TPS625 **Poster Session**

NRG-BR007: A phase III trial evaluating de-escalation of breast radiation (DEBRA) following breast-conserving surgery of stage 1, HR+, HER2-, RS ≤18 breast cancer.

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Background: Approximately 50% of newly diagnosed invasive breast cancers are stage 1, with the majority being ER/PR-positive, HER2-negative. Genomic assays such as the Oncotype DX have identified patients (pts) with reduced risk of distant metastasis and without benefit from chemotherapy added to endocrine therapy (ET), freeing them from excess toxicity. Genomic assays are also recognized as prognostic for in-breast recurrence (IBR) after breast-conserving surgery (BCS) and could similarly allow de-escalation of adjuvant radiotherapy (RT). Reducing overtreatment is of interest to pts, providers, and payers. **Methods:** We hypothesize that BCS alone is non-inferior to BCS plus RT for IBR and breast preservation in women intending ET for stage 1 invasive breast cancer (ER and/or PR-positive, HER2-negative with an Oncotype DX Recurrence Score [RS] of ≤18). Stratification is by age (<60; ≥60), tumor size (≤1 cm; >1-2cm), and RS (≤11, >11-18/MammaPrint Low). Pts are randomized post-BCS to Arm 1 with breast RT using standard methods (moderate or ultra hypo- or conventional-fractionated whole breast RT with/without boost, or APBI) with ≥5 yrs of ET (tamoxifen or AI) or Arm 2 with ≥5 yrs of ET (tamoxifen or AI) alone. The specific regimen of ET in both arms is at the treating physician's discretion. Eligible pts are stage 1: pT1 (≤2 cm), pN0, age ≥50 to <70 yrs, s/p BCS with negative margins (no ink on tumor), s/p axillary nodal staging (SNB or ALND), ER and/or PR-positive (ASCO/CAP), HER2-negative (ASCO/CAP), and Oncotype DX RS ≤18 (diagnostic core biopsy or resected specimen). A "low risk" MammaPrint is permissible if completed as part of usual care prior to screening. Primary endpoint is IBR (invasive breast cancer or DCIS). Secondary endpoints are breast conservation rate, invasive in-breast recurrence, relapse-free interval, distant disease-free survival, overall survival, patient-reported breast pain, patient-reported worry about recurrence, and adherence to ET. We assume a clinically acceptable difference in IBR of 4% at 10 yrs to judge omission of RT as non-inferior (10-yr event-free survival for RT group is 95.6% *v* 91.6% for the omission-of-RT group). BR007 is powered to detect non-inferiority with 80% power and a one-sided α=0.025, assuming that there would be a ramp-up in accrual in the first two years (leveling off in Yrs 3-5); 1,670 pts (835 per arm) are required for randomization. Conservative loss to follow-up is 1%/yr. Some T1a pts screened may have Oncotype DX scores >18, making them ineligible for the study. In the accrual process, 1,714 pts will be required to register to ensure that our final randomized cohort is 1,670 pts. As of 1-6-2025: 1,168/1,670 pts have been randomly assigned, and 1,294 screened. Support: U10 CA180868, -180822, UG1 CA189867. Clinical trial information: NCT04852887. Research Sponsor: National Cancer Institute; U10 CA180868; National Cancer Institute; UG1CA189867; National Cancer Institute; UG1 CA189867.