NICE National Institute for Health and Care Excellence

NICE guideline

Advanced breast cancer: diagnosis and treatment

Clinical guideline
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www.nice.org.uk/guidance/cg81

Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guideline replaces TA30, TA54 and TA62.

This guideline is partially replaced by NG101.

This guideline is the basis of QS12.

Overview

This guideline covers care and support for people with advanced (stage 4) breast cancer. It aims to help them and their healthcare professionals make shared decisions about tests and treatments to improve outcomes and quality of life.

Who is it for?

- Healthcare professionals
- Palliative care services
- People with advanced breast cancer, their families and carers

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Diagnosis and assessment

Imaging assessment

1.1.1 Assess the presence and extent of visceral metastases using a combination of plain radiography, ultrasound, computed tomography (CT) scans and magnetic resonance imaging (MRI). **[2009]**

1.1.2 Assess the presence and extent of metastases in the bones of the axial skeleton using bone windows on a CT scan or MRI or bone scintigraphy. **[2009]**

1.1.3 Assess proximal limb bones for the risk of pathological fracture in patients with evidence of bone metastases elsewhere, using bone scintigraphy and/or plain radiography. **[2009]**

1.1.4 Use MRI to assess bony metastases if other imaging is equivocal for metastatic disease or if more information is needed (for example, if there are lytic metastases encroaching on the spinal canal). **[2009]**

1.1.5 Positron emission tomography fused with computed tomography (PET-CT) should only be used to make a new diagnosis of metastases for patients with breast cancer whose imaging is suspicious but not diagnostic of metastatic

disease. **[2009]**

Pathological assessment

1.1.6 On recurrence, consider reassessing oestrogen receptor (ER) and human epidermal growth factor 2 receptor (HER2) status if a change in receptor status will lead to a change in management. **[2017]**

Monitoring disease status

1.1.7 Do not use bone scintigraphy to monitor the response of bone metastases to treatment. **[2009]**

1.1.8 Do not use PET-CT to monitor advanced breast cancer. **[2009]**

1.2 Providing information and support for decision making

1.2.1 Assess the patient's individual preference for the level and type of information. Reassess this as circumstances change. **[2009]**

1.2.2 On the basis of this assessment, offer patients consistent, relevant information and clear explanations, and provide opportunities for patients to discuss issues and ask questions. **[2009]**

1.2.3 Assess the patient's individual preference for how much they wish to be involved in decision making. Reassess this as circumstances change. **[2009]**

1.2.4 Be aware of the value of decision aids and the range available. Make the most appropriate decision aid available to the patient. **[2009]**

1.3 Systemic disease-modifying therapy

1.3.1 Offer endocrine therapy as first-line treatment for the majority of patients with ER-positive advanced breast cancer. **[2009]**

1.3.2 Offer chemotherapy as first-line treatment for patients with ER positive advanced breast cancer whose disease is imminently life-threatening or requires early relief of symptoms because of significant visceral organ involvement, providing they understand and are prepared to accept the toxicity. **[2009]**

1.3.3 For patients with ER-positive advanced breast cancer who have been treated with chemotherapy as their first-line treatment, offer endocrine therapy following the completion of chemotherapy. **[2009]**

Endocrine therapy

1.3.4 Offer an aromatase inhibitor (either non-steroidal or steroidal) to:

- postmenopausal women with ER-positive breast cancer and no prior history of endocrine therapy
- postmenopausal women with ER-positive breast cancer previously treated with tamoxifen. **[2009]**

1.3.5 Offer tamoxifen and ovarian suppression as first-line treatment to premenopausal and perimenopausal women with ER-positive advanced breast cancer not previously treated with tamoxifen. **[2009]**

1.3.6 Offer ovarian suppression to premenopausal and perimenopausal women who have previously been treated with tamoxifen and then experience disease progression. **[2009]**

1.3.7 Offer tamoxifen as first-line treatment to men with ER-positive advanced breast cancer. **[2009]**

Chemotherapy

1.3.8 On disease progression, offer systemic sequential therapy to the majority of patients with advanced breast cancer who have decided to be treated with chemotherapy. **[2009]**

1.3.9 Consider using combination chemotherapy to treat patients with advanced breast cancer for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity. **[2009]**

1.3.10 For patients with advanced breast cancer who are not suitable for anthracyclines (because they are contraindicated or because of prior anthracycline treatment either in the adjuvant or metastatic setting), systemic chemotherapy should be offered in the following sequence:

- first line: single-agent docetaxel
- second line: single-agent vinorelbine or capecitabine
- third line: single-agent capecitabine or vinorelbine (whichever was not used as second-line treatment). **[2009]**

1.3.11 Gemcitabine in combination with paclitaxel, within its licensed indication, is recommended as an option for the treatment of metastatic breast cancer only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate. (This recommendation is from NICE's technology appraisal guidance on gemcitabine for the treatment of metastatic breast cancer.) **[2009]**

