



EPICS

# EPICS in Small Cell Lung Cancer (SCLC)

June 29, 2022

Content	Slide
Meeting Snapshot	3 
Faculty Panel	4 
Meeting Agenda	5 
Key Insights and Strategic Recommendations	6 
Standards of Care Across the SCLC Treatment Continuum	11 
Biomarkers in SCLC	17 
Recent Progress and Emerging Therapies in Second Line and Beyond	24 

EPICS

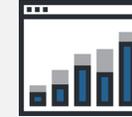
## VIRTUAL CLOSED-DOOR ROUNDTABLE



**DATE:**  
June 29, 2022



**DISEASE-STATE AND  
DATA PRESENTATIONS**  
by key experts



**INSIGHTS REPORT**  
including postmeeting  
analyses and actionable  
recommendations

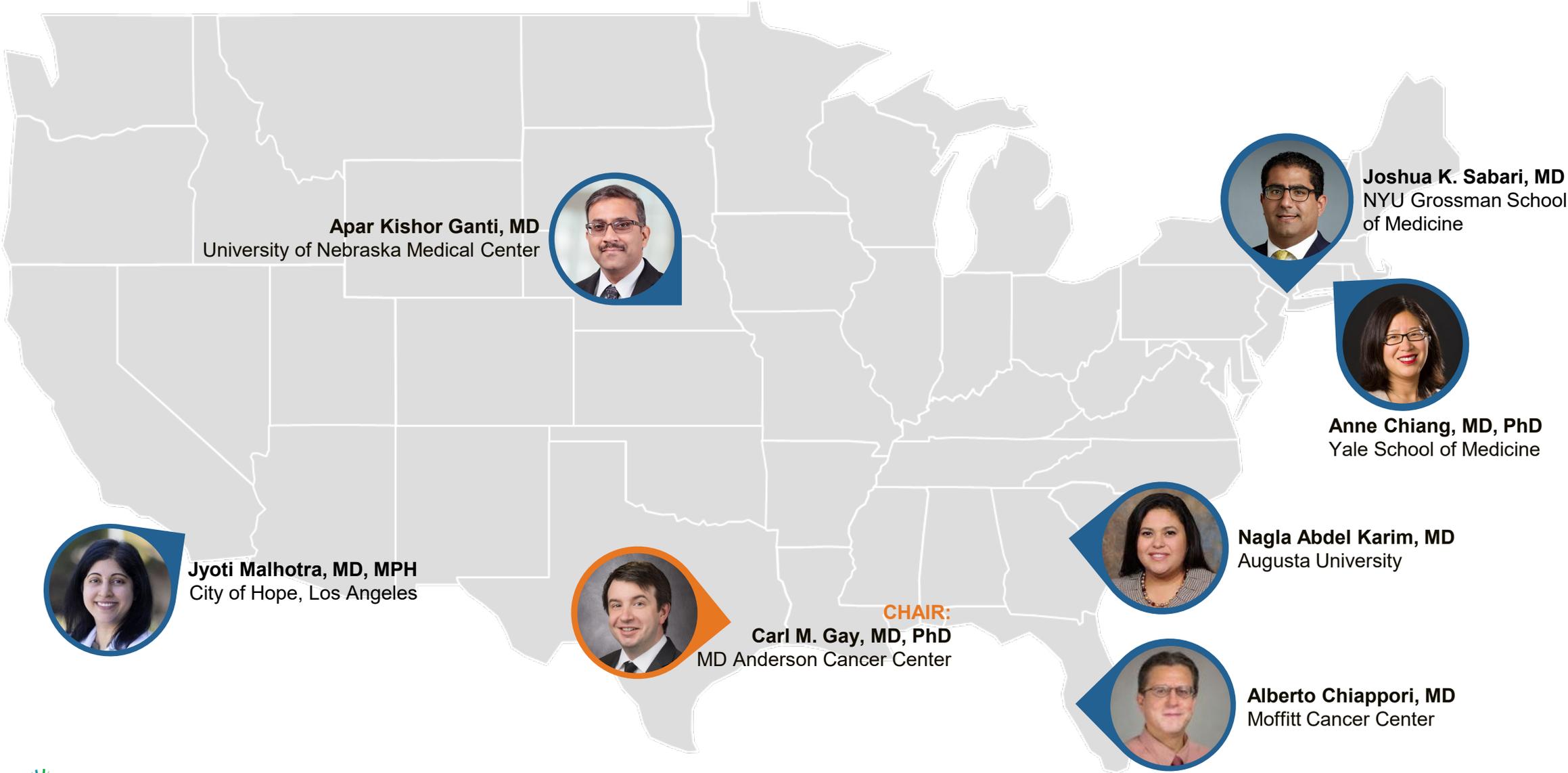


**PANEL:** 7 key experts  
in SCLC in 7 states in  
the US



**SCLC-SPECIFIC  
DISCUSSIONS** on the latest  
research updates,  
therapeutic advances, and  
their application in clinical  
decision-making

# Panel Consisting of 7 US Small Cell Lung Cancer Experts



# Meeting Agenda

EPICS

Time	Topic	Speaker/Moderator
6.00 PM – 6.05 PM	Welcome and Introductions	Carl M. Gay, MD, PhD
6.05 PM – 6.15 PM	Standards of Care Across the SCLC Treatment Continuum	Nagla Abdel Karim, MD
6.15 PM – 6.30 PM	Key Questions and Topics for Discussion	All Faculty
6.30 PM – 6.35 PM	Key Takeaways	Nagla Abdel Karim, MD
6.35 PM – 6.40 PM	Biomarkers in SCLC	Joshua K. Sabari, MD
6.40 PM – 7.00 PM	Key Questions and Topics for Discussion	All Faculty
7.00 PM – 7.05 PM	Key Takeaways	Joshua K. Sabari, MD
7.05 PM – 7.15 PM	Recent Progress and Emerging Therapies in Second Line and Beyond	Apar Kishor Ganti, MD
7.15 PM – 7.50 PM	Key Questions and Topics for Discussion	All Faculty
7.50 PM – 7.55 PM	Key Takeaways	Apar Kishor Ganti, MD
7.55 PM – 8.00 PM	Summary and Meeting Close	Carl M. Gay, MD, PhD



