# LANCS & SOUTH CUMBRIA BREAST CRG

# REFERENCE MANUAL

# FOR THE MANAGEMENT OF

# BREAST CANCER

**Guidelines agreed by:**

| | |
|---|---|
| Breast CRG members | January 2023 |
| Version | V4 2023 |
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| **Please destroy all previous versions of this guideline** | |

## SECTION 1

## NICE Guidance and Breast Cancer

The following guidance has been published by NICE. This guidance is designed to cover most of the patients most of the time. They are not designed as a textbook on breast cancer management and do not cover every eventuality. Topics covered are driven by the stakeholders.

NICE confines itself to peer reviewed published data and is exclusive of abstracts and conference presentations. All guidance issued should be applied to each individual patient.
NICE guidance is available at www.nice.org.uk/index

**SECTION 2**

# CLINICAL GUIDELINES

# FOR THE MANAGEMENT OF

# BREAST CANCER

# WITHIN

# LANCASHIRE & SOUTH CUMBRIA

## Introduction

- This manual sets out the guidelines on the management of breast cancer to be adopted by the cancer centre and units in the Lancashire and South Cumbria Cancer Network.
- All new patients with breast cancer should be discussed by a multi-disciplinary team.
- Patients should be considered for clinical trials.
- Patients may be treated outside this guidance, but this must be agreed by the MDT and the reasons appropriately recorded in the patients notes and SCR.

## Breast MDT

The MDT lead should be a single named clinician who is also a core team member.

**The MDT core team should include:**

- Two designated breast surgeons
- Clinical Oncologist
- Medical Oncologist * (where the responsibility of chemotherapy is not undertaken by the clinical oncology core team member).
- An imaging specialist * (the role of imaging specialist can be met by a group of named specialists provided each meets the required workload).
- A histopathologist (taking part in the specialist EQA for breast cancer) * (the role of histopathology specialist can be met by a group of named specialists provided each meets the required workload).
- Two breast nurse specialists
- MDT co-ordinator/secretary
- At least one clinical core member of the team with direct clinical contact should have completed the training necessary to enable them to practice at level 2 for the psychological support of cancer patients and carers and should receive a minimum of 1 hour's clinical supervision by a level 3 or level 4 practitioner per month.
- An NHS employed member of the core or extended team should be nominated as having specific responsibility for users' issues and information for patients and carers.
- A member of the core team nominated as the person responsible for ensuring that recruitment into clinical trials and other well-designed studies is integrated into the MDT.

Conduct is governed by local policy but should be polite and respectful.

file://nas02.xlthtr.nhs.uk/userdata$/rachel.ellis/Downloads/NCATMDTCharacteristics_FINAL%20(1).pdf

The MDT may be a forum for teaching and learning. The case presentations should be concise and relevant, the question addressed to the MDT should be clearly framed. Time thresholds for placing the patient on the MDT should be adhered to except in case of urgency. These cases should be discussed with the relevant clinician prior to the meeting. Adequate time should be allocated in clinicians' timetables to attend. The meeting should be of a reasonable duration and a reasonable case load should be presented. It is important that a narrative is recorded from the MDT decision making on the Cancer Register wherever possible and appropriate.

The MDTM time is a precious resource, and every attempt should be made to use it efficiently. The NHSE and NHSI document Streamlining Multi-Disciplinary Team Meeting 2019 refers to proposed changes and can be accessed at: Streamlining (england.nhs.uk).

## Imaging in the Diagnosis of Breast Lumps

- Age >40 years
    - Digital mammo
    - ± Ultrasound

- Age <40 years
    - Ultrasound

- Specific indications for ultrasound

    - Evaluating breast lumps
    - Identifying a discrete mass lesion in a nodular area
    - Evaluating cystic lesions of the breast
    - Assessing lesions identified by mammography
    - Monitoring malignant and benign lesions where appropriate
    - Image-guided core biopsies
    - Assessment of axilla along with FNA/core were indicated

## Diagnosis

- All discrete masses presenting symptomatically must be assessed by imaging **(see above)** and fine needle aspiration (FNA) or biopsy, usually core biopsy. It is now accepted that we should rely primarily on core biopsies, which should preferably be done under ultrasound guidance. FNA should be reserved for exceptional situation where core biopsy is not feasible.
- If FNA result is C4 (suspicious), or C3 (atypical), a core biopsy should be performed to complete assessment
- If FNA result is C1 (inadequate/non-diagnostic), when the clinical and imaging findings are equivocal or malignant, a repeat FNA, or preferably a core biopsy must be done to obtain a tissue diagnosis.
- Core biopsy can be used in conjunction with FNA, particularly in multi-focal disease. Core biopsy should be performed in all suspected cancers (Baso Guidelines 2009). Ultrasound guided core biopsy is preferred where possible.
- FNA of axillary lymph nodes that are equivocal or suspicious on ultrasound should form the part of full assessment of axilla. Core biopsy of the axillary node should be performed where the breast primary is occult.

**Basic information**

The information required on all patients is as follows: -

- Histologically confirmed diagnosis
- Clinical history and examination
- Age and menopausal status
- Past or concurrent medical illnesses
- Family history

## Staging Investigations

**Early breast cancer**
Routine blood tests or imaging are not routinely indicated for early breast cancers

**LABC (Locally advanced breast cancer) and High-risk patients**

Staging investigations should be considered in these groups of patients:

- Locally advanced breast cancer patients.

- Chest wall fixity excluding pec major, skin involvement with epithelial breach, fixed matted axillary LNs.
- Clinically N2 or 4 or more involved lymph nodes on histology.
- T3 disease with nodal involvement or T4 disease.
- Axillary US suggesting N2 disease where clinically axillary disease not feasible to assess satisfactorily.
- Inflammatory breast cancer.
- Recurrent invasive ipsilateral breast cancer (Previous DCIS leading to invasive recurrence or contralateral new primary does not require staging).
- Any patient deemed by the MDT to be high risk.
- Chest x-ray is not the standard investigation for diagnosis of lung metastases, although they can be followed up, if visible, by this modality.

**Staging Imaging**

- Contrast CT of Chest, abdomen and Pelvis is considered to be the optimum investigation imaging.
- Isotope bone scan is no longer considered to be an essential imaging due to lack of useful information in absence of a symptom. However, it can be considered as felt appropriate in the MDT meeting.
- Other investigations skeletal x-rays, ultrasound/MRI scan of liver/bone/soft tissue should only be done as indicated by symptoms, signs or the biochemical profile or prompted by equivocal CT findings.

## Pathology Reporting

Reporting will follow the guidelines given in the RCPath document, **"Guidelines for non-operative diagnostic procedures and reporting in breast cancer screening August 2021".**

G150-Non-op-reporting-breast-cancer-screening.pdf (rcpath.org)

And also, “Pathology reporting of breast disease in surgical excision specimens incorporating the dataset for histological reporting of breast cancer June 2016”.

G148_BreastDataset-hires-Jun16.pdf (rcpath.org)

These cover scoring for hormone receptors and sentinel node reporting.

- Tumour size
- Histological grade
- ER/PR status
- HER 2 status
- Upfront PDL 1 testing for TNBC
- PI3K receptor mutation analysis

- Despite the lack of evidence supporting its use, PR testing is currently recommended by NICE, in addition to ER and HER 2, and these will continue to be tested at present.
  Early and locally advanced breast cancer: diagnosis and management (nice.org.uk)
- The ER and PR results will continue to be expressed as an Allred score.
- HER-2 status is recommended in all patients.
- HER-2: Every attempt will be made to make the HER-2 result available within 2 weeks to help with medical treatment, due to the widened indication of HER2 positive and TNBC. This includes ongoing efforts to validate ISH testing for HER2 within the network. They should certainly be available at the time of making recommendation on systemic therapy.
- All receptor requests should be processed routinely. Nodal status: sentinel LN biopsy should form the standard of care for all patients (within RCS guidelines).
- The reporting pathologist will ensure that receptor status is available on all breast cancers as soon as possible.

Minimum information requirement for Adjuvant therapy recommendation:

- Patients details (age, comorbidities, menopausal status, any specific circumstances/needs)
- Tumour characteristics- Grade, size, LVI, Histological subtypes, Receptors status (ER PR and Her2)
- Nodal status
- Oncotype DX should be offered where clinically appropriate.
- Ki67 may be requested for additional information where it will aid decisions regarding chemotherapy. However, scoring methodology is yet to be agreed.

**Recording of MDT outcome**

The information presented at MDT should be prospectively recorded in the Cancer Register used by the individual Trusts.

In the North Lancs and South Cumbria network this is in form of the **Somerset Cancer Registry**.

To record the agreed minimum COSD (Cancer Outcome and Service Dataset) recommended fields, but every attempt should be made to enter clinical information to make it a useful resource.

Information on COSD can be accessed at
Cancer Outcomes and Services Dataset (COSD) (ncin.org.uk)

SACT (Systemic Anti-cancer Therapy) Dataset/VARIAN to record systemic chemotherapy
Information on SACT dataset can be found at
SACT Homepage (chemodataset.nhs.uk)

## The Role of Other Imaging Modalities in Breast Cancer

### MRI Scanning

Indications:

- Screening of genetic high-risk patients, according to family history guidelines. http://guidance.nice.org.uk/CG164/NICEGuidance/pdf/English
- Screening of patients following mantle radiotherapy.
- Mammographically occult breast cancer.
- For diagnosis of occult breast primary cancer, suspected on clinical grounds, in patients for whom conventional imaging is unsuccessful.
- For patients with a discrepancy in size between clinical findings and imaging.
- For significant discrepancy on mammogram and ultrasound size.
- Lobular cancer being considered for breast conserving surgery.
- To assess response to neo-adjuvant chemotherapy.
- Assessment of patients who have breast implants and have been diagnosed with primary breast cancer.

### PET Scanning

No routine indications exist presently but can be requested if felt appropriate by the MDT.

**Axillary US already included in minimum assessment for all newly diagnosed cancers**

## Male Breast Cancer

Men with breast cancer should be offered surgery which would take the form of a mastectomy. The axilla would be staged in the normal way with pre-operative ultrasound and sentinel node biopsy where nodes are not involved.

Radiotherapy and chemotherapy would be offered in the normal way based on the results of pathological staging.

Tamoxifen is recommended if the tumour is oestrogen receptor positive, but less information is available about safety of aromatase inhibitors as adjuvant endocrine therapy in men. If an AI is used androgen blockade is required with GNRH antagonist.

Covered in assessment and diagnosis - follow up should be annual mammograms for 5 years.

## Ductal carcinoma in situ (DCIS)

### Introduction

- 20 – 30% of malignant disease found at breast screening.
- Pre-invasive disease with risk of development of invasive disease in future.
- May present as a mass, with Paget's disease or nipple discharge but more commonly as micro calcification on screening mammography.
- Local recurrence associated with size, histology, and completeness of excision. 50% of local relapses are invasive.
- Local recurrence after surgery alone is 20% and after surgery and radiotherapy is 10% (Fisher B. et al NSAPB B 17. J. Clin Oncol 1998:16:441-52. Julien J. P. et al EORTC 10853. Lancet 2000;355:528-23).
- Lymph node staging is not normally required; however, it should be offered to patients undergoing mastectomy for DCIS and the other relative indications include:
  - Suspicion of invasive disease.
  - DCIS associated with mass.

### Surgical treatment of DCIS

Breast conservation alone with no adjuvant breast radiotherapy

- Clear excision margins (1mm or more)
- Low and intermediate grade histology

### Breast conservation and adjuvant breast radiotherapy

- Clear margins (1mm or more)
- High grade histology

### Mastectomy

- Multicentric/extensive multifocal disease proven with core biopsy.
- Inadequate (less than 1 mm) margins after reasonable attempts at excision (usually two).
- Immediate reconstruction should be considered as with any mastectomy.
- The axilla should be staged in the case of a mastectomy for DCIS.

## Lobular Neoplasia (ALH and LCIS) and ADH

- Not a pre-cancerous lesion but risk indicators
- Usually, an incidental finding
- High risk of invasive cancer in both breasts
- Close monitoring advised (annual screening) for 5 years

- There is no indication for adjuvant hormone therapy outside clinical trials.
- Chemoprevention can be discussed in cases of LCIS.
- Pleomorphic LCIS is treated as high grade DCIS.

## The Management of Invasive Breast Cancers – Indications for Surgery

### Surgical treatment

The patient's treatment should have been discussed in the diagnostic MDT.
This plan may be modified at the time of surgery according to clinical and patient requirements.

All appropriate treatment options, including breast conserving surgery, mastectomy, immediate or delayed reconstruction should be discussed and be available. If an appropriate option is not locally available, the patient should be offered this option in the next closest part of the network.

All units should offer all breast surgical techniques with the exception of free flap based reconstructive work (e.g., DIEP flap). In this case a referral pathway should exist.

An Oncoplastic MDT should exist with access to a plastic surgeon to aid the decision-making for patients requiring complex oncoplastic or reconstructive procedures.

Surgical technique is to be of the standard set out by the RCS ABS Guidelines.

A single -pre-operative dose of antibiotics may be administered (Cochrane review)

**Breast conservation**

Patient selection and management

- Technically suitable for breast conservation (acceptable tumour to breast volume ratio).
- Neoadjuvant chemotherapy or endocrine treatment should be considered in appropriate cases to facilitate BCS.
- Patient should be agreeable to radiotherapy (RT) and no contraindication for RT should exist.
- Consider “Therapeutic Mammoplasty”, partial reconstruction where appropriate.
- All BCS should be done in line with Oncoplastic BCS principles.
- Clips to mark the cavity in all patients (to aid radiotherapy planning).
- Orientation of specimen is important to help optimum margin-reporting by the pathologists.
- Margins must be assessed using a method acceptable to the local MDT (>1mm).
- Clearance of margins documented and discussed at MDT.
- Multifocal disease limited to one quadrant can be offered- BCS if there is reasonable chance of achieving a satisfactory margin with or without therapeutic mammoplasty or a partial reconstruction.
- Multi-centric disease should generally be taken as a contraindication to BCS as safety of multiple wide local excisions in not established. However, in low risk (DCIS/Grade 1/2) small volume (T1) disease it can be considered on a case-to-case basis where patients opt against mastectomy and are properly discussed in the MDT meeting. The lack of evidence of safety of multiple WLEs must be explained to the patient.

**Mastectomy**

Patient selection and management:

- Multiple lesions or widespread DCIS (see section on DCIS)
- Inflammatory cancer
- Size of breast would give unacceptable cosmetic result with conservation surgery and not suitable for partial reconstruction
- Recurrence after breast conservation and RT
- Patient refuses breast RT
- Contraindication for RT such as previous RT (Mantle field)
- Patient choice

**Axillary Management**

The aim of axillary management is two-fold:

- To provide staging information
- Therapeutic (in high volume axillary disease)

At the time of diagnostic evaluation of a suspected breast lesion, the axilla should be examined ultrasonographically and any equivocal or suspicious nodes (for metastatic involvement) should be assessed by FNAC/Core biopsy.

If the FNAC contains malignant cells the axilla should be treated with ALND.

If the axilla is clear on US or FNAC a SLNB should be undertaken.

All breast cancer patients undergoing BCS/ mastectomy for invasive disease and Mastectomy for DCIS and should have staging of the axilla

Patients undergoing chemotherapy for down-staging who are clinically node negative are eligible for SN biopsy prior to or after chemotherapy. It is now generally accepted that post NACT SLNB is safe in clinically negative axilla, and there is no need for pre NACT SLNB as this delays the start of systemic therapy in usually a high-risk disease scenario. Unless selectively recommended by MDT in high-risk tumours.

Sentinel node biopsy should be performed with dual tracer technique (Radioactive isotope and Patent Blue).

Patent blue dye is avoided in cases of known allergy, multiple allergies, pregnancy and lactating patient. In cases where there is good uptake of radioisotope in axillary SLN, blue dye injection could be avoided to minimise the risk of blue dye allergy. This, however, should be explained to the patient during consenting process.

Newer techniques eg. Magtrace for SLNB can also be used potentially leading to reduction in use of patent blue dye and isotope tracers.

**Axillary Management after SLNB**

- Isolated tumour cells and micro-metastases do not require further axillary treatment.
- Macrometastases (1-2 nodes) and has had a mastectomy or WLE, they need to be offered a clearance or radiotherapy to the axilla as part of axillary management. Merits of axillary dissection or radiotherapy should be considered in individual cases in the MDT. Avoidance of further axillary management could be considered in low-risk cancers as outlined in ABS consensus statement on axillary management.
  The statement can be accessed at:
  management-of-the-malignant-axilla-in-early-breast-cancer.pdf (associationofbreastsurgery.org.uk)

  Note, at present further treatment is normally considered but as data develops and de-escalation of treatment of the axilla may be considered in the MDT for appropriate patients as per ESMO, ASCO and ESTRO guidelines.

