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

RTP
RESEARCH
TO PRACTICE

Current Questions and Controversies in the Management of Lung Cancer

An Interactive Meet The Professor Series

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

Commercial Support

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

Dr Love — Disclosures

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

RTP
RESEARCH
TO PRACTICE

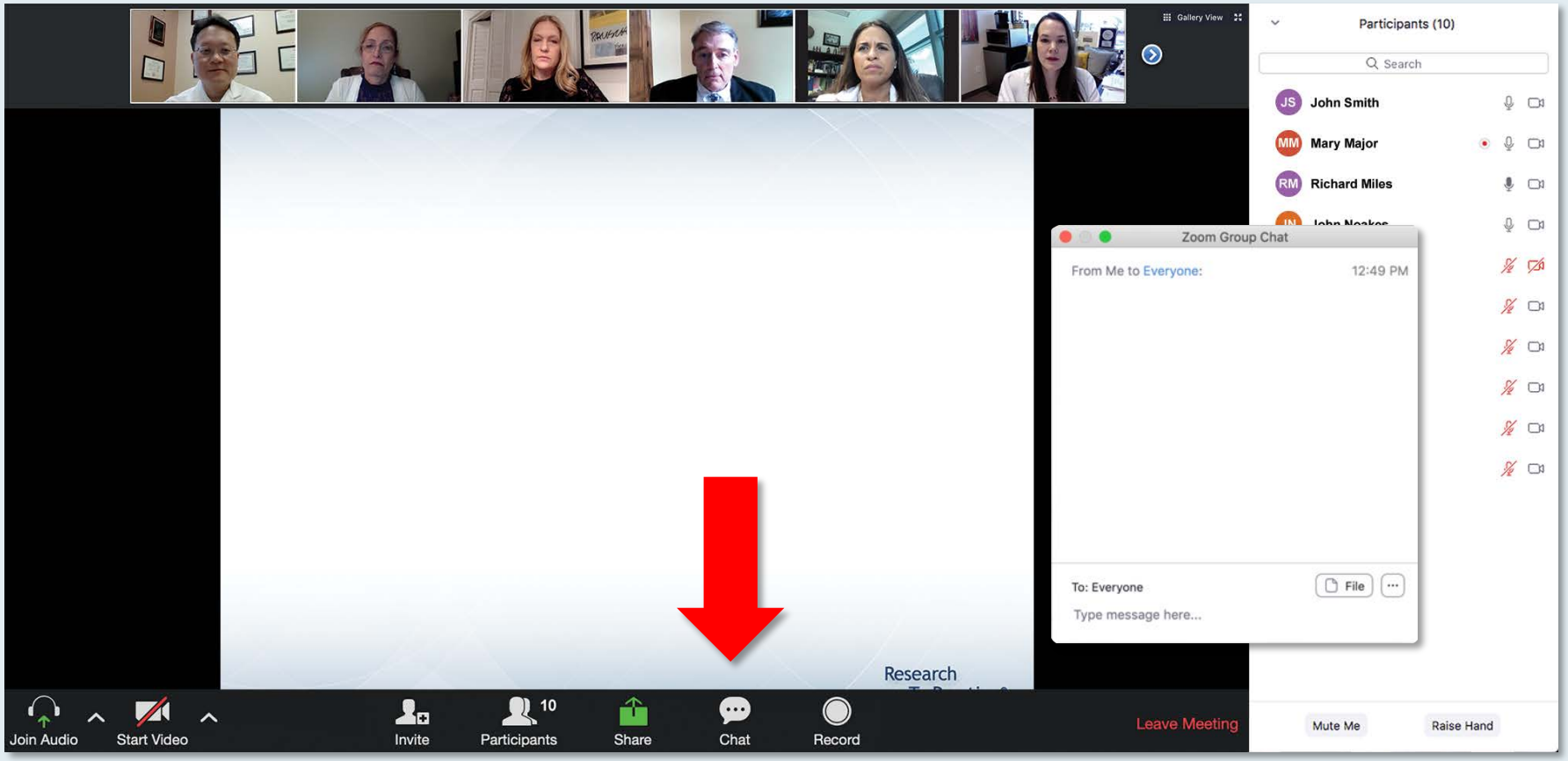
Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Spigel — Disclosures

Consulting Agreements	Aptitude Health, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Celgene Corporation, Dracen Pharmaceuticals, EMD Serono Inc, Evelo Biosciences Inc, Genentech, a member of the Roche Group, GlaxoSmithKline, Iksuda Therapeutics, Illumina, Merck, Molecular Templates, Nektar, Novartis, Pfizer Inc, PharmaMar, Roche Laboratories Inc, Seattle Genetics, Takeda Pharmaceutical Company Limited, Triptych Health Partners, TRM Oncology
Contracted Research	Aeglea BioTherapeutics, Astellas, AstraZeneca Pharmaceuticals LP, BIND Therapeutics Inc, Bristol-Myers Squibb Company, Celgene Corporation, Celldex Therapeutics, Clovis Oncology, Daiichi Sankyo Inc, Eisai Inc, EMD Serono Inc, G1 Therapeutics, Genentech, a member of the Roche Group, GRAIL, ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, ImmunoGen Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Lilly, Merck, Molecular Partners, Nektar, Neon Therapeutics, Novartis, Takeda Oncology, Transgene, UT Southwestern Medical Center

We Encourage Clinicians in Practice to Submit Questions

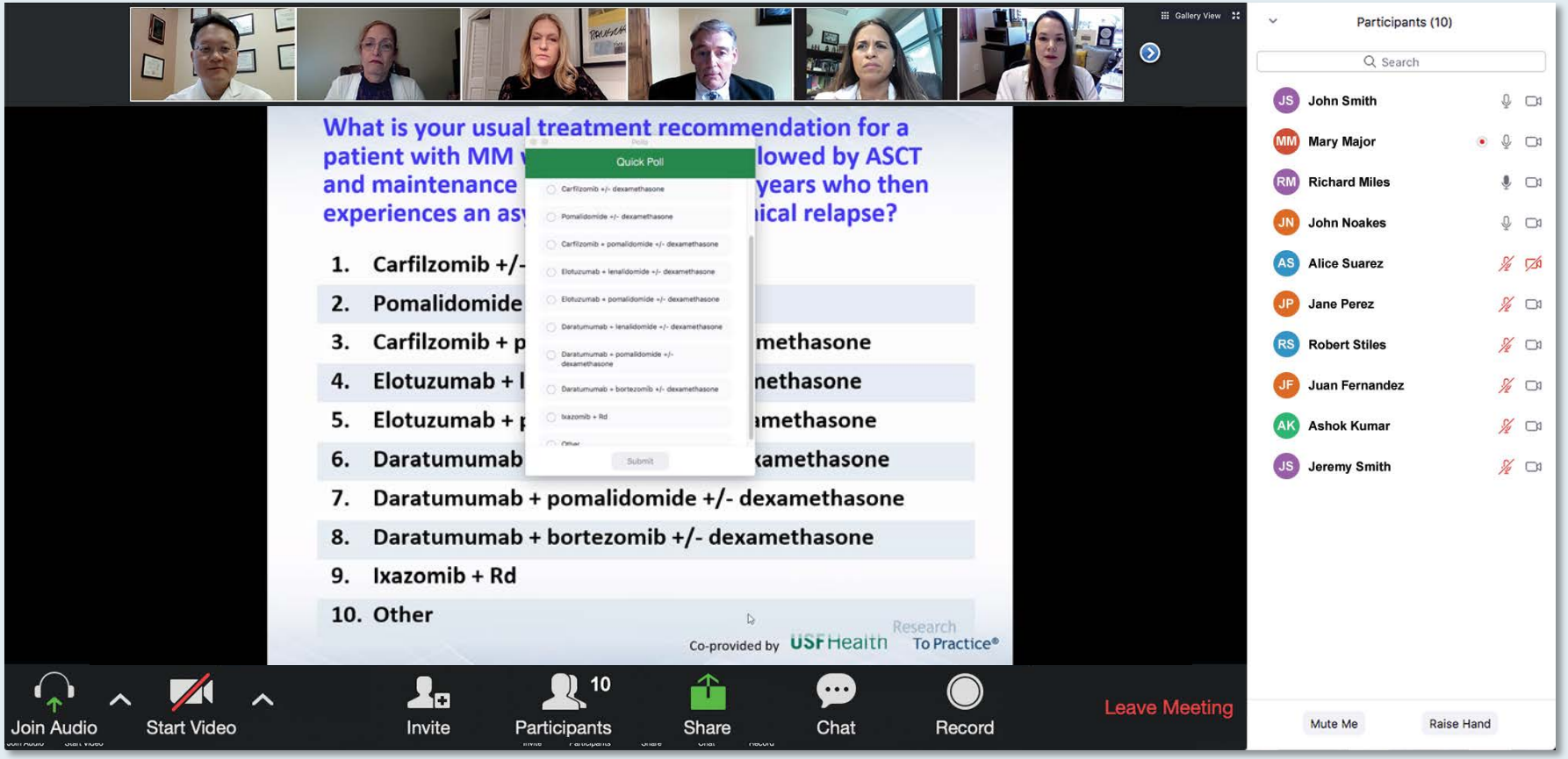


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

How to answer poll questions



When a poll question pops up, click your answer choice from the available options.

