Oncotype DX tumor gene expression profiling in stage II colon cancer

**Application: Prognostic, risk prediction**

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Elizabeth M. Webber, Jennifer S. Lin, Evelyn P. Whitlock


**Abstract**

Overall five-year survival for patients with stage-II colon cancer averages 75% after surgery alone. However, some of these patients have poorer outcomes, similar to patients with stage-III disease. The proposed use of the Oncotype DX assay is to improve risk stratification for recurrence in stage-II colon cancer.

**Clinical Scenario**

Onco type DX is used for profiling tumor gene expression in patients with Stage-II colon cancer to predict recurrence risk and inform treatment decisions following surgery.

**Test Development**

Four studies (n=1851) reported the results of the initial development of the Oncotype Dx assay in colon cancer. These studies were conducted by the manufacturer in partnership with the National Surgical Adjuvant Breast and Bowel Project and the Cleveland Clinic. [1][2][3] During initial development the assay comprised an 18-gene panel that included 7 genes for relapse-free survival prognosis in colon cancer to yield a prognostic recurrence score (RS), 6 genes to predict response to 5-fluorouracil/leucovorin (5FU/LV) chemotherapy to yield a predictive treatment score (TS), and 5 reference genes. Further development of the 12-gene RS in these four studies found that there were no apparent differences in gene expression patterns between stage-II and stage-III colon cancer patients. [4]

Subsequent validation of the 18 gene panel found that the RS score was a valid predictor of relapse-free survival. The TS score, however, was not found to be a valid predictor of treatment response.[5][6] Because of this result, these 6 predictive TS genes were not included in the test currently marketed by Genomic Health.

**Test Description**

Oncotype DX is a quantitative multi-gene, real-time polymerase chain reaction (RT-PCR) assay that measures gene expression in paraffin-embedded tumor tissues. [5] The Oncotype type DX assay that Genomic Health plans to market in 2010 will include 7 genes for relapse-free survival prognosis and 5 reference genes and yields a prognostic recurrence score (RS).[6]

**Public Health Importance**

Colorectal cancer is the third most common non-dermatological cancer in the United States and is the second leading cause of cancer-related death in the United States. The American Cancer Society estimates that 106,100 new cases of colon cancer (52,010 in men and 54,090 in women) were diagnosed in 2009. [7][8] Ongoing controversy exists as to whether adjuvant chemotherapy should be advised for patients with stage-II colon cancer. [9] Identification of patients at higher risk of recurrence may help to inform decisions surrounding the use of adjuvant chemotherapy to potentially improve prognosis after surgery.

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Limitations

Overall, we found very little evidence, most identified studies related to the Onco type DX assay for colorectal cancer were development or initial validation studies. Most studies were also presented as meeting abstracts and not as complete publications, including the only two studies related the clinical validity. Full critical appraisal and confirmation of reported results are not possible without more details on these studies. The validation studies represent retrospective analyses on only a subset of the patients in the prospectively designed QUASAR trial. It is not clear if these samples represent the full spectrum of patients or a specially selected group that may over-estimate the assay's performance. In addition, risk prediction was calculated as relative estimates between low-, intermediate, and high-risk categories, with a fairly narrow range across groups. The lack of a calculated absolute risk may lead to some difficulty in implementing this assay into clinical practice decisions and determining its true benefit. Further, no net benefit can be determined from validations studies that consider test performance only.
Conclusions

There is currently not enough evidence for a full evaluation of this assay. Although Genomic Health launched the Onco\textsuperscript{type} Dx colon cancer assay worldwide in January 2010, additional research is clearly needed before the value of this assay for clinical practice can be determined. The manufacturer has indicated that their reference laboratory will perform the Onco\textsuperscript{type} Dx colon cancer assay. At this point FDA approval will not be required for this assay because the assay will be performed in house by the Genomic Health commercial laboratory that is regulated and certified under the Clinical Laboratory Improvement Amendments (CLIA). [7]

Links


- For recent additions to the literature, see Pubmed special query
- U.S. Food and Drug Administration: Search FDA 510(k) database

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Competing interests

The authors have declared that no competing interests exist.

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