Meet The Professor

Current and Future Role of Immunotherapy in the Management of Lung Cancer

Sarah B Goldberg, MD, MPH
Associate Professor of Medicine
Medical Oncology, Yale School of Medicine
New Haven, Connecticut

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Commercial Support

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Dr Love — Disclosures

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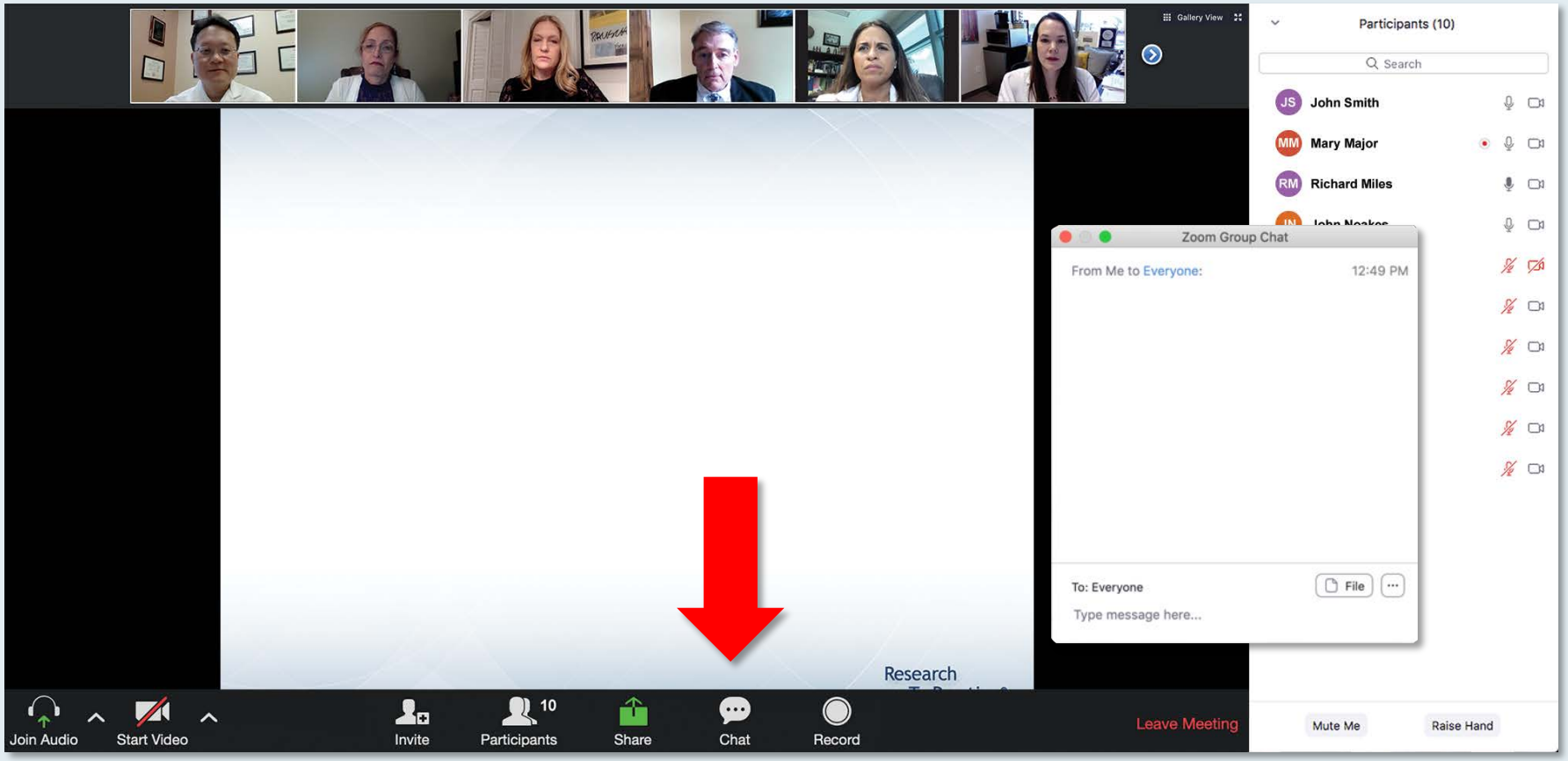
Contracted Research	AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc

We Encourage Clinicians in Practice to Submit Questions



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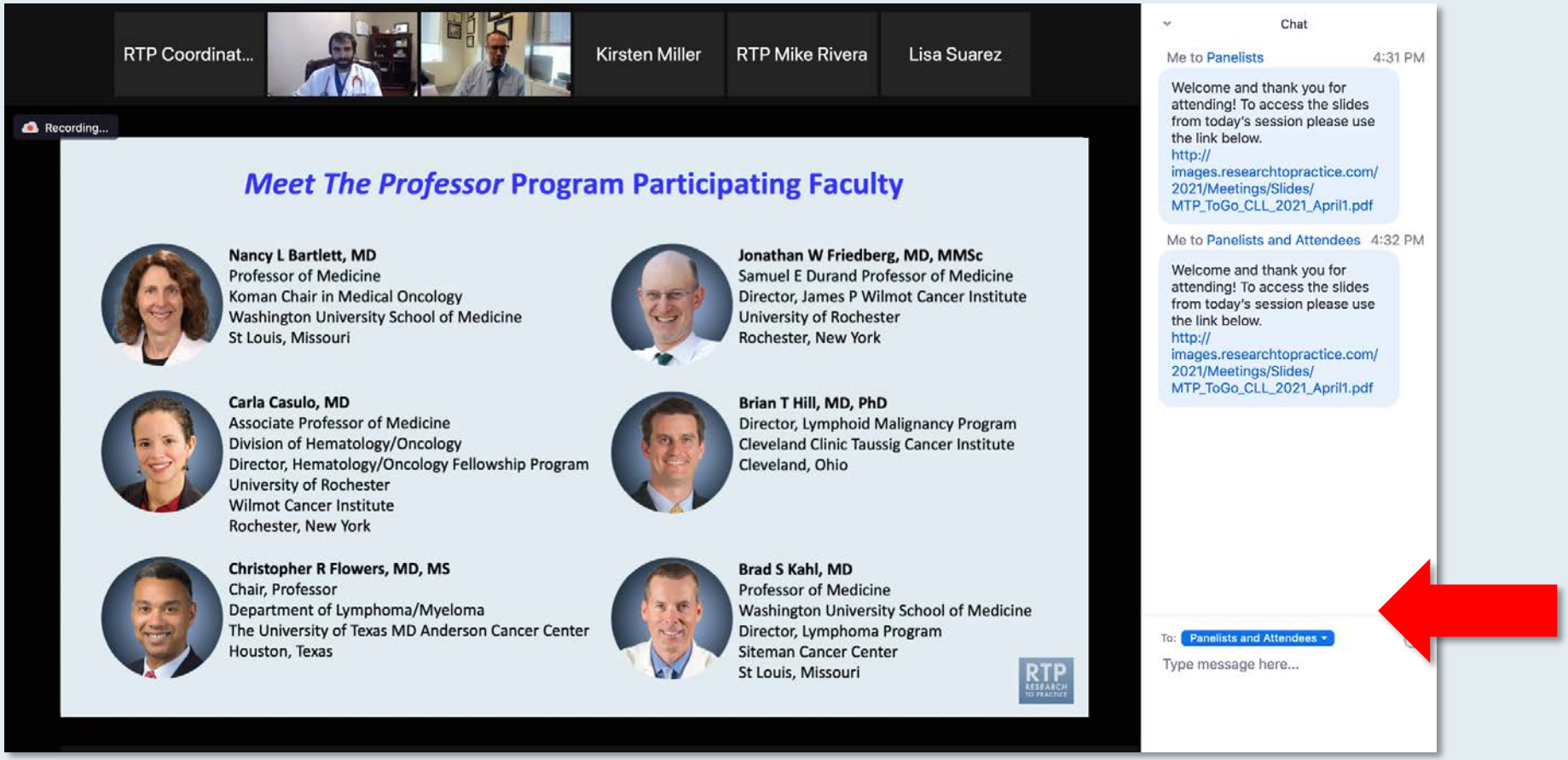

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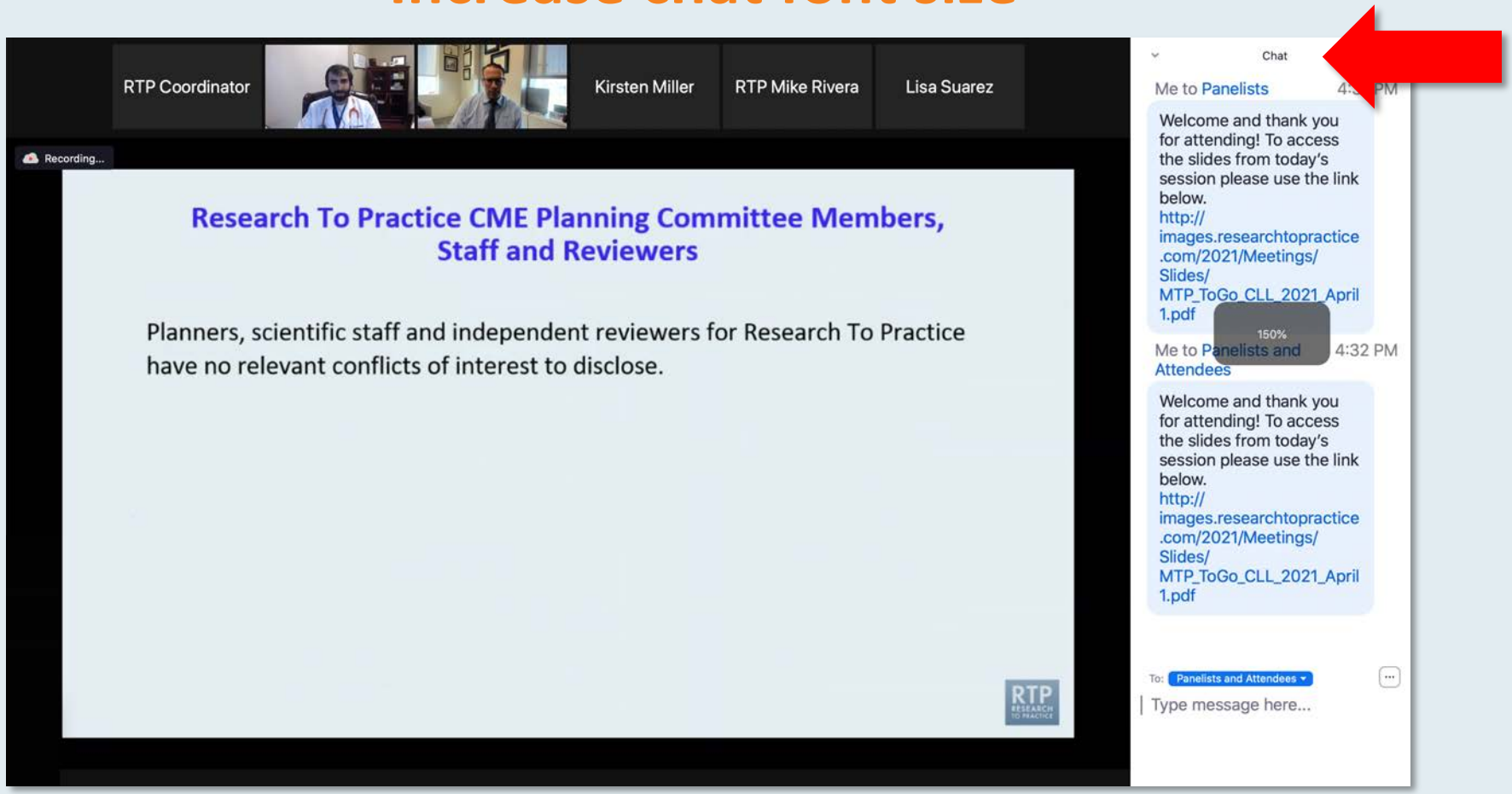

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

NSCLC with EGFR Exon 20 Insertion Mutations

DR GREGORY RIELY
MEMORIAL SLOAN KETTERING CANCER CENTER

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Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 31, 2022
5:00 PM – 6:00 PM ET

Faculty

Kerry Rogers, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Myelodysplastic Syndromes

Tuesday, April 5, 2022
5:00 PM – 6:00 PM ET

Faculty

Rami Komrokji, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Wednesday, April 6, 2022
5:00 PM – 6:00 PM ET

Faculty

Andrew M Evens, DO, MSc

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Management of Myelofibrosis

Thursday, April 7, 2022
5:00 PM – 6:00 PM ET

Faculty

Professor Claire Harrison

Moderator

Neil Love, MD

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Year in Review:
Prostate Cancer

Tuesday, April 12, 2022
5:00 PM – 6:00 PM ET

Faculty

Emmanuel S Antonarakis, MD

Additional faculty to be announced

Moderator

Neil Love, MD

RTP Year in Review 2022

"What I Tell My Patients"
16th Annual RTP/ONS CE Seminar Series
ONS Congress, Anaheim, California — April 27 - May 1, 2022

Thursday April 28	**Prostate Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Ovarian Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Non–Small Cell Lung Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
	Hepatobiliary Cancers 8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)
Friday April 29	**Small Cell Lung Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Chronic Lymphocytic Leukemia 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Breast Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
Saturday April 30	**Cervical and Endometrial Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Bladder Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

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Thank you for joining us!

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

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New Haven, Connecticut

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Meet The Professor Program Participating Faculty

Charu Aggarwal, MD
Leslye M Heisler Associate Professor
for Lung Cancer Excellence
University of Pennsylvania
Abramson Cancer Center
Philadelphia, Pennsylvania

Sarah B Goldberg, MD, MPH
Associate Professor of Medicine
Medical Oncology
Yale School of Medicine
New Haven, Connecticut

Stephen V Liu, MD
Associate Professor of Medicine
Georgetown University Hospital
Washington, DC

Jarushka Naidoo, MB BCH, MHS
Consultant Medical Oncologist
Beaumont Hospital
Dublin, Ireland
Adjunct Assistant Professor of Oncology
Johns Hopkins University
Baltimore, Maryland

MODERATOR
Neil Love, MD
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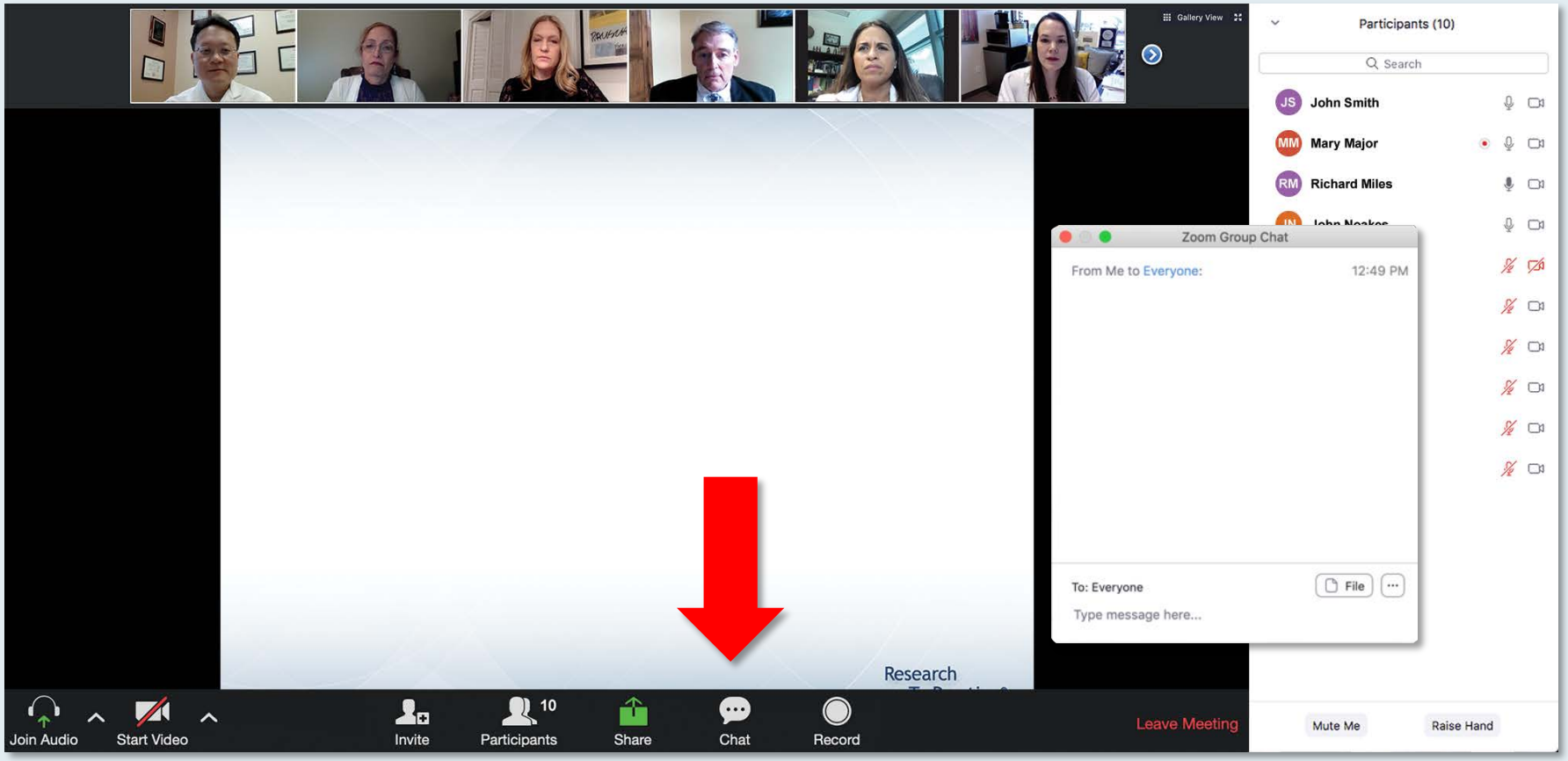

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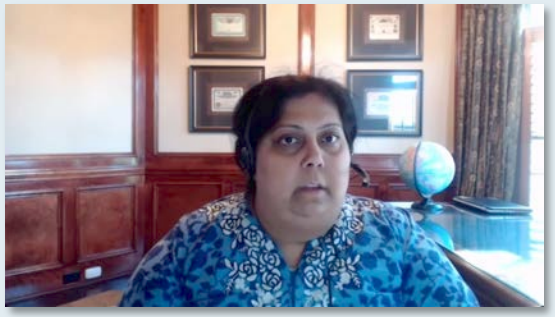
Daniel R Carrizosa, MD, MS
Atrium Health
Levine Cancer Institute
Charlotte, North Carolina



Niyati A Nathwani, MD
Carolina Blood
and Cancer Care Associates
Charlotte, North Carolina

Zanetta S Lamar, MD
Florida Cancer Specialists
Naples, Florida

G Richard Polkinghorn, MD
Maine General Health
Augusta, Maine

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

John Yang, MD
Fall River, Massachusetts

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Meet The Professor with Dr Goldberg

MODULE 1: Case Presentation

- Dr Polkinghorn: A 62-year-old woman metastatic non-small cell lung cancer (NSCLC) and multiple sclerosis

MODULE 2: Case Presentation

- Dr Yang: A 77-year-old woman with progressive metastatic adenocarcinoma of the lung — PD-L1 90%

MODULE 3: PEARLS/KEYNOTE-091 Phase III Study of Adjuvant Pembrolizumab

MODULE 4: Case Presentations

- Dr Morganstein: A 65-year-old man who presents with seizures associated with multiple brain metastases from NSCLC
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MODULE 5: Journal Club with Dr Goldberg

MODULE 6: Faculty Survey

MODULE 7: Appendix of Key Data Sets

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Genentech Provides Update on Phase III SKYSCRAPER-02 Study in Extensive-Stage Small Cell Lung Cancer

Press Release – March 30, 2022

- *SKYSCRAPER-02, the first randomized study of tiragolumab in extensive-stage small cell lung cancer (ES-SCLC), did not meet its co-primary endpoint of progression-free survival*
- *ES-SCLC is a hard-to-treat disease and atezolizumab plus chemotherapy remains a standard of care*
- *Tiragolumab continues to be evaluated in non-small cell lung cancer and other cancer types through additional Phase III trials as planned*

"….the Phase III SKYSCRAPER-02 study, evaluating the investigational anti-TIGIT immunotherapy tiragolumab plus atezolizumab and chemotherapy (carboplatin and etoposide) as an initial (first-line) treatment for people with extensive-stage small cell lung cancer (ES-SCLC), did not meet its co-primary endpoint of progression-free survival. The co-primary endpoint of overall survival was not met at its interim analysis and is unlikely to reach statistical significance at the planned final analysis. Data suggest tiragolumab plus atezolizumab and chemotherapy was well-tolerated and no new safety signals were identified when adding tiragolumab. Data will be presented at an upcoming medical meeting."

https://finance.yahoo.com/news/genentech-provides-phase-iii-skyscraper-051000966.html

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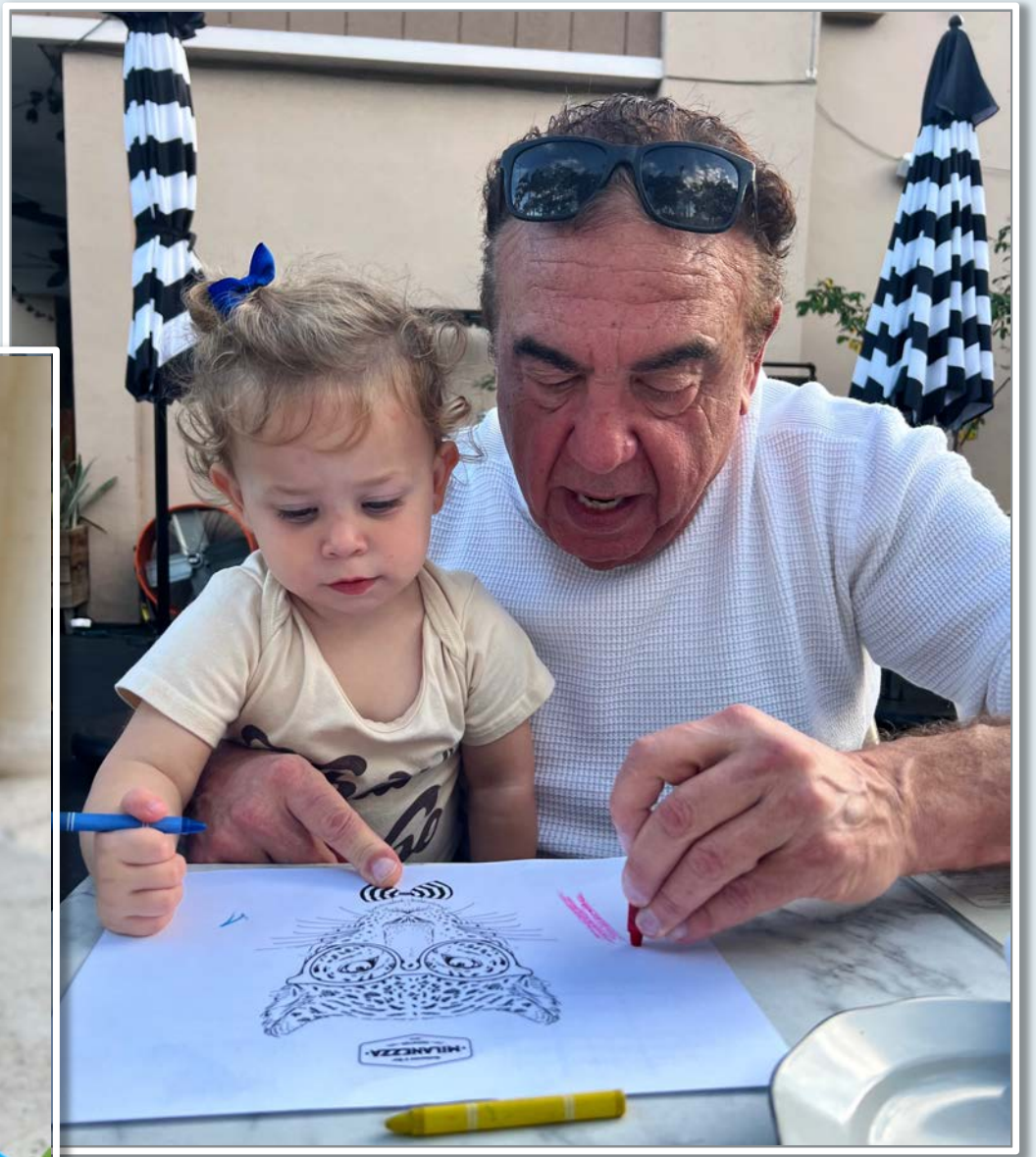

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Have you administered or would you administer an anti-PD-1/PD-L1 antibody to a patient with multiple sclerosis?

1. I have
2. I have not but would for the right patient
3. I would not
4. I would but only on clinical trial

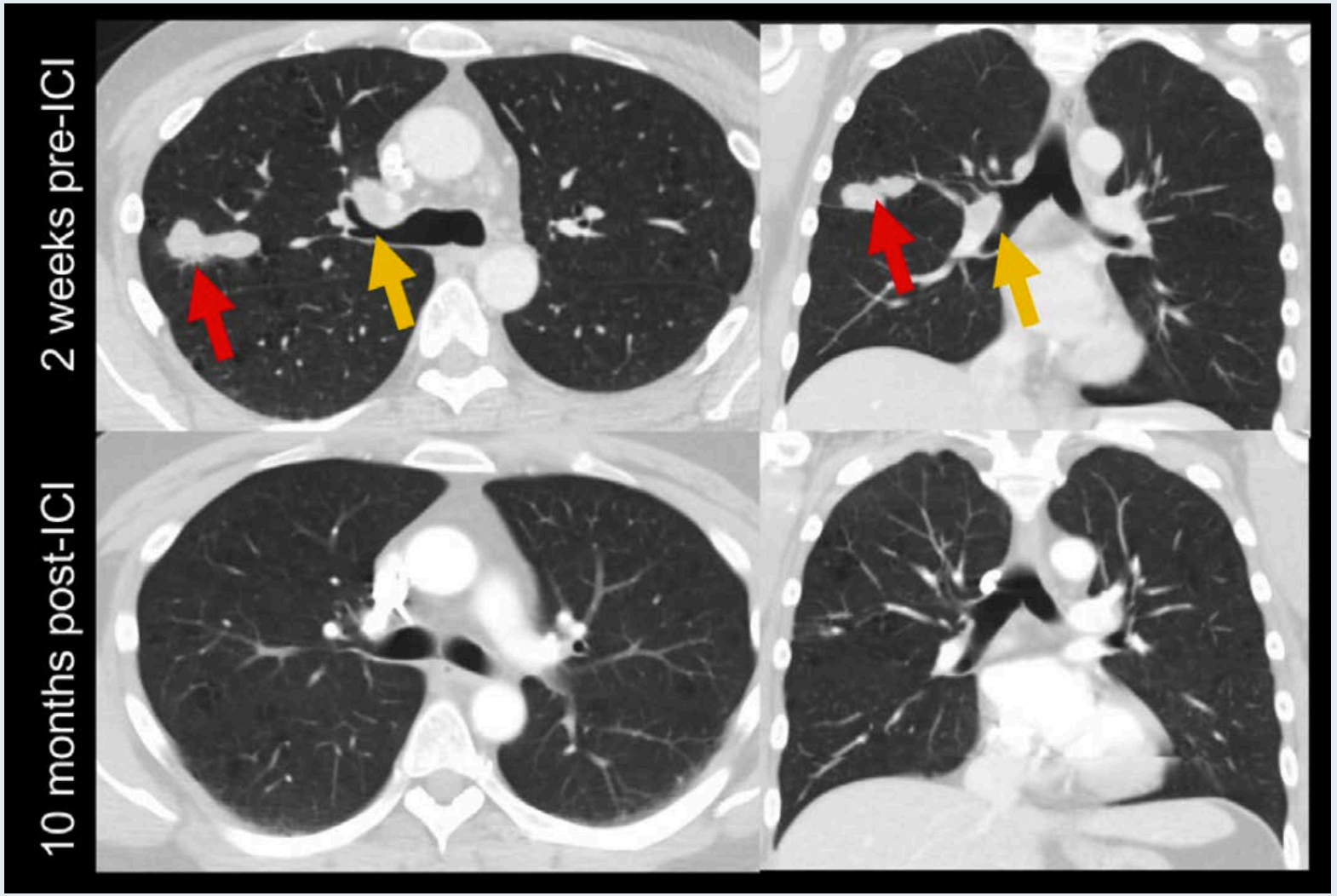
JTO Clin Res Rep 2021;2(6):100183

CASE REPORT

Intracranial Complications From Immune Checkpoint Therapy in a Patient With NSCLC and Multiple Sclerosis: Case Report

Benjamin Y. Lu, MD,[a] Cigdem Isitan, MD,[b,c] Amit Mahajan, MD,[d] Veronica Chiang, MD,[e] Anita Huttner, MD,[f] Jackson Robinson Mitzner, BS,[c] Sarah F. Wesley, MD,[b] Sarah B. Goldberg, MD, MPH[a,*]

CT Images of the Primary Lung Tumor 2 Weeks Before (top) and 10 Months After (bottom) Immune Checkpoint Inhibitor (ICI) Therapy



Lu BY et al. *JTO Clin Res Rep* 2021;2(6):100183.

