Facilitating an integrated approach to the diagnosis and treatment of breast cancer

This guide provides an explanation of the Prosigna Patient Report generated by the nCounter® Dx Analysis System, which may help interpret and present results.

**Intended use:** The Prosigna Breast Cancer Prognostic Gene Signature Assay is an in vitro diagnostic assay which is performed on the NanoString nCounter® Dx Analysis System using FFPE breast tumor tissue previously diagnosed as invasive breast carcinoma. This qualitative assay utilizes gene expression data, weighted together with clinical variables to generate a risk category and numerical score, to assess a patient’s risk of distant recurrence of disease.¹

**Special conditions for use:** Prosigna is not intended for diagnosis, to predict or detect response to therapy, or to help select the optimal therapy for patients.¹
**Understanding the Prosigna™ Patient Report**

Page 1 of the Prosigna Patient Report provides two customized outputs to determine your patient’s probability of distant recurrence over 10 years:

- **Prosigna Score**: Derived from a proprietary algorithm based on the PAM50 gene signature, the Prosigna Score is a numerical value on a 0 to 100 scale that correlates with the probability of distant recurrence within 10 years.¹

- **Risk group**: Based on the Prosigna Score and nodal status, risk group is provided to allow interpretation of the Prosigna Score by using cutoffs related to clinical outcome in tested patient populations.²

The patient’s tumor size and nodal status are required to determine her Prosigna Score and risk group.³

---

**Page 2 of the Prosigna Patient Report** provides context for your patient’s reported risk group based on the results of a large clinical validation study; ABCSG-8.⁴ Both the Prosigna Score and risk group add statistically significant prognostic information beyond other clinical variables for node-negative and node-positive patients (P<0.0001).¹²

- **Node-negative patients**: 10-year distant recurrence-free survival (DRFS) rates were >95% for the low-risk group, 90.4% for the intermediate-risk group, and <85% for the high-risk group.⁵

- **Node-positive patients**: 10-year DRFS rates were 94.2% for the low-risk group and 75.8% for the high-risk group.¹

---

Prosigna assay results are based on a large validation data set of postmenopausal women with early-stage breast cancer, including both node-negative and node-positive patients (see table at right).¹ The Prosigna Patient Report is customized and includes only those results relevant to your patient’s nodal status.

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Nodal status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1047</td>
<td>Node-negative</td>
</tr>
<tr>
<td>382</td>
<td>Node-positive</td>
</tr>
</tbody>
</table>

The data and table in the Clinical Trial Results section reflect results seen in your patient’s nodal status and risk group from the broader ABCSG-8 validation study population.

The Kaplan-Meier plot shows the probability of distant recurrence (DR) for each risk group, based on DRFS within the similar nodal status patient population from the clinical validation study.³

**REFERENCES:**

2. Gnant M, P2-10-02, Clinical Validation of the PAM50 risk of recurrence (ROR) score for predicting residual risk of distant recurrence (DR) after endocrine therapy in postmenopausal women with HR+ early breast cancer (EBC): An ABCSG study, SABCS 2012.
4. Prosigna Package Insert
The Prosigna Score is related to an individual patient’s 10-year risk of DR:
- Low risk: <10% predicted risk
- Intermediate risk: 10% to 20% predicted risk
- High risk: >20% predicted risk

### Clinical Trial Results
Prosigna has been validated in a large clinical validation study (N=1478) that includes both node-negative and node-positive patients. Results from the node-negative patient population are presented on page 2 of the Prosigna Patient Report, so you can interpret your patient's Prosigna Score in the context of the results seen in similar patients from the clinical validation study.

**Summary of ABCSG-8 study**
- **Samples:** 1478 FFPE breast tumor samples from postmenopausal women with hormone receptor-positive breast cancer who were randomized prior to treatment to 2 years of adjuvant taxotere, followed by either 3 years of anastrozole or 3 years of adjuvant tamoxifen.
- **Objective:** Determine if the Prosigna Score and risk group add prognostic information beyond other clinical variables.
- **Conclusions:** The Prosigna Score and risk group add statistically significant prognostic information beyond other clinical variables (P=0.0001). Risk groups stratify patients according to DRFS, with 10-year DRFS rates of >95% for the low-risk group, 90.4% for the intermediate-risk group, and <85% for the high-risk group.
Node-positive Prosigna™ Patient Report

**Patient Prosigna Score**

The Prosigna algorithm was used in retrospective analysis of the ABCSG-8 clinical trial which included more than 1400 patients with varying risks of distant recurrence. The analysis for node-positive patients was limited to two risk categories since the ABCSG-8 study included a smaller number of node-positive patients (n=382) relative to the number of node-negative patients (n=1047). The Prosigna Score classifies node-positive (1–3 nodes) patients as low or high risk based on prespecified thresholds for risk classification. Prosigna Score cutoffs greater than 40 corresponded high risk, and the score <40 is low-risk.

