

# Association of a genomic index of sensitivity to endocrine therapy with locoregional recurrence of breast cancer

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## Introduction

- The sensitivity to endocrine therapy (SET) index is a genomic index<sup>1</sup>
  - Measures transcriptional activity of 18 genes related to ER and PR relative to 10 reference genes
  - Adjusted for baseline prognostic factors (cT, cN, RNA4)
- Higher SET index is predictive of greater intrinsic tumoral sensitivity to endocrine therapy (ET)
- SET index has been shown to be associated with distant recurrence and risk of death<sup>1</sup>
- We evaluated the association of SET index and locoregional recurrence in a cohort with high-risk breast cancer

## Methods

- Single institution, retrospective study from 2000-2009
- Inclusion criteria:
  - Female patients ≥ 18 years
  - Diagnosis of hormone receptor-positive, Her2-negative invasive breast cancer
  - Received neoadjuvant chemotherapy
  - Took adjuvant ET (Tamoxifen and/or aromatase inhibitor)
- Patients censored at time of last follow up or death
- SET index was defined as a binary variable (high vs low) based on a pre-defined cutpoint
- Descriptive statistics and Kaplan-Meier estimates of LRR-free survival were done
- Univariate analysis of factors associated with LRR was performed

## Results

- Median follow-up time of 110 months (5 – 204)

**Table 1. Characteristics of the cohort (N = 292)**

	n (%)
Age	
Median (Range)	50 (23-79)
≤ 50 years	155 (53.1)
> 50 years	137 (46.9)
Histology	232 (79.5)
Ductal	25 (8.5)
Lobular	30 (10.3)
Mixed Ductal/Lobular	5 (1.7)
Clinical T-stage	
T1	23 (7.9)
T2	173 (59.2)
T3	56 (19.2)
T4	39 (13.4)
Unknown*	1 (0.3)
Clinical N-stage	
N0	91 (31.1)
N1	136 (46.6)
N2	23 (7.9)
N3	42 (14.4)
Grade	
I	19 (6.5)
II	144 (49.4)
III	128 (43.8)
Unknown	1 (0.3)
Definitive surgical procedure	
Mastectomy	194 (66.4)
Breast Conservation	98 (33.6)
Definitive axillary procedure	
ALND	227 (77.8)
SLND	64 (21.9)
None	1 (0.3)
Adjuvant radiation therapy	
Yes	246 (84.3)
No	46 (15.7)
SET index	
High	125 (42.8)
Low	167 (57.2)
RCB	
0 (pCR)	28 (9.6)
I	25 (8.6)
II	152 (52.0)
III	75 (25.7)
Unknown	12 (4.1)

