CANCER EDUCATION AND ADVOCACY FOUNDATION OF NIGERIA (CEAFON)

In Collaboration with

THE FEDERAL MINISTRY OF HEALTH (FMOH)

CANCER TREATMENT POCKET GUIDELINES SERIES

BREAST CANCER 2016
GUIDELINES COMMITTEE

CHAIR:

SUNDAY ADEYEMI ADEWUYI
Professor of Clinical & Radiation Oncology
Department Of Radiology
Ahmadu Bello University, Zaria - Nigeria

EDITORIAL BOARD:

FRANCIS ABAYOMI DUROSINMI-ETTI
Professor of Clinical & Radiation Oncology
Department of Radiology
Lagos University Teaching Hospital, Lagos - Nigeria

RAMATU HASSAN
National Coordinator
National Cancer Control Programme /Head Nuclear Medicine Programme.

SUBJECT EDITORS:

JIBRIN PAUL
Consultant, Pathologist
National Hospital Abuja- Nigeria

JOHN C. OJUKWU
Specialist Consultant, Minimally Invasive Surgery, Surgical Oncology
Advanced Videoscopic & Laparoscopic Surgery Centre (AVLSC), Lagos- Nigeria

OLADAPO B. CAMPBELL
Professor of Clinical & Radiation Oncology
Department of Radiology
University College Hospital, Ibadan, Oyo- NIGERIA

OBINNA M. NWANERI
Associate Professor - Internal Medicine
Medical Director - Iowa Oncology Network
University of Iowa Holden Comprehensive Cancer Center,
Iowa City, Iowa, USA
GUIDELINES COMMITTEE

DEPUTY SUBJECT EDITORS:

OLAYIDE AGODIRIN
Consultant General and Laparoscopic Surgeon
University of Ilorin Teaching hospital, Ilorin, Kwara- Nigeria

OMOLOLA SALAKO
Consultant, Clinical and Radiation Oncologist
Lagos University Teaching Hospital, Lagos- Nigeria

ANTHONIA SOWUNMI
Consultant, Clinical and Radiation Oncologist
Lagos University Teaching Hospital, Lagos- Nigeria

TEMITOPE OLATUNJI
Consultant, Clinical and Radiation Oncologist
Lagos University Teaching Hospital, Lagos- Nigeria

MARCUS INYAMA
Consultant, Hemato-Oncologist
University of Calabar Teaching Hospital, Calabar
Cross River- Nigeria

EDITORIAL ASSISTANT:

YETUNDE BASHORUN
Administrative Officer
Cancer Education and Advocacy Foundation of Nigeria (CEAFON)
Lagos-Nigeria
CEAFON CANCER TREATMENT POCKET GUIDELINES PROVIDES YOU WITH A CONCISE SUMMARY OF THE FUNDAMENTAL RECOMMENDATIONS MADE BY VARIOUS EXPERTS ON BREAST CANCER MANAGEMENT AND ADOPTED FROM ESMO, ASCO AND NCCN GUIDELINES.

The key content includes Diagnostic Criteria, Staging of disease, Treatment plans and follow up. It is intended to provide you with a set of recommendations for the best standards of care for Breast Cancer using evidence-based Medicine. It will also facilitate knowledge uptake and helps you to deliver an appropriate quality of focused care to your patients.

This booklet can be used as a quick reference guide to access key content on evidence-based management of Breast Cancer.

Chemotherapy regimen for Breast Cancer has passed through a period of vigorous development in recent years. Any attempt to compile a list of the most important treatment schedules (mono- and poly-chemotherapy) suggested in the literature must remain incomplete. Even if, as goes without saying, strictly objective criteria are applied, it always remains an open question as to which schedules are “important” and which are of “only” local significance. This compilation for Nigerian use must be seen in this light.

This compilation thus does not replace the usual textbooks, compendia or manufacturers’ brochures. These should be consulted particularly in respect of dosage modifications, side effects, contraindications, interactions, co-medications, etc.

Any comments and suggestions on how to improve this pocket guideline would be appreciated.

Prof. S. A. Adewuyi
Email: info@ceafon.com
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>GENERAL CONSIDERATIONS</td>
<td>6</td>
</tr>
<tr>
<td>EARLY OPERABLE BREAST CANCER</td>
<td>6</td>
</tr>
<tr>
<td>LOCALLY ADVANCED BREAST CANCER</td>
<td>10</td>
</tr>
<tr>
<td>METASTATIC AND RECURRENT BREAST CANCER</td>
<td>11</td>
</tr>
<tr>
<td>TRIPLE NEGATIVE BREAST CANCER (TNBC)</td>
<td>12</td>
</tr>
<tr>
<td>MALE BREAST CANCER</td>
<td>12</td>
</tr>
<tr>
<td>MINIMUM DIAGNOSTIC WORKUP</td>
<td>13</td>
</tr>
<tr>
<td>DEFINITIONS</td>
<td>14</td>
</tr>
<tr>
<td>BREAST CANCER GROUP STAGING (TNM)</td>
<td>15</td>
</tr>
<tr>
<td>PRIMARY BREAST CANCER</td>
<td>16</td>
</tr>
<tr>
<td>DIAGNOSTIC WORKUP FOR EARLY BREAST CANCER</td>
<td>16</td>
</tr>
<tr>
<td>STAGING AND RISK ASSESSMENT</td>
<td>18</td>
</tr>
<tr>
<td>MANAGEMENT OF LOCAL / LOCOREGIONAL DISEASE</td>
<td>19</td>
</tr>
<tr>
<td>MINIMUM REQUIREMENT FOR PATHOLOGY DIAGNOSIS</td>
<td>20</td>
</tr>
<tr>
<td>LOCAL TREATMENT FOR BREAST CANCER</td>
<td>21</td>
</tr>
<tr>
<td>GENERAL CONSIDERATION FOR SURGERY</td>
<td>21</td>
</tr>
<tr>
<td>BREAST CONSERVING SURGERY</td>
<td>21</td>
</tr>
<tr>
<td>MASTECTOMY</td>
<td>22</td>
</tr>
<tr>
<td>SURGERY AFTER PRIMARY SYSTEMIC THERAPY</td>
<td>22</td>
</tr>
<tr>
<td>RADIOTHERAPY</td>
<td>23</td>
</tr>
<tr>
<td>RT AFTER BREAST CONSERVING SURGERY (BCS)</td>
<td>24</td>
</tr>
<tr>
<td>RADIOTHERAPY DOSES AND FRACTIONATION</td>
<td>25</td>
</tr>
<tr>
<td>BREAST CANCER CHEMOTHERAPY GUIDELINES</td>
<td>26</td>
</tr>
<tr>
<td>ADJUVANT SYSTEMIC TREATMENT</td>
<td>27</td>
</tr>
<tr>
<td>LATE STAGE DISEASE THERAPY</td>
<td>29</td>
</tr>
<tr>
<td>EARLY STAGE DISEASE THERAPY</td>
<td>30</td>
</tr>
<tr>
<td>ENDOCRINE THERAPY (ET)</td>
<td>31</td>
</tr>
<tr>
<td>HER2-DIRECTED THERAPY</td>
<td>33</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>34</td>
</tr>
</tbody>
</table>
GENERAL CONSIDERATIONS

