Meet The Professor
Optimizing the Management of Small Cell Lung Cancer

Jacob Sands, MD
Physician
Dana-Farber Cancer Institute
Assistant Professor
Harvard Medical School
Boston, Massachusetts

Commercial Support

This activity is supported by an educational grant from Jazz Pharmaceuticals Inc.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

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Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

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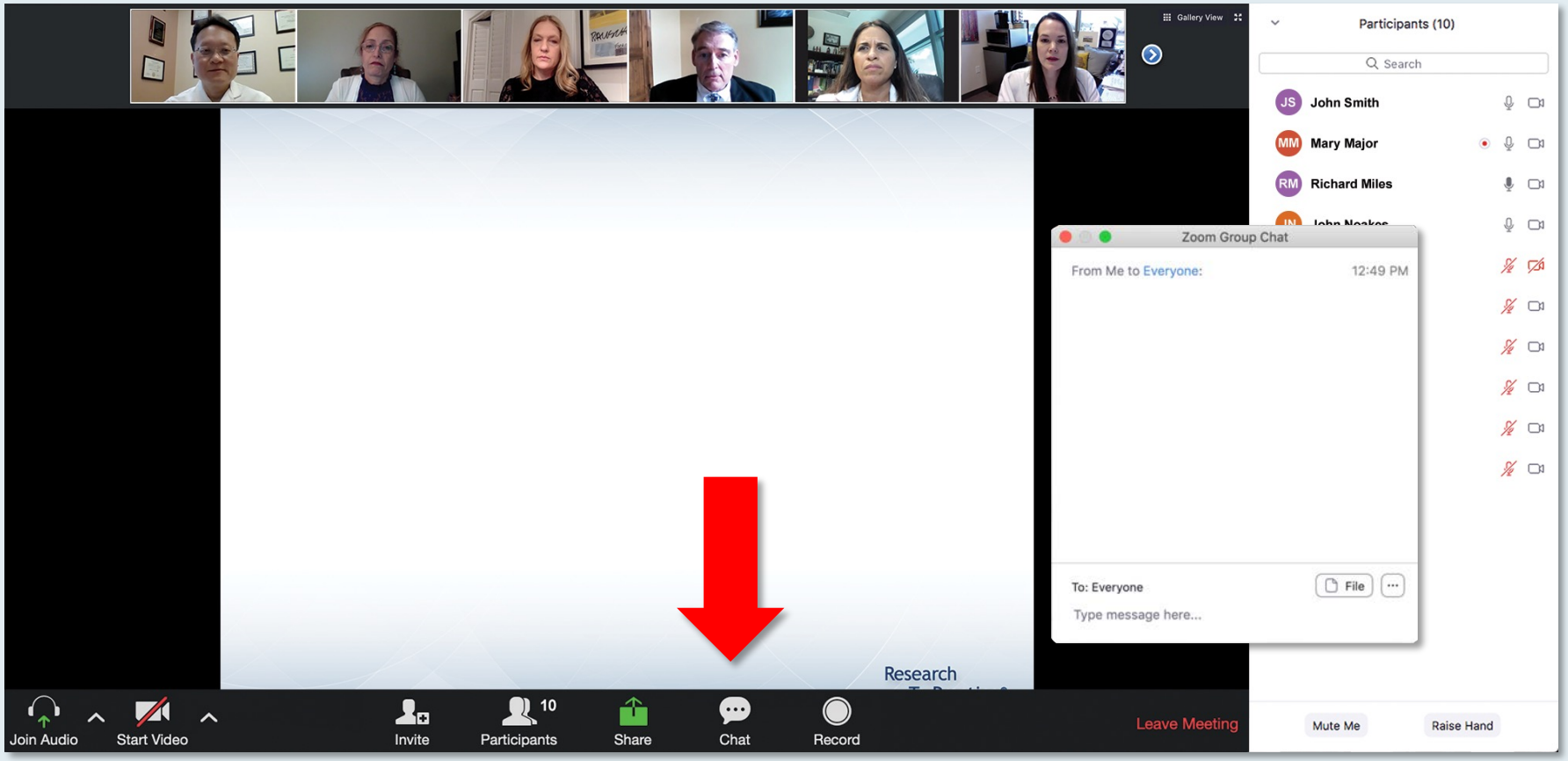
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

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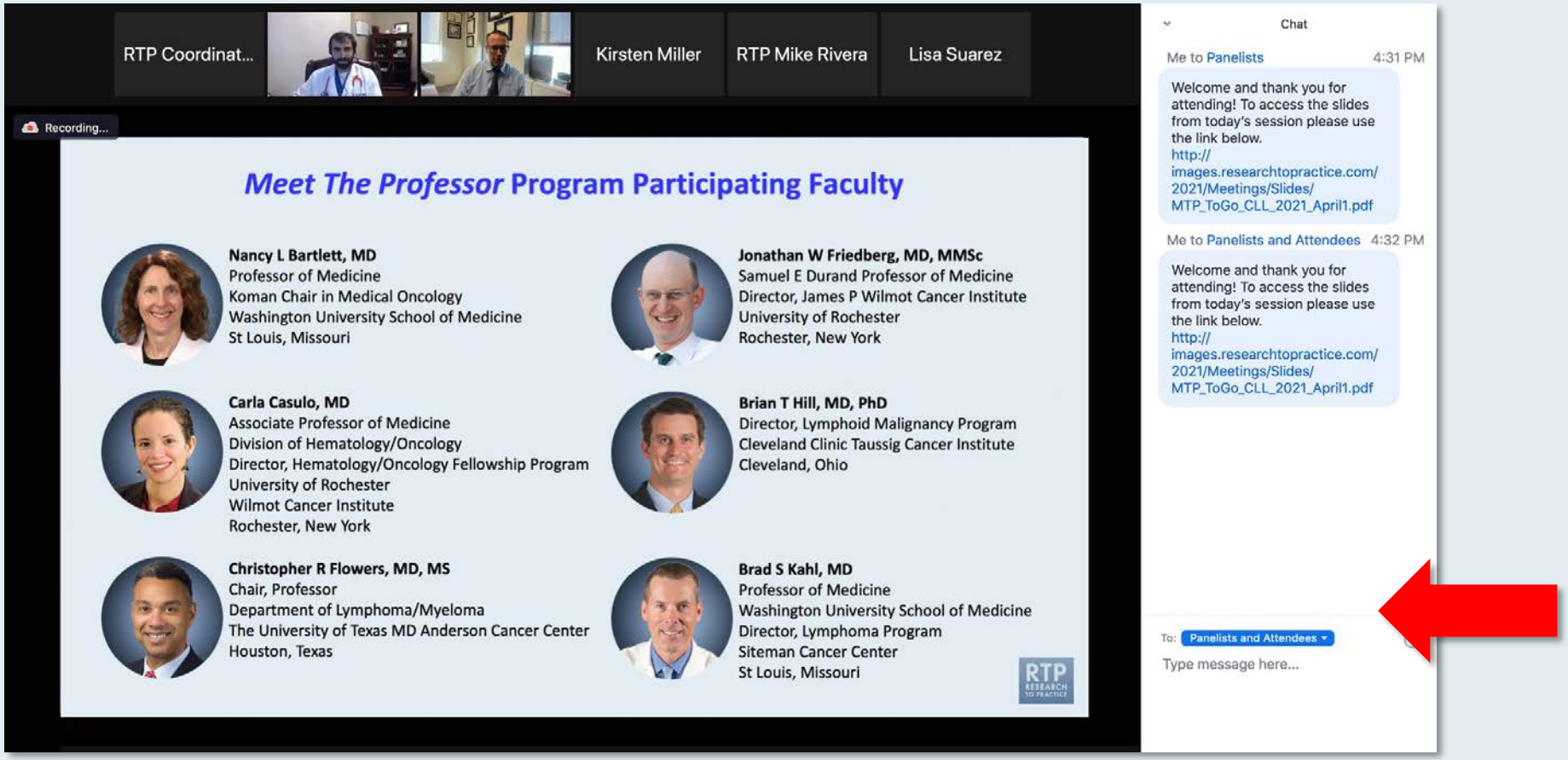
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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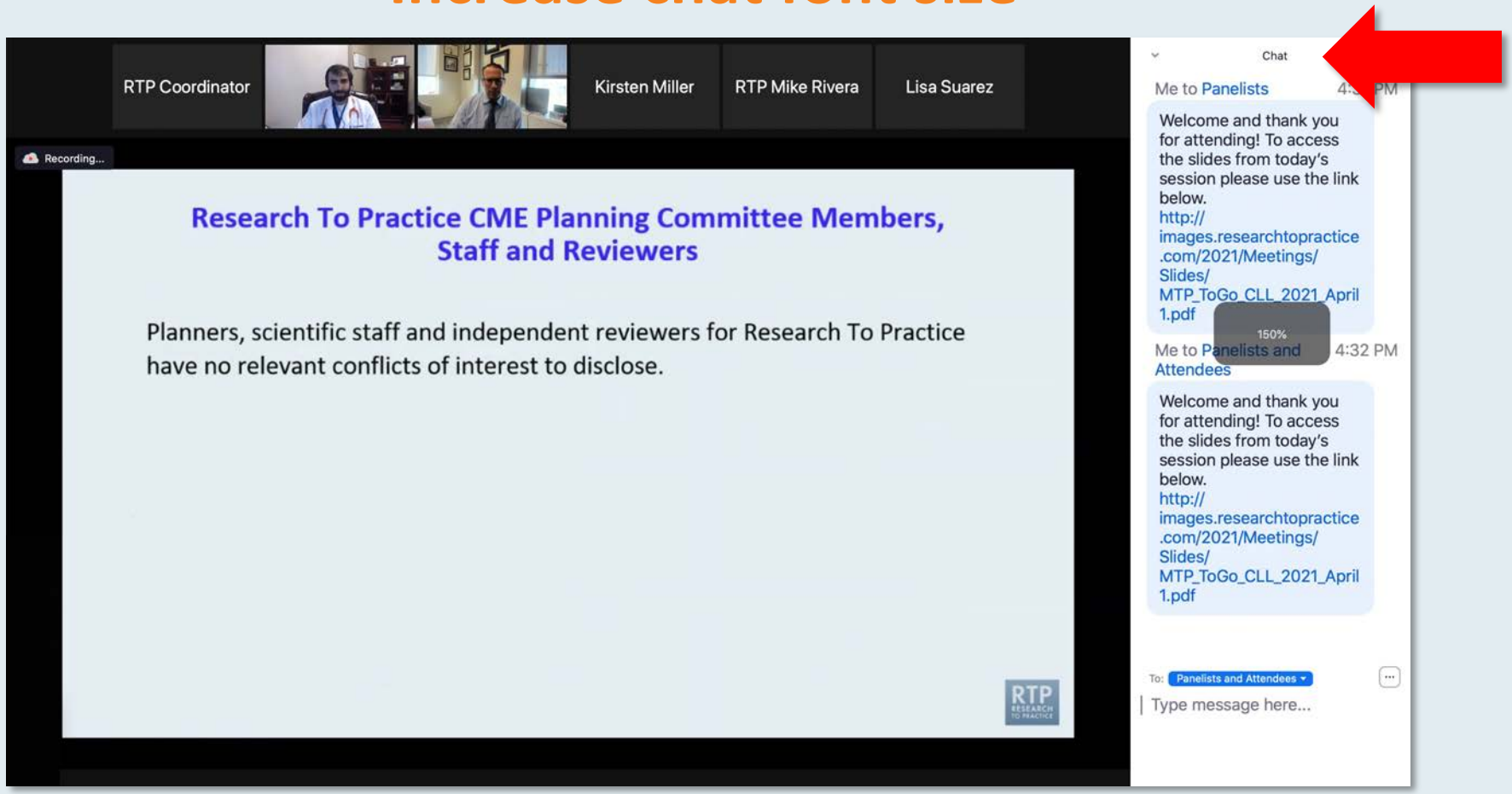

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Management of Unresectable Stage III Non-Small Cell Lung Cancer

DR JEFFREY BRADLEY

EMORY UNIVERSITY SCHOOL OF MEDICINE

DR DAVID R SPIGEL

SARAH CANNON RESEARCH INSTITUTE

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Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Wednesday, August 17, 2022
5:00 PM – 6:00 PM ET

Faculty

John Strickler, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Ovarian Cancer

Thursday, August 25, 2022
5:00 PM – 6:00 PM ET

Faculty

Richard T Penson, MD, MRCP

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Wednesday, August 31, 2022
5:00 PM – 6:00 PM ET

Faculty

Lecia V Sequist, MD, MPH

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of HER2-Positive Breast Cancer

Thursday, September 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Mark D Pegram, MD

Moderator

Neil Love, MD

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Exploring Current Considerations and Promising Investigational Approaches for Patients with Myelodysplastic Syndromes

CME/MOC-Accredited Virtual Symposium in Conjunction with the Society of Hematologic Oncology 2022 Annual Meeting

Thursday, September 8, 2022

5:00 PM – 6:00 PM ET

Faculty

Gail J Roboz, MD

David Sallman, MD

Additional faculty to be announced

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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Meet The Professor
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Assistant Professor
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Meet The Professor Program Participating Faculty

Jacob Sands, MD
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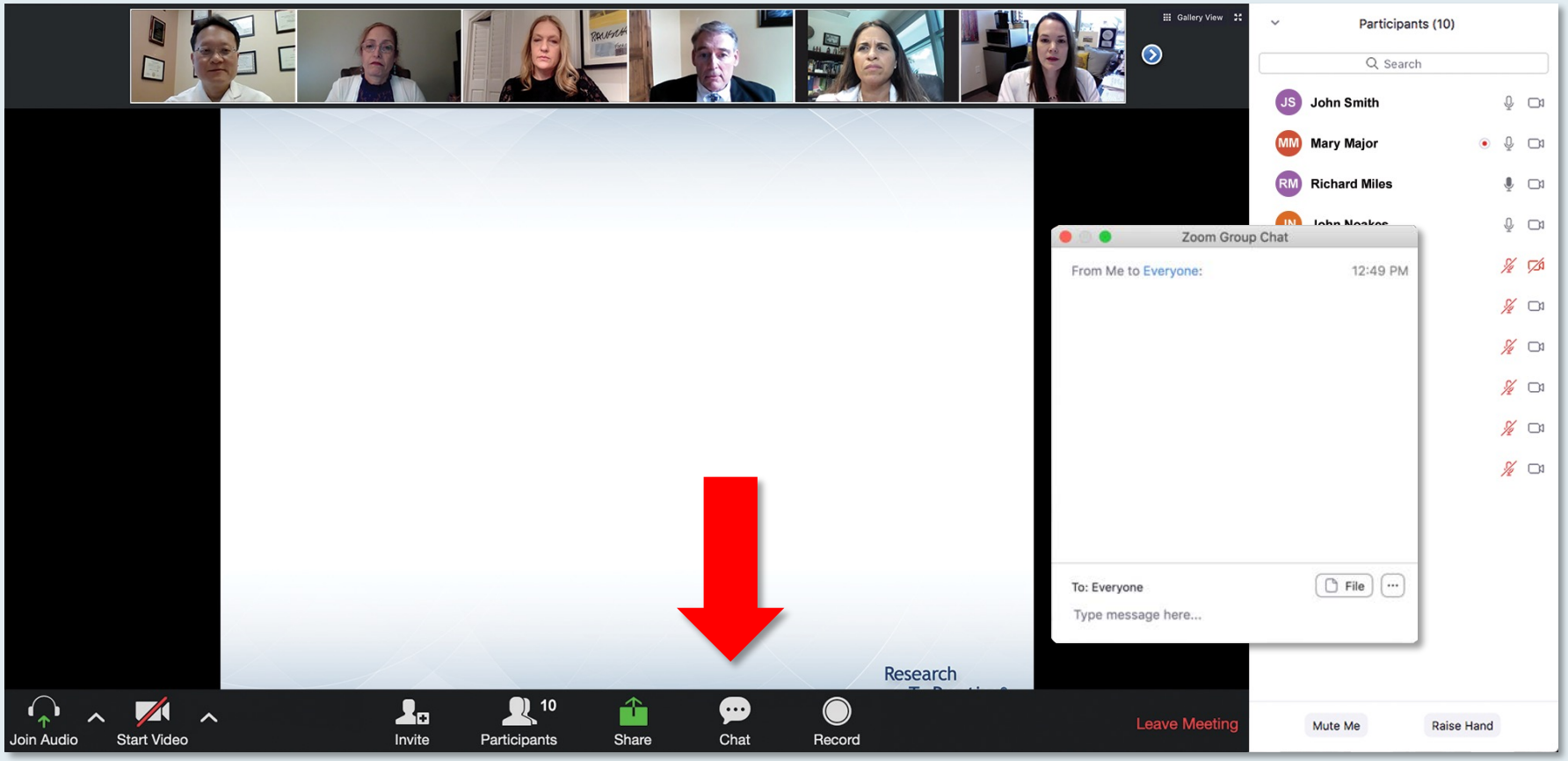

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WITH DR NEIL LOVE

Management of Unresectable Stage III Non-Small Cell Lung Cancer

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Harold C Simmons Comprehensive Cancer Center
Richardson, Texas

Kapisthalam (KS) Kumar, MD
Florida Cancer Specialists
Trinity, Florida

Ferdy Santiago, MD
Florida Cancer Specialists
Naples, Florida

Adam R Miller, MD
Mass General/North Shore Cancer Center
Danvers, Massachusetts

John Yang, MD
Fall River, Massachusetts

Mohamed K Mohamed, MD, PhD
Cone Health Cancer Center
Greensboro, North Carolina

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Meet The Professor with Dr Sands

Introduction: Journal Club

MODULE 1: Case Presentations

MODULE 2: Appendix of Key Publications

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J Thorac Oncol 2021 January;16(1):37-53.

IASLC

STATE OF THE ART: CONCISE REVIEW

Lung Screening Benefits and Challenges: A Review of The Data and Outline for Implementation

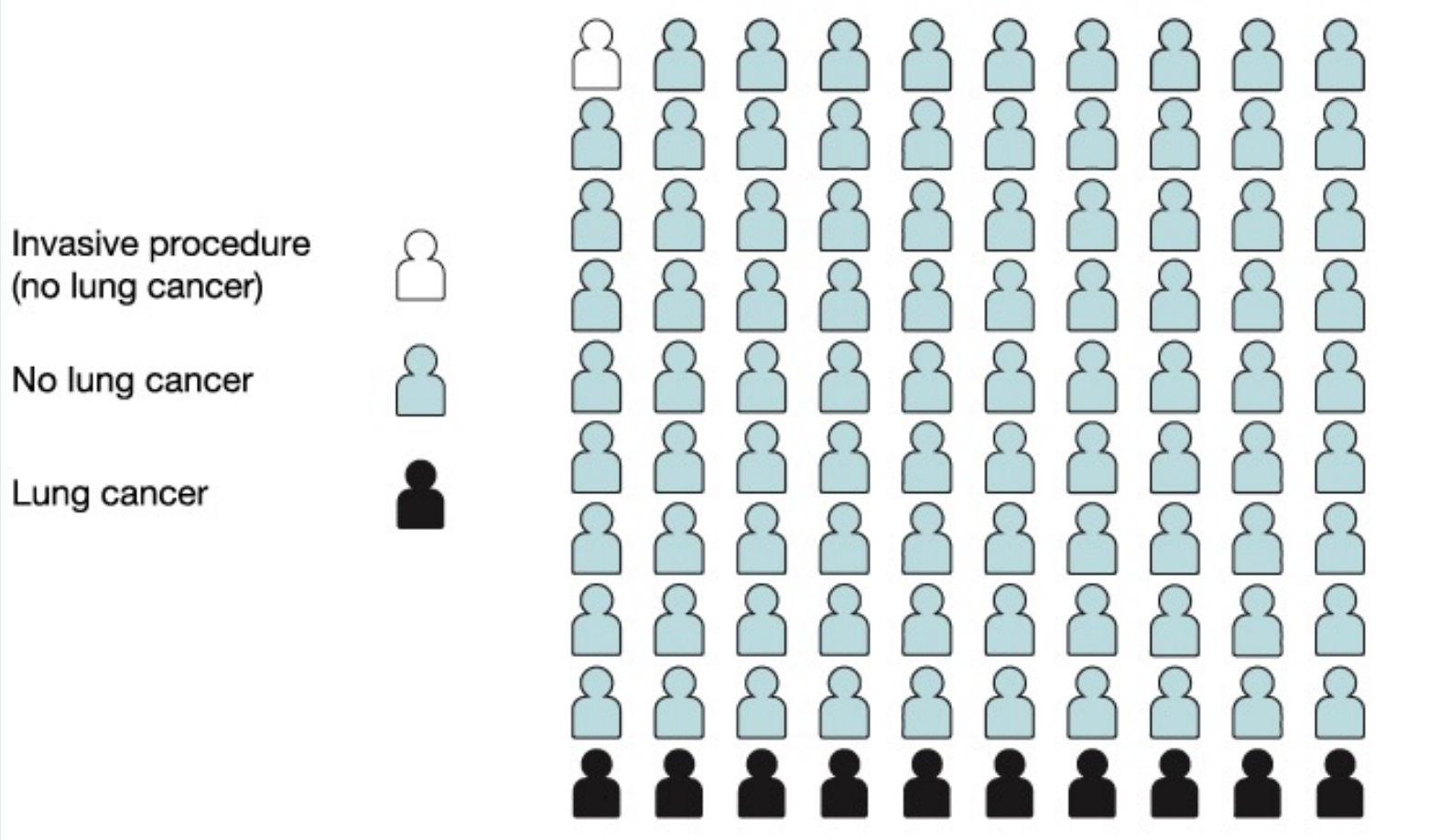
Check for updates

Jacob Sands, MD,[a,*] Martin C. Tammemägi, PhD,[b] Sebastien Couraud, MD, PhD,[c] David R. Baldwin, MD, FRCP,[d] Andrea Borondy-Kitts, MS, MPH,[e] David Yankelevitz, MD,[f] Jennifer Lewis, MD,[g,h,i] Fred Grannis, MD,[j] Hans-Ulrich Kauczor, MD,[k] Oyunbileg von Stackelberg, PhD,[k] Lecia Sequist, MD,[l] Ugo Pastorino, MD,[m] Brady McKee, MD[n]

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

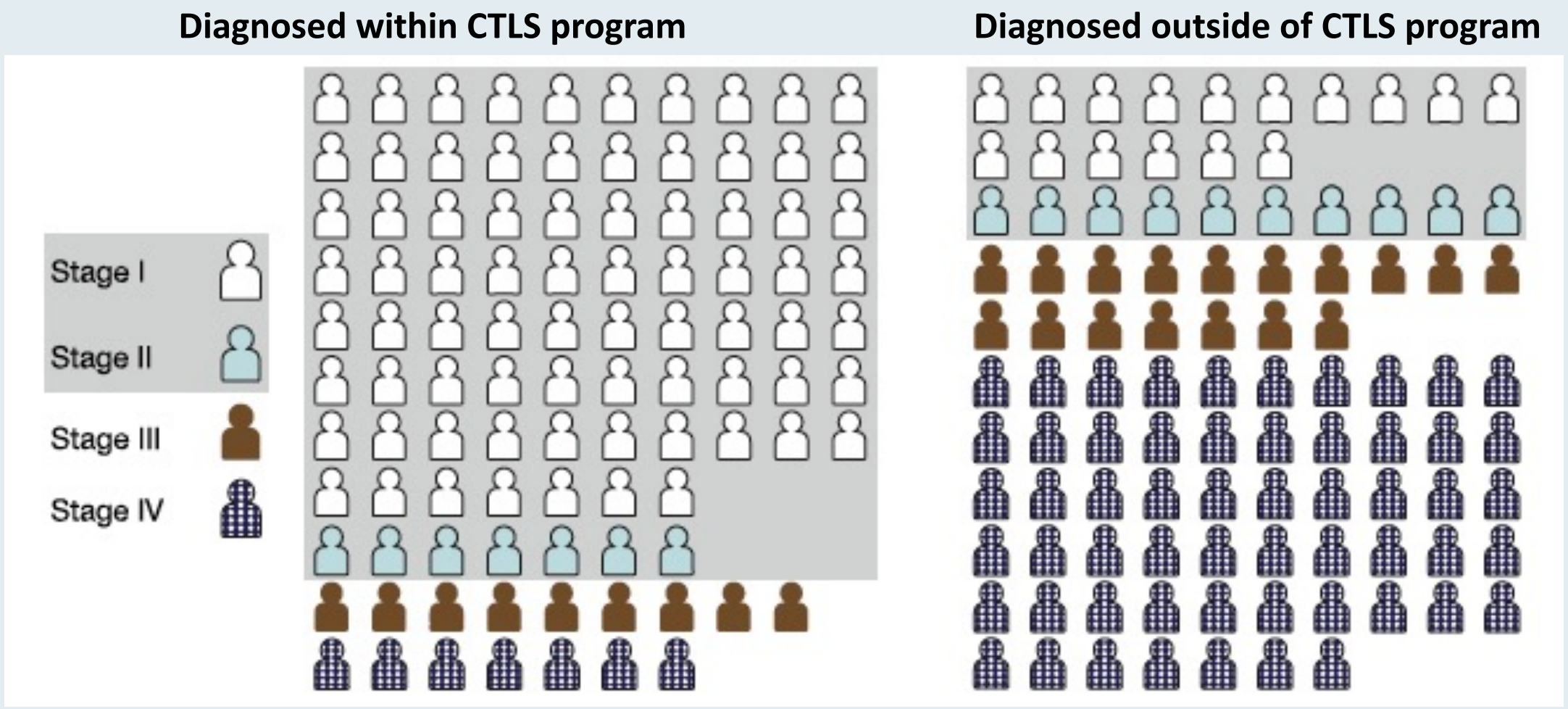
Updated Decision Aid to Support Shared Decision-Making in Practice: Lung Screening Outcomes

Lung screening outcomes of 100 high-risk individuals during full duration of screening eligibility



Sands J et al. *J Thorac Oncol* 2021 January;16(1):37-53.

Updated Decision Aid to Support Shared Decision-Making in Practice: Lung Cancer Stage at Diagnosis



Sands J et al. *J Thorac Oncol* 2021 January;16(1):37-53.

J Thorac Oncol 2021 September;16(9):1437-9.

EDITORIAL

Yet Another Reminder of the Value of Lung Cancer Screening

Anurag K. Singh, MD,* Jacob M. Sands, MD

J Thorac Oncol 2021 September;16(9):1479-89.

IASLC

ORIGINAL ARTICLE

Impact of Low-Dose Computed Tomography Screening for Primary Lung Cancer on Subsequent Risk of Brain Metastasis

Chloe C. Su, BS,[a,b] Julie T. Wu, MD, PhD,[c] Joel W. Neal, MD, PhD,[c,d] Rita A. Popat, PhD,[b] Allison W. Kurian, MD, MSc,[c,d] Leah M. Backhus, MD, MPH,[d,e,f] Seema Nagpal, MD,[d,g,h] Ann N. Leung, MD,[i] Heather A. Wakelee, MD,[c,d] Summer S. Han, PhD[a,d,h,*]

Stage of Lung Cancer Diagnosed in Patients Randomized to CT Screening: Screen Detected versus Nonscreen Detected

	NLST		NELSON	
Stage	Screen Detected (%)	Nonscreen Detected (%)	Screen Detected (%)	Nonscreen Detected (%)
IA	329 (52)	82 (23)	95 (47)	10 (7)
IB	71 (11)	31 (9)	24 (12)	10 (7)
IIA	26 (4)	7 (2)	8 (4)	4 (3)
IIB	20 (3)	15 (4)	11 (5)	6 (4)
IIIA	59 (9)	37 (10)	20 (10)	14 (10)
IIIB	49 (8)	58 (16)	13 (6)	14 (10)
IV	81 (13)	131 (36)	19 (9)	73 (52)

CT, computed tomography; NLST, National Lung Screening Trial.

Singh AK, Sands JM. *J Thorac Oncol* 2021 September;16(9):1437-39.

Recent Stage Shifts and Changes in the Treatment of Stage I Small Cell Lung Cancer in the United States

Haridas CS et al.

IASLC 2022;Abstract EP14.05-003.

Clinical Stage of SCLC Treated in the United States

Baseline Characteristics	2010-2013 (n=55,335)	2014-2017 (n=59,907)	p-value
Clinical Stage:			
I	3.9%	4.5%	<0.001
II	3.2%	3.6%	
III	20.5%	21.4%	
IV	61.5%	62.5%	
Not staged	10.9%	8.0%	

Haridas CS et al. IASLC 2022;Abstract EP14.05-003.

Meet The Professor with Dr Sands

Introduction: Journal Club

MODULE 1: Case Presentations

MODULE 2: Appendix of Key Publications

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Cancers (Basel) 2021 February 10;13(4):727.

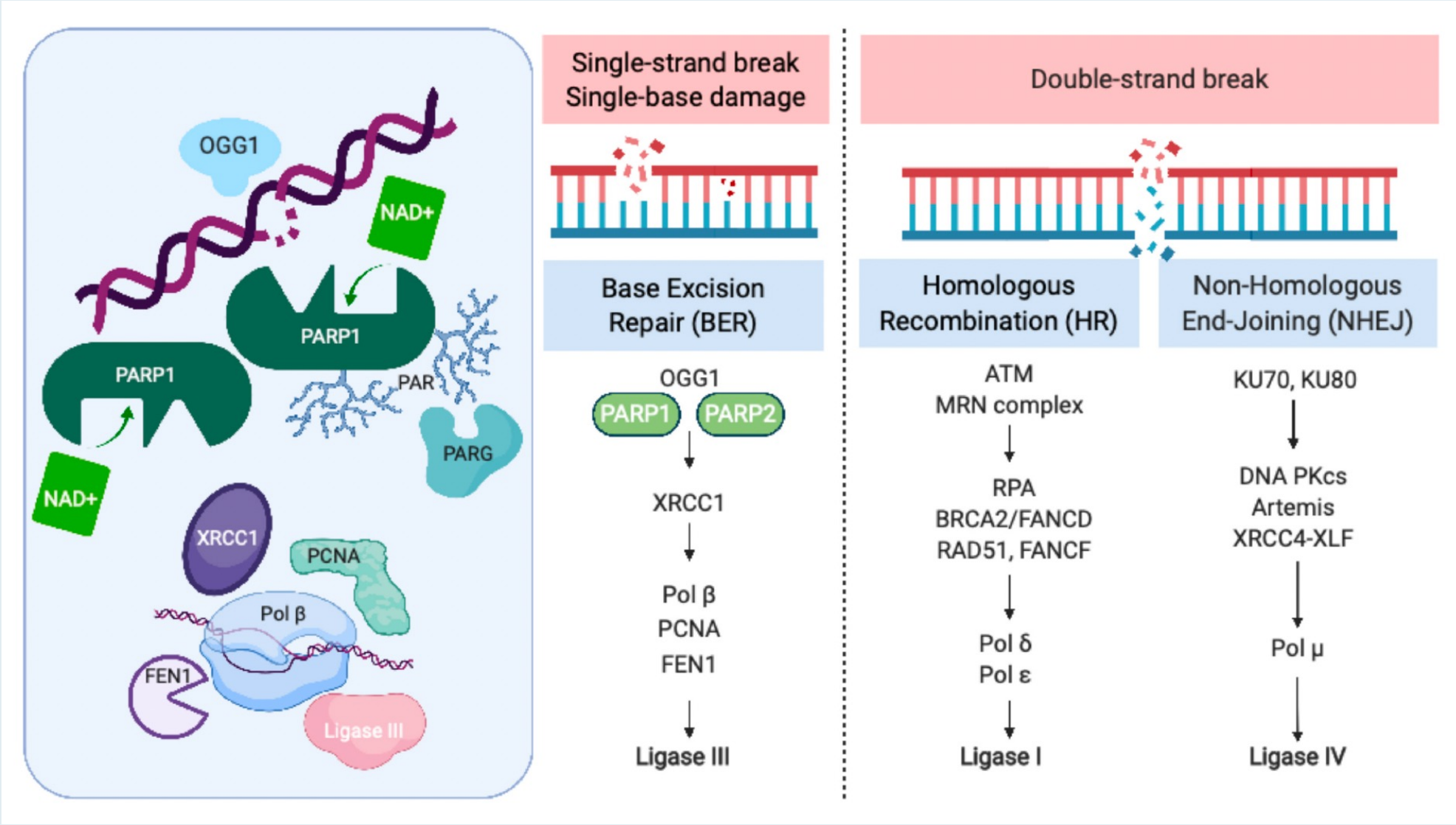
cancers

Review

PARP Inhibitors in Small-Cell Lung Cancer: Rational Combinations to Improve Responses

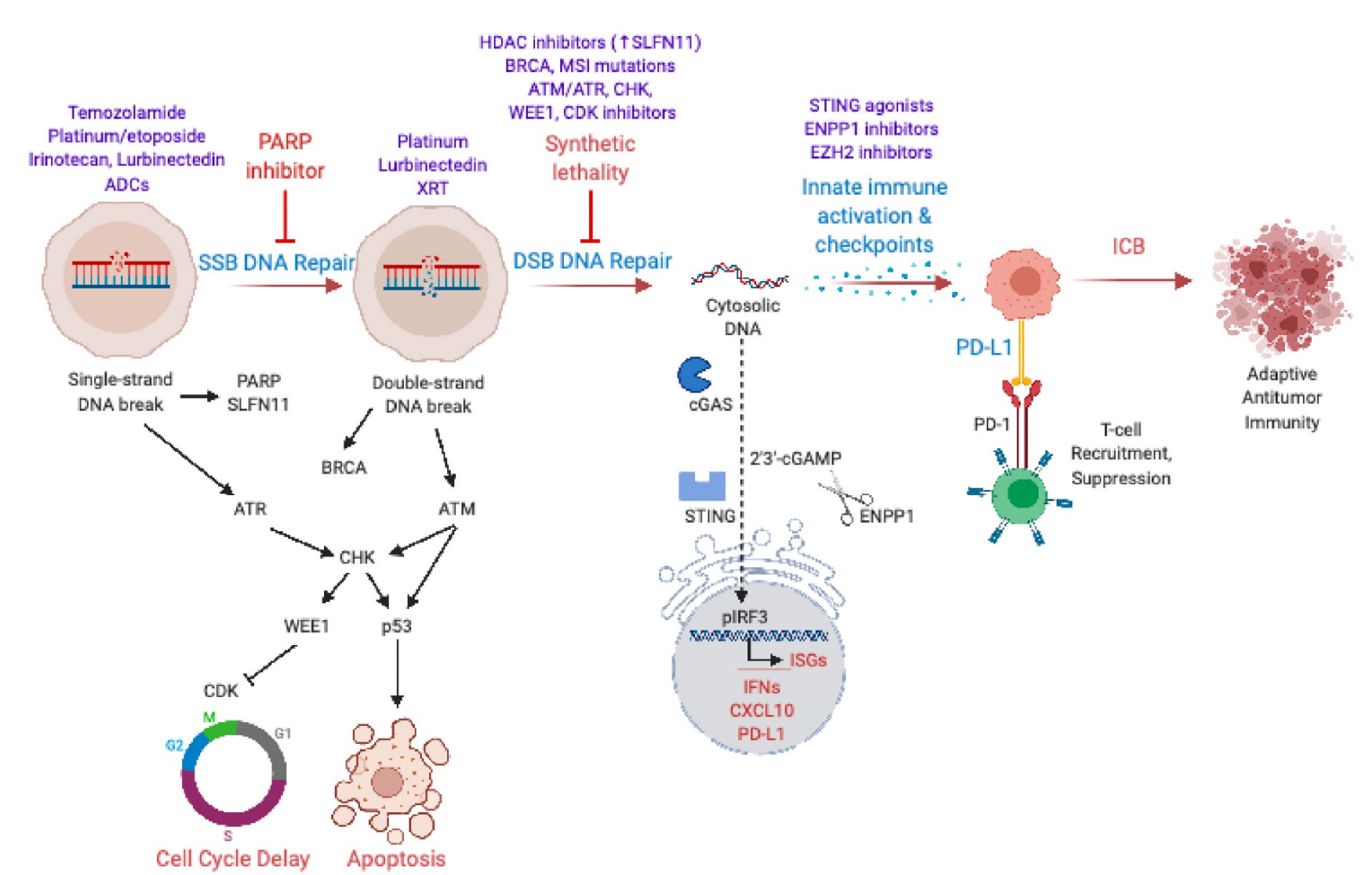
Erik H. Knelson [1], Shetal A. Patel [2] and Jacob M. Sands [1,*]

The Role of PARP in the DNA Damage Response



Knelson EH et al. *Cancers (Basel)* 2021 February 10;13(4):727.

PARP Inhibitor Combinations



Knelson EH et al. *Cancers (Basel)* 2021 February 10;13(4):727.

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KeyVibe-008: Randomized, Phase 3 Study of First-Line Vibostolimab plus Pembrolizumab plus Etoposide/Platinum versus Atezolizumab plus EP in Extensive-Stage Small Cell Lung Cancer

Sands J et al.

ASCO 2022;Abstract TPS8606.

