Background Determination of programmed death-ligand 1 (PD-L1) level in tumor by immunohistochemistry (IHC) is widely used to predict response to check point inhibitor therapy. In particular, the Dako PD-L1 (22C3) antibody is a common companion diagnostic to the monoclonal antibody drug Keytruda (pembrolizumab) in non-small cell lung cancer (NSCLC). However, for the practicing pathologist, interpretation of the PD-L1 (22C3) assay is cumbersome and time consuming. Manual pathologist scoring also suffers from poor intra- and inter-pathologist precision, particularly around the cut-off point. In this clinical validation study, we developed an image analysis (IA) based solution to accurately and precisely score digital images obtained from PD-L1 stained NSCLC tissues for making clinical enrollment decisions.

Methods 10 NSCLC tissue samples were purchased from a qualified vendor and IHC stained for PD-L1; 4 of these samples had serial sections stained on two separate days. Stained slides were scanned at 20X magnification and analyzed using Flagship Biosciences’ IA solutions that quantify PD-L1 expression and separate tumor and stromal compartments. Resulting image markups of cell detection and PD-L1 expression were reviewed by an MD pathologist for acceptance. PD-L1 staining was evaluated by digital IA in the sample’s tumor compartment for Total Proportion Score (TPS,%). Assay specificity was defined by ≥ 90% of the tissue cohort exhibiting appropriate cell recognition (≥ 90% cells correctly recognized as determined by the pathologist), with ≤ 10% false positive rate for staining classification. Sensitivity was defined by ≥ 90% of the cohort exhibiting appropriate cell identification (≥ 90% cells correctly identified), with ≤ 10% false negative rate for staining classification. Accuracy was defined by the combination of sensitivity and specificity and precision was defined by concordance of the binned TPS (<1%, ≥ 1%, ≥ 50%) in ≥ 80% of the samples stained on multiple days.

Results The preliminary results show that IA can yield high analytical sensitivity, specificity, accuracy, and precision in the determination of the PD-L1 score. 100% of the tissue cohort met criteria for analytical specificity, sensitivity, and accuracy and 100% of the samples stained on multiple days met the precision criteria.

Conclusions This data demonstrates the feasibility of an IA approach as applied to PD-L1 (22C3) scoring. Ongoing experiments include application of the developed 22C3 algorithm on a separate cohort of 20 NSCLC samples to determine the correlation of digital scoring and scoring obtained by three pathologists. Additionally, we will evaluate the precision obtained by digital scoring in relation to the intra- and inter-pathologist concordance.

REFERENCES