Diagnosis and treatment of advanced breast cancer: Summary of NICE guidance

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PRACTICE

GUIDELINES

Diagnosis and treatment of advanced breast cancer: summary of NICE guidance

N Murray *senior lecturer and honorary consultant*[1], J Winstanley *consultant surgeon*[2], A Bennett *assistant centre manager*[3], K Francis *researcher*[3], on behalf of the Guideline Development Group

[1]Cancer Research UK Clinical Centre, University of Southampton, Somers Cancer Research Building, Southampton General Hospital, Southampton SO16 6YD; [2]Royal Bolton Hospital, Bolton BL4 0RJ; [3]National Collaborating Centre for Cancer, Cardiff CF10 3AF

This is one of a series of *BMJ* summaries of new guidelines, which are based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists.

Why read this summary?

Breast cancer is the most common cancer in women and the second most common cause of death from cancer in women in the United Kingdom. Each year in the UK more than 12 300 women and 70 men will die from advanced breast cancer having lived with this condition for an average of two to three years before death.[1-4] Management of advanced breast cancer requires the input of a wide range of healthcare professionals, usually in primary, secondary, and tertiary healthcare settings. Clinical practice and availability of certain treatments and procedures are known to vary across the UK. This article summarises the most recent recommendations from the National Institute for Health and Clinical Excellence (NICE) on the diagnosis and treatment of advanced breast cancer.[5]

Recommendations

NICE recommendations are based on systematic reviews of best available evidence. When minimal evidence is available, recommendations are based on the Guideline Development Group's opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

Diagnosis and assessment

Imaging assessment

- Assess the presence and extent of metastases in the bones of the axial skeleton using bone windows on a computed tomography (CT) scan or magnetic resonance imaging (MRI) or using bone scintigraphy.
- 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. [*Based on evidence from small comparative studies or case series and on the opinion of the Guideline Development Group*]
- Use MRI to assess bony metastases if other imaging is equivocal for metastatic disease or if more information is needed (for example, if lytic metastases are encroaching on the spinal canal).
- Positron emission tomography fused with computed tomography (PET-CT) should be used to make a new diagnosis of metastases only for patients with breast cancer whose imaging is suspicious but not diagnostic of metastatic disease. [*Based on the opinion of the Guideline Development Group*]

Pathological assessment

- Assess oestrogen receptor and human epidermal growth factor receptor 2 (HER2) status at the time of disease recurrence if receptor status was not assessed at the time of initial diagnosis. In the absence of tumour tissue from the primary tumour, and if feasible, obtain a biopsy of a metastasis to assess oestrogen receptor and HER2 status. [*Based on the opinion of the Guideline Development Group*]
- Patients with tumours of known oestrogen receptor status whose disease recurs should not have a further biopsy just to reassess that status.
- Patients with tumours of known HER2 status whose disease recurs should not have a further biopsy just to reassess that status. [*Based on limited evidence from observational studies and on the opinion of the Guideline Development Group*]

Correspondence to: N Murray nickm@soton.ac.uk

Providing information and support for decision making

- Assess the patient's individual preference for the level and type of information. Reassess this as circumstances change.
- 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.
- Assess the patient's individual preference for how much they wish to be involved in decision making. Reassess this as circumstances change.
- Be aware of the value of decision aids and the range available. Ensure that the most appropriate decision aid is available to the patient. [*Based on moderate quality randomised trials*]

Systemic disease modifying therapy

Endocrine therapy

- Offer endocrine therapy as first line treatment for most patients with oestrogen receptor positive advanced breast cancer. However, if in such patients the disease is imminently life threatening or requires early relief of symptoms resulting from significant visceral organ involvement, offer chemotherapy as first line treatment instead, provided that the patients understand and are prepared to accept the toxicity. [*Based on a high quality systematic review and on the opinion of the Guideline Development Group*]
- Offer an aromatase inhibitor (non-steroidal or steroidal) to:

  -Postmenopausal women with oestrogen receptor positive breast cancer and no prior history of endocrine therapy

  -Postmenopausal women with oestrogen receptor positive breast cancer previously treated with tamoxifen. [*Based on high quality evidence of clinical and cost effectiveness*]
- Offer tamoxifen and ovarian suppression as first line treatment to premenopausal and perimenopausal women with oestrogen receptor positive advanced breast cancer not previously treated with tamoxifen.
- Offer ovarian suppression to premenopausal and perimenopausal women who have previously been treated with tamoxifen and who then experience disease progression. [*Based on a moderate quality randomised controlled trial and a high quality systematic review of randomised trials*]
- Offer tamoxifen as first line treatment to men with oestrogen receptor positive advanced breast cancer. [*Based on low quality retrospective case series and on the opinion of the Guideline Development Group*]

Chemotherapy

- For most patients who experience disease progression, offer chemotherapy as a course of treatment with a single recommended chemotherapy drug. [*Based on a limited randomised trial and on the opinion of the Guideline Development Group*]
- Consider using combination chemotherapy in patients for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity. [*Based on randomised trial evidence*]
- For patients who are not suitable for anthracyclines (because they are contraindicated or because of prior anthracycline treatment either in the adjuvant or metastatic setting), offer systemic chemotherapy in the following sequence:

  -First line: single agent docetaxel

  -Second line: single agent vinorelbine or capecitabine

  -Third line: single agent vinorelbine or capecitabine (whichever was not used as second line treatment).

