Anaplastic lymphoma kinase immunohistochemistry testing comparable to fluorescence in situ hybridization testing

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Sixteen institutions across Europe collaborated together to show for the first time that a semi-quantitative anaplastic lymphoma kinase (ALK) protein expression test, immunohistochemistry (IHC), is reliable amongst several laboratories and reviewers when test methodology and result interpretation are strictly standardized and the scoring pathologists are appropriately trained on the test.

ALK tyrosine kinase inhibitors (TKIs) shrink tumors and increase progression-free survival in late-stage non-small cell lung cancer (NSCLC) patients positive for ALK as determined by the fluorescence in situ hybridization (FISH) test, a test for DNA rearrangement within the gene. Testing positive for ALK is required in order to be prescribed the therapeutic inhibitors. However, the FISH test is expensive, time-consuming, and requires specialized equipment and expertise. Many other studies have shown comparable results between IHC and FISH but none have compared a highly standardized test and scoring methodology performed at multiple institutions in numerous countries.

Fifteen well-characterized NSCLC specimens were tested and scored for IHC at 16 institutes of pathology in Belgium, Denmark, France, Germany, Scotland, Spain, Sweden and Switzerland. The specimens were pre-tested 3 times by FISH at 2 separate institutions in Germany. Prior to the IHC testing all the equipment was standardized between all the institutions and the scoring pathologists all attended an internet-based

training session with teaching cases.

The results published in the November issue of the *Journal of Thoracic Oncology*, the official journal for the International Association for the Study of Lung Cancer (IASLC), show that all 16 institutions agreed with 100% concordance on the 7 FISH/IHC negative and on 4 FISH/IHC positive specimens. There was also 100% concordance from all institutions on 2 obvious IHC positive cases that were uncertain by FISH ("borderline"). These 2 cases were confirmed ALK positive by a third test, reverse transcription-polymerase chain reaction (RT-PCR). The last 2 cases were ALK-FISH positive and were scored IHC positive by 15/16 and 12/16 institutions, respectively. However, those not scoring these 2 cases as unequivocal ALK IHC positive, called them IHC equivocal and would have demanded an additional ALK test (FISH, PCR) under diagnostic conditions.

The authors conclude "after harmonization of the staining instruments and training of the observers, the ALK IHC assay can be regarded as a reliable multicenter technique for the detection of ALK protein expression". For the future the authors note "there is need to compare validated ALK IHC assays and ALK-FISH in clinical trials as therapy response data of patients with differing ALK IHC and FISH results will help to implement ALK-IHC not only as a prescreening tool, but also as a potential stand-alone test (at least in cases displaying a clear staining pattern). Until then ALK diagnosis should be based on the rational application of both methods adapted to the given case as FISH has some disadvantages and even validated IHC may produce equivocal staining patterns."

More information: journals.lww.com/jto/Abstract/ … K_Testing_of.15.aspx

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