

Meet The Professor

Management of Lung Cancer

Corey J Langer, MD

Director of Thoracic Oncology

Abramson Cancer Center

Professor of Medicine

Perelman School of Medicine

University of Pennsylvania

Philadelphia, Pennsylvania

Commercial Support

This activity is supported by an educational grant from AstraZeneca Pharmaceuticals LP.

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 commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Exelixis Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Genomic Health Inc, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seagen Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc and Verastem Inc.

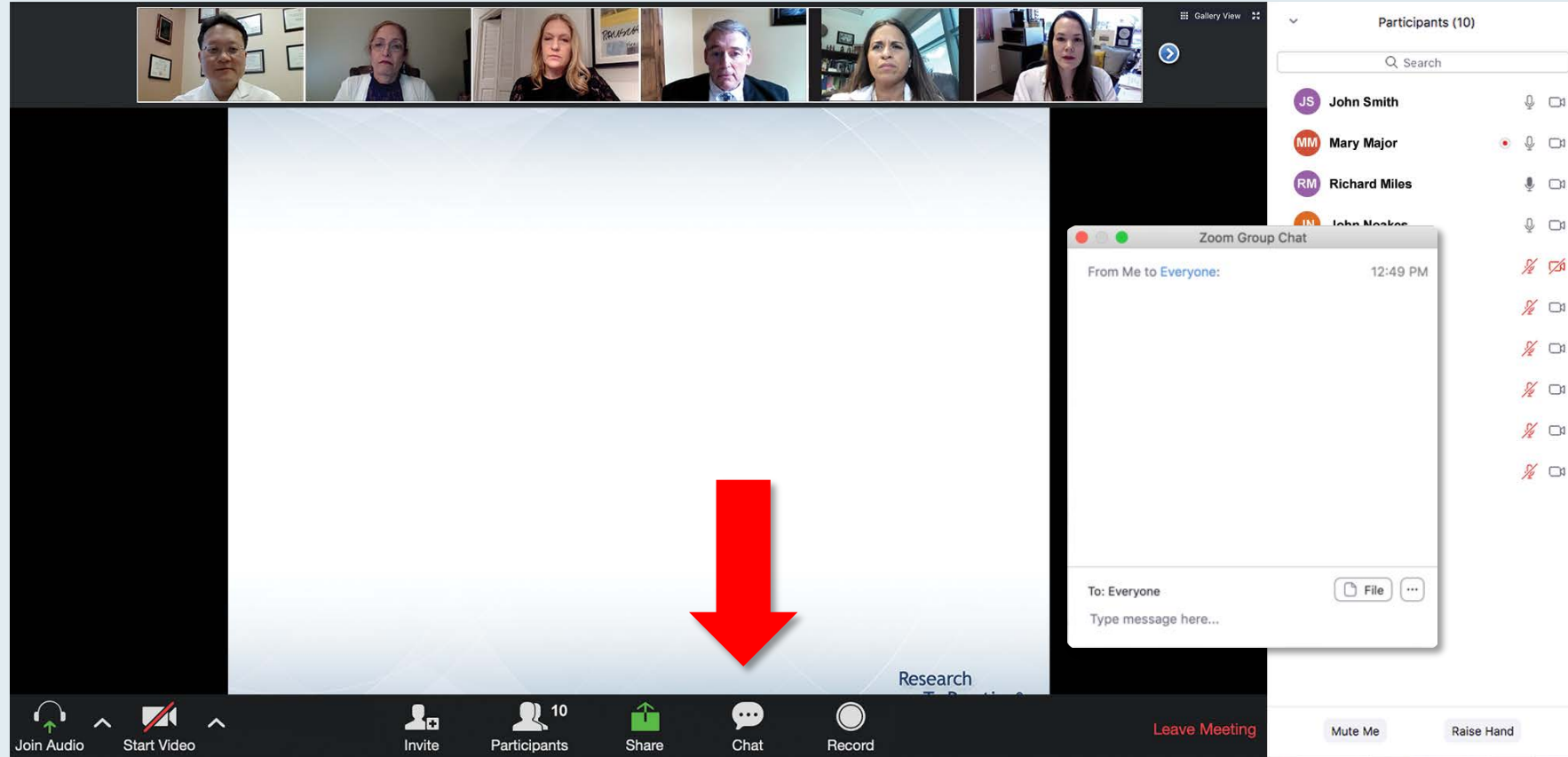
Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Langer— Disclosures

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We Encourage Clinicians in Practice to Submit Questions



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

Familiarizing Yourself with the Zoom Interface

How to answer poll questions

The screenshot displays a Zoom meeting interface. At the top, a gallery view shows six participants. The main screen displays a poll question: "What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?". Below the question is a list of ten treatment options, each preceded by a number. A "Quick Poll" window is open, showing the same list of options with radio buttons for selection. The bottom of the screen features a toolbar with icons for "Join Audio", "Start Video", "Invite", "Participants" (showing 10), "Share", "Chat", "Record", and a "Leave Meeting" button. On the right side, a "Participants (10)" list is visible, showing names and status icons.

What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

Quick Poll

- ☐ Carfilzomib +/- dexamethasone
- ☐ Pomalidomide +/- dexamethasone
- ☐ Carfilzomib + pomalidomide +/- dexamethasone
- ☐ Elotuzumab + lenalidomide +/- dexamethasone
- ☐ Elotuzumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + lenalidomide +/- dexamethasone
- ☐ Daratumumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + bortezomib +/- dexamethasone
- ☐ Ixazomib + Rd
- ☐ Other

Submit

Co-provided by USF Health Research To Practice®

Join Audio Start Video Invite Participants 10 Share Chat Record Leave Meeting Mute Me Raise Hand

Participants (10)

Search

- JS John Smith
- MM Mary Major
- RM Richard Miles
- JN John Noakes
- AS Alice Suarez
- JP Jane Perez
- RS Robert Stiles
- JF Juan Fernandez
- AK Ashok Kumar
- JS Jeremy Smith

When a poll question pops up, click your answer choice from the available options.
Results will be shown after everyone has answered.

Upcoming Webinars

**Thursday, November 12, 2020
12:00 PM – 1:00 PM ET**

**Meet The Professor: Management
of Multiple Myeloma**

Faculty

Sergio Giralt, MD

Moderator

Neil Love, MD

**Friday, November 13, 2020
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**Meet The Professor:
Immunotherapy and Novel
Agents in Gynecologic Cancers**

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**Meet The Professor: Management
of Chronic Lymphocytic
Leukemia**

Faculty

Prof John G Gribben, MD, DSc, FMedSci

Moderator

Neil Love, MD

Thank you for joining us!

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

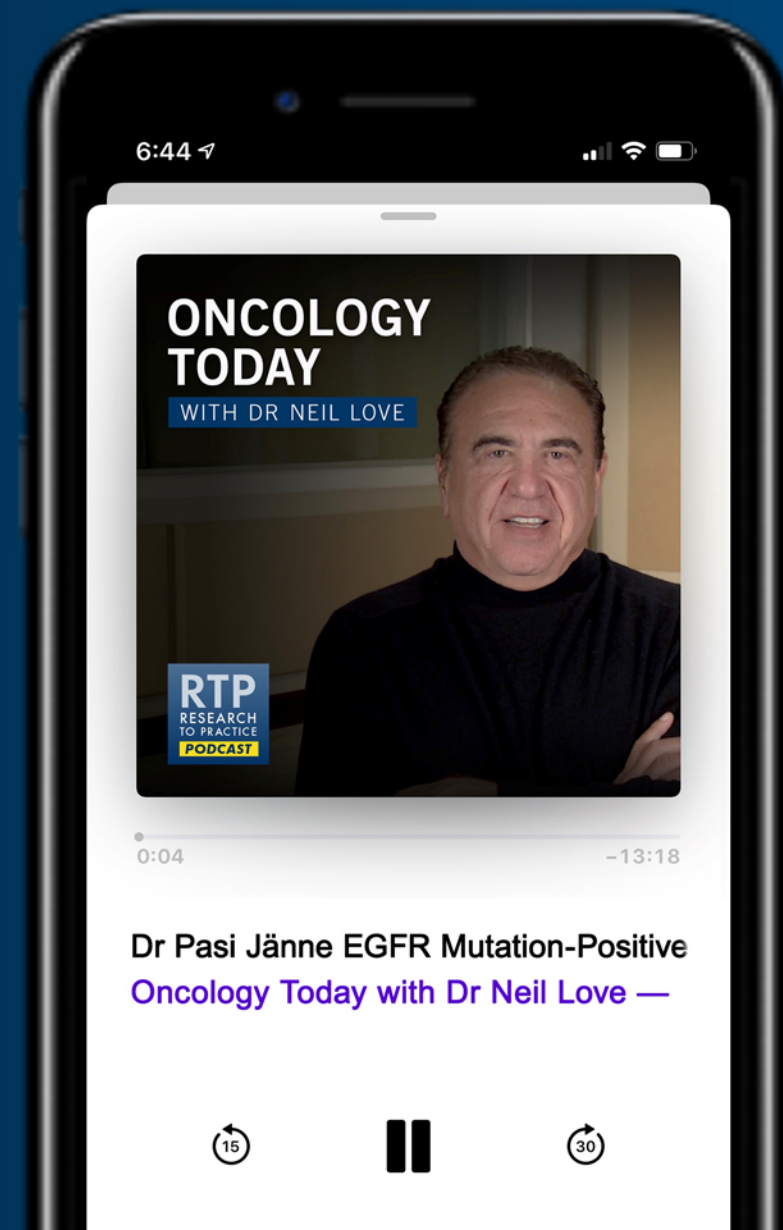
ONCOLOGY TODAY

SPECIAL EDITION: EGFR MUTATION-POSITIVE NON-SMALL CELL LUNG CANCER

WITH DR NEIL LOVE



DR PASI JÄNNE
DANA-FARBER CANCER INSTITUTE



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Meet The Professor Program Participating Faculty



John V Heymach, MD, PhD
Professor and Chair
Thoracic/Head and Neck Medical Oncology
The University of Texas
MD Anderson Cancer Center
Houston, Texas



Benjamin Levy, MD
Associate Professor
Johns Hopkins School of Medicine
Clinical Director
Medical Director, Thoracic Oncology Program
Johns Hopkins Sidney Kimmel Cancer Center
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Leora Horn, MD, MSc
Ingram Associate Professor of Cancer Research
Director, Thoracic Oncology Research Program
Assistant Vice Chairman for Faculty
Development
Vanderbilt University
Medical Center
Nashville, Tennessee



Professor Tony SK Mok, MD
Chairman, Department of Clinical Oncology
The Chinese University of Hong Kong
Hong Kong, China



Corey J Langer, MD
Director of Thoracic Oncology
Abramson Cancer Center
Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania



Joel W Neal, MD, PhD
Associate Professor of Medicine
Division of Oncology
Department of Medicine
Stanford Cancer Institute
Stanford University
Palo Alto, California

Meet The Professor Program Participating Faculty



Paul K Paik, MD

Associate Attending Physician
Clinical Director, Thoracic Oncology Service
Memorial Sloan Kettering Cancer Center
New York, New York



Lecia V Sequist, MD, MPH

Director, Center for Innovation in Early
Cancer Detection
Massachusetts General Hospital Cancer Center
The Landry Family Professor of Medicine
Harvard Medical School
Boston, Massachusetts



Nathan A Pennell, MD, PhD

Professor, Hematology and
Medical Oncology
Cleveland Clinic Lerner College
of Medicine of Case Western
Reserve University
Director, Cleveland Clinic Lung
Cancer Medical Oncology Program
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Program Director
Lung Cancer Research
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Professor Solange Peters, MD, PhD

Head, Medical Oncology
Chair, Thoracic Malignancies
Oncology Department
Lausanne University Hospital (CHUV)
Lausanne, Switzerland

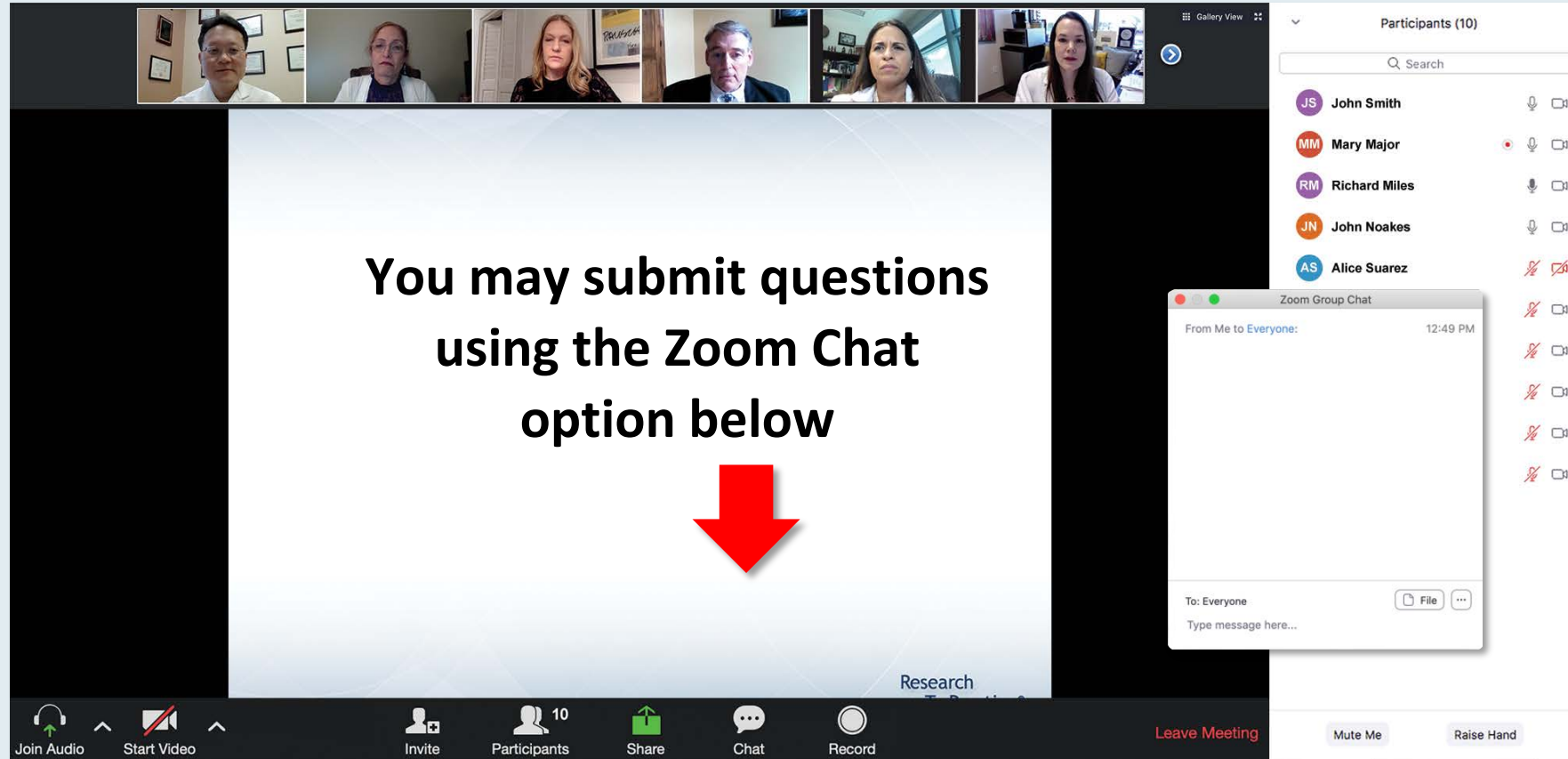


Project Chair

Neil Love, MD

Research To Practice
Miami, Florida

We Encourage Clinicians in Practice to Submit Questions



The screenshot displays a Zoom meeting interface. At the top, a gallery view shows six participants. The main screen displays a presentation slide with the text: "You may submit questions using the Zoom Chat option below". A large red arrow points downwards from this text. On the right side, a "Participants (10)" list is visible, showing names like John Smith, Mary Major, Richard Miles, John Noakes, and Alice Suarez. Below the participants list, a "Zoom Group Chat" window is open, showing a message from "Me to Everyone" at 12:49 PM. The bottom toolbar includes icons for "Join Audio", "Start Video", "Invite", "Participants", "Share", "Chat", and "Record". A "Leave Meeting" button is also present.

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- ☐ Ixazomib + Rd
- ☐ Other

Participants (10)

Name	Status
John Smith	Microphone On, Video On
Mary Major	Microphone On, Video On
Richard Miles	Microphone On, Video On
John Noakes	Microphone On, Video On
Alice Suarez	Microphone Off, Video Off
Jane Perez	Microphone Off, Video Off
Robert Stiles	Microphone Off, Video Off
Juan Fernandez	Microphone Off, Video Off
Ashok Kumar	Microphone Off, Video Off
Jeremy Smith	Microphone Off, Video Off

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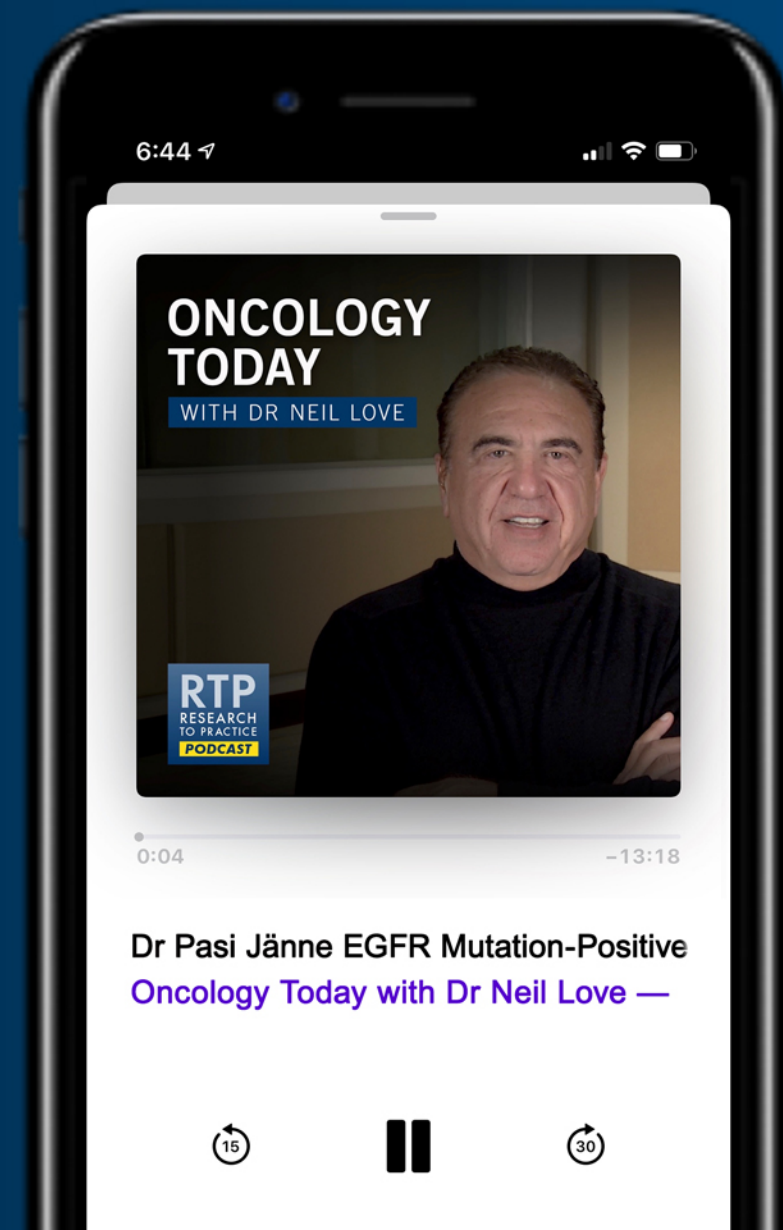
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Joshua Bauml, MD

Assistant Professor of Medicine, Division of Hematology/Oncology
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, Pennsylvania

Meet The Professor with Dr Langer

Module 1: Cases from Dr Bauml

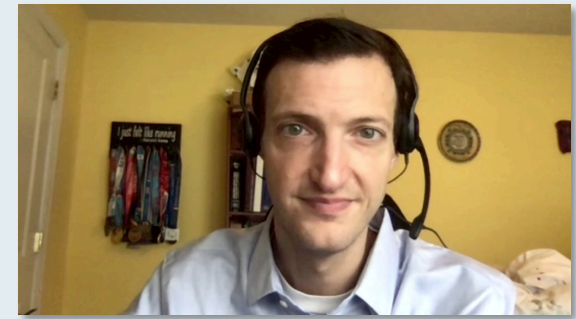
- A 75-year-old woman with locally advanced squamous cell carcinoma of the lung
- A 65-year-old woman with metastatic adenocarcinoma of the lung – ALK translocation
- A 66-year-old woman with metastatic small cell lung cancer
- A 53-year-old woman with metastatic adenocarcinoma of the lung – EGFR exon 19 deletion
- Questions and Comments: MET alterations and amplification in NSCLC

Module 2: Lung Cancer Journal Club with Dr Langer

Module 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

Module 4: Key Papers and Recent Approvals

Case Presentation – Dr Bauml: A 75-year-old woman with locally advanced squamous cell carcinoma of the lung



