Thank you for joining us.
The program will commence momentarily.

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Current Questions and Controversies in the Management of Lung Cancer

An Interactive Meet The Professor Series

Nathan A Pennell, MD, PhD
Professor, Hematology and Medical Oncology
Cleveland Clinic Lerner College
of Medicine of Case Western Reserve University
Director, Cleveland Clinic Lung Cancer Medical Oncology Program
Cleveland, Ohio

Commercial Support

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

Dr Love — Disclosures

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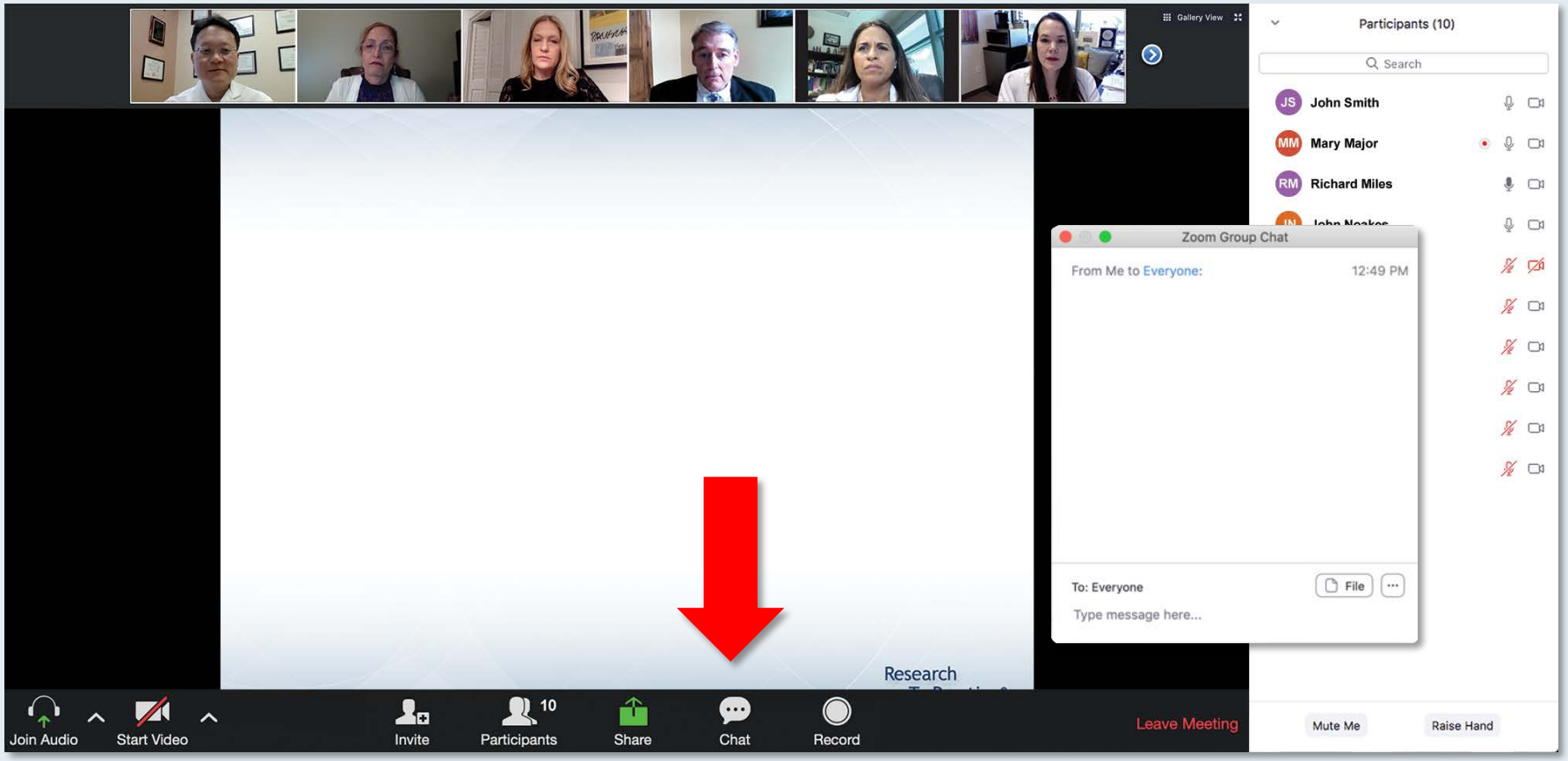
We Encourage Clinicians in Practice to Submit Questions



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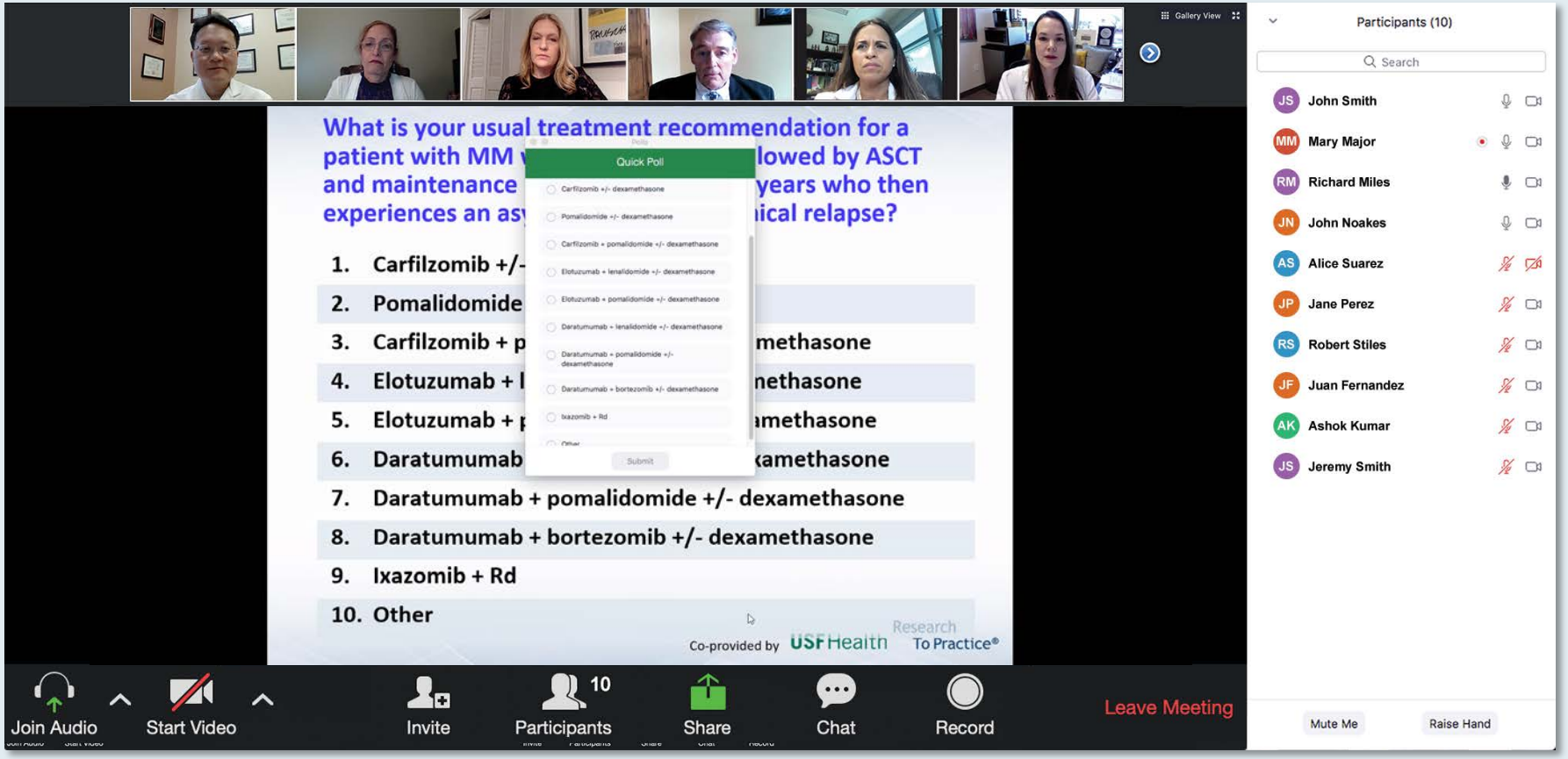
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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Upcoming Live Webinars

Friday, September 11, 2020
12:00 PM – 1:00 PM ET

Clinical Investigator Perspectives on the Current and Future Role of PARP Inhibition in the Management of Ovarian Cancer

Faculty
Robert L Coleman, MD

Moderator
Neil Love, MD

Monday, September 14, 2020
12:00 PM – 1:00 PM ET

Optimizing the Selection and Sequencing of Therapy for Patients with Chronic Lymphocytic Leukemia

Faculty
Ian W Flinn, MD, PhD

Moderator
Neil Love, MD

Upcoming Live Webinars

Wednesday, September 16, 2020
12:00 PM – 1:00 PM ET

Clinical Investigator Perspectives on the Current and Future Management of Multiple Myeloma

Faculty
Jonathan L Kaufman, MD

Moderator
Neil Love, MD

Friday, September 18, 2020
12:00 PM – 1:00 PM ET

Optimizing the Selection and Sequencing of Therapy for Patients with Chronic Lymphocytic Leukemia

Faculty
Matthew S Davids, MD, MMSc

Moderator
Neil Love, MD

Thank you for joining us!

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

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WITH DR NEIL LOVE

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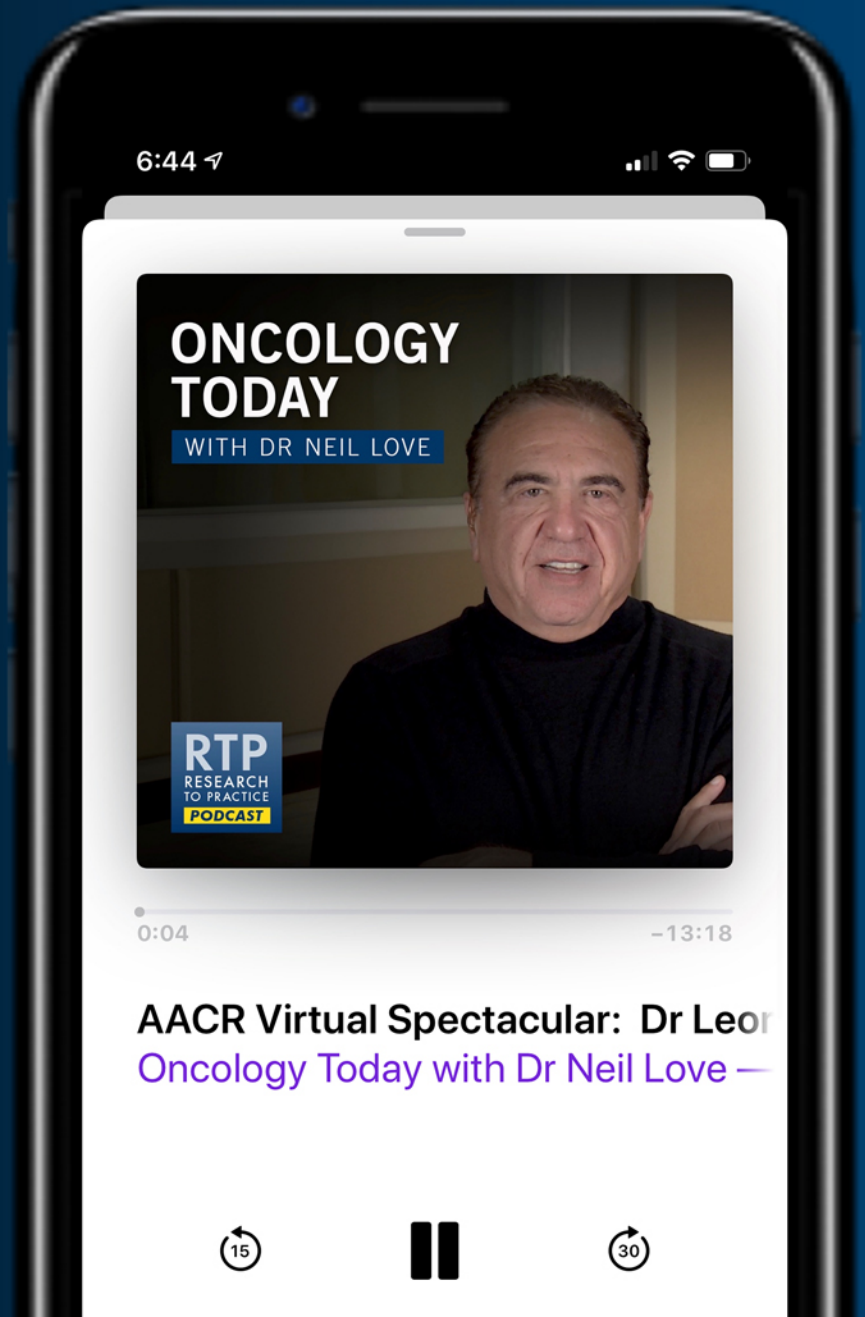

