Meet The Professor
Management of Lung Cancer

Martin Reck, MD, PhD
Head of Department of Thoracic Oncology
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Commercial Support

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Dr Love — Disclosures

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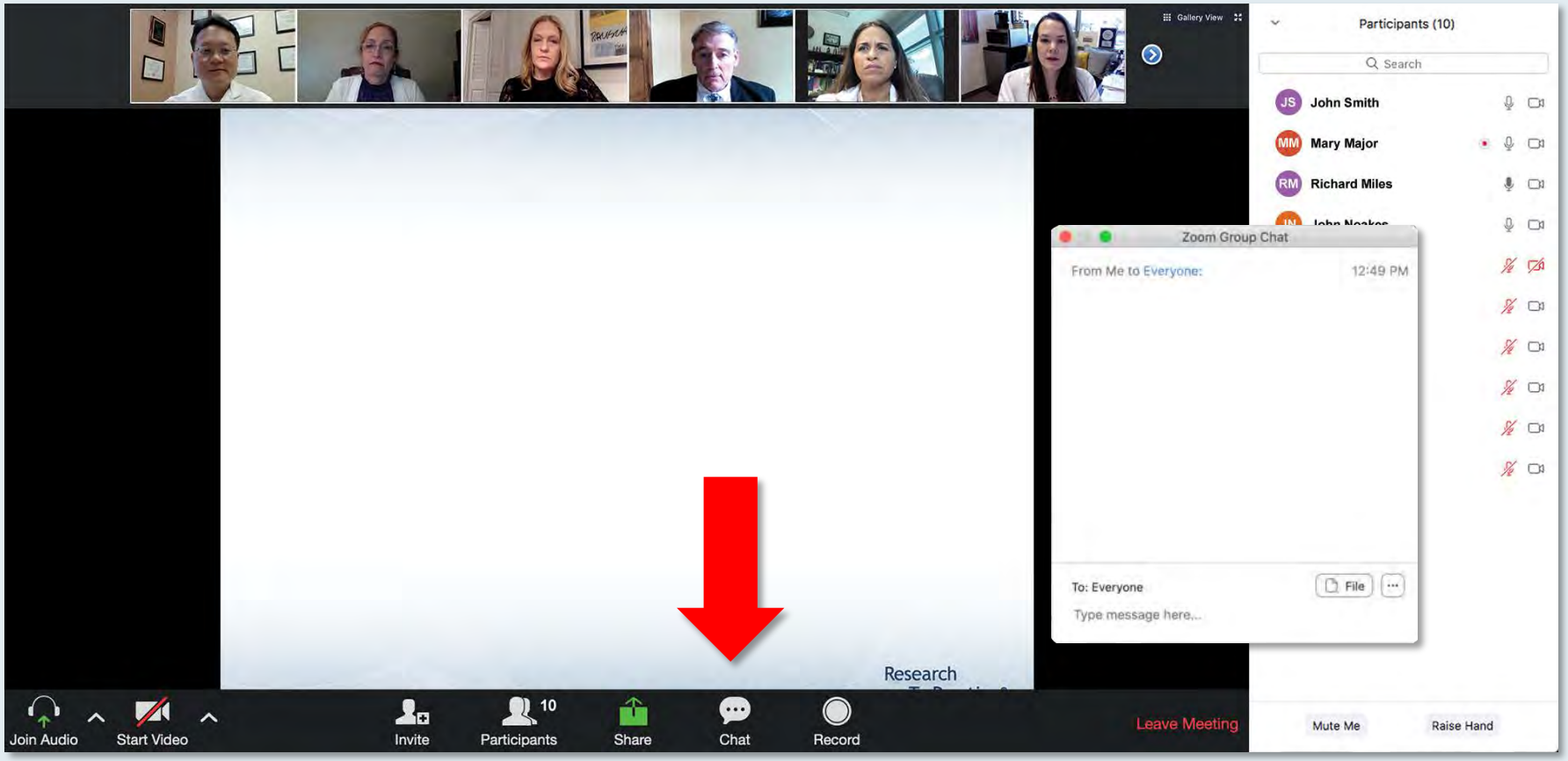
We Encourage Clinicians in Practice to Submit Questions



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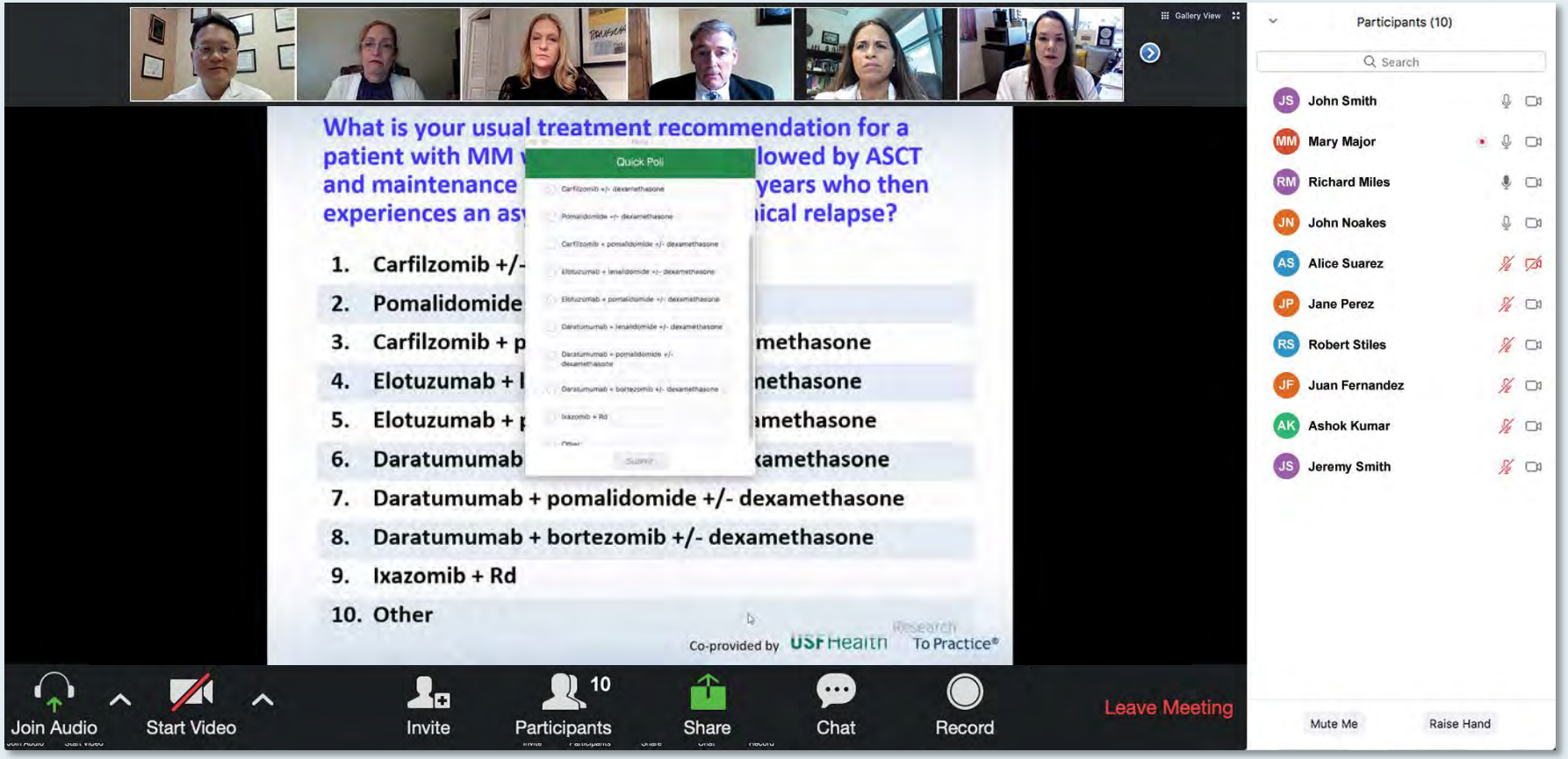
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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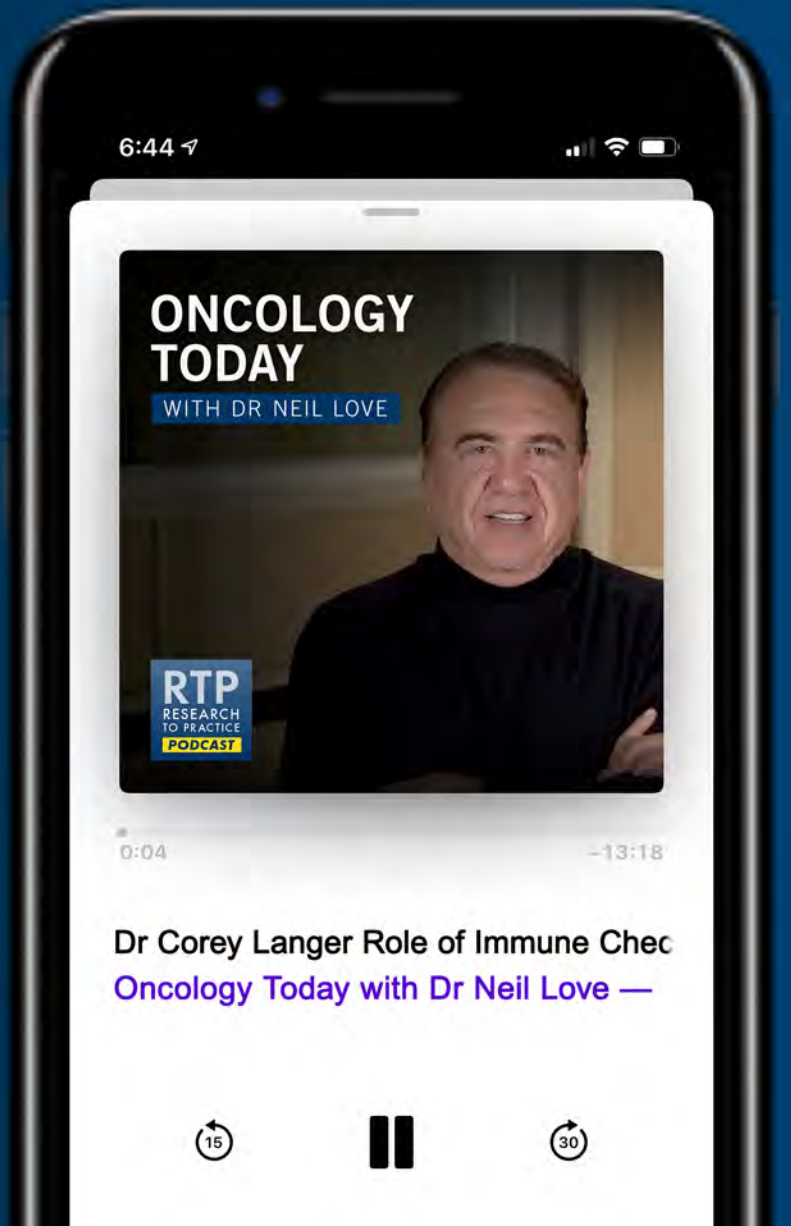

Recent Advances in Hematologic Oncology: A 4-Part Live Webinar Series Reviewing Key Data and Presentations from the 62nd ASH Annual Meeting

Part 4 — Chronic Lymphocytic Leukemia

Wednesday, February 24, 2021
5:00 PM – 6:00 PM ET

Faculty

Paul M Barr, MD
Matthew S Davids, MD, MMSc
Kerry Rogers, MD

Moderator

Neil Love, MD

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Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Prostate Cancer (Part 1 of a 3-Part Series)

Thursday, February 25, 2021
5:00 PM – 6:30 PM ET

Faculty

Tanya B Dorff, MD
Fred Saad, MD
A Oliver Sartor, MD
Matthew R Smith, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Renal Cell Carcinoma (Part 2 of a 3-Part Series)

Monday, March 1, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas E Hutson, DO, PharmD
Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

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Meet The Professor
Management of Ovarian Cancer

Tuesday, March 2, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas J Herzog, MD

Moderator

Neil Love, MD

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Meet The Professor
Management of Multiple Myeloma

Wednesday, March 3, 2021
5:00 PM – 6:00 PM ET

Faculty

Morie A Gertz, MD, MACP

Moderator

Neil Love, MD

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Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Urothelial Bladder Carcinoma (Part 3 of a 3-Part Series)

Thursday, March 4, 2021
5:00 PM – 6:15 PM ET

Faculty

Arjun Balar, MD
Elisabeth I Heath, MD
Jonathan E Rosenberg, MD

Moderator

Neil Love, MD

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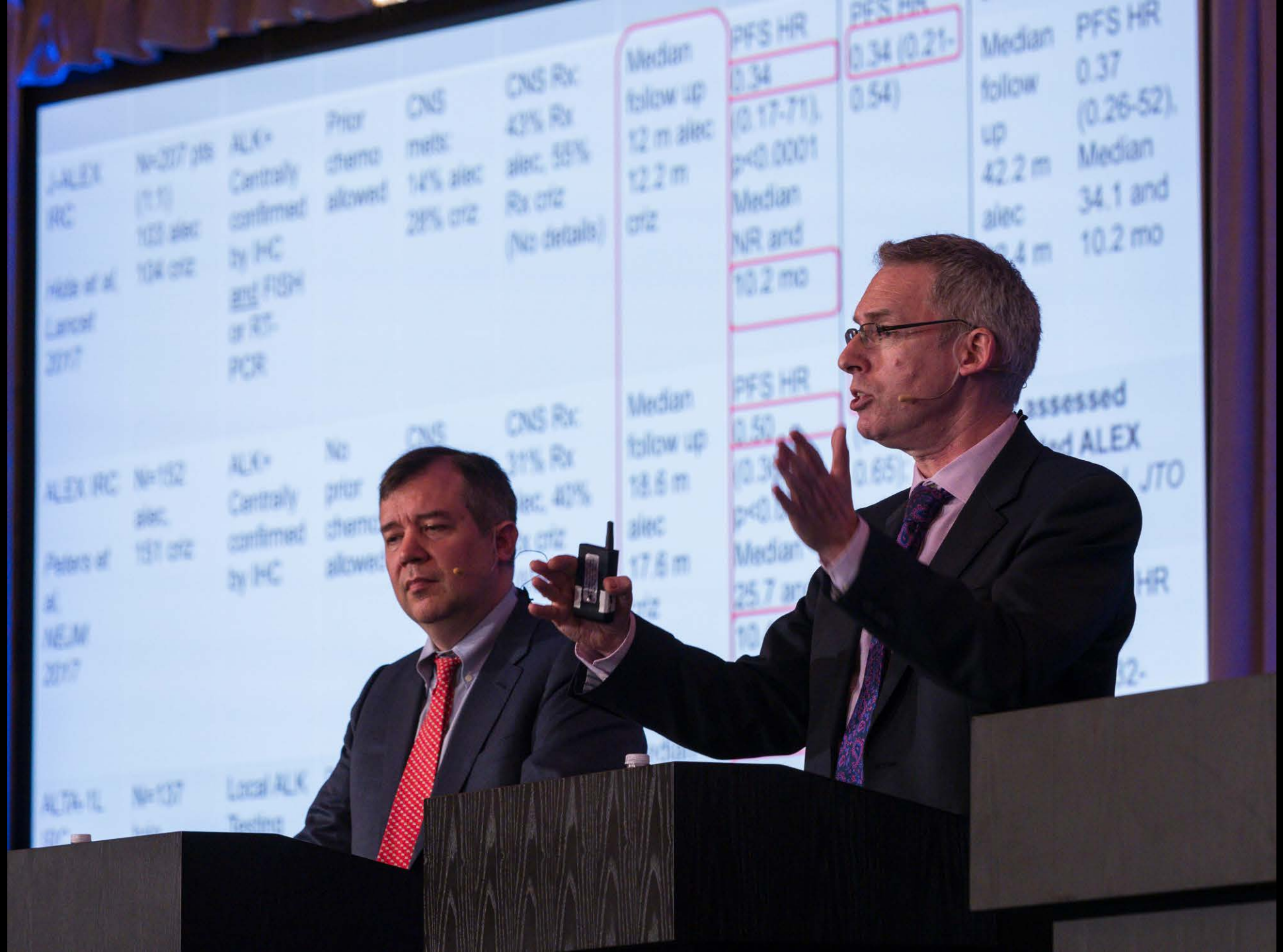
Thank you for joining us!

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


with an NTRK gene fusion?
32%
5%
10%
3%


J-ALEX IRC
Hida et al. Lancet 2017
N=207 pts (1:1) 103 alec 104 crz
ALK+ Centrally confirmed by IHC and FISH or RT-PCR
Prior chemo allowed
CNS mets: 14% alec 29% crz
CNS Rx: 43% Rx alec, 55% Rx crz (No details)
Median follow up 12 m alec 12.2 m crz
PFS HR
0.34 (0.17-71), p<0.0001
Median NR and 10.2 mo
0.34 (0.21-0.54)
Median follow up 42.2 m alec
PFS HR 0.37 (0.26-52). Median 34.1 and 10.2 mo
ALEX IRC
Peters et al. NEJM 2017
N=152 alec, 151 crz
ALK+ Centrally confirmed by IHC
No prior chemo allowed
CNS
CNS Rx: 31% Rx alec, 40% Rx crz
Median follow up 18.6 m alec 17.6 m crz
PFS HR
0.50
Median 25.7 mo
0.65
ssessed
ALEX
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ALTA-1L
N=137
Local ALK Testing


THE WESTIN
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Meet The Professor
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Martin Reck, MD, PhD
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Meet The Professor Program Participating Faculty

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University of Pennsylvania
Philadelphia, Pennsylvania

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The University of Texas
MD Anderson Cancer Center
Houston, Texas

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Director, Thoracic Oncology Research Program
Assistant Vice Chairman for Faculty Development
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Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
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Clinical Director
Medical Director, Thoracic Oncology Program
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Division of Oncology
Department of Medicine
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Chairman, Department of Clinical Oncology
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Director, Cleveland Clinic Lung Cancer Medical
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Massachusetts General Hospital Cancer Center
The Landry Family Professor of Medicine
Harvard Medical School
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Lausanne, Switzerland

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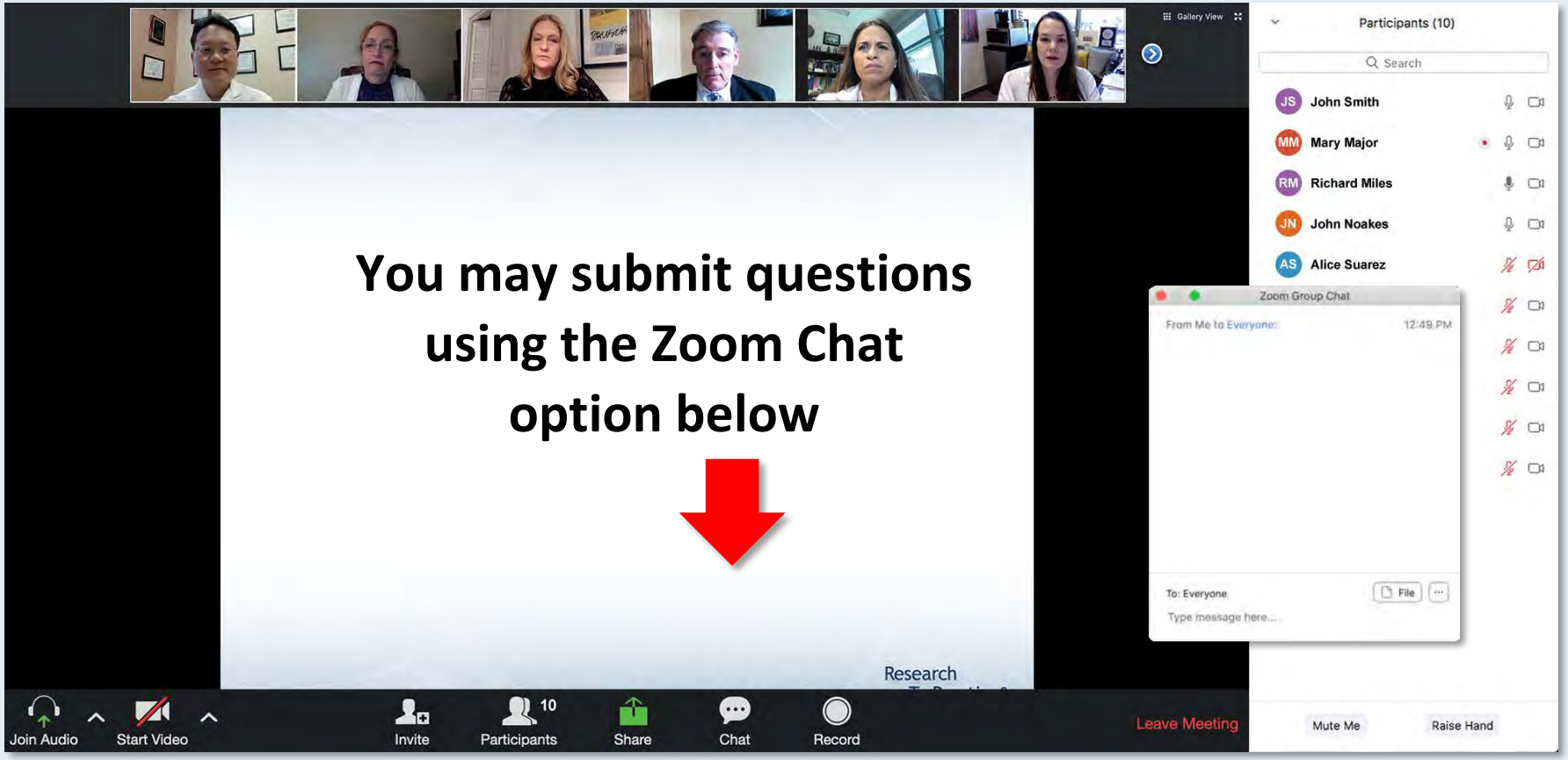

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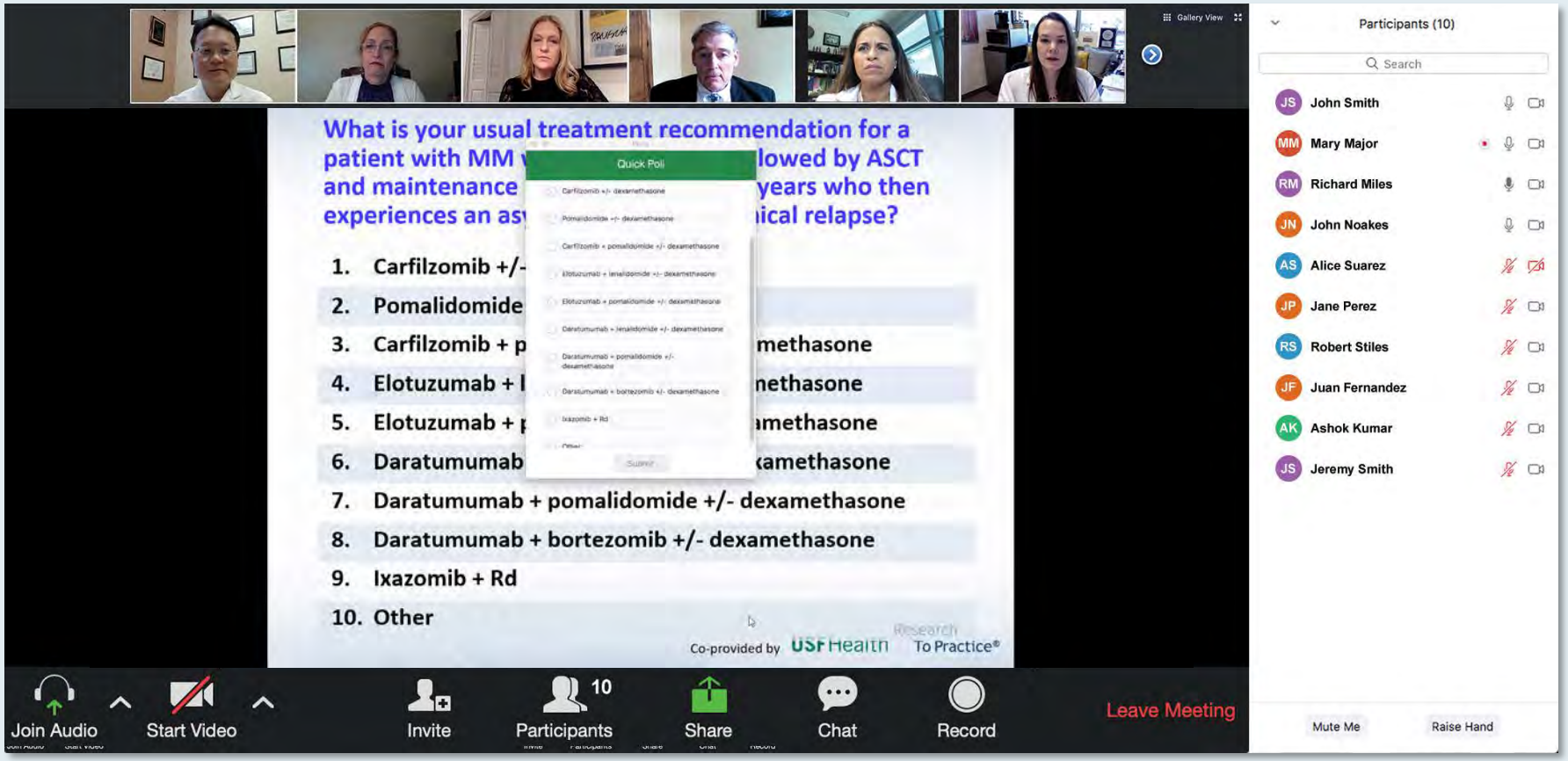

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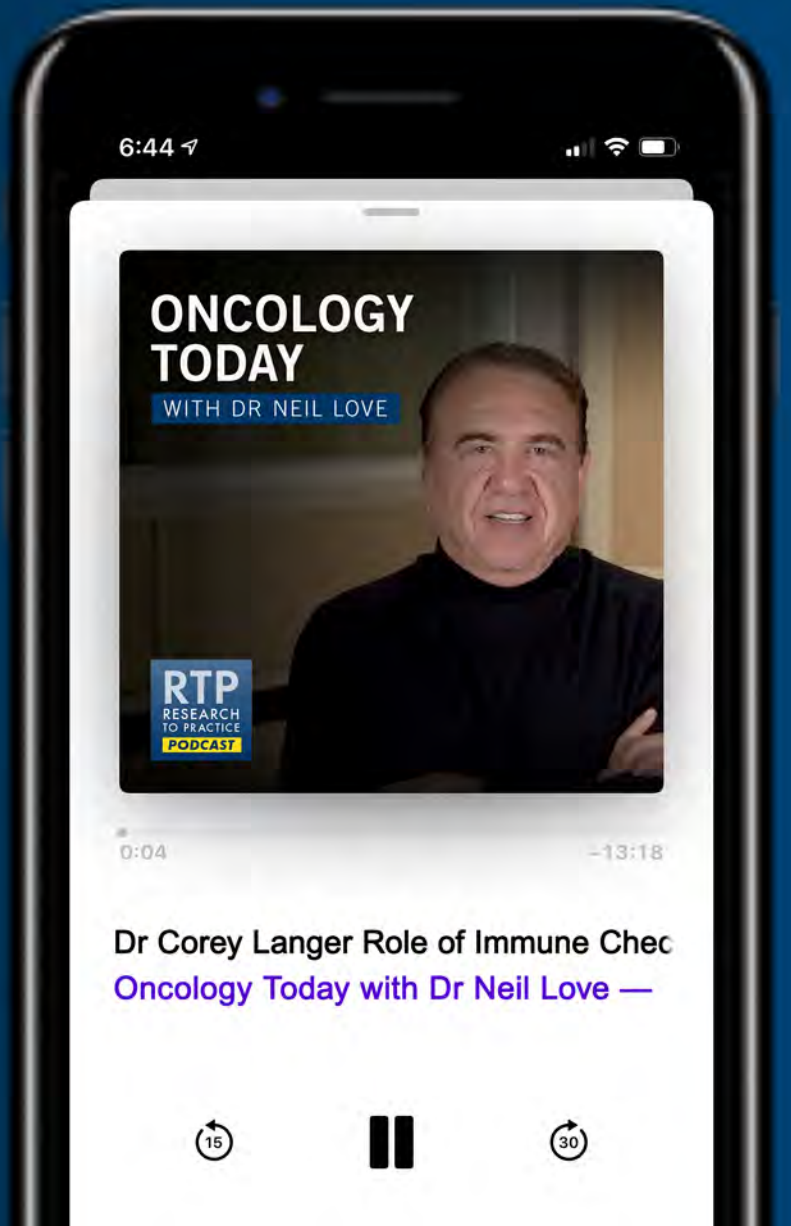

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LungenClinic Grosshansdorf
Grosshansdorf, Germany

Namrata I Peswani, MD
Hematologist Oncologist
Harold C Simmons Comprehensive Cancer Center
UT Southwestern Medical Center
Richardson, Texas

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Meet The Professor with Dr Reck

Module 1: Cases from Dr Peswani

- An otherwise healthy 80-year-old man with extremely symptomatic extensive-stage small cell lung cancer (SCLC)
  - Parts 1 and 2
- A 76-year-old woman with extensive-stage SCLC
- A 45-year-old man and never smoker with de novo metastatic non-small cell lung cancer (NSCLC) – EGFR exon 21 mutation
- An 80-year-old woman and never smoker with metastatic NSCLC – EGFR exon 21 mutation

Module 2: Lung Cancer Journal Club with Dr Reck

Module 3: Other Key Papers and Recent Approvals for Discussion

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Case Presentation – Dr Peswani: An otherwise healthy 80-year-old man with extremely symptomatic extensive-stage SCLC – Part 1

Dr Namrata Peswani

- ES-SCLC, extremely symptomatic from 12.4-cm LUL mass,
  - Mediastinal invasion and circumferential encasement of the left main pulmonary artery and mainstem bronchus with occlusion of the left upper lobe bronchus
  - Liver and bone mets

Questions

- Are there any differences between carboplatin/etoposide with atezolizumab versus with durvalumab?
- In this healthy 80-year-old patient I was able to give triplet therapy, but in frail patients are you using instead single-agent immunotherapy?

Case Presentation – Dr Peswani: An otherwise healthy 80-year-old man with extremely symptomatic extensive-stage SCLC – Part 2

Dr Namrata Peswani

- ES-SCLC, extremely symptomatic from 12.4-cm LUL mass,
  - Mediastinal invasion and circumferential encasement of the left main pulmonary artery and mainstem bronchus with occlusion of the left upper lobe bronchus
  - Liver and bone mets
- ***Carboplatin/etoposide/atezolizumab x 6 with near CR in lung, stable bone and liver disease***
- ***Maintenance atezolizumab x 2 → Recurrence of symptoms***
- ***CT: Worsening disease in lungs and new liver lesion***

Questions

- ***What treatment would you recommend next?***
- ***What side effects have you observed with lurbinectedin and how are you monitoring patients who are on this agent?***

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Case Presentation – Dr Peswani: A 76-year-old woman with extensive-stage SCLC

Dr Namrata Peswani

- ES-SCLC, with liver and bone metastases
- Carboplatin/etoposide/atezolizumab x 6, with near CR in lung, stable disease in bone and liver
- Maintenance atezolizumab

Questions

- Since this patient had a more defined lung mass and responded well to her initial therapy, is there a role for consolidation radiation therapy?
- What is the role of prophylactic cranial irradiation, which I believe now people are considering omitting for some of these patients?

Case Presentation – Dr Peswani: A 45-year-old man and never smoker with de novo metastatic NSCLC – EGFR exon 21 mutation

Dr Namrata Peswani

- 12/2019: Unprovoked DVT
- 6/2020: Developed severe hip and shoulder pain
- CT scan: Lytic lesions in the right scapula and left hip as well as a lung mass
- Biopsy lung mass: NSCLC, EGFR exon 21 mutation
- Osimertinib, with plan for SBRT to oligometastatic disease after response to therapy
  - 3-month scans: Initial response
  - 6-month scans: Progressive disease
- Next generation sequencing ordered

Questions

- What is our understanding about the mechanisms for osimertinib resistance?
- Are there any agents available to overcome that resistance?

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Trial in Progress

ERRAMOSI trial

Phase III study in first-line metastatic NSCLC with EGFR exon 19 or exon 21 L858R mutations

Randomization arms

- Erlotinib → followed by usual care (T790-osi)
- Erlotinib/ramucirumab → followed by usual care (T790-osi)
- Osimertinib → followed by usual care

Primary endpoints

❑ Time to first progression

❑ Time to second progression

❑ Overall survival

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Case Presentation – Dr Peswani: An 80-year-old woman and never smoker with metastatic NSCLC – EGFR exon 21 mutation

Dr Namrata Peswani

- 2018: Stage I RLL NSCLC s/p SBRT (not a surgical candidate)
- Surveillance scan: Increase in size of RLL lesion
  - PET: No distant disease
  - MRI brain: 2 brain metastases
  - Re-checked 2018 biopsy specimen: EGFR exon 21

Questions

- Should she get radiation to her brain metastases, or should we treat with osimertinib and then consider radiation therapy based on her response to osimertinib?

FDA Approves Osimertinib as Adjuvant Therapy for NSCLC with EGFR Mutations

Press Release — December 18, 2020

- The FDA approved osimertinib as adjuvant therapy after tumor resection in patients with NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- Efficacy was demonstrated in the randomized, double-blind, placebo-controlled ADAURA trial for patients with EGFR exon 19 deletions or exon 21 L858R mutation-positive NSCLC who had complete tumor resection, with or without prior adjuvant chemotherapy.
- Eligible patients with resectable tumors (stage IB – IIIA) were required to have predominantly non-squamous histology and EGFR exon 19 deletions or exon 21 L858R mutations identified prospectively from tumor tissue in a central laboratory EGFR Mutation Test.

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-osimertinib-adjuvant-therapy-non-small-cell-lung-cancer-egfr-mutations

The NEW ENGLAND JOURNAL of MEDICINE

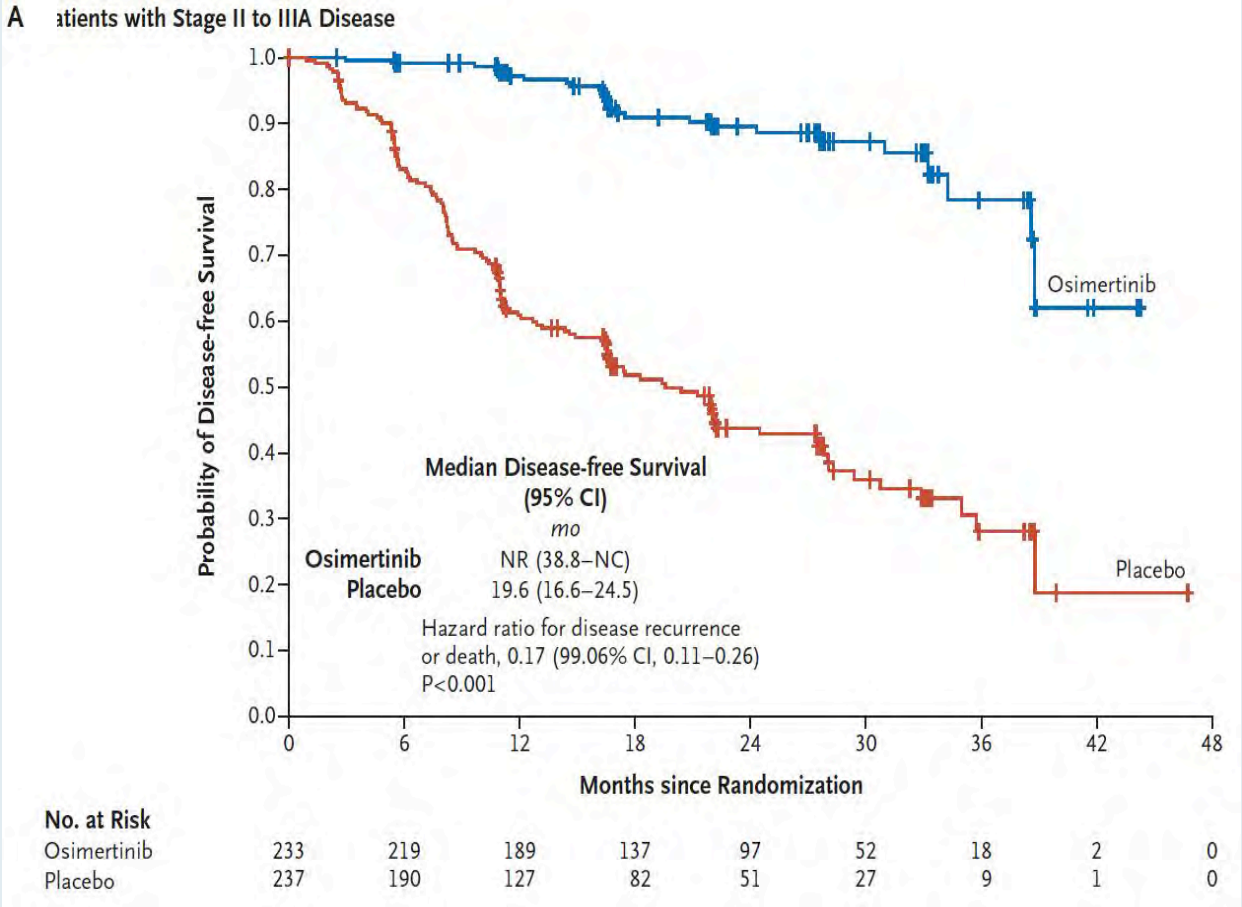
ORIGINAL ARTICLE

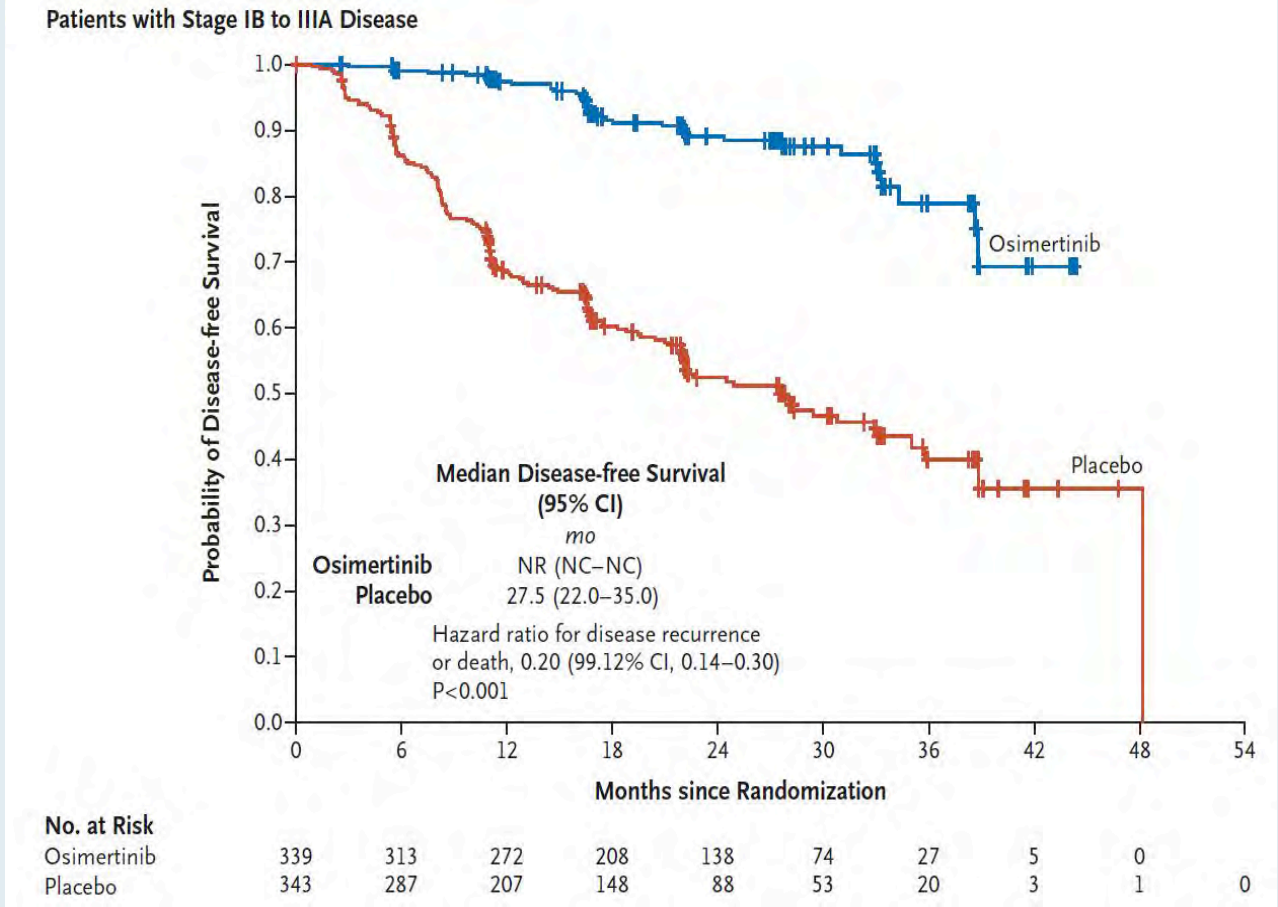
Osimertinib in Resected *EGFR*-Mutated Non–Small-Cell Lung Cancer

Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Terufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., Kye-Young Lee, M.D., Ph.D., Charuwan Akewanlop, M.D., Chong-Jen Yu, M.D., Ph.D., Filippo de Marinis, M.D., Laura Bonanno, M.D., Manuel Domine, M.D., Ph.D., Frances A. Shepherd, M.D., Lingmin Zeng, Ph.D., Rachel Hodge, M.Sc., Ajlan Atasoy, M.D., Yuri Rukazenkov, M.D., Ph.D., and Roy S. Herbst, M.D., Ph.D.,

***N Engl J Med* 2020;383(18):1711-23.**

ADAURA: Disease-Free Survival by Stage





Wu YL et al. *N Engl J Med* 2020;383(18):1711-23.

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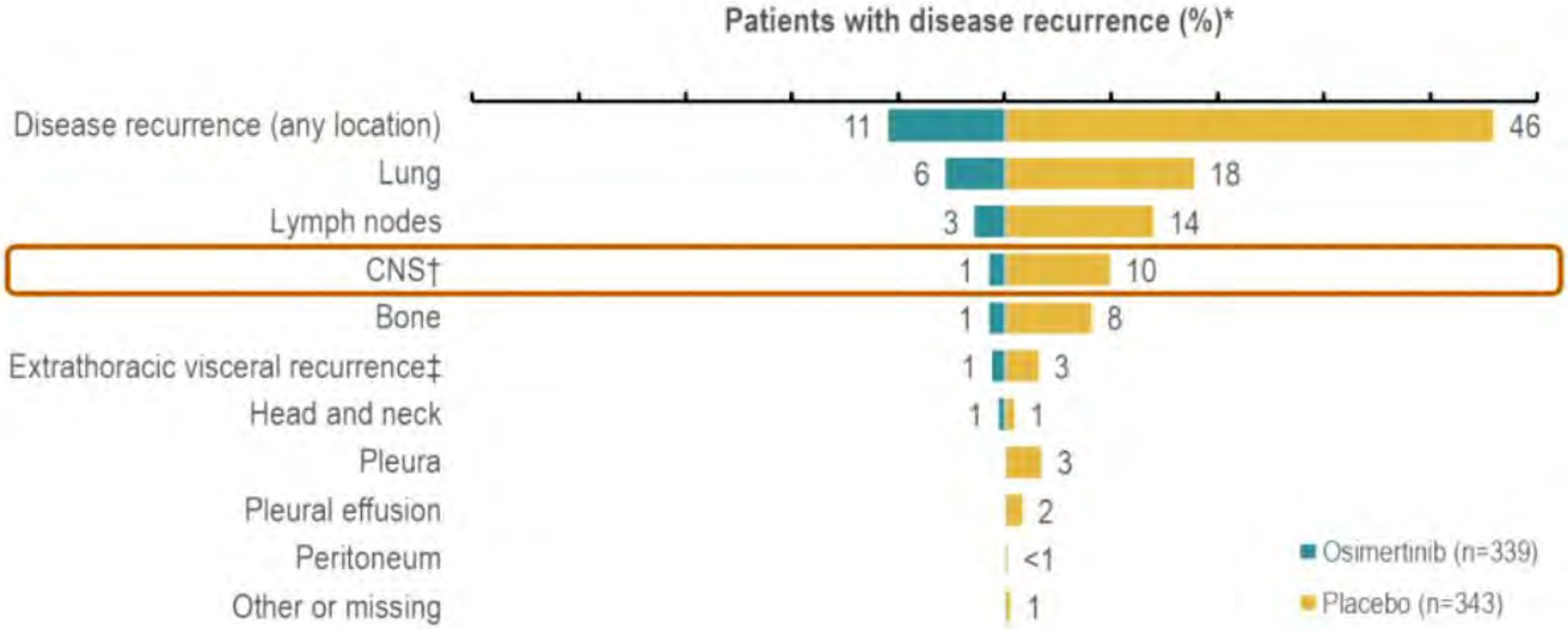
Osimertinib Adjuvant Therapy in Patients (pts) with Resected EGFR Mutated (EGFRm) NSCLC (ADAURA): Central Nervous System (CNS) Disease Recurrence

Tsuboi M et al.

ESMO 2020;Abstract LBA1.

ADAURA: Sites of Disease Recurrence



Tsuboi M et al. ESMO 2020;Abstract LBA1.

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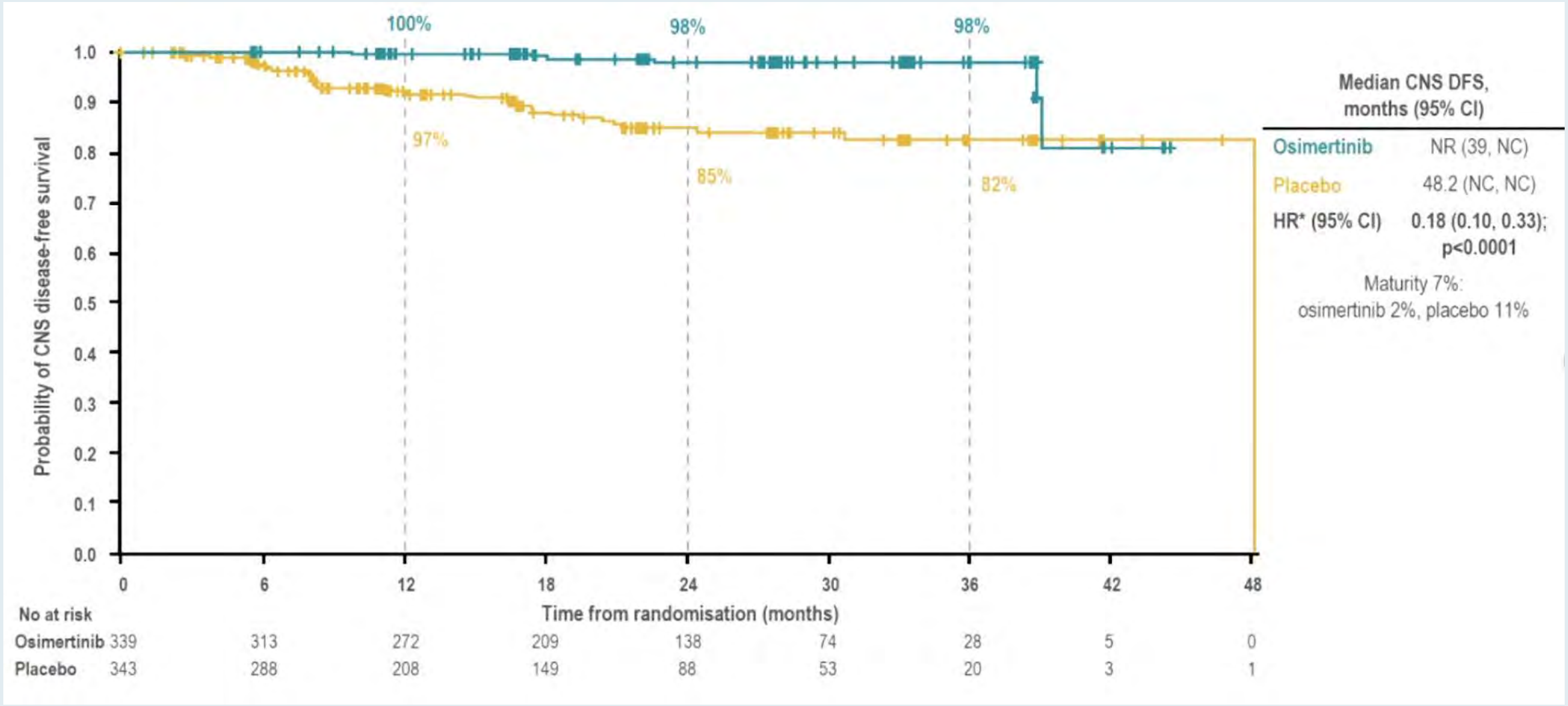
ADAURA: CNS DFS Events

- 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.

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

1. Durvalumab
2. Osimertinib
3. Durvalumab + osimertinib
4. Durvalumab followed by osimertinib
5. Other

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The ADAURA trial is the first major step forward in the adjuvant setting in 20 years.

1. Agree
2. Agree, but IOs are coming soon
3. Disagree

What does the adjuvant treatment of melanoma, gastroesophageal cancer, and bladder cancer have in common that does not apply to non-small cell lung cancer?

Meet The Professor with Dr Reck

Module 1: Cases from Dr Peswani

Module 2: Lung Cancer Journal Club with Dr Reck

- First-line ICI for advanced NSCLC: State of the art and future directions
- KEYNOTE-598: Pembrolizumab/ipilimumab for metastatic NSCLC with PD-L1 TPS ≥ 50%
- PACIFIC: 4-year survival update with consolidation durvalumab after chemoradiation therapy
- Immune checkpoint inhibitors in non-metastatic NSCLC: Chance for cure?
- Combination of immunotherapy and radiotherapy -The next magic step in the management of lung cancer?
- CheckMate 9LA: Nivolumab/ipilimumab combined with first-line chemotherapy
- Patient-reported outcomes in Part 1 of the CheckMate 227 trial: First-line nivolumab/ipilimumab vs chemotherapy
- IMpower133: Long-term survivors with first-line chemotherapy ± atezolizumab in extensive-stage SCLC
- STIMULI trial: Consolidation ipilimumab/nivolumab in limited-stage SCLC

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Meet The Professor with Dr Reck

Module 1: Cases from Dr Peswani

Module 2: Lung Cancer Journal Club with Dr Reck (continued)

- Anti-angiogenic agents in the age of resistance to immune checkpoint inhibitors: Do they have a role in non-oncogene-addicted NSCLC?
- Serial liquid biopsies to detect treatment failure and profile resistance mechanisms in ALK rearranged NSCLC
- Longitudinal therapy monitoring of ALK-positive NSCLC by combined copy number and targeted mutation profiling of cell-free DNA
- DESTINY-LUNG01: Trastuzumab deruxtecan in HER2-overexpressing metastatic NSCLC
- Perceived relatedness, death acceptance, and demoralization in patients with cancer

Module 3: Other Key Papers and Recent Approvals for Discussion

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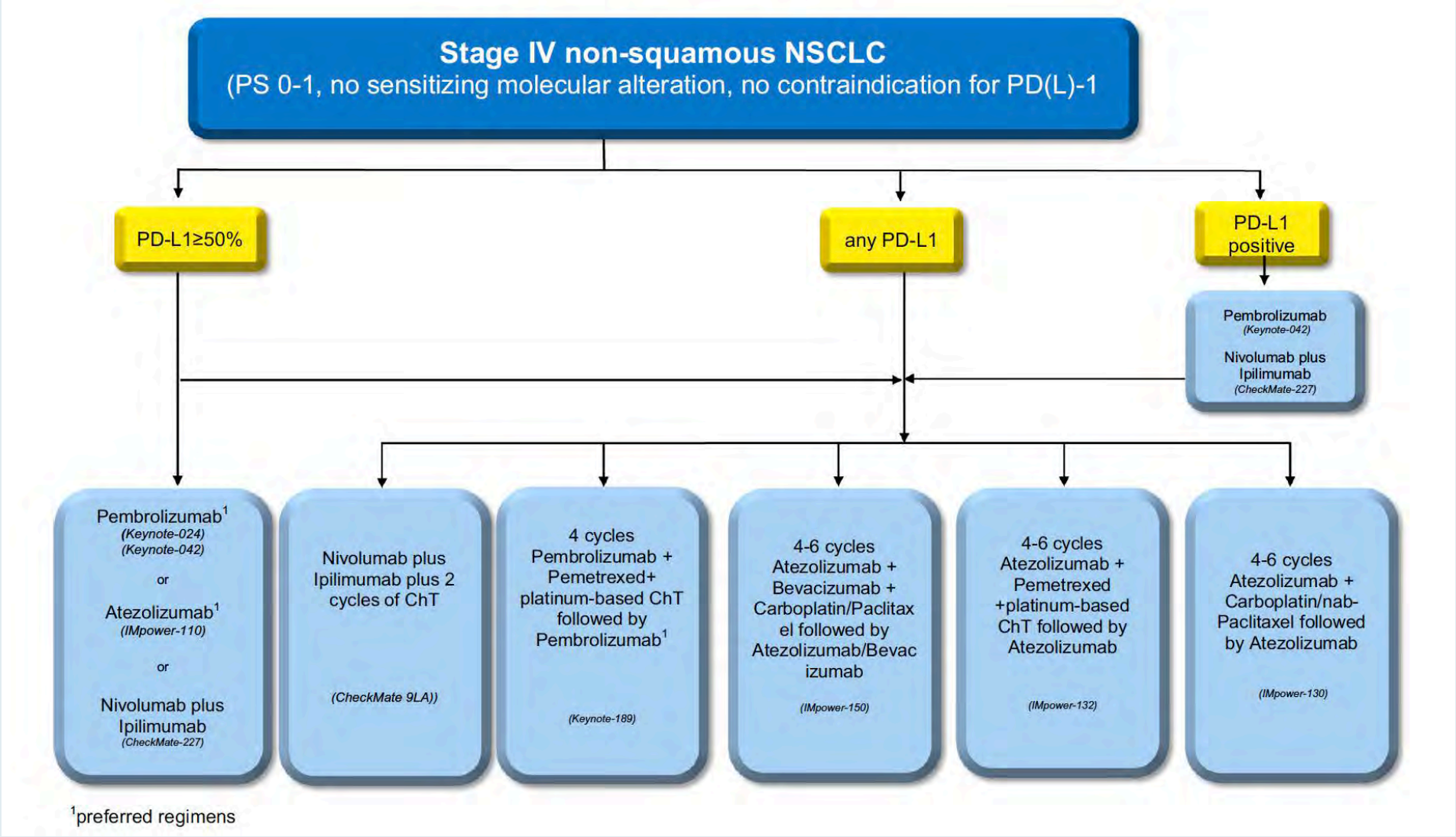
Drugs (2020) 80:1783–1797
https://doi.org/10.1007/s40265-020-01409-6

REVIEW ARTICLE

First-Line Immune Checkpoint Inhibition for Advanced Non-Small-Cell Lung Cancer: State of the Art and Future Directions

Christoph Jakob Ackermann[1] · Helen Adderley[2] · Ana Ortega-Franco[2] · Adeel Khan[2] · Martin Reck[3] · Raffaele Califano[2,4,5]

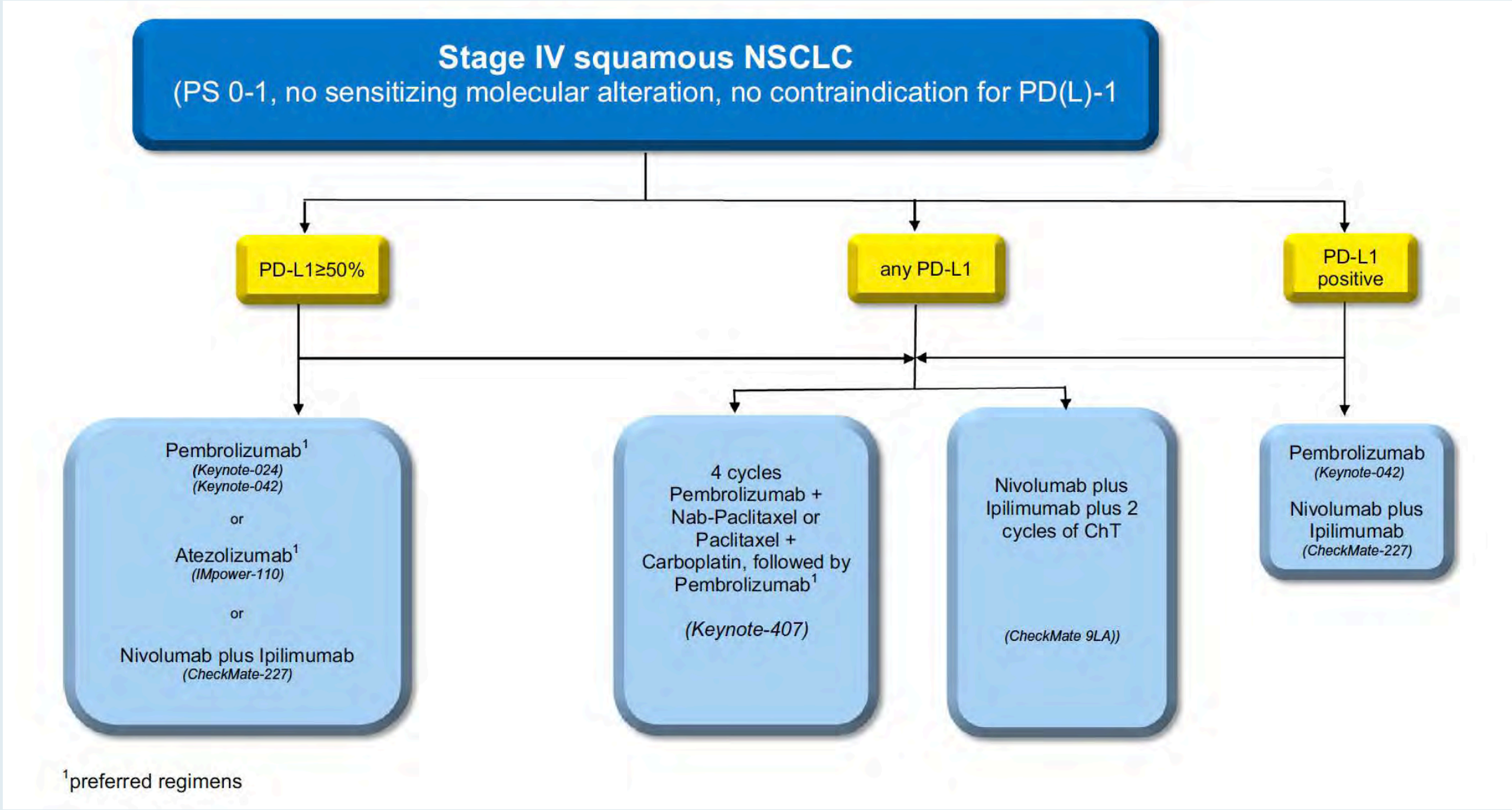
CPI-Based Treatment First-Line Options for Advanced Nonsquamous NSCLC



Ackermann CJ et al. *Drugs* 2020;80(17):1783-97.

RTP RESEARCH TO PRACTICE

CPI-Based Treatment First-Line Options for Advanced Squamous NSCLC



Ackermann CJ et al. *Drugs* 2020;80(17):1783-97.

rapid communications

Pembrolizumab Plus Ipilimumab or Placebo for Metastatic Non–Small-Cell Lung Cancer With PD-L1 Tumor Proportion Score ≥ 50%: Randomized, Double-Blind Phase III KEYNOTE-598 Study

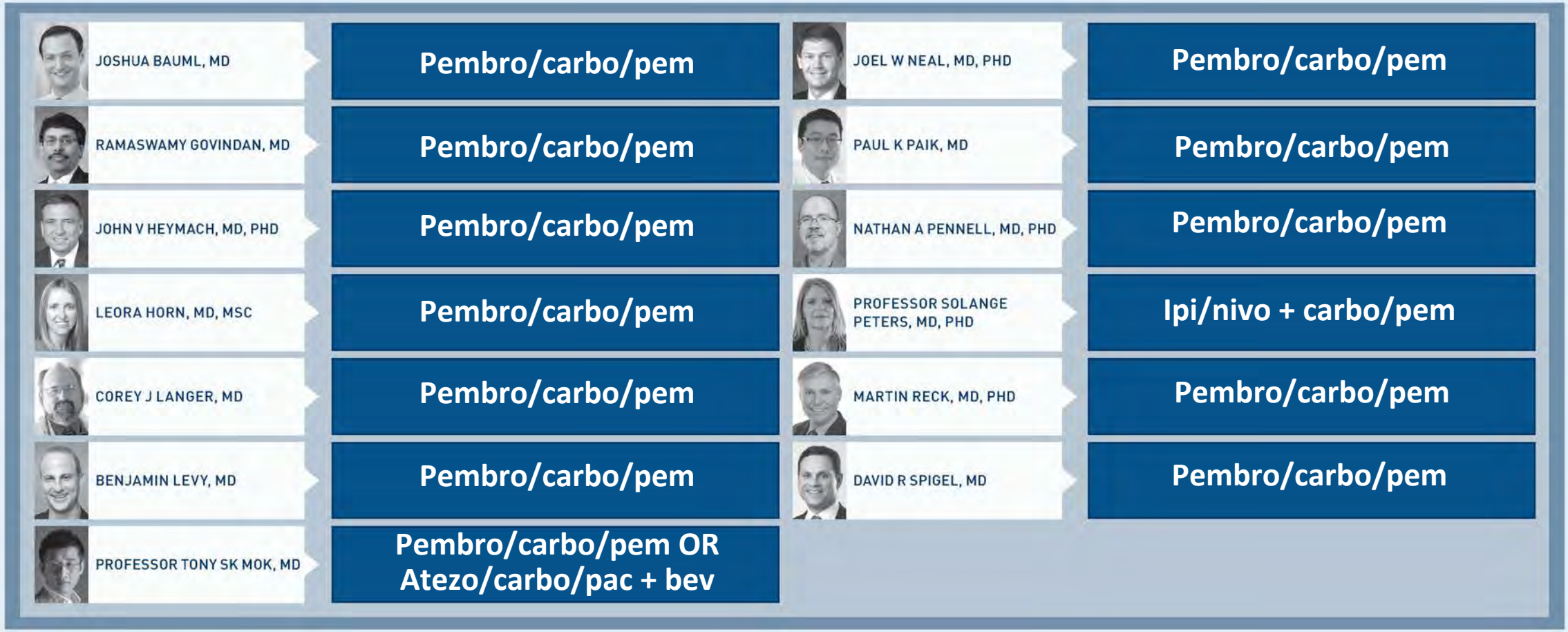
Michael Boyer, MBBS, PhD[1]; Mehmet A. N. Şendur, MD[2]; Delvys Rodríguez-Abreu, MD[3]; Keunchil Park, MD, PhD[4]; Dae Ho Lee, MD, PhD[5]; Irfan Çiçin, MD[6]; Perran Fulden Yumuk, MD[7]; Francisco J. Orlandi, MD[8]; Ticiana A. Leal, MD[9]; Olivier Molinier, MD[10]; Nopadol Soparattanapaisam, MD[11]; Adrian Langleben, MD[12]; Raffaele Califano, MD[13]; Balazs Medgyasszay, MD[14]; Te-Chun Hsia, MD[15]; Gregory A. Otterson, MD[16]; Lu Xu, PhD[17]; Bilal Piperdi, MD[17]; Ayman Samkari, MD[17]; and Martin Reck, MD, PhD[18] for the KEYNOTE-598 Investigators

J Clin Oncol 2021;[Online ahead of print]

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 10%?

1. Chemotherapy +/- bevacizumab
2. Anti-PD-1/PD-L1 antibody alone
3. Carboplatin/pemetrexed/pembrolizumab
4. Atezolizumab/carboplatin/*nab* paclitaxel
5. Atezolizumab/carboplatin/paclitaxel/bevacizumab
6. Ipilimumab/nivolumab
7. Ipilimumab/nivolumab + chemotherapy
8. Other

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 10%?



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

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%?

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

* Likely dose-reduced chemotherapy

RTP RESEARCH TO PRACTICE

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

1. Chemotherapy +/- bevacizumab
2. Anti-PD-1/PD-L1 antibody alone
3. Carboplatin/pemetrexed/pembrolizumab
4. Atezolizumab/carboplatin/*nab* paclitaxel
5. Atezolizumab/carboplatin/paclitaxel/bevacizumab
6. Ipilimumab/nivolumab
7. Ipilimumab/nivolumab + chemotherapy
8. Other

RTP RESEARCH TO PRACTICE

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

 JOSHUA BAUML, MD	Pembro
 RAMASWAMY GOVINDAN, MD	Pembro/carbo/pem
 JOHN V HEYMACH, MD, PHD	Pembro
 LEORA HORN, MD, MSC	Pembro
 COREY J LANGER, MD	Pembro*
 BENJAMIN LEVY, MD	Pembro
 PROFESSOR TONY SK MOK, MD	Pembro
 JOEL W NEAL, MD, PHD	Pembro +/- carbo/pem
 PAUL K PAIK, MD	Pembro
 NATHAN A PENNELL, MD, PHD	Pembro
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro
 MARTIN RECK, MD, PHD	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%?

 JOSHUA BAUML, MD	Pembro
 RAMASWAMY GOVINDAN, MD	Pembro
 JOHN V HEYMACH, MD, PHD	Pembro
 LEORA HORN, MD, MSC	Pembro
 COREY J LANGER, MD	Pembro
 BENJAMIN LEVY, MD	Pembro
 PROFESSOR TONY SK MOK, MD	Pembro
 JOEL W NEAL, MD, PHD	Pembro
 PAUL K PAIK, MD	Pembro
 NATHAN A PENNELL, MD, PHD	Pembro
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro
 MARTIN RECK, MD, PHD	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%?

 JOSHUA BAUML, MD	Pembro/carbo/pac
 RAMASWAMY GOVINDAN, MD	Pembro/carbo/*nab*-P
 JOHN V HEYMACH, MD, PHD	Pembro/carbo/*nab*-P
 LEORA HORN, MD, MSC	Pembro/carbo/*nab*-P
 COREY J LANGER, MD	Pembro/carbo/*nab*-P
 BENJAMIN LEVY, MD	Pembro/carbo/*nab*-P
 PROFESSOR TONY SK MOK, MD	Pembro/carbo/*nab*-P or Pembro/carbo/pac

 JOEL W NEAL, MD, PHD	Pembro/carbo/ *nab*-P or pac
 PAUL K PAIK, MD	Pembro/carbo/pac
 NATHAN A PENNELL, MD, PHD	Pembro/carbo/*nab*-P
 PROFESSOR SOLANGE PETERS, MD, PHD	Ipi/nivo + carbo/pac
 MARTIN RECK, MD, PHD	Pembro/carbo/pac
 DAVID R SPIGEL, MD	Pembro/carbo/*nab*-P

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%?

 JOSHUA BAUML, MD	Pembro/carbo/pac
 RAMASWAMY GOVINDAN, MD	Pembro
 JOHN V HEYMACH, MD, PHD	Pembro
 LEORA HORN, MD, MSC	Pembro/carbo/*nab*-P
 COREY J LANGER, MD	Pembro/carbo/*nab*-P
 BENJAMIN LEVY, MD	Pembro/carbo/pac
 PROFESSOR TONY SK MOK, MD	Pembro
 JOEL W NEAL, MD, PHD	Pembro/carbo/*nab*-P
 PAUL K PAIK, MD	Pembro/carbo/pac
 NATHAN A PENNELL, MD, PHD	Pembro/carbo/pac
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro/carbo/pac
 MARTIN RECK, MD, PHD	Carbo/*nab*-P
 DAVID R SPIGEL, MD	Pembro/carbo/*nab*-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%?

 JOSHUA BAUML, MD	Pembro
 RAMASWAMY GOVINDAN, MD	Pembro/carbo/*nab*-P
 JOHN V HEYMACH, MD, PHD	Pembro
 LEORA HORN, MD, MSC	Pembro
 COREY J LANGER, MD	Pembro
 BENJAMIN LEVY, MD	Pembro
 PROFESSOR TONY SK MOK, MD	Pembro or Atezo
 JOEL W NEAL, MD, PHD	Pembro +/- carbo/ *nab*-P or pac
 PAUL K PAIK, MD	Pembro
 NATHAN A PENNELL, MD, PHD	Pembro
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro
 MARTIN RECK, MD, PHD	Pembro
 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%?

 JOSHUA BAUML, MD	Pembro
 RAMASWAMY GOVINDAN, MD	Pembro
 JOHN V HEYMACH, MD, PHD	Pembro
 LEORA HORN, MD, MSC	Pembro
 COREY J LANGER, MD	Pembro
 BENJAMIN LEVY, MD	Pembro
 PROFESSOR TONY SK MOK, MD	Pembro or Atezo
 JOEL W NEAL, MD, PHD	Pembro +/- carbo/ *nab*-P
 PAUL K PAIK, MD	Pembro
 NATHAN A PENNELL, MD, PHD	Pembro
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro
 MARTIN RECK, MD, PHD	Pembro
 DAVID R SPIGEL, MD	Pembro

RTP RESEARCH TO PRACTICE

J Thorac Oncol 2021:S1556-0864(21)00022-8

BRIEF REPORT

Four-Year Survival With Durvalumab After Chemoradiotherapy in Stage III NSCLC—an Update From the PACIFIC Trial

Corinne Faivre-Finn, MD, PhD,[a,b,*] David Vicente, MD,[c] Takayasu Kurata, MD,[d] David Planchard, MD, PhD,[e] Luis Paz-Ares, MD, PhD,[f,g] Johan F. Vansteenkiste, MD, PhD,[h] David R. Spigel, MD,[i] Marina C. Garassino, MD,[j] Martin Reck, MD, PhD,[k] Suresh Senan, PhD,[l] Jarushka Naidoo, MBBCH, MHS,[m,n] Andreas Rimner, MD,[o] Yi-Long Wu, MD,[p] Jhanelle E. Gray, MD,[q] Mustafa Özgüroğlu, MD,[r] Ki H. Lee, MD,[s] Byoung C. Cho, MD, PhD,[t] Terufumi Kato, MD,[u] Maike de Wit, MD, PhD,[v] Michael Newton, PharmD,[w] Lu Wang, PhD,[w] Piruntha Thiyagarajah, MD,[x] Scott J. Antonia, MD, PhD[q]

VIRTUAL 2020 ESMO congress

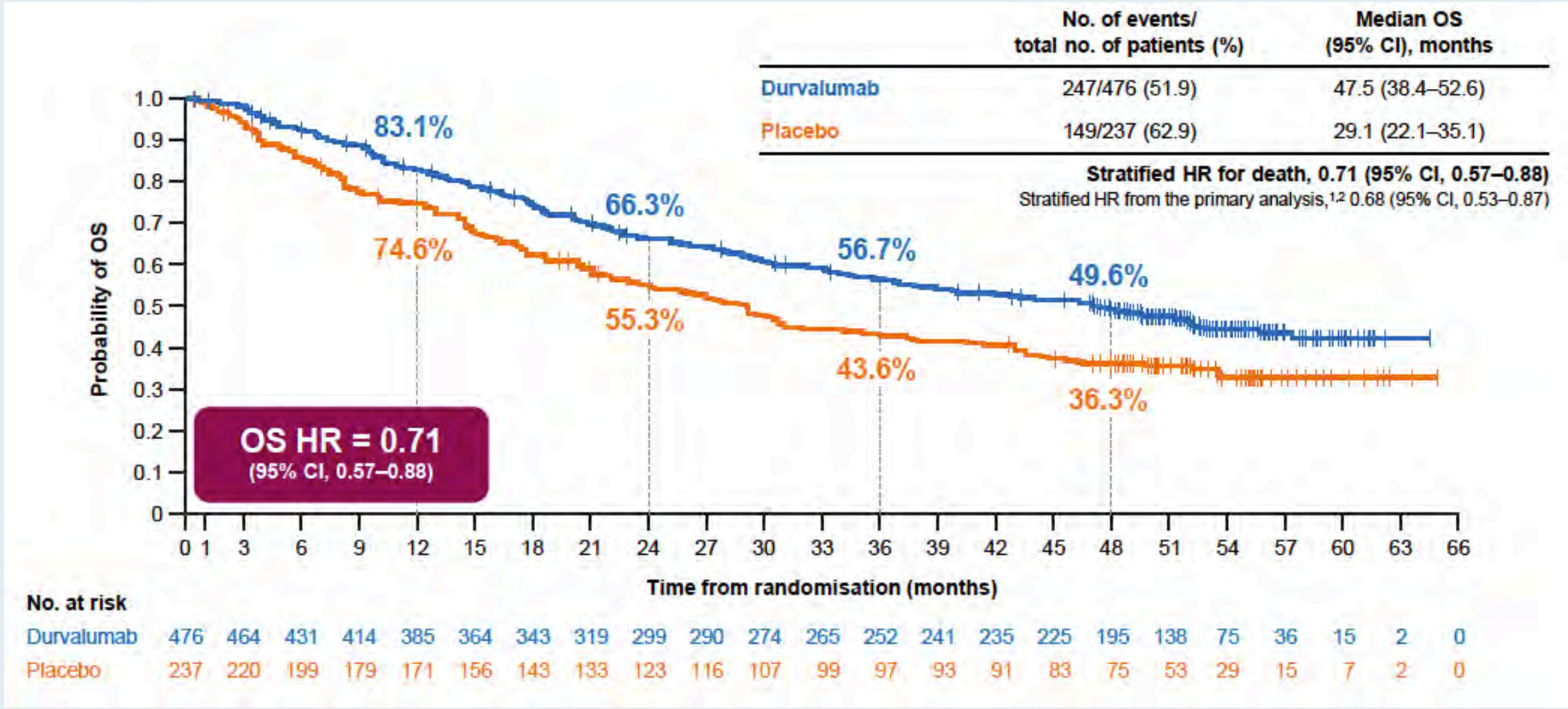
Durvalumab after chemoradiotherapy in Stage III NSCLC: 4-year survival update from the Phase 3 PACIFIC trial

Corinne Faivre-Finn[1], David Vicente[2], Takayasu Kurata[3], David Planchard[4], Luis Paz-Ares[5], Johan F. Vansteenkiste[6], David R. Spigel[7], Marina C. Garassino[8], Martin Reck[9], Suresh Senan[10], Jarushka Naidoo[11,12], Andreas Rimner[13], Yi-Long Wu[14], Jhanelle E. Gray[15], Mustafa Özgüroğlu[16], Ki Hyeong Lee[17], Michael Newton[18], Lu Wang[18], Piruntha Thiyagarajah[19], Scott J. Antonia[15]

[1]The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [2]Hospital Universitario Virgen Macarena, Seville, Spain; [3]Kansai Medical University Hospital, Hirakata, Japan; [4]Gustave Roussy, Department of Medical Oncology, Thoracic Unit, Villejuif, France; [5]Hospital Universitario 12 de Octubre, CiberOnc, Universidad Complutense and CNIO, Madrid, Spain; [6]Department of Respiratory Oncology, University Hospitals KU Leuven, Leuven, Belgium; [7]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, Tennessee, USA; [8]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [9]Lung Clinic Grosshansdorf, Airway Research Center North, German Center for Lung Research, Grosshansdorf, Germany; [10]Department of Radiation Oncology, Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, The Netherlands; [11]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD, USA; [12]Bloomberg-Kimmel Institute for Cancer Immunotherapy at John Hopkins University, Baltimore, MD, USA; [13]Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, New York, USA; [14]Department of Pulmonary Oncology, Guangdong Lung Cancer Institute, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou, China; [15]H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, USA; [16]Istanbul University – Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; [17]Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, South Korea; [18]AstraZeneca, Gaithersburg, MD, USA; [19]AstraZeneca, Cambridge, UK

ESMO 2020;Abstract LBA49

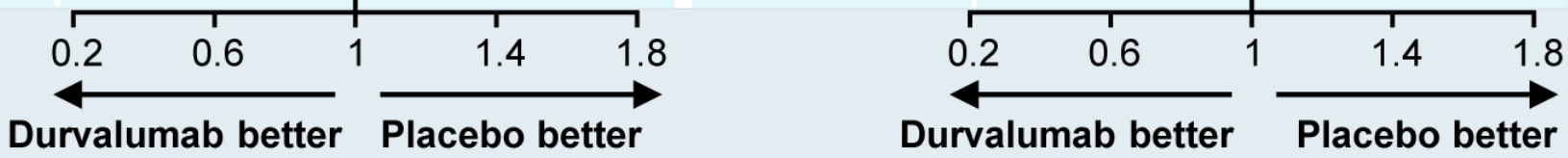
PACIFIC: 4-Year Overall Survival – Intent-To-Treat Population



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

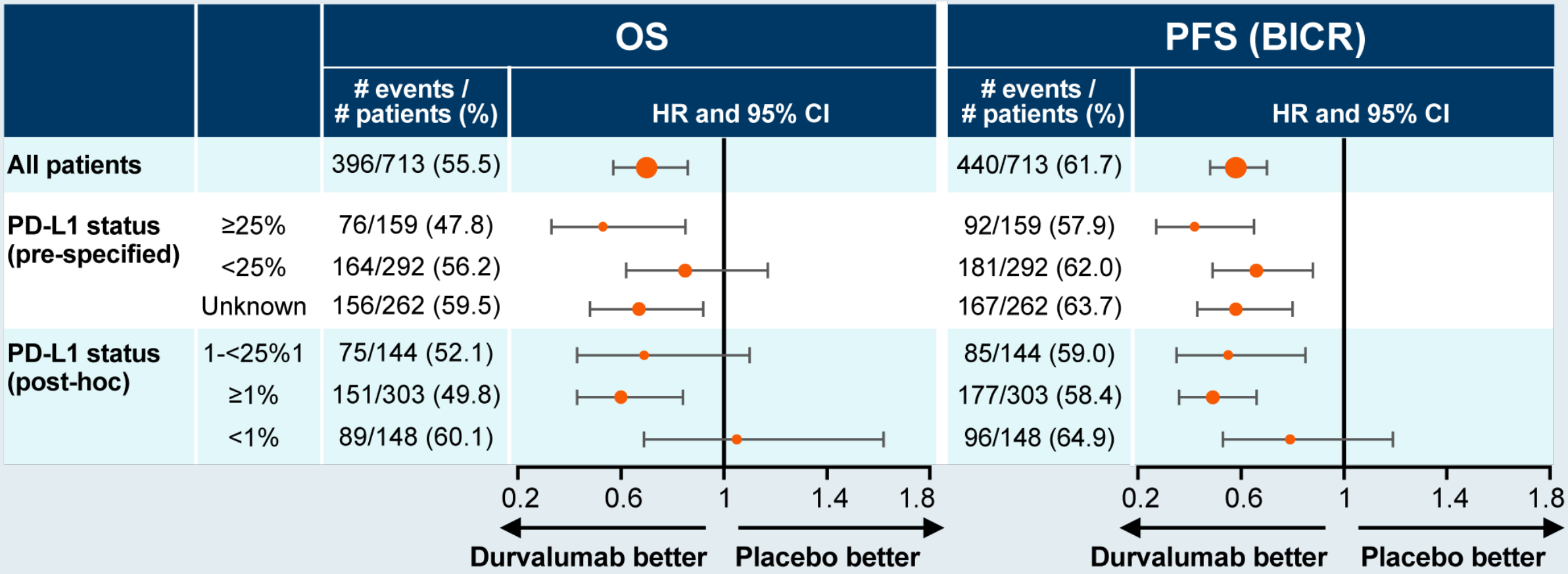
PACIFIC: Updated Outcomes by EGFR Status

		OS		PFS (BICR)	
		# events / # patients (%)	HR and 95% CI	# events / # patients (%)	HR and 95% CI
***EGFR* mutation**	Positive	24/43 (55.8)		32/43 (74.4)	
	Negative	261/482 (54.1)		290/482 (60.2)	
	Unknown	111/188 (59.0)		118/188 (62.8)	



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

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)
  - PD-L1 expression-level cutoff of 1% was part of an unplanned post-hoc analysis requested by the EMA

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

Drugs (2019) 79:1937–1945
https://doi.org/10.1007/s40265-019-01222-w

REVIEW ARTICLE

Immune Checkpoint Inhibition in Non-metastatic Non-small Cell Lung Cancer: Chance for Cure?

David F. Heigener[1,2] · Martin Reck[3,4]

EDITORIAL

IASLC

Combination of Immunotherapy and Radiotherapy—The Next Magic Step in the Management of Lung Cancer?

Lizza E. L. Hendriks, MD, PhD,[a,*] Jessica Menis, MD,[b,c]
Dirk K. M. De Ruysscher, MD, PhD,[d] Martin Reck, MD, PhD[e]

J Thorac Oncol 2021;[Online ahead of print]

ORIGINAL ARTICLE

First-Line Nivolumab Plus Ipilimumab Versus Chemotherapy in Advanced NSCLC With 1% or Greater Tumor PD-L1 Expression: Patient-Reported Outcomes From CheckMate 227 Part 1

Martin Reck, MD, PhD,[a,*] Tudor-Eliade Ciuleanu, MD, PhD,[b] Jong-Seok Lee, MD,[c] Michael Schenker, MD,[d] Clarisse Audigier-Valette, MD,[e] Bogdan Zurawski, MD, PhD,[f] Helena Linardou, MD, PhD,[g] Gregory A. Otterson, MD,[h] Pamela Salman, MD,[i] Makoto Nishio, MD, PhD,[j] Emmanuel de la MoraJimenez, MD,[k] Krysztof Lesniewski-Kmak, MD,[l] István Albert, MD,[m] Samreen Ahmed, FRCP, MD,[n] Konstantinos Syrigos, MD, PhD,[o] John R. Penrod, PhD,[p] Yong Yuan, PhD,[p] Steven I. Blum, MBA, MA,[p] Faith E. Nathan, MD,[p] Xiaowu Sun, PhD,[q] Alejandro Moreno-Koehler, MPH,[q] Fiona Taylor, MBiochem,[q] Kenneth John O'Byrne, MD[r]

VIRTUAL 2020 ESMO congress

ESMO 2020;Abstract 1781MO

IMpower133: characterisation of long-term survivors treated with first line chemotherapy ± atezolizumab in extensive-stage small cell lung cancer

Stephen V. Liu,[1] Leora Horn,[2] Tony S. K. Mok,[3] Aaron S. Mansfield,[4] Richard De Boer,[5] Gyorgy Losonczy,[6] Shunichi Sugawara,[7] Rafal Dziadziuszko,[8] Maciej Krzakowski,[9] Alexey Smolin,[10] Maximilian Hochmair,[11] Marina Garassino,[12] Sivuonthanh Lam,[13] Mark McCleland,[13] Andres Cardona,[14] Stefanie Morris,[14] Martin Reck[15]

RTP RESEARCH TO PRACTICE

original reports

Updated Overall Survival and PD-L1 Subgroup Analysis of Patients With Extensive-Stage Small-Cell Lung Cancer Treated With Atezolizumab, Carboplatin, and Etoposide (IMpower133)

Stephen V. Liu, MD[1]; Martin Reck, MD, PhD[2]; Aaron S. Mansfield, MD[3]; Tony Mok, MD[4]; Arnaud Scherpereel, MD, PhD[5]; Niels Reinmuth, MD, PhD[6]; Marina Chiara Garassino, MD[7]; Javier De Castro Carpeno, MD[8]; Raffaele Califano, MD[9]; Makoto Nishio, MD[10]; Francisco Orlandi, MD[11]; Jorge Alatorre-Alexander, MD[12]; Ticiana Leal, MD[13]; Ying Cheng, MD[14]; Jong-Seok Lee, MD[15]; Sivuonthanh Lam, PharmD[16]; Mark McCleland, PhD[16]; Yu Deng, PhD[16]; See Phan, MD[16]; and Leora Horn, MD[17]

J Clin Oncol 2021;[Online ahead of print]

Consolidation nivolumab and ipilimumab vs observation in limited stage SCLC after chemo-radiotherapy – Results from the randomized phase II ETOP/IFCT 4-12 STIMULI trial

etop
Information | Research

Solange Peters, Jean-Louis Pujol, Urania Dafni, Jesús Andrade, Annemarie Becker, Manuel Dómine, Alessandra Curioni-Fontecedro, Olivier Molinier, Denis Moro-Sibilot, Kristiaan Nackaerts, Amelia Insa Mollá, Guillermo López Vivanco, Jeannick Madelaine, Sanjay Popat, Martin Reck, Heidi Roschitzki-Voser, Paul Mitchell, Dirk De Ruysscher, Cécile Le Pechoux, Rolf Stahel

ESMO 2020;Abstract LBA84

VIRTUAL 2020 ESMO congress

RTP RESEARCH TO PRACTICE

Lung Cancer 144 (2020) 76–84

Contents lists available at ScienceDirect

Lung Cancer

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

Review

Anti-angiogenic agents in the age of resistance to immune checkpoint inhibitors: Do they have a role in non-oncogene-addicted non-small cell lung cancer?

Sanjay Popat[a,b,*], Christian Grohé[c], Jesus Corral[d], Martin Reck[e], Silvia Novello[f], Maya Gottfried[g], Dejan Radonjic[h], Rolf Kaiser[h,i]

COLD SPRING HARBOR
Molecular Case Studies

RAPID CANCER COMMUNICATION

Cold Spring Harb Mol Case Stud 2019;5(6):a004630

Serial liquid biopsies for detection of treatment failure and profiling of resistance mechanisms in *KLC1–ALK*-rearranged lung cancer

Steffen Dietz,[1,2,11] Petros Christopoulos,[2,3,4,11] Lisa Gu,[1,2] Anna-Lena Volckmar,[5] Volker Endris,[5] Zhao Yuan,[6] Simon J. Ogrodnik,[1,2] Tomasz Zemojtel,[7] Claus-Peter Heussel,[2,8] Marc A. Schneider,[2,4] Michael Meister,[2,4] Thomas Muley,[2,4] Martin Reck,[9] Matthias Schlesner,[2,6] Michael Thomas,[2,3] Albrecht Stenzinger,[2,5,10,11] and Holger Sültmann[1,2,11]

EBioMedicine 62 (2020) 103103

Contents lists available at ScienceDirect

EBioMedicine

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

Research paper

Longitudinal therapy monitoring of ALK-positive lung cancer by combined copy number and targeted mutation profiling of cell-free DNA

Steffen Dietz[1,2,*], Petros Christopoulos[2,3,*], Zhao Yuan[5], Arlou Kristina Angeles[1,2], Lisa Gu[1,2], Anna-Lena Volckmar[4], Simon J. Ogrodnik[1,2], Florian Janke[1,2,6], Chiara Dalle Fratte[1,7], Tomasz Zemojtel[8], Marc A. Schneider[2,9], Daniel Kazdal[2,4], Volker Endris[4], Michael Meister[2,9], Thomas Muley[2,9], Erika Cecchin[7], Martin Reck[10], Matthias Schlesner[2,5], Michael Thomas[2,3], Albrecht Stenzinger[4,11], Holger Sültmann[1,2,#]

FDA Grants Breakthrough Therapy Designation to Trastuzumab Deruxtecan for Metastatic NSCLC with a HER2 Mutation

Press Release – May 18, 2020

- The FDA has granted breakthrough therapy designation to trastuzumab deruxtecan for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumours have a HER2 mutation and with disease progression on or after platinum-based therapy.
- The designation was granted based on data from the ongoing Phase II DESTINY-Lung01 trial currently testing trastuzumab deruxtecan, a HER2-directed antibody drug conjugate (ADC), in patients with HER2-mutant metastatic NSCLC.

https://www.astrazeneca.com/media-centre/press-releases/2020/enhertu-granted-breakthrough-therapy-designation-in-the-us-for-her2-mutant-metastatic-non-small-cell-lung-cancer.html

RTP RESEARCH TO PRACTICE

Trastuzumab Deruxtecan in HER2-Mutated Metastatic Non-Small Cell Lung Cancer (NSCLC): Interim Results of DESTINY-Lung01[1]

Trastuzumab Deruxtecan in HER2-Overexpressing Metastatic Non-Small Cell Lung Cancer (NSCLC): Interim Results of DESTINY-Lung01[2]

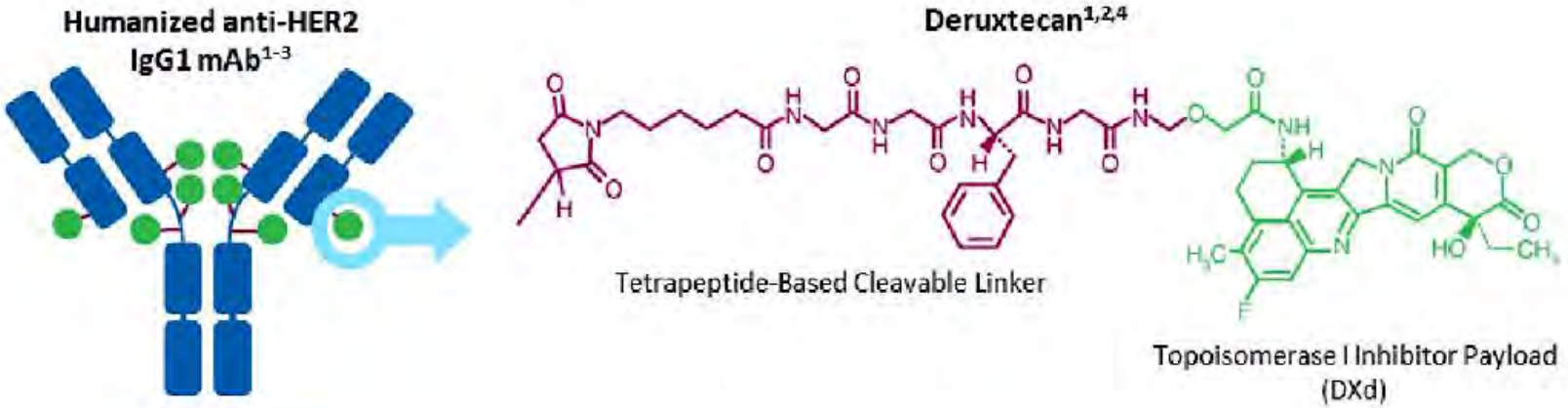
[1] Smit EF et al.
WCLC 2021;Abstract MA11.03.

[2] Nakagawa K et al.
WCLC 2021;Abstract OA04.05.

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

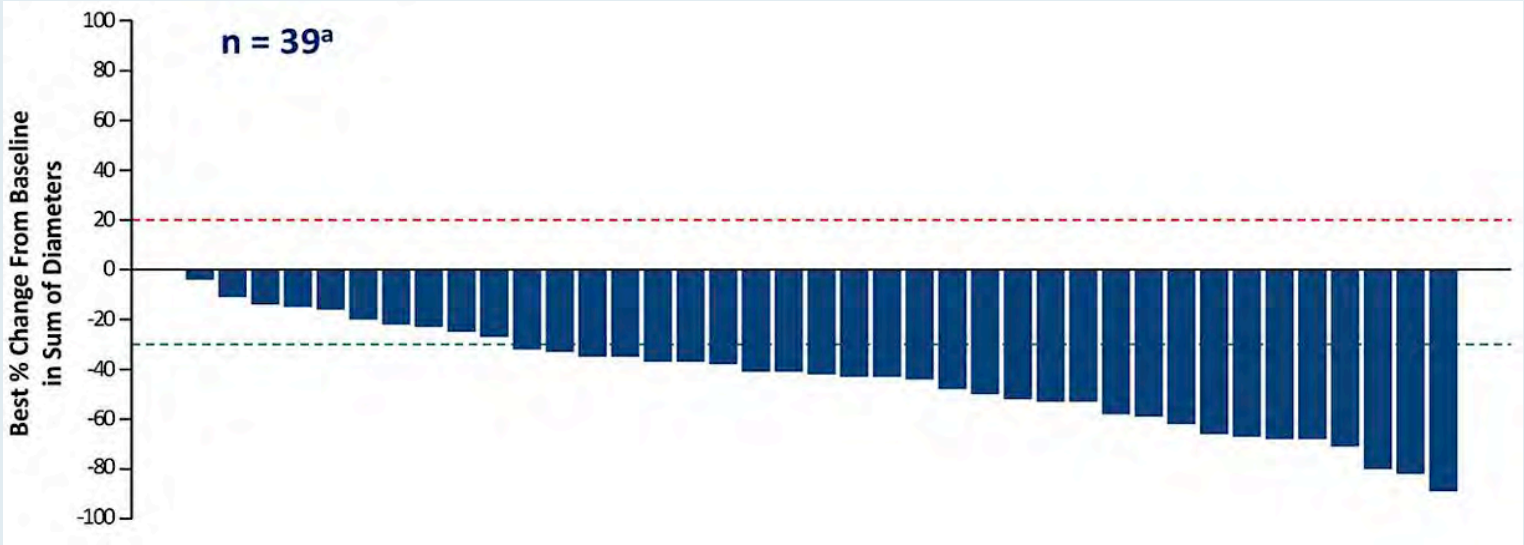


Payload mechanism of action: topoisomerase I inhibitor
High potency of payload
High drug to antibody ratio ≈ 8
Payload with short systemic half-life
Stable linker-payload
Tumor-selective cleavable linker
Membrane-permeable payload

Smit EF et al. ASCO 2020;Abstract 9504.

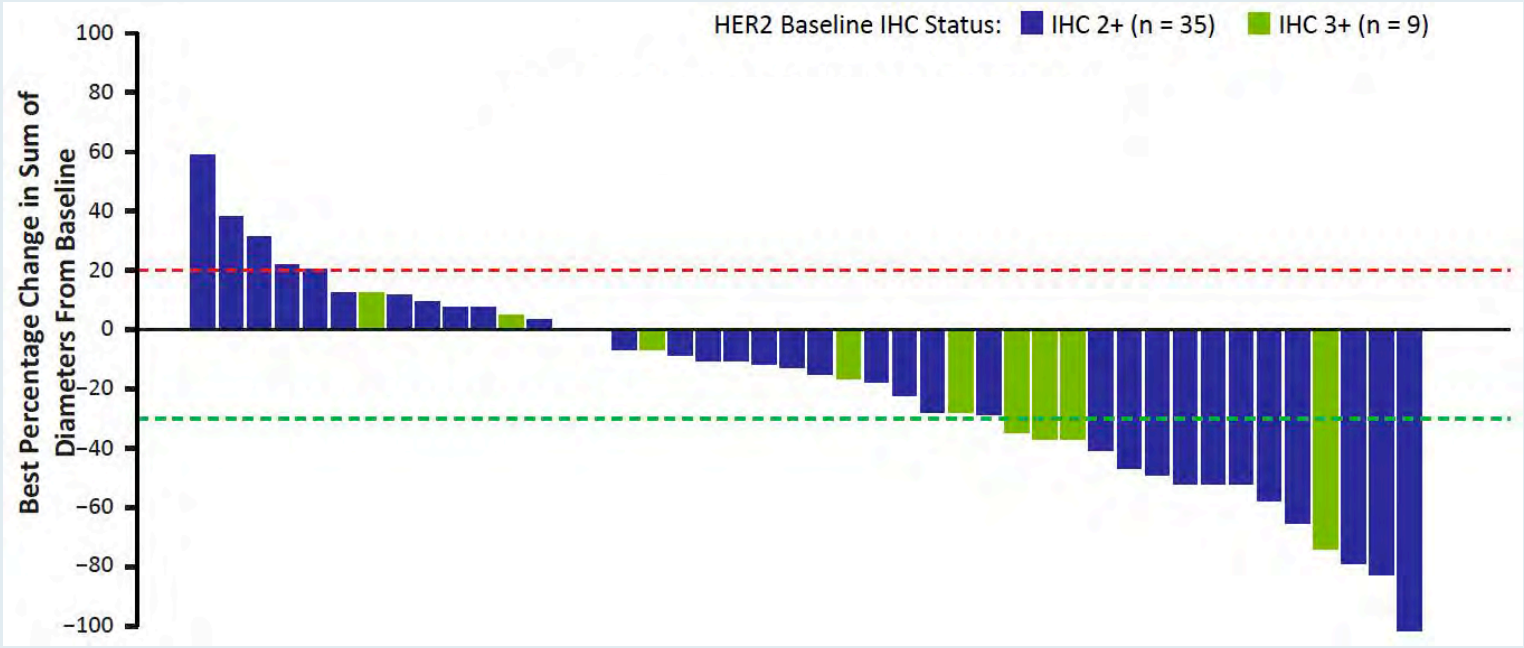
DESTINY-Lung01: Best Percentage Change in Tumor Size with T-Dxd in HER2-Mutant versus Overexpressing NSCLC

Mutant



Confirmed ORR = 61.9%
DCR = 90.5%
Median DoR = not reached
Median PFS = 14.0 months

Overexpressing



Confirmed ORR = 24.5%
DCR = 69.4%
Median DoR = 6.0 months
Median PFS = 5.4 months

Smit EF et al. WCLC 2021;Abstract MA11.03; Nakagawa K et al. WCLC 2021;Abstract OA04.05.

RTP RESEARCH TO PRACTICE

Supportive Care in Cancer (2020) 28:2693–2700
https://doi.org/10.1007/s00520-019-05088-2

ORIGINAL ARTICLE

Perceived relatedness, death acceptance, and demoralization in patients with cancer

Rebecca Philipp[1] · Anja Mehnert[2] · Volkmar Müller[3] · Martin Reck[4] · Sigrun Vehling[1]

Meet The Professor with Dr Reck

Module 1: Cases from Dr Peswani

Module 2: Lung Cancer Journal Club with Dr Reck

Module 3: Other Key Papers and Recent Approvals for Discussion

RTP
RESEARCH
TO PRACTICE

Targeted Therapies

FDA Approves Ramucirumab with Erlotinib for First-Line NSCLC

Press Release – May 29, 2020

"The Food and Drug Administration approved ramucirumab in combination with erlotinib for first-line treatment of metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.

Efficacy was evaluated in RELAY (NCT02411448), a multinational, randomized, double-blind, placebo-controlled, multicenter study in patients with previously untreated metastatic NSCLC whose tumors have EGFR exon 19 deletion or exon 21 (L858R) substitution mutations. A total of 449 patients were randomized (1:1) to receive either ramucirumab 10 mg/kg or placebo every 2 weeks as an intravenous infusion, in combination with erlotinib 150 mg orally once daily, until disease progression or unacceptable toxicity."

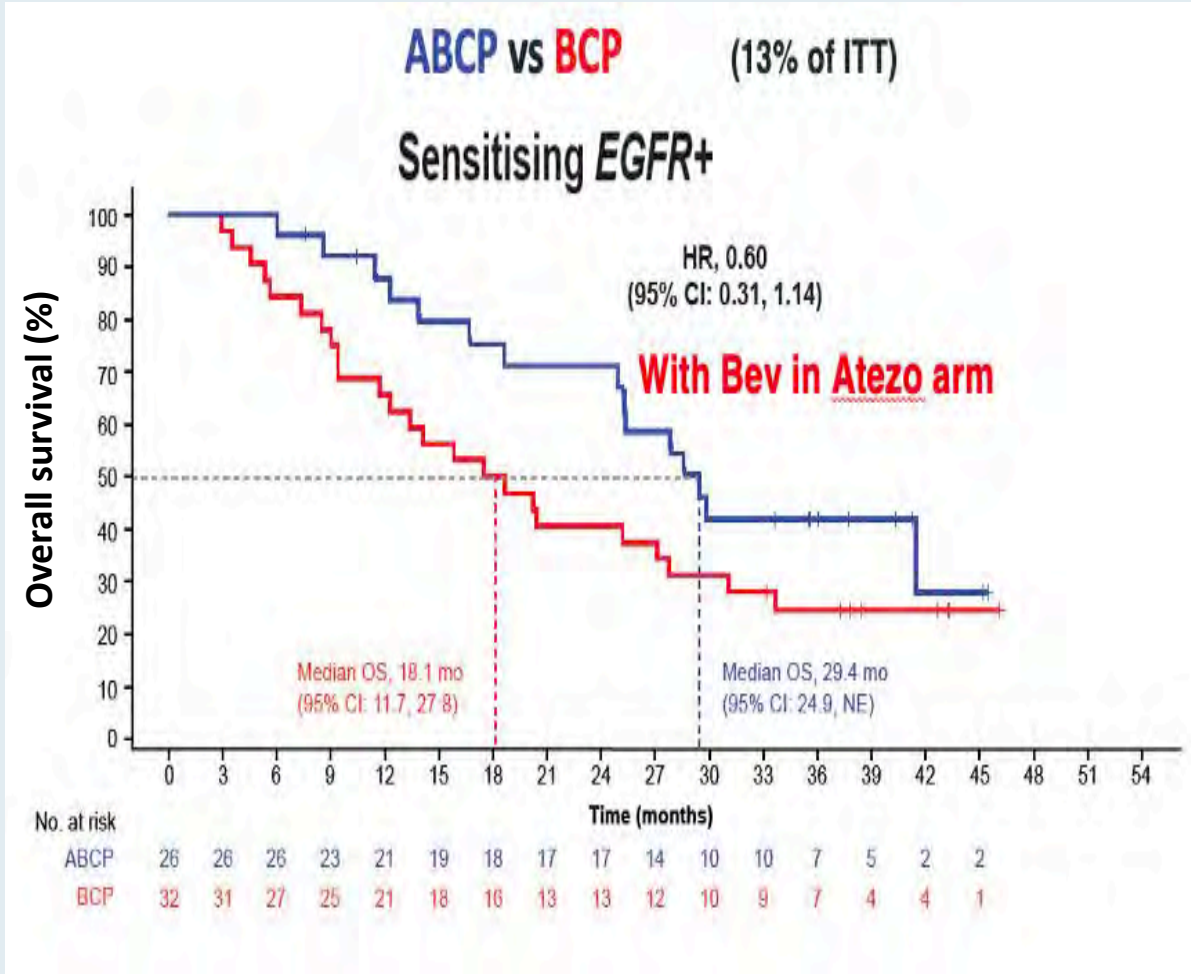
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-ramucirumab-plus-erlotinib-first-line-metastatic-nsclc

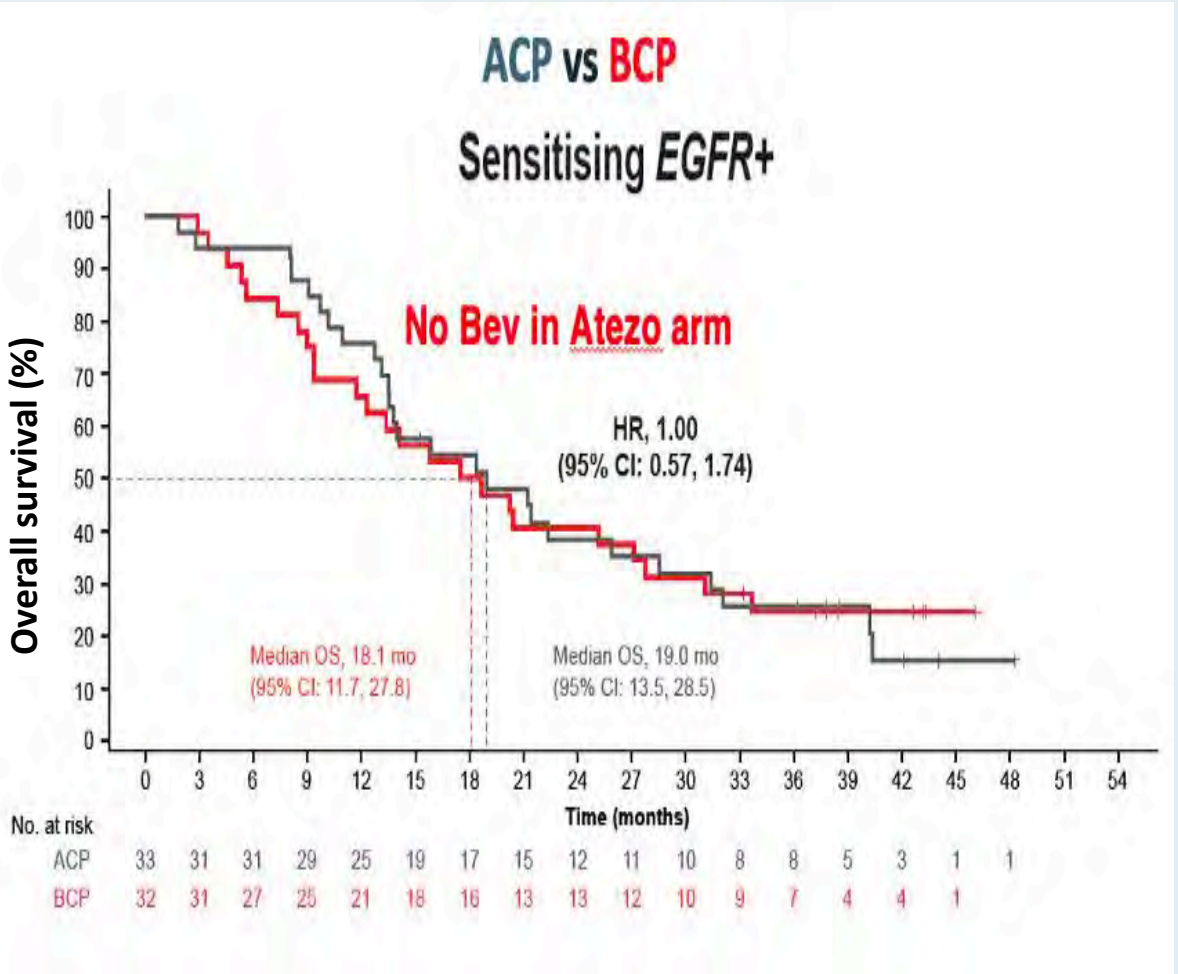
IMpower150: Updated Efficacy Analysis in Patients with EGFR Mutations

Reck M et al.

ESMO 2020;Abstract 1293P.

IMpower150 Trial: OS Benefit of First-Line Atezolizumab for Patients with Metastatic NSCLC with EGFR Tumor Mutations





ABCP = atezolizumab + bevacizumab/carboplatin/paclitaxel; BCP = bevacizumab/carboplatin/paclitaxel

Reck M et al. ESMO 2020;Abstract 1293P.

RTP RESEARCH TO PRACTICE

FDA Approves Brigatinib for ALK-Positive Metastatic NSCLC

Press Release – May 22, 2020

The Food and Drug Administration approved brigatinib for adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.

Today, the FDA also approved the Vysis ALK Break Apart FISH Probe Kit as a companion diagnostic for brigatinib.

Efficacy was investigated in ALTA 1L (NCT02737501), a randomized (1:1), open-label, multicenter trial in adult patients with advanced ALK-positive NSCLC who had not previously received an ALK-targeted therapy. The trial required patients to have an ALK rearrangement based on a local standard of care testing. The trial randomized 275 patients to receive brigatinib 180 mg orally once daily with a 7-day lead-in at 90 mg once daily (n=137) or crizotinib 250 mg orally twice daily (n=138). A subset of the clinical samples was retrospectively tested with the Vysis ALK Break Apart FISH Probe Kit. Of the enrolled patients, 239 had positive results using the Vysis diagnostic test (central results were negative for 20 patients and unavailable for 16 patients).

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-brigatinib-alk-positive-metastatic-nsclc

The NEW ENGLAND JOURNAL of MEDICINE

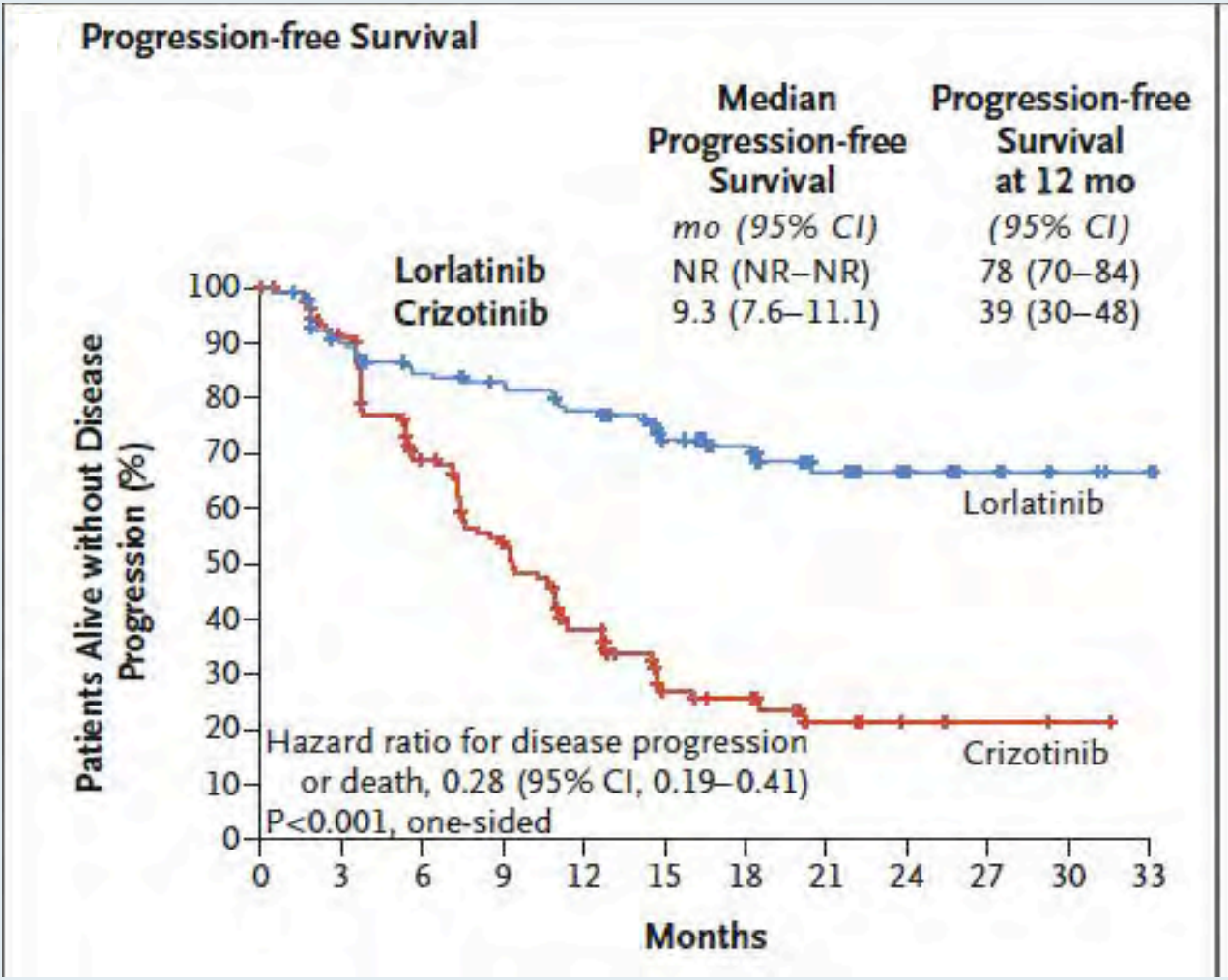
ORIGINAL ARTICLE

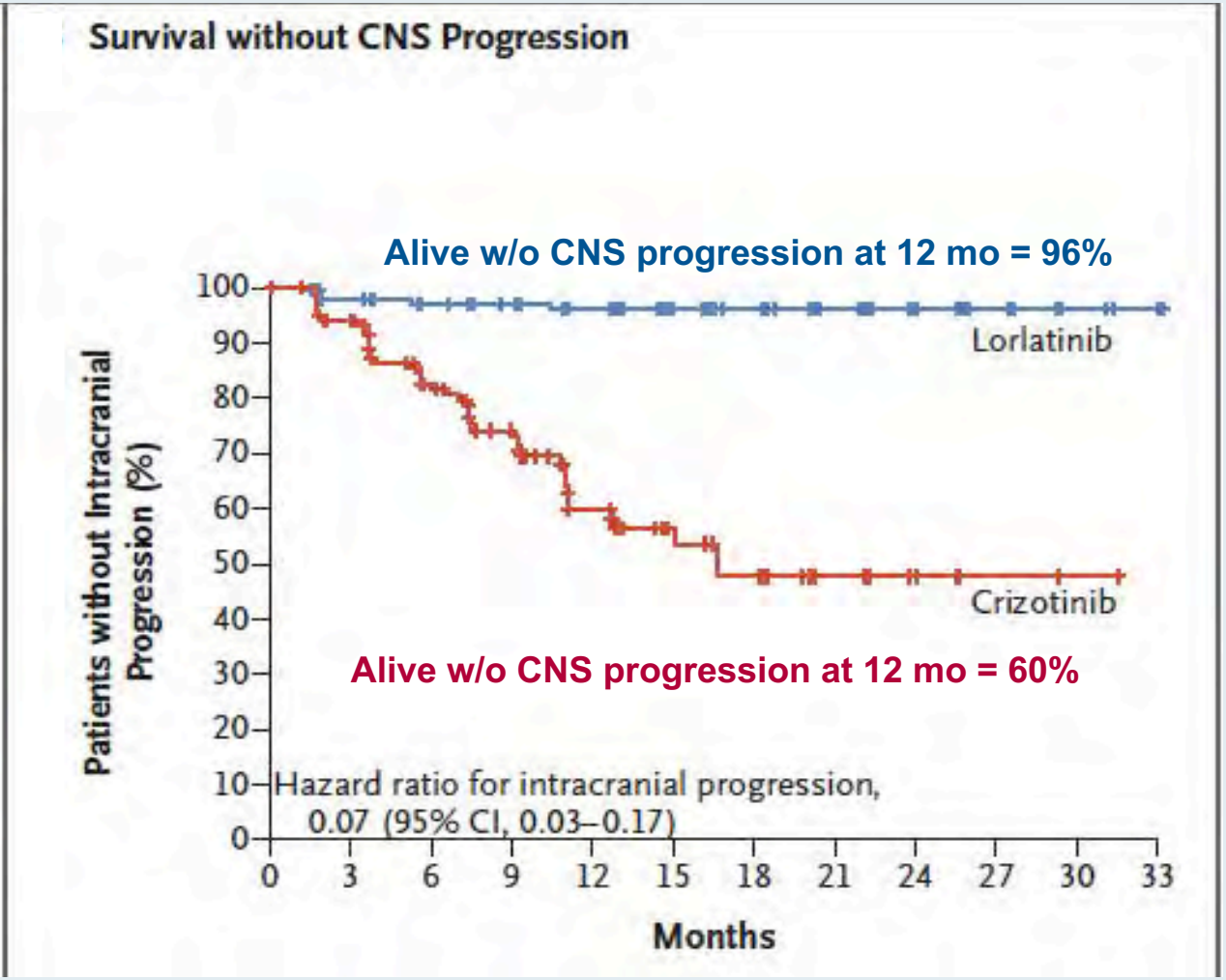
First-Line Lorlatinib or Crizotinib in Advanced *ALK*-Positive Lung Cancer

Alice T. Shaw, M.D., Ph.D., Todd M. Bauer, M.D., Filippo de Marinis, M.D., Ph.D., Enriqueta Felip, M.D., Ph.D., Yasushi Goto, M.D., Ph.D., Geoffrey Liu, M.D., Julien Mazieres, M.D., Ph.D., Dong-Wan Kim, M.D., Ph.D., Tony Mok, M.D., Anna Polli, B.Sc., Holger Thurm, M.D., Anna M. Calella, Ph.D., Gerson Peltz, M.D., M.P.H., and Benjamin J. Solomon, M.B., B.S., Ph.D., for the CROWN Trial Investigators*

N Engl J Med 2020;383(21):2018-29.

CROWN: PFS and Survival without Intracranial Progression



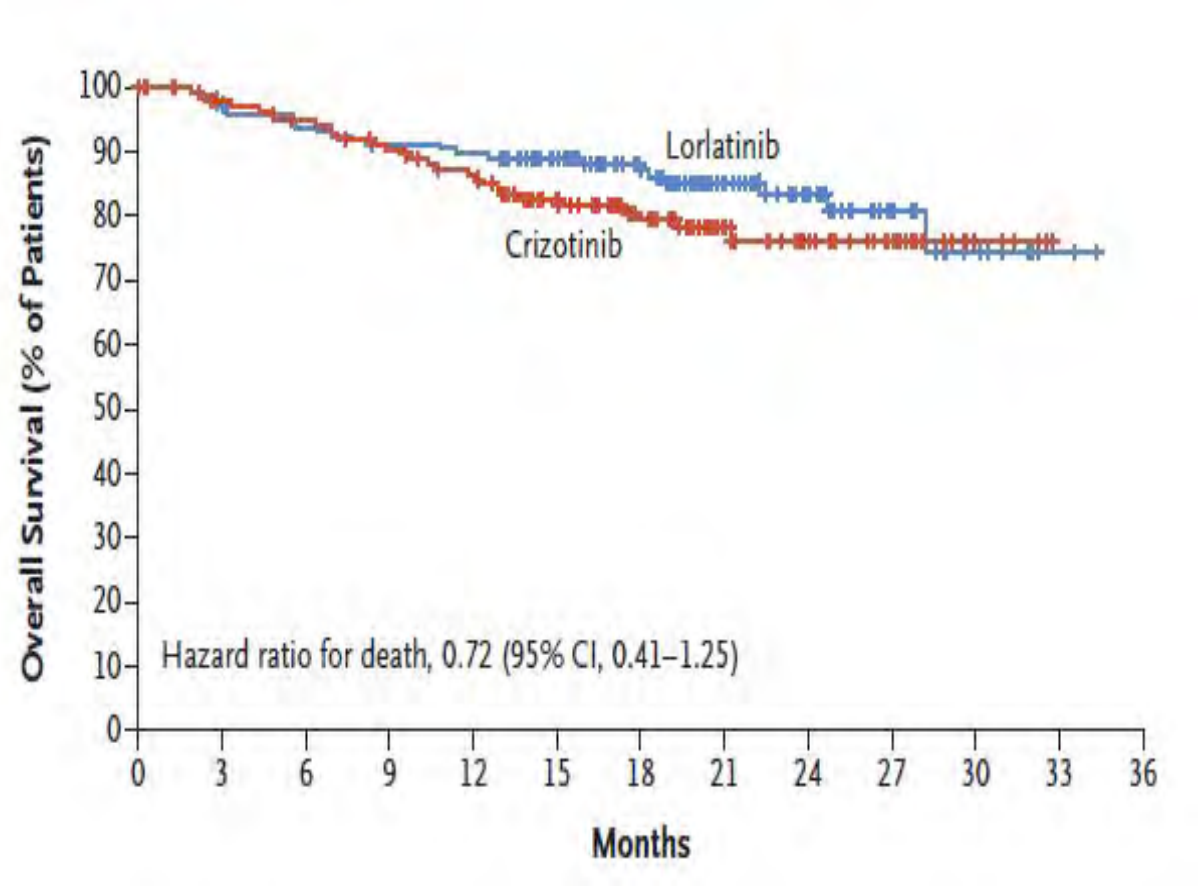


Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29.

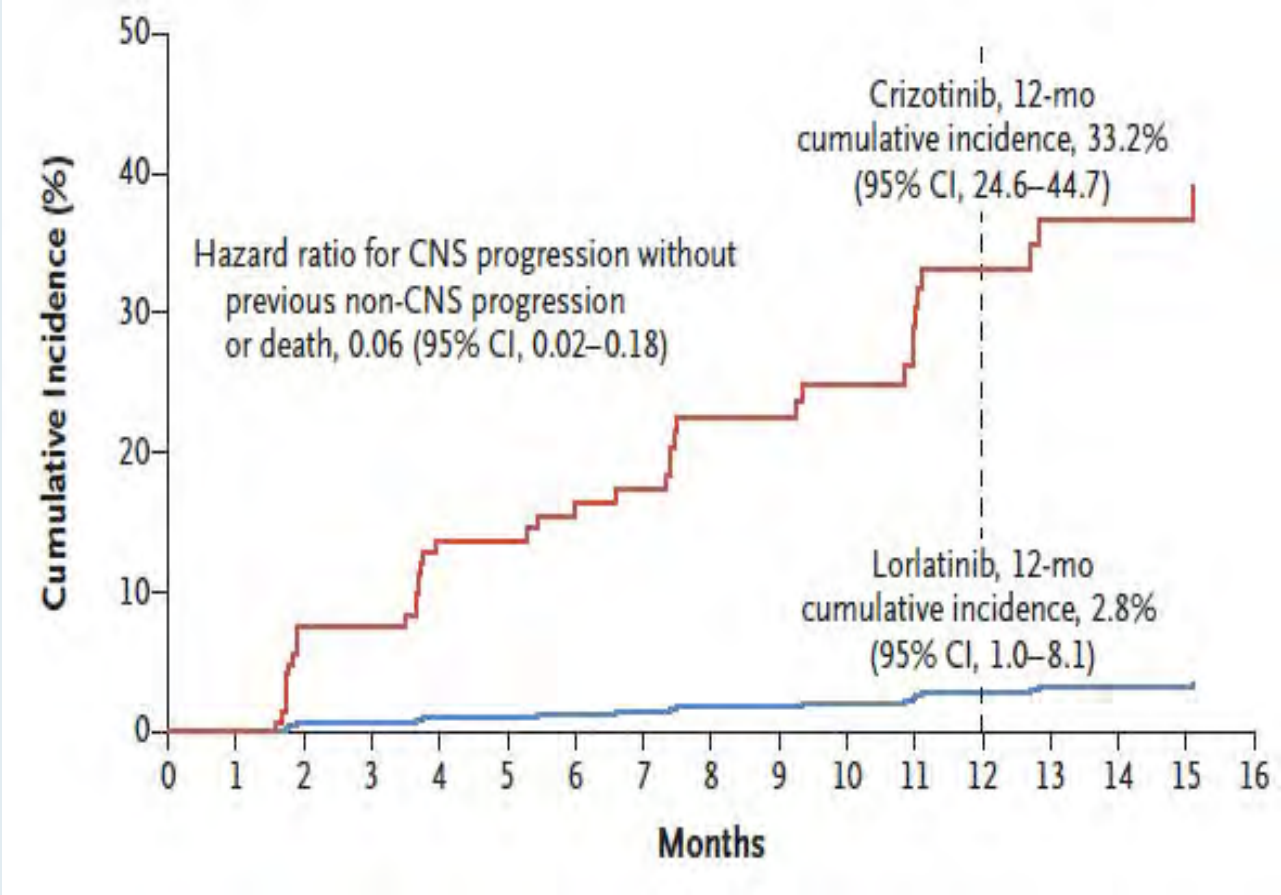
RTP RESEARCH TO PRACTICE

CROWN: OS and Cumulative Incidence of CNS Progression

Overall Survival



Cumulative Incidence of CNS Progression as First Event



Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29.

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

The NEW ENGLAND JOURNAL of MEDICINE

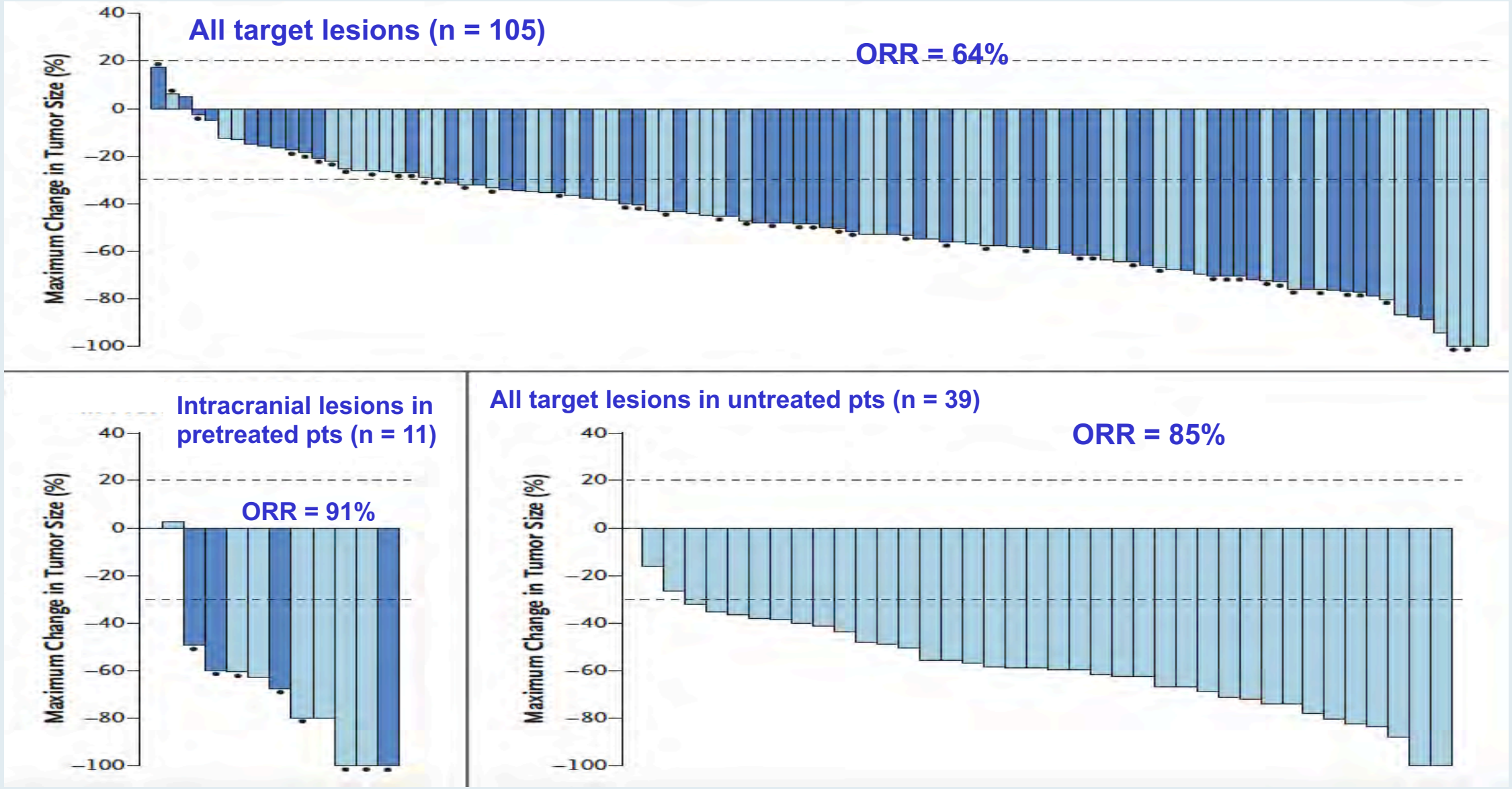
ESTABLISHED IN 1812 AUGUST 27, 2020 VOL. 383 NO. 9

Efficacy of Selpercatinib in *RET* Fusion–Positive Non–Small-Cell Lung Cancer

A. Drilon, G.R. Oxnard, D.S.W. Tan, H.H.F. Loong, M. Johnson, J. Gainor, C.E. McCoach, O. Gautschi, B. Besse, B.C. Cho, N. Peled, J. Weiss, Y.-J. Kim, Y. Ohe, M. Nishio, K. Park, J. Patel, T. Seto, T. Sakamoto, E. Rosen, M.H. Shah, F. Barlesi, P.A. Cassier, L. Bazhenova, F. De Braud, E. Garralda, V. Velcheti, M. Satouchi, K. Ohashi, N.A. Pennell, K.L. Reckamp, G.K. Dy, J. Wolf, B. Solomon, G. Falchook, K. Ebata, M. Nguyen, B. Nair, E.Y. Zhu, L. Yang, X. Huang, E. Olek, S.M. Rothenberg, K. Goto, and V. Subbiah

N Engl J Med 2020;383(9):813-24.

LIBRETTO-001: Response by Independent Review



Drilon A et al. *N Engl J Med* 2020;383(9):813-24.

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

Press Release – September 4, 2020

"On September 4, 2020, the Food and Drug Administration granted accelerated approval to pralsetinib for adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.

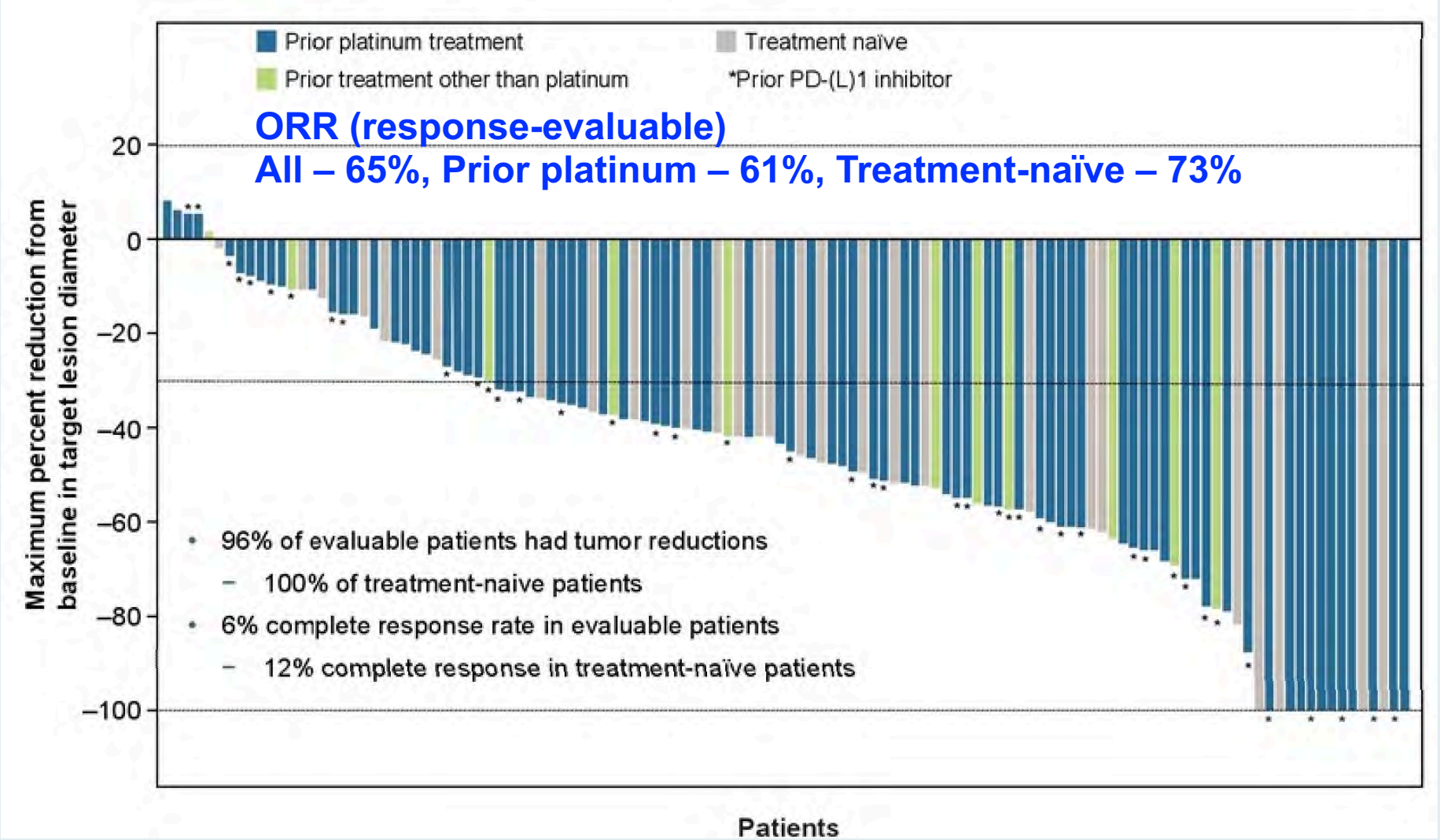
Today, FDA also approved the Oncomine Dx Target (ODxT) Test as a companion diagnostic for pralsetinib.

Efficacy was investigated in a multicenter, open-label, multi-cohort clinical trial (ARROW, NCT03037385) in patients whose tumors had RET alterations. Identification of RET gene alterations was prospectively determined in local laboratories using either next generation sequencing, fluorescence in situ hybridization, or other tests. The main efficacy outcome measures were overall response rate (ORR) and response duration determined by a blinded independent review committee using RECIST 1.1."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pralsetinib-lung-cancer-ret-gene-fusions

RTP RESEARCH TO PRACTICE

ARROW Primary Endpoint: Response to Pralsetinib



Gainor JF et al. ASCO 2020;Abstract 9515.

RTP RESEARCH TO PRACTICE

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

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

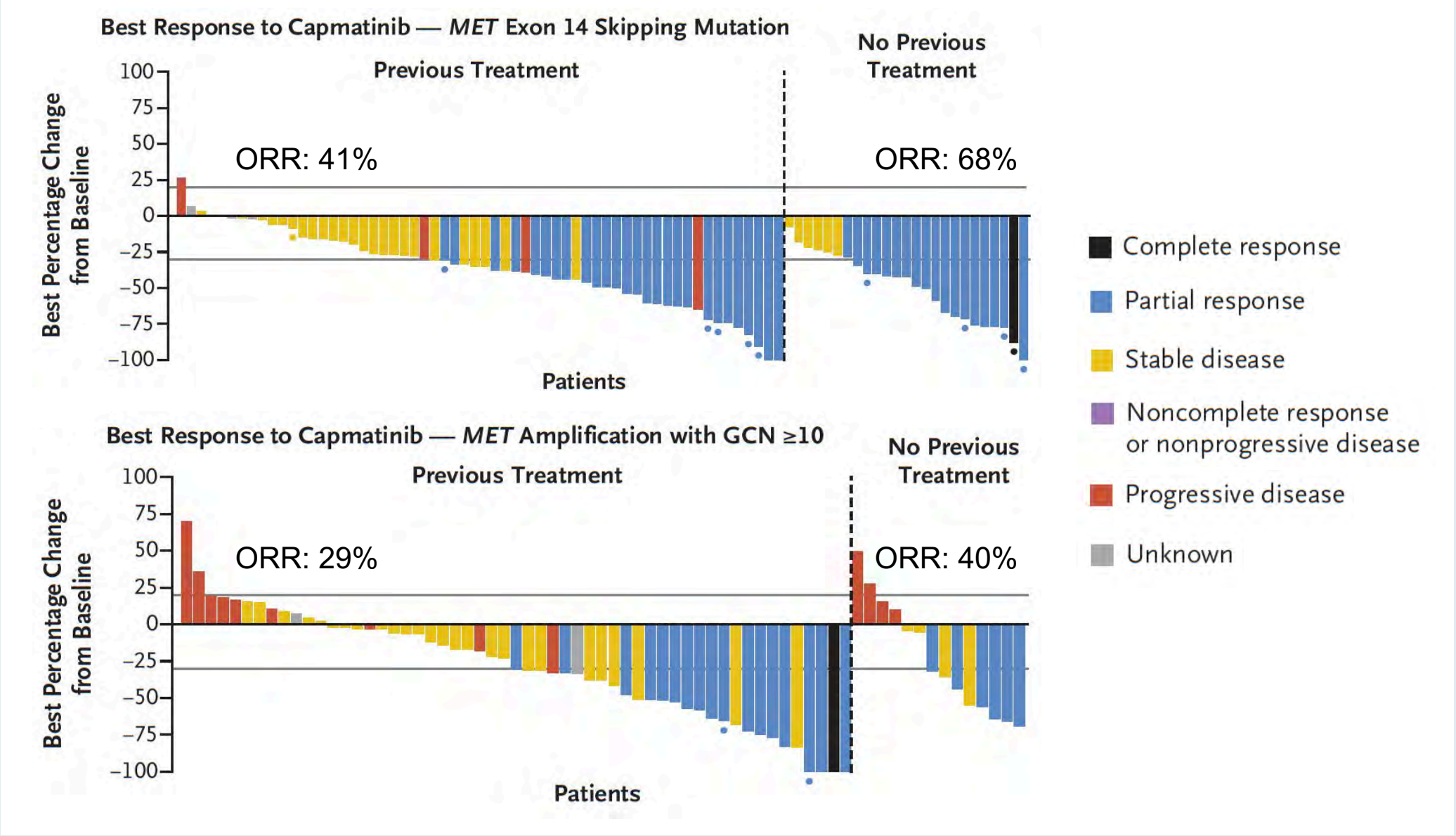
Capmatinib in *MET* Exon 14–Mutated or *MET*-Amplified Non–Small-Cell Lung Cancer

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.

RTP RESEARCH TO PRACTICE

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

Press Release — February 03, 2021

"On February 3, 2021, the Food and Drug Administration granted accelerated approval to tepotinib for adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (MET) exon 14 skipping alterations.

Efficacy was demonstrated in the VISION trial (NCT02864992), a multicenter, non-randomized, open-label, multicohort study enrolling 152 patients with advanced or metastatic NSCLC with MET exon 14 skipping alterations. Patients received tepotinib 450 mg orally once daily until disease progression or unacceptable toxicity."

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

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

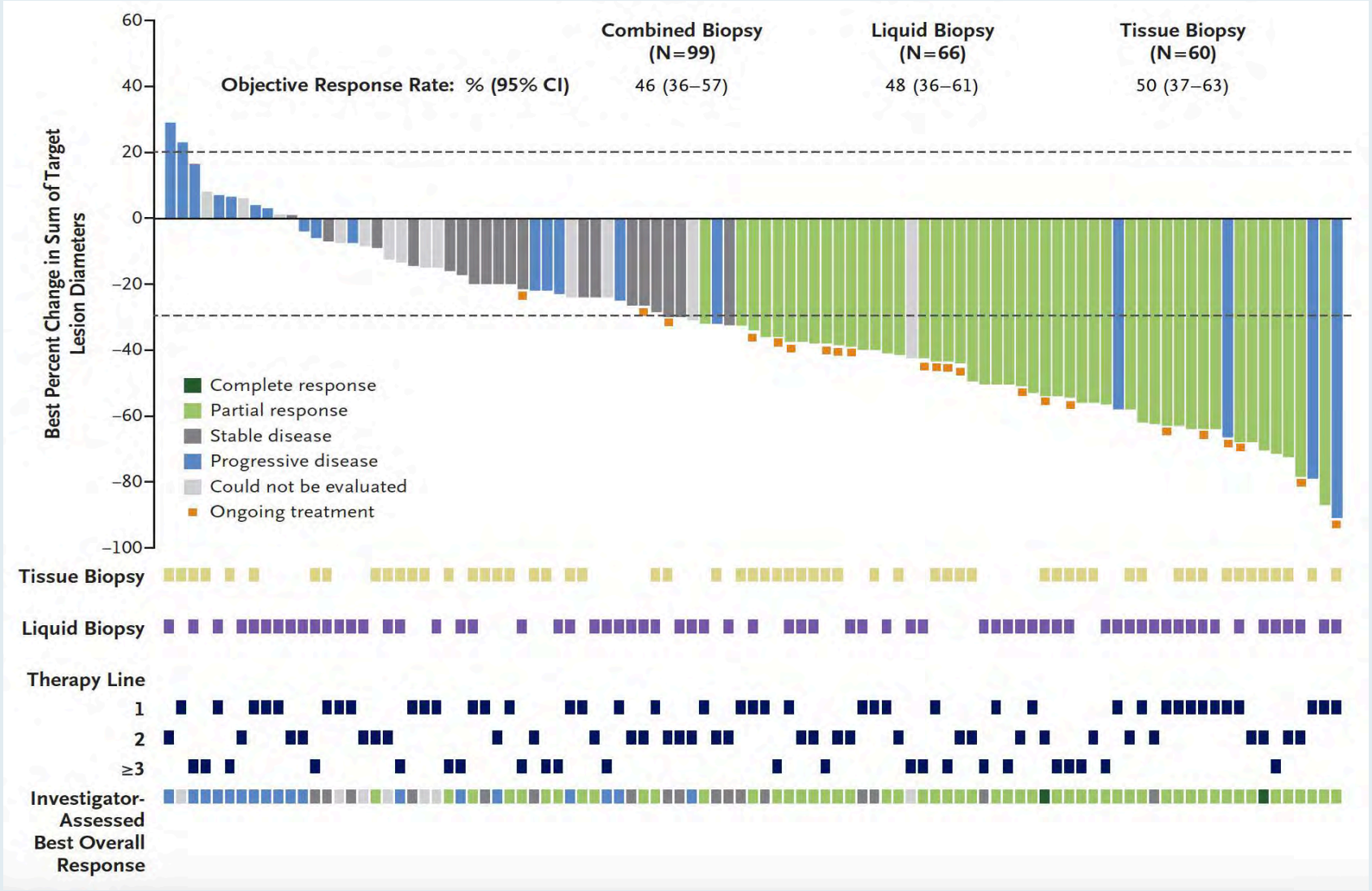
ORIGINAL ARTICLE

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.

VISION Trial of Tepotinib: Response Rate and Change from Baseline in Tumor Burden



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

FDA Grants Breakthrough Therapy Designation to Sotorasib for NSCLC with a KRAS G12C Mutation

Press Release – December 08, 2020

- "The FDA has granted breakthrough therapy designation to the investigational KRASG12C inhibitor, sotorasib, for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a *KRAS G12C* mutation, as determined by an FDA-approved test, following at least 1 prior systemic therapy.
- The designation is supported by positive phase 2 results from the CodeBreaK 100 clinical study in patients with advanced NSCLC whose cancer had progressed despite prior treatment with chemotherapy and/or immunotherapy.
  - In the study, treatment with sotorasib provided patients with durable anticancer activity and a positive benefit-risk profile.
- Notably, *KRAS G12C* is the most common *KRAS* mutation in NSCLC"

https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-designation-to-sotorasib-for-nsclc-with-kras-g12c-mutation

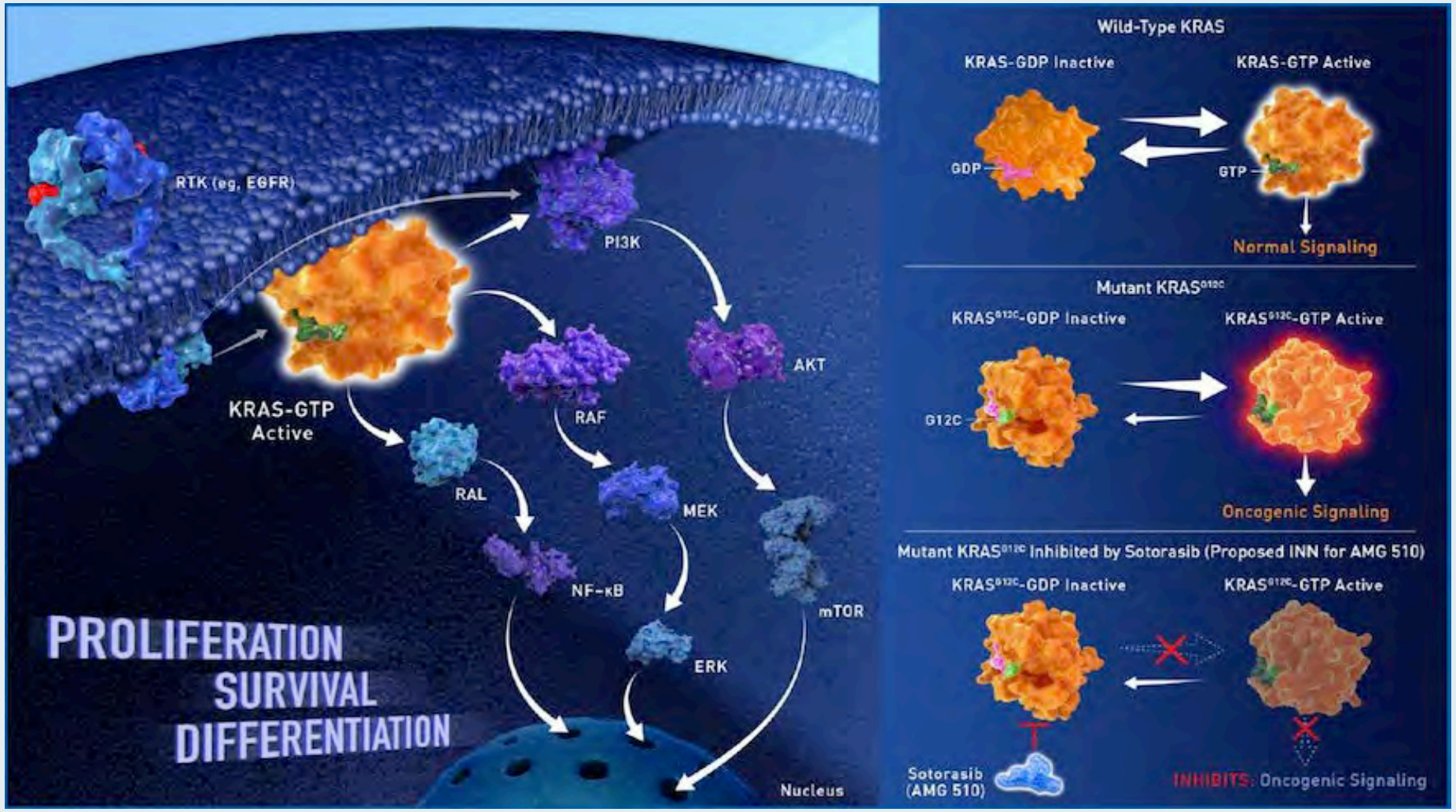
RTP RESEARCH TO PRACTICE

CodeBreaK100: Registrational Phase 2 Trial of Sotorasib in KRASp.G12C Mutated Non-small Cell Lung Cancer

Li BT et al.

WCLC 2021;Abstract PS01.07.

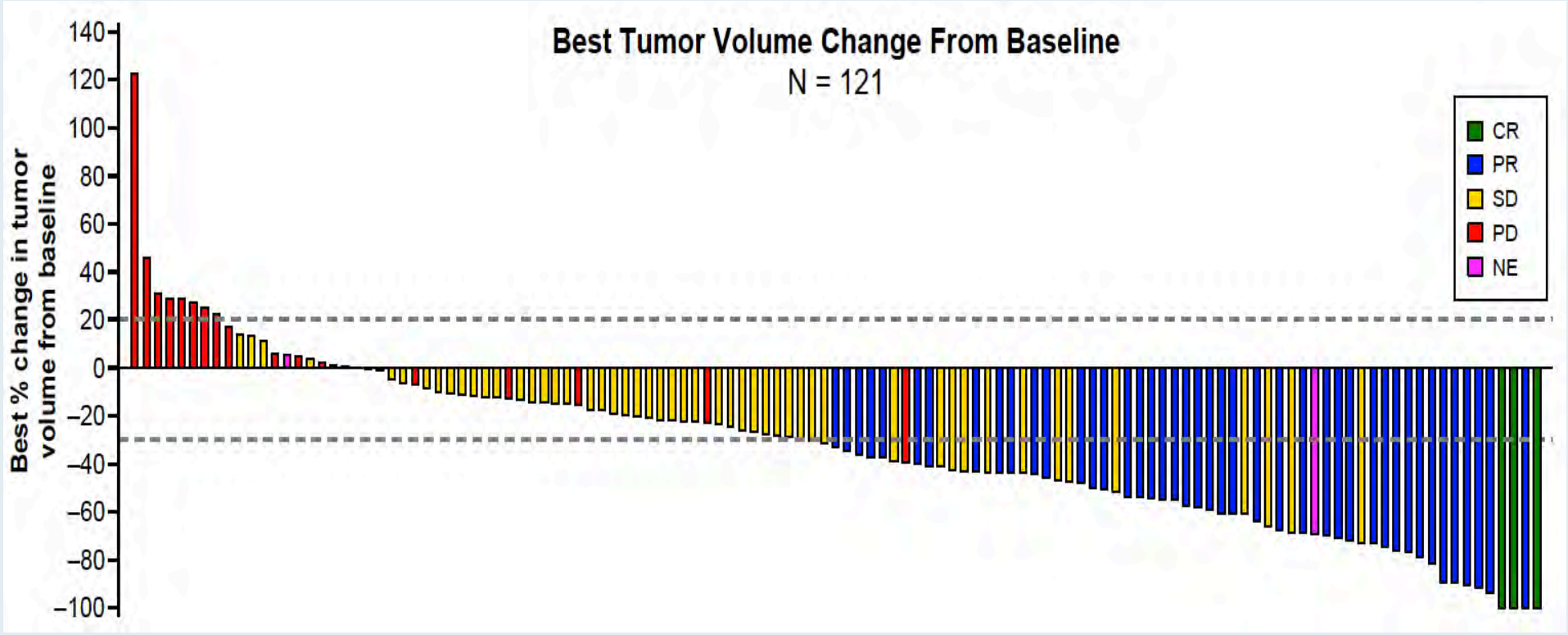
Mechanism of Action of Sotorasib (AMG 510) – KRASG12C inhibitor



Fakih M et al. ASCO 2020;Abstract 4018.

RTP RESEARCH TO PRACTICE

CodeBreak 100 Trial: Response and Survival Outcomes



Outcome	960 mg (n = 124)
ORR	37.1%
DCR	80.6%
PR	43.0%
mPFS	6.8 mo
mOS	Not evaluable

Data cutoff: December 1, 2020; median follow-up time: 12.2 months

Li BT et al. WCLC 2021;Abstract PS01.07.

RTP RESEARCH TO PRACTICE

Immunotherapies

FDA-Approved Immunotherapy Options for the First-Line Treatment of Metastatic NSCLC

Combination regimen	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab + Platinum and pemetrexed[1]	8/20/18	KEYNOTE-189	Nonsquamous	0.49
Pembrolizumab + Carboplatin, paclitaxel or *nab* paclitaxel[2]	10/30/18	KEYNOTE-407	Squamous	0.64
Atezolizumab + Carboplatin and paclitaxel and bevacizumab[3]	12/6/18	IMpower150	Nonsquamous	0.78
Atezolizumab + Carboplatin and *nab* paclitaxel[4]	12/3/19	IMpower130	Nonsquamous	0.79
Nivolumab + Ipilimumab[5]	5/15/20	CheckMate-227	PD-L1 TPS≥1, EGFR and/or ALK *wt*	0.62
Nivolumab + Ipilimumab and chemotherapy[6]	5/26/20	CheckMate-9LA	EGFR and/or ALK *wt*	0.69
Monotherapy	**FDA approval**	**Pivotal study**	**Histologic type**	**HR (OS)**
Pembrolizumab[7,8]	4/11/19 10/24/16	KEYNOTE-042 KEYNOTE-024	PD-L1 TPS≥1%	0.63
Atezolizumab[9]	5/18/20	IMpower110	PD-L1 TPS≥50, EGFR and/or ALK *wt*	0.59

[1] Gandhi L et al. *NEJM* 2018;378(22):2078-92. [2] Paz-Ares L et al. *NEJM* 2018;379(21):2040-51.
[3] Socinski MA et al. *NEJM* 2018;378(24):2288-301. [4] West H et al. *Lancet Oncol* 2019;20(7):924-37.
[5] Hellmann MD et al. *N Engl J Med* 2019;381(21):2020-31. [6] Reck M et al. ASCO 2020;Abstract 9501.
[7] Mok TSK et al. *Lancet* 2019;393(10183):1819-30. [8] Reck M et al. *J Clin Oncol* 2019;37(7):537-46.
[9] Spigel DR et al. ESMO 2019;Abstract LBA78

FDA Approves Nivolumab with Ipilimumab for First-Line Metastatic NSCLC with PD-L1 Tumor Expression ≥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(≥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 ≥1% were randomized to receive either the combination of nivolumab plus with ipilimumab (n=396) or platinum-doublet chemotherapy (n=397)."

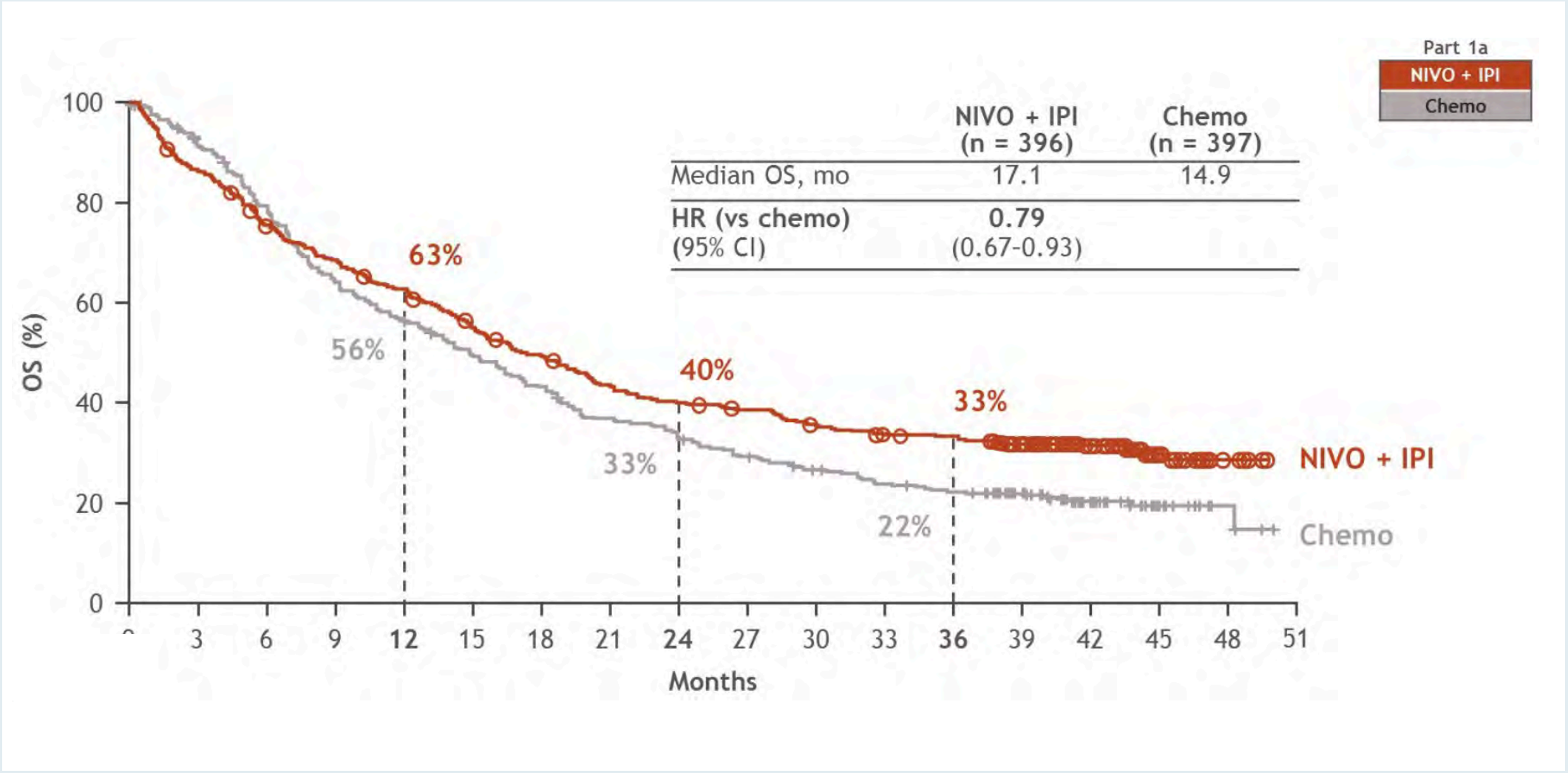
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-nivolumab-plus-ipilimumab-first-line-mnsclc-pd-l1-tumor-expression-1

RTP RESEARCH TO PRACTICE

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.

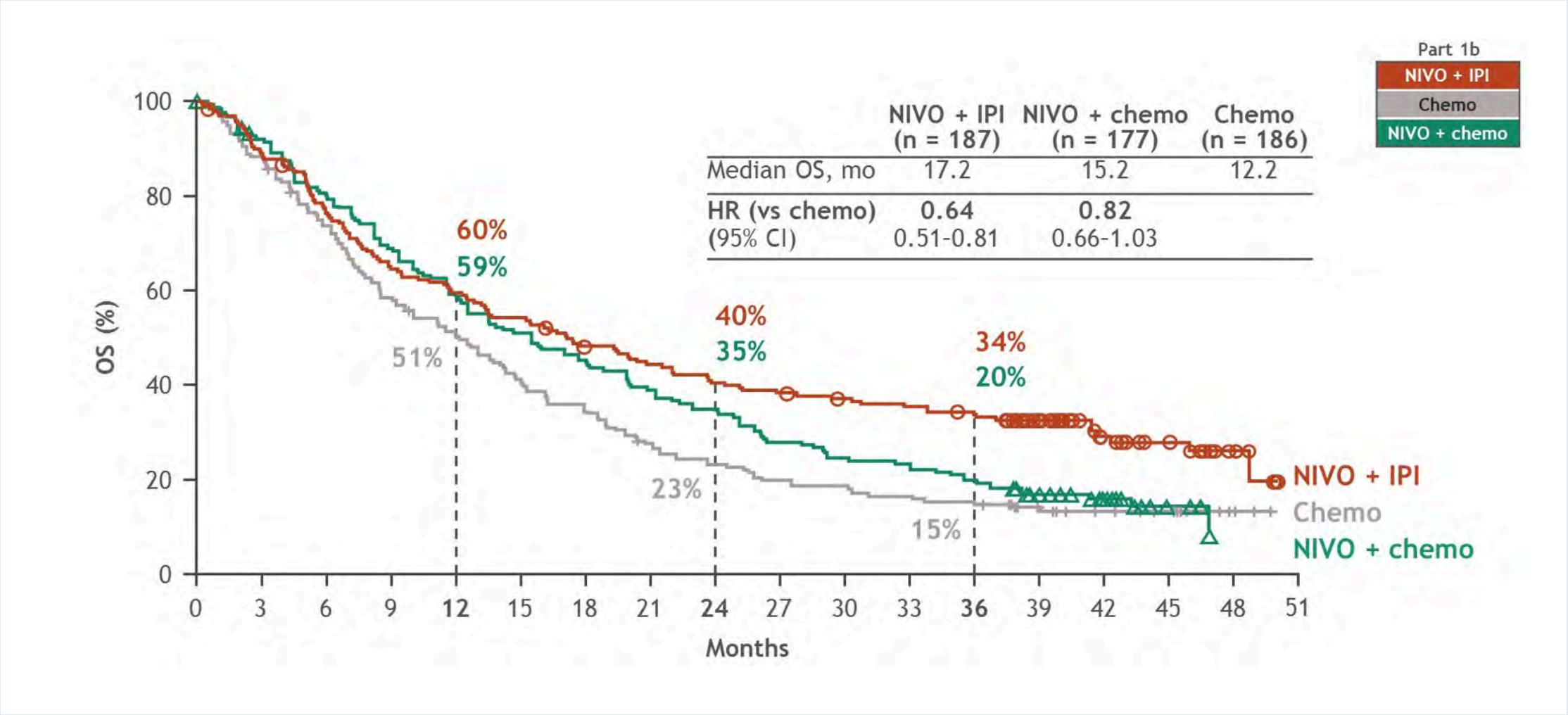
Three-Year Update: OS with IPI + Nivo vs Chemo (PD-L1 ≥1%)



Ramalingam SS et al. ASCO 2020;Abstract 9500.

RTP RESEARCH TO PRACTICE

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



Ramalingam SS et al. ASCO 2020;Abstract 9500.

RTP RESEARCH TO PRACTICE

FDA Approves Cemiplimab-rwlc for Non-Small Cell Lung Cancer with High PD-L1 Expression

Press Release — February 22, 2021

"The Food and Drug Administration approved cemiplimab-rwlc for the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) (locally advanced who are not candidates for surgical resection or definitive chemoradiation or metastatic) whose tumors have high PD-L1 expression (Tumor Proportion Score [TPS] > 50%) as determined by an FDA-approved test, with no EGFR, ALK or ROS1 aberrations.

Efficacy was evaluated in Study 1624 (NCT03088540), a multi-center, randomized, open-label trial in 710 patients with locally advanced NSCLC who were not candidates for surgical resection or definitive chemoradiation or with metastatic NSCLC. Patients were randomized (1:1) to receive cemiplimab-rwlc 350 mg intravenously every 3 weeks for up to 108 weeks or a platinum-based chemotherapy. The main efficacy outcome measures were overall survival (OS) and progression-free survival (PFS) per blinded independent central review (BICR)"

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-cemiplimab-rwlc-non-small-cell-lung-cancer-high-pd-l1-expression?utm_medium=email&utm_source=govdelivery

RTP RESEARCH TO PRACTICE

FDA Grants Priority Review to Front-Line Cemiplimab for PD-L1-High Advanced or Metastatic NSCLC

Press Release — October 29, 2020

"The FDA has accepted the supplemental Biologics License Application (sBLA) for cemiplimab-rwlc and granted it Priority Review for the frontline treatment of patients with locally advanced or metastatic non–small cell lung cancer (NSCLC) with ≥50% PD-L1 expression. The Prescription Drug User Fee Act target action date for this potential approval is set to February 28, 2021.

The sBLA for cemiplimab as treatment of this patient population was supported by findings from the phase 3 EMPOWER-Lung 1 clinical trial of cemiplimab versus chemotherapy in patients with advanced or metastatic PD-L1–positive NSCLC, for which topline results were recently presented during the European Society of Medical Oncology (ESMO) Virtual Annual Congress 2020."

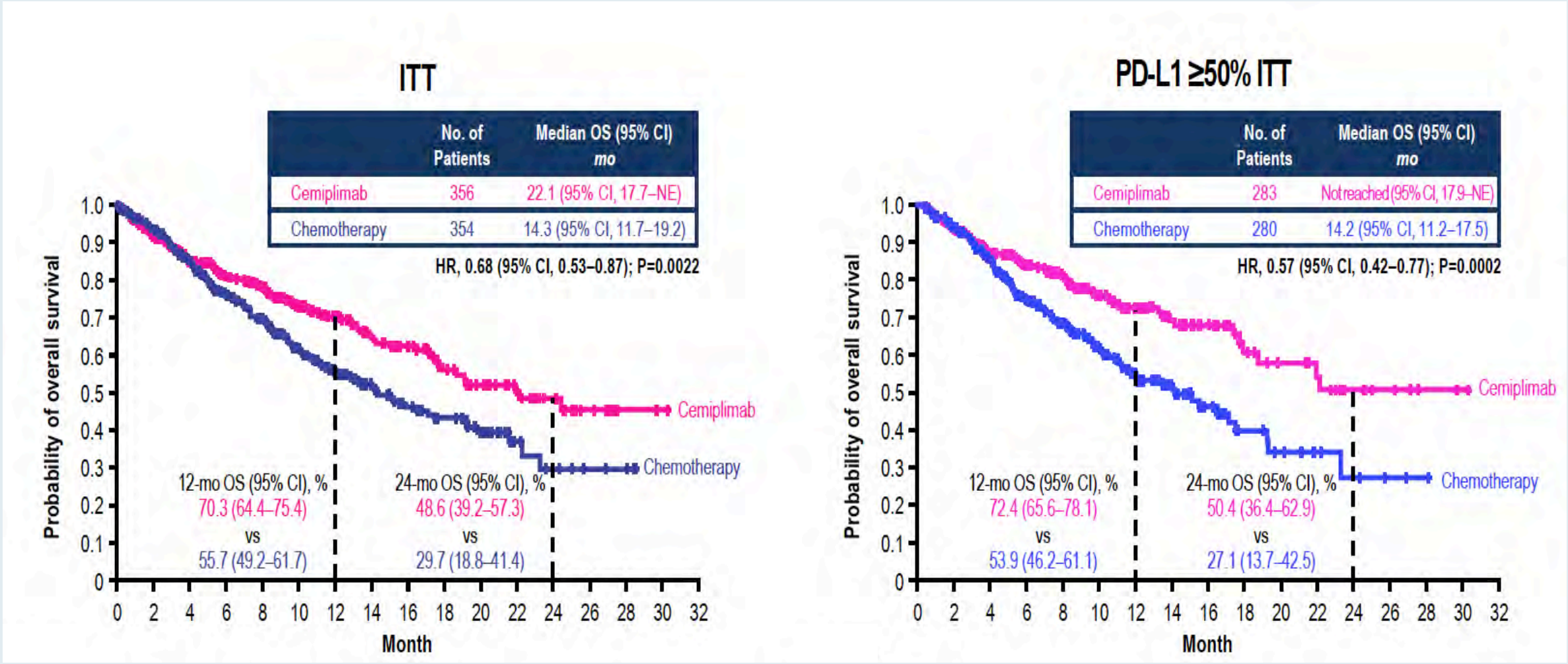
https://www.targetedonc.com/view/fda-grants-priority-review-to-frontline-cemiplimab-for-pd-l1-high-advanced-or-metastatic-nsclc

EMPOWER-Lung 1: Phase 3 First-Line (1L) Cemiplimab Monotherapy vs Platinum-Doublet Chemotherapy (Chemo) in Advanced Non-Small Cell Lung Cancer (NSCLC) with Programmed Cell Death-Ligand 1 (PD-L1) ≥50%

Sezer A et al.

ESMO 2020;Abstract LBA52.

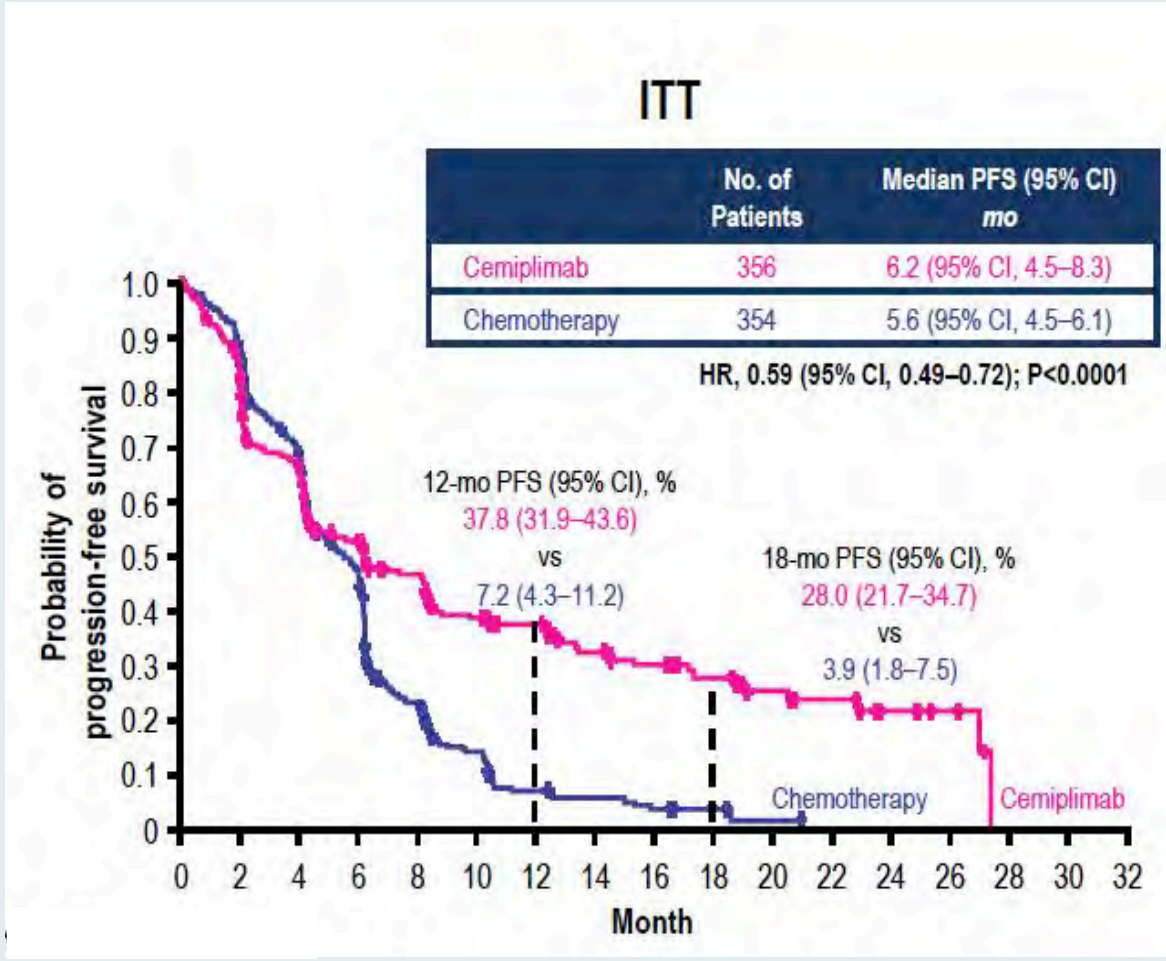
EMPOWER-Lung 1 Trial of 1L Cemiplimab: OS

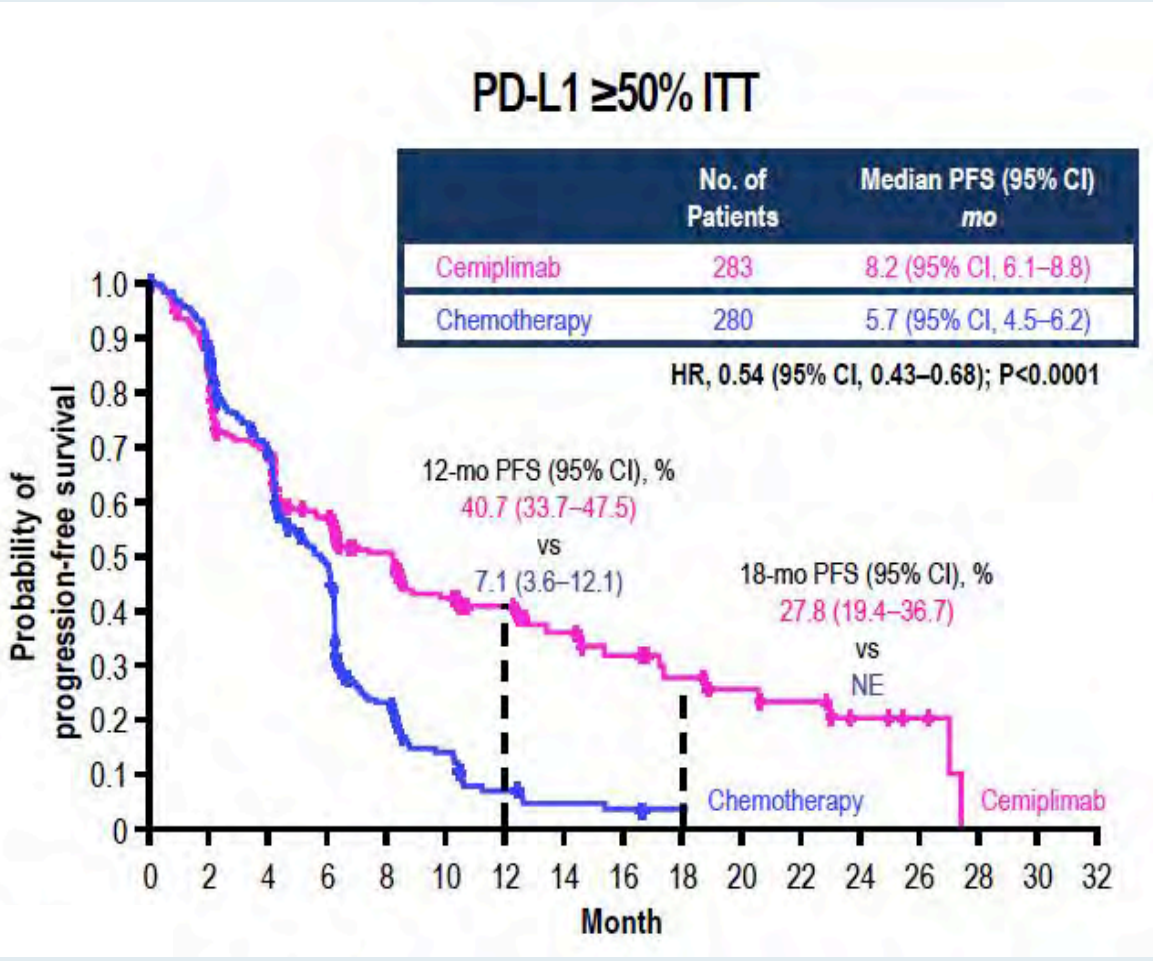


Sezer A et al. ESMO 2020;Abstract LBA52.

RTP RESEARCH TO PRACTICE

EMPOWER-Lung 1 Trial of 1L Cemiplimab: PFS





Sezer A et al. ESMO 2020;Abstract LBA52.

Stage III NSCLC

CheckMate 816 Met a Primary Endpoint of Improved pCR with Neoadjuvant Nivolumab in Combination with Chemotherapy

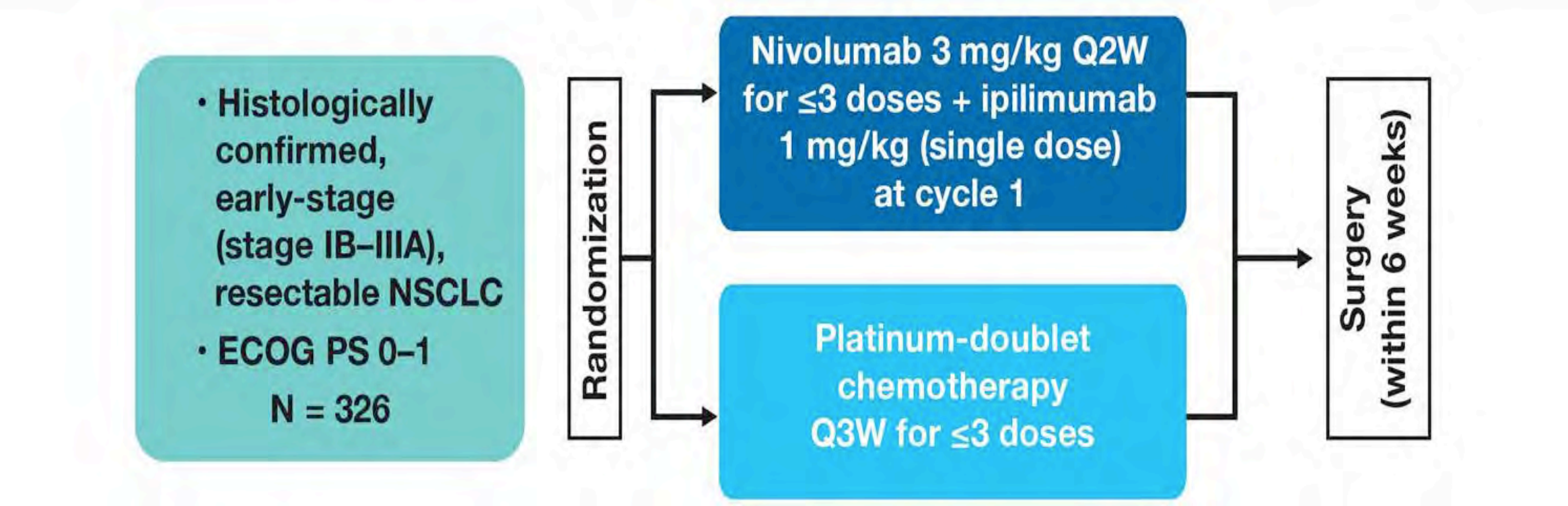
Press Release — October 07, 2020

"The Phase 3 CheckMate 816 trial met a primary endpoint of pathologic complete response (pCR) in resectable non-small cell lung cancer (NSCLC). In the trial, significantly more patients treated with nivolumab plus chemotherapy before surgery showed no evidence of cancer cells in their resected tissue compared to those treated with chemotherapy alone. CheckMate 816 is the first and only Phase 3 trial to demonstrate a benefit with an immune checkpoint inhibitor in combination with chemotherapy as a neoadjuvant treatment in non-metastatic NSCLC.

Patients in the experimental arm of the trial received up to three doses of nivolumab plus chemotherapy prior to surgery, a standard number of cycles of therapy in the neoadjuvant setting. The safety profile of nivolumab plus chemotherapy was consistent with previously reported studies in NSCLC."

https://news.bms.com/news/details/2020/Opdivo-nivolumab-Plus-Chemotherapy-Shows-Statistically-Significant-Improvement-in-Pathologic-Complete-Response-as-Neoadjuvant-Treatment-of-Resectable-Non-Small-Cell-Lung-Cancer-in-Phase-3-CheckMate--816-Trial/default.aspx

Phase III CheckMate 816 Trial Design



Primary endpoints: EFS and pCR
Secondary endpoints include: OS, major pathological response, time to death or distant metastases

Forde PM et al. ASCO 2017;Abstract TPS8577.

Small Cell Lung Cancer

RTP
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TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

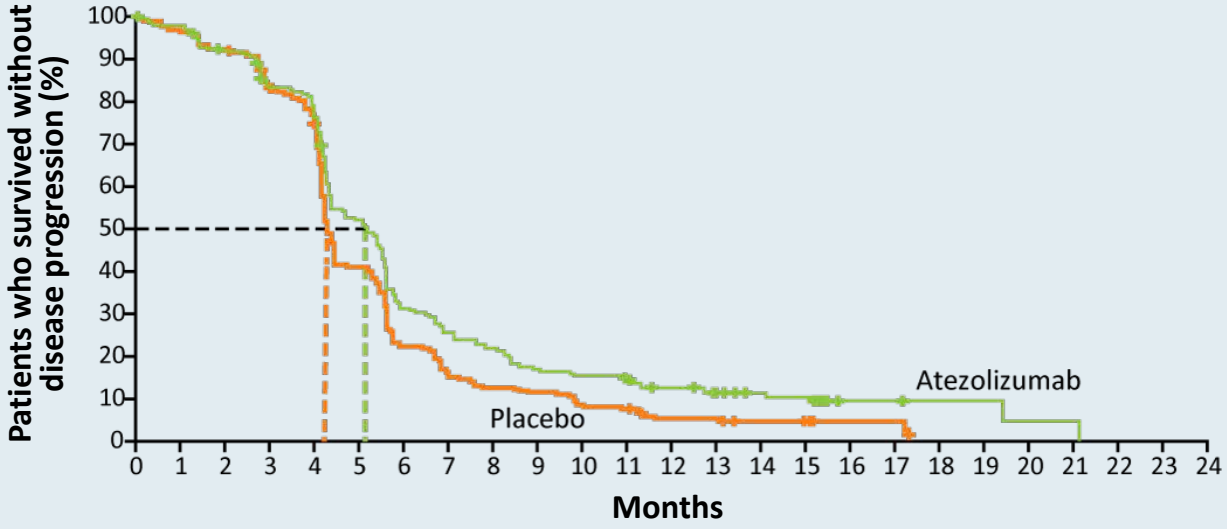
First-Line Atezolizumab plus Chemotherapy in Extensive-Stage Small-Cell Lung Cancer

L. Horn, A.S. Mansfield, A. Szczęsna, L. Havel, M. Krzakowski, M.J. Hochmair, F. Huemer, G. Losonczy, M.L. Johnson, M. Nishio, M. Reck, T. Mok, S. Lam, D.S. Shames, J. Liu, B. Ding, A. Lopez-Chavez, F. Kabbinavar, W. Lin, A. Sandler, and S.V. Liu, for the IMpower133 Study Group*

N Engl J Med 2018;379(23):2220-9.

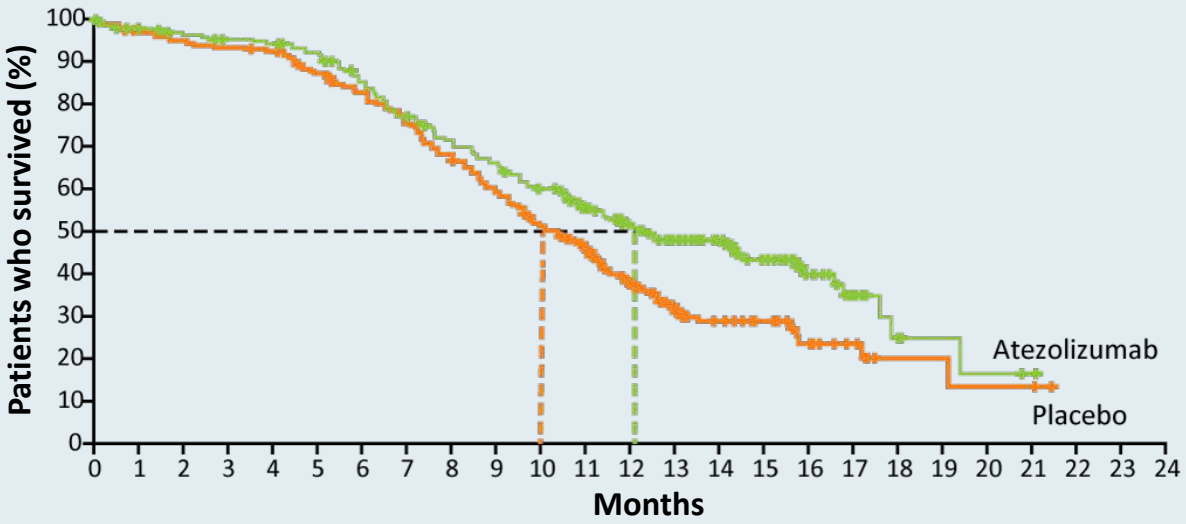
IMpower133: Survival Outcomes

Progression-free survival (PFS)



	Median PFS	12-mo PFS	HR	*p*-value
Atezolizumab	5.2 mo	12.6%	0.77	0.02
Placebo	4.3 mo	5.4%		

Overall survival (OS)



	Median OS	12-mo OS	HR	*p*-value
Atezolizumab	12.3 mo	51.7%	0.70	0.007
Placebo	10.3 mo	38.2%		

- The safety profile of atezolizumab + carboplatin and etoposide was consistent with the previously reported safety profile of the individual agents; no new findings were observed.

Horn L et al. *N Engl J Med* 2018;379(23):2220-9.

FDA Approves Durvalumab for Extensive-stage Small Cell Lung Cancer

Press Release — March 27, 2020

"On March 27, 2020, the Food and Drug Administration approved durvalumab in combination with etoposide and either carboplatin or cisplatin as first-line treatment of patients with extensive-stage small cell lung cancer (ES-SCLC).

Efficacy of this combination in patients with previously untreated ES-SCLC was investigated in CASPIAN, a randomized, multicenter, active-controlled, open-label, trial (NCT03043872). The evaluation was based on the comparison of patients randomized to durvalumab plus chemotherapy vs. chemotherapy alone. The major efficacy outcome measure was overall survival (OS). Additional efficacy outcome measures were investigator-assessed progression-free survival (PFS) and objective response rate (ORR), per RECIST v1.1."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-durvalumab-extensive-stage-small-cell-lung-cancer

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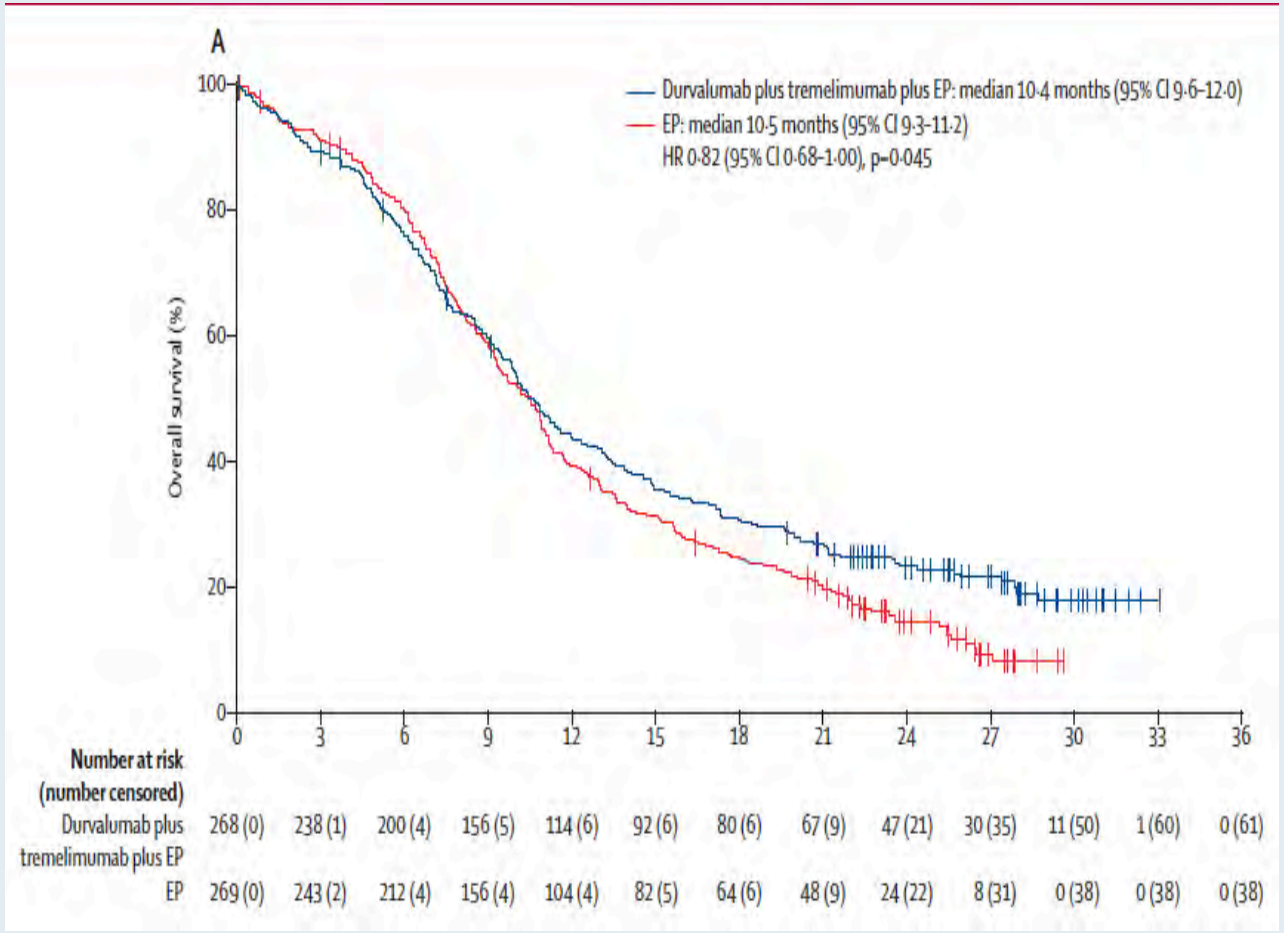
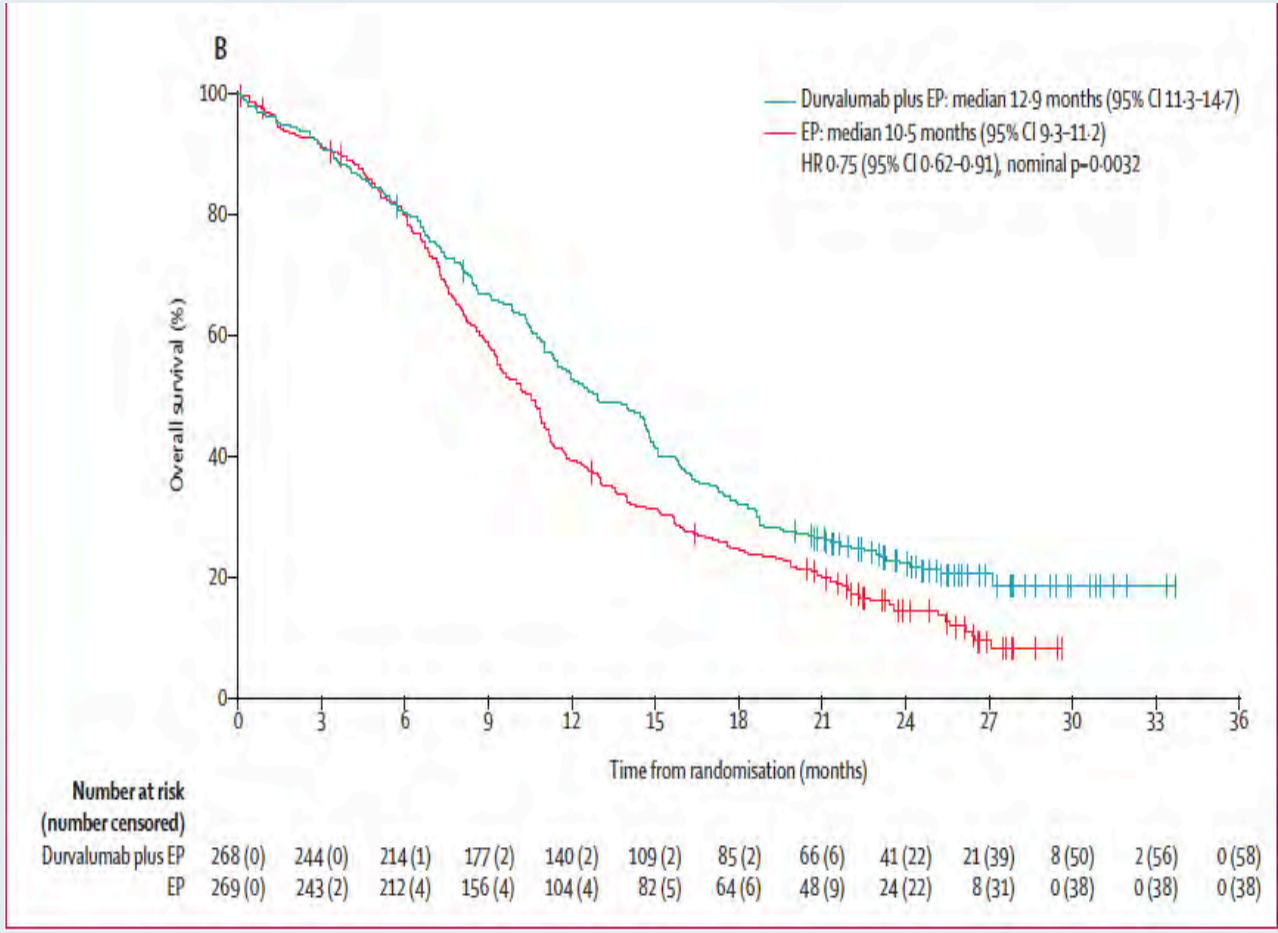
Durvalumab, with or without tremelimumab, plus platinum–etoposide versus platinum–etoposide alone in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): updated results from a randomised, controlled, open-label, phase 3 trial

*Jonathan W Goldman, Mikhail Dvorkin, Yuanbin Chen, Niels Reinmuth, Katsuyuki Hotta, Dmytro Trukhin, Galina Statsenko, Maximilian J Hochmair, Mustafa Özgüroğlu, Jun Ho Ji, Marina Chiara Garassino, Oleksandr Voitko, Artem Poltoratskiy, Santiago Ponce, Francesco Verderame, Libor Havel, Igor Bondarenko, Andrzej Każarnowicz, György Losonczy, Nikolay V Conev, Jon Armstrong, Natalie Byrne, Piruntha Thiyagarajah, Haiyi Jiang, Luis Paz-Ares, for the CASPIAN investigators**

CASPIAN: Updated OS Analyses in ITT Population

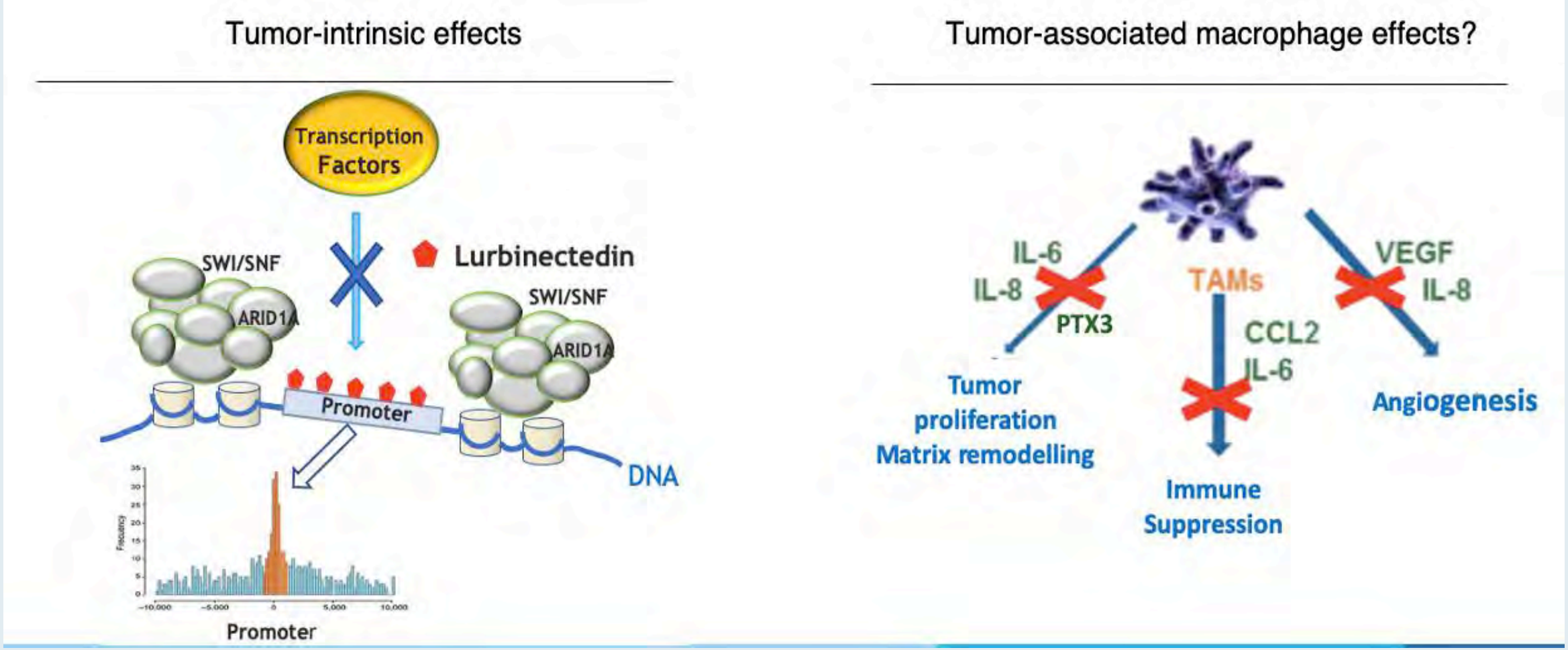




Goldman JW et al. *Lancet Oncol* 2021;22(1):51-65.

RTP RESEARCH TO PRACTICE

Lurbinectedin: A Selective Inhibitor of Oncogenic Transcription



How does it work?

- **Alkylator**
- **Minor groove DNA binder**

Paz-Ares LG et al. ASCO 2019;Abstract 8506.

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.

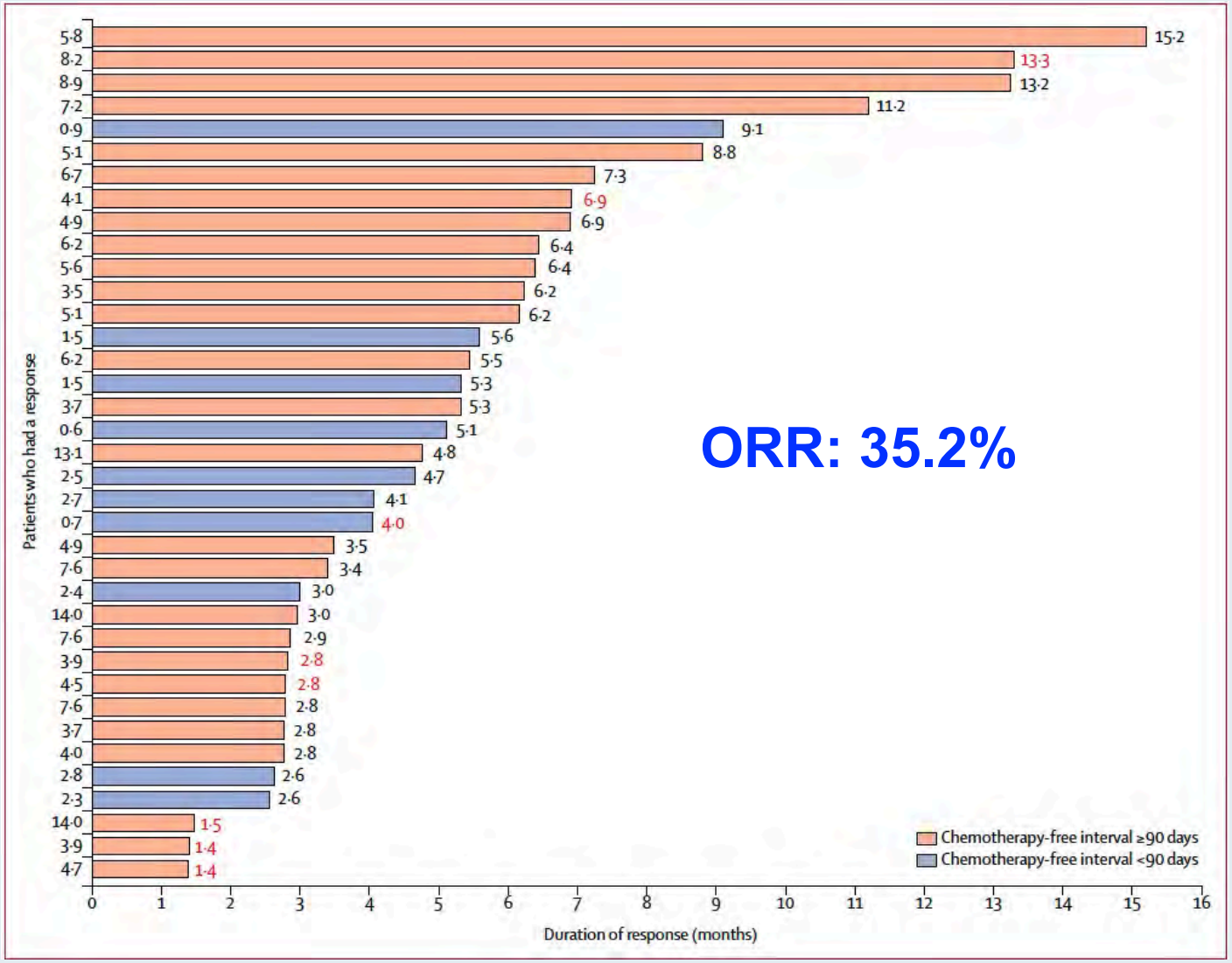
RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21:645-54.

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*

Rate and Duration of Response with Lurbinectedin as Second-Line Therapy in SCLC



Trigo J et al. *Lancet Oncol* 2020;21(5):645-54.

ATLANTIS Trial Did Not Meet the Prespecified Criteria for Significance of the Primary Endpoint of Overall Survival

Press Release — December 03, 2020

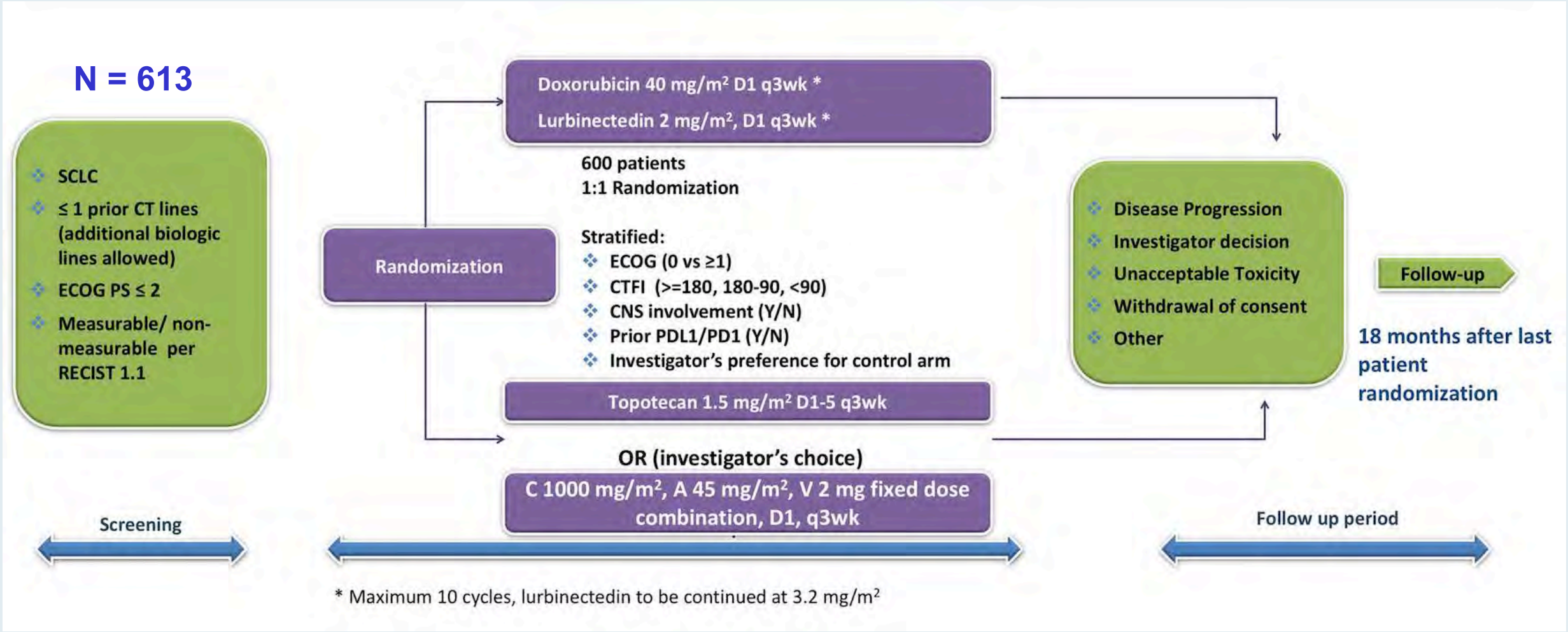
"Results [were announced] from the ATLANTIS Phase 3 multicenter, randomized, controlled study evaluating lurbinectedin in combination with doxorubicin versus physician's choice of topotecan or cyclophosphamide/doxorubicin/vincristine (CAV) for adult patients with SCLC whose disease progressed following one prior platinum-containing line. Patients received lurbinectedin at 2.0 mg/m^2 in the combination arm, which is lower than the FDA approved dose of lurbinectedin at 3.2 mg/m^2.

The study did not meet the pre-specified criteria of significance for the primary endpoint of overall survival (OS) in the intent-to-treat (ITT) population comparing lurbinectedin in combination with doxorubicin to the control arm, though there was no adverse effect on OS with the experimental arm. Based on the study design, no additional hypotheses were formally tested. Importantly, key secondary and subgroup analyses favored the lurbinectedin combination arm. Lurbinectedin monotherapy was not tested in ATLANTIS.

The safety data in this study was consistent with the known safety profile of lurbinectedin monotherapy with no new safety signals observed."

https://investor.jazzpharma.com/news-releases/news-release-details/jazz-pharmaceuticals-and-pharmamar-announce-results-atlantis

Ongoing Phase III ATLANTIS Trial



Clinicaltrials.gov (NCT02566993); Accessed February 2021; Farago AF et al. ASCO 2018;Abstract TPS8587.

Recent Advances in Hematologic Oncology: A 4-Part Live Webinar Series Reviewing Key Data and Presentations from the 62nd ASH Annual Meeting

Part 4 — Chronic Lymphocytic Leukemia

Wednesday, February 24, 2021
5:00 PM – 6:00 PM ET

Faculty

Paul M Barr, MD
Matthew S Davids, MD, MMSc
Kerry Rogers, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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