



MMM116410

# Breast Cancer Gene Expression Profile



**CONFIDENTIAL**

**ORDERING PHYSICIAN**

**Bob Doctor MD**

123 Grand Ave  
Anywhere, NV 89109

Pathologist: Jonathan Pathologist MD

**SPECIMEN**

Specimen Type: **Resection**  
Tissue: **Breast**  
Surgery Date: **Oct 13, 2017**  
TRF Received: **Jan 2, 2018**  
Sample Received: **Jan 2, 2018**  
Report Date: **Jan 5, 2018**

**PATIENT**

Last Name: **Pt Last Name**  
First Name: **Pt First Name**  
Date of Birth: **Jan 7, 1968**  
Patient ID: **Patient id**  
Gender: **Female**  
Accession #: **07001035-BLD**  
Requisition #: **07001035**

**Block(s) Analyzed:**

12-GENE MOLECULAR SCORE:	<b>3.7</b>	
TUMOR STAGE:	<b>pT1b</b> (>0.5 cm but ≤1 cm)	
NODAL STATUS:	<b>pN0</b> (zero positive nodes)	

EndoPredict® is a gene expression assay for patients with ER+, HER2-early-stage breast cancer. From this genomic analysis, a 12-Gene Molecular Score is assigned. This score, combined with tumor size and nodal status, contributes to the EPclin Risk Score, from which the risks of distant recurrence (10-year and 5 to 15-years) with 5 years of adjuvant endocrine therapy alone and the estimated absolute benefit of chemotherapy (at 10 years) are determined.

<b>INITIAL</b> Treatment Planning	<b>0-10 YEAR LIKELIHOOD OF DISTANT RECURRENCE</b> <i>(For patients treated with 5 years of endocrine therapy alone)</i>	<b>2.9%</b>
	<b>ESTIMATED ABSOLUTE CHEMOTHERAPY BENEFIT AT 10 YEARS</b>	<b>0.3%</b>

<b>LONG-TERM</b> Treatment Planning	<b>LIKELIHOOD OF LATE DISTANT RECURRENCE YEARS 5-15</b> <i>(For patients with no recurrence after 5 years of endocrine therapy and no chemotherapy administered)</i>	<b>2.3%</b>
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**Note:** Recurrence risk and chemotherapy benefit estimates contained within this report are based on analysis of multiple cohorts of post-menopausal women with resected ER+/HER2- invasive female breast cancer who have not been treated prior to resection with neo-adjuvant therapy (e.g. chemotherapy, radiation therapy or endocrine therapy) and who do not have a current or prior diagnosis of an additional cancer.<sup>1-3</sup> Risks may differ for individuals who do not meet the aforementioned clinical characteristics. Reported recurrence risks assume that this patient will receive endocrine therapy (with or without localized radiation therapy) alone. If adjuvant chemotherapy is administered after resection, the reported 10-year likelihood of distant recurrence and the likelihood of late recurrence (years 5-15) will not reflect actual patient risks. This test result is invalid if the patient has already experienced a distant recurrence.



