



An advanced gene expression test for predicting the risk of distant recurrence in breast cancer.

*Risk of Breast Cancer Recurrence • Benefits of Chemotherapy
Suitability for Extended Endocrine Therapy*

Partial
**MEDICARE
REBATE**
Coming Soon



Providing prognostic precision for women with ER+,HER2- primary breast cancer

EndoPredict is an in vitro diagnostic test that provides highly important and clear information for different stages of treatment planning for patients with estrogen receptor-positive, HER2-negative primary breast cancer.

Initial treatment planning:

10-year risk of recurrence for patients with node-negative or node-positive disease,¹ and estimated absolute chemotherapy benefit at 10 years based on modern treatment regimens.⁶

Long-term treatment planning:

Breast cancer recurrence risk out to 15 years.⁷ The gene expression assay adds additional information to common prognostic factors so that a specific prognosis and prediction can be established for each individual patient.

Patients at low risk of distant recurrence are usually treated without chemotherapy. Under endocrine therapy alone without chemotherapy, more than 95% of low-risk patients do not experience a distant recurrence, even more than 10 years after diagnosis.¹ Compared to risk

“Breast cancer patients and their treating doctors must make complex, highly-personalised treatment decisions. Prognostic tools, such as EndoPredict, can play a vital role in determining the type of treatment and prognosis for the patient through assisting with adjuvant therapy decision-making in ER-positive breast cancer.

Molecular assays in breast cancer

Studies of gene expression conducted in the early 2000s highlighted the potential of molecular assays to provide additional information beyond traditional pathology regarding prognosis. These assays have all been shown to provide useful prognostic information to ER-positive patients regarding their risk of developing breast cancer recurrence, and their use is supported by international

EndoPredict has been validated in four prospective-retrospective studies, providing level 1 evidence.^{1,3,5}

TARGET GROUP CHECK

- ✓ ER-Positive
- ✓ HER2/neu-Negative
- ✓ 0-3 pos. Lymph node
- ✓ Pre-/Post-Menopausal
- ✓ Size: pT1-3

stratification using other gene expression tests or clinical parameters, EndoPredict identifies the largest group of women with breast cancer at low risk (<10% chance of distant recurrence in 10 years) who might safely avoid chemotherapy.^{2,3,4}

In addition EndoPredict predicts the individual absolute chemotherapy benefit at 10 years⁶ and is the only test that provides the individual risk of breast cancer late distant recurrence within years 5-15⁷ to help in deciding whether a patient can avoid extended endocrine therapy.

EndoPredict is performed on FFPE tumor tissue from biopsy or surgical specimens. The 12-gene molecular score (also called EP Score in publications) is determined initially. As soon as information on tumor size and nodal status is available, it is combined with the 12-gene molecular score to calculate the EPclin Risk Score.

guidelines. A number of studies have shown that the second-generation assays, such as EndoPredict, which also incorporate clinical variables like lymph node status and tumour size, are better able to predict late recurrence (5-10 years post treatment) and may also identify a larger group of low-risk patients.^{3,4}

High quality pathology is a vital part of breast cancer diagnosis and management, and molecular assays such as EndoPredict can provide important additional information to support complex decision-making about the use of chemotherapy in ER-positive breast cancer.”

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EndoPredict Result Report: basis of the treatment decision

EndoPredict provides a comprehensive test result and an individualized EPclin Risk Score. The EPclin Risk Score algorithm integrates a 12-gene molecular score, tumor size, and nodal status. All three factors contributed significant information with respect to risk assessment in an independent clinical validation study.¹

In addition to the percentage risk of recurrence up to 10 years, the absolute chemotherapy benefit based on current treatment regimens and the risk of recurrence between 5 and 15 years after diagnosis* is indicated. The patient is classified as "low risk" or "high risk." The treating physician receives the report and can plan further treatment based on the results.

Result Report
Created by: EndoPredict Report Generator* CE EndoPredict

Sample Name: **Sample Aa**
Note:
Report Created: **2019-02-08 10:55 AM (CET)**

12-GENE MOLECULAR SCORE: (Range 0-15) **10.1**

TUMOR SIZE: **pT1c (>1cm but <=2cm)**

NODAL STATUS: **1 to 3 positive lymph nodes (incl. pN1mic)**

RESULT
EPclin RISK SCORE 4.8 **EPclin RISK CLASS HIGH**

EndoPredict* is a gene expression assay for patients with ER-positive, HER2-negative 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. The EPclin Risk Class refers to the risk of distant recurrence with 5 years of adjuvant endocrine therapy alone.

