prosigna®

Breast Cancer Prognostic Gene Signature Assay

What is Prosigna?

- Prosigna is the only PAM50-based, early-stage breast cancer assay to deliver a highly accurate assessment of risk of distant recurrence with a personalized prognostic score that identifies your patient's 10-year risk.
- Prosigna together with the nCounter® Dx Analysis System delivers genomic testing results with meaningful decreased turnaround times from local qualified laboratories.
- Prosigna accurately classifies breast cancer into one of the 4 intrinsic subtypes: Luminal A, Luminal B, HER-2 enriched, or Basal-like. Correct knowledge of the biological classification of the tumour type allows better prediction of how the disease will behave.

What is PAM50?

- A gene classifier algorithm that uses a 50-gene expression profile to assign breast cancer to one of four PAM50 molecular subtypes determined by the tumour's molecular profile.
- Gene expression data are weighted with clinical variables to determine the Prosigna score, an integer score from 0-100 indicative of the probability of distant recurrence.
- Prosigna Score is based on tumour size, proliferation score, and the gene expression profile of PAM50 molecular subtypes.

Why choose Prosigna?

Prosigna provides a risk category and numerical score for assessment of the risk of distant recurrence of disease at 10 years, helping to inform clinical decisions with prognostic information beyond standard clinical variables (age, grade, tumour size, nodal status, and adjuvant therapy).

- Validated on 2,479 samples in the combined ABCSG-8 and TransATAC studies.
- CE-marked for FFPE breast tumour tissue on the nCounter® Dx Analysis System.
- Recognized and listed in multiple international guidelines including ASCO, NCCN, and ESMO.
- Positive opinions of prognostic ability during St Gallen consensus vote:
  - 80% of experts agree that Prosigna risk assessment is valuable during years 1-5 in pN0 ER+ HER2- disease.[1]
  - 75% agree that Prosigna risk assessment is valuable during years 1-5 for pN+ (i.e. in 1-3 involved lymph nodes).[1]
  - 63% agree that Prosigna risk assessment is valuable beyond 5 years.[2]

Which patients are appropriate for Prosigna?

Postmenopausal women with hormone receptor-positive, node-negative (Stage I or Stage II), or node-positive (Stage II and IIIA) breast cancer to be treated with adjuvant endocrine therapy.

LAS
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(주)엘에이에스 | LAS Inc. T. 02-3486-0911~2 / info@lascience.co.kr / www.lascience.co.kr

Example Reports

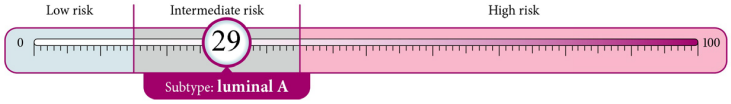
Patient	Specimen	Run Set ID: RPT Test 1
Tumor Size: > 2cm	**ID #:** n1-r29-LA	**Comments:** Comment for n1-r29-LA
Lymph Nodes: node-positive (1-3 nodes)	**Date Reported:** September 21, 2012	

prosigna® Breast cancer prognostic gene signature assay

ID #: n1-r29-LA **Tumor Size:** > 2cm **Lymph Nodes:** node-positive (1-3 nodes)

Assay Description: The Prosigna® breast cancer gene signature assay measures the expression of 50 different genes to identify subtype and report a Risk of Recurrence Score (ROR), which is used to assign the patient to a predefined risk group. These results are derived from a proprietary algorithm based on the PAM50 gene signature, intrinsic subtype, and clinical variables including tumor size and nodal status.

Risk of Recurrence*:

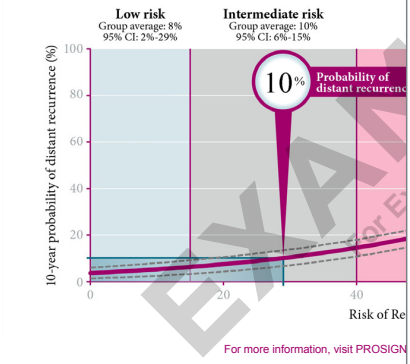


* The ROR ranges from 0 through 100 and correlates with the probability of distant recurrence (DR) in the tested patient population. The risk classification is provided to guide the interpretation of the ROR using cutoffs related to clinical outcome.

