

IO102-IO103 cancer vaccine plus pembrolizumab for first line (1L) treatment of advanced solid tumors: final results of a phase 2 basket trial

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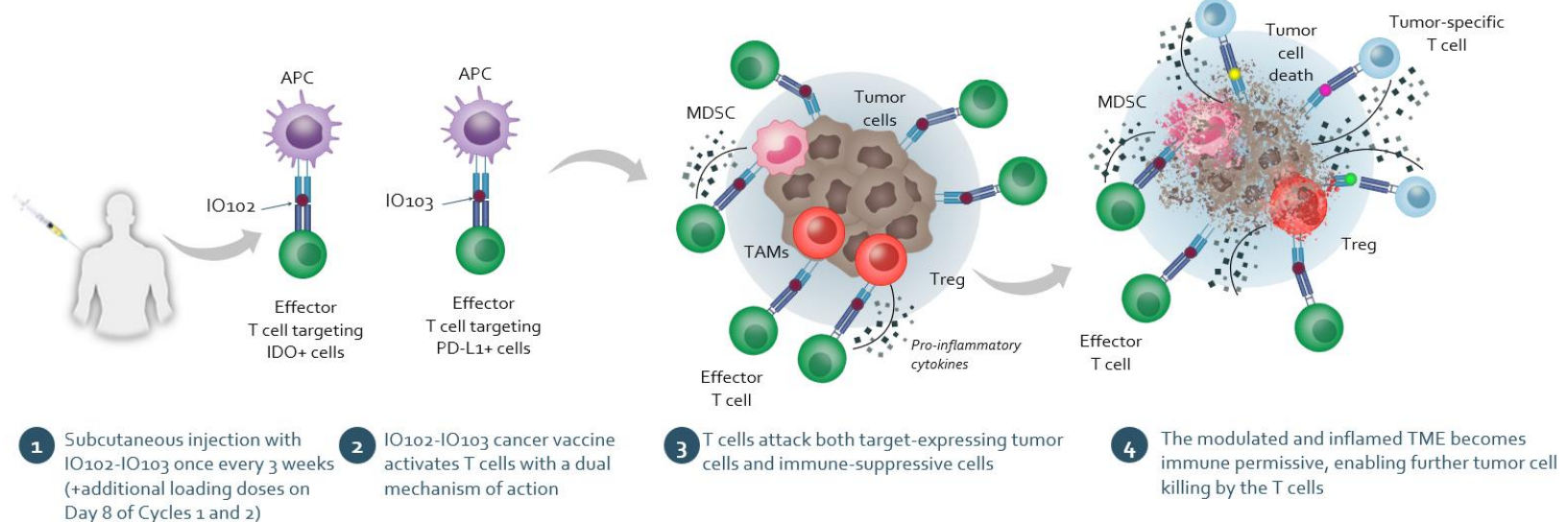


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Background

IO102-IO103 is an investigational immuno-modulatory therapeutic cancer vaccine designed to kill both tumor cells and immune-suppressive cells in the tumor microenvironment. Co-administration of IO102 and IO103 is hypothesized to benefit patient outcomes since the dual antigen vaccine can impact two separate immune-resistant pathways (IDO1 and PD-L1, respectively).¹ Efficacy and safety data from IOB-013/KN-D18, a randomized phase 3 trial with IO102-IO103 plus pembrolizumab versus pembrolizumab in 1L advanced melanoma, will also be presented at this conference.²



Study design

IOB-022/KN-D38 is a phase 2, non-comparative, open-label, multicenter, basket trial designed to assess the efficacy and safety of treatment with IO102-IO103 in combination with pembrolizumab in patients with non-small cell lung cancer (NSCLC) or squamous cell carcinoma of the head and neck (SCCHN).

Eligibility criteria	Treatment and assessments	Endpoints
NSCLC cohort: - Metastatic lung adenocarcinoma - PD-L1 TPS ≥50% - No prior first-line therapy SCCHN cohort: - Recurrent or metastatic SCCHN - PD-L1 CPS ≥20 - No prior first-line therapy	Q3W IO102-IO103 85 µg each + pembrolizumab 200 mg Tumor imaging schedule: First year: Q9W Second year: Q12W For up to 2 years	Primary endpoint: - ORR per investigator RECIST 1.1* Secondary/exploratory endpoints: - PFS per investigator RECIST 1.1** - OS*** - Safety

*Assessed in efficacy evaluable patients (patients who have completed at least 2 cycles of study treatment).

