Breast Cancer – Invasive

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.

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

### INITIAL MULTIDISCIPLINARY EVALUATION
- Pathology review
- 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 imaging 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

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>- Breast conservation therapy&lt;sup&gt;4&lt;/sup&gt; with sentinel&lt;sup&gt;6&lt;/sup&gt; lymph node (SLN) surgery</td>
</tr>
<tr>
<td>I/II</td>
<td>- Total mastectomy with SLN&lt;sup&gt;6&lt;/sup&gt; surgery with or without reconstruction&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>II</td>
<td>- Consider neoadjuvant chemotherapy&lt;sup&gt;8&lt;/sup&gt; for biologically aggressive tumors when appropriate. Confirm placement of radio-opaque markers.&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
<tr>
<td>IIB/III</td>
<td>- Consider neoadjuvant chemotherapy&lt;sup&gt;8&lt;/sup&gt; or neoadjuvant endocrine therapy&lt;sup&gt;10&lt;/sup&gt;</td>
</tr>
<tr>
<td>IIB</td>
<td>- Confirm placement radio-opaque markers&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

### TREATMENT

- Breast conservation therapy<sup>5</sup> with sentinel<sup>6</sup> lymph node (SLN) surgery
- Total mastectomy with SLN<sup>6</sup> surgery with or without reconstruction<sup>1</sup>
- Consider neoadjuvant chemotherapy<sup>8</sup> for biologically aggressive tumors when appropriate. Confirm placement of radio-opaque markers.<sup>9</sup>
- Consider neoadjuvant chemotherapy<sup>8</sup> or neoadjuvant endocrine therapy<sup>10</sup>
- Confirm placement radio-opaque markers<sup>9</sup>
- Breast conservation therapy<sup>5</sup> with axillary surgery<sup>11</sup>
- Total mastectomy with axillary lymph node surgery with or without reconstruction<sup>7</sup> or
- Consider neoadjuvant chemotherapy<sup>8</sup> (see page 2)
- Breast conservation therapy<sup>5</sup> with SLN<sup>6</sup> surgery
- Total mastectomy with SLN<sup>6</sup> surgery with or without reconstruction<sup>7</sup>
- Consider neoadjuvant chemotherapy<sup>8</sup>

---

<sup>1</sup>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
- Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
- Tumor size
- Lymph node status
- Composite histologic grade
- HER2
- Margin status
- Extracapsular extension
- Size of metastasis

<sup>2</sup>Pathology Review to include:
- Tumor size
- Lymph node status
- Histologic type
- HER2
- Margin status
- Extracapsular extension
- Size of metastasis


<sup>4</sup>Biody imaging: CT abdomen, bone scan, chest x-ray preferred for initial imaging. CT chest optional. PET-CT for inflammatory breast cancer.

<sup>5</sup>Candidates 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

<sup>6</sup>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 surgery as the initial and primary means of evaluating nodal status for selected patients who are clinically node negative.

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

<sup>8</sup>See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options

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

<sup>10</sup>See Page 11 for Endocrine Systemic Adjuvant Therapy Options

<sup>11</sup>Candidates for limited axillary surgery with a prior biopsy proven 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.

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

### ADJUVANT THERAPY FOLLOWING SURGERY AS LOCAL TREATMENT

**PATHOLOGICAL STAGING**

**POST-SURGERY**

<table>
<thead>
<tr>
<th>Positive Nodes?</th>
<th>Tumor less than or equal to 0.5 cm</th>
<th>Tumor greater than 0.5 to 1 cm</th>
<th>Tumor greater than 1 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No further axillary surgery</td>
<td>Completion Axillary Lymph Node Dissection (ALND)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Consider endocrine therapy if tumor is hormone receptor positive</td>
<td>● Consider adjuvant chemotherapy for adverse prognostic features</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Anti-HER2 based therapy if HER2 positive</td>
<td>● Use anti-HER2 based therapy for HER2 positive disease (consider weekly paclitaxel as chemotherapy backbone)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Adjuvant chemotherapy with weekly anthracycline/taxane-based regimen</td>
<td>● Adjuvant endocrine therapy if tumor is hormone receptor positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Anti-HER2 based therapy regimen if HER2 positive</td>
<td>● Adjuvant endocrine therapy if tumor is hormone receptor positive</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td>● Consider multi-gene prognostic assays, see Appendix B</td>
</tr>
</tbody>
</table>

