Disclaimer: These are general guidelines and must be considered with value judgements for individual patients.

Essential: mandatory

Preferred /Desirable / Optimal: cost effective with evidence of efficacy

Optional: can be considered, minimal evidence, cost is an issue

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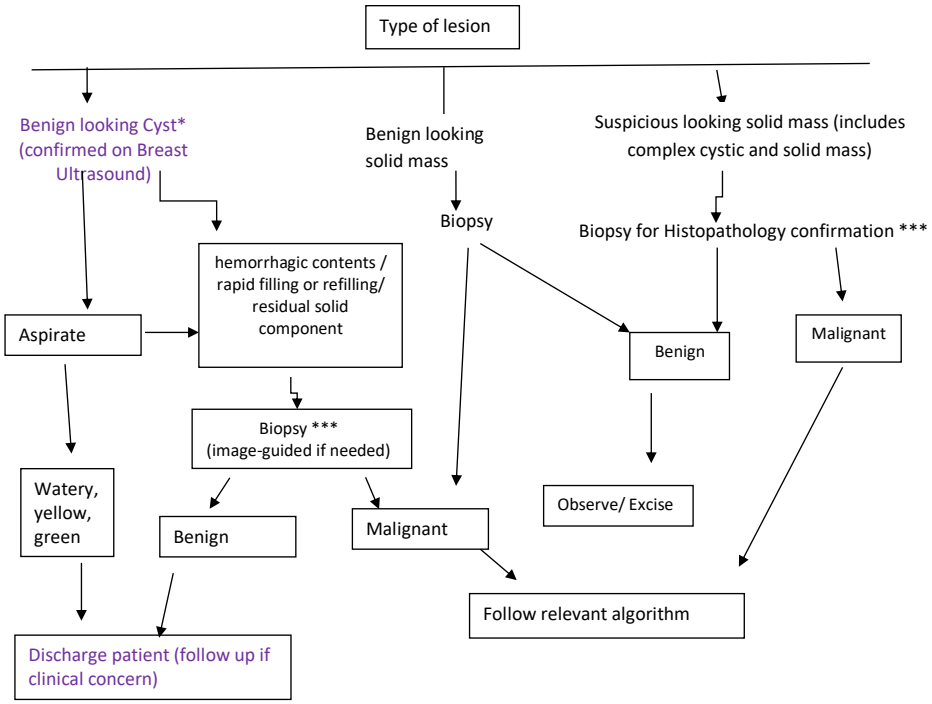
Evaluation of a breast Lump

All women with a breast lump should undergo a TRIPLE TEST which comprising of

1. **Clinical Examination by an experienced clinician preferably a breast surgeon**
2. **Bilateral imaging: a bilateral mammogram and/or Ultrasound/ MRI as appropriate##**
3. **Histopathology** (Core biopsy preferred or FNAC) # Incisional biopsy may be considered in exceptional cases**



**Solitary and multiple simple cysts can be observed and do not need to be aspirated.*

****Core Biopsy is preferred in cases where neo-adjuvant therapy is planned (for grading and receptor status) and for guided non palpable-lesions and if MRM considered. FNAC is acceptable if patient cannot afford Core Biopsy. IHC evaluation is mandatory prior to neo adjuvant therapy. Histo/cyto pathology confirmation is a MUST before initiating cancer directed treatment (surgery/ chemotherapy/ other systemic treatment). Exception: in case where frozen section is required for primary diagnosis*

