

# Guidance for the management of early breast cancer Recommendations and practice points

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# **Contents**

Context	1
Treatment planning, information & support	2
Multidisciplinary care and Care coordination	2
Patient information and support	2
Assessment and referral	3
Complementary and alternative therapies	5
Pathology and imaging prior to treatment	5
Treatment	7
Research and clinical trials	7
Neoadjuvant therapy	7
Surgery	8
Surgery timing	8
Breast conserving surgery (BCS) and mastectomy	8
Breast reconstruction	9
Sentinel node biopsy (SNB) and axilla management	10
Risk-reducing strategies	12
Systemic therapy	12
Systemic therapy planning	12
Chemotherapy	14
Anti-HER2 therapy	15
Cardiac dysfunction during treatment	16
Endocrine therapy	16
Bone-modifying agents and bone health	18
Radiation therapy	19
Radiation therapy timing	19
Radiation therapy after neoadjuvant chemotherapy	19
Radiation therapy after breast-conserving surgery	19
Radiation therapy after mastectomy	20
Radiation therapy of nodal regions	21
Radiation therapy and adverse events	21
Follow-up and survivorship care	22
Continuity of care and patient information	22
Follow-up care providers and plan	22
Patient information	22

Surveillance and imaging	23
Follow-up surveillance	23
Follow-up imaging	24
Management of long-term and late effects	24
Lymphoedema	24
Menopausal symptoms	25
Reproductive and sexual health	26
Fatigue and sleep disorders	26
Pain	27
Cognitive impairment	27
Psychosocial needs	27

## Context

This document contains a list of recommendations and practice points that have been developed to assist health professionals in the management and care of early breast cancer. The Guidance has been developed using a meta-guideline approach as described in the Methods report.

The purpose of this Guidance is to provide health professionals with up-to-date evidence-based guidance for the management of patients with early breast cancer that is relevant to the Australian health care setting. This Guidance aims to support the delivery of best practice patient-centred care and to assist health professionals and patients in shared decision-making regarding the management of early breast cancer.

Early breast cancer is defined as invasive breast cancer that is contained in the breast and may or may not have spread to the lymph nodes in the breast or armpit. The scope of this guidance covers the management of early breast cancer in women and men. The scope does not include the management of ductal carcinoma in situ (DCIS) which is non-invasive, or the management of advanced or metastatic cancer.

Guidance is included for the management and care of early breast cancer across the patient journey from the point of breast cancer diagnosis, including treatment planning and information and support for patients before treatment, treatment delivery, and follow-up of after active treatment and survivorship care for people living with and beyond early breast cancer. Screening and initial detection of early breast cancer are not included.

This Guidance is presented in full on a featured website to assist access to the information: www.guidancebreastcancer.gov.au. The website contains a webpage for each guidance point, with text describing how each guidance point was developed, the source information, and links to useful resources.

The Guidance is considered appropriate practice but does not replace clinical judgement and should be considered in relation to patient preferences. Practice is also underpinned by the seven key Principles of care, which are part of the Optimal Care Pathway for patients with breast cancer.

Breast cancer care is an area of high research activity and hence evidence-based practice can rapidly change. These recommendations and practice points are informed by the best-available evidence and information at the time the guidance was prepared.

1

# Treatment planning, information & support

## Multidisciplinary care and Care coordination

#### **Recommendation**

A key contact person, ideally a breast care nurse and/or a cancer care coordinator, should be agreed as soon as possible to support communication and coordination of patient-centred care. If appropriate, consultations may be via telephone and/or video conferencing calls, especially in regional or remote areas.

#### **Practice Point**

Discuss all cases of breast cancer within a multidisciplinary team (MDT) treatment planning meeting at least once, and ideally before any treatment, including surgery, is initiated so that a treatment plan can be recommended that takes account of patient comorbidities and includes consideration for neoadjuvant systemic therapy. If possible, results of all relevant tests and imaging should be available for the MDT discussion. Consider a follow-up discussion if there is significant change in the course of the disease after commencement of therapy.

#### **Practice Point**

Include obstetricians and perinatologists in the multidisciplinary team (MDT) for the treatment of patients with breast cancer during pregnancy. Particular attention should be paid to each woman's preferences and psychosocial needs due to the higher likelihood of distress.

## **Practice Point**

Close and early collaboration between oncologists and cardiologists is recommended for those patients that require treatment with a potentially cardiotoxic treatment, particularly in the context of existing cardiovascular disease or multiple cardiovascular risk factors.

## **Recommendation**

Generally, age alone should not dictate treatment decisions, however all management decisions for an older patient should consider life expectancy; potential risks versus absolute benefits; treatment tolerance; patient preferences; potential barriers to treatment; polypharmacy; and assessment of functional status, comorbidities, falls, depression, cognition, nutritional status and social situation.

## Patient information and support

#### Recommendation

All patients with a potential or known diagnosis of breast cancer should have access to information and support at every stage of diagnosis, treatment, and follow-up.

#### **Recommendation**

Assess each patient's information and support needs in relation to breast cancer and its treatment, side effects and other health concerns; and provide culturally appropriate resources and referral to available support services to meet these needs.

#### **Practice Point**

All clinicians involved in the care of patients with breast cancer should consider clinicianpatient communication training. It is essential that training is based on sound educational principles with a focus on ongoing acquisition and enhancement of skills.

#### **Recommendation**

Advise all patients with breast cancer that a healthy lifestyle is associated with a lower risk of recurrence and improved survival. Discuss how a healthy lifestyle includes achieving and maintaining a healthy weight, limiting alcohol intake, cessation of smoking and undertaking regular physical activity.

#### **Recommendation**

All patients with breast cancer should be advised to avoid inactivity and continue normal daily activities after diagnosis, and during and after breast cancer treatment, where possible.

#### **Recommendation**

Advise patients to undertake regular aerobic exercise and resistance exercise (strength training) before, during and after breast cancer treatment appropriate to their treatment and tailored to their general health, medical condition, and fitness.

