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A phase II study of Monalizumab in patients with recurrent/metastatic (RM) squamous cell carcinoma of the head and neck (SCCHN): results of the I1 cohort of the EORTC-HNCG-1559 trial (UPSTREAM).

Background

Patients (pts) with RM SCCHN progressing after platinum have a median overall survival (OS) of 7-8 months with nivolumab or pembrolizumab. No other drug has shown meaningful activity in this setting. HLA-E is a non-classical MHC molecule that is highly expressed in 70% of SCCHN. By binding to the NKG2A receptor expressed on NK cells and T-lymphocytes, HLA-E inhibits their cytotoxic function. Monalizumab (mona) is a human IgG4 antibody targeting the NKG2A receptor.

Methods

The UPSTREAM trial is a biomarker-driven umbrella trial of several targeted therapies and immunotherapy for RM SCCHN (post platinum, ECOG 0-1, measurable disease). The immunotherapy 1 (I1) cohort was a phase II, single arm, proof-of-concept substudy evaluating the efficacy of single agent mona. Non-eligible pts for the biomarker-driven cohorts were included in the I1 cohort. Mona was given as an infusion (10 mg/kg) on day 1 of each cycle (14 days). The primary endpoint was objective response rate (RECISTv1.1) during the first 16 weeks. A two-stage Simon design was used (H1 15%, H0 3%, α 8%, power 90%) with planned interruption of accrual if no response was seen after 25 pts. Secondary endpoints included toxicity (CTCAEv4.03), progression-free survival (PFS), response duration and OS.

Results

27 RM SCCHN pts were included in the 1st stage (median age: 62 yrs, oral cavity (26%), oropharynx (41%), hypopharynx (26%), larynx (7%)). 16 (59%) were pretreated with anti-PD(-L)1 compounds. No objective response was recorded. Stable disease was observed in 6 pts (22%). Disease progression was recorded in all but one patient and the median PFS was 7.4 wks (95% CI: 6.6-7.9 wks). Based on 16/27 deaths currently recorded, median OS was 27.7 wks (95% CI: 13-53.9 wks). Mona showed a favorable safety profile: 59% pts reported grade $\geq$ 3 adverse events, none of them treatment-related. The final results of these preliminary data will be presented at ESMO.

Conclusion

The substudy of mona in monotherapy did not meet its primary objective and was closed at interim for futility. Median PFS was 7.4 wks. Mona has a favorable safety profile and is under investigation in combination with durvalumab within the UPSTREAM trial.

Clinical trial registration: ClinicalTrials.gov: NCT03088059