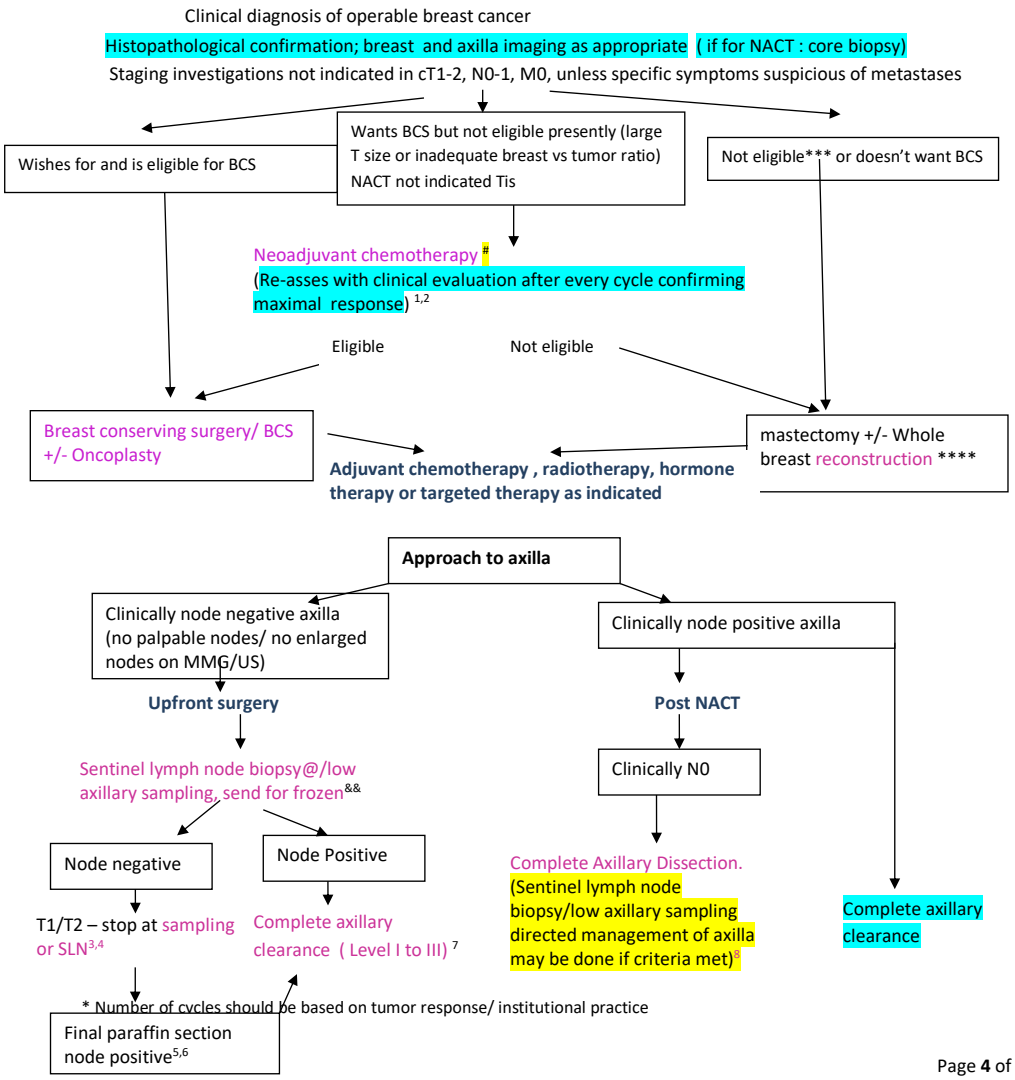
Primary diagnostic procedure should not be Excision Biospy prior to failure of routine procedures.

**** Histo/cyto pathology confirmation is a MUST before initiating cancer directed treatment (surgery/ chemotherapy/ other systemic treatment*

#: In cases of discordance in triple test, further evaluation must be considered.

MRI breast may be considered in cases with extremely dense breast with clinical or imaging based suspicion of multiple tumors, high risk women with dense breast.

Management Schema for Operable breast cancer (Tis,T1-2, N0-1, M0)



Tailoring treatment based on IHC , to be able to consider post NACT adjuvant therapy to non responders can be discussed with patients

***: Contraindications to BCS include: diffuse microcalcification, EIC+ with margin positive, poor patient compliance, previous chest or breast radiation, relative contraindication is multicentricity. Contra-indications to radiotherapy e.g. collagen vascular diseases.

3: SNB can be performed either using dual dye- radiocolloid and blue dye (preferred method) OR using blue dye alone. 1 to 2 ml peri-tumoral and/or sub-areolar injection / sub-dermal injection of patent blue dye or 2% methylene blue 10 minutes prior to the surgical incision and 40 MBq in 0.5ml of 99m-technetium–labeled sulphur/ antimony colloid peri-tumoral and/or sub-areolar injection / sub-dermal injection 2 to 12 hours prior to surgery.

