Poster #214

Serplulimab versus placebo plus chemotherapy as first-line treatment for extensive-stage small-cell lung cancer: efficacy and safety from the end-of-study analysis of the international phase 3 ASTRUM-005 study

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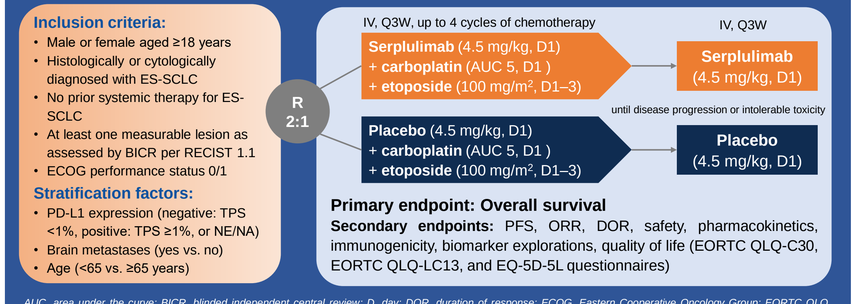
Background

- Extensive-stage small-cell lung cancer (ES-SCLC) is associated with rapid disease progression and poor prognosis, with a 5-year survival rate of 7%[1,2]. Following over three decades of platinum-etoposide chemotherapy, combination therapy of a programmed death 1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor with chemotherapy has become the standard of care as first-line treatment for ES-SCLC.
- In the IMpower133 and CASPIAN phase 3 studies, addition of PD-L1 inhibitor atezolizumab, and durvalumab to chemotherapy prolonged the median overall survival (OS) by 2.0[3] and 2.7 months[4], respectively. Other PD-(L)1 inhibitors, including adebrelimab, tislelizumab, and toripalimab, have also shown survival benefit in studies conducted in China, prolonging median OS by 2.5[5], 2.0[6], and 1.3 months[7], respectively.
- ASTRUM-005 is an international, randomized, double-blind, placebo-controlled phase 3 trial that was the first to show significantly improved OS upon addition of a PD-1 inhibitor, serplulimab, to chemotherapy for first-line treatment of ES-SCLC, with a median OS extension by 4.5 months[8]. An updated analysis at 32-month median follow-up showed sustained survival benefit[9]. Here we present the efficacy and safety findings from the end-of-study analysis of ASTRUM-005 at a median follow-up duration of 42.4 months.

Methods

- Previously untreated patients with ES-SCLC were randomized in a 2:1 ratio to receive serplulimab + carboplatin + etoposide (serplulimab group) or placebo + carboplatin + etoposide (placebo group) in 3-week cycles (**Figure 1**).

Figure 1. Study design



AUC, area under the curve; BICR, blinded independent central review; D, day; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; EORTC QLQ, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; EQ-5D-5L, European Quality of Life 5 Dimensions-5 Level; ES-SCLC, extensive-stage small-cell lung cancer; IV, intravenous; NA, not available; NE, not evaluable; ORR, objective response rate; PD-L1, programmed death ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; TPS, tumor proportion score.

Conclusions

The end-of-study analysis demonstrated long-term survival benefit of serplulimab combined with carboplatin and etoposide for previously untreated patients with ES-SCLC, supporting this therapy as a first-line standard of care for ES-SCLC treatment.

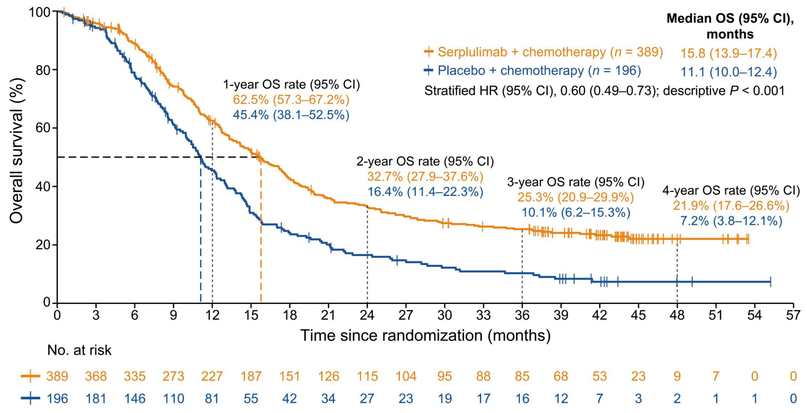
Results

- Baseline demographics and characteristics of each group have been reported previously[8].
- By data cutoff on May 7, 2024, the median follow-up duration was 42.4 months. 585 patients were enrolled and randomized to the serplulimab group (*n* = 389) and the placebo group (*n* = 196). In total, there were 401 Asian (68.5%) and 184 (31.5%) non-Asian patients; all non-Asian patients were White.
- In total, 77 (19.8%) patients in the serplulimab group and 12 (6.1%) in the placebo group had completed the study, and 312 (80.2%) and 184 (93.9%) had discontinued from the study, respectively. The most common reason for study discontinuation was death (72.2% vs. 84.7%).
- 206 (53.0%) patients in the serplulimab group and 94 (48.0%) in the placebo group received subsequent systemic anticancer treatment after the first disease progression, with chemotherapy being the most common drug modality.

