Miami Breast Cancer Conference 2016

Title: A multi-marker test for recurrence risk after BCS +/- RT for DCIS

Background: Reducing overtreatment is an important unmet need for DCIS patients. To develop a biomarker signature for recurrence risk we used cross-validation modeling within two large patient cohorts treated with and without RT after BCS.

Material and Methods: Patients were from Uppsala University Hospital (UUH), diagnosed 1986 - 2004, and University of Massachusetts (UMass), diagnosed 1999 - 2008, treated with BCS with (56%) or without (44%) RT. Biomarkers (p16/INK4A, Ki-67, COX-2, PgR, HER2, FOXA1, SIAH2 via IHC/ISH) from FFPE tissue were assessed by board certified pathologists. Pathology and clinical data were collected from medical records.

Two recurrence risk signatures were developed, one for invasive and another for overall ipsilateral breast events (IBEs). Targeting 5% for the "low risk" groups, parameters and biomarker thresholds were determined by multiple cross-validation on the combined patient sets (n=600, 8.1 year median follow-up). Each partition divided patients into independent training and testing subsets. Invasive and overall consensus risk scores were generated for each patient on continuous scales, and thresholds stratified them into risk groups for statistical analysis. 10-year IBE risk (10yRR) rates were calculated using Kaplan-Meier analysis.

Results: Over 2/3 of patients had a low risk invasive signature. Over 1/3 of patients had a low risk overall IBE signature. 10yRR was substantially lower for patients with low risk signatures ($p<.001$, invasive and overall). Both algorithms maintained significance when adjusted for nuclear grade, tumor size, age, necrosis and margin status. Invasive and overall IBE risks were similar regardless of RT in low risk patients. Patients whose risk signatures were not low - and who had RT - had less than half the 10yRR of those without RT.

Conclusions: The risk stratification algorithms accurately identify patients at risk for invasive and overall IBEs in cross-validation, and they currently are being evaluated in multiple independent validation studies. In low risk patients 10yRR without RT is low and similar to that with RT.

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10-YEAR IPSILATERAL RISK						
	BCS, No RT			BCS, RT		
	Risk±95% CI	Prevalence	N	Risk±95% CI	Prevalence	N
Baseline Invasive Risk	13%±5%	44%	264	6%±6%	56%	344
Invasive Signature *"Low"*	**4%**±3%	70%	184	**5%**±4%	71%	242
Invasive Signature *not "Low"*	**30%**±11%	30%	80	**6%**±6%	29%	97
Baseline Overall Risk	24%±6%	44%	264	12%±4%	56%	344
Overall Signature *"Low"*	**8%**±6%	36%	95	**7%**±6%	45%	153
Overall Signature *not "Low"*	**32%**±8%	64%	169	**15%**±6%	55%	186

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