

## Update on breast cancer diagnosis and management:

new topics for primary care

Over 49 000 women each year in the UK are diagnosed with breast cancer, making it the most prevalent cancer in women.<sup>1</sup> Most primary breast cancers in the UK are diagnosed through two routes. The NHS Breast Screening Programme (NHSBSP) offers mammography every 3 years to women between the ages of 50 and 70. The breast screening services diagnose about a third of breast cancers. The remaining two-thirds of patients with breast cancer present, generally, to primary care, with symptoms, including a breast lump, nipple discharge, breast pain, and nipple inversion. In the UK, demand for symptomatic breast services continues to increase annually, despite a relative plateau in the number of new cases of breast cancer diagnosed. From NHS Digital data (derived from Hospital Episode Statistics data), there were 612 619 first appointments at NHS breast clinics in 2017–2018, an increase from 591 800 in 2016–2017, and 583 676 in 2015–2016.<sup>2</sup>

Breast cancer survival depends on the stage of the disease at diagnosis, the treatment received, and the biology of the tumour. More than 90% of women diagnosed with early breast cancer survive for at least 5 years, and 78% survive for 10 years. In contrast, only 13% of those diagnosed with advanced disease survive for >5 years.

Currently, there are three topics of interest and changing practice in the area of breast cancer diagnosis and management that are relevant to primary care: the use of neoadjuvant chemotherapy; genomic markers and profiling in breast cancer; and breast implant-associated anaplastic large-cell lymphoma, a new disease entity.

### USE OF NEOADJUVANT CHEMOTHERAPY

Early breast cancer is traditionally treated with surgery first and adjuvant (postoperative) systemic treatments (chemotherapy, endocrine treatment, targeted treatments) and radiotherapy to reduce the risks of both systemic and local recurrence. Adjuvant treatment recommendations are based on

stage and biology of the tumour as well as the patient's fitness.

Neoadjuvant therapy refers to the systemic treatment of breast cancer prior to definitive surgical treatment, that is, preoperative therapy. Typically, neoadjuvant treatment has taken the form of chemotherapy (NACT), although there is increased interest in expanding the role of neoadjuvant endocrine treatment in certain situations. One of the goals of NACT is to downstage the breast tumour, which may permit less extensive surgery on the breast and the axilla, avoiding the risks associated with breast reconstruction. This enables the patient to be able to undergo breast-conserving surgery instead of mastectomy, improving cosmetic outcomes, and reducing postoperative complications such as lymphoedema.

Also, NACT permits evaluation of the effectiveness of systemic treatment, which can then be used to guide decision making about adjuvant, postoperative treatment. The response of the cancer to neoadjuvant therapy is a strong prognostic factor for recurrence, especially in triple-negative breast cancer and human epidermal growth factor receptor 2 (HER2)-positive breast cancer. Emerging studies suggest that the NACT may allow a tailored approach to systemic treatments after breast surgery. In particular, studies have shown that addition of capecitabine as adjuvant treatment in women with triple-negative breast cancer and residual cancer after NACT,<sup>3</sup> or adding trastuzumab emtansine in women with HER2-positive breast cancer and residual cancer after NACT, can improve long-term outcomes.<sup>4</sup>

Although it was hypothesised that overall survival may be improved by neoadjuvant therapy because of earlier initiation of systemic treatment in patients at high risk of recurrence, randomised trials have demonstrated equivalent survival for pre- and postoperative chemotherapy.

The use of new or adjuvant chemotherapy is associated with an increased frequency of breast-conserving surgery (65% versus 49%).

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Submitted: 10 March 2020; Editor's response: 23 March 2020; final acceptance: 29 March 2020.

©British Journal of General Practice 2020; 70: 515–516.

DOI: <https://doi.org/10.3399/bjgp20X712985>

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It was also associated with increased risk of local recurrence (15 years local recurrence rate 21.4% versus 15.9%), which has been attributed to the increased use of breast-conserving surgery.<sup>5</sup>

Since the early trials there have been many advances in selecting patients for neoadjuvant treatment as well as demonstration of benefit of selecting subsequent treatment based on response.

