Exploratory Biomarker Analysis of Ociperlimab Plus Tislelizumab in Patients with PD-L1 Positive Non-Small Cell Lung Cancer in AdvanTIG-105

Yan Yu[1], Yanyan Peng[2], Wei Tan[2], Guohua Yu[3], Jun Zhang[4], Se Hyun Kim[5], Han Yan[6], Hanying Li[2], Yun Zhang[6], Zinan Bao[2], Yunxia Zuo[2], David S. Shames[7], Shun Lu[8]

[1]Harbin Medical University Cancer Hospital, Harbin, Heilongjiang, China; [2]BeOne Medicines, Ltd, Shanghai, China; [3]Weifang People's Hospital, Weifang, Shandong, China; [4]OSF Healthcare Cancer Institute, Peoria, IL, USA; [5]Seoul National University Bundang Hospital, Seongnam, South Korea; [6]Beone Medicines, Ltd, Beijing, China; [7]BeOne Medicines, Ltd, San Carlos, CA, USA; [8]Shanghai Chest Hospital, Shanghai, China

CONCLUSIONS

- In patients with NSCLC with PD-L1 TC ≥25%, or TIGIT IC ≥5%, there was a trend toward longer PFS and higher ORR compared with low PD-L1 or low TIGIT subgroups when treated with OCI plus TIS
- A trend toward longer PFS was observed in PD-L1 TC ≥25% or TIGIT IC ≥5% subgroups in patients with NSQ- versus SQ-NSCLC and may be associated with biological differences in histology
- PD-L1 TC combined with TIGIT IC or TIGIT MOA-related immune cells signatures (NK cell, Treg and macrophage) can further enrich PFS benefit compared with other subgroups
- The biomarker findings were based on a single-arm study with limited sample size. Confirmation of these results will require prospective evaluation of OCI plus TIS in randomized studies

INTRODUCTION

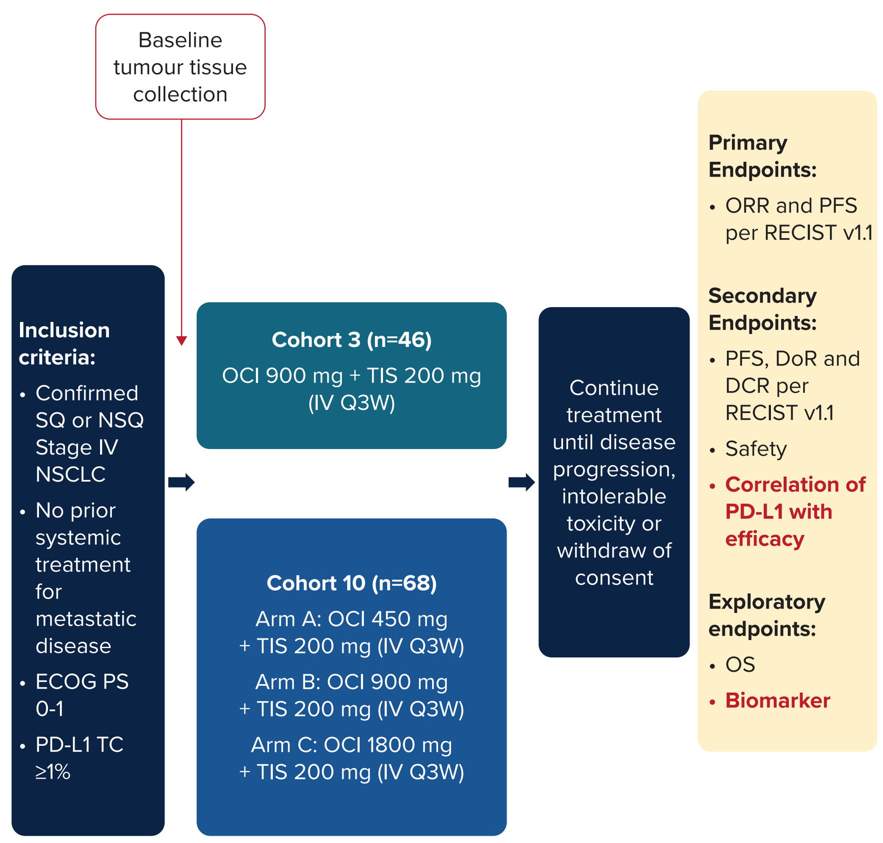
- Ociperlimab (OCI), an anti-T cell immunoreceptor with Ig and ITIM domains (TIGIT) antibody, plus tislelizumab (TIS), an anti-programmed cell death protein 1 antibody, may enhance antitumour immune responses in advanced solid tumours
- In a retrospective biomarker analysis of patients in AdvanTIG-105 (NCT04047862),[1] a phase 1/1b open-label study of OCI plus TIS for treatment naïve metastatic non-squamous (NSQ) and squamous (SQ) programmed cell death ligand 1 (PD-L1) positive (tumor cells [TC] ≥1%) non-small cell lung cancer (NSCLC), we examined PD-L1 expression on TC, TIGIT expression on immune cells (IC), and gene expression profiling (GEP), and analysed their associations with objective response rate (ORR) and progression-free survival (PFS)

