REDISCOVER-2

TRIAL TITLE
Phase 3 Study of RLY-2608 Plus Fulvestrant Compared With Capivasertib Plus Fulvestrant for Locally Advanced or Metastatic PIK3CA-mutant HR+/HER2- Breast Cancer (ReDiscover-2)

TRIAL STATUS
Recruiting

TRIAL NUMBER
NCT06982521

TRIAL PHASE
Phase 3

PARTICIPANTS INCLUDED IN THE STUDY*:

- Adults with locally advanced or metastatic breast cancer that cannot be treated with surgery or radiation.
- Both men and women are eligible; pre-menopausal women must be willing and able to receive ovarian suppression therapy starting at least 4 weeks before the trial.
- Cancer must be hormone receptor-positive (HR+) and HER2-negative (HER2-) with one or more *PIK3CA* mutations.
- Cancer must have progressed after prior treatment, specifically:
  - One to two lines of prior hormone therapy (such as letrozole, tamoxifen or fulvestrant).
  - Exactly one prior treatment with a CDK4/6 inhibitor (such as palbociclib/Ibrance, ribociclib/Kisqali or abemaciclib/Verzenio) for advanced disease.
- Participants must not have already received treatment with PI3K, AKT or mTOR inhibitors (such as alpelisib/Piqray or everolimus/Afinitor) or an antibody-drug conjugate (such as trastuzumab deruxtecan/Enhertu).
- Participants must not have uncontrolled diabetes, significant heart or lung disease, or untreated brain metastases.

*Additional eligibility criteria may have applied.

Breast Cancer Breakthroughs
FACT SHEET

TRIAL DETAILS:

- ReDiscover-2 is a global, randomized, open-label, multicenter Phase 3 clinical trial.
- The study is testing whether RLY-2608 (an investigational PI3Kα inhibitor) plus fulvestrant (a hormone therapy) works better than capivasertib/Truqap (an AKT inhibitor) plus fulvestrant in people with HR+/HER2- metastatic breast cancer and a *PIK3CA* mutation.
- Approximately 540 participants will take part in the study.
- Participants will be assigned to receive either RLY-2608 with fulvestrant or capivasertib with fulvestrant.
- The goal is to see which combination delays cancer progression longer and improves survival while also studying quality of life, side effects and overall safety.

ABOUT HR+/HER2- BREAST CANCER, PIK3CA MUTATIONS AND RLY-2608:

- HR+/HER2- breast cancer is the most common type of breast cancer. It grows in response to hormones but does not overexpress the HER2 protein.
- Metastatic HR+/HER2- breast cancer can develop resistance to treatments, due to genetic changes in the tumor, like a *PIK3CA* mutation. *PIK3CA* mutations occur in approximately 40% of metastatic HR+/HER2- breast cancers.
- RLY-2608 is an investigational drug that selectively blocks the mutant forms of the PI3Kα protein. By sparing the wildtype form of the PI3Kα protein, RLY-2608 may result in fewer side effects while slowing cancer growth.
- This study will help determine whether RLY-2608 in combination with fulvestrant offers better outcomes than the FDA-approved drug capivasertib in combination with fulvestrant in people whose cancer has progressed after taking hormone therapy plus a CDK4/6 inhibitor.

References:

1. Relay Therapeutics. Phase 3 Study of RLY-2608 Plus Fulvestrant Compared With Capivasertib Plus Fulvestrant for Locally Advanced or Metastatic PIK3CA-mutant HR+/HER2- Breast Cancer (ReDiscover-2) (NCT06982521). ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06982521
2. Susan G. Komen. "Hormone Receptor-Positive Breast Cancer: Why Your HR Status Matters for Treatment Decisions." *Know More* (blog), March 28, 2025. https://www.komen.org/blog/know-more-hr-positive-breast-cancer/
3. Susan G. Komen. "Tumor Characteristics That Affect Prognosis." *Tumor Characteristics*, Susan G. Komen, Accessed September 2025. https://www.komen.org/breast-cancer/diagnosis/factors-that-affect-prognosis/tumor-characteristics/

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