Meet The Professor with Dr Sands

MODULE 1: Case Presentations

- Dr Miller: A 55-year-old woman with extensive-stage small cell lung cancer (ES-SCLC) who had an excellent response to chemo-IO and has been on maintenance IO for 2 years
- Dr Peswani: A 66-year-old woman with ES-SCLC who presented with SVC syndrome and has a near CR with chemo-IO
- Dr Yang: An 87-year-old woman with metastatic SCLC possibly of adrenal origin who has an excellent response to chemo-IO
- Dr Santiago: A 74-year-old man with recurrent ES-SCLC who has prolonged disease control on topetecan/trilaciclib
- Dr Miller: A 59-year-old woman with ES-SCLC and brain metastases who responds to chemo-IO but later has PD and has toxicity with topotecan
- Dr Mohamed: A 69-year-old woman with ES-SCLC who has PD on chemo-IO but responds to lurbinectidin with only mild toxicity
- Dr Carrizosa: A 73-year-old man with synchronous Stage III SCLC and Stage I NSCLC who receives concurrent CRT
- Dr Kumar: A 60-year-old woman with ES-SCLC who has a PR with chemo-IO but a residual splenic hilar lymph node
- Dr Miller: A 64-year-old woman with ES-SCLC who responds to chemo-IO but develops CNS oligometastasis on IO maintenance

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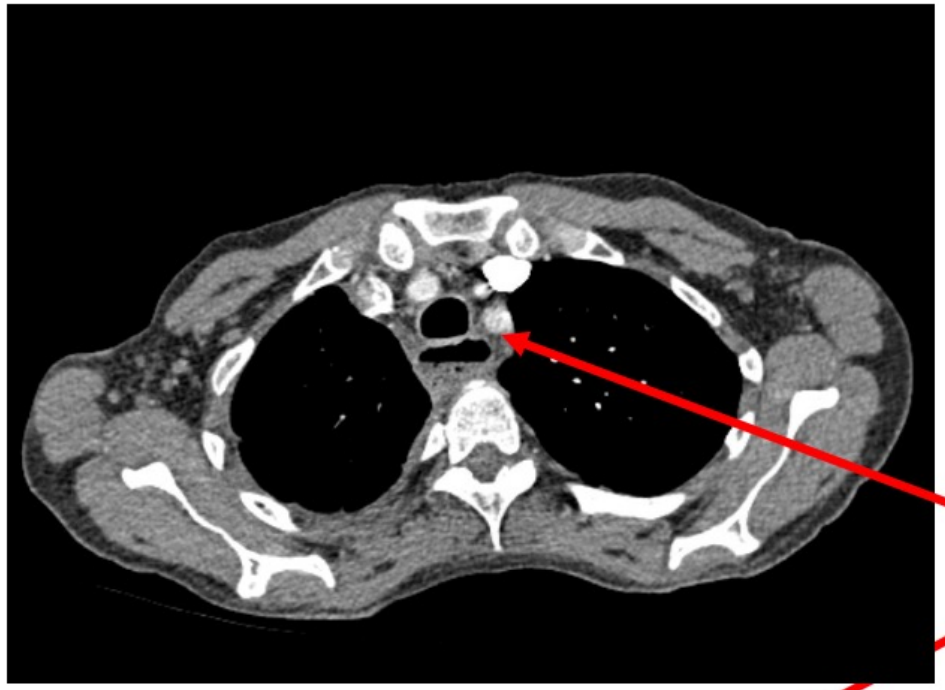
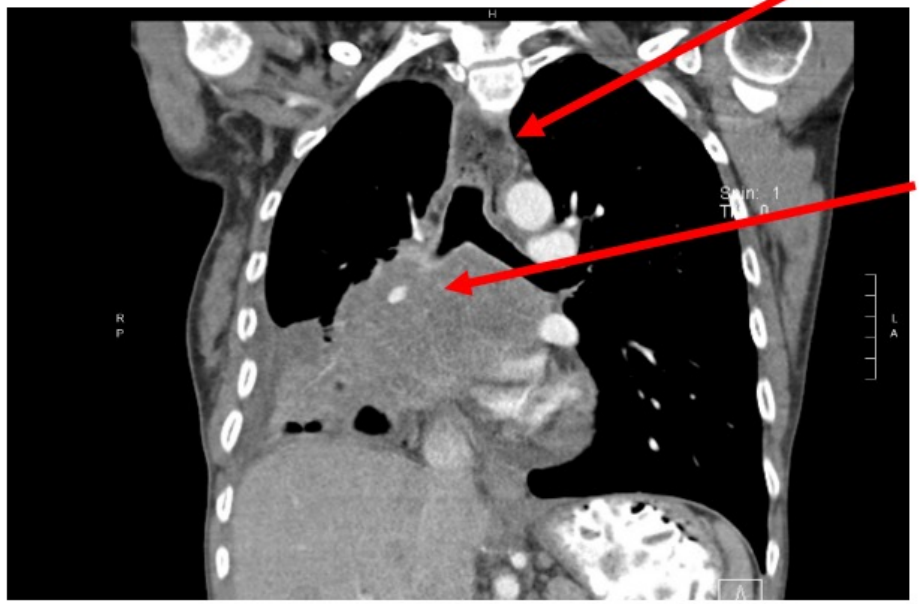
Case Presentation: A 55-year-old woman with ES-SCLC who had an excellent response to chemo-IO and has been on maintenance IO for 2 years

Dr Adam Miller (Danvers, Massachusetts)



Dilated esophagus from mass effect, with contents in proximal esophagus



Large conglomerate RIGHT hilar/mediastinal mass

Case Presentation: A 66-year-old woman with ES-SCLC who presented with SVC syndrome and has a near CR with chemo-IO

Dr Namrata Peswani (Richardson, Texas)

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Case Presentation: An 87-year-old woman with metastatic SCLC possibly of adrenal origin who has an excellent response to chemo-IO

Dr John Yang (Fall River, Massachusetts)

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Case Presentation: A 74-year-old man with recurrent ES-SCLC who has prolonged disease control on topetecan/trilaciclib

Dr Ferdy Santiago (Naples, Florida)

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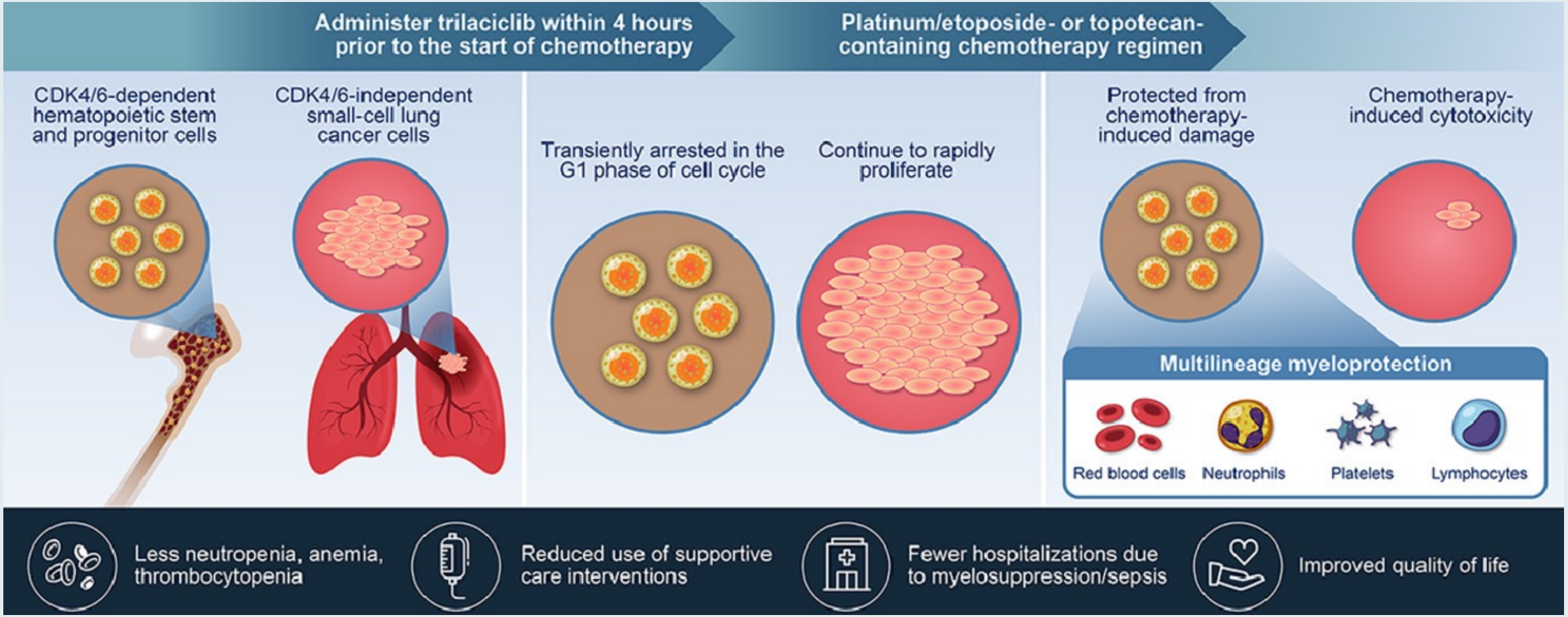
Trilaciclib: Mechanism of Action



Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

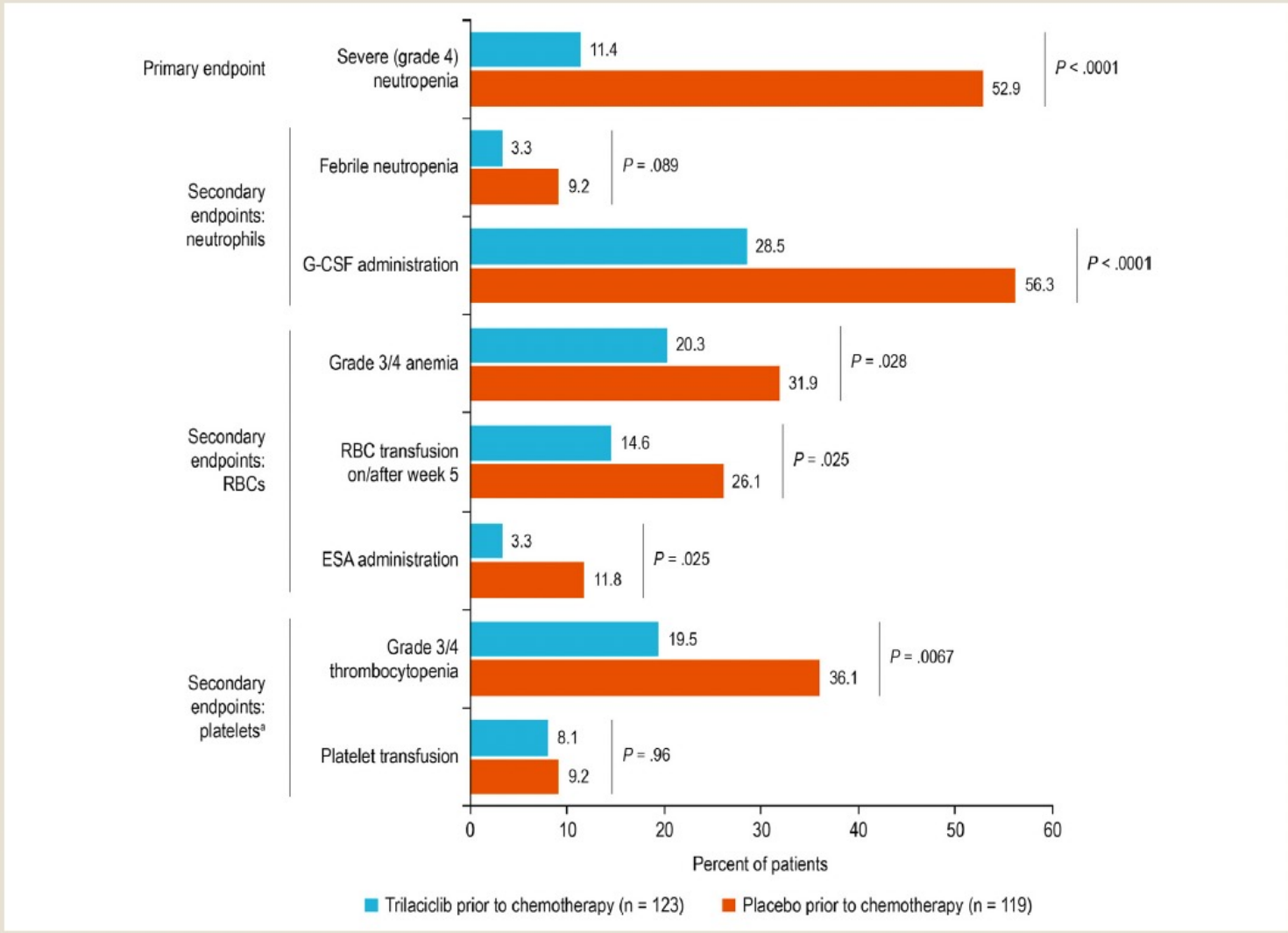
Clin Lung Cancer 2021;22(5):449-60.

Original Study

Effects of Trilaciclib on Chemotherapy-Induced Myelosuppression and Patient-Reported Outcomes in Patients with Extensive-Stage Small Cell Lung Cancer: Pooled Results from Three Phase II Randomized, Double-Blind, Placebo-Controlled Studies

Jared Weiss,[1] Jerome Goldschmidt,[2] Zoran Andric,[3] Konstantin H. Dragnev,[4] Chad Gwaltney,[5] Konstantina Skaltsa,[6] Yili Pritchett,[7] Joyce M. Antal,[7] Shannon R. Morris,[7] Davey Daniel[8,9]

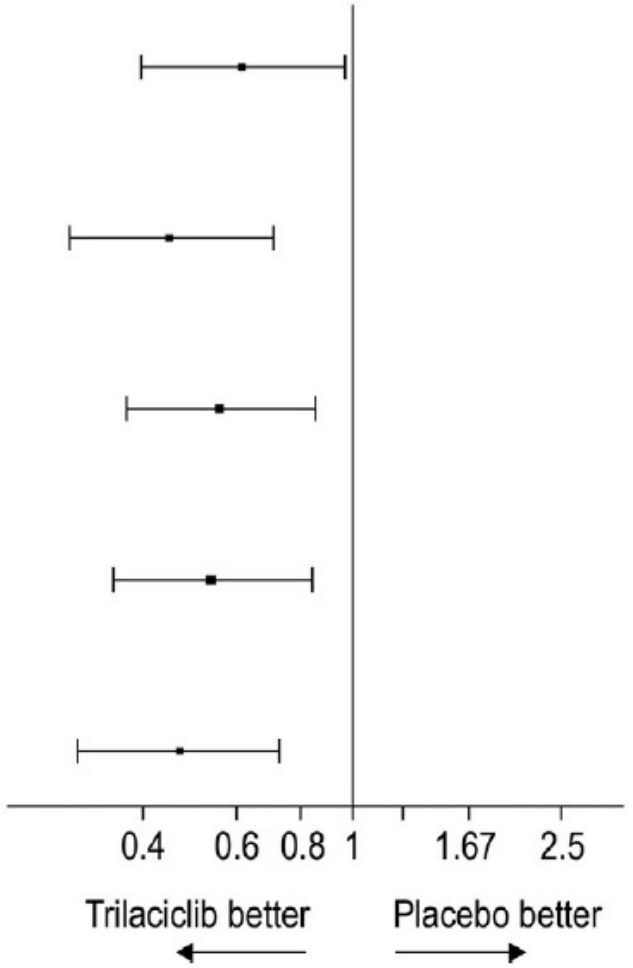
Myelopreservation Benefits with Trilaciclib Administered Prior to Chemotherapy



Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

Time to Confirmed Deterioration (TTCD) in Selected Patient-Reported Outcome Measures with Trilaciclib

Domain	Events, n Trilaciclib/placebo	TTCD, months Trilaciclib/placebo	Hazard ratio (95% CI)
Physical wellbeing	32/51	NYR/5.16	0.62 (0.40–0.97)
Functional wellbeing	31/55	7.62/3.78	0.45 (0.29–0.71)
Fatigue	39/61	7.03/2.33	0.56 (0.37–0.85)
Anemia trial outcome index	33/55	7.20/3.78	0.54 (0.35–0.84)
FACT-An total	31/58	NYR/3.48	0.47 (0.30–0.73)



Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

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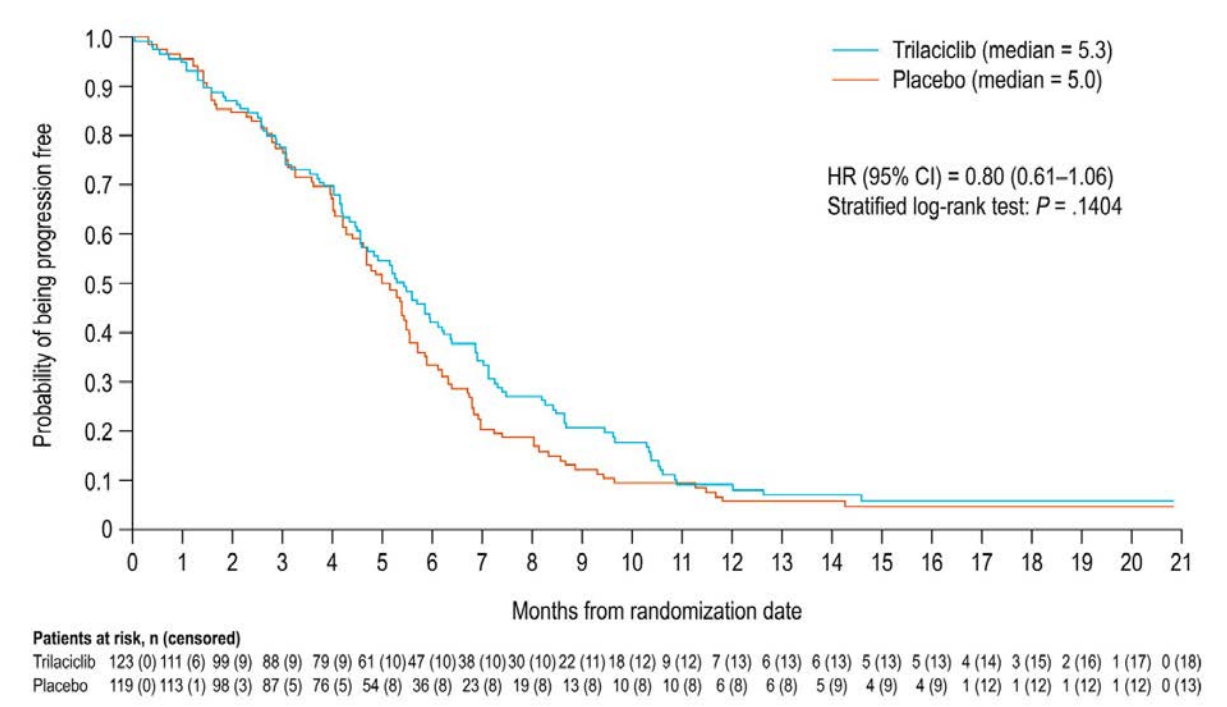
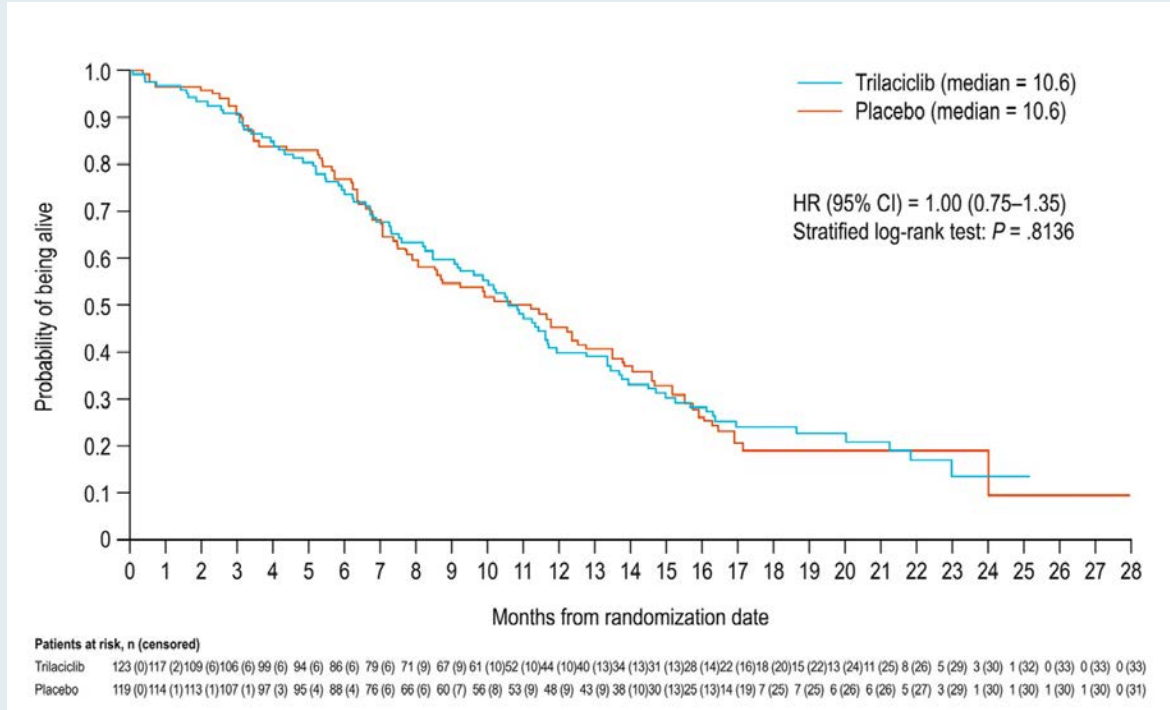
Progression-Free and Overall Survival for Patients Who Received Trilaciclib versus Placebo





Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

Summary of Adverse Events (AEs) in the Pooled Safety Population

Event	*n* (%)	
	Trilaciclib Prior to Chemotherapy (*n* = 122)	Placebo Prior to Chemotherapy (*n* = 118)
Any AE	115 (94.3)	114 (96.6)
Any placebo-/trilaciclib-related AE	45 (36.9)	49 (41.5)
Any serious AE	36 (29.5)	30 (25.4)
Any placebo-/trilaciclib-related serious AE	2 (1.6)	1 (0.8)
Any AE of grade ≥3	73 (59.8)	98 (83.1)
Any AE of grade ≥4	30 (24.6)	62 (52.5)
Any placebo-/trilaciclib-related AE of grade ≥3	10 (8.2)	18 (15.3)
Any hematologic AE	82 (67.2)	106 (89.8)
Any hematologic AE of grade ≥3	54 (44.3)	91 (77.1)
Any hematologic AE of grade ≥4	19 (15.6)	62 (52.5)
AESIs for trilaciclib	23 (18.9)	10 (8.5)
Any AE leading to discontinuation of any study drug	11 (9.0)	13 (11.0)
All-cause hospitalization	30 (24.6)	30 (25.4)
Hospitalization due to CIM or sepsis	5 (4.1)	16 (13.6)
Any AE leading to death	6 (4.9)	3 (2.5)

AESIs = adverse events of special interest

Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

Case Presentation: A 59-year-old woman with ES-SCLC and brain metastases who responds to chemo-IO but later has PD and has toxicity with topotecan

Dr Adam Miller (Danvers, Massachusetts)

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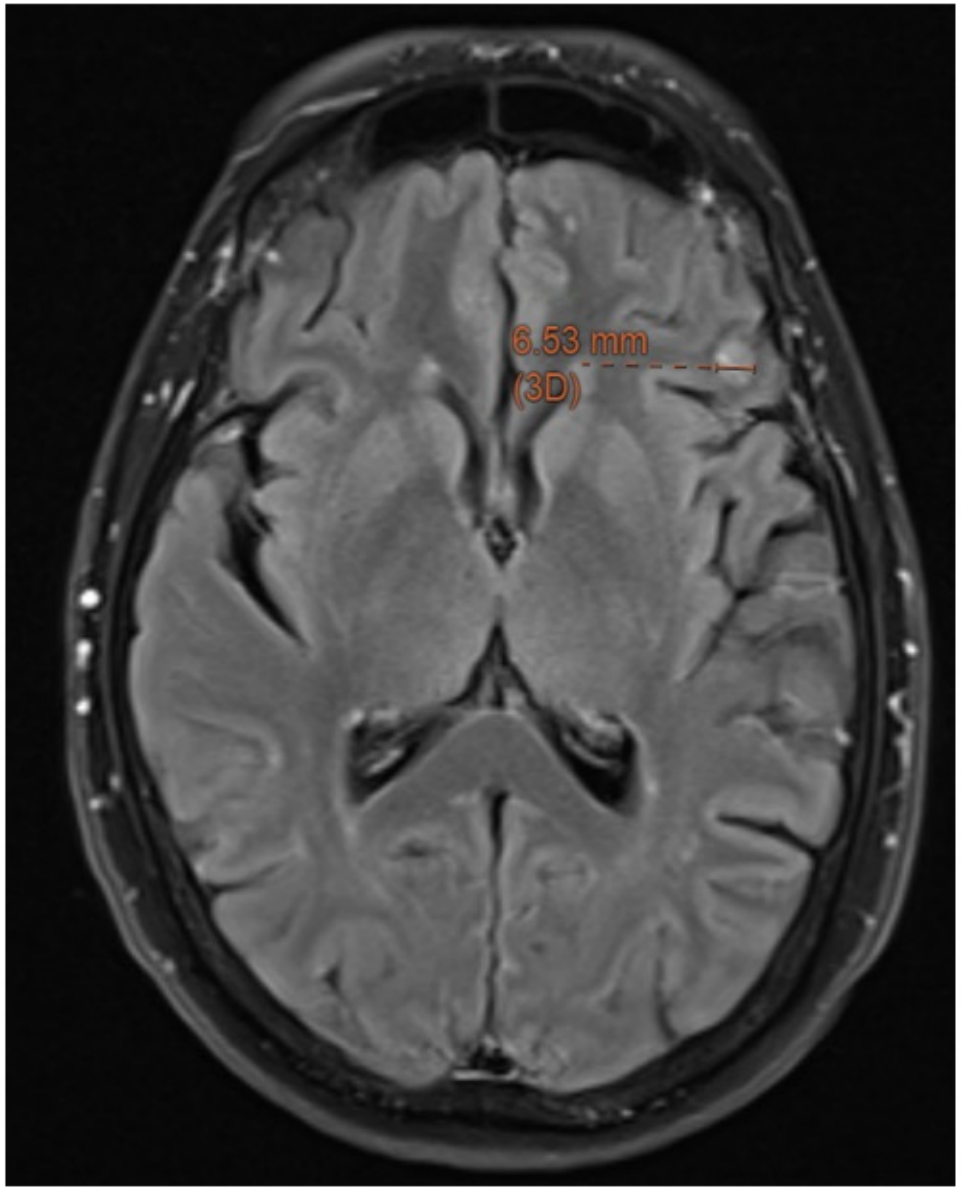
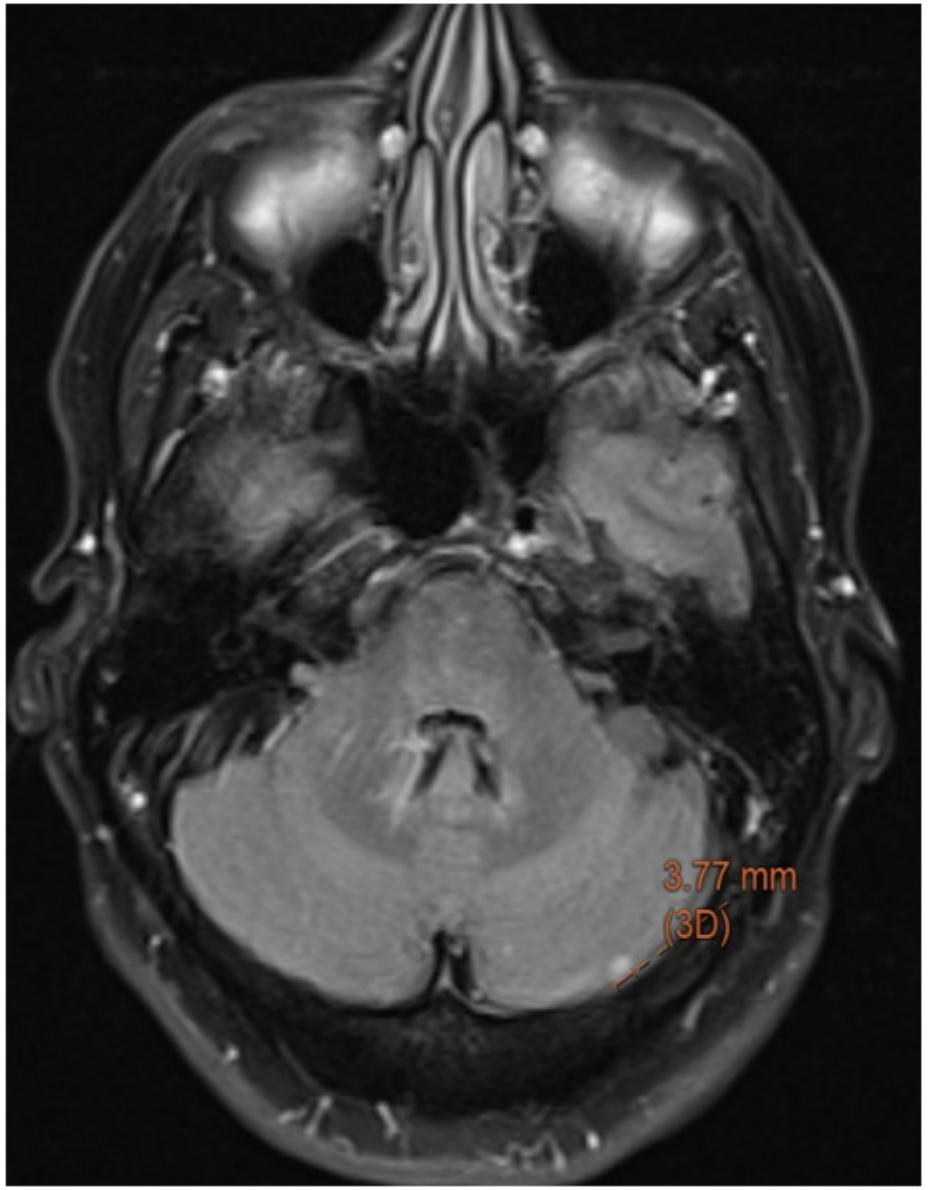
Left frontal lesion ~ 6.5 mm



3.7 mm left cerebellar lesion



Case Presentation: A 59-year-old woman with ES-SCLC and brain metastases who responds to chemo-IO and later has PD and has toxicity with topotecan (cont)

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Case Presentation: A 69-year-old woman with ES-SCLC who has PD on chemo-IO but responds to lurbinectidin with only mild toxicity

Dr Mohamed Mohamed (Greensboro, North Carolina)

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Therapeutic Advances in Medical Oncology *Review*

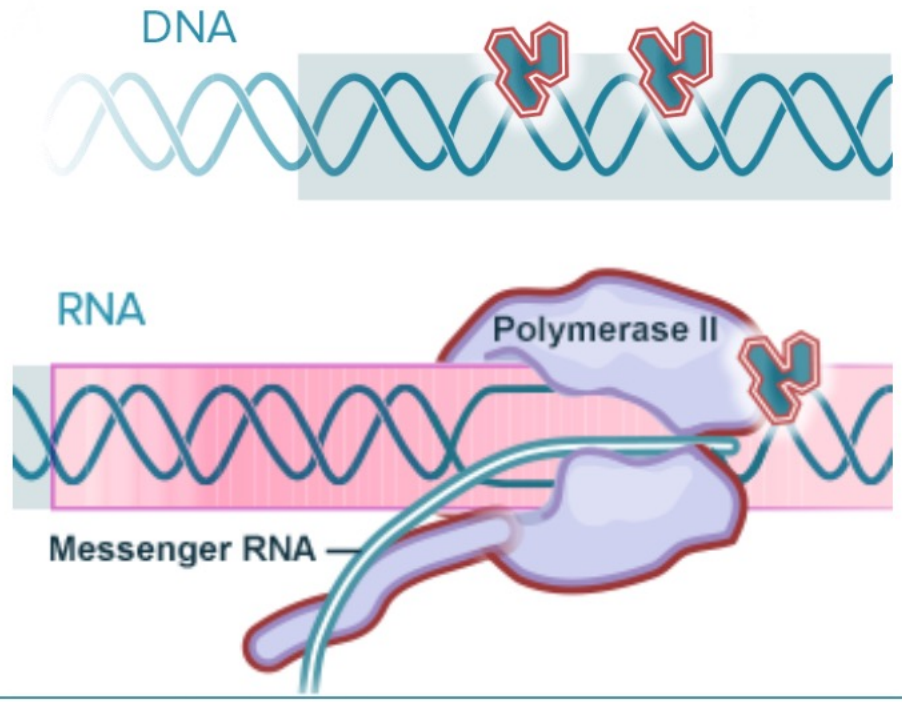
An overview of lurbinectedin as a new second-line treatment option for small cell lung cancer

Ther Adv Med Oncol
2021, Vol. 13: 1–9

Shetal Patel, William Jeffrey Petty and Jacob M. Sands

Lurbinectedin Mechanism of Action

Effects on the tumor



- Binds to guanine residues in the minor groove of DNA
- Affects activity of transcription factors

- Stalls RNA polymerase II
- Affects DNA repair pathways
- Results in eventual cell death

https://www.zepzelcapro.com/mechanism-of-action/

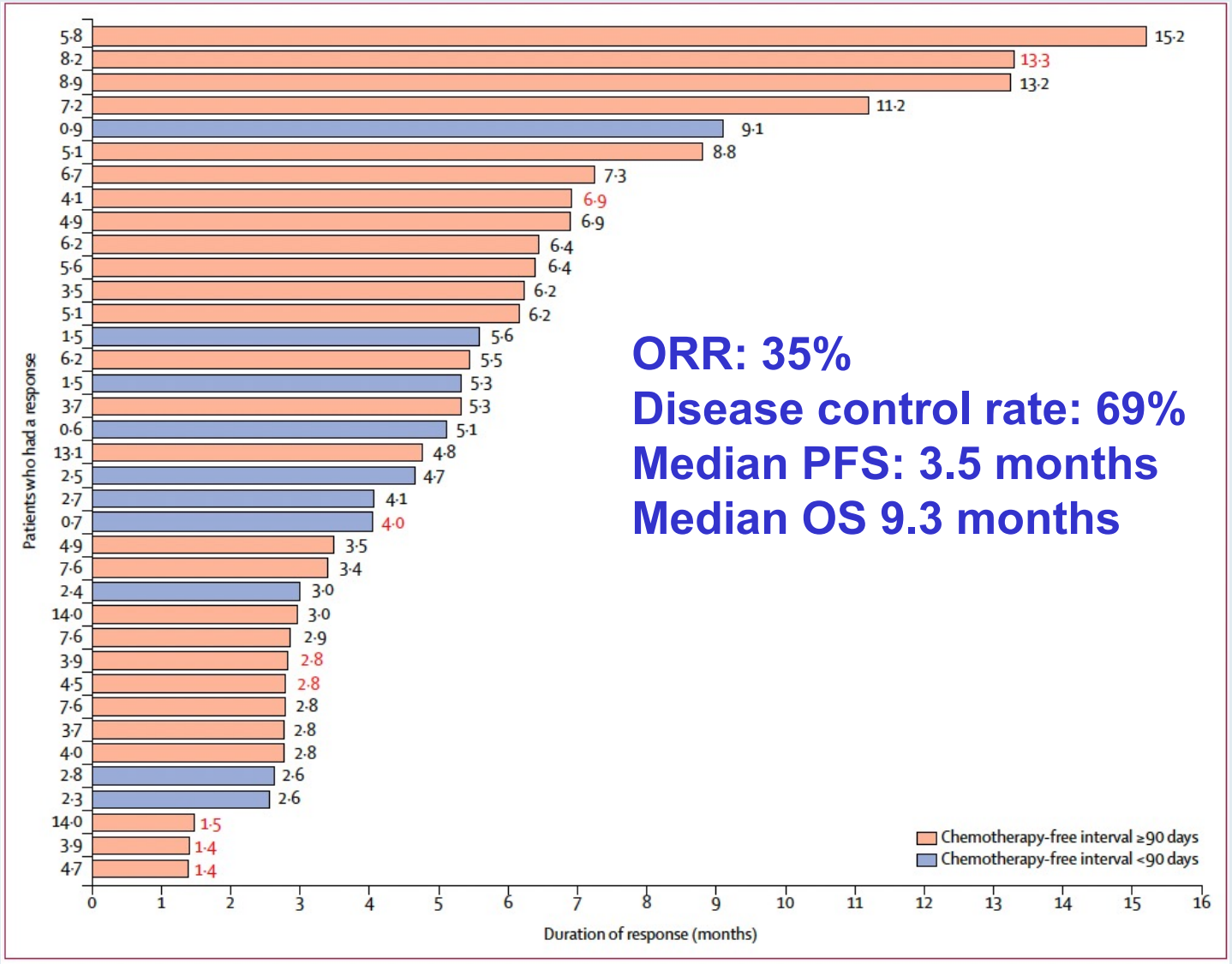
RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21(5):645-54.

Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial

José Trigo, Vivek Subbiah*, Benjamin Besse, Victor Moreno, Rafael López, María Angeles Sala, Solange Peters, Santiago Ponce, Cristian Fernández, Vicente Alfaro, Javier Gómez, Carmen Kahatt, Ali Zeaiter, Khalil Zaman, Valentina Boni, Jennifer Arrondeau, Maite Martínez, Jean-Pierre Delord, Ahmad Awada, Rebecca Kristeleit, Maria Eugenia Olmedo, Luciano Wannesson, Javier Valdivia, María Jesús Rubio, Antonio Anton, John Sarantopoulos, Sant P Chawla, Joaquín Mosquera-Martinez, Manolo D'Arcangelo, Armando Santoro, Victor M Villalobos, Jacob Sands, Luis Paz-Ares*

Response, Survival and Common AEs in the Pivotal Phase II Study of Lurbinectedin for SCLC After 1 Line of Chemotherapy



Common treatment-related adverse events		
	Grade 1-2	Grade 3-4
Anemia	87%	9%
Leukopenia	50%	29%
Neutropenia	26%	46%
Thrombocytopenia	37%	7%

AEs = adverse events; ORR = overall response rate;
PFS = progression-free survival; OS = overall survival

Trigo J et al. *Lancet Oncol* 2020;21(5):645-54.