Biological therapy

1.3.12 For patients who are receiving treatment with trastuzumab for advanced breast cancer, discontinue treatment with trastuzumab at the time of disease progression outside the central nervous system. Do not discontinue trastuzumab if disease progression is within the central nervous system alone. (Recommendations on the use of trastuzumab are covered by NICE's technology appraisal guidance on the use of trastuzumab for the treatment of advanced breast cancer). **[2009]**

For all technology appraisal guidance relevant to this section, including genomic biomarker-based therapy, see the NICE topic page on breast cancer. The point at which to use genomic biomarker-based therapy in solid tumour treatment pathways is uncertain. See the NICE topic page on genomic biomarker-based therapy.

1.4 Supportive care

1.4.1 Healthcare professionals involved in the care of patients with advanced breast cancer should ensure that the organisation and provision of supportive care services comply with the recommendations made in NICE's cancer service guidance on improving outcomes in breast cancer and improving supportive and palliative care for adults with cancer, in particular the following two recommendations:

- 'Assessment and discussion of patients' needs for physical, psychological, social, spiritual and financial support should be undertaken at key points (such as diagnosis; at commencement, during, and at the end of treatment; at relapse; and when death is approaching).'
- 'Mechanisms should be developed to promote continuity of care, which might include the nomination of a person to take on the role of "key worker" for individual patients.' **[2009]**

1.5 Managing complications

Lymphoedema

Recommendations in this section have been stood down as they have been superseded by the February 2025 update on lymphoedema early identification, risk reduction and management in the NICE guideline on early and locally advanced breast cancer: diagnosis and management.

1.5.1 This recommendation has been stood down.

1.5.2 This recommendation has been stood down.

1.5.3 This recommendation has been stood down.

1.5.4 This recommendation has been stood down.

1.5.5 This recommendation has been stood down.

1.5.6 This recommendation has been stood down.

1.5.7 This recommendation has been stood down.

Cancer-related fatigue

1.5.8 Offer all patients with advanced breast cancer for whom cancer-related fatigue is a significant problem an assessment to identify any treatable causative factors, and offer appropriate management as necessary. **[2009]**

1.5.9 Provide clear, written information about cancer-related fatigue, organisations that offer psychosocial support and patient led groups. **[2009]**

1.5.10 Provide information about and timely access to an exercise programme for all patients with advanced breast cancer experiencing cancer-related fatigue. **[2009]**

Uncontrolled local disease

1.5.11 A breast cancer multidisciplinary team should assess all patients presenting with uncontrolled local disease and discuss the therapeutic options for controlling the disease and relieving symptoms. **[2009]**

1.5.12 A wound care team should see all patients with fungating tumours to plan a dressing regimen and supervise management with the breast care team. **[2009]**

1.5.13 A palliative care team should assess all patients with uncontrolled local disease in order to plan a symptom management strategy and provide psychological support. **[2009]**

Bone metastases

1.5.14 Consider offering bisphosphonates to patients newly diagnosed with bone metastases to prevent skeletal-related events and reduce pain. **[2009]**

1.5.15 The choice of bisphosphonate for patients with bone metastases should be a local decision, taking into account patient preference and limited to preparations licensed for this indication. **[2009]**

1.5.16 Use external beam radiotherapy in a single fraction of 8 Gy to treat patients with bone metastases and pain. **[2009]**

1.5.17 An orthopaedic surgeon should assess all patients at risk of a long bone fracture, to consider prophylactic surgery. **[2009]**

Brain metastases

1.5.18 Offer surgery followed by whole brain radiotherapy to patients who have a single or small number of potentially resectable brain metastases, a good performance status and who have no or well controlled other metastatic disease. **[2009]**

1.5.19 Offer whole brain radiotherapy to patients for whom surgery is not appropriate, unless they have a very poor prognosis. **[2009]**

1.5.20 Offer active rehabilitation to patients who have surgery and/or whole brain radiotherapy. **[2009]**

1.5.21 Offer referral to specialist palliative care to patients for whom active treatment for brain metastases would be inappropriate. **[2009]**

Recommendations for research

The 2014 and 2009 guideline committees made the following recommendations for research.

1 Assessment of the role of exercise

What is the role of arm and shoulder specific exercises compared with and/or used as an adjunct to established lymphoedema treatments (such as compression garments and complex decongestive therapy)?

Why this is important

Well-designed randomised controlled trials should consider differing arm and shoulder-specific aerobic and/or resistive exercises that focus on strength and flexibility to improve local lymph flow, for example, swimming, weight lifting, tai chi and yoga. The studies should have a follow-up period that is sufficient to capture long-term outcomes including changes to current lymphoedema or any new-onset lymphoedema in other parts of the limb. Outcomes for this research should include quality-of-life measures. **[2014]**

2 Endocrine therapy

Clinical trials are needed to investigate the most effective endocrine therapy for postmenopausal women with ER-positive tumours who progress on treatment with an aromatase inhibitor.