EPICS

# Standards of Care Across the SCLC Treatment Continuum



**Nagla Abdel Karim, MD**  
Augusta University  
Augusta, GA

# Phase III SKYSCRAPER-02 Primary Results: Tiragolumab in Combination With Atezolizumab + Etoposide in Patients With Untreated ES-SCLC – Efficacy

Charles Rodin, et al. 2022. ASCO LBA8507

## STUDY POPULATION (N = 490)

> Phase III trial in ES-SCLC

## PRIMARY ENDPOINTS

PFS: Primary Analysis Set

Figure 1: Primary Analysis Set (PFS)



Figure 2: Overall Survival (OS) for Tiragolumab + Atezolizumab + Etoposide (T+A+E) and Atezolizumab + Etoposide (A+E)



# Phase III SKYSCRAPER-02 Primary Results: Tiragolumab in Combination With Atezolizumab + Etoposide in Patients With Untreated ES-SCLC – Safety

Charles Rodin, et al. 2022. ASCO LBA8507

## OUTCOME

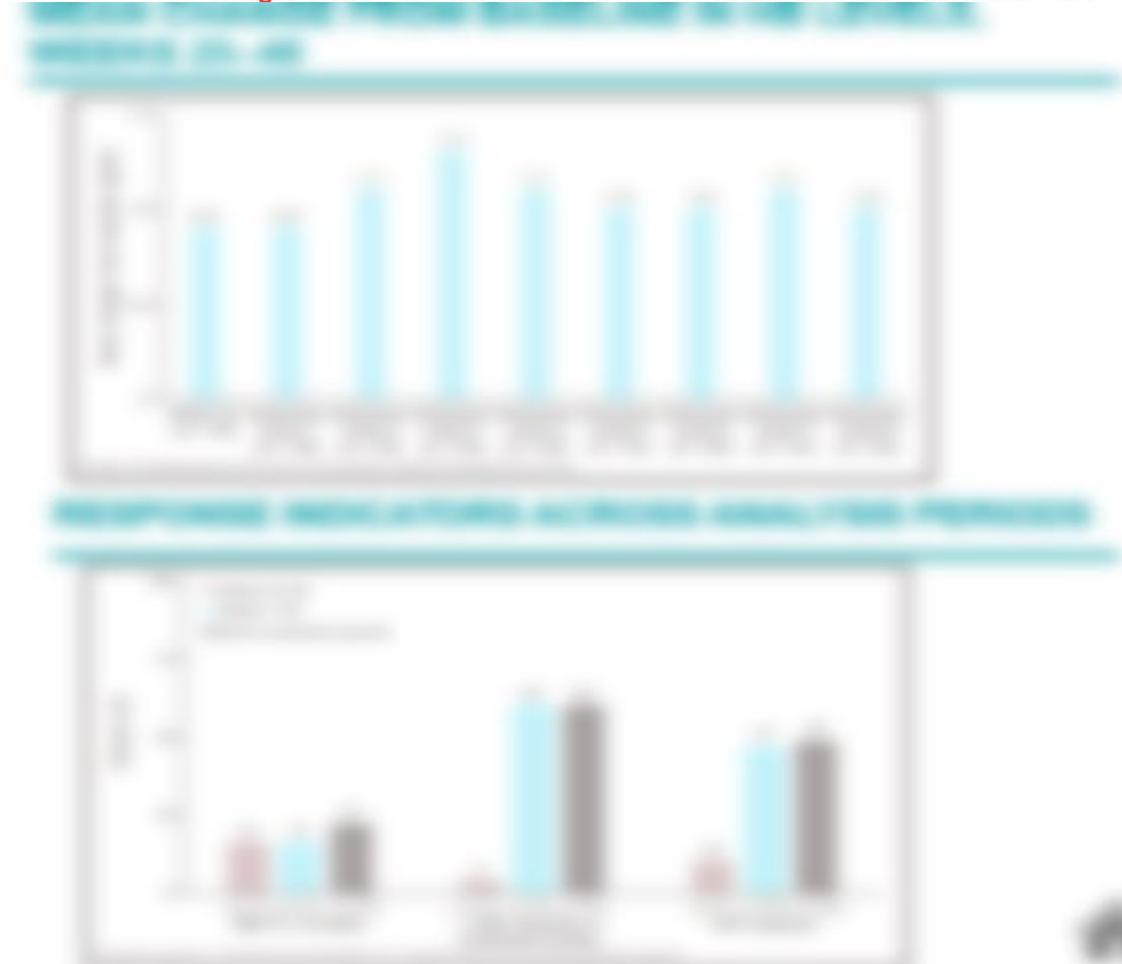
> Grade 3/4 TRAEs occurred in 52.3% of the

## SAFETY OVERVIEW

n (%)

Tiragolumab + atezolizumab + CE

Placebo + atezolizumab + CE



# SLFN11 Predicted Improved PFS and OS in Veliparib (PARPi) + Temozolomide (TMZ) Combination Cohort

M. Catherine Pietanza, et al. J Clin Oncol. 2018;36:2386-2394

## METHODS (N = 490)

> A total of 104 patients with recurrent SCLC were randomly assigned 1:1 to oral

## OVERALL SURVIVAL

**STUDY POPULATION**

1. 490 patients with recurrent SCLC were randomly assigned 1:1 to oral veliparib (PARPi) + temozolomide (TMZ) or oral TMZ alone. The PARPi + TMZ cohort had a median age of 63 years, 85% were male, and 75% had ECOG performance grade 0-1. The TMZ cohort had a median age of 63 years, 85% were male, and 75% had ECOG performance grade 0-1. The PARPi + TMZ cohort had a median age of 63 years, 85% were male, and 75% had ECOG performance grade 0-1. The TMZ cohort had a median age of 63 years, 85% were male, and 75% had ECOG performance grade 0-1.