Dr Joshua Bauml

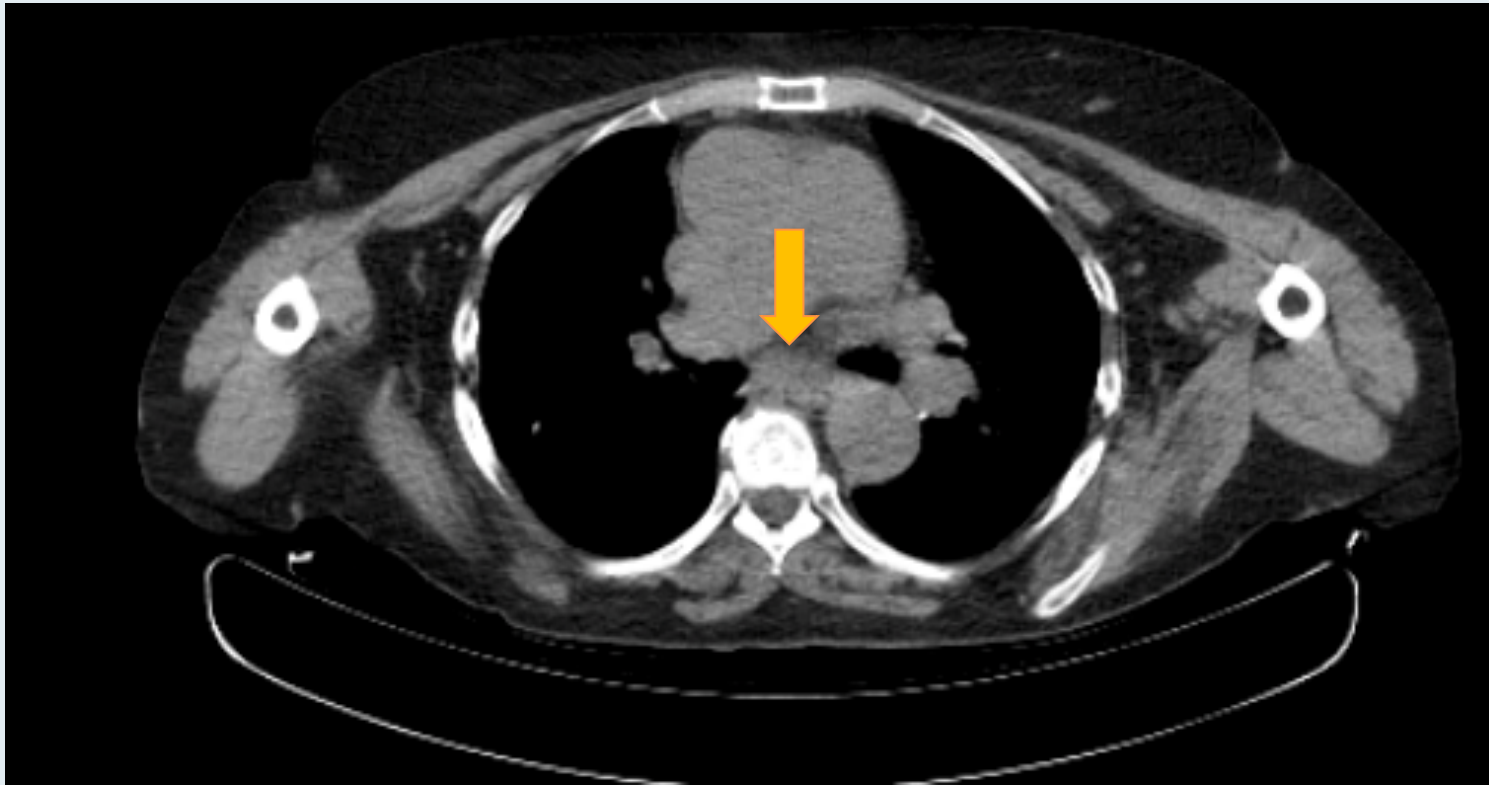
- Two prior lung cancer diagnoses s/p surgery not requiring adjuvant therapy > 5 years ago
- Surveillance imaging: Increasing size of subcarinal lymphadenopathy
- No evidence of distant metastases
- Biopsy: Squamous cell carcinoma, PD-L1: 0%
- Concurrent chemoradiation therapy, with carboplatin/paclitaxel
 - Radiation pneumonitis requiring oxygen and steroids 3 weeks after completion of therapy
 - Consolidation durvalumab not administered due to pneumonitis, declining PS
- Currently, remains NED

Question

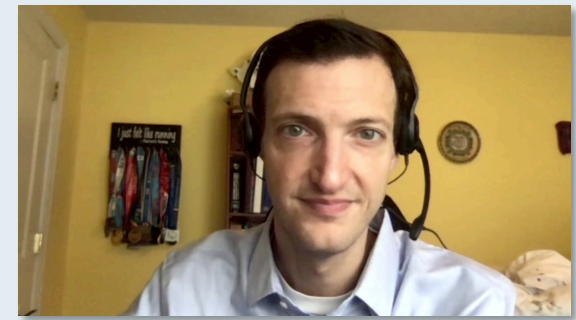
- How do you manage a patient whose performance status declines significantly after chemoradiation therapy? How do you incorporate durvalumab, or do you?

Case Presentation – Dr Bauml: A 75-year-old woman with locally advanced squamous cell carcinoma of the lung

Subcarinal adenopathy



Case Presentation – Dr Bauml: A 65-year-old woman with metastatic adenocarcinoma of the lung – ALK translocation



Dr Joshua Bauml

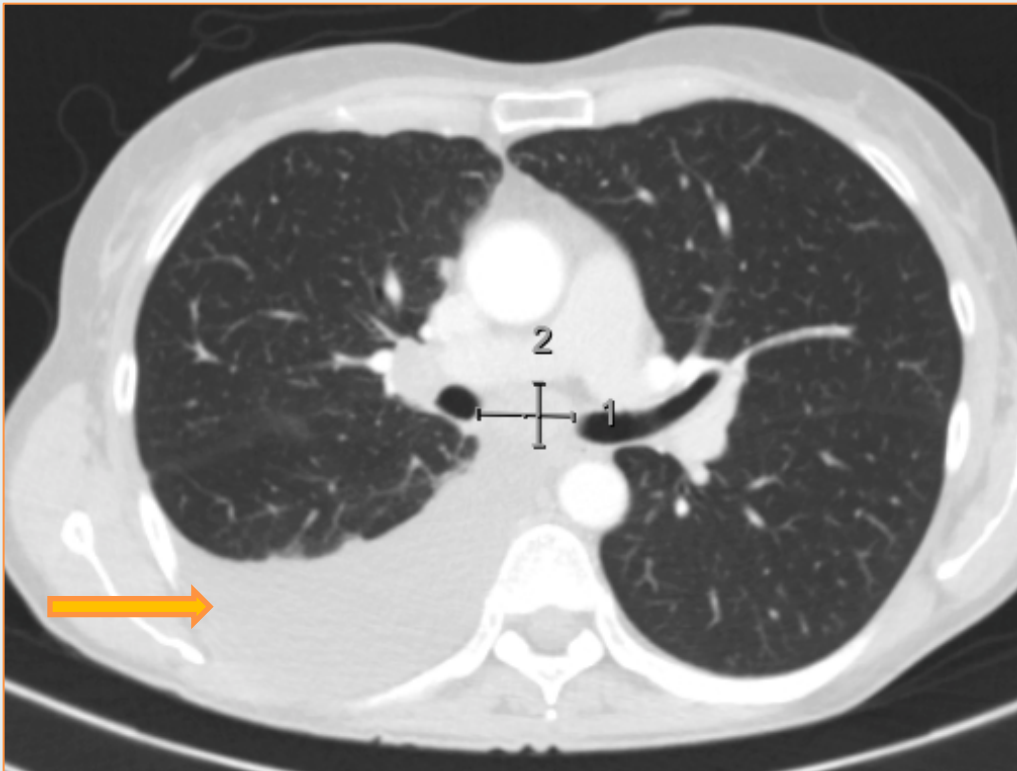
- Presents with abdominal bloating and mild SOB
- CT: Ascites, peritoneal carcinomatosis
- Biopsy: Adenocarcinoma, TTF1-positive
- IHC: ALK-positive; FISH confirms ALK translocation
- Alectinib, with rapid response

Questions

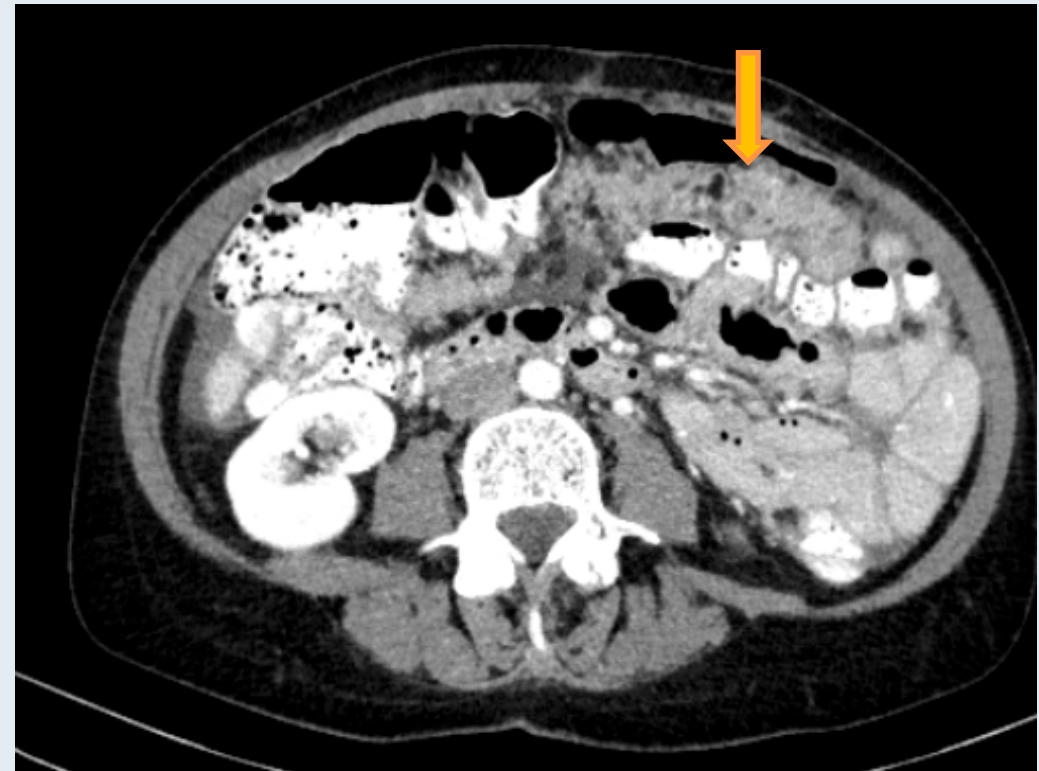
- What is your first-line approach for a patient with metastatic, ALK-translocated NSCLC?
- How do you manage patients who are progressing on alectinib? Do you do molecular testing at the time of progression? And if so, what do you do with that information?

Case Presentation – Dr Bauml: A 65-year-old woman with metastatic adenocarcinoma of the lung – ALK translocation

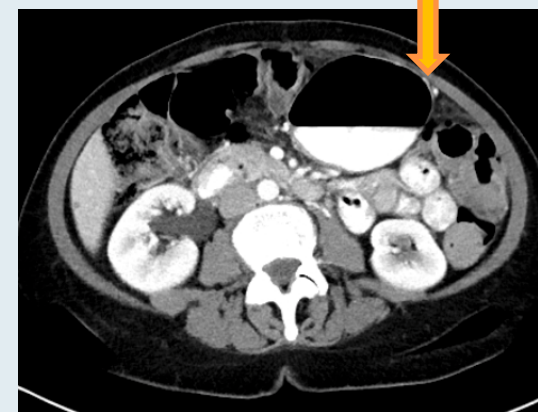
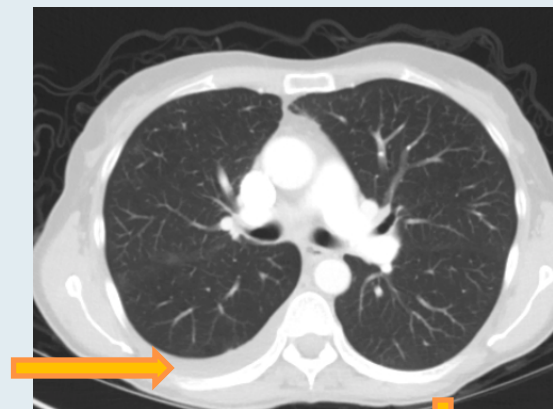
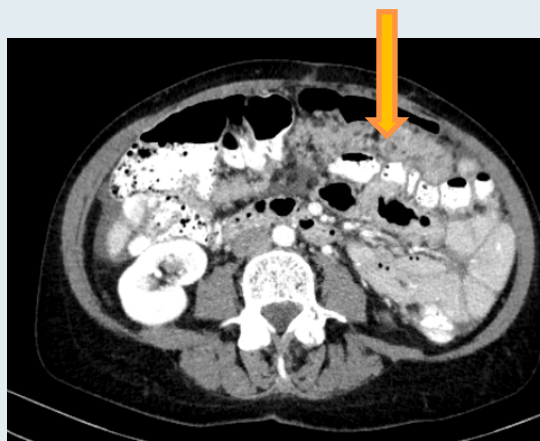
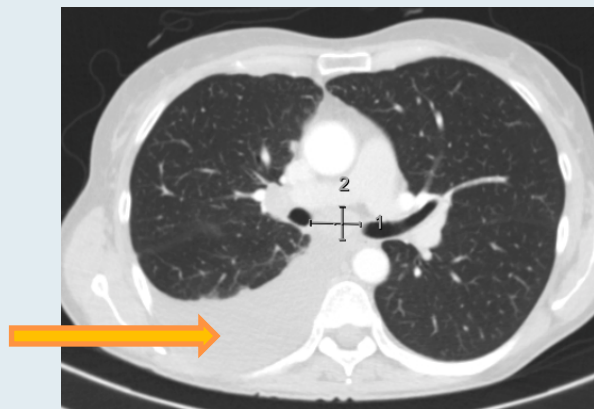
Pleural effusion



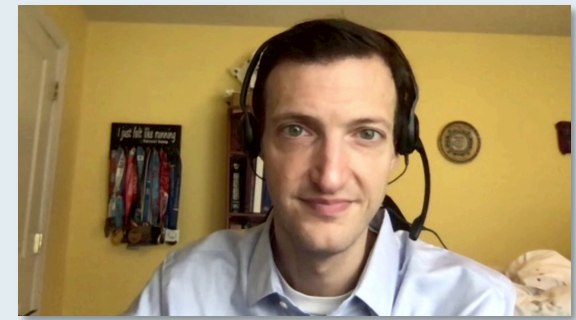
Peritoneal carcinomatosis and ascites



Case Presentation – Dr Bauml: A 65-year-old woman with metastatic adenocarcinoma of the lung – ALK translocation — Scans after initiation of alectinib



Case Presentation – Dr Bauml: A 66-year-old woman with metastatic small cell lung cancer



Dr Joshua Bauml

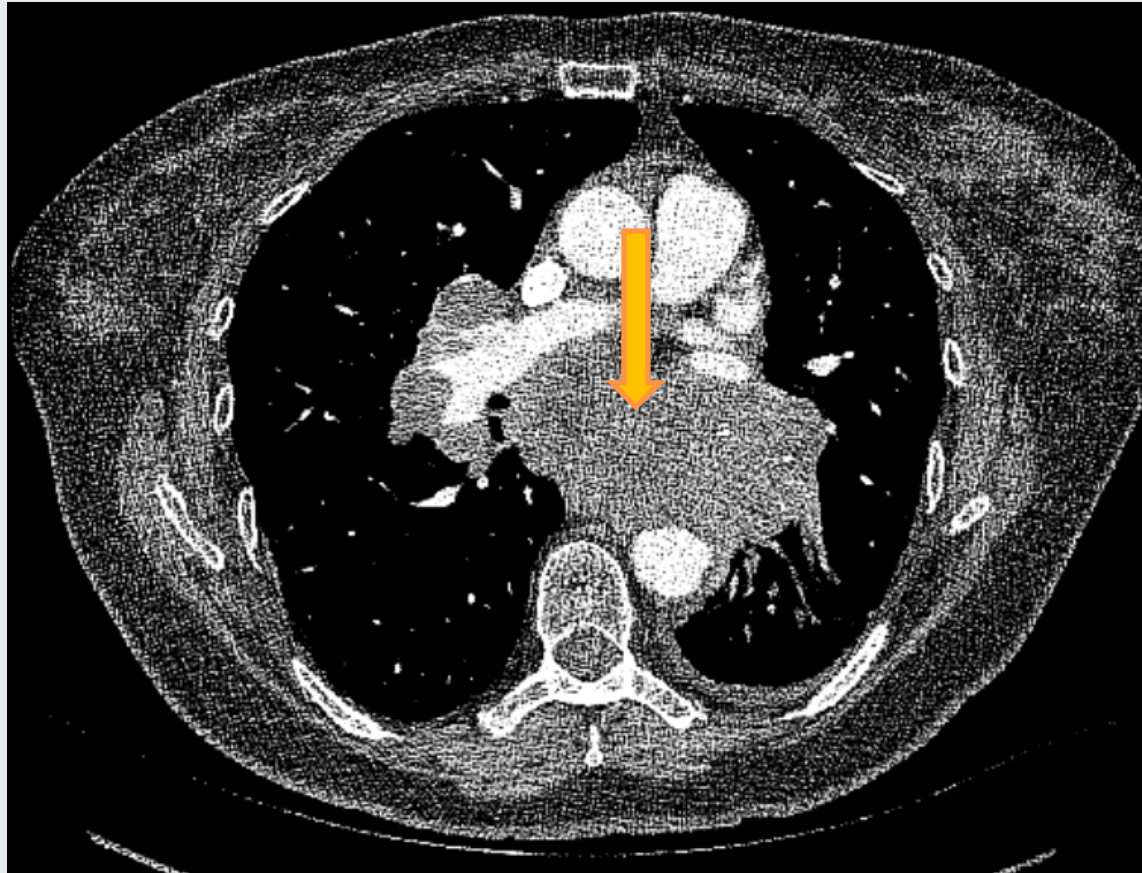
- Presents with PCP, cough and rapidly progressing SOB
- CT chest: Mediastinal mass
- Bronchoscopic biopsy: SCLC
- PET: Extensive hepatic metastases

Questions

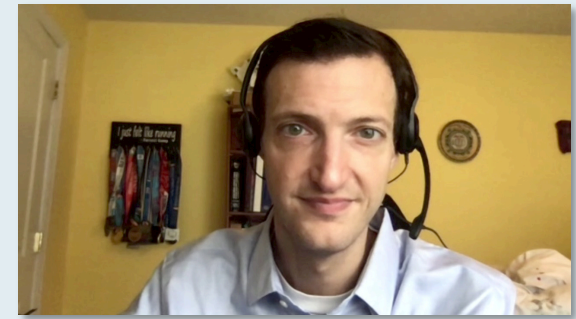
- How do you choose between the different immunotherapies that are currently approved for the management of extensive-stage SCLC?
- When do you incorporate cisplatin versus carboplatin in the management of extensive-stage SCLC?
- If you have apalutamide with disseminated small cell lung cancer and concurrent brain metastases, how do you incorporate directed management of those brain metastases into your overall care plan?

Case Presentation – Dr Bauml: A 66-year-old woman with metastatic SCLC – CT scans

Mediastinal mass, subcarinal lymph node compressing both main bronchi



Case Presentation – Dr Bauml: A 66-year-old woman with metastatic SCLC (continued)



Dr Joshua Bauml

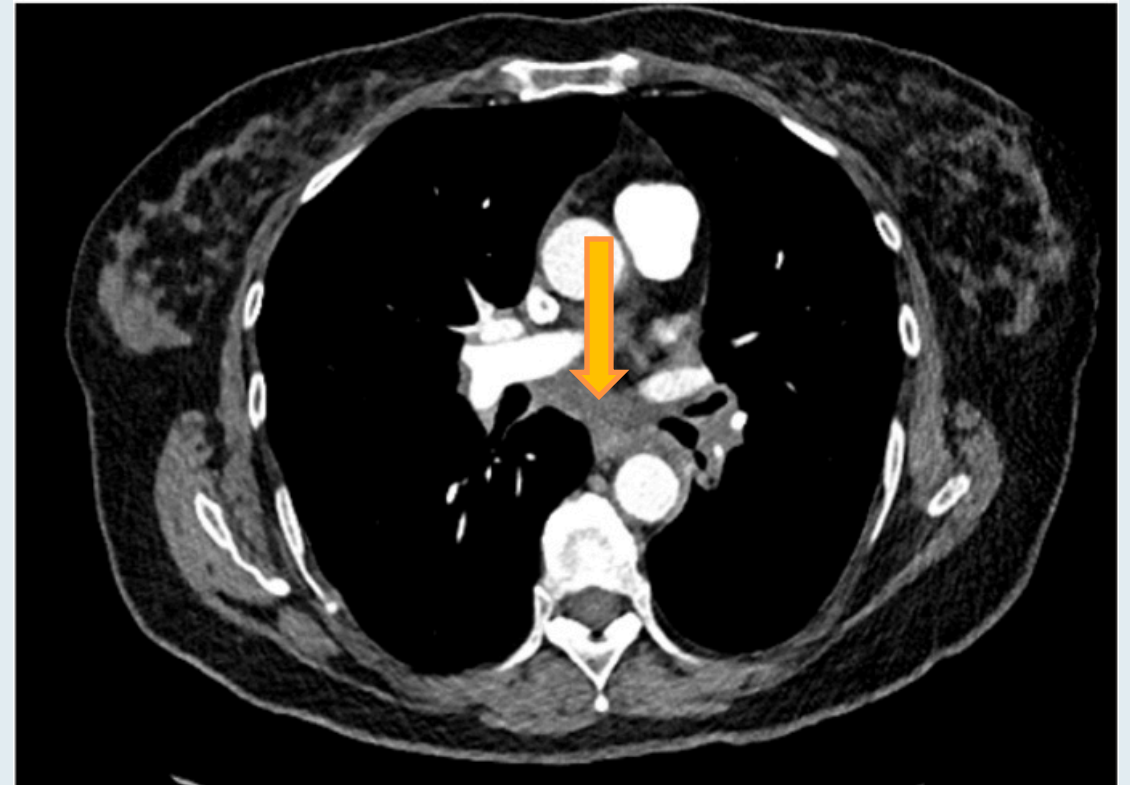
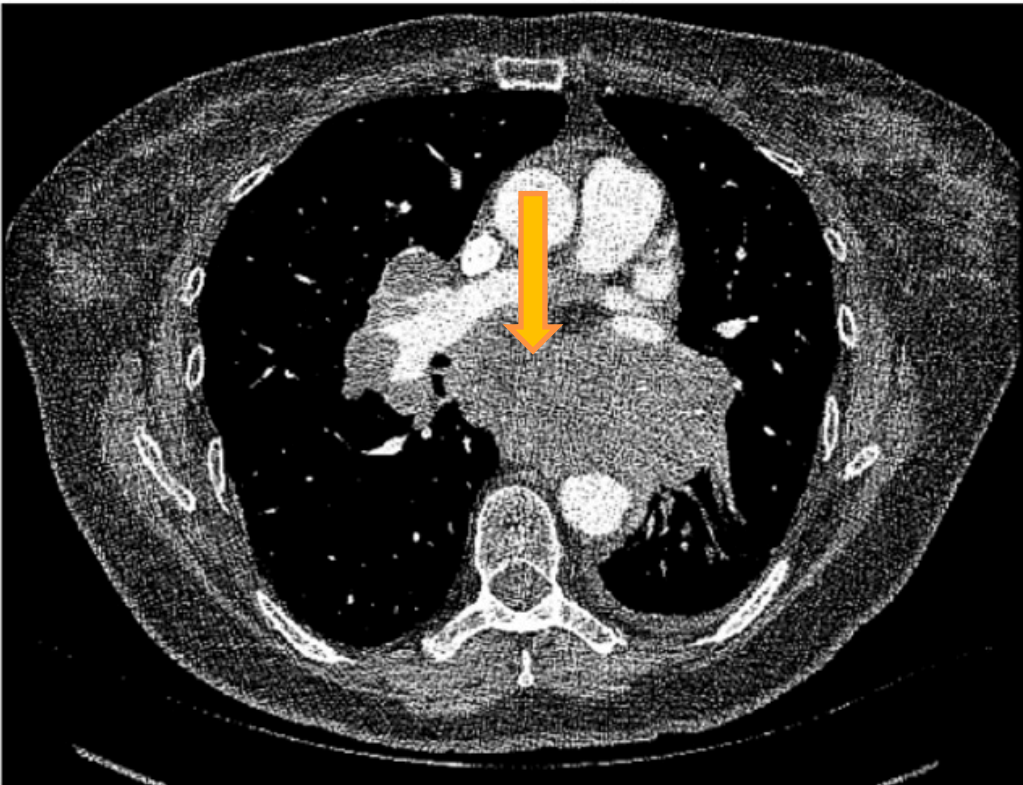
- Presents with PCP, cough and rapidly progressing SOB
- CT chest: Mediastinal mass
- Bronchoscopic biopsy: SCLC
- PET: Extensive hepatic metastases
- ***Carboplatin / etoposide / atezolizumab***

Question

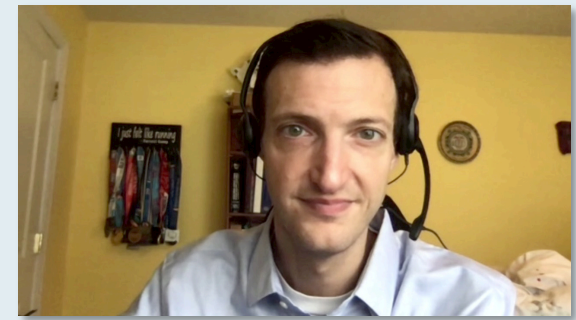
- Which biomarkers will be important, moving forward, to guide our use of immunotherapy in SCLC? Do you use TMB? PD-L1? And, if so, how?

