# *Meet The Professor*
# Management of Lung Cancer

**Professor Solange Peters, MD, PhD**
Head, Medical Oncology
Chair, Thoracic Malignancies
Oncology Department
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Lausanne, Switzerland

# Commercial Support

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# Dr Love — Disclosures

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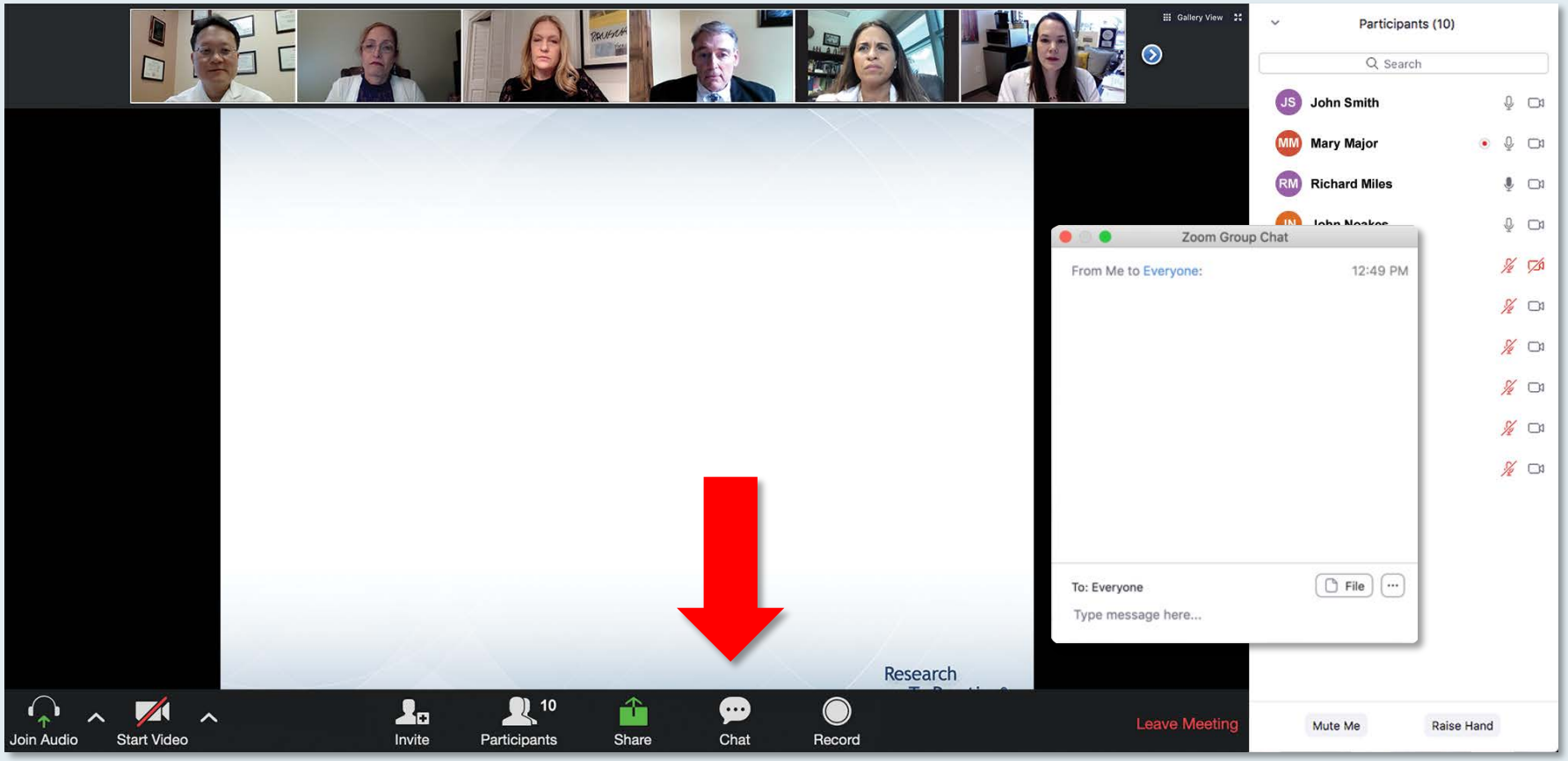


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# Familiarizing Yourself with the Zoom Interface

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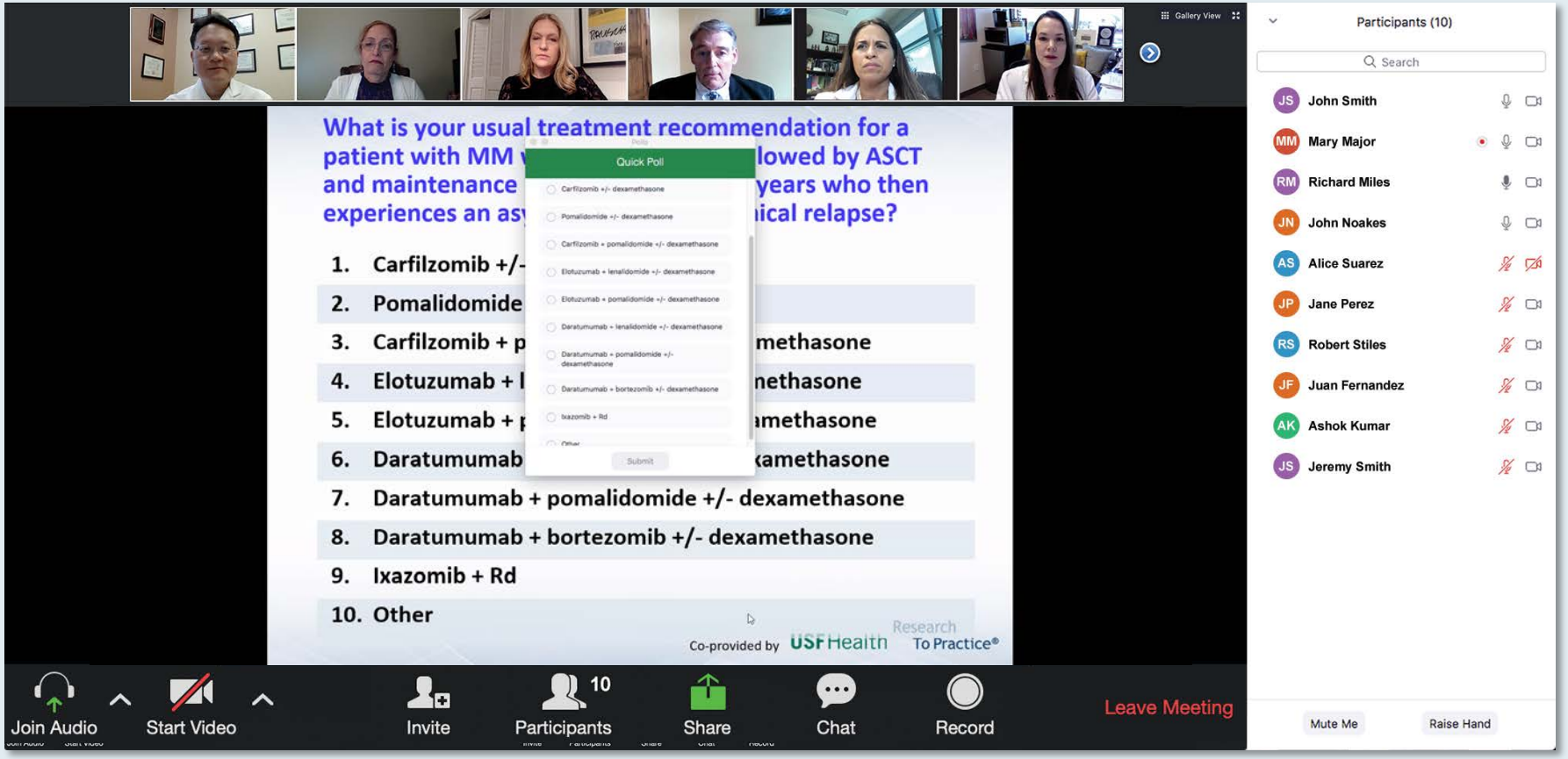


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## Upcoming Webinars

### Friday, October 30, 2020
### 12:30 PM – 1:30 PM ET

**Meet The Professor: Immunotherapy and Novel Agents in Gynecologic Cancers**

**Faculty**
Richard T Penson, MD, MRCP

**Moderator**
Neil Love, MD

### Friday, November 6, 2020
### 12:00 PM – 1:00 PM ET

**Meet The Professor: Management of Ovarian Cancer**

**Faculty**
Mansoor Raza Mirza, MD

**Moderator**
Neil Love, MD

*Thank you for joining us!*

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

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## WITH DR NEIL LOVE

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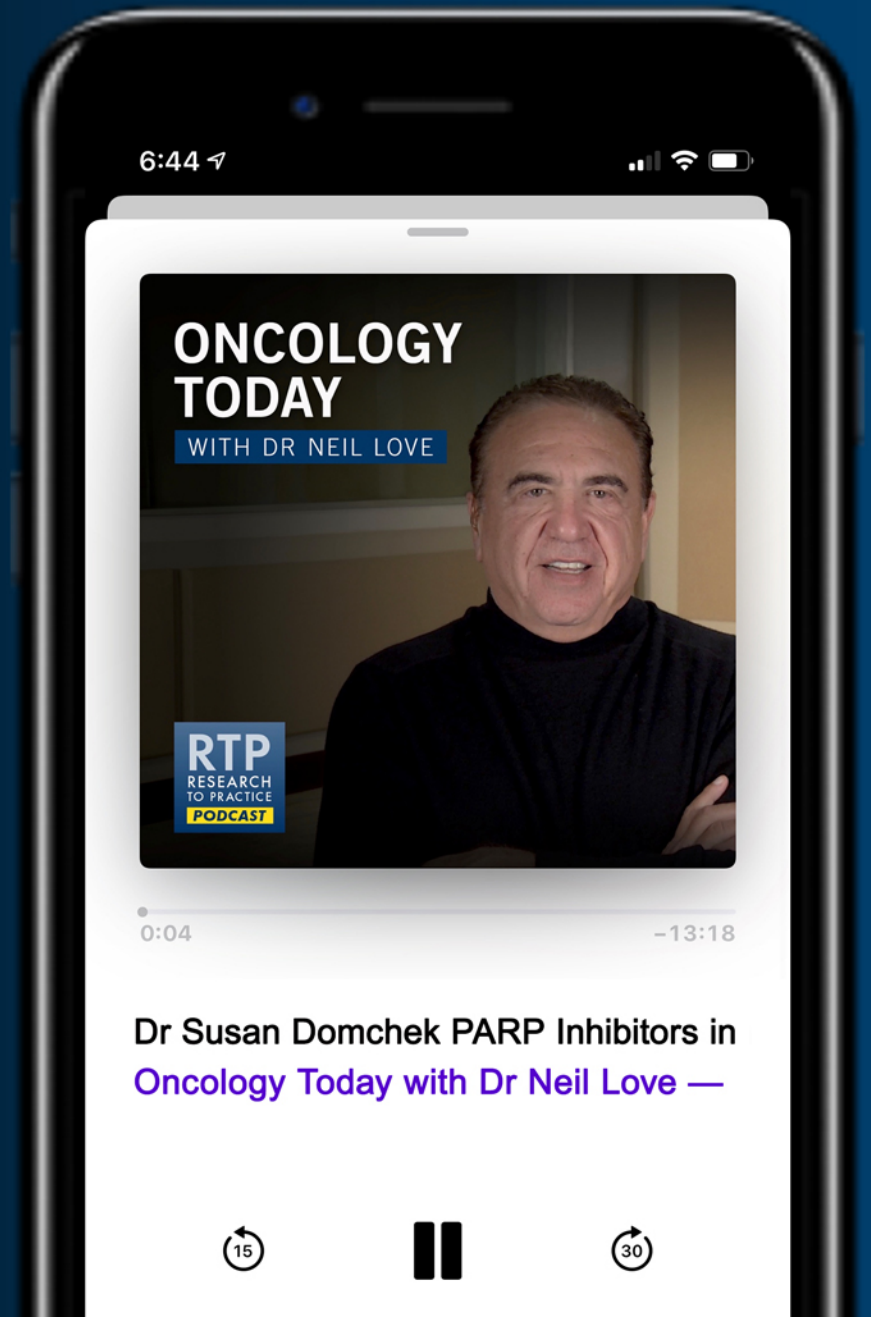

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# *Meet The Professor* Program Participating Faculty

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Director, Thoracic Oncology Research Program
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Vanderbilt University
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Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

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Johns Hopkins School of Medicine
Clinical Director
Medical Director, Thoracic Oncology Program
Johns Hopkins Sidney Kimmel Cancer Center at Sibley Memorial
Washington, DC

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

**Joel W Neal, MD, PhD**
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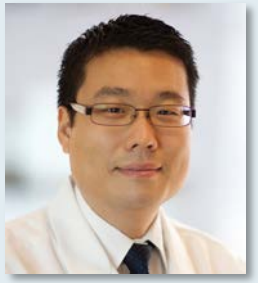

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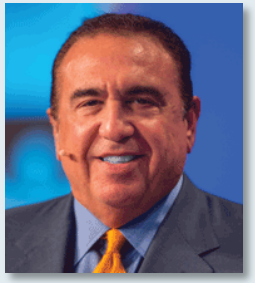

