TPS6112 **Poster Session**

A phase 2 study of fianlimab (anti–LAG-3) plus cemiplimab (anti–PD-1) versus cemiplimab plus placebo in patients with recurrent/metastatic head and neck squamous cell carcinoma (HNSCC) with positive PD-L1 expression.

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Background: Concurrent blockade of lymphocyte activation gene 3 (LAG-3) may enhance the efficacy of anti–programmed cell death-1 (PD-1) therapies. In a multicohort study, fianlimab (anti–LAG-3) plus cemiplimab (anti–PD-1) showed signs of clinical activity with durable responses and a generally manageable safety profile in patients with recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) warranting further investigation. **Methods:** This randomized, multicenter, Phase 2 study (NCT06769698) will investigate fianlimab (anti–LAG-3) plus cemiplimab (anti–PD-1) versus cemiplimab plus placebo in patients with R/M HNSCC with positive programmed cell death-ligand 1 (PD-L1) expression. The primary objective is to evaluate investigator-assessed objective response rate (ORR) with combination therapy (fianlimab + cemiplimab) versus cemiplimab monotherapy (cemiplimab + placebo). Key inclusion criteria: (1) aged ≥18 years; (2) histologically confirmed R/M HNSCC; (3) primary tumor location of oral cavity, oropharynx, larynx, or hypopharynx; (4) confirmed positive PD-L1 expression status with a Combined Positive Score of ≥1 based on a previous immunohistochemistry (IHC) test performed on a surgical/core biopsy specimen; (5) for patients with oropharynx disease, human papillomavirus (HPV) status must be established by p16 IHC or HPV DNA or RNA *in situ* hybridization (ISH) test; biopsy can be from primary tumor or nodal/distant metastasis; (6) for patients with squamous cell carcinoma of neck node with occult primary, a positive HPV DNA or RNA ISH test; (7) measurable disease per Response Evaluation Criteria in Solid Tumors version 1.1; (8) Eastern Cooperative Oncology Group performance status of ≤1; (9) adequate bone marrow, hepatic, and renal function. Key exclusion criteria: (1) patients who have progressive disease within 6 months of completion of curatively intended systemic treatment for locoregionally advanced HNSCC; (2) patients who have received prior systemic anticancer therapy in the R/M HNSCC setting. Approximately 120 patients will be enrolled across two cohorts. Patients will receive fianlimab + cemiplimab intravenously (IV) every 3 weeks (Q3W) or cemiplimab (350 mg) + placebo IV Q3W. Cohort 1 (n=60, HPV positive HNSCC) will be randomized 1:1 to receive: a) fianlimab + cemiplimab, b) placebo + cemiplimab. Cohort 2 (n=60, HPV negative HNSCC) will be randomized 1:1 to receive: a) fianlimab + cemiplimab, b) placebo + cemiplimab. The primary endpoint is ORR per investigator assessment. The secondary endpoints are progression-free survival, disease control rate, duration of response, safety, pharmacokinetics, and immunogenicity. Clinical trial information: NCT06769698. Research Sponsor: Regeneron Pharmaceuticals, Inc.