# Breast Cancer – Metastatic Disease

Disclaimers: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other healthcare providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

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ECOG = Eastern Cooperative Oncology Group  
HER = human epidermal growth factor receptor  
HR = hormone receptor
Note: Consider Clinical Trials as treatment options for eligible patients.

EVALUATION FOR METASTASIS

- Biopsy to confirm metastatic disease, histology, ER/PR and HER2 status
- CT with contrast, PET/CT, or MRI to encompass chest, abdomen and pelvis
  - If imaging does not include PET/CT, obtain radionuclide bone scan
- CBC with differential and chemistries including renal and liver enzymes
- Consider tumor markers as an adjunctive test for monitoring response to therapy
- Assessment of symptoms and metastatic sites for clinical scenarios requiring individualized therapy
- All patients with metastatic breast cancer, regardless of subtype and family history, should have genetic testing performed via referral to Clinical Genetics or by provider ordered genetic testing pathway
- Lifestyle risk assessment
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative

TREATMENT

- Multidisciplinary team discussion to determine appropriate sequencing of treatment options
  - Surgical and Radiation Oncology consult as indicated (see Principles of Radiation)
  - Systemic therapy
    - HR-positive/HER2-negative, see Page 3
    - HR-positive/HER2-positive, see Page 4
    - HR-negative/HER2-positive, see Page 5
    - HR-negative/HER2-negative (triple negative breast cancer), see Page 6

- Tumor genomic analysis to identify actionable mutations of interest including ESR1, PIK3CA, NTRK, TMB, MSI-H, dMMR, etc

- HR-positive/HER2-negative
- See Page 3

- HR-positive/HER2-positive
- See Page 4

- HR-negative/HER2-positive
- See Page 5

- HR-negative/HER2-negative (triple negative breast cancer)
- See Page 6

Note: Patients with bone metastases and life expectancy > 12 weeks should receive a bisphosphonate if creatinine clearance ≥ 30 mL/minute or denosumab after dental evaluation, in addition to other anti-cancer therapy.

1 For patients eligible for systemic therapy and/or clinical trials, molecular testing on tumor biopsy should be done at initial recurrence or next line of therapy for both standard of care options (including rarer aberrations that may qualify for agnostic treatments, e.g., NTRK, BRAF, RET, TMB, MSI-H, dMMR) or eligibility for clinical trials. While tumor testing may be more sensitive for mutations/tumor mutational burden, ESR1 mutations are more easily detected on liquid biopsy.

2 If bone scan shows substantial lesions in weight-bearing areas that are not included in the CTs, then additional views are indicated to rule out impending fractures

3 See Appendix A

4 See Genetic Counseling algorithm

5 See Physical Activity, Nutrition, and Tobacco Cessation Treatment algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

6 GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

7 HER2-positive by either immunohistochemistry 3+ or FISH, (HER2/CEP17 ratio ≥ 2)
Postmenopausal patients²,³:

First line therapy
- Aromatase inhibitor (AI) or fulvestrant with ribociclib or abemaciclib⁴
- If prior AI therapy within one year, consider fulvestrant plus CDK4/6 inhibitor
- For select patients⁵, consider endocrine therapy only

Second line therapy (or within one year of completing adjuvant endocrine therapy with AI)
- If fulvestrant not given previously⁶:
  - Patients who relapsed within a year of completion of adjuvant endocrine therapy are considered candidates for CDK4/6 combination with fulvestrant regardless of PIK3CA status
- If prior CDK4/6 therapy was given and PIK3CA mutation present, fulvestrant with alpelisib or capivasertib
- If prior CDK4/6 therapy and PIK3CA/PTEN- or AKT1- or PTEN-alteration, capivasertib and fulvestrant
- If neither PIK3CA mutation nor PIK3CA/PTEN- or AKT1- or PTEN-alterations are present, consider fulvestrant or exemestane or tamoxifen (depending on prior endocrine therapy exposure) with everolimus
- If prior CDK4/6 therapy was palbociclib, consider changing endocrine therapy and switch to ribociclib
  - If germline mutation (e.g., BRCA 1 or 2, PALB2), talazoparib or olaparib
  - If ESR1 mutation, single agent elacestrant
  - If MSI-H/dMMR, pembrolizumab or dostarlimab
  - If HER2 mutation, neratinib/fulvestrant/trastuzumab
  - For select patients⁷, consider endocrine therapy only