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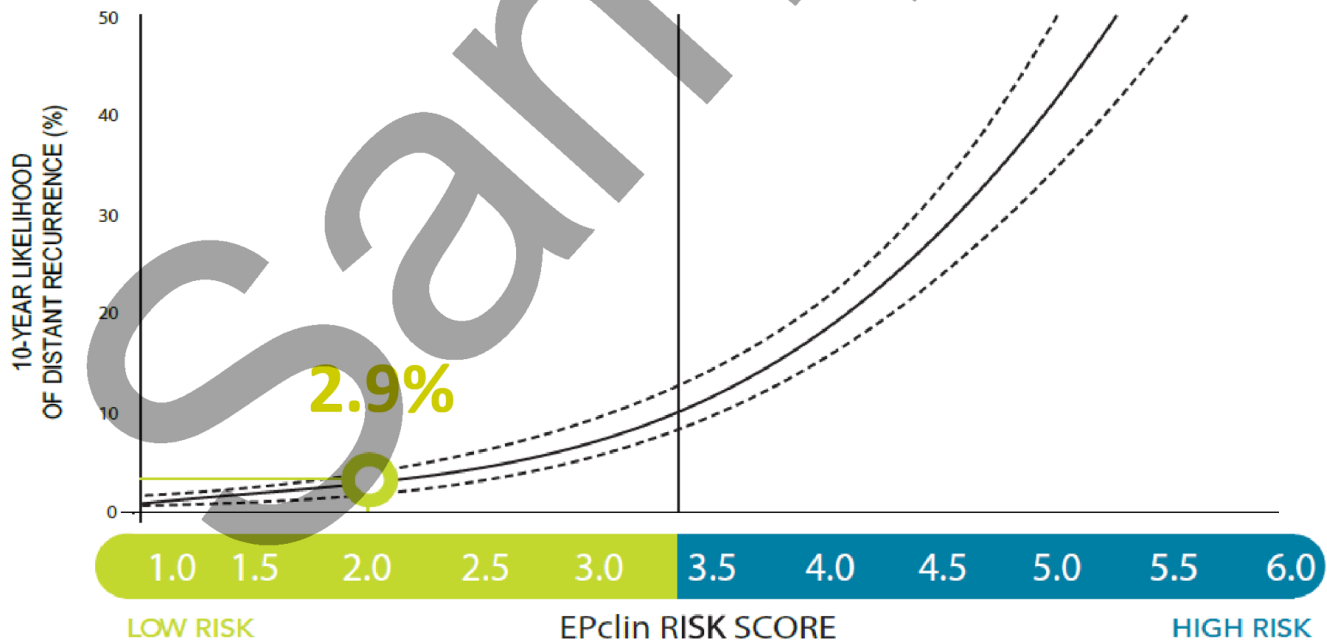
## Initial Treatment Planning 10 Year Prognostic



**CONFIDENTIAL**

12-GENE MOLECULAR SCORE: **3.7**TUMOR STAGE: **pT1b** (>0.5 cm but ≤1 cm)NODAL STATUS: **pN0** (zero positive nodes)EPclin  
RISK SCORE **2.0**

TREATMENT:

**AFTER 5 YEARS ENDOCRINE  
THERAPY ALONE****Result Interpretation:** An EPclin Score of 2.0 is categorized as LOW RISK and is associated with a 2.9% (95% CI: 2.0% - 4.1%) 10-year likelihood of experiencing a distant recurrence when treated with 5 years of endocrine therapy alone.**LIKELIHOOD OF DISTANT RECURRENCE  
(YEARS 0-10)**

