Year in Review: Immunotherapy and Other Nontargeted Approaches for Lung Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, June 18, 2024
5:00 PM – 6:00 PM ET

Faculty

Matthew Gubens, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

Faculty

Matthew Gubens, MD, MS
Professor of Medicine
Medical Director, Thoracic Medical Oncology
University of California, San Francisco
San Francisco, California

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP and Daiichi Sankyo 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, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma, a Sobi Company, 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 US Inc, Gilead Sciences Inc, Grail Inc, GSK, 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, Kronos Bio Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology 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, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, 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.

Dr Gubens — Disclosures

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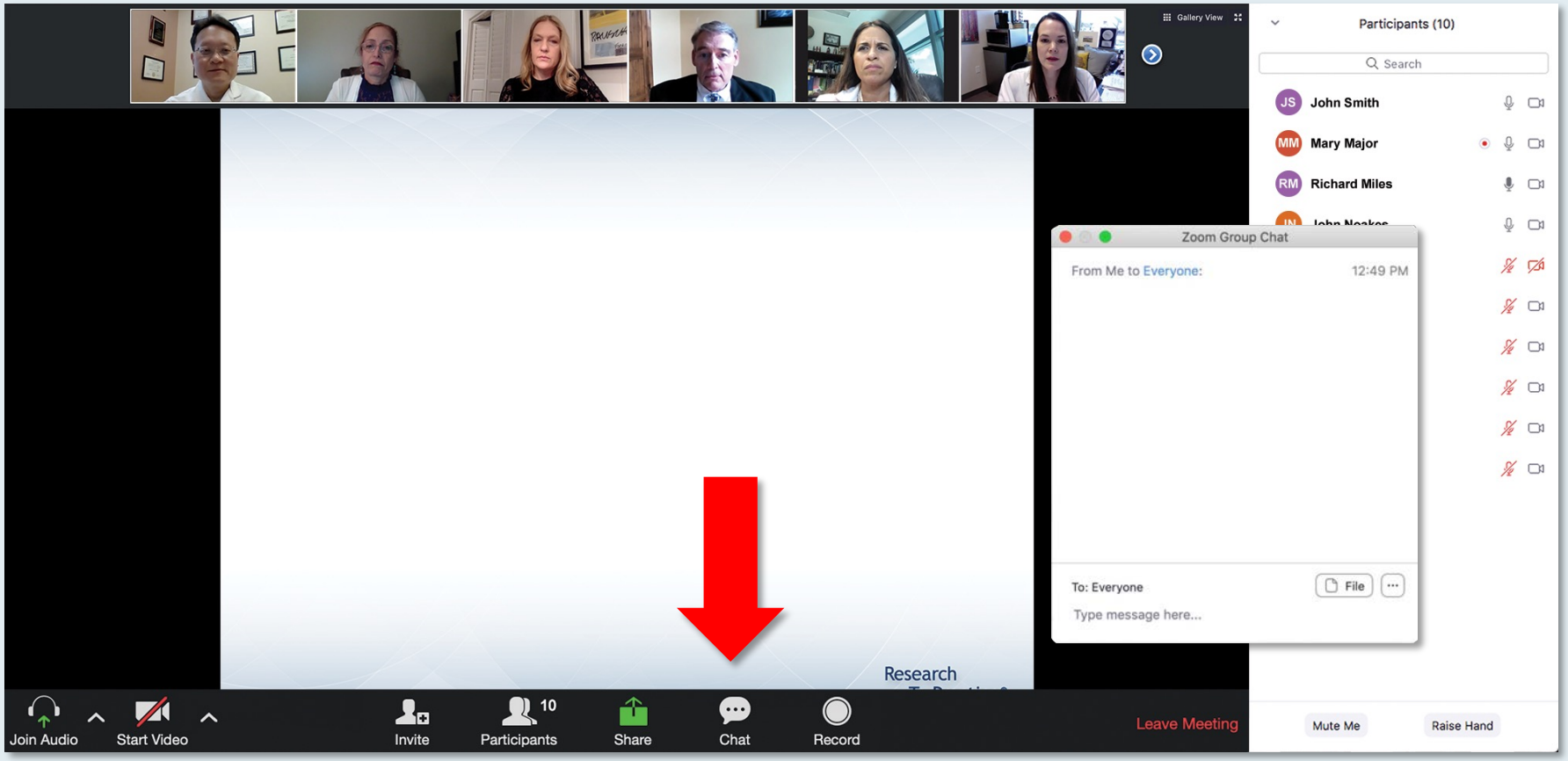
Contracted Research	Amgen Inc, Johnson & Johnson Pharmaceuticals, Merck, Trizell
Data and Safety Monitoring Board/Committee	Samsung Bioepis

We Encourage Clinicians in Practice to Submit Questions



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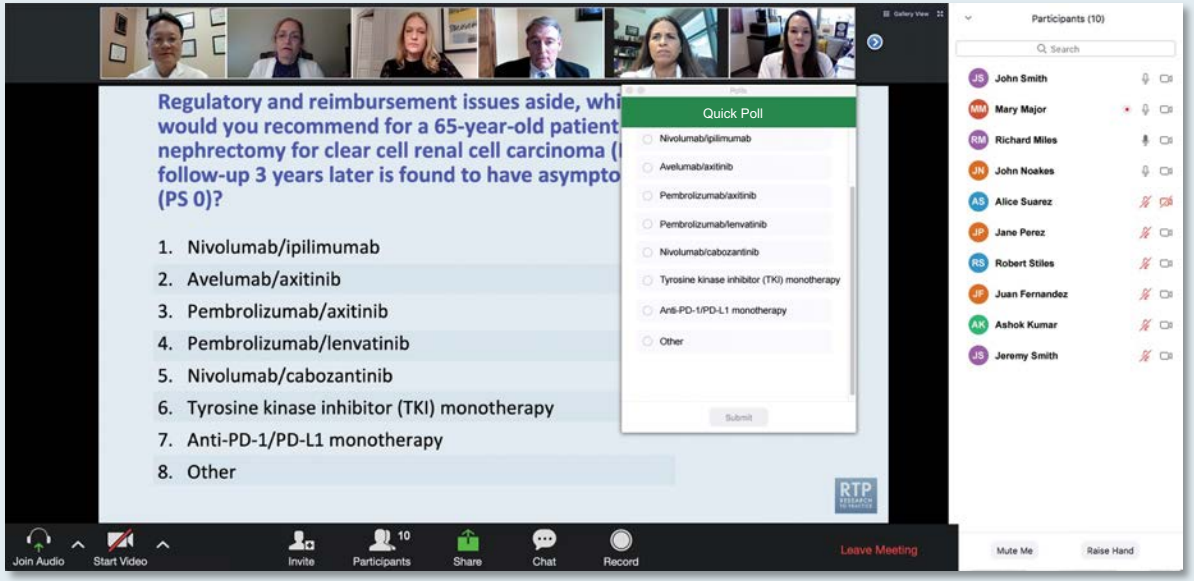

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ONCOLOGY TODAY

WITH DR NEIL LOVE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Targeted Therapy for Non-Small Cell Lung Cancer

DR JUSTIN F GAINOR
MASSACHUSETTS GENERAL HOSPITAL

DR KAREN RECKAMP
CEDARS-SINAI CANCER

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Investigator Perspectives on Available Research and Challenging Questions in Renal Cell Carcinoma: A Post-ASCO Annual Review

A CME/MOC-Accredited Live Webinar

Wednesday, June 19, 2024
5:00 PM – 6:00 PM ET

Faculty

Rana R McKay, MD
Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

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What Clinicians Want to Know About the Management of Triple-Negative Breast Cancer

A CME/MOC-Accredited Live Webinar

Thursday, June 20, 2024
5:00 PM – 6:00 PM ET

Faculty

Kevin Kalinsky, MD, MS
Heather McArthur, MD, MPH

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Year in Review: Gynecologic Oncology

A CME/MOC-Accredited Live Webinar

Tuesday, June 25, 2024
5:00 PM – 6:00 PM ET

Faculty

Dana M Chase, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Year in Review: Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Tuesday, July 9, 2024
5:00 PM – 6:00 PM ET

Faculty

Jesús G Berdeja, MD
Thomas Martin, MD

Moderator

Neil Love, MD

RTP Year in Review 2024

Inside the Issue: Integrating Antibody-Drug Conjugates into the Management of HR-Positive and Triple-Negative Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 17, 2024
5:00 PM – 6:00 PM ET

Faculty

Professor Peter Schmid, FRCP, MD, PhD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Inside the Issue: Integrating ALK-Targeted Therapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, July 18, 2024
5:00 PM – 6:00 PM ET

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Professor Solange Peters, MD, PhD
Professor Ben Solomon, MBBS, PhD

Moderator

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MODULE 4: Novel Agents and Strategies

MODULE 5: Immunotherapy for NSCLC with a Targetable Mutation

MODULE 6: Small Cell Lung Cancer

Thank you for joining us!

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

RTP Year in Review 2024

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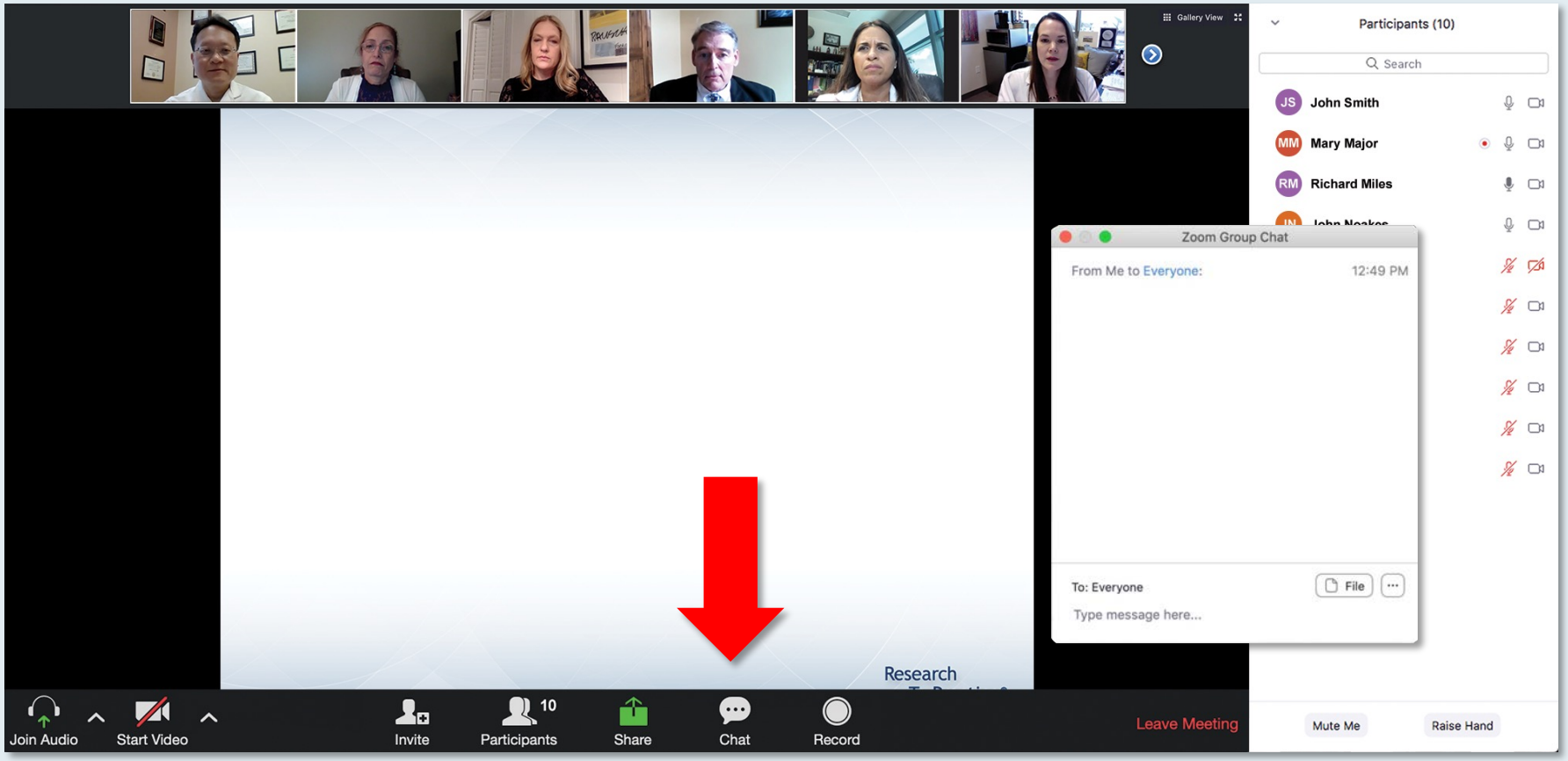

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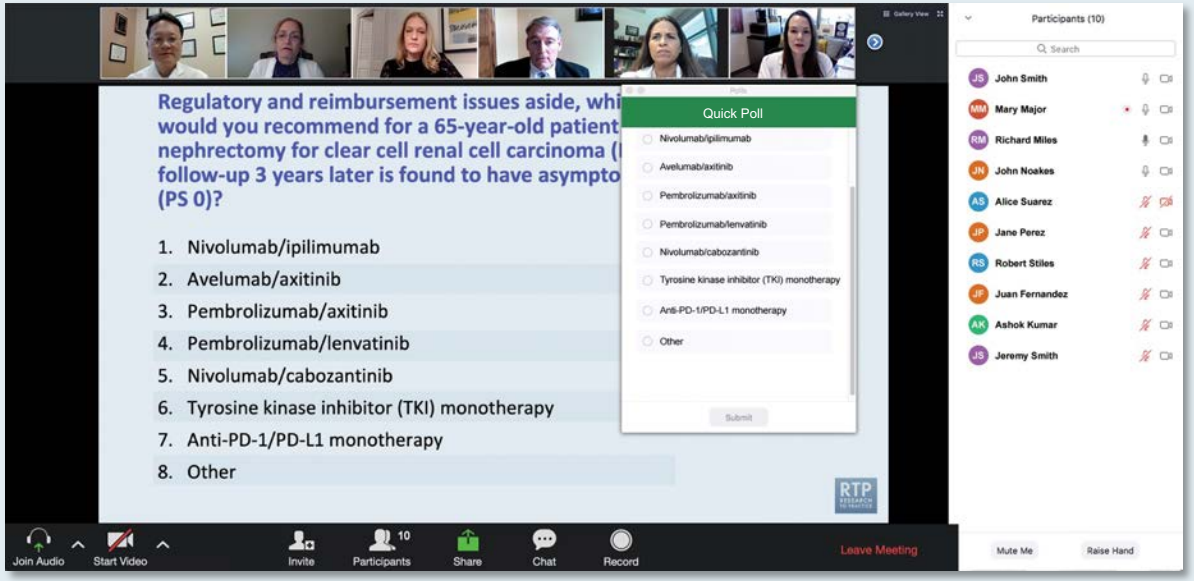

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Dr Gubens — Disclosures

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Contracted Research	Amgen Inc, Johnson & Johnson Pharmaceuticals, Merck, Trizell
Data and Safety Monitoring Board/Committee	Samsung Bioepis

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

Key Data Sets

- Spicer J et al. **Neoadjuvant nivolumab** (NIVO) + **chemotherapy** (chemo) vs chemo in patients (pts) with resectable NSCLC: **4-year update** from **CheckMate 816**. ASCO 2024;Abstract LBA8010.
- Cascone T et al. **Perioperative nivolumab** in resectable lung cancer. *N Engl J Med* 2024 May 16;390(19):1756-69.
- Cascone T et al. Clinical outcomes with **perioperative nivolumab** (NIVO) by nodal status among patients (pts) with stage III resectable NSCLC: Results from the **phase 3 CheckMate 77T study**. ASCO 2024;Abstract LBA8007.
- Wakelee H et al. **Perioperative pembrolizumab** for early-stage NSCLC. *N Engl J Med* 2023;389(6):491-503.
- Garassino MC et al. Health-related quality of life (HRQoL) outcomes from the randomized, double-blind **phase 3 KEYNOTE-671** study of **perioperative pembrolizumab** for early-stage non-small-cell lung cancer (NSCLC). ASCO 2024;Abstract 8012.
- Heymach J et al. Outcomes with **perioperative durvalumab** (D) in pts with resectable NSCLC and baseline N2 lymph node involvement (N2 R-NSCLC): An **exploratory subgroup** analysis of **AEGEAN**. ASCO 2024;Abstract 8011.

Key Data Sets (Continued)

- Felip E et al. Overall survival with **adjuvant atezolizumab** after chemotherapy in resected stage II-IIIA NSCLC (**IMpower010**): A randomised, multicentre, open-label, **phase III trial**. *Ann Oncol* 2023;34(10):907-19.
- Oselin K et al. **Pembrolizumab** vs placebo for early-stage NSCLC after resection and adjuvant therapy: **Subgroup analysis** of patients who received adjuvant chemotherapy in the **phase III PEARLS/KEYNOTE-091** study. ASCO 2023;Abstract 8520.
- Khan S et al. **ctDNA-Lung-DETECT**: **ctDNA outcomes** for resected early-stage non-small cell lung cancers at 12 months. ASCO 2024;Abstract 8018.
- Rodrigues G et al**. American Radium Society** appropriate use criteria for unresectable locally advanced non-small cell lung cancer. *JAMA Oncol* 2024 April 11;[Online ahead of print].
- Ramalingam SS et al.
- Filippi AR et al. **Real-world outcomes** with **durvalumab** after **chemoradiotherapy** in patients with unresectable stage III NSCLC: Interim analysis of overall survival from **PACIFIC-R**. *ESMO Open* 2024 June 3;9(6):103464.

Key Data Sets (Continued)

- Filippi ARR et al. **Durvalumab** after **radiotherapy** in patients with unresectable stage III NSCLC ineligible for chemotherapy: **Primary results** from the **DUART** study. ESMO 2023;Abstract LBA62.
- de Castro G Jr et al. **Five-year outcomes** with **pembrolizumab** versus **chemotherapy** as **first-line** therapy in patients with NSCLC and PD-L1 tumor proportion score ≥1% in the **KEYNOTE-042** study. *J Clin Oncol* 2023;41(11):1986-91.
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- Novello S et al. **Pembrolizumab plus chemotherapy** in squamous NSCLC: 5-year update of the phase III KEYNOTE-407 study. *J Clin Oncol* 2023;41(11):1999-2006.
- Ramalingam SS et al. **Six-year survival** and HRQoL outcomes with **1L nivolumab + ipilimumab** in patients with metastatic NSCLC (mNSCLC) from **CheckMate227**. WCLC 2023;Abstract OA14.03.
- Reck M et al. **Five-year outcomes** with **first-line (1L) nivolumab + ipilimumab + chemotherapy** (N + I + C) vs C in patients (pts) with metastatic NSCLC (mNSCLC) in **CheckMate 9LA**. ASCO 2024;Abstract 8560.

Key Data Sets (Continued)

- Johnson ML et al. **Durvalumab** with or without **tremelimumab** in combination with **chemotherapy** as **first-line therapy** for mNSCLC: The **phase III POSEIDON study**. *J Clin Oncol* 2023;41(6):1213-27.
- Peters S et al. **Durvalumab ± tremelimumab + chemotherapy** in **first-line** metastatic NSCLC: **5-year overall survival** update from the **POSEIDON study**. ESMO Immuno-Oncology 2023;Abstract LBA3.
- Ahn M-J et al. **Datopotamab deruxtecan (Dato-DXd)** vs docetaxel in previously treated advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC): Results of the randomized **phase 3 study TROPION-Lung01**. ESMO Asia 2023;Abstract 509MO.
- Goto Y et al. **TROPION-Lung02: Dato-DXd** plus **pembrolizumab** with or without platinum **chemotherapy** in advanced NSCLC. ASCO 2023;Abstract 9004.
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Key Data Sets (Continued)

- Planchard D et al. **ICARUS-LUNG01**: A phase 2 study of **datopotomab deruxtecan (Dato-DXd)** in patients with previously treated advanced non-small cell lung cancer (NSCLC), with sequential tissue biopsies and biomarkers analysis to predict treatment outcome. ASCO 2024;Abstract 8501.
- Paz-Ares L et al. **TROPION-Lung05: Datopotamab deruxtecan (Dato-DXd)** in previously treated non-small cell lung cancer (NSCLC) with **actionable genomic alterations (AGAs).** ESMO 2023;Abstract 1314MO.
- Lisberg A et al. **Intracranial efficacy** of **datopotamab deruxtecan (Dato-DXd)** in patients (pts) with previously treated advanced/metastatic non-small cell lung cancer (a/m NSCLC) with actionable genomic alterations (AGA): Results from TROPION-Lung05. ASCO 2024;Abstract 8593.
- Benjamin DJ et al. The role of **chemotherapy plus immune checkpoint inhibitors** in **oncogenic-driven NSCLC**: A University of California Lung Cancer Consortium retrospective study. *JTO Clin Res Rep* 2022 October 29;3(12):100427.
- Middleton G et al. A phase II trial of **ceralasertib** and **durvalumab** in advanced NSCLC with and without RAS mutations: Results of **NLMT arm J**. WCLC 2023;Abstract MA06.06.

Key Data Sets (Continued)

- Besse B et al. **Biomarker-directed targeted therapy** plus **durvalumab** in advanced non-small-cell lung cancer: A phase 2 umbrella trial. *Nat Med* 2024;30(3):716-29.
- Spigel DR et al. **ADRIATIC: Durvalumab** (D) as **consolidation** treatment (tx) for patients (pts) with **limited-stage small-cell lung cancer** (LS-SCLC). ASCO 2024;Abstract LBA5.
- Lee S-H et al. A phase II, open-label, combination therapy of **durvalumab** and **ceralasertib** in relapsed and refractory **small cell lung cancer (SUKSES-N4**). ASCO 2024;Abstract 8104.
- Johnson M et al. **Ifinatamab deruxtecan (I-DXd; DS-7300)** in patients with **refractory SCLC**: A subgroup analysis of a phase 1/2 study. WCLC 2023;Abstract OA05.05.
- Dowlati A et al. **Sacituzumab govitecan** as **second-line** treatment for **extensive SCLC**: **Preliminary results** from the phase II **TROPiCS-03 basket trial**. ESMO 2023;Abstract 1990MO.
- Paz-Ares L et al. **Tarlatamab**, a first-in-class DLL3-targeted bispecific T-cell engager, in **recurrent SCLC**: An open-label, phase I study. *J Clin Oncol* 2023;41(16):2893-903.
- Paz-Ares L et al. **Tarlatamab** for patients with **previously treated SCLC**: **Primary analysis** of the phase II **DeLLphi-301 study**. ESMO 2023;Abstract LBA92.

Agenda

INTRODUCTION: Risk of Autoimmune Toxicity with Checkpoint Inhibitors

MODULE 1: Immunotherapy in the Neoadjuvant/Adjuvant Setting

MODULE 2: Immunotherapy for Locally Advanced NSCLC

MODULE 3: First-Line Immunotherapy for Metastatic NSCLC

MODULE 4: Novel Agents and Strategies

MODULE 5: Immunotherapy for NSCLC with a Targetable Mutation

MODULE 6: Small Cell Lung Cancer

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The Current and Future Role of Oncologic Immunotherapies in the Management of Genitourinary Cancers

Friday, February 27, 2015
7:15 PM – 9:15 PM
Orlando, Florida

Moderator
Neil Love, MD

Faculty
Charles G Drake, MD, PhD
David F McDermott, MD
Daniel P Petrylak, MD
David I Quinn, MBBS, PhD
Nicholas J Vogelzang, MD

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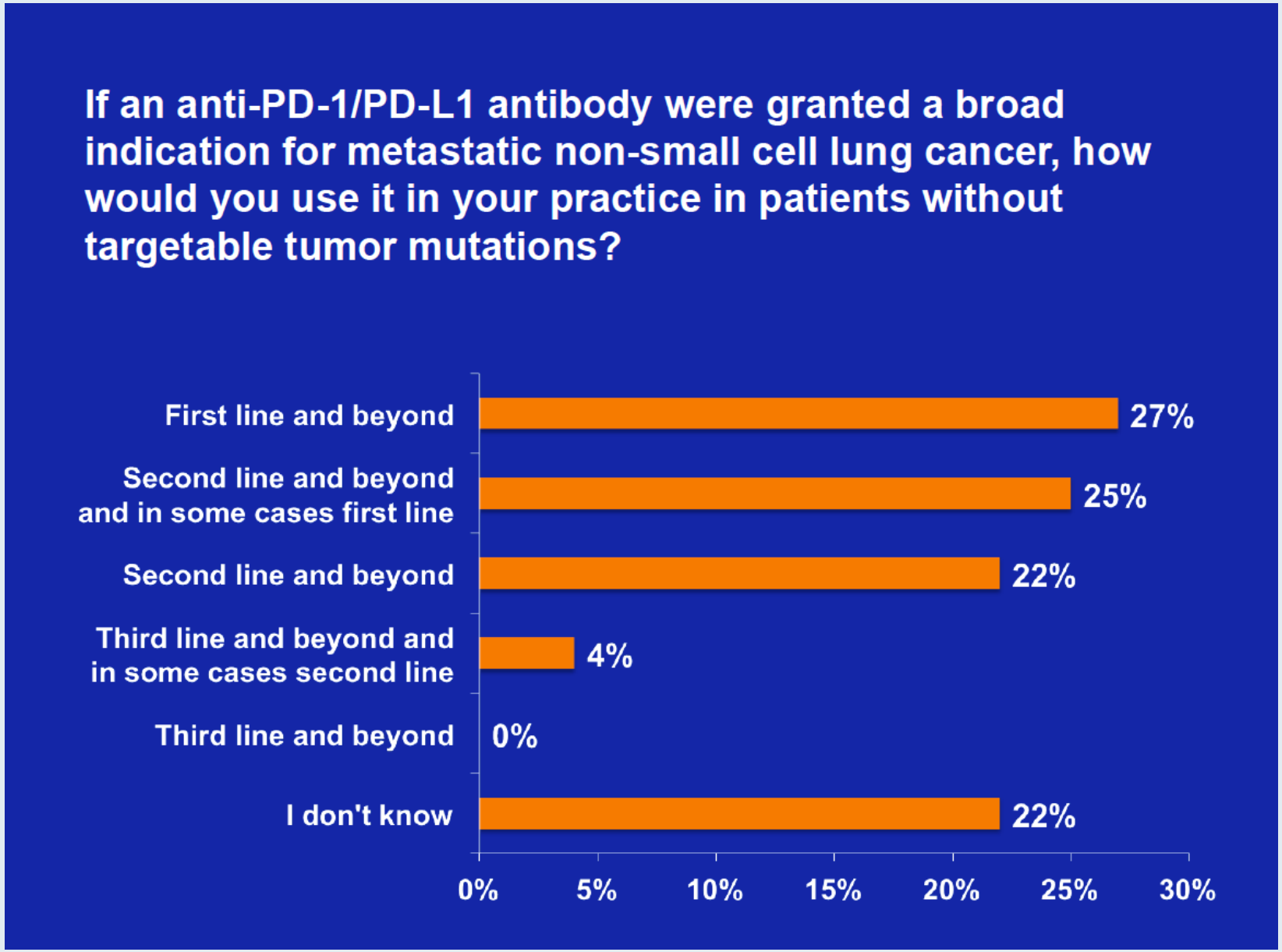
ASCO Genitourinary Cancers Symposium, February 27, 2015.



ASCO Genitourinary Cancers Symposium, February 27, 2015.

2024 ASCO® ANNUAL MEETING

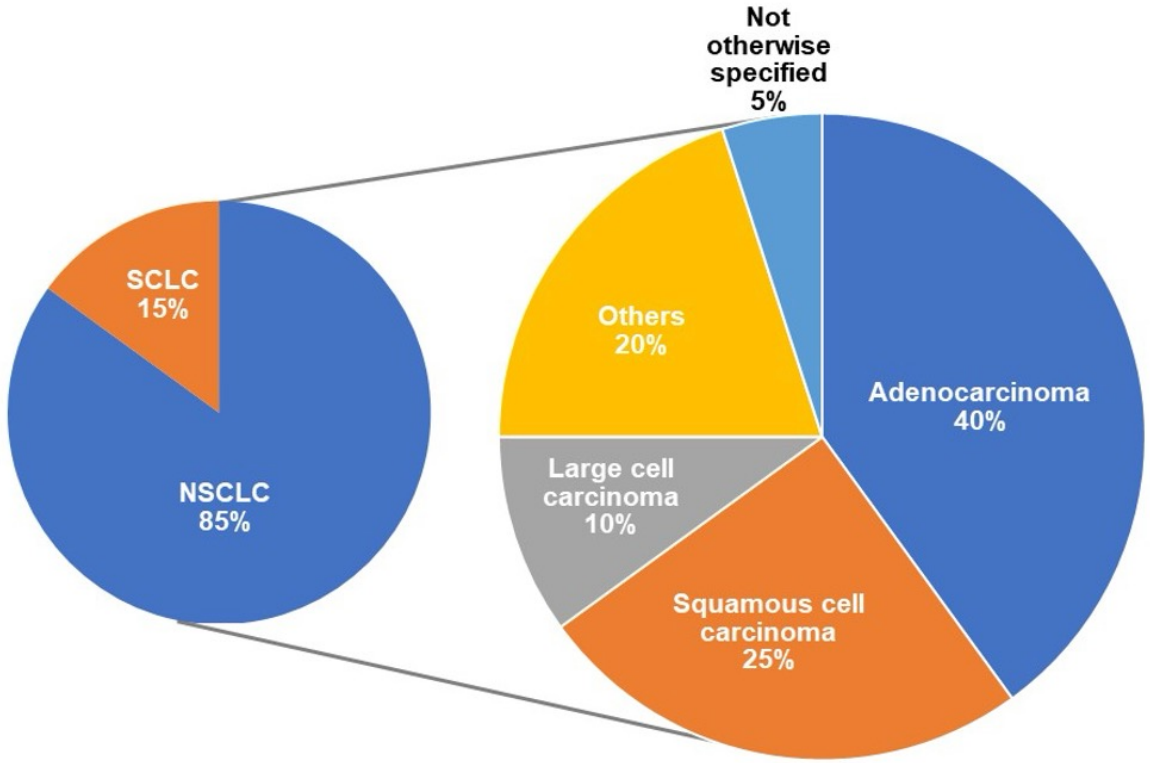
Metastatic NSCLC with Actionable Genomic Alterations

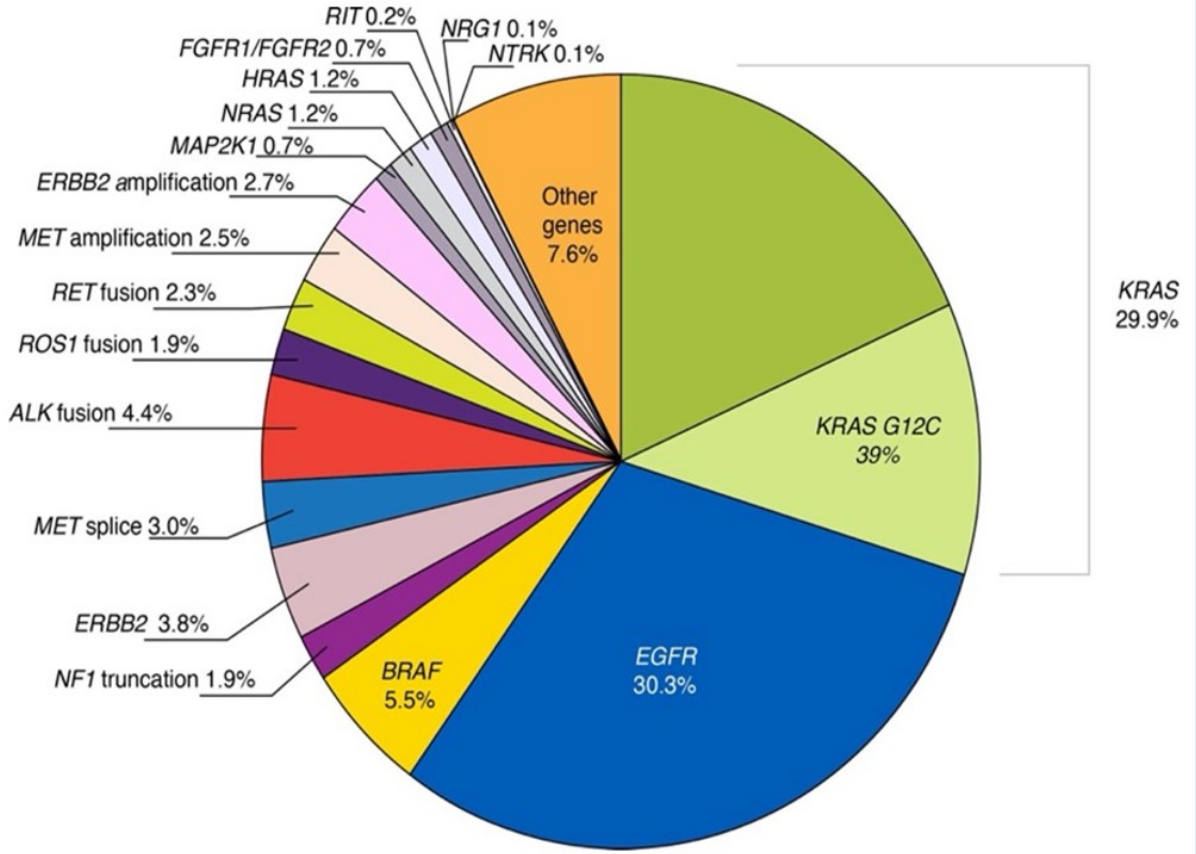
Education Session
Advanced Lung Cancer: State-of-the-Art Approaches and Insights

Matthew Gubens, MD, MS, FASCO
Professor of Medicine
Medical Director, Thoracic Medical Oncology
Chair, UCSF Comprehensive Cancer Center Protocol Review and Monitoring Committee
University of California, San Francisco

RTP Year in Review 2024

Landscape of Lung Cancer



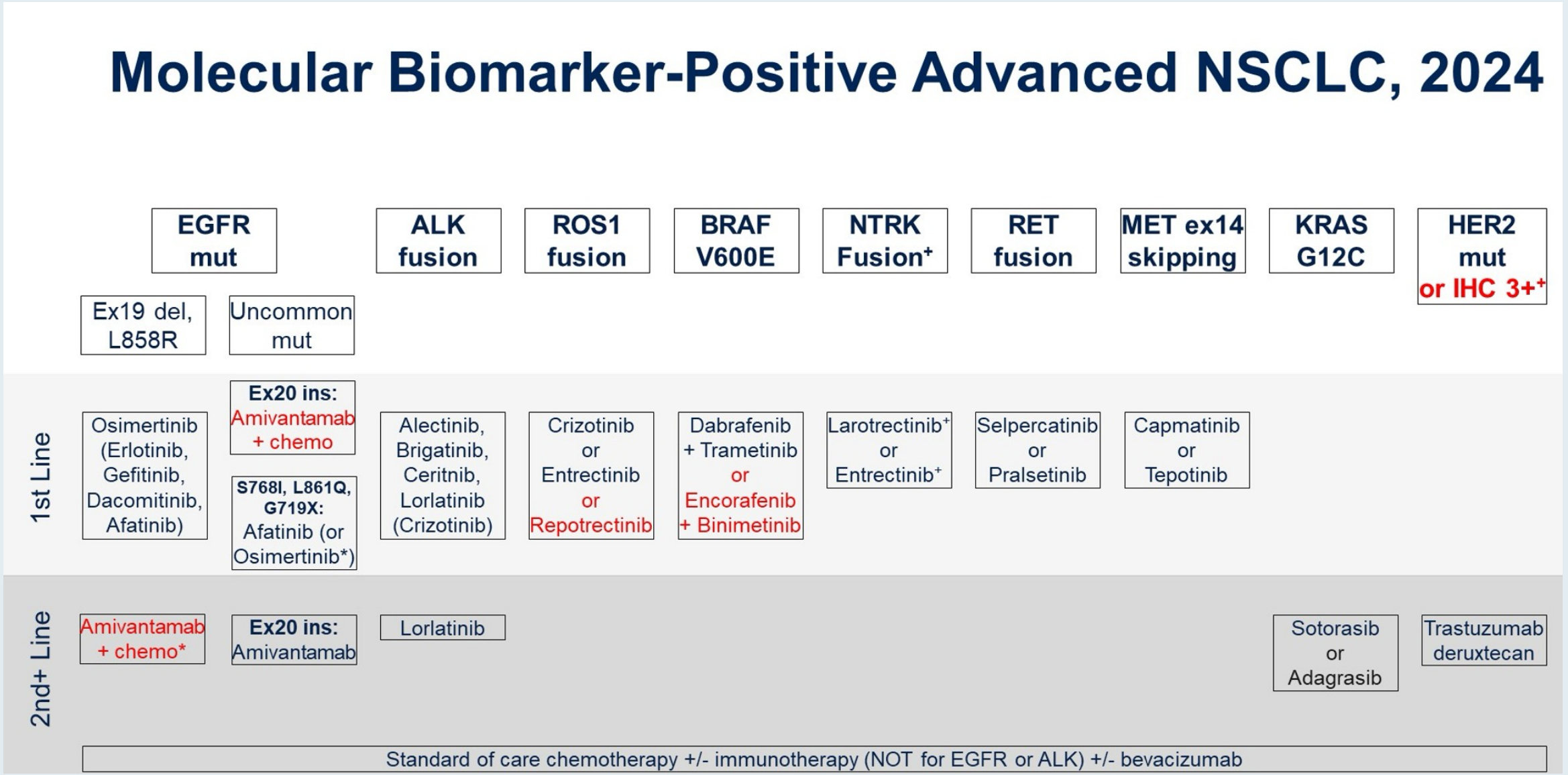


PD-L1 expression
(Tumor mutational burden)

Gubens M. ASCO 2024 Education Session.

