WHAT IS THE IDEAL SCREENING STRATEGY FOR DOUBLE HIT LYMPHOMA?

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Background
The trend towards less invasive testing has brought to the forefront the question of how the provided material can be used most efficiently. "Double hit" lymphoma (DHL), characterized by rearrangements of MYC, and BCL2 and/or BCL6 genes, is treated differently than other subtypes of aggressive B cell lymphoma. However, there is a lack of consensus regarding how to best direct fluorescence in situ hybridization (FISH) testing based on the clinical, morphologic, and immunophenotypic features. The challenge stems from the relatively low prevalence of DHL and the morphologic and immunophenotypic overlap with diffuse large B cell lymphoma (DLBCL). We devised guidelines for the complete work-up of aggressive B cell lymphoma which included morphology review, immunohistochemical (IHC) assessment to assess germinal center (GC) and double expresser (DE) phenotypes, and FISH studies.

Objectives
The aims of this study were: to assess the effectiveness of several quality improvement (QI) initiatives designed to overcome some of the challenges of dealing with limited samples; and to analyze the clinical and pathologic data gathered from using an unselected approach to FISH testing, in order to identify most efficient screening algorithm for DHL for our patient population.

Methods
From October 2016 to December 2017, the number of cases of newly diagnosed aggressive B cell lymphoma lacking a complete work-up were compared before and 2 QI initiatives: bundling immunohistochemical (IHC) orders into standardized panels, and preferentially sending FISH studies on the flow cytometry sample, rather than the paraffin tissue block. In cases with a complete work-up, the following clinical and pathologic parameters were correlated with the FISH results: the International Prognostic Index (IPI); typical DLBCL-like morphology; GC vs non-GC phenotype; DE vs non-DE phenotype.

Results
After implementation of a standardized IHC panel, there was an 81% reduction in missing IHC stains. None of the cases lacking material for FISH benefited from preferentially sending the flow sample, since the flow sample was not diagnostic. Of the clinical and pathologic parameters assessed, only GC+MYC+ ($p=0.046$) or GC+ DE ($p=0.029$) distinguished DHL from other aggressive B cell lymphomas. Directing FISH testing to GC+MYC+ cases provides a sensitivity of 100% and would reduce unnecessary FISH testing by 77%.

Discussion
Implementation of a standardized IHC panel and directing FISH testing to GC+MYC+ cases are efficient strategies in characterization of aggressive B cell lymphomas within our core biopsy-predominant sample population.