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MMM130815

Initial Treatment Planning  
**Adjuvant Chemotherapy Benefit**

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Name: Last Name, First Name

DOB: Jan 7, 1968

Accession #: 07001035-BLD

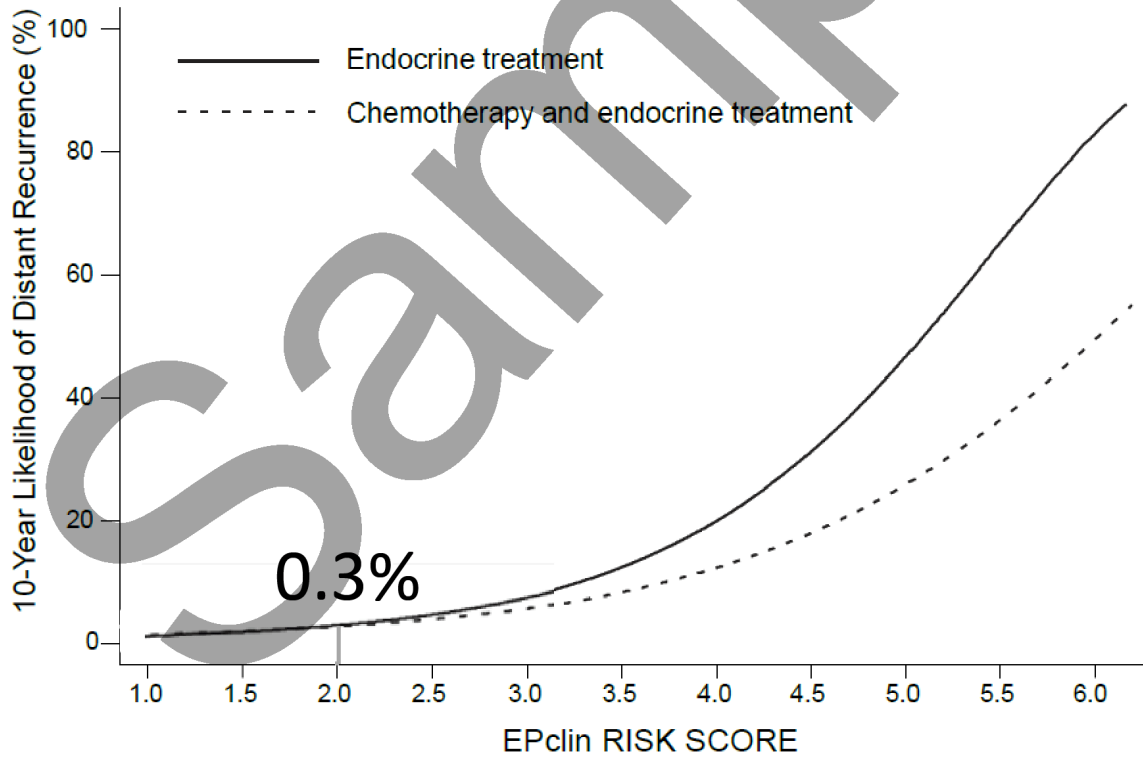
Report Date: Jan 5, 2018

12-GENE MOLECULAR SCORE: **3.7**TUMOR STAGE: **pT1b** (>0.5 cm but ≤1 cm)NODAL STATUS: **pN0** (zero positive nodes)EPclin  
RISK SCORE **2.0**

TREATMENT:

**CHEMOTHERAPY AND/OR  
5 YEARS ENDOCRINE THERAPY****Result Interpretation:** At 10 years, an EPclin Risk Score of 2.0 is associated with an estimated 0.3% (95% CI: -1.1% - 1.4%) absolute benefit from chemotherapy, when used in combination with endocrine treatment, compared to endocrine treatment alone.

## PREDICTION OF CHEMOTHERAPY BENEFIT AT 10 YEARS



**ESTIMATED ABSOLUTE CHEMOTHERAPY BENEFIT AT 10 YEARS**  
**0.3%**



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### Long-term Treatment Planning 5-15 Year Prognostic



**CONFIDENTIAL**

Name: Last Name, First Name      DOB: Jan 7, 1968      Accession #: 07001035-BLD      Report Date: Jan 5, 2018

12-GENE MOLECULAR SCORE:	<b>3.7</b>	<b>EPclin RISK SCORE</b> <span style="font-size: 2em;"><b>2.0</b></span>
TUMOR STAGE:	<b>pT1b</b> (>0.5 cm but ≤1 cm)	
NODAL STATUS:	<b>pN0</b> (zero positive nodes)	

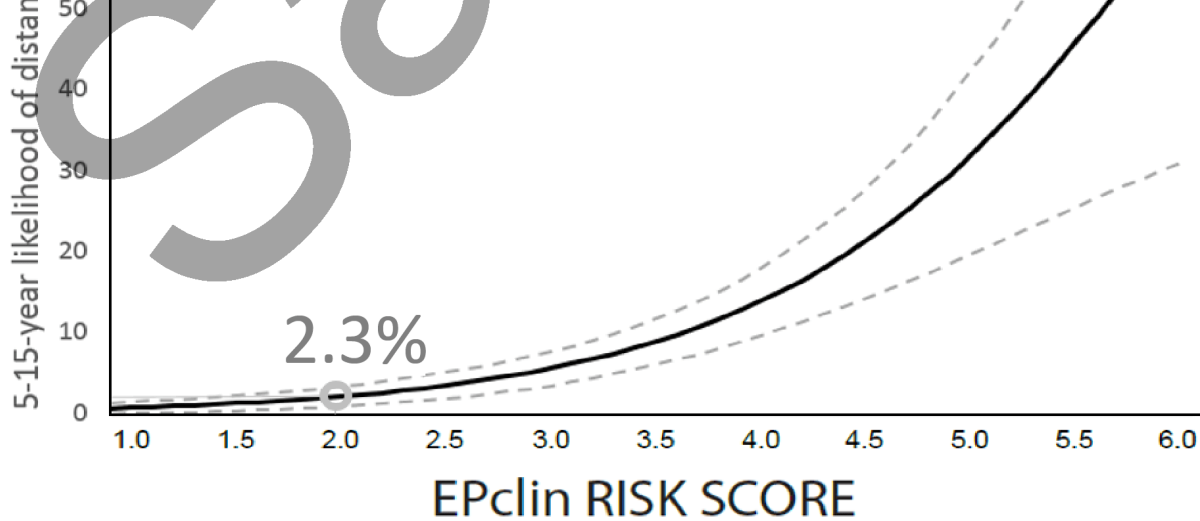
**TREATMENT:**  
**AFTER 5 YEARS ENDOCRINE THERAPY ALONE**

**Result Interpretation:** An EPclin Risk Score of 2.0 is associated with a 2.3% (95% CI: 1.0% - 3.6%) likelihood of experiencing a distant recurrence within 5-15 years of diagnosis. Estimates of distant recurrence at 15 years apply to patients who are distant recurrence-free after 5 years of endocrine therapy alone.