RTP Year in Review 2024

Molecular Biomarker-Positive Advanced NSCLC, 2024



Gubens M. ASCO 2024 Education Session.

nature communications

Article

https://doi.org/10.1038/s41467-023-44512-4

Polygenic risk score for ulcerative colitis predicts immune checkpoint inhibitor-mediated colitis

Received: 22 May 2023

Accepted: 15 December 2023

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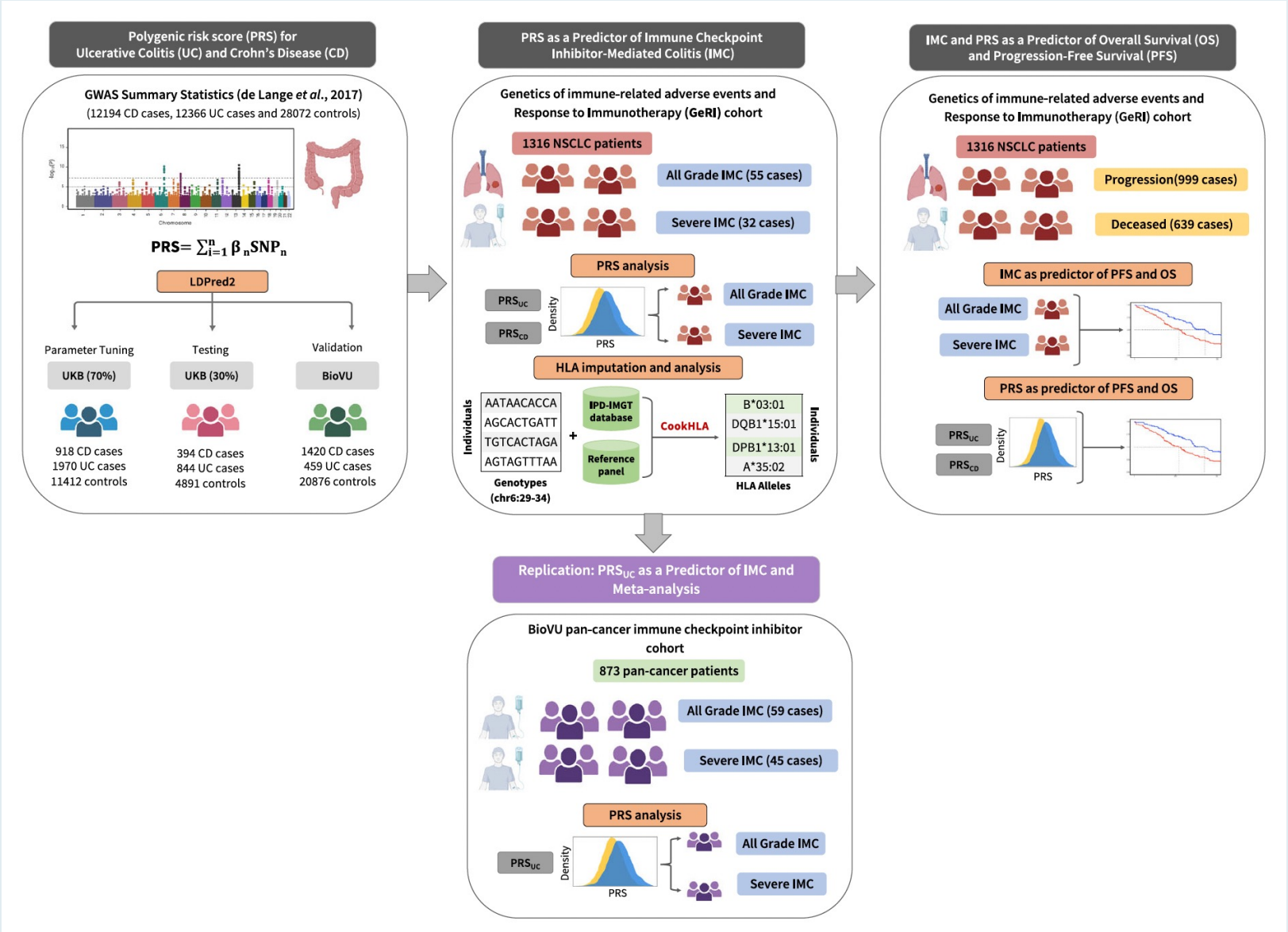
Check for updates

Pooja Middha[1], Rohit Thummalapalli[2], Michael J. Betti[3], Lydia Yao[4], Zoe Quandt[5,6], Karmugi Balaratnam[7], Cosmin A. Bejan[8], Eduardo Cardenas[1], Christina J. Falcon[9], David M. Faleck[10], Princess Margaret Lung Group*, Matthew A. Gubens[11,12], Scott Huntsman[1], Douglas B. Johnson[13], Linda Kachuri[14,15], Khaleeq Khan[7], Min Li[1], Christine M. Lovly[16], Megan H. Murray[4], Devalben Patel[7], Kristin Werking[17], Yaomin Xu[4], Luna Jia Zhan[7], Justin M. Balko[13], Geoffrey Liu[7,18,19], Melinda C. Aldrich[3], Adam J. Schoenfeld[20] & Elad Ziv[1,12,21,22]

Polygenic Risk Score for Ulcerative Colitis Predicts Immune Checkpoint Inhibitor-Mediated Colitis



Middha P et al. *Nat Commun* 2024 March 26;[Online ahead of print].

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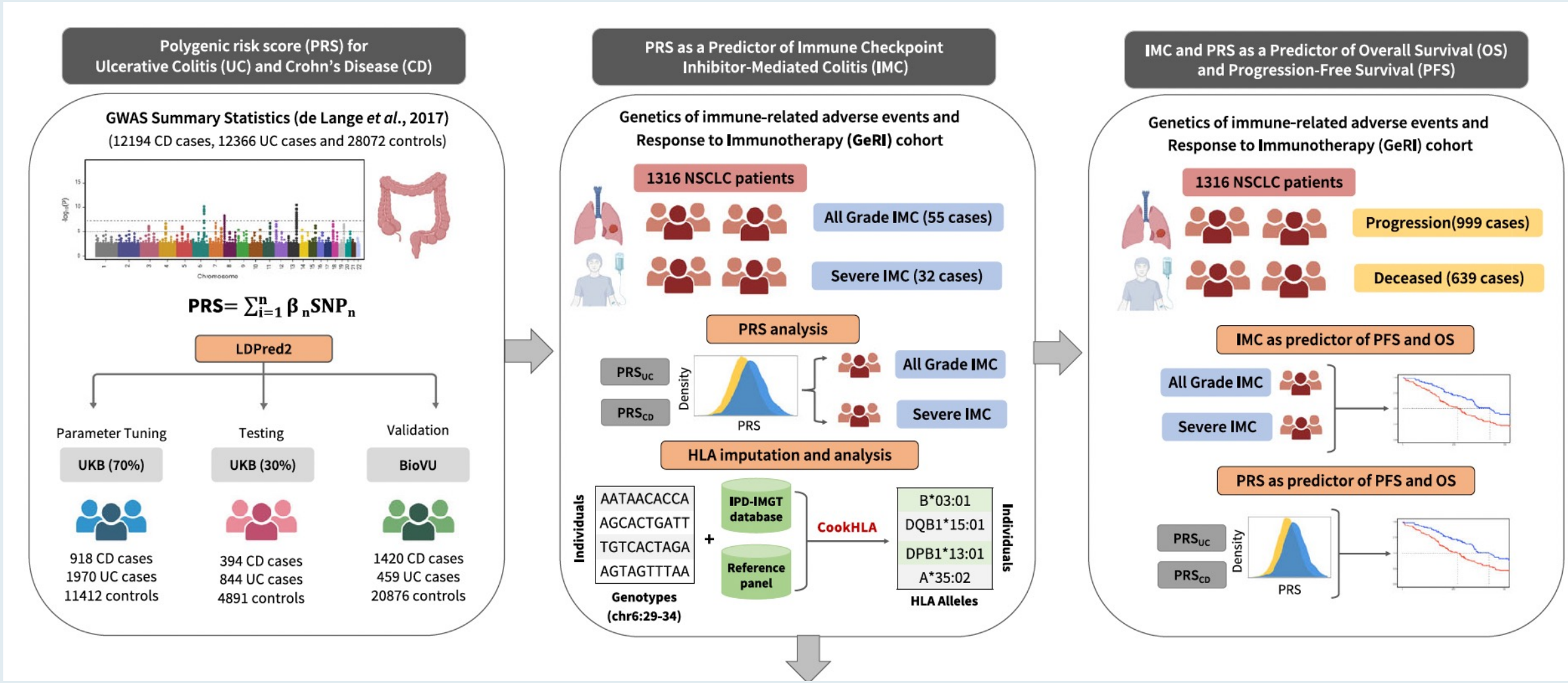
Polygenic Risk Score for Ulcerative Colitis Predicts Immune Checkpoint Inhibitor-Mediated Colitis (Continued)



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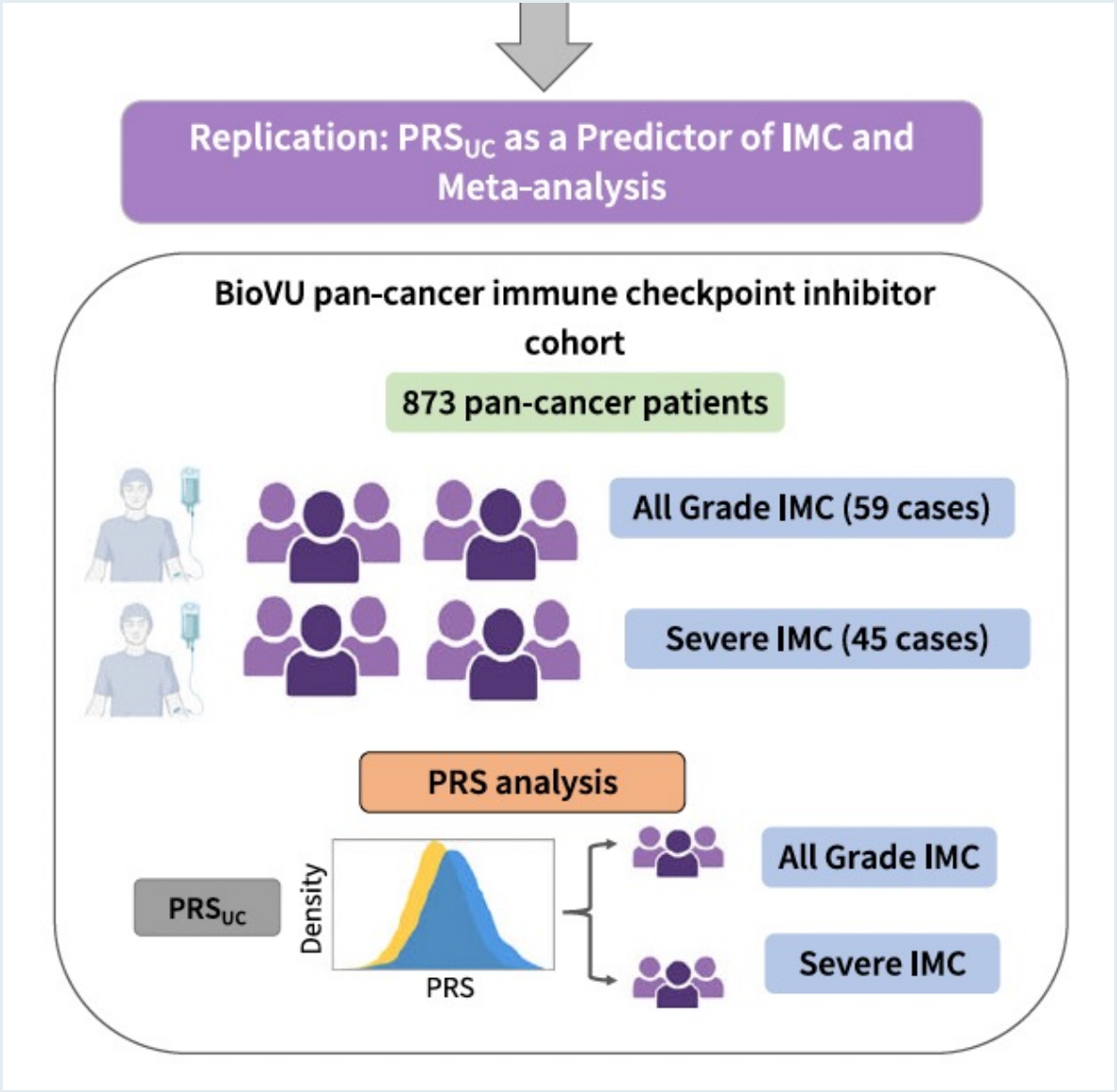

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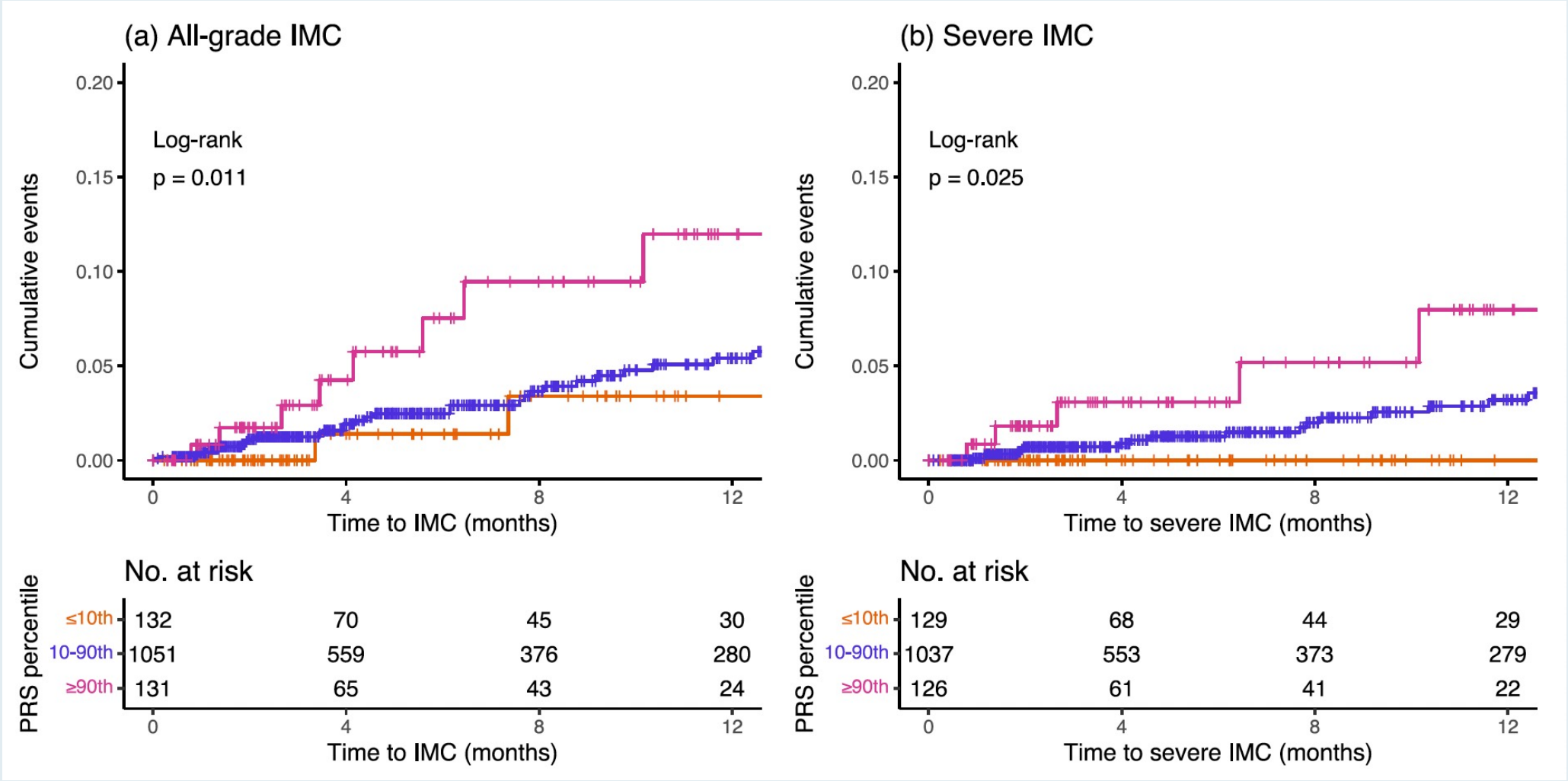
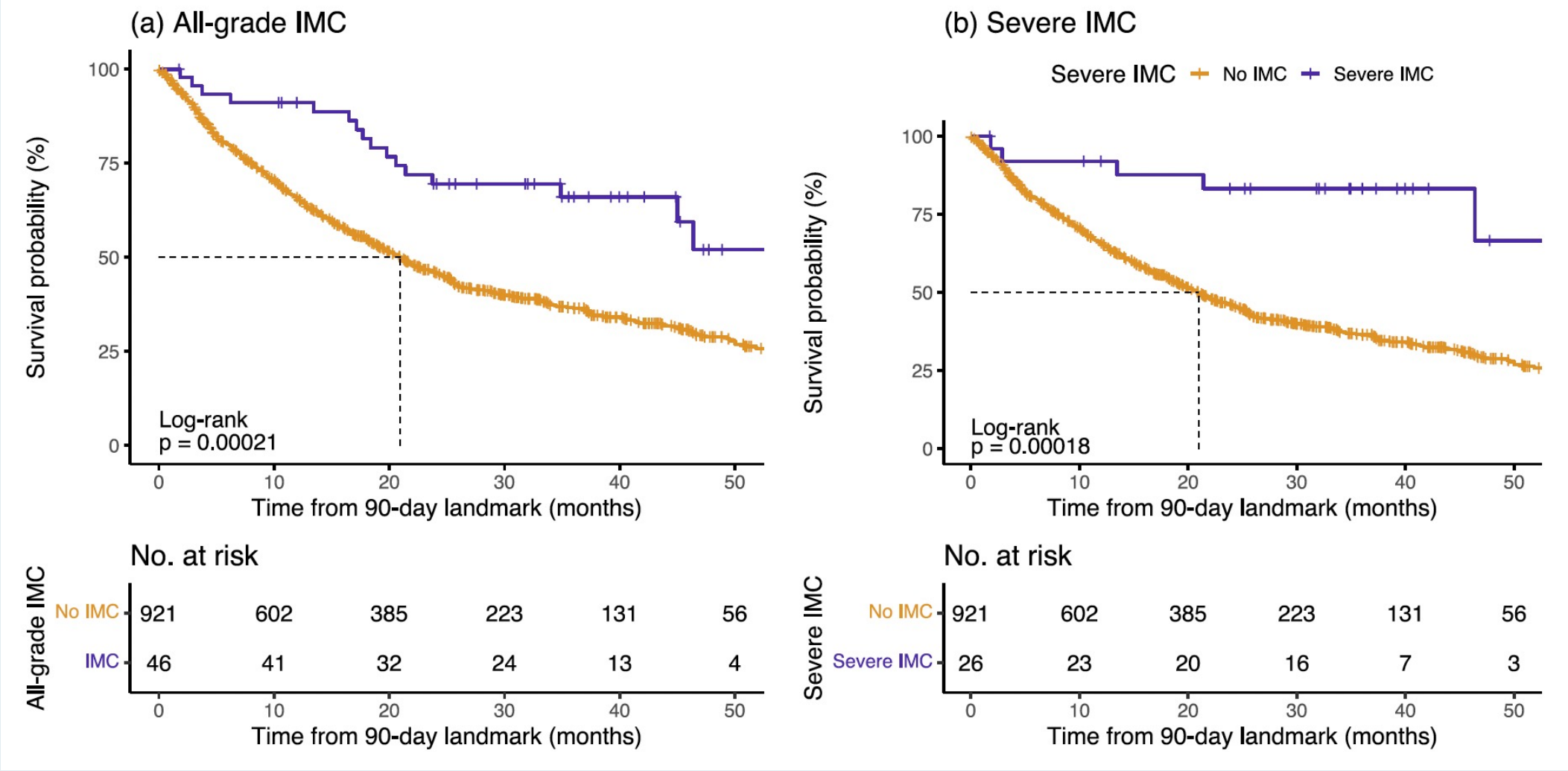
All-Grade and Severe Immune Checkpoint Inhibitor-Mediated Colitis by Polygenic Risk Score for Ulcerative Colitis in the GeRI Cohort



GeRI = genetics of immune-related adverse events and response to immunotherapy

Middha P et al. *Nat Commun* 2024 March 26;[Online ahead of print].

Immune Checkpoint Inhibitor-Mediated Colitis as a Predictor of Overall Survival in the Entire GeRI Cohort



Middha P et al. *Nat Commun* 2024 March 26;[Online ahead of print].

Agenda

INTRODUCTION: Risk of Autoimmune Toxicity with Checkpoint Inhibitors

MODULE 1: Immunotherapy in the Neoadjuvant/Adjuvant Setting

MODULE 2: Immunotherapy for Locally Advanced NSCLC

MODULE 3: First-Line Immunotherapy for Metastatic NSCLC

MODULE 4: Novel Agents and Strategies

MODULE 5: Immunotherapy for NSCLC with a Targetable Mutation

MODULE 6: Small Cell Lung Cancer

Neoadjuvant and Perioperative Immunotherapy for NSCLC

- Spicer J et al. **Neoadjuvant nivolumab** (NIVO) + **chemotherapy** (chemo) vs chemo in patients (pts) with resectable NSCLC: **4-year update** from **CheckMate 816**. ASCO 2024;Abstract LBA8010.
- Cascone T et al. **Perioperative nivolumab** in resectable lung cancer. *N Engl J Med* 2024 May 16;390(19):1756-69.
- Cascone T et al. Clinical outcomes with **perioperative nivolumab** (NIVO) by nodal status among patients (pts) with stage III resectable NSCLC: Results from the **phase 3 CheckMate 77T study**. ASCO 2024;Abstract LBA8007.
- Wakelee H et al. **Perioperative pembrolizumab** for early-stage NSCLC. *N Engl J Med* 2023;389(6):491-503.
- Garassino MC et al. Health-related quality of life (HRQoL) outcomes from the randomized, double-blind **phase 3 KEYNOTE-671** study of **perioperative pembrolizumab** for early-stage non-small-cell lung cancer (NSCLC). ASCO 2024;Abstract 8012.
- Heymach J et al. Outcomes with **perioperative durvalumab** (D) in pts with resectable NSCLC and baseline N2 lymph node involvement (N2 R-NSCLC): An **exploratory subgroup** analysis of **AEGEAN**. ASCO 2024;Abstract 8011.

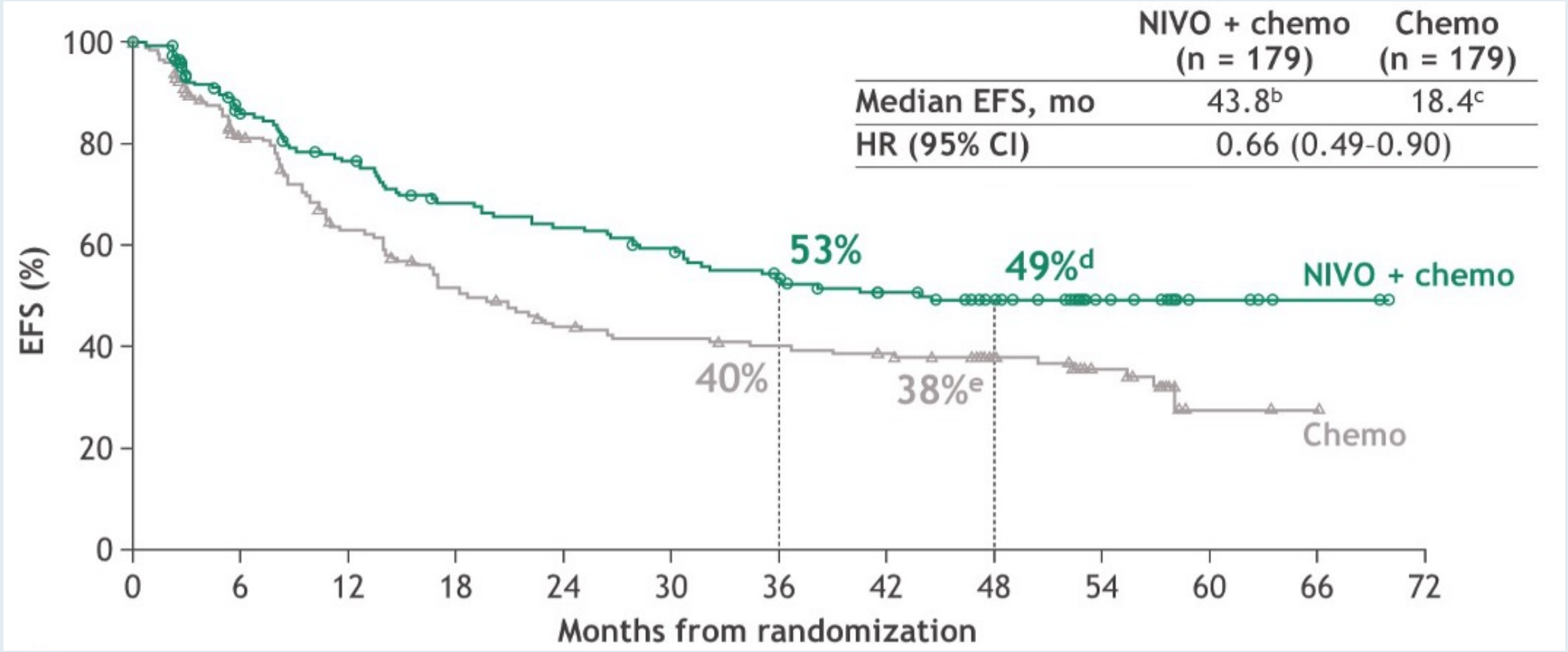
2024 ASCO ANNUAL MEETING

Abstract LBA8010

Neoadjuvant nivolumab plus chemotherapy vs chemotherapy in patients with resectable NSCLC: 4-year update from CheckMate 816

Jonathan D. Spicer,[1] Nicolas Girard,[2] Mariano Provencio Pulla,[3] Changli Wang,[4] Tetsuya Mitsudomi,[5] Mark M. Awad,[6] Everett E. Vokes,[7] Janis M. Taube,[8] Lorena Lupinacci,[9] Gene B. Saylors,[10] Fumihiro Tanaka,[11] Moishe Liberman,[12] Sung Yong Lee,[13] Aurelia Alexandru,[14] Manolo D'Arcangelo,[15] Phuong Tran,[16] Javed Mahmood,[16] Vishwanath Gharpure,[16] Apurva Bhingare,[16] Patrick M. Forde[8]

CheckMate 816 4-Year Update: Event-Free Survival (EFS)



Spicer J et al. ASCO 2024;Abstract LBA8010.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Perioperative Nivolumab in Resectable Lung Cancer

T. Cascone, M.M. Awad, J.D. Spicer, J. He, S. Lu, B. Sepesi, F. Tanaka, J.M. Taube, R. Cornelissen, L. Havel,* N. Karaseva, J. Kuzdzal, L.B. Petruzelka, L. Wu, J.-L. Pujol, H. Ito, T.-E. Ciuleanu, L. de Oliveira Muniz Koch, A. Janssens, A. Alexandru, S. Bohnet, F.V. Moiseyenko, Y. Gao, Y. Watanabe, C. Coronado Erdmann, P. Sathyanarayana, S. Meadows-Shropshire, S.I. Blum, and M. Provencio Pulla, for the CheckMate 77T Investigators†

2024 May 16;390(19):1756-69

2024 ASCO ANNUAL MEETING

Abstract LBA8007

Clinical outcomes with perioperative nivolumab by nodal status among patients with stage III resectable NSCLC: results from the phase 3 CheckMate 77T study

Mariano Provencio Pulla,[1] Mark M. Awad,[2] Jonathan D. Spicer,[3] Annelies Janssens,[4] Fedor Moiseyenko,[5] Yang Gao,[6] Yasutaka Watanabe,[7] Aurelia Alexandru,[8] Florian Guisier,[9] Nikolaj Frost,[10] Fabio Franke,[11] T. Jeroen Nicolaas Hiltermann,[12] Jie He,[13] Fumihiro Tanaka,[14] Shun Lu,[15] Cinthya Coronado Erdmann,[16] Padma Sathyanarayana,[16] Phuong Tran,[16] Vipul Devas,[16] Tina Cascone[17]

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 10, 2023 VOL. 389 NO. 6

Perioperative Pembrolizumab for Early-Stage Non–Small-Cell Lung Cancer

H. Wakelee, M. Liberman, T. Kato, M. Tsuboi, S.-H. Lee, S. Gao, K.-N. Chen, C. Dooms, M. Majem, E. Eigendorff, G.L. Martinengo, O. Bylicki, D. Rodríguez-Abreu, J.E. Chaft, S. Novello, J. Yang, S.M. Keller, A. Samkari, and J.D. Spicer, for the KEYNOTE-671 Investigators*

2023;389(6):491-503

2024 ASCO ANNUAL MEETING

Abstract 8012

Health-Related Quality of Life Outcomes From the Randomized, Double-Blind Phase 3 KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC

Marina C Garassino, Heather Wakelee, Jonathan D Spicer, Moishe Liberman, Terufumi Kato, Masahiro Tsuboi, Se-Hoon Lee, Ke-Neng Chen, Christophe Dooms, Margarita Majem, Ekkehard Eigendorff, Gastón L Martinengo, Olivier Bylicki, Delvys Rodríguez-Abreu, Jamie Chaft, Jing Yang, Ashwini Arunachalam, Josephine M Norquist, Steven M Keller, Shugeng Gao

2024 ASCO ANNUAL MEETING

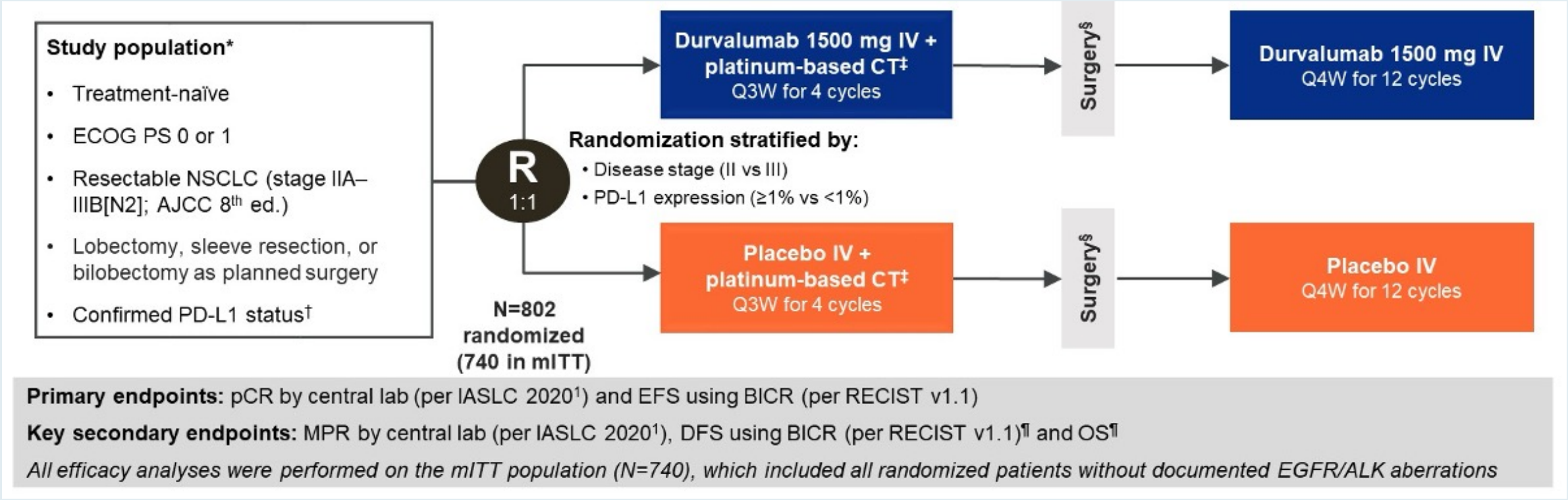
Abstract 8011

Outcomes with Perioperative Durvalumab in Patients with Resectable NSCLC and Baseline N2 Lymph Node Involvement (N2 R-NSCLC)

An Exploratory Subgroup Analysis of AEGEAN

John V. Heymach,[1] Martin Reck,[2] Tetsuya Mitsudomi,[3] Janis M. Taube,[4] Alexander Spira,[5] Jamie Chaft,[6] Gary J. Doherty,[7] Helen Mann,[7] Tamer M. Fouad,[8] David Harpole[9]

AEGEAN: Phase III Study Design



Heymach J et al. ASCO 2024;Abstract 8011.