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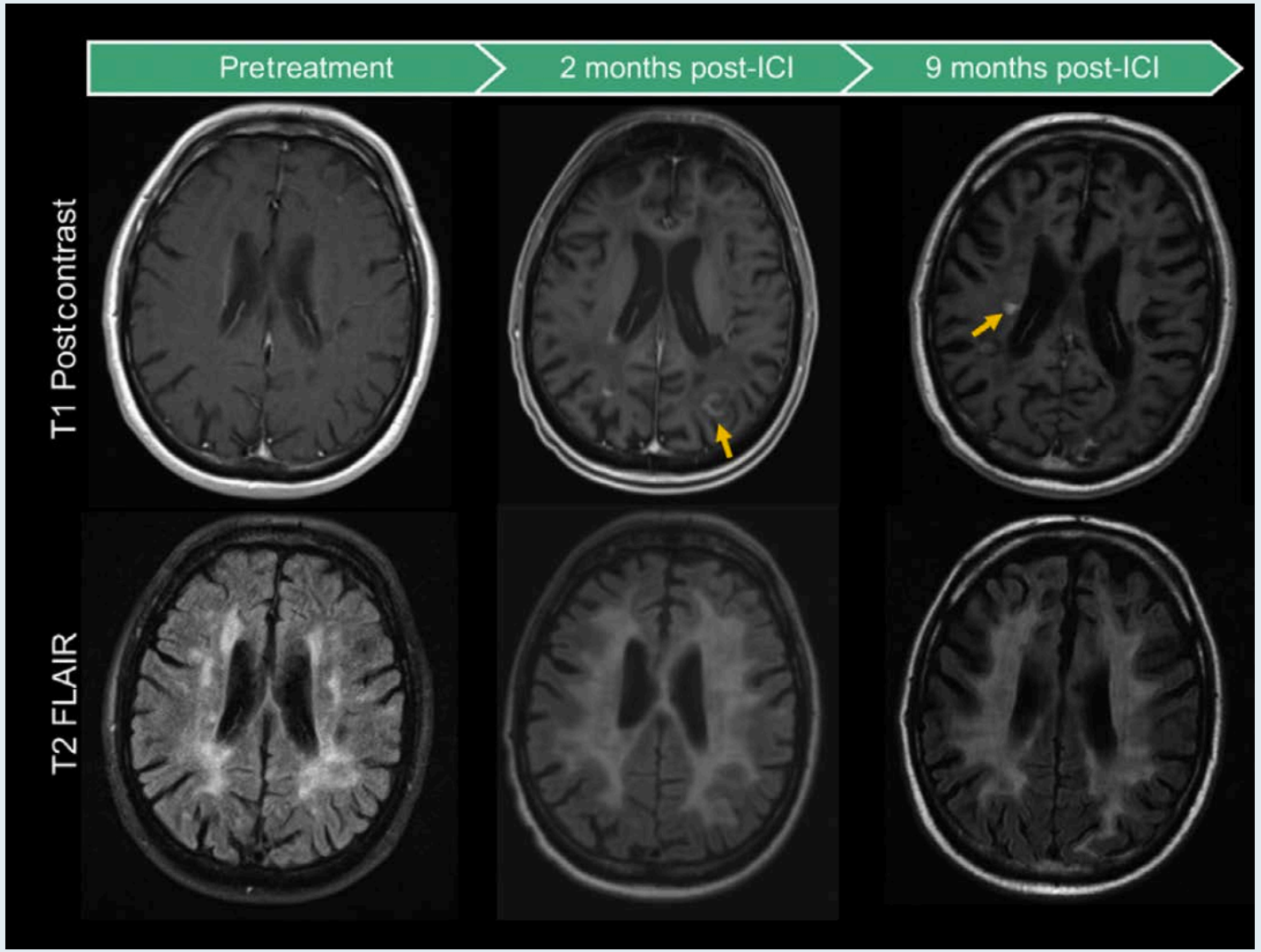
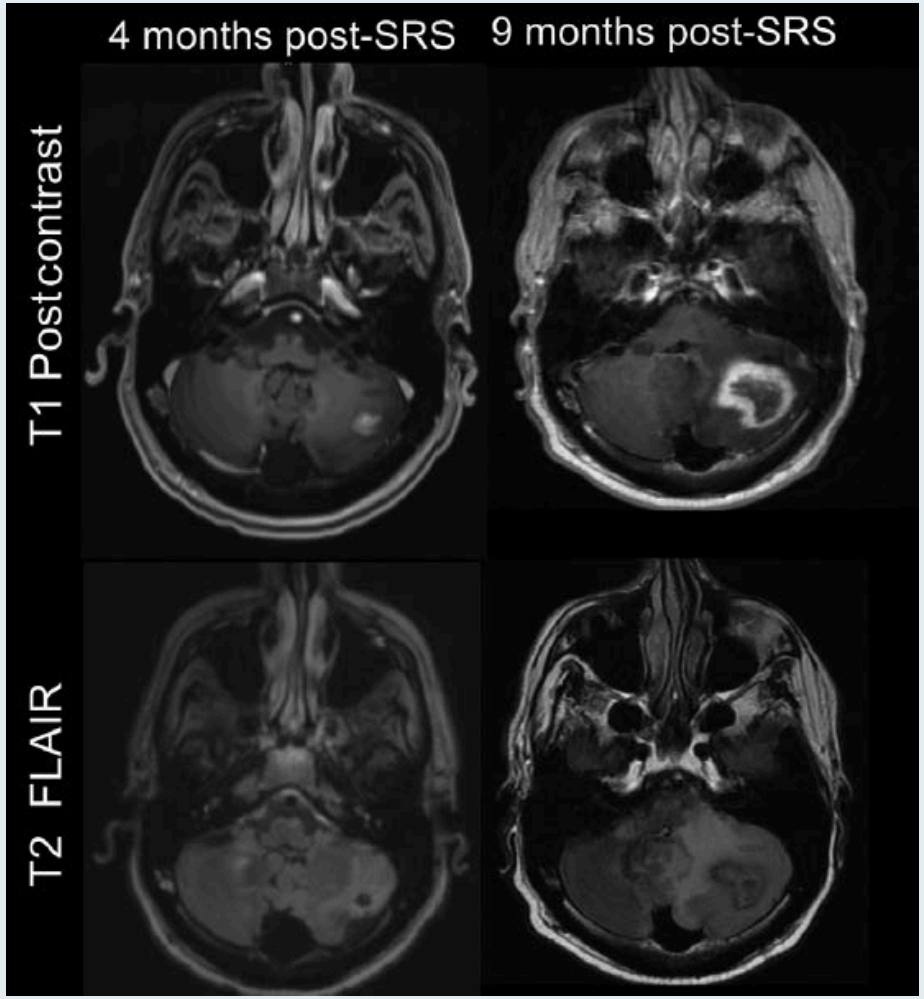
MR Images of the Brain Before Any Therapy (left), 2 Months After Atezolizumab (middle), and 9 Months After Atezolizumab (right)



Lu BY et al. *JTO Clin Res Rep* 2021;2(6):100183.

MR Images 4 Months (left) and 9 Months (right) After Stereotactic Radiosurgery (SRS) to a Left Cerebellar Lesion in the T1 Postgadolinium Contrast (top row) and T2 FLAIR (bottom row) Sequences



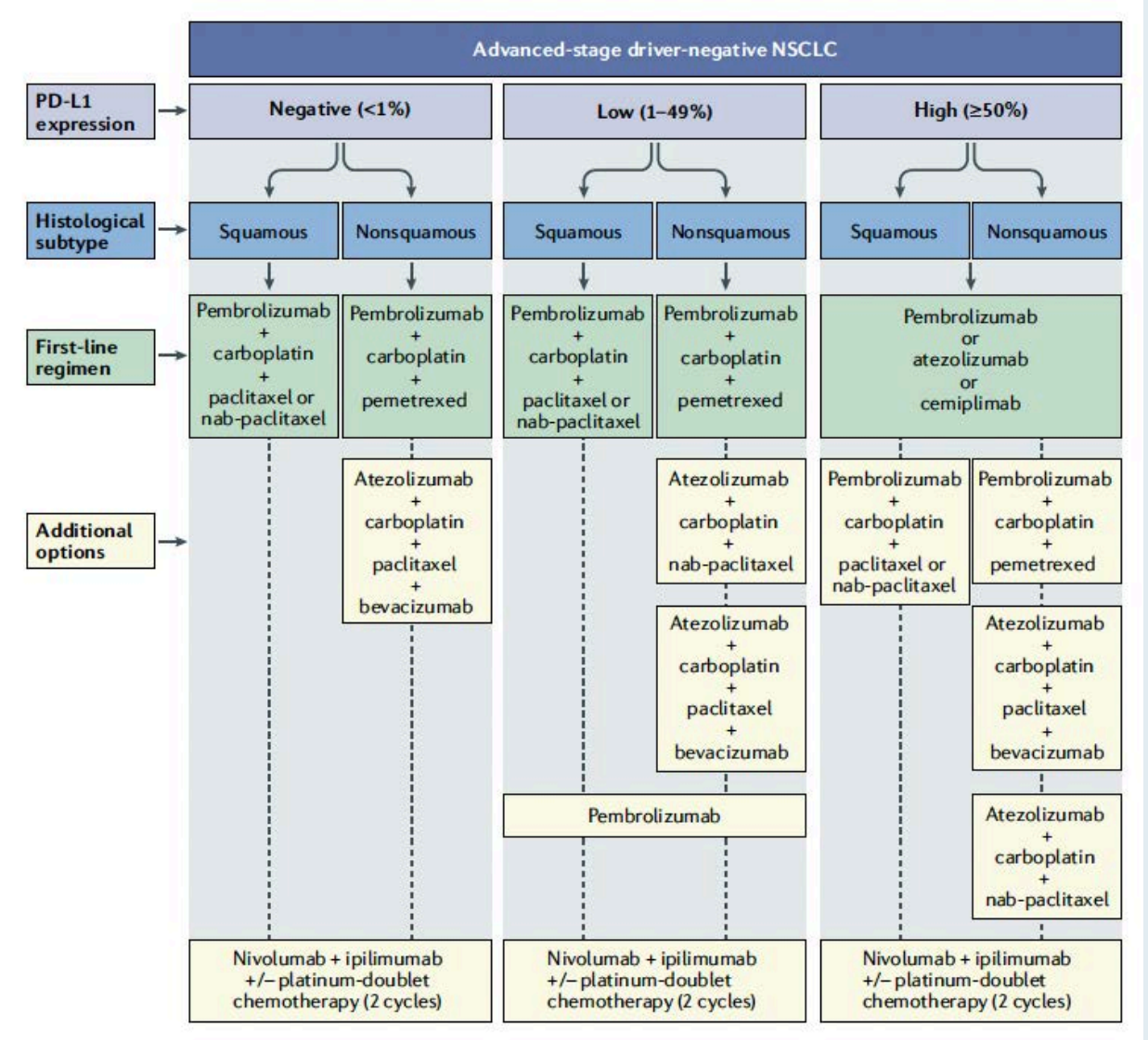
Lu BY et al. *JTO Clin Res Rep* 2021;2(6):100183.

Nat Rev Clin Oncol 2021;18(10):625-44

Selecting the optimal immunotherapy regimen in driver-negative metastatic NSCLC

Michael J. Grant, Roy S. Herbst and Sarah B. Goldberg✉

Immunotherapy-Based Management of Advanced-Stage Driver-Negative NSCLC



Grant MJ et al. *Nat Rev Clin Oncol* 2021;18(10):625-44.

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Case Presentation: A 62-year-old woman with metastatic NSCLC and multiple sclerosis

Dr Richard Polkinghorn (Augusta, Maine)

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Which of the following 3 agents has the best risk-benefit profile when administered as monotherapy for a patient with metastatic NSCLC with no targetable mutations and a high PD-L1 TPS (≥50%) ?

1. Pembrolizumab
2. Atezolizumab
3. Cemiplimab
4. There is no significant difference between the 3 agents

For a patient with metastatic NSCLC and a high PD-L1 TPS (>50%) to whom you've decided to administer anti-PD-1/PD-L1 antibody monotherapy, if one of the 3 approved agents, pembrolizumab, atezolizumab or cemiplimab, were priced 50% below the other 2 agents, would you preferentially use it?

1. Yes
2. Yes, depending on the agent
3. No

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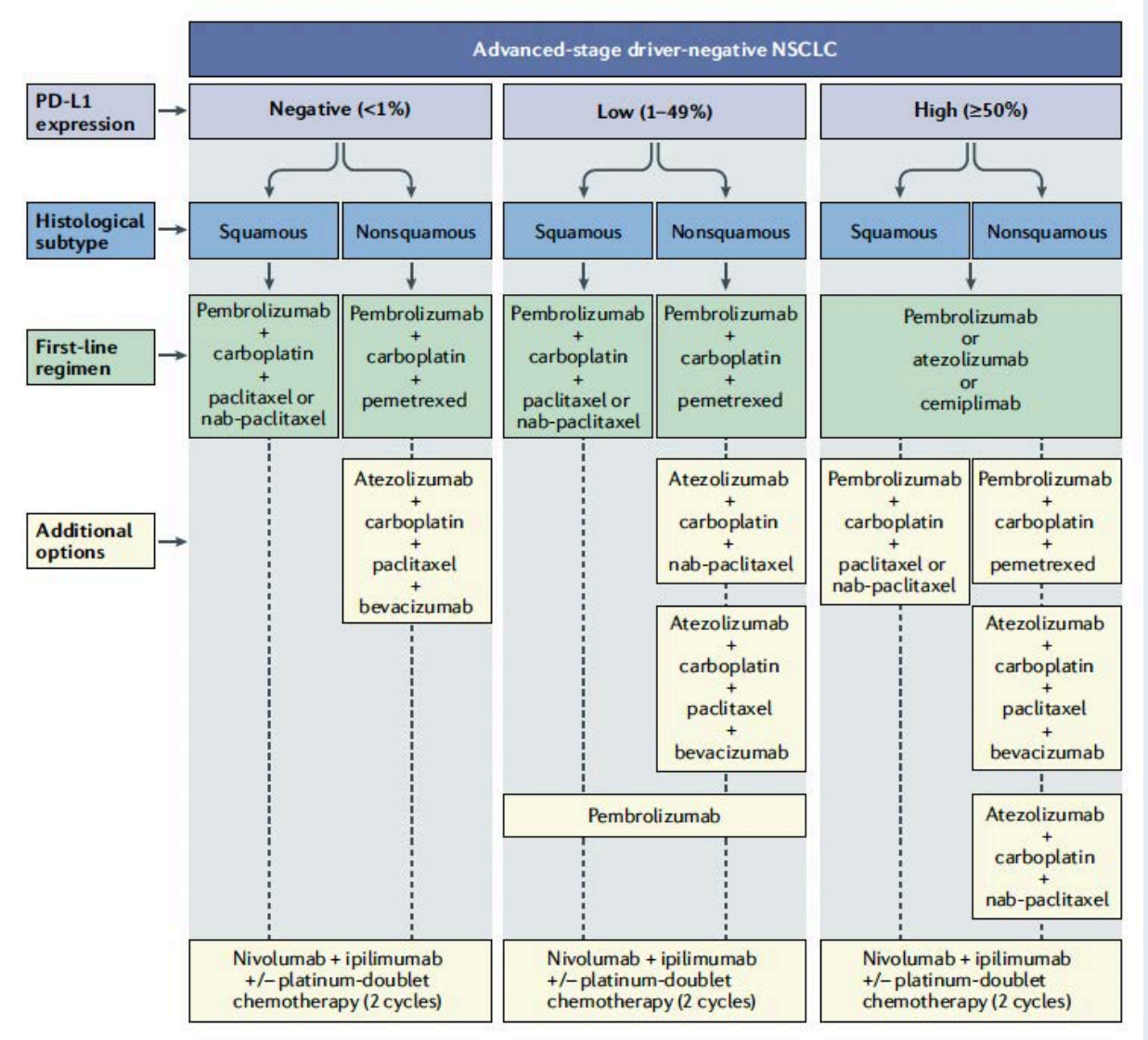
Immunotherapy-Based Management of Advanced-Stage Driver-Negative NSCLC



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A recent meta-analysis evaluating the benefits of immunotherapy (IO) alone versus an IO with chemotherapy for patients with NSCLC and high PD-1 demonstrated which outcome?

1. IO with chemotherapy improves response rate (RR), progression-free survival (PFS) and overall survival
2. IO with chemotherapy improves RR and PFS
3. I am not familiar with these data

Case Presentation: A 77-year-old woman with progressive metastatic adenocarcinoma of the lung — PD-L1 90%

Dr John Yang (Fall River, Massachusetts)

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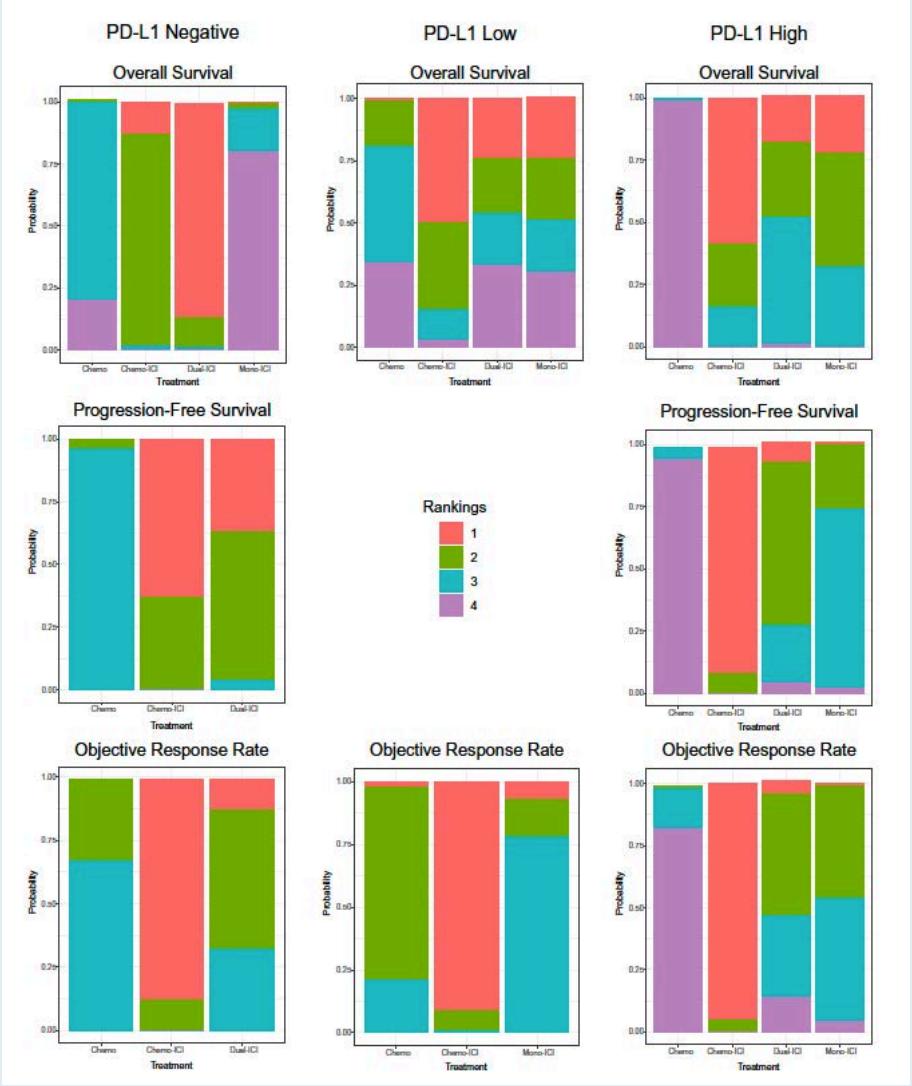
Cancer 2021;127(5):709-19.

Original Article

Comparative Efficacy of Chemoimmunotherapy Versus Immunotherapy for Advanced Non–Small Cell Lung Cancer: A Network Meta-Analysis of Randomized Trials

Ranjan Pathak, MBBS, MHS [1]; Gilberto De Lima Lopes, MD, MPH[2]; Han Yu, MBBS, PhD[3]; Madan Raj Aryal, MBBS[3,4]; Wenyan Ji, MA[3]; Katherine Stemmer Frumento, MLS, MBA[5]; Christopher J. D. Wallis, MD, PhD [6]; Zachary Klaassen, MD, MSc [7,8]; Henry S. Park, MD, MPH [9]; and Sarah B. Goldberg, MD, MPH [1]

Bayesian Ranking Profiles of the Efficacy of First-Line Treatments for Advanced NSCLC Stratified by PD-L1 Subset



Pathak R et al. *Cancer* 2021;127(5):709-19.

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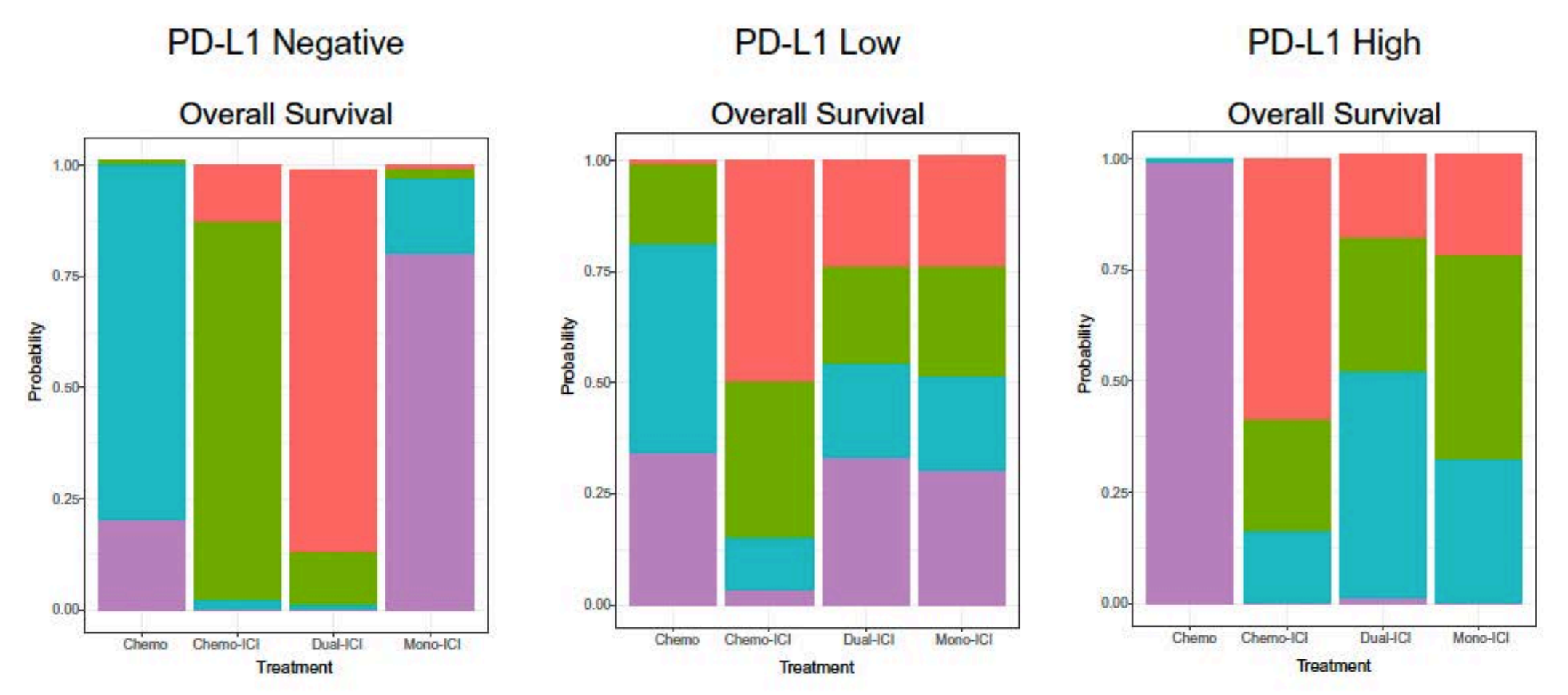
Bayesian Ranking Profiles of the Efficacy of First-Line Treatments for Advanced NSCLC Stratified by PD-L1 Subset: Overall Survival



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Exploring the Potential Benefits of Various Adjuvant and Neoadjuvant Therapeutic Approaches for Patients with Early-Stage Non-Small Cell Lung Cancer

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Localized Lung Survey Respondents

Medical Oncologists

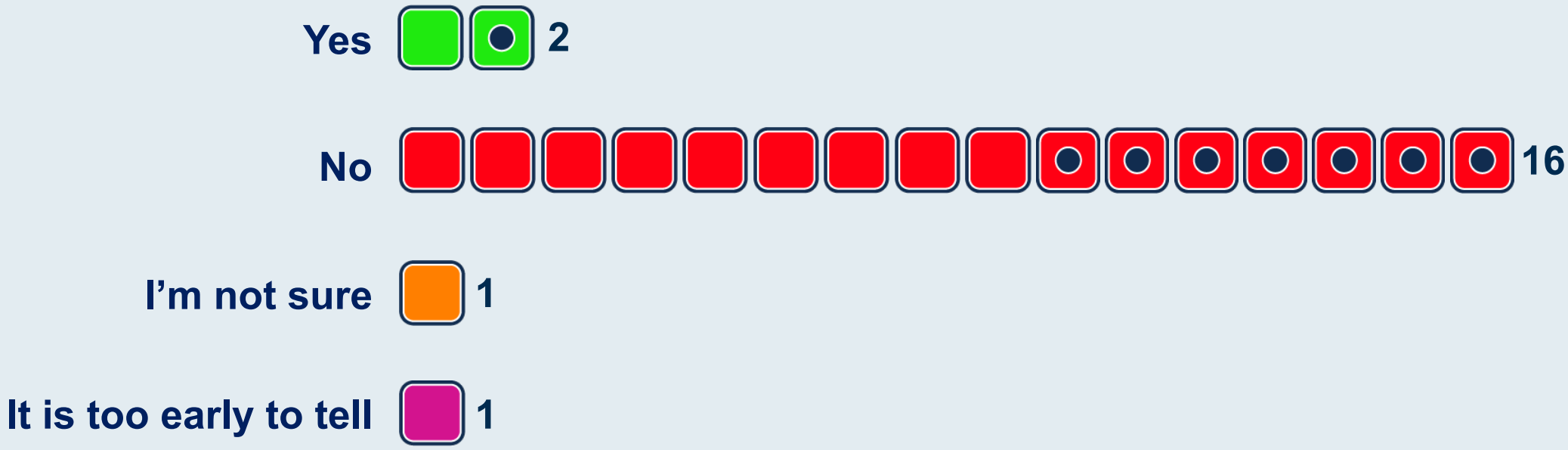
Julie R Brahmer, MD, MSc
D Ross Camidge, MD, PhD
Jamie E Chaft, MD
Matthew Gubens, MD, MS
Corey J Langer, MD
Daniel Morgensztern, MD
Solange Peters, MD, PhD
Gregory J Riely, MD, PhD
Jonathan W Riess, MD, MS
Lecia V Sequist, MD, MPH
David R Spigel, MD
Anne S Tsao, MD, MBA

Thoracic Surgeons

Mara Antonoff, MD
Leah Backhus, MD, MPH
Jules Lin, MD
Bernard J Park, MD
Harvey I Pass, MD
Brendon M Stiles, MD
Eric Vallieres, MD
Stephen C Yang, MD

RTP RESEARCH TO PRACTICE

Based on available data and your clinical experience, does neoadjuvant immunotherapy (alone or with chemotherapy) increase the risk of surgical complications for patients with NSCLC?



Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

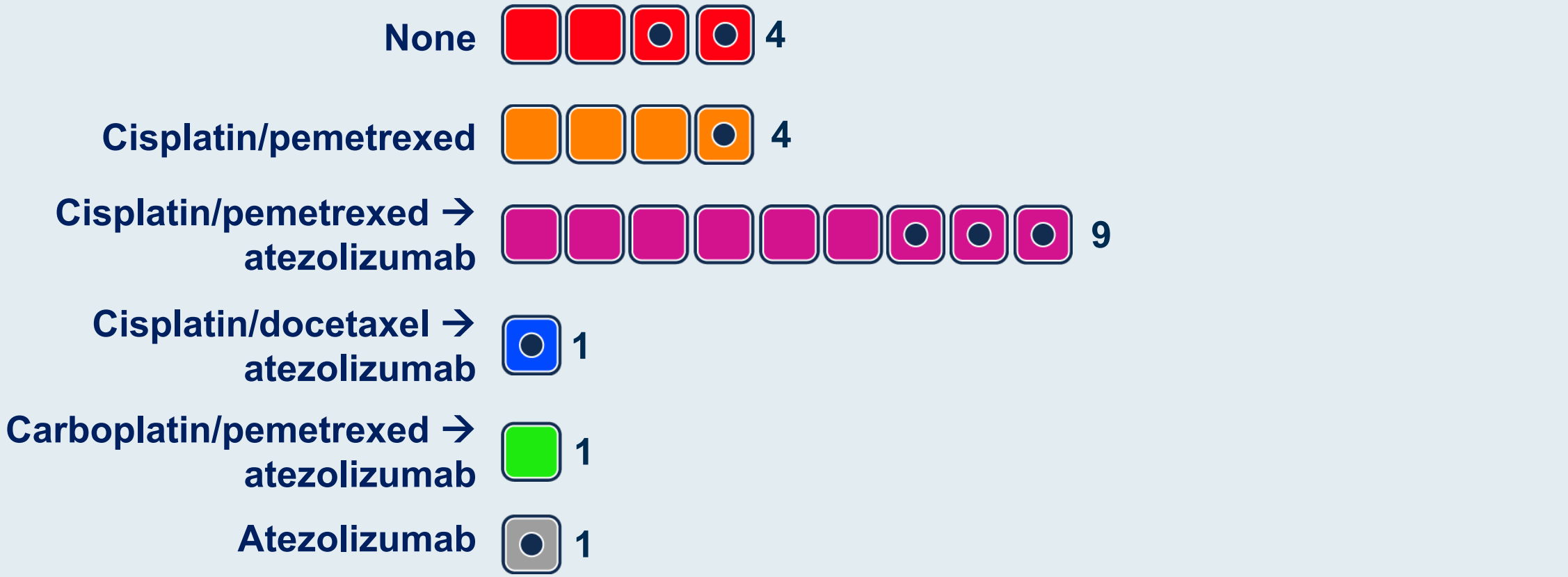
In general, which adjuvant treatment, if any, would you recommend for an otherwise healthy 65-year-old patient with Stage IB nonsquamous NSCLC and a PD-L1 TPS of 5%?

