Do you have locally advanced or metastatic breast cancer? If so, you may be able to participate in this study of a potential new treatment.

**A Randomized Phase III Trial of Endocrine Therapy Plus Entinostat or Placebo in Patients With Hormone Receptor–Positive Advanced Breast Cancer**

**WHY consider participating in this study**

- Clinical studies are an important way to test the effectiveness of new drugs for treating breast cancer that is not able to be removed by surgery (locally advanced) or has spread (metastasized) to another part of the body
- All study patients will receive the standard hormonal treatment (exemestane)
- Some study patients will also receive an oral investigational drug, entinostat, which has been shown to inhibit breast cancer in preclinical studies and has shown encouraging data in a randomized phase II study. This study will assess its effects in combination with exemestane.
- Once enrolled in the trial, patients can withdraw from the study at any time

**WHAT this study involves**

- If you choose to enroll in this study, you will be assigned by chance (randomized) to one of two study groups, as shown in the diagram
  - Group A will receive exemestane + entinostat
  - Group B will receive exemestane + placebo (an inactive pill)
  
  Neither you nor your doctor will know which treatment you are receiving. In the event of an emergency, this information can be made available to your doctor.
- Participation involves a variety of tests, exams, and procedures, including questions about your general well-being, physical exams, blood work, and CT scans. These are part of regular cancer care and may be done even if you do not join the study.

**Diagram**

- **Enrollment**
- **Randomization** (You will be in one of two groups)
  - **Group A**
    - Exemestane (25 mg) taken by mouth daily
    - Entinostat (5 mg) taken by mouth once a week
  - **Group B**
    - Exemestane (25 mg) taken by mouth daily
    - Placebo (5 mg) taken by mouth once a week

Continue until you, your doctor, or the study sponsor decides to stop your participation

End of study assessments and follow-up
**WHO will take part in the study**

- Approximately 600 women and men in the United States and selected other countries will be included in this study. It is open to pre-, peri-, and postmenopausal women and all men with hormone receptor-positive and/or progesterone receptor–positive breast cancer that cannot be removed by surgery (locally advanced) or has spread (metastasized) to another part of the body. Patients will not be eligible if they are HER2 (human epidermal growth factor receptor-2)-positive.

- Individuals who participate must have recovered from side effects of past therapies

- Hormone receptor–positive cancers may be more likely to respond to hormone therapies, such as exemestane. Patients must have completed prior endocrine therapy at least two weeks before being assigned a study group; an exception is exemestane, which is allowed in patients with metastatic disease if they started exemestane within four weeks of being assigned to a study group. Patients who received everolimus, prior palbociclib, or other cyclin-dependent kinase (CDK) inhibitor (ribociclib, abemaciclib) and prior fulvestrant use are allowed and may participate as long as the drug was completed two weeks before being assigned a study group. Patients may not participate if they have been treated with entinostat, valproic acid (Depakote®, Epilim®, Valparin, Vlapro, Stavzor®), or vorinostat (Zolinza®).

**WHAT are the costs of taking part in this study**

- You and/or your health plan or insurance company will need to pay some or all of the costs of treating your cancer in this study. If you are male or a pre/perimenopausal woman, you will receive goserelin, which will be covered by your insurance. Some health plans will not pay these costs; check with your health plan or insurance company to find out what they will pay for.

- The NCI will supply the exemestane and the entinostat or placebo at no charge while you take part in this study. If a problem with getting exemestane or entinostat/placebo occurs, your study doctor will talk to you about the options.

- For more information on insurance coverage and clinical trials, visit the National Cancer Institute (NCI) website at: www.cancer.gov/clinicaltrials/learningabout/payingfor or call 1-800-4-CANCER (1-800-422-6237)

**IF you would like to know more**

- About the E2112 study
  - Ask your doctor
  - Visit www.ecog-acrin.org/patients and select Trial Educational Materials, then select the link to E2112. If you are seeking information about medical facilities where this trial is available, scroll down the page to Contacts and Locations.
  - Call the NCI Cancer Information Service at 1-800-4-CANCER (1-800-422-6237)

- About entinostat or exemestane
  - Visit www.cancer.gov/drugdictionary

- About clinical trials and general cancer information
  - Visit the NCI website at www.cancer.gov

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**About ECOG-ACRIN**

The ECOG-ACRIN Cancer Research Group is a scientific organization that designs and conducts biomarker-driven cancer research involving adults who have or are at risk of developing cancer. The Group is dedicated to achieving research advances in all aspects of cancer care and improving the quality of life and survival in patients. For more information about ECOG-ACRIN, visit www.ecog-acrin.org.

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