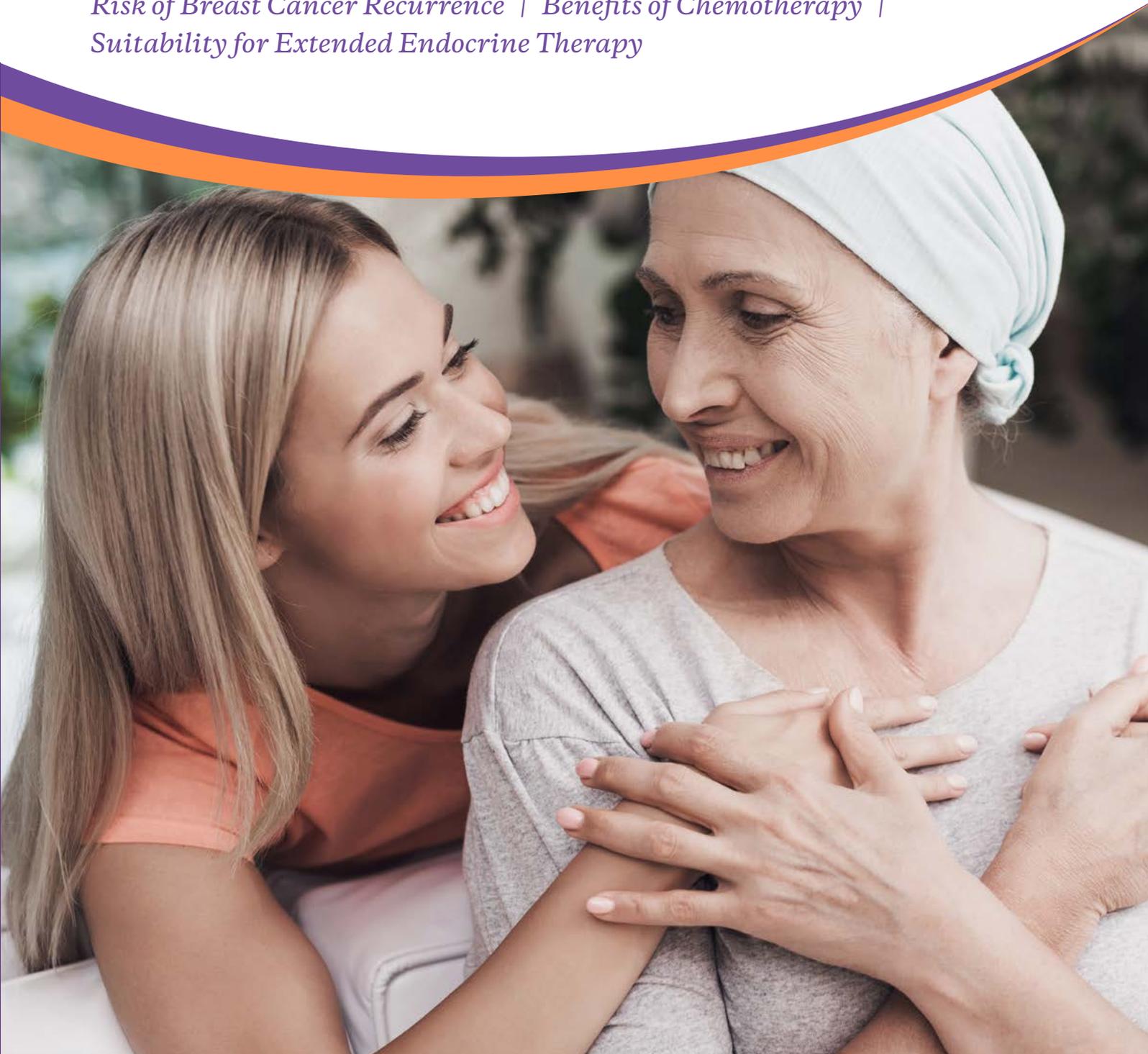


*An advanced gene expression test for predicting the risk of distant recurrence in breast cancer.*