Third or subsequent lines of therapy (other endocrine or biological treatments)
- If HER2-low (IHC 1+ or 2+), fam-trastuzumab deruxtecan-nxki
  - Consider sunitinib/gemcitabine or second line therapy options if not given previously
  - Abemaciclib if no previous CDK4/6 inhibitor
  - Tamoxifen + Estrogens (estradiol) + Progestins (megestrol acetate)
  - For other chemotherapy options not used in first or second line therapy, see Appendix B

EVALUATION
- Provide supportive care with symptom management as indicated
- Monitor identified target lesions after every 2-3 cycles (months) of treatment by physical exam and/or imaging, as indicated
- Continue current treatment until progressive disease or unacceptable toxicity, then consider alternate endocrine therapy¹,⁵
- If progressive or unacceptable toxicity and no further endocrine options consider systemic chemotherapy until progressive disease or abemaciclib if no previous CDK4/6 inhibitor¹,⁶
- For patients with HR-positive, HER2-low tumors, use fam-trastuzumab deruxtecan-nxki after one line of systemic chemotherapy in metastatic setting

Note: Patients with bone metastases and life expectancy > 12 weeks should receive a bisphosphonate if creatinine clearance ≥ 30 mL/minute or denosumab after dental evaluation, in addition to other anti-cancer therapy.

¹ See Appendix B: Recurrent or Metastatic Breast Cancer Systemic Therapy Treatment Options
² Status post surgical bilateral salpingo oophorectomy (BSO), clinically suppressed on gonadotropin analogues, > 2 years without clinical menses if stopped early due to chemotherapy, or naturally ceased menses for 1 year. For patients after hysterectomy or < 55 years old, consider verifying with estrogen, analogues, > 2 years without clinical menses if stopped early due to chemotherapy, or naturally ceased menses
³ Palbociclib can be considered if patient intolerant to ribociclib and/or abemaciclib
⁴ Select patients include patients at high risk for morbidity from biological options, low burden and low grade disease, clinically sensitive to endocrine therapy, etc
⁵ Consider breast surgery for patients with limited responding metastatic disease who have an intact primary

Note: Consider Clinical Trials as treatment options for eligible patients.

CDK = cyclin-dependent kinase  
IHC = immunohistochemical
dMMR = deficient mismatch repair  
HER = human epidermal growth factor receptor
HR = hormone receptor  
MSI-H = high levels of microsatellite instability

Appendix B: Recurrent or Metastatic Breast Cancer Systemic Therapy Treatment Options
Appendix C: Zubrod/ECOG Performance Status
Department of Clinical Effectiveness V2
Approved by Executive Committee of the Medical Staff on 03/19/2024
**Breast Cancer – Metastatic Disease**

**PRESENTATION**

**TREATMENT**

Postmenopausal patients \(^{3,4}\):
- **First line therapy** \(^{5}\):  
  - If no prior trastuzumab \(^{6}\) or > 6 months since adjuvant trastuzumab:  
    - Docetaxel or paclitaxel plus trastuzumab and pertuzumab \(^{6}\)  
    - For select patients, aromatase-inhibitor (AI) with trastuzumab or lapatinib or trastuzumab plus lapatinib
  - If ≤ 6 months from adjuvant trastuzumab or if prior (neo) adjuvant pertuzumab:  
    - Fam-trastuzumab deruxtecan-nxki or consider alternate HER2 directed therapies

