9027: A Protocol Pre-specified Interim Overall Survival (OS) Analysis of GEMSTONE-302: A Phase 3 Study of Sugemalimab versus Placebo plus Platinum-based Chemotherapy (Chemo) as First-line (1L) Treatment for Patients with Metastatic Non-small Cell Lung Cancer

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BACKGROUND

- Sugemalimab is a full length, fully human anti-PD-L1 (programmed death ligand-1) immunoglobulin G4 (IgG4, s228p) monoclonal antibody
- GEMSTONE-302, a randomised, double-blind, phase 3 study, previously met its primary endpoint and demonstrated statistically significant and clinically meaningful prolongation of investigator-assessed progression-free survival (PFS) with sugemalimab + chemo vs placebo + chemo as a first-line treatment in patients with metastatic NSCLC
- PFS benefit was observed in both squamous (sq) and non-squamous (nsq) NSCLC, regardless of PD-L1 expression levels[1]
- Sugemalimab in combination with chemotherapy has been approved in China for the first-line treatment of patients with metastatic NSCLC[2]
- Here we report the data from a protocol pre-specified interim OS analysis

METHODS

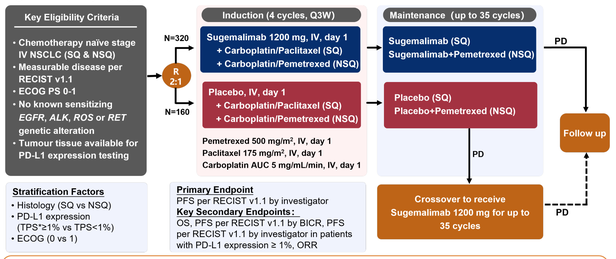
Study Design

Patients with systemic treatment-naive stage IV NSCLC, measurable disease per RECIST v1.1, ECOG PS 0-1, and no known EGFR, ALK, ROS1 and RET alterations were randomised 2:1 to receive sugemalimab (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: sugemalimab/placebo; nsq-NSCLC: sugemalimab/placebo + pemetrexed). Patients in placebo group could cross over to receive sugemalimab monotherapy upon disease progression.

Endpoints

- Primary endpoint was investigator-assessed PFS
- Key secondary endpoints included OS, investigator-assessed PFS in patients with tumor PD-L1 expression ≥1%, and investigator-assessed ORR

Figure 1. Study Design and Statistical Considerations of GEMSTONE-302



Stratification Factors
- Histology (SQ vs NSQ)
- PD-L1 expression (TPS*≥1% vs TPS<1%)
- ECOG (0 vs 1)

Primary Endpoint
PFS per RECIST v1.1 by investigator
Key Secondary Endpoints:
OS, PFS per RECIST v1.1 by BICR, PFS per RECIST v1.1 by investigator in patients with PD-L1 expression ≥ 1%, ORR

Statistical Considerations: Sequential testing method was used to control overall type I error in the following order: investigator assessed PFS in ITT population, OS, investigator assessed PFS in patients with tumour PD-L1 expression ≥1%, and investigator assessed ORR. The Lan–DeMets method with an approximate Pocock boundary was used to control for type I error to account for a preplanned interim analysis of overall survival. The two-sided P value boundary was 0·0396 (calculated according to 253 events observed at the interim overall survival analysis).

Abbreviations: NSQ=non-squamous; SQ=squamous; PD=progression disease; IV=intravenous injection; BICR=blinded independent central radiologic review; ITT=intent-to-treat
*Percentage of tumour cells with membranous PD-L1 staining assessed using VENTANA PD-L1 (SP263) immunohistochemistry

RESULTS

Baseline Characteristics and Patient Disposition

- As of 22 Nov 2021, among all 479 enrolled patients, 51 (15.9%) and 7 (4.4%), respectively, remained on treatment with sugemalimab + chemo or placebo + chemo
- 174 (54.4%) patients in sugemalimab + chemo group and 113 (71.1%) patients in placebo + chemo group discontinued from study, most discontinuations were due to death
- The median follow-up was 25.4 and 24.9 months, respectively
- 49.1% and 65.4% of the patients received ≥1 subsequent anti-cancer therapy, respectively. Among which, 17.8% and 43.4% of the patients, respectively, received anti-PD-(L)1-containing therapies, including 45 (28.3%) patients in the placebo+chemo group received on-study crossover sugemalimab treatment post disease progression (**Tab 2**)