Case Presentation – Dr Bauml: A 66-year-old woman with metastatic SCLC – CT scans

After carboplatin / etoposide / atezolizumab



Case Presentation – Dr Bauml: A 53-year-old woman with metastatic adenocarcinoma of the lung – EGFR exon 19 deletion

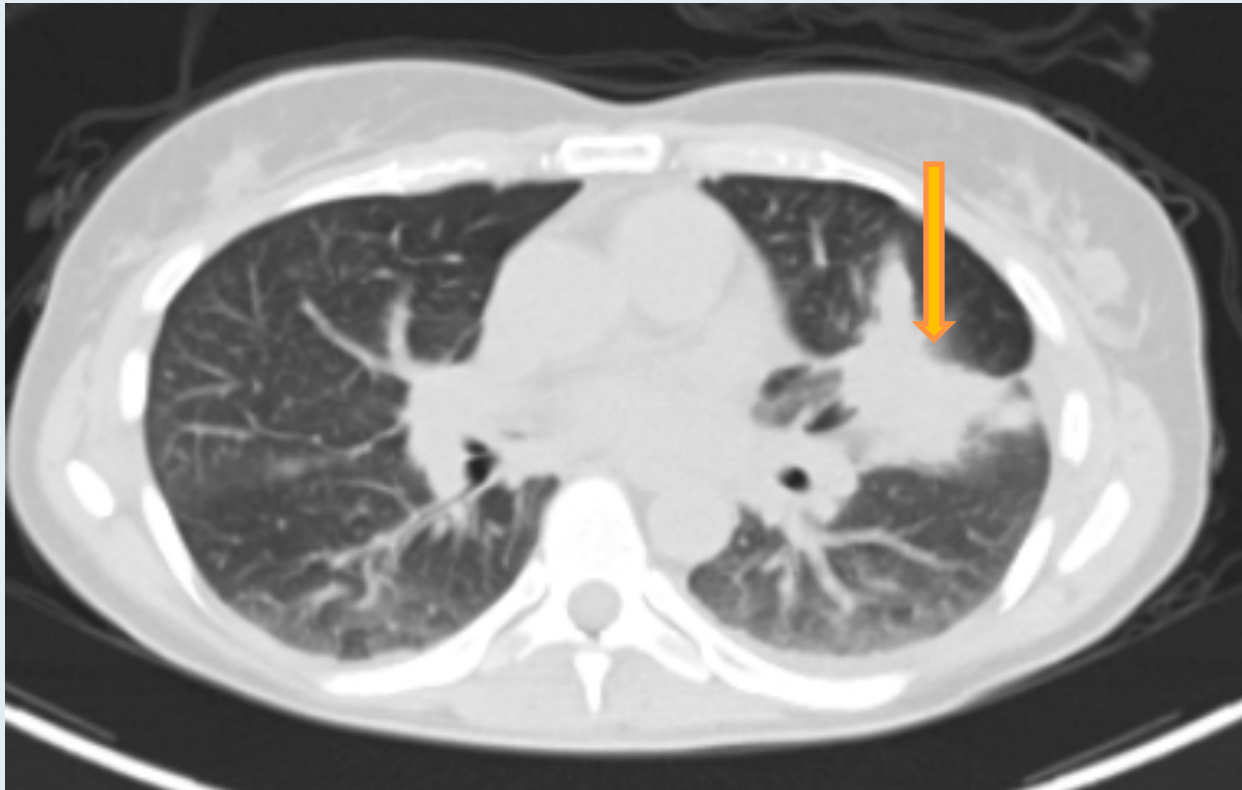


Dr Joshua Bauml

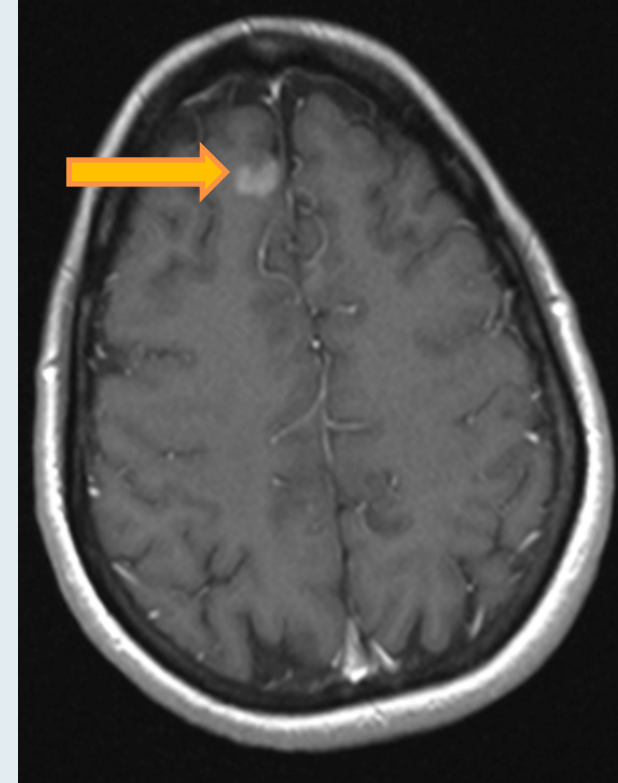
- Presents with back pain, worsening cough after MVA
- Imaging: Bilateral lung masses
- Biopsy: Adenocarcinoma of the lung, EGFR exon 19 deletion, PD-L1-negative
- Brain MRI: 2 separate brain metastases
- Osimertinib 80 mg daily
 - Radiation oncologist recommends SRS

Case Presentation – Dr Bauml: A 53-year-old woman with metastatic adenocarcinoma of the lung – EGFR exon 19 deletion

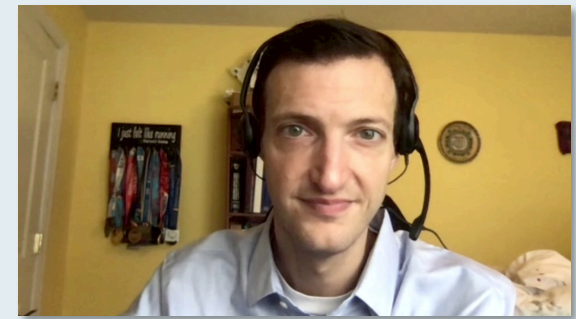
Bilateral Lung Masses



Brain Metastases



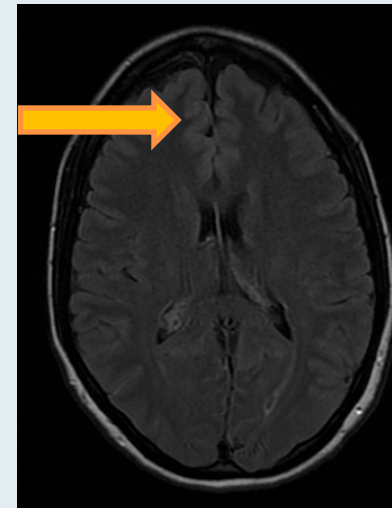
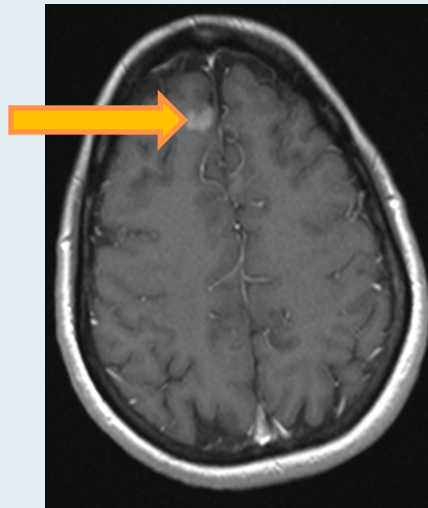
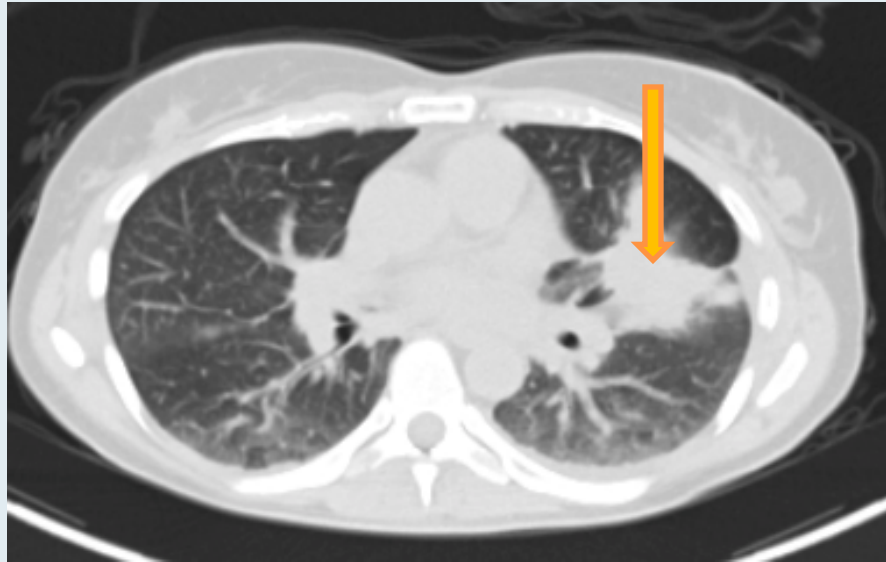
Case Presentation – Dr Bauml: A 53-year-old woman with metastatic adenocarcinoma of the lung – EGFR exon 19 deletion (continued)



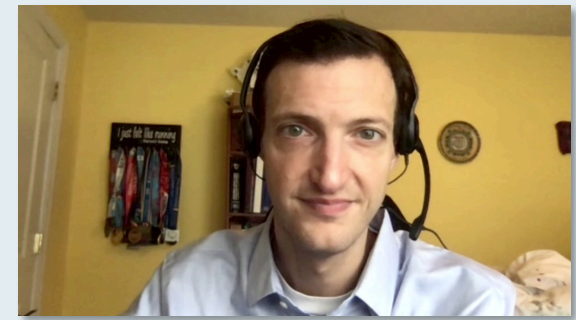
Dr Joshua Bauml

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- Imaging: Bilateral lung masses
- Biopsy: Adenocarcinoma of the lung, EGFR exon 19 deletion, PD-L1-negative
- Brain MRI: 2 separate brain metastases
- Osimertinib 80 mg daily
 - Radiation oncologist recommends SRS but patient refuses
 - ***Excellent response to osimertinib in the lung and brain***
 - ***Nine months later: Rapidly progressing bilateral pleural effusions***
- ***MET FISH: MET amplified x 7***
- ***Capmatinib / osimertinib, with remarkable response***

Case Presentation – Dr Bauml: A 53-year-old woman with metastatic adenocarcinoma of the lung – EGFR exon 19 deletion, osimertinib 80 mg daily, no brain RT



Case Presentation – Dr Bauml: A 53-year-old woman with metastatic adenocarcinoma of the lung – EGFR exon 19 deletion (continued)



Dr Joshua Bauml

- Osimertinib 80 mg daily
 - Radiation oncologist recommends SRS but patient refuses
 - Excellent response to osimertinib in the lung and brain
 - Nine months later: Rapidly progressing bilateral pleural effusions
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- ***Capmatinib / osimertinib, with remarkable response***

Questions

- In patients with NSCLC and an EGFR tumor mutation, does the size of the brain metastases influence how you proceed with treatment?
- If a patient presents with leptomeningeal disease at diagnosis, what dose of osimertinib do you tend to utilize – 80 mg/day or 160 mg/day?
- In patients progressing on first-line osimertinib, what is your approach to assessment of molecular mechanisms of resistance? Tissue biopsy? Liquid biopsy? Both?
- If no mechanisms of resistance are identified, what is your approach – Osimertinib/chemo? Chemo/IO? IO alone?

Questions and Comments: MET alterations and amplification in NSCLC



Dr Joshua Bauml

Meet The Professor with Dr Langer

Module 1: Cases from Dr Bauml

Module 2: Lung Cancer Journal Club with Dr Langer


- Pembrolizumab with chemotherapy versus chemotherapy alone for metastatic NSCLC (mNSCLC)
- Baseline plasma TMB as a marker to predict response to pembrolizumab-based therapy in mNSCLC
- Concurrent chemoradiation therapy and pembrolizumab for locally advanced NSCLC
- Pembrolizumab for the treatment of malignant pleural mesothelioma
- Managing locally advanced NSCLC in older patients
- Treatment for patients with NSCLC harboring rare oncogenic mutations
- Concurrent chemoradiation therapy and the HIV inhibitor nelfinavir for Stage IIIA/IIIB NSCLC
- Varenicline for tobacco use among patients with cancer
- Management of lung cancer during the COVID-19 pandemic
- Gene signatures predictive of response to immune checkpoint blockade in NSCLC

Module 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

Module 4: Key Papers and Recent Approvals

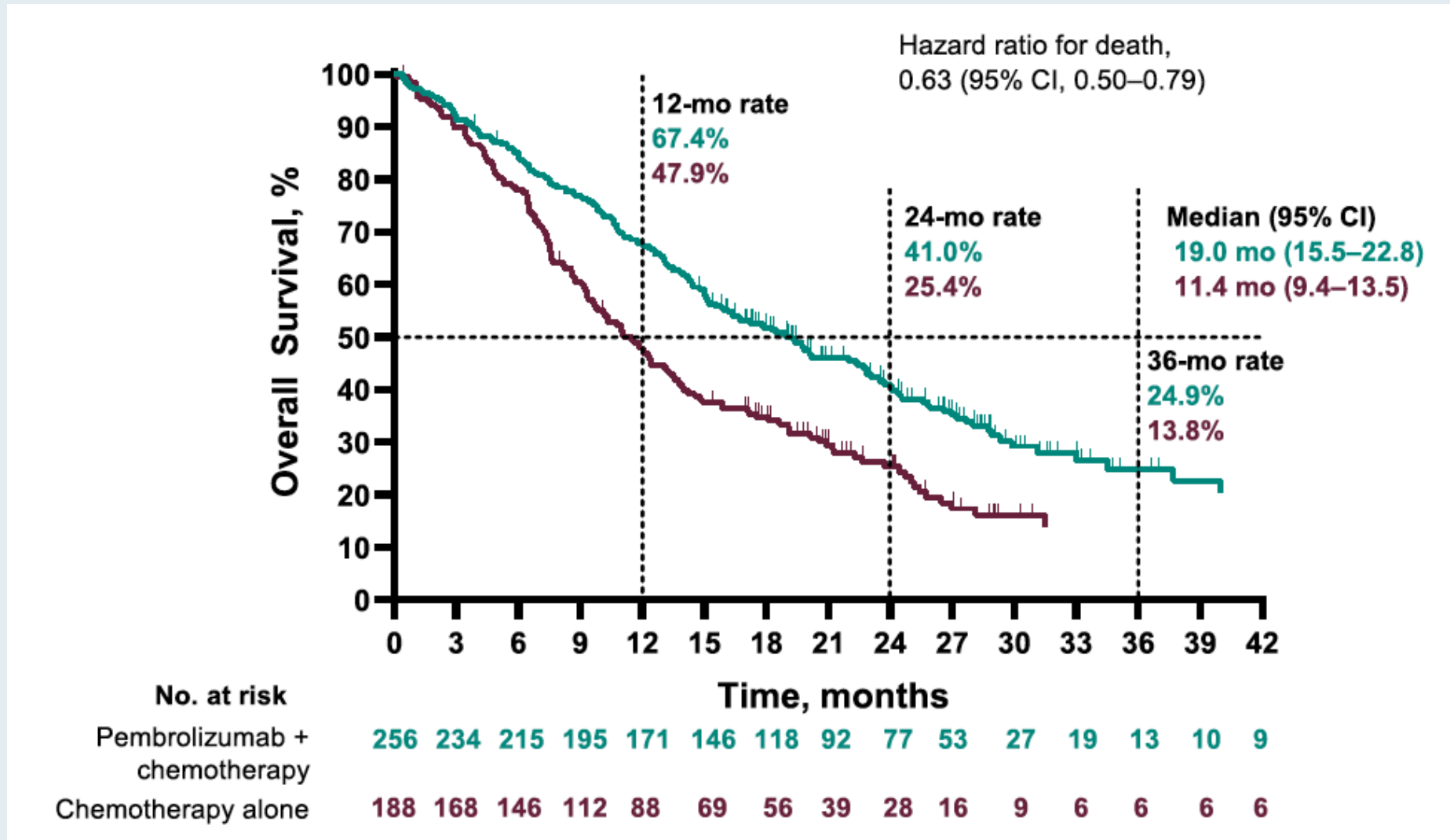
Original Article

Pembrolizumab Plus Chemotherapy Versus Chemotherapy Alone in Patients With Advanced Non-Small Cell Lung Cancer Without Tumor PD-L1 Expression: A Pooled Analysis of 3 Randomized Controlled Trials

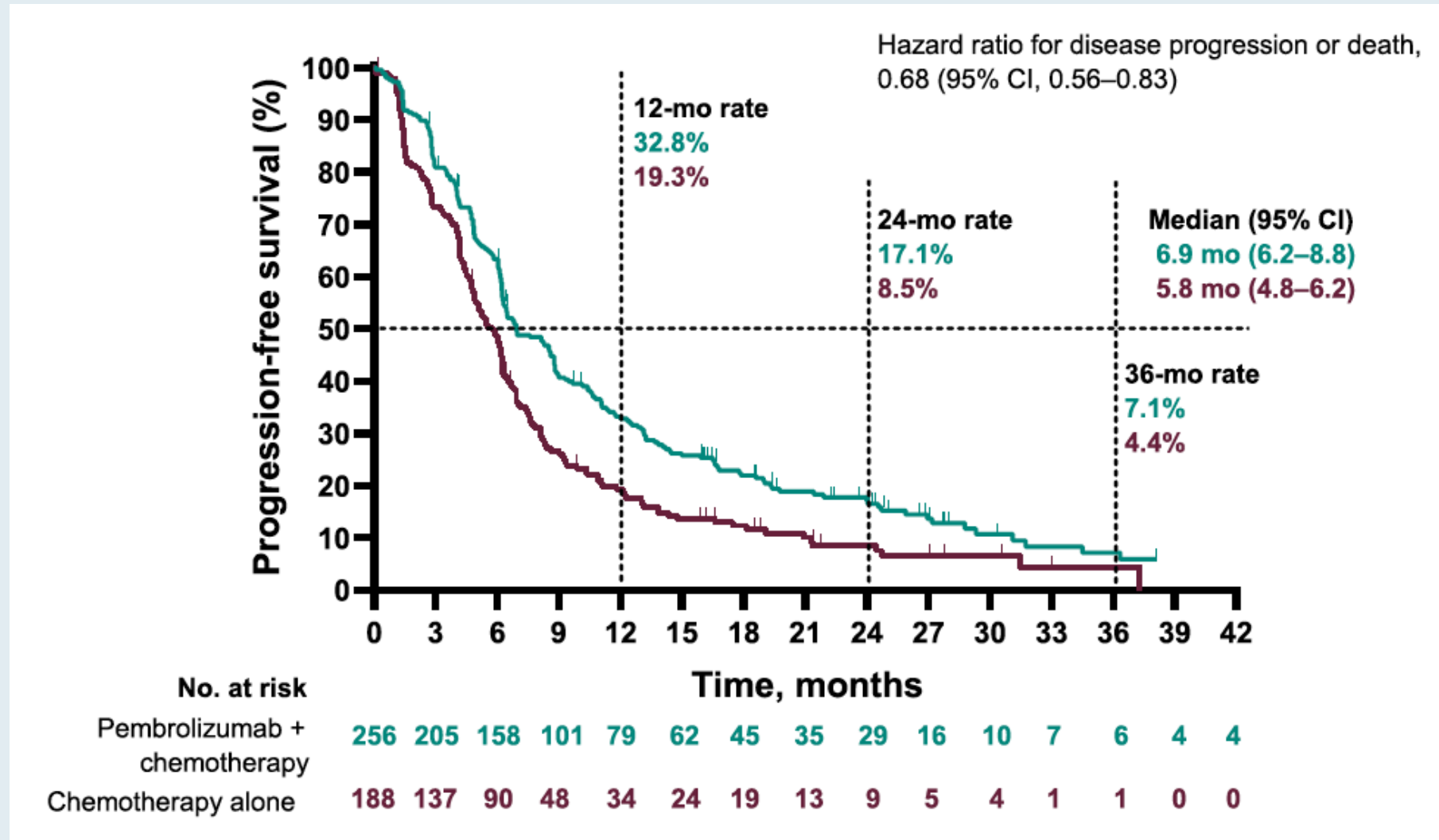
Hossein Borghaei, DO ¹; Corey J. Langer, MD²; Luis Paz-Ares, MD³; Delvys Rodríguez-Abreu, MD⁴; Balazs Halmos, MD⁵; Marina C. Garassino, MD⁶; Baerin Houghton, MD⁷; Takayasu Kurata, MD⁸; Ying Cheng, MD⁹; Jianxin Lin, MS¹⁰; M. Catherine Pietanza, MD¹⁰; Bilal Piperdi, MD¹⁰; and Shirish M. Gadgeel, MD¹¹

Cancer 2020;126(22):4867-77.