**Clinical Trial Results: Clinical Validation Study**

Prosigina has been validated in a large clinical validation study (N=1478) that includes both node-negative and node-positive patients. Results from the node-positive patient population are presented on page 2 of the Prosigna Patient Report, so you can interpret your patient’s Prosigna Score in the context of the results seen in similar patients from the clinical validation study.

**Summary of ABCSG-8 study**

- **Samples:** 1478 FFPE breast tumor samples from postmenopausal women with hormone receptor–positive breast cancer who were randomized prior to treatment to 2 years of adjuvant tamoxifen, followed by either 3 years of anastrozole or 3 years of adjuvant tamoxifen. 1,2
- **Objective:** Determine if the Prosigna Score and risk group add prognostic information beyond other clinical variables. 1,2
- **Conclusions:** The Prosigna Score and risk group add statistically significant prognostic information beyond other clinical variables (P<0.0001). Risk groups stratify patients according to DRFS, with 10-year DRFS rates of 94.2% for the low-risk group and 75.8% for the high-risk group. 1,2

---

**Node-negative patients are classified into one of 2 risk groups based on their Prosigna Score. The cutoff between low risk and high risk is 40.**

---

**Node-positive patients are classified into one of 2 risk groups based on their Prosigna Score. The cutoff between low risk and high risk is 40.**

---

**The Kaplan-Meier plot shows the 10-year DRFS rate for each risk group within the node-positive patient population from the ABCSG-8 clinical validation study. The high-risk group is significantly different from the low-risk group.**

---

**Patient Prosigna Score**

The analysis for node-positive patients was limited to two risk categories since the ABCSG-8 study included a smaller number of node-positive patients (n=382) relative to the number of node-negative patients (n=1047). The scale and cutoffs between risk groups differ for node-negative and node-positive patients, as shown below.

<table>
<thead>
<tr>
<th>Node-negative</th>
<th>Low risk</th>
<th>Intermediate risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosigna Score</td>
<td>0-40</td>
<td>40-80</td>
<td>&gt;80</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Node-positive</th>
<th>Low risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosigna Score</td>
<td>0-40</td>
<td>&gt;40</td>
</tr>
</tbody>
</table>

The Kaplan-Meier plot shows the 10-year DRFS rate for each risk group within the node-positive patient population from the ABCSG-8 clinical validation study. The high-risk group is significantly different from the low-risk group.

---

**Probability of Distant Recurrence at 10 Years (%)**

- **Low risk:** 6%
- **High risk:** 40%

---

**To determine the relationship between the Prosigna Score and estimated 10-year risk of DR, plot your patient’s score along the x-axis, then draw a horizontal line to the y-axis. Due to the small sample size of node-positive patients with scores >80, the exact relationship of the Prosigna Score to probability of DR could not be established beyond 80.**

---

**Clinical Trial Results: Clinical Validation Study**

Prosigina has been validated in a large clinical validation study (N=1478) that includes both node-negative and node-positive patients. Results from the node-positive patient population are presented on page 2 of the Prosigna Patient Report, so you can interpret your patient’s Prosigna Score in the context of the results seen in similar patients from the clinical validation study.

**Summary of ABCSG-8 study**

- **Samples:** 1478 FFPE breast tumor samples from postmenopausal women with hormone receptor–positive breast cancer who were randomized prior to treatment to 2 years of adjuvant tamoxifen, followed by either 3 years of anastrozole or 3 years of adjuvant tamoxifen. 1,2
- **Objective:** Determine if the Prosigna Score and risk group add prognostic information beyond other clinical variables. 1,2
- **Conclusions:** The Prosigna Score and risk group add statistically significant prognostic information beyond other clinical variables (P<0.0001). Risk groups stratify patients according to DRFS, with 10-year DRFS rates of 94.2% for the low-risk group and 75.8% for the high-risk group. 1,2

---

**Node-positive Prosigna Score**

The analysis for node-positive patients was limited to two risk categories since the ABCSG-8 study included a smaller number of node-positive patients (n=382) relative to the number of node-negative patients (n=1047). The scale and cutoffs between risk groups differ for node-negative and node-positive patients, as shown below.
Contact us to learn how Prosigna™
can enhance your clinical practice

For more information, visit Prosigna.com
or e-mail info@prosigna.com


US contact information:
NanoString Technologies, Inc.
530 Fairview Ave N, Suite 2000
Seattle, WA 98109

Phone: 888-358-NANO
(888-358-6266)
Fax: 206-378-6288
Web site: nanostring.com