EndoPredict®

One Test – Three Clinical Answers

eurobio SCIENTIFIC

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

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

Partial MEDICARE REBATE *Available*

Only available at

AUSTRALIAN Clinicalabs

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 *ER* positive, *HER2* negative primary breast cancer.

TARGET GROUP CHECK

- *HER2* negative
- *ER* positive
- Lymph node positive or negative
- Pre- and postmenopausal
- Tumour size pT1 to pT3
- Grade 1 to 3

"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 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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National Director of Molecular Genetics

EndoPredict is trusted in global clinical routine and is recommended in all major guidelines:

- ✓ **European Society of Medical Oncology (ESMO) 2024**
- ✓ **American Society of Clinical Oncology (ASCO) 2022**
- ✓ **St. Gallen International Expert Consensus 2023**
- ✓ **American Joint Committee on Cancer (AJCC) 2017**
- ✓ **National Comprehensive Cancer Network (NCCN) 2024**
- ✓ **National Institute for Health and Care Excellence (NICE) 2024**

EndoPredict provides highly important and clear information for different stages of treatment planning.

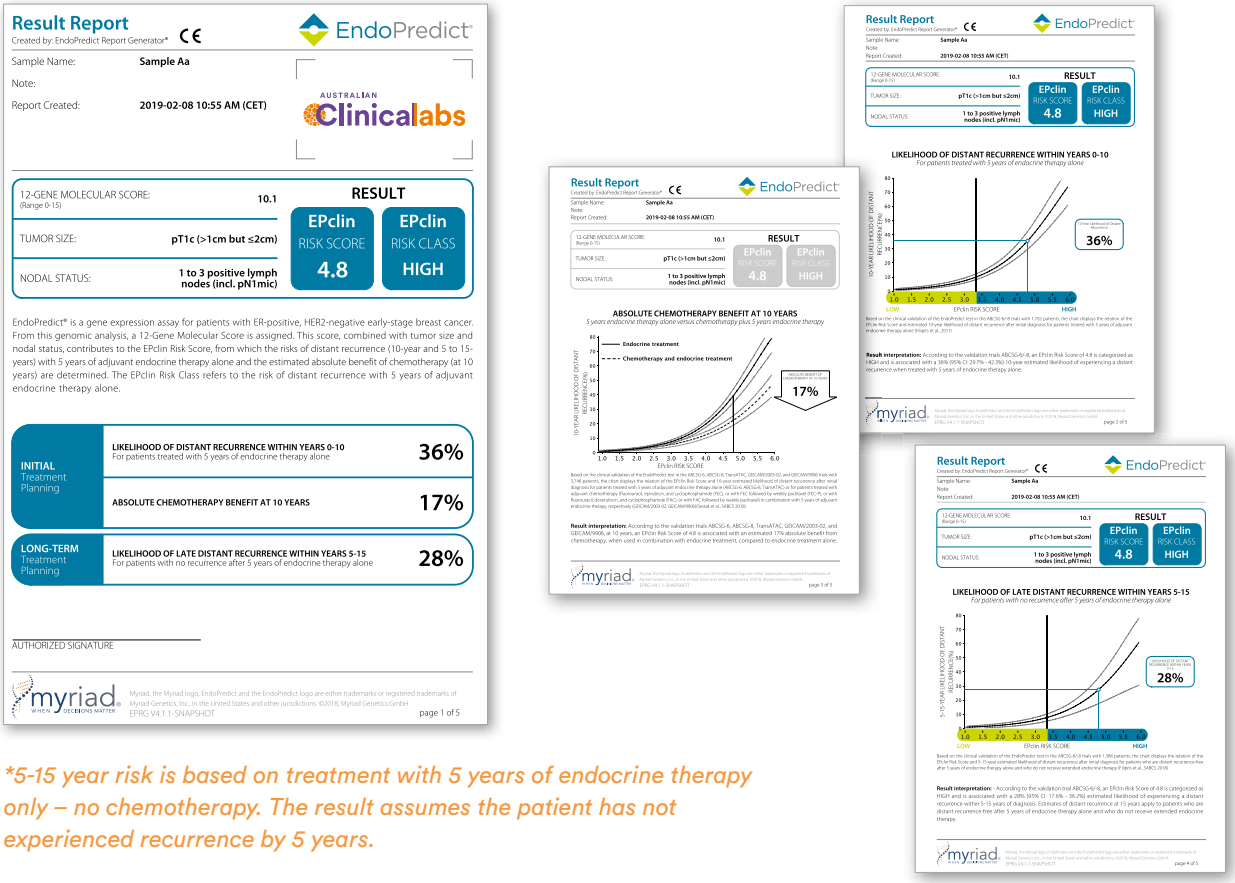
- **Initial treatment planning:**
  10-year risk of recurrence for patients with node-negative or node-positive disease,[1] and estimated absolute chemotherapy benefit at 10 years based on modern treatment regimens.[6]
- **Long-term treatment planning:**
  Breast cancer recurrence risk out to 15 years.[7]

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 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 years[6] and is the only test that provides the individual risk of breast cancer late distant recurrence within years 5-15[7] to help in deciding whether a patient can avoid extended endocrine therapy.