Results will be shown after everyone has answered.

RTP RESEARCH TO PRACTICE

Upcoming Live Webinars

Wednesday, September 23, 2020
12:00 PM – 1:00 PM ET

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

Faculty
Jeff Sharman, MD

Moderator
Neil Love, MD

Thursday, September 24, 2020
12:00 PM – 1:00 PM ET

Exploring the Role of Immune Checkpoint Inhibitor Therapy and Other Novel Strategies in Gynecologic Cancers

Faculty
David M O'Malley, MD

Moderator
Neil Love, MD

Upcoming Live Webinars

Tuesday, September 29, 2020
12:00 PM – 1:00 PM ET

Current Questions and Controversies in the Management of Lung Cancer

Faculty
Benjamin Levy, MD

Moderator
Neil Love, MD

Thursday, October 1, 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
Ursula Matulonis, MD

Moderator
Neil Love, MD

Upcoming Live Webinars

Friday, October 2, 2020
12:00 PM – 1:00 PM ET

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

Faculty
William G Wierda, MD, PhD

Moderator
Neil Love, MD

Thank you for joining us!

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

RTP
RESEARCH
TO PRACTICE

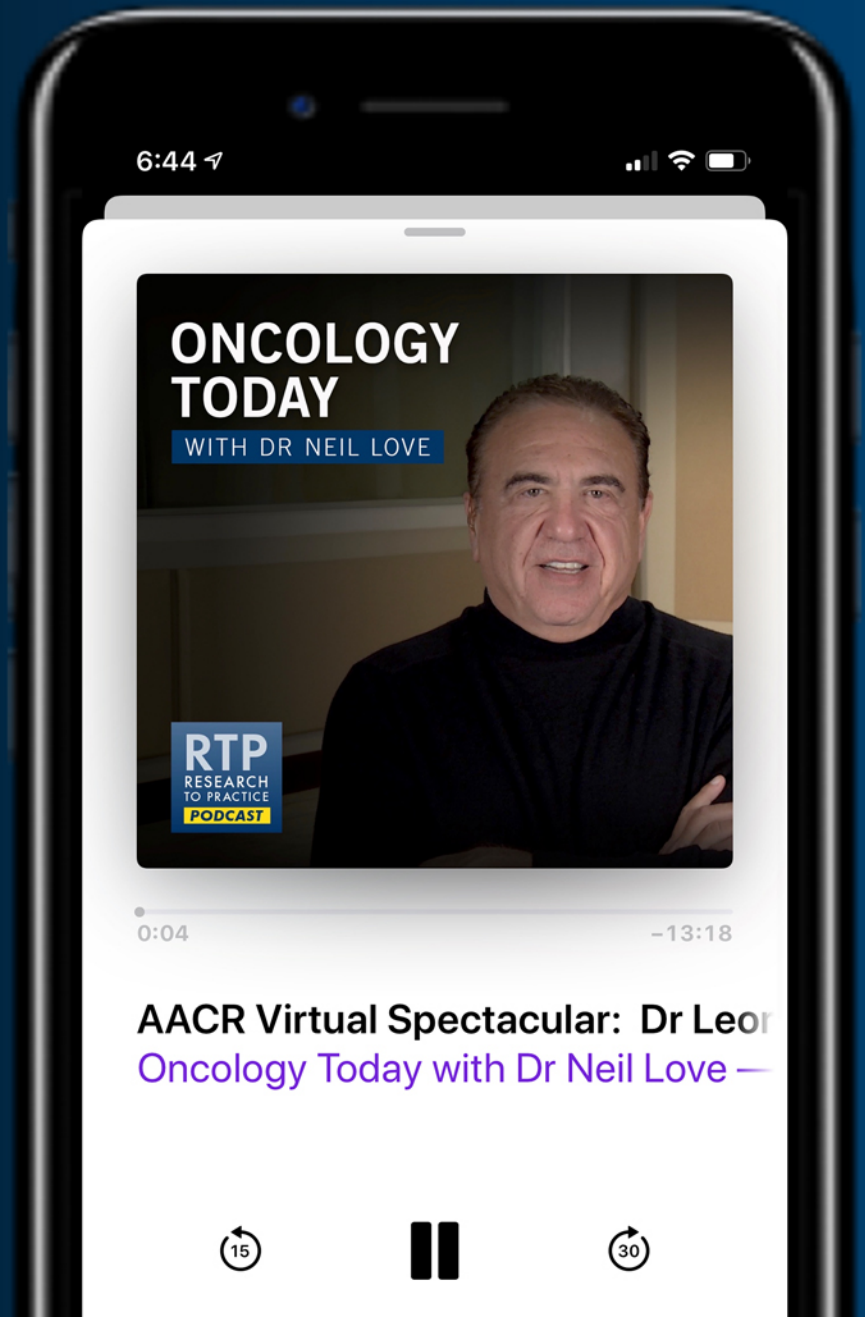
ONCOLOGY TODAY

WITH DR NEIL LOVE

Listen on Apple Podcasts

Spotify®

Listen on Google Podcasts



Current Questions and Controversies in the Management of Lung Cancer

An Interactive Meet The Professor Series

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

Meet The Professor Program Participating Faculty

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

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

Leora Horn, MD, MSc
Ingram Associate Professor
of Cancer Research
Director, Thoracic Oncology
Research Program
Assistant Vice Chairman for
Faculty Development
Vanderbilt University
Medical Center
Nashville, Tennessee

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

RTP
RESEARCH
TO PRACTICE

Meet The Professor Program Participating Faculty

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

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

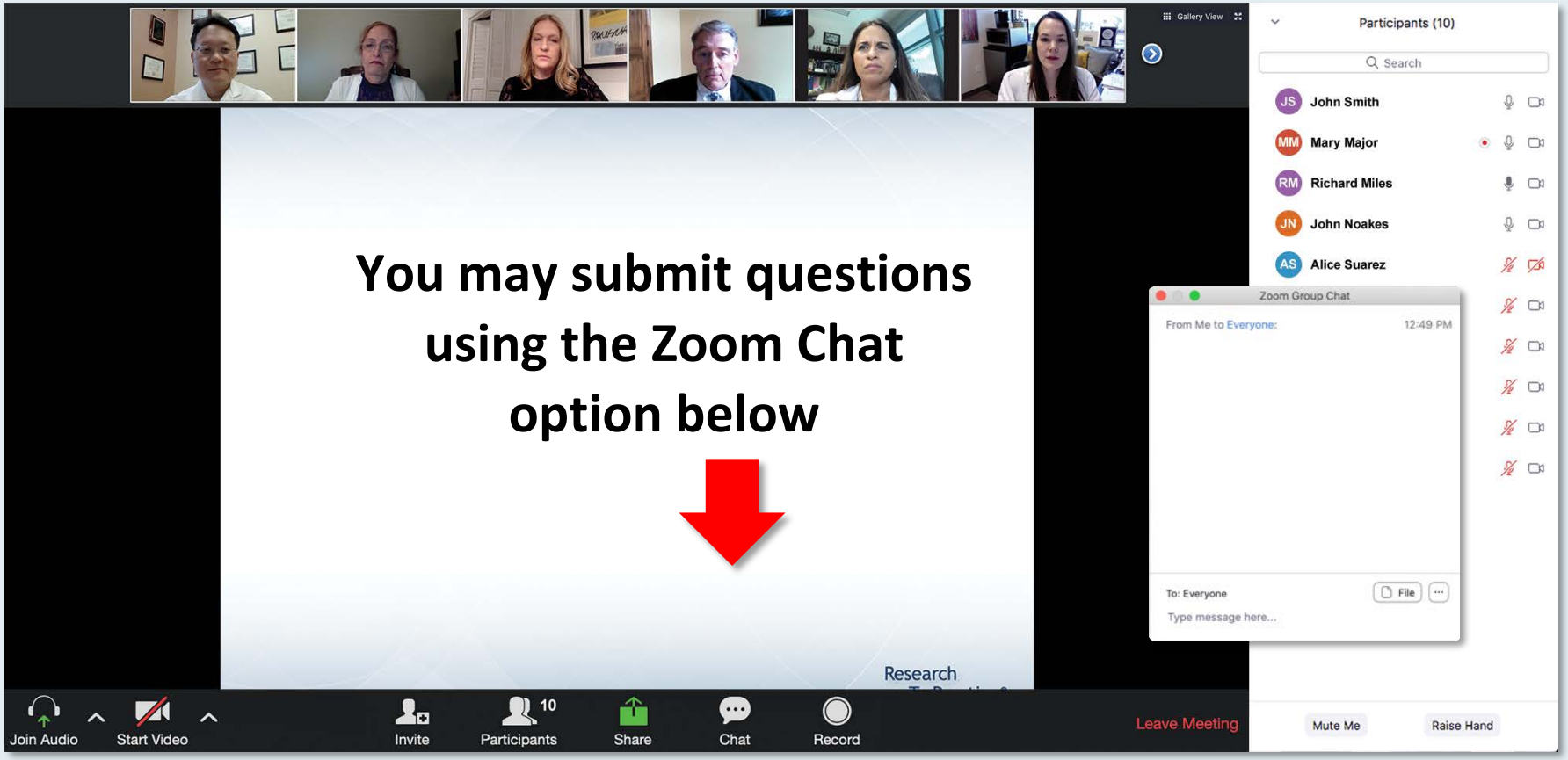
Lecia V Sequist, MD, MPH
Director, Center for Innovation in Early
Cancer Detection
Massachusetts General Hospital Cancer Center
The Landry Family Professor of Medicine
Harvard Medical School
Boston, Massachusetts