**Benchmarks for mPFS are 6.5 months for NSCLC (TPS ≥50%)³ and 3.4 months for SCCHN (CPS ≥20).⁴

***Benchmarks for mOS are 20 months for NSCLC (TPS ≥50%)³ and 14.8 months for SCCHN (CPS ≥20).⁴

Baseline characteristics

Baseline characteristics	NSCLC (adenocarcinoma*) (N=37)	SCCHN (N=21)
Age, median (range) years	71 (55–80)	69 (58–86)
Gender, male, n (%)	18 (48.6)	14 (66.7)
Smoking status, current/prior smoker, n (%)	34 (91.9)	14 (66.7)
ECOG PS 0, n (%)	13 (35.1)	5 (23.8)
ECOG PS 1, n (%)	24 (64.9)	16 (76.2)
Stage IVA	15 (40.5)	7 (33.3)
Stage IVB	22 (59.5)	2 (9.5)
Stage IVC	NA	12 (57.1)

*One patient had squamous cell carcinoma, which was only identified after initiation of study treatment; this patient was not included in the efficacy evaluable population.

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References

- 1) Chapellier M, et al. *Cancer Res.* 2025;85(8 Suppl 1):2241.
- 2) Hassel JC, et al. *ESMO* 2025. Proffered paper presentation 3212.
- 3) de Castro G, Jr., et al. *J Clin Oncol.* 2023;41(11):1986–1991.
- 4) Burtness B, et al. *Lancet.* 2019;394 (10212):1915–1928.
- 5) Riess JW, et al. *Ann Oncol.* 2024;35 (Suppl 2):S691.
- 6) Riess JW, et al. *J Immunother Cancer.* 2024;12 (Suppl 2): A1–A1683.

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Abbreviations: AE, adverse event; APC, adenomatous polyposis coli; BOR, best overall response; cDNA, cell-free DNA; CI, confidence interval; CPS, combined positive score; CR, complete response; ctDNA, circulating tumor DNA; DE, differential expression; DMSO, dimethyl sulfoxide; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ELISpot, enzyme-linked immunospot; EOT, end of treatment; ID, identification; IDO, indoleamine 2,3-dioxygenase; IMS, immune-modulatory signature; MDSC, myeloid-derived suppressor cell; mOS, median overall survival; mPFS, median progression-free survival; N, number of patients; NA, not applicable; NE, not estimable; NSCLC, non-small cell lung cancer; OS, overall survival; ORR, overall response rate; PBMC, peripheral blood mononuclear cell; PD, progressive disease; PD-L, programmed death ligand; PFS, progression-free survival; PS, partial survival; PR, partial response; PT, patient; Q3W, once every 3 weeks; Q9W, once every 9 weeks; Q12W, once every 12 weeks; RECIST, response evaluation criteria in solid tumors; RNA, ribonucleic acid; SCCHN, squamous cell carcinoma of the head and neck; SD, stable disease; TAM, tumor associated macrophage; TME, tumor microenvironment; TPS, tumor proportion score; Treg, regulatory T cell; VAF, variant allele frequency.

Safety results

All patients received at least one cycle of study treatment. At data cut-off (Sep 1st, 2025), three patients remained on treatment. All discontinued patients were followed for AEs until 100 days after the last dose.

Adverse event summary, n, (%)	NSCLC (N=37)	SCCHN (N=21)
Number of patients with at least one AE	35 (94.6)	21 (100.0)
Related AE (any study treatment)	30 (81.1)	17 (81.0)
Serious AE	19 (51.4)	8 (38.1)
Serious related AE (any study treatment)	5 (13.5)	2 (9.5)
Grade 3 or 4 AE	21 (56.8)	10 (47.6)
Grade 3 or 4 AE related to any study treatment	9 (24.3)	5 (23.8)
AE leading to discontinuation of any study treatment	8 (21.6)	4 (19.0)
AE leading to death*	4 (10.8)	1 (4.8)
Number of patients with immune mediated AE	10 (27.0)	5 (23.8)

*One of these AEs (stroke) was considered possibly treatment-related by investigator: the patient (NSCLC) had an underlying hyper-coagulable condition possibly exacerbated by the study treatment.