### LIKELIHOOD OF LATE DISTANT RECURRENCE (Years 5-15)

After 5 years of endocrine therapy alone and no chemotherapy administered





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## Breast Cancer Gene Expression Profile



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Pathologist: Jonathan Pathologist MD

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 Patient ID: **Patient id**  
 Gender: **Female**  
 Accession #: **07001035-BLD**  
 Requisition #: **07001035**

**Block(s) Analyzed:**

**Test Description:** EndoPredict is a gene expression test that predicts the risks of distant recurrence (10-year and 5 to 15-years), with 5 years of adjuvant endocrine therapy alone, and the estimated absolute benefit of chemotherapy (at 10 years) for patients with estrogen receptor-positive and HER2-negative invasive female breast cancer.<sup>1-3</sup> The test result categorizes patients into "Low" or "High" risk of distant metastasis within 10 years. Analysis is performed on RNA extracted from FFPE blocks of the primary tumor. This test utilizes quantitative RT-PCR to measure the expression of eight target genes, three normalization genes, and one control gene, from which a 12-Gene Molecular Score is calculated.<sup>1</sup> The risk association based solely on this molecular fingerprint is assessed on a scale of 0-15, with lower risk molecular scores being <5 and higher risk scores being ≥5. The 12-Gene Molecular Score can be combined with clinicopathologic features (tumor size and lymph node status) to generate an EPclin Risk Score, which is a more significant predictor metastatic disease.<sup>1,3</sup> The threshold differentiating "Low" and "High" risk EPclin Risk Scores was established during assay development and is pre-specified during testing of current samples. EPclin Risk Scores from 1.0 through 3.3 are reported as "Low Risk" and are associated with an estimated 10-year risk of recurrence of less than 10%. EPclin Risk Scores from 3.4 through 6.0 are reported as "High Risk" and are associated with an estimated 10-year risk of recurrence equal to or greater than 10%. For patients who are distant recurrence-free at 5 years and have been treated for 5 years with endocrine therapy alone, the distant recurrence risk at 15 years without extended endocrine therapy is also provided.

Therapeutic decisions made subsequent to testing should take into account all relevant clinical parameters, including patient's age, overall health, etc.

Please contact Myriad Professional Support at 1-844-887-3636 or email [EndoPredict@myriad.com](mailto:EndoPredict@myriad.com) to discuss any questions regarding this result.

**References**

1. Filipits M, Rudas M, Jakesz R, et al. A new molecular predictor of distant recurrence in ER-positive, HER2-negative breast cancer adds independent information to conventional clinical risk factors. *Clin Cancer Res.* 2011;17(18):6012-6020.
2. Muller BM, Brase JC, Haufe F, et al. Comparison of the RNA-based EndoPredict multigene test between core biopsies and corresponding surgical breast cancer sections. *J Clin Pathol.* 2012;65(7):660-662.
3. Data on file.

**Note:** Myriad deems information provided on the Test Request Form to be definitive, and to supersede information provided in any other form (e.g., pathology report). Clinicopathologic parameters provided by the healthcare provider(s), in whatever form, have not been verified by Myriad.

