The Oncotype DX® Assay in the Contemporary Management of Invasive Early-stage Breast Cancer

Cancer – The Biology Century

- Understanding and treating the underlying tumor biology
  - Cancer genetic studies demonstrate the transition of basic research to clinical application (i.e. BRCA testing)
  - Targeted cancer therapies developed based on the unique tumor genetic characteristics (i.e. tamoxifen and trastuzumab)
  - Sequencing of the human genome
  - Gene expression profiling shown to predict clinical outcome

Scientific breakthroughs making personalized medicine in cancer a reality

Key Questions When Evaluating Genomic Classifiers

- Fit for purpose
  - Incoporated in research protocols?
  - What is the level of evidence?
  - Prevision of individualized therapy?

Clinical Validation of the Oncotype DX® Breast Cancer Assay in Node-Negative Disease
Onco
type DX® Clinical Validation: NSABP B-14

- Objective: Prospectively validate the Recurrence Score® result as a predictor of distant recurrence in node-negative, ER+ patients

- Multicenter study with prespecified 21-gene assay, algorithm, endpoints, analysis plan

- Placebo—not eligible
- Tamoxifen—eligible
- Randomized
- Registered

Randomized
Registered

Tamoxifen—eligible

Onco
type DX® Clinical Validation: NSABP B-14, Distant Recurrence

Distant recurrence over time

- 10-Year rate of recurrence = 8.8%
- 95% CI: 4.0%, 9.6%

- 10-Year rate of recurrence = 14.3%
- 95% CI: 8.3%, 19.3%


RS, Recurrence Score® result

10-Year rate of recurrence comparison between low-risk and high-risk groups: P < 0.001

All patients (N=668)

Distant recurrence-free at 10 Years

- All Patients
- Low Risk (RS <18)
- Int Risk (RS 18-30)
- High Risk (RS ≥31)

Onco
type DX® Clinical Validation: NSABP B-14, Subgroup Analysis by Tumor Size

All patients (N=668)

Size ≤1 cm

Size 1-2 cm

Size 2-4 cm

Size >4 cm

RS, Recurrence Score® result

% Distant Recurrence-free at 10 Years


10-Year rate of recurrence comparison between low-risk and high-risk groups: P < 0.001

All Patients

Low Risk (RS <18)

Int Risk (RS 18-30)

High Risk (RS ≥31)

Onco
type DX® Clinical Validation: NSABP B-14, Clinical Validation: Subgroup Analysis by Tumor Grade

All patients N=668

Well

Moderate

Poor

% Distant Recurrence-free at 10 Years


RS, Recurrence Score® result

10-Year rate of recurrence comparison between low-risk and high-risk groups: P < 0.001

All Patients

Low Risk (RS <18)

Int Risk (RS 18-30)

High Risk (RS ≥31)

Onco
type DX® Clinical Validation: NSABP B-20

- Objective: Prospectively determine the relationship between Recurrence Score® result and chemotherapy benefit in node-negative, ER+ patients

- Multicenter study with prespecified 21-gene assay, algorithm, endpoints, analysis plan

Randomized

Tam + MF

Tam + CMF

Tam
High Recurrence Score® Result Correlates with Greater Benefit from Chemotherapy (NSABP B-20)

**Graph:**
- X-axis: Years
- Y-axis: Proportion without distant recurrence
- Data points show a trend indicating greater benefit from chemotherapy as Recurrence Score increases.

**Table:**
- **RS ≥ 31** (Tam + CMF/MF vs Tam)
  - N: 117, 47
  - Events: 13, 18
  - P < 0.001

**Graph:**
- X-axis: 0 to 100 Recurrence Score
- Y-axis: 0 to 100
- Data points indicating a significant difference in distant recurrence between low and high RS groups.

**Table:**
- **Recurrence Score < 18**
  - N: 218, 135
  - Events: 8, 4
  - P = 0.61

**Table:**
- **Recurrence Score 18 - 30**
  - N: 89, 45
  - Events: 9, 4
  - P = 0.39

**Table:**
- **Recurrence Score ≥ 31**
  - N: 117, 47
  - Events: 13, 18
  - P < 0.001

**Figure:**
- **Node Negative, ER-Positive Breast Cancer Chemotherapy Benefit**
  - Comparison of chemotherapy benefit across different Recurrence Score ranges.

**Figure:**
- **NSABP B-20: Many Younger Patients Have Low Recurrence Score® Disease**
  - Age distribution by Recurrence Score category.

**Figure:**
- **NSABP B-20: Significant Proportion of High-Grade Tumors Have Low Recurrence Score® Disease**
  - Tumor grade vs Recurrence Score distribution.

**Figure:**
- **NSABP B-20: Many Small Tumors Have Intermediate to High Recurrence Score® Disease**
  - Tumor size vs Recurrence Score distribution.