Breast cancer is a heterogenous disease, which includes at least four or five very different subtypes. The first step in the recognition of the heterogeneity was the demonstration of the presence of functional hormonal receptors (HR) in nearly two thirds of breast cancer specimens. This finding, which established a first classification in HR-positive and HR-negative, was followed by the demonstration of HER2/neu gene alteration, present in nearly 20% of tumours. Depending on the stage and biology of the disease as well as on the patient’s characteristics, breast cancer management involves surgery, radiation, endocrine, cytostatic /chemotherapy and biological therapies. It is often multidisciplinary employing these therapy modalities in various combinations and sequences.

EARLY OPERABLE BREAST CANCER (EOBC)

The primary treatment of early operable breast cancer typically is surgery (breast-conserving segmental mastectomy or total mastectomy) both in combination with axillary staging (sentinel node biopsy or full nodal clearance). Breast radiotherapy is strongly recommended after breast-conserving surgery and should also be considered after total mastectomy for patients with four or more positive axillary nodes as well as T3 or T4 tumours and/or tumours invading the skin or adjacent musculature independent of the nodal status. Risk-adapted adjuvant systemic therapy, which is tailored according to potential responsiveness to endocrine therapy increases the chance of long-term survival.

<table>
<thead>
<tr>
<th>EARLY OPERABLE BREAST CANCER</th>
<th>Primary Treatment</th>
<th>Recommendation after Primary Treatment</th>
<th>Adjuvant Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EARLY OPERABLE BREAST CANCER</strong></td>
<td>Surgery (breast-conserving segmental mastectomy or total mastectomy) both in combination with axillary staging (sentinel node biopsy or full nodal clearance)</td>
<td>Breast radiotherapy is strongly recommended after breast-conserving surgery and should also be considered after total mastectomy for patients with four or more positive axillary nodes as well as T3 or T4 tumours and/or tumours invading the skin or adjacent musculature independent of the nodal status</td>
<td>Risk-adapted adjuvant systemic therapy, which is tailored according to potential responsiveness to endocrine therapy, increases the chance of long-term survival.</td>
</tr>
</tbody>
</table>

- CT = chemotherapy, ET = endocrine therapy, PgR = progesterone receptor.
- * When combining CT with tamoxifen, the latter should be started after the end of CT. It is unclear whether aromatase inhibitors should be started concurrently with or sequentially after CT. In premenopausal patients GnRH can be started concurrently with CT, leading to rapid amenorrhea. Addition of trastuzumab when HER2-positive.
### Adjuvant systemic treatment for patients with operable breast cancer – treatment according to responsiveness to endocrine therapies

<table>
<thead>
<tr>
<th>Risk</th>
<th>Endocrine-responsiveness</th>
<th>Risk</th>
<th>Endocrine-responsiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>ET or nil</td>
<td>Intermediate Risk</td>
<td>ET alone or CT → ET*</td>
</tr>
<tr>
<td></td>
<td>ET or nil</td>
<td></td>
<td>CT → ET*</td>
</tr>
<tr>
<td>High Risk</td>
<td>CT → ET*</td>
<td></td>
<td>CT → ET*</td>
</tr>
</tbody>
</table>

### Definition of risk categories for patients with operable breast cancer

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Node-negative and all of the following features</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• pT ≤ 2 cm</td>
</tr>
<tr>
<td></td>
<td>• Grade 1</td>
</tr>
<tr>
<td></td>
<td>• Absence of extensive peritumoural vascular invasion</td>
</tr>
<tr>
<td></td>
<td>• ER and/or PgR expressed</td>
</tr>
<tr>
<td></td>
<td>• HER2/neu gene neither overexpressed nor amplified</td>
</tr>
<tr>
<td></td>
<td>• Age ≥ 35 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intermediate Risk</th>
<th>Node-negative and at least one of the following features</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• pT &gt; 2 cm</td>
</tr>
<tr>
<td></td>
<td>• Grade 2-3</td>
</tr>
<tr>
<td></td>
<td>• Presence of extensive peritumoural vascular invasion</td>
</tr>
<tr>
<td></td>
<td>• ER and/or PgR absent</td>
</tr>
<tr>
<td></td>
<td>• HER2/neu gene expression or amplified</td>
</tr>
<tr>
<td></td>
<td>• Age &lt; 35 years</td>
</tr>
</tbody>
</table>

**Node-positive (1-3 involved nodes)**
- ER and/or PgR expressed
- HER2/neu gene neither overexpressed nor amplified

<table>
<thead>
<tr>
<th>High Risk</th>
<th>Node-positive (1-3 involved nodes) and</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ER and/or PgR absent</td>
</tr>
<tr>
<td></td>
<td>HER2/neu gene overexpressed or amplified</td>
</tr>
</tbody>
</table>

**Node-positive (1-4 involved nodes)**

*CT = chemotherapy, ET = endocrine therapy, PgR = progesterone receptor.

