

# ASTRUM-005 Randomized Clinical Trial

## 1L Serplulimab vs. Placebo added to Chemotherapy on Survival Patients with ES- SCLC

### Effect of First-Line Serplulimab vs Placebo Added to Chemotherapy on Survival in Patients With Extensive-Stage Small Cell Lung Cancer

#### The ASTRUM-005 Randomized Clinical Trial

**Importance** Programmed cell death ligand 1 inhibitors combined with chemotherapy has changed the approach to first-line treatment in patients with extensive-stage small cell lung cancer (SCLC). It remained unknown whether adding a programmed cell death 1 (PD-1) inhibitor to chemotherapy provided similar or better benefits in patients with extensive-stage SCLC, which would add evidence on the efficacy of checkpoint inhibitors in the treatment of extensive-stage SCLC.

**Objective** To evaluate the efficacy and adverse event profile of the PD-1 inhibitor serplulimab plus chemotherapy compared with placebo plus chemotherapy as first-line treatment in patients with extensive-stage SCLC.

**Design, Setting, and Participants** This international, double-blind, phase 3 randomized clinical trial (ASTRUM-005) enrolled patients at **114 hospital sites in 6 countries** between September 12, 2019, and April 27, 2021. Of **894 patients who were screened, 585 with extensive-stage SCLC who had not previously received systemic therapy were randomized**. Patients were followed up through October 22, 2021.

**Interventions** Patients were randomized 2:1 to receive either 4.5 mg/kg of serplulimab (n = 389) or placebo (n = 196) intravenously every 3 weeks. All patients received intravenous carboplatin and etoposide every 3 weeks for up to 12 weeks.

**Main Outcomes and Measures** The primary outcome was overall survival (prespecified significance threshold at the interim analysis, 2-sided  $P < .012$ ). There were 13 secondary outcomes, including progression-free survival and adverse events.

**Results** Among the 585 patients who were randomized (mean age, 61.1 [SD, 8.67] years; 104 [17.8%] women), 246 (42.1%) completed the trial and 465 (79.5%) discontinued study treatment. All patients received study treatment and were included in the primary analyses. As of the data cutoff (October 22, 2021) for this interim analysis, the median duration of follow-up was 12.3 months (range, 0.2-24.8 months). The median overall survival was significantly longer in the serplulimab group (15.4 months [95% CI, 13.3 months-not evaluable]) than in the placebo group (10.9 months [95% CI, 10.0-14.3 months]) (hazard ratio, 0.63 [95% CI, 0.49-0.82];  $P < .001$ ). The median progression-free survival (assessed by an independent radiology review committee) also was longer in the serplulimab group (5.7 months [95% CI, 5.5-6.9 months]) than in the placebo group (4.3 months [95% CI, 4.2-4.5 months]) (hazard ratio, 0.48 [95% CI, 0.38-0.59]). Treatment-related adverse events that were grade 3 or higher occurred in 129 patients (33.2%) in the serplulimab group and in 54 patients (27.6%) in the placebo group.

**Conclusions and Relevance** Among patients with previously untreated extensive-stage SCLC, serplulimab plus chemotherapy significantly improved overall survival compared with chemotherapy alone, supporting the use of serplulimab plus chemotherapy as the first-line treatment for this patient population.

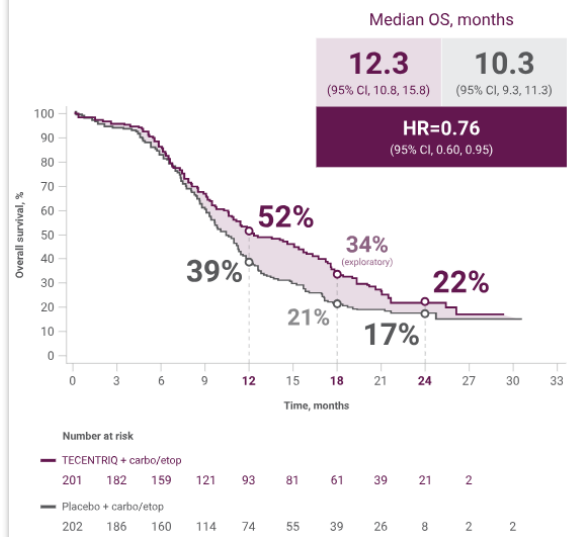
**Trial Registration** ClinicalTrials.gov Identifier: [NCT04063163](https://clinicaltrials.gov/ct2/show/study/NCT04063163)

