DCISionRT®

American Society of Radiation Oncology Annual Meeting 2021

Title: Biosignatures to Optimize Adjuvant Radiation Therapy Use in Patients with DCIS with High Risk Clinicopathologic Features

Purpose/Objective: There is an unmet need to identify women diagnosed with DCIS who have a low recurrence risk and could omit radiotherapy (RT) after breast conserving surgery (BCS), or an elevated recurrence risk after treatment with BCS plus RT.

Methods: Pathology, clinical data, and FFPE tissue samples were evaluable for 485 women treated for DCIS with BCS with negative margins, with or without whole breast RT, at centers in Sweden, US and Australia. A subset with large tumor size (>2.5 cm) &/or nuclear grade III DCIS was assessed (n=250). A validated biosignature (Prelude, Laguna Hills CA) and a novel response subtype biosignature to RT after BCS were determined using protein biomarkers (p16/INK4A, Ki-67, COX-2, PgR, HER2, FOXA1, SIAH2) assayed on FFPE tissue. The two biosignatures classified women into three risk groups: Low risk, Elevated risk with a good response subtype (Rst) and Elevated risk with a poor Rst to RT after BCS. Ipsilateral breast tumor recurrence (IBTR) included DCIS or Invasive Breast Cancer (IBC) that was local, regional, or metastatic. Hazard ratios and 10-year risks were calculated using Cox proportional hazards and Kaplan-Meier analyses.

Results: Of 250 women with nuclear grade III DCIS &/or size >2.5 cm, biosignatures classified 72% (n=179) of patients into an Elevated risk group consisting of those with a good (n=122) or a poor (n=57) response subtype (Rst) to RT after BCS. The remaining 28% of women were classified into a Low risk group (n=71). In the Low risk group (n=71), women treated without RT had good 10-year outcomes with no (0%) 10-year IBC events, and derived no significant RT benefit (1%) in 10-year IBTR rates (IBTR p=0.81). Of all women treated without RT (n=102), those in the Elevated risk group (good and poor Rst combined, n=61) had significantly worse 10-year IBTR/IBC rates (31%/17%) than those in the Low risk group, (IBTR HR=12, p=0.01). Women treated with RT in the Elevated risk group with a good Rst (n=77) had significantly reduced 10-year IBTR/IBC rates of 5%/3%. However, no significant benefit to RT was noted for women within the Elevated risk group with a poor Rst (n=41) who had 10-year IBTR/IBC rates of 25%/20%. Of all women treated with RT in the Elevated risk group (n=118), those with a poor Rst had significantly worse outcomes than those with a good Rst (IBTR HR=4.1, p=0.035, IBC HR=8, p=0.053).

Conclusions: In women with nuclear grade III DCIS &/or size >2.5 cm, DCISionRT combined with a novel response subtype biosignature (Rst) identified an Elevated risk group with two distinct subtypes of women: (1) a poor Rst that had high IBTR/IBC rates with or without RT and (2) a good Rst deriving significant benefit from adjuvant RT. Women in the corresponding Low risk group had low 10-year IBTR/IBC rates and derived no significant benefit from adjuvant RT.

Table 1.

	Low Risk Group (n=71)				Elevated Risk Group (n=179)		
	n	% 10-year rates			*n*	% 10-year rates	
		IBTR	IBC only			IBTR	IBC only
BCS without RT	41	2	0	**BCS without RT**			
				Good and Poor Rst	61	31	17
BCS plus RT	30	3	0	**BCS plus RT**			
				Good Rst	77	5	3
				Poor Rst	41	25	20

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Authors:

Frank A. Vicini, MD, FASTRO
Michigan Healthcare Professionals, Farmington Hills, MI

Chirag S. Shah, MD
Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland OH

Pat W. Whitworth, MD
Nashville Breast Center, Nashville, TN

Steve Shivers, PhD
PreludeDx, Laguna Hills, CA

Fredrik Wärnberg, MD, PhD
University of Gothenburg, Gothenburg, Sweden

G Bruce Mann, MD, PhD
The Royal Melbourne and Royal Women's Hospital Parkville, Australia

Troy Bremer, PhD
PreludeDx, Laguna Hills, CA