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## Paving the way for personalised medicine

### Why the Oncotype DX Breast Recurrence Score® test is leading the way in a new age of medicine

In a consumer society with bespoke demands, broad choice and online identities, we are often told that everything is becoming more individual. Think, for example, of the 80,000 different combinations of coffee order available at Starbucks, or the huge variety of colours and features available when buying a new car.

The latest clinical approaches to medicine are no exception to this trend of ensuring that everything is tailored with maximum precision.

Traditionally, drugs have been developed to target an entire population, the so-called 'one size fits all' approach. However, such an approach fails to take into account the wide variety in responses to medicine across different patients. It is a rarely cited, yet widely accepted, scientific fact that most advanced medicines only work for a proportion of the population [1] – GlaxoSmithKline's late head of genetics, Allen Roses, once ruffled feathers by admitting that 90% of therapies are only effective in 30 to 50% of people [2].

Breast cancer is a disease which certainly requires a personal approach. Often regarded as a single disease best treated with chemotherapy, there are in fact many forms of breast cancer, all

of which develop differently and require different treatment plans.

*The Lancet's* recent overview of the benefits of adjuvant systemic therapy found that cytotoxic chemotherapy and hormonal therapy increased disease-free and overall survival for patients with stage I or stage II breast cancer. However the picture is much more complicated than simply "chemotherapy improves survival rates": the odds of recurrence and mortality vary widely between patients with different forms of breast cancer, treated with various types of chemotherapy.

Use of chemotherapy has since been widely recommended for selected patients with node-negative breast cancer due to the high risk of distant spread and the absolute survival benefit of up to 10% [3,4].

However, between 70 and 95% of node-negative patients remain disease-free after hormone therapy alone at 10 years [5]. As such, the key is in identifying high-risk patients who may benefit from chemotherapy, and patients at low risk of recurrence who may be able to avoid the physical and emotional toll taken by such aggressive treatment. This is where the Oncotype DX® test comes into play.

Examining the expression of 21 genes in a patient's breast tumour tissue, the Oncotype DX Breast Recurrence Score test provides personalised information for tailoring treatment based on the biology of the patient's individual disease. The results of the analysis are fed into a formula that gives a number known as the Recurrence Score® result. This value – a number from 0 to 100 – can provide information about how likely the individual's breast cancer is to recur within 10 years of diagnosis and, crucially for an individual, the likelihood that the patient will benefit from chemotherapy.

Recurrence scores of 18 or less identify patients at low risk of recurrence and absence of benefit from chemotherapy. A high risk recurrence scores of 31 or more identifies women with a 1 in 5 risk of recurrence and a 28% improved survival rate with chemotherapy after surgery. The test is recommended care in four Breast Cancer International Guidelines [6] and recent data from clinical trials has confirmed its value [7].

Recommended by the National Institute for Health and Clinical Excellence (NICE) in 2013,

researchers analyse Oncotype DX test results at Genomic Health's laboratories in Redwood City, California



the test informs adjuvant chemotherapy decisions for patients with node-negative, oestrogen receptor positive (ER+), and human epidermal growth factor receptor 2 negative (HER2-) [8]. Through gene expression profiling, it can accurately identify breast cancer patients with a low risk of recurrence who are predicted to derive minimal benefit from chemotherapy. This personalised approach to treatment is revolutionising the way in which breast cancer – in addition to other types of the disease – is treated, and is crucial to optimising patient care.

A recent study addressed the extent to which the test has helped breast cancer patients avoid unnecessary chemotherapy. Prior to the NICE recommendation, the Breast Recurrence Score™ was evaluated in a pilot study from May to December 2012 in Greater Manchester. The study assessed both node-negative and node-positive patients who were considered as needing chemotherapy by their clinicians, with the aim of evaluating the impact of the Oncotype DX test on chemotherapy use [9]. The study assessed 201 patients treated for early stage breast cancer, all with ER+ and HER2-negative breast cancer. The Recurrence Score result had a significant impact on treatment recommendations, with only 74 patients (36.8%) receiving chemotherapy.

The remaining 127 patients (63.2%) received endocrine therapy only as their form of treatment. Testing with Oncotype DX spared two-thirds of women from unnecessary chemotherapy, a significant proportion.

Sparing patients from chemotherapy offers two major advantages. First and foremost, patients are spared an often debilitating physical toll. It is well known that chemotherapy is associated with a range of side effects which include

cardiotoxicity, secondary leukaemia, hair loss and infections, as well as having a dramatic impact on quality of life. There are also psychological effects to consider. Cognitive impairment, which affects up to half of all treated women, had a huge effect on patients' working life following chemotherapy, often leading to increased absenteeism and a reduction or loss in workplace activity [10].

Patients undergoing chemotherapy treatment often rate stress as one of the emotional side-effects of breast cancer treatment [11]. Patients may feel fearful, anxious, angry, or depressed at some points during their treatment, and are striving for a sense of normality. The inability to return to work can exacerbate these problems further.

There is also an economic aspect, which is highly significant – particularly for a budget-limited NHS. Within the Manchester study, the estimated cost of chemotherapy for the patient group would have been over £1.2 million, had no testing taken place. Given that only 74 of the 201 patients underwent chemotherapy, the total cost of treatment, including the cost of the test, stood at £975,986. The total cost saving was over £250,000. This demonstrates that the Oncotype DX test not only makes clinical sense – allowing two-thirds of women to avoid unnecessary chemotherapy – but also financial sense, making the need for a personalised care approach ever more crucial.

It is important to note that the cost saving estimates contained within the Manchester study were conservative calculations, based on the list price for the Oncotype DX test. The true potential savings for the NHS are much greater, as the NHS has access to the test at a confidential price significantly lower than the published list price.

Although the test has yet to be recommended by NICE for node-positive patients, findings have shown that Oncotype DX can be equally as beneficial in such cases. For instance, a German study of patients with high-risk node-negative or node-positive disease reported a 94% disease-free survival at 5 years for patients with a Recurrence Score result of 11 or less. Once again, the Oncotype DX test was proven to reliably identify both node-negative and node-positive patients who are unlikely to benefit from chemotherapy but would have suffered the short and long-term effects of treatment [12].

The benefits of this personalised approach to medicine are not limited to breast cancer treatment, but can be reaped across the board. Testimony to this fact is the Government's 100,000 Genomes Project that aims to bring the benefits of personalised medicine to the NHS. To seek to ensure that patients benefit from innovations in genomics, the Government has committed to sequencing 100,000 whole human genomes, from 70,000 patients, by the end of 2017. As the NHS states itself, whilst the main aim is to improve the lives of patients, there are potentially many economic benefits for the nation and the UK tax-payer also. At such a crucial time for NHS funding, such measures cannot come quick enough.

The Oncotype DX test is a key part of this changing landscape and is now becoming part of routine clinical practice in the UK. In both node-negative and node-positive patients, the test has the potential to maintain patients' quality of life and reduce the economic burden of breast cancer care. For personalised medicine, this is just the beginning.

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