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Etcamah in combination with a CDK4/6 inhibitor approved in the US for 1st-line advanced HR-positive breast cancer

Approval based on SERENA-6 Phase III trial results which showed combination reduced the risk of disease progression or death by 56% in patients with an emergent ESR1 tumour mutation

Innovative treatment strategy has potential to reshape 1st-line treatment paradigm for patients in this setting

AstraZeneca's *Etcamah* (camizestrant) in combination with a cyclin-dependent kinase (CDK) 4/6 inhibitor (abemaciclib, palbociclib or ribociclib) has been approved in the US for the treatment of adult patients with hormone receptor (HR)-positive, HER2-negative, locally advanced or metastatic breast cancer upon detection of *ESR1* mutation during aromatase inhibitor (AI) and CDK4/6 inhibitor therapy, based on a US Food and Drug Administration (FDA)-authorised test.

The accelerated approval was based on results from the pivotal SERENA-6 Phase III trial presented at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting and simultaneously published in *The New England Journal of Medicine*.[1]

Kevin Kalinsky, MD, MS, FASCO, Division Director of Medical Oncology, Winship Cancer Institute of Emory University and investigator for the trial, said: "This combination provides an important new option for the one in three patients with this form of advanced breast cancer whose tumours develop *ESR1* mutations before clinical or radiographic disease progression. Today's approval will enable clinicians to promptly intervene and change therapeutic strategy at an earlier opportunity ahead of disease progression, rather than waiting until the cancer becomes harder to treat, and patient outcomes and quality of life worsen."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "Today's approval is the tenth granted by the FDA this year across AstraZeneca's portfolio and our fourth in breast cancer alone. The *Etcamah* combination reflects AstraZeneca's leadership in redefining breast cancer care by pioneering a new approach using circulating tumour DNA and is the first and only medicine of its type in the 1st-line setting."

In a planned interim analysis of the SERENA-6 trial, *Etcamah* in combination with a CDK4/6 inhibitor reduced the risk of disease progression or death by 56% versus standard-of-care treatment with an AI (anastrozole or letrozole) in combination with a CDK4/6 inhibitor (based on a hazard ratio [HR] of 0.44; 95% confidence interval [CI]:0.31-0.60; p<0.00001; median PFS 16.0 versus 9.2 months). While data for the key secondary endpoints of time to second disease progression (PFS2) and overall survival (OS) were immature at the time of the interim analysis, a subsequent pre-planned analysis demonstrated a statistically significant and clinically meaningful PFS2 benefit of 25.7 months versus 19.1 months in favour of the *Etcamah* combination (HR: 0.63; 95% CI: 0.46-0.86; p=0.00373), and OS continued to mature in favour of the *Etcamah* combination (HR: 0.87; 95% CI: 0.57-1.30). The trial will continue to assess OS as a key secondary endpoint.

The safety profile of *Etcamah* in combination with palbociclib, ribociclib or abemaciclib in the SERENA-6 trial was consistent with the known safety profile of each medicine. No new safety concerns were identified, and discontinuations were very low and similar in both arms.[1]

In the US, breast cancer is the most common cancer in women, with more than 300,000 new patients diagnosed annually, and more than 42,000 deaths.[2] Approximately 37,000 patients with HR-positive metastatic breast cancer in the US are treated with a medicine in the 1st-line setting, most frequently with endocrine therapies that target estrogen receptor (ER)-driven disease, which are often paired with CDK4/6 inhibitors.[3-5] However, resistance to these therapies frequently develop in many patients.[5] Once this occurs, treatment options are limited and survival rates are low with just over a third of patients anticipated to live beyond five years after diagnosis.[5,6] Mutations in the *ESR1* gene are a key driver of endocrine resistance and are associated with poor outcomes, emerging during treatment of the disease

and becoming more prevalent as the disease progresses.[7,8] Approximately 30% of patients with endocrine sensitive HR-positive disease develop *ESR1* mutations during 1st-line treatment before disease progression.[3]

