

THE BREAST CANCER INDEXSM (BCI) TEST REPORT



Risk Of Distant Recurrence & Extended Endocrine Benefit (Report Page 1 of 2)

Physician Information

Treating Physician First Last, M.D. Facility Name Facility Address City, State Zip Phone: (512) 421-4100 Fax: (512) 451-3709	Pathologist First Last, M.D. Laboratory Name Laboratory Address City, State Zip Phone: (XXX) XXX-XXXX Fax: (XXX) XXX-XXXX
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Patient & Order Information

Order ID	BDX15-654321
Patient Name:	First Last
DOB (Gender):	X/X/XXXX (F) XX Yrs
Sample ID:	
Date of Collection:	
Date Received:	
Date Reported:	

BCI Prognostic

**HIGH Risk of Late Recurrence
(8.3% between years 5-10)**

**Your Test
Summary**

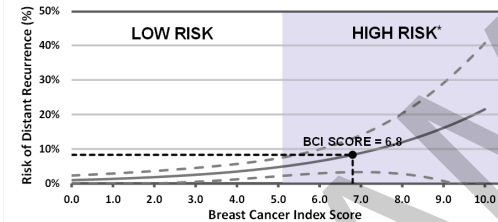
BCI Predictive

**LOW
Likelihood of Benefit**

HIGH RISK CATEGORY*

8.3% RISK[†] (95% CI: 3.3% - 13.1%)
**OF DISTANT RECURRENCE FOR ER+,
LYMPH NODE-NEGATIVE PATIENTS AFTER YEAR 5¹**

LOW LIKELIHOOD OF BENEFIT FROM EXTENDED ENDOCRINE THERAPY³



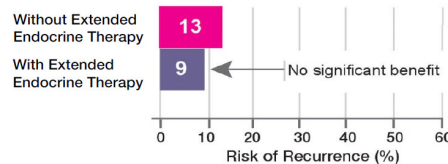
Your Result
Low BCI Predictive

BCI Predictive was validated in a cohort that included both LN- and LN+ (1-3 nodes) patients; however, the study was not designed or powered to assess LN+ and LN- groups separately.

[†] Risk of Recurrence estimate is based on analysis of BCI Prognostic in the Stockholm clinical study¹ and provides residual risk of distant recurrence beyond year 5 in patients treated with a maximum of 5 years of adjuvant endocrine therapy only (no adjuvant chemotherapy or extended endocrine therapy). Risk of recurrence applies only to LN- patients. Positive LN status increases risk, and LN+ patients should be considered at high risk of recurrence.²

TREATMENT BENEFIT BASED ON INDEPENDENT VALIDATION DATA OF BCI PREDICTIVE IN MA.17³

Patients with a Low BCI Predictive result had **NO SIGNIFICANT RISK REDUCTION (p=0.35)** when treated with extended endocrine therapy in the MA.17 validation study³



Additional Comments:

Laboratory Director: Sue Beruti, M.D. CLIA #: 05-D1065727 CLF334843 Electronically Signed By: Sue Beruti, M.D.

Biotheranostics, Inc. 9640 Towne Center Drive, Suite 200 • San Diego, CA 92121 Tel: 877.886.6739

Result Summary

BCI reports two independent genomic signatures. Four combinations of BCI risk category and Likelihood of Benefit from extended endocrine therapy are possible.

Prognostic Result (5-10 y)

Individualized risk of late recurrence is presented as a percentage in the Summary section, and is plotted on a continuous risk curve.

Patient result is also categorized as LOW or HIGH risk by BCI

Predictive Result

Patient's individualized likelihood of benefit from extended endocrine therapy

Predictive Validation in MA.17

Treatment benefit in the extended setting for LOW BCI Predictive patients:

- No significant benefit/risk reduction

Clinically Actionable Information*

- Consider additional and other therapeutic options for risk reduction
- Monitor closely

*For node-negative patients. BCI Prognostic was validated in a cohort that included LN- patients only. Any LN+ patient should be viewed as higher risk and managed accordingly.