***Project Chair***
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Research To Practice
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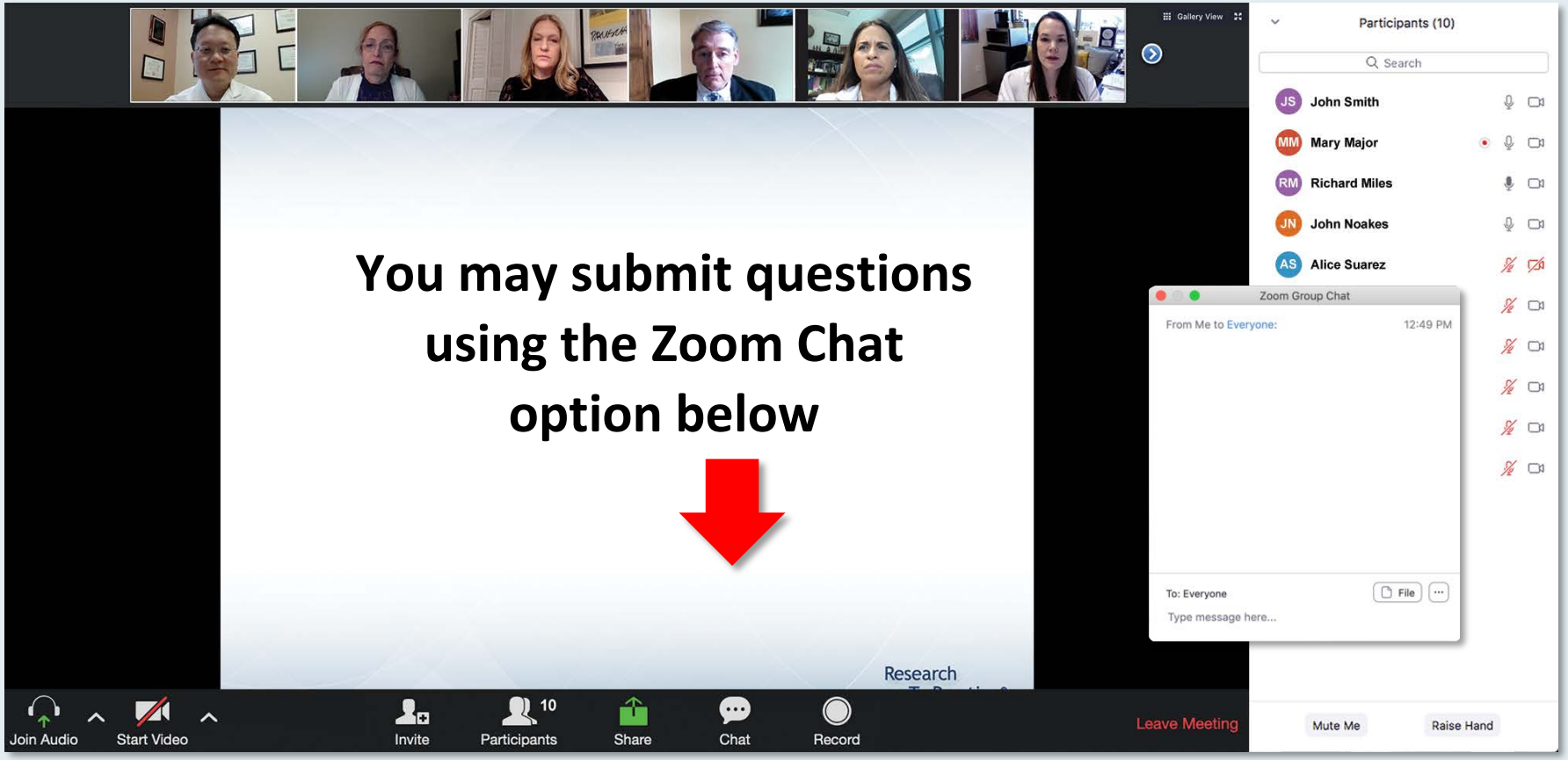


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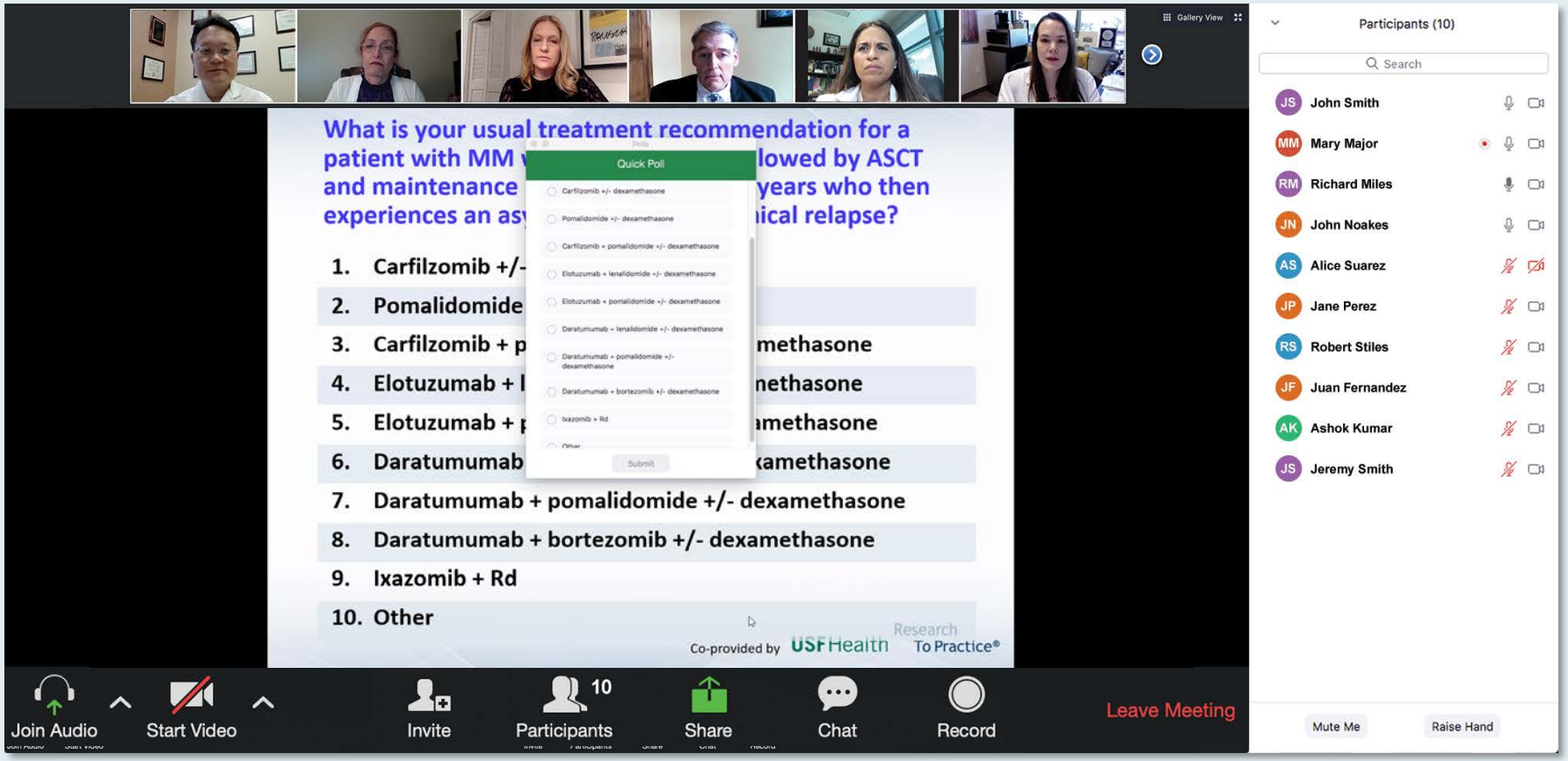


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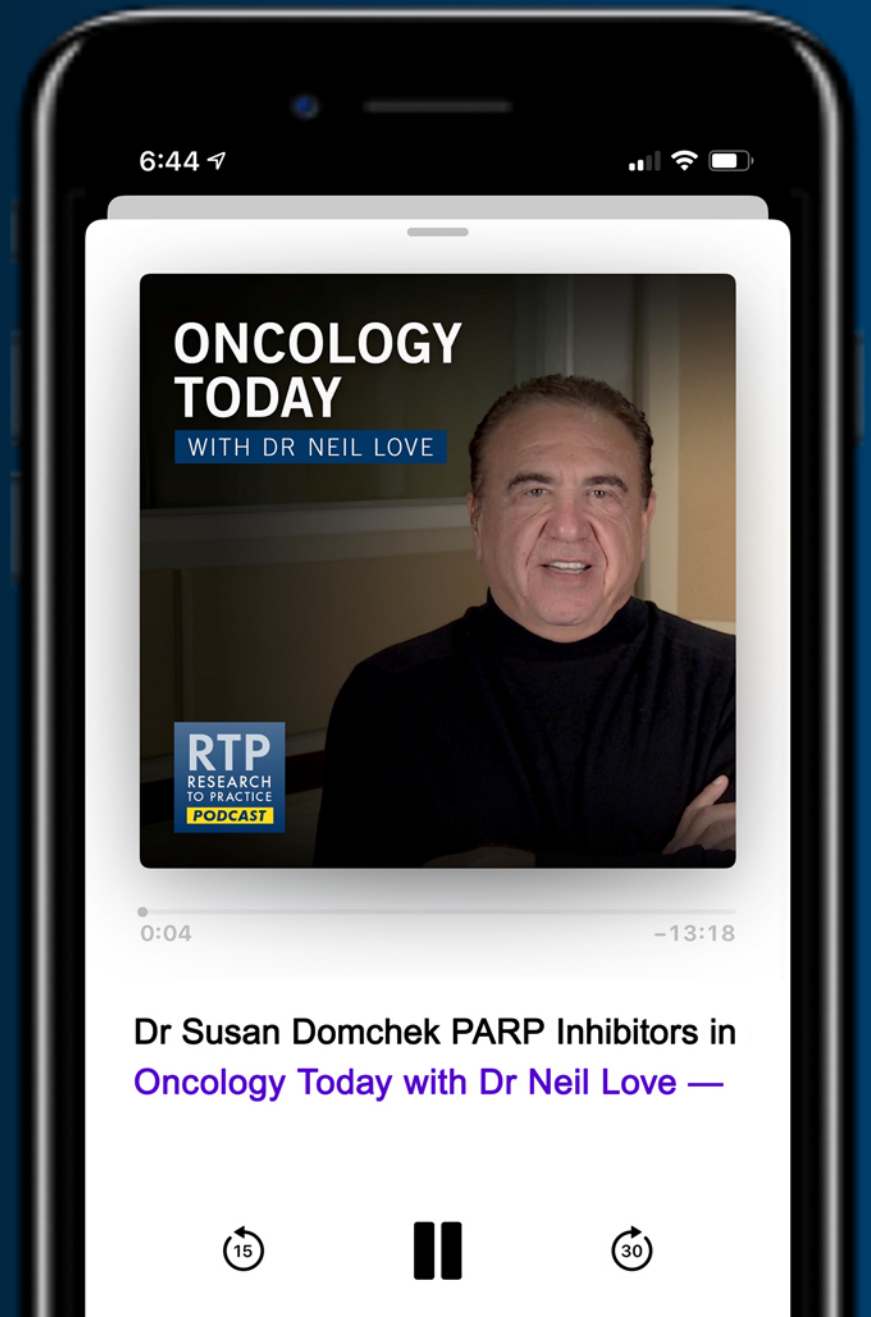

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**Allan Freedman, MD**
Physician with Suburban Hematology-Oncology Associates
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**Benjamin Parsons, DO**
Hematology/Oncology
Gundersen Health System Cancer and Blood Disorders
Adult Hematology Section Chair and Pediatric Hematology Oncology Section Chair
Gundersen Health Site Director for Precision Medicine Molecular Tumor Board
Clinical Adjunct Professor, University of Wisconsin–Madison
Madison, Wisconsin

# Meet The Professor with Prof Peters

## Module 1: Cases from Drs Freedman and Parsons

- Dr Freedman: A 62-year-old woman with metastatic adenocarcinoma of the lung – TMB 25 mut/Mb, no actionable mutations
- Dr Parsons: A frail 82-year-old man and smoker with Stage IIIB non-small cell lung cancer (NSCLC) and no identified targetable mutations
- Dr Parsons: A 61-year-old man and smoker with Stage IB NSCLC and no identified targetable mutations
- Dr Freedman: An 81-year-old woman with metastatic adenocarcinoma of the lung and brain metastases – EGFR C797S mutation
- Dr Parsons: Questions and Comments: Selection and sequencing of agents in small cell lung cancer (SCLC)
- Dr Freedman: A 71-year-old woman with metastatic adenocarcinoma of the lung and solitary cerebellar metastasis – pan wild-type

## Module 2: Lung Cancer Journal Club with Prof Peters

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

## Module 4: Key Papers and Recent Approvals

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# Patients with metastatic adenocarcinoma of the lung should generally have a “liquid biopsy” ordered…

1. At diagnosis
2. At diagnosis if insufficient tissue for NGS
3. Neither

# What is your usual first-line treatment for a patient with metastatic NSCLC, no actionable mutations and PD-L1 level of 0?

1. Pemetrexed/pembrolizumab/carboplatin
2. Chemotherapy
3. Chemotherapy + bevacizumab
4. Ipilimumab/nivolumab
5. Other

# Case Presentation – Dr Freedman: A 62-year-old woman with metastatic adenocarcinoma of the lung – TMB 25 mut/Mb, no actionable mutations

Dr Allan Freedman

- 1/2014: Diagnosed with Stage IB adenocarcinoma of the lung – pan-wildtype
- RUL lobectomy → Adjuvant cisplatin/pemetrexed x 4 → disease free x 5 years
- 12/2018: Seizure
  - MRI: Solitary right parietal lobe metastasis
  - PET: No extracranial disease
- Neurosurgery → SRS to resection site
- NGS: TMB 25 mut/Mb, PD-L1 10%, no actionable mutations; Liquid biopsy: Same
- 7/2020: Local recurrence at edge of resection margin in brain; No extracranial disease
  - Second neurosurgical resection: Two foci of tumor and fragments of dura positive
  - Second course of SRS planned

**Question**

- Should we just continue to observe her and wait for the next event?

**A 60-year-old patient presents with unresectable Stage IIIB adenocarcinoma of the lung and is also found to have an EGFR exon 19 deletion. Reimbursement issues aside, what is your likely treatment strategy?**

1. Chemoradiation and durvalumab consolidation
2. Chemoradiation and durvalumab consolidation → osimertinib
3. Osimertinib
4. Chemoradiation → osimertinib
5. Other

# Case Presentation – Dr Parsons: A frail 82-year-old man with Stage IIIB NSCLC and no identified targetable mutations

**Dr Benjamin Parsons**

- 2019: Diagnosed with Stage IIIB right lower lobe adenocarcinoma of the lung (cT3N2M0)
- Liquid biopsy ordered
  - Limited tissue available for testing
  - Liquid biopsy reveals no identified targetable mutations
  - PD-1/PD-L1 status undetermined
- Chemoradiation therapy → durvalumab maintenance
- 2020: Disease progression

**Questions**

- What therapy would you offer next for this patient?
- Do you prefer single versus doublet cytotoxic regimens in frail, older patients? What are your experiences with the tolerability of cytotoxic doublets in these patients?