**Management of the axilla in patients undergoing neoadjuvant chemotherapy**

- All patients should have their axilla assessed by USS at the time of diagnostic imaging and any suspicious axillary LNs should have an FNA or core biopsy.
- Any patient with positive axillary lymph nodes, pre-neoadjuvant chemotherapy, should have axillary clearance at the time of surgery (both ACOSOG 71071 and SENTINA trial show unacceptable false negative rate from SLNB in this group of patients even if clinically node negative following neoadjuvant chemotherapy).

- In clinically node negative patients, sentinel node biopsy may be performed after chemotherapy.
- Patients with negative SLNB, prior to neoadjuvant chemotherapy, do not require any further axillary surgery
- Patients who have isolated tumour cells (ITC) or micrometastasis on SLNB after neoadjuvant chemotherapy should be offered axillary dissection because of the high risk of them having further axillary disease.
- In carefully selected patients with solitary nodal involvement on US and FNA/core before NACT, SLNB can be considered. In such cases dual technique SLNB must be used and at least 3 nodes must be harvested.
- Post NACT Targeted axillary dissection (TAD) has been adopted in several centres and has potential benefit for patients who show complete radiological response from NACT. However, there is no consensus on its safety and criteria. The Clinical Reference Group (CRG) should consider participation in the ATNEC trial which offers a structured use of TAD. Evidence in relation to axillary management could be accessed at ABS MDT guideline on axillary management after NACT and Consensus Guideline of American Association of Breast surgeons respectively:

  Axillary Surgery Following Neoadjuvant Chemotherapy - Multidisciplinary Guidance From the Association of Breast Surgery, Faculty of Clinical Oncology of the Royal College of Radiologists, UK Breast Cancer Group, National Coordinating Committee for Breast Pathology and British Society of Breast Radiology

  Consensus Guideline on the Management of the Axilla in Patients With Invasive/In-Situ Breast Cancer (breastsurgeons.org)

## Reconstruction after Mastectomy

Immediate reconstruction should be discussed with all women needing mastectomy even if only to say why IBR is not appropriate.

- Stage I/II women undergoing mastectomy should be offered reconstruction – immediate or delayed, if immediate reconstruction not advisable or taken up by the patient delayed breast reconstruction should be offered.
- Skin sparing mastectomy should be the standard unless skin involvement or oncologically not safe. Nipple sparing mastectomy should be offered where oncologically safe.
- Autologous tissue transfer reconstruction should be offered to all eligible patients irrespective of whether locally available or not.
- Pre-reconstruction RT prevents use of implants/tissue expanders without tissue transfer protection.
- RT can be given to skin flaps post reconstruction including implants, but cosmetic results will deteriorate with time and risk of grade 3/4 capsular contraction is higher.
- Patients offered implant-based reconstruction should be offered information on the risks of silicone implants including BIA-ALCL.
- Smokers and medically unfit may not be suitable for tissue transfer or implant-based reconstruction and risk of failure of reconstruction should be fully explained if undertaken.
- All patients who are offered breast reconstruction should be given an opportunity to discuss their options with BCNs before making the decision.

### Axillary recurrence

- Best treated by axillary node clearance if this has not already been carried out. All such patients should be staged prior to surgery and offered appropriate systemic therapy post-surgery.

### Medically unfit patients

- Biopsy is required to confirm diagnosis and establish endocrine responsiveness.

- Primary endocrine therapy using Letrozole in postmenopausal women if endocrine responsive (Eierman W. et al Annals of Oncol vol 12 no. 11 (2001) pp 1527-1532). Tamoxifen should be used in pre-menopausal women. There is very little evidence of use of Tamoxifen solely as primary endocrine treatment in premenopausal women and appropriate ovarian ablation should be considered as adjunct.
- Surgery is best for control of local disease either wide-local excision or mastectomy and should always be considered if safe.
- Anaesthetic options may include local or regional anaesthetic with Paravertebral and pectoral block.
- Management of the axilla is individually determined according to the performance status, stage and patients' wishes.
- If inoperable and not suitable/unresponsive to endocrine treatment, consider:
    - Radiotherapy
    - Other systemic therapies as felt appropriate in MDT
    - Palliative Care

## Indications for Radiation Treatment

The standards and techniques of radiotherapy are held in the Rosemere Cancer Centre (http://lthqpradapp/QPulseDocumentService/Documents.svc/documents/active/attachment?number=CP-054). The prescribing clinician must possess the appropriate competency. Radiotherapy will be delivered according to the relevant standards. **Please see Appendix 4 for full Network guidelines (p.37-39)**

**Timing of radiotherapy and other considerations:**

Enough time between surgery and commencement of radiotherapy should be given to allow time for surgical wound healing, reasonable resolution of seroma, and/or resolution of post-operative inflammation/infection. The timing will also help to avoid radiotherapy causing surgical wound breakdown. Delay should be kept to a minimum. National guidelines for second and subsequent treatment timings will be adhered to.

Where adjuvant systemic chemotherapy is indicated, this should be undertaken first, then followed by the radiotherapy.
Radiotherapy is delivered concurrently with Hormone Therapy (HT) in ER+/PR+ disease.
Radiotherapy can be given concurrently with adjuvant Trastuzumab in Her2+ patients.
Patient(s) with a Pacemaker in situ will require assessment of the location of the Pacemaker, dosimetric analysis and liaison with the Cardiology/Pace-maker team before, during and after the course of the radiotherapy.

Heart sparing techniques will be used whenever possible.
(Techniques are referred to in document as being located in radiotherapy dept)

**Adjuvant therapy**

- Aims of treatment
    - Reduce incidence of local recurrence following breast conserving surgery
    - Reduce incidence of local recurrence of DCIS (see section on the management of DCIS)
    - Reduce incidence of local recurrence in selected patients following mastectomy
    - Increase overall survival (8-9%)

- Treatment Techniques
    - The protocols for radiotherapy administration are located in the Radiotherapy Department.
    - These include treatment guidelines, Quality Assurance and mechanistic protocols.

| Indication | Rosemere | RCR (consensus 2016) | NICE | Change | Fractionation |
|---|---|---|---|---|---|
| **DCIS** | High grade only, post WLE (Breast) | No further recommendation | Consider adjuvant XRT, discuss pros and cons | nil | 26/5#/7days |
| **WLE** | Default, all except >70yrs and <3cm, G1 or G2 (Breast) | No further recommendation | | nil | 26/5#/7days Or 27.5 in 5# fractions over 5 weeks |
| **Partial volume Breast** | Large breast (difficult anatomy) or Low risk LR (G1, 2, T1, -N0, ve margins, Ductal ca, ER +ve, Her 2 -ve) (TB + 1cm) | Exclude if lobular ca. and/or if LVSI present Consider if G1 or 2, <3cm | <3cm, G1, 2, N0, ER+ve, Her 2 -ve, >50y/o, will have endocrine therapy for 5yrs | nil | 26/5/7days |
| **IORT** | Not routinely recommended, follow NICE guidance | As per NICE | See Guidance on IORT | nil | NA |
| **No XRT** | Discuss if >70yrs and <3cm, G1 or G2 | Discuss if >70yrs and <3cm, G1 or G2 | T1N0, ER+ve, Her 2-ve, G1 or 2, >65y/o 5yrs Endocrine therapy | Reduction in age to >65y/o, see table 5 p24 NICE guidance | Discuss avoidance if >65y/o, (see table 5 p24 NICE guidance) |
| **Boost** | +ve margins, and/or <50y/o, and/or extensive DCIS (Tumour bed +1cm) | +ve margins, and/or <50y/o, and/or extensive DCIS | Offer if high risk of local recurrence | nil | 10/5/1wk 16/8/1.5 wks |
| **Mastectomy Node -ve** | +ve margins >5cm (Chest wall) | No further treatment | Consider for T3 and T4 and/or +ve margins | nil | 26/5#/7days |
| **Mastectomy 1-3 LN +ve, (any T)** | (Chest wall) | Follow trial evidence, treat if high risk and nodal areas being treated | Consider if N1 or greater | We haven't offered if <3+ve LN Discuss with patient | 40/15/3wks |

| Indication | Rosemere | RCR (consensus 2016) | NICE | Change | Fractionation |
|---|---|---|---|---|---|
| **SCF** | 4-9 +ve LN (breast/chest wall + SCF) | N0 no further treatment<br>1-2 +ve LN follow trial evidence<br>>3LN further axillary treatment recommended/ | Offer if >4 involved LN<br>Offer if 1-3 +ve LN, T3/4, G3, poor prognostic factors and PS 0/1 | No change, see comment re ANC below | 40/15/3wks |
| **Peripheral (SCF and Axilla)** | +ve sample<br>≥10 +ve LN<br><10 +ve LN, +ve margins and significant extra capsular spread (Breast/chest wall and peripheral) | As above | Do not offer after ANC, see comments below | Discuss with patient | 40/15/3wks |
| **IMC** | +ve LN (IMC plus breast/chest wall) | Consider if high risk recurrence, (e.g., T3/4 and or N2-3)<br>Consider intermediate risk (1-3 LN and central/medial disease) | Consider if LN +ve | Threshold for IMC XRT lowered; suggest wait until SUPREMO published. Until then discuss with patient | 40/15/3wks |
| **Reconstruction** | +ve margin, >5cm, >3 +ve LN, T4 | use standard fractionation | No recommendation | nil | 26/5#/7days |

Specific points for consideration abstracted from NICE guidance and RCR Consensus statements.

**NICE Guidance**

1. Use technique to minimise heart and lung dose
    a. Forward planned IMRT, DIBH on left
    b. 3 field solution not yet complete, some centres use DIBH to reduce lung on right
2. Nodal areas- do not offer if LN-ve
3. Do not offer nodal XRT after ANC
    a. In general, we would not offer XRT post ANC unless >10LN or residual disease in axilla; for individual case by case discussion

**RCR Breast Consensus statement (2016)**

**Cardiac-sparing radiotherapy should be considered the standard of care for patients with left-sided breast cancer.**

- The heart should routinely be excluded from the radiotherapy field.
- All UK radiotherapy departments should have a breath-hold technique available.

- A target mean heart dose would help departments to implement breath-hold.
- For left-breast-affected patients undergoing radiotherapy not including the internal mammary chain (IMC), >90% of patients should be treated to a mean heart dose of <2 Gray (Gy).

**Tumour bed boost**

- A tumour bed boost should be considered for all patients with invasive breast cancer who are less than 50 years old.
- Consider the benefit of a tumour bed boost for those over 50 years with higher risk pathological features (especially Grade 3 and/or extensive intraductal component).
- A hypo-fractionated boost using a similar fraction size as the whole breast is acceptable; it should be equivalent to 16 Gray (Gy) in eight fractions.

**Breast-conserving surgery and tumour bed clips**

Tumour bed clips should be considered the standard of care to improve planning (and delivery) of the boost.

**Avoidance of radiotherapy should be considered:**

Radiotherapy can be avoided in the low-risk population aged 65 and over.

In women deemed to be at very low risk of local recurrence, for example patients ≥70 years out of a research study and ≥60 years in study with T1N0 oestrogen receptor positive (ER+), progesterone receptor positive (PR+), human epidermal growth factor receptor negative (HER2-), Grade 1–2 tumours AND who are willing to take adjuvant endocrine therapy for a minimum of five years AND have regular mammograms for ten years. These criteria are best fulfilled within the UK PRIMETIME bio-marker directed study and participation is recommended.

**Internal mammary chain radiotherapy**

- Internal mammary chain (IMC) radiotherapy should be considered in patients at high risk of recurrence (that is, T4 and/or N2–3 disease).
- IMC radiotherapy should be considered in patients at intermediate risk of recurrence (that is, 1–3 axillary macro-metastases and central/medial disease, who have been recommended loco-regional irradiation).
- IMC radiotherapy should be given using techniques which minimise doses to organs-at-risk. Every centre should have a breath-hold technique available for patients undergoing IMC radiotherapy.
- The following dose constraints are recommended for IMC radiotherapy: heart $V_{17\ Gray\ (Gy)}$ <10%, ipsilateral lung $V_{17Gy}$ <35%, mean contralateral breast dose <3.5 Gy; in patients at intermediate risk of recurrence, a mean heart dose <6 Gy is considered a reasonable objective.

**Hypofractionation**

There is no indication to use more than 15 fractions for the breast, chest wall or nodal areas for standard adjuvant treatment. Five fractions is now the current national standard.

**Partial breast radiotherapy after breast-conserving surgery**

- Can be considered for patients ≥50 years, Grade 1–2, ≤3 centimetres (cm), oestrogen receptor positive (ER+), human epidermal growth factor receptor negative (HER2-), N0 with minimum 1 millimeter (mm) radial excision margins for invasive disease, using either (i) external beam radiotherapy with 40 Gray (Gy) in 15 fractions over three weeks or (ii) multi-catheter brachytherapy using fractionation schedules as per the Groupe Européen de Curiethérapie and European Society for Radiotherapy and Oncology (GEC-ESTRO) trial.
- Classical lobular cancer and/or lymphovascular space invasion should be excluded.

**Locally recurrent breast cancer**

- Exclude distant metastases.
- Resect, if possible, consider initial with hormonal therapy if endocrine responsive, chemotherapy if not, if initially unresectable.
- Post-operative radiotherapy if surgical margins close and if previous radiotherapy has not exceeded a tolerance dose.
- To treat fungating breast cancer.
- To reduce bleeding in a fungating lesion.

**Metastatic breast cancer**

- Painful bone metastases
- Spinal cord compression
- Troublesome tumour deposits (e.g. skin, nodes, choroids, for fractionation see Radiotherapy Dept Protocols)
- Brain metastases consider referral for stereotactic radiotherapy

**Angiosarcoma**

- Usually, radiation induced and occurring in irradiated volume
- Post-operative hyper fractionated radiotherapy is standard of care. However, as these are rare and infrequent a literature search reflecting the current treatment should be undertaken prior to commencement of therapy.

## Systemic Therapy for Breast Cancer

- For all patients receiving systemic therapy for breast cancer consider entry into appropriate clinical trials if available.
- All treatment decisions should be discussed at MDT.

**Neo-adjuvant (preoperative) systemic therapy**

## Neoadjuvant Chemotherapy

**Indications**

- Inoperable locally advanced (LABC) breast cancer to permit later surgery.
- Inflammatory breast cancer.
- Large tumour relative to the size of the breast to facilitate breast conserving surgery.
- To avoid delays to initiation of chemotherapy where mastectomy with immediate reconstruction is the intended surgical treatment for high-risk tumour types (i.e., HER2-positive and Triple Negative).
- Breast surgery for local control following initial chemotherapy may be appropriate for patients with limited-volume metastatic disease.
- TNBC and HER2 positive (T2N0 or T1N1)

**Patient selection**

- All patients for consideration of neo-adjuvant chemotherapy should be discussed in the breast MDT.
- Pathology from core biopsy including ER/PR and HER2 status should be available at MDT to make decision regarding neo-adjuvant treatment.
- Patients with high grade and particularly ER/PR –'ve or HER2+'ve cancers are most likely to respond favourably to neo-adjuvant chemotherapy and should largely form the subset of patients in whom this approach is offered.

**Pre-treatment assessment**

- Patients undergoing neo-adjuvant systemic treatment should have axillary U/S (+ core biopsy/ FNAC if nodes are suspicious).
- In clinically node negative patients sentinel node biopsy may be performed either before or after chemotherapy.
- A marker clip should be inserted to identify the tumour bed. This is particularly important for those patients thought likely to achieve a complete clinical response e.g., with HR –ve or smaller tumours, especially where there is no microcalcification.
- Patients undergoing neo-adjuvant chemotherapy should ordinarily be staged if the tumour is locally advanced or inflammatory (T3-4), or if there are involved lymph nodes determined by U/S and core/ FNAC.
- Axillary clips if undergoing TAD (please see section above regarding indications for TAD)

**Monitoring**

- All patients must have regular clinical review of tumour response.
- Ultrasound is the most practical imaging for on treatment tumour response monitoring.
- A mid-point ultrasound is recommended.
- The choice of imaging modality to determine treatment response should be made by the MDT on the basis of pre-treatment imaging assessment.

**Post-chemotherapy**

- The timing and plan for surgery should be discussed by the MDT following end of chemotherapy response assessment.
- Surgery should normally be performed 3-6 weeks from the final cycle of chemotherapy.

- Breast radiotherapy for local control once maximum response has been achieved, can be considered if surgery is not possible.
- Management of axilla post neoadjuvant chemotherapy is described on pages 13-14.

**Neoadjuvant regimens**

- See (neo)adjuvant algorithm summary table (**appendix II**) for details of recommended chemotherapy regimens.

## Neoadjuvant Endocrine Therapy

**Indications**

- For the down-staging of primary breast cancer to enable breast conserving surgery (usually for post-menopausal patients with low-grade and HER2 –ve tumours, or who are not suitable for chemotherapy)
- To render inoperable locally advanced disease operable or amenable to radiotherapy.
- For disease control in patients who are unfit for surgery or for who surgery needs to be delayed.
- Breast surgery for local control after a period of primary endocrine therapy may be appropriate for patients with limited-volume metastatic disease.

