TPS6109 Poster Session

HexAgon-HN: Phase 2/3, randomized study of the hexavalent OX40 agonist INBRX-106 in combination with pembrolizumab vs pembrolizumab alone as first-line treatment for recurrent/metastatic head and neck cancer with a PD-L1 combined positive score of ≥20.

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Background: Pembrolizumab (pembro) ± chemotherapy is a standard-of-care first-line treatment option for recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). Pembro monotherapy is commonly used in patients with a PD-L1 combined positive score (CPS) of ≥20, with an objective response rate (ORR) of <25% and median overall survival (OS) of <15 months.[1] Therefore, a high unmet need exists for more effective, non–chemotherapy-based treatment options. INBRX-106 is a novel, hexavalent OX40 agonist designed to promote higher-order clustering of the costimulatory receptor OX40, leading to more potent agonism than the bivalent first generation of OX40 agonists. Combining INBRX-106 with pembro may amplify and prolong the antitumor immune response. In an ongoing phase 1/2 study (NCT04198766), INBRX-106 + pembro has demonstrated robust pharmacodynamics, a favorable safety profile, and promising clinical activity in multiple tumor types, including R/M HNSCC. These findings supported the initiation of HexAgon-HN (NCT06295731), a phase 2/3, randomized study evaluating INBRX-106 + pembro vs pembro alone as first-line treatment for R/M HNSCC with a PD-L1 CPS of ≥20. **Methods:** Eligible patients must have biopsy-confirmed R/M HNSCC that is considered incurable; a primary tumor in the oral cavity, oropharynx, hypopharynx, or larynx; no previous receipt of therapy for R/M disease; a centrally confirmed PD-L1 CPS of ≥20; measurable disease per RECIST 1.1; and an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1. Prior curative-intent treatment for locoregionally advanced HNSCC is allowed if progressive disease occurred ≥6 months (≥12 months if immunotherapy) after completion of treatment. Up to 410 patients will be randomized 1:1 (stratified by locoregional advanced vs distant metastatic disease, HPV status, and ECOG PS) to INBRX-106 + pembro 200 mg every 3 weeks or pembro (alone in the open-label, phase 2 part or in combination with placebo in the double-blind, phase 3 part). If the phase 2 part (N≈60) shows favorable results for the primary efficacy endpoint (ORR) and secondary safety and efficacy endpoints (eg, duration of response [DOR], progression-free survival [PFS] rate at 6 months, and clinical benefit rate [CBR]), the study can seamlessly proceed to the phase 3 part. The phase 3 part (N≈350) has dual primary efficacy endpoints of PFS and OS; secondary endpoints include ORR, DOR, CBR, time to chemotherapy, safety, and patient-reported quality of life. This study is currently enrolling in the US (30 sites), Europe (40 sites), and Asia-Pacific region (15 sites). 1. Burtness B, et al. *Lancet*. 2019;394:1915-1928. Clinical trial information: NCT06295731. Research Sponsor: Inhibrx Biosciences, Inc.