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

Project Chair
Neil Love, MD
Research To Practice
Miami, Florida

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions

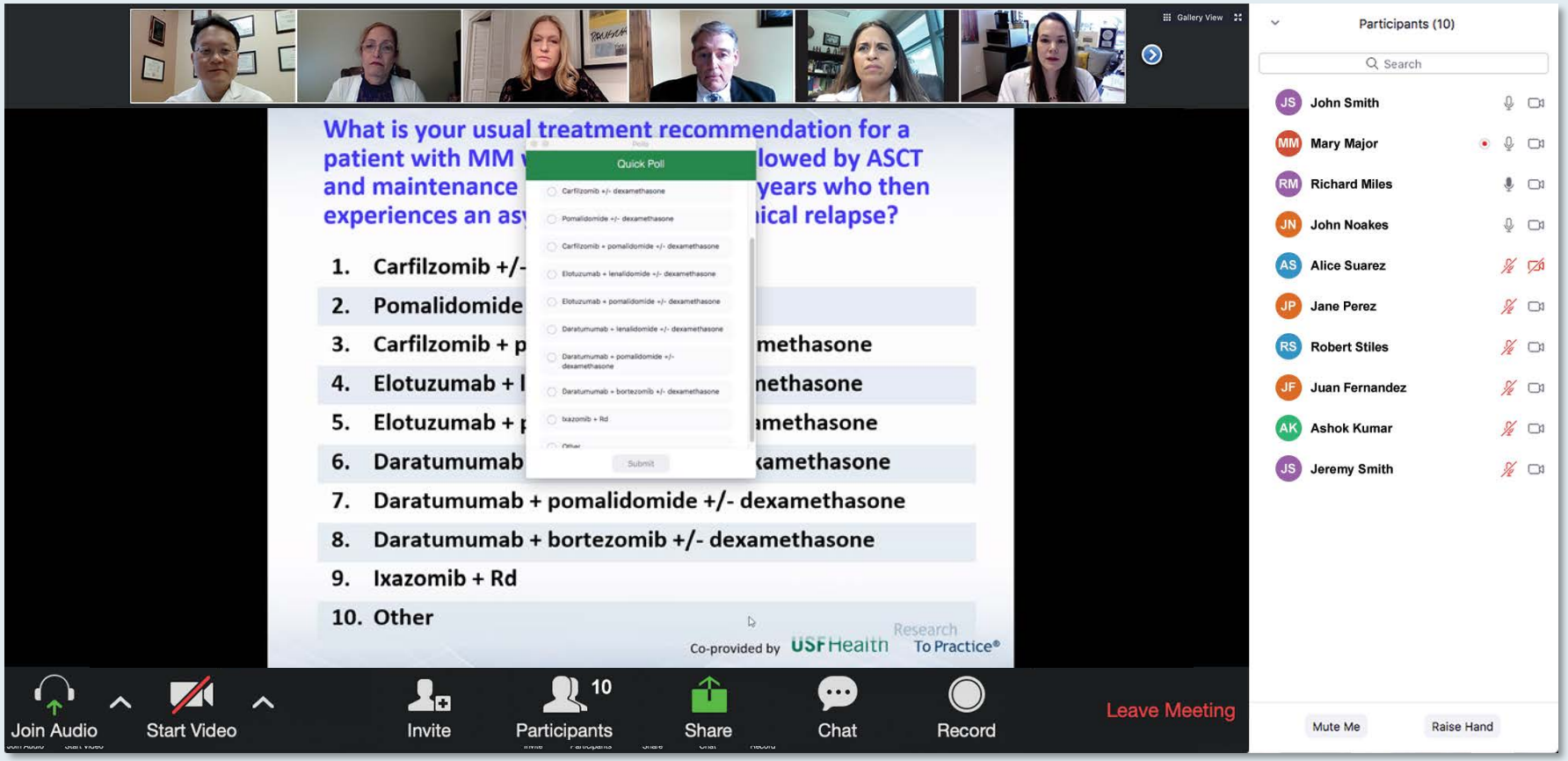


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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

RTP RESEARCH TO PRACTICE

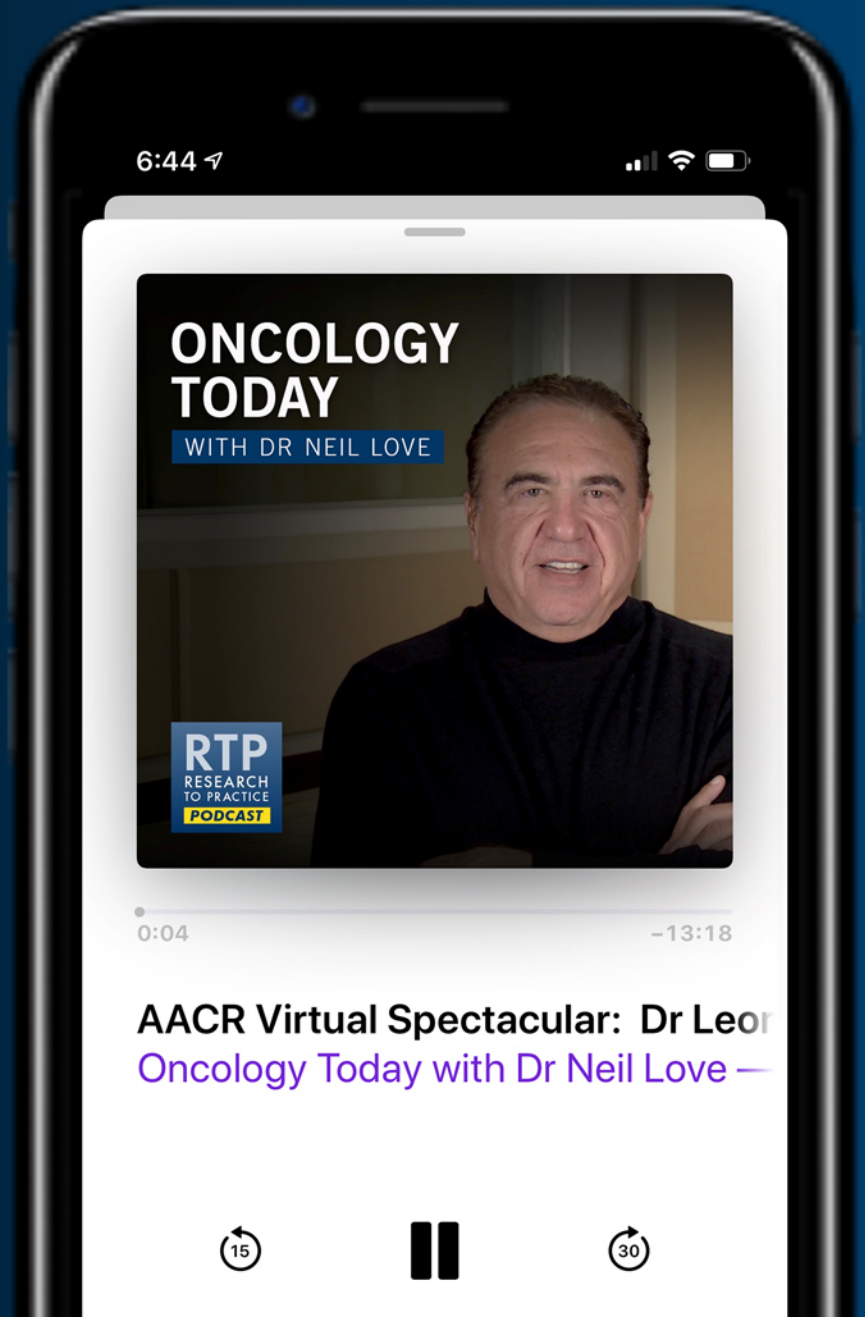
ONCOLOGY TODAY

WITH DR NEIL LOVE

Listen on Apple Podcasts

Spotify®

Listen on Google Podcasts



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

A Meet The Professor Series

Wednesday, September 23, 2020
12:00 PM – 1:00 PM ET

Faculty
Jeff Sharman, MD

Moderator
Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Exploring the Role of Immune Checkpoint Inhibitor Therapy and Other Novel Strategies in Gynecologic Cancers