**Second line therapy** \(^{6}\):
- Fam-trastuzumab deruxtecan-nxki if not previously given

**Third or subsequent lines of therapy** \(^{5,8}\):
- Ado-trastuzumab emtansine, if not previously given
- Tucatinib plus trastuzumab and capecitabine
- Capecitabine plus lapatinib or trastuzumab
- Neratinib plus capecitabine
- Margetuximab-cmkb plus chemotherapy (capecitabine, vinorelbine, gemcitabine or eribulin)
- Trastuzumab plus a taxane, with or without carboplatin
- Trastuzumab plus lapatinib
- Trastuzumab plus chemotherapy (vinorelbine, gemcitabine, capecitabine or eribulin)
- Trastuzumab plus pertuzumab (if pertuzumab not previously given)
- Other endocrine therapy not previously used (tamoxifen, estrogens, progestins or androgens)

**EVALUATION**

- Provide supportive care with symptom management as indicated
- Monitor identified target lesions after every 2-3 cycles (months) of treatment by physical examination and/or imaging, as indicated
- Continue current treatment until progressive disease or unacceptable toxicity, then consider alternate anti-HER2 therapy (with or without endocrine therapy) \(^{3,9}\)
- If progressive or unacceptable toxicity and no other anti-HER2 therapy or endocrine options are available, consider chemotherapy or other systemic therapy until progressive disease \(^{3,9}\)
- Monitor neurological symptoms and if suspicious, obtain central nervous system (CNS) imaging as clinically indicated

Note: Consider Clinical Trials as treatment options for eligible patients.

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**HER = human epidermal growth factor receptor**  
**HR = hormone receptor**

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\(^{1}\) See Appendix B: Recurrent or Metastatic Breast Cancer Systemic Therapy Treatment Options

\(^{2}\) HER-2 positive by either immunohistochemistry 3+ or fluorescence in situ hybridization (FISH), (HER2/CEP17 ratio ≥ 2)

\(^{3}\) Status post surgical bilateral salpingo oophorectomy (BSO), clinically suppressed on gonadotropin analogues, > 2 years without clinical menses if stopped early due to chemotherapy, or naturally ceased menses for 1 year

\(^{4}\) If premenopausal, add ovarian function suppression or ablation for patients receiving endocrine therapy

\(^{5}\) In patients with central nervous system metastases, tucatinib-containing regimens are preferred

\(^{6}\) Obtain cardiac evaluation at baseline and as clinically indicated

\(^{7}\) After 4-6 months with no progression or unacceptable toxicity, chemotherapy may be discontinued with continuation of trastuzumab and pertuzumab with endocrine therapy

\(^{8}\) Endocrine therapy may be used for maintenance of response if toxicity prompts discontinuation of anti-HER2 therapy. Endocrine therapy alone may also be used for third and subsequent lines therapy, although anti-HER2 regimens are preferred

\(^{9}\) Consider breast surgery for patients with limited responding metastatic disease who have an intact primary

\(^{10}\) See Appendix C: Zubrod/ECOG Performance Status

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Note: Patients with bone metastases and life expectancy > 12 weeks should receive a bisphosphonate if creatinine clearance ≥ 30 mL/minute or denosumab after dental evaluation, in addition to other anti-cancer therapy.

\(^{1}\) HER-2 positive by either immunohistochemistry 3+ or fluorescence in situ hybridization (FISH), (HER2/CEP17 ratio ≥ 2)

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\(^{7}\) Endocrine therapy may be used for maintenance of response if toxicity prompts discontinuation of anti-HER2 therapy. Endocrine therapy alone may also be used for third and subsequent lines therapy, although anti-HER2 regimens are preferred

\(^{8}\) Consider breast surgery for patients with limited responding metastatic disease who have an intact primary

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Approved by Executive Committee of the Medical Staff on 03/19/2024
**Breast Cancer – Metastatic Disease**

