PATIENTS AND METHODS

• Immunosenesence is a progressive remodeling of immune functions with a multifactorial etiology (aging, chronic inflammation, persistent infectious cancer).
• CMV has been shown to act as chronic antigenic stressor and to accelerate immune aging by affecting peripheral blood T cell phenotyping, including loss of CD28 or overexpression of CD57.
• Latent viral infections were shown to be associated with chronic type I IFN signature that might promote lymphocyte senescence.
• We defined SIP as the proportion of CD28-CD57+KLRG1+CD8+ circulating T cells. We showed that a high pretreatment SIP (>39.5%) was associated with resistance to ICB in patients with aNSCLC.

OBJECTIVE

We aimed to assess the role of SIP combined to CMV status on outcomes in aNSCLC patients and the association between SIP and chronic type I IFN signature.

RESULTS

Baseline SIP status was assessed by flow cytometry on fresh blood samples from ICB-treated and polychemotherapy-treated (PCT) aNSCLC patients. Type I IFN score was calculated by the sum of relative expression of 5 IFN-stimulated genes (IFIT4, IFIT1, IFITM1, LY6E, MX1), determined by RT-qPCR. Soluble factors associated to interferons (IFNα, IFNβ, IFNA, IP-10, PD-L1) were quantified using the MSD assay.

Fig. 1: SIP and CMV status
Fig. 2: PFS and OS according to CMV status
Fig. 3: PFS and OS in CMV+ patients according to SIP status

CONCLUSION

203 aNSCLC patients (142 ICB-treated, 61 PCT-treated) were evaluable for SIP (19.7% SIP+) and 180 patients (89%) for CMV status. CMV+ patients rate was significantly higher in IFN compared to SIP- patients (91.4% vs 50%, p<0.0001). Among CMV+ patients, SIP+ patients had lower PFS (1.9 vs 3.3 months, p=0.0087) and OS (6.2 vs 22.8 months, p=0.0008) than SIP- (Fig.3). Otherwise, at baseline, no association between SIP and type I IFN signature nor plasmatic levels of IFN-related factors was found (Fig.4).

SIP+ patients are CMV+. SIP+ identifies patients with poorer outcomes in CMV+ ICB-treated aNSCLC. No association between type I IFN signature or IFN-related plasmatic factors and SIP was found.

BACKGROUND

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