5: If the Patient and Tumor characteristics meet the ACOZOG Z-11 (T1 , micro metastasis in node , Low grade tumor, ER /PR positive, BCS done, whole breast RT using tangential fields planned) and 1-2 SLN positive, no further axillary surgery may be considered.

****Breast reconstruction may be be performed by surgeons in motivated and suitable patients following mastectomy . Implant or autologous flap reconstruction can be performed based on patients suitability and choice of surgeon .

7.If cN0 prior to NACT or an OBC with cN1 post chemotherapy cN): can be considered for SLN/ Low axillary sampling

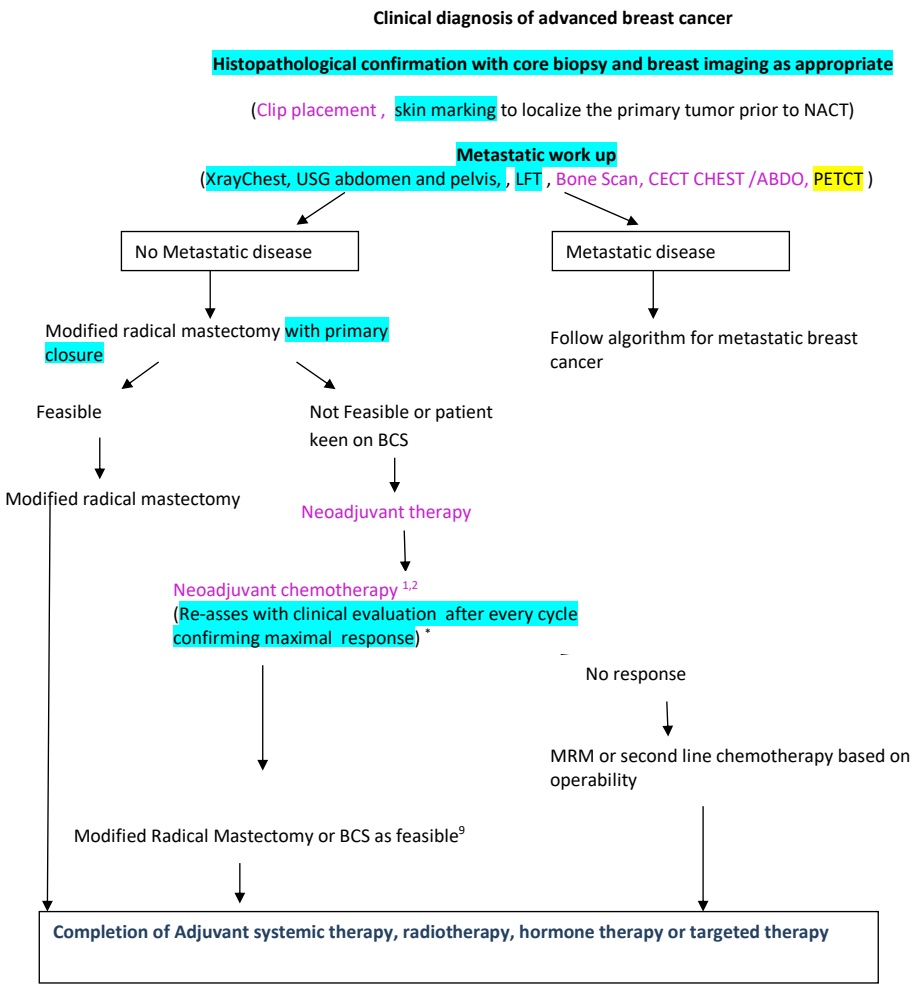
&&: if FS not available: LAS and final HPR or ALND (level II if no gross enlarged nodes)

Margins in BCS : negative margin defined as no tumor on inked surface. In case of positive margins, should be revised . In case of persistent positive margins, MRM to be considered

