Meet The Professor
Management of Lung Cancer

Paul K Paik, MD
Associate Attending Physician
Clinical Director, Thoracic Oncology Service
Memorial Sloan Kettering Cancer Center
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Commercial Support

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Dr Love — Disclosures

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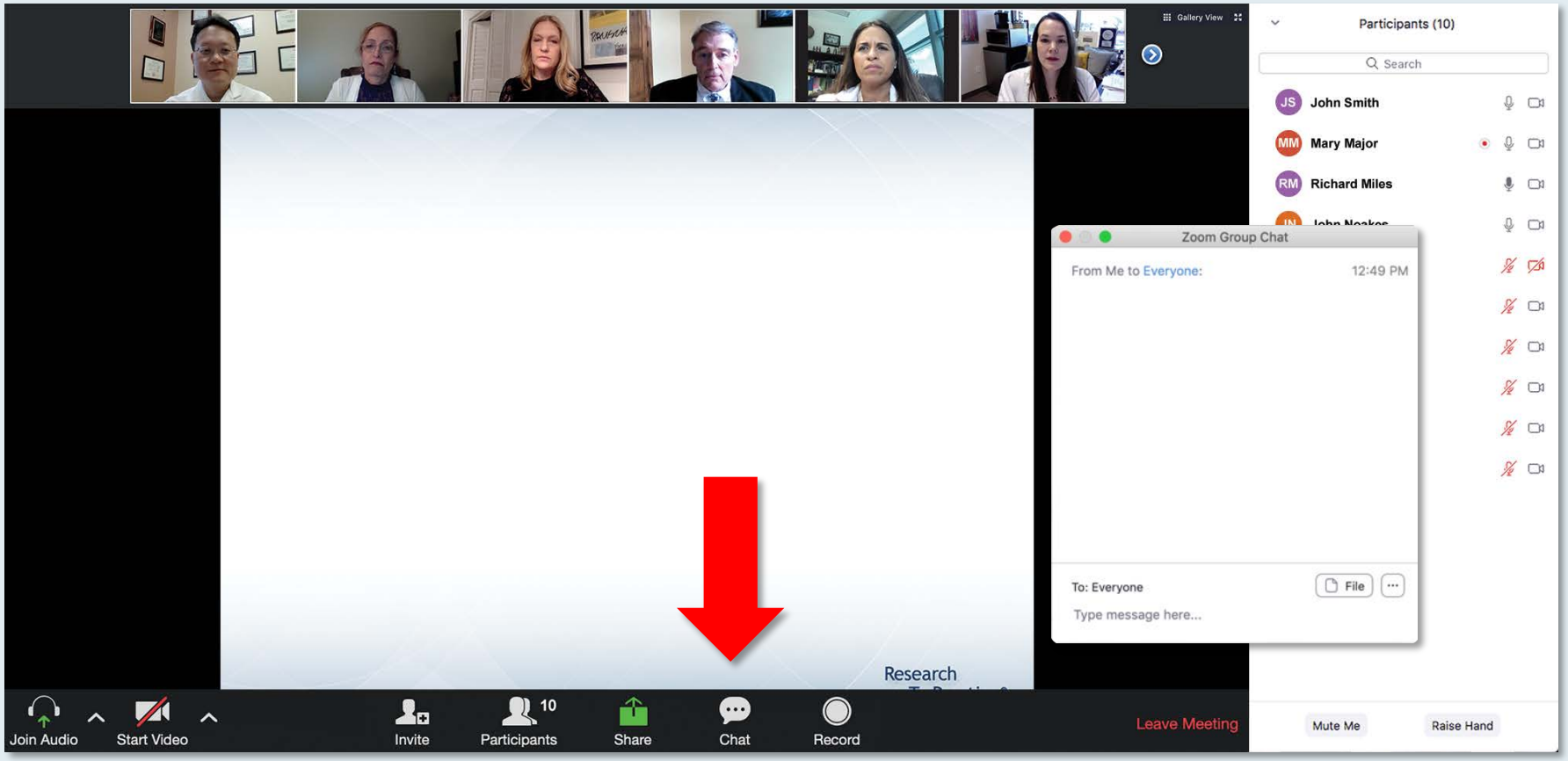
We Encourage Clinicians in Practice to Submit Questions



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

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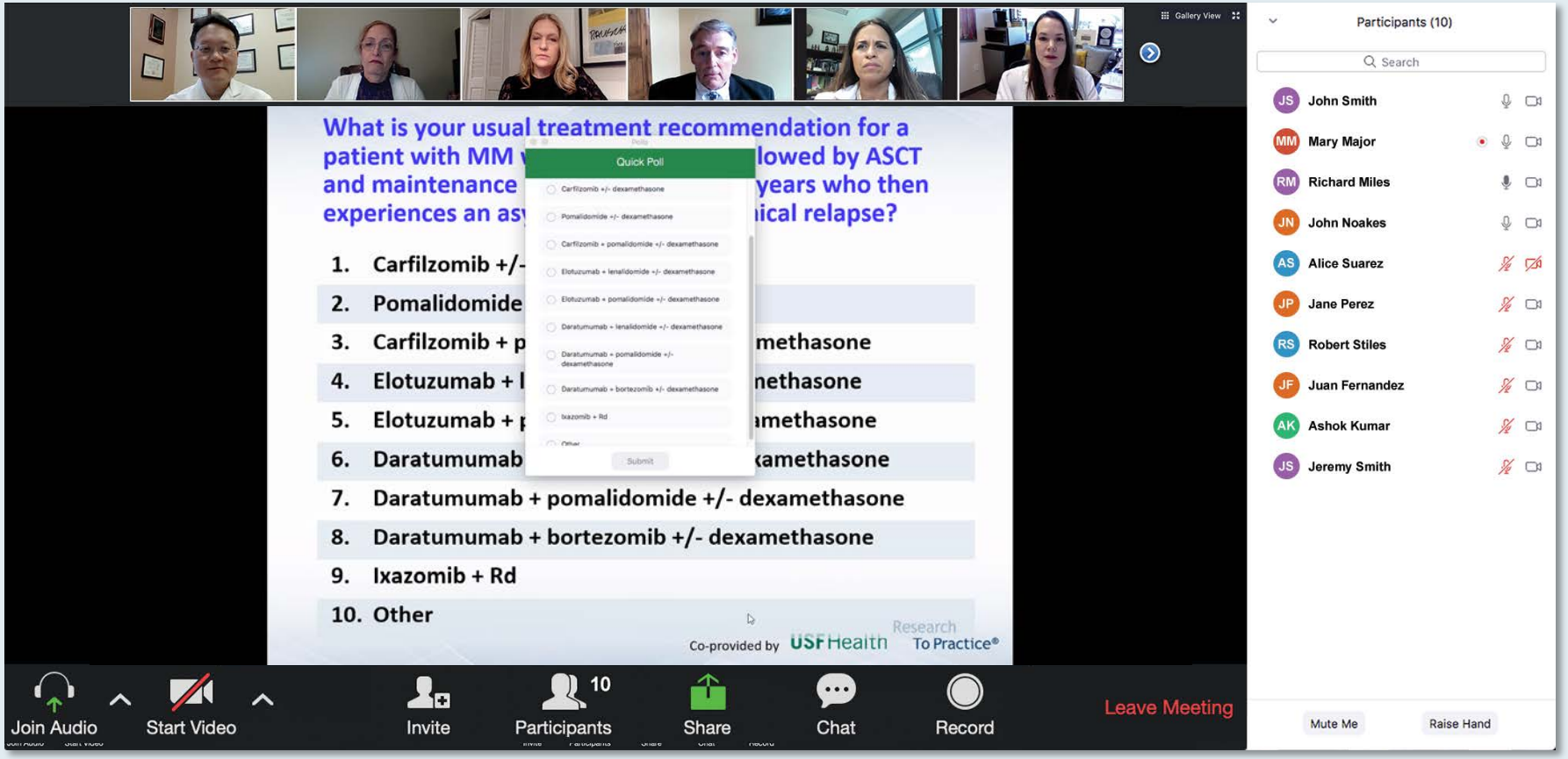

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Upcoming Webinars

Wednesday, October 14, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Chronic Lymphocytic Leukemia

Faculty
John M Pagel, MD, PhD

Moderator
Neil Love, MD

Thursday, October 15, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Ovarian Cancer

Faculty
Kathleen Moore, MD

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Upcoming Webinars

Friday, October 16, 2020
11:00 AM – 12:00 PM ET

Addressing Current Questions and Controversies in the Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Faculty
Roy S Herbst, MD, PhD
Suresh S Ramalingam, MD
Helena Yu, MD

Moderator
Neil Love, MD

Tuesday, October 20, 2020
5:00 PM – 6:00 PM ET

Optimizing the Role of Radiation Oncologists and Other Multidisciplinary Team Members in the Management of Locally Advanced Non-Small Cell Lung Cancer

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Saturday, October 24, 2020
8:30 AM – 4:30 PM ET

Current Concepts and Recent Advances in Oncology: A Daylong Clinical Summit Hosted in Partnership with Florida Cancer Specialists

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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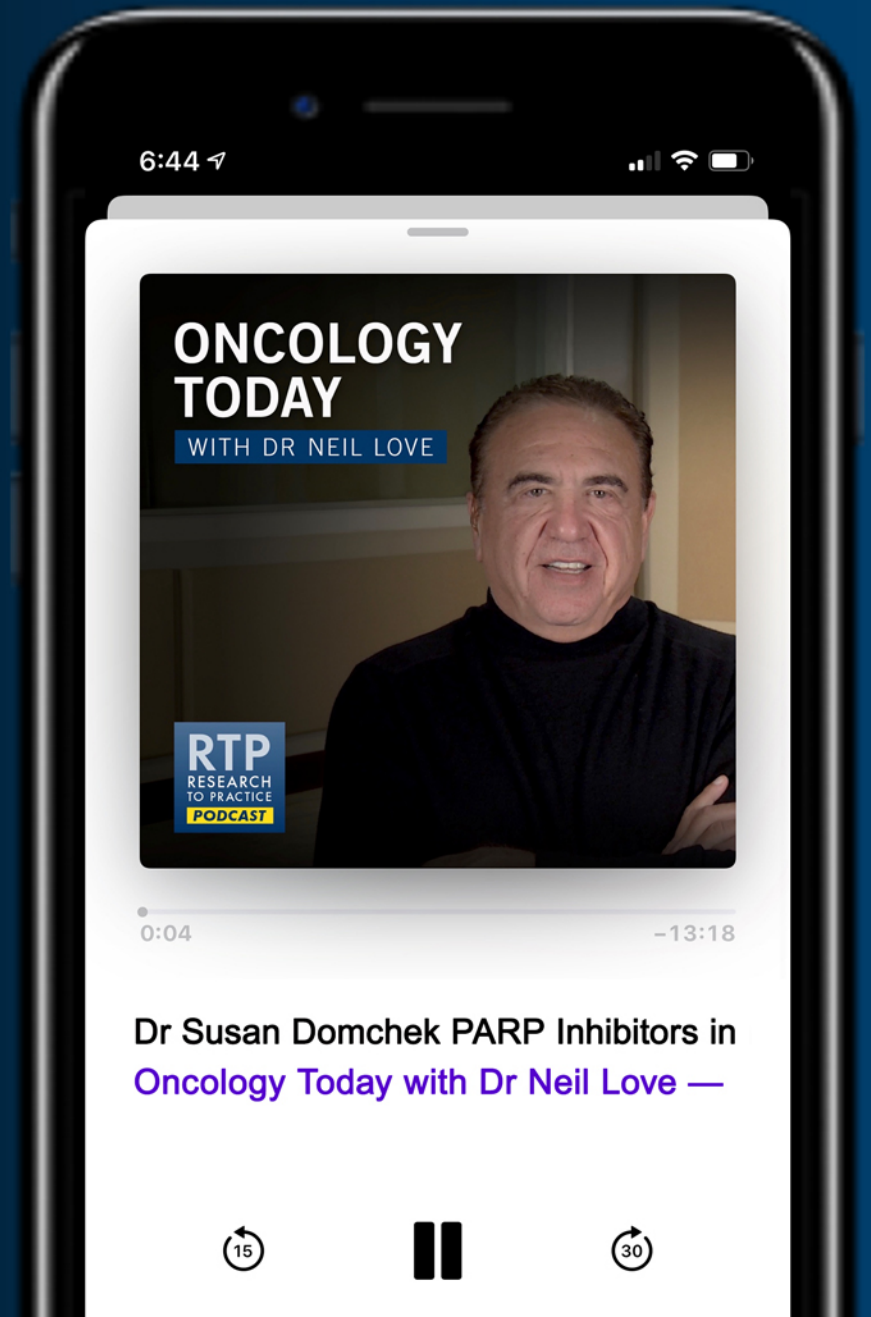

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Meet The Professor Program Participating Faculty

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Director, Thoracic Oncology
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Assistant Vice Chairman for
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Medical Center
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Benjamin Levy, MD
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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

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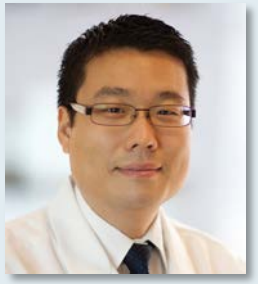
Associate Professor of Medicine
Division of Oncology
Department of Medicine
Stanford Cancer Institute
Stanford University
Palo Alto, California



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Director, Cleveland Clinic Lung
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Lecia V Sequist, MD, MPH
Director, Center for Innovation in Early
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Massachusetts General Hospital Cancer Center
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Harvard Medical School
Boston, Massachusetts

David R Spigel, MD
Chief Scientific Officer
Program Director
Lung Cancer Research
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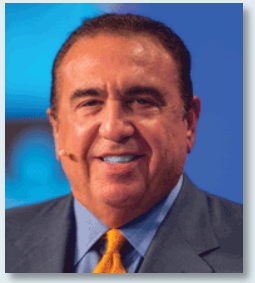
Nashville, Tennessee



