FDA approves AstraZeneca's Etcamah, opening ctDNA-guided treatment paradigm in breast cancer

In a rare divergence from its own expert panel, the FDA has granted accelerated approval to AstraZeneca's camizestrant, turning a contentious regulatory review into a landmark win that opens a new treatment paradigm for molecular-guided cancer care.

The oral SERD, to be marketed as Etcamah, has been approved in combination with a CDK4/6 inhibitor for the treatment of HR-positive, HER2-negative breast cancer, but only upon detection of ESR1 mutation during initial first-line treatment with an aromatase inhibitor and a CDK4/6 drug.

Etcamah survived a hesitant FDA and an overwhelming rejection by an advisory committee to secure Friday's surprise approval.

As Jefferies analysts framed in a Sunday note, Etcamah's approval is an important moment in breast cancer, "not because of the drug itself, but because it validates an entirely new treatment paradigm of ctDNA-guided intervention before radiographic progression."

The approval is based on the phase 3 Serena-6 trial, which enrolled HR+/HER2- breast cancer patients who had not progressed on first-line aromatase inhibitors and CDK4/6 inhibitors, as determined by scans, but who had emergent ESR1 mutation detected in circulating tumor DNA.

Compared with patients who stayed on their original treatment, those who switched to the Etcamah-CDK4/6 regimen enjoyed a 56% lower risk of disease progression or death. Median progression free survival was 16 months for the novel therapy, versus 9.2 months in the comparator arm.

The Etcamah group also went longer before tumor progression on next-line treatment or death with 23% in risk reduction. Overall survival data, while not mature, showed a trend in favor of AZ's regimen.

Roche's ctDNA-guided approach in post-surgical bladder cancer pays off with Tecentriq nod

Despite the positive readout, the FDA's initial review took a more skeptical view toward its interpretation. Because other oral SERDs have become standard second-line therapy in certain HR+/HER2- breast cancer cases, the FDA initially took issue with Serena-6's trial design because it didn't compare the novel first-line switch approach to the standard practice of waiting until disease progression. The trial did not allow crossover to Etcamah, and only 14% of control-arm patients received other oral SERDs for subsequent treatment.

At that time, the FDA recognized that its decision on AZ's application would have far-reaching implications beyond just Etcamah, because it would signify an endorsement of a new treatment paradigm based on detection of a biomarker in liquid biopsy before conventional tumor progression.

During April's advisory committee deliberation, experts largely sided with the FDA. Even though AZ's first-line switch method is trailblazing, several FDA advisors were concerned that Serena-6's design was flawed by not offering enough patients an oral SERD as second-line treatment.

Following overwhelmingly negative reviews by both the FDA and the agency's advisors, AZ submitted additional ctDNA analyses at the FDA's request. It showed that by Week 8, total ctDNA levels were reduced by 99% in the Etcamah arm, versus an increase of 64% in the control arm, according to results presented at ASCO 2026. An exploratory analysis also linked reduction of total ctDNA to a 61% improvement in overall survival.

Now, after a review extension, the FDA has apparently changed its mind. The accelerated approval means AZ is obligated to provide confirmatory evidence in the future. The phase 3 Serena-4 trial evaluating Etcamah as a first-line treatment regimen is expected to read out topline results this year.

“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,” Dave Fredrickson, AZ’s head of oncology hematology business unit, said in a Sept. 4 statement.

By AZ’s estimate, about 37,000 patients with HR-positive metastatic breast cancer in the U.S. are treated with a medicine, mostly with endocrine therapies, paired with CDK4/6 inhibitors. However, about 30% of patients may develop ESR1 mutations, which may drive endocrine resistance, during their first-line treatments before 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,” Kevin Kalinsky, M.D., from Emory University and investigator for Serena-6, said in a statement.

AZ has pegged Etcamah to reach more than $5 billion in peak annual sales, although the currently approved first-line switch label is only a small part of that ambition. The majority of the revenue target, according to Jefferies, likely lies in the early breast cancer setting.

Etcamah faces some tough oral SERD competitors in the Menarini Group’s Orserdu, Eli Lilly’s Inluriyo and Roche’s giredestrant, all targeting the adjuvant setting.

News Source:

https://www.fiercepharma.com/pharma/fda-approves-astrazeneca-etcamah-opening-ctdna-guided-treatment-shift-breast-cancer