The survive heroes study: targeting molecular relapse in breast cancer

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Abstract

Background: Current research on circulating tumor DNA (ctDNA) in the adjuvant setting of early breast cancer (eBC) underscores its strong prognostic significance. Patients who are ctDNA-positive but show no radiological signs of relapse (i.e., molecular relapse) exhibit reduced disease-free and overall survival. Secondary adjuvant intervention studies represent an innovative and promising therapeutic approach.

Objective: Treating ctDNA-positive patients without radiographic evidence of recurrence is a novel therapeutic strategy. If SURVIVE HERoes and similar studies targeting minimal residual disease (MRD) yield positive results, they could pave the way for a new molecularly driven individualized treatment approach aimed at improving survival or even achieving cure by liquid biopsy triggered early intervention in this new therapeutic window of pre-symptomatic MRD.

Methods: SURVIVE HERoes is a phase III randomized clinical trial comparing the potent antibody-drug conjugate trastuzumab deruxtecan to standard of care (SoC) in patients with HER2-positive or HER2-low eBC and molecular residual or recurrent disease (ctDNA-positive, cM0) following primary therapy. Patients tested positive for ctDNA in a tumor-informed approach are eligible, if staging examinations do not show any residual or recurrent cancer. Participants are randomized in a 2:1 ratio to receive trastuzumab deruxtecan (+ endocrine therapy for HR+ patients) or SoC therapy. Stratification factors include hormonal receptor status (positive versus negative) and HER2 status (positive versus low).

The primary endpoint is ctDNA clearance rate after 12 months of therapeutic intervention. Secondary endpoints include relapse-free survival, overall survival, safety, and quality of life (QoL). The trial will enroll a total of 180 participants across 50 centers in Germany. Staging examinations and ctDNA assessments will be performed at regular intervals. The study is accompanied by a comprehensive translational research program. Recruitment began in Q1/2025 and is anticipated to continue until 2030.

Do you have any conflicts of interest?

Yes, I have a conflict of interest.

Funding by Astra Zeneca