Meet The Professor
Management of Lung Cancer

Ramaswamy Govindan, MD
Professor of Medicine
Director, Section of Oncology
Anheuser-Busch Endowed Chair in Medical Oncology
Washington University School of Medicine
St Louis, Missouri

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, Karyopharm Therapeutics, 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, Seagen Inc, 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.

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Dr Govindan — Disclosures

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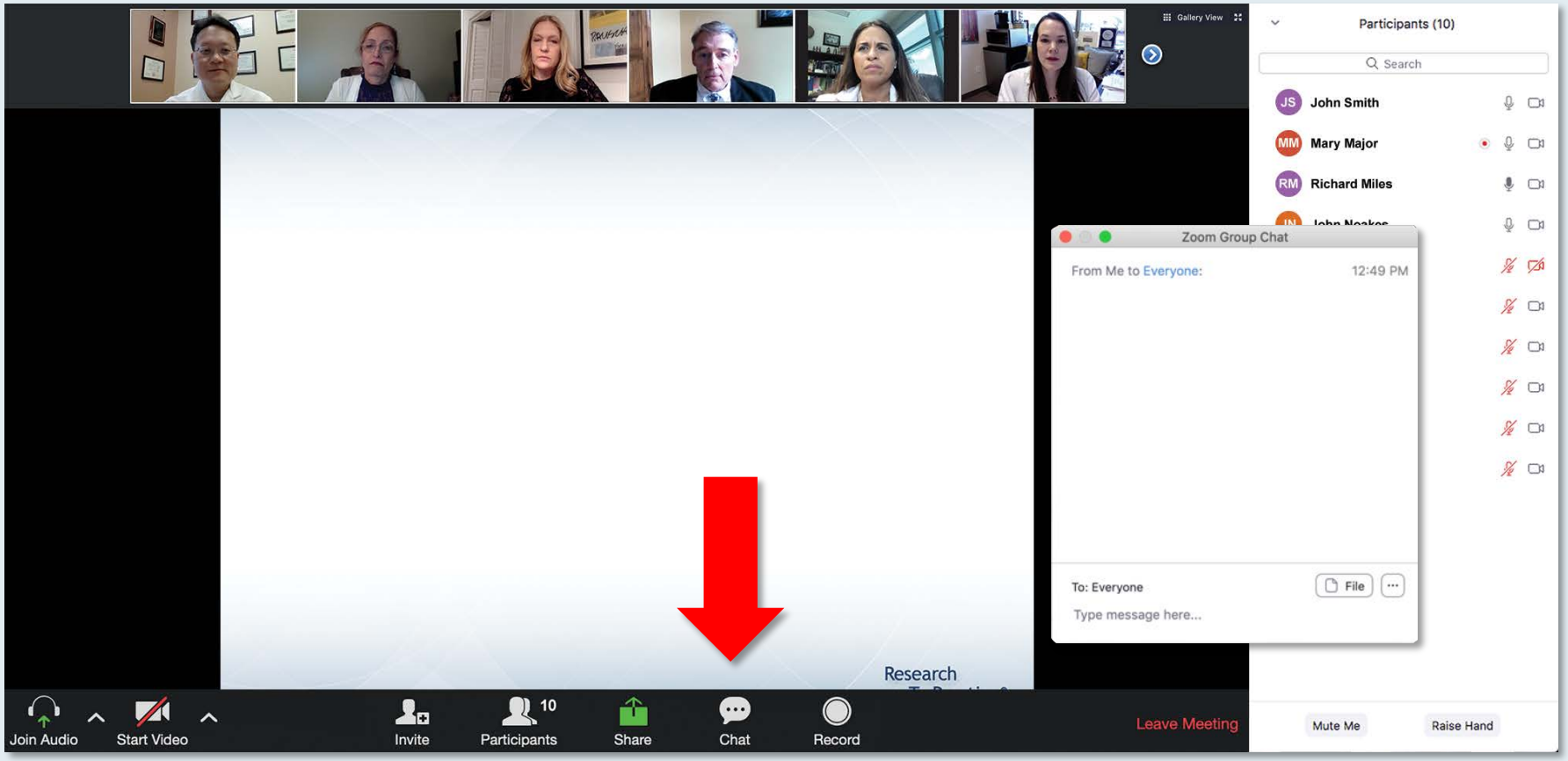
We Encourage Clinicians in Practice to Submit Questions



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

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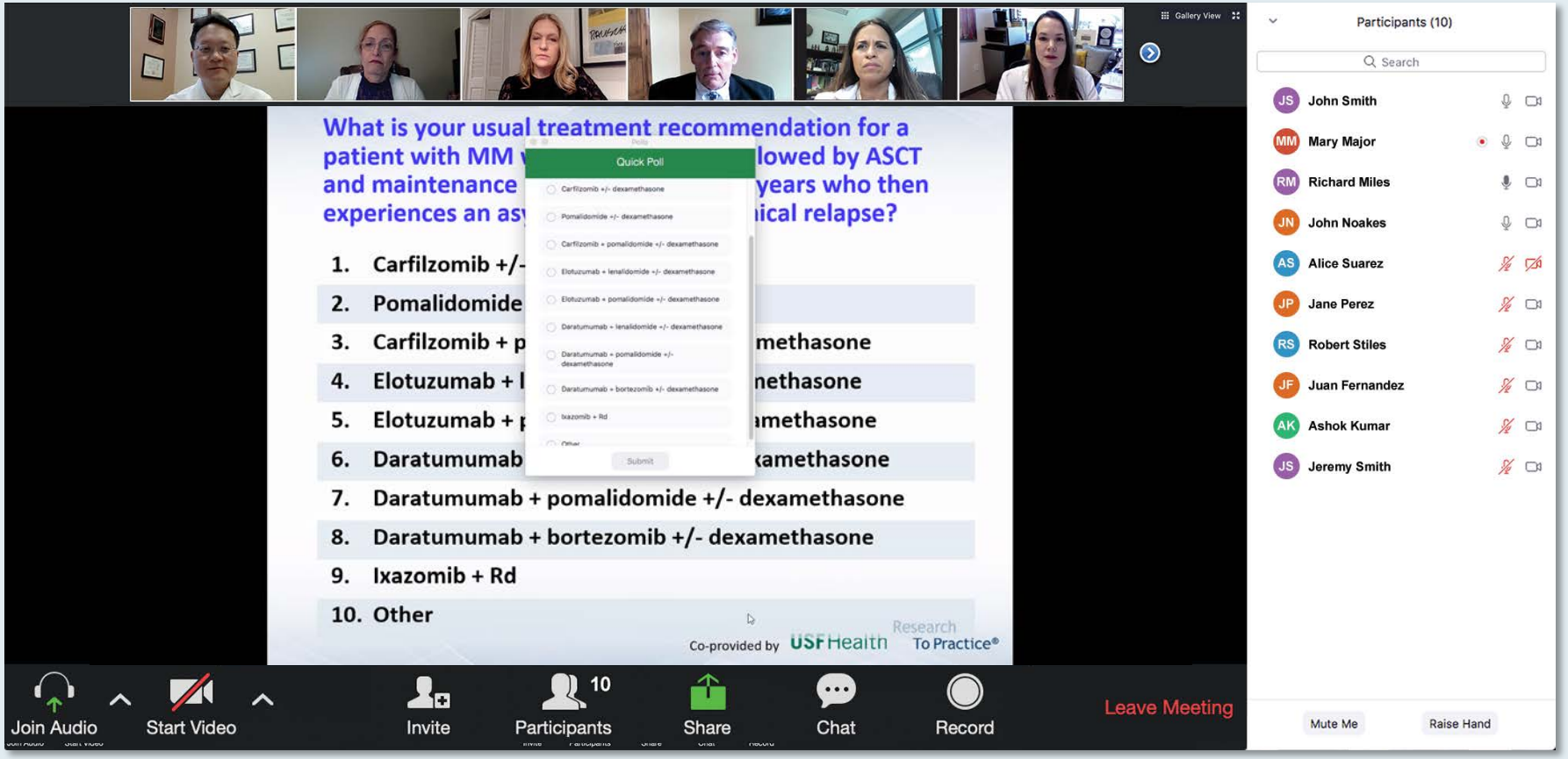
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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Upcoming Webinars

Friday, December 4, 2020

Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Hematologic Cancers

A 4-Part Friday Satellite Symposia Live Webinar Series Preceding the 62nd ASH Annual Meeting

Moderator
Neil Love, MD

Tuesday, December 8, 2020
5:00 PM – 6:00 PM ET

Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology
Colorectal and Gastroesophageal Cancers

Faculty
Peter C Enzinger, MD
Zev Wainberg, MD, MSc

Moderator
Neil Love, MD

Upcoming Webinars

Thursday, December 10, 2020
8:30 PM – 10:00 PM ET

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

Faculty

Carey K Anders, MD
Erika Hamilton, MD
Sara Hurvitz, MD
Mark D Pegram, MD
Sara M Tolaney, MD, MPH

Moderator

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Friday, December 11, 2020
8:30 PM – 10:00 PM ET

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Triple-Negative Breast Cancer

Faculty

P Kelly Marcom, MD
Joyce O'Shaughnessy, MD
Hope S Rugo, MD
Professor Peter Schmid, MD, PhD

Moderator

Neil Love, MD

Thank you for joining us!

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

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ONCOLOGY TODAY

WITH DR NEIL LOVE

EGFR MUTATION-POSITIVE NON-SMALL CELL LUNG CANCER

DR PASI JÄNNE
DANA-FARBER CANCER INSTITUTE

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Director, Section of Oncology
Anheuser-Busch Endowed Chair in Medical Oncology
Washington University School of Medicine
St Louis, Missouri

Leora Horn, MD, MSc
Ingram Associate Professor of Cancer Research
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Director of Thoracic Oncology
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Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

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Meet The Professor Program Participating Faculty

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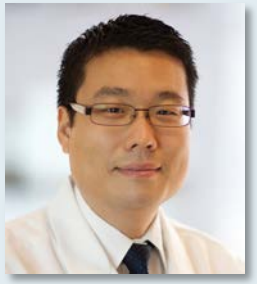
at Sibley Memorial
Washington, DC

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

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



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

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Meet The Professor Program Participating Faculty

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

Professor Solange Peters, MD, PhD
Head, Medical Oncology
Chair, Thoracic Malignancies
Oncology Department
Lausanne University Hospital (CHUV)
Lausanne, Switzerland

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

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

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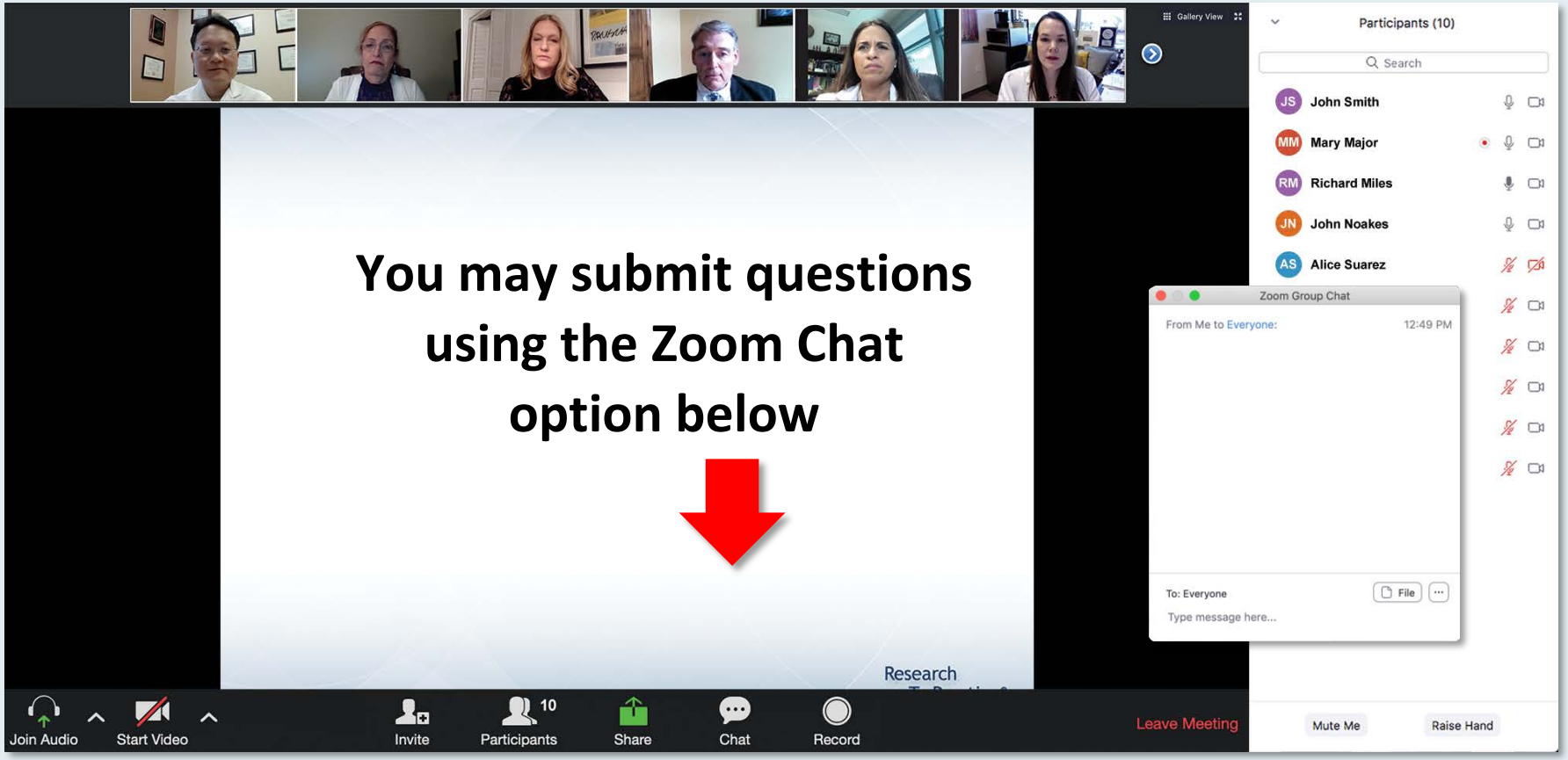
We Encourage Clinicians in Practice to Submit Questions



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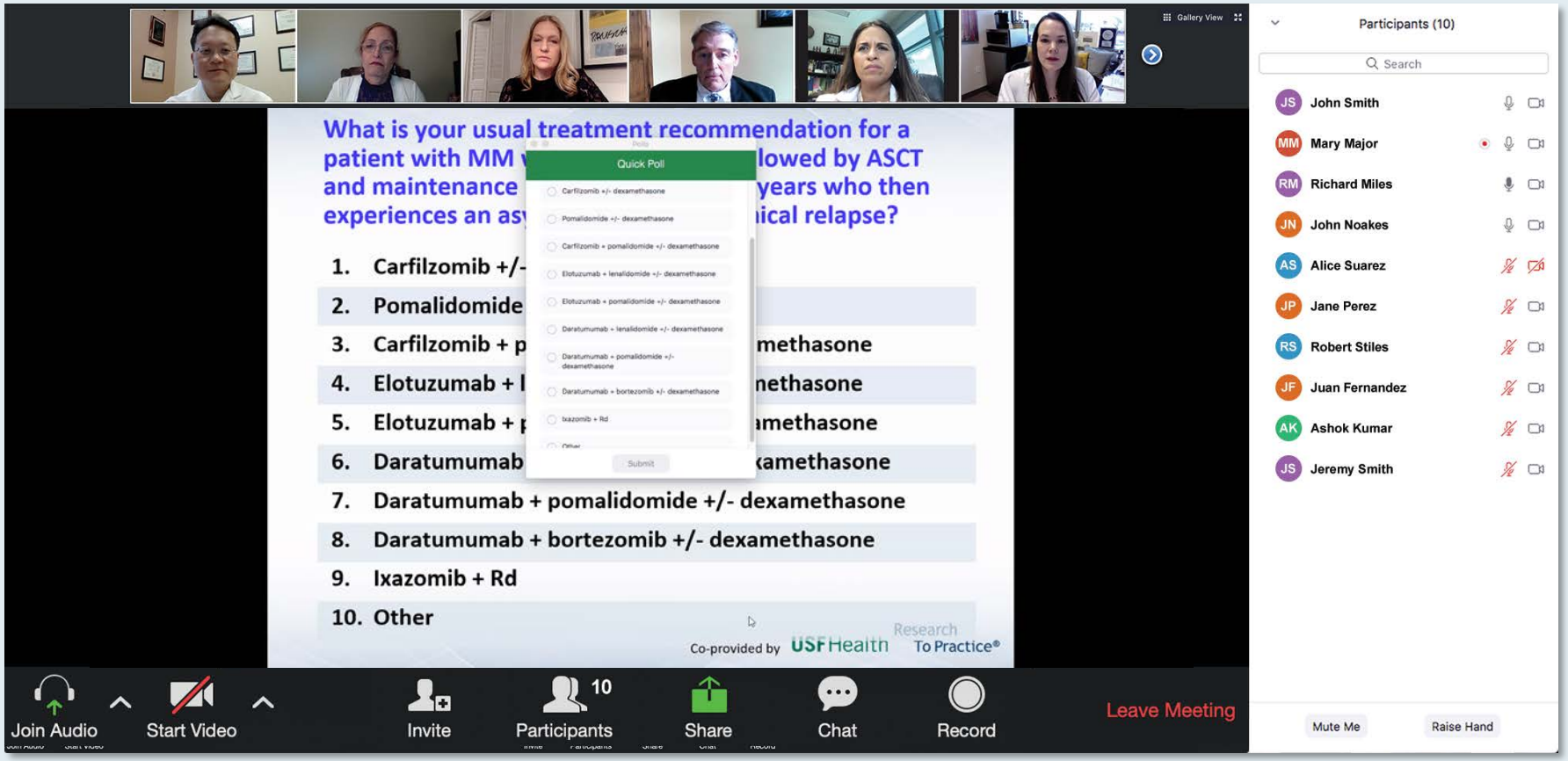

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EGFR MUTATION-POSITIVE NON-SMALL CELL LUNG CANCER

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Multiple Myeloma
8:30 AM – 10:00 AM Pacific Time
(11:30 AM – 1:00 PM ET)

Chronic Lymphocytic Leukemia
12:00 PM – 1:30 PM Pacific Time
(3:00 PM – 4:30 PM ET)