*When combining CT with tamoxifen, the latter should be started after the end of CT. It is unclear whether aromatase inhibitors should be started concurrently with or sequentially after CT. In premenopausal patients GnRH can be started concurrently with CT, leading to rapid amenorrhea. Addition of trastuzumab when HER2-positive.*
Based on the results of large randomized clinical trials, meta-analyses and following internationally accepted treatment guidelines the vast majority of patients with early breast cancer (exceptions might be patients older than 70 years or selected patients having very small tumours <1 cm or low grade) is offered adjuvant systemic therapy.

Patients with tumours considered **endocrine responsive** receive endocrine treatment alone or a combination of endocrine and chemotherapy, whereas those with tumours of uncertain endocrine responsiveness are usually treated with a combination of endocrine and chemotherapy.

### Pre-menopausal

<table>
<thead>
<tr>
<th>First line Treatment</th>
<th>Additional Treatment</th>
<th>Second Line Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>A gonadotrophin releasing hormone (GnRH) analog, like goserelin, and / or the antiestrogen like tamoxifen are first-line endocrine options. GnRH analogs induce reversible ovarian suppression and amenorrhea, which has been associated with a favorable impact on survival and allows younger women to retain fertility.</td>
<td>Literature indicates that adjuvant therapy with zoledronic acid and possibly other Bisphosphonates may lower the risk of breast cancer recurrence in patients treated with endocrine therapy.</td>
<td>Surgical or Radiation - induced ovarian ablation is an appropriate second-line therapy.</td>
</tr>
</tbody>
</table>
### Post-menopausal

<table>
<thead>
<tr>
<th>First line Treatment</th>
<th>Additional Treatment</th>
<th>Second Line Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant endocrine therapy should include one of the third generation aromatase inhibitors (AIs). AIs increase disease-free survival when compared with tamoxifen. This has been shown for anastrozole &amp; letrozole given upfront, for exemestane &amp; anastrozole given after 2-3 years of tamoxifen, and for letrozole &amp; anastrozole compared with placebo given after 5 years of tamoxifen.</td>
<td>Therapy with AIs can be complicated by accelerated bone loss and increased fracture risk. Women treated with AIs therefore should be protected against bone loss with vitamin D and calcium supplements, and – in presence of risk factors for bone fracture – also Bisphosphonates. Adjuvant therapy with zoledronic acid and possibly other Bisphosphonates may also lower the risk of breast cancer recurrence in patients treated with AIs.</td>
<td>The sequential administration of endocrine therapy and chemotherapy provides additional benefit for patients with a higher risk of relapse.</td>
</tr>
</tbody>
</table>

Patients of all ages with **endocrine non-responsive** tumours derive benefit from adjuvant chemotherapy. Since the mid 1970s when it was shown that cyclophosphamide / methotrexate / fluorouracil (CMF) resulted in statistically significant and clinically meaningful improvements in disease-free and overall survival, the use of adjuvant chemotherapy has become common practice. In selected patients (e.g. elderly, cardiac contraindications, triple-negative node-negative) CMF is still an appropriate option. The optimal duration of adjuvant chemotherapy is not known. However, at least four cycles should be administered, generally aiming for six to eight cycles. Dose reductions below the standard range are associated with inferior results.
Patients with **HER2 overexpression** (e.g. 3+ using Hercep Test/IHC) or **amplification** (measured by CISH or FISH) can benefit from adjuvant treatment with the monoclonal antibody trastuzumab. One year of trastuzumab given in combination with or sequenced with adjuvant chemotherapy significantly improved disease-free survival and overall survival.

**LOCALLY ADVANCED BREAST CANCER**  
This includes advanced primary tumours, advanced nodal disease and inflammatory carcinomas. It requires a coordinated treatment planning between the medical, surgical and radiation oncologist.

### Primary (neoadjuvant) Systemic Therapy

*Provides the earliest possible treatment against;*  
- Micrometastases,  
- Offers selected patients with large operable tumours the chance of breast conservation  
- Renders inoperable tumours resectable  
- Allows a response-adapted individualization of subsequent postoperative therapy

### Hormone Receptor-positive tumours

- Aromatase inhibitors give an increased response rate and a higher rate of breast-conserving surgery compared with tamoxifen

### Hormone Receptor-negative tumours

- Anthracyclines- and taxanes-based chemotherapy improves the chance of achieving both higher breast-conserving surgery and pCR rates compared with less intensive standard regimes. At least six cycles should be completed before surgery.

### HER2-positive breast cancer

- Patients who have operable, locally advanced, HER2-positive breast cancer should receive neoadjuvant paclitaxel plus trastuzumab followed by 5-fluorouracil, epirubicin and cyclophosphamide plus trastuzumab.

**Inflammatory breast cancer** is the most aggressive manifestation of locally advanced breast cancer. Nowadays, multidisciplinary management including neoadjuvant chemotherapy (often based on anthracyclines and taxanes), surgery, radiotherapy and in hormone receptor-positive disease, hormonal therapy represents the mainstay of treatment.
Current therapies for patients with metastatic or recurrent disease are mainly aimed at maintaining/improving the quality of life, symptoms control and prolongation of survival. Although the treatment may include surgery and radiation therapy, management is generally focused on systemic therapies.

For patients with **hormone receptor-positive** breast cancer, endocrine treatments provide therapeutic options that generally have better safety profiles than cytotoxic chemotherapies.

For **premenopausal women** not having had prior adjuvant tamoxifen at all or having discontinued it for at least 12 months, a combined therapy approach with tamoxifen and ovarian ablation (GnRH analogs, surgery or radiation) is the standard therapy for these patients. Third-generation AIs may be considered after or in combination with ovarian ablation.

For **postmenopausal women**, third-generation AIs were found to be superior to tamoxifen in first-line therapy. Nonetheless, tamoxifen still remain acceptable in selected patients. In case of disease progression, salvage hormone therapy may include AIs, fulvestrant, megestrol acetate and androgens.