\*Occult primary breast tumor

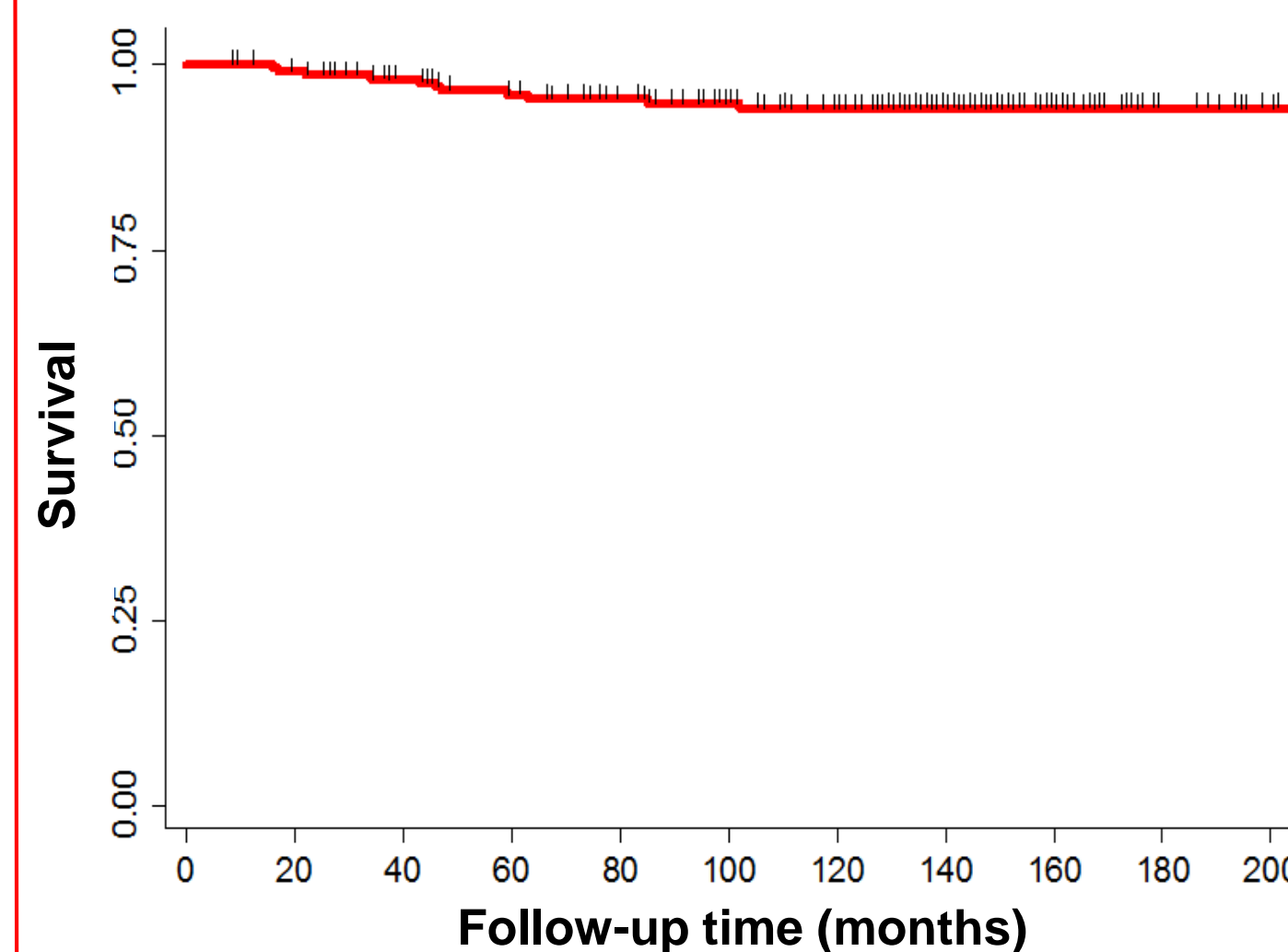
**Table 2. Sites of locoregional recurrence, N = 11**

	n (%)
Local (ipsilateral breast, skin, chest wall)	7 (63.6)
Regional (axillary, ipsilateral internal mammary or supraclavicular lymph nodes)	3 (23.3)
Both	1 (9.1)

