

 A decorative graphic on the left side of the slide, consisting of several thick, curved lines in various colors (teal, green, orange, grey, light blue) arranged in a circular pattern.

EPICS

Small Cell Lung Cancer (SCLC) in 2022 and Beyond – Region 2

August 17, 2022

Content	Slide
Meeting Snapshot	3 
Faculty Panel	4 
Meeting Agenda	5 
Key Insights and Strategic Recommendations	6 
Biomarkers in SCLC	10 
Recent Progress and Emerging Therapies in Second Line and Beyond	17 
Standards of Care Across the SCLC Treatment Continuum	25 

EPICS

VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
August 17, 2022



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



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations

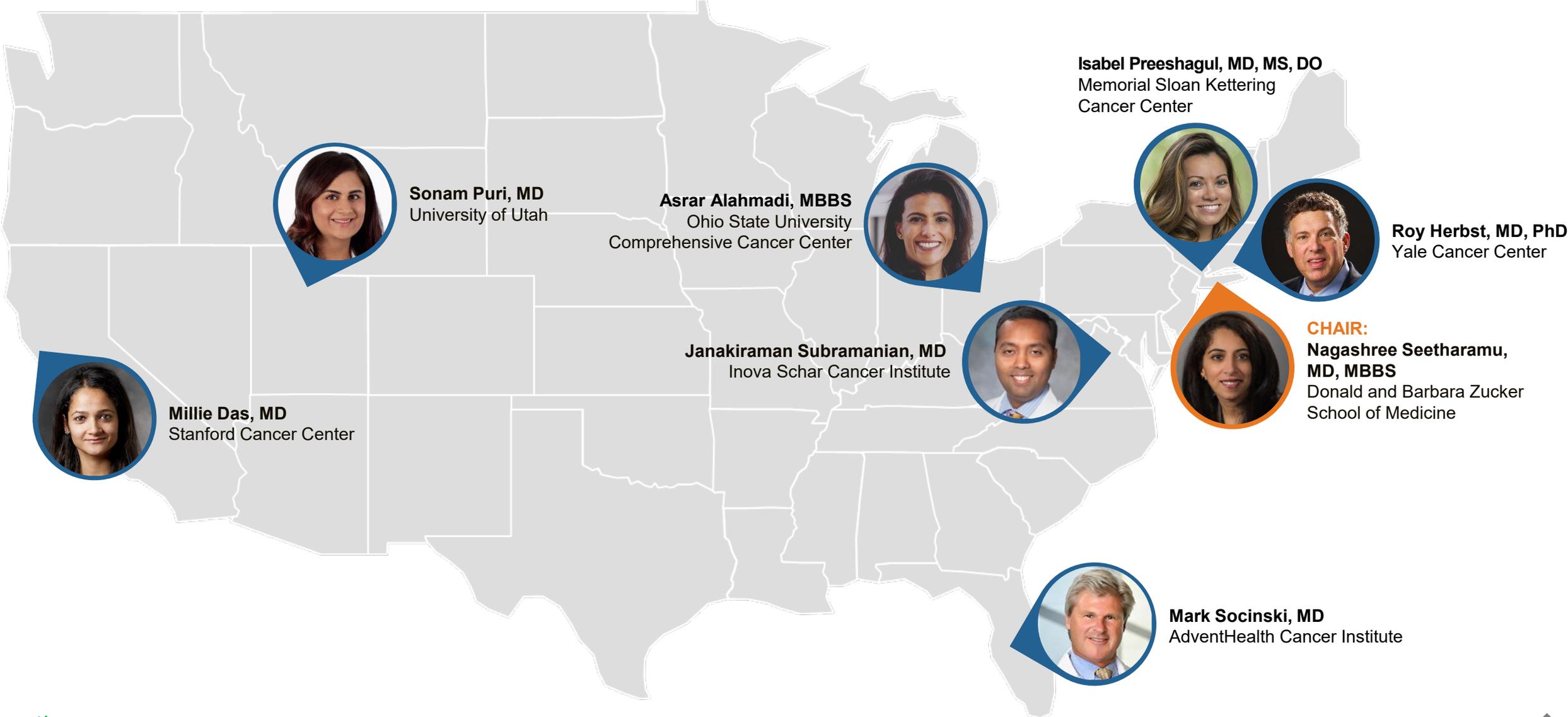


PANEL: 8 key experts
in SCLC in 7 states in
the US



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

Panel Consisting of 8 US Small Cell Lung Cancer Experts



Meeting Agenda

EPICS

Time	Topic	Speaker/Moderator
6.00 PM – 6.05 PM	Welcome and Introductions	Nagashree Seetharamu, MD, MBBS
6.05 PM – 6.15 PM	Biomarkers in SCLC	Sonam Puri, MD
6.15 PM – 6.30 PM	Key Questions and Topics for Discussion	All Faculty
6.30 PM – 6.35 PM	Key Takeaways	Sonam Puri, MD
6.35 PM – 6.45 PM	Recent Progress and Emerging Therapies in Second Line and Beyond	Mark Socinski, MD
6.45 PM – 7.20 PM	Key Questions and Topics for Discussion	All Faculty
7.20 PM – 7.25 PM	Key Takeaways	Mark Socinski, MD
7.25 PM – 7.35 PM	Standards of Care Across the SCLC Treatment Continuum	Roy Herbst, MD, PhD
7.35 PM – 7.50 PM	Key Questions and Topics for Discussion	All Faculty
7.50 PM – 7.55 PM	Key Takeaways	Roy Herbst, MD, PhD
7.55 PM – 8.00 PM	Summary and Meeting Close	Nagashree Seetharamu, MD, MBBS



EPICS

Biomarkers in SCLC



Sonam Puri, MD
University of Utah

Current State of Biomarkers in SCLC and Immune Checkpoint Inhibitors

BIOMARKERS REPRESENT THE NEXT STEP IN IMPROVING SCLC TREATMENT PATHWAYS

> Biomarkers are needed to develop personalized medicine in SCLC

- [Faded text]



SCLC SUBTYPES

Phase I study - (NCT01042370)

- Experts believe the inclusion of molecular phenotypes is possible in real time, and these subtypes can potentially be targeted