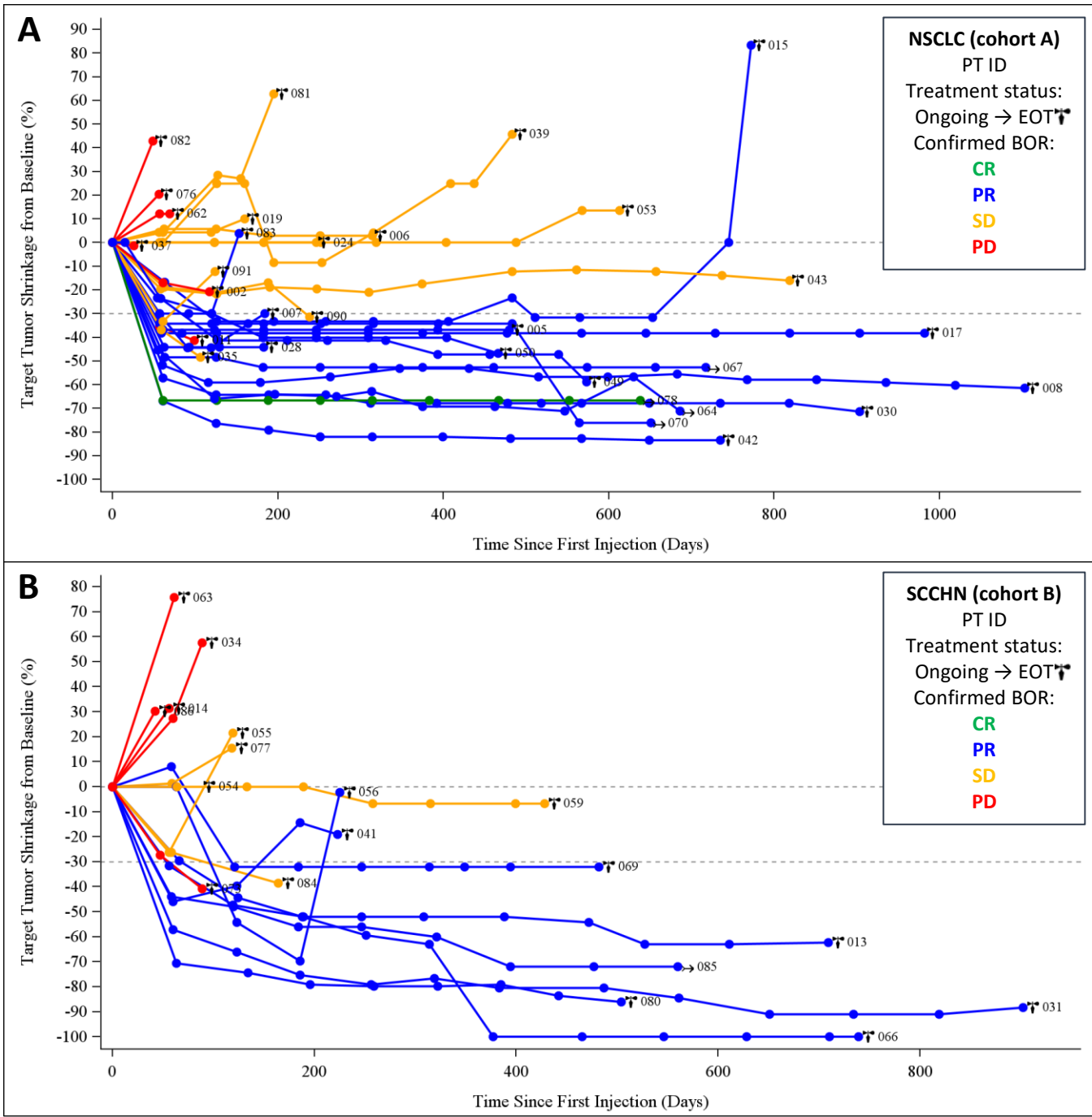
Treatment-related AEs occurring in ≥10%	NSCLC (N=37)	SCCHN (N=21)
Injection-site reactions (All Grade 1–2)	15 (40.5)	4 (19.0)
Fatigue	7 (18.9)	5 (23.8)
Asthenia	8 (21.6)	0
Rash	5 (13.5)	3 (14.3)
Pruritus	4 (10.8)	2 (9.5)
Diarrhea	4 (10.8)	3 (14.3)
ALT increase	4 (10.8)	3 (14.3)
AST increase	3 (8.1)	4 (19.0)
Hypothyroidism	3 (8.1)	4 (19.0)

