Breast Cancer – Invasive

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NOTE: Consider clinical trials as treatment options for eligible patients.

INITIAL MULTIDISCIPLINARY EVALUATION

- Pathology review2,3
- Bilateral diagnostic mammography
- History and Physical
- CBC, platelets, liver function tests (total bilirubin, alkaline phosphatase, transaminases), creatinine
- Diagnostic imaging of breast and regional nodal basins with FNA of suspicious nodes
- In patients with clinical suspicion of distant metastasis body imaging4 recommended, consider for clinical stage Iib and III
- Consider need for genetic counseling, fertility preservation, and pregnancy testing
- Pre-operative lymphedema education and screening

CLINICAL STAGING

Clinical Stage I

Candidate for breast conservation5 at presentation?

Yes

Breast conservation therapy6 with sentinel6 lymph node (SLN) surgery

Consider neoadjuvant chemotherapy8 for biologically aggressive tumors when appropriate. Confirm placement of radio-opaque markers.9

Total mastectomy with SLN6 surgery with or without reconstruction7

Total mastectomy with axillary lymph node surgery

Breast conservation therapy5 with axillary surgery11

Breast conservation therapy5 with axillary lymph node surgery with or without reconstruction7 or

Total mastectomy with axillary lymph node surgery with or without reconstruction7 or

Total mastectomy with SLN6 surgery with or without reconstruction7

No

Breast conservation therapy5 with axillary surgery11

Consider neoadjuvant chemotherapy8 for biologically aggressive tumors when appropriate. Confirm placement of radio-opaque markers.9

Total mastectomy with axillary lymph node surgery

Breast conservation therapy5 with axillary lymph node surgery with or without reconstruction7 or

Total mastectomy with axillary lymph node surgery with or without reconstruction7 or

Total mastectomy with SLN6 surgery with or without reconstruction7

Surgery

See Page 2, Post-Surgery

See Page 3

See Page 2, Post-Surgery

1There are special circumstances in which these guidelines do not apply. These include, but are not limited to:
- Sarcoma of the breast
- Lymphoma of the breast
- Patients with lupus and scleroderma
- Special histologies (i.e., tubular, medullary, pure papillary, or colloid)

2Pathology Review to include:
- Tumor size
- Composite histologic grade
- HER2
- Margin status
- Lympathic/Vascular invasion
- Size of metastasis
- Size of lymph node


4Body imaging: CT abdomen, bone scan, chest x-ray preferred for initial imaging. CT chest optional. PET-CT for inflammatory breast cancer.

5Candidates for breast conservation therapy:
- unicentric disease
- tumor to breast size ratio allows for acceptable cosmetic result
- Negative margins
- resolution of any skin edema after systemic therapy
- no evidence of diffuse calcifications on mammogram
- No contraindication to radiotherapy

6Surgeons with an established record of lymphatic mapping experience for breast cancer (a minimum of 20 cases with an identification rate of greater than 85% and a false negative rate of less than 5%) may consider sentinel lymph node surgery as the initial and primary means of evaluating nodal status for selected patients who are clinically node negative.

7For patients with stage II disease requiring post-mastectomy radiation, consider delayed reconstruction. For patients with stage III disease, delayed reconstruction is preferred.

8See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options

9Radio-opaque markers should be placed as close to initiation of therapy as possible if not done at time of diagnosis.

10See Page 11 for Endocrine Systemic Adjuvant Therapy Options

11Candidates for limited axillary surgery with a prior biopsy proved axillary lymph node: documented removal of the prior biopsied and clipped lymph node demonstrating no metastases using sentinel lymph node dissection with targeted axillary dissection to ensure that lymph node with prior documented carcinoma is removed and tested.
Breast Cancer – Invasive

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NOTE: Consider clinical trials as treatment options for eligible patients.

PATHOLOGICAL STAGING

POST-SURGERY

Meets Z0011 criteria? Yes No

Completion Axillary Lymph Node Dissection (ALND)

No further axillary surgery

Tumor less than or equal to 0.5 cm

Yes

No

Tumor greater than 0.5 to 1 cm

Positive Nodes?