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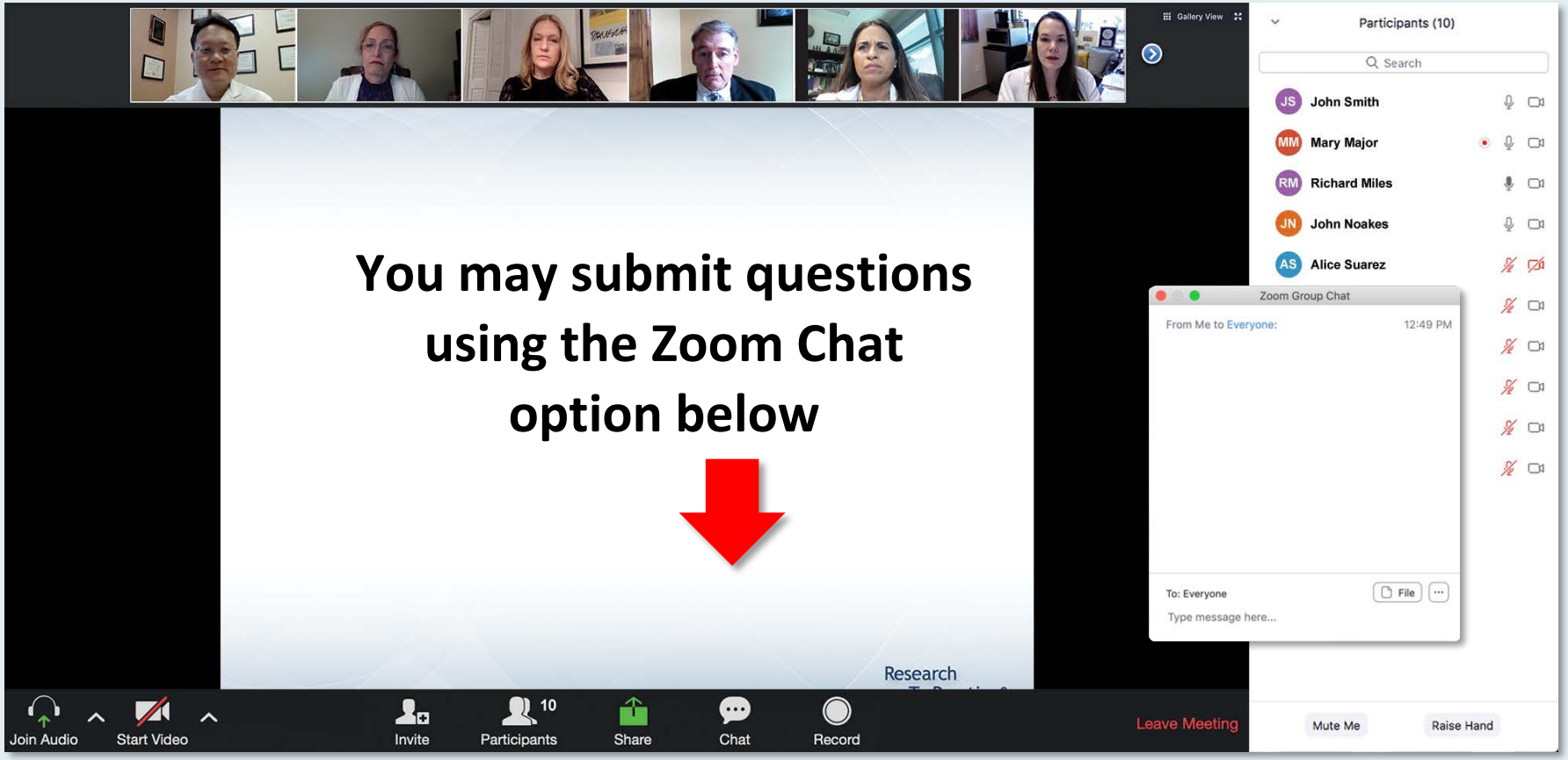

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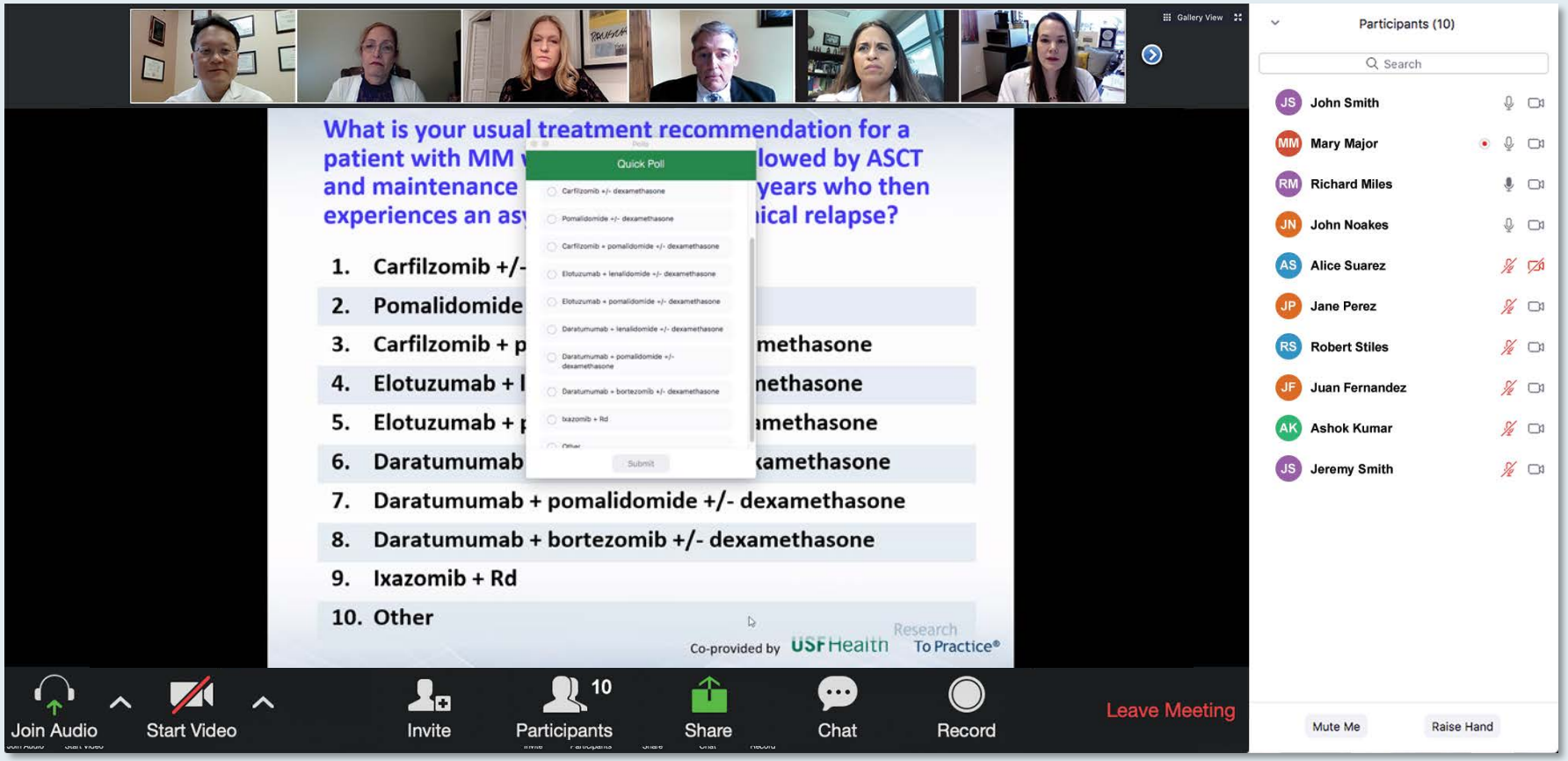

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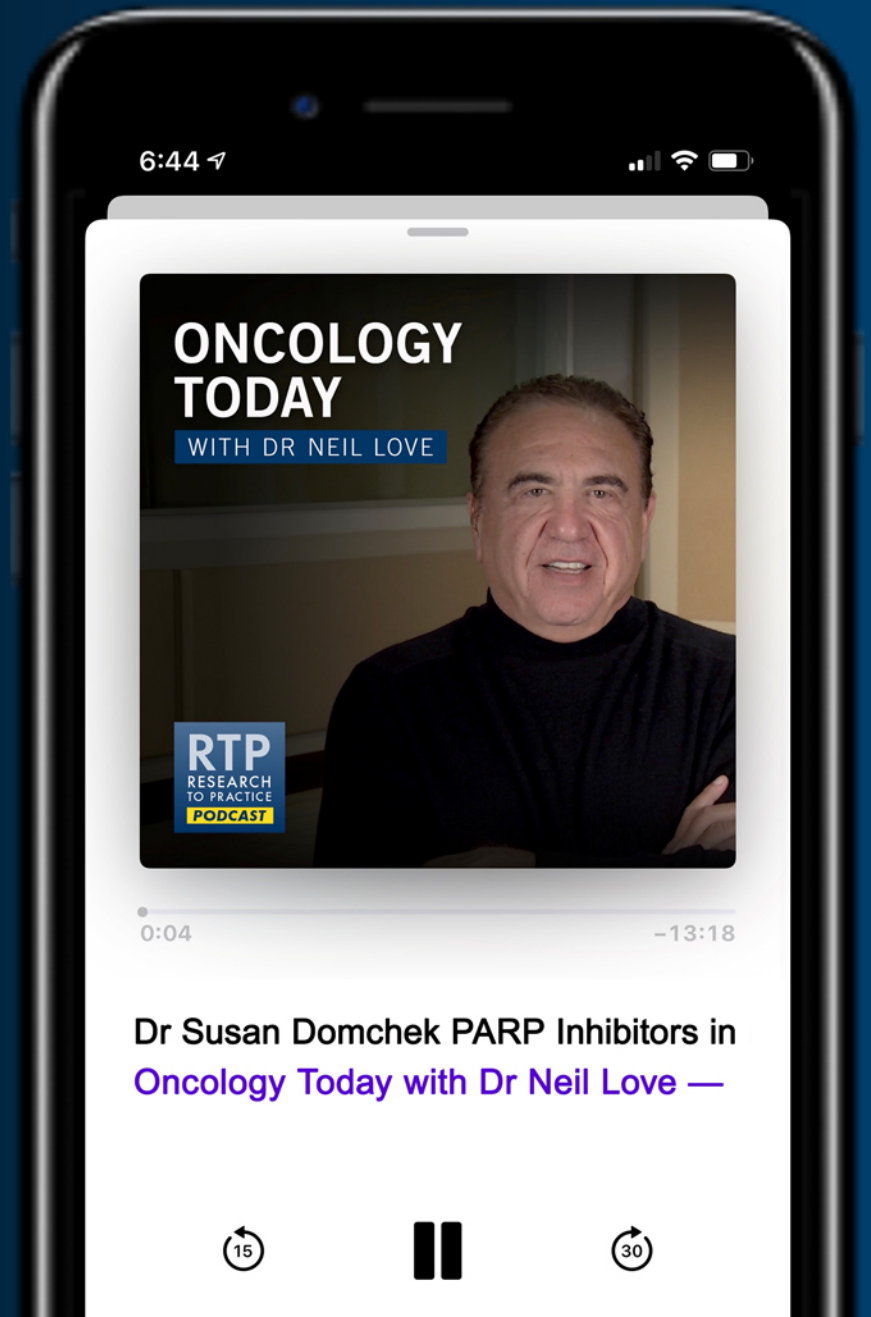

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Axel Grothey, MD
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Shaji K Kumar, MD
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David R Spigel, MD
Sara M Tolaney, MD, MPH

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Medical Group
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Tower Health – McGlinn Cancer Institute
West Reading, Pennsylvania

Syed Farhan Zafar, MD
Hematologist and Medical Oncologist
Florida Cancer Specialists and Research Institute
Chief, Division of Hematology and Oncology, Lee Health
Fort Myers, Florida

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Meet The Professor with Dr Paik

Module 1: Cases from Drs Chen, Rupard and Zafar

- Dr Zafar: A 64-year-old woman and never-smoker with metastatic NSCLC and discordant BRAF mutation testing results
- Questions and Comments: Immune checkpoint inhibitors alone or in combination with chemotherapy
- Dr Zafar: A 46-year-old woman and never-smoker with mixed-histology NSCLC and an ALK mutation
- Dr Rupard: A 53-year-old woman with metastatic NSCLC with pleural disease and an ALK mutation
- Dr Chen: A 70-year-old woman with an extensive smoking history and NSCLC with pleural disease, PD-L1 70%

Module 2: Lung Cancer Journal Club with Dr Paik

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

Module 4: Key Papers and Recent Approvals

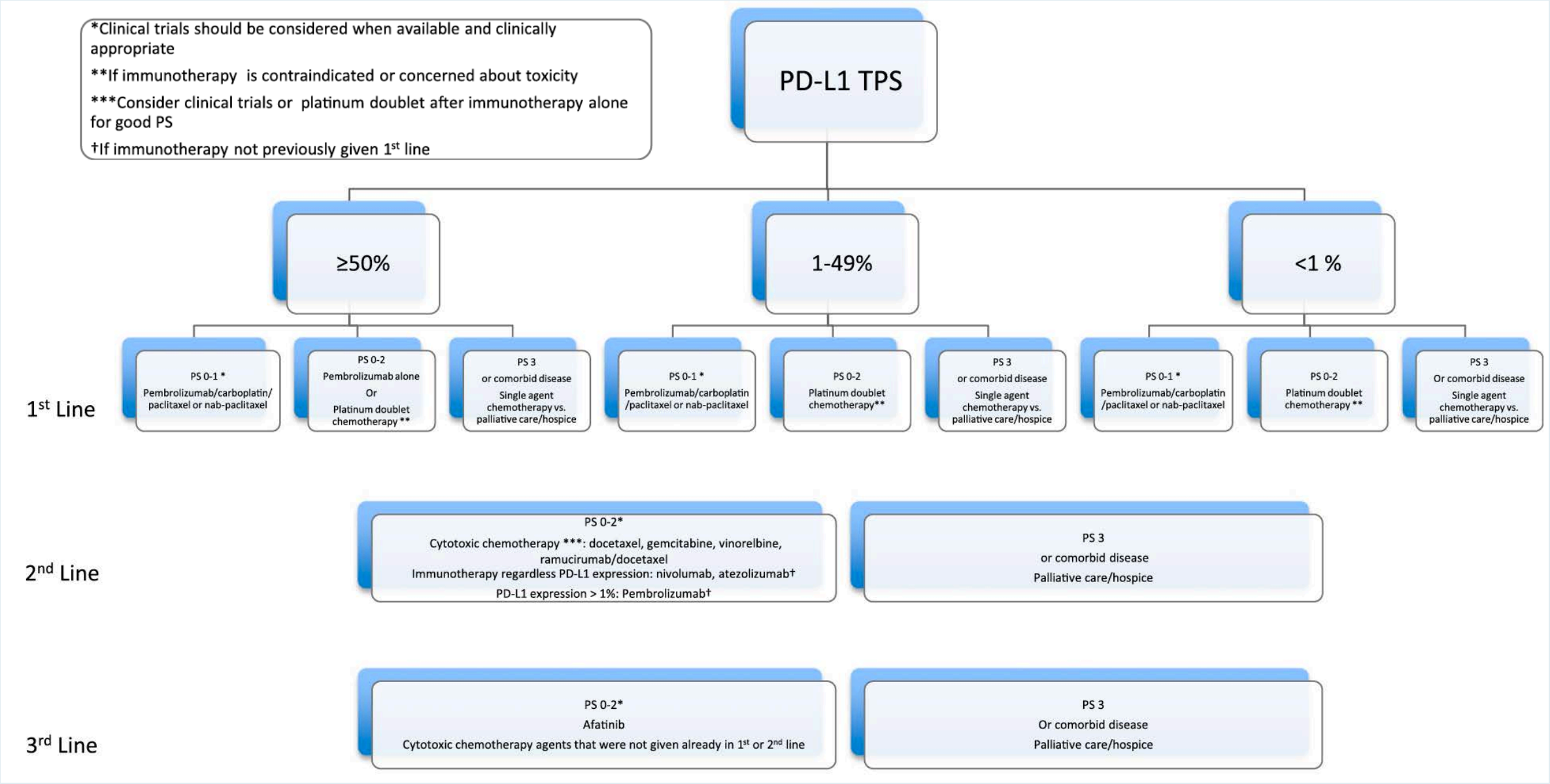
LUNG CANCER

New Treatment Options in Advanced Squamous Cell Lung Cancer

Paul K. Paik, MD[1,2]; Rathi Narayana Pillai, MD[3]; Christopher S. Lathan, MD, MS, MPH[4]; Sylvia A. Velasco, MD[4]; and Vassiliki Papadimitrakopoulou, MD[5]

Am Soc Clin Oncol Educ Book 2019;39:e198-206.

