

**ORIGINAL RESEARCH** TARGIT-A randomised clinical trial

**Long term survival and local control outcomes from single dose targeted intraoperative radiotherapy during lumpectomy (TARGIT-IORT) for early breast cancer**

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**Study question** Can risk adapted targeted intraoperative radiotherapy (TARGIT-IORT) delivered as a single dose during lumpectomy effectively replace postoperative whole breast external beam radiotherapy (EBRT) for early breast cancer, and what are the long term outcomes?

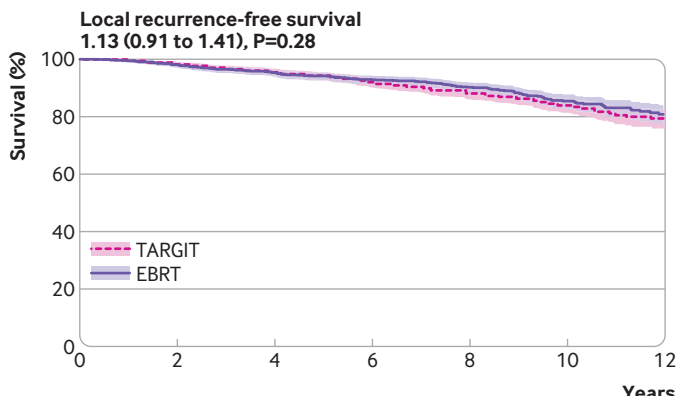
**Methods** The TARGIT-A international randomised controlled trial (32 centres in 10 countries in the United Kingdom, Europe, Australia, and North America) recruited 2298 women aged 45 years and older with invasive ductal carcinoma up to 3.5 cm (lymph node stage cN0-N1) who were eligible for breast conservation. Participants were randomised before lumpectomy to either single dose TARGIT-IORT or EBRT (standard daily fractionated course over three to six weeks). The main outcome measures were non-inferiority at a margin of 2.5% for five year local recurrence rate, and long term survival.

**Study answer and limitations** 1140 patients were randomised to TARGIT-IORT and 1158 to EBRT. The study found that TARGIT-IORT was non-inferior to EBRT for local recurrence. At five year complete follow-up the local recurrence risk was 2.11% (24/1140) for TARGIT-IORT compared with 0.95% (11/1158) for EBRT (difference 1.16%, 90% confidence interval 0.32% to 1.99%). 14 fewer deaths occurred with TARGIT-IORT than with EBRT (42/1140 v 56/1158). With long term follow-up (median 8.6 years) no statistically significant difference in any breast cancer outcome was found (such as local recurrence-free survival, mastectomy-free survival, and breast cancer mortality), and mortality from other causes was significantly lower in the TARGIT-IORT arm (45 v 74 deaths, hazard ratio 0.59, 95% confidence interval 0.40 to 0.86, P=0.005). Two major risk factors for cardiovascular disease and malignant disease were collected (age and body mass index), and they were well balanced between the two randomised arms of this large trial.

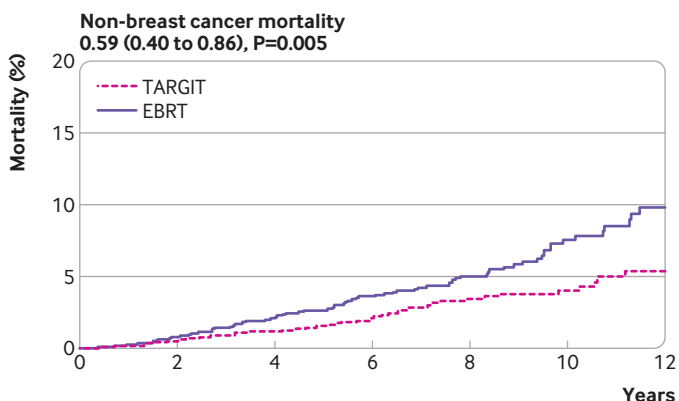
**What this study adds** For most patients with early breast cancer, immediate single dose TARGIT-IORT during lumpectomy was an effective alternative to EBRT, with comparable long term efficacy for cancer control and lower non-breast cancer mortality. TARGIT-IORT should be discussed with eligible patients when breast conserving surgery is planned.

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Trial registration ISRCTN34086741, NCT00983684.



No at risk		0	2	4	6	8	10	12
TARGIT		1140	1081	1043	960	662	363	144
EBRT		1158	1086	1034	972	666	366	139



No at risk		0	2	4	6	8	10	12
TARGIT		1140	1089	1059	989	689	378	152
EBRT		1158	1088	1041	978	672	371	143

Long term outcomes of the randomised TARGIT-A trial comparing risk adapted targeted intraoperative radiotherapy (TARGIT) delivered as single dose during lumpectomy with postoperative whole breast external beam radiotherapy (EBRT) for early breast cancer. Data under titles are hazard ratios (95% confidence intervals) and log rank test P values