Concurrently with this approval, the FDA also approved a companion diagnostic test to detect emerging *ESR1* resistance mutations in the circulating tumour DNA (ctDNA) of patients with HR-positive, HER2-negative advanced or metastatic breast cancer. SERENA-6 is the first global, double-blind, registrational Phase III trial to use a ctDNA-guided approach to detect the emergence of endocrine resistance and inform a switch in therapy before disease progression. The innovative trial design used ctDNA monitoring via a blood test at the time of routine tumour scans every two to three months to identify patients for early signs of endocrine resistance via the emergence of *ESR1* mutations. Following detection of an *ESR1* mutation without disease progression, the endocrine therapy of patients was switched to *Etcamah* from ongoing treatment with an AI, while continuing combination with the same CDK4/6 inhibitor.

Etcamah is also approved in more than 30 countries across the globe, including in the EU, Japan, Canada, the UK and several other countries based on the SERENA-6 Phase III trial.

Notes

HR-positive breast cancer
Breast cancer is the second most common cancer and one of the leading causes of cancer-related deaths worldwide.[9] More than two million patients were diagnosed with breast cancer in 2024, with more than 690,000 deaths globally.[9] While survival rates are high for those diagnosed with early breast cancer, only about 30% of patients diagnosed with or who progress to metastatic disease are expected to live five years following diagnosis.[6]

HR-positive breast cancer, characterised by the expression of estrogen or progesterone receptors, or both, is the most common subtype of breast cancer with 70% of tumours considered HR-positive and HER2-negative.[6] ERs often drive the growth of HR-positive breast cancer cells.[10]

Globally, more than 200,000 patients with HR-positive breast cancer are treated with a medicine in the 1st-line setting; most frequently with endocrine therapies that target ER-driven disease, which are often paired with CDK4/6 inhibitors.[3-5]

The optimisation of endocrine therapy and overcoming resistance to enable patients to continue benefiting from these treatments, as well as identifying new therapies for those who are less likely to benefit, are active areas of focus for breast cancer research.

SERENA-6
SERENA-6 is a Phase III, double-blind, randomised trial evaluating the efficacy and safety of *Etcamah* in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) versus treatment with an AI (anastrozole or letrozole) in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) in patients with HR-positive, HER2-negative advanced breast cancer (patients with either locally advanced disease, or metastatic disease) whose tumours have an emergent *ESR1* mutation.

The global trial enrolled 315 adult patients with histologically confirmed HR-positive, HER2-negative advanced breast cancer, undergoing treatment with an AI in combination with a CDK4/6 inhibitor as 1st-line treatment. The primary endpoint of the SERENA-6 trial is PFS as assessed by investigator, with secondary endpoints including OS, and PFS2 by investigator assessment.

Etcamah
Etcamah is a potent, next-generation oral selective estrogen receptor degrader (SERD) and complete ER antagonist, administered orally, once daily. The recommended dose of *Etcamah* in combination with a CDK4/6 inhibitor is 75mg.

Etcamah in combination with a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib) is approved in the US, EU, Japan and several other countries for the treatment of adult patients with HR-positive (or ER-positive), HER2-negative locally advanced or metastatic breast cancer upon detection or

emergence of *ESR1* mutation and without disease progression during 1st-line endocrine therapy based on the results from the SERENA-6 Phase III trial.

The broad, robust and innovative *Etcamah* clinical development programme, including the SERENA-4, CAMBRIA-1 and CAMBRIA-2 Phase III trials, is evaluating the safety and efficacy of *Etcamah* when used as a monotherapy or in combination with CDK4/6 inhibitors to address a number of areas of unmet need in HR-positive, HER2-negative breast cancer.

AstraZeneca in breast cancer
Driven by a growing understanding of breast cancer biology, AstraZeneca is challenging, and redefining, the current clinical paradigm for how breast cancer is classified and treated to deliver even more effective treatments to patients in need - with the bold ambition to one day eliminate breast cancer as a cause of death.

