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Phase 2 study of abemaciclib in combination with endocrine therapy with or without paclitaxel induction in patients with hormone receptor-positive, HER2-negative advanced breast cancer and aggressive disease criteria: ABIGAIL

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BACKGROUND

- Endocrine therapy (ET) is the preferred therapy option for patients with hormone receptor-positive (HR[+]), HER2-negative (HER2[-]) advanced breast cancer (ABC). However, patients presenting with visceral crisis or severe symptoms usually deserve an induction chemotherapy regimen to achieve rapid disease control [1,2].
- Cyclin-dependent kinases 4/6 inhibitors have improved the effectiveness of ET across all HR[+]/HER2[-] subgroups, with impressive rates of objective response [3]. An exploratory analysis revealed that the addition of abemaciclib to ET conferred the largest benefit in patients with poor prognostic characteristics (liver metastases, high grade tumors, short disease-free interval, or progesterone receptor (PgR)[-]) [4].
- ABIGAIL aims to provide consistent evidence that abemaciclib plus ET is non-inferior to paclitaxel in terms of early overall response as first-line regimen in HR[+], HER2[-] ABC patients with poor prognostic factors.

METHODS

- ABIGAIL is a multicenter, randomized, open-label, investigator-initiated phase 2 study (NCT04603183).
- Patients will be allocated in a 1:1 ratio to receive a 12-week induction therapy consisting of either abemaciclib plus ET (± LHRH analog if men, pre-/peri-menopausal women) **(arm A)** or paclitaxel **(arm B)**.
- After 12-week induction period, in the absence of progression or unacceptable toxicity, patients in **arm A** will continue abemaciclib + ET. Patients in **arm B** will receive crossover abemaciclib plus ET immediately after induction period or up to 12 weeks later as a further three cycles of paclitaxel could be given at discretion of the clinician.
- Patients in **arm B** presenting unacceptable toxicity or progression on paclitaxel will be offered to receive crossover abemaciclib plus ET at discretion of the clinician.
- Tumor assessment through CT-scan or MRI-scan will be performed once every three cycles (or at treatment discontinuation if earlier) until end of study. Response will be assessed as best response according to response evaluation criteria in solid tumors (RECIST) 1.1.
- An overview of the study design is shown in **Figure 1**.

STUDY OBJECTIVES

Primary Objective

- To compare the efficacy –in terms of 12-week overall response rate (ORR) by blinded independent central review per RECIST 1.1– of abemaciclib plus ET (**arm A**) versus paclitaxel (**arm B**).

Secondary Objectives

- To compare the efficacy –in terms of investigator-assessed ORR, clinical benefit rate, 12-week progression-free survival (PFS), PFS, time to response, duration of response, overall survival, maximum tumor shrinkage, time to first subsequent therapy, time to second subsequent therapy, and the time to first chemotherapy– of abemaciclib plus ET (arm A) versus paclitaxel (arm B).
- To assess the safety and tolerability of study drugs, and the health-related quality of life in either arms.

Exploratory Objectives

- To investigate predictive/prognostic biomarkers and their pharmacodynamic changes on tissue biopsies and blood samples.
- To characterize the gut microbiome and metabolomic profile in stool samples of patients allocated to **arm A**.

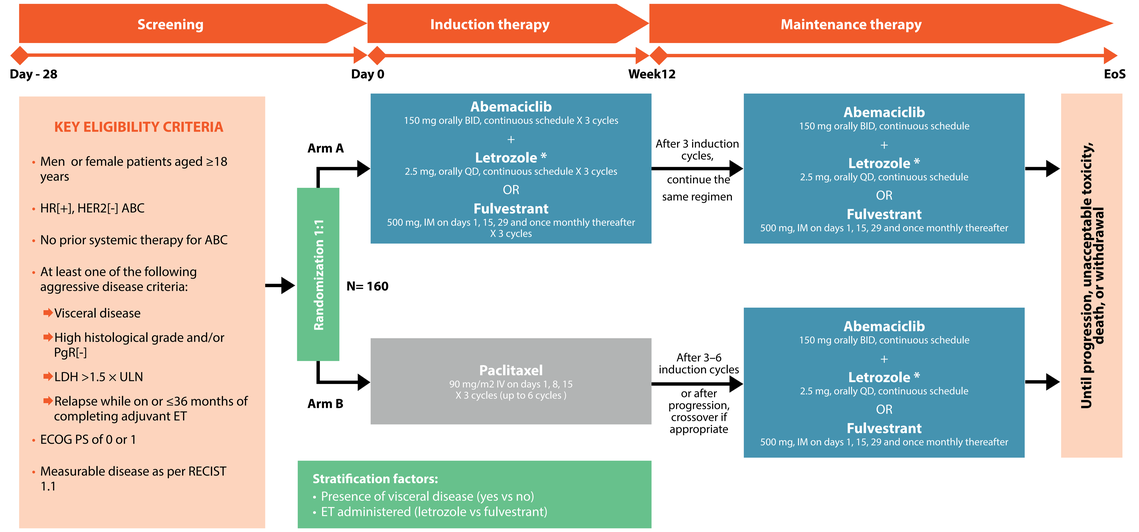
STATISTICS

Statistical Assumptions

- The sample size assumes the comparison of two proportions in an asymptotical normal test.
- We expect 30% versus 15% 12-week ORR in **arm A** versus **arm B**, respectively, with a 5% non-inferiority margin.
- Based on a 10% dropout rate, a sample size of 160 patients is necessary to attain 80% power at nominal level of two-sided alpha of 0.05.
- We will test the superiority of abemaciclib plus ET if the non-inferiority objective is achieved. Both analyses, will be conducted with the Newcombe hybrid score method for confidence intervals.

STUDY DESIGN

Figure 1. ABIGAIL Study Profile



* Letrozole is highly recommended for patients who are sensitive to AI, while fulvestrant for AI-resistant patients. Men and pre-/peri-menopausal women will receive LHRH if randomized to receive abemaciclib plus ET.
Abbreviations: ABC, unresectable locally advanced or metastatic breast cancer not amenable to resection with curative intent; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; HR, hormone receptor; IM, intramuscular injection; IV; intravenously; LDH, lactate dehydrogenase; PgR, progesterone receptor; ULN, the upper limit of normal.

STUDY ENROLLMENT

- ABIGAIL was opened to accrual in May 2021 and currently recruiting in 16 institutions from Spain.
- An additional three countries (France, Italy, and Portugal) are participating.

REFERENCES

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