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2018 ASTRO Annual Meeting Late-breaking Abstract Selections

LBA1

Randomized Trial Evaluating Radiation following Surgical Excision for "Good Risk" DCIS: 12-Year Report from NRG/RTOG 9804

B. McCormick; *Memorial Sloan Kettering Cancer Center, New York, NY*

Purpose/Objective(s): NRG/RTOG 9804 is the only prospective randomized trial to assess the impact of whole breast radiation (WBRT) versus observation (OBS) in women with "good risk" DCIS, following breast conservation surgery. The primary objective is local recurrence (LR) in the treated breast. Long-term results of this trial are presented here.

Materials/Methods: "Good risk" DCIS was defined for this trial as clinically occult DCIS, found by mammogram or incidental finding at surgery, with size ≤2.5 cm, final margins ≥3 mm, with low or intermediate nuclear grade. Consented patients were randomly assigned to WBRT with standard doses or OBS; boosts were not allowed. The use of Tamoxifen (Tam) for 5 years was optional. Cumulative incidence was used to estimate LR, Gray's test to compare treatments, and Fine-Gray regression for hazard ratios (HRs). Intended accrual was 1790, to detect LR HR = 0.58.

Results: 636 women were randomized from 1999 - 2006 and initial results were reported in 2013. For this long-term update, in addition to the analyses for the 585 eligible patients with follow-up, sensitivity analyses were also done including all patients with follow-up (n = 629). As analyses were essentially the same, the reported results are based on all patients with follow-up. Median age was 58 years and 76% were post-menopausal. Mean pathologic tumor size was 0.60 cm, 61% ≤ 0.5 cm, and 65% had a margin width ≥1.0 cm or a completely negative re-excision specimen. Highest nuclear grade was 1 in 44% and 2 in 56%. Intention to use Tam was indicated for 69% of patients, equally between treatment arms; however actually receiving Tam was different at 58% WBRT vs. 65% OBS (p = 0.05). With a median follow-up time of 12.4 years, the 12-year cumulative incidence of LR was 2.8% (95% CI: 1.1, 5.6) with WBRT and 11.4% (7.7, 15.8) with OBS (p = 0.0001; HR = 0.26, 95% CI: 0.13, 0.54). The 12-year cumulative incidence of invasive (INV) LR was 1.5% (0.4, 4.0) with WBRT and 5.8% (3.2, 9.5) with OBS (p = 0.016; HR = 0.34, 95% CI: 0.14, 0.85). On multivariable analysis, only WBRT (HR = 0.25, 95% CI: 0.12, 0.53; p = 0.0003) and the use of Tamoxifen (HR = 0.50, 95% CI: 0.27, 0.91; p = 0.024) were associated with reduced LR. Age (< 50 vs. ≥ 50) and pathologic tumor size were not significant for all LR, nor INV LR. As expected, no significant differences were observed in survival, disease-free survival or mastectomy use.

Conclusion: Whole breast radiation significantly reduced LR and INV LR in this "good risk" DCIS population. The larger than expected WBRT effect has yielded meaningful results despite not meeting targeted accrual. These results should not be presented to the patient as an absolute indication for WBRT in the defined "good risk" group, but rather should inform a meaningful patient-physician discussion that includes risks, benefits and the patient's own degree of comfort, which can vary greatly, with the differences in LR with and without radiation.

LBA2

FAST Phase III RCT of Radiotherapy Hypofractionation for Treatment of Early Breast Cancer: 10-Year Results (CRUKE/04/015)

A.M. Brunt,[1] J. Haviland,[2] M. Sydenham,[2] H. Algurafi,[3] A. Alhasso,[4] P. Bliss,[5] D. Bloomfield,[6] M. Emson,[2] A. Goodman,[7] A. Harnett,[8] H. Passant,[9] Y.M. Tsang,[10] D. Wheatley,[11] J. Bliss,[2] and J. Yarnold[12]; *[1]Institute of Cancer Research, London, United Kingdom, [2]The Institute of Cancer Research, Sutton, United Kingdom, [3]Southend Hospital, Southend, United Kingdom, [4]Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom, [5]Torbay General Hospital, Torbay, United Kingdom, [6]Royal Sussex County Hospital, Brighton, United Kingdom, [7]Royal Devon and Exeter Hospital, Exeter, United Kingdom, [8]Norfolk and Norwich University Hospital, Norwich, United Kingdom, [9]Velindre Hospital, Cardiff, United Kingdom, [10]Mount Vernon Cancer Centre, London, United Kingdom, [11]Royal Cornwall Hospital, Truro, United Kingdom, [12]Division of Radiotherapy and Imaging, the Institute of Cancer Research, London, United Kingdom*

