For newly diagnosed patients with node-negative or node-positive, ER-positive, HER2-negative invasive breast cancer

The Onco
type DX® Breast Cancer Assay reveals the underlying biology that changes treatment decisions 37% of the time

Even when treatment decisions based on traditional measures seem conclusive, Onco
type DX can lead to a different approach

For newly diagnosed patients with node-negative or node-positive, ER-positive, HER2-negative invasive breast cancer

Uncover the Unexpected®
Individualized Recurrence Score® (RS) results assess the potential benefit of chemotherapy and the likelihood of distant breast cancer recurrence. Treatment decisions were changed even when definitive treatment decisions had already been made for these patients*†:

- **33%** of the overall population switched from **CT + HT** to **HT** alone based on a low Recurrence Score result‡.
- **4%** of the overall population switched from **HT** only to **CT + HT** based on a high Recurrence Score result‡.

The Onco type DX® Breast Cancer Assay results change treatment decisions across 7 independent studies§:

<table>
<thead>
<tr>
<th>Before RS → After RS</th>
<th>CT + HT → HT (n=297)</th>
<th>HT → HT (n=303)</th>
<th>CT + HT → CT + HT (n=271)</th>
<th>HT → CT + HT (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asad et al* (n=81)</td>
<td>36</td>
<td>13</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>Henry et al* (n=29)</td>
<td>7</td>
<td>14</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Klang et al* (n=313)</td>
<td>105</td>
<td>119</td>
<td>69</td>
<td>20</td>
</tr>
<tr>
<td>Liang et al* (n=260)</td>
<td>85</td>
<td>47</td>
<td>125</td>
<td>3</td>
</tr>
<tr>
<td>Lo et al* (n=83)</td>
<td>20</td>
<td>40</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Oratz et al* (n=68)</td>
<td>14</td>
<td>32</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>Thanasoulis et al* (n=78)</td>
<td>30</td>
<td>38</td>
<td>8</td>
<td>2</td>
</tr>
</tbody>
</table>

% with changed treatment decisions **33%**

Studies have shown that Recurrence Score results reduce chemotherapy use, spare patients the negative health and quality of life impact of unnecessary chemotherapy, and reduce the costs to society and the healthcare system1,6,9,10.
Oncotype DX® is the only multigene breast cancer assay incorporated into 3 major clinical guidelines

Clinical practice guidelines

<table>
<thead>
<tr>
<th>NCCN Guidelines</th>
<th>Consider use in &gt;0.5 cm, HR+, HER2-negative disease pT1, pT2, or pT3; and pN0 or pN1mi (≤2 mm axillary node metastasis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCO® Guidelines</td>
<td>Newly diagnosed patients with node-negative, ER+ breast cancer who will receive tamoxifen</td>
</tr>
<tr>
<td>St Gallen Consensus Guidelines</td>
<td>Oncotype DX has been shown to predict chemotherapy benefit among patients with HR+ disease</td>
</tr>
</tbody>
</table>

*National Cancer Institute.

The Oncotype DX assay analyzes the expression of 21 genes to provide a Recurrence Score® unique to each patient

- The Recurrence Score predicts chemotherapy benefit and indicates the 10-year risk of distant recurrence

The Oncotype DX assay provides an individualized Recurrence Score result

The Recurrence Score reflects an individual’s unique tumor biology

For Recurrence Score >50, group average rate of distant recurrence and 95% CI shown.

Low Recurrence Score disease:
- Indolent
- Hormone therapy–sensitive
- Minimal, if any, chemotherapy benefit

High Recurrence Score disease:
- Aggressive
- Less sensitive to hormone therapy
- Large chemotherapy benefit
Patient age and tumor size cannot predict the Recurrence Score® result

The Oncotype DX® assay Recurrence Score results provide additional insight into underlying tumor biology.®

NSABP B-20 trial (n=651)®

Patient age (years)

- Younger patients can have low Recurrence Score results
- Older patients can have high Recurrence Score results

Clinical tumor size (cm)

- Patients with small tumors can have high Recurrence Score results
- Patients with large tumors can have low Recurrence Score results

Recurrence Score result
- <18
- 18–30
- ≥31
Tumor grade cannot predict the Recurrence Score result

The Oncotype DX assay reveals critical information that changes treatment decisions.

