

INSTITUTIONAL EXPERIENCE, GAINS AND LESSONS, IN REGARDS TO ONCOTYPE DX TESTING AT LANDMARK MEDICAL CENTER

WOONSOCKET, RI:

Introduction: Oncotype DX, developed by Genomic Health, is a diagnostic test that quantifies the likelihood of disease recurrence in women with early-stage hormone estrogen receptor (ER) positive only breast cancer (*prognostic* significance) and assesses the likely benefit from certain types of chemotherapy (*predictive* significance).

Oncotype DX analyzes a panel of 21 genes within a tumor to determine a Recurrence Score. The Recurrence Score is a number between 0 and 100 that corresponds to a specific likelihood of breast cancer recurrence within 10 years of the initial diagnosis, though the score is not validated, though the buckets of Low, Intermediate or High Risk are when the patient receives / abides to 5 years of Tamoxifen. With this information, it may be possible for doctors and patients to make more informed decisions about breast cancer treatment options.

Oncotype DX was initially developed for women with early-stage invasive breast cancer with ER+ cancers whose lymph nodes do not contain tumor (**node-negative**). Typically in these cases, treatment with anti-hormonal therapy, such as tamoxifen or aromatase inhibitors, is planned, and the test can help define whether chemotherapy should or should not be added to that anti-hormone treatment. Oncotype DX is a noninvasive test that is performed on a small amount of the tissue removed during the original surgery lumpectomy, mastectomy, or core biopsy, which means no additional invasive procedure is required. To perform Oncotype DX, the pathologist will send several thin sections of the formalin-fixed, paraffin-embedded tissue sample to Genomic Health. Oncotype DX uses a highly reproducible laboratory process known as RT-PCR to determine the expression of the 21-gene panel. The Oncotype DX test results are then integrated with other laboratory test results to help doctors formulate a treatment plan based on the unique characteristics of the tumor. Since Oncotype DX became available in 2004, it has been used by over 10,000 physicians to help guide treatment for over 200,000 patients in 60+ countries.

Cost and cost-effectiveness: The current list price of Oncotype DX is \$4,175.00. Several studies indicate that the use of the Oncotype DX test is cost-effective. Average cost of adjuvant chemotherapy for breast cancer can be anywhere from 50,000 to 90,000\$. Thus with proper utilization of Onco Type Dx testing significant impact can be made on the wise utility of resources.

Key clinical studies: In collaboration with several independent investigators, Oncotype DX was evaluated in numerous studies involving over 3,300 patients. The results of three key studies appear below.

- **NSABP Study B-14:** Oncotype DX was clinically validated in a large, independent multi-center trial of patient samples from the NSABP Study B-14.2 Results demonstrate that Oncotype DX is an accurate and reliable predictor of breast cancer recurrence.

Study conclusion: The Recurrence Score has been validated as quantifying the likelihood of distant recurrence in tamoxifen-treated patients with node-negative, estrogen receptor-positive breast cancer.

- **NSABP Study B-20:** Samples of cancer tissue from a clinical trial (NSABP B-20) were used to show that Oncotype DX can predict chemotherapy benefit.¹⁸¹

Study conclusion: The Recurrence Score assay not only quantifies the likelihood of breast cancer recurrence in women with node-negative, estrogen receptor-positive breast cancer, but also predicts the magnitude of chemotherapy benefit.

- **Kaiser Permanente study:** A large clinical study conducted by Kaiser Permanente confirmed in a community setting that Oncotype DX helps predict the likelihood of breast cancer survival at 10 years.

Study conclusion: In a large, population-based study of lymph node-negative patients not treated with chemotherapy, the Recurrence Score was strongly associated with risk of breast cancer death among ER-positive, tamoxifen-treated and -untreated patients.

- **SWOG 8814 study:** In ER-positive, mainly post-menopausal tamoxifen-treated lymph node-positive women the Recurrence Score assay quantified the likelihood of breast cancer recurrence and also predicted the magnitude of chemotherapy benefit.

Oncotype DX TAILORx Trial:

Since the validation of the Oncotype DX Breast Cancer Assay Recurrence Score used a designed study of archived tumor samples from a randomized clinical trial it might be considered Level of Evidence I, a position that Genomic Health has taken. Others, including the NCCN, have considered this as retrospective evidence. Additionally, Oncotype DX is being evaluated in node negative, estrogen-receptor positive breast cancer in a prospective trial, the Trial Assigning Individualized Options for Treatment (**Rx**) (TAILORx), launched 2006 May, enrolled 10,000 people with intermediate results on the test; results are estimated to be completed in 2014.

UTILITY OF ONCOTYPE DX TESTING AT LAMDMARK MEDICAL CENTER:

Objective: To assess underutilization of Oncotype Dx testing and conceivable over utility of adjuvant chemotherapy in early stage hormone positive node negative breast cancer.

Methods: Retrospective review of cases of breast cancer; early stage, hormone positive, lymph node negative diagnosed at LMC during the years 2010 – 2012. Recurrence score through oncotype Dx testing was reviewed to see its impact on treatment.

Results: Breast Cancer Cases @ Landmark 2010-2012

- 50 cases; Stage 1-2 ER/PR positive and lymph node negative
- 18 Patients had oncotype testing performed
 - 12 with score of 25 or less – all received hormone treatment
 - 3 with score of 56, 20 & 24 – received chemotherapy
 - 2 with score of 4 and 12 – both refused any further treatment
 - 1 with score of 35-prior breast primary-only underwent bilateral mastectomies
- 5 Patients received chemotherapy with no Oncotype testing done, two of which had
 - bilateral breast CA at diagnosis; 1 with Stage 2A & 3B received chemo & hormones; the other with Stage 1 & 2 also received chemo & hormones
- 15 Patients received hormonal treatment – no oncotype testing done
- 12 Patients received no further treatment – no oncotype testing done

CONCLUSIONS:

At our institution we have observed that of all pertinent cases of breast cancers diagnosed in between 2010 – 2012, oncotype Dx testing was ordered in only 36% of the cases. Treatment proposed on the basis of recurrence score was as per the NCCN guidelines. 10% of the cases treated with adjuvant chemotherapy could have benefitted from the oncotype Dx testing. Hence, we need to focus on proper utilization of resources and checking of Oncotype Dx Testing in all early stage, stage I to II, ER positive, node negative breast cancer.