AEGEAN Subgroup Analysis: Author Conclusions

- Among patients with baseline N2 nodal status, perioperative durvalumab + neoadjuvant CT prolonged EFS and increased the pCR rate versus neoadjuvant CT alone, similar to that observed in the mITT population[1]; in this subgroup:
  - EFS HR = 0.63 (95% CI: 0.43–0.90), with benefit in both single- and multi-station disease (HR = 0.61 and 0.69)
  - Difference in pCR rate = 11.7% (95% CI: 5.6–18.4)
- In the N2 subgroup, the approach, type, and timing of surgery were similar between arms and consistent with the overall trial[1,2]
  - The proportion that completed surgery was slightly less in the N2 subgroup vs the mITT population (72.7% vs 77.2%)
  - Of those who completed surgery, R0 resection rates were numerically higher in the D vs PBO arm (94.7% vs 91.7%)
- In the N2 subgroup, the perioperative regimen had a manageable safety profile, similar to that with neoadjuvant CT alone and consistent with the overall trial[1]

With clinically meaningful improvement in efficacy, no adverse impact on surgical outcomes and a manageable safety profile, the addition of perioperative durvalumab to neoadjuvant CT remains a potential new treatment option for patients with N2 R-NSCLC

Heymach J et al. ASCO 2024;Abstract 8011.

Adjuvant Immunotherapy for NSCLC

- Felip E et al. Overall survival with **adjuvant atezolizumab** after chemotherapy in resected stage II-IIIA NSCLC (**IMpower010**): A randomised, multicentre, open-label, **phase III trial**. *Ann Oncol* 2023;34(10):907-19.
- Oselin K et al. **Pembrolizumab** vs placebo for early-stage NSCLC after resection and adjuvant therapy: **Subgroup analysis** of patients who received adjuvant chemotherapy in the **phase III PEARLS/KEYNOTE-091** study. ASCO 2023;Abstract 8520.
- Khan S et al. **ctDNA-Lung-DETECT**: **ctDNA outcomes** for resected early-stage non-small cell lung cancers at 12 months. ASCO 2024;Abstract 8018.

2024 ASCO ANNUAL MEETING

Abstract 8018

CONQUER CANCER® THE ASCO FOUNDATION MERIT AWARD

ctDNA-Lung-DETECT: rate of ctDNA detection and outcomes for clinical stage I NSCLC

Sam Khan[1], Jamie Feng[1], Tom Waddell[2], Kazuhiro Yasufuku[2], Andrew Pierre[2], Shaf Keshavjee[2], Jonathan Yeung[2], Marcelo Cypel[2], Laura Donahoe[2], Elliot Wakeam[2], Marc de Perrot[2], Najib Safieddine[3], Michael Ko[4], David Parente[4], Mary Rabey[1], Michael Cabanero[4], Lisa Le[5], Christodoulos Pipinikas[6], Amber Chevalier[6], Natasha B. Leighl[1]

ctDNA-Lung-DETECT: Author Conclusions

In this study of patients with **clinical stage I** NSCLC:

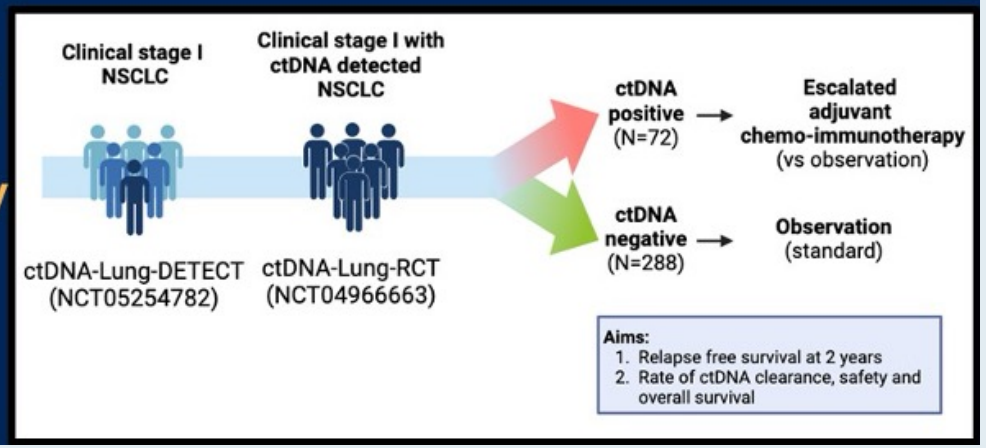
- Pre-operative ctDNA was detected in 22.7% using a tumour-informed assay
- Post-operative ctDNA was only detected in the setting of pathologic upstaging (occult N2 disease)
- In patients with pathologic stage I NSCLC, pre-operative ctDNA was detected in 14.0%

- Recurrence-free survival was significantly associated with detection of pre-operative ctDNA [HR 3.69, 95% CI: 1.12-12.1]
- Pathologic invasive tumour size but not radiographic size associated with pre-operative ctDNA detection
- ctDNA detection was more frequent in patients with high risk pathologic features and tumour suppressor alterations

Pre-operative ctDNA identifies stage I NSCLC patients at higher risk of relapse that may benefit from intensified curative therapy

Demonstration of the clinical utility of this approach is underway

More sensitive assays are needed to increase the value of this promising technology in clinical practice



Khan S et al. ASCO 2024;Abstract 8018.

Agenda

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MODULE 5: Immunotherapy for NSCLC with a Targetable Mutation

MODULE 6: Small Cell Lung Cancer

Consolidation for Locally Advanced NSCLC

- Rodrigues G et al**. American Radium Society** appropriate use **criteria for unresectable locally advanced non-small cell lung cancer**. *JAMA Oncol* 2024 April 11;[Online ahead of print].
- Lu S et al. **Osimertinib** after Chemoradiotherapy in **Stage III EGFR-Mutated** NSCLC. *N Engl J Med* 2024; Jun 2 [online ahead of print]
- Filippi AR et al. **Real-world outcomes** with **durvalumab** after **chemoradiotherapy** in patients with unresectable stage III NSCLC: Interim analysis of overall survival from **PACIFIC-R**. *ESMO Open* 2024 June 3;9(6):103464.
- Filippi ARR et al. **Durvalumab** after **radiotherapy** in patients with unresectable stage III NSCLC ineligible for chemotherapy: **Primary results** from the **DUART** study. ESMO 2023;Abstract LBA62.

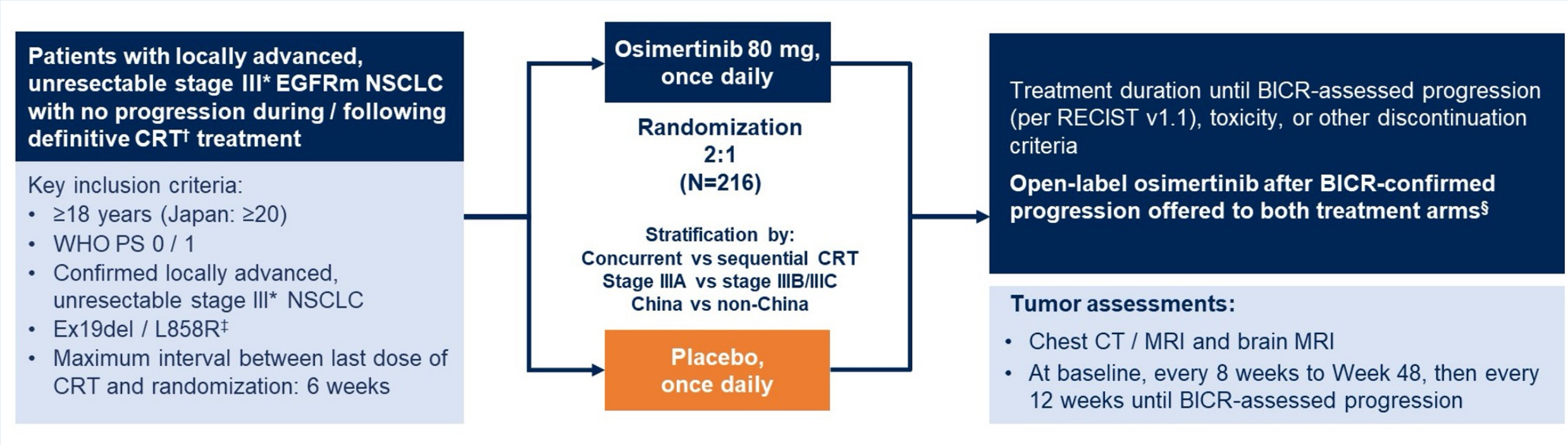
JAMA Oncology | Special Communication

American Radium Society Appropriate Use Criteria for Unresectable Locally Advanced Non-Small Cell Lung Cancer

George Rodrigues, MD, PhD; Kristin A. Higgins, MD; Andreas Rimner, MD; Arya Amini, MD; Joe Y. Chang, MD, PhD; Stephen G. Chun, MD; Jessica Donington, MD; Martin J. Edelman, MD; Matthew A. Gubens, MD; Puneeth Iyengar, MD, PhD; Benjamin Movsas, MD; Matthew S. Ning, MD; Henry S. Park, MD, MPH; Andrea Wolf, MD; Charles B. Simone II, MD

JAMA Oncol 2024; April 11;[Online ahead of print].

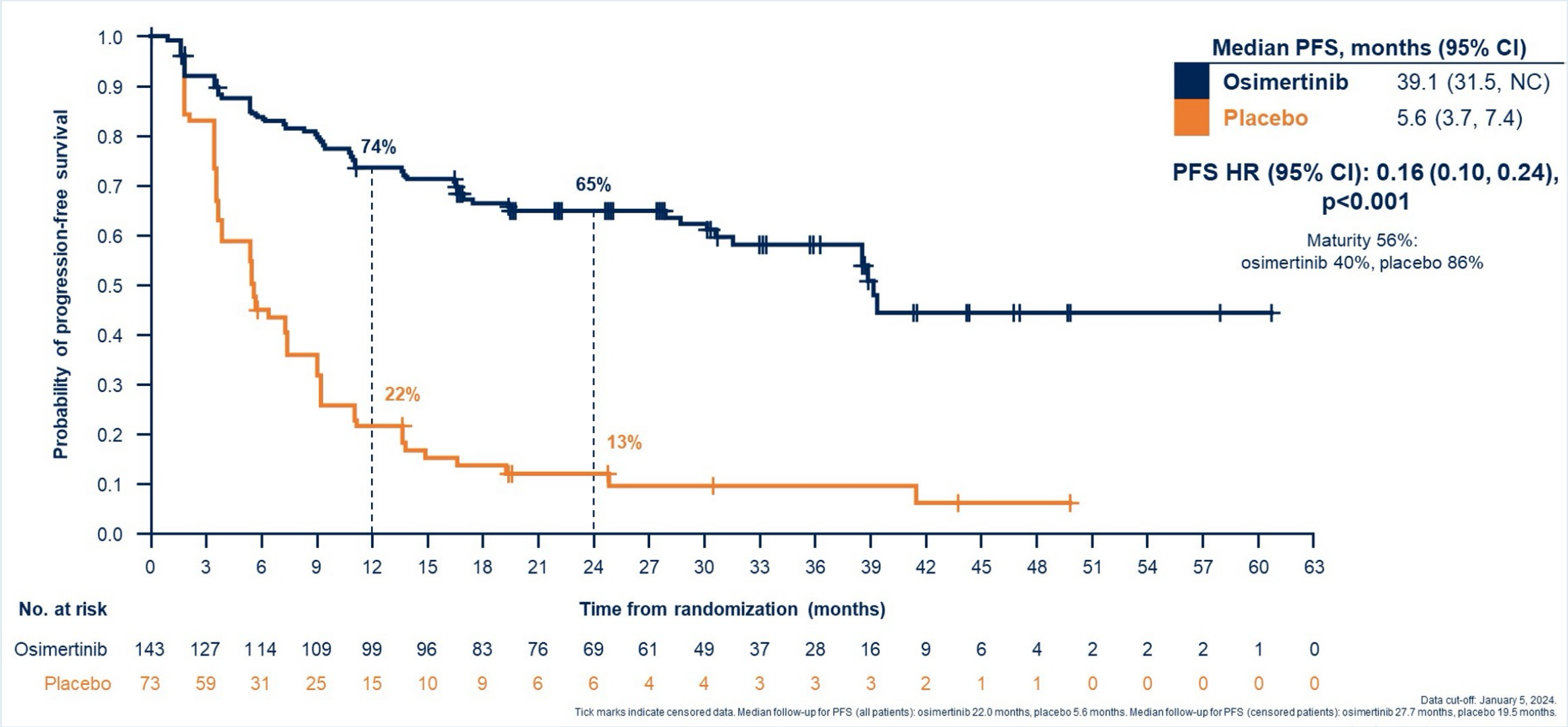
LAURA Phase III Study



Characteristics, %	Osimertinib (n=143)	Placebo (n=73)
AJCC / UICC staging (8th edition) at diagnosis: IIIA / IIIB / IIIC	36 / 47 / 17	33 / 52 / 15
Histology: adenocarcinoma / other	97 / 3	95 / 5
EGFR mutation at randomization:* Ex19del / L858R	52 / 48†	59 / 41
Type of CRT: concurrent CRT / sequential CRT	92 / 8	85 / 15
Response to prior CRT: CR / PR / SD / PD / NE	3 / 47 / 43 / 0 / 8	4 / 37 / 51 / 0 / 8
Target lesion size by BICR:‡ mean (SD), mm	33 (18)	36 (17)

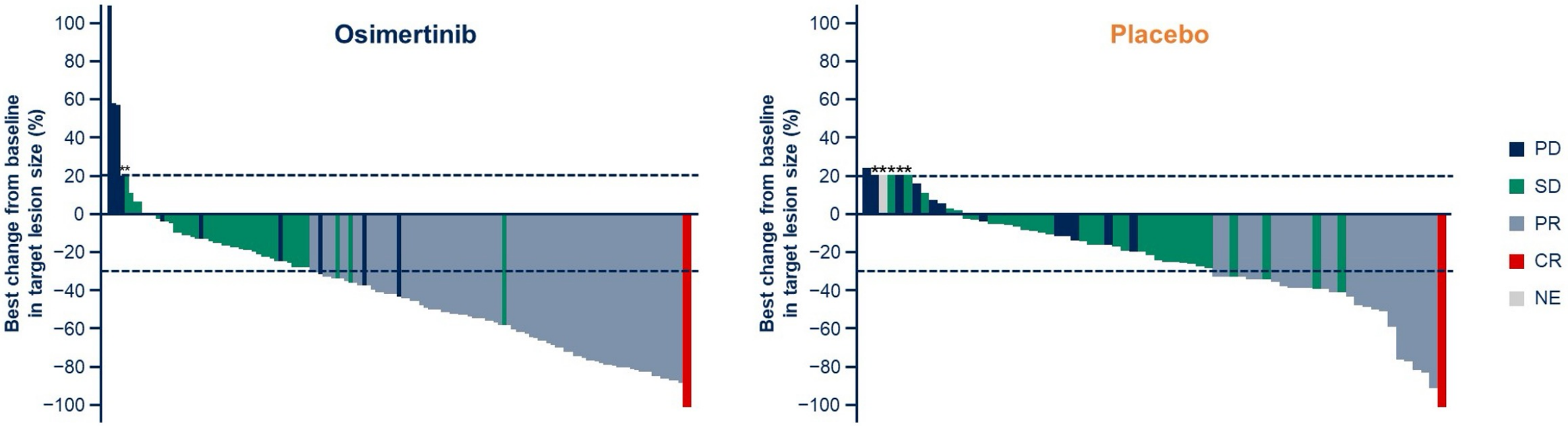
Ramalingam SS et al. ASCO 2024;Abstract LBA4. Lu S et al. *N Engl J Med* 2024 June 2;[Online ahead of print].

LAURA: PFS Outcomes by BICR



Ramalingam SS et al. ASCO 2024;Abstract LBA4. Lu S et al. *N Engl J Med* 2024 June 2;[Online ahead of print]

LAURA: Tumor Response by BICR

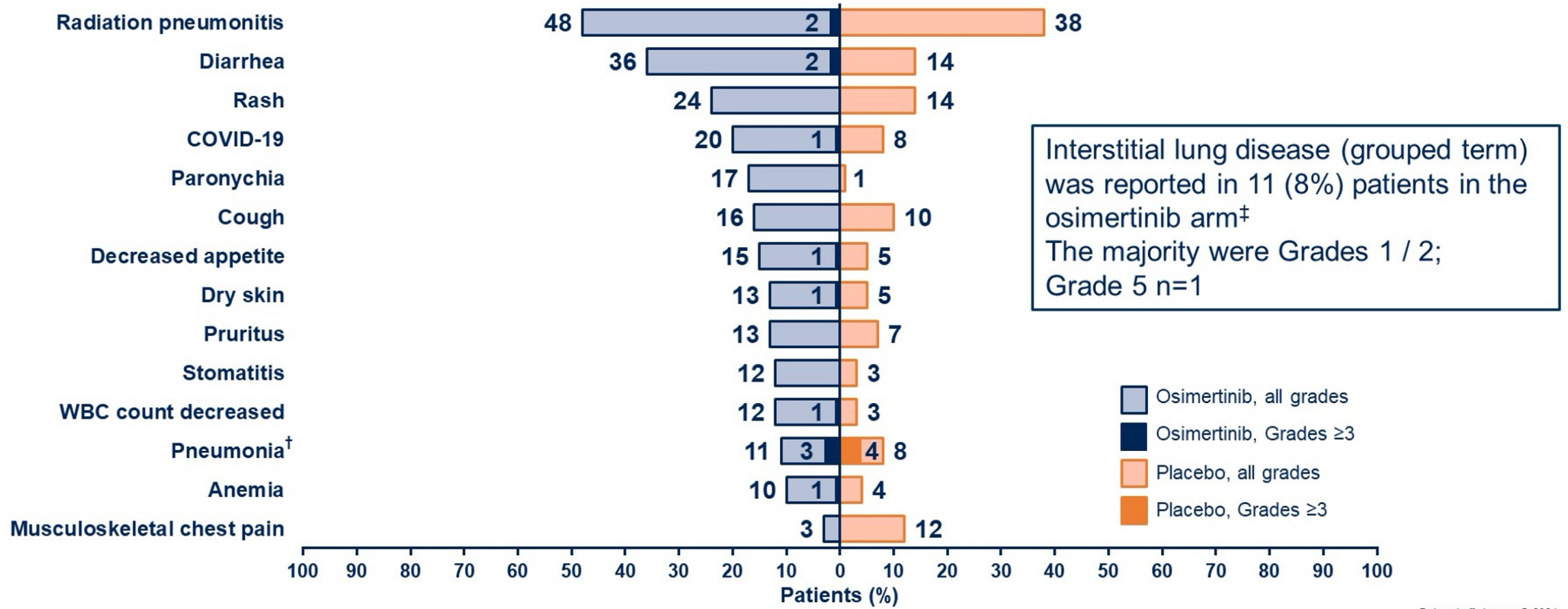


	Osimertinib (n=143)	Placebo (n=73)
Objective response rate, % (95% CI)	57 (49, 66)	33 (22, 45)
Disease control rate, % (95% CI)	89 (83, 94)	79 (68, 88)
Median duration of response, months (95% CI)	36.9 (30.1, NC)	6.5 (3.6, 8.3)

Ramalingam SS et al. ASCO 2024;Abstract LBA4.

LAURA: Safety Profile

The most common AE in both arms was radiation pneumonitis; the majority were low grade (no Grade 4 / 5), non-serious and manageable



Interstitial lung disease (grouped term) was reported in 11 (8%) patients in the osimertinib arm‡
The majority were Grades 1 / 2; Grade 5 n=1

Data cut-off: January 5, 2024.

*AEs with incidence of 10% or more in either treatment arm are shown. Patients with multiple events in the same category counted only once in that category. Patients with events in more than one category are counted once in each of those categories. Includes AEs with an onset date on or after the date of first dose and up to and including 28 days following the discontinuation of study treatment and before starting subsequent cancer therapy; †One grade 5 AE of pneumonia was reported in the osimertinib arm; ‡Interstitial lung disease (grouped term) was reported in 1 patient (1%) in placebo arm; AE was pneumonitis, Grade 1.

Ramalingam SS et al. ASCO 2024;Abstract LBA4.

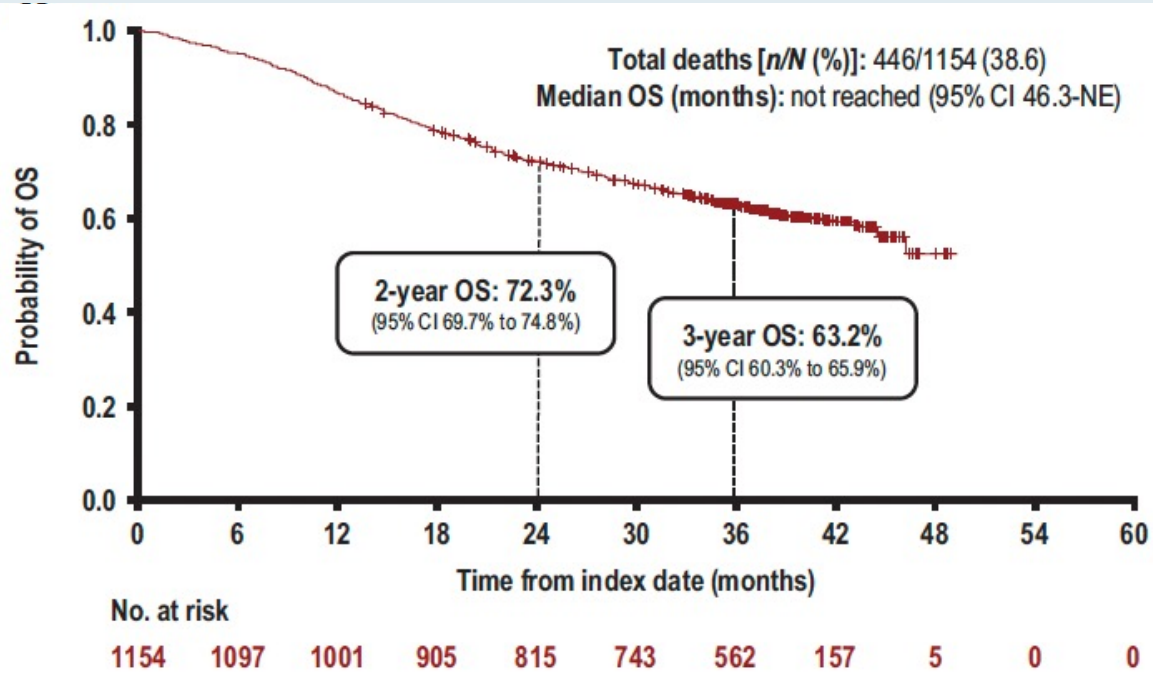
ORIGINAL RESEARCH

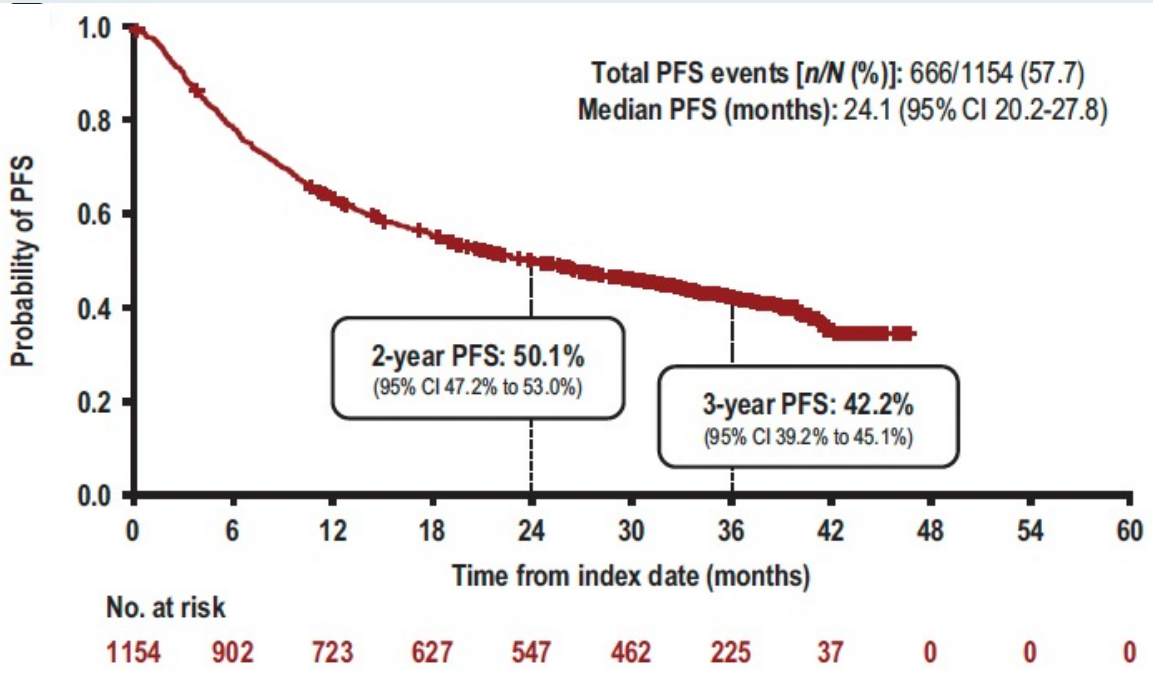
Real-world outcomes with durvalumab after chemoradiotherapy in patients with unresectable stage III NSCLC: interim analysis of overall survival from PACIFIC-R

A. R. Filippi[1*†], J. Bar[2,3], C. Chouaid[4], D. C. Christoph[5], J. K. Field[6], R. Fietkau[7], M. C. Garassino[8], P. Garrido[9], V. D. Haakensen[10], S. Kao[11], B. Markman[12], F. McDonald[13], F. Mornex[14], M. Moskovitz[15‡], S. Peters[16], A. Sibille[17], S. Siva[18], M. van den Heuvel[19], P. Vercauter[20], S. Anand[21], P. Chander[21], M. Licour[22], A. R. de Lima[21], Y. Qiao[21] & N. Girard[23,24]

ESMO Open 2024 June 3;9(6):103464

PACIFIC-R Study: Overall Survival (OS) and Investigator-Assessed Progression-Free Survival (PFS) in the Full Analysis Set





Filippi AR et al. *ESMO Open* 2024 June 3;9(6):103464.

MADRID 2023 ESMO congress

LBA62

Durvalumab after Radiotherapy in Patients with Unresectable Stage III NSCLC Ineligible for Chemotherapy

Primary Results from the DUART Study

Andrea R. Filippi,[1] Maria Rosario García Campelo,[2] Jean-Baptiste Paoli,[3] Dariusz Kowalski,[4] Chiara Bennati,[5] Paolo Borghetti,[6] Diego Cortinovis,[7] Angelo Delmonte,[8] Carlo Genova,[9] Sylvie Van Hulst,[10] Robert Mroz,[11] Sergiusz Nawrocki,[12] Ivan Toledano,[13] Giuseppe Tonini,[14] Ignacio Diaz Perez,[15] Nefeli Georgoulia,[15] Kayhan Foroutanpour,[15] Rafał Dziadziuszko[16]

[1]Fondazione IRCCS Policlinico San Matteo and University of Pavia, Pavia, Italy; [2]University Hospital A Coruña, A Coruña, Spain; [3]Hôpital Privé Clairval, Marseille, France; [4]Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [5]S Maria delle Croci Hospital, AUSL della Romagna, Ravenna, Italy; [6]ASST Spedali Civili and University of Brescia, Brescia, Italy; [7]Fondazione IRCCS San Gerardo dei Tintori Monza and Milano Bicocca University, Monza, Italy; [8]IRCCS Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori" (IRST), Meldola, Italy; [9]IRCCS Ospedale Policlinico San Martino and University of Genoa, Genova, Italy; [10]University Hospital of Nimes, Nimes France; [11]Medical University of Bialystok, Białystok, Poland; [12]University of Warmia and Mazury in Olsztyn, Olsztyn, Poland; [13]CCGM, Clinique Clémentville, Montpellier, France; [14]Fondazione Policlinico Universitario Campus Bio-Medico and Università Campus Bio-Medico di Roma, Roma, Italy; [15]AstraZeneca, Gaithersburg, MD, USA; [16]Medical University of Gdansk, Gdansk, Poland

DUART: Objective Response Rate (ORR)

Endpoint	Cohort A (standard RT; n=59)	Cohort B (palliative RT; n=43)	Total (N=102)
Confirmed ORR*, % (95% CI)†	28.8 (17.8–42.1)	23.3 (11.8–38.6)	26.5 (18.2–36.1)
Response status, n (%)			
Complete response	0	0	0
Partial response	17 (28.8)	10 (23.3)	**27 (26.5)**
Stable disease	25 (42.4)	22 (51.2)	**47 (46.1)**
Progression	10 (16.9)	6 (14.0)	16 (15.7)
RECIST v1.1 progression	6 (10.2)	5 (11.6)	11 (10.8)
Death	4 (6.8)	1 (2.3)	5 (4.9)
Not evaluable	7 (11.9)	5 (11.6)	12 (11.8)

- The confirmed ORR was 26.5% and 46.1% of patients had stable disease

Filippi AR et al. ESMO 2023;Abstract LBA62.

DUART: Conclusions

- Durvalumab following thoracic RT had a similar safety profile to that observed with durvalumab after cCRT in the PACIFIC trial and showed encouraging preliminary efficacy in this frailer and older population that are ineligible for CT[1,2*]
- Only 10 of 102 patients (9.8%) had grade 3/4 PRAEs within 6 months of starting Tx (primary endpoint), demonstrating that RT followed by consolidation durvalumab is well-tolerated in patients who are ineligible for CT, including patients with PS 2
- Median PFS was 8.0 months and ~35% of patients were alive and progression free at 1 year after starting durvalumab
  - Median PFS was numerically higher in the 60 Gy cohort (9.0 months), with ~40% alive and progression free at 1 year after starting durvalumab
- Median OS was 15.9 months and ~62% of patients were alive at 1 year after starting durvalumab
  - Notwithstanding changes in modern RT techniques, this compares favourably to historical cohorts treated with RT alone, in which patients experienced a median survival of approximately 8–14 months[3–6]
- **The combination of thoracic RT followed by durvalumab provides a novel option for this common subset of elderly and more fragile patients**

Filippi AR et al. ESMO 2023;Abstract LBA62.

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MODULE 6: Small Cell Lung Cancer

First-Line Immunotherapy for Metastatic NSCLC

- de Castro G Jr et al. **Five-year outcomes** with **pembrolizumab** versus **chemotherapy** as **first-line** therapy in patients with NSCLC and PD-L1 tumor proportion score ≥1% in the **KEYNOTE-042** study. *J Clin Oncol* 2023;41(11):1986-91.
- Garassino MC et al. **Pembrolizumab** plus **pemetrexed** and **platinum** in nonsquamous NSCLC: **5-year outcomes** from the **phase III KEYNOTE-189 study**. *J Clin Oncol* 2023;41(11):1992-8.
- Novello S et al. **Pembrolizumab plus chemotherapy** in **squamous** NSCLC: 5-year update of the phase III **KEYNOTE-407** study. *J Clin Oncol* 2023;41(11):1999-2006.
- Ramalingam SS et al. **Six-year survival** and HRQoL outcomes with **1L nivolumab + ipilimumab** in patients with metastatic NSCLC (mNSCLC) from **CheckMate227**. WCLC 2023;Abstract OA14.03.
- Reck M et al. **Five-year outcomes** with **first-line (1L) nivolumab + ipilimumab + chemotherapy** (N + I + C) vs C in patients (pts) with metastatic NSCLC (mNSCLC) in **CheckMate 9LA**. ASCO 2024;Abstract 8560.
- Johnson ML et al. **Durvalumab** with or without **tremelimumab** in combination with **chemotherapy** as **first-line therapy** for mNSCLC: The **phase III POSEIDON study**. *J Clin Oncol* 2023;41(6):1213-27.
- Peters S et al. **Durvalumab ± tremelimumab + chemotherapy** in **first-line** metastatic NSCLC: **5-year overall survival** update from the **POSEIDON study**. ESMO Immuno-Oncology 2023;Abstract LBA3.

First-Line Pembrolizumab as Monotherapy or Combined with Chemotherapy: 5-Year Updates

Monotherapy	Histologic type	Study arms	Median 5-year OS HR
KEYNOTE-042[1]	PD-L1 TPS ≥1% nonsquamous squamous	Pembrolizumab vs chemotherapy	PD-L1 TPS ≥1%: 0.79 PD-L1 TPS ≥20%: 0.75 PD-L1 TPS ≥50%: 0.68
Combination regimen			
KEYNOTE-189[2]	Nonsquamous	Pembrolizumab + platinum/pemetrexed vs placebo + platinum/pemetrexed	ITT: 0.60 PD-L1 TPS <1%: 0.55 PD-L1 TPS 1%-49%: 0.65 PD-L1 TPS ≥50%: 0.68
KEYNOTE-407[3]	Squamous	Pembrolizumab + carboplatin, paclitaxel or *nab* paclitaxel vs placebo + carboplatin, paclitaxel or *nab* paclitaxel	ITT: 0.71 PD-L1 TPS <1%: 0.83 PD-L1 TPS 1%-49%: 0.61 PD-L1 TPS ≥50%: 0.68

OS = overall survival; HR = hazard ratio; TPS = tumor proportion score; ITT = intention to treat

[1] de Castro G Jr et al. *J Clin Oncol* 2023;41(11):1986-91. [2] Garassino MC et al. *J Clin Oncol* 2023;41(11):1992-8.
[3] Novello S et al. *J Clin Oncol* 2023;41(11):1999-2006.