Medical oncologist

Thoracic surgeon

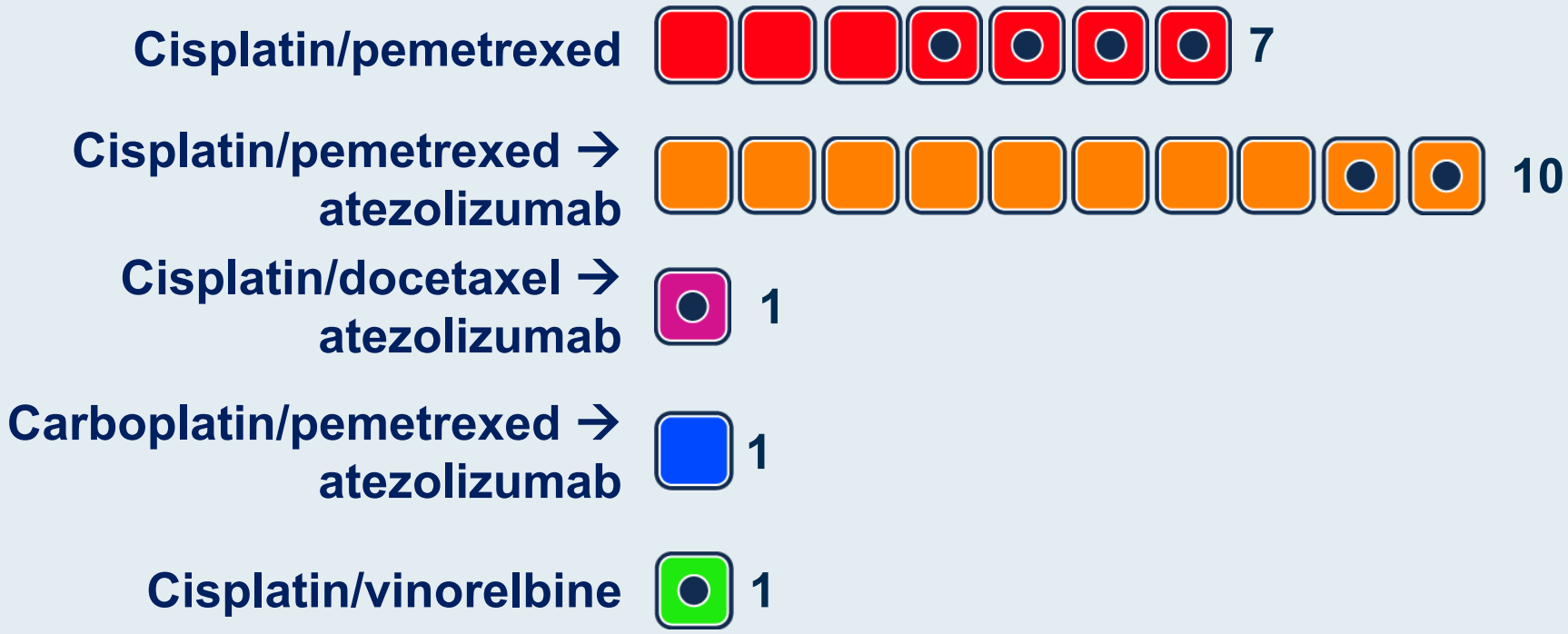
Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

In general, which adjuvant treatment, if any, would you recommend for an otherwise healthy 65-year-old patient with Stage IB nonsquamous NSCLC and a PD-L1 TPS of 50%?



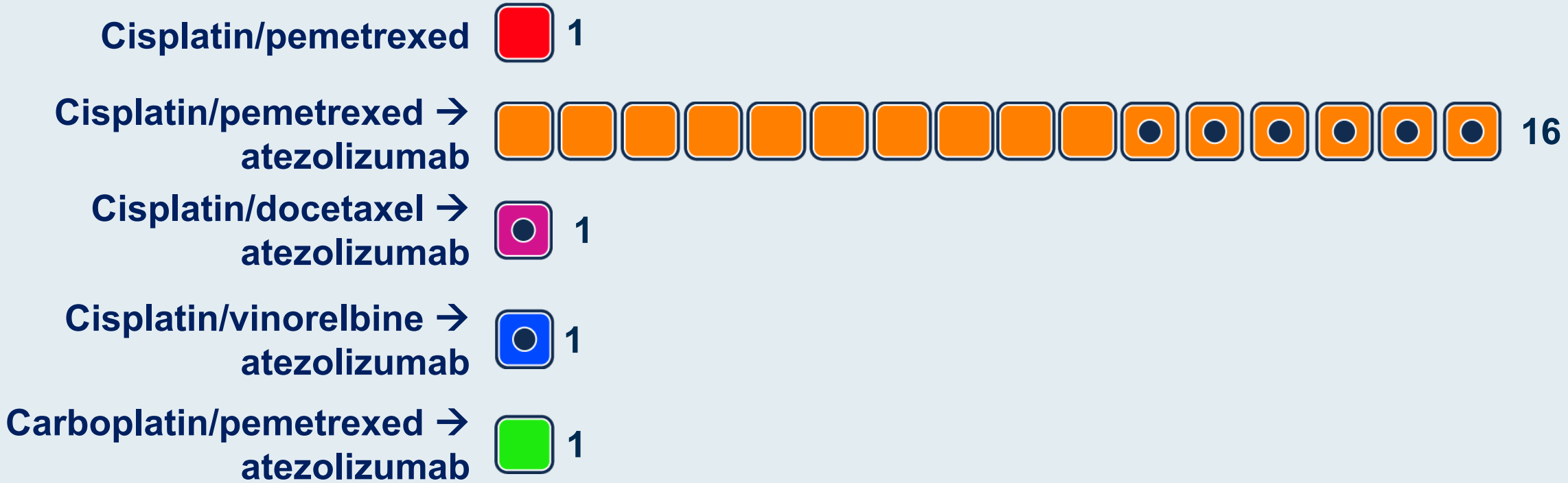
Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

In general, which adjuvant treatment, if any, would you recommend for an otherwise healthy 65-year-old patient with Stage IIA nonsquamous NSCLC and a PD-L1 TPS of 5%?



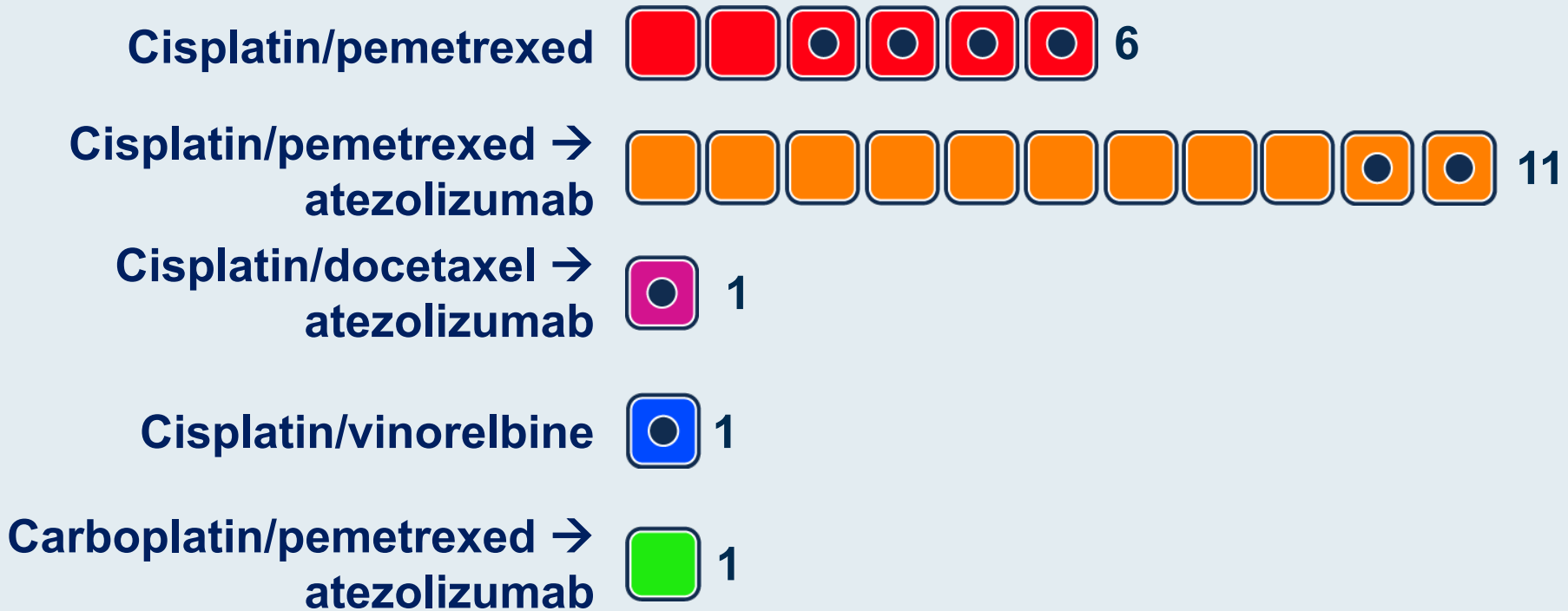
Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

In general, which adjuvant treatment, if any, would you recommend for an otherwise healthy 65-year-old patient with Stage IIA nonsquamous NSCLC and a PD-L1 TPS of 50%?



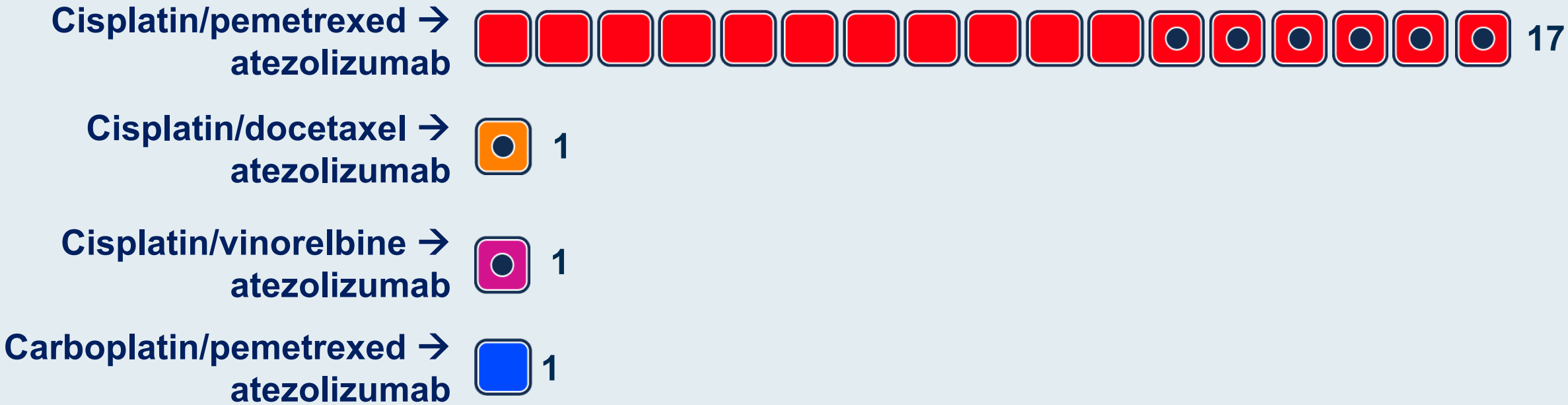
Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

In general, which adjuvant treatment, if any, would you recommend for an otherwise healthy 65-year-old patient with Stage IIB nonsquamous NSCLC and a PD-L1 TPS of 5%?



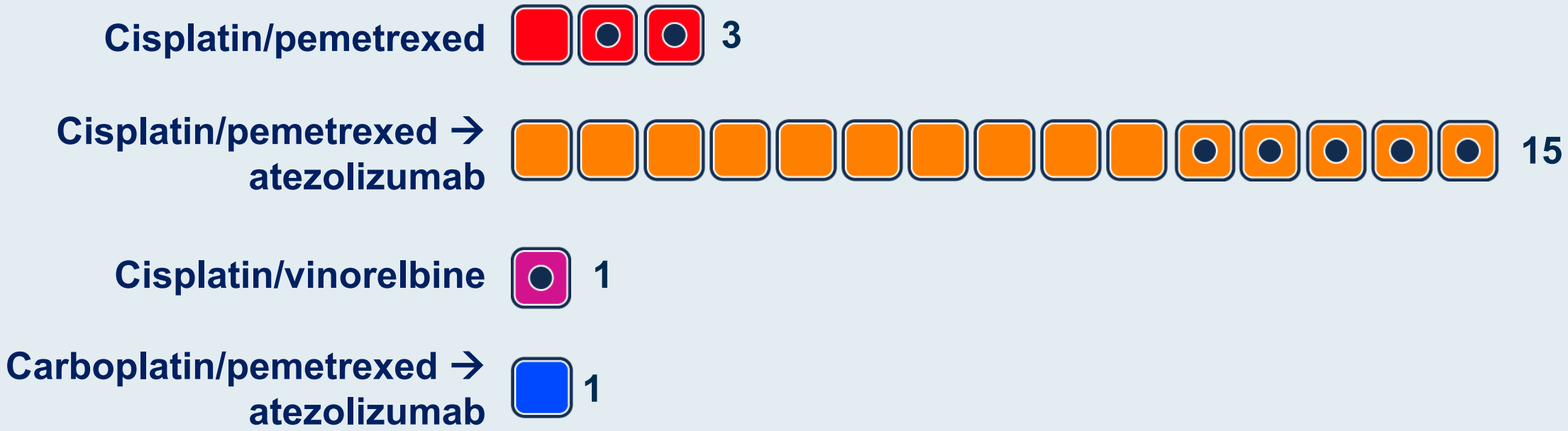
Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

In general, which adjuvant treatment, if any, would you recommend for an otherwise healthy 65-year-old patient with Stage IIB nonsquamous NSCLC and a PD-L1 TPS of 50%?



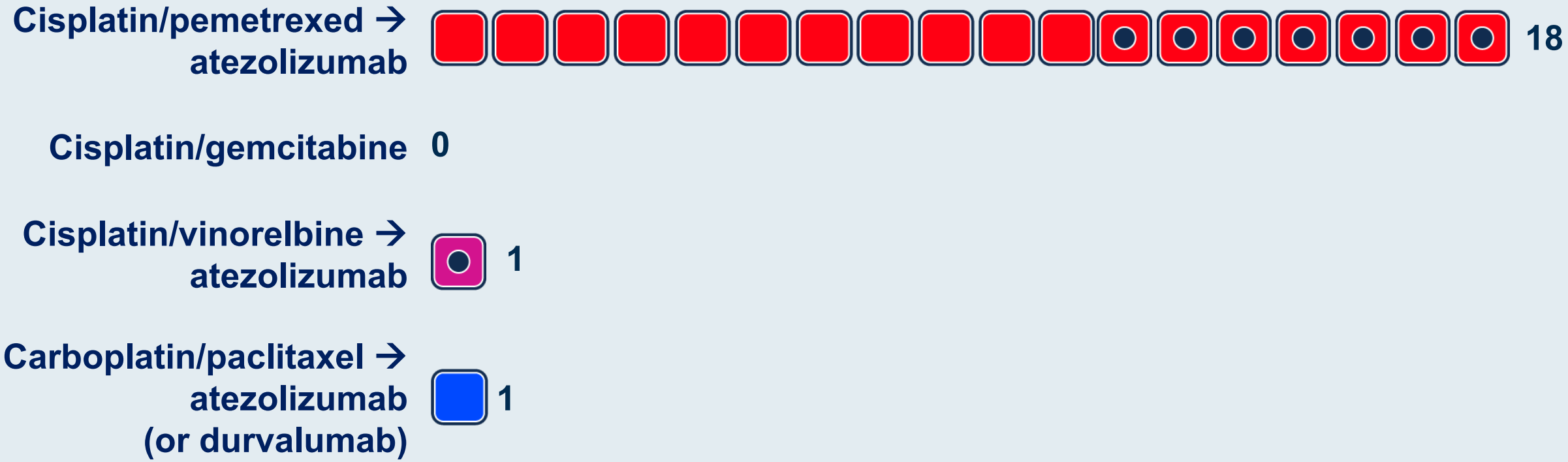
Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

In general, which adjuvant treatment, if any, would you recommend for an otherwise healthy 65-year-old patient with Stage IIIA nonsquamous NSCLC and a PD-L1 TPS of 5%?



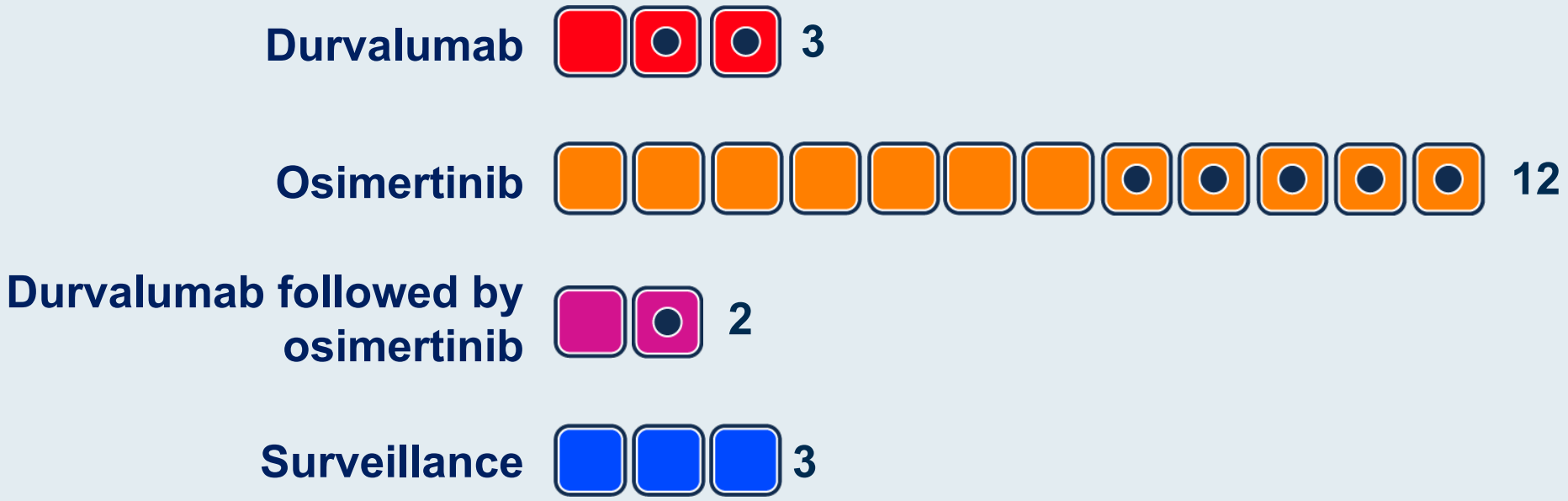
Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

In general, which adjuvant treatment, if any, would you recommend for an otherwise healthy 65-year-old patient with Stage IIIA nonsquamous NSCLC and a PD-L1 TPS of 50%?



Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

What would you most likely recommend as consolidation treatment for a patient with locally advanced NSCLC who has completed chemoradiation therapy and is found to have an EGFR activating mutation?

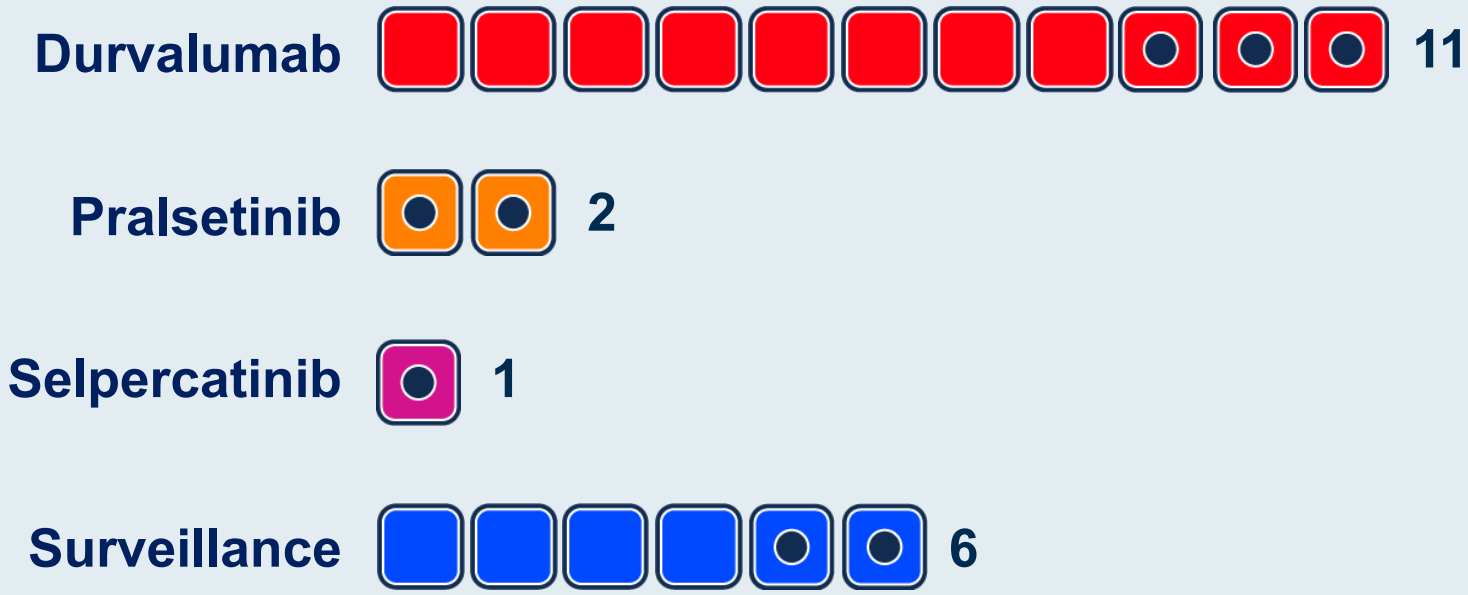


Medical oncologist

Thoracic surgeon

Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

What would you most likely recommend as consolidation treatment for a patient with locally advanced NSCLC who has completed chemoradiation therapy and is found to have a RET fusion?



Survey of medical oncologists who specialize in lung cancer and thoracic surgeons

Recent Advances in Adjuvant Systemic Treatment of Solid Tumors

Disease	Agent or regimen			
NSCLC	Atezolizumab (10-15-21)	Osimertinib (12-18-20)	Durvalumab (2-16-18)	Nivolumab/chemotherapy*
Breast	Abemaciclib (10-13-21)	Olaparib	Pembrolizumab (7-26-21)	T-DM1 (5-3-19)
Upper GI	Nivolumab (5-20-21)			
RCC	Pembrolizumab (11-17-21)			
Bladder	Nivolumab (8-19-21)	Pembrolizumab† (1-8-2020)		
Ovarian	Olaparib/bevacizumab (5-8-20)	Niraparib (4-29-20)	Olaparib (12-19-18)	
Melanoma	Dabrafenib/trametinib (4-30-18)	Pembrolizumab (2-15-19)	Nivolumab (12-20-17)	
Prostate	Abiraterone (+ LHRH agonist)			

* Neoadjuvant therapy

† Indicated for patients with non-muscle-invasive bladder cancer who are not eligible for cystectomy but who may have undergone TURBT

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EORTC European Organisation for Research and Treatment of Cancer
The future of cancer therapy

etop
Information | Research

Pembrolizumab Versus Placebo For Early-Stage NSCLC Following Complete Resection and Adjuvant Chemotherapy When Indicated: Randomized, Triple-Blind, Phase 3 EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 Study

L. Paz-Ares,[1*] M. O'Brien,[2*] M. Mauer,[3] U. Dafni,[4] K. Oselin,[5] L. Havel,[6] E. Esteban,[7] D. Isla,[8] A. Martinez-Marti,[9] M. Faehling,[10] M. Tsuboi,[11] J.S. Lee,[12] K. Nakagawa,[13] J. Yang,[14] S.M. Keller,[14] N. Jha,[3] S. Marreaud,[3] R. Stahel,[15] S. Peters,[16**] B. Besse[17**] on behalf of the PEARLS/KEYNOTE-091 Investigators

[1]Hospital Universitario 12 de Octubre, CNIO, Ciberonc & Universidad Complutense, Madrid, Spain; [2]Royal Marsden Hospital, London, UK; [3]European Organisation for Research and Treatment of Cancer, Headquarters Brussels, Belgium; [4]National and Kapodistrian University of Athens and Frontier Science Foundation Hellas; [5]North Estonia Medical Centre, Tallinn, Estonia; [6]Charles University and Thomayer Hospital, Prague, Czech Republic; [7]Hospital Universitario Central de Asturias, Oviedo, Spain; [8]University Hospital Lozano Blesa, IIS Aragon, Zaragoza, Spain; [9]Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; [10]Klinikum Esslingen, Esslingen, Germany; [11]National Cancer Center Hospital East, Kashiwa, Japan; [12]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea; [13]Kindai University Faculty of Medicine, Osaka, Japan; [14]Merck & Co., Inc., Kenilworth, NJ, USA; [15]European Thoracic Oncology Platform, Bern, Switzerland; [16]Lausanne University Hospital, Lausanne, Switzerland; [17]Institut Gustave Roussy, Villejuif, France
*Drs. Paz-Ares and O'Brien contributed equally to this presentation. **Drs. Peters and Besse contributed equally to this presentation.

ESMO

Early-Stage Non-Small-Cell Lung Cancer (NSCLC)

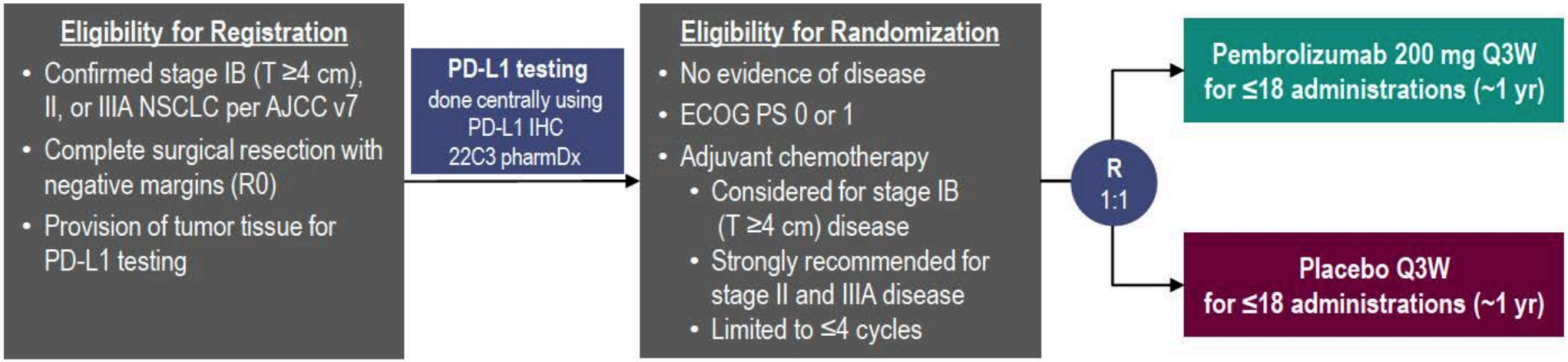
- Encompasses stage I to IIIA disease
- Accounts for ~50% of all NSCLC diagnoses[1]
- Standard treatment is resection followed by adjuvant platinum-based chemotherapy for stage IB (T ≥4 cm) to IIIA disease[2]
- Absolute 5-year overall survival benefit for adjuvant chemotherapy is modest at 5% over observation alone[3,4]
- Atezolizumab (anti–PD-L1) improved DFS versus best supportive care following complete resection and adjuvant chemotherapy for stage II to IIIA NSCLC that expresses PD-L1 on ≥1% of tumor cells[5]

1. Ganti AK et al. *JAMA Oncol* 2021;7:1824-32. 2. Remon J et al. *Ann Oncol* 2021;32:1637-42. 3. Pignon JP et al. *J Clin Oncol* 2008;26:3552-9.
4. NSCLC Meta-analyses Collaborative Group et al. *Lancet* 2010;375:1267-77. 5. Felip E et al. *Lancet* 2021;398:1344-57.

Paz-Ares L et al. ESMO Virtual Plenary 2022;Abstract VP3-2022.

PEARLS/KEYNOTE-091 Study Design

Randomized, Triple-Blind, Phase 3 Trial



Stratification Factors

- Disease stage (IB vs II vs IIIA)
- PD-L1 TPS (<1% vs 1-49% vs ≥50%)
- Receipt of adjuvant chemotherapy (yes vs no)
- Geographic region (Asia vs Eastern Europe vs Western Europe vs rest of world)

Dual Primary End Points

- DFS in the overall population
- DFS in the PD-L1 TPS ≥50% population

Secondary End Points

- DFS in the PD-L1 TPS ≥1% population
- OS in the overall, PD-L1 TPS ≥50%, and PD-L1 TPS ≥1% populations
- Lung cancer-specific survival in the overall population
- Safety

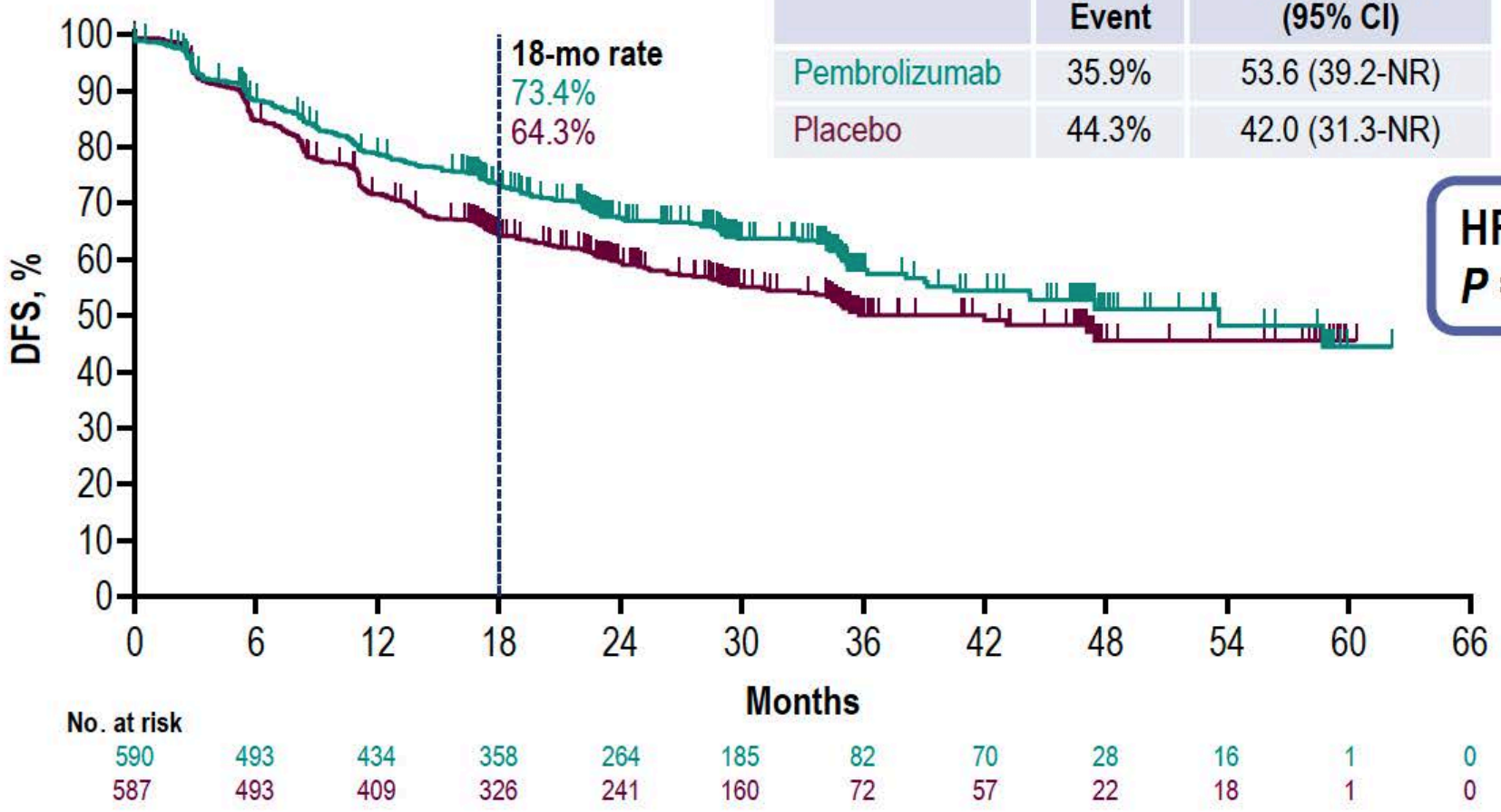
ESMO VIRTUAL PLENARY

ClinicalTrials.gov number, NCT02504372.

