Small Cell Lung Cancer Landscape Overview

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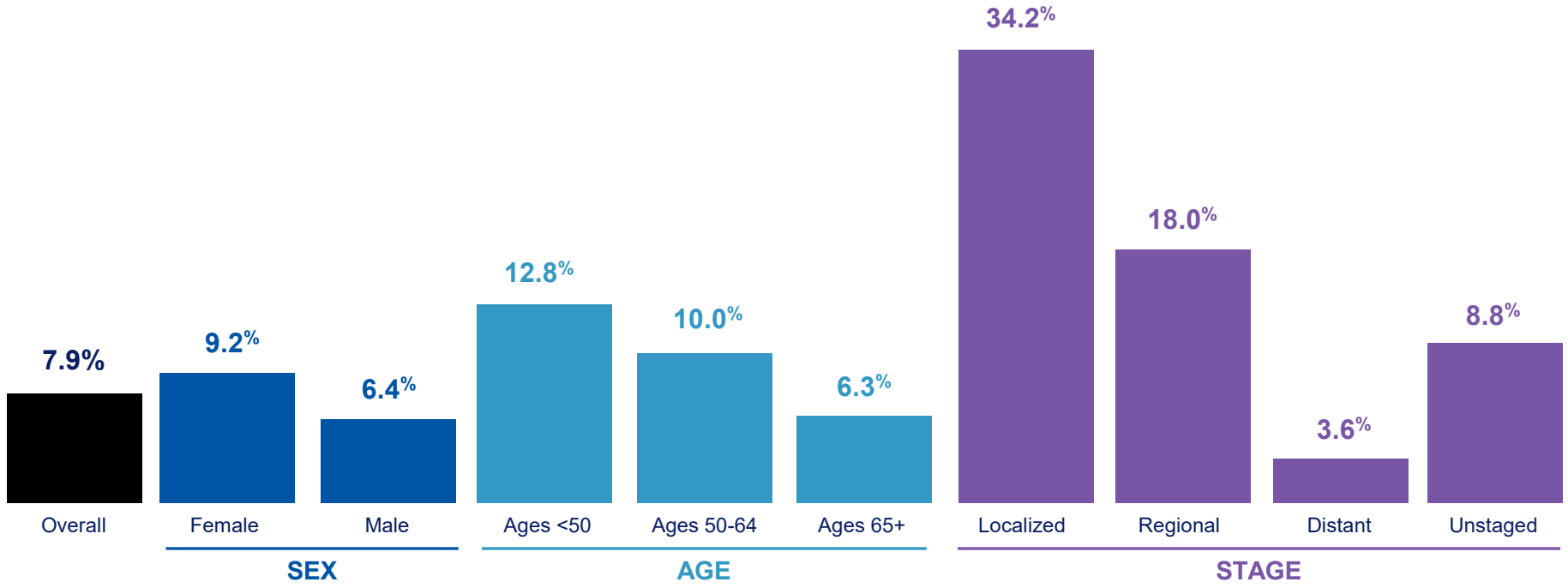
SER-MED-001-v2.0-08/2024

SCLC Is a Rapidly Progressing Lung Cancer

- SCLC is characterized by rapid tumor progression with a 5-year survival of only 7.9% and accounts for ~13% of all lung cancer cases[1-3]

SCLC 5-Year Relative Survival Rate (%) per Sex, Age, and Stage at Diagnosis in 2015[3]



SCLC=small cell lung cancer.

1. Ganti AK, et al. *JAMA Oncol*. 2021;7(12):1824-1832. 2. Wang Q, et al. *J Thorac Oncol*. 2023;18(1):31-46. 3. SEER*Explorer. Surveillance Research Program, National Cancer Institute; 2023. Updated November 16, 2023. Accessed March 22, 2024. https://seer.cancer.gov.statistics-network/explorer

