–Negative Localized Breast Cancer

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What is ER+/HER2- early 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-)**

For patients with **early breast cancer**, the tumor is confined to the breast and nearby lymph nodes and **has not** spread to distant organs

What are some common treatments for ER+/HER2- early breast cancer?

Surgery is one of the most common treatments for people with early and localized 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

Chemotherapy is a treatment that damages cancer cells. People will often receive chemotherapy before surgery to shrink the size of their tumor (as a form of neoadjuvant therapy), after surgery to kill remaining cancer cells, or if their cancer has spread beyond the breast

Neoadjuvant therapy is a treatment given to people before surgery to shrink the size of their tumor and slow the growth of localized breast cancer. Neoadjuvant therapies can include endocrine therapy, such as anastrozole, or chemotherapy

What is vepdegestrant?

Vepdegestrant, also called **ARV-471**, is an investigational drug taken by mouth as a pill that researchers are testing for the treatment of ER+ breast cancer. It is a **PROteolysis TArgeting Chimera (PROTAC) estrogen receptor degrader**

- PROTAC protein degraders are designed to 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

Why is vepdegestrant being evaluated in this study?

As a PROTAC estrogen receptor degrader, vepdegestrant offers a distinct approach from existing endocrine therapies

Treatment with vepdegestrant has been well tolerated in previous clinical studies of patients with ER+/HER2- advanced breast cancer, supporting further evaluation of vepdegestrant as a neoadjuvant treatment option

This summary describes results from a clinical study evaluating vepdegestrant or anastrozole as neoadjuvant therapy in people with ER+/HER2- early breast cancer who had no prior treatment for their cancer

This was a non-comparative study; each treatment group was analyzed on its own, and the study was not designed to test which treatment worked better

The **main aim** of the study was to find out

- **If vepdegestrant could slow cancer from growing before breast cancer surgery. One way to determine this is by measuring the levels of the protein Ki-67 in the tumor, which is an indicator of how fast the cancer is growing**

This summary describes

- **How well vepdegestrant slowed the growth of tumors before surgery**
- **The percentage of women who were able to have breast cancer surgery after taking vepdegestrant**
- **The side effects people experienced while taking vepdegestrant**

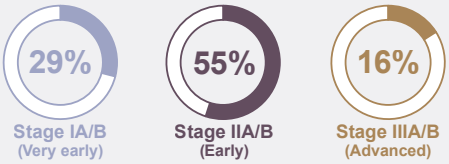
Analysis Population

WHO PARTICIPATED IN THIS STUDY?

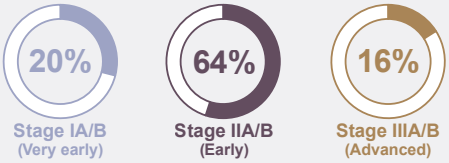
152 postmenopausal women living with ER+/HER2- early breast cancer **who did not receive previous treatment for their cancer** participated in this study and were randomly assigned to receive vepdegestrant or anastrozole

Before the study

Among the 102 people assigned to receive **vepdegestrant**, their stages of breast cancer were:



Among the 50 people assigned to receive anastrozole, their stages of breast cancer were:



During the study

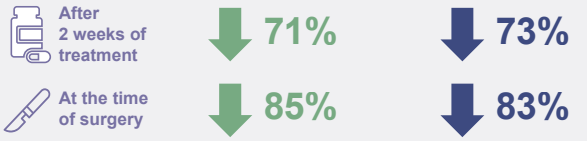
Participants were randomized 2:1 to receive either vepdegestrant (200 mg) or anastrozole (1 mg) as pills by mouth once daily for approximately 5.5 months before undergoing surgery

Results

WHAT WERE THE RESULTS OF THIS PHASE 2 STUDY?

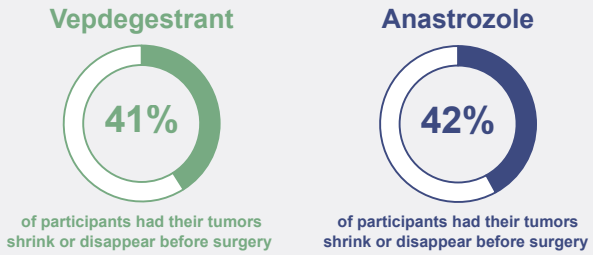
How much did the protein Ki-67 decrease in tumors?

Ki-67 is an indicator of how fast the cancer is growing



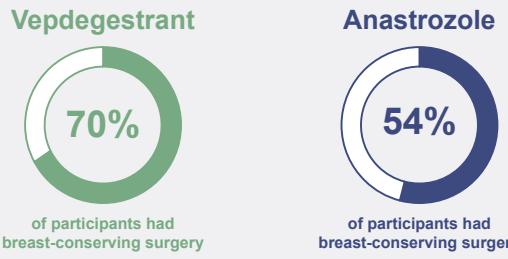
Did tumors stop growing or shrink?

Tumors were imaged during the month leading up to surgery



What percentage of women had breast cancer surgery?

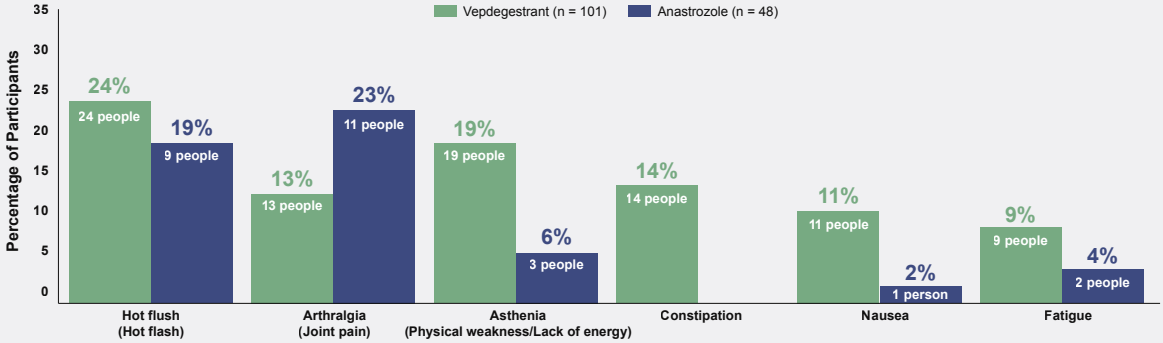
Breast-conserving surgery aims to remove the cancer while preserving the breast



64% of people experienced side effects related to vepdegestrant, and 48% of people experienced side effects related to anastrozole

The most common side effects related to treatment that participants experienced during the study were hot flush with vepdegestrant and arthralgia with anastrozole

Most side effects were mild or moderate



TAKE-HOME MESSAGES

Treatment with **vepdegestrant stopped cancer from growing and reduced tumor size when used as therapy before surgery** in some people living with ER+/HER2- early breast cancer who did not receive previous treatment

Most people had side effects with vepdegestrant that were **mild or moderate**

Who sponsored the study?

This study is sponsored by **Arvinas Estrogen Receptor, Inc., in collaboration with Pfizer, 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