Yes

No

Tumor greater 1 cm

See Page 4 For Radiotherapy Options

ADJUVANT THERAPY FOLLOWING SURGERY AS LOCAL TREATMENT

- Adjuvant chemotherapy with weekly anthracycline/taxane-based regimen
- Anti-HER2 based therapy regimen if HER2 positive
- Adjuvant endocrine therapy if tumor is hormone receptor positive

- Consider endocrine therapy if tumor is hormone receptor positive
- Anti-HER2 based therapy if HER2 positive (consider weekly paclitaxel as chemotherapy backbone)

- Consider adjuvant chemotherapy for adverse prognostic features
- Use anti-HER2 based therapy for HER2 positive disease (consider weekly paclitaxel as chemotherapy backbone)
- Adjuvant endocrine therapy if tumor is hormone receptor positive
- Consider multi-gene prognostic assays, see Appendix B

- Consider adjuvant chemotherapy when appropriate
- Anti-HER2 based therapy if HER2 positive
- Adjuvant endocrine therapy if tumor is hormone receptor positive
- Consider multi-gene prognostic assays, see Appendix B

1 There are special circumstances in which these guidelines do not apply. These include, but are not limited to:
- Sarcoma of the breast
- Lymphoma of the breast
- Patients with lupus and scleroderma
- Patients with limited life expectancy
- Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
- Cancer during pregnancy
- Lymphovascular invasion (LVI), triple receptor negative, High-grade 3.
- Tumors of favorable histology less than 3.0 cm (tubular, mucinous) can be considered lower risk and treated appropriately.

2 Z0011 criteria: Clinical T1 or T2, N0, M0, lumpectomy and sentinel lymph node surgery, and tumor positive sentinel node (up to two nodes positive on sentinel node surgery) planned for whole breast irradiation and systemic therapy.

3 See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options

4 See Page 11 for Endocrine Systemic Adjuvant Therapy Options

5 Cardiac evaluation at baseline and as clinically indicated

6 Lymphovascular invasion (LVI), triple receptor negative, High-grade 3.
Breast Cancer – Invasive

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Clinical Stage/Presentation

- Assess tumor size at least every 6 weeks and at completion of systemic treatment with physical exam
- Imaging with mammogram and/or ultrasound at completion of systemic treatment, if undergoing breast conserving surgery
- Consider mid-treatment ultrasound or other imaging at any point for clinical suspicion of disease progression

Breast Conservation Therapy Candidate?

- If candidate for breast conservation therapy, place radiopaque markers
- If candidate for breast conservation therapy following neoadjuvant therapy, place radiopaque markers

Primary Systemic Therapy

- Neoadjuvant systemic chemotherapy OR neoadjuvant endocrine therapy as clinically indicated
- If candidate for breast conservation therapy following neoadjuvant therapy, place radiopaque markers

Chemotherapy (or hormone therapy options if appropriate) for HER2-negative breast cancer

- If clinically node negative at diagnosis, proceed with sentinel node surgery followed by axillary node surgery if sentinel node is positive
- If clinically node positive, confirmed by needle biopsy proceed with axillary node dissection or if limited axillary nodal disease is no longer evident, consider SLN biopsy with documented clip removal and if no metastases proceed to radiotherapy without axillary lymph node dissection

Breast Conserving Surgery

- See Pathological Findings on Page 4

Local Treatment

1. Cardiac evaluation at baseline and as clinically indicated
2. Surgeons with an established record of lymphatic mapping experience for breast cancer (a minimum of 20 cases with an identification rate of greater than 85% and a false negative rate of less than 5%) may consider sentinel lymph node dissection as the initial and primary means of evaluating nodal status for selected patients who are clinically node negative.
3. Candidates for breast conservation therapy:
   - unicentric disease
   - tumor to breast size ratio allows for acceptable cosmetic result
   - no evidence of diffuse calcification on mammogram
   - resolution of any skin edema after systemic therapy
   - margins greater than or equal to 2 mm, No contraindication to radiotherapy
4. Patients with stage I disease requiring post-mastectomy radiation, consider delayed reconstruction. For patients with stage III disease, delayed reconstruction is preferred.
5. Candidates for breast conservation therapy:
   - Sarcoma of the breast
   - Lymphoma of the breast
   - Patients with lupus and scleroderma
   - Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
   - Patients with limited life expectancy
   - Cancer during pregnancy
6. See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options
7. See Page 11 for Endocrine Systemic Adjuvant Therapy Options. Higher risk patients could be considered for post-operative chemotherapy.
8. Candidate reconstruction and plastic surgery consult

