**Topic:** Soluble mediators

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**ANALYSIS OF SOLUBLE MARKERS AS PREDICTIVE AND PROGNOSTIC BIOMARKERS TO IMMUNOTHERAPY WITH ANTI-PD1 MONOCLONAL ANTIBODIES IN SECOND LINE TREATMENT OF ADVANCED NON-SMALL-CELL LUNG CANCER (NSCLC)**

**Background:** Immunotherapy with anti-PD1/PDL1 monoclonal antibodies has become the second-line standard treatment for most patients with advanced NSCLC. Efficacy of these treatments seems to be higher in patients with PDL1-positive tumors. However, the difficulty to achieve tumor samples to analyze PDL1 expression requires the search of new biomarkers able to predict efficacy. The aim of study was to assess the utility of circulating biomarkers, sPDL1, sPDL2, sCD137, sIDO and sGITR, for predicting immunotherapy response in NSCLC patients.

**Material and Methods:** Blood samples from 50 NSCLC were collected before anti-PD1/PDL1 treatment in second-line. Plasma biomarker levels were measured by Multiplex bead-based assays. Non-parametric test was used for correlating analytical variables with clinico-pathological characteristics. Continuous variables were dichotomized using the median as cut-off. For progression free survival-PFS and overall survival-OS analyses, Cox Regression and Kaplan Meier curves were performed. SPSS was used for statistical analyses.

**Results:** sCD137, sGITR and sIDO correlated significantly with response (p= 0.016, p= 0.018, p= 0.030, respectively), while sPDL1 showed a trend. Three groups of patients were established according to high or low levels of these 4 markers: G1, patients with low levels of 3/4 markers; G2, patients with low levels of 2 and high levels of 2 markers; G3, patients with high levels of 3/4 markers. G1 patients showed significantly lower response rate (p= 0.011), and G3 patients
had better OS (Not reached vs. 8.6 vs. 6.33 months, p= 0.010). Individually, patients with higher levels of sIDO and sGITR exhibited a tendency toward improved PFS and OS, compared to those with lower levels. Regarding sPDL1, patients with higher levels had significant increase in PFS (Not Reached vs. 3 months, p=0.017) and a trend toward OS benefit (Not Reached vs. 8.27 months, p= 0.081). Multivariate analysis for OS revealed that combination of these 4 markers has independent prognostic value in this cohort (HR=0.595, p= 0.04).

**Conclusion:** In patients treated with anti-PD1 antibodies, sCD137, sIDO, sGITR and sPDL1 seem to be related to degree of response or PFS, and combination of these markers may be an independent prognostic factor for OS. Further investigations using larger patient cohorts are needed to confirm these results.

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