**Pre-treatment assessment**

- Patients undergoing neo-adjuvant systemic treatment should have axillary nodal status determined by axillary U/S (+ core biopsy/ FNAC if nodes are suspicious).
- Patients with positive axillary lymph nodes should undergo clearance at the time of definitive local surgery.
- Patients undergoing neo-adjuvant endocrine therapy should undergo staging to exclude metastatic disease where the tumour is locally advanced (T3-4) or where there is overt nodal involvement.
- The choice of imaging modality to determine treatment response should be made by the MDT on the basis of pre-treatment imaging assessment.

**Monitoring**

- All patients undergoing neo-adjuvant endocrine treatment must have regular review of tumour response and discussion in MDT regarding timing/extent of surgery (or radiotherapy).
- Ultrasound is the most practical imaging technology for on-treatment tumour response monitoring.
- Patients should be reviewed 6 weeks after starting treatment to exclude early progression and thereafter at least every 3 months.
- The optimal duration of treatment is not established. Significant response is unusual in less than 3 months. There is a significant risk of acquired resistance when the duration of treatment exceeds 12 months

**Neoadjuvant endocrine regimens**

- Letrozole 2.5mg OD for postmenopausal patients
- Tamoxifen 20mg OD FOR pre-menopausal patients (or Letrozole 2.5mg daily in combination with zoladex)
- Data supporting neoadjuvant endocrine therapy in premenopausal patients is limited.

# Adjuvant Systemic therapy

## Risk stratification and Prognostication and Prediction

- PREDICT (www.predict.nhs.uk ) is recommended to support estimates of individual prognosis and the absolute benefit of adjuvant treatment over a ten-year period.
- Nottingham Prognostic Index (NPI) may be used to estimate prognosis but does not predict treatment benefit
- Oncotype DX Recurrence Score, Prosigna or EndoPredict (EPclin score) should be requested for eligible patients for whom adjuvant chemotherapy is an option to help guide decision making. Eligible patients are those who are ER positive, HER2 negative and lymph node negative (including micrometastatic disease) if they are considered to have an intermediate risk of distant recurrence using a validated tool (PREDICT or the Nottingham Prognostic Index). (See NICE Diagnostics Guidance DG34).
- Patients with ER positive, HER2 negative and lymph node positive disease could be offered the Optima clinical trial.

# Adjuvant Chemotherapy

- Discuss chemotherapy in patients with:
  - ER negative breast cancer
  - HER2 positive breast cancer
  - ER positive breast cancer where benefit of chemotherapy in addition to endocrine therapy is estimated as >3% increase in 10-year overall survival by AoL/ PREDICT)
- For patients with ER positive, HER2 negative and lymph node negative tumours genomic testing as above provides a more accurate estimate of individual patient risk.
- Decision making should be based on risk or relapse/mortality, co-morbidity and patient preference.
- Risk of long-term complications should be considered when selecting chemotherapy regimen – e.g., limit or avoid anthracycline exposure for patients with hypertension and LV hypertrophy, use taxanes cautiously for patients with diabetes at risk of peripheral neuropathy.
- Chemotherapy should be started within 31 days of completion of surgery (NICE CG 80) and given prior to radiotherapy and endocrine therapy (if indicated.
- Advice re wigs, scarfs etc should be available to all patients before starting treatment.
- The use of PICC/Hickman lines to facilitate chemotherapy administration and reduce the risk of venous damage should be considered for all women receiving anthracycline chemotherapy, particularly Epirubicin.
- Pre-menopausal women should be given advice concerning menopause and if appropriate, the risk of infertility and should be given the opportunity of fertility preservation at or before the initial chemotherapy consultation (Urgent referral to Department of Reproductive Medicine at St Mary's Hospital, Manchester).
- Where anthracycline use is planned formal measurement of ejection fraction should be performed if there is a cardiac history or significant cardiac risk factors including age >65.
- Patients should be involved in the treatment decision and have sufficient information regarding benefits and potential toxicities (as well as written information) to make an informed choice.
- See (neo)adjuvant algorithm summary table (**appendix II**) for details of recommended chemotherapy regimens
- TCx4 (taxotere and cyclophosphamide) is an option for high-risk patients unsuitable for anthracyclines.
- Dose intensity is important and primary prophylaxis with G-CSF should be considered for all patients.

### Adjuvant HER2 targeted therapy

- See (neo)adjuvant algorithm summary table (**appendix II**) for details of recommended chemotherapy regimens.
- Patients with HER2 positive tumours (IHC 3+ or FISH positive) should be considered for adjuvant trastuzumab 3 weekly combined with chemotherapy.
- Patients with confirmed lymph node positive disease at diagnosis or following surgery should be considered for dual HER2 targeted therapy with pertuzumab and trastuzumab.
- The duration of trastuzumab (+/- pertuzumab) treatment is for 1 year (18 doses in total).
- All patients starting HER2 targeted therapy should have cardiac assessment at baseline including blood pressure and must have LVEF >50%
- Assessment of LVEF should be pre-chemotherapy, then pre-trastuzumab and then 4 monthly whilst on treatment (See **appendix I** on cardiac monitoring for trastuzumab for monitoring and management of cardiac compromise).
- An alternative trastuzumab containing regimen in patients who need to avoid anthracyclines is TCH (Taxotere, Carboplatin and trastuzumab) which has significantly less cardiac risk compared with anthracycline regimens (BCIRG 006).
- Women with T1/N0/HER-2+ cancers, or patients unfit for standard chemotherapy options should be considered for 12 weeks weekly Taxol and trastuzumab as an alternative to standard regimes.
- Patients with ER+ve early-stage breast cancer can be considered for neratinib as extended anti HER2 therapy if they have completed adjuvant trastuzumab-based therapy less than 1 year ago, trastuzumab is the only HER2 directed adjuvant treatment they have had, and if they had neoadjuvant chemotherapy-based regimens they still had residual invasive disease in the breast or axilla following the neoadjuvant treatment.
- Endocrine treatment should be offered to all women with ER positive disease; treatment should be concurrent with targeted therapy and started following completion of chemotherapy.
- Radiotherapy should be given as per guidelines but concurrent with targeted therapy.

### Chemotherapy, its administration, and side effect management

- Departmental protocols exist describing the indications and administration for all chemotherapy protocols.
- Network wide prescriptions are in use and all chemotherapy is prescribed electronically. New regimes should have a protocol drawn up as soon as possible and should be approved by the Breast Cancer Lead Clinician.
- All protocols should state the anti-emetic protocol. These are agreed centrally and if alternatives employed the reason should be stated in the notes.
- All patients should be reviewed between chemotherapy cycles by an oncologist (or appropriate nurse specialist) and toxicities assessed.

## Adjuvant Endocrine therapy

- All patients with ER-positive (defined as Allred/Quick Score ≥3) breast cancer should be offered adjuvant endocrine therapy (See summary adjuvant hormone therapy guidelines table 2019 below).
- The benefit of adjuvant endocrine therapy is not clear for patients with borderline ER positive disease.
- The duration of endocrine therapy should be at least 5 years with consideration given to extending the treatment to 10 years for women considered to have a higher risk of late relapse (whilst bearing in mind potential side effects of longer treatment).
- Patients should be advised at the start of treatment of the likely planned duration of endocrine treatment, accepting that this may change as new evidence becomes available.
- Endocrine therapy is started after chemotherapy (if given) but should be given concurrently with anti-HER2 therapy.
- Initiation of endocrine therapy should not be delayed for radiotherapy.

**Premenopausal patients**

- Tamoxifen 20 mg/day should be offered to all patients for at least 5 years.
- Aromatase inhibitors (AI) may only be used when combined with ovarian suppression.
- Ovarian suppression (OS) in addition to anti-oestrogens should be considered following chemotherapy for women with high-risk disease who either maintain or recover menses or have biochemical evidence of premenopausal state within eight months of completing chemotherapy.
- Consideration should be given to the toxicities of ovarian suppression before initiating treatment.
- OS should be combined with either tamoxifen or an AI.
- OS/AI combination may be considered in selected patients <35 yrs or at high risk of recurrence. If an AI is used extra care in monitoring bone health is required.
- If chemotherapy is indicated (but declined) consider ovarian suppression/ablation.
- OS is unlikely to benefit those with low-risk disease.
- The optimal duration of ovarian suppression is not established – durations between 2 and 5 years are effective; longer is likely to be better.
- For achieving consistent OS, only the preparations of goserelin and triptorelin for monthly administration are recommended (the three-monthly preparations are not licensed and oestradiol suppression may be less complete).

**Postmenopausal patients**

- Most post-menopausal women with ER-positive and/or PR-positive breast cancer should be considered for an aromatase inhibitor as part of their adjuvant endocrine treatment although patients with very good prognosis disease (e.g. NPI score ≤3.4 with predicted 10-year survival >93%) may be treated with tamoxifen alone.
- Available strategies include up-front AI, Tamoxifen 2-3 years then switch to AI or AI for 3-5 years in women who have completed 5 years of Tamoxifen
- The recommendation will also depend on co-morbidity (e.g. osteoporosis, history of venous thromboembolism etc) and patient preference.
- For **low risk** - node negative, low grade, HER2 negative, strong ER expression – additional AI benefit is likely to be small and side effect profile/patient preference is crucial.
- For **high risk** – larger, node positive, adverse molecular features – relative gains may be more important so include at some point.
- Women receiving AI therapy who require vaginal oestrogens for atrophic vaginitis should be treated with low-strength preparations (e.g. estriol 0.01%) and for limited duration or switched to tamoxifen with which topical oestrogens pose no risk.
- At the time of starting an AI a DEXA scan should be undertaken and the need for calcium /vitamin D supplement be assessed (see guide on page 22). The scan should be repeated according to local and national guidance once the BMD has been determined.

- **Uncertain menopausal status**
- Definition of menopause
  - Age >45 and natural amenorrhoea of at least 1 year's duration.
  - Bilateral surgical oophorectomy.
  - For amenorrhoea not fulfilling the above criteria the diagnosis of postmenopausal status should be supported by hormone measurement: FSH levels must be > 25IU/L with low oestradiol (i.e. within the locally defined postmenopausal range), in the event of doubt measure on 2 occasions preferably 4-6 weeks apart.
  - Women who have undergone hysterectomy without bilateral surgical oophorectomy and are age >60 may be considered postmenopausal.
  - Women who are peri-menopausal naturally should NOT be given AI until such time as menopause is established as defined above
  - The diagnosis of menopause in women who have undergone or are undergoing systemic anticancer treatment should be made with great caution. The likelihood of developing a chemotherapy-induced menopause increases with age and is greatest for women receiving cyclophosphamide and docetaxel-containing regimens and those >45. However ovarian function may recover up to 2 years after

completion of chemotherapy. Tamoxifen may also suppress menstruation, especially following chemotherapy.

**Adjuvant treatment with CDK4/6 inhibitors**

- Abemaciclib is indicated for high-risk disease (2 years treatment).

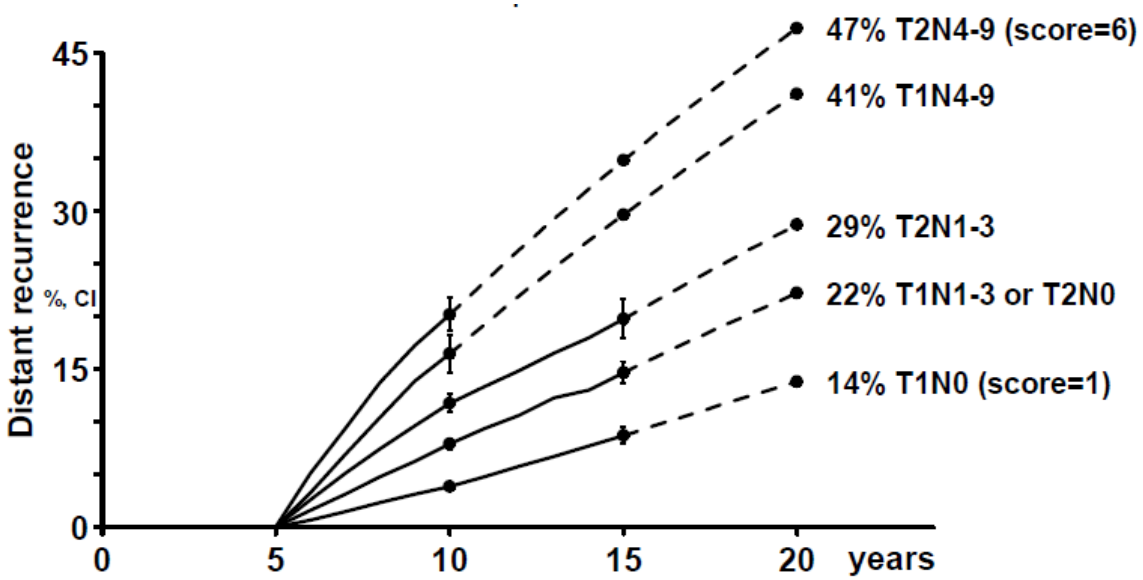
**Adjuvant bisphosphonates**

- Indicated for post-menopausal high-risk disease.

<table>
<tr><th colspan="3">Summary adjuvant hormone therapy guidelines 2019</th></tr>
<tr><td colspan="3">Premenopausal Patients</td></tr>
<tr><td>1-5 years</td><td>6-10 years</td><td>Notes</td></tr>
<tr><td>Tamoxifen<br><br>Consider OFS if high risk – see notes</td><td>Tamoxifen, or<br><br>AI (if has become post-menopausal)</td><td>- All patients should have an endocrine review at end of year 5<br>- The risks/benefits of continuing treatment should be discussed taking into account individual risks of recurrence and side effects of treatment.<br>- Pre-menopausal patients should be offered tamoxifen until menopause has been biochemically confirmed, noting the unreliability of biochemical testing in patients on or recently taking tamoxifen<br><br>OFS<br>Consider Ovarian Suppression in patients at higher risk of recurrence i.e. remaining Premenopausal post chemotherapy, lymph node positive or <35 yrs (? Grade 3)<br>Women >40 with low grade, node negative cancers are unlikely to benefit and may experience more side effects<br><br>Tamoxifen vs Exemestane<br>Exe/OFS combination may be considered in selected patients <35 yrs. or 4+ lymph nodes and at high risk of recurrence but has no proven survival benefit</td></tr>
<tr><td colspan="3">Postmenopausal Patients</td></tr>
<tr><td colspan="2">Node-Positive</td><td rowspan="2">Notes</td></tr>
<tr><td>1-5 years</td><td>6-10 years</td></tr>
<tr><td>AI or<br>Tamoxifen or<br>Sequence</td><td>AI or<br>Tamoxifen</td><td rowspan="4">AI vs Tamoxifen<br>Low risk – node negative, low grade, HER2 negative, Strong ER expression – additional AI benefit likely small and side-effect profile/patient preference is crucial<br><br>High risk – Larger, node positive, adverse molecular features – relative AI gains may be more important so include at some point<br><br>5yrs or 10yrs</td></tr>
<tr><td colspan="2">Node-Negative</td></tr>
<tr><td>1-5 years</td><td>6-10 years</td></tr>
</table>

| | | |
|---|---|---|
| AI or<br>Tamoxifen or<br>sequence | AI or<br>Tamoxifen | All patients should have an endocrine review at end of year 5. The risks/benefits of continuing treatment should be discussed taking into account individual risks of recurrence and side effects of treatment.<br>If considering additional AI beyond 5 yrs. repeat dexa scan |