**RESULTS**

1. The PARPi + TMZ cohort had a median OS of 11.1 months, compared with 9.7 months for the TMZ cohort. The PARPi + TMZ cohort had a median PFS of 4.2 months, compared with 3.8 months for the TMZ cohort.

**CONCLUSIONS**

1. The PARPi + TMZ combination significantly improved OS and PFS compared with TMZ alone in patients with recurrent SCLC.



**EPICS**

# **Standards of Care Across the SCLC Treatment Continuum – Discussion of SKYSCRAPER-02**

Key Takeaways

# Discussion Highlights: Standards of Care Across the SCLC Treatment Continuum

## RECENT UPDATES AND ADVANCES IN SCLC TREATMENT

**Key Message:**

The focus of contemporary SCLC care has shifted towards the front-line setting for optimal outcomes. For untreated SCLC, an optimal regimen is now 1, or 2, or 3, or 4 drugs versus traditional treatment selection.

- 1. There is a strong emphasis on front-line therapy to treat recurrent disease has shifted from chemotherapy-based optimal treatment (combination chemotherapy or combination and sequencing that will need to be further addressed in future clinical trials).
- 2. In recurrent disease practice, experts usually opt for an alternative (2nd or 3rd generation setting to treat recurrent disease).
- 3. In addition, several studies with recurrent disease and/or recurrent to a 2nd setting, suggest that alternative regimens including immunotherapy, and various novel sequencing strategies (2nd or 3rd generation) are being explored in various clinical trials.
- 4. There is a strong emphasis on front-line therapy to treat recurrent disease with immunotherapy and novel agents. The front-line setting is being explored in various clinical trials. The front-line setting is being explored in various clinical trials.
- 5. There is a strong emphasis on front-line therapy to treat recurrent disease with immunotherapy and novel agents. The front-line setting is being explored in various clinical trials.

**Key Message:**

Optimal combination of treatment should be individualized for each patient.

- 1. There is a strong emphasis on front-line therapy to treat recurrent disease with immunotherapy and novel agents. The front-line setting is being explored in various clinical trials.



**Dr. [Name]**

...the focus of contemporary SCLC care has shifted towards the front-line setting for optimal outcomes. For untreated SCLC, an optimal regimen is now 1, or 2, or 3, or 4 drugs versus traditional treatment selection.



**Dr. [Name]**

...the focus of contemporary SCLC care has shifted towards the front-line setting for optimal outcomes. For untreated SCLC, an optimal regimen is now 1, or 2, or 3, or 4 drugs versus traditional treatment selection.

EPICS

## Biomarkers in SCLC



**Joshua K. Sabari, MD**  
NYU Grossman School of Medicine  
New York, NY

# Current State of Biomarkers in SCLC and Immune Checkpoint Inhibitors

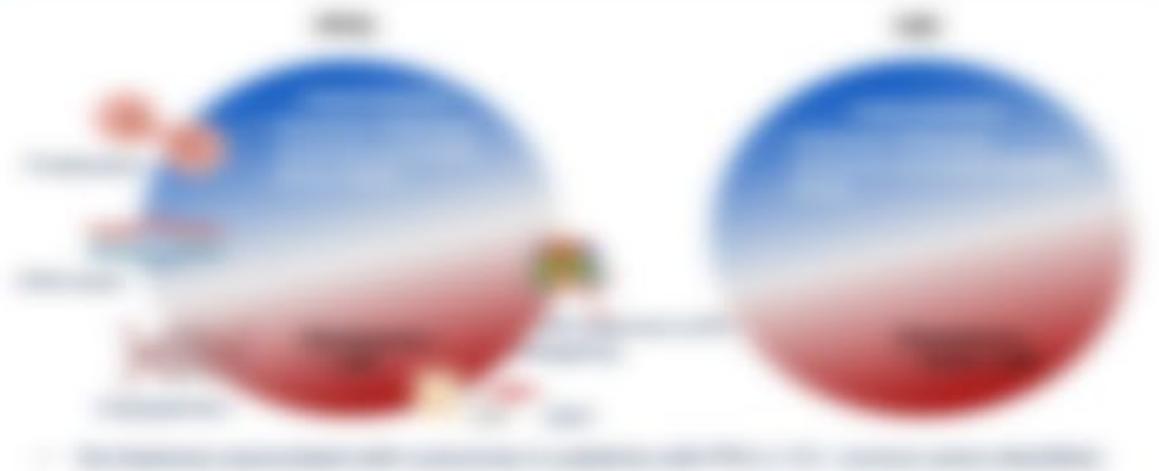
## A SLOW AND ONGOING SEARCH FOR BIOMARKERS

> Despite many years of research, no markers that could help improve

## SIGNALING PATHWAYS AND PHYSIOLOGIC DOMAINS IN SCLC



### THE TUMOR MICROENVIRONMENT WITH IMMUNE CELLULARITY



Blurred text area containing detailed information about signaling pathways and physiologic domains in SCLC.

