DCISionRT®

Society of Surgical Oncology 2021

Title: DCIS Biologic Risk Signature Predicts Risk of Recurrence and RT Benefit After BCS

Background: Radiation therapy (RT) after breast conserving surgery (BCS) for DCIS reduces the risk of ipsilateral breast events (IBE) without altering survival. Its use varies widely due to differing assessments of the risk/benefit ratio of this treatment. Precise assessment of post-BCS RT benefit would allow individualized treatment decisions. We performed validation of a biologic risk signature, DCISionRT (PreludeDx, Laguna Hills, CA), to assess IBE risk after BCS and the benefit of RT.

Methods: Women with DCIS meeting eligibility criteria were identified from a retrospective Australian cohort. Medical records were reviewed to collect treatment and outcomes, and FFPE tissue was provided to the PreludeDx CLIA lab for blinded testing of a panel of biomarkers (HER2, PR, Ki-67, COX2, p16, FOXA1 and SIAH2) scored by board-certified pathologists. The prognostic effect of DS for IBE risk was assessed by multivariate Cox proportional hazards (CPH) analyses, adjusting for adjuvant treatments. The predictive effect of DS for RT IBE benefit was assessed by multivariate CPH analysis, including the RT:DS interaction.

Results: 183 women had Decision Scores (DS) and outcomes available with a median follow-up of 73 months. 72 of these women received RT (39%) and 66 received endocrine therapy (ET, 36%). The total cohort had 5-year IBE risks of 10%, while women treated with RT had 4% risks and those treated without RT had 14% risks. After BCS and no ET, women with higher DS results had greater IBE risk (DS per 5 units HR=2.4), after adjusting for RT. Elevated categorical DS (DS>3) predicted increased IBE risk in all women, adjusting for ET, RT. In women treated without ET, elevated continuous DS had greater IBE risk (HR=3.6) and greater relative RT benefit (RT:DS HR = 0.1), compared to lower DS.

Conclusions: Women with elevated DS had a significantly higher risk of IBE. Most importantly, women with higher DS had a greater relative benefit from RT compared to women with lower DS. This validation supports previous findings that DCISionRT provides prognostic and predictive information to allow personalized treatment decisions.

Table 1: Multivariate Cox Proportional Hazards Analysis of DCISionRT for IBE Risk and RT Benefit

	Hazard Ratio (HR)	95% Confidence Interval	p-value
Prognostic for IBE Risk (multivariate analysis)			
No ET (adjusted for RT, n=117) Continuous DS (per 5 units)[1]	2.4	1.2 - 4.8	0.0098
All patients (adjusted for RT and ET, n=183) Continuous DS (per 5 units)[2]	2.1	1.2 - 3.8	0.0082
Predictive of RT Benefit (multivariate analysis)			
No ET (n=117, DS:RT interaction) Continuous DS (per 5 units)	3.6	1.7 - 7.5	0.0007
RT (alone)	1.4	0.3 - 6.7	0.67
RT:DS (per 5 units)[3]	0.1	0.01 - 0.95	0.045

1) Multivariate analysis of DS adjusted for RT in women treated with BCS without endocrine treatment, n=117. 2) Multivariate analysis of DS adjusted for RT and ET in women treated with BCS, n=183. 3) Multivariate analysis of DS testing interaction of DS on RT in women treated with BCS without endocrine treatment.

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