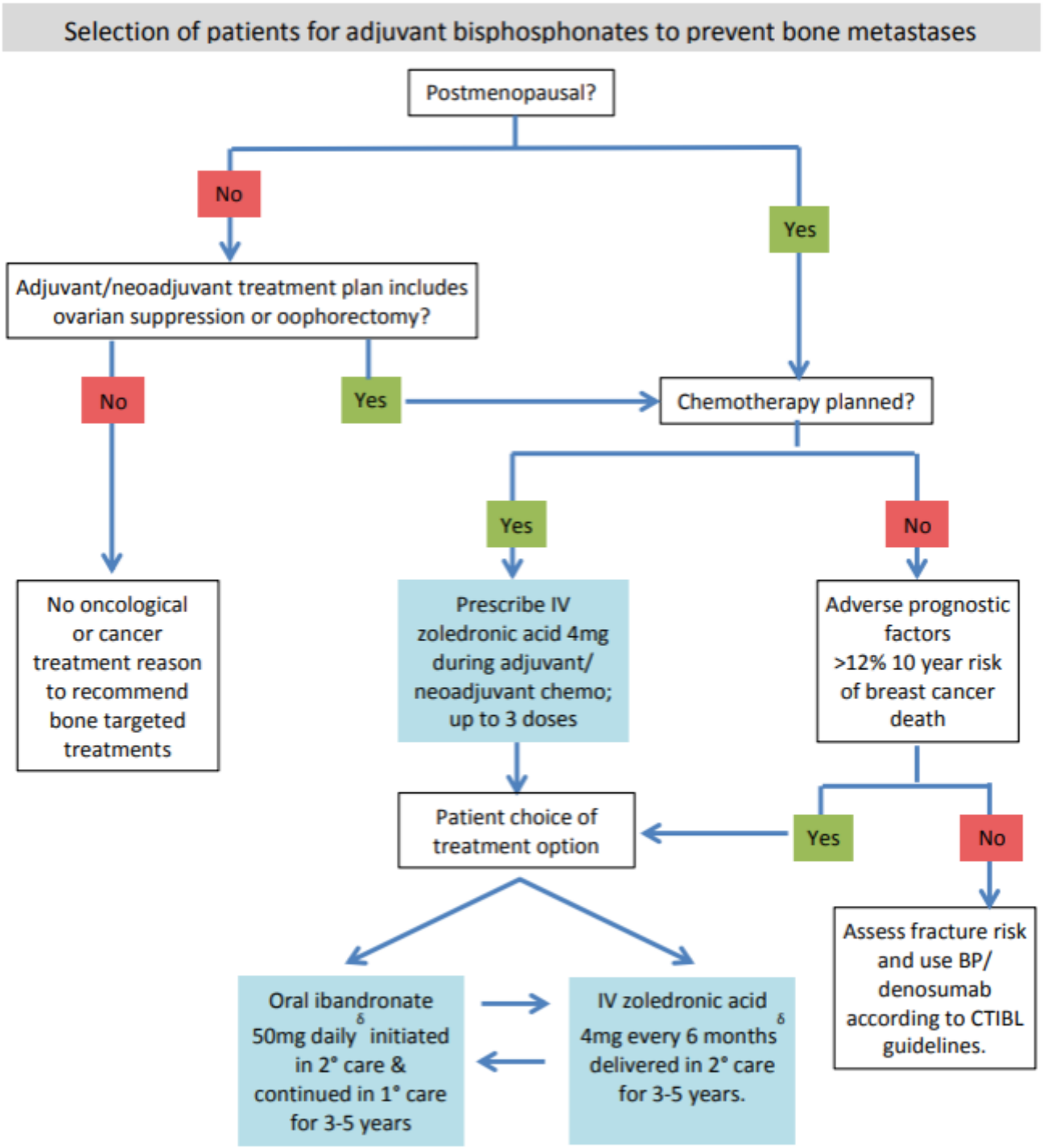
- Note - A 20-year perspective is needed on ER+ disease. Distant recurrences continue steadily into years 5–20 when stopping endocrine therapy after 5 years. Without further endocrine therapy, distant recurrence risk in years 5–20 is around 14% for T1N0 and much greater for T2N0 or N+ disease (see graph below from EBCTCG data (ASCO 2016)




**<u>Long-term</u> recurrence risks after use of endocrine therapy for only 5 years:** Relevance of breast tumour characteristics (EBCTCG ASCO 2016)

# Adjuvant Bisphosphonates and Bone Health

## Bisphosphonates




**Selection of Patients Suitable for Adjuvant Bisphosphonate Therapy to Prevent Skeletal Metastases (modified from ukbcg.org)**

- Bisphosphonates are recommended for post-menopausal women (either naturally or as a result of ovarian suppression therapy) as part of routine clinical practice to prevent skeletal metastases, regardless of breast cancer sub-type. Treatment is ineffective for pre- and peri-menopausal women.
- Offer to patients with intermediate- or high-risk breast cancer (>12% 10-year risk of breast cancer death)
- The optimal agent and schedule/ duration of administration has not been established.
- Prior to commencing adjuvant bisphosphonate therapy:
- Patients should be advised to have a dental health assessment
- Baseline vitamin D analysis (vitamin D loading if <50nmol/L followed by maintenance dose). Additional calcium supplementation if patient has a low calcium diet.

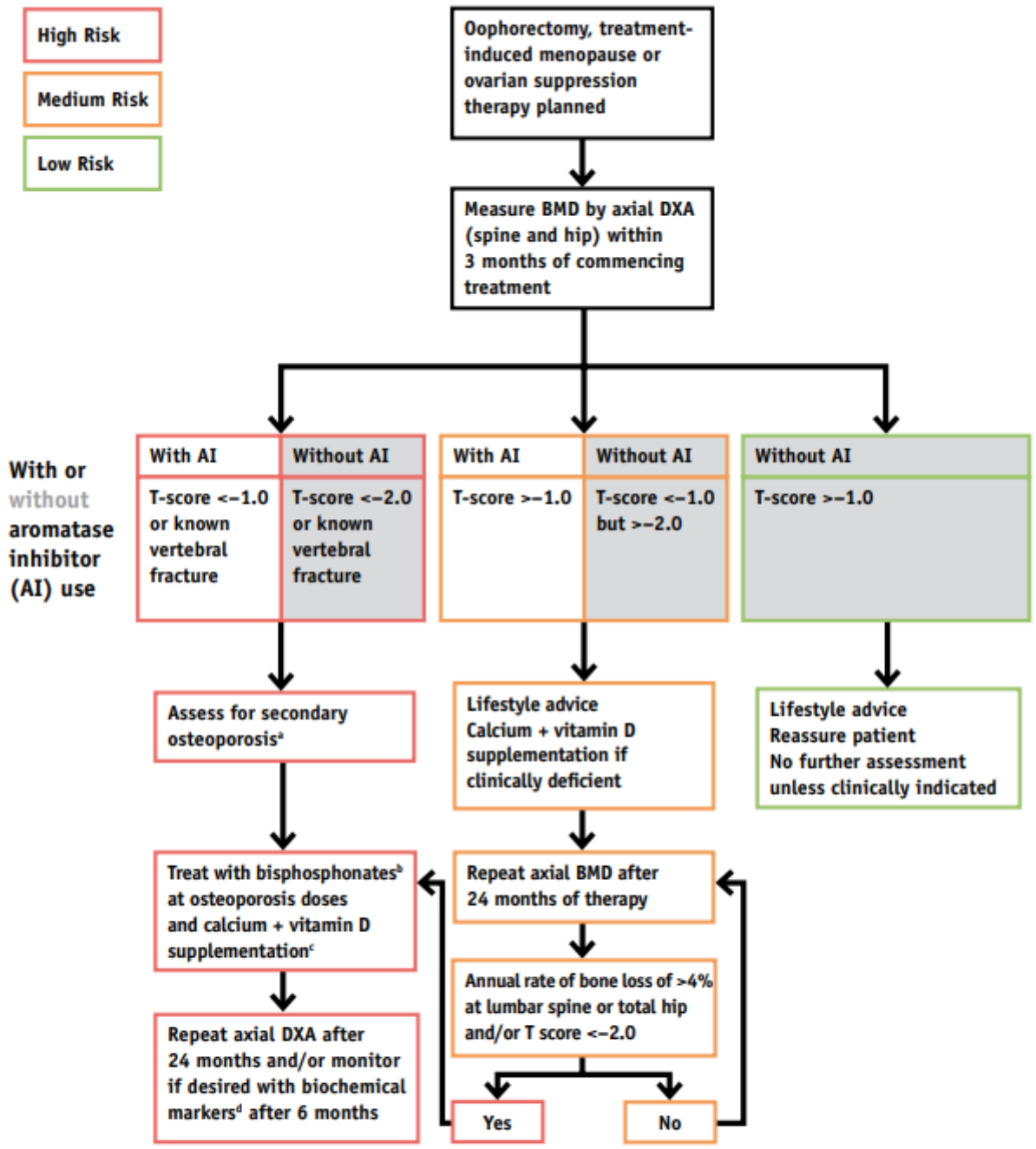
- Reference: Early Breast Cancer Trialists' Collaborative Group (2015) Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials. Lancet 386: 1353–61. doi: 10.1016/S0140-6736(15)60908-4

**Bone Health**

- After menopause a reduction in bone mineral density occurs at a rate that can be as high as 5% per year for the first 3 years reducing to about 0.5% annually.
- All aromatase inhibitors are associated with significant bone loss related to further oestrogen deprivation, and an increased risk of osteoporosis and fracture rate compared with either tamoxifen or placebo.
- Post-menopausal patients treated with an AI who are not treated with adjuvant bisphosphonates because they are at low-risk or decline treatment, or who are not treated for other reasons are at risk of accelerated bone loss and osteoporosis.
- Pre-menopausal patients who are treated with ovarian suppression are also at risk of accelerated bone loss.
- Bone health for patients treated with an AI should be managed according to the national guidelines.
- Patients starting on AI should have a baseline bone mineral density assessment within 3 months of starting an AI.
    - This result should be communicated to the patient and the GP with appropriate advice regarding management of bone health in primary care.
    - If BMD is normal then further routine assessment of BMD during adjuvant therapy is not required.
    - For patients with osteoporosis or at risk of osteoporosis, appropriate treatment should be initiated with monitoring of BMD according to the Bone Health Guidelines.
    - There are 2 algorithms to follow as shown on next two pages:

**Reference**: Reid DM, Doughty J, Eastell R, Heys SD, Howell A, McCloskey EV, Powles T, Selby P, Coleman RE. Guidance for the management of breast cancer treatment-induced bone loss: a consensus position statement from a UK Expert Group. Cancer Treat Rev 2008;34:S1–S18

**Algorithm 1:** Adjuvant treatment associated with ovarian suppression/failure with or without concomitant aromatase inhibitor use in women who experience premature menopause

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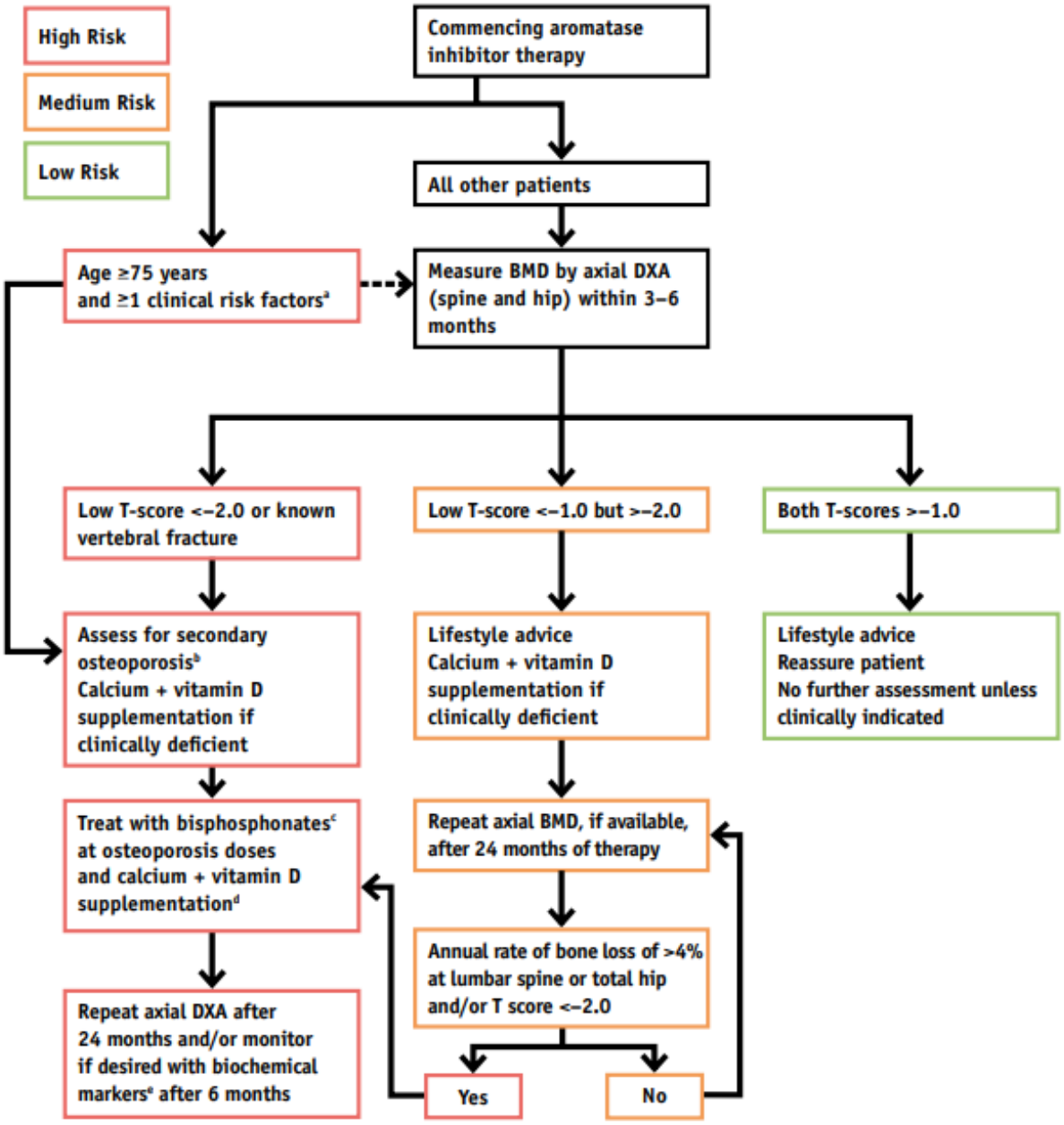
**a** ESR, FBC, bone and liver function (calcium, phosphate, alkaline phosphatase, albumin, AST / GT), serum creatinine, endomysial antibodies, serum thyroid-stimulating hormone

**b** Alendronate 70 mg per week, risedronate 35 mg per week, ibandronate (150 mg po monthly or 3 mg iv 3-monthly), zoledronic acid 4 mg iv 6-monthly

**c** To be given as ≥1 g of calcium + ≥800 IU of vitamin D

**d** Biochemical markers such as serum C-terminal telopeptide of type I collagen or urinary N-telopeptide of type I collagen

**Algorithm 2:** Postmenopausal adjuvant treatment with aromatase inhibitors




**a** Previous low-trauma fracture after age 50, parental history of hip fracture, alcohol intake of ≥4 units/day, diseases associated with secondary osteoporosis, prior corticosteroids for >6 months, low BMI (<22)

**b** ESR, FBC, bone and liver function (calcium, phosphate, alkaline phosphatase, albumin, AST / GT), serum creatinine, endomysial antibodies, serum thyroid stimulating hormone

**c** Alendronate 70 mg per week, risedronate 35 mg per week, ibandronate (150 mg po monthly or 3 mg iv 3-monthly), zoledronic acid 4 mg iv 6-monthly

**d** To be given as ≥1 g of calcium + ≥800 IU of vitamin D

**e** Biochemical markers such as serum C-terminal telopeptide of type I collagen or urinary N-telopeptide of type I collagen

## Systemic Therapy for Metastatic Disease

- Patients should have access to a Breast Care Nurse trained in the management of patients with metastatic disease.
- Early referral to supportive/palliative care team and access to benefits should be considered for all patients.
- Recruitment to relevant clinical trials should be considered if this is an option.

- Ensure ER/PR/HER2 status is known from original biopsy.
- Consider biopsy of metastasis to re-evaluate receptor status, as this may change on recurrence. Biopsy may be especially valuable where original receptor status is uncertain or unavailable, or where the disease-free interval is long. N.B. Receptor determination by immunohistochemistry on de-calcified bone biopsy is not considered reliable.

- In selecting systemic treatment consider previous treatment history, endocrine responsiveness, HER2 status, performance status, disease-free interval, disease-burden, threat from visceral disease, co-morbidity and patient preference.
- Treatment options are considered separately according to tumour receptor subtype - See metastatic breast cancer treatment algorithm (**Appendix III**).

- For ER-positive disease that is not immediately life threatening endocrine treatment should be considered as initial therapy in most cases.
- CDK4/6 inhibitors should be used alongside AI's either as first or second therapy in suitable patients.
- In situations where a faster response is desired or a response to endocrine treatment is unlikely, chemotherapy should be considered.
- In most situations serial single agent chemotherapy is preferred to multi-agent combinations.
- Consider the early use of platinum containing regimens in patients with TNBC or BRCA mutations.

- **Bone Metastasis**
- Bone prophylaxis with denosumab is recommended for all patients with bone metastases.
- Treatment is normally at 3-4 weekly intervals but may be given less frequently. Treatment should be continued indefinitely.
- Patients are advised to take regular Vitamin D/Calcium supplements.
- Denosumab is associated with a risk of osteonecrosis of the jaw (ONJ). Patients are advised to have a dental check-up and complete any required surgical treatment prior to commencing therapy.

