Oncotype DX Breast DCIS

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

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<th>Procedure addressed by this guideline</th>
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<td>Oncotype DX Breast DCIS Assay</td>
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What is Oncotype DX for breast cancer prognosis

Definition

Oncotype DX® is a gene expression assay designed to determine the risk of a breast cancer recurrence within 10 years of the original diagnosis.¹

- It is intended for early stage, hormone receptor-positive, lymph node-negative breast cancer.¹⁴
- Oncotype DX should be used with other standard methods of breast cancer assessment such as disease staging, grading, and other tumor markers.¹,²
- Oncotype DX results appear to correlate with chemotherapy benefit, which may help with the decision between tamoxifen only and adjuvant chemotherapy.⁵,⁶ Studies have demonstrated that the addition of Oncotype DX results changed treatment recommendations and decisions in 25% to 44% of patients, with the majority of recommendations changing from chemotherapy plus tamoxifen to tamoxifen only.⁷-⁹
- Oncotype DX can be used in individuals with ductal carcinoma in situ (DCIS) in addition to individuals with invasive carcinoma.

Test information

- Depending on the risk being calculated (local or distant metastasis), either a DCIS Breast Score® (DCIS or invasive carcinoma) or a Breast Recurrence Score® (invasive carcinoma) is calculated.¹⁰-¹³
- The Oncotype DX DCIS Breast Score® algorithm is intended for use in women with DCIS treated by local excision, with or without tamoxifen treatment. The score result is reported as a number between 0 and 100, with lower scores representing a low chance of recurrence and a higher score representing a high chance of recurrence within 10 years.¹⁰-¹³
• Oncotype DX measures the expression level of 21 genes (16 cancer and 5 reference) from paraffin-embedded breast tumor tissue.\textsuperscript{1} These sixteen genes consistently correlated with distant recurrence-free survival in three studies that explored the expression of 250 genes in breast tumor samples.\textsuperscript{5}

• The Oncotype DX DCIS score is calculated using a subset of 12 of the 21 gene Oncotype DX panel, including 7 cancer-related and 5 reference genes. On the patient report, average 10 year rates for any local/same breast recurrence (DCIS and invasive) as well as local invasive rate only are reported for a given DCIS Breast Score. Results of the DCIS Breast Score have the potential to change the treatment decision based on risk of local recurrence.\textsuperscript{10-13}

• The results are provided as a Recurrence Score\textsuperscript{®} (RS, 0-100) with higher scores reflecting higher risk of recurrence. Three risk categories help characterize prognosis:\textsuperscript{1,2}
  - Low risk (RS<18), \textasciitilde50% of patients tested
    - Least aggressive tumors
    - Metastasis unlikely
    - 7% recurrence by 10 yrs
  - Intermediate risk (RS 18-30), \textasciitilde25% of patients tested
    - More aggressive tumors
    - Metastasis more likely
    - 14% recurrence by 10 yrs
  - High risk (RS 31 or higher), \textasciitilde25% of patients tested
    - Most aggressive tumors
    - Metastasis most likely
    - 31% recurrence by 10 yrs

• Patients with high scores benefit the most from chemotherapy, showing a substantial reduction in 10 year recurrence. Patients with intermediate scores show questionable benefit from chemotherapy, whereas those with low scores benefit the least from chemotherapy.\textsuperscript{2,5,6}

**Guidelines and evidence**

• The National Comprehensive Cancer Network (NCCN, 2018) breast cancer treatment guidelines recommend the 21-gene Oncotype DX Breast assay in their treatment algorithm for hormone receptor-positive, HER2-negative breast cancer in both node-negative (category of evidence 1, predictive and prognostic purposes,
preferred test status) and node-positive (category of evidence 2A, prognostic purposes only) cancer.\(^1\)