# Serplulimab Yielded 15.8 mOS at 32 Months Follow-up



## 2-year OS Data

Additional survival data based on nearly 2 years of follow-up<sup>3</sup>



Tecentriq demonstrated OS benefit with up to 2 years of follow-up, but has not shared 3-year OS data despite being first-to-market



## 3-year OS Data

OVERALL SURVIVAL AT 3-YEAR PLANNED EXPLORATORY ANALYSIS<sup>1†</sup>  
(median duration of follow-up: 39.4 months)

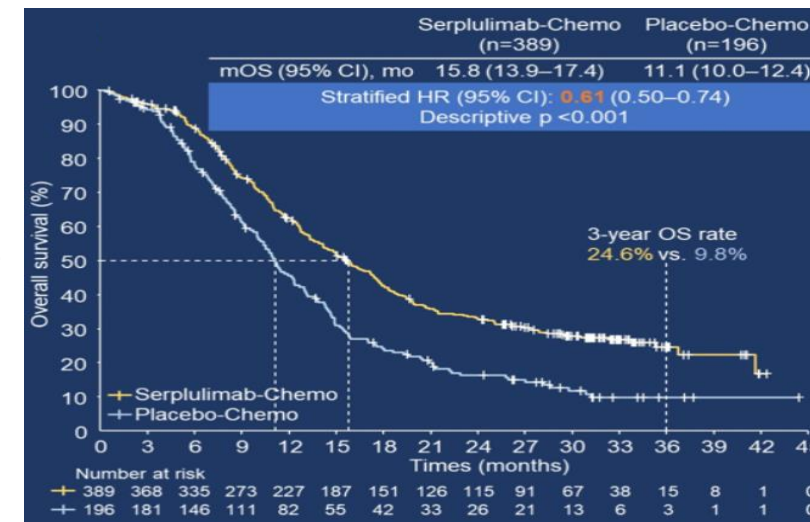


Imfinzi + EP<sup>1</sup> has demonstrated ~3x OS benefit vs. EP<sup>1</sup> alone at 3 years

In ASTRUM-005, 585 patients were enrolled. 31.5% of patients were non-Asian. By the data cutoff of June 13, 2023 (data presented at ASCO 2024), with a median follow-up of 31.6 mo, Serplulimab showed a mOS of 15.8 mo. vs. 11.1 mo in the placebo arm<sup>2</sup>, stratified HR (95% CI): 0.61 (0.50-0.74), descriptive p<0.001.

## Serplulimab

## 31.6-month OS Data



Serplulimab may significantly increase 3-year OS benefit compared to SOC competitors; Caucasian and Asian patients show comparable outcomes

Therapy	3-year OS (Global)
Placebo + Chemo	9.8% (95% CI 5.6–15.4)
Serplulimab + Chemo	24.6% (95% CI 19.5–30.1)

Sources:  
 Tecentriq [HCP website](#); Imfinzi [HCP website](#); Henlius Corporate [Presentation](#)

1. Platinum based chemotherapy: carboplatin or cisplatin + etoposide.  
 2. ASTRUM-005 used placebo as a comparator and these results are not reflective of a head-to-head trial with actual standard of care including immunotherapy.

# ASTRUM Data Presented in Leading Journals and Conferences

JAMA

**QUESTION** Does the programmed cell death 1 inhibitor serplulimab, when added to chemotherapy during the first line of treatment, improve outcomes in patients with extensive-stage small cell lung cancer?

**CONCLUSION** In patients with extensive-stage small cell lung cancer, serplulimab plus chemotherapy as the first-line treatment resulted in improved overall survival compared with chemotherapy alone.