# Appendix 1

## Monitoring of Cardiac Ejection Fraction for Patients with Breast Cancer Receiving Trastuzumab

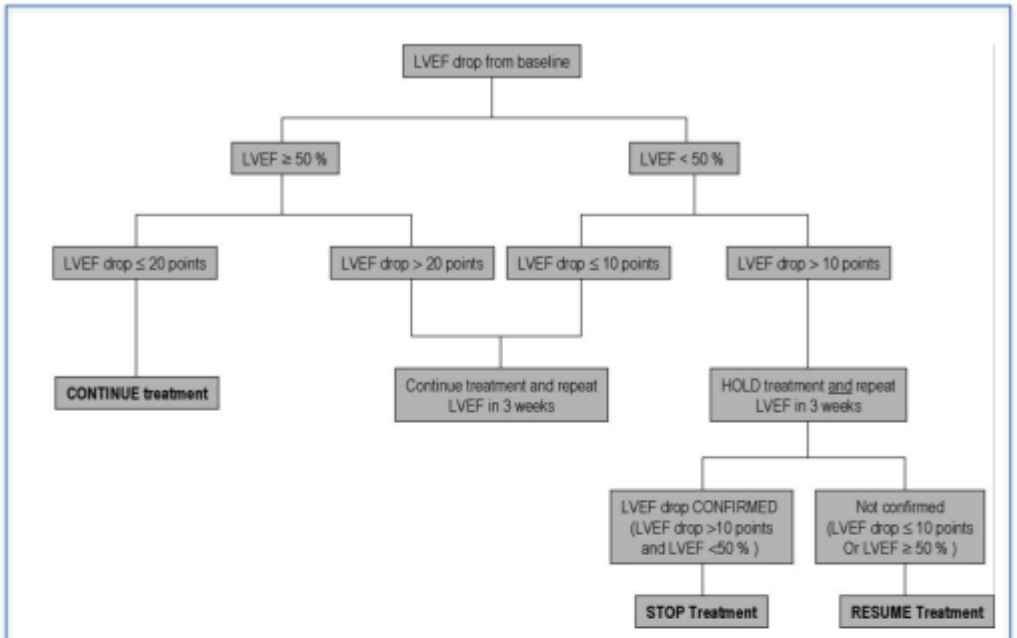



**Figure 1**. Algorithm for treating falls in LVEF while on adjuvant trastuzumab (Taken from Aphinity protocol). N.B. while the same general principles apply for metastatic disease it is not necessary to be so stringent.

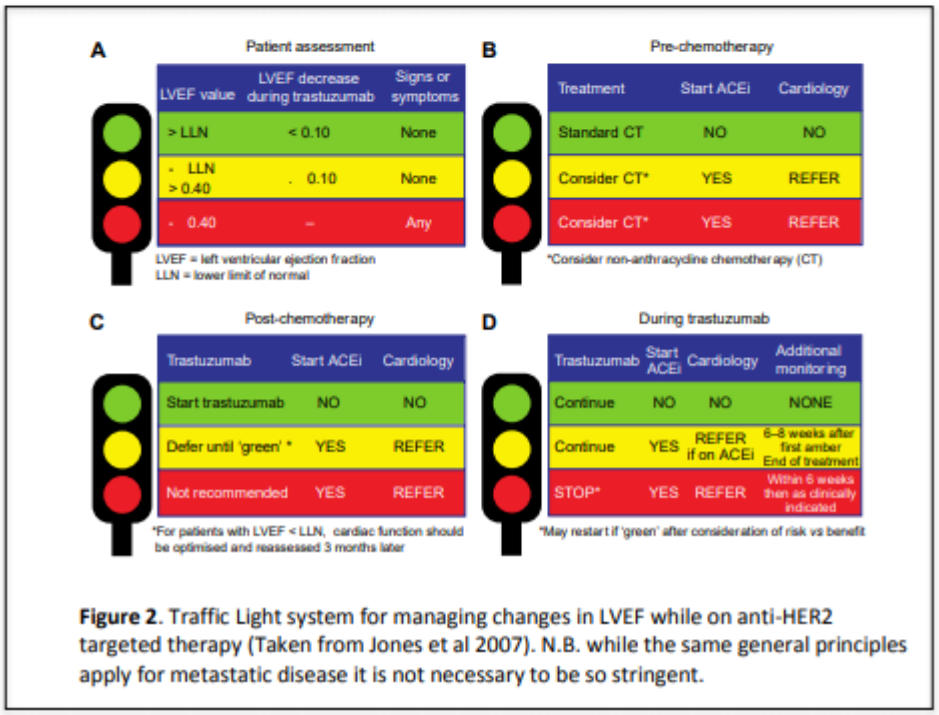



**Figure 2**. Traffic Light system for managing changes in LVEF while on anti-HER2 targeted therapy (Taken from Jones et al 2007). N.B. while the same general principles apply for metastatic disease it is not necessary to be so stringent.

**Figure taken from London Cancer Breast systemic treatment guidelines, Aug 2017**

- All patients require a baseline MUGA or Echo and a cardiovascular assessment.
- If a patient's blood pressure is >145/85 mmHg for a sustained period (>3 measurements over time) then an ACEi should be initiated.

- Patients should have assessment of ejection fraction pre trastuzumab.
- Assessment should be repeated every 4 months.

**Starting ACEi and Beta blockers**

- Start an ACEi first followed by a Beta blocker a few days after
- Start both at the lowest doses possible then titrate up to target doses (see box)
- Double doses at not less than two weekly intervals

| Starting dose | Target dose |
|---|---|
| **ACEi** | |
| **Enalapril 2.5mg BD** | **10-20mg BD** |
| **Lisinopril 2.5mg OD** | **30-35mg OD** |
| **Ramipril 2.5mg OD** | **5-10mg OD** |
| **Beta blockers** | |
| **Bisoprolol 1.25mg OD** | **10mg OD** |
| **Cavedilol 3.125mg BD** | **25-50mg BD** |
| **Metoprolol CR/XL 12.5-25mg OD** | **200mg OD** |

**OD=once daily, BD twice daily, TDS three times**

**Guidelines on initiation of ACEi treatment**

- High risk patients need very close monitoring – these include patients with:
  - Severe heart failure - e.g., on high dose diuretic therapy which cannot be discontinued, or large doses of vasodilators
  - dehydration - hypotension (systolic BP less than 90 mmHg)
  - substantial renal impairment (e.g., creatinine over 300 micromol/l)

- Monitoring of U&Es is recommended as table:
- Advise patient regarding dizziness in the first few days of treatment and cough

| Week | Low risk | High risk |
|---|---|---|
| 1 | No monitoring | Check blood and BP at 4 days |
| 2 | Check blood and BP between 7-10 days | Check blood and BP at 10 days |
| 3 | Increase dose if required | Increase dose if required |
| 4 | Check bloods when at full dose of ACEi | Check blood if dose of ACEi increased |

**Guidelines on initiation of Beta Blocker treatment**

- Start 48 hours following ACEi if patient has tolerated the ACEi – if ACEi not initially well tolerated wait 1 week then commence Beta blocker
- Caution using in asthma, patients with heart rate <60 and systolic BP <90, patients with heart block
- Stop diltiazem/verapamil if patient already taking
- Monitor HR, BP
- Check blood biochemistry 1-2 weeks after initiation and 1-2 weeks after final dose titration

- If patient develops fatigue or marked bradycardia <50 beats per min then halve beta blocker

## References


Jones AL, Barlow M, Barrett-Lee PJ, Canney PA, Gilmour IM, Robb SD, Plummer CJ, Wardley AM, Verrill MW. Management of cardiac health in trastuzumab-treated patients with breast cancer: updated United Kingdom National Cancer Research Institute recommendations for monitoring. Br J Cancer. 2009 Mar 10;100(5):684-92

McMurray J, Cohen-Solal A, Dietz R, Eichhorn E, Erhardt L, Hobbs FD, Krum H, Maggioni A, McKelvie RS, Piña IL, Soler-Soler J, Swedberg K. Practical recommendations for the use of ACE inhibitors, beta-blockers and spironolactone in heart failure: putting guidelines into practice. Eur J Heart Fail. 2005 Aug;7(5):710-21.

National Clinical Guideline Centre. (2010) Chronic heart failure: the management of chronic heart failure in adults in primary and secondary care. London: National Clinical Guideline Centre. Available from: http://guidance.nice.org.uk/CG108/Guidance/pdf/English

# Appendix 2

**(Neo)-adjuvant Chemotherapy Treatment Algorithm**

## (Neo-)Adjuvant Chemotherapy in Early Stage Breast Cancer

NHS Lancashire and South Cumbria Integrated Care Board | Cancer Alliance

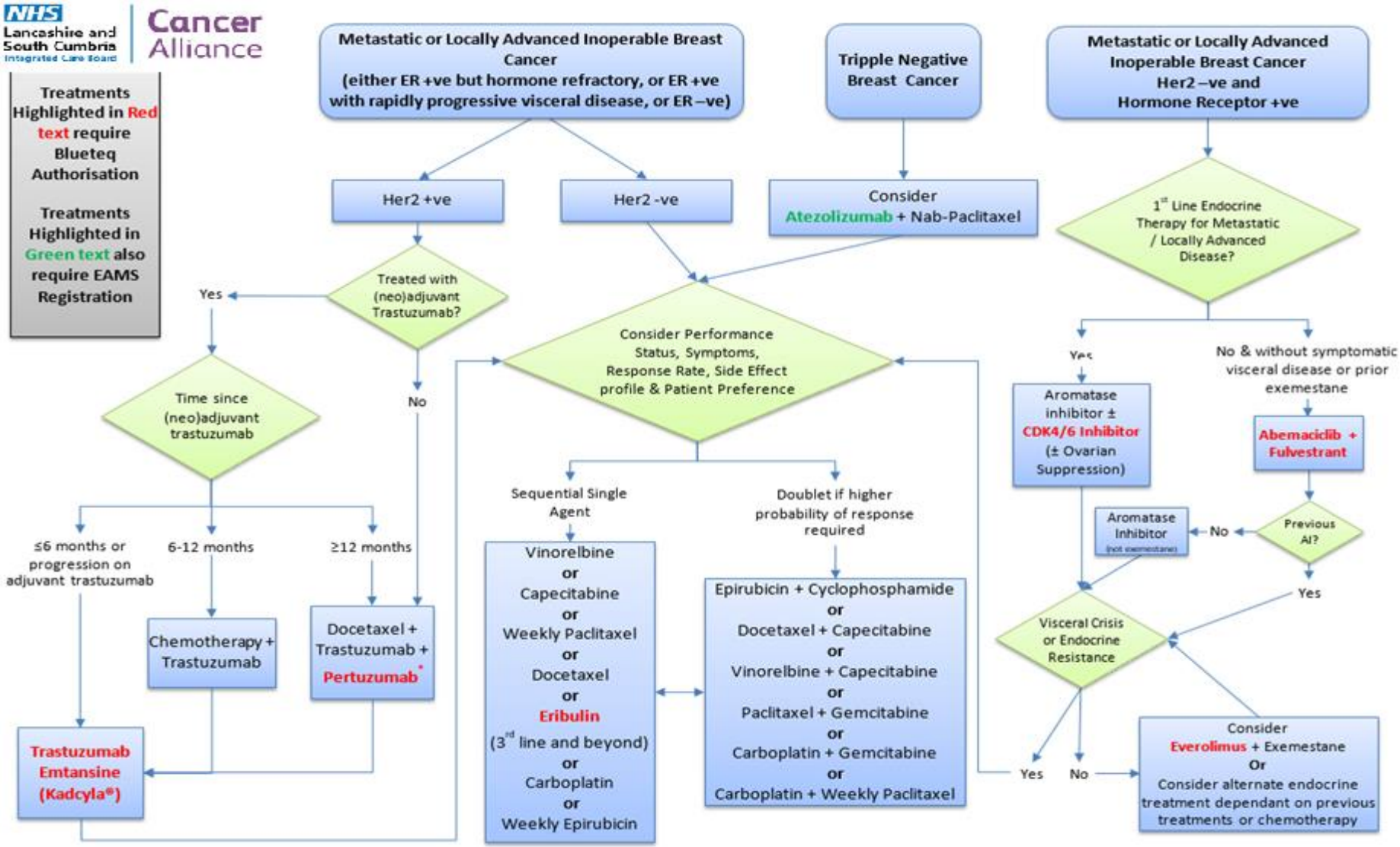
| | Node –ve | | Node +ve or high risk node –ve | | Triple Negative Consider: |
|---|---|---|---|---|---|
| | Her2 -ve | Her2 +ve | Her2 -ve | Her2 +ve | |
| **Neo-adjuvant** | AC (dose dense) - Weekly Paclitaxel × 12 weeks **OR** $EC_{100}$-T* | Docetaxel* + Carboplatin + Trastuzumab + **Pertuzumab**** (TCHP) **OR** $EC_{100}$-T*HP** | AC (dose dense)- Weekly Paclitaxel × 12 weeks **OR** $EC_{100}$-T* | Docetaxel* + Carboplatin + Trastuzumab + **Pertuzumab** (TCHP) **OR** $EC_{100}$-T*HP | 3 Weekly Carboplatin + Weekly Paclitaxel × 12 weeks **followed by:** AC(dose dense) × 4 cycles **OR** $EC_{100}$ × 3 cycles |
| **Adjuvant** | $EC_{100}$-T* **OR** TC × 4 cycles | $EC_{100}$-T*H **OR** Weekly Paclitaxel × 12 weeks + Trastuzumab **OR** Docetaxel + Carboplatin + Trastuzumab (TCH) | AC (dose dense) - Weekly Paclitaxel × 12 weeks **OR** $FEC_{100}$-T* | $EC_{100}$-T*PH **OR** Docetaxel + Carboplatin + Trastuzumab + **Pertuzumab** (TCHP) | AC (dose dense) - Weekly Paclitaxel × 12 weeks **OR** $EC_{100}$-T* |
| **Contraindication to anthracycline or patient unsuitable for sequential anthracycline-taxane chemotherapy (neo-adjuvant or adjuvant)** | Docetaxel + Cyclophosphamide × 4 cycles | Docetaxel + Carboplatin + Trastuzumab (TCH) (if neo-adjuvant add **Pertuzumab**) **OR** Weekly Paclitaxel × 12 weeks + Trastuzumab | Docetaxel + Cyclophosphamide × 4 cycles | Docetaxel* + Carboplatin + Trastuzumab + **Pertuzumab** (TCHP) **OR** Weekly Paclitaxel × 12 weeks + Trastuzumab | Docetaxel + Cyclophosphamide × 4 cycles |
| **Plus for:** **Postmenopausal women or Premenopausal women with a medical menopause.** **AND** **Patients with sufficient risk of relapse to benefit from this adjuvant treatment (consider in all node positive, ER negative and /or HER2 positive as well as high risk ER positive)** | Adjuvant Zoledronic acid 6 monthly x 3 years | | | | |

*Docetaxel may be substituted with Weekly Paclitaxel to cover the same treatment period. **Pertuzumab only if tumour is >=2cm if node negative disease.

**Treatments Highlighted in Red text require Blueteq Authorisation**

# Appendix 3

## Metastatic Breast Cancer Treatment Algorithm



# Appendix 4

**Network Guidelines for Breast Radiotherapy**

*These Network guidelines follow the RCR's current published guidance for breast radiotherapy [1, 7]. Entry into clinical trials should be considered where available.*

**Indications.**

Radiotherapy is given to the whole breast after breast conserving surgery for invasive breast cancer and DCIS with higher risk of local recurrence.

Partial breast radiotherapy may be considered in patients ≥50 years old with ≤3 cm N0, ER positive HER2 negative, ductal tumours with clear margins.

Radiotherapy to the breast may be omitted in patients with invasive breast cancer deemed at very low risk of local recurrence, e.g. patients ≥65 with G1-2 T1N0, ER positive HER2 negative, ductal cancers who are willing to take adjuvant endocrine therapy and have annual mammography for a minimum of 5 years.

Radiotherapy to the breast may be omitted in patients after excision of DCIS considered low risk of recurrence, for example low/intermediate tumours less than 15 mm with clear margins in postmenopausal women. Decision making tools such as the VNPI [2] may be useful.

Post-mastectomy chest wall radiotherapy is indicated for ≥ 4 involved axillary nodes, ≥T3 tumours (> 5 cm), involved excision margins; and in the presence of 2 or more relative indications: 1-3 nodes, grade 3, lymphovascular invasion.

Management of a positive sentinel node biopsy (*NB 'axillary treatment' = radiotherapy or surgery)*

Isolated tumour cells, micrometastases: no axillary treatment

1-2 positive macrometastases: axillary treatment is not mandatory in some patients with lower risk disease, e.g., postmenopausal, G1-2 T1, ER positive HER2 negative. Encourage entry into clinical trials, e.g., POSNOC [3].

≥3 nodes should have further axillary treatment.

Supraclavicular fossa is usually irradiated if ≥4 axillary nodes are positive. Consider SCF radiotherapy if 1-3 nodes are positive with other poor prognostic factors, e.g., G3, triple negative phenotype, lymphovascular space invasion.

SCF and chest wall usually irradiated following neoadjuvant chemotherapy for inflammatory or locally advanced breast cancer

Internal mammary chain radiotherapy should be considered in patients with high risk of recurrence, e.g. T4 and/or and N2/3 disease or in patients with intermediate risk of recurrence, e.g. 1-3 axillary macrometastases with central/medial disease

Tumour bed boost should be offered in all patients ≤50 years old. Should also be offered in patients over 50 years of age with additional risk factors of local recurrence (grade III and/or extensive intraductal component. positive margins where further excision deemed impossible

Radiotherapy to axilla after neoadjuvant chemotherapy for patients presenting with cN1 disease.