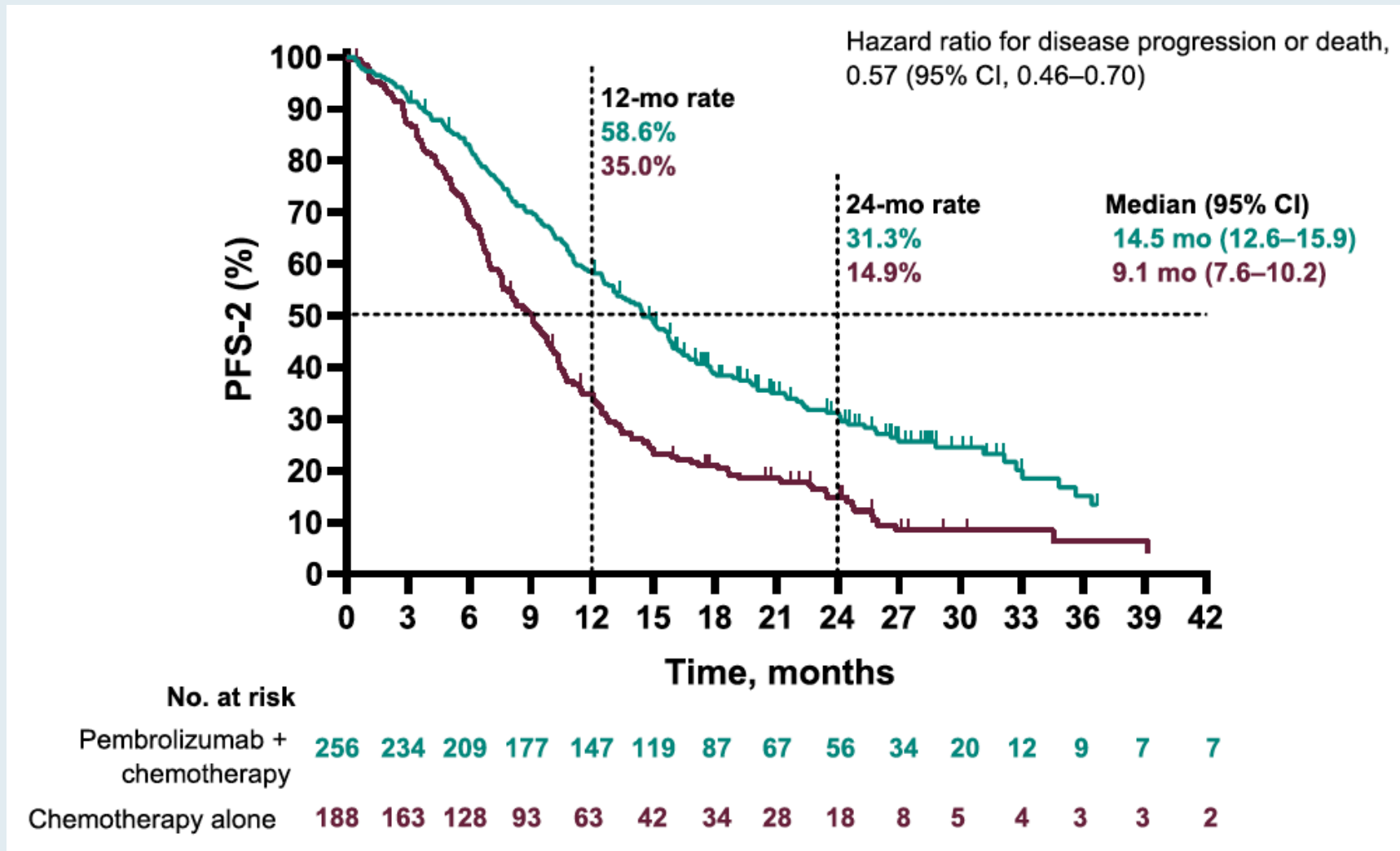
OS for Patients with No PD-L1 Expression (TPS <1%)



PFS for Patients with No PD-L1 Expression (TPS <1%)



PFS-2 for Patients with No PD-L1 Expression (TPS <1%)



Long-Term Overall Survival From KEYNOTE-021 Cohort G: Pemetrexed and Carboplatin With or Without Pembrolizumab as First-Line Therapy for Advanced Nonsquamous NSCLC

Mark M. Awad, MD, PhD,^{a,*} Shirish M. Gadgeel, MD,^b Hossein Borghaei, DO, MS,^c Amita Patnaik, MD,^d James Chih-Hsin Yang, MD, PhD,^e Steven F. Powell, MD,^f Ryan D. Gentzler, MD,^g Renato G. Martins, MD, MPH,^h James P. Stevenson, MD,ⁱ Mehmet Altan, MD,^j Shadia I. Jalal, MD,^k Amit Panwalkar, MD,^l Matthew Gubens, MD, MS,^m Lecia V. Sequist, MD,ⁿ Sanatan Saraf, PhD,^o Bin Zhao, MD, PhD,^o Bilal Piperdi, MD,^o Corey J. Langer, MD^p

J Thorac Oncol 2020;[Online ahead of print].

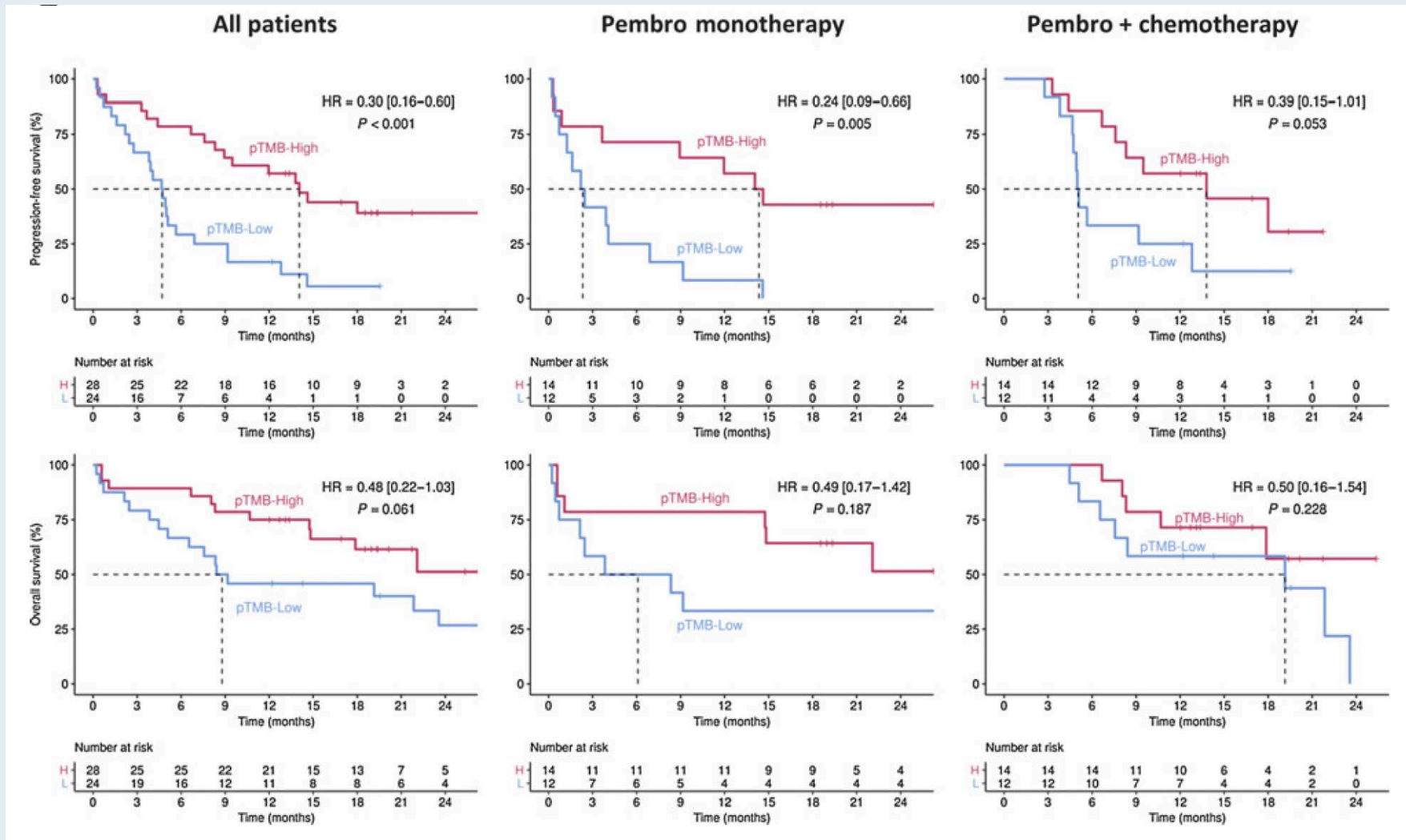
Baseline Plasma Tumor Mutation Burden Predicts Response to Pembrolizumab-based Therapy in Patients with Metastatic Non-Small Cell Lung Cancer


Charu Aggarwal¹, Jeffrey C. Thompson², Austin L. Chien¹, Katie J. Quinn³, Wei-Ting Hwang⁴, Taylor A. Black¹, Stephanie S. Yee¹, Theresa E. Christensen¹, Michael J. LaRiviere⁵, Benjamin A. Silva¹, Kimberly C. Banks³, Rebecca J. Nagy³, Elena Helman³, Abigail T. Berman⁵, Christine A. Ciunci¹, Aditi P. Singh¹, Jeffrey S. Wasser⁶, Joshua M. Bauml¹, Corey J. Langer¹, Roger B. Cohen¹, and Erica L. Carpenter¹

Cancer Res 2020;26(10):2354-61.

Survival Curves Using Cutoff of 16 Mut/Mb in Evaluable Patients

N = 52 evaluable patients (26 pembrolizumab monotherapy and 26 platinum pemetrexed-based therapy)





Research

JAMA Oncology | **Original Investigation**

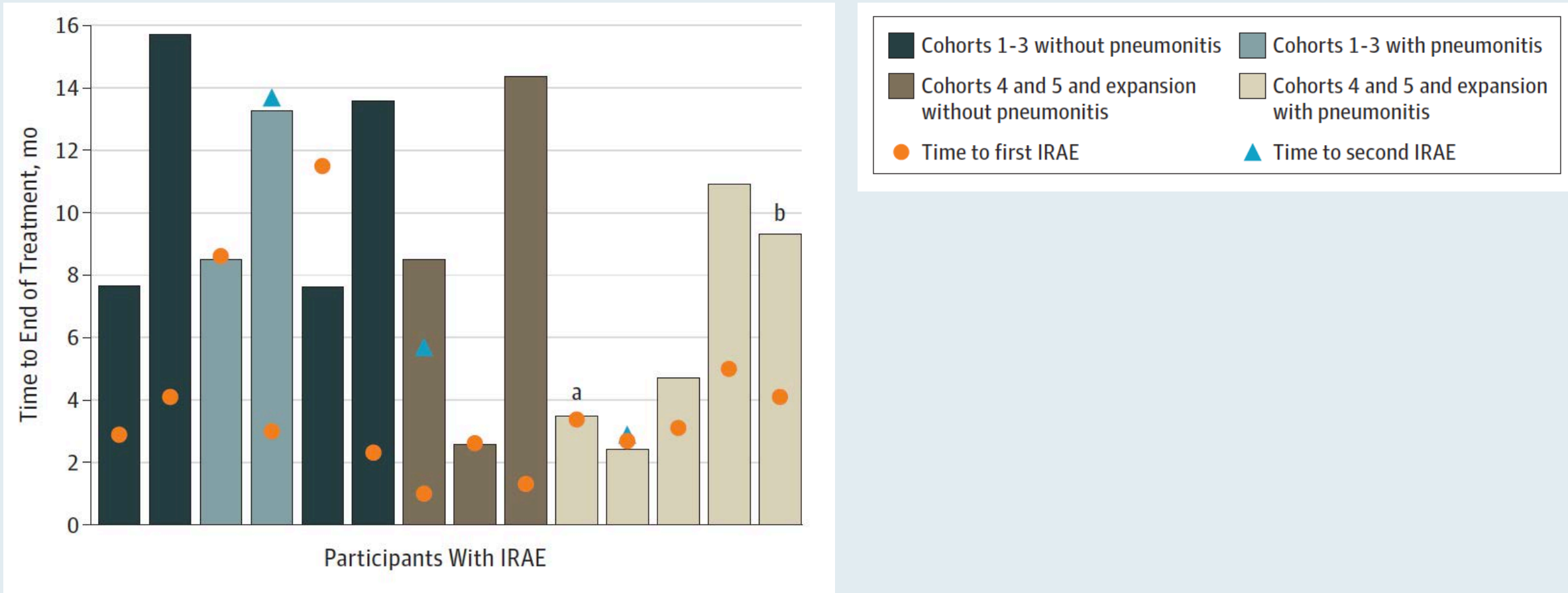
Phase 1 Trial of Pembrolizumab Administered Concurrently With Chemoradiotherapy for Locally Advanced Non-Small Cell Lung Cancer A Nonrandomized Controlled Trial

Salma K. Jabbour, MD; Abigail T. Berman, MD, MSCE; Roy H. Decker, MD, PhD; Yong Lin, PhD;
Steven J. Feigenberg, MD; Scott N. Gettinger, MD; Charu Aggarwal, MD, MPH; Corey J. Langer, MD;
Charles B. Simone II, MD; Jeffrey D. Bradley, MD; Joseph Aisner, MD; Jyoti Malhotra, MD, MPH

JAMA Oncol 2020;6(6):848-55.

Time to Immune-Related Adverse Events

N = 14 patients who developed IRAEs of at least Grade 2



PEMBROLIZUMAB IN THE TREATMENT OF PATIENTS WITH MALIGNANT PLEURAL MESOTHELIOMA FOLLOWING PROGRESSION AFTER INITIAL CHEMOTHERAPY

do not

go gentle

into that

good night

rage rage

against the

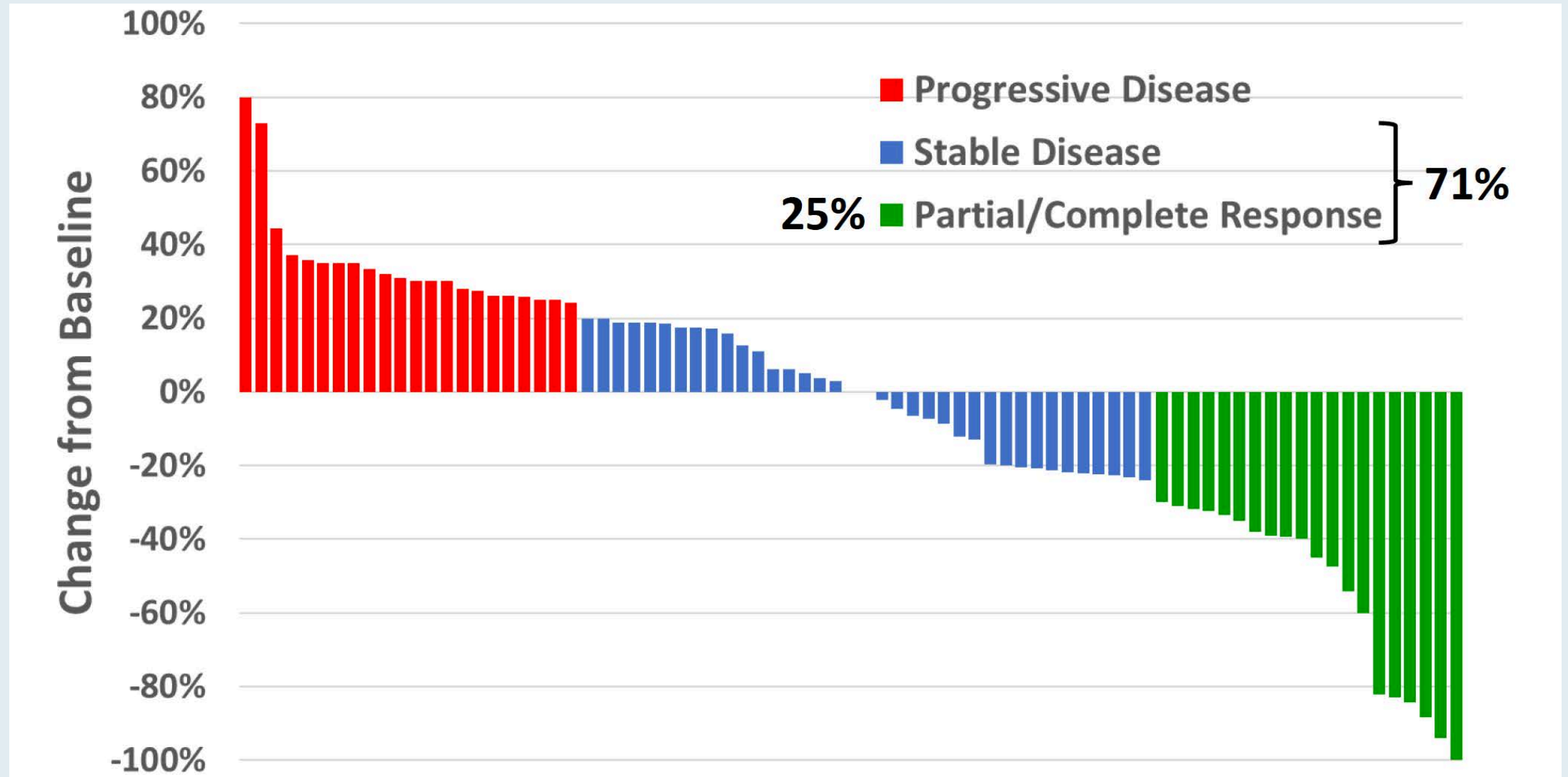
dying of

the light

Keith A. Cengel, MD, PhD
Director, Photodynamic Therapy Program
Executive Director Penn Mesothelioma Program
Department of Radiation Oncology
University of Pennsylvania

V. Grover

Overall Response to Pembrolizumab



Impact of Prior Radiation Pneumonitis on Incidence of Immunotherapy Related Pneumonitis

Kier M et al.