CheckMate 227 Study: 6-Year Outcomes with First-Line Nivolumab and Ipilimumab for Metastatic NSCLC

	PD-L1 ≥1%		PD-L1 <1%	
	Nivolumab[a] + ipilimumab[b]	Chemotherapy	Nivolumab[a] + ipilimumab[b]	Chemotherapy
Randomized patients, n	396	397	187	186
Median OS, months (95% CI)	17.1 (15.0-20.2)	14.9 (12.7-16.7)	17.4 (13.2-22.0)	12.2 (9.2-14.3)
OS HR (95% CI)	0.78 (0.67-0.91)		0.65 (0.52-0.81)	
6-year OS rate, %	22	13	16	5
6-year PFS rate, %	11	2	8	NA
ORR, n (%)	144 (36)	118 (30)	51 (27)	43 (23)
Median DOR, months (95% CI)	24.5 (15.5-34.5)			

Ramalingam SS et al. WCLC 2023;Abstract OA14.03.

CheckMate 9LA Study: 5-Year Outcomes with First-Line Nivolumab and Ipilimumab for Metastatic NSCLC

Endpoint	All randomized		PD-L1 < 1%		PD-L1 ≥1%		Squamous		Nonsquamous	
	Nivo + ipi (n = 368)	Chemo (n = 358)	Nivo + ipi (n = 135)	Chemo (n = 129)	Nivo + ipi (n = 204)	Chemo (n = 204)	Nivo + ipi (n = 115)	Chemo (n = 112)	Nivo + ipi (n = 246)	Chemo (n = 246)
Median OS	15.8 mo	11.0 mo	17.7 mo	9.8 mo	15.8 mo	10.9 mo	14.5 mo	9.1 mo	17.8 mo	12.0 mo
OS HR	0.73		0.63		0.73		0.63		0.77	
5-year OS rate	18%	11%	22%	8%	18%	11%	18%	7%	19%	12%
Median PFS	6.7 mo	5.3 mo	5.8 mo	5.0 mo	6.9 mo	4.7 mo	5.6 mo	4.3 mo	6.9 mo	5.6 mo
PFS HR	0.70		0.71		0.70		0.65		0.75	
5-year PFS rate	10%	4%	9%	3%	10%	5%	8%	4%	10%	4%

nivo = nivolumab; ipi = ipilimumab; PFS = progression-free survival

Reck M et al. ASCO 2024;Abstract 8560.

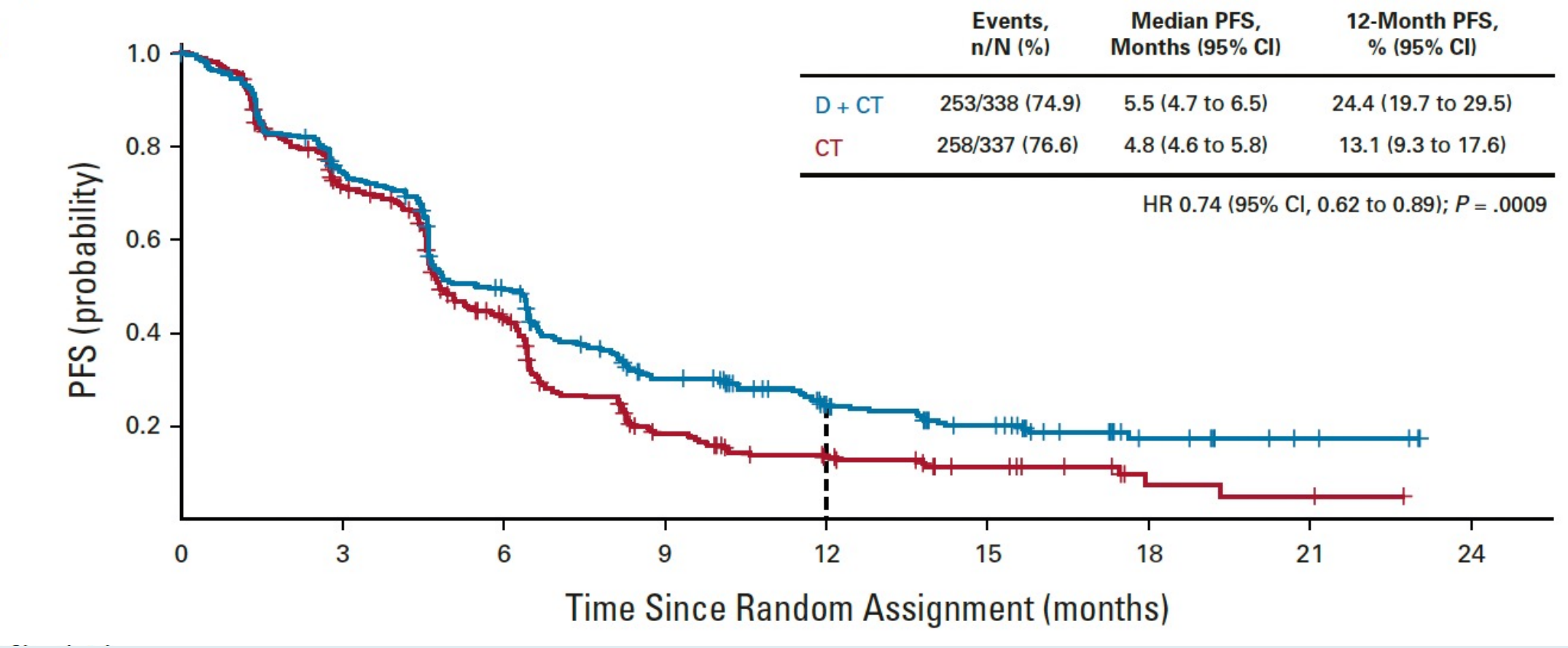
original reports

Durvalumab With or Without Tremelimumab in Combination With Chemotherapy as First-Line Therapy for Metastatic Non–Small-Cell Lung Cancer: The Phase III POSEIDON Study

Melissa L. Johnson, MD[1]; Byoung Chul Cho, MD, PhD[2]; Alexander Luft, MD[3]; Jorge Alatorre-Alexander, MD[4]; Sarayut Lucien Geater, MD[5]; Konstantin Laktionov, MD[6]; Sang-We Kim, MD, PhD[7]; Grygorii Ursol, MD[8]; Maen Hussein, MD[9]; Farah Louise Lim, MBBS, MRCP[10]; Cheng-Ta Yang, MD[11]; Luiz Henrique Araujo, MD, PhD[12]; Haruhiro Saito, MD, PhD[13]; Niels Reinmuth, MD, PhD[14]; Xiaojin Shi, MD[15]; Lynne Poole, MSc[16]; Solange Peters, MD, PhD[17]; Edward B. Garon, MD[18]; and Tony Mok, MD[19] for the POSEIDON investigators

J Clin Oncol 2023;41:1213-27

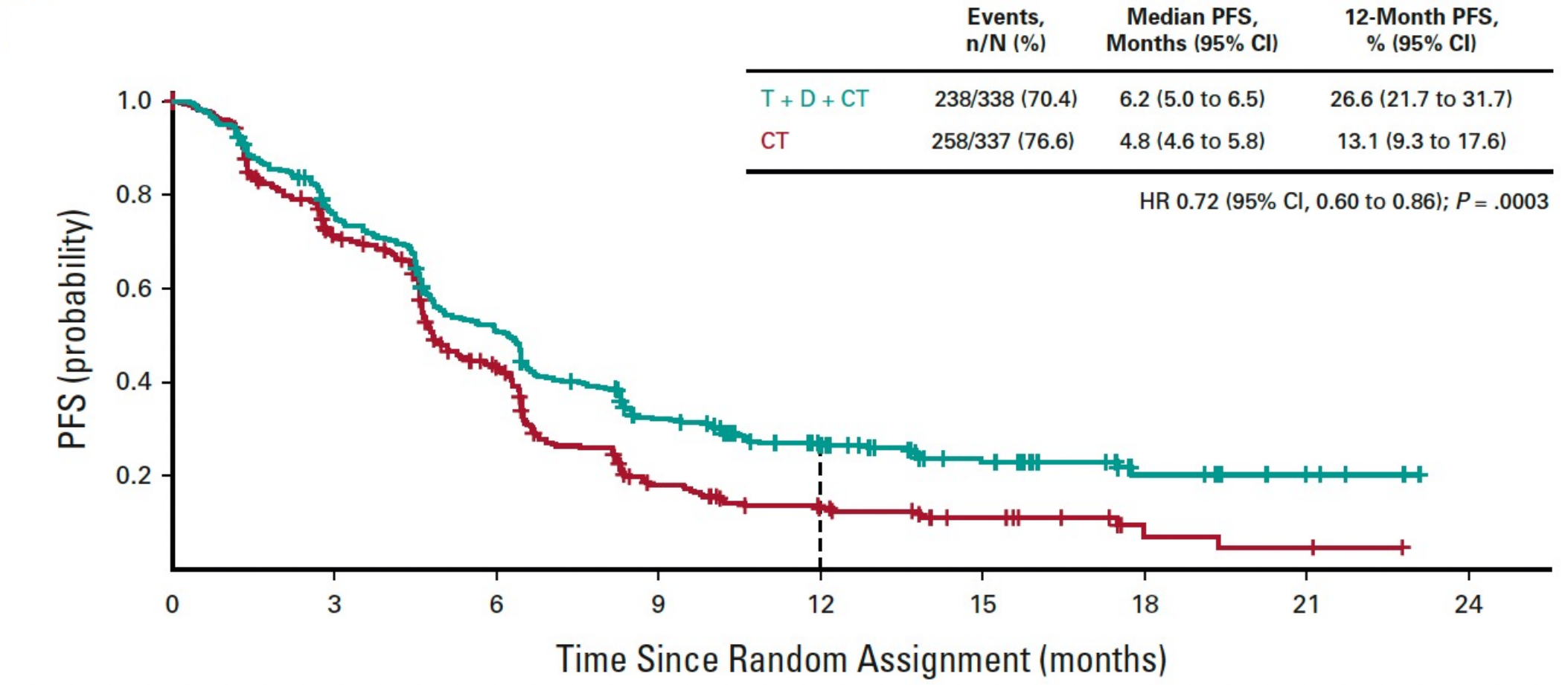
POSEIDON: Progression-Free Survival with Durvalumab and Chemotherapy versus Chemotherapy



D = durvalumab; CT = chemotherapy

Johnson ML et al. *J Clin Oncol* 2023;41:1213-27.

POSEIDON: Progression-Free Survival with Durvalumab, Tremelimumab and Chemotherapy versus Chemotherapy



	Events, n/N (%)	Median PFS, Months (95% CI)	12-Month PFS, % (95% CI)
T + D + CT	238/338 (70.4)	6.2 (5.0 to 6.5)	26.6 (21.7 to 31.7)
CT	258/337 (76.6)	4.8 (4.6 to 5.8)	13.1 (9.3 to 17.6)

HR 0.72 (95% CI, 0.60 to 0.86); $P = .0003$

T = tremelimumab

Johnson ML et al. *J Clin Oncol* 2023;41:1213-27.

2023 ESMO IMMUNO-ONCOLOGY

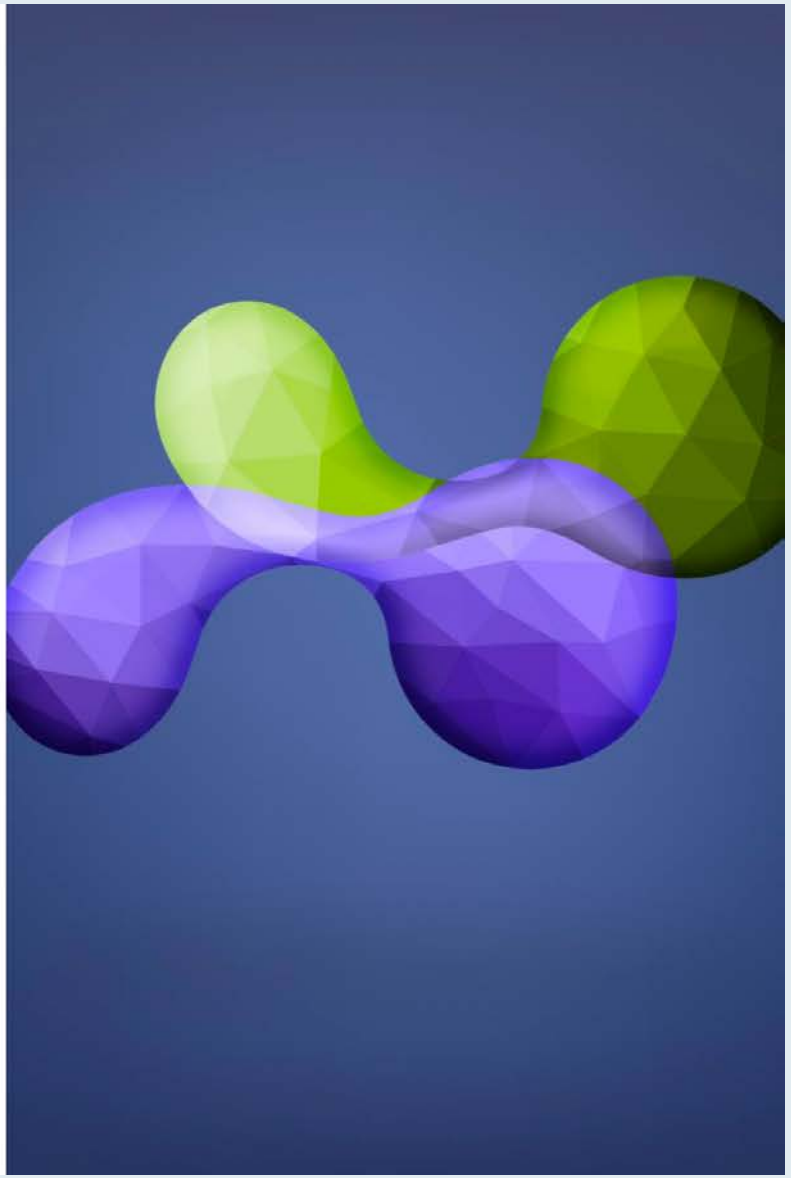
Annual Congress

LBA3 – Durvalumab ± Tremelimumab + Chemotherapy in First-Line Metastatic NSCLC: 5-Year Overall Survival Update from the POSEIDON Study

Solange Peters,[1] Byoung Chul Cho,[2] Alexander Luft,[3] Jorge Alatorre-Alexander,[4] Sarayut Lucien Geater,[5] Konstantin Laktionov,[6] Dmytro Trukhin,[7] Sang-We Kim,[8] Grygorii Ursol,[9] Maen Hussein,[10] Farah Louise Lim,[11] Cheng-Ta Yang,[12] Luiz Henrique Araujo,[13] Haruhiro Saito,[14] Niels Reinmuth,[15] Leah Szadkowski,[16] Caitlin Lowery,[17] Edward B. Garon,[18] Tony Mok,[19] Melissa L. Johnson[20]

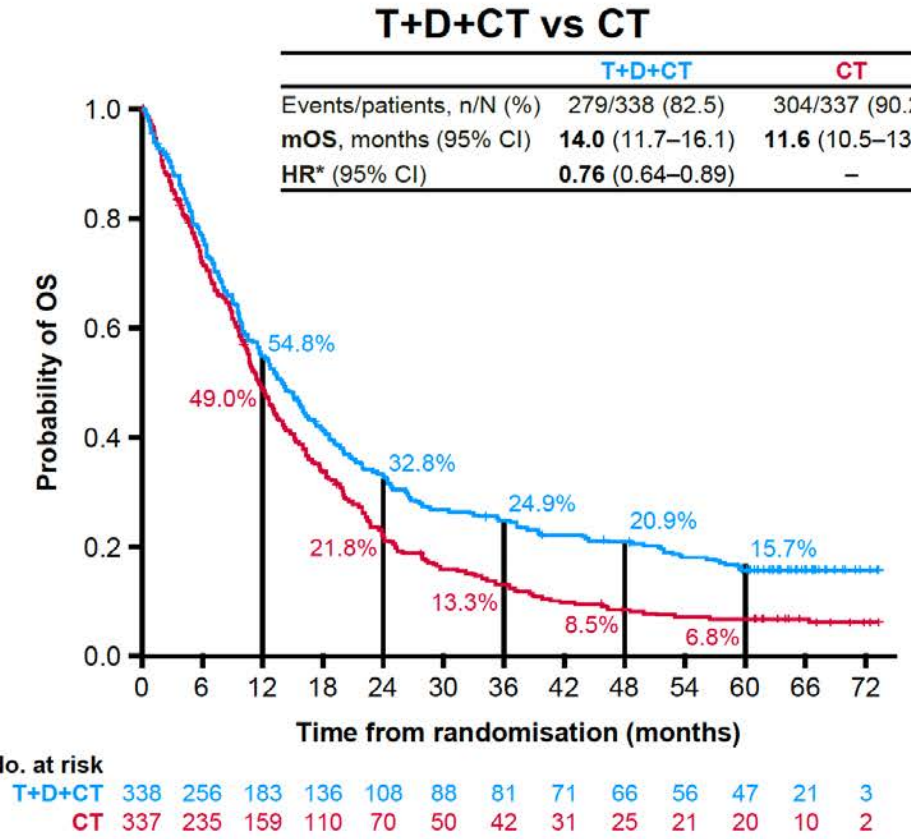
[1]Centre Hospitalier Universitaire Vaudois, Lausanne University, Lausanne, Switzerland; [2]Yonsei Cancer Center, Seoul, Republic of Korea; [3]Leningrad Regional Clinical Hospital, St Petersburg, Russia; [4]Health Pharma Professional Research, Mexico City, Mexico; [5]Prince of Songkla University, Songkhla, Thailand; [6]Federal State Budgetary Institution "N.N. Blokhin National Medical Research Center of Oncology" of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia; [7]Odessa Regional Oncological Dispensary, Odessa, Ukraine; [8]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [9]Acinus, Kropyvnytskyi, Ukraine; [10]Florida Cancer Specialists – Sarah Cannon Research Institute, Leesburg, FL, USA; [11]Queen Mary University of London, London, United Kingdom; [12]Chang Gung Memorial Hospital, Taoyuan City, Taiwan; [13]Instituto Nacional de Cancer-INCA, Rio de Janeiro, Brazil; [14]Kanagawa Cancer Center, Yokohama, Japan; [15]Asklepios Lung Clinic, Munich-Gauting, Germany; [16]AstraZeneca, Mississauga, ON, Canada; [17]AstraZeneca, Gaithersburg, MD, USA; [18]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [19]Chinese University of Hong Kong, Hong Kong, China; [20]Sarah Cannon Research Institute, Tennessee Oncology, PLLC, Nashville, TN, USA

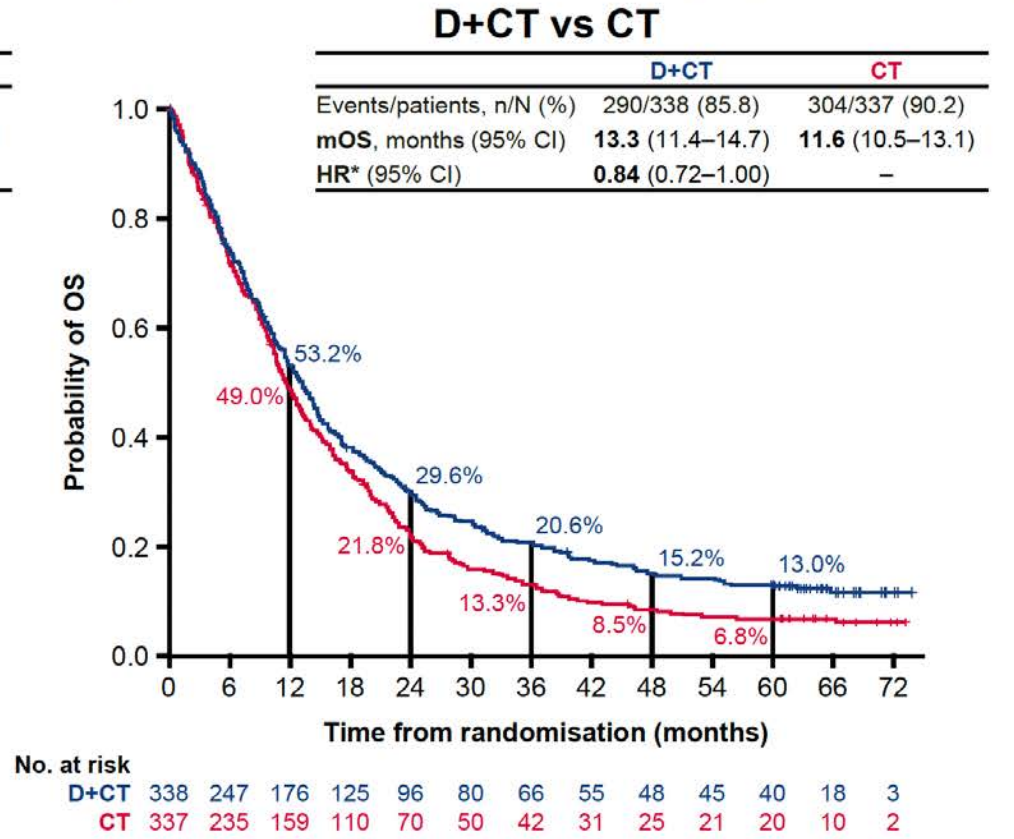
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE



POSEIDON: 5-Year Overall Survival Update

Sustained OS benefit for T+D+CT vs CT with HR 0.76 and 5-yr OS rates more than twice as high (15.7% vs 6.8%)





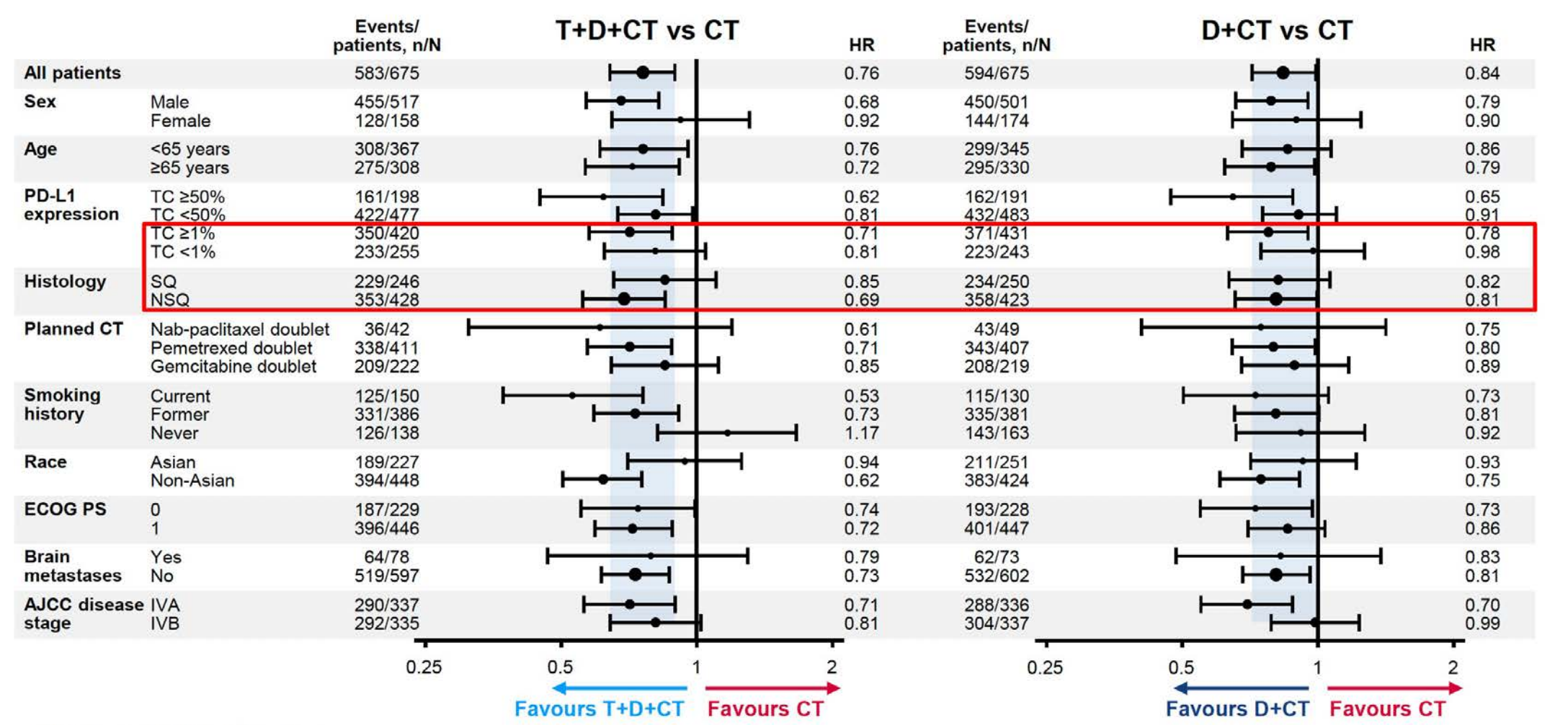
Median follow-up in censored patients at DCO: 63.4 months (range 0.0–73.9)

*HR <1 favours D(±T)+CT vs CT (stratified analysis); DCO, 24 Aug 2023

mOS, median OS; yr, year

Peters S et al. ESMO Immuno-Oncology 2023;Abstract LBA3.

POSEIDON: 5-Year Overall Survival Update Subgroup Analysis



AJCC, American Joint Committee on Cancer

HR <1 favours D(±T)+CT vs CT (all patients analysis stratified, subgroup analysis unstratified); size of circle is proportional to the number of events across both treatment groups; DCO, 24 Aug 2023

Peters S et al. ESMO Immuno-Oncology 2023;Abstract LBA3.

Agenda

INTRODUCTION: Risk of Autoimmune Toxicity with Checkpoint Inhibitors

MODULE 1: Immunotherapy in the Neoadjuvant/Adjuvant Setting

MODULE 2: Immunotherapy for Locally Advanced NSCLC

MODULE 3: First-Line Immunotherapy for Metastatic NSCLC

MODULE 4: Novel Agents and Strategies

MODULE 5: Immunotherapy for NSCLC with a Targetable Mutation

MODULE 6: Small Cell Lung Cancer

Novel Agents and Strategies for mNSCLC

- Ahn M-J et al. **Datopotamab deruxtecan (Dato-DXd)** vs docetaxel in previously treated advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC): Results of the randomized **phase 3 study TROPION-Lung01**. ESMO Asia 2023;Abstract 509MO.
- Goto Y et al. **TROPION-Lung02: Dato-DXd** plus **pembrolizumab** with or without platinum **chemotherapy** in advanced NSCLC. ASCO 2023;Abstract 9004.
- Levy B et al. **Datopotamab deruxtecan (Dato-DXd)** plus **pembrolizumab** (pembro) with or without platinum **chemotherapy** (Pt-CT) as **first-line** (1L) therapy for advanced non-small cell lung cancer (aNSCLC): **Subgroup analysis** from **TROPION-Lung02**. ASCO 2024;Abstract 8617.
- Planchard D et al. **ICARUS-LUNG01**: A phase 2 study of **datopotomab deruxtecan (Dato-DXd)** in patients with previously treated advanced non-small cell lung cancer (NSCLC), with sequential tissue biopsies and biomarkers analysis to predict treatment outcome. ASCO 2024;Abstract 8501.

Novel Agents and Strategies for mNSCLC (Continued)

- Paz-Ares L et al. **TROPION-Lung05: Datopotamab deruxtecan (Dato-DXd)** in previously treated non-small cell lung cancer (NSCLC) with **actionable genomic alterations (AGAs).** ESMO 2023;Abstract 1314MO.
- Lisberg A et al. **Intracranial efficacy** of **datopotamab deruxtecan (Dato-DXd)** in patients (pts) with previously treated advanced/metastatic non-small cell lung cancer (a/m NSCLC) with actionable genomic alterations (AGA): Results from TROPION-Lung05. ASCO 2024;Abstract 8593.

SINGAPORE 2023 ESMO ASIA

Abstract 509MO

Datopotamab deruxtecan (Dato-DXd) vs docetaxel in previously treated advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC): Results of the randomized phase 3 study TROPION-Lung01

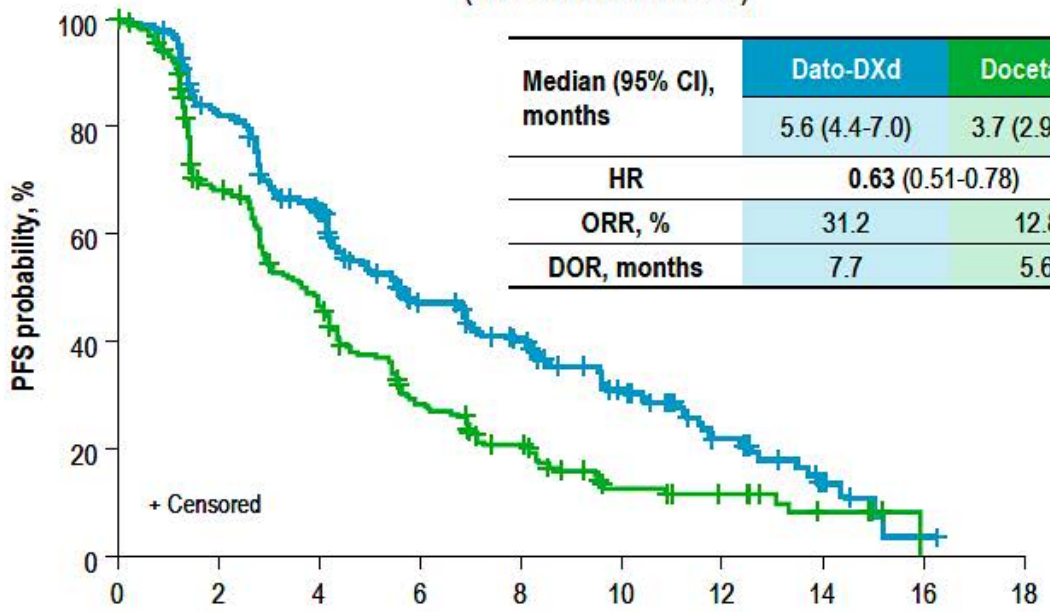
Myung-Ju Ahn,[1,a,b] Aaron Lisberg,[2,a] Luis Paz-Ares,[3] Robin Cornelissen,[4] Nicolas Girard,[5] Elvire Pons-Tostivint,[6] David Vicente Baz,[7] Shunichi Sugawara,[8] Manuel Angel Cobo,[9] Maurice Pérol,[10] Céline Mascaux,[11] Elena Poddubskaya,[12] Satoru Kitazono,[13] Hidetoshi Hayashi,[14] Jacob Sands,[15] Richard Hall,[16] Yong Zhang,[17] Hong Zebger-Gong,[18] Deise Uema,[17] Isamu Okamoto[19]

[a]Equal contribution as first author. [b]Indicates presenting author.