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# Case Presentation – Dr Parsons: A 61-year-old man with Stage IB NSCLC and no identified targetable mutations

**Dr Benjamin Parsons**

- 2017: Diagnosed with Stage IB left lobe adenocarcinoma of the lung
  - Greatest dimension – 3.2 cm; high grade with LVI and N0 status
  - Diabetes and other risk factors for chronic kidney disease
- NGS panel ordered
  - NGS reveals no identified targetable mutations
  - High PD-1/PD-L1 status
- Adjuvant carboplatin/pemetrexed x 4

**Questions**

- Any updates in management of T2N0 NSCLC? Current role for (neo)adjuvant chemotherapy?
- What is your comfort level with substituting carboplatin for cisplatin in this setting?
- Would you offer adjuvant immunotherapy in a patient with a high PD-L1 score?

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# Case Presentation – Dr Freedman: An 81-year-old woman with metastatic adenocarcinoma of the lung and brain metastases – EGFR C797S mutation

Dr Allan Freedman

- 5/2018: Presents with de novo metastatic adenocarcinoma of the lung
  - Destructive mass in the lateral first rib and involvement of the pedicle of T4
- Biopsy: EGFR missense in exon 18 and missense in exon 20
- Radiation therapy to rib → osimertinib and denosumab
- 5/2019: Oligoprogression of disease in the LUL → SBRT, continued systemic therapy
- 5/2020: PD in spine treated with radiation therapy
- 9/2020: Gait instability; MRI of brain: Right temporal and frontal lesions, left temporal lesion, 2 cerebellar lesions → radiation therapy
- Liquid biopsy: Low-level mutations – EGFR C797S mutation and PIK3CA mutation

**Questions**

- What is the significance of these less common EGFR mutations? Do these affect the type of therapy we choose, how we follow them and our subsequent treatments?
- Should we continue the present therapy? When would you consider switching to a second-line treatment, and what should that be? Should we be looking at immunotherapy? Chemotherapy?
- What is your approach to managing brain metastases in an older patient? Should we continue the TKI?

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# Questions and Comments: Selection and sequencing of agents in SCLC?

**Dr Benjamin Parsons**

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# Case Presentation – Dr Freedman: A 71-year-old woman with metastatic adenocarcinoma of the lung and solitary cerebellar metastasis – pan wild-type

Dr Allan Freedman

- 2016: Diagnosed with moderately differentiated adenocarcinoma, pan-wildtype
- Work-up: Solitary cerebellar metastasis (Stage IV with oligometastatic disease)
- Treated with curative intent: Paclitaxel/carboplatin → SRS to brain
- Maintenance pemetrexed x 11 months
- 9/2017: Radiographic progression in lung and cerebellum
- Second course of SRS to CNS → nivolumab x 43 treatments over 3 years
  - In 2018 a third cerebellar metastasis was treated with XRT
- Currently, remains disease free

**Questions**

- Currently, what is considered the optimum number of cycles of treatment with immunotherapy?
- Is it worthwhile to test him now with liquid biopsy or to wait for actual progression of disease?

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# Meet The Professor with Prof Peters

## Module 1: Cases from Drs Freedman and Parsons

## Module 2: Lung Cancer Journal Club with Prof Peters

- Prognostic factors, testing and defining outcomes in patients with cancer in the COVID-19 era
- Brain metastases
- Stage III NSCLC: Real-world consolidation durvalumab; neoadjuvant durvalumab/chemotherapy
- METeoric rise of MET in lung cancer; targeting MET in EGFR resistance
- Novel approaches in SCLC: Lurbinectedin and consolidation ipilimumab/nivolumab
- KEYNOTE-604: Pembrolizumab with etoposide/platinum as first-line therapy for extensive-stage SCLC
- First-line immunotherapy in metastatic NSCLC
- Immune-related adverse events with checkpoint inhibitors (CI); feasibility of CI rechallenge
- Mobocertinib as first-line treatment for NSCLC with EGFR exon 20 insertions
- ALEX: Updated overall survival, safety data
- Quantifying the confounders of panel-based tumor mutational burden measurement

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

## Module 4: Key Papers and Recent Approvals

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# Assessment of Clinical and Laboratory Prognostic Factors in Patients with Cancer and SARS-CoV-2 Infection: The COVID-19 and Cancer Consortium (CCC19)

Grivas P et al.

ESMO 2020;Abstract LBA72.

# Defining COVID-19 Outcomes in Thoracic Cancer Patients: TERAVOLT (Thoracic cancERs International CoVid 19 cOLlaboraTion)

Espinar JB et al.

ESMO 2020;Abstract LBA75.

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ANNALS OF ONCOLOGY driving innovation in oncology

EDITORIAL

# Testing for COVID-19 in lung cancer patients

Passaro A et al. *Annal Oncol* 2020;[Online ahead of print].

Cancer Cell

CellPress

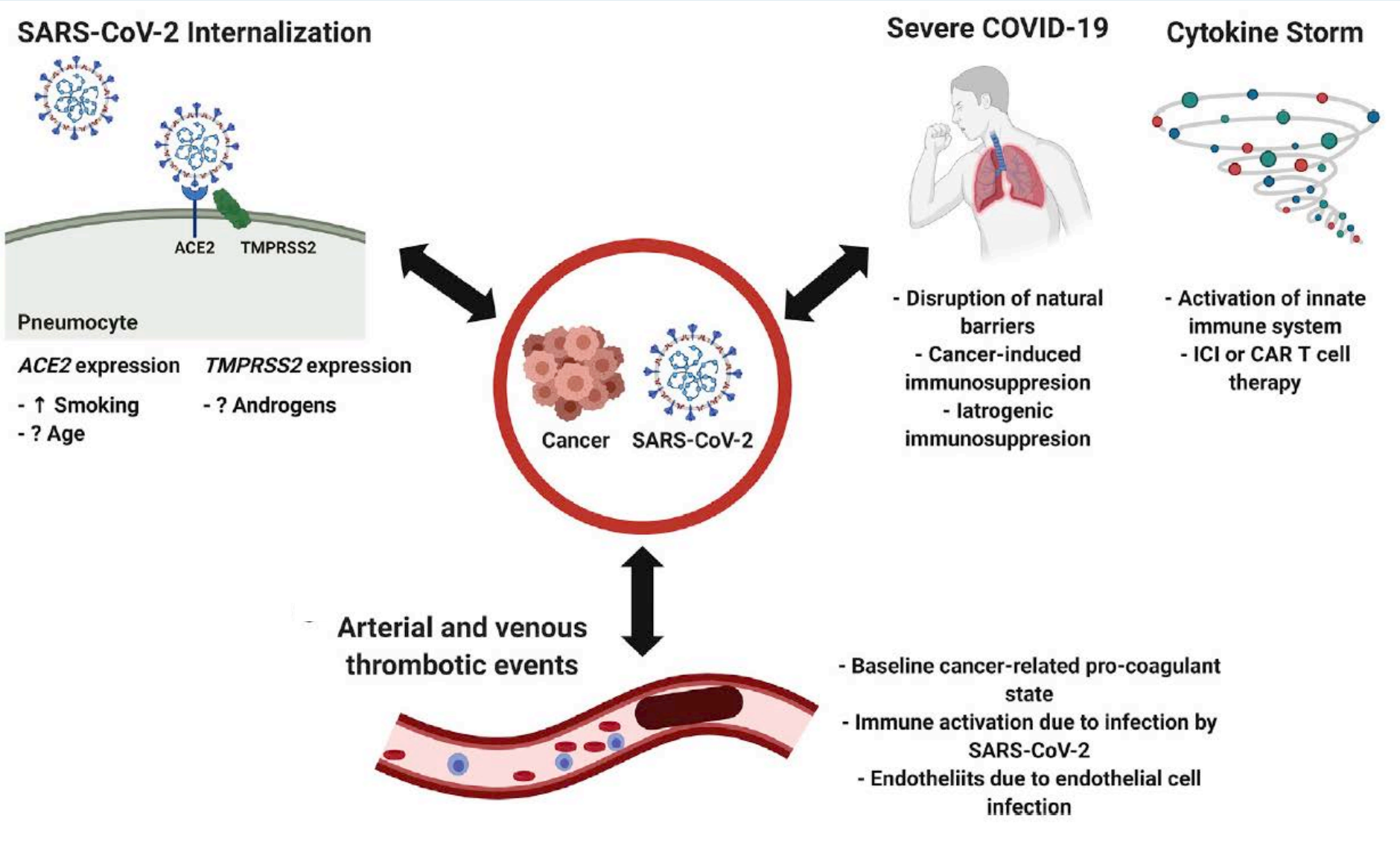
Review

# COVID-19 and Cancer: Current Challenges and Perspectives

Ziad Bakouny,[1,7] Jessica E. Hawley,[2,7] Toni K. Choueiri,[1] Solange Peters,[3] Brian I. Rini,[4] Jeremy L. Warner,[4,5] and Corrie A. Painter[6,*]

*Cancer Cell* 2020;[Online ahead of print].

# Interplay between SARS-CoV-2 and Cancer Biology




Bakouny Z et al. *Cancer Cell* 2020;[Online ahead of print].

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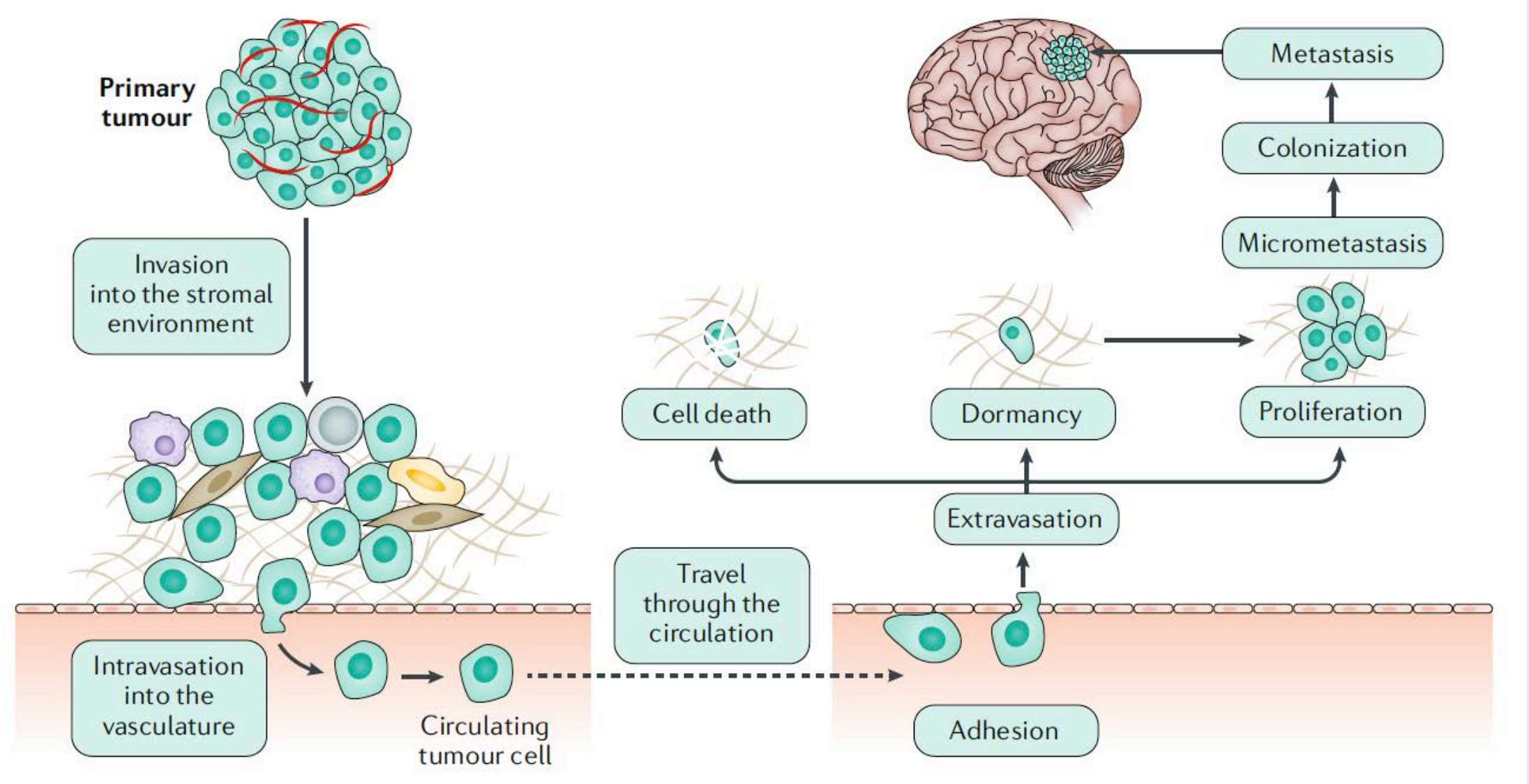
# Brain metastases

*Achal Singh Achrol[1]*, Robert C. Rennert[2]*, Carey Anders[3], Riccardo Soffietti[4], Manmeet S. Ahluwalia[5], Lakshmi Nayak[6], Solange Peters[7], Nils D. Arvold[8], Griffith R. Harsh[9], Patricia S. Steeg[10] and Steven D. Chang[9]**

***Nat Rev Dis Primers 2019;5(1):5.***

# Cancer Cell Metastatic Dissemination




Achrol AS et al. *Nat Rev Dis Primers* 2019;5(1):5.

