Advanced breast cancer: diagnosis and treatment

NICE guideline Draft for consultation, August 2008

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.

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Introduction

Breast cancer is the most common cancer for women in England and Wales, with about 37,000 new cases diagnosed¹² and 11,000 deaths³ recorded in England and Wales each year. In men breast cancer is rare, with about 270 cases diagnosed^{1, 2} and 70 deaths³ in England and Wales each year. Of these new cases in women and men, around 10% are diagnosed in the advanced stages, when the tumour has spread significantly within the breast or to other organs of the body. In addition, there is 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 these patients 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. A clinical guideline will help to address these issues and offer guidance on best practice.

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

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¹ Office for National Statistics (2005) Cancer statistics registrations: registrations of cancer diagnosed in 2002, England, Series MB1 number 33, London: National Statistics.

² Welsh Cancer Intelligence and Surveillance Unit (2005) Cancer incidence in Wales 1992–2002. Cardiff: Welsh Cancer Intelligence and Surveillance Unit.

³ Office for National Statistics (2003) Mortality statistics: cause. England and Wales 2003. London: The Stationery Office.

Patient-centred care

This guideline offers best practice advice on the care of patients with advanced breast cancer.

Treatment and care should take into account patients' needs and preferences. People with advanced breast cancer should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – 'Reference guide to consent for examination or treatment' (2001) (available from www.dh.gov.uk). Healthcare professionals should also follow a code of practice accompanying the Mental Capacity Act (summary available from www.publicguardian.gov.uk).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

Key priorities for implementation

Presentation and diagnosis

- 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. 1.1.1.5
- If receptor status (oestrogen receptor and HER2) was not assessed at the time of initial diagnosis, then it should be assessed at the time of tumour recurrence. In the absence of any tumour tissue from the primary tumour a biopsy of a metastasis should be obtained if feasible. 1.1.1.8

Systemic disease-modifying therapy

- For patients with hormone receptor-positive advanced breast cancer, offer endocrine therapy as first-line treatment unless there is a clinical need to achieve a rapid tumour response. 1.3.1.1
- For patients with advanced breast cancer who are not suitable for anthracyclines (adjuvant anthracyclines or first-line metastatic anthracyclines, or contraindicated), 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). 1.3.3.3
- Patients who are receiving treatment with trastuzumab should not continue trastuzumab at the time of disease progression outside the central nervous system. 1.3.4.4

Community-based treatment and supportive care

 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 previous NICE guidance documents ('Improving outcomes in breast cancer: Manual update' [2002] and 'Improving supportive and palliative

care for adults with cancer' [2004]), 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.' 1.4.1.1

Management of specific problems

- 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. 1.5.3.1
- Offer bisphosphonates to patients newly diagnosed with bone metastases,
 to prevent skeletal-related events and to reduce pain. 1.5.4.1
- Use external beam radiotherapy in a single fraction of 8 Gy to treat patients with bone metastases and pain. 1.5.4.3
- 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. 1.5.5.1

1 Guidance

The following guidance is based on the best available evidence. The full guideline ([add hyperlink]) gives details of the methods and the evidence used to develop the guidance.

1.1 Presentation and diagnosis

1.1.1 Making a diagnosis

Imaging

- 1.1.1.1 Assess visceral metastases using an appropriate combination of plain radiography, ultrasound, CT scan and MRI.
- 1.1.1.2 Use either bone windows on a CT scan, MRI or bone scintigraphy to assess the presence and extent of metastases in the bones of the axial skeleton.
- 1.1.1.3 Assess proximal limb bones in patients with evidence of bone metastases elsewhere, for the risk of pathological fracture, using either bone scintigraphy and/or plain radiographs.
- 1.1.1.4 Use MRI to assess bony metastases if other imaging is equivocal for metastatic disease or if more information is needed (for example lytic metastases encroaching on the spinal canal).
- 1.1.1.5 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.

Pathology

1.1.1.6 Patients with tumours of known oestrogen receptor status whose disease recurs should not have a further biopsy to reassess oestrogen receptor status.