**Authorized Signature:**

Benjamin B. Roa, Ph.D.  
 Diplomate ABMG  
 Senior Laboratory Director

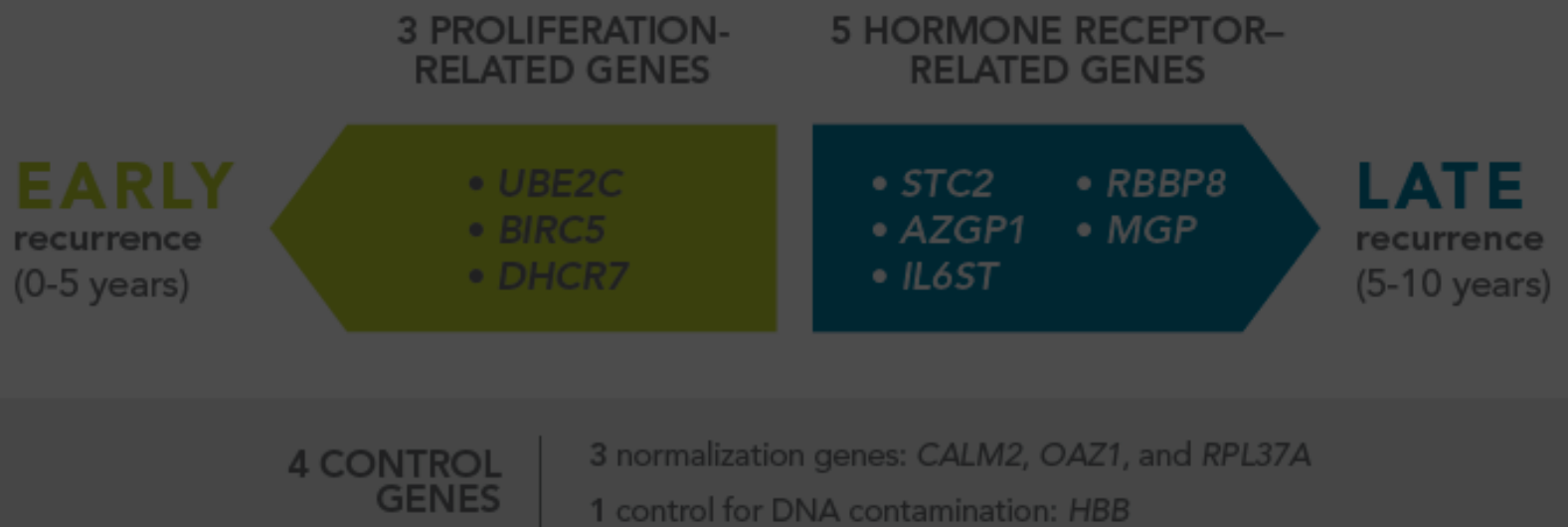
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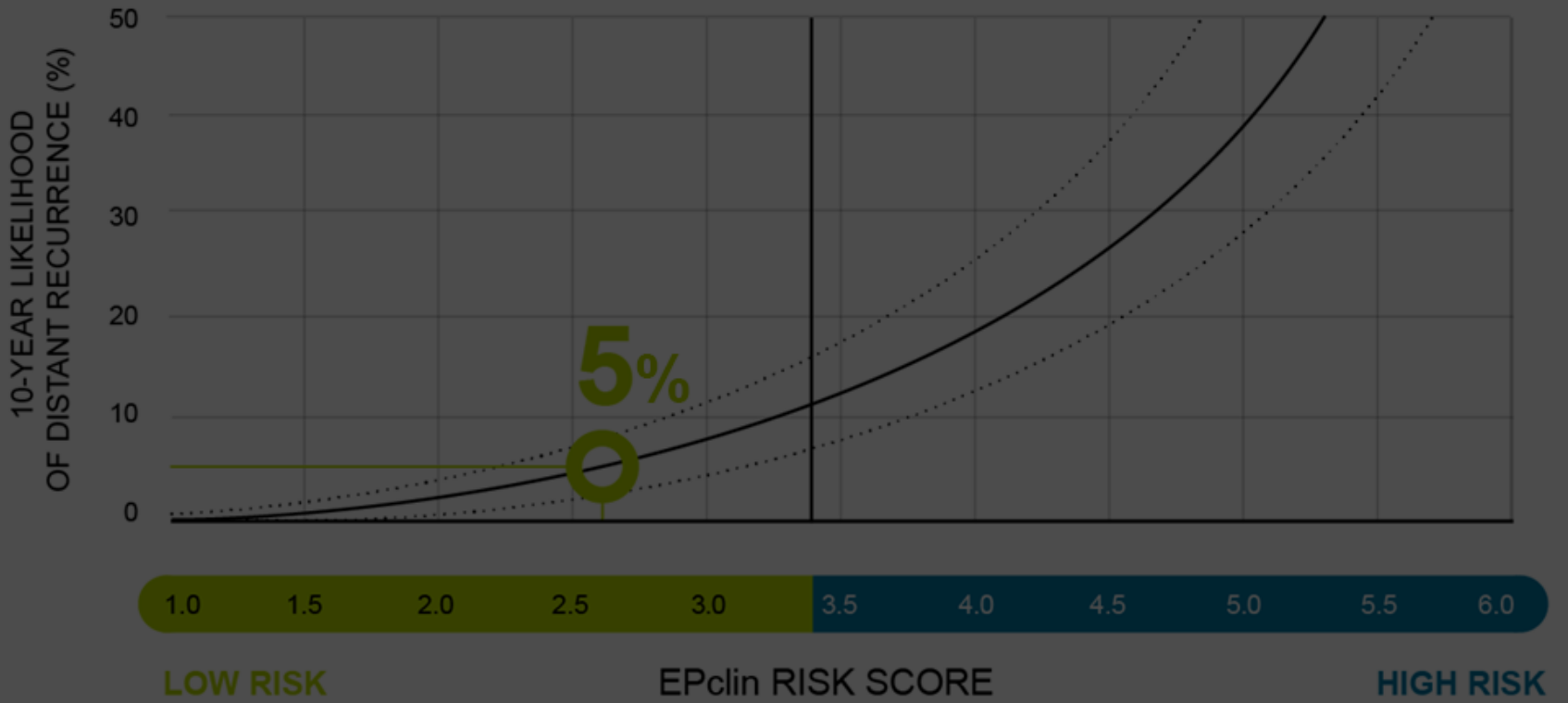
## 12-gene molecular score for early and late recurrence