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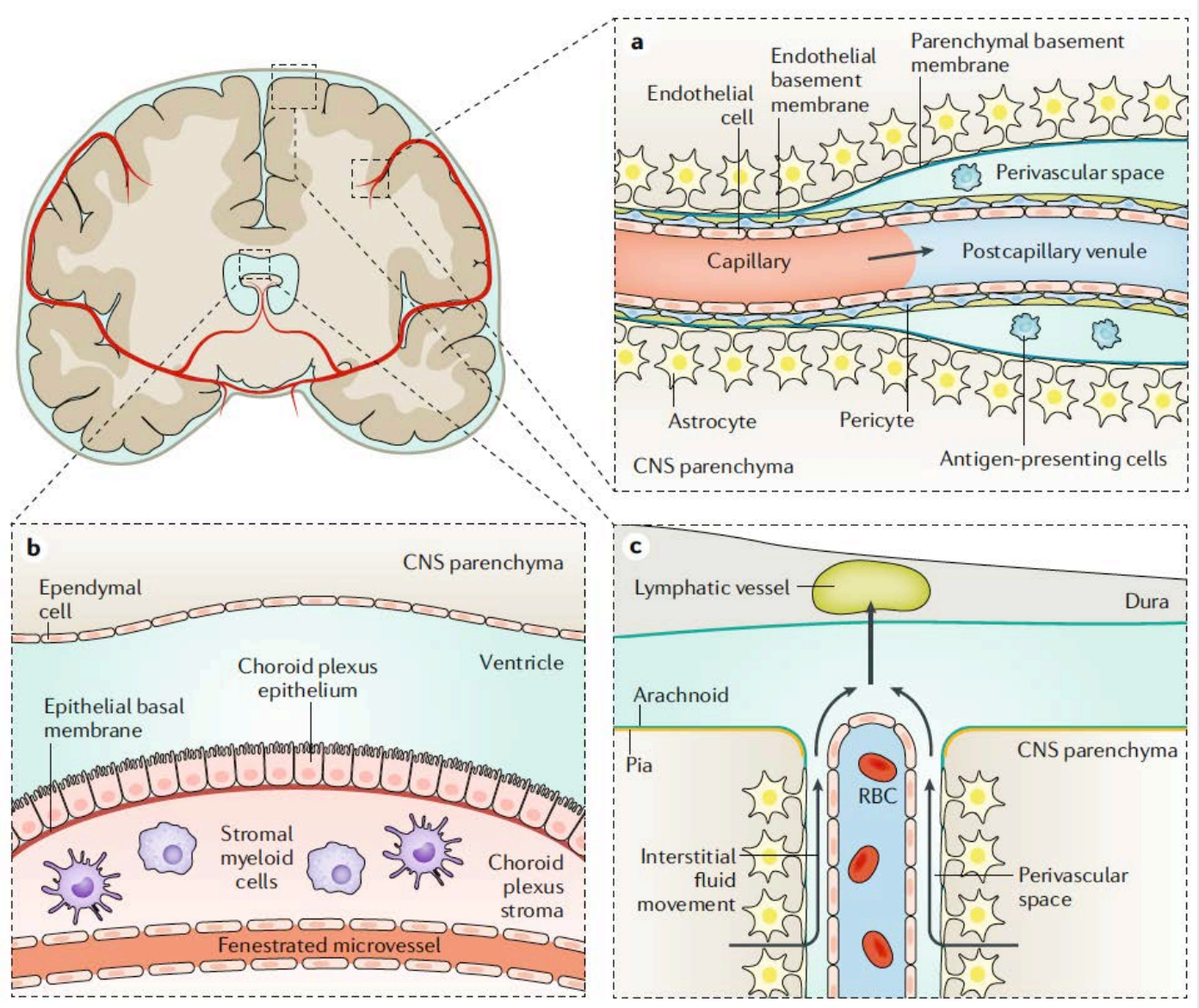
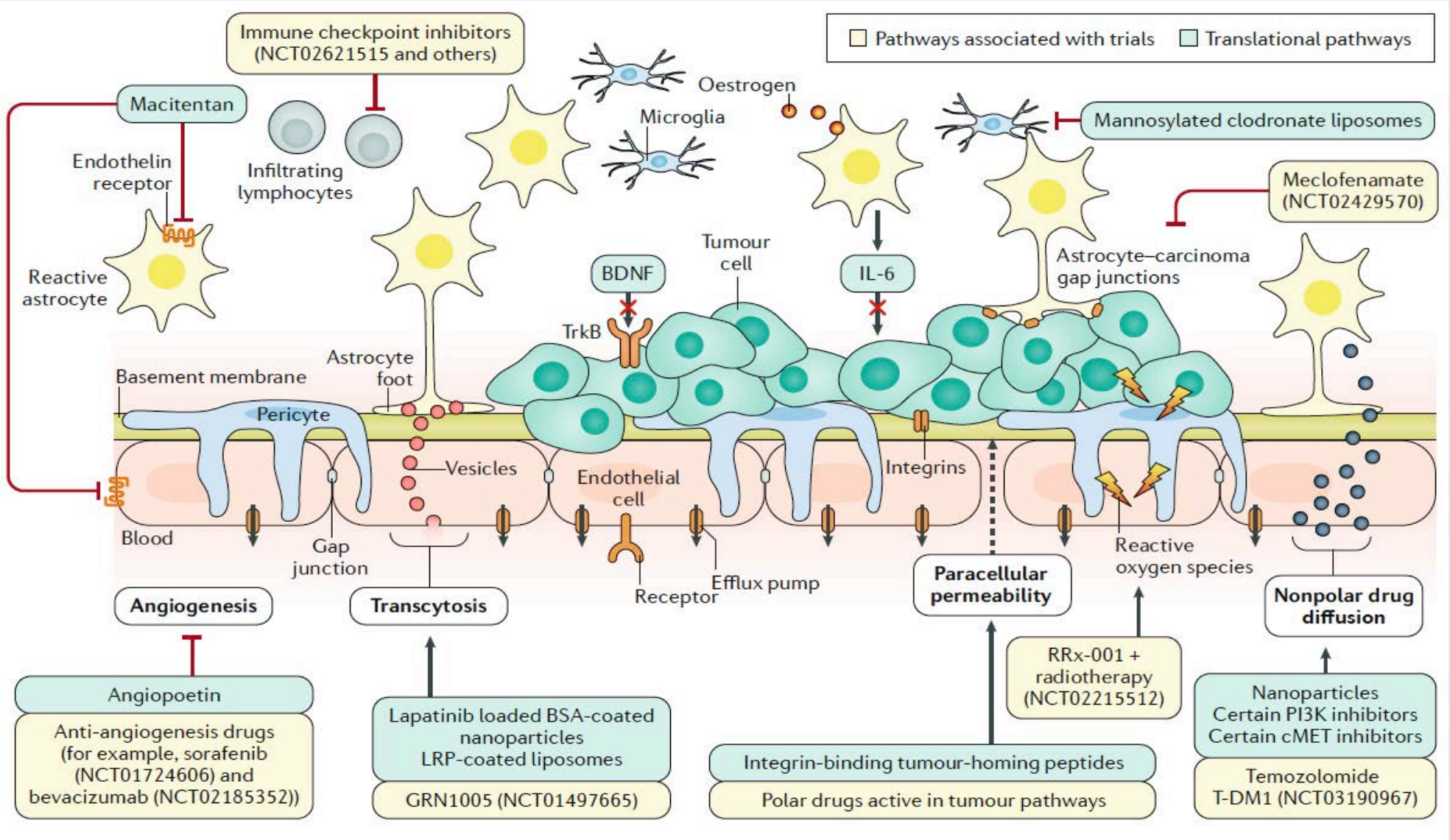
# Central Nervous System Barriers




Achrol AS et al. *Nat Rev Dis Primers* 2019;5(1):5.

# Selected Potential Targets in the Blood-Tumor Microenvironment for Future Therapies




Achrol AS et al. *Nat Rev Dis Primers* 2019;5(1):5.

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# 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.

Review

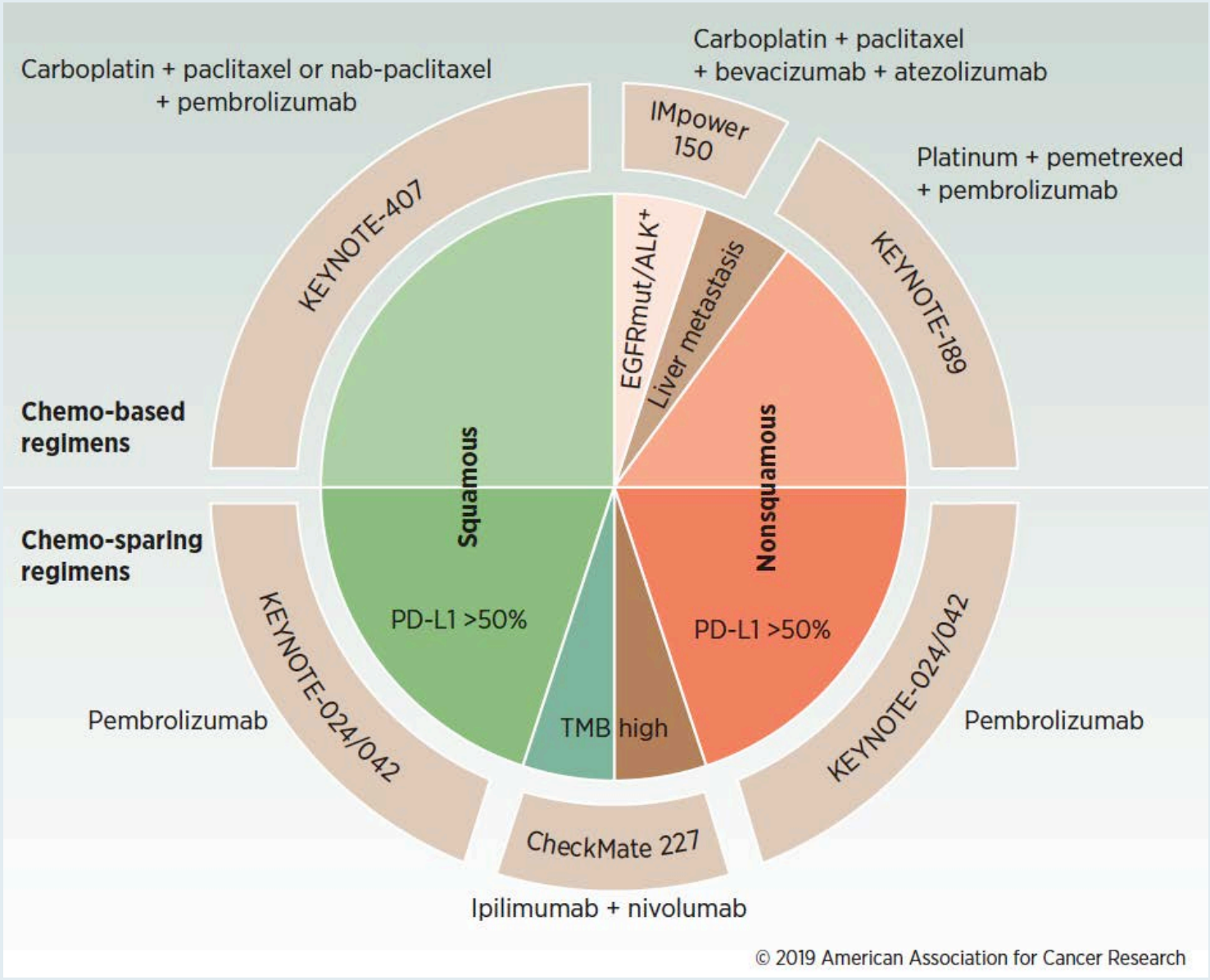
Clinical Cancer Research

# Immunotherapy for the First-Line Treatment of Patients with Metastatic Non–Small Cell Lung Cancer

Pablo Martinez[1], Solange Peters[2], Timothy Stammers[3], and Jean-Charles Soria[3,4]

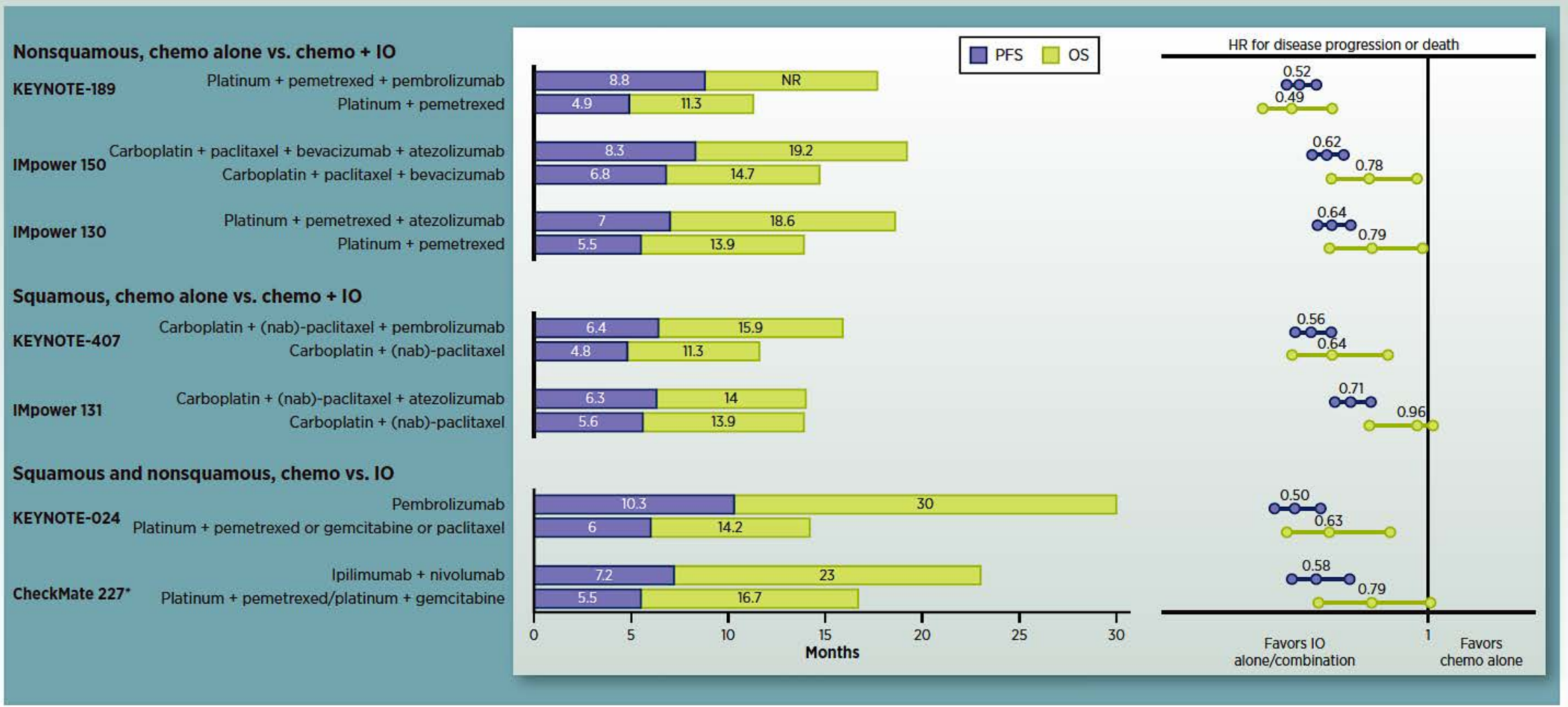
*Clin Cancer Res* 2019;25(9):2691-8.