**Note:** Consider Clinical Trials as treatment options for eligible patients.

### PRESENTATION

**HR-negative/HER2-positive**

- **First line therapy**
  - If no prior trastuzumab or > 6 months since adjuvant trastuzumab:
    - Paclitaxel (or docetaxel) plus trastuzumab and pertuzumab
  - If ≤ 6 months from adjuvant trastuzumab or if prior (neo) adjuvant pertuzumab:
    - Fam-trastuzumab deruxtecan-nxki or consider alternate HER2 directed therapies

- **Second line therapy**
  - Fam-trastuzumab deruxtecan-nxki if not previously given

- **Third or subsequent lines of therapy**
  - Ado-trastuzumab emtansine, if not previously given
  - Tucatinib plus trastuzumab and capecitabine
  - Neratinib plus capecitabine
  - Margituximab-cmkb plus chemotherapy (capecitabine, vinorelbine, gemcitabine or eribulin)
  - Trastuzumab plus a taxane, with or without carboplatin
  - Trastuzumab plus lapatinib
  - Trastuzumab plus chemotherapy (vinorelbine, gemcitabine, capecitabine or eribulin)
  - Trastuzumab plus pertuzumab (if pertuzumab not previously given)

### TREATMENT

- **Provide supportive care with symptom management as indicated**
- **Monitor identified target lesions after every 2-3 cycles (months) of treatment by physical exam and/or imaging, as indicated**
- **Continue current treatment until progressive disease or unacceptable toxicity, then consider alternate anti-HER2 therapy**
- **If progressive or unacceptable toxicity and no other anti-HER2 therapy options are available, consider chemotherapy until progressive disease**
- **If failure to respond to multiple anti-HER2 therapies or deterioration of Zubrod/Eastern Cooperative Oncology Group (ECOG) performance status to ≥ 3, consider supportive care alone**

**EVALUATION**

**Note:** Patients with bone metastases and life expectancy > 12 weeks should receive a bisphosphonate if creatinine clearance ≥ 30 mL/minute or denosumab after dental evaluation, in addition to other anti-cancer therapy.

1 See Appendix B: Recurrent or Metastatic Breast Cancer Systemic Therapy Treatment Options
2 HER2-positive by either immunohistochemistry 3+ or FISH, (HER2/CEP17 ratio ≥ 2)
3 In patients with central nervous system metastases, tucatinib-containing regimens are preferred
4 Obtain cardiac evaluation at baseline and as clinically indicated
5 After 4-6 months with no progression or unacceptable toxicity, chemotherapy may be discontinued with continuation of trastuzumab and pertuzumab
6 Consider breast surgery for patients with limited responding metastatic disease who have an intact primary

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**Breast Cancer – Metastatic Disease**

**Note:** Consider Clinical Trials as treatment options for eligible patients.

### PRESENTATION

**HR-negative/** 
**HER2-negative**  
(**triple negative breast cancer**)

- **First line therapy**
  - If PD-L1 expression is present:
    - Pembrolizumab plus chemotherapy (albumin-bound paclitaxel, paclitaxel, or gemcitabine/carboplatin)
  - If PD-L1 expression is absent:
    - For chemotherapy options, see **Appendix B**
    - Single-agent therapy is preferred, except for patients with impending visceral crisis or very symptomatic disease
      - Gemcitabine/carboplatin is an option if recent progression on a taxane
    - Combination chemotherapy is also preferred for patients with oligometastases

- **Second line therapy**
  - For chemotherapy options not used in first line therapy, see **Appendix B**
  - Sacituzumab govitecan-hziy
  - If germline mutation (*e.g.*, BRCA 1 or 2, PALB2), talazoparib or olaparib
  - If NTKR fusion, larotrectinib or entrectinib
  - If MSI-H/dMMR, pembrolizumab or dostarlimab
  - If RET fusion, selpercatinib
  - If BRAF V600E, dabrafenib and trametinib

- **Third or subsequent lines of therapy**
  - If HER2-low (IHC 1+ or 2+), fam-trastuzumab deruxtecan-nxki
  - For other chemotherapy options not used in first or second line therapy, see **Appendix B**

