

ONCOLOGY



EndoPredict®

Understanding the EndoPredict® Test Report

**ENDOPREDICT® IS A GENOMIC TEST FOR WOMEN
WITH ER+/HER2-, EARLY-STAGE BREAST CANCER**

This guide is not medical advice and is intended to help you understand your patient's EndoPredict results.

What Does EndoPredict® Do?


EndoPredict provides three separate results you and your patient can use when determining the treatments that are right for her. **These three results answer the following questions:**

- What is the chance that her cancer will return within 10 years?
- How will her cancer potentially respond to chemotherapy?
- Can she safely stop hormone treatment (aka endocrine therapy) at five years?


EndoPredict measures the activity of 12 genes in your patient's tumor that are associated with the risk of her cancer returning and the likelihood it will respond to chemotherapy.^{1,2} This molecular result is combined with tumor size and nodal status to create an EPclin Risk Score. Your patient's individualized EPclin Score will estimate if her cancer is at low (<10%) or high (≥10%) risk of coming back in the next 10 years.

The EndoPredict test report includes a summary page and three separate results

EXAMPLE OF A LOW RISK RESULT SUMMARY PAGE


MMM496039

Breast Cancer Gene Expression Profile



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ORDERING PHYSICIAN	SPECIMEN	PATIENT
Bob Doctor MD 123 Grand Ave Anywhere, NV 89109 Pathologist: Joey Pathologist MD	Specimen Type: Resection Tissue: Breast Surgery Date: Mar 13, 2018 TRF Received: Nov 6, 2018 Sample Received: Nov 6, 2018 Report Date: Nov 29, 2018	Last Name: Pt Last Name First Name: Pt First Name Date of Birth: Jan 7, 1968 Patient ID: Patient id Gender: Female Accession #: 07000342-BLD Requisition #: 07000342

Block(s) Analyzed:

12-GENE MOLECULAR SCORE:	2.0
TUMOR STAGE:	pT1c (>1 cm but ≤2 cm)
NODAL STATUS:	pN1 (1-3 positive nodes)

EPclin

2.5

RISK SCORE


LOW RISK

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.

A	INITIAL Treatment Planning 0-10 YEAR LIKELIHOOD OF DISTANT RECURRENCE <small>(For patients treated with 5 years of endocrine therapy alone)</small>	4.6%
B	ESTIMATED ABSOLUTE CHEMOTHERAPY BENEFIT AT 10 YEARS	0.8%

C	LONG-TERM Treatment Planning LIKELIHOOD OF LATE DISTANT RECURRENCE YEARS 5-15 <small>(For patients with no recurrence after 5 years of endocrine therapy and no chemotherapy administered)</small>	3.7%
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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.^{1,3} 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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Your patient's 12-gene molecular score, tumor size/stage, and nodal status are shown here. These 3 components are combined to give the EPclin Risk Score.


WHAT RESULTS DOES ENDO-PREDICT PROVIDE?

- A** Risk of distant recurrence in years 0-10
- B** Absolute benefit from chemotherapy
- C** Risk of late recurrence in years 5-15.

The EPclin Risk Score can range from 1.0 to 6.0. Scores of 3.3 or less mean the cancer is at **LOW RISK (<10%)** of coming back while scores of 3.4 or more mean the cancer is at **HIGH RISK (≥10%)** of coming back.

EndoPredict can be ordered on biopsy to provide you with accurate results even faster. When ordering on biopsy, your patient's report will still provide a molecular score, but it will not have the EPclin Risk Score. This report will provide a table showing her risk score projections based on the molecular score and their nodal status and tumor size that will be obtained from the pathology report after surgery.

