



Systemic Therapy for SCLC

ASCO-OH (CCO) Guideline

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Overview

1. Background & Methodology

- Introduction
- Guideline Development Methodology
- Clinical Questions
- Target Population and Audience

2. Summary of Recommendations

3. Discussion

- Patient and Clinician Communication
- Health Disparities
- Additional Resources
- Expert Panel Members



1

Background & Methodology

Introduction

- SCLC is an aggressive, poorly differentiated, neuroendocrine carcinoma with more than 150,000 people diagnosed worldwide each year.^{1,2}
- SCLC is usually staged using the Veterans Administration Lung Study Group staging system which defines limited-stage (LS-SCLC) as disease confined to one hemithorax within a tolerable radiation field, and extensive-stage (ES-SCLC) as disease extending beyond LS-SCLC, including malignant pleural effusion, contralateral lung involvement, and hematogenous metastases.³
- Over two-thirds of patients present with extensive-stage disease at diagnosis.
- LS-SCLC is potentially curable when treated with concurrent chemoradiotherapy, with 5-year OS rates reported as up to 34%.⁴
- ES-SCLC remains an incurable disease with a 5-year OS rate of < 5%.^{2,5}
- Until recently, the major improvements in outcomes achieved for patients with SCLC were due to advances in radiotherapy, particularly in those with limited-stage disease.^{6,7}

Introduction

- Since the last ASCO update in SCLC management in 2015,⁸ there have been significant advances in the systemic treatment of ES-SCLC with the incorporation of immune checkpoint inhibitors into first-line therapy,^{9,10} and additional options for subsequent treatment of recurrent disease.^{11,12}
- Importantly, any discussion of the management of patients with small cell lung cancer would be incomplete without a strong recommendation for smoking cessation, not only to decrease the risk of developing lung cancer, but also to improve the outcomes of people already diagnosed with lung cancer.
- Numerous studies have reported that smoking cessation results in superior outcomes in terms of cancer recurrence, tolerance of and response to treatment, and overall survival for patients with both early-stage and advanced lung cancer.¹³⁻¹⁷
- The purpose of this ASCO and OH updated guideline is to summarize recommendations for systemic therapy in the management of patients with SCLC in light of recent advances.
- In addition, ASCO endorses the ASTRO guidelines on radiotherapy for patients with SCLC.¹⁸



Guideline Development Methodology

- The ASCO Evidence Based Medicine Committee (EBMC) guideline process includes:
 - a systematic literature review by ASCO guidelines staff
 - an expert panel provides critical review and evidence interpretation to inform guideline recommendations
 - final guideline approval by ASCO EBMC
- The full ASCO Guideline methodology manual can be found at: www.asco.org/guideline-methodology

Clinical Questions

This clinical practice guideline addresses eight clinical questions:

1. What is the optimal treatment regimen for adjuvant systemic therapy in patients with resected SCLC?
2. What is the optimal systemic therapy for use with concurrent radiotherapy in patients with LS-SCLC?
3. What is the optimal first-line systemic therapy for patients with ES-SCLC?
4. What systemic therapy options are available for treating relapsed SCLC?
5. What is the best management approach for treatment naïve patients who are older or who have poor PS?
6. What is optimal systemic therapy for patients with NSCLC harboring an *EGFR* mutation that has transformed to SCLC?
7. What is the role of biomarkers, including molecular profiling in guiding therapy for patients with SCLC?
8. Which myeloid supportive agents may be considered for use in patients with SCLC?



Target Population and Audience

Target Population

- Patients with SCLC

Target Audience

- Medical oncologists, radiation oncologists, thoracic surgeons, pulmonologists, pathologists, radiologists, primary care physicians, nurse practitioners, physician assistants, pharmacists, nurses, and other providers.



2

Summary of Recommendations

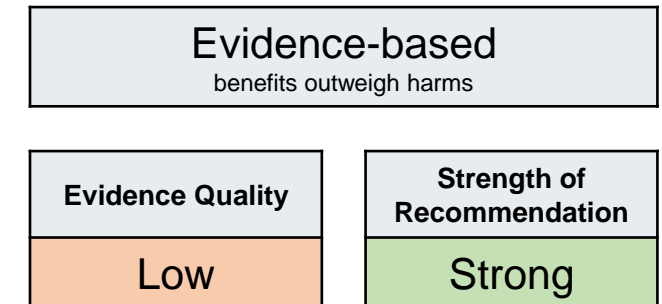
Summary of Recommendations

Clinical Question 1

- What is the optimal treatment regimen for adjuvant systemic therapy in patients with resected SCLC?