Treatment Algorithm for Advanced Squamous Cell Lung Cancer



Paik PK et al. *Am Soc Clin Oncol Educ Book* 2019;39:e198-206.

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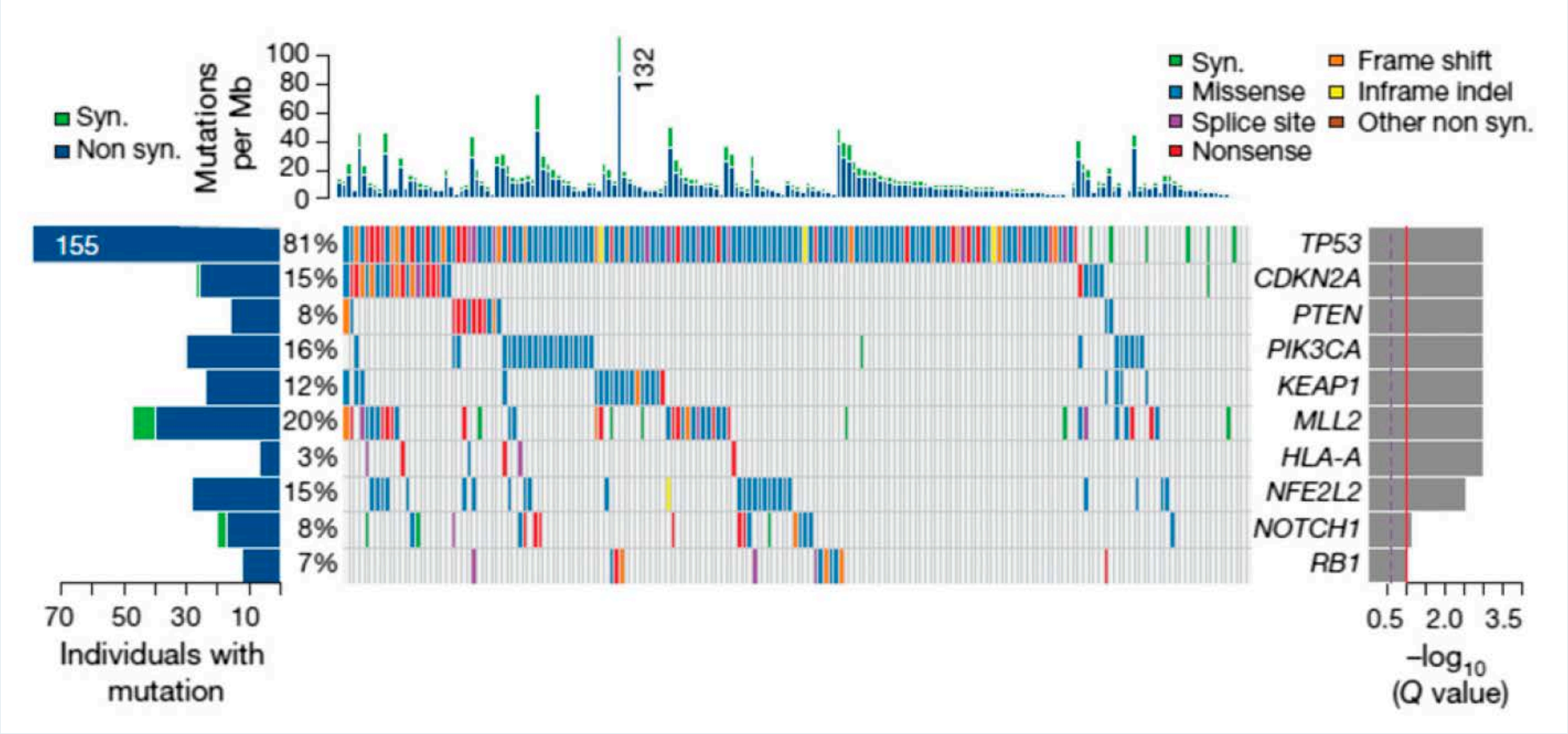
Significant Gene Mutations in Squamous Cell Lung Cancer



Paik PK et al. *Am Soc Clin Oncol Educ Book* 2019;39:e198-206.

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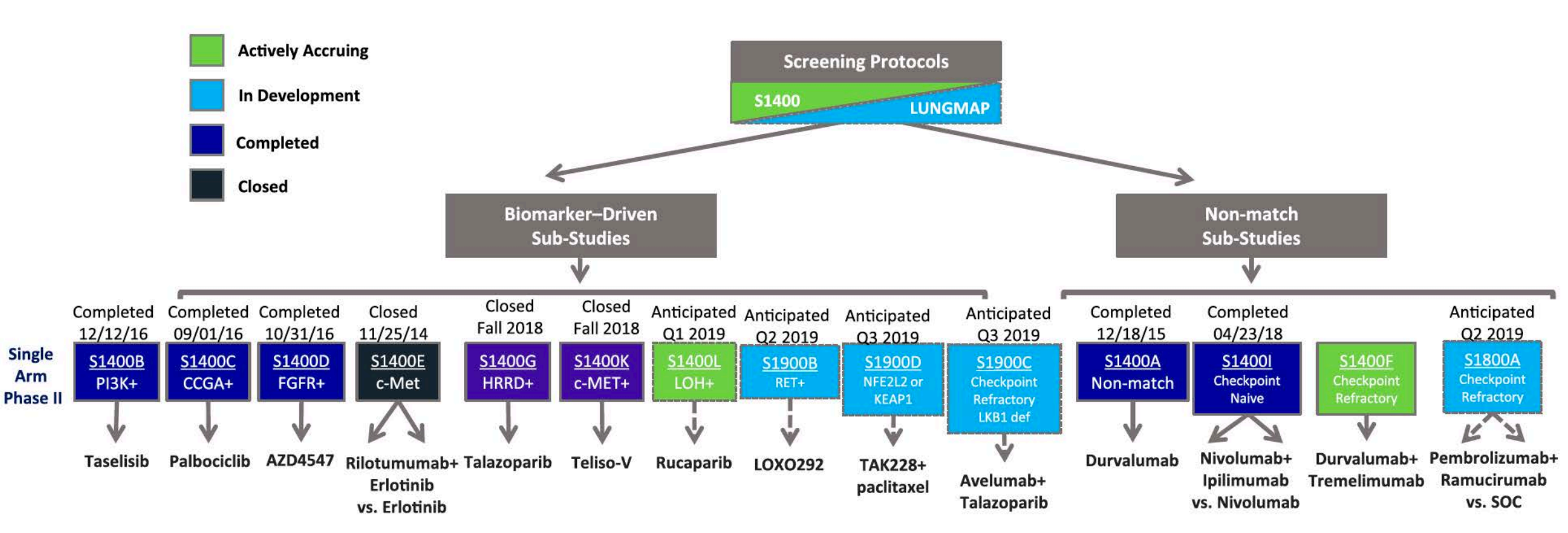
Summary of Early-Phase Targeted Therapy Clinical Trial Results

Target	Drug	ORR (%)	Median PFS (95% CI)
PI3K	Taselisib	4	2.8 (1.7–4.0)
PI3K	Buparlisib	4.5	2.8 (1.4–3.7)
G1/S checkpoint	Palbociclib	6	1.8 (1.6–2.9)
FGFR1	AZD4547	7	2.7 (1.4–4.5)
FGFR1	Dovitinib	11.5	2.9 (1.5–4.3)
FGFR1	BGJ398	11	NA

Paik PK et al. *Am Soc Clin Oncol Educ Book* 2019;39:e198-206.

Lung-MAP Schema



Paik PK et al. *Am Soc Clin Oncol Educ Book* 2019;39:e198-206.

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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

Case Presentation – Dr Zafar: A 64-year-old woman and never-smoker with metastatic NSCLC and discordant BRAF mutation testing results

Dr Syed Zafar

- 2020: Diagnosed with metastatic adenocarcinoma with several pulmonary lesions, mediastinal lymphadenopathy, and brain metastases
- Liquid biopsy and NGS ordered
  - Liquid biopsy reveals BRAF V600E mutation
  - NGS results do not reveal any actionable targets

Questions

- What could cause the discordance in mutation testing results? Which assay result should I trust?

Case Presentation – Dr Zafar: A 64-year-old woman with discordant BRAF mutation testing results (cont)

Dr Syed Zafar

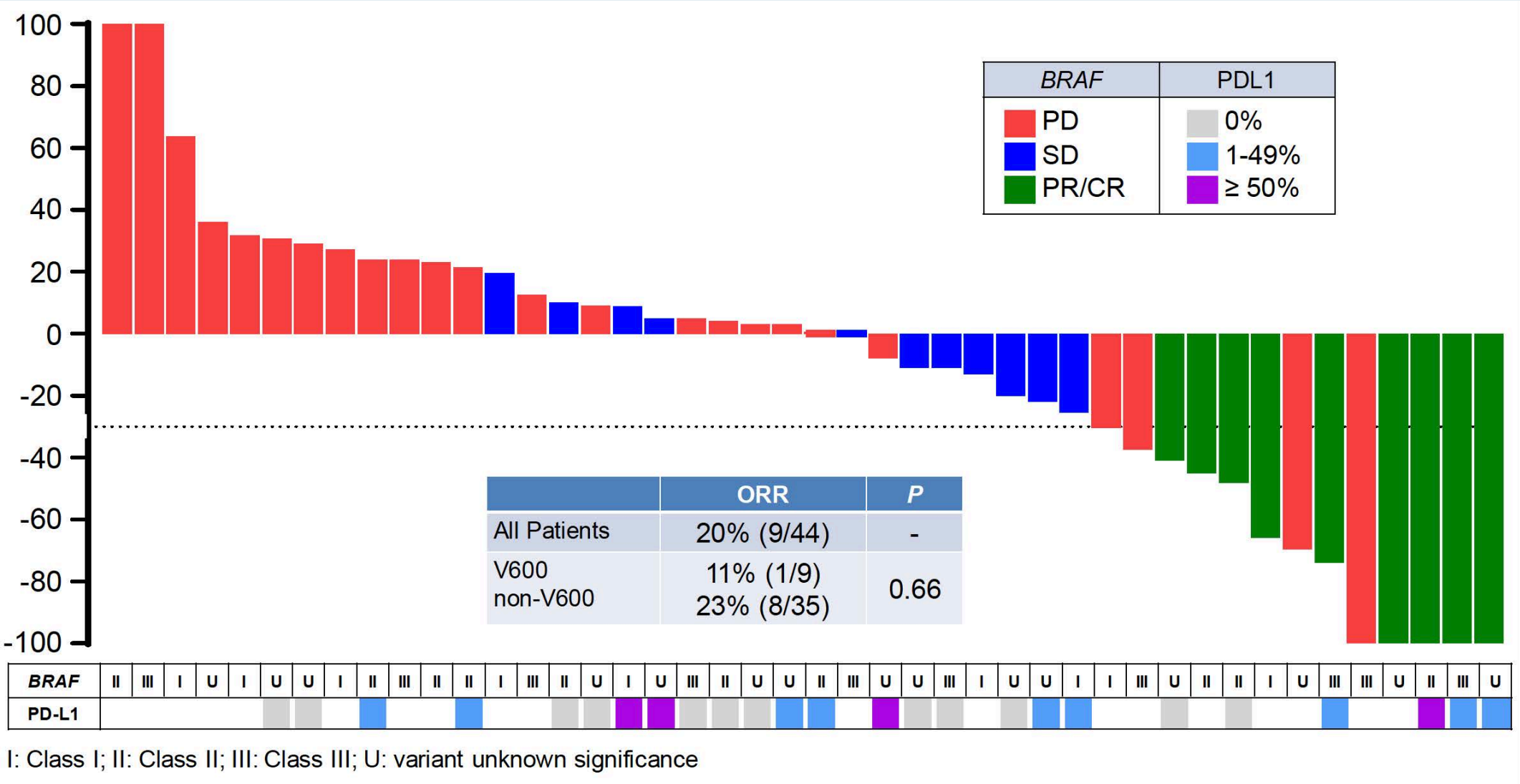
- Patient is symptomatic: Cough, shortness of breath, effusion
- PD-L1-positive
- Considering symptomatology of patient, chemotherapy/IO combination initiated
- Patient's symptoms have improved on treatment
- Holding BRAF-targeted treatment in reserve as potential future therapy

Molecular Characteristics, Immunophenotype, and Immune Checkpoint Inhibitor Response in BRAF Non-V600 Mutant Lung Cancers

Offin M et al.

