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## Breast

### Comparison of Radiation With or Without Concurrent Trastuzumab for HER2-Positive Ductal Carcinoma In Situ Resected by Lumpectomy: A Phase III Clinical Trial.

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#### PURPOSE

Preclinical studies report that trastuzumab (T) can boost radiotherapy (RT) effectiveness. The primary aim of the B-43 trial was to assess the efficacy of RT alone vs concurrent RT plus T in preventing recurrence of ipsilateral breast cancer (IBTR) in women with ductal carcinoma in situ (DCIS).

#### PATIENTS AND METHODS

Eligibility: Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1, DCIS resected by lumpectomy, known estrogen receptor (ER) and/or progesterone receptor (PgR), and human epidermal growth factor receptor 2 (HER2) status by centralised testing. Whole-breast RT was given concurrently with T. Stratification was by menopausal status, adjuvant endocrine therapy plan, and nuclear grade. Definitive intent-to-treat primary analysis was to be conducted when either 163 IBTR events occurred or all accrued patients were on study  $\geq$  five years.

#### RESULTS

There were 2,014 participants who were randomly assigned. Median follow-up time as of December 31, 2019, was 79.2 months. At primary definitive analysis, 114 IBTR events occurred: RT arm, 63 and RT plus T arm, 51 (hazard ratio [HR], 0.81; 95% CI, 0.56 to 1.17; P value = .26). There were 34 who were invasive: RT arm, 18 and RT plus T arm, 20 (HR, 1.11; 95% CI, 0.59 to 2.10; P value = .71). Seventy-six were DCIS: RT arm, 45 and RT plus T arm, 31 (HR, 0.68; 95% CI, 0.43 to 1.08; P value = .11). Annual IBTR event rates were: RT arm, 0.99%/y and RT plus T arm, 0.79%/y. The study did not reach the 163 protocol-specified events, so the definitive analysis was triggered by all patients having been on study for  $\geq$  five years.

#### CONCLUSION

Addition of T to RT did not achieve the objective of 36% reduction in IBTR rate but did achieve a modest but statistically nonsignificant reduction of 19%. Nonetheless, this trial had negative results. Further exploration of RT plus T is needed in HER2-positive DCIS before its routine delivery in patients with DCIS resected by lumpectomy.