Phase II study - (NCT01042370)

- The approach is seen as effective, working well, and broadly applicable to many cancers

Phase III study - (NCT01042370)

- This approach is seen as a great option for a patient population in which going unstratified is difficult. It is seen as effective and safe

Phase IV study - (NCT01042370)

- Experts believe the combination of subtypes with treatment is safe. However, they would like to see phase II data to confirm its activity in this setting

Phase V study - (NCT01042370)

- The NCT01042370 approach is seen as useful in the specific patient population with advanced disease. It was seen to be effective, very safe, and well-tolerated. Some of the responses were seen fairly early in the study

GENOMIC PROFILING THROUGH DNA TESTING



[The following text is heavily blurred and illegible. It appears to be a list of bullet points or a series of short paragraphs, likely describing the clinical applications and benefits of genomic profiling through DNA testing.]



Focus on SLFN11 and c-MYC (protein based)

SLFN11

Placebo and TMZ

Veliparib and TMZ

TWO PROTEINS AS POTENTIAL BIOMARKERS

> SLFN11: DNA/RNA helicase. High expression levels of SLFN11

EPICS

Biomarkers in SCLC

Key Takeaways

Discussion Highlight: Biomarkers in SCLC

SCLC IS ONE OF THE RARE REMAINING SOLID TUMOR TYPES WHERE THERE IS NO APPROVED COMPANION BIOMARKER



Dr Puri:
Circulating free DNA is the most promising test

> Currently, biomarkers are not being used in the clinic and are mostly considered in the context of

[Faded text area containing multiple paragraphs and bullet points, likely representing a list of biomarkers or clinical trial results.]

EPICS

Recent Progress and Emerging Therapies in Second Line and Beyond



Mark Socinski, MD
AdventHealth Cancer Institute

Treatment Options for Relapsed ES-SCLC

NCCN CLINICAL PRACTICE GUIDELINES FOR SECOND-LINE SCLC

> Treatment recommendation depends on CTFI

STUDY POPULATION

1. Patients with relapsed ES-SCLC who have received 1-2 prior lines of systemic therapy, including platinum-based chemotherapy, and have a CTFI of 0-3. The population includes patients who did not receive platinum-based chemotherapy in the first line of treatment.

