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The SURVIVE HERoes study (NCT06643585): Targeting molecular relapse in breast cancer.

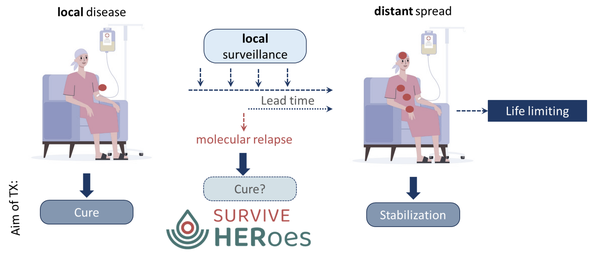
A secondary adjuvant intervention study of trastuzumab deruxtecan versus SOC treatment in patients with HER2 positive or HER2 low early breast cancer and ctDNA positivity after primary therapy.

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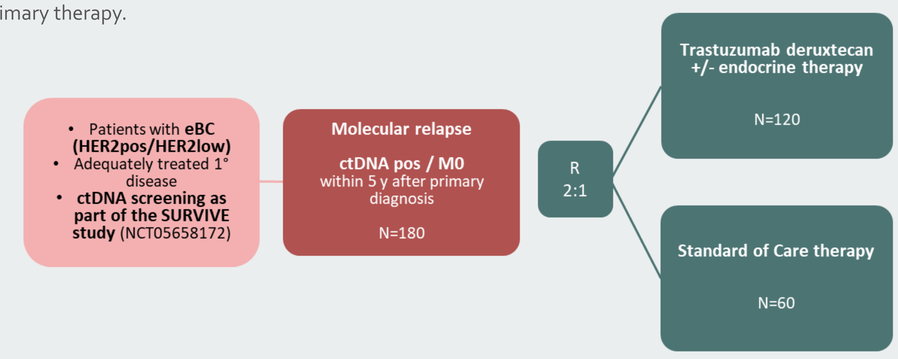
Background

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.



Trial design

SURVIVE HERoes is a phase III randomized open-label clinical trial comparing the antibody-drug conjugate trastuzumab deruxtecan to standard of care (SoC) in 180 patients with HER2-positive or HER2-low eBC and molecular residual or recurrent disease (ctDNA-positive, cM0) following primary therapy.



Stratification Factors

- HER2 status (low versus positive)
- Hormone receptor status (positive (≥ 1%) versus negative)

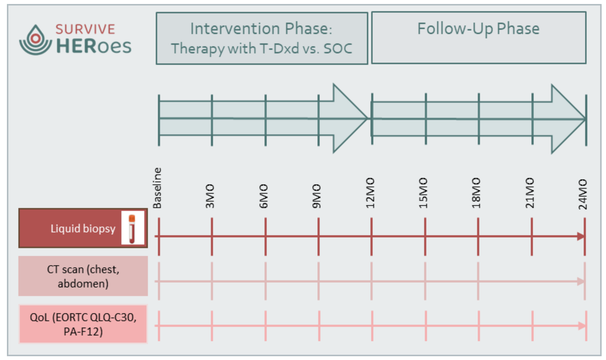
Study Homepage Clinicaltrials.gov Contact Survive-heroes@uniklinik-ulm.de

Endpoints

Primary endpoint: ctDNA clearance after 12 months

Secondary endpoints: Distant disease-free survival (DDFS), Invasive disease-free survival (IDFS), Overall Survival (OS), Quality of Live (QoL), safety, ctDNA and CTC dynamics and clearance

Study Interventions



After the 12 month Follow-Up phase in HERoes, the participants enter the intensified surveillance of the SURVIVE study.

ctDNA using a tumor-informed approach (RaDaR)

CTC with HER2 co-staining (CellSearch®)

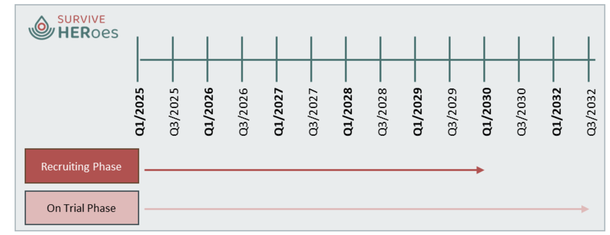
Key Inclusion Criteria

- Early breast cancer, HER2 positive or HER2 low
- Primary therapy (operation +/- radiotherapy +/- (neo) adjuvant chemotherapy) completed
- ctDNA positive (RaDaR)
- No signs of relapse (M0)
- Adequate organ function
- Age 18-75 years; ECOG 0-1

Key Exclusion Criteria

- Metastatic (stage IV) breast cancer
- Patients with a history of any secondary primary malignancy are ineligible with the exceptions of DCIS or other in-situ diseases
- Prior treatment with T-DXd
- History of ILD
- Prolonged QTc interval

Current status and timeline



- Enrolment started in Q2/2025
- 50 centers across Germany planned, currently 27 registered and/or initiated (see map)



Conclusion

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 achieving cure by liquid biopsy triggered early intervention in this new therapeutic window of pre-symptomatic MRD after early breast cancer.

Roles and Acknowledgements

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