IASLC 2023 World Conference on Lung Cancer
SEPTEMBER 9-12, 2023 | SINGAPORE

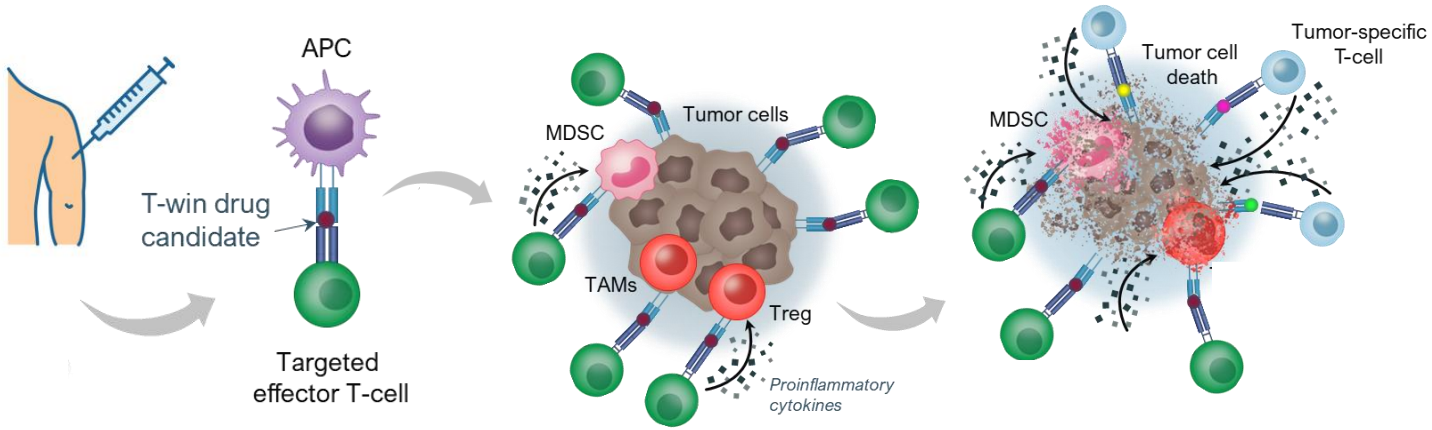
Phase 2 trial of IO102-IO103 vaccine plus pembrolizumab: preliminary results for the first-line treatment of lung adenocarcinoma IOB-022 / KN-D38

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

1. University of California Davis Comprehensive Cancer Center, Sacramento, CA, USA; 2. University of California, San Diego, CA, USA; 3. Oregon Health & Science University, Portland, OR, USA; 4. Velindre Cancer Centre, Cardiff, UK; 5. Fundación Jiménez Díaz University Hospital, Madrid, Spain; 6. Unidad de Gestión Clínica (UGC) Oncología Médica Hospital Regional y Universitario de Málaga, Instituto de Investigación Biomédica 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

IO102-IO103 immuno-modulating cancer vaccine background

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



1. Subcutaneous injection with vaccine to activate T cells
2. Vaccine-activated T cells attack immune suppressive targeted antigen positive cells
3. Inflamed TME becomes immune-permissive, enabling further tumor cell killing by the recruited tumor-specific T cells

Proof of concept in melanoma[1,2]:

- N=30; IO102-IO103 + nivolumab
- Anti-PD1 naïve metastatic melanoma
- Overall Response Rate = 80%
- Complete Response Rate = 50%
- mPFS = ~26 months
- Vaccine-specific T cell responses observed in blood and tumor
- Systemic toxicity observed comparable to nivolumab monotherapy

1. Kjeldsen et al. *Nat Med* 2021
2. Lorentzen et al. *J Immunother Cancer* 2023

APC, antigen-presenting cell; IDO, Indoleamine 2,3-dioxygenase; MDSC, myeloid-derived suppressor cell; mPFS, median progression-free survival; PD-(L)1, programmed cell death (ligand) protein 1; TAMs, tumor-associated macrophages; TME, tumor microenvironment; Treg, regulatory T cell

Phase 2 Trial Design, demographics and baseline characteristics

Non-comparative, open-label, multi-cohort trial (NCT05077709)

Eligibility criteria – Cohort A

- Treatment naive in the first-line setting NSCLC adenocarcinoma
- PD-L1 expression TPS ≥50%
- Measurable disease (RECIST 1.1)
- ECOG PS 0 or 1

IO102-IO103 vaccine
(85-85µg SC D1 and D8 of C1 and C2 followed by q3w)
+ pembrolizumab IV 200mg q3w

For up to 35 cycles

Primary endpoint
Objective response rate

Secondary endpoints
PFS, DoR, CR, DCR, OS, safety

Pre-defined interim analysis: First 15 patients with ≥2 cycles and either ≥2 post-baseline tumor assessments or discontinued

