

San Antonio Breast Cancer Symposium 2017

Abstract: 851741

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Title: A validation of DCIS biological risk profile in a randomised study for radiation therapy with 20 year follow-up (SweDCIS)

Background: Women diagnosed with ductal carcinoma in situ (DCIS) and their physicians need tools that assess individualized risk and predict treatment benefit. A DCIS biologic signature was previously validated in an observational study at Kaiser Permanente NW. We evaluated the results of the signature for predictive utility in a national randomized clinical trial (SweDCIS) by assessing the 10-year benefit of adjuvant radiotherapy (RT) on ipsilateral breast event (IBE) and invasive breast cancer (IBC) risks.

Methods: The signature was validated in a prospective-retrospective study in women from the SweDCIS trial (n=1046) performed by the Swedish Breast Cancer Group. Women were treated with breast conserving surgery (BCS) between 1987-1999 and randomized to RT or no RT. A central pathology review of paraffin embedded tissue blocks (n=873) was performed at Uppsala University (UU). Freshly cut slides were provided to PreludeDx for biomarker testing. Extended follow-up of SweDCIS was published in 2014.

A panel of biomarkers (HER2, PR, Ki67, COX2, p16/INK4A, FOXA1 and SIAH2) were assayed and scored in PreludeDx's CLIA lab by board-certified pathologists. Continuous Decision Scores (DS) were calculated with the biologic signature using the biomarker and clinical factors (age, size, margin, and palpability) blinded to patient outcome. The DS results were provided to the Uppsala Regional Cancer Center for analysis. A predefined and co-developed statistical analysis plan was executed. Absolute 10-year RT benefit was assessed using Kaplan-Meier survival analysis. Hazard ratios (HR) were determined using Cox proportional hazards analysis and the interaction of the DS and RT benefit was assessed.

Results: Complete biomarker and clinical information was available in 584 women. In women with clear margins (n=506), 78 IBEs, including 31 IBCs, were recorded within 10 years of diagnosis. The multivariate analysis of DS (0-10 unit scale) and the RT interaction was significant for risk of IBC (p=0.048) and IBE (p<0.001) at 10 years. The DS defined an elevated risk group (>3) for which there was pronounced 10-year benefit of RT (p=0.01) with an absolute risk reduction of 9% for IBC (Table 1). The corresponding low risk group (≤3), which included 48% of all patients, demonstrated no significant RT benefit (p=0.70) with an absolute risk reduction of 1%. The continuous DS variable was correlated with IBE risk, HR 1.49/per 5 units 95%CI[1.02,2.18] (p=0.038), in addition to the RT benefit for IBE in low (p=0.04) and elevated (p<0.001) risk groups.

Discussion: Evaluation of the SweDCIS trial validated prognostic and RT predictive utility of the biologic signature. Women diagnosed with DCIS and treated with BCS±RT were stratified into clinically relevant low and elevated risk groups (≤3 vs >3). Women in the elevated risk group had twice the treatment benefit for IBC from RT compared to prior randomized trials, while the low risk group had no benefit from RT.

Table 1. 10-year RT benefit in women from the SweDCIS trial.

Decision Score Risk Groups	n	Invasive Breast Cancer (IBC)		
		Absolute RT Benefit	HR	p-value
Low Risk (DS≤3)	243	1%	0.84 [0.32 to 2.22]	0.70
Elevated Risk (DS>3)	263	9%	0.24 [0.08 to 0.76]	0.012

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