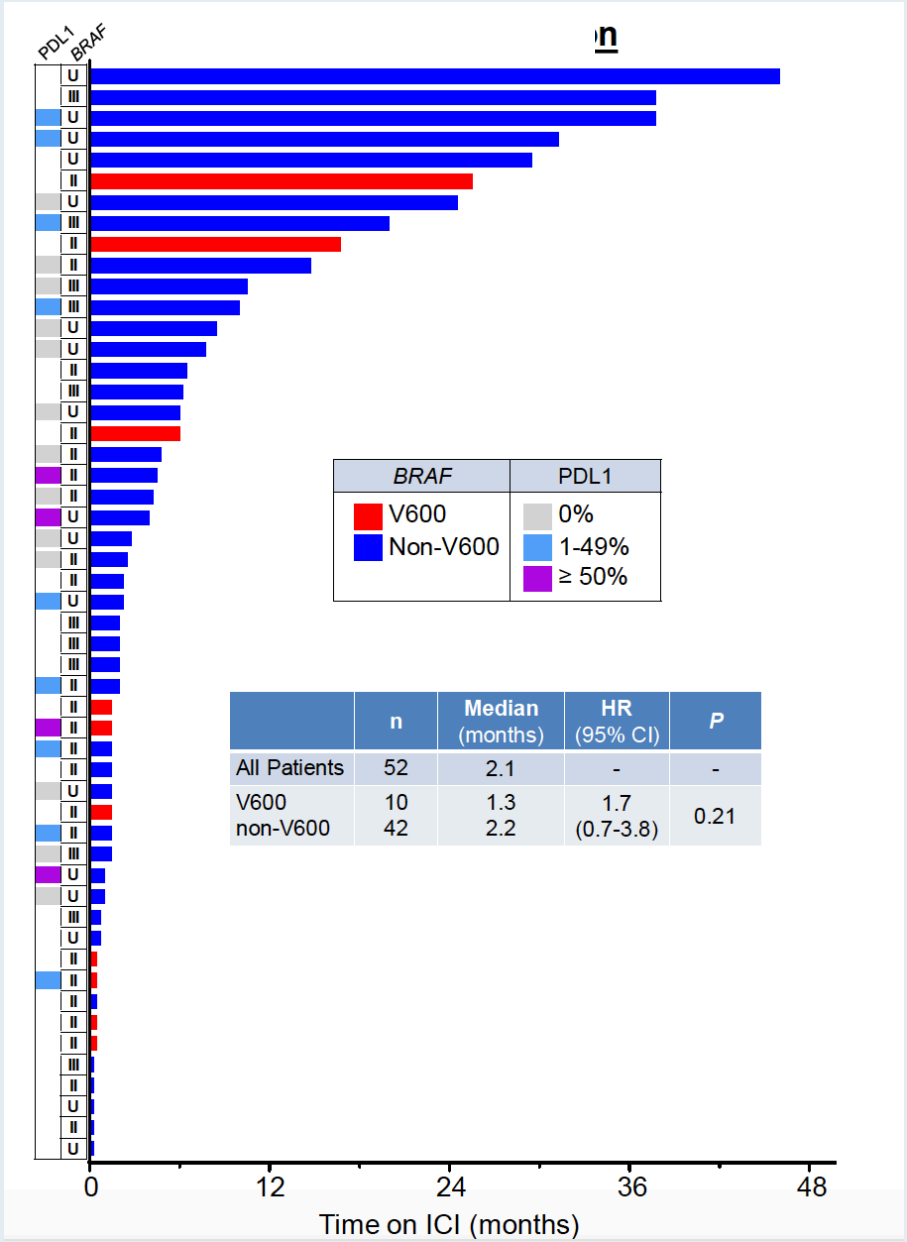
IASLC 2019;Abstract P1.04-39.

Overall Response Rate



Offin M et al. IASLC 2019;Abstract P1.04-39.

Time to Immune Checkpoint Inhibitor Discontinuation



	n	Median (months)	HR (95% CI)	P
All Patients	52	2.1	-	-
V600	10	1.3	1.7 (0.7-3.8)	0.21
non-V600	42	2.2		

Offin M et al. IASLC 2019;Abstract P1.04-39.

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Case Presentation – Dr Zafar: A 46-year-old woman and never-smoker with mixed-histology NSCLC and an ALK mutation

Dr Syed Zafar

- 2016: Diagnosed with poorly differentiated adenocarcinoma with focal squamous differentiation
  - NGS detects EML4-ALK fusion mutation
- 2016: Crizotinib initiated due to presence of multiple brain metastases
- 2017: Progression in brain → alectinib
- 2018: Progression in brain → resection of 8-mm parieto-occipital lesion → radiotherapy
- 2020: Presents with seizures → new brain metastases detected → right frontal stereotactic craniotomy

Questions

- Considering administering lorlatinib if patient continues to have brain progression, but are there other options I should consider for her? Is there anything exciting on the horizon, any clinical trails?

Case Presentation – Dr Rupard: A 53-year-old woman with metastatic NSCLC with pleural disease and an ALK mutation

Dr Erik Rupard

- 2013: Presented with pneumonia, and mass in right upper lobe detected; pleural biopsy demonstrates ALK mutation-positive adenocarcinoma
- 2013 – 2017: Progressed through multiple lines of therapy:
  - Crizotinib → Ceritinib → NGS detects G1202R ALK mutation predictive of response to lorlatinib
  - Lorlatinib not available → Carboplatin/pemetrexed/bev followed by maintenance bev
- 2017: Developed right upper quadrant pain → CT scan reveals 8-cm tumor in liver
  - Within several weeks tumor size increased to 20 cm
  - Local therapies unsuccessful

Questions

- Have you seen such cases of pleural disease extending down to the abdomen? How would you have approached treatment of this patient – would you have administered the anti-PD-1 agent before chemo?
- What is your experience with lorlatinib and how common is the G1202R ALK mutation?

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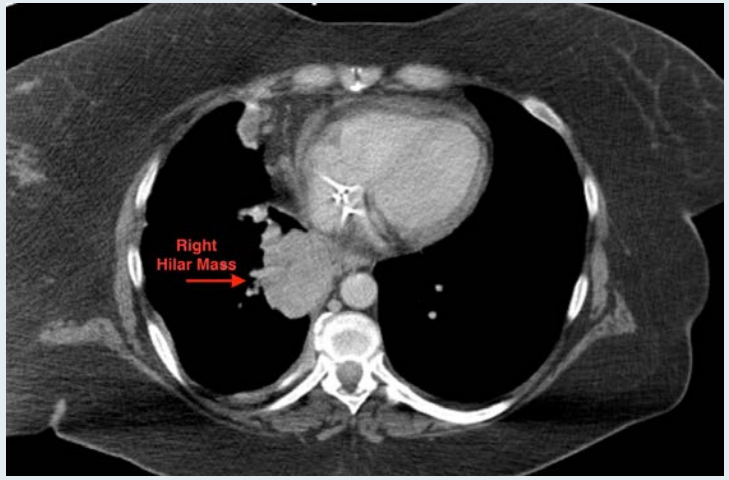
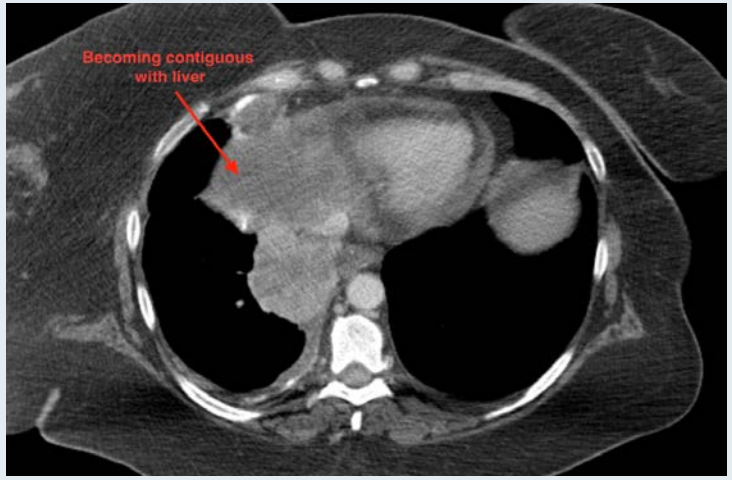
Case Presentation – Dr Rupard: A 53-year-old woman with pleural disease and liver metastasis

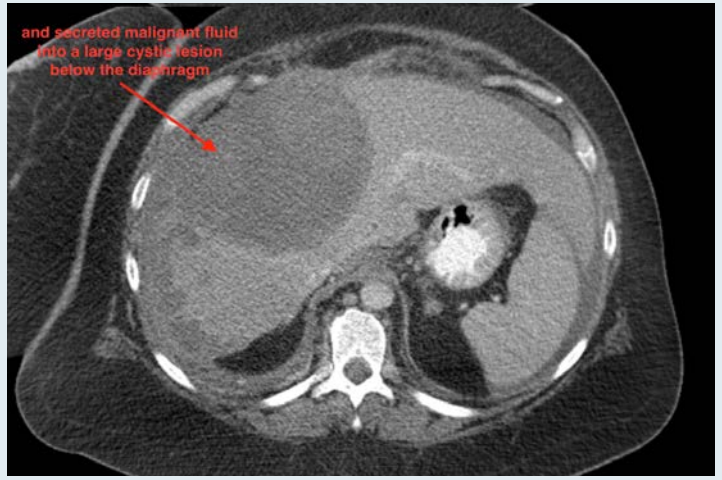
Right hilar mass



Becoming contiguous with liver



Large cystic lesion of secreted malignant fluid below diaphragm



Case Presentation – Dr Chen: A 70-year-old woman with an extensive smoking history and NSCLC with pleural disease, PD-L1 70%

Dr Gigi Chen

- 9/2020: Presents to ER with progressive dyspnea and 70-pound weight loss over the last year; 35-year smoking history
  - Found to have right pleural effusion; cytology shows adenocarcinoma
- Bronchoscopy, right thoracoscopy, extensive decortication, talc pleurodesis and pleura biopsy
- Mutation testing is negative for EGFR, ALK, ROS, BRAF, and MET
- PD-L1 70%
- Have discussed single-agent pembrolizumab as next treatment

Questions

- If this patient receives single-agent pembrolizumab and progresses, what would be the best second-line treatment for her? Would ipilimumab/nivolumab be appropriate for this patient?

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Module 1: Cases from Drs Chen, Rupard and Zafar

Module 2: Lung Cancer Journal Club with Dr Paik

- Phase II trial of *nab* paclitaxel and gemcitabine for Stage IV squamous cell lung cancer
- Tepotinib for NSCLC with MET exon 14 skipping mutations
- Capmatinib for NSCLC with MET exon 14 mutation or MET amplification
- Ramucirumab and docetaxel before or after immune checkpoint inhibitors
- Early resistance mechanisms to first-line osimertinib

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

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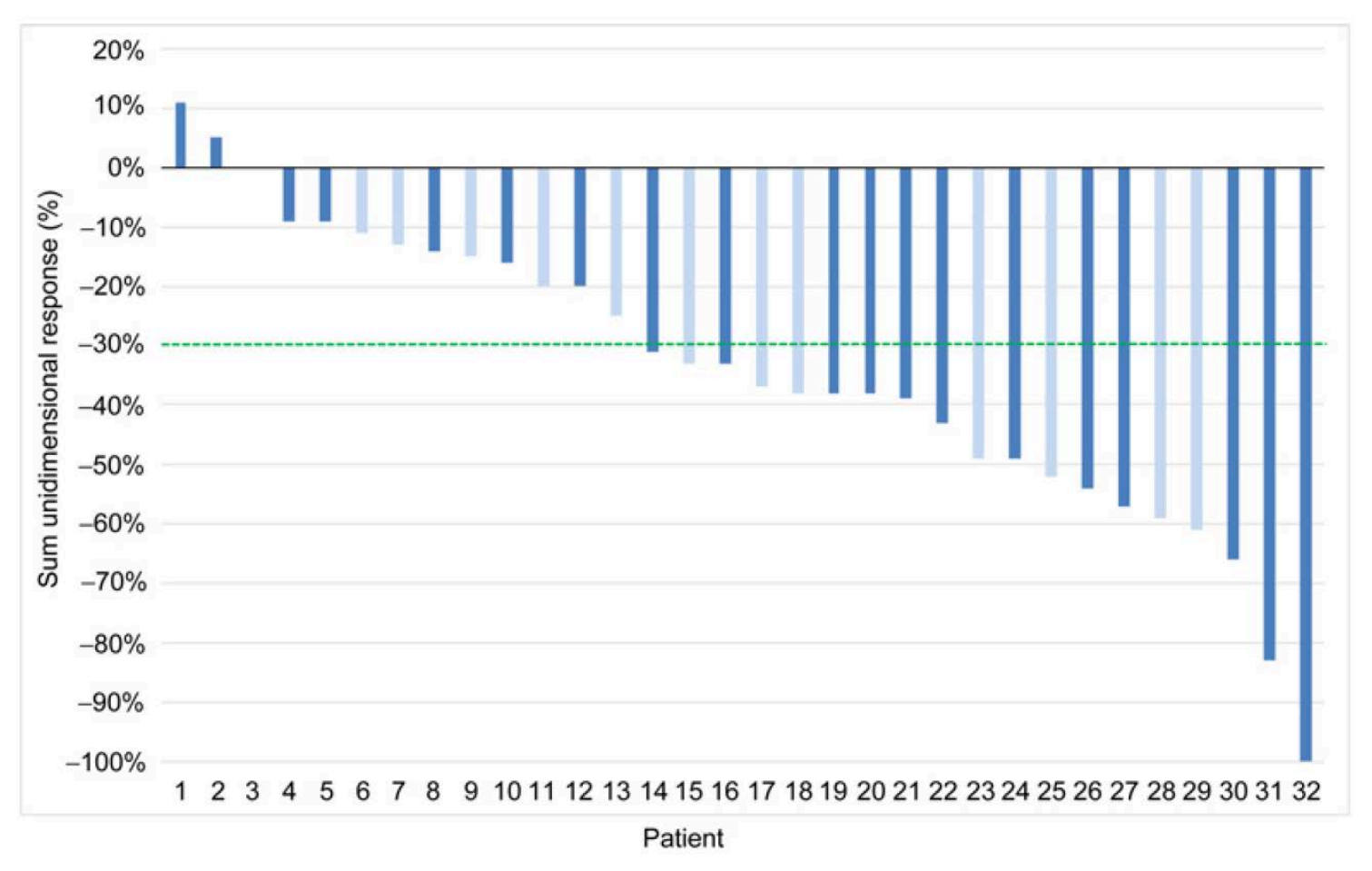
CLINICAL CANCER RESEARCH | RESEARCH BRIEFS: CLINICAL TRIAL BRIEF REPORT

A Phase II Trial of Albumin-Bound Paclitaxel and Gemcitabine in Patients with Newly Diagnosed Stage IV Squamous Cell Lung Cancers

Paul K. Paik[1,2], Rachel K. Kim[1], Linda Ahn[1], Andrew J. Plodkowski[3], Ai Ni[4], Mark T.A. Donoghue[5], Philip Jonsson[5], Miguel Villalona-Calero[6], Kenneth Ng[1,2], Daniel McFarland[1,2], John J. Fiore[1,2], Afsheen Iqbal[1,2], Juliana Eng[1,2], Mark G. Kris[1,2], and Charles M. Rudin[1,2]

Clin Cancer Res 2020;26(8):1796-802.

