Randomized phase II, open-label, multicenter study evaluating the addition of Elacestrant to Olaparib (Standard PARP-Inhibitor) compared to olaparib monotherapy in patients with HR+/HER2- locally advanced or metastatic breast cancer with germline *BRCA1/2* mutations – ELEMENT

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Background

- Elacestrant, a selective estrogen receptor degrader (SERD), proved safe and efficient in heavily pretreated patients (pts) with estrogen receptor-positive (ER+), human epidermal growth factor-2 negative (HER2-) metastatic BC (mBC) who had disease progression following ≥ 1 line of endocrine therapy (ET) including CDK4/6 inhibitor. Efficacy was superior in pts with estrogen receptor-1 (*ESR1*) .[1]
- Olaparib, a poly-ADP ribose polymerase (PARP) inhibitor, proved safe and efficient in pretreated HER2- mBC with deleterious/suspected deleterious germline (g)*BRCA1/2* mutation.[2]
- Extended follow-up of olaparib revealed a potential overall survival (OS) benefit in pts not previously treated with chemotherapy in the metastatic setting as well as no evidence of cumulative toxicity.[3,4]
- These data support early germline BRCA1/2 testing, ideally at first diagnosis of metastatic disease, to optimize treatment sequencing.
- The purpose of this study is to evaluate whether the addition of the oral SERD elacestrant to olaparib standard therapy can improve progression-free survival (PFS) and potentially delay the need for chemotherapy when compared to olaparib alone in patients with hormone receptor-positive (HR+)/HER2- locally advanced or mBC with a g*BRCA1/2* mutation.

Study objectives

Primary objective:

To evaluate the impact on **PFS** of elacestrant with olaparib vs. olaparib alone in patients with HR+/HER2- locally advanced/mBC and g*BRCA1/2* mutation. PFS is the time from randomization to first progression as assessed by the investigator, or death, whichever occurs first.

Secondary objectives:

- To compare **time-to-treatment failure (TTF)** between treatment arms.
- To compare **OS** between treatment arms.
- To assess and compare **patient reported outcomes (PROs)** and **quality of life (QoL)** between treatment arms.
- To compare **overall response rate (ORR)** between treatment arms.
- To compare the **clinical benefit rate (CBR)** between treatment arms.
- To assess and compare **safety** and **compliance** between treatment arms.

Translational research objectives:

- To assess *BRCA1/2* and *ESR1* mutation status via liquid biopsy.
- To assess ctDNA at baseline, during treatment, and at disease progression.
- To explore predictive biomarkers for efficacy, PFS, and resistance.

Study design

ELEMENT (GBG114; EU-CT: 2023-504925-38) is a phase II, prospective, multicenter, randomized, open-label, parallel group study in pts with HR+/HER2- locally advanced or mBC with g*BRCA1/2* mutations. Pts are randomized 2:1 to elacestrant + olaparib (arm A) or olaparib (arm B). See **Figure 1**.

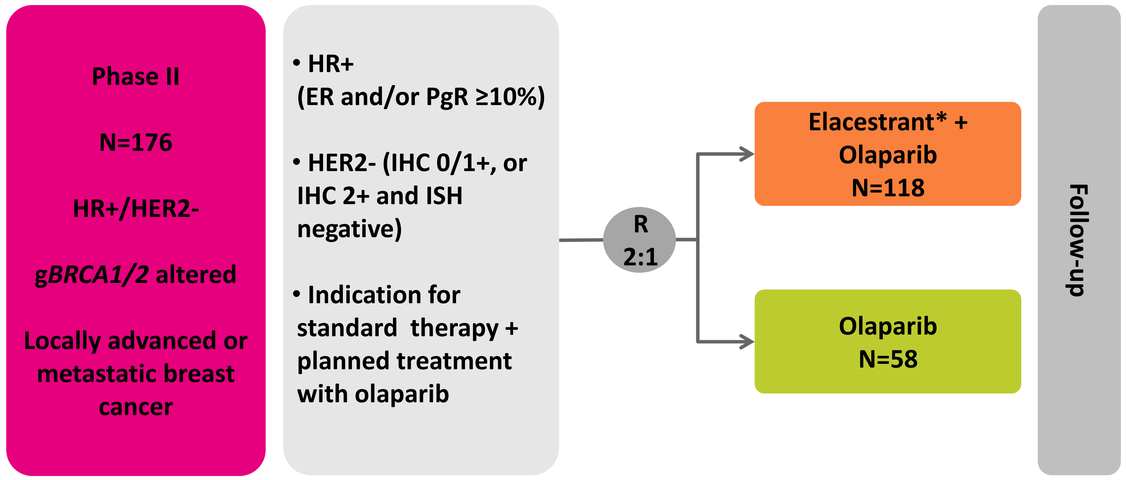

Figure 1. ELEMENT trial study design

Study Treatment:

Arm A: 400 mg tablet of elacestrant dihydrochloride (345 mg elacestrant)* QD and 300 mg of olaparib BID

Arm B: 300 mg of olaparib BID

Dose interruptions and reductions are permitted as specified in the protocol.

Treatment in either arm will be given until disease progression, unacceptable toxicity, withdrawal of patient's consent to study participation, or end of study (EOS).

*Together with GnRH analogue in pre- and perimenopausal women, and in men, at least two weeks prior to treatment.

Collection of biomaterials

Study requirements	Treatment Phase			Follow-up phase
	Pre-treatment	During treatment	EOT	At relapse
FFPE tumor tissue	X			X
Plasma liquid biopsy (ctDNA)	X	After 28 days, then Q3 months	X	X
Whole blood	X			

Follow-up

- Follow-up data (including first new therapy, subsequent disease progression data, and death) is collected every 3 months until progression or EOS, whichever occurs first.
- After progression (incl. pts who experience progression during the treatment phase), data will be collected every 6 months until EOS.

Key eligibility criteria

- Age ≥ 18 years, female or male patients.
- Locally advanced HR+/HER2- mBC according to ASCO/CAP guidelines.
- Pts with deleterious or suspected deleterious g*BRCA1/2* mutations upon local testing.
- Indication for standard-of-care therapy and planned treatment with olaparib.
- No prior treatment with PARP inhibitors.
- No known hypersensitivity to or contraindication against one of the substances used in the study.
- No active or newly diagnosed CNS metastases, including leptomeningeal carcinomatosis, carcinomatous meningitis, or radiographic signs of CNS hemorrhage. Pts with stable brain metastases are eligible.
- No symptomatic metastatic visceral disease at risk of life-threatening complications in short term.
- Willingness and ability to provide archived formalin fixed paraffin embedded tissue (FFPE) block or a partial block from archived tumor or metastasis.
- Adequate organ function prior to enrolment.
- ECOG performance status 0-2.
- Life-expectancy > 6 months.

Interim analysis

An interim safety analysis will be performed in the study after the first 15 pts in the elacestrant arm have completed 8 weeks of treatment.

Recruitment

- The ELEMENT study plans to enroll patients across ~40 sites in Germany.
- Until 27 January 2026, 16 pts have been randomized.
- Enrollment is currently taking place across 34 active sites.
- Additional sites are being activated.

References

1. Bardia et al., J Clin Oncol 2021. 2. Robson et al., N Engl J Med 2017.
3. Robson et al., Ann Oncol 2019. 4. Robson et al., Eur J Cancer 2023.

Conflicts of interest

Thomas Decker declares to participate in advisory boards for Novartis, Roche, IOMEDICO, and AstraZeneca.

The 37th German Cancer Congress (Deutscher Krebskongress – DKK), Berlin, February 18 – February 21, 2026.

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