Acute Myeloid Leukemia
3:00 PM – 4:30 PM Pacific Time
(6:00 PM – 7:30 PM ET)

Hodgkin and Non-Hodgkin Lymphoma
7:00 PM – 8:30 PM Pacific Time
(10:00 PM – 11:30 PM ET)

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

D Ross Camidge, MD, PhD
Professor of Medicine/Oncology
Joyce Zeff Chair in Lung Cancer Research
Director of Thoracic Oncology
University of Colorado, Anschutz Medical Campus
Denver, Colorado

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Meet The Professor with Dr Govindan

Module 1: Cases from Dr Zafar

- A 66-year-old man, smoker with metastatic adenocarcinoma of the lung – ALK fusion, PD-L1 high (Part 1)
- A 66-year-old man, smoker with metastatic adenocarcinoma of the lung – ALK fusion, PD-L1 high (Part 2)
- Second Opinion from Dr Camidge: A 66-year-old man, smoker with metastatic adenocarcinoma of the lung – ALK fusion, PD-L1 high (Part 3)
- A 53-year-old man, previous smoker with Stage IIIA adenocarcinoma of the lung – ALK fusion

Module 2: Lung Cancer Journal Club with Dr Govindan

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

Module 4: Key Papers and Recent Approvals

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Case Presentation – Dr Zafar: A 66-year-old man, smoker with metastatic adenocarcinoma of the lung – ALK fusion, PD-L1 high (Part 1)

Dr Syed Zafar

- 2017: Adenocarcinoma of the lung, with solitary brain metastasis
  - NGS: Quantity/quality not sufficient
- Platinum/pemetrexed, Stereotactic RT to brain metastasis
- NGS (tissue biopsy): ALK fusion-positive, High PD-L1 (TPS > 90%), EGFR wildtype
- Switched to alectinib → PD 13 months later
- Repeat tissue biopsy, NGS: ALK-EML4 fusion (variant 2), EGFR D761N, TP53, MSS, High PD-L1

Case Presentation – Dr Zafar: A 66-year-old man, smoker with metastatic adenocarcinoma of the lung – ALK fusion, PD-L1 high (Part 2)

Dr Syed Zafar

- 2017: Adenocarcinoma of the lung, with solitary brain metastasis
- Platinum/pemetrexed, Stereotactic RT to brain metastasis
- NGS (tissue biopsy): ALK fusion-positive, High PD-L1 (TPS > 90%), EGFR wildtype
- Switched to alectinib → PD 13 months later
- Repeat tissue biopsy, NGS: ALK-EML4 fusion (variant 2), EGFR D761N, TP53, MSS, High PD-L1
- **Switched to lorlatinib x 9 months**
  - **Required dose reductions – cognitive declines and depression resolved after discontinuation**
- **MRI brain: Stable**
- **Liquid biopsy (See report)**

Questions

- He still has the EML4-ALK transfusion, the uncommon EGFR mutation and some MET alteration. What should I try next – another ALK inhibitor, like brigatinib? Chemotherapy?

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Case Presentation – Dr Zafar: A 66-year-old man – NGS (liquid biopsy)

Dr Syed Zafar

FGFR2 D336D	0.1%	ND → 0.1%	Synonymous Alteration §
MET R1327C	0.1%	0.1% → 0.1%	Variant of Uncertain Significance §
MET C545Y	ND	0.2% → ND	
EGFR D761N	ND	0.5% → ND	
EML4-ALK Fusion	ND	0.2% → ND	
ESR1 L378I	ND	0.1% → ND	
TP53 P278S	ND	0.8% → ND	
GNAS R201C	ND		

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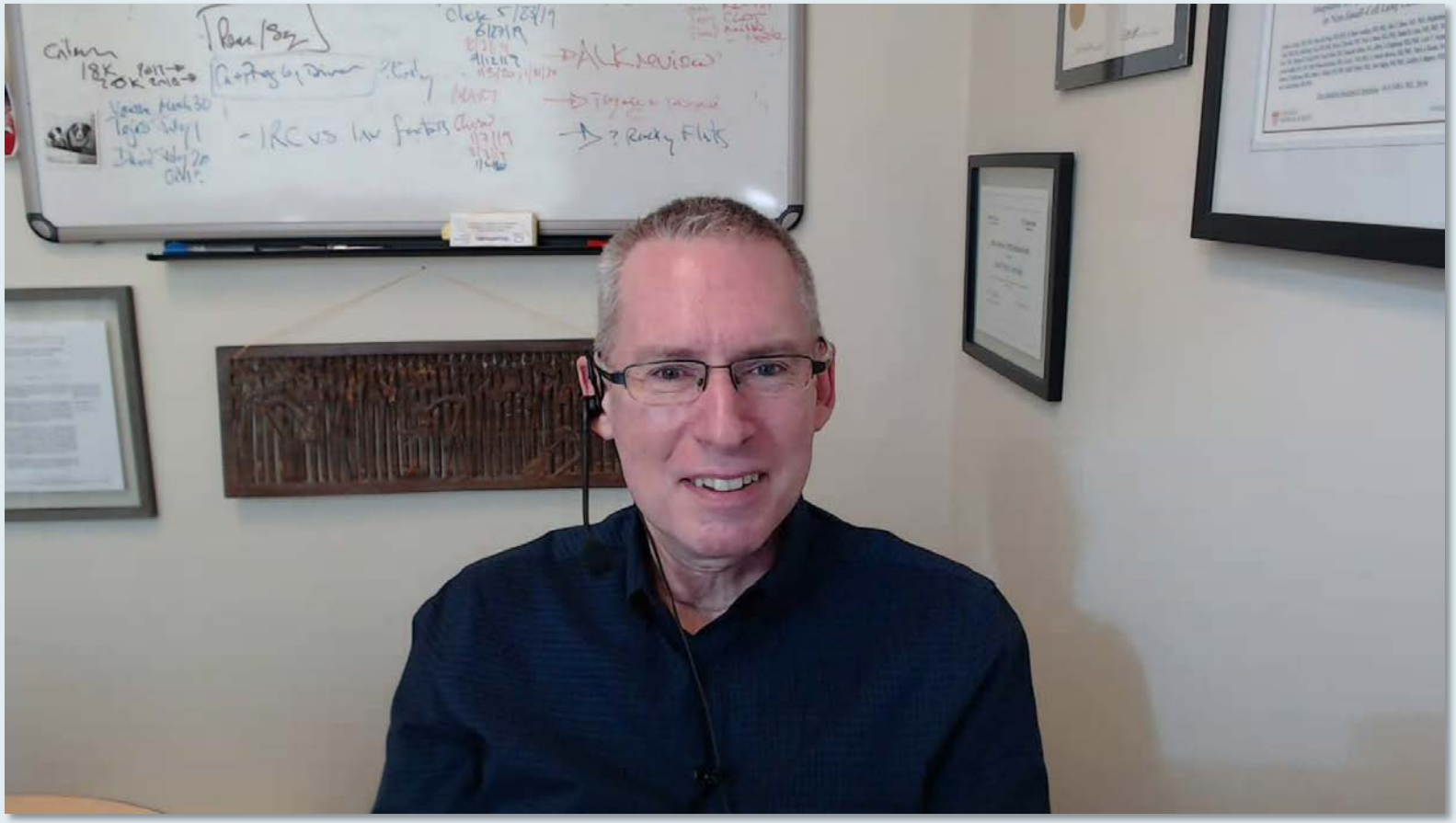
Second Opinion: A 66-year-old man, smoker with metastatic adenocarcinoma of the lung – ALK fusion, PD-L1 high (Part 3)



Dr Ross Camidge

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

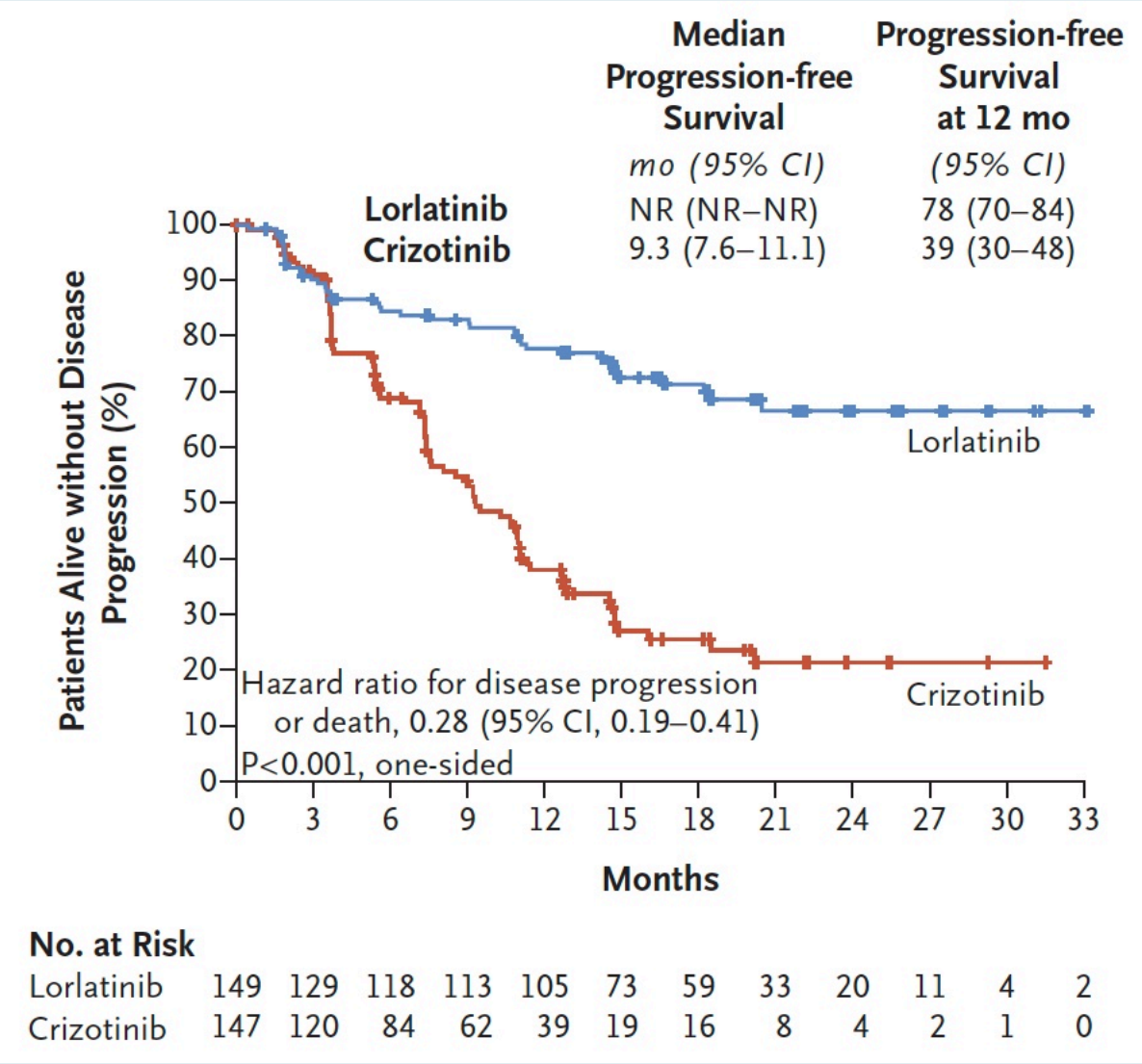
The NEW ENGLAND JOURNAL of MEDICINE

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*

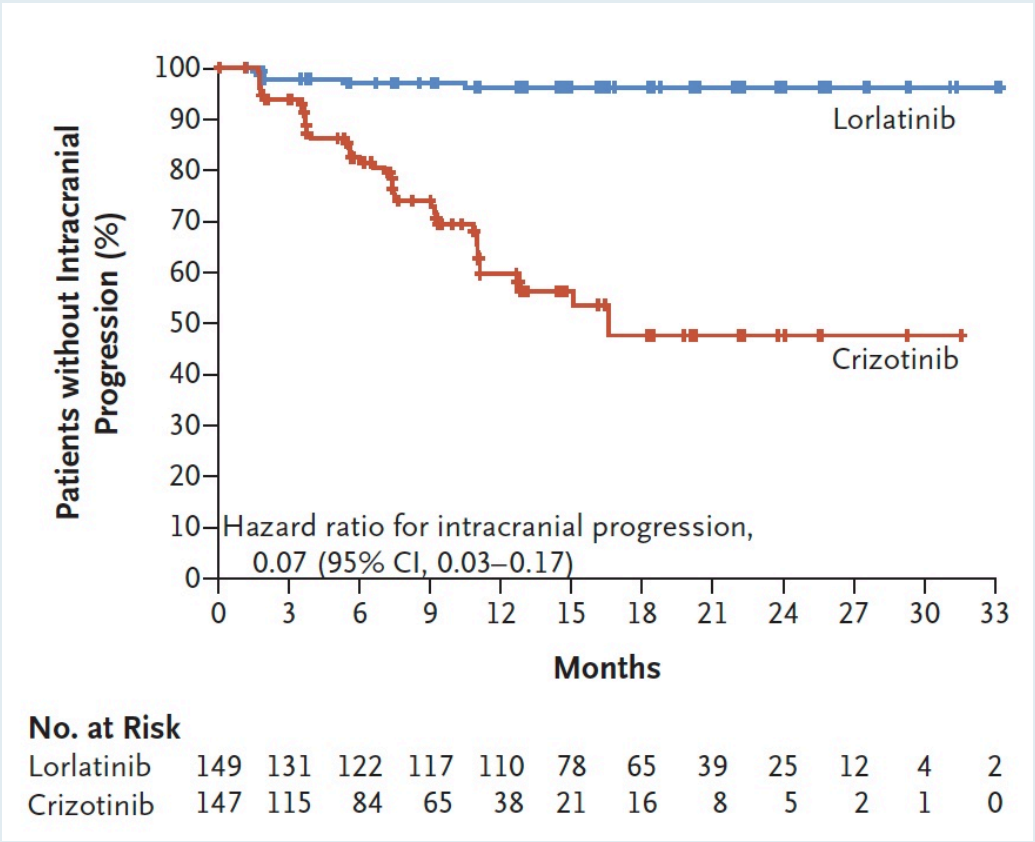
CROWN Trial: Progression-Free Survival



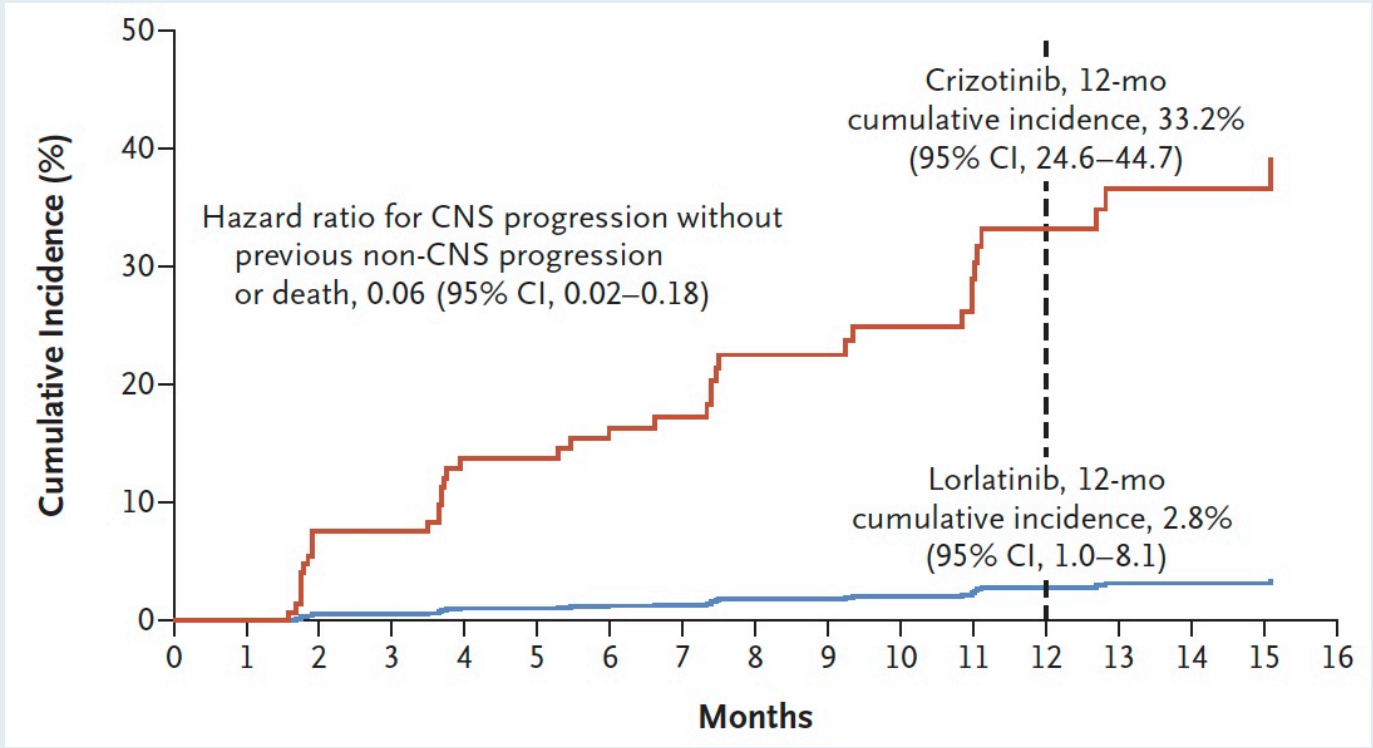
Shaw AT et al. *N Engl J Med* 2020;383:2018-29.

CROWN: CNS Progression

Survival without CNS Progression



Cumulative Incidence of CNS Progression as First Event



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

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CROWN: Select Adverse Events

Adverse event	Lorlatinib (n = 149)		Crizotinib (n = 142)	
	Grade 3	Grade 4	Grade 3	Grade 4
Increased weight	17%	0	2%	0
Hypercholesterolemia	15%	1%	0	0
Hypertriglyceridemia	13%	7%	0	0
Hypertension	10%	0	0	0
Edema	4%	0	1%	0
Anemia	3%	0	3%	0
Peripheral neuropathy	2%	0	1%	0
Cognitive effects	2%	0	0	0
Mood effects	1%	0	0	0

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

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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Case Presentation – Dr Zafar: A 53-year-old man, previous smoker with Stage IIIA adenocarcinoma of the lung – ALK fusion

Dr Syed Zafar

- Stage IIIA lung adenocarcinoma
  - Surgery → platinum/pemetrexed → radiation therapy
- NGS: ALK fusion, PD-L1 TPS 1% (See report)

Question

- Should an ALK inhibitor be recommended?

