A Novel Biosignature to Assess Residual Risk in Early Stage Invasive Breast Cancer After Standard Breast Conserving Surgery

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PURPOSE/OBJECTIVE(S)

Despite continually improving outcomes for women diagnosed with early stage breast cancer, there is an unmet need to identify those with elevated risk after standard treatment for whom enhanced treatment strategies should be considered. A poor response-type (RSt) signature has been assessed in women treated with breast conserving surgery.

MATERIAL & METHODS

This study includes patients from two separate hospitals in Sweden diagnosed with early stage breast cancer (tumor size 20 mm or less) and treated with breast conserving therapy between 1987 and 2004. Women with positive margins, lymph node metastases, or those treated with mastectomy or chemotherapy were excluded. The RSt biosignature was calculated using biomarkers (ER, p16/INK4A, Ki-67, COX-2, PgR, HER2, FOXA1, SIAH2) scored by board certified pathologists in a CLIA certified laboratory. Pathology and clinical data were collected from medical records. There were 284 eligible patients with biomarker data and 102 received hormone therapy and 233 received radiation therapy. Multivariate Cox proportional hazards and survival analysis were used to assess cumulative incidence risk differences, hazard ratios, and 10-year risks.

RESULTS

Women with a poor RSt remained at particularly elevated risk after treatment with breast conserving surgery and radiation therapy with a 17% 10-yr risk and HR=3.7 (95%CI 2.0-7.10), p<0.0001 (Figure 1, Table 2). The distribution of size and grade were similar for good versus poor RSt. Patients with a poor RSt had an elevated risk of disease-specific death; HR=2.9 (95%CI 1.3-6.7), p=0.01.

- A new biosignature identified a Poor Response Type in women with early stage invasive breast cancer
- Women with a Poor Response Type had high risk for ipsilateral breast events after BCS + RT
- Women with a Good Response Type had an excellent outcome after BCS + RT

Figure 1. 10-Year Risks by Response Type (Radiation Treated)

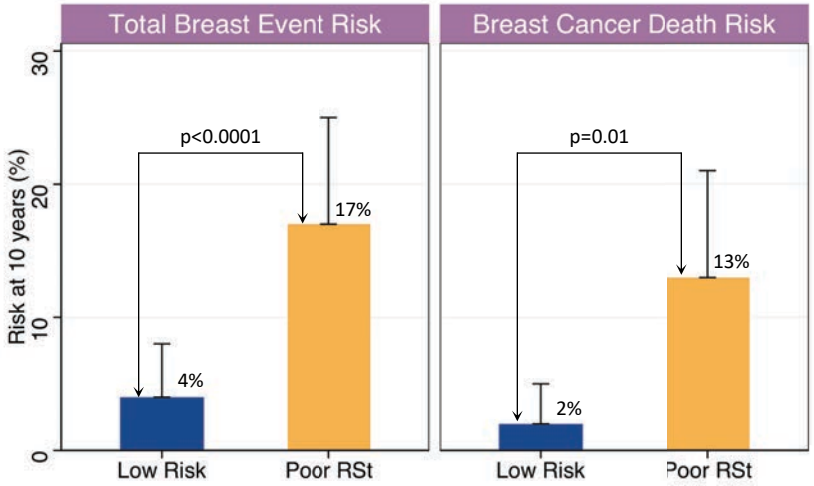

Table 1. Clinical Pathology by Response Type (Radiation Treated)

	Good RSt		Poor RSt		Total	
	n	%	n	%	n	%
Grade*						
Grade 1 or 2	122	81%	45	69%	167	78%
Grade 3	28	19%	20	31%	48	22%
Size*						
≤ 10 mm	89	56%	40	61%	129	57%
> 10 mm	71	44%	26	39%	97	43%
Age						
50 and under	46	28%	16	24%	62	27%
Over 50	119	72%	52	76%	171	73%
Hormone Therapy (HT)						
no HT	106	64%	49	72%	155	67%
+ HT	59	36%	19	28%	78	33%

* Grade (n=18) or size (n=7) was unknown for some patients.

Table 2. 10-year Breast Event and Breast Cancer Death by Response Type (Radiation Treated)

RSt Group	Patients	Events	10-year Event Risk (95% CI)	Local Regional Events	10-year Specific Death (95%CI)	Breast Cancer Deaths
Good RSt	165	7	4% (1-8)	5	2% (0-5)	2
Poor RSt	68	11	17% (7-25)	5	13% (5-21)	9

SUMMARY/CONCLUSION

A novel biosignature identified women diagnosed with early stage invasive breast cancer with a good and a poor RSt. Women with a poor RSt remained at particularly elevated risk even after RT, and thus enhanced treatment strategies should be considered for these women.

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