Radiographic Responses



Light blue: Patients treated during Stage I. Dark blue: Patients treated during Stage II.

Paik PK et al. *Clin Cancer Res* 2020;26(8):1796-802.

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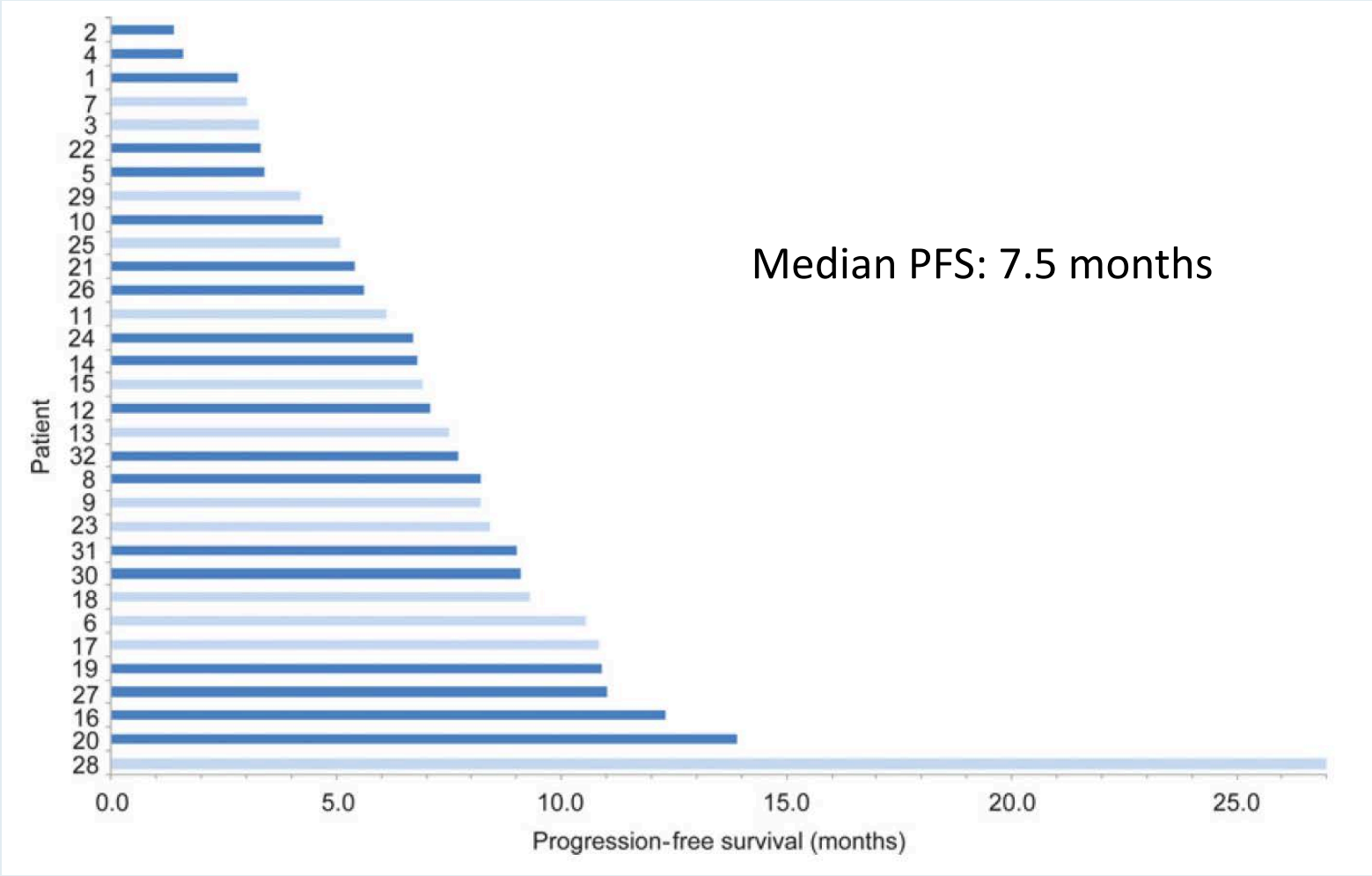
Progression-Free Survival



Median PFS: 7.5 months

Light blue: Patients treated during Stage I. Dark blue: Patients treated during Stage II.

Paik PK et al. *Clin Cancer Res* 2020;26(8):1796-802.

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The NEW ENGLAND JOURNAL of MEDICINE

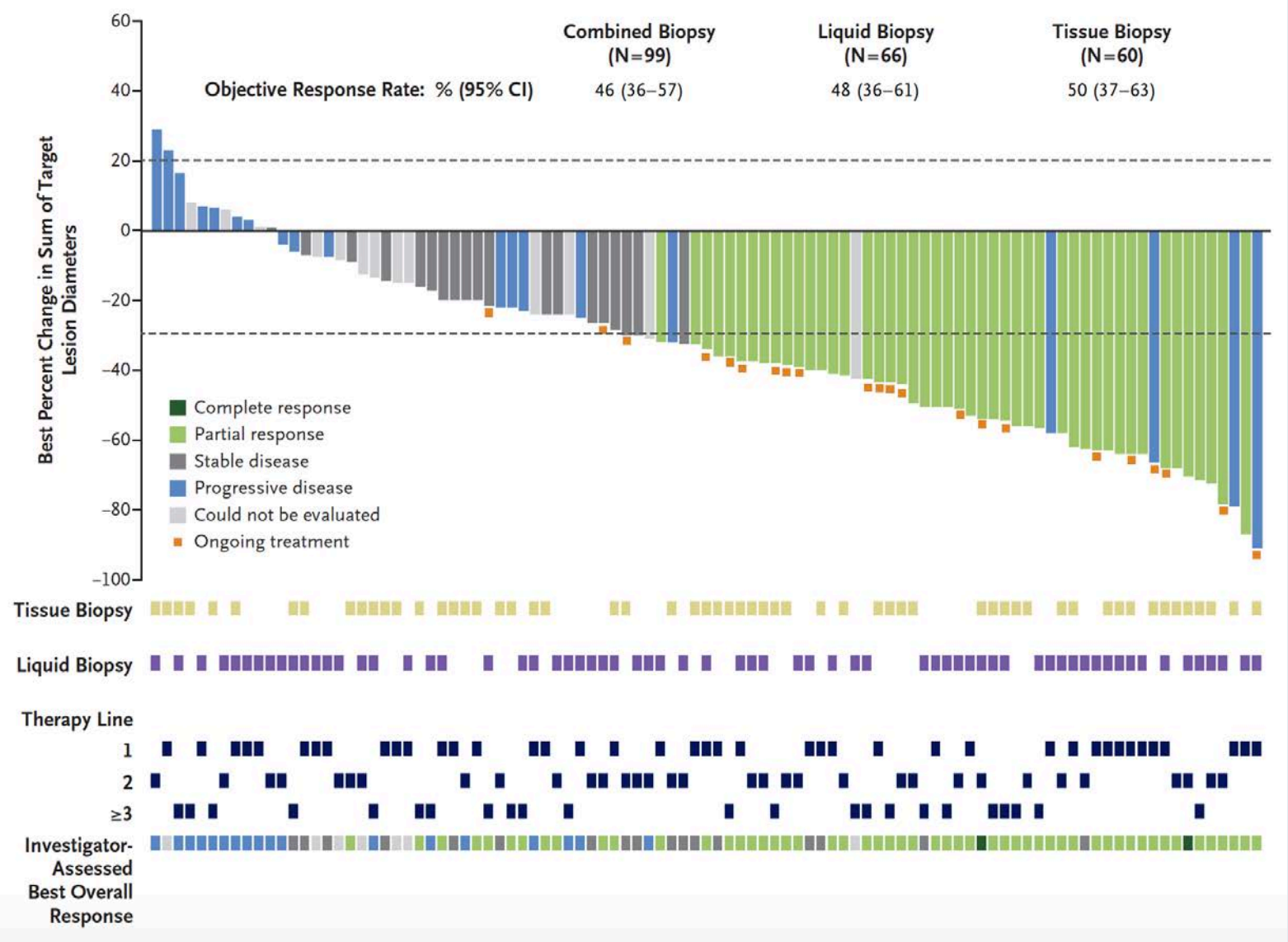
ORIGINAL ARTICLE

Tepotinib in Non–Small-Cell Lung Cancer with *MET* Exon 14 Skipping Mutations

P.K. Paik, E. Felip, R. Veillon, H. Sakai, A.B. Cortot, M.C. Garassino, J. Mazieres, S. Viteri, H. Senellart, J. Van Meerbeeck, J. Raskin, N. Reinmuth, P. Conte, D. Kowalski, B.C. Cho, J.D. Patel, L. Horn, F. Griesinger, J.-Y. Han, Y.-C. Kim, G.-C. Chang, C.-L. Tsai, J.C.-H. Yang, Y.-M. Chen, E.F. Smit, A.J. van der Wekken, T. Kato, D. Juraeva, C. Stroh, R. Bruns, J. Straub, A. Johne, J. Scheele, J.V. Heymach, and X. Le

***N Engl J Med* 2020;383(10):931-43.**

Tepotinib: Response Rate and Change from Baseline in Tumor Burden



Paik PK et al. *N Engl J Med* 2020;383(10):931-43.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

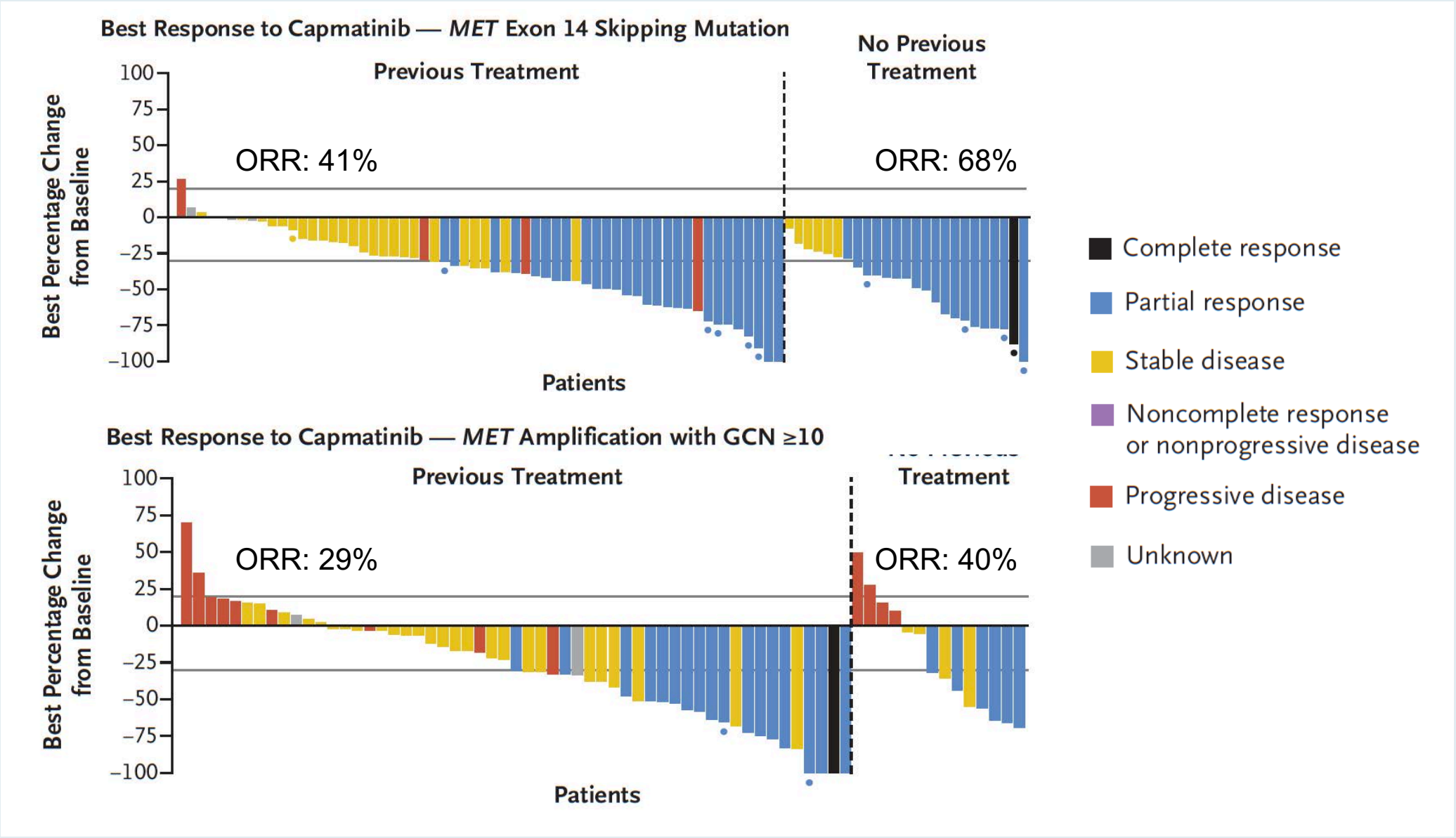
Capmatinib in *MET* Exon 14–Mutated or *MET*-Amplified Non–Small-Cell Lung Cancer

J. Wolf, T. Seto, J.-Y. Han, N. Reguart, E.B. Garon, H.J.M. Groen, D.S.W. Tan, T. Hida, M. de Jonge, S.V. Orlov, E.F. Smit, P.-J. Souquet, J. Vansteenkiste, M. Hochmair, E. Felip, M. Nishio, M. Thomas, K. Ohashi, R. Toyozawa, T.R. Overbeck, F. de Marinis, T.-M. Kim, E. Laack, A. Robeva, S. Le Mouhaer, M. Waldron-Lynch, B. Sankaran, O.A. Balbin, X. Cui, M. Giovannini, M. Akimov, and R.S. Heist, for the GEOMETRY mono-1 Investigators*

ABSTRACT

N Engl J Med 2020;383(10):944-57.

