



GUIDELINES FOR MANAGEMENT OF BREAST CANCER

in the State of Qatar

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This document is a best practice guide intended to assist in the diagnosis, management, treatment and care of breast cancer in the State of Qatar compiled by members of the Breast Tumour Board and Supreme Council of Health and based on guidelines from Hamad Medical Corporation, the National Comprehensive Cancer Network (NCCN) and the Scottish Intercollegiate Guidelines Network (SIGN).

This guideline is subject to ongoing review on a 12 monthly basis.

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INTRODUCTION

1. Introduction

Breast cancer is the most common cancer in GCC and in State of Qatar. In 2013, breast cancer accounted for 41% of all female cancer cases in Qatar¹. Worldwide, the estimated incidence of breast cancer (age standardized rate) is 29.1%².

In Qatar, the majority of women with breast cancer below 60 years of age present with advanced stage disease. The introduction of a national screening programme for women above the age of 45 years will aid early detection, timely management with optimal outcomes for all women consequently.

The aetiology of the majority of breast cancer is unknown. However, numerous risk factors of the disease have been established. These risk factors for the disease include: female gender; increasing patient age. Other risk factors associated with a minority of the breast cancers include family history of breast cancer at a young age; early menarche; late menopause; older age at first live childbirth; prolonged hormone replacement therapy; previous exposure to therapeutic chest wall irradiation; benign proliferative breast disease; increased mammographic breast density and genetic mutations of the BRCA1/ 2 genes³.

1.1 Purpose of the Guideline

This guideline is intended to articulate the agreed standards of care for the treatment of breast cancer within the State of Qatar and to assist clinical staff to provide appropriate care and treatment for patients with breast cancer.

1.2 End Users of the Guideline – Professional and Patient Groups

This guideline is relevant to all healthcare professionals (physicians, nurses, allied health professionals, others) who come into contact with women with breast cancer, as well as to the women themselves and their carers.

This guideline is relevant to patients with histologically proven diagnoses of breast cancer and includes the management of patients with breast cancers such as ductal, lobular and Paget disease and does not include the management of benign breast disease. There is a separate national guideline for the breast cancer screening of all women including asymptomatic, symptomatic and high risk family history patients in the state of Qatar.

It is also expected that this guideline will be of value to those involved in clinical governance in both primary, secondary care and private healthcare to help ensure that arrangements are in place to deliver appropriate care to this group of women.

1.3 Target Areas

This guideline is intended as a reference for the following departments: surgery, diagnostic radiology, pathology/ laboratory, medical oncology, radiation oncology, nursing, pharmacy and medical genetics.

GENERAL PRINCIPLES OF CARE

2. General Principles of Care

The main recommendations are that:

- Patients should be managed by a multidisciplinary team in a designated breast unit, which treats more than 100 new cancer cases per year.
- Patients should be informed of the different treatment options (including no treatment) and should be involved in the decision making process to the extent that they wish.
- All patients should be offered access to a breast cancer advanced clinical nurse specialist to support them through their cancer experience.
- Patients should be offered prompt access to specialist psychological support and, if appropriate psychiatric services.
- Patients should be made aware of, and have the choice to enter clinical trials if available.
- Following the MDT discussion, the decision is validated and 'signed off' by members present. The MDT outcome proforma is then uploaded onto the patient's records. This ensures that those involved in the patients care can access the decision; this includes the patient's primary health care physician. The recommended decision for patients from the private sector is fed back to the referring clinician.

THE SPECIALIST MULTI-DISCIPLINARY TEAM (MDT)

3. The Specialist Multi-Disciplinary Team (MDT)

The MDT is the group of people from different health care disciplines, who meet regularly to discuss an agreed cohort of patients. This forum allows each specialist to independently contribute to the diagnosis and management of patients with suspected or diagnosed breast cancer. This forum also recommends treatment regimens for individual patients.

Referrals for discussion at the MDT are managed by the MDT coordinator. These referrals are accepted from the membership of the MDT as well as other professionals, who are involved in the management of patients with suspected or diagnosed breast cancer i.e. private providers, other MDT meetings, general surgeons and clinicians within the National Centre for Cancer Care and Research (NCCCR).

Prior to the MDT meeting, a list of patients for discussion is generated from the referrals made and is circulated to the MDT members for review. A deadline is set for referrals for discussion to enable the members to prepare for the MDT discussion.

3.1 Criteria for Discussion at MDT

Patients who meet the following criteria should be referred for discussion by the MDT:

- Patients with newly suspected cases once assessment is complete (clinical review, imaging and biopsy) enabling a diagnosis to be made and initial treatment plan agreed.
- Patients presenting post operatively for pathology review and further management decision making.
- Patients presenting with relapsed or progressive disease whilst on or after treatment.
- All patients with a diagnosis of breast cancer prior to commencing treatment.
- Patients requiring delayed reconstructive surgery
- Patients requesting prophylactic bilateral mastectomy with respect to BRCA mutation will need to be discussed in high risk breast cancer MDT with representation from the plastic surgery department.

3.2 Individual Patient Treatment Plans

The core function of the MDT is to agree and record individual patient's treatment plans. During the MDT meeting, a record is made of the case discussion, and the agreed management plan including plans for further investigation, clinical review and treatment. The MDT individualized treatment plan includes the following information:

- The patient identity (patient name and medical number)
- Summary of clinical presentation
- Summary of investigations completed and summary of results
- The MDT agreed treatment planning decision

The MDT discussion and decision is validated and 'signed off' by members present. The MDT outcome proforma is then uploaded onto the electronic patient's records. This ensures that those involved in the patient's care can access the decision including the patient's primary health care physician. The recommended decision for patients from the private sector is fed back to the referring clinician.

Referrals for patients requiring chemotherapy is undertaken when the patient is seen in the breast clinic.

3.3 Arrangements for Decision Making Outside of the Regular MDT Forum

Decisions in the management of breast cancer are rarely made urgently (without due consideration), and therefore every effort should be made for the patient to be discussed by the MDT prior to commencing treatment. In the event that this is required, discussion should occur between at least 2 core members of the MDT of different disciplines and the patient should be listed for discussion at the next available MDT meeting.

3.4 The MDT Relationship with the Tumour Board

The lead clinician of the breast cancer MDT must be a member of the Qatar breast cancer tumour board. The lead clinician must attend the meetings of these forums or must nominate another core member of the MDT to attend. The attendance at the tumour board will be recorded and demonstrated in the team's annual report.

REFERRAL GUIDELINES AND PATIENT PATHWAY

4. Referral Guidelines and Patient Pathway

Patients are referred to the breast cancer specialist team through the following routes:

- Primary Healthcare Centres (PHC) by using the Urgent Suspected Cancer (USC) form or through routine referral
- Internal HMC referrals from the emergency department, breast surgeons, other consultants and oncologists.
- The national screening programme.
- Other cancer MDTs.
- Referrals from private providers or from those returning to Qatar following treatment overseas.

Patients referred to the breast cancer service should be seen in a specialist clinic by a clinician who has been designated as privileged for this specialty.

Patients should be referred to a breast surgeon first if there is a suspicion of breast cancer, or if the patient has a diagnosis of breast cancer preoperatively or 4 weeks postoperatively.

4.1 Criteria for using the USC Form in Breast Cancer Referral

- New, discrete lump in breast or axilla
- Altered breast contour/ dimpling
- Persistent asymmetrical nodularity/ thickening
- Breast abscess/ inflammation not responsive to one course of antibiotics
- Bloodstained, persistent/ troublesome nipple discharge
- Recent nipple retraction/ distortion or eczema suspected Paget's disease
- Abnormal Mammogram (BIRADS 4 or more)

4.2 Management of Referrals at HMC

- I. Referrals of all new tertiary cancer patient referrals using the USC form and internal referrals within HMC are managed by the Referral Management Office (RMO).

Any provider who wishes to refer a patient to cancer services at HMC using an urgent suspicion of cancer referral form should complete the USC form and phone the request through to the RMO and then send the USC form to the RMO.

The **RMO** contact details are as follows:

Telephone: +974 40250116

Fax: +974 44398975

Email: suspectedcancer@hamad.qa

- II. Referral of patients from all providers for discussion and/ or opinion at the MDT on confirmed or uncertain/difficult diagnosis of cancer are managed by the MDT coordinator.

Other referrals managed by the MDT coordinator include

- Re-referrals of patients already discussed at the MDT meeting but who have had a change or cessation in agreed treatment plan.
- Referrals between teams communicated by the MDT coordinators to each other by specific tumour type.

The **MDT coordinator** can be contacted on:

Telephone: +974 55231962/ 44398106

Fax: +974 40151082

Email: afigueroa@hamad.qa

The referral should be made by a faxed referral letter or copy of HMC's completed MDT referral proforma. Any relevant imaging and pathology (both report and blocks where possible) should be made available for review as part of the MDT discussion.

The MDT will agree the next steps for the patient and the appropriate appointment will be made. The patient pathway coordinator will take responsibility for facilitating access to the required service.

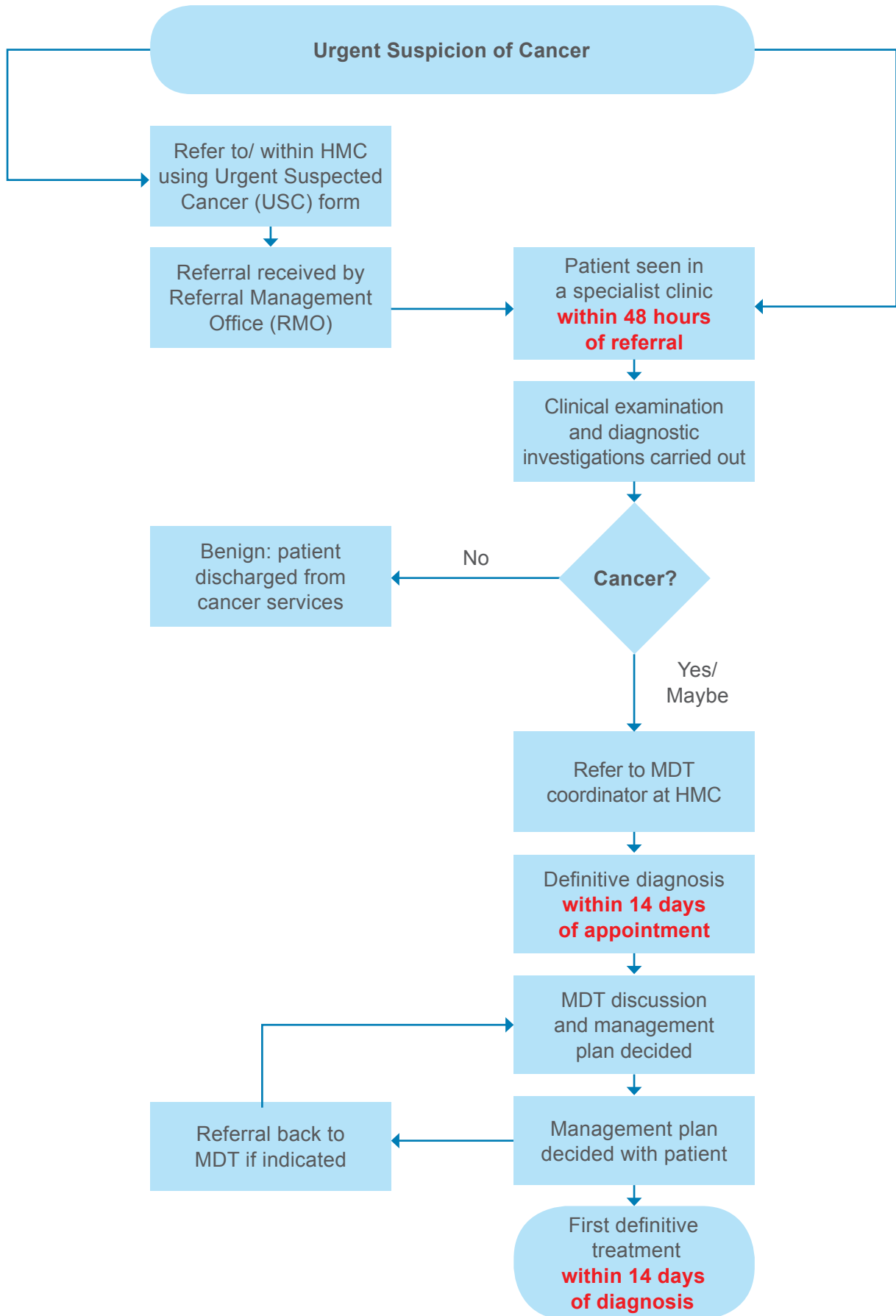
4.3 The Patient Referral Pathway in Qatar