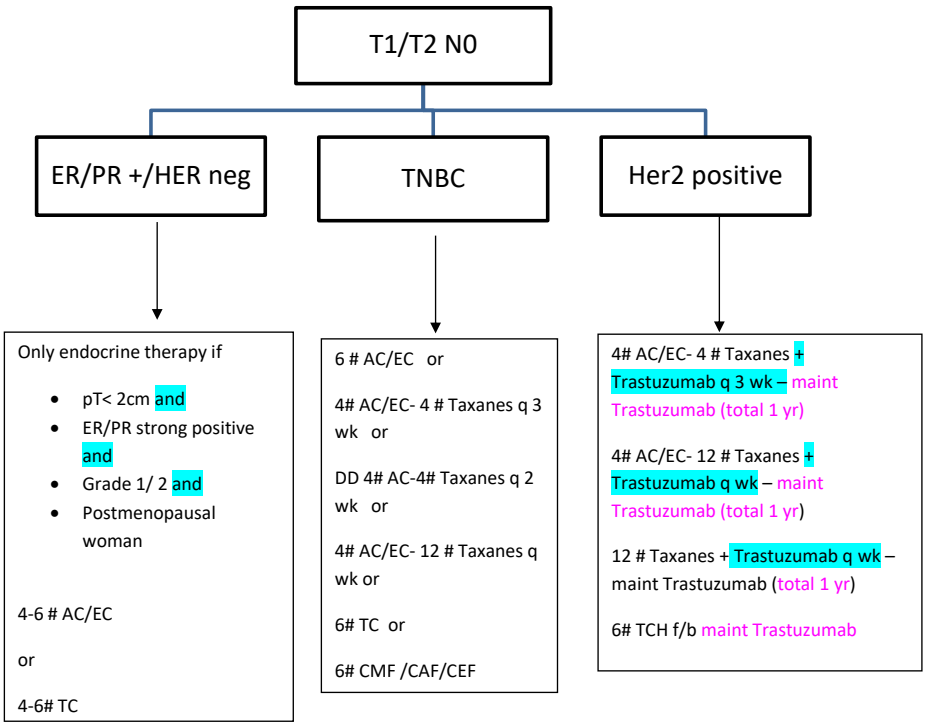
In patients with family history of cancer, younger than 40 years, male breast cancer or patients with synchronous and metachronous breast cancer, can be referred for genetic counselling and those who are willing may be considered for testing to rule-out presence of germline pathogenic variant.

Screen detected Low grade DCIS undergoing lumpectomy may not require axillary assessment.

Management Schema for locally Advanced breast cancer (T3-4, any N, N2-3 any T)

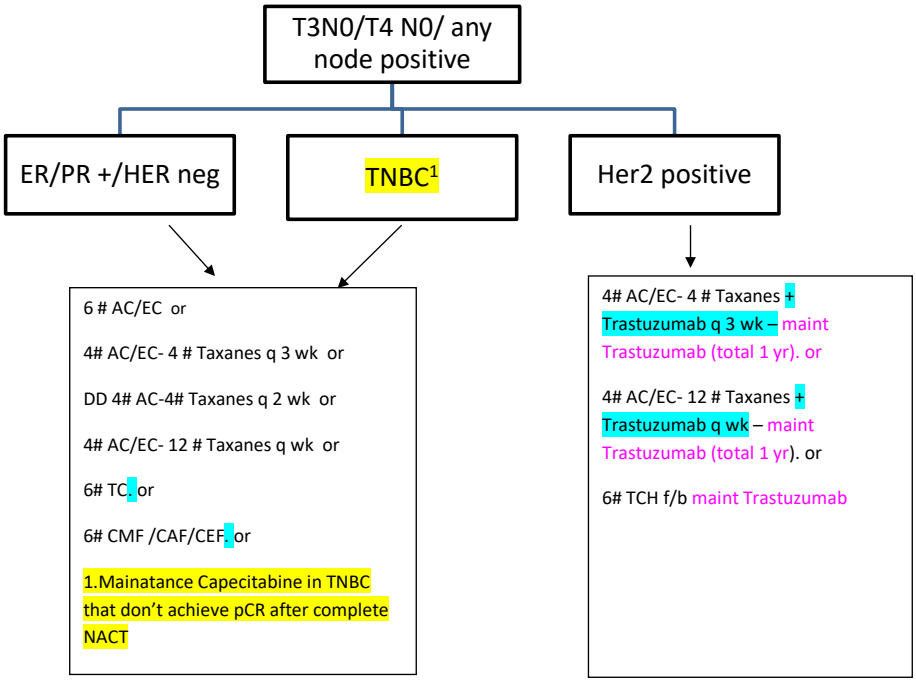


Systemic therapy*



- Choice of chemotherapy to be given depends upon patient's and tumour characteristics .
- Rare pathological subtypes : treatment to be individualised.