Second-generation prognostic tests include genes that predict both early and late recurrence.

EPclin integrates 12-gene molecular score with clinicopathological features

12-GENE MOLECULAR SCORE:	<b>4.6</b>	<b>EPclin</b> RISK SCORE <b>2.6</b> LOW RISK	10-YEAR LIKELIHOOD OF DISTANT RECURRENCE <b>5%</b> LOW RISK
TUMOR STAGE:	<b>T1c</b> (>1 cm but ≤2 cm)		
NODAL STATUS:	<b>N0</b> (zero positive nodes)		





**References:** 1. Filipits M, Rudas M, Jakesz R, et al. A new molecular predictor of distant recurrence in ER-positive, HER2-negative breast cancer adds independent prognostic information to conventional clinical risk factors. *Clin Cancer Res.* 2011;17(18):6012-6020. 2. Sestak I, Buus R, Cuzick J, et al. Comparison of the performance of 6 prognostic signatures for estrogen receptor-positive breast cancer: A secondary analysis of a randomized clinical trial. *JAMA Oncol.* 2018;4(4):545-553. 3. Pan H, Gray R, Braybrooke J, et al. 20-year risk for breast-cancer recurrence after stopping endocrine therapy at 5 years. *N Eng J Med.* 2017; 377:1836-1846. 4. Hortobagyi G, Connolly J, D'Orsi C, et al. *AJCC Cancer Staging Manual*, 8th Ed. New York: Springer; 2017.

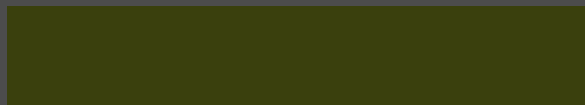
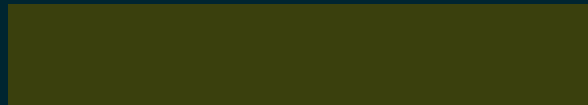