METHODS

Patients and Biomarker Evaluation

- AdvanTIG-105 cohort 3 and cohort 10 study design is shown in **Figure 1**
- PD-L1 TC was measured using the Roche SP263 immunohistochemistry (IHC) assay
- TIGIT IC was measured using the Roche SP410 IHC assay
- GEP was performed using TrueSeq RNA Access (Illumina)

Figure 1. AdvanTIG-105 Cohort 3 and Cohort 10 Study Design



Abbreviations: DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IV, intravenous; OS, overall survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Statistical Analysis

- Gene signature scores were evaluated with single sample gene set enrichment analysis (ssGSEA) and gene lists used for signature score were from published BostonGene[2]
- The survival distribution of PFS was estimated using Kaplan-Meier Method; hazard ratio (HR) of PFS was estimated by Cox proportional hazards model
- Differences between ORRs were tested using Fisher exact method
- All *P*-values were reported for descriptive purposes

RESULTS

Baseline Characteristics

- Baseline characteristics were comparable across cohorts and between intent-to-treat (ITT) and biomarker evaluable patients (BEP) (**Table 1**)
- At Aug 2024 data-cut-off, median follow-up was 19.7 months (m; range: 0.7-41.6 m) for cohort 3 and 9.8 m (range: 0.3-21.4 m) for cohort 10