# Subtypes of Small Cell Lung Cancer

## SCLC Molecular Subtypes Identified by Their Key Transcription Regulator

**Neuroendocrine Subtype**

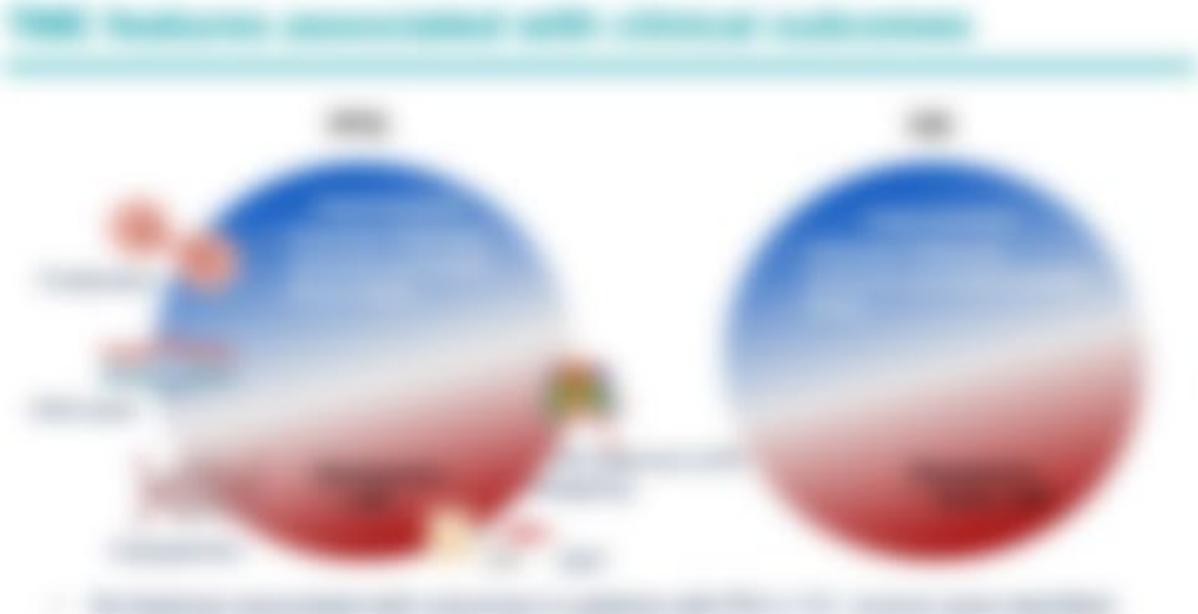
Characterized by high expression of neuroendocrine markers and transcription factors such as POU5F1, SOX2, and ASCL1. This subtype is the most common and is highly aggressive.

**Neuroendocrine-Like Subtype**

Characterized by a mixture of neuroendocrine and non-neuroendocrine markers. This subtype is less common and may have a different clinical course compared to the neuroendocrine subtype.

**Non-Neuroendocrine Subtype**

Characterized by low expression of neuroendocrine markers and high expression of non-neuroendocrine markers. This subtype is the least common and may have a different clinical course compared to the other subtypes.



## DLL3

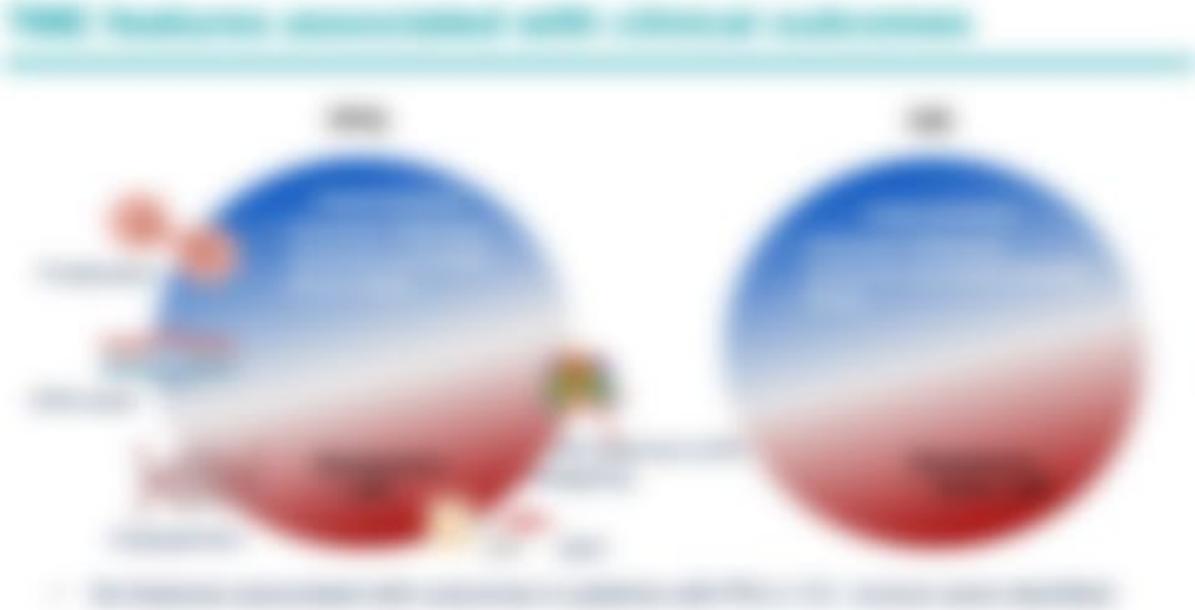
> Direct transcriptional target of ASCL1. Its highest expression is in the SCLC-A subtype (ASCL1 high)

**Background**

DLL3 is a member of the Notch signaling pathway. It is a transmembrane protein that binds to Notch receptors and plays a role in cell differentiation and proliferation. In the context of cancer, DLL3 is overexpressed in several tumor types, including small cell lung cancer (SCLC).

**Targeting DLL3**

Targeting DLL3 with antibodies or small molecules is a promising therapeutic strategy for SCLC. This approach aims to block the DLL3-Notch signaling pathway, which is essential for the growth and survival of SCLC cells.



**EPICS**

# **Biomarkers in SCLC**

Key Takeaways

# Discussion Highlights: Biomarkers in SCLC (1/2)

## Key Messages

The success of immunotherapy against lung cancer depends on the immune system's ability to recognize and kill cancer cells. Biomarkers can help identify patients who are most likely to benefit from immunotherapy.

- 1. Biomarkers can help identify patients who are most likely to benefit from immunotherapy.
- 2. Biomarkers can help identify patients who are most likely to benefit from immunotherapy.
- 3. Biomarkers can help identify patients who are most likely to benefit from immunotherapy.