INITIAL Treatment Planning
LIKELIHOOD OF DISTANT RECURRENCE WITHIN YEARS 0-10 For patients treated with 5 years of endocrine therapy alone **36%**

ABSOLUTE CHEMOTHERAPY BENEFIT AT 10 YEARS **17%**

LONG-TERM Treatment Planning
LIKELIHOOD OF LATE DISTANT RECURRENCE WITHIN YEARS 5-15 For patients with no recurrence after 5 years of endocrine therapy alone **28%**

AUTHORIZED SIGNATURE

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Result Report CE EndoPredict

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RESULT
EPclin RISK SCORE 4.8 **EPclin RISK CLASS HIGH**

ABSOLUTE CHEMOTHERAPY BENEFIT AT 10 YEARS
5 years endocrine therapy alone versus chemotherapy plus 5 years endocrine therapy

Based on the clinical validation of the EndoPredict test in the ABCSG 8 trial, the EPclin Risk Score of 4.8 is associated with an estimated 17% absolute benefit from chemotherapy, when used in combination with endocrine treatment, compared to endocrine treatment alone.

myriad

Result Report CE EndoPredict

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TUMOR SIZE: **pT1c (>1cm but <=2cm)**

NODAL STATUS: **1 to 3 positive lymph nodes (incl. pN1mic)**

RESULT
EPclin RISK SCORE 4.8 **EPclin RISK CLASS HIGH**

LIKELIHOOD OF DISTANT RECURRENCE WITHIN YEARS 0-10
For patients treated with 5 years of endocrine therapy alone

Based on the clinical validation of the EndoPredict test in the ABCSG 8 trial with 1702 patients, the risk of distant recurrence after 10 years of adjuvant endocrine therapy alone is associated with a 36% (95% CI: 29%-42.2%) 10-year estimated likelihood of experiencing a distant recurrence when treated with 5 years of endocrine therapy alone.

myriad

Result Report CE EndoPredict

Sample Name: **Sample Aa**
Report Created: **2019-02-08 10:55 AM (CET)**

12-GENE MOLECULAR SCORE: (Range 0-15) **10.1**

TUMOR SIZE: **pT1c (>1cm but <=2cm)**

NODAL STATUS: **1 to 3 positive lymph nodes (incl. pN1mic)**

RESULT
EPclin RISK SCORE 4.8 **EPclin RISK CLASS HIGH**

LIKELIHOOD OF LATE DISTANT RECURRENCE WITHIN YEARS 5-15
For patients with no recurrence after 5 years of endocrine therapy alone

Based on the clinical validation of the EndoPredict test in the ABCSG 8 trial with 1702 patients, the risk of distant recurrence after 5 to 15 years of adjuvant endocrine therapy alone is associated with a 28% (95% CI: 19.9%-36.2%) estimated likelihood of experiencing a distant recurrence after 5 years of endocrine therapy alone and who do not receive endocrine endocrine therapy.

myriad

**5-15 year risk is based on treatment with 5 years of endocrine therapy only – no chemotherapy. The result assumes the patient has not experienced recurrence by 5 years.*

12-Gene Molecular Score

The 12-Gene Molecular Score independently assesses risk of recurrence based upon quantitative reverse transcription polymerase chain reaction (qRT-PCR) of 8 signature genes, 3 normalization genes, and 1 control gene. The 12-Gene Molecular Score includes genes that predict both early and late metastasis to provide improved prognostic power.

The 12-Gene Molecular Score significantly improved prognostic performance when added to the following measures:

- Nodal status, tumor size, age, and grade
- Quantitative ER levels
- Quantitative KI-67 levels
- Adjuvant! Online

12-gene molecular score for early and late recurrence

EARLY recurrence (0-5 years)

3 PROLIFERATION-RELATED GENES

- UBE2C
- BIRC5
- DHCR7

5 HORMONE RECEPTOR-RELATED GENES

- STC2
- A2GP1
- IL6ST
- RBBP8
- MGP

4 CONTROL GENES

3 normalization genes: CALM2, OAZ1, and RPL37A
1 control for DNA contamination HBB

LATE recurrence (5-10 years)

Variable	0-5 years HR (95% CI)	P-value	>5 years HR (95% CI)	P-value
PROLIFERATION	1.60 (1.33-1.92)	<0.001	1.19 (0.85-1.67)	0.298
ER SIGNALING	0.89 (0.75-1.06)	0.204	0.61 (0.46-0.81)	<0.001

