Oncotype DX for Colorectal Cancer Recurrence Risk

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 Colon Cancer Assay</td>
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What is the Oncotype DX Colon Cancer Assay

Definition

The Oncotype DX® Colon Cancer Assay measures the expression of a panel of genes in stage II colon cancer tumors to predict the risk of future recurrence.¹

- Stage II colon cancer is defined by a primary tumor that has grown into or through the outermost layers of the colon, but has not spread to nearby lymph nodes or more distant metastasis.² At least 12 to 13 lymph nodes should be evaluated.³,⁴
- Stage II colon cancer is often treated with surgery alone with good prognosis.³,⁴ Adjuvant chemotherapy is not routinely recommended because it does not appear to improve 5-year survival rates by more than 5% among all people with stage II disease.³,⁴
- However, up to 25% of people with stage II disease will have a recurrence within 5 years.³ The decision about adjuvant chemotherapy is currently influenced by factors that help predict a higher recurrence risk, including:³,⁴
  - Inadequately sampled lymph nodes
  - Tumor characteristics such as T4 lesion (tumor penetrates to visceral peritoneum or adheres/invaded other organs²), perforation, poorly differentiated histology
  - Microsatellite instability and/or mismatch repair expression test results (particularly if considering 5-FU therapy only)
- These prognostic markers are imperfect and the need for additional validated prognostic markers is recognized.³
- The Oncotype DX Colon Cancer Assay proposes an additional method for stratifying recurrence risk to assist in the adjuvant chemotherapy decision. Genomic
Health, who markets the assay, suggests the optimal use may be for people with “standard risk” stage II colon cancer (T3 tumor, mismatch repair proficient/microsatellite stable) following surgery, where other accepted prognostic factors do not make the chemotherapy decision clearer.¹

Test information

- The Oncotype DX Colon Cancer Assay quantifies the expression of 12 genes from paraffin-embedded primary colon cancer tissue samples.¹
  - Seven cancer genes associated with recurrence-free interval: Ki-67, C-MYC, MYBL2, FAP, BGN, INHBA, GADD45B
  - Five reference genes (to normalize expression levels): ATP5E, PGK1, GPX1, UBB, VDAC2
- The results are provided as a Recurrence Score, which translates into a percent recurrence risk at three years. Further risk information is provided based on such characteristics as T3/T4 tumor grade and mismatch repair results.¹

Guidelines and evidence

National Comprehensive Cancer Network

- The National Comprehensive Cancer Network (NCCN, 2018) colon cancer guidelines state the following:⁴
  - “Several multigene assays have been developed in hopes of providing prognostic and predictive information to aid in decisions regarding adjuvant therapy in patients with stage II or III colon cancer.”
  - “In summary, the information from these tests can further inform the risk of recurrence over other risk factors, but the panel questions the value added. Furthermore, there is no evidence of predictive value in terms of the potential benefit of chemotherapy to any of the available multigene assays. The panel believes that there are insufficient data to recommend the use of multigene assays to determine adjuvant chemotherapy.”

Literature Review

There is insufficient evidence of clinical validity and clinical utility for the use of Oncotype DX for colon cancer as a prognostic or predictive assay among stage II and stage III A/B colon cancer patients.⁵-¹⁴ Several decision impact studies suggest that use of Oncotype DX leads to changes in treatment management, but study authors do not evaluate if such changes lead to improved survival or other health outcomes. No studies directly assessed clinical utility.
Overall, it is still unclear if use of this assay will accurately identify a subset of patients with stage II/III A/B colon cancer who can safely avoid the complications of unnecessary treatments, or if use of the assay will accurately identify a subset of patients who would most benefit from a particular chemotherapy regimen.

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