# Regimens Evaluated in First-Line NSCLC Immunotherapy Studies




Martinez P et al. *Clin Cancer Res* 2019;25(9):2691-8.

# First-Line NSCLC Immunotherapy Studies: Survival Outcomes




Martinez P et al. *Clin Cancer Res* 2019;25(9):2691-8.

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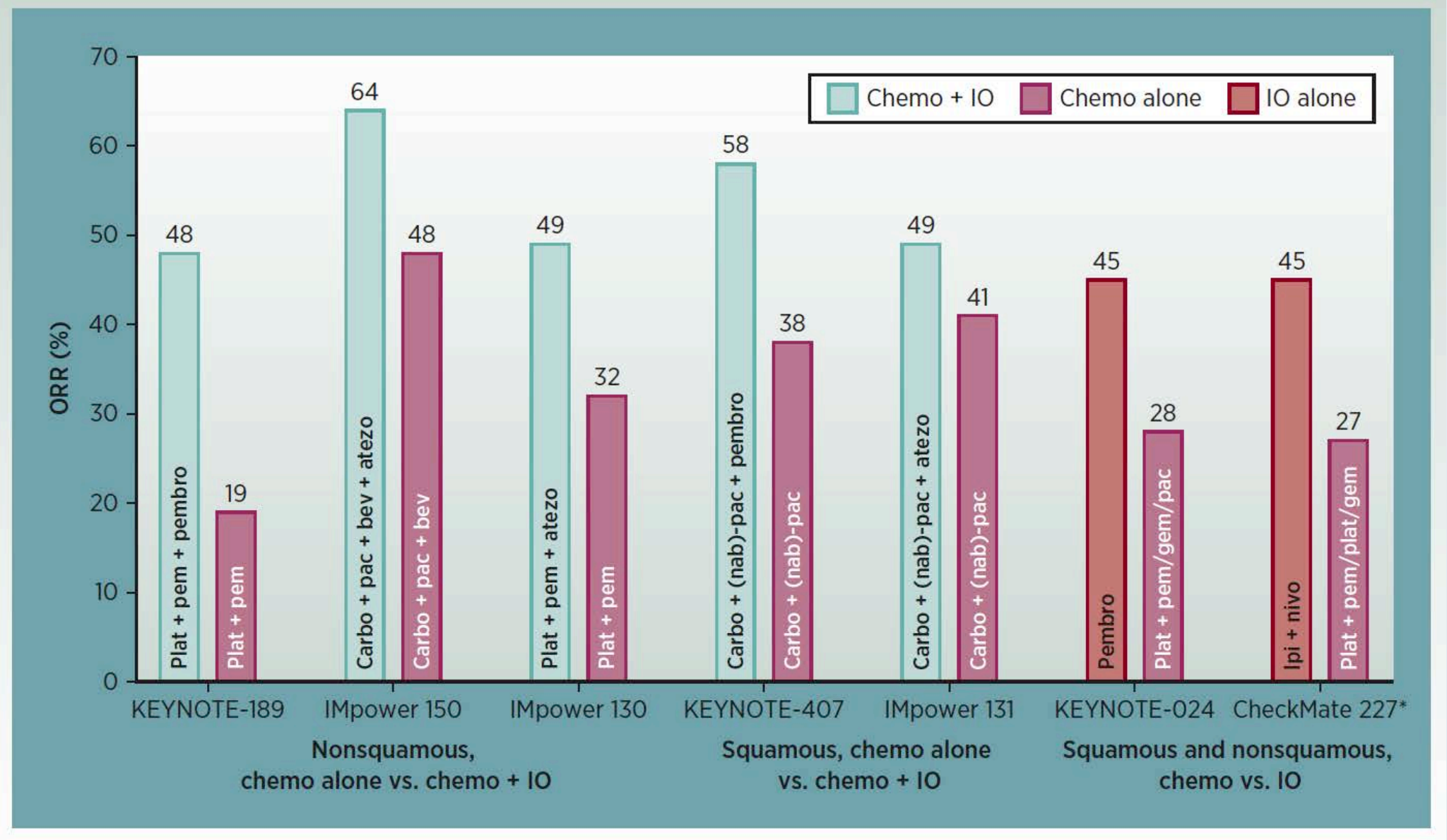
# First-Line NSCLC Immunotherapy Studies: Response Rates




Martinez P et al. *Clin Cancer Res* 2019;25(9):2691-8.

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# Long-Lasting, Irreversible and Late-Onset Immune-Related Adverse Events (irAEs) from Immune Checkpoint Inhibitors (ICIs): A Real-World Data Analysis

Ghisoni E et al.

ASCO 2020;Abstract e15095.

# Rechallenge patients with immune checkpoint inhibitors following severe immune-related adverse events: review of the literature and suggested prophylactic strategy

John Haanen,[1] Marc Ernstoff,[2] Yinghong Wang ,[3] Alexander Menzies,[4,5] Igor Puzanov,[2] Petros Grivas,[6] James Larkin,[7] Solange Peters,[8] John Thompson,[6] Michel Obeid[9,10]

*J Immunother Cancer* 2020;8(1):e000604.

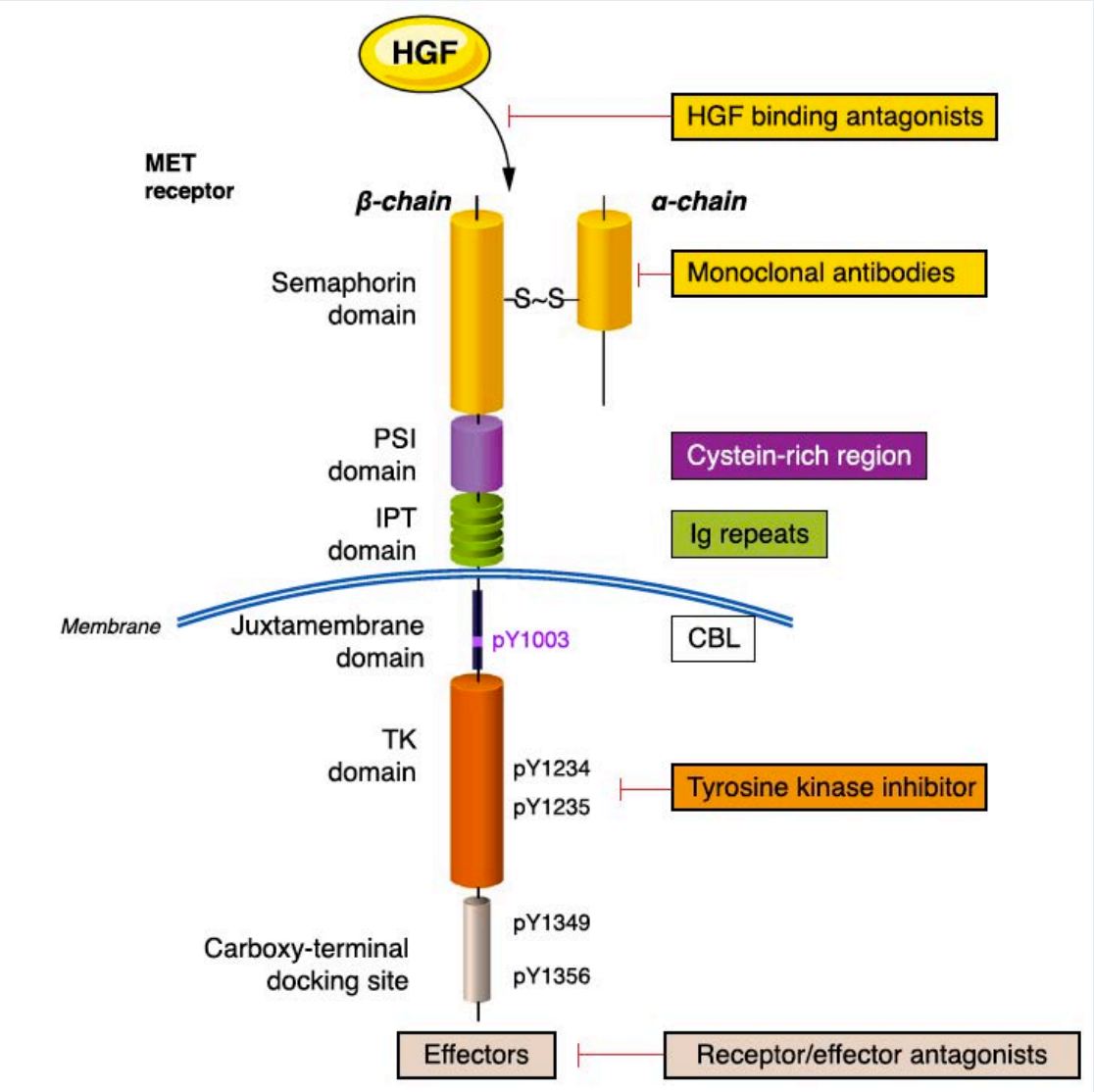
Review Article

# The METeoric Rise of MET in Lung Cancer

Alex Friedlaender, MD [1]; Alexander Drilon, PhD [2,3]; Giuseppe Luigi Banna, MD [4]; Solange Peters, PhD [5]; and Alfredo Addeo, MD [1]

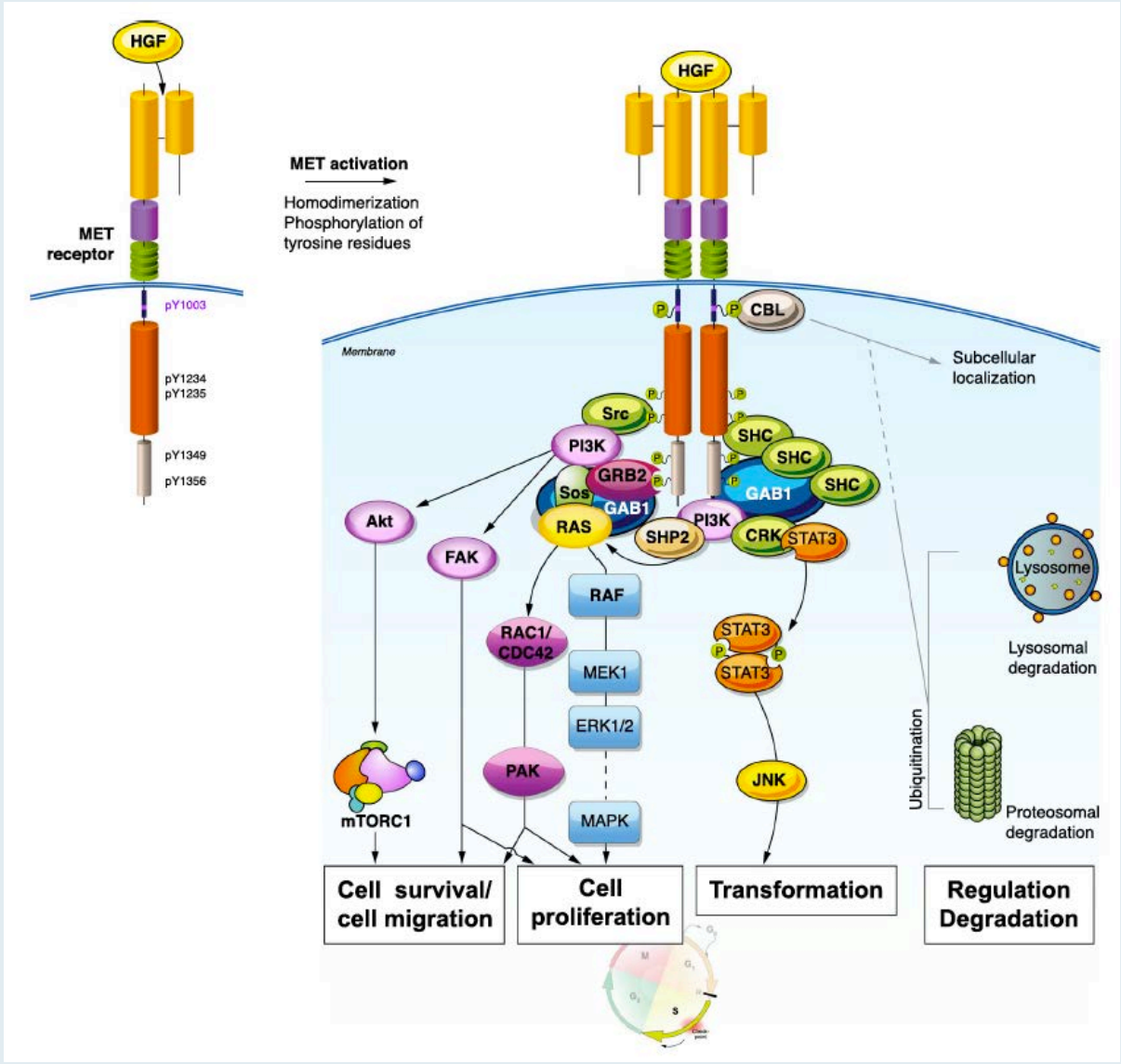
*Cancer* 2020;126:4826-37.