- 1.1.1.7 Patients with tumours of known HER2 status whose disease recurs should not have a further biopsy to reassess HER2 status
- 1.1.1.8 If receptor status (oestrogen receptor and HER2) was not assessed at the time of initial diagnosis then it should be assessed at the time of tumour recurrence. In the absence of any tumour tissue from the primary tumour a biopsy of a metastasis should be obtained if feasible.

1.1.2 Monitoring disease progress

- 1.1.2.1 Do not use bone scintigraphy to monitor the response of bone metastases to treatment.
- 1.1.2.2 Do not use PET-CT for monitoring patients with advanced breast cancer.

1.2 Providing information and support for decision making

- 1.2.1.1 Assess the patient's individual preference for the level and type of information, and reassess this as circumstances change.
- 1.2.1.2 On the basis of this assessment, offer consistent, relevant information and clear explanations, and provide opportunities for patients to discuss issues and ask questions.
- 1.2.1.3 Assess the patient's individual preference for how much they wish to be involved in decision making, and reassess this as circumstances change.
- 1.2.1.4 Help patients make difficult decisions about their treatment. Be aware of the range and value of decision aids available and make the most appropriate aid available to the patient.

1.3 Systemic disease-modifying therapy

- 1.3.1.1 For patients with hormone receptor-positive advanced breast cancer, offer endocrine therapy as first-line treatment unless there is a clinical need to achieve a rapid tumour response.
- 1.3.1.2 For patients with hormone receptor-positive advanced breast cancer whose disease is imminently life-threatening or requires early relief of symptoms because of significant visceral organ involvement, offer chemotherapy as first-line treatment if they are fit enough and are prepared to accept the toxicity.
- 1.3.1.3 For patients with hormone receptor-positive advanced breast cancer, offer endocrine therapy following chemotherapy.

1.3.2 Endocrine therapy

- 1.3.2.1 Offer a third-generation aromatase inhibitor (either non-steroidal or steroidal) to:
 - postmenopausal women with hormone receptor-positive breast cancer and no prior history of endocrine therapy
 - postmenopausal women with hormone receptor-positive breast cancer who have previously been treated with tamoxifen.
- 1.3.2.2 Offer tamoxifen as first-line treatment to pre-menopausal and peri-menopausal women with hormone receptor-positive advanced breast cancer not previously treated with tamoxifen.
- 1.3.2.3 Offer ovarian suppression to pre-menopausal and peri-menopausal women who have responded to tamoxifen and then develop progressive disease.
- 1.3.2.4 Offer tamoxifen as first-line treatment to men with oestrogen receptor-positive advanced breast cancer.

1.3.3 Chemotherapy

- 1.3.3.1 Use sequential single agents on disease progression to treat the majority of patients with advanced breast cancer who require chemotherapy.
- 1.3.3.2 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.
- 1.3.3.3 For patients with advanced breast cancer who are not suitable for anthracyclines (adjuvant anthracyclines or first-line metastatic anthracyclines, or contraindicated), 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).
- 1.3.3.4 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 appropriate⁴.

1.3.4 Biological response modifiers

1.3.4.1 Trastuzumab in combination with paclitaxel (combination trastuzumab is currently only licensed for use with paclitaxel) is recommended as an option for people with tumours expressing human epidermal growth factor receptor 2 (HER2) scored at levels

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⁴ This recommendation is from 'Gemcitabine for the treatment of metastatic breast cancer', NICE technology appraisal guidance 116 (2007). It has been incorporated into this guideline in line with NICE procedures for developing clinical guidelines.

- of 3+ who have not received chemotherapy for metastatic breast cancer and for whom anthracycline treatment is inappropriate.⁵
- 1.3.4.2 Trastuzumab monotherapy is recommended as an option for people with tumours expressing HER2 scored at levels of 3+ who have received at least two chemotherapy regimens for metastatic breast cancer. Prior chemotherapy must have included at least an anthracycline and a taxane where these treatments are appropriate. It should also have included hormonal therapy in suitable oestrogen receptor positive patients.⁵
- 1.3.4.3 HER2 levels should be scored using validated immunohistochemical techniques and in accordance with published guidelines. Laboratories offering tissue sample immunocytochemical or other predictive tests for therapy response should use validated standardised assay methods and participate in and demonstrate satisfactory performance in a recognised external quality assurance scheme.⁵
- 1.3.4.4 Patients who are receiving treatment with trastuzumab should not continue trastuzumab at the time of disease progression outside the central nervous system.