Case Presentation – Dr Zafar: A 53-year-old man – NGS

Dr Syed Zafar

Diagnosis: Adenocarcinoma, NOS **All Testing Completed:** 06-Dec-2019

Results with Therapy Associations

BIOMARKER	METHOD	ANALYTE	RESULT	THERAPY ASSOCIATION		BIOMARKER LEVEL*
ALK	Seq	RNA-Tumor	Fusion Detected	BENEFIT	alectinib, brigatinib	Level 1
	IHC	Protein	Positive | 3+, 95%	BENEFIT	ceritinib	Level 1
				BENEFIT	crizotinib	Level 1
PD-L1 (22c3)	IHC	Protein	Positive, Low Expression, TPS: 1%	BENEFIT	pembrolizumab	Level 1
				BENEFIT	atezolizumab	Level 2
				BENEFIT	durvalumab, nivolumab	Level 3A
EGFR	Seq	DNA-Tumor	Mutation Not Detected	LACK OF BENEFIT	erlotinib, gefitinib	Level 1

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Meet The Professor with Dr Govindan

Module 1: Cases from Dr Zafar

Module 2: Lung Cancer Journal Club with Dr Govindan

- Sex and gender: modifiers of health, disease and medicine
- Adjuvant targeted therapy or immunotherapy (SELECT, ALCHEMIST studies)
- Role of tumor mutational burden in selecting patients for first-line immunotherapy
- New approaches to therapy for small cell lung cancer
- Validation of prognostic mRNA signatures in early-stage squamous lung cancer
- Whole-genome characterization of lung adenocarcinomas lacking alterations in RTK/RAS/RAF/MAPK pathway
- Mastering the complex targeted therapy for non-small cell lung cancer
- Biomarker-driven staging
- Untangling the evolutionary roots of lung cancer
- Proteogenomic characterization reveals therapeutic vulnerabilities in lung adenocarcinoma
- Pan-cancer analysis of whole genomes
- $KRAS^{G12C}$-inhibitor sotorasib (AMG 510)
- AMG 757 HLE BiTE® immune therapy targeting DLL3

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

Module 4: Key Papers and Recent Approvals

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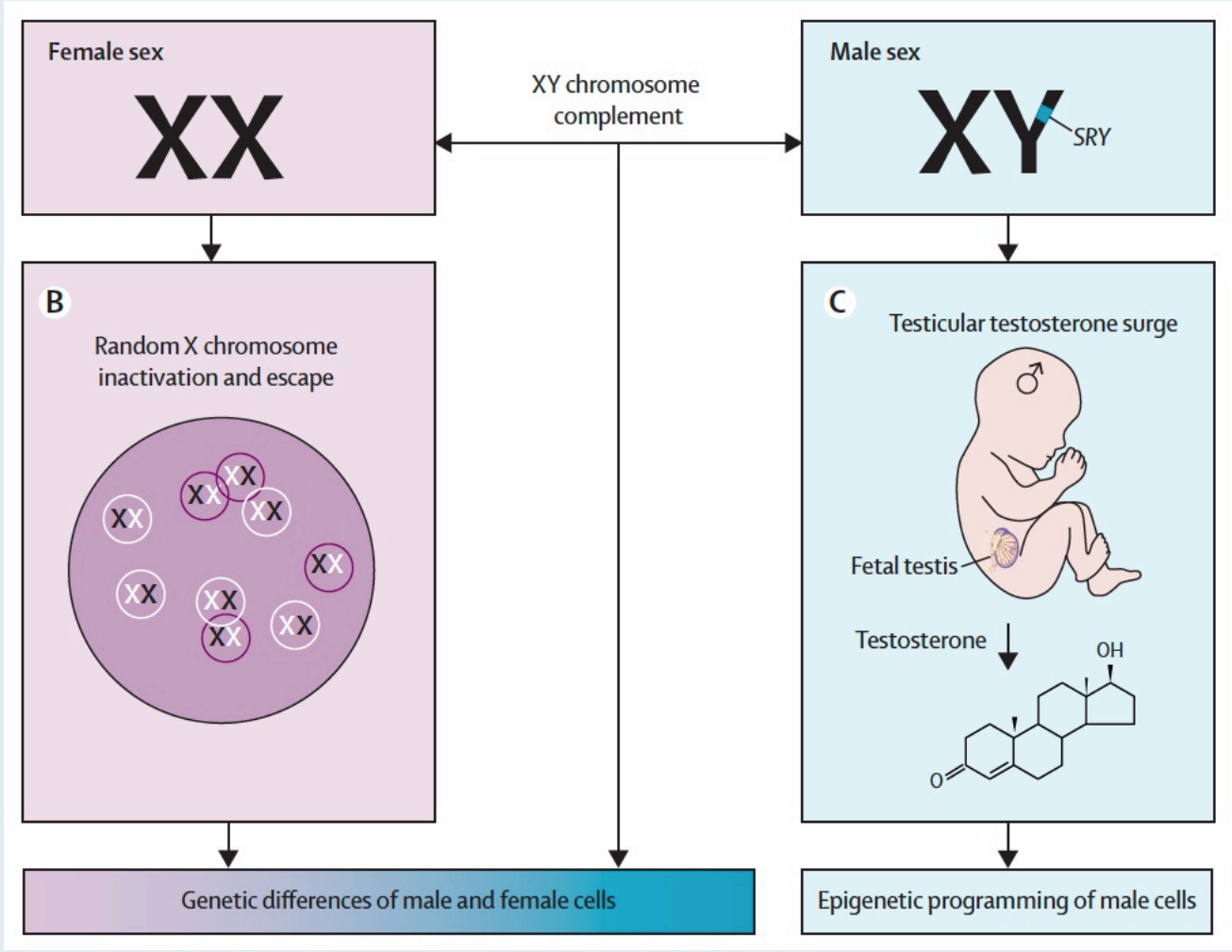
Lancet 2020;396(10250):565-82.

Review

Sex and gender: modifiers of health, disease, and medicine

Franck Mauvais-Jarvis, Noel Bairey Merz, Peter J Barnes, Roberta D Brinton, Juan-Jesus Carrero, Dawn L DeMeo, Geert J De Vries, C Neill Epperson, Ramaswamy Govindan, Sabra L Klein, Amedeo Lonardo, Pauline M Maki, Louise D McCullough, Vera Regitz-Zagrosek, Judith G Regensteiner, Joshua B Rubin, Kathryn Sandberg, Ayako Suzuki

Genetic Causes of Sex Differences



Mauvais-Jarvis F et al. *Lancet* 2020;396(10250):565-82.

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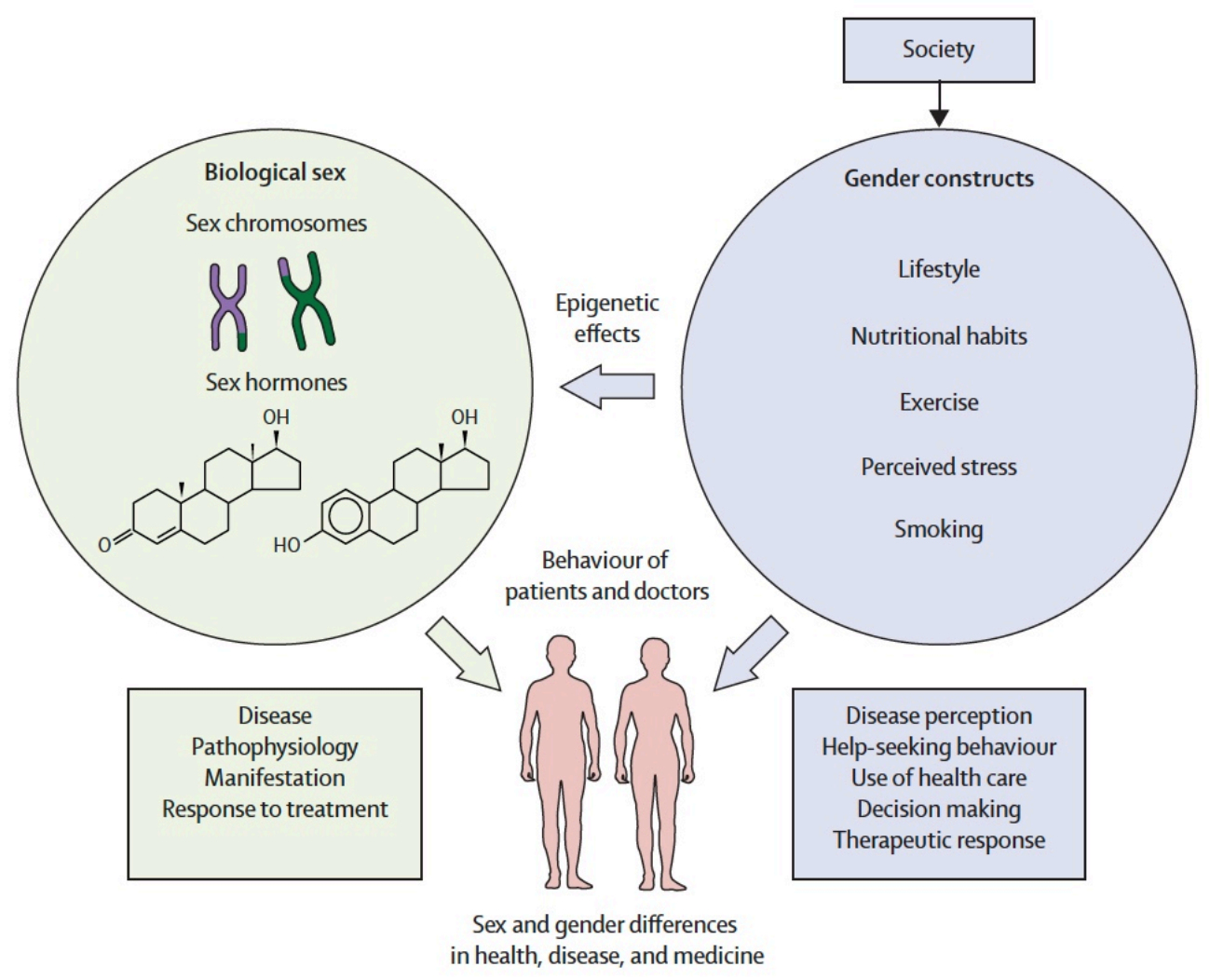
Interrelation between Sex and Gender in Health, Diseases and Medicine



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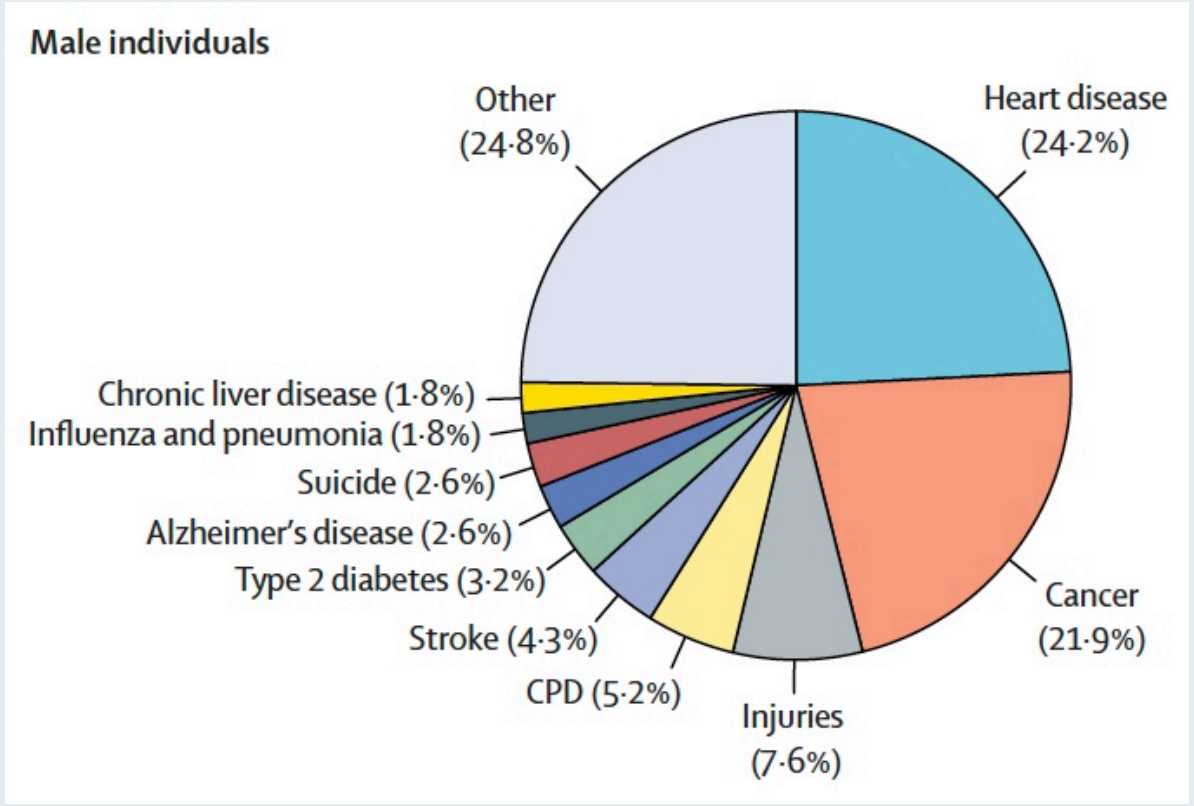
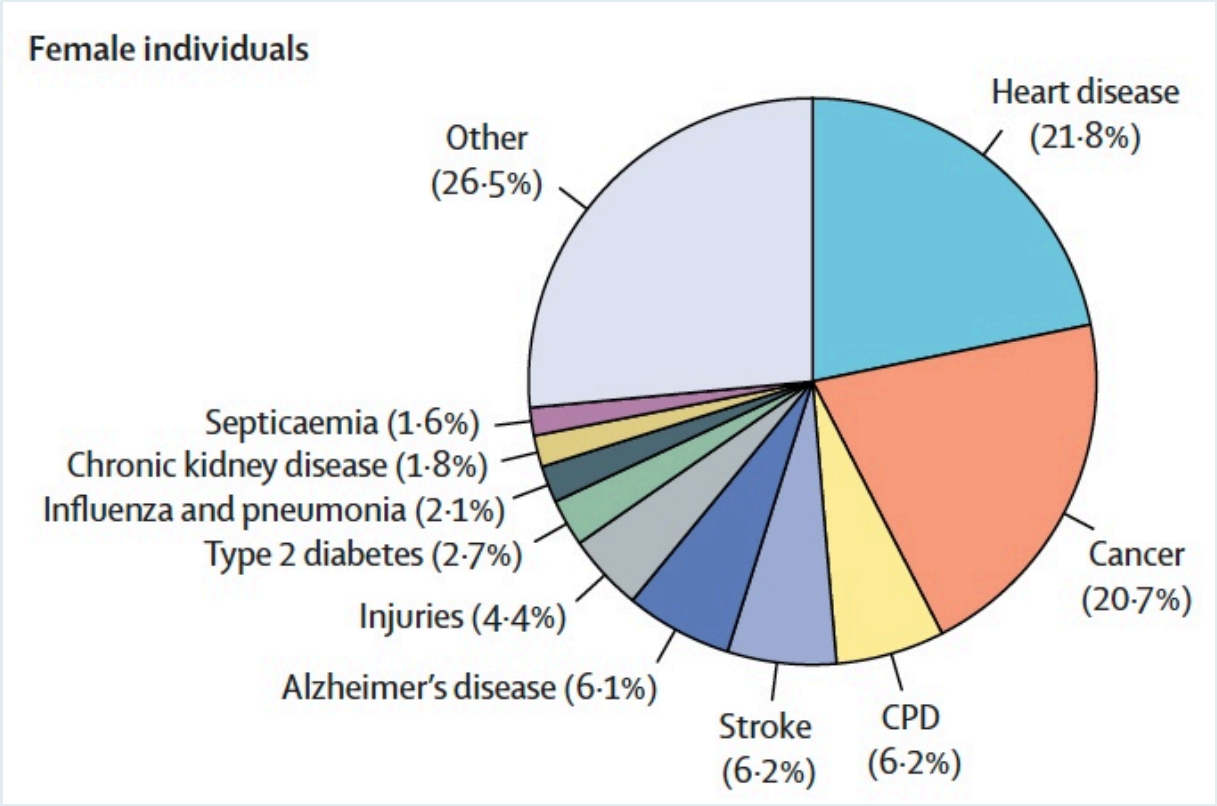
Distribution of the 10 Leading Causes of Death, by Sex





