TPS615 Poster Session

A phase III trial evaluating addition of adjuvant chemotherapy to ovarian function suppression + endocrine therapy in premenopausal women with pN0-1, HR+/HER2- breast cancer (BC) and oncotype recurrence score (RS) ≤25 (OFSET): NRG-BR009.

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Background: The TAILORx and RxPONDER trials demonstrated that RS identifies many postmenopausal pts with node-neg and node-pos BC and RS ≤25, who do not benefit from addition of ACT to endocrine therapy (ET). Both trials also showed that certain subsets of premenopausal pts (node-neg/high clinical risk/RS 16-20, node-neg/RS 21-25, and node-pos/RS ≤25) benefited from adding ACT to ET. Most premenopausal pts in these trials did not receive ovarian function suppression (OFS) as part of their ET regimen. Given the observed benefit from OFS in high-risk premenopausal pts with HR+/HER2- BC in the SOFT/TEXT trials, many questioned whether all or part of the observed ACT benefit in the TAILORx/RxPONDER trials may have been the result of chemotherapy-induced OFS. To address this question, we developed OFSET, a phase III, multicenter clinical trial comparing OFS+ET *v* ACT+OFS+ET. **Methods:** We hypothesize that addition of ACT to OFS+ET is superior to OFS+ET in improving invasive breast cancer-free survival (IBCFS) among premenopausal, early-stage BC pts with HR+/HER2- tumors, and a 21-gene RS between 16-25 (for pN0 pts) and 0-25 (for pN1 pts). Secondary objectives include invasive disease-free survival, overall survival, distant recurrence-free interval, breast cancer-free interval, and health-related quality of life (HRQOL). Pts must be node-neg with RS 16-20 (plus high clinical risk), or RS 21-25, or have 1-3 positive nodes with RS ≤25. Stratification is by nodal status/RS status (pN0 RS 16-25 *v* pN1 RS 0-15 and pN1 RS 16-25), intent to receive CDK4/6 inhibitor (yes; no), and age (18-39 *v* ≥40). Pts are randomized after surgery to either OFS+ET or ACT+OFS+ET*v* ET is an aromatase inhibitor (AI). Choice is per investigator discretion; tamoxifen is allowed if AI is not tolerated or if OFS is incomplete. Radiotherapy will be administered per investigator discretion per protocol guidelines. The HRQOL sub-study will assess differences in severe menopausal symptoms, measured by the FACT ESS-19 score between arms, as well as increased pain severity (PROMIS). Blood and tumor specimens will be collected for future research. Accrual of 3,960 pts is anticipated to be completed in 7 yrs, 7 mos. Per NSABP B-28 and RxPONDER data, 5yr IBCFS of pN1 pts on the ACT+OFS+ET arm is estimated at 92.3%. Based on TAILORx data, 5yr IBCFS of pN0 pts on the ACT arm is ~95%. Assuming 56% of pts to be pN0 and 44% pN1, and a 0.5% annual loss-to-follow-up rate, the definitive analyses to detect a hazard ratio: 0.75 with ACT+OFS+ET *v* OFS+ET, with one-sided α of 0.025 and 80% power, will require 380 IBCFS events, expected to occur~11 yrs after study initiation. OFSETwas activated Aug 2023. As of 1-6-25, accrual is: 188/3,960. NCT #: NCT05879926. Support: U10CA180868, -80822, UG1CA189867, U24CA196067. Clinical trial information: NCT05879926. Research Sponsor: National Cancer Institute; U10CA180868; National Cancer Institute; U10CA180822; National Cancer Institute; UG1CA189867; National Cancer Institute; U24CA196067.