

Real-world evidence of elacestrant in adults with HR+, HER2– *ESR1*-mutated metastatic breast cancer



This summary describes **studies evaluating real-world outcomes of elacestrant** that were presented in Lloyd MR, et al. *Clin Cancer Res.* 2025 and Rugo HS, et al. *Clin Cancer Res.* 2025. An explanation of the studies and their findings are summarized below.

What is elacestrant used for?

Elacestrant is a prescription medicine to treat women who have gone through menopause and adult men with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, *ESR1*-mutated advanced breast cancer or breast cancer that has spread to other parts of the body (metastatic), and whose disease has progressed after endocrine therapy.¹

Why were these studies performed?

After elacestrant was FDA approved in January 2023 and sufficient time had passed, researchers wanted to better understand how elacestrant works in a real-world setting. **Real-world studies** can **leverage large datasets** to evaluate **treatment patterns** and **explore biomarker associations with patient outcomes**.^{1,2}

What are the limitations of real-world data?

Real-world data analyses can address some of the limitations of clinical trials; however, they also present distinct challenges. Real-world differences between routine clinical care and prospective trials may be due to multiple factors impacting patient selection, like:



Treatment heterogeneity



Genomic profile



Tumor burden



Censoring



Follow-up duration from the time of first elacestrant treatment



Clinical interpretation of surrogate outcomes, incomplete or missing data, and imprecise or inconsistent definitions of lines of therapy

Due to the retrospective, observational design of these analyses, only **associations** between treatments and outcomes can be inferred, **not causation**.

- ✓ These results can not be directly compared with clinical trials
- ✓ There is the potential for missing, inaccurate, or incomplete data
- ✓ Results are not adjusted for potential bias
- ✓ Since this analysis was based on data collected in the US, the results may not be generalizable to other patient populations
- ✓ Variations in patient populations and baseline characteristics might require further research

What does real-world mean in this analysis?

Real-world means that researchers analyzed insurance claims or electronic health records of patients who were not enrolled in a clinical trial but took elacestrant as part of their routine cancer care.

Elacestrant and the EMERALD clinical trial^{1,3,4}

What did the EMERALD clinical trial evaluate?

In the EMERALD clinical trial, researchers wanted to evaluate if elacestrant reduced the risk of breast cancer worsening or death compared to standard endocrine therapy for patients with previously treated ER+, HER2- advanced or metastatic breast cancer.

Elacestrant is an estrogen receptor antagonist, a type of endocrine therapy (ET), indicated for the treatment of postmenopausal women or adult men with ER+, HER2-, *ESR1*-mutated advanced or metastatic breast cancer that has progressed following at least one prior line of ET

EMERALD was a clinical study that supported the FDA approval of elacestrant and is separate from the real-world studies shown on the following pages.

ER+, HER2- Advanced or Metastatic Breast Cancer

- Mostly females
- All received 1–2 lines of prior ET plus a CDK4/6 inhibitor
- Mostly 60- to 65-year-olds

478 patients randomly divided into 2 groups

239 patients

239 patients

Elacestrant

Standard of Care (SOC) ET

Fulvestrant, exemestane, anastrozole, or letrozole

What were the key results?

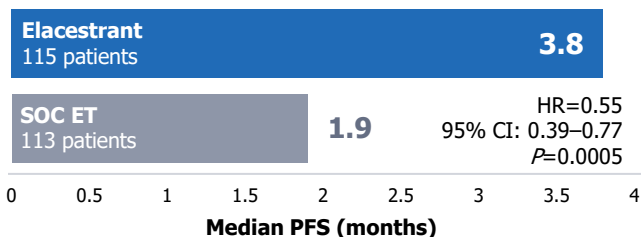
Patients who had advanced or metastatic breast cancer with ***ESR1*-mutated** tumors who took elacestrant had a 45% reduction in the risk of their cancer growing, spreading, or getting worse when compared to people who took SOC ETs. The **median progression-free survival** (mPFS) was 3.8 months for elacestrant compared to 1.9 months with other ETs.

