The median age of the patients was 70 years, and the majority of the patients (60.5%) were male. The cohort included patients with NSCLC of various histologies such as adenocarcinoma (n=314, 61.8%), and squamous cell carcinoma (n=75, 23.9%). Patients (33.4%) had targetable genetic alterations (EGFR/ALK-Ros1). CRP measurement was available for 285 patients (92.7%), and 55 patients (17.5%) received PD-L1 targeted treatments. Demographics are presented in detail in Table 1.

In the whole cohort (n=314), CRP level of ≥5mg/l was associated with improved overall survival (OS) in univariate (HR 1.0, CI 95% 0.22-0.41) and multivariate analyzes (HR 0.42, CI 95% 0.28-0.66) (Figure 1, Table 2).

Among the PD-L1 treated (n=55), both CRP of ≥10mg/l and PD-L1 TPS of ≥50 were associated with increased progression free survival (PFS) (HR 0.66, CI 95% 0.42-0.97) and OS (HR 0.39, CI 95% 0.18-0.86) while CRP level of ≥10mg/l was statistically significant_association (HR 0.21, CI 95% 0.12-0.38) (Table 3).

The combination of high PD-L1 TPS (≥50) and CRP (≥10) carried a high negative predictive value among the ICI treated with a median PFS of 2.22 months (CI 0.56-6.75-77) which was very similar to patients with low PD-L1 3.35 months (CI 0.59-1.35-77) (Figure 2).

To our knowledge, our study is the first to use pre-treatment tumor PD-L1 score and circulating CRP levels as a biomarker for ICIs benefit. Our results show that both bare independent predictive value for ICIs therapies (PFS), and PD-L1 also for OS. More importantly, the benefit from ICIs therapies in PD-L1 score (≥50) is driven mostly by patients with low CRP levels (≥10mg/l) while limited ICIs benefit is seen with high CRP levels. Furthermore, since the obtainability of tumor biopsies can be challenging especially in lung cancers, biomarkers analyzable from peripheral blood could be more feasible.

Conclusions

Adding plasma CRP levels to PD-L1 significantly increased the predictive power of sole PD-L1. Patients with high CRP little benefit from PD-L1 regardless of PD-L1 scores regardless of PD-L1.

The study highlights combined evaluation of plasma CRP and PD-L1 TPS as negative predictive marker for ICIs therapies.

Figure 1. Overall Survival according to CRP (A) and PD-L1 (B).

Table 1. Patient demographics.

Table 2. Univariate and multivariate analysis for OS.

Table 3. Univariate and multivariate analyzes for PFS and OS for the PD-L1 treated (from the 1st dose).

References