# Potential Therapeutic Targets of the MET Receptor



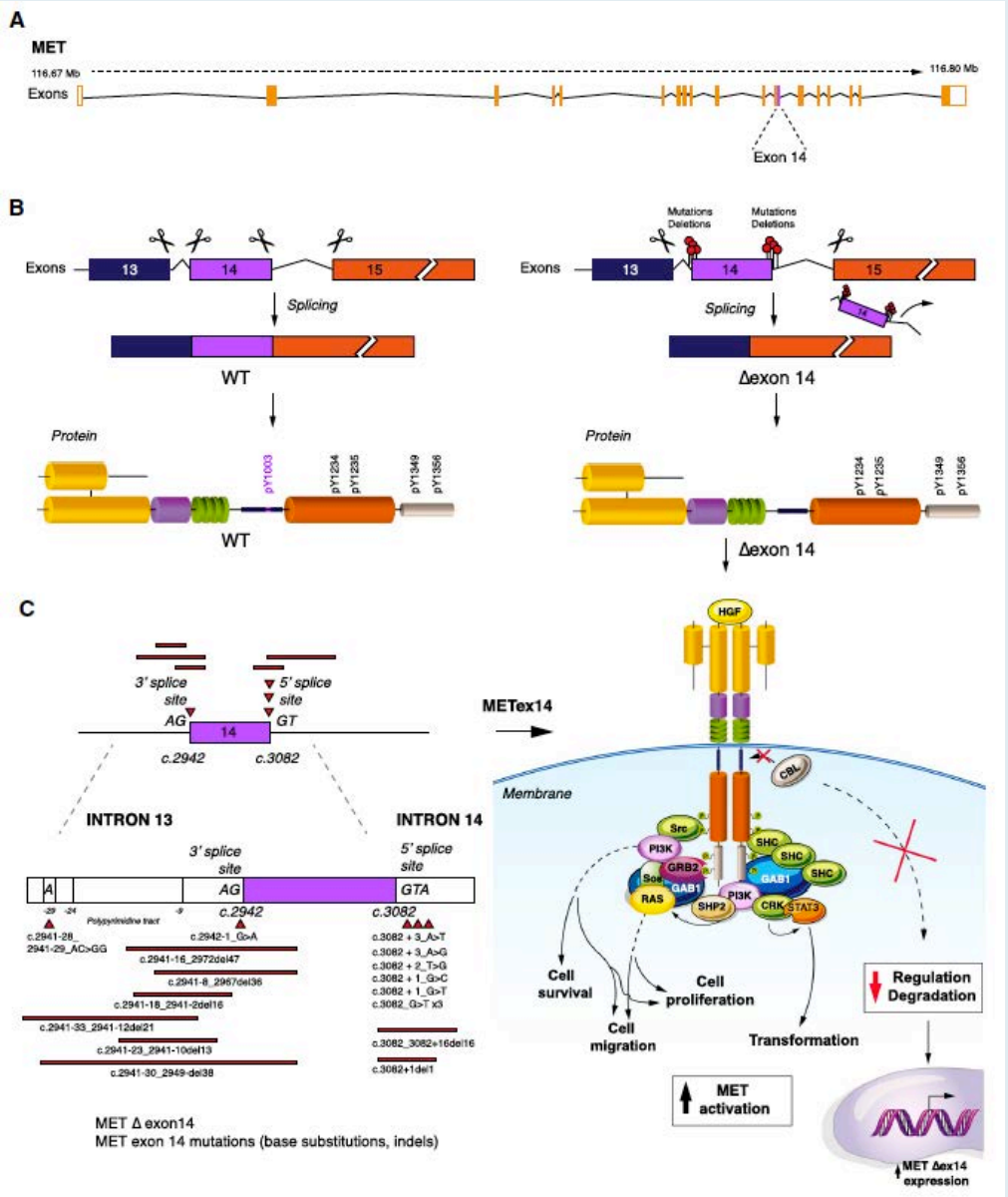

Friedlaender A et al. *Cancer* 2020;126:4826-37.

# MET Signaling Pathways and Their Effector Functions




Friedlaender A et al. *Cancer* 2020;126:4826-37.

# Pathophysiology of Exon 14 Alterations




Friedlaender A et al. *Cancer* 2020;126:4826-37.

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# Targeting MET in EGFR resistance in non-small-cell lung cancer—ready for daily practice?

Schmid S et al. *Lancet Oncol* 2020;21(3):320-2.

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TO PRACTICE

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

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

*Lancet Oncol* 2020; 21: 645–54

rapid communications

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

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

*J Clin Oncol* 2020;38:2369-79.

Rudin CM et al. ASCO 2020;Abstract 9001. Oral

# Consolidation Ipilimumab and Nivolumab vs Observation in Limited Stage SCLC After Chemo-Radiotherapy: Results from the ETOP/IFCT 4-12 STIMULI Trial

Peters S et al.

ESMO 2020;Abstract LBA84.

# Mobocertinib (TAK-788) as First-Line Treatment vs Platinum-Based Chemotherapy (CT) for NSCLC with EGFR Exon 20 Insertions (Exon20ins)

Jänne PA et al.

ESMO 2020;Abstract 1412TiP.

# Updated Overall Survival (OS) and Safety Data from the Randomized, Phase III ALEX Study of Alectinib (ALC) versus Crizotinib (CRZ) in Untreated Advanced ALK+ NSCLC

Peters S et al.

ASCO 2020;Abstract 9518.

# SAKK 16/14: Anti-PD-L1 Antibody Durvalumab in Addition to Neoadjuvant Chemotherapy in Patients with Stage IIIA (N2) Non-Small Cell Lung Cancer (NSCLC) – A Multicenter Single-Arm Phase II Trial

Rothschild SI et al.

ESMO 2020;Abstract 1237MO.

# Quantifying the Confounders of Panel-Based Tumor Mutational Burden (TMB) Measurement

Budczies J et al.

AACR 2020;Abstract 3093.

# Meet The Professor with Prof Peters

## Module 1: Cases from Drs Freedman and Parsons

## Module 2: Lung Cancer Journal Club with Prof Peters

- Prognostic factors, testing and defining outcomes in patients with cancer in the COVID-19 era
- Brain metastases
- Stage III NSCLC: Real-world consolidation durvalumab; neoadjuvant durvalumab/chemotherapy
- METeoric rise of MET in lung cancer; targeting MET in EGFR resistance
- Novel approaches in SCLC: Lurbinectedin and consolidation ipilimumab/nivolumab
- KEYNOTE-604: Pembrolizumab with etoposide/platinum as first-line therapy for extensive-stage SCLC
- First-line immunotherapy in metastatic NSCLC
- Immune-related adverse events with checkpoint inhibitors (CI); feasibility of CI rechallenge
- Mobocertinib as first-line treatment for NSCLC with EGFR exon 20 insertions
- ALEX: Updated overall survival, safety data
- Quantifying the confounders of panel-based tumor mutational burden measurement

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

## Module 4: Key Papers and Recent Approvals

RTP RESEARCH TO PRACTICE

**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

RTP
RESEARCH
TO PRACTICE

# 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

RTP RESEARCH TO PRACTICE

# 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

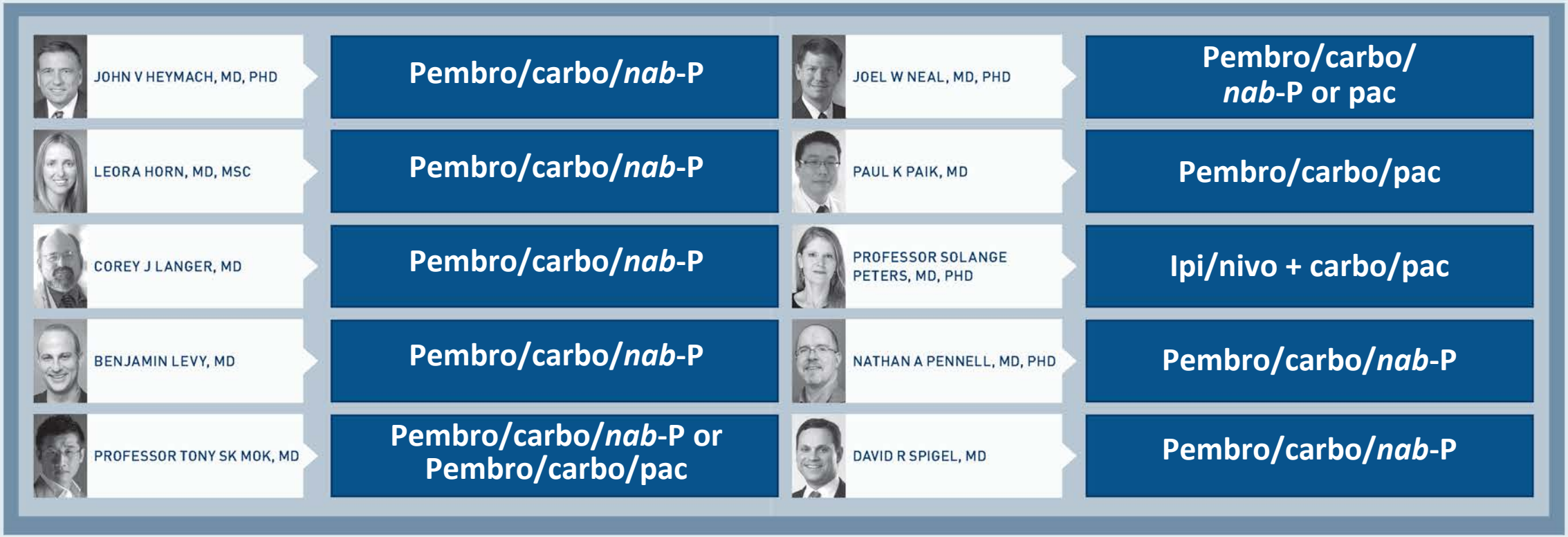
RTP RESEARCH TO PRACTICE

# 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%?

| | | | |
|---|---|---|---|
|  JOHN V HEYMACH, MD, PHD | Pembro |  JOEL W NEAL, MD, PHD | Pembro |
|  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 |

RTP RESEARCH TO PRACTICE

# 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%?




*Nab*-P = nanoparticle albumin-bound paclitaxel

RTP RESEARCH TO PRACTICE

# 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/*nab*-P |
|  LEORA HORN, MD, MSC | Pembro/carbo/*nab*-P |  PAUL K PAIK, MD | Pembro/carbo/pac |
|  COREY J LANGER, MD | Pembro/carbo/*nab*-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/*nab*-P |

RTP RESEARCH TO PRACTICE

# 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/ *nab*-P or pac |
|  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 |

RTP RESEARCH TO PRACTICE

# 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%?

| | | | |
|---|---|---|---|
|  JOHN V HEYMACH, MD, PHD | Pembro |  JOEL W NEAL, MD, PHD | Pembro +/- carbo/ *nab*-P |
|  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 |

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

# 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?

| | | | |
|---|---|---|---|
|  JOHN V HEYMACH, MD, PHD | Indefinitely or until PD/toxicity |  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 | Indefinitely or until PD/toxicity |
|  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 | Indefinitely or until PD/toxicity |

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

# 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 |

RTP RESEARCH TO PRACTICE

# 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

RTP RESEARCH TO PRACTICE

# Meet The Professor with Prof Peters

## Module 1: Cases from Drs Freedman and Parsons

## Module 2: Lung Cancer Journal Club with Prof Peters

- Prognostic factors, testing and defining outcomes in patients with cancer in the COVID-19 era
- Brain metastases
- Stage III NSCLC: Real-world consolidation durvalumab; neoadjuvant durvalumab/chemotherapy
- METeoric rise of MET in lung cancer; targeting MET in EGFR resistance
- Novel approaches in SCLC: Lurbinectedin and consolidation ipilimumab/nivolumab
- KEYNOTE-604: Pembrolizumab with etoposide/platinum as first-line therapy for extensive-stage SCLC
- First-line immunotherapy in metastatic NSCLC
- Immune-related adverse events with checkpoint inhibitors (CI); feasibility of CI rechallenge
- Mobocertinib as first-line treatment for NSCLC with EGFR exon 20 insertions
- ALEX: Updated overall survival, safety data
- Quantifying the confounders of panel-based tumor mutational burden measurement

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

## Module 4: Key Papers and Recent Approvals

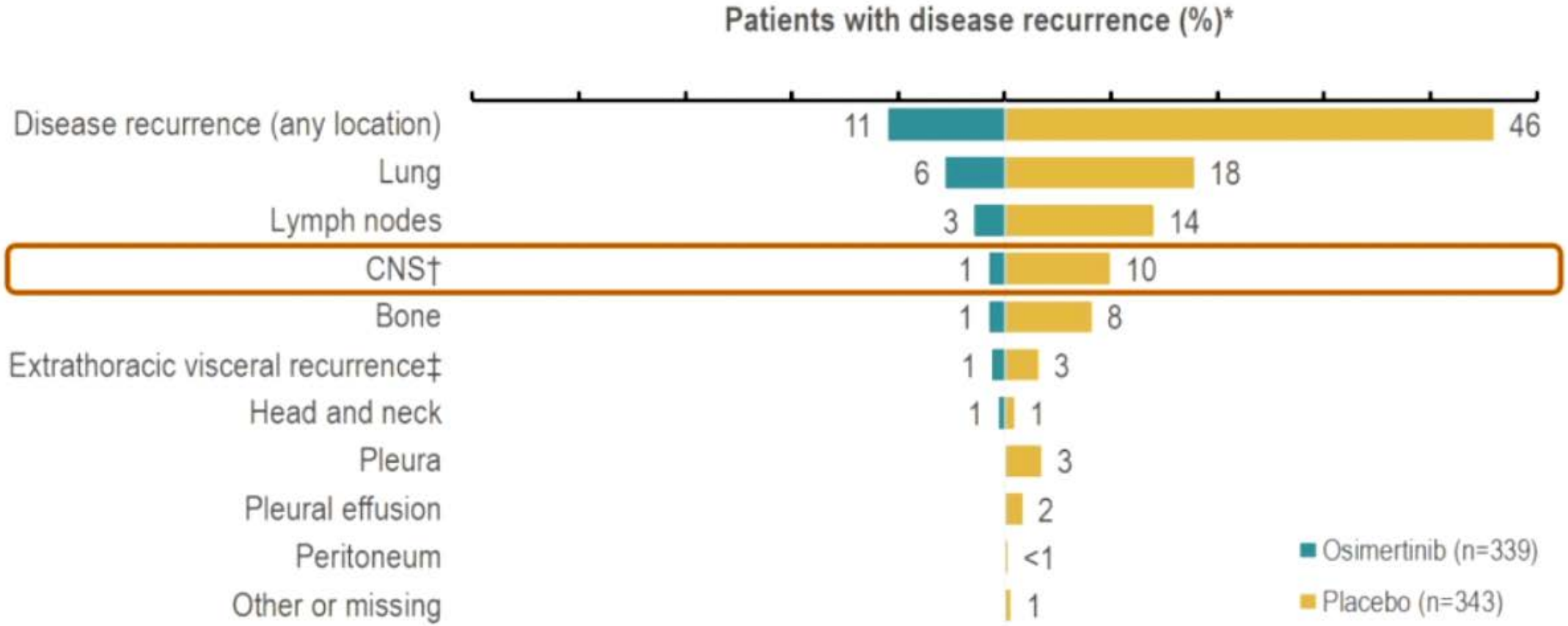
RTP RESEARCH TO PRACTICE

# 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




Tsuboi M et al. ESMO 2020;Abstract LBA1.