Lurbinectedin/doxorubicin *versus* CAV or topotecan in relapsed SCLC patients: Phase III randomized ATLANTIS trial

Luis Paz-Ares[1]

[1]Hospital Universitario 12 de Octubre, Madrid, Spain

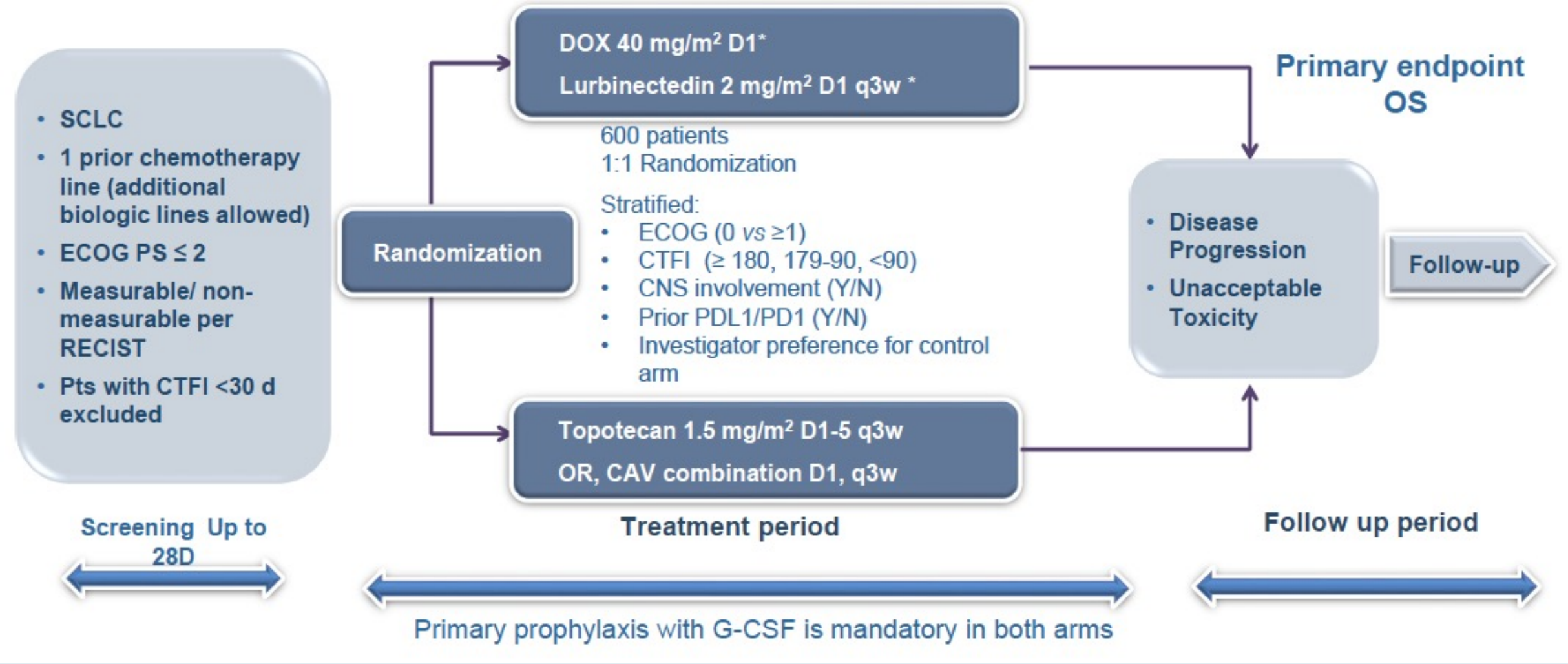
Tudor Eliade Ciuleanu[2], Alejandro Navarro[3], Andrea Fulop[4], Sophie Cousin[5], Laura Bonanno[6], Egbert Smit[7], Alberto Chiappori[8], Mª Eugenia Olmedo[9], Ildiko Horvath[10], Christian Gröhé[11], José Antonio López-Vilariño[12], Rafael Núñez[12], Antonio Nieto[12], Martin Cullell-Young[12], Noelia Vasco[12], Carmen Kahatt[12], Ali Zeaiter[12], Enric Carcereny[13], Jaromir Roubec[14], Konstantios Syrigos[15], Gregory Lo[16], Isidoro Barneto[17].

[2]Institutul Oncologic Prof. Dr. Ion Chiricuta, și Universitatea de medicina și farmacie Iuliu Hatieganu , Cluj-Napoca, Romania. [3]Hospital Vall d´Hebrón, Barcelona, Spain. [4]Orszagos Koranyi TBC es Pulmonologiai Intezet, 6, Budapest, Hungary. [5] CRLCC Institut Bergonie, Bordeaux, France. [6]Istituto Oncologico Veneto, Padova, Italy. [7]Antonie van Leeuwenhoek Ziekenhuis, Amsterdam, The Netherlands. [8]H. Lee Moffitt Cancer Center & Research Institute, Tampa (FL), USA. [9]Hospital Universitario Ramón y Cajal, Madrid, Spain. [10]Orszagos Koranyi TBC es Pulmonologiai Intezet, 14, Budapest, Hungary. [11]Evangelische Lungenklinik, Berlin, Germany. [12]Pharma Mar, S.A., Colmenar Viejo, Madrid, Spain. [13] Institut Català d'Oncologia-Hospital Germans Trias i Pujol B-ARGO GROUP, Badalona, Spain. [14]Nemocnice AGEL, Ostrava-Vitkovice, Czech Republic. [15]3rd Department of Medicine, National & Kapodistrian University of Athens. [16]Lakeridege Hospital, Oshawa (ON), Canada. [17]Hospital Reina Sofía, Córdoba, Spain.

IASLC 2021 World Conference on Lung Cancer
SEPTEMBER 8 - 14, 2021 I WORLDWIDE VIRTUAL EVENT

Abstract PL02.03

ATLANTIS: Phase III Trial Design

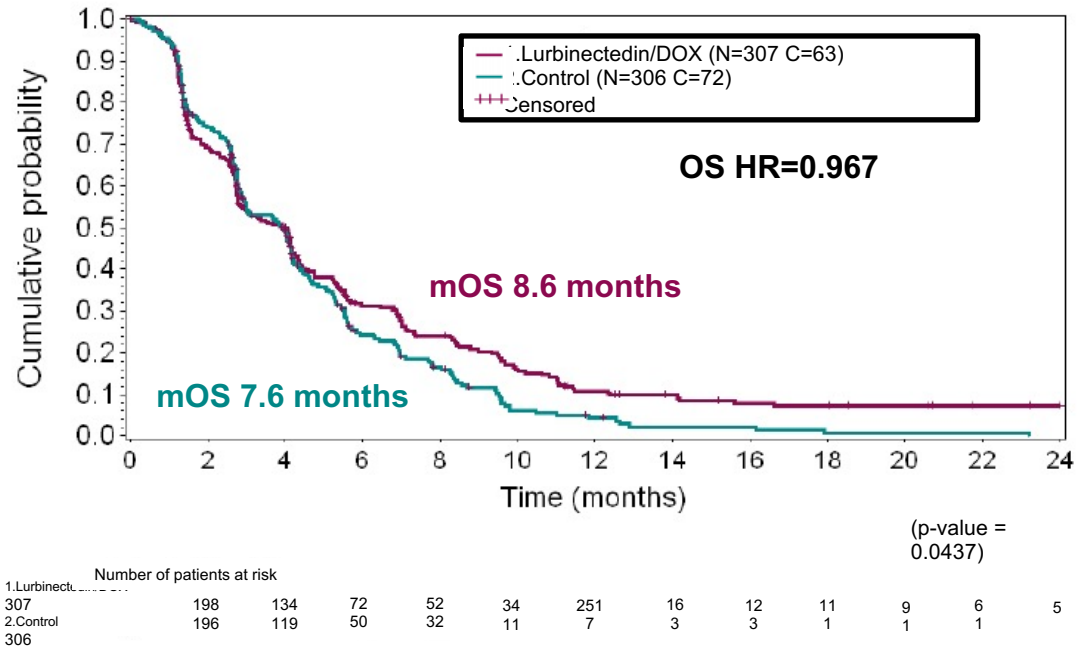


DOX = doxorubicin; OS = overall survival; CTFI = chemotherapy-free interval; CAV = cyclophosphamide, doxorubicin and vincristine

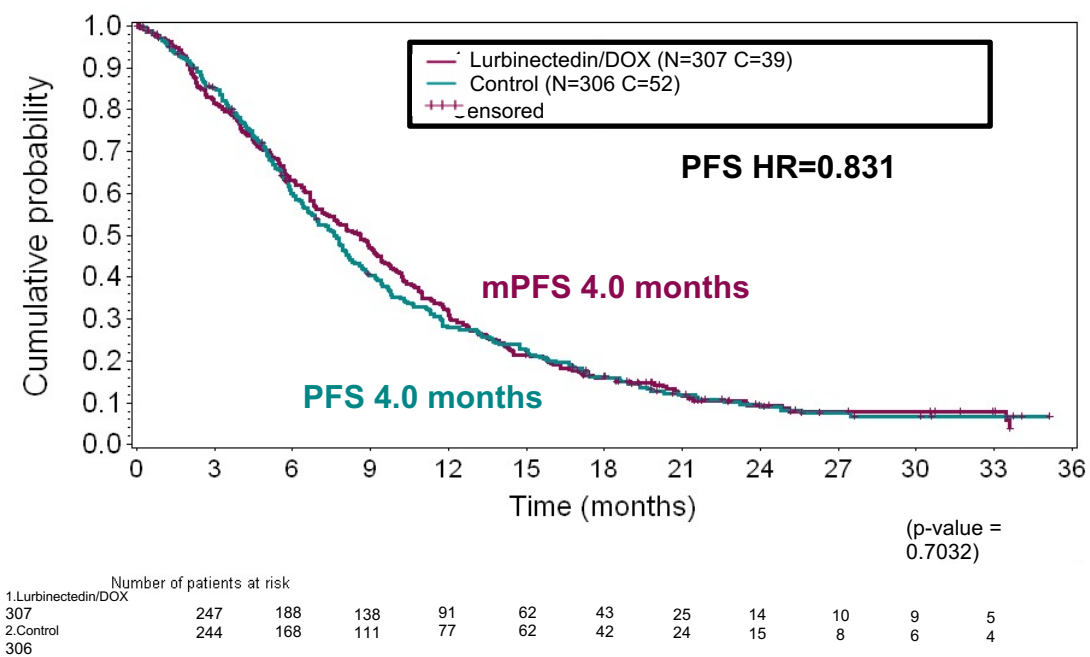
Paz-Ares et al. WCLC 2021;Abstract PL02.03.

ATLANTIS: Lurbinectedin with Doxorubicin versus CAV or Topotecan for Patients with Relapsed SCLC

Overall Survival



Progression-free Survival



CAV = cyclophosphamide, doxorubicin and vincristine; DOX = doxorubicin; OS = overall survival; mOS = median OS; PFS = progression-free survival; mPFS = median PFS

Paz-Ares et al. WCLC 2021;Abstract PL02.03.

ATLANTIS: Safety Summary

Hematological	Lurbinectedin+DOX (n=303)	Control (n=289)	
	Grade ≥3	Grade ≥3	p-value
Anaemia	44 (14.5)	90 (31.1)	<0.0001
Neutropenia	112 (37.0)	200 (69.2)	<0.0001
Febrile neutropenia	12 (4.0)	24 (8.3)	0.0377
Thrombocytopenia	42 (13.9)	90 (31.1)	<0.0001

Non hematological	Lurbinectedin+DOX (n=303)	Control (n=289)	
	Grade ≥3	Grade ≥3	p-value
ALT increased	6 (2.0)	3 (1.0)	0.5057
AP increased	2 (0.7)	3 (1.0)	0.6783
AST increased	7 (2.3)	4 (1.4)	0.5463
Fatigue	26 (8.6)	31 (10.7)	0.4051
Nausea	6 (2.0)	4 (1.4)	0.7525
Vomiting	4 (1.3)	0	0.1242

	Lurbinectedin+DOX (n=303) n (%)	Control (n=289) n (%)
Any AE treatment-related	268 (88.4)	266 (92.0)
Any grade ≥3 AE	**143 (47.2)**	**218 (75.4)**
Any grade 4 AE	**49 (16.2)**	**158 (54.7)**
Any grade ≥3 SAE	38 (12.5)	83 (28.7)
Death associated with AEs	**1 (0.3)**	**10 (3.5)**
Treatment discontinuations associated with AEs	23 (7.6)	45 (15.6)
Delays associated with AEs	79 (26.1)	99 (34.3)
Reductions associated with AEs	66 (21.8)	138 (47.8)

DOX = doxorubicin; AE = adverse event; SAE = serious AE

Paz-Ares et al. WCLC 2021;Abstract PL02.03.

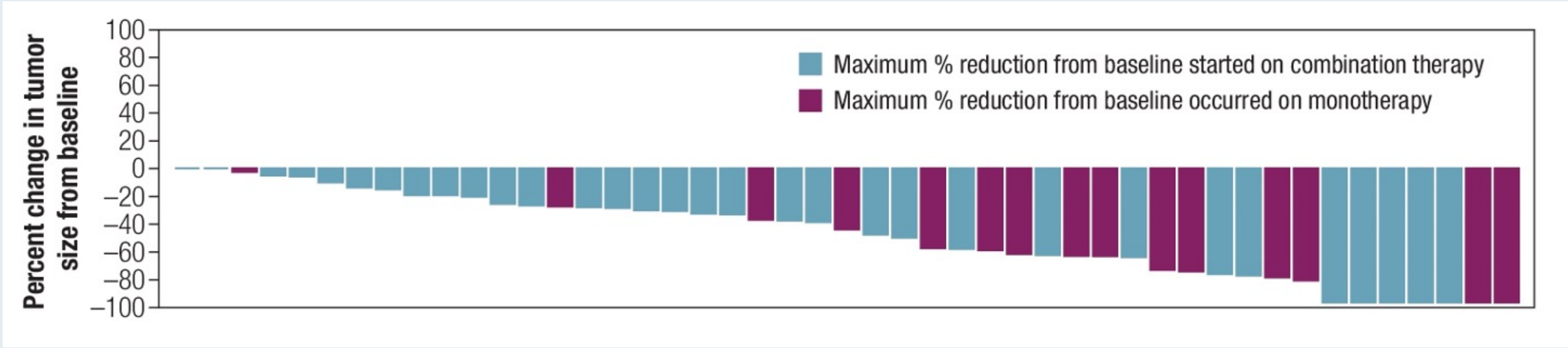
Analysis of Patients With Relapsed Small Cell Lung Cancer (SCLC) Receiving Single-agent Lurbinectedin in the Phase 3 ATLANTIS Trial

Alejandro Navarro,[1,*] Santiago Ponce Aix,[2,3] Isidoro C. Barneto,[4] Egbert F. Smit,[5] José Antonio López-Vilariño,[6] Antonio Nieto,[6] Carmen Kahatt,[6] Ali Zeaiter,[6] Sophie Cousin,[7] Helge Bischoff,[8] Jaromir Roubec,[9] Konstantinos Syrigos,[10] Luis Paz-Ares[3]

ASCO 2022 | Abstract 8524

RTP RESEARCH TO PRACTICE

ATLANTIS: Change in Tumor Size from Baseline During Combination Therapy or Monotherapy (IRC)



Navarro A et al. ASCO 2022;Abstract 8524.

RTP RESEARCH TO PRACTICE

ATLANTIS: Change in Tumor Size from Baseline During Combination Therapy or Monotherapy (IRC)

Best response to lurbinectedin + doxorubicin	Best response on lurbinectedin monotherapy 3.2 mg/m²			
	CR	PR	SD	PD
CR (n = 3)	3			
PR (n = 26)	3	15		8
SD (n = 19)	1	2	8	8
	Improving response ⟵		⟶ Declining response	

The majority (32/48) of patients who switched to lurbinectedin monotherapy maintained or improved the tumor response achieved on combination therapy (16 patients had progressive disease)

Navarro A et al. ASCO 2022;Abstract 8524.

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.

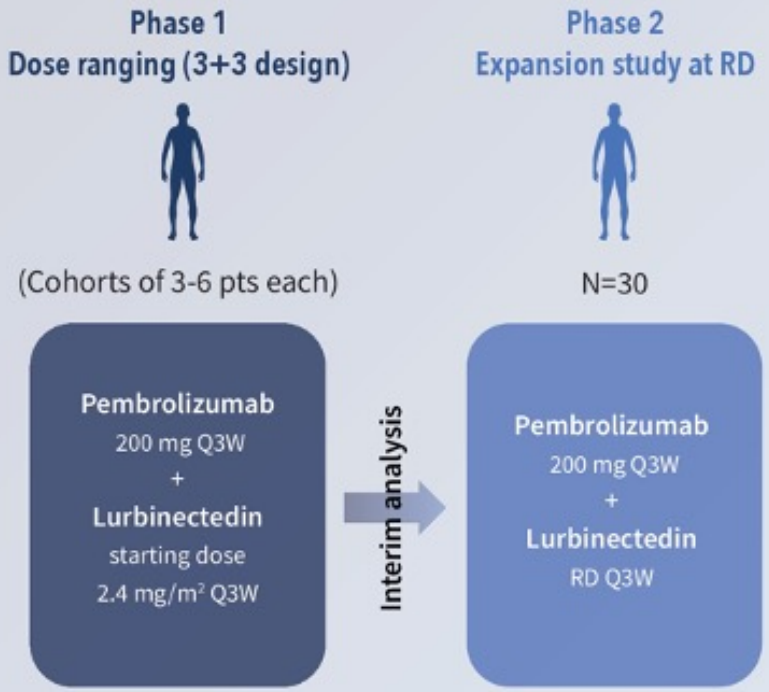
ASCO 2022;Abstract 8581.

LUPER Phase I/II Study Design

Prospective phase I/II, multicenter, open-label study (NCT04358237)

Key inclusion criteria

- ≥18 years with confirmed SCLC
- ECOG PS 0-1
- Measurable disease as per RECIST v.1.1
- Progression to a CT-containing regimen (≥4 weeks before study initiation)
- Previous immunotherapy NOT allowed
- Pts with treated, stable, asymptomatic brain metastases (BMs) are allowed



The RP2D was the highest DL at which 0/3 pts or ≤1/6 pts experienced DLTs during the first cycle.
P and L will be administered Day 1 Q3W until disease progression, unacceptable toxicity, or consent withdrawal.

Primary endpoints

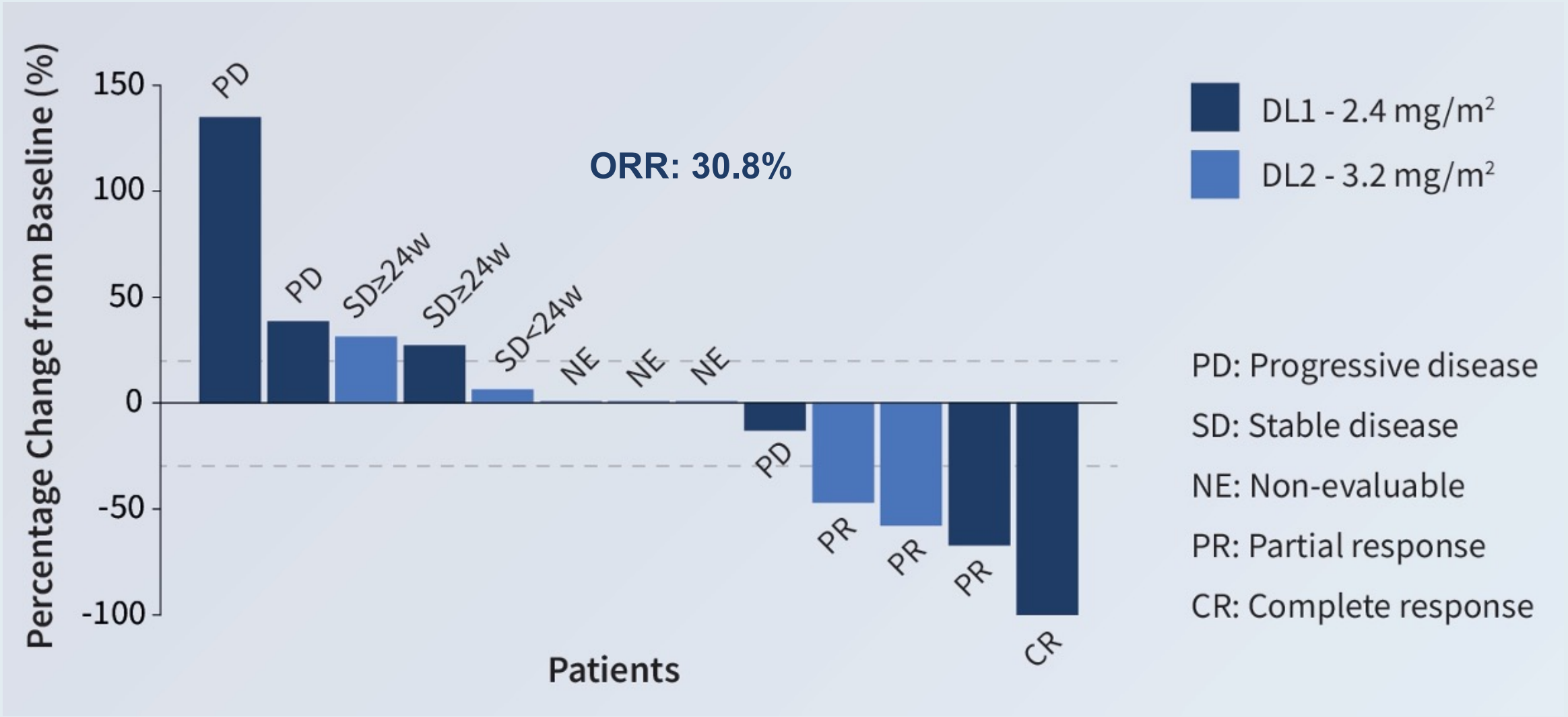
- Phase 1: MTD and RD of L in combination with P for phase II in pts with relapsed SCLC.
- Phase 2: Efficacy of L in combination with P in terms of ORR, according to RECIST 1.1, in pts with relapsed SCLC.

Secondary endpoints

- Safety as per CTCAE 5.0, preliminary efficacy, and pharmacokinetics.

Calles A et al. ASCO 2022;Abstract 8581.

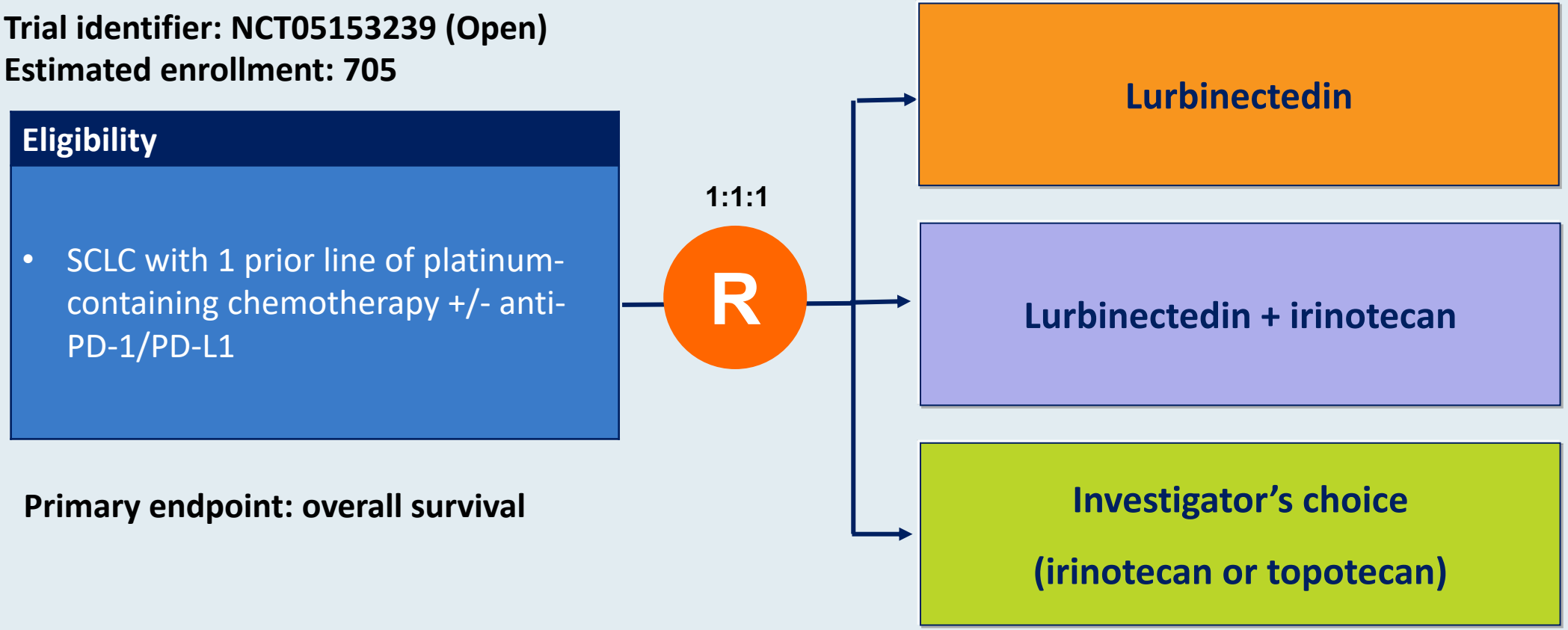
LUPER: Best Overall Response



Calles A et al. ASCO 2022;Abstract 8581.

Ongoing Phase III LAGOON Study Design

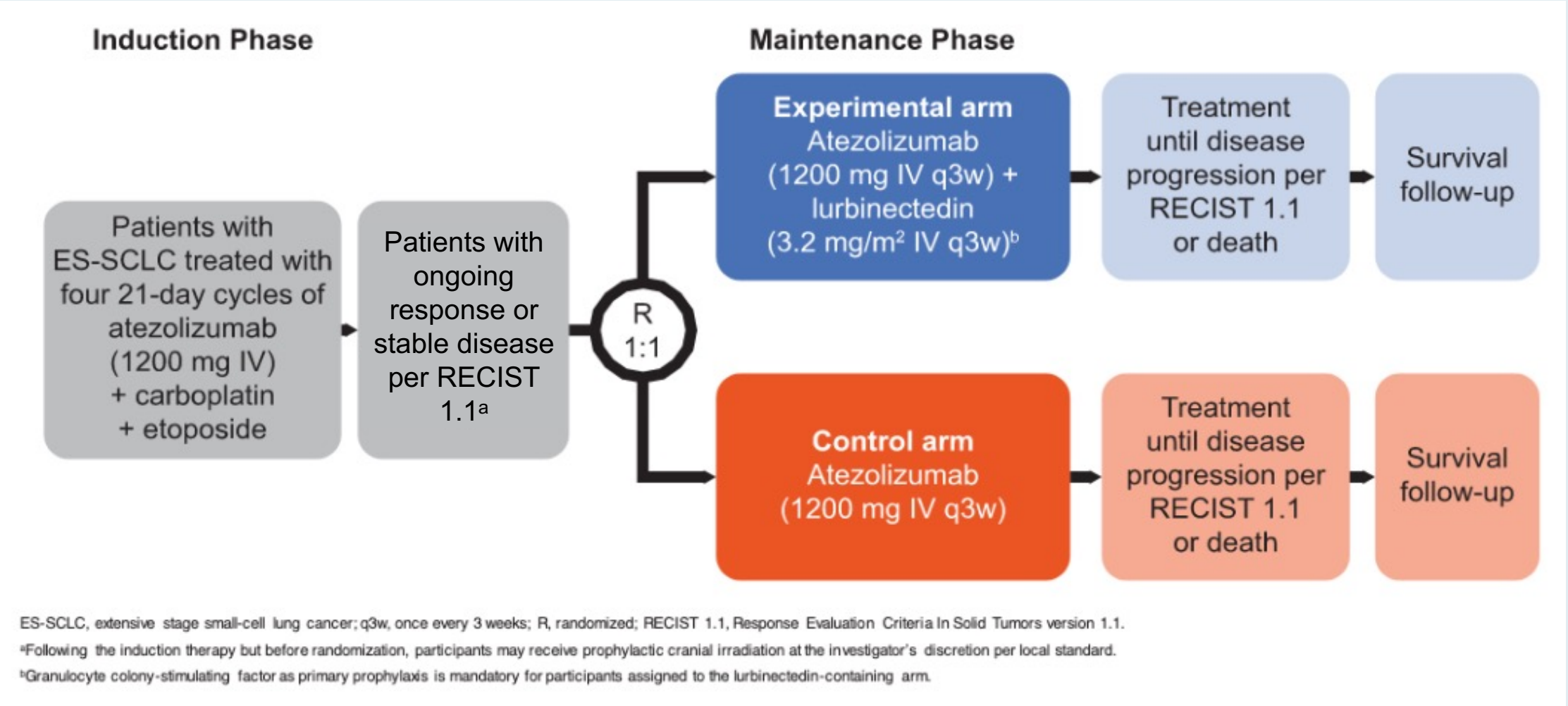
Trial identifier: NCT05153239 (Open)
Estimated enrollment: 705



Primary endpoint: overall survival

www.clinicaltrials.gov. NCT05153239. Accessed July 2022.

IMforte Phase III Study Schema: Maintenance Therapy with Lurbinectedin and Atezolizumab versus Atezolizumab



ES-SCLC, extensive stage small-cell lung cancer; q3w, once every 3 weeks; R, randomized; RECIST 1.1, Response Evaluation Criteria In Solid Tumors version 1.1.

[a]Following the induction therapy but before randomization, participants may receive prophylactic cranial irradiation at the investigator's discretion per local standard.

[b]Granulocyte colony-stimulating factor as primary prophylaxis is mandatory for participants assigned to the lurbinectedin-containing arm.

Paz-Ares L et al. IASLC 2022;Abstract EP14.02-015.

Case Presentation: A 73-year-old man with synchronous Stage III SCLC and Stage I NSCLC who receives concurrent CRT

Dr Daniel Carrizosa (Charlotte, North Carolina)

RTP RESEARCH TO PRACTICE

Case Presentation: A 60-year-old woman with ES-SCLC who has a PR with chemo-IO but has a residual splenic hilar lymph node

Dr KS Kumar (Trinity, Florida)

RTP RESEARCH TO PRACTICE

Case Presentation: A 64-year-old woman with ES-SCLC who responds to chemo-IO but develops CNS oligometastasis on IO maintenance

Dr Adam Miller (Danvers, Massachusetts)

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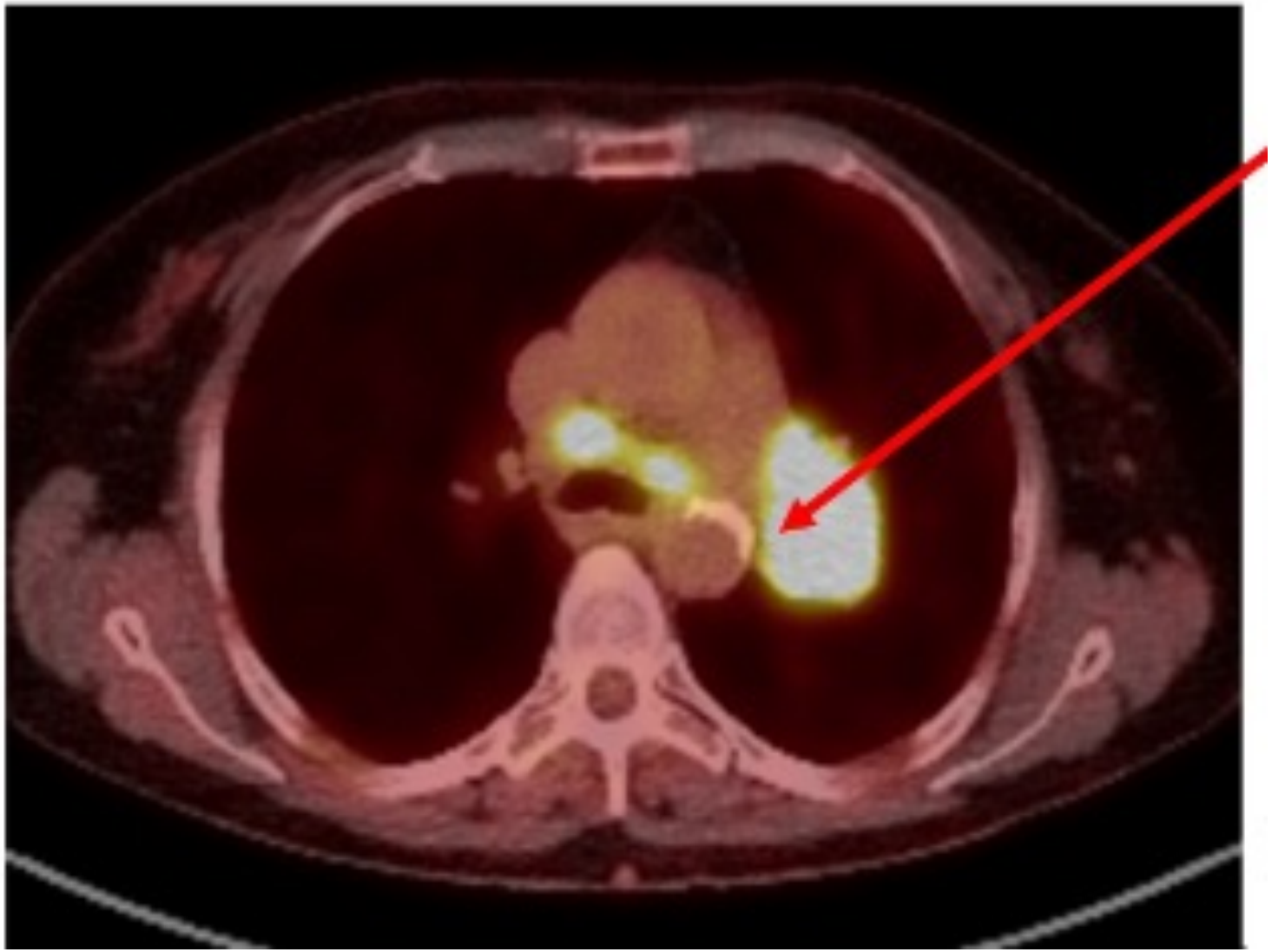
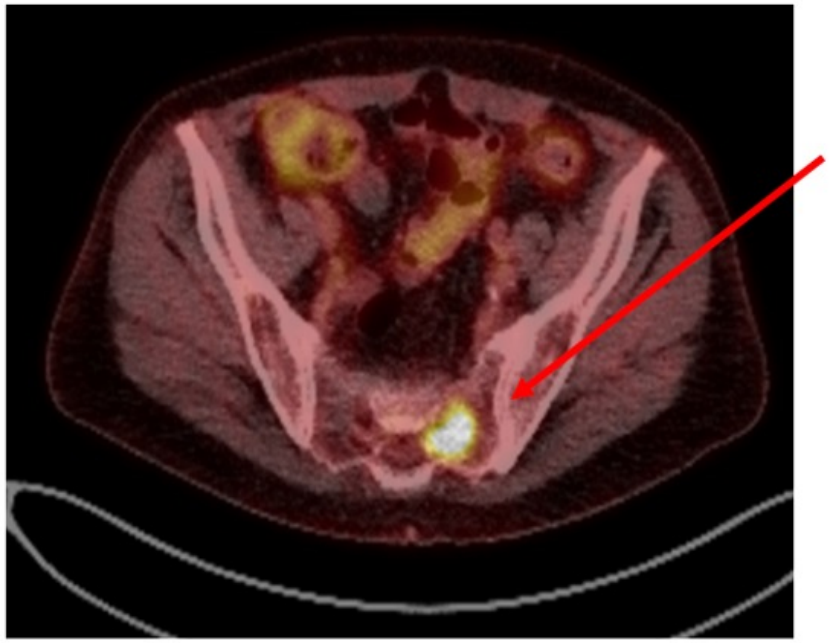
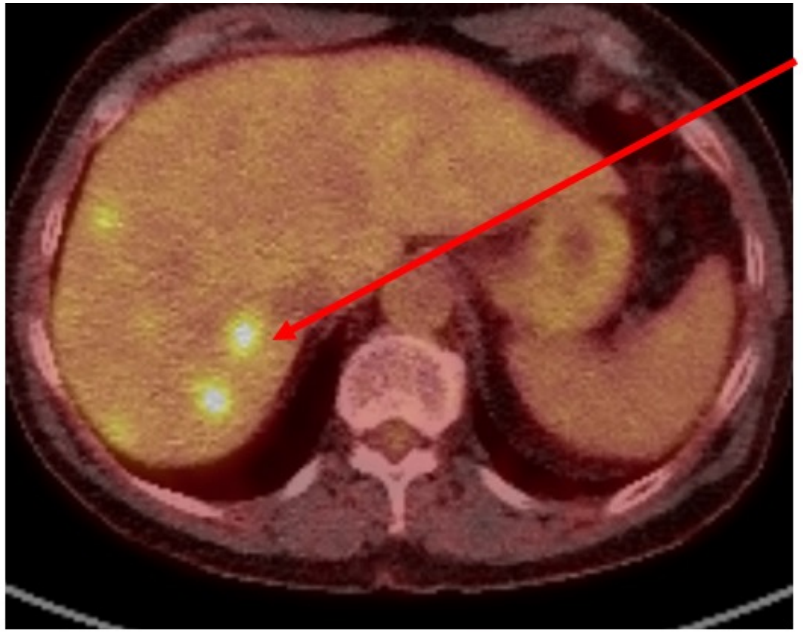


Chest CT: Left hilar FDG-avid mass with FDG-avid mediastinal lymphadenopathy



Pelvis: FDG-avid bone metastasis



Liver: FDG-avid hepatic metastasis

Meet The Professor with Dr Sands

Introduction: Journal Club

MODULE 1: Case Presentations

MODULE 2: Appendix of Key Publications

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RESEARCH
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First-Line Therapy for Extensive-Stage Small Cell Lung Cancer (ES-SCLC)

original reports

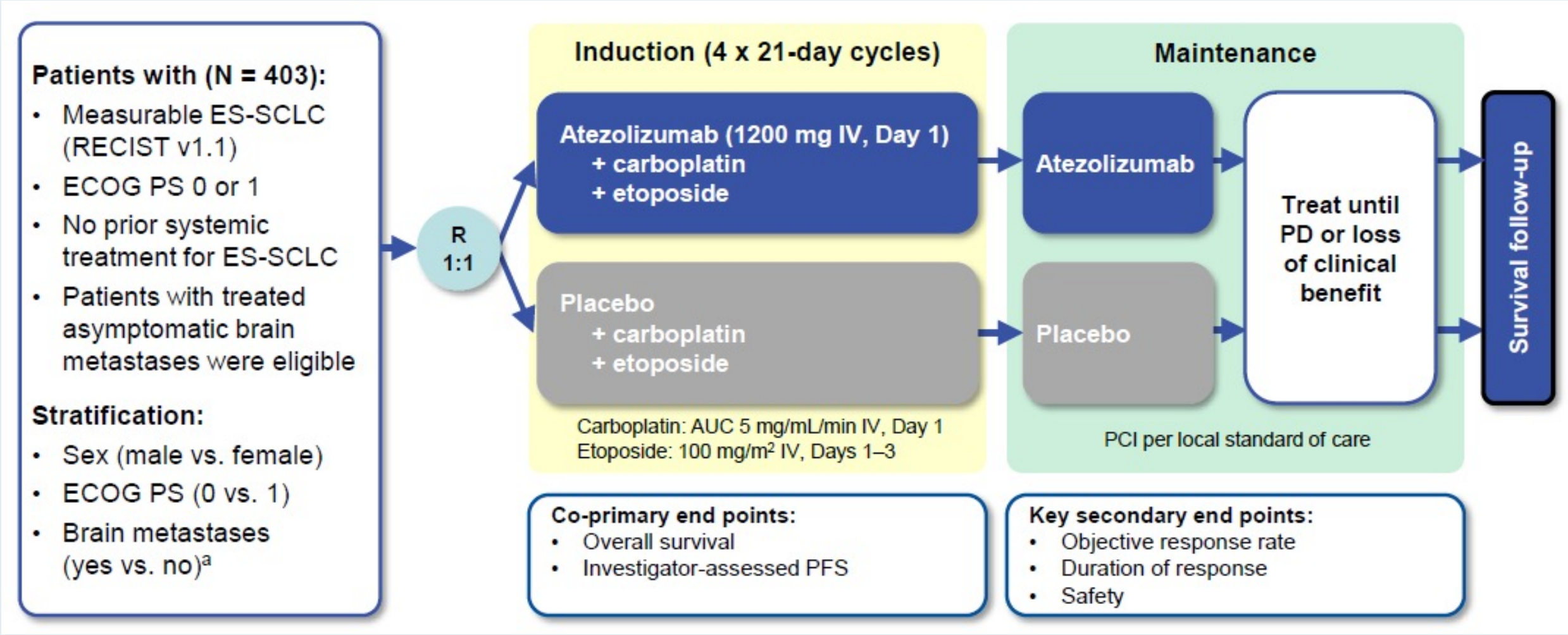
Updated Overall Survival and PD-L1 Subgroup Analysis of Patients With Extensive-Stage Small-Cell Lung Cancer Treated With Atezolizumab, Carboplatin, and Etoposide (IMpower133)

Stephen V. Liu, MD[1]; Martin Reck, MD, PhD[2]; Aaron S. Mansfield, MD[3]; Tony Mok, MD[4]; Arnaud Scherpereel, MD, PhD[5]; Niels Reinmuth, MD, PhD[6]; Marina Chiara Garassino, MD[7]; Javier De Castro Carpeno, MD[8]; Raffaele Califano, MD[9]; Makoto Nishio, MD[10]; Francisco Orlandi, MD[11]; Jorge Alatorre-Alexander, MD[12]; Ticiana Leal, MD[13]; Ying Cheng, MD[14]; Jong-Seok Lee, MD[15]; Sivuonthanh Lam, PharmD[16]; Mark McCleland, PhD[16]; Yu Deng, PhD[16]; See Phan, MD[16]; and Leora Horn, MD[17]

J Clin Oncol 2021;39(6):619-30.