1.4 Community-based treatment and supportive care

1.4.1.1 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 previous NICE guidance documents ('Improving outcomes in breast cancer: Manual update' [2002] and 'Improving supportive and palliative care for adults with cancer' [2004]), in particular the following two recommendations:

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⁵ This recommendation is from 'The clinical effectiveness and cost effectiveness of trastuzumab for breast cancer', NICE technology appraisal guidance 34 (2005). It has been incorporated into this guideline in line with NICE procedures for developing clinical guidelines.

- '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.'

1.5 Management of specific problems

1.5.1 Lymphoedema

- 1.5.1.1 Assess patients with advanced breast cancer and lymphoedema for treatable underlying factors before starting any lymphoedema management programme.
- 1.5.1.2 Offer all patients with lymphoedema related to advanced breast cancer complex decongestive therapy (CDT) as the first form of lymphoedema management.
- 1.5.1.3 Consider using multi-layer lymphoedema bandaging (MLLB) for volume reduction, as a first treatment option before compression hosiery.
- 1.5.1.4 Provide patients with advanced breast cancer and lymphoedema with at least two suitable compression garments. These should be of the appropriate class and size, and a choice of fabrics and colours should be available.
- 1.5.1.5 Provide patients with advanced breast cancer and lymphoedema with the contact details of local and national lymphoedema support groups.

1.5.2 Cancer-related fatigue

- 1.5.2.1 Offer all patients with advanced breast cancer for whom fatigue is a significant problem an assessment to identify any treatable causative factors and offer appropriate management as necessary.
- 1.5.2.2 Provide clear, written information about fatigue, organisations that offer psychosocial support and patient-led groups.
- 1.5.2.3 Provide information about and timely access to an exercise programme for all patients with advanced breast cancer experiencing cancer-related fatigue.

1.5.3 Uncontrolled local disease

- 1.5.3.1 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.
- 1.5.3.2 A wound care team should see all patients with fungating tumours to plan a dressing regimen and supervise management with the breast care team.
- 1.5.3.3 A palliative care team should assess all patients with uncontrolled local disease and their families in order to plan a symptom management strategy and to provide psychological support.

1.5.4 Bone metastases

- 1.5.4.1 Offer bisphosphonates to patients newly diagnosed with bone metastases, to prevent skeletal-related events and to reduce pain.
- 1.5.4.2 The choice of which bisphosphonate to use for patients with bone metastases should be a local decision, taking into account patient preference and limited to preparations licensed for this indication.
- 1.5.4.3 Use external beam radiotherapy in a single fraction of 8 Gy to treat patients with bone metastases and pain.

1.5.4.4 An orthopaedic surgeon should assess all patients at risk of a long bone fracture, to consider prophylactic surgery.

1.5.5 Brain metastases

- 1.5.5.1 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.
- 1.5.5.2 Offer whole brain radiotherapy to patients for whom surgery is not appropriate, unless they have a very poor prognosis.
- 1.5.5.3 Offer active rehabilitation to patients who have surgery and/or whole brain radiotherapy.
- 1.5.5.4 Patients for whom active treatment for brain metastases would be inappropriate should be referred for specialist palliative care.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available from http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11655

Groups that will be covered

 Women and men with invasive adenocarcinoma of the breast of clinical stage 4 (that is, with known metastatic disease).

Groups that will not be covered

- Women and men with invasive adenocarcinoma of the breast of clinical stages 1, 2 and 3 (this will be covered by the NICE guideline on 'Early breast cancer: diagnosis and treatment').
- Women and men with metastases to the breast from other primary tumours.
- Women and men with rare breast tumours (for example, angiosarcoma, lymphoma).
- Women and men with benign breast tumours (for example, fibroadenoma, benign phyllodes tumours).

How this guideline was developed

NICE commissioned the National Collaborating Centre for Cancer to develop this guideline. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see appendix B).

There is more information in the booklet: 'The guideline development process: an overview for stakeholders, the public and the NHS' (third edition, published April 2007), which is available from www.nice.org.uk/guidelinesprocess or from NICE publications (phone 0845 003 7783 or email publications@nice.org.uk and quote reference N1233).

