



The Oncotype DX Recurrence Score® Test: A Brief Summary of the Assay that Revolutionized the Treatment Landscape for Early-Stage Hormone Receptor-Positive Breast Cancer

The one size fits all approach: a thing of the past

The majority of invasive breast cancer diagnoses are hormone receptor-positive (HR+), meaning that the cancerous cells have high levels of estrogen receptors and/or progesterone receptors. Thus, these cells grow in response to the hormone estrogen. Historically, all women with this type of diagnosis were offered a surgical intervention, followed by chemotherapy, and lastly a regimen of estrogen blocking therapy such as tamoxifen. Despite the unpleasant side effects related to chemotherapy, experts continued to recommend it due to the known benefits of reducing local and distant recurrence.

As advances in research began to focus on the molecular basis of breast cancer, we began to see physicians shift to more individualized treatment options rather than a “one size fits all” approach. Emerging data revealed that certain tumor characteristics could potentially predict which patients were likely to have a breast cancer recurrence and thus would benefit from chemotherapy. On the contrary, this also suggested that some individuals could safely forgo chemotherapy, meaning that many women were potentially receiving unnecessary treatments.

The Oncotype Dx Breast Recurrence Score® test predicts who will benefit from chemotherapy

The development of the 21-gene assay known as the Oncotype DX Breast Recurrence Score® test [Genomic Health (now Exact Sciences)] in 2004 revolutionized the concept of personalized medicine [1]. Since 2008, the Oncotype DX Breast Recurrence Score® test has been recommended by multiple national guidelines as a way to prevent the overtreatment of early stage hormone-receptor-positive, HER2-negative, axillary lymph node-negative breast cancer [1].



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This test uses genomic material from breast tumor samples removed during surgery. Samples are carefully analyzed for genes that regulate cancer growth. Based on this analysis, a Recurrence Score ranging from 0 to 100 is generated. Scores of 15 or less are associated with a low risk of distant recurrence and, therefore, these individuals with these low scores can safely forgo chemotherapy. Recurrence scores of 26 or higher, however, are predictive of an increased risk of recurrence, and thus chemotherapy is recommended. Until 2018, scores between 16 and 25 were considered intermediate and were not associated with a definitive treatment option.

The TAILORx trial shows further precision of the Oncotype DX® test

In 2018, long-term data from the landmark clinical trial known as TAILORx confirmed that women with low Recurrence Scores could be spared chemotherapy without increasing their risk of their cancer coming back. The trial also finally answered the question about ‘intermediate’ Recurrence Scores. Researchers saw that in women with scores between 16 and 25, outcomes were highly dependent upon menopausal status and/or age, as shown in Figure 1. These data allowed researchers to establish new treatment recommendations based on Recurrence Score, at least for post-menopausal women. The TAILORx trial established that women 50+ years old with Recurrence Scores between 0 and 25 would not benefit from chemotherapy. The majority of women in this age group score between 0 and 25, thus these new parameters will likely spare thousands of women from unnecessary treatments. But, the TAILORx trial *also* revealed that these scores may mean something different for women <50 years old. While younger women with scores between 0 and 15 showed no benefit from chemotherapy, individuals with scores between 16 and 25 showed some benefit from chemotherapy. For instance, scores between 16 and 20 showed a ~1.6% benefit from chemotherapy, and scores between 21 and 25 showed ~6.5% benefit. Prior to



Figure 1: Chemotherapy benefits among women >50 and 50 y.o. base on recurrence scores (RS). Images adapted from <https://www.oncotypeiq.com> [6].

the trial, the exact benefit of chemotherapy within these ranges was unclear. This suggests that reviewing the risks and benefits of chemotherapy are more important than ever for premenopausal women with Recurrence Scores between 16 and 25, and shared-decision making is essential for women in this group.

The RxPONDER trial tells us that Oncotype DX® can predict chemotherapy benefits for post-menopausal women with 1-3 positive lymph nodes.