RTP RESEARCH TO PRACTICE

IMpower133: Phase III Study Design

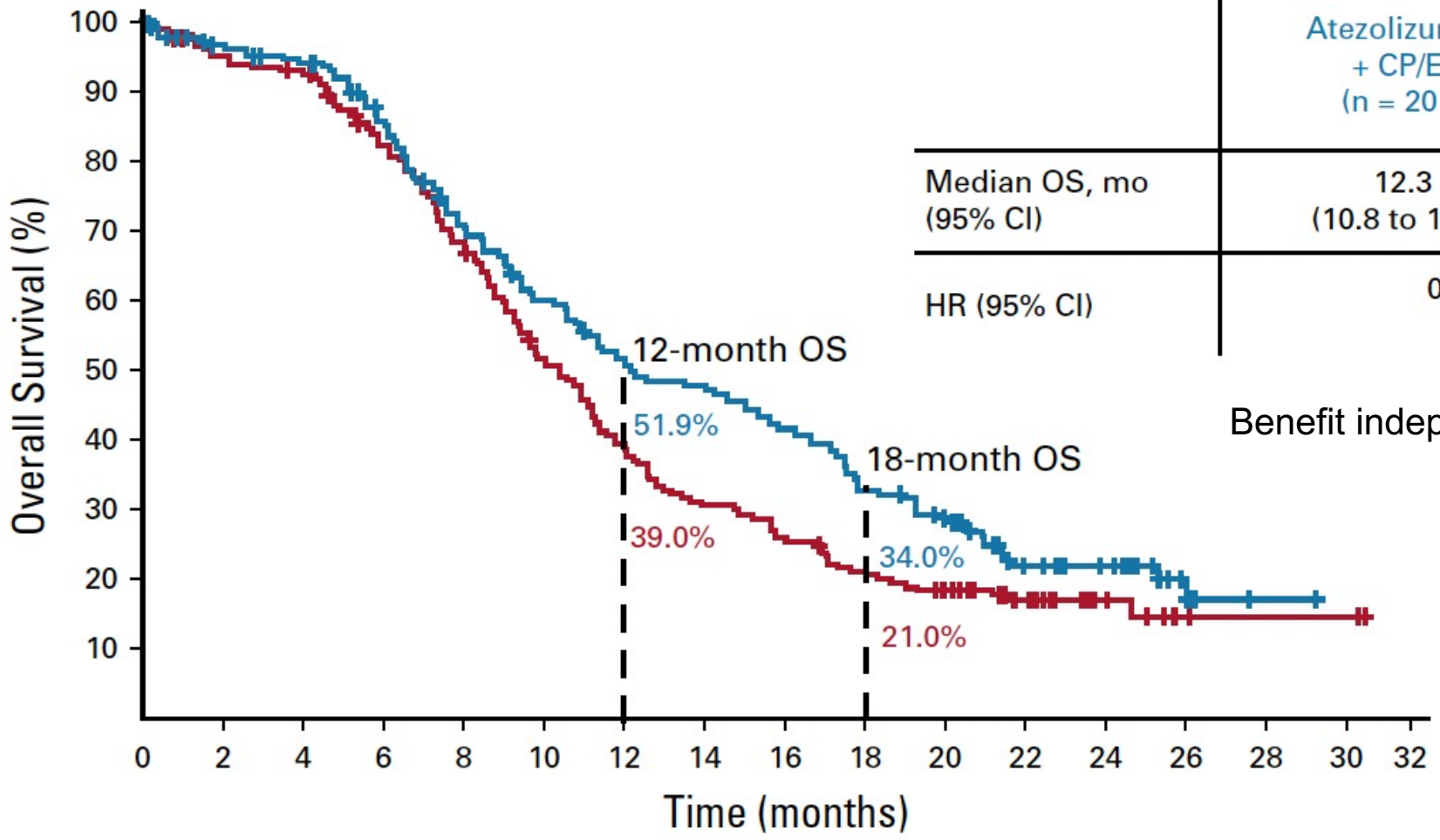


ES-SCLC = extensive-stage small cell lung cancer; PD = disease progression; PFS = progression-free survival

Liu SV et al. *J Clin Oncol* 2021;39(6):619-30.

IMpower133: Updated OS (ITT Population)

Median follow up: 22.9 mo



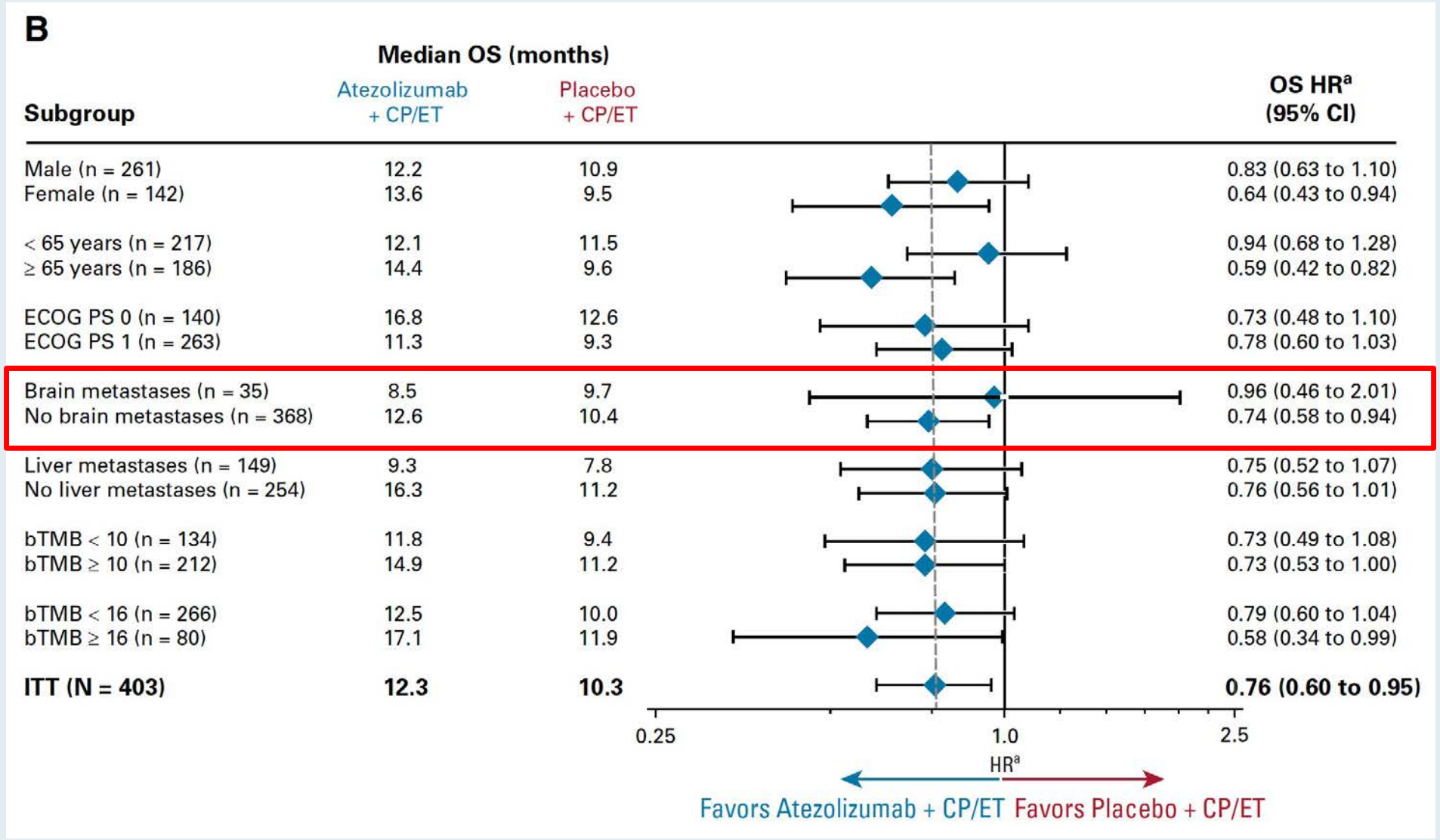
	Atezolizumab + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8 to 15.8)	10.3 (9.3 to 11.3)
HR (95% CI)	0.76 (0.60 to 0.95) *P* = .0154*	

Benefit independent of PD-L1 status

OS = overall survival; CP = carboplatin; EP = etoposide

Liu SV et al. *J Clin Oncol* 2021;39(6):619-30.

IMpower133: OS Subgroup Analyses



OS = overall survival; CP/ET = carboplatin with etoposide

Liu SV et al. *J Clin Oncol* 2021;39(6):619-30.

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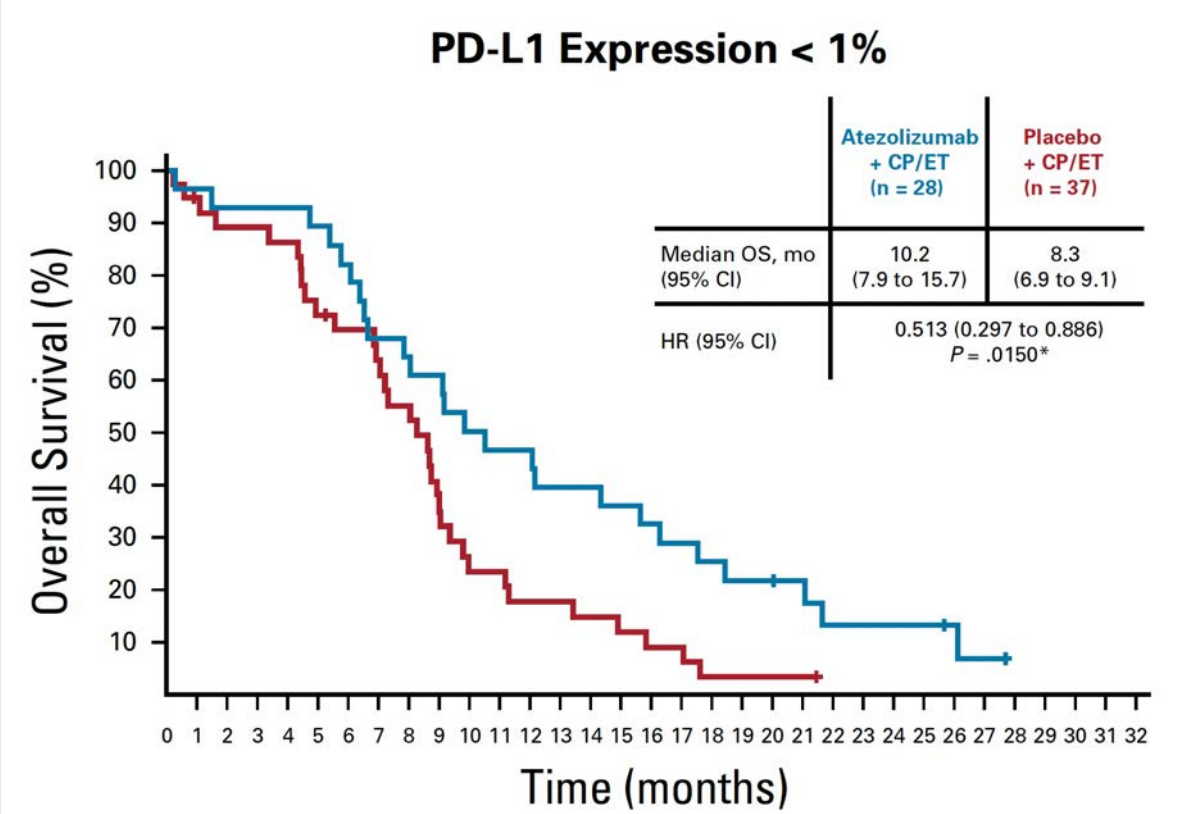
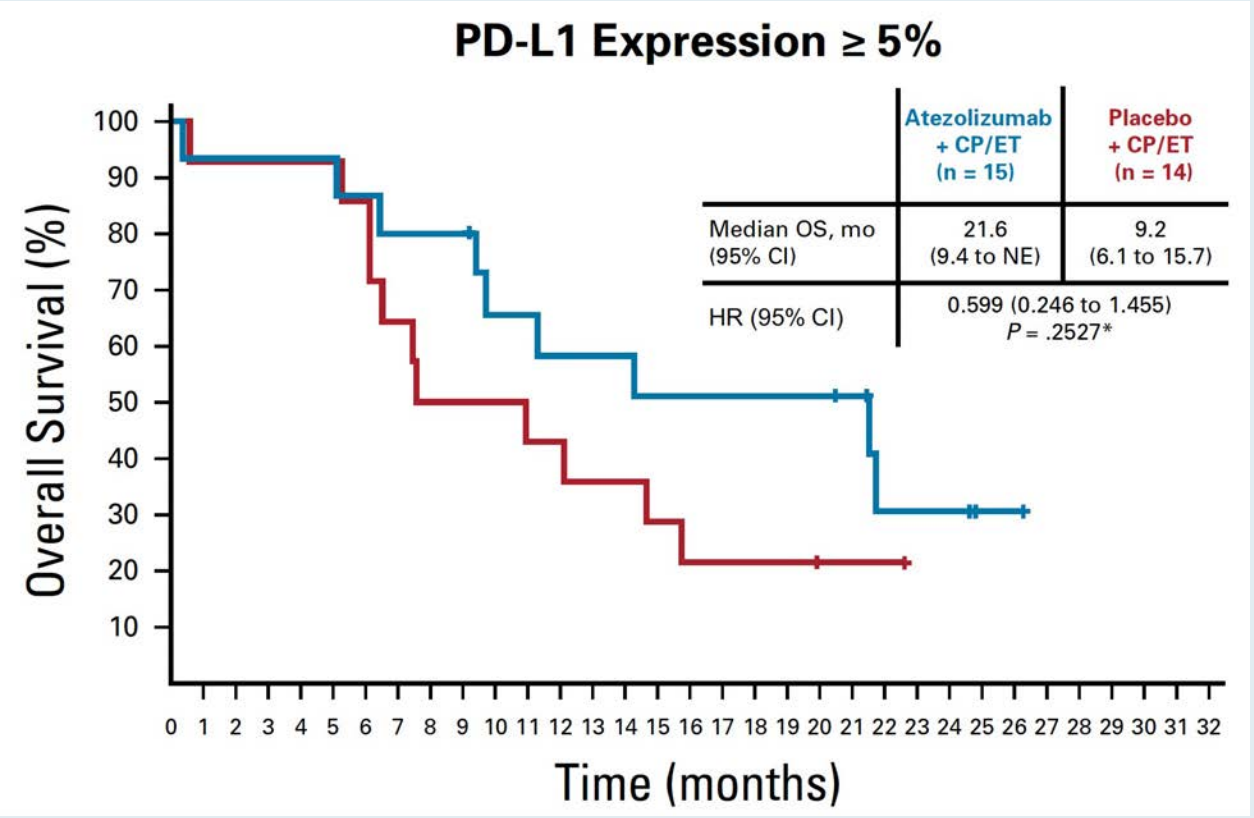
IMpower133: OS by PD-L1 Expression (<1% versus ≥5%)





OS = overall survival; CP/ET = carboplatin with etoposide

Liu SV et al. *J Clin Oncol* 2021;39(6):619-30.

RTP RESEARCH TO PRACTICE

IMpower133: Adverse Events (AEs)

Patients — no. (%)	Atezolizumab + CP/ET (N = 198)	Placebo + CP/ET (N = 196)
Patients with ≥ 1 AE	198 (100)	189 (96.4)
Grade 3–4 AEs	133 (67.2)	125 (63.8)
Treatment-related AEs[a]	188 (94.9)	181 (92.3)
Serious AEs	74 (37.4)	68 (34.7)
Immune-related AEs	79 (39.9)	48 (24.5)
AEs leading to withdrawal from any treatment[a]	22 (11.1)	6 (3.1)
AEs leading to withdrawal from atezolizumab/placebo	21 (10.6)	5 (2.6)
AEs leading to withdrawal from carboplatin	5 (2.5)	1 (0.5)
AEs leading to withdrawal from etoposide	8 (4.0)	2 (1.0)
Treatment-related deaths	3 (1.5)	3 (1.5)

- Median duration of treatment with atezolizumab was 4.7 months (range: 0 to 21)
- Median number of doses received:
  - Atezolizumab: 7 (range: 1 to 30)
  - Chemotherapy: 4 doses for carboplatin; 12 doses for etoposide (same for both treatment groups)

Liu SV et al. WCLC 2018;Abstract PL02.07.

ESMO Open 2022;7(2):100408.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN | CANCER HORIZONS

ORIGINAL RESEARCH

Durvalumab, with or without tremelimumab, plus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer: 3-year overall survival update from CASPIAN☆

L. Paz-Ares[1*], Y. Chen[2], N. Reinmuth[3], K. Hotta[4], D. Trukhin[5], G. Statsenko[6], M. J. Hochmair[7], M. Özgüroğlu[8], J. H. Ji[9], M. C. Garassino[10,11], O. Voitko[12], A. Poltoratskiy[13], E. Musso[14], L. Havel[15], I. Bondarenko[16], G. Losonczy[17], N. Conev[18], H. Mann[19], T. B. Dalvi[20], H. Jiang[20] & J. W. Goldman[21]

RTP RESEARCH TO PRACTICE

CASPIAN: Phase III Study Design

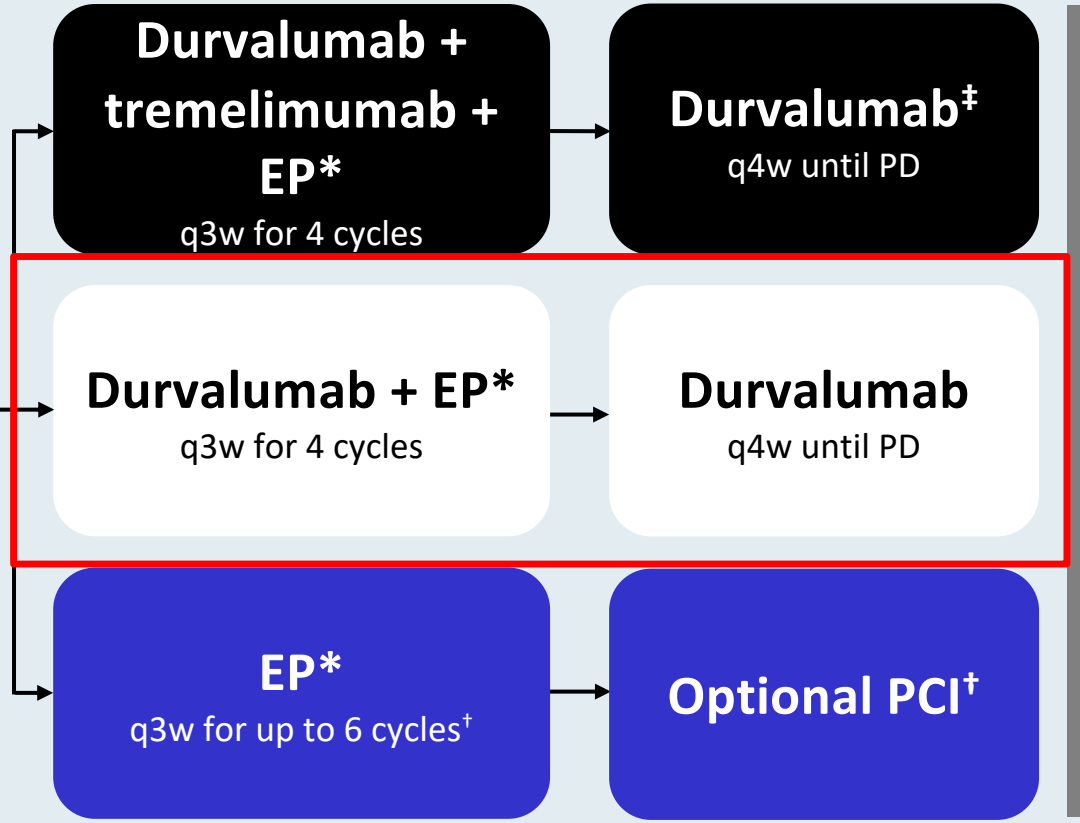
- Treatment-naïve ES-SCLC
- WHO PS 0 or 1
- Asymptomatic or treated and stable brain metastases permitted
- Life expectancy ≥12 weeks
- Measurable disease per RECIST v1.1

N = 805 (randomized)

1:1:1

R

Stratified by planned platinum (carboplatin vs cisplatin)



Primary endpoint

- OS

Secondary endpoints

- PFS §
- ORR §
- Safety & tolerability
- PROs

* EP consists of etoposide 80–100 mg/m^2 with either carboplatin AUC 5-6 or cisplatin 75-80 mg/m^2, durvalumab dosed at 1,500 mg, tremelimumab dosed at 75 mg

† Patients could receive an additional 2 cycles of EP (up to 6 cycles total) and PCI at the investigator's discretion

‡ Patients received an additional dose of tremelimumab post-EP; § By investigator assessment per RECIST v1.1

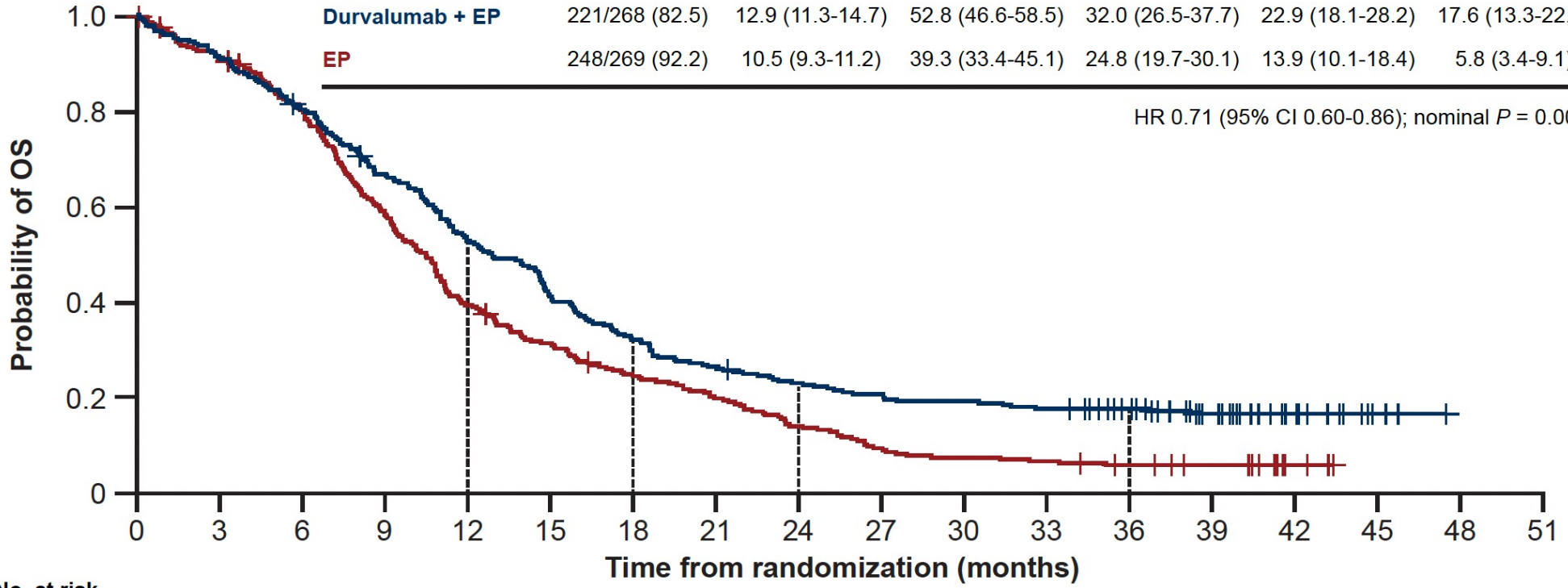
PS = performance status; PD = disease progression; PCI = prophylactic cranial irradiation; OS = overall survival; PFS = progression-free survival; ORR = objective response rate; PROs = patient-reported outcomes; AUC = area under the curve

Paz-Ares L et al. ASCO 2020;Abstract 9002.

CASPIAN OS (ITT Population): Durvalumab with EP versus EP

	Events/ patients, *n* (%)	Median OS (95% CI), months	12-month OS rate (95% CI), %	18-month OS rate (95% CI), %	24-month OS rate (95% CI), %	36-month OS rate (95% CI), %
Durvalumab + EP	221/268 (82.5)	12.9 (11.3-14.7)	52.8 (46.6-58.5)	32.0 (26.5-37.7)	22.9 (18.1-28.2)	17.6 (13.3-22.4)
EP	248/269 (92.2)	10.5 (9.3-11.2)	39.3 (33.4-45.1)	24.8 (19.7-30.1)	13.9 (10.1-18.4)	5.8 (3.4-9.1)

HR 0.71 (95% CI 0.60-0.86); nominal *P* = 0.0003

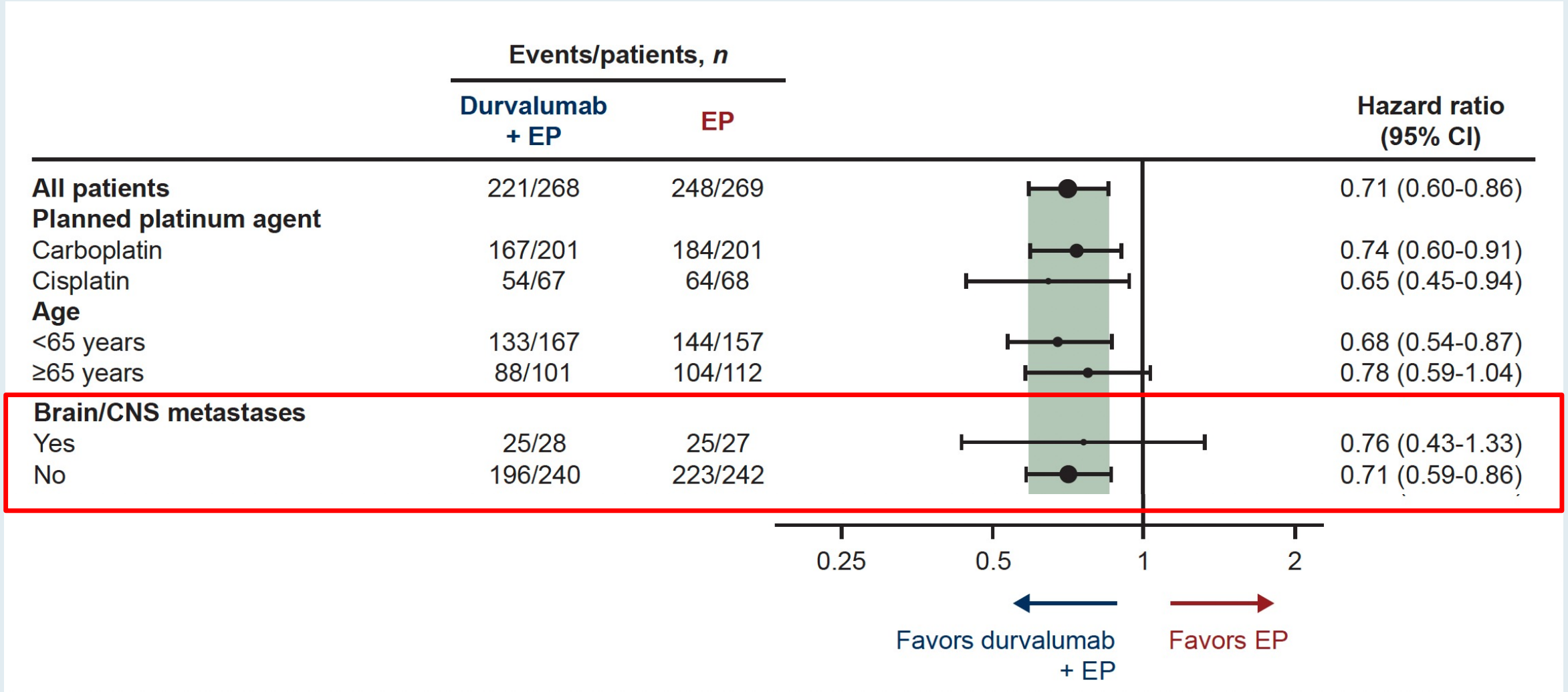


No. at risk																	
Durvalumab + EP	268	244	214	177	140	109	85	70	60	54	50	46	39	25	13	3	0	0
EP	269	243	212	156	104	82	64	51	36	24	19	17	13	10	3	0	0	0

OS = overall survival; EP = carboplatin or cisplatin with etoposide

Paz-Ares L et al. *ESMO Open* 2022;7(2):100408.

CASPIAN Forest Plot of OS: Durvalumab with EP versus EP

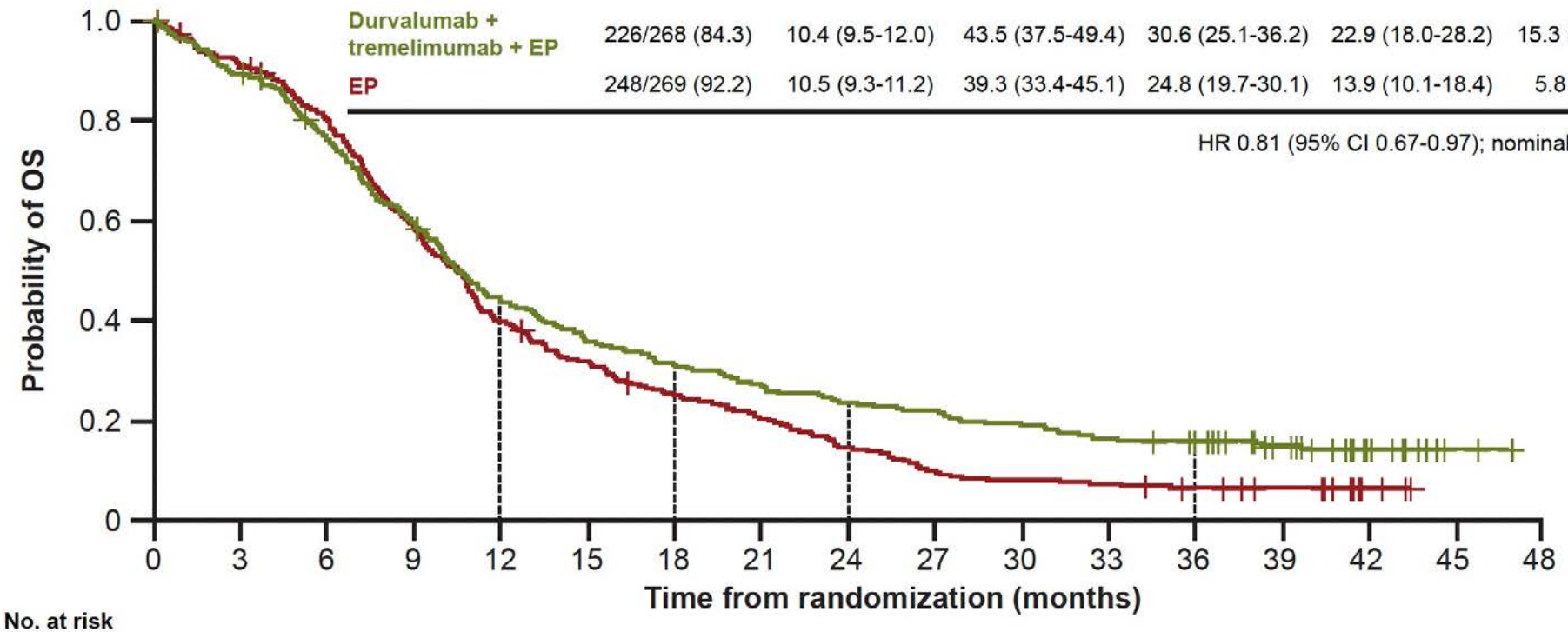


OS = overall survival; EP = carboplatin or cisplatin with etoposide

Paz-Ares L et al. *ESMO Open* 2022;7(2):100408.

CASPIAN OS (ITT Population): Durvalumab with Tremelimumab and EP versus EP

	Events/ patients, *n* (%)	Median OS (95% CI), months	12-month OS rate (95% CI), %	18-month OS rate (95% CI), %	24-month OS rate (95% CI), %	36-month OS rate (95% CI), %
Durvalumab + tremelimumab + EP	226/268 (84.3)	10.4 (9.5-12.0)	43.5 (37.5-49.4)	30.6 (25.1-36.2)	22.9 (18.0-28.2)	15.3 (11.2-19.9)
EP	248/269 (92.2)	10.5 (9.3-11.2)	39.3 (33.4-45.1)	24.8 (19.7-30.1)	13.9 (10.1-18.4)	5.8 (3.4-9.1)



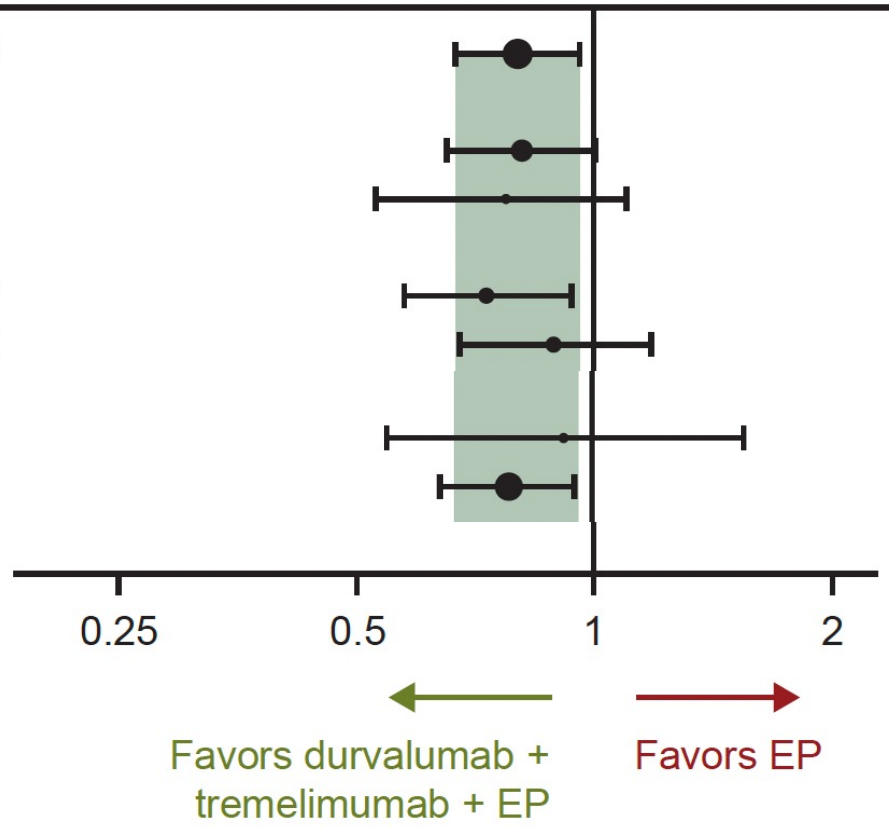
OS = overall survival; EP = carboplatin or cisplatin with etoposide

Paz-Ares L et al. *ESMO Open* 2022;7(2):100408.

RTP RESEARCH TO PRACTICE

CASPIAN Forest Plot of OS: Durvalumab with Tremelimumab and EP versus EP

	Events/patients, *n*		Hazard ratio (95% CI)
	Durvalumab + tremelimumab + EP	EP	
All patients	226/268	248/269	0.81 (0.67-0.97)
Planned platinum agent			
Carboplatin	169/200	184/201	0.82 (0.66-1.01)
Cisplatin	57/68	64/68	0.78 (0.54-1.11)
Age			
<65 years	126/154	144/157	0.74 (0.58-0.94)
≥65 years	100/114	104/112	0.90 (0.69-1.19)
Brain/CNS metastases			
Yes	35/38	25/27	0.92 (0.55-1.56)
No	191/230	223/242	0.79 (0.65-0.95)



OS = overall survival; EP = carboplatin or cisplatin with etoposide

Paz-Ares L et al. *ESMO Open* 2022;7(2):100408.

CASPIAN: Response and Progression-Free Survival (PFS)

	Durvalumab plus EP (n = 27)	Durvalumab plus tremelimumab plus EP (n = 19)
Best objective response[a]		
Responders, *n* (%)	23 (85.2)	19 (100.0)
Complete response[b]	6 (22.2)	4 (21.1)
Partial response[b]	17 (63.0)	15 (78.9)
Non-responders, *n* (%)	4 (14.8)	0
Stable disease ≥6 weeks	2 (7.4)	0
Progression	2 (7.4)	0
PFS[a]		
Progression events, *n* (%)	6 (22.2)	4 (21.1)
New lesions only	2 (7.4)	4 (21.1)
Target lesions only	4 (14.8)	0
PFS rate at 12 months, % (95% CI)[c]	85.2 (65.2-94.2)	84.2 (58.7-94.6)
PFS rate at 24 months, % (95% CI)[c]	81.5 (61.1-91.8)	78.9 (53.2-91.5)

EP = carboplatin or cisplatin with etoposide

Paz-Ares L et al. *ESMO Open* 2022;7(2):100408.

