Mammostrat Breast Cancer Recurrence Assay

Definition

The Mammostrat® Breast Cancer Recurrence Assay is an immunohistochemical (IHC) assay that measures levels of five proteins in tumor tissue associated with risk of breast cancer recurrence.¹

- It is used in people with newly diagnosed, early stage breast cancer.
- The assay looks at five proteins and determines their expression levels in the tumor. The expression levels of these five markers are thought to influence whether the tumor will metastasize, increasing the patient’s chance of recurrence. These levels are then translated into a risk index, given as a percent chance of recurrence over 10 years.
- Physicians and patients may use the risk index as one factor in determining the course of treatment. Patients in the high risk category may benefit more from aggressive treatment, whereas patients in the low risk category may elect to forgo the aggressive chemotherapy.²

Test information

- The Mammostrat assay measures the expression level of five proteins by immunohistochemistry. These markers are believed to be associated with breast cancer recurrence.³
  - p53 plays a role in cell cycle regulation. Mutations in the p53 gene are associated with tumor growth.
  - HTF9C is implicated in DNA replication and cell cycle control.
- CEACAM5 is normally expressed in embryonic tissue, but is also found in some tumors.
- NDRG1 may have a role in helping tumors survive aggressive treatment.
- SLC7A5 can, when overexpressed, help sustain the high growth rate of cancer.

These levels are then translated into a quantitative “risk index” via a proprietary algorithm, which divides patients into groups with low, moderate, or high risk of recurrence:

<table>
<thead>
<tr>
<th>Risk index</th>
<th>Risk of breast cancer recurrence over 10 years</th>
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<tbody>
<tr>
<td>Low</td>
<td>7.6%</td>
</tr>
<tr>
<td>Moderate</td>
<td>16.3%</td>
</tr>
<tr>
<td>High</td>
<td>20.9%</td>
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</tbody>
</table>

**Guidelines and evidence**

- The NCCN does not specifically mention the use of Mammostrat in its most recent guidelines.
- The American Society of Clinical Oncology (ASCO, 2016) published a clinical practice guideline on the use of biomarkers to guide decision-making in women with early-stage invasive breast cancer. They recommend:
  - “If a patient has ER/PgR-positive, HER2-negative (node-positive or node-negative) breast cancer, the clinician should not use the five-protein assay (Mammostrat; Clarient, a GE Healthcare company, Aliso Viejo, CA) to guide decisions on adjuvant systemic therapy. Type: evidence based. Evidence quality: intermediate. Strength of recommendation: moderate.”
  - “If a patient has HER2-positive breast cancer or TN breast cancer, the clinician should not use the five-protein assay (Mammostrat) to guide decisions on adjuvant systemic therapy. Type: informal consensus. Evidence quality: insufficient. Strength of recommendation: strong.”
- A 2010 clinical study tested the assay’s ability to accurately predict risk of breast cancer recurrence in a cohort of 1,812 women with early stage breast cancer:
  - “The Mammostrat markers are biologically independent of one another and measure aspects of physiology distinct from proliferation, HER2 status, and hormone receptor status already assessed by IHC assays that are standard of care. Collectively these data add support to a potential role for Mammostrat in management of early-stage breast cancer.”
Criteria
• This test is considered investigational and/or experimental.

  o Investigational and experimental (I&E) molecular and genomic (MolGen) tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact, which typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), and/or performs better than an existing standard of care medical management option. Such tests are also not generally accepted as standard of care in the evaluation or management of a particular condition.

  o In the case of MolGen testing, FDA clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight and FDA clearance often does not assess clinical utility.

References