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TRANSLATIONAL RESEARCH

23P Immunosenescence (iSenescence) correlates with progression (PD) to PD-(L)1 inhibitors (IO) and not to platinum-chemotherapy (PCT) in advanced non-small cell lung cancer (aNSCLC) patients (pts)

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Background: iSenescence is a remodeling of immune functions with a multifactorial etiology (i.e. aging, chronic inflammation, cancer). Although the absence of CD28 and the expression of CD57 and KLRG1 on circulating T-lymphocytes are hallmarks of iSenescence, the characterization of such phenotype in aNSCLC pts and the correlation with clinical characteristics and benefit from IO or PCT are currently unknown.

Methods: A senescent immune phenotype (SIP) defined as % of circulating $CD8^+CD28^-CD57^+KLRG1^+$ T-lymphocytes was assessed by flow cytometry (FC) on fresh blood from aNSCLC pts treated with IO or PCT in a single institution. A log-rank

maximization method was used to identify a SIP cut-off level and dichotomize pts accordingly. The objective was to correlate SIP with clinical characteristics and RECIST response by univariate logistic regression analysis.

Results: 37 aNSCLC pts were evaluable for SIP before IO: 32% $\geq$ 65 years, 91% non-squamous, 43% KRAS mutated, 51% with PD-L1 expression $\geq$1%, 8% chemotherapy naïve. 43% had PD, 41% stability (SD), 16% partial response (PR). Median PFS and OS were 2.7 (95% CI 1.8; 7.3) and 13 (95% CI 4.8-NR) months, respectively, median follow-up was 9.3 (95% CI 6.2-14.9) months. SIP (% $CD28^-CD57^+KLRG1^+$) median value on circulating $CD8^+$ lymphocytes was 12.2% (min 1.7%, max 56.1%). 32% of pts had >20.47% $CD8^+$ lymphocytes with a $CD28^-CD57^+KLRG1^+$ phenotype, being classified SIP^+. SIP status did not significantly correlate with age, pts' characteristics or CT exposure. 2 (17%) of 12 SIP^+ had PR/SD (DCR), vs 19 (76%) of 25 SIP^- pts ($p = 0.001$); median PFS was significantly lower in SIP^+ (1.5 months 95% CI 1;2.2) vs SIP^- pts (7.4 months 95% CI 5.5, 9.3) ($p = 0.001$). Among 61 aNSCLC pts treated with 1st line PCT, 18% had PD, 43% SD, 39% PR. SIP median value on circulating $CD8^+$ lymphocytes was 17.9% (min 0.89%, max 66.1%), 43% of pts were SIP^+. SIP did not significantly correlate with DCR (OR: 0.82, 95% CI 0.22-3.13, $p = 0.82$) upon PCT.

Conclusions: iSenescence, monitored by FC measurement of 3 surface molecules on circulating $CD8^+$ lymphocytes, is observed in 32% and 43% of aNSCLC pts before IO or PCT, respectively. SIP correlated with lower DCR upon IO and not PCT.

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