The American Society of Clinical Oncology (ASCO) today issued two clinical practice guidelines on treating women with advanced, HER2-positive breast cancer. The first guideline lists the appropriate systemic therapies for women newly-diagnosed with advanced disease and those whose early-stage disease progressed to advanced cancer. The second guideline provides recommendations for treating brain metastases in women with HER2-positive advanced breast cancer.

**First Evidence-Based Guideline on Systemic Therapy for Advanced, HER2-positive Breast Cancer**

ASCO’s new guideline provides evidence-based recommendations for using systemic targeted therapies in treating advanced (inoperable locally advanced and metastatic), HER2-positive breast cancer. The recommendations will help standardize care and maximize the potential benefit from HER2-targeted therapies.

“We have several treatments for advanced HER2-positive breast cancer, all of which are associated with improved survival,” said Eric P. Winer, MD, co-chair of ASCO’s Expert Panel that developed the guideline. “We’re very fortunate that now we have multiple studies that give us a clear picture of how these newer agents should be used.”

About 15 to 20 percent of breast cancers are HER2-positive, meaning that they have high levels of HER2 protein, which makes cancer cells grow and divide faster. Approximately half of all HER2-positive breast cancer is also hormone receptor-positive. Currently, there are four targeted therapy drugs approved by the Food and Drug Administration (FDA) for treatment of advanced HER2-positive breast cancer: lapatinib, trastuzumab, pertuzumab, and trastuzumab emtansine (T-DM1).
While these treatments (sometimes used in combination with other drugs) are not curative, they can substantially extend the life of person living with cancer if used appropriately. These targeted therapies also have fewer side effects compared with standard chemotherapy. However, congestive heart failure is a contraindication for HER2 targeted therapy, in general.

To develop this clinical practice guideline, an ASCO Expert Panel conducted a formal systematic review of relevant medical literature. The review identified 19 randomized phase III clinical trials on HER2-targeted therapies, three of which addressed the role of hormonal therapy for HER2-positive, hormone receptor-positive advanced breast cancer. Based on the review, the panel made recommendations for three lines of therapy.

Key recommendations of the guideline are:

- **First-line therapy:** combination of chemotherapy, trastuzumab and pertuzumab. For select patients, such as those with contraindications and/or slow growing hormone receptor-positive cancer, hormonal therapy administered with or without either trastuzumab or lapatinib may be substituted for a chemotherapy-based HER2-targeted regimen because it may have fewer side effects. However, hormonal therapy is not appropriate for all patients with advanced, hormone receptor-positive breast cancer and it has not been associated with a survival benefit in this setting.
- **Second-line therapy:** T-DM1
- **Third-line line therapy and beyond:** treatment depends on what patients have received in the first- and second-lines. Options may include T-DM1, hormonal therapy or chemotherapy with trastuzumab and in some cases with lapatinib, the combination of trastuzumab and lapatinib, or pertuzumab-based regimen if the patient had not previously received pertuzumab.

The guideline, *Systemic Therapy for Patients with Advanced HER2-Positive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline*, was published today in the *Journal of Clinical Oncology*.

**First Consensus Recommendations for Treating Brain Metastases in Patients with HER2-positive Breast Cancer**

Brain metastases occur in 30 to 40 percent of women living with HER2-positive breast cancer. However, there is relatively limited research in this setting and no systemic treatments are specifically approved for brain metastases. This clinical practice guideline provides consensus-based recommendations for use of local and systemic therapies in patients with HER2 positive breast cancer that has spread to the brain and is the first guideline specifically for patients with HER2-positive metastatic breast cancer.

“Brain metastases can compromise neurologic function, and treatments are designed to preserve neurologic function and minimize the decline in quality of life,” said Sharon Giordano, MD, co-chair of the ASCO Expert Panel. “But at the same time, some of the treatments for brain metastases
have side effects that can negatively affect cognitive function. We hope that this guideline will help standardize care for these patients and balance toxicities and benefits of treatment.”

Women with HER2-positive breast cancer can live two years or more after initial diagnosis of brain metastases. While it is uncertain whether the treatments for brain metastases prolong survival, many may be effective in managing the symptoms and some may well extend life.

Key recommendations of the guideline are:

- For patients with favorable prognosis for survival, surgery and/or radiotherapy are recommended, depending on the size and number of metastases, resectability, and symptoms.
- For patients with a poor prognosis for survival, options include surgery, whole brain radiation therapy, and systemic therapies with some evidence of activity in the setting of brain metastases, such as lapatinib and capecitabine.
- Additional options include best supportive care, enrollment in a clinical trial, and/or palliative care.

This guideline is ASCO’s first formal expert consensus-based clinical practice guideline, undertaken due to the paucity of specific evidence for this population, and included multidisciplinary expert input, including from neurosurgeons and radiation oncologists.

The guideline, Recommendations on Disease Management for Patients with Advanced HER2-Positive Breast Cancer and Brain Metastases: American Society of Clinical Oncology Clinical Practice Guideline, was published today in the Journal of Clinical Oncology.

Information explaining these recommendations and what they mean for patients is available at www.cancer.net/recommendations. The guidelines are available at http://www.asco.org/guidelines/breast-cancer.

About ASCO:

Founded in 1964, the American Society of Clinical Oncology (ASCO) is the world’s leading professional organization representing physicians who care for people with cancer. With more than 35,000 members, ASCO is committed to improving cancer care through scientific meetings, educational programs and peer-reviewed journals. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation, which funds groundbreaking research and programs that make a tangible difference in the lives of people with cancer. For ASCO information and resources, visit asco.org. Patient-oriented cancer information is available at Cancer.Net.