RTP RESEARCH TO PRACTICE

CASPIAN 3-Year Update: Serious Adverse Events

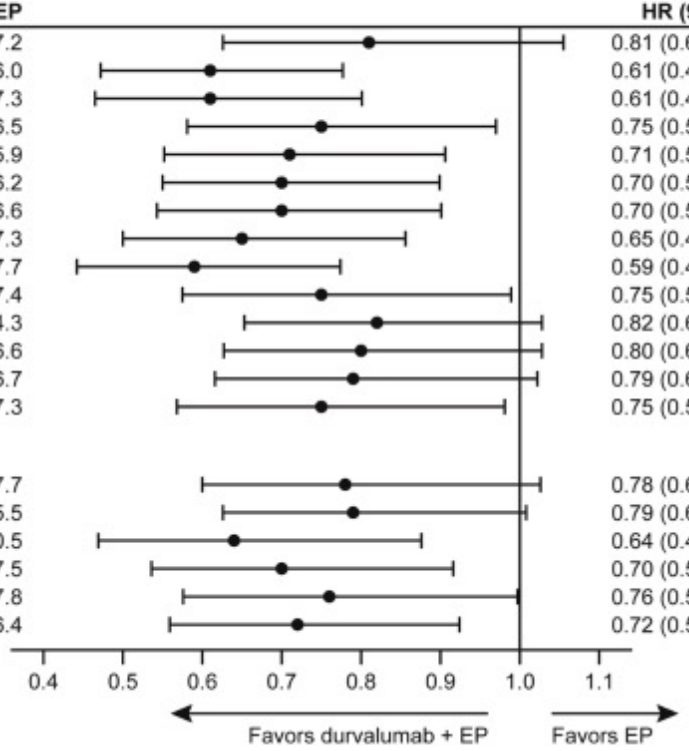
	D+EP (n=265)	D+T+EP (n=266)	EP (n=266)
Serious AEs (all cause), n (%)*	86 (32.5)	126 (47.4)	97 (36.5)
Febrile neutropenia	12 (4.5)	11 (4.1)	12 (4.5)
Pneumonia	6 (2.3)	16 (6.0)	11 (4.1)
Anaemia	5 (1.9)	9 (3.4)	12 (4.5)
Thrombocytopenia	1 (0.4)	6 (2.3)	9 (3.4)
Hyponatremia	2 (0.8)	9 (3.4)	4 (1.5)
Neutropenia	2 (0.8)	5 (1.9)	7 (2.6)
Diarrhoea	2 (0.8)	7 (2.6)	4 (1.5)
Pulmonary embolism	1 (0.4)	7 (2.6)	0
AEs leading to death (all cause), n (%)†	14 (5.3)	29 (10.9)	16 (6.0)
Treatment-related AEs leading to death	6 (2.3)	12 (4.5)	2 (0.8)

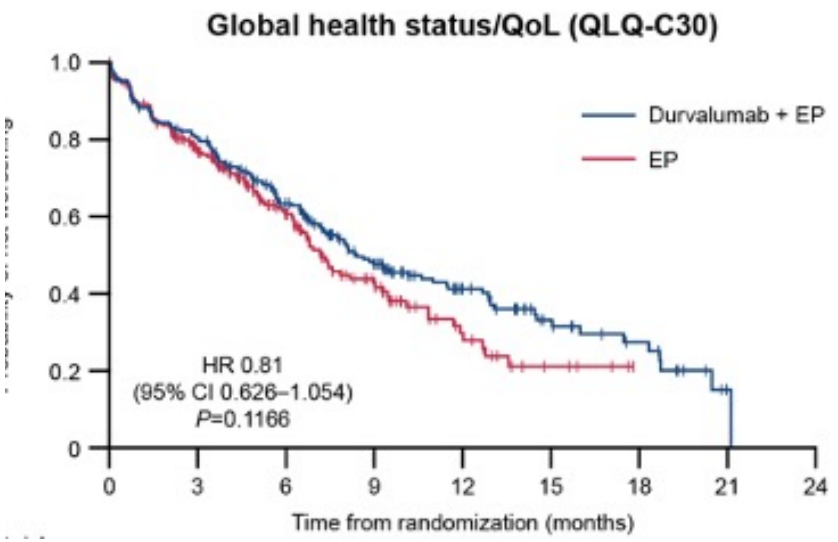
D = durvalumab; EP = carboplatin or cisplatin with etoposide; T = tremelimumab; AEs = adverse events

Paz-Ares LG et al. ESMO 2021;Abstract LBA61.

CASPIAN: Quality of Life

QLQ-C30	Events/ patients, n	Median TTD, months Durvalumab + EP	Median TTD, months EP	HR (95% CI)	Nominal *P* value
Global health status/QoL	240/470	8.4	7.2	0.81 (0.626–1.054)	0.1166
Cognitive functioning	261/486	8.4	6.0	0.61 (0.472–0.776)	<0.0001
Emotional functioning	216/481	12.9	7.3	0.61 (0.464–0.800)	0.0003
Physical functioning	246/483	8.5	6.5	0.75 (0.581–0.970)	0.0276
Role functioning	262/456	7.4	5.9	0.71 (0.550–0.904)	0.0059
Social functioning	264/472	7.6	6.2	0.70 (0.549–0.897)	0.0048
Appetite loss	251/454	8.3	6.6	0.70 (0.542–0.899)	0.0054
Constipation	225/468	11.1	7.3	0.65 (0.499–0.855)	0.0018
Diarrhea	208/487	14.6	7.7	0.59 (0.442–0.774)	0.0002
Dyspnea	220/442	9.0	7.4	0.75 (0.574–0.989)	0.0406
Fatigue	309/475	5.5	4.3	0.82 (0.653–1.027)	0.0835
Nausea/vomiting	260/488	8.4	6.6	0.80 (0.626–1.027)	0.0809
Pain	250/472	7.8	6.7	0.79 (0.615–1.021)	0.0718
Insomnia	220/435	8.6	7.3	0.75 (0.568–0.980)	0.0349
QLQ-LC13					
Cough	221/459	9.3	7.7	0.78 (0.600–1.026)	0.0747
Dyspnea	284/480	6.5	5.5	0.79 (0.625–1.006)	0.0578
Hemoptysis	165/487	18.3	10.5	0.64 (0.469–0.876)	0.0049
Arm/shoulder pain	224/478	9.9	7.5	0.70 (0.535–0.915)	0.0088
Chest pain	215/478	10.6	7.8	0.76 (0.575–0.996)	0.0464
Other pain	255/466	7.8	6.4	0.72 (0.558–0.923)	0.0096





EP = carboplatin or cisplatin with etoposide; QoL = quality of life; D = durvalumab

Goldman JW et al. *Lung Cancer* 2020;149:46-52.

LUMINANCE: A Phase IIIb Study of Durvalumab plus Platinum-Etoposide for the First-Line Treatment of Extensive-Stage SCLC

Reinmuth N et al.

IASLC 2022;Abstract EP14.05-015.

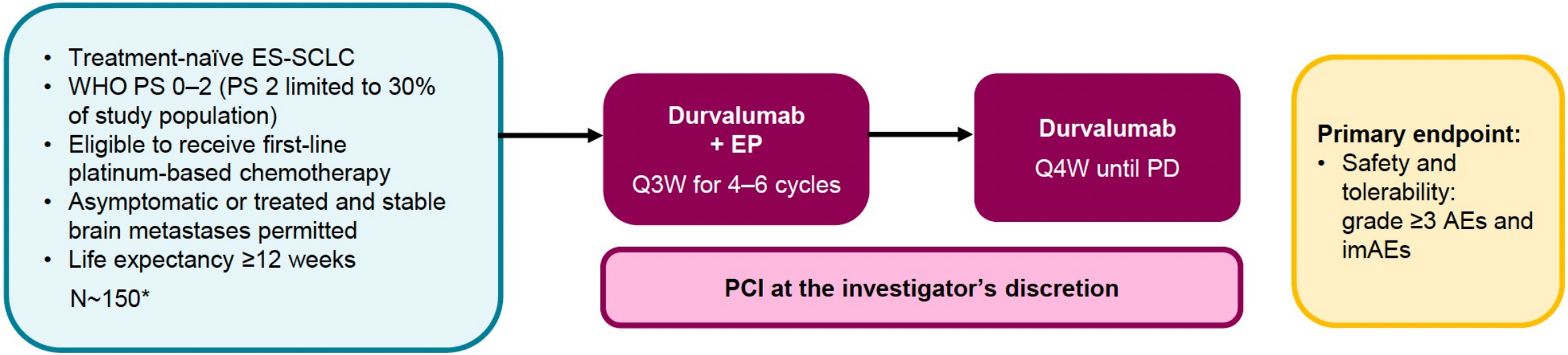
LUMINANCE Phase IIIb Study Rationale

- In common with most registrational Phase III studies, the patient inclusion and exclusion criteria in CASPIAN resulted in a study population that did not fully represent that encountered in real-world clinical practice.
  - Many patients with ES-SCLC have poor performance status (WHO PS ≥2) at diagnosis, but recruitment in CASPIAN was limited to patients with WHO PS 0 or 1.
  - Although 4 cycles of EP is standard for ES-SCLC, an additional 2 cycles are often administered; in CASPIAN up to 6 cycles were permitted in the etoposide (EP) arm only.
  - The role of prophylactic cranial irradiation (PCI) remains controversial in ES-SCLC, but is sometimes used in the real world at the discretion of the treating physician; in CASPIAN, PCI was permitted only in the EP arm.
- The Phase IIIb LUMINANCE study will provide safety and efficacy data for patients with ES-SCLC, including those with WHO PS 2, with durvalumab in combination with up to 6 cycles of EP, with or without PCI, to help inform treatment decisions in real-world practice.
- In addition, LUMINANCE will potentially help address important scientific questions, including the identification of potential biomarkers to distinguish patients who might benefit most from durvalumab.

Reinmuth N et al. IASLC 2022;Abstract EP14.05-015.

LUMINANCE Phase IIIb Study Design

- The safety and efficacy of durvalumab in combination with up to 6 cycles of EP, with or without PCI, will be evaluated in ~150 patients with previously untreated ES-SCLC, including patients with WHO PS 2.
- Durvalumab will be administered intravenously concurrently with platinum-based chemotherapy (investigator's choice of cisplatin or carboplatin) and etoposide Q3W for 4–6 cycles, followed by durvalumab Q4W until PD.
  - Drug dosages: durvalumab 1500 mg; cisplatin 75–80 mg/m^2 or carboplatin AUC5–6 (for patients with WHO PS 2, a dose of AUC4 is permitted); etoposide 80–100 mg/m^2.



Reinmuth N et al. IASLC 2022;Abstract EP14.05-015.

2022 ASCO ANNUAL MEETING

Abstract 8505

ASTRUM-005: Serplulimab, A Novel Anti-PD-1 Antibody, Plus Chemotherapy versus Chemotherapy as First-Line Treatment for Extensive-Stage Small-Cell Lung Cancer: An International Randomized Phase 3 Study

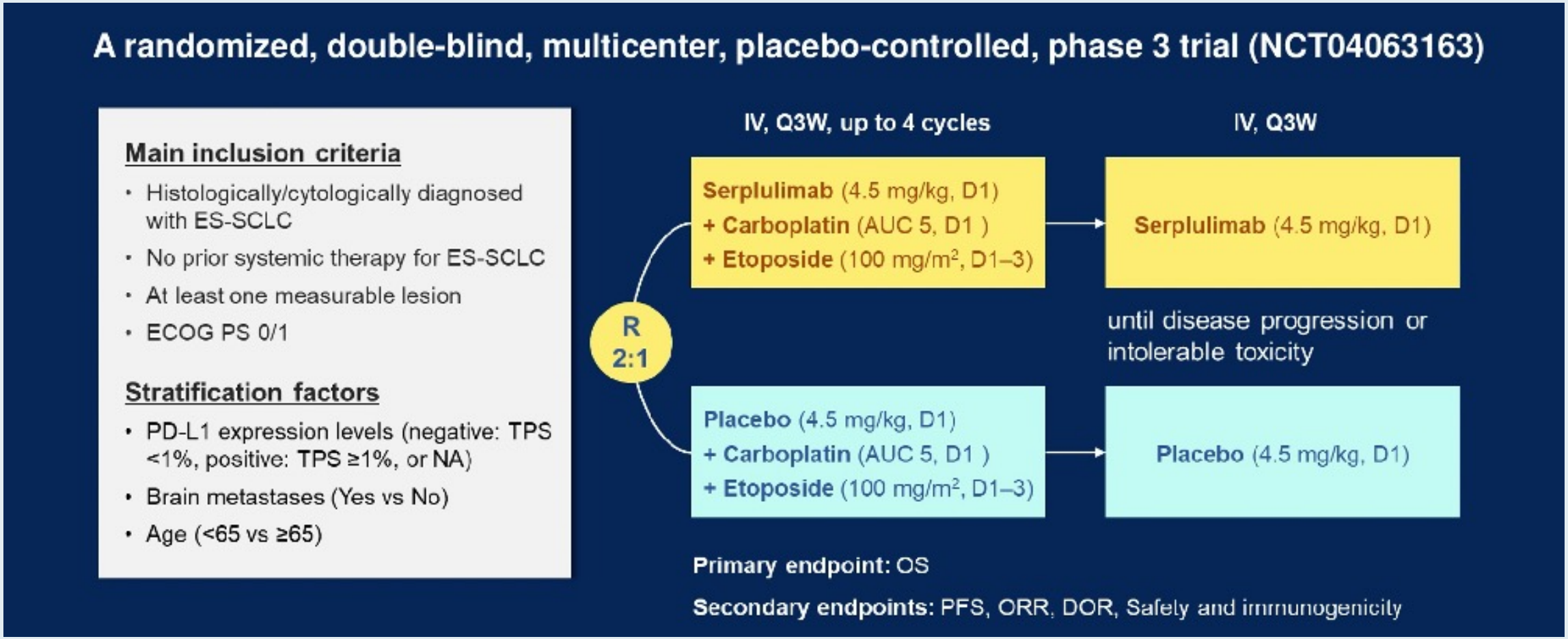
Ying Cheng, MD

Jilin Cancer Hospital, Changchun, China

Ying Cheng[1], Liang Han[2], Lin Wu[3], Jun Chen[4], Hongmei Sun[5], Guilan Wen[6], Yinghua Ji[7], Mikhail Dvorkin[8], Jianhua Shi[9], Zhijie Pan[10], Jinsheng Shi[11], Xicheng Wang[12], Yuansong Bai[13], Tamar Melkadze[14], Yueyin Pan[15], Xuhong Min[16], Maksym Viguro[17], Wenying Kang[18], Qingyu Wang[18], Jun Zhu[18], ASTRUM-005 Investigators;

[1]Jilin Cancer Hospital, Changchun, China; [2]Xuzhou Central Hospital, Xuzhou, China; [3]Hunan Cancer Hospital, Changsha, China; [4]Tianjin Medical University General Hospital, Tianjin, China; [5]Jiamusi Cancer Hospital, Jiamusi, China; [6]The First Affiliated Hospital of Nanchang University, Nanchang, China; [7]The First Affiliated Hospital of Xinxiang Medical University, Xinxiang, China; [8]Budgetary Healthcare Institution of Omsk Region "Clinical Oncology Dispensary", Omsk, Russia; [9]Linyi Cancer Hospital, Linyi, China; [10]The First Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China; [11]Cangzhou People's Hospital, Cangzhou, China; [12]The First Affiliated Hospital of Guangdong Pharmaceutical University, Guangzhou, China; [13]China-Japan Union Hospital of Jilin University, Changchun, China; [14]Acad.Fridon Todua Medical Center, Research Institute of Clinical Medicine, Tbilisi, Georgia; [15]Anhui Provincial Hospital, Hefei, China; [16]Anhui Chest Hospital, Hefei, China; [17]Medical Center "Mriya Med-Service", Kryvyi Rih, Ukraine; [18]Shanghai Henlius Biotech, Inc., Shanghai, China

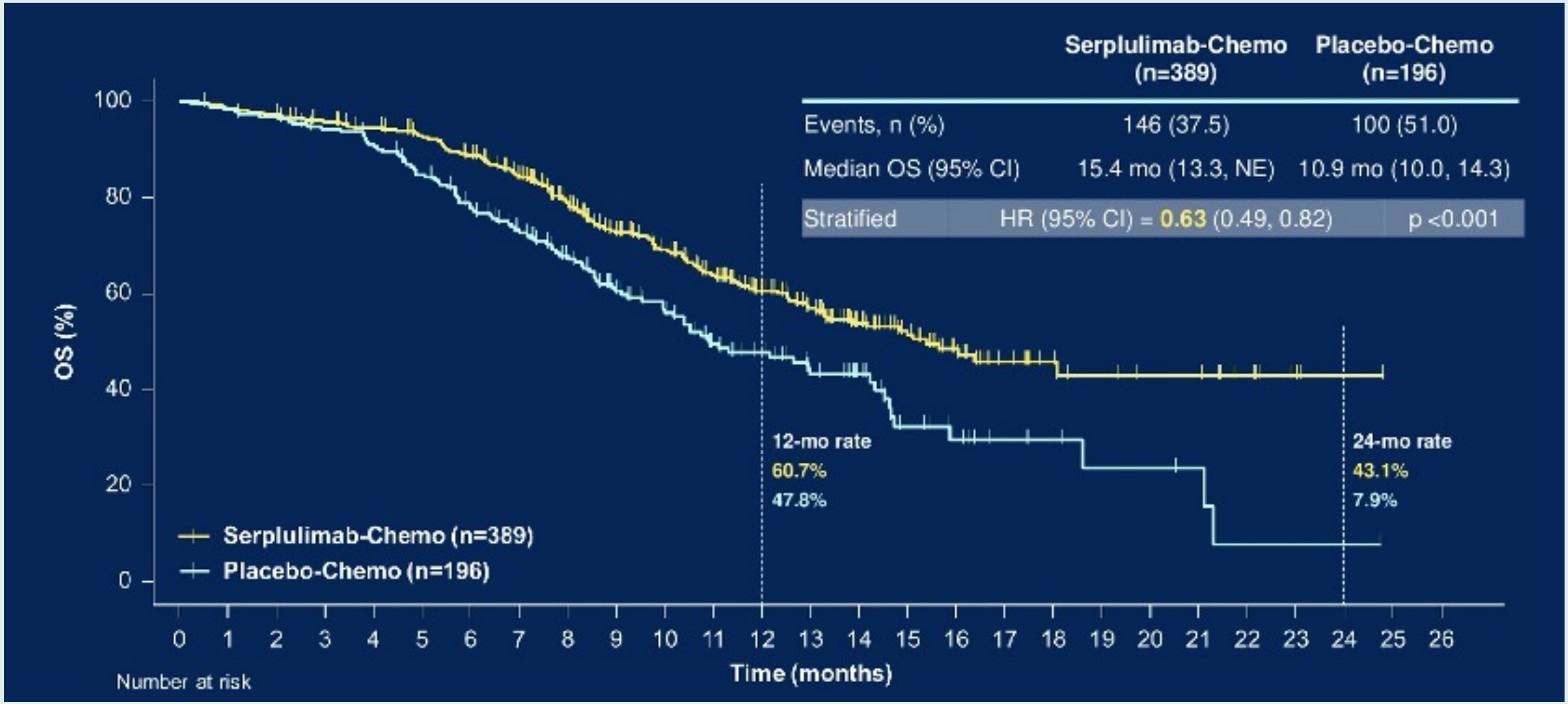
ASTRUM-005 Study Design



ES-SCLC = extensive-stage small cell lung cancer; TPS = tumor proportion score; OS = overall survival; PFS = progression-free survival; ORR = objective response rate; DOR = duration of response

Cheng Y et al. ASCO 2022;Abstract 8505.

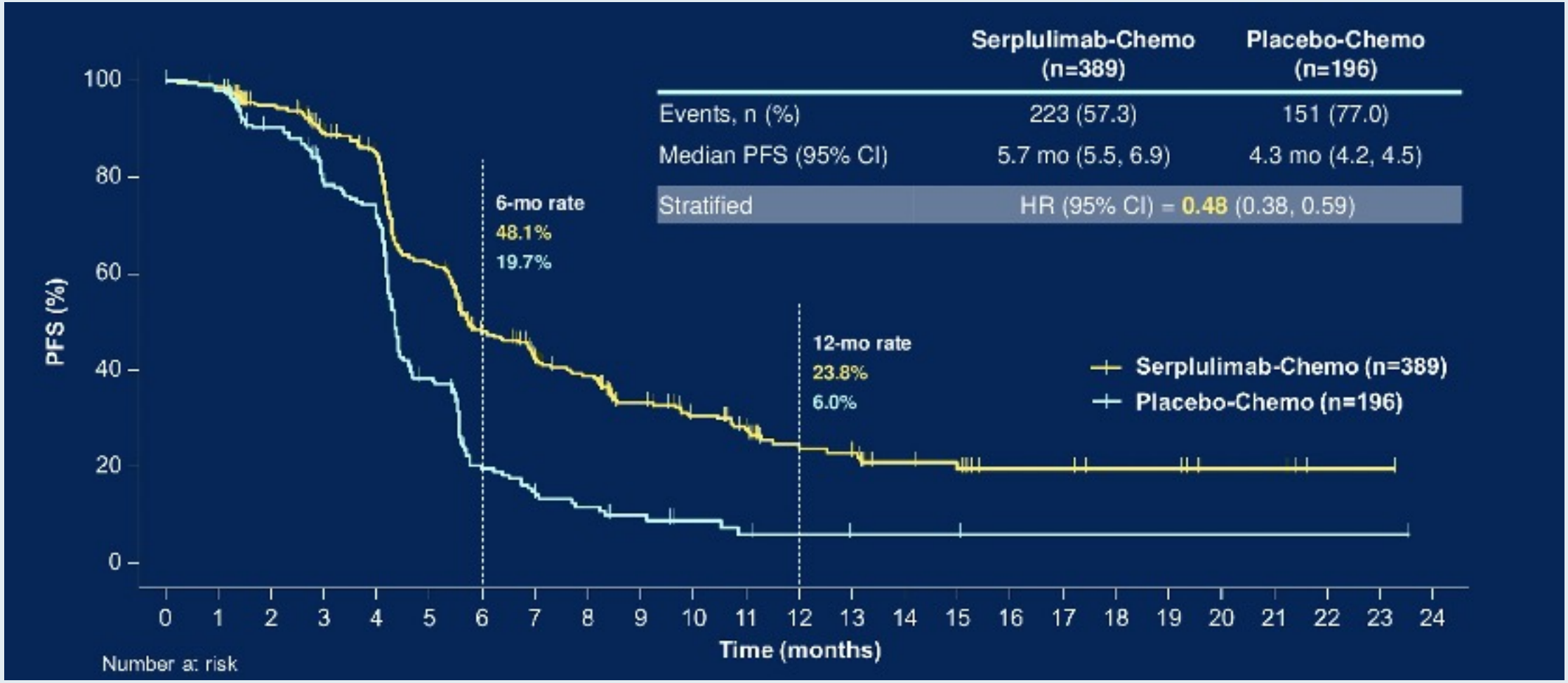
ASTRUM-005: Overall Survival (OS)



Cheng Y et al. ASCO 2022;Abstract 8505.

RTP RESEARCH TO PRACTICE

ASTRUM-005: Progression-Free Survival (PFS)

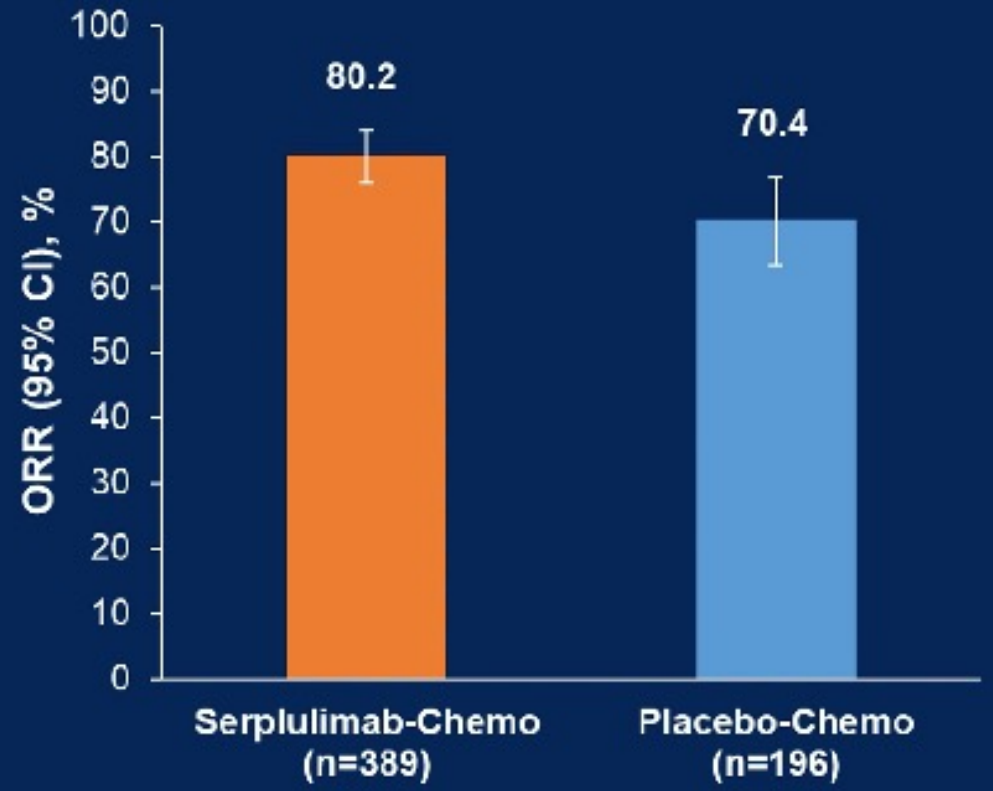


Cheng Y et al. ASCO 2022;Abstract 8505.

RTP RESEARCH TO PRACTICE

ASTRUM-005: Response

	Serplulimab-Chemo (n=389)	Placebo-Chemo (n=196)
ORR, n (%) [95% CI]	**312 (80.2)** [75.9, 84.1]	**138 (70.4)** [63.5, 76.7]
Best overall response, n (%)		
CR	**3 (0.8)**	**0**
PR	309 (79.4)	138 (70.4)
SD	49 (12.6)	37 (18.9)
PD	9 (2.3)	11 (5.6)
NE or missing	19 (4.9)	10 (5.1)



ORR = objective response rate; CR = complete response; PR = partial response; SD = stable disease; PD = disease progression; NE = not estimable

Cheng Y et al. ASCO 2022;Abstract 8505.

ASTRUM-005: Safety Profile

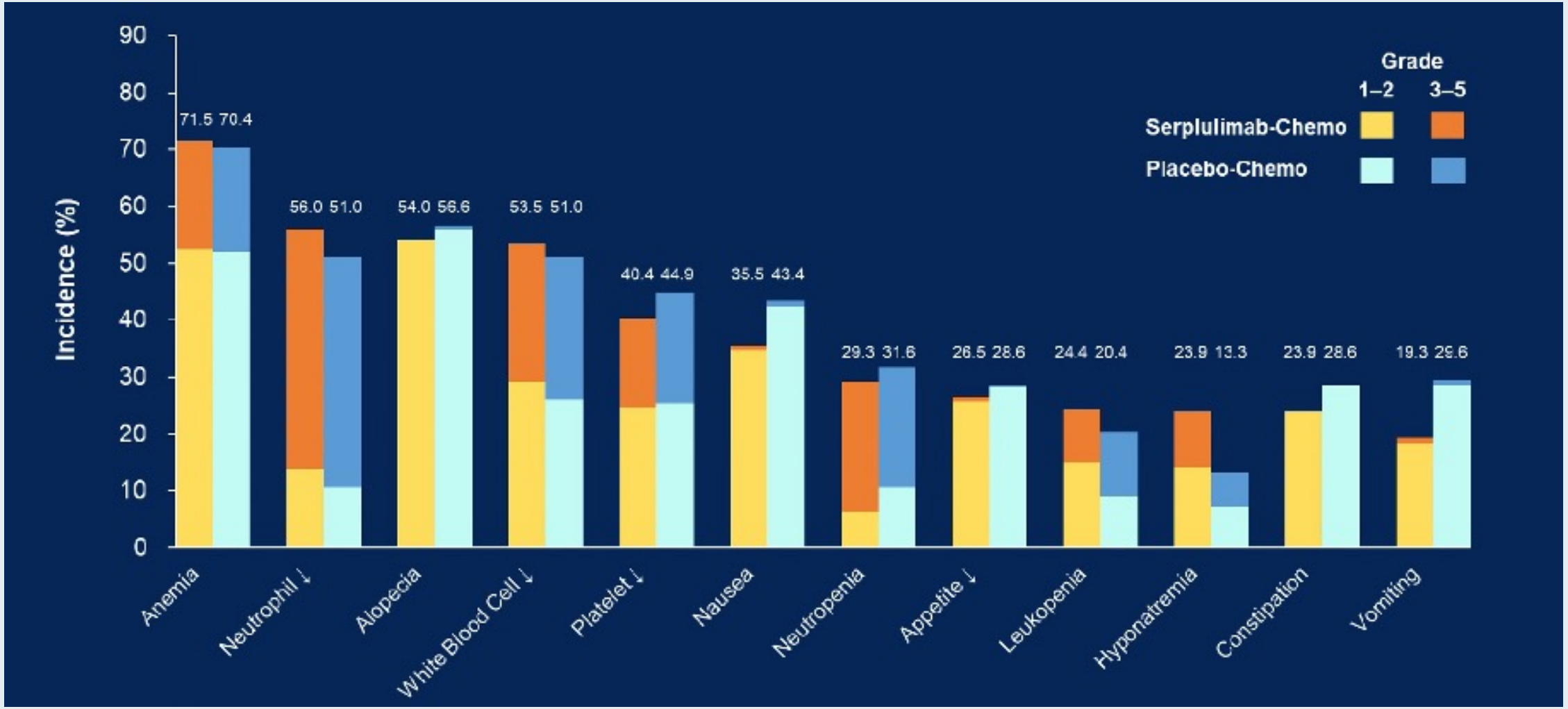
	Serplulimab-Chemo (n=389)	Placebo-Chemo (n=196)
TEAEs, n (%)	372 (95.6)	191 (97.4)
CTCAE grade ≥3	321 (82.5)	157 (80.1)
SAEs	136 (35.0)	69 (35.2)
AESIs		
IRRs	7 (1.8)	1 (0.5)
irAEs	144 (37.0)	36 (18.4)
TRAEs related to serplulimab/placebo, n (%)	272 (69.9)	110 (56.1)
CTCAE grade ≥3	129 (33.2)	54 (27.6)
Leading to treatment discontinuation	19 (4.9)	8 (4.1)
Leading to death	3 (0.8)	1 (0.5)

- The most common irAEs in serplulimab group were: hypothyroidism (11.6%), hyperthyroidism (9.0%), and rash (3.1%)

TEAEs = treatment-emergent adverse events; CTCAE = Common Terminology Criteria for Adverse Events; SAEs = serious adverse events; AESIs = adverse events of special interest; IRRs = infusion-related reactions; irAEs = immune-related adverse events

Cheng Y et al. ASCO 2022;Abstract 8505.

ASTRUM-005: Common Adverse Events



Cheng Y et al. ASCO 2022;Abstract 8505.

Novel PD-1 Inhibitor Serplulimab Granted Orphan Drug Designation by FDA for SCLC

Press Release: April 9, 2022

"The FDA has granted serplulimab an orphan drug designation for the treatment of small cell lung cancer (SCLC), according to a press release from [its] developer.

The designation was granted to continue the development of serplulimab and to take advantage of a policy that allows for better support of registration and commercialization within the United States. Further plans in 2022 for serplulimab include submitting a new drug application in China and a marketing authorization application in Europe, which could potentially make serplulimab the first PD-1 inhibitor to be used in the frontline setting for patients with SCLC.

Serplulimab was also assessed in combination with chemotherapy in a phase 3 trial (NCT04063163) of patients with previously untreated extensive-stage SCLC (ES-SCLC). At the first interim analysis, the combination met the primary end point, yielding a significant improvement in overall survival (OS) compared with chemotherapy alone. Additionally, the combination demonstrated a positive safety profile with no new safety findings."

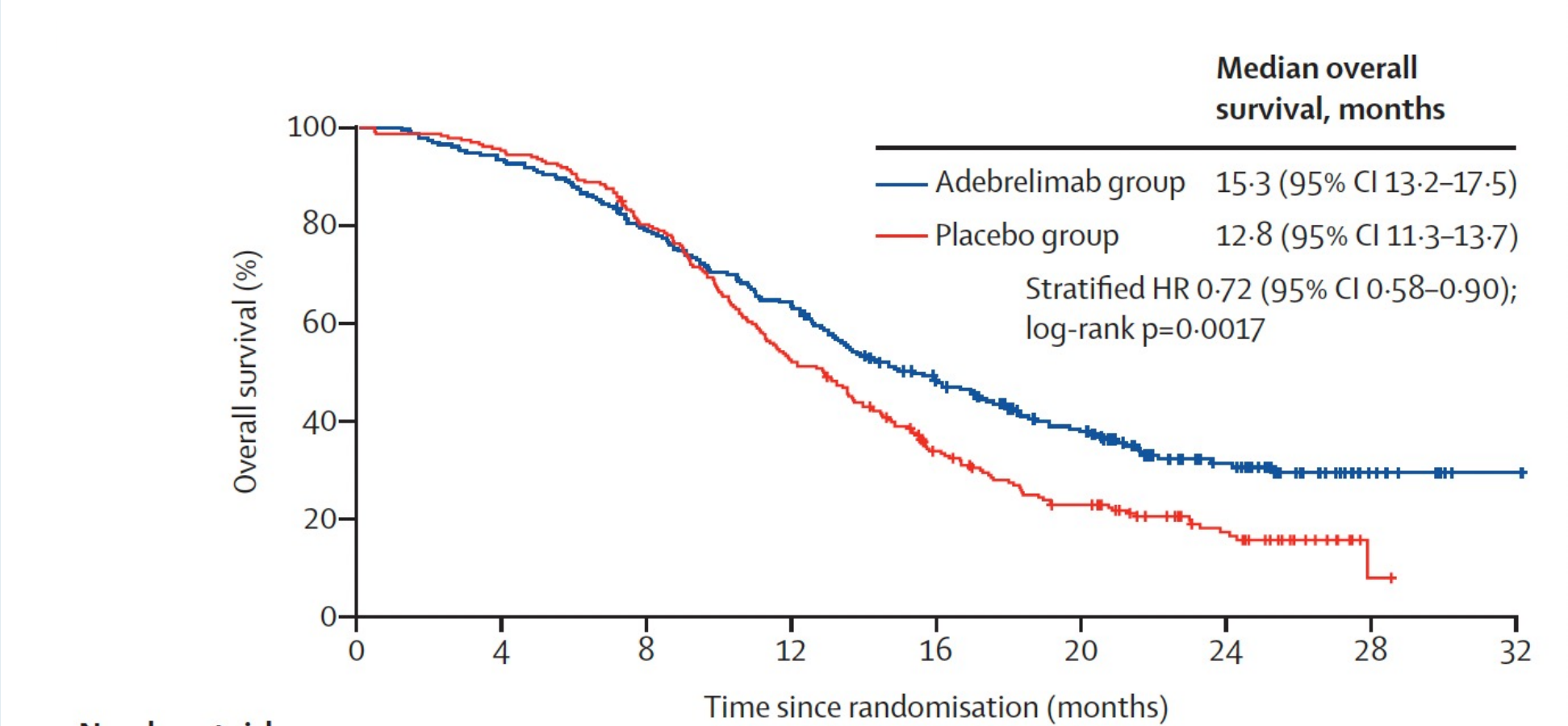
https://www.cancernetwork.com/view/serplulimab-granted-orphan-drug-designation-by-fda-in-sclc

Lancet Oncol 2022;23(6):739-47.

Adebrelimab or placebo plus carboplatin and etoposide as first-line treatment for extensive-stage small-cell lung cancer (CAPSTONE-1): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

*Jie Wang, Caicun Zhou, Wenxiu Yao, Qiming Wang, Xuhong Min, Gongyan Chen, Xingxiang Xu, Xingya Li, Fei Xu, Yong Fang, Runxiang Yang, Guohua Yu, Youling Gong, Jun Zhao, Yun Fan, Quan Liu, Lejie Cao, Yu Yao, Yunpeng Liu, Xiaoling Li, Jingxun Wu, Zhiyong He, Kaihua Lu, Liyan Jiang, Chengping Hu, Wenhua Zhao, Ben Zhang, Wei Shi, Xiaojing Zhang, Ying Cheng, for the CAPSTONE-1 Study Group**

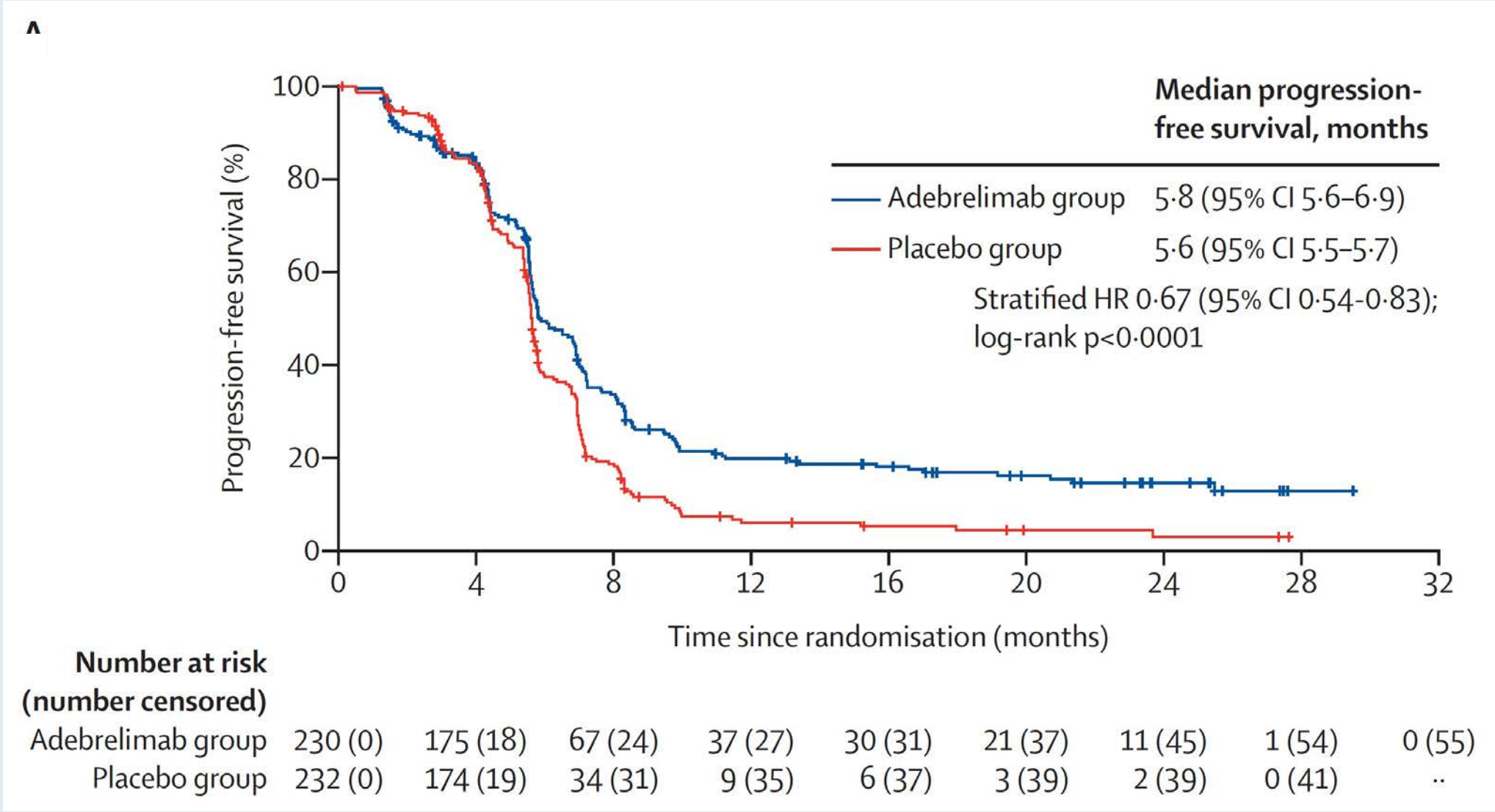
CAPSTONE-1: Overall Survival



Number at risk (number censored)									
Adebrelimab group	230 (0)	215 (0)	180 (1)	144 (1)	101 (10)	72 (19)	37 (44)	8 (71)	1 (78)
Placebo group	232 (0)	221 (0)	185 (1)	120 (1)	70 (10)	44 (14)	21 (29)	1 (46)	0 (47)

Wang J et al. *Lancet Oncol* 2022;23(6):739-47.