[*The last bullet point, about patients not suitable for anthracyclines, is based on a health economic analysis comparing the cost effectiveness of various sequences of single agent and combination chemotherapy regimens*]

Biological therapy

- For patients receiving treatment with trastuzumab[6] 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. [*Based on limited evidence of clinical benefit and a lack of evidence of cost effectiveness*]

Managing complications

Lymphoedema

- Offer all patients with lymphoedema complex decongestive therapy[7] as the first stage of lymphoedema management.
- Consider using multilayer lymphoedema bandaging for volume reduction as a first treatment option before compression hosiery. [*Based on the opinion of the Guideline Development Group*]

Cancer related fatigue

- Provide information about and timely access to an exercise programme for all patients experiencing cancer related fatigue. [*Based on a high quality systematic review and meta-analysis and on the opinion of the Guideline Development Group*]

Uncontrolled local disease

- 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. [*Based on poor quality evidence from small case series, on expert position papers, and on the opinion of the Guideline Development Group*]

Bone metastases

- Consider offering bisphosphonates to patients with a new diagnosis of bone metastases to prevent skeletal related events and to reduce pain. [*Based on a high quality systematic review and meta-analysis and moderate quality evidence of cost effectiveness*]

Brain metastases

- 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 no or well controlled metastatic disease elsewhere.

- Offer whole brain radiotherapy to patients for whom surgery is not appropriate, unless they have a very poor prognosis. [*Based on moderate quality retrospective case series*]

Overcoming barriers

Some of these recommendations have cost implications and/or will require provision of services not previously provided in many areas of Britain. Breast cancer has not previously been listed as an approved indication for PET-CT in the NHS, but the number of patients needing this procedure in any given healthcare trust is likely to be small. Provision of lymphoedema services is patchy around the UK, and the recommendations are likely to require an increase in staff and facilities. Currently very few areas are likely to provide access to an exercise programme for cancer related fatigue, so providers will need to consider how best to provide this. Timeliness of access to appropriate neurosurgical services may vary, and implementing the recommendations may require new protocols in some cancer networks. The use of trastuzumab beyond disease progression in HER-2 positive disease varies widely around the UK. Providers should ensure they have processes that provide complete transparency about the indication for prescribing trastuzumab. Processes should be in place to ensure that trastuzumab is used only in accordance with the indications agreed by purchasers.

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Further information on the guidance

Breast cancer is an important condition causing substantial mortality and morbidity in the United Kingdom, with heavy use of healthcare resources. Introduction of newer and more costly treatments has often proved controversial, with widespread variation in levels of provision between different areas (so called postcode variation), which has been reduced since the establishment of NICE. Although some of the more pressing controversies about availability of treatments were managed using the technology appraisal processes (the appraisal process used by NICE to make binding recommendations about the adoption (or not) of new therapies by the NHS), it is logical to have a single guideline incorporating recommendations about currently available treatments.

Little is new in this guideline, and the Guideline Development Group believes that it reflects what should be current best practice around the UK. As outlined in the main text, some cancer centres and units may need to introduce changes to comply with some guideline recommendations.

The use of trastuzumab at the time of disease progression is thought to vary considerably around the UK. This use is an unlicensed indication, for which no formal cost effectiveness analysis has been submitted to NICE. The Guideline Development Group feels that in the interests of equity, trastuzumab beyond progression is not a treatment that should be used in the NHS unless and until a proper appraisal has been performed.

Methods

The development of this guideline was based on methods outlined by the NICE guidelines manual.[8]

Management of advanced breast cancer involves different treatments over time. Limited information was available in the published literature about comparisons of different sequences of treatments, in particular chemotherapy. In the light of this the development group and health economists from the London School of Hygiene and Tropical Medicine developed a new health economic model for chemotherapy, to incorporate the available data from published randomised trials in a manner that permitted a cost effectiveness evaluation. The development group was aware of the potential limitations of such a model but believed that this model represented a substantial step forward for considering the “whole of life” treatment of a cancer that will ultimately cause death. It will undoubtedly be refined by others in the future. It was reassuring that the final output of the model was consistent with what the development group believes to be the most common practices of oncologists treating breast cancer around the UK.

Future research and remaining uncertainties

The quality of evidence with which to formulate recommendations for managing advanced breast cancer was surprisingly poor. Many published randomised trials on advanced breast cancer are, in isolation, of an acceptable quality regarding the questions they pose about the population eligible for the trial. However, it is extremely difficult to put the results of such trials into the context of a whole of life treatment plan. Substantial further research is required in this area. The quality of health economic information available from most trials is also poor, and this too needs to be resolved.