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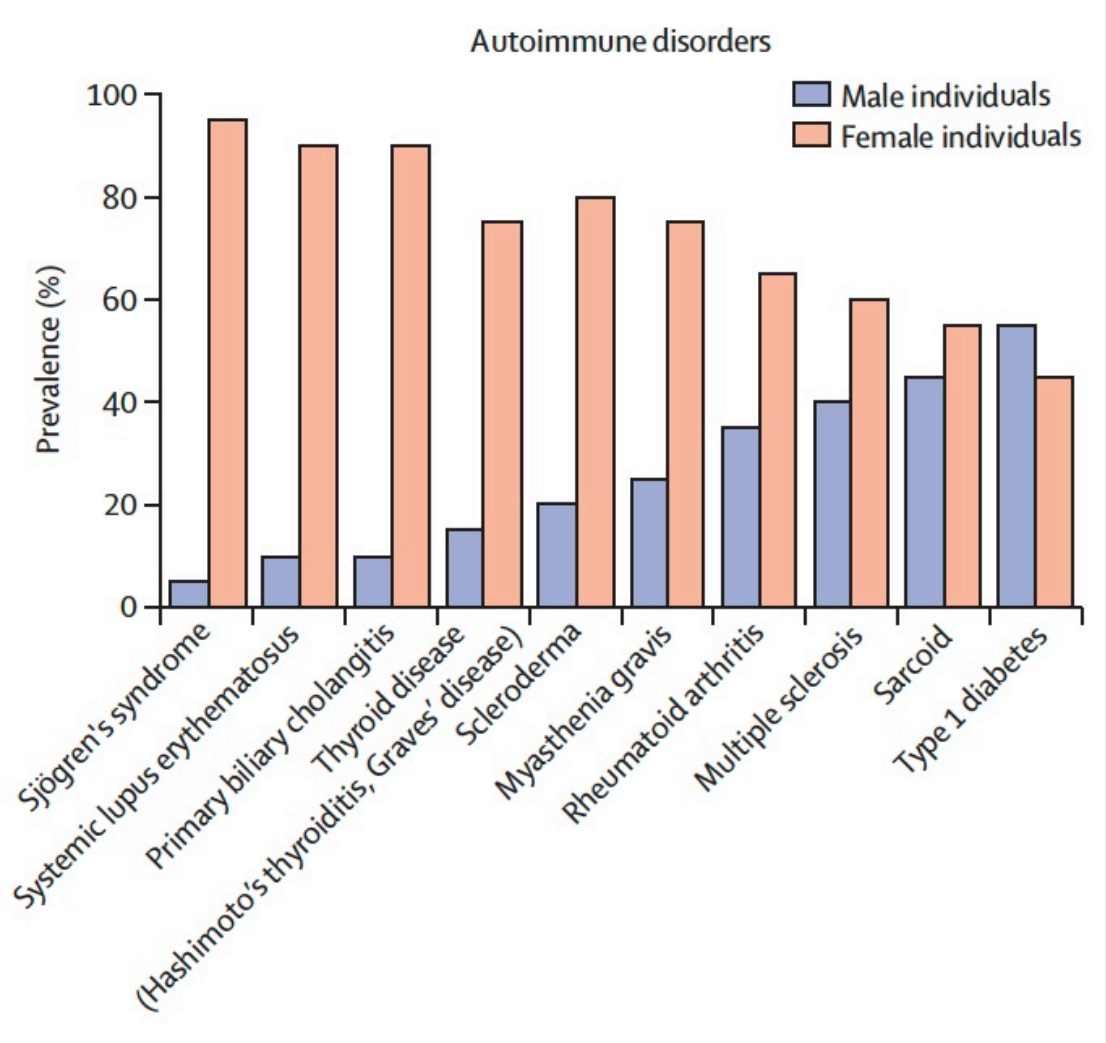
Disabling Disorders with High Sex Influence on Prevalence: Autoimmune Disorders



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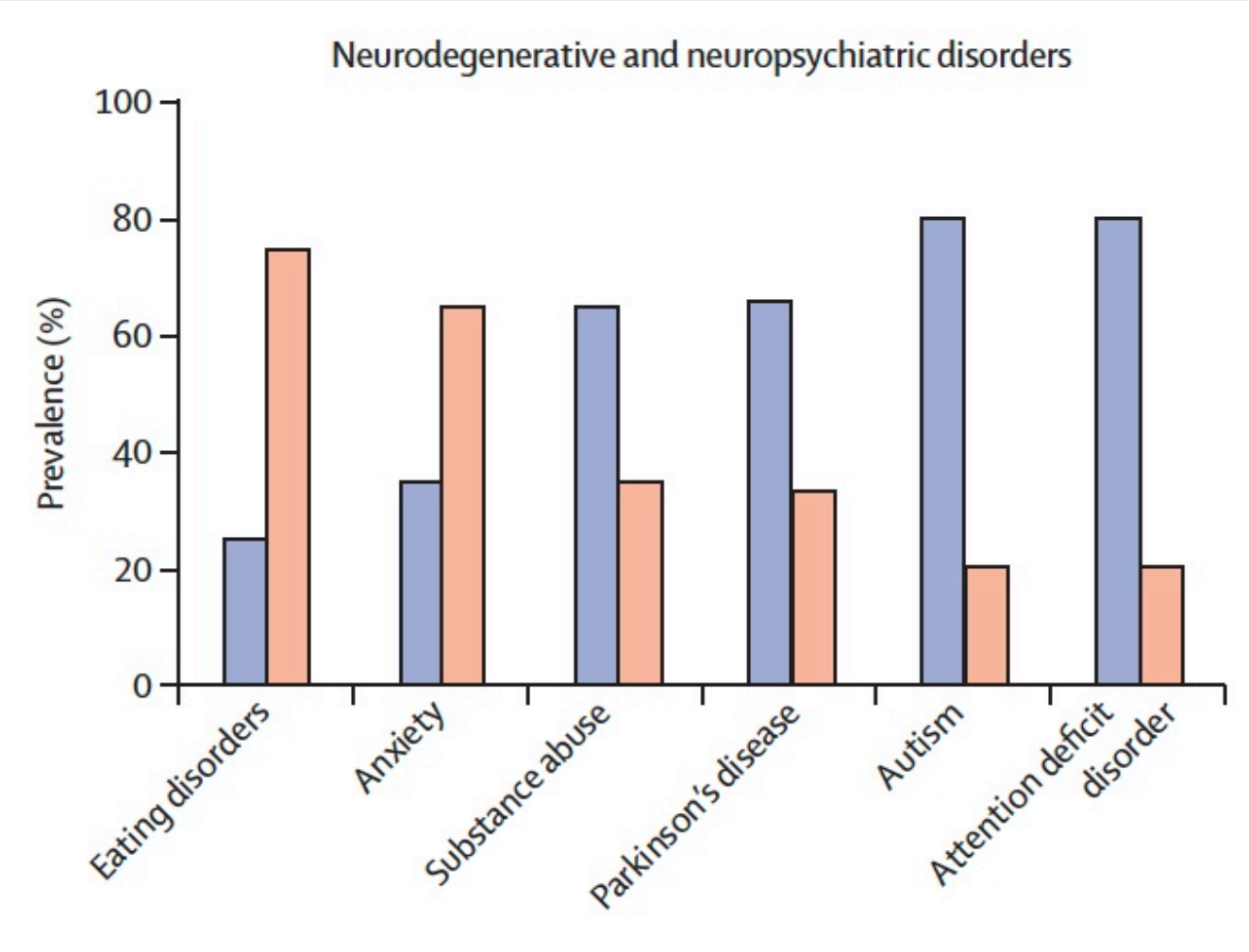
Disabling Disorders with High Sex Influence on Prevalence: Neurodegenerative and Neuropsychiatric Disorders



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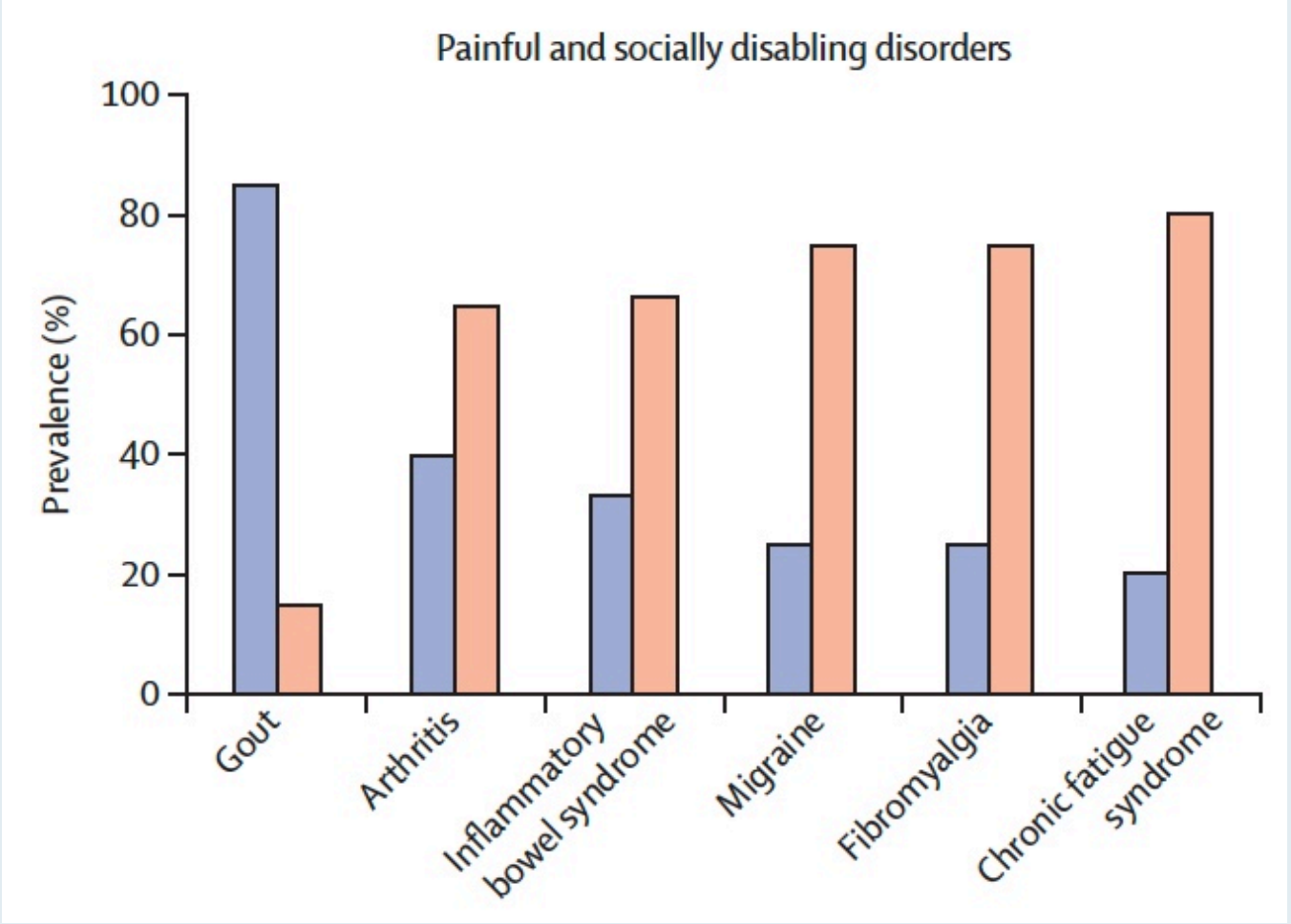
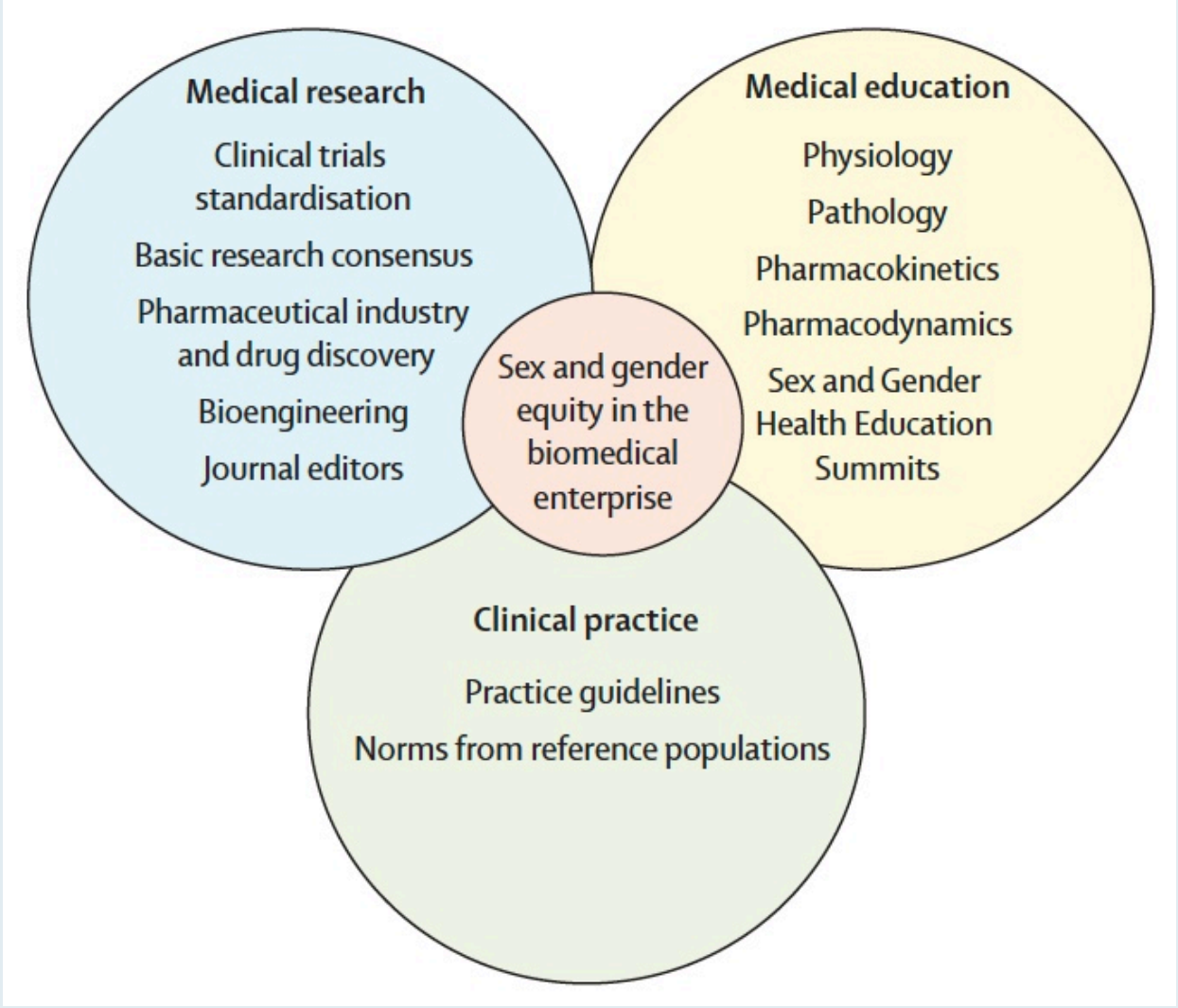
Disabling Disorders with High Sex Influence on Prevalence: Painful and Socially Disabling Disorders



Mauvais-Jarvis F et al. *Lancet* 2020;396(10250):565-82.

Summary of Recommendations to Promote Sex and Gender Equity in the Biomedical Enterprise



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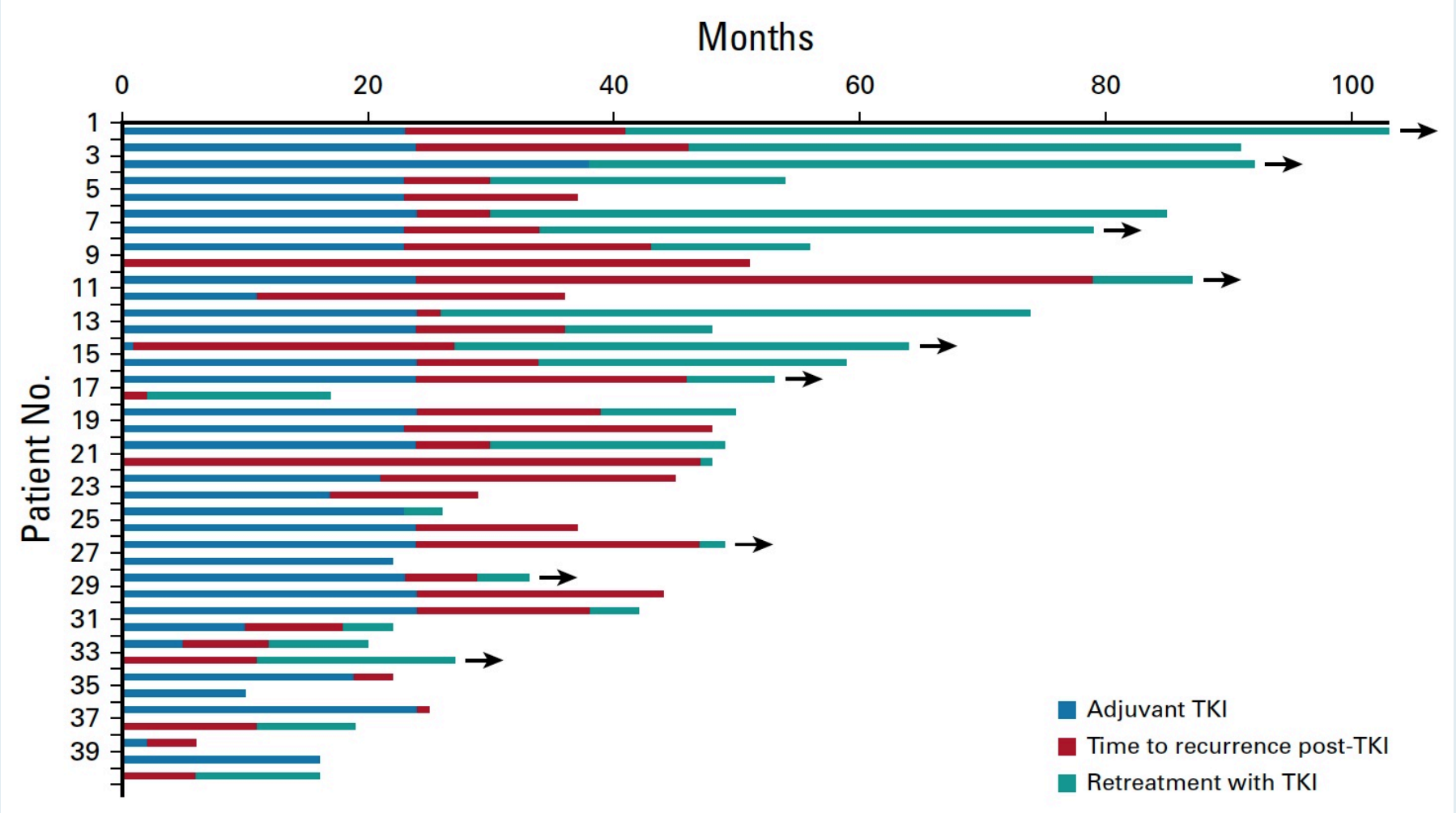
original report

SELECT: A Phase II Trial of Adjuvant Erlotinib in Patients With Resected Epidermal Growth Factor Receptor–Mutant Non–Small-Cell Lung Cancer

Nathan A. Pennell, MD, PhD[1]; Joel W. Neal, MD, PhD[2]; Jamie E. Chaft, MD[3]; Christopher G. Azzoli, MD[4]; Pasi A. Jänne, MD, PhD[5]; Ramaswamy Govindan, MD[6]; Tracey L. Evans, MD[7]; Daniel B. Costa, MD[8]; Heather A. Wakelee, MD[2]; Rebecca S. Heist, MD[4]; Marc A. Shapiro, MD[1]; Alona Muzikansky, MA[4]; Sudish Murthy, MD, PhD[1]; Michael Lanuti, MD[4]; Valerie W. Rusch, MD[3]; Mark G. Kris, MD[3]; and Lecia V. Sequist, MD[4]

J Clin Oncol 2019;37(2):97-104.