A Meet The Professor Series

Thursday, September 24, 2020
12:00 PM – 1:00 PM ET

Faculty
David M O'Malley, MD

Moderator
Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Current Questions and Controversies in the Management of Lung Cancer

A Meet The Professor Series

Tuesday, September 29, 2020
12:00 PM – 1:00 PM ET

Faculty
Benjamin Levy, MD

Moderator
Neil Love, MD

RTP
RESEARCH
TO PRACTICE

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

A Meet The Professor Series

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

Faculty
Ursula Matulonis, MD

Moderator
Neil Love, MD

RTP
RESEARCH TO PRACTICE

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

A Meet The Professor Series

Friday, October 2, 2020
12:00 PM – 1:00 PM ET

Faculty
William G Wierda, MD, PhD

Moderator
Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Current Questions and Controversies in the Management of Lung Cancer

An Interactive Meet The Professor Series

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

Ranju Gupta, MD
Attending Physician
Co-Director, Cardio-Oncology Program
LVPG Hematology Oncology Associates
Lehigh Valley Health Network
Bethlehem, Pennsylvania

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

Meet The Professor with Dr Spigel

Module 1: Cases from the Community – Drs Peles and Gupta

- Dr Peles: An 80-year-old woman with high-risk MDS/AML and metastatic adenocarcinoma of the lung – PD-L1 95%
- Dr Gupta: A 48-year-old woman and never smoker with metastatic adenocarcinoma of the lung – PD-L1 50%
- Dr Gupta: A 79-year-old woman and never smoker with recurrent locally advanced NSCLC – MET exon 14 mutation
- Dr Gupta: A 42-year-old Asian woman and never smoker with adenocarcinoma of the lung – ROS1 fusion
- Dr Gupta: A 76-year-old man with recurrent mediastinal disease, pleural effusion

Module 2: Lung Cancer Journal Club with Dr Spigel

- ADAURA trial: Adjuvant osimertinib
- CheckMate 153 trial: Continuous vs 1-year fixed-duration nivolumab for previously treated mNSCLC
- ASCO guidelines for NSCLC without driver mutations
- PACIFIC trial: Three-year OS with durvalumab after chemoradiation therapy
- Five-year survival with nivolumab for advanced melanoma, renal cell carcinoma, NSCLC
- Clinical, genomic and response analysis with anti-MET therapy for patients with MET exon 14 mutation
- CheckMate 568 trial: First-line nivolumab/ipilimumab with chemotherapy
- RESILIENT trial: Liposomal irinotecan for small cell lung cancer progressing after platinum-based therapy
- ESMO 2020 highlights

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

Module 4: Key Papers and Recent Approvals

RTP
RESEARCH TO PRACTICE

Case Presentation – Dr Peles: An 80-year-old woman with high-risk MDS/AML and metastatic adenocarcinoma of the lung – PD-L1 95%

Dr Shachar Peles

- High risk MDS/AML on azacitidine/venetoclax
  - Cytopenias, admitted with pneumonia
- March 2019: LUL lung and right hepatic lesions
  - Liver biopsy: Metastatic poorly differentiated adenocarcinoma of the lung (CK 7, TTF-1 positive)
  - PD-L1: 95%. EGFR, ALK, MET, RET Rearrangement negative
- Pembrolizumab, with complete remission
- June 2020 PET/CT: No suspicious foci of increased FDG avidity

Questions

- In a patient with NSCLC and a very high disease burden, with PD-L1 >60%, would you still add chemotherapy for 2-4 cycles to the immunotherapy to ensure a response? Or, would you have faith in the checkpoint inhibitor alone?
- How do you tease out which patients to give chemoimmunotherapy versus ipilimumab/nivolumab? And to which patients would you give chemo plus ipilimumab/nivolumab?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Gupta: A 48-year-old woman and never smoker with metastatic adenocarcinoma of the lung – PD-L1 50%

Dr Ranju Gupta

- March 2017: Stage IIIb adenocarcinoma of the right lung
- Concurrent cisplatin/pemetrexed/RT, good response except persistent disease in L retroclavicular lymph node
  - Pathology: Adenocarcinoma, ALK, ROS1, EGFR mutation-negative, PD-L1 50%
- January 2018: Atezolizumab x 2 years → NED, no side effects
  - Patient is keen to discontinue immunotherapy if it can be done safely
  - Most recent PET scan: Persistent FDG avid in the right hilar lymph node
  - Status post bronchoscopy and biopsies: Inflammation

Questions

- Is it okay to discontinue immunotherapy in this patient, who has received atezolizumab for 2.5 years and is not experiencing toxicity?

Case Presentation – Dr Gupta: A 79-year-old woman and never smoker with recurrent locally advanced NSCLC – MET exon 14 mutation

Dr Ranju Gupta

- November 2018: Stage IIIA squamous cell NSCLC
  - Not a surgical candidate
- Carboplatin/paclitaxel/RT → Durvalumab x 1 year
  - Recurrence in the right lung after 20 cycles of durvalumab
- Next generation sequencing: MET exon 14 splice site mutation, MSS, TMB 4 mut/Mb, PD-L1 30%, STK11, myc amplification
- Capmatinib

Questions

- What would be your first treatment recommendation, since her PD-L1 is 30%?
- What happens when she experiences disease progression on capmatinib? Immunotherapy?

Case Presentation – Dr Gupta: A 42-year-old Asian woman and never smoker with adenocarcinoma of the lung – ROS1 fusion

Dr Ranju Gupta

- May 2020: Admitted with SOB, right shoulder pain
  - CT scan: Pulmonary embolism, SVC syndrome and left lung opacification → SVC venogram with stent placement and anticoagulation
  - Bilateral pleural effusions → S/p catheter placement
  - Bronchoscopy and biopsy confirmed adenocarcinoma, lung primary
- Next generation sequencing (liquid biopsy): Negative for actionable mutations
- Multiple hospitalizations for recurrent thrombosis in her arms, worsening pleural effusions
- Carboplatin/paclitaxel
- NGS (tissue): ROS1 Fusion, PD-L1 TPS 25, TP53
- Chemotherapy discontinued after 2 cycles (no clinical response)
- July 2020: Entrectinib 400 mg bid (lower dose due to transaminitis) on compassionate basis

Questions

- Should we be using entrectinib instead of crizotinib, just like we now use osimertinib instead of erlotinib? Or, should I have gone with crizotinib?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Gupta: A 76-year-old man with recurrent mediastinal disease, pleural effusion

Dr Ranju Gupta

- 2016: Early-stage lung cancer s/p lobectomy, no adjuvant treatment indicated
- 2019 on routine scans: Recurrent disease in mediastinal lymph nodes, left pleural effusion
- Carboplatin/pemetrexed/pembrolizumab, with response on restaging scans
- Hospitalized in June with diabetic ketoacidosis: Autoimmune thyroiditis
  - Diagnosed to have autoimmune diabetes, since anti-islet positive → Endocrinology
  - Pembrolizumab held
- Pleural fluid sent for next generation sequencing: PD-L1 TPS 0, ERBB2 (HER2) positive, PIK3CA-G106R
- TAPUR trial: Started on trastuzumab/pertuzumab
  - First CT scan: Stable to slightly decreased mediastinal lymphadenopathy, smaller left pleural effusion

Questions

- Would you be comfortable re-starting immunotherapy in this patient?
- What are your thoughts about trastuzumab deruxtecan for patients with HER2-positive NSCLC?

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

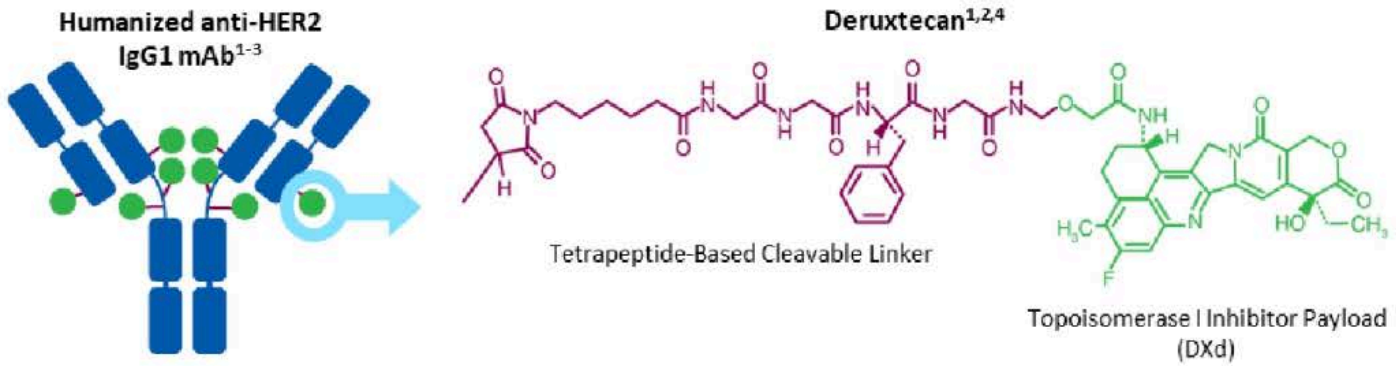
Smit EF et al.