Recommendation 1.1

- Adjuvant chemotherapy should be offered to patients with resected limited-stage SCLC who have adequate performance status.



Summary of Recommendations

Recommendation 1.2

- Adjuvant chemotherapy should consist of 4 cycles of cisplatin or carboplatin plus etoposide.

Recommendation 1.3

- Adjuvant chemotherapy should be initiated within 8 weeks from resection.

Informal consensus
benefits outweigh harms

Evidence Quality
N/A

Strength of Recommendation
Weak

Informal consensus
benefits outweigh harms

Evidence Quality
N/A

Strength of Recommendation
Weak



Summary of Recommendations

Clinical Question 2

- What is the optimal treatment regimen for adjuvant systemic therapy in patients with resected SCLC?

Recommendation 2.1

- Cisplatin and etoposide should be administered with concurrent radiotherapy in patients with LS-SCLC.

Evidence-based benefits outweigh harms	
Evidence Quality	Strength of Recommendation
High	Strong

Summary of Recommendations

Recommendation 2.2

- Carboplatin and etoposide may be offered as systemic therapy concurrent with radiation for patients with LS-SCLC and contraindications to the use of cisplatin.

Recommendation 2.3

- Chemotherapy should be commenced as soon as possible in patients with LS-SCLC and not deferred until radiation therapy can be started.

Evidence-based
benefits outweigh harms

Evidence Quality
Low

Strength of Recommendation
Strong

Informal consensus
benefits outweigh harms

Evidence Quality
Low

Strength of Recommendation
Strong

Summary of Recommendations

Clinical Question 3

- What is the optimal first-line systemic therapy for patients with ES-SCLC?

Recommendation 3.1

- First-line systemic therapy with carboplatin or cisplatin plus etoposide plus immunotherapy (atezolizumab or durvalumab) followed by maintenance immunotherapy should be offered to patients with ES-SCLC if there are no contraindications to immunotherapy.

Evidence-based benefits outweigh harms	
Evidence Quality	Strength of Recommendation
High	Strong

Summary of Recommendations

Clinical Question 4

- What systemic therapy options are available for treating relapsed SCLC?

Recommendation 4.1

- In patients with relapsed SCLC with a chemotherapy-free interval of less than 90 days, single-agent chemotherapy may be offered. Preferred agents are topotecan or lurbinectedin.

Qualifying statement: Single-agent chemotherapy is preferred over multi-agent chemotherapy due to concerns regarding the balance of risks versus benefits.

Evidence-based benefits outweigh harms	
Evidence Quality	Strength of Recommendation
Moderate	Strong

Summary of Recommendations

Recommendation 4.2

- In patients with relapsed SCLC with a chemotherapy-free interval of at least 90 days, re-challenge with a platinum-based regimen or single-agent chemotherapy (preferred agents are topotecan or lurbinectedin) may be offered.

Recommendation 4.3

- In patients with relapsed SCLC who had progression while on maintenance immunotherapy, there is no evidence to support continuation of immunotherapy.

Evidence-based
benefits outweigh harms

Evidence Quality
Moderate

Strength of Recommendation
Strong

Informal consensus
benefit to harm ratio not assessable

Evidence Quality
N/A

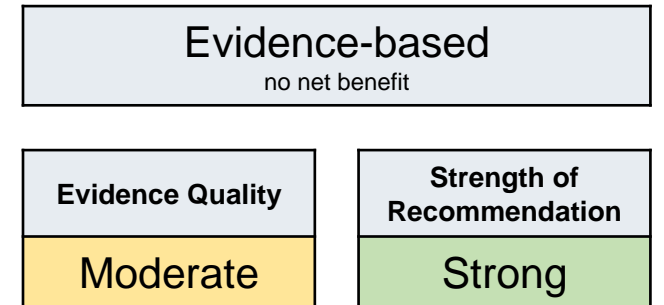
Strength of Recommendation
Strong



Summary of Recommendations

Recommendation 4.4

- In an immunotherapy-naïve patient, second-line immunotherapy alone is not recommended outside of the clinical trial setting. Participation in clinical trials to better identify predictive biomarkers is encouraged.



