Evaluation of PD-L1 Expression in Primary Lung Tumor and Metastatic Lymph Nodes in the Presence of Immune Cells

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Background

Immunotherapies against programmed death ligand-1 (PD-L1) have been established as an effective treatment for a subset of lung cancer patients. Even though it is critical for a successful therapy to know prevalent PD-L1 expression patterns in all affected tissues, information on matching lymph node metastases and immune cells is particularly limited. The purpose of this study was thus to evaluate comparative PD-L1 expression profiles in those tissues.

Methods

FDA-approved IHC assays for PD-L1 (Dako 22C3) were performed on a lung tissue array (LC814A, US Biomax) according to manufacturer's instructions. Histopathological analysis by H-scoring was performed to determine the rate and intensity of positive tumor and immune cell staining for each of the 80 cores. The H score was calculated as follows: A total of up to 300 cells were assessed, per specimen, at 40x high-power magnification (typically over 7-10 fields). A staining level of 0-3 was then assigned to each cell, to designate the intensity of specific positive membranous-to-cytoplasmic staining. The H score was subsequently calculated as % cells staining at level 1 (x1) + % cells staining at level 2 (x2) + % cells staining at level 3 (x3) = total H score per sample. This resulted in a maximum possible H score of 300.

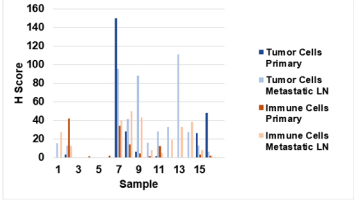

Figure 1: PD-L1 Staining in Adenocarcinoma; LN = lymph nodes

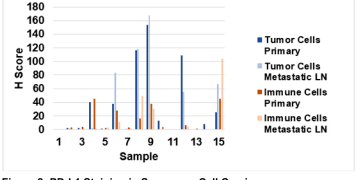

Figure 2: PD-L1 Staining in Squamous Cell Carcinoma

Results

Of the 16 adenocarcinoma tumor samples with a valid staining, 7 (44%) showed positive PD-L1 staining for tumor cells and 10 (63%) for primary immune cells. Importantly, 9 matching metastatic lymph node samples out of the 16 samples (56%) showed an increased PD-L1 H score compared to primary tumors for both tumor cells and immune cells (Figure 1). Of the 15 squamous cell **carcinoma** samples with a valid staining, 11 (73%) showed detectable PD-L1 expression levels in the primary tumor and 12 (80%) in the primary immune cells, while 7 (47%) and 9 (60%) showed lower scores in matching metastatic lymph node tumor cells and their immune cells, respectively (Figure 2). Very low or no expression of PD-L1 was detected in small cell lung **cancer**, as to be expected from previous studies.

Conclusions

Squamous cell carcinomas and adenocarcinomas display significant heterogeneity with regard to PD-L1 expression in associated lymph node metastases. While the reasons for this frequent discordant PD-L1 expression pattern involving both tumor and immune cells need to be investigated further, our findings may help guide the proper interpretation of PD-L1 companion diagnostic **test results and subsequent therapeutic decisions.**

Disclosure

The views in this Poster have not been formally disseminated by the U.S. Food and Drug Administration and should not be construed to represent any agency determination or policy.