As per multi-institutional guidelines [4] for patients presenting with cN1 disease who undergo an SLNB post NACT (four nodes removed with dual mapping), axillary radiotherapy can be offered for those who achieve pCR within the nodes after discussion in MDT. Consider entry into the ATNEC study [4].

If SNLB shows isolated tumours cells, micrometastases or macrometastases, offer axillary treatment.

**Radiotherapy technique**

Localisation as per local guidelines, radiopaque markers on lateral and medial reference points. CT dataset acquired.

Virtually simulated, isocentric, coplanar back-edge aligned tangential fields. A cardiac sparing technique, e.g., deep inspiration breath hold should be used for all left-sided treatments.

Radiotherapy planning with inverse planned IMRT using 6 and 10 MV photon beams.

CTV is whole breast volume enclosed by the tangential fields excluding 5 mm from the skin and lung. PTV = CTV +1 cm.

Partial breast radiotherapy CTV is the tumour bed +15 mm excluding 5 mm from skin and long. PTV =CTV +1 cm. The whole breast tangents are reduced to cover PTV by 1 cm superiorly/inferiorly.

Critical structures: heart (mean dose to heart <2Gy), ipsilateral lung (e.g. V18 < 15%, mean dose <6Gy), contralateral lung receiving 2.5Gy should be <10%, mean doss to contralateral breast should be <1.5Gy.

Dose and fractionation
Prescribed as per local protocol, e.g., 100% to the middle of breast/chest wall/partial breast volume, or to 100% isodose. Hotspots should be below 107% and 90-95% isodose should cover breast.

Radical adjuvant doses:

26 Gy/5f/7d for all patients not requiring tumour bed boost or nodal radiotherapy. [6,7]

40 Gy/15 f/21 days to breast and nodes. Consider for chest wall after immediate reconstruction. [7]

28.5/5f / 5 weeks [8] for patients with significant co-morbidity and/or frailty that makes daily radiotherapy difficult.

40 Gy/15 f/21 days with sequential boost, for example 10Gy/5f, or 12Gy/4f.

48Gy/15f/21 days simultaneous integrated boost

Palliative dose:

30-36Gy/5-6f/5-6 weeks

Imaging is with cone beam CT and/or kV imaging depending on fractionation, clinical scenario, (e.g. breast swelling) etc. See local protocol.

**References**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3. http://www.posnoc.co.uk/
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5. https://warwick.ac.uk/fac/sci/med/research/ctu/trials/atnec
6. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. Brunt et al. The Lancet, May 2020. Vol 395, issue 10237, P1613-1626
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## Appendix 5

### Treatment Summary

# Treatment Summary for Patients Diagnosed with Breast Cancer

**Patient Name**
**Patient Address**

**Hospital Name**
**Hospital Address**

**Date of Birth: 00/00/0000**
**Hospital No: 01234567**
**NHS No: 999 999 9999**

Dear ***[INSERT PATIENT NAME]***
Please find below the summary of your diagnosis, treatment and the ongoing management plan that we discussed. A copy of this has also been sent to your GP. Everyone's management plan is different, as it is based on their diagnosis and treatment. This plan is specific to your needs.
At East Lancashire Hospitals NHS Trust Breast Cancer Unit, our Treatment Summary has been designed to increase your knowledge and wellbeing and to help you move forward now that your initial treatment has finished. Please remember that if you do feel anxious or would like further advice at any time you are welcome to contact your Breast Care Nurse who can recommend a wide range of resources and services that have been designed to help you.

**Key Contact Numbers:**

| | |
|---|---|
| **Breast Care Nurse** | **Name:**<br>**Contact Number:** |
| **Breast Cancer Support Worker** | **Name:** **Contact Number:** |
| | |

**Diagnosis and Treatment to Date:**

| | | | |
|---|---|---|---|
| **Diagnosis:** | *Please give full details* | **Date of Diagnosis**: | |
| **Histology:** | | | |
| **Summary of Treatment and relevant dates:** | | | |
| *Please be specific and give full details, avoiding jargon.* | | | |
| **Treatment aim:** | | | |

**Further Treatment and Management [Delete AS APPROPRIATE]**

| | |
|---|---|
| **Further Treatment** | |
| Radiotherapy | Leaflet given ☐ |
| Chemotherapy | Leaflet given ☐ |
| Hormone therapy (endocrine) | Leaflet given ☐ |
| Herceptin | Leaflet given ☐ |
| Bisphosphonates | Leaflet given ☐ |
| **Further Management** | |

You will be called for a mammogram every year for 5 years following diagnosis.
If after 5 years, you are still under the age of 50, you will continue to have annual mammograms until your 50th birthday. ☐
(Please note: If you have had bilateral mastectomies, you will not have annual mammogram surveillance)

Bone density (DEXA) scan **[PLEASE ADD DETAILS]** ☐

If you have any concerns about breast symptoms between mammograms it is important that you contact your Breast Care Nurse.

## Possible Side Effects from the treatment(s) you have had

Some side effects can improve quickly, however some, such as fatigue, may take longer to improve. **If you are struggling to cope with side effects, or if the side effects are getting worse rather than better, please contact your Breast Care Nurse for advice.**

**[DELETE IF NOT APPROPRIATE]**

### Possible side-effects from surgery

- Changes in the look and feel of the breast, chest wall or armpit due to scarring from surgery.
- Numbness and/or long-term pain/discomfort around the site of surgery and upper arm.
- Swelling/Fluid build-up in the arm, hand or breast (lymphoedema) - please contact your Breast Care Nurse if this occurs so that they can arrange further assessment.

### Possible side-effects from endocrine treatment

- Hot flushes.
- Aches and pains in joints.
- Feeling of tiredness or exhaustion (fatigue).
- Mood swings.
- Reduced libido (sex drive) and vaginal dryness.

### Possible side-effects from radiotherapy

- Changes in the appearance of the breast, skin or nipple.
- Tiny visible blood vessels on the skin surface (often called ‘spider veins’ or ‘telangiectasia’).
- Long-term pain or discomfort of the breast or chest wall.
- Swelling/fluid build-up in the arm, hand or breast (lymphoedema) – please contact your Breast Care Nurse if this occurs so that they can arrange further assessment.
- Feeling of tiredness or exhaustion (fatigue).

### Possible side-effects from Herceptin

- Feeling of tiredness or exhaustion (fatigue).
- Joint and muscle pains.
- Flu-like symptoms.
- Heart problems – your heart will be carefully monitored whilst taking Herceptin.

Your Herceptin Team will give further advice and details and address any issues at your appointment: **[ADD CONTACT DETAILS].**

### Possible side-effects from chemotherapy

- Feeling of tiredness or exhaustion (fatigue) (may persist for several months after chemotherapy).
- Difficulty with concentration and memory (may persist for 1-2 years after treatment).
- Tingling, numbness or pain in fingers and toes (known as ‘peripheral neuropathy’).
- Increased risk of early menopause or infertility.
- Rare risk of developing second cancers.

**Possible Immediate effects from Bisphosphonates**

- Feeling of tiredness or exhaustion (fatigue).
- Flu-like symptoms.
- Poor blood supply to the jaw (Osteonecrosis). This is a rare side effect. If you have persistent jaw pain, loose teeth, swelling, redness or ulcers on the gums you should inform your Breast Care Nurse and see your dentist urgently.
- Thigh bone (femoral) fracture. This is a rare side effect. If you have persistent pain in your thigh, hip or groin, you should inform your Breast Care Nurse.

**Although a common side effect there are also steps you can take to reduce the risk of developing lymphoedema. Your Breast Care Nurse can explain these and provide you with further information.**

**Additional information relating to lifestyle and support needs:**

**What can be done to reduce the risk of breast cancer returning?**

- **Taking medication as advised**
- **Regular physical activity**
- **Maintaining a healthy weight**
- **Reducing alcohol intake**
- **Stopping smoking**

**Your Breast Care Nurse can give you details of support with any of the above**.

**National Breast Screening Programme**

Once you have completed your breast cancer follow up (usually 5 years of annual mammograms) you should continue to have mammograms every 3 years:

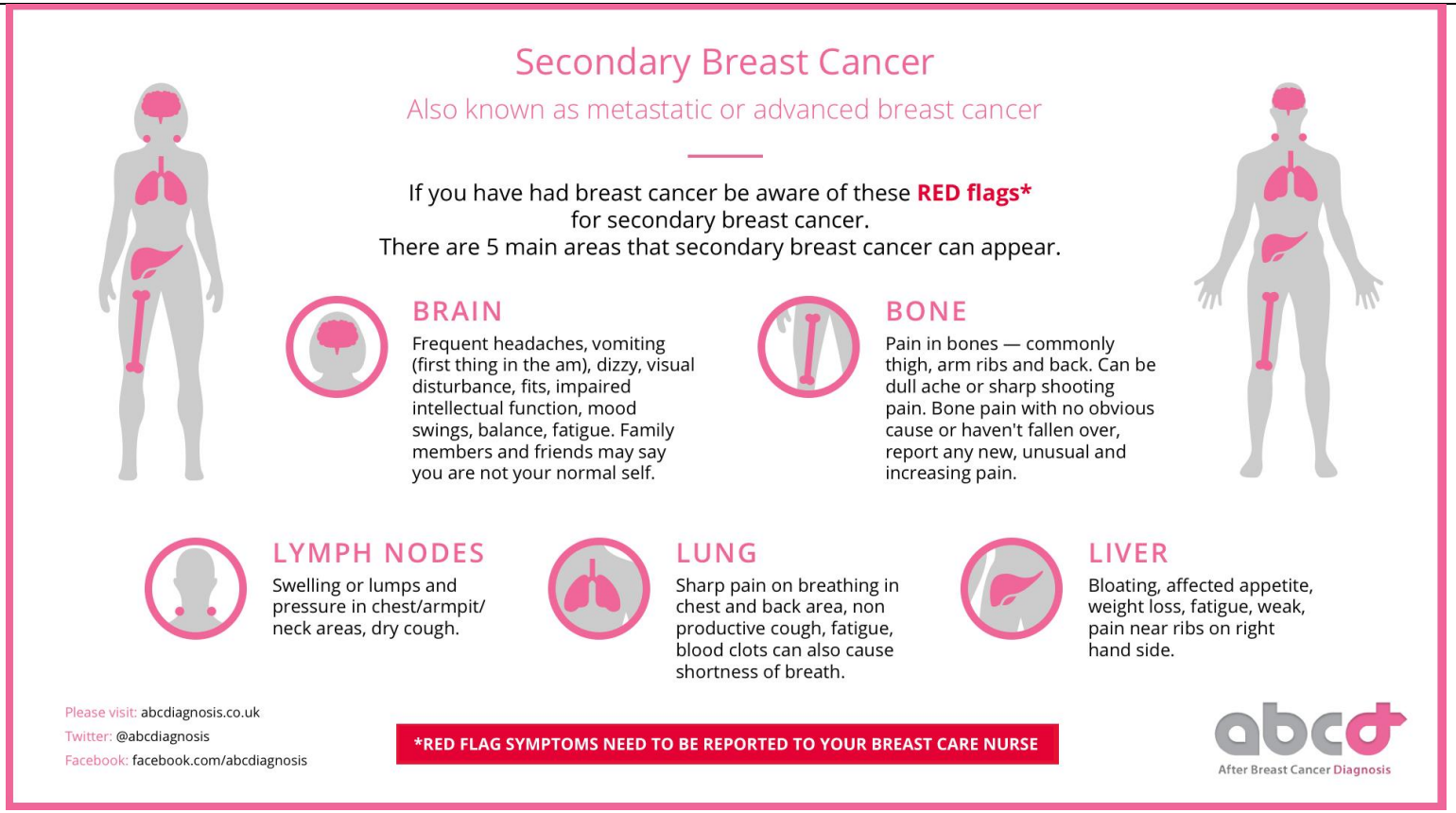
- The national breast screening programme invites women aged 50-70 for a mammogram every 3 years.
- If you are under 50 at the end of your cancer follow-up you will continue to have mammograms with your breast cancer team until you reach the age of 50 and then join the national breast screening programme.
- If you have been told you are a gene carrier you will join the national breast screening programme at the end of your breast cancer follow-up, regardless of your age.
- If you have had both breasts removed (a bilateral mastectomy} and are invited for breast screening, ask your breast screening unit for an opt-out letter or your GP can write to the Breast Screening Unit to inform them you do not require screening.
- If you are over the age of 70 yrs, you can self-refer for mammogram surveillance every 3 years.

## Symptoms of possible recurrence that will require investigation

Recurrence is uncommon but occasionally breast cancer can return in the breast, chest wall or armpit (**local recurrence**) or in a different part of the body (**secondary breast cancer**).

**If you notice any new lumps in your breast (either side), armpit, or mastectomy scar, or new changes to the breast shape, skin or nipple, it is important that you contact your Breast Care Nurse to arrange assessment.**

The image below shows the possible symptoms of secondary breast cancer. If you experience these symptoms, with no obvious other cause (e.g. a common cold, a back injury etc) they need to be reported to your Breast Care Nurse.




For additional information please visit abcdiagnosis.co.uk.

**Other Useful Contact Numbers:** ***[DELETE AS APPROPRIATE]***

| | |
|---|---|
| Surgical Secretary | ***[INSERT CONTACT DETAILS]*** |
| Prosthetic Nurse | ***[INSERT CONTACT DETAILS]*** |
| Herceptin Team | ***[INSERT CONTACT DETAILS]*** |
| Bisphosphonates Team | ***[INSERT CONTACT DETAILS]*** |
| Psychologist | ***[INSERT CONTACT DETAILS]*** |
| Other ***[INSERT DETAILS]*** | ***[INSERT CONTACT DETAILS]*** |
| Other ***[INSERT DETAILS]*** | ***[INSERT CONTACT DETAILS]*** |

| **Treatment Summary Completed by:** | |
|---|---|
| Copy sent to GP: | □ |
| Copy sent to Consultant: | □ |
| Copy sent to other Health Care Professional(s): | **[INSERT DETAILS]** |

**Suggested actions for GP include duration of Endocrine Therapy, Bone Health management etc.**

## Follow-up arrangements

### Early-Stage Disease (low/intermediate/high risk)

- Asymptomatic breast cancer patients will be followed up by a surgical team (when adjuvant chemotherapy and radiotherapy are completed). This should now be in the context of Stratified Follow up triggered by patients. All such patient should be offered education in supported self-management, this should be either face to face or virtual.

- There is no evidence-based guidance regarding the timing or frequency of review visits, so no recommendation is made here. Pragmatically, there should be availability of appointments for patients when problems arise.

- Routine follow up may be undertaken by any appropriately skilled professional group surgeon, oncologist, breast care nurse, Advanced Clinical Practitioner only in appropriate settings such as reconstruction, primary endocrine treatments, ongoing issues, part of clinical trials

- The Surgeon or their deputy in the surgical follow-up clinic, will be responsible for requesting and organising follow-up for imaging surveillance which remains the key for surveillance.

- At the end of primary treatment, the patient and specialist should agree a written care plan. Please see Appendix 5 for a Treatment summary template. Patients should have a contact number for the specialist breast cancer nurse whom they can contact for advice. If following a patient enquiry, it is felt that patient should be referred for an outpatient consultation, the breast cancer nurse will make the appropriate arrangements, either for referral to a nurse-led, surgical or oncology clinic. For advice out of hours, patients are advised to contact their GP or NHS direct.

- NICE guidance enables the patient to choose preferred follow up whether in primary or secondary care.

- Mammographic follow up is annually for 5 years or until reaching screening age if too young for screening at 5 years. Exceptions to this include patients enrolled on trials i.e. Primetime.

- B3 lesions should be managed as per the NHS Breast Screening multidisciplinary working group guidelines for the diagnosis and management of breast lesions of uncertain malignant potential on core biopsy (B3 lesions)
  NHS Breast Screening multidisciplinary working group guidelines for the diagnosis and management of breast lesions of uncertain malignant potential on core biopsy (B3 lesions) (associationofbreastsurgery.org.uk)

- Local protocols should be agreed for recall arrangements and access to specialist clinics following discharge from clinical surveillance.

Open access should be encouraged

### Locally advanced and metastatic disease

- Follow up by medical team (clinical or medical oncology).

- Close co-operation with the palliative care team is often necessary especially for patients with metastatic disease and transfer of care may be appropriate.

- Assessment and discussion of patients' needs for physical, psychological, social, spiritual and financial support should be undertaken at key points (such as diagnosis, at commencement, during and at the end of treatment; at relapses; and when death is approaching).
  (NICE guidance September 2013)

- Mechanisms should be developed to promote continuity of care, which might include the nomination of a person to take on the role of 'key worker' for individual patients.
  (NICE guidance September 2013)

- Patients with symptoms of adjustment disorder, anxiety, or depression, should be referred for psychological interventions and possibly for psychiatric assessment and treatment.