Table 1. Patient Baseline Characteristics

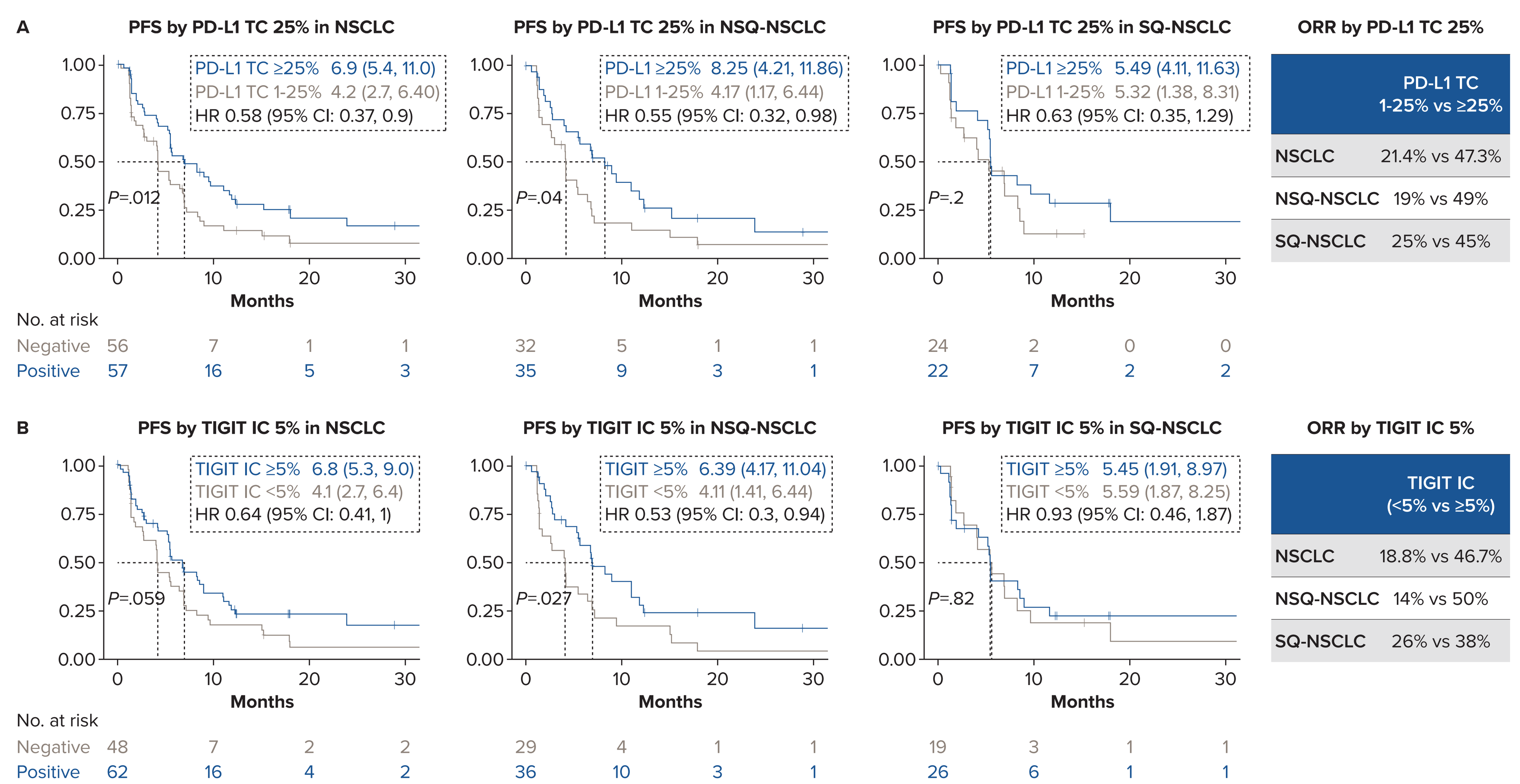
	Cohort 10 Arm A	Cohort 10 Arm B	Cohort 10 Arm C	Cohort 3 ITT	Cohorts 3 and 10 ITT	Cohorts 3 and 10 GEP BEP*
n	24	21	23	46	113	93
Age (mean, SD)	61.54 (10.46)	64.00 (7.05)	65.39 (8.98)	64.96 (8.91)	64.15 (8.97)	64.10 (9.20)
Sex=M (n, %)	17 (70.8)	17 (81.0)	17 (73.9)	29 (63.0)	80 (70.2)	65 (69.9)
Race=Asian (n, %)	22 (91.7)	19 (90.5)	17 (73.9)	34 (73.9)	92 (80.7)	73 (78.5)
ECOG=1 (n, %)	21 (87.5)	16 (76.2)	18 (78.3)	34 (75.6)	89 (78.1)	71 (76.3)
BMI (mean, SD)	22.78 (4.47)	23.17 (3.69)	24.01 (3.72)	24.30 (5.92)	23.71 (4.84)	23.77 (4.60)
PD-L1 TC ≥25%	9 (37.5)	9 (42.9)	12 (52.2)	27 (60.0)	57 (50.0)	50 (53.8)
TIGIT IC ≥5%	14 (58.3)	8 (38.1)	13 (56.5)	27 (60.0)	62 (54.4)	51 (54.8)

*PD-L1 IHC results were available for all patients. TIGIT IHC results were available for 96% of patients (109/113).
Abbreviations: BMI, body mass index; M, male.

PFS and ORR Benefits in NSQ- and SQ-NSCLC with PD-L1 TC ≥25% or TIGIT IC ≥5%

- PD-L1 TC ≥25% was associated with a trend toward longer PFS and higher ORR versus <25% primarily in patients with NSQ-NSCLC (**Figure 2A**)
- TIGIT IC ≥5% was associated with a trend toward longer PFS and higher ORR versus <5% primarily in NSQ-NSCLC (**Figure 2B**)

