DCISionRT®

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Title: Comparing Risk Stratification and Radiotherapy Benefit for Patients with DCIS Using a 7-Gene Biosignature as Compared to a Clinicopathologic Nomogram

Background: Multiple prospective trials show over 70% of women with ductal carcinoma in situ (DCIS) do not recur after breast conserving surgery (BCS) alone and that radiotherapy (RT) had a clinically meaningful reduction in 10-yr risk after BCS. Clinicopathologic (CP) factor-based criteria or nomograms have been used to select for whom to de-escalate treatment, assessing 10-yr ipsilateral breast recurrence (IBR) rate after BCS. In this study, we compared classification of women by a CP model similar to the MSKCC DCIS nomogram with the 7-gene biosignature and their associated total 10-yr IBR rates with and without RT.

Material and Methods: DCIS patients (n=926) from four international cohorts treated with BCS with negative margins (no-ink on tumor) with or without RT (CP details previously published) were analyzed with both a CP model and the 7-gene biosignature with residual risk subtype (RRt). Biosignature decision score (DS) was categorized as Low Risk (DS≤2.8 without RRt) vs Elevated Risk (DS>2.8 with or without RRt). CP model used MSKCC DCIS nomogram factors and weighting, but omitted number of excisions and close margin and was categorized using score<220 as CP low-risk. 10-yr total IBR rates were evaluated using Cox Proportional Hazards and Kaplan Meier analysis by treatment, and risk groups in patients treated with and without RT.

Results: The biosignature classified 338 patients (37%) as DS Low Risk with a 5.6% 10-yr IBR rate for BCS without RT and no risk reduction with RT (4.8%, HR=0.8, 95%CI(.3, 2.3), p=0.7). The CP-model classified 320 patients (34%) as CP low-risk (score<220) with an 8.3% 10-yr IBR rate for BCS without RT and a non-significant slightly lower rate with RT (4.7%, HR=0.5, 95%CI(.2, 1.2), p=0.12). However, the biosignature reclassified 63% of these CP low-risk patients as DS Elevated Risk with 10-yr IBR rates of 12.3% for BCS without RT and 4.8% with RT (HR 0.2, 95%CI(.1, .8), p< 0.01).

Conclusions: Using 10-yr outcome data (n=926) from multiple contemporary published validation studies, the biosignature re-classified nearly 2/3 of patients in the CP low-risk (MSKCC nomogram-like) group as Elevated Risk. The re-classified CP low-risk patients had elevated 10-year IBR rates after BCS without RT and had an 80% relative benefit from RT, demonstrating they potentially could have been undertreated. This demonstrates the ability of the 7-gene biosignature to better risk-stratify patients with DCIS following BCS and identify patients with low-risk CP who may benefit from RT.

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