Probability of Distant Recurrence:

In the clinical validation studies, patients who were node-positive (1-3 nodes), luminal A subtype, with an ROR score of 29 were in the intermediate probability of distant recurrence at 10 years.

The Prosigna® algorithm has been validated by 2 randomized clinical trials inclu of these 2 clinical validation studies shows that the probability of distant recurren a significantly greater probability of distant recurrence.†



For more information, visit PROSIGN

†Data apply to patients being treated with hormone therapy for 5 years as in the tested patie patient population. It is unknown whether these findings can be extended to other patient pop

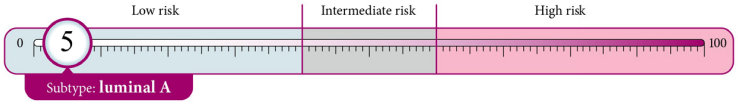
Patient	Specimen	Run Set ID: RPT Test 1
Tumor Size: <= 2cm	**ID #:** n0-r5-LA	**Comments:** Comment for n0-r5-LA
Lymph Nodes: node-negative	**Date Reported:** September 18, 2012	

prosigna® Breast cancer prognostic gene signature assay

ID #: n0-r5-LA **Tumor Size:** <= 2cm **Lymph Nodes:** node-negative

Assay Description: The Prosigna® breast cancer gene signature assay measures the expression of 50 different genes to identify subtype and report a Risk of Recurrence Score (ROR), which is used to assign the patient to a predefined risk group. These results are derived from a proprietary algorithm based on the PAM50 gene signature, intrinsic subtype, and clinical variables including tumor size and nodal status.

Risk of Recurrence*:

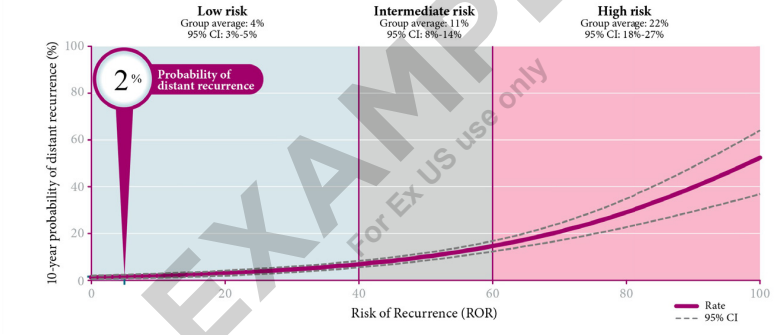


* The ROR ranges from 0 through 100 and correlates with the probability of distant recurrence (DR) in the tested patient population. The risk classification is provided to guide the interpretation of the ROR using cutoffs related to clinical outcome.

Probability of Distant Recurrence:

In the clinical validation studies, patients who were node-negative, luminal A subtype, with an ROR score of 5 were in the low-risk group. This group averaged a 4% probability of distant recurrence at 10 years.

The Prosigna® algorithm has been validated by 2 randomized clinical trials including more than 2400 patients with varying rates of distant recurrence. An analysis of these 2 clinical validation studies shows that the probability of distant recurrence for the low-risk population is 4%, while the high-risk population has a significantly greater probability of distant recurrence.†



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

†Data apply to patients being treated with hormone therapy for 5 years as in the tested patient population. See Package Insert for further information on therapy regimens and tested patient population. It is unknown whether these findings can be extended to other patient populations or treatment schedules.

Key Clinical Trial Findings

- In node-negative patients, the 10-year distant recurrence-free survival (DRFS) rates were[3]:
  - 96.2% for low risk [95% CI: 94.7% - 97.3%]
  - 89.2% for intermediate risk [95% CI: 86.1% - 91.7%]
  - 77.7% for high risk [95% CI: 72.8% - 81.9%]
- In node-positive patients, the 10-year DRFS rates were[3]:
  - 91.7% for low risk [95% CI: 70.6% - 97.8%]
  - 90.4% for intermediate risk [95% CI: 85.2% - 93.9%]
  - 71.8% for high risk [95% CI: 66.3% - 76.6%]
- Significant insight into late recurrence between years 5 and 10 after diagnosis[3]:
  - Distant recurrence rate for low risk group five years after DR-free completion of treatment from 5-10 years in node-negative patients was 1.7% [95% CI: 0.8% - 2.6%]
  - Distant recurrence rate for low/intermediate risk group five years after DR-free completion of treatment from 5-10 years in node-positive patients was 5.3% [95% CI: 2.0% - 8.4%]
- 2016 San Antonio Breast Cancer Symposium released data on a comprehensive comparison of prognostic signatures for breast cancer in TransATAC[4].
  - Phase III prospectively-designed retrospective analysis with outcomes directly comparing multiple assays (Oncotype Dx, Prosigna, EndoPredict, Breast Cancer Index).
  - Prosigna Score (ROR) demonstrated improved prognostic performance compared to all other multi-gene tests in the hormone receptor positive, HER2 and node-negative population in predicting the risk of recurrence at both 0-10 years and 5-10 years.
    - In the node-negative population, Prosigna had the lowest rate of distant recurrence for low risk patients in years 0-10 (3%) and years 5-10 (1.4%).
  - The TransATAC comprehensive comparison provides evidence that Prosigna accurately predicts the risk of recurrence up to 10 years after diagnosis, as well as the risk of late recurrence (between 5 and 10 years after diagnosis).