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. 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


7. Tumors of favorable histology less than 3.0 cm (tubular, mucinous) can be considered lower risk and treated appropriately.
Breast Cancer – Invasive

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

CLINICAL STAGE/ PRESENTATION

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

HER2 positive?

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

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

LOCAL TREATMENT

Breast conserving therapy candidate?

- 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 Conserving Surgery
- 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

Total mastectomy with nodal treatment as determined by initial nodal status:
- If clinically node negative at diagnosis, proceed with sentinel node biopsy 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

Consider reconstruction and plastic surgery consult.

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

See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options
See Page 11 for Endocrine Systemic Adjuvant Therapy Options. Higher risk patients could be considered for post-operative chemotherapy.

Candidates for breast conservation therapy:
- unicentric disease
- resolution of any skin edema after systemic therapy
- tumor to breast size ratio allows for acceptable cosmetic result
- no evidence of diffuse calcification on mammogram
- margins greater than or equal to 2 mm
- No contraindication to radiotherapy

Cardiac evaluation at baseline and as clinically indicated

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.

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

- Stage I - II disease, with 0-3 involved lymph node(s)
- Stage III disease or 4 or more involved lymph nodes

#### From local treatment

- 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.

#### 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

### TREATMENT

- 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.

- Endocrine therapy\(^3\) for hormone receptor positive tumors sequential after chemotherapy\(^2\) and local therapy
- Trastuzumab to complete one year if HER2-positive tumor

#### SURVEILLANCE

- 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

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

**EVALUATION FOR METASTASIS**

Distant metastasis<sup>1,2</sup>

- 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

HER2 negative

- ER negative or
- ER positive and extensive visceral disease or
- Symptomatic disease

HER2 positive by either Immuno-histochemistry 3+ or FISH → See Page 6

**TREATMENT FOR METASTASIS**

**Pre-menopausal endocrine options**

- Tamoxifen with or without ovarian ablation
- In premenopausal patient following ovarian ablation use post-menopausal endocrine options

**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

**Chemotherapy** until progressive disease or maximum benefit can include:

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

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

Continue current treatment until progressive disease or unacceptable toxicity then consider alternate endocrine therapy<sup>3</sup>

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.

---

<sup>1</sup>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
- Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
- Cancer during pregnancy

<sup>2</sup>See Appendix B for scenarios requiring individualized therapy.

<sup>3</sup>See Page 11 for Endocrine Systemic Adjutvant Therapy Options. Male patients should be treated similarly to premenopausal patients. Use of aromatase inhibitors or fulvestrant should be accompanied by androgen deprivation therapy (medical/surgical).

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**Breast Cancer – Invasive**

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Breast Cancer – Invasive

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

TREATMENT FOR METASTASIS

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

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

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.

HER2 positive by either Immunohistochemistry 3+ or FISH

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

Her2 positive by either Immunohistochemistry 3+ or FISH

Continued from previous page

Progressive disease

- 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

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

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

1 There are special circumstances in which these guidelines do not apply. These include, but are not limited to:
2 See Appendix A - Neoadjuvant/Adjuvant Chemotherapy Options
3 See Appendix C - Recurrent or Metastatic Breast Cancer Treatment Options

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**Breast Cancer – Invasive**

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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

**TREATMENT FOR RECURRENCE**

- Consider systemic therapy
- Consider pre-operative chemotherapy

Invasive histology?