Efficacy

- Consistent with previous analyses, median OS in the serplulimab group increased by 4.7 months compared to placebo group. Median OS was 15.8 months (95% confidence interval [CI], 13.9–17.4) in the serplulimab group and 11.1 months (95% CI, 10.0–12.4) in the placebo group (hazard ratio [HR] = 0.60, 95% CI, 0.49–0.73, descriptive *P* < 0.001; **Figure 2**).
- This end-of-study analysis provided the first report on the 4-year OS rates, which was higher in the serplulimab group (21.9%) than in the placebo group (7.2%).

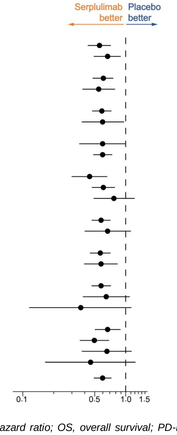
Figure 2. End-of-study analysis of overall survival in the intent-to-treat population



CI, confidence interval; HR, hazard ratio; No., number; OS, overall survival.

Figure 3. Forest plot of overall survival in patient subgroups

Subgroup	Number of events/patients: Serplulimab	Number of events/patients: Placebo	Median OS (months): Serplulimab	Median OS (months): Placebo	HR (95% CI)
Age					
< 65 years	160/235	97/119	16.8	11.7	0.56 (0.43–0.72)
≥ 65 years	120/154	69/77	14.9	10.0	0.67 (0.49–0.90)
Race					
Asian	194/262	119/139	15.8	11.1	0.61 (0.48–0.76)
Non-Asian	86/127	47/57	15.6	11.2	0.55 (0.38–0.79)
Sex					
Male	228/317	139/164	15.5	10.9	0.59 (0.48–0.73)
Female	52/72	27/32	16.6	13.8	0.60 (0.38–0.96)
Baseline ECOG performance status					
0	46/71	22/32	19.7	11.1	0.60 (0.36–0.99)
1	234/318	144/164	14.8	11.1	0.60 (0.49–0.74)
Smoking history					
Current	64/102	43/47	15.5	10.7	0.45 (0.30–0.67)
Former	154/206	96/114	16.3	10.9	0.61 (0.47–0.79)
Never	62/81	27/35	14.4	13.1	0.77 (0.49–1.22)
Brain metastasis					
No	241/339	142/168	15.9	11.3	0.58 (0.47–0.72)
Yes	39/50	24/28	13.9	9.1	0.67 (0.40–1.12)
Liver metastasis					
No	196/290	121/145	17.7	12.2	0.57 (0.45–0.72)
Yes	84/99	45/51	10.8	7.8	0.58 (0.40–0.84)
PD-L1 expression level (TPS)					
TPS < 1%	236/322	133/154	15.8	10.5	0.58 (0.47–0.72)
TPS ≥ 1%	38/58	24/32	15.1	12.9	0.65 (0.39–1.10)
Not evaluable/ Not available	6/9	9/10	17.3	11.4	0.37 (0.12–1.14)
PD-L1 expression level (CPS)					
CPS < 1	135/175	74/90	14.2	10.0	0.67 (0.50–0.89)
1 ≤ CPS < 10	94/131	64/71	15.9	11.1	0.50 (0.36–0.69)
CPS ≥ 10	43/70	18/25	19.7	14.7	0.66 (0.38–1.14)
Not evaluable/ Not available	8/13	10/10	17.3	12.8	0.46 (0.17–1.24)
Overall	**280/389**	**166/196**	**15.8**	**11.1**	**0.60 (0.49–0.73)**



HR was unstratified for patient subgroups and stratified for the overall population.
CI, confidence interval; CPS, combined positive score; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; OS, overall survival; PD-L1, programmed death ligand 1; TPS, tumor proportion score.

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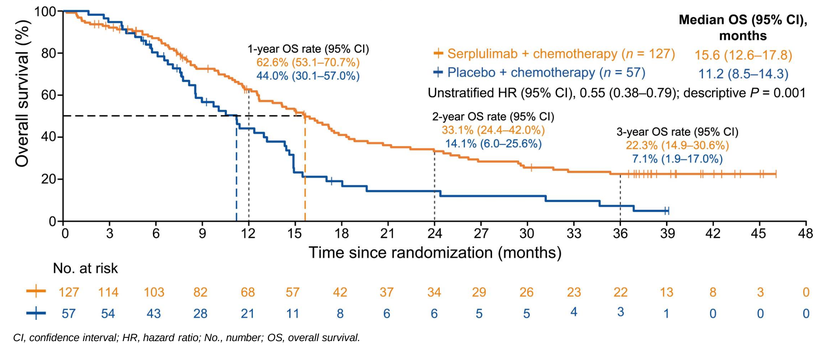
- OS benefit was observed across subgroups by age, race, sex, Eastern Cooperative Oncology Group performance status, smoking history, brain metastasis, liver metastasis, or PD-L1 expression level (**Figure 3**).
- In non-Asian patients, median OS was 15.6 vs. 11.2 months in the respective groups (unstratified HR = 0.55, 95% CI, 0.38–0.79, **Figure 4**).