#### **Recommendation**

Strongly encourage all patients with breast cancer to stop smoking. Advise patients that smoking increases the risk of complications of treatment (e.g. wound infection, deep vein thrombosis) and breast cancer recurrence, and worsens vasomotor symptoms.

## **Recommendation**

Inform all patients with breast cancer about the risk of developing lymphoedema and provide relevant information before treatment with surgery or radiation therapy.

## **Practice Point**

Inform patients and their GPs of potential cardiac risks associated with treatment, the importance of ongoing monitoring and management of cardiac health and cardiovascular risk factors based on their baseline and future risk of cardiac dysfunction, and, encourage a heart-healthy lifestyle.

## Assessment and referral

#### **Practice Point**

Pay attention to the emotional needs of the person diagnosed with breast cancer and undertake psychosocial screening as soon as possible after breast cancer diagnosis and at the commencement of any new treatment. Use a validated and reliable measure that features reportable scores that are clinically meaningful, with established cut-offs.

A detailed psychosocial assessment should be undertaken for patients at a higher risk of depression, e.g. patients with a history of mental health issues, patients with caring responsibilities, patients under financial stress, young patients, and those with multiple stressors.

#### Recommendation

If signs of distress, depression, or anxiety are present, consider offering patients referral to counselling and/or appropriate psycho-oncology and mental health resources as clinically indicated.

#### **Recommendation**

All patients with breast cancer should be assessed at or around the time of diagnosis for familial and genetic risk factors as indicated in current eviQ guidelines, which include relevant pathogenic variants in adult blood relatives, gender, ancestry, breast cancer characteristics, and personal and family cancer history.

#### **Recommendation**

In accordance with eviQ guidelines, patients suspected of having high familial or genetic cancer risk should be referred to a family cancer clinic for genetic counselling and genetic testing as appropriate.

#### **Practice Point**

Discuss fertility issues and the implications of premature menopause with all premenopausal women. Arrange early referral to a fertility specialist to maximise the opportunity for consideration of fertility preservation if appropriate and feasible.

#### **Recommendation**

Premenopausal women should be counselled regarding the risk of becoming pregnant while on chemotherapy, endocrine therapy, anti-HER2 therapy, or during radiation therapy, even in the presence of amenorrhoea.

#### **Recommendation**

Discuss and offer barrier contraceptive options (condoms or diaphragms, a copper intrauterine device, or surgical options) for premenopausal women with breast cancer, noting that systemic hormonal contraception is contraindicated irrespective of disease subtype.

#### **Practice Point**

Premenopausal women should be advised not to use a levonorgestrel-releasing intra-uterine device (LNG-IUD) and to use alternative non-hormonal contraception, as the safety of the LNG-IUD among women with breast cancer has not been determined.

#### **Recommendation**

A screening geriatric assessment is a reasonable first step in identifying patients who may benefit from an extended comprehensive geriatric assessment.

#### **Practice Point**

Patients at higher risk of lymphoedema (e.g. those in whom axillary clearance or axillary radiation therapy is planned, or patients with lymphatic insufficiency) should be referred to a lymphoedema therapist for assessment prior to breast cancer treatment, and for regular monitoring after breast cancer treatment. Bioimpedance measurements may be part of the clinical assessment.

#### **Recommendation**

A baseline cardiac risk assessment, including an echocardiogram, should be undertaken for patients whose treatment will include chemotherapy (especially anthracyclines) or HER2 therapy (especially trastuzumab) or left-sided radiation therapy.

#### **Recommendation**

Avoid or minimise the use of potentially cardiotoxic therapies if established alternatives exist that would not compromise cancer-specific outcomes.

# Complementary and alternative therapies

#### **Practice Point**

Facilitate open disclosure and non-judgmental dialogue with patients regarding existing or planned use of complementary medicines or alternative therapies.

#### **Practice Point**

Advise all patients with breast cancer that complementary medicines or alternative therapies should not be used instead of standard therapies for the purpose of improving breast cancer survival.

## **Practice Point**

Offer information regarding effective evidence-based complementary therapies (such as yoga, acupuncture, and meditation) for symptom control in patients with breast cancer.

# Pathology and imaging prior to treatment

## **Practice Point**

For patients with a breast lesion where the results of conventional diagnostic imaging (mammography or tomosynthesis and ultrasound) are inconclusive but suspicious for the presence of breast cancer and biopsy has not been possible, consider the use of contrast mammography or magnetic resonance imaging (MRI).

#### **Practice Point**

For patients with breast cancer where a discrepancy exists between clinical assessment and conventional diagnostic imaging (mammography or tomosynthesis and ultrasound), or there is a discrepancy in conventional imaging, consider the use of magnetic resonance imaging (MRI) if the results from this imaging are expected to alter treatment planning.

## **Practice Point**

Consider imaging with magnetic resonance imaging (MRI) or Contrast Enhanced Spectral Mammography (CESM) (where available) for patients with lobular breast cancer.

#### **Practice Point**

For patients who are considered suitable for active treatment and in whom staging of locally advanced (stage III) breast cancer is required or there is a high index of suspected metastatic breast cancer, consider the use of 18F-FDG positron emission tomography (PET).

## **Practice Point**

(a) Report breast pathology findings according to the Structured Reporting Protocols of Royal College of Pathologists of Australasia (RCPA); (b) Report breast imaging findings according to the standards of the Royal Australian and New Zealand College of Radiologists (RANZCR), Faculty of Clinical Radiology.

# **Treatment**

## Research and clinical trials

#### **Practice Point**

Strongly encourage and support patients with breast cancer to participate in clinical trials where a suitable trial is available.

# **Neoadjuvant therapy**

#### **Practice Point**

In patients with large tumours (who might not be candidates for breast-conserving surgery), consider the use of neoadjuvant systemic therapies to reduce tumour size and potentially enable breast-conserving surgery instead of mastectomy.