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No (e.g. DCIS)
  - Surveillance and endocrine therapy if estrogen receptor positive

**Endocrine therapy**

- Yes
  - Consider additional systemic therapy
  - Consider endocrine therapy if hormone receptor positive
  - Consider chemotherapy

- No
  - No

**Previous chest wall radiotherapy?**

- Yes
  - Radiotherapy to chest wall and regional lymphatics, if not DCIS alone

- No
  - No

**Persistent disease?**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Previous breast radiotherapy?**

- Yes
  - Total mastectomy with lymph node surgery consider sentinel lymph node surgery if clinically node negative
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Breast intact?**

- Yes
  - Total mastectomy with lymph node surgery consider sentinel lymph node surgery if clinically node negative
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Resectable?**

- Yes
  - Total mastectomy with lymph node surgery consider sentinel lymph node surgery if clinically node negative
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Wide local excision (WLE) with margin assessment**

- Yes
  - Consider neoadjuvant systemic therapy prior to WLE

- No
  - No

**Total mastectomy with lymph node surgery**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Ultrasound of affected breast including regional nodal basins**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider body imaging for invasive recurrence**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider preoperative systemic therapy**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider biomarkers**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider systemic therapy**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider additional systemic therapy**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider endocrine therapy if hormone receptor positive**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider chemotherapy**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider systemic therapy**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider systemic therapy**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider endocrine therapy if hormone receptor positive**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

**Consider chemotherapy**

- Yes
  - Consider systemic therapy
  - Consider pre-operative chemotherapy

- No
  - No

---

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
- Special histologies (i.e., tubular, medullary, pure papillary, or colloid)
- 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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### STAGING

#### Stage III
- HER2 negative: neoadjuvant doxorubicin and taxane based chemotherapy
- HER2 positive: dual anti-HER2 therapy containing regimen with chemotherapy
- Consider clinical trial(s)

#### Stage IV (de novo)
- Single/multi-agent systemic therapy
- Symptom management (Supportive care)
- Clinical trials

### TREATMENT

#### Operable
- HER2 positive: dual anti-HER2 therapy containing regimen with chemotherapy
- Consider clinical trial(s)

#### Inflammatory Breast Cancer
- Modified radical mastectomy
- Radiotherapy to chest wall and regional lymphatics, if no previous radiation
- Adjuvant endocrine therapy if tumor is hormone receptor positive

#### HER2 positive
- HER2 maintenance therapy
- Additional systemic therapy with or without radiotherapy
- Symptom management (Supportive care)
- Consider clinical trial(s)

#### HER2 negative
- HER2 negative: neoadjuvant doxorubicin and taxane based chemotherapy
- Consider clinical trial(s)

#### Multidisciplinary evaluation of response

#### Diagnosis 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)

#### 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).

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

---

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- 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:
- 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)

---

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### APPENDIX A: Neoadjuvant/Adjuvant Chemotherapy Options

#### HER-2 negative disease

**Preferred regimens:**
- 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
- Fluorouracil, doxorubicin, and cyclophosphamide (FAC) followed or preceded by weekly paclitaxel

**Other regimens:**
- Dose-dense doxorubicin and cyclophosphamide (AC) followed or preceded by paclitaxel every 2 weeks
- Docetaxel and cyclophosphamide (TC)
- Dose-dense doxorubicin and cyclophosphamide (AC) followed or preceded by docetaxel every 3 weeks

#### HER-2 positive disease

**Preferred regimens:**
- Doxorubicin and cyclophosphamide (AC) followed by paclitaxel plus trastuzumab and pertuzumab cycles/ days vary
- Docetaxel, carboplatin, trastuzumab (TCH) plus pertuzumab
- For Stage II or higher, consider addition of pertuzumab with chemotherapy portion of regimen.