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Risk Of Distant Recurrence & Extended Endocrine Benefit (Report Page 2 of 2)

Physician Information

Treating Physician
First Last, M.D.
Facility Name
Fax: (XXX) XXX-XXXX

Patient & Order Information

Order ID: BDX15-654321
Patient Name: First Last
DOB (Gender): X/X/XXXX (F) XX Yrs Old
Date Reported:

ADDITIONAL RESULTS APPLICABLE IF BCI ORDERED AT TIME OF DIAGNOSIS

BCI Prognostic

HIGH Risk of Overall Recurrence
(15.3% between years 0-10)

HIGH RISK CATEGORY*

15.3% RISK[†] (95% CI: 8.9% - 21.2%)
OF DISTANT RECURRENCE FOR ER+, LYMPH NODE -
NEGATIVE PATIENTS FROM YEARS 0-10¹

[†] Risk of Recurrence estimate is based on analysis of BCI Prognostic in the Stockholm clinical study¹ and provides risk of recurrence from years 0-10 post-diagnosis in patients treated with a maximum of 5 years of adjuvant endocrine therapy only (no adjuvant chemotherapy or extended endocrine therapy). Risk of recurrence applies only to LN- patients. Positive LN status increases risk, and LN+ patients should be considered at high risk of recurrence.²

BCI Predictive

LOW Likelihood of Benefit

LOW LIKELIHOOD OF BENEFIT

FROM EXTENDED ENDOCRINE THERAPY³

BCI Predictive was validated in a cohort that included both LN- and LN+ (1-3 nodes) patients; however, the study was not designed or powered to assess LN+ and LN- groups separately.

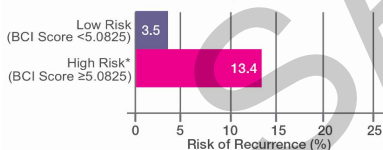
Test Description and Clinical Evidence

BCI is a multi-gene quantitative RT-PCR assay that provides two outputs based on unique gene expression signatures: BCI Prognostic and BCI Predictive.

BCI Predictive provides a prediction of likelihood of benefit from extended (>5 years) endocrine therapy (EET).³ Patient results for this test are categorized as either High or Low Likelihood of Benefit. BCI Predictive was validated in the NCIC-CTG MA.17 trial.^{3,4}
BCI Prognostic provides an individualized estimate for a patient's risk for distant recurrence in the late (5-10 years post-diagnosis) and overall (0-10 years post-diagnosis) time frames.^{1,2} For each time frame, a risk category is provided based on pre-specified cut points. BCI Prognostic has been validated in 3 independent cohorts.^{1,2}

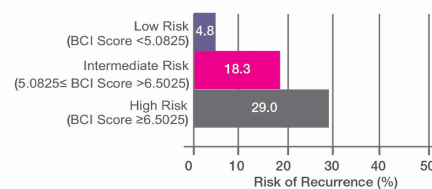
Independent validation data of BCI Prognostic in TransATAC²

Risk of recurrence for lymph node-negative patients from years 5-10 by BCI risk groups in TransATAC²



*In clinical studies, BCI Intermediate risk had a statistically similar risk of late (5-10 year) recurrence as the BCI High risk group;^{1,2} thus risk categories are reported as Low or High risk only

Risk of recurrence for lymph node-negative patients from years 0-10 by BCI risk groups in TransATAC²



Further Information

For additional information including test description, methodology, clinical report and interpretation, please see: www.breastcancerindex.com/ordering

References

- Zhang Y, et al. *Clin Cancer Res*. 2013;19:4196205. 2. Sgroi D, et al. *Lancet Oncol*. 2013; 14:1067-76. 3. Sgroi D, et al. *J Natl Cancer Inst*. 2013; 105:1036-42. 4. Goss PE, et al. *N Engl J Med* 2003; 349:1793-802.

Laboratory Director: Sue Beruti, M.D.

CLIA #: 05-D1065727 CLF334843

Electronically Signed By: Sue Beruti, M.D.

Intended Use

The Breast Cancer Index (BCI) Risk of Recurrence & Extended Endocrine Benefit Test is indicated for patients diagnosed with estrogen receptor-positive (ER+), early-stage breast cancer, who are distant recurrence-free, and provides: 1) a quantitative assessment of the likelihood of both late (post-5 years) and overall (0-10 year) distant recurrence in lymph node-negative (LN-) patients treated with initial adjuvant endocrine therapy, and 2) prediction of likelihood of benefit from extended (>5 year) endocrine therapy in patients who are recurrence-free after an initial 5 years of adjuvant endocrine therapy. Treatment decisions require correlation with all other clinical findings.

This test was developed and its performance characteristics determined by Biotherapeutics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration. This test is used for clinical purposes. It should not be regarded as investigational or for research. How this information is used to guide patient care is the responsibility of the physician. Biotherapeutics is certified under the Clinical Laboratory Improvement Amendments of 1988 to perform high complexity clinical laboratory testing.

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Results if BCI Ordered at Time of Diagnosis

Test Description and Clinical Evidence

Validation - Risk of late recurrence: In clinical studies, BCI Intermediate risk had a statistically similar risk of late recurrence as the BCI High risk group; thus, risk categories are reported as Low or High risk only

Validation - Risk of overall recurrence: BCI separates patients into three distinct categories for patients in which BCI is ordered to assess overall risk of recurrence (0-10 years)