[1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [2]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [3]Hospital Universitario 12 de Octubre, CNIO-H12O Lung Cancer Unit, Universidad Complutense & CiberOnc, Madrid, Spain; [4]Erasmus MC Cancer Institute, Rotterdam, The Netherlands; [5]Institut Curie, Paris, France; [6]Centre Hospitalier Universitaire de Nantes, Nantes, France; [7]Hospital Universitario Virgen Macarena, Seville, Spain; [8]Sendai Kousei Hospital, Sendai, Japan; [9]FEA Oncología Médica, Medical Oncology Intercenter Unit, Regional and Virgen de la Victoria University Hospitals, IBIMA, Málaga, Spain; [10]Centre Léon Bérard, Lyon, France; [11]Hôpitaux Universitaires de Strasbourg (CHRU), Strasbourg, France; [12]Vitamed LLC, Moscow, Russia; [13]The Cancer Institute Hospital of JFCR, Tokyo, Japan; [14]Kindai University, Osaka, Japan; [15]Dana-Farber Cancer Institute, Boston, MA, USA; [16]University of Virginia Health System, Charlottesville, VA, USA; [17]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [18]Daiichi Sankyo Europe GmbH, Munich, Germany; [19]Kyushu University Hospital, Fukuoka, Japan

TROPION-Lung01: PFS by Histology

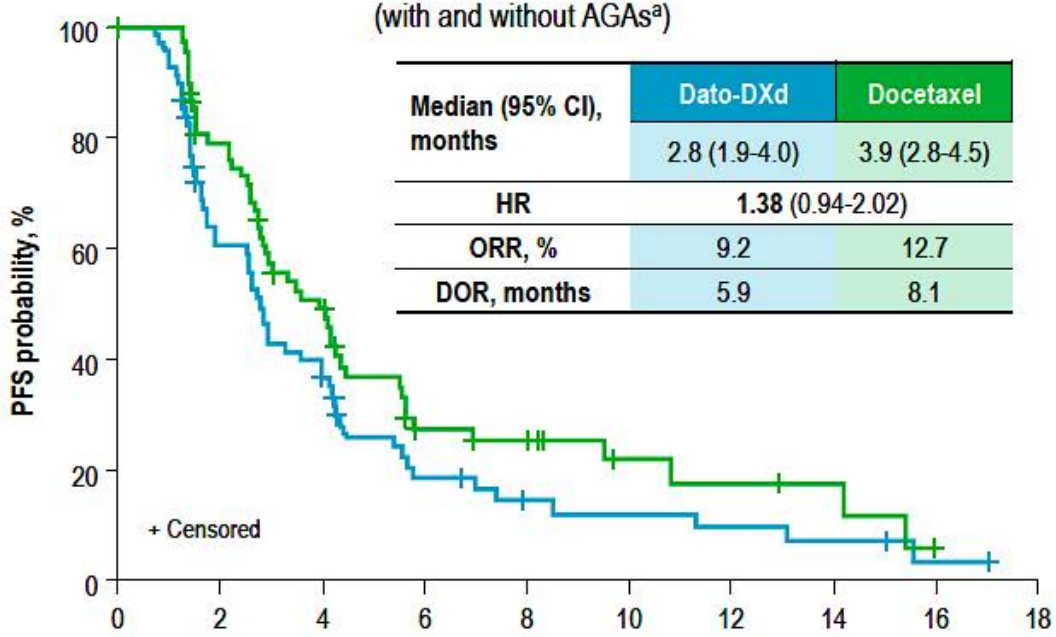
Non-squamous
(with and without AGAs)



Median (95% CI), months	Dato-DXd	Docetaxel
	5.6 (4.4-7.0)	3.7 (2.9-4.2)
HR	**0.63** (0.51-0.78)	
ORR, %	31.2	12.8
DOR, months	7.7	5.6

No. at risk										
Dato-DXd	229	178	134	86	68	41	20	7	1	0
Docetaxel	232	135	90	50	32	14	10	4	0	0

Squamous
(with and without AGAs[a])



Median (95% CI), months	Dato-DXd	Docetaxel
	2.8 (1.9-4.0)	3.9 (2.8-4.5)
HR	**1.38** (0.94-2.02)	
ORR, %	9.2	12.7
DOR, months	5.9	8.1

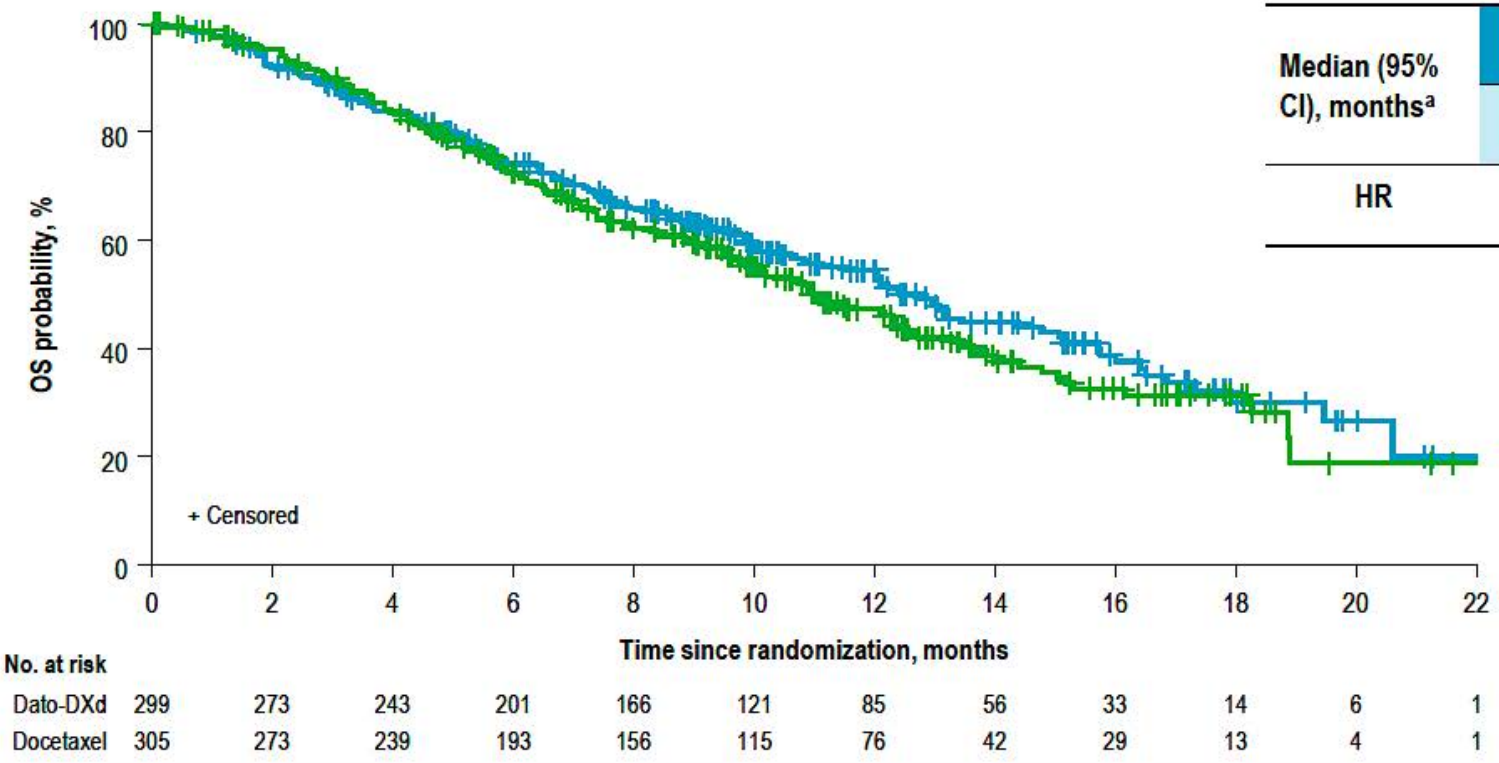
No. at risk										
Dato-DXd	70	38	22	10	6	5	4	3	1	0
Docetaxel	73	51	30	13	10	5	4	3	0	0

PFS HR for non-squamous without AGAs: 0.71 (0.56, 0.91)

AGA, actionable genomic alteration; DOR, duration of response; HR, hazard ratio; ORR, objective response rate; PFS, progression-free survival.
[a]Squamous subset included 3 patients with AGAs.

Ahn M-J et al. ESMO Asia 2023;Abstract 509MO.

TROPION-Lung01: Interim OS Analysis



Median (95% CI), months[a]	Dato-DXd	Docetaxel
	12.4 (10.8-14.8)	11.0 (9.8-12.5)
HR	**0.90** (0.72-1.13)	

Information fraction at interim analysis (events/total events required): **74%.**

Non-squamous HR (95% CI): **0.77** (0.59-1.01); **Squamous HR** (95% CI): **1.32** (0.87-2.00)

Trial is continuing to final OS analysis

HR, hazard ratio; ITT, intention to treat; OS, overall survival.
[a]Median OS follow-up was 11.8 (95% CI, 11.3-12.7) and 11.7 (95% CI, 10.9-12.9) months for Dato-DXd and docetaxel, respectively.

Ahn M-J et al. ESMO Asia 2023;Abstract 509MO.

TROPION-Lung01: Adverse Events of Special Interest

AESI, n (%)	Dato-DXd N=297	Docetaxel N=290
Stomatitis/oral mucositis[a]		
All grades	160 (54)	59 (20)
Grade ≥3	19 (6)	4 (1)
Ocular events[b]		
All grades	57 (19)	27 (9)
Grade ≥3	5 (2)[c]	0
Adjudicated drug-related ILD[d]		
All grades	25 (8)	12 (4)
Grade ≥3	10 (3)	4 (1)
Grade 5	7 (2)	1 (0.3)

- Stomatitis/oral mucositis associated with Dato-DXd resulted in a low rate of discontinuation (0.7%)
- Dry eye was the most common ocular event seen with Dato-DXd (6.1%; primarily grade ≤2), followed by increased lacrimation (5.4%)
- Seven adjudicated drug-related grade 5 ILD events
  - Primary cause of death in 4 out of 7 was attributed to disease progression by investigator
  - Non-squamous: 4 of 232 patients (1.7%); Squamous: 3 of 65 patients (4.6%)[e]
- IRRs were observed in 8% of patients in each arm, all were grade ≤2 with the exception of 1 grade 3 event with Dato-DXd

AESI, adverse event of special interest; ILD, interstitial lung disease; IRR, infusion-related reaction; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; SMQ, standardized MedDRA query; SOC, system organ class. AESIs listed in this slide are treatment emergent and include all PTs that define the medical concept.

[a]Events included the selected PTs oral mucositis/stomatitis, oropharyngeal pain, mouth ulceration, odynophagia, dysphagia, oral pain, glossitis, pharyngeal inflammation, aphthous ulcer, and oral mucosa erosion. [b]Ocular events included selected PTs from the corneal disorder SMQ and selected relevant PTs from the eye disorder SOC. [c]Included 4 cases of keratitis and 1 case of ulcerative keratitis. [d]ILD includes events that were adjudicated as ILD and related to use of Dato-DXd or docetaxel (includes cases of potential ILD/pneumonitis based on MedDRA v26.0 for the narrow ILD SMQ, selected terms from the broad ILD SMQ, and PTs of respiratory failure and acute respiratory failure). [e]Among treated patients, histology information per the case report form.

Ahn M-J et al. ESMO Asia 2023;Abstract 509MO.

ASCO 2024

Abstract # 8617

Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab with or without platinum chemotherapy as first-line therapy for advanced non-small cell lung cancer (NSCLC); subgroup analysis from TROPION-Lung02

Benjamin Levy,[1] Luis Paz Ares,[2] Wu Chou Su,[3] Scott Herbert,[4] Tsung Ying Yang,[5] Anthony Tolcher,[6,7] Yanyan Lou,[8] Yoshitaka Zenke,[9] Diego Cortinovis,[10] Enriqueta Felip,[11] Manuel Domine,[12] Konstantinos Leventakos,[13] Emiliano Calvo,[14] Atsushi Horiike,[15] Edward Pan,[16] Daisy Lin,[16] Xiaoyu Jia,[16] Priyanka Basak,[16] Michael J. Chisamore,[17] Yasushi Goto[18]

TROPION-Lung02 Subgroup Analysis: First-Line Efficacy Outcomes

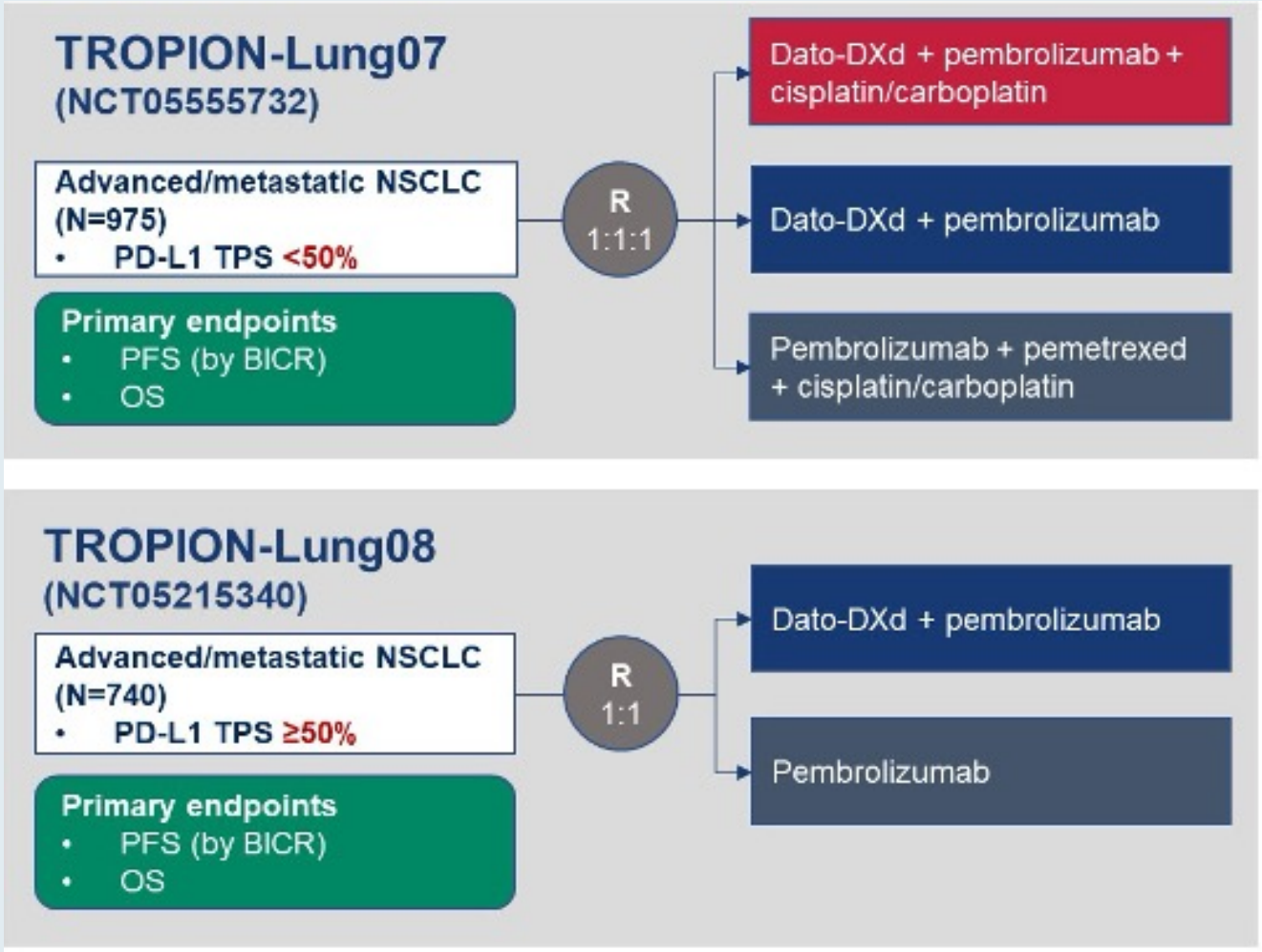
	All 1L (n=96)		1L PD-L1 <1% (n=34)		1L PD-L1 1–49% (n=42)		1L PD-L1 ≥50% (n=20)	
	Doublet (n=42)	Triplet (n=54)	Doublet (n=18)	Triplet (n=16)	Doublet (n=19)	Triplet (n=23)	Doublet (n=5)	Triplet (n=15)
ORR, n (%)	22 (52)	30 (56)	8 (44)	5 (31)	9 (47)	17 (74)	5 (100)	8 (53)
[95% CI]	[36–68]	[41–69]	[22–69]	[11–59]	[24–71]	[52–90]	[48–100]	[27–79]
BOR, n (%)								
CR	1 (2)	1 (2)	1 (6)	0	0	1 (4)	0	0
PR	21 (50)	29 (54)	7 (39)	5 (31)	9 (47)	16 (70)	5 (100)	8 (53)
SD	15 (36)	18 (33)	8 (44)	10 (63)	7 (37)	3 (13)	0	5 (33)
PD	3 (7)	2 (4)	1 (6)	1 (6)	2 (11)	1 (4)	0	0
NE	2 (5)	4 (7)	1 (6)	0	1 (5)	2 (9)	0	2 (13)
DCR, n (%)	37 (88)	48 (89)	16 (89)	15 (94)	16 (84)	20 (87)	5 (100)	13 (87)
[95% CI]	[74–96]	[77–96]	[65–99]	[70–100]	[60–97]	[66–97]	[48–100]	[60–98]
Median TTR, months	1.4	1.4	1.4	1.5	1.5	1.4	1.4	1.5
[Range]	[1.2–7.0]	[1.2–9.6]	[1.2–6.9]	[1.2–9.6]	[1.2–7.0]	[1.2–7.0]	[1.3–2.8]	[1.2–8.3]
Median DoR, months	NE	12.9	NE	12.9	12.0	14.6	NE	18.1
[95% CI]	[9.7–NE]	[5.7–NE]	NE	[4.1–NE]	[4.2–NE]	[4.2–NE]	[5.5–NE]	[4.1–NE]

[a]Evaluated locally by tumor proportion score using immunohistochemistry (22C3 assay). [b]Responses with confirmed CR/PR.

ORR = objective response rate; BOR = best overall response; CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; NE = not evaluable; DCR = disease control rate; TTR = time to response; DoR = duration of response

Levy B et al. ASCO 2024;Abstract 8617.

Ongoing Phase III Trials of Dato-DXd with Pembrolizumab for Advanced/Metastatic NSCLC



BICR = blinded independent central review

Goto Y et al. ASCO 2023;Abstract 9004.

2024 ASCO ANNUAL MEETING

Abstract 8501

ICARUS-LUNG01: A phase 2 Study of Dato-DXd in patients with previously treated advanced NSCLC, with sequential tissue biopsies and biomarkers analysis to predict treatment outcome

D. Planchard[1,2], N. Cozic[3], M. Wislez[4], C. Chouaid[5], H. Curcio[6], S. Cousin[7], C. Mascaux[8], J. Cadranel[9], M. Geier[10], M. R. Ghigna[11], G. Nachabeh[12], R. Zwirtes[13], R. Chiaverelli[13], R. Cheikh-Hussin[14], N. Corcos[14], F. Mosele[1,15], F. André[1,2,15], G. Montagnac[14], B. Pistilli[1,14]

ICARUS-LUNG01 Study Design

Multi-center, single-arm, phase 2 study (NCT04940325)

KEY ELIGIBILITY CRITERIA

- NSCLC (stage IIIB, IIIC, or IV)
- ECOG PS of 0 or 1
- Progressed on prior 1-3 lines:
  - Without known mutations: anti PD-1/PDL-1 containing therapy and a platinum-doublet regimen
  - With known EGFR, BRAF, MET ALK, ROS1, RET, NTRK alterations: one line of an approved targeted agent and one platinum-doublet regimen
- Asymptomatic brain metastases

Dato-DXd 6 mg/kg Q3W until PD or unacceptable toxicity

Primary Endpoint:

- Investigator-assessed ORR*

Secondary Endpoints:

- DOR, PFS, CBR, OS
- Safety and tolerability

Mandatory sample collection :

- Tumor biopsy (1 Frozen + 3 FFPE)
- Blood (5 to 69 ml)

Exploratory Endpoints:

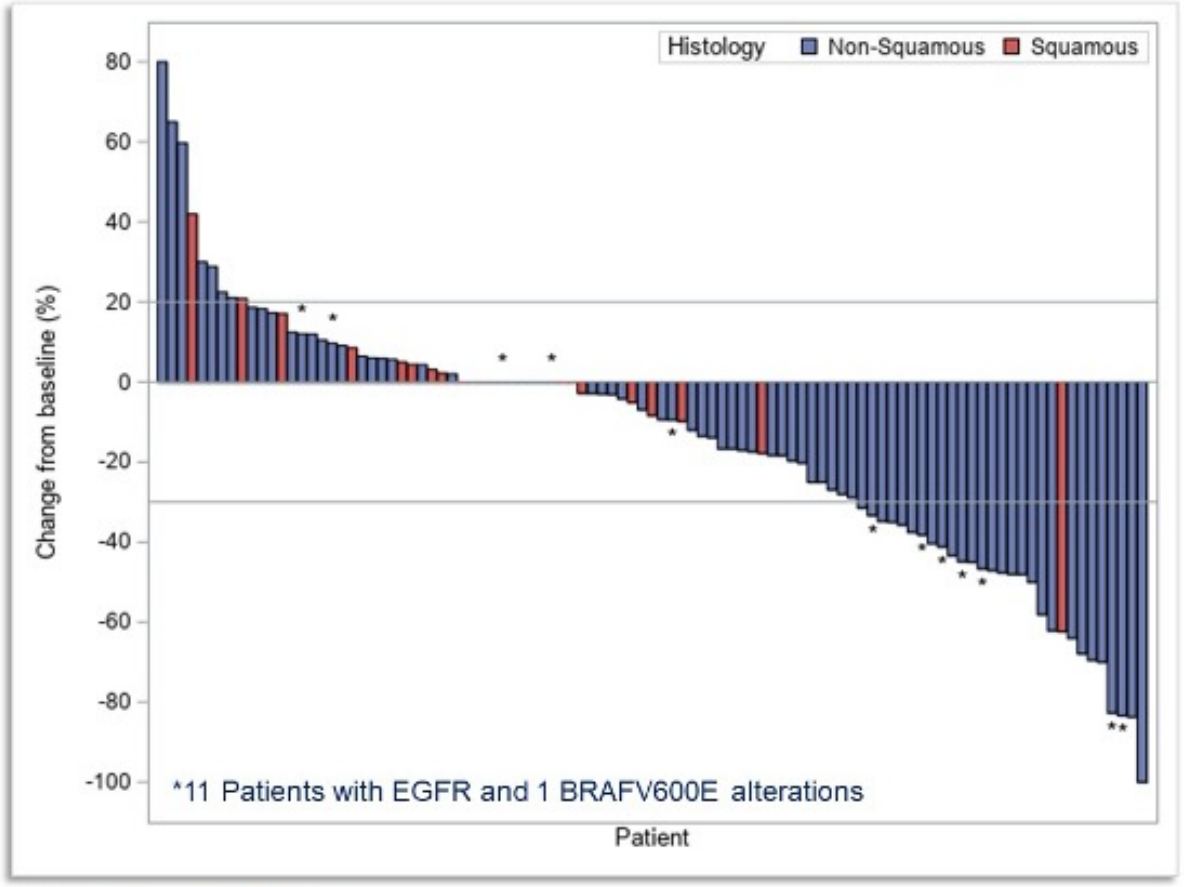
- Predictors of response/resistance
- Dynamics of TROP2 expression before and after treatment
- CTCs levels during treatment

ECOG PS: Eastern Cooperative Oncology Group Performance Status, FFPE: Formalin-Fixed Paraffin-Embedded, Q3W: every 3 weeks, PD: Progressive Disease, C: Cycle, D: Day , EOT: End of Treatment; ORR: Objective Response Rate, DOR: Duration of Response, CBR: Clinical Benefit Rate, CTCs: Circulating Tumor Cells

** Confirmed ORR as per RECIST V1.1 assessment every 6 weeks until objective progressive disease*

Planchard D et al. ASCO 2024;Abstract 8501.

ICARUS-LUNG01: Objective Response Rates with Dato-DXd for Previously Treated Advanced NSCLC



Overall population, N=100	
Confirmed ORR[a] , % [95%CI]	26.0 [17.4 ; 34.6]
DOR, median (months) [95%CI]	7.0 [5.5 ; 11.9]
CBR[b], % [95%CI]	36 [26.6 ; 45.4]

ORR by histology (N=100)/genomic alterations (N=85)		
ORR by histology, % [95%CI]	NSQ (N=82) 30.5 [20.8 ; 41.6]	SCC (N=18) 5.6 [0.14 ; 27.3]
ORR by EGFR, BRAF mut[c], % [95%CI]	Present (N=12) 50.0 [21.1 ; 78.9]	Absent (N=73) 23.2 [14.2 ; 34.7]

H0 : p0 ≤10% is rejected, p value<.0001

KRAS mut[d] (N=11) ORR: 63.6% [30.8; 89.1%]
KRAS wt (N=74) ORR: 21.6% [12.9; 32.7%]

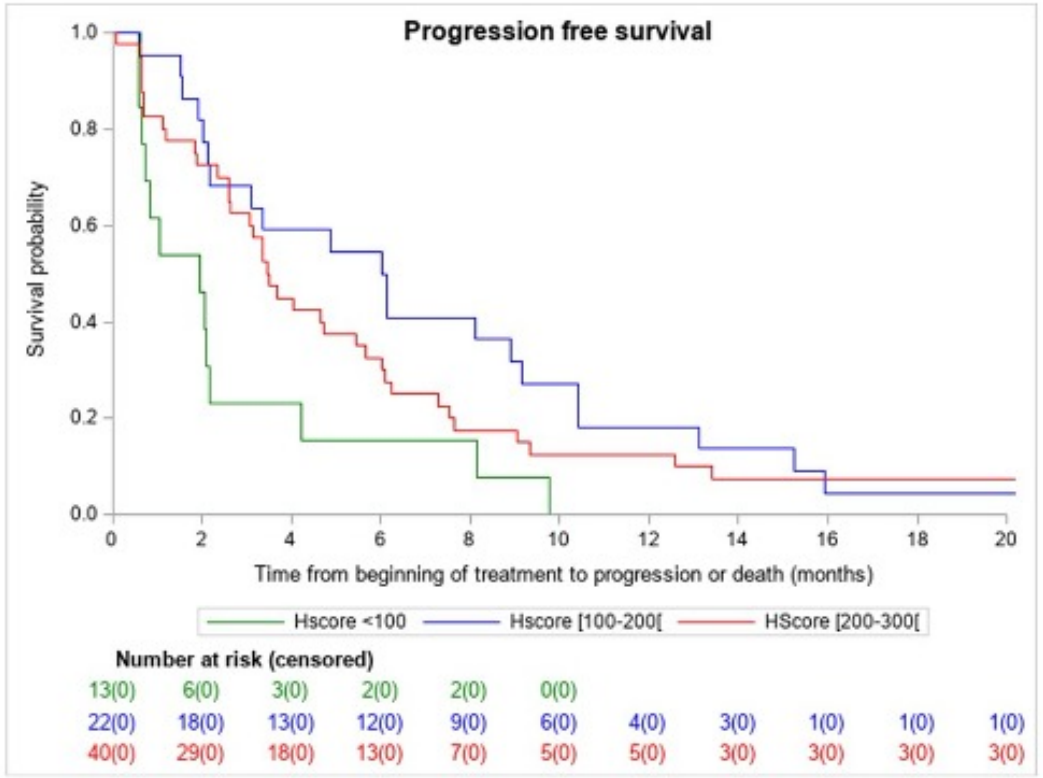
NSQ: Non Squamous Cell Carcinoma

[a]Confirmed ORR; clopper-Pearson (Exact) method was used for confidence interval; [b]Defined as the presence of ≥ 1 partial or complete response, or a stable disease for >6 months under treatment, [c]11 EGFR: exon 19, 20, 21; 1 BRAFV600E; [d]KRAS G12C (n=7)

CBR = clinical benefit rate; NSQ = nonsquamous; SCC = squamous cell carcinoma

Planchard D et al. ASCO 2024;Abstract 8501.

ICARUS-LUNG01: TROP2 Expression and PFS with Dato-DXd for Previously Treated Advanced NSCLC



TROP2 (H-score)*	<100 (N = 13)	100-200 (N = 22)	≥200 (N = 40)
Median PFS, months [95% CI]	**2.0** [0.7 ; 2.2]	**6.1** [2.1 ; 9.2]	**3.5** [2.6 ; 5.5]
HR** [95% CI]	**ref**	**0.37** [0.18-0.75]	**0.50** [0.26-0.94]

TROP2 (EPR20043) FLA IHC; H-Score: autocalculation of tumor cells staining intensity in the membrane compartment= (1[MEMBRANE 1+]) + (2*[MEMBRANE 2+]) + (3*[MEMBRANE 3+])

**p value = 0.02

Patients with a wide range of **TROP2 expression** may benefit from Dato-DXd §

§ No statistically significant association with ORR

Of the 78 patients with H-Score available at baseline, 3 were omitted due to lack of tumor cells (% of tumor cells < 10%).

Planchard D et al. ASCO 2024;Abstract 8501.

MADRID 2023 ESMO congress

Abstract 1314MO

TROPION-Lung05: Datopotamab deruxtecan (Dato-DXd) in previously treated non-small cell lung cancer with actionable genomic alterations

Luis Paz-Ares,[1] Myung-Ju Ahn,[2] Aaron Lisberg,[3] Satoru Kitazono,[4] Byoung Chul Cho,[5] George Blumenschein Jr,[6] Elaine Shum,[7] Elvire Pons Tostivint,[8] Yasushi Goto,[9] Kiyotaka Yoh,[10] Rebecca Heist,[11] Paul Baas,[12] David Planchard,[13] Maurice Pérol,[14] Enriqueta Felip,[15] Wu-Chou Su,[16] Hong Zebger-Gong,[17] Lan Lan,[18] Chelsea Liu,[18] Jacob Sands[19]

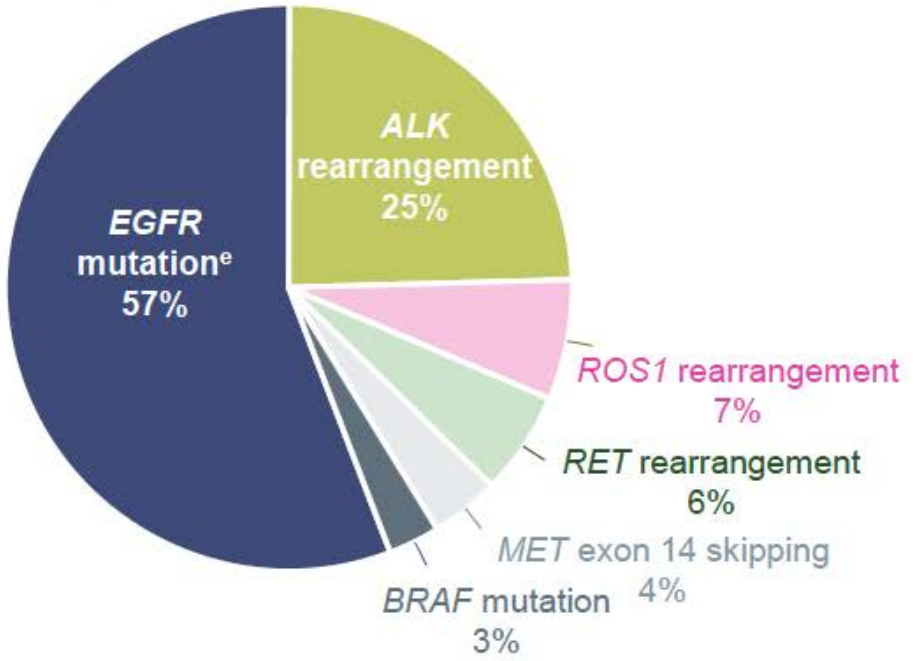
[1]Hospital Universitario 12 de Octubre, Madrid, Spain; [2]Samsung Medical Center, Seoul, South Korea; [3]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [4]The Cancer Institute Hospital of JFCR, Tokyo, Japan; [5]Severance Hospital, Seoul, South Korea; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]NYU Langone Health Perlmutter Cancer Center, New York, NY, USA; [8]University Hospital of Nantes, Nantes, France; [9]National Cancer Center Hospital, Tokyo, Japan; [10]National Cancer Center Hospital East, Kashiwa, Japan; [11]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [12]The Netherlands Cancer Institute, Amsterdam, the Netherlands; [13]Gustave Roussy, Villejuif, France; [14]Centre Léon Bérard, Lyon, France; [15]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [16]National Cheng Kung University Hospital, Tainan, Taiwan; [17]Daiichi Sankyo Europe GmbH, Munich, Germany; [18]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [19]Dana-Farber Cancer Institute, Boston, MA, USA

RTP Year in Review 2024

TROPION-Lung05: Patient Characteristics and Disposition

Demographic characteristics	Dato-DXd (N=137)
Median age (range), years	60 (29-79)
Female, n (%)	83 (61)
Histology, n (%)	
Adenocarcinoma	130 (95)
History of brain metastasis, n (%)[a]	70 (51)
Median prior lines of therapy for adv/met disease	3
Prior lines of therapy, n (%)	137 (100)
≥3 prior lines of therapy for adv/met disease	98 (72)
Prior platinum chemotherapy	137 (100)
Prior anti–PD-1/anti–PD-L1 immunotherapy	49 (36)
≥2 prior lines of targeted therapies for indicated genomic alteration	82 (60)

Relative Frequency of Genomic Alterations[b-d]



Disposition

At the time of data cutoff (December 14, 2022):

- Median (range) treatment duration was 4 (1-21) months
- 60 participants (44%) were ongoing in study
- 20 participants (15%) were ongoing on study treatment

adv/met, advanced/metastatic; Dato-DXd, datopotamab deruxtecan; PD-1, programmed cell death 1 protein; PD-L1, programmed cell death 1 ligand 1.

[a]Patients with clinically inactive brain metastases and patients with treated brain metastases who are no longer symptomatic, require no treatment with corticosteroids or anticonvulsants, and have recovered from radiotherapy may be included in the study. [b]Patients whose tumors harbor *KRAS* mutations, in the absence of the genomic alterations *EGFR, ALK, ROS1, NTRK, BRAF, MET* exon 14 skipping, and *RET*, were excluded from the study. [c]Three patients had tumors with *MET* amplification. [d]Patients had co-occurring alteration types; thus, percentages do not sum to 100%. [e]Protocol requires enrollment of ≈50% of patients with *EGFR*-mutated tumors, among whom 80% should have received prior osimertinib.

Paz-Ares L et al. ESMO 2023;Abstract 1314MO.

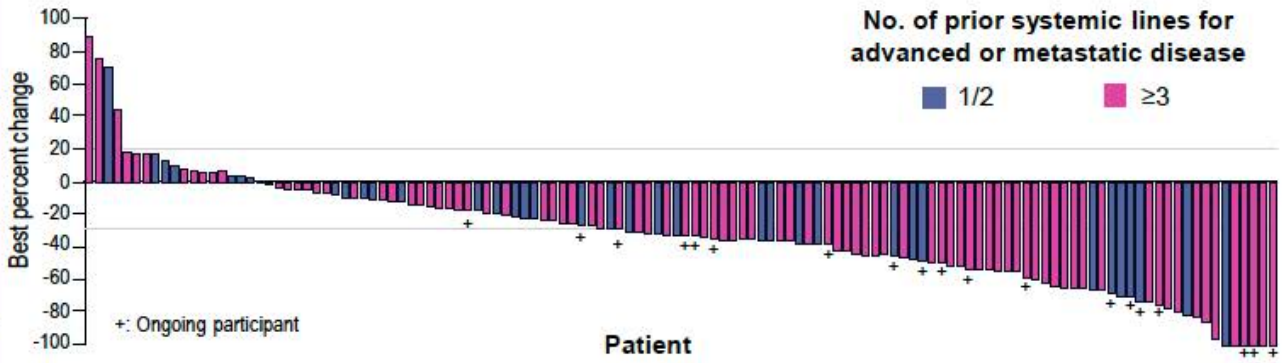
TROPION-Lung05: Efficacy Summary

Response per BICR	All treated patients (N=137)	Patients with *EGFR* mutations (N=78)	Patients with *ALK* rearrangement (N=34)
ORR confirmed, n (%) [95% CI][a]	49 (35.8) [27.8-44.4]	34 (43.6) [32.4-55.3]	8 (23.5) [10.7-41.2]
Median DOR (95% CI), months	7.0 (4.2-9.8)	7.0 (4.2-10.2)	7.0 (2.8-8.4)
DCR confirmed, n (%) [95% CI][a]	108 (78.8) [71.0-85.3]	64 (82.1) [71.7-89.8]	25 (73.5) [55.6-87.1]
Median PFS, (95% CI), months[b]	5.4 (4.7-7.0)	5.8 (5.4-8.3)	4.3 (2.6-6.9)

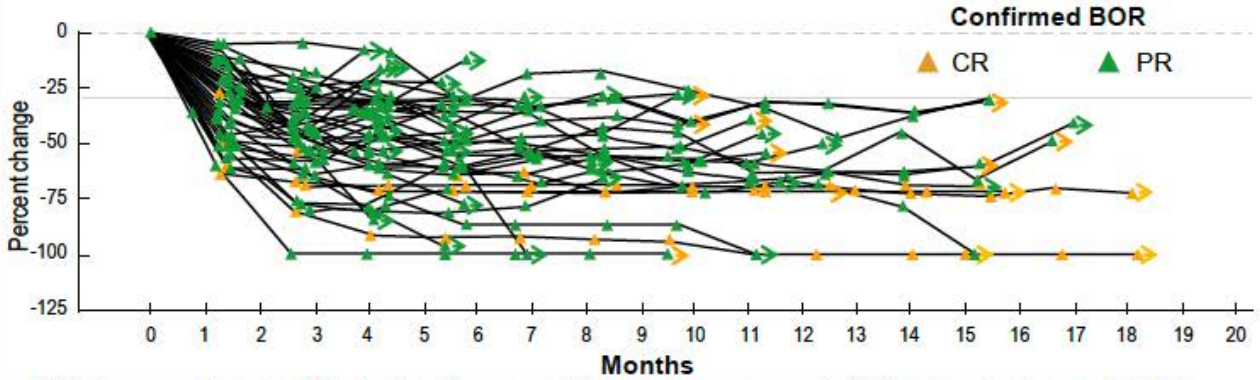
BOR: In the overall population (N=137), 4 patients (3%) achieved a CR and 45 (33%) achieved a PR

***EGFR* subset:** Among patients with sensitizing or T790M mutations (N=68), the ORR was 49.1% in those previously treated with osimertinib

Best Percent Change From Baseline in Sum of Diameters of Target Lesions



Percent Change From Baseline in Sum of Diameters of Target Lesions in Patients With Confirmed CR/PR[c]



BICR, blinded independent central review; BOR, best overall response; CR, complete response; DCR, disease control rate; DOR, duration of response; ORR, objective response rate; PFS, progression-free survival; PR, partial response.