#### **Practice Point**

In patients with breast cancer who are treated with neoadjuvant systemic therapy, use imaging prior to the commencement of therapy and at the completion of therapy, to assist with surgical planning. The type of imaging (ultrasound or MRI) will be dependent on the histopathology of the breast lesion. In addition, use localisation techniques in the breast lesion and in any biopsy-proven positive lymph nodes before therapy is commenced.

#### **Practice Point**

In patients with breast cancer who are treated with neoadjuvant systemic therapy, consider using imaging for assessment of response after initiation of therapy to allow treatment modification.

#### **Recommendation**

Neoadjuvant systemic therapy should start as soon as diagnosis and staging is completed (ideally within 2-4 weeks).

## **Recommendation**

Consider neoadjuvant chemotherapy for suitable patients with breast cancer whose disease type is likely to show rapid response to chemotherapy and whose disease burden as assessed pre-operatively indicates a need for chemotherapy. Suitable patients may include those with triple negative breast cancer, HER2-positive breast cancer, or luminal B hormonal cancer.

## Recommendation

Discuss the benefits and risks of neoadjuvant chemotherapy, including toxicity (with consideration of regulatory status), and effects on breast conservation rate, pathological complete response rate, and survival.

Suitable neoadjuvant chemotherapy regimens include those used for adjuvant chemotherapy. Consider the addition of a platinum-based agent for patients with triple negative breast cancer.

#### **Recommendation**

Consider neoadjuvant endocrine therapy for postmenopausal women with ER-positive breast cancer as an option to reduce tumour size if there is no definite indication for chemotherapy.

# Surgery

## Surgery timing

#### **Practice Point**

Perform surgery within 4-6 weeks after neoadjuvant systemic therapy, allowing for recovery from myelosuppression.

#### **Practice Point**

Perform surgery within 1 month of a decision to treat with surgery among those patients who do not receive neoadjuvant therapy.

# Breast conserving surgery (BCS) and mastectomy

## **Recommendation**

In patients with breast cancer who are undergoing breast surgery, offer the choice of either breast-conserving surgery (if technically possible) followed by radiation therapy, or a mastectomy.

## Recommendation

Inform patients with breast cancer who are undergoing breast surgery, that radiation therapy is usually required following breast-conserving surgery and that further surgery may be required if the surgical margins are positive or close.

#### **Recommendation**

In patients with breast cancer with a confirmed germline mutation (e.g. BRCA1/2) that predisposes to an increased risk of breast cancer, discuss the options of breast-conserving surgery, mastectomy or bilateral mastectomy, noting that there is a higher risk of a second malignancy if the breast is conserved, but that this risk is reduced by adjuvant systemic therapy.

#### **Practice Point**

Ensure optimal fixation (and labelling) of breast cancer specimens for accurate pathological examination and biomarker assessment.

#### **Practice Point**

Conduct post-excisional specimen imaging of image-guided excisions. The specimen should be suitably labelled with sutures and clips to allow orientation and margin assessment. Imaging can be specimen mammogram or ultrasound, performed by either the radiologist or surgeon.

#### **Recommendation**

Offer further surgery (re-excision or mastectomy, as appropriate) after breast-conserving surgery where invasive cancer and/or DCIS is present at the radial margins (as defined by tumour on ink, 0 mm).

#### Recommendation

Consider further surgery (re-excision or mastectomy, as appropriate) after breast-conserving surgery where there is invasive cancer and/or DCIS within 2mm of but not at the radial margins (>0mm and <2 mm).

#### **Practice Point**

In patients with Paget's disease of the nipple, perform breast imaging prior to surgery to exclude underlying breast malignancy.

#### Recommendation

In patients with Paget's disease of the nipple with or without underlying breast cancer, offer breast-conserving surgery with removal of the nipple/areolar complex followed by whole breast radiation therapy, as an alternative to mastectomy.

## **Recommendation**

In patients with Paget's disease of the nipple treated with breast-conserving surgery with removal of the nipple/areolar complex, offer nipple reconstruction, based on the individual patient's preferences.

## **Breast reconstruction**

#### Recommendation

Before a mastectomy is performed, discuss the benefits and risks of all reconstruction options with reference to timing (immediate or delayed), technique (implant-based or tissue-based reconstruction) and breast symmetrising procedures, regardless of whether these procedures are available locally, and implications for future surveillance. Be aware that some patients may prefer not to have breast reconstruction surgery, and some may prefer to discuss reconstruction later.

#### **Practice Point**

Inform patients that chemotherapy may be delayed if complications arise from reconstructive surgery.

Skin-sparing mastectomy or nipple-sparing mastectomy with immediate breast reconstruction can be offered to patients undergoing risk-reducing mastectomy.

#### **Practice Point**

For patients who are contemplating delayed breast reconstruction, and who have had chest wall radiation therapy, tissue-based reconstruction is preferred.

#### Recommendation

For patients undergoing implant-based breast reconstruction, no recommendations can be made for or against the use of specific collagen-based or non-biological matrices.

#### Recommendation

For patients undergoing breast reconstruction, no recommendations can be made for or against the routine use of autologous fat grafting for aesthetic purposes, noting that its use should be based on clinical need.

#### **Practice Point**

Consider nipple-sparing mastectomy for all patients with breast cancer without clinical or radiological nipple involvement but be cautious for patients with the following clinical features: extensive DCIS, significant ptosis (unless staging procedure considered), invasive cancer close to the nipple, large breasts, or the presence of risk factors for skin flap ischaemia (such as smoking, diabetes, or general poor health).

## Recommendation

Nipple-sparing mastectomy and areola-sparing mastectomy are not recommended in inflammatory breast cancer or where the cancer involves the nipple/areolar complex.

## Sentinel node biopsy (SNB) and axilla management

## Recommendation

Offer sentinel node biopsy to breast cancer patients with no clinical or radiological evidence of axillary lymph node metastases at initial diagnosis.

## **Practice Point**

Perform sentinel node biopsy (SNB) in clinically node negative T1 tumours. SNB can be performed in node negative T2/T3 or multicentric/multifocal cancer, noting that SNB is associated with a higher false negative rate in these cancers.