**Patient Led Follow-Up (PLFU)**

Patients who are eligible for PLFU, according to the guidelines, will be entered into the programme. They will be offered either a face-to-face education day or online resources which is then followed by annual mammograms with or without a questionnaire. In addition, there is access to OSC/Rapid Access Clinic via the Breast Care Nurses, Cancer Support Worker, and ACP's.

Patients who are not suitable for Patient Led Follow-Up are followed up in the traditional ways mentioned above.

To continue to develop a safe/robust digital surveillance (welLPRES) and help shape the patient portal to enable equity of access to health needs and health and wellbeing information.

**Survivorship**

There have been significant improvements in breast cancer survival rates in the UK over the past two decades, with over two thirds of women diagnosed now surviving for more than 20 years (CRUK 2014).

As cancer survival rates increase, research has focused on the effect of diagnosis and treatment on individuals' quality of life after completion of treatment and its ongoing consequences (Sherman *et al* 2012).

The Cancer Reform Strategy (Department of Health (DH) 2007) and Improving Outcomes in Cancer Strategy (DH 2011) proposed the need to re-consider how care is delivered for individuals living with and beyond the disease.

A number of alternative measures are being or have been developed for patients after treatment for early breast cancer (Tsianakas *et al* 2012).

## Guidelines for Patients with a Family History of Breast Cancer

- Each cancer unit should have access to a nurse led breast cancer family history assessment clinic.
- On receipt of a referral a questionnaire will be sent out alongside standard written information as outlined in NICE guidance and a clinic appointment arranged unless low risk (these patients may be discharged by letter).
- Assessment will place patients in low, moderate, and high-risk categories.
- High risk patients will be offered referral to a tertiary centre and/or screening locally as per high-risk guidelines.
- Patients should be offered a written summary of their consultation with standard written information as per NICE guidance.
- CanRisk should be used where possible as an assessment tool for risk, this is the RGC preferred tool. If not available BOADICEA and the Manchester score can be used.

**Referral Guidelines from Primary Care**

- One first-degree female relative diagnosed with breast cancer at younger than age 40 years **or**
- One first-degree male relative diagnosed with breast cancer at any age **or**
- One first-degree relative with bilateral breast cancer where the first primary was diagnosed at younger than age 50 years **or**
- Two first-degree relatives, or one first-degree **and** one second-degree relative, diagnosed with breast cancer at any age **or**
- One first-degree or second-degree relative diagnosed with breast cancer at any age **and** one first-degree or second-degree relative diagnosed with ovarian cancer at any age (one of these should be a first-degree relative) **or**
- Three first-degree or second-degree relatives diagnosed with breast cancer at any age

Guidelines for Secondary Care Patients who **do not require** referral to a Specialist Genetic Clinic

- One first-degree relative diagnosed with breast cancer at younger than 40 years **or**
- Two first-degree or second-degree relatives diagnosed with breast cancer at an average age of older than 50 years **or**
- Three first-degree or second-degree relatives diagnosed with breast cancer at an average age of older than 60 years **or**
- a formal risk assessment (usually carried out in a specialist genetic clinic) or a family history pattern is likely to give risks of greater than 3-8% risk in the next 10 years for women aged 40 years, or a lifetime risk of 17% or greater but less than 30% provided certain other specific are not present (See NICE Guidelines page 23)

Guidelines for Secondary Care Patients **who should be** offered a referral to Specialist Genetic Clinic

- At least the following female breast cancers only in the family
    - Two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 50 years (at least one must be a first-degree relative) **or**
    - three first-degree or second-degree relatives diagnosed with breast cancer at younger than average age of 60 years (at least one must be a first degree relative) **or**

    - four relatives diagnosed with breast cancer at any age (at least one must be a first-degree relative) **or**

- Families containing one relative with ovarian cancer at any age **and,** on the same side of the family
    - One first-degree relative (including the relative with ovarian cancer) or second-degree relative diagnosed with breast cancer at younger than age 50 years **or**
    - Two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years **or**
    - Another ovarian cancer at any age **or**

- Families affected by bilateral cancer (each breast cancer has the same count value as one relative)
    - One first-degree relative with cancer diagnosed in both breasts at younger than an average age of 50 years **or**
    - One first-degree relative diagnosed with bilateral cancer and one first or second degree relative diagnosed with breast cancer at younger than an average age of 60 years **or**

- Families containing male breast cancer at any age **and,** on the same side of the family, at least
    - One first-degree or second-degree relative diagnosed with breast cancer at younger than age 50 years **or**
    - Two first-degree or second-degree relative diagnosed with breast cancer at younger than an average age of 60 years **or**

- A formal risk assessment has given risk assessments of
    - A 10% or greater chance of a gene mutation being harboured in the family **or**
    - A greater than 8% risk of developing breast cancer in the next 10 years **or**
    - A 30% or greater lifetime risk of developing breast cancer

- Further advice for specific families (as per NICE 2013) from a Specific Genetic Service

**Genetic Testing for those with a family history**

- Use a carrier probability calculation method (CanRisk +/or Manchester Scoring System) as well as family history to determine who should be offered referral to a specialist genetic clinic.
- Offer testing > 10% chance of BRCA1/2 orTP53 mutation in family.
- Start with testing an affected family member to avoid risk of false negative.
- Can now offer to an unaffected individual if no affected relative available.

**Management of patients with increased risk identified**

- Advise all women on breast awareness
- Do not routinely offer USS surveillance
- **Offer** annual mammography for moderate 40-50 years and 40-59 years high risk patients
- **Offer** annual mammography 40-59 years to women who have **not** had genetic testing but have a greater than 30% probability of being a BRCA carrier

- **Offer** annual mammograms aged 40-69 to women with a known BRCA1 or BRCA2 mutation

**Consider** annual mammogram for:

- Women aged 30-39 at high risk
- Women aged 30-39 years who have not had genetic testing but >than 30% chance of being a BRCA carrier
- Women aged 30-39 with a known BRCA1 and BRCA2
- **Consider** Aged 50-59 women at moderate risk
- We can offer mammograms from 35 if 10 year risk is over 3%, however this isn't in NICE guidelines so RGC support required on an individual basis. These are Manchester Guidelines.

<u>MRI Surveillance</u>

- **Offer** annual MRI to women age 30-49 who have not had genetic testing but have a greater risk than 30% of being a BRCA carrier
- **Offer** 30-49 years with a known BRCA1 or BRCA2 mutation
- **Offer** 20-49 years who have not had genetic testing but have a greater than 30% probability of being a TP53 carrier
- **Offer** 20-49 years with a known TP53 mutation
- **Consider** annual MRI surveillance for women aged 50-69 years with a known TP53 mutation

<u>Chemoprevention for women with no personal history of breast cancer</u>

- **Offer** Tamoxifen or Raloxifine to pre and post-menopausal women at high risk.
- **Do not offer** Tamoxifen or Raloxifine to high-risk women who have had bilateral mastectomy.
- **Consider** Tamoxifen or Raloxifine for 5 years for pre and post-menopausal women at moderate risk.
- Risk and benefits of tamoxifen should be discussed in family history clinics.
- Prescription should be done by GP.
- **Do not** continue treatment with Tamoxifen or Raloxifine beyond 5 years.
- Inform women that they should stop Tamoxifen at least 2 months before trying to conceive and 6 weeks before elective surgery.
- **Please see NICE guideline 164 for more specific guidance**

**Summary of surveillance recommendations for women with no personal history of breast cancer (sourced and adapted form NICE 2013)**

| Age (years) | Moderate risk | High risk | High risk with more than 30% chance of a faulty BRCA gene | High risk with a faulty BRCA1 or BRCA2 gene | High risk with more than 30% chance of a faulty TP53 gene | High risk with a faulty TP53 gene |
|---|---|---|---|---|---|---|
| 20-29 | None | None | None | None | Yearly MRI | Yearly MRI |

| | | | | | | |
|---|---|---|---|---|---|---|
| 30-39 | None | You may have a yearly mammogram | Yearly MRI and possibly yearly mammogram | Yearly MRI and possibly yearly mammogram | Yearly MRI | Yearly MRI |
| 40-49 | Yearly mammogram | Yearly mammogram | Yearly mammogram and yearly MRI | Yearly mammogram and yearly MRI | Yearly MRI | Yearly MRI |
| 50-59 | You may have a yearly mammogram | Yearly mammogram | Yearly mammogram<br><br>MRI if mammogram shows dense breasts | Yearly mammogram<br><br>MRI if mammogram shows dense breasts | Mammogram as part of the population screening programme | MRI if mammogram shows dense breasts. You may have yearly MRI |
| 60-69 | Mammogram as part of the NHS screening programme | Mammogram as part of the NHS screening programme | Mammogram as part of the NHS screening programme<br><br>MRI if mammogram shows dense breasts | Yearly mammogram<br><br>MRI if mammogram shows dense breasts | Mammogram as part of the NHS screening programme<br><br>MRI if mammogram shows dense breasts | You may have yearly MRI |
| 70+ | Mammogram as part of the NHS screening programme | Mammogram as part of the NHS screening programme | Mammogram as part of the NHS screening programme | Mammogram as part of the NHS screening programme | Mammogram as part of the NHS screening programme | None |

## Genetic Testing Guidelines for Patients Diagnosed with Breast Cancer

- Use the protocol for Genomic Testing of Patients with a Diagnosis of Breast Cancer (Appendix 6) for determining who is eligible for testing and referral to the clinical genetics team. http://gmcancer.org.uk/breast/genetic-testing.

<u>Surveillance for women with a personal and family history of breast cancer</u>

- Ensure that all women with breast cancer are offered annual mammography for a minimum 5 years in line with NICE guidance 80. Some patients need extended surveillance if high risk in line with NICE guidance.

<u>Risk Management Advice</u>

- Advice on oral contraceptives as per NICE guideline 164
- Breast feed if possible
- HRT as per above guideline
- Alcohol, smoking and weight/physical advice as per above guideline

## Risk-reducing mastectomy/oophorectomy for women with personal history of breast cancer

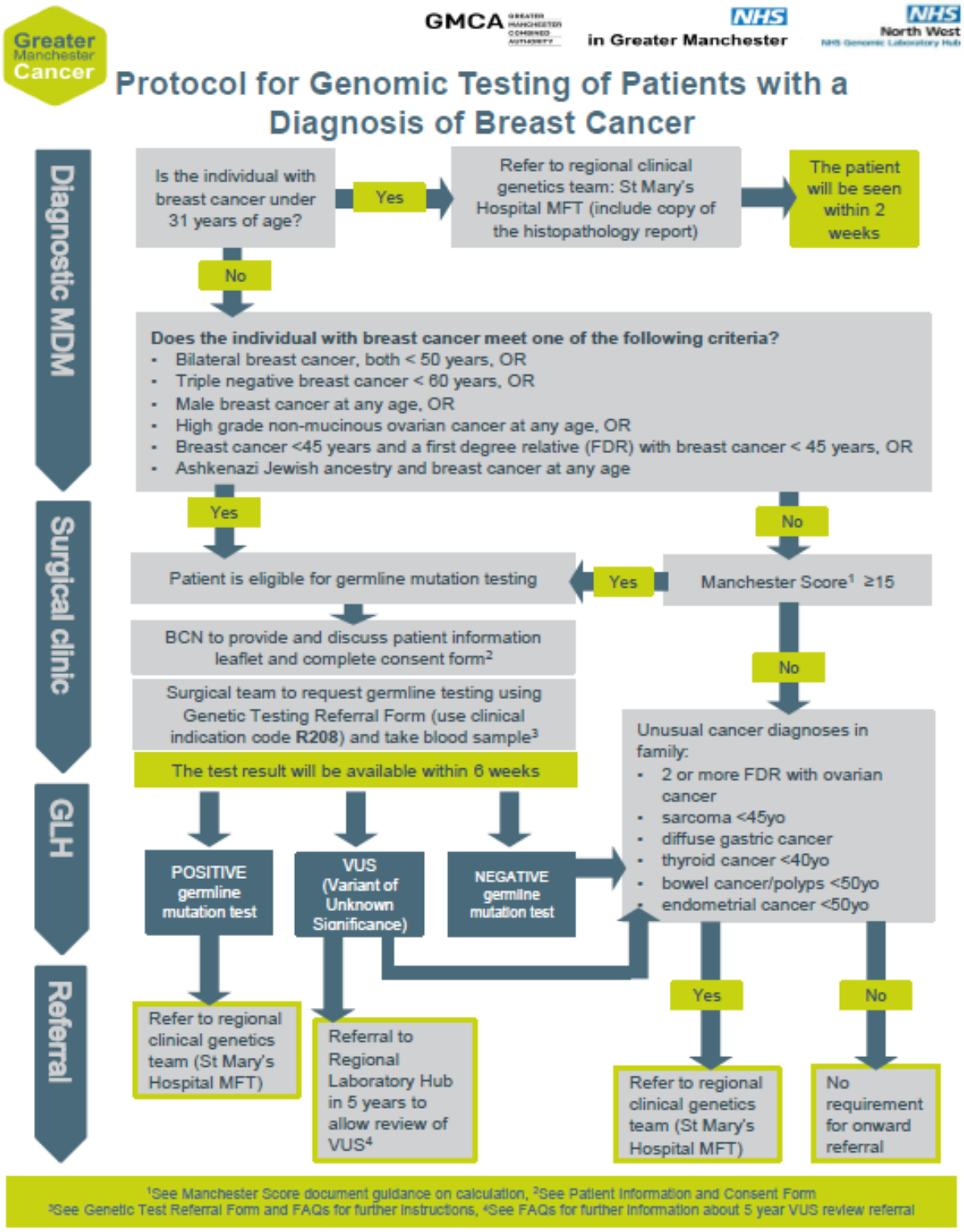
- Bilateral risk-reducing is appropriate for only a small proportion of women who are high risk.
- Bilateral mastectomy should be raised as a risk-reducing strategy option with all women at high risk.

- Women considering this surgery should be seen in a Specialist Genetic Clinic to aid decision making, to discuss risk factors and to have appropriate counselling, preparation and support.
- Bilateral oophorectomy is appropriate for small numbers of women from high-risk families.
- The effects of early menopause should be discussed with all women considering this surgery.
- **Please see NICE guideline 164 for more specific guidance.**

# Appendix 6

## Protocol for Genomic Testing

https://gmcancer.org.uk/wp-content/uploads/2022/08/Breast-Cancer-Genetic-Testing-Pathway-Algorithm-V2.0-21August2022.pdf

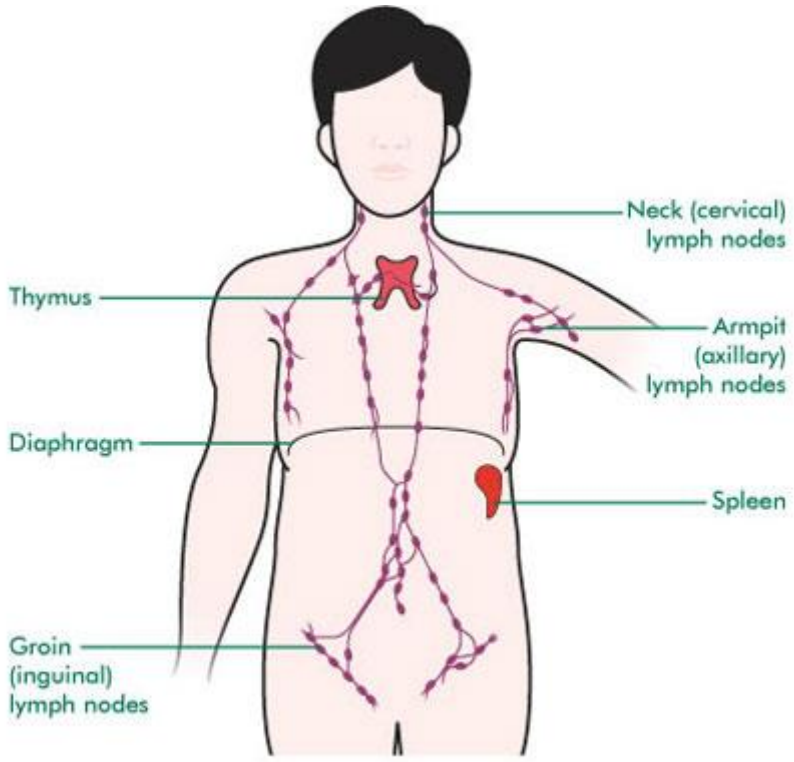



Breast Cancer Genetic Testing Pathway: Algorithm V1.0 28April2021

## Cancer-related Lymphoedema

Also called **secondary lymphoedema**, this is caused by cancer or its treatment and recurrent episodes of infection in the affected area. It can occur if the lymph nodes are blocked with cancer or if they have been removed by surgery. Radiotherapy and chemotherapy can also cause lymphoedema by causing fibrosis within the remaining lymphatic pathways. However, the majority of patients who have surgery or radiotherapy to the breast and axilla will not develop lymphoedema.