[a]The 2-sided 95% CIs are based on the Clopper-Pearson exact binomial method. [b]Median PFS and PFS probabilities are based on the Kaplan-Meier method. [c]Per BICR.

Paz-Ares L et al. ESMO 2023;Abstract 1314MO.

Abstract # 8593

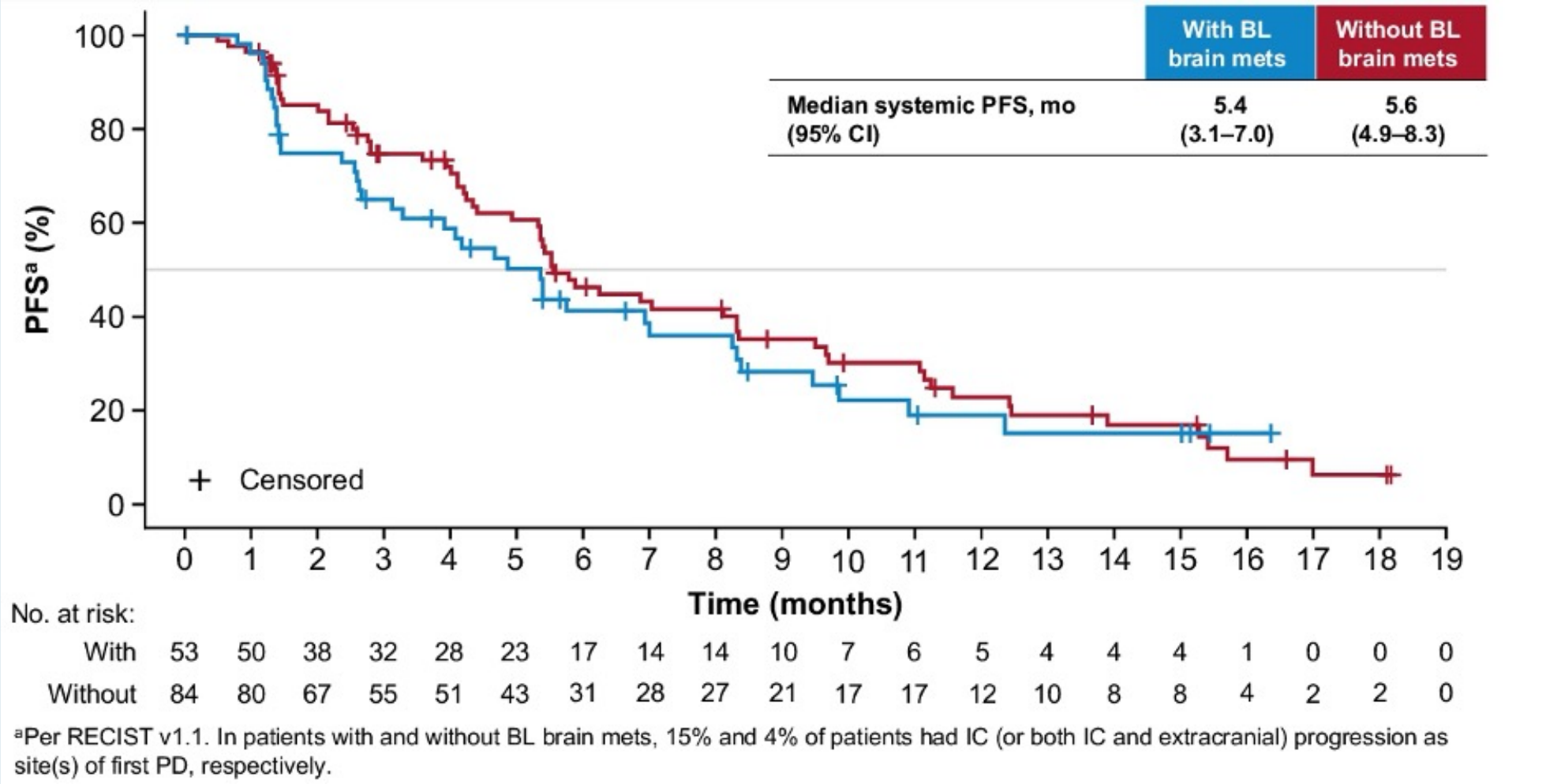
ASCO 2024

Intracranial efficacy of datopotamab deruxtecan in patients with previously treated advanced/metastatic non-small cell lung cancer with actionable genomic alterations: results from TROPION-Lung05

Aaron Lisberg,[1] Myung-Ju Ahn,[2] Satoru Kitazono,[3] Byoung Chul Cho,[4] George Blumenschein Jr,[5] Elaine Shum,[6] Elvire Pons Tostivint,[7] Yasushi Goto,[8] Kiyotaka Yoh,[9] Luis Paz-Ares,[10] Rebecca Heist,[11] Paul Baas,[12] David Planchard,[13,14] Maurice Pérol,[15] Enriqueta Felip,[16] Wu-Chou Su,[17] Hong Zebger-Gong,[18] Lan Lan,[19] Chelsea Liu[19]

[1]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [2]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [3]The Cancer Institute Hospital of JFCR, Tokyo, Japan; [4]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [6]NYU Langone Health Perlmutter Cancer Center, New York, NY, USA; [7]University Hospital of Nantes, Nantes, France; [8]National Cancer Center Hospital, Tokyo, Japan; [9]National Cancer Center Hospital East, Kashiwa, Japan; [10]Hospital Universitario 12 de Octubre, Madrid, Spain; [11]Massachusetts General Hospital Cancer Center, Harvard Medical School, Harvard University, Boston, MA, USA; [12]The Netherlands Cancer Institute, Amsterdam, the Netherlands; [13]Gustave Roussy, Department of Medical Oncology, Thoracic Group, Villejuif, France; [14]Faculty of Medicine, Paris-Saclay University, Paris, France; [15]Centre Léon Bérard, Lyon, France; [16]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [17]National Cheng Kung University Hospital, Tainan, Taiwan; [18]Daiichi Sankyo Europe GmbH, Munich, Germany; [19]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA

TROPION-Lung05: Intracranial PFS in Patients With and Without Baseline Brain Metastases



[a]Per RECIST v1.1. In patients with and without BL brain mets, 15% and 4% of patients had IC (or both IC and extracranial) progression as site(s) of first PD, respectively.

Lisberg A et al. ASCO 2024;Abstract 8593.

Agenda

INTRODUCTION: Risk of Autoimmune Toxicity with Checkpoint Inhibitors

MODULE 1: Immunotherapy in the Neoadjuvant/Adjuvant Setting

MODULE 2: Immunotherapy for Locally Advanced NSCLC

MODULE 3: First-Line Immunotherapy for Metastatic NSCLC

MODULE 4: Novel Agents and Strategies

MODULE 5: Immunotherapy for NSCLC with a Targetable Mutation

MODULE 6: Small Cell Lung Cancer

Immunotherapy for NSCLC with a Targetable Mutation

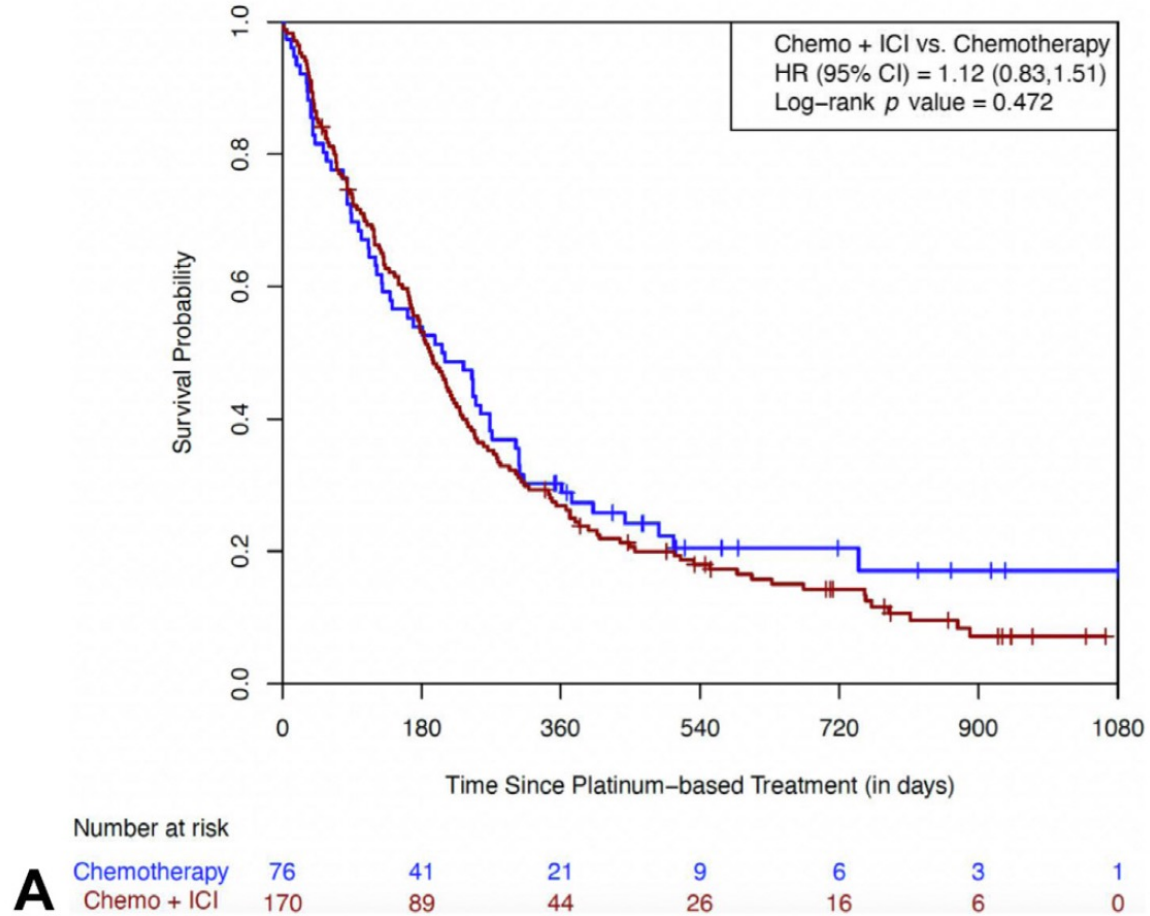
- Benjamin DJ et al. The role of **chemotherapy plus immune checkpoint inhibitors** in **oncogenic-driven NSCLC**: A University of California Lung Cancer Consortium retrospective study. *JTO Clin Res Rep* 2022 October 29;3(12):100427.
- Middleton G et al. A phase II trial of **ceralasertib** and **durvalumab** in advanced NSCLC with and without RAS mutations: Results of **NLMT arm J**. WCLC 2023;Abstract MA06.06.
- Besse B et al. **Biomarker-directed targeted therapy** plus **durvalumab** in advanced non-small-cell lung cancer: A phase 2 umbrella trial. *Nat Med* 2024;30(3):716-29.

The Role of Chemotherapy Plus Immune Checkpoint Inhibitors in Oncogenic-Driven NSCLC: A University of California Lung Cancer Consortium Retrospective Study

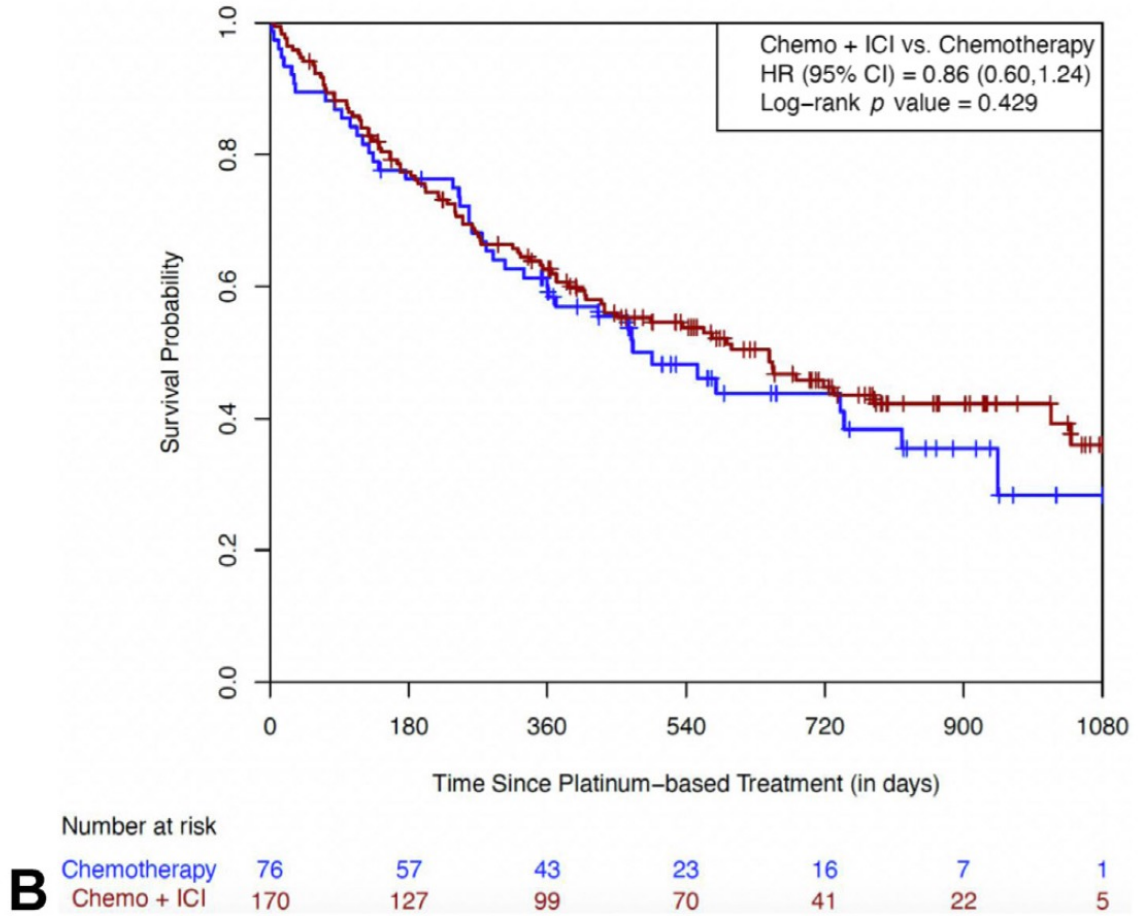
David J. Benjamin, MD,[a,l] Shuai Chen, PhD,[b] Joanna B. Eldredge, MD,[c] Shiruyeh Schokrpur, MD,[d] Debory Li,[e] Zhikuan Quan, MS,[b] Jason W. Chan, MD,[f] Amy L. Cummings, MD,[g] Megan E. Daly, MD,[h] Jonathan W. Goldman, MD,[g] Matthew A. Gubens, MD,[i] Jeremy P. Harris, MD,[j] Mark W. Onaitis, MD,[d,k] Viola W. Zhu, MD, PhD,[a,m] Sandip P. Patel, MD,[d] Karen Kelly, MD[c,n,*]

JTO Clin Res Rep 2022;3(12):100427.

PFS and OS in Study Cohort (n = 246)



A

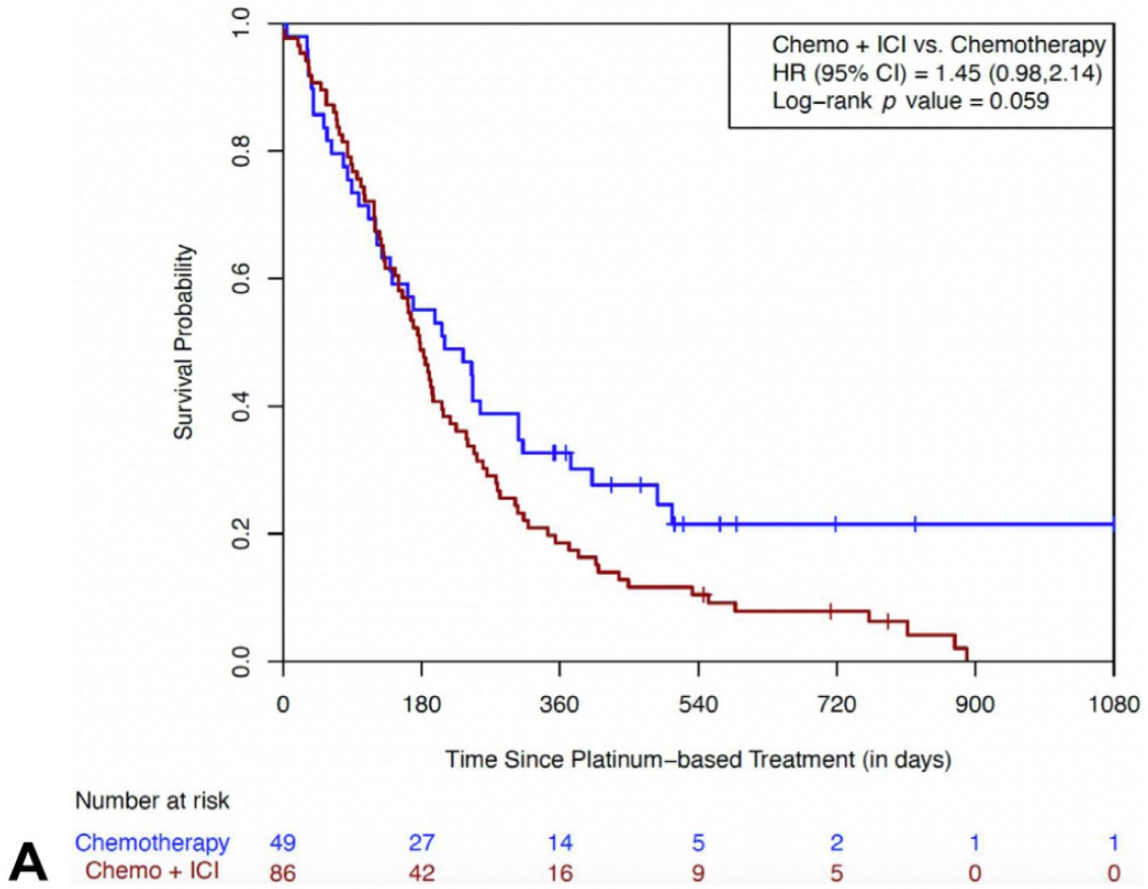


B

Figure 1. (*A*) Progression-free survival in the study cohort. (*B*) Overall survival in the study cohort. Chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; ICI, immune checkpoint inhibitor.

Benjamin DJ et al. *JTO Clin Res Rep* 2022;3(12):100427.

Possible Detriment of Immune Checkpoint Inhibition After EGFR Tyrosine Kinase Inhibitor for NSCLC with EGFR Mutation



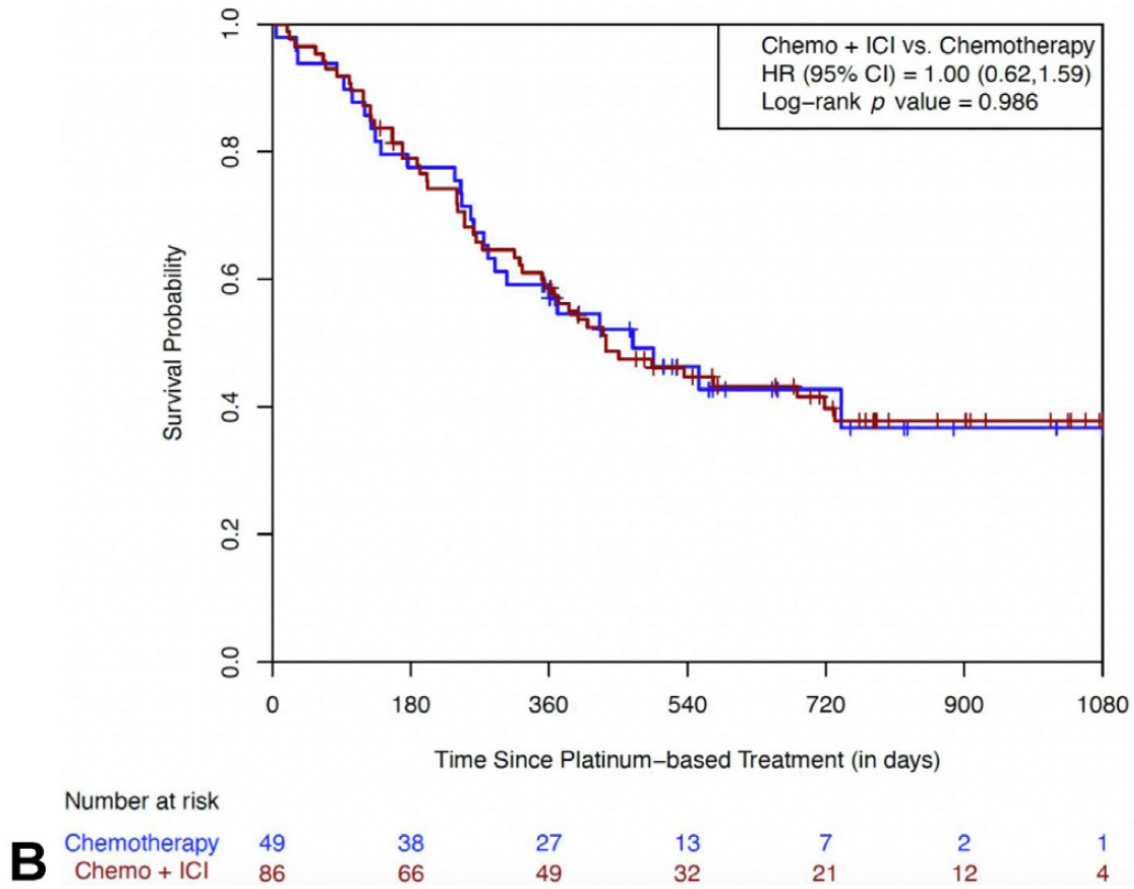


Figure 2. (*A*) Progression-free survival in the *EGFR* subgroup. (*B*) Overall survival in the *EGFR* subgroup. Chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; ICI, immune checkpoint inhibitor.

Benjamin DJ et al. *JTO Clin Res Rep* 2022;3(12):100427.

IASLC
2023 World Conference on Lung Cancer
SEPTEMBER 9-12, 2023 | SINGAPORE

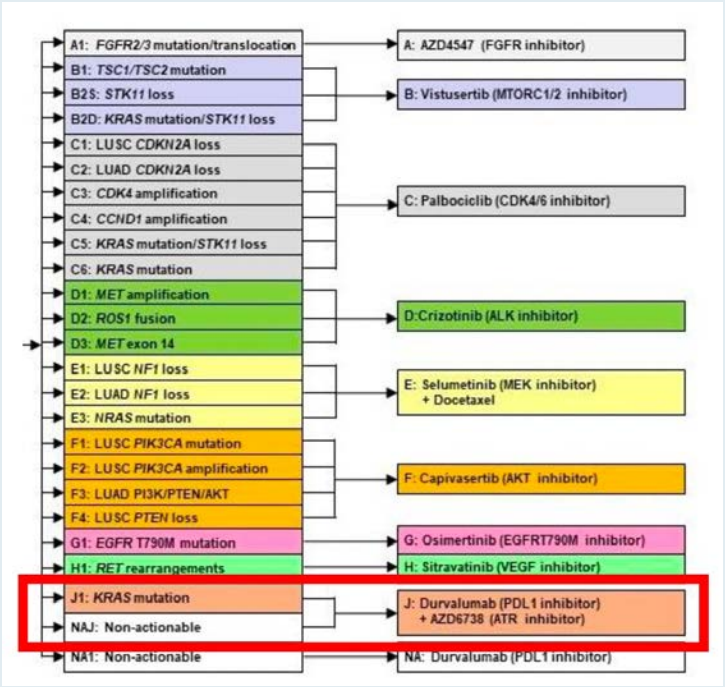
A Phase II Trial of Ceralasertib and Durvalumab in Advanced Non-Small Cell Lung Cancer (NSCLC) with and without RAS Mutations: Results of NLMT Arm J

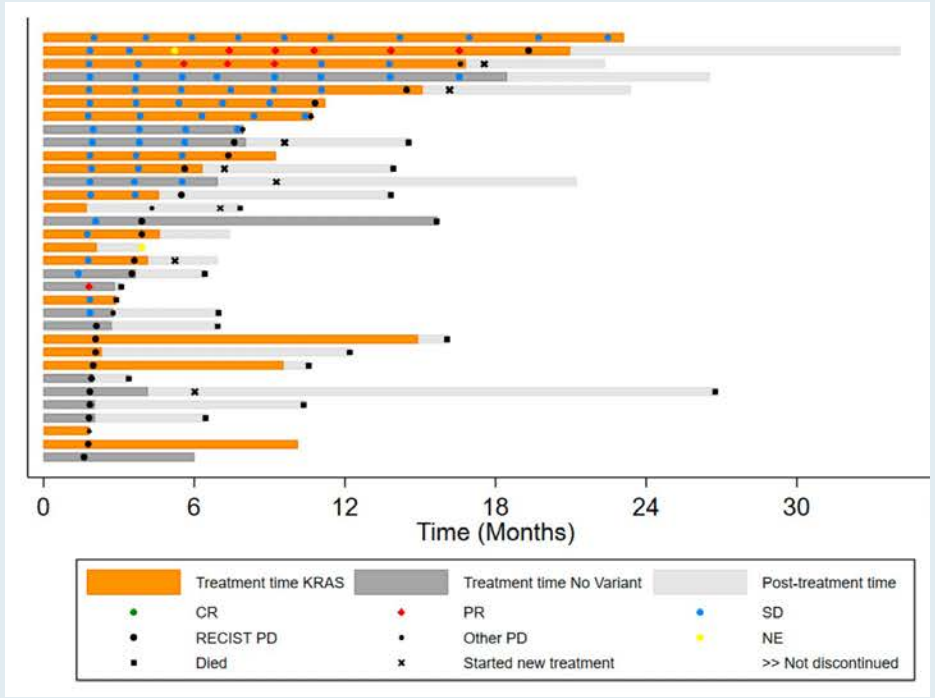
Gary Middleton, Peter Fletcher, Joshua Savage, Manita Mehmi, Alastair Greystoke, Adam Dangoor, Judith Cave, C. Escriu, Paul Shaw, Nicola Steele, Pooja Jain, S. Popat, M. Forster, James Spicer, Nicholas Coupe, Sarah Danson, David Gilligan, Dakshinamoorthy Muthukumar, Gillian Price, Yvonne Summers, Elizabeth Toy, Lucinda Billingham

Cancer Research UK Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom

Sponsor: University of Birmingham
Funders: Cancer Research UK: C11497/A19363, C11497/A22209
Pharmaceutical Industry partner: AstraZeneca

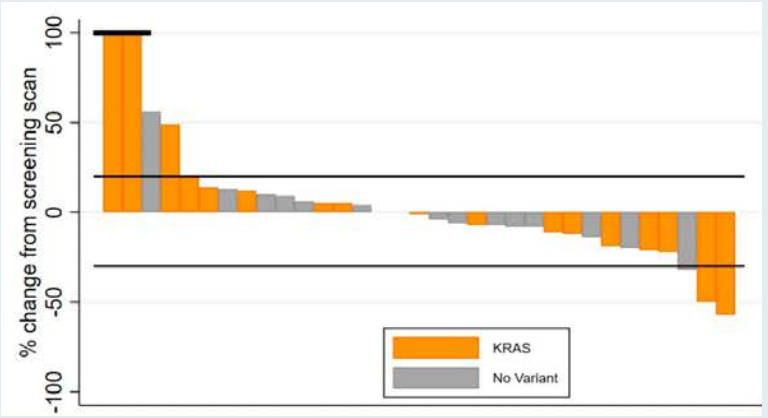
National Lung Matrix Trial Arm J: Response and Survival Among Patients Who Received Prior Immune Checkpoint Blockade (ICB)

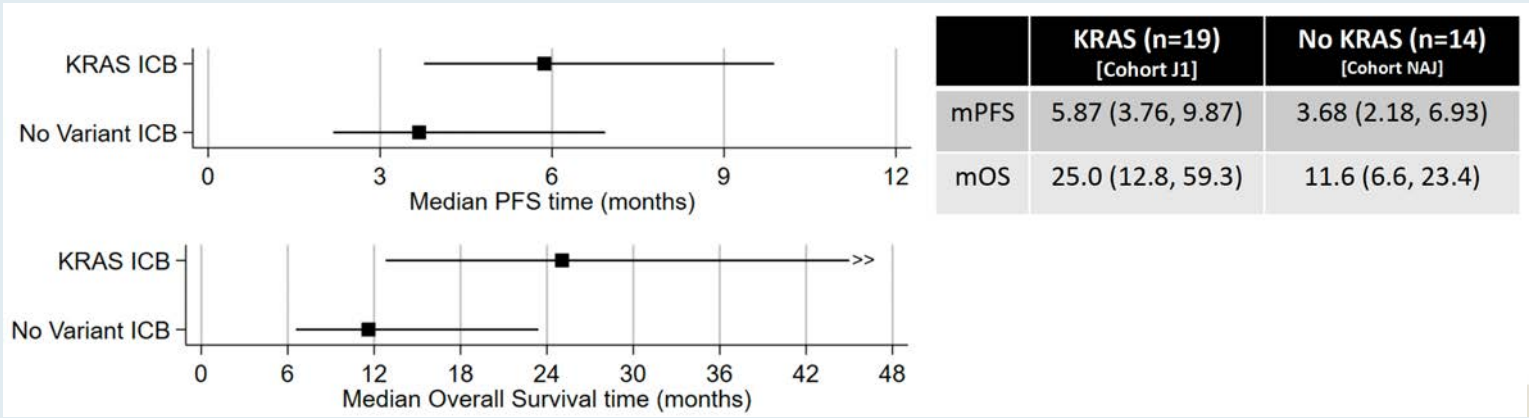




	KRAS (n=19) [Cohort J1]	No KRAS (n=14) [Cohort NAJ]
DCB rate Prob(> 30%)	39.7% (20.3, 61.6) 0.82	30.5% (11.8, 55.1) 0.52
OR rate Prob(>30%)	13.1% (3.2, 31.7) 0.04	4.5% (0.2, 21.8) < 0.01

DCB = durable clinical benefit; OR = objective response





	KRAS (n=19) [Cohort J1]	No KRAS (n=14) [Cohort NAJ]
mPFS	5.87 (3.76, 9.87)	3.68 (2.18, 6.93)
mOS	25.0 (12.8, 59.3)	11.6 (6.6, 23.4)

Middleton G et al. WCLC 2023;Abstract MA06.06.

nature medicine

Article

https://doi.org/10.1038/s41591-024-02808-y

Biomarker-directed targeted therapy plus durvalumab in advanced non-small-cell lung cancer: a phase 2 umbrella trial

Benjamin Besse[1], Elvire Pons-Tostivint[2], Keunchil Park[3,32], Sylvia Hartl[4,33], Patrick M. Forde[5], Maximilian J. Hochmair[6], Mark M. Awad[7], Michael Thomas[8], Glenwood Goss[9], Paul Wheatley-Price[9], Frances A. Shepherd[10], Marie Florescu[11], Parneet Cheema[12], Quincy S. C. Chu[13], Sang-We Kim[14], Daniel Morgensztern[15], Melissa L. Johnson[16], Sophie Cousin[17], Dong-Wan Kim[18], Mor T. Moskovitz[19,34], David Vicente[20], Boaz Aronson[21], Rosalind Hobson[22], Helen J. Ambrose[23], Sajan Khosla[24], Avinash Reddy[25], Deanna L. Russell[26], Mohamed Reda Keddar[27], James P. Conway[28], J. Carl Barrett[26], Emma Dean[29], Rakesh Kumar[30], Marlene Dressman[30], Philip J. Jewsbury[29], Sonia Iyer[26], Simon T. Barry[29], Jan Cosaert[29] & John V. Heymach[31]

Nat Med 2024;30:716-29

HUDSON Study: Treatment Efficacy with Durvalumab/Ceralasertib and with Other Regimens in Previously Treated Advanced NSCLC

Efficacy parameter	Durvalumab-ceralasertib, *n* = 79	Durvalumab plus olaparib, danvatirsen or oleclumab, *n* = 189
Objective response rate, n (%)	11 (13.9)	5 (2.6)
Partial response rate, n (%)	11 (13.9)	5 (2.6)
Stable disease ≥35 days, n (%)[a]	37 (46.8)	89 (47.1)
Unconfirmed partial or complete response, n (%)	3 (3.8)	4 (2.1)
Progression, n (%)	20 (25.3)	91 (48.1)
RECIST disease progression, n (%)	17 (21.5)	70 (37.0)
Died, n (%)	3 (3.8)	21 (11.1)
Not evaluable, n (%)	11 (13.9)	4 (2.1)
Disease control at 12 weeks, n (%)	40 (50.6)	61 (32.3)
Disease control at 24 weeks, n (%)	28 (35.4)	30 (15.9)
PFS, median (80% CI), months	5.8 (4.6-7.4)	2.7 (1.8-2.8)
OS, median (80% CI), months	17.4 (14.1-20.3)	9.4 (7.5-10.6)

[a]≥40 days for durvalumab plus danvatirsen or ceralasertib.

CI, confidence interval; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumours.

Besse B et al. *Nat Med* 2024;30:716-29.

Agenda

INTRODUCTION: Risk of Autoimmune Toxicity with Checkpoint Inhibitors

MODULE 1: Immunotherapy in the Neoadjuvant/Adjuvant Setting

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MODULE 4: Novel Agents and Strategies

MODULE 5: Immunotherapy for NSCLC with a Targetable Mutation

MODULE 6: Small Cell Lung Cancer

Durvalumab Consolidation for Limited-Stage SCLC

- Spigel DR et al. **ADRIATIC: Durvalumab** (D) as **consolidation** treatment (tx) for patients (pts) with **limited-stage small-cell lung cancer** (LS-SCLC). ASCO 2024;Abstract LBA5.