#### **Practice Point**

Sentinel node biopsy is not required when performing risk-reducing mastectomy, provided the patient has had adequate pre-operative imaging.

Sentinel node biopsy should not be performed in patients who have inflammatory breast cancer.

#### **Practice Point**

In pregnant women with breast cancer with no clinical or radiological evidence of axillary lymph node metastases at initial diagnosis, consider the use of radioactive tracers but do not use Patent Blue dye if undertaking sentinel node biopsy.

#### **Practice Point**

Where possible, lymphatic mapping with pre-operative lymphoscintigraphy in combination with intraoperative use of the gamma probe and Patent Blue dye should be used to locate the sentinel node(s), noting that the theatre team and anaesthetist must be aware of the potential for Patent Blue dye to cause anaphylaxis.

#### **Practice Point**

Where combination technique is not available or suitable, the use of radioisotope alone or Patent Blue dye alone (where no nuclear facilities are available) may be considered, noting that the theatre team and anaesthetist must be aware of the potential for Patent Blue dye to cause anaphylaxis.

#### **Practice Point**

Excise all identified sentinel nodes, including internal mammary nodes where access is possible.

## **Practice Point**

Do not routinely perform intraoperative assessment of the sentinel node.

#### **Recommendation**

In order to allow staging as per American Joint Committee on Cancer (AJCC) criteria, sentinel lymph nodes must be examined pathologically by a method which ensures detection of all clinically significant metastases (i.e. 2 mm or greater). All lymph node tissue should be processed. Immunohistochemistry can be used selectively.

#### **Recommendation**

Offer axillary node clearance to patients with breast cancer who have a pre-operative ultrasound-guided needle biopsy with pathologically proven lymph node metastases.

#### **Recommendation**

Discuss further axillary treatment (axillary node clearance or radiation therapy) in patients who have more than two macrometastases.

Discuss the benefits and risks of having no further axillary treatment after mastectomy or after breast-conserving surgery in patients who have one or two sentinel lymph node macrometastases and have been advised to have radiation therapy and adjuvant systemic therapy.

#### **Recommendation**

Do not offer further axillary treatment after breast-conserving surgery and breast radiation therapy or mastectomy to patients who have only micrometastases (0.2 - ≤2 mm) in their sentinel lymph nodes, or who have only isolated tumour cells (<0.2 mm) in their sentinel lymph nodes.

#### **Practice Point**

Management of an axilla that becomes sentinel node negative after neoadjuvant systemic therapy is an emerging aspect of care and no definitive guidance can currently be given.

## Risk-reducing strategies

#### **Recommendation**

In patients with breast cancer with a population risk of contralateral breast cancer (that is, no genetic predisposition) do not routinely offer risk-reducing mastectomy for the contralateral breast.

#### **Recommendation**

In premenopausal women with breast cancer with a confirmed germline mutation (e.g. BRCA 1/2) that predisposes to an increased risk of breast cancer, discuss risk-reducing strategies (e.g. contralateral risk-reducing mastectomy or endocrine therapy/ risk-reducing medication).

#### **Recommendation**

In women with breast cancer with a confirmed germline mutation (e.g. BRCA 1/2) that predisposes to an increased risk of ovarian/fallopian tube cancer, refer to a gynaecological oncologist for discussion of the benefits and risks of bilateral salpingo-oophorectomy (BSO).

# Systemic therapy

## Systemic therapy planning

#### Recommendation

Request simultaneously the oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth receptor 2 (HER2) status of all core biopsies of invasive breast cancers, at the time of initial histopathological diagnosis.

Assess the ER, PR and HER2 status of all invasive breast cancers using standardised and quality-assured immunohistochemical techniques and report the results quantitatively. Ensure receptor status test results are available and recorded at the preoperative and postoperative multidisciplinary team meetings when systemic treatment is discussed.

#### **Practice Point**

Perform in situ hybridisation testing for HER2 status on core biopsy material if neoadjuvant systemic therapy is being considered, noting that receptor status between core and surgical specimens may be different.

#### **Practice Point**

If considering the use of tumour gene expression profiling tests to inform decisions about the use of adjuvant chemotherapy for patients with breast cancer, be aware that the clinical utility of these tests has not yet been established. Discuss with the patient the potential benefits (reduced adverse events due to avoiding chemotherapy) and potential harm (breast cancer recurrence that might have been prevented) of using these.

#### **Practice Point**

Repeat receptor status testing on any residual disease after neoadjuvant systemic therapy.

## Recommendation

Consider adjuvant systemic therapy after surgery for patients with invasive breast cancer, individualising treatment based on a multidisciplinary assessment of prognostic and predictive factors and the possible risks and benefits of treatment. Ensure that recommendations for treatment are recorded at a multidisciplinary team meeting.

## **Recommendation**

In patients with breast cancer consider use of the PREDICT tool to estimate prognosis and the absolute benefits of adjuvant systemic therapy, recognising that the PREDICT tool is less accurate in some women and has not been validated in men or in an Australian population. Ki67 should be used in conjunction with other clinicopathological variables and should not be used alone in any patient to make treatment decisions.

#### **Recommendation**

Offer temporary ovarian suppression with a gonadotrophin releasing hormone (GnRH) agonist such as goserelin during chemotherapy to all premenopausal breast cancer patients undergoing chemotherapy who are interested in preventing early menopause and/or preserving fertility. Commence goserelin at least one week prior to the commencement of chemotherapy.

## **Practice Point**

Advise women with breast cancer who are receiving chemotherapy, anti-HER2 therapy, or tamoxifen, to avoid pregnancy as these therapies are potentially teratogenic.

In pregnant women with breast cancer, chemotherapy can be considered after 14 weeks of gestation.

#### **Practice Point**

The dosage of chemotherapeutic agents should be the same for pregnant women as compared to non-pregnant women. A lower pre-pregnant weight should not be used.

#### **Practice Point**

Breastfeeding is not recommended during chemotherapy or endocrine therapy.