EXAMPLE OF A BIOPSY RESULT SUMMARY PAGE



MMM116615

CONFIDENTIAL

Breast Cancer Recurrence Test Result

ORDERING PHYSICIAN Bob Doctor MD 123 Grand Ave Anywhere, NV 89109 Pathologist: Jonathan Pathologist MD	SPECIMEN Specimen Type: Biopsy Tissue: Breast Surgery Date: Mar 13, 2018 TRF Received: Apr 12, 2018 Sample Received: Apr 12, 2018 Report Date: Apr 15, 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 #: 07001224-BLD Requisition #: 07001224
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Block(s) Analyzed:

12-GENE MOLECULAR SCORE: 5.0 HIGH RISK	Estimated risk is based on the 12-Gene Molecular Score alone. Once both tumor stage and nodal status are known, the EPclin RISK SCORE, which is a superior predictor of the 10-YEAR LIKELIHOOD OF DISTANT RECURRENCE, can be calculated using the EPclin Risk Score table below.
TUMOR STAGE: pTx	
NODAL STATUS: Not Provided	

Result Interpretation: Based on the 12-Gene Molecular Score alone, this patient is at HIGH RISK for distant recurrence within 10 years. (The molecular score ranges from 0-15 with high risk patients having scores ≥5.0.)

12-Gene Molecular Score

5.0




0 5 15

12-Gene Molecular Score

		TUMOR STAGE				
		pT1a	pT1b	pT1c	pT2	pT3
NODAL STATUS	pN0	LOW RISK EPclin: 2.4 Rec. Risk: 4.2% <small>(95% CI: 3.1% - 5.7%)</small>	LOW RISK EPclin: 2.4 Rec. Risk: 4.2% <small>(95% CI: 3.1% - 5.7%)</small>	LOW RISK EPclin: 2.7 Rec. Risk: 5.6% <small>(95% CI: 4.3% - 7.3%)</small>	LOW RISK EPclin: 3.1 Rec. Risk: 8.1% <small>(95% CI: 6.5% - 10.2%)</small>	HIGH RISK EPclin: 3.4 Rec. Risk: 10% <small>(95% CI: 8% - 12%)</small>
	pN1 pN1mi	LOW RISK EPclin: 3.0 Rec. Risk: 7.4% <small>(95% CI: 5.9% - 9.3%)</small>	LOW RISK EPclin: 3.0 Rec. Risk: 7.4% <small>(95% CI: 5.9% - 9.3%)</small>	HIGH RISK EPclin: 3.4 Rec. Risk: 10% <small>(95% CI: 8% - 12%)</small>	HIGH RISK EPclin: 3.7 Rec. Risk: 14% <small>(95% CI: 12% - 17%)</small>	HIGH RISK EPclin: 4.1 Rec. Risk: 20% <small>(95% CI: 17% - 24%)</small>

*EPclin Risk Scores and 10-year distant recurrence risks (i.e. "Rec. Risk") are specific to a 12-Gene Molecular Score of 5.0. The 10-year likelihoods of distant recurrence are based on analysis of a cohort of post-menopausal women with resected ER+/HER2-invasive female breast cancer who have not been treated prior to resection with systemic neoadjuvant therapy (e.g. chemotherapy, radiation therapy, or endocrine therapy) and who do not have a current or prior diagnosis of an additional cancer. These risks may differ for individuals who do not meet the aforementioned clinical characteristics. These recurrence risks also assume that patients will receive endocrine therapy (with or without localized radiation therapy) alone. If adjuvant chemotherapy is administered after resection, these recurrence risks will not reflect actual patient risk. This test result is invalid if this patient has already experienced a distant recurrence.



The EPclin Risk Score and risk classification will be undefined on a biopsy report, but the table will allow you to see her risk based on additional factors.

The table shows low and high risk projections based on various nodal status and tumor size outcomes in surgery.

Providers can send the pathology report post-surgery to receive an amended full report to review with their patient.

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EndoPredict combines a 12-gene molecular score with tumor size and nodal status to provide more prognostic power.^{6,7}

Even as the **12-gene Molecular Score** **A** remains consistent, as **Tumor Stage** and **Nodal Status** **B** change, the **EPclin Risk Score** **C** is affected to be High or Low Risk.

A 12-GENE MOLECULAR SCORE: **7.9**

TUMOR STAGE: **pT1b** (>0.5 cm but ≤ 1m)

B NODAL STATUS: **pN0** (zero positive nodes)

C EPclin RISK SCORE: **3.2**
LOW RISK

10-YEAR LIKELIHOOD OF DISTANT RECURRENCE: **8.9%**
LOW RISK

Result Interpretation: An EPclin Score of 3.2 is categorized as LOW RISK and is associated with a 8.9% (95% CI: 7.2% - 11%) 10-year likelihood of experiencing a distant recurrence.