Systemic therapy (Adjuvant/ Neoadjuvant)



AC – adriamycin/cyclophosphamide, EC- epirubicin/ cyclophosphamide, TC – docetaxel/ cyclophosphamide, CMF – cyclophosphamide, methotrexate,5-fluorouracil, P- Paclitaxel, TCH – docetaxel,Carboplatin,trastuzumab

Choice of chemotherapy depends on patient and tumor characteristics

Hormone Therapy for all ER &/or PR positive

- Adjuvant hormonal therapy for all ER/PR(+) patients (start 2 weeks after last cycle of chemotherapy) for minimum 5 years

- Tamoxifen for 5years in premenopausal patients is standard adjuvant hormonal therapy
  For premenopausal women with high risk disease Tamoxifen with ovarian suppression may be considered
  Switch therapy: 2-5 years Tamoxifen AI for 5 years may be considered after confirming post menopausal status before starting AI.
  Tamoxifen for 10 years to be considered in high risk patients/node positive patients.

  AI - in postmenopausal patients for a minimum of 5 years. Letrozole/ Anastrazole or Exemestane are the options, with no difference in efficacy/ adverse effects. Any one can be used, based on physician's choice, availability
  5 years of AI fb 5 years of Tamoxifen or 7-10 years of AI can be considered in high risk cases.

- Her2 positive patients (invasive cancer) –Adjuvant Trastuzumab for 1 year is the standard practice, minimum 12 weeks therapy is recommended.

- Adjuvant chemotherapy can be considered in some cases of pT1 (<0.5 cm)/N0/M0 TNBC based on patient and tumour characteristics.

- Adjuvant chemotherapy and targeted therapy can be considered in some cases of pT1 (<0.5 cm)/N0/M0 ER/PR negative/ HER 2 positive patients based on patient and tumour characteristics.

Guidelines for Radiation therapy in breast cancer [22-25]

A] INDICATIONS AND TARGET VOLUMES OF ADJUVANT RADIOTHERAPY

Stage	Post-Mastectomy				Post Breast Conservation Surgery				
	Chest Wall	**SCF**	**Axilla**	**IMN**	**Whole Breast**	**Boost**	**SCF**	**Axilla**	**IMN**
DCIS	No indication for RT				Yes (Exception: Low grade, <2cm, HR +, elderly patients)	High grade, focal positive margins, age ≤50 years	No indication for RT		
T1/2 N0	No indication for RT				Yes (Exception: Highly select patients as per PRIME study[28])	Yes[23]	No indication for RT		
T1/2 N1	In all cases except select low risk pN1 cases	In all cases except select low risk pN1 cases	If SNB / AS positive & axilla not cleared	X	Yes	Yes[23]	In all cases except select low risk pN1 cases	If SNB / AS positive & axilla not cleared	X
T3 N0	Yes	Individualized	X	X	Yes	Yes[23]	Individualized	X	X
Any N2, T3 N1-3, any T4	Yes	Yes	Only for residual disease after AC	For IMN positive on scans or histology	Yes	Yes[23]	Yes	Only for residual disease after AC	For IMN positive on scans or histology

Special considerations:

1) Ductal carcinoma in situ: Adjuvant radiotherapy (RT) is not indicated after mastectomy. After breast conservation, majority of patients will be eligible for whole breast RT with or without boost to the tumor bed. Sequential boost is recommended for high grade tumors, young patients (≤50 years) or close margins (< 2 mm). Elderly women with screen detected lesions may be observed after lumpectomy.
(2) Accelerated partial breast irradiation (APBI): APBI can be offered in select cases in centres having experience as well as maintaining clinical audit of the APBI technique used in their centre. The eligibility criteria include women with early breast cancers having age> 40 years, pathological tumor size up to 3 cm, clear marginsand absent lympho-vascular emboli and extensive intraductal component.[24]
(3) Oligo-metastatic breast cancer (OMBC): Oligometastatic disease is defined as low volume metastatic disease with limited number and size of metastatic lesions (up to 5, single organ), potentially amenable for local treatment, aimed at achieving a complete remission status. Loco-regional radiotherapy should be offered only if it is possible to ablate all the oligometastatic sites either with surgery, radiotherapy or other modality without causing undue toxicity.