# Chemotherapy

#### Recommendation

Consider adjuvant chemotherapy for all patients with breast cancer whose disease is at high risk of recurrence and has a subtype likely to respond to adjuvant chemotherapy (e.g. triple negative; HER2-postive; luminal B).

#### **Recommendation**

The choice of neoadjuvant or adjuvant chemotherapy should be determined by a patient's comorbidities, physical function, and degree of frailty, and not by gene mutation status or age alone.

#### Recommendation

Ideally adjuvant chemotherapy should commence within 4 to 6 weeks of the date of surgery. If adjuvant chemotherapy and radiation therapy are indicated, the chemotherapy should be given first.

#### **Practice Point**

Chemotherapy can be given concurrently with the gonadotropin-releasing hormone (GnRH) agonist goserelin, but not with tamoxifen.

#### **Recommendation**

The cumulative dose of anthracycline in a two-drug regimen should not exceed 240 mg/m2 for doxorubicin, or 720 mg/m2 for epirubicin.

## Recommendation

When choosing a chemotherapy regimen, consider the cumulative toxicity when an anthracycline and a taxane are used together.

#### **Recommendation**

For patients in whom an anthracycline-taxane regimen is contraindicated, cyclophosphamide-methotrexate-fluorouracil (CMF) with oral cyclophosphamide is an acceptable chemotherapy alternative.

Refer to eviQ for the preferred adjuvant chemotherapy regimens (including dose-dense regimens and alternatives to doxorubicin-cyclophosphamide x 4).

#### **Practice Point**

Treat all patients with growth factor support if dose-dense adjuvant systemic therapy is being prescribed and for other regimens where the risk of febrile neutropenia is higher than 20%.

#### Recommendation

Offer trastuzumab emtansine as additional adjuvant treatment for patients with HER2-positive breast cancer who have residual disease after a neoadjuvant taxane-trastuzumab regimen.

#### **Practice Point**

For patients with triple negative breast cancer with residual disease after neoadjuvant chemotherapy, consider the addition of capecitabine to a post-neoadjuvant anthracycline-taxane regimen.

#### **Practice Point**

Use adequate antiemetics when treating patients with systemic therapy.

#### **Recommendation**

Consider scalp cooling to reduce the risk of hair loss for patients receiving chemotherapy, noting scalp cooling may be less effective with anthracycline-containing regimens.

## Anti-HER2 therapy

## **Recommendation**

Offer adjuvant trastuzumab (with or without pertuzumab) for patients with at least T1c, HER2-positive breast cancer (given at 3-week intervals for 1 year) in combination with surgery, chemotherapy, and radiation therapy as appropriate.

#### **Recommendation**

Consider trastuzumab in addition to chemotherapy as adjuvant treatment for patients with T1a/T1b HER2-positive breast cancer, taking into account any comorbidities, prognostic features and possible toxicity of chemotherapy.

## Recommendation

Ideally adjuvant trastuzumab (with or without pertuzumab) should be given concurrently with taxane-based regimens but should not be given concurrently with anthracyclines.

#### **Practice Point**

Consider adding neratinib to high risk ER-positive/HER2-positive patients who complete one year of trastuzumab and remain disease-free.

In patients receiving trastuzumab, consider monitoring cardiac function during treatment (e.g. every 3 months) and follow-up. Early referral to a cardiologist should be considered in cases of deterioration in cardiac function.

# **Cardiac dysfunction during treatment**

#### **Recommendation**

Consider routine surveillance during treatment, preferably with an echocardiogram, of asymptomatic patients considered to be at increased risk of developing cardiac dysfunction. Frequency of surveillance should be determined by patient baseline and future risk of cardiotoxicity.

#### **Recommendation**

In patients with clinical signs or symptoms of cardiac dysfunction during routine clinical assessment throughout treatment, the following approaches are recommended:

- i. Echocardiogram for diagnostic workup
- ii. Cardiac MRI can be performed if echocardiogram is not available or is not technically feasible (e.g. poor image quality). Alternatively, gated heart pool scan can be considered
- iii. Serum cardiac biomarkers (troponins, natriuretic peptides) as an adjunct to imaging and clinical assessment
- iv. Refer to a cardiologist based on clinical context and findings.

Consider deferral or cessation of cardiotoxic treatment where clinically indicated, in collaboration with a cardiologist.

# **Endocrine therapy**

#### Recommendation

Adjuvant endocrine therapy should be considered in all patients with ER-positive cancer, defined as ER immunohistochemistry (IHC) staining ≥1%. Discuss the benefits and risks of endocrine therapy with patients whose cancers contain low levels of ER-positive cells (1%-10% weakly positive cells by IHC).

## Recommendation

Consider adjuvant endocrine therapy in patients with ER-negative but PR-positive tumours, noting that this scenario is extremely unusual, and consideration should be given to repeat confirmatory testing.

#### **Practice Point**

Endocrine therapy should start as soon as appropriate, after completion of chemotherapy and/or radiation therapy (and in some cases will be started prior to chemotherapy).

In patients with ER-positive tumours who do not commence adjuvant endocrine therapy immediately after surgery or chemotherapy, delayed endocrine therapy is still clinically beneficial.

#### Recommendation

Primary endocrine therapy (endocrine therapy alone without surgery) should only be offered to older patients with ER-positive tumours who have a short-estimated life expectancy (<2–3 years), who are considered unfit for surgery after optimisation of comorbid medical conditions, or who decline surgery. The involvement of a geriatrician is strongly recommended to estimate life expectancy and guide management of reversible comorbidities. It is reasonable to choose tamoxifen, or an aromatase inhibitor based on potential side-effects.

#### **Recommendation**

Omission of adjuvant endocrine therapy is an option for older patients with a very low risk tumour (pT1aN0) or those with life-limiting comorbidities.

#### **Practice Point**

Advise patients commencing endocrine therapy on the importance of weight-bearing exercise and on adequate calcium intake and vitamin D levels.

## Recommendation

Offer tamoxifen as the initial adjuvant endocrine therapy for men, and for premenopausal women with ER-positive invasive breast cancer with low risk of recurrence.