A 12-GENE MOLECULAR SCORE: **7.9**

TUMOR STAGE: **pT2** (>2 cm but ≤5m)

B NODAL STATUS: **pN0** (zero positive nodes)

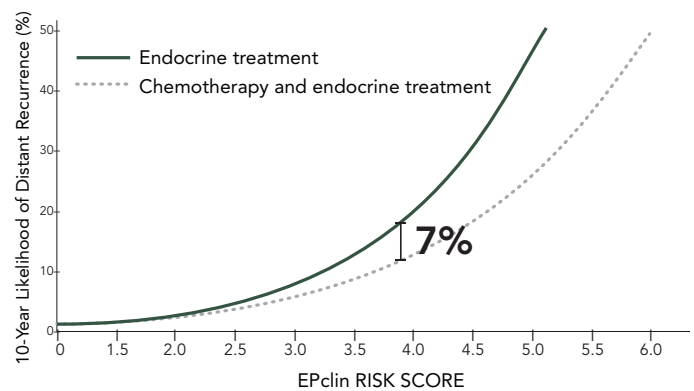
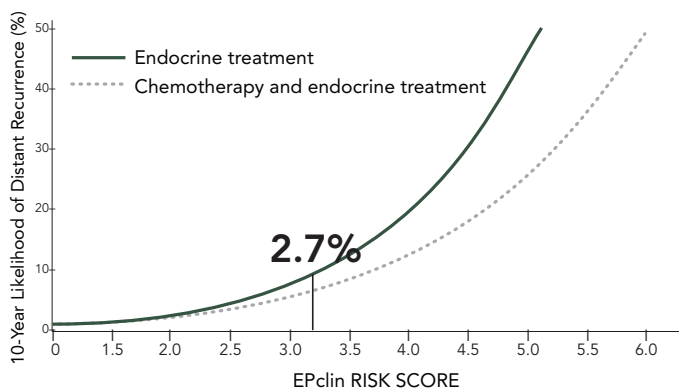
C EPclin RISK SCORE: **3.9**
HIGH RISK

10-YEAR LIKELIHOOD OF DISTANT RECURRENCE: **17%**
HIGH RISK

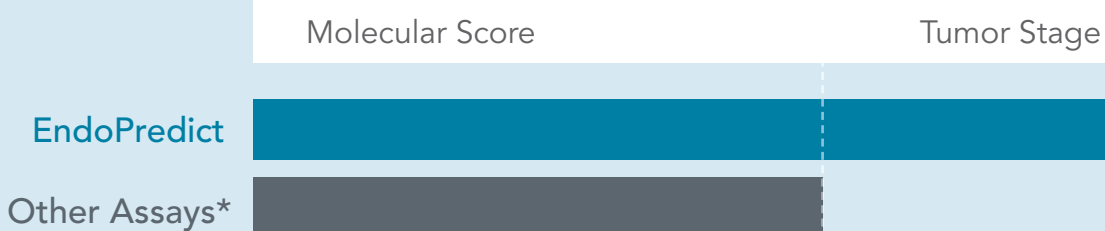
Result Interpretation: An EPclin Score of 3.9 is categorized as HIGH RISK and is associated with a 17% (95% CI: 14% - 20%) 10-year likelihood of experiencing a distant recurrence.

ESTIMATED ABSOLUTE CHEMOTHERAPY BENEFIT AT 10 YEARS: **2.7%**

ESTIMATED ABSOLUTE CHEMOTHERAPY BENEFIT AT 10 YEARS: **7%**



PROGNOSTIC POWER



*OncotypeDX, MammaPrint

Molecular Score

Tumor Size

Nodal Status

+

EPclin Risk Score

A 12-GENE MOLECULAR SCORE: 7.9

TUMOR STAGE: pT2 (>2 cm but ≤5m)

