Breast

Hypofractionated Breast Radiotherapy for One Week Versus Three Weeks (FAST-Forward): Five-year Efficacy and Late Normal Tissue Effects Results From a Multicentre, Non-Inferiority, Randomised, Phase 3 Trial

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BACKGROUND

We aimed to identify a five-fraction schedule of adjuvant radiotherapy (radiation therapy) delivered in one week that is non-inferior in terms of local cancer control and is as safe as an international standard 15-fraction regimen after primary surgery for early breast cancer. Here, we present five-year results of the FAST-Forward trial.

METHODS

FAST-Forward is a multicentre, phase 3, randomised, non-inferiority trial done at 97 hospitals (47 radiotherapy centres and 50 referring hospitals) in the UK. Patients aged at least 18 years with invasive carcinoma of the breast (pT1-3, pN0-1, M0) after breast conservation surgery or mastectomy were eligible. We randomly allocated patients to either 40 Gy in 15 fractions (over three weeks), 27 Gy in five fractions (over one week), or 26 Gy in five fractions (over one week) to the whole breast or chest wall. Allocation was not masked because of the nature of the intervention. The primary endpoint was ipsilateral breast tumour relapse; assuming a 2% five-year incidence for 40 Gy, non-inferiority was predefined as ≤1·6% excess for five-fraction schedules (critical hazard ratio [HR] of 1·81). Normal tissue effects were assessed by clinicians, patients, and from photographs. This trial is registered at isrctn.com, ISRCTN19906132.

FINDINGS

Between 24 November 2011 and 19 June 2014 we recruited and obtained consent from 4096 patients from 97 UK centres, of whom 1361 were assigned to the 40 Gy schedule, 1367 to the 27 Gy schedule, and 1368 to the 26 Gy schedule. At a median follow-up of 71.5 months (IQR 71.3 to 71.7), the primary endpoint event occurred in 79 patients (31 in the 40 Gy group, 27 in the 27 Gy group, and 21 in the 26 Gy group); HRs versus 40 Gy in 15 fractions were 0.86 (95% CI 0.51 to 1.44) for 27 Gy in five fractions and 0.67 (0.38 to 1.16) for 26 Gy in five fractions. Five-year incidence of ipsilateral breast tumour relapse after 40 Gy was 2.1% (1.4 to 3.1); estimated absolute differences versus 40 Gy in 15 fractions were -0.3% (-1.0 to 0.9) for 27 Gy in five fractions (probability of incorrectly accepting an inferior five-fraction schedule: p=0.0022 vs. 40 Gy in 15 fractions) and -0.7% (-1.3 to 0.3) for 26 Gy in five fractions (p=0.00019 vs. 40 Gy in 15 fractions). At five years, any moderate or marked clinician-assessed normal tissue effects in the breast or chest wall was reported for 98 of 986 (9.9%) 40 Gy patients, 155 of 1005 (15.4%) 27 Gy patients, and 121 of 1020 (11.9%) 26 Gy patients. Across all clinician assessments from one to five years, odds ratios versus 40 Gy in 15 fractions were 1.55

(95% CI 1.32 to 1.83, p<0.0001) for 27 Gy in five fractions and 1.12 (0.94 to 1.34, p=0.20) for 26 Gy in five fractions. Patient and photographic assessments showed higher normal tissue effect risk for 27 Gy versus 40 Gy but not for 26 Gy versus 40 Gy.

INTERPRETATION

26 Gy in five fractions over one week is non-inferior to the standard of 40 Gy in 15 fractions over three weeks for local tumour control, and is as safe in terms of normal tissue effects up to five years for patients prescribed adjuvant local radiotherapy after primary surgery for early-stage breast cancer.