Efficacy results

Data cut-off (Sep 1st, 2025): Efficacy data set represents eligible patients with at least two cycles of treatment. ORR was reported previously.^{5,6}

Endpoints	NSCLC (N=31)	SCCHN (N=18)
Objective response rate % (95% CI)	48.4 (30.2, 66.9)	44.4 (21.5, 69.2)
Median follow-up (months)	32.3	23.8
Median PFS, months (95% CI)	8.1 (4.2, 17.7)	7.0 (2.0, 13.1)
18-month PFS, (95% CI)	31% (16, 48)	22% (7, 43)
Median OS, months (95% CI)	22.6 (16.6, NE)	22.3 (9.4, NE)
18-month OS, (95% CI)	64% (44, 78)	61% (35, 79)

Figure 1: Depth and duration of target lesion response for (A) NSCLC and (B) SCCHN. Each timepoint shows the change in sum of diameters compared to baseline.



Gene expression signature

Figure 2. Kaplan-Meier of PFS stratified for immune-modulatory signature (IMS) showing prolonged median PFS for patients with IMS-high signature.

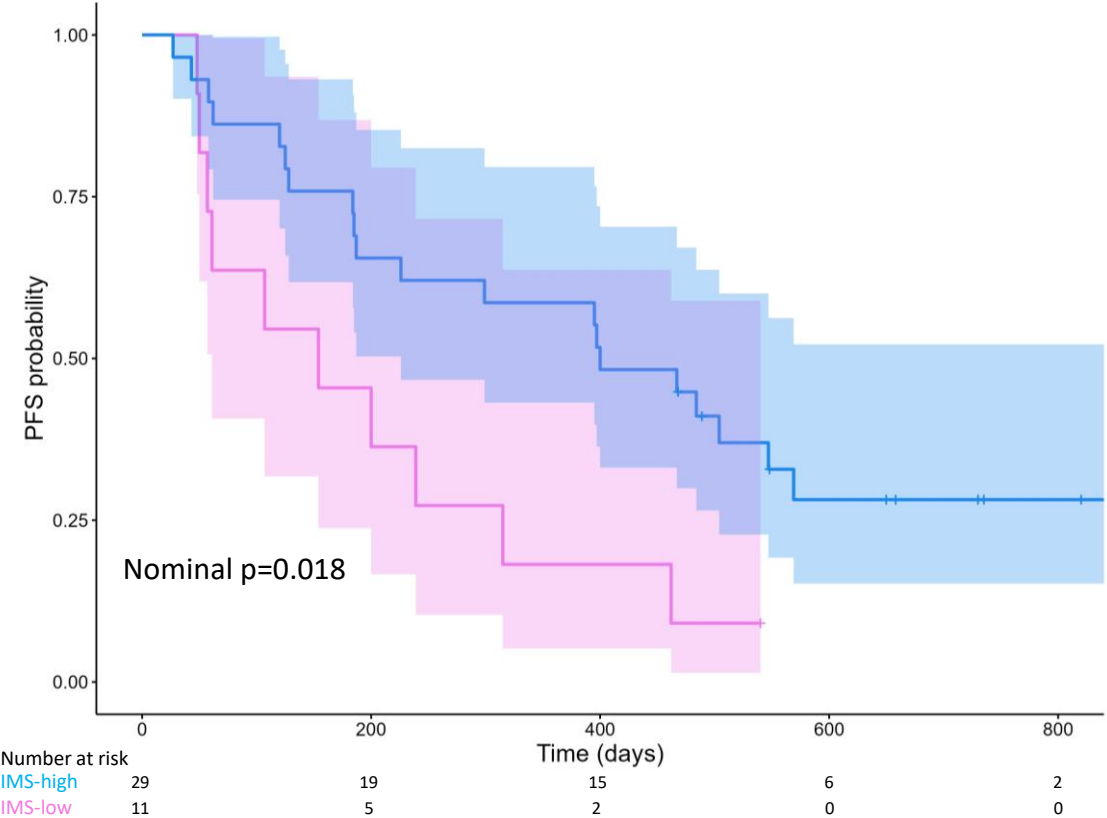
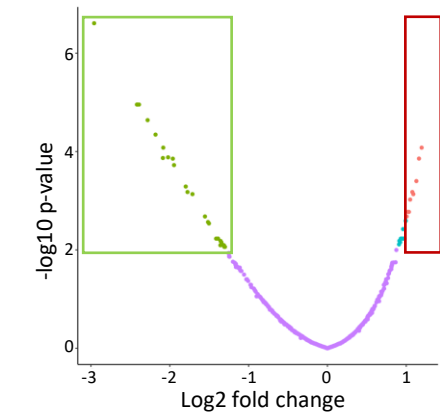