Capmatinib: Response Rate and Change from Baseline in Tumor Burden



Wolf J et al. *N Engl J Med* 2020;383(10):944-57.

Efficacy of Ramucirumab and Docetaxel Given Either Before or After Immune Checkpoint Inhibitors in Patients with Lung Cancers

Offin M et al.

ASCO 2019;Abstract 9078.

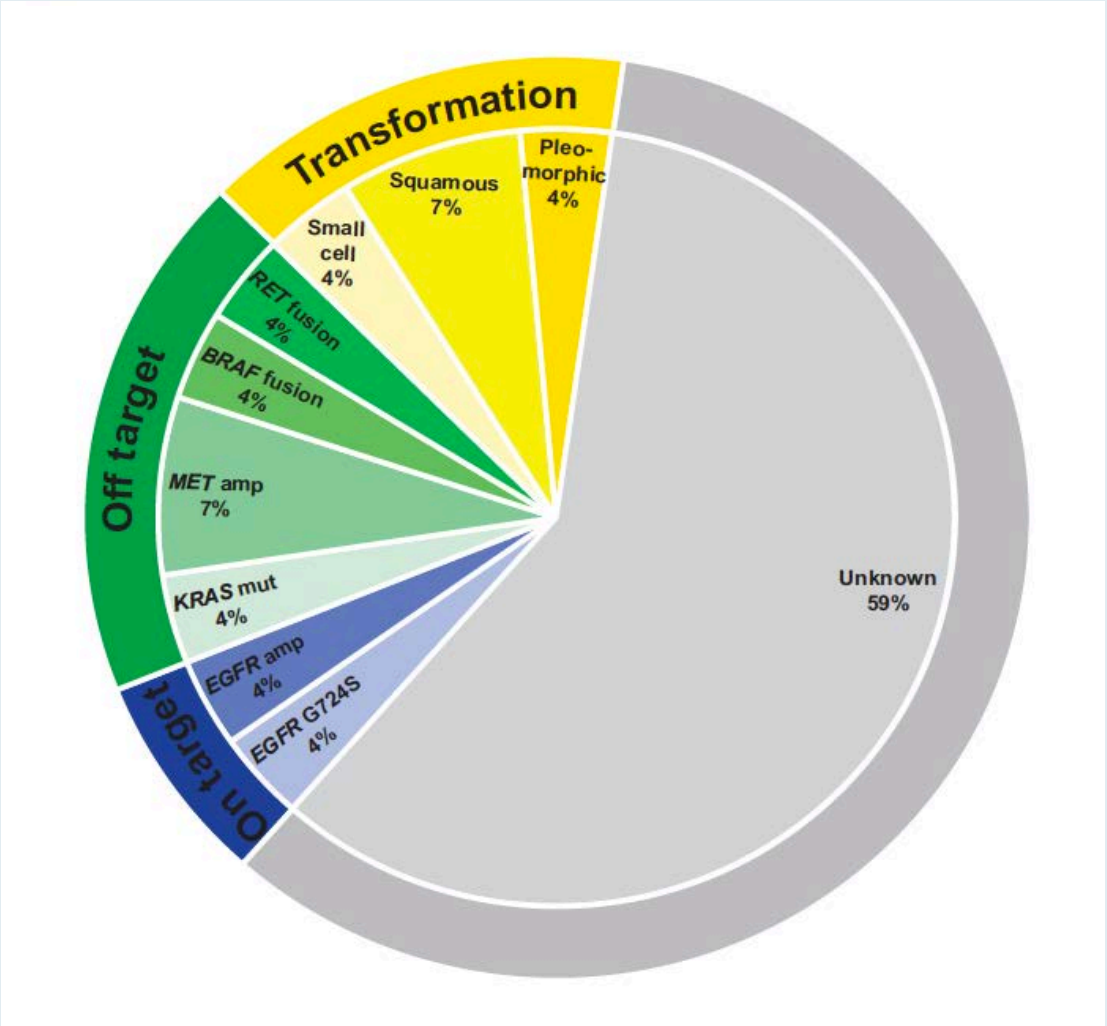
CLINICAL CANCER RESEARCH | TRANSLATIONAL CANCER MECHANISMS AND THERAPY

Tumor Analyses Reveal Squamous Transformation and Off-Target Alterations As Early Resistance Mechanisms to First-line Osimertinib in *EGFR*-Mutant Lung Cancer

Adam J. Schoenfeld[1], Joseph M. Chan[1], Daisuke Kubota[2], Hiroki Sato[3], Hira Rizvi[1,4], Yahya Daneshbod[2], Jason C. Chang[2], Paul K. Paik[1], Michael Offin[1], Maria E. Arcila[2], Monika A. Davare[5], Ujwal Shinde[6], Dana Pe'er[7], Natasha Rekhtman[2], Mark G. Kris[1], Romel Somwar[2], Gregory J. Riely[1], Marc Ladanyi[2], and Helena A. Yu[1]

Clin Cancer Res 2020;26(11):2654-63.

Distribution of Established Mechanisms of Resistance in Patients Receiving First-Line Osimertinib Therapy



Schoenfeld AJ et al. *Clin Cancer Res* 2020;26(11):2654-63.

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Paik

Module 1: Cases from Drs Chen, Rupard and Zafar

Module 2: Lung Cancer Journal Club with Dr Paik

- Phase II trial of *nab* paclitaxel and gemcitabine for Stage IV squamous cell lung cancer
- Tepotinib for NSCLC with MET exon 14 skipping mutations
- Capmatinib for NSCLC with MET exon 14 mutation or MET amplification
- Ramucirumab and docetaxel before or after immune checkpoint inhibitors
- Early resistance mechanisms to first-line osimertinib

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

Module 4: Key Papers and Recent Approvals

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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

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Which first-line treatment regimen would you recommend for a patient with metastatic nonsquamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 10%? Of 60%?

	TPS of 10%		TPS of 60%	
	Age 65	Age 80	Age 65	Age 80
 JOHN V HEYMACH, MD, PHD	Pembro/carbo/pem	Pembro	Pembro	Pembro
 LEORA HORN, MD, MSC	Pembro/carbo/pem	Pembro or Hospice	Pembro	Pembro
 COREY J LANGER, MD	Pembro/carbo/pem	Pembro	Pembro*	Pembro
 BENJAMIN LEVY, MD	Pembro/carbo/pem	Pembro	Pembro	Pembro
 PROFESSOR TONY SK MOK, MD	Pembro/carbo/pem OR Atezo/carbo/pac + bev	Pembro	Pembro	Pembro
 JOEL W NEAL, MD, PHD	Pembro/carbo/pem	Pembro	Pembro +/- carbo/pem	Pembro
 PAUL K PAIK, MD	Pembro/carbo/pem	Pembro/carbo/pem	Pembro	Pembro
 NATHAN A PENNELL, MD, PHD	Pembro/carbo/pem	Pembro/carbo/pem†	Pembro	Pembro
 DAVID R SPIGEL, MD	Pembro/carbo/pem	Pembro/carbo/pem	Pembro	Pembro

Pembro = pembrolizumab; carbo = carboplatin; pem = pemetrexed; atezo = atezolizumab; pac = paclitaxel; bev = bevacizumab * If very symptomatic, pembro/carbo/pem; † Likely dose-reduced chemotherapy

Which first-line treatment regimen would you recommend for a patient with metastatic squamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 10%? Of 60%?

	TPS of 10%		TPS of 60%	
	Age 65	Age 80	Age 65	Age 80
 JOHN V HEYMACH, MD, PHD	Pembro/carbo/ *nab*-P	Pembro	Pembro	Pembro
 LEORA HORN, MD, MSC	Pembro/carbo/ *nab*-P	Pembro/carbo/*nab*-P	Pembro	Pembro
 COREY J LANGER, MD	Pembro/carbo/*nab*-P	Pembro/carbo/*nab*-P	Pembro	Pembro
 BENJAMIN LEVY, MD	Pembro/carbo/ *nab*-P	Pembro/carbo/pac	Pembro	Pembro
 PROFESSOR TONY SK MOK, MD	Pembro/carbo/*nab*-P or Pembro/carbo/pac	Pembro	Pembro or Atezo	Pembro or Atezo
 JOEL W NEAL, MD, PHD	Pembro/carbo/ *nab*-P or pac	Pembro/carbo/*nab*-P	Pembro +/- carbo/ *nab*-P or pac	Pembro+/- carbo/ *nab*-P
 PAUL K PAIK, MD	Pembro/carbo/pac	Pembro/carbo/pac	Pembro	Pembro
 NATHAN A PENNELL, MD, PHD	Pembro/carbo/*nab*-P	Pembro/carbo/pac	Pembro	Pembro
 DAVID R SPIGEL, MD	Pembro/carbo/*nab*-P	Pembro/carbo/*nab*-P	Pembro	Pembro

Nab-P = nanoparticle albumin-bound paclitaxel

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

PD = progressive disease

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 patient with extensive-stage SCLC?

	Age 65	Age 80
 JOHN V HEYMACH, MD, PHD	Carbo/etoposide + atezolizumab	Carbo/etoposide + atezolizumab
 LEORA HORN, MD, MSC	Carbo/etoposide + atezolizumab	Carbo/etoposide + atezolizumab
 COREY J LANGER, MD	Carbo/etoposide + atezolizumab or durvalumab	Carbo/etoposide + durvalumab
 BENJAMIN LEVY, MD	Carbo/etoposide + atezolizumab	Carbo/etoposide + atezolizumab
 PROFESSOR TONY SK MOK, MD	Carbo/etoposide + atezolizumab	Carbo/etoposide OR Carbo/etoposide + atezolizumab or durvalumab
 JOEL W NEAL, MD, PHD	Carbo/etoposide + atezolizumab	Carbo/etoposide + atezolizumab or durvalumab
 PAUL K PAIK, MD	Carbo/etoposide + atezolizumab	Carbo/etoposide + atezolizumab
 NATHAN A PENNELL, MD, PHD	Carbo/etoposide + atezolizumab	Carbo/etoposide + atezolizumab
 DAVID R SPIGEL, MD	Carbo/etoposide + durvalumab	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
 LEORA HORN, MD, MSC	Carboplatin/etoposide
 COREY J LANGER, MD	Carboplatin/etoposide + atezolizumab or durvalumab
 BENJAMIN LEVY, MD	Carboplatin/etoposide
 PROFESSOR TONY SK MOK, MD	Carboplatin/etoposide
 JOEL W NEAL, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 PAUL K PAIK, MD	Carboplatin/etoposide
 NATHAN A PENNELL, MD, PHD	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
 LEORA HORN, MD, MSC	Carboplatin/etoposide + atezolizumab
 COREY J LANGER, MD	Carboplatin/etoposide + atezolizumab or durvalumab
 BENJAMIN LEVY, MD	Carboplatin/etoposide + atezolizumab
 PROFESSOR TONY SK MOK, MD	Carbo/etoposide OR Carbo/etoposide + atezolizumab or durvalumab
 JOEL W NEAL, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 PAUL K PAIK, MD	Carboplatin/etoposide + atezolizumab
 NATHAN A PENNELL, MD, PHD	Carboplatin/etoposide + atezolizumab
 DAVID R SPIGEL, MD	Carboplatin/etoposide + durvalumab

SIADH = syndrome of inappropriate antidiuretic hormone secretion

Meet The Professor with Dr Paik

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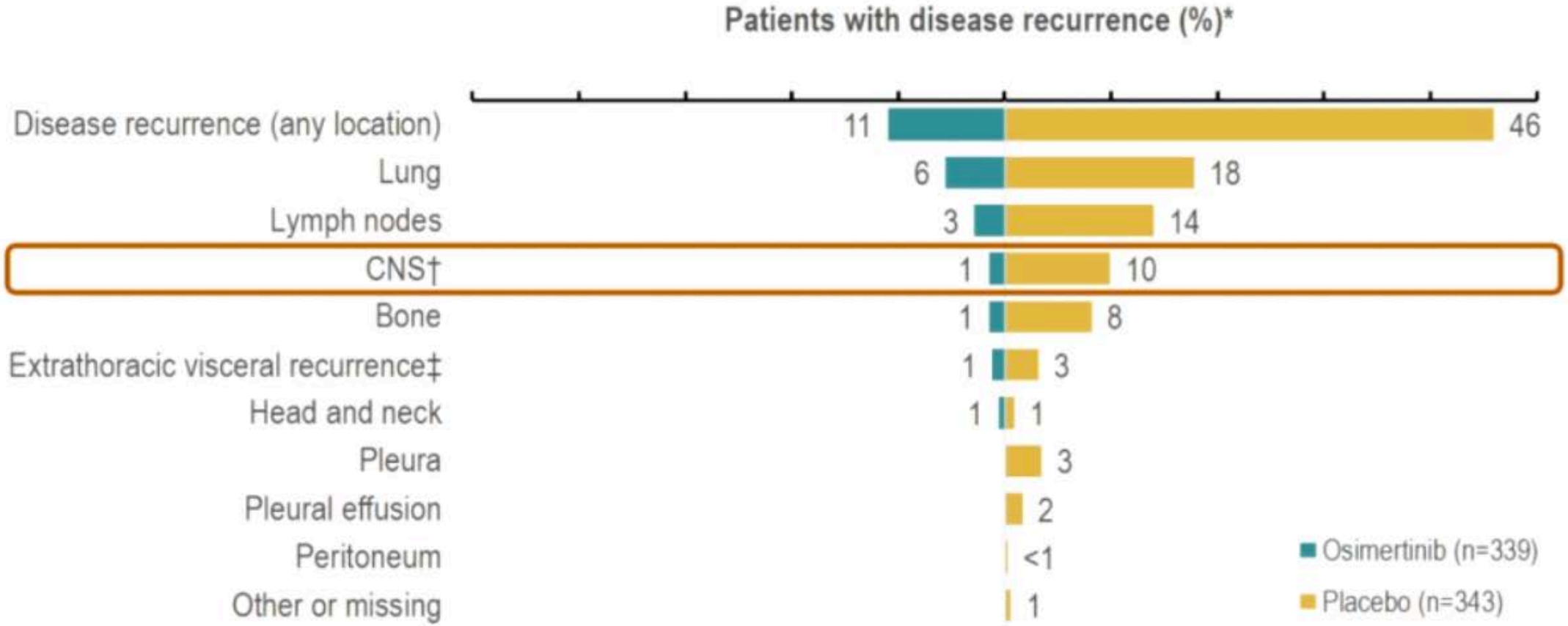
Osimertinib Adjuvant Therapy in Patients (pts) with Resected EGFR Mutated (EGFRm) NSCLC (ADAURA): Central Nervous System (CNS) Disease Recurrence

