A randomized Phase 2 trial of the IO102-IO103 (IDO and PD-L1) cancer vaccine plus pembrolizumab as neoadjuvant/adjuvant treatment of patients with solid tumors

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Background

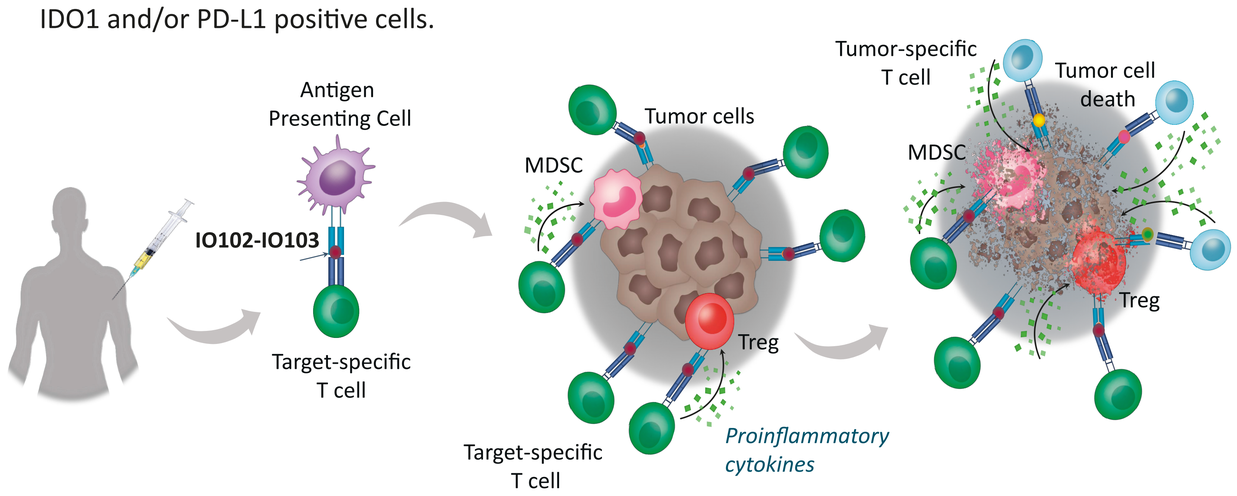
Immune checkpoint inhibitors have transformed the treatment of multiple tumor types, including melanoma and SCCHN.

However, some patients with locally advanced disease still recur after surgery and adjuvant therapies.

- In melanoma, neoadjuvant pembrolizumab followed by adjuvant pembrolizumab was shown to improve EFS compared to adjuvant pembrolizumab only.[1]
- In SCCHN, two cycles of neoadjuvant pembrolizumab resulted in a two-fold increase in the frequency of pathological tumor response compared with one cycle.[2]

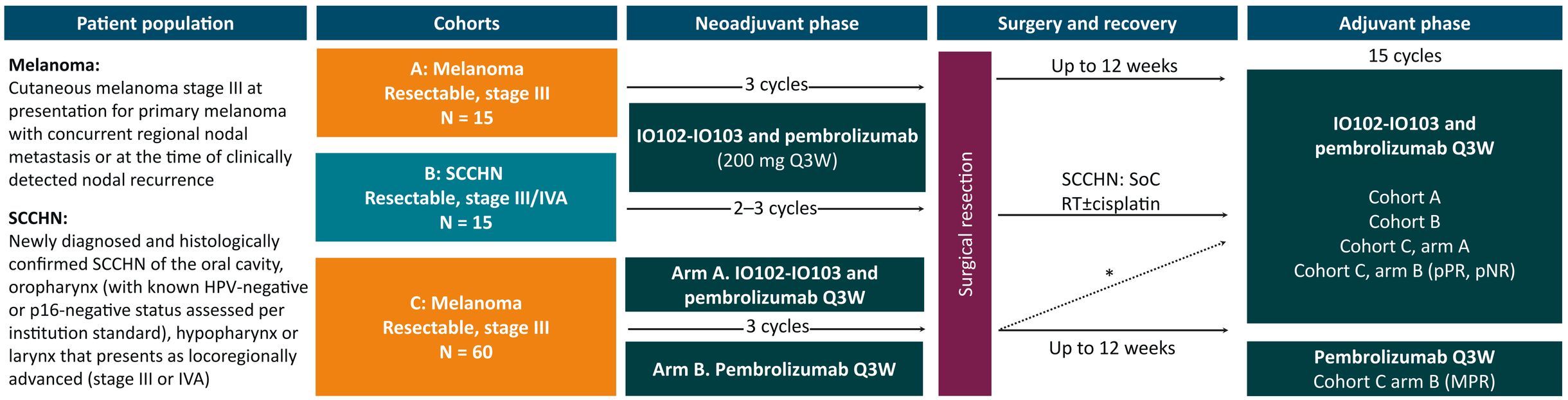
Treatment with IO102-IO103 plus nivolumab in anti-PD-1-naïve metastatic melanoma showed 80% objective response rate (95% CI, 62.7–90.5), including 50% complete response and was well tolerated in a Phase 1/2 trial.[3,4] We aim to investigate the activity of IO102-IO103 plus pembrolizumab in the perioperative setting in melanoma and SCCHN.

