Allina Health

Oncology Clinical Service Line
System-wide Consensus Guidelines:
Oncotype DX Assay Testing for Treatment of Breast Cancer

These guidelines apply to clinical interventions that have well-documented outcomes, but whose outcomes may not be desirable for all patients

Reference #: SYS-PC-OCSL-CG-009

Origination Date: March 2018
Next Review Date: March 2021
Effective Date: March 2018

Approved Date: March 2018
Approval By: Allina Health Quality Council

System-wide Ownership Group: Allina Health Breast Cancer Program Committee

System-wide Information Resource: Manager of Clinical Programs

Hospital Division Quality Council: February 2018

Stakeholder Groups
Virginia Piper Cancer Institute

SCOPE:

Sites, Facilities, Business Units	Departments, Divisions, Operational Areas	People applicable to
All Facilities that perform breast conserving therapy for invasive carcinoma; Abbott Northwestern Hospital, Buffalo Hospital, Cambridge Medical Center, District One Hospital, Mercy Hospital, Mercy Hospital – Unity Campus, New Ulm Medical Center, River Falls Area Hospital, Regina Hospital, St. Francis Medical Center, United Hospital	Breast Surgeons Pathology Radiation Oncology Medical Oncology	Physicians, Advanced Practice Providers

PICO (TS) Framework

Population: Breast cancer patients

Intervention: Ordering of Oncotype DX Assay Testing for treatment by treating physician

Comparison: NA

Outcomes: Ensure Oncotype DX Assay Testing is performed in appropriate patients at the right interval

Timing: After breast cancer diagnosis.

Setting: Outpatient; Oncology

CLINICAL PRACTICE GUIDELINES:

1. When ordered, the Oncotype DX should be performed no less than 14 days after discharge from an Allina hospital.
2. Oncotype DX may be ordered by the treating physician, after discussion with the patient.
3. Oncotype DX is recommended in patients with stage: pT1b, pT1c, pT2, pT3 and N0 or N1(mi)
4. Oncotype DX is also to be considered in select patients with 1-3 positive axillary lymph nodes
5. In patients with multiple tumors:
   a. If the tumors are histologically and phenotypically similar (in regards to type, grade, and hormone expression), only the larger tumor should be sent for Oncotype DX testing.
   b. If the tumors are histologically different, attempts should be made to determine if testing is necessary on more than one tumor. The larger and / or higher grade tumor is generally the best choice for Oncotype DX testing. (suggested by pathology)
6. Oncotype DX should not be ordered in ER negative, HER2 positive tumors, or stage IV
7. In patients with DCIS there is currently (2017) insufficient evidence to recommend performing Oncotype DX to guide treatment decisions

SUPPORTING EVIDENCE:

Although the current NCCN guidelines do not mandate the use of molecular gene expression assays such as Oncotype DX, based on the increasing body of evidence, it is suggested as an additional prognostic/predictive test that can be considered in certain subsets of patients to aid in decisions regarding the benefit of adjuvant chemotherapy (1).

As of 2017, based on the available data, the NCCN Panel Members believe that that the 21-gene assay (Oncotype DX) is the most validated multigene assay to predict who is most likely to respond to systemic chemotherapy.

The 21-gene assay (Oncotype DX) is among the best validated prognostic and predictive gene assays. Patients with a high risk score (>31) clearly benefit from chemotherapy, whereas patients with a low risk score (<18) do not appear to benefit from the addition of chemotherapy, regardless of the number of positive lymph nodes (5). Multiple studies have shown that the 21-gene assay recurrence score is predictive of recurrence in postmenopausal women treated with Tamoxifen or Aromatase inhibitors (2, 3, 4, 5, 6, and 7). The Oncotype DX recurrence score has also shown to predict response to adjuvant chemotherapy (5,6,7), regardless of the number of axillary lymph nodes involved, although the largest studies in node positive patients were retrospective (5,7). The TAILORx study showed prospectively that patients with a low risk recurrence score (<11) do not benefit from chemotherapy, as their 5-year risk of systemic recurrence without receiving chemotherapy was 1% (13).

The additional benefit from adjuvant chemotherapy in addition to endocrine therapy in patients with an intermediate Recurrence Score (18-25) is currently still unclear. The TAILORx study is prospectively collecting that information (13). The ongoing RxPONDER trial is evaluating whether adjuvant chemotherapy is beneficial in patients with hormone receptor positive, HER-2 negative breast cancer with positive axillary nodes and a recurrence score of 25 or less (14).

We believe that the decision to order Oncotype DX or other molecular predictive assay, should be made in conjunction with the discussion of the short and long term toxicity risks of chemotherapy, therefore should be deferred to the Medical Oncologist and involve the participation of the patient.

