Use of Biomarkers to Guide Decisions on Systemic Therapy for Women With Metastatic Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline
Introduction

The purpose of this guideline is to provide evidence-based recommendations to practicing oncologists and other stakeholders on the appropriate use of results from assays of breast tumor biomarkers to guide or influence decisions on systemic therapy in women with metastatic breast cancer.
ASCO Guideline Development Methodology

The ASCO Clinical Practice Guidelines Committee guideline process includes:

• a systematic literature review by ASCO guidelines staff
• an expert panel provides critical review and evidence interpretation to inform guideline recommendations
• final guideline approval by ASCO CPGC

The full ASCO Guideline methodology supplement can be found at:
www.asco.org/guidelines/metastaticbreastmarkers

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Clinical Questions

(1) Under what circumstances (ie, for which patients) should metastases be biopsied or otherwise sampled to test for changes from the primary tumor with respect to endocrine receptor or HER2 status?

(2) For women with metastatic breast cancer and with known endocrine receptor and HER2 status, which additional tumor markers have demonstrated clinical utility to guide initiation of systemic therapy or direct selection of a new systemic therapy regimen?

(3) For women with metastatic breast cancer and with known estrogen receptor (ER), progesterone receptor (PR), and HER2 status, which additional tumor markers have demonstrated clinical utility to guide decisions on whether to switch to a different drug or regimen or discontinue treatment?

(4) For each tumor biomarker shown to have clinical utility for guiding decisions on systemic therapy for metastatic disease in questions 2 or 3, what are the appropriate assays, timing, and frequency of measurement?
Target Population and Audience

Target Population
Women with metastatic breast cancer being considered for systemic therapy or for changes in the drug or regimen they are receiving.

Target Audience
Any physician caring for patients with breast cancer, including medical, surgical, and radiation oncologists, oncology nurses and physician assistants, and pathologists; patients
Summary of Guideline Recommendations

Q1. Circumstances for Metastases Biopsy

- Patients with accessible, newly diagnosed metastases from primary breast cancer should be offered biopsy for confirmation of disease process and testing of ER, PR, and HER2 status.
- They should also be informed that if discordances are found, evidence is lacking to determine whether outcomes are better with treatment regimens based on receptor status in the metastases or the primary tumor.
- With discordance of results between primary and metastatic tissues, the panel consensus is to preferentially use the ER, PR, and HER2 status from the metastasis to direct therapy if supported by the clinical scenario and the patient’s goals for care.
Summary of Guideline Recommendations
Q2. Additional Tumor Markers for Systemic Therapy

• Decisions on initiating systemic therapy for metastatic breast cancer should be based on clinical evaluation, judgment, and patient preferences.
• There is no evidence at this time that initiating therapy solely on the basis of biomarker results beyond that of ER, PR, and HER2 improves health outcomes.
• Decisions about initiating or selecting therapy for metastatic breast cancer should be based solely on ER, PR, and HER2 status and the specific clinical scenario.

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Summary of Guideline Recommendations
Q3. Additional Tumor Markers for Switching or Discontinuing Treatment

• Recommendations for tissue biomarkers:
  – In patients who are already receiving systemic therapy for metastatic breast cancer, decisions on changing to a new drug or regimen or discontinuing treatment should be based on the patient’s goals for care and clinical evaluation and judgment of disease progression or response, given that there is no evidence at this time that changing therapy solely on the basis of biomarker results beyond ER, PR, and HER2 improves health outcomes, quality of life, or cost-effectiveness.

• Recommendations for circulating tumor markers:
  – In patients already receiving systemic therapy for metastatic breast cancer, decisions on changing to a new drug or regimen, or discontinuing treatment, should be based on the patient’s goals for care and clinical evaluation and judgment of disease progression or response, given that there is no evidence at this time that changing therapy solely on the basis of circulating biomarker results improves health outcomes, quality of life, or cost-effectiveness.
  – Carcinoembryonic antigen, (CEA), cancer antigen (CA) 15-3, and CA 27.29 may be used as adjunctive assessments to contribute to decisions regarding therapy for metastatic breast cancer. Data are insufficient to recommend use of CEA, CA 15-3, and CA 27.29 alone for monitoring response to treatment.
Summary of Guideline Recommendations

Q4. Appropriate Assays, Timing, and Frequency of Measurement

- Decisions for systemic therapy should be influenced by ER, PR, and HER2. To date, clinical utility has not been demonstrated for any additional biomarkers.
Health Disparities

• It is important to note that many patients have limited access to medical care.
• Racial and ethnic disparities in health care contribute significantly to this problem in the United States. Patients with cancer who are members of racial/ethnic minorities suffer disproportionately from comorbidities, experience more substantial obstacles to receiving care, are more likely to be uninsured, and are at greater risk of receiving poor-quality care than are other Americans.
• Many other patients lack access to care because of their geographic location and distance from appropriate treatment facilities. Awareness of these disparities in access to care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the highest level of cancer care to these vulnerable populations.

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Health Disparities

• The biomarker distribution of ER, PR, and HER2 status can vary across tumors from patients with differing ethnic and racial backgrounds.

• In addition to the biologic variability of ER, PR, and HER2 expression within the breast cancer, there is evidence that disparities exist in the frequency of biomarker testing in certain populations and that these disparities are influenced by health insurance coverage.
Multiple Chronic Conditions

• Creating evidence-based recommendations to inform treatment of patients with additional chronic conditions, a situation in which the patient may have two or more such conditions—referred to as multiple chronic conditions (MCC)—is challenging.

• There have been reports of liver dysfunction and renal dysfunction affecting the values of serum tumor markers, which demonstrates that MCC may confuse the interpretation of serum tumor markers.

• There is insufficient evidence to calibrate how MCC may affect the results of biomarker testing.

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Future Directions

• One of the most important conclusions from this guideline is the compelling need for further research on this topic.

• The study of biomarkers continues to lag behind that of the therapies themselves, because historically this has not been an area of robust research.

• In this era of molecular medicine and patient-centered care, it is critical that the medical community continue to lobby for and conduct high-quality biomarker research for women with advanced breast cancer.
Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at

www.asco.org/metastaticbreastmarkers

Patient information is available at www.cancer.net
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