



June 27, 2014

To: submissions@nccn.org

Re: Submission Request – Breast Cancer

Submitted by:

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Date of request: 6/27/2014

NCCN Guidelines Panel: Breast Cancer- July 20, 2014

On behalf of Genomic Health Inc., I respectfully request the **NCCN Breast Panel** to review the enclosed data for inclusion of the **Oncotype DX® Breast Cancer Assay** in the recurrence risk assessment of patients with 1-3 Node Positive, ER Positive, HER-2 negative early stage breast cancer.

Specific change: Recommend the Oncotype DX Breast Cancer Assay as a component of the treatment guideline for HER-2 negative, ER-positive tumors (BINV-6) as an additional bullet (Proposed bullet: The panel recommends that Oncotype DX Breast Cancer assay be considered for patients with 1-3 Node Positive, ER Positive, HER-2 negative early stage breast cancer to inform the individualized adjuvant treatment discussion).

FDA Clearance: FDA clearance is not required for this assay because the assay is performed in the central laboratory at Genomic Health that is regulated and certified under the Clinical Laboratory Improvement Amendments (CLIA) and the College of American Pathologists (CAP).

Rationale: Inclusion of this assay (studied in over 3,500 N+ patients) in the treatment decision algorithm for patients with 1-3 positive nodes, ER+, HER-2-neg early stage breast cancer will reduce variability of recurrence risk assessment and provide prediction of chemotherapy benefit, which will lead to a more informed treatment decision based on the individual patient's tumor biology and thus, increasing the confidence of physicians and patients in the estimates of recurrence risk and expected chemotherapy benefit.

The following articles are submitted in support of this proposed change.

Analytical validation studies:

1. Cronin M et al. *Am J Pathol.* 2004; 164(1):35–42.
2. Cronin M et al. *Clin Chem.* 2007; 53(6):1084-91.

Clinical validation studies in node-positive patients:

3. Albain KS et al. *Lancet Oncol.* 2010; 11(1): 55-65.
4. Dowsett M et al. *J Clin Oncol.* 2010; 28 (11): 1829-34.

Additional clinical studies in node-positive patients (supportive):

5. Gianni L et al. *J Clin Oncol.* 2005; 23(29): 7265-77.
6. Badve SS et al. *J Clin Oncol.* 2008; 26(15):2473-81.
7. Chang J et al. *Breast Cancer Res Treat.* 2008; 108(2): 233-40.
8. Akashi-Tanaka S et al. *Breast.* 2009; 18(3): 171-4.
9. Mamounas EP et al. ASCO Breast Cancer Symposium; September 2012; San Francisco, CA. Abstract #1.
10. Vacirca J et al. American Society for Clinical Oncology; June 2013; Chicago, IL. Abstract #565.
11. Penault-Llorca FM et al. American Society for Clinical Oncology; June 2014; Chicago, IL. Abstract #11052.

Clinical utility studies in node-positive patients:

12. de Boer RH et al. *Med J Aus.* 2013;199: 205-8.
13. Eiermann W et al. *Ann Oncol.* 2013; 24(3): 618-24.
14. Yamauchi H et al. *Clin Breast Cancer.* 2014; 14(3):191-7.
15. Oratz R et al. *J Oncol Pract.* 2011; 7(2): 94-9.
16. Bargallo JER et al. European Society for Medical Oncology Congress; September 2012; Vienna, Austria. Abstract 289P.

Sincerely,



Amy P. Sing, MD Senior Director, Medical Affairs

Additional Information:

Clinical and Economic Utility: Since the 2011 NCCN Task Force publication the assay has demonstrated clinical utility to physicians, patients, society and payers in multiple clinical and economic utility studies. Numerous studies from around the world have shown that use of the Recurrence Score result in clinical practice is cost-effective/cost-saving. The following studies support the health economic utility of the assay in US patient populations:

17. Hornberger J et al. *J Oncol Pract.* 2011; 7(3 Suppl): e38s-45s.
18. Hornberger J et al. *J Natl Cancer Inst.* 2012;104(14):1068-79.
19. Reed SD et al. *Genet Med.* 2013;15(3):203-11.

Additionally, Genomic Health data based on tests ordered suggests that *Oncotype DX* is utilized outside the investigational setting in many NCCN centers and that a significant number of node-positive patients tested have a low Recurrence Score result. Published and non-published data suggest that oncologists rely upon the evidence showing that, similar to node-neg patients, the *Oncotype DX* assay predicts magnitude of response to adjuvant chemotherapy and/or predicts the 10-yr risk of distant recurrence for patients with node-positive disease and supports treatment of a majority of these low risk patients with hormonal therapy alone.

Overall testing resulted in less frequent recommendations for chemotherapy in low risk patients

- The clinical utility studies have shown consistency regarding the assay's impact on physician's treatment recommendations. Treatment recommendations changed on average 30% of the time.¹²⁻¹⁶
- Consistency was also seen across the studies in the percentage of recommendations for increasing and decreasing treatment intensity.
- Similar to the node-neg studies, the *Oncotype DX* Breast Cancer Assay has been evaluated in multiple health economic analyses, suggesting that use of the test will potentially reduce overall cost by reducing chemotherapy use.¹⁷⁻¹⁹

In summary, *Oncotype DX* guided treatment decisions improve outcomes for node-positive patients and society. The consistent high rate of decision change likely reflects how the quantitative information provided by the Recurrence Score result is clinically meaningful to physicians and patients, and addresses the less precise nature of risk assignment based on the conventional clinical and pathologic characteristics, which can lead to a lack of confidence in the overall treatment plan.