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



# 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-receptorpositive, HER2-negative, primary breast cancer.

## Initial treatment planning:

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

## Long-term treatment planning:

Breast cancer recurrence risk out to 15 years.<sup>7</sup>

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

*“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 about prognosis. These assays have all been shown to provide useful prognostic information to ER positive patients about their risk of developing breast cancer recurrence and their use is supported by international guidelines. A number

EndoPredict has been validated in four prospective-retrospective studies, providing level 1 evidence.<sup>1,3,5</sup>

## TARGET GROUP CHECK

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

a distant recurrence, even more than 10 years after diagnosis.<sup>1</sup> Compared to risk 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.<sup>2,3,4</sup>

In addition EndoPredict predicts the individual absolute chemotherapy benefit at 10 years<sup>6</sup> and is the only test that provides the individual risk of breast cancer late distant recurrence within years 5-15<sup>7</sup> 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.

of studies have shown that the second generation assays such as EndoPredict (provided by Clinical Labs), which also incorporate clinical variables such as 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.<sup>3,4</sup>

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.”

Prof. Sandra O’Toole,  
MB, BS (HONS), BSC MED (HONS),  
PhD, FRCPA



# 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.<sup>1</sup>

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:** 10.1 (Range 0-13)  
**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-Genes 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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**LIKELIHOOD OF LATE DISTANT RECURRENCE WITHIN YEARS 5-15**  
For patients with no recurrence after 5 years of endocrine therapy alone: **28%**

## 12-Genes Molecular Score

The 12-Genes 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-Genes Molecular Score includes genes that predict both early and late metastasis to provide improved prognostic power.

The 12-Genes 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**

**3 PROLIFERATION-RELATED GENES**  
**EARLY recurrence (0-5 years)**  
 • UBE2C  
 • BIRC5  
 • DHCR7

**5 HORMONE RECEPTOR-RELATED GENES**  
**LATE recurrence (5-10 years)**  
 • STC2  
 • AZGP1  
 • IL6ST  
 • RBBP8  
 • MGP

**4 CONTROL GENES** > 3 normalization genes: CALM2, OAZ1, and RPL37A  
 1 control for DNA contamination HBB

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

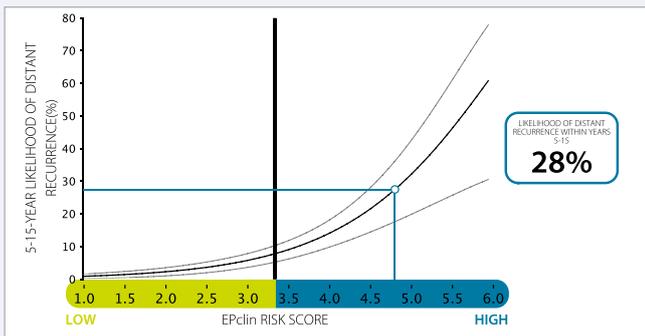
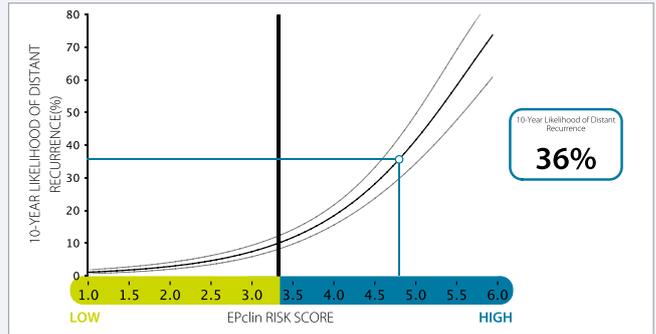
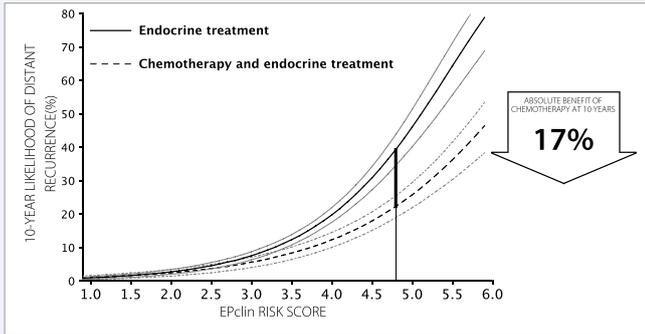
*Proliferation genes provide important additional prognostic information within the first five years, while ER-associated genes are critical to predict late recurrences.<sup>11</sup>*

## Tumor size and nodal status

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

EPclin integrates 12-gene molecular score with clinicopathological features

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



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.<sup>1,2,3,5</sup>

## 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.<sup>4</sup>

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.