Purpose/Objective(s): The UK FAST trial tested 5 fractions (Fr) of 5.7 Gy and 6.0 Gy against 25 Fr of 2.0 Gy in women prescribed whole breast radiotherapy (no boost) after local excision of early breast cancer. Analysis of primary endpoint (normal tissue effects [by photograph]) showed that the 28.5 Gy/5 Fr regimen appeared similar to control. Further follow-up now enables analysis of 10-year outcomes.

Materials/Methods: The FAST trial (ISRCTN62488883) randomised women aged ≥50 years with invasive breast carcinoma (pT1-2 pN0) to 3 whole breast radiotherapy schedules: 50 Gy in 25 Fr over 5 weeks (control), 30 Gy or 28.5 Gy in 5 Fr over 5 weeks (1:1:1). Exclusion criteria were planned lymphatic/breast boost radiotherapy or (neo)adjuvant cytotoxic therapy. Normal tissue effects (NTE) were assessed annually to 10 years by clinicians and photographs at 2 and 5 years compared with a pre-radiotherapy baseline. Breast tumour recurrence was a secondary endpoint.

Results: 915 women were recruited from 18 UK centres (2004-2007). Composite endpoint of any clinician-assessed breast NTE showed significantly higher levels at 5 and 10 years for 30 Gy compared with 50 Gy (Table). Prevalence of marked NTEs at 5 and 10 years were very low. Compared with 50Gy excess of moderate/marked effects for 30Gy were: 5 years +10.5%, 95%CI 4.9 to 16.1%; 10 years +9.4%, 95%CI 1.1 to 17.6% and for 28.5 Gy, were +2.4%, 95%CI -2.5 to 7.3% at 5 years and +5.5%, 95%CI -2.3 to 13.3% at 10 years. At 9.9 years median follow up, 10 local recurrences (50 Gy: 3, 30 Gy: 3, 28.5 Gy: 4) and 96 deaths (50 Gy: 33, 30 Gy: 33, 28.5 Gy: 30) have been reported.

Conclusion: Marked NTEs were rare for all schedules. Late moderate/marked NTE after 28.5Gy/5 Fr/5 weeks were similar to 50Gy/25 Fr/5 weeks, but higher after 30Gy/5 Fr/5 weeks. Local recurrence rates were very low at 10 years for all schedules. Further research of a 5-Fr regimen is

Abstract LBA2; Table 1 Clinician assessments of NTE at 5 and 10 years

Worst grade of any NTE in the breast[1]	50Gy/25Fr (5 weeks) n (%)	30Gy/5Fr (5 weeks) n (%)	28.5Gy/5Fr (5 weeks) n (%)
At 5 years:	**N = 254**	**N = 267**	**N = 253**
None	160 (63.0)	152 (56.9)	155 (61.3)
Mild	75 (29.5)	67 (25.1)	73 (28.8)
Moderate	15 (5.9)	40 (15.0)	24 (9.5)
Marked	4 (1.6)	8 (3.0)	1 (0.4)
P-value[2]	-	*0.008*	*0.475*
At 10 years:	**N = 132**	**N = 130**	**N = 130**
None	90 (68.2)	66 (50.8)	72 (55.4)
Mild	30 (22.7)	40 (30.8)	39 (30.0)
Moderate	11 (8.3)	18 (13.8)	17 (13.1)
Marked	1 (0.8)	6 (4.6)	2 (1.5)
P-value[2]	-	*0.003*	*0.034*

[1] Shrinkage, induration, telangiectasia, edema;
[2] χ^2 trend test (none, mild, moderate/marked); comparison with 50Gy/25Fr