Data cut-off: July 10th, 2023

Patients	n = 25
Age (years), Median	71.0
Sex	
Female	14 (56%)
Male	11 (44%)
ECOG performance status	
0	9 (36%)
1	16 (64%)
Stage at study entry	
IVA-B	25 (100%)

C, cycle; CR, complete response; D, day; DCR, disease control rate; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; IV, intravenously; NSCLC, non-small cell lung cancer; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; SC, subcutaneously; q3w, once every three weeks;

Safety and pre-defined interim efficacy analysis

All patients who received at least 1 dose of IO102-IO103 + pembrolizumab	n = 25	Events*
Treatment-related adverse events	19 (76%)	
Serious related AE	2 (8%)	*Fatigue (1), pneumonitis (1)*
TRAE Leading to discontinuation	3 (12%)	*Colitis (2), pneumonitis (1)*
TRAE Grade 3–4 (no TRAE Grade 5**)	4 (16%)	*Asthenia (1), fatigue (1), malaise (1), pneumonitis (1), rash maculo-papular (1)*
TRAE immune-mediated	6 (24%)	*Hypothyroidism (2), colitis (2), hypophysitis (1) pneumonitis (1), rash maculo-papular (1)*
Most common TRAE (≥10%)		
Injection site reaction	9 (36%)	
Fatigue/asthenia	5 (20%)	
Diarrhea	3 (12%)	
Arthralgia	4 (16%)	

Causality of AEs was assessed against any treatment (IO102-IO103 and pembrolizumab)

Interim efficacy analysis: n = 15 with ≥2 cycles and either ≥2 post-baseline tumor assessments or discontinued

Best overall response	n = 15
ORR 95% CI	**8 (53.3%)** [26.6, 78.7]
PR	8 (53.3%)
SD	4 (26.7%)
PD	3 (20.0%)

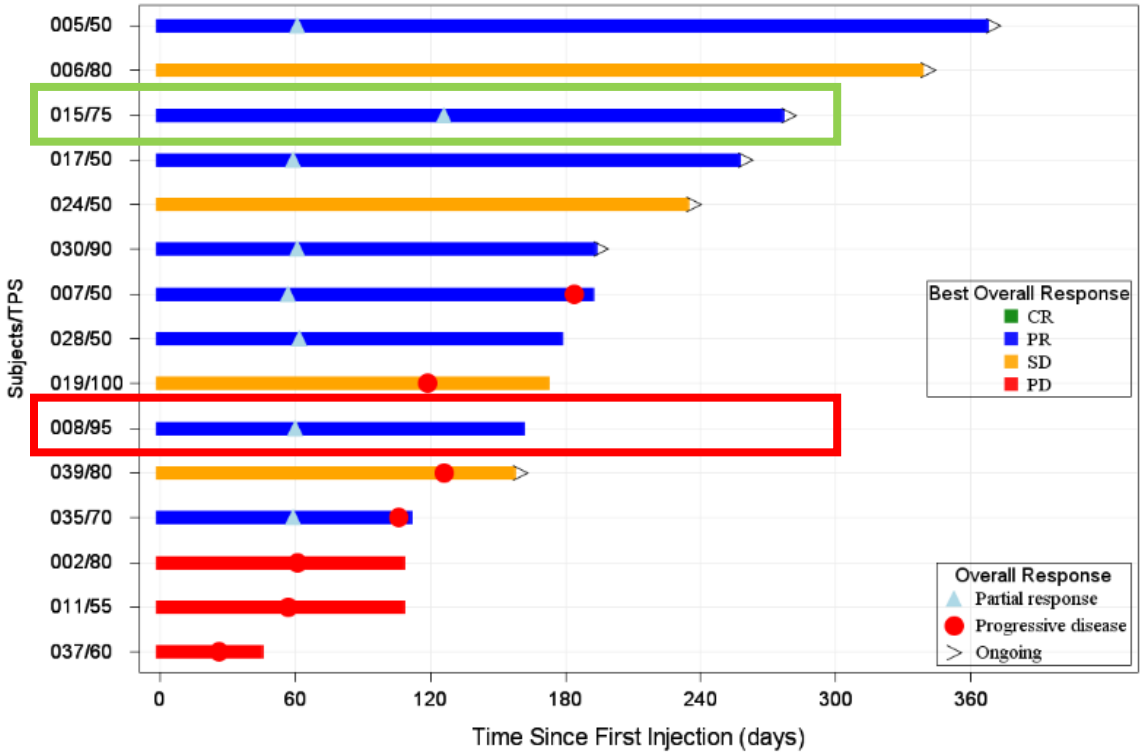
Median duration of exposure to IO102-IO103 = 15 weeks (min-max 0–52)