DEFINITIONS: N/A
SPECIAL ENTITIES: N/A
FORMS: N/A
ALGORITHM: N/A
EXCEPTIONS N/A

ADDENDUM: Plan for Monitoring and Adherence
Who will be measured for guideline adherence?
- Physicians

Where is the data located?
- EDW/Tumor registry

How will the guideline adherence be monitored?
- It will be monitored through the Breast Program Committee

What will be measured?
- % patients getting inappropriate Oncotype DX
- % Candidates for Oncotype DX receiving test
- % Candidates for Oncotype DX not tested but receiving chemo

When will adherence data be collected?
- A minimum of yearly

Allina Health

REFERENCES:

1. Jeffrey SS, Lonning PE, Hillner BE. Genomics-based prognosis and therapeutic prediction in breast cancer. J Natl Compr Canc Netw 2005; 3:291-300. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16002001

2. Paik S, Shak S, Tang G, et al. A multigene assay to predict recurrence of Tamoxifen-treated node negative breast cancer. N Engl J Med 2004; 351:2817-2826. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15591335

3. Dowsett M, Cuzick J, Wale C, et al. Prediction of risk of distant recurrence using the 21-gene recurrence score in node negative and node positive postmenopausal patients with breast cancer treated with anastrozole or tamoxifen: a TransATAC study. J Clin Oncol 2010; 28: 1829-1834. Available at: http://www.ncbi.nlm.nih.gov.pubmed/20212256

4. Mamounas EP, Tang G, Fisher B, et al. Association between the 21-gene recurrence score assay and the risk of locoregional recurrence in node-negative, estrogen receptor –positive breast cancer: results from NSABP-B14 and NSABP B-20. J Clin Oncol 2010; 28:1677-1683. Available at: http://www.ncbi.nlm.nih.gov.pubmed/20065188

5. Albain KS, Barlow WE, Shak S, et al. Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, estrogen receptor-positive breast cancer on chemotherapy: a retrospective analysis of a randomized trial. Lancet Oncol 2010; 11:55-65. Available at: http://www.ncbi.nlm.nih.gov.pubmed/20005174

6. Paik S, Tang G, Shak S et al. Gene expression and benefit of chemotherapy in women with node negative, estrogen receptor-positive breast cancer. J Clin Oncol 2006; 24:3726-3734. Available at: http://www.ncbi.nlm.nih.gov.pubmed/16720680

7. Tang G, Shak S, Paik S, et al. Comparison of the prognostic and predictive utilities of the 21-gene Recurrence Score assay and Adjuvant! for women with node-negative, ER-positive breast cancer: results from NSABP B-14 and NSABP B-20. Breast Cancer Res treat 2011; 127:133-142. Available at: http://www.ncbi.nlm.nih.gov.pubmed/21221771

8. Van de Vijer MJ, He YD, van't Veer LJ, et al. A gene-expression profiling predicts clinical outcome of breast cancer. Nature. 2002; 415:530-536. Available at: http://www.ncbi.nlm.nih.gov.pubmed/11823860

9. Knauer M, Mook S, Rutgers EJ, et al. The predictive value of the 70-gene signature for adjuvant chemotherapy in early breast cancer. Breast Cancer Res Treat 2010; 120:655-661. Available at: http://www.ncbi.nlm.nih.gov.pubmed/20204499

10. Dowsett M, Sestak I, Lopez-Knowles E, et al. Comparison of PAM50 risk of recurrence score with Oncotype DX and IHC4 for predicting risk of distant recurrence after endocrine therapy. J Clin Oncol 2013; 31:2783-2790. Available at: http://www.ncbi.nlm.nih.gov.pubmed/23816962

11. Sestak I, Cuzick J, Dowsett M at al. Prediction of late distant recurrence after 5 years of endocrine treatment: a combined analysis of patients from the Austrian breast and colorectal cancer study group 8 and arimidex, tamoxifen alone or in combination randomized trials using the PAM50 risk of recurrence score. J Clin Oncol 2015; 33; 916-922. Available at: http://www.ncbi.nlm.nih.gov.pubmed/25332252

12. Sparano JA, Gray RJ, Makower DF et al. Prospective validation of a 21-gene expression assay in breast cancer. New England J of Med 2015; 373:2005-2014. Available at: http://www.nejm.org/doi/full/10.1056/NEJMoa1510764

13. Clinical trial underway: Hormone therapy with or without combination chemotherapy in treating women who have undergone surgery for node negative breast cancer (the TAILORx trial), Clinical trial ID: NCT00310180. Available at:http://clinicaltrials.gov/ct2/show/NCT00310180?term=TAILORx&rank=2

14. Clinical trial underway: A phase III, randomized clinical trial of standard adjuvant endocrine therapy +/- chemotherapy in patients with 1-3 positive nodes, hormone receptor positive and HER2 negative breast cancer with recurrence score (RS) of 25 or less. RXPONDER: A clinical trial RX for positive node, endocrine responsive breast cancer. Clinical trial ID: NCT01272037. Available at: http://clinicaltrials.gov/show/NCT01272037

15. Cardoso F, van't Veer LJ, Bogaerts J, et al. 70-gene signature as an aid to treatment decisions in early breast cancer. The MINDACT trial. N Engl J Med, 2016; 375(8):717-729. Available at: http://www.ncbi.nlm.nih.gov.pubmed/27557300

Related Guidelines/Documents

Name	Content ID	Business Unit where Originated
N/A		

Guidelines/Documents Replacing

Name	Content ID	Business Unit where Originated
N/A		