The patients most at risk are those patients who undergo an axillary node clearance followed by axillary radiotherapy.




The most common areas for lymphoedema to occur after cancer treatment are:

- in the arm or breast after breast cancer treatment to the armpit or breast.
- in the leg if cancer or its treatment affects nodes in the groin area or the pelvis.

The affected area, arm or leg may become swollen, stiff, uncomfortable and awkward to move, making it difficult to do daily activities, such as dressing or washing. Lymphoedema can develop weeks, months or even years after cancer treatment and it is difficult to know who will be affected or how severe the lymphoedema will be. However, most lymphoedema is detected in the early stage with patients noticing mild swelling to the area affected.

Although lymphoedema is usually found in an arm or leg, other parts of the body can become swollen. There may be swelling of the chest or abdomen (trunk) or groin. Swelling of the breast or chest area can sometimes occur after breast-conserving surgery. If the lymph nodes in the neck are affected, the face may swell, but this is rare.

Lymphoedema may cause the following symptoms in the affected area:

- A feeling of fullness, stiffness or heaviness
- Swelling, tightness and stretching of the skin.
- Clothes, shoes or jewelry (rings or watches) may feel tighter than usual.
- Skin changes – the skin in the area may feel tight or stretched and sometimes the texture can feel thicker. Skin may also be dry, flaky, rough or scaly.
- Aching and discomfort with reduced movement of the joints.

The aim of treatment is to reduce the swelling, which in turn will relieve the symptoms associated with it as mentioned above such as discomfort.

There are many treatment modalities, often used in combination but it is a chronic problem. Although the swelling can usually be reduced, there is always a risk of it coming back and may not completely go away. It may take several weeks or months before there is any real improvement, but with treatment the affected part of the body should become less swollen, easier to move and less uncomfortable.

There are different aspects of treatment:

- Skin care and preventing infection
- Self-massage, known as Simple Lymphatic Drainage.
- Limb positioning and movement
- Support using compression garments such as sleeves, stockings and wraps.
- Specific exercises
- Kiniseo taping
- Intensive treatments such as - Low level light laser therapy; Compression pumps, multi-layer bandaging; Manual lymphatic drainage

The therapies may need to be done every day to give the best results. Patients will be shown how to carry them out at home. Many people soon develop a routine that builds their lymphoedema care into their everyday activities.

Good skin care plays a vital part in the treatment of lymphoedema. Lymphoedema can make the skin become dry and itchy and it may crack. Good moisturising can help to prevent this. Suitable creams are available from local chemists or patients can get them on prescription from their general practitioner.

Any break in the skin, however small, may lead to the potential of infection (cellulitis) and the swollen part becomes red, hot and painful. Patients may experience a high temperature, flu-like symptoms, feel generally unwell and lose their appetite. Medical advice should be sought immediately, and antibiotics are usually given to treat the infection and should be started straight away and generally taken for two weeks. Patients should be made aware of the symptoms at an early stage and encouraged to see their general practitioner as soon as they suspect they have an infection.

It is important that patients are referred appropriately to a Lymphoedema Service for symptoms which are classed more than mild, for appropriate advice and treatment. There is also a Network Lymphoedema patient leaflet available for patients, which has been developed and explains what lymphoedema is and the symptoms patients might experience.

**Antibiotics for cellulitis in lymphodema** [a]

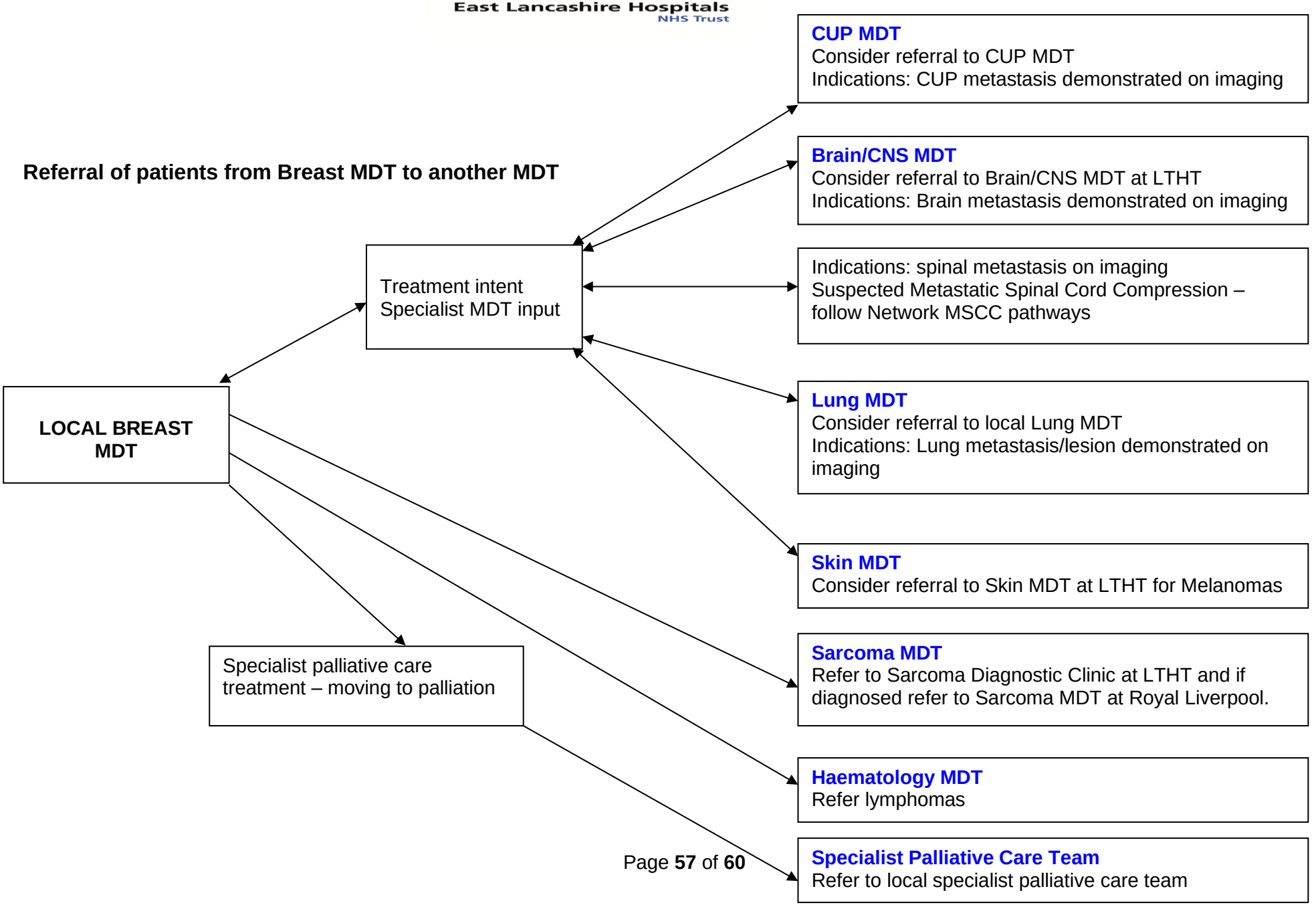
| Situation | First-line antibiotics | If allergic to penicillin | Second-line antibiotics | Comments |
|---|---|---|---|---|
| Acute cellulitis + septicaemia (inpatient admission) | Flucloxacillin IV 2g q6h or benzylpenicillin IV 1200-2400mg q6h + gentamycin IV 5mg/kg o.d. | Clindamycin IV 600mg q6h | Clindamycin IV 600mg q6h (if poor or no response by 48h) | Switch to amoxicillin 500mg q8h when:<br>➢ Temperature down for 48h<br>➢ Inflammation much resolved<br>➢ CRP <30mg/L |
| Acute cellulitis (home care) | Amoxicillin 500mg q8h ± Flucloxacilllin 500mg q6h[b] | Erythromycin 500mg q6h or clarithromycin 500mg q12h | If fails to resolve, convert to IV regimen as in row 1, column 2 | Treat for at least 14 days or until signs of inflammation have resolved |
| Prophylaxis to prevent recurrent cellulitis (if 2+ attacks p.a.) | Penicillin V 250 mg b.d. (500mg if weight >75kg) | Erythromycin 250mg bd. | Clindamycin 150mg o.d. or clarithromycin 250mg o.d. | After one year, halve dose of penicillin to 250mg o.d. (500mg if weight >75kg) |
| Emergency supply of antibiotics "in case of need" (when away from home) | Amoxicillin 500mg q8h | erythromycin 500mg q6h or clarithromycin 500mg q12h | If fails to resolve, or constitutional symptoms develop, convert to IV regimen as in row 1, column 2 above | |

a. PO unless stated otherwise
b. Add if suspect Staphylococcus aureous infection e.g. folliculitis, pus formation, crusted dermatitis

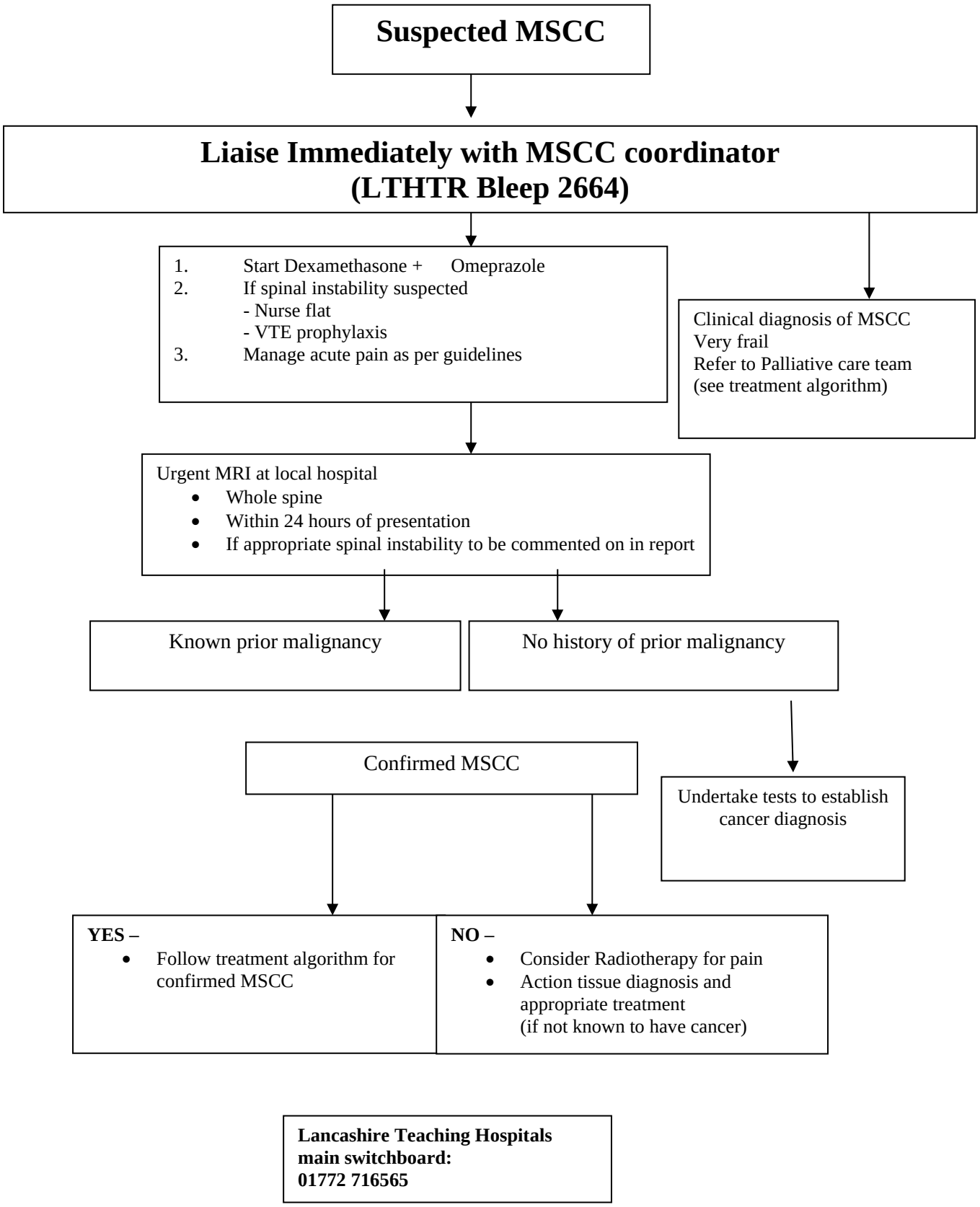
Reference; British Lymphology Society; Consensus Document on the management of Cellulitis in Lymphoedema. Revised March 2013

http://www.lymphoedema.org/Menu3/Cellulitis%20Consensus.pdf

## Referral of patients from Breast MDT to another MDT

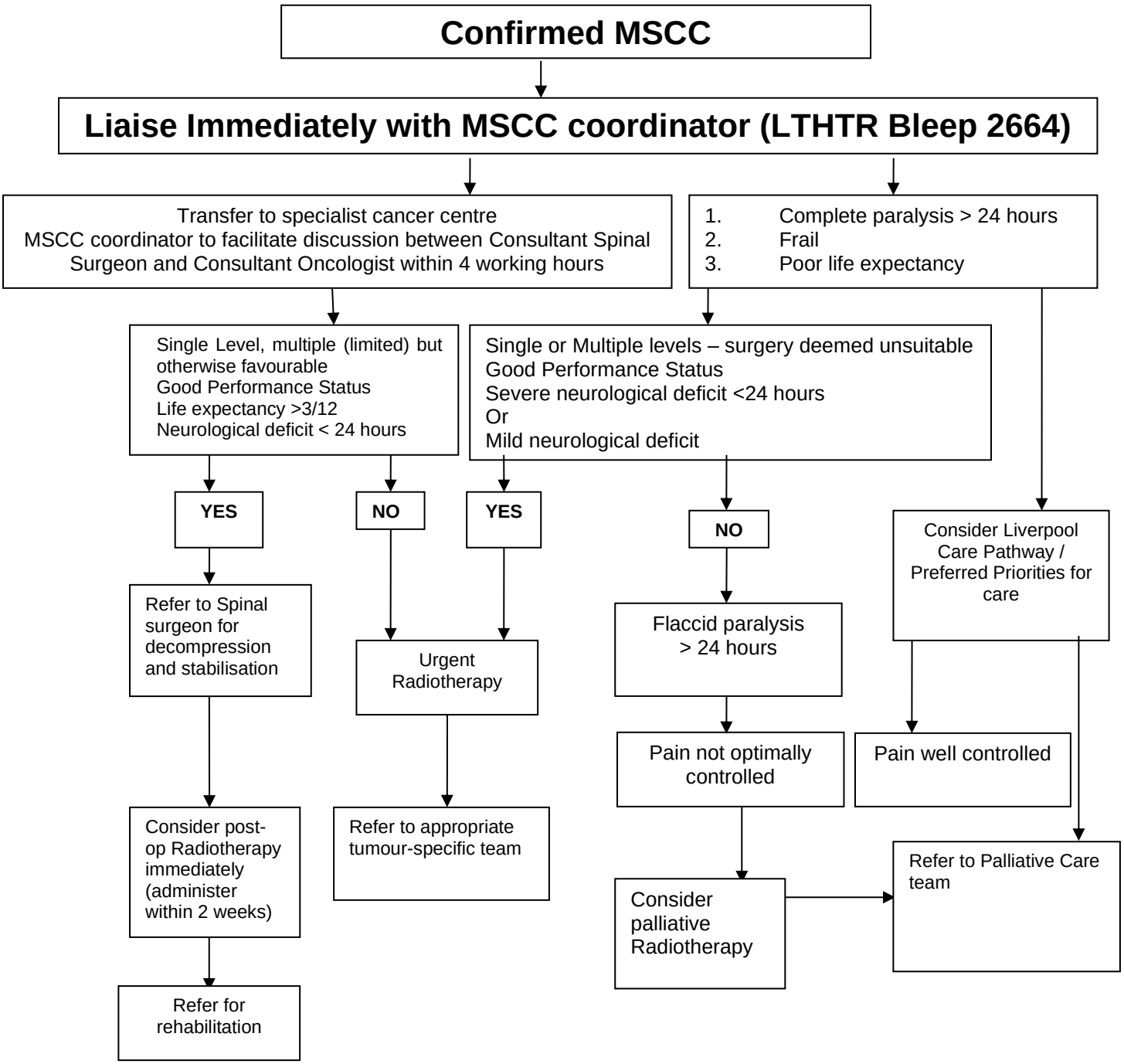


# Diagnostic Algorithm for Suspected Metastatic Spinal Cord Compression (MSCC)




**Lancashire Teaching Hospitals main switchboard: 01772 716565**

# Treatment Algorithm for Metastatic Spinal Cord Compression (MSCC)

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This document has been developed and agreed by members of the Lancashire & South Cumbria Breast CRG (part of the Northwest Coast SCN).