RTP RESEARCH TO PRACTICE

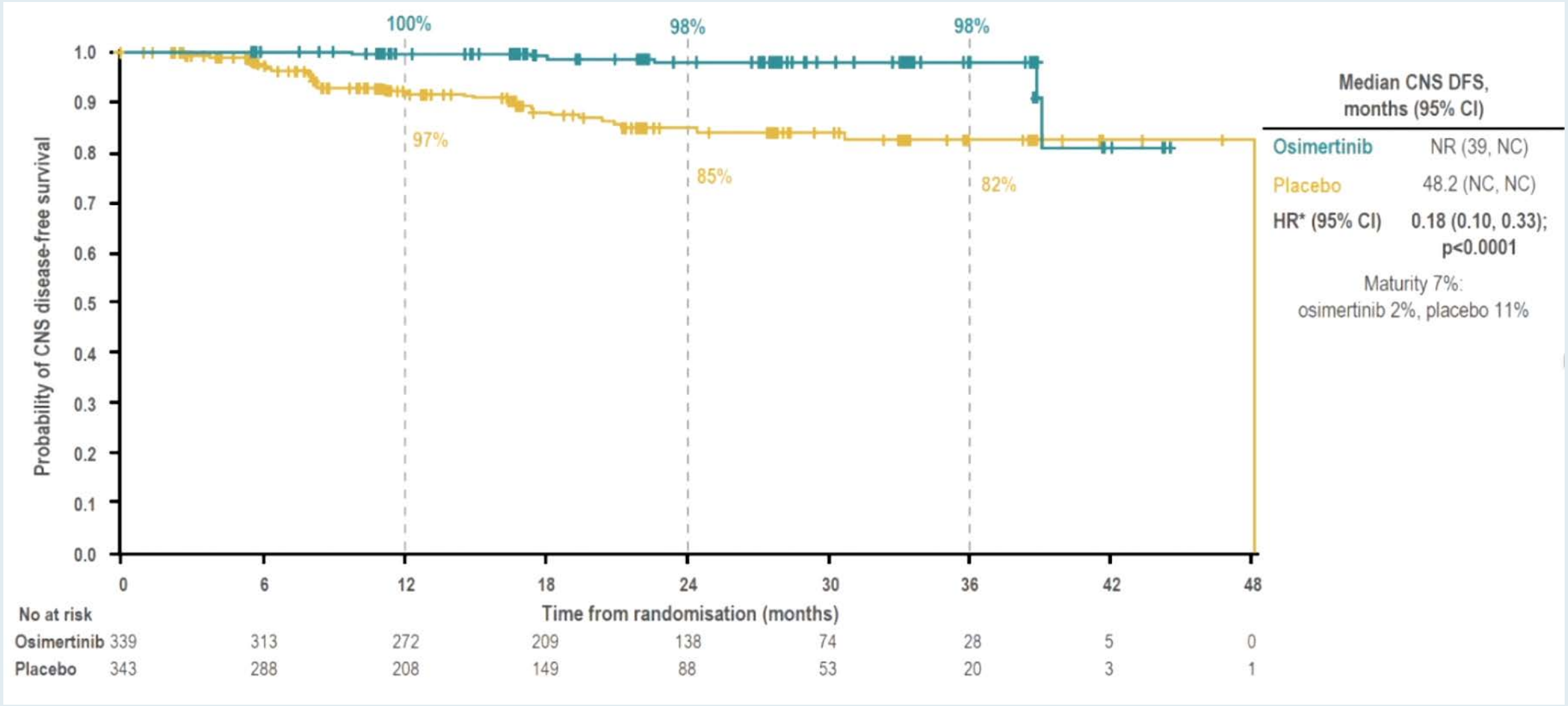
# ADAURA: CNS DFS Events

- 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%) |

Tsuboi M et al. ESMO 2020;Abstract LBA1.

# ADAURA: CNS DFS in Overall Population




Tsuboi M et al. ESMO 2020;Abstract LBA1.

RTP RESEARCH TO PRACTICE

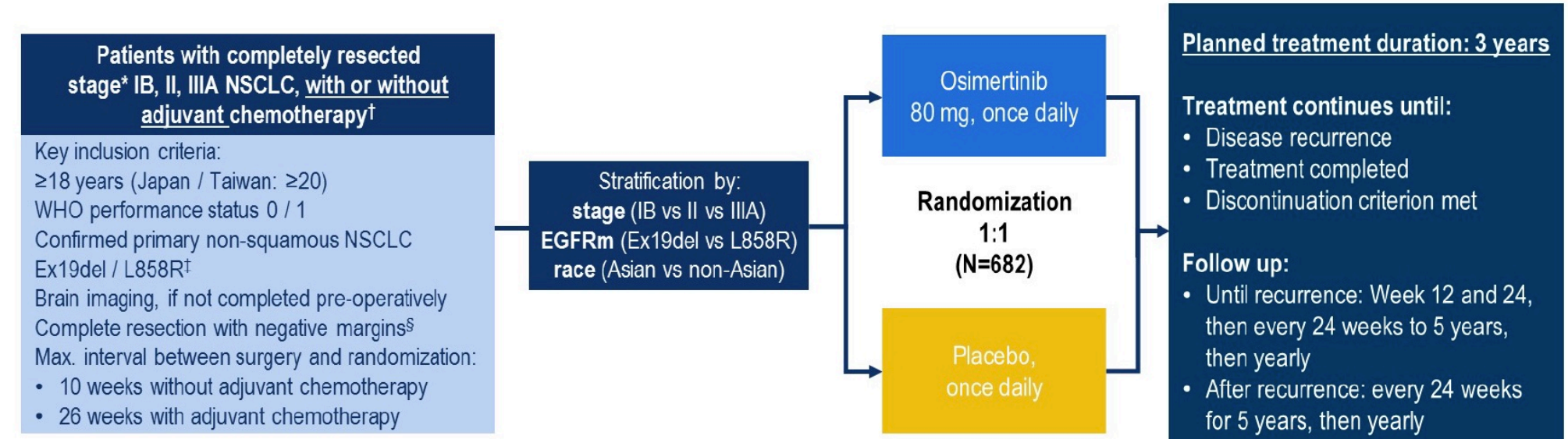
# Osimertinib as Adjuvant Therapy in Patients (pts) with Stage IB–IIIA EGFR Mutation Positive (EGFRm) NSCLC After Complete Tumor Resection: ADAURA

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



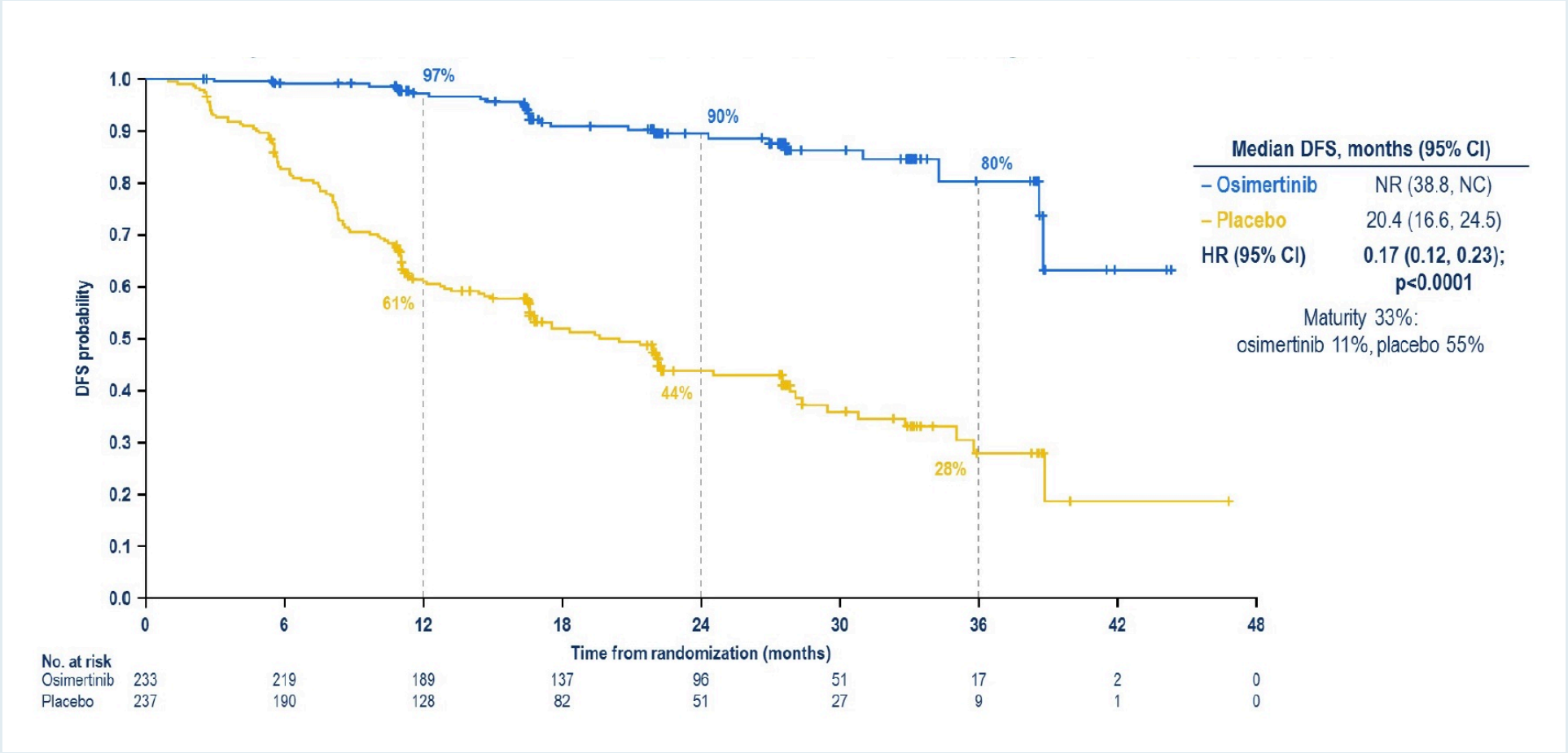

**Endpoints**

- **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**

Herbst RS et al. ASCO 2020;Abstract LBA5.

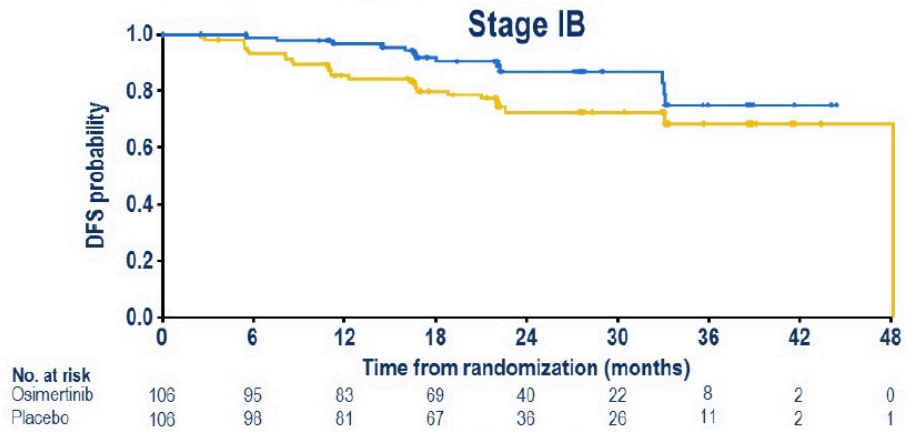
# ADAURA Primary Endpoint: Inv-Assessed DFS (Stage II/IIIA)

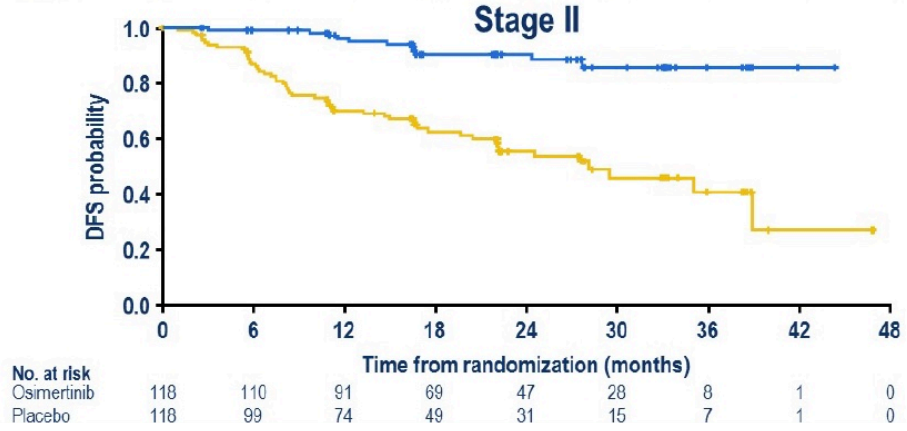



Herbst RS et al. ASCO 2020;Abstract LBA5.

