

# New Rules to Boost Cancer Test Accuracy

► **Breaking new ground, oncodiagnostics are changing how pathologists test for breast cancer**

►► ***GEO SUMMARY: Recent developments in breast cancer testing are leading to changes in pathology. Oncologists and pathologists have issued new guidelines regarding HER2 testing and new research suggests changes may be coming for estrogen-receptor testing as well. For the first time, the new guidelines require a certain level of testing and new procedures for pre-analytical processing.***

**C**ONCERN THAT CERTAIN WIDELY USED BREAST CANCER TESTS may underestimate the number of patients who test positive for breast cancer has fostered three recent developments regarding laboratory testing that may affect the patient's ability to receive hormone therapy.

Each of these developments signals a shift in acceptance for molecular testing. Further, each represents recognition that the quality of molecular tests results can vary, leading to false negatives and a call for more definitive testing.

First, the **American Society of Clinical Oncology (ASCO)** and **College of American Pathologists (CAP)** made news in December when they jointly recommended practice guidelines for HER2 testing for breast cancer. The issue was the subject of a cover story in *CAP Today*. Second, **UnitedHealthcare** followed the CAP-ASCO announcement with a decision to cover members who had earlier tested for breast cancer, and wanted retesting due to concern that the earlier test was inaccurate. UnitedHealthcare encouraged its members to discuss the issue with their

oncologists to determine if retesting was appropriate.

Third was the publication of a study in the December 20, 2006, issue of the *Journal of Clinical Oncology*. Researchers determined that a new anti-estrogen receptor antibody reagent for identifying estrogen receptors (ER) in breast cancer specimens is significantly more sensitive and specific than current reagents. Participating in the study were several laboratories, including **PhenoPath Laboratories** in Seattle, Washington.

## ► **Deficiencies In Gene Testing**

Research shows that 14% to 16% of patients are incorrectly labeled with over-expression of HER2/neu gene and 18% to 22% are incorrectly reported with gene underexpression. These deficiencies in HER2 testing led to the new guidelines.

"The new guidelines are significant for two reasons," said Allen M. Gown, M.D., Medical Director and Chief Pathologist at PhenoPath. "First, pathologists and oncologists developed them jointly. Researchers know that such tests require close collabo-

ration between the two specialists. These new guidelines reflect that knowledge. Second, the guidelines address the issue of fixation time in specimen processing, a first in pathology.”

Similar error rates are occurring in HER2 and ER testing and inadequate fixation may cause false negatives in both HER2 and ER testing, Gown said. A minimum fixation of six hours is needed for ER testing, he added.

“One significant factor that affects the accuracy of such testing is pre-analytical variables, and the most critical is fixation time,” Gown said. “The new guidelines require six to 24 hours of fixation.”

In an interview with THE DARK REPORT, Gown said, “These developments are a reminder that lab testing for anything is a work in progress. Our latest research shows, for example, that we may not necessarily be using the best reagents for estrogen receptors. Laboratorians should study these developments and determine if they are using optimal tests. If they are not using optimal tests, they could be failing to identify cancer cases.

“The new ASCO-CAP guidelines do not actually tell labs what reagents to use, but they do specify a certain way to conduct testing to achieve a level of accuracy that equals 90%,” Gown said. “Now that standards for HER2 testing have been announced, we can assume that ASCO and CAP will consider guidelines for ER testing, based on the new research.

“For example, here at PhenoPath, in our most recent research, we evaluated a new anti-ER antibody called SP1 and compared its performance with that of the older 1D5 antibody,” Gown explained. “We found the new SP1 antibody was more sensitive than the older 1D5 antibody. About 8% of the patients were characterized as ER-negative with the older 1D5 reagent. But, these patients were positive with the new SP1 antibody, and this group of patients clearly demonstrated improved survival.

“When you do the math, it’s clear that 8% of patients could be 15,000 to 20,000 casts of cases of cancer that are missed each year,” Gown explained.

“For this reason alone, it is important for laboratorians to take notice that this research was published in an oncology journal, the *Journal of Clinical Oncology*,” Gown said. “This type of research gets published in oncology journals because it has important implications for tumor treatment. For this reason, pathologists should be reading oncology journals. This is where the field is going, and it’s where all the new developments in oncodiagnostics are reported.”

### ► From Research to Action

THE DARK REPORT has several observations on this issue. First, research into the lack of consistency and accuracy in performing the HER2 and ER testing demonstrates how the healthcare system is moving quickly to measure outcomes, identify areas for improvement, and then implement those improvements in the form of published guidelines. Second, the collaboration between oncologists and pathologists to improve HER2 and ER testing shows how molecular diagnostics require pathologists to have a more active ongoing role with clinicians.

Third, as Gown noted, pathologists seeking to stay informed about the latest developments in oncology, infectious disease, and other fields need to be aware of the literature in other specialties. This development is another sign of growing clinical collaboration between pathology and most medical specialties.

In the coming years, the most effective pathologists will be those who reach outside the walls of the laboratory to interact with and support clinicians in getting the right answer at diagnosis, and then consulting with these specialists so that they provide the most appropriate therapies for patients.

**TDR**

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