Swimmer Plot for All Patients Who Experienced Disease Recurrence (N = 40)



Pennell NA et al. *J Clin Oncol* 2019;37(2):97-104.

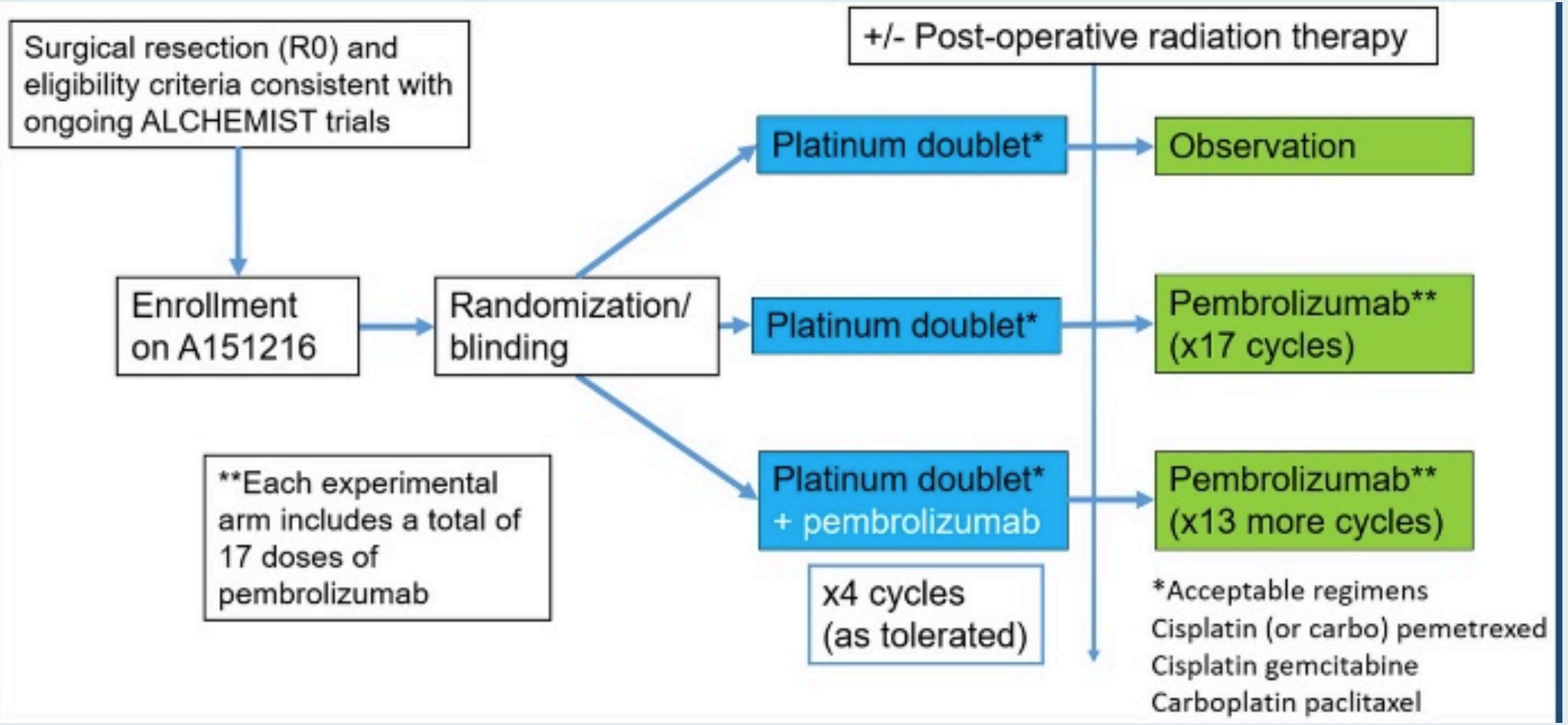
RTP RESEARCH TO PRACTICE

ALCHEMIST: Adjuvant Targeted Therapy or Immunotherapy for High-Risk Resected NSCLC

Sands J et al.

ASCO 2020;Abstract TPS9077.

ALCHEMIST Trial Design



Sands J et al. ASCO 2020;Abstract TPS9077.

Research

JAMA Oncol 2020;6(5):661-74.

JAMA Oncology | Original Investigation

Durvalumab With or Without Tremelimumab vs Standard Chemotherapy in First-line Treatment of Metastatic Non–Small Cell Lung Cancer
The MYSTIC Phase 3 Randomized Clinical Trial

Naiyer A. Rizvi, MD; Byoung Chul Cho, MD, PhD; Niels Reinmuth, MD, PhD; Ki Hyeong Lee, MD, PhD; Alexander Luft, MD; Myung-Ju Ahn, MD; Michel M. van den Heuvel, MD, PhD; Manuel Cobo, MD, PhD; David Vicente, MD; Alexey Smolin, MD; Vladimir Moiseyenko, MD, PhD; Scott J. Antonia, MD, PhD; Sylvestre Le Moulec, MD; Gilles Robinet, MD; Ronald Natale, MD; Jeffrey Schneider, MD; Frances A. Shepherd, MD; Sarayut Lucien Geater, MD; Edward B. Garon, MD; Edward S. Kim, MD; Sarah B. Goldberg, MD; Kazuhiko Nakagawa, MD, PhD; Rajiv Raja, PhD; Brandon W. Higgs, PhD; Anne-Marie Boothman, DPhil; Luping Zhao, PhD; Urban Scheuring, MD, PhD; Paul K. Stockman, MBChB, PhD; Vikram K. Chand, MBBS; Solange Peters, MD, PhD; for the MYSTIC Investigators

Invited Commentary

The Mystic Role of Tumor Mutational Burden in Selecting Patients With Lung Cancer for First-Line Immunotherapy

Saiama N. Waqar, MBBS, MSCI; Ramaswamy Govindan, MD

JAMA Oncol 2020;6(5):674-5.

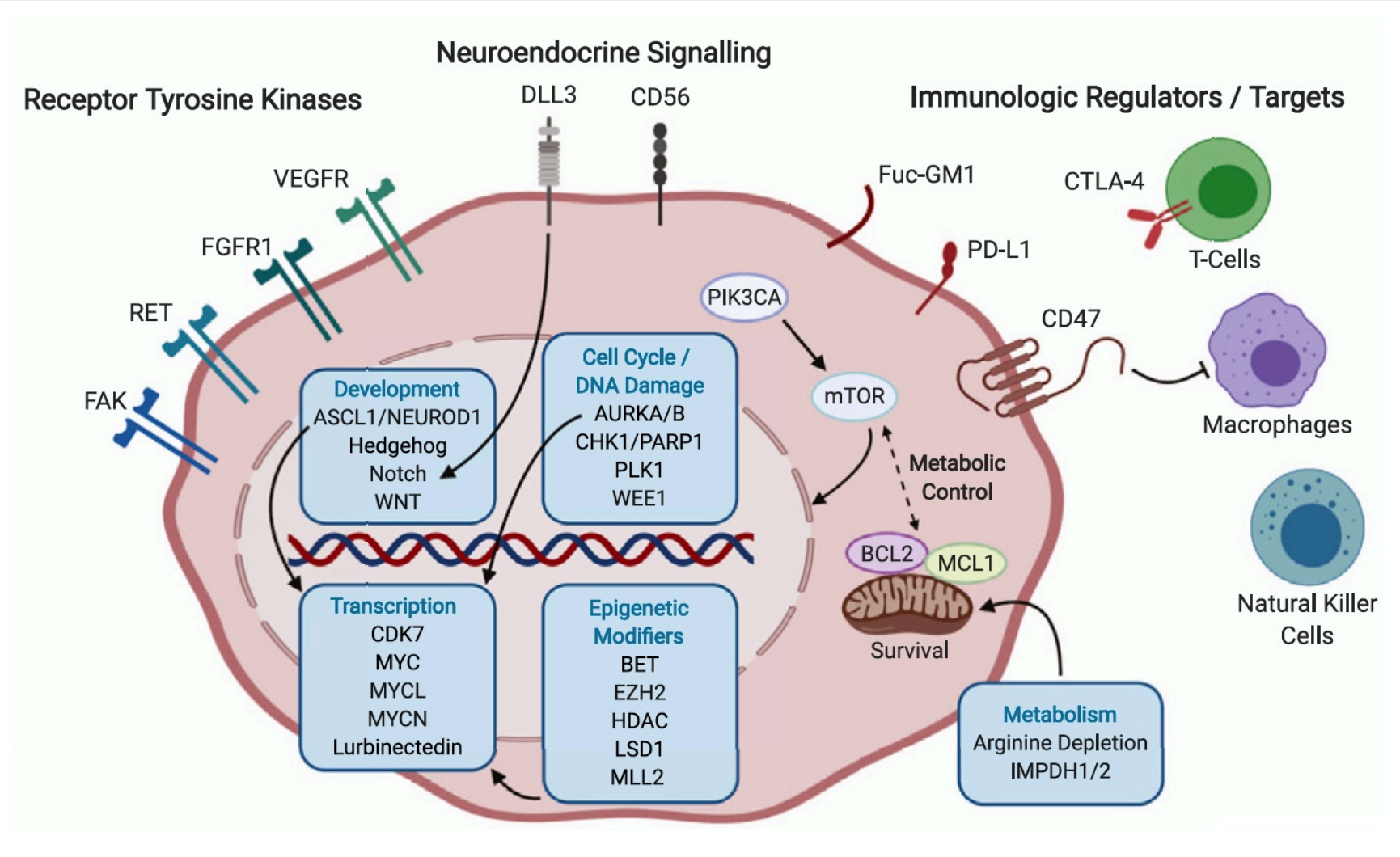
J Thorac Oncol 2020;15(4):520-40.

REVIEW ARTICLE

New Approaches to SCLC Therapy: From the Laboratory to the Clinic

John T. Poirier, PhD,[a] Julie George, PhD,[b] Taofeek K. Owonikoko, MD, PhD,[c] Anton Berns, PhD,[d] Elisabeth Brambilla, MD, PhD,[e] Lauren A. Byers, MD,[f] David Carbone, PhD, MD,[g] Huanhuan J. Chen, PhD,[h] Camilla L. Christensen, PhD,[i] Caroline Dive, PhD,[j] Anna F. Farago, PhD, MD,[k] Ramaswamy Govindan, MD,[l] Christine Hann, MD, PhD,[m] Matthew D. Hellmann, MD,[n] Leora Horn, MD, FRCPC,[o]

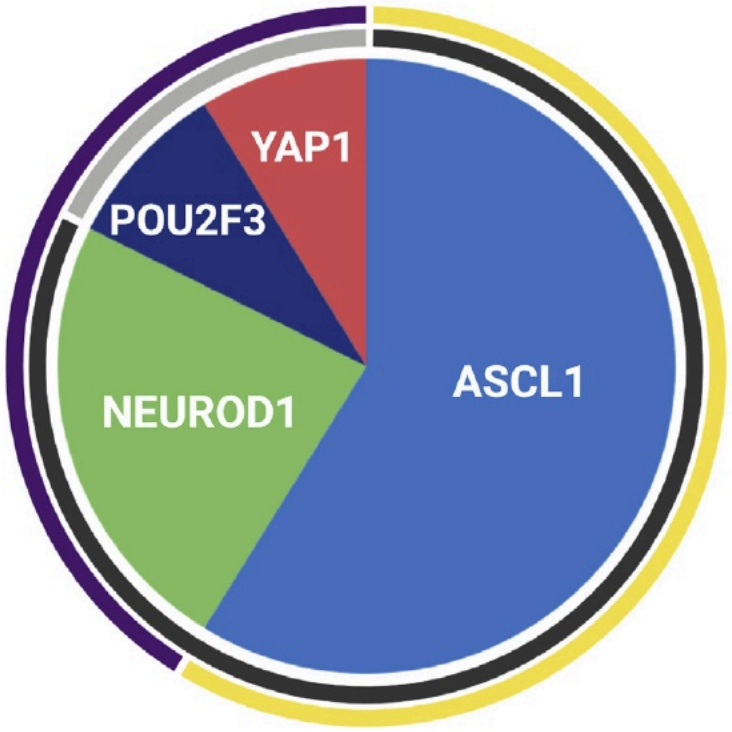
Some of the Many Areas of Current Therapeutic Interest in SCLC



Poirier JT et al. *J Thorac Oncol* 2020;15(4):520-40.

RTP RESEARCH TO PRACTICE

Relative Abundance, MYC Status and Neuroendocrine Character of the 4 Molecular Subtypes of SCLC, Identified by Key Transcriptional Regulator



	ASCL1	NEUROD1	POU2F3	YAP1
Targeted Therapies	BCL2 CREBBP DLL3 LSD1	Arginine Deprivation AURKA/B CHK1 IMPDH LSD1	Arginine Deprivation AURKA/B CHK1 IGF-R1 IMPDH	Arginine Deprivation AURKA/B CHK1 IMPDH IO

Poirier JT et al. *J Thorac Oncol* 2020;15(4):520-40.

Clin Cancer Res. 2019 October 15; 25(20): 6119–6126.

Circulating Tumor DNA Profiling in Small Cell Lung Cancer Identifies Potentially Targetable Alterations

Siddhartha Devarakonda[1,2], Sumithra Sankararaman[1], Brett H. Herzog[1], Kathryn A. Gold[3], Saiama N. Waqar[1,2], Jeffrey Ward[1,2], Victoria M. Raymond[4], Richard B. Lanman[4], Aadel Chaudhuri[1,2], Taofeek K. Owonikoko[5], Bob T. Li[6], John T. Poirier[6], Charles M. Rudin[6], Ramaswamy Govindan[1,2], Daniel Morgensztern[1,2]

J Thorac Oncol 2020;15(11):1748-57.

ORIGINAL ARTICLE

Multi-Institutional Prospective Validation of Prognostic mRNA Signatures in Early Stage Squamous Lung Cancer (Alliance)

Raphael Bueno, MD,[a,*] William G. Richards, PhD,[a] David H. Harpole, MD,[b] Karla V. Ballman, PhD,[c] Ming-Sound Tsao, MD,[d] Zhengming Chen, PhD,[c] Xiaofei Wang, PhD,[e] Guoan Chen, PhD,[f] Lucian R. Chirieac, MD,[g] M. Herman Chui, MD,[h] Wilbur A. Franklin, MD,[i] Thomas J. Giordano, MD,[j] Ramaswamy Govindan, MD,[k] Mary-Beth Joshi, MPH,[b] Daniel T. Merrick, MD,[i] Christopher J. Rivard, PhD,[l] Thomas Sporn, MD,[b] Adrie van Bokhoven, PhD,[i] Hui Yu, MD, PhD,[l] Frances A. Shepherd, MD,[m] Mark A. Watson, MD, PhD,[n] David G. Beer, PhD,[f] Fred R. Hirsch, MD, PhD[l,o]

Whole-Genome Characterization of Lung Adenocarcinomas Lacking Alterations in RTK/RAS/RAF/MAPK Pathway

Carrot-Zhang J et al.

AACR 2020;Abstract 5895.

Cancer Cell 2020;38(3):320-2.

CellPress

Cancer Cell

Spotlight

Mastering the Complex Targeted Therapy for Non-small Cell Lung Cancer

Siddhartha Devarakonda,[1] Ramaswamy Govindan,[1] and Daniel Morgensztern[1,*]

[1]Alvin Siteman Cancer Center at Washington University, Washington University School of Medicine, 660 S Euclid Box 8056, St. Louis, MO, USA

*Correspondence: Danielmorgensztern@wustl.edu

https://doi.org/10.1016/j.ccell.2020.07.011

JAMA Network Open

JAMA Netw Open 2019;2(12):e1917062

Original Investigation | Oncology

Comparison of Conventional TNM and Novel TNMB Staging Systems for Non–Small Cell Lung Cancer

Greg J. Haro, MD; Bonnie Sheu, MD; Nancy R. Cook, ScD; Gavitt A. Woodard, MD; Michael J. Mann, MD; Johannes R. Kratz, MD

JAMA Network Open

JAMA Netw Open 2019;2(12):e1917052

Invited Commentary | Oncology

Biomarker-Driven Staging—Are We There Yet?

Siddhartha Devarakonda, MD; Ramaswamy Govindan, MD

nature COMMUNICATIONS

Nat Commun 2019;10(1):2979.

COMMENT

https://doi.org/10.1038/s41467-019-10879-6 OPEN

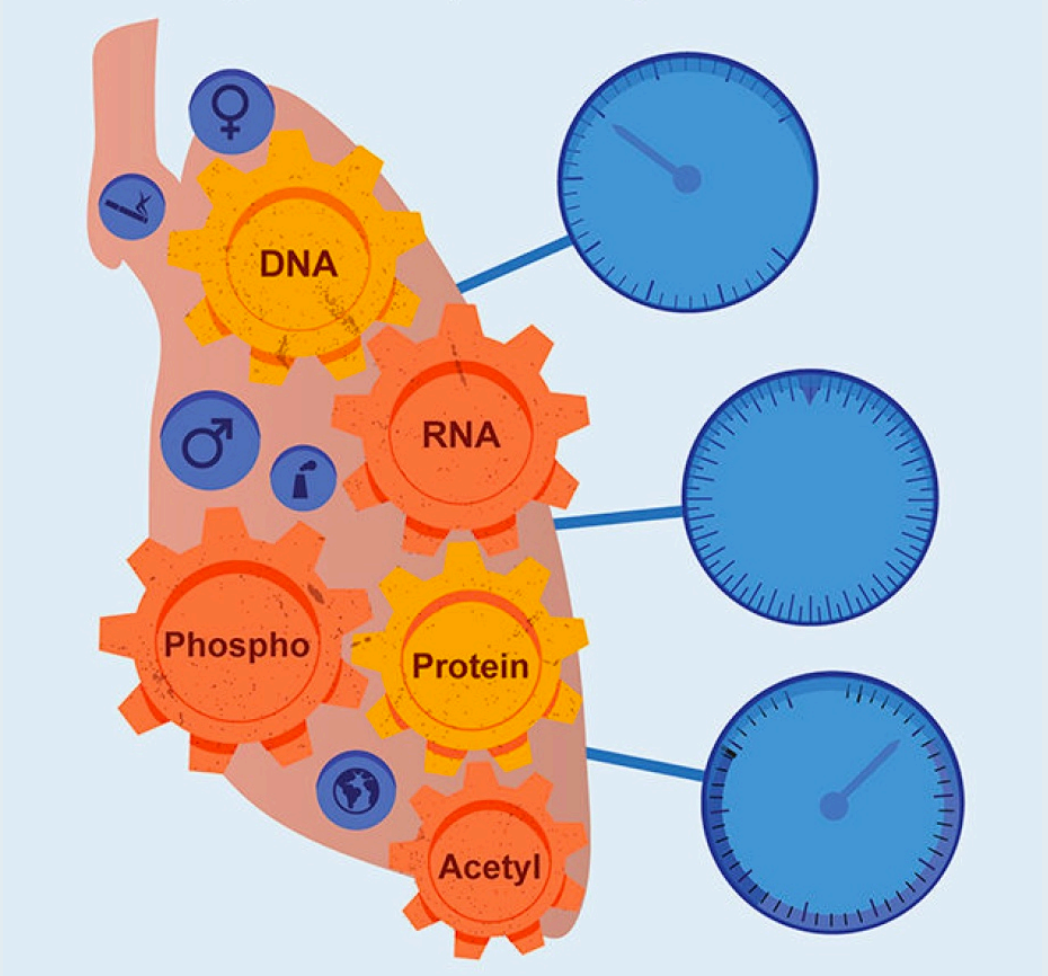
Untangling the evolutionary roots of lung cancer

Siddhartha Devarakonda[1,2,3] & Ramaswamy Govindan[1,2,3]

Gillette MA et al; Clinical Proteomic Tumor Analysis Consortium.
Cell 2020;182(1):200-25.e35

Proteogenomic characterization reveals therapeutic vulnerabilities in lung adenocarcinoma

Proteogenomic Analysis of Lung Adenocarcinoma



Gillette MA, et al; Clinical Proteomic Tumor Analysis Consortium. *Cell* 2020;182(1):200-25.e35

RTP RESEARCH TO PRACTICE

Nature 2020;578(7793):82-93.