The following diagram (Figure 1) presents an overview of a cancer patient referral pathway in the State of Qatar.

Significant Timelines in the Patient Referral Pathway

- i. **Referral to Specialist Clinic:**
 - Those referred using the USC form should be seen **within 48 hours of referral**.
- ii. **Time to Definitive Diagnosis:**
 - Once a patient is seen, **a definitive diagnosis should be reached in 14 days** using a combination of imaging, pathology and physical examinations. This applies to any patient referred to a specialist clinic and found to have a diagnosis of cancer, regardless of the referral route.
- iii. **Time to Treatment:**
 - There must be **no more than 14 days between the date of confirmed diagnosis at MDT and the date of first definitive treatment**. This applies to any patient, with a confirmed diagnosis of cancer, regardless of the referral route.

Patient Referral Pathway in Qatar



INVESTIGATIONS AND DIAGNOSIS – PRE-TREATMENT ASSESSMENT

5. Investigations and Diagnosis – Pre-treatment Assessment

5.1 The Primary Investigations

- History & physical examination
- Bilateral mammogram and Ultrasound of the breast.
- Complete blood count, platelets, kidney and liver function tests (LFTs), alkaline phosphatase (AP).
- Biopsy - Core needle biopsy.
- Body imaging can be done preoperatively or postoperatively according to clinical staging and MDT recommendation as necessary: ultrasound of abdomen, magnetic resonance imaging (MRI), diagnostic computerized tomography (CT) scan of chest.
- Echocardiogram if chemotherapy is planned.
- Serum hormonal levels - Estradiol, FSH and LH, if needed to assess menopause status. Fertility counselling if premenopausal to be decided by the MDT.
- Referral to high risk clinic if patient is at high risk for hereditary breast cancer.
- Pathology review if undertaken outside tertiary centre.

5.2 Imaging

Imaging techniques are useful for detecting metastases and tumour recurrence. Anatomic imaging techniques include radiographs, ultrasound, CT, and MRI. Provisional treatment intent (radical or non-radical) needs to be decided before decisions on imaging are made.

Radiological staging work up depends on clinical staging and includes CT of chest, abdomen, pelvis, and bone scan, brain imaging for neurological symptoms or signs. PET/ CT to be considered in stage III or IV or if there is contraindication to staging CT. Radiological staging should not delay surgery in early breast cancers - stages I and II.

The impression or conclusion of the bilateral mammogram and/ or ultrasound is based on the BI-RADS classification by the American College of Radiology:

BIRADS Classification

Table 1

Category	Diagnosis	Number of Criteria and Recommendation
0	Incomplete	The mammogram or ultrasound didn't give the radiologist enough information to make a clear diagnosis. Follow-up imaging is necessary.
1	Negative	There is nothing to comment on. Routine screening recommended.
2	Benign	A definite benign finding. Routine screening is recommended.
3	Probably benign	Findings that have a high probability of being benign (> 98%). For six-month short interval follow-up.
4	Suspicious abnormality	Not characteristic of breast cancer, but reasonable probability of being malignant (3 to 94%). Biopsy should be considered.
5	Highly suggestive of malignancy	Lesion that has a high probability of being malignant (≥ 95%). Appropriate action should be taken.
6	Known biopsy - proven malignancy	Lesions known to be malignant, that is being imaged prior to definitive treatment. Ensure that treatment is completed.

Breast MRI Indications:

- To check any discrepancy between clinical and mammographic or ultrasound imaging.
- Invasive lobular carcinoma
- Breast density precludes assessment of tumour size
- Assessment of response to primary chemotherapy (pre-, mid- and at completion of therapy)
- Assessment of symptoms/ signs associated with silicone breast implants - to rule out any suspicion of multifocal, multicentric carcinoma in the ipsilateral breast or as screening of the contralateral breast cancer.

5.3 Breast Biopsy

- Core needle biopsy (CNB) is the procedure of choice for evaluation of most of palpable and non-palpable breast lesions. CNB can be obtained by clinical or ultrasound or stereotactic guidance of the suspicious lesion in the breast or metastatic site.
- Fine needle aspiration (FNA) of the breast can be performed in any of the following:
 - In cases of cysts or obviously benign lesions
 - On lymph nodes when metastasis is suspected
 - In case of contraindications to perform core needle biopsy.
- Excision biopsy under wire localization for non palpable breast lesion seen by breast imaging.

The specimens should be oriented for the pathologist and specific requests for determination of biomarkers should be stated (ER, PR, HER-2 status). In reporting, the core biopsy should include cancer type, grade, LVI, receptor and HER-2 status.

PATHOLOGY ASSESSMENT AND STAGING

6. Pathology Assessment and Staging

6.1 General Considerations

A central component to the treatment of breast cancer is full knowledge of extent of disease and biologic features. These factors contribute to the determination of the stage of the disease, assist in the risk estimation that the cancer will recur, and provide information that predicts response to therapy (e.g. ER, PR, and HER-2). Accurate pathology reporting requires communication between the clinician and the pathologist relating to

- Relevant patient history
- Prior breast biopsies
- Prior irradiation to the chest
- Pregnancy status
- Characteristics of the abnormality biopsied
- Clinical state of lymph nodes
- Presence of inflammatory change or other skin abnormality
- Any prior treatment administered (e.g. chemotherapy, radiotherapy).

Medical documentation must include TNM staging and the outcome of the MDT discussion. Preoperative clinical stage (TNM Staging) should be documented by the operating surgeon and postoperative pTNM staging by the pathologist.

Pathological evaluation and interpretation of the operated (resection) specimen should follow the College of American Pathologists (CAP) guidelines published in October 2009 based on AJCC/ UICC/ TNM, 7th Edition and should include at least the following parameters:

- i. Presence or absence of carcinoma
- ii. Type of carcinoma (invasive vs. In-situ)
- iii. Histomorphologic type of carcinoma (ductal vs. lobular vs. other)
- iv. Size of tumour
- v. Multifocality and multicentricity
- vi. Modified SBR grade of the tumour
- vii. Lymphovascular invasion
- viii. Perineural infiltration
- ix. Margins status
- x. Skin, areola and nipple status
- xi. Micro calcifications
- xii. Number of axillary lymph nodes sampled
- xiii. Number of lymph nodes positive
- xiv. Size of largest node metastasis and presence of extracapsular spread in the lymph nodes
- xv. Receptor status of oestrogen, progesterone (ER/ PR) - detailed hormone receptor reporting as per ACSCO/ CAP guidelines.⁶

- xvi. Receptor status of HER-2 (human epidermal growth factor receptor 2) - detailed hormone receptor reporting as per ASCO/ CAP guidelines.⁶
- xvii. Pathological stage (TNM)

6.2 Determination of Receptor Status

ER/ PR: ER status should be determined for all samples of DCIS, and ER and PR tumour status should be determined for all samples of invasive breast cancer. ER and PR tumour status is normally determined by immunohistochemistry (IHC) testing.

HER-2: HER-2 tumour status should be determined for all newly diagnosed invasive breast cancers and for first recurrences of breast cancer whenever possible. HER-2 status is initially assessed by immunohistochemistry (IHC) and reported according to ASCO/ CAP guidelines, as negative (0 - 1+), equivocal (2+) and positive (3+). If the findings by IHC are equivocal, then reflex testing with insitu hybridization (ISH) is performed and reported as amplified, not amplified or equivocal.

6.3 Staging (TNM)

All patients with breast cancer should be assigned a clinical stage of disease and if appropriate evaluation is available, a pathologic stage of disease. The routine use of staging allows for efficient identification of local treatment options, assists in identifying systemic treatment options and provides baseline prognostic information.

Clinical staging of the axilla (examination and ultrasound) includes the FNAC/ Core biopsy of suspicious looking lymph nodes. Clinical staging is based on the TNM 2009 classification from the AJCC Cancer Staging Manual, 7th edition.