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Meet The Professor Program Participating Faculty

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Professor and Chair
Thoracic/Head and Neck Medical Oncology
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Corey J Langer, MD
Director of Thoracic Oncology
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Director, Thoracic Oncology
Research Program
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Johns Hopkins School of Medicine
Clinical Director
Medical Director, Thoracic
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Cancer Center at Sibley Memorial
Washington, DC

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Meet The Professor Program Participating Faculty

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

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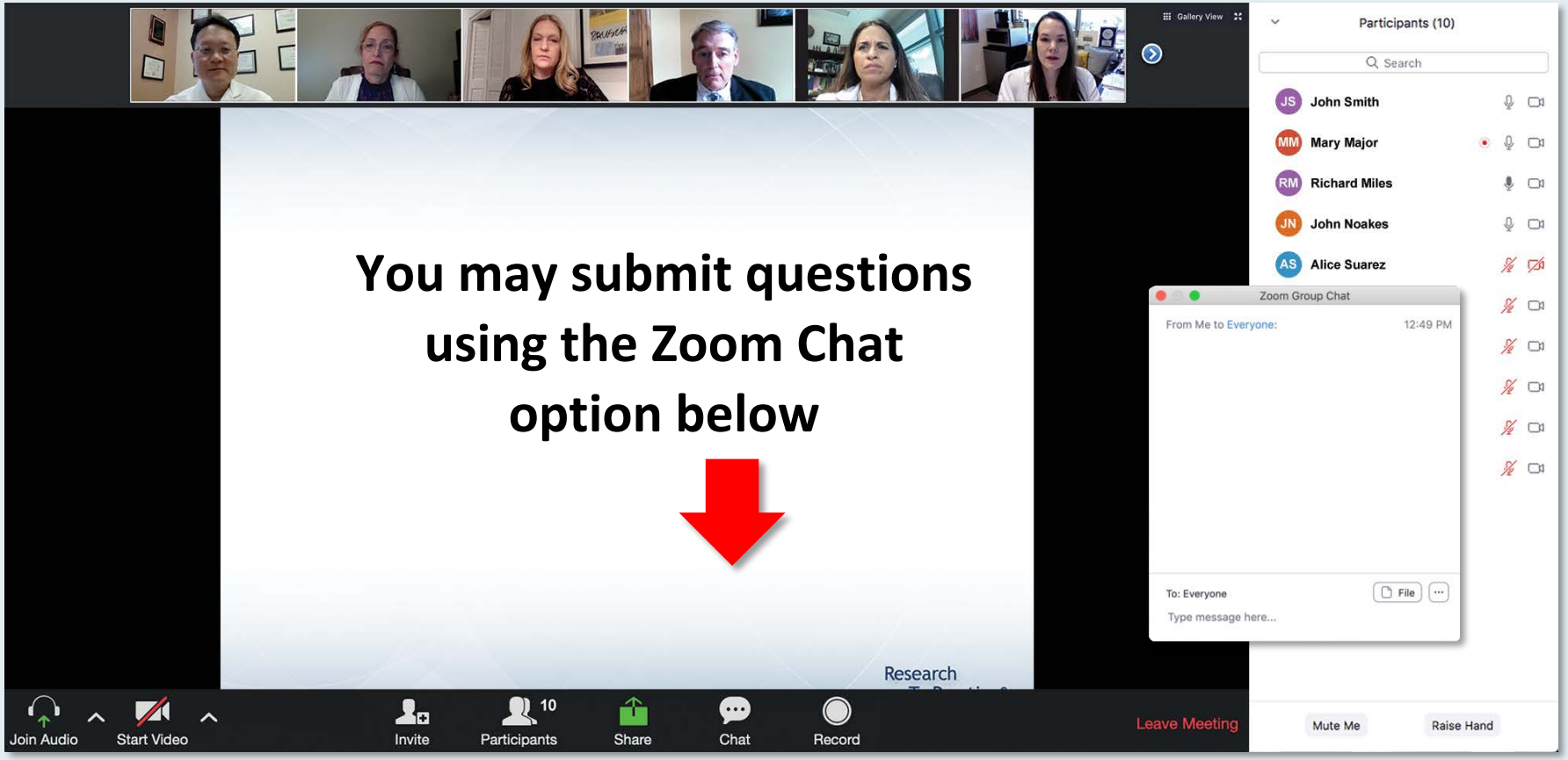

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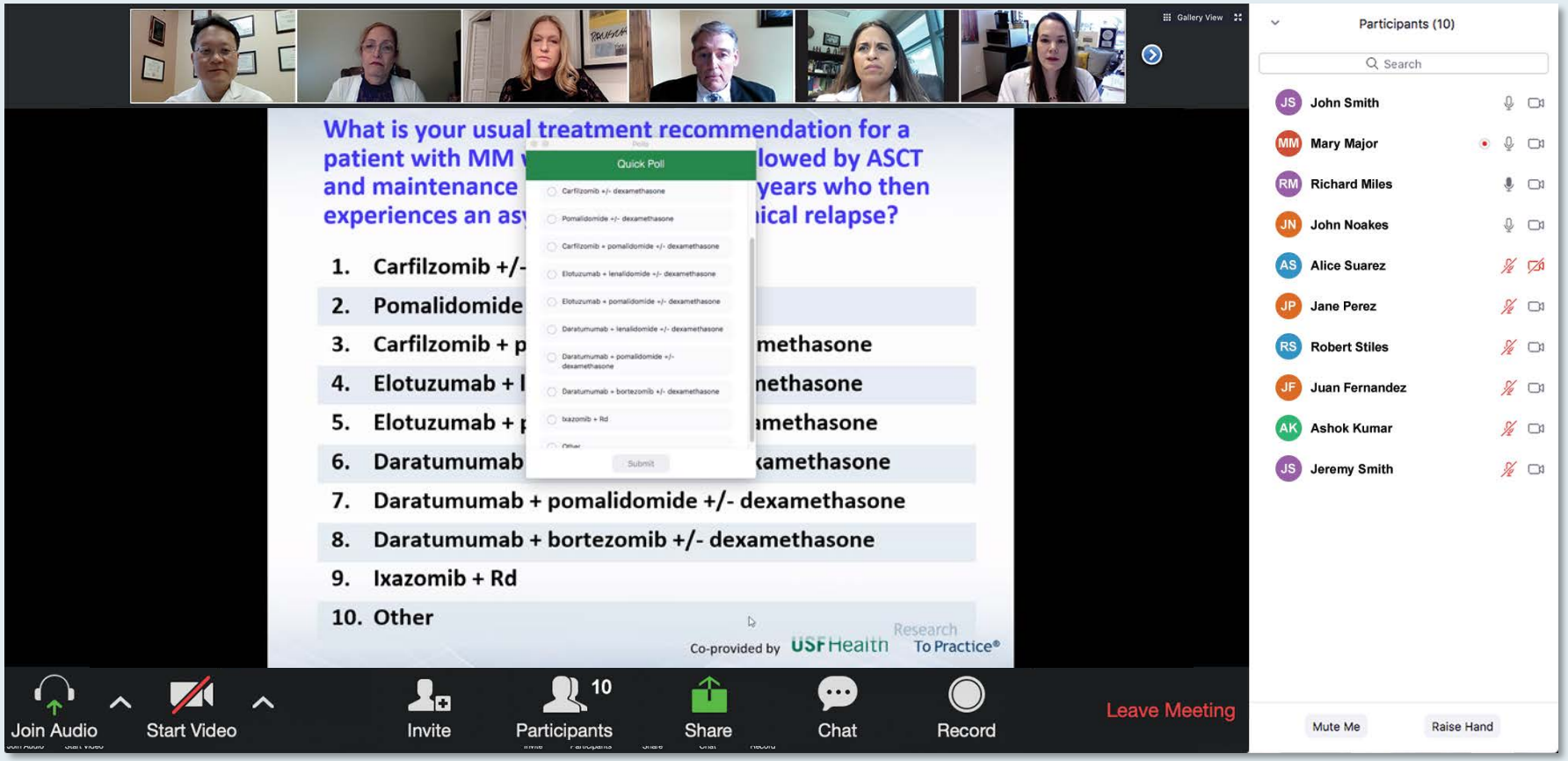

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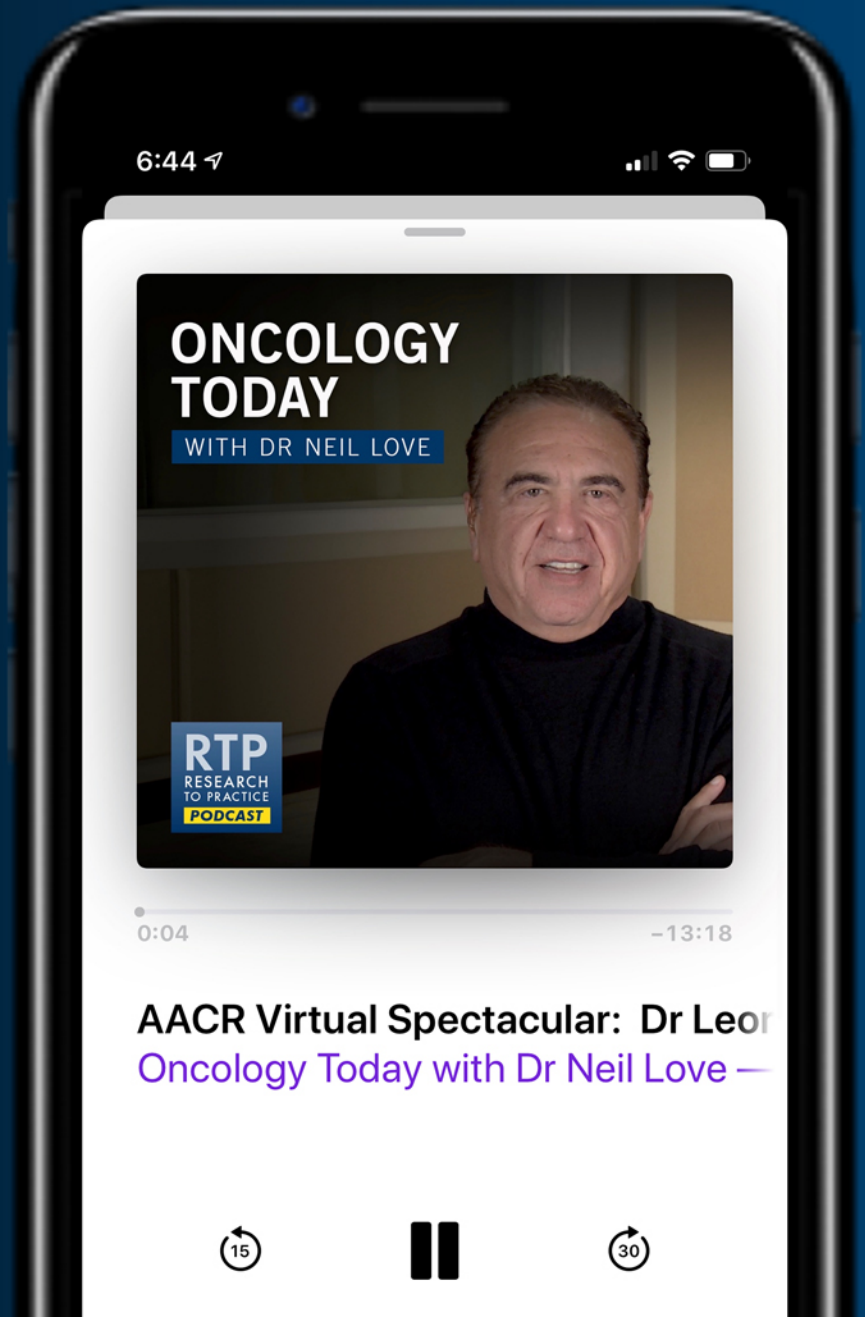