# EndoPredict at a Glance

## EndoPredict Superior Prognostic Performance 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 N0 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

### SCREENING

- Palpatory findings
- Mammography



### CLINICAL DIAGNOSIS

- Biopsy
- Imaging



### PATHOLOGICAL DIAGNOSIS

- ER, PR, and HER2 status
- Other parameters



### SURGERY

- Tumor size
- Nodal status



### ADJUVANT THERAPY DECISION

- Endocrine therapy
- Chemotherapy if necessary



PATIENT JOURNEY

  
EndoPredict



## Our Expert Pathologists

### Prof. Sandra O'Toole



**MB, BS (HONS), BSC MED (HONS), PhD, FRCPA**  
 Anatomical Pathology, Histopathology,  
 Molecular Biology

Phone: 1300 134 111  
 State: **New South Wales**  
 Email: [sandra.otoole@clinicallabs.com.au](mailto:sandra.otoole@clinicallabs.com.au)

### Assoc.Prof. Mirette Saad



**MBBS (HONS), MD (HONS), MAACB, FRCPA, PhD**  
 Chemical Pathology, PhD Molecular Genetics

Phone: 03 9538 6777  
 State: **Victoria**  
 Email: [mirette.saad@clinicallabs.com.au](mailto:mirette.saad@clinicallabs.com.au)

# HOW TO ORDER

- 1 Download the request form
- 2 Fill in the patients details and clinical history
- 3 Tick "EndoPredict"
- 4 Ensure the referring clinician details are complete
- 5 If known, provide the specimen details
- 6 If you would like a copy report to be sent, please provide the details of the other clinician
- 7 Fill in payment details

EndoPredict resources and request forms are available at [www.clinicallabs.com.au/endorpredict](http://www.clinicallabs.com.au/endorpredict)

For further information, or to enquire about ordering EndoPredict please contact Australian Clinical Labs Molecular department on (03) 9538 2259.

#### References

1. Filipits M. 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. Dubsky P. et al.: EndoPredict improves the prognostic classification derived from common clinical guidelines in ER-positive, HER2-negative early breast cancer. Ann Oncol 2013, 24 :640-647
3. Buus et al. Comparison of EndoPredict and EPclin With Oncotype DX Recurrence Score for Prediction of Risk of Distant Recurrence After Endocrine Therapy. J Natl Cancer Inst, 2016, Vol. 108, No. 11
4. Sestak I. et al. Comparison of the Performance of 6 Prognostic Signatures for Estrogen Receptor- Positive Breast Cancer. A Secondary Analysis of a Randomized Clinical Trial. JAM Oncology Published online February 15, 2018
5. Martin M. et al.: Clinical validation of the EndoPredict test in node-positive, chemotherapy-treated ER+/HER2- breast cancer patients: results from the GEICAM 9906 trial. BCR 2014, 16:R3
6. Sestak I, et al.: Prediction of Distant Recurrence by EndoPredict in Patients with Estrogen Receptor-Positive, HER2-Negative Breast Cancer who Received Adjuvant Endocrine Therapy plus Chemotherapy (ET+C) or Endocrine Therapy Alone (ET). SABCS 2018
7. Filipits M, et al.: Prediction of distant recurrence using EndoPredict among women with ER-positive, HER2-negative breast cancer with a maximum follow-up of 16 years. SABCS 2018
8. Dubsky P. et al.: The EndoPredict score provides prognostic information on late distant metastases in ER+/HER2- breast cancer patients. BJC. 2013; 109, 2959–2964

**1300 134 111** VIC NSW SA NT  
**1300 367 674** Western Australia  
[www.clinicallabs.com.au](http://www.clinicallabs.com.au)