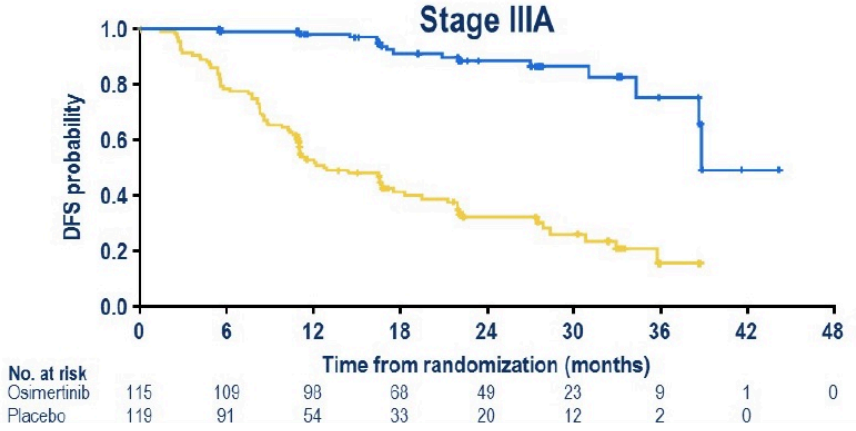
RTP RESEARCH TO PRACTICE

# ADAURA: DFS by Stage



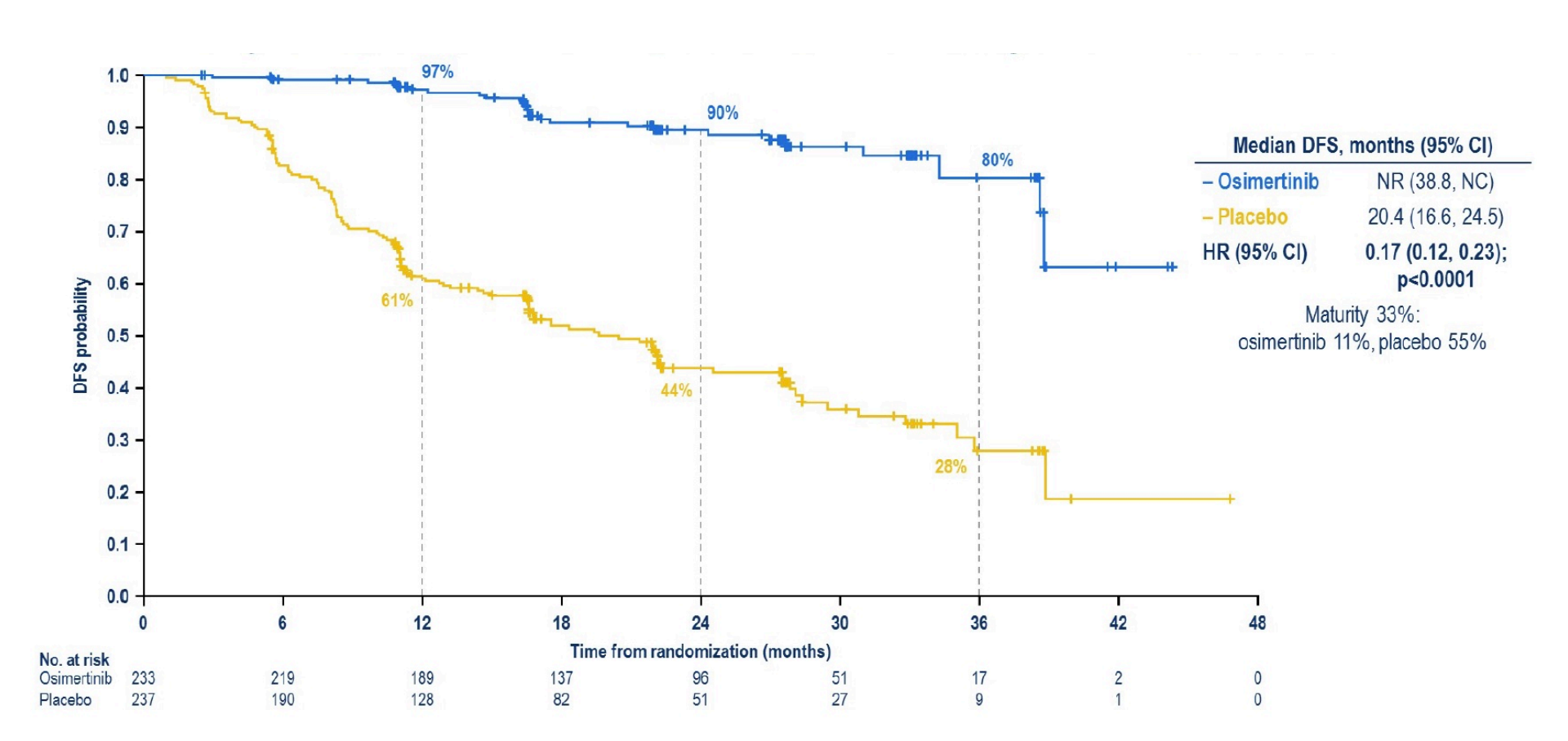




| | Stage IB | Stage II | Stage IIIA |
|---|---|---|---|
| 2 year DFS rate, % (95% CI) | | | |
| – Osimertinib | 87 (77, 93) | 91 (82, 95) | 88 (79, 94) |
| – Placebo | 73 (62, 81) | 56 (45, 65) | 32 (23, 42) |
| Overall HR (95% CI) | 0.50 (0.25, 0.96) | 0.17 (0.08, 0.31) | 0.12 (0.07, 0.20) |




Herbst RS et al. ASCO 2020;Abstract LBA5.

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




Herbst RS et al. ASCO 2020;Abstract LBA5.

# 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/$m^2$ by intravenous infusion every 21 days until disease progression or unacceptable toxicity.

The recommended lurbinectedin dose is 3.2 mg/$m^2$ every 21 days."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-lurbinectedin-metastatic-small-cell-lung-cancer.

# 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."

https://www.globenewswire.com/news-release/2020/09/07/2089388/0/en/Roche-announces-FDA-approval-of-Gavreto-pralsetinib-for-the-treatment-of-adults-with-metastatic-RET-fusion-positive-non-small-cell-lung-cancer.html

RTP RESEARCH TO PRACTICE

# 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."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-selpercatinib-lung-and-thyroid-cancers-ret-gene-mutations-or-fusions

# 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."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-capmatinib-metastatic-non-small-cell-lung-cancer

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

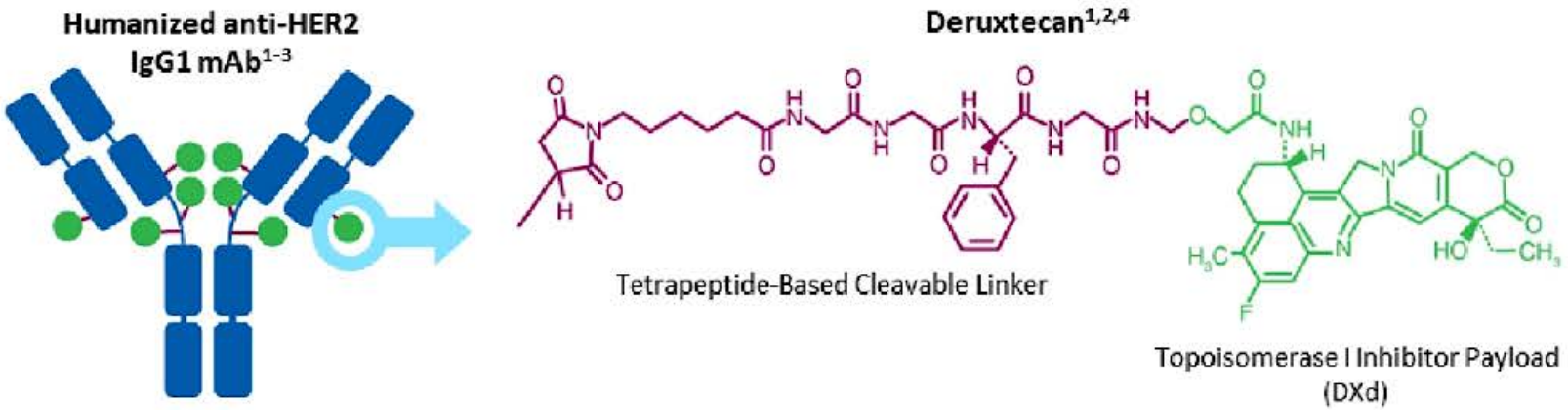
Smit EF et al.

ASCO 2020;Abstract 9504.

# Antibody-Drug Conjugate
# Trastuzumab Deruxtecan

## T-DXd is an ADC with 3 components:

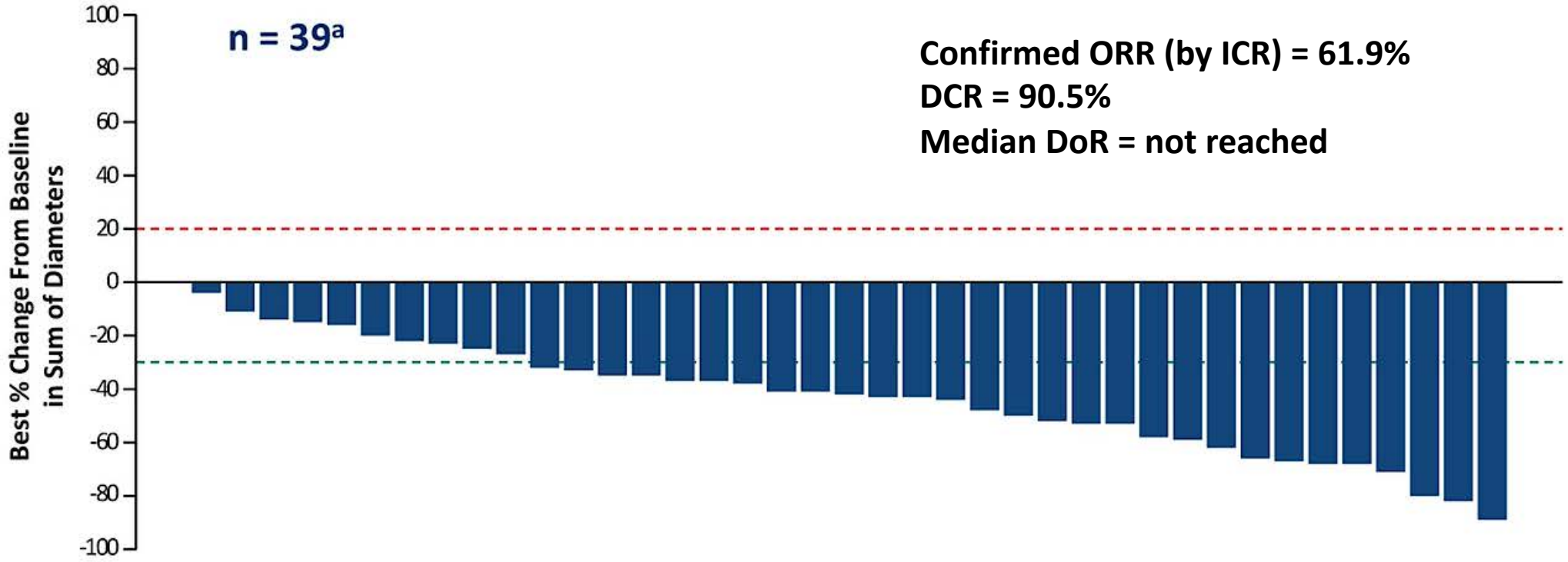
- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker




| |
|---|
| 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 |

Smit EF et al. ASCO 2020;Abstract 9504.

# DESTINY-Lung01: Efficacy



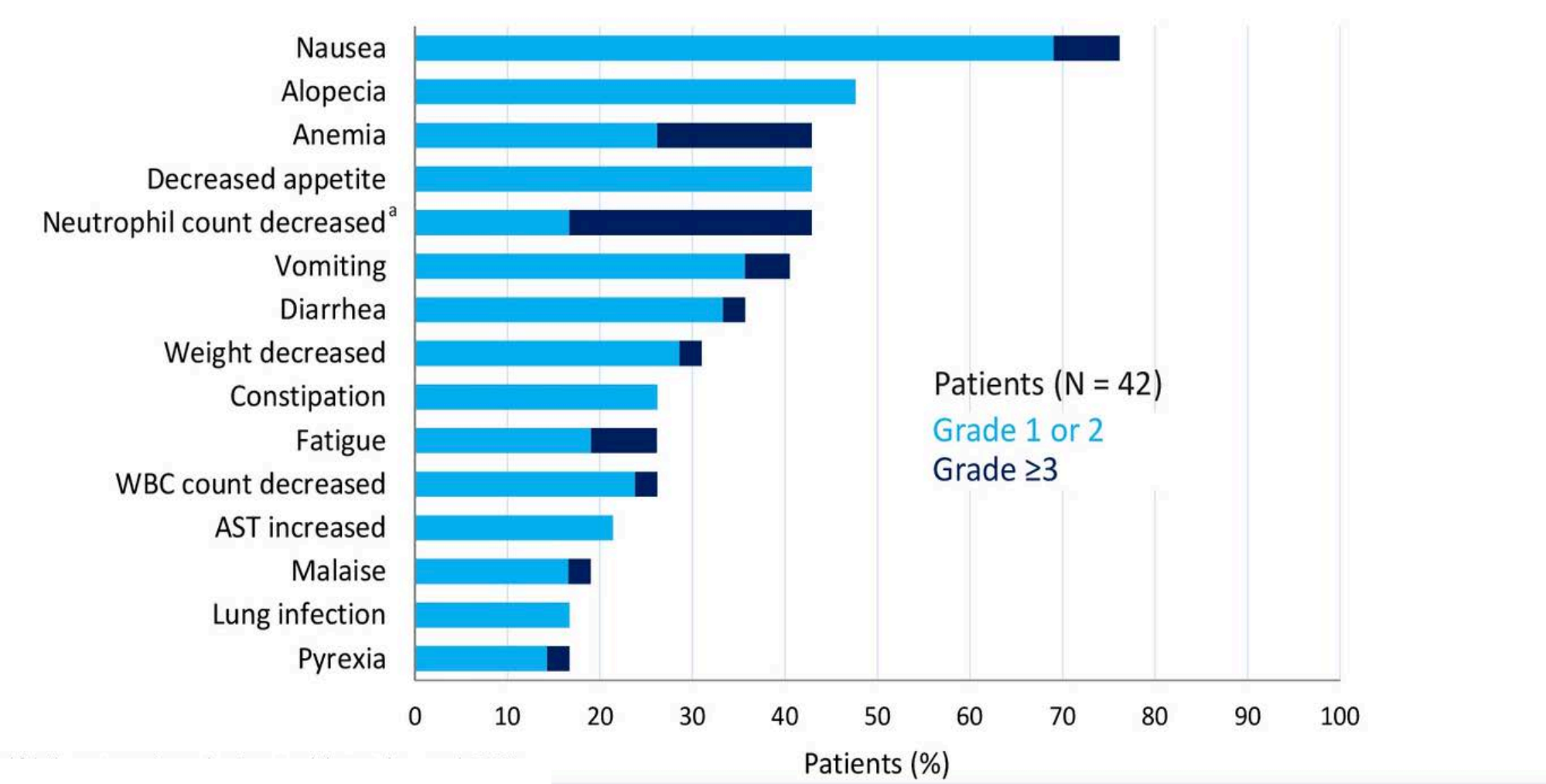

Based on independent central review. Baseline is last measurement taken before enrollment. Shown is best (minimum) percent change from baseline in the sum of diameters for all target lesions.

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

- Median PFS = 14.0 months

Smit EF et al. ASCO 2020;Abstract 9504.

# DESTINY-Lung01: Treatment-Emergent AEs




Smit EF et al. ASCO 2020;Abstract 9504.

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

| | All Patients (N = 42) | | | | | |
|---|---|---|---|---|---|---|
| n (%) | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 | Any Grade/ Total |
| 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

Smit EF et al. ASCO 2020;Abstract 9504.

# *Meet The Professor*
# Immunotherapy and Novel Agents in Gynecologic Cancers

**Friday, October 30, 2020**
**12:30 PM – 1:30 PM ET**

## Faculty

**Richard T Penson, MD, MRCP**

## 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 days.*

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