EndoPredict®

Breast Cancer Prognostic Test

eurobio SCIENTIFIC

Pathology Guide

INTENDED USE: The EndoPredict® QS Kit is an in vitro diagnostic product for patients with estrogen-receptor-positive, HER2-negative (ER+/HER2-) primary breast cancer to determine the risk of distant recurrence and to estimate the adjuvant chemotherapy benefit.

1. Selection of tissue sample

- FFPE (Formalin Fixed Paraffin Embedded) breast tumor tissue should be used.
- The portion of the tumor in the tissue section must be at least 30% (ratio of invasive tumor tissue to total tissue area) and should be determined by a pathologist using the adjacent H&E (Hematoxylin and Eosin stained) section. Adipose tissue is not to be considered as tissue.
- Both biopsy and surgical specimens can be used.
- The specimen material may be submitted as blocks or slides.
- If the block cannot be sent, one charged H&E slide cut at 2-5 microns, plus five charged, consecutive unstained 10-micron section slides are required.
- Ensure there is a specimen identification number on each block or slide submitted.
- The specimen should be prepared and stored at room temperature prior to shipping.

2. Clinical information required

- pN: pathological lymph node status (number of affected lymph nodes).
- pT: pathological tumor size.

3. Limitations

Performance characteristics of the EndoPredict test have only been established for patients with ER+/HER2- primary breast cancer who have not received any radiation or systemic treatment for their disease.

Treatment prior to biopsy or resection of the primary breast tumor (e.g., neoadjuvant chemotherapy, radiation treatment) may affect test performance, potentially resulting in inaccurate test results. Therefore, patient samples exposed to radiation or systemic treatment are not suitable for testing.

4. Fixation

Tissue removal, fixation, paraffin embedding, and storage can be performed according to local standard operating procedures with the following restrictions:

- The time until fixation should not exceed one hour at room temperature.
- 10% neutral buffered formalin must be used as a fixative (corresponds to 4% formaldehyde). Fixation should not exceed three days.

Breast cancer suitable for testing

The scenarios below are not exhaustive. If you have a query, please contact either your local EndoPredict testing laboratory or email the team at Eurobio directly on kitsupport@eurobio-scientific.de.

T1 – T3 tumors	EndoPredict is validated for T1 – T3 tumors. Note, there is no data for pT1mic. The EPclin score cannot be calculated.
Node negative and node positive breast cancer	EndoPredict is validated for patients with node negative and node positive breast cancer. Although patients with >3 positive lymph nodes were included in clinical and analytical validation studies, use of EndoPredict is not recommended in this group according to current guidelines and manufacturer guidance. Further information: a) National and international guidelines (ESMO[1], NCCN[2], ASCO[3]) recommend gene expression testing for patients with up to three affected lymph nodes. b) In clinical studies, more than 98% of patients with >3 positive lymph nodes were classified as 'high-risk' by EPclin. Micrometastatic disease in the lymph nodes (pN1mic) is considered as node positive within the EndoPredict algorithm.
Biopsy tissue	EndoPredict is validated for use on a pre-surgical biopsy. Analytically equivalent results have been demonstrated between breast tumor biopsy and paired surgical resection samples.[4] As for tumor resection tissue, the needle biopsy must be fixed in formalin and embedded in paraffin. If both biopsy and surgical specimen are available, it is recommended to select the surgical specimen.
Histological subtypes	EndoPredict is validated for primary invasive ER+/HER2- breast cancer, independent from histological subtype. Primary breast tumors with invasive ductal, invasive lobular, mixed histology (with both invasive ductal and invasive lobular characteristics), and primary invasive breast tumors with no specified histology are all acceptable for testing. Subgroup analyses in lobular and ductal breast cancer show no difference in prognostic power between the two subgroups.
Simultaneous multifocal and multicentric diseae	EndoPredict is validated for use in simultaneous ipsilateral tumors. To determine the 12-Gene Molecular EP Score, the pathologist should select the tumor with **the most aggressive histopathological features** (higher grading, higher Ki67, lower ER/PR) which may not be the largest tumor. For calculation of the EPclin Score, **the largest tumor size** should be used (regardless of the tumor selected for the gene expression test). This is in line with TNM stage classification of simultaneous ipsilateral tumors.[5] The EPclin result will thus reflect the molecular signature of the most aggressive tumor (according to histopathological features) combined with the risk determined by the T stage of the disease.
Simultaneous bilateral disease	EndoPredict is validated for use in bilateral tumors. To determine the 12-Gene Molecular EP Score, the pathologist should select the tumor with **the most aggressive histopathological features** (higher grading, higher Ki67, lower ER/PR) which may not be the largest tumor. For calculation of the EPclin Score, **pT and pN of the side of the tested tumor** should be used. This is in line with TNM classification for simultaneous bilateral tumors.
Simultaneous disease - the option to test more than one tumor	If the option of testing more than one tumor is feasible, then the best strategy may be to test sequentially. The more aggressive tumor, based on standard parameters, should be tested first. If the result is high-risk, then testing on a subsequent tumor is unnecessary. If the result of the first tumor is low-risk, then testing a subsequent tumor may be considered.

Samples not suitable for testing

Fresh frozen tissue	Fresh frozen tissue is not suitable for testing. EndoPredict is validated for use in FFPE tissue only.
pT1mi and pT4 tumors	EndoPredict is not validated for pT1mi or pT4 tumors. The EPclin score cannot be calculated.
Non-invasive	EndoPredict is not validated for non-invasive breast cancer such as DCIS (ductal carcinoma in situ) or LCIS (lobular carcinoma in situ).
Local or distant relapse	EndoPredict is not validated for use in either a local or a distant relapse.
Second primary tumors	EndoPredict is validated for primary breast cancer only. This includes simultaneous tumors. EndoPredict is not validated for use on a second primary tumor, regardless of whether the patient has received prior treatment or not.
Lymph node tissue	EndoPredict is not validated for use in lymph node tissue.
Pregnancy	EndoPredict is not validated for use in patients that are pregnant.

References

1. Loibl S. et al., Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2024;35:159-182. **2.** NCCN Guidelines Version V3.2025: Breast Cancer (2025). **3.** Andre F. et al., Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update. J Clin Oncol. 2022 Jun 1;40(16):1816-1837. **4.** Müller BM. Et al., Comparison of the RNA-based EndoPredict multigene test between core biopsies and corresponding surgical breast cancer sections. J Clin Pathol. 2012 Jul;65(7):660-2. **5.** American Joint Committee on Cancer, Cancer Staging Manual, eighth edition.

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This in vitro diagnostic medical device is a regulated health product that bears the CE marking under this regulation. Intended for healthcare professionals.

Please read the instructions in the user manual carefully.

NABM code: not applicable.

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