Table 2

Stage	Tumour	Node	Metastases
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T0 T1 T2	N1 N1 N0	M0 M0 M0
Stage IIB	T2 T3	N1 N0	M0 M0
Stage IIIA	T0 T1 T2 T3	N2 N2 N2 N1 - 2	M0 M0 M0 M0
Stage IIIB	T4 T4 T4	N0 N1 N2	M0 M0 M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

Table 3

Primary tumour (T)*•Δ	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
Tis (Paget's)	Paget's disease (Paget disease) of the nipple NOT associated with invasive carcinoma and/ or carcinoma in situ (DCIS and/ or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget's disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget's disease should still be noted.
T1	Tumour ≤ 20 mm in greatest dimension
T1mi	Tumour ≤ 1 mm in greatest dimension
T1a	Tumour > 1 mm but ≤ 5 mm in greatest dimension
T1b	Tumour > 5 mm but ≤ 10 mm in greatest dimension
T1c	Tumour > 10 mm but ≤ 20 mm in greatest dimension
T2	Tumour > 20 mm but ≤ 50 mm in greatest dimension
T3	Tumour > 50 mm in greatest dimension
T4◇	Tumour of any size with direct extension to the chest wall and/ or to the skin (ulceration or skin nodules)
T4a	Extension to the chest wall, not including only pectoralis muscle adherence/ invasion
T4b	Ulceration and/ or ipsilateral satellite nodules and/ or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma
T4c	Both T4a and T4b
T4d	Inflammatory carcinoma§
<p>Post-treatment ypT.¥ The use of neoadjuvant therapy does not change the clinical (pre-treatment) stage. Clinical (pre-treatment) T will be defined by clinical and radiographic findings, while y pathologic (post-treatment) T will be determined by pathologic size and extension. The ypT will be measured as the largest single focus of invasive tumour, with the modifier "m" indicating multiple foci. The measurement of the largest tumour focus should not include areas of fibrosis within the tumour bed.</p>	
Regional lymph nodes (N)	
Clinical	
NX	Regional lymph nodes cannot be assessed (e.g., previously removed)
N0	No regional lymph node metastases
N1	Metastases to movable ipsilateral level I, II axillary lymph node(s)
N2	Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detected‡ ipsilateral internal mammary nodes in the <i>absence</i> of clinically evident axillary lymph node metastases
N2a	Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures
N2b	Metastases only in clinically detected‡ ipsilateral internal mammary nodes and in the <i>absence</i> of clinically evident level I, II axillary lymph node metastases
N3	Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected‡ ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement

Regional lymph nodes (N)	
N3a	Metastases in ipsilateral infraclavicular lymph node(s)
N3b	Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
N3c	Metastases in ipsilateral supraclavicular lymph node(s)
Pathologic (pN)†**	
pNX	Regional lymph nodes cannot be assessed (e.g., previously removed, or not removed for pathologic study)
pN0	No regional lymph node metastasis identified histologically
pN0(i-)	No regional lymph node metastases histologically, negative immunohistochemistry (IHC)
pN0(i+)	Malignant cells in regional lymph node(s) no greater than 0.2 mm (detected by H&E or IHC including isolated tumour cell clusters (ITC))
pN0(mol-)	No regional lymph node metastases histologically, negative molecular findings (RT-PCR)**
pN0(mol+)	Positive molecular findings (RT-PCR)**, but no regional lymph node metastases detected by histology or IHC
pN1	Micrometastases; or metastases in 1 - 3 axillary lymph nodes; and/ or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected ΔΔ
pN1mi	Micrometastases (greater than 0.2 mm and/ or more than 200 cells, but none greater than 2.0 mm)
pN1a	Metastases in 1 - 3 axillary lymph nodes, at least one metastasis greater than 2.0 mm
pN1b	Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected ΔΔ
pN1c	Metastases in 1 - 3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected
pN2	Metastases in 4 - 9 axillary lymph nodes; or in clinically detected◊◊ internal mammary lymph nodes in the <i>absence</i> of axillary lymph node metastases
pN2a	Metastases in 4 - 9 axillary lymph nodes (at least one tumour deposit greater than 2.0 mm)
pN2b	Metastases in clinically detected◊◊ internal mammary lymph nodes in the <i>absence</i> of axillary lymph node metastases
pN3	Metastases in ten or more axillary lymph nodes; or in infraclavicular (level III axillary) lymph nodes; or in clinically detected◊◊ ipsilateral internal mammary lymph nodes in the <i>presence</i> of one or more positive level I, II axillary lymph nodes; or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected ΔΔ; or in ipsilateral supraclavicular lymph nodes
pN3a	Metastases in ten or more axillary lymph nodes (at least one tumour deposit greater than 2.0 mm); or metastases to the infraclavicular (level III axillary lymph) nodes
pN3b	Metastases in clinically detected◊◊ ipsilateral internal mammary lymph nodes in the <i>presence</i> of one or more positive axillary lymph nodes; or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected ΔΔ
pN3c	Metastases in ipsilateral supraclavicular lymph nodes
Post-treatment ypN	
<p>- Post-treatment yp "N" should be evaluated as for clinical (pre-treatment) "N" methods above. The modifier "sn" is used only if a sentinel node evaluation was performed after treatment. If no subscript is attached, it is assumed that the axillary nodal evaluation was by axillary node dissection (AND).</p> <p>- The X classification will be used (ypNX) if no yp post-treatment SN or AND was performed</p> <p>- N categories are the same as those for pN</p>	

Distant metastasis (M)			
M0	No clinical or radiographic evidence of distant metastases		
cM0(i+)	No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumour cells in circulating blood, bone marrow, or other non-regional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastases		
M1	Distant detectable metastases as determined by classic clinical and radiographic means and/ or histologically proven larger than 0.2 mm		
Post-treatment yp M classification. The M category for patients treated with neoadjuvant therapy is the category assigned in the clinical stage, prior to initiation of neoadjuvant therapy. Identification of distant metastases after the start of therapy in cases where pre-therapy evaluation showed no metastases is considered progression of disease. If a patient was designated to have detectable distant metastases (M1) before chemotherapy, the patient will be designated as M1 throughout.			
Anatomic stage/ prognostic groups§§			
0	Tis	N0	M0
IA	T1 ¥¥	N0	M0
IB	T0	N1mi	M0
	T1 ¥¥	N1mi	M0
IIA	T0	N1 ‡‡	M0
	T1 ¥¥	N1 ‡‡	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1 ¥	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
	Any T	Any N	M1

Distant metastasis (M)

* The T classification of the primary tumour is the same regardless of whether it is based on clinical or pathologic criteria, or both. Designation should be made with the subscript “c” or “p” modifier to indicate whether the T classification was determined by clinical (physical examination or radiologic) or pathologic measurements, respectively. In general, pathologic determination should take precedence over clinical determination of T size.

- Size should be measured to the nearest millimeter. If the tumour size is slightly less than or greater than a cutoff for a given T classification, it is recommended that the size be rounded to the millimeter reading that is closest to the cutoff.

Δ Multiple simultaneous ipsilateral primary carcinomas are defined as infiltrating carcinomas in the same breast, which are grossly or macroscopically distinct and measurable. T stage is based only on the largest tumour. The presence and sizes of the smaller tumour(s) should be recorded using the “(m)” modifier.

◇ Invasion of the dermis alone does not qualify as T4; dimpling of the skin, nipple retraction, or any other skin change except those described under T4b and T4d may occur in T1, T2, or T3 without changing the classification. The chest wall includes ribs, intercostal muscles, and serratus anterior muscle, but not the pectoralis muscles.

§ Inflammatory carcinoma is a clinical-pathologic entity characterized by diffuse erythema and oedema (peau d’orange) involving a third or more of the skin of the breast. These skin changes are due to lymphoedema caused by tumour emboli within dermal lymphatics. Although dermal lymphatic involvement supports the diagnosis of inflammatory breast cancer, it is neither necessary nor sufficient, in the absence of classical clinical findings, for the diagnosis of inflammatory breast cancer.

¥ If a cancer was designated as inflammatory before neoadjuvant chemotherapy, the patient will be designated to have inflammatory breast cancer throughout, even if the patient has complete resolution of inflammatory findings.

‡ Clinically detected is defined as detecting by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration biopsy with cytologic examination. Confirmation of clinically detected metastatic disease by fine needle aspiration without excision biopsy is designated with an (f) suffix, for example, cN3a(f). Excisional biopsy of a lymph node or biopsy of a sentinel node, in the absence of assignment of a pT, is classified as a clinical N, for example, cN1. Information regarding the confirmation of the nodal status will be designated in site specific factors as clinical, fine needle aspiration, core biopsy, or sentinel lymph node biopsy. Pathologic classification (pN) is used for excision or sentinel lymph node biopsy only in conjunction with a pathologic T assignment.

† Classification is based on axillary lymph node dissection with or without sentinel lymph node biopsy. Classification based solely on sentinel lymph node biopsy without subsequent axillary lymph node dissection is designated (sn) for “sentinel node,” for example, pN0(sn).

** Isolated tumour cell clusters (ITC) are defined as small clusters of cells not greater than 0.2 mm, or single tumour cells, or a cluster of fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by immunohistochemical (IHC) methods. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification but should be included in the total number of nodes evaluated.

•• RT-PCR: reverse transcriptase/ polymerase chain reaction.

ΔΔ “Not clinically detected” is defined as not detected by imaging studies (excluding lymphoscintigraphy) or not detected by clinical examination.

◇◇ “Clinically detected” is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration biopsy with cytologist examination.

§§ Anatomic stage:

- M0 includes M0(i+).

- The designation pM0 is not valid; any M0 should be clinical.

- If a patient presents with M1 prior to neoadjuvant systemic therapy, the stage is considered Stage IV and remains Stage IV regardless of response to neoadjuvant therapy.- Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.

- Post-neoadjuvant therapy is designated with the “y” prefix. For patients with a pathologic complete response (pCR) to neoadjuvant therapy, no stage group is assigned (i.e., yT0N0M0).

¥¥ T1 includes T1mi.

‡‡ T0 and T1 tumours with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.

7. Management of Breast Cancer

Treatment and care should take into account the patient's needs and preferences. Patients with breast cancer should have the opportunity to make informed decisions about their care and treatment in partnership with their healthcare professionals. Treatment decisions should take into account the quality of life as well as survival.

Patients with breast cancer should be offered individualized information tailored to their needs. Patient preference is a major component of the decision-making process, especially in situations in which survival rates are equivalent among the available treatment options. Healthcare professionals should discuss all relevant management options recommended in this guideline with patients and with their carers.

The management of patients with breast cancer includes the treatment of local disease with surgery, radiation therapy, or both and the treatment of systemic disease with chemotherapy, endocrine therapy, biologic therapy, or a combination of these.

Ligaclips should be placed in the cavity (2 clips in each circumferential margin and 2 clips posteriorly/ deep). Whenever downsizing of the tumour size by neoadjuvant chemotherapy is being contemplated, radiological clips should be considered.

- **Surgery (covered in detail in Chapter 8)**
- **Systemic therapy (covered in detail in Chapter 9)** Systemic therapy should be considered for all patients with breast cancer where benefit outweighs the risk and includes:
 - Endocrine therapy (adjuvant and neoadjuvant).
 - Chemotherapy (adjuvant and neoadjuvant).
 - Biologic therapy (including hormone therapy, Immunotherapy).
- **Radiotherapy (covered in detail in Chapter 10)**

In terms of treatment, breast cancer may be divided into

- i. The pure non-invasive carcinomas - lobular carcinoma in situ (LCIS) and ductal carcinoma in situ (DCIS) (stage 0)
- ii. Operable, locoregional invasive carcinoma with or without associated non-invasive carcinoma (clinical stage I, stage II, and some stage IIIA tumours)
- iii. Inoperable locoregional invasive carcinoma with or without associated non-invasive carcinoma (clinical stage IIIB, stage IIIC, and some stage IIIA tumours)
- iv. Metastatic (stage IV) or recurrent carcinoma.

7.1 Management of Breast Cancer in Pregnancy

General Considerations

First trimester: Discuss termination or continuation of pregnancy with breast surgery and axillary staging. Begin adjuvant/ neoadjuvant treatment in second trimester followed by adjuvant systemic treatment (hormone, anti HER-2 if indicated) and radiotherapy postpartum if indicated.

Second to Early Third trimester: Neoadjuvant chemotherapy with mastectomy or BCS axillary staging followed by adjuvant systemic and radiotherapy postpartum.

Late Third trimester: Mastectomy or breast conservation surgery (BCS) axillary staging followed by adjuvant systemic and radiotherapy postpartum.