Why this is important

Although there is good evidence to support the use of aromatase inhibitors for postmenopausal women with ER-positive tumours, there is little evidence to determine what is the best sequence of alternative hormone treatments when they progress. **[2009]**

3 Chemotherapy

Randomised clinical trials should evaluate the clinical and cost effectiveness of different

sequences of chemotherapy for advanced breast cancer.

Why this is important

Most patients with advanced breast cancer who receive chemotherapy will be given at least two different regimens and many will receive three. The available evidence to support decisions about the most clinically and cost effective sequence in which to use these drugs is extremely limited. There is also very little good-quality evidence about the relative clinical and cost effectiveness of currently recommended treatments, either in combination or in sequence. Following on from the recommendations in this guideline, it would be important to establish clinical trials to investigate this problem in a more systematic fashion than hitherto. **[2009]**

4 Biological response modifiers (progressive metastatic disease)

The use of continued trastuzumab in patients with progressive metastatic disease should be investigated as part of a randomised controlled trial. Trial design should incorporate collection of data required for prospective cost-effectiveness analysis.

Why this is important

There is currently no high-quality published evidence about whether continuing trastuzumab is effective in prolonging survival in patients with HER2-positive advanced breast cancer who develop progressive disease (outside the central nervous system) during or after first-line treatment with trastuzumab and cytotoxic chemotherapy. Any studies should be carefully planned to permit a high quality cost-effectiveness analysis. **[2009]**

5 Biological response modifiers (adjuvant trastuzumab)

Randomised controlled trials are needed to assess whether patients who have had adjuvant trastuzumab should be offered further biological response modifiers. Trial design should incorporate collection of data required for prospective cost-effectiveness analysis.

Why this is important

As more patients with HER2-positive advanced breast cancer have trastuzumab as part of their initial adjuvant treatment following a diagnosis of early breast cancer, an increasing number of patients with advanced breast cancer will have had previous exposure to this agent. There is no evidence currently about whether trastuzumab or other biological therapies are effective in this situation. **[2009]**

6 Uncontrolled local disease

The relevant research organisations should be encouraged to address the topic of uncontrolled local disease and devise appropriate research studies. This might include development of a national register.

Why this is important

The problem of how best to manage uncontrolled local disease is very poorly addressed by the current evidence. Although it is probably quite an uncommon condition, it is likely that across the country there are enough patients to generate evidence from well-coordinated national studies. A national register should be considered as part of this because of the current uncertainties about the frequency of the problem. **[2009]**

Context

Breast cancer is the most common cancer affecting women in England and Wales, with about 40,500 new cases diagnosed and 10,900 deaths recorded in England and Wales each year. In men breast cancer is rare, with about 260 cases diagnosed and 68 deaths in England and Wales each year (Office for National Statistics, Cancer statistics registrations: registrations of cancer diagnosed in 2005, England; Welsh Cancer Intelligence and Surveillance Unit, Cancer incidence in Wales 1992–2002). Of these new cases in women and men, a small proportion is diagnosed in the advanced stages, when the tumour has spread significantly within the breast or to other organs of the body. In addition, there are a significant number of women who have been previously treated with curative intent who subsequently develop either a local recurrence or metastases. Over recent years there have been important developments in the investigation and management of patients with advanced breast cancer, including new chemotherapy, and biological and hormonal agents. There is some evidence of practice variation across the country and of patchy availability of certain treatments and procedures. This clinical guideline helps to address these issues and offers guidance on best practice.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE topic page on breast cancer.

For full details of the evidence and the guideline committee's discussions, see the full guideline. You can also find information about how the guideline was developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put NICE guidance into practice.

Update information

February 2025: Recommendations in the section on lymphoedema (recommendations 1.5.1 to 1.5.7) have been stood down as they have been superseded by the update on lymphoedema early identification, risk reduction and management in the NICE guideline on early and locally advanced breast cancer: diagnosis and management.

August 2017: We reviewed the evidence and updated recommendations in section 1.1 on assessing oestrogen receptor (ER) and human epidermal growth factor receptor 2 (HER2) status on disease recurrence.

July 2014: We reviewed the evidence on exercise for people with or at risk of lymphoedema and added 2 recommendations to section 1.5.

Recommendations are marked as **[2017]**, **[2014]** or **[2009]**.

[2017] indicates that the evidence was reviewed and the recommendation updated in 2017.

[2014] indicates that the evidence was reviewed and the recommendation added in 2014.

[2009] indicates that the evidence was reviewed in 2009.

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