Paz-Ares L et al. ESMO Virtual Plenary 2022;Abstract VP3-2022.

DFS, Overall Population

	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	35.9%	53.6 (39.2-NR)
Placebo	44.3%	42.0 (31.3-NR)



HR 0.76 (95% CI, 0.63-0.91)
***P* = 0.0014**

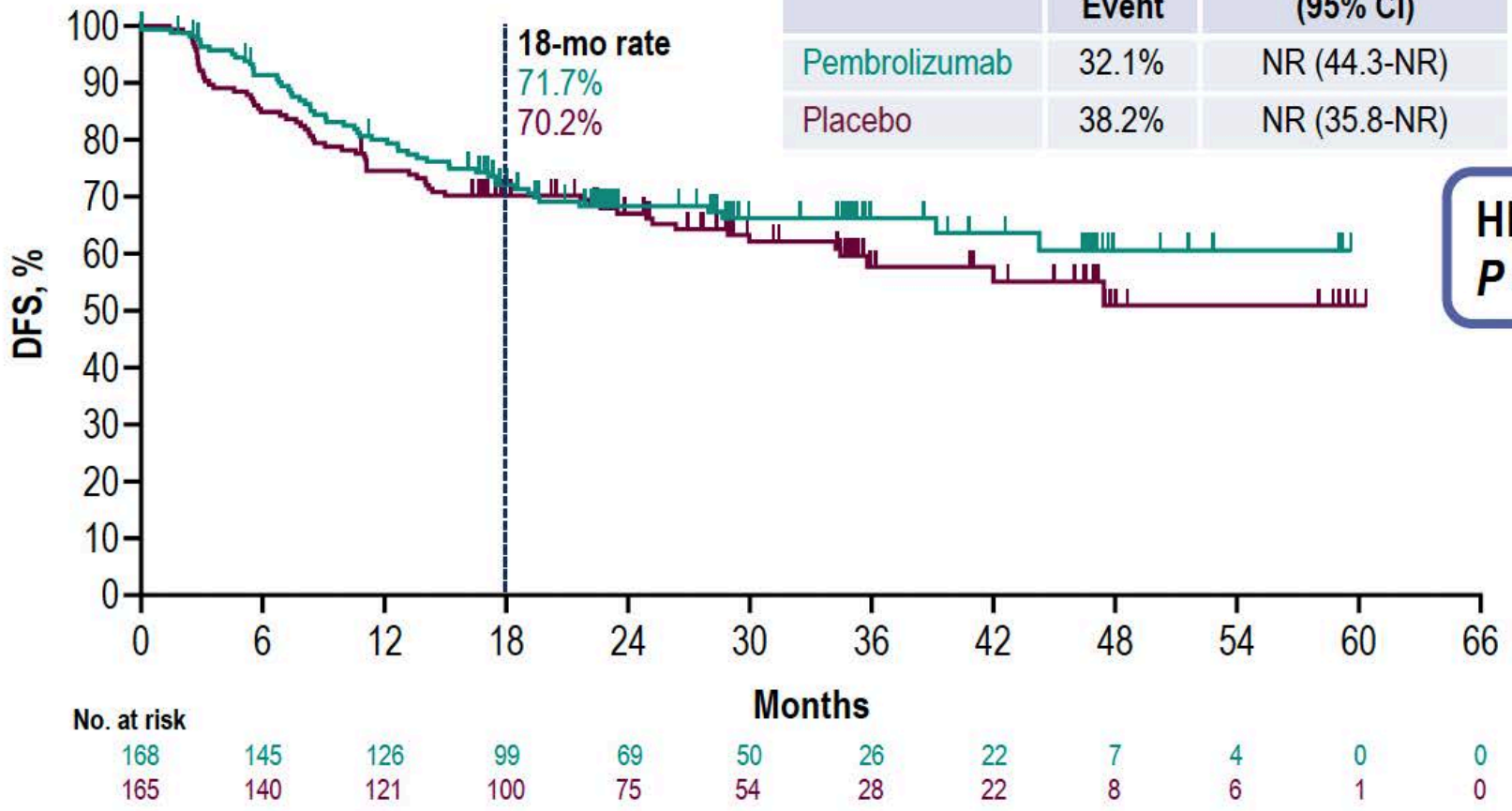
ESMO VIRTUAL PLENARY

Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: September 20, 2021

Paz-Ares L et al. ESMO Virtual Plenary 2022;Abstract VP3-2022.

DFS, PD-L1 TPS ≥50% Population

	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	32.1%	NR (44.3-NR)
Placebo	38.2%	NR (35.8-NR)



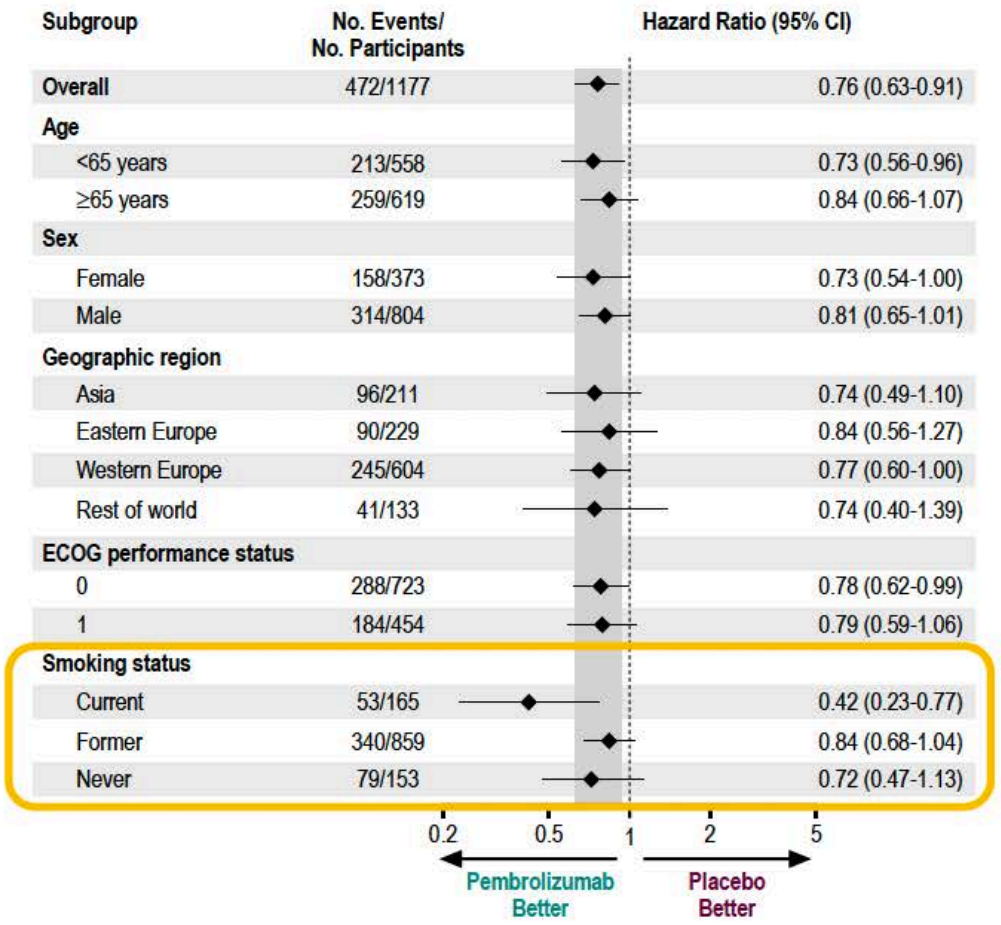
HR 0.82 (95% CI, 0.57-1.18)
***P* = 0.14**

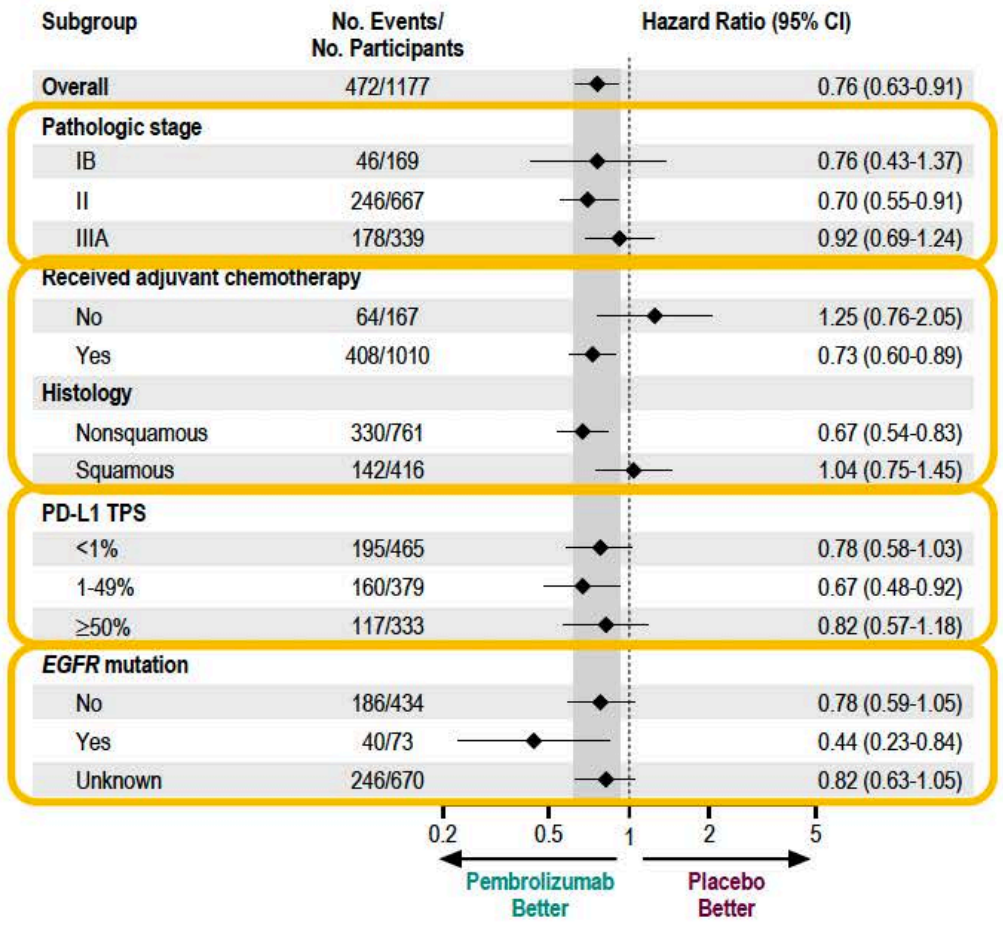
ESMO VIRTUAL PLENARY

Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: September 20, 2021

Paz-Ares L et al. ESMO Virtual Plenary 2022;Abstract VP3-2022.

DFS in Key Subgroups, Overall Population





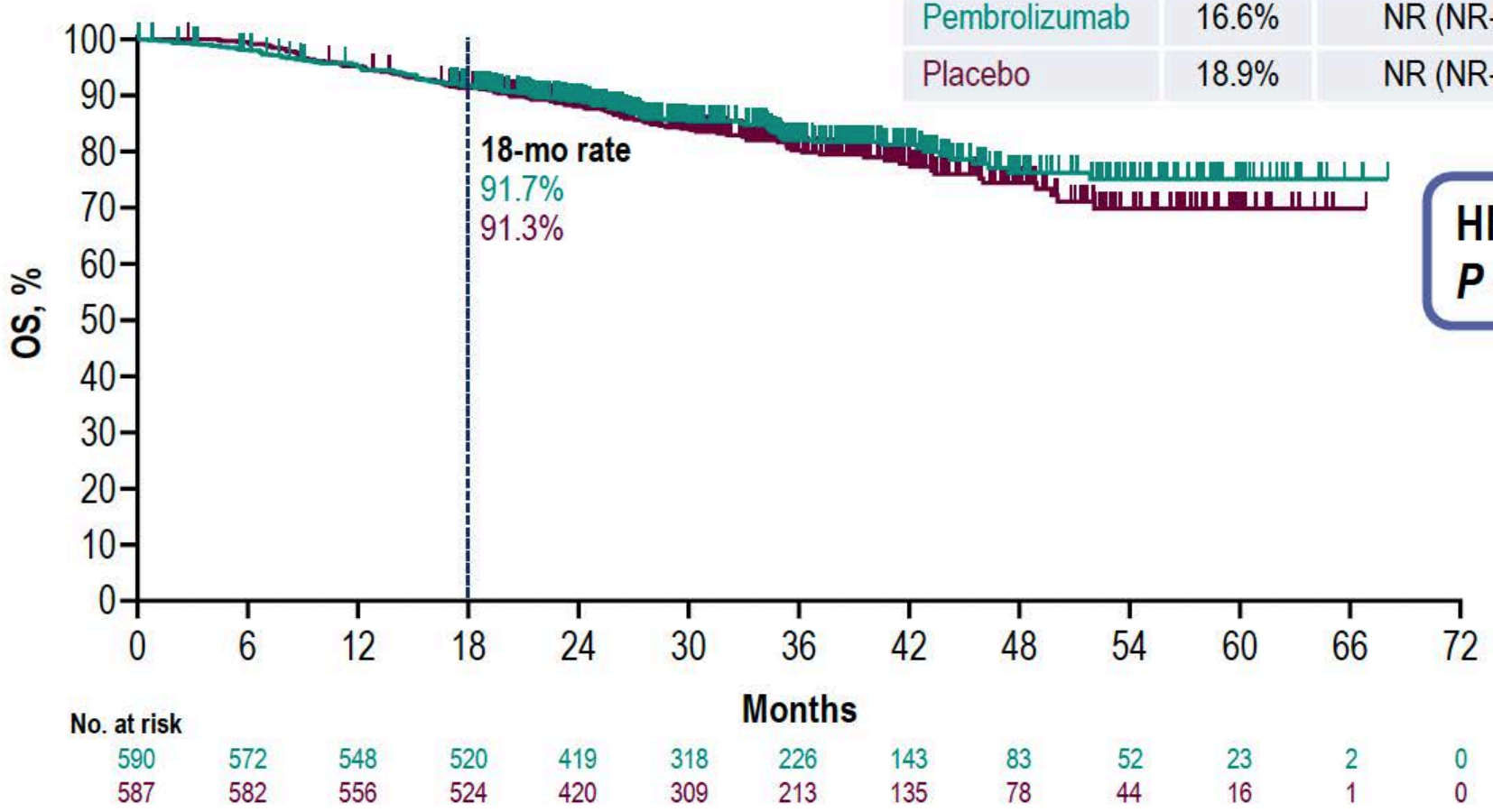
ESMO VIRTUAL PLENARY

Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: September 20, 2021

Paz-Ares L et al. ESMO Virtual Plenary 2022;Abstract VP3-2022.

OS, Overall Population

	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	16.6%	NR (NR-NR)
Placebo	18.9%	NR (NR-NR)



HR 0.87 (95% CI, 0.67-1.15)
***P* = 0.17**

ESMO VIRTUAL PLENARY

Data cutoff date: September 20, 2021

Paz-Ares L et al. ESMO Virtual Plenary 2022;Abstract VP3-2022.

Summary and Conclusions

- Pembrolizumab provided statistically significant, clinically meaningful DFS improvement versus placebo in the overall population
  - Median DFS of 53.6 months with pembrolizumab vs 42.0 months with placebo (HR, 0.76)
  - Generally consistent DFS benefit in participants with PD-L1 TPS <1%, 1-49%, and ≥50%
  - OS data are immature
  - DFS in the PD-L1-defined populations and OS will be tested at future analyses according to the analysis plan
- Pembrolizumab safety profile as expected
- **Data suggest pembrolizumab has the potential to be a new adjuvant treatment option for patients with stage IB (T ≥4 cm) to IIIA NSCLC following complete resection and adjuvant chemotherapy when recommended, regardless of PD-L1 expression**

ESMO VIRTUAL PLENARY

RTP RESEARCH TO PRACTICE

Paz-Ares L et al. ESMO Virtual Plenary 2022;Abstract VP3-2022.

ESMO VIRTUAL PLENARY

Pembrolizumab Versus Placebo For Early-Stage NSCLC Following Complete Resection and Adjuvant Chemotherapy When Indicated: Randomized, Triple-Blind, Phase 3 EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 Study

Lessons to learn….

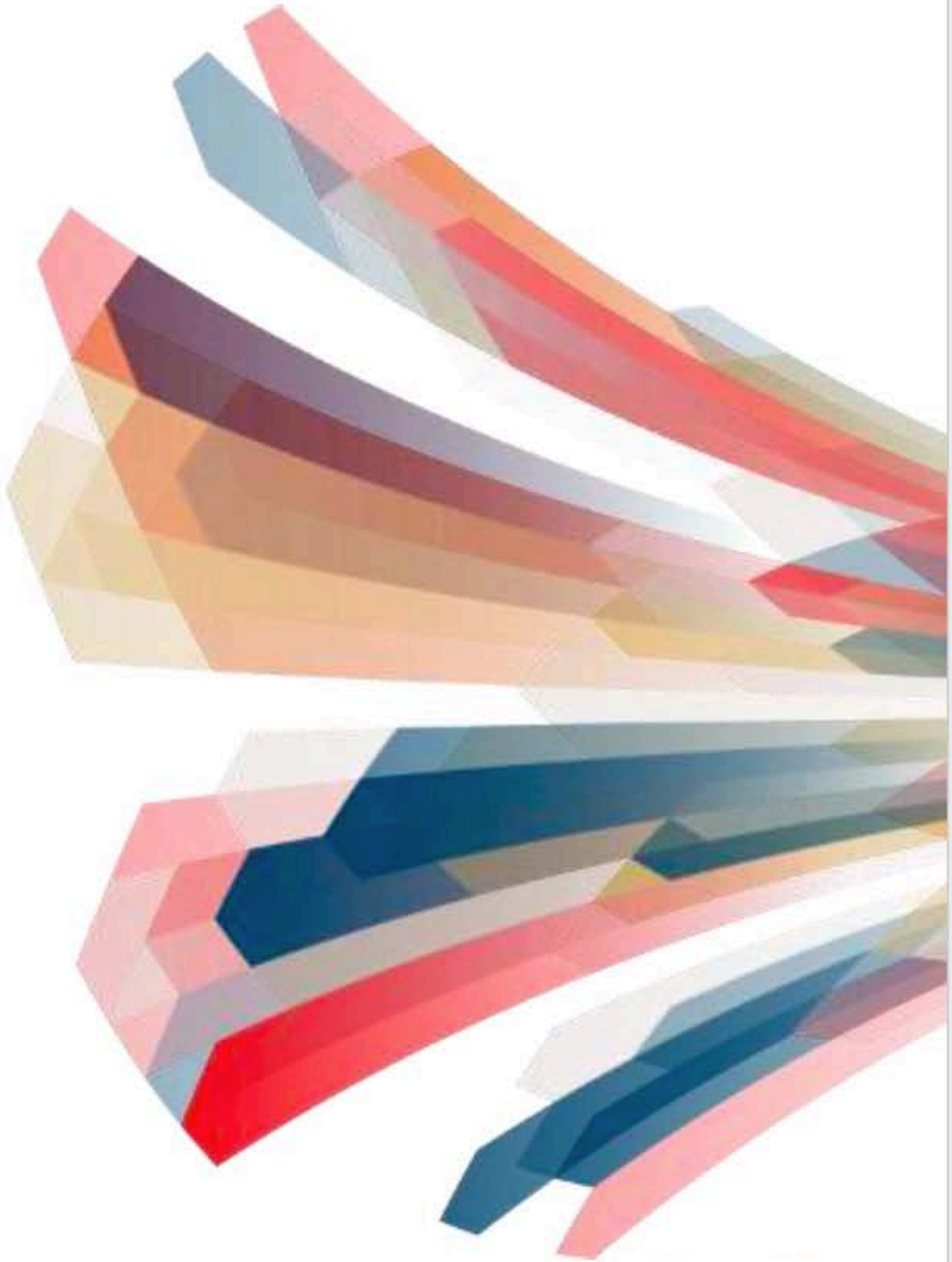
Martin Reck

Department of Thoracic Oncology

Airway Research Center North, German Center for Lung Research

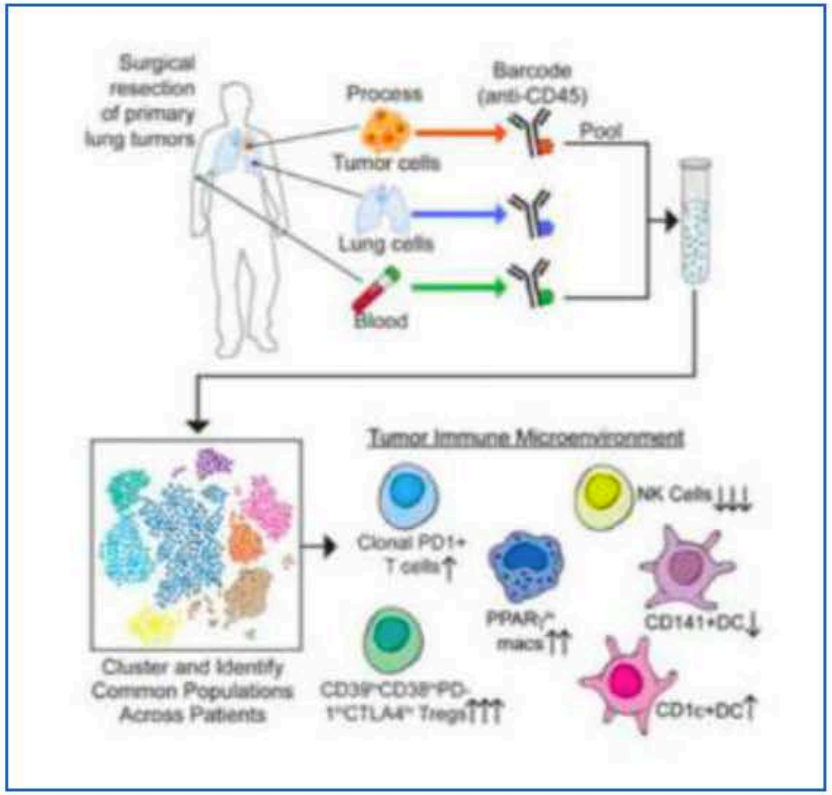
LungenClinic Grosshansdorf

Germany



EARLY NSCLC – AN ATTRACTIVE TARGET FOR IMMUNOTHERAPY

Immunosuppressive Microenvironment in early stage, resectable Adenocarcinoma



Lavin Y et al, Cell 2017

Reck M. ESMO Virtual Plenary 2022; Discussant

COMMON GROUNDS AND DISCREPANCIES

	Impower 010	PEARLS
Control arm	BSC	Placebo
Primary EP	DFS II-IIIa, PDL-1 =/> 1% Hierarchical testing DFS II-IIIa all comers	DFS Ib-IIIa all comers DFS Ib-IIIa PD-L1 =/> 50%
Randomized patients	1280	1177
Stage I/II/IIIa	11.8%, 46.7%, 41.1%	14.3%, 56.7%, 28.8%
PD-L1	44% <1%, 53.5% > 1% (SP263)	39.5% < 1%, 32.3% 1-49%, 28.3% =/> 50% (22C3 Dako)
Adjuvant chemotherapy	1-4 cycles cisplatinum based CT oblig.	Recommended in stage II/IIIa
Follow up	32.8 m	35.6 m

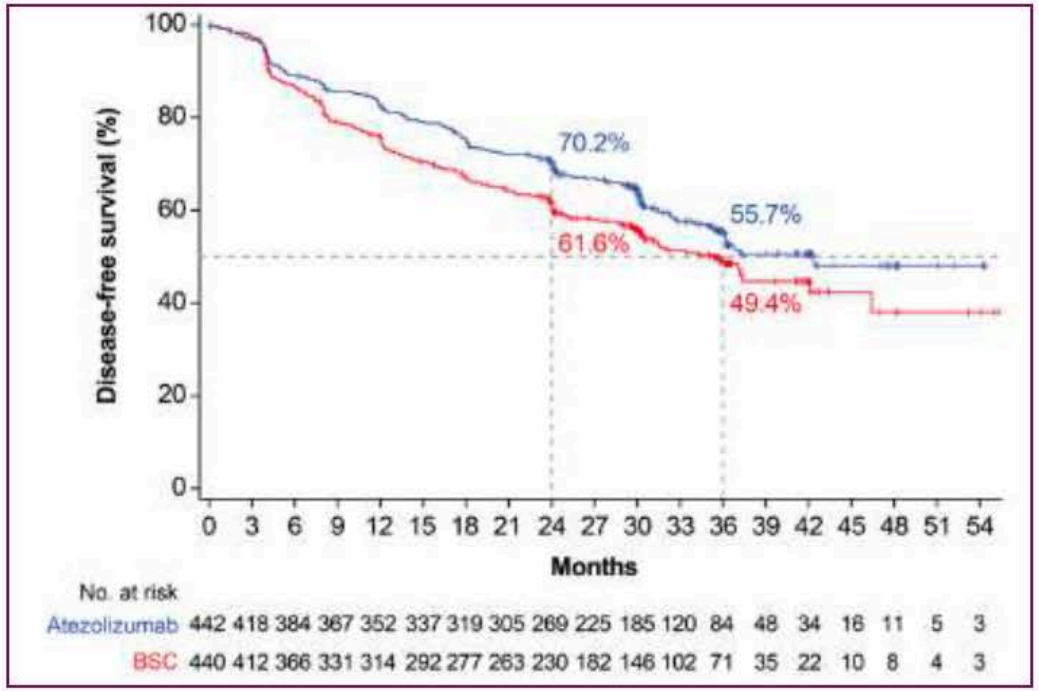
Felip E et al, Lancet 2021, Paz-Ares L et al, ESMO Plenary 2022

ESMO VIRTUAL PLENARY

OUTCOMES – NOT SO DIFFERENT

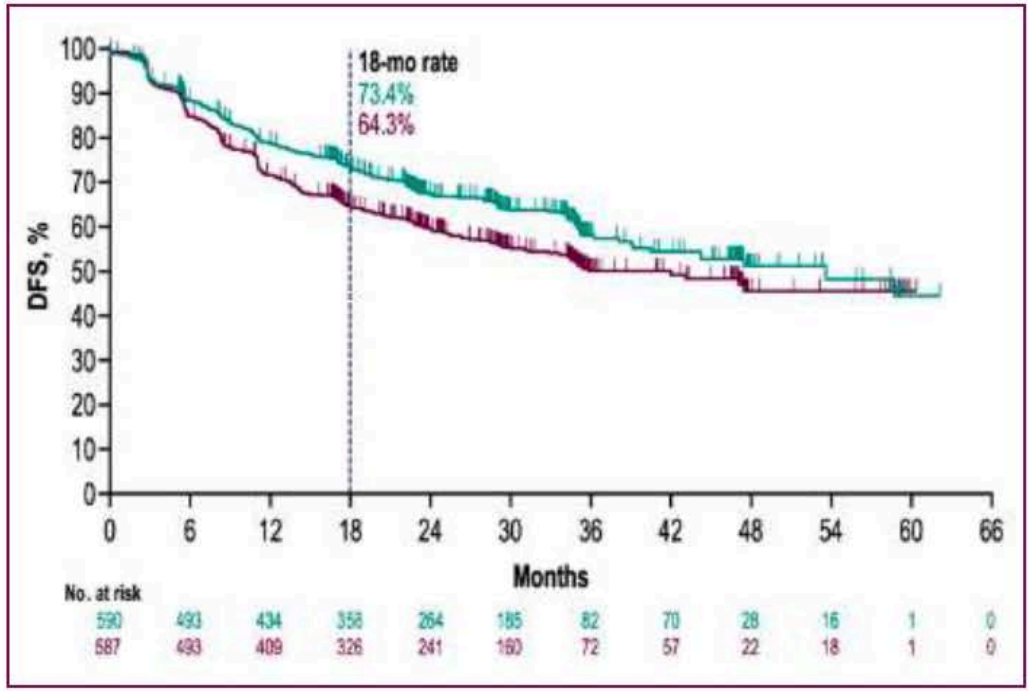
Wakelee, H et al, ASCO 2021, Paz-Ares L et al, ESMO Plenary 2022

Impower 010 – DFS stage II-IIIa (all comers)



HR 0.79 (0.49, 0.96), p 0.02

PEARLS – DFS stage Ib-IIIa (all comers)



HR 0.76 (0.63, 0.91), p 0.0014

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RTP RESEARCH TO PRACTICE

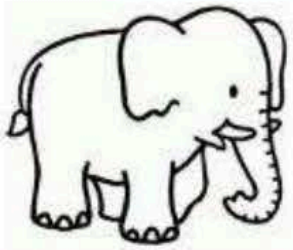
WHERE IS THE ELEPHANT IN THE ROOM?

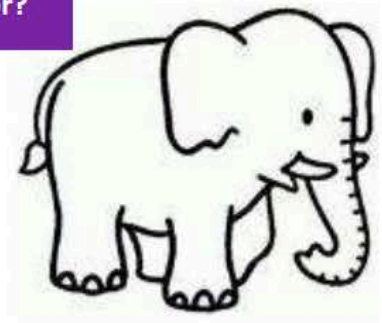
https://www.istockphoto.com/de/fotos/elephant-in-the-room

SO MANY ELEPHANTS!

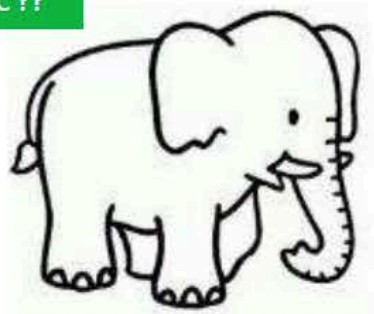
PD-L1 – a good prognostic factor?

Marker?



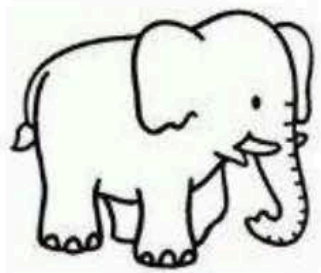


Immunotherapy in EGFR mutated NSCLC ??

