1417P Preliminary results of PRINCiPe (predictors of resistance to immunotherapy with nivolumab [NIV]) study in advanced pretreated non-small cell lung cancer (APNSCLC), investigating the role of an immune genomic signature (IGS) including JAK2, JAK3, PIAS4, PTPN2, STAT3, IFNAR2 alterations

S. Pilotto[1], G. Grizzi[1], I. Sperduti[2], M. Simbolo[3], C. Vicentini[3], A. Calió[3], M. Caccese[1], A. Mafficini[3], L. Carbognin[1], V. Corbo[3], A. Gkountakos[3], A. Santo[1], M. Infante[4], M. Brunelli[3], A. Scarpa[5], G. Tortora[1], E. Bria[6]

[1]Medical Oncology, University of Verona, AOUI Verona, Verona, Italy, [2]Biostatistics, Regina Elena National Cancer Institute, Rome, Italy, [3]Department of Diagnostics and Public Health, Section of Anatomical Pathology, University and Hospital Trust of Verona, Verona, Italy, [4]Thoracic Surgery, AOUI Verona, Verona, Italy, [5]ARC-Net Research Centre and Department of Diagnostics and Public Health, AOU Verona, Verona, Italy, [6]UOC Oncologia Medica, Università Cattolica del Sacro Cuore - Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background: Although immunotherapy impressively improved the outcome of APNSCLC, many patients (pts) rapidly progress. The mechanism of resistance may be influenced by genomic abnormalities in immune-escape/editing genes.

Methods: FFPE-tumor blocks of APNSCLC pts undergone NIV were retrospectively sequenced for Somatic Mutations/Copy Number Variations (SM/CNV) (Ampliseq 17-genes customized panel: APLNR, B2M, IFNAR1, IFNAR2, IFNGR1, IFNGR2, IRF9, JAK1, JAK2, JAK3, PIAS4, PTPN2, SOCS1, STAT1, STAT2, STAT3, TYK2). End-points of PRINCiPe study: overall-, progression-free-survival (OS/PFS) and objective response rate (ORR).

Results: 24 APNSCLC pts were gathered (median age 69.5 yrs, median number of previous lines 3 [2-5], 2nd line NIV [70.8%], male/female 79.2/20.8%, squamous/non-squamous 41.7/58.3%, EGFR mutant 5 [20.8%], median follow-up 6.8 months [range 1-23], deaths 14 [58.3%]). JAK3/JAK2 (6/3 pts, 25/12.5%) CNV, and IFNAR2/STAT3 SM (2 pts, 8.3%) were the most frequent abnormalities. Pts (12) with JAK3, PIAS4, PTPN2, STAT3, IFNAR2 SM and/or JAK2/3 CNV (IGS+) had a significantly lower OS/PFS than those without (IGS-). At multivariate analysis, IGS+ was independently associated with shorter OS (HR 4.90, 95% CI 1.40-16.5, p = 0.01) and PFS (HR 6.10, 95% CI 2.0-18.7, p = 0.001); the (previous) surgery was significantly associated

with longer PFS (HR 4.20, 95% CI 1.1-11.4, p = 0.03). IGS+ pts were significantly more associated with the presence of liver metastases (p = 0.04). A trend towards lower activity of NIV in EGFR+ pts was found.

Table: 1417P

	IGS+	IGS-	p-value
ORR (%, 95% CI)	-	16.6% (2-31)	0.09
Median OS (months, 95% CI)	4 (1-8)	13 (n.e.)	0.046
Median PFS (months, 95% CI)	3 (2-3.5)	6 (5-9)	0.002

Conclusions: The derived IGS appears to identify APNSCLC pts with a lower chance to benefit from NIV, supporting intrinsic resistance. Given the small sample, a prospective larger and external validation is ongoing.

Legal entity responsible for the study: Emilio Bria.

Funding: University of Verona.

Disclosure: All authors have declared no conflicts of interest.