The evaluation of pregnant women with suspected breast cancer includes:

- History and physical exam
- Mammogram (with shielding)
- Ultrasound of the breast and regional lymph node
- Guided biopsy
- Core biopsy.
- Staging for
 - **cT1 - T2 CN negative:** Chest x-ray (with shielding), abdominal ultrasound, liver and renal function tests, CBC with differential.
 - **cT3:** In addition to above tests to consider MRI staging for thoracic and lumbar spine without contrast.

A sentinel lymph node biopsy (SLNB) should not offered to pregnant women under 30 gestational weeks as there is limited data regarding the use of radioactive tracer. Radio-labelled sulphur appears to be safe in pregnancy. Isosulfan blue or methylene blue dye for SNLB is discouraged during pregnancy.

Systemic Therapy during Pregnancy

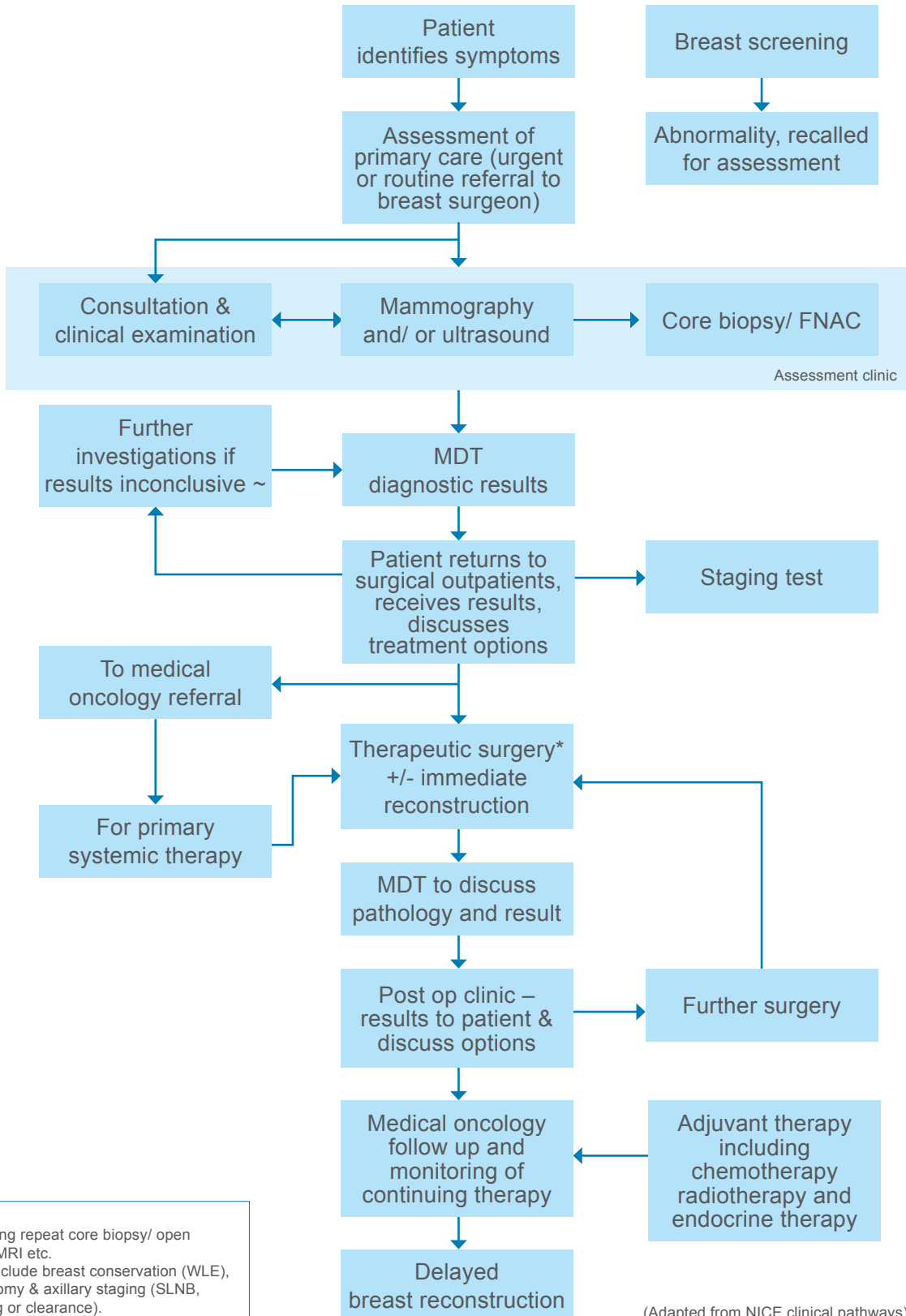
The indication of systemic chemotherapy is the same as for non pregnant women however; chemotherapy is contraindicated during first trimester of pregnancy. Postpartum systemic treatment will be same as non-pregnant. Preferred chemotherapy regimens during pregnancy include:

- **FAC** (doxorubicin, cyclophosphamide, and fluorouracil)
- **FEC** (epirubicin, cyclophosphamide, and fluorouracil).

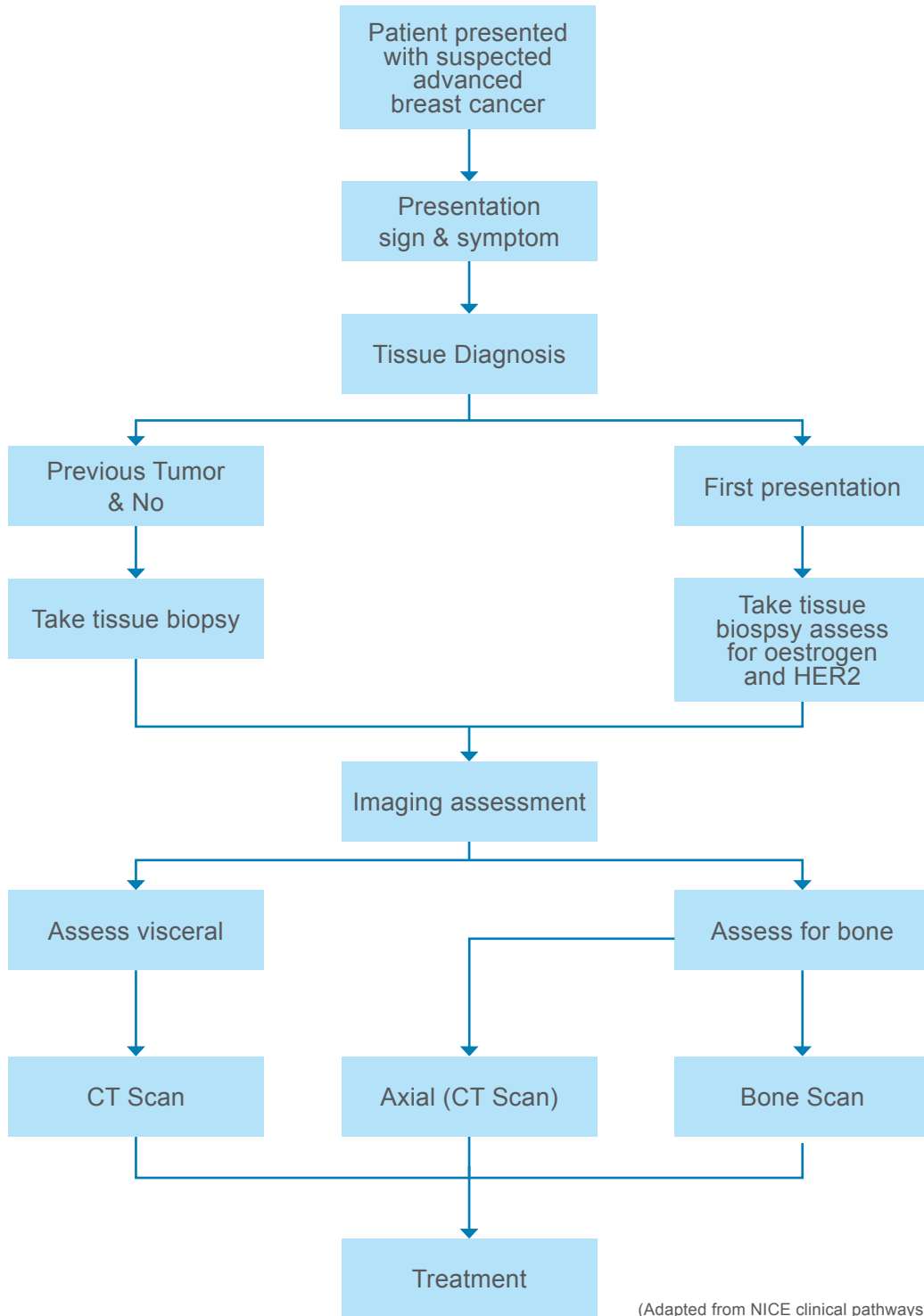
Paclitaxel (weekly) after the first trimester is acceptable; however, there are insufficient safety data to recommend general use of taxanes during pregnancy. Trastuzumab and Pertuzumab are contraindicated in pregnancy.

Early consultation with an obstetrician is recommended in order to assess any pregnancy-related complications and to monitor the well-being of foetus before the estimated delivery date.

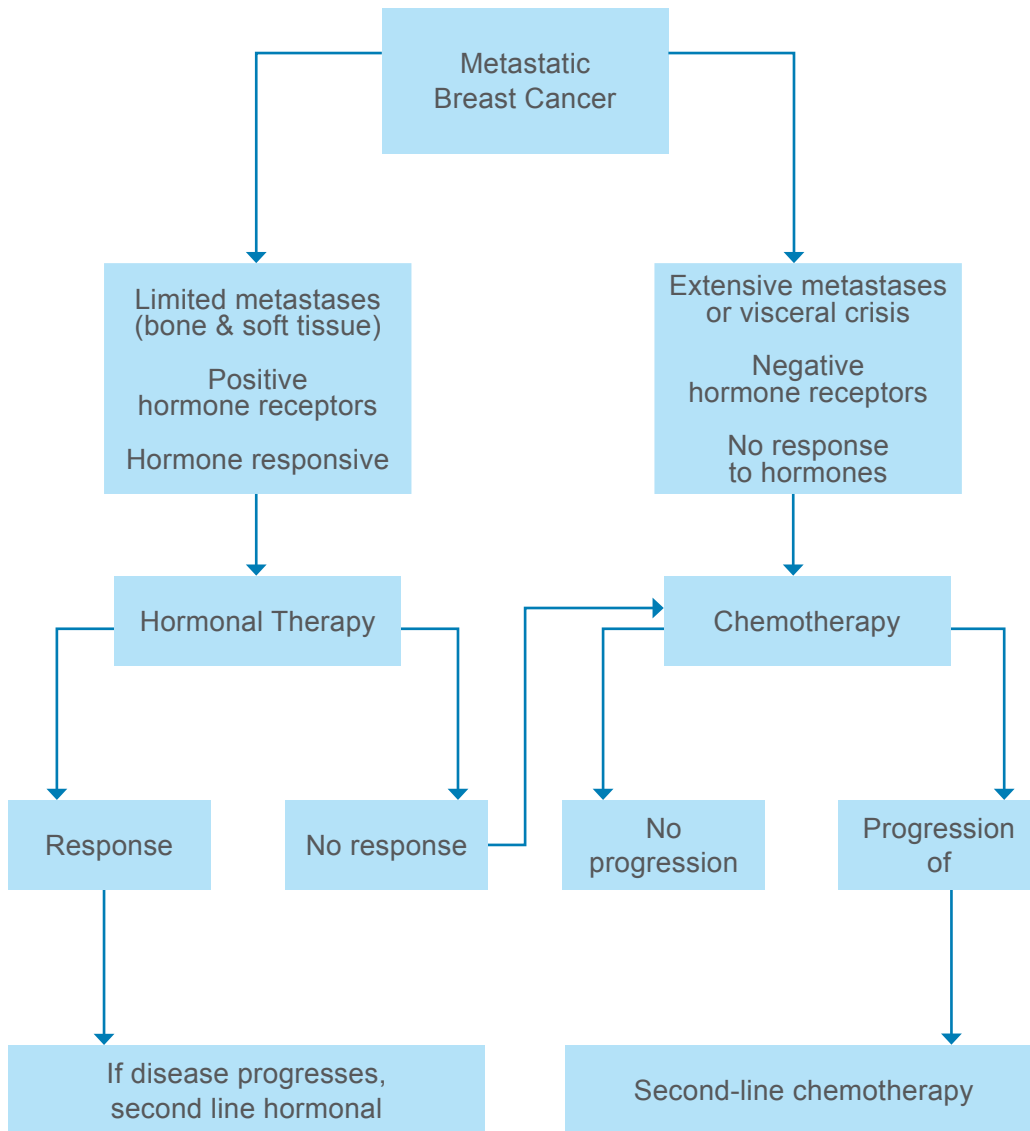
Treatment Pathway of Early Breast Cancer