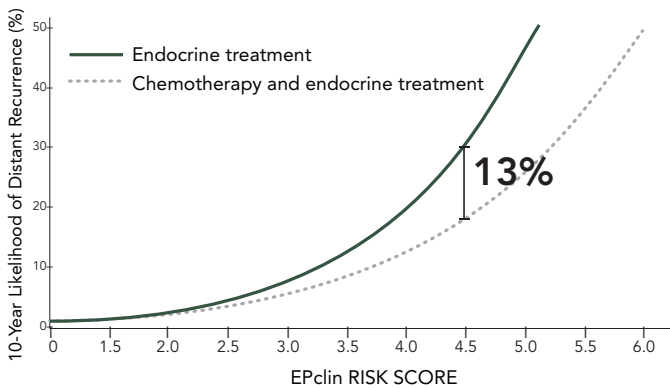
B NODAL STATUS: pN1 (1-3 positive nodes)

C EPclin RISK SCORE
4.5
HIGH RISK

10-YEAR LIKELIHOOD OF DISTANT RECURRENCE
28%
HIGH RISK

Result Interpretation: An EPclin Score of 4.5 is categorized as HIGH RISK and is associated with a 28% (95% CI: 24% - 33%) 10-year likelihood of experiencing a distant recurrence.

ESTIMATED ABSOLUTE CHEMOTHERAPY BENEFIT AT 10 YEARS **13%**




Nodal Status



How Will My Patient's Cancer Potentially Respond to Chemotherapy?

Page three of the EndoPredict report provides a 10-year absolute chemotherapy benefit. This shows how much adding chemotherapy to five years of hormone (aka endocrine) therapy will reduce the likelihood of your patient's cancer coming back within ten years of diagnosis.²

EXAMPLE OF A LOW RISK RESULT - 3RD PAGE



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: **2.0**

TUMOR STAGE: **pT1c** (>1 cm but ≤2 cm)

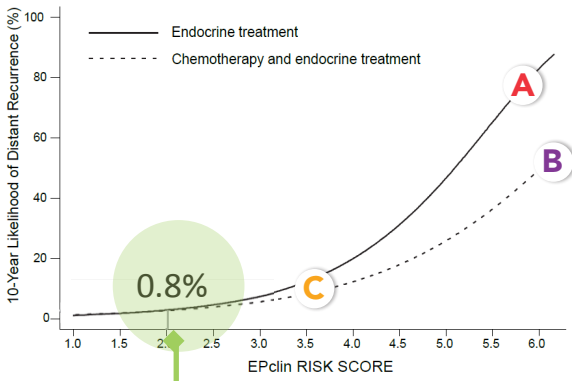
NODAL STATUS: **pN1** (1-3 positive nodes)

EPclin RISK SCORE **2.5**

TREATMENT: **CHEMOTHERAPY AND/OR 5 YEARS ENDOCRINE THERAPY**

Result Interpretation: At 10 years, an EPclin Risk Score of 2.5 is associated with an estimated 0.8% (95% CI: 2.3% - 1.0%) 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


0.8%

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The higher the EPclin Risk Score the more likely your patient will benefit from chemotherapy:²


