Processing of Breast Cancer Risk of Recurrence Results Following Genomic Tumor Testing

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Precision Medicine through Tumor Genomic Profiling

NATIONAL CANCER INSTITUTE
PRECISION MEDICINE IN CANCER TREATMENT

Discovering unique therapies that treat an individual’s cancer based on the specific genetic abnormalities of that person’s tumor.
Genomic Testing for Risk for Recurrence

• Gene expression tumor analysis for early stage, ER+ breast cancers:
  • Estimate risk of recurrence
  • Aid prognosis
  • Predict treatment benefit
    • Chemotherapy
    • Extending hormonal therapy
NSABP B-14 Study
10-year rate of distant recurrence was significantly lower for patients with low Recurrence Score results compared to high results.¹
NSABP B-20 Study
Low Recurrence Score result predicted little to no benefit from chemotherapy\(^2\)

**LOW RECURRENCE SCORE RESULT (< 18)**
LITTLE TO NO CHEMOTHERAPY BENEFIT

**INTERMEDIATE RECURRENCE SCORE RESULT (18–30)**
NO SUBSTANTIAL CHEMOTHERAPY BENEFIT

**NSABP B-20 Study**
High Recurrence Score result predicted large benefit from chemotherapy\(^2\)

**HIGH RECURRENCE SCORE RESULT (≥31)**
LARGE CHEMOTHERAPY BENEFIT

\(88\%\) vs \(60\%\) absolute benefit from TAM + CHEMOTHERAPY
Rates of testing by year (2006-2011)

O’Neill et al., 2015

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Testing = Standard of Care

12th St. Gallen International Breast Cancer Conference
Primary Therapy of Early Breast Cancer with Treatment Consensus Update
16 - 19 March 2011
St. Gallen, Switzerland
Sample Report

Breast Cancer Report - Node Negative

Prognosis

Patient ID: DOE JANE ELIZABETH
Gender: Female
Date of Birth: 01-Jan-1950
Medical Record/Project #: 55967771
Date of Collection: 10-Oct-2015
Specimen Type/ID: BreastCRP0770YO
Study #: ReportID0989965

Recurrence Score

OncoTypeDX Breast Cancer Assay uses RT-PCR to determine the expression of a panel of 21 genes in tumor tissue. The Recurrence Score result is calculated from the gene expression results and ranges from 0-100.

The findings are applicable to women who have stage I or II node-negative (N0), estrogen receptor-positive (ER+) breast cancer and will be treated with 5 years of tamoxifen therapy. It is unknown whether the findings apply to other patients outside these criteria.

Clinical Experience: The following results are from a clinical validation study that included 688 patients from the NSABP B-14 study. The study included female patients with stage I or II, ER+, non-breast cancer. Patients were randomized to either tamoxifen or tamoxifen plus chemotherapy. Patients in the pre-specified group with Recurrence Score results ≥ 11, the group average 10-year risk was 90% (95% CI) of distant recurrence were 10% (5%, 54%) for tamoxifen alone and 12% (8%, 18%) for tamoxifen + CMF/AMF.

Recurrence Score Result

6

Prognosis: 10-Year Risk of Distant Recurrence after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-14)

10-Year Risk of Distant Recurrence

Tam Alone
5% (85% CI: 3%-75%)

Low Risk
10-Year Risk: 5% (95% CI: 4%-12%)
Intermediate Risk
10-Year Risk: 14% (95% CI: 8%-22%)
High Risk
10-Year Risk: 34% (95% CI: 24%-57%)

Prediction of Chemotherapy Benefit after 5 Years of Tam, Based on the Recurrence Score Result (from NSABP B-20)

Tam Alone

Tam + Chemo

Absolute Benefit of Chemotherapy at 10 Years by Recurrence Score Risk Group
EGAPP Recommendations--2015

• Research gaps:
  – “Further research (is needed) to clarify how women understand and use the risk information.”
What we know to date:

• Most women accurately recall their perceived risk of recurrence
  • 71% of tested women recalled a perceived risk of recurrence within 4% of the Recurrence Score
  • Mean perceived risk for recurrence for women with low (9.6%), intermediate (18%) and high (25.8%) Recurrence Score reflected actual risk

Tzeng et al., 2010
Questions:

How do women perceive their risk of recurrence before and after the receipt of their Recurrence Score?