What is an *ESR1* mutation? Some ER+ breast cancers may develop an acquired mutation in the estrogen receptor 1 gene (*ESR1*) that causes certain ETs to be less effective

What is median PFS? PFS is the length of time people in the study are alive and their cancer does not grow or spread after the start of treatment. Since the median is the middle number in a group of numbers arranged from lowest to highest, median PFS is the time at which half of the patients were alive, and their cancer had not progressed

What did the data show?

mPFS in patients with advanced or metastatic breast cancer and *ESR1*-mutated tumors



45%

Less risk of progression with elacestrant compared to SOC ET

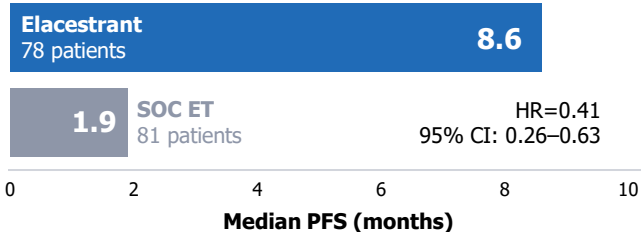
What did the safety data show?

Most common side effects in at least 10% of all patients treated in the trial

	Elacestrant 237 patients	SOC ET 230 patients
Muscle pain	41%	39%
Nausea	35%	19%
Vomiting	19%	9%
Diarrhea	13%	10%
Constipation	12%	6%
Abdominal pain	11%	10%
Indigestion	10%	2.6%
Fatigue	26%	27%
Decreased appetite	15%	10%
Headache	12%	12%
Hot flush	11%	8%

A **post-hoc analysis** suggested that elacestrant was associated with an improvement in mPFS compared to SOC ET in patients who received longer prior treatment with ET plus a CDK4/6 inhibitor for at least 12 months.

mPFS for patients with *ESR1* mutation who received prior ET plus a CDK4/6 inhibitor for at least 12 months³



What is a post-hoc analysis? A post-hoc analysis takes a closer look at data from a study after it is completed to see if there are any interesting findings to help researchers discover new insights and better understand the treatment. These analyses were done after the main EMERALD trial ended and could represent chance findings. While they provide additional information, only **associations** can be inferred, **not causation**. It is recommended that other trials be done to confirm these findings

Clinical and genomic factors associated with elacestrant outcomes in *ESR1*-mutant metastatic breast cancer⁵

What was the main goal of the study?

This study was a **retrospective** analysis of information collected from a large clinical-genomic database.

Researchers assessed **clinical and genomic factors** associated with differences in elacestrant outcomes, which was measured via **time-to-next-treatment (TTNT)**.

Safety with elacestrant was not evaluated in this study.

What does retrospective mean?

A retrospective analysis means that researchers review events that have already taken place

What is time-to-next-treatment?

The time from the start of one line of therapy to the next line of therapy, or death (whichever occurs first)

Who were the patients in the study?

756 patients with **HR+, HER2- *ESR1*-mutated metastatic breast cancer** identified for analysis via the GuardantINFORM database and treated with a line of elacestrant therapy after FDA approval in January 2023. The patients also had an *ESR1*-mutation detected on circulating tumor DNA (ctDNA) within 6 months of elacestrant initiation. The mean age was **63 years**.