1. *Gnant M et. al St. Gallen/Vienna 2017: A Brief Summary of the Consensus Discussion. Breast Care 2017; 12:102-107*
2. *Gnant M et. al St. Gallen/Vienna 2015: A Brief Summary of the Consensus Discussion. Breast Care 2015; 10:124-130*
3. *Prosigna [Package Insert], Seattle, WA: NanoString Technologies, Inc; 2017.*
4. *Comprehensive Comparison of Prognostic Signatures for Breast Cancer Recurrence in TransATAC presentation; SABCS Dec, 2016. The TransATAC data were generated after 510(k) clearance of Prosigna.*

Patient	Specimen	
Tumor Size: > 2cm	**ID #:** n0-g2-14-LR-LA	**Run Set ID:** Prosigna Sample 2
Lymph Nodes: node-negative	**Date Reported:** September 20, 2017	**Comments:** Comment for n0-g2-14-LR-LA

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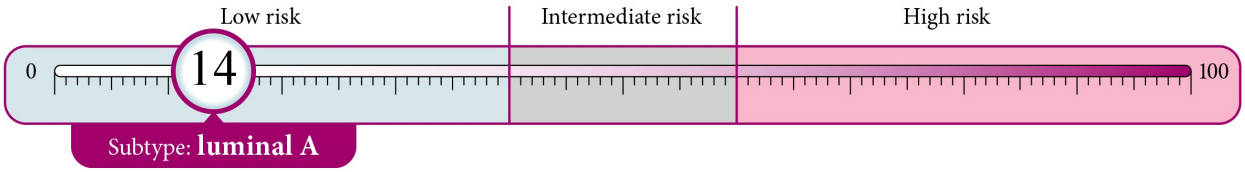
ID #: n0-g2-14-LR-LA **Tumor Size:** > 2cm **Lymph Nodes:** node-negative

Assay Description: The Prosigna® breast cancer gene signature assay measures the expression of 50 different genes to identify subtype and report a Risk of Recurrence Score (ROR), which is used to assign the patient to a predefined risk group. These results are derived from a proprietary algorithm based on the PAM50 gene signature, intrinsic subtype, and clinical variables including tumor size and nodal status.

Risk of Recurrence*:

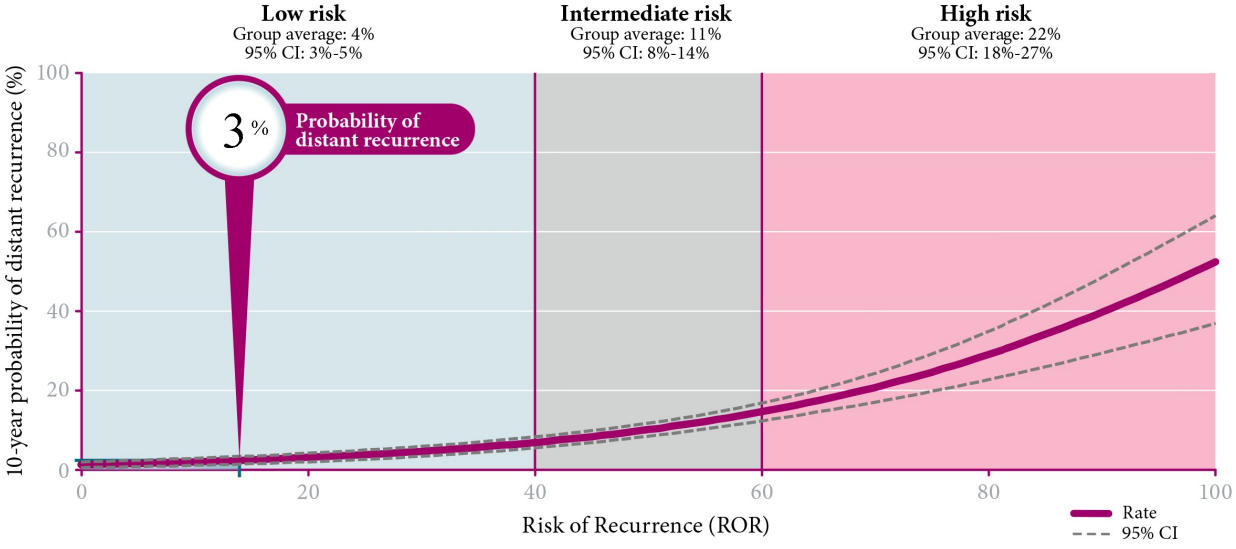


* The ROR ranges from 0 through 100 and correlates with the probability of distant recurrence (DR) in the tested patient population. The risk classification is provided to guide the interpretation of the ROR using cutoffs related to clinical outcome.

Probability of Distant Recurrence:

In the clinical validation studies, patients who were node-negative, luminal A subtype, with an ROR score of 14 were in the low-risk group. This group averaged a 4% probability of distant recurrence at 10 years.

The Prosigna® algorithm has been validated by 2 randomized clinical trials including more than 2400 patients with varying rates of distant recurrence. An analysis of these 2 clinical validation studies shows that the probability of distant recurrence for the low-risk population is 4%, while the high-risk population has a significantly greater probability of distant recurrence.†



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†Data apply to patients being treated with hormone therapy for 5 years as in the tested patient population. See Package Insert for further information on therapy regimens and tested patient population. It is unknown whether these findings can be extended to other patient populations or treatment schedules.

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ID #: n0-g2-14-LR-LA **Tumor Size:** > 2cm **Lymph Nodes:** node-negative

Clinical Validation Studies: Prognosis for node-negative, luminal A, low-risk breast cancer patients was determined based on the rate of distant recurrence (DR) of this population in 2 prospective-retrospective clinical studies. These studies analyzed more than 2400 samples from postmenopausal women with early stage, hormone receptor-positive breast cancer, using a prospectively defined analysis plan. The data shown are for postmenopausal women with early stage, hormone receptor-positive breast cancer who received 5 years of endocrine therapy after surgical resection of the primary tumor.

Rate of Distant Recurrence (DR) for Node-Negative Patients

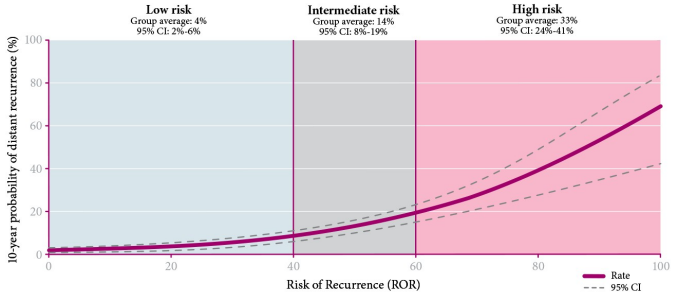
Subtype	Luminal A [95% CI]	Luminal B [95% CI]	HER2-enriched	Basal-like
Rate of DR	**5%** [4%-7%]	**18%** [15%-22%]	*	*

*There were insufficient numbers of basal-like and HER2-enriched patients in these studies to produce data.