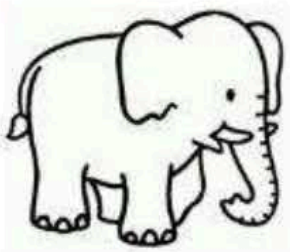


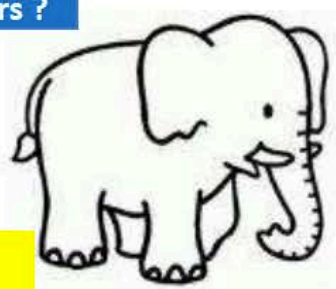
Immunotherapy in PD-L1 negative tumors ??

No Benefit in PD-L1 high expressors ?



DFS = OS??





Adjuvant chemotherapy required for immunotherapy?

Neoadjuvant vs adjuvant Immunotherapy ??

https://ausmalbilder-tiere.com/elefanten-15/

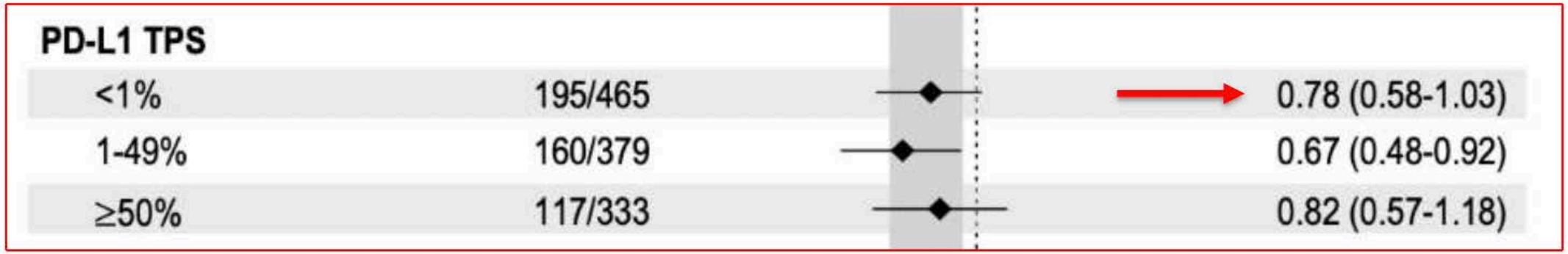
ESMO VIRTUAL PLENARY

Martin Reck

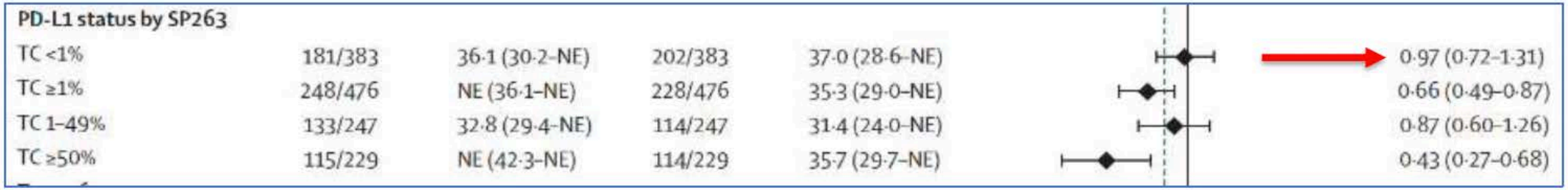
Reck M. ESMO Virtual Plenary 2022; Discussant

WHAT ABOUT THE PD-L1 NEGATIVES?

PEARLS Trial



Impower 010



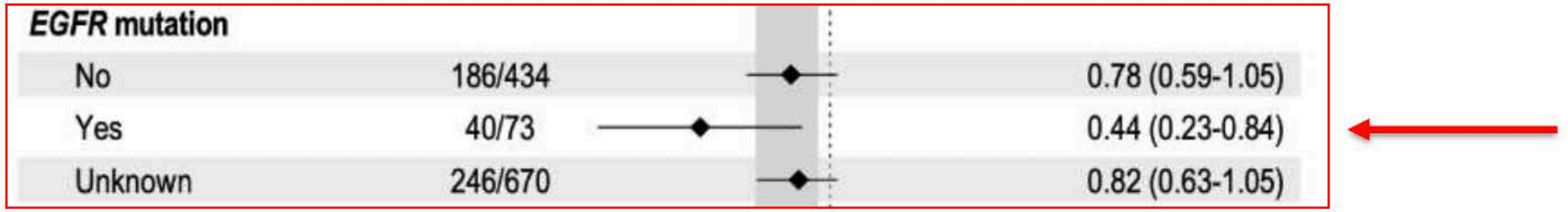
Felip E et al, Lancet 2021, Paz-Ares L et al ESMO Plenary 2022

ESMO VIRTUAL PLENARY

Reck M. ESMO Virtual Plenary 2022; Discussant

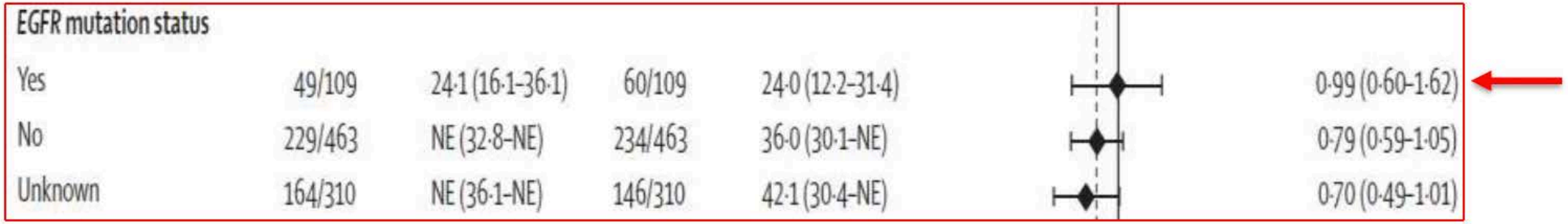
EGFR-MUTATIONS

PEARLS Trial



56% (670/1177) unknown

Impower 010



35% (361/1005) unknown

Felip E et al, Lancet 2021, Paz-Ares L et al ESMO Plenary 2022

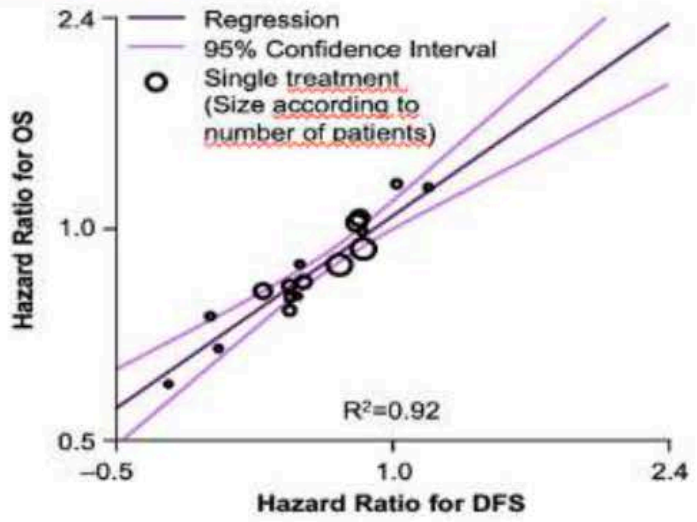
ESMO VIRTUAL PLENARY

Reck M. ESMO Virtual Plenary 2022; Discussant

DFS = OS?

Tibetanian Prayer Wheel

Correlation between DFS and OS in adjuvant Chemotherapy of NSCLC[1]



- Somewhat convincing data, that DFS might be a surrogate marker for OS
- However – so far only data for adjuvant chemotherapy, but not for *adjuvant immuno- or targeted therapies*
- In this early days of adjuvant immunotherapy assesment of more mature OS data essential

Mauguen A, et al. Lancet Oncol 2013

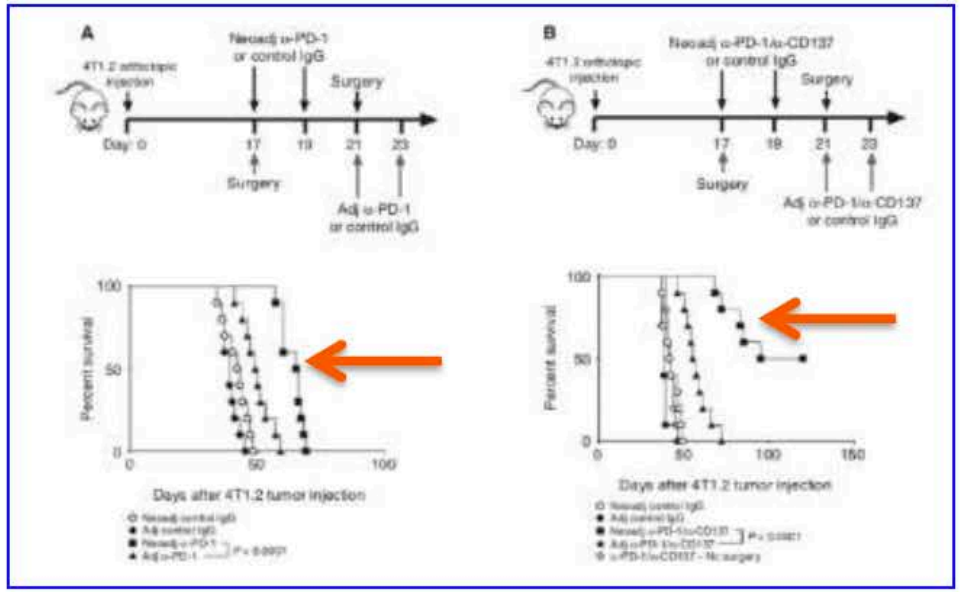
Reck M. ESMO Virtual Plenary 2022; Discussant

NEOADJUVANT VS ADJUVANT IMMUNOTHERAPY

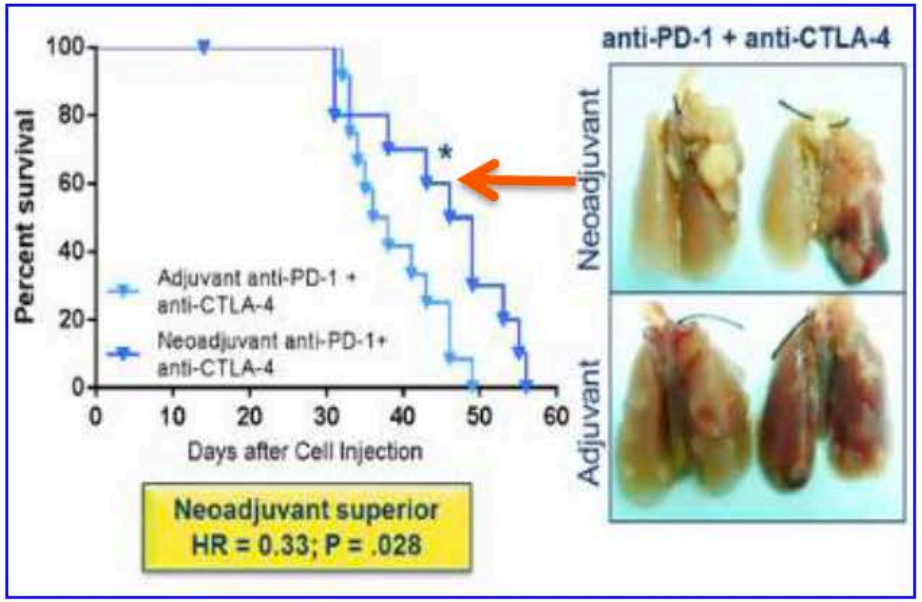
There are multiple arguments for one or the other approach, which already been discussed in multiple meetings…

Potential Benefit for neoadjuvant immunotherapy only seen in preclinical trials, but..

Breast Model



NSCLC Model



Liu J et al, Cancer Discovery 2016; Cascone T et al, AACR 2019

ESMO VIRTUAL PLENARY

Martin Reck

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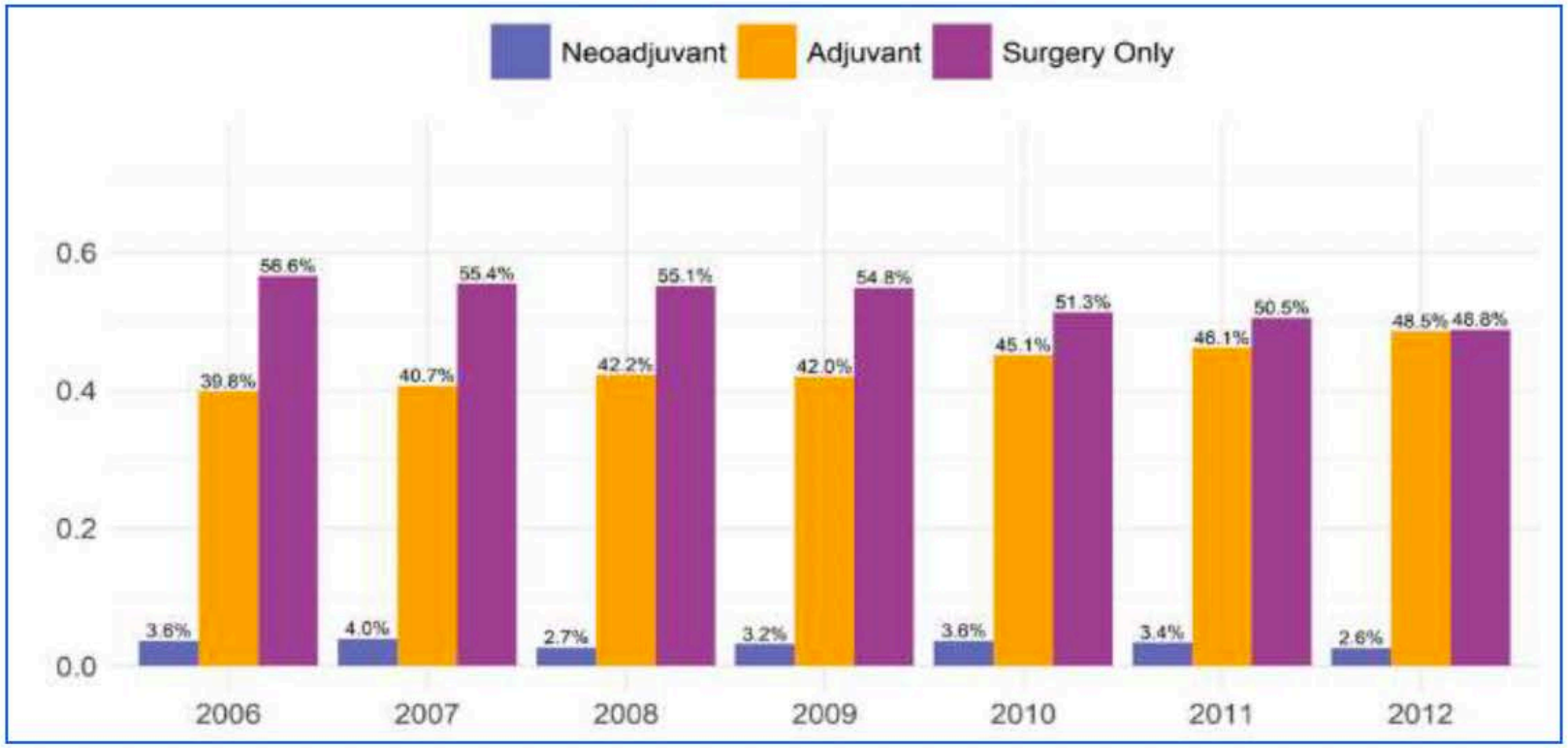
DATA FROM THE NATIONAL CANCER DATABASE

35.134 patients with surgery +/- neo or adjuvant chemotherapy



Adjuvant Therapy	Appr. 53%
Neoadjuvant Therapy	Appr. 3%
Neoadjuvant Therapy Stage II	2.4%

ESMO VIRTUAL PLENARY

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Mac Lean M et al, Oncotarget 2018

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PERHAPS MORE A PHILOSOPHICAL QUESTION…

Current perioperative trials

ESMO VIRTUAL PLENARY

Martin Reck

Courtesy of Jordi Remon

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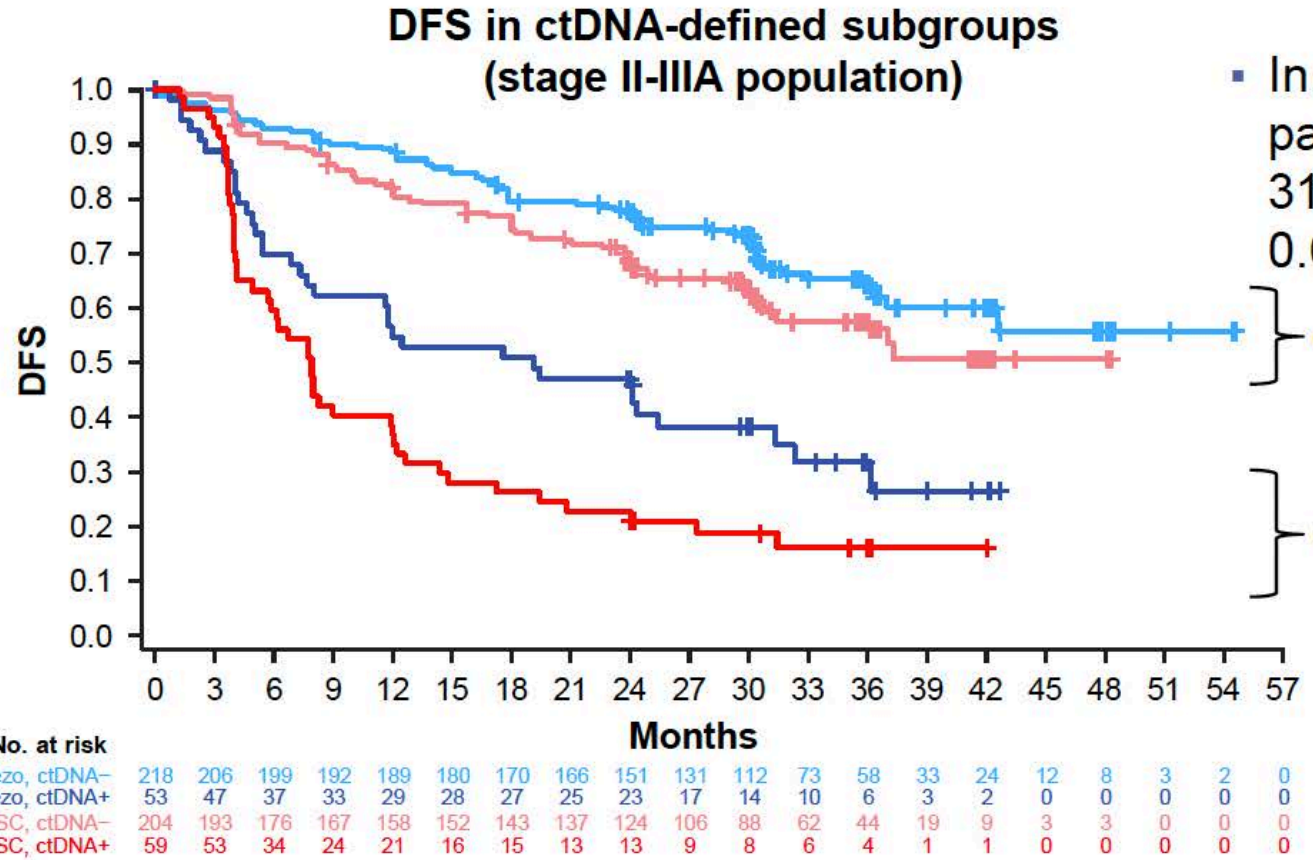
Zhou C et al, ESMO IO 2021

Impower 010 – Exploratory results for ctDNA



- In all ctDNA-evaluable stage II-IIIA patients, mDFS was NR (atezo) vs 31.4 months (BSC), with an HR of 0.69 (95% CI: 0.53, 0.89)

ctDNA−	Atezo (n=218)	BSC (n=204)
mDFS, mo	NR	NR
HR (95% CI)	0.72 (0.52, 1.00)	

ctDNA+	Atezo (n=53)	BSC (n=59)
mDFS, mo	19.1	7.9
HR (95% CI)	0.61 (0.39, 0.94)	

Clinical cutoff: 21 January 2021. Unstratified HRs are shown.

Reck M. ESMO Virtual Plenary 2022; Discussant

CONCLUSIONS

- Thanks to the authors for sharing the presentation and being available for so many questions!

- We are entering the times of perioperative immunotherapies
- First signals of efficacy for adjuvant immunotherapy in two large randomised trials
- More Follow ups and Maturation urgently required with new questions from the PEARLS trial:
  - Role of PD-L1 expression
  - Role of EGFR mutations
  - Role of adjuvant chemotherapy / potential role of adjuvant immunotherapy
- The future might become challenging!

Reck M. ESMO Virtual Plenary 2022; Discussant

Meet The Professor with Dr Goldberg

MODULE 1: Case Presentation

- Dr Polkinghorn: A 62-year-old woman metastatic non-small cell lung cancer (NSCLC) and multiple sclerosis

MODULE 2: Case Presentation

- Dr Yang: A 77-year-old woman with progressive metastatic adenocarcinoma of the lung — PD-L1 90%

MODULE 3: PEARLS/KEYNOTE-091 Phase III Study of Adjuvant Pembrolizumab

MODULE 4: Case Presentations

- Dr Morganstein: A 65-year-old man who presents with seizures associated with multiple brain metastases from NSCLC
- Dr Lamar: A 63-year-old woman with a 3.1-cm hilar mass, adenopathy and significant cardiac comorbidities
- Dr Nathwani: A 77-year-old man with high-grade neuroendocrine cancer of the lung
- Dr Carrizosa: A 77-year-old woman with malignant mesothelioma and multiple comorbidities
- Dr Yang: An 87-year-old man with extensive-stage small cell lung cancer — PD-L1 >50%

MODULE 5: Journal Club with Dr Goldberg

MODULE 6: Faculty Survey

MODULE 7: Appendix of Key Data Sets

RTP RESEARCH TO PRACTICE

Case Presentation: A 65-year-old man who presents with seizures associated with multiple brain metastases from NSCLC

Dr Neil Morganstein (Summit, New Jersey)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 63-year-old woman with a 3.1-cm hilar mass, adenopathy and significant cardiac comorbidities

Dr Zanetta Lamar (Naples, Florida)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 77-year-old man with high-grade neuroendocrine cancer of the lung

Dr Niyati Nathwani (Charlotte, North Carolina)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 77-year-old woman with malignant mesothelioma and multiple comorbidities

Dr Daniel Carrizosa (Charlotte, North Carolina)

RTP
RESEARCH
TO PRACTICE

Case Presentation: An 87-year-old man with extensive-stage small cell lung cancer — PD-L1 >50%

Dr John Yang (Fall River, Massachusetts)

RTP
RESEARCH
TO PRACTICE

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RTP RESEARCH TO PRACTICE

Adoption of Consolidative Durvalumab Among Patients with Locally Advanced Non-Small Cell Lung Cancer

Jairam V et al.

ASCO 2021;Abstract e20550.

Gibson JA et al. *Lancet Oncol* 2021;22(3):306-7.

Perspectives

Snapshot

Yale Cancer Center Precision Medicine Tumor Board: molecular findings alter a diagnosis and treatment plan

Grant MJ et al. *Lancet Oncol* 2022;23(3):337-8.

Snapshot

Yale Precision Medicine Tumor Board: reawakening the guardian of the genome

Open access Short report

Journal for ImmunoTherapy of Cancer

Spatially resolved analysis of the T cell immune contexture in lung cancer-associated brain metastases

Benjamin Y Lu ,[1] Richa Gupta,[2] Adam Aguirre-Ducler,[2] Nicole Gianino,[2] Hailey Wyatt,[2] Matthew Ribeiro,[1] Veronica L Chiang,[3] Joseph N Contessa,[4,5] Adebowale J Adeniran,[2] Lucia B Jilaveanu,[1] Harriet M Kluger,[1] Kurt A Schalper,[2] Sarah B Goldberg[1]

J Immunother Cancer 2021;9(10):e002684

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RTP RESEARCH TO PRACTICE

In what situations, if any, are you currently recommending neoadjuvant chemotherapy (with or without an anti-PD-1/PD-L1 antibody) for your patients with NSCLC?

 Dr Aggarwal	None	 Dr Hanna	None
 Dr Goldberg	Select patients with Stage III disease	 Dr Liu	Resectable N2+ disease
 Dr Govindan	N2 disease with adequate pulmonary reserve	 Dr Ramalingam	Resectable N2 disease

RTP RESEARCH TO PRACTICE

Which first-line treatment regimen would you recommend for a 65-year-old patient with metastatic nonsquamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 0%?

 Dr Aggarwal	Carboplatin/pemetrexed/ pembrolizumab	 Dr Hanna	Carboplatin/pemetrexed/ pembrolizumab
 Dr Goldberg	Carboplatin/pemetrexed/ pembrolizumab	 Dr Liu	Carboplatin/pemetrexed/ pembrolizumab
 Dr Govindan	Carboplatin/pemetrexed/ pembrolizumab	 Dr Ramalingam	Ipilimumab/nivolumab

RTP RESEARCH TO PRACTICE

In general, what would be your preferred first-line treatment regimen for a 65-year-old patient with extensive-stage small cell lung cancer (SCLC)?

 Dr Aggarwal	Carboplatin/etoposide + atezolizumab	 Dr Hanna	Carboplatin/etoposide + atezolizumab
 Dr Goldberg	Carboplatin/etoposide + atezolizumab	 Dr Liu	Carboplatin/etoposide + atezolizumab
 Dr Govindan	Carboplatin/etoposide + atezolizumab	 Dr Ramalingam	Carboplatin/etoposide + atezolizumab

RTP RESEARCH TO PRACTICE

In what situations if any, do you administer trilaciclib to patients with extensive-stage SCLC who are receiving platinum/etoposide- or topotecan-containing regimens to reduce the incidence of chemotherapy-induced myelosuppression?

 Dr Aggarwal	I do not	 Dr Hanna	I have not yet done so
 Dr Goldberg	Intolerance to G-CSF	 Dr Liu	I have not used trilaciclib but might consider it if multilineage myelosuppression noted with topotecan
 Dr Govindan	None	 Dr Ramalingam	I have not used this in my practice

RTP RESEARCH TO PRACTICE

The benefits and risks of adding durvalumab to platinum/etoposide and of adding atezolizumab to carboplatin/etoposide are very similar, and from a clinical point of view selecting between the 2 regimens as first-line treatment for a patient with extensive-stage SCLC can be considered a “coin flip.”

 Dr Aggarwal	Agree	 Dr Hanna	Agree
 Dr Goldberg	Agree	 Dr Liu	Agree
 Dr Govindan	Agree	 Dr Ramalingam	Agree

RTP RESEARCH TO PRACTICE

In general, what is your preferred second-line treatment for a patient with extensive-stage SCLC with metastases and disease progression on chemotherapy/atezolizumab?

 Dr Aggarwal	Lurbinectedin	 Dr Hanna	Lurbinectedin
 Dr Goldberg	Lurbinectedin	 Dr Liu	Lurbinectedin
 Dr Govindan	Topotecan or irinotecan	 Dr Ramalingam	Lurbinectedin

RTP RESEARCH TO PRACTICE

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RTP RESEARCH TO PRACTICE

Appendix

FDA Approves Atezolizumab as Adjuvant Treatment for NSCLC

Press Release – October 15, 2021

"The Food and Drug Administration approved atezolizumab for adjuvant treatment following resection and platinum-based chemotherapy in patients with stage II to IIIA non-small cell lung cancer (NSCLC) whose tumors have PD-L1 expression on ≥ 1% of tumor cells, as determined by an FDA-approved test.

Today, the FDA also approved the VENTANA PD-L1 (SP263) Assay (Ventana Medical Systems, Inc.) as a companion diagnostic device to select patients with NSCLC for adjuvant treatment with atezolizumab.