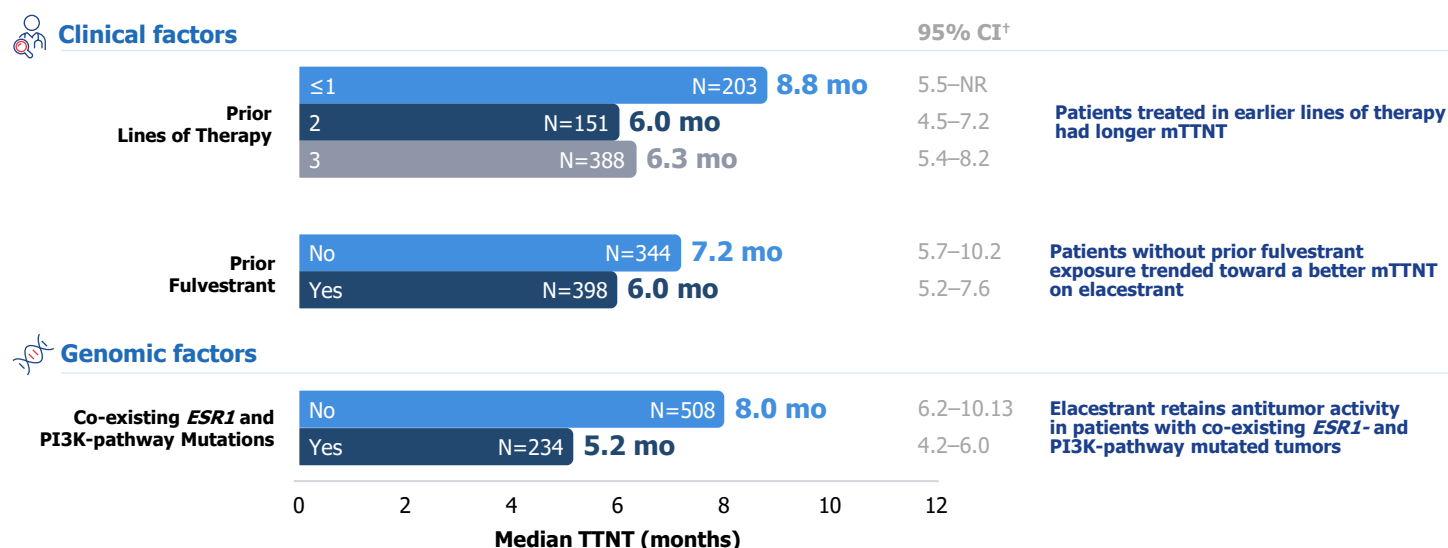


What were the key results of the study?

In this real-world study, patients treated with elacestrant had longer median TTNT (mTTNT) in earlier lines of therapy, despite being more heavily pre-treated with therapies like fulvestrant, chemotherapy, and ADCs, than patients in the EMERALD clinical trial.*

These findings emphasize the importance of **personalized therapy selection** and **treatment sequencing** in *ESR1*-mutant metastatic breast cancer and support the **routine clinical use of elacestrant** in patients previously exposed to endocrine and CDK4/6 inhibitor therapy, with or without coexisting PI3K pathway alterations.

Median TTNT since elacestrant initiation across:



*Elacestrant is indicated for use after progression on endocrine therapy. †The 95% confidence interval is a way to describe how precise a sample estimate is. A narrower interval indicates a more precise estimate, while a wider one indicates more uncertainty.

Outcomes of elacestrant in ER+, HER2– *ESR1*-mutant metastatic breast cancer⁶

What was the main goal of the study?

This study was a **retrospective** analysis of information collected from US insurance claims data from the Komodo Research Dataset (KRD).

Researchers also assessed **clinical and genomic factors** from the linked Foundation Medicine Inc. clinical-genomic (FMICG) data and investigated differences in elacestrant outcomes, which was measured via **time-to-next-treatment (TTNT)**.

Safety with elacestrant was not evaluated in this study.

What does retrospective mean?

A retrospective analysis means that researchers review events that have already taken place

What is time-to-next-treatment?

The time from the start of one line of therapy to the next line of therapy, or death (whichever occurs first)

Who were the patients in the study?

306 patients with **ER+, HER2– *ESR1*-mutated metastatic breast cancer** who were treated with elacestrant, were ET eligible, and had an eligible line of therapy. The median age was **64 years**.

