## 1416P Immunosenescence (iSenescence) correlates with disease progression in advanced non-small cell lung cancer (aNSCLC) patients treated with PD-(L)1 inhibitors (IO)

R. Ferrara[1], M. Naigeon[1], E. Auclin[2], B. Duchemann[1], L. Cassard[1], J. Medhi[1], L. Boselli[1], J. Grivel[1], A. Desnoyer[1], L. Mezquita[3], F. Aboubakar[3], L. Hendriks[3], D. Planchard[3], C. Caramella[4], J. Remon[3], M. Ngocamus[5], C. Nicotra[5], B. Besse[3], N. Chaput[1]

*[1]Laboratory of Immune Oncology, Institut Gustave Roussy, Villejuif, France, [2]Oncology, Hopital European George Pompidou, Paris, France, [3]Department of Medical Oncology, Gustave Roussy Institute, Villejuif, France, [4]Radiology, Institut Gustave Roussy, Villejuif, France, [5]Drug Development Department, Institut Gustave Roussy, Villejuif, France*

**Background:** iSenescence is a progressive 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 Killer-cell lectin-like receptor G1 (KLRG1) on peripheral T-lymphocytes are potential hallmarks of iSenescence, the characterization of such phenotype in IO-treated aNSCLC patients and the correlation with clinical characteristics and benefit from immunotherapy are currently unknown.

**Methods:** A senescent immune phenotype (SIP) defined as a percentage of circulating $CD8^+CD28^-CD57^+KLRG1^+$ T-lymphocytes was assessed by flow cytometry (FC) on fresh blood from aNSCLC patients treated with IO in a single institution (03/2017–04/2018). A log-rank maximization method was used to identify a SIP cut-off level and dichotomize patients accordingly. The objective was to correlate SIP with clinical characteristics and RECIST response by univariate logistic regression analysis.

**Results:** 39 aNSCLC patients were evaluable for SIP before IO: 38% $\geq$ 65 years, 87% non-squamous, 38% KRAS mutated, 54% with PD-L1 expression $\geq$1%, 13% chemotherapy naïve. Among 30 patients evaluable for IO response, 53% had progression (PD), 27% stability (SD), 20% partial response (PR). Median PFS was 1.9 months (95% CI 1.5; 2.5). OS was not calculated due to the short follow-up [6 months (95% CI 4-11)]. SIP (% $CD28^-CD57^+KLRG1^+$) median value on circulating $CD8^+$ lymphocytes was 15.26% (min 1.87%, max 56.28%). Overall, 13 (33%) of 39 patients had >22.25% $CD8^+$ lymphocytes with a $CD28^-CD57^+KLRG1^+$ phenotype, being classified as $SIP^+$. SIP status did not significantly correlate with age, IO-baseline patients' characteristics or previous chemotherapy exposure. Among patients evaluable for IO response, only 1 (10%) of 10 $SIP^+$ experienced disease control (PR/SD), compared to 13 (65%) of 20 $SIP^-$ patients; similarly, PD rate was significantly higher in $SIP^+$ compared to $SIP^-$ patients (90% vs 35%, $p = 0.007$).

**Conclusions:** iSenescence, monitored by FC measurement of 3 surface molecules on circulating $CD8^+$ lymphocytes, is observed in 33% of aNSCLC patients, is independent of age and correlates with lower disease control rate upon IO.

**Legal entity responsible for the study:** Institut Gustave Roussy.

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

**Disclosure:** All authors have declared no conflicts of interest.