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GEMSTONE-302: A Phase 3 Study of Platinum-Based Chemotherapy with Placebo or Sugemalimab, a PD-L1 mAb, for metastatic NSCLC

Type: Late Breaking Abstract (LBA)

Topic: Immunotherapy (Phase II/III Trials)

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Introduction

Sugemalimab is a full-length, fully human PD-L1 targeted immunoglobin G4 (IgG4, s228p) mAb. GEMSTONE-302 is a randomized, double-blind, phase 3 study to evaluate the efficacy and safety of sugemalimab or placebo in combination with chemotherapy as first-line treatment in metastatic squamous (sq) or non-squamous (nsq) NSCLC. The PFS interim analysis data as of 08 June 2020 showed that sugemalimab plus chemotherapy demonstrated a clinically meaningful and statistically significant prolongation of PFS with a well-tolerated safety profile in metastatic NSCLC patients irrespective of tumor pathology and PD-L1 expression. Sugemalimab plus chemotherapy was also associated with higher ORRs and durable responses and an OS benefit trend. Here, we report the results from the final PFS analysis and an updated OS analysis of this study. To our knowledge, this is a data report from the first randomized, double-blind, phase 3 study of anti-PD-L1 monoclonal antibody plus platinum-based chemotherapy as first-line treatment for stage IV sq or nsq NSCLC.

Methods

Patients with Stage IV NSCLC and measurable disease per RECIST v1.1, no prior systemic treatment, ECOG PS 0-1, wild-type *EGFR* or *ALK* were randomized 2:1 to sugemalimab or placebo in combination with chemotherapy. Randomization was stratified by subtype of NSCLC (sq *vs.* nsq), PD-L1 expression (≥1% *vs.* <1%), and ECOG PS (0 *vs.* 1). Patients received sugemalimab (1200 mg, IV, 4 cycles, Q3W) or placebo plus chemotherapy (sq-NSCLC: carboplatin, AUC=5, IV; paclitaxel, 175 mg/m2, IV. nsq-NSCLC: carboplatin, AUC=5, IV; pemetrexed, 500 mg/m2, IV), followed by maintenance therapy with sugemalimab or placebo in sq-NSCLC patients and sugemalimab or placebo plus pemetrexed in nsq-NSCLC patients (up to 35 cycles). The primary endpoint was investigator-assessed PFS.

Types of Analysis and Data Reporting

Results

As of 15 March 2021, amongst the 479 patients enrolled, 79 (24.7%) vs 12 (7.5%) were still on treatment in the sugemalimab+chemotherapy and placebo+chemotherapy groups, respectively. The median follow-up duration was 17.8 and 17.5 months, respectively. Compared with placebo+chemotherapy, sugemalimab+chemotherapy continued to provide longer PFS (358 events, [99.4% of the final PFS analysis], median PFS 9.03 *vs.* 4.90 months, stratified HR 0.48 [0.39-0.60]) and OS (198 events [55.0% of the final OS

analysis], median OS 22.83 *vs.* 17.68 months, stratified HR 0.67 [0.50-0.90]). Twelve-month PFS rates were 36.4% *vs.* 14.8% and 24-month OS rates were 47.1% *vs.* 38.1%. ORR per investigator was 63.4% in sugemalimab+chemotherapy group and 40.3% in placebo+chemotherapy group, median DoRs were 9.82 *vs.* 4.37 months, respectively. Clinical benefits were observed across all the subgroups including different pathologic types and PD-L1 expression levels. Incidences of Grade≥3 TEAEs were reported in 64.1% and 61.6% of patients in sugemalimab+chemotherapy and placebo+chemotherapy groups, respectively. No new safety signals were found.

Conclusion

In this phase 3 trial, sugemalimab was associated with a statistically and clinically significant improvement in both PFS and OS when combined with standard chemotherapy in patients with Stage IV NSCLC. These improvements were consistent in patients regardless of PD-L1 expression status or histology (squamous and non-squamous). These results support sugemalimab+chemotherapy as a potential new treatment option as the first-line treatment of patients with metastatic NSCLC.