Genomic Health

oncotype DX® Breast Recurrence Score

Oncotype DX Breast Recurrence Score® Report

Micromets & Node Positive (1-3)*

PATIENT, SAMPLE

Date of Birth: **01-Jan-1950** Gender: **Female** Report Number: **OR000123456-3021** Report Date: **03-Dec-2018**

Specimen Source/ID: **Breast/SP-16_0123456**

Ordering Physician: **Dr. First-Name I. Ordering-Physician-Last-Name**

Recurrence Score® Result (RS)

10

Distant Recurrence Risk at 9 Years

With AI or TAM Alone

12%

TransATAC

Absolute Chemotherapy Benefit

RS 0-17

No Apparent Benefit

SWOG 8814

AI = Aromatase Inhibitor / TAM = Tamoxifen

Real World Evidence of SEER Registry Outcomes in Patients Treated Without Chemotherapy Based on RS Results

	RS 0-10	RS 11-15	RS 16-20	RS 21-25	RS 26-100
# of Patients	1808	2196	1754	692	364
BCSS at 9 Years	98.2%	99.0%	96.7%	93.1%	84.2%

BCSS = Breast cancer-specific survival

Quantitative Single-Gene Scores

10.8 ER Positive

<3.7 6.5 ≥12.5

7.3 PR Positive

<3.2 5.5 ≥10.0

10.0 HER2 Negative

<7.6 10.7 11.5 ≥13.0

Laboratory Director(s): S. Shak, MD; F. Baehner, MD; H. Bailey, MD & P. Joseph, MD

Genomic Health, Inc., 301 Penobscot Drive, Redwood City, CA 94063, USA - CLIA Number 05D1018272

This test was developed and its performance characteristics determined by Genomic Health, Inc. It has not been cleared or approved by the FDA, nor is it currently required to be. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research.

Genomic Health

oncotype DX® Breast Recurrence Score

Oncotype DX Breast Recurrence Score® Report

Micromets & Node Positive (1-3)*

PATIENT, SAMPLE

Date of Birth: **01-Jan-1950** Gender: **Female** Report Number: **OR000123456-3021** Report Date: **03-Dec-2018**

Specimen Source/ID: **Breast/SP-16_0123456**

Ordering Physician: **Dr. First-Name I. Ordering-Physician-Last-Name**

Medical Record/Patient #: **1234567-01** Client: **Community Medical Center**

Date of Collection: **18-Nov-2018**

Specimen Received: **20-Nov-2018**

Additional Recipient: **Dr. First-Name I. Recipient-Physician-Last-Name**

Pathologist: **Dr. First-Name I. Pathologist-Last-Name**

The Oncotype DX Breast Recurrence Score test uses RT-PCR to determine the expression of a panel of 21 genes (16 cancer-related, 5 reference) in tumor tissue.

The Oncotype DX Breast Recurrence Score test uses RT-PCR to provide prognostic and predictive information to guide the systemic treatment decisions with hormonal therapy and/or chemotherapy for patients diagnosed with ER+, HER2- invasive breast cancer. Decisions on treatment should also be based on independent medical judgment of the treating physician taking into consideration all available information concerning the patient's medical condition, including other pathological tests, in accordance with your communities' standard of care.

*Results in this report are based on studies including both micrometastases and 1-3 positive nodes.
Advances in histopathological techniques and changes in staging criteria have resulted in an increase in the number of patients diagnosed with lymph node micrometastases (0.2 mm - 2.0 mm). Previous study results varied regarding their clinical significance. BCSS in SEER[1] for patients with RS 0-17 treated without chemotherapy are similarly favorable for patients with negative nodes, micrometastases, and 1-3 positive nodes.

The **Recurrence Score Result (RS)**, which ranges from 0-100, is calculated from the quantitative RT-PCR analysis of the 21 genes.

The **Distant Recurrence Risk** at 9 Years (Prognosis), in patients treated with tamoxifen or arimidex alone, is provided by the TransATAC[2] trial. Risk is for individual RS results. The 95% confidence intervals for distant recurrence at 9 years are ±3 to ±6% for RS 0-22, and range from ±6 to ±12% as RS increases from RS 23-50. The TransATAC trial enrolled 1,231 patients and 243 patients had 1-3 positive nodes, including micrometastases.

The **Absolute Benefit of Chemotherapy** is provided by the SWOG 8814[3] trial. Results for reduction in distant recurrence or death at 5 years are for the RS groups 0-17, 18-30, and 31-100. The SWOG 8814 trial enrolled 367 patients with N+ (including micrometastases), ER+ breast cancer who were randomized to tamoxifen alone or tamoxifen plus CAF (anthracycline-containing) chemotherapy. The benefit of chemotherapy increased with an increase in the RS result.
**The upper bound of the 95% confidence interval for RS 18-30 was 7% absolute chemotherapy benefit.

Real World Evidence of SEER Registry Outcomes in Patients Treated Without Chemotherapy Based on RS Results
SEER had 6,814 patients with HR+, HER2-, node positive (1-3 positive nodes or micrometastases) breast cancer, diagnosed between January 2004 and December 2014, who were reported to have no or unknown chemotherapy use. Two additional prospective studies also demonstrated favorable outcomes with endocrine therapy alone for patients with 1-3 positive nodes and RS 0-11 (PlanB[4]) or RS 0-17 (Clalit[5]).

Quantitative Single-Gene Scores for quality control. The Oncotype DX test uses quantitative RT-PCR to determine the RNA expression of ER, PR, and HER2, using the published validated cut-offs[6]. The standard deviations of single-gene results are less than 0.5 units. The RT-PCR single-gene results may differ from ER, PR, or HER2 results reported using other methods or reported by other laboratories.

References:
1. Roberts et al. *Breast Cancer Res Treat.* 2017.; Genomic Health (data on file). 2. Dowsett et al. *J Clin Oncol.* 2010. 3. Albain et al. *Lancet Oncol.* 2010.; Genomic Health (data on file).
4. Nitz et al. *Breast Cancer Res Treat.* 2017. 5. Stemmer et al. *npj Breast Cancer* 2017. 6. Badve et al. *J Clin Oncol.* 2008.; Baehner et al. *J Clin Oncol.* 2010.