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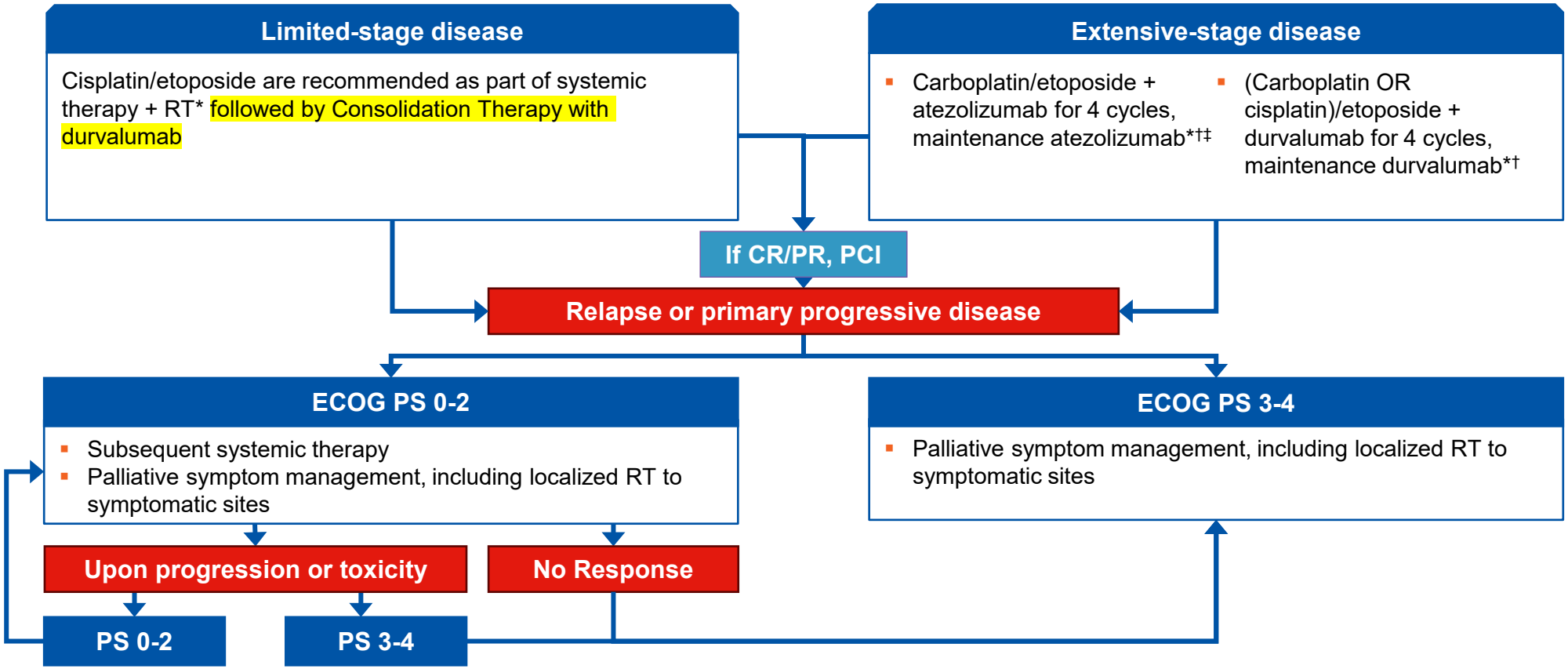
Overview of Preferred SCLC Systemic Therapies Includes PD-L1–Targeted Immune Checkpoint Inhibitors Based on the Latest NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)



*Category 1 recommendation. †Contraindications for treatment with programmed death-1 (PD-1)/programmed death ligand-1 inhibitors may include active or previously documented autoimmune disease and/or concurrent use of immunosuppressive agents. For safety reasons, do not use ICIs in patients who have recently received tyrosine kinase inhibitors. Maintenance immunotherapy with either atezolizumab or durvalumab should continue until progression or intolerable toxicity. ‡Category 2A for maintenance atezolizumab 1680 mg day 1, every 28 days.

CR=complete response; ECOG PS=Eastern Cooperative Oncology Group performance status; IV=intravenous; PCI=prophylactic cranial irradiation; PR=partial response; RT=radiation therapy; SCLC=small cell lung cancer.

Adapted from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer V.3.2025.

Progress Continues to Be Made With Immune Checkpoint Inhibitors for the Treatment of SCLC

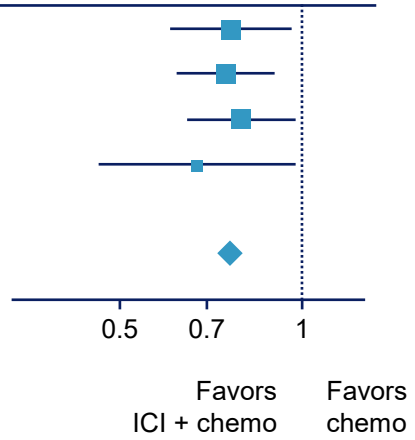
- Despite improvements in OS with approved PD-L1 inhibitors for the treatment of ES-SCLC, there is still a clinical need for more effective treatments among these patients[1,2]
  - In IMpower133, the mOS was 12.3 months (95% CI: 10.8–15.8) with atezolizumab + chemotherapy and 10.3 months (95% CI: 9.3–11.3) with chemotherapy alone[3]*
  - In CASPIAN, a 3-year analysis showed that the mOS was 13.0 months (95% CI: 11.5–14.8) with durvalumab + chemotherapy and 10.3 months (95% CI: 9.3–11.2) with chemotherapy alone[3]†

OS Among Patients With ES-SCLC Treated With PD-1/PD-L1 ICI Plus Platinum-etoposide Chemotherapy[4]‡

