TPS1120 Poster Session

A phase III randomized trial of radiotherapy optimization for low-risk HER2-positive breast cancer (HERO): NRG-BR008.

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Background: Breast radiotherapy (RT) is the standard of care for patients with early-stage breast cancer (BC) who undergo breast-conserving surgery (BCS). However, the magnitude of benefit of RT is less clear in BCS patients with low-risk disease who receive effective systemic therapy. Among patients with early-stage HER2-positive (HER2+) BC, 10-year locoregional recurrence has been reported as low as 1.5% following BCS, adjuvant chemotherapy and HER2-targeted therapy, and RT. Given these exceedingly favorable outcomes, with the addition of HER2-directed therapy, we seek to evaluate the feasibility of omitting RT among patients with early-stage HER2+ BC following BCS and appropriate systemic therapy. **Methods:** This is a phase III randomized trial for patients ≥18 years with early-stage, node-negative, HER2+ (IHC/FISH) BC treated with BCS with negative margins and sentinel lymph node biopsy or axillary dissection. Patients undergoing primary surgery must have pathologic T1-2 (≤3 cm) N0 disease, whereas patients receiving neoadjuvant therapy must have clinical T1-2 (with radiographically T≤5 cm) N0 disease and exhibit a pathologic complete response (ypT0N0) at surgery (residual DCIS [ypTis] spanning ≤1 cm is permitted, and surgical margins are negative for DCIS). All patients must receive cytotoxic chemotherapy and HER2-targeted therapy, either in the adjuvant or neoadjuvant setting. Stratification is by age (<60; ≥60), tumor size (≤1 cm; >1 cm), estrogen-receptor status (positive; negative), and systemic therapy sequencing (adjuvant *v* neoadjuvant). Patients will be randomized to standard breast RT in addition to continuation of trastuzumab to complete one year of treatment (Arm 1), or trastuzumab alone (Arm 2). Endocrine therapy will be recommended for patients with hormone-receptor-positive tumors. The primary endpoint is the recurrence-free interval (RFI). Secondary endpoints include time to ipsilateral breast recurrence, locoregional recurrence, disease-free survival, and overall survival, in addition to the 7-year ipsilateral breast recurrence rate among those not receiving RT. A health-related quality of life sub-study will assess differences in patient-reported breast pain and worry. We estimate a 7-year RFI of 97.5% with RT and allow for a clinically acceptable decrement of 3.63% without RT (7-year RFI of 93.87%; HR 2.5) to establish omission of RT as non-inferior. NRG-BR008 aims to enroll 1,300 patients over 7.25 years, yielding 80% power to detect the non-inferiority of RT omission with a one-sided α=0.05. We expect to observe the required 38 RFI events within 4.5 years of additional follow-up. The NRG-BR008/HERO trial opened to accrual in March 2023. Accrual is 64/1,300 as of 1/23/24. NCT #: NCT05705401. Support: U10 CA180868, -180822, UG1 CA189867, U24 CA196067. Clinical trial information: NCT05705401. Research Sponsor: National Cancer Institute; U10CA180868; National Cancer Institute; U10CA180822; National Cancer Institute; UG1CA189867; National Cancer Institute; U24CA196067.