B] DOSE FRACTIONATION:

1) Whole breast or chest wall RT with or without supraclavicular nodal irradiation

1. **Standard regimen (hypofractionation):** 40Gy/15#/3weeks or 42.5Gy/16#/3.5 weeks
2. **Alternative regimen (conventional fractionation):** 50Gy/25#/5 weeks if high cardiac doses or involves axillary or internal mammary nodal irradiation

2) Tumor bed boost:

- 10-14 Gy with 2.0-2.5Gy daily fractionas sequential boost.
- 48 Gy in 15 fractions over 3 weeks as per RTOG 1005 protocol if delivered simultaneously along with whole breast radiotherapy.[31]

3) Oligo-metastases: Doses for SBRT may range from 24-30Gy single fraction to 30Gy/5 fr or may be further fractionated depending upon the clinician's judgement.

If facility for SBRT not available to consider referral to specialized center. Alternatively, treat them with protracted hypofractionated regime with conventional technique 30 Gy in 10 fractions or 40 Gy in 15 fractions.

C] RADIOTHEARPY TECHNIQUE:

1) Standard technique (Bi-tangential): CT based planning is preferred in all cases but preferable / mandatory when conventional planning shows maximum heart distance > 1 cm or there is a large breast with major difference in contours at different levels of the breast or irregular chest wall contour or inter-field separation >18 cm. 3 D conformal radiotherapy using field-in-field technique in free breathing to achieve a homogenous distribution. Maximum cardiac sparing using multi-leaf collimator or block must be used for left sided cancers while ensuring appropriate target coverage. Treatment in linear accelerator is advisable.

2) Standard technique for boost: Enface electrons or photons both are acceptable. If clinically indicated, patients may be re-simulated for boost planning. **Centres with expertise may deliver boost using interstitial brachytherapy.**

3) Special techniques (IMRT/IGRT/DIBH/prone): There will be greater clinical benefit in the following case scenarios:

1. Left sided breast cancer in which standard bi-tangential technique is unable to achieve acceptable dosimetry to the normal tissues on 3D (desired dose constraints to be achieved for OARS) or 2D planning (maximum heart distance > 1cm, central lung distance >3cm).
2. Target volumes include internal mammary nodal chain or oligo-metastatic sites
3. Patients with pre-existing cardio-pulmonary conditions entailing maximum sparing of normal tissues.
4. Large breast or chest wall separation causing dose inhomogeneity within the target volumes.

4) Stereotactic radio-surgery (SRS)/Stereotactic body radiotherapy (SBRT): These are recommended for the following indications:

1. Radical treatment of oligometastatic sites such as bones/ liver/ lung/ brain and adrenal metastases. For spine without epidural spinal soft tissue compression.
2. Re-irradiation of previously treated site in cases of palliative treatment.

Follow-up of patients after completion of primary treatment, (OBC /LABC)[26,27]

Follow up visit 3-6 months (or when symptomatic) after completion of adjuvant treatment for the first five years

