
Background

Unmet need

- Although outcomes in patients with R/M HNSCC have been improved with first-line treatment with immunotherapies such as the PD-1 inhibitor pembrolizumab, there remains an unmet need for new treatment options as not all patients derive benefit due to inherent or emerging resistance to immune checkpoint blockade.

ICOS as a target in HNSCC

- ICOS is a co-stimulatory receptor that promotes T-cell proliferation and survival, making it a promising target for immunotherapy.1

GSK3359609 is an ICOS agonist antibody with both T-cell-co-stimulating effects via antibody-dependent cellular toxicity (ADCC) and the ability to directly activate ICOS+ T cells.2

HNSCC has elevated expression of immune checkpoint modulators, including PD-1 and ICOS, and OS rates are higher in patients with HNSCC tumors that have high ICOS expression and/or HPV− compared with those that are HPV+ or have low ICOS expression.3

Rationale for ICOS and PD-1 combination

- Combining immunomodulatory agents targeting different components of the cancer immunity cycle may generate more effective immune responses and overcome possible escape mechanisms.4

- Co-targeting PD-1 and ICOS may both directly counteract tumor-induced immune evasion and enhance adaptive antitumor immunity.5

- GSK3359609 has demonstrated antitumor activity in combination with pembrolizumab in nonclinical models.6

Key inclusion criteria

- Age ≥18 years with R/M HNSCC considered incurable by local therapies and no prior systemic therapy for R/M HNSCC
- Primary tumor of head and neck, oropharynx, hypopharynx, or larynx
- Progression of disease
- ECOG PS 0–2
- PD-L1 IN CPS ≥1 and known HPV status (opharyngeal cancer)7

Key exclusion criteria

- Prior therapy with anti-PD-1/L1/L2 and/or ICOS-directed agent
- Prior therapy ≥120 days or major surgery ≥42 days prior to randomization
- CNS metastases, active autoimmune diseases, or immune deficiencies
- Other invasive malignancy within 3 years

This trial (NCT04128696) is

- Randomized
- Phase II/III
- Double-blind

Utilizing a 2×1 adaptive Phase II design,8 with the option to seamlessly expand the initial Phase II study into a Phase III study, without changing eligibility criteria, endpoints, or randomization schemes.

Primary endpoints

- OS by PD-L1 status
- IRC of PD-L1 CPS ≥1 vs ≤0 population

Secondary endpoints

Key secondary endpoints

- OS by PD-L1 status in the total population
- OS by PD-L1 CPS ≥1 vs ≤0

Exploratory endpoints

- ORR, ORi, ORR plus PD-L1 CPS ≥1 vs ≤0
- OS of 12 months and 2 years in the ≥1 vs ≤0 population
- OS, ORR, ORi, and PD-L1 CPS at ≤1 by PD-L1 status
- PK

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Trial status

- INDUCE-3 is currently active and recruiting globally

*For questions, please contact the presenting author: Aaron.Hansen@uhn.ca

Abbreviations

- APC: antigen-presenting cell
- CNS: central nervous system
- CPS: combined positive score
- CR: complete response
- CTLA-4: cytotoxic T-lymphocyte–associated protein-4
- CXCR5: C-X-C motif chemokine receptor 5
- DCR: disease control rate
- DoR: duration of response
- ECOG PS: Eastern Cooperative Oncology Group performance status
- HPV: human papillomavirus
- HRQoL: health-related quality of life
- IN: immunohistochemical
- IRB: institutional review board
- IV: intravenous
- MLR: mixed leukocyte reaction
- PD-L1: programmed death-ligand 1
- PD-1: programmed death 1
- PC: Pharmaceutics
- R/M: recurrent/metastatic
- RCT: randomized clinical trial
- RCT: randomized controlled trial
- SD: stable disease
- TCR: T-cell receptor
- TCR: T-cell receptor
- TCPM: tumor cell proliferation model
- TNM: tumor-node-metastasis
- TS: time to survival
- TS: time to survival
- VEGF: vascular endothelial growth factor
- VRF: vascular risk factor
- VS: vascular space
- VS: vascular space
- WHO: World Health Organization
- YWH: Yukon Hospice Society

References


Acknowledgments

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Disclosures

No disclosures were reported for this presentation.