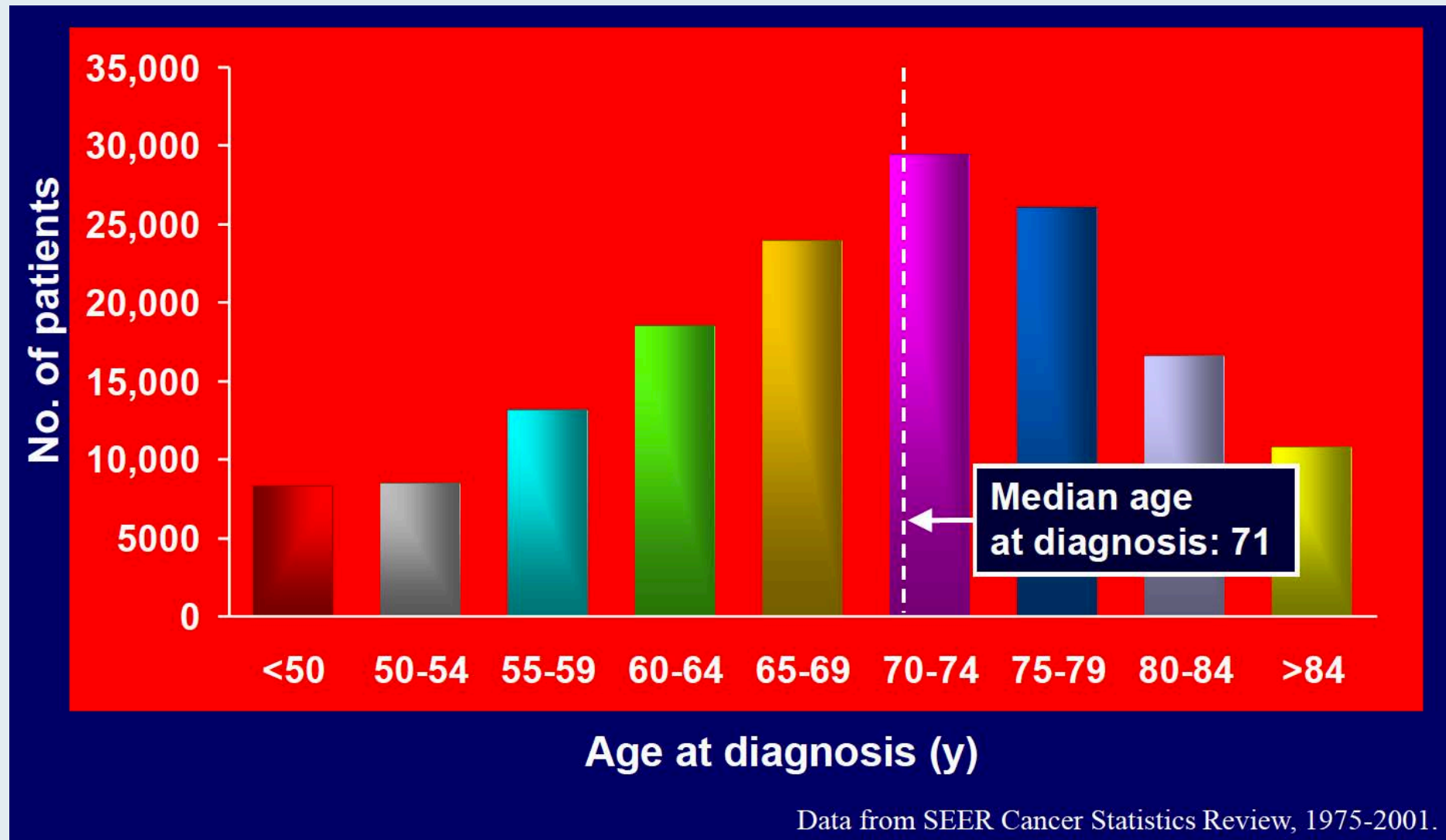
IASLC 2019;Abstract P1.01-63.

Managing Locally Advanced NSCLC in the Elderly in 2019

Langer CJ et al.

IASLC 2019;Abstract IBS03.01.

Incidence of NSCLC in the US by Age at Diagnosis



Elderly Challenges

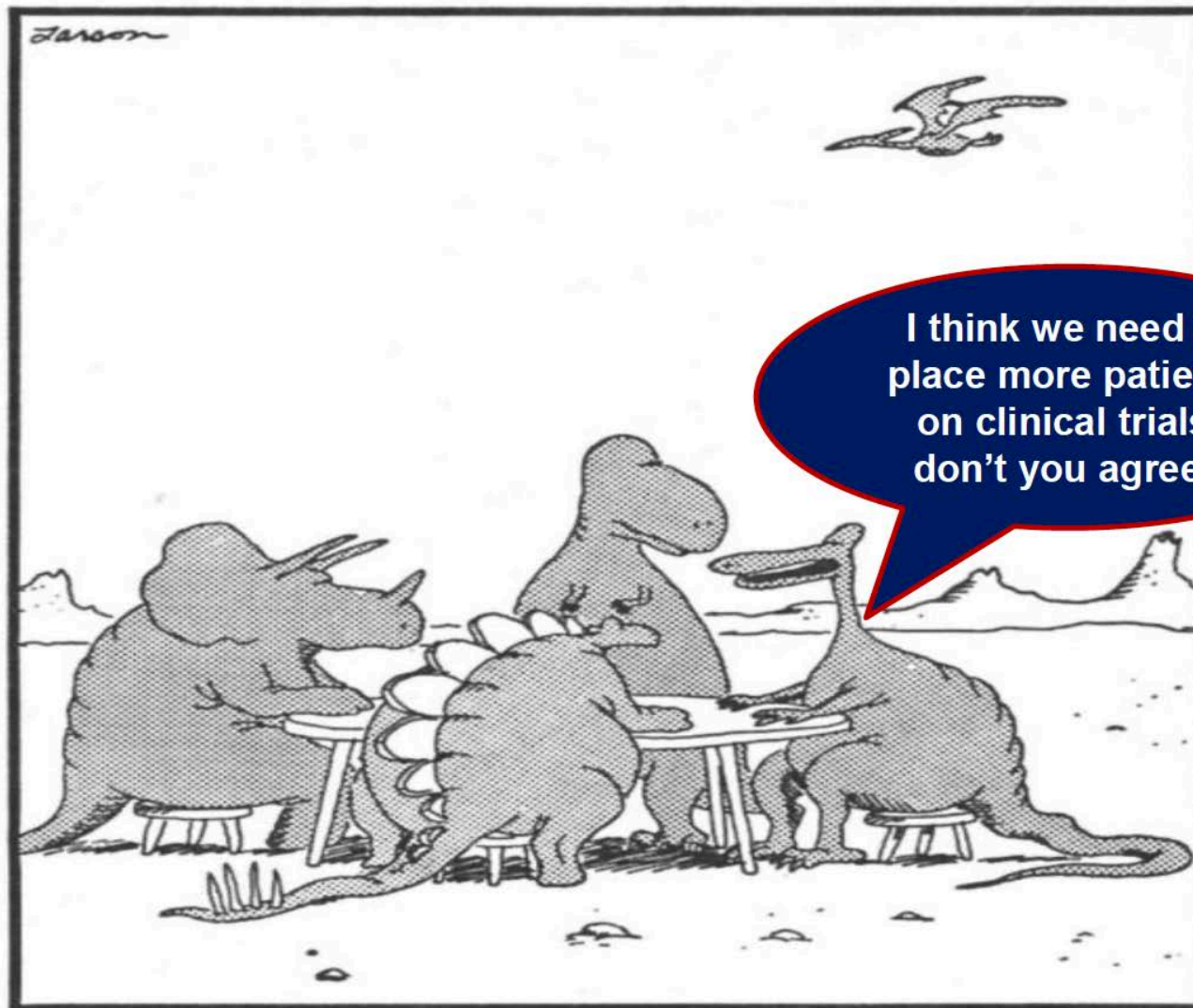


- Definition: ≥ 65 vs 70 vs 75 years
- Decreased drug clearance
- Decreased marrow reserve
- Higher degree of co-morbidities
- Immunologic vulnerabilities and immune senescence

A photograph of a man with a beard and glasses, wearing a straw hat with a red band, standing next to a brown horse. The man is looking at the horse. The horse is wearing a green halter. In the background, there are trees and a white tent. Two speech bubbles are overlaid on the image. The first speech bubble is blue and contains the text "You are never too old to sign up for this protocol !". The second speech bubble is purple and contains the text "Doc, Give me the pen....".

**You are never too old to
sign up for this protocol !**

**Doc, Give
me the pen....**



"Well, time for our weekly brain-stem-storming session."

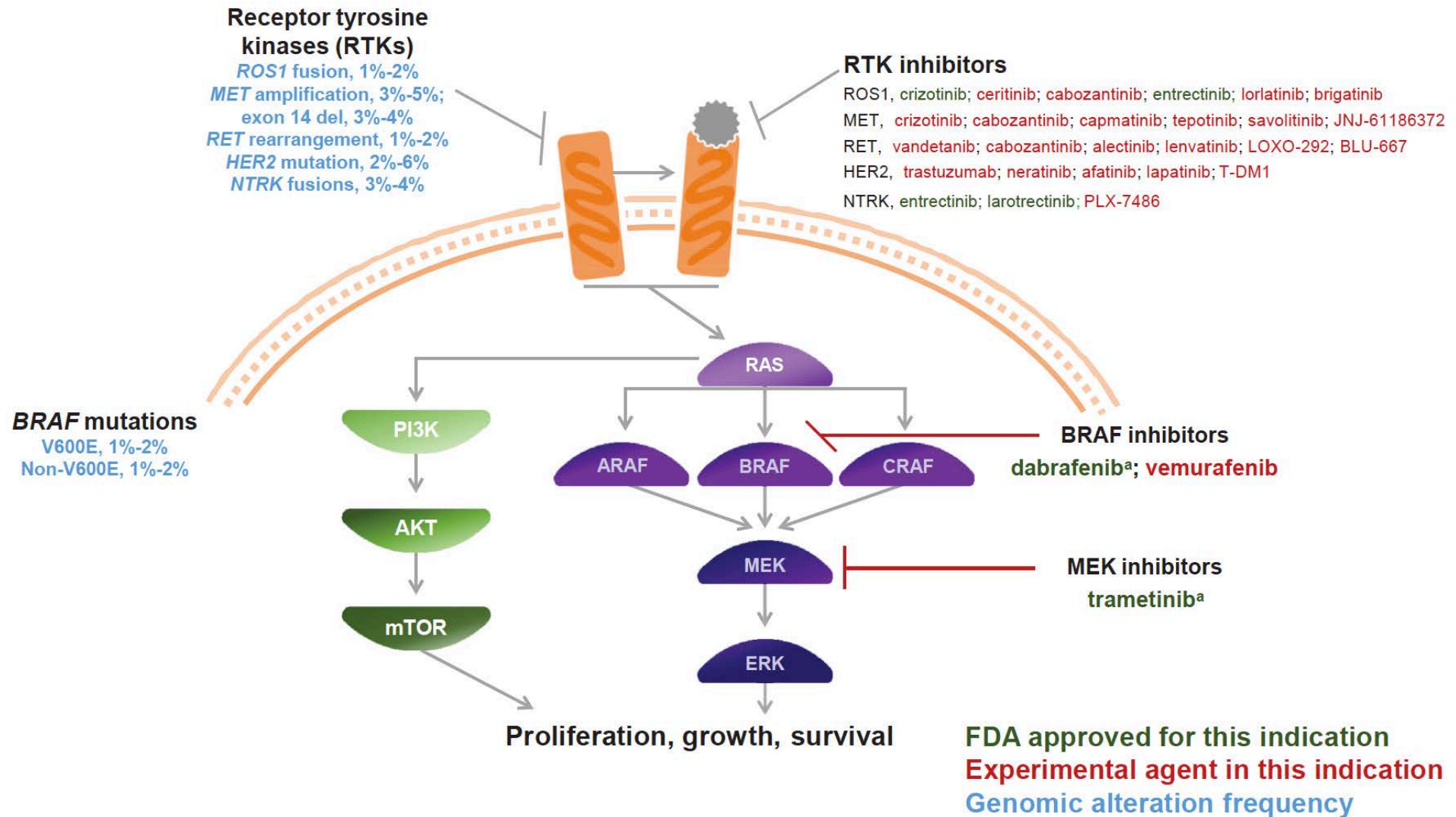
**Corey Langer preaching to the choir at the weekly
Friday thoracic tumor board**

Treatment of Patients With Non—Small-Cell Lung Cancer Harboring Rare Oncogenic Mutations

Melina E. Marmarelis, Corey J. Langer

Clin Lung Cancer 2020;21(5):395-406.

Targeting Rare Oncogenic Alterations in Non-Small Cell Lung Cancer



^a Approved by the FDA as combination therapy for treatment of patients with *BRAF* V600E-mutant metastatic NSCLC.

Research

JAMA Oncology | **Original Investigation**

Clinical Outcomes of the HIV Protease Inhibitor Nelfinavir With Concurrent Chemoradiotherapy for Unresectable Stage IIIA/IIIB Non-Small Cell Lung Cancer A Phase 1/2 Trial

Ramesh Rengan, MD, PhD; Rosemarie Mick, MS; Daniel A. Pryma, MD; Lilie Leming Lin, MD; John Christodouleas, MD; John P. Plastaras, MD, PhD; Charles B. Simone II, MD; Anjali K. Gupta, MD; Tracey L. Evans, MD; James P. Stevenson, MD; Corey J. Langer, MD; John Kucharczuk, MD; Joseph Friedberg, MD; Sarah Lam, BS; Dana Patsch, BS; Stephen M. Hahn, MD; Amit Maity, MD, PhD

JAMA Oncol 2019;5(10):1464-72.

Psychooncology. 2019;28(3):561-9. doi:10.1002/pon.4978.

A Randomized Controlled Trial of 24-Weeks of Varenicline for Tobacco Use among Cancer Patients: Efficacy, Safety, and Adherence

Robert Schnoll^{a,1}, Frank Leone^b, Anna Veluz-Wilkins^c, Andrew Miele^a, Anita Hole^a, Nancy C. Jao^c, E. Paul Wileyto^d, Allison J. Carroll^c, Ravi Kalhan^{c,e}, Jyoti Patel^f, Corey Langer^g, Su Fen Lubitz^a, Brian Hitsman^c

Management of Lung Cancer During the COVID-19 Pandemic

Aditi P. Singh, MD^{1,2}; Abigail T. Berman, MD^{2,3}; Melina E. Marmarelis, MD^{1,2}; Andrew R. Haas, MD, PhD⁴; Steven J. Feigenberg, MD^{2,3}; Jennifer Braun, RN, BSN, MHA²; Christine A. Ciunci, MD^{1,2}; Joshua M. Bauml, MD^{1,2}; Roger B. Cohen, MD^{1,2}; John C. Kucharczuk, MD⁵; Lawrence N. Shulman, MD^{1,2}; Corey J. Langer, MD^{1,2}; and Charu Aggarwal, MD, MPH^{1,2}

JCO Oncol Pract 2020;16(9):579-86.

Gene signature of antigen processing and presentation machinery predicts response to checkpoint blockade in non-small cell lung cancer (NSCLC) and melanoma

Jeffrey C Thompson ,¹ Christiana Davis,² Charuhas Deshpande,³ Wei-Ting Hwang,⁴ Seth Jeffries,² Alexander Huang,² Tara C Mitchell,² Corey J Langer,² Steven M Albelda¹

J Immunother Cancer 2020;8(2):e000974.



ELSEVIER

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

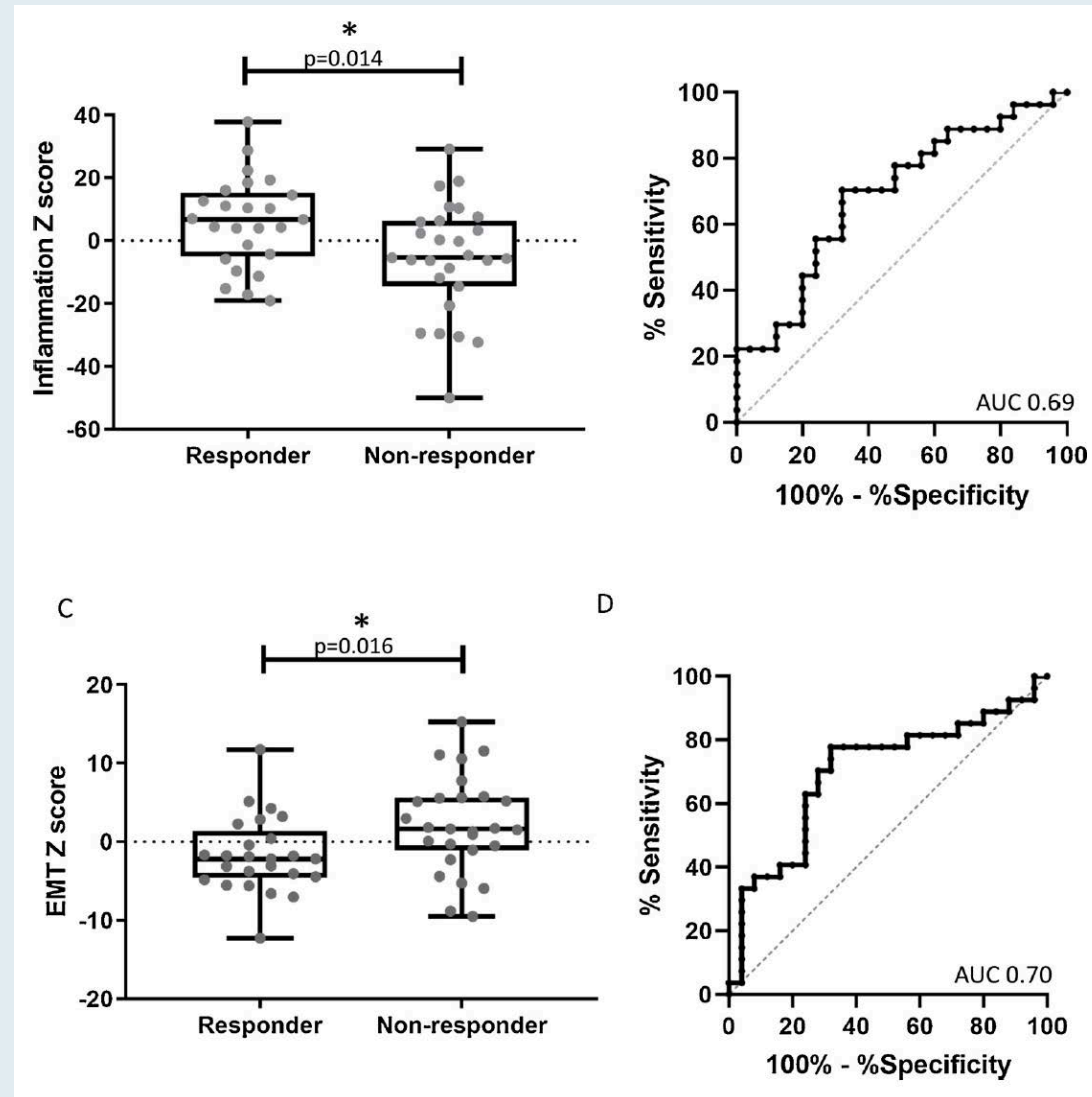
Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Gene signatures of tumor inflammation and epithelial-to-mesenchymal transition (EMT) predict responses to immune checkpoint blockade in lung cancer with high accuracy

Jeffrey C. Thompson^{a,*}, Wei-Ting Hwang^{b,e}, Christiana Davis^c, Charuhas Deshpande^{d,e}, Seth Jeffries^c, Yashoda Rajpurohit^f, Vinod Krishna^f, Denis Smirnov^f, Raluca Verona^f, Matthew V. Lorenzi^f, Corey J. Langer^{c,e}, Steven M. Albelda^{a,e}

Analysis of the Inflammatory and EMT Signatures and Response to Checkpoint Blockade



Meet The Professor with Dr Langer

Module 1: Cases from Dr Bauml

Module 2: Lung Cancer Journal Club with Dr Langer

- Pembrolizumab with chemotherapy versus chemotherapy alone for metastatic NSCLC (mNSCLC)
- Baseline plasma TMB as a marker to predict response to pembrolizumab-based therapy in mNSCLC
- Concurrent chemoradiation therapy and pembrolizumab for locally advanced NSCLC
- Pembrolizumab for the treatment of malignant pleural mesothelioma
- Managing locally advanced NSCLC in older patients
- Treatment for patients with NSCLC harboring rare oncogenic mutations
- Concurrent chemoradiation therapy and the HIV inhibitor nelfinavir for Stage IIIA/IIIB NSCLC
- Varenicline for tobacco use among patients with cancer
- Management of lung cancer during the COVID-19 pandemic
- Gene signatures predictive of response to immune checkpoint blockade in NSCLC











Module 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

Module 4: Key Papers and Recent Approvals

Regulatory and reimbursement issues aside, which adjuvant systemic therapy would you generally recommend for a patient with Stage IIB nonsquamous NSCLC and an EGFR exon 19 deletion?











1. Chemotherapy
2. Osimertinib
3. Chemotherapy followed by osimertinib
4. Other

Which first-line treatment regimen would you recommend for an 65-year-old patient with metastatic nonsquamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 10%?

 JOHN V HEYMACH, MD, PHD	Pembro/carbo/pem	 JOEL W NEAL, MD, PHD	Pembro/carbo/pem
 LEORA HORN, MD, MSC	Pembro/carbo/pem	 PAUL K PAIK, MD	Pembro/carbo/pem
 COREY J LANGER, MD	Pembro/carbo/pem	 PROFESSOR SOLANGE PETERS, MD, PHD	Ipi/nivo + carbo/pem
 BENJAMIN LEVY, MD	Pembro/carbo/pem	 NATHAN A PENNELL, MD, PHD	Pembro/carbo/pem
 PROFESSOR TONY SK MOK, MD	Pembro/carbo/pem OR Atezo/carbo/pac + bev	 DAVID R SPIGEL, MD	Pembro/carbo/pem











Pembro = pembrolizumab; carbo = carboplatin; pem = pemetrexed; ipi = ipilimumab; nivo = nivolumab; atezo = atezolizumab; pac = paclitaxel; bev = bevacizumab

Which first-line treatment regimen would you recommend for an 80-year-old patient with metastatic nonsquamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 10%?

 JOHN V HEYMACH, MD, PHD	Pembro	 JOEL W NEAL, MD, PHD	Pembro
 LEORA HORN, MD, MSC	Pembro or Hospice	 PAUL K PAIK, MD	Pembro/carbo/pem
 COREY J LANGER, MD	Pembro	 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro/carbo/pem
 BENJAMIN LEVY, MD	Pembro	 NATHAN A PENNELL, MD, PHD	Pembro/carbo/pem*
 PROFESSOR TONY SK MOK, MD	Pembro	 DAVID R SPIGEL, MD	Pembro/carbo/pem











* Likely dose-reduced chemotherapy

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 60%?











 JOHN V HEYMACH, MD, PHD	Pembro	 JOEL W NEAL, MD, PHD	Pembro +/- carbo/pem
 LEORA HORN, MD, MSC	Pembro	 PAUL K PAIK, MD	Pembro
 COREY J LANGER, MD	Pembro*	 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro
 BENJAMIN LEVY, MD	Pembro	 NATHAN A PENNELL, MD, PHD	Pembro
 PROFESSOR TONY SK MOK, MD	Pembro	 DAVID R SPIGEL, MD	Pembro

* If very symptomatic, pembro/carbo/pem

Which first-line treatment regimen would you recommend for an 80-year-old patient with metastatic nonsquamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 60%?