ASCO 2020;Abstract 9504.

Antibody-Drug Conjugate
Trastuzumab Deruxtecan

T-DXd is an ADC with 3 components:

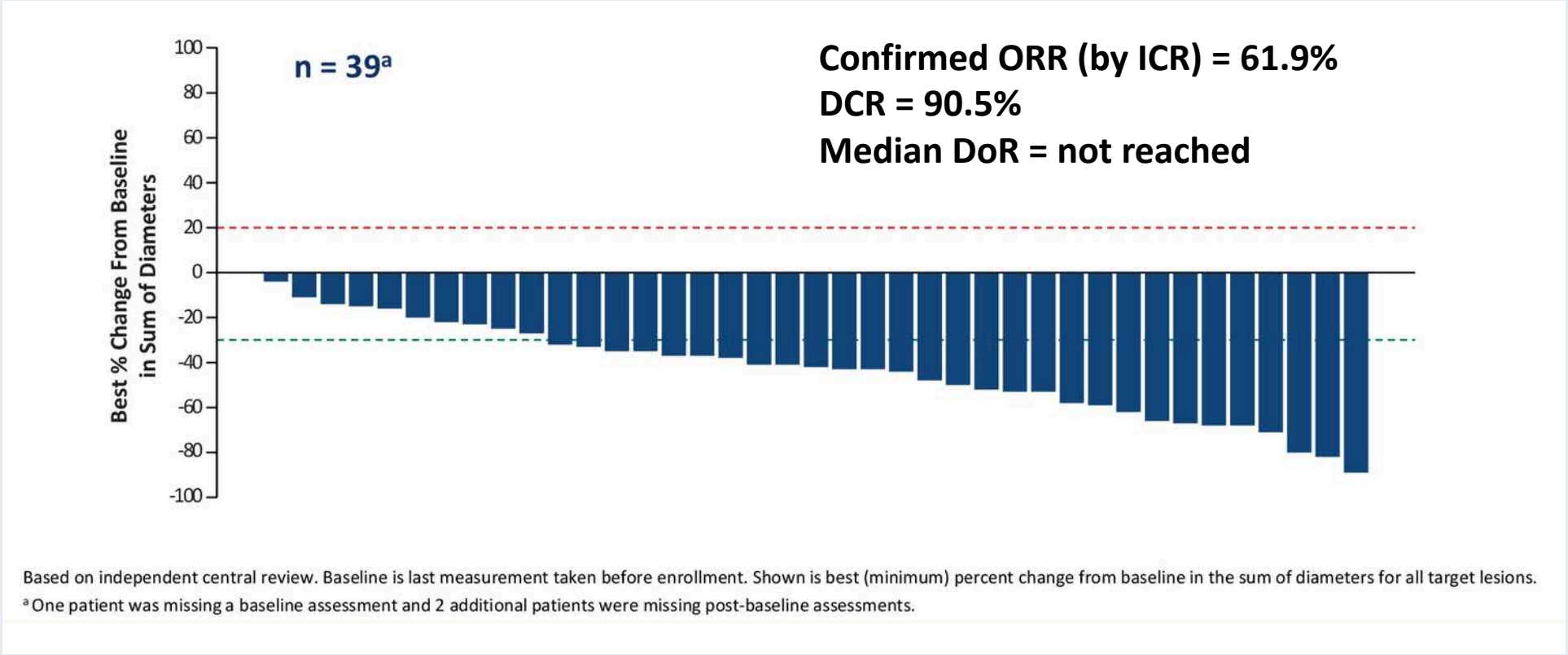
- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



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.

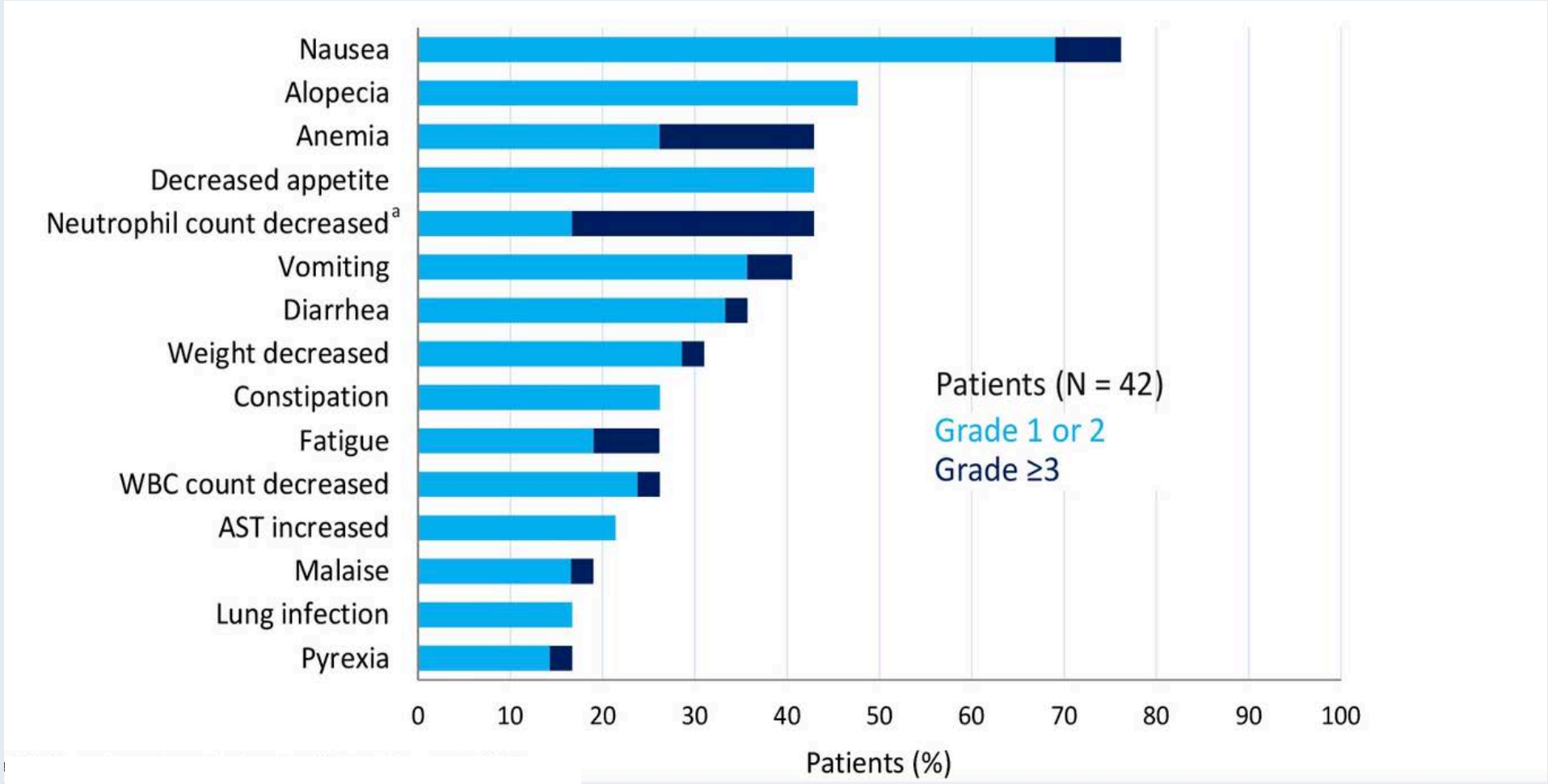
DESTINY-Lung01: Efficacy



- 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.

Meet The Professor with Dr Spigel

Module 1: Cases from the Community – Drs Peles and Gupta

- Dr Peles: An 80-year-old woman with high-risk MDS/AML and metastatic adenocarcinoma of the lung – PD-L1 95%
- Dr Gupta: A 48-year-old woman and never smoker with metastatic adenocarcinoma of the lung – PD-L1 50%
- Dr Gupta: A 79-year-old woman and never smoker with recurrent locally advanced NSCLC – MET exon 14 mutation
- Dr Gupta: A 42-year-old Asian woman and never smoker with adenocarcinoma of the lung – ROS1 fusion
- Dr Gupta: A 76-year-old man with recurrent mediastinal disease, pleural effusion

Module 2: Lung Cancer Journal Club with Dr Spigel

- ADAURA trial: Adjuvant osimertinib
- CheckMate 153 trial: Continuous vs 1-year fixed-duration nivolumab for previously treated mNSCLC
- PACIFIC trial: Three-year OS with durvalumab after chemoradiation therapy
- Five-year survival with nivolumab for advanced melanoma, renal cell carcinoma, NSCLC
- Clinical, genomic and response analysis with anti-MET therapy for patients with MET exon 14 mutation
- CheckMate 568 trial: First-line nivolumab/ipilimumab with chemotherapy
- RESILIENT trial: Liposomal irinotecan for small cell lung cancer progressing after platinum-based therapy
- ESMO 2020 highlights

