Abstract 540P: Phase 3 study of serplulimab plus chemotherapy as first-line therapy for advanced squamous non-small-cell lung cancer: ASTRUM-004 Asian subgroup

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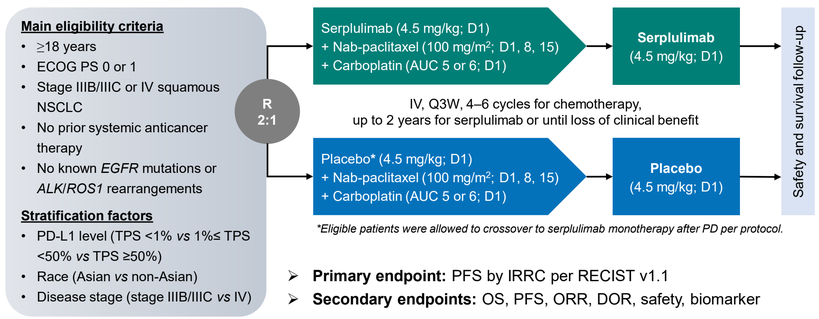
Background

- Squamous non-small cell lung cancer (NSCLC) accounts for 25–30% of NSCLC cases[1], with low frequency of targetable gene alterations[2,3].
- Adding PD-1/PD-L1 inhibitor to chemotherapy has demonstrated improved outcomes in the first-line setting[4–9]. However, preferred treatment options with a favourable risk-benefit ratio are still limited in the global setting.
- **Serplulimab**, a novel anti-PD-1 monoclonal antibody, improved survival in patients with various tumour types, and has been approved by China NMPA for MSI-H solid tumours, extensive-stage small cell lung cancer, squamous NSCLC, and CPS ≥1 oesophageal squamous cell carcinoma.
- The results from the final analysis of the phase 3 ASTRUM-004 study evaluating the efficacy and safety of serplulimab versus placebo, combined with carboplatin/nab-paclitaxel, as a first-line treatment for locally advanced or metastatic squamous NSCLC have been previously reported in WCLC 2023.
- Here we report results from the Asian subgroup final analysis of ASTRUM-004.

Methods

- This is a randomised, double-blind, multicentre, international phase 3 trial (NCT04033354).
- Statistical analysis: The 1st interim analysis of OS was performed at the time of PFS final analysis, when approximately 99 deaths had occurred. The 2nd interim analysis of OS was performed when 198 deaths were observed. The final OS analysis was performed when 299 deaths had occurred. PFS and OS were tested sequentially at an overall 2-sided α level of 0.05. The multiplicity-adjusted 2-sided α level was 0.0002, 0.012, and 0.046 for OS at the 1st and the 2nd interim analysis, and the final analysis, respectively.

Figure 1. Study design



**Eligible patients were allowed to crossover to serplulimab monotherapy after PD per protocol.*

- **Primary endpoint:** PFS by IRRC per RECIST v1.1
- **Secondary endpoints:** OS, PFS, ORR, DOR, safety, biomarker

D, day; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group perform status; IRRC, Independent Radiological Review Committee; IV, intravenous; NSCLC, non-small-cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; TPS, tumour proportion score.

Results

- As of 31 January 2023, 537 patients were randomised, of which 359 patients were Asian (serplulimab-chemo, n=240; placebo-chemo, n=119).
- The median follow-up duration was 32.9 months.
- Baseline demographics and characteristics are shown in Table 1.

References

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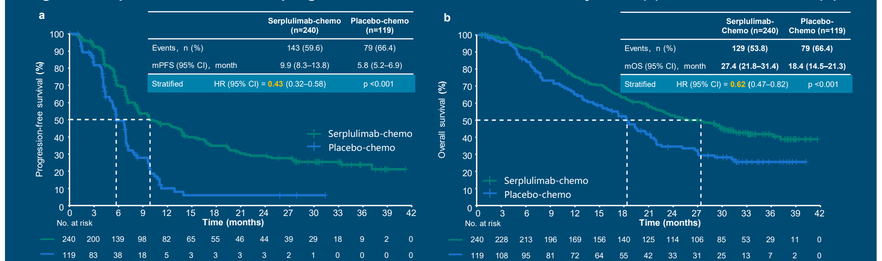
Superior efficacy and a manageable safety profile were observed with the addition of serplulimab to chemotherapy in Asian patients with previously untreated advanced squamous NSCLC.