 <div>JOHN V HEYMACH, MD, PHD</div>	Pembro	 <div>JOEL W NEAL, MD, PHD</div>	Pembro
 <div>LEORA HORN, MD, MSC</div>	Pembro	 <div>PAUL K PAIK, MD</div>	Pembro
 <div>COREY J LANGER, MD</div>	Pembro	 <div>PROFESSOR SOLANGE PETERS, MD, PHD</div>	Pembro
 <div>BENJAMIN LEVY, MD</div>	Pembro	 <div>NATHAN A PENNELL, MD, PHD</div>	Pembro
 <div>PROFESSOR TONY SK MOK, MD</div>	Pembro	 <div>DAVID R SPIGEL, MD</div>	Pembro

Which first-line treatment regimen would you recommend for a 65-year-old patient with metastatic squamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 10%?











 JOHN V HEYMACH, MD, PHD	Pembro/carbo/ <i>nab</i> -P	 JOEL W NEAL, MD, PHD	Pembro/carbo/ <i>nab</i> -P or pac
 LEORA HORN, MD, MSC	Pembro/carbo/ <i>nab</i> -P	 PAUL K PAIK, MD	Pembro/carbo/pac
 COREY J LANGER, MD	Pembro/carbo/ <i>nab</i> -P	 PROFESSOR SOLANGE PETERS, MD, PHD	Ipi/nivo + carbo/pac
 BENJAMIN LEVY, MD	Pembro/carbo/ <i>nab</i> -P	 NATHAN A PENNELL, MD, PHD	Pembro/carbo/ <i>nab</i> -P
 PROFESSOR TONY SK MOK, MD	Pembro/carbo/ <i>nab</i> -P or Pembro/carbo/pac	 DAVID R SPIGEL, MD	Pembro/carbo/ <i>nab</i> -P

Nab-P = nanoparticle albumin-bound paclitaxel











Which first-line treatment regimen would you recommend for an 80-year-old patient with metastatic squamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 10%?

 JOHN V HEYMACH, MD, PHD	Pembro	 JOEL W NEAL, MD, PHD	Pembro/carbo/ <i>nab</i> -P
 LEORA HORN, MD, MSC	Pembro/carbo/ <i>nab</i> -P	 PAUL K PAIK, MD	Pembro/carbo/pac
 COREY J LANGER, MD	Pembro/carbo/ <i>nab</i> -P	 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro/carbo/pac
 BENJAMIN LEVY, MD	Pembro/carbo/pac	 NATHAN A PENNELL, MD, PHD	Pembro/carbo/pac
 PROFESSOR TONY SK MOK, MD	Pembro	 DAVID R SPIGEL, MD	Pembro/carbo/ <i>nab</i> -P

Which first-line treatment regimen would you recommend for a 65-year-old patient with metastatic squamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 60%?

 JOHN V HEYMACH, MD, PHD	Pembro	 JOEL W NEAL, MD, PHD	Pembro +/- carbo/ <i>nab-P</i> or <i>pac</i>
 LEORA HORN, MD, MSC	Pembro	 PAUL K PAIK, MD	Pembro
 COREY J LANGER, MD	Pembro	 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro
 BENJAMIN LEVY, MD	Pembro	 NATHAN A PENNELL, MD, PHD	Pembro
 PROFESSOR TONY SK MOK, MD	Pembro or Atezo	 DAVID R SPIGEL, MD	Pembro

Which first-line treatment regimen would you recommend for an 80-year-old patient with metastatic squamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 60%?

 <div>JOHN V HEYMACH, MD, PHD</div>	Pembro	 <div>JOEL W NEAL, MD, PHD</div>	Pembro +/- carbo/ <i>nab-P</i>
 <div>LEORA HORN, MD, MSC</div>	Pembro	 <div>PAUL K PAIK, MD</div>	Pembro
 <div>COREY J LANGER, MD</div>	Pembro	 <div>PROFESSOR SOLANGE PETERS, MD, PHD</div>	Pembro
 <div>BENJAMIN LEVY, MD</div>	Pembro	 <div>NATHAN A PENNELL, MD, PHD</div>	Pembro
 <div>PROFESSOR TONY SK MOK, MD</div>	Pembro or Atezo	 <div>DAVID R SPIGEL, MD</div>	Pembro

How long would you continue treatment for a patient with metastatic NSCLC who is receiving an anti-PD-1/PD-L1 antibody and at first evaluation is tolerating it well and has a complete clinical response?

 JOHN V HEYMACH, MD, PHD	2 years	 JOEL W NEAL, MD, PHD	2 years
 LEORA HORN, MD, MSC	2 years	 PAUL K PAIK, MD	Indefinitely or until PD/toxicity
 COREY J LANGER, MD	2 years (min)	 PROFESSOR SOLANGE PETERS, MD, PHD	2 years (discuss unknowns)
 BENJAMIN LEVY, MD	Indefinitely or until PD/toxicity	 NATHAN A PENNELL, MD, PHD	2 years
 PROFESSOR TONY SK MOK, MD	2 years	 DAVID R SPIGEL, MD	Likely 2 years but CR duration dependent











How long would you continue treatment for a patient with metastatic NSCLC who is receiving an anti-PD-1/PD-L1 antibody and at first evaluation is tolerating it well and has a partial clinical response?

 <div>JOHN V HEYMACH, MD, PHD</div>	Indefinitely or until PD/toxicity	 <div>JOEL W NEAL, MD, PHD</div>	2 years
 <div>LEORA HORN, MD, MSC</div>	2 years	 <div>PAUL K PAIK, MD</div>	Indefinitely or until PD/toxicity
 <div>COREY J LANGER, MD</div>	2 years (min)	 <div>PROFESSOR SOLANGE PETERS, MD, PHD</div>	Indefinitely or until PD/toxicity
 <div>BENJAMIN LEVY, MD</div>	Indefinitely or until PD/toxicity	 <div>NATHAN A PENNELL, MD, PHD</div>	2 years
 <div>PROFESSOR TONY SK MOK, MD</div>	2 years	 <div>DAVID R SPIGEL, MD</div>	Indefinitely or until PD/toxicity











What is your preferred second-line treatment for a patient with extensive-stage small cell cancer of the lung with metastases and disease progression on chemotherapy/atezolizumab?

1. Topotecan or irinotecan
2. Lurbinectedin
3. Nivolumab/ipilimumab
4. Pembrolizumab
5. Nivolumab
6. Other

Regulatory and reimbursement issues aside, what would be your preferred first-line treatment regimen for a 65-year-old patient with extensive-stage SCLC?

 JOHN V HEYMACH, MD, PHD	Carbo/etoposide + atezolizumab	 JOEL W NEAL, MD, PHD	Carbo/etoposide + atezolizumab
 LEORA HORN, MD, MSC	Carbo/etoposide + atezolizumab	 PAUL K PAIK, MD	Carbo/etoposide + atezolizumab
 COREY J LANGER, MD	Carbo/etoposide + atezolizumab or durvalumab	 PROFESSOR SOLANGE PETERS, MD, PHD	Carbo/etoposide + atezolizumab or durvalumab
 BENJAMIN LEVY, MD	Carbo/etoposide + atezolizumab	 NATHAN A PENNELL, MD, PHD	Carbo/etoposide + atezolizumab
 PROFESSOR TONY SK MOK, MD	Carbo/etoposide + atezolizumab	 DAVID R SPIGEL, MD	Carbo/etoposide + durvalumab











Regulatory and reimbursement issues aside, what would be your preferred first-line treatment regimen for an 80-year-old patient with extensive-stage SCLC?

 JOHN V HEYMACH, MD, PHD	Carbo/etoposide + atezolizumab	 JOEL W NEAL, MD, PHD	Carbo/etoposide + atezolizumab or durvalumab
 LEORA HORN, MD, MSC	Carbo/etoposide + atezolizumab	 PAUL K PAIK, MD	Carbo/etoposide + atezolizumab
 COREY J LANGER, MD	Carbo/etoposide + durvalumab	 PROFESSOR SOLANGE PETERS, MD, PHD	Carbo/etoposide + atezolizumab or durvalumab
 BENJAMIN LEVY, MD	Carbo/etoposide + atezolizumab	 NATHAN A PENNELL, MD, PHD	Carbo/etoposide + atezolizumab
 PROFESSOR TONY SK MOK, MD	Carbo/etoposide OR Carbo/etoposide + atezolizumab or durvalumab	 DAVID R SPIGEL, MD	Carbo/etoposide + durvalumab

Regulatory and reimbursement issues aside, what would be your preferred first-line treatment regimen for a 65-year-old patient with extensive-stage SCLC and neurologic paraneoplastic syndrome causing moderate to severe proximal myopathy?

 JOHN V HEYMACH, MD, PHD	Carboplatin/etoposide	 JOEL W NEAL, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 LEORA HORN, MD, MSC	Carboplatin/etoposide	 PAUL K PAIK, MD	Carboplatin/etoposide
 COREY J LANGER, MD	Carboplatin/etoposide + atezolizumab or durvalumab	 PROFESSOR SOLANGE PETERS, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 BENJAMIN LEVY, MD	Carboplatin/etoposide	 NATHAN A PENNELL, MD, PHD	Carboplatin/etoposide
 PROFESSOR TONY SK MOK, MD	Carboplatin/etoposide	 DAVID R SPIGEL, MD	Carboplatin/etoposide + durvalumab

Regulatory and reimbursement issues aside, what would be your preferred first-line treatment for a 65-year-old patient with extensive-stage SCLC and symptomatic SIADH, in addition to standard treatment for SIADH?

 JOHN V HEYMACH, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab	 JOEL W NEAL, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 LEORA HORN, MD, MSC	Carboplatin/etoposide + atezolizumab	 PAUL K PAIK, MD	Carboplatin/etoposide + atezolizumab
 COREY J LANGER, MD	Carboplatin/etoposide + atezolizumab or durvalumab	 PROFESSOR SOLANGE PETERS, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 BENJAMIN LEVY, MD	Carboplatin/etoposide + atezolizumab	 NATHAN A PENNELL, MD, PHD	Carboplatin/etoposide + atezolizumab
 PROFESSOR TONY SK MOK, MD	Carbo/etoposide OR Carbo/etoposide + atezolizumab or durvalumab	 DAVID R SPIGEL, MD	Carboplatin/etoposide + atezolizumab

SIADH = syndrome of inappropriate antidiuretic hormone secretion

Meet The Professor with Dr Langer

Module 1: Cases from Dr Bauml

Module 2: Lung Cancer Journal Club with Dr Langer

- Pembrolizumab with chemotherapy versus chemotherapy alone for metastatic NSCLC (mNSCLC)
- Baseline plasma TMB as a marker to predict response to pembrolizumab-based therapy in mNSCLC
- Concurrent chemoradiation therapy and pembrolizumab for locally advanced NSCLC
- Pembrolizumab for the treatment of malignant pleural mesothelioma
- Managing locally advanced NSCLC in older patients
- Treatment for patients with NSCLC harboring rare oncogenic mutations
- Concurrent chemoradiation therapy and the HIV inhibitor nelfinavir for Stage IIIA/IIIB NSCLC
- Varenicline for tobacco use among patients with cancer
- Management of lung cancer during the COVID-19 pandemic
- Gene signatures predictive of response to immune checkpoint blockade in NSCLC

Module 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

Module 4: Key Papers and Recent Approvals

Osimertinib Adjuvant Therapy in Patients (pts) with Resected EGFR Mutated (EGFRm) NSCLC (ADAURA): Central Nervous System (CNS) Disease Recurrence

Tsuboi M et al.

ESMO 2020;Abstract LBA1.

ADAURA: Sites of Disease Recurrence

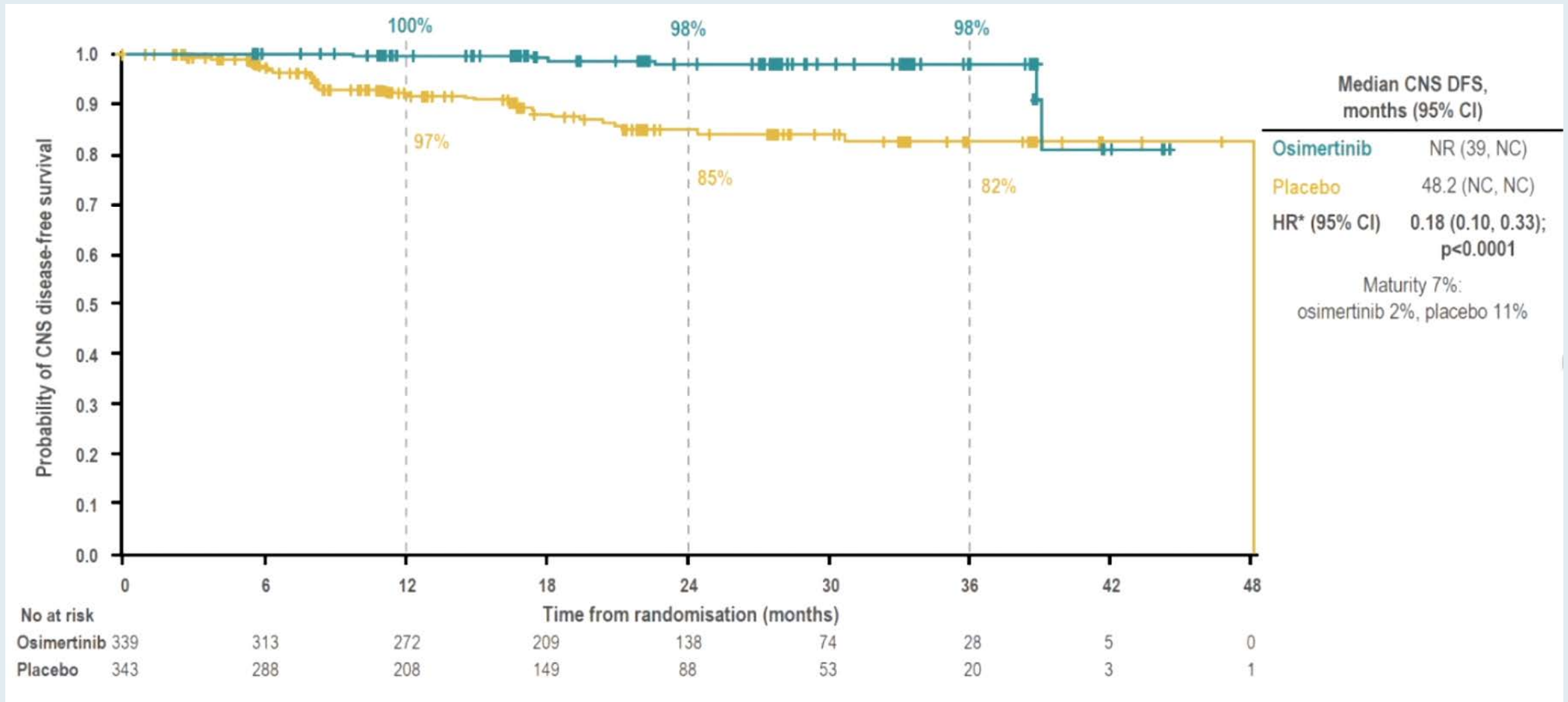


ADAURA: CNS DFS Events

- Overall, 45 patients (osimertinib n=6, placebo n=39) had CNS DFS events

Overall population		
Patients, n (%)	Osimertinib n=339	Placebo n=343
CNS DFS events:	6 (2%)	39 (11%)
CNS recurrence	4 (1%)	33 (10%)
Death	2 (1%)	6 (2%)

ADAURA: CNS DFS in Overall Population



Osimertinib as Adjuvant Therapy in Patients (pts) with Stage IB–IIIA EGFR Mutation Positive (EGFRm) NSCLC After Complete Tumor Resection: ADAURA

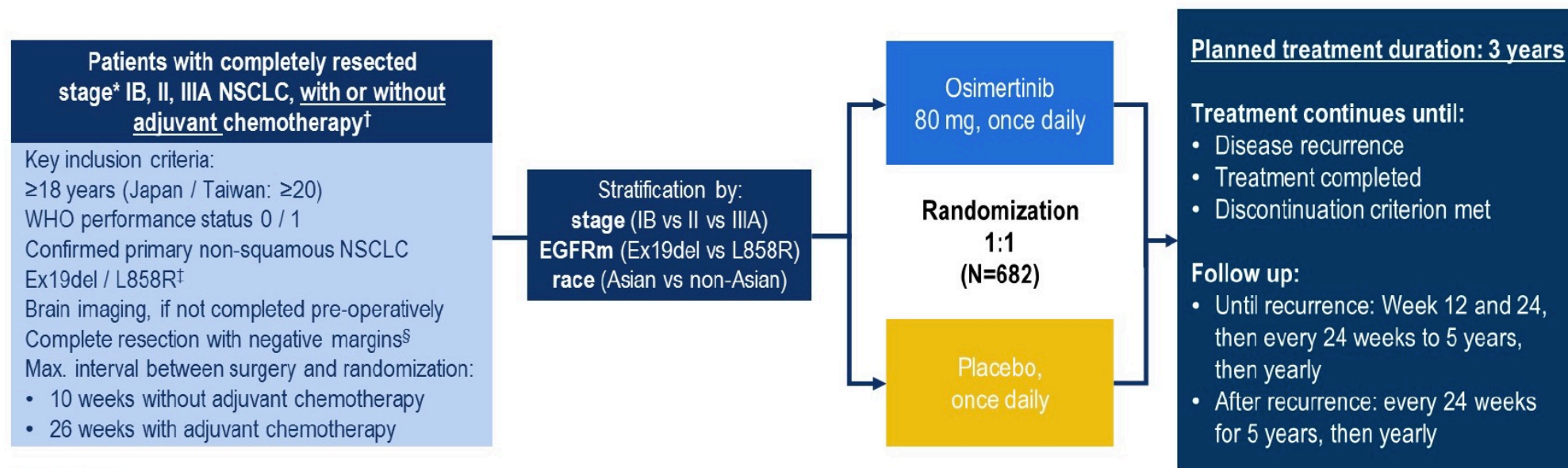
Herbst RS et al.

ASCO 2020;Abstract LBA5.

Discussion of LBA5

Discussant: David R Spigel, MD, FASCO | Sarah Cannon Research Institute

ADAURA Phase III Trial Schema

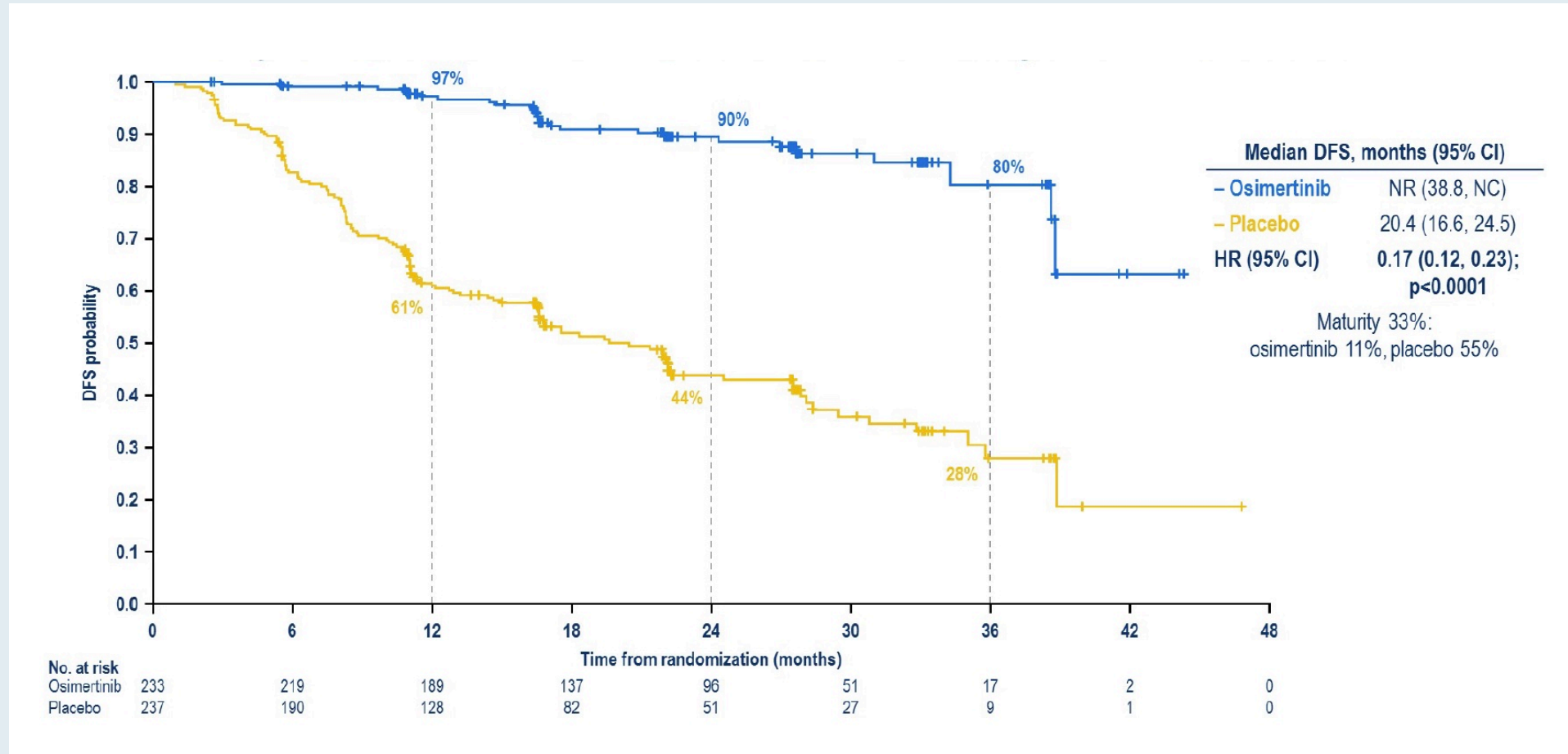


Endpoints

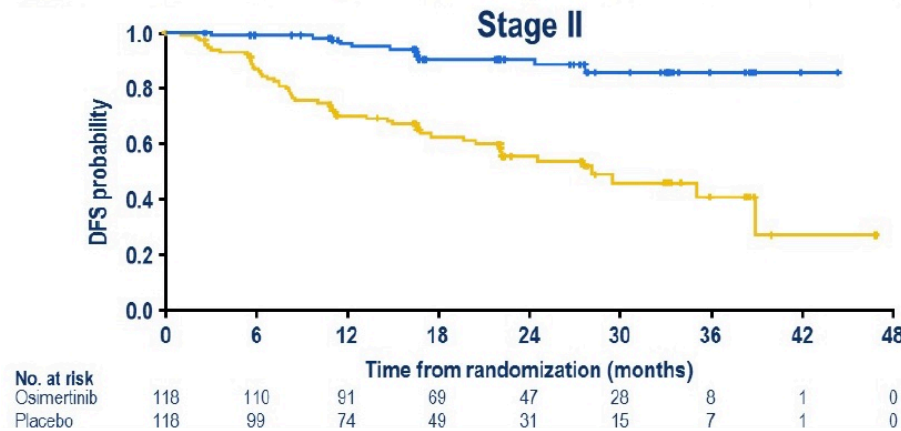
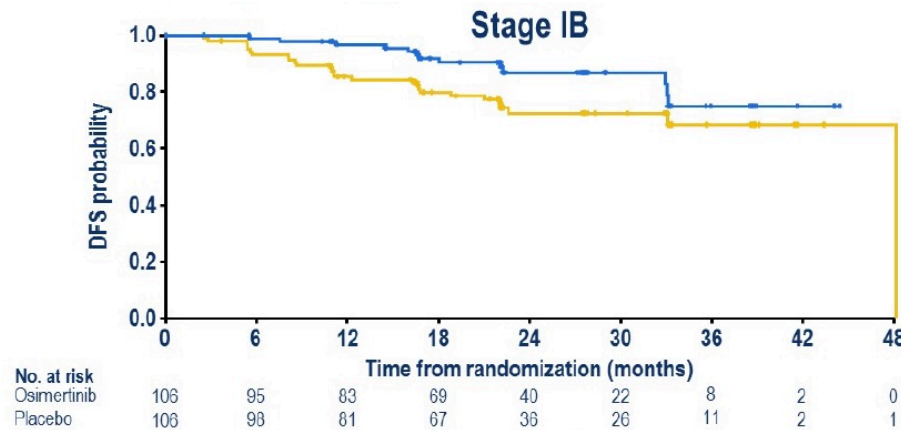
- **Primary:** DFS, by investigator assessment, in stage II/IIIA patients; designed for superiority under the assumed DFS HR of 0.70
- **Secondary:** DFS in the overall population¶, DFS at 2, 3, 4, and 5 years, OS, safety, health-related quality of life

