A MULTICENTRE PHASE 1B STUDY OF NG-641, A NOVEL TRANSGENE-ARMED AND TUMOUR-SELECTIVE ADENOVIRAL VECTOR, AND PEMBROLIZUMAB AS NEOADJUVANT TREATMENT FOR SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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Background Despite multimodal management strategies, outcomes for patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN) remain poor. Immune checkpoint inhibitors have demonstrated promise as a neoadjuvant strategy to reduce relapse rates¹; however, the immunosuppressive SCCHN tumour microenvironment (TME) has limited the efficacy of immunotherapy to date. This 'cold' TME is characterised by an absence of T-cell activation/inflammation² and high levels of stromal fibroblast activating protein (FAP),³ indicative of immunosuppressive cancer-associated fibroblasts (CAFs). Novel approaches to ameliorate this immunosuppressive TME are required to realise the full benefit of immunotherapy in SCCHN. NG-641 is a next-generation blood-stable and transgene-armed Tumour-Specific Immuno Gene Therapy (T-SiGn) adenoviral vector that selectively replicates in epithelial tumour cells. NG-641 encodes four immunostimulatory transgenes: a FAP-directed bi-specific T-cell activator antibody to target CAFs, interferon alpha 2 to promote innate and adaptive immune responses, and C-X-C motif chemokine ligands 9 and 10 to induce T cell infiltration.⁴ Together, these transgenes are designed to locally re-programme the immunosuppressive TME and promote functional anti-cancer immune responses while minimising systemic immune-related toxicities. This mechanism of action is particularly suited to SCCHN and should complement anti-PD-1 inhibitors. We, therefore, designed a study to assess neoadjuvant treatment with NG-641 and pembrolizumab in locally advanced SCCHN.

Methods The mode-of-action transgene (MOAT) study is a multicentre, open-label, dose-escalating, phase 1b study of NG-641 as monotherapy or with pembrolizumab. Patients are eligible if they have newly diagnosed or recurrent locally advanced SCCHN and have definitive surgery planned within 8 weeks of screening. In Part A, patients will receive three doses of intravenous NG-641 monotherapy prior to surgery (figure 1). Once NG-641 transgene expression is confirmed in excised tumour tissues, Part A will close and NG-641 dose-escalation can continue in Part B. Patients will then also receive a single dose of pembrolizumab given ~5 days after NG-641 to minimize toxicity and take advantage of the mechanism of NG-641 prior to PD-1 blockade. The primary objective is to characterise the safety and tolerability of NG-641 ± pembrolizumab in SCCHN; secondary objectives are to identify a recommended dose of NG-641 plus pembrolizumab and to assess treatment outcomes, including pathological tumour responses and overall survival. Pharmacodynamic outcomes will be assessed following NG-641 ± pembrolizumab, including characterising immune/inflammatory biomarkers in both tumour and blood. The study is to be conducted at 4 sites in the UK; up to 36 patients will be enrolled.

Abstract 437 Figure 1 MOAT study schematic

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Trial Registration This trial is registered as NCT04830592 on clinicaltrials.gov.

REFERENCES

- Uppaluri R, Campbell KM, Egloff AM, et al. Neoadjuvant and Adjuvant Pembrolizumab in Resectable Locally Advanced, Human Papillomavirus-Unrelated Head and Neck Cancer: A Multicenter, Phase II Trial. *Clin Cancer Res* 2020;**26**:5140–52.
- Cristescu R, Mogg R, Ayers M, et al. Pan-tumor genomic biomarkers for PD-1 checkpoint blockade-based immunotherapy. *Science* 2018;**362**:eaar3593.
- Dolzign H, Schweifer N, Puri C, et al. Characterization of cancer stroma markers: In silico analysis of an mRNA expression database for fibroblast activation protein and endosialin. *Cancer Immun* 2005;**5**:10.
- Champion BR, Besneux M, Patsalidou M, et al. NG-641: An oncolytic T-SiGn virus targeting cancer-associated fibroblasts in the stromal microenvironment of human carcinomas. *Cancer Res* 2019;**79**:5013.

Ethics Approval This study was approved by a central United Kingdom Research Ethics Committee (South Central - Oxford A Research Ethics Committee); approval reference 20/SC/0425, Integrated Research Application System ID 290504. All participants must provide informed consent prior to enrolment.

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