CAPSTONE-1: Progression-Free Survival



Wang J et al. *Lancet Oncol* 2022;23(6):739-47.

CAPSTONE-1: Treatment-Related Adverse Events (>15%)

	Adebrelimab group (n=230)				Placebo group (n=232)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Any treatment-related adverse event	32 (14%)	85 (37%)	110 (48%)	2 (1%)	32 (14%)	110 (47%)	85 (37%)	2 (1%)
Neutrophil count decreased	44 (19%)	82 (36%)	92 (40%)	0	45 (19%)	103 (44%)	72 (31%)	0
White blood cell count decreased	111 (48%)	99 (43%)	7 (3%)	0	127 (55%)	78 (34%)	10 (4%)	0
Platelet count decreased	103 (45%)	65 (28%)	23 (10%)	0	113 (49%)	56 (24%)	22 (9%)	0
Alanine aminotransferase increased	90 (39%)	5 (2%)	0	0	69 (30%)	4 (2%)	0	0
Aspartate aminotransferase increased	78 (34%)	2 (1%)	1 (<1%)	0	56 (24%)	4 (2%)	0	0
γ-glutamyltransferase increased	24 (10%)	4 (2%)	0	0	22 (9%)	1 (<1%)	0	0
Anaemia	131 (57%)	63 (27%)	1 (<1%)	0	141 (61%)	66 (28%)	0	0
Nausea	90 (39%)	2 (1%)	0	0	107 (46%)	0	0	0
Vomiting	58 (25%)	2 (1%)	0	0	53 (23%)	1 (<1%)	0	0
Constipation	40 (17%)	0	0	0	42 (18%)	0	0	0
Alopecia	102 (44%)	0	0	0	98 (42%)	0	0	0
Decreased appetite	63 (27%)	5 (2%)	0	0	60 (26%)	2 (1%)	0	0
Hypoalbuminaemia	26 (11%)	0	0	0	24 (10%)	0	0	0
Asthenia	41 (18%)	1 (<1%)	0	0	44 (19%)	1 (<1%)	0	0

Wang J et al. *Lancet Oncol* 2022;23(6):739-47.

IASLC 2022 World Conference on Lung Cancer

AUGUST 6-9, 2022 | VIENNA, AUSTRIA

Abstract OA12.05

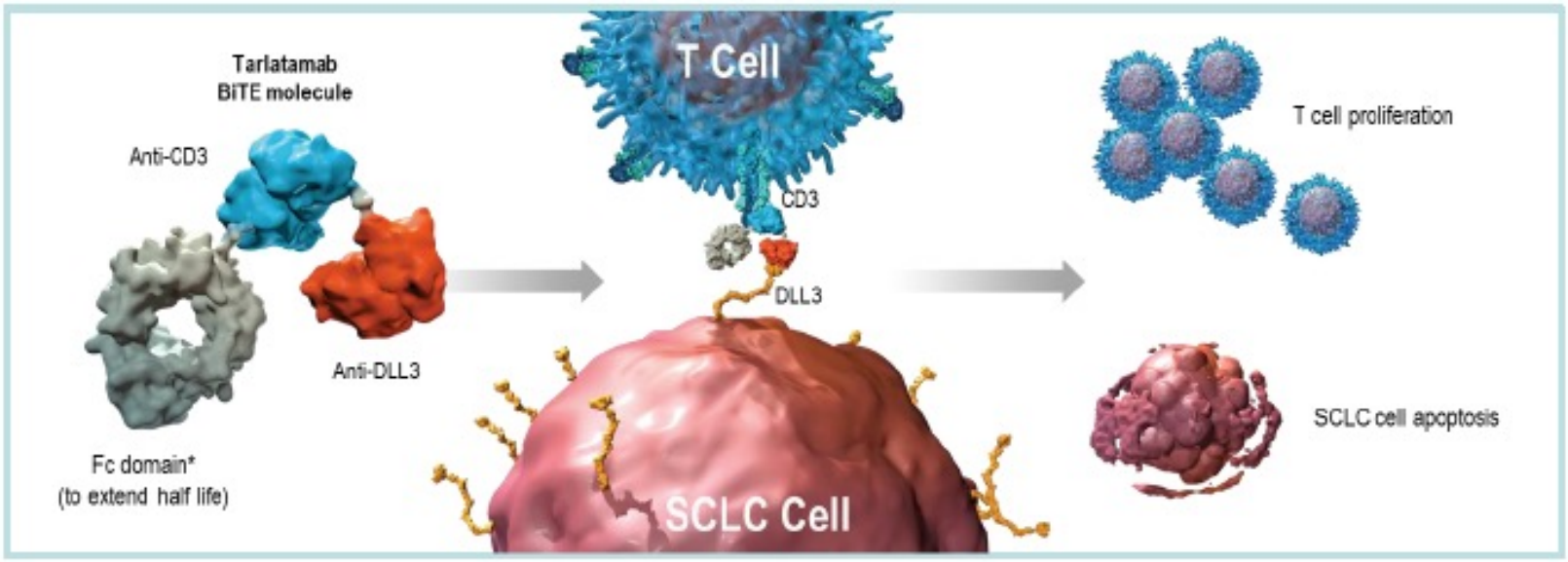
Phase 1 Updated Exploration and First Expansion Data for DLL3-Targeted T-cell Engager Tarlatamab in SCLC (DeLLphi-300 Study)

Hossein Borghaei,[1*] Luis Paz-Ares,[2] Melissa Johnson,[3] Stephane Champiat,[4] Taofeek Owonikoko,[5] Victoria Lai,[6] Michael Boyer,[7] Horst-Dieter Hummel,[8] Ramaswamy Govindan,[9] Neeltje Steeghs,[10] Fiona Blackhall,[11] Noemi Reguart,[12] Afshin Dowlati,[13] Yiran Zhang,[14] Nooshin Hashemi Sadraei,[14] Amanda Goldrick,[14] Hiroki Izumi[15]

RTP RESEARCH TO PRACTICE

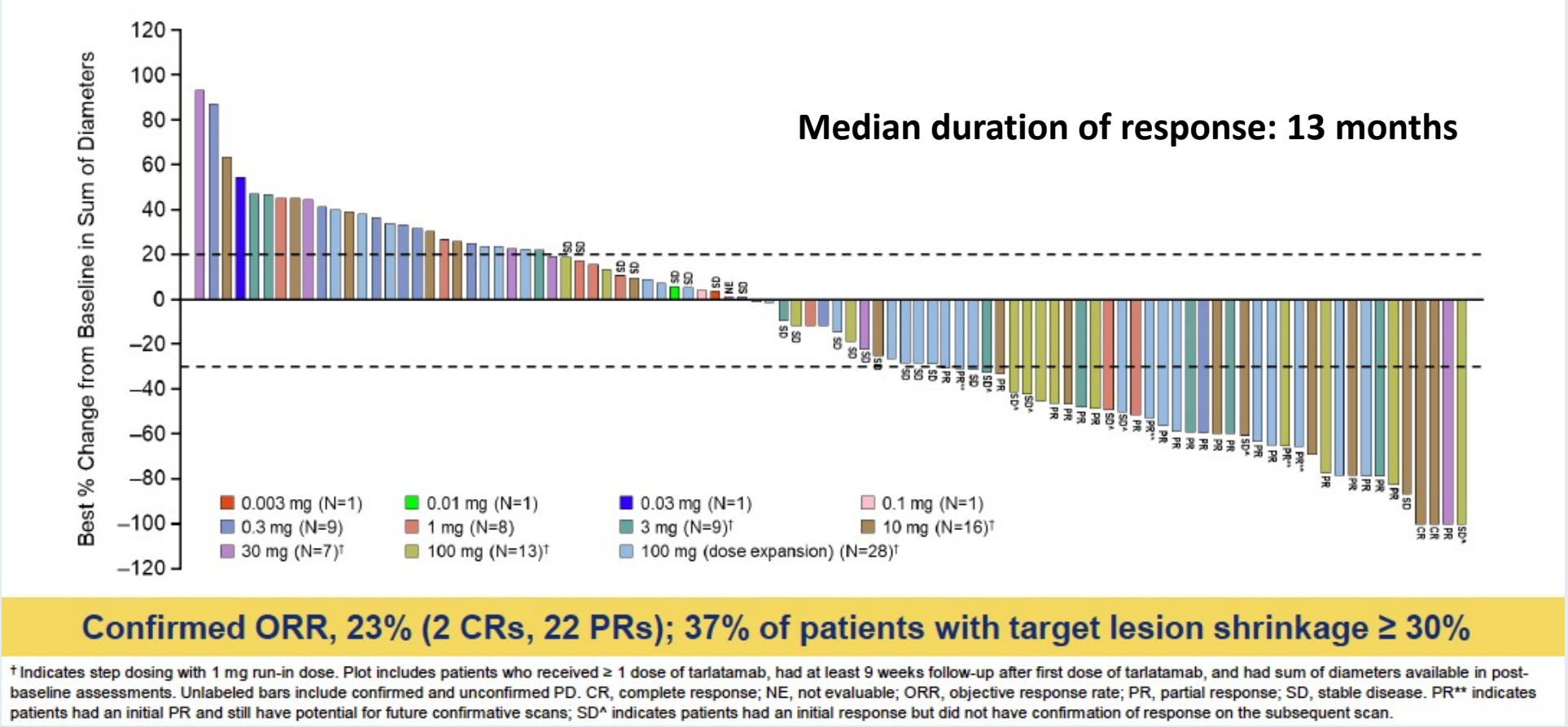
AMG 757: A Half-Life Extended BiTE (Bispecific T-Cell Engager) Targeting DLL3 for SCLC

- Notch ligand delta-like ligand 3 (DLL3) is aberrantly expressed on the surface of SCLC cells
- Tarlatamab is a bispecific T cell engager (BiTE®) immune therapy that binds DLL3 and CD3 leading to T cell-mediated tumor lysis
  - Interim phase 1 dose exploration data show preliminary efficacy and acceptable safety in SCLC patients



Borghaei H et al. IASLC 2022;Abstract OA12.05.

DeLLphi-300: Summary of Tarlatamab (AMG 757) Efficacy in a Phase I Study for Previously Treated SCLC



† Indicates step dosing with 1 mg run-in dose. Plot includes patients who received ≥ 1 dose of tarlatamab, had at least 9 weeks follow-up after first dose of tarlatamab, and had sum of diameters available in post-baseline assessments. Unlabeled bars include confirmed and unconfirmed PD. CR, complete response; NE, not evaluable; ORR, objective response rate; PR, partial response; SD, stable disease. PR** indicates patients had an initial PR and still have potential for future confirmative scans; SD^ indicates patients had an initial response but did not have confirmation of response on the subsequent scan.

- Median progression-free survival: 3.7 months
- Median overall survival: 13.2 months

Borghaei H et al. IASLC 2022;Abstract OA12.05.

RTP RESEARCH TO PRACTICE

DeLLphi-300: Treatment-Related Adverse Events Summary for Tarlatamab

Treatment-related AEs (by preferred term)	Patients (N = 106)	
	All Grades, n (%)	Grade ≥ 3, n (%)*
Any treatment-related AE	97 (92)	33 (31)
Treatment-related AEs occurring in > 15% of patients (by preferred term)		
CRS	56 (53)	1 (1)
Pyrexia	40 (38)	2 (2)
Dysgeusia	24 (23)	0
Fatigue	23 (22)	3 (3)
Nausea	21 (20)	0

- 4/106 (4%) patients discontinued tarlatamab due to treatment-related AEs: encephalopathy (n=1), neurotoxicity (n=1), and pneumonitis (n=2, including one grade 5 AE)

Tarlatamab showed a manageable safety profile across evaluated doses

*Includes one patient with grade 5 pneumonitis; AE, adverse event; CRS, cytokine release syndrome.

Borghaei H et al. IASLC 2022;Abstract OA12.05.

DeLLphi-300: Treatment-Related Adverse Events of Interest for Tarlatamab

Events of Interest (AMQN)	All Patients (N = 106)	
	All grades n (%)	Grade ≥ 3 n (%)
CRS*	56 (53)	1 (1)
Neurologic events†	53 (50)	7 (7)
Neutropenia‡	17 (16)	10 (9)

- CRS AEs (Lee, 2014) were mostly grade 1, occurred in cycle 1 and rarely recurred in subsequent cycles, and were generally manageable; no grade 4/5 CRS
  - 8/106 patients [8%] required tocilizumab for CRS
- Treatment-related neurologic events (NEs) were predominantly grade 1 and either dysgeusia or headache
  - Confusion was the most common grade ≥ 3 treatment-related NE (n=5). Confusion was the only grade 4 NE on the study (n=1)
- Grade 4 treatment-related neutropenia occurred in 4 patients (4%); no cases of febrile neutropenia

AMQN, Amgen MedDRA query narrow; CRS, cytokine release syndrome; NE, neurologic event. *CRS includes cytokine abnormal, cytokine release syndrome, cytokine storm, cytokine test; †Neurologic Events based on "Central neuropsychiatric events due to direct neurotoxicities" search and was graded using CTCAE version 4.0; ‡Neutropenia based on AMQN search and graded using CTCAE version 4.0.

Borghaei H et al. IASLC 2022;Abstract OA12.05.

2022 ASCO ANNUAL MEETING

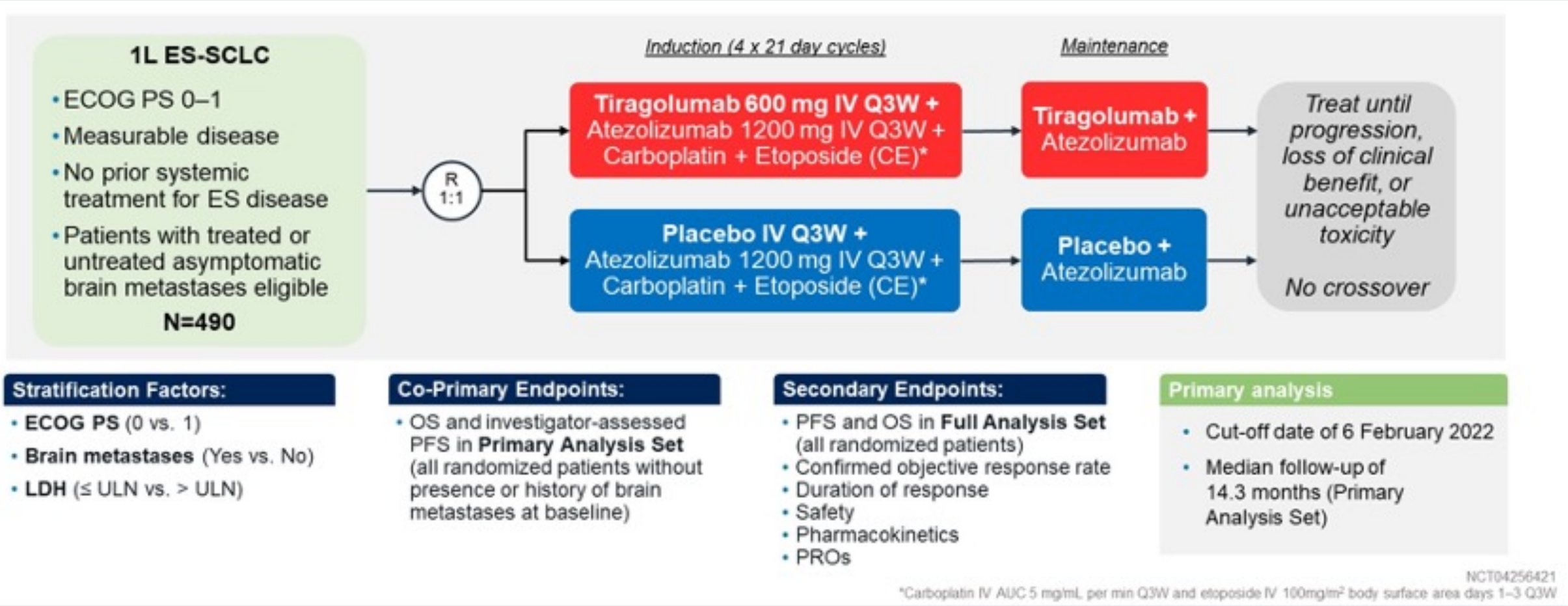
Abstract LBA8507

SKYSCRAPER-02: Primary results of a phase III, randomized, double-blind, placebo-controlled study of atezolizumab + carboplatin + etoposide with or without tiragolumab in patients with untreated extensive-stage small cell lung cancer

Charles M. Rudin,[1] Stephen V. Liu,[2] Shun Lu,[3] Ross A. Soo,[4] Min Hee Hong,[5] Jong-Seok Lee,[6] Maciej Bryl,[7] Daphne Dumoulin,[8] Achim Rittmeyer,[9] Chao-Hua Chiu,[10] Ozgur Ozyilkan,[11] Alejandro Navarro,[12] Silvia Novello,[13] Yuichi Ozawa,[14] Anthony Lee,[15] Meilin Huang,[15] Xiaohui Wen,[15] Tien Hoang,[15] Raymond Meng,[15] Martin Reck[16]

RTP RESEARCH TO PRACTICE

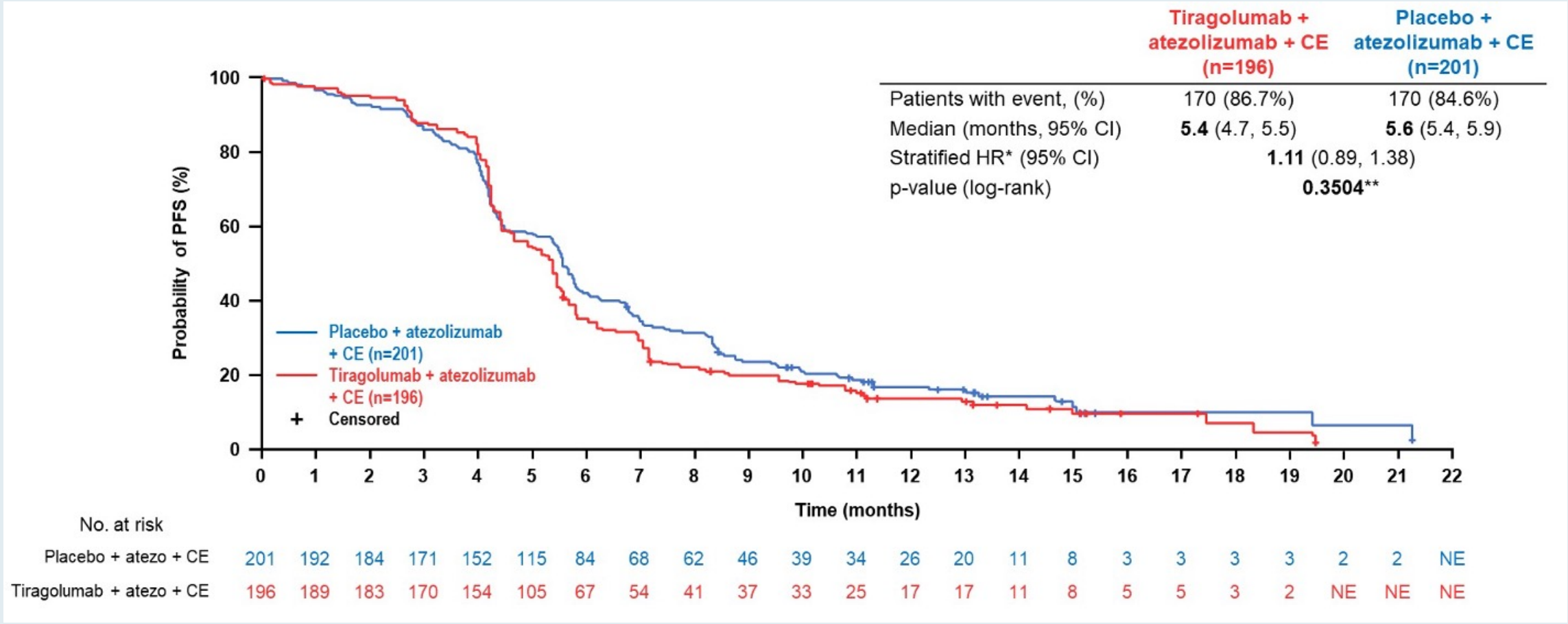
SKYSCRAPER-02: Phase III Trial Schema



Rudin CM et al. ASCO 2022;Abstract LBA8507.

RTP RESEARCH TO PRACTICE

SKYSCRAPER-02: PFS in the Primary Analysis Set

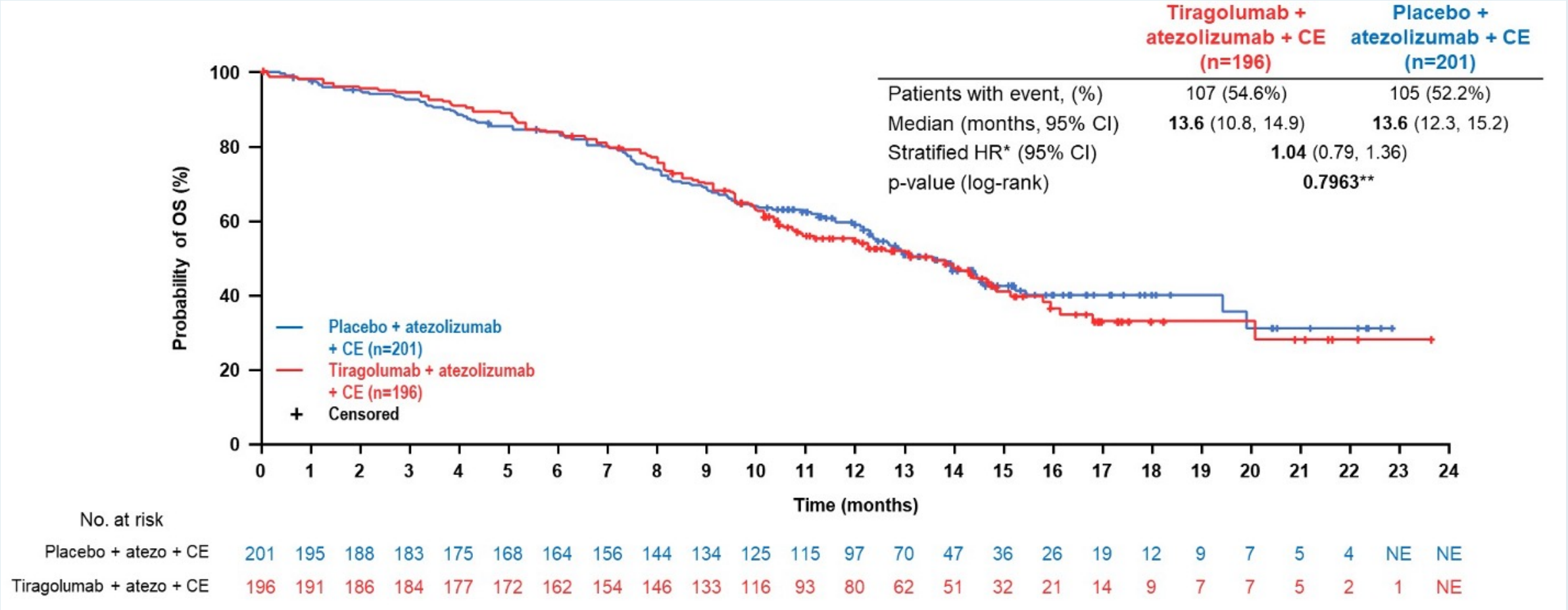


	Tiragolumab + atezolizumab + CE (n=196)	Placebo + atezolizumab + CE (n=201)
Patients with event, (%)	170 (86.7%)	170 (84.6%)
Median (months, 95% CI)	**5.4** (4.7, 5.5)	**5.6** (5.4, 5.9)
Stratified HR* (95% CI)	**1.11** (0.89, 1.38)	
p-value (log-rank)	**0.3504****	

PFS = progression-free survival; CE = carboplatin and etoposide

Rudin CM et al. ASCO 2022;Abstract LBA8507.

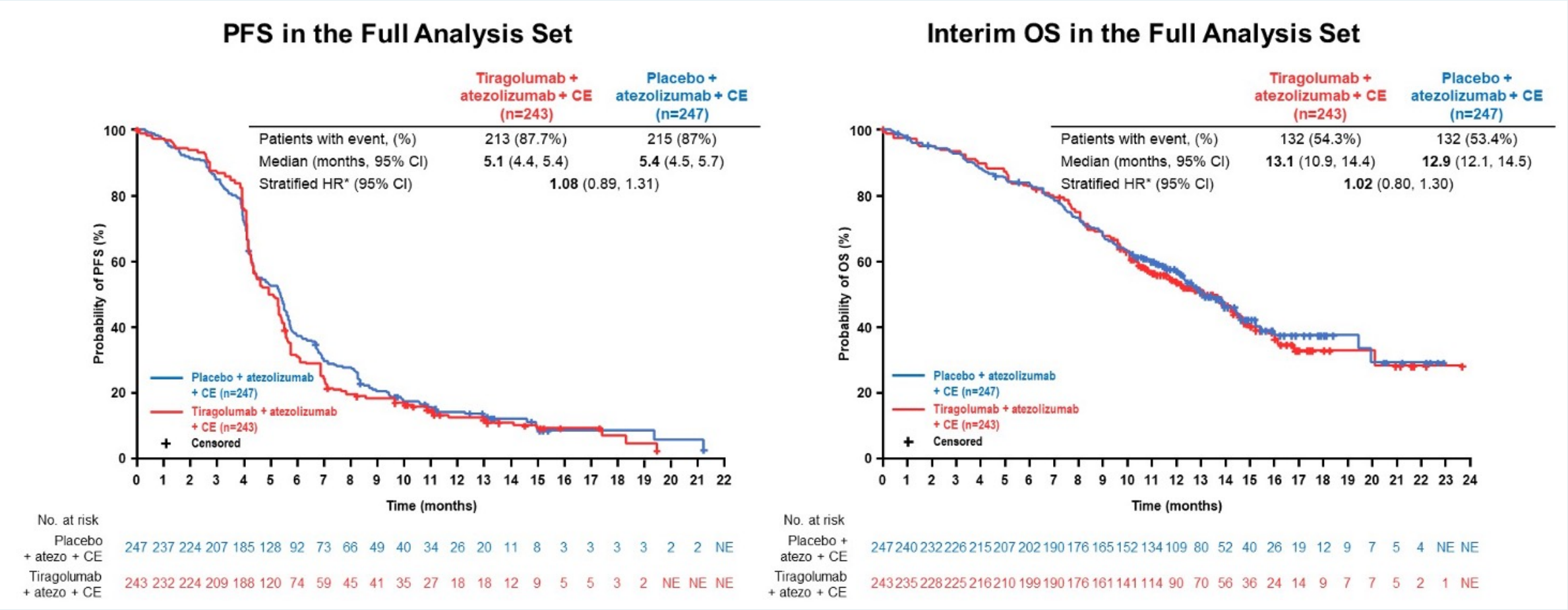
SKYSCRAPER-02: OS in the Primary Analysis Set



OS = overall survival; CE = carboplatin and etoposide

Rudin CM et al. ASCO 2022;Abstract LBA8507.

SKYSCRAPER-02: PFS and OS in the Full Analysis Set



PFS = progression-free survival; OS = overall survival; CE = carboplatin and etoposide

Rudin CM et al. ASCO 2022;Abstract LBA8507.

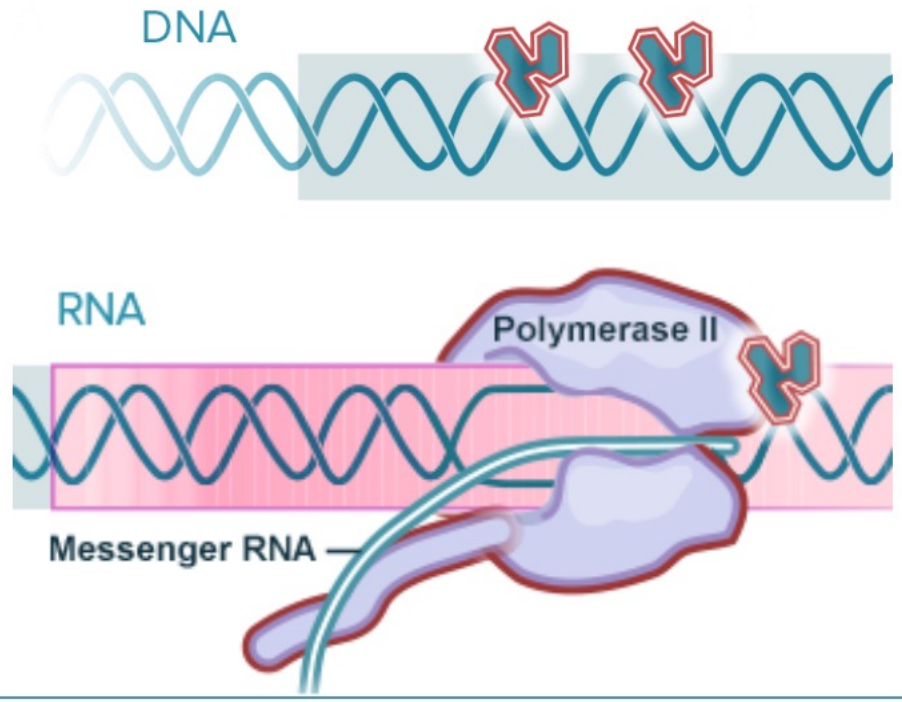
Select Ongoing Phase III Trials of Anti-PD-1/PD-L1 Antibodies Combined with Other Therapeutic Approaches as Initial Therapy for ES-SCLC

Trial identifier	N	Study arms	Estimated primary completion date
IMforte (NCT05091567)	690	• Atezolizumab + carboplatin/etoposide → atezolizumab + lurbinectedin • Atezolizumab + carboplatin/etoposide	April 2025
KEYVIBE-008 (NCT05224141)	450	• Pembrolizumab/vibostolimab + platinum/etoposide → pembrolizumab/vibostolimab • Atezolizumab + platinum/etoposide → atezolizumab	May 2025
RAPTOR (NCT04402788)	138	• Atezolizumab + radiation therapy • Atezolizumab	April 2027

Selection and Sequencing of Therapy for Patients with Relapsed SCLC

Lurbinectedin Mechanism of Action

Effects on the tumor



- Binds to guanine residues in the minor groove of DNA
- Affects activity of transcription factors

- Stalls RNA polymerase II
- Affects DNA repair pathways
- Results in eventual cell death

https://www.zepzelcapro.com/mechanism-of-action/

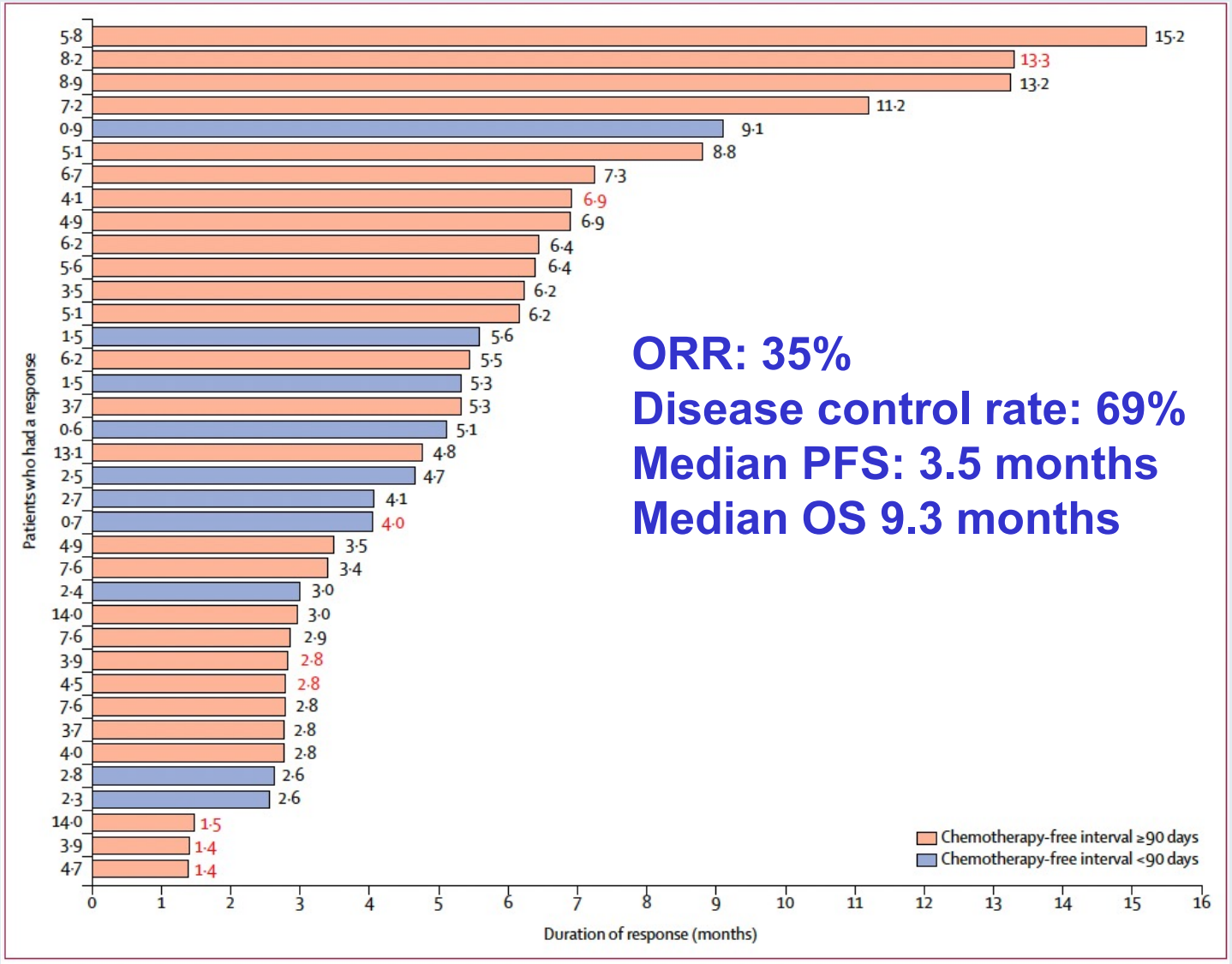
RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21(5):645-54.

Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial

José Trigo, Vivek Subbiah*, Benjamin Besse, Victor Moreno, Rafael López, María Angeles Sala, Solange Peters, Santiago Ponce, Cristian Fernández, Vicente Alfaro, Javier Gómez, Carmen Kahatt, Ali Zeaiter, Khalil Zaman, Valentina Boni, Jennifer Arrondeau, Maite Martínez, Jean-Pierre Delord, Ahmad Awada, Rebecca Kristeleit, Maria Eugenia Olmedo, Luciano Wannesson, Javier Valdivia, María Jesús Rubio, Antonio Anton, John Sarantopoulos, Sant P Chawla, Joaquín Mosquera-Martinez, Manolo D'Arcangelo, Armando Santoro, Victor M Villalobos, Jacob Sands, Luis Paz-Ares*

Response, Survival and Common AEs in the Pivotal Phase II Study of Lurbinectedin for SCLC After 1 Line of Chemotherapy



Common treatment-related adverse events		
	Grade 1-2	Grade 3-4
Anemia	87%	9%
Leukopenia	50%	29%
Neutropenia	26%	46%
Thrombocytopenia	37%	7%

AEs = adverse events; ORR = overall response rate;
PFS = progression-free survival; OS = overall survival

Trigo J et al. *Lancet Oncol* 2020;21(5):645-54.