In summary, neoadjuvant systemic treatment could offer an advantage for a selected group of patients, although for the majority of breast cancers surgery first remains the recommended treatment strategy. Discussion between members of the breast multidisciplinary team and patient involvement in decision making about treatments are paramount for appropriate patient selection.

## GENOMIC MARKERS AND PROFILING

The widespread application of adjuvant systemic therapy has reduced mortality from breast cancer. Prognostic factors (providing information on risk and clinical outcomes independent of therapy) and predictive factors (providing information of likelihood of response to a given treatment) are used in making treatment decisions on adjuvant systemic treatments. Several factors in breast cancer are both prognostic and predictive.

Traditionally, patient-related factors (such as age), stage (such as tumour size and nodal involvement), and pathological factors (such as oestrogen receptor and HER2 expression and grade) have been used as prognostic and/or predictive factors in advising on adjuvant treatments. Unfortunately, even when taking this information into consideration, treatments cannot be rationalised with complete accuracy, with some patients being overtreated and others undertreated.

The emergence of genomic techniques and the ability to measure expression of genes has led to the development of biologically based tests to aid recommendation for adjuvant systemic treatments. New NICE guidance was published in 2018 about genomic markers to tailor oncology decision making regarding chemotherapy.<sup>6</sup> EndoPredict, Oncotype DX Breast Recurrence Score, and Prosigna are recommended as options for guiding adjuvant chemotherapy decisions for people with oestrogen receptor (ER)-positive, HER2-negative, and lymph node (LN)-negative/lymph node micro-metastasis-only early breast cancer.<sup>6</sup> Oncotype DX Breast Recurrence Score is the most well-validated assay to identify patients who are most and least likely to derive benefit from adjuvant chemotherapy. At this time, it is indicated for

women with node-negative or node micro-metastasis-only, oestrogen receptor-positive, and HER2-negative breast cancer. Work to define the Oncotype DX role in patients with 1–3 nodes involved is ongoing.

After breast surgery and when all the above information is available, the case is discussed in a multidisciplinary team meeting and recommendations are made. Oncologists will see the patient to discuss the risks from the tumour and possible benefits from systemic treatment so informed treatment decisions are undertaken.

## BREAST IMPLANT-ASSOCIATED ALAC

Primary care practitioners should also be aware of breast implant-associated anaplastic large-cell lymphoma (BIA-ALCL), an uncommon peripheral T-cell lymphoma arising around textured-surface breast implants placed for either reconstructive or cosmetic indications. The incidence of ALCL in patients who have had textured implants inserted is in the order of 1 in 7000. The association of breast implants with a cancer of the immune system has created understandable concern among patients, plastic and breast surgeons, and oncologists.<sup>7</sup>

Initial studies suggest that BIA-ALCL follows a relatively indolent course in most patients. Those patients with early-stage disease have an excellent prognosis. Reports of disseminated cancer and deaths attributed to the disease emphasise the importance of appropriate surveillance, timely diagnosis, and adequate treatment.

BIA-ALCL is a rare condition: clinicians must maintain a high index of suspicion, particularly regarding the development of a new seroma around an existing breast implant, in which case the diagnosis is usually made by aspiration of the seroma under ultrasound control. Most cases present approximately 10 years after implant placement, although earlier or later presentations can be seen. Practitioners in primary care need to be aware of this condition. Any patient presenting with new swelling, diffuse or localised, around an existing implant needs to be referred to a one-stop breast clinic for a full triple assessment.

Considerable advances have been made in tailoring the treatment of patients with breast cancer, to allow treatment escalation for high-risk disease and treatment de-escalation for low-risk good prognostic tumours. This progress requires, as does the diagnosis of ALCL, careful multidisciplinary team working between oncologists, surgeons, radiologists, and pathologists to deliver the highest possible standards of care for patients, involving patients and informing their choices.

## Provenance

Freely submitted; externally peer reviewed.

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