OUTLINE

1. Patients with a CTFI of 0-1 should receive a platinum-based doublet. Patients with a CTFI of 2-3 should receive a platinum-based doublet or a platinum-based triplet.

KEY POINT CONCLUSIONS

Continuing platinum-based treatment beyond week 20 provides clinical benefit in all subgroups and decreases the proportion of patients who are progression-free.

KEY POINT CONCLUSIONS: PATIENTS WITH A CTFI OF 0-1



RESPONSE: PROPORTION OF PATIENTS WHO ARE PROGRESSION-FREE



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

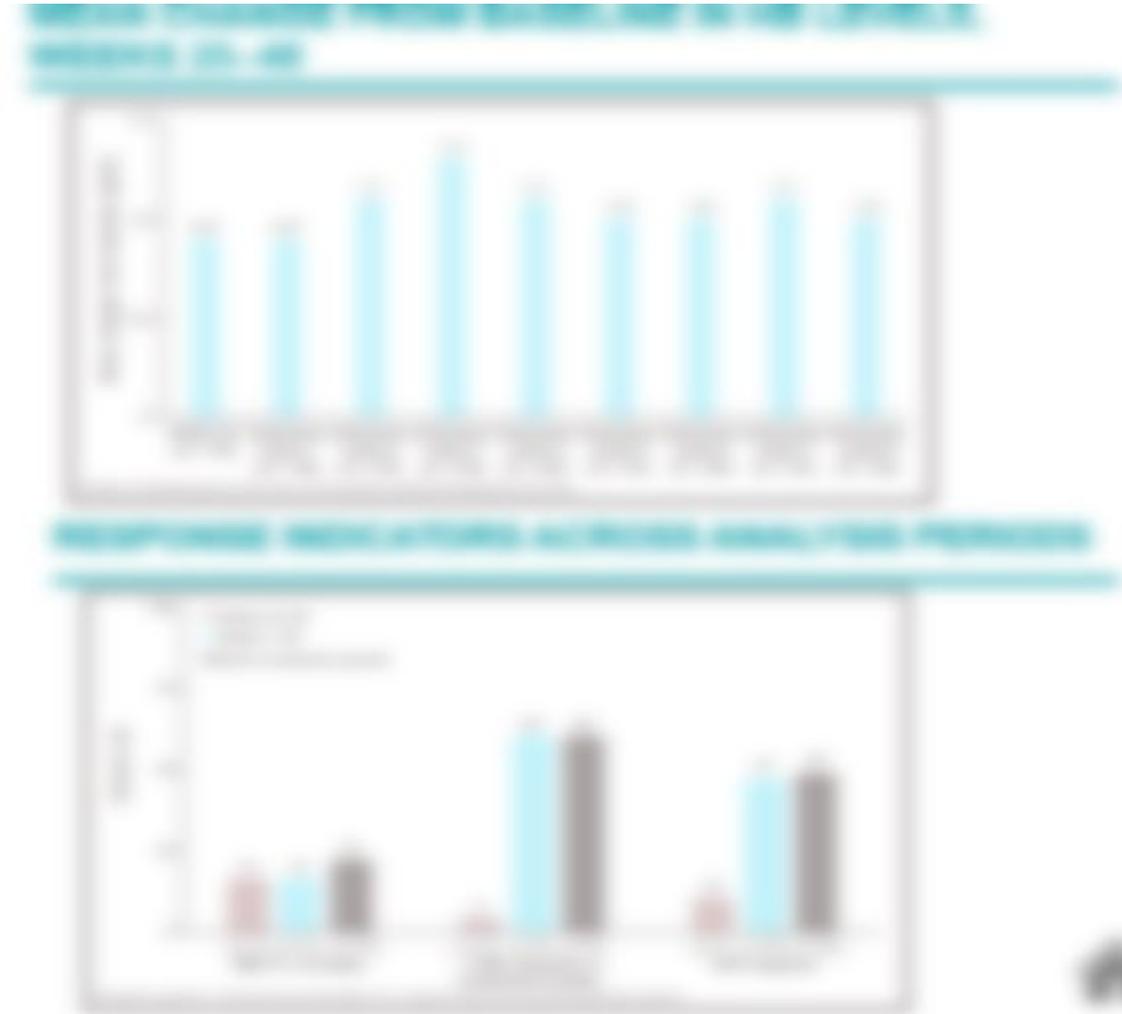
Cheng Y, et al. 2022 ASCO #8580

EPICS

DOSE-EXPANSION ARM

> Dose escalation: from 2.5 to 3.2 mg/m² as 1-hr

RESULTS – EFFICACY AND CTFI LENGTH



ATLANTIS Trial: Phase III Randomized Study of Lurbinectedin + DOX in 2L SCLC

Navarro A, et al. 2022 ASCO #8524

ATLANTIS trial design

Key eligibility criteria

Experimental arm^{a,b}

Primary endpoint

STUDY POPULATION

1. Eastern Cooperative Oncology Group (ECOG) performance grade 0-1, age ≥ 18 years, histologically confirmed small cell lung cancer (SCLC) with a confirmed relapse after first-line treatment with a platinum-based doublet, and no prior treatment with a second-line systemic therapy.

2. Eastern Cooperative Oncology Group (ECOG) performance grade 0-1, age ≥ 18 years, histologically confirmed SCLC with a confirmed relapse after first-line treatment with a platinum-based doublet, and no prior treatment with a second-line systemic therapy.

3. Eastern Cooperative Oncology Group (ECOG) performance grade 0-1, age ≥ 18 years, histologically confirmed SCLC with a confirmed relapse after first-line treatment with a platinum-based doublet, and no prior treatment with a second-line systemic therapy.

INTERVENTIONS

1. Lurbinectedin 1.5 mg/m² intravenously (IV) on days 1, 8, and 15 of a 21-day cycle, plus doxorubicin 45 mg/m² IV on day 1, every 21 days for up to 6 cycles.

2. Doxorubicin 45 mg/m² IV on day 1, every 21 days for up to 6 cycles.

PRIMARY ENDPOINTS

1. Overall survival (OS) at 12 weeks.