Article

Pan-cancer analysis of whole genomes

https://doi.org/10.1038/s41586-020-1969-6

The ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium

Online resources for data access, visualization and analysis

The PCAWG landing page (http://docs.icgc.org/pcawg) provides links to several data resources for interactive online browsing, analysis and download of PCAWG data and results (Supplementary Table 4).

Direct download of PCAWG data

Aligned PCAWG read data in BAM format are also available at the European Genome Phenome Archive (EGA; https://www.ebi.ac.uk/ega/search/site/pcawg under accession number EGAS00001001692). In addition, all open-tier PCAWG genomics data, as well as reference datasets used for analysis, can be downloaded from the ICGC Data Portal at http://docs.icgc.org/pcawg/data/. Controlled-tier genomic data, including SNVs and indels that originated from TCGA projects (in VCF format) and aligned reads (in BAM format) can be downloaded using the Score (https://www.overture.bio/) software package, which has accelerated and secure file transfer, as well as BAM slicing facilities to selectively download defined regions of genomic alignments.

PCAWG computational pipelines

The core alignment, somatic variant-calling, quality-control and variant consensus-generation pipelines used by PCAWG have each been packaged into portable cross-platform images using the Dockstore system[84] and released under an Open Source licence that enables unrestricted use and redistribution. All PCAWG Dockstore images are available to the public at https://dockstore.org/organizations/PCAWG/collections/PCAWG.

ICGC Data Portal

The ICGC Data Portal[85] (https://dcc.icgc.org) serves as the main entry point for accessing PCAWG datasets with a single uniform web interface and a high-performance data-download client. This uniform interface provides users with easy access to the myriad of PCAWG sequencing data and variant calls that reside in many repositories and compute clouds worldwide. Streaming technology[86] provides users with high-level visualizations in real time of BAM and VCF files stored remotely on the Cancer Genome Collaboratory.

UCSC Xena

UCSC Xena[87] (https://pcawg.xenahubs.net) visualizes all PCAWG primary results, including copy-number, gene-expression, gene-fusion and promoter-usage alterations, simple somatic mutations, large somatic structural variations, mutational signatures and phenotypic data. These open-access data are available through a public Xena hub, and consensus simple somatic mutations can be loaded to the local computer of a user via a private Xena hub. Kaplan–Meier plots, histograms, box plots, scatter plots and transcript-specific views offer additional visualization options and statistical analyses.

The Expression Atlas

The Expression Atlas (https://www.ebi.ac.uk/gxa/home) contains RNA-sequencing and expression microarray data for querying gene expression across tissues, cell types, developmental stages and/or experimental conditions[88]. Two different views of the data are provided: summarized expression levels for each tumour type and gene expression at the level of individual samples, including reference-gene expression datasets for matching normal tissues.

PCAWG Scout

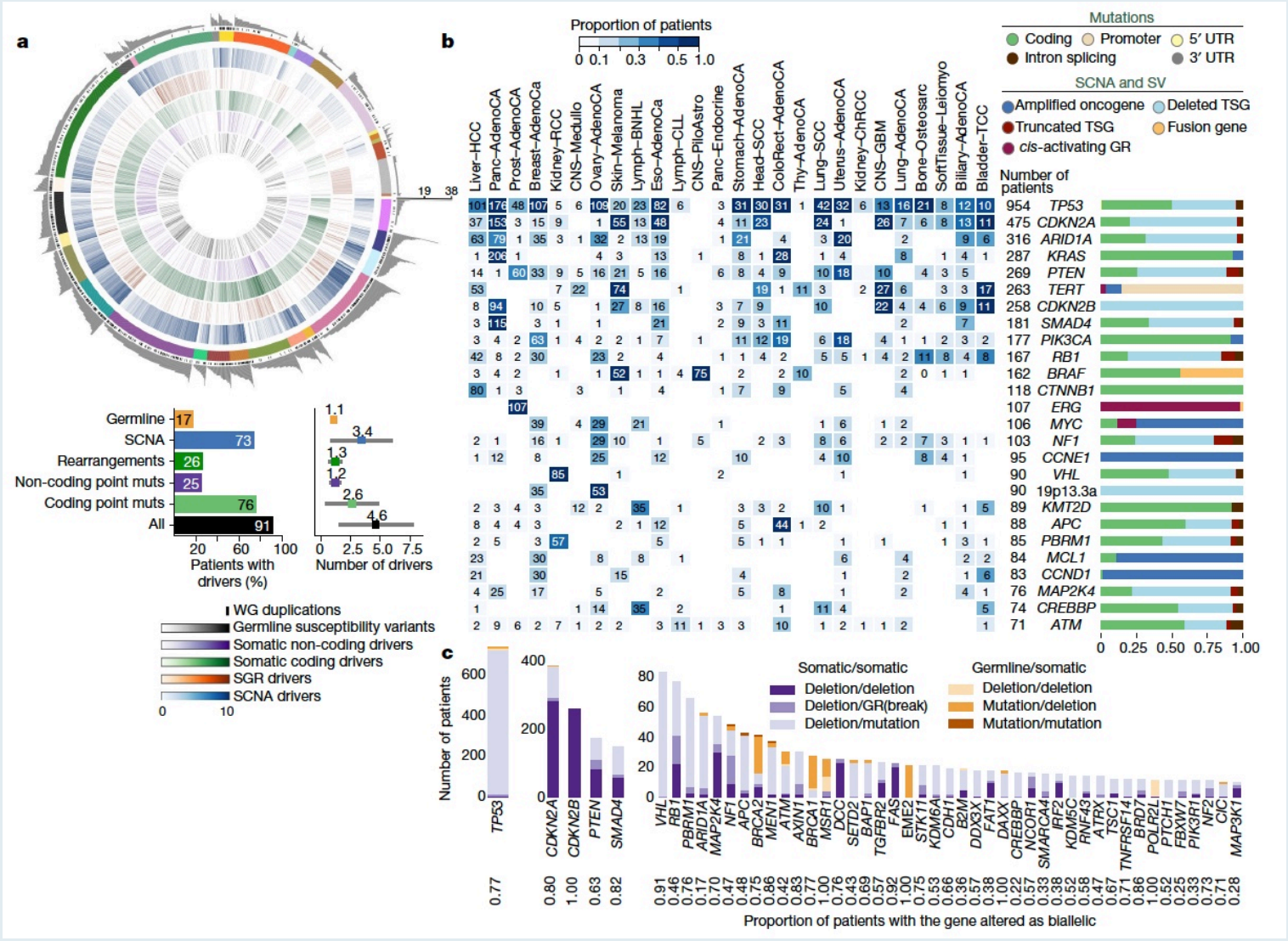
PCAWG Scout (http://pcawgscout.bsc.es/) provides a framework for -omics workflow and website templating to generate on-demand, in-depth analyses of the PCAWG data that are openly available to the whole research community. Views of protected data are available that still safeguard sensitive data. Through the PCAWG Scout web interface, users can access an array of reports and visualizations that leverage on-demand bioinformatic computing infrastructure to produce results in real time, allowing users to discover trends as well as form and test hypotheses.

Chromothripsis Explorer

Chromothripsis Explorer (http://compbio.med.harvard.edu/chromothripsis/) is a portal that allows structural variation in the PCAWG dataset to be explored on an individual patient basis through the use of circos plots. Patterns of chromothripsis can also be explored in aggregated formats.

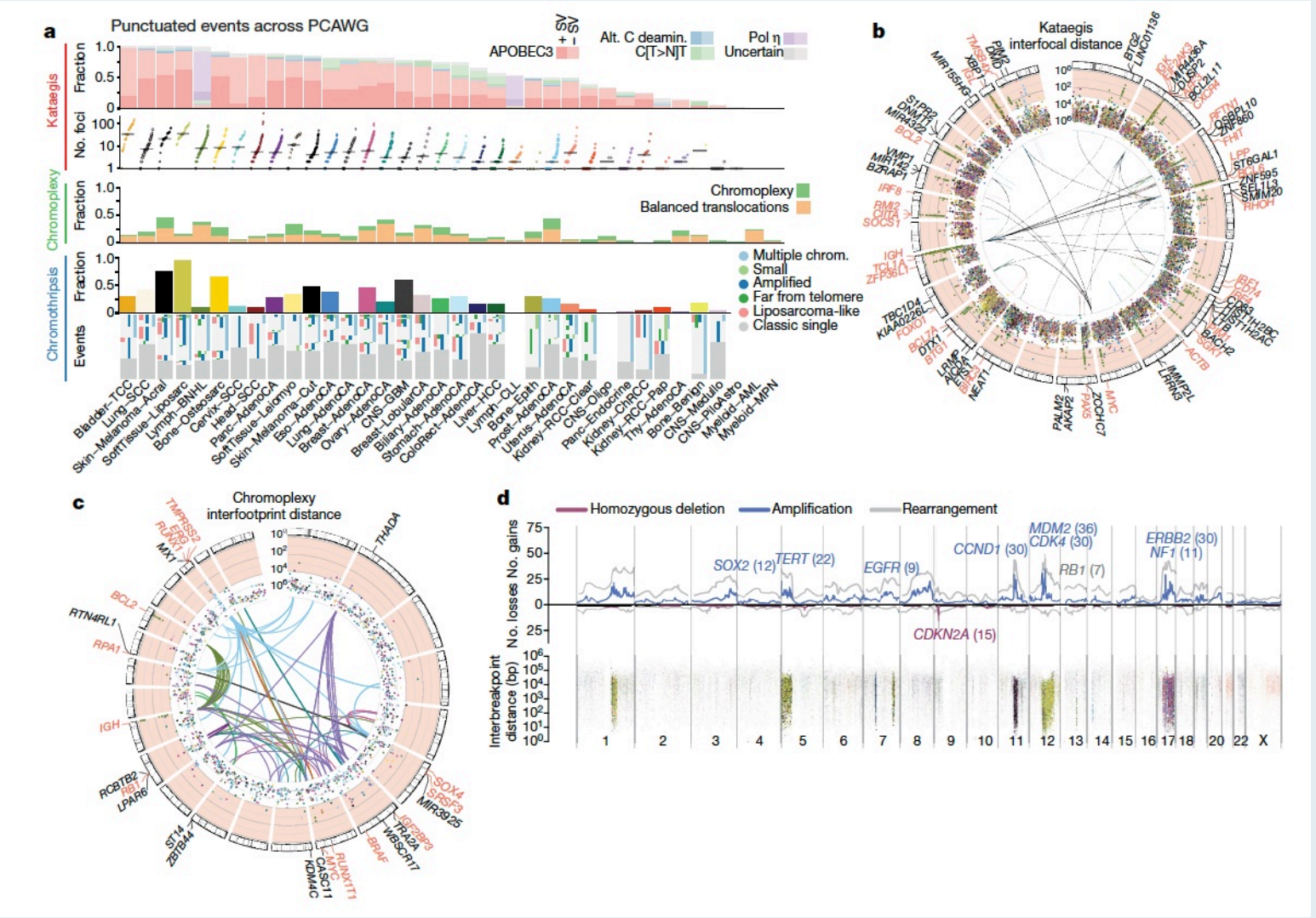
ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium. *Nature* 2020;578(7793):82-93.

Panorama of Driver Mutations in PCAWG



ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium. *Nature* 2020;578(7793):82-93.

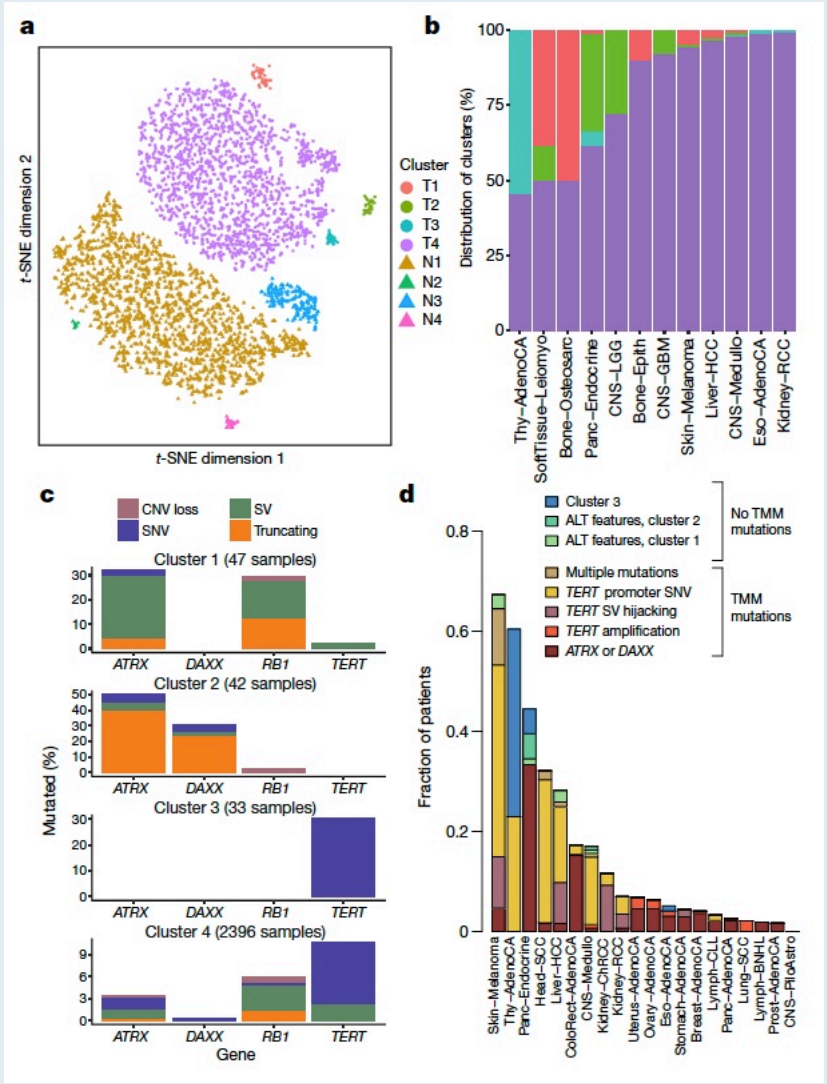
Patterns of Clustered Mutational Processes in PCAWG



ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium. *Nature* 2020;578(7793):82-93.

RTP RESEARCH TO PRACTICE

Telomere Sequence Patterns Across PCAWG



ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium. *Nature* 2020;578(7793):82-93.