#### Recommendation

For premenopausal women with ER-positive breast cancer at higher risk of recurrence, consider ovarian function suppression with a gonadotrophin releasing hormone (GnRH) agonist in addition to endocrine therapy (tamoxifen or aromatase inhibitors), noting that a GnRH agonist must be used with aromatase inhibitors.

## **Recommendation**

If a gonadotropin-releasing hormone (GnRH) agonist is used in premenopausal women, it should be given on a monthly basis to optimise ovarian suppression.

#### Recommendation

Offer an aromatase inhibitor as the initial adjuvant endocrine therapy for postmenopausal women with lobular cancer or ER-positive breast cancer who are at intermediate or high risk of recurrence. Offer tamoxifen or aromatase inhibitors to postmenopausal women who are at low risk of recurrence. Offer tamoxifen if aromatase inhibitors are not tolerated or are contraindicated.

Consider extending the duration of tamoxifen therapy beyond 5 years for both premenopausal and postmenopausal women with ER-positive breast cancer.

#### Recommendation

Offer extended therapy (total duration of endocrine therapy of more than 5 years) with an aromatase inhibitor for postmenopausal women with ER-positive breast cancer who are at intermediate or high risk of late recurrence and who have been taking tamoxifen for 2 to 5 years.

#### **Recommendation**

Consider extended therapy (total duration of endocrine therapy of more than 5 years) with an aromatase inhibitor for postmenopausal women with ER-positive breast cancer who are at intermediate or high risk of late recurrence and who have been taking tamoxifen for 2 to 5 years.

#### **Practice Point**

Be aware that alternative strategies for extended endocrine therapy with aromatase inhibitors, depending on risk of recurrence and tolerance of therapy, include: continuous therapy to 7.5 years, therapy up to 10 years with a 3-month break each year, and continuous therapy for up to 10 years.

# Bone-modifying agents and bone health

## **Recommendation**

Consider imaging with dual energy x-ray (DEXA) to measure bone mineral density in patients with breast cancer treated with chemotherapy and/or endocrine therapy.

#### Recommendation

Consider the use of zoledronic acid or denosumab for the management of treatment-induced bone loss in patients with breast cancer.

#### Recommendation

Before commencing treatment with a bone-modifying agent (denosumab or zoledronic acid) discuss the benefits, common and rare side effects, risks (including unknown harms to future offspring) and regulatory status of the treatments.

#### **Practice Point**

Refer all patients to a dentist for preventative and ongoing dental care before commencing treatment with a bone-modifying agent.

#### **Recommendation**

Consider the use of zoledronic acid as adjuvant therapy for premenopausal women receiving ovarian suppression.

Consider the use of zoledronic acid as adjuvant therapy for postmenopausal women with breast cancer with a moderate to high risk of recurrence.

## Radiation therapy

# Radiation therapy timing

#### **Practice Point**

In patients who have completed definitive surgery for breast cancer, commence radiation therapy as soon as possible after wound healing within 8 weeks of surgery or typically within 3-4 weeks of completion of adjuvant chemotherapy.

#### **Practice Point**

For patients requiring mastectomy and radiation therapy offer breast reconstruction with the opportunity to discuss the risks and benefits of early or delayed reconstruction, taking into account different surgical techniques, reconstruction methods and patient preferences. In patients considering breast reconstruction, discuss the risk of complications and reconstructive failure in relation to the timing of radiation therapy.

#### **Practice Point**

The ideal sequencing of radiation therapy, neoadjuvant systemic therapy and reconstruction is unknown and therefore should be discussed by a multidisciplinary team (MDT), ideally before surgery or radiation therapy.

## Radiation therapy after neoadjuvant chemotherapy

#### **Recommendation**

For patients with locally advanced breast cancer and/or involved lymph nodes at presentation who have received neoadjuvant chemotherapy, consider post-mastectomy radiation therapy with or without nodal radiation therapy.

## Recommendation

For patients with inflammatory breast cancer who have been treated with neoadjuvant chemotherapy, offer local/regional treatment with mastectomy followed by radiation therapy.

# Radiation therapy after breast-conserving surgery

## Recommendation

Offer breast radiation therapy to patients with breast cancer who have had breast-conserving surgery with clear surgical margins.

In patients who have undergone breast-conserving surgery and who are at high risk of local recurrence (age ≤50 years with any grade, age 51-70 years with higher grade, or a positive margin), offer radiation therapy boost following whole-breast radiation therapy.

#### Recommendation

Discuss the benefits and risks of omitting radiation therapy after breast-conserving surgery in women over 70 years of age with very low risk of local recurrence and who are suitable and willing to take endocrine therapy for five years.

#### **Recommendation**

In patients with breast cancer (excluding lobular type) who have undergone breast-conserving surgery with clear surgical margins and who have a very low risk of local recurrence, partial breast irradiation can be considered if patients are suitable and willing to take adjuvant endocrine therapy for five years.

#### **Recommendation**

Offer a hypofractionated course of radiation therapy to women with breast cancer who have undergone breast-conserving surgery with clear surgical margins and who require post-operative whole breast radiation therapy.

# Radiation therapy after mastectomy

#### **Recommendation**

For patients with breast cancer who have undergone a mastectomy and have at least four positive lymph nodes and a T3 or T4 tumour or involved surgical margins, offer adjuvant radiation therapy to the chest wall.

## **Recommendation**

For patients with breast cancer who have undergone a mastectomy and have macrometastases in 1-3 lymph nodes, consider adjuvant radiation therapy to the chest wall.

#### **Recommendation**

For patients with breast cancer who have undergone a mastectomy and have lymph nodenegative T3 or T4 cancer, consider adjuvant radiation therapy to the chest wall.

#### Recommendation

For patients with breast cancer who have undergone mastectomy and who are at low risk of local recurrence (e.g. most people who have lymph node-negative breast cancer), do not offer radiation therapy to the chest wall.

# Radiation therapy of nodal regions

#### **Practice Point**

For patients with 4 or more nodes involved, offer radiation of the nodal basins in addition to the chest wall or whole breast.