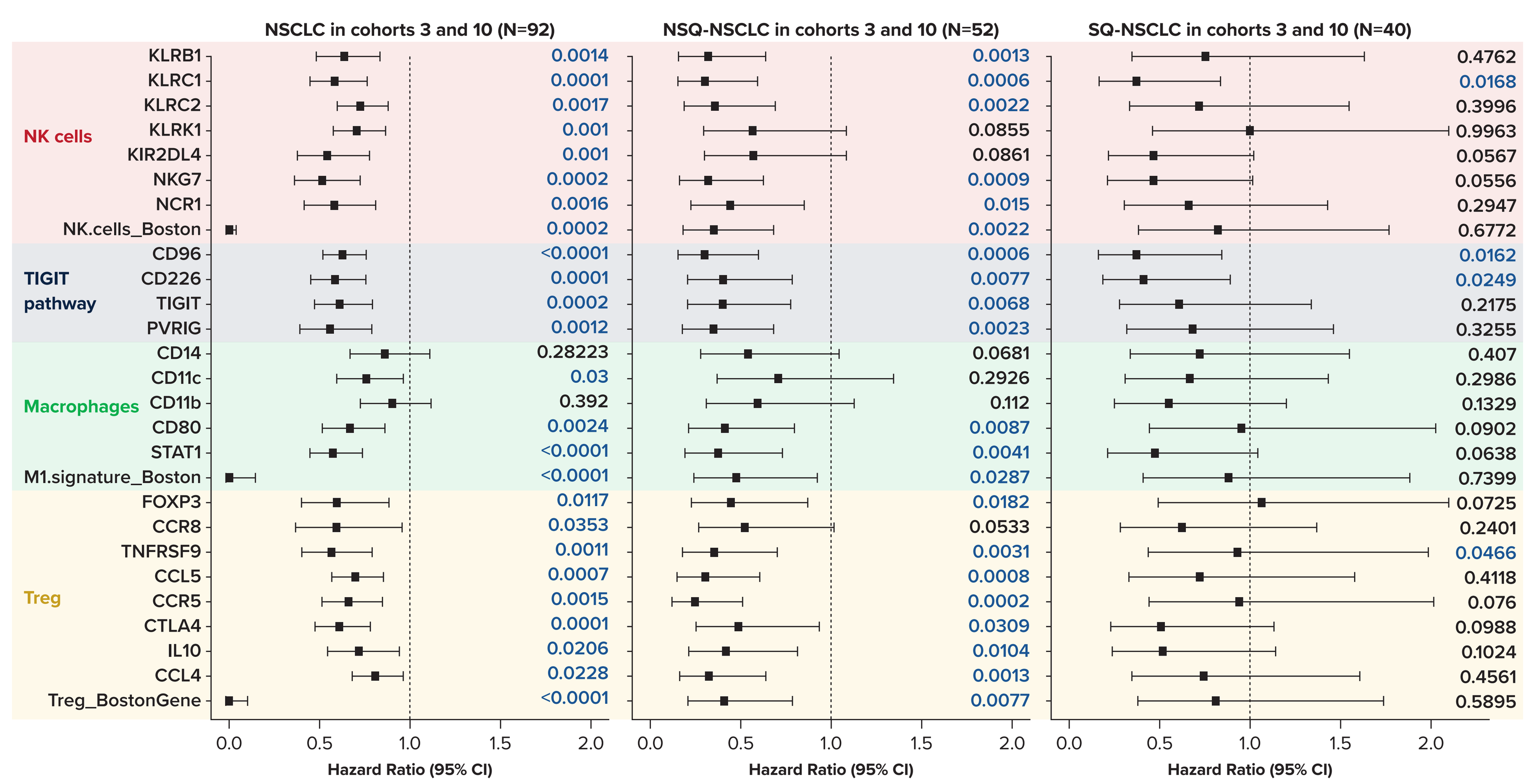
Figure 2. PFS and ORR by PD-L1 and TIGIT Expression Status in Patients with NSQ-NSCLC and SQ-NSCLC



Anti-TIGIT Mechanism of Action (MOA) Related Pathways and Immune Cell Signatures Associated with PFS primarily in NSQ-NSCLC

- Anti-TIGIT MOA related GEP signatures (natural killer [NK] cells, regulatory T cells [Treg], and macrophages) were strongly correlated with a trend toward longer PFS primarily in patients with NSQ-NSCLC
- The observed wider HR 95% CI observed in SQ-NSCLC may indicate increased tumour heterogeneity or be due to smaller patient size

Figure 3. Association of Gene Expression Signatures with PFS in NSQ- vs SQ-NSCLC*