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

Module 4: Key Papers and Recent Approvals

RTP
RESEARCH
TO PRACTICE

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

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

RTP
RESEARCH
TO PRACTICE

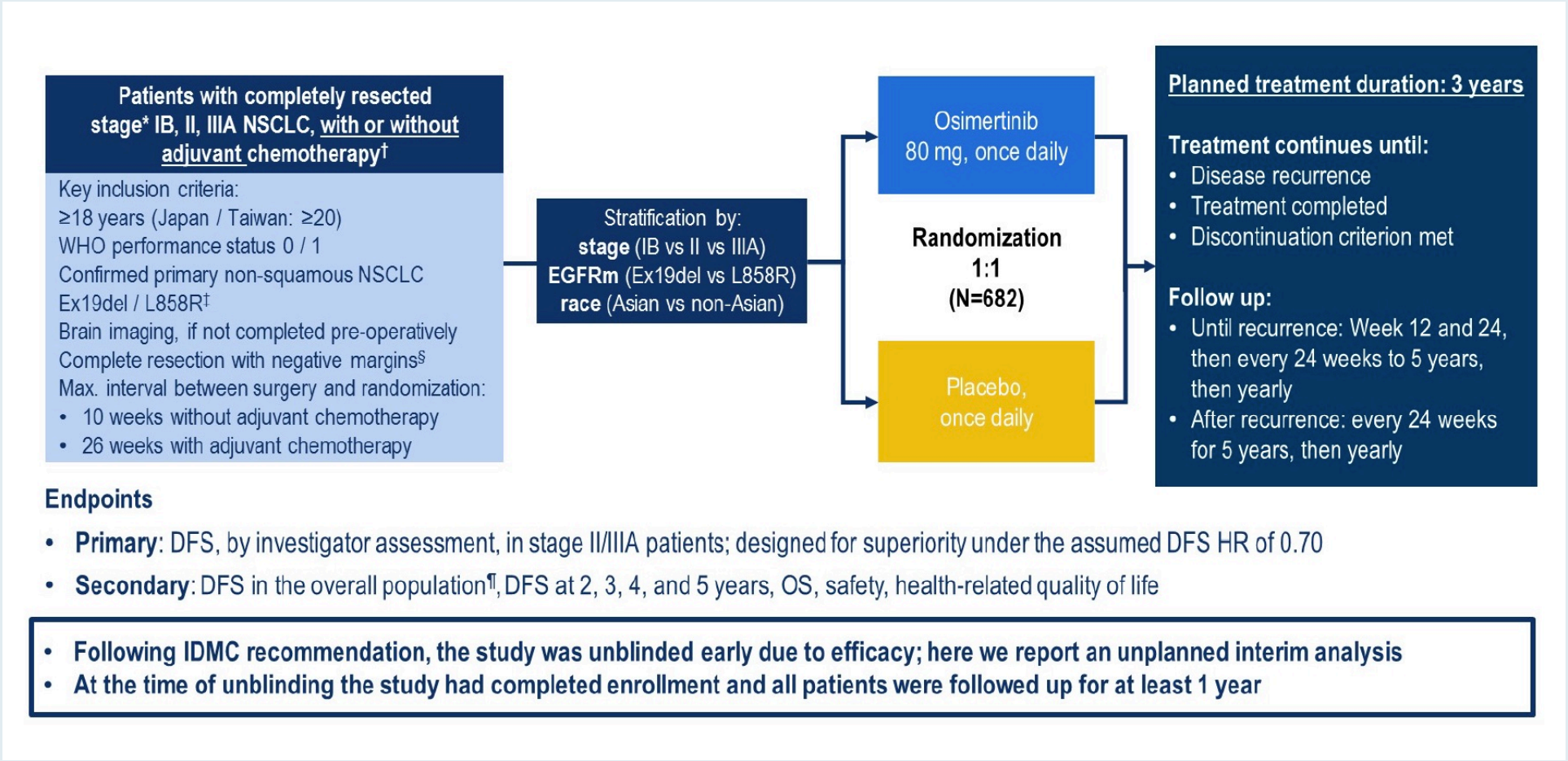
Osimertinib as Adjuvant Therapy in Patients (pts) with Stage IB–IIIA EGFR Mutation Positive (EGFRm) NSCLC After Complete Tumor Resection: ADAURA

Herbst RS et al.
ASCO 2020;Abstract LBA5.

Discussion of LBA5

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

ADAURA Phase III Trial Schema



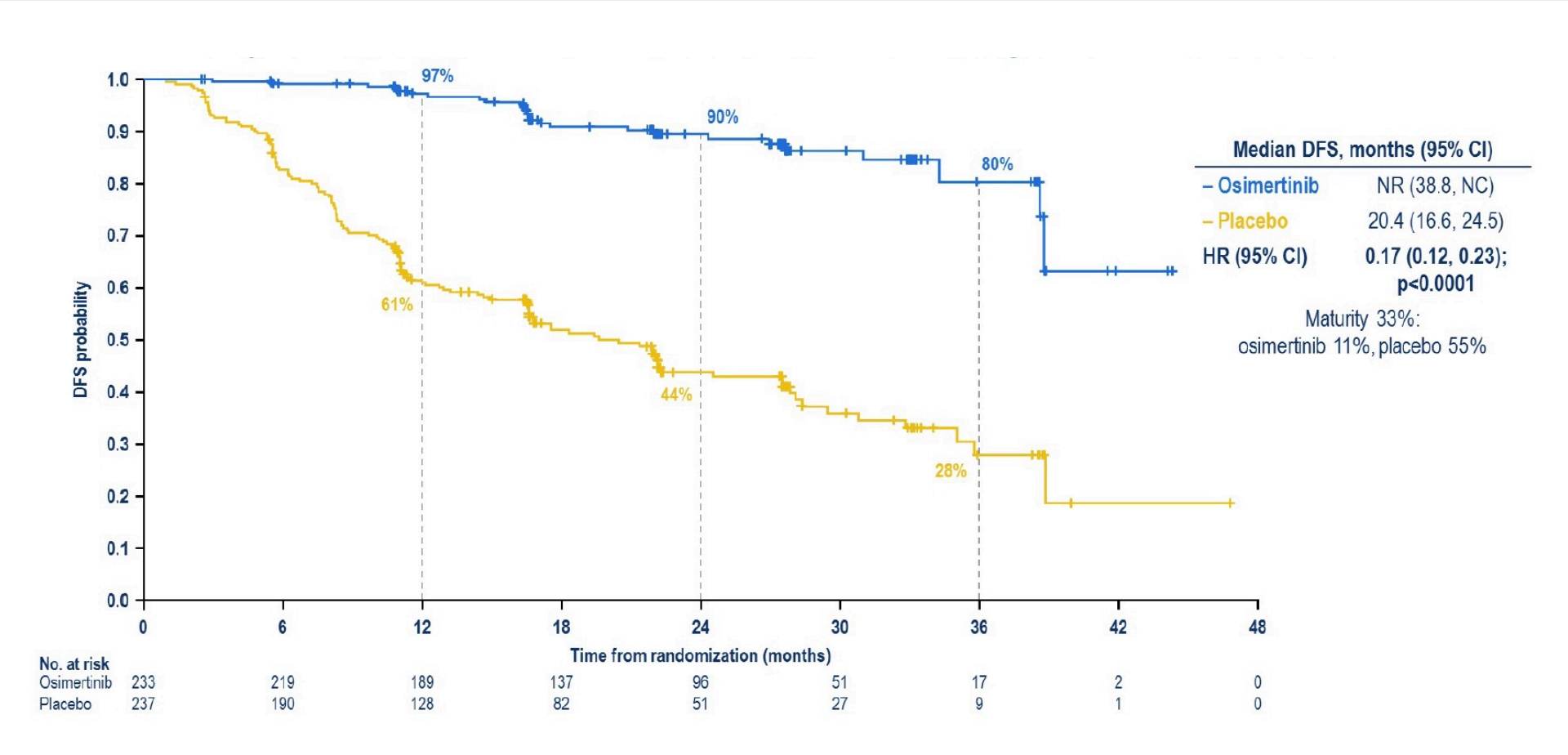
Endpoints

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

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

Herbst RS et al. ASCO 2020;Abstract LBA5.