#### **Practice Point**

For patients with 1-3 lymph nodes involved, consider radiation of the nodal basins in addition to the chest wall or whole breast.

#### **Practice Point**

For patients where involvement of the internal mammary lymph nodes is identified during sentinel node biopsy or an 18F-FDG PET study, consider radiation to the internal mammary lymph node chain.

# Radiation therapy and adverse events

#### Recommendation

In patients undergoing radiation therapy use techniques that minimise the dose to the lung and heart, including deep inspiratory breath-holding for left-sided cancer.

#### **Practice Point**

Wherever possible, avoid radiation therapy in patients with p53 genetic mutations.

#### **Practice Point**

In pregnant women with breast cancer with a high risk of recurrence, the multidisciplinary team should consider the risks and benefits of radiation therapy to the woman and the fetus, and these should be discussed with the woman.

## **Practice Point**

In pregnant women with breast cancer with a low to intermediate risk of recurrence, delay radiation therapy until after delivery of the baby.

# Follow-up and survivorship care

## Continuity of care and patient information

# Follow-up care providers and plan

#### **Recommendation**

- (a) The selection of the provider of follow-up care (specialist(s) and/or general practitioner (GP)) should be a decision made by the multidisciplinary team and the patient, and be based on the purpose of follow-up and the individual patient's needs, risk of recurrence, circumstances, health literacy, and preferences for shared follow-up care. This decision should be reviewed over time.
- (b) All patients should be offered the opportunity for their follow-up care to be shared between a GP and a specialist, to provide more accessible, whole-person care.
- (c) All patients should be informed about the benefits of GP involvement in their follow-up care and other relevant information to make an informed choice.

#### **Recommendation**

A patient's follow-up care plan should be developed in consultation with the patient, the GP, and the multidisciplinary team following completion of active treatment. To support coordination of care, the care plan should be provided to the multidisciplinary team, including the GP, and indicate the health professional(s) designated to provide follow-up care and the patient's individual follow-up schedule.

## Recommendation

The patient should be provided with an agreed follow-up schedule and shared care plan.

#### Patient information

#### **Recommendation**

All patients should be provided with information about the symptoms and signs of local or regional recurrence and their individual risk of recurrence.

#### Recommendation

Patients prescribed adjuvant endocrine therapy should be provided with information and support to continue their full course of therapy.

22

## Surveillance and imaging

## Follow-up surveillance

#### **Practice Point**

In patients with breast cancer ensure that follow-up care includes ongoing assessment for possible long-term toxicities and late effects of adjuvant treatments (including secondary cancers, cardiovascular toxicity, lymphoedema, mental health (including distress, depression, anxiety, body image), sexual health, premature menopause, infertility, fatigue, weight gain, impaired cognitive function, musculoskeletal health, pain and neuropathy, and bone health).

#### **Recommendation**

Patient history and clinical examination should occur every 3-6 months for the first 2 years, every 6-12 months for the next 3 years and annually after 5 years.

#### Recommendation

In patients who have been treated for breast cancer and who are not experiencing symptoms, do not perform intensive testing (full blood count, biochemistry or tumour markers) or intensive imaging (chest x-ray, PET, CT or radionuclide bone scans) as part of standard follow-up.

#### Recommendation

All patients who have received treatment for breast cancer should be encouraged to participate in other cancer screening programs as for the general population.

## Recommendation

In patients who have undergone a mastectomy and breast reconstruction surveillance should consist of regular clinical examination of the chest wall and reconstructed breast at every routine follow-up visit.

#### Recommendation

In asymptomatic patients considered to be at increased risk of cardiac dysfunction, perform cardiac imaging (preferably an echocardiogram, or a cardiac MRI or a gated heart pool scan) between 6-12 months and at 24 months after completion of cancer-directed therapy.

## **Practice Point**

Patients who have undergone treatment for breast cancer and are found to have breast symptoms, signs, or imaging results suggestive of a breast cancer recurrence during follow-up should be rapidly referred to a specialist for further assessment.

# Follow-up imaging

#### Recommendation

Patients who have undergone breast-conserving surgery should be referred for annual mammography of both breasts.

Patients who have undergone a unilateral mastectomy should be referred for annual mammography on the intact breast.

Patients may choose to return to BreastScreen for routine annual mammographic surveillance after 5 years.

Consider the addition of ultrasound to mammography for follow-up, when indicated on clinical or radiological grounds.

#### **Practice Point**

In patients less than 50 years of age who are carriers of high-risk gene mutations (e.g. BRCA1/2) and who have not undergone risk-reducing mastectomy, consider the use of annual magnetic resonance imaging (MRI) of both breasts during follow-up.

#### **Recommendation**

In patients who have undergone breast-conserving surgery or a mastectomy and breast reconstruction, diagnostic imaging (mammography, ultrasound, or magnetic resonance imaging) is useful in the evaluation of new symptoms (e.g. lumps, skin changes).

#### **Recommendation**

In patients who have undergone a mastectomy and breast reconstruction and who are asymptomatic, routine imaging of the reconstructed breast is not recommended.

#### Recommendation

In patients who have undergone a mastectomy and breast reconstruction diagnostic imaging (mammography, ultrasound, or magnetic resonance imaging) is useful in the evaluation of new symptoms (e.g., lumps, skin changes).

## Management of long-term and late effects

# Lymphoedema

#### **Recommendation**

For patients who have had treatment for breast cancer, give advice on skin care and how to prevent and manage infection that may cause or exacerbate lymphoedema.

#### Recommendation

When informing patients with breast cancer about the risk of developing lymphoedema or breast or chest wall oedema, advise them of the importance of using the treated arm in daily activities, of regular participation in physical activities, and maintenance of a healthy weight, to minimise the risk of lymphoedema/oedema.

Low risk medical procedures (such as injections, blood tests, or intravenous administration of medicines) can be performed on the arm of the treated side if needed, as such procedures will not cause or worsen lymphoedema. In patients with lymphoedema, blood pressure monitoring on the arm of the treated side should depend on clinical need.

