

From Tumour Tissue to Treatment Decision: The Role of Oncotype DX

Dr Janet Jincy Moni



Introduction

Breast cancer is a heterogeneous disease comprising several biological subtypes with distinct prognostic and therapeutic implications. Over the past three decades, advances in molecular pathology have transformed breast cancer management from a "one-size-fits-all" approach to a personalised treatment strategy. One of the most significant developments has been the introduction of genomic assays such as Oncotype DX, which help clinicians identify patients who are likely to benefit from chemotherapy and those who can be safely treated with endocrine therapy alone.

Historical Background

The foundations of personalised treatment in breast cancer were established through landmark clinical trials conducted during the 1980s and 1990s.

The NSABP B-14 trial investigated women with oestrogen receptor (ER)-positive, lymph node-negative breast cancer and demonstrated that five years of tamoxifen significantly reduced breast cancer recurrence and improved long-term outcomes compared with placebo. This study established endocrine therapy as the standard treatment for many patients with hormone receptor-positive disease.

Subsequently, the NSABP B-20 trial demonstrated that adding chemotherapy to tamoxifen further reduced recurrence risk in some women with ER-positive, node-negative breast cancer. The benefit was particularly evident in younger women, highlighting the need to identify which patients genuinely benefit from chemotherapy and which could avoid unnecessary treatment.

These studies raised an important clinical question: how can clinicians accurately identify patients who will benefit from chemotherapy?

Why Is It Important to Identify Those Who Benefit from Chemotherapy?

Although chemotherapy can significantly reduce recurrence risk in selected patients, it is associated with considerable toxicity and long-term adverse effects. These include:

- Reduced fertility
 - Cardiotoxicity and heart damage
 - Fatigue
 - Hair loss
 - Increased infection risk
 - Potential long-term effects on quality of life
- Avoiding unnecessary chemotherapy therefore remains a major objective in modern breast cancer care.

The Development of Oncotype DX

To address this challenge, researchers developed the Oncotype DX Breast Recurrence Score® assay, a genomic test that evaluates the biological behaviour of breast cancers at the molecular level.

The test is performed on a formalin-fixed, paraffin-embedded tumour specimen. The pathologist selects the tumour block containing the most representative and highest-grade invasive carcinoma. The selected tissue is then sent to a specialised laboratory for molecular analysis.

The assay analyses the expression of 21 genes, including 16 cancer-related genes and 5 reference genes, to generate a personalised Recurrence Score.

Understanding the Recurrence Score

The Recurrence Score (RS) ranges from 0 to 100 and provides information regarding both prognosis and the likely benefit of chemotherapy.

Historically, recurrence scores were classified as:

Low risk: RS <18

Intermediate risk: RS 18–30

High risk: RS ≥31

Following the landmark TAILORx trial, recurrence score interpretation was refined:

RS 0–25: Most women with node-negative disease derive little or no benefit from chemotherapy and can be treated effectively with endocrine therapy alone.

RS 26–100: Significant benefit from chemotherapy is observed, and adjuvant chemotherapy is generally recommended.

The recurrence score therefore provides information beyond traditional clinicopathological factors such as tumour size, grade, and patient age, allowing truly personalised treatment decisions.

Prognostic and Predictive Value

A major strength of Oncotype DX is that it provides both prognostic and predictive information.

Prognostic Value

The test estimates the risk of distant recurrence despite endocrine therapy alone, such as tamoxifen. Patients with low recurrence scores generally have excellent long-term outcomes with endocrine therapy alone.

Predictive Value

The assay predicts the likelihood that chemotherapy will reduce recurrence risk. Patients with high recurrence scores derive the greatest benefit from chemotherapy, whereas those with low scores gain little additional advantage.

Key Clinical Evidence

NSABP B-14

Paik and colleagues analysed tumour samples from the NSABP B-14 trial and demonstrated that the recurrence score was a powerful predictor of distant recurrence in patients treated with tamoxifen.

NSABP B-20

Further analysis of the NSABP B-20 trial showed that patients with high recurrence scores experienced substantial benefit from chemotherapy, while those with low scores did not.

TAILORx Trial

The TAILORx trial enrolled more than 10,000 women with hormone receptor-positive, HER2-negative, node-negative breast cancer. The study demonstrated that most women with recurrence scores between 0 and 25 could safely avoid chemotherapy without compromising survival outcomes.

RxPONDER Trial

The RxPONDER study extended the use of recurrence score testing to patients with limited node-positive disease and demonstrated that postmenopausal women with recurrence scores of 25 or less could often avoid chemotherapy, whereas some premenopausal women still benefited from treatment.

Together, these studies established Oncotype DX as one of the most clinically validated genomic assays in breast cancer management.

Economic Benefits of Oncotype DX

In addition to its clinical value, Oncotype DX offers important economic benefits.

Using a representative cohort of 100 women with early-stage ER-positive, node-negative breast cancer, the average chemotherapy-related cost is estimated to be approximately £5,000 per patient, including:

- Chemotherapy drugs
- Administration costs

- Monitoring and investigations
- Supportive medications
- Management of treatment-related complications

Without genomic testing, the total chemotherapy-related expenditure for 100 patients may approach **£500,000**.

By identifying patients who are unlikely to benefit from chemotherapy, Oncotype DX can substantially reduce unnecessary treatment. In a typical cohort:

- Approximately 20% of patients would have a high recurrence score and receive chemotherapy.
- Approximately 30% would fall into an intermediate category requiring individualised discussion.
- Approximately 50% would have a low recurrence score and safely avoid chemotherapy.

This approach has been estimated to generate savings of approximately £168,400 per 100 patients, while simultaneously reducing treatment-related toxicity and improving quality of life.

Additional benefits include:

- Fewer chemotherapy-related side effects
- Reduced hospital attendances
- Lower supportive care requirements
- Reduced emergency admissions
- Improved patient experience
- More efficient utilisation of NHS resources

Conclusion

The introduction of Oncotype DX has transformed the management of early-stage hormone receptor-positive breast cancer. Building on evidence from NSABP B-14 and NSABP B-20, the assay provides both prognostic and predictive information that helps clinicians individualise treatment decisions.

The Recurrence Score enables identification of patients who can safely avoid chemotherapy while ensuring that those most likely to benefit receive appropriate treatment. Landmark studies such as TAILORx and RxPONDER have further validated its role in contemporary breast cancer practice.

Beyond its clinical benefits, Oncotype DX also contributes to more efficient healthcare delivery through the reduction of unnecessary chemotherapy and associated costs. By integrating pathology, molecular diagnostics, and evidence-based medicine, Oncotype DX truly transforms tumour tissue into informed treatment decisions.

References

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