

Leading Health Care Organizations Recommend to Test All Patients with Invasive Breast Cancer for HER2 Status

NORTHFIELD, Ill., Oct. 7, 2013 /PRNewswire-USNewswire/ -- The College of American Pathologists (CAP) and the American Society of Clinical Oncology (ASCO) today issued a joint, updated guideline aimed at improving the accuracy and reporting of human epidermal growth factor receptor 2 (HER2) testing in patients with invasive breast cancer. The guideline update is based on a systematic review of medical research literature, providing oncologists and pathologists with detailed recommendations for how to test for HER2 overexpression, interpret the results, and recommend HER2-targeted therapies. The guideline, originally issued in 2007, was published as an early online release in the CAP's [Archives](#)

[of Pathology & Laboratory Medicine](#)

and ASCO's

Journal of Clinical Oncology

(JCO). The joint guideline was prepared by an ASCO/CAP Update Committee consisting of experts in breast cancer and cancer biomarkers.

Approximately 15 percent of all newly diagnosed breast cancers are HER2-positive, meaning that the tumors have extra copies of the *HER2* gene and/or high levels of the HER2 protein, which controls breast cancer cell growth and spread. HER2-positive tumors usually grow faster compared to HER2-negative tumors. The purpose of HER2 testing is to identify patients who could benefit from effective HER2-targeted therapies, such as trastuzumab (Herceptin), lapatinib (Tykerb), pertuzumab (Perjeta), and T-DM1 (Kadcyla). These treatments can substantially improve survival in patients with HER2-positive invasive breast cancer. It is therefore important to accurately determine the HER2 status to ensure that patients most likely to benefit are offered a HER2-targeted treatment. At the same time, those that are unlikely to benefit can avoid side effects and costs associated with those drugs.

"Our ability to identify cancer subtypes that will lead to more individualized therapeutic decisions and that are shown to improve clinical outcomes is rapidly improving. Consequently, and more than ever before, society must demand access to high-quality cancer biomarker tests that can help cancer specialists match the right treatments with the right patients. This guideline update strengthens and clarifies recommendations for HER2 testing based on new evidence," says Ant

onio C. Wolff

, MD, FACP, FASCO, co-chair of the ASCO/CAP HER2 Testing in Breast Cancer Panel and professor of oncology at the Johns Hopkins Kimmel Comprehensive Cancer Center.

The two FDA-approved methods currently used in the United States to test for HER2 are immunohistochemistry (IHC) and in-situ hybridization (ISH). IHC testing assesses how much HER2 protein is present on the surface of tumor cells, whereas ISH testing measures how many copies of the *HER2* gene are present inside each cancer cell. The original guideline focused on IHC and fluorescence in-situ hybridization (FISH), whereas the updated guideline adds recommendations for a newer diagnostic technique known as bright-field ISH. This technique also evaluates for amplification of the *HER2* gene, and uses a regular light microscope rather than a fluorescent microscope. Some sources of variability may be reduced with this technique as the invasive component can be more easily identified using bright-field microscopy.

The guideline recommends the following:

- Always test HER2 status on all newly diagnosed invasive breast cancers (primary site and/or metastatic site).
- Ensure that at least one tumor sample is tested for either HER2 protein expression (immunohistochemistry [IHC] assay) or (in situ hybridization [ISH assay]) for *HER2* gene amplification.
- Discuss the role of HER2-targeted therapy if the HER2 test result is positive and if there is no apparent histopathologic discordance with HER2 testing.
- Delay the decision to recommend HER2-targeted therapy if the HER2 test result is equivocal. Mandatory retesting should be done on the same specimen using the alternative test if the initial HER2 test result is equivocal or on an alternative specimen.
- Do not administer HER2-targeted therapy if the HER2 test result is negative. If there is apparent histopathologic discordance with the HER2 test result, additional HER2 testing should be considered.
- Report a HER2 test result as indeterminate if technical issues prevent one or both tests (IHC and ISH) from being done in a tumor specimen, or prevent the test (or tests) from being reported as positive, negative, or equivocal.
- Confirm that the testing laboratory conforms to standards set for accreditation by CAP or an equivalent accreditation authority.

In rare cases, it may be difficult to know for sure if the result is positive or negative. If additional

testing on other tissue specimens is not possible, pathologists and oncologists should consider all available clinical data on the patient prior to recommending HER2-targeted therapy.

According to M. Elizabeth H. Hammond, MD, FCAP, co-chair of the ASCO/CAP HER2 Testing in Breast Cancer Panel and professor of pathology at the University of Utah

School of Medicine, "The number of patients with equivocal HER2 test results used to be rather large. But evidence suggests that the quality of HER2 testing is improving and the frequency of equivocal and inaccurate results is decreasing. We believe that this is at least in part due to our earlier recommendations in 2007. We hope the current guideline will resolve remaining challenges in the field, and ultimately result in better outcomes for all patients with breast cancer."

The guideline panel also commented on the large increase in the number of pathology laboratories participating in programs designed to evaluate the quality of testing of established breast cancer biomarkers, like estrogen receptor and HER2. The updated guideline contains more detailed recommendations on key points doctors should discuss with patients regarding HER2 status, such as the reasons for HER2 testing, types of tests used, interpretation of test results, and the potential need for retesting in case of disease recurrence. It also emphasizes the critical need for a close collaboration by all physicians and health systems involved in the care of breast cancer patients and in the performance of tests that can be used to influence decisions about treatment.

In conjunction with publication of the guideline, the CAP and ASCO have developed clinical tools and resources for pathologists and oncologists that summarize the findings and recommendations. The resources include supplemental information on clinical questions, as well as IHC and ISH test result interpretation criteria and reporting elements. The CAP and ASCO have also developed a companion patient guide, available on cap.org and ASCO's cancer information website, <http://www.cancer.net/>, respectively.

More information on the new guideline and clinical tools and resources can be found at: [CAP Guidelines](http://cap.org/guidelines)

or at

www.asco.org/guidelines/her2

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About the College of American Pathologists As the leading organization for board-certified pathologists, the College of American Pathologists (CAP) serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. With more than 18,000 physician members, the CAP has led laboratory accreditation for more than 50 years with more than 7,500 CAP-accredited laboratories in 50 countries. Find more information about the CAP at

cap.org

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About ASCO 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 30,000 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 ground-breaking research and programs that make a tangible difference in the lives of people with cancer. For ASCO information and resources, visit <http://www.asco.org/> . Patient-oriented cancer information is available at

<http://www.cancer.net/>

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