	<b>EndoPredict</b>	Oncotype DX	MammaPrint	Breast Cancer Index	Prosigna
Reported Outcome Data	<b>15 Years</b>	9 Years	5 Years	10 Years	10 Years
Extended Endocrine Therapy Report	<b>5-15 year late recurrence</b>	--	--	5-10 year late recurrence & extended endocrine benefit	--
Chemotherapy Benefit Result	✓	✓	✓	--	--
Chemotherapy Benefit Regimen	<b>FEC±P FAC±wP<sup>1</sup></b>	CMF or MF <sup>2</sup> CAF <sup>3</sup>	--	--	--
Patients in Chemotherapy Benefit Validation	<b>3746 (NO, N+)<sup>1</sup></b>	1018 (NO, N+) <sup>2,3</sup>	--	--	--
Consistency in Report Cutoffs	<b>Same report cutoff across validations and patient types</b>	Multiple cutoffs for different validations and patient types	Same report cutoffs across patient types	Different cutoffs for 5-10 and 0-10 year reports	Different cutoffs for NO and N1 reports
Training Data	<b>ER+ HER2- NO/+<sup>4</sup></b>	ER+ HER2+/- NO <sup>5</sup>	ER+/- HER2+/- NO <sup>6</sup>	ER+/- HER2 status: unknown NO/N+ <sup>7</sup>	ER+/- HER2+/- NO/N+ <sup>8</sup>
Guideline Inclusion	<b>NCCN<sup>9</sup>, ASCO<sup>10</sup>, St. Gallen<sup>11</sup>, ESMO<sup>12</sup>, NICE<sup>13</sup></b>	NCCN <sup>9</sup> , ASCO <sup>10</sup> , St. Gallen <sup>11</sup> , ESMO <sup>12</sup> , NICE <sup>13</sup>	NCCN <sup>9</sup> , ASCO <sup>14</sup> , St. Gallen <sup>11</sup> , ESMO <sup>12</sup>	NCCN <sup>9</sup> , ASCO <sup>10</sup> , St. Gallen <sup>11</sup>	NCCN <sup>9</sup> , ASCO <sup>10</sup> , St. Gallen <sup>11</sup> , ESMO <sup>12</sup> , NICE <sup>13</sup>





# EndoPredict®



**References:** 1. Sestak I, Martín M, Dubsky P, et al. Prediction of chemotherapy benefit by EndoPredict in patients with breast cancer who received adjuvant endocrine therapy plus chemotherapy or endocrine therapy alone. *Breast Cancer Res Treat*. [published online ahead of print April 30, 2019]. <https://doi.org/10.1007/s10549-019-05226-8>. 2. Paik S, Tang G, Shak S, et al; Gene Expression and Benefit of Chemotherapy in Women with Node-Negative, Estrogen Receptor-Positive Breast Cancer. *J Clin Oncol* 2006; 24:3726-3734. 3. Albain K, Barlow W, Shak S, et al; Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive oestrogen-receptor-positive breast cancer on chemotherapy: a retrospective analysis of a randomized trial. *Lancet Oncol* 2010;11:55-65. 4. Filipits M, Rudas M, Jakesz R, et al; for EP Investigators. A new molecular predictor of distant recurrence in ER-positive, HER2-negative breast cancer adds independent information to conventional clinical risk factors. *Clin Cancer Res* . 2011;17(18):6012-6020. 5. Paik S, Shak S, Tang G, et al; A Multigene Assay to Predict Recurrence of Tamoxifen-Treated, Node-Negative Breast Cancer. *N Engl J Med* 2004; 351:2817-26. 6. van't Veer L, Dai H, van de Vijver M, et al; Gene expression profiling predicts clinical outcome of breast cancer. *Nature* 2002;415:530-6. 7. Jerevall P, Ma X, Li H, et al; Prognostic utility of HOXB13:IL17BR and molecular grade index in early-stage breast cancer patients from the Stockholm trial. *Br J Cancer* 2011;104:1762-1769. 8. Wallden B, Storhoff J, Nielsen T, et al; Development and verification of the PAM50-based Prosigna breast cancer gene signature assay. *BMC Medical Genomics* 2015; 8:54. 9. National Comprehensive Cancer Network. Breast Cancer (Version 2.2018) [https://www.nccn.org/professionals/physician\\_gls/pdf/breast.pdf](https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf). Accessed October 18, 2018. 10. Harris LN, Ismaila N, McShane LM, et al. Use of biomarkers to guide decisions on adjuvant systemic therapy for women with early-stage invasive breast cancer: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol* 2016;34(10):1134-1150. 11. Curigliano G, Burstein H, Winer E, et al; De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer. *Ann Oncol* 2017;28:1700-1712. 12. Senkus E, Kyriakides S, Ohno S, et al; ESMO Guidelines Committee. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2015;26(Suppl 5):v8-v30. 13. National Institute for Health and Care Excellence. Tumor profiling tests to guide adjuvant chemotherapy decisions in early breast cancer. <http://nice.org.uk/guidance/dg34>. Accessed February 26, 2019. 14. Krop I, Ismaila N, Andre A, et al; Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Focused Update. *J Clin Oncol* 35:2838-2847. 15. Simon R, Paik S, Hayes D; Use of Archived Specimens in Evaluations of Prognostic and Predictive Biomarkers. *J Natl Cancer Inst* 2009;101:1446-1452.