3 Implementation

The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' (available from www.dh.gov.uk).

Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CGXXX). [NICE to amend list as needed at time of publication]

- Slides highlighting key messages for local discussion.
- Costing tools:
 - costing report to estimate the national savings and costs associated with implementation
 - costing template to estimate the local costs and savings involved.
- Implementation advice on how to put the guidance into practice and national initiatives that support this locally.

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Audit support for monitoring local practice.

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline (see section 5).

4.1 Endocrine therapy

Clinical trials are needed to investigate the most effective endocrine therapy for postmenopausal women with oestrogen receptor positive tumours who progress on treatment with a third-generation aromatase inhibitor.

Why this is important

Although there is good evidence to support the use of third-generation aromatase inhibitors for postmenopausal women with oestrogen receptor-positive tumours, there is little evidence to determine what is the best sequence of alternative hormone treatments when they progress.

4.2 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 this guideline's recommendations, it would be important to establish clinical trials that investigate this problem in a more systematic fashion than hitherto.

4.3 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.

Why this is important

There is currently no high-quality published evidence about whether continuing trastuzumab is effective in prolonging survival in HER2-positive patients 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.

4.4 Biological response modifiers (adjuvant trastuzumab)

Randomised controlled trials are needed to assess whether patients who have had adjuvant trastuzumab should receive further biological response modifiers.

Why this is important

As more HER2-positive patients 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 response modifiers are effective in this situation.

4.5 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

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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.

5 Other versions of this guideline

5.1 Full guideline

The full guideline, 'Advanced breast cancer: diagnosis and treatment' contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Cancer, and is available from [NCC website details to be added], our website (www.nice.org.uk/CGXXXfullguideline) and the National Library for Health (www.nlh.nhs.uk). [Note: these details will apply to the published full guideline.]

5.2 Quick reference guide

A quick reference guide for healthcare professionals is available from www.nice.org.uk/CGXXXquickrefguide

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

5.3 'Understanding NICE guidance'

Information for patients and carers ('Understanding NICE guidance') is available from www.nice.org.uk/CGXXXpublicinfo

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about advanced breast cancer.

6 Related NICE guidance

Published

Referral guidelines for suspected cancer. NICE clinical guideline 27 (2005). Available from www.nice.org.uk/CG027

Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (partial update of NICE clinical guideline 14). NICE clinical guideline 41 (2006). Available from www.nice.org.uk/CG041

Improving supportive and palliative care for adults with cancer. Cancer service guidance (2004). Available from www.nice.org.uk/csgsp

Improving outcomes in breast cancer – manual update. Cancer service guidance (2002). Available from www.nice.org.uk/csgbc

Bisphosphonates (alendronate, etidronate, risedronate), selective oestrogen receptor modulators (raloxifene) and parathyroid hormone (teriparatide) for the secondary prevention of osteoporotic fragility fractures in postmenopausal women. NICE technology appraisal guidance 87 (2005). Available from www.nice.org.uk/TA087

Guidance on the use of trastuzumab for the treatment of advanced breast cancer. NICE technology appraisal guidance 34 (2002). Available from www.nice.org.uk/TA034

Gemcitabine for the treatment of locally advanced or metastatic breast cancer. NICE technology appraisal guidance 116 (2007). Available from www.nice.org.uk/TA116

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

 Early and locally advanced breast cancer: diagnosis and treatment. NICE clinical guideline (publication expected Feburary 2009).

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- Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women. NICE technology appraisal update (publication date to be confirmed).
- Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women. NICE technology appraisal (publication date to be confirmed).
- Osteoporosis: assessment of fracture risk and the prevention of osteoporotic fractures in individuals at high risk. NICE clinical guideline (publication date to be confirmed.)

