AB029. PS01.11. Thymomas are the potential candidates for the immune checkpoint inhibitors therapy

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Background: A robust development of targeted therapy including immunotherapy with checkpoint inhibitors for a lung carcinoma occurred in the last years. The immunotherapy is the most effective in the group of patients with a high expression of a programmed cell death ligand-1 (PD-L1) detected by immunohistochemical tests on the neoplastic cells. One of these tests uses antibody clone 22C3 that serves as a predictive biomarker for pembrolizumab therapy. The aim of our study was an analysis of the PD-L1/22C3 expression on the thymic epithelial tumors (TETs) cells.

Methods: The histological sections obtained from 90 TETs of different histological types (WHO classification, 2015) and stages (Masaoka-Koga staging system) were analyzed immunohistochemically. The study was performed on Link 48 Autostainer and a clone 22C3 (Dako) was used. A membrane staining at any intensity, complete circumferential or partial seen on the epithelial cells was regarded as positive. The results were reported as a percentage of positive tumor cells. The cutoff point that would be the criterion for the therapy is not established yet for TETs. The basic clinical data (patients' gender, myasthenic symptoms) were acquired. Five more TETs after chemotherapy were analyzed to compare the quality of immunohistochemical test in the samples from the same patient before and after treatment.

Results: Seventy-two thymomas and 18 thymic carcinomas (TCs) were analyzed. Median value of PD-L1-positive tumor cells in thymomas reached 70% and was especially high in B-types: in B1 [6] 68% of cells were positive, in B2 [14] 90%, B3 [3] 98%, B2B3 [17] 90% and B1B2 [3] 70% as well as in micronodular thymoma with lymphoid stroma [4] 68%. In A [2], atypical A [4] and AB [18] types the PD-L1 expression was presented by 3%, 8% and 10% of cells, respectively. In the group of TCs the median value of positive tumor cells was 1%. Only 5/18 TCs (4 squamous cell and 1 combined neuroendocrine carcinoma) showed high expression (≥50% of positive tumor cells) of PD-L1. The expression was two times higher (>80% of positive cells) in TETs of stages 3 or 4 than in less advanced tumors (40% of cells). The immunohistochemical reaction was often heterogenic in intensity but usually evenly distributed across the tumor. The thymocytes were negative but mature inflammatory lymphocytes in the stroma of thymic carcinomas revealed the expression. Twenty-one TETs were accompanied by myasthenia. Median value of PD-L1 expression in the tumors with myasthenic symptoms was 80% of cells in contrast to 30% in the other group. The PD-L1 expression in the tumors before and after chemotherapy was identical in all cases but one, in which the values were: 80% before *vs.* 70% after treatment. Statistical analysis will be the next step of the study.

Conclusions: Over half of B type thymomas (B2, B3, B1 and their combinations) and micronodular thymomas with lymphoid stroma showed high expression of PD-L1 (>50% of positive tumor cells) hence these groups, from biological point of view, seem to be the best candidate for immunotherapy with pembrolizumab. However, clinicopathological correlation is mandatory. Neuroendocrine thymic carcinomas were not reactive for PD-L1 and these tumors probably will not respond to this therapy. The reaction was usually evenly distributed in the tumors, so even small sample should be representative for analysis. Cytological material requires further analysis.

Keywords: Thymoma; immunotherapy; programmed cell death ligand-1 (PD-L1); thymic carcinoma

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