GS2-02: Impact of Tamoxifen Only after Breast Conservation Surgery for "Good Risk" Duct Carcinoma in Situ: Results from the NRG Oncology/RTOG 9804 and ECOG-ACRIN E5194 Trial

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Abstract Number: SESS-3482

Background
The NRG/RTOG 9804 and ECOG-ACRIN E5194 studies sub-classified duct carcinoma in situ (DCIS) into different risk groups after breast conservation surgery (BCS) based on size, DCIS grade, and margin width. NRG/RTOG 9804 randomized patients with "good risk" DCIS (size ≤2.5 cm, grade 1-2, margin ≥3mm) to whole breast radiation (RT) or none, and ECOG-ACRIN E5194 had 2 cohorts, one observing patients with the same "good risk" characteristics after BCS without RT. In both trials, the use of tamoxifen) was optional but tracked. This ancillary analysis of both trials was undertaken to assess the role of tamoxifen alone on ipsilateral breast recurrence (IBR) in this "good risk" group not receiving RT.
Methods
A combined database from the non-RT arm of NRG/RTOG 9804 and the "good risk" cohort from ECOG-ACRIN E5194 was created and distributions of patient and DCIS characteristics by tamoxifen use (yes vs. no) were compared using the Chi-square test. IBR, invasive IBR, DCIS IBR and contralateral breast event (CBE) were estimated by the cumulative incidence method and distributions between tamoxifen use were compared using Gray's test. A 2-sided significance level of 0.05 was used. Univariate and multivariable Fine-Gray regression was used to analyze the effects of factors, in addition to tamoxifen use, that may be associated with endpoints.
Results
878 patients were analyzed, 317 patients from NRG/RTOG 9804, and 561 from ECOG-ACRIN E5194. Median age was 59, margin width was ≥3mm or negative by re-excision in 97.8%, size was ≤5mm in 48.1%, and grade was 1-2 in 87.5%. The use of tamoxifen in the combined no-RT group was 43.1% (65.6% in NRG/RTOG 9804 and 30.3% in ECOG-ACRIN E5194). Median follow up of all patients was 14.85 years.
There were 117 IBR, 65 invasive and 52 DCIS. There was a statistically significant association for reduced IBR with tamoxifen use (p=0.001); estimated 15-year IBR (95% CI) with tamoxifen is 11.4% (7.9%, 15.5%) and without is 19.0% (15.3%, 22.9%). Further analysis showed the reduction to be significantly associated with tamoxifen use for invasive IBR (p=0.0048) but not for DCIS IBR (p=0.089). No associations were seen for CBE.
On univariable analysis, pathologic size (≤ 5 mm vs. > 10 mm) was significantly associated with IBR (p=0.0001) as was DCIS grade (1 vs 2, p=0.042). On multivariable analysis for IBR, DCIS grade fell out of the model and after adjusting for pathologic size, tamoxifen use remained statistically significantly associated with reduced IBR. On multivariable analysis for invasive IBR, size fell out of the model and adjusting for grade, tamoxifen use remained statistically significantly associated with reduced invasive IBR. Patients who received tamoxifen were 44% less likely to have any IBR (HR =

0.56, 95% CI: 0.38, 0.84; p=0.0044), and 51% less likely to have invasive IBR (HR=0.49, 95% CI: 0.28, 0.84; p=0.0092), as compared to patients with no tamoxifen.
Conclusions
For women with “good risk” DCIS who opt for BCS without RT, the use of tamoxifen is significantly associated with a reduction in IBR overall and specifically invasive IBR, not DCIS IBR.