The major efficacy outcome measure was disease-free survival (DFS) as assessed by the investigator in the primary efficacy analysis population (n=476) of patients with stage II-IIIA NSCLC with PD-L1 expression on ≥1% of tumor cells (PD-L1 ≥1% TC). Median DFS was not reached (95% CI: 36.1, NE) in patients on the atezolizumab arm compared with 35.3 months (95% CI: 29.0, NE) on the BSC arm (HR 0.66; 95% CI: 0.50, 0.88; p=0.004)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-atezolizumab-adjuvant-treatment-non-small-cell-lung-cancer

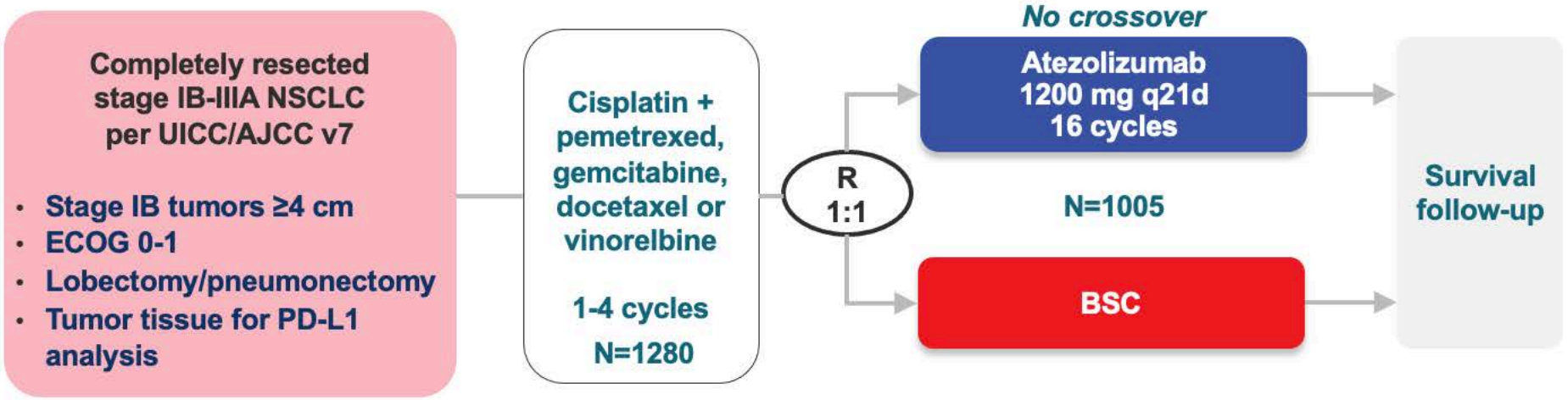
RTP RESEARCH TO PRACTICE

Lancet 2021;398:1344-57

Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB–IIIA non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial

*Enriqueta Felip, Nasser Altorki, Caicun Zhou, Tibor Csőszi, Ihor Vynnychenko, Oleksandr Goloborodko, Alexander Luft, Andrey Akopov, Alex Martinez-Marti, Hirotsugu Kenmotsu, Yuh-Min Chen, Antonio Chella, Shunichi Sugawara, David Voong, Fan Wu, Jing Yi, Yu Deng, Mark McCleland, Elizabeth Bennett, Barbara Gitlitz, Heather Wakelee, for the IMpower010 Investigators**

IMpower010: A Phase III Trial of Adjuvant Atezolizumab After Chemotherapy for Resected Stage IB-IIIA NSCLC



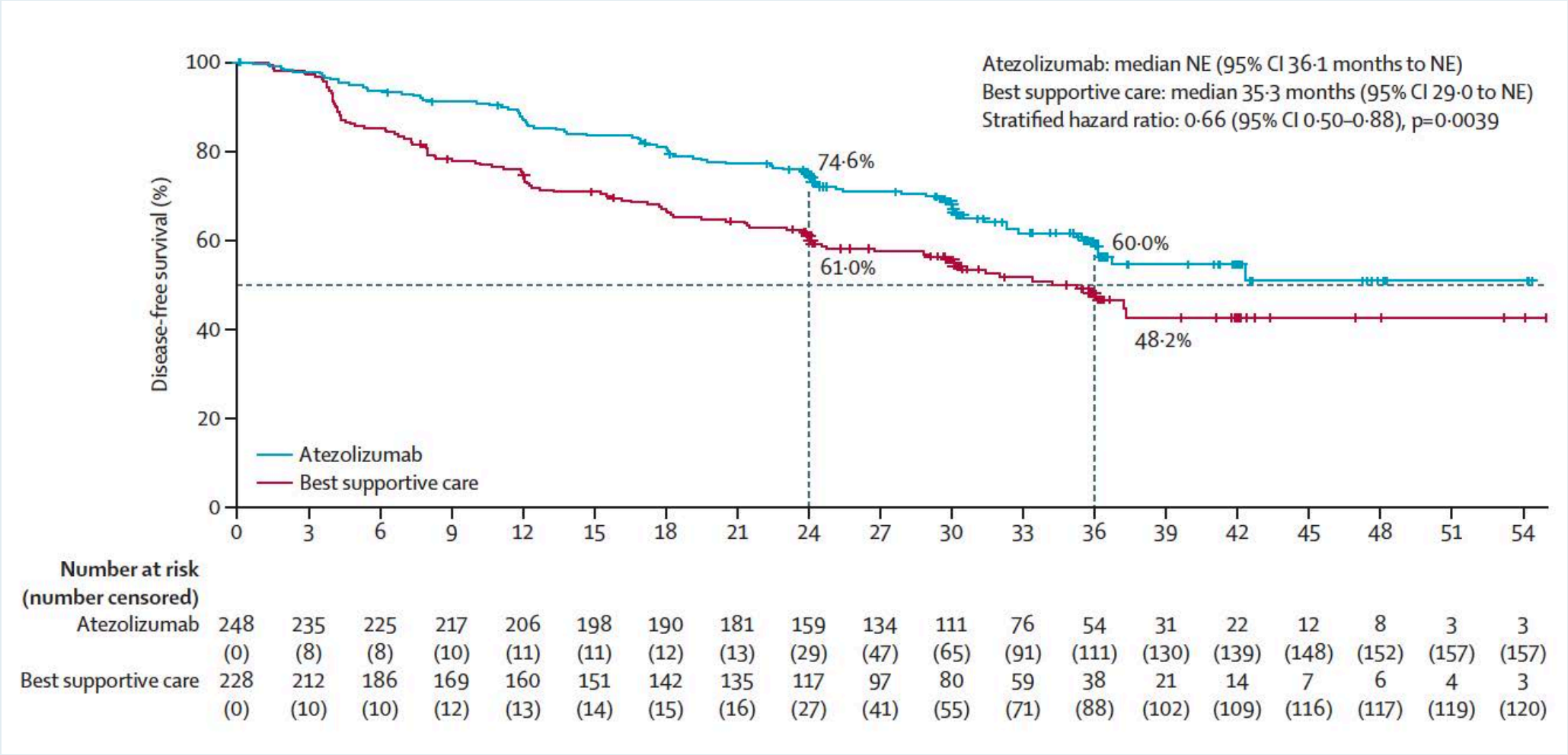
Stratification factors
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints
- Investigator-assessed DFS tested hierarchically:
  - **PD-L1 TC ≥1% (per SP263) stage II-IIIA population**
  - **All-randomized stage II-IIIA population**
  - **ITT population (stage IB-IIIA)**

Key secondary endpoints
- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

Wakelee HA et al. ASCO 2021;Abstract 8500.

IMpower010 Primary Endpoint: Disease-Free Survival in the PD-L1 ≥1% Tumor Cells Stage II-IIIA Population



Felip E et al. *Lancet* 2021;398(10308):1344-57.

IMpower010: Characterization of Stage IB-IIIA NSCLC Patients by Type and Extent of Therapy Prior to Adjuvant Atezolizumab

Nasser Altorki,[1] Enriqueta Felip,[2] Caicun Zhou,[3] Eric Vallieres,[4] Vladimir Moiseyenko,[5] Alexey Smolin,[6] Achim Rittmeyer,[7] Roman Vereshchako,[8] Maurice Perol,[9] Wolfgang Schutte,[10] Jian Fang,[11] Min Tao,[12] Encarnacao Teixeira,[13] Young-Chul Kim,[14] Virginia McNally,[15] Fan Wu,[16] Yu Deng,[17] Elizabeth Bennett,[17] Barbara Gitlitz,[17] Heather Wakelee[18]

[1] New York-Presbyterian Hospital, Weill Cornell Medicine, New York, NY; [2] Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [3] Tongji University Affiliated Shanghai Pulmonary Hospital, Shanghai, China; [4] Swedish Cancer Institute, Seattle, WA; [5] GBUZ Saint Petersburg Clinical Research Center of Specialized Types of Care (Oncology), Saint Petersburg, Russia; [6] Principal Military Clinical Hospital n.a. N.N. Burdenko, Moscow, Russia; [7] Lungenfachklinik Immenhausen, Immenhausen, Germany; [8] Kyiv Railway Clinical Hospital #3 of Branch Health Center of the PJSC Ukrainian Railway, Kyiv, Ukraine; [9] Centre Léon Bérard, Lyon, France; [10] Krankenhaus Martha-Maria; Halle-Dolau gGmbH, Halle, Germany; [11] Beijing Cancer Hospital, Beijing, China; [12] First Affiliated Hospital of Soochow University, Jiangsu, China; [13] Centro Hospitalar de Lisboa Norte E.P.E – Hospital Pulido Valente, Lisbon, Portugal; [14] Chonnam National University Medical School, and CNU Hwasun Hospital, Jeollanam-do, South Korea; [15] F. Hoffmann-La Roche Ltd., Basel, Switzerland; [16] Roche (China) Holding Ltd, Shanghai, China; [17] Genentech Inc, South San Francisco, CA; [18] Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA

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

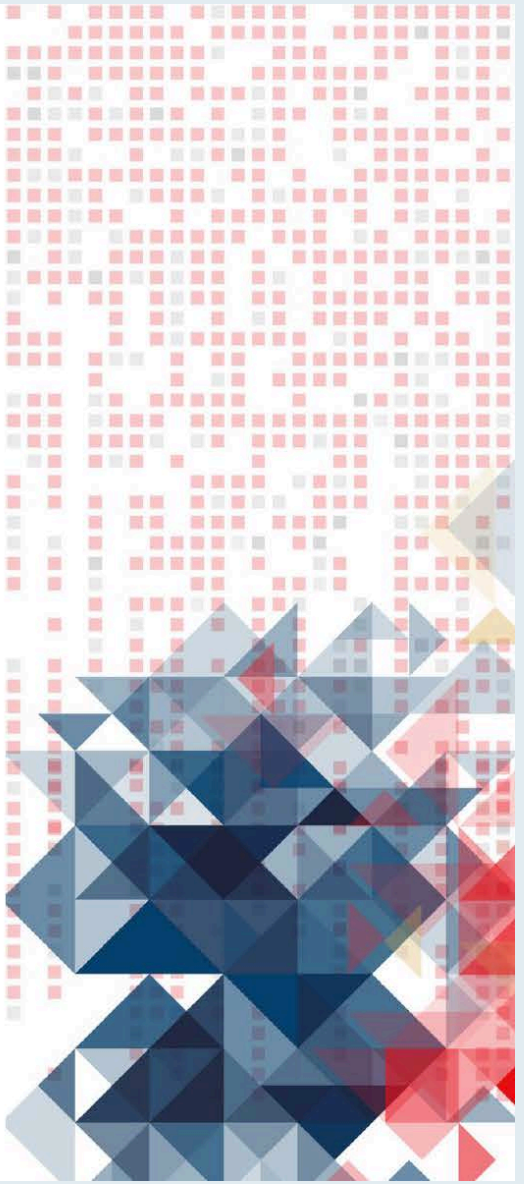
Abstract PL0205

2021 ESMO congress

IMpower010: Sites of Relapse and Subsequent Therapy From a Phase 3 Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA NSCLC

Enriqueta Felip,[1] Eric Vallieres,[2] Caicun Zhou,[3] Heather Wakelee,[4] Igor Bondarenko,[5] Hiroshi Sakai,[6] Haruhiro Saito,[7] Grygorii Ursol,[8] Koji Kawaguchi,[9] Yunpeng Liu,[10] Evgeny Levchenko,[11] Nikolay Kislov,[12] Martin Reck,[13] Rüdiger Liersch,[14] Virginia McNally,[15] Qian Zhu,[16] Beiying Ding,[16] Elizabeth Bennett,[16] Barbara Gitlitz,[16] Nasser Altorki[17]

[1]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [2]Swedish Cancer Institute, Seattle, WA, USA; [3]Tongji University Affiliated Shanghai Pulmonary Hospital, Shanghai, China; [4]Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA; [5]Dnipro State Medical University, Dnipro, Ukraine; [6]Saitama Cancer Center, Saitama, Japan; [7]Kanagawa Cancer Center, Yokohama, Japan; [8]Acinus, Kropyvnytskyi, Ukraine; [9]Mie University Graduate School of Medicine, Mie, Japan; [10]First Hospital, China Medical University, Shenyang, China; [11]Scientific Research Oncology Institute, St Petersburg, Russia; [12]Regional Clinical Oncology Hospital, Yaroslavl, Russia; [13]Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany; [14]Clemenshospital Münster, Münster, Germany; [15]Roche Products Ltd, Welwyn Garden City, United Kingdom; [16]Genentech Inc, South San Francisco, CA, USA; [17]New York-Presbyterian Hospital, Weill Cornell Medicine, New York, NY, USA



Abstract LBA9

RTP RESEARCH TO PRACTICE

FDA Approves Neoadjuvant Nivolumab and Platinum-Doublet Chemotherapy for Localized NSCLC

Press Release – March 4, 2022

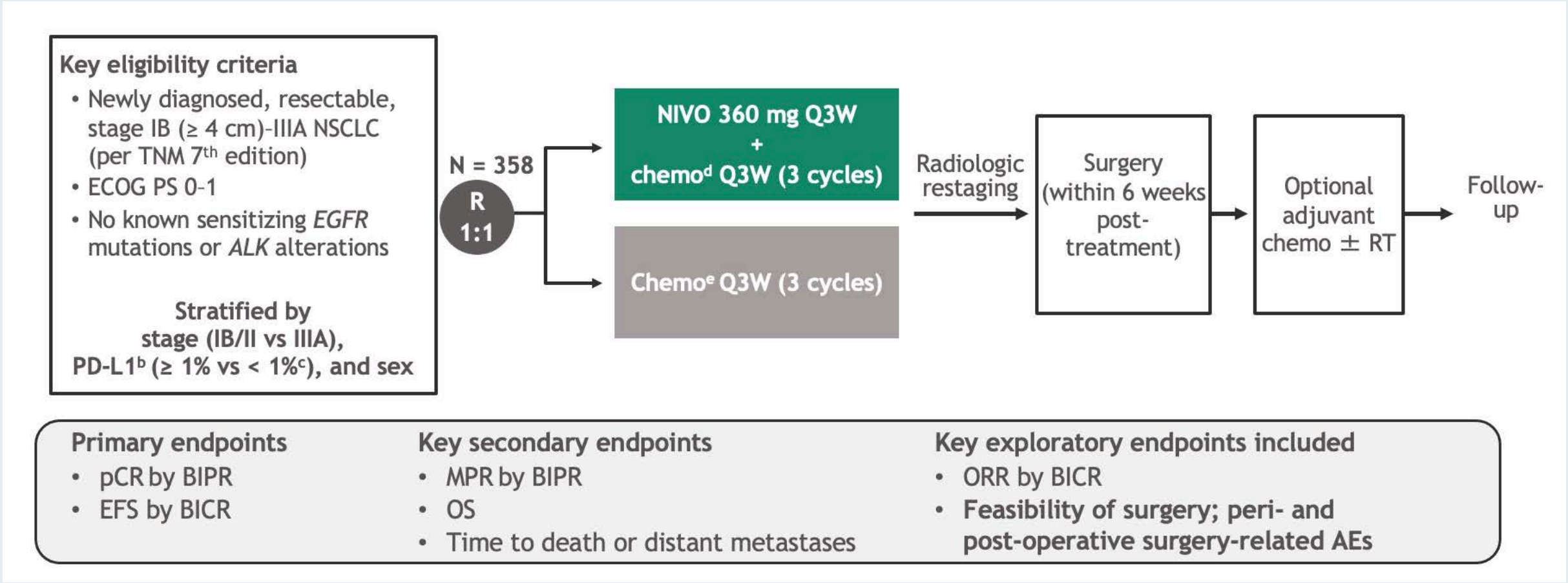
"The Food and Drug Administration approved nivolumab with platinum-doublet chemotherapy for adult patients with resectable non-small cell lung cancer (NSCLC) in the neoadjuvant setting. This represents the first FDA approval for neoadjuvant therapy for early-stage NSCLC.

Efficacy was evaluated in CHECKMATE-816 (NCT02998528), a randomized, open label trial in patients with resectable, histologically confirmed Stage IB (≥4 cm), II, or IIIA NSCLC (AJCC/UICC staging criteria) and measurable disease (RECIST v1.1.). Patients were enrolled regardless of the tumor PD-L1 status. A total of 358 patients were randomized to receive either nivolumab plus platinum-doublet chemotherapy administered every 3 weeks for up to 3 cycles, or platinum-chemotherapy alone administered on the same schedule.

The main efficacy outcome measures were event-free survival (EFS) and pathologic complete response (pCR) by blinded independent central review. Median EFS was 31.6 months in the nivolumab plus chemotherapy arm and 20.8 months for those receiving chemotherapy alone. The hazard ratio was 0.63 (p=0.0052). The pCR rate was 24% in the nivolumab plus chemotherapy arm and 2.2% in the chemotherapy alone arm."

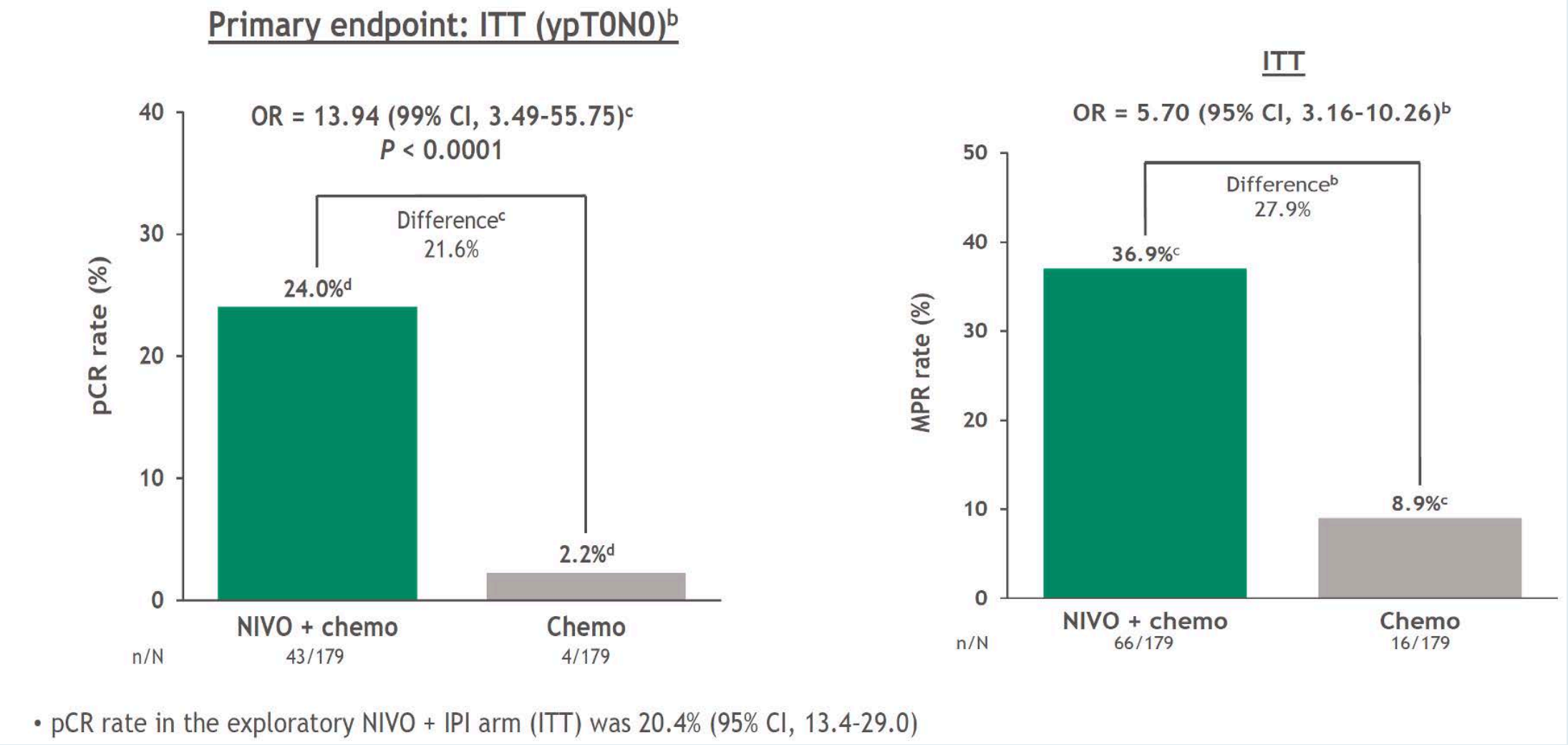
www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-neoadjuvant-nivolumab-and-platinum-doublet-chemotherapy-early-stage-non-small-cell-lung

CheckMate 816: A Phase III Trial of Neoadjuvant Nivolumab with Chemotherapy for Newly Diagnosed, Resectable, Stage IB-IIIA NSCLC



Spicer J et al. ASCO 2021;Abstract 8503.

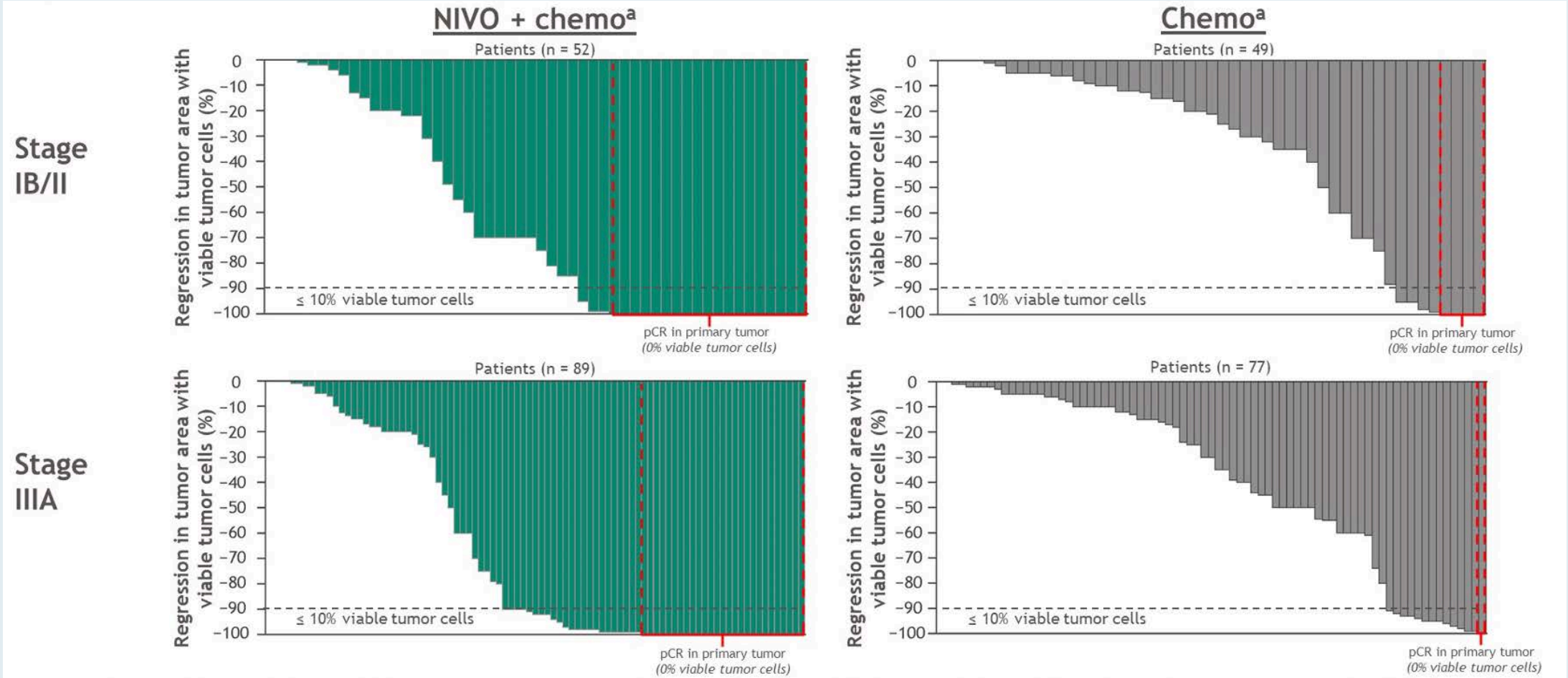
CheckMate 816 Coprimary Endpoint: Pathologic Complete Response (pCR)



- pCR rate in the exploratory NIVO + IPI arm (ITT) was 20.4% (95% CI, 13.4-29.0)

Forde PM et al. AACR 2021;Abstract CT003.

CheckMate 816: Depth of Pathologic Regression in Primary Tumor by Stage



- The median residual viable tumor percentage in stage IB/II and IIIA was 28% and 8% with NIVO + chemo vs 79% and 70% with chemo, respectively

[a]Response-evaluable patients.

Spicer J et al. ASCO 2021;Abstract 8503.

RTP RESEARCH TO PRACTICE

CheckMate 816: Impact of Neoadjuvant Immunotherapy on Surgery

Neoadjuvant immunotherapy did not negatively affect surgery outcomes

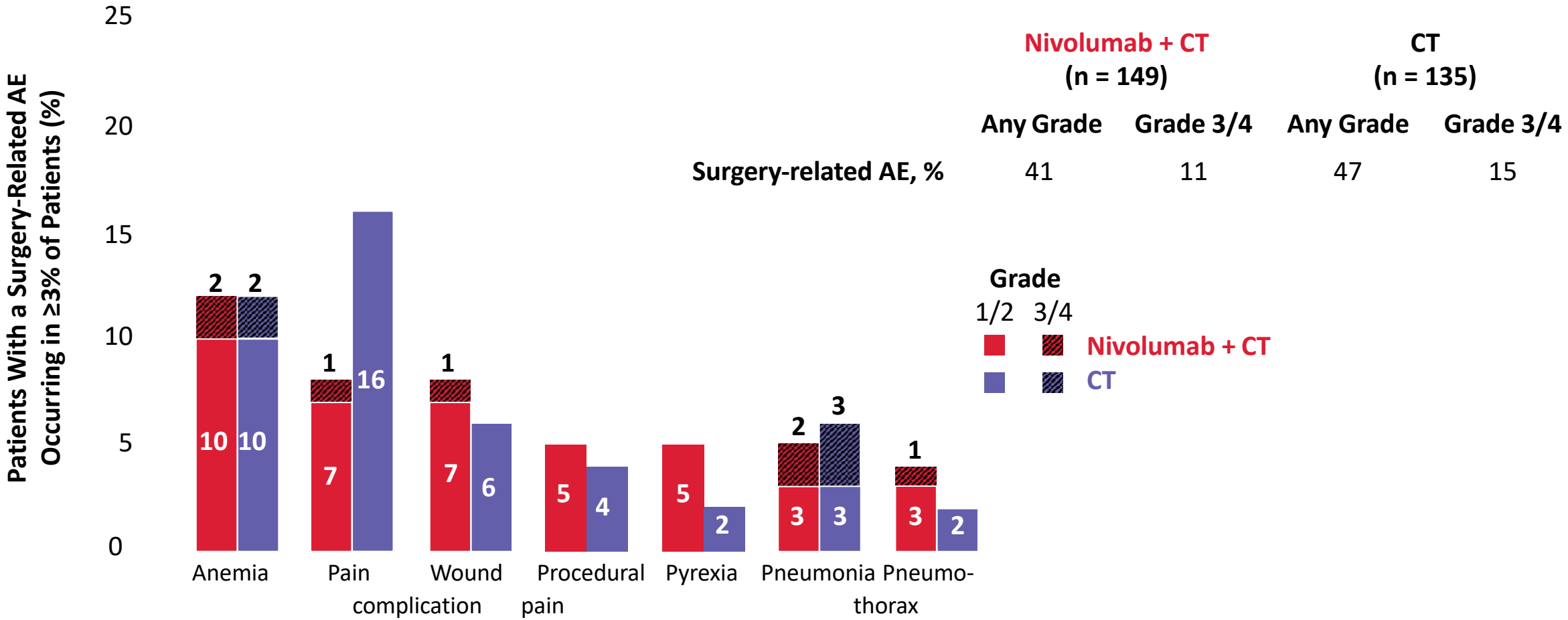
Surgery-Related Parameter in All Randomized Patients	Nivolumab + CT (n = 179)	CT (n = 179)
Surgery received/cancelled, %	83/16	75/21
	184 (130-252)*	217 (150-283)†
Surgery approach, % ▪ Thoracotomy ▪ Minimally invasive ▪ Minimally invasive → open	 59‡ 30‡ 11‡	 63§ 22§ 16§
Type of surgery, %# ▪ Lobectomy ▪ Pneumonectomy	 77‡ 17‡	 61§ 25§
Complete resection (R0), %	83	78

*n = 122. †n = 121. ‡n = 149. §n = 135. #Calculated from patients who received definitive surgery. Patients may have had ≥1 surgery type. Patients who received other types of surgery (eg, sleeve lobectomy, bilobectomy) not shown.

Courtesy of Roy S Herbst, MD, PhD

Spicer. ASCO 2021. Abstr 8503.

CheckMate 816: Surgery-Related Complications up to 90 Days After Definitive Surgery



Surgery-related AEs not shown: subcutaneous emphysema, atrial fibrillation, cough, pleural effusion, nausea, dyspnea, pulmonary fistula, non-cardiac chest pain. n = 2 grade 5 surgery-related AEs (pulmonary embolism, aortic rupture) in nivolumab + CT arm considered unrelated to study drug by investigator. n = 2 intraoperative complications (intraoperative hemorrhage, aortic rupture) in nivolumab + CT arm deemed not related to study drug.

Spicer. ASCO 2021. Abstr 8503.

Courtesy of Roy S Herbst, MD, PhD

Select Ongoing Phase III Trials of Immunotherapy in the Neoadjuvant Setting

Trial identifier	N	Patient population	Study arms
IMpower030 (NCT03456063)	453	Resectable Stage II, IIIA or select IIIB (T3N2 only) NSCLC Squamous or nonsquamous histology	• Atezolizumab + platinum-based chemotherapy • Placebo + platinum-based chemotherapy
KEYNOTE-671 (NCT03425643)	786	Resectable Stage II, IIIA or resectable IIIB (T3-4N2) NSCLC	• Pembrolizumab + platinum-based chemotherapy • Placebo + platinum-based chemotherapy
AEGEAN (NCT03800134)	800	Resectable Stage IIA to select (ie, N2) Stage IIIB NSCLC	• Durvalumab + platinum-based chemotherapy • Placebo + platinum-based chemotherapy

www.clinicaltrials.gov; Accessed November 2021.

Select Ongoing Phase III Trials of Immunotherapy in the Adjuvant Setting

Trial identifier	N	Patient population	Study arms
BR31 (NCT02273375)	1,360	Stage IB (≥4 cm in the longest diameter), II or IIIA after complete resection	• Durvalumab • Placebo
KEYNOTE-091/ PEARLS (NCT02504372)	1,177	Stage IB with T ≥4 cm, II-IIIA NSCLC after complete surgical resection with or without adjuvant chemotherapy	• Pembrolizumab • Placebo
ANVIL (NCT02595944)	903	Complete surgical resection of Stage IB (≥4 cm), II or IIIA NSCLC with adjuvant chemotherapy Negative for ALK translocation and EGFR exon 19 deletion or exon 21 L858R mutation	• Nivolumab • Placebo

www.clinicaltrials.gov; Accessed November 2021.