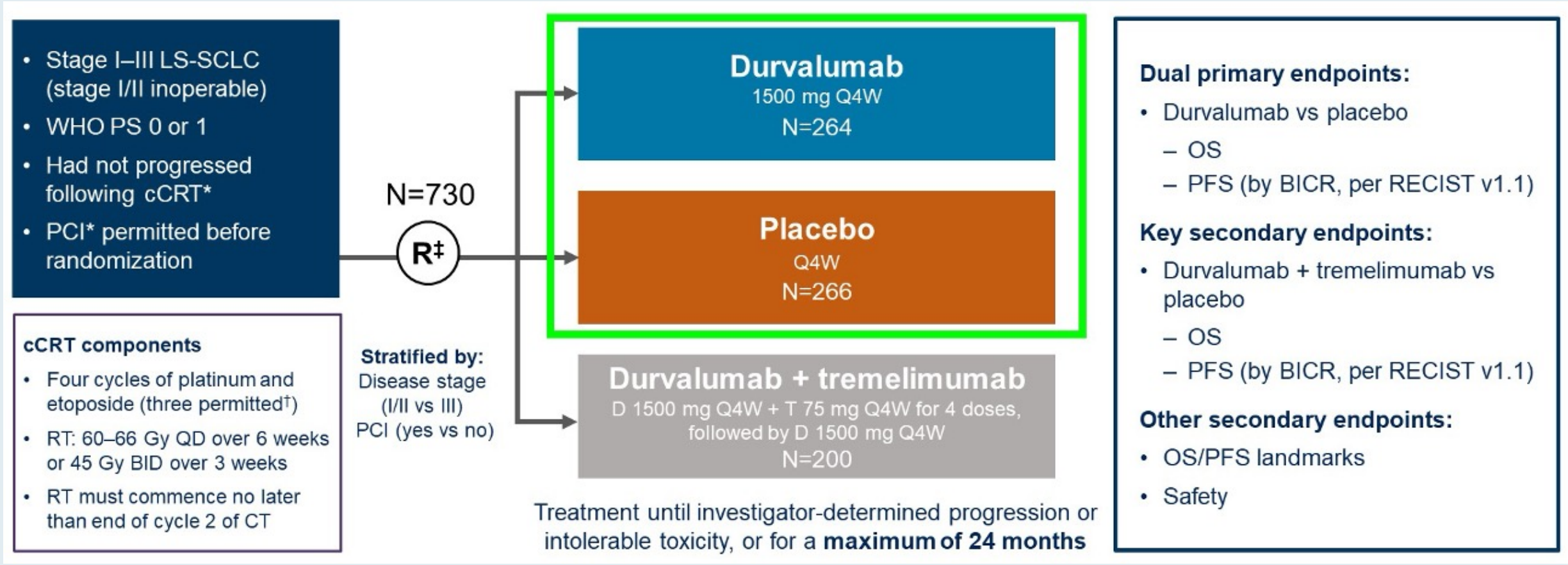
2024 ASCO ANNUAL MEETING

Abstract LBA5

ADRIATIC: durvalumab as consolidation treatment for patients with limited-stage small-cell lung cancer (LS-SCLC)

David R. Spigel, Ying Cheng, Byoung Chul Cho, Konstantin Laktionov, Jian Fang, Yuanbin Chen, Yoshitaka Zenke, Ki Hyeong Lee, Qiming Wang, Alejandro Navarro, Reyes Bernabe, Eva Buchmeier, John Wen-Cheng Chang, Isamu Okamoto, Sema Sezgin Goksu, Andrzej Badzio, Bethany Gill, Hema Gowda, Haiyi Jiang, Suresh Senan

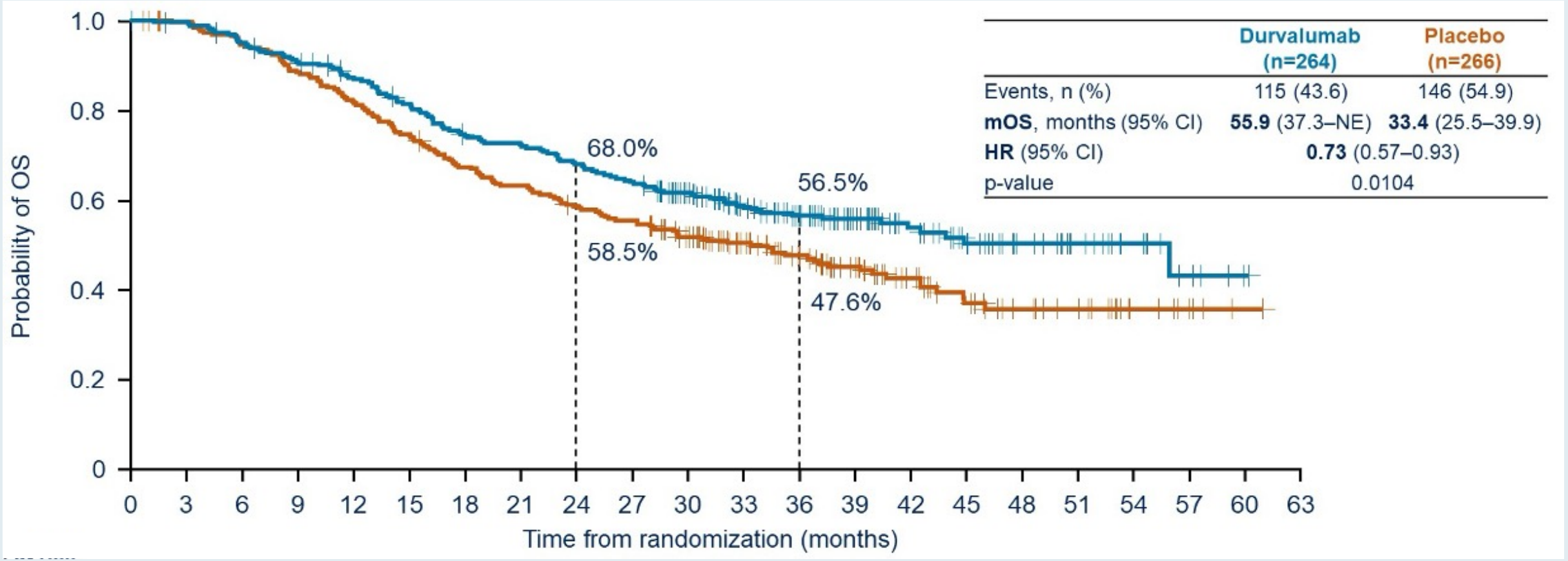
ADRIATIC: Phase III Study Design



cCRT = concurrent chemoradiation therapy; PCI = prophylactic cranial irradiation; RT = radiation therapy

Spigel DR et al. ASCO 2024;Abstract LBA5.

ADRIATIC: Overall Survival (Dual Primary Endpoint)

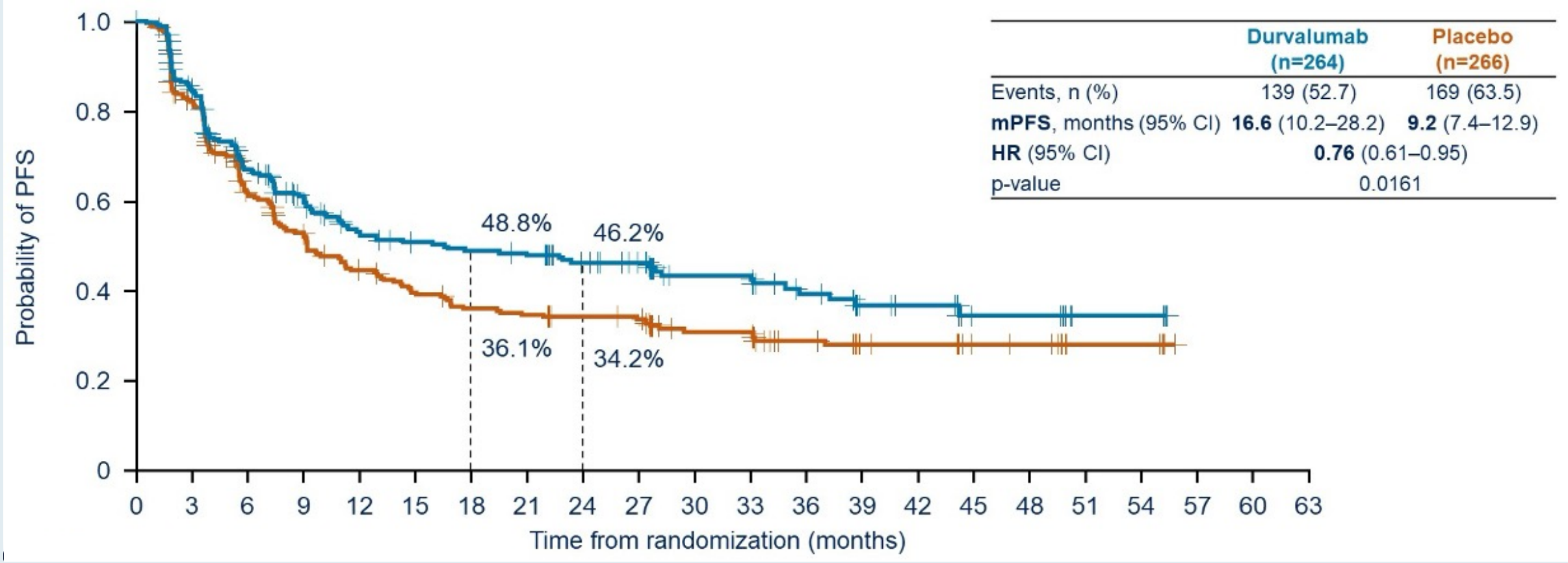


	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

mOS = median overall survival

Spigel DR et al. ASCO 2024;Abstract LBA5.

ADRIATIC: Progression-Free Survival (Dual Primary Endpoint)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	139 (52.7)	169 (63.5)
mPFS, months (95% CI)	**16.6** (10.2–28.2)	**9.2** (7.4–12.9)
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

mPFS = median progression-free survival

Spigel DR et al. ASCO 2024;Abstract LBA5.

ADRIATIC: Author Conclusions

- **Durvalumab as consolidation treatment after cCRT demonstrated statistically significant and clinically meaningful improvement in OS and PFS compared with placebo in patients with LS-SCLC**
  - **OS HR 0.73** (95% CI 0.57–0.93), p=0.0104; mOS 55.9 (95% CI 37.3–NE) vs 33.4 (95% CI 25.5–39.9) months
  - **PFS HR 0.76** (95% CI 0.61–0.95), p=0.0161; mPFS 16.6 (95% CI 10.2–28.2) vs 9.2 (95% CI 7.4–12.9) months
  - Treatment benefit was generally consistent across predefined patient subgroups for both OS and PFS
- **Durvalumab consolidation treatment for up to 2 years was well tolerated, and safety findings were consistent with the known safety profile of durvalumab monotherapy in the post-cCRT setting**

Consolidation durvalumab will become the new standard of care for patients with LS-SCLC who have not progressed after cCRT

Spigel DR et al. ASCO 2024;Abstract LBA5.

Anti-PD-1/PD-L1-Based Therapies for Extensive-Stage SCLC

- Paz-Ares L et al. **Durvalumab ± tremelimumab + platinum-etoposide** in **extensive-stage SCLC (CASPIAN)**: Outcomes by PD-L1 expression and tissue tumor mutational burden. *Clin Cancer Res* 2024 February 16;30(4):824-35.
- Liu SV et al. Five-year survival in patients with **ES-SCLC** treated with **atezolizumab** in **IMpower133: IMbrella A** extension study results. WCLC 2023;Abstract OA01.04.

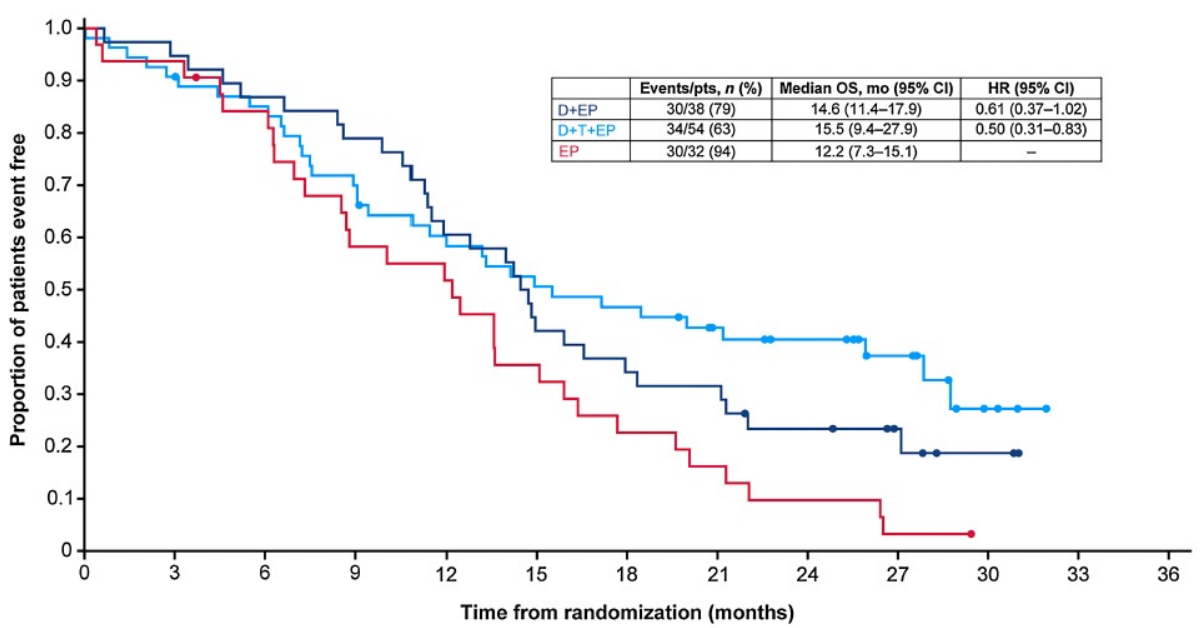
Durvalumab ± Tremelimumab + Platinum-Etoposide in Extensive-Stage Small Cell Lung Cancer (CASPIAN): Outcomes by PD-L1 Expression and Tissue Tumor Mutational Burden

Luis Paz-Ares[1], Marina Chiara Garassino[2,3], Yuanbin Chen[4], Niels Reinmuth[5], Katsuyuki Hotta[6], Artem Poltoratskiy[7], Dmytro Trukhin[8], Maximilian J. Hochmair[9], Mustafa Özgüroğlu[10], Jun Ho Ji[11], Galina Statsenko[12], Nikolay Conev[13], Igor Bondarenko[14], Libor Havel[15], György Losonczy[16], Mingchao Xie[17], Zhongwu Lai[18], Nadia Godin-Heymann[19], Helen Mann[19], Haiyi Jiang[18], Yashaswi Shrestha[18], and Jonathan W. Goldman[20]

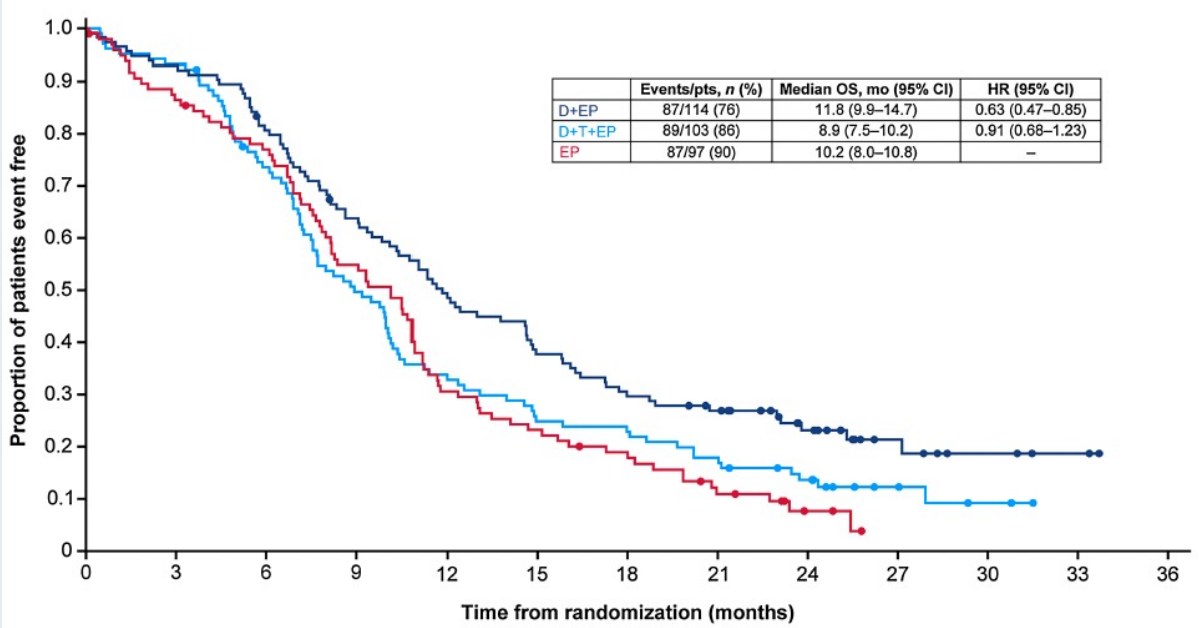
Clin Cancer Res 2024 February 16;30(4):824-35

CASPIAN: OS Analysis by Subgroup

PD-L1 TC or IC ≥1%



PD-L1 TC and IC <1%



Author Conclusions: *These results support treatment benefit with first-line durvalumab plus EP in patients with ES-SCLC irrespective of biomarker status; there was no evidence that either PD-L1 expression or tTMB can be used to select patients or predict outcomes with durvalumab plus EP in this disease setting. However, our observations in the durvalumab plus tremelimumab plus EP arm suggest that PD-L1 expression may yet prove to be a useful biomarker for combined treatment with PD-(L)1 and CTLA-4 inhibition, although this requires confirmation with a prospective and independent dataset.*

TC = tumor cell; IC = immune cell; ES-SCLC = extensive-stage small cell lung cancer

Paz-Ares L et al. *Clin Cancer Res* 2024 February 16;30(4):824-35.

Novel Agents and Strategies for Patients with SCLC

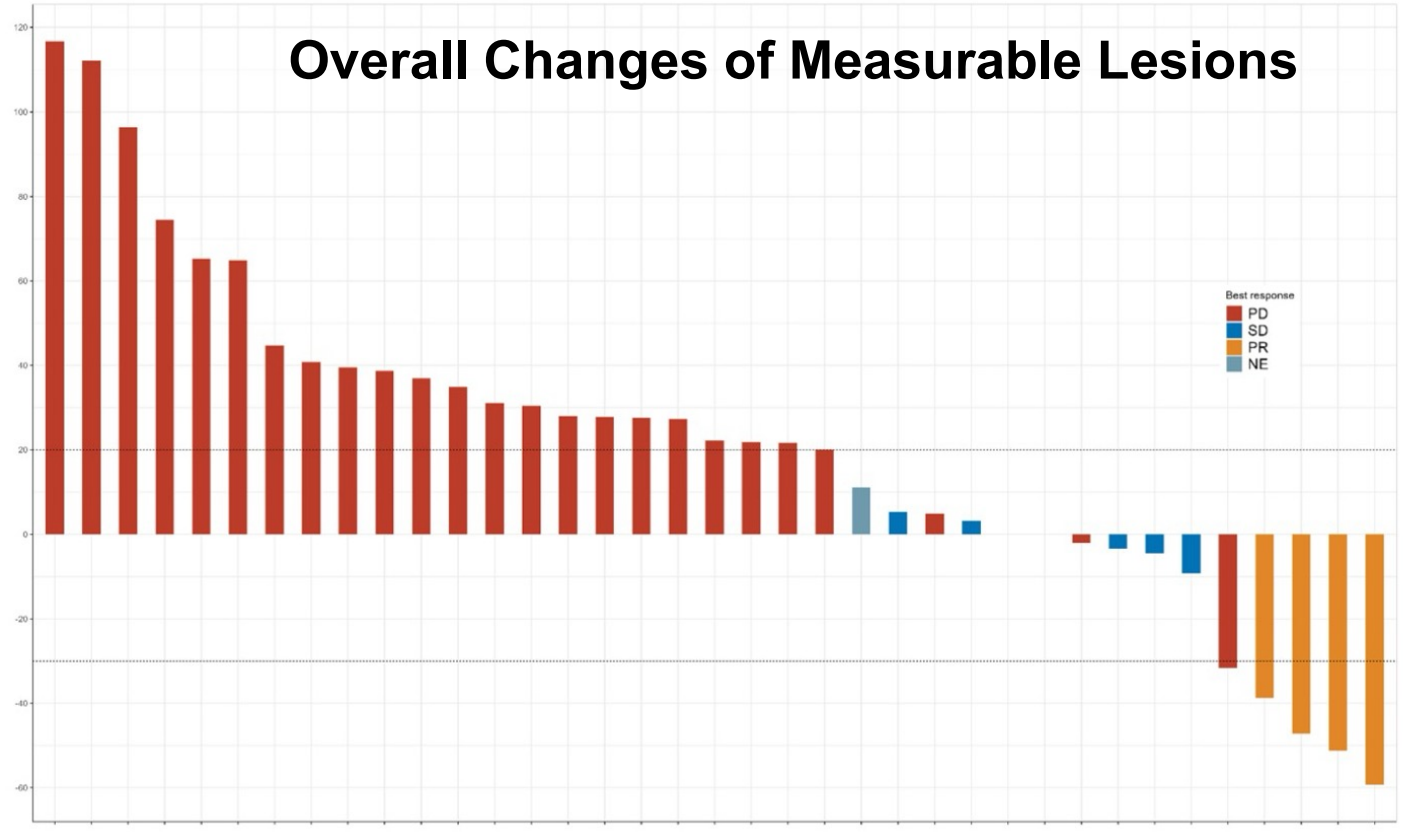
- Lee S-H et al. A phase II, open-label, combination therapy of **durvalumab** and **ceralasertib** in relapsed and refractory **small cell lung cancer (SUKSES-N4**). ASCO 2024;Abstract 8104.
- Johnson M et al. **Ifinatamab deruxtecan (I-DXd; DS-7300)** in patients with **refractory SCLC:** A subgroup analysis of a phase 1/2 study. WCLC 2023;Abstract OA05.05.
- Rudin C et al. A phase II study of **ifinatamab deruxtecan (I-DXd; DS-7300**) in patients with previously treated **ES-SCLC**. WCLC 2023;Abstract P2.16-06.
- Dowlati A et al. **Sacituzumab govitecan** as **second-line** treatment for **extensive SCLC**: **Preliminary results** from the phase II **TROPiCS-03 basket trial**. ESMO 2023;Abstract 1990MO.
- Paz-Ares L et al. **Tarlatamab**, a first-in-class DLL3-targeted bispecific T-cell engager, in **recurrent SCLC**: An open-label, phase I study. *J Clin Oncol* 2023;41(16):2893-903.
- Paz-Ares L et al. **Tarlatamab** for patients with **previously treated SCLC**: **Primary analysis** of the phase II **DeLLphi-301 study**. ESMO 2023;Abstract LBA92.

A Phase II, Open-Label, Combination Therapy of Durvalumab and Ceralasertib in Relapsed and Refractory Small Cell Lung Cancer (SUKSES-N4)

Lee S-H et al.

ASCO 2024;Abstract 8104.

SUKSES-N4: A Phase II Study of Durvalumab with Ceralasertib for Relapsed/Refractory SCLC



Measure	N (%)
Number of patients	42
Median follow-up duration	7.16 (6.07-13.0)
Best objective response	
Complete response	0
Partial response	4 (9.5)
Stable disease	7 (16.7)
Progression	29 (69.0)
Not evaluable	2 (4.8)
ORR (%)	9.5
DCR (%)	26.2
Number of PFS events	40 (95.2)
Median PFS, months (95% CI)	1.64 (1.61-1.97)
Number of OS events	37 (88.1)
Median OS, months (95% CI)	7.16 (6.07-13.9)

Lee S-H et al. ASCO 2024;Abstract 8104.

SUKSES-N4: Safety Profile of Durvalumab and Ceralasertib for Relapsed/Refractory SCLC

Number of patients (count with the highest grade)			
	Grade 1 or 2	Grade 3	Grade 4
Among 30 patients with IP related AE	14	6	10

IP related adverse event n (%) (Observed at least 2 or more pts)	Grade 1 or 2	Grade 3	Grade 4
Thrombocytopenia	4 (9.5)	3 (7.1)	9 (21.4)
Anemia	2 (4.8)	3 (7.1)	-
Neutropenia	-	1 (2.4)	3 (7.1)
Increased lipase	-	-	1 (2.4)
Asthenia	2 (4.8)	2 (4.8)	-
Pneumonitis	-	2 (4.8)	-
Hemoptysis	-	1 (2.4)	-
Nausea	11 (@6.2)	-	-
Skin rash	6 (14.3)	-	-
Anorexia	6 (14.3)	-	-
Dizziness	4 (9.5)	-	-
Headache	4 (9.5)	-	-
Itching	3 (7.1)	-	-
Vomiting	3 (7.1)	-	-
Hypothyroidism	3 (7.1)	-	-
Fatigue	2 (4.8)	-	-

Lee S-H et al. ASCO 2024;Abstract 8104.

FDA Grants Accelerated Approval to Tarlatamab for Extensive-Stage Small Cell Lung Cancer

Press Release: May 16, 2024

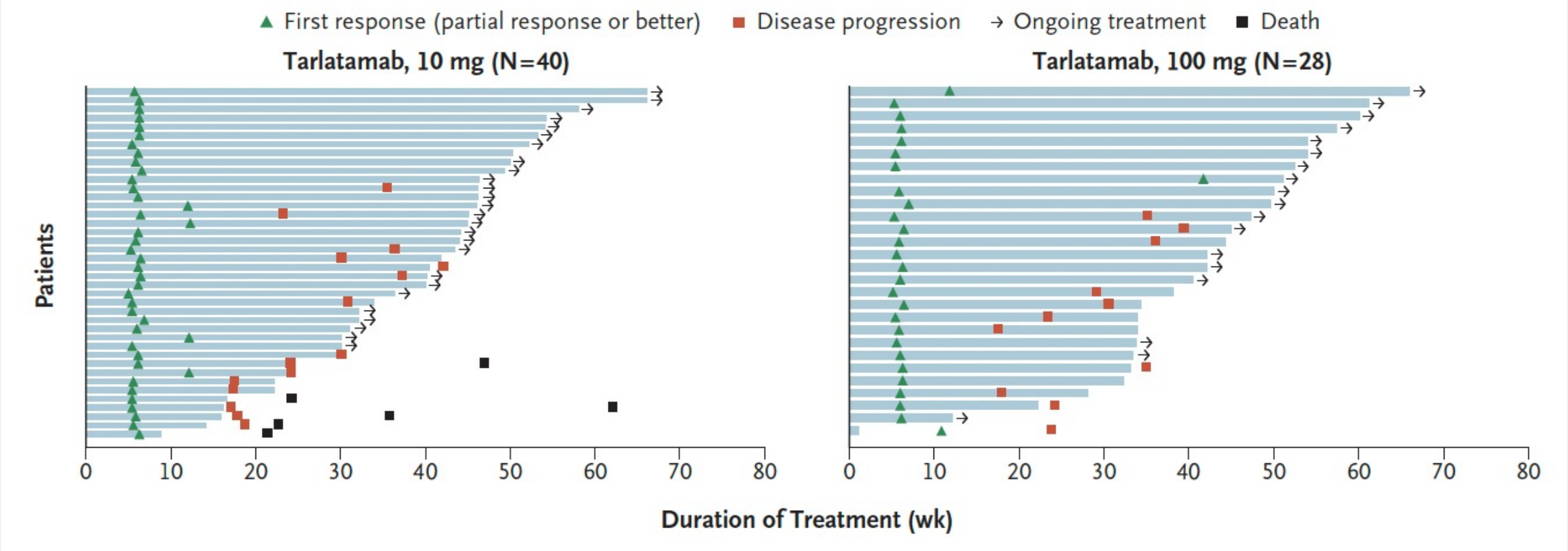
"On May 16, 2024, the Food and Drug Administration granted accelerated approval to tarlatamab-dlle for extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy. The major efficacy outcome measures were overall response rate (ORR) per RECIST 1.1 and duration of response (DOR), as assessed by blinded independent central review. ORR was 40% and median DOR was 9.7 months.

The prescribing information for tarlatamab includes a Boxed Warning for serious or life-threatening cytokine release syndrome (CRS) and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS). The most common adverse reactions (>20%) were CRS, fatigue, pyrexia, dysgeusia, decreased appetite, musculoskeletal pain, and constipation, anemia and nausea. The most common Grade 3 or 4 laboratory abnormalities (≥5%) were decreased lymphocytes, decreased sodium, increased uric acid, decreased total neutrophils, decreased hemoglobin, increased activated partial thromboplastin time, and decreased potassium.

The recommended tarlatamab dose is an initial dose of 1 mg administered as an intravenous infusion over 1 hour on Cycle 1 Day 1, followed by 10 mg on Cycle 1 Day 8 and Day 15 then every 2 weeks thereafter until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-tarlatamab-dlle-extensive-stage-small-cell-lung-cancer

DeLLphi-301 Trial: Onset and Duration of Response



Paz-Ares L et al. *N Engl J Med* 2023 November 30;389(22):2063-75.

DeLLphi-301: Efficacy Analysis Set per ITT Analysis

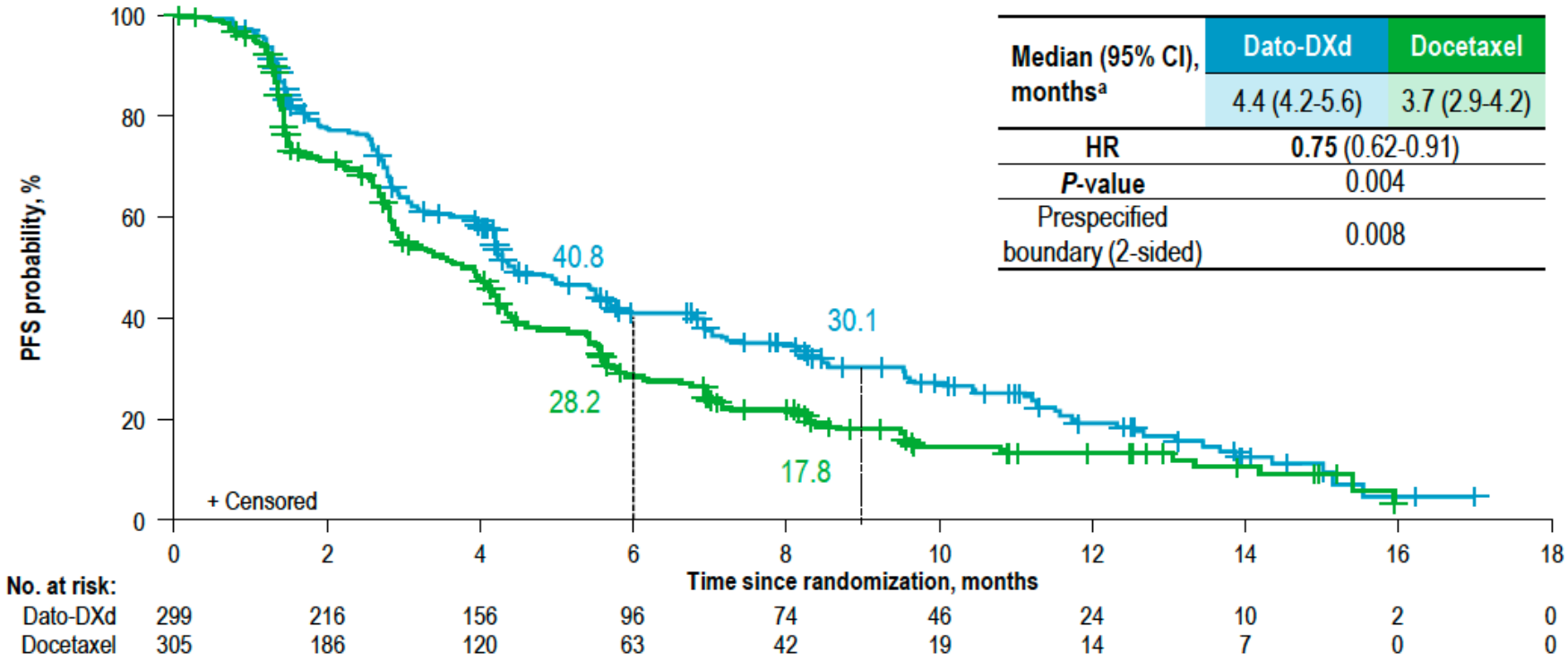
	10 mg (n = 100)*	100 mg (n = 88)*
ORR, % (97.5% CI)	40.0 (29.1—51.7)	31.8 (21.1—44.1)
Complete response, n (%)	1 (1.0)	7 (8.0)
Partial response, n (%)	39 (39.0)	21 (23.9)
Stable disease, n (%)	30 (30.0)	27 (30.7)
Progressive disease, n (%)	20 (20.0)	13 (14.8)
Not evaluable, n (%)	2 (2.0)	4 (4.5)
Death before post-baseline scan, n (%)	6 (6.0)	13 (14.8)
No post-baseline scan, n (%)	2 (2.0)	3 (3.4)
mDoR, mo (95% CI)	NE (5.9—NE)	NE (6.6—NE)
Disease control rate % (95% CI)	70.0 (60.0, 78.8)	62.5 (51.5, 72.6)
mOS, mo (95% CI)	14.3 (10.8—NE)	NE (12.4—NE)
mPFS, mo (95% CI)	4.9 (2.9—6.7)	3.9 (2.6—4.4)

ITT = intent to treat; ORR = objective response rate

Paz-Ares L et al. ESMO 2023;Abstract LBA92.

APPENDIX

TROPION-Lung01: PFS in ITT Population



Median (95% CI), months[a]	Dato-DXd	Docetaxel
	4.4 (4.2-5.6)	3.7 (2.9-4.2)
HR	**0.75** (0.62-0.91)	
P-value	0.004	
Prespecified boundary (2-sided)	0.008	

	Dato-DXd	Docetaxel
ORR (95% CI), %[b]	**26.4** (21.5-31.8)	**12.8** (9.3-17.1)
DOR (95% CI), mo	**7.1** (5.6-10.9)	**5.6** (5.4-8.1)

CR, complete response; DOR, duration of response; HR, hazard ratio; ITT, intention to treat; ORR, objective response rate; PFS, progression-free survival; PR, partial response.
[a]Median PFS follow-up was 10.9 (95% CI, 9.8-12.5) and 9.6 (95% CI, 8.2-11.9) months for Dato-DXd and docetaxel, respectively. [b]Included 4 CRs and 75 PRs for Dato-DXd and 39 PRs for docetaxel.

Ahn M-J et al. ESMO Asia 2023;Abstract 509MO.