In December 2021, the highly anticipated RxPONDER trial results were published in *The New England Journal of Medicine* [3]. Previous interim analyses showed such significant impact that the use of the test for HR+/HER2 node-positive diagnoses had already been incorporated into the National Comprehensive Cancer Network (NCCN) guidelines, but under the caveat of its being classified as Category 2 level of evidence. The highest level of evidence is Category 1 [4].

The newest results show that post-menopausal women with HR+/HER2-breast cancer with one to three positive lymph nodes and a Recurrence Score between 0 and 25 can forgo chemotherapy regardless of tumor size, grade, or number of lymph nodes involved. Data from the study showed that at five years of follow-up, post-menopausal women with this diagnosis that underwent both chemotherapy plus endocrine therapy had similar outcomes as women that received endocrine therapy alone. This means that chemotherapy did not benefit this group of women [3].

In contrast, the data also show that pre-menopausal women with HR+/HER2-breast cancer with one to three positive lymph nodes and a Recurrence Score between 0 and 25 significantly benefit from chemotherapy. Data showed that at five years of follow-up, pre-menopausal women that underwent both chemotherapy plus endocrine therapy had significantly better outcomes than women that received endocrine therapy alone. This means that the chemotherapy plays a critical role in reducing the risk of recurrence in this group of women. It is currently thought that this benefit may be related to the suppression of ovarian function that accompanies chemotherapy, however, this hypothesis has yet to be tested.

Because of the RxPONDER trial, a node-positive breast cancer diagnosis no longer automatically means that chemotherapy is recommended. Instead, an Oncotype DX Breast Recurrence Score® test result and menopausal status can be used to carefully tailor recommendations to the individual patient.

Other applications of the Oncotype Dx Breast Recurrence Score® test for women with HR+/HER2- Breast Cancer

Previous studies have suggested that Oncotype DX® may be useful in predicting patients that may benefit from neoadjuvant therapies (therapy before surgery) [7,8]. However, national guidelines do not currently recommend the Oncotype DX® to guide clinical decision making for neoadjuvant therapies. Due to the groundbreaking paradigm shifts made as a result of Oncotype DX®, it is likely that future clinical trials will be focused on understanding its utility in a wider range of chemotherapy applications.

What does this mean for Bay Area Cancer Connection clients?

Women with early-stage, hormone receptor-positive, HER2-negative breast cancer may be able to forgo chemotherapy depending on their lymph node status, age, and Oncotype DX Recurrence Score® test results. If women are unsure if they are candidates for this test, or if they have already had this test and do not understand their results, Personalized Cancer Information and Education Specialists at Bay Area Cancer Connections can guide them through the most recent clinical trials and national guidelines to help them understand their unique situation.

References:

1. Exact Sciences.com, Company History. 2021. Accessed December 2021.
2. Sparano J.A., Gray R.J., Makower, D.A., et al. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. *N Engl J Med* 2018; 379:111-121, doi: 10.1056/NEJMoa1804710
3. Kalinsky K., Barlow W.E., Gralow J.R., et al. 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer. *N Engl J Med*, 2021. doi: 10.1056/NEJMoa2108873
4. National Cancer Comprehensive Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version. 1.2022-November 24, 2021.
5. Genomic Health Inc. About the Oncotype DX Breast Recurrence Score® Test. 2021
6. (<https://www.oncotypeiq.com/en-US/breast-cancer/healthcare-professionals/oncotype-dx-breast-recurrence-score/about-the-test>) Accessed December 2021.
7. Iwata H, Masudet N., Yamamoto Y., al. Validation of the 21-gene test as a predictor of clinical response to neoadjuvant hormonal therapy for ER+, HER2-negative breast cancer: the TransNEOS study. *Breast Cancer Res Treat.* 2019 Jan;173(1):123-133. doi:10.1007/s10549-018-4964-y
8. Pease A.M., Riba L.A., Gruner R.A., et al.. Oncotype DX Recurrence Score as a Predictor of Response to Neoadjuvant Chemotherapy. *Ann Surg Oncol.* 2018, 26(2):366-371 doi: 10.1245/s10434-018-07107-8