### TREATMENT

1. Provide supportive care with symptom management, as indicated
2. Monitor identified target lesions after every 2-3 cycles (months) of treatment by physical exam and/or imaging, as indicated
3. Continue current treatment until progressive disease or unacceptable toxicity, then consider alternate chemotherapy or targeted therapy
4. Monitor neurological symptoms and if suspicious, obtain central nervous system (CNS) imaging, as clinically indicated
5. If progressive or unacceptable toxicity and no further systemic therapy options remain, consider supportive care alone

### EVALUATION

- Provide supportive care with symptom management, as indicated
- Monitor identified target lesions after every 2-3 cycles (months) of treatment by physical exam and/or imaging, as indicated
- Continue current treatment until progressive disease or unacceptable toxicity, then consider alternate chemotherapy or targeted therapy
- Monitor neurological symptoms and if suspicious, obtain central nervous system (CNS) imaging, as clinically indicated
- If progressive or unacceptable toxicity and no further systemic therapy options remain, consider supportive care alone

**Note:** Patients with bone metastases and life expectancy > 12 weeks should receive a bisphosphonate if creatinine clearance ≥ 30 mL/minute or denosumab after dental evaluation, in addition to other anti-cancer therapy

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CNS = central nervous system  
HR = hormone receptor  
dMMR = deficient mismatch repair  
HER = human epidermal growth factor receptor  
MSI-H = high levels of microsatellite instability  
IHC = immunohistochemical  
PD-L1 = programmed death-ligand 1  
HR-negative/HER2-negative = hormone receptor negative / human epidermal growth factor receptor negative

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1 See **Appendix B**: Recurrent or Metastatic Breast Cancer Systemic Therapy Treatment Options
2 PD-L1 expression is evaluated with PD-L1 IHC (immunohistochemical assay) 22C3 and considered to be present if Combined Positive Score (CPS) is ≥ 10
3 Consider breast surgery for patients with limited responding metastatic disease who have an intact primary
### APPENDIX A: Clinical Scenarios Requiring Individualized Therapy

- Oligometastasis\(^1\) or Stage IV NED\(^2\)
- Brain metastases (refer to Brain Metastases Management algorithm)
- Leptomeningeal disease (refer to Leptomeningeal Metastases algorithm)
- Choroid metastases
- Cord compression (refer to Spinal Cord Compression Management in Cancer Patients algorithm)
- Plexopathy/radiculopathy
- Extensive local-regional disease
- Pathologic fracture
- Impeding pathologic fracture
- Pleural effusion\(^3\) (refer to Management of Malignant Pleural Effusion - Adult algorithm)
- Pericardial effusion\(^4\)
- Superior vena cava syndrome
- Biliary obstruction
- Ureteral obstruction
- Pregnancy\(^5\)
- de novo M1 inflammatory breast cancer (refer to Breast Cancer - Inflammatory (IBC) algorithm)

\(^{1}\) Oligometastases includes selected patients with up to 5 metastatic lesions in the same or different organ sites. These patients may be considered for definitive treatment with curative intent.

\(^{2}\) Stage IV NED is considered to include patients with up to 5 metastatic lesions in the same or different organ sites who have been treated with surgical or other ablative therapy. These patients may be considered for definitive treatment with curative intent.

