NCI National Clinical Trials Network

E2112

ECOG-ACRIN cancer research group
Reshaping the future of patient care

For Patients with Advanced Breast Cancer

E2112 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase III Trial of Endocrine Therapy plus Entinostat/Placebo in Patients with Hormone Receptor-Positive Advanced Breast Cancer

Patient Population

See Section 3.0 for Complete Eligibility Details

- ER and/or PR positive histologically confirmed adenocarcinoma of the breast with staining of ≥ 1% cells
- Must *not* have tumors that are HER2 IHC 3+, ISH ≥ 2.0, or average HER2 copy number ≥ 6.0 signals per cell
- Must have measurable or non-measurable Stage III/locally advanced or metastatic carcinoma of the breast per protocol, where local therapy with curative intent is not possible
- Pre/peri– and postmenopausal women and all men are eligible; pre/perimenopausal women and men must agree to receive concomitant LHRH agonist
- Must not have known CNS metastasis or a history of CNS metastases; patients with leptomeningeal disease are not eligible
- Must meet either: 1) disease progression any time after non-steroidal AI use in the advanced disease setting, or 2) relapse while on or within ≤ 12 months of end of adjuvant non-steroidal AI therapy with no prior endocrine therapy for advanced disease (see protocol for additional details)
- Patients may have received 1 prior chemo regimen for metastatic disease (must be completed ≥ 3 weeks prior to randomization); may be treated with bone modifying agents
- Prior RT must be completed ≥ 2 weeks prior to randomization (must be recovered from toxicity)
- Must not receive concurrent anti-cancer therapy or investigational agent unless specified in protocol
- Must not be receiving valproic acid, a HDAC inhibitor (must not have previously received any HDAC inhibitor)
- Must have no known allergies to imidazole drugs, exemestane, or entinostat
- Must have recovered from all clinically relevant AEs to grade1 or baseline due to previous agents administered (except alopecia)
- Adequate lab values, ECOG PS 0-1, age ≥ 18 years, and life expectancy ≥ 12 weeks; must be able to swallow pills
- HIV-positive patients should have a CD4 count > 250/mm³

Treatment Plan

See Section 5.0 for Complete Treatment Details

One Cycle = 4 weeks (28 days). A complete cycle of treatment is defined as 28 days (+/- 3 days) of once daily continuous treatment of exemestane in combination with entinostat/placebo. A new cycle start is defined as the first planned date of entinostat/placebo for the cycle

Arm X (Arms A Entinostat and B Placebo; double-blind trial):

- Exemestane 25 mg PO (single dose), Days 1-28
- Entinostat/placebo 5 mg PO (single dose), Days 1, 8, 15, & 22
- Goserelin (pre/perimenopausal female and all male participants only) 3.6 mg SubQ injection Day 1
- Repeat cycles every 28 days until disease progression or unacceptable toxicity

Note:

- *Entinostat/placebo should be taken on an empty stomach, at least 1 hour before or 2 hours after a meal/ snack*
- *Missed doses should not be made up*

Study Chair:
Roisin Connolly, M.B., B.Ch.

Co-Chair:
Kathy D. Miller, M.D.

Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org

Protocol Information

ECOG-ACRIN Operations-Boston: 617-632-3610, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

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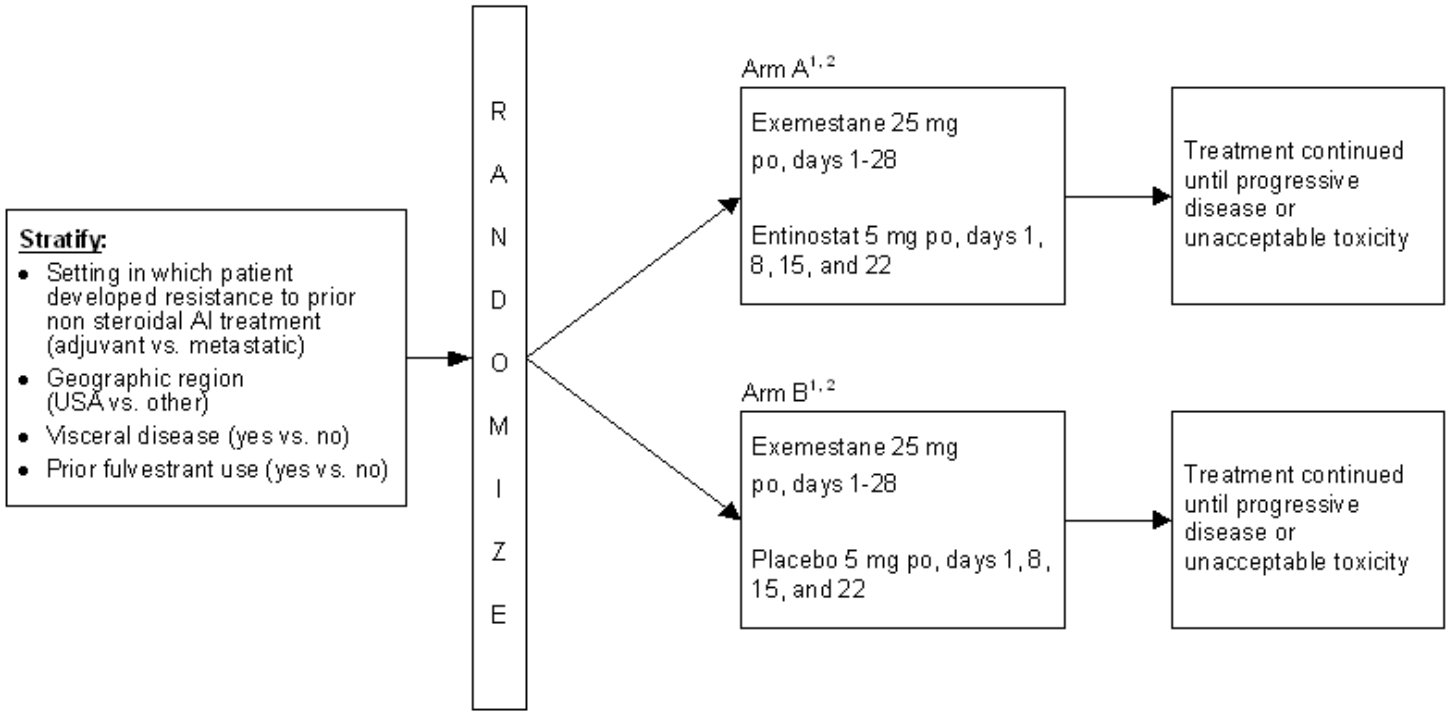
Schema



Accrual Goal = 600 patients
Cycle = 28 days

1. Treatment is blinded. Confirmation of randomization will indicate that patient is on Arm X.
2. Male participants and pre/perimenopausal women will receive Goserelin 3.6 mg SubQ injection on day 1.