Study or Subgroups	ICI+ Chemo-therapy Total, n	Chemo-therapy Total, n	Weight	Hazard Ratio (95% CI)
IMpower133	201	202	25.2%	0.76 (0.60–0.95)
CASPIAN	268	269	36.3%	0.75 (0.62–0.91)
KEYNOTE-604	228	225	29.3%	0.80 (0.64–0.98)
ECOG-ACRIN EA5161	80	80	9.3%	0.67 (0.46–0.98)
Total (95% CI)	777	776	100.0%	0.76 (0.68–0.85)

Heterogeneity: $Chi^2 = 0.63$, df = 3 (P=0.89); $I^2 = 0\%$

Test for overall effect: Z = 4.75 (P<0.00001)



*Phase 3, randomized trial that assessed the addition of atezolizumab to carboplatin plus etoposide in 403 patients with previously ES-SCLC and compared outcomes to carboplatin plus etoposide alone.[3] †Phase 3 randomized trial that assessed adding durvalumab to etoposide and either carboplatin or cisplatin followed by maintenance durvalumab in 537 patients with previously untreated ES-SCLC and compared response to platinum plus etoposide alone.[3] ‡Based on a systematic review and meta-analysis of randomized clinical trials evaluating the addition of PD-1/PD-L1 ICIs to first-line chemotherapy in SCLC.[4]

ES-SCLC=extensive-stage small cell lung cancer; ICI=immune checkpoint inhibitor; mOS=median overall survival; OS=overall survival; PD-1=programmed death-1; PD-L1=programmed death ligand-1; SCLC=small cell lung cancer.

1. Goldman JW, et al. *Lancet Oncol*. 2021;22(1):51-65. 2. Liu SV, et al. *J Clin Oncol*. 2021;39(6):619-630. 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer V.2.2024. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed March 4, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. 4. Facchinetti F, Di Maio M, Tiseo M. *Cancers (Basel)*. 2020;12(9):2645.

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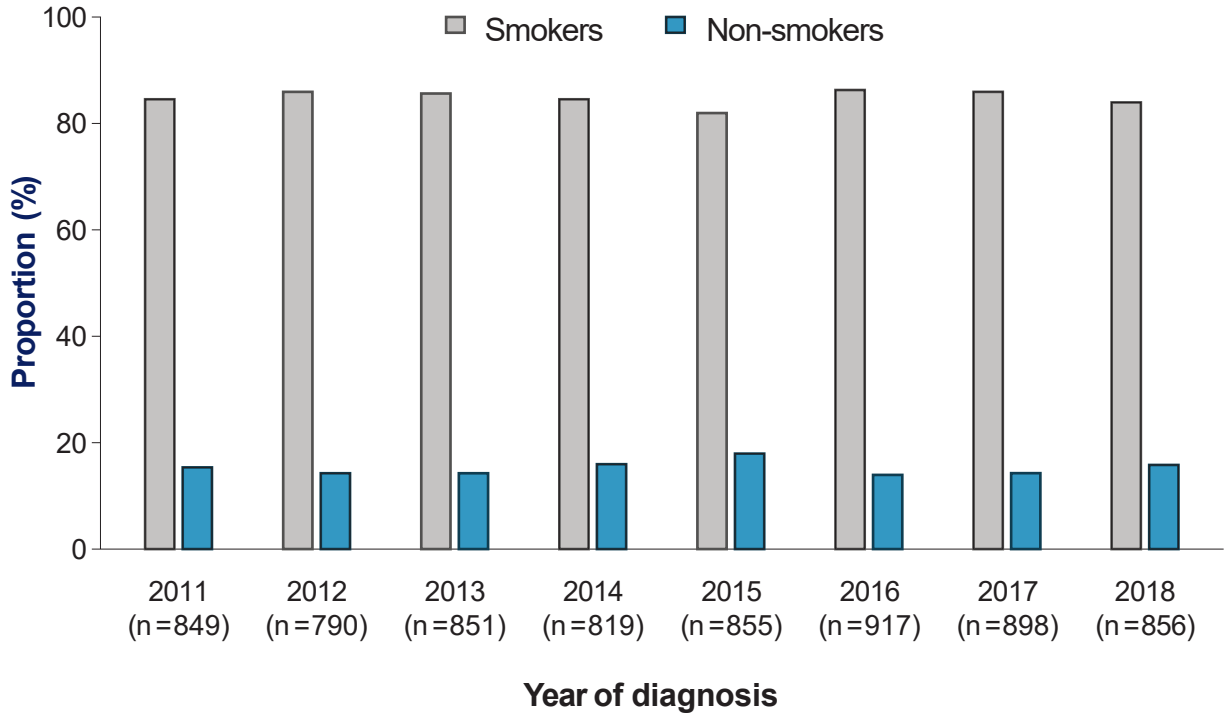
While SCLC Occurs Mostly in Smokers, Some Patients Presenting With SCLC Are Reported as Never-Smokers

- Smoking status affects the clinical presentations of lung cancer, which may differ by ethnicity
  - Among patients from Asian countries (ie, China, Korea, and Taiwan), 15%-20% of patients with SCLC were reported as “never-smokers”*
  - Among non-Asian populations, “never-smokers” accounted for only 2%-6% of all SCLC cases
- The percentage of never-smokers varied little in the SCLC population among Asian patients over time: 15.5% in 2011 and 16.1% in 2018
- Potential exposures: secondhand tobacco, residential radon

Smoking Status Among Asian Patients With SCLC From 2011 to 2018†



*Based on studies conducted in patients from China, Korea, and Taiwan. †Based on a retrospective cohort study using data from the national Taiwan Cancer Registry that analyzed the data on lung cancer occurring from January 1996 to December 2018.