**POPULATION** 481 Men  
**INTERVENTION** Serplulimab + chemotherapy vs. Placebo + chemotherapy  
**FINDINGS** Median overall survival

SINGAPORE 2022  
ESMO ASIA

ASTRUM-005  
Updated results  
versus placebo  
in extensive-stage  
small cell lung cancer  
An international  
randomized, double-blind, phase 3 trial

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2 December 2022

**Abstract #8100: Serplulimab vs. placebo combined with chemotherapy as first-line treatment for extensive-stage small-cell lung cancer: Extended follow-up results and patient-reported outcomes from the international phase 3 ASTRUM-005 study**

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**Background**  
Anti-PD-L1 plus chemotherapy has become the standard first-line therapy for extensive-stage small-cell lung cancer (ES-SCLC). However, benefits in overall survival (OS) are still modest (improvement in median OS, 2.0-2.5 months).<sup>1-3</sup>  
ASTRUM-005 was an international phase 3 trial comparing efficacy and safety of serplulimab vs. placebo, combined with chemotherapy, as first-line treatment for ES-SCLC. Interim analysis showed a 4.5-month improvement of median OS in serplulimab-chemotherapy group, making serplulimab the first approved PD-1 inhibitor for ES-SCLC. Continuing improvements were seen in all efficacy endpoints in an updated analysis reported at ESMO Asia Congress 2022.  
Here we present the updated efficacy with extended follow-up and patient-reported outcomes.

**Methods**  
This randomized, double-blind, phase 3 trial (Figure 1) screened patients at 114 hospital sites in 6 countries. Detailed methods have been reported previously.<sup>4</sup>  
**Figure 1. Study design**  
**Inclusion criteria:**  
• Male or female aged ≥18 years  
• histologically or cytologically diagnosed with ES-SCLC  
• No prior systemic therapy for ES-SCLC  
• At least one measurable lesion as assessed by RECIST 1.1 (4.5 mg/kg, D1) or ECOG PS 0-1  
**Stratification factor**  
• PD-L1 expression (tumor TPS <1% vs ≥1%, median TPS 14% vs 16%)  
• Brain metastases (yes vs no)  
• Age (≤70 vs >70 years)  
**Primary endpoints: Overall survival**  
• Serplulimab (4.5 mg/kg, D1) + Carboplatin (AUC 5, D1) + Etoposide (100 mg/m<sup>2</sup>, D1-3) vs Placebo (4.5 mg/kg, D1) + Carboplatin (AUC 5, D1) + Etoposide (100 mg/m<sup>2</sup>, D1-3)  
**Secondary endpoints: PFS, ORR, DOR, safety, pharmacokinetics, immunogenicity, biomarker explorations, quality of life (EORTC QLQ-C30, EORTC QLQ-L13), and EQ-5D-5L questionnaire**  
**Results**  
• By the data cutoff of June 13, 2023, the median follow-up duration was 31.6 months. 565 patients were enrolled and randomized to the serplulimab-chemotherapy group (n = 389) and the placebo-chemotherapy group (n = 176). 31.5% of patients were non-Asian (all White).  
• Baseline demographics and characteristics of each group have been reported previously.<sup>4</sup>  
**Table 1. Updated secondary efficacy endpoints**

Endpoint	Serplulimab-chemotherapy (n=389)	Placebo-chemotherapy (n=176)
Median PFS by RRRC, mo (95% CI)	5.8 (5.6-6.9)	4.3 (4.2-4.4)
Hazard ratio (95% CI)	0.46 (0.38-0.57)	
Confirmed ORR by RRRC, % (95% CI)	68.9 (64.0-73.5)	58.7 (51.4-65.6)
Complete response, n (%)	6 (1.5)	0
Partial response, n (%)	262 (67.4)	105 (59.7)
Median DOR by RRRC, mo (95% CI)	6.8 (5.5-7.9)	4.2 (3.1-4.2)

**Table 2. Updated overall survival in subgroups**

Stratification factor	Serplulimab-Chemo (n=389)	Placebo-Chemo (n=176)	Hazard ratio (95% CI)
Age			
≤70 years	101/254	45/107	0.50 (0.42-0.72)
>70 years	190/135	131/76	0.50 (0.51-0.34)
Sex			
Male	292/217	128/84	0.50 (0.44-0.56)
Female	97/172	48/92	0.50 (0.51-0.71)
Race			
Asian	188/202	100/109	0.51 (0.46-0.71)
Non-Asian	201/187	76/67	0.50 (0.39-0.63)
ECOG PS			
0	43/11	20/23	0.50 (0.31-0.86)
1	346/178	156/153	0.49 (0.45-0.76)
ECOG PS			
0	61/52	41/46	0.49 (0.35-0.77)
1	328/337	135/130	0.50 (0.47-0.76)
TPS			
<1%	38/25	20/25	0.50 (0.31-0.86)
≥1%	351/364	156/151	0.49 (0.45-0.76)
Brain metastases			
Yes	38/25	20/25	0.50 (0.31-0.86)
No	351/364	156/151	0.49 (0.45-0.76)