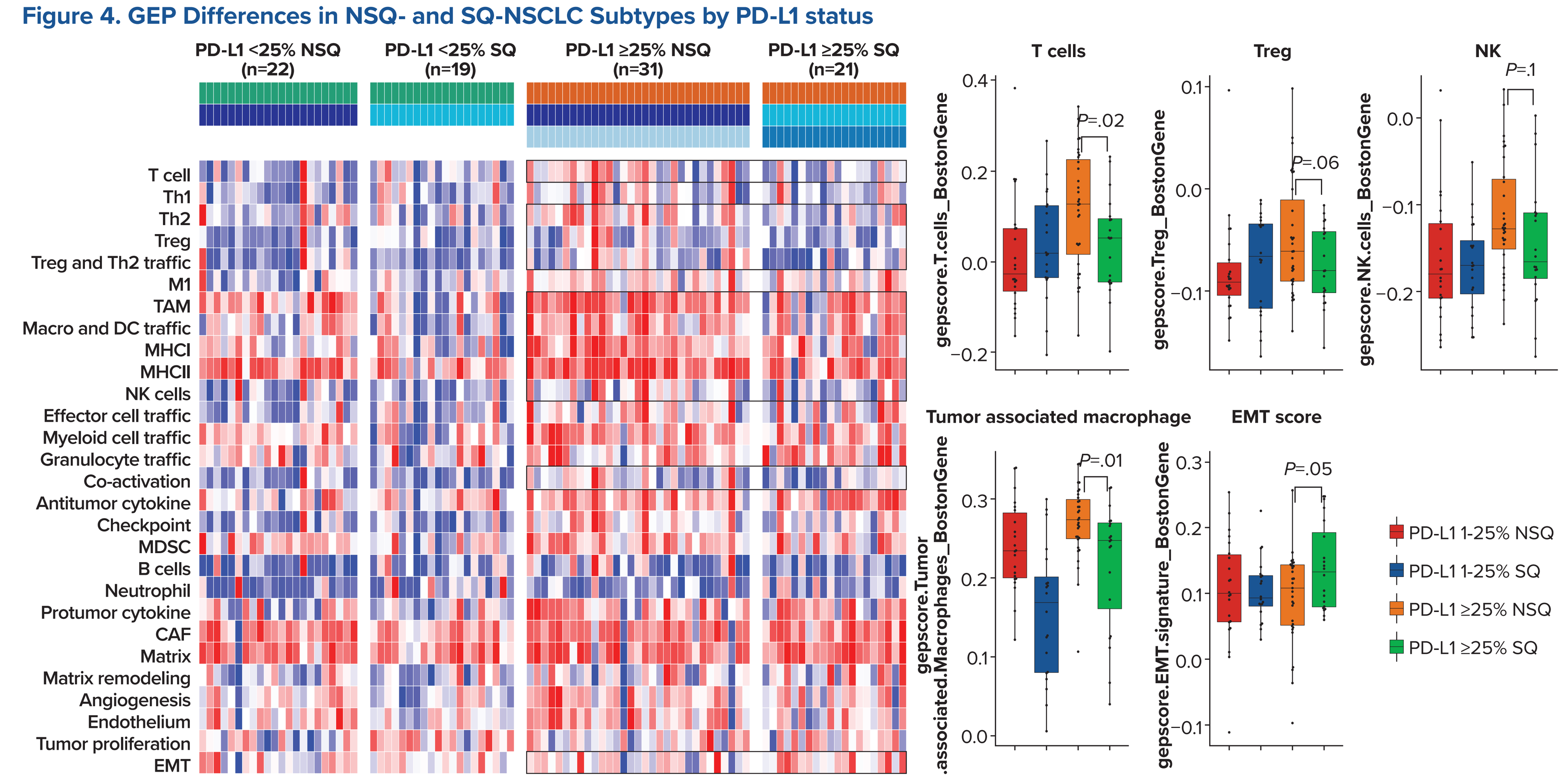


*P≤.05 highlighted in blue.

Biological Differences in PD-L1 High NSCLC NSQ and SQ Subtypes

- T cells, Treg, NK cells, tumor associated macrophages (TAM), major histocompatibility complex class II (MHCII), and co-activation cytokines signatures were higher in PD-L1 TC ≥25% NSQ-NSCLC compared with SQ-NSCLC (**Figure 4**)
- Epithelial-to-mesenchymal transition (EMT) signature was lower in PD-L1 TC ≥25% NSQ-NSCLC compared with SQ-NSCLC (**Figure 4**)
- The enrichment of immune reactive factors in the PD-L1 TC ≥25% NSQ-NSCLC subgroup may be associated with the observed trend toward longer PFS versus SQ-NSCLC subgroup