**Question:**
- Does the Recurrence Score® Impact Treatment Decisions?
**Meta-Analysis: Overall Impact of Recurrence Score® on Treatment Decisions**

<table>
<thead>
<tr>
<th>Treatment plan prior to OncoType DX®</th>
<th>Treatment plan after RS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT + HT</td>
<td>CT + HT</td>
</tr>
<tr>
<td>88%</td>
<td>38%</td>
</tr>
<tr>
<td>62%</td>
<td>52%</td>
</tr>
<tr>
<td>4% change</td>
<td>4% change</td>
</tr>
</tbody>
</table>

Overall, the RS led to a 37% change in treatment decisions:
- 33% from CT + HT → HT
- 4% from HT → CT + HT

**Most Patients Were Positively Influenced by the Recurrence Score® Result**

<table>
<thead>
<tr>
<th>I am glad I took the RS assay</th>
<th>RS results were easy to understand</th>
<th>I think the RS helped support treatment decision</th>
<th>I would have made the same treatment decision without RS</th>
<th>I feel the RS influenced my treatment decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>10</td>
</tr>
</tbody>
</table>

*Those not satisfied noted a negative impact on QOL, treatment side effects including aches, hot flashes, pain, mood alteration, and negative impact on self image.

In addition, the Recurrence Score® result helped reduce patients’ anxiety and decisional conflict.

**Can You Guess the Recurrence Score®?**

**PATIENT A**
- 68-year-old patient with 1.1-cm tumor
- Menopausal Status: Postmenopausal
- Tumor Type: Infiltrating Ductal Carcinoma (IDC)
- Tumor Size: 1.1 cm
- ER Status (IHC): Positive
- PR Status (IHC): Positive
- HER2 Status: Negative
- Histologic Grade: 2
- Lymph Node Status: Negative
- General Health: Fair

**PATIENT B**
- 69-year-old patient with 1.3-cm tumor
- Menopausal Status: Postmenopausal
- Tumor Type: Infiltrating Ductal Carcinoma (IDC)
- Tumor Size: 1.3 cm
- ER Status (IHC): Positive (2)
- PR Status (IHC): Positive (2)
- HER2 Status: Negative (IHC)
- Histologic Grade: 3
- Lymph Node Status: Negative
- General Health: PS 0

**Patient Cases**

**Can You Guess the Recurrence Score®?**

**PATIENT A**
- 68-year-old patient with 1.1-cm tumor
- Menopausal Status: Postmenopausal
- Tumor Type: Infiltrating Ductal Carcinoma (IDC)
- Tumor Size: 1.1 cm
- ER Status (IHC): Positive
- PR Status (IHC): Positive
- HER2 Status: Negative
- Histologic Grade: 2
- Lymph Node Status: Negative
- General Health: Fair

**PATIENT B**
- 69-year-old patient with 1.3-cm tumor
- Menopausal Status: Postmenopausal
- Tumor Type: Infiltrating Ductal Carcinoma (IDC)
- Tumor Size: 1.3 cm
- ER Status (IHC): Positive (2)
- PR Status (IHC): Positive (2)
- HER2 Status: Negative (IHC)
- Histologic Grade: 3
- Lymph Node Status: Negative
- General Health: PS 0

**Is the Oncotype DX® Assay Included in Treatment Guidelines?**

**The Oncotype DX® Assay**
- The Only Multi-gene Assay Incorporated into 4 Major Guidelines to Predict Adjuvant Chemotherapy Benefit in ER+, HER2- Early Stage Breast Cancer

- NCCN Guidelines
  | Quantifies risk of recurrence as a continuous variable and predicts responsiveness to both tamoxifen and chemotherapy
- ASCO® guidelines
  | Predicts the risk of recurrence and may be used to identify patients likely to benefit from tamoxifen or chemotherapy
- St Gallen Consensus
  | Provides not only prognostic but also predictive information regarding the utility of cytotoxic therapy in addition to endocrine therapy
- NICE guidelines
  | Recommended as an option for guidance of chemotherapy decisions in patients at intermediate risk of distant recurrence

**Patient Cases**

**Is the Oncotype DX® Assay Included in Treatment Guidelines?**

**The Oncotype DX® Assay**
- The Only Multi-gene Assay Incorporated into 4 Major Guidelines to Predict Adjuvant Chemotherapy Benefit in ER+, HER2- Early Stage Breast Cancer

- NCCN Guidelines
  | Quantifies risk of recurrence as a continuous variable and predicts responsiveness to both tamoxifen and chemotherapy
- ASCO® guidelines
  | Predicts the risk of recurrence and may be used to identify patients likely to benefit from tamoxifen or chemotherapy
- St Gallen Consensus
  | Provides not only prognostic but also predictive information regarding the utility of cytotoxic therapy in addition to endocrine therapy
- NICE guidelines
  | Recommended as an option for guidance of chemotherapy decisions in patients at intermediate risk of distant recurrence