7 Updating the guideline

NICE clinical guidelines are updated as needed so that recommendations take into account important new information. We check for new evidence 2 and 4 years after publication, to decide whether all or part of the guideline should be updated. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

Appendix A: The Guideline Development Group

Mr John Winstanley (Chair)⁶

Consultant Surgeon, Royal Bolton Hospital

Dr Sarah Wilson (Chair)⁷

Medical Director, InHealth

Dr Nick Murray (Lead Clinician)

Senior Lecturer and Honorary Consultant Medical Oncologist, Cancer Research UK Clinical Centre, University of Southampton

Dr Murray Brunt

Consultant Clinical Oncologist, University Hospital of North Staffordshire NHS Trust

Dr Helen Burrell

Consultant Radiologist, Nottingham University Hospitals NHS Trust

Dr Susan Closs

Lead Consultant in Palliative Medicine/ Network Chair in Palliative Care (South West Wales Cancer Network), Swansea NHS Trust

Mrs Debbie Collins

Macmillan Radiotherapy Specialist, Kent Oncology Centre

Dr Dermott Davison

GP, County Antrim, Northern Ireland

Dr Chris Gaffney⁸

Consultant Clinical Oncologist, Velindre Cancer Centre, Cardiff

Mrs Kathleen Jenkins

Retired Clinical Nurse Specialist

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From February 2008 – February 2009
 From June 2006 to February 2008

⁸ From September 2007 – February 2009

Mrs Mary Milne⁹

Nurse Consultant, The Parapet Breast Unit

Mrs Susan Raettig

Patient/carer representative, Chair, Hull and East Riding Cancer Patient **Involvement Group**

Miss Jane Rankin

Lead Cancer Physiotherapist, Belfast City Hospital

Mrs Claire Ryan¹⁰

Lead Research Nurse, Oncology Clinical Trials, Kent Oncology Research Centre

Mr John Winstanley¹¹

Consultant Surgeon, Royal Bolton Hospital

Mrs Netta Wooles

Patient/carer representative

Miss Anna Wood¹²

Head of Policy and Campaigns, Breast Cancer Care

⁹ From June 2006 to July 2007

¹⁰ From November 2007 to February 2009 ¹¹ From June 2006 to February 2008

¹² From June 2006 to May 2008

Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

Dr John Hyslop (Chair)

Consultant Radiologist, Royal Cornwall Hospital NHS Trust

Dr Ash Paul

Deputy Medical Director, Health Commission Wales

Professor Liam Smeeth

Professor of Clinical Epidemiology, London School of Hygiene and Tropical Medicine