EndoPredict Result Report: basis of the treatment decision

EndoPredict provides a comprehensive test result and an individualised EPclin Risk Score. The EPclin Risk Score algorithm integrates a 12-gene molecular score, tumour 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.



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.

The 12-Gene Molecular Score

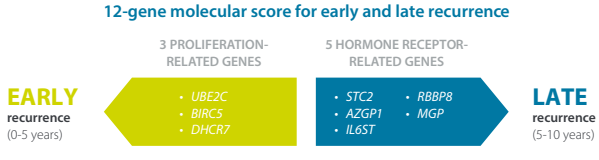
EndoPredict is performed on FFPE tumour tissue from biopsy or surgical specimens. The 12-gene molecular score (also called EP Score in publications) is determined initially. As soon as information on tumour size and nodal status is available, it is combined with the 12-gene molecular score to calculate the EPclin Risk 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, tumour size, age, and grade
- Quantitative ER levels
- Quantitative KI-67 levels
- Adjuvant! Online

12-gene molecular score for early and late recurrence



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

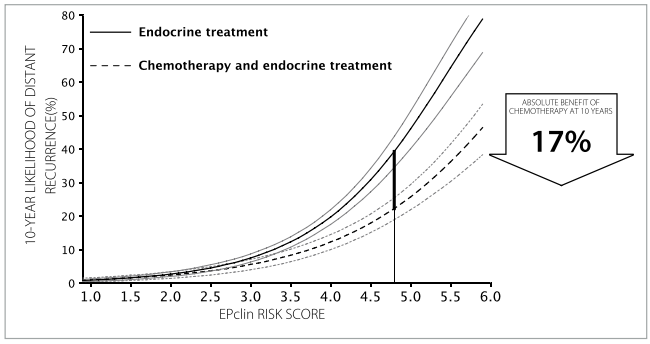
Proliferation genes provide important additional prognostic information within the first five years, while ER-associated genes are critical to predict late recurrences.[17]

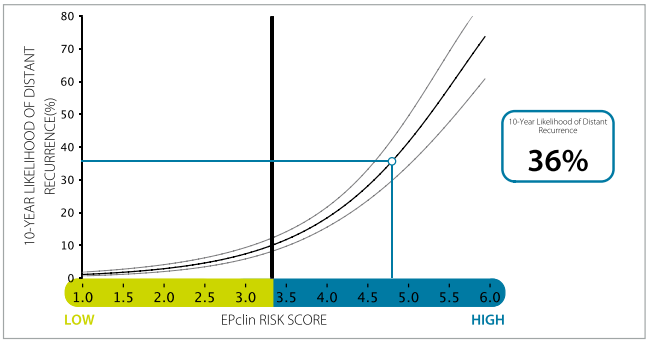
Tumour size and nodal status

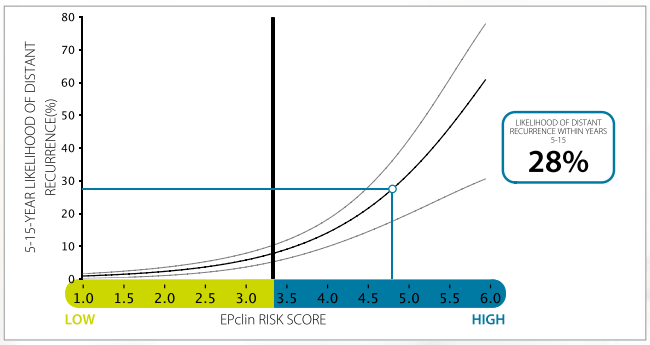
Tumour size and nodal status are established prognostic markers routinely used to stage invasive breast cancer.[4] Both clinicopathological factors independently contribute significant prognostic information. The integration of the 12-Gene Molecular Score with tumour size and lymph node status (EPclin)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

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

EPclin integrates 12-gene molecular score with clinopathological features







EndoPredict offers a clear low- or high-risk result presented on continuous curves – providing an individualised 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.