\(^{3}\) If patient is symptomatic, a multidisciplinary team discussion is required

\(^{4}\) Refer to Management of Pregnant Patients with Cancer Policy (#CLN0582)
APPENDIX B: Recurrent or Metastatic Breast Cancer Systemic Therapy Treatment Options

## Chemotherapy

### Preferred single agents:

<table>
<thead>
<tr>
<th>Anthracyclines</th>
<th>Taxanes</th>
<th>Anti-metabolites</th>
<th>Other microtubule inhibitors</th>
<th>Other single agents:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>Paclitaxel</td>
<td>Capecitabine</td>
<td>Vinorelbine</td>
<td>Carboplatin</td>
</tr>
<tr>
<td>Pegylated liposomal doxorubicin</td>
<td>Albumin-bound paclitaxel</td>
<td>Gemcitabine</td>
<td>Eribulin</td>
<td>Sacituzumab govitecan-hziy</td>
</tr>
</tbody>
</table>

### Other single agents:

- Cyclophosphamide
- Epirubicin
- Cisplatin
- Docetaxel
- Ixabepilone
- Mitomycin C

### Combination chemotherapy regimens:

- FAC/CAF (cyclophosphamide, doxorubicin, and fluorouracil)
- EC (epirubicin and cyclophosphamide)
- CMF (cyclophosphamide, methotrexate, and fluorouracil)
- Gemcitabine and carboplatin
- Docetaxel and capecitabine
- Gemcitabine and paclitaxel

## HER2 Based Therapies

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

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

### Other options (not considered preferred first options):

- Trastuzumab with docetaxel
- Trastuzumab with paclitaxel with or without carboplatin
- Trastuzumab with vinorelbine
- Trastuzumab with capecitabine
- Trastuzumab plus pertuzumab (if pertuzumab not previously given)

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

- Fam-trastuzumab deruxtecan-nxki
- Ado-trastuzumab emtansine
- Tucatinib plus trastuzumab plus capecitabine
- Trastuzumab plus lapatinib without cytotoxic therapy
- Trastuzumab plus chemotherapy (capecitabine, vinorelbine, gemcitabine or eribulin)

<table>
<thead>
<tr>
<th>ER = estrogen receptor</th>
<th>PR = progesterone receptor</th>
</tr>
</thead>
</table>

1. Dose-dense AC is not indicated for treatment of metastatic breast cancer
2. After maximal benefit achieved with chemotherapy, consider continuous anti-HER2 therapy alone, if ER or PR positive, in combination with appropriate endocrine therapy (does not apply to ado-trastuzumab emtansine)
### APPENDIX B: Recurrent or Metastatic Breast Cancer Systemic Therapy Treatment Options - continued

#### Endocrine Based Therapies

- **Aromatase inhibitors (AI)**
  - AI with or without CDK 4/6 inhibitor (abemaciclib or ribociclib)
  - Anastrozole
  - Letrozole
  - Exemestane
  - Exemestane, fulvestrant, or tamoxifen with everolimus
- **Tamoxifen**
- **Elacestrant**
- **Fulvestrant**
  - Fulvestrant with alpelisib for PIK3CA mutation
  - Fulvestrant with capivasertib for PIK3CA/PI3/AKT1/PTEN alterations
  - Fulvestrant with or without CDK 4/6 inhibitor (abemaciclib, palbociclib, or ribociclib)
  - Fulvestrant with AI
- **Abemaciclib single agent**
- **Progestin (megestrol acetate)**
- **Estrogen (estradiol)**

#### Other Therapies

- **HR-negative/HER2-negative (triple negative breast cancer):**
  - With PD-L1 expression: Pembrolizumab plus chemotherapy (albumin-bound paclitaxel, paclitaxel, or gemcitabine and carboplatin)
  - If NTKR fusion, larotrectinib or entrectinib
  - If RET fusion, selpercatinib
  - If BRAF V600E, dabrafenib, and trametinib
  - If MSI-H/dMMR, pembrolizumab, or dostarlimab

- **BRCA-positive directed therapies:**
  - Talazoparib
  - Olaparib

- **Molecularly targeted agents along with NTRK fusion-directed:**
  - Larotrectinib and Entrectinib

- **Total Mutation Burden-High (TMB-H: ≥ 10 muts/mb/dMMR positive):**
  - Pembrolizumab

- **Bone-directed therapies:**
  - Pamidronate disodium
  - Zoledronic acid
  - Denosumab
  - Strontium-89
  - Samarium Sm 153 lexidronam

