

**6P Predictive score using clinical and blood biomarkers in advanced non-small cell lung cancer (aNSCLC) patients treated with immunotherapy**

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**Background:** Despite the overall survival (OS) benefit, only 18-20% of aNSCLC patients respond to immune-checkpoint inhibitors (ICI) as second-line therapy with a median progression-free survival (mPFS) of 2-4 months. The identification of predictive and prognostic biomarkers to select patients most likely to respond to ICI is greatly needed in guiding clinical practice.

**Methods:** We conducted a retrospective monocentric analysis of 154 aNSCLC patients receiving single-agent Nivolumab or Pembrolizumab as second-line (68%) and >3<sup>rd</sup> line (32%). We collected complete blood cell count at baseline and evaluated LDH, absolute neutrophil count (ANC), lymphocyte count (ALC), monocyte count (AMC) and eosinophil count (AEC) and their ratio such as neutrophil-lymphocyte ratio (NLR), derived-NLR (dNLR) and lymphocyte-monocyte ratio (LMR). Univariate and multivariate analyses were performed to identified independent predictors factors for immunotherapy (using Kaplan–Meier and Cox Progression analyses).

**Results:** The multivariate analysis on clinical factors showed the negative predictive role of ECOG PS 2 and liver metastasis and the positive predictive role of smoking status. The multivariate analysis for PFS showed the negative predictive role of higher ANC (>6000/mL) and LDH (>400 mg/dl) and positive predictive role of higher ALC (>2200/mL). Also, according to stepwise regression analyses, NLR>4 plays negative predictive and prognostic role at baseline. Finally, five predictive clinical and blood biomarkers at baseline (smoking status, ECOG PS, liver metastases, LDH and NLR), were used to create a predictive score for immunotherapy. Three predictive groups were defined as high, intermediate and low with a mPFS of 10.2 vs 4.9 vs 1.7 months respectively (HR 4.18 95% IC 2.64–6.62, p < 0.001).

**Table: 6P**

Predictive Factor	Assessment	Point
ECOG PS	0-1 2	0 1
Smoking (pack-years)	> 43 < 43	0 1
Liver metastases	No Yes	0 1
LDH (mg/dl)	< 400 > 400	0 1
NLR	< 4 > 4	0 1
Predictive groups	PFS (months):	HR 4.18 95%
(Points): 1 = 0	10.2 4.9 1.7	IC (2.64 – 6.62)
2 = 1-2		p < 0.001
3 = 3-5		

**Conclusions:** In advanced NSCLC patients treated with second-line immunotherapy, the identification of five and predictive clinical and blood biomarkers at baseline, combined in a predictive score, may help identify patients most likely to benefit from immunotherapy.

**Legal entity responsible for the study:** Clinical Cancer Center Giovanni Paolo II, Bari, Italy.

**Funding:** Has not received any funding.

**Disclosure:** G. Domenico: Advisory board: Bristol-Myers Squibb. All other authors have declared no conflicts of interest.