#### **Recommendation**

Patients who have been treated for breast cancer who develop lymphoedema should have access to a lymphoedema therapist.

# **Menopausal symptoms**

## **Recommendation**

Discuss the risks and benefits of therapies for managing menopausal symptoms (hot flushes, night sweats and vaginal dryness) associated with breast cancer treatments, noting that all forms of systemic menopausal hormonal therapy (MHT) including oestrogen-only, combined oestrogen and progestogen, tibolone, and compounded or bioidentical hormones are contraindicated in women with a personal history of breast cancer.

#### Recommendation

Consider first-line treatment with cognitive behavioural therapy (CBT) delivered in person or online for the management of moderate to severe hot flushes or night sweats and sleep disturbance in women with a history of breast cancer.

#### **Recommendation**

Consider second-line treatment with non-endocrine systemic therapies (venlafaxine, desvenlafaxine, paroxetine, escitalopram, clonidine, or gabapentin) at doses shown to be effective in the management of moderate to severe hot flushes or night sweats in women with a history of breast cancer. Women treated with any of these drugs should be monitored for the development of adverse effects which may include sexual dysfunction, gastrointestinal symptoms, anxiety, sleep disturbance, or in rare cases suicidal ideation. Be aware that paroxetine should be avoided in women treated with tamoxifen.

## **Recommendation**

In breast cancer patients experiencing sleep disturbance due to vasomotor symptoms and that is impacting on their quality of life, consider the second-line use of non-endocrine systemic therapies (desvenlafaxine, paroxetine, gabapentin) at doses shown to be effective in the management of sleep disturbance due to vasomotor symptoms. Be aware that paroxetine should be avoided in women treated with tamoxifen.

#### **Practice Point**

Advise patients that there is negative or insufficient evidence of the effectiveness of complementary or alternative therapies for the management of hot flushes, night sweats or vaginal dryness.

# Reproductive and sexual health

#### **Recommendation**

Ask patients about concerns with sexual intimacy, and refer for further therapy, if appropriate.

#### **Practice Point**

In women with a history of breast cancer who have vaginal dryness, offer first-line treatment with non-alcohol based vaginal lubricants during sexual activity. Consider topical lidocaine treatments to the vulvovaginal area for women experiencing pain with sexual activity.

#### **Practice Point**

In women with a personal history of breast cancer who have persistent vulvovaginal symptoms that are unresponsive to non-hormonal treatments, consider second-line treatment with vaginal oestrogens (low dose vaginal oestradiol, or vaginal oestriol).

#### **Recommendation**

Exogenous testosterone is not recommended as a treatment to improve sexual function in women with a personal history of breast cancer, as the efficacy and long-term safety after breast cancer has not been established.

#### **Recommendation**

Patients of childbearing age who experience infertility after treatment for breast cancer should be referred to a specialist in reproductive endocrinology and infertility as soon as possible.

## Fatigue and sleep disorders

#### **Recommendation**

Assess all patients with breast cancer for fatigue and advise patients on the importance of good sleep hygiene practices.

## Recommendation

Offer therapy or referral, as appropriate, for factors that may impact on or cause fatigue (e.g. depression, sleep disturbance, pain, anaemia, lymphoedema, thyroid or cardiac dysfunction). For those patients who do not have an otherwise identifiable cause of fatigue, offer referral to appropriate assessment and treatment services (such as a psychologist).

#### **Practice Point**

In patients with breast cancer who are experiencing fatigue, encourage physical activity as exercise counteracts the adverse effects of cancer and its treatment.

#### **Pain**

#### **Practice Point**

Assess for pain and contributing factors with the use of a simple pain scale and comprehensive history of the patient's condition. Be aware of the importance of assessing ongoing and persistent or new pain and consider the possibility of local recurrence.

#### Recommendation

Where treatment-related pain is present, offer interventions such as paracetamol and non-steroidal anti-inflammatory drugs. Consider referral to a specialist practitioner (e.g. lymphoedema therapist, occupational therapist, or pain specialist) as appropriate, depending on the underlying cause of the pain.

#### **Practice Point**

In patients with breast cancer who are experiencing arthralgia, encourage physical activity as exercise can reduce musculoskeletal symptoms. If exercise or NSAIDs are unsuccessful, consider changing to a different aromatase inhibitor, use of duloxetine, or switching to tamoxifen.

#### **Recommendation**

Assess for peripheral neuropathy in relation to chemotherapy by asking patients about their symptoms, specifically symmetrical numbness and tingling in their hands and/or feet, and the characteristics of the symptoms. Physical activity and/or duloxetine may be helpful in the treatment of peripheral neuropathic pain, numbness, and tingling. Be aware that asymmetrical numbness of the hands may be due to carpal tunnel syndrome, which is more common in women with breast cancer on endocrine therapy and will require different management.

## Cognitive impairment

## Recommendation

If cognitive impairment in association with breast cancer or its treatment is suspected, assess for and treat reversible contributing factors (e.g. thyroid dysfunction), discuss coping strategies, and offer referral to an appropriate health professional (geriatrician, neurologist, psychiatrist or psychologist) experienced in the assessment and management of cognitive impairment.

## **Psychosocial needs**

#### **Practice Point**

Diagnose and treat anxiety and depression in patients with breast cancer the same way as in the general population, noting that anxiety and depression reduce an individual's ability to cope with disease and treatment burden. Be aware that menopausal symptoms and anxiety and depression are interconnected: treatment of menopausal symptoms may improve anxiety and depression (particularly via the resolution of sleep disturbance), while treatment of anxiety and depression may improve an individual's ability to cope with menopausal symptoms.

## **Practice Point**

Ask patients if they're worried about the cancer recurring. Assess whether these worries are having a significant impact on their life and if so, offer referral to a psychologist.

## **Practice Point**

Be aware that returning to work or caring duties after breast cancer treatment is often a challenge and that extra professional support may be needed (e.g. psychological services).

## **Practice Point**

For patients contemplating returning to work, consider referral for vocational rehabilitation programs where available.