SCLC=small cell lung cancer.

Tseng JS, et al. *JAMA Netw Open*. 2022;5(3):e224830.

Serplulimab, an Anti-PD-1 Monoclonal Antibody for the Treatment of SCLC

A unique mode of recognition

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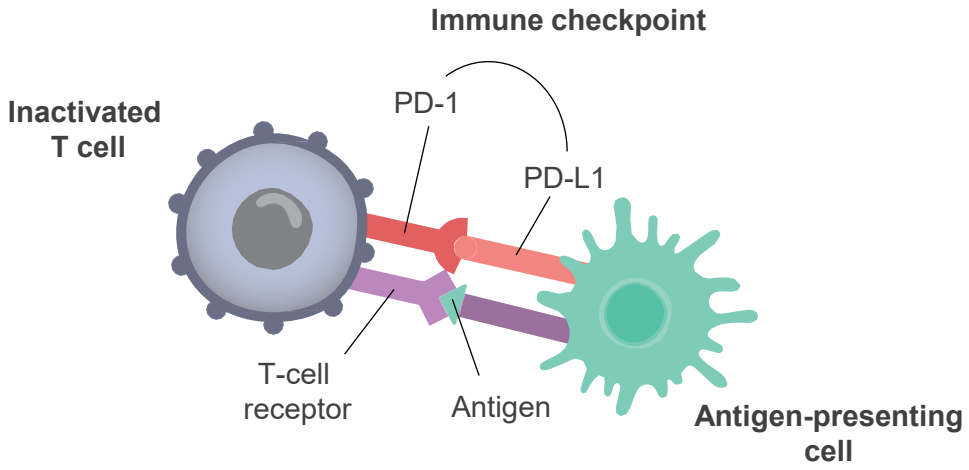
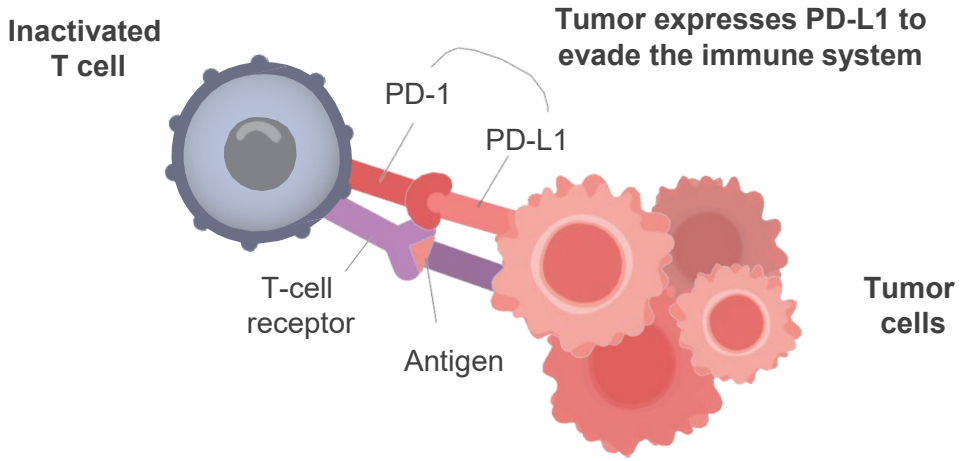
The PD-1/PD-L1 Pathway Is an Important Regulator of the Immune System



- PD-1 is a co-inhibitory receptor expressed on the surface of activated T cells and other immune cells. Its ligands, PD-L1 and PD-L2, are mainly expressed on antigen-presenting cells and tumor cells
- The binding of PD-1 to its ligands regulates T-cell effector functions during various physiological responses—such as acute and chronic infection—and the maintenance of immune tolerance



Cancer cells use the PD-1/PD-L1 pathway to escape T-cell–mediated destruction.

- PD-L1 is highly expressed in a variety of cancers, including lung cancer
- Increased expression of PD-L1 in tumor tissues and on antigen-presenting cells in the tumor microenvironment results in T-cell immunosuppression, exhaustion of tumor-specific T cells, and cancer escape

Issafras H, et al. *PLoS One*. 2021;16(12):e0257972.