Because high and low Oncotype DX Recurrence Score results reflect different intrinsic tumor biology, physicians can make decisions based on underlying disease.
The OncoType DX® assay provides prognostic information for node-negative patients

Prognostic*: The Recurrence Score® (RS) result is directly correlated with the rate of distant recurrence.

- A low Recurrence Score result correlated with a lower rate of distant recurrence, while a high Recurrence Score result correlated with a higher rate of distant recurrence.

**NSABP B-14:** 10-year rate of distant recurrence was significantly lower for patients with low Recurrence Score results.

- Low Risk: RS < 18
  - 6.8%
  - 95% CI: 4%–9.6%

- Intermediate Risk: RS 18–30
  - 14.3%
  - 95% CI: 8.3%–20.3%

- High Risk: RS ≥ 31
  - 30.5%
  - 95% CI: 23.6%–37.4%

**NSABP B-14:** The majority of patients had low Recurrence Score results.

- 51% RS < 18
- 27% RS ≥ 31
- 22% RS 18–30

*Prognostic: Any measurement available at the time of diagnosis or surgery associated with clinical outcome in the absence of systematic adjuvant therapy or following the standard of care treatment.

**NSABP B-14**
Prospective analysis of archived tissue from 668 stage I or II patients with ER-positive, node-negative invasive breast cancer treated with tamoxifen. Twenty-nine percent of patients were <50 years of age and 62% had tumors that were ≤2.0 cm in size. The 10-year distant recurrence rate for the overall study population was 15%.
**Predictive**: Any measurement associated with benefit or lack of benefit from a particular therapy.

**NSABP B-20**

Prospective analysis of archived tissue from 651 patients with ER-positive, node-negative invasive breast cancer treated with tamoxifen or tamoxifen plus CMF/MF. Approximately 45% of the patients were <50 years of age, two-thirds of tumors were ≤2.0 cm in size, and 20% of tumors were PR-negative.

*Predictive*: The Recurrence Score® is associated with the level of benefit from chemotherapy

**NSABP B-20**: A high Recurrence Score result predicted a significant benefit from chemotherapy (n=651)

<table>
<thead>
<tr>
<th>Recurrence Score Result</th>
<th>Proportion without distant recurrence</th>
<th>P-value</th>
<th>Tam + chemo</th>
<th>Tam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (&lt;18)</td>
<td>0.97/0.96</td>
<td>≥0.61</td>
<td>218/135</td>
<td>8/4</td>
</tr>
<tr>
<td>Intermediate (18–30)</td>
<td>0.91/0.89</td>
<td>&lt;0.39</td>
<td>89/45</td>
<td>9/4</td>
</tr>
<tr>
<td>High (≥31)</td>
<td>0.88/0.60</td>
<td>&lt;0.001</td>
<td>117/47</td>
<td>13/18</td>
</tr>
</tbody>
</table>

*Only the OncoType DX® assay provides predictive information for node-negative patients*
The Oncotype DX® assay provides recurrence risk information for both node-negative and node-positive patients.

Trans ATAC: Recurrence risks seen in node-negative patients and patients with 1–3 positive nodes who had low Recurrence Score® results (n=1,178)²⁸

- The risk of 9-year distant recurrence increased with the number of positive nodes and the Recurrence Score result.
- For low Recurrence Score results, the risk of 9-year distant recurrence for node-negative patients and those with 1–3 positive nodes was similar.

Trans ATAC
Prospective analysis of archived tissue from 1,231 postmenopausal patients with invasive breast cancer treated with tamoxifen or an aromatase inhibitor, of whom 1,178 were ER-positive and either node-negative or node-positive. Of 306 node-positive patients: 79% had 1–3 positive nodes, 21% had 4 or more positive nodes, and 4% had unknown nodal status. The mean age was 64 years and 67% of tumors were ≤2.0 cm in size.
The Oncotype DX® assay predicts the benefit of chemotherapy in node-positive patients

SWOG 8814: Significant chemotherapy benefit only in the high Recurrence Score® result group (n=367)⁹