RTP RESEARCH TO PRACTICE

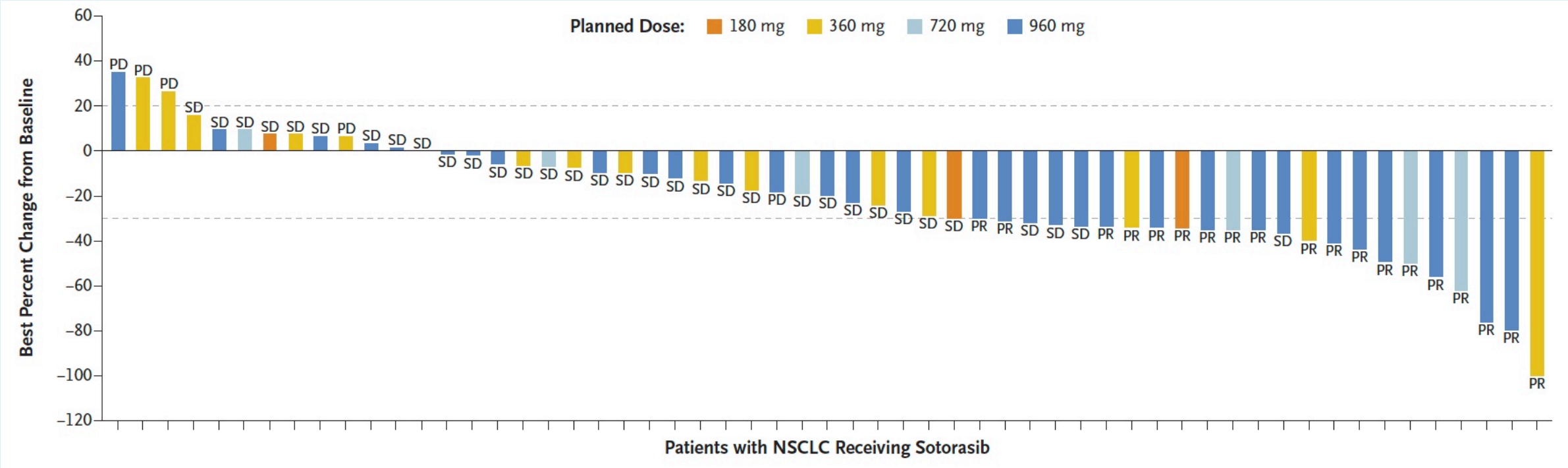
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 24, 2020 VOL. 383 NO. 13

KRAS^{G12C} Inhibition with Sotorasib in Advanced Solid Tumors

D.S. Hong, M.G. Fakih, J.H. Strickler, J. Desai, G.A. Durm, G.I. Shapiro, G.S. Falchook, T.J. Price, A. Sacher, C.S. Denlinger, Y.-J. Bang, G.K. Dy, J.C. Krauss, Y. Kuboki, J.C. Kuo, A.L. Coveler, K. Park, T.W. Kim, F. Barlesi, P.N. Munster, S.S. Ramalingam, T.F. Burns, F. Meric-Bernstam, H. Henary, J. Ngang, G. Ngarmchamnanrith, J. Kim, B.E. Houk, J. Canon, J.R. Lipford, G. Friberg, P. Lito, R. Govindan, and B.T. Li

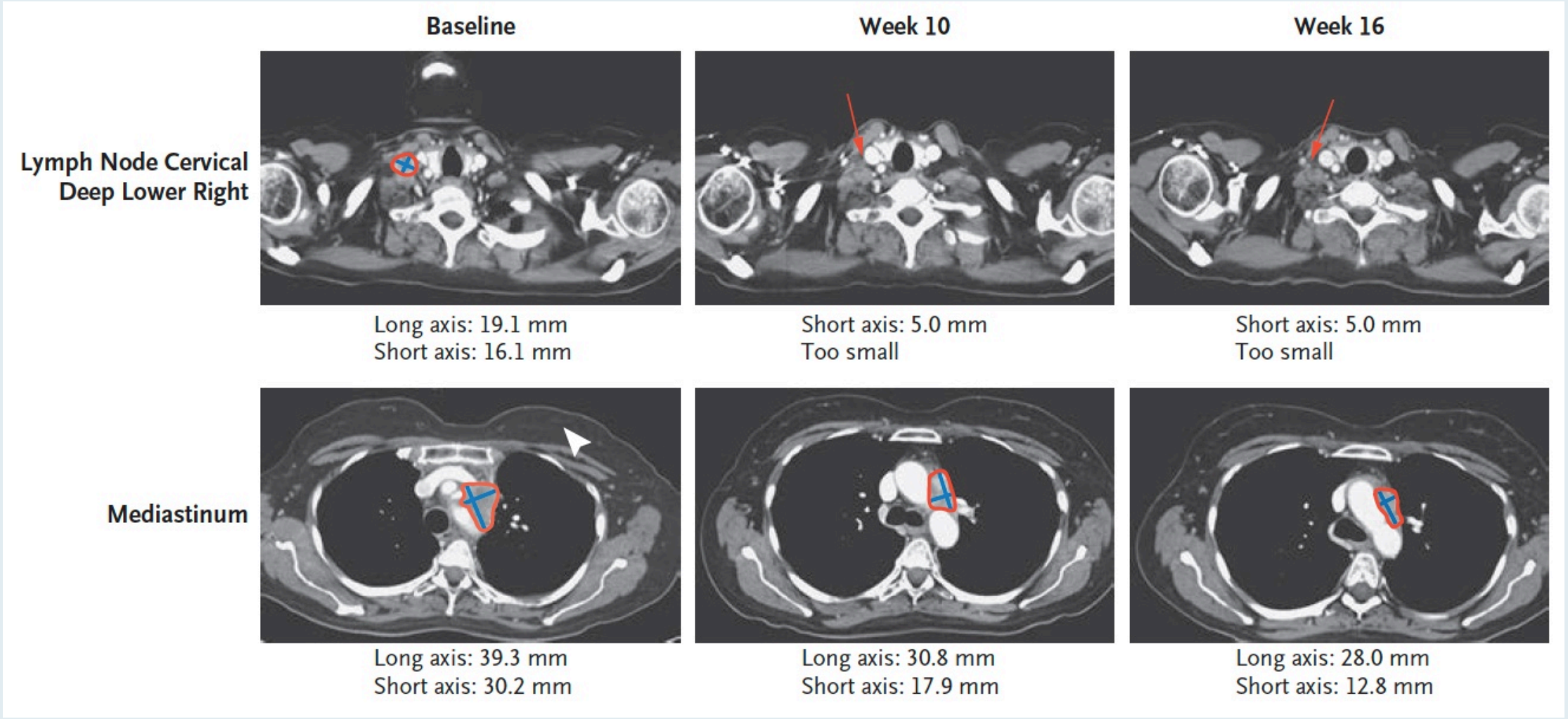
Change from Baseline in Tumor Burden



Hong DS et al. *N Engl J Med* 2020;383(13):1207-17.

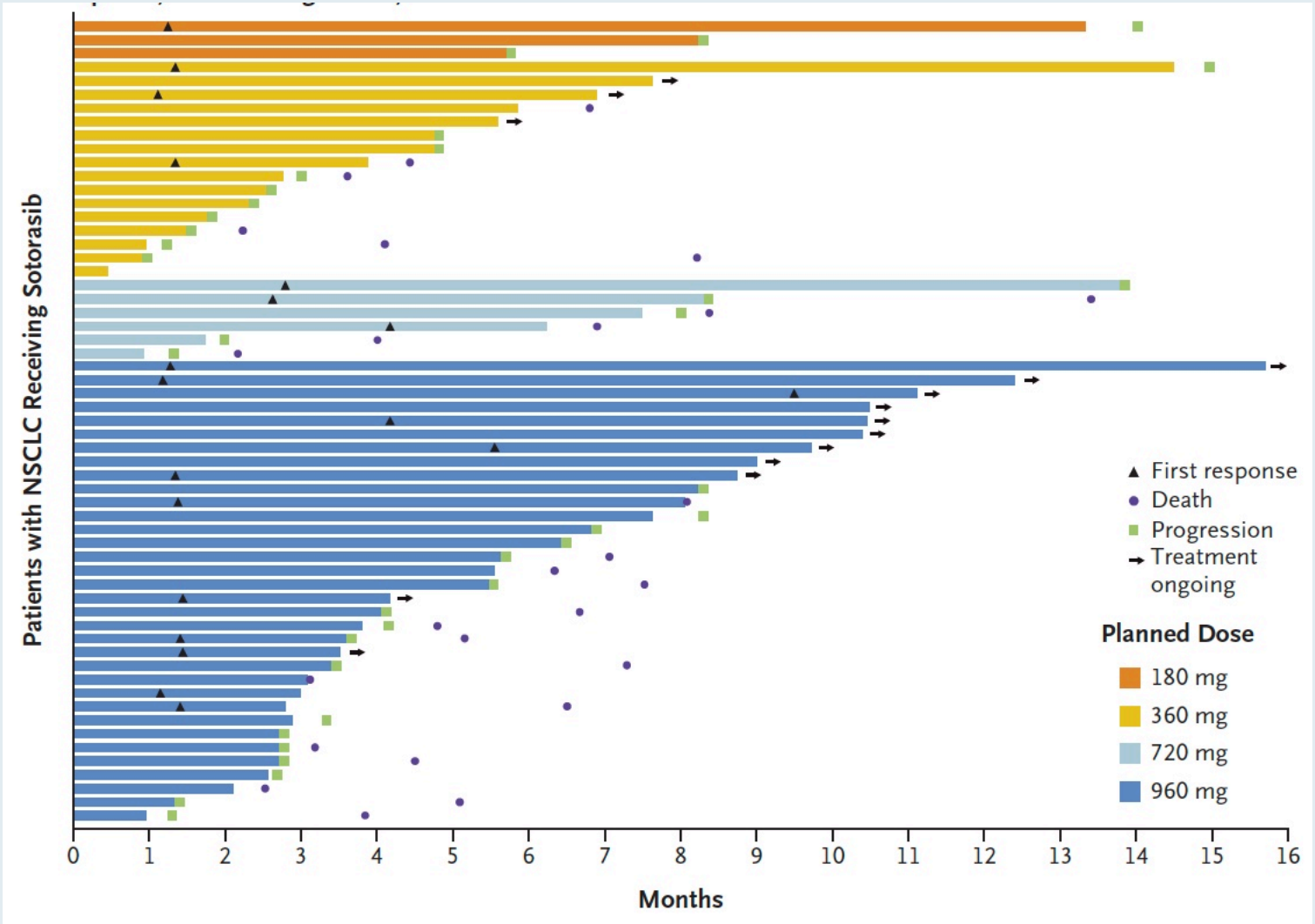
RTP RESEARCH TO PRACTICE

Effect of Sotorasib in a Patient with NSCLC



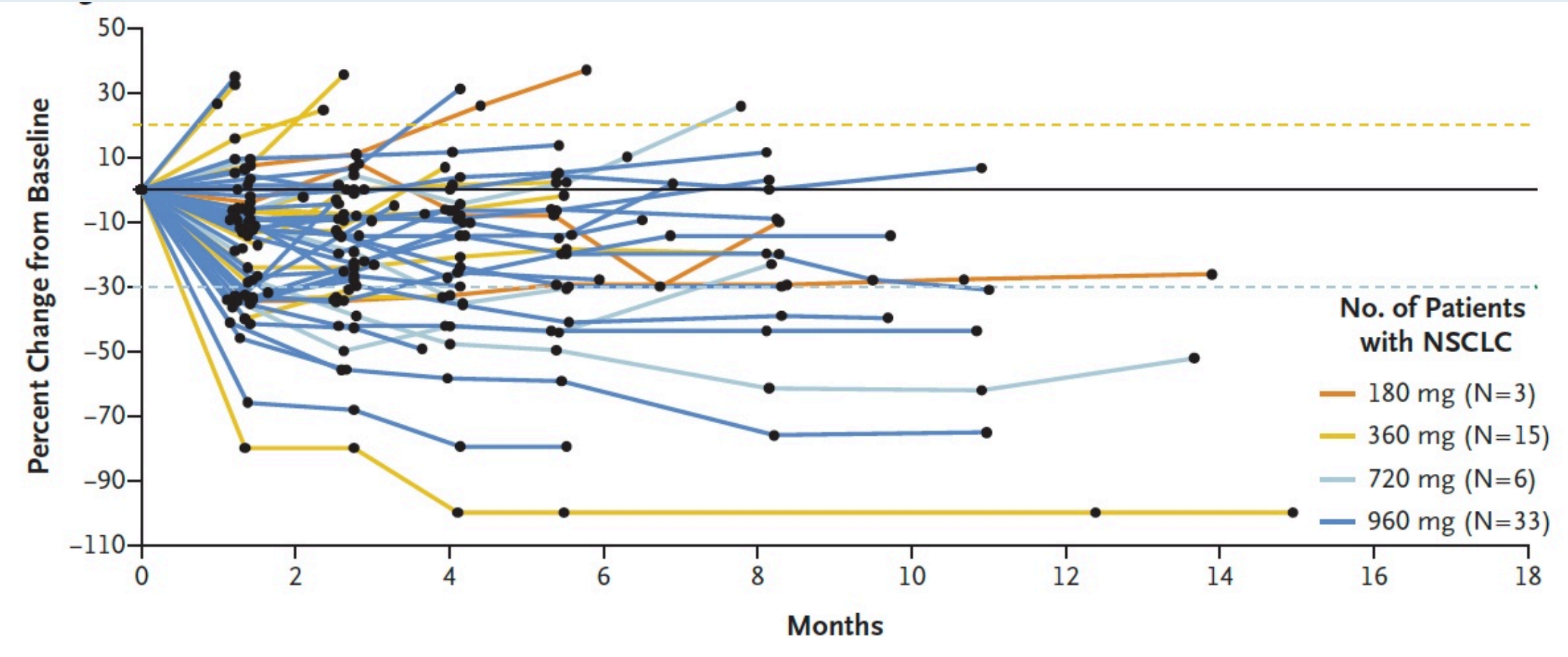
Hong DS et al. *N Engl J Med* 2020;383(13):1207-17.

Time to Response, Time to Disease Progression and Treatment Duration with Sotorasib



Hong DS et al. *N Engl J Med* 2020;383(13):1207-17.

Change in Tumor Burden over Time



Hong DS et al. *N Engl J Med* 2020;383(13):1207-17.

Nature 2019;575(7781):217-23.

Article

The clinical KRAS(G12C) inhibitor AMG 510 drives anti-tumour immunity

https://doi.org/10.1038/s41586-019-1694-1

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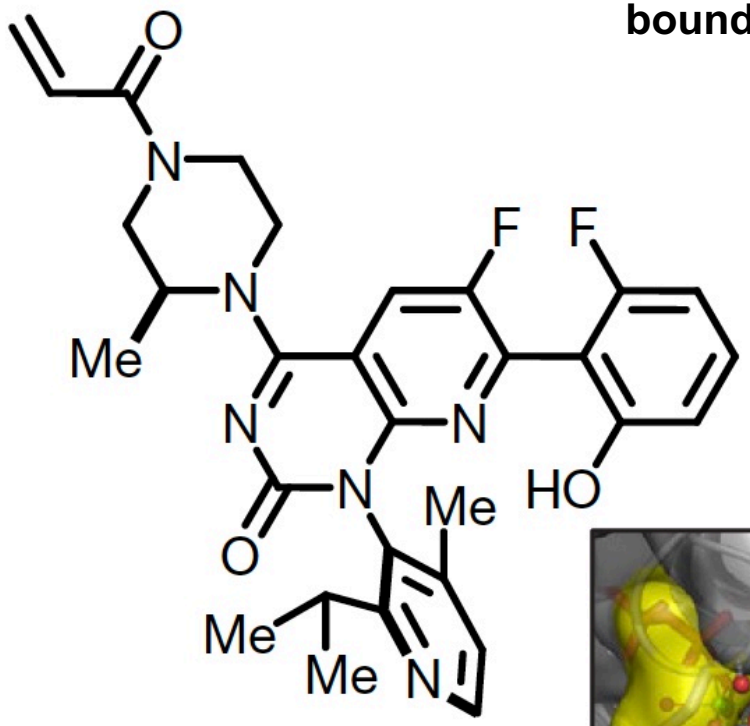
Accepted: 18 September 2019

Published online: 30 October 2019

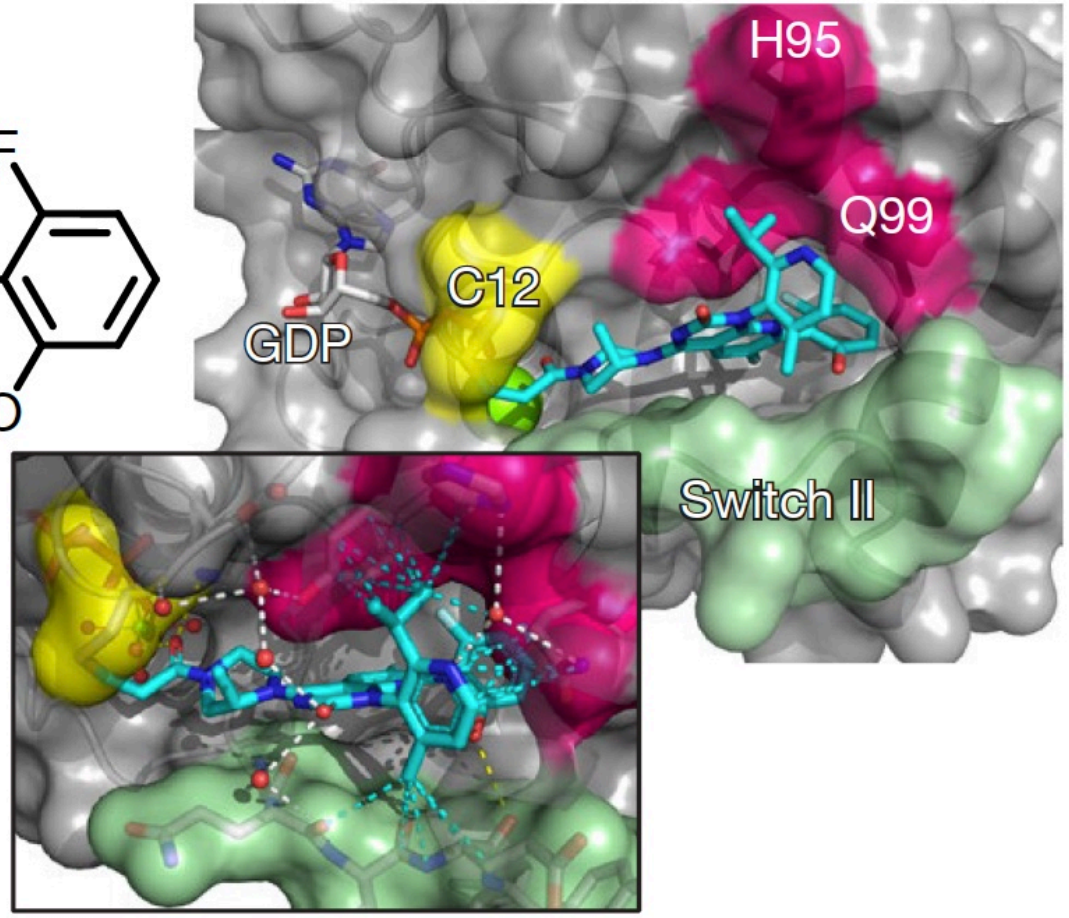
Jude Canon[1*], Karen Rex[1,17], Anne Y. Saiki[1,17], Christopher Mohr[1], Keegan Cooke[1], Dhanashri Bagal[2], Kevin Gaida[1], Tyler Holt[1], Charles G. Knutson[3], Neelima Koppada[3], Brian A. Lanman[1], Jonathan Werner[1], Aaron S. Rapaport[2], Tisha San Miguel[1], Roberto Ortiz[3,14], Tao Osgood[1], Ji-Rong Sun[1], Xiaochun Zhu[3,15], John D. McCarter[1], Laurie P. Volak[3,16], Brett E. Houk[4], Marwan G. Fakih[5], Bert H. O'Neil[6], Timothy J. Price[7,8], Gerald S. Falchook[9], Jayesh Desai[10], James Kuo[11], Ramaswamy Govindan[12], David S. Hong[13], Wenjun Ouyang[2], Haby Henary[4], Tara Arvedson[2], Victor J. Cee[1] & J. Russell Lipford[1*]

Sotorasib (AMG 510) Exploits a Cryptic Groove in KRAS(G12C) to Enhance Potency and Selectivity

AMG 510



X-ray co-crystal structure of KRAS (G12C/C51S/C80L/C118S) bound to GDP and AMG 510



Canon J et al. *Nature* 2019;575(7781):217-23.