Treatment Pathway for Metastatic Breast Cancer



SYSTEMIC TREATMENT APPROACH FOR METASTATIC BREAST CANCER



SURGICAL MANAGEMENT

8. Surgical Management

Established surgical procedures for the local treatment of invasive or in situ breast cancer disease include:

- **Breast conservation surgery**, which involves removal of the tumour together with a rim of surrounding normal breast tissue with retention of the breast, and
- **Mastectomy**, which involves removal of the whole breast. Patients having a mastectomy should be counselled for reconstruction.

The choice of surgery must be tailored to the individual patient, who should be fully informed of the options and made aware that breast irradiation is required following conservation, and that further surgery may be required if the margins are not clear of tumour.

8.1 Management of the Axilla

Spread of metastatic disease to axillary nodes is the most significant prognostic indicator and is used as one of the major determinants of appropriate systemic adjuvant therapy. Therefore, all patients with operable breast cancer should have axillary surgery (with the exception of cases where knowledge of nodal status will not affect treatment, and only after an MDT decision). Axillary surgery is necessary for adequate staging and treatment of invasive breast cancer.

- A minimum of 10 lymph nodes is considered adequate for staging the axilla.
- If there is proven axillary lymph node disease preoperatively, axillary lymph node (ALN) dissection (or axillary node clearance) should be undertaken;
- If there is no proven disease, the optimal axillary procedure is a sentinel lymph node biopsy (SLNB). If SLNB is not available, the patient should be referred to a centre where SLNB can be performed.

8.1.1 Sentinel Lymph Node Biopsy

Sentinel lymph node biopsy (SLNB) is appropriate for most patients with early breast cancer (T1-T3) without known presence of axillary metastasis confirmed by histopathology. All patients with clinically negative axilla and T2 -T3 tumours, having neoadjuvant chemotherapy, to downsize the tumour, should have SLNB before starting systemic therapy

SLNB should be performed in all cases of early breast cancer except:

- Pathologically positive lymph nodes (regardless of the clinical assessment)
- Pregnancy less than 30 weeks,
- After neoadjuvant systemic treatment outside clinical trials.

On performing the SLNB, it is recommended that:

- Where sentinel node is not identified - Proceed to axillary lymph node dissection (ALND) level I/ II in cases.
- Regardless of the sentinel node status, if the lymph nodes are metastatic on gross inspection - Proceed to axillary clearance.
- If there is gross disease apparent in the level II nodes - Proceed to level III axillary clearance only.

8.1.2 Axillary Lymph Node Dissection

Axillary lymph nodes dissection (ALND) depends on the analysis of the SLNB as follows:

- Negative Sentinel Node - no further axillary dissection
- Positive Sentinel Node - Isolated tumour cells < 0.2 mm - no further axillary dissection.
- No further axillary management is required for patients undergoing breast conservation surgery and radiotherapy for T1 or T2 and clinically node-negative breast cancer and who have 1 or 2 positive nodes at SLNB.
- In all other cases of **positive nodes at SLNB**, axillary lymph node dissection (ALND) level I and/ or II is recommended and should be performed prior to adjuvant therapy.
- Axillary clearance (axillary lymph node dissection level III) also serves to treat metastatic disease in the axilla by surgical removal.

8.2 Breast Conserving Surgery

The use of breast conserving therapy is predicated on achieving a pathologically negative margin of resection. Margins should be evaluated on all surgical specimens from breast-conserving surgery. Requirements for optimal margin evaluation include:

- Orientation of the surgical specimens.
- Description of the gross and microscopic margin status
- Reporting of the distance, orientation and type of tumour (invasive or DCIS) in relation to the closest margin.

8.2.1 Orientation of the Surgical Specimen (Lumpectomy)

Appropriate orientation of the specimen with suture and/ or clips is important to help the pathologist/ radiologist assess the margin status. This must be done according to the local protocols. Re-excision of cavity margin should have an orientation stitch at the new margin site (unless if it is a global re-excision) to be discussed with the pathologist.

8.3 Mastectomy

The indications include:

Table 4

Absolute:	Relative:
<ul style="list-style-type: none"> • Multicenter tumours, • Large tumours (> 4 cm) in relation to breast size especially when no neo-adjuvant therapy is planned, • Multiple positive margins after re excision. • Inflammatory breast cancer, • Patient's choice, • Prior radiation to the breast or chest wall, • To avoid radiation therapy during early pregnancy (first and second trimester). 	<ul style="list-style-type: none"> • Includes active connective tissue disease such as (scleroderma, systemic lupus erythematosus). • Patients known to have <i>BRCA 1</i>, <i>BRCA 2</i> gene mutation where bilateral mastectomies are recommended. • Contralateral risk-reducing mastectomy in <i>BRCA</i> mutation negative patients (only undertaken at patient's choice) • Recurrent breast cancer

Mastectomy results in loss of the breast for breastfeeding, loss of sensation in the skin of the breast and nipple-areolar complex (NAC), and loss of the breast for cosmetic, body image and psychosocial purposes. The nipple-areolar complex is sacrificed with skin sparing mastectomy for the cancer therapy (currently only performed within the confines of prospective clinical trials).

The nipple-areolar complex can be spared in prophylactic mastectomy. When post-mastectomy radiation is required, and patient is having skin sparing mastectomy, immediate breast reconstruction is preferred.

8.4 Breast Reconstruction

All women undergoing breast cancer treatment should be educated about breast reconstructive options as adapted to their individual clinical situation. The decision regarding type of reconstruction includes patient preference, body habitus, smoking history, co-morbidities, plans for irradiation, and expertise and experience of the reconstruction team.

All breast reconstruction procedures have to be performed only by privileged surgeons. The privileged surgeon should work in a coordinated multidisciplinary fashion to properly guide the patient's decision; and to determine optimal sequences of the reconstructive procedures in relation to adjuvant therapies.

Patients undergoing mastectomy should always be counselled for reconstruction. Breast reconstruction can be performed at the same time as mastectomy (**immediate** with saline expander) or after completion of cancer treatment (**delayed**).

Following mastectomy, factors to be considered in the decision-making include the types of breast reconstruction that are:

- Implant only reconstruction
- Autologous tissue (flap)
 - latissimus dorsi (LD) flap
 - transverse rectus abdominus myocutaneous (TRAM) flap
 - gluteus maximus myocutaneous flap
 - free flaps (when available)
- Combination of both types (autologous + implant)

Delayed reconstruction is generally preferred after completion of radiation therapy in **autologous tissue reconstruction** due to reported loss in reconstruction cosmesis.

Immediate reconstruction is preferred when **implant reconstruction** is used, in order to avoid tissue expansion of radiated skin flaps. Tissue expansion of irradiated skin can result in significantly increased risk of capsular contracture, malposition, poor cosmesis, and implant exposure. In a previously radiated patient, the use of tissue expanders/ implants is relatively contraindicated.

Women who are not satisfied with the cosmetic outcome following completion of breast cancer treatment should be offered a privileged surgery consultation.

Cases of *BRCA* positive genes with positive family history could have a risk-reducing subcutaneous mastectomy with immediate reconstruction.

Cases with fungating adherent tumour can be treated by mastectomy as palliative procedure and immediate chest wall reconstruction using autologous flap or skin grafting depends on appropriate patient selection.

The relative contra-indications to reconstruction include:

- Metastatic disease
- Obesity
- Diabetes
- Cardiovascular disease
- Excessive use of nicotine

8.5 Surgical Management Based on TNM Staging:

8.5.1 Ductal Carcinoma in situ (Stage 0, Tis, N0, M0):

- Primary treatment is through:
 - (Wide local excision) Breast conservation without lymph node surgery + whole breast radiation therapy OR
 - Total mastectomy with or without sentinel node biopsy + reconstruction

Surgery must ensure complete pathological excision of the disease with a minimum of 2mm radial margin. In patients with multifocal DCIS or extending for more than 4cm, mastectomy will be considered.

Complete ALND should not be performed in the absence of evidence of invasive cancer or proven axillary metastatic disease in women with apparent pure DCIS.

In patients with seemingly pure DCIS to be treated with mastectomy or with excision in an anatomical location, which could compromise the performance of a future SLN procedure, a SLN procedure may be performed.

Complete resection should be documented by analysis of margins and specimen radiography.

8.5.2 Lobular Carcinoma in situ (Stage 0, Tis, N0, M0):

- Primary treatment is through a core needle biopsy followed by a surgical excision of the area.

No further surgery is necessary following incidental finding of LCIS on diagnostic surgical biopsy (at present, surgical clearance of LCIS is not required).

If malignancy is not discovered following surgical excision, a programme of mammographic surveillance until screening age will be offered to the patient.

8.5.3 Invasive Breast Cancer Stage I, IIA, IIB/ IIIA (T3, N1, M0):

- Primary treatment is through wide local excision (breast conservation) OR mastectomy with surgical staging of axilla.

Surgery must ensure complete pathological excision of the disease with a minimum of tumour inked margins to 2mm radial pathological margin.

Central tumours will require central resections not compromising nipple areola complex if it is ≥ 2 cm away from it. Impalpable lesions will require radiological wire localization prior to surgery.