Regular communication with your healthcare provider is essential to ensure you are receiving the most appropriate care for your condition.



**Dr. [Name]**  
[Speaker's name and affiliation]



**Dr. [Name]**  
[Speaker's name and affiliation]

## Key Messages

The success of immunotherapy against lung cancer depends on the immune system's ability to recognize and kill cancer cells. Biomarkers can help identify patients who are most likely to benefit from immunotherapy.

- 1. Biomarkers can help identify patients who are most likely to benefit from immunotherapy.
- 2. Biomarkers can help identify patients who are most likely to benefit from immunotherapy.
- 3. Biomarkers can help identify patients who are most likely to benefit from immunotherapy.

Regular communication with your healthcare provider is essential to ensure you are receiving the most appropriate care for your condition.

- 1. Regular communication with your healthcare provider is essential to ensure you are receiving the most appropriate care for your condition.



**Dr. [Name]**  
[Text]



**Dr. [Name]**  
[Text]

**EPICS**

# Recent Progress and Emerging Therapies in Second Line and Beyond



**Apar Kishor Ganti, MD**  
University of Nebraska Medical Center  
Omaha, NE

# Efficacy and Safety of Lurbinectedin as Second-Line Therapy in Chinese Patients With Small Cell Lung Cancer: Preliminary Results of a Phase 1 Study

Cheng Y, et al. 2022. ASCO 8580

EPICS

## STUDY POPULATION

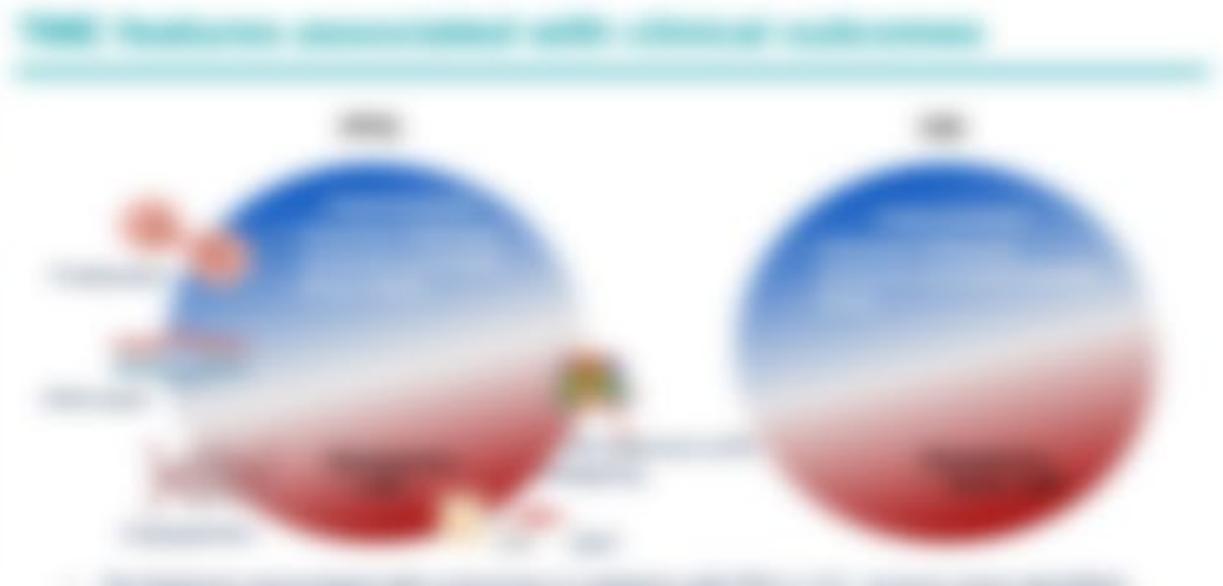
## STUDY DESIGN

**STUDY POPULATION**

Chinese patients with histologically confirmed SCLC, ECOG performance grade 0-1, and no prior systemic anticancer therapy for SCLC. Patients were stratified by ECOG performance grade (0 vs 1) and by prior platinum-based therapy (yes vs no).

**STUDY DESIGN**

A phase 1, open-label, multicenter study. The study was conducted in two cohorts: Cohort 1 (ECOG 0) and Cohort 2 (ECOG 1). The study was stratified by ECOG performance grade (0 vs 1) and by prior platinum-based therapy (yes vs no). The study was conducted in two cohorts: Cohort 1 (ECOG 0) and Cohort 2 (ECOG 1). The study was stratified by ECOG performance grade (0 vs 1) and by prior platinum-based therapy (yes vs no).



**STUDY DESIGN**

A phase 1, open-label, multicenter study. The study was conducted in two cohorts: Cohort 1 (ECOG 0) and Cohort 2 (ECOG 1). The study was stratified by ECOG performance grade (0 vs 1) and by prior platinum-based therapy (yes vs no). The study was conducted in two cohorts: Cohort 1 (ECOG 0) and Cohort 2 (ECOG 1). The study was stratified by ECOG performance grade (0 vs 1) and by prior platinum-based therapy (yes vs no).