AstraZeneca has a comprehensive portfolio of approved and promising compounds in development that leverage different mechanisms of action to address the biologically diverse breast cancer tumour environment.

With *Enhertu* (trastuzumab deruxtecan), a HER2-directed antibody drug conjugate (ADC), AstraZeneca and Daiichi Sankyo are aiming to improve outcomes in previously treated HER2-positive, HER2-low and HER2-ultralow metastatic breast cancer and are exploring its potential in earlier lines of treatment and in new breast cancer settings.

In HR-positive breast cancer, AstraZeneca continues to improve outcomes with foundational medicines *Faslodex* and *Zoladex* (goserelin) and aims to reshape the HR-positive space with first-in-class AKT inhibitor, *Truqap* (capivasertib), the TROP-2-directed ADC, *Datroway* (datopotamab deruxtecan) and next-generation oral SERD, *Etcamah*.

PARP inhibitor *Lynparza* (olaparib) is a targeted treatment option that has been studied in early and metastatic breast cancer patients with an inherited *BRCA* mutation. AstraZeneca with MSD (Merck & Co., Inc. in the US and Canada) continue to research *Lynparza* in these settings. AstraZeneca is also exploring the potential of saruparib, a potent and selective inhibitor of PARP1, in combination with *Etcamah* in *BRCA*-mutated, HR-positive, HER2-negative advanced breast cancer.

To bring much-needed treatment options to patients with triple-negative breast cancer, an aggressive form of breast cancer, AstraZeneca is collaborating with Daiichi Sankyo to evaluate the potential of *Datroway* alone and in combination with immunotherapy *Imfinzi* (durvalumab).

AstraZeneca in oncology
AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyse changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death.

AstraZeneca
AstraZeneca (LSE/STO/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Disease, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Social Media @AstraZeneca.

Contacts
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References

1. Bidard FC, et al. First-Line Camizestrant for Emerging ESR1-Mutated Advanced Breast Cancer. *N Engl J Med* 2025; DOI: 10.1056/NEJMoa2502929.
2. American Cancer Society. Key Statistics for Breast Cancer. Available at: https://www.cancer.org/cancer/types/breast-cancer/about/how-common-is-breast-cancer.html. Accessed September 2026.
3. Cerner CancerMPact database. Accessed September 2026.
4. Lin M, et al. Comparative Overall Survival of CDK4/6 Inhibitors Plus Endocrine Therapy vs. Endocrine Therapy Alone for Hormone receptor-positive, HER2-negative metastatic breast cancer. *J Cancer*. 2020; 10.7150/jca.48944.
5. Lloyd M R, et al. Mechanisms of Resistance to CDK4/6 Blockade in Advanced Hormone Receptor-positive, HER2-negative Breast Cancer and Emerging Therapeutic Opportunities. *Clin Cancer Res*. 2022; 28(5):821-30.
6. National Cancer Institute. Cancer Stat facts: Female breast cancer subtypes. Available at: https://seer.cancer.gov/statfacts/html/breast-subtypes.html. Accessed September 2026.
7. Brett O, et al. ESR1 mutation as an emerging clinical biomarker in metastatic hormone receptor-positive breast cancer. *Breast Cancer Res*. 2021; 23:85.
8. Zundelevich A, et al. ESR1 mutations are frequent in newly diagnosed metastatic and loco-regional recurrence of endocrine-treated breast cancer and carry worse prognosis. *Breast Cancer Res*. 2020; 22:16.
9. Sung H, et al. Global cancer statistics 2024: GLOBOCAN estimates of incidence and mortality worldwide for 34 cancers in 186 countries. *CA Cancer J Clin*. 2026; DOI: 10.3322/caac.70090.
10. Scabia V, et al. Estrogen receptor positive breast cancers have patient specific hormone sensitivities and rely on progesterone receptor. *Nat Commun*. 2022; 10.1038/s41467-022-30898-0.

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