2. Time to progression (TTP) at 12 weeks.



ATLANTIS Clinical Trial: Overall Survival and Posthoc Analysis

Navarro A, et al. 2022 ASCO #8524

RESULTS – EFFICACY

10

POSTHOC ANALYSIS

> 50 patients completed 10 cycles of lurbi + DOX and

STUDY POPULATION

100 patients were enrolled in the study, with 50 patients in each arm. The study population was composed of patients with advanced solid tumors, including breast, lung, and colorectal cancer. The patients were randomized to receive either the experimental treatment or the control treatment. The study was conducted in a multicenter setting across several countries. The primary endpoint of the study was overall survival. The study was designed as a phase III, randomized, controlled trial. The patients were stratified by cancer type and performance status. The study was approved by the relevant ethics committees and regulatory authorities. The study was conducted in accordance with the principles of Good Clinical Practice (GCP). The study was registered in the ClinicalTrials.gov database.

RESULTS

The overall survival results showed that the experimental treatment group had a significantly better overall survival compared to the control treatment group. The median overall survival was significantly longer in the experimental group. The results were consistent across different cancer types and performance status groups. The overall survival benefit was statistically significant. The results were consistent across different cancer types and performance status groups. The overall survival benefit was statistically significant.

CONCLUSIONS

The study demonstrated that the experimental treatment significantly improved overall survival compared to the control treatment. The results were consistent across different cancer types and performance status groups. The overall survival benefit was statistically significant. The results were consistent across different cancer types and performance status groups. The overall survival benefit was statistically significant.

