B-1
Immune Checkpoint Markers in Pulmonary Large Cell Neuroendocrine Carcinomas

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BACKGROUND: The overall prognosis for pulmonary large cell neuroendocrine carcinoma (LCNEC) patients is poor despite treatment with front line systemic chemotherapy regimens for small cell lung cancer (SCLC) or non-SCLC (NSCLC). Given the efficacy and recent success with immunotherapy in a number of tumor types, we set out to determine the level of a number of immune markers in addition to other proteins which could potentially further help in classification of pulmonary LCNECs.

METHODS: Immunohistochemistry analyses were performed on a pulmonary LCNEC tissue microarray (TMA) from US Biomax consisting of 24 treatment naïve cases (3 cores/patient) of varying stages ranging from I-IIIb using antibodies against Ki67, p53, PD-1 and PDL-1. All stained slides were scored by a pathologist.

RESULTS: There was no correlation between the percent of Ki67, a tumor proliferation marker and the disease stage. Moreover, p53 and most likely the mutant form of the protein was detected in 7/24 cases with 5/7 having greater than 70% expression. With regards to PD-L1, tumoral expression was present in 5/24 (21%) cases although 2 only had 1% or less tumoral staining in at least one core. PD-L1 positive stromal lymphocytes occurred in 10/24 (42%) cases with overall staining of 5% of the cells or less, except in one case. PD-1-positive stromal lymphocytes were present in 10/24 (42%) cases with 5 cases expressing 2% or less positive cells.

CONCLUSION: There was no apparent correlation between any of the markers tested and disease stage. Additionally, presence of p53 staining could potentially serve as a marker to guide the choice of a SCLC over NSCLC therapeutic regimen for patients. Overall, these preliminary findings are being further validated in a larger number of samples. This characterization will help optimize the timing of immunotherapy with respect to the other standard of care therapeutic approaches employed to date.