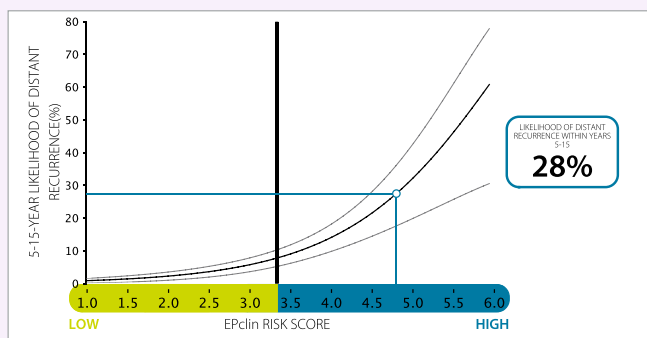
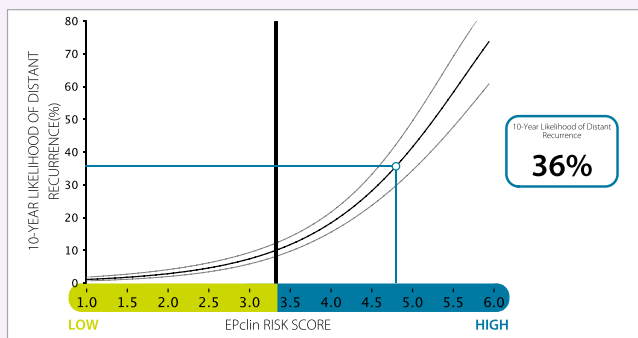
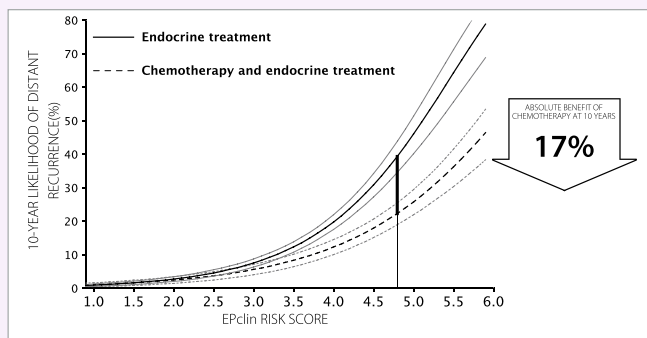
Proliferation genes provide important additional prognostic information within the first five years, while ER-associated genes are critical to predict late recurrences.¹¹

Tumor size and nodal status

Tumor size and nodal status are established prognostic markers routinely used to stage invasive breast cancer.⁴ Both clinicopathological factors independently contribute significant prognostic information. The integration of the 12-Genes Molecular Score with tumor size and lymph node status (EPclin) resulted in a statistically significant improvement in prognostic power above the clinicopathological factors alone.¹

EPclin integrates 12-gene molecular score with clinicopathological features

12-GENE MOLECULAR SCORE: <small>(Range 0-15)</small>	10.1	RESULT	
TUMOR SIZE:	pT1c (>1cm but ≤2cm)	EPclin RISK SCORE	EPclin RISK CLASS
NODAL STATUS:	1 to 3 positive lymph nodes (incl. pN1mic)	4.8	HIGH



EndoPredict offers a clear low- or high-risk result presented on continuous curves – providing an individualized risk of distant recurrence and the absolute chemotherapy benefit for each patient.

Clear risk groups identified in different subgroups

EndoPredict supplies additional prognostic information to supplement all common prognostic factors, as demonstrated by four validation studies with more than 3,100 patients.^{1,2,3,5}

Comparison with other Prognostic Tests

When compared to other gene expression tests, EndoPredict was the most prognostic signature for distant recurrence, both in years 0-10 and in years 5-10, in all patients.⁴

EndoPredict identified the largest group of women with breast cancer, both in node-negative and node-positive disease:

- at low risk (<10% chance in 10 years) of distant recurrence who might safely avoid chemotherapy
- at low risk of late distant recurrence for whom an extended endocrine therapy might not be justified.

When to use

EndoPredict is performed on FFPE tumour tissue from biopsy or surgical specimens from patients who have not received systemic endocrine therapy and/or chemotherapy.

Screening	Clinical Diagnosis	Pathological Diagnosis	Surgery	Adjuvant Therapy Decision
Palpatory findings	Biopsy	ER, PR, and HER2 status	Tumour size	Endocrine therapy
Mammography	Imaging	Other parameters	Nodal status	Chemotherapy if necessary
▼	▼	▼	▼	▼
PATIENT JOURNEY				▶
				▲ EndoPredict

Superior prognostic performance with results you can trust

- **Only prognostic test that can answer**
 - whether your patient can safely avoid chemotherapy
 - how beneficial chemotherapy would be
 - whether your patient can avoid extended endocrine therapy
- **Largest “true” low risk group for safe reduction of chemotherapy**
 - more than 70% of NO patients
 - up to 30% of N+ patients
- **Second-generation gene expression test for superior prognostic power**
- **Unique gene selection for accurate early and late risk assessment**
- **Consistent study cohorts and constant cutoff**
- **Clear low and high-risk category**
- **Rapid results**



Our Expert Pathologist

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Ordering EndoPredict with Clinical Labs

How to order

Please download the EndoPredict request form, which can be found at clinicallylabs.com.au/endopredict. Fill in patient details and clinical history, and select “EndoPredict”. Ensure that referring clinician details are complete, and if known, provide specimen details. If you would like a copy of the report to be sent to another clinician, please provide the necessary details. The payment process can be found on the request form.

Specimens required

EndoPredict is performed on FFPE tumour tissue from biopsy or surgical specimens.

Turnaround time

4–5 business days from the sample receipt date.

Test cost

Partial Medicare rebate coming soon.

For current pricing and more information, please visit clinicallylabs.com.au/endopredict

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