Lurbinectedin/doxorubicin *versus* CAV or topotecan in relapsed SCLC patients: Phase III randomized ATLANTIS trial

Luis Paz-Ares[1]

[1]Hospital Universitario 12 de Octubre, Madrid, Spain

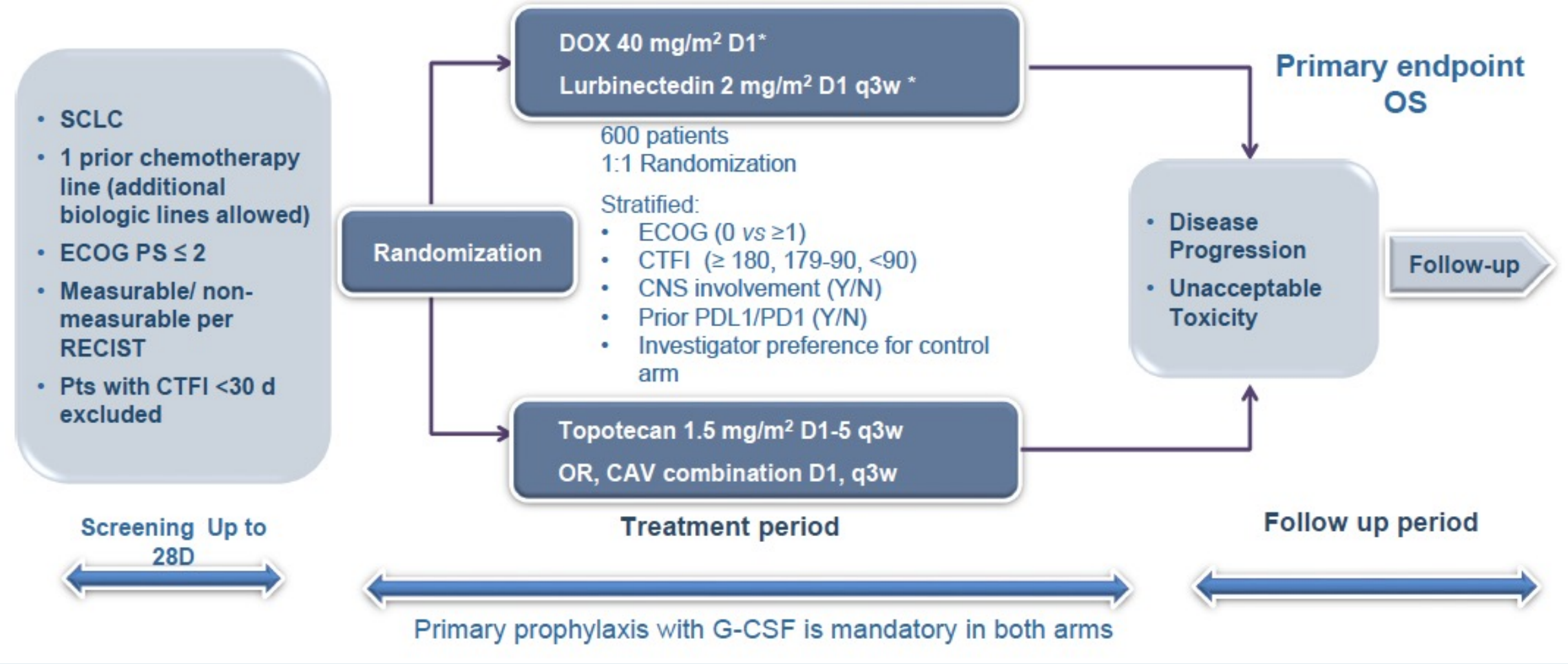
Tudor Eliade Ciuleanu[2], Alejandro Navarro[3], Andrea Fulop[4], Sophie Cousin[5], Laura Bonanno[6], Egbert Smit[7], Alberto Chiappori[8], Mª Eugenia Olmedo[9], Ildiko Horvath[10], Christian Gröhé[11], José Antonio López-Vilariño[12], Rafael Núñez[12], Antonio Nieto[12], Martin Cullell-Young[12], Noelia Vasco[12], Carmen Kahatt[12], Ali Zeaiter[12], Enric Carcereny[13], Jaromir Roubec[14], Konstantios Syrigos[15], Gregory Lo[16], Isidoro Barneto[17].

[2]Institutul Oncologic Prof. Dr. Ion Chiricuta, și Universitatea de medicina și farmacie Iuliu Hatieganu , Cluj-Napoca, Romania. [3]Hospital Vall d´Hebrón, Barcelona, Spain. [4]Orszagos Koranyi TBC es Pulmonologiai Intezet, 6, Budapest, Hungary. [5] CRLCC Institut Bergonie, Bordeaux, France. [6]Istituto Oncologico Veneto, Padova, Italy. [7]Antonie van Leeuwenhoek Ziekenhuis, Amsterdam, The Netherlands. [8]H. Lee Moffitt Cancer Center & Research Institute, Tampa (FL), USA. [9]Hospital Universitario Ramón y Cajal, Madrid, Spain. [10]Orszagos Koranyi TBC es Pulmonologiai Intezet, 14, Budapest, Hungary. [11]Evangelische Lungenklinik, Berlin, Germany. [12]Pharma Mar, S.A., Colmenar Viejo, Madrid, Spain. [13] Institut Català d'Oncologia-Hospital Germans Trias i Pujol B-ARGO GROUP, Badalona, Spain. [14]Nemocnice AGEL, Ostrava-Vitkovice, Czech Republic. [15]3rd Department of Medicine, National & Kapodistrian University of Athens. [16]Lakeridege Hospital, Oshawa (ON), Canada. [17]Hospital Reina Sofía, Córdoba, Spain.

IASLC 2021 World Conference on Lung Cancer
SEPTEMBER 8 - 14, 2021 I WORLDWIDE VIRTUAL EVENT

Abstract PL02.03

ATLANTIS: Phase III Trial Design

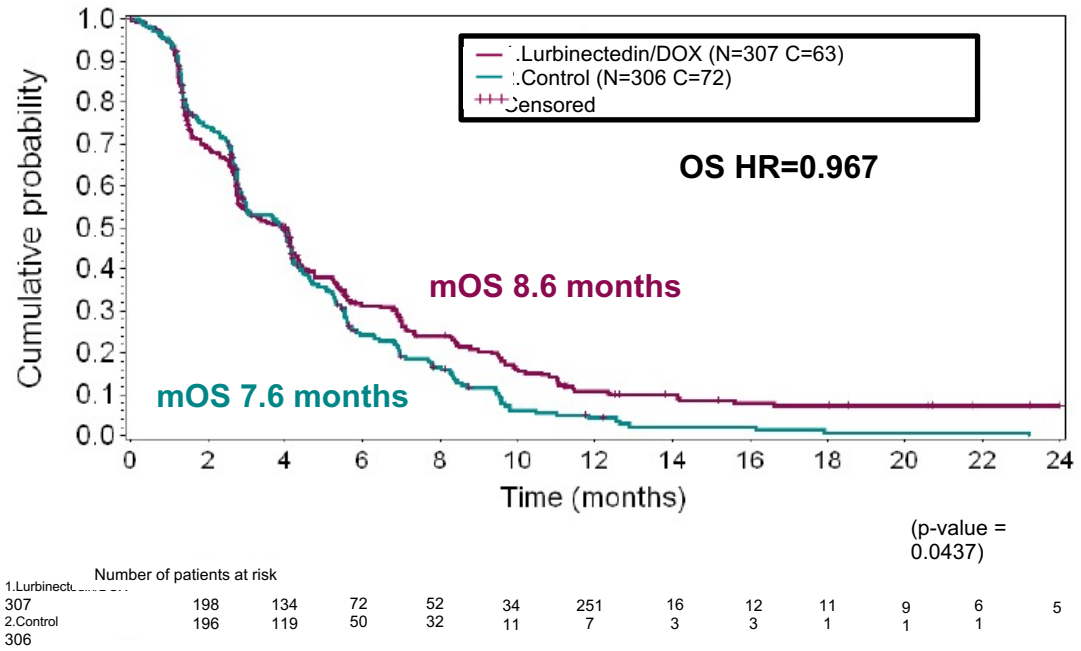


DOX = doxorubicin; OS = overall survival; CTFI = chemotherapy-free interval; CAV = cyclophosphamide, doxorubicin and vincristine

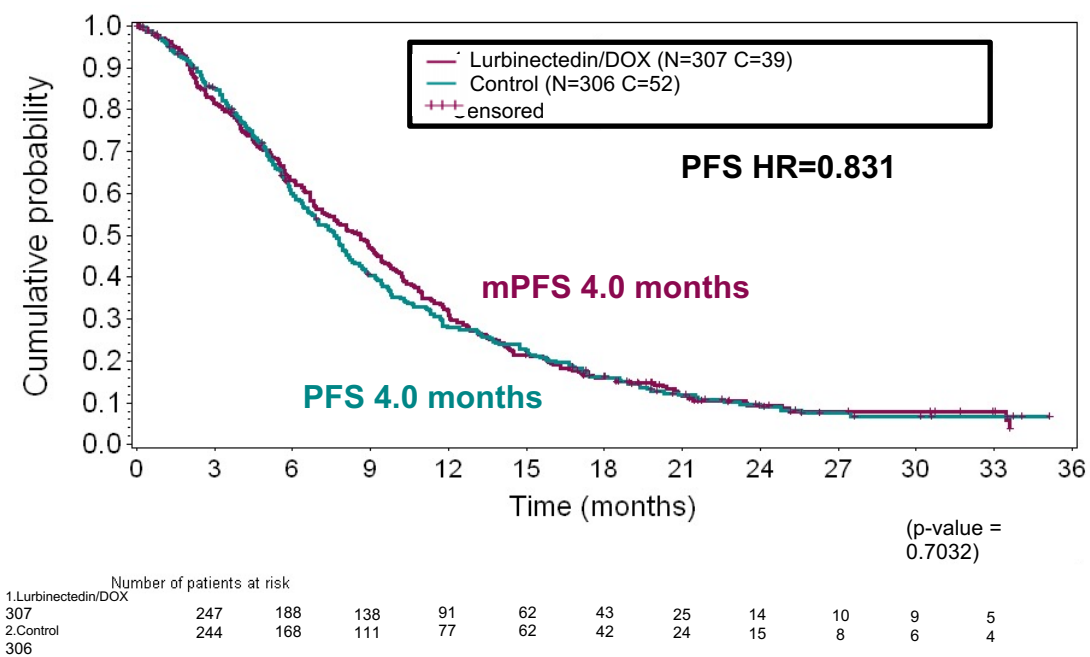
Paz-Ares et al. WCLC 2021;Abstract PL02.03.

ATLANTIS: Lurbinectedin with Doxorubicin versus CAV or Topotecan for Patients with Relapsed SCLC

Overall Survival



Progression-free Survival



CAV = cyclophosphamide, doxorubicin and vincristine; DOX = doxorubicin; OS = overall survival; mOS = median OS; PFS = progression-free survival; mPFS = median PFS

Paz-Ares et al. WCLC 2021;Abstract PL02.03.

ATLANTIS: Safety Summary

Hematological	Lurbinectedin+DOX (n=303)	Control (n=289)	
	Grade ≥3	Grade ≥3	p-value
Anaemia	44 (14.5)	90 (31.1)	<0.0001
Neutropenia	112 (37.0)	200 (69.2)	<0.0001
Febrile neutropenia	12 (4.0)	24 (8.3)	0.0377
Thrombocytopenia	42 (13.9)	90 (31.1)	<0.0001

Non hematological	Lurbinectedin+DOX (n=303)	Control (n=289)	
	Grade ≥3	Grade ≥3	p-value
ALT increased	6 (2.0)	3 (1.0)	0.5057
AP increased	2 (0.7)	3 (1.0)	0.6783
AST increased	7 (2.3)	4 (1.4)	0.5463
Fatigue	26 (8.6)	31 (10.7)	0.4051
Nausea	6 (2.0)	4 (1.4)	0.7525
Vomiting	4 (1.3)	0	0.1242

	Lurbinectedin+DOX (n=303) n (%)	Control (n=289) n (%)
Any AE treatment-related	268 (88.4)	266 (92.0)
Any grade ≥3 AE	**143 (47.2)**	**218 (75.4)**
Any grade 4 AE	**49 (16.2)**	**158 (54.7)**
Any grade ≥3 SAE	38 (12.5)	83 (28.7)
Death associated with AEs	**1 (0.3)**	**10 (3.5)**
Treatment discontinuations associated with AEs	23 (7.6)	45 (15.6)
Delays associated with AEs	79 (26.1)	99 (34.3)
Reductions associated with AEs	66 (21.8)	138 (47.8)

DOX = doxorubicin; AE = adverse event; SAE = serious AE

Paz-Ares et al. WCLC 2021;Abstract PL02.03.

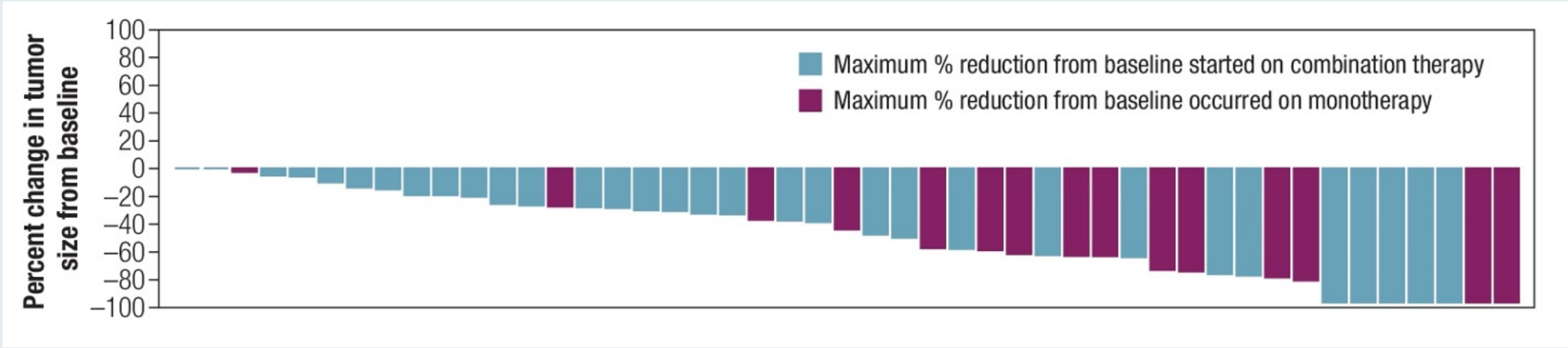
Analysis of Patients With Relapsed Small Cell Lung Cancer (SCLC) Receiving Single-agent Lurbinectedin in the Phase 3 ATLANTIS Trial

Alejandro Navarro,[1,*] Santiago Ponce Aix,[2,3] Isidoro C. Barneto,[4] Egbert F. Smit,[5] José Antonio López-Vilariño,[6] Antonio Nieto,[6] Carmen Kahatt,[6] Ali Zeaiter,[6] Sophie Cousin,[7] Helge Bischoff,[8] Jaromir Roubec,[9] Konstantinos Syrigos,[10] Luis Paz-Ares[3]

ASCO 2022 | Abstract 8524

RTP RESEARCH TO PRACTICE

ATLANTIS: Change in Tumor Size from Baseline During Combination Therapy or Monotherapy (IRC)



Navarro A et al. ASCO 2022;Abstract 8524.

RTP RESEARCH TO PRACTICE

ATLANTIS: Change in Tumor Size from Baseline During Combination Therapy or Monotherapy (IRC)

Best response to lurbinectedin + doxorubicin	Best response on lurbinectedin monotherapy 3.2 mg/m²			
	CR	PR	SD	PD
CR (n = 3)	3			
PR (n = 26)	3	15		8
SD (n = 19)	1	2	8	8
	Improving response ⟵		⟶ Declining response	

The majority (32/48) of patients who switched to lurbinectedin monotherapy maintained or improved the tumor response achieved on combination therapy (16 patients had progressive disease)

Navarro A et al. ASCO 2022;Abstract 8524.

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.

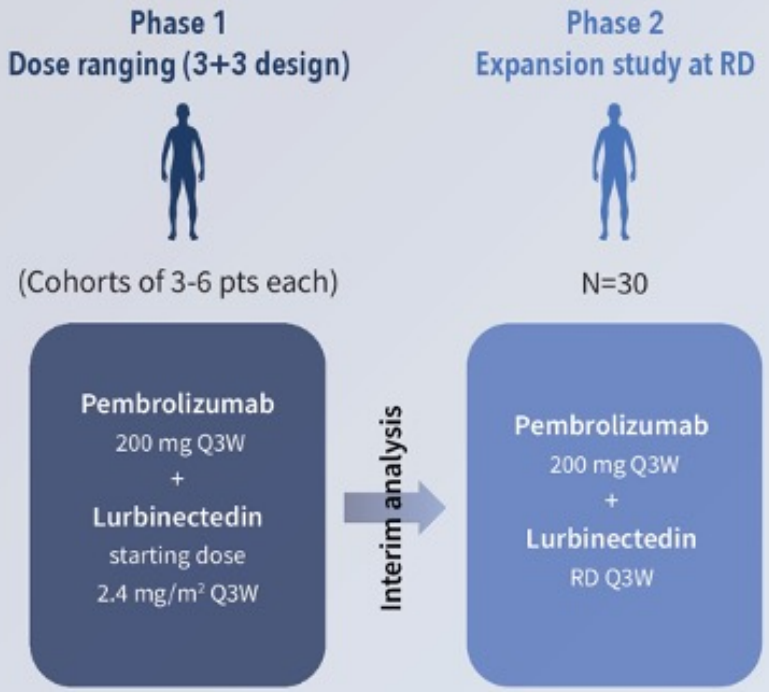
ASCO 2022;Abstract 8581.

LUPER Phase I/II Study Design

Prospective phase I/II, multicenter, open-label study (NCT04358237)

Key inclusion criteria

- ≥18 years with confirmed SCLC
- ECOG PS 0-1
- Measurable disease as per RECIST v.1.1
- Progression to a CT-containing regimen (≥4 weeks before study initiation)
- Previous immunotherapy NOT allowed
- Pts with treated, stable, asymptomatic brain metastases (BMs) are allowed



The RP2D was the highest DL at which 0/3 pts or ≤1/6 pts experienced DLTs during the first cycle.
P and L will be administered Day 1 Q3W until disease progression, unacceptable toxicity, or consent withdrawal.

Primary endpoints

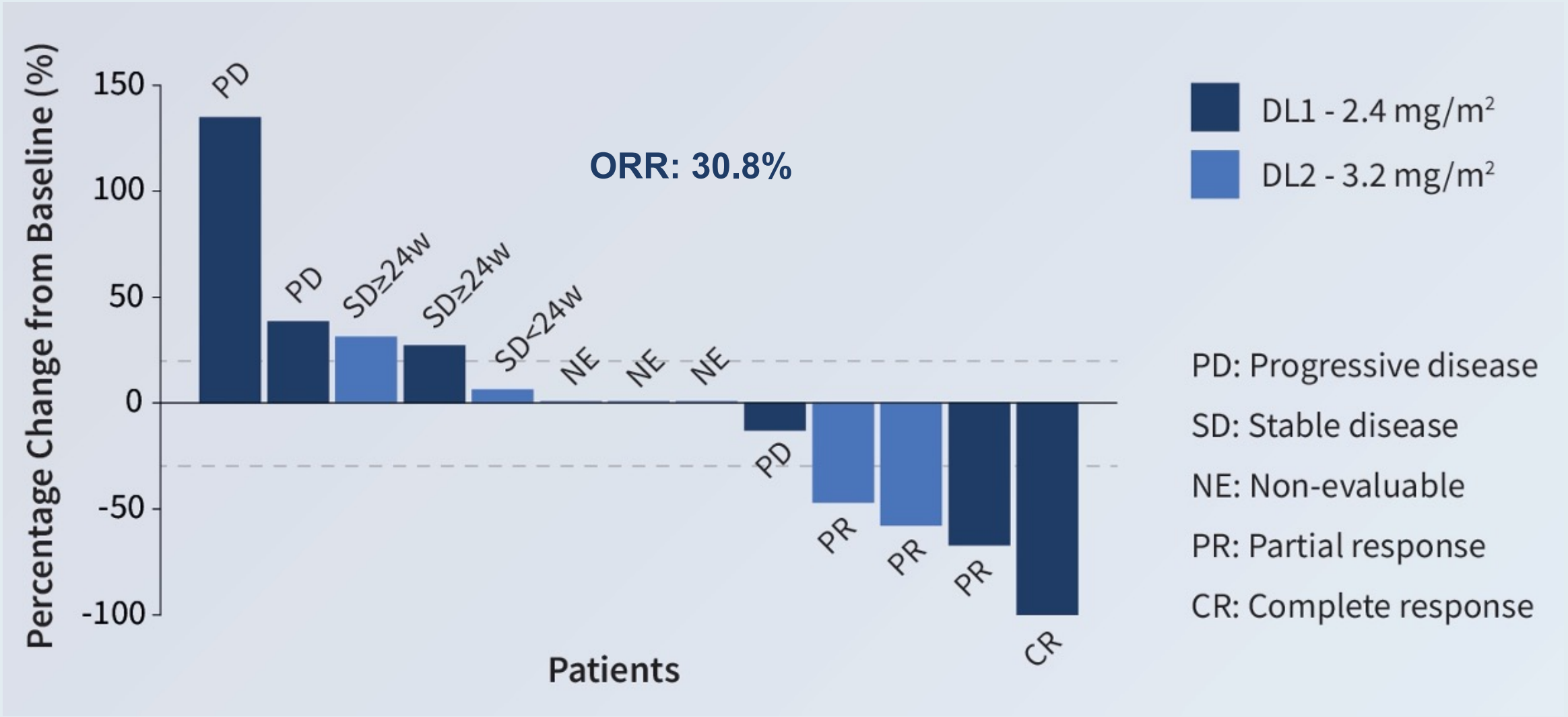
- Phase 1: MTD and RD of L in combination with P for phase II in pts with relapsed SCLC.
- Phase 2: Efficacy of L in combination with P in terms of ORR, according to RECIST 1.1, in pts with relapsed SCLC.

Secondary endpoints

- Safety as per CTCAE 5.0, preliminary efficacy, and pharmacokinetics.

Calles A et al. ASCO 2022;Abstract 8581.

LUPER: Best Overall Response



Calles A et al. ASCO 2022;Abstract 8581.

LUPER: Safety Analysis

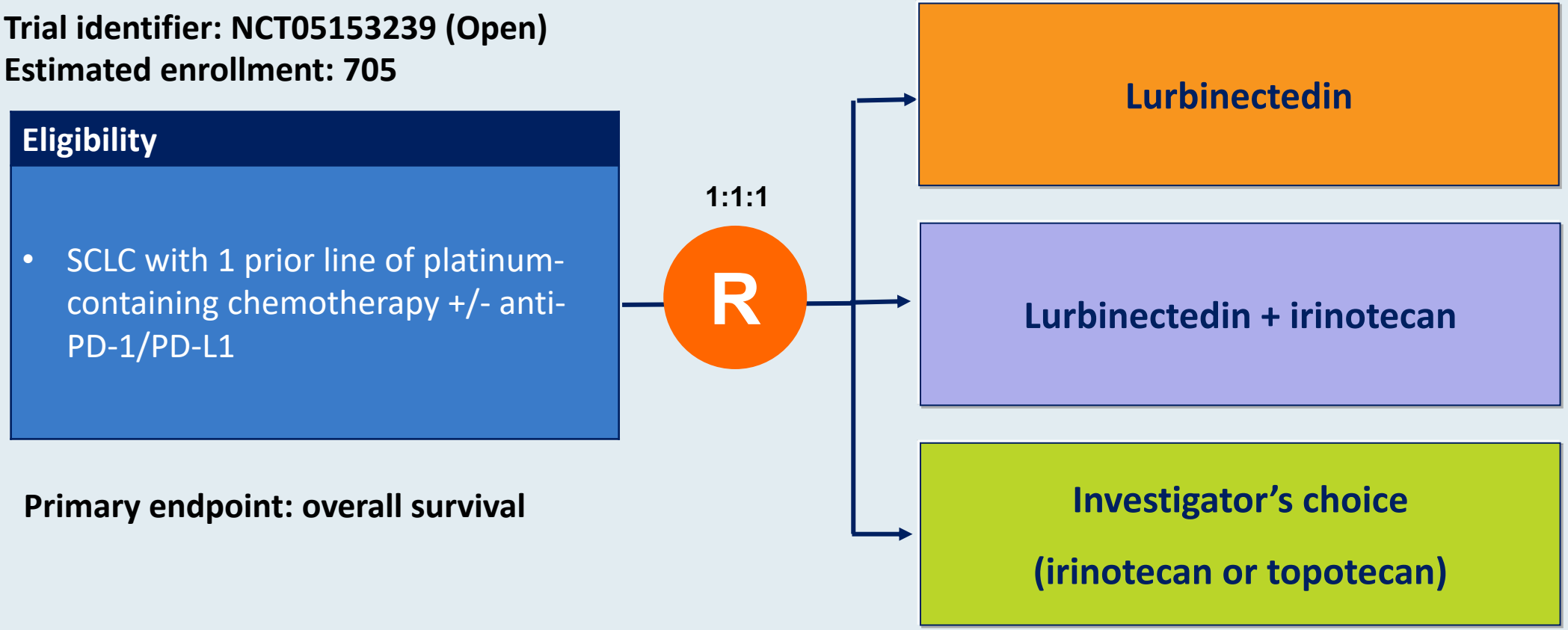
Overall (N=13)	Any grade n (%)	Grade 3 n (%)	Grade 4 n (%)
TEAEs	11 (84.6)	7 (53.9)	2 (15.4)
Haematologic	8 (61.5)	3 (23.1)	2 (15.4)
Neutropenia	7 (53.9)	3 (23.1)	2 (15.4)
Thrombocytopenia	3 (23.1)	1 (7.7)	0 (0.0)
Anaemia	2 (15.4)	0 (0.0)	0 (0.0)
Non-haematologic	11 (84.6)	4 (30.8)	0 (0.0)
Fatigue	10 (76.9)	1 (7.7)	0 (0.0)
Nausea	7 (53.9)	0 (0.0)	0 (0.0)
ALT increased	4 (30.8)	3 (23.1)	0 (0.0)
Decreased appetite	4 (30.8)	0 (0.0)	0 (0.0)
Vomiting	2 (15.4)	0 (0.0)	0 (0.0)
Constipation	2 (15.4)	0 (0.0)	0 (0.0)
AST increased	3 (23.1)	2 (15.4)	0 (0.0)
Dyspnoea	2 (15.4)	0 (0.0)	0 (0.0)

TAEAs = treatment-emergent adverse events

Calles A et al. ASCO 2022;Abstract 8581.

Ongoing Phase III LAGOON Study Design

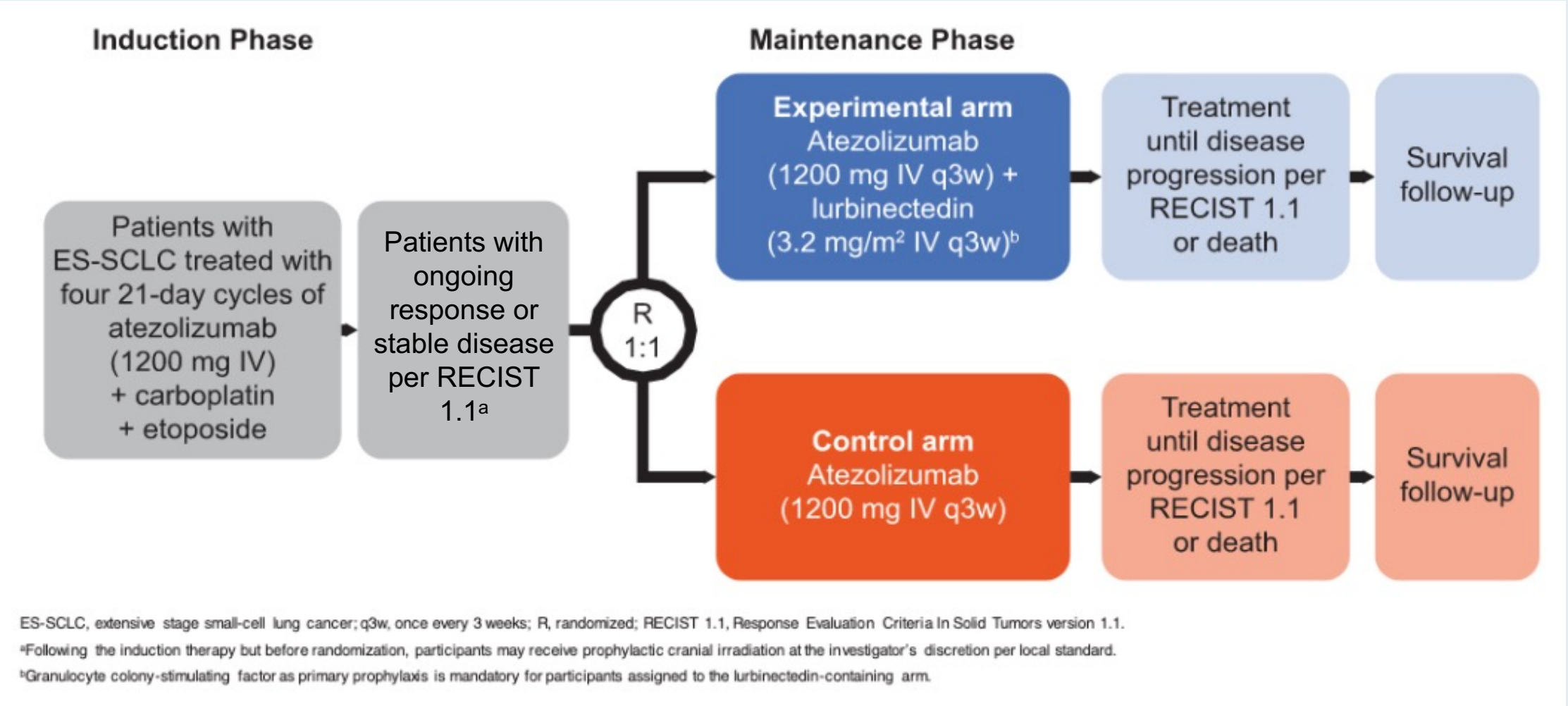
Trial identifier: NCT05153239 (Open)
Estimated enrollment: 705



Primary endpoint: overall survival

www.clinicaltrials.gov. NCT05153239. Accessed July 2022.

IMforte Phase III Study Schema: Maintenance Therapy with Lurbinectedin and Atezolizumab versus Atezolizumab



ES-SCLC, extensive stage small-cell lung cancer; q3w, once every 3 weeks; R, randomized; RECIST 1.1, Response Evaluation Criteria In Solid Tumors version 1.1.

[a]Following the induction therapy but before randomization, participants may receive prophylactic cranial irradiation at the investigator's discretion per local standard.

[b]Granulocyte colony-stimulating factor as primary prophylaxis is mandatory for participants assigned to the lurbinectedin-containing arm.

Paz-Ares L et al. IASLC 2022;Abstract EP14.02-015.

Nivolumab Indication for Small Cell Lung Cancer Withdrawn

Press Release: January 25, 2021

"On December 29, Bristol Myers Squibb issued the following statement on nivolumab's small cell lung cancer (SCLC) indication in the United States.

In 2018, nivolumab was granted accelerated approval by the US Food and Drug Administration (FDA) for the treatment of patients with SCLC whose disease has progressed after platinum-based chemotherapy and at least one other line of therapy. The accelerated approval was based on nivolumab's effect on surrogate endpoints from the phase I/II CheckMate 032 trial for patients with advanced or metastatic solid tumors. The trial demonstrated encouraging response rates and duration of response with nivolumab in SCLC, an aggressive and difficult-to-treat cancer. However, subsequent confirmatory studies in different treatment settings—CheckMate 451 and CheckMate 331—did not meet their primary endpoints of overall survival."

https://ascopost.com/issues/january-25-2021/nivolumab-indication-in-small-cell-lung-cancer-withdrawn-in-us-market/

original reports

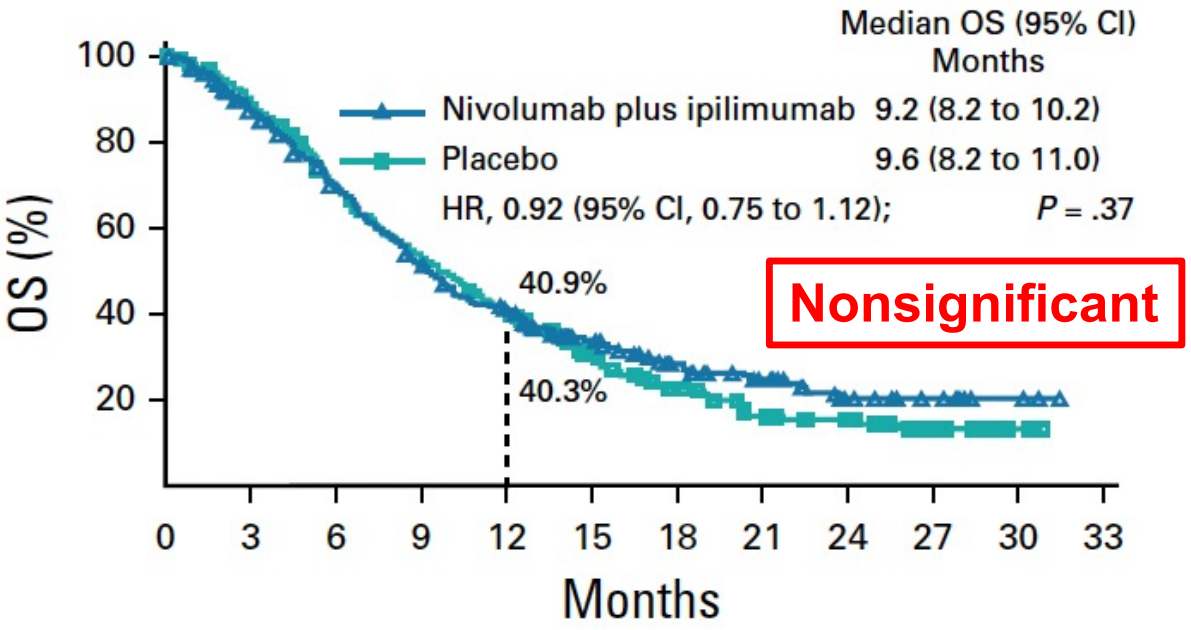
Nivolumab and Ipilimumab as Maintenance Therapy in Extensive-Disease Small-Cell Lung Cancer: CheckMate 451

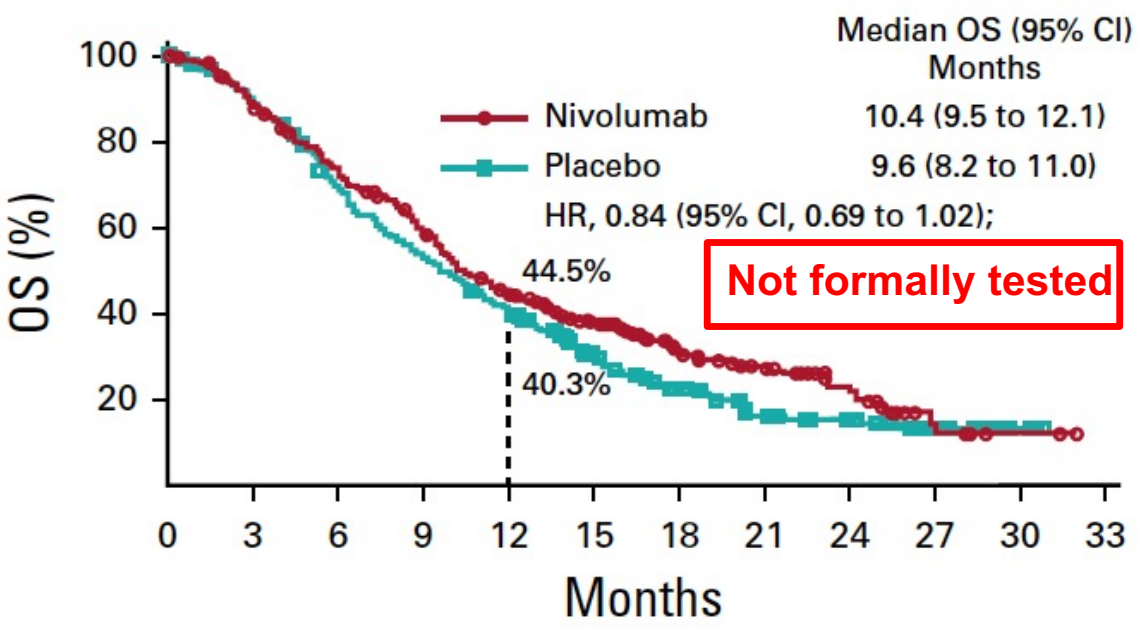
Taofeek K. Owonikoko, MD, PhD[1]; Keunchil Park, MD, PhD[2]; Ramaswamy Govindan, MD[3]; Neal Ready, MD, PhD[4]; Martin Reck, MD, PhD[5]; Solange Peters, MD, PhD[6]; Shaker R. Dakhil, MD[7]; Alejandro Navarro, MD[8]; Jerónimo Rodríguez-Cid, MD[9]; Michael Schenker, MD, PhD[10]; Jong-Seok Lee, MD, PhD[11]; Vanesa Gutierrez, MD[12]; Ivor Percent, MD[13]; Daniel Morgensztern, MD[3]; Carlos H. Barrios, MD[14]; Laurent Greillier, MD, PhD[15]; Sofia Baka, MD, PhD[16]; Miten Patel, MD[17]; Wen Hong Lin, MD[18]; Giovanni Selvaggi, MD[18]; Christine Baudelet, PhD[18]; Jonathan Baden, MSc[18]; Dimple Pandya, MD[18]; Parul Doshi, PhD[18]; and Hye Ryun Kim, MD, PhD[19]

J Clin Oncol 2021;39(12):1349-59.

RTP RESEARCH TO PRACTICE

CheckMate 451: Overall Survival (Primary Endpoint Not Met)





Owonikoko TK et al. *J Clin Oncol* 2021;39(12):1349-59.