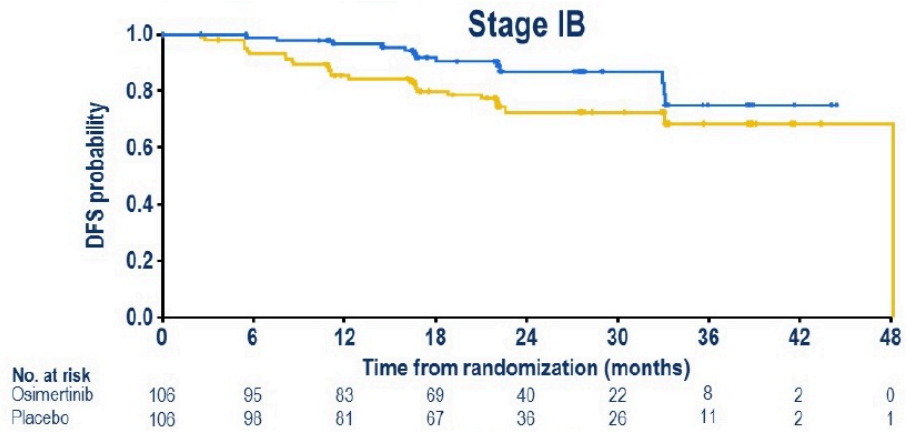
ADAURA Primary Endpoint: Inv-Assessed DFS (Stage II/IIIA)



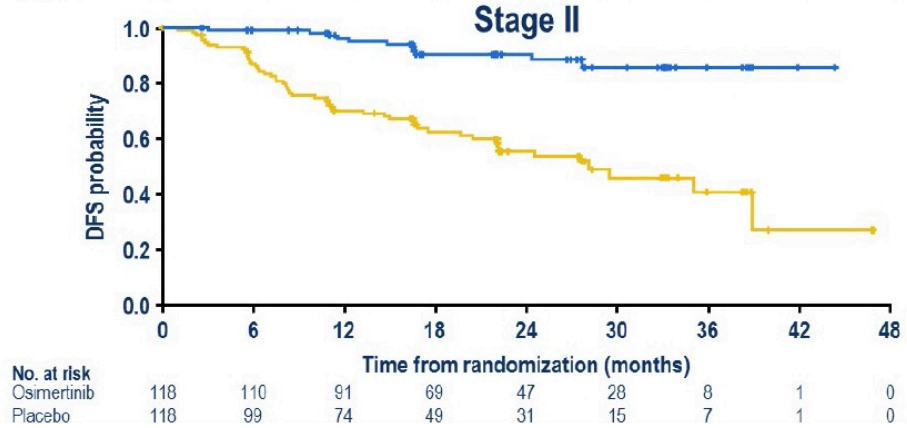
Herbst RS et al. ASCO 2020;Abstract LBA5.

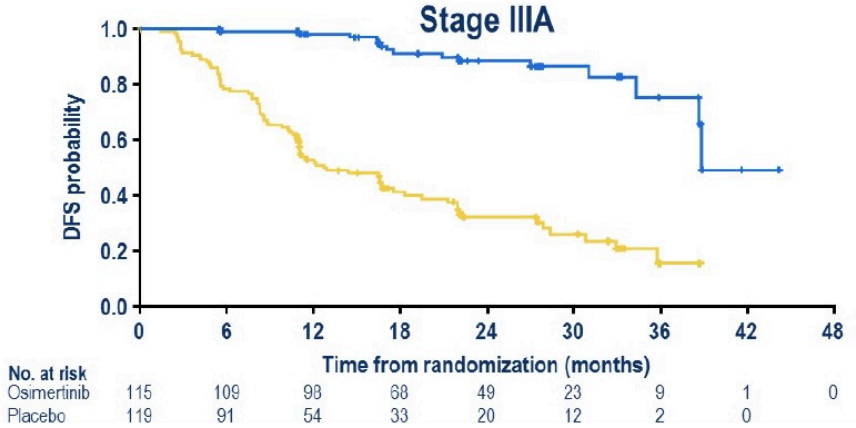
RTP RESEARCH TO PRACTICE

ADAURA: DFS by Stage



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

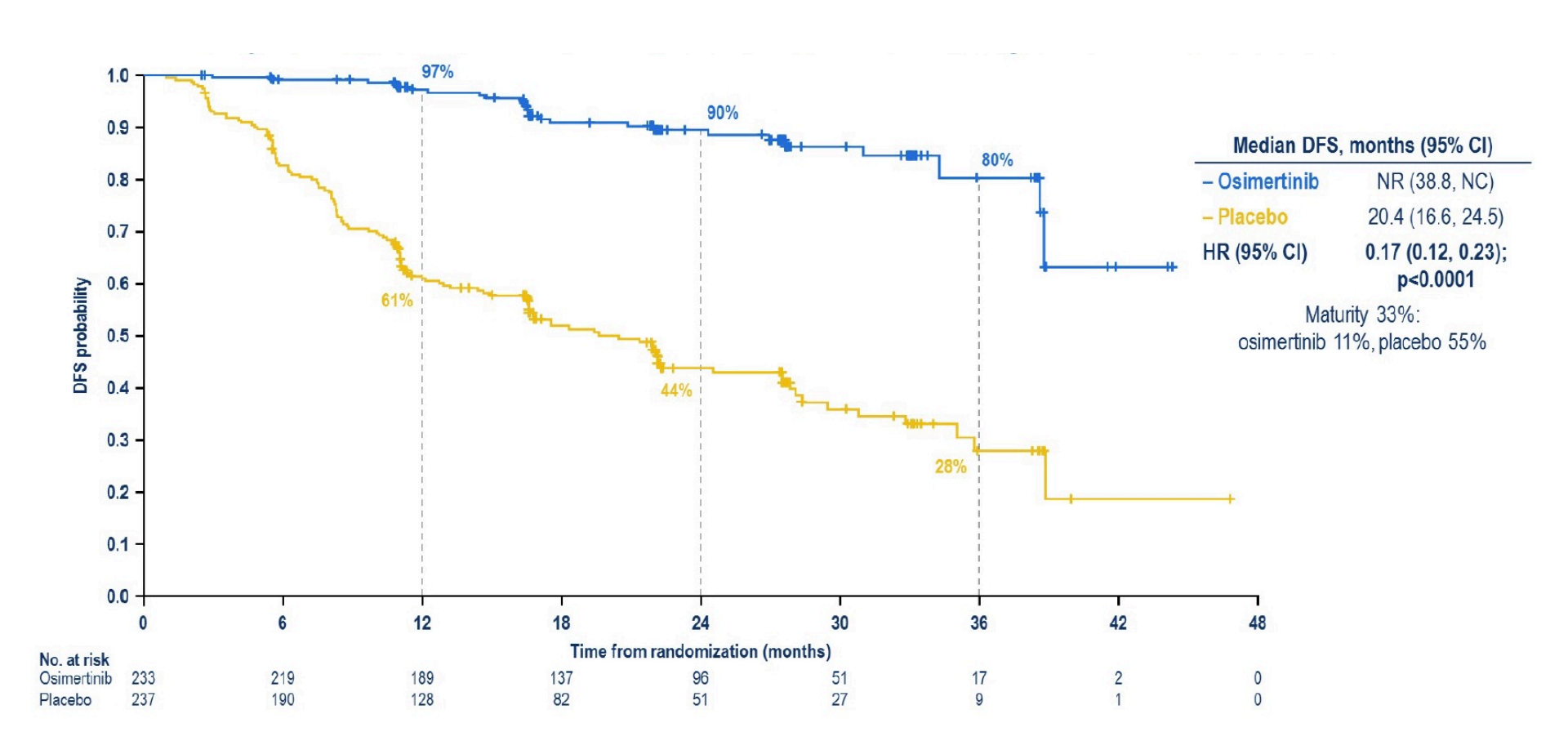




Herbst RS et al. ASCO 2020;Abstract LBA5.

RTP RESEARCH TO PRACTICE

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



Herbst RS et al. ASCO 2020;Abstract LBA5.

PALLAS: A Randomized Phase III Trial of Adjuvant Palbociclib with Endocrine Therapy versus Endocrine Therapy Alone for HR+/HER2- Early Breast Cancer

Mayer EL et al.

ESMO 2020;Abstract LBA12.

Abemaciclib Combined with Endocrine Therapy for the Adjuvant Treatment of HR+, HER2- Node-Positive, High-Risk, Early Breast Cancer (monarchE)

Johnston SRD et al.
ESMO 2020;Abstract LBA5_PR;
J Clin Oncol 2020;[Online ahead of print].

Gaining Ground: Targeting EGFR in Early Stage NSCLC
Discussion of LBA5

Spigel D.

ASCO 2020;Abstract LBA5 – Discussant

Finding Meaning and Moving Ahead

- Opportunity to help more (high-risk Stage I, unresectable Stage III?)
- cfDNA and residual disease
- Duration, next-generation inhibitors, chemotherapy value
- Revising the regulatory path
- Molecular testing in early-stage NSCLC

Spigel D. ASCO 2020;Abstract LBA5 – Discussant

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.

A Randomized Phase II Study of Osimertinib with or without Bevacizumab in Advanced Lung Adenocarcinoma Patients with EGFR T790M Mutation (West Japan Oncology Group 8715L)

Toi Y et al.

ESMO 2020;Abstract 1259O.

