Breast

Intraoperative irradiation for early breast cancer (ELIOT): long-term recurrence and survival outcomes from a single-centre, randomised, phase III equivalence trial

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BACKGROUND

In the randomised, phase III equivalence trial on electron intraoperative radiotherapy (ELIOT), accelerated partial breast irradiation (APBI) with the use of intraoperative radiotherapy was associated with a higher rate of ipsilateral breast tumour recurrence (IBTR) than whole-breast irradiation (WBI) in patients with early-stage breast cancer. Here, we aimed to examine the planned long-term recurrence and survival outcomes from the ELIOT trial.

METHODS

This single-centre, randomised, phase III equivalence trial was done at the European Institute of Oncology (Milan, Italy). Eligible women, aged 48-75 years with a clinical diagnosis of a unicentric breast carcinoma with an ultrasound diameter not exceeding 25 mm, clinically negative axillary lymph nodes, and who were suitable for breast-conserving surgery, were randomly assigned (1:1) via a web-based system, with a random permuted block design (block size of 16) and stratified by clinical tumour size, to receive post-operative WBI with conventional fractionation (50 Gy given as 25 fractions of 2.0 Gy, plus a 10 Gy boost), or 21 Gy intraoperative radiotherapy with electrons (ELIOT) in a single dose to the tumour bed during surgery. The trial was open label and no-one was masked to treatment group assignment. The primary endpoint was the occurrence of IBTR. The trial was designed assuming a five-year IBTR rate of 3.0% in the WBI group and equivalence of the two groups, if the five -year IBTR rate in the ELIOT group did not exceed a 2·5 times excess, corresponding to 7·5%. Overall survival was the secondary endpoint. The main analysis was done by intention to treat. The cumulative incidence of IBTR events and overall survival were assessed at five, 10, and 15 years of follow-up. This trial is registered with ClinicalTrials.gov, NCT01849133.

FINDINGS

Between 20 Nov 2000, and 27 Dec 2007, 1305 women were enrolled and randomly assigned: 654 to the WBI group and 651 to the ELIOT group. After a median follow-up of 12·4 years (IQR 9·7-14·7), 86 (7%) patients developed IBTR, with 70 (11%) cases in the ELIOT group and 16 (2%) in the WBI group, corresponding to an absolute excess of 54 IBTRs in the ELIOT group (HR 4·62, 95% CI 2·68-7·95, p<0·0001). In the ELIOT group, the five-year IBTR rate was 4·2% (95% CI 2·8-5·9), the 10-year rate was 8·1% (6·1-10·3), and the 15-year rate was 12·6% (9·8-15·9). In the WBI group, the five-year IBTR rate was 0·5% (95% CI 0·1-1·3), the 10-year rate was 1·1% (0·5-2·2), and the 15-year rate was 2·4% (1·4-4·0). At final follow-up on 11 March 2019, 193 (15%) women had died from any cause, with no difference between the two groups (98 deaths in the ELIOT group vs 95 in the WBI group; HR 1·03, 95% CI 0·77-1·36, p=0·85). In the ELIOT group, the overall survival rate was 96·8% (95% CI 95·1-97·9) at five years, 90·7% (88·2-92·7) at 10 years, and 83·4% (79·7-86·4) at 15 years; and in the WBI group, the overall survival rate was 96·8% (95·1-97·9) at five years, 92·7% (90·4-94·4) at 10 years, and 82·4% (78·5-85·6) at 15 years. We did not collect long-term data on adverse events.

INTERPRETATION

The long-term results of this trial confirmed the higher rate of IBTR in the ELIOT group than in the WBI group, without any differences in overall survival. ELIOT should be offered to selected patients at low-risk of IBTR.