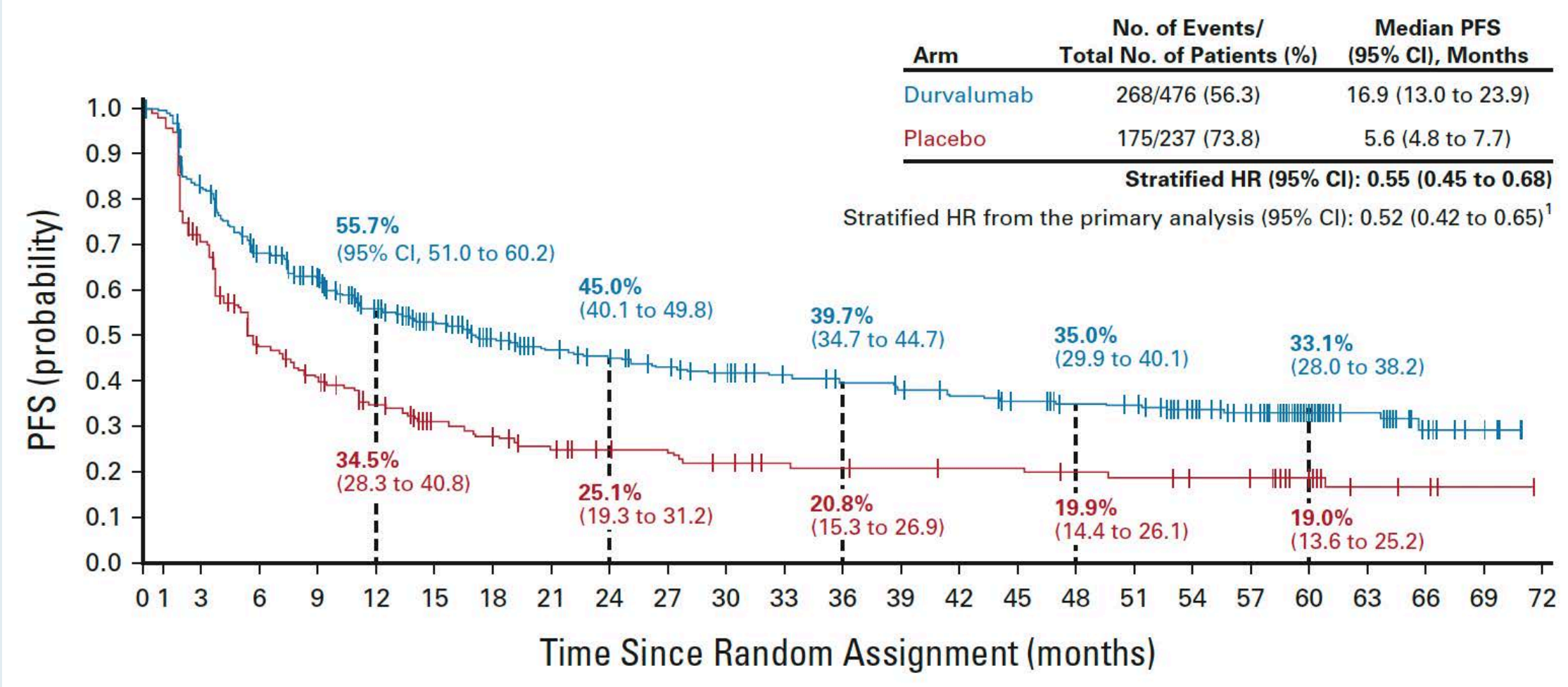
original reports

Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

David R. Spigel, MD[1]; Corinne Faivre-Finn, MD, PhD[2]; Jhanelle E. Gray, MD[3]; David Vicente, MD[4]; David Planchard, MD, PhD[5]; Luis Paz-Ares, MD, PhD[6]; Johan F. Vansteenkiste, MD, PhD[7]; Marina C. Garassino, MD[8,9]; Rina Hui, PhD[10]; Xavier Quantin, MD, PhD[11]; Andreas Rimner, MD[12]; Yi-Long Wu, MD[13]; Mustafa Özgüroğlu, MD[14]; Ki H. Lee, MD[15]; Terufumi Kato, MD[16]; Maike de Wit, MD, PhD[17]; Takayasu Kurata, MD[18]; Martin Reck, MD, PhD[19]; Byoung C. Cho, MD, PhD[20]; Suresh Senan, PhD[21]; Jarushka Naidoo, MBBCH, MHS[22]; Helen Mann, MSc[23]; Michael Newton, PharmD[24]; Piruntha Thiyagarajah, MD[23]; and Scott J. Antonia, MD, PhD[3]; on behalf of the PACIFIC Investigators

J Clin Oncol 2022;[Online ahead of print].

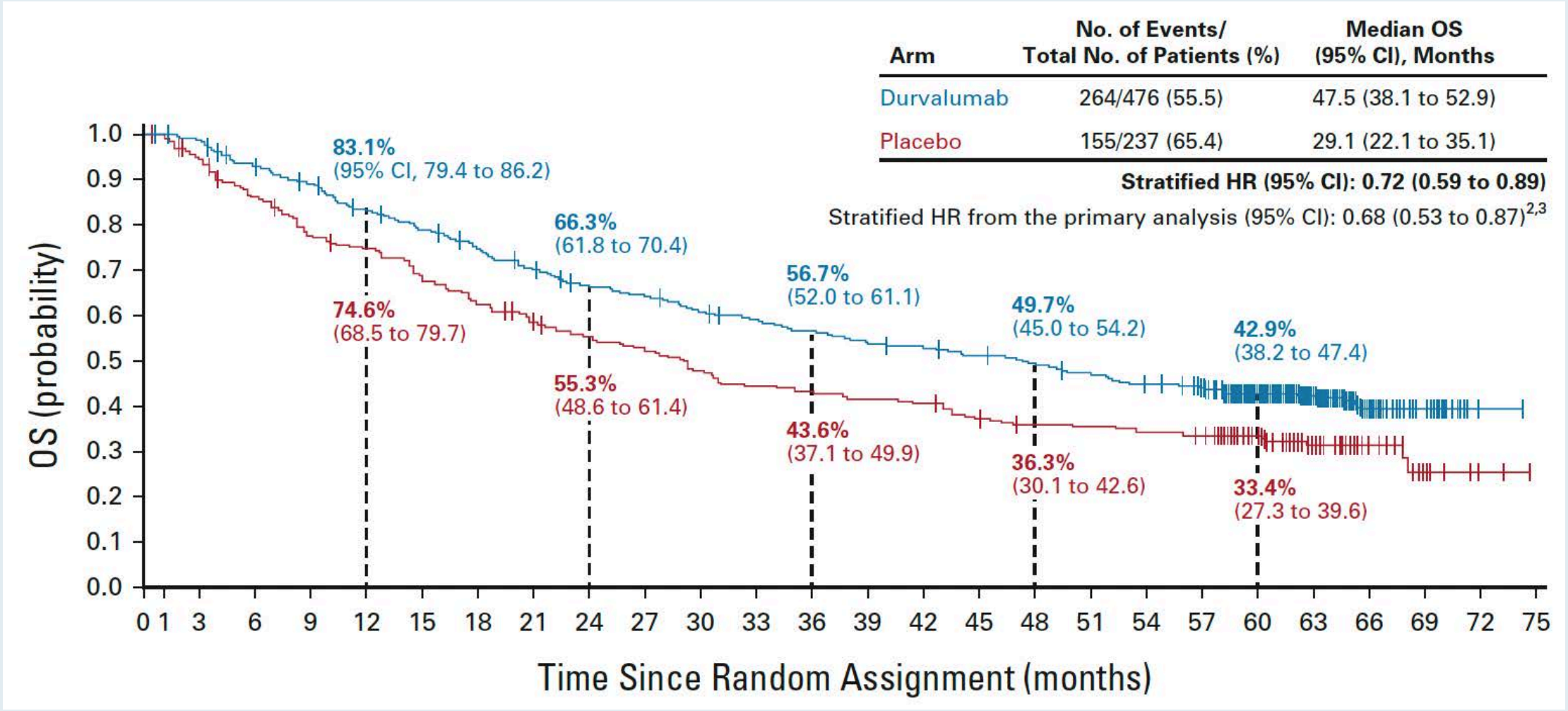
PACIFIC: Five-Year Progression-Free Survival (PFS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



Spigel DR et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

PACIFIC: Five-Year Overall Survival (OS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



Spigel DR et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

FDA Approves Durvalumab for Fixed-Dose Use in NSCLC, Bladder Cancer Indications

Press Release – November 20, 2020

"The FDA has approved durvalumab for an additional dosing option, a fixed dose of 1500 mg every 4 weeks, in the approved indications of unresectable stage III non-small cell lung cancer after chemoradiation and previously treated advanced bladder cancer.

This new dosing option is consistent with the dosing for the agent that has been approved in extensive-stage small cell lung cancer (ES-SCLC); this will serve as an alternative option for patients who weigh more than 30 kg rather than the weight-based dosing of 10 mg/kg that is administered every 2 weeks.

The regulatory decision was based on data from several clinical trials examining the agent, including the phase 3 PACIFIC trial (NCT02125461), which supported the 2-week, weight-based dosing in patients with unresectable stage III NSCLC, and the phase 3 CASPIAN trial (NCT03043872), which examined a 4-week, fixed-dose during maintenance treatment in patients with ES-SCLC."

https://www.onclive.com/view/fda-approves-durvalumab-for-fixed-dose-use-in-nsclc-bladder-cancer-indications

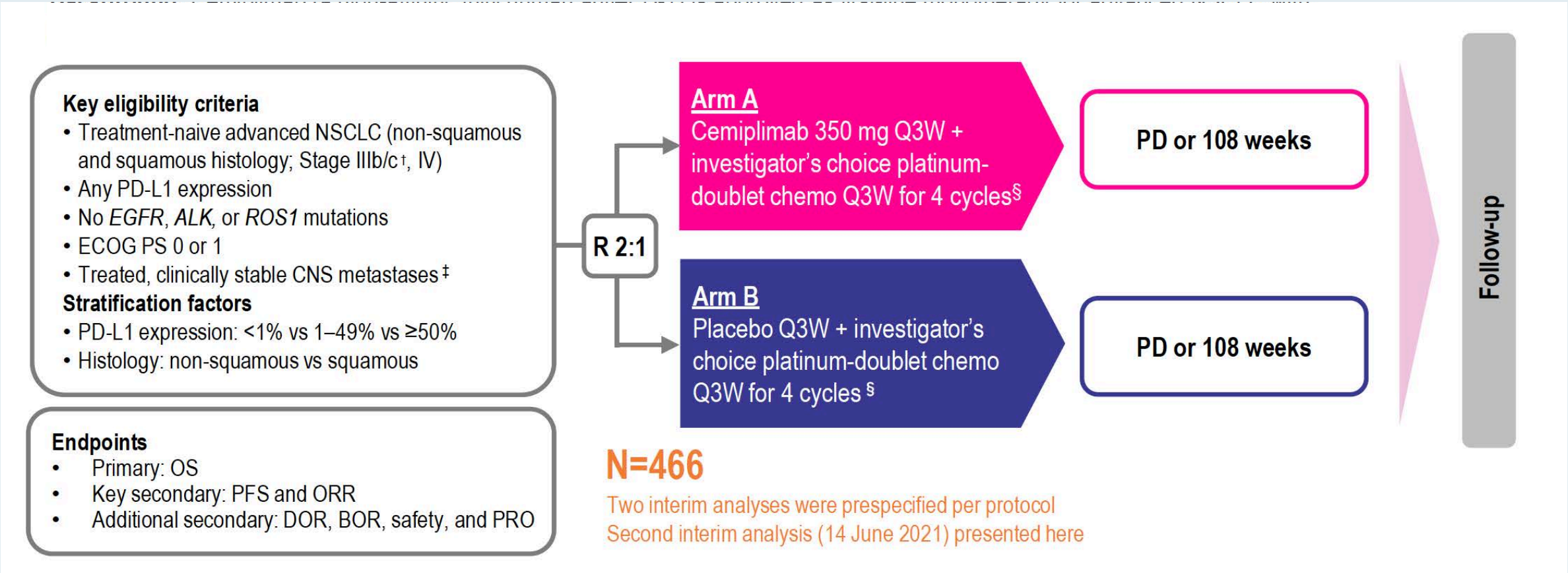
RTP RESEARCH TO PRACTICE

FDA-Approved Single-Agent Immunotherapy Options for First-Line Therapy

Monotherapy	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab[1,2] (q3wk or q6wk)	4/11/19 10/24/16	KEYNOTE-042 KEYNOTE-024	PD-L1 TPS ≥1%	0.63
Atezolizumab[3] (q2wk, q3wk or q4wk)	5/18/20	IMpower110	PD-L1 TPS ≥50, EGFR and/or ALK wt	0.59
Cemiplimab[4] (q3wk)	2/22/21	EMPOWER-Lung 1 (Study 1624)	PD-L1 TPS ≥50, EGFR and/or ALK and/or ROS1 wt	0.57

[1] Mok. *Lancet* 2019. [2] Reck. *J Clin Oncol* 2019. [3] Herbst. *N Engl J Med* 2020. [4] Sezer. *Lancet* 2021.

EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC



Gogishvili M et al. ESMO 2021;Abstract LBA51.

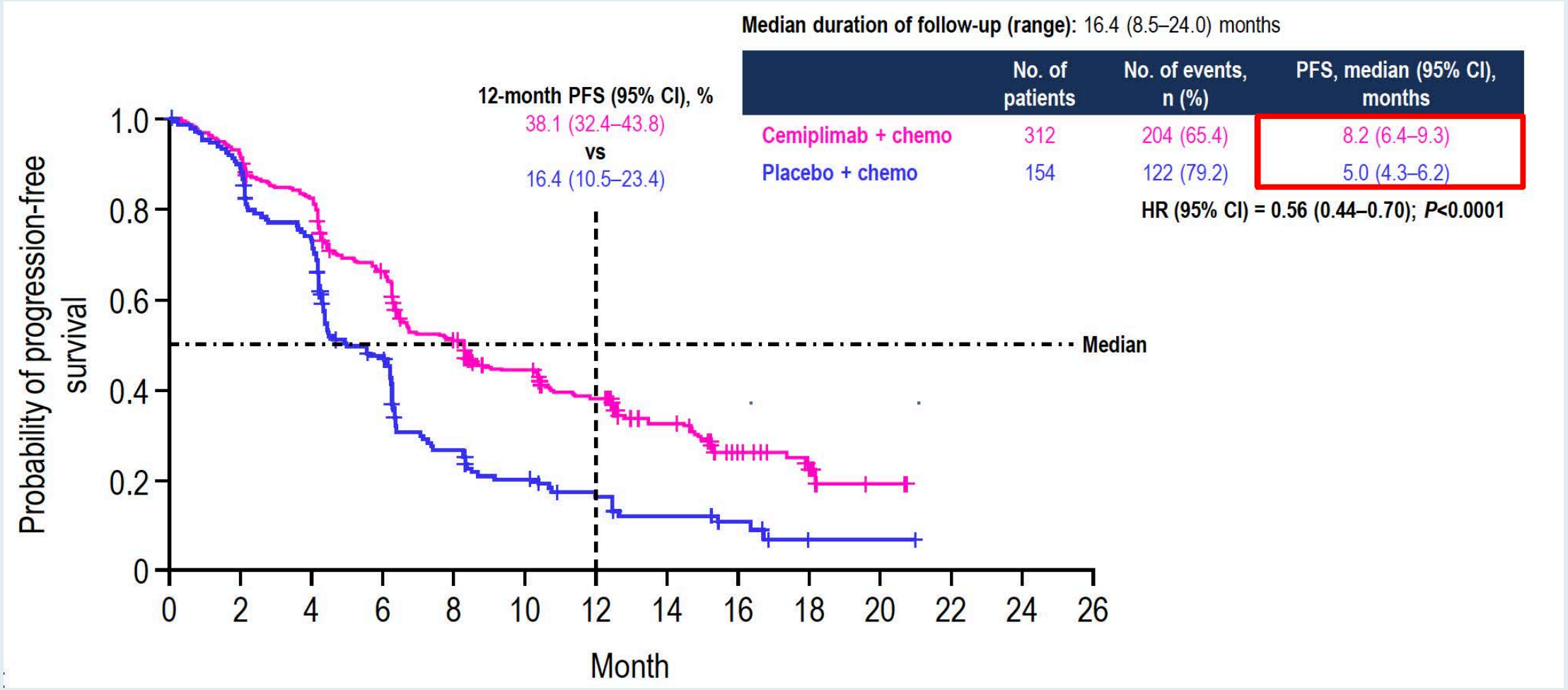
RTP RESEARCH TO PRACTICE

EMPOWER-Lung 3: Progression-Free Survival

Median duration of follow-up (range): 16.4 (8.5–24.0) months

	No. of patients	No. of events, n (%)	PFS, median (95% CI), months
Cemiplimab + chemo	312	204 (65.4)	8.2 (6.4–9.3)
Placebo + chemo	154	122 (79.2)	5.0 (4.3–6.2)

HR (95% CI) = 0.56 (0.44–0.70); *P*<0.0001



Gogishvili M et al. ESMO 2021;Abstract LBA51.

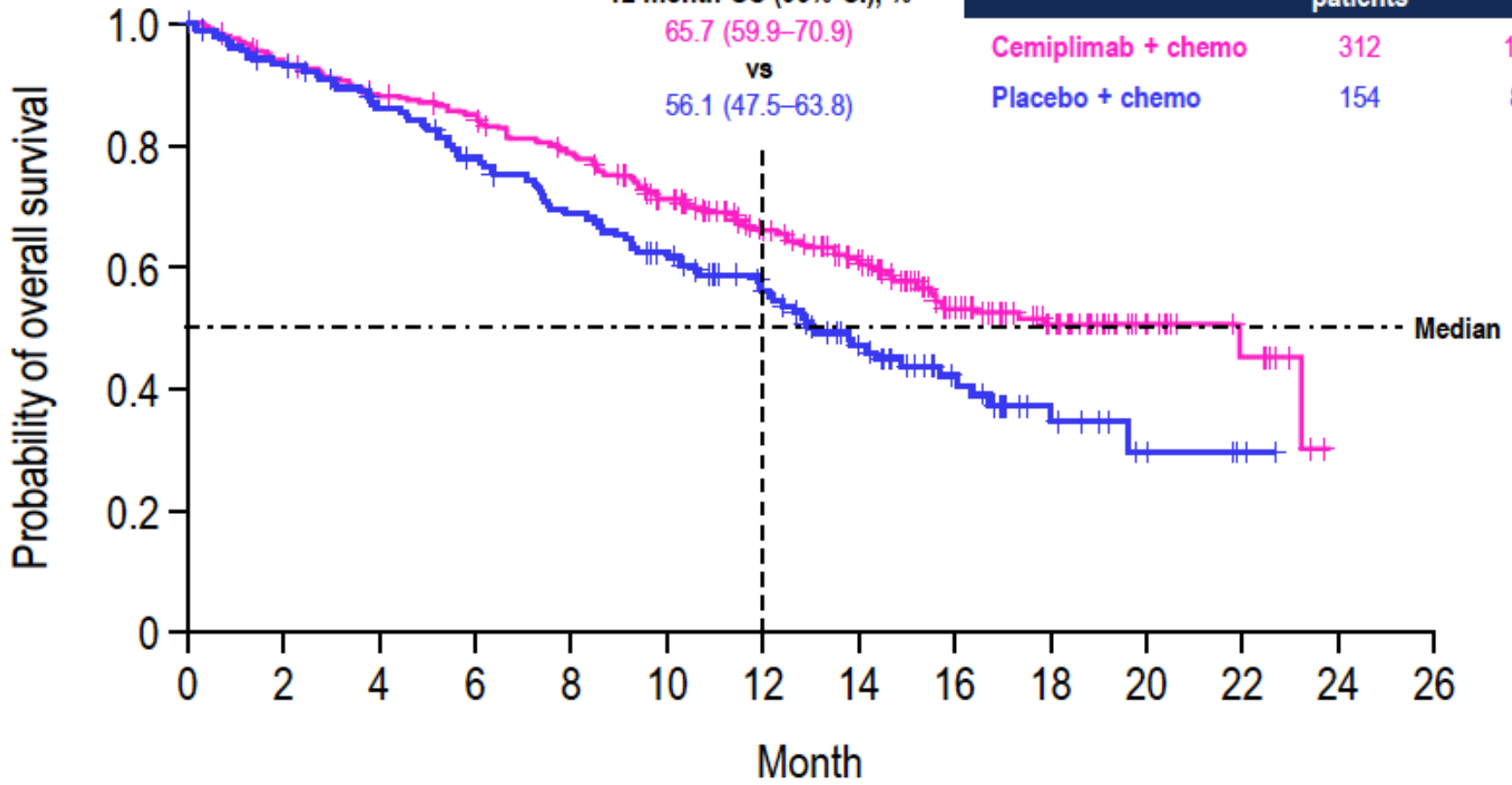
RTP RESEARCH TO PRACTICE

EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC

Median duration of follow-up (range): 16.4 (8.5–24.0) months

	No. of patients	No. of events, n (%)	OS, median (95% CI), months
Cemiplimab + chemo	312	132 (42.3)	21.9 (15.5–NE)
Placebo + chemo	154	82 (53.2)	13.0 (11.9–16.1)

HR (95% CI) = 0.71 (0.53–0.93); *P*=0.014

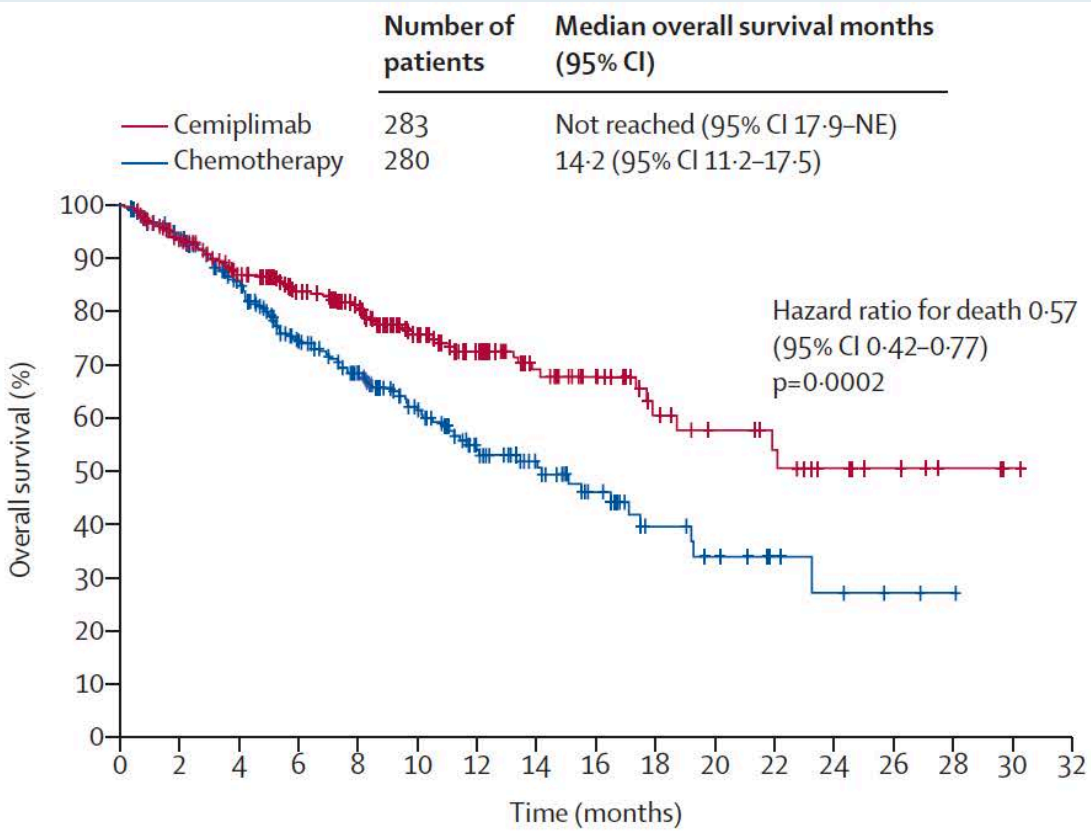


Gogishvili M et al. ESMO 2021;Abstract LBA51.

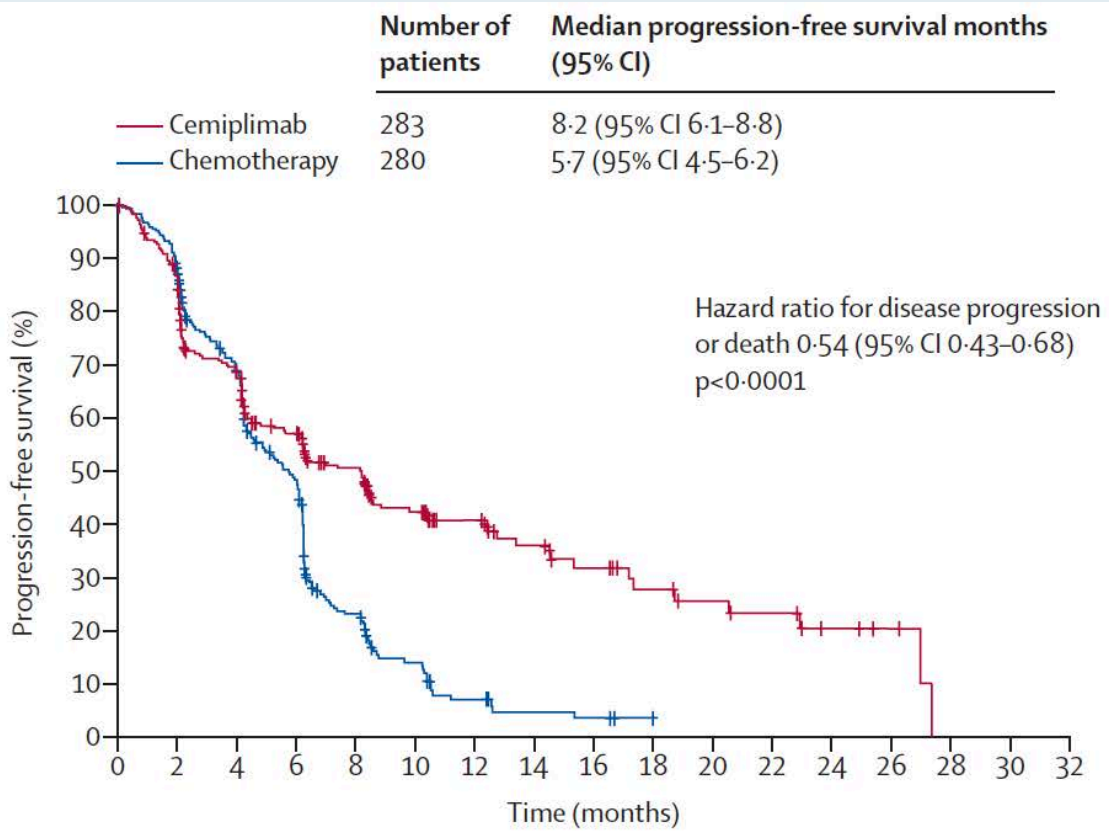
RTP RESEARCH TO PRACTICE

EMPOWER-Lung 1: A Phase III Trial of Cemiplimab Monotherapy for First-Line Treatment of NSCLC with PD-L1 ≥50%

Overall Survival



Progression-Free Survival



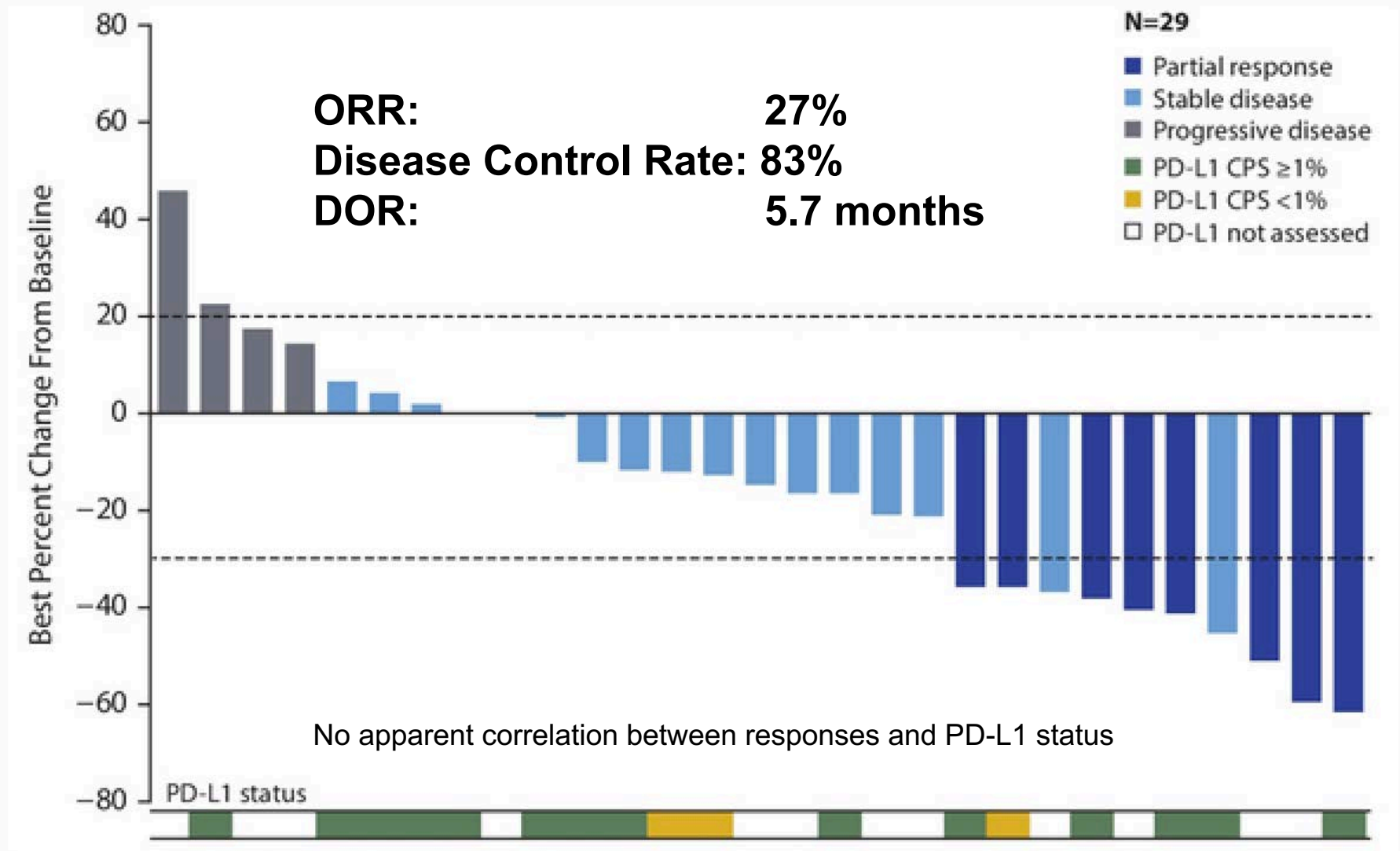
Sezer A et al. *Lancet* 2021;397:592-604.

FDA-Approved Immunotherapy Combination Options for First-Line Therapy

Combination regimen	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab (q3wk or q6wk) + Platinum and pemetrexed[1]	8/20/18	KEYNOTE-189	Nonsquamous	0.56
Pembrolizumab (q3wk or q6wk) + Carboplatin, paclitaxel or *nab* paclitaxel[2]	10/30/18	KEYNOTE-407	Squamous	0.71
Atezolizumab (q3wk) + Carboplatin and paclitaxel and bevacizumab[3]	12/6/18	IMpower150	Nonsquamous	0.80
Atezolizumab (q3wk) + Carboplatin and *nab* paclitaxel[4]	12/3/19	IMpower130	Nonsquamous	0.79
Nivolumab (q2wk) + Ipilimumab[5]	5/15/20	CheckMate 227	PD-L1 TPS ≥1, EGFR and/or ALK wt	0.76
Nivolumab (q3wk) + Ipilimumab and chemotherapy[6]	5/26/20	CheckMate 9LA	EGFR and/or ALK wt	0.72

[1] Rodriguez-Abreu. *Ann Oncol* 2021. [2] Paz-Ares. *J Thorac Oncol* 2020. [3] Socinski *J Thorac Oncol* 2021. [4] West. *Lancet Oncol* 2019.
[5] Paz-Ares. ASCO 2021;Abstract 9016. [6] Reck. ASCO 2021;Abstract 9000.