**Patient Cases**

**Is the Oncotype DX® Assay Included in Treatment Guidelines?**

**The Oncotype DX® Assay**
- The Only Multi-gene Assay Incorporated into 4 Major Guidelines to Predict Adjuvant Chemotherapy Benefit in ER+, HER2- Early Stage Breast Cancer

- NCCN Guidelines
  | Quantifies risk of recurrence as a continuous variable and predicts responsiveness to both tamoxifen and chemotherapy
- ASCO® guidelines
  | Predicts the risk of recurrence and may be used to identify patients likely to benefit from tamoxifen or chemotherapy
- St Gallen Consensus
  | Provides not only prognostic but also predictive information regarding the utility of cytotoxic therapy in addition to endocrine therapy
- NICE guidelines
  | Recommended as an option for guidance of chemotherapy decisions in patients at intermediate risk of distant recurrence

**Patient Cases**

**Is the Oncotype DX® Assay Included in Treatment Guidelines?**

**The Oncotype DX® Assay**
- The Only Multi-gene Assay Incorporated into 4 Major Guidelines to Predict Adjuvant Chemotherapy Benefit in ER+, HER2- Early Stage Breast Cancer

- NCCN Guidelines
  | Quantifies risk of recurrence as a continuous variable and predicts responsiveness to both tamoxifen and chemotherapy
- ASCO® guidelines
  | Predicts the risk of recurrence and may be used to identify patients likely to benefit from tamoxifen or chemotherapy
- St Gallen Consensus
  | Provides not only prognostic but also predictive information regarding the utility of cytotoxic therapy in addition to endocrine therapy
- NICE guidelines
  | Recommended as an option for guidance of chemotherapy decisions in patients at intermediate risk of distant recurrence

**Patient Cases**

**Is the Oncotype DX® Assay Included in Treatment Guidelines?**

**The Oncotype DX® Assay**
- The Only Multi-gene Assay Incorporated into 4 Major Guidelines to Predict Adjuvant Chemotherapy Benefit in ER+, HER2- Early Stage Breast Cancer

- NCCN Guidelines
  | Quantifies risk of recurrence as a continuous variable and predicts responsiveness to both tamoxifen and chemotherapy
- ASCO® guidelines
  | Predicts the risk of recurrence and may be used to identify patients likely to benefit from tamoxifen or chemotherapy
- St Gallen Consensus
  | Provides not only prognostic but also predictive information regarding the utility of cytotoxic therapy in addition to endocrine therapy
- NICE guidelines
  | Recommended as an option for guidance of chemotherapy decisions in patients at intermediate risk of distant recurrence

**Patient Cases**
PATIENT B RESULTS
Clinical Experience
Patients with a Recurrence Score of 11 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 7% (95% CI: 5%-10%).

5

Can You Guess the Recurrence Score®?
68 & 69 year-old patients, small node-negative tumors, grade 2 & 3

PATIENT B RESULTS
Clinical Experience
Patients with a Recurrence Score of 11 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 7% (95% CI: 5%-10%).

PATIENT A RESULTS
Clinical Experience
Patients with a Recurrence Score of 34 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 23% (95% CI: 18%-28%).

Can You Guess the Recurrence Score®?
45 & 46 year-old patients, small node-negative tumors, grade 2 & 3

PATIENT A RESULTS
Clinical Experience
Patients with a Recurrence Score of 15 in the clinical validation study had an Average Rate of Distant Recurrence at 10 years of 10% (95% CI: 7%-12%).

Conclusions
The Onco type DX® Report Provides Valuable Information Along a Continuum of ER+ Breast Cancer

- The Onco type DX report provides valuable information on:
  - Node-negative prognosis
  - Node-negative predicted chemotherapy benefit
  - Quantitative data on ER/PR/HER2
- Node-positive report contains an additional page with prognosis and predicted chemo benefit information specific to node-positive patients

The Onco type DX® Breast Cancer Assay

- Quantitatively predicts the likelihood of breast cancer recurrence and assesses the benefit from both hormonal therapy and chemotherapy (Level I Evidence)
- High and low Recurrence Score® results reflect different intrinsic tumor biology
- You cannot predict the risk of distant recurrence or chemotherapy benefit by relying on clinical and pathological variables
- Changes treatment decisions based on traditional measures 37% of time, sparing patients the negative health and QOL impact of unnecessary chemotherapy and resulting in cost savings
- Only assay incorporated into ASCO®, NCCN® and St. Gallen’s clinical practice guidelines
- Longest history of commercial genomic assays with over 200,000 patients tested worldwide

ASCO is a trademark of the American Society of Clinical Oncology and NCCN is a trademark of the National Comprehensive Cancer Network.
ASCO and NCCN do not endorse any therapy or product.