↓

Followed by every 12months check up for 5-10years

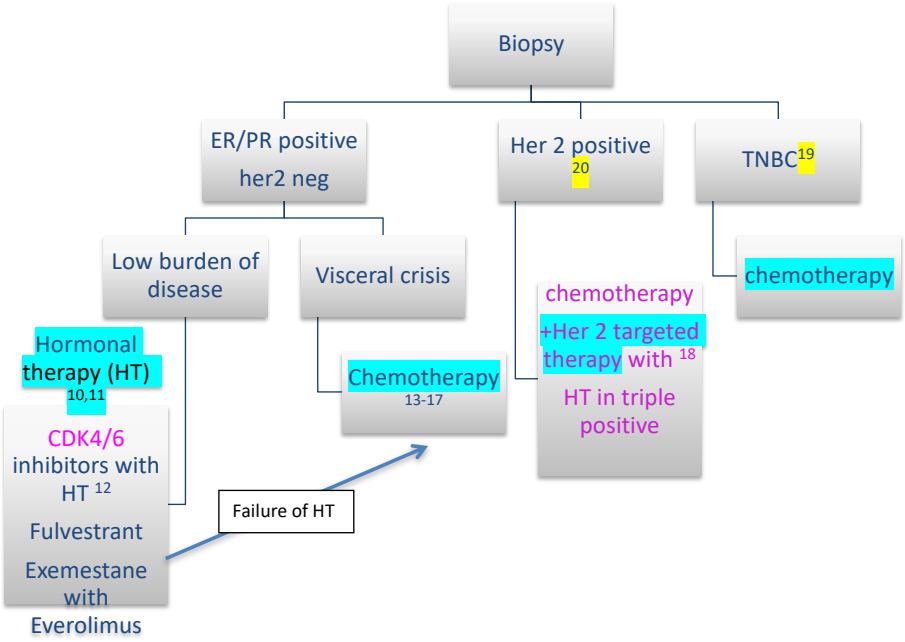
↓

Every 2 yearly check up after 10 years

Follow up visit includes

- History
- Clinical breast examination
- NO INVESTIGATION unless doubtful history s/o metastasis/suspicious clinical findings
- Follow up mammography every 12-24 months

Guideline for Metastatic Breast Cancer*



*: early institution of palliative therapy

10) Premenopausal women should receive Tamoxifen; they may receive regimens indicated for postmenopausal women if they have undergone ovarian ablation.

11) Consideration of front-line hormonal therapy is based on previous therapy received for early-stage disease

12) CDK 4/6 inhibitors in combination with hormonal therapy may be considered in the front-line/ second line setting

13) Chemotherapy can be considered at any time point in case of visceral crisis or no response to hormonal therapy.

14) Taxane in combination with trastuzumab and pertuzumab[19] is the preferred first-line regimen; especially in treatment naive patients or in those who received trastuzumab in adjuvant or neoadjuvant setting. Trastuzumab with chemotherapy may be considered if pertuzumab is not feasible. Other options are: Lapatinib with chemotherapy or trastuzumab with Lapatinib.

15) TDM-1 indicates trastuzumab emtansine, in next line treatment for patients progressing on a trastuzumab-based regimen.

16) PARP inhibitors / Immunotherapy can be considered[21]

Surgery in MBC: Surgery is performed only for palliation of symptoms (Fungation or bleeding ulcer).

Surgery can be considered following systemic treatment in otherwise fit patients with oligo-metastatic disease (as previously defined), especially if skeletal or soft tissue metastasis only, with favorable histology, ER/PR strongly positive tumors.

Palliative radiotherapy[28-33]

Bone metastases

1. 8 Gray single fraction to symptomatic bone/s in case of uncomplicated metastases
2. In case a patient with wide spread metastases having multiple confluent regions of bone pain, they may be considered for magna-field irradiation. (Dose 6 Gy single fraction for the upper hemi-body and 8 Gy single fraction for lower hemi-body). Patients who receive hemi-body radiation should not be given early systemic chemotherapy and therefore such hemi-body radiation is reserved for patients with extensive bone only metastases. Keep a gap of 4-6 weeks before initiating chemotherapy. Avoid upper hemi-body in patients with compromised lung function.
3. 20 Gray /5# for patients with a) Impending fracture b) cord compression c) large adjacent soft tissue.
4. Bisphosphonates to all patients of bone metastasis

Brain metastasis

1. Whole brain irradiation – 20 Gray/5 #/1 week or 30Gray/10#/2 weeks in case of multiple lesion and/or uncontrolled primary
2. In case of patients with single brain metastasis, controlled primary and no other site of systemic disease, consider referral for surgery or stereotactic radiosurgery (SRS) alone or whole brain radiotherapy followed by SRS boost.
3. For centers with lack of neurosurgery and SRS, whole brain radiation therapy to a dose of 30y/10 fr
4. Best supportive care if poor performance status and unfit for whole brain RT

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