Plain Language Summary of Data Presented at SABCS 2024

EMBER-3 Trial: Results

What is this summary about?

Here, we summarize the results of the EMBER-3 study presented at the 47th San Antonio Breast Cancer Symposium in 2024. To help you understand the results, see the description of the study below.

EMBER-3: a study of imlunestrant with or without abemaciclib in patients with ER+, HER2- advanced breast cancer following progression on a previous hormone therapy

- Advanced breast cancer means that the cancer has spread to another part of the body outside of the breast. This is also sometimes called metastatic breast cancer
- Disease recurrence means that the cancer has come back after hormone therapy. Disease progression means that the cancer has spread and worsened on hormone therapy
- The *ESR1*-mutated population includes those with advanced breast cancer and a mutation in the estrogen receptor 1 gene. This mutation causes certain hormone therapies to be less effective
- The study analyzed patients in two ways. First, in all patients enrolled in the study. Second, in only patients whose tumors had the *ESR1* mutation

How was the study designed and what was the main goal?

ER+, HER2- advanced breast cancer

874 patients were randomized 1:1:1

- **Imlunestrant (study drug)**
- **Older approved hormone therapies of the physician's choice (fulvestrant or exemestane)**
- **Imlunestrant (study drug) and abemaciclib**

ER+ cancer cells have receptors that allow the hormone estrogen to attach, allowing cancer cells to grow.

HER2 proteins control how breast cells grow. In certain cancers, there are too many of these proteins causing the cancer to grow and spread.

Patients who participated in this trial were placed into one of three different treatment groups.

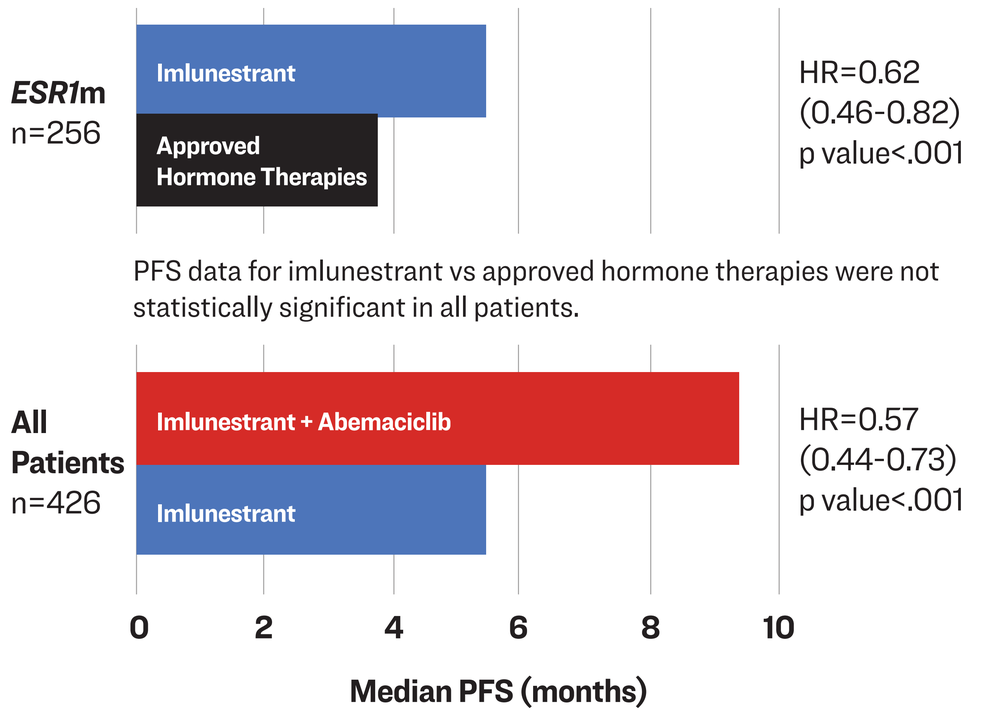
Main goals of study

The study had 3 goals.

- First, to determine if imlunestrant was better than older approved hormone therapies in patients with *ESR1*-mutated breast cancer
- Second, to understand if imlunestrant was better than older hormone therapies in all patients in the trial
- Lastly, to determine if the combination of imlunestrant plus abemaciclib was better than imlunestrant alone in all patients tested

What were the results?

- Imlunestrant improved PFS (meaning a delay in disease progression or death) in patients with ER+, HER2- advanced breast cancer who also had an *ESR1* mutation
- The data also showed that the addition of abemaciclib to imlunestrant improved PFS in patients with ER+, HER2- advanced breast cancer, regardless of *ESR1* mutation status

What was evaluated?	What did the data show?	What does it mean?
PFS PFS, or progression-free survival, is the length of time people in the study are alive and their cancer does not grow or spread after the start of treatment. ***ESR1* mutation** *ESR1* mutation means the cancer has a mutation in the estrogen receptor 1 gene. This means the cancer is resistant to older forms of hormone therapy, like aromatase inhibitors.	 PFS data for imlunestrant vs approved hormone therapies were not statistically significant in all patients.	**Imlunestrant** worked better than older hormone therapies if the cancer had an *ESR1* mutation. These patients had a **38% reduction** in the risk of cancer spreading. **Imlunestrant and abemaciclib** worked better than imlunestrant alone. These patients had a **43% reduction** in the risk of cancer spreading. This treatment effect was seen in cancers with or without an *ESR1* mutation.

What about safety?

Side effects were generally mild. Most patients did not need to reduce dose, hold doses, or stop the imlunestrant because of side effects.

The most common side effects with **imlunestrant** were:

- Fatigue (23%)
- Diarrhea (21%)
- Nausea (17%)
- Arthralgia (14%)
- AST increase (13%)
- Back pain (11%)

2% needed to lower the dose and 4% needed to stop the medicine; imlunestrant had a generally favorable safety profile.

The most common side effects with **imlunestrant and abemaciclib** were:

- Diarrhea (86%)
- Nausea (49%)
- Low white blood cells (48%)
- Anemia (44%)
- Fatigue (39%)
- Vomiting (31%)

39% needed a lower dose of one or both drugs and 6% needed to stop both medicines; the safety of imlunestrant plus abemaciclib was consistent with the known safety profile for the combination of abemaciclib with fulvestrant.

In EMBER-3, imlunestrant showed a treatment effect in patients with *ESR1*-mutated ER+, HER2- advanced breast cancer, and imlunestrant plus abemaciclib showed a treatment effect in patients with ER+, HER2- advanced breast cancer.

Reference: SABCS 2024 Presentation. Komal L. Jhaveri, et al. Abstract GS1-01: Imlunestrant, an Oral Selective Estrogen Receptor Degrader (SERD), as Monotherapy and Combined with Abemaciclib, for Patients with ER+, HER2- Advanced Breast Cancer (ABC), Pretreated with Endocrine Therapy (ET): Results of the Phase 3 EMBER-3 trial.

Abbreviations: AST=aspartate aminotransferase; ER=estrogen receptor; *ESR1*=estrogen receptor 1 gene; HER2=human epidermal growth factor receptor 2; HR=hazard ratio; m=mutated; PFS=progression-free survival.

ClinicalTrials.gov Identifier: NCT04975308.