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CONTACT: Kennesha Baldwin
703-299-1085
baldwink@asco.org

Anthony Phipps
847-832-7574
tphipp@cap.org

ONCOLOGY AND PATHOLOGY GROUPS RELEASE PRACTICE GUIDELINE RECOMMENDATIONS FOR HER2 TESTING FOR BREAST CANCER

Alexandria, VA—The American Society of Clinical Oncology (ASCO) and the College of American Pathologists (CAP) published a clinical practice guideline on improving the accuracy of HER2 testing for breast cancer patients. Predictive and prognostic markers are being increasingly used to guide therapy selection, and accurate identification of the HER2 status is key to identifying patients that could benefit from specific treatments, while identifying others that could be spared potentially toxic and costly therapies. This is the first time that these two organizations join forces to address a critical issue that affects all patients with a new diagnosis of invasive breast cancer.

The human epidermal growth factor receptor 2 (HER2) is a receptor that sits on the outside of cells and controls cancer cell growth, invasion, and the spread of cancer to other parts of the body. Every healthy breast cell contains two copies of the HER2 gene, but extra copies of the gene occur in approximately 20% of women with invasive breast cancer. Tumors that are “HER2-positive” tend to grow more quickly than other types of breast cancer, and patients with this breast cancer type have a higher risk of cancer recurrence and death. They are also less likely to respond to certain treatments while responding better to others.

Results from HER2 testing help the oncologist determine the appropriate treatment for patients with breast cancer, including specific drugs that target the HER2 protein. Anti-HER2 antibody therapy is associated with significant potential benefits, but also risks. Therefore, accurate HER2 testing results are critical to ensuring that patients who may benefit from the anti-HER2 antibody therapy are identified and patients not expected to benefit are not unnecessarily exposed to potential toxicities.

“As molecular testing and pharmagenomics advance, pathologists and clinicians must work together to develop effective practice guidelines for the testing and treatment of patients. Testing for HER2 expression in breast cancer is a perfect example of this,” said Elizabeth Hammond, MD, FCAP, co-lead author of the guideline and pathologist at LDS Hospital and Professor of Pathology, University of Utah School of Medicine. “These new HER2 guidelines are a tremendous step forward. They provide practical guidance for the medical laboratory community on how this testing should be conducted and reported. This will help ensure that patients receive the most appropriate, most effective treatment available.”

The two methods most commonly used to test for HER2 are immunohistochemistry (IHC) and fluorescence in-situ hybridization (FISH). IHC testing can show how much of the HER2 protein is present on the surface of tumor cells, while FISH testing measures

the number of HER2 gene copies in the nucleus of each cell. This gene is responsible for high levels of expression of the HER2 protein on the tumor cells.

The guideline recommends a testing algorithm that defines positive, negative, and equivocal values for both the IHC and FISH tests. Equivocal results form a new category and require repeat testing or the use of a different test. The guideline does not recommend initial use of one test over another in general circumstances (special circumstances may lead to the recommendation of one test over another), but recommends strategies to ensure that all tests are correctly performed, validated, and reproducible.

The guideline also recommends that laboratories adhere on stringent quality improvement standards including assessment of HER2 testing concordance of 95% with another validated HER2 test for both positive and negative assay values, participation in ongoing internal testing performance evaluation, and participation in external knowledge testing (proficiency testing). Biannual examination of these activities will occur through laboratory accreditation by a valid accrediting agency like CAP.

"Based on available data, the Panel did not recommend one test over another but focused its efforts on improving the accuracy of HER2 testing, regardless of the test used," said Antonio C. Wolff, MD, FACP, co-lead guideline author and Associate Professor of Oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University. "Because the results of HER2 testing can predict a patient's likely response to different treatments, including chemotherapy, hormone therapy, and trastuzumab, it is crucial that testing with IHC and/or FISH produces accurate results especially if it is being used as the sole determinant of therapy selection."

As a result of the panel's recommendations, CAP will require all of the laboratories it accredits to participate in HER2 proficiency testing if they wish to conduct HER2 testing. Proficiency testing deficiencies can result from improper use of a test system, through improper calibration of the test system, or unacceptable precision.

HER2 proficiency testing will include a series of specimen challenges that are sent to laboratories for testing a few times a year. Findings will be reported back and then graded to determine performance. Failure to perform adequately on proficiency testing can result in the laboratory being asked to cease testing until the cause of the failures is identified and corrected. CAP-accredited laboratories also will be required to adhere to the rest of the guidelines when conducting and reporting HER2 testing. These guidelines are intended for use with both types of HER2 testing currently in use. It is hoped that other accrediting agencies will swiftly adopt similar accreditation standards.

"The collaboration between CAP and ASCO has resulted in tangible improvements to the way HER2 testing should and will be conducted, and those improvements will have a direct positive impact on the treatment of patients," said Dr. Hammond. "These new accreditation and proficiency testing requirements for CAP-accredited labs reflect the expanding role laboratories play in not only the diagnosis of disease, but also in the treatments that patients receive. These guidelines are a real victory for patients."

Along with the new guideline, ASCO and CAP have developed a corresponding patient guide that is available to the public on ASCO's patient website, People Living With Cancer, at www.plwc.org, as well as on the CAP website, www.cap.org.

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“American Society of Clinical Oncology/ College of American Pathologists Guideline Recommendations for HER2 Testing in Breast Cancer.” A. C. Wolff, MD, et al, Johns Hopkins Kimmel Cancer Center, Baltimore, MD.

This guideline is being published in both the January 1 print issue of the *Journal of Clinical Oncology (JCO)*, the semi-monthly peer-reviewed journal of the American Society of Clinical Oncology (ASCO), and the January issue of the *Archives of Pathology and Laboratory Medicine*, the peer-reviewed journal of the College of American Pathologists. It is also available online at both www.cap.org and www.asco.org. In addition to the guidelines for physicians, a patient guide is available on ASCO's patient website at www.plwc.org.

For a copy of the guideline and available companion pieces, visit www.asco.org/guidelines/HER2, call 703-299-1180, or e-mail: guidelines@asco.org or www.cap.org, call 847-832-7574.

The American Society of Clinical Oncology (ASCO) is the world's leading professional organization representing physicians of all oncology subspecialties who care for people with cancer. ASCO's more than 20,000 members from the United States and abroad set the standard for patient care and lead the efforts to discover more effective cancer treatments, increase funding for clinical and translational research, and, ultimately, improve cancer care for the estimated 10 million people diagnosed with cancer worldwide each year. ASCO publishes the *Journal of Clinical Oncology (JCO)*, the preeminent, peer-reviewed, medical journal on clinical cancer research, and produces People Living With Cancer (www.plwc.org), a comprehensive consumer website providing oncologist-vetted cancer information to help patients and families make informed health-care decisions.

The College of American Pathologists is a medical society that serves nearly 16,000 physician members and the laboratory community throughout the world. It is the world's largest association composed exclusively of pathologists and is widely considered the leader in laboratory quality assurance. The College is an advocate for high-quality and cost-effective medical care. *Archives of Pathology and Laboratory Medicine*, the leading peer-reviewed medical journal for pathologists worldwide, is published by the College. The College also produces MyHealthTestReminder.com (<http://www.myhealthtestreminder.com>), an e-mail reminder web site, to help patients remember to schedule their life-saving health tests such as mammograms, Pap tests, colon cancer screenings, diabetes screenings, cholesterol testing, and to schedule their next blood donation. The site also provides preventive patient information, developed by pathologists, on these diseases. For more information, contact CAP at 800-323-4040 or visit <http://www.cap.org>.