A Phase 2 trial of the IO102-IO103 cancer vaccine plus pembrolizumab: preliminary analysis for first line treatment of NSCLC and SCCHN

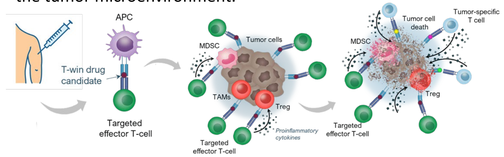
Jonathan W. Riess[1], Ezra Cohen[2], James Spicer[3], Paul Shaw[4], Jaime Rubio Perez[5], Laura Medina Rodriguez[6], Marya F. Chaney[7], Shane O'Neill[8], Ayako Wakatsuki Pedersen[8], Diane Opatt McDowell[8], Eva Ehrnrooth[8], Pilar Garrido[9]

[1]UC Davis Comprehensive Cancer Center, Sacramento, CA, USA; [2]University of California, San Diego, CA, USA; [3]King's College London, London, UK; [4]Velindre Cancer Centre, Cardiff, UK; [5]Fundación Jiménez Díaz University Hospital, Madrid, Spain; [6]Unidad de gestión clínica (UGI) Oncología Médica Hospital Regional y Universitario de Málaga, Instituto de Investigación de Biotecnología de Málaga (IBIMA), Málaga, Spain; [7]Merck & Co., Inc., Rahway, NJ, USA; [8]IO Biotech, Copenhagen, Denmark; [9]Hospital Universitario Ramon y Cajal, Madrid, Spain

Presentation 1038P
EudraCT: 2021-003026-69
ClinicalTrials.gov: NCT05077709

Background

IO102-IO103 stimulates activation of T cells against IDO+ and PD-L1+ cells, resulting in modulation of the tumor microenvironment.[1]

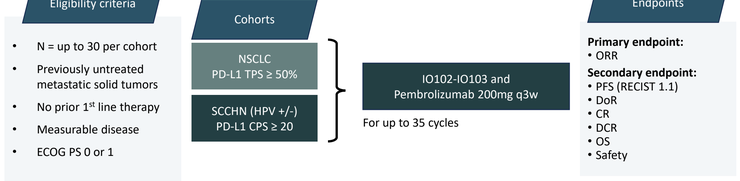


Proof of concept in melanoma[1,2]:
N=30; IO102-IO103 + nivolumab
Anti-PD1 naïve metastatic
Overall response rate = 80%
Complete response rate = 50%
Median PFS = ~26 months

1. Subcutaneous injection with vaccine to activate T cells
2. Vaccine-activated T cells attack and kill target-expressing immunosuppressive cells in the tumor microenvironment
3. The inflamed TME becomes immune-permissive, enabling further tumor cell killing by the recruited tumor-specific T cells

Study design

IOB-022/KN-D38: Phase 2, non-comparative, open-label, basket trial



Baseline characteristics

At data-cut-off (21st August 2023)

Patients	NSCLC N=28	SCCHN N=14
Age (years), median	71.0	70.0
Sex Male	14 (50%)	10 (71%)
ECOG performance status 0 1	11 (39%) 17 (61%)	2 (14%) 12 (86%)
HPV/p16 status Positive Negative Unknown	- - -	7 (50%) 5 (36%) 2 (14%)

References:
1. Kjeldsen JW *et al. Nat Med* 2021;27:2212–32
2. Lorentzen *et al. J Immunother Cancer* 2023;11(5):e006755

Abbreviations: *AE, adverse event; C, cycle; CI, confidence interval; CPS, combined positive score; CR, complete response; ctDNA, circulating tumor CVA, cerebrovascular accident; DNA; D, day; DCR, disease control rate; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; GGT, gama glutamil transferase; HPV, human papillomavirus; IDO, indoleamine 2,3-dioxygenase; IFN, interferon; N, number of patients; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; p16, cyclin-dependent kinase inhibitor 2A gene; PD, progressive disease; PD1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PFS, progression-free survival; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha gene; PR, partial response; Pts, patients; SCC, squamous cell carcinoma; SD, stable disease; SCCHN, squamous cell carcinoma of the head and neck; TME, tumor microenvironment; TP53, tumor protein p53 gene; TPS, tumor proportion score; TRAE, treatment-related adverse event; q3w, once every three weeks.*

Safety results

Safety set: all patients who received at least 1 dose of any of the study medications

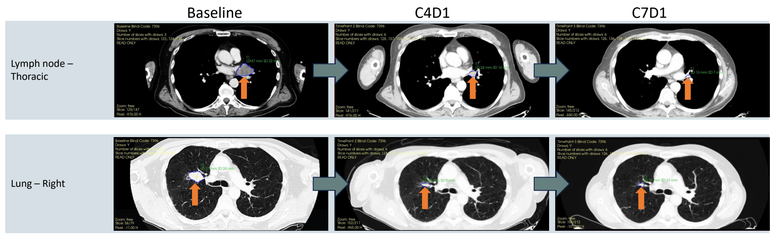
Summary of adverse events	Total pts N = 42	NSCLC (N = 28)	SCCHN (N = 14)
Any AE	39 (92.9%)	27 (96.4%)	12 (85.7%)
TRAEs	32 (76.2%)	23 (82.1%)	9 (64.3%)
	N = 42	List of Events (*some patients experienced more than one event*)	
Serious related AE	2 (4.8%)	*Fatigue (1), pneumonitis (1), CVA (1)*	
TRAEs leading to discontinuation	4 (9.5%)	*Colitis (2), pulmonary embolism (1), skin rash maculo-papular (1)*	
TRAE Grade 3–5*	5 (11.9%)	*Asthenia (1), fatigue (1), malaise (1), GGT increased (1), pneumonitis (1), rash maculo-papular (1), pulmonary embolism (1), CVA** (1)*	
TRAE immune-mediated	8 (19%)	*Hypothyroidism (3), colitis (2), adrenal insufficiency (1), hypophysitis (1), pneumonitis (1), rash maculo-papular (1)*	
Most common TRAE (≥10%) Injection site reaction Fatigue Rash	11 (26.2%) 6 (14.3%) 5 (11.9%)		