NOTE: Consider clinical trials as treatment options for eligible patients.
NOTE: Consider clinical trials as treatment options for eligible patients.

<table>
<thead>
<tr>
<th>PATHOLOGICAL FINDINGS</th>
<th>TREATMENT</th>
<th>SURVEILLANCE</th>
</tr>
</thead>
</table>
| Stage I - II disease, with 0-3 involved lymph node(s) | • Whole breast radiotherapy\(^2\) for breast conservation therapy with or without regional lymphatics.  
• Consider partial breast radiotherapy for tumors less than or equal to 3 cm and negative lymph nodes.  
• XRT consult for consideration of chest wall radiotherapy with or without regional lymphatics for patients with total mastectomy and tumor greater than 5 cm or any positive lymph nodes. | • Physical exam at least every 6 months for 5 years, then annually after year 5  
• If breast conservation therapy, mammogram of treated breast at 6-12 months, then annually  
• Annual gynecologic exam, if receiving tamoxifen  
• Assess bone health (See Breast Cancer Survivorship: Bone Health Algorithm)  
• Encourage age appropriate cancer and general health guidelines  
• Educate, screen and refer for lymphedema management as needed |
| Stage III disease or 4 or more involved lymph nodes | • Post mastectomy radiotherapy to chest wall and regional lymphatics  
• Whole breast radiotherapy\(^2\) with regional lymphatics for breast conservation therapy | • Endocrine therapy\(^3\) for hormone receptor positive tumors sequential after chemotherapy\(^2\) and local therapy  
• Trastuzumab to complete one year if HER2-positive tumor |

\(^1\) There are special circumstances in which these guidelines do not apply. These include, but are not limited to:
• Sarcoma of the breast  
• Lymphoma of the breast  
• Patients with lupus and scleroderma  
• Patients with limited life expectancy  
• Special histologies (i.e., tubular, medullary, pure papillary, or colloid)  
• Cancer during pregnancy

\(^2\) Radiotherapy for BCT and post-mastectomy radiotherapy, are generally delivered at completion of chemotherapy. For early stage node negative patients, radiotherapy may be delivered before or after chemotherapy.

\(^3\) See Page 11 for Endocrine Systemic Adjuvant Therapy Options

\(^4\) See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options
Breast Cancer – Invasive

NOTE: Consider clinical trials as treatment options for eligible patients.

EVALUATION FOR METASTASIS

- Biopsy to confirm metastatic disease, histology, ER/PR and HER2 status
- Bone Scan
- CT, PET/CT or MRI to encompass chest, abdomen and pelvis
- Consider chest x-ray if no CT is performed
- Complete blood count and chemistries including renal and liver function
- Consider CA15-3 as an adjunctive test for monitoring response to therapy

Distant metastasis

- ER positive and bone or soft tissue metastasis only or
- Limited visceral disease

Post-menopausal endocrine options

- Non-steroidal aromatase inhibitors with or without fulvestrant (if no prior aromatase inhibitor or tamoxifen)
- Tamoxifen (if no prior tamoxifen)
- Letrozole with or without Palbociclib

Second line therapy:

- Exemestane with or without everolimus
- Fulvestrant with or without Palbociclib
- Other endocrine treatments:
  - Estrogens
  - Progestins
  - Androgens

Disease response or clinical benefit?