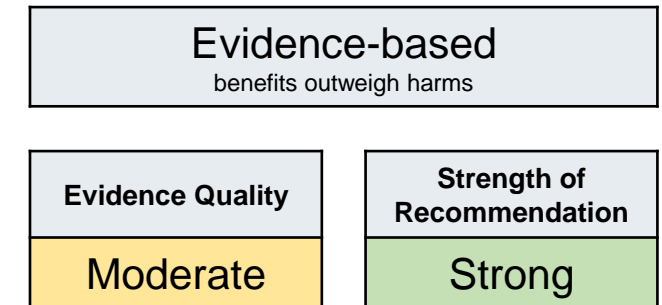
Summary of Recommendations

Clinical Question 5

- What is the best management approach for treatment naïve patients who are older or who have poor PS?

Recommendation 5.1

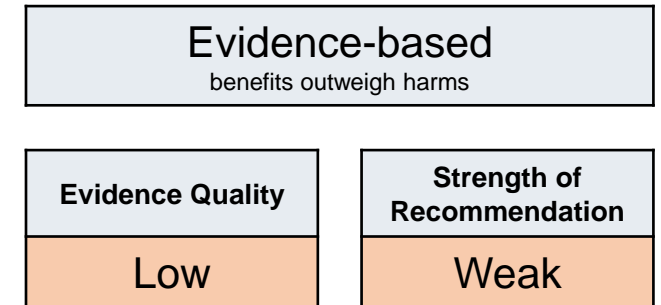
- Older patients with LS-SCLC and ECOG PS 0-1 may be offered standard treatment with concurrent chemoradiotherapy with curative intent.



Summary of Recommendations

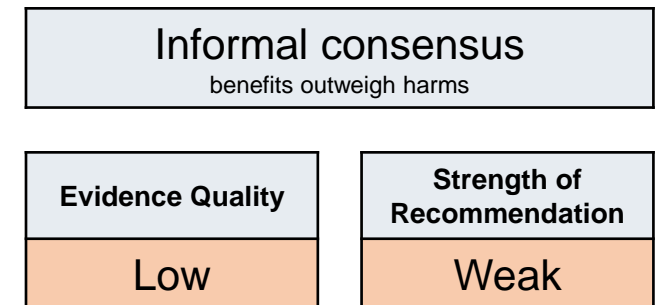
Recommendation 5.2

- Patients with LS-SCLC and ECOG PS 2 due to SCLC may be offered standard treatment with concurrent chemoradiotherapy with curative intent.



Recommendation 5.3

- Patients with LS-SCLC and ECOG PS 3-4 due to SCLC may be offered initial chemotherapy followed by sequential radiotherapy if there is improvement in PS.



Summary of Recommendations

Recommendation 5.4

- Older patients with ES-SCLC and ECOG PS 0-1 may be offered standard treatment with carboplatin and etoposide plus immunotherapy (atezolizumab or durvalumab) followed by maintenance immunotherapy.

Recommendation 5.5

- Patients with ES-SCLC and ECOG PS 2 may be offered carboplatin and etoposide plus immunotherapy.

Evidence-based
benefits outweigh harms

Evidence Quality
Moderate

Strength of Recommendation
Strong

Informal consensus
benefits outweigh harms

Evidence Quality
Low

Strength of Recommendation
Weak



Summary of Recommendations

Recommendation 5.6

- Patients with ES-SCLC and ECOG PS 3-4 due to SCLC may be offered chemotherapy.

Informal consensus benefits outweigh harms	
Evidence Quality	Strength of Recommendation
Low	Weak



Summary of Recommendations

Clinical Question 6

- What is optimal systemic therapy for patients with NSCLC harboring an EGFR mutation that has transformed to SCLC?

Recommendation 6.1

- Patients with NSCLC harboring an *EGFR* mutation that has transformed to SCLC should be managed with carboplatin or cisplatin plus etoposide.

Qualifying statement: There is insufficient evidence to support the use of immunotherapy in this setting. Clinical trial enrollment should be offered whenever possible.

Informal consensus benefits outweigh harms	
Evidence Quality	Strength of Recommendation
Low	Weak

Summary of Recommendations

Recommendation 6.2

- EGFR inhibitor may be continued with chemotherapy in patients with NSCLC harboring an *EGFR* mutation that has transformed to SCLC.

Informal consensus benefits outweigh harms	
Evidence Quality	Strength of Recommendation
Low	Weak

Summary of Recommendations

Clinical Question 7

- What is the role of biomarkers, including molecular profiling in guiding therapy for patients with SCLC?

Recommendation 7.1

- There is no evidence to support the use of molecular profiling and biomarker analysis to guide standard treatment in patients with *de novo* SCLC.

Evidence-based benefit to harm ratio not assessable	
Evidence Quality	Strength of Recommendation
Low	Weak

Summary of Recommendations

Clinical Question 8

- Which myeloid supportive agents may be considered for use in patients with SCLC?

