PLEURAL MALIGNANT MESOTHELIOMAS OVER-EXPRESS PD-L1

A. Voss1, J. Xiu2, S. Millis2, Z. Gatalica3
1Oncology, Caris Life Sciences, Basel, Switzerland
2Medical Affairs, Caris Life Sciences, Phoenix, AZ, USA
3Pathology, Caris Life Sciences, Phoenix, AZ, USA

Aim: Prognosis of pleural malignant mesothelioma (PLMM) remains poor, especially at progression after initial surgical treatment. Pemetrexed and platinum combination chemotherapy are the mainstay therapy for unresectable disease. New immune-modulation therapies may offer additional benefit for a selected group of patients. We investigated expression of PD-L1 and PD-1 as potential biomarkers in mesotheliomas.

Methods: Fourteen (M:F = 9:5) patients (age range 41-80 years) with PLMM and seven (M:F= 2:5) patients (age range 40-86 years) with peritoneal malignant mesotheliomas (PEMM) were analyzed using immunohistochemistry (IHC), in-situ hybridization (ISH) and molecular (NGS) methods (Caris Life Sciences), in search for biomarkers of targeted therapies.

Results: Overexpression of PD-L1 (defined as 2+ in ≥5% of cells) was identified in 10/14 cases of PLMM. In contrast, PEMM less frequently over-expressed PD-L1 (2/7 cases). Tumor infiltration with PD-1 positive lymphocytes was a characteristic of malignant mesotheliomas in both locations. Simultaneous over-expression of PD-L1 (mesothelioma cells) and PD-1 (tumor infiltrating lymphocytes) was seen in 9 cases of PLMM. Four of the PD-L1 positive PLMM also presented with low expression of thymidylate synthase (TS). Additional biomarkers of targeted therapies included over-expression of c-Met in both pleural and peritoneal mesotheliomas, with a similar frequency (4/13 PLMM and 3/7 PEMM), without gene amplification. No activating mutations were found in several tyrosine kinase genes (e.g. HER2, EGFR and c-MET).

Conclusions: Malignant mesotheliomas of pleura frequently (>70%) overexpress PD-L1 which makes them potential candidates for the targeted immune therapies aimed at inhibition of PD-1/PD-L1 interaction. Combination of immune therapies with conventional pemetrexed chemotherapy may be plausible in a significant portion of PD-L1 positive patients, as suggested by a concurrent low expression of TS.