继续 current treatment until progressive disease or maximum benefit can include:

- Anthracyclines based upon lifetime exposure to anthracyclines
- Capecitabine
- Carboplatin
- Cisplatin
- Erbulin
- Gemcitabine
- Ixabepilone
- Taxanes
- Vinorelbine

Fail to respond to 3 sequential regimens or Zubrod status greater than or equal to 3, discontinue chemotherapy

Palliative care

NOTE: All patients with bone metastases and life expectancy greater than 12 weeks should consider after dental evaluation: a bisphosphonate (creatinine clearance is 30 or greater) or denosumab.
Breast Cancer – Invasive

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NOTE: Consider clinical trials as treatment options for eligible patients.

TREATMENT FOR METASTASIS

Continued from previous page

HER2 positive by either Immuno-histochemistry 3+ or FISH

If no prior trastuzumab or greater than 1 year since adjuvant trastuzumab:
- Taxane chemotherapy plus trastuzumab plus pertuzumab
- Alternate therapy based on hormone receptor status if not candidate for anti-HER2 or cytotoxic therapy
  - If less than 6 to 12 months from adjuvant trastuzumab or if prior (neo)adjuvant pertuzumab:
    - T-DM1 (Ado-trastuzumab emtansine)
    - Consider HER2 directed therapies

Progressive disease

Proceed to one of the following regimens, and can follow by another regimen below if the patient continues to be a candidate for antineoplastic therapy:
- T-DM1 if not previously given
- Capecitabine plus lapatinib
- Trastuzumab plus lapatanib
- Trastuzumab plus other chemotherapy (preferred options - Vinorelbine, gemcitabine, capecitabine, eribulin)
- Chemotherapy or hormonal therapy (if ER or PR positive)
- Consider HER2 directed therapies

Palliative care

NOTE: All patients with bone metastases and life expectancy greater than 12 weeks should consider after dental evaluation: a bisphosphonate (creatinine clearance is 30 or greater) or denosumab.

1There are special circumstances in which these guidelines do not apply. These include, but are not limited to:
- Sarcoma of the breast
- Lymphoma of the breast
- Patients with lupus and scleroderma
- Patients with limited life expectancy
- Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
- Cancer during pregnancy

1See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options
2See Appendix C - Recurrent or Metastatic Breast Cancer Treatment Options

ER = Estrogen Receptor  FISH = Fluorescence In Situ Hybridization
HER2 = Human Epidermal Growth Factor Receptor 2
PR = Progesterone Receptor

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**EVALUATION FOR LOCAL RECURRENCE**

Ipsilateral breast/chest wall recurrence or ipsilateral regional recurrence without distant metastasis

- Biopsy to confirm recurrence with:
  - Consider body imaging for invasive recurrence
  - If intact breast, bilateral diagnostic mammogram
  - Ultrasound of affected breast including regional nodal basins
  - Consider preoperative systemic therapy
  - Consider biomarkers\(^2\)

- Consider systemic therapy\(^3\)
- Consider pre-operative chemotherapy\(^3\)
- Consider chemotherapy

**TREATMENT FOR RECURRENCE**

- **Total mastectomy with lymph node surgery** consider sentinel lymph node surgery if clinically node negative
- Consider systemic therapy\(^3\)
- Consider pre-operative chemotherapy\(^3\)

- **Breast conservation therapy** with margin assessment, or
- **Total mastectomy; lymph node surgery; radiation therapy consult**

- **Wide local excision (WLE) with margin assessment**
- Consider neoadjuvant systemic therapy prior to WLE

- **Surgical resection with margin assessment**
  - Consider additional systemic therapy
  - **Surveillance and endocrine therapy if hormone receptor positive**

- **Radiotherapy to chest wall and regional lymphatics**:
  - if no previous radiation

- **Persistent disease?**
  - **Consider systemic therapy**
  - **Consider pre-operative chemotheraphy\(^1\)**

**NOTE:** Consider clinical trials as treatment options for eligible patients.

---

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- Sarcoma of the breast
- Lymphoma of the breast
- Patients with limited life expectancy
- Cancer during pregnancy


\(^3\) See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options

\(^4\) See Page 11 for Endocrine Systemic Adjuvant Therapy Options

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### Breast Cancer – Invasive

