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Laboratory News

VOL. 39, NO. 6 - SEPTEMBER 1, 2016

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HER2 REFLEX CHANGE

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Effective September 1, 2016, Marshfield Labs will modify the HER2 testing algorithm for breast and gastroesophageal cancers (test codes: **HER2NEU**, **ERA/PRA**, **FHER2**). In addition to cases interpreted as 2+ by immunohistochemistry (IHC), those read as 1+ will also reflex to fluorescence in-situ hybridization (FISH). This change will help ensure that patients eligible for HER2 directed therapies are more consistently identified.

Marshfield Labs switched from a polyclonal to a monoclonal antibody for HER2 IHC in January, 2016. Although this provided greater specificity, it also resulted in more 1+ cases of which about 10% are amplified by FISH (usually low-level amplification) using the 2013 American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) Guidelines. Using our current algorithm, these cases would have been considered negative and would not have undergone further testing.

Until now, Marshfield Labs has used the most common algorithm starting with IHC (read on a scale of 0 to 3+), [with 0/1+ negative, 2+ equivocal and 3+ positive] and reflexing only 2+ cases to FISH. Cases interpreted as 3+ (regardless of FISH results) or FISH positive are treatment-eligible. IHC is less resource intensive than FISH, making it an attractive first tier test if a significant number of cases can forgo FISH testing. With the proposed 1+/2+ algorithm, it is estimated that about half of cases will be reflexed to FISH. Cases interpreted as 0 or 3+ by IHC will not be reflexed.

Trastuzumab (Herceptin), along with other more recently

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developed therapies directed at HER2-positive cancers, have significantly improved outcomes for these patients, who historically have had an unfavorable prognosis. Thus, Marshfield Clinic oncologists feel that the sensitive detection of these patients is paramount.

QUESTIONS

• Gene Shaw, MD, Clinical Pathology; Phone number: 800-222-5835.

HER2 SPECIMEN REQUIREMENTS: RECORDING UPDATE AND TISSUE HANDLING REMINDER

Faith Bosmans, Pathologists' Assistant, Pathology Lab

RECORDING UPDATE

In 2013, to improve testing accuracy and reduce the risks associated with false positive and false negative results, ASCO/CAP collaborated in developing specimen handling and fixation guidelines for HER2, Estrogen Receptor (ERA), and Progesterone Receptor (PRA) testing. These guidelines currently target breast tissues *only,* not gastrointestinal tissues. The Histology Requisition forms and web portal are being updated to ensure the following information is recorded:

1. **Specimen removal time and time placed in fixative** (This will allow calculation of the *cold ischemic time*, i.e., the amount of time between removal from the body and placement in fixative.) This time should be less than one hour.
2. **Fixative type** – should be 10% neutral buffered formalin (NBF).
3. **Fixative duration** – should be more than 6 hours but less than 72 hours. If histology staff process the tissue, they will calculate fixative duration.

Previous Histology Requisition forms should be discarded after receiving Marshfield Labs' updated Histology forms. Please call Marshfield Labs Customer Service at 800-222-5835 to order new forms.

SPECIMEN HANDLING

Breast specimens must be inked and cut into before being placed in formalin!

1. BEFORE breast is cut into, it needs to be inked so the true margin is not compromised. Marshfield Labs inks as follows:
   - Superior - Blue
   - Inferior - Green
   - Medial - Red
   - Lateral - Orange
   - Anterior - Yellow
   - Posterior - Black
2. Breast specimens need to be CUT INTO so that the formalin fixative can come in direct contact with the tumor. Since formalin only penetrates tissue at a rate of 1 mm/hr., it may not fix the tumor for hours or even days, resulting in autolysis and potentially inaccurate hormone testing results. Suggested cuts are: 1-2 cuts for smaller lumpectomy specimens, 2-3 cuts for larger lumpectomy specimens, 3-4 cuts for a mastectomy specimen.
3. The breast tissue must be placed into formalin ASAP, but no later than one hour after being removed from the patient. The time removed and time placed in formalin must be indicated.

QUESTIONS

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