Serplulimab: An Anti-Programmed Cell Death 1 (PD-1) mAb With a Favorable Binding Profile

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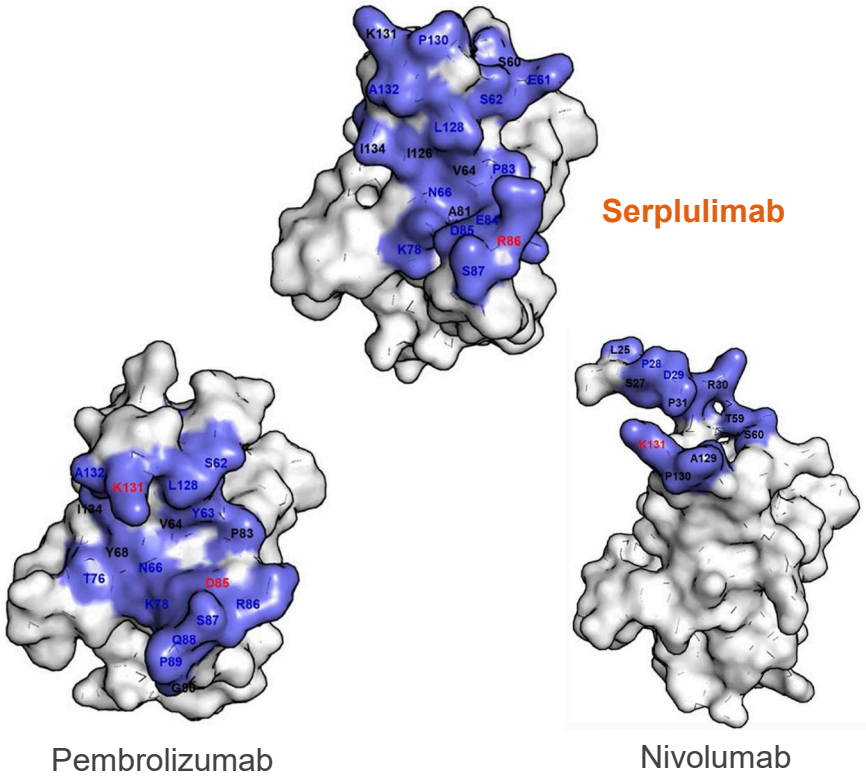
- Novel fully humanized anti–PD-1 IgG4 mAb
- Activates T-cell proliferation and cytokine secretion in T-cells in in vivo studies
- Similar or better PD-L1 and PD-L2 blockade than a nivolumab analogue based on flow cytometry
- Similar antitumor activity compared with pembrolizumab based on in vivo mouse models
- Unique mode of recognition of the PD-1 receptor when comparing complex structure models with currently available anti–PD-1 mAbs

Comparison of Binding Epitope Regions (Blue) of Serplulimab With Pembrolizumab and Nivolumab



MOA is hypothesized and is not meant to imply clinical efficacy.

Serplulimab is not approved for use in the United States (US). Clinical investigation of serplulimab in the US is underway.

IgG4=human immunoglobulin G4; mAb=monocolonal antibody; PD-1=programmed death-1; PD-L1=programmed death ligand-1; PD-L2=programmed death ligand-2.