Patients with T2/ T3 tumours requiring mastectomy will be considered for neoadjuvant chemotherapy if this might make them suitable for breast conserving surgery with tumour down-sizing (however, this may not be the case and still neoadjuvant chemotherapy is given).

Patients with T1 to T3 tumours with positive axillary nodes should be considered for neoadjuvant chemotherapy followed by surgery.

8.5.4 Stage IIIA (T0-3, N2, M0), IIIB, IIIC

Neoadjuvant chemotherapy followed by wide local excision (breast conservation)/ mastectomy and axillary lymph node clearance level I/ II/ (Consider level III only if suspicious looking nodes are present at level II).

8.5.5 Stage IV

Stage IV is a systemic disease and would require systemic treatment. Local regional control could be obtained by mastectomy and axillary lymph node dissection level I/ II or radiotherapy, following systemic treatment; based on MDT discussion.

8.6 Surgical Management of Specific Pathologies

8.6.1 Paget Disease of the Nipple

If conventional imaging fails to reveal extensive micro calcification or an invasive tumour, a breast MRI should be performed. Surgical management is as follows:

- Local disease - central resection.
- Extensive/ multifocal disease - mastectomy.
- Axillary staging is the same as for invasive cancer.

8.6.2 Inflammatory Breast Cancer

It is characterized by erythema and oedema (peau d'orange) of a third or more of the skin of the breast and with a palpable border to the erythema. Pathologically, tumour is typically present in the dermal lymphatics of the involved skin.

Management is by neoadjuvant chemotherapy followed by mastectomy and axillary lymph node clearance levels I/ II followed by radiotherapy.

8.6.3 Local/ Regional Recurrent Disease

- If initial treatment was lumpectomy and radiotherapy, then next procedure is mastectomy.
- If initial treatment was mastectomy, then next procedure is surgical resection, if possible.
- In axillary recurrence consider surgical resection if possible followed by radiotherapy.
- Consider systemic treatment in all cases of recurrent disease in addition to restaging.

SYSTEMIC THERAPY

9. Systemic Therapy

Systemic therapy in the management of breast cancer includes

- i. **Chemotherapy:** treatment using drugs to kill or damage cancer cells.
- ii. **Endocrine therapy:** cancer treatment in which drugs are used to slow tumor growth by blocking the effect or synthesis of female hormones based on hormonal response in the tumour.
 - a. Tumours with an incomplete (some expression) or high degree of expression of estrogen receptor (ER) and/ or progesterone receptor (PgR) are considered **endocrine responsive**.
 - b. Tumours with no detectable expression of ER and PgR are considered **endocrine non-responsive**.
- iii. **Biologic therapy**
 - a. **Immunotherapy:** Treatment that works via the immune system

The medical oncologist should assess a patient's risk stratification and document in the patient's file according to St. Gallen criteria 2007. In patients who are estrogen-receptor positive (ER+), with intermediate risk, options to discuss include either to undergo chemotherapy followed by hormone treatment or to consider the Oncotype DX test.

The Oncotype DX genomic test analyzes the activity of 21 genes that can influence how likely a cancer is to grow and respond to treatment. It is both a prognostic and a predictive test as it predicts the likelihood of benefit from chemotherapy. The test results assign a Recurrence score - a number between 0 and 100 - to the early-stage breast cancer.

- **Low recurrence score (< 18)** - low risk of recurrence - administer adjuvant endocrine therapy.
- **Intermediate recurrence score (18-30)** - intermediate risk of recurrence - give administer adjuvant endocrine therapy + adjuvant chemotherapy
- **High recurrence score (≥ 31)** - adjuvant endocrine therapy + adjuvant chemotherapy.

Table 5: Risk categories and suggested treatment for patients with operated breast cancer

Risk category	Characteristics present	Recommended Treatment
Low risk	Node-negative tumour and all of the following features: pT ≤ 2 cm Grade 1 Absence of extensive peri-tumoural vascular invasion ER and/ or PgR expressed HER-2 gene neither over expressed nor amplified Age ≥ 35 years	HER-2 negative: Consider Endocrine therapy (ET). Estimated risk of recurrence in 10 years (< 10%)
Intermediate risk	Node-negative and at least one of the following features: pT > 2 cm Grade 2-3 Presence of extensive peri-tumoural vascular invasion ER and PgR absent Age < 35 years OR Node-positive (1-3 involved nodes) AND ER and/ or PgR expressed AND HER-2 gene neither over expressed nor amplified	Highly endocrine responsive tumour and HER-2 negative: Consider Endocrine therapy OR Chemotherapy with/ without endocrine therapy + Trastuzumab Estimated risk of recurrence in 10 years (10-50%) If patient has ER, PR positive, HER-2 neu negative, consider OncoType DX test
High risk	Node-positive (1-3 involved nodes) AND ER and PgR absent OR HER-2 gene over expressed or amplified OR Node-positive (4 or more involved nodes)	Chemotherapy with/ without endocrine therapy + trastuzumab HER-2 positive and tumour size > 0.5cm: Consider Trastuzumab + Chemotherapy (CT) Estimated risk of recurrence in 10 years (> 50%)

Table 6: Choice of treatment modalities according to hormone responsiveness and HER-2 status

HER-2 Status	Highly endocrine responsive	Incompletely endocrine responsive	Endocrine non-responsive
Negative	ET (consider adding CT according to risk)	ET (consider adding CT according to risk)	CT
Positive and tumour size > 0.5cm	ET + Trastuzumab + CT	ET + Trastuzumab + CT	Trastuzumab + CT

9.1 Endocrine Therapy

9.1.1 Indications for Endocrine Therapy

The goal of adjuvant endocrine therapy is to reduce the availability of oestrogen to the cancer cells. This can be achieved by

- blocking oestrogen receptors with drugs such as Tamoxifen;
- suppression of ovarian oestrogen synthesis by luteinising hormone releasing hormone (LHRH) agonists (also known as gonadotropin-releasing hormone analogues (GnRHs)) OR
- ovarian function ablation surgically - irreversible.
- aromatase inhibitors (AIs), anastrozole, exemestane and letrozole, prevent the synthesis of oestrogen from androgens.

GnRHs, for example goserelin, provide effective ovarian suppression in premenopausal women and are an effective alternative to oophorectomy. They induce a menopausal status that is usually reversible on cessation of therapy.

AIs use are associated with long-term skeletal adverse effects - risk of bone density loss, osteoporosis associated fractures, joint stiffness, etc. It is recommended that women treated with AIs should have their vitamin D levels checked and supplemented.

Menopause is generally the permanent cessation of menses and includes a profound and permanent decrease in ovarian oestrogen synthesis. Reasonable criteria for determining menopause include any of the following:

- Prior bilateral oophorectomy
- Age \geq 60y
- Age < 60y and amenorrhic for 12 or more months in the absence of chemotherapy, tamoxifen, toremifene, or ovarian suppression and follicle-stimulating hormone (FSH) and estradiol in the postmenopausal range
- If taking tamoxifen or toremifene, and age < 60y, then FSH and plasma estradiol level in postmenopausal ranges.

The total duration of optimal adjuvant endocrine treatment is between 5 to 10 years; with 5 years for Tamoxifen alone being standard in premenopausal women and aromatase inhibitors (AI) for postmenopausal women. Sequential rather than concurrent administration of cytotoxic and endocrine therapies should be used.

Women are to receive a bisphosphonate if on assessment of bone mineral density by DEXA, a T- score of less than -2.5 SD which equals to osteoporosis, is received. Patients on AI should use vitamin D and calcium as prophylaxis even in the absence of osteoporosis/ osteopenia.

The choice and sequencing of specific adjuvant endocrine therapy should be agreed following consideration of benefits and side effects for each treatment.

9.1.2 Endocrine Treatment in Early Invasive Breast Cancer

Patients with early invasive breast cancer should have a baseline DEXA scan to assess bone mineral density if they:

- are starting adjuvant aromatase inhibitors,
- have treatment-induced menopause,
- are starting ovarian suppression therapy.

Tumour type	Pre-menopausal	Post-menopausal
Ductal carcinoma in situ (DCIS)	For ER positive, PgR positive in histopathology specimen, treat with Tamoxifen for 5 years	For ER positive, PgR positive in histopathology specimen, treat with Aromatase Inhibitor (AI) for 5 years and use Tamoxifen if there is a contraindication to AI.
Lobular carcinoma in situ	Counselling regarding risk reduction	Counselling regarding risk reduction
Invasive Early Breast Cancer (pT1a,b,c), pT2, pT3 +N0, N1mi.	<p>1st line: Treat with Tamoxifen for at least 5years, to a total of 10years, unless there are contraindications or side effects</p> <p>2nd line: Consider ovarian ablation with AI (Exemestane) for patients with contraindications to Tamoxifen or in high risk group.</p> <p>3rd line: Consider ovarian ablation plus Tamoxifen for patients intolerant to AI.</p>	<p>1st line: Treat with AI for at least 5years.</p> <p>2nd line: Tamoxifen for 2 to 3 years, then switch to AI for a total of 2 to 5 years.</p>

9.1.3 Endocrine Treatment in Metastatic Breast Cancer

- Hormone receptor positive metastatic breast cancer:** Patients with slowly progressive disease, no visceral involvement, and minimal symptoms, e.g. in cases with a long relapse-free interval, isolated bone and soft tissue involvement and prior response to endocrine therapy. Treatment of endocrine responsive patients is according to the menopausal status.
- Hormone receptor negative metastatic breast cancer:** Patients with hormone receptor-negative metastatic breast cancer and those with proven hormone resistant disease should receive cytotoxic chemotherapy to control this aggressive type of breast cancer.

Table 8: Hormone receptor positive metastatic breast cancer

Pre-menopausal	Post-menopausal
<p>1st line: Treat with Tamoxifen - if no proven Tamoxifen resistance or if > 12months after discontinuation of Tamoxifen.</p> <p>2nd line: Consider AI (letrozole, anastrozole or exemestane) + ovarian suppression or ablation if resistant to Tamoxifen or < 12months after discontinuation of Tamoxifen.</p>	<p>1st line: Treat with non-steroidal AI (Anastrozole, Letrozole) if no prior AI treatment.</p> <p>2nd line: Treat with Tamoxifen, Letrozole, Anastrozole or Steroidal AI (Exemestane) or Fulvestrant. Exemestane + Everolimus if patient has progressed within 12 months in non-steroidal AI or Tamoxifen.</p>

Endocrine therapy should be continued till disease progression or unacceptable toxicity. If the disease progressed after 3 consecutive endocrine regimens or a visceral crisis developed, the patient should be shifted to chemotherapy.

9.2 Chemotherapy

Systemic chemotherapy can be given with different intents:

- Neoadjuvant chemotherapy is widely recommended as part of a multimodal treatment approach prior to surgery for patients with potentially operable (locally advanced or inflammatory) breast cancer.
- Adjuvant chemotherapy is given in early breast cancer in high-risk category, post surgery to reduce risk of recurrence and improve survival.
- Palliative chemotherapy is given in the metastatic setting for disease control.