Efficacy

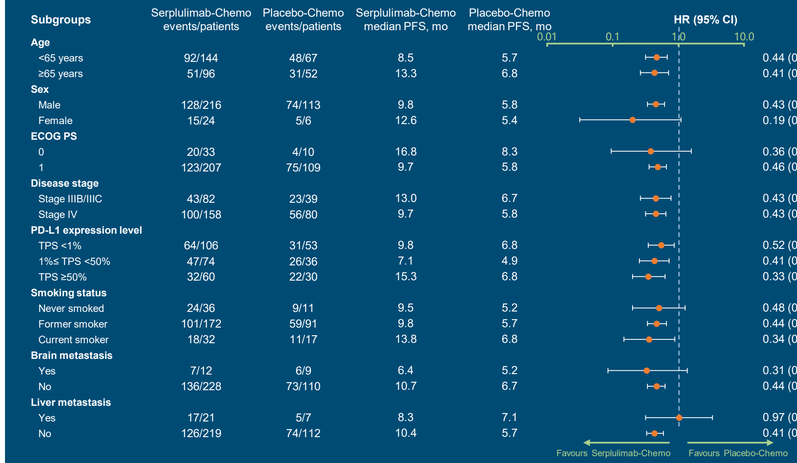
Figure 2. Kaplan–Meier curves of progression-free survival as assessed by IRRC (a) and overall survival (b)



CI, confidence interval; HR, hazard ratio; m, median; IRRC, Independent Radiological Review Committee; No., number; OS, overall survival; PFS, progression-free survival.

- In Asian patients, serplulimab-chemo group showed promising benefits in the primary endpoint of PFS (9.9 *vs* 5.8 months, HR=0.43 [95% CI 0.32–0.58]).
- Prolonged OS was also observed with the combination of serplulimab and chemotherapy (27.4 *vs* 18.4 months, HR=0.62 [95% CI 0.47–0.82]).
- 74 patients in the placebo-chemo group crossed over to serplulimab. After adjustment with 2-stage model, the risk of death was reduced by 63% with serplulimab-chemo (27.4 *vs* 10.7 months; HR 0.37 [95% CI 0.25–0.49]).

Figure 3. Forest plot analysis of progression-free survival as assessed by IRRC per RECIST v1.1



- Analyses in the subgroups demonstrated generally consistent results with that in overall Asian population.
- At final analysis, the confirmed objective response rate was 67.5% (95% CI 61.2–73.4) in the serplulimab-chemo group and 44.5% (95% CI 35.4–53.9) in the placebo-chemo group (odds ratio 2.59 [95% CI 1.65–4.06]). The confirmed median duration of response was 12.3 months (95% CI 8.7–16.8) and 5.6 months (95% CI 4.4–7.1) in the respective groups (HR 0.43 [95% CI 0.28–0.65]).