Table 1. Baseline Characteristics

	Sugemalimab + Chemo N = 320	Placebo + Chemo N = 159
Age, Median (range), Years	62.0 (29 - 75)	64.0 (36 - 75)
Sex, Male, n (%)	254 (79.4%)	129 (81.1%)
ECOG performance status, n (%)		
0	59 (18.4%)	25 (15.7%)
1	261 (81.6%)	134 (84.3%)
Tumour pathological type, n (%)		
Squamous Cell Carcinoma	129 (40.3%)	63 (39.6%)
Non-squamous Cell Carcinoma	191 (59.7%)	96 (60.4%)
Tumour PD-L1 expression, n (%)		
<1%	124 (38.8%)	64 (40.3%)
≥1%	196 (61.3%)	95 (59.7%)
Smoking status, n (%)		
Never	88 (27.5%)	40 (25.2%)
Current or former	232 (72.5%)	119 (74.8%)
Baseline liver metastasis, Yes, n (%)	39 (12.2%)	18 (11.3%)
Baseline brain metastasis, Yes, n (%)	50 (15.6%)	17 (10.7%)

Table 2. Subsequent Anti-cancer Therapy

	Sugemalimab + Chemo N = 320	Placebo + Chemo N = 159
Number (%) of patients with ≥1 subsequent therapies#	157 (49.1%)	104 (65.4%)
Anti-PD-(L)1-containing therapies*	57 (17.8%)	69 (43.4%)
Non-study PD-(L)1	41 (12.8%)	29 (18.2%)
On study cross-over sugemalimab	18 (5.6%)	45 (28.3%)
Others	148 (46.3%)	85 (53.5%)

Subsequent anti-cancer therapies are not mutually exclusive, patients may have received more than one therapies
*The patients may have received both non-study PD-(L)1 and on study cross-over sugemalimab

Efficacy

Overall Survival

- Median OS was 25.4 months in sugemalimab + 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% (**Fig 2A**)
- OS benefits were observed across all subgroups including different tumor pathology (sq: median OS 23.3 vs. 12.2 months, HR = 0.56; nsq: median OS 26.9 vs. 19.8 months, HR = 0.72) and PD-L1 expression levels (≥1%: median OS 27.0 vs. 19.0 months, HR = 0.64; <1%: median OS 19.4 vs. 14.8 months, HR = 0.66) (**Fig 2B**)

Figure 2. Overall Survival (A) Kaplan–Meier estimates of overall survival in the intent-to-treat (ITT) population

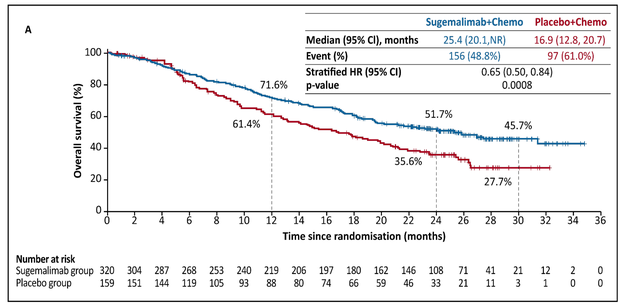
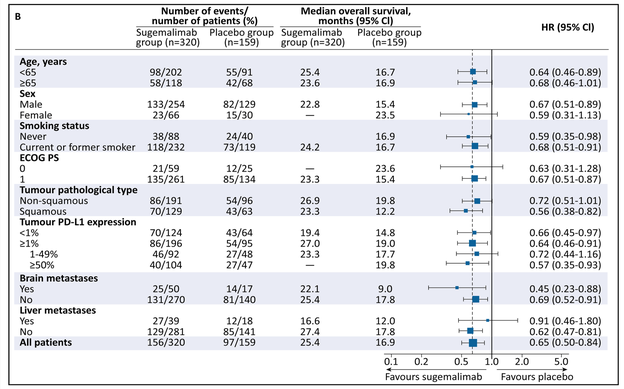


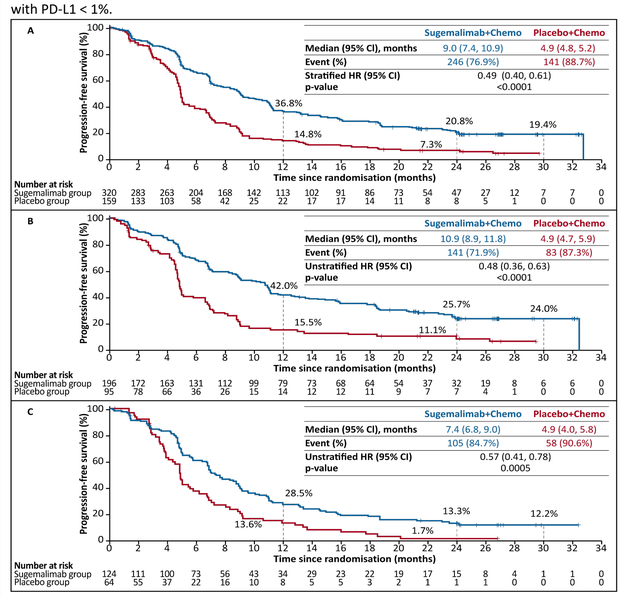
Figure 2. Overall Survival (B) Subgroup analysis of overall survival.