**2 AE Grade 5: 2 patients died after C1, prior C2 (cause unknown) and reported as not related to study treatment.*
***Patient discontinued due to pulmonary embolism followed by a cerebrovascular accident which was a fatal event.*

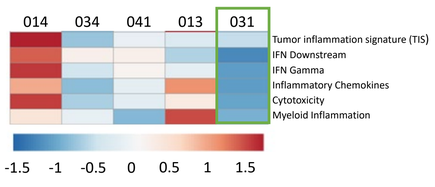
SCCHN case-study

Patient 031: recurrent oropharyngeal squamous cell carcinoma

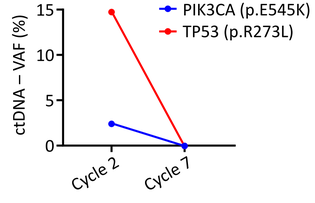
- 63 years old male
- Stage IVc (Tx, Nx, pNx, M1) – PD-L1 CPS 50 – HPV negative
- Partial response at C4D1 (week 10) with -57.1% tumor shrinkage
- Patient is ongoing with 13 cycles completed (37 weeks)



Immune signatures (NanoString)



ctDNA: undetectable at cycle 7



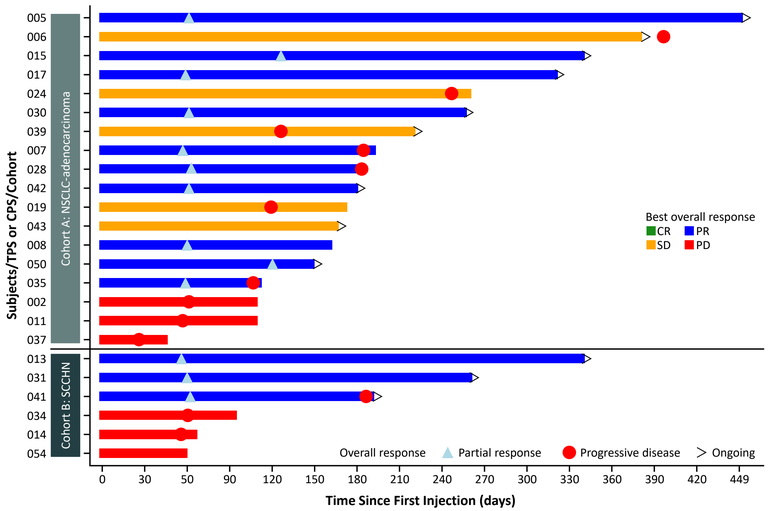
Figures legend:
NanoString: Heatmap of select signature scores from Nanostring PanCancer 360
ctDNA: Cell-free total nucleic acid extracted from plasma samples was sequenced using the Oncomine Pan-Cancer Cell-Free Assay (Thermo Fisher). Individual ctDNA mutated variants identified at the indicated time points are represented as their percentage out of the total cfDNA (%VAF) sequenced

Efficacy results

Efficacy set: all patients with at least 2 post-baseline tumor assessments or who discontinued after 2 cycles of study treatment

NSCLC Best overall response	N = 18
ORR (95% CI)	10 (56%) [30.8; 78.5]
Partial Response (PR)	10 (56%)
Stable Disease (SD)	5 (28%)
Progressive Disease (PD)	3 (17%)

SCCHN Best overall response	N = 6
ORR	3 /6
Partial Response	3
Stable Disease	0
Progressive Disease	3



Note: 8 out of the 10 NSCLC patients and the 3 SCCHN patients had PR confirmed per RECIST 1.1.; patient 035 experienced PD at the following scan and patient 050 had not yet had their second scan at the time of data cut off. Patient 008 discontinued study treatment due to toxicity.

Conclusion

Encouraging preliminary clinical data supports continuation of recruitment:

- PR as best response in 10/18 NSCLC patients (56%, 95% CI 30.8; 78.5) and in 3/6 SCCHN patients
- Supports accrual of more patients and longer follow-up for PFS and DoR
- While data is still evolving, 5/10 NSCLC and 3/3 SCCHN partial responses have more than 180 days PFS and are ongoing
- Safety is consistent with prior studies[1] of IO102-IO103 in combination with checkpoint inhibitors, with no noted additional significant systemic toxicity
  → Enrolment is still ongoing (NCT05077709)

Contact details for presenting author: Jonathan W. Riess: jwriess@ucdavis.edu

Acknowledgements and disclosures:
This study is funded and conducted by IO Biotech ApS in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. Medical writing support for the development of this poster, under the direction of the authors, was provided by Edward Potts and Beverly La Ferla of Ashfield MedComms (GmbH), an Inizio company, and funded by IO Biotech ApS (supported by IO Biotech ApS).

Jonathan W. Riess has received research funding from AstraZeneca, Boehringer Ingelheim, Merck, Novartis, Revolution Medicines, ArriVent, and Spectrum; has participated in advisory boards for Bayer, Beigene, Biodesix, Regeneron, Turning Point, Bristol-Myers Squibb, Daiichi Sankyo, Roche/Genentech, Janssen, Seattle Genetics, Jazz Pharmaceuticals, Mervis, and Sanofi; and had acted as a consultant for Blueprint, Boehringer Ingelheim, EMD Serono, and Novartis.

Presented at the European Society for Medical Oncology (ESMO) congress, 20–24 October 2023, Madrid, Spain.