Background
Although immune checkpoint inhibitors (ICIs) have significantly changed the treatment algorithm of patients with advanced non-small cell lung cancer (aNSCLC), the discovery of clinically useful biomarkers remain a challenging issue. Recently, a new score, Patras Immunotherapy Score (PIOS), has been proposed by our group focusing on the results of aNSCLC patients treated with nivolumab or pembrolizumab. The aim of the current study was to investigate the prognostic and predictive value of PIOS in aNSCLC patients treated with combination immunotherapy with chemotherapy.

Methods
PIOS score is calculated as $PS\times BMI/LOT\times AGE$ with $PS$ representing the Performance Status, $BMI$ Body Mass Index, $LOT$ Line Of Treatment and $AGE$ the age at diagnosis. In the current study, 189 patients with confirmed aNSCLC, who were treated with chemotherapy combined with immunotherapy, were finally enrolled in order to investigate the prognostic value of PIOS. To assess specificity of PIOS for immunotherapy, a second group with 513 aNSCLC patients, treated with chemotherapy alone, were also retrospectively included.

Results
- Higher PIOS score was related to improved progression free survival (PFS) not only in univariate (HR 0.56, $p=0.015$), but also in multivariable analysis using as co-factor the PD-L1 expression (Fig.1a, HR 0.53, $p=0.012$).
- Furthermore, PIOS score was also associated with overall survival (OS) ($p=0.002$). The favorable group with higher PIOS had median OS of 1067 days compared to 528 days for the unfavorable group with low PIOS score at univariate analysis (Fig.1b, HR 0.39, $p<0.001$), while this association remained significant in multivariable analysis (HR 0.43, $p=0.001$).
- Predictiveness of PIOS for patients treated with immunotherapy was confirmed in the combined analysis of both subgroups of patients ($n=189+513$) with a significant interaction between PIOS and the specific treatment being observed (HR = 0.066 with $p<0.001$).
- Specificity of PIOS score for the combination was also confirmed by using the second group of patients ($n=513$), who were treated with chemotherapy alone. No prognostic significance for PIOS was observed in this group (Fig.1c).

Conclusions
This study confirmed the prognostic value as well as the predictive value of PIOS formula in aNSCLC patients treated with immunotherapy/chemotherapy combination.