- Following IDMC recommendation, the study was unblinded early due to efficacy; here we report an unplanned interim analysis
- At the time of unblinding the study had completed enrollment and all patients were followed up for at least 1 year

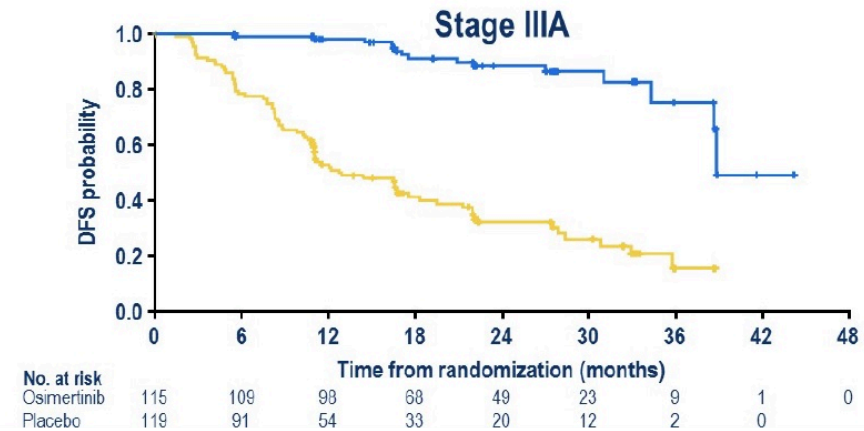
ADAURA Primary Endpoint: Inv-Assessed DFS (Stage II/IIIA)



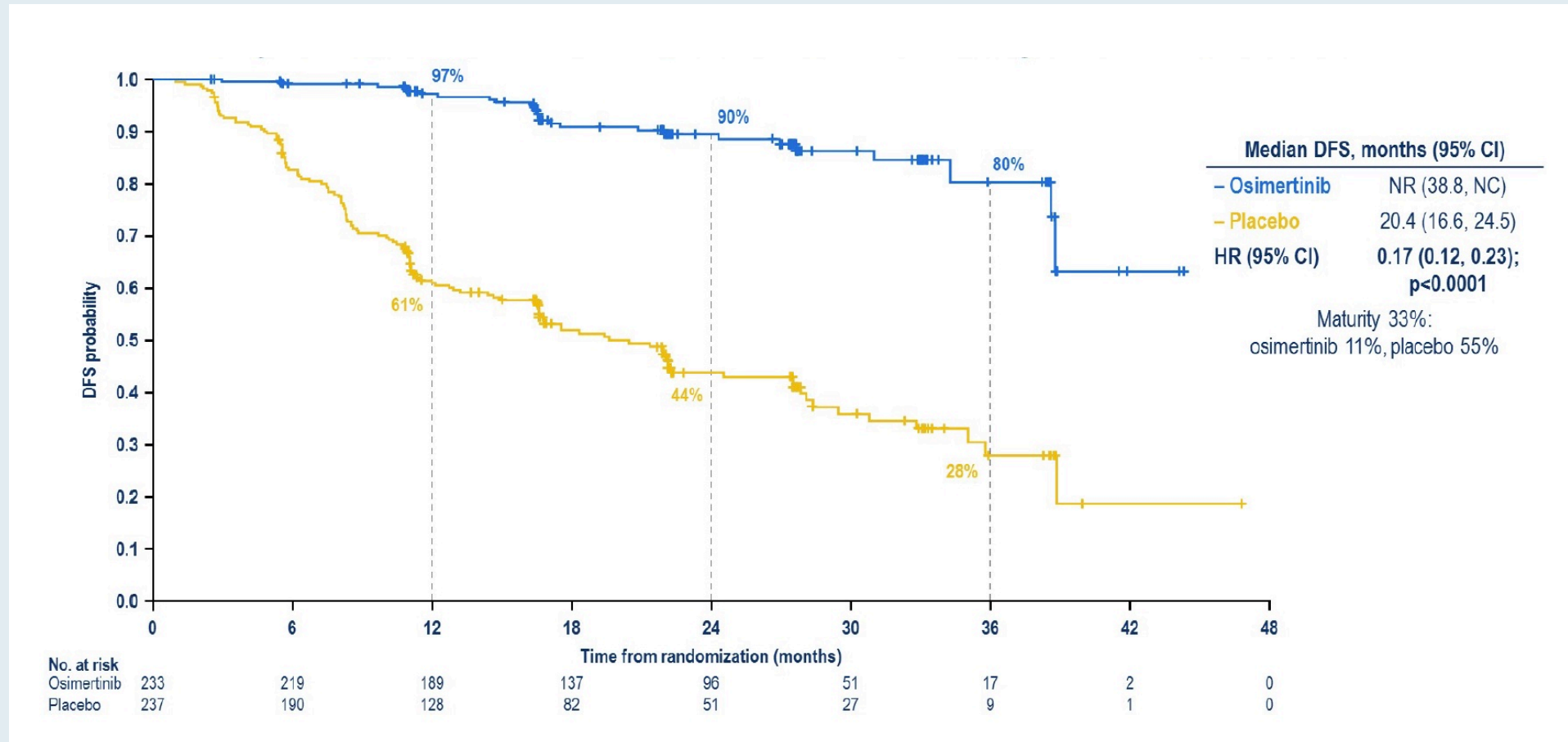
ADAURA: DFS by Stage



	Stage IB	Stage II	Stage IIIA
2 year DFS rate, % (95% CI)			
– Osimertinib	87 (77, 93)	91 (82, 95)	88 (79, 94)
– Placebo	73 (62, 81)	56 (45, 65)	32 (23, 42)
Overall HR (95% CI)	0.50 (0.25, 0.96)	0.17 (0.08, 0.31)	0.12 (0.07, 0.20)



ADAURA Secondary Endpoint: Inv-Assessed DFS in the Overall Population (Stage IB/II/IIIA)



FDA Approves Nivolumab with Ipilimumab for First-Line Metastatic NSCLC (PD-L1 Tumor Expression $\geq 1\%$)

Press Release — May 15, 2020

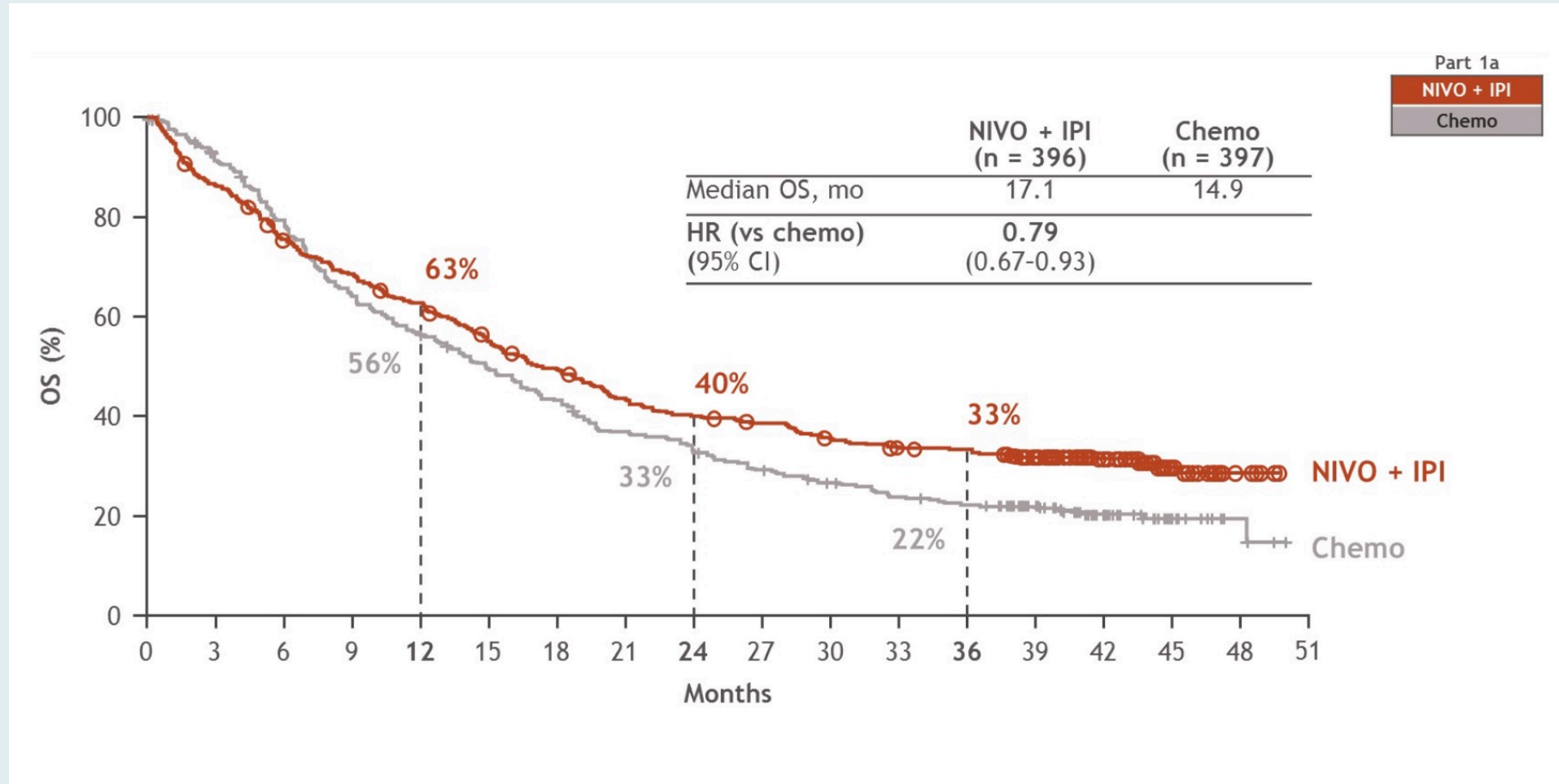
“The Food and Drug Administration approved the combination of nivolumab plus ipilimumab as first-line treatment for patients with metastatic non-small cell lung cancer whose tumors express PD-L1($\geq 1\%$), as determined by an FDA-approved test, with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.

Efficacy was investigated in CHECKMATE-227 (NCT02477826), a randomized, open-label, multi-part trial in patients with metastatic or recurrent NSCLC and no prior anticancer therapy. In Part 1a of the trial, 793 patients with PD-L1 tumor expression $\geq 1\%$ were randomized to receive either the combination of nivolumab plus with ipilimumab (n=396) or platinum-doublet chemotherapy (n=397).”

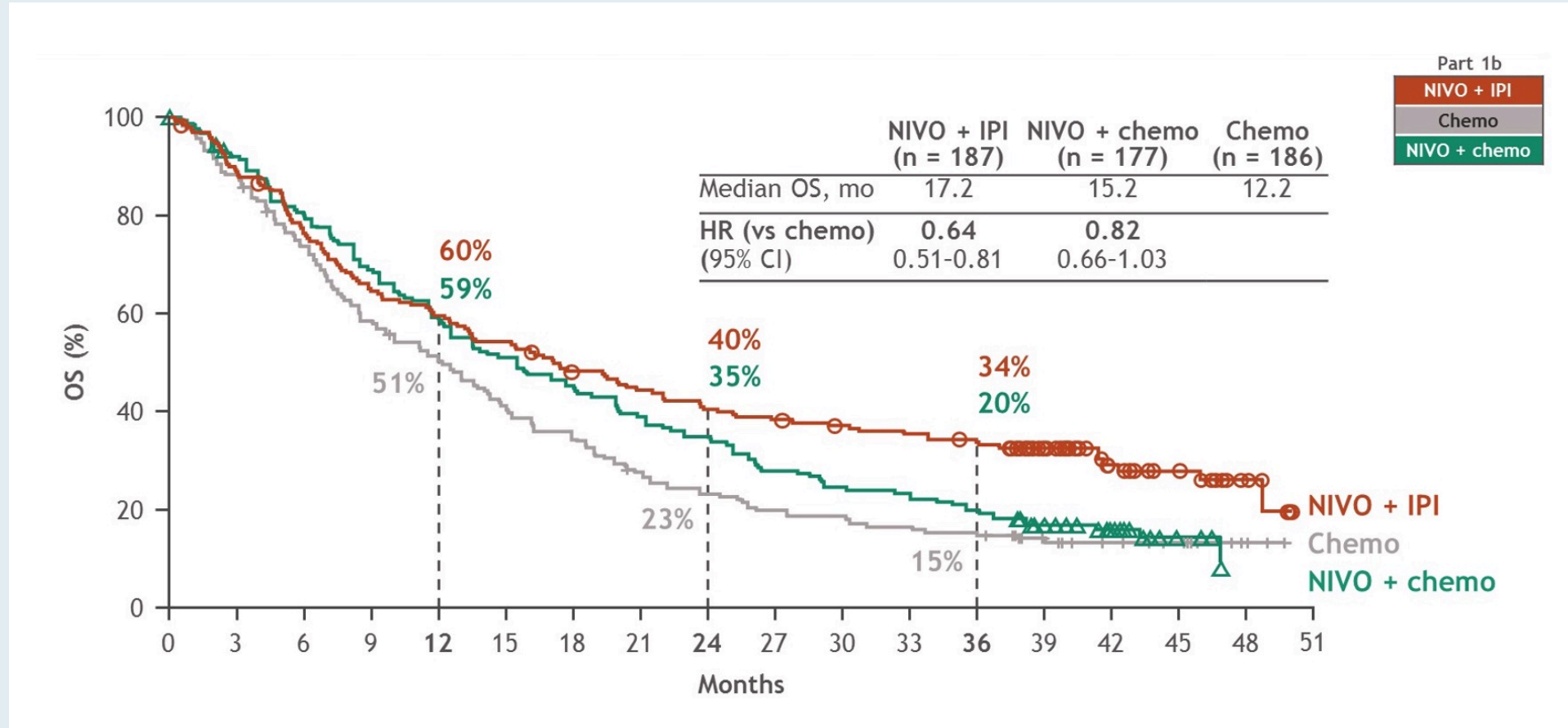
Nivolumab + Ipilimumab versus Platinum-Doublet Chemotherapy as First-Line Treatment for Advanced Non-Small Cell Lung Cancer: Three-Year Update from CheckMate 227 Part 1

Ramalingam SS et al.
ASCO 2020;Abstract 9500.

3-Year Update: OS with IPI + Nivo vs Chemo (PD-L1 $\geq 1\%$)



3-Year Update: OS with IPI + Nivo vs Chemo vs Nivo + Chemo (PD-L1 < 1%)



FDA Approves Nivolumab with Ipilimumab and Chemotherapy for First-Line Treatment of Metastatic NSCLC

Press Release — May 26, 2020

“The Food and Drug Administration approved the combination of nivolumab plus ipilimumab and 2 cycles of platinum-doublet chemotherapy as first-line treatment for patients with metastatic or recurrent non-small cell lung cancer (NSCLC), with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.

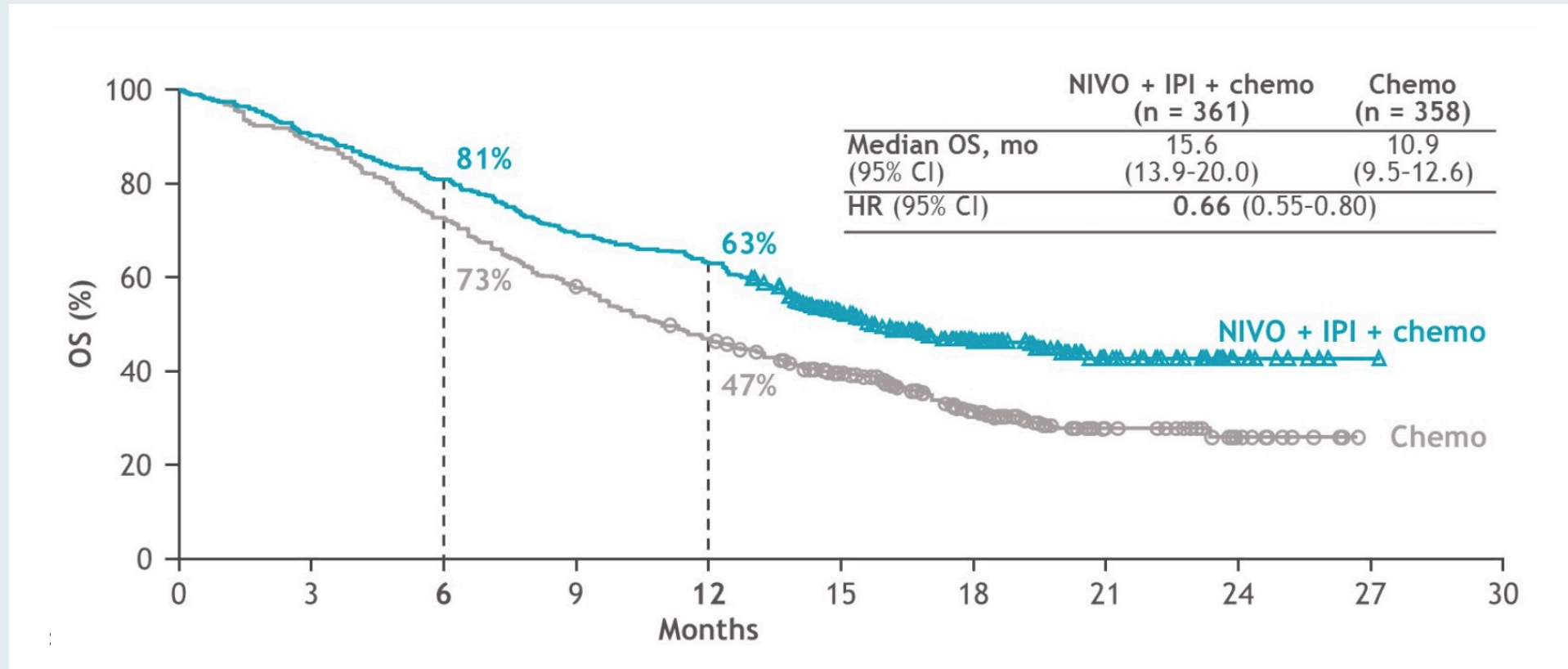
Efficacy was investigated in CHECKMATE-9LA (NCT03215706), a randomized, open-label trial in patients with metastatic or recurrent NSCLC. Patients were randomized to receive either the combination of nivolumab plus ipilimumab and 2 cycles of platinum-doublet chemotherapy (n=361) or platinum-doublet chemotherapy for 4 cycles (n=358).”

Nivolumab (NIVO) + Ipilimumab (IPI) + 2 Cycles of Platinum-Doublet Chemotherapy (Chemo) vs 4 Cycles Chemo as First-Line (1L) Treatment (tx) for Stage IV/Recurrent Non-Small Cell Lung Cancer (NSCLC): CheckMate 9LA

Reck M et al.

ASCO 2020;Abstract 9501.

