

[77] Validation of Prognostic Utility of HOXB13:IL17BR and Molecular Grade Index in Early Stage Breast Cancer.

Stål O, Jerevall P-L, Ma X-J, Li H, Salunga R, Erlander M, Sgroi D, Holmlund B, Skoog L, Fornander T Linköping University, Linköping, Sweden; bioTheranostics, San Diego, CA; Massachusetts General Hospital and Harvard Medical School, Boston, MA; Karolinska Institute, Stockholm, Sweden

Background. HOXB13:IL17BR (H:I) is a two gene expression index, which has been shown to be an independent prognostic factor in estrogen receptor (ER)-positive lymph node-negative (N0) breast cancer. A molecular grade index (MGI) measures the expression of five proliferation-related genes. An algorithm based on dichotomized H:I and MGI stratifying patients into three risk groups has been shown to be superior to either alone in predicting risk of distant metastasis in ER+/N0 patients. Further validation in larger cohorts is needed to establish its clinical performance. A continuous predictor combining H:I and MGI is desirable for making individualized risk assessment in the clinical setting.

Methods. During 1976 through 1990 the Stockholm Breast Cancer Group conducted a randomized clinical trial comparing adjuvant tamoxifen with control in 1780 postmenopausal women considered to be at low risk of recurrence (N0 and tumor size < 3 cm). We measured H:I and MGI using a real time PCR assay in 769 patients from this trial based on sample availability. Correlation of gene expression indices with distant metastasis and death due to breast cancer was evaluated by Kaplan-Meier analysis and Cox proportional hazard regression. Modeling was also used to develop a continuous risk index as a function of both H:I and MGI.

Results. Using pre-specified cutoff points and combination algorithm, H:I, MGI and their combination each was significantly associated with both distant metastasis-free survival and breast cancer-specific survival (Table 1). Furthermore, we used the ER+ tamoxifen-treated subset (n=314) to develop a continuous risk model (Breast Cancer Index or BCI) combining both H:I and MGI. The prognostic utility of BCI was then successfully validated in the untreated subset in this trial and three additional previously published cohorts. BCI consistently identified ~50% patients with a very low 10-year recurrence risk (< 5%).

Discussion. This large retrospective analysis of a randomized clinical trial cohort validated the prognostic utility of H:I, MGI, and their combination. With the continuous risk model, this RT-PCR-based assay allows prediction of risk of recurrence at the individual level, which may help tailor personalized treatment strategy.

Table 1. Univariate Cox regression analysis of H:I, MGI, and H:I+MGI

		Distant Metastasis		Breast Cancer Death	
		Tam (n=398)	No Tam (n=371)	Tam (n=398)	No Tam (n=371)
		Hazard Ratio (95%)		Hazard Ratio (95%)	
H:I	high vs low	1.93 (1.07-3.47) _ p=2.80E-02	2.50 (1.54-4.07) p=2.26E-04	2.40 (1.28-4.52) p=6.49E-03	2.23 (1.35-3.69) p=1.74E-03
MGI	high vs low	4.62 (2.29-9.32) _ p=1.86E-05	1.93 (1.19-3.12) p=7.71E-03	5.25 (2.43-11.34) p=2.48E-05	2.67 (1.56-4.58) p=3.50E-04
H:I+MGI	inter. vs low	3.86 (1.71-8.69) _ p=1.24E-03	1.32 (0.69-2.50) p=4.00E-01	3.99 (1.63-2.82) p=2.46E-03	2.08 (1.07-4.03) p=3.06E-02
	high vs low	5.29 (2.51-11.18) p=1.26E-05	2.42 (1.44-4.06) p=8.00E-04	6.34 (2.82-14.24) p=7.77E-06	3.14 (1.77-5.57) p=9.67E-05

Saturday, December 12, 2009 4:45 PM

General Session VI (3:15 PM-5:30 PM)

[Terms of Service.](#)