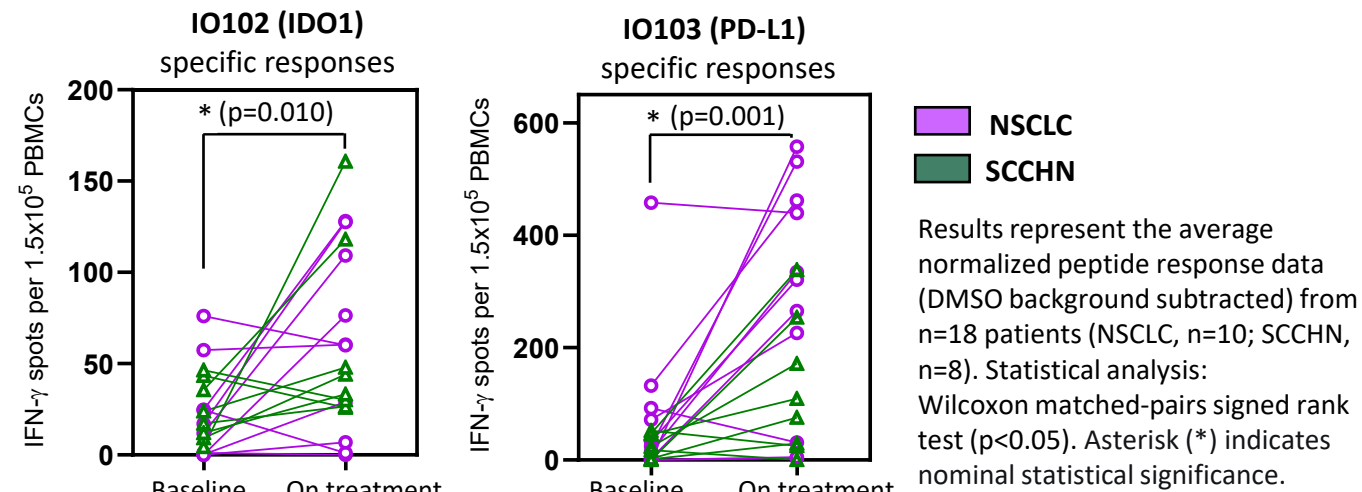
Figure 3. Volcano plot.



The IMS signature was developed using genes from differential gene expression analysis based on NanoString PanCancer IO360 panel expression comparing RNA from baseline tumor tissue from clinical responders versus non-responders from both NSCLC (N=25) and SCCHN (N=15) cohorts. Genes significantly up-regulated (red) or down-regulated (green) in responders were assessed for functional relevance according to the expected immune-response to the vaccine. The final IMS signature consists of a 12-gene profile, which remains to be validated in a larger cohort.