- The 2007 evidence-based guidelines from the American Society of Clinical Oncology (ASCO) about breast cancer tumor marker use state:
  
  o “In newly diagnosed patients with node-negative, estrogen-receptor positive breast cancer, the Oncotype DX assay can be used to predict the risk of recurrence in patients treated with tamoxifen. Oncotype DX may be used to identify patients who are predicted to obtain the most therapeutic benefit from adjuvant tamoxifen and may not require adjuvant chemotherapy. In addition, patients with high recurrence scores appear to achieve relatively more benefit from adjuvant chemotherapy (specifically (C)MF) than from tamoxifen. There are insufficient data at present to comment on whether these conclusions generalize to hormonal therapies other than tamoxifen, or whether this assay applies to other chemotherapy regimens.”\(^3\)
  
  o In 2016, the American Society of Clinical Oncology (ASCO), stated: “If a patient has ER/PgR-positive, HER2-negative (node-negative) breast cancer, the clinician may use the 21-gene recurrence score (RS; Oncotype DX; Genomic Health, Redwood City, CA) to guide decisions on adjuvant systemic chemotherapy. Type: evidence based. Evidence quality: high. Strength of recommendation: strong.”\(^4\)

- The Evaluation of Genomic Applications in Practice and Prevention Working Group (EGAPP, 2009 and updated in 2016) found:
  
  o “Insufficient evidence to make a recommendation for or against the use of tumor gene expression profiles to improve outcomes in defined populations of women with breast cancer. In the updated 2016 publication, “evidence of clinical validity for Oncotype DX was confirmed as adequate. With regard to clinical utility, although there was evidence from prospective retrospective studies that the Oncotype DX test predicts benefit from chemotherapy, and there was adequate evidence that the use of Oncotype DX gene expression profiling in clinical practice changes treatment decisions regarding chemotherapy, no direct evidence was found that the use of Oncotype DX testing leads to improved clinical outcomes. Until definitive evidence for clinical utility is available, clinicians must decide on a case-by-case basis whether to offer the test to patients.”\(^5,6\)

- The 14th St Gallen International Breast Cancer Conference (2015) Expert Panel confirmed previously published recommendations:
  
  o Regarding Oncotype DX, the 2011 recommendations stated: “Several tests are available which define prognosis. These may indicate a prognosis so good that the doctor and patient decide that chemotherapy is not required. A strong majority of the Panel agreed that the 21-gene signature (Oncotype DX) may also be used where available to predict chemotherapy responsiveness in an
endocrine responsive cohort where uncertainty remains after consideration of other tests..." 17

- In 2015, the Panel “considered the role of multiparameter molecular marker assays for prognosis separately in years 1-5 and beyond 5 years and their value in selecting patients who require chemotherapy.” The Panel concluded that “only Oncotype DX commanded a majority in favor of its value in predicting the usefulness of chemotherapy.” 18

- Literature Review

  - Rakovitch et al. (2015) conducted a population cohort study (n=3320 women with DCIS) with a median follow-up period of 9.6 years. 19 Study authors demonstrated that the DCIS Score independently predicted the risk of local recurrence in women with DCIS treated with breast conserving surgery (HR, 2.15; 95% CI, 1.43-3.22). Patients considered low risk via the DCIS Score (62%) had 10-year local recurrence of 13%; intermediate risk (17%) patients had 10-year local recurrence of 33%; and high risk (21%) patients had 10-year local recurrence of 28%. The DCIS Score is intended to provide a quantified risk score for local recurrence to help clinicians guide treatment decisions and potentially reduced the effects of overtreatment with radiotherapy.

  - Study results of this trial and others indicate that despite the ability of Oncotype DX to reclassify patients into different risk groups, it is not clear if the risk estimation is accurate enough to induce changes in treatment strategies or disease management, or if the 10-year local recurrence of approximately 13% is still low enough for patients to successfully avoid radiation therapy and the risk of its associated complications. 20

Criteria

- This test is considered investigational and/or experimental.

  - 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.

  - 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


