1813P Prevalence and prognostic value of PD-L1 expression in molecular subtypes of metastatic large cell neuroendocrine carcinoma (LCNEC)

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Background: Pulmonary LCNEC is a rare tumor. Two mutually exclusive subtypes of LCNEC are recognized, the co-mutated TP53 and RB1 and the STK11/KEAP1 (predominantly RB1 wildtype) group. We investigated PD-L1 expression in a well characterized stage IV LCNEC cohort and compared expression in the two subtypes.

Methods: Panel-consensus pathology revision was performed along with targeted next generation sequencing (TNGS) for genes TP53, RB1, STK11 and KEAP1 and immunohistochemical (IHC) analysis of RB1, on pretreatment tumor samples of stage IV LCNEC treated with chemotherapy (Derks et al. CCR 2018). IHC staining for PD-L1 (DAKO 28-8) was performed according to standard protocols on the DAKO autostainer and evaluated by an experienced screener. Tumors were scored positive if $>1\%$ of tumor cells showed any membranous staining. Overall survival (OS) was evaluated by Kaplan Meier analysis and differences estimated with Log-Rank test. Cox-regression analysis included PD-L1, age and gender.

Results: PD-L1 IHC expression data could be generated in 98/147 confirmed LCNEC samples along with RB1 IHC (n = 97) of which 77 passed quality control for TNGS. PD-L1 expression was positive in 16/98 cases (16%); n = 5 (5%) with >50%, n = 11 (11%) having >1-50% and n = 82 (82%) with ≤1% membranous staining, respectively. No significant correlation of PD-L1 expression with molecular subtyping of LCNEC was identified (Table). PD-L1 expression was correlated with a superior OS, hazard ratio (HR) 0.54 ((95% Confidence interval (CI), 0.31-0.96) P = 0.034.

Table: 1813P Expression of PD-L1 in LCNEC, correlated to molecular data

	PD-L1 +	PD-L1 -	P-value
LCNEC (n = 98)	16%	84%	-
1-5%	7 %	-	-
5-20	4%	-	-
>50	5%	-	-
Rb1 IHC (n = 97)			
RB1 (+) (n = 29)	10%	90%	NS
RB1 (-) (n = 68)	19%	81%	
Mutation status (n = 76)			
RB1/TP53 mutated (n = 33)	15%	85%	NS
RB1 wildtype (n = 43)	16%	84%	
OS in months (95% CI)	8.9 (4.2-13.6)	6.6 (5.7-7.6)	HR 0.54 (0.31-0.96) P = 0.034

Conclusions: PD-L1 expression was positive in 16% of stage IV LCNEC tumors. PD-L1 expression is an independent process from LCNEC molecular subgroups. In LCNEC patients with PD-L1 expression superior OS is observed compared to those with negative PD-L1 tumors.

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