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

Continuous Versus 1-Year Fixed-Duration Nivolumab in Previously Treated Advanced Non–Small-Cell Lung Cancer: CheckMate 153

David M. Waterhouse, MD, MPH[1]; Edward B. Garon, MD, MS[2]; Jason Chandler, MD[3]; Michael McCleod, DO[4]; Maen Hussein, MD[5]; Robert Jotte, MD, PhD[6]; Leora Horn, MD, MS[7]; Davey B. Daniel, MD[8]; George Keogh, MD[9]; Ben Creelan, MD[10]; Lawrence H. Einhorn, MD[11]; Justin Baker, MD[12]; Samer Kasbari, MD[13]; Petros Nikolinakos, MD[14]; Sunil Babu, MD[15]; Felix Couture, MD[16]; Natasha B. Leighl, MD, MMS[17]; Craig Reynolds, MD[18]; George Blumenschein Jr, MD[19]; Vijay Gunuganti, MD[20]; Ang Li, MS[21]; Nivedita Aanur, MD[21]; and David R. Spigel, MD[22]

J CLIN ONCOL 2020 SEP 10 | ONLINE AHEAD OF PRINT

BRIEF REPORT

Three-Year Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC—Update from PACIFIC

Jhanelle E. Gray, MD,[a,*] Augusto Villegas, MD,[b] Davey Daniel, MD,[c,d] David Vicente, MD,[e] Shuji Murakami, MD,[f] Rina Hui, MD,[g,h] Takayasu Kurata, MD,[i] Alberto Chiappori, MD,[a] Ki Hyeong Lee, MD,[j] Byoung Chul Cho, MD,[k] David Planchard, MD,[l] Luis Paz-Ares, MD,[m,n] Corinne Faivre-Finn, MD,[o] Johan F. Vansteenkiste, MD,[p] David R. Spigel, MD,[d] Catherine Wadsworth, BVSc,[q] Maria Taboada, MSc,[r] Phillip A. Dennis, MD,[s] Mustafa Özgüroğlu, MD,[t] Scott J. Antonia, MD[a]

J THORAC ONCOL 2020 | VOLUME 15 | ISSUE 2

Research

JAMA Oncology | Original Investigation

Five-Year Survival and Correlates Among Patients With Advanced Melanoma, Renal Cell Carcinoma, or Non–Small Cell Lung Cancer Treated With Nivolumab

Suzanne L. Topalian, MD; F. Stephen Hodi, MD; Julie R. Brahmer, MD; Scott N. Gettinger, MD; David C. Smith, MD; David F. McDermott, MD; John D. Powderly, MD; Jeffrey A. Sosman, MD; Michael B. Atkins, MD; Philip D. Leming, MD; David R. Spigel, MD; Scott J. Antonia, MD, PhD; Alexander Drilon, MD; Jedd D. Wolchok, MD, PhD; Richard D. Carvajal, MD; M. Brent McHenry, PhD; Fareeda Hosein, MD; Christopher T. Harbison, PhD; Joseph F. Grosso, PhD; Mario Sznol, MD

JAMA ONCOL 2019 | VOLUME 5 | ISSUE 10

Clinical and Genomic Analysis of Non-Small Cell Lung Cancer (NSCLC) Patients with MET Exon14 Skipping (METex14) Mutations and Responses to Anti-MET Therapy

McKenzie A et al.

ASCO 2020;Abstract 9613.

Nivolumab (NIVO) plus Ipilimumab (IPI) with Two Cycles of Chemotherapy (Chemo) in First-Line Metastatic Non-Small Cell Lung Cancer (NSCLC): CheckMate 568 Part 2

Gainor JF et al.

ASCO 2020;Abstract 9560.

RESILIENT Part II: An Open-Label, Randomized, Phase III Study of Liposomal Irinotecan Injection in Patients with Small-Cell Lung Cancer Who Have Progressed with Platinum-Based First-Line Therapy

Paz-Ares LG et al.

ASCO 2020;Abstract TPS9081.

RESILIENT Part I, an Open-Label, Safety Run-in of Liposomal Irinotecan in Adults with Small Cell Lung Cancer (SCLC) Who Have Progressed with Platinum-Based First-Line (1L) Therapy: Subgroup Analyses by Platinum Sensitivity

Spigel DR et al.

ASCO 2020;Abstract 9069.

Lorlatinib vs Crizotinib in the First-Line Treatment of Patients (pts) with Advanced ALK-Positive Non-Small Cell Lung Cancer (NSCLC): Results of the Phase 3 CROWN Study

Solomon B et al.

ESMO 2020;Abstract LBA2.

Neoadjuvant Durvalumab in Resectable Non-Small Cell Lung Cancer (NSCLC): Preliminary Results from a Multicenter Study (IFCT-1601 IONESCO)

Wislez M et al.

ESMO 2020;Abstract 1214O.

Neoadjuvant Atezolizumab (A) for Resectable Non-Small Cell Lung Cancer (NSCLC): Results from the Phase II PRINCEPS Trial

Besse B et al.

ESMO 2020;Abstract 1215O.

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

Peters S et al.

ESMO 2020;Abstract LBA84.

Durability of Clinical Benefit and Biomarkers in Patients (pts) with Advanced Non-Small Cell Lung Cancer (NSCLC) Treated with AMG 510 (Sotorasib)

Hong D et al.

ESMO 2020;Abstract 1257O.

KEYNOTE-024 5-Year OS Update: First-Line (1L) Pembrolizumab (Pembro) vs Platinum-Based Chemotherapy (Chemo) in Patients (pts) with Metastatic NSCLC and PD-L1 Tumor Proportion Score (TPS) ≥50%

Brahmer J et al.

ESMO 2020;Abstract LBA51.

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.

WJOG @Be Study: A Phase II Study of Atezolizumab (Atez) with Bevacizumab (Bev) for Non-Squamous (Sq) Non-Small-Cell Lung Cancer (NSCLC) with High PD-L1 Expression

Seto T et al.

ESMO 2020;Abstract LBA55.

Meet The Professor with Dr Spigel

Module 1: Cases from the Community – Drs Peles and Gupta

- Dr Peles: An 80-year-old woman with high-risk MDS/AML and metastatic adenocarcinoma of the lung – PD-L1 95%
- Dr Gupta: A 48-year-old woman and never smoker with metastatic adenocarcinoma of the lung – PD-L1 50%
- Dr Gupta: A 79-year-old woman and never smoker with recurrent locally advanced NSCLC – MET exon 14 mutation
- Dr Gupta: A 42-year-old Asian woman and never smoker with adenocarcinoma of the lung – ROS1 fusion
- Dr Gupta: A 76-year-old man with recurrent mediastinal disease, pleural effusion

Module 2: Lung Cancer Journal Club with Dr Spigel

- ADAURA trial: Adjuvant osimertinib
- CheckMate 153 trial: Continuous vs 1-year fixed-duration nivolumab for previously treated mNSCLC
- PACIFIC trial: Three-year OS with durvalumab after chemoradiation therapy
- Five-year survival with nivolumab for advanced melanoma, renal cell carcinoma, NSCLC
- Clinical, genomic and response analysis with anti-MET therapy for patients with MET exon 14 mutation
- CheckMate 568 trial: First-line nivolumab/ipilimumab with chemotherapy
- RESILIENT trial: Liposomal irinotecan for small cell lung cancer progressing after platinum-based therapy
- ESMO 2020 highlights

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

Module 4: Key Papers and Recent Approvals

RTP
RESEARCH
TO PRACTICE

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

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

Regulatory and reimbursement issues aside, what would be your preferred first-line treatment regimen for a 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

RTP RESEARCH TO PRACTICE

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

 JOHN V HEYMACH, MD, PHD	Carboplatin/etoposide
 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

RTP RESEARCH TO PRACTICE

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

 JOHN V HEYMACH, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 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

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Spigel

Module 1: Cases from the Community – Drs Peles and Gupta

- Dr Peles: An 80-year-old woman with high-risk MDS/AML and metastatic adenocarcinoma of the lung – PD-L1 95%
- Dr Gupta: A 48-year-old woman and never smoker with metastatic adenocarcinoma of the lung – PD-L1 50%
- Dr Gupta: A 79-year-old woman and never smoker with recurrent locally advanced NSCLC – MET exon 14 mutation
- Dr Gupta: A 42-year-old Asian woman and never smoker with adenocarcinoma of the lung – ROS1 fusion
- Dr Gupta: A 76-year-old man with recurrent mediastinal disease, pleural effusion

Module 2: Lung Cancer Journal Club with Dr Spigel

- ADAURA trial: Adjuvant osimertinib
- CheckMate 153 trial: Continuous vs 1-year fixed-duration nivolumab for previously treated mNSCLC
- PACIFIC trial: Three-year OS with durvalumab after chemoradiation therapy
- Five-year survival with nivolumab for advanced melanoma, renal cell carcinoma, NSCLC
- Clinical, genomic and response analysis with anti-MET therapy for patients with MET exon 14 mutation
- CheckMate 568 trial: First-line nivolumab/ipilimumab with chemotherapy
- RESILIENT trial: Liposomal irinotecan for small cell lung cancer progressing after platinum-based therapy
- ESMO 2020 highlights

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

Module 4: Key Papers and Recent Approvals

RTP
RESEARCH
TO PRACTICE

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

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

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

A Meet The Professor Series

Wednesday, September 23, 2020
12:00 PM – 1:00 PM ET

Faculty
Jeff Sharman, MD

Moderator
Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

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

RTP
RESEARCH
TO PRACTICE