#### Inflammatory Breast Cancer

**TREATMENT**

- **HER2 negative:**
  - Neoadjuvant doxorubicin and taxane-based chemotherapy
  - Consider clinical trial(s)

- **HER2 positive:**
  - Dual anti-HER2 therapy containing regimen with chemotherapy
  - Consider clinical trial(s)

#### Stage III

**Operable?**

- Yes
  - Multidisciplinary evaluation of response
  - Operable?
    - Yes
      - Modified radical mastectomy
      - Radiotherapy to chest wall and regional lymphatics, if no previous radiation
      - Adjuvant endocrine therapy if tumor is hormone receptor positive
    - No
      - Additional systemic therapy with or without radiotherapy
      - Multidisciplinary evaluation of response
      - Operable?
        - Yes
          - HER2+ maintenance therapy
        - No
          - HER2 positive
            - Hormone receptor positive
              - Adjuvant endocrine therapy
            - No
              - Additional systemic therapy
                - Symptom management (supportive care)
                - Consider clinical trial(s)

#### Stage IV (de novo)

**Operable?**

- No
  - Additional systemic therapy
  - Symptom management (supportive care)
  - Consider clinical trial(s)

### STAGING

- **HER2 negative:**
  - Neoadjuvant doxorubicin and taxane-based chemotherapy
  - Consider clinical trial(s)

- **HER2 positive:**
  - Dual anti-HER2 therapy containing regimen with chemotherapy
  - Consider clinical trial(s)

### Multidisciplinary Evaluation of Response

- **Operable?**
  - Yes
    - Modified radical mastectomy
    - Radiotherapy to chest wall and regional lymphatics, if no previous radiation
    - Adjuvant endocrine therapy if tumor is hormone receptor positive
  - No
    - Additional systemic therapy with or without radiotherapy
    - Multidisciplinary evaluation of response
    - Operable?
      - Yes
        - HER2+ maintenance therapy
      - No
        - HER2 positive
          - Hormone receptor positive
            - Adjuvant endocrine therapy
          - No
            - Additional systemic therapy
              - Symptom management (supportive care)
              - Consider clinical trial(s)

### Diagnostic Workup:

- Medical history and physical
- Obtain photograph to establish baseline clinical appearance and follow up medical photography for a treatment response documentation.
- PET scan/CT scan - If PET/CT scan not possible: neck (if clinically indicated) in addition to chest/abdominal pelvic CT with bone scan.
- Obtain skin biopsy and ultrasound-guided core biopsy of the tumor (random biopsies if mass not present)

### Additional Systemic Therapy

- Additional systemic therapy
- Symptom management (supportive care)
- Consider clinical trial(s)

### Her2+ Maintenance Therapy

- HER2+ maintenance therapy

### HER2 Positive

- HER2 positive
  - Hormone receptor positive
    - Adjuvant endocrine therapy
  - No
    - Additional systemic therapy
      - Symptom management (supportive care)
      - Consider clinical trial(s)

### Adjuvant Endocrine Therapy

- Adjuvant endocrine therapy

### Additional Systemic Therapy

- Additional systemic therapy

### Symptom Management (Supportive Care)

- Symptom management (supportive care)

### Consider Clinical Trial(s)

- Consider clinical trial(s)

### Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options

- See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options

### Endocrine Systemic Adjuvant Therapy Options

- See Page 11 for Endocrine Systemic Adjuvant Therapy Options

### Sarcoma of the Breast

- Patients with lupus and scleroderma

### Lymphoma of the Breast

- Patients with limited life expectancy

### Special Histologies

- Cancer during pregnancy

### NOTE:

- Consider clinical trials as treatment options for eligible patients.