# Efficacy and Safety of Lurbinectedin as Second-Line Therapy in Chinese Patients With Small Cell Lung Cancer: Preliminary Results of a Phase 1 Study

Cheng Y, et al. 2022. ASCO 8580

EPICS

## RESULTS – DOSE-EXPANSION ARM

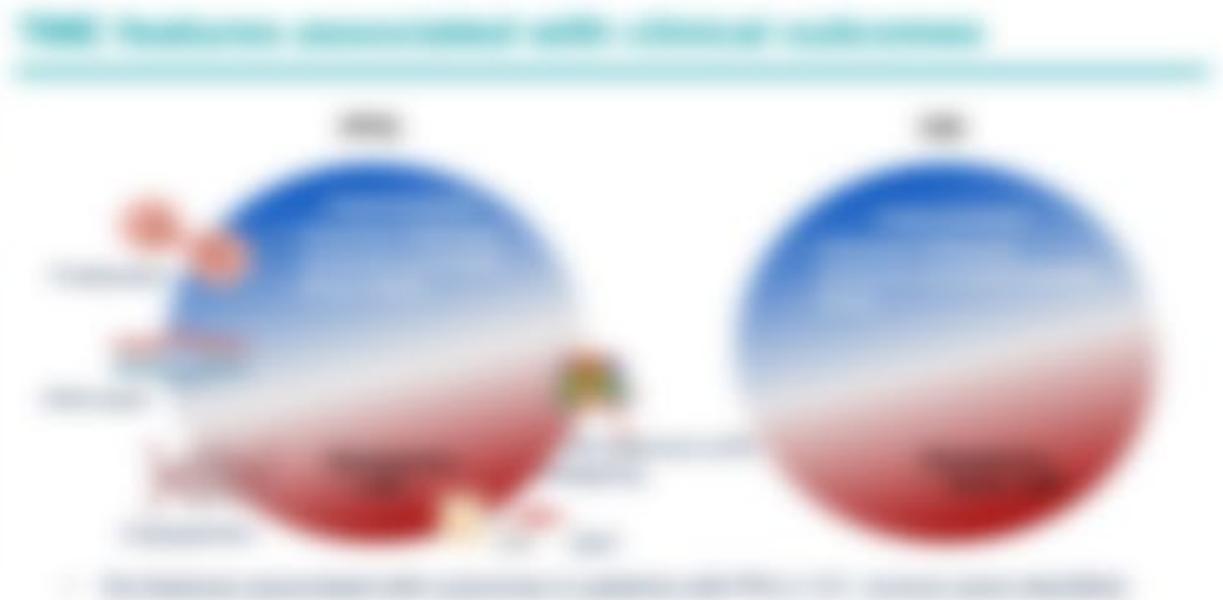
## RESULTS – EFFICACY AND CTFI LENGTH

**Background:** Lurbinectedin is a novel cytotoxic agent with a unique mechanism of action. It is a topoisomerase II inhibitor that binds to DNA, forming a cross-link and blocking the DNA replication fork. Lurbinectedin has been shown to be effective in the treatment of small cell lung cancer (SCLC) in a phase 1 study. The purpose of this study was to evaluate the efficacy and safety of lurbinectedin as second-line therapy in Chinese patients with SCLC.

**Methods:** This phase 1 study was a dose-expansion study. The study included 24 Chinese patients with SCLC who had received at least one prior systemic therapy. The patients were randomized to receive lurbinectedin at two different doses: 1.5 mg/m<sup>2</sup> and 2.0 mg/m<sup>2</sup>. The primary endpoint was the maximum tolerated dose (MTD). Secondary endpoints included objective response rate (ORR), duration of response (DOR), and overall survival (OS).

**Results:** The MTD was 2.0 mg/m<sup>2</sup>. The ORR was 50% (12/24) in the 2.0 mg/m<sup>2</sup> group. The DOR was 12.1 months (95% CI, 8.1–16.1). The OS was 12.1 months (95% CI, 8.1–16.1). The most common adverse events were neutropenia, anemia, and thrombocytopenia.

**Conclusion:** Lurbinectedin is well-tolerated and effective as second-line therapy in Chinese patients with SCLC. The MTD is 2.0 mg/m<sup>2</sup>. The ORR is 50% and the DOR is 12.1 months. The OS is 12.1 months. Lurbinectedin is a promising agent for the treatment of SCLC.



# A Phase 1/2 Trial of Lurbinectedin (L) in Combination With Pembrolizumab (P) in Relapsed Small Cell Lung Cancer (SCLC): The LUPER Study

Calles A, et al. 2022. ASCO 8581

## KEY INCLUSION CRITERIA

## RESULTS – SAFETY

**KEY INCLUSION CRITERIA**

1. Histologically confirmed relapsed SCLC with a confirmed diagnosis of SCLC within 12 months of the start of the study.

2. Eastern Cooperative Oncology Group (ECOG) performance grade 0-1.

3. Adequate organ function: Hemoglobin  $\geq 10$  g/dL, platelets  $\geq 100,000$  /mm<sup>3</sup>, neutrophils  $\geq 1,500$  /mm<sup>3</sup>, creatinine  $\leq 1.5$  times upper limit of normal (ULN), and bilirubin  $\leq 1.5$  times ULN.

4. No prior treatment with a platinum-based chemotherapy regimen for SCLC.

5. No prior treatment with a PD-1/PD-L1 inhibitor.

6. No prior treatment with Lurbinectedin.

7. No concurrent or planned use of other anticancer therapy within 14 days before and 14 days after the start of the study.