Subtype and Prognosis:

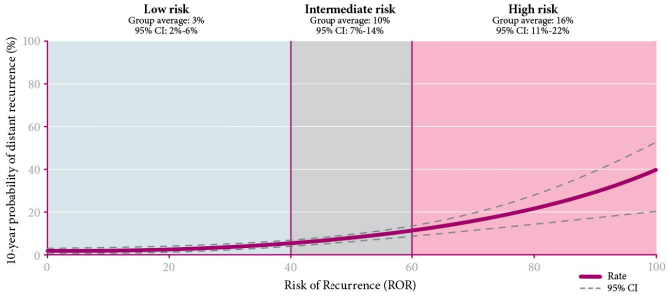
Intrinsic subtype is related to prognosis in the tested patient population. The most common subtypes of breast cancer are the luminal subtypes: luminal A and luminal B. In the combined analysis of 2 clinical validation studies of hormone receptor-positive patients, 68% of the tested patient population was found to be luminal A, and 27% was luminal B.[1] The gene expression pattern of these subtypes resembles the luminal epithelial component of the breast.[3] These tumors are characterized by high expression of estrogen receptor (ER), progesterone receptor (PR), and genes associated with ER activation.[3] Luminal A breast cancers exhibit low expression of genes associated with cell cycle activation and generally have a better prognosis than luminal B.

TransATAC clinical validation study[1]:



The TransATAC study analyzed 1007 samples using a prospectively defined analysis plan. Data shown are for postmenopausal stage I or II, node-negative, hormone receptor-positive breast cancer patients that received 5 years of endocrine therapy.*

ABCSG-8 clinical validation study[2]:



The ABCSG-8 study analyzed 1478 samples using a prospectively defined analysis plan. Data shown are for postmenopausal stage I or II, node-negative, hormone receptor-positive breast cancer patients that received 5 years of endocrine therapy.*

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*See Package Insert for further information on therapy regimens and tested patient population. It is unknown whether these findings can be extended to other patient populations or treatment schedules.

REFERENCES: **1.** Dowsett M, Lopez-Knowles E, Sidhu K, et al. Comparison of PAM50 risk of recurrence (ROR) score with Oncotype DX and IHC4 for predicting residual risk of RFS and distant-(D)RFS after endocrine therapy: A TransATAC Study. Program and abstracts of the 34th Annual San Antonio Breast Cancer Symposium; December 6-10, 2011; San Antonio, Texas. Abstract S4-5.

2. Gnant M, et al., 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.

3. Parker JS, Mullins M, Cheang MC, et al. Supervised risk predictor of breast cancer based on intrinsic subtypes. *J Clin Oncol*. 2009;27(8):1160-1167

Patient	Specimen	
Tumor Size: <= 2cm	**ID #:** n0-l2-70-HR-LB	**Run Set ID:** Prosigna Sample 2
Lymph Nodes: node-negative	**Date Reported:** September 20, 2017	**Comments:** Comment for n0-l2-70-HR-LB

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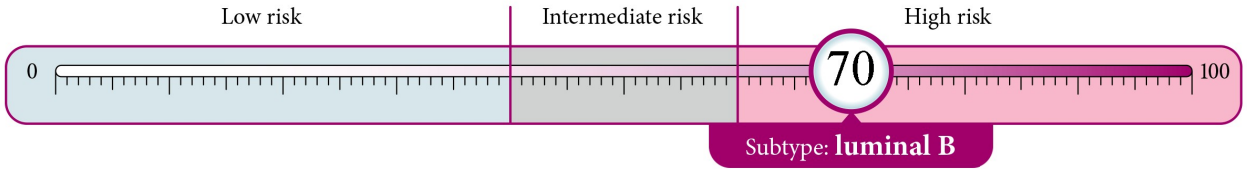
ID #: n0-l2-70-HR-LB **Tumor Size:** <= 2cm **Lymph Nodes:** node-negative

Assay Description: The Prosigna® breast cancer gene signature assay measures the expression of 50 different genes to identify subtype and report a Risk of Recurrence Score (ROR), which is used to assign the patient to a predefined risk group. These results are derived from a proprietary algorithm based on the PAM50 gene signature, intrinsic subtype, and clinical variables including tumor size and nodal status.

Risk of Recurrence*:



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Probability of Distant Recurrence:

In the clinical validation studies, patients who were node-negative, luminal B subtype, with an ROR score of 70 were in the high-risk group. This group averaged a 22% probability of distant recurrence at 10 years.