- **LOW RECURRENCE SCORE RESULT (<18)**
  - Tam only: 92%, 87%
  - CAF-T: 91, 10
  - P = 0.56

- **INTERMEDIATE RECURRENCE SCORE RESULT (18–30)**
  - Tam only: 81%, 70%
  - CAF-T: 57, 10
  - P = 0.89

- **HIGH RECURRENCE SCORE RESULT (≥31)**
  - Tam only: 73%, 54%
  - CAF-T: 71, 18
  - P = 0.033

- No substantial benefit in breast cancer-specific survival from anthracycline-based chemotherapy for node-positive patients with low Recurrence Score results
- Substantial benefit in breast cancer-specific survival from anthracycline-based chemotherapy for node-positive patients with high Recurrence Score results

SWOG 8814
Prospective analysis of archived tissue from 367 postmenopausal, hormone receptor–positive, node-positive patients with invasive breast cancer treated with tamoxifen or tamoxifen plus CAF. Approximately 62% had 1–3 positive nodes and the remainder had 4 or more. Mean age was 60 years (range 42–81), 20% were PR-negative, and 64% of tumors were 2–5 cm in size.
21 genes reveal the underlying biology that provides prognostic and predictive information

### Sample report

**Genes responsible for generating the Recurrence Score (RS) result and report**

**PROLIFERATION**
- Ki-67
- STK15
- Survivin
- Cyclin B1
- MYBL2

**INVASION**
- Stromelysin 3
- Cathepsin L2

**HER2**
- GRB7
- HER2

**REFERENCE**
- Beta-actin
- GAPDH
- RPLPO
- GUS
- TFRC

**ESTROGEN**
- ER
- PR
- Bcl-2
- SCUBE2

**OTHER**
- GSTM1
- CD68
- BAG1

### RS formula

\[
RS = +0.47 \times \text{HER2 group score} - 0.34 \times \text{Estrogen group score} + 1.04 \times \text{Proliferation group score} + 0.10 \times \text{Invasion group score} + 0.05 \times \text{CD68} - 0.08 \times \text{GSTM1} - 0.07 \times \text{BAG1}
\]

### 16 cancer genes

- Cyclin B1
- Survivin
- SCUBE2
- Ki-67
- Cathepsin L2
- ER
- PR
- Bcl-2
- GSTM1
- CD68
- BAG1
- GRB7
- HER2
- STK15
- Survivin
- Cyclin B1
- MYBL2

### 5 reference genes

- Beta-actin
- GAPDH
- RPLPO
- GUS
- TFRC

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Also available for node-positive patients and patients with ductal carcinoma in situ.
Genomic Health® is committed to making Oncofotype DX® available to your patients

Sign up now for the Customer Portal at https://online.genomichealth.com for online ordering and results

Call Customer Service at 866-ONCOTYPE to open an account

Ensuring access to the Oncofotype DX assay for invasive breast cancer

- Extensively reimbursed in node-negative disease: more than 95% of privately insured lives and Medicare beneficiaries are covered
  - Expanding coverage in node-positive patients
- Provides comprehensive services to ease the reimbursement process for you, your staff, and your patients through the Genomic Access Program (GAP)
  - GAP provides several assistance programs designed to help patients based on financial eligibility

Genomic Health is a CLIA-certified, CAP-accredited reference laboratory

Oncotype DX is now available for patients with ductal carcinoma in situ (DCIS) and stage II colon cancer

References:
Even when treatment decisions based on traditional measures seem conclusive, Oncotype DX can lead to a different approach

**Oncotype DX:**

- Provides an individualized Recurrence Score® result that cannot be predicted by traditional clinicopathologic variables
- Is the only assay incorporated into NCCN®, ASCO®, and St Gallen clinical practice guidelines
- Is the first commercial multigene expression assay to predict the benefit of chemotherapy in patients with ER-positive, HER2-negative breast cancer
- Fulfills the criteria for National Cancer Institute Level I, Category B evidence, with consistent results in more than one prospective validation study using archived samples
- Has been clinically validated in 13 studies with over 4,000 breast cancer patients
- Can spare patients the negative health and quality of life impact of unnecessary chemotherapy and result in cost savings
- Has the longest history and track record of commercial genomic assays with over 300,000 patients tested

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