How many women over- or under-estimate their risk?

What are the correlates of over- or underestimation?
Methods and Participants

Newly diagnosed breast cancer patients (N = 193)

- Stage I/II
- Pre-test/Post-test design
- High RS = 17
- Intermediate RS = 60
- Low RS = 116

Demographics

- Mean age = 57 (range = 37-83)
- 65% White, 27% African American, 5% Asian, 3% Other
- 60% college degree
Perceived Risk of Recurrence:

“What do you think the chance is that your breast cancer will come back or spread to other parts of your body? Please choose a number from 0-100?”

Accuracy: Alignment of post-test perceived risk and their Oncotype category
• Perceived risk = 0--underestimate
Correlates of over- and under-estimation:

- Recurrence Score
- Receipt of chemotherapy
- Age
- Race
- Education
- Cancer-related distress
- Perceived communication quality
Low Risk of Recurrence

(t = 3.61, p < .001)

- Pretest Perceived Risk of Recurrence
- Posttest Perceived Risk of Recurrence
- Mean Recurrence Score
Intermediate Risk of Recurrence

(t = .75, p = .46)

- Pretest Perceived Risk of Recurrence
- Posttest Perceived Risk of Recurrence
- Mean Recurrence Score
High Risk of Recurrence

(t = 0.28, p < 0.78)

- Pretest Perceived Risk of Recurrence
- Posttest Perceived Risk of Recurrence
- Mean Recurrence Score
Over- and under-estimation of risk

Overall N

- Red: Underestimate
- Blue: Accurate
- Green: Overestimate

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## Correlates of over- and under-estimation

<table>
<thead>
<tr>
<th></th>
<th>Overestimated OR (95% CI)</th>
<th>Underestimated OR (95% CI)</th>
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<tbody>
<tr>
<td>Oncotype Score</td>
<td></td>
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<tr>
<td>Low Score v. Intermediate</td>
<td>0.19 (0.03-1.39) +</td>
<td>0.08 (0.02-0.41)**</td>
</tr>
<tr>
<td>Low Score v. High</td>
<td>2.88 (0.71-11.69)</td>
<td>0.03 (0.01-0.09)*****</td>
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<tr>
<td>Age</td>
<td>1.01 (0.97-1.06)</td>
<td>0.95 (0.90-0.98)**</td>
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<tr>
<td>White v. non-White</td>
<td>1.36 (0.57-3.25)</td>
<td>2.18 (0.69-6.85)</td>
</tr>
<tr>
<td>College v. non-College</td>
<td>0.31 (0.13-0.75)**</td>
<td>2.50 (0.82-7.63)</td>
</tr>
<tr>
<td>Chemotherapy v. None</td>
<td>0.52 (0.12-2.18)</td>
<td>0.65 (0.17-2.51)</td>
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<tr>
<td>Post-test distress</td>
<td>1.03 (0.99-1.07)</td>
<td>0.97 (0.92-1.02)</td>
</tr>
<tr>
<td>Communication quality</td>
<td>0.88 (0.80-0.97)**</td>
<td>1.09 (0.97-1.22)</td>
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+<.10; *<.05; **<.01; ***<.001
Perceived risk: Women with high RS tumors

• Accurate integration of the risk-reduction afforded by chemotherapy

OR

• Defensive processing of high risk of recurrence
Over- and under-estimation

• Older women more likely to underestimate their risk for developing breast cancer (Jones et al., 2011)

• Lower levels of education is a common correlate of overestimation (Skinner et al., 1998; Leblond et al., 2012)

• Effective communication = greater accuracy
  • Family members (Himes et al., 2016)
  • Oncologists (Kelly et al., 2013)
Conclusions

• Perceived risk of recurrence does not uniformly reflect women’s Recurrence Score results

• Future work will examine the impact of this for longer-term outcomes
  – Extend to 1 year post-dx
  – Adherence to treatment and surveillance
  – Quality of life
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