Clinical utility of a biologic signature to assess DCIS recurrence risk in patients meeting 'good-risk' criteria (RTOG 9804, ECOG E5194): interim analysis of the DCISionRT PREDICT study

Chirag Shah[1], Frank Vicini[2], Steven C Shivers[3], Pat W Whitworth[4], Rakesh Patel[5], Charles E Cox[6] and Troy Bremer[3]

[1]Cleveland Clinic, Cleveland, OH; [2]21st Century Oncology, Farmington, MI; [3]PreludeDx, Laguna Hills, CA; [4]Nashville Breast Center, Nashville, TN; [5]Good Samaritan Cancer Center, Los Gatos, CA; [6]University of South Florida, Tampa, FL

Background

- When considering health-related, quality-of-life and monetary costs associated with post-surgical treatments for women diagnosed with Ductal Carcinoma In Situ (DCIS), there remains a need for prognostic and predictive tools to help design individual treatment planning.
- DCISionRT (PreludeDx, Laguna Hills, CA) is a validated biologic signature[1-3] to assess the 10-year event risk for DCIS patients managed with breast conserving surgery (BCS).
- The 10-year risks are provided separately for patients treated with and without adjuvant radiation therapy (RT) after BCS.
- The study was designed to measure the change in adjuvant RT recommendation. This is a planned interim analysis of the study, which will eventually comprise up to 2,500 patients and 100 sites.

Materials and Methods

- The registry includes females over the age of 25 who are candidates for breast conserving surgery and eligible for RT. Survey forms are completed pre- and post-DCISionRT test to capture treatment recommendations and patient preferences.
- This interim analysis was performed to assess changes in RT recommendation for patients treated with BCS in different clinicopathologic subgroups.
- Specifically, 'good risk' profiles were based on the RTOG 9804 and ECOG 5194 study designs. RTOG 9804 like criteria was screening detected tumors with nuclear grade of 1 or 2, size of ≤ 2.5 cm, and clear (≥ 2 mm) surgical margins.
- ECOG 5194 like criteria was tumors with nuclear grade of 1 or 2, size of ≤ 2.5 cm, and clear surgical margins, or nuclear grade of 3, size of ≤ 1 cm, and clear surgical margins.
- Statistics were provided as percentages and counts, and McNemar's test was used to assess change in RT with a p-value of <0.05 considered statistically significant.

Results

- There were 513 patients from 32 sites with testing completed after treatment with BCS.
- Of these patients, 16% were ≤ 50 years of age, 60% were ≥ 60 years of age, and 26% were ≥ 70 years of age. The DCIS tumor nuclear grade was high in 32% of patients, and the size of the tumor was ≤ 1 cm for 68% of patients.
- There were 49% of patients who met RTOG 9804 like criteria, 51% who met the ECOG 5194 (grade 1 or 2) criteria, and 17% of patients who met the ECOG 5194 (grade 3) criteria.
- RT was recommended to 52% and 53% patients for RTOG 9804/ECOG 5194 (grade 1 or 2) criteria pre-testing, and 42% post-testing. For ECOG 5194 (grade 3) like criteria, 84% of patients were recommended RT pre-test, and 47% were recommended RT post-test.
- In all criteria groups, for patients who were initially recommended RT pre-test, 48% to 54% were not recommended RT post-test, while patients initially not recommended RT pre-test, 21% to 37% were recommended RT post-test.
- Overall, the post-test RT recommendation was significantly changed from between 44% and 46% for patients with 'good-risk' clinicopathologic criteria.

1) Bremer, Clin Cancer Res Dec 2018; 2)Wärnberg, Cancer Res Feb 2018; 3) Weinman, Clin Cancer Res Aug 2020.

- DCISionRT demonstrates high clinical utility by impacting radiation therapy recommend-ations in 45% of women overall
- Recommendations for RT increased 37% in patients initially recommended to omit RT in clinicopathologic low risk groups
- DCISionRT may help to prevent over- and under- treatment of DCIS

Table 1. Change in RT Recommendations in Patients meeting 'Good Risk' Criteria

RTOG 9804

	Pre-Test	Post-Test	Δ RT
RT	132	105	-27
No RT	120	147	
% RT	**52%**	**42%**	**-11%**

Pre- to Post-Test	Δ RT	% Change
Pre-Test RT → Post-Test no RT	71/132	54%
Pre-Test no RT → Post-Test RT	44/120	37%
Overall Change	**115/252**	**46%**
	p-value	**0.012**

ECOG E5194 Grade 1 & 2

	Pre-Test	Post-Test	Δ RT
RT	138	110	-28
No RT	124	152	
% RT	**53%**	**42%**	**-11%**

Pre- to Post-Test	Δ RT	% Change
Pre-Test RT → Post-Test no RT	73/138	53%
Pre-Test no RT → Post-Test RT	45/124	36%
Overall Change	**118/262**	**45%**
	p-value	**0.0099**

ECOG E5194 Grade 3

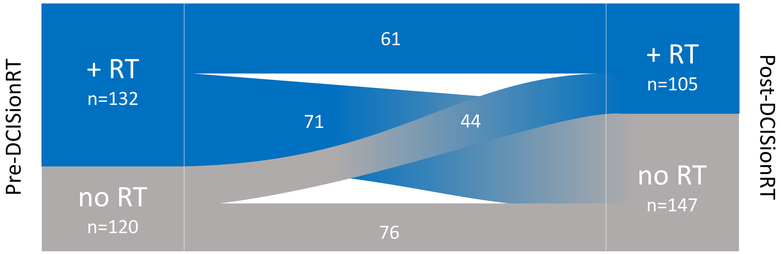
	Pre-Test	Post-Test	Δ RT
RT	71	40	-31
No RT	14	45	
% RT	**84%**	**47%**	**-36%**

Pre- to Post-Test	Δ RT	% Change
Pre-Test RT → Post-Test no RT	34/71	48%
Pre-Test no RT → Post-Test RT	3/14	21%
Overall Change	**37/85**	**44%**
	p-value	**3.4E-06**

Table 2. Δ in RT Recommendation by DCISionRT by Clinicopathology Criteria

	Group	n	%	% Change	95% CI
All	All Patients	513	100%	43%	39% to 47%
Age	Age < 50	80	16%	36%	27% to 47%
	Age ≥ 50	433	84%	44%	39% to 49%
	Age ≥ 60	308	60%	43%	38% to 49%
	Age ≥ 70	133	26%	41%	33% to 50%
Grade	Grade I/II	349	68%	45%	40% to 50%
	Grade III	164	32%	38%	31% to 45%
Size	Size ≤ 1 cm	347	68%	46%	41% to 52%
	Size > 1 cm	166	32%	35%	28% to 43%
'Good Risk' Criteria	RTOG 9804	252	49%	46%	40% to 52%
	ECOG E5194 Grade 1/2	262	51%	45%	39% to 51%
	ECOG E5194 Grade 3	85	17%	44%	34% to 54%

Figure 1. DCISionRT Decision Impact on RT Recommendation



Conclusions

- This second PREDICT interim analysis demonstrates a significant net change in RT recommendation based on DCISionRT for 513 patients. This is consistent with the previous analysis.
- Treatment recommendations were changed post-assay in 45% of women for RT and 15% of women for HT.
- The integration of DCISionRT into clinical-decision processes will help enable clinicians and patients to identify optimal treatments while preventing over- or under-treatment.