TPS6113 Poster Session

A multicenter, randomized, double-blind, phase 2/3 study of ficerafusp alfa (BCA101) or placebo in combination with pembrolizumab for first-line treatment of PD-L1-positive, recurrent or metastatic head and neck squamous cell carcinoma: The FORTIFI-HN01 study.

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Background: HPV-negative head and neck squamous cell carcinoma (HNSCC) is an aggressive disease characterized by high rates of recurrence, metastasis, and resistance to standard treatments. Over 80% of HPV-negative HNSCC cases overexpress TGF-β, a key driver of poor survival and treatment resistance. Ficerafusp alfa, a first-in-class bifunctional antibody, targets epidermal growth factor receptor (EGFR) while neutralizing TGF-β in the tumor microenvironment. In a Phase 1/1b trial (NCT04429542), ficerafusp alfa demonstrated promising efficacy and a manageable safety profile in first-line recurrent/metastatic (R/M) HNSCC. The ongoing FORTIFI-HN01 study (NCT06788990) is a randomized, double-blind, placebo-controlled Phase 2/3 trial designed to assess the efficacy and safety of ficerafusp alfa combined with pembrolizumab versus placebo plus pembrolizumab in patients with PD-L1 positive first-line R/M HPV-negative HNSCC. **Methods:** Eligible patients must have histologically confirmed R/M HNSCC with primary lesions in the oral cavity, larynx, or hypopharynx, or OPSCC, excluding HPV-positive OPSCC confirmed by central laboratory testing. Additional criteria include no prior systemic therapy for R/M disease, PD-L1 positive tumors (CPS ≥1), measurable disease per RECIST v1.1 assessed by BICR, and ECOG performance status of 0 or 1. The Phase 2 objective is to determine the optimal biological dose (OBD) of ficerafusp alfa through an integrated analysis of safety, tolerability, PK, PD, and efficacy. Subjects will be randomized 1:1:1 to receive high-dose ficerafusp alfa, low-dose ficerafusp alfa, or placebo, each combined with pembrolizumab. Randomization is stratified by PD-L1 CPS (1-19 vs. ≥20) and disease extent (local/regional recurrence only, distant metastasis only, or both). After OBD determination, the trial will transition seamlessly into Phase 3 with a 2:1 randomization (OBD vs. control).Patients will receive pembrolizumab (200 mg i.v. every 3 weeks for up to 35 cycles) and either ficerafusp alfa (1500 mg or 750 mg) or placebo weekly until disease progression or unacceptable toxicity. Tumor imaging will occur every 6 weeks during the first year and every 9 weeks thereafter. The primary endpoints are objective response rate (ORR) per RECIST v1.1 (BICR) and overall survival (OS). Secondary endpoints include safety, additional efficacy measures, and patient-reported outcomes (PROs). The trial is actively recruiting, with a planned enrollment of (NCT06788990). Clinical trial information: NCT06788990. Research Sponsor: Study funded by Bicara Therapeutics Inc.