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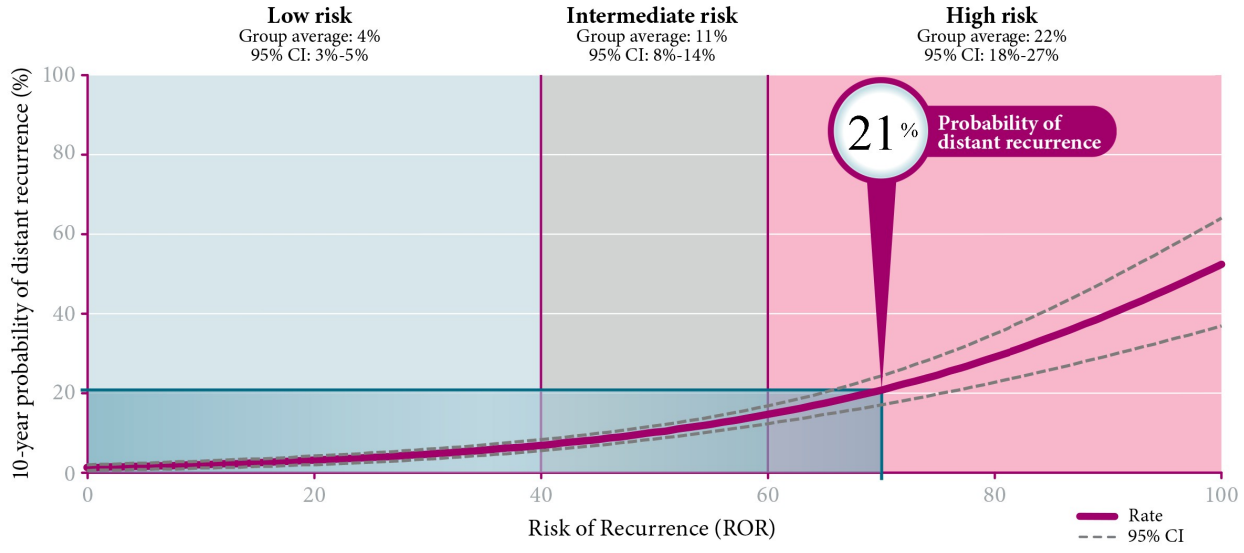

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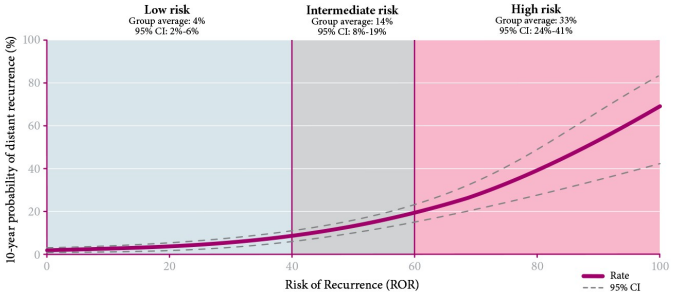

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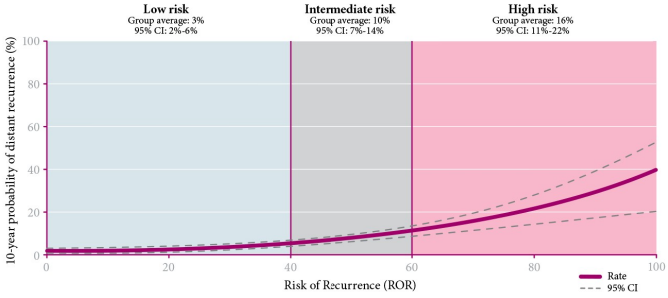

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3. Parker JS, Mullins M, Cheang MC, et al. Supervised risk predictor of breast cancer based on intrinsic subtypes. *J Clin Oncol*. 2009;27(8):1160-1167

Ordering Information

PRODUCT DESCRIPTION	CATALOG NUMBER	UNIT
Prosigna® Gene Signature Assay Complete kit for running Prosigna tests. Includes all CodeSet and Master Kit components; does not include RNA Isolation Kit.	PROSIGNA-001 PROSIGNA-002 PROSIGNA-003 PROSIGNA-004 PROSIGNA-010	One kit of 1 patient assay One kit of 2 patient assays One kit of 3 patient assays One kit of 4 patient assays One kit of 10 patient assays
Roche FFPET RNA Isolation Kit Includes 25 isolations per kit.	Roche-FFPET-025	Each

nanoString® TECHNOLOGIES

NanoString Technologies, Inc.
530 Fairview Ave N
Seattle, WA 98109

CONTACT

For more information and details on how to offer Prosigna from your institution, please contact

(주)엘에이에스 | LAS Inc.
10136 김포시 아라육로 16 6F
T. 02-3486-0911~2
info@lascience.co.kr
www.lascience.co.kr

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