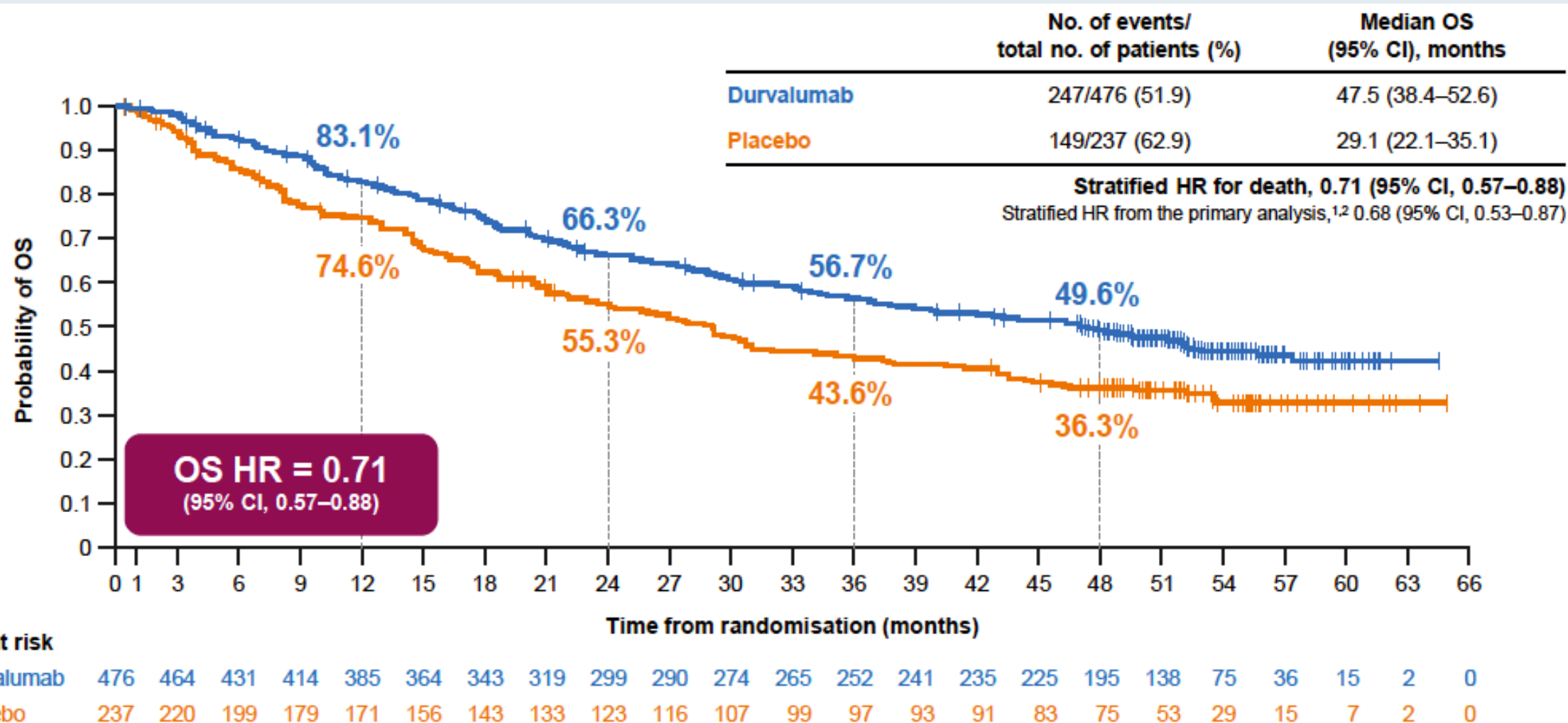
CheckMate 9LA: Updated OS



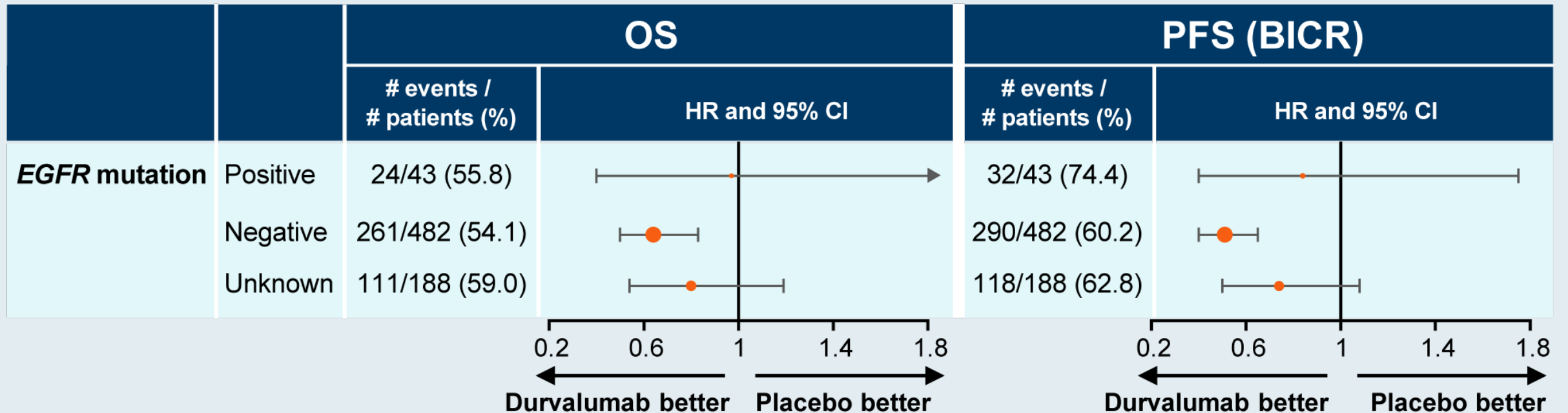
Durvalumab After Chemoradiotherapy in Stage III NSCLC: 4-Year Survival Update from the Phase III PACIFIC Trial

Faivre-Finn C et al.
ESMO 2020;Abstract LBA49.

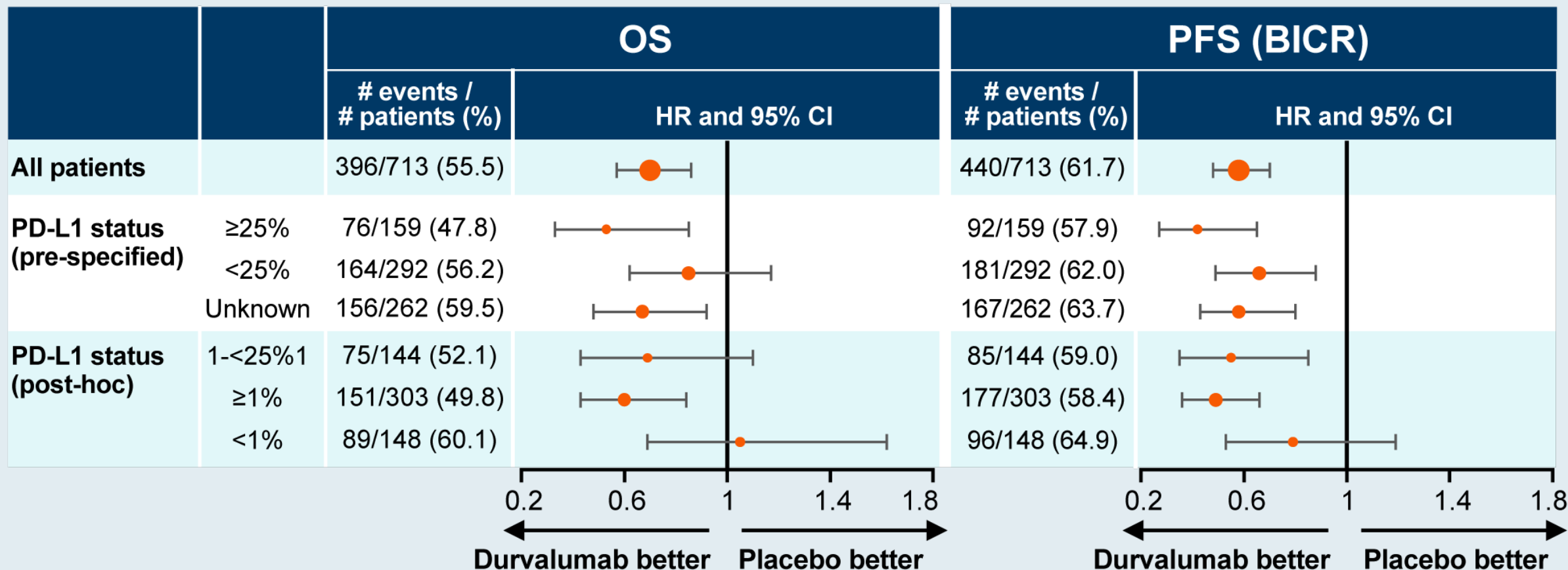
PACIFIC: 4-Year Overall Survival – Intent-To-Treat Population



PACIFIC: Updated Outcomes by EGFR Status



PACIFIC: Updated Outcomes by PD-L1 Status



- Important facts regarding PD-L1 status:
 - PD-L1 testing was not required and 37% of all randomised patients had unknown PD-L1 status
 - PD-L1 status was determined from tumour tissue obtained pre-CRT (getting a sample post-CRT medically not feasible)
 - PDL1 expression-level cutoff of 1% was part of an unplanned post-hoc analysis requested by the EMA

Characteristics of the First 615 Patients Enrolled in Pacific R: A Study of the First Real-World Data on Unresectable Stage III NSCLC Patients Treated with Durvalumab After Chemoradiotherapy

Girard N et al.

ESMO 2020;Abstract 1242P.

Pacific R: Biomarker Status

Biomarker evaluated	Tested, n (%)	Positive, n (%)	Inconclusive, n (%)
PD-L1 expression	442 (71.9)	324 (73.3)	27 (6.1)
EGFR mutation	262 (42.8)	19 (7.3)	7 (2.7)
ALK translocation	256 (41.9)	6 (2.3)	12 (4.7)
BRAF mutation	164 (26.8)	14 (8.5)	5 (3.0)
KRAS mutation	180 (29.5)	44 (24.4)	6 (3.3)

Accelerated Approval of Lurbinectedin for Metastatic SCLC

Press Release – June 15, 2020

“On June 15, 2020, the Food and Drug Administration granted accelerated approval to lurbinectedin for adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

Efficacy was demonstrated in the PM1183-B-005-14 trial (Study B-005; NCT02454972), a multicenter open-label, multi-cohort study enrolling 105 patients with metastatic SCLC who had disease progression on or after platinum-based chemotherapy. Patients received lurbinectedin 3.2 mg/m² by intravenous infusion every 21 days until disease progression or unacceptable toxicity.

The recommended lurbinectedin dose is 3.2 mg/m² every 21 days.”

FDA Grants Approval of Pralsetinib for the Treatment of Metastatic NSCLC with RET Fusion

Press Release – September 7, 2020

“The Food and Drug Administration has approved pralsetinib for the treatment of adults with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test. This indication was approved under the FDA’s Accelerated Approval programme, based on data from the phase I/II ARROW study. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. Pralsetinib is a once-daily, oral precision therapy designed to selectively target RET alterations, including fusions and mutations.

The approval is based on the results from the phase I/II ARROW study, in which pralsetinib produced durable clinical responses in people with RET fusion-positive NSCLC with or without prior therapy, and regardless of RET fusion partner or central nervous system involvement. Pralsetinib demonstrated an overall response rate (ORR) of 57% ... and complete response (CR) rate of 5.7% in the 87 people with NSCLC previously treated with platinum-based chemotherapy. In the 27 people with treatment-naïve NSCLC, the ORR was 70%, with an 11% CR rate.”

FDA Approves Selpercatinib for Lung and Thyroid Cancer with RET Gene Mutations or Fusions

Press Release — May 8, 2020

“On May 8, 2020, the Food and Drug Administration granted accelerated approval to selpercatinib for the following indications:

- Adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC);
- Adult and pediatric patients ≥ 12 years of age with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy;
- Adult and pediatric patients ≥ 12 years of age with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

Efficacy was investigated in a multicenter, open-label, multi-cohort clinical trial (LIBRETTO-001) in patients whose tumors had RET alterations.”

FDA Grants Accelerated Approval to Capmatinib for Metastatic Non-Small Cell Lung Cancer

Press Release — May 6, 2020

“On May 6, 2020, the Food and Drug Administration granted accelerated approval to capmatinib for adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping as detected by an FDA-approved test.

The FDA also approved the FoundationOne CDx assay as a companion diagnostic for capmatinib.

Efficacy was demonstrated in the GEOMETRY mono-1 trial (NCT02414139), a multicenter, non-randomized, open-label, multicohort study enrolling 97 patients with metastatic NSCLC with confirmed MET exon 14 skipping.

The recommended capmatinib dose is 400 mg orally twice daily with or without food.”

Trastuzumab Deruxtecan (T-DXd; DS-8201) in Patients with HER2-Mutated Metastatic Non-Small Cell Lung Cancer (NSCLC): Interim Results of DESTINY-Lung01

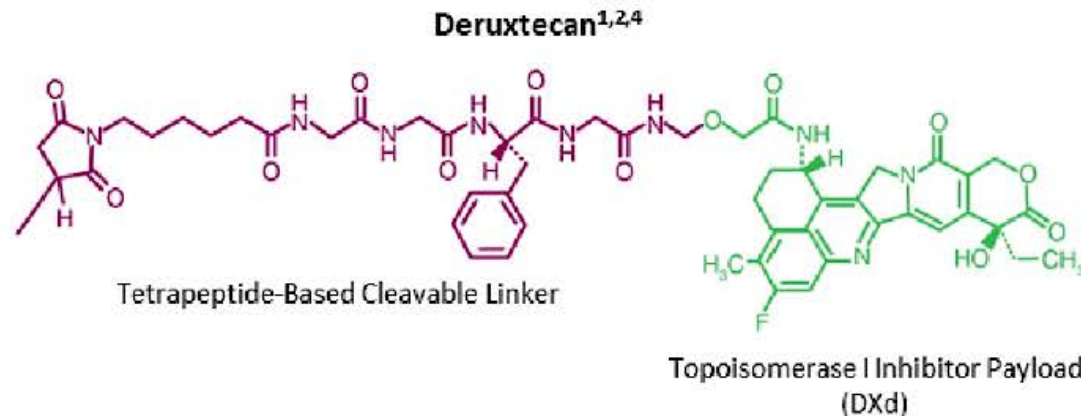
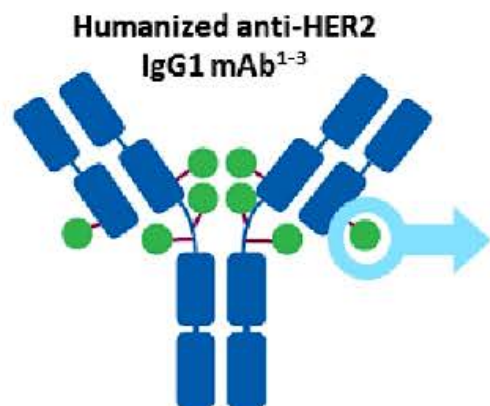
Smit EF et al.

ASCO 2020;Abstract 9504.

Antibody-Drug Conjugate Trastuzumab Deruxtecan

T-DXd is an ADC with 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



Payload mechanism of action:
topoisomerase I inhibitor

High potency of payload

High drug to antibody ratio ≈ 8

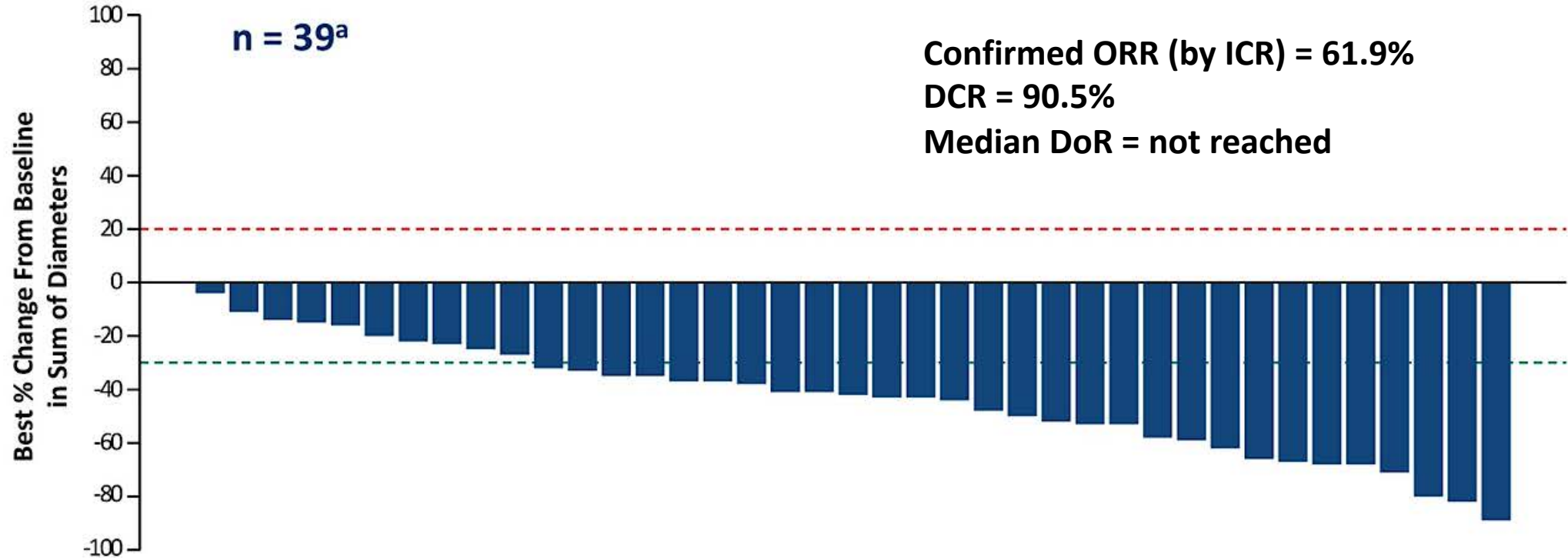
Payload with short systemic half-life

Stable linker-payload

Tumor-selective cleavable linker

Membrane-permeable payload

DESTINY-Lung01: Efficacy

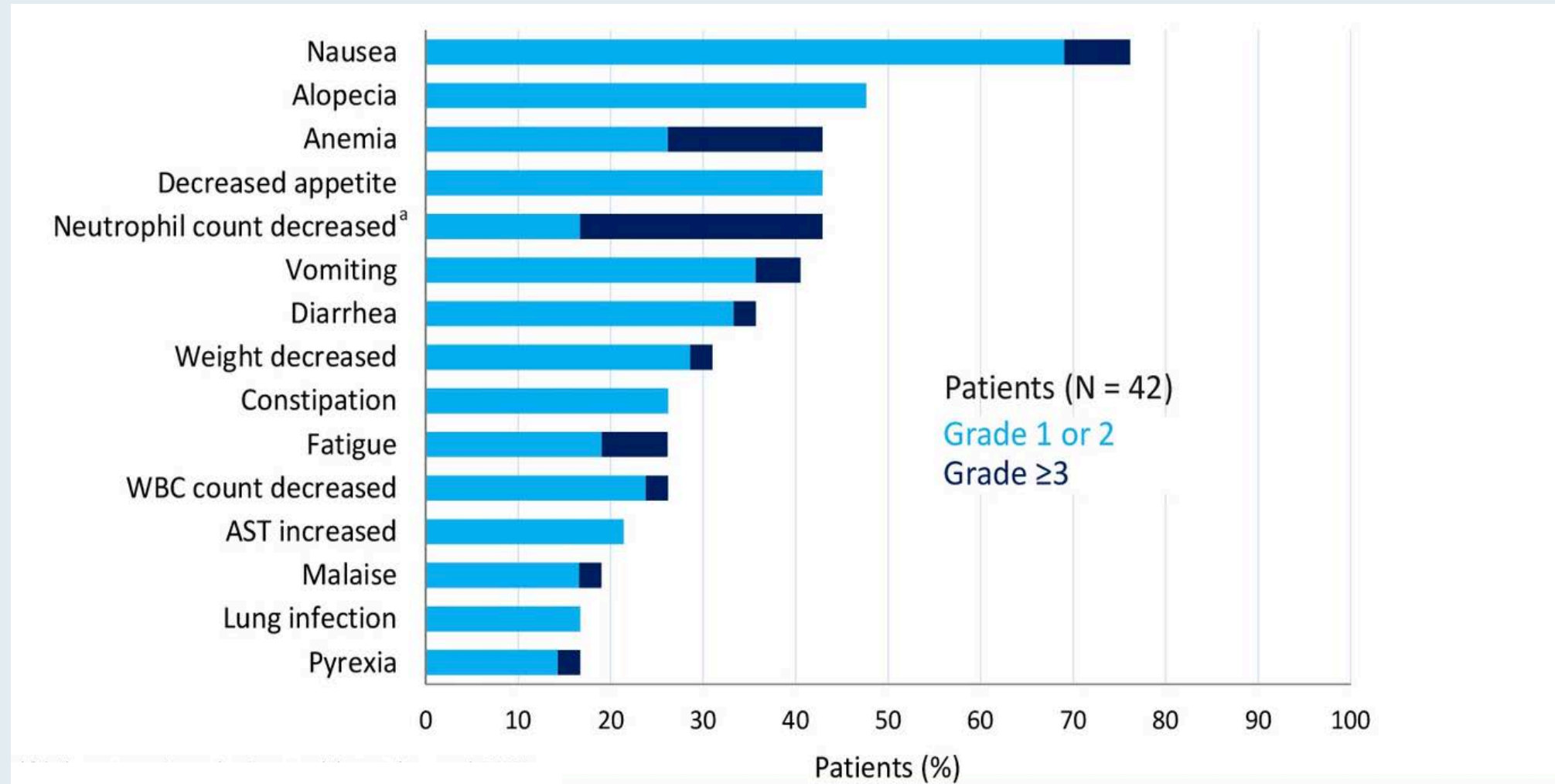


Based on independent central review. Baseline is last measurement taken before enrollment. Shown is best (minimum) percent change from baseline in the sum of diameters for all target lesions.

^a One patient was missing a baseline assessment and 2 additional patients were missing post-baseline assessments.

- Median PFS = 14.0 months

DESTINY-Lung01: Treatment-Emergent AEs



DESTINY-Lung01: AEs of Special Interest – Interstitial Lung Disease

n (%)	All Patients (N = 42)					Any Grade/ Total
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	
Interstitial lung disease	0 ^a	5 (11.9)	0	0	0	5 (11.9)

- Median time to onset of investigator-reported ILD was at 86 days (range, 41-255 days)
- 4 patients had drug withdrawn and 1 had drug interrupted
- All patients received steroid treatment
- 2 patients recovered, 1 recovered with sequelae, 1 was recovering, and 1 had not recovered by data-cutoff
- No grade 5 ILD was observed in this cohort

Meet The Professor

Management of Multiple Myeloma

Thursday, November 12, 2020
12:00 PM – 1:00 PM ET

Faculty

Sergio Giralt, MD

Moderator

Neil Love, MD

Thank you for joining us!

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