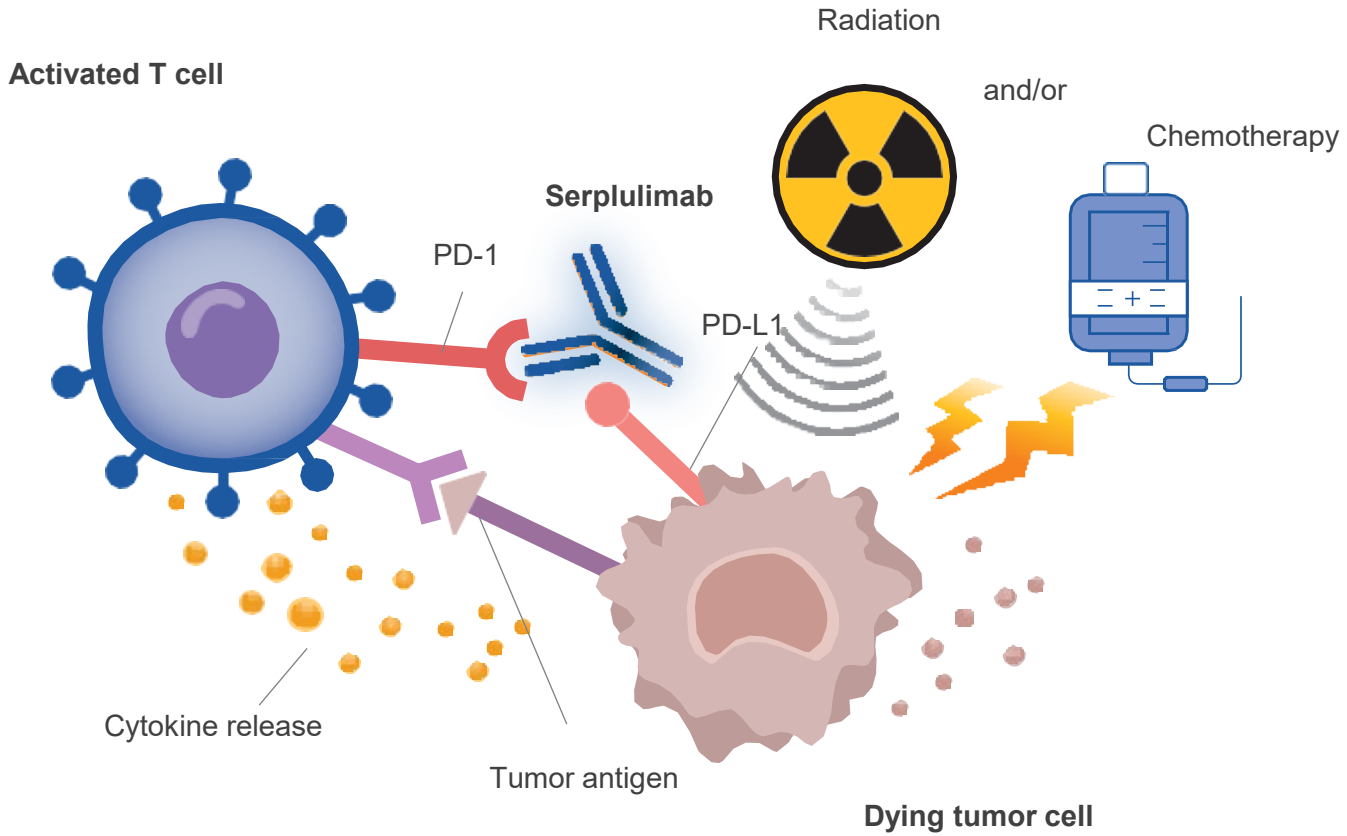
Issafras H, et al. *PLoS One*. 2021;16(12):e0257972.

Serplulimab Can Restore T-cell Immunity by Blocking the PD-1/PD-L1 Pathway[1]

- Inhibition of the PD-1/PD-L1 pathway can enable tumor-reactive T cells to recognize tumor antigens and enhance the T-cell anti-tumor response[1]

Serplulimab works synergistically with chemotherapy and/or radiation to enhance tumor-killing effects[2,3]

- The cytotoxic effects of chemotherapy and/or radiation on tumor cells increase the release and presentation of tumor antigens to T cells[2]
- Inhibition of the PD-1/PD-L1 pathway and subsequent restoration of T-cell immunity with serplulimab may produce a stronger and more durable response against these tumor antigens[1]



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1. Issafras H, et al. *PLoS One*. 2021;16(12):e0257972. 2. Fabian KP, Wolfson B, Hodge JW. *Front Oncol*. 2021;11:728018. 3. Cheng Y, et al; ASTRUM-005 Study Group. *JAMA*. 2022;328(12):1223-1232.