---

1 There are special circumstances in which these guidelines do not apply. These include, but are not limited to:

- Sarcoma of the breast
- Lymphoma of the breast
- Patients with lupus and scleroderma
- Patients with limited life expectancy
- Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
- Cancer during pregnancy

2 Diagnostic Workup:

- Obtain photograph to establish baseline clinical appearance and follow up medical photography for a treatment response documentation.
- PET scan/CT scan - If PET/CT scan not possible: neck (if clinically indicated) in addition to chest/abdominal pelvic CT with bone scan.
- Obtain skin biopsy and ultrasound-guided core biopsy of the tumor (random biopsies if mass not present)

3 Evaluate pathology response:

- Minimal residual disease or pathologic complete response, age over 45 and negative margins, daily radiation to 66 Gy (2 Gy/fraction, primary fields to 50).
- Significant residual disease, age less than 45 or close or positive margins, twice daily radiation to 66 Gy (1.5 Gy per fraction, primary fields to 51).

4 See Page 11 for Endocrine Systemic Adjuvant Therapy Options

5 See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options
APPENDIX A: Neoadjuvant/Adjuvant Chemotherapy Options

<table>
<thead>
<tr>
<th>HER-2 negative disease³</th>
<th>Preferred regimens:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Doxorubicin and cyclophosphamide (AC) either every 3 weeks or every 2 weeks (dose dense) followed or preceded by weekly paclitaxel x 12, or dose dense paclitaxel every 2 weeks</td>
</tr>
<tr>
<td></td>
<td>• Fluorouracil, doxorubicin, and cyclophosphamide (FAC) followed or preceded by weekly paclitaxel</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HER-2 positive disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred regimens:</td>
</tr>
<tr>
<td>• Doxorubicin and cyclophosphamide (AC) followed by paclitaxel plus trastuzumab and pertuzumab cycles/ days vary</td>
</tr>
<tr>
<td>• Docetaxel, carboplatin, trastuzumab (TCH) plus pertuzumab</td>
</tr>
<tr>
<td>• For Stage II or higher, consider addition of pertuzumab with chemotherapy portion of regimen.</td>
</tr>
</tbody>
</table>

Other regimens⁴:

- Weekly paclitaxel plus trastuzumab (for low-risk disease, such as Stage I)

APPENDIX B: Clinical Scenarios Requiring Individualized Therapy

- Brain metastases
- Ureteral obstruction
- Leptomeningeal disease
- Impending pathologic fracture
-choroid metastases
- Pathologic fracture
- Extensive local-regional disease
- Pleural effusion
- Cord compression
- Pericardial effusion
- Plexopathy/radiculopathy
- Biliary obstruction
- Superior vena cava syndrome
- Stage IV NED
- Oligometastasis³
- Pregnancy

¹There are special circumstances in which these guidelines do not apply. These include, but are not limited to:
- Sarcoma of the breast
- Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
- Lymphoma of the breast
- Patients with lupus and scleroderma
- Cancer during pregnancy
- Patients with limited life expectancy

²Refer to NCCN Guidelines Version 3.2015 for specific doses and number of cycles.

³Optimal duration of adjuvant HER-2 therapy is one year.

⁴May consider other neoadjuvant/adjuvant regimens per NCCN guidelines

⁵Oligometastases – selected patients with isolated metastatic breast cancer may be considered for definitive treatment.
### APPENDIX C: Recurrent or Metastatic Breast Cancer Treatment Options

<table>
<thead>
<tr>
<th>Preferred Single Agents:</th>
<th>Taxanes</th>
<th>Anti-metabolites</th>
<th>Other microtubule inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthracyclines</td>
<td>Doxorubicin, Pegylated liposomal doxorubicin</td>
<td>Paclitaxel</td>
<td>Capecitabine, Gemcitabine</td>
</tr>
<tr>
<td>Taxanes</td>
<td>Paclitaxel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-metabolites</td>
<td>Capecitabine, Gemcitabine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other microtubule inhibitors</td>
<td>Vinorelbine, Eribulin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Single Agents:</th>
<th>Docetaxel, Albumin-bound paclitaxel</th>
<th>Cisplatin, Epirubicin, Ixabepilone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Docetaxel</td>
<td>Cisplatin</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Albumin-bound paclitaxel</td>
<td>Epirubicin</td>
</tr>
<tr>
<td>Other Single Agents</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combination Chemotherapy Regimens:</th>
<th>Docetaxel and capecitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAC/CAF (cyclophosphamide, doxorubicin, and fluorouracil)</td>
<td>Gemcitabine and paclitaxel</td>
</tr>
<tr>
<td>FEC (fluorouracil, epirubicin, and cyclophosphamide)</td>
<td>Gemcitabine and carboplatin</td>
</tr>
<tr>
<td>AC (doxorubicin and cyclophosphamide)</td>
<td>Ixabepilone/capcitabine</td>
</tr>
<tr>
<td>EC (epirubicin and cyclophosphamide)</td>
<td></td>
</tr>
<tr>
<td>CMF (cyclophosphamide, methotrexate, and fluorouracil)</td>
<td></td>
</tr>
</tbody>
</table>