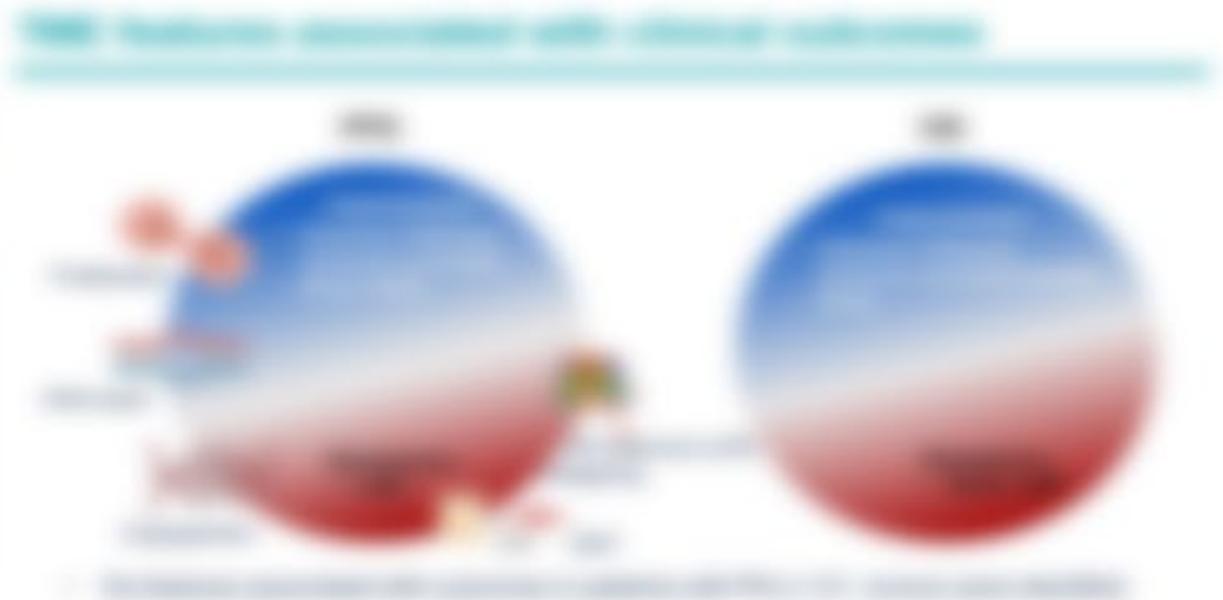
8. No history of active or uncontrolled chronic infection, including but not limited to hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), tuberculosis, or other opportunistic infections.

9. No history of autoimmune disease, including but not limited to rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, or other autoimmune conditions.

10. No history of organ transplant.

11. No history of pregnancy or breastfeeding.

12. No history of second primary malignancy within 5 years before the start of the study.



**RESULTS – SAFETY**

The safety profile of the combination of Lurbinectedin and Pembrolizumab was evaluated in the LUPER study. The most common adverse events (AE) were Grade 1-2, including fatigue, nausea, and constipation. There were no Grade 4 adverse events reported. The overall safety profile was consistent with the known safety profiles of the individual agents.

# Analysis of Patients With Relapsed Small Cell Lung Cancer (SCLC) Receiving Single-Agent Lurbinectedin in the Phase 3 ATLANTIS Trial

Navarro A, et al. 2022 ASCO #8524

## TREATMENT

## TRIAL OVERVIEW

**Background**

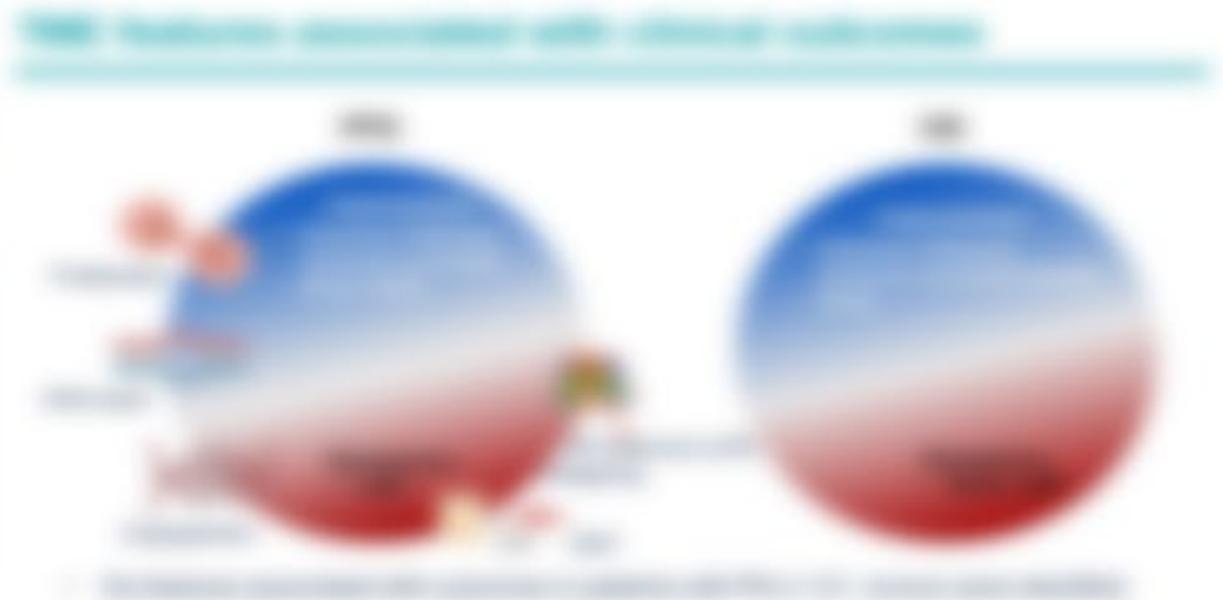
Small cell lung cancer (SCLC) is a highly aggressive malignancy with a poor prognosis. The standard of care for relapsed SCLC is a combination of cyclophosphamide, Adriamycin, and vincristine (CAV). Lurbinectedin is a novel, orally active, cytotoxic agent that has shown promising activity in SCLC. The ATLANTIS trial is a phase 3, randomized, controlled trial comparing lurbinectedin to CAV in patients with relapsed SCLC. The primary endpoint is overall survival (OS). The secondary endpoints include progression-free survival (PFS), quality of life, and toxicity.

**Methods**

The ATLANTIS trial is a phase 3, randomized, controlled trial comparing lurbinectedin to CAV in patients with relapsed SCLC. The trial is stratified by performance status (PS) and prior treatment. The primary endpoint is OS. The secondary endpoints include PFS, quality of life, and toxicity.

**Results**

The results of the ATLANTIS trial show that lurbinectedin is superior to CAV in terms of OS. The median OS for the lurbinectedin group was significantly longer than that of the CAV group. The results also show that lurbinectedin is well-tolerated and has a favorable toxicity profile compared to CAV.