2023 ASCO ANNUAL MEETING

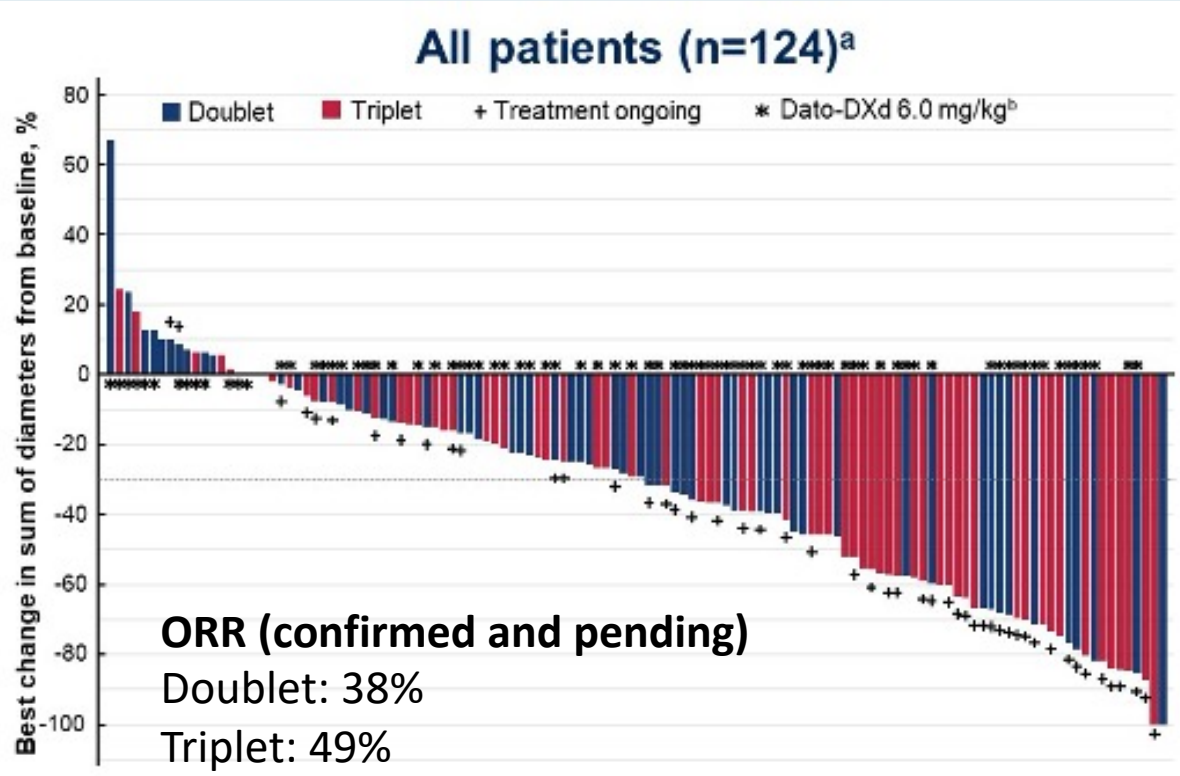
Abstract 9004

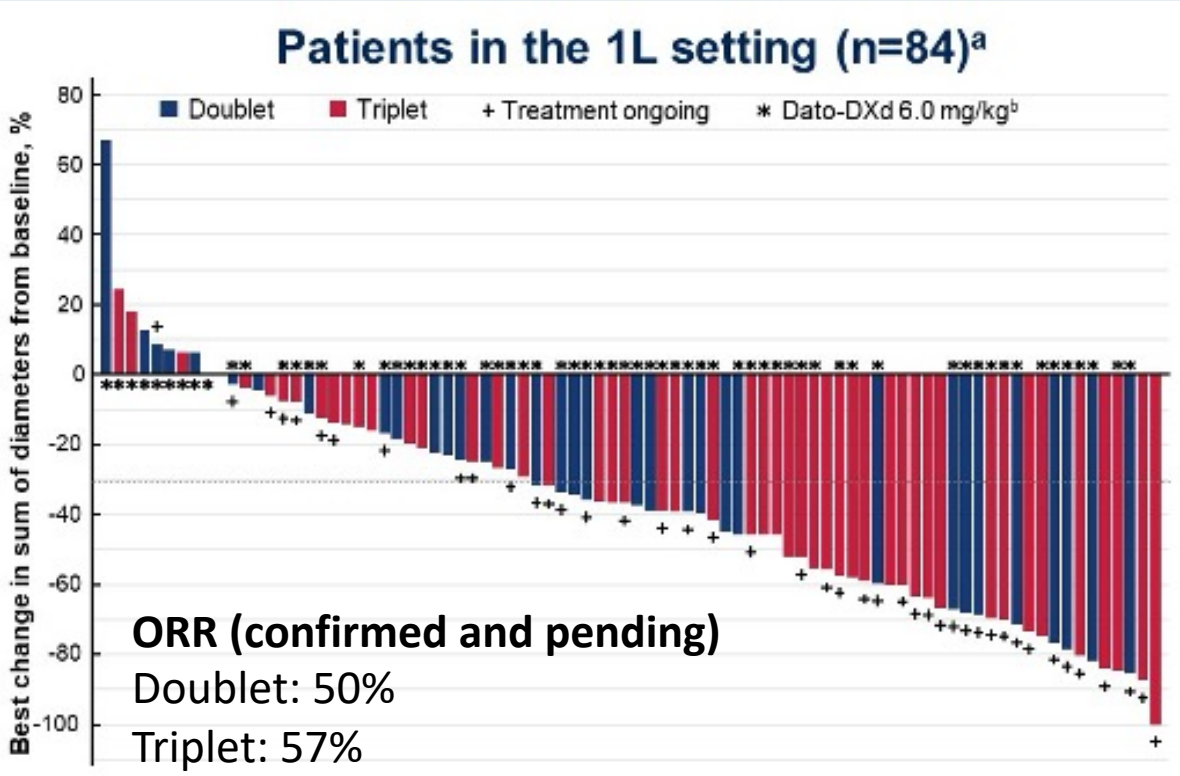
TROPION-Lung02: Datopotamab Deruxtecan (Dato-DXd) Plus Pembrolizumab With or Without Platinum Chemotherapy in Advanced Non-Small Cell Lung Cancer

Yasushi Goto, MD, PhD,[1] Wu Chou Su, MD,[2] Benjamin Levy, MD,[3] Olivier Rixe, MD, PhD,[4,5] Tsung Ying Yang, MD, PhD,[6] Anthony Tolcher, MD,[7] Yanyan Lou, MD, PhD,[8] Yoshitaka Zenke, MD, PhD,[9] Panayiotis Savvides, MD,[10] Enriqueta Felip, MD, PhD,[11] Manuel Domine, MD, PhD,[12] Konstantinos Leventakos, MD, PhD,[13] Mariano Provencio Pulla, MD, PhD,[14] Atsushi Horiike, MD, PhD,[15] Edward Pan, MD,[5] Daisy Lin, PhD,[5] Jessie Gu, PhD, MS,[5] Priyanka Basak, MD, MBE,[5] Michael Chisamore, PhD,[16] Luis Paz-Ares, MD, PhD[17]

[1]National Cancer Center Hospital, Tokyo, Japan; [2]Department of Oncology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [3]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; [4]Quantum Santa Fe, Santa Fe, NM; [5]Daiichi Sankyo, Inc, Basking Ridge, NJ; [6]Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; [7]NEXT Oncology, San Antonio, TX; [8]Mayo Clinic, Jacksonville, FL; [9]Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [10]Mayo Clinic, Phoenix, AZ; [11]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [12]Department of Oncology, Hospital Universitario Fundación Jiménez Díaz (IIS-FJD), Madrid, Spain; [13]Mayo Clinic, Rochester, MN; [14]Department of Medical Oncology, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain; [15]Division of Medical Oncology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan; [16]Merck & Co, Inc, Rahway, NJ; [17]Hospital Universitario 12 de Octubre, CNIO-H12O Lung Cancer Unit, Universidad Complutense and CIBERONC, Madrid, Spain

TROPION-Lung02: Tumor Response with Dato-DXd and Pembrolizumab with or without Platinum Chemotherapy



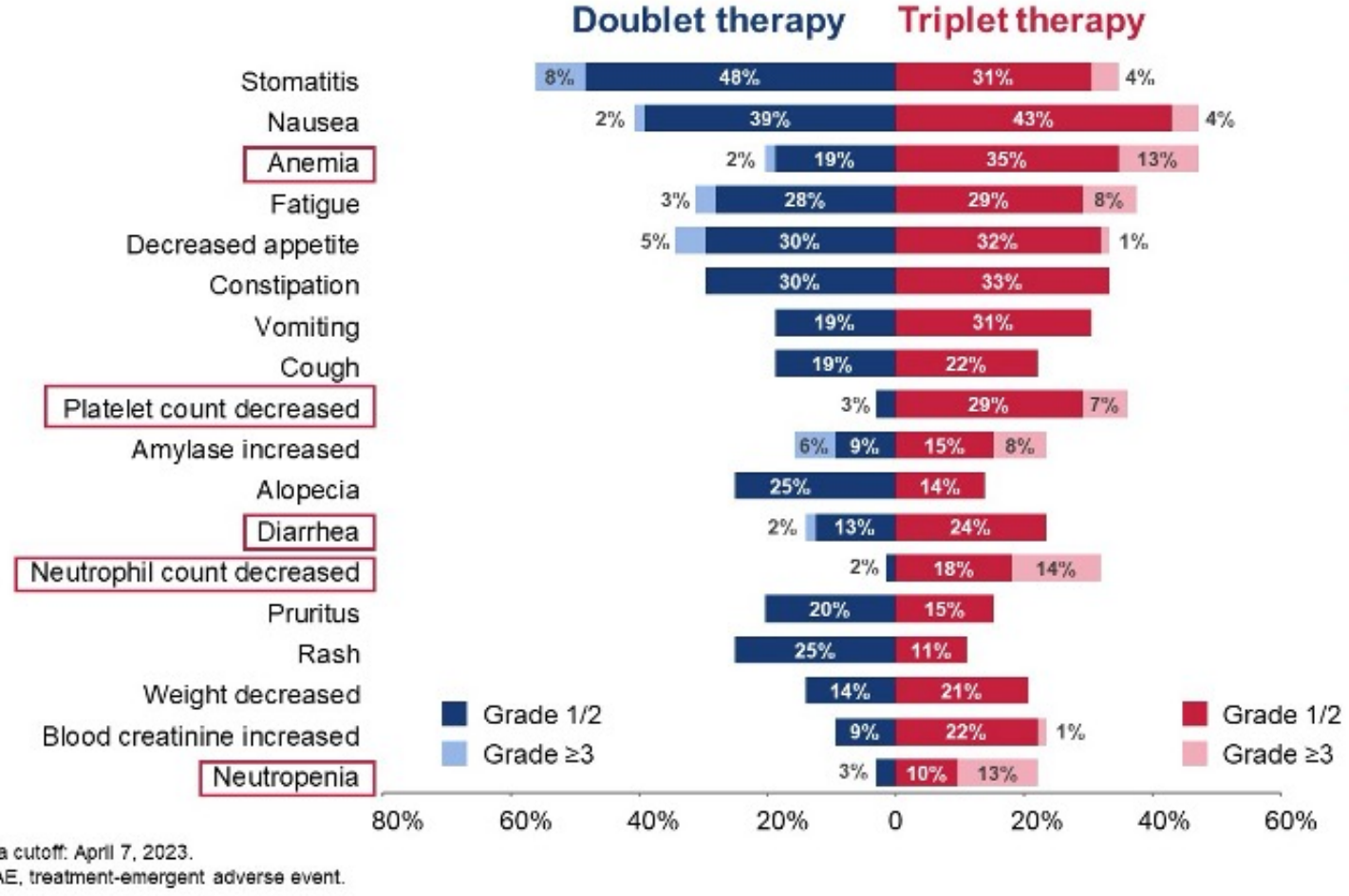


Data cutoff: April 7, 2023.
1L, first line.
[a] Patients with no baseline target lesions or no postbaseline tumor assessments were excluded from the waterfall plots. [b] Planned dose level.

ORR = objective response rate

Goto Y et al. ASCO 2023;Abstract 9004.

TROPION-Lung02: Treatment-Emergent Adverse Events (TEAEs) with Dato-DXd and Pembrolizumab with or without Platinum Chemotherapy



- The most frequent TEAEs of any grade were stomatitis, nausea, anemia, and fatigue
- In general, hematologic TEAEs, particularly those of grade ≥3, were more frequently observed with triplet therapy than with doublet therapy

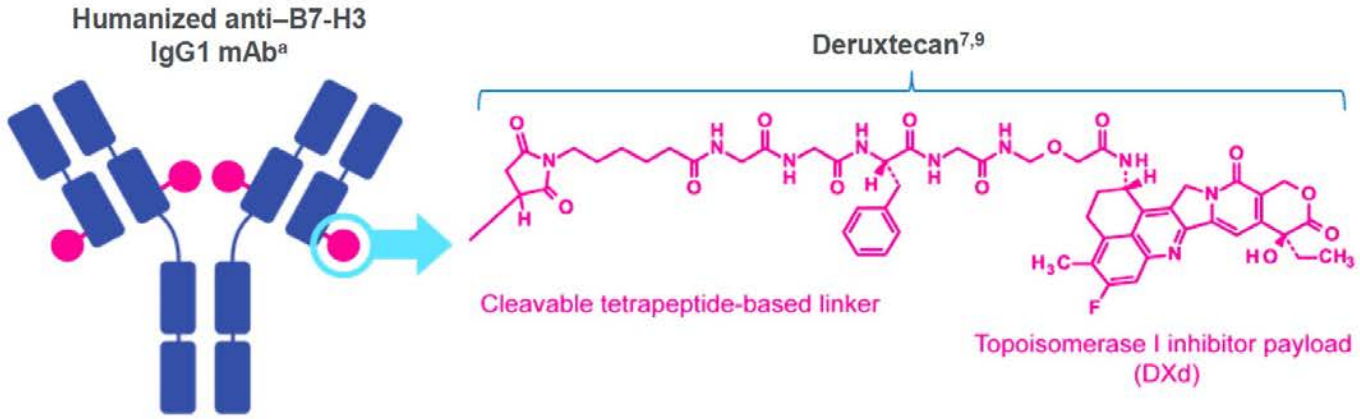
Data cutoff: April 7, 2023.
TEAE, treatment-emergent adverse event.

Goto Y et al. ASCO 2023;Abstract 9004.

Ifinatamab Detuxtecan: Mechanism of Action

Ifinatamab Deruxtecan (I-DXd; DS-7300) Was Designed With 7 Key Attributes

- B7-H3 is overexpressed in a wide range of cancer types and is associated with disease progression and lower survival[1–5]
- I-DXd is a B7-H3 (CD276)-directed ADC composed of 3 parts:[6–9,11]
  - A humanized anti–B7-H3 IgG1 monoclonal antibody[9,11]
  - A topoisomerase I inhibitor payload (an exatecan derivative, DXd)
  - A tetrapeptide-based cleavable linker that covalently bonds the other 2 components

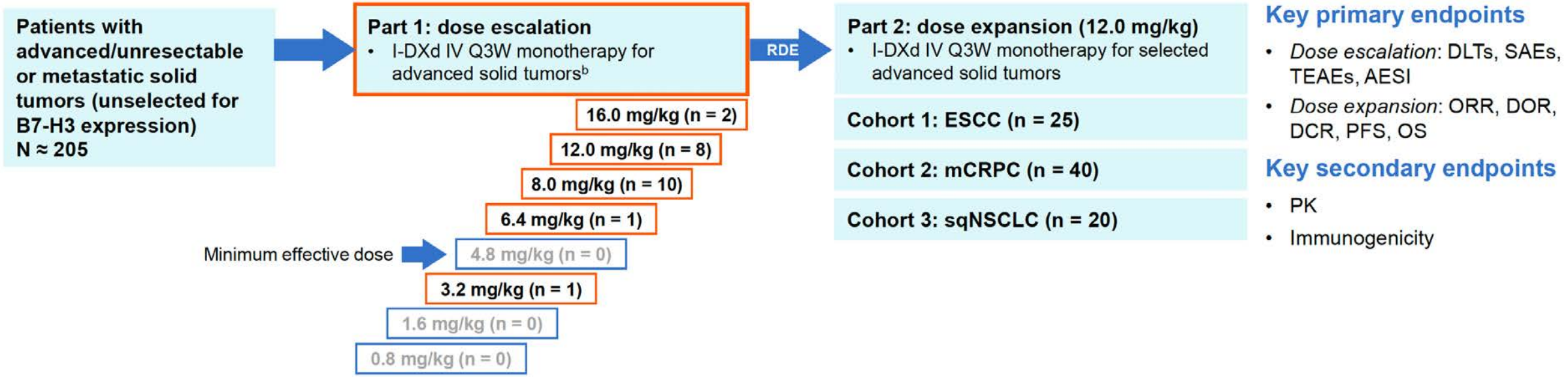


Payload mechanism of action: topoisomerase I inhibitor[7,9,11,b]
High potency of payload[9,11,b]
Optimized drug-to-antibody ratio ≈ 4[6–8,10,b]
Payload with short systemic half-life[9,11,b,c]
Stable linker-payload[9,11,b]
Tumor-selective cleavable linker[9,11,b]
Bystander antitumor effect[7,10,11,b]

Johnson et al. WCLC 2023;Abstract OA05.05.

DS7300-A-J101 Study Design

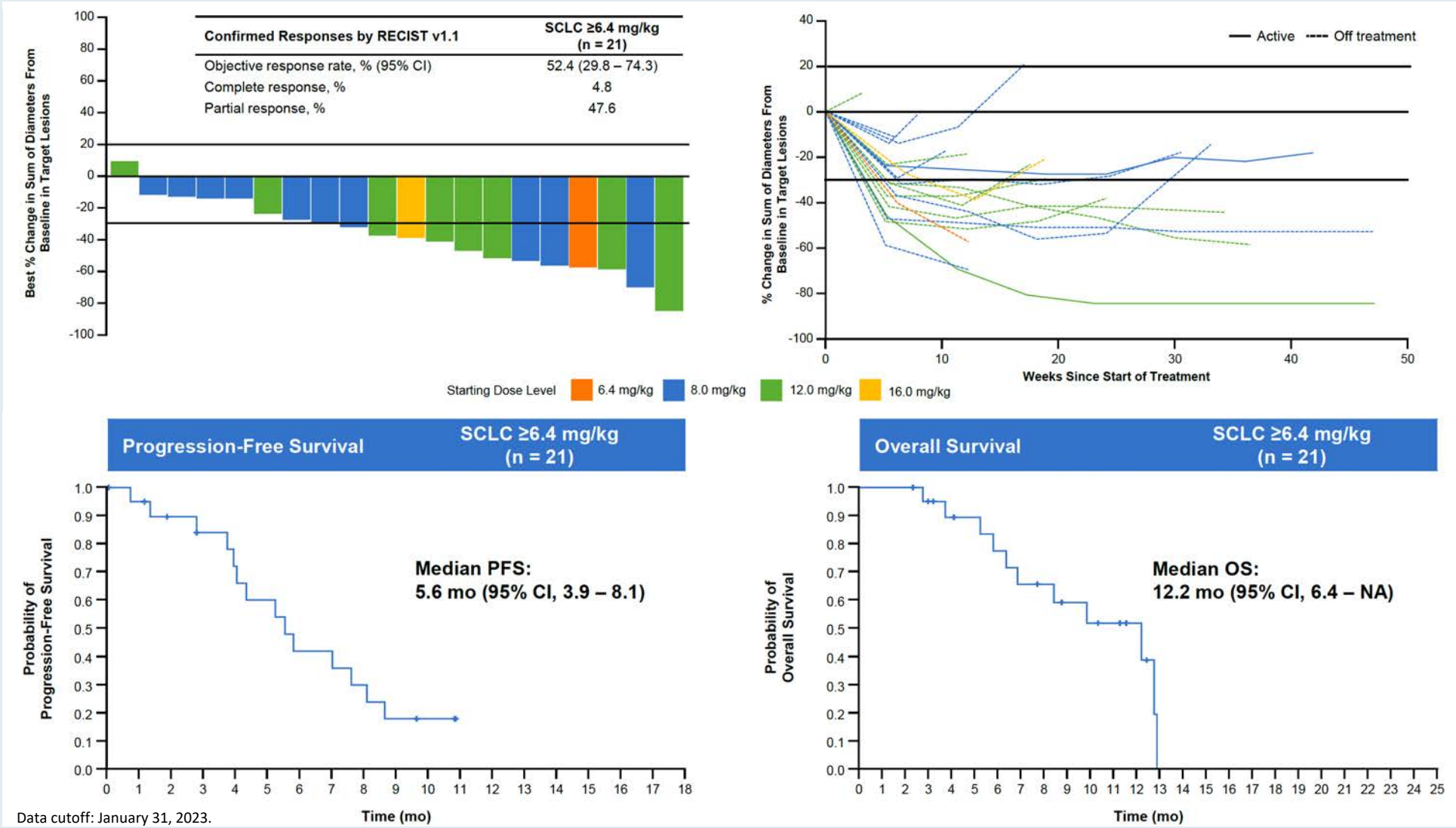
- I-DXd is generally well tolerated with early signs of antitumor activity[1,2]
- **We present a subgroup analysis of patients with SCLC (N = 22[a]) from part 1 treated with I-DXd at all doses studied**
  - Patients dosed at ≥6.4 mg/kg (n = 21) were evaluable for efficacy
  - Baseline tumor biopsies were retrospectively examined for B7-H3 protein level by IHC and used for correlative analysis in biomarker-evaluable patients dosed at ≥6.4 mg/kg (n = 17)



Johnson M et al. WCLC 2023;Abstract OA05.05.

DS7300-A-J101: Ifinatamab Deruxtecan Antitumor Activity

- Nearly all patients with postbaseline scans had a reduction in target lesions
- Median time to response was 1.2 months (95% CI, 1.2-1.4)
- Median duration of response was 5.9 months (95% CI, 2.8-7.5); 2 patients remain on treatment
- Median follow-up was 11.7 months (95% CI, 4.63-12.88)



Data cutoff: January 31, 2023.

Johnson M et al. WCLC 2023;Abstract OA05.05.

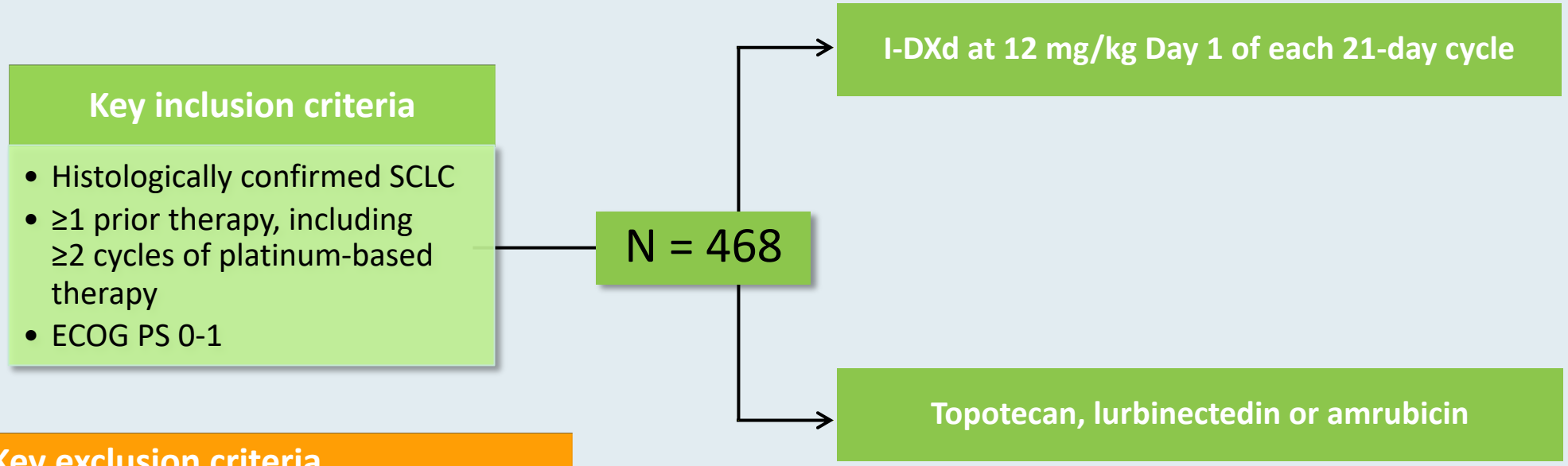
DS7300-A-J101: Ifinatamab Deruxtecan Most Common (≥10%) All-Grade TEAEs Regardless of Causality

System Organ Class Preferred Term, n (%)	SCLC (N = 22)	
	Any Grade	Grade ≥3
Nausea	13 (59.1)	1 (4.5)
Fatigue	11 (50.0)	0 (0.0)
Anemia	6 (27.3)	1 (4.5)
Vomiting	6 (27.3)	0 (0.0)
Decreased appetite	5 (22.7)	1 (4.5)
Pyrexia	4 (18.2)	0 (0.0)
Constipation	4 (18.2)	1 (4.5)
IRR	3 (13.6)	0 (0.0)
Diarrhea	3 (13.6)	0 (0.0)
Dehydration	3 (13.6)	0 (0.0)
Dyspnea	3 (13.6)	0 (0.0)
Platelet count decreased	3 (13.6)	0 (0.0)
Arthralgia	3 (13.6)	0 (0.0)
Hyponatremia	3 (13.6)	0 (0.0)

- A total of 3 patients (13.6%) experienced an interstitial lung disease (ILD) or pneumonitis event (2 Grade 1, 1 Grade 2).
  - All events were adjudicated by the ILD adjudication committee, of which 1 was adjudicated as drug-related ILD (Grade 2, 8.0 mg/kg), and treatment was discontinued per protocol.
- Prophylactic premedication for nausea, vomiting and infusion-related reaction were not permitted for primary prophylaxis during cycle 1 of dose escalation.

Johnson M et al. WCLC 2023;Abstract OA05.05.

IDeate-Lung02: A Phase III Study of Ifinatamab Deruxtecan versus Treatment of Physician's Choice for Relapsed SCLC



Key exclusion criteria

- Prior orlotamab, enoblituzumab or other B7-H3-targeted agents (including I-DXd)
- Prior ADC that consists of an exatecan derivative (eg, T-DXd)
- Received the study comparators or any topoisomerase I inhibitor
- Any history of ILD/pneumonitis

Outcomes

- Primary endpoints: ORR and OS (up to 4.5 years)
- Key secondary endpoints: PFS, DOR, safety (up to 4.5 years)

I-DXd = ifinatamab deruxtecan; ADC = antibody-drug conjugate; ILD = interstitial lung disease; ORR = overall response rate

www.clinicaltrials.gov. NCT06203210. Accessed June 2024.

MADRID 2023 ESMO congress

Sacituzumab govitecan as second-line treatment for extensive stage small cell lung cancer

Preliminary results from the phase 2 TROPiCS-03 basket trial

Afshin Dowlati,[1] Andres Cervantes,[2] Sunil Babu,[3] Erika Hamilton,[4] Shu Fen Wong,[5] Andrea Tazbirkova,[6] Ivana Gabriela Sullivan,[7] Cédric van Marcke,[8] Antoine Italiano,[9] Jilpa Patel,[10] Sabeen Mekan,[10] Tia Wu,[10] Anne C. Chiang[11]

[1]University Hospitals Seidman Cancer Center and Case Western Reserve University, Cleveland, OH, USA; [2]INCLIVA Instituto de Investigación Sanitaria, University of Valencia, Valencia, Spain; [3]Fort Wayne Medical Oncology and Hematology, Fort Wayne, IN, USA; [4]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [5]Andrew Love Cancer Centre, Geelong, Australia; [6]Pindara Private Hospital, Benowa, Queensland, Australia; [7]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [8]Cliniques Universitaires Saint-Luc, Brussels, Belgium; [9]Institut Bergonié, Bordeaux, France; [10]Gilead Sciences, Inc., Foster City, CA, USA; [11]Yale School of Medicine, New Haven, CT, USA

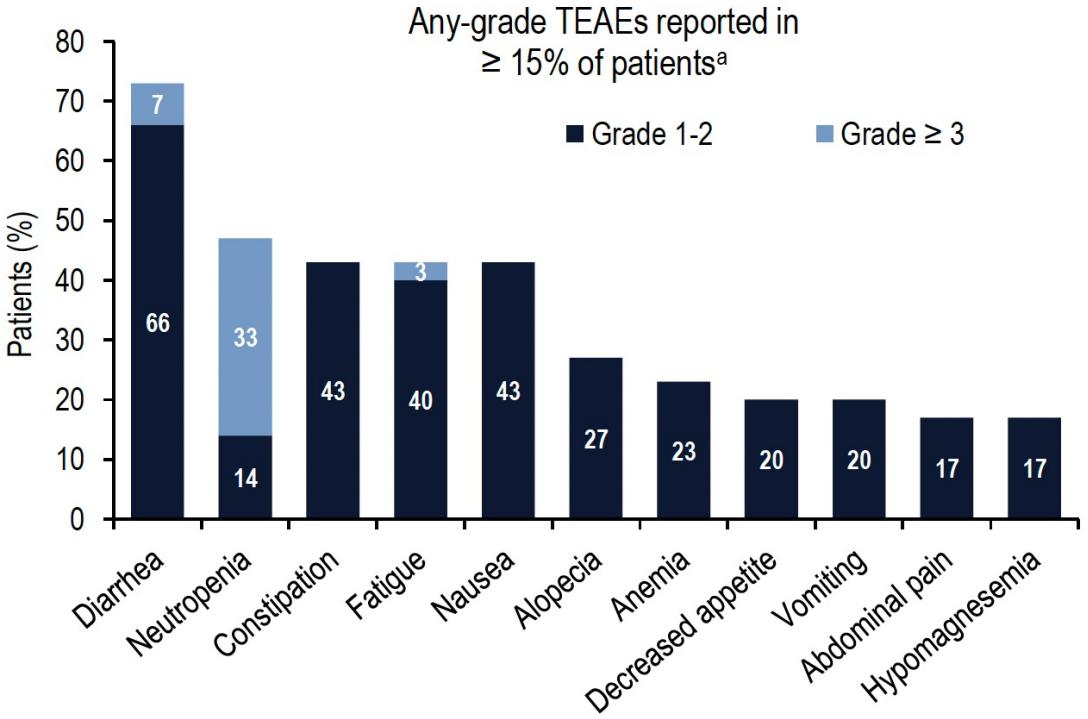
Presenter: Afshin Dowlati, MD

Saturday, October 21, 2023, 14:55-15:00
FPN: 1990MO

TROPiCS-03: Safety Summary with Sacituzumab Govitecan for ES-SCLC

The adverse event profile observed in this trial was consistent with the observed safety of SG in other tumor types

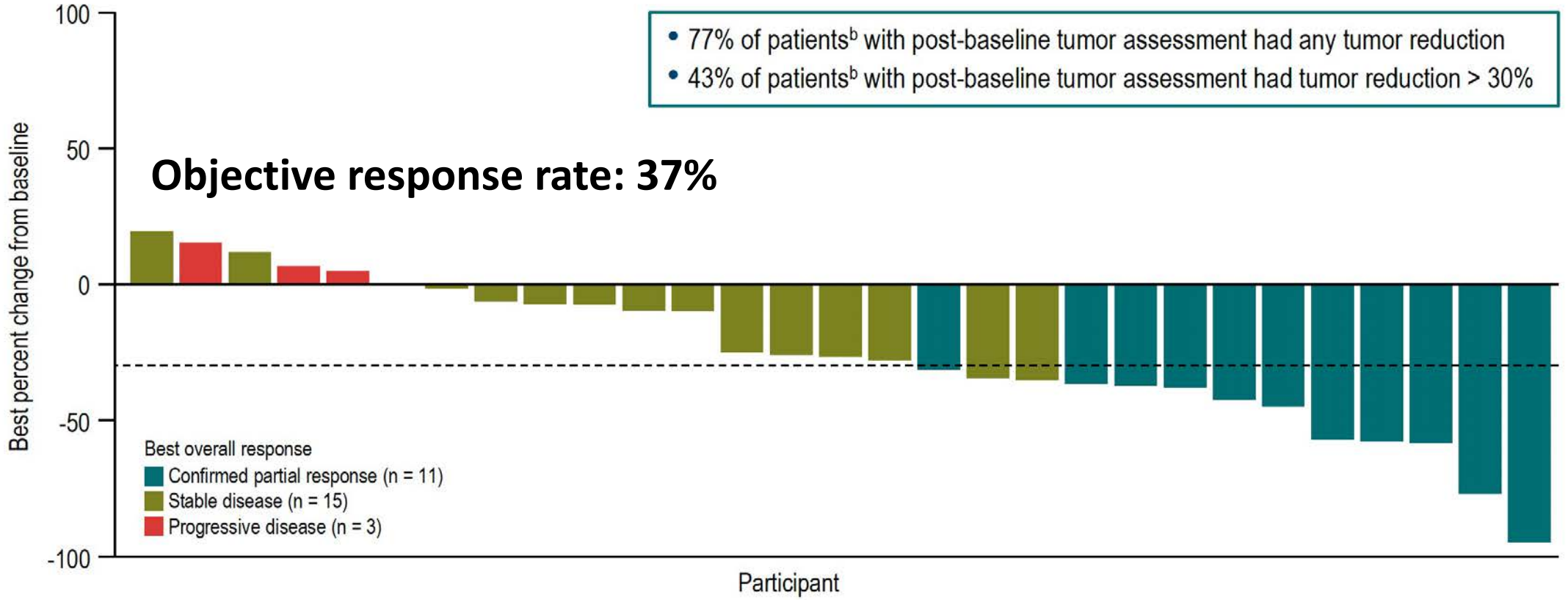
Safety-evaluable patients, n (%)	ES-SCLC N = 30[a]
Any-grade TEAEs	30 (100)
Related to study treatment	28 (93)
Grade ≥ 3 TEAEs	18 (60)
Related to study treatment	15 (50)
Serious TEAEs	9 (30)
Related to study treatment	4 (13)
TEAEs leading to dose reduction	8 (27)
TEAEs leading to discontinuation	0
Related to study treatment	0
TEAEs leading to death	0
Related to study treatment	0



TEAE is defined as any adverse event with an onset date on or after the study treatment start date and no later than 30 days after the last dose of study treatment. ES-SCLC, extensive-stage squamous cell lung cancer; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event. [a]Includes patients enrolled on or before 27 April 2023.

Dowlati A et al. ESMO 2023;Abstract 1990MO.

TROPiCS-03: Tumor Response with Sacituzumab Govitecan for ES-SCLC



Includes patients enrolled on or before 27 April 2023. RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1. [a]By investigator assessment per RECIST v1.1. [b]Percentages were calculated using the total number of patients (N = 30).

Dowlati A et al. ESMO 2023;Abstract 1990MO.

Investigator Perspectives on Available Research and Challenging Questions in Renal Cell Carcinoma: A Post-ASCO Annual Review

A CME/MOC-Accredited Live Webinar

Wednesday, June 19, 2024
5:00 PM – 6:00 PM ET

Faculty

Rana R McKay, MD
Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

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RTP Year in Review 2024