**First-line Regimens for HER2-positive disease**: (trastuzumab naïve patients or those who recurred after 6 to 12 months after adjuvant trastuzumab)

- Pertuzumab plus trastuzumab and docetaxel
- Pertuzumab plus trastuzumab and paclitaxel

**Other Options, but should not be considered preferred first options:**

- Trastuzumab with docetaxel
- Trastuzumab with paclitaxel with or without carboplatin
- Trastuzumab with vinorelbine
- Trastuzumab with capcitabine

**Regimens for trastuzumab-exposed HER2-positive disease**:  

- Ado-trastuzumab emtansine (T-DM1) for recurrence (6 to 12 months from adjuvant trastuzumab)
- Lapatinib plus capcitabine
- Trastuzumab plus capcitabine
- Trastuzumab plus lapatinib without cytotoxic therapy
- Trastuzumab plus other agents

---

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- Sarcoma of the breast
- Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
- Lymphoma of the breast
- Cancer during pregnancy
- Patients with limited life expectancy

2After maximal benefit achieved with chemotherapy, consider continuous anti-HER2 therapy alone, if ER or PR positive in combination with appropriate hormonal therapy (This does not apply to Ado-trastuzumab emtansine [T-DM1])
Breast Cancer – Invasive

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Endocrine Systemic Adjuvant Therapy Options

1 There are special circumstances in which these guidelines do not apply. These include, but are not limited to:
   - Sarcoma of the breast
   - Lymphoma of the breast
   - Patients with lupus and scleroderma
   - Patients with limited life expectancy
   - Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
   - Cancer during pregnancy

2 Male patients should be treated similarly to premenopausal patients. Use of aromatase inhibitors or fulvestrant should be accompanied by androgen deprivation therapy (medical/surgical).

3 Aromatase inhibitors may not be an option if the patient is intolerant, concerns over bone density or patient declines therapy.

NOTE: Consider clinical trials as treatment options for eligible patients.

**Premenopausal at diagnosis**
- Tamoxifen for 5 years with or without ovarian suppression or ablation
- Ovarian ablation plus aromatase inhibitor for at least 5 years

**Postmenopausal after initial 5 years?**
- Yes: Aromatase inhibitor for 5 years or Consider tamoxifen for an additional 5 years (10 years total)
- No: Consider tamoxifen for an additional 5 years (10 years total)

**Premenopausal at diagnosis**
- Tamoxifen for 5 years or Consider tamoxifen for up to 10 years

**Postmenopausal at diagnosis**
- Yes: Aromatase inhibitor for at least 5 years or Tamoxifen for 2-3 years followed by aromatase inhibitor to complete at least 5 years of endocrine therapy or Aromatase inhibitor for 2-3 years followed by tamoxifen to complete at least 5 years of endocrine therapy or Tamoxifen for 4 ½ to 6 years followed by aromatase inhibitor to for at least 5 years or Tamoxifen for 4 ½ to 6 years, then consider tamoxifen for an additional at least 5 years for a total of 10 years of endocrine therapy
- No: Tamoxifen for 5 years or Consider tamoxifen for up to 10 years
This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.

SUGGESTED READINGS


This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.

SUGGESTED READINGS - Continued


SUGGESTED READINGS - Continued


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**SUGGESTED READINGS – Chemotherapy Regimens for Metastatic Breast Cancer and in Combination with Transtuzumab**


This practice consensus algorithm is based on majority expert opinion of the Breast Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following breast multidisciplinary team members.

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