✓ **EndoPredict validated in four prospective-retrospective studies, providing level 1 evidence.[1,3,5]**

✓ **ESMO early breast cancer guidelines in 2024 recognise EndoPredict as having the highest level of clinical evidence alongside other genomic assays.[9]**

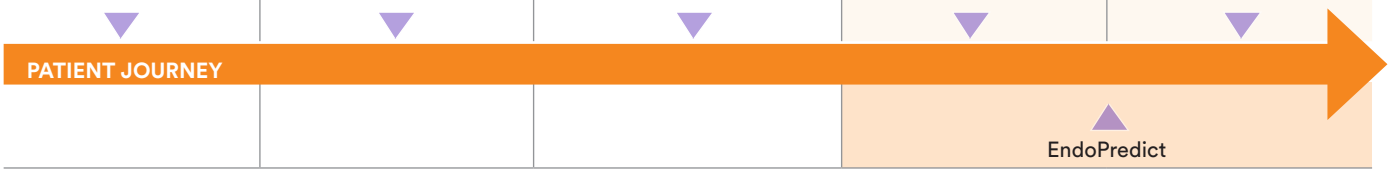
✓ **NICE in the UK now recommends EndoPredict for tailored treatment of lymph node positive and negative early breast cancer.[10]**

✓ **New prospective data from two studies (UNIRAD and TUM) confirm prognostic and predictive accuracy for EndoPredict in making treatment decisions for early-stage breast cancer study.[11]**

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



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 N0 patients
  - up to 30% of N+ patients
- **Consistent study cohorts and constant cutoff**
- **Partial Medicare rebate available**
- **Performed locally in Australia with rapid results**
- **Second-generation gene expression test for superior prognostic power**
- **Unique gene selection for accurate early and late risk assessment**
- **Clear low and high-risk category**

References

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2. Dubsky P. et al.: EndoPredict improves the prognostic classification derived from common clinicalguidelines 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
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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
9. Loibl, S., et al. "Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up." Annals of Oncology, vol 35, no. 2, 2024, pp. 159-182.
10. National Institute for Health and Care Excellence. Tumour profiling tests to guide adjuvant chemotherapy decisions in early breast cancer (Diagnostics guidance [DG58]). 2024.
11. Klein, E., et al. "Long-term prospective outcome data using EndoPredict as risk stratification and chemotherapy decision biomarker in hormone receptor-positive, HER2-negative early breast cancer." Breast Cancer Research and Treatment, 2024.

Our Expert Pathologist

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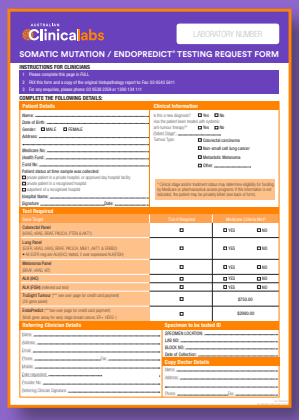
Associate Professor Mirette Saad is an RCPA Consultant Chemical Pathologist and the National Director of Molecular Genetics at Australian Clinical Labs. She obtained a PhD in Molecular Genetics from Melbourne University and Peter MacCallum Cancer Institute. A/P Saad chairs the RCPA Chemical Pathology Advisory Committee and is a member of the AACB and RCPA Genetic Advisory Committee.

Ordering EndoPredict with Clinical Labs


SOMATIC MUTATION / ENDOPREDICT® TESTING REQUEST FORM

How to order

Please download the EndoPredict request form, which can be found at clinicallabs.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.

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

A partial Medicare rebate is available under item number 73306.

Patients are required to pay for EndoPredict prior to our laboratory conducting the test. Clinical Labs will contact your patient via SMS or phone call with payment instructions—please advise them to expect this communication in the days following the test request. After making the payment online, Clinical Labs will send your patient a receipt, which they can use to claim the partial Medicare rebate directly from Medicare.

*For current pricing and further information, please visit **clinicallabs.com.au/endopredict***

Medicare Eligibility Criteria

Gene expression profiling testing using EndoPredict, for the purpose of profiling gene expression in formalin-fixed, paraffin-embedded primary breast cancer tissue from core needle biopsy or surgical tumour sample to estimate the risk of distant recurrence of breast cancer within 10 years, if:

(a) the sample is from a new primary breast cancer, which is suitable for adjuvant chemotherapy; and
(b) the sample has been determined to be oestrogen receptor positive and *HER2* negative by IHC and ISH respectively on surgically removed tumour; and
(c) the sample is axillary node negative or positive (up to 3 nodes) with a tumour size of at least 1 cm and no more than 5 cm determined by histopathology on surgically removed tumour; and
(d) the sample has no evidence of distal metastasis; and
(e) pre-testing of intermediate risk of distant metastases has shown that the tumour is defined by at least one of the following characteristics: (i) histopathological grade 2 or 3; (ii) one to 3 lymph nodes involved in metastatic disease (including micrometastases but not isolated tumour cells); and
(f) the service is not administered for the purpose of altering treatment decisions

Applicable once per new primary breast cancer diagnosis for any particular patient

Please contact your local Clinical Labs representative if you require our EndoPredict patient brochures.

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