**Other regimens:**
- 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
- Oligometastasis
- Pregnancy

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

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

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

4. May consider other neoadjuvant/adjuvant regimens per NCCN guidelines.

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

### Preferred Single Agents:

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

### Other Single Agents:

- Cyclophosphamide
- Carboplatin
- Docetaxel
- Albumin-bound paclitaxel
- Cisplatin
- Epirubicin
- Vinorelbine
- Ixabepilone

### Combination Chemotherapy Regimens:

- FAC/CAF (cyclophosphamide, doxorubicin, and fluorouracil)
- FEC (fluorouracil, epirubicin, and cyclophosphamide)
- AC (doxorubicin and cyclophosphamide)
- EC (epirubicin and cyclophosphamide)
- CMF (cyclophosphamide, methotrexate, and fluorouracil)

### First-line Regimens for HER2-positive disease:

- 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 capecitabine

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

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

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1. There 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
   - Cancer during pregnancy

2. After 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

Premenopausal at diagnosis

Tamoxifen for 5 years with or without ovarian suppression or ablation

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)
- No further endocrine therapy

Ovarian ablation plus aromatase inhibitor for at least 5 years

Premenopausal at diagnosis

Tamoxifen for 5 years with or without ovarian suppression or ablation

Aromatase inhibitor an option?

Yes

- Tamoxifen for 5 years or
- Consider tamoxifen for an additional 5 years (10 years total)

No

- 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
- Tamoxifen for 2-3 years followed by aromatase inhibitor for at least 5 years or
- Aromatase inhibitor for 2-3 years followed by tamoxifen to complete at least 5 years of endocrine therapy
- 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

Postmenopausal at diagnosis

- 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
- Tamoxifen for 2-3 years followed by aromatase inhibitor for at least 5 years or
- Aromatase inhibitor for 2-3 years followed by tamoxifen to complete at least 5 years of endocrine therapy
- 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

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
- Patients with bone density concerns

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.
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SUGGESTED READINGS


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SUGGESTED READINGS - Continued


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.

Sausan Abouharb, MD
Beatriz Adrada, MD
Catherine Akay, MD
Constance Albarracin, MD
Frederick Ames, MD
Elsa Arribas, MD
Banu K. Arun, MD
Carlos Barcenas, MD
Robert C. Bast, MD
Gildy Babiera, MD
Isabelle Bedrosian, MD
Daniel J. Booser, MD
Shon Black, MD
Abenna Brewster, MD
Powel Brown, MD
Thomas Buchholz, MD
Aman U. Buzdar, MD
Abigail Caudle, MD
Mariana Chavez-Mac Gregor, MD
Hui Chen, MD
Alejandro Contreras, MD
Sarah DeSnyder, MD
Mark Dryden, MD
Mary Edgerton, MD
Barry Feig, MD
Bruno Fornage, MD
Michael Gilcrease, MD
Sharon Giordano, MD
Tamara Haygood, MD
Karen Hoffman, MD
Gabriel N. Hortobagyi, MD
Kelly K. Hunt, MD
Lei Huo, MD
Rosa Hwang, MD
Nuhad K. Ibrahim, MD
Meghan Karuturi, MD
Kimberly Koenig, MD
Savithri Krishnamurthy, MD
Henry M. Kuerer, MD, PhD
Deanna Lane, MD
Huong Le-Petross, MD
Jennifer Litton, MD
Anthony Lucci, MD
Funda Meric-Bermstam, MD
Lavinia Middleton, MD
Elizabeth Mittendorf, MD
Stacy Moulder, MD
James L. Murray, III, MD
Rashmi Murthy, MD
George Perkins, MD
Erika Resekova, MD
Merrick I. Ross, MD
Aysegul A. Sahin, MD
Lumarie Santiago, MD
Simona Shaitelman, MD
Benjamin Smith, MD
Nour Sneige, MD
Tanya Moseley, MD
Michael Stauder, MD
Eric Strom, MD
Fraser W. Symmans, MD
Welela Tereffé, MD
Mediget Teshome, MD
Alastair Thompson, MD
Debasish Tripathy, MD
Naoto T. Ueno, MD, PhD
Vicente Valero, MD
Ronald Walters, MD
Gary Whitman, MD
Wendy Woodward, MD
Yun Wu, MD
Wei Yang, MD
Amy Zhang, MD