EPclin Risk Score

LOW



HIGH

LOW



HIGH

Chemotherapy Benefit

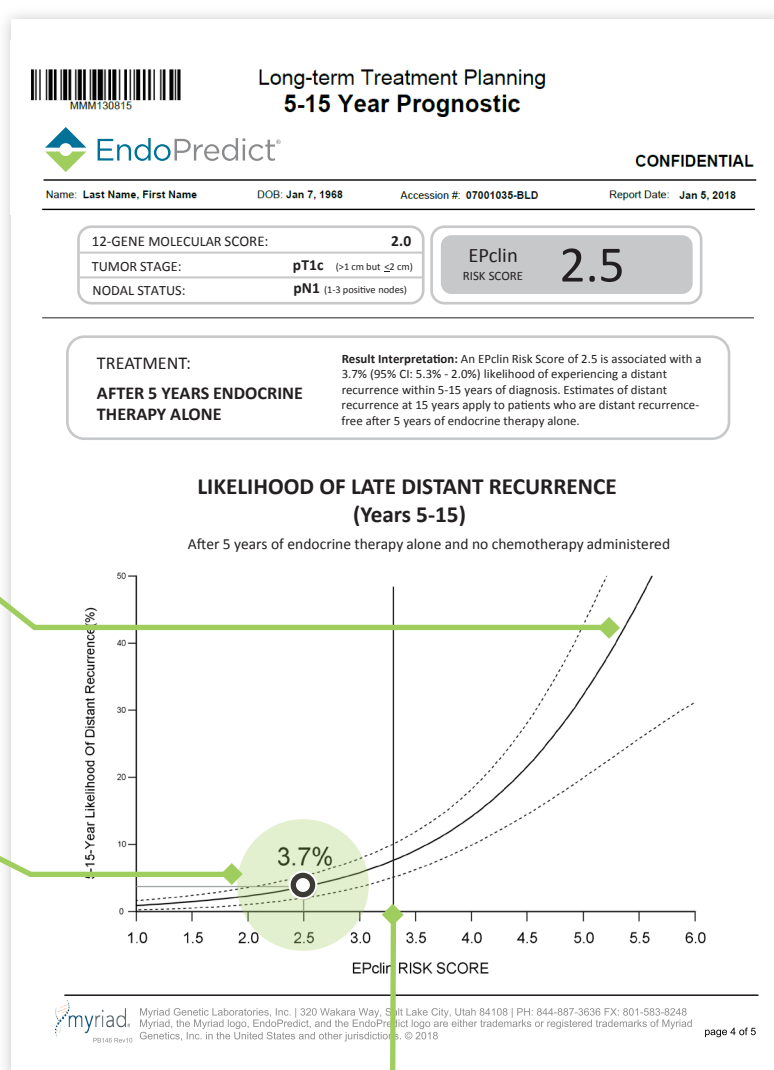
- A
The solid line shows the 10-year risk of cancer coming back when treated with only 5 years of hormone therapy
- B
The dashed line shows the 10-year risk of cancer coming back when treated with chemotherapy plus 5 years of hormone therapy
- C
The difference between these two lines is your patient's benefit from chemotherapy based on her **individualized** EPclin score

Your patient's benefit from chemotherapy is shown on the graph and in the grey box.

Can My Patient Safely Stop Hormone Treatment at Five Years?

Page four of the EndoPredict report helps inform long-term treatment decisions and provides a likelihood of late distant recurrence - this is the risk that your patient's breast cancer will return in a part of their body other than the breast in years five through fifteen.³ This risk estimate assumes that your patient will take hormone (aka endocrine) treatments as prescribed for the first five years after diagnosis and that her cancer does not recur within the first five years.

EXAMPLE OF A LOW RISK RESULT - 4TH PAGE



As the EPclin score increases along the bottom of the graph, the 5-15 year risk of recurrence increases also.³

Your patient's individualized risk of distant recurrence in years 5-15 is shown on the graph.

3.3 = Low/High Risk cut-off point

Why EndoPredict®?

Prognostic power providing low-risk results you can trust.

EndoPredict is for ER+, HER2– early-stage breast cancer patients (N0 or N+, up to 3 nodes, pre- or postmenopausal)



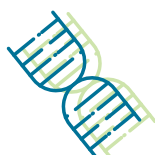
Lower cost vs other breast cancer recurrence tests



Fast 7-day turnaround



Individualized Low/High Result with chemotherapy benefit



Inclusion of proliferation- and hormone receptor-related genes contributes to accurate assessment of early and late recurrence risk



Better identifies a large percentage of low-risk patients (average of 6% recurrence)

More than 70%  Up to 30% of  N+ patients



For information on ordering EndoPredict visit endopredict.com



Supporting broad access for patients
For more information, visit myriadpromise.com



References:

1. Filipits M, Rudas M, Jakesz R, et al; for EP Investigators. A new molecular predictor of distant recurrence for ER-positive, HER2-negative breast cancer adds independent information to conventional clinical risk factors. *Clin Cancer Res.* 2011;17(18):6012-6020.
2. Sestak I, Martin 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* (2019) <https://doi.org/10.1007/s10549-019-05226-8>.
3. Filipits M, Dubsky P, Rudas M, et al; Prediction of distant recurrence using EndoPredict among women with ER+, HER2- node-positive and node-negative breast cancer treated with endocrine therapy only. *Clin Cancer Res.* (2019) <https://doi.org/10.1158/1078-0432.CCR-19-0376>.