POSTHOC ANALYSIS



RESPONSE RATES AND TOXICITY ANALYSIS



EPICS

Recent Progress and Emerging Therapies in Second Line and Beyond

Key Takeaways

Discussion Highlight: Lurbinectedin and Other Treatment Options for Second-Line Treatment of SCLC

SECOND-LINE TREATMENT OPTIONS FOR SCLC PATIENTS AND THERAPEUTIC LANDSCAPE



“

> SCLC is viewed by the experts as a graveyard for new drugs, on the basis of the

[Blurred text block]

[Blurred text block]

[Blurred text block]

Discussion Highlight: Lurbinectedin in Second-Line Treatment of SCLC



BIOMARKERS USE IN THE SECOND LINE

- > Experts suggested patients should be tested early, as the disease can progress rapidly. They argued that by the time the disease progresses, there might not be

EPICS

Standards of Care Across the SCLC Treatment Continuum



Roy Herbst, MD, PhD
Yale Cancer Center

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; enrollment criteria

PRIMARY ENDPOINTS

PFS: Primary Analysis Set

Timeline of FDA Approvals for HER2+ Breast Cancer

Year	2018	2019	2020	2021	2022	2023
HER2+ Breast Cancer						
Trastuzumab		2013		2013	2013	2013
Trastuzumab Derivat						2018

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

SAFETY OVERVIEW

OUTCOME

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

[Blurred content area]



First-Line Pembrolizumab or Placebo Combined With Etoposide and Platinum for ES-SCLC: KEYNOTE-604 Long-term Follow-up Results

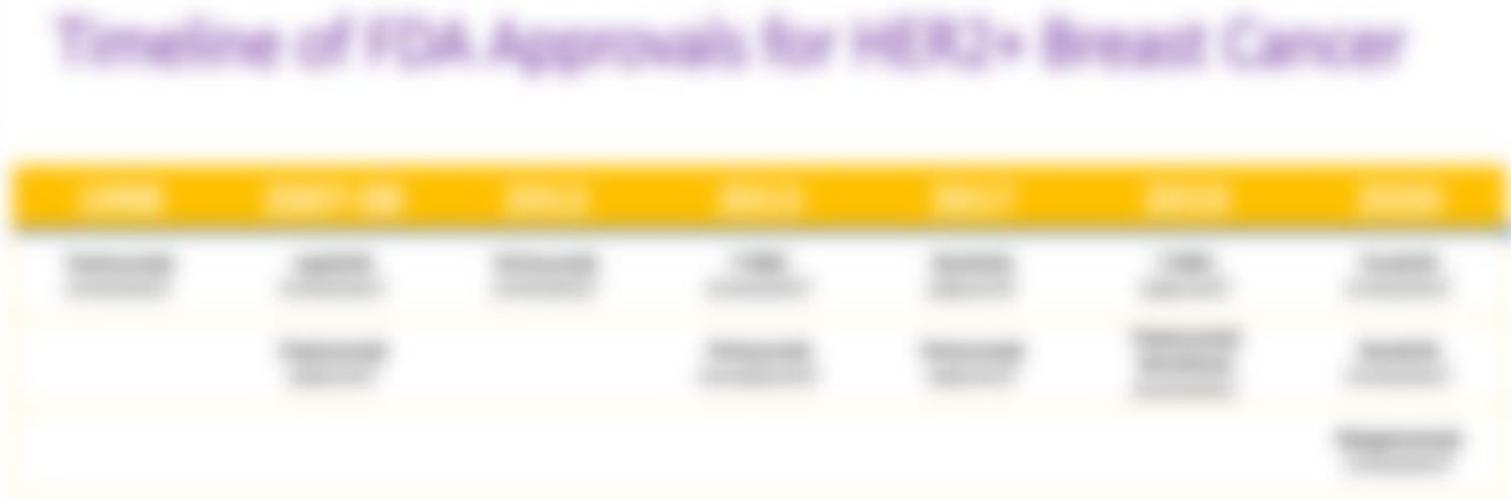
Rudin CM, et al. WCLC 2022 #OA12.06

OVERALL SURVIVAL

METHODS (N = 453)

> Selection criteria

[Blurred text area containing details of the study's selection criteria and methodology.]



EPICS

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

Key Takeaways

Discussion Highlight: Standards of Care Across the SCLC Treatment Continuum

RECENT UPDATES AND ADVANCES IN SCLC TREATMENT

> The relevance of trilaciclib support with chemotherapy was discussed



[Blurred text area containing the main discussion content]



[Blurred text area containing a quote or additional discussion content]