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

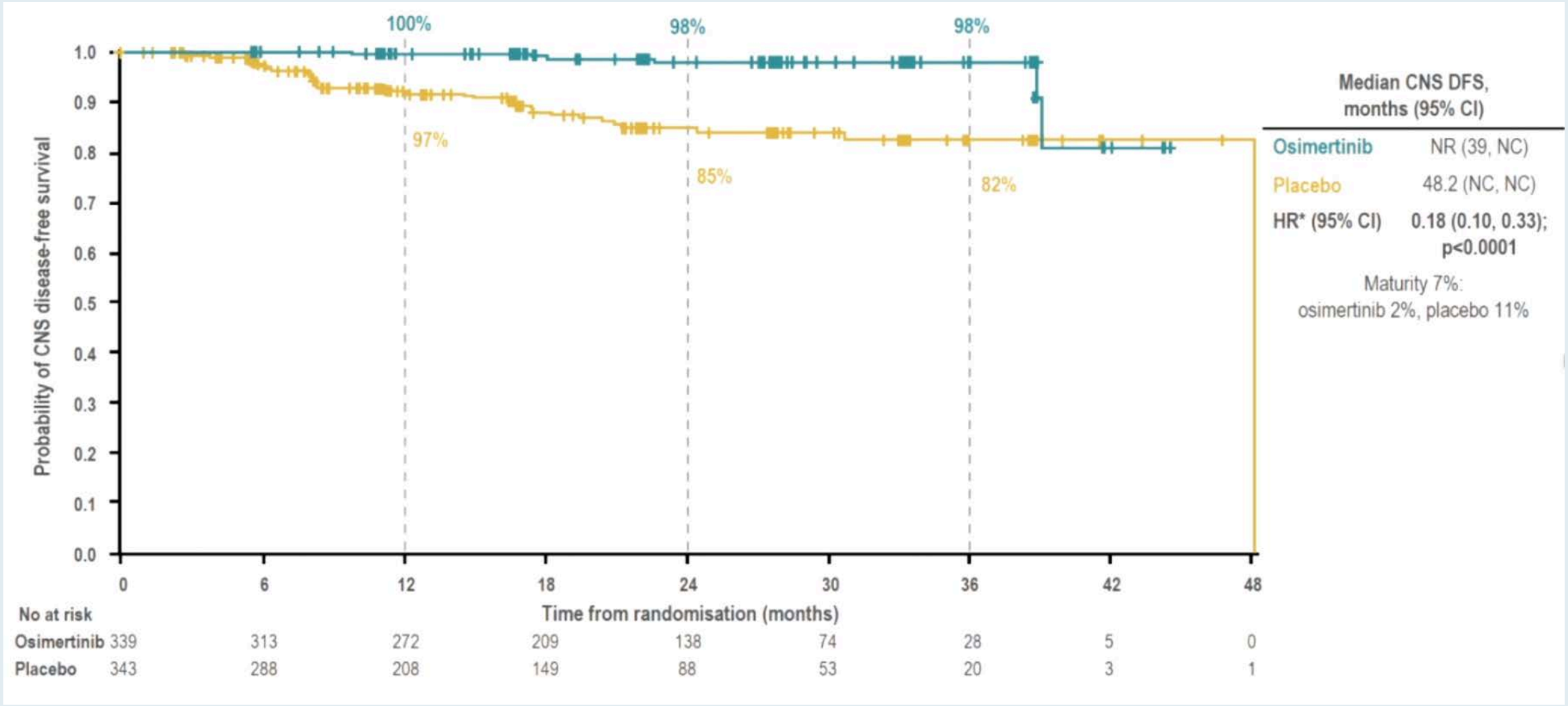
ADAURA: CNS DFS Events

- 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

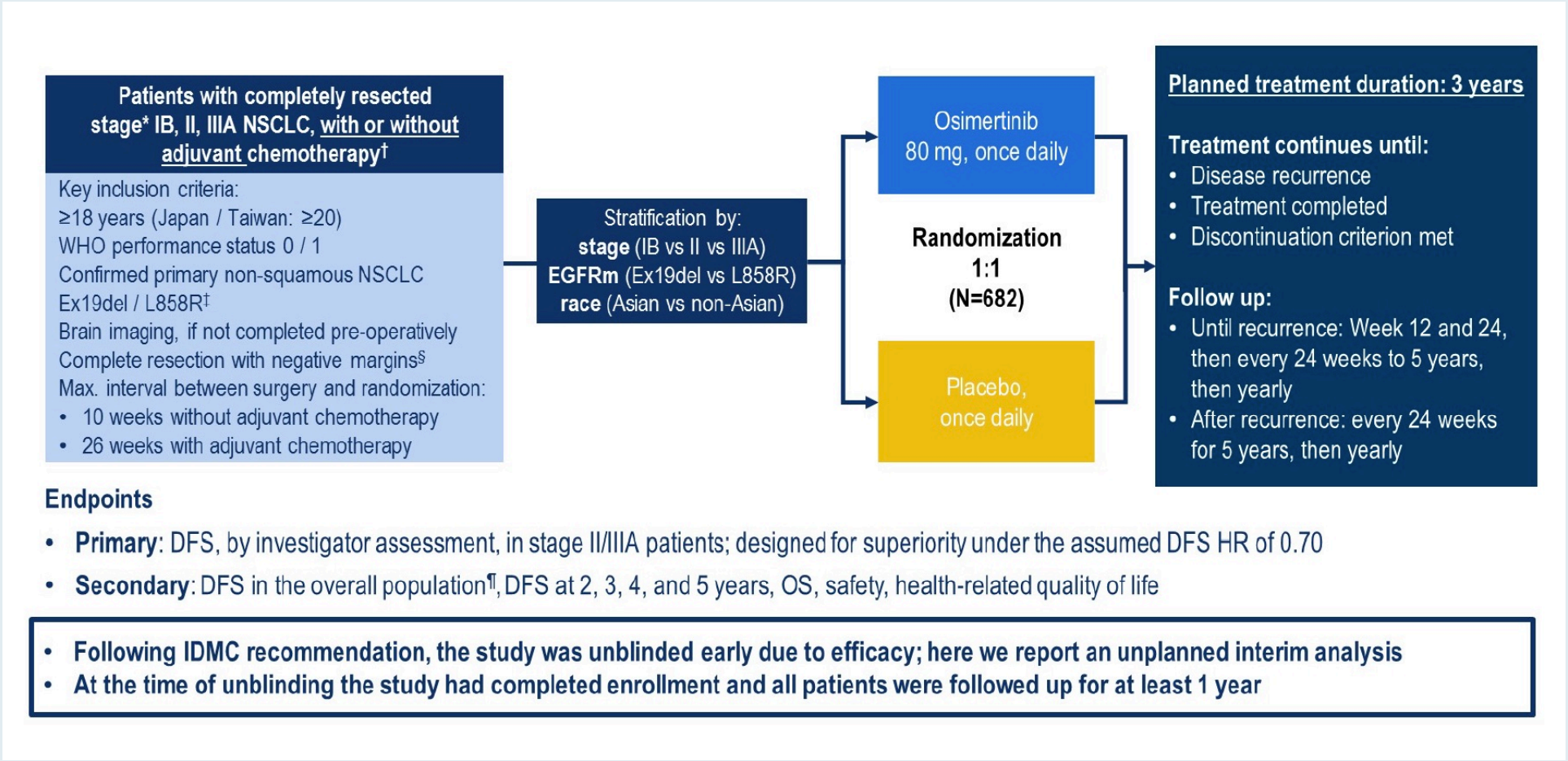
Osimertinib as Adjuvant Therapy in Patients (pts) with Stage IB–IIIA EGFR Mutation Positive (EGFRm) NSCLC After Complete Tumor Resection: ADAURA

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



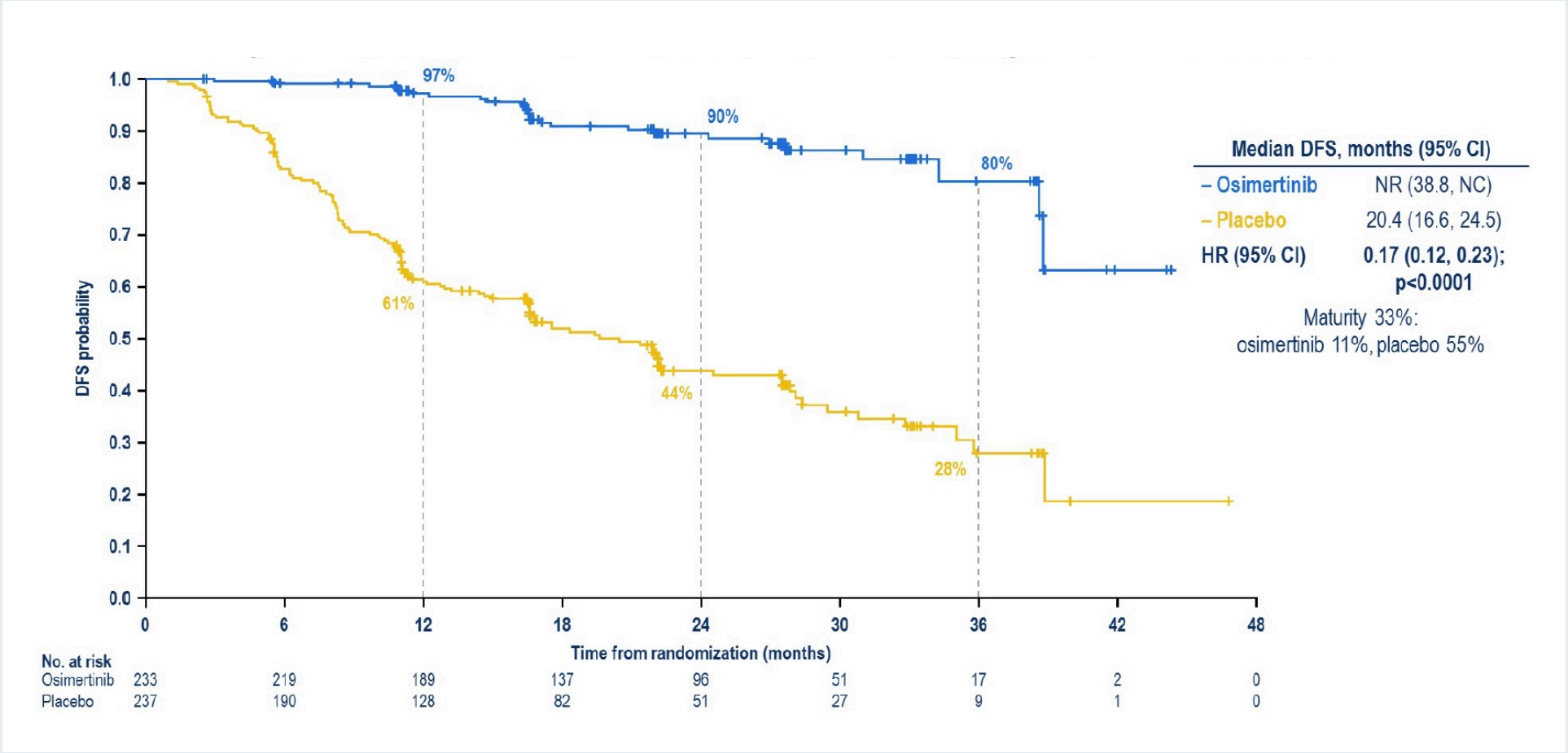
Endpoints

- **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.

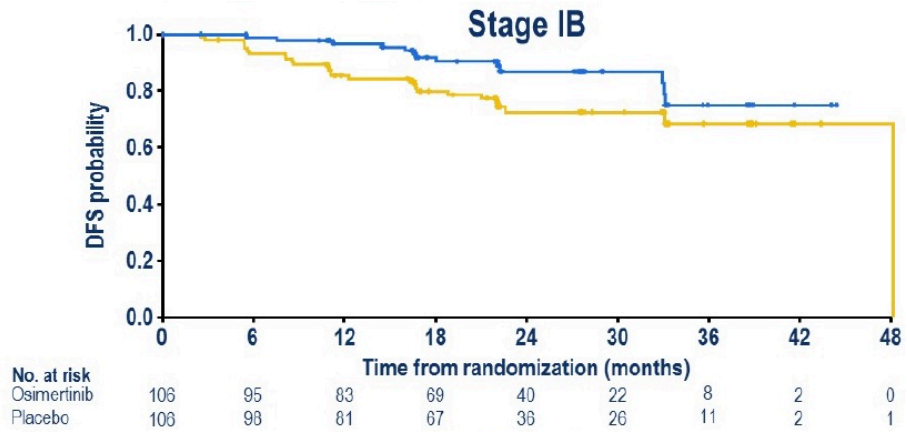
ADAURA Primary Endpoint: Inv-Assessed DFS (Stage II/IIIA)

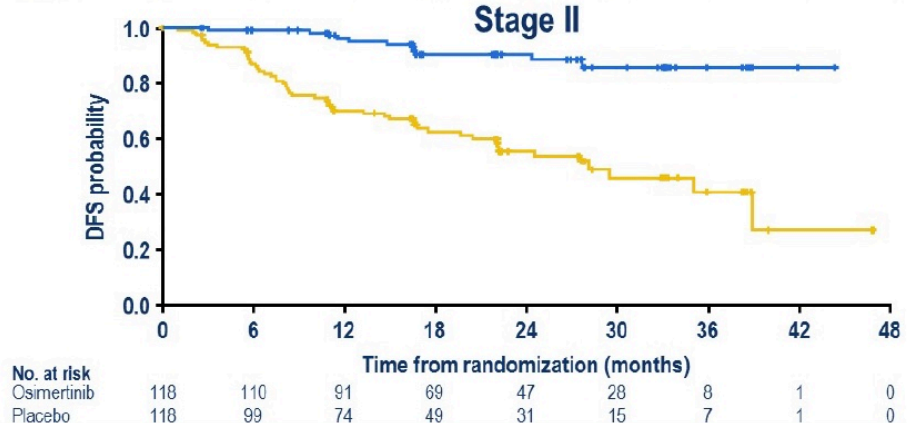


Herbst RS et al. ASCO 2020;Abstract LBA5.