IO102-IO103 is an investigational therapeutic cancer vaccine that targets both tumor cells and immune-suppressive cells in the tumor microenvironment. IO102-IO103 promotes inflammation and potentiates anti-tumor activity via activation and expansion of T cells against IDO1 and/or PD-L1 positive cells.



Methods

TRIAL DESIGN: IOB-032/PN-E40 (NCT05280314) is a Phase 2, open-label, multi-cohort trial aiming to evaluate safety, anti-tumor and immunological activity of the IO102-IO103 cancer vaccine in combination with pembrolizumab as neoadjuvant and adjuvant treatment in patients with solid tumors.



*Patients in cohort C with poor pathological response to pembrolizumab alone in the neoadjuvant phase (>10% residual viable tumor) may cross over to receive the combination treatment post-surgery at the discretion of the investigator.

KEY INCLUSION CRITERIA:
- Candidate for surgical resection with curative intent
- Measurable disease per RECIST 1.1
- ECOG PS 0–1

KEY EXCLUSION CRITERIA:
- Prior systemic therapy for the tumor under study
- History of in-transit/satellite metastases within the last 6 months

LOCATIONS: US, Europe and Australia
ENROLMENT STATUS: Recruitment commenced in December 2023

PRIMARY ENDPOINT:
- Major pathological response: ≤10% residual viable tumor per central assessment

KEY SECONDARY ENDPOINTS:
- EFS
- Disease-free survival
- Safety

TRANSLATIONAL RESEARCH:
- Measure expansion of treatment-induced IO102-IO103 specific T-cells in blood
- Immune infiltration and changes in the tumor/TME (TCR seq, immune cell expression)
- Explore predictive biomarkers (PD-L1, TMB, immune expression signature)

STATISTICAL METHODS:
The tumor bed is defined as the area in the resected specimen (including nodal metastasis, if applicable) taken up by viable tumor cells, necrosis and stroma. The percentage area taken up by residual viable tumor will be determined according to the guidelines from Tetzlaff *et al*.[5] The percentage of patients with MPR including 95% CIs will be reported for each cohort, and for cohorts A and C combined.

Abbreviations
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EFS, event-free survival; HPV, human papillomavirus; IDO, indoleamine 2,3-dioxygenase; MDSC, myeloid-derived suppressor cells; MPR, major pathologic response; N, number of patients; p16, cyclin-dependent kinase inhibitor 2A; PD-1, programmed death protein 1; PD-L1, programmed death ligand 1; pNR, partial negative response; pPR, partial positive response; Q3W, once every 3 weeks; RECIST 1.1, Response Evaluation Criteria in Solid Tumours v1.1; SCCHN, squamous cell carcinoma of head and neck; SoC RT, standard-of-care radiotherapy; TCR, T-cell receptor; TMB, tumor mutational burden; TME, tumor microenvironment; Treg, regulatory T-cell

References
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