Updated investigator-assessed PFS

- In the intent-to-treat population, median PFS was 9.0 months with sugemalimab + 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% (**Fig 3A**)
- In patients with PD-L1 ≥ 1%, the median PFS was 10.9 vs. 4.9 months (HR = 0.48 [0.36-0.63], p < 0.0001) (**Fig 3B**); In patient with PD-L1<1%, the median PFS was 7.4 vs. 4.9 months (HR=0.57 [0.41-0.78], nominal p=0.0005) (**Fig 3C**)

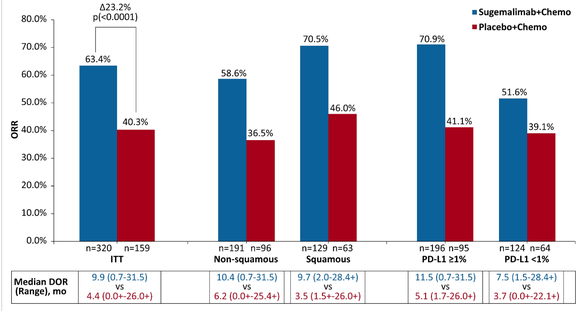
Figure 3. Investigator-assessed PFS (A) ITT population. (B) Patients with PD-L1 ≥ 1%. (C) Patients with PD-L1 < 1%.



ORR and DOR

- ORR was 63.4% vs. 40.3% (p < 0.0001) in sugemalimab + chemo group vs. placebo + chemo group; Median DOR was 9.9 vs. 4.4 months, respectively (**Fig 4**)

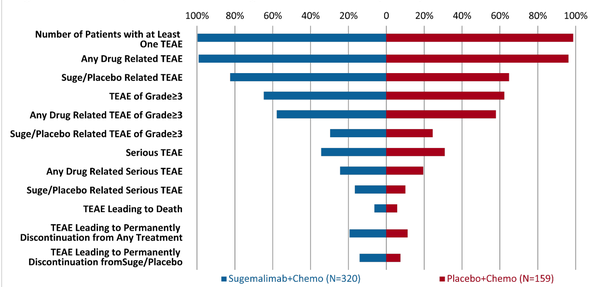
Figure 4. ORR and DOR Assessed by Investigator



Safety

- Sugemalimab + chemo had a manageable safety profile and no new safety signals were identified after a longer follow-up since last report at 2021 WCLC Congress (**Fig 5**)

Figure 5. Summary of Treatment-emergent Adverse Events (TEAEs)



CONCLUSION

- Sugemalimab plus chemo demonstrated statistically significant and clinically meaningful PFS, OS and ORR improvement compared with placebo plus chemo, the benefit was irrespective of tumour pathology or PD-L1 expression levels
  - Median OS: 25.4 vs. 16.9 months, HR = 0.65, p=0.0008
  - Median PFS: 9.0 vs. 4.9 months, HR = 0.49, p<0.0001
  - ORR: 63.4% vs. 40.3%, p<0.0001
- The combination had a manageable safety profile and no new safety signals were identified
- These data support sugemalimab plus chemo as a 1L treatment for patients with metastatic NSCLC

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DISCLOSURES

- C. Zhou: Honorarium as a speaker: Amoy Diagnostics, Boehringer Ingelheim, CStone Pharmaceuticals, Eli Lilly China, Hengrui Medicine, Innovent Biologics, Luye Pharma, MSD, Qilu Pharmaceutical, Roche, Sanofi, TopAlliance Biosciences; Advisor: Hengrui Medicine, Innovent Biologics, Qilu Pharmaceutical, TopAlliance Biosciences
- Z. Wang, M. Sun, L. Cao, Z. Ma, R. Wu, Y. Yu, W. Yao, S. Sun, J. Chen, W. Zhuang, J. Cui, X. Chen, Y. Lu, and C. Hu have declared no conflicts of interests.
- J. Wang, R. Chen, M. Qin, H. W., J. Yang are employees of CStone Pharmaceuticals (Su Zhou) Co., Ltd.

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Reference: 1. Dhillon S, Duggan S. *Drugs*. 2022;10.1007/s40265-022-01693-4. 2. Zhou C, Wang Z, Sun Y, et al. *Lancet Oncol*. 2022;23(2):220-233.