General considerations

- Informed consent needs to be obtained from the patient by the medical oncologist before chemotherapy is started.
- The use of anthracyclines is recommended for all patients and especially for patients with HER-2-positive breast cancer. The use of taxanes may be limited to high-risk patients.
- The use of non-anthracycline-containing regimens such as CMF, docetaxel and cyclophosphamide may still be appropriate for some patients (elderly, cardiac contraindication). A shorter duration of chemotherapy (12-16 weeks) may be suitable for elderly patients, for whom the role of chemotherapy remains uncertain.
- The optimal duration of the treatment is not known. However, at least four cycles (12-16 weeks) should be administered, with the general aim of six to eight cycles (18-24 weeks).
- The use of dose-dense schedules with prophylactic G-CSF is controversial, while high-dose therapy requiring peripheral blood stem cell support is not recommended.

9.2.1 Neoadjuvant Chemotherapy.

For HER-2 positive breast cancer:

- TCH (docetaxel/ carboplatin/ trastuzumab) + Pertuzumab x 6 cycles.
- Pertuzumab + trastuzumab + docetaxel x 4 cycles followed by FEC x 4 cycles.
- Pertuzumab + trastuzumab + paclitaxel weekly x 12 cycles followed by FEC x 4 cycles.
- Docetaxel/ cyclophosphamide/ pertuzumab + trastuzumab x 6 cycles.

For HER-2 negative breast cancer:

- FEC x 3 - 4 cycles followed by D x 3 - 4 cycles (fluorouracil/ epirubicin/ cyclophosphamide followed by docetaxel).
- FEC/ AC x 4 cycles followed by 12 cycles of paclitaxel weekly.

Table 9: Commonly prescribed chemotherapy in neoadjuvant setting for HER-2 negative breast cancer

Regimen	Dose	No. of cycles	Duration of cycles (weeks)
FEC-D	Flourouracil 500mg/m ² Epirubicin 100mg/m ² Cyclophosphamide 500mg/m ² Docetaxel 100mg/m ²	3 - 3	3 - 3
FEC 100-75	Flourouracil 500mg/m ² Epirubicin 100mg/m ² Cyclophosphamide 500mg/m ²	6	3
DC	Docetaxel 75mg/m ² Cyclophosphamide 600mg/m ²	4	3
FEC-T	Flourouracil 500mg/m ² Epirubicin 90mg/m ² Cyclophosphamide 500mg/m ² Taxol 80mg/m ²	4 - (8-12)	3 - 1

Table 10: Commonly prescribed chemotherapy in neoadjuvant setting for HER-2 positive breast cancer

Regimen	Dose	No. of cycles	Duration of cycles (weeks)
PTH - P followed by FEC	Trastuzumab 8mg/kg (1 st cycle), 6 mg/kg (2 nd cycle) + Pertuzumab 840mg (1 st cycle), 420 mg (2 nd cycle) + Paclitaxel 80mg/m ² (weekly)	4 - 12	3 - 1
PTH - D followed by FEC	Trastuzumab 8mg/kg (1 st cycle), 6 mg/kg (2 nd cycle) + Pertuzumab 840mg (1 st cycle), 420 mg (2 nd cycle) + Docetaxel 75mg/m ²	4 - 4	3 - 3
FEC	Fluorouracil 500mg/m ² Epirubicin 100mg/m ² Cyclophosphamide 500mg/m ²	4	3
PTCH	Carboplatin AUC6 + Trastuzumab 8mg/kg (1 st cycle), 6 mg/kg (2 nd cycle) + Pertuzumab 840mg (1 st cycle), 420 mg (2 nd cycle), Docetaxel 75 mg/m ²	6	3

9.2.2 Adjuvant Chemotherapy

High Risk (according to St. Gallen criteria or OncoType DX > 30):

For HER-2 positive breast cancer:

- TCH (docetaxel/ carboplatin/ trastuzumab) x 6 cycles.
- FEC x 3 - 4 cycles followed by trastuzumab + docetaxel x 3 - 4 cycles
- FEC x 4 cycles followed by trastuzumab + paclitaxel weekly x 12 cycles
- Docetaxel/ cyclophosphamide +trastuzumab x 6 cycles.

For HER-2 negative breast cancer:

- FEC x 3 - 4 cycles followed by D x 3 - 4 cycles (fluorouracil/ epirubicin/ cyclophosphamide followed by docetaxel).
- FEC/ AC x 4 cycles followed by 12 cycles of paclitaxel weekly.

Intermediate Risk (according to St. Gallen criteria or OncoType DX 18 - 30):

- AC x 4 cycles.
- AC x 4 cycles followed by Taxol weekly x 12 cycles.
- CMF (Cyclophosphamide/ Methotrexate/ Fluorouracil) x 6 cycles if patient has poor performance status or has cardiac dysfunction.

Table 11: Commonly prescribed chemotherapy in adjuvant setting for HER-2 negative breast cancer

Regimen	Dose	No. of cycles	Duration of cycles (weeks)
CMF	Cyclophosphamide 600mg/m ² Methotrexate 40mg/m ² Fluorouracil 600mg/m ²	6	4
AC-D	Doxorubicin 60mg/m ² Cyclophosphamide 600mg/m ² Docetaxel 100mg/m ²	4 - 4	3 - 3
FAC	Cyclophosphamide 500mg/ m ² Doxorubicin 50mg/m ² Fluorouracil 500mg/m ²	6	4
AC-Tw	Doxorubicin 60mg/m ² Cyclophosphamide 600mg/m ² Paclitaxel 80mg/m ²	4 - 12	3 - 1
DAC	Docetaxel 75mg/m ² Doxorubicin 50mg/ m ² Cyclophosphamide 500mg/m ²	6	3

9.2.3 Chemotherapy Regimens for Metastatic Breast Cancer

There is no approved standard chemotherapy for metastatic breast cancer except the taxane-based regimen for patient progressing after the anthracycline-based chemotherapy. For the majority of patients, overall survival outcome from sequential use of single cytotoxic drugs seems to be equivalent to that after combination chemotherapy. Duration of each regimen and number of regimens should be tailored to each individual patient.

The choice between chemotherapy protocols should be made according to the risk assessment, HER-2 neu status, performance status of the patient and the need for rapid disease control. Low risk or friable patients can be offered single agent chemotherapy with sequential changing after progression. High risk patients with aggressive disease and visceral metastasis, who are in need of rapid disease control, should be considered for combination of chemotherapy.

HER-2 positive metastatic breast cancer
(Detailed information about chemotherapeutic agents and regimens provided below under Immunotherapy).

Chemotherapy	Dose	Frequency
Doxorubicin	60-75mg/m ²	Every 21 days
Doxorubicin	20mg/m ²	Every week
Epirubicin	60-90mg/m ²	Every 21 days
Liposomal Doxorubicin	50mg/m ²	Every 28 days
Paclitaxel	175mg/m ²	Every 21 days
Paclitaxel	80mg/m ²	Every week
Docetaxel	60-100mg/m ²	Every 21 days
Docetaxel	40mg/m ²	Every week
Albumin bound Paclitaxel	100-150mg/m ² day 1,8 & 15	Every 28 days
Gemcitabine	800-1250mg/m ² day 1,8 & 15	Every 28 days
Vinorelbine	25mg/m ² - 30 mg/m ²	Every week

Chemotherapy	Dose	Frequency
Paclitaxel	90mg/m ² day 1,8 & 15	Every 28 days
Bevacizumab	10mg/kg day 1 & 15	

Table 14: Preferred Chemotherapy Combinations for Metastatic Breast Cancer (MBC)

	Chemotherapy	Dose	Frequency
PTD	Pertuzumab	840 mg IV day 1 followed by 420 mg IV	Every 21 days x 6 Then maintenance with pertuzumab and trastuzumab for 1 year
	Trastuzumab	8mg/kg IV day 1 followed by 6 mg/kg IV	
	Docetaxel	75-100 mg/m ² IV day 1 cycled every 21 days	
PTP	Pertuzumab	840 mg IV day 1 followed by 420 mg IV cycled every 21 days	Every 21 days (Pertuzumab Trastuzumab every 21 days and paclitaxel weekly)
	Trastuzumab	4 mg/kg IV day 1 followed by 2 mg/ kg IV weekly or 8mg/kg IV day 1 followed by 6 mg/kg IV cycled every 21 days	
	Paclitaxel	80 mg/m ² IV day 1 weekly	
T-DM1	Ado-trastuzumab emtansine (T-DM1)	3.6 mg/kg IV day 1	Every 21 days
FAC	Cyclophosphamide	500mg/m ²	Every 21 days
	Doxorubicin	50mg/m ²	
	Fluorouracil	500mg/m ²	
FEC	Fluorouracil	500mg/m ²	Every 21 days
	Epirubicin	50mg/m ²	
	Cyclophosphamide	400mg/m ²	
AC	Doxorubicin	60mg/m ²	Every 21 days
	Cyclophosphamide	600mg/m ²	
EC	Epirubicin	75mg/m ²	Every 21 days
	Cyclophosphamide	600mg/m ²	
AT	Doxorubicin	60mg/m ²	Every 21 days
	Paclitaxel	125-200mg/m ²	
CMF	Cyclophosphamide	600mg/m ²	Every 21 days
	Methotrexate	40mg/m ²	
	Fluorouracil	600mg/m ²	
	Docetaxel	75mg/m ²	Every 21 days
	Capecitabine	1000/m ² PO BID day 1-14	
GT	Gemcitabine	1250mg/m ² IV days 1 & 8	Every 21 days
	Paclitaxel	175mg/m ² IV day 1	
	Ixabepilone	40mg/m ²	Every 21 days
	Capecitabine	1000mg/m ² PO BID day 1-14	

Table 15: Preferred Agents with Trastuzumab for HER-2-positive MBC

Chemotherapy	Dose	Frequency
Trastuzumab (component) OR	4mg/kg day 1 followed by 2mg/kg	Weekly
Trastuzumab	8mg/kg day 1 followed by 6mg/kg	3 weeks
Carboplatin	AUC 6	Every 21 days
Paclitaxel	175mg/m ²	
Carboplatin	AUC 2	Every 28 days
Paclitaxel	80mg/m ²	
Capecitabine	1000mg/m ² PO BID day 1-14	Every 21 days
Lapatinib	1250mg orally daily day 1-21	
Single Agents with Trastuzumab		
Chemotherapy	Dose	Frequency
Paclitaxel	175mg/m ²	Every 21 days

Agent	Dose	Frequency
Paclitaxel	80-90mg/m ²	Weekly
Docetaxel	80-100mg/m ²	Every 21 days
Docetaxel	35mg/m ²	Weekly
Vinorelbine	25mg/m ² - 30mg/m ²	Weekly
Capecitabine	1000-1250mg/m ² PO BID day 1-14	Every 21 days
Lapatinib	1000mg PO daily	

9.3 Immunotherapy

Patients with HER-2 positive breast cancer should receive trastuzumab, either as adjuvant treatment or with neoadjuvant chemotherapy following risk assessment and performance status. The standard duration of treatment with trastuzumab is currently one year.