Patients with metastatic breast cancer are considered candidates for chemotherapy if they are inappropriate to receive hormonal therapy (**hormone receptor-negative status or progression on hormonal therapies**), or if they have **rapidly progressing symptomatic or bulky disease**. More recently, bevacizumab, an anti-angiogenic agent, has been approved for use in combination with paclitaxel as first-line treatment of metastatic breast cancer after showing benefit in progression-free (but not overall) survival. Aggressive combination chemotherapy is particularly indicated for patients requiring urgent reduction in their tumour burden, whereas a sequential administration of single agents potentially reduces the risk of toxicity and may be especially appropriate in frail and elderly patients or in patients with slowly growing tumours.

The treatment of patients with **progressive metastatic breast cancer** still is a challenge, although several newer agents – either alone or in combination with other cytostatics – are active in this setting (and also in first-line treatment). These include vinorelbine, gemcitabine, capecitabine, (non-)pegylated liposomal doxorubicin, nab-paclitaxel, epothilones like ixabepilone, antiangiogenic agents like bevacizumab as well as poly (ADP-ribose) polymerase (PARP) inhibitors (e.g. olaparib).

Patient with metastatic breast cancer with **overexpression of HER2** may receive the monoclonal antibody trastuzumab. It can be used in combination with chemotherapy. Trastuzumab was found to be active in heavily pre-treated patients.
TRIPLE NEGATIVE BREAST CANCER (TNBC)

TNBC is defined by lack of or minimal expression of oestrogen and progesterone receptors and the absence of HER2 overexpression / amplification. TNBC is often managed with chemotherapy regimens based on DNA-damaging agents, such as anthracyclines, platinum derivatives and cyclophosphamide because of the absence of specific treatment guidelines for this subgroup and the lack of targets for current tailored therapies.

MALE BREAST CANCER

The treatment of male breast cancer, which is a rare disease, has been extrapolated from the knowledge of female breast cancer, despite differences in the pathogenesis, biology and genetics of these two disease entities, especially the differences with regard to the role of male hormones as well as oestrogens compared with female disease. Mastectomy with axillary dissection remains the standard surgical treatment. Sentinel lymph node biopsy could be proposed in small tumours. Locoregional radiotherapy is very often indicated. Indications for adjuvant therapies are similar to those in women. Tamoxifen is the standard adjuvant treatment, but chemotherapy is proposed in young men with axillary nodal involvement and/or negative HR status. For metastatic disease, tamoxifen is still the mainstay for HR-positive disease. For HR-negative disease, doxorubicin-based chemotherapy regimens are used.

MINIMUM DIAGNOSTIC WORKUP

The diagnostic workup for patients with malignancies will include investigation to diagnose and confirm malignancy and to assess the extent of disease i.e. metastatic survey. These are different from the investigations required prior to administration of chemotherapy which is meant to assess patient’s fitness for chemotherapy.

The investigations include:

- Full Blood Counts & Differentials
- Urea and Electrolytes
- Serum Creatinine
- Liver Function Tests
- Serum calcium and phosphates and proteins
- Retroviral screening
- Chest X-rays
- X-rays of relevant anatomic areas
- CT scans/ MRI when indicated
- Ultrasound of the Abdomen & Pelvis
- Urinalysis
- Bone scans and Echocardiography
The diagnostic workup for patients with malignancies will include investigation to diagnose and confirm malignancy and to assess the extent of disease i.e. metastatic survey. These are different from the investigations required prior to administration of chemotherapy which is meant to assess patient’s fitness for chemotherapy.

The investigations include:

- Full Blood Counts & Differentials
- Urea and Electrolytes
- Serum Creatinine
- Liver Function Tests
- Serum calcium
- phosphates and proteins
- Retroviral screening
- Chest X-rays
- X-rays of relevant anatomic areas
- CT scans/ MRI when indicated
- Ultrasound of the Abdomen & Pelvis
- Urinalysis
- Bone scans and
- Echocardiography
## PRIMARY TUMOUR
- **TX**: Primary tumour cannot be assessed
- **T0**: No evidence of primary tumour
- **Tis**: In situ cancer or isolated Paget’s disease of the nipple without tumour
  - (DCIS): Ductal Carcinoma in situ
  - (LCIS): Lobular carcinoma in situ
  
  Note: Paget’s disease associated with a tumour is classified according to the size of the tumour.

### T1
- Tumour 2 cm or less in greatest dimension
  - **T1mic**: Micro metastases 0.1 cm or less
  - **T1a**: >0.1 - 0.5 cm
  - **T1b**: >0.5 - 1.0 cm
  - **T1c**: >1.0 – 2.0 cm

### T2
- Tumour more 2 cm but not more than 5 cm in greatest dimension

### T3
- Tumour more than 5 cm in greatest dimension

### T4
- Tumour of any size with direct extension to chest wall or skin
  - **T4a**: Extension to the chest wall
  - **T4b**: Oedema, ulceration of the skin or satellite skin nodules
  - **T4c**: Both (T4a + T4b)
  - **T4d**: Inflammatory carcinoma

## REGIONAL LYMPH NODE
- **NX**: Regional lymph nodes cannot be assessed (e.g. previously removed)
- **N0**: No regional lymph node metastases
- **N1**: Metastases to movable ipsilateral Axillary lymph node(s)
- **N2**: Metastases to ipsilateral Axillary lymph node(s) fixed to one another or to other structures
- **N3**: Metastases to ipsilateral infraclavicular (N3a), ipsilateral internal mammary (N3b), and / or ipsilateral supraclavicular lymph nodes (N3c)

## DISTANT METASTASES
- **M0**: No clinical or radiographic evidence of distant metastases
- **M1**: Distant metastases present
<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1*</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T0</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1*</td>
<td>N1**</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T0, T1,* T2</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1, N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
PRIMARY BREAST CANCER
SCREENING, DIAGNOSIS AND PATHOLOGY/MOLECULAR BIOLOGY

- Breast Self-Examination (BSE) is advised in all adults, especially women.
- Yearly Clinician or trained Nurse Examination of the breast is encouraged.
- Regular mammography is recommended in women aged 50-69 years.
- Diagnosis is based on clinical examination in combination with imaging and confirmed by pathological assessment.

Diagnostic workup for early breast cancer

Clinical Assessment
- Includes bimanual palpation of the breasts and loco regional lymph nodes and assessment for distant metastases (bones, liver and lungs).