Figure 4. Overall survival in non-Asian patients (all White)



CI, confidence interval; HR, hazard ratio; No., number; OS, overall survival.

- Patients in the serplulimab group had improved PFS, DOR, and ORR compared to the placebo group (**Table 1 and Table 2**).

Table 1. BICR or investigator-assessed PFS

	Serplulimab group (*n* = 389)	Placebo group (*n* = 196)
Median PFS by BICR, months (95% CI)	5.8 (5.6–6.9)	4.3 (4.2–4.4)
Stratified HR (95% CI)	0.47 (0.38–0.57); descriptive *P* < 0.001	
Median PFS by investigator, months (95% CI)	5.5 (5.0–5.7)	4.3 (4.2–4.4)
Stratified HR (95% CI)	0.57 (0.47–0.69); descriptive *P* < 0.001	

Table 2. BICR-assessed ORR and DOR

	Serplulimab group (*n* = 389)	Placebo group (*n* = 196)
Confirmed ORR, % (95% CI)	68.9 (64.0–73.5)	58.7 (51.4–65.6)
Complete response, *n* (%)	9 (2.3)	0 (0)
Partial response, *n* (%)	259 (66.6)	115 (58.7)
Median DOR, months (95% CI)	6.8 (5.5–8.3)	4.2 (3.1–4.2)
Stratified HR (95% CI)	0.45 (0.35–0.58); descriptive *P* < 0.001	

All P-values in these tables were for descriptive analysis.
BICR, blinded independent central review; CI, confidence interval; DOR, duration of response; HR, hazard ratio; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

Safety

- The safety profiles were highly similar to those from the previous analysis. No new safety signals were identified.
- Treatment-emergent adverse events (TEAEs) were reported in 96.4% and 98.0% of patients in the serplulimab group and the placebo group, respectively (**Table 3**). Grade ≥3 TEAEs were reported in 84.8% vs. 83.2% of patients, respectively, and the incidences were 80.2% vs. 77.0% after excluding deaths resulting from disease progression or COVID-19.
- Serplulimab- or placebo-related TEAEs occurred in 71.7% (grade ≥3, 35.0%) vs. 57.7% (grade ≥3, 29.1%) of patients in the respective groups (**Table 3**).
- The most common TEAEs were hematological toxicities (**Table 4**).

Table 3. End-of-study safety analysis

	Serplulimab group (*n* = 389)	Placebo group (*n* = 196)
Any TEAE, *n* (%)	375 (96.4)	192 (98.0)
Grade ≥3	330 (84.8)	163 (83.2)
Grade ≥3*	312 (80.2)	151 (77.0)
Leading to death	39 (10.0)	27 (13.8)
Leading to death*	21 (5.4)	15 (7.7)
Serious TEAE	155 (39.8)	77 (39.3)
Immune-related TEAE	148 (38.0)	37 (18.9)
Serplulimab or placebo-related TEAE, *n* (%)	279 (71.7)	113 (57.7)
Grade ≥ 3	136 (35.0)	57 (29.1)
Leading to treatment discontinuation	25 (6.4)	10 (5.1)

Table 4. Most common TEAEs (≥ 25% in either group)

Adverse event, *n* (%)	Serplulimab group (*n* = 389) Any grade	Serplulimab group (*n* = 389) Grade ≥3	Placebo group (*n* = 196) Any grade	Placebo group (*n* = 196) Grade ≥3
Anemia	281 (72.2)	75 (19.3)	140 (71.4)	36 (18.4)
Neutrophil count decreased	220 (56.6)	167 (42.9)	101 (51.5)	79 (40.3)
Alopecia	211 (54.2)	0	111 (56.6)	1 (0.5)
White blood cell count decreased	211 (54.2)	95 (24.4)	100 (51.0)	49 (25.0)
Platelet count decreased	162 (41.6)	62 (15.9)	88 (44.9)	38 (19.4)
Nausea	141 (36.2)	4 (1.0)	86 (43.9)	2 (1.0)
Neutropenia	117 (30.1)	91 (23.4)	63 (32.1)	41 (20.9)
Decreased appetite	110 (28.3)	3 (0.8)	56 (28.6)	1 (0.5)
Hyponatremia	99 (25.4)	39 (10.0)	26 (13.3)	12 (6.1)
Constipation	96 (24.7)	0	58 (29.6)	0
Vomiting	79 (20.3)	5 (1.3)	58 (29.6)	2 (1.0)

** Excluding disease progression or COVID-19.*
COVID-19, coronavirus disease 2019; PD, progressive disease; TEAE, treatment-emergent adverse event.

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