Title: A protocol pre-specified interim overall survival (OS) analysis of GEMSTONE-302: a phase 3 study of sugemalimab (suge) versus placebo plus platinum-based chemotherapy (chemo) as first-line (1L) treatment for patients (pts) with metastatic non-small cell lung cancer (NSCLC)

Category: Lung Cancer-Non-Small Cell Metastatic

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Background

GEMSTONE-302, a randomized, double-blind, phase 3 study, previously met its primary endpoint and demonstrated statistically significant and clinically meaningful prolongation of progression-free survival (PFS) with suge+chemo vs placebo+chemo as a 1L treatment in pts with metastatic NSCLC. PFS benefit was observed in both squamous (sq) and non-squamous (nsq) NSCLC, regardless of PD-L1 expression levels. Here we report the data from a protocol pre-specified interim OS analysis.

Methods

Pts with systemic treatment-naïve stage IV NSCLC, measurable disease per RECIST v1.1, ECOG PS 0-1, and no known EGFR, ALK, ROS1 and RET alterations were randomized 2:1 to receive suge (1200 mg, IV) or placebo plus chemo (sq-NSCLC: carboplatin+paclitaxel; nsq-NSCLC: carboplatin+pemetrexed) every 3 weeks for up to 4 cycles, followed by maintenance therapy (sq-NSCLC: suge/placebo; nsq-NSCLC: suge/placebo+pemetrexed) for up to 35 cycles. The primary endpoint was investigator assessed PFS (INV-PFS). Key secondary endpoints included OS, INV-PFS in pts with tumor PD-L1 expression ≥1%, and ORR. Pts in the placebo group could cross over to receive suge monotherapy upon disease progression.

Results

As of 22 Nov 2021, among all 479 enrolled pts, 51 (15.9%) and 7 (4.4%), respectively, remained on treatment with suge+chemo or placebo+chemo. The median follow-up was 25.4 and 24.9 months, respectively. Following treatment discontinuation, 17.8% and 43.4% of the pts, respectively, received cross-over suge or other non-study anti-PD-(L)1-containing therapies. Median OS was 25.4 months in suge+chemo group vs 16.9 months in placebo+chemo group (HR=0.65 [95%CI, 0.50-0.84], p=0.0008), and 2-year OS rate was 51.7% vs 35.6%. OS benefits were observed across all subgroups including different tumor histologies (sq: HR=0.56; nsq: HR=0.72) and PD-L1 expression levels (≥1%: HR=0.64; <1%: HR=0.66). In the intent-to-treat population, median PFS was 9.0 months with suge+chemo vs 4.9 months with placebo+chemo (HR=0.49 [0.40-0.61]), and 2-year PFS rate was 20.8% vs 7.3%. In pts with PD-L1≥1%, the median PFS was 10.9 vs 4.9 months (HR=0.48 [0.36-0.63], p<0.0001). ORR was 63.4% vs 40.3% (p<0.0001). Among pts with baseline brain metastases, suge+chemo improved their OS (HR=0.45) and intracranial INV-PFS (post-hoc analysis, HR=0.33) vs placebo+chemo. Safety profile was consistent with previously reported results.

Conclusions

Suge plus chemo demonstrated statistically significant and clinically meaningful OS improvement compared with placebo plus chemo, irrespective of tumor histology or PD-L1 expression levels, in pts with newly diagnosed metastatic NSCLC, offering a new 1L treatment option for this group of pts.

Clinical trial information: Clinicaltrials.gov: NCT03789604.