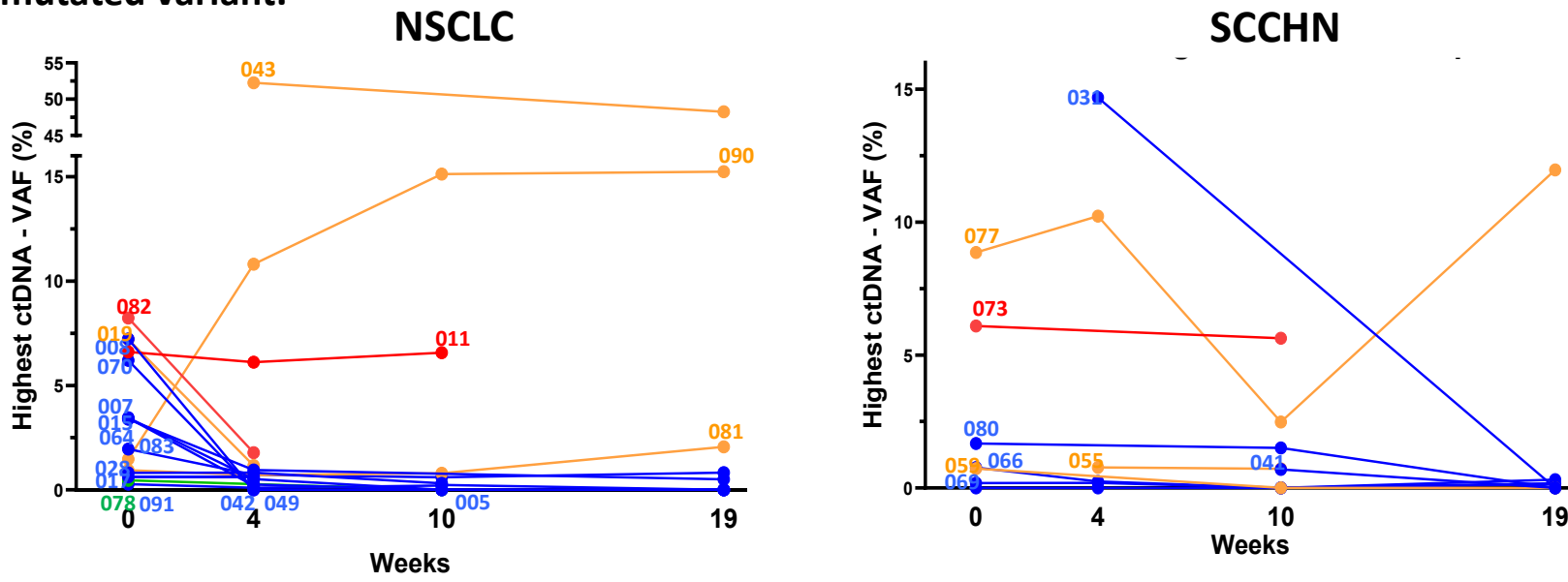
Vaccine-specific immune response

Figure 4: ELISpot comparing baseline and on-treatment (best response) immune responses to IDO1 and PD-L1 peptides in PBMCs.



Kinetics of ctDNA changes

Figure 5: Change over time (Baseline, Week 4, Week 10, Week 19) of the ctDNA highest mutated variant.



NSCLC (n=19, left) SCCHN (n=10, right). Colors indicate clinical response status (PD: Red, SD: Orange, PR: Blue, CR: Green). ctDNA mutations were determined by sequencing plasma ctDNA with the OncoPrint™ Pan-Cancer Cell-Free Assay

Conclusions

- The primary endpoint was met with an ORR of 44% in efficacy evaluable patients with recurrent/metastatic PD-L1-high SCCHN (CPS ≥20).
- Mature mPFS and mOS presented here for NSCLC and SCCHN compare favorably to historical benchmarks for pembrolizumab monotherapy.^{3,4}
- No new safety signals were observed: Injection-site reactions were all Grade 1–2 and systemic reactions were consistent with known safety profile for pembrolizumab monotherapy.
- Clinical responders showed upregulation of treatment specific pathways and genes compared with non-responders; the IMS signature could be a valuable predictive biomarker to be validated in a larger cohort.
- Together with promising data from the IOB-013/KN-D18 randomized phase 3 trial in first-line advanced melanoma, these data support further development of IO102-IO103 plus anti-PD-1 therapy in NSCLC and SCCHN first-line settings.