# ATLANTIS Clinical Trial – the Efficacy and Safety of Single-Agent Lurbinectedin Were Analyzed in a Post-hoc Analysis

Navarro A, et al. 2022 ASCO #8524

## OUTCOMES

## RESULTS – EFFICACY

**Primary Endpoints**

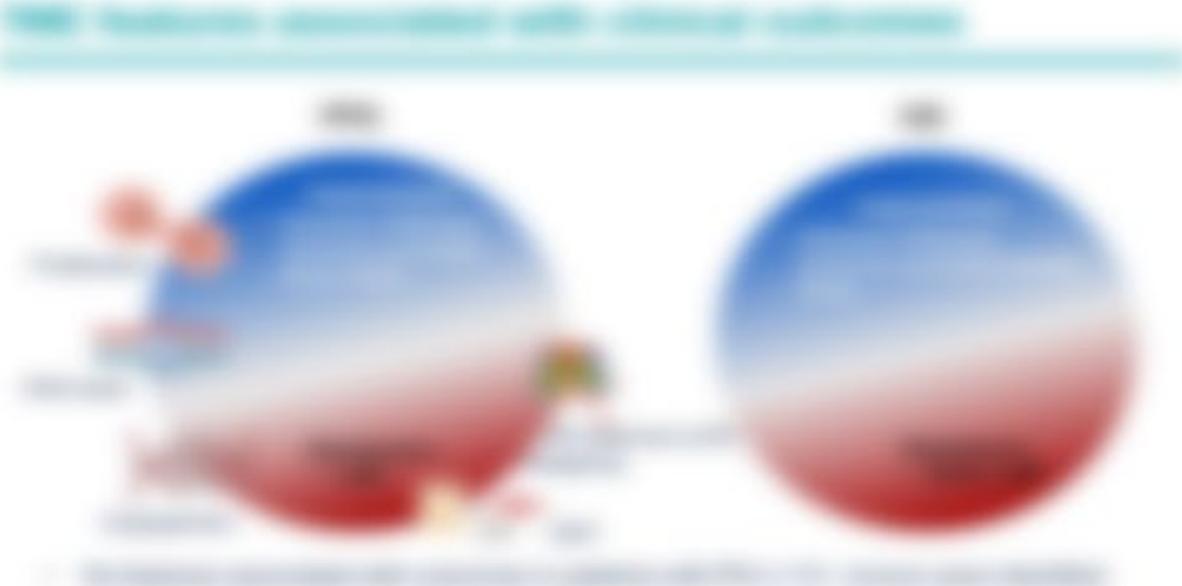
**Overall Survival (OS)**

**Time to Progression (TTP)**

**Quality of Life (QoL)**

**Secondary Endpoints**

**Adverse Events (AE)**



EPICS

# Recent Progress and Emerging Therapies in Second Line and Beyond

Key Takeaways

# Discussion Highlights: Lurbinectedin in Second-Line Treatment of SCLC (1/2)

**MOST EXPERTS VIEW LURBINECTEDIN FAVORABLY AND USE IT IN THEIR PRACTICE DESPITE WHAT THEY CONSIDER TO BE MODEST EFFICACY RESULTS**

---

**KEY TAKEAWAYS**

- Most experts view lurbinectedin favorably and use it in their practice despite what they consider to be modest efficacy results.
- Experts are generally positive about the drug's safety profile and its ability to be used in combination with other therapies.
- There is a strong belief in the drug's potential to improve patient outcomes in the second-line setting.

**EXPERT OPINIONS**

Experts are generally positive about the drug's safety profile and its ability to be used in combination with other therapies. There is a strong belief in the drug's potential to improve patient outcomes in the second-line setting.



# Discussion Highlights: Lurbinectedin in Second-Line Treatment of SCLC (2/2)

## TREATMENT SEQUENCING PAST THE FIRST LINE

**KEY TAKEAWAYS**

- 1. Lurbinectedin is a novel, orally active, cytotoxic agent that targets DNA topoisomerase II and DNA topoisomerase I, leading to DNA damage and cell death.
- 2. In a phase 1 study, lurbinectedin was well-tolerated and showed promising activity in SCLC patients, including those with prior platinum-based therapy.
- 3. Lurbinectedin is currently being evaluated in several phase 2 studies, including a study comparing lurbinectedin to irinotecan in second-line SCLC.

**CLINICAL TRIALS**

Several clinical trials are currently evaluating lurbinectedin in SCLC, including:

- A phase 2 study comparing lurbinectedin to irinotecan in second-line SCLC.
- A phase 2 study evaluating lurbinectedin in combination with durvalumab in SCLC.
- A phase 2 study evaluating lurbinectedin in combination with pembrolizumab in SCLC.



**CONCLUSION**

Lurbinectedin is a promising agent for the treatment of SCLC, particularly in the second-line setting. Further clinical studies are needed to confirm its efficacy and safety in this population.

# Discussion Highlights: Other Key Takeaways for the Treatment of SCLC in the Second Line

## RECENT DEVELOPMENTS IN THE SECOND-LINE TREATMENT FOR SCLC AND POTENTIAL NEW AREAS OF INTEREST

**KEY TAKEAWAYS**

The second-line treatment landscape for SCLC is rapidly evolving. Key takeaways include the importance of biomarker testing, particularly for PD-L1 expression and potential future targets like MET and HER2. The integration of immunotherapy, such as atezolizumab, remains a cornerstone of treatment, often combined with chemotherapy. Emerging data on novel agents and combinations are being closely monitored for their impact on overall survival and quality of life.

**CLINICAL TRIALS**

Several clinical trials are currently underway, focusing on novel drug combinations and biomarker-guided therapy. These trials aim to identify more effective and less toxic treatment options for patients with relapsed SCLC. Key areas of interest include the use of targeted therapies and immunomodulators in combination with standard-of-care treatments.



A circular speaker icon is positioned to the left of a text box. The text box contains several lines of text, which are blurred in this view. The text likely represents a key point or a quote from a speaker during the discussion.