Table 1. Patient demographics and baseline characteristics

	Serplulimab-Chemo (n = 240)	Placebo-Chemo (n = 119)
Median age (range), years	63.0 (43–75)	64.0 (35–75)
Sex, n (%)		
Male	216 (90.0)	113 (95.0)
Female	24 (10.0)	6 (5.0)
Race, n (%)		
Asian	240 (100)	119 (100)
Other	0	0
Median BMI (range), kg/m²	22.0 (15.6–34.1)	21.1 (15.2–30.4)
ECOG PS, n (%)		
0	33 (13.8)	10 (8.4)
1	207 (86.3)	109 (91.6)
Disease stage, n (%)		
IIIB/IIIC	82 (34.2)	39 (32.8)
IV	158 (65.8)	80 (67.2)
PD-L1 expression, n (%)		
TPS <1%	106 (44.2)	53 (44.5)
1%≤ TPS <50%	74 (30.8)	36 (30.3)
TPS ≥50%	60 (25.0)	30 (25.2)
Smoking status, n (%)		
Current smoker	32 (13.3)	17 (14.3)
Former smoker	172 (71.7)	91 (76.5)
Never smoked	36 (15.0)	11 (9.2)
Liver metastasis, n (%)	21 (8.8)	7 (5.9)
Brain metastasis, n (%)	12 (5.0)	9 (7.6)

BMI, body mass index; chemo, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death-ligand 1; TPS, tumour proportion score.

Safety

- The incidence and severity of TEAEs and TRAEs were similar between the two treatment groups (Table 2).
- 41.3% and 23.5% patients reported irAEs, most commonly hypothyroidism (9.6% *vs* 0.8%), rash (7.5% *vs* 0.8%), and immune-mediated lung disease (6.3% *vs* 0.8%), which were similar to that reported in previous PD-1/PD-L1 inhibitor studies. Most irAEs were grade 1–2.
- Most common TRAEs[a] are listed in Table 3. The most common (incidence ≥15%) grade ≥3 TRAEs[a] by PT were neutrophil count decreased (22.1% *vs* 21.8%), anaemia (17.5% *vs* 16.0%), and white blood cell count decreased (15.0% *vs* 16.8%) in the serplulimab-chemo group and the placebo group.

Table 2. Summary of TEAEs

n (%)	Serplulimab-Chemo (n = 240)	Placebo-Chemo (n = 119)
Any TEAE	239 (99.6)	119 (100)
Grade 1	1 (0.4)	0
Grade 2	15 (6.3)	16 (13.4)
Grade 3	117 (48.8)	67 (56.3)
Grade 4	86 (35.8)	28 (23.5)
Grade 5	20 (8.3)	8 (6.7)
Grade ≥3	223 (92.9)	103 (86.6)
TRAE[a]	205 (85.4)	93 (78.2)
Grade ≥3 TRAE[a]	107 (44.6)	46 (38.7)
Serious TEAEs	138 (57.5)	57 (47.9)
TEAEs leading to drug discontinuation[b]	42 (17.5)	9 (7.6)
TEAEs leading to death	20 (8.3)	8 (6.7)
AESIs	102 (42.5)	28 (23.5)
IRRs	4 (1.7)	0
irAEs	99 (41.3)	28 (23.5)

Table 3. Most common TRAEs[a] (≥ 15%[c])

SOC PT	Serplulimab-Chemo (n = 240)	Placebo-Chemo (n = 119)
TRAE[a], n (%)	205 (85.4)	93 (78.2)
Investigations, n (%)	152 (63.3)	69 (58.0)
Neutrophil count decreased	79 (32.9)	38 (31.9)
White blood cell count decreased	78 (32.5)	40 (33.6)
Platelet count decreased	67 (27.9)	33 (27.7)
Alanine aminotransferase increased	44 (18.3)	12 (10.1)
Aspartate aminotransferase increased	44 (18.3)	8 (6.7)
Blood and lymphatic system disorders, n (%)	111 (46.3)	52 (43.7)
Anaemia	107 (44.6)	48 (40.3)
Metabolism and nutrition disorders, n (%)	90 (37.5)	35 (29.4)
Decreased appetite	49 (20.4)	24 (20.2)
Skin and subcutaneous tissue disorders, n (%)	87(36.3)	24 (20.2)
Rash	37 (15.4)	6 (5.0)

[a] Related to serplulimab/placebo; [b] Discontinuation of serplulimab/placebo; [c] ≥15% in serplulimab-chemo group

AESI, adverse event of special interest; chemo, chemotherapy; irAE, immune-related adverse event; IRR, infusion-related reaction; PT, preferred term; SOC, system organ class; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

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