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RTP RESEARCH TO PRACTICE

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Zanetta S Lamar, MD
Florida Cancer Specialists
and Research Institute
Naples, Florida

Shachar Peles, MD
Florida Cancer Specialists
and Research Institute
Atlantis, Florida

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Meet The Professor with Dr Pennell

Module 1: Cases from the Community

- Dr Peles: A 69-year-old man and smoker with Stage IIIA squamous cell lung carcinoma
- Dr Lamar: An 83-year-old woman with Stage IIIB NSCLC – EGFR exon 21 mutation
- Comments: Pneumonitis in patients with Stage III disease and COPD receiving durvalumab
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- Dr Peles: A 73-year-old woman with extensive-stage small cell lung cancer

Module 2: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

Module 3: Journal Club

- EGFR mutation-positive disease (ADAURA trial)
- Checkpoint inhibitors (ipilimumab/nivolumab, treatment intervals, locally advanced disease)
- HER2-positive disease (trastuzumab deruxtecan)

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The Oncologist 2020;25:1–4

The Oncologist®

Precision Medicine Clinic: Molecular Tumor Board

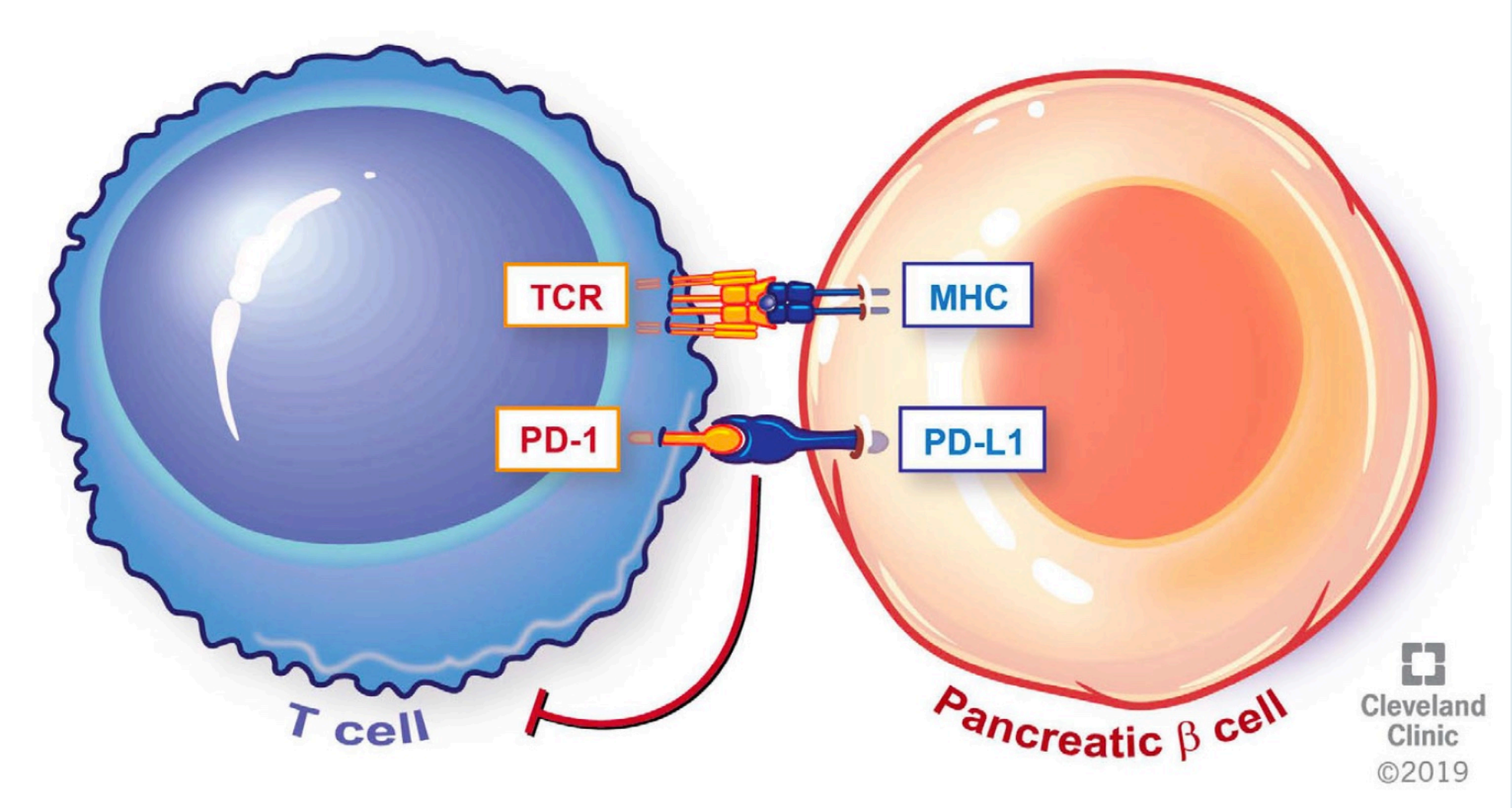
Cases from the Immune-Related Adverse Event Tumor Board: Diagnosis and Management of Immune Checkpoint Blockade Induced Diabetes

Alexia Zagouras,[a] Pradnya D. Patil,[b] Divya Yogi-Morren,[c] Nathan A. Pennell[b]

[a]Cleveland Clinic Lerner College of Medicine, Cleveland, Ohio, USA; [b]Department of Hematology and Oncology, Taussig Cancer Institute and [c]Department of Endocrinology, Diabetes and Metabolism, Cleveland Clinic, Cleveland, Ohio, USA

Physiologic Interaction between Pancreatic β Cell and T Cells

Engagement of the PD-1/PD-L1 Axis Leads to Self-Tolerance and Immune Homeostasis



Zagouras A et al. *The Oncologist* 2020;25:1–4.

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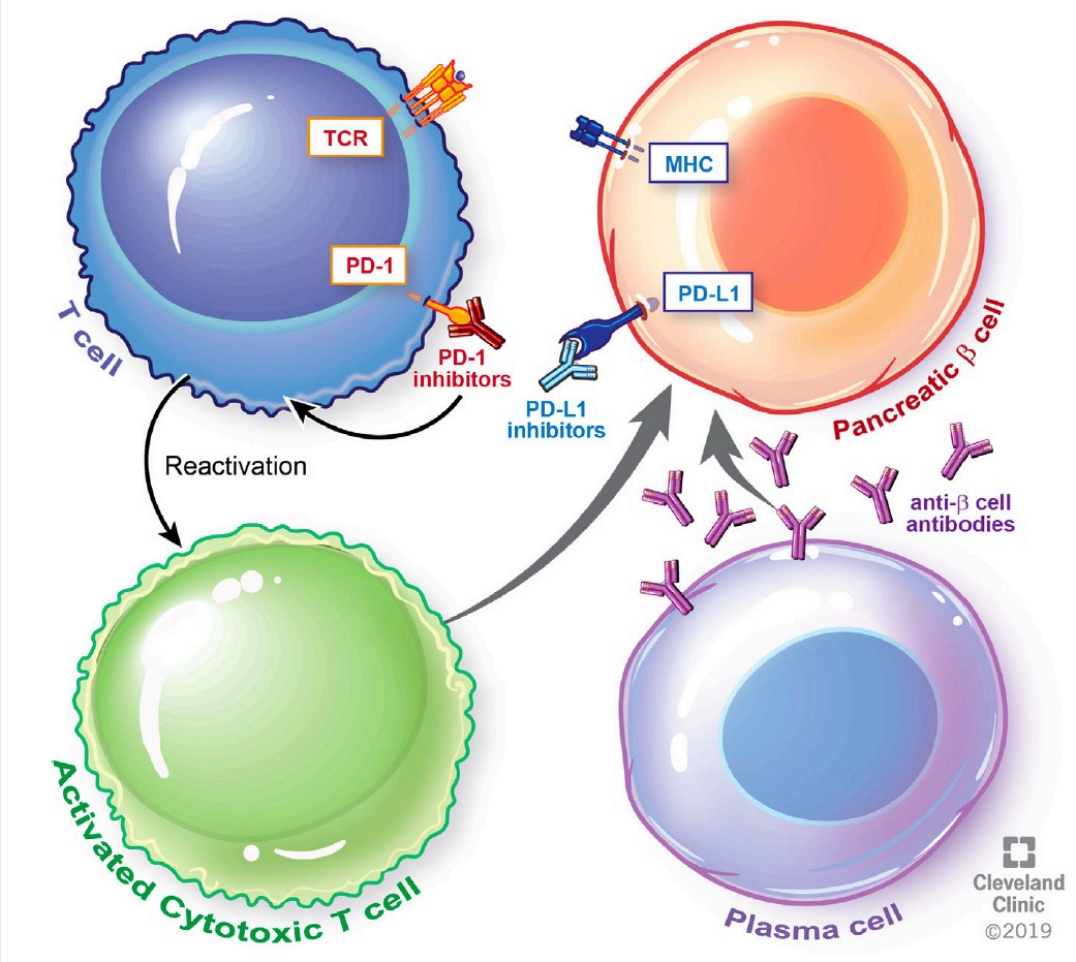
Disruption of the Physiologic Immune Tolerance Mechanisms Due to Immune Checkpoint Blockade Leads to Reactivation of Self-Reactive T Cells and Immune Mediated Destruction of the Pancreatic β Cells Resulting in Diabetes



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Case Presentation – Dr Peles: A 69-year-old man and smoker with Stage IIIA squamous cell lung carcinoma

Shachar Peles, MD

- May 2020: RUL mass, Stage IIIA poorly differentiated squamous cell carcinoma
- June 2020 lymph node 4R FNA: Metastatic poorly differentiated squamous cell carcinoma
- Currently, RT/cisplatin/etoposide

Questions

- Would you proceed with surgery if deemed resectable after chemoradiation therapy? Or would you treat with definitive chemoradiation therapy and then consolidate with durvalumab?
- Would you administer consolidation durvalumab if surgery is performed?

Case Presentation – Dr Lamar: An 83-year-old woman with Stage IIIB NSCLC – EGFR exon 21 mutation

Zanetta S Lamar, MD

- 2018: Diagnosed with Stage IA lung adenocarcinoma
- Left upper lobectomy, mediastinal node dissection and observation
- June 2020 repeat PET scan: Multiple hypermetabolic bilateral mediastinal lymph nodes
  - No evidence of distant disease
  - Brain MRI: Negative
  - Molecular testing: EGFR exon 21; PD-L1 TPS 0%; ALK, ROS1 and RET negative.
  - Performance status: 1, occasional memory problems

Questions

- What treatment would you recommended next?
- Would you consider concurrent chemoradiation therapy? Would you consider Osimertinib?