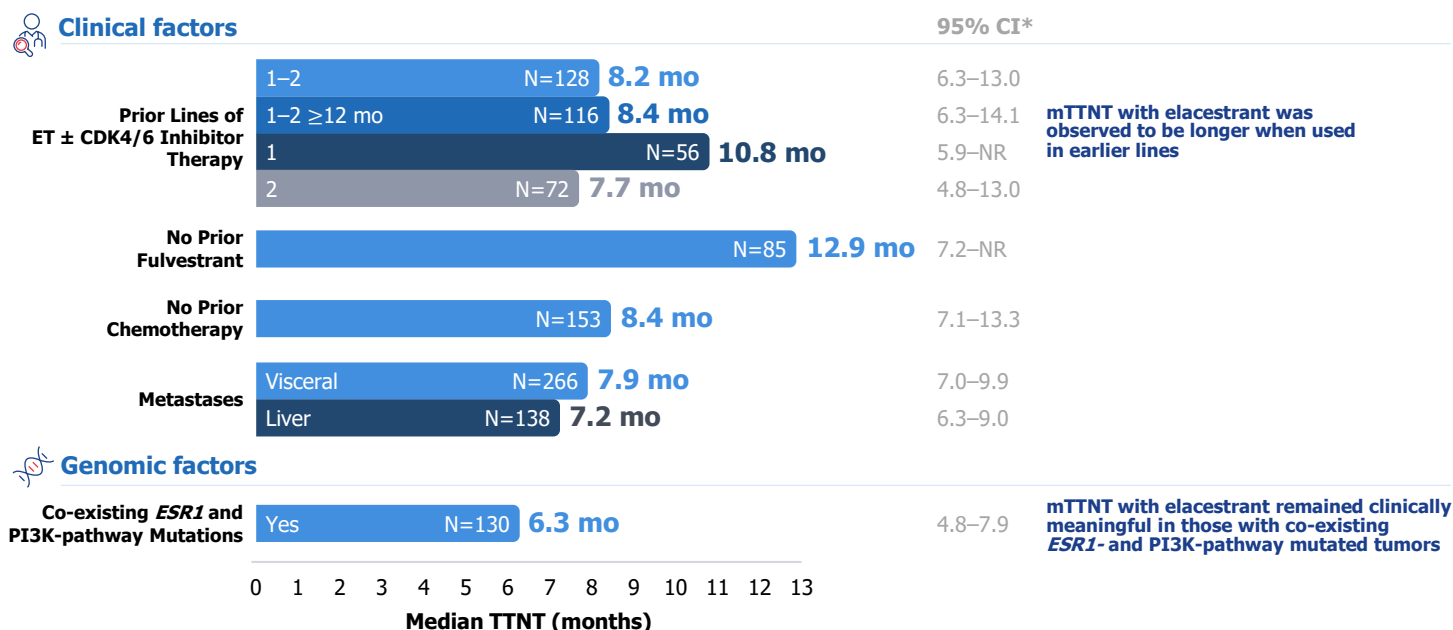


What were the key results of the study?

The median TTNT (mTTNT) with elacestrant was observed to be longer when used in earlier lines of therapy and remained clinically meaningful in patients who have both *ESR1* and PI3K-pathway mutated tumors.

These findings support recommendations to **test for *ESR1*-mutations in liquid biopsy at each progression** and **reinforces the role of elacestrant in personalized ET sequencing strategies** prior to targeted combinations, chemotherapy, or antibody-drug conjugates for the management of ER+, HER2– mBC after first line ET+CDK4/6i.

Median TTNT since elacestrant initiation across:



*The 95% confidence interval is a way to describe how precise a sample estimate is. A narrower interval indicates a more precise estimate, while a wider one indicates more uncertainty. 1. Orserdu Package Insert. Stemline Therapeutics; 2023. 2. Cottu P, et al. *Breast*. 2022;61:118-122. 3. Bidard FC, et al. *J Clin Oncol*. 2022;40(28):3246-3256. 4. Bardia A, et al. *Clin Cancer Res*. 2024;30(19):4299-4309. 5. Lloyd MR, et al. *Clin Cancer Res*. Published online November 7, 2025. 6. Rugo HS, et al. *Clin Cancer Res*. Published online November 14, 2025.