Serplulimab vs atezolizumab added to chemotherapy in patients with treatment-naive ES-SCLC in the United States – ASTRIDE trial

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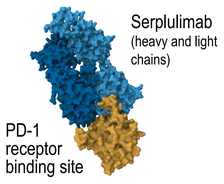
Background

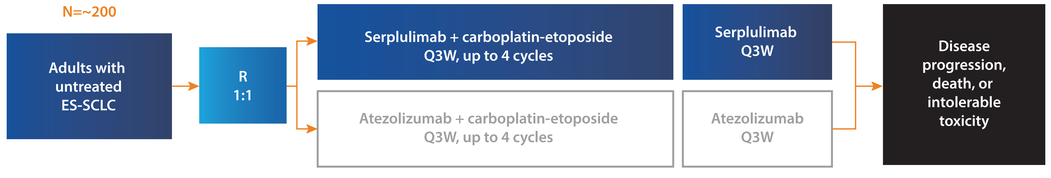
- Small cell lung cancer (SCLC) is the most aggressive subtype of lung cancer, accounting for ~15% of all lung cancer cases[1]
- SCLC is classified as either limited stage small cell lung cancer (LS-SCLC) or extensive stage small cell lung cancer (ES-SCLC)[1]
  - Approximately 2 out of 3 patients with SCLC have ES-SCLC when diagnosed[1]
- Following approvals of atezolizumab (2019) and durvalumab (2020) combination therapies based on the Phase 3 IMpower133 and CASPIAN studies, respectively, anti–PD-L1 + etoposide-platinum chemotherapy became the SOC in ES-SCLC; these therapies have offered ~2 month OS benefit compared to chemotherapy alone[2-4]
- Due to significant unmet medical need for SCLC, there are multiple ongoing studies of serplulimab, exploring its safety and efficacy in patients with both LS-SCLC and ES-SCLC[5]
- Results from the ASTRUM-005 study, a global, randomized, placebo-controlled Phase 3 clinical study, led to the approval of serplulimab for the 1L treatment of ES-SCLC in China, making it the world's first anti–PD-1 monoclonal antibody (mAb) to be approved in SCLC[6,7]
  - Serplulimab + chemotherapy showed an improvement in median OS by 4.7 months vs placebo + chemotherapy (15.8 months vs 11.1 months; HR 0.62 [95% CI: 0.50-0.76]; *P*<0.001) in treatment-naive patients with ES-SCLC[8]
- Fosun Pharma entered into an exclusive license agreement with Shanghai Henlius Biotech, Inc. for the commercialization of serplulimab in the US[9]
- ASTRIDE, a head-to-head, US-based study of serplulimab + chemotherapy vs atezolizumab + chemotherapy for the treatment of 1L ES-SCLC, aims to confirm the ASTRUM-005 findings in a US-based ES-SCLC population[10]

Mechanism of action of serplulimab

- Serplulimab is a novel anti–PD-1 mAb with a unique mode of recognition of the PD-1 receptor compared with currently available anti–PD-1 mAbs[11]
  - While serplulimab shows greater overlap of its epitope region with pembrolizumab than nivolumab, it has an opposite heavy chain and light chain usage vs pembrolizumab, resulting in a different spatial interaction with PD-1[11,12]
- In vitro, serplulimab was able to specifically bind the PD-1 receptor and efficiently block the PD-L1 and PD-L2 signaling pathway with relatively higher potency than nivolumab[11]
- In vivo, serplulimab demonstrated similar antitumor activity as pembrolizumab and the potential for complete tumor eradication, while nivolumab only demonstrated tumor growth inhibition[11]



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



Key endpoints

Primary: OS

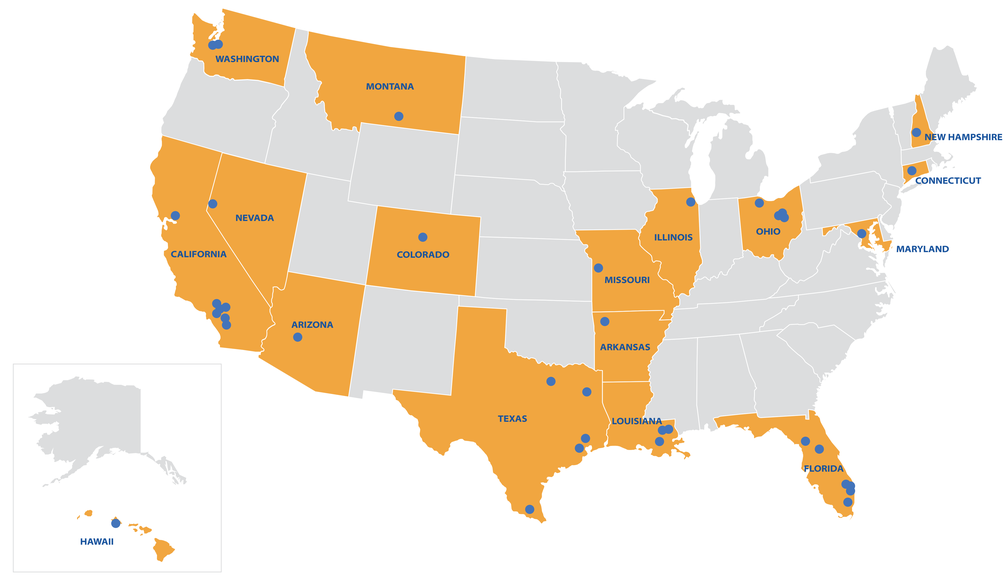
Secondary: PFS, ORR, DOR, QoL, PK/PD, correlative biomarker analyses

Safety: AEs

Study status

- ASTRIDE is currently recruiting participants; an estimated 200 participants from 90 sites across the US will be enrolled
- This is an ongoing study; enrollment began on November 18, 2022
- The study has an estimated primary completion date of June 2024

ASTRIDE sites



More information about this study can be found at https://clinicaltrials.gov/study/NCT05468489.

Key inclusion criteria

- 18 years and older
- Histologically or cytologically diagnosed with ES-SCLC
- ≥1 measurable lesion
- Stable and treated brain metastases
- ECOG PS 0 or 1
- No significant organ dysfunction
- Expected survival ≥12 weeks

Key exclusion criteria

- Histologically or cytologically confirmed mixed-stage SCLC
- Prior systemic SCLC treatments
- Grade ≥2 peripheral neuropathy
- Ejection fraction <50% or NYHA class III to IV cardiac insufficiency
- Pregnant or breastfeeding females

Support and contact

- This study is sponsored by Shanghai Henlius Biotechnology Co., Ltd
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Acknowledgements

- Thank you to the patients and their families who make this trial possible
- Thank you to the clinical study teams and investigators for their work and contributions
- This study is supported by Shanghai Henlius Biotech, Inc. and Fosun Pharma
- All authors contributed to and approved this presentation; writing and editorial assistance were provided by Christine Schwall-Pecci of BGB Group, funded by Fosun Pharma

Abbreviations
1L, first-line; AE, adverse event; DOR, duration of response; ES-SCLC, extensive stage small cell lung cancer; LS-SCLC, limited stage small cell lung cancer; mAb, monoclonal antibody; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PD-1, programmed cell death 1; PD-L1, programmed death-ligand 1; PD-L2, programmed death-ligand 2; PFS, progression-free survival; PK, pharmacokinetics; PS, performance status; Q3W, every 3 weeks; QoL, quality of life; R, randomization; SCLC, small cell lung cancer; SOC, standard of care.

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