*Some patients experienced more than one event; ***2 AE Grade 5: 2 patients died after C1, prior C2 (cause unknown) and reported as not related to study treatment*

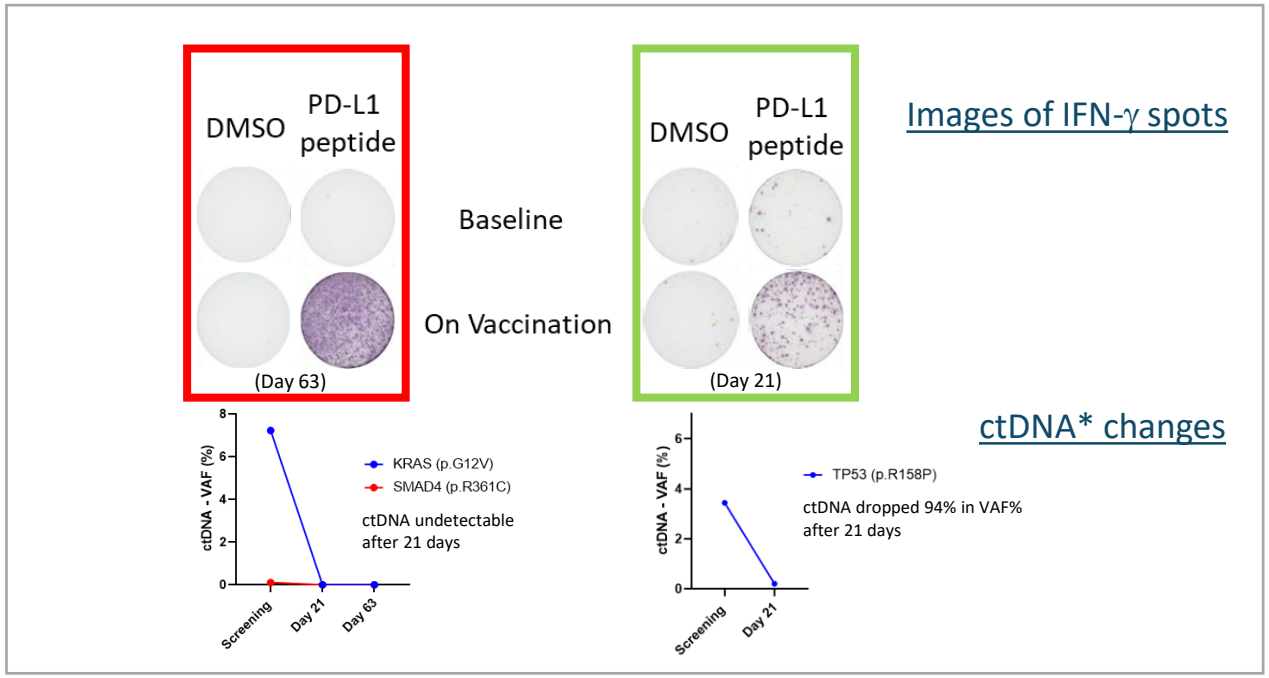
AE, adverse event; C, cycle; CI, confidence interval; IMP, investigational medicinal product; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; TRAE, treatment-related adverse event

Preliminary response and biomarker analysis

Preliminary response data from eligible patients



Biomarker data from responding patients 008 (left) and 015 (right)



- ctDNA data* indicates a reduced tumor burden (with complete clearance or a considerable drop in VAF%) 21 days after the 1st dose
- On vaccination T cell expansion was observed

**ctDNA analysis conducted using Thermo Fisher Scientific Oncomine cfDNA assay*

CI, confidence interval; CR, complete response; cfDNA, cell-free DNA; ctDNA, circulating tumor DNA; DMSO, dimethyl sulfoxide; IFN-γ, interferon-gamma; *ORR, objective response rate; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease; TPS, tumor proportion score; VAF, variant allele frequency*

Conclusions

- This is a preliminary analysis of IO102-IO103 immuno-modulating cancer vaccine in combination with pembrolizumab as first-line treatment in patients with metastatic NSCLC adenocarcinoma and PD-L1 TPS ≥50%

- Encouraging early clinical and biomarker data
  - Confirmed PR as best overall response in 8/15 patients (53.3%)
  - Supports accrual of more patients and longer follow-up for PFS and DoR
  - Safety consistent with pembrolizumab monotherapy with no noted additional significant systemic toxicity

→ Enrollment is still ongoing (NCT05077709)

DoR, duration of response; CI, confidence interval; ctDNA, circulating tumor DNA; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; PD-L1, programmed death-ligand 1; PR, partial response; TPS, tumor proportion score

Acknowledgments

We wish to thank all patients, family members, and clinical trial staff that is participating in the trial.

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 and editorial support for the development of this mini oral presentation, under the direction of the authors, were provided by Ashfield MedComms, an Inizio company