Figure 4. GEP Differences in NSQ- and SQ-NSCLC Subtypes by PD-L1 status

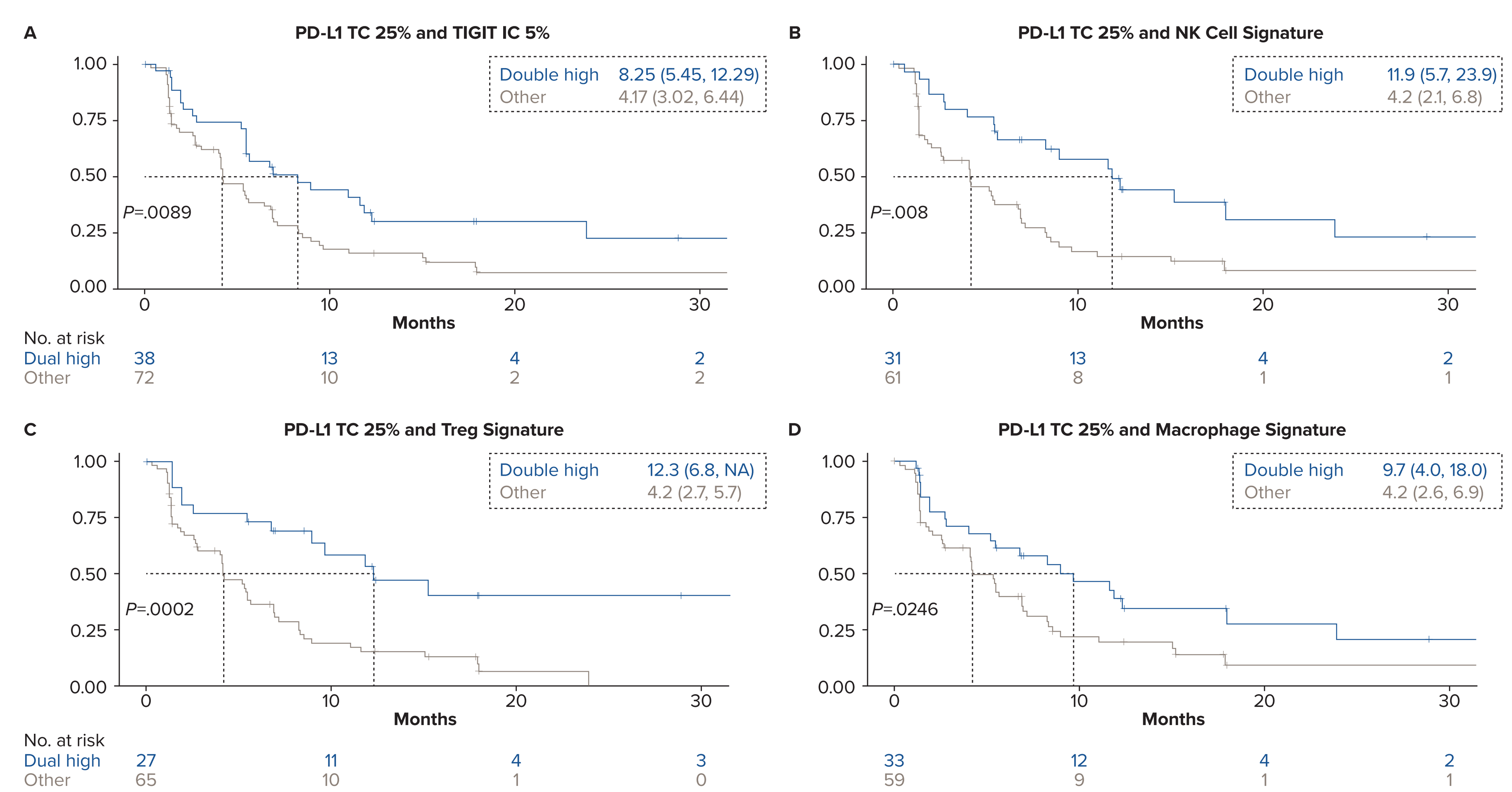


Abbreviations: CAF, cancer-associated fibroblast; MDSC, myeloid-derived suppressor cell; Th, T helper cell.

PD-L1 TC ≥25% Combined with TIGIT IC ≥5%, or Signatures of NK Cells, Treg, and Macrophages Can Further Enrich PFS Benefit

- Patients with PD-L1 and TIGIT double high (**Figure 5A**), PD-L1 and NK signature double high (**Figure 5B**), PD-L1 and Treg signature double high (**Figure 5C**), PD-L1 and macrophage signature double high (**Figure 5D**) achieved prolonged PFS benefits compared with other subgroups

Figure 5. PD-L1 TC 25% in Combination with TIGIT IC 5%, NK Cells, Treg, or Macrophage Signatures, and Associations with PFS Benefit



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DISCLOSURES

YY: No disclosures.

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