Imaging
- Includes bilateral mammography and ultrasound of breast and regional lymph nodes.
- Where facilities abound, Breast MRI can be considered for some patients. It should be done before neoadjuvant chemotherapy, when evaluating response to primary systemic therapy or when the findings of conventional imaging are inconclusive.

Other Assessment
- Include: complete medical history, family history of cancers, physical examination, a minimum blood workup (full blood count, liver function tests, urea and electrolytes, serum creatinine, alkaline phosphatase and calcium levels), chest x-ray and menopausal status.
Diagnostic workup for early breast cancer

Evaluation of cardiac function
- With cardiac ultrasound or ECHO is essential prior to planned treatment with anthracyclines and/or trastuzumab.

Pathological examination
- Of the primary tumour and cytology/histology of the axillary nodes (if involvement is suspected) are required
  - Core needle biopsy, with ultrasound or stereotactic guidance, is recommended, with ultrasound-guided fine needle aspiration as a minimum.
  - Core needle biopsy is mandatory for planned preoperative systemic therapy to confirm invasive disease and assess biomarkers.
- A marker should be placed into the tumour at biopsy to ensure surgical resection of the correct site.
- Sentinel lymph node biopsy should be done. The best time to carry out sentinel lymph node biopsy (SLNB) when the axilla is negative both clinically and on imaging remains controversial.
- Final pathological diagnosis should be made according to the World Health Organization (WHO) classification and the tumour-node-metastasis (TNM) staging system.
- Pathology report should include the histological type, grade, immunohistochemistry (IHC) evaluation of oestrogen receptor (ER) status, progesterone receptor (PgR) and human epidermal growth factor receptor 2 (HER2) expressions.
- Proliferation markers, such as Ki67, can give additional useful information.
- Where biopsy specimens are negative for ER/PgR and HER2, retesting of the surgical specimen is advised.
- Tumours should be grouped into surrogate intrinsic subtypes, defined by histology and IHC data, to assist prognostication and treatment decision making (Luminal A, Luminal B, HER2 over-expression, “Basal-like”/ triple negative).
### STAGING AND RISK ASSESSMENT

<table>
<thead>
<tr>
<th>Blood Workup</th>
<th>A minimum blood workup, as outlined for diagnosis, is recommended before surgery and systemic (neo) adjuvant therapy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other Investigations</td>
<td>Further investigations such as abdominal ultrasound, CT chest and bone scan can be considered for patients with clinically positive axillary nodes, large tumours, aggressive biology and should be performed in case of clinical signs, symptoms or laboratory values suggesting the presence of metastases.</td>
</tr>
<tr>
<td>Pathology</td>
<td>Pathological assessment of surgical specimens should include: the number, location and maximum diameter of tumours removed, the number of removed and positive lymph nodes, the extent of lymph nodes metastases, the pathological type and grade of the tumour, evaluation of resection margins (including location and minimum distance of the margin), vascular invasion and a biomarker analysis.</td>
</tr>
</tbody>
</table>

The most important prognostic factors are:

- ER/PgR expression
- HER2 and proliferation markers
- Number of involved regional nodes
- Tumour histology
- Size, grade and presence of peri-tumoural vascular invasion
- Status of the surgical margins (in patients undergoing breast conserving therapy).
- After neoadjuvant systemic treatment, the response to treatment and amount of residual disease are important prognostic factors.
  - Post-treatment tumour TNM staging should be included.
MANAGEMENT OF LOCAL / LOCOREGIONAL DISEASE

- Treatment should be carried out in specialized institutions / departments that care for a high volume of breast cancer patients.
- Treatment should be provided by a multidisciplinary team specialized in breast cancer and including at least a surgeon, radiation oncologist, medical oncologist, radiologist, pathologist and breast nurse.
- Where any of the above is not available in the institution, consultation should be done prior to commencement of therapy.
- Treatment decisions should be based on tumour burden / location and biology as well as age and general health status of the patient and should take into account the patient’s preference after extensive discussion.
- The possibility of hereditary cancer should be explored with discussions of genetic testing (where the facilities exist) and prophylactic procedures as required.
- Fertility issues should be discussed with premenopausal patients.
MINIMUM REQUIREMENT FOR PATHOLOGY DIAGNOSIS

- Tissue diagnosis is the gold standard in the management of any malignancy
- Multidisciplinary team is pivotal to management of Breast cancer
- Minimum information required from the oncologist
- Minimum information expected in the pathology report
- Tissue handling and Quality control issue are key to any useful pathology diagnosis

<table>
<thead>
<tr>
<th>Minimum clinical information required</th>
<th>Minimum information in pathology report</th>
<th>Tissue handling and Quality Control (QC)</th>
</tr>
</thead>
</table>
| • Name of the patient, sex and age   | • Report of Breast carcinoma with ER/PgR & HER2 assay is mandatory  
• Clinical presentation  
• Clinical impression (working diagnosis)  
• Family history, history of pregnancy  
• Information on previous treatments received (surgery, chemotherapy, targeted therapy and radiotherapy)  
• Cytological and radiological feature and diagnosis  
• Specimen type, minimum of trucut biopsy is required for evaluation of breast pathology  
• Specimen must be submitted fixed in 10% neutral buffer formalin (NBF). | • Tissue must be fixed in 10% NBF within 1hr of surgery for minimum of 6hrs and maximum of 48hrs.  
• Turnaround time for H&E diagnosis should not be more than 1 week and ER/PgR status should not be more than 10 days  
• QC/QA program is mandatory  
• Laboratory revolving funds should be established to avoid out of stock syndrome  
• Continuous Medical Education (CME) for the pathologist and technician is mandatory |

LOCAL TREATMENT FOR BREAST CANCER

SURGERY

General Consideration for Surgery
- MDT should be involved de novo and all the way through investigations and treatment
- The surgical input should preferably be in the following order
- A tissue diagnosis is imperative. Trucut biopsies offer the advantages of a diagnosis, grading, immunohistochemistry and mitotic activity. FNAC is a distant option with limitations.
- Early breast cancer should be accorded the option of sentinel node biopsy and breast conservation where all modalities are present and possible.
- All surgical considerations should weigh the risk of lymphedema and any changes to overall survival.
- Histology of mastectomy specimen should include 10 axillary nodes and inked margins. IHC is imperative.
- Most senior surgeon should be responsible for filling pathology forms and preservation in 10% buffered formalin within 1 hour of surgery.
- Continuous updates in surgical oncology is advised

