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mammaprint®
70-Gene Breast Cancer Recurrence Test

MammaPrint®: Recommended in international breast cancer clinical practice guidelines

Following the publication of the results of MINDACT[1] in the New England Journal of Medicine in August 2016, the medical societies that reviewed the findings have included or expanded their recommendation of MammaPrint based on this landmark clinical trial

1. American Society of Clinical Oncology (ASCO)

New recommendation in 2017

Issued: July 2017

- Focused update dedicated exclusively to MammaPrint and triggered by the 'practice-changing' results of the MINDACT trial in August 2016[II]
- ASCO recommends MammaPrint:
  - For clinical high risk, hormone receptor-positive, HER2-negative breast cancer, to inform decisions on withholding chemotherapy
  - As currently the only genomic test to guide treatment decisions for 1-3 lymph node-positive early-stage breast cancer patients

Patient group	Recommendation	Evidence rating
ER/PgR-positive, HER2-negative, **lymph node-negative** breast cancer	MammaPrint may be used in patients with high clinical risk per MINDACT categorization to inform decisions on withholding adjuvant systemic chemotherapy due to its ability to identify a good prognosis population with potentially limited chemotherapy benefit	Type: **evidence-based** Evidence quality: **high** Strength: **strong**
ER-positive, HER2-negative, **lymph node-positive** breast cancer	MammaPrint may be used in patients at high clinical risk per MINDACT categorization to inform decisions on withholding adjuvant systemic chemotherapy. However, such patients should be informed that a benefit of chemotherapy cannot be excluded, particularly in patients with greater than one involved lymph node	Type: **evidence-based** Evidence quality: **high** Strength: **moderate**

Adapted from Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline.

2. St. Gallen International Breast Cancer Consensus

New recommendation in 2017

Issued: June 2017

- Third time that the biennial guidelines have recommended MammaPrint[III]
- 2017 update expands consensus on MammaPrint as a prognostic tool to make treatment decisions for adjuvant chemotherapy in patients with lymph-node positive breast cancer
- Before the publication of MINDACT in 2016, MammaPrint was already recommended for lymph-node negative patients

Patient group	Recommendation
ER-positive, HER2-negative, **lymph node-negative** breast cancer	MammaPrint is endorsed as a prognostic marker for adjuvant endocrine therapy in node-negative breast cancers. It is also recommended for guiding the decision on adjuvant chemotherapy in node-negative tumors, identifying cases at low risk, with an excellent prognosis that would not warrant chemotherapy
ER-positive, HER2-negative, **lymph node-positive** breast cancer	Gene expression signatures were not uniformly endorsed for making treatment decisions regarding adjuvant chemotherapy in node-positive cases. Only MammaPrint and Oncotype DX was recommended. Patients with low risk tumor scores and a limited degree of nodal involvement appear to have a good prognosis with or without chemotherapy

Adapted from De-escalating and Escalating Treatments for Early Stage Breast Cancer: The St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017.

[I]Cardoso F, van't Veer LJ, Bogaerts J et al. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer. N Engl J Med 2016; 375: 717-29.

[II]Krop I, Ismaila N, Andre F et al. Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Focused Update. DOI: 10.1200/JCO.2017.74.0472 Journal of Clinical Oncology – published online before print July 10, 2017

[III]Curigliano G, Burnstein H, Winer E et al. De-escalating and Escalating Treatments for Early Stage Breast Cancer: The St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017. Ann Oncol 2017 mdx308.

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3. European Group on Tumour Markers (EGTM)

New recommendation in 2017

Issued: March 2017

- MammaPrint is the first and only multi-gene test to receive level 1A status, based on findings of the MINDACT trial[IV]
- Update based on evaluation of the most recent validation data available for all multigene tests

Patient group	Recommendation	Level of evidence
ER-positive, HER2-negative, **lymph node-negative** and **1-3 lymph node-positive** breast cancer	MammaPrint is recommended for determining prognosis and aiding decision-making for the administration of adjuvant chemotherapy to patients with ER-positive, HER2-negative, lymph node-negative and lymph node-positive (1-3 nodes) disease	1A

Adapted from Clinical use of biomarkers in breast cancer: Updated guidelines from the European Group on Tumor Markers (EGTM)

4. German Gynecological Oncology Group (AGO)

New recommendation in 2017

Issued: March 2017

- Update for the "Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer" gave MammaPrint a level 1A recommendation to justify withholding potentially unnecessary chemotherapy[V]

Factor	LOE[2009] (Level of Evidence)	CTS (Category of tumor marker study)
MammaPrint	1*	A*

* Simon et al, J Natl Cancer Inst 101: 1446-1452, 2009
Adapted from Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer, AGO 2017.

5. American Joint Committee on Cancer (AJCC)

Issued: 2016

- The AJCC has included the use of molecular biomarkers or "Multigene Panels" as "Stage Modifiers"[VI]
- This is the first time that genomic testing has been formally incorporated to help inform more accurate disease classification

Patient group	Change	Details of change
Hormone receptor-positive, HER2-negative, **lymph node-negative** breast cancer	Inclusion of Multigene Panels (when available) as Stage Modifiers - **MammaPrint**	A MammaPrint low risk score, regardless of tumor size, places the tumor in the same prognostic category as T1a-T1b N0 M0 (Level II)

Adapted from the AJCC TNM Cancer Staging Manual, Eighth Edition. Published October 2016.

6. European Society of Medical Oncology (ESMO)

Issued: 2015

- Clinical Practice Guidelines recommend MammaPrint for staging and risk assessment and to inform adjuvant chemotherapy treatment[VII]
- MammaPrint may be used to gain additional prognostic and/or predictive information to complement pathology assessment and to predict response to adjuvant chemotherapy
- In case of uncertainty regarding indications for adjuvant chemotherapy MammaPrint may be used to determine the individual recurrence risk and predict the benefit from chemotherapy

7. National BorstKanker Overleg Nederland (NABON) Dutch breast cancer guidelines

Issued: 2012

- NABON guidelines recommend MammaPrint may be used in individual cases with a hormone sensitive invasive ductal carcinoma if there is doubt about the indication for adjuvant chemotherapy on the basis of traditional prognostic factors[VIII]
- In 2016, NABON issued an update letter in response to the impact of the publication of the MINDACT trial. It provisionally concluded that MammaPrint may have added value in patients with pT1-2N0 and pT1-N1, ER-positive and HER2-negative invasive ductal breast cancer who are considered for chemotherapy

Learn more about how the MammaPrint test can help to personalize management decisions for early-stage breast cancer patients by visiting www.agendia.com, or keep up to date by following us on Twitter, Facebook or LinkedIn.

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[IV] Duffy MJ, et al. Clinical use of biomarkers in breast cancer: Updated guidelines from the European Group on Tumor Markers (EGTM). Eur J Cancer. 2017 Feb 27;75:284-298.
[V] AGO Breast Committee. Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer. Recommendations 2017. http://www.ago-online.de/en/guidelines-mamma/april-2017/
[VI] American Joint Committee on Cancer 2017. M.B.Amin et al. (eds.) AJCC Cancer Staging Manual, 8th Edition.
[VII] Senkus E, Kyriakides S, Ohno S, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol (2015) 26 (suppl_5): v8-v30
[VIII] Online Version of Dutch Guidelines Accessed – 13 July 2017(http://richtlijnendatabase.nl/en/richtlijn/breast_cancer/risk_profiling/gene_expression_profiles/prognostic_value.html)

MammaPrint is a US FDA cleared and CE-marked IVD intended for risk of recurrence for distant metastasis in early stage I and II breast cancer patients.

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