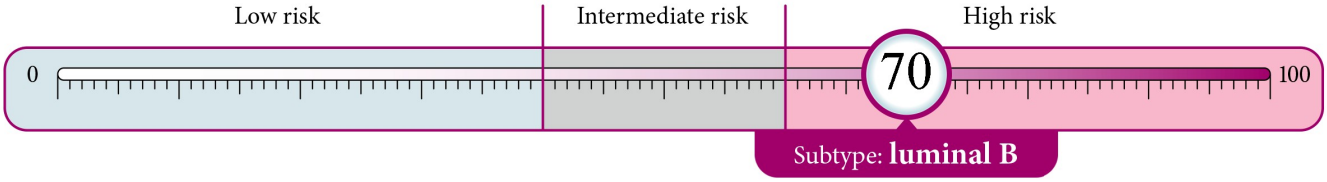
Patient	Specimen	
Tumor Size: <= 2cm	**ID #:** n0-l2-70-HR-LB	**Run Set ID:** Prosigna Sample 2
Lymph Nodes: node-negative	**Date Reported:** September 20, 2017	**Comments:** Comment for n0-l2-70-HR-LB

prosigna®
Breast cancer
prognostic gene signature assay

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*:

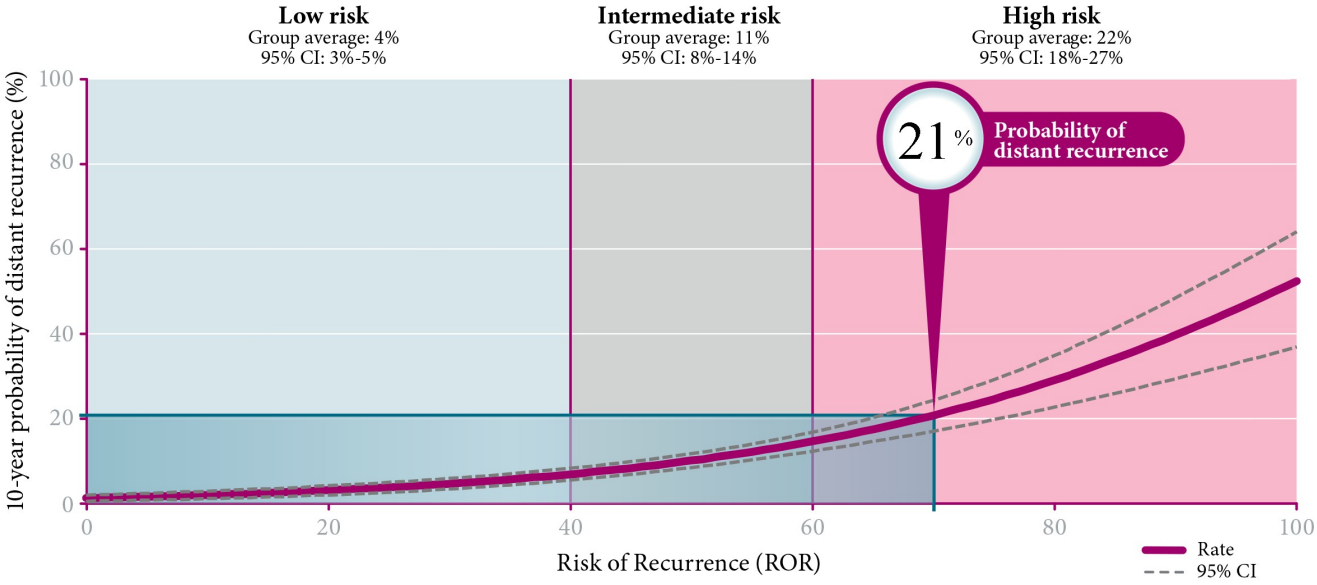


* The ROR ranges from 0 through 100 and correlates with the probability of distant recurrence (DR) in the tested patient population. The risk classification is provided to guide the interpretation of the ROR using cutoffs related to clinical outcome.

Probability of Distant Recurrence:

In the clinical validation studies, patients who were node-negative, luminal 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.

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 high-risk population is 22%.†



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.

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

prosigna®
Breast cancer
prognostic gene signature assay

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

Clinical Validation Studies: Prognosis for node-negative, luminal B, high-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

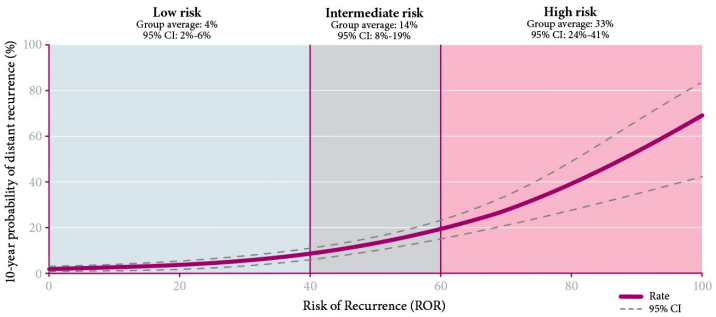
Subtype	Luminal A [95% CI]	Luminal B [95% CI]	HER2-enriched	Basal-like
Rate of DR	**5%** [4%-7%]	**18%** [15%-22%]	*	*

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

Subtype and Prognosis:

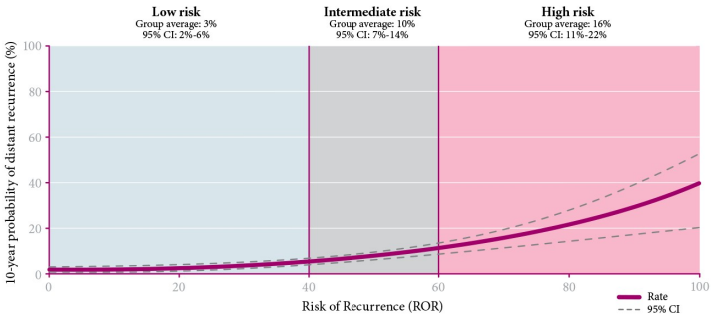
Intrinsic subtype is related to prognosis in the tested patient population. The most common subtypes of breast cancer are the luminal subtypes: luminal A and luminal B. In the combined analysis of 2 clinical validation studies of hormone receptor-positive patients, 68% of the tested patient population 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.*

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

*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