Breast Conserving Surgery
- BCT (wide local excision and radiotherapy [RT]) is appropriate for most newly diagnosed early breast cancers.
- Efforts to achieve acceptable cosmesis should be made.
- Histological assessment of resection margins is essential and margin status should be reported.
- Marking the tumour bed with clips facilitates accurate planning of the radiation boost field.
LOCAL TREATMENT FOR BREAST CANCER

SURGERY

General Consideration for Surgery

- MDT should be involved de novo and all the way through investigations and treatment
- The surgical input should preferably be in the following order

<table>
<thead>
<tr>
<th>Surgical Oncologist</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Surgeon in a dedicated Breast Team</td>
</tr>
<tr>
<td>General surgeon (Emphasis being on regular updates)</td>
</tr>
</tbody>
</table>

- A tissue diagnosis is imperative. Trucut biopsies offer the advantages of a diagnosis, grading, immunohistochemistry and mitotic activity. FNAC is a distant option with limitations.
- Early breast cancer should be accorded the option of sentinel node biopsy and breast conservation where all modalities are present and possible.
- All surgical considerations should weigh the risk of lymphedema and any changes to overall survival.
- Histology of mastectomy specimen should include 10 axillary nodes and inked margins. IHC is imperative.
- Most senior surgeon should be responsible for filling pathology forms and preservation in 10% buffered formalin within 1 hour of surgery.
- Continuous updates in surgical oncology is advised

Breast Conserving Surgery

- BCT (wide local excision and radiotherapy [RT]) is appropriate for most newly diagnosed early breast cancers.
- Efforts to achieve acceptable cosmesis should be made.
- Histological assessment of resection margins is essential and margin status should be reported.
- Marking the tumour bed with clips facilitates accurate planning of the radiation boost field.
**Mastectomy**

- Mastectomy may be carried out due to tumour size, tumour multicentricity, failure to achieve negative surgical margins after multiple resections, prior radiotherapy (RT) to the chest wall/breast or other contraindications to RT or patient choice.
- Breast reconstruction should be available and the best technique for each patient discussed.
- SLNB rather than full nodal clearance is the standard of care for axillary staging in early, clinically node-negative breast cancer.
- Ductal carcinoma in-situ (DCIS) can be treated with total mastectomy or BCT provided that clear resection margins can be achieved.
- Axillary node evaluation with SLNB is not required with in-situ malignancy but may be reasonable in large and/or high-grade tumours especially when mastectomy is required.

---

**Surgery after primary systemic therapy**

- Downsizing of a large unifocal primary tumour with neoadjuvant therapy will allow BCT to be undertaken in a substantial proportion of patients
  - Multifocal disease or more limited reduction of the primary tumour will necessitate mastectomy.
Management should be carried out by a multi-disciplinary team and in an individualized approach per breast cancer patient. In a situation where a patient received surgery outside the radiotherapy facility, the referring doctor should send a detailed medical report, operation findings, slides, blocks, pathology reports, imaging studies etc.

**Indications for adjuvant radical radiotherapy**
- Primary tumour \( \geq 5\)cm \(T3\)
- Node positive \(N1-N3\)
- Positive resections or involved margins (<10mm)
- After breast conservation surgery (lumpectomy, wide local excision)

**Indications of pre-operative radical radiotherapy**
- Locally advanced disease not responding to chemotherapy
- Fungating tumour
- To control tumour haemorrhage

**Palliative radiotherapy**
- To relieve oncologic emergencies such as:
  o Superior vena cava obstruction
  o Imminent spinal cord compression
  o Increased intracranial pressure
  o Pathological fracture
  o Intractable bone pain
  o Multiple brain metastases

**Sequencing**
- Adjuvant chest wall or whole breast radiotherapy should be done within 6 weeks post-chemotherapy.
- In Pre-operative radiotherapy setting, surgery should be done within 4 – 6 weeks post radiotherapy.
**Assessment of disease**
The radiation oncologist ideally should conduct a breast examination pre operatively. Breast and nodal examination, TNM staging, breast imaging, histology and immunohistochemistry report be documented. A radiation oncologist must assess the risk of local recurrence and rule out metastases before irradiating the whole breast or chest wall. Patient assessment and relevant investigations should be done prior to radiotherapy.

<table>
<thead>
<tr>
<th>RT after breast conserving surgery (BCS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Whole breast radiotherapy</strong></td>
</tr>
<tr>
<td>• Whole breast RT (WBRT) is recommended, with boost irradiation for patients with unfavourable risk factors, such as age &lt;50 years, grade 3 tumours, vascular invasion and non-radical excision.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Accelerated partial breast irradiation only</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Accelerated partial breast irradiation (APBI) might be considered for patients with low risk of local recurrence, for example ≥ 50 years with unicentric, unifocal, node-negative, non-lobular breast cancer, up to 3 cm without extensive intraductal components or vascular invasion and with negative margins, particularly if they will receive adjuvant hormonal treatment.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Radiation after mastectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Post-mastectomy RT (PMRT) is recommended for high-risk patients, including involved resection margins, involved axillary lymph nodes and T3-T4 tumours independent of nodal status.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regional irradiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Comprehensive locoregional RT encompassing the chest wall and regional nodes is recommended for patients with involved axillary lymph nodes.</td>
</tr>
<tr>
<td>• Following axillary lymph node dissection, the resected part of the axilla should not be irradiated, except in cases of residual disease after surgery.</td>
</tr>
</tbody>
</table>
Radiotherapy doses and fractionation

- Traditionally, 45-50 Gy in 25-28 fractions of 1.8-2.0 Gy, with a typical boost of 10-16 Gy in 2 Gy single doses, has been used.
- Shorter fractionation schedules (eg 15-16 fractions with 2.5-2.67 Gy single dose) have comparable efficacy and safety.
  - These data are not fully validated in young patients and in patients with mastectomy and/or additional regional irradiation.