Recommendation 8.1

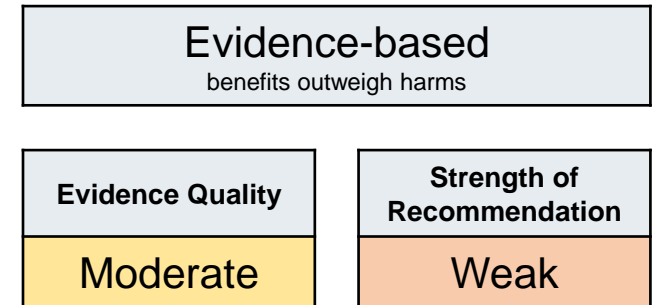
- Trilaciclib or G-CSF may be offered as a myeloid supportive agent for patients with untreated or previously treated ES-SCLC who are undergoing treatment with chemotherapy or chemoimmunotherapy.

Evidence-based benefits outweigh harms	
Evidence Quality	Strength of Recommendation
Moderate	Weak

Summary of Recommendations

Recommendation 8.2

- G-CSF may be offered in patients with LS-SCLC who are undergoing chemoradiotherapy.



3

Discussion

Patient and Clinician Communication

- The cancer symptoms and side effects from treatment can significantly impact a person's quality of life, and patient-clinician communication is key to the patient's experience.
- Expert Panel suggestions include the below:
 - Get to know your patients
 - Treating SCLC is complex, and evidence may be incomplete or conflicting. Data should be applied in the content of patients and their caregivers
 - Overall survival is not the only important endpoint for patients and their families
 - Have difficult conversations about goals of care ahead of treatment – what is important and meaningful in their life, patient's fears, and tradeoffs they're willing to make
 - People with SCLC are the experts in their own lived experience and symptoms, side effects, and severity
 - Words matter, and smoking-related stigma is an important issue
 - The [IASLC Language guide](#) has best practices for talking or writing about lung cancer
 - Provide hope with reality for patients



Health Disparities

- Although ASCO clinical practice guidelines represent expert recommendations on the best practices in disease management to provide the highest level of cancer care, it is important to note that many patients have limited access to medical care and/or receive fragmented care.
- Studies have found that Black race, lack of insurance or having non-private insurance, lower education, and older age were factors associated with lower odds of receiving systemic treatment for ES-SCLC.
- In addition to racial disparities in the delivery of chemotherapy for patients with ES-SCLC, other studies have reported that Black patients are less likely to receive prophylactic cranial irradiation and effective doses of consolidative thoracic radiotherapy.
- Socioeconomic factors such as type of health insurance may also affect receipt of chemotherapy and survival. Higher education was associated with an increased likelihood of receiving chemotherapy.
- Older patients have a higher incidence of comorbidities and tend to have worse outcomes in general. The poorer OS in older patients with SCLC could be related to decreased tolerance or dose limitations of chemotherapy or RT, in addition to noncancer-related causes of death.¹⁹



Health Disparities

- Studies also show that older patients and non-Hispanic black patients are less likely to receive guidelines concordant treatment across most clinical subgroups of lung cancer.²⁰
- Awareness of these disparities in access to care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the highest level of cancer care to these vulnerable populations.
- Achieving health equity requires efforts that inform, educate, and empower all individuals.
- Stakeholders should work toward achieving health equity by ensuring equitable access to both high-quality cancer and research, and addressing the structural barriers that preserve health inequities.²¹



Additional Resources

- More information, including a supplement and clinical tools and resources, is available at www.asco.org/thoracic-cancer-guidelines
- Patient information is available at www.cancer.net

Guideline Panel Members

Name	Affiliation/Institution	Role/Area of Expertise
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Abbreviations

- ASCO, American Society of Clinical Oncology
- ASTRO, American Society for Radiation Oncology
- CCO, Cancer Care Ontario
- EBMC, Evidence Based Medicine Committee
- ECOG, Eastern Cooperative Oncology Group
- EGFR, epidermal growth factor receptor
- ES-SCLC, extensive-stage small-cell lung cancer
- G-CSF, granulocyte colony stimulating factor
- IASLC, International Association for the Study of Lung Cancer
- LS-SCLC, limited-stage small-cell lung cancer
- N/A, not applicable
- NSCLC, non-small-cell lung cancer
- OH, Ontario Health
- OS, overall survival
- PS, performance status
- RT, radiation therapy
- SCLC, small-cell lung cancer

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