### Chemotherapy and Targeted Therapy for Patients With Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer That is Either Endocrine-Pretreated or Hormone Receptor-Negative: ASCO Guideline Update

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| **Is there an optimal sequence of chemotherapy and/or targeted therapy (first-line, second-line or greater) for patients with triple-negative metastatic breast cancer (with or without BRCA1 or BRCA2 germline mutations)?** | 1.1. Patients with metastatic triple-negative breast cancer with expression of programmed cell death ligand-1 (PD-L1-positive) and no existing contraindications may be offered the addition of immune checkpoint inhibitor to chemotherapy (atezolizumab plus nab-paclitaxel or pembrolizumab plus chemotherapy) as first-line therapy. | Type: Evidence based, benefits outweigh harms  
Evidence quality: Moderate  
Strength of recommendation: Strong |
|                   | 1.2. Patients with metastatic triple-negative breast cancer without expression of programmed cell death ligand-1 (PD-L1-negative) should be offered single agent chemotherapy rather than combination chemotherapy as first-line treatment, although combination regimens may be offered for symptomatic or immediately life-threatening disease for which time may allow only one potential chance for therapy. | Type: Evidence based; benefits outweigh harms  
Evidence quality: Moderate  
Strength of recommendation: Strong |
|                   | Practical Information: Patients may be offered either platinum-based or non-platinum-based regimens based on individualized patient and provider assessment of preferences, risks, and benefits. | |
|                   | 1.3. Patients with metastatic triple-negative breast cancer who have received at least two prior therapies for metastatic disease should be offered treatment with sacituzumab govitecan. | Type: Evidence based; benefits outweigh harms  
Evidence quality: High  
Strength of recommendation: Strong |
|                   | 1.4. Patients with metastatic triple-negative breast cancer with germline BRCA1 or 2 mutations who have previously been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic disease setting may be offered an oral PARP inhibitor (olaparib or talazoparib) rather than chemotherapy. | Type: Evidence based; benefits outweigh harms  
Evidence quality: Moderate  
Strength of recommendation: Strong |
|                   | Practical Information: Small single-arm studies show that oral PARP inhibitor therapy demonstrates high response rates in metastatic breast cancer encoding DNA repair defects, such as germline PALB2 mutation carriers and somatic BRCA mutations. It should also be noted that the randomized PARP inhibitor trials made no direct comparison with taxanes, anthracyclines, or platinums; comparative efficacy against these compounds is unknown. | |
## Chemotherapy and Targeted Therapy for Patients With Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer That is Either Endocrine-Pretreated or Hormone Receptor-Negative: ASCO Guideline Update

| Clinical Question                                                                 | Recommendation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Evidence Rating                                                                                                                                                                                                                       |
|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| What are the indications for chemotherapy versus endocrine therapy in endocrine-pretreated ER-positive metastatic breast cancer?                                                                 |
| 2.1. Patients with metastatic hormone receptor-positive (HR-positive) breast cancer with disease progression on a prior endocrine agent with or without targeted therapy may be offered treatment with either endocrine therapy with or without targeted therapy (refer to the companion ASCO guideline on Endocrine Therapy and Targeted Therapy for Hormone Receptor-Positive Metastatic Breast Cancer for details) or single-agent chemotherapy. | Type: Evidence based; benefits outweigh harms Evidence quality: Moderate Strength of recommendation: Strong  
*Practical Information: Treatment choice should be based on individualized patient and provider assessment of preferences, risks, and benefits.* |
| Is there an optimal sequence of non-endocrine agents for patients with hormone receptor-positive but HER2-negative metastatic breast cancer that are no longer benefiting from endocrine therapy (with or without BRCA1 or BRCA2 germline mutations)? | 3.1. Patients with metastatic HR-positive but HER2-negative breast cancer with germline BRCA1 or 2 mutations who are no longer benefiting from endocrine therapy may be offered an oral PARP inhibitor in the first- through to third-line setting rather than chemotherapy.  
*Practical Information: Small single-arm studies show that oral PARP inhibitor therapy demonstrates high response rates in metastatic breast cancer encoding DNA repair defects, such as germline PALB2 mutation carriers and somatic BRCA mutations. It should also be noted that the randomized PARP inhibitor trials made no direct comparison with taxanes, anthracyclines, or platinums; comparative efficacy against these compounds is unknown.* | Type: Evidence based; benefits outweigh harms Evidence quality: Moderate Strength of recommendation: Strong  
*Practical Information: Choice of chemotherapy agent should be based on individualized patient and provider assessment of preferences, risks, and benefits.* |
| 3.2. Patients with HR-positive HER2-negative metastatic breast cancer no longer benefiting from endocrine therapy should be offered single agent chemotherapy rather than combination therapy, although combination regimens may be offered for symptomatic or immediately life-threatening disease for which time may allow only one potential chance for therapy. | Type: Evidence based; benefits outweigh harms Evidence quality: Moderate Strength of recommendation: Strong  
*Practical Information: Choice of chemotherapy agent should be based on individualized patient and provider assessment of preferences, risks, and benefits.* |
| At what point should a patient be transitioned to hospice or best supportive care only? | 4.1. No recommendation regarding at which point a patient’s care should be transitioned to hospice or best supportive care only is possible at this time.  
*Practical Information: Given the heterogeneity of breast cancer and the treatment goals of patients with breast cancer it is not possible to identify a universal optimal time to transition to hospice or best supportive care. When to transition is a decision that should be shared between the patient and clinician in the context of an ongoing conversation regarding goals of care. The conversation about integration of supportive care and eventual consideration of hospice care should start early in the management of metastatic breast cancer.* | Type: Consensus; benefits/harms ratio unknown Evidence quality: N/A Strength of recommendation: Strong |