Cardiac function should be monitored every three months in patients treated with anthracyclines and/ or trastuzumab. Trastuzumab should be used with caution in patients with significant cardiac comorbidity. The benefits should be weighed with the harms in these patients and treatment should only be recommended after careful consideration.

Adjuvant trastuzumab should not be given concurrently with anthracyclines but may be given either concurrently with taxane-based regimens or sequentially.

9.3.1 In Adjuvant Setting:

- Trastuzumab with endocrine therapy without chemotherapy is not supported by clinical trial evidence.
- Trastuzumab can be used in women with a primary tumour between 510 mm in size however its use for women with tumour < 5mm needs to be discussed.
- Based on pharmacokinetic analyses, a 3-weekly schedule (6 mg/kg) is considered equivalent to a weekly schedule (2 mg/kg).

9.3.2 In the Neoadjuvant Setting:

- For locally advanced breast cancer, use trastuzumab and pertuzumab in combination with chemotherapy.
- Avoid trastuzumab in patients with low left ventricular ejection fraction (< 50%). A reassessment of LVEF should occur after completing chemotherapy and before starting trastuzumab.

9.3.3 Metastatic Breast Cancer

In metastatic breast cancer, treatment with trastuzumab should be started early. Cardiac monitoring should be performed before and during treatment with trastuzumab. Treatment with Trastuzumab should be continued till disease progression in metastatic setting.

In metastatic breast cancer after first disease progression,

- **1st line treatment:** Consider Trastuzumab + Pertuzumab in combination with chemotherapy
- **2nd line treatment:** Consider TDM1 or Capecitabine + Lapatinib.
- **3rd line treatment:** Consider dual HER-2 blockade using both Trastuzumab and Lapatinib shows better survival when used after progression on trastuzumab.

RADIOTHERAPY

10. Radiotherapy

10.1 General Considerations

Radiation therapy should follow chemotherapy when chemotherapy is indicated.

- Postoperative radiotherapy in early breast cancer is indicated for all patients undergoing breast conservative surgery. This can be through:
 - Whole breast radiation with radiotherapy boost to the tumour bed. The radiotherapy boost is recommended in patients at higher risk (age < 50, high-grade disease) and all patients receiving radiotherapy after breast conservation surgery.
 - Supraclavicular area radiation if ≥ 4 positive lymph nodes and can still be considered if < 4 positive axillary nodes are present.
- Post-mastectomy radiotherapy is indicated in patients with lymph node-positive breast cancer and a high risk of recurrence - T3/ T4 primary tumour and ≥ 4 positive axillary lymph nodes.
- Chest wall and supraclavicular area radiation is indicated and can still be considered if < 4 positive axillary nodes are present.
- Post-mastectomy radiotherapy may also be considered in patients with lymph node-negative breast cancer and intermediate risk of recurrence - tumour < 5cm and margins < 1 mm. Only chest wall radiation is indicated.

All metastatic breast cancer patients are treated with systemic therapy. Individualized local treatment for each patient can be added. Palliative surgery or radiation is indicated for symptomatic metastasis or impending local organ damage due to metastasis.

All patients are seen by a radiation oncologist after referral from the weekly MDT meeting. A signed and informed consent is gained before the patient proceeds with radiotherapy treatment planning.

10.2 Dose Prescription:

10.2.1 Target Volumes Definitions

Target volume definitions are based on clinical and imaging information. It is important to individualize delivery of radiation therapy and considerations such as patient positioning (i.e. prone vs. supine) will be decided during simulation and adopted during the administration of radiation therapy.

Whole Breast Radiation: Target volume definition includes the entire breast tissue, and is done by both clinical assessment and CT-based treatment planning (according to ICRU report 50). A uniform dose distribution and minimal normal tissue toxicity are the goals and can be accomplished using compensators such as wedges, forward planning using segments, intensity-modulated radiation therapy (IMRT), respiratory gating, or prone positioning amongst other techniques.

Chest Wall Radiation (including breast reconstruction): The target includes the ipsilateral chest wall, mastectomy scar, and drain sites where possible. Depending on whether the patient has been reconstructed or not, several techniques using photons and/ or electrons are appropriate. CT-based treatment planning is recommended in order to identify lung and heart volumes amongst other organs at risk and minimize exposure of these organs. Special consideration should be given to the use of bolus material when photon fields are used to ensure that the skin dose is adequate when clinically indicated.

10.2.2 Dose to Target Volumes

Post-mastectomy radiotherapy:

- Chest wall TV receives a dose of 50 Gy in 25 fractions.
- Boost TV to the scar region receives a dose of 10 to 16 Gy in 5 to 8 fractions.

Breast conservation therapy:

- Whole breast TV receives a dose of 50 Gy in 25 fractions.
- Boost TV to the tumour bed receives a dose of 10 to 16 Gy in 5 to 8 fractions.
- Lymphatic drainage areas - treated if clinically indicated.
- Supraclavicular and axillary nodal PTV receives a dose of 45 Gy in 25 fractions.

10.2.3 Fractionation

Hypo-fraction regimes can be considered in patients with poor performance status, elderly patients; for patients with metastatic disease who are indicated for local therapy, and/ or informed patients who request an accelerated fractionation regimen.

Post-mastectomy radiotherapy:

- Chest wall PTV receives a dose of 40 Gy in 15 fractions.
- Boost PTV to the scar region receives a dose of 10 Gy in 5 fractions.

Breast Conservation Therapy:

- Whole breast PTV receives a dose of 40 Gy in 15 fractions.
- Boost PTV to the tumour bed receives a dose of 10 Gy in 5 fractions.
- Lymphatic drainage areas -- treated if clinically indicated
- Supraclavicular and axillary nodal PTV receives a dose of 40 Gy in 15 fractions.

10.2.4 Palliative Radiotherapy

Palliative Radiotherapy is indicated for relieving symptoms or preventing threatening complications from locally advanced or metastatic disease. Target volume in palliative setting is determined individually.

- Patients with painful bone metastases can also be considered for palliative treatment with Magnetic Resonance Guided Focused Ultrasound (MRgFUS).
- There are several effective conventional radiotherapy regimens, including 30 Gy in 10 fractions, 20 Gy in 5 fractions, and 8 Gy in 1 fraction.
- The selection of an appropriate fractionation schedule and treatment technique should take into consideration several factors, including the patient's general condition, site and extent of metastatic disease, threatening symptoms, past treatment, prognosis and remaining treatment options.

10.2.5 Stereotactic Radiotherapy or Radiosurgery

Stereotactic radiotherapy or radiosurgery is an alternative to neurosurgery in patients with limited volume brain metastatic disease. Patients who are candidates for stereotactic irradiation techniques should be discussed at the neuro-oncology MDT. Whole brain irradiation should be considered in patients with multiple brain metastases.

10.3 Radiotherapy Treatment Planning

Treatment planning is done on the treatment planning system and is reviewed and approved by the radiation oncologist.

Surgical clips (which can be identified in the Planning CT Scan), placed in the tumour bed at the time of surgery will be helpful in radiotherapy planning.

The Plan review includes (but is not limited to) analysis of dose volume histogram, isodose distribution, radiation beam parameters and suggestions for plan improvement.

The proposed treatment plan and dose prescription should be documented. Any modification to treatment plan will need to be clearly documented. Each plan is subject to intra-departmental peer review by the radiation oncology team, including radiation oncologists, medical physicists, and radiation therapists.

Intensity modulated radiation therapy (IMRT) as well as 3D-conformal radiation therapy (EBRT) is used in breast cancer radiotherapy. The radiotherapy boost is delivered with electron beam or photon fields or brachytherapy.

10.4 Treatment Delivery

Patients are treated according to the standard treatment instructions. The radiation oncologist is present for the first fraction of radiation. Imaging is done according to the imaging protocol and typically includes MV imaging and kVkv during boost delivery with on-line review by the radiation therapist and radiation oncologist on day 1 (when indicated), and off-line review by the radiation oncologist.

Patients will be reviewed once a week by the radiation oncologist for assessing treatment progress and toxicity. The radiation oncologist will evaluate and manage any radiation related side effects.

10.5 Follow up

Oncological follow up is performed by the medical oncologist. Radiotherapy-specific follow up is performed by the radiation oncologist. The first radiotherapy-specific follow up should be performed 8 weeks after treatment and thereafter on a yearly basis.

The aims of follow-up include:

- To discover early local recurrences or contralateral breast cancer.
- To evaluate and treat possible treatment related complications such as menopausal symptoms and osteoporosis.
- To provide psychological support and information in order to enhance patients return to normal life.
- To provide appropriate palliative services to patients with metastatic breast cancer in order to improve symptoms and quality of life.

10.5.1 Early and Local/ Regionally Advanced Breast Cancer Follow-up

Follow-up will be done alternately between surgeons and medical oncologist and should be tailored according to patient's risk stratification and clinical needs. Every visit should include history taking, eliciting of symptoms and a physical examination. Further investigations will be guided according to patient's symptoms. The schedule is as follows:

- The first 2 years: patients to be seen every three months;
- Years 2 to 5 years: patients are seen every six months;
- More than 5 years: patients are seen annually.

Ipsilateral (after BCS) and contralateral clinical mammography is recommended yearly for premenopausal women and postmenopausal women for the first five years and then according to national screening guidelines.

There are no data to indicate that performing blood counts, chest X-ray, bone scan, liver ultrasound, CT scans of chest and abdomen or any tumour markers such as CA 15-3 or CEA on asymptomatic patients produces a survival benefit.

A DEXA scan should be performed for women experiencing a premature menopause (< 45 years); those on an aromatase inhibitor with a baseline T score of less than -1 SD and repeated every 2 years.

10.5.2 Metastatic Breast Cancer Follow-up

Investigations are directed according to the symptoms of patients. Response to the treatment in the metastatic sites needs to be assessed every two to three months.

- Hormone therapy follow-up assessment is to be performed on average every 1 to 2 months.
- Chemotherapy follow-up assessment is to be performed after 1 to 2 cycles.

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THE GUIDELINE DEVELOPMENT GROUP (GDG)

12. The Guideline Development Group (GDG)

The breast cancer clinical guidelines have been produced with the assistance of a multidisciplinary group of clinicians to provide a comprehensive overview of the breast cancer patient's journey from referral to treatment and support.

The guideline development process was supported by staff from Hamad Medical Corporation (HMC) and Supreme Council of Health (SCH). The draft of the guideline was prepared by HMC and SCH staff in partnership with the breast tumour board chair and lead clinicians. This draft was then discussed and agreed with the tumour board and subsequently forwarded to the stakeholders for consultation.

Following the consultation period, staff from HMC and SCH finalized the recommendations and the final document was sent to the National Cancer Committee (NCC) for approval. On receipt of the NCC approval, publication and dissemination occurred in the state of Qatar. The following are members of Breast GDG as follows:

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Updating the Guideline

One year after publication of the guideline, the breast tumour board will review the guideline to determine whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an early update.

Disclaimer

The GDG assumes that healthcare professionals will use clinical judgment, knowledge and expertise when deciding whether it is appropriate to apply these guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the practitioner in light of individual patient circumstances, the wishes of the patient and clinical expertise.

The SCH disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.