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Breast

Effect of Delayed Targeted Intraoperative Radiotherapy vs Whole-Breast Radiotherapy on Local Recurrence and Survival: Long-term Results from the TARGIT-A Randomised Clinical Trial in Early Breast Cancer.

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JAMA Oncol. 2020 Apr 2:e200249. doi: 10.1001/jamaoncol.2020.0249

IMPORTANCE:

Conventional adjuvant radiotherapy for breast cancer given daily for several weeks is onerous and expensive. Some patients may be obliged to choose a mastectomy instead, and some may forgo radiotherapy altogether. We proposed a clinical trial to test whether radiotherapy could be safely limited to the tumour bed.

OBJECTIVE:

To determine whether delayed second-procedure targeted intraoperative radiotherapy (TARGIT-IORT) is non-inferior to whole-breast external beam radiotherapy (EBRT) in terms of local control.

Design, Setting, and Participants:

In this prospective, randomised (1:1 ratio) non-inferiority trial, 1153 patients aged 45 years or older with invasive ductal breast carcinoma smaller than 3.5 cm treated with breast conservation were enrolled from 28 centres in nine countries. Data were locked in on July 3, 2019.

INTERVENTIONS:

The TARGIT-A trial was started in March 2000; patients were randomised after needle biopsy to receive TARGIT-IORT immediately after lumpectomy under the same anaesthetic vs. EBRT and results have been shown to be non-inferior. A parallel study, described in this article, was initiated in 2004; patients who had their cancer excised were randomly allocated using separate randomisation tables to receive EBRT or delayed TARGIT-IORT given as a second procedure by reopening the lumpectomy wound.

MAIN OUTCOMES AND MEASURES:

A non-inferiority margin for local recurrence rate of 2.5% at five years, and long-term survival outcomes.

RESULTS:

Overall, 581 women (mean [SD] age, 63 [7] years) were randomised to delayed TARGIT-IORT and 572 patients (mean [SD] age, 63 [8] years) were randomised to EBRT. Sixty patients (5%) had tumours larger than 2 cm, or had positive nodes, and only 32 (2.7%) were younger than 50 years. Delayed TARGIT-IORT was not non-inferior to EBRT. The local recurrence rates at five-year complete follow-up were: delayed TARGIT-IORT vs EBRT (23/581 [3.96%] vs 6/572 [1.05%]), respectively; difference, 2.91%; upper 90% CI, 4.4%). With long-term follow-up (median [IQR], 9.0 [7.5-10.5] years), there was no statistically significant difference in local recurrence-free survival (HR, 0.75; 95% CI, 0.57-1.003; P=0.052), mastectomy-free survival (HR, 0.88; 95% CI, 0.65-1.18; P=0.38), distant disease-free survival (HR, 1.00; 95% CI, 0.72-1.39; P=0.98), or overall survival (HR, 0.96; 95% CI, 0.68-1.35; P=0.80).

CONCLUSIONS AND RELEVANCE:

These long-term data show that despite an increase in the number of local recurrences with delayed TARGIT-IORT, there was no statistically significant decrease in mastectomy-free survival, distant disease-free survival, or overall survival.