COSMIC-021 (Cohort 7): Best Change from Baseline with Cabozantinib/Atezolizumab for Metastatic NSCLC



Patient population

- Radiographic progression on or after 1 prior ICI treatment
- ≤2 lines of prior systemic anticancer therapy for metastatic NSCLC
- No EGFR mutations, ALK or ROS1 rearrangements or BRAF V600E mutation

Neal JW et al. ASCO 2020;Abstract 9610.

RTP RESEARCH TO PRACTICE

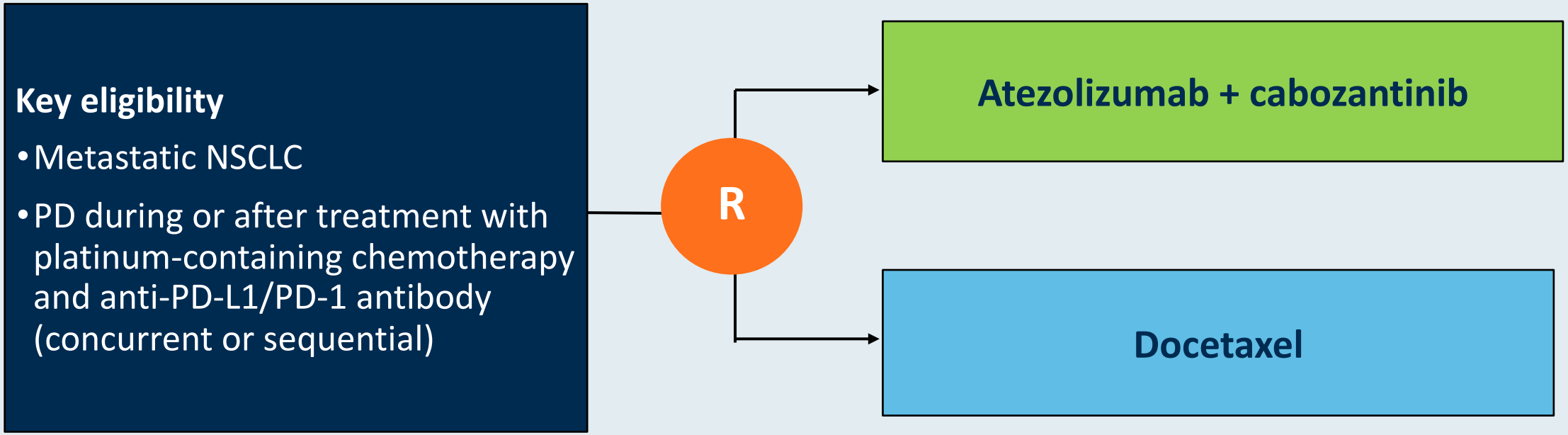
COSMIC-021 (Cohort 7): Immune-Related Adverse Events with Cabozantinib/Atezolizumab for Metastatic NSCLC

	NSCLC Cohort 7 (N=30)	
	Any Grade	Grade 3
Any AE, n (%)	6 (20)	0
Hyperthyroidism	1 (3.3)	0
Hypothyroidism	1 (3.3)	0
Lipase increased	1 (3.3)	0
Myocarditis*	1 (3.3)	0
Pain	1 (3.3)	0
Pneumonitis*	1 (3.3)	0
Rash	1 (3.3)	0

*One patient experienced grade 5 pneumonitis and myocarditis; pneumonitis was assessed as the cause of death

Neal JW et al. ASCO 2020;Abstract 9610.

CONTACT-01 Phase III Study Design



Primary endpoint: Overall survival
Secondary endpoints: PFS, ORR, DOR, others

www.clinicaltrials.gov. NCT04471428. Accessed November 2021.

Background: TIGIT Pathway

- TIGIT (T cell immunoreceptor with Ig and ITIM domains) is a novel inhibitory receptor expressed on multiple immune cells, including T cells and NK cells[1-3]
- TIGIT inhibits T cells and NK cells by binding to its ligand PVR on tumor cells and antigen-presenting cells (APCs)
- TIGIT expression strongly correlates with PD-1 expression, especially in tumor-infiltrating T cells in lung cancer
- *Hypothesis*: Anti-TIGIT antibodies, which prevent TIGIT from binding to its ligand, could restore the anti-tumor response and could complement the activity of anti-PD-L1/PD-1 antibodies

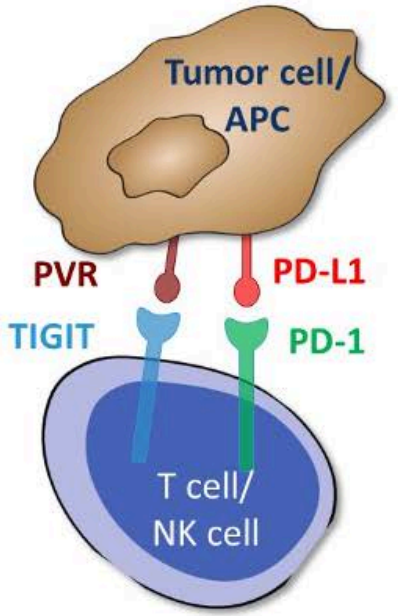


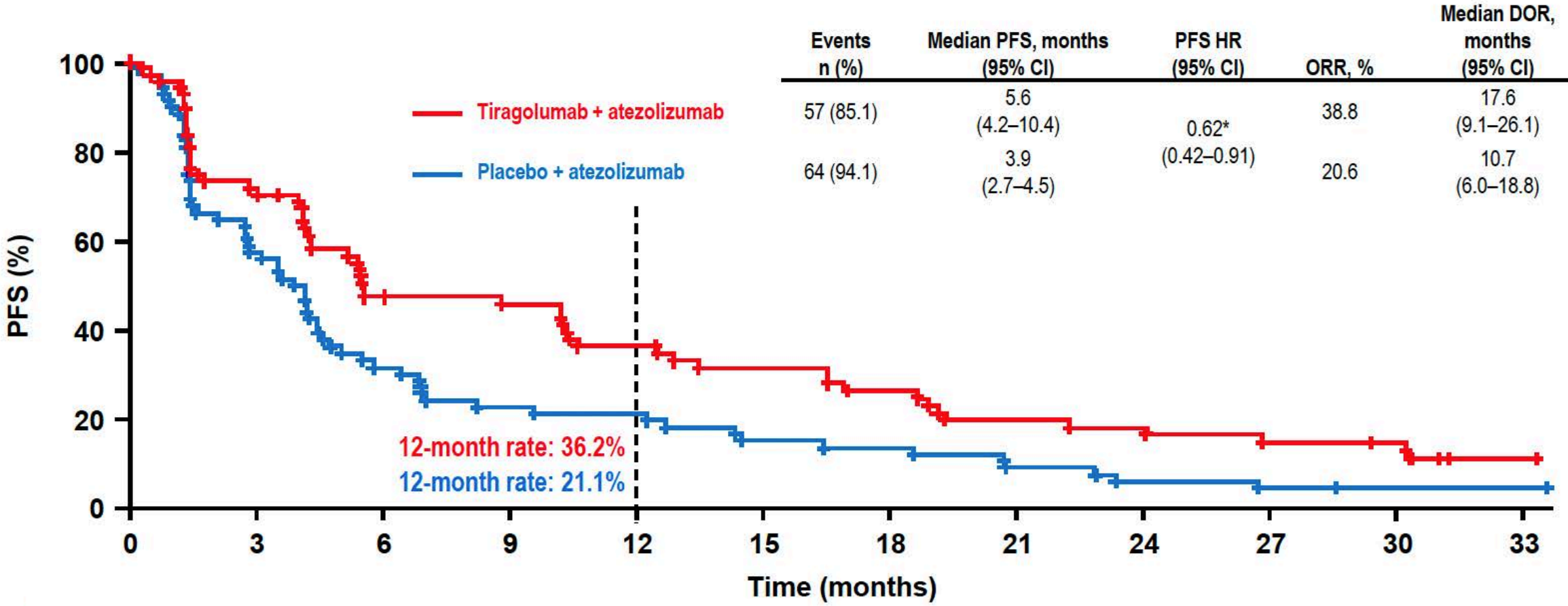
Figure adapted from Manieri et al. *Trends Immunology* 2017

NK, natural killer; PVR, poliovirus receptor

[1] Manieri et al. *Trends Immunology* 2017; [2] Rotte et al. *Annals of Oncology* 2018; [3] Yu et al. *Nature Immunology* 2009

Rodriguez-Abreu D et al. ASCO 2020;Abstract 9503.

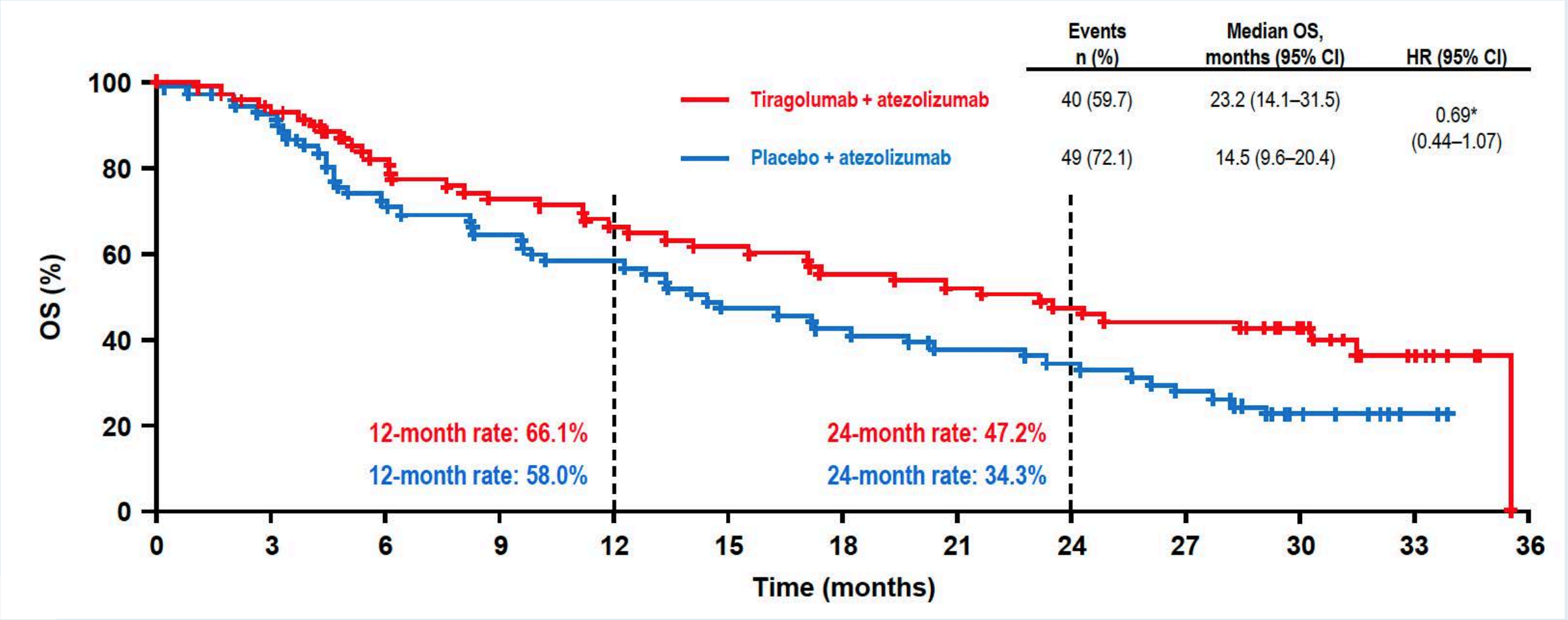
CITYSCAPE: Investigator-Assessed PFS (ITT)



	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tiragolumab + atezolizumab	57 (85.1)	5.6 (4.2–10.4)	0.62* (0.42–0.91)	38.8	17.6 (9.1–26.1)
Placebo + atezolizumab	64 (94.1)	3.9 (2.7–4.5)		20.6	10.7 (6.0–18.8)

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Investigator-Assessed OS (ITT)



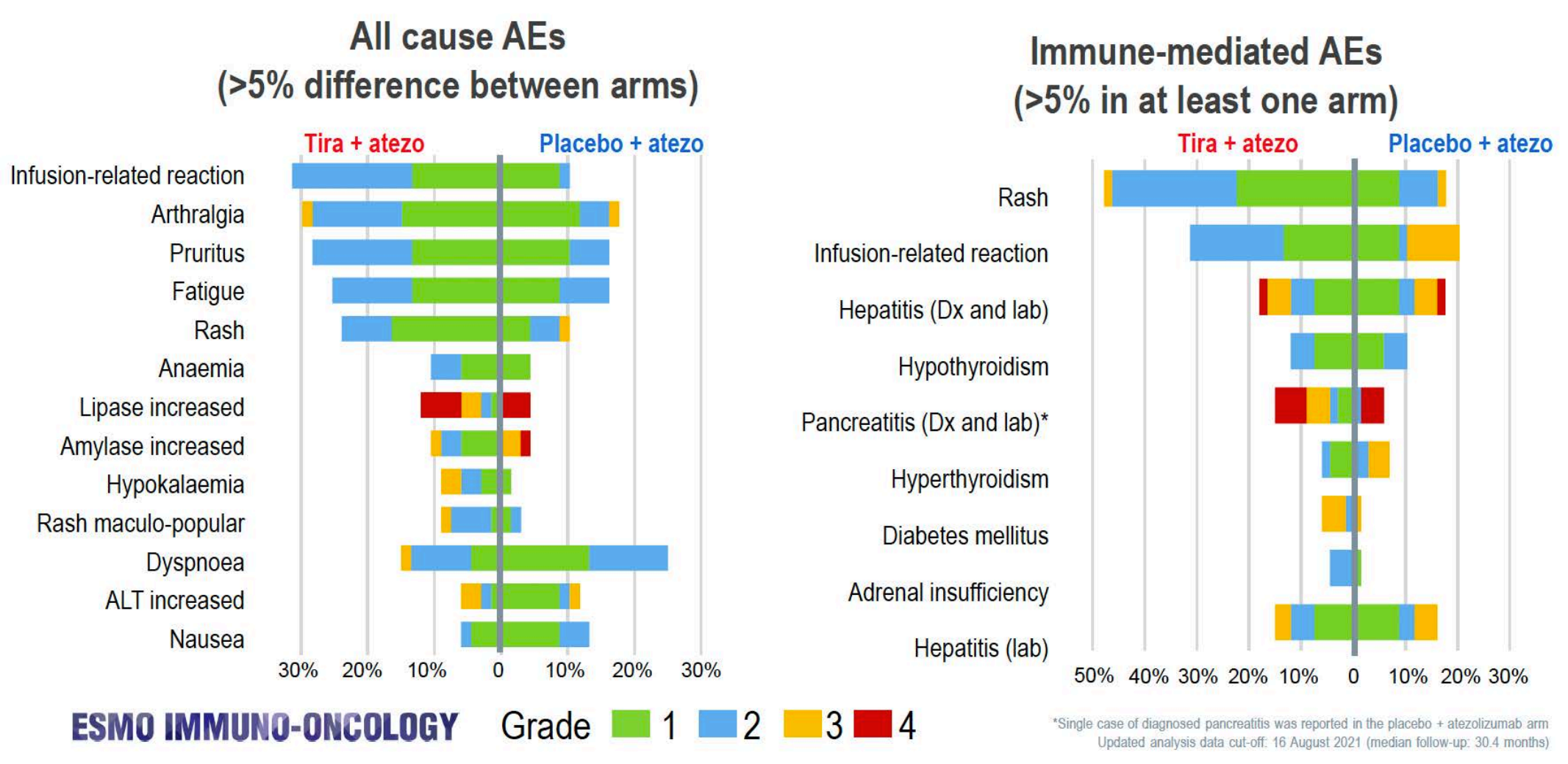
Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Safety Summary

	Tiragolumab + atezolizumab (n=67)	Placebo + atezolizumab (n=68)
Median treatment duration, months (min–max)	4.99 (0–34.5)	2.81 (0–30.3)
Any-cause AEs, n (%)	66 (98.5)	66 (97.1)
Grade 3–4 AEs	35 (52.2)	27 (39.7)
Grade 5	3 (4.5)	7 (10.3)
Serious AEs	35 (52.2)	28 (41.2)
Treatment-related AEs, n (%)	55 (82.1)	48 (70.6)
Grade 3–4 AEs	15 (22.4)	17 (25.0)
Grade 5*	2 (3.0)	0
Serious AEs	14 (20.9)	12 (17.6)
Immune-mediated AEs, n (%)	51 (76.1)	32 (47.1)
Grade 3–4	13 (19.4)	11 (16.2)
AEs leading to dose modification/interruption, n (%)	33 (49.3)	24 (35.3)
AEs leading to treatment withdrawal, n (%)	10 (14.9)	9 (13.2)

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Incidence of Adverse Events



Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

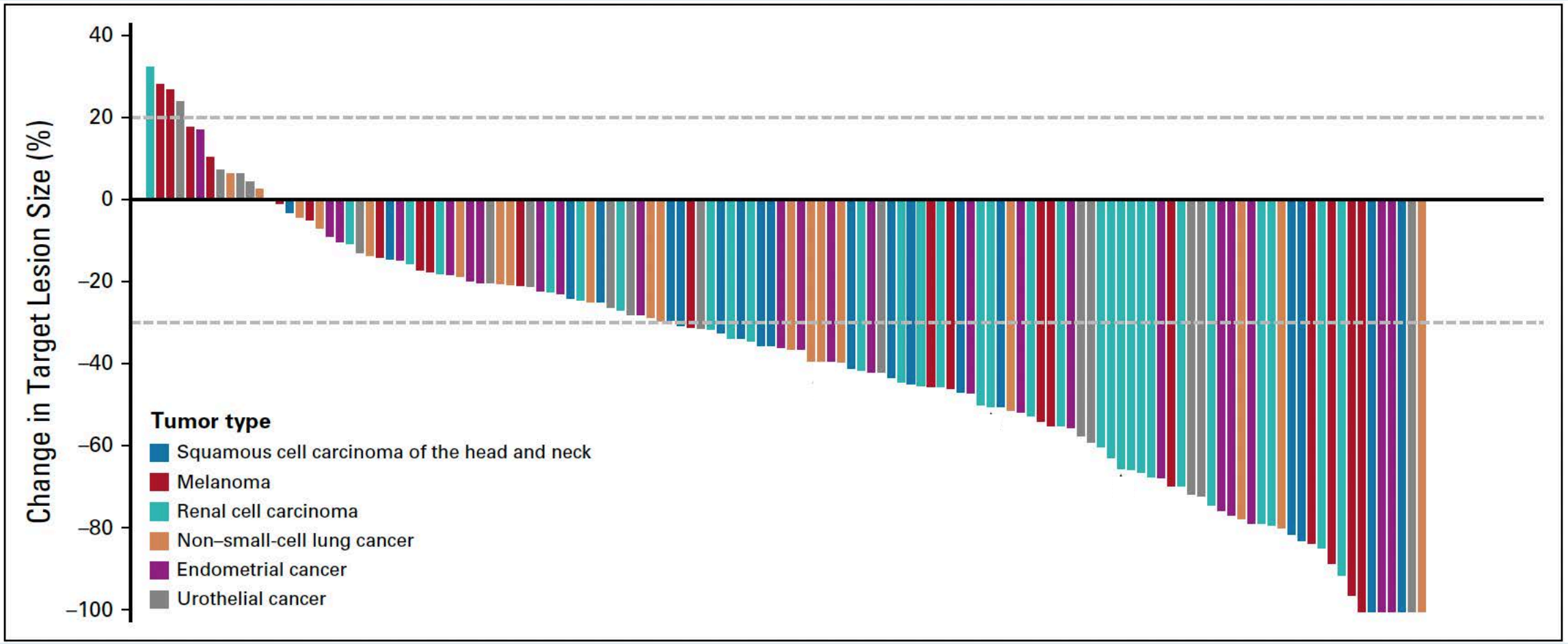
original reports

Phase IB/II Trial of Lenvatinib Plus Pembrolizumab in Patients With Advanced Renal Cell Carcinoma, Endometrial Cancer, and Other Selected Advanced Solid Tumors

Matthew H. Taylor, MD[1]; Chung-Han Lee, MD, PhD[2]; Vicky Makker, MD[2]; Drew Rasco, MD[3]; Corina E. Dutcus, MD[4]; Jane Wu, PhD[4]; Daniel E. Stepan, MD[5]; Robert C. Shumaker, PhD[4]; and Robert J. Motzer, MD[2]

J Clin Oncol 2020;38:154-63

KEYNOTE-146: Maximum Change in Target Lesion Size (All Patients)



Taylor MH et al. *J Clin Oncol* 2020;38:154-63.

KEYNOTE-146: Phase IB/II Trial of Lenvatinib/Pembrolizumab in Advanced Solid Cancers

Efficacy in the Metastatic NSCLC Population				
N	**Line of therapy**	**ORR**	**Median DOR**	**Median PFS**
21	Any	33%	10.9 mo	5.9 mo

DOR = duration of response

Summary of Treatment-Related Adverse Events (TREAs): All Patients	
Parameter	**(N = 137)**
Serious AEs	26%
TREAs leading to pembrolizumab dose interruption	45%
TREAs leading to pembrolizumab discontinuation	15%
TREAs leading to lenvatinib dose reduction and/or interruption	85%
TREAs leading to lenvatinib discontinuation	13%

Taylor MH et al. *J Clin Oncol* 2020;38:154-63.

Ongoing LEAP Phase III Trials in NSCLC

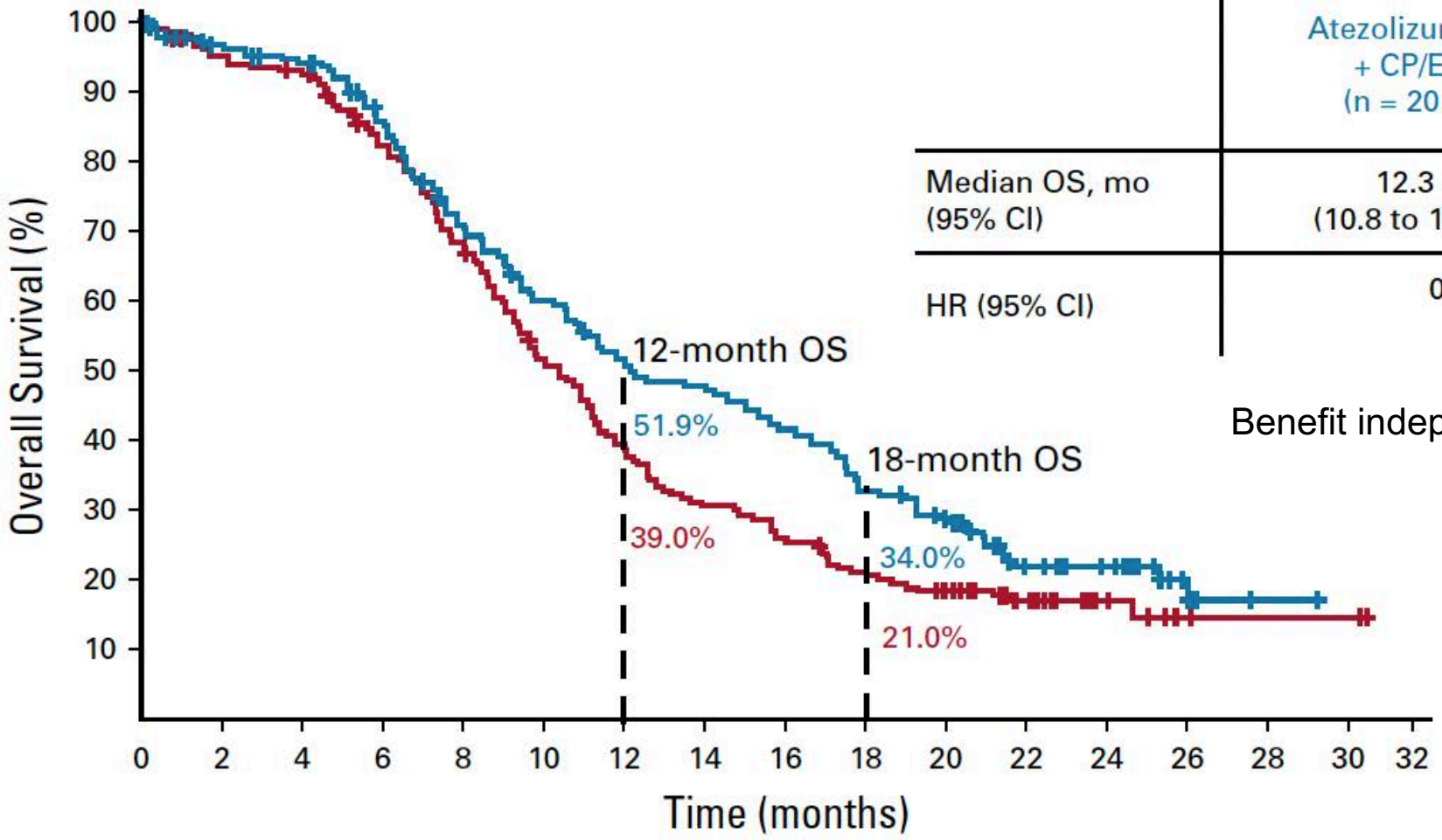
Trial ID	N	Patient population	Line of therapy	Treatment
LEAP-006	726	Previously untreated metastatic nonsquamous NSCLC	1L	• Pemetrexed + platinum chemo + Pembrolizumab + lenvatinib • Pemetrexed + platinum chemo + pembrolizumab + placebo
LEAP-007	620	Previously untreated, advanced (Stage IV), PD-L1 positive (TPS ≥1%) NSCLC	1L	• Lenvatinib + pembrolizumab • Placebo + pembrolizumab
LEAP-008	405	Metastatic NSCLC that progressed during/after platinum doublet chemotherapy or on treatment with anti-PD-1/PD-L1 monoclonal antibody as monotherapy or combination therapy	≥2L	• Lenvatinib + pembrolizumab • Standard chemotherapy • Lenvatinib

Taylor MH et al. *Futur Oncol* 2021;17(6):637-47. www.clinicaltrials.gov. NCT03829319, NCT03829332, NCT03976375. Accessed November 2021.

RTP RESEARCH TO PRACTICE

IMpower133: Updated OS in Extensive-Stage SCLC (ES-SCLC) Treated with First-Line Atezolizumab, Carboplatin and Etoposide

Median follow up: 22.9 mo



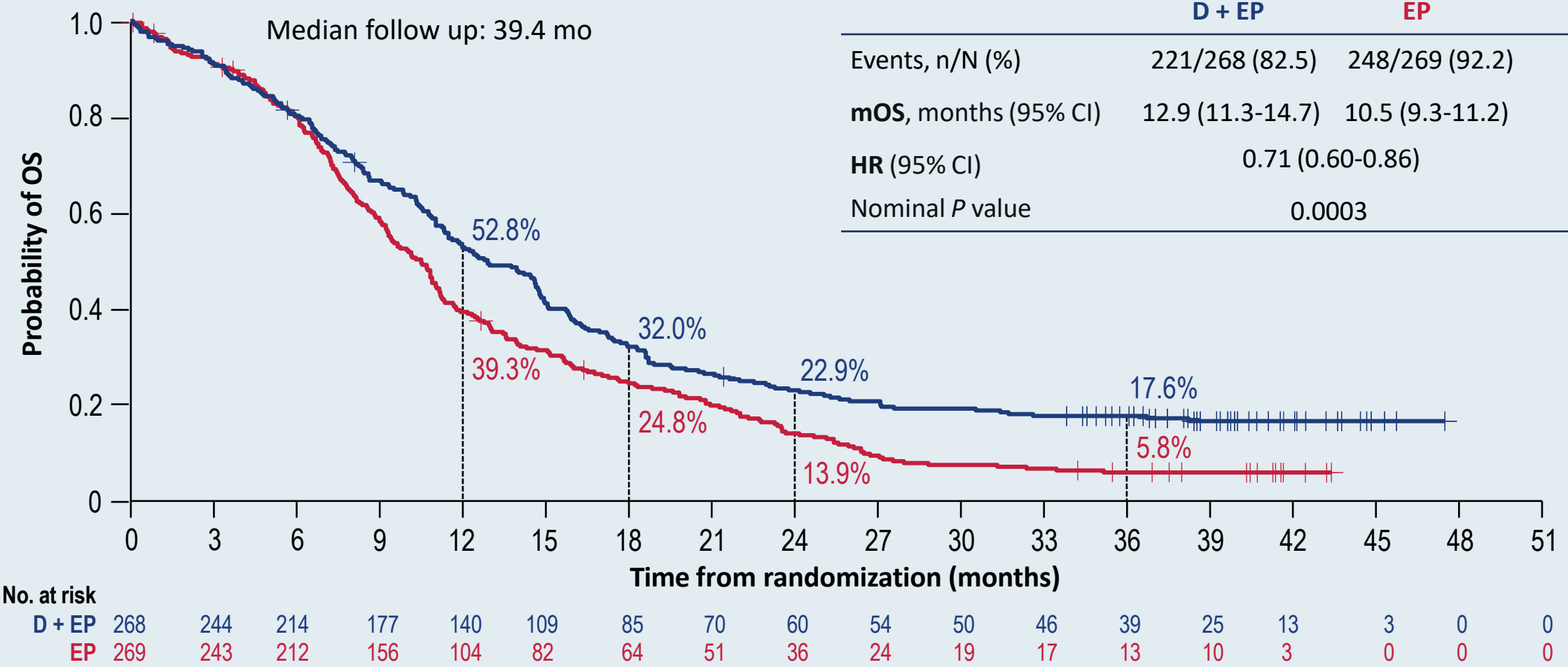
	Atezolizumab + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8 to 15.8)	10.3 (9.3 to 11.3)
HR (95% CI)	0.76 (0.60 to 0.95) *P* = .0154*	

Benefit independent of PD-L1 status

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

RTP RESEARCH TO PRACTICE

CASPIAN: Three-Year Updated OS with First-Line Durvalumab, Platinum and Etoposide for ES-SCLC



	D + EP	EP
Events, n/N (%)	221/268 (82.5)	248/269 (92.2)
mOS, months (95% CI)	12.9 (11.3-14.7)	10.5 (9.3-11.2)
HR (95% CI)	0.71 (0.60-0.86)	
Nominal *P* value	0.0003	

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

RTP RESEARCH TO PRACTICE

SKYSCRAPER-02: A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of Atezolizumab plus Carboplatin and Etoposide with or without Tiragolumab in Patients with Untreated Extensive-Stage SCLC

Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 31, 2022
5:00 PM – 6:00 PM ET

Faculty

Kerry Rogers, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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