11P - Senescent Immune Phenotype (SIP) status that predicts resistance to Immune Checkpoint Blockers (ICB) among CMV+ advanced Non-Small Cell Lung Cancer (aNSCLC) patients is not associated with chronic type I IFN signature

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BACKGROUND

- Immunosenescence is a progressive remodeling of immune functions with a multifactorial etiology (aging, chronic inflammation, persistent infections, cancer).
- CMV has been shown to act as chronic antigenic stressor and to accelerate immune ageing by affecting peripheral blood T cell phenotypes, 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%, SIP+) was associated with resistance to ICB in patients with aNSCLC[a].

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.

PATIENTS AND METHODS

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 (*IFI44, IFIT1, IFITM1, LY6E, MX1*), determined by RT-qPCR. Soluble factors associated to interferons (IFNα, IFNβ, IFNλ, IP-10, PD-L1) were quantified using the MSD assay.

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RESULTS

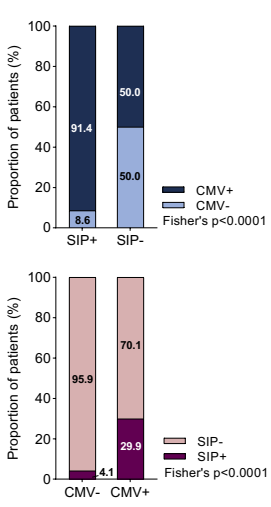

Fig. 1: SIP and CMV status

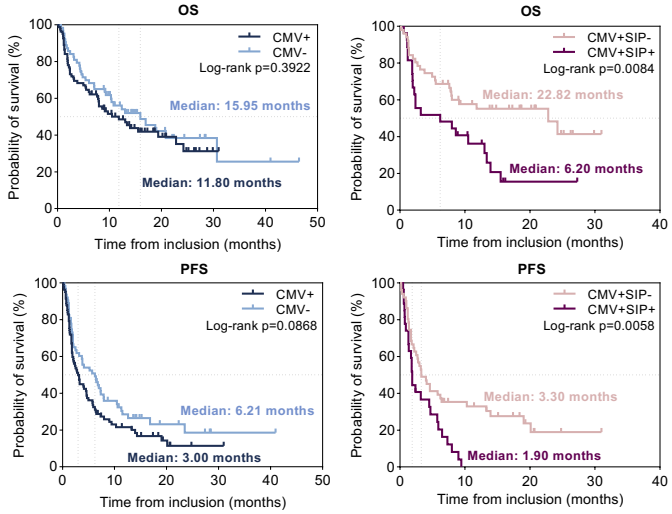

Fig. 2: PFS and OS according to CMV status

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

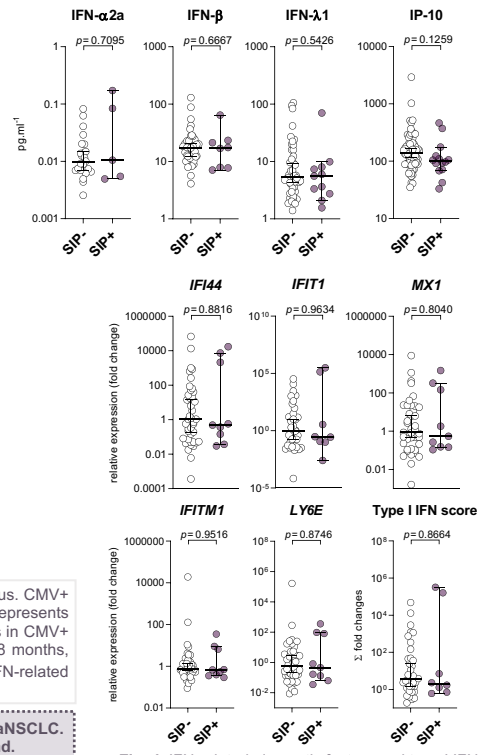

Fig. 4: IFN-related plasmatic factors and type I IFN signature according to SIP status

203 aNSCLC patients (142 ICB-treated, 61 PCT-treated) were evaluable for SIP (19.7% SIP+) and 180 patients (89%) for CMV status. CMV+ patient's rate was significantly higher in SIP+ compared to SIP- patients (91.4% vs 50%, p<0.0001). Among CMV+ patients, SIP+ represents only 30% (Fig.1). In ICB-treated patients, CMV status was not sufficient to predict outcomes (median PFS 6.21 in CMV- vs 3 months in CMV+ patients, p=0.087) (Fig.2). Among CMV+ patients, SIP+ patients had lower PFS (1.9 vs 3.3 months, p=0.006) and OS (6.2 vs 22.8 months, p=0.008) 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).

CONCLUSION

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.

[a]Ferrara R, Naigeon M, et al. Clin Cancer Res. 2021 Jan 15