The survive study – standard surveillance vs. intensified liquid biopsy-based surveillance in early breast cancer survivors

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Abstract

Background: Current breast cancer (BC) follow-up relies on clinical examinations and breast imaging, as studies from the 1980s demonstrated no survival benefit from distant metastasis screening. However, with advancements in treatment strategies and the diagnostic potential of liquid biopsies, this approach warrants re-evaluation. To enable pre-symptomatic detection of distant relapse, we propose assessing a liquid biopsy-guided surveillance strategy incorporating serum tumor markers (CA 27.29, CA 125, CEA), circulating tumor cells (CTCs), and circulating tumor DNA (ctDNA).

Objective: We aim to determine whether liquid biopsy-guided follow-up enables earlier, sensitive, and specific detection of distant (oligo-)metastases, facilitating timely intervention and improving OS.

Methods: The SURVIVE study (NCT05658172), funded by the German Federal Ministry of Education and Research, is a multicenter, randomized controlled trial evaluating the benefits of intensified surveillance versus standard surveillance in 3500 survivors of primary invasive intermediate-to-high risk early breast cancer (eBC). All subtypes are eligible. Intermediate-to-high risk is defined as the indication for (neo-)adjuvant chemotherapy, tumor size >50 mm, positive lymph nodes (≥pN1mi), or high grade (≥G3). Patients are randomized 1:1 to either standard follow-up or liquid biopsy-guided intensified follow-up. Patients must have completed primary therapy (surgery, adjuvant chemo- or radiotherapy), while ongoing adjuvant endocrine, antibody, or targeted therapy is allowed. In both arms, guideline-based follow-up is performed, with additional blood samples collected longitudinally at regular intervals. In the intervention arm, these samples are analyzed for serum tumor markers, CTCs, and ctDNA (tumor-informed RaDaR assay). Abnormal findings indicating minimal residual disease (MRD) trigger full staging. In the case of M0 status, liquid biopsy testing and staging continue, with the option for inclusion in interventional trials in the presence of MRD, if applicable. Recurrence is managed according to national guidelines. The study is currently recruiting, and as of February 2025, 1023 patients have been randomized.

The two primary objectives are to evaluate the lead time effect obtained by liquid biopsy marker testing in the intensified follow-up arm and to test whether intensified, liquid biopsy-guided surveillance improves overall survival (OS) compared to standard follow-up. Secondary endpoints include IDFS, DDFS, DRFS, BCSS, and QoL as well as biomarker sensitivities and specificities obtained in the intensified follow-up arm.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.