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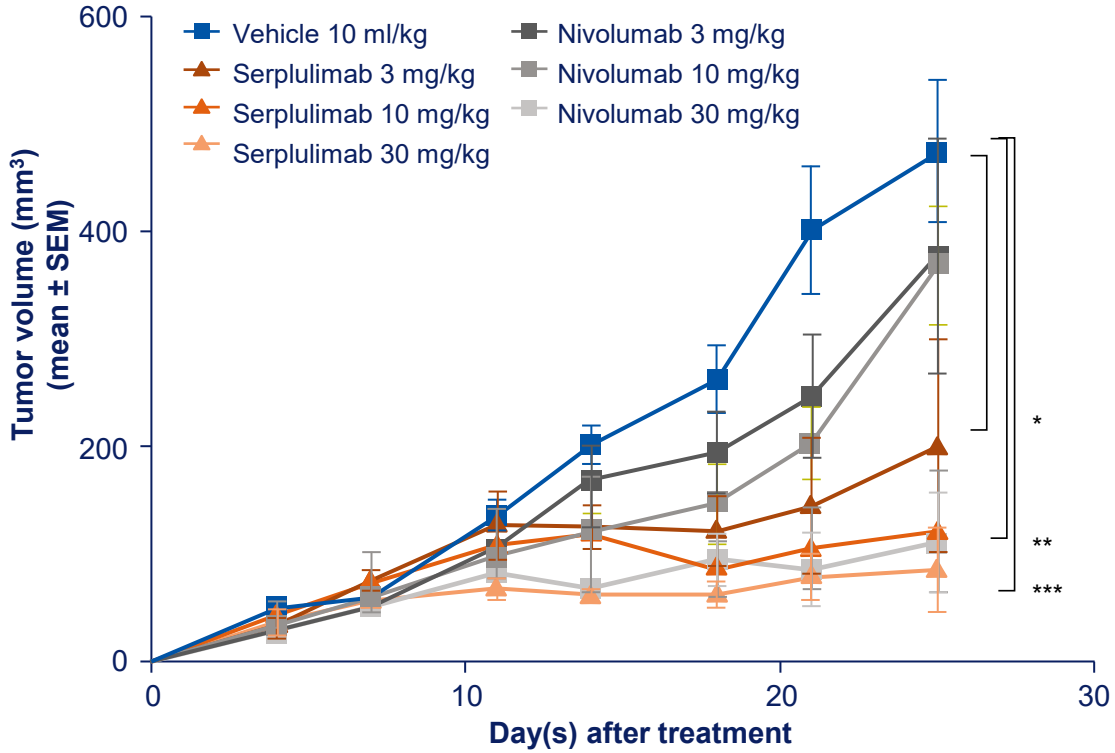
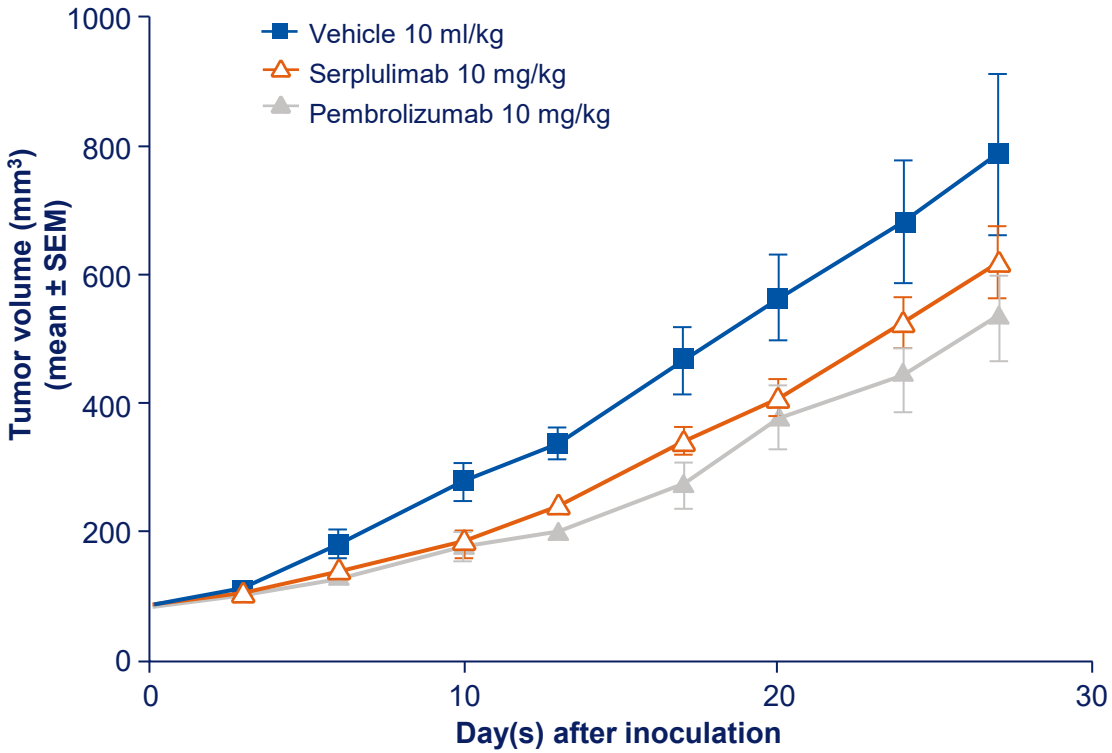
Antitumor Activity With Serplulimab Showed a Pronounced Effect on Tumor Growth In Vivo

When compared with currently available anti–PD-1 antibodies in in vivo mouse models, serplulimab showed similar or better PD-L1 blockade and antitumor activity





*P<0.05. **P<0.001. ***P<0.0001.

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mAb=monocolonal antibody; PD-1=programmed death-1; PD-L1=programmed death ligand-1; SEM=standard error of the mean.

Issafras H, et al. *PLoS One*. 2021;16(12):e0257972.