Patients with unresectable disease

- Patients with disease becoming resectable after primary systemic therapy should receive surgery then RT.
- Where disease remains unresectable, RT (50 Gy) to regions with a high likelihood of subclinical disease, with boost (up to 60-70 Gy) to all sites of macroscopic disease is recommended.
- Regular evaluation to assess the possibility of resection after 45-50 Gy is advised.
- If relevant, a CT scan taken in the treatment position prior to primary systemic therapy may improve later localisation of target volumes.

Non-invasive carcinoma (intraepithelial neoplasia)

- WBRT is recommended for the majority of women with DCIS.
- Total mastectomy with clear margins is curative in DCIS and PMRT is not recommended.
- RT is not warranted for lobular neoplasia, with the exception of the pleomorphic subtype.

Palliative radiotherapy

- 8 Gy single fraction for most bone metastases for relief of pain.
- 20 Gy in 5 daily fractions of 4 Gray given in 1 week may be used for sites such as cervical spine, meningeal disease and nodal masses.
- 36 Gray in 6 fractions of 6 Gray once or twice weekly, given in 6 weeks for fungating primary tumours, especially in frail patients.

**NB:** multiple options exists, determined by life expectancy, performance status and frailty of patients, waiting time, etc.
Treatment break
- The deleterious effect of treatment break is recognised, avoidance of breaks is an important consideration for all radiotherapy departments.
- If break occurs, it should be compensated.
- Treatment break < 5 days should be compensated with 0.6 Gy daily for the duration of break in treatment.

Breast Cancer Chemotherapy Guidelines

Who
- Chemotherapy should be administered in dedicated chemotherapy centres and only by expert and appropriately trained medical personnel which includes (but not limited to):
  o Doctors: surgical oncologist, radiation oncologist, medical oncologist, general surgeons, internal medicine doctors, family practice doctors, general practitioners.
  o Nurses: Trained Oncology nurses; experienced with over 3-5 years of experience.
  o Pharmacists: Trained Oncology Pharmacists; experienced with over 3-5 years experience.
  o Others – with appropriate training and/or requisite 3-5 years experience.
  o All of whom should be trained in the appropriate storage handling, monitoring effects and safe administration of chemotherapeutic agents.
  o All chemotherapy administration should follow a formal institutional SOP for chemotherapy administration.

Where
- All chemotherapy should be administered in a properly registered health care facility (within the laws and regulations of the location of the health care facility) with immediate availability of emergency care in case any life-threatening chemotherapy complications occur.
- Ability to summon ambulance services will suffice.
- The most senior doctor should evaluate patient every 2-3 cycles, especially in neo-adjuvant setting. This will help guide therapy.
When

- Chemotherapy should be administered (if indicated) within 4-6 weeks of definitive surgical therapy.
- In patients whose treatment will require combination chemotherapy, hormonal therapy, biological therapy and radiation; chemotherapy should be administered prior to radiation.
- Care should be taken on the timing and/or combination of anthracyclines and trastuzumab, which can precipitate severe/irreversible cardiac damage.
- Chemotherapy should not be administered with selective estrogen receptor modulators like tamoxifen or aromatase inhibitors.
- Radiation therapy should be started after the systemic effects have resolved and the patient has fully recovered functional status.

Adjuvant Systemic Treatment

- Treatment choice should be based on the predicted sensitivity to treatment types, the benefit from their use and an individual’s risk of relapse and should incorporate the treatment sequelae, patients’ biological age, general health status, comorbidities and preferences.
- Treatment should start within 2-6 weeks after surgery
  - Efficacy decreases with administration >12 weeks after surgery.
- The most frequently used regimens contain anthracyclines and/or taxanes, although CMF may be used in selected patients.
  - 4 cycles of doxorubicin and cyclophosphamide are considered to be equivalent to 6 cycles of CMF
- The addition of taxanes improves the efficacy of chemotherapy but increases non-cardiac toxicity.
- Non-anthracycline, taxanes-based regimens, such as 4 cycles of docetaxel and cyclophosphamide, may be an alternative for selected patients, for example, those at risk of cardiac complications.
- The routine use of platinum compounds in the adjuvant setting cannot be recommended.
- Chemotherapy is usually administered for 12-24 weeks (4-8 cycles).
- The use of dose-dense schedules (with granulocyte colony-stimulating factor support) should be considered, particularly in highly proliferative tumours.
Elderly Patients

- Treatment decisions should be based on biological rather than formal age and “fit” elderly patients should receive identical treatments to their younger counterparts.
- A standard multidrug regimen should be used with doses of drugs whenever feasible.
- In frail elderly patients, single-agent pegylated liposomal doxorubicin and metronomic cyclophosphamide plus methotrexate is feasible and demonstrates similar activity, although efficacy compared with standard chemotherapy is not known.

Chemotherapy:

Lines of therapy suggestions: all node+ → taxane. Trastuzumab is always used in HER+ disease for 12 months total. Any of these therapies can be used in a neoadjuvant fashion however all therapy should be completed prior to surgical management and evaluation.
Add taxane to all node positive disease.

Adjuvant Therapy

<table>
<thead>
<tr>
<th>Adjuvant therapy – ER+, PR+, HER+: node negative/node positive</th>
<th>Adjuvant therapy – ER+, PR+, HER-: node negative/node positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide + anthracycline + trastuzumab +/- taxane x 4-6 cycles</td>
<td>Cyclophosphamide + anthracycline +/-taxane x 4-6 cycles</td>
</tr>
<tr>
<td>Platinum + taxane + trastuzumab x 4-6 cycles either regimen followed by hormonal therapy</td>
<td>Cyclophosphamide + taxane x 4-6 cycles either regimen followed by hormonal therapy</td>
</tr>
</tbody>
</table>
### Adjuvant Therapy

<table>
<thead>
<tr>
<th>Adjuvant therapy – ER-, PR-, HER-: node negative/node positive</th>
<th>Adjuvant therapy – ER-, PR-, HER+: node negative/node positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cyclophosphamide + anthracycline +/-taxane x 4-6 cycles</td>
<td>• Cyclophosphamide + anthracycline + trastuzumab x 4-6 cycles</td>
</tr>
<tr>
<td>• platinum + taxane x 4-6 cycles</td>
<td>• Cyclophosphamide + taxane + trastuzumab x 4-6 cycles do not give anthracycline concurrently with trastuzumab</td>
</tr>
</tbody>
</table>