Mr Peter Gosling

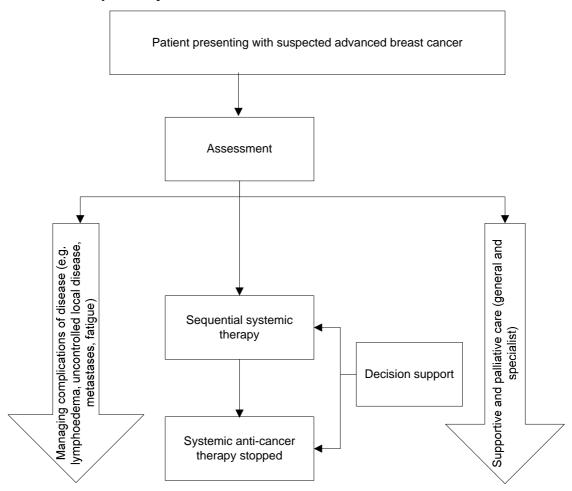
Lay member

Mr Jonathan Hopper

Medical Director (Northern Europe), ConvaTec Ltd

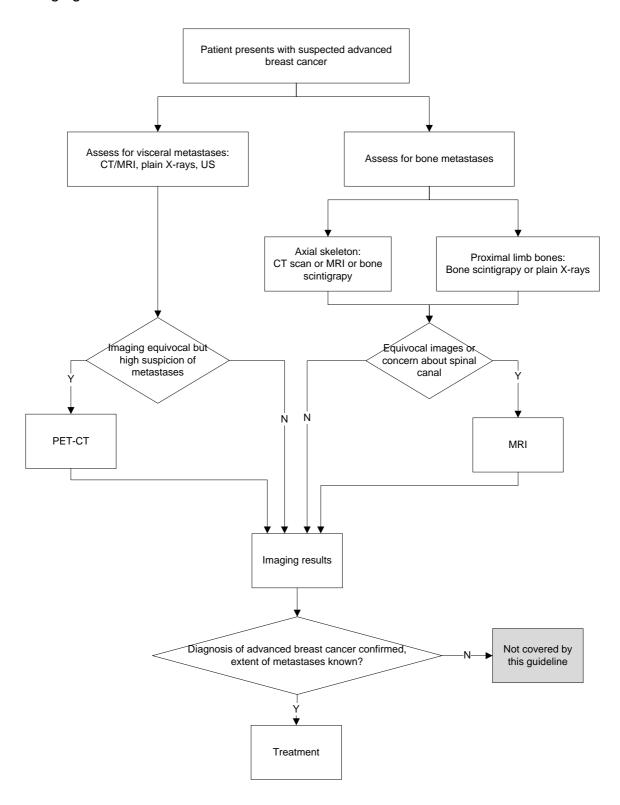
Appendix C: The algorithms

Overview of pathway

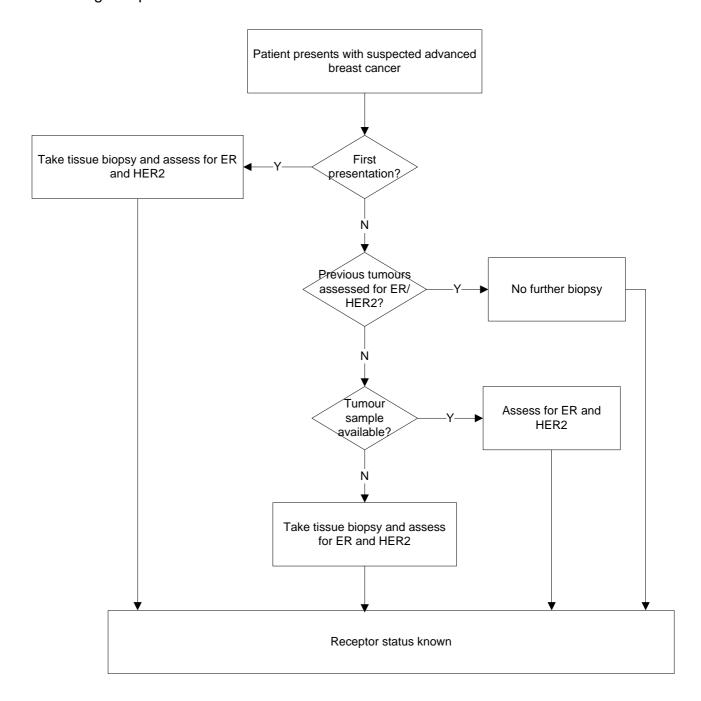


Diagnosing Advanced Breast Cancer

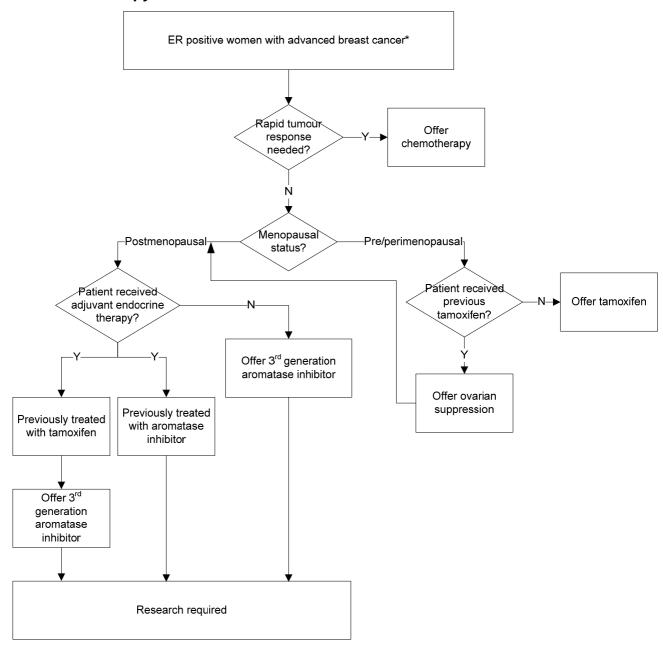
Imaging assessment



Assessing receptor status



Endocrine therapy



*For ER-positive men with advanced breast cancer offer tamoxifen as the first-line treatment

Chemotherapy



^{*}Consider combination therapy for patients in whom a greater probability of response is important and who understand/are likely to tolerate the additional toxicity