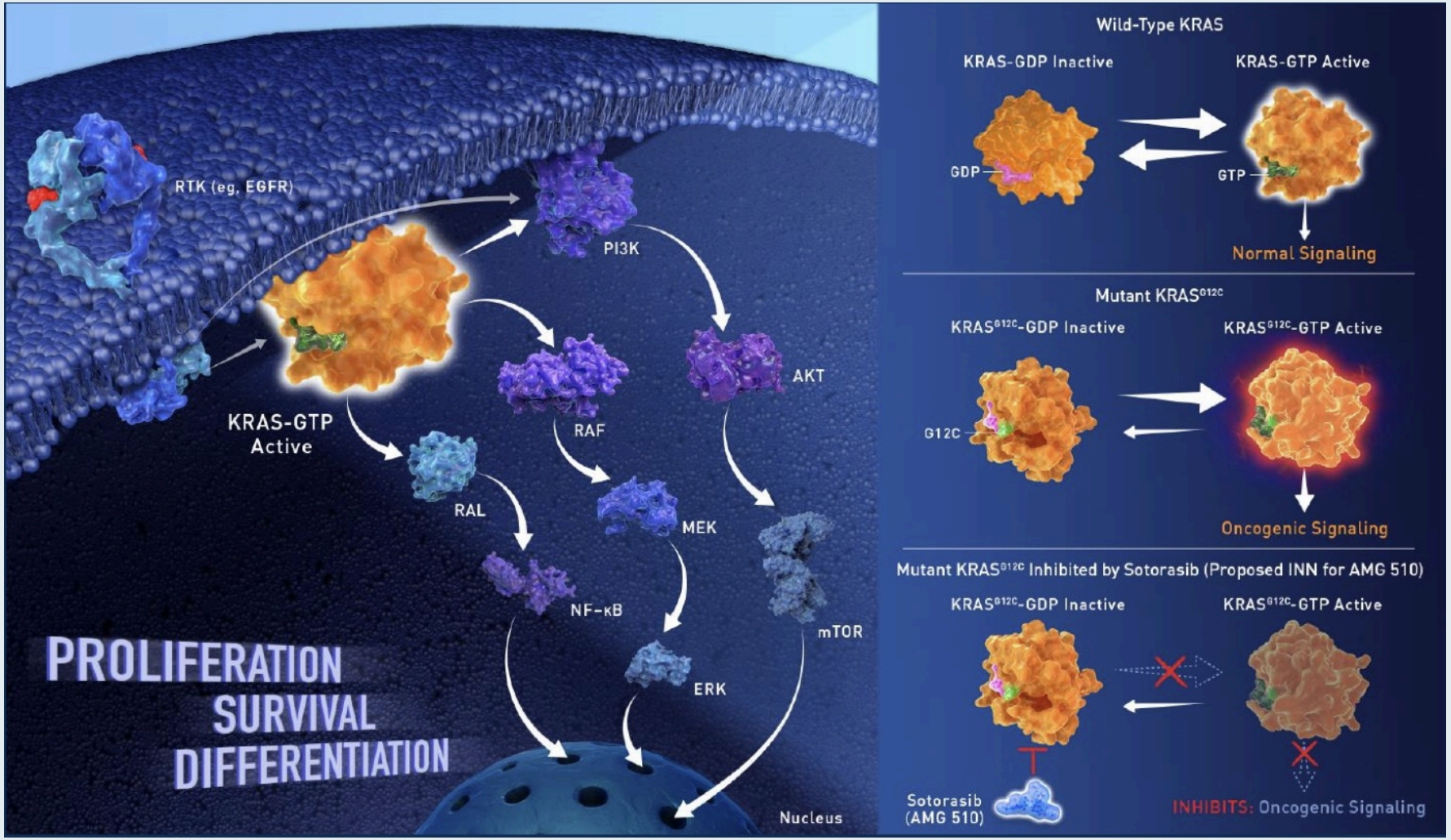
RTP RESEARCH TO PRACTICE

Trial in Progress: A Phase Ib Study of AMG 510, a Specific and Irreversible KRASG12C Inhibitor, in Combination with Other Anticancer Therapies in Patients with Advanced Solid Tumors Harboring KRAS p.G12C Mutation (CodeBreak 101)

Fakih M et al.

ASCO 2020;Abstract TPS3661.

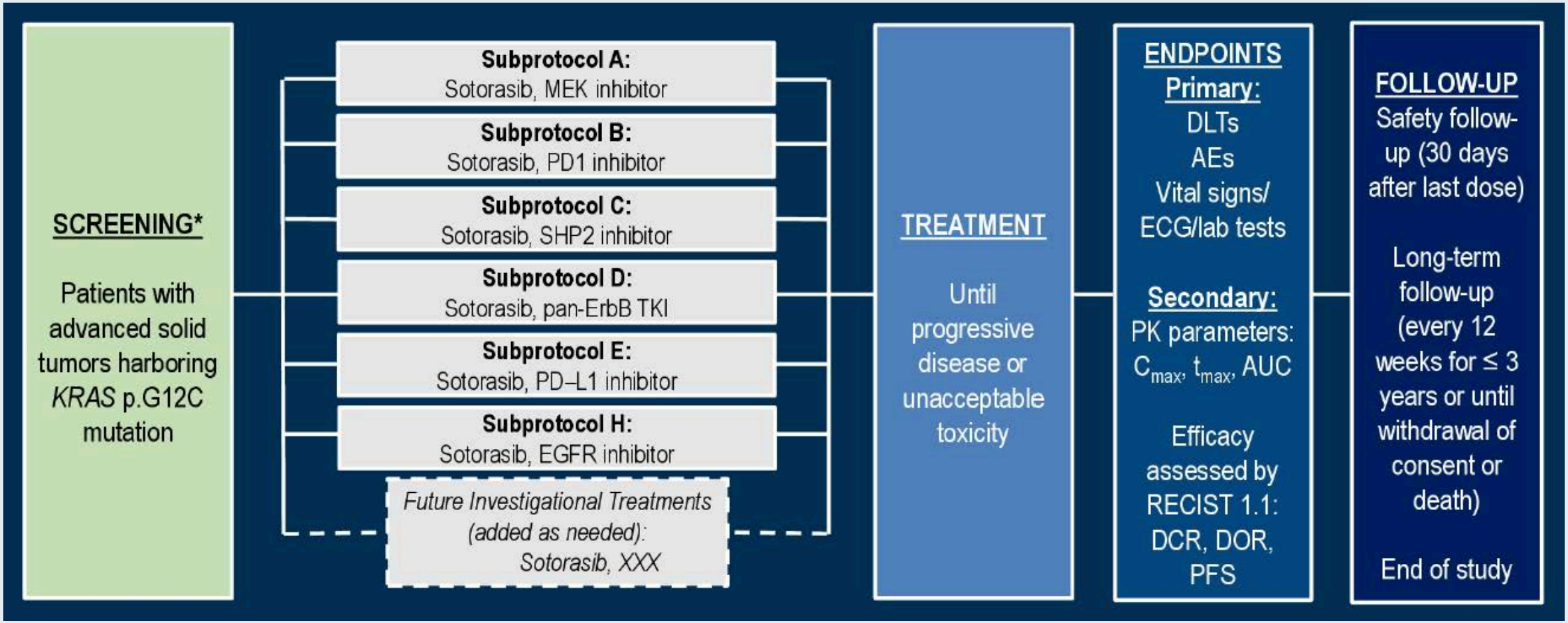
Sotorasib (AMG 510) Locks KRAS^{G12C} in the Inactive State, Inhibiting Oncogenic Signaling



Fakih M et al. ASCO 2020;Abstract TPS3661.

RTP RESEARCH TO PRACTICE

Master Study Design



Fakih M et al. ASCO 2020;Abstract TPS3661.

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

Hong DS et al.

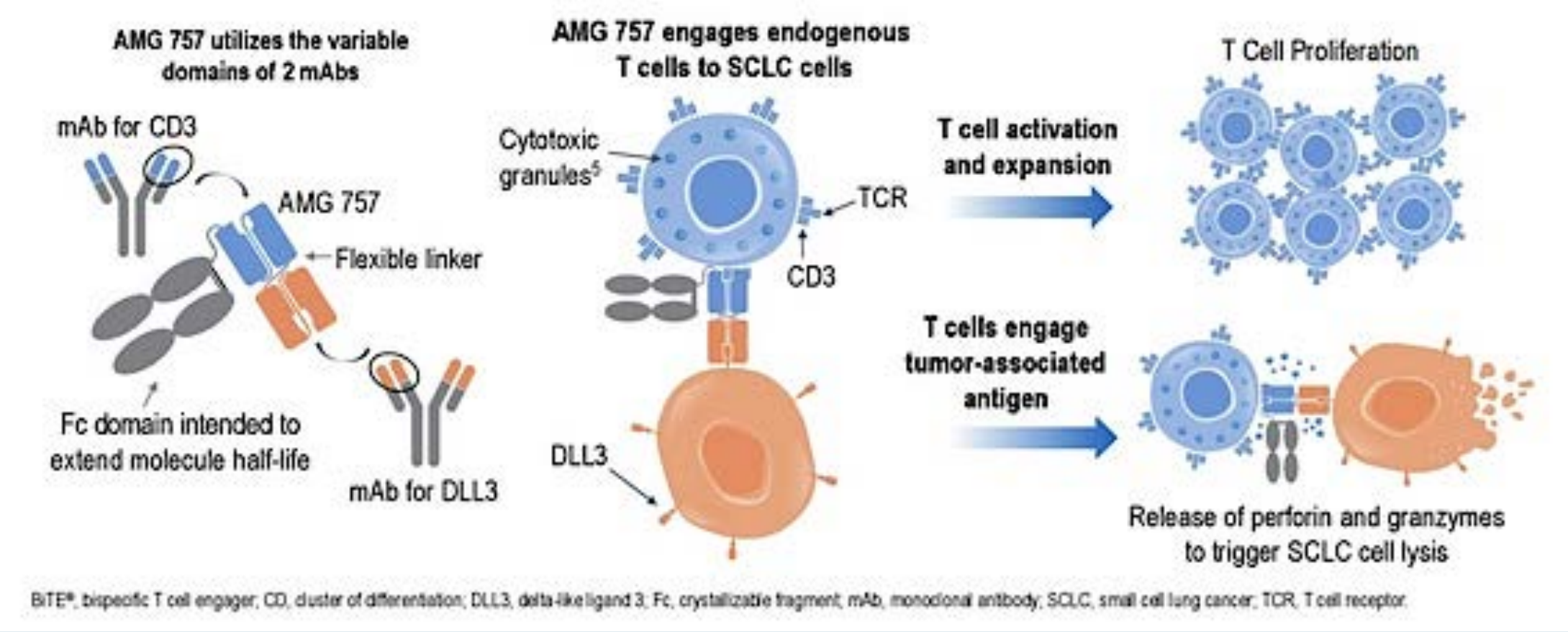
ESMO 2020;Abstract 1257O.

Phase I Study of AMG 757, a Half-Life Extended Bispecific T-Cell Engager (HLE BiTE Immune Therapy) Targeting DLL3, in Patients with Small Cell Lung Cancer (SCLC)

Owonikoko TK et al.

ASCO 2020;Abstract TPS9080.

AMG 757 is a Half-Life Extended BiTE Immune Therapy Designed to Engage and Bridge a Patient's Own T Cells to DLL3 on SCLC Cells



BiTE®, bispecific T cell engager; CD, cluster of differentiation; DLL3, delta-like ligand 3; Fc, crystallizable fragment; mAb, monoclonal antibody; SCLC, small cell lung cancer; TCR, T cell receptor.

Owonikoko TK et al. ASCO 2020;Abstract TPS9080.

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Govindan

Module 1: Cases from Dr Zafar

Module 2: Lung Cancer Journal Club with Dr Govindan

- Sex and gender: modifiers of health, disease and medicine
- Adjuvant targeted therapy or immunotherapy (SELECT, ALCHEMIST studies)
- Role of tumor mutational burden in selecting patients for first-line immunotherapy
- New approaches to therapy for small cell lung cancer
- Validation of prognostic mRNA signatures in early-stage squamous lung cancer
- Whole-genome characterization of lung adenocarcinomas lacking alterations in RTK/RAS/RAF/MAPK pathway
- Mastering the complex targeted therapy for non-small cell lung cancer
- Biomarker-driven staging
- Untangling the evolutionary roots of lung cancer
- Proteogenomic characterization reveals therapeutic vulnerabilities in lung adenocarcinoma
- Pan-cancer analysis of whole genomes
- $KRAS^{G12C}$-inhibitor sotorasib (AMG 510)
- AMG 757 HLE BiTE® immune therapy targeting DLL3

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

Module 4: Key Papers and Recent Approvals

RTP
RESEARCH
TO PRACTICE

Which first-line treatment regimen would you recommend for an 65-year-old patient with metastatic nonsquamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 10%?

 RAMASWAMY GOVINDAN, MD	Pembro/carbo/pem
 JOHN V HEYMACH, MD, PHD	Pembro/carbo/pem
 LEORA HORN, MD, MSC	Pembro/carbo/pem
 COREY J LANGER, MD	Pembro/carbo/pem
 BENJAMIN LEVY, MD	Pembro/carbo/pem
 PROFESSOR TONY SK MOK, MD	Pembro/carbo/pem OR Atezo/carbo/pac + bev
 JOEL W NEAL, MD, PHD	Pembro/carbo/pem
 PAUL K PAIK, MD	Pembro/carbo/pem
 PROFESSOR SOLANGE PETERS, MD, PHD	Ipi/nivo + carbo/pem
 NATHAN A PENNELL, MD, PHD	Pembro/carbo/pem
 DAVID R SPIGEL, MD	Pembro/carbo/pem

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

RTP RESEARCH TO PRACTICE

Which first-line treatment regimen would you recommend for an 80-year-old patient with metastatic nonsquamous lung cancer, no identified targetable mutations and a PD-L1 TPS of 10%?

 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
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro/carbo/pem
 NATHAN A PENNELL, MD, PHD	Pembro/carbo/pem*
 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%?

 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
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro
 NATHAN A PENNELL, 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%?

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

 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
 PROFESSOR SOLANGE PETERS, MD, PHD	Ipi/nivo + carbo/pac
 NATHAN A PENNELL, MD, PHD	Pembro/carbo/*nab*-P
 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%?

 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
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro/carbo/pac
 NATHAN A PENNELL, MD, PHD	Pembro/carbo/pac
 DAVID R SPIGEL, MD	Pembro/carbo/*nab*-P

RTP RESEARCH TO PRACTICE

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

 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
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro
 NATHAN A PENNELL, 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%?

 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
 PROFESSOR SOLANGE PETERS, MD, PHD	Pembro
 NATHAN A PENNELL, MD, PHD	Pembro
 DAVID R SPIGEL, MD	Pembro

RTP RESEARCH TO PRACTICE

How long would you continue treatment for a patient with metastatic NSCLC who is receiving an anti-PD-1/PD-L1 antibody and at first evaluation is tolerating it well and has a complete clinical response?

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

RTP RESEARCH TO PRACTICE

How long would you continue treatment for a patient with metastatic NSCLC who is receiving an anti-PD-1/PD-L1 antibody and at first evaluation is tolerating it well and has a partial clinical response?

 RAMASWAMY GOVINDAN, MD	Indefinitely or until PD/toxicity
 JOHN V HEYMACH, MD, PHD	Indefinitely or until PD/toxicity
 LEORA HORN, MD, MSC	2 years
 COREY J LANGER, MD	2 years (min)
 BENJAMIN LEVY, MD	Indefinitely or until PD/toxicity
 PROFESSOR TONY SK MOK, MD	2 years
 JOEL W NEAL, MD, PHD	2 years
 PAUL K PAIK, MD	Indefinitely or until PD/toxicity
 PROFESSOR SOLANGE PETERS, MD, PHD	Indefinitely or until PD/toxicity
 NATHAN A PENNELL, MD, PHD	2 years
 DAVID R SPIGEL, MD	Indefinitely or until PD/toxicity

RTP RESEARCH TO PRACTICE

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

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

Regulatory and reimbursement issues aside, what would be your preferred first-line treatment regimen for a 65-year-old patient with extensive-stage SCLC?

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

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would be your preferred first-line treatment regimen for an 80-year-old patient with extensive-stage SCLC?

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

RTP RESEARCH TO PRACTICE

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

 RAMASWAMY GOVINDAN, MD	Carboplatin/etoposide
 JOHN V HEYMACH, MD, PHD	Carboplatin/etoposide
 LEORA HORN, MD, MSC	Carboplatin/etoposide
 COREY J LANGER, MD	Carboplatin/etoposide + atezolizumab or durvalumab
 BENJAMIN LEVY, MD	Carboplatin/etoposide
 PROFESSOR TONY SK MOK, MD	Carboplatin/etoposide
 JOEL W NEAL, MD, PHD	Carboplatin/etoposide + atezolizumab or durvalumab
 PAUL K PAIK, MD	Carboplatin/etoposide
 PROFESSOR SOLANGE PETERS, 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?

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

SIADH = syndrome of inappropriate antidiuretic hormone secretion

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Govindan

Module 1: Cases from Dr Zafar

Module 2: Lung Cancer Journal Club with Dr Govindan

- Sex and gender: modifiers of health, disease and medicine
- Adjuvant targeted therapy or immunotherapy (SELECT, ALCHEMIST studies)
- Role of tumor mutational burden in selecting patients for first-line immunotherapy
- New approaches to therapy for small cell lung cancer
- Validation of prognostic mRNA signatures in early-stage squamous lung cancer
- Whole-genome characterization of lung adenocarcinomas lacking alterations in RTK/RAS/RAF/MAPK pathway
- Mastering the complex targeted therapy for non-small cell lung cancer
- Biomarker-driven staging
- Untangling the evolutionary roots of lung cancer
- Proteogenomic characterization reveals therapeutic vulnerabilities in lung adenocarcinoma
- Pan-cancer analysis of whole genomes
- $KRAS^{G12C}$-inhibitor sotorasib (AMG 510)
- AMG 757 HLE BiTE® immune therapy targeting DLL3

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

Module 4: Key Papers and Recent Approvals

