Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial.

The TARGIT-A trial compared risk-adapted radiotherapy using single-dose targeted intraoperative radiotherapy (TARGIT) versus fractionated external beam radiotherapy (EBRT) for breast cancer. We report 5-year results for local recurrence and the first analysis of overall survival from the TARGIT-A randomised trial.
reopening the wound). Patients in the TARGIT group received supplemental EBRT (excluding a boost) if unforeseen adverse features were detected on final pathology, thus radiotherapy was risk-adapted. The primary outcome was absolute difference in local recurrence in the conserved breast, with a prespecified non-inferiority margin of 2.5% at 5 years; prespecified analyses included outcomes as per timing of randomisation in relation to lumpectomy. Secondary outcomes included complications and mortality. This study is registered with ClinicalTrials.gov, number NCT00983684. Patients were enrolled at 33 centres in 11 countries, between March 24, 2000, and June 25, 2012. 1721 patients were randomised to TARGIT and 1730 to EBRT. Supplemental EBRT after TARGIT was necessary in 15.2% [239 of 1571] of patients who received TARGIT (21.6% prepathology, 3.6% postpathology). 3451 patients had a median follow-up of 2 years and 5 months (IQR 12-52 months), 2020 of 4 years, and 1222 of 5 years. The 5-year risk for local recurrence in the conserved breast was 3.3% (95% CI 2.1-5.1) for TARGIT versus 1.3% (0.7-2.5) for EBRT (p=0.042). TARGIT concurrently with lumpectomy (prepathology, n=2298) had much the same results as EBRT: 2.1% (1.1-4.2) versus 1.1% (0.5-2.5; p=0.31). With delayed TARGIT (postpathology, n=1153) the between-group difference was larger than 2.5% (TARGIT 5.4% [3.0-9.7] vs EBRT 1.7% [0.6-4.9]; p=0.069). Overall, breast cancer mortality was much the same between groups (2.6% [1.5-4.3] for TARGIT vs 1.9% [1.1-3.2] for EBRT; p=0.56) but there were significantly fewer non-breast-cancer deaths with TARGIT (1.4% [0.8-2.5] vs 3.5% [2.3-5.2]; p=0.0086), attributable to fewer deaths from cardiovascular causes and other cancers. Overall mortality was 3.9% (2.7-5.8) for TARGIT versus 5.3% (3.9-7.3) for EBRT (p=0.099). Wound-related complications were much the same between groups but grade 3 or 4 skin complications were significantly reduced with TARGIT (four of 1720 vs 13 of 1731, p=0.029). TARGIT concurrent with lumpectomy within a risk-adapted approach should be considered as an option for eligible patients with breast cancer carefully selected as per the TARGIT-A trial protocol, as an alternative to postoperative EBRT. University College London Hospitals (UCLH)/UCL Comprehensive Biomedical Research Centre, UCLH Charities, National Institute for Health Research Health Technology Assessment programme, Ninewells Cancer Campaign, National Health and Medical Research Council, and German Federal Ministry of Education and Research.