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CDK = cyclin-dependent kinase  |  MSI-H = high levels of microsatellite instability  |  dMMR = deficient mismatch repair

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APPENDIX C: Zubrod/ECOG Performance Status

<table>
<thead>
<tr>
<th>Description</th>
<th>Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
<td>0</td>
</tr>
<tr>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (e.g., light house work, office)</td>
<td>1</td>
</tr>
<tr>
<td>Ambulatory and capable of self care but unable to perform any work activities; up and about &gt; 50% of waking hours</td>
<td>2</td>
</tr>
<tr>
<td>Capable of only limited self care, confined to bed or chair &gt; 50% of waking hours</td>
<td>3</td>
</tr>
<tr>
<td>Completely disabled, cannot carry on any self care, totally confined to bed or chair</td>
<td>4</td>
</tr>
<tr>
<td>Dead</td>
<td>5</td>
</tr>
</tbody>
</table>

ECOG = Eastern Cooperative Oncology Group
Breast Cancer – Metastatic Disease

PRINCIPLES OF BREAST ONCOLOGIC SURGERY

Stage IV disease
• Traditionally, surgical management of the primary and regional nodes are not recommended in the setting of stage IV disease
• In patients with oligometastatic disease and excellent response to systemic therapy locoregional therapy may be considered in carefully selected patients evaluated by the multidisciplinary team
• Given data indicating no survival benefit for surgery in patients with metastatic disease, surgery within the context of a clinical trial would be appropriate
• Radiation therapy and/or palliative mastectomy may be considered in patients with advanced local progression, symptomatic fungating and/or bleeding tumors not responsive to systemic therapy

Oligometastatic Disease
• For patients with oligometastatic disease who have undergone definitive surgery, conventional treatment with whole breast or chest wall and undissected draining lymphatics, to include the internal mammary nodes (IMN), supraclavicular (SCV), and level III axilla is recommended. Include level I/II axilla if axillary lymph node dissection (ALND) not performed.
• Enrollment in a trial for randomization to treatment is recommended for treatment of the oligometastatic disease site, (e.g., bone, lung, liver). Off trial, patients being considered for definitive treatment should be discussed both in a multidisciplinary setting and within the radiation oncology service
• Additional treatment of the oligometastatic disease site, (e.g., bone, lung, liver) with radiation therapy or enrollment in a trial for randomization to treatment is also recommended. Trial radiation doses may be reasonable for patients being considered for definitive treatment off trial.
• Consultation to other radiation services based on oligometastatic disease site may be warranted as follows:
  o Brain with < 10 metastatic lesions: Central nervous system (CNS) Radiation Oncology
  o Spine with limited (1-2) vertebral body involvement: CNS Radiation Oncology for stereotactic treatment
  o Skull base: Head and Neck Radiation Oncology
  o Lung metastases: Thoracic Radiation Oncology
  o Liver metastases: Gastrointestinal Radiation Oncology
  o Limited bone metastases: Breast Radiation Oncology

PRINCIPLES OF RADIATION

Widely Metastatic Disease
• Consultation to other radiation services for non-oligometastatic disease should be considered for the following:
  o Brain with ≥ 10 metastatic lesions or diffuse spine disease: Breast Radiation Oncology
  o Leptomeningeal disease (LMD): CNS Radiation Oncology
  o Diffuse bone disease, including spine or bone disease causing pain or at risk of fracture: Radiation Oncology Bone Metastatic Clinic or Breast Radiation Oncology
  o Bleeding and/or painful and/or fungating primary mass: Breast Radiation Oncology

1 Patients who are not candidates for radiation, or in select highly chemo/biotherapy-sensitive cases, treatment with systemic bio-chemotherapy regimens used for non-CNS metastatic disease can be considered
**SUGGESTED READINGS**


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SUGGESTED READINGS - continued


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SUGGESTED READINGS - continued


Breast Cancer – Metastatic Disease

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