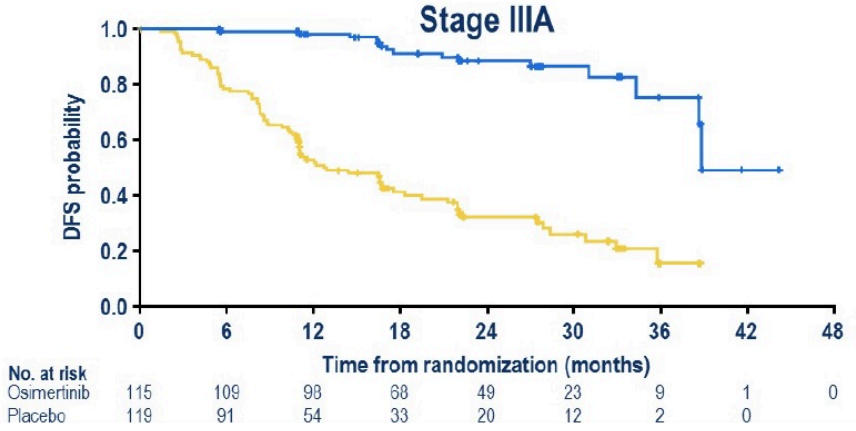
RTP RESEARCH TO PRACTICE

ADAURA: DFS by Stage



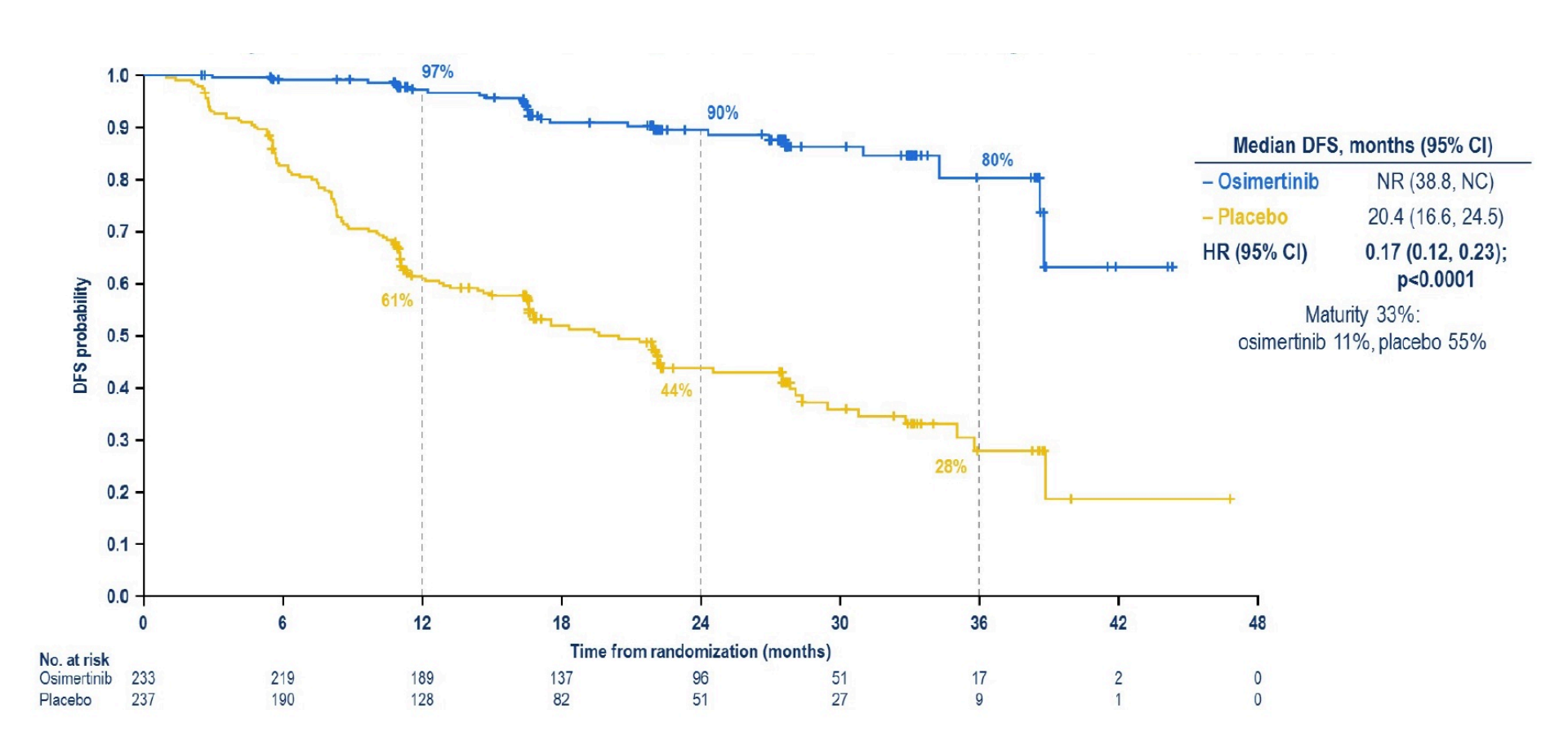


	Stage IB	Stage II	Stage IIIA
2 year DFS rate, % (95% CI)			
– Osimertinib	87 (77, 93)	91 (82, 95)	88 (79, 94)
– Placebo	73 (62, 81)	56 (45, 65)	32 (23, 42)
Overall HR (95% CI)	0.50 (0.25, 0.96)	0.17 (0.08, 0.31)	0.12 (0.07, 0.20)



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

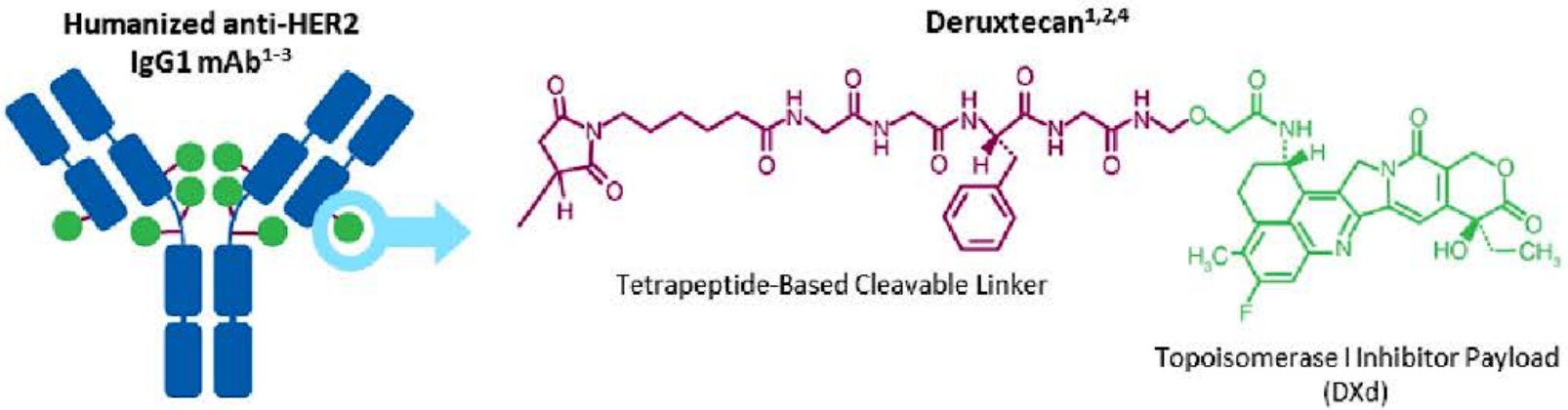
Smit EF et al.

ASCO 2020;Abstract 9504.

Antibody-Drug Conjugate
Trastuzumab Deruxtecan

T-DXd is an ADC with 3 components:

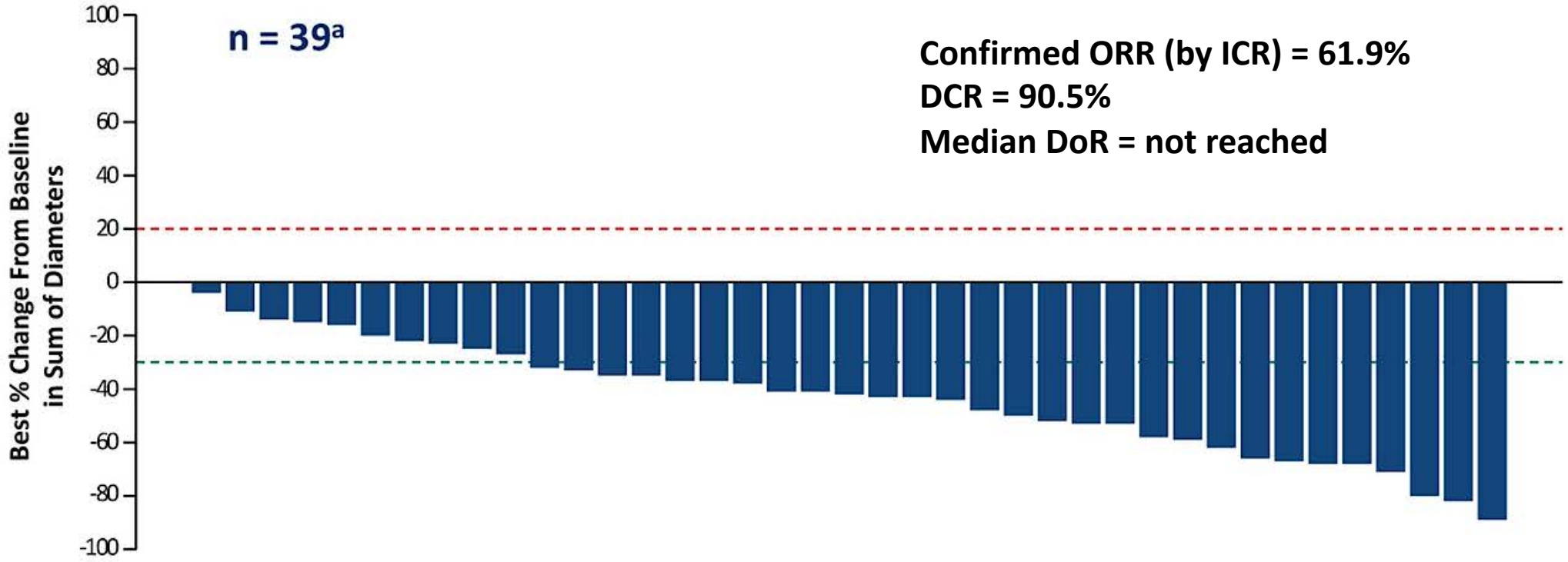
- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



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



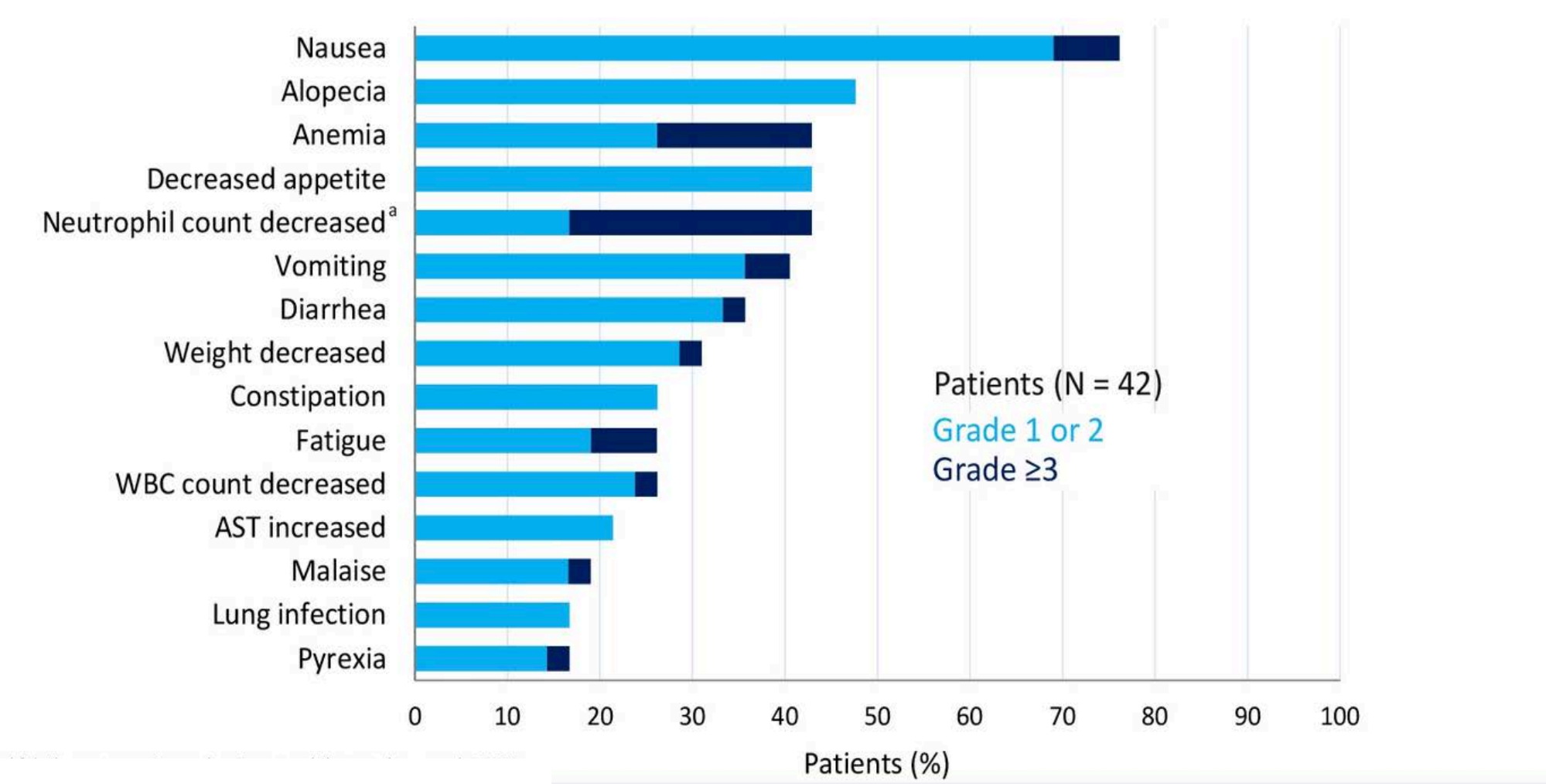
Based on independent central review. Baseline is last measurement taken before enrollment. Shown is best (minimum) percent change from baseline in the sum of diameters for all target lesions.

[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

Management of Chronic Lymphocytic Leukemia

Wednesday, October 14, 2020
12:00 PM – 1:00 PM ET

Faculty

John M Pagel, MD, PhD

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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