### Late Stage Disease Therapy

<table>
<thead>
<tr>
<th>Late stage disease therapy (III/IV) – ER+, PR+, HER-/+</th>
<th>Late stage disease therapy (III/IV) – ER-, PR-, HER-/+</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hormonal therapy is the first line – know menopausal status</td>
<td>• Single agent should be the first chemotherapy – taxane or capecitabine +/- trastuzumab</td>
</tr>
<tr>
<td>• single agent should be the first chemotherapy – taxane or capecitabine</td>
<td>• Cyclophosphamide +/- anthracycline +/- taxane x unknown - cycles</td>
</tr>
<tr>
<td>• Cyclophosphamide +/-anthracycline x unknown - cycles</td>
<td>• Platinum+/-taxane x unknown cycles</td>
</tr>
<tr>
<td>• Cyclophosphamide +/-taxane x unknown cycles</td>
<td></td>
</tr>
</tbody>
</table>
Early Stage Disease Therapy

Early stage disease – node+/-, ER+, PR+, HER+/- (indigent)

i. No role for 9 weeks of trastuzumab
ii. Standard of care is one year of trastuzumab
iii. Consider – CMF – old regimen + much less expensive

- Post Chemotherapy, monitor patients every 3-4 months for 24 months, then every 6 months for another 2 years, then annually.
- 2nd opinion evaluation or guidance from nearby specialized centre is always recommended.
- Do not assume a patient cannot afford a specific intervention. Offer it and let the patient/family decline before choosing a less optimal therapeutic intervention for logistic/financial reasons.
- Be cognizant of cumulative doses of anthracyclines in the above regimen. Periodically monitor EF before, during and after trastuzumab and other agents.
- In locally advanced and large operable tumours, neoadjuvant systemic therapy may reduce the extent of surgery required.
- The whole planned course of systemic therapy (except Endocrine therapy ET) should be delivered pre-operatively, to increase the probability of achieving a pathological complete response (pCR)
- A sequential regimen of anthracyclines and taxanes is recommended for the vast majority of patients.
- After delivery of 4-8 cycles of anthracyclines and taxanes, no additional chemotherapy should be administered in the adjuvant setting.
- Advanced breast cancer should be accorded the option of neo-adjuvant therapy.
**ENDOCRINE THERAPY (ET)**

ET is indicated in all patients with detectable ER expression (≥ 1% of invasive cancer cells) irrespective of the use of chemotherapy and / or targeted therapy.

**Premenopausal Patients**

- Tamoxifen 20 mg/day for 5-10 years is a standard.
- Patients becoming post-menopausal during the first 5 years of tamoxifen can switch to the aromatase inhibitor (AI).
- A combination of ovarian ablation and tamoxifen in ER-positive patients can be used as an alternative to cyclophosphamide/ methotrexate/fluorouracil (CMF)-type chemotherapy.
- Ovarian suppressive treatment is generally administered for 2-5 years.

In patients with stage 1 or 2 disease desirous of childbearing post treatment

- Goserelin subcute 3.6mg (monthly) for 3 – 5 years
- This is withdrawn 6 months prior to period of planned pregnancy, patient is monitored closely during pregnancy and allowed to breastfeed for 6 months
- After a total of 24 months post discontinuation of Goserelin, patient is recommenced on tab Tamoxifen 20mg daily
- Aromatase inhibitor can also be used after attaining menopause.
- While on Goserelin, patient must have intra uterine contraceptive device (IUCD) in place.
### Post-Menopausal

- Patients with age >60 years
- Amenorrhea for more than 12 months in the absence of chemotherapy (not induced by chemotherapy)
- Biochemical evidence of menopause
- Patient may require bisphosphonate to manage osteoporosis

### Post-Menopausal Patients

- Aromatase inhibitors (AIs) and tamoxifen are valid options
- AIs can be used upfront, after 2-3 years of tamoxifen (non-steroidal AI and exemestane in both cases) or as extended adjuvant therapy after 5 years of tamoxifen (letrozole and anastrozole).
- There is no benefit for routine AI use >5 years.
- Caution should be exercised when using tamoxifen in patients with conditions predisposing to thromboembolic complications and endometrial hyperplasia.
- Adequate calcium and vitamin D3 intake are essential in patients undergoing ovarian suppression and / or treated with AI and periodic assessment of bone mineral density should be conducted.
- In neoadjuvant setting in post-menopausal patients, pre-surgery ET is generally given for 4-8 months, or until maximum response, and continued post-operatively.

### Ovarian Ablation For Premenopausal Patients

- Bilateral oophorectomy
- Ovarian ablation using ionizing radiation (pelvic radiotherapy)
- Chemotherapy induced

### Bisphosphonates

- Prophylactic use of Bisphosphonates can prolong disease-free survival and breast cancer-specific survival in women with low oestrogen status (post-menopause, patients on AIs).
- Bisphosphonates can reduce the risk of skeletal complications in patients with treatment-related bone loss.
HER2-Directed Therapy

- It is indicated in patients with tumour with over-expression of HER2/neu 3+
- Trastuzumab is approved in patients with node-positive disease and in node-negative disease with tumours >1 cm.
  - It can also be considered for patients with N0 tumours <1 cm, particularly in ER-negative disease.
- In line with the new American Society of Clinical Oncology (ASCO) HER2 guidelines, HER2-targeted therapy may also be considered if a HER2 test result is equivocal
- A 1-year treatment duration is standard for trastuzumab.
- Patient selection should be based on baseline cardiac function and 3-4 months monitoring of cardiac function during treatment is recommended.
- Trastuzumab should not be routinely administered concomitantly with anthracyclines, but combination with taxanes, RT and ET is safe.
REFERENCES

1. European Society for Medical Oncology (ESMO)
2. American Society of Clinical Oncology (ASCO)
3. National Comprehensive Cancer Network (NCCN)
STOP CANCER