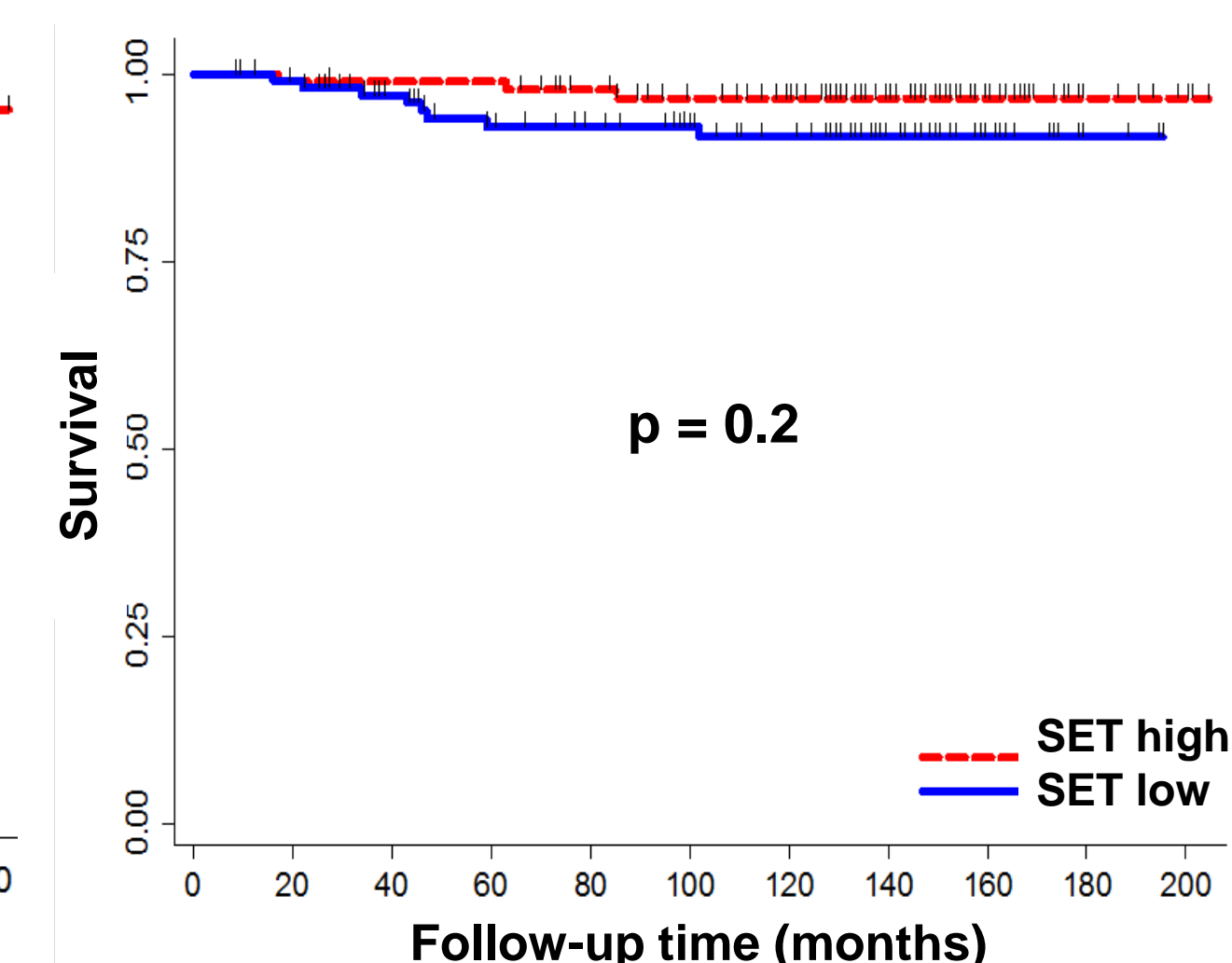
10-year overall survival: 80.0%

10-year LRR-free survival: 95.2%

**Figure 1. Locoregional recurrence-free survival**



**Figure 2. Recurrence-free survival by SET index**



**Table 4. Univariable analysis of factors associated with locoregional recurrence**

Factor	HR	SE	p-value	95% CI
Age	1.0	0.03	0.5	0.9-1.0
T-stage	1.6	0.6	0.2	0.8-3.2
N-stage	1.4	0.5	0.4	0.6-3.0
Grade	1.7	0.9	0.3	0.6-4.9
SET index - low vs high	2.4	1.6	0.2	0.6-9.1
RCB class	1.5	0.6	0.3	0.7-6.5
Mastectomy vs BCS	0.9	0.6	0.9	0.3-3.1

HR = hazard ratio. SE = standard error. 95% CI = confidence interval

## Conclusions

- In a high-risk HR+/Her2-negative population, clinical and biologic factors were not associated with risk of locoregional failure
- There was no association between SET index and locoregional recurrence
- With a median follow-up of 9 years, LRR in this high-risk population remained low, 3.8%
- While 10-year OS was 80%, LRR-free survival was greater than 95% reflecting the low rate of LRRs
- Limitations of this study include:
  - Retrospective nature
  - Single institution
  - Length of follow-up
- SET index does not appear to reflect the biology of LRRs in this cohort
- Larger cohorts of patients with longer follow-up times are indicated to determine whether SET index can help identify patients at high risk of LRR

## References

- Symmans WF et al. Genomic index of sensitivity to endocrine therapy for breast cancer. *Journal of Clinical Oncology*. 2010;28:4111-19.