**Figure 2. Updated overall survival in overall population (A) and non-Asian (all White) patients (B)**

**Figure 3. Updated overall survival in subgroups**

**Figure 4. Change from baseline to Week 18 in functional and symptom domains**

**Table 2. "Pain in other parts" by Week 18**

**Table 3. Time to deterioration**

**Outcomes in non-Asian patients (all White) may serve as a proof of concept for ASTRIDE bridging trial currently accruing patients in the United States (NCT05468489).**

**Acknowledgments and Disclosures**  
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Jing Li, Alex Aitkin, Qingyu Wang, and Jun Zhu are employees of Shanghai Fosun Pharma, Inc.  
2024 American Society of Clinical Oncology (ASCO) Annual Meeting, May 31 - June 4, 2024

High priority  
Publications from  
the US perspective:

Smoking-related genomic mutation patterns in patients with small cell lung cancer treated in ASTRUM-005 study

Abstract accepted and to be presented at ESMO 24

Serplulimab MoA

Full manuscript submitted to mAB (IF 5.3)

ASTRUM-005 Long term Follow-up: Backbone of regulatory filing in the US

Full manuscript submitted to Cancer Discovery (IF 28.2)

Past presentations

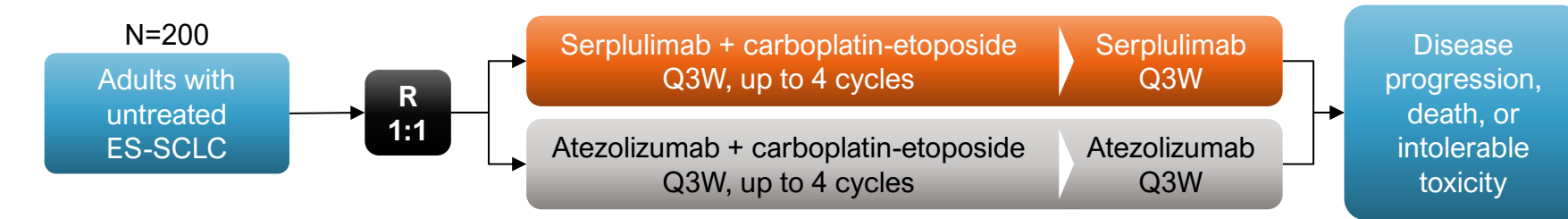
Planned



# ASTRIDE Trial Design - U.S. Bridging Trial Ongoing

First study in ES-SCLC with current SOC as the comparator arm

## Study design: Phase 3, randomized, open-label study



Key endpoints	Key inclusion criteria	Key exclusion criteria	Enrollment
<p><b>Primary:</b> OS</p> <p><b>Secondary:</b> PFS, ORR, DOR, QoL, PK/PD, correlative biomarker analyses</p> <p><b>Safety:</b> AEs</p>	<ul style="list-style-type: none"> <li>• 18 years and older</li> <li>• Histologically or cytologically diagnosed with ES-SCLC</li> <li>• ≥1 measurable lesion</li> <li>• Stable and treated brain metastases</li> <li>• ECOG PS 0 or 1</li> <li>• No significant organ dysfunction</li> <li>• Expected survival ≥12 weeks</li> </ul>	<ul style="list-style-type: none"> <li>• Histologically or cytologically confirmed mixed-stage SCLC</li> <li>• Prior systemic SCLC treatments</li> <li>• Grade 2 peripheral neuropathy</li> <li>• Ejection fraction &lt;50% or NYHA class III to IV cardiac insufficiency</li> <li>• Pregnant or breastfeeding females</li> </ul>	<p>Aligned with FDA requirements for diversity and inclusion of minorities in clinical trials</p>

AE=adverse event, DOR=duration of response, ORR=objective response rate, OS=overall survival, PD=pharmacodynamic, PFS=progression-free survival, PK=pharmacokinetic, QoL=quality of life.  
Data on File, Protocol Number HLX10-005-SCLC301-E, Fosun Pharma USA.