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Comments and Questions: Identifying pneumonitis in patients with Stage III disease receiving durvalumab who have underlying COPD

Shachar Peles, MD

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Case Presentation – Dr Lamar: A 94-year-old woman with metastatic NSCLC – PD-L1 75%, no EGFR mutation

Zanetta S Lamar, MD

- ECOG performance status of 3 at diagnosis
- Pembrolizumab, with significant partial response after 4 cycles
- ECOG performance status of 0; “best she has ever felt”

Questions

- How long do you continue single-agent PD-L1 inhibitors in responding patients? Do you stop after 2 years?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Peles: A 60-year-old man with metastatic adenocarcinoma of the lung – PD-L1 100%

Shachar Peles, MD

- November 2017: RUL, poorly differentiated adenocarcinoma
  - MRI brain: Multiple enhancing masses (largest 2.7 x 2.5 cm), extensive edema
  - CT chest: 10 cm RUL lung mass with mediastinal lymphadenopathy
- Completed WBRT
- December 2017: Pembrolizumab
- April 2020 PET/CT: Continued decrease with contraction of right apical pulmonary lesion with low grade activity. Stable minimally prominent right paratracheal lymph nodes and mild metabolic activity

Questions

- How long would you continue the pembrolizumab? Would you continue indefinitely?
- If his PD-L1 levels were known earlier, would it have been reasonable, with this amount of CNS disease, to initiate the checkpoint inhibitor and forgo radiation therapy?

Case Presentation – Dr Peles: A 73-year-old woman with extensive-stage small cell lung cancer

Shachar Peles, MD

- November 2019: Admitted with abdominal pain, weight loss, weakness
  - Left hilar mass, liver metastases, osseous metastases
  - Liver, core needle biopsy: Poorly differentiated neuroendocrine carcinoma (small cell carcinoma)
- Carboplatin/etoposide/atezolizumab x 4 → atezolizumab
  - 2/2020: Interval improvement with resolution of lung lesions, decrease in size of liver lesions, and osseous mets more extensive and sclerotic
- June 2020: Completes atezolizumab, but left sided chest pain, weight loss, nausea → PD

Questions

- Is there a preference for which PD-L1 inhibitor to combine with platinum/etoposide? Is there a benefit of using cisplatin over carboplatin?
- What is the best second line option for recurrent SCLC – topotecan, lurbinectedin?

Meet The Professor with Dr Pennell

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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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For a patient with metastatic nonsquamous NSCLC with an EGFR exon 19 deletion and a PD-L1 TPS of 60% who receives first-line osimertinib with response followed by disease progression, would you recommend repeat mutation testing? What treatment would you recommend if no further actionable mutations were identified?

	Recommend repeat testing?	Second-line treatment
 JOHN V HEYMACH, MD, PHD	Yes, tissue	Atezo/carbo/paclitaxel + bev
 LEORA HORN, MD, MSC	Yes, liquid; if negative, tissue	Carbo/pemetrexed
 COREY J LANGER, MD	Yes, liquid and tissue	Continue osimertinib, add carbo/pemetrexed/bev*
 BENJAMIN LEVY, MD	Yes, liquid and tissue	Atezo/carbo/paclitaxel + bev
 JOEL W NEAL, MD, PHD	Yes, tissue	Pembro/carbo/pemetrexed or Atezo/carbo/paclitaxel + bev
 NATHAN A PENNELL, MD, PHD	Yes, tissue	Pembro/carbo/pemetrexed
 DAVID R SPIGEL, MD	Yes, liquid	Continue osimertinib, add carbo/pemetrexed

Atezo = atezolizumab; carbo = carboplatin; bev = bevacizumab; pembro = pembrolizumab

* Atezo/carbo/paclitaxel + bev if very symptomatic

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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
 JOEL W NEAL, MD, PHD	Pembro/carbo/pem	Pembro	Pembro +/- carbo/pem	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

Pem = pemetrexed

* If very symptomatic, pembro/carbo/pem; † Likely dose-reduced chemotherapy

RTP RESEARCH TO PRACTICE

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/P	Pembro	Pembro
 JOEL W NEAL, MD, PHD	Pembro/carbo/ *nab*-P or P	Pembro/carbo/*nab*-P	Pembro +/- carbo/ *nab*-P or P	Pembro+/- carbo/ *nab*-P
 NATHAN A PENNELL, MD, PHD	Pembro/carbo/*nab*-P	Pembro/carbo/P	Pembro	Pembro
 DAVID R SPIGEL, MD	Pembro/carbo/*nab*-P	Pembro/carbo/*nab*-P	Pembro	Pembro

Nab-P = nanoparticle albumin-bound paclitaxel; P = paclitaxel

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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
 JOEL W NEAL, MD, PHD	2 years	2 years
 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

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Should PD-L1 levels generally be tested in patients with locally advanced NSCLC? In general, do you recommend durvalumab as consolidation treatment for patients with locally advanced NSCLC who have no disease progression after chemoradiation therapy?

		Recommend consolidation durvalumab?		
	Test for PD-L1?	PD-L1 ≤1%	EGFR mutation	ALK rearrangement
 JOHN V HEYMACH, MD, PHD	No	Yes	Yes	Yes
 LEORA HORN, MD, MSC	No	Yes	No	No
 COREY J LANGER, MD	Yes	Yes	Yes	Yes
 BENJAMIN LEVY, MD	Yes	Yes	Yes	Yes
 JOEL W NEAL, MD, PHD	Yes	Yes	Yes	No
 NATHAN A PENNELL, MD, PHD	No	Yes	Yes	Yes
 DAVID R SPIGEL, MD	No	Yes	Yes	Yes

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A patient who successfully received chemoradiation therapy for locally advanced NSCLC is about to start durvalumab. Pretreatment imaging shows changes consistent with radiation effect. Would you use durvalumab?

In general, would you recommend consolidation durvalumab for similar patients who are experiencing mild esophagitis or mildly symptomatic pneumonitis?

	Radiation effect	Mild esophagitis	Mildly symptomatic pneumonia
 JOHN V HEYMACH, MD, PHD	Yes	Yes	No
 LEORA HORN, MD, MSC	Yes	Yes	No, wait until improvement
 COREY J LANGER, MD	Yes	Yes	Yes*
 BENJAMIN LEVY, MD	Yes	Yes	Yes
 JOEL W NEAL, MD, PHD	Yes	Yes	Yes
 NATHAN A PENNELL, MD, PHD	Yes	Yes	No
 DAVID R SPIGEL, MD	Yes	Yes	Yes

* If Grade 1 and do not require steroids

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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
 JOEL W NEAL, MD, PHD	Carbo/etoposide + atezolizumab	Carbo/etoposide + atezolizumab or durvalumab
 NATHAN A PENNELL, MD, PHD	Carbo/etoposide + atezolizumab	Carbo/etoposide + atezolizumab
 DAVID R SPIGEL, MD	Carbo/etoposide + durvalumab	Carbo/etoposide + durvalumab

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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
 JOEL W NEAL, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 NATHAN A PENNELL, MD, PHD	Carboplatin/etoposide
 DAVID R SPIGEL, MD	Carboplatin/etoposide + durvalumab

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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
 JOEL W NEAL, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 NATHAN A PENNELL, MD, PHD	Carboplatin/etoposide/atezolizumab
 DAVID R SPIGEL, MD	Carboplatin/etoposide + durvalumab

SIADH = syndrome of inappropriate antidiuretic hormone secretion

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- Dr Peles: A 69-year-old man and smoker with Stage IIIA squamous cell lung carcinoma
- Dr Lamar: An 83-year-old woman with Stage IIIB NSCLC – EGFR exon 21 mutation
- Comments: Pneumonitis in patients with Stage III disease and COPD receiving durvalumab
- Dr Lamar: A 94-year-old woman with metastatic NSCLC – PD-L1 75%, no EGFR mutation
- Dr Peles: A 60-year-old man with metastatic adenocarcinoma of the lung – PD-L1 100%
- Dr Peles: A 73-year-old woman with extensive-stage small cell lung cancer

Module 2: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

Module 3: Journal Club

- EGFR mutation-positive disease (ADAURA trial)
- Checkpoint inhibitors (ipilimumab/nivolumab, treatment intervals, locally advanced disease)
- HER2-positive disease (trastuzumab deruxtecan)

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Journal of Cancer Research and Clinical Oncology (2020) 146:2329–2338
https://doi.org/10.1007/s00432-020-03296-6

REVIEW – CLINICAL ONCOLOGY

Non-small cell lung cancer patients with ex19del or exon 21 L858R mutation: distinct mechanisms, different efficacies to treatments

W.-Q. Li[1] · J.-W. Cui[1]

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

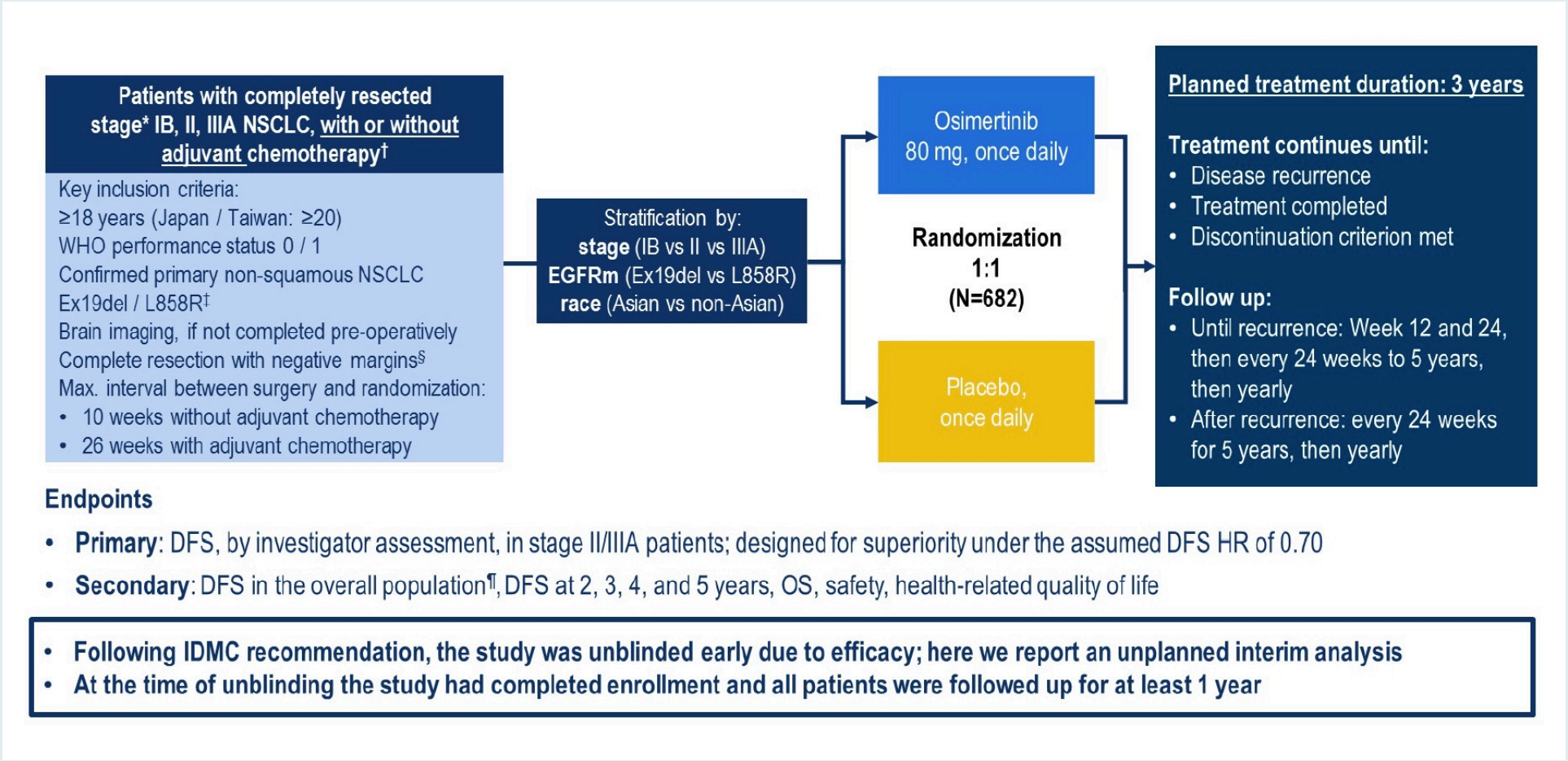
Herbst RS et al.