Global and US Development Pathway for Serplulimab

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Global Development Pathway for Serplulimab, an Anti-PD-1 Monoclonal Antibody for the Treatment of ES-SCLC

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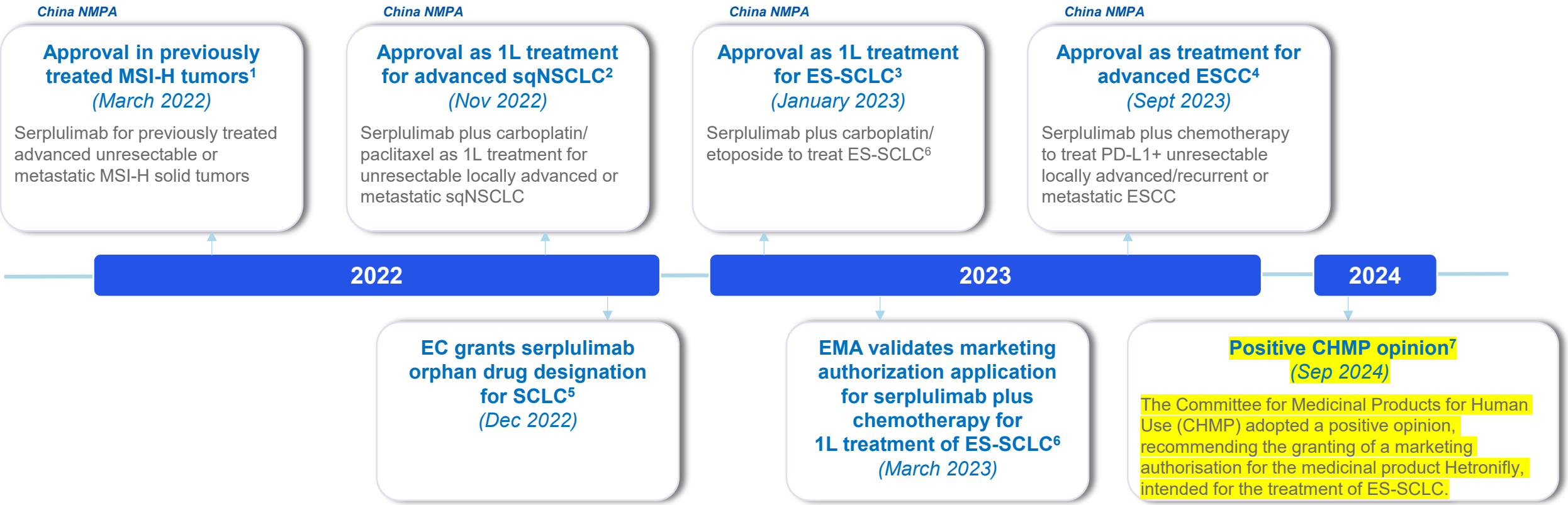

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1L=first-line; EC=European Commission; EMA=European Medical Agency; ESCC=esophageal squamous cell carcinoma; ES-SCLC=extensive-stage small cell lung cancer; MSI-H=microsatellite instability–high; NMPA=National Medical Products Administration; PD-1=programmed death-1; PD-L1=programmed death ligand-1; SCLC=small cell lung cancer; sqNSCLC=squamous non-small cell lung cancer.

1. Press release. Shanghai Henlius Biotech, Inc. March 25, 2022. https://www.henlius.com/en/NewsDetails-3512-26.html 2. Press release. Shanghai Henlius Biotech, Inc. November 1, 2022. https://www.henlius.com/en/NewsDetails-3837-26.html 3. Press release. Shanghai Henlius Biotech, Inc. January 17, 2023. https://www.henlius.com/en/NewsDetails-3949-26.html 4. Press release. Shanghai Henlius Biotech, Inc. September 22, 2023. https://www.henlius.com/en/NewsDetails-4283-26.html 5. Press release. Shanghai Fosun Pharmaceutical Co., Ltd. December 15, 2022. https://www.fosunpharma.com/en/content/details38_12122.html 6. Press release. Shanghai Helius Biotech, Inc. March 23, 2023. https://www.henlius.com/en/NewsDetails-4074-26.html
7. Press release. Shanghai Henlius Biotech, Inc. September 21, 2024. https://www.henlius.com/en/NewsDetails-4712-26.html

Development Pathway for Serplulimab in the US

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Serplulimab is not approved for use in the United States (US). Clinical investigation of serplulimab in the US is underway.

1L=first-line; ES-SCLC=extensive-stage small cell lung cancer; FDA=US Food and Drug Administration; LS-SCLC=limited-stage small cell lung cancer; NDA=new drug application; SCLC=small cell lung cancer.

1. Press release. Shanghai Henlius Biotech, Inc. April 7, 2022. https://www.henlius.com/en/NewsDetails-3525-26.html 2. Press release. Shanghai Henlius Biotech, Inc. September 28, 2022. https://www.henlius.com/en/NewsDetails-3768-26.html 3. Press release. Shanghai Henlius Biotech, Inc. November 29, 2022. https://www.henlius.com/en/NewsDetails-3880-26.html 4. Press release. Shanghai Henlius Biotech, Inc. January 5, 2023. https://www.henlius.com/en/NewsDetails-3935-26.html 5. ClinicalTrials.gov. NCT05353257. https://classic.clinicaltrials.gov/ct2/show/NCT05353257 6. ClinicalTrials.gov. NCT05468489. https://classic.clinicaltrials.gov/ct2/show/NCT05468489