RTP RESEARCH TO PRACTICE

Ann Oncol 2021;32(5):631-41.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

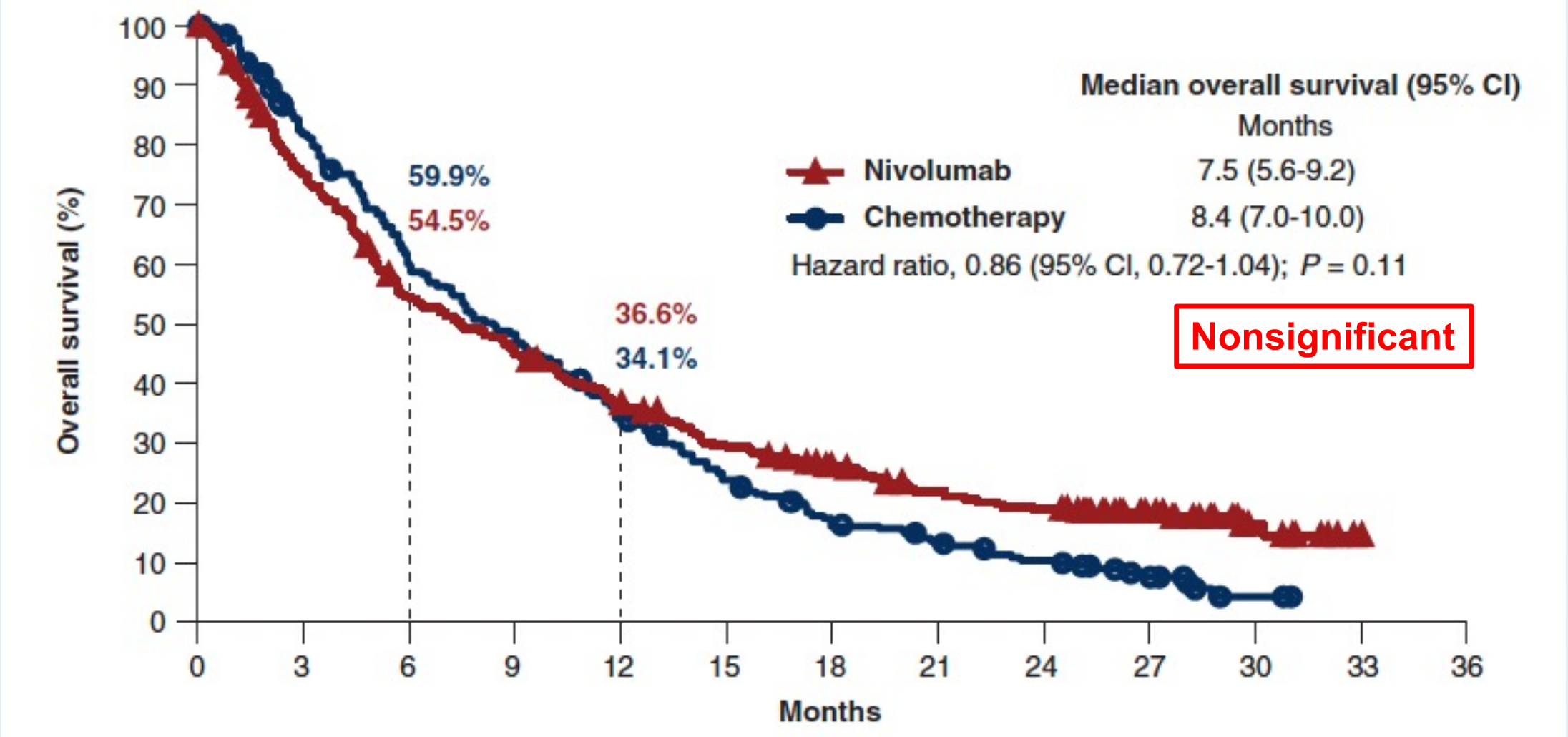
ORIGINAL ARTICLE

Second-line nivolumab in relapsed small-cell lung cancer: CheckMate 331☆

D. R. Spigel[1*], D. Vicente[2], T. E. Ciuleanu[3], S. Gettinger[4], S. Peters[5], L. Horn[6], C. Audigier-Valette[7], N. Pardo Aranda[8], O. Juan-Vidal[9], Y. Cheng[10], H. Zhang[11], M. Shi[12], A. Luft[13], J. Wolf[14], S. Antonia[15†], K. Nakagawa[16], J. Fairchild[17†], C. Baudelet[18], D. Pandya[19], P. Doshi[20], H. Chang[21] & M. Reck[22]

RTP RESEARCH TO PRACTICE

CheckMate 331: Overall Survival (Primary Endpoint Not Met)



Spigel DR et al. *Ann Oncol* 2021;32(5):631-41.

RTP RESEARCH TO PRACTICE

Small Cell Lung Cancer Indication for Pembrolizumab Is Withdrawn

Press Release: March 2, 2021

"On March 1, Merck announced the company is voluntarily withdrawing the US indication for pembrolizumab for the treatment of patients with metastatic small cell lung cancer with disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy. The withdrawal of this indication was done in consultation with the U.S. Food and Drug Administration (FDA), and Merck is working to complete this process over the coming weeks. This decision does not affect other indications for pembrolizumab.

The confirmatory phase III trial for this indication, KEYNOTE-604, met one of its dual primary endpoints of progression-free survival but did not reach statistical significance for the other primary endpoint of overall survival."

https://ascopost.com/news/march-2021/pembrolizumabs-indication-in-small-cell-lung-cancer-is-withdrawn/

RTP RESEARCH TO PRACTICE

rapid communications

Pembrolizumab or Placebo Plus Etoposide and Platinum as First-Line Therapy for Extensive-Stage Small-Cell Lung Cancer: Randomized, Double-Blind, Phase III KEYNOTE-604 Study

Charles M. Rudin, MD, PhD[1]; Mark M. Awad, MD, PhD[2]; Alejandro Navarro, MD[3]; Maya Gottfried, MD[4]; Solange Peters, MD, PhD[5]; Tibor Csőszi, MD[6]; Parneet K. Cheema, MD[7]; Delvys Rodriguez-Abreu, MD[8]; Mirjana Wollner, MD[9]; James Chih-Hsin Yang, MD, PhD[10]; Julien Mazieres, MD, PhD[11]; Francisco J. Orlandi, MD[12]; Alexander Luft, PhD, MD[13]; Mahmut Gümüş, MD[14]; Terufumi Kato, MD[15]; Gregory P. Kalemkerian, MD[16]; Yiwen Luo, PhD[17]; Victoria Ebiana, MD[17]; M. Catherine Pietanza, MD[17]; and Hye Ryun Kim, MD[18] on behalf of the KEYNOTE-604 Investigators

J Clin Oncol 2020;38(21):2369-79.

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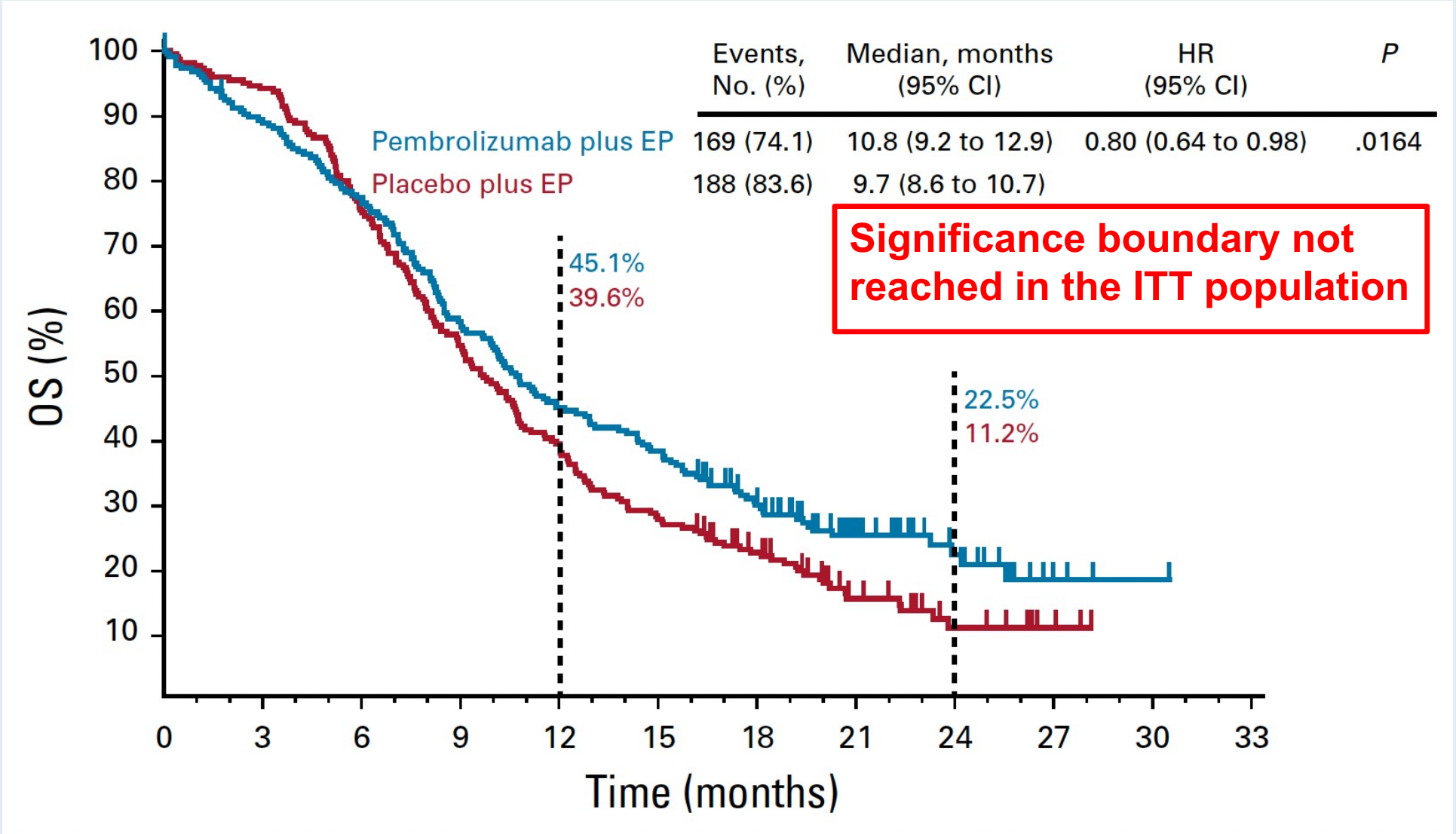
KEYNOTE-604: Final Overall Survival (Coprimary Endpoint Not Met)



EP = etoposide and platinum

Rudin CM et al. *J Clin Oncol* 2020;38(21):2369-79.

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

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IASLC 2022;Abstract OA12.06

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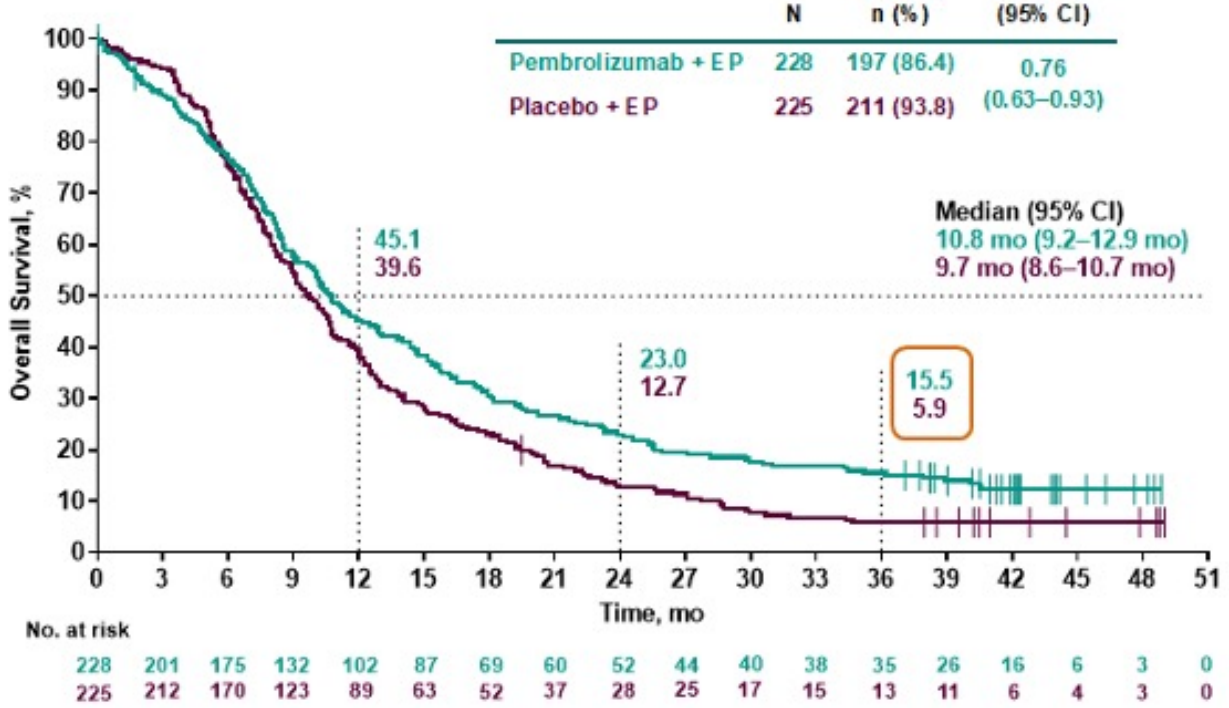
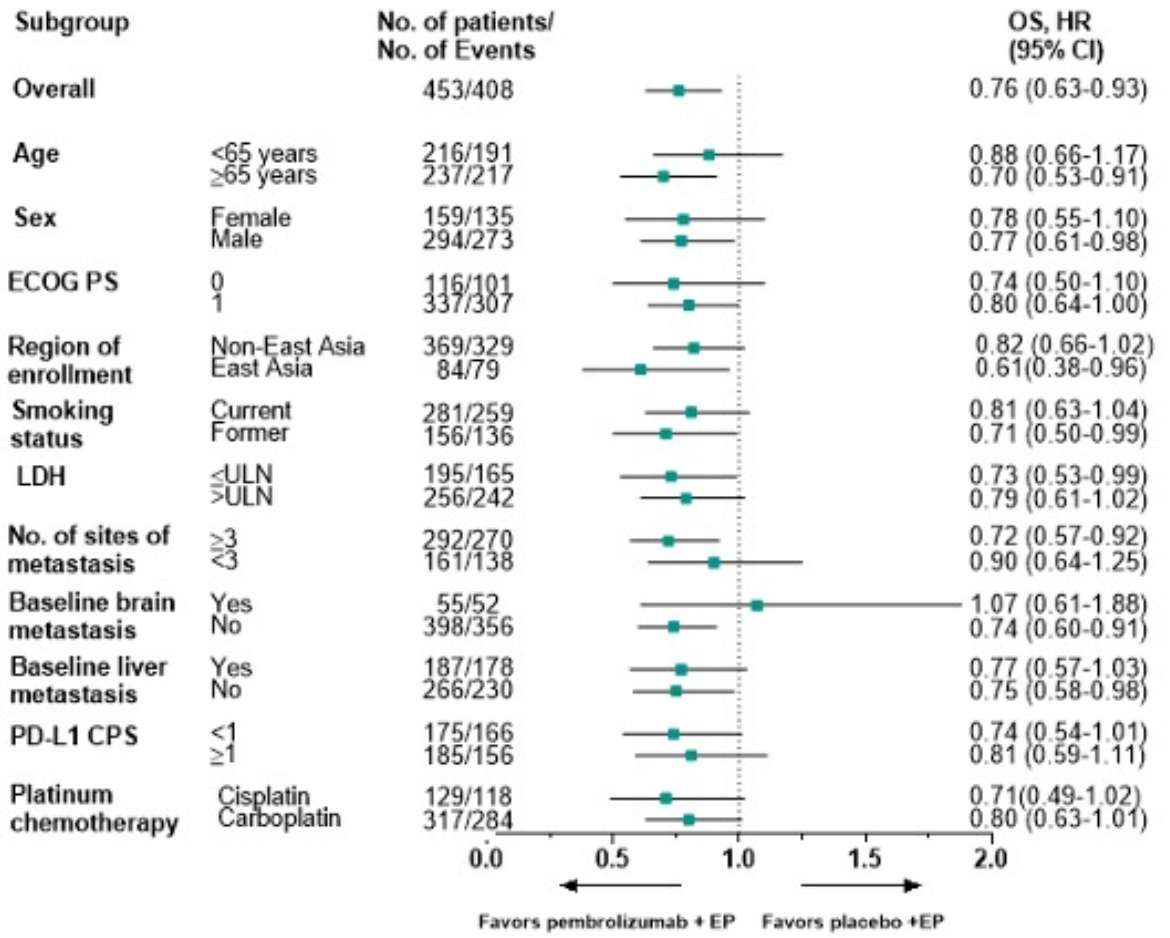
KEYNOTE-604: Long-Term Follow-Up of Overall Survival in the ITT Population

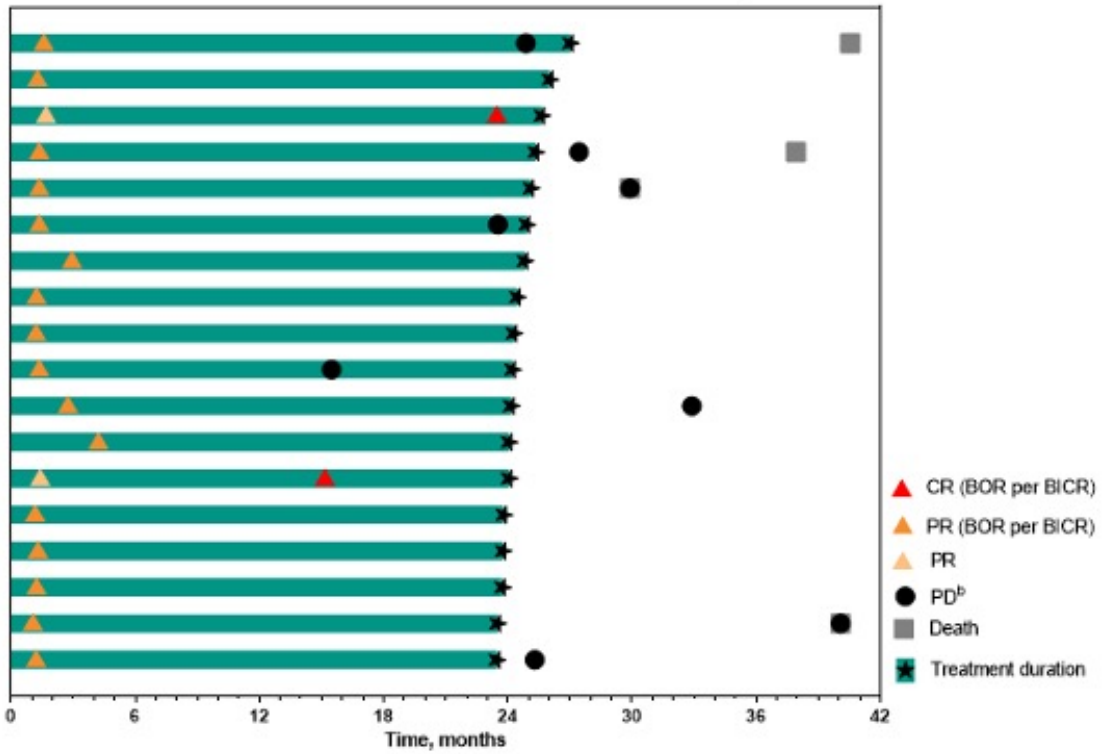




Rudin CM et al. IASLC 2022;Abstract OA12.06.

KEYNOTE-604: Response Summary with Long-Term Follow-Up

Treatment Duration and Time to Response



Summary of OS and Response

	Completed 35 cycles n = 18
Median OS (95% CI),[c] mo	NR (16.6–NR)
2-year OS rate after completing 35 cycles (95% CI),[d] %	72.2 (39.5–89.2)
ORR (95% CI),[e] %	100.0 (81.5–100.0)
Best overall response,[e] n (%)	
CR	2 (11.1)
PR	16 (88.9)
DOR, median (range),[c,e] mo	NR (14.1 to 46.8+)
DOR ≥12 mo, %	100.0
DOR ≥24 mo, %	83.3

- 14 patients (77.8% of 18 and 6.1% of 228) were alive as of last assessment before data cutoff
- 2/225 (0.9%) patients in the placebo + EP arm completed 35 cycles and were alive as of data cutoff

NR, not reached. '+' indicates no PD by the time of last assessment.
[a]Median time from randomization to data cutoff was 42.5 (range, 38.2–49.5) mo.
[b]Of 3 patients who had PD after completion of 35 cycles of pembrolizumab, 1 patient started pembrolizumab 6 months after PD and 2 patients had not received subsequent therapy as of database cutoff.
[c]OS and DOR estimates are based on the Kaplan-Meier method.
[d]Corresponds to approximately 4 years after randomization.
[e]Based on RECIST v1.1 by BICR.
Database cutoff date: September 21, 2021.

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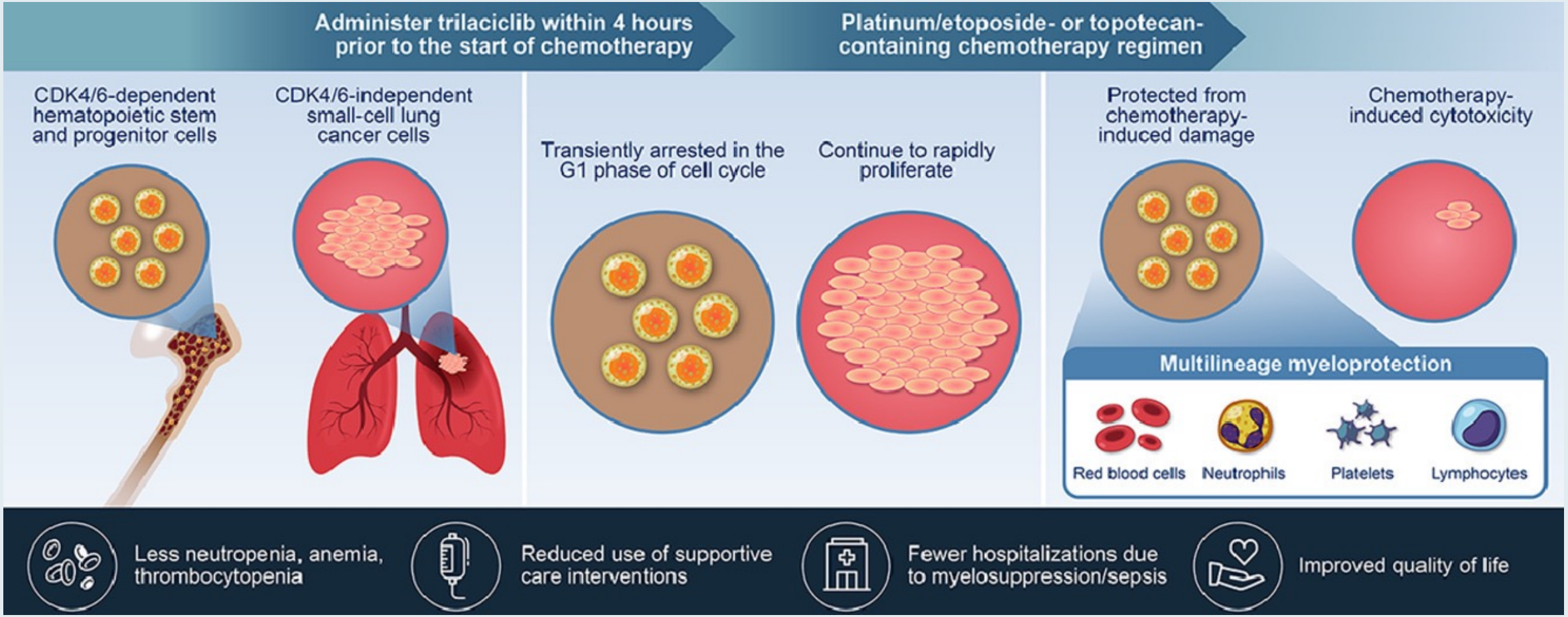
Safety and Tolerability Issues with Available Therapies for SCLC

Trilaciclib: Mechanism of Action



Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

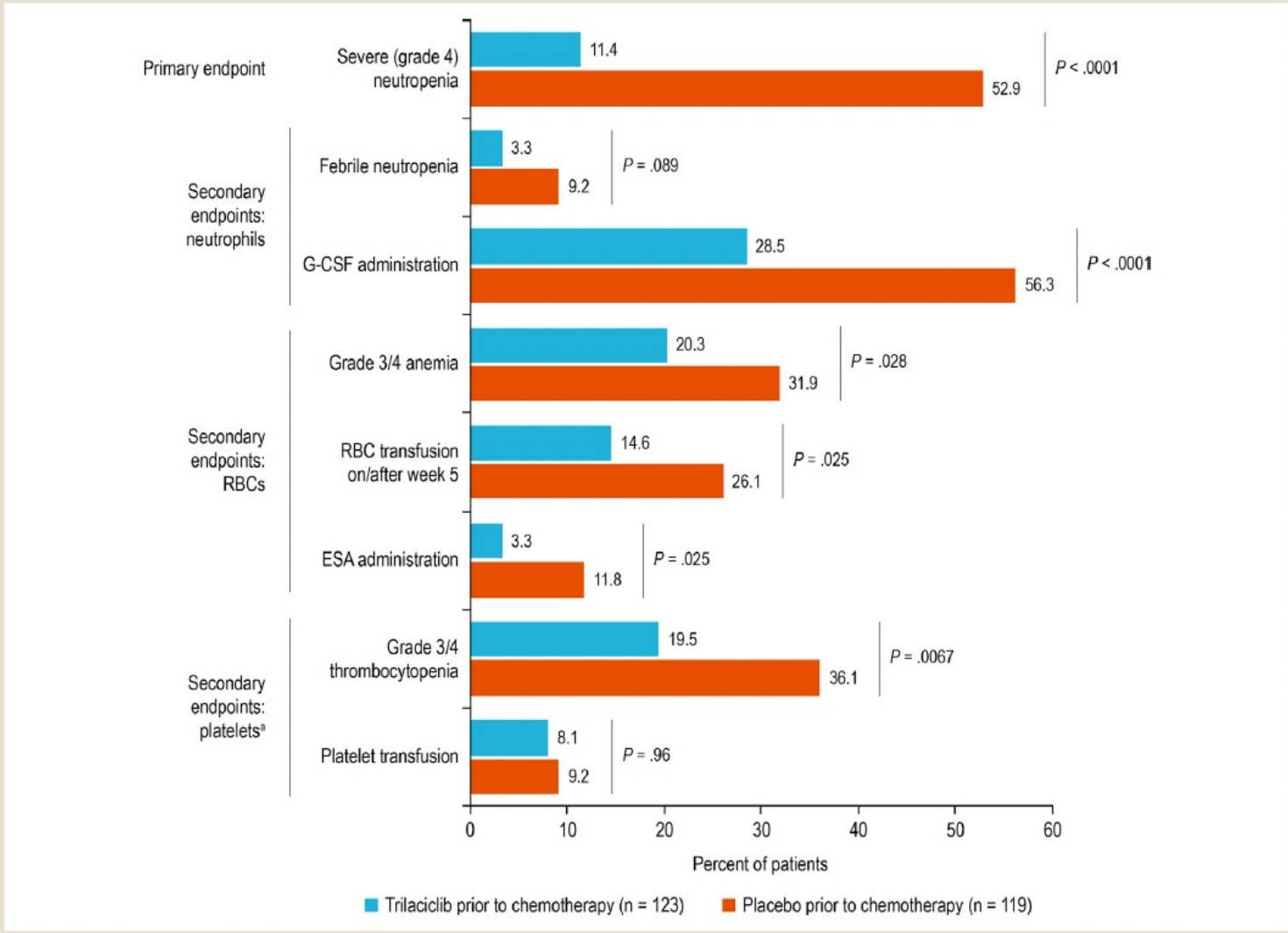
Clin Lung Cancer 2021;22(5):449-60.

Original Study

Effects of Trilaciclib on Chemotherapy-Induced Myelosuppression and Patient-Reported Outcomes in Patients with Extensive-Stage Small Cell Lung Cancer: Pooled Results from Three Phase II Randomized, Double-Blind, Placebo-Controlled Studies

Jared Weiss,[1] Jerome Goldschmidt,[2] Zoran Andric,[3] Konstantin H. Dragnev,[4] Chad Gwaltney,[5] Konstantina Skaltsa,[6] Yili Pritchett,[7] Joyce M. Antal,[7] Shannon R. Morris,[7] Davey Daniel[8,9]

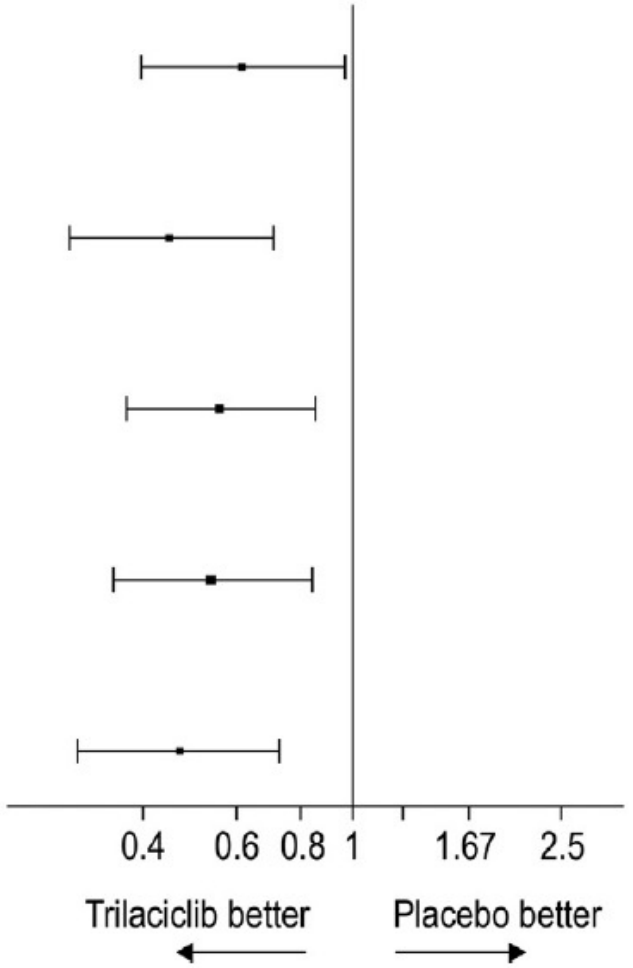
Myelopreservation Benefits with Trilaciclib Administered Prior to Chemotherapy



Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

Time to Confirmed Deterioration (TTCD) in Selected Patient-Reported Outcome Measures with Trilaciclib

Domain	Events, n Trilaciclib/placebo	TTCD, months Trilaciclib/placebo	Hazard ratio (95% CI)
Physical wellbeing	32/51	NYR/5.16	0.62 (0.40–0.97)
Functional wellbeing	31/55	7.62/3.78	0.45 (0.29–0.71)
Fatigue	39/61	7.03/2.33	0.56 (0.37–0.85)
Anemia trial outcome index	33/55	7.20/3.78	0.54 (0.35–0.84)
FACT-An total	31/58	NYR/3.48	0.47 (0.30–0.73)



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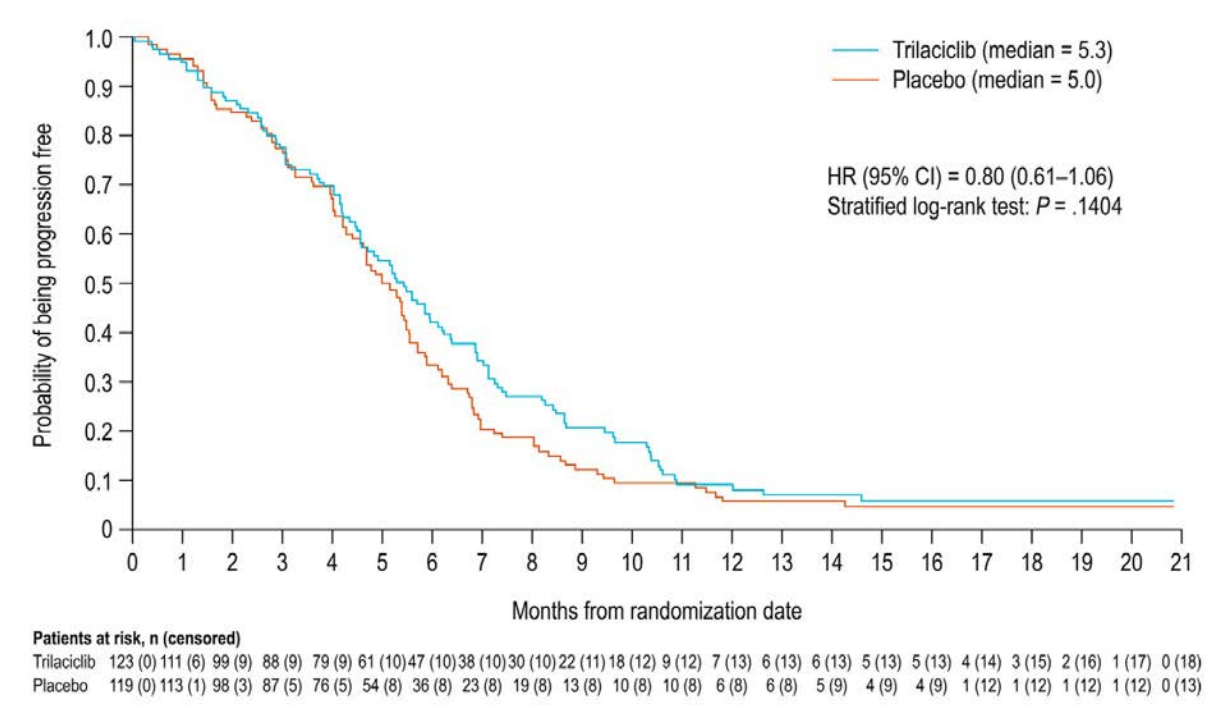
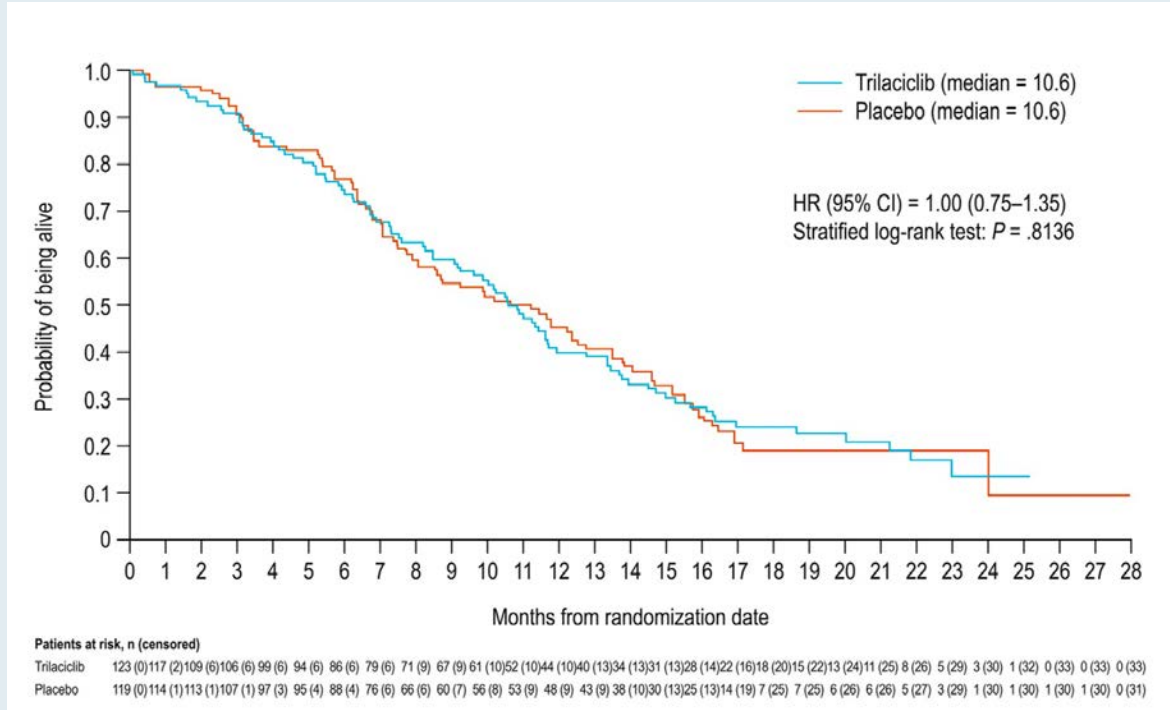
Progression-Free and Overall Survival for Patients Who Received Trilaciclib versus Placebo





Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

Summary of Adverse Events (AEs) in the Pooled Safety Population

Event	*n* (%)	
	Trilaciclib Prior to Chemotherapy (*n* = 122)	Placebo Prior to Chemotherapy (*n* = 118)
Any AE	115 (94.3)	114 (96.6)
Any placebo-/trilaciclib-related AE	45 (36.9)	49 (41.5)
Any serious AE	36 (29.5)	30 (25.4)
Any placebo-/trilaciclib-related serious AE	2 (1.6)	1 (0.8)
Any AE of grade ≥3	73 (59.8)	98 (83.1)
Any AE of grade ≥4	30 (24.6)	62 (52.5)
Any placebo-/trilaciclib-related AE of grade ≥3	10 (8.2)	18 (15.3)
Any hematologic AE	82 (67.2)	106 (89.8)
Any hematologic AE of grade ≥3	54 (44.3)	91 (77.1)
Any hematologic AE of grade ≥4	19 (15.6)	62 (52.5)
AESIs for trilaciclib	23 (18.9)	10 (8.5)
Any AE leading to discontinuation of any study drug	11 (9.0)	13 (11.0)
All-cause hospitalization	30 (24.6)	30 (25.4)
Hospitalization due to CIM or sepsis	5 (4.1)	16 (13.6)
Any AE leading to death	6 (4.9)	3 (2.5)

AESIs = adverse events of special interest

Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

Common Adverse Events (AEs)

Event	*n* (%)	
	Trilaciclib Prior to Chemotherapy (*n* = 122)	Placebo Prior to Chemotherapy (*n* = 118)
Most common AEs (occurring in ≥10% of patients)[a]		
Neutropenia	51 (41.8)	78 (66.1)
Anemia	46 (37.7)	71 (60.2)
Nausea	41 (33.6)	39 (33.1)
Fatigue	41 (33.6)	32 (27.1)
Thrombocytopenia	37 (30.3)	50 (42.4)
Dyspnea	20 (16.4)	20 (16.9)
Pyrexia	17 (13.9)	13 (11.0)
Alopecia	16 (13.1)	30 (25.4)
Diarrhea	16 (13.1)	21 (17.8)
Decreased appetite	16 (13.1)	15 (12.7)
Headache	16 (13.1)	11 (9.3)
Constipation	14 (11.5)	23 (19.5)
Vomiting	11 (9.0)	19 (16.1)
Leukopenia	10 (8.2)	28 (23.7)
Platelet count decreased	9 (7.4)	19 (16.1)
Dizziness	9 (7.4)	18 (15.3)
Neutrophil count decreased	8 (6.6)	21 (17.8)

Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

Adverse Events of Special Interest

Adverse event	Trilaciclib before chemotherapy	Placebo before chemotherapy
Injection site reactions	13.9%	2.5%
Phlebitis/thrombophlebitis	9.0%	0.8%
Acute drug hypersensitivity reactions	4.1%	3.4%

Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

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Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

Wednesday, August 17, 2022
5:00 PM – 6:00 PM ET

Faculty

John Strickler, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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