ASCO 2020;Abstract LBA5.

Discussion of LBA5

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

ADAURA Phase III Trial Schema



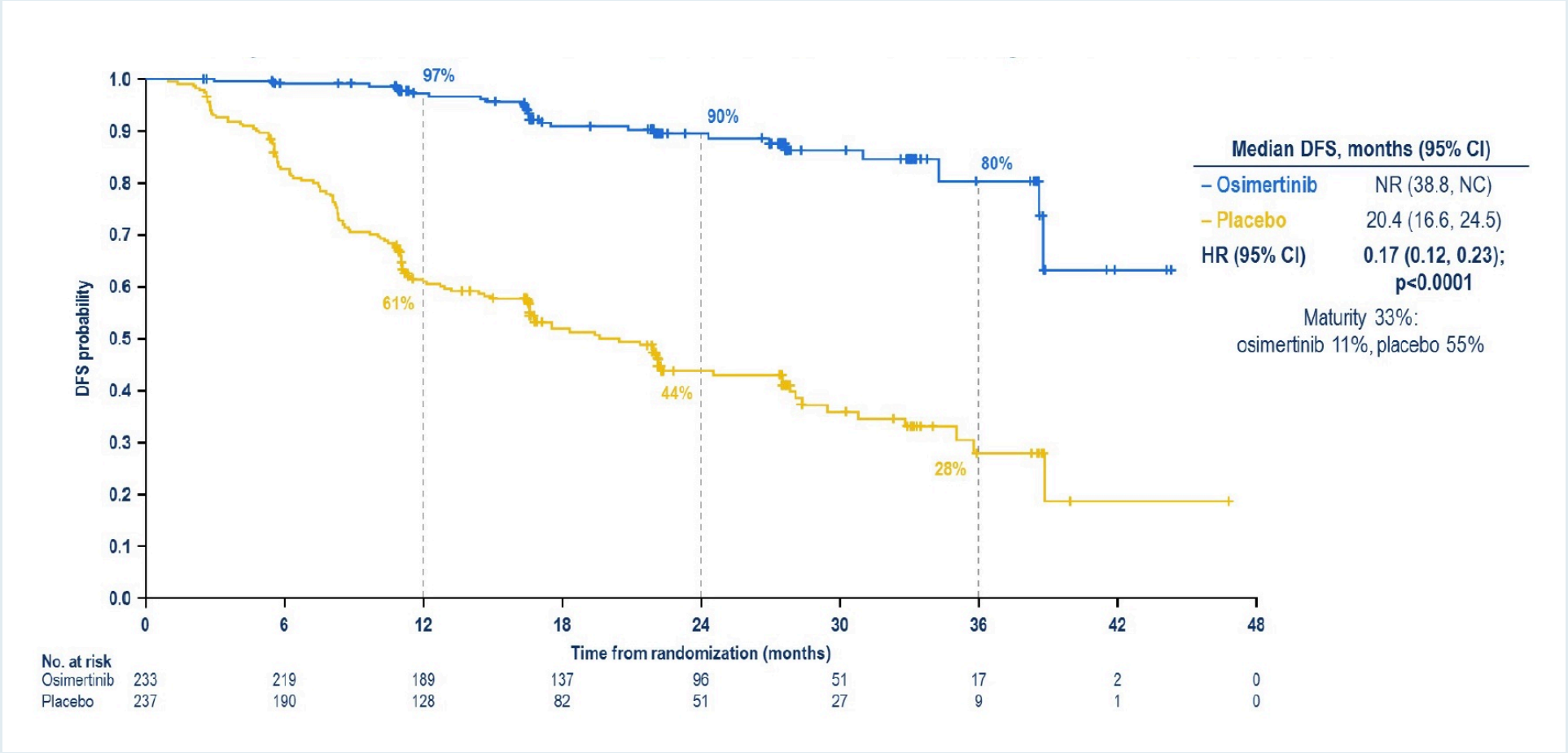
Endpoints

- **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.

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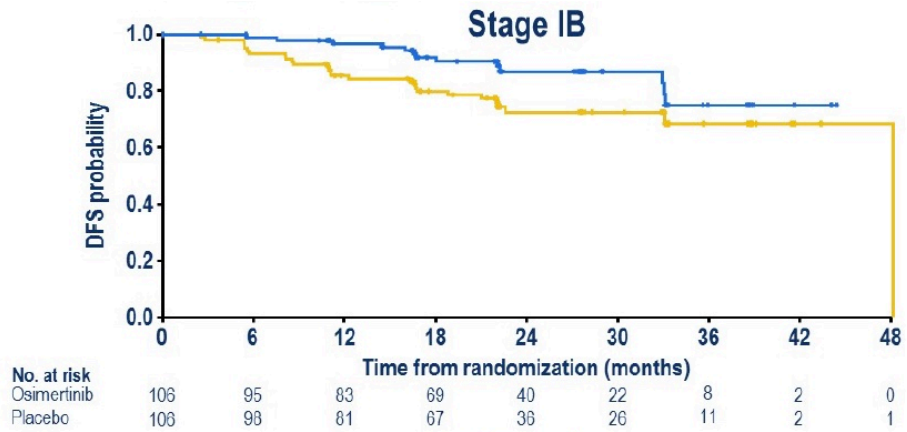
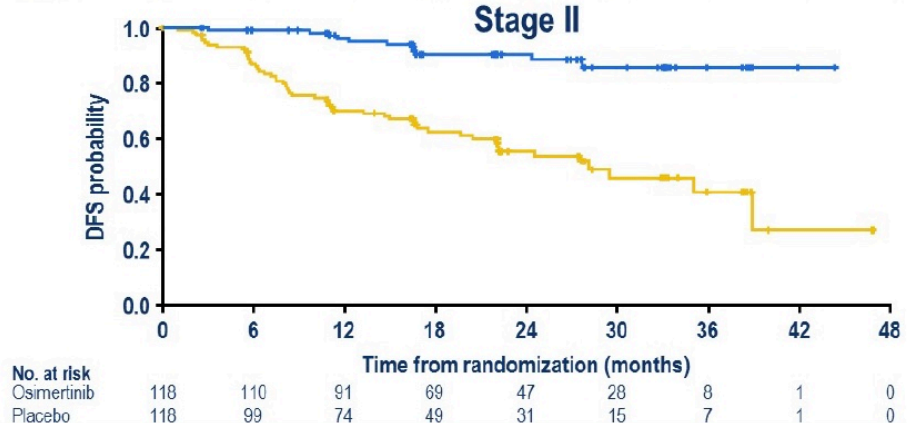
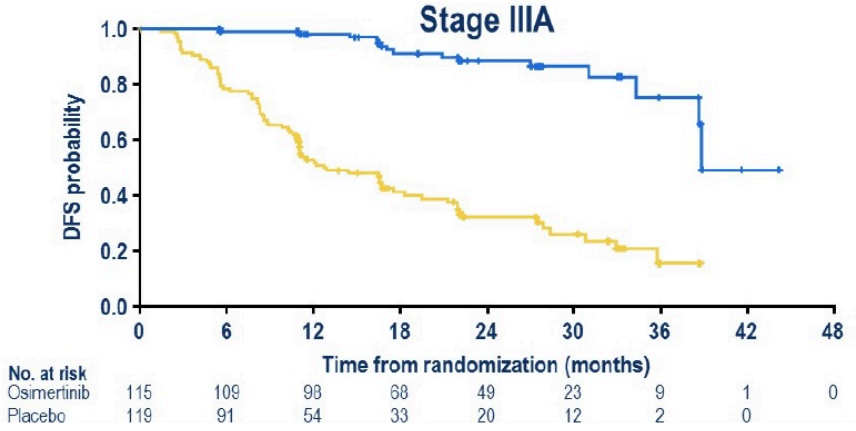
ADAURA: DFS by Stage



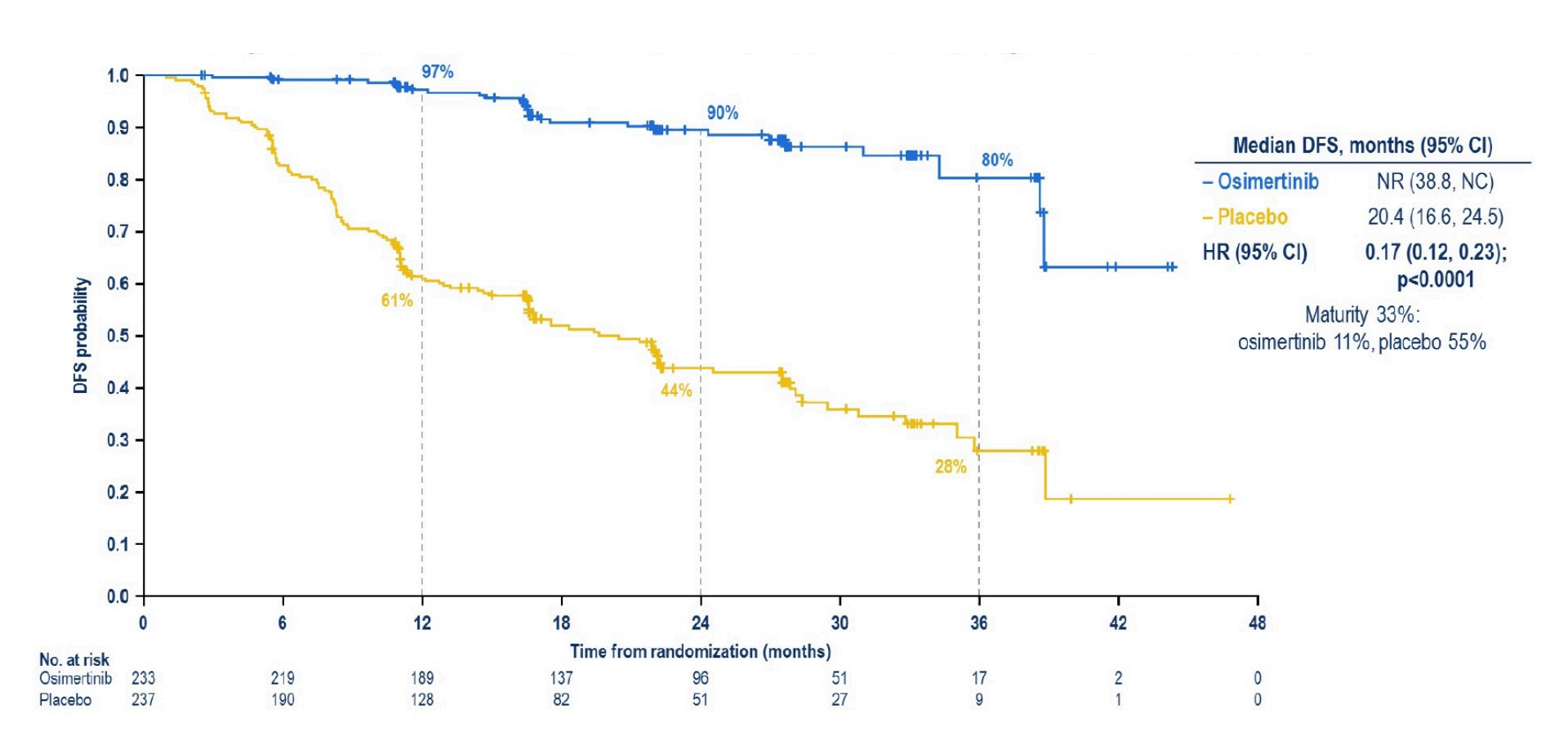


	Stage IB	Stage II	Stage IIIA
2 year DFS rate, % (95% CI)			
– Osimertinib	87 (77, 93)	91 (82, 95)	88 (79, 94)
– Placebo	73 (62, 81)	56 (45, 65)	32 (23, 42)
Overall HR (95% CI)	0.50 (0.25, 0.96)	0.17 (0.08, 0.31)	0.12 (0.07, 0.20)



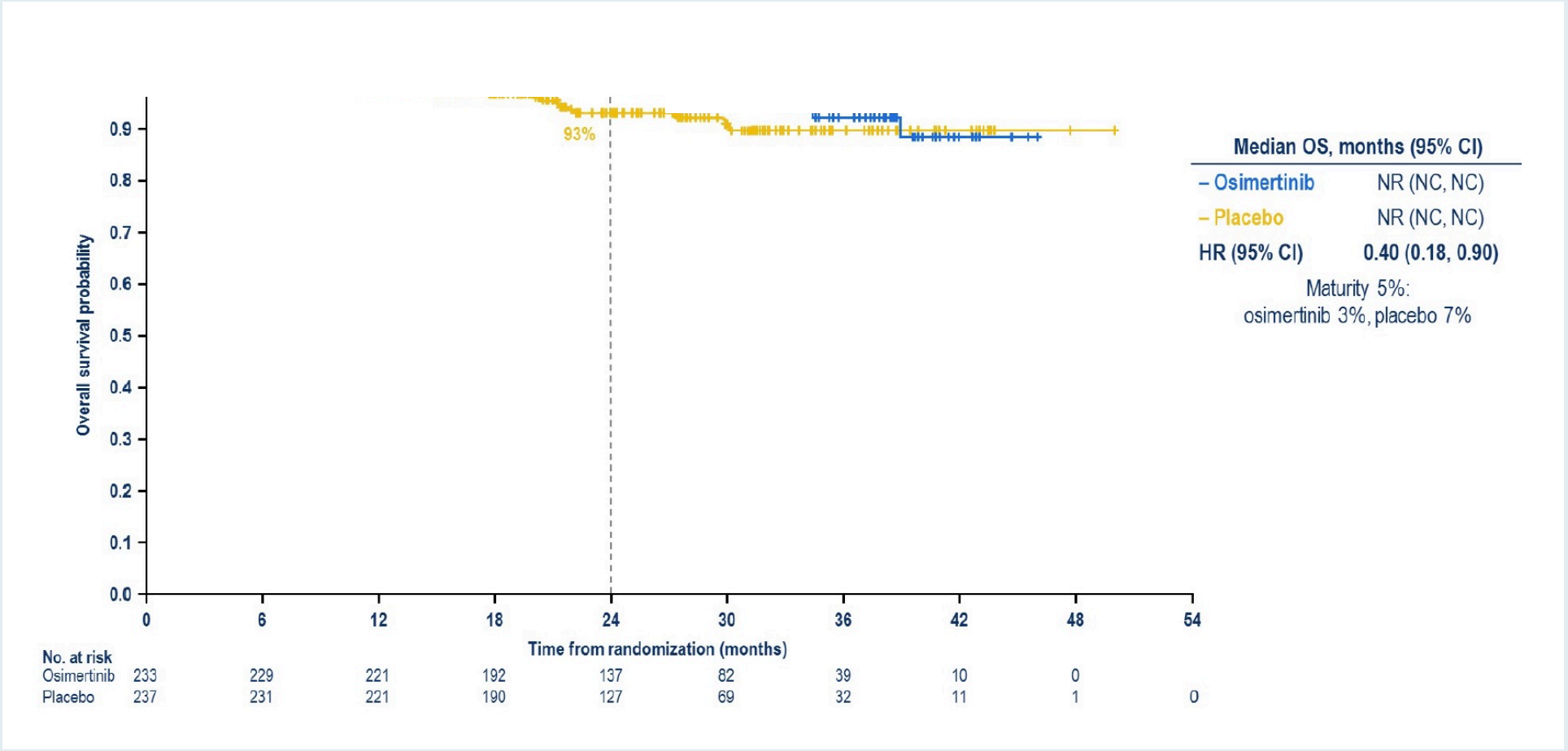
Herbst RS et al. ASCO 2020;Abstract LBA5.

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



Herbst RS et al. ASCO 2020;Abstract LBA5.

ADAURA: Early Snapshot of OS (Stage II/IIIA)



Herbst RS et al. ASCO 2020;Abstract LBA5.

RTP RESEARCH TO PRACTICE

ADAURA: Safety Summary

AE, any cause*, n (%)	Osimertinib (n=336)	Placebo (n=343)
Any AE	327 (97)	306 (89)
Any AE Grade ≥3	68 (20)	48 (14)
Any AE leading to death	0	1 (<1)
Any serious AE	54 (16)	44 (13)
Any AE leading to discontinuation	38 (11)	15 (4)
Any AE leading to dose reduction	25 (7)	2 (1)
AE, possibly causally related†, n (%)		
Any AE	303 (90)	190 (55)
Any AE Grade ≥3	32 (10)	9 (3)
Any AE leading to death	0	0
Any serious AE	9 (3)	2 (1)

Herbst RS et al. ASCO 2020;Abstract LBA5.

frontiers in Oncology

REVIEW
published: 23 June 2020
doi: 10.3389/fonc.2020.01193

Extended-Interval Dosing Strategy of Immune Checkpoint Inhibitors in Lung Cancer: Will it Outlast the COVID-19 Pandemic?

Kartik Sehgal[1,2*], *Daniel B. Costa*[1] *and Deepa Rangachari*[1*]

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	0.56
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] Gadgeel S et al. *J Clin Oncol* 2020;38(14):1505-17. [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 (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)."

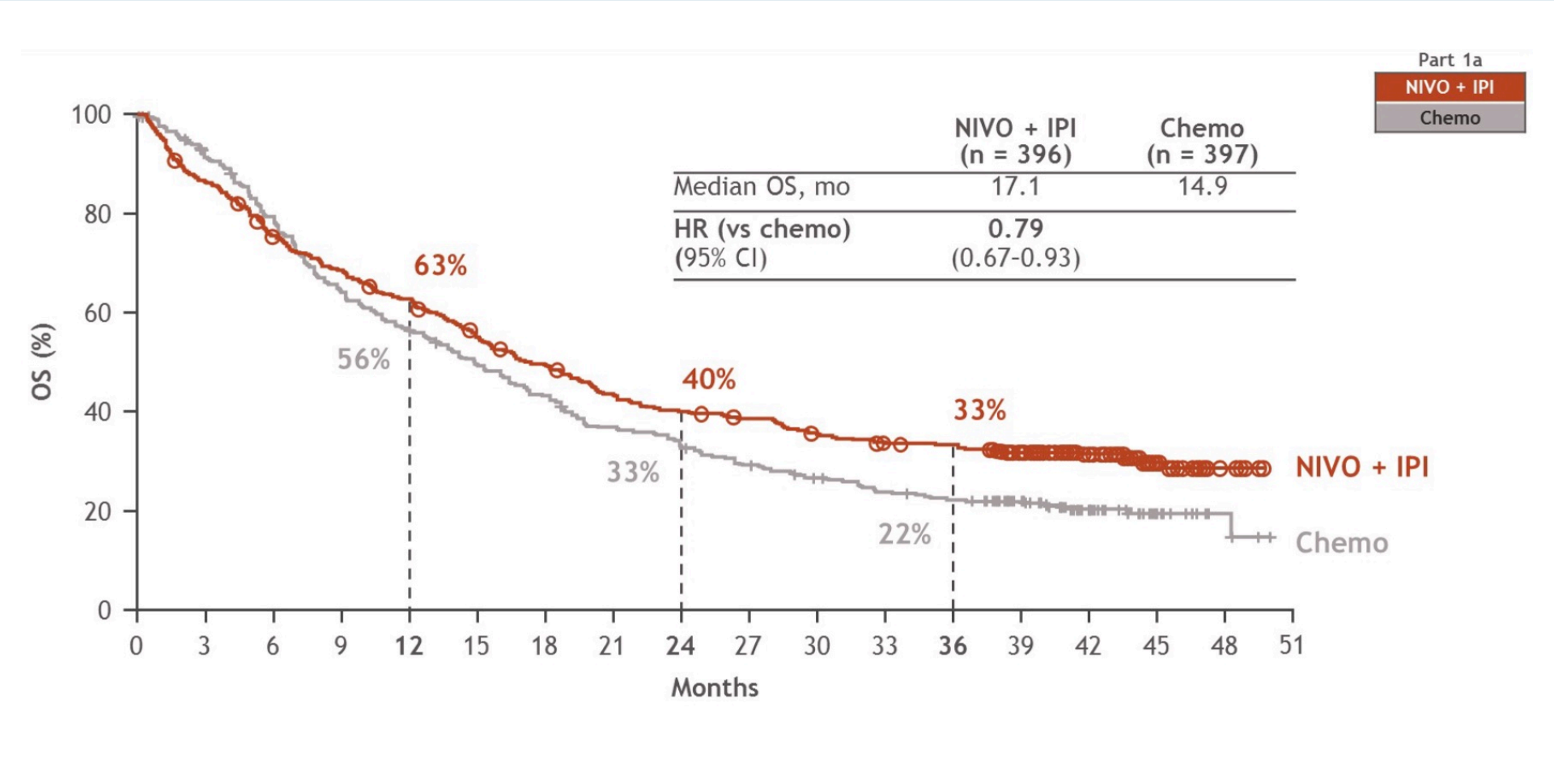
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-nivolumab-plus-ipilimumab-first-line-mnsclc-pd-l1-tumor-expression-1

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

Ramalingam SS et al.

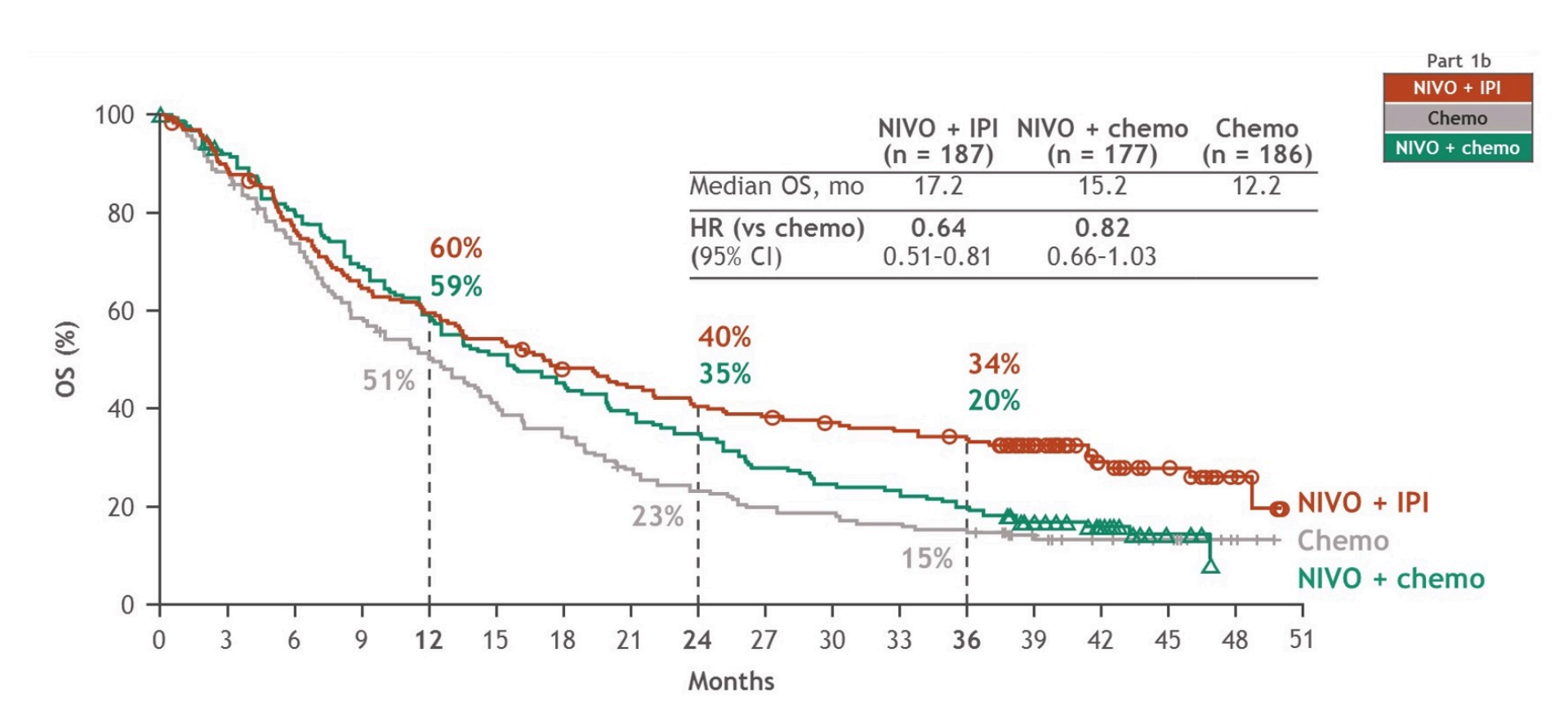
ASCO 2020;Abstract 9500.

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



Ramalingam SS et al. ASCO 2020;Abstract 9500.

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



Ramalingam SS et al. ASCO 2020;Abstract 9500.

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Landmark Analysis of OS by Response Status at 6 Months with PD-L1 ≥ 1% (IPI + Nivo vs Chemo)

	Ipi + Nivo (n = 295) versus Chemo (n = 306)			
Response status	Response at 6 mo	1-yr OS rate	2-yr OS rate	3-yr OS rate
CR or PR	39% vs 25%	90% vs 73%	76% vs 51%	70% vs 39%
SD	14% vs 18%	69% vs 54%	45% vs 38%	34% vs 33%
PD	46% vs 58%	44% vs 47%	22% vs 25%	19% vs 17%

Ramalingam SS et al. ASCO 2020;Abstract 9500.

CheckMate 227: Treatment-Related AEs

Select AE	Nivo/Ipi (n = 576)		Chemo (n = 570)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Diarrhea	17.0%	1.7%	9.6%	0.7%
Rash	17.0%	1.6%	5.3%	0
Fatigue	14.4%	1.7%	18.9%	1.4%
Decreased appetite	13.2%	0.7%	19.6%	1.2%
Nausea	9.9%	0.5%	36.1%	2.1%
Anemia	3.8%	1.4%	33.0%	11.6%
Neutropenia	0.2%	0	17.2%	9.5%

- Treatment-related serious **AEs (any grade)**: 24.5% (Nivo/Ipi) vs 13.9% (chemo)
- Treatment-related AEs leading to **discontinuation (any grade)**: 18.1% (Nivo/Ipi) vs 9.1% (chemo)
- Treatment-related **death (any grade)**: 1.4% (Nivo/Ipi) vs 1.1% (chemo)

Hellmann MD et al. *N Engl J Med* 2019;381(21):2020-31.

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

Press Release — May 26, 2020

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

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

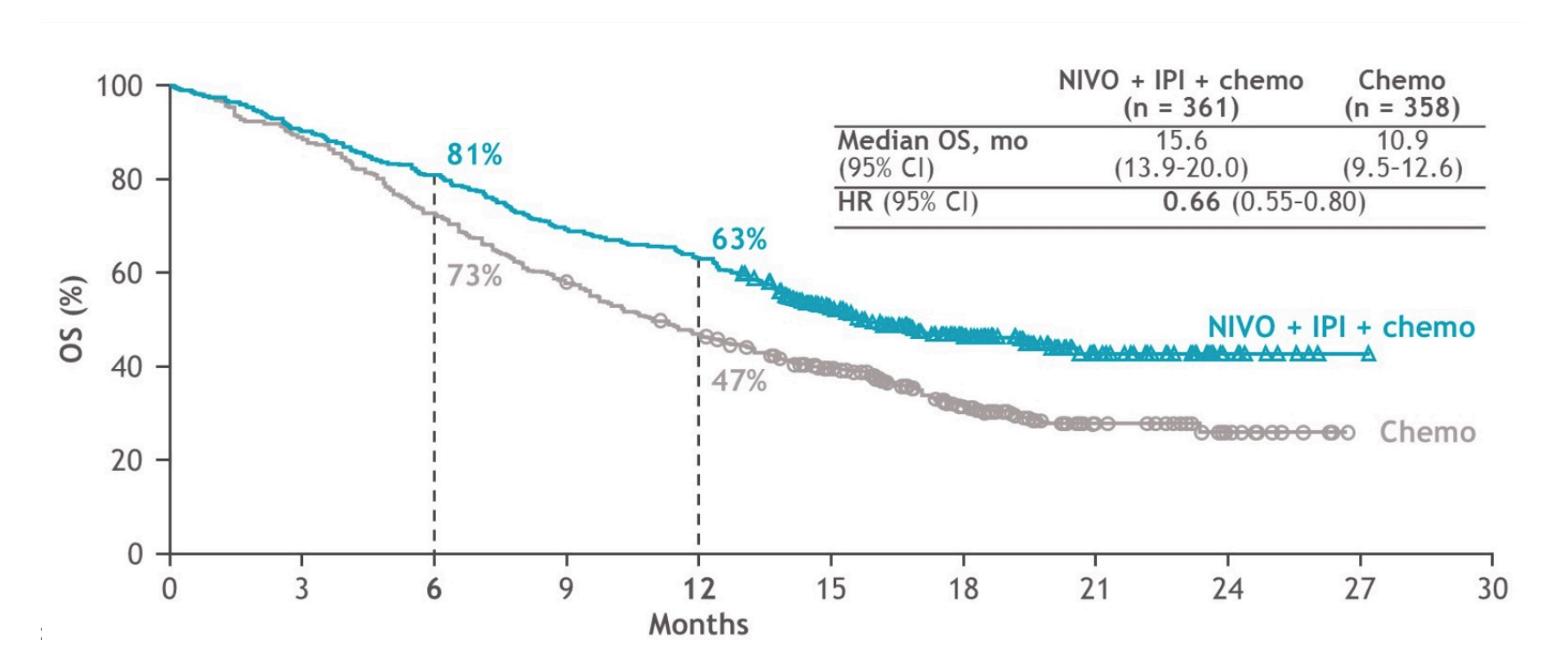
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-nivolumab-plus-ipilimumab-and-chemotherapy-first-line-treatment-metastatic-nsclc

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

Reck M et al.

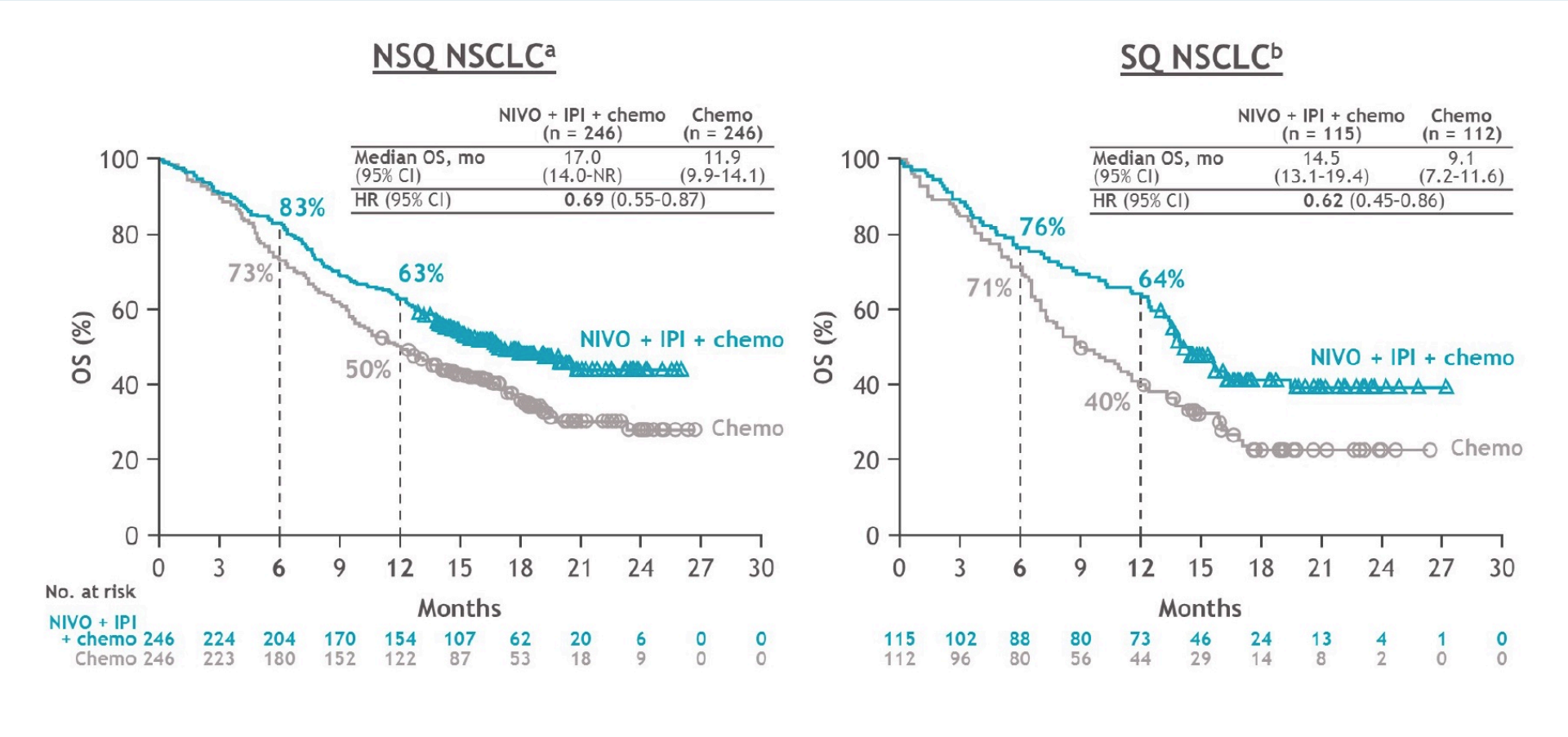
ASCO 2020;Abstract 9501.

CheckMate 9LA: Updated OS



Reck M et al. ASCO 2020;Abstract 9501.

CheckMate 9LA: Updated OS by Histology



Reck M et al. ASCO 2020;Abstract 9501.

RTP RESEARCH TO PRACTICE

CheckMate 9LA: Safety Summary

TRAE,[a] %	NIVO + IPI + chemo (n = 358)		Chemo (n = 349)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Any TRAE	92	47	88	38
TRAEs leading to discontinuation of any component of the regimen	19	16	7	5
Serious TRAEs	30	25.4	18	15
Treatment-related deaths[b]	2		2	

- Median (range) duration of therapy was 6.1 (0-23.5) months and 2.4 (0-24.0) months for NIVO + IPI + chemo versus chemo, respectively
- Most common any-grade TRAEs (≥ 15%) were nausea, anemia, asthenia and diarrhea

Reck M et al. ASCO 2020;Abstract 9501.

Real-World Rates of Pneumonitis After Consolidation Durvalumab

Real-World Survey of Pneumonitis/Radiation Pneumonitis in LA-NSCLC After Approval of Durvalumab: HOPE-005/CRIMSON Retrospective Cohort Study

- >80% developed pneumonitis
- More than half of them were asymptomatic, but 5% needed HOT and 1.5% developed fatal pneumonitis
- V20 was an independent risk factor for symptomatic pneumonitis (Grade ≥2)
- With careful consideration, durvalumab-rechallenge could be an option after corticosteroid therapy for pneumonitis

Incidence of Pneumonitis in US Veterans with NSCLC Receiving Durvalumab After Chemoradiation Therapy

- In this real-world cohort, clinical significant pneumonitis was:
  - More frequent compared to clinical trial reports
    - Asymptomatic infiltrates on imaging: 39.8%
    - Clinically significant pneumonitis: 21.1%
      - Grade 2 (7.3%), Grade 3 (11.4%), Grade 4 (1.6%), Grade 5 (0.8%)
  - Not associated with increased risk of death

Saito et al. ASCO 2020; Abstract 9039. Thomas T et al. ASCO 2020; Abstract 9034.

RTP RESEARCH TO PRACTICE

LUNG CANCER

Making Checkpoint Inhibitors Part of Treatment of Patients With Locally Advanced Lung Cancers: The Time Is Now

Mark G. Kris, MD[1]; Corinne Faivre-Finn, MD, PhD[2]; Tiana Kordbacheh, MD[2]; Jamie Chaft, MD[1]; Jia Luo, MD[1]; Anne Tsao, MD[3]; and Stephen Swisher, MD[3]

2020 ASCO EDUCATIONAL BOOK | asco.org/edbook

A Phase I Safety and Feasibility Study of Neoadjuvant Chemoradiation plus Pembrolizumab Followed by Consolidation Pembrolizumab in Resectable Stage IIIA Non-Small Cell Lung Cancer

Lemmon C et al.

ASCO 2020;Abstract 9009.

Cancer Treatment Reviews 86 (2020) 101996

Contents lists available at ScienceDirect

Cancer Treatment Reviews

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

Anti-tumour Treatment

The force of HER2 – A druggable target in NSCLC?

M. Jebbink[a], A.J. de Langen[a], M.C. Boelens[b], K. Monkhorst[b], E.F. Smit[a,*]

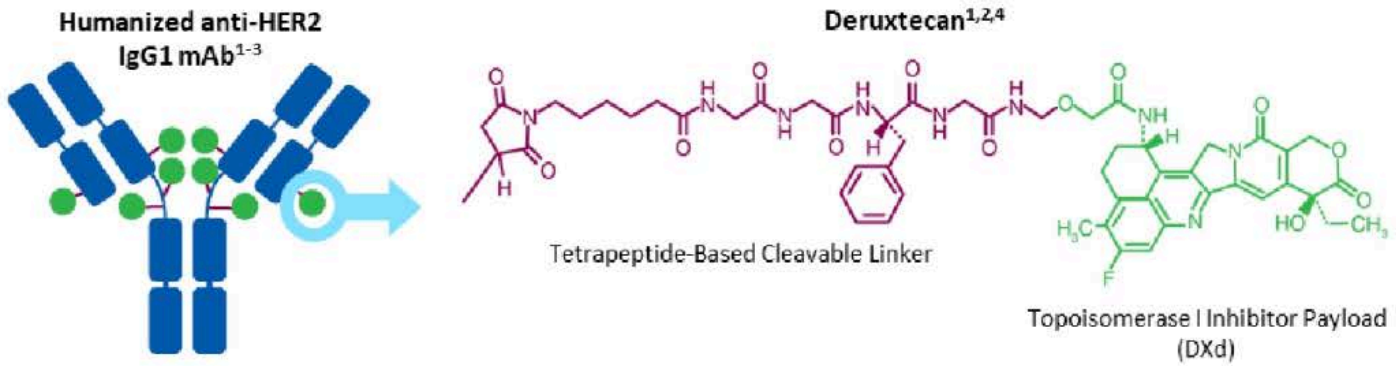
Trastuzumab Deruxtecan (T-DXd; DS-8201) in Patients with HER2-Mutated Metastatic Non-Small Cell Lung Cancer (NSCLC): Interim Results of DESTINY-Lung01

Smit EF et al.
ASCO 2020;Abstract 9504.

Antibody-Drug Conjugate
Trastuzumab Deruxtecan

T-DXd is an ADC with 3 components:

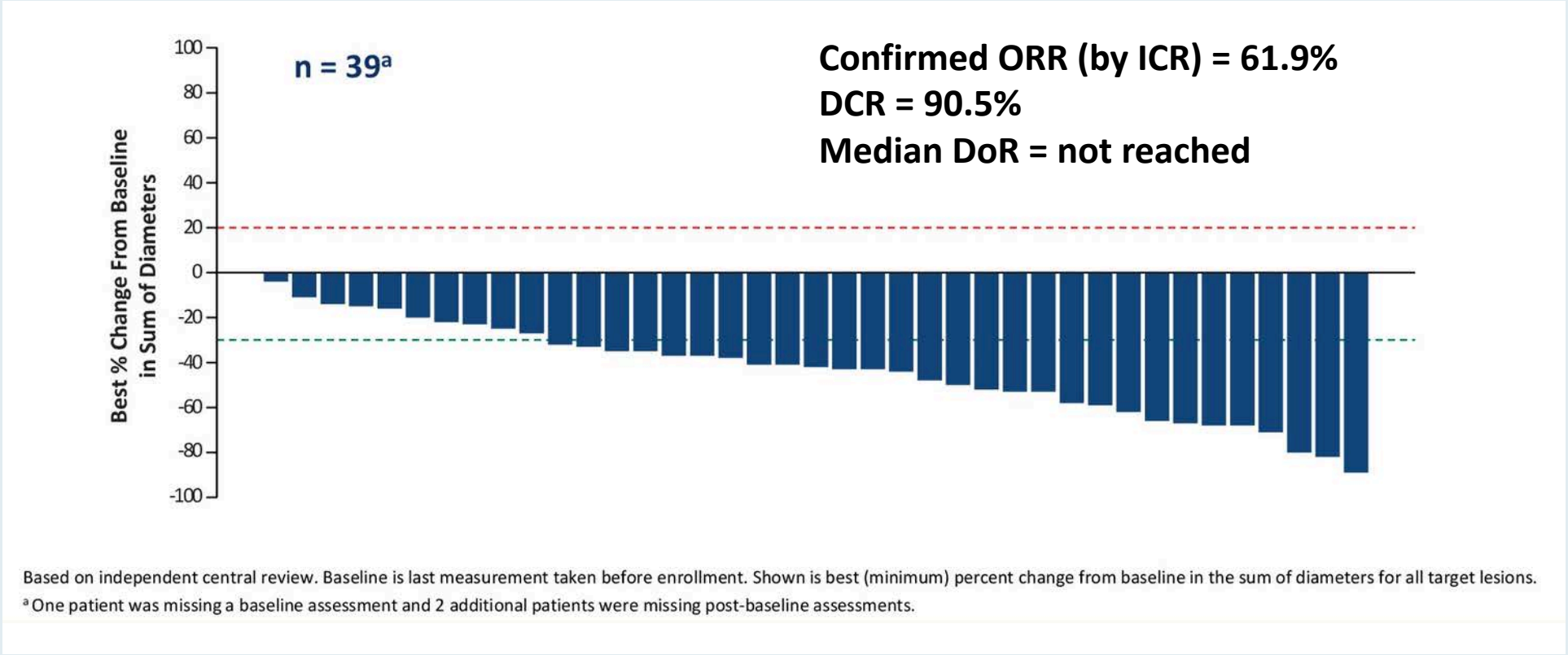
- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



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. *Proc ASCO* 2020;Abstract 9504.

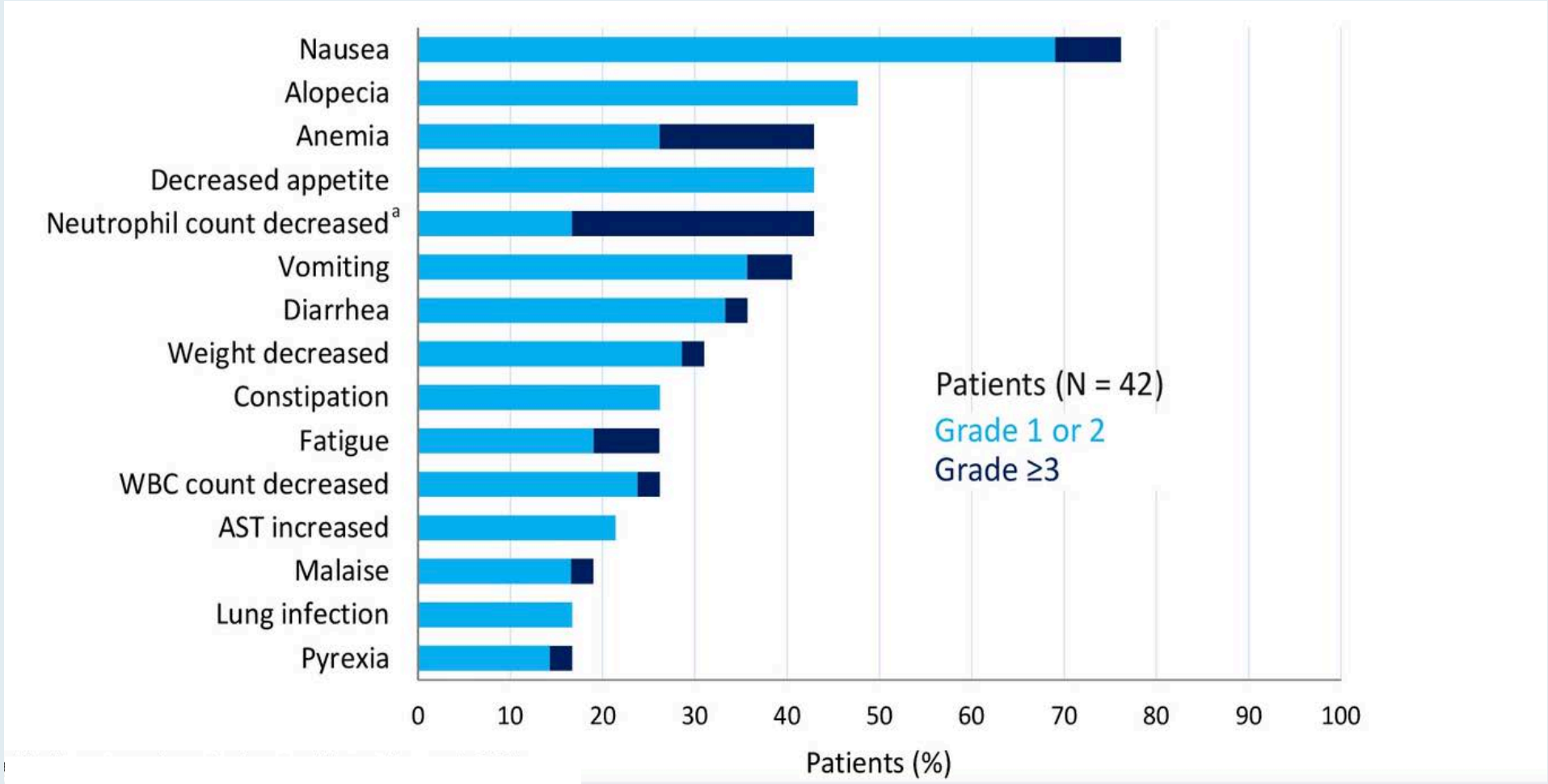
DESTINY-Lung01: Efficacy



- Median PFS = 14.0 mos

Smit EF et al. *Proc ASCO* 2020;Abstract 9504.

DESTINY-Lung01: Treatment-Emergent AEs



Smit EF et al. *Proc 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. *Proc ASCO* 2020;Abstract 9504.

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

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.

Clinical Investigator Perspectives on the Current and Future Role of PARP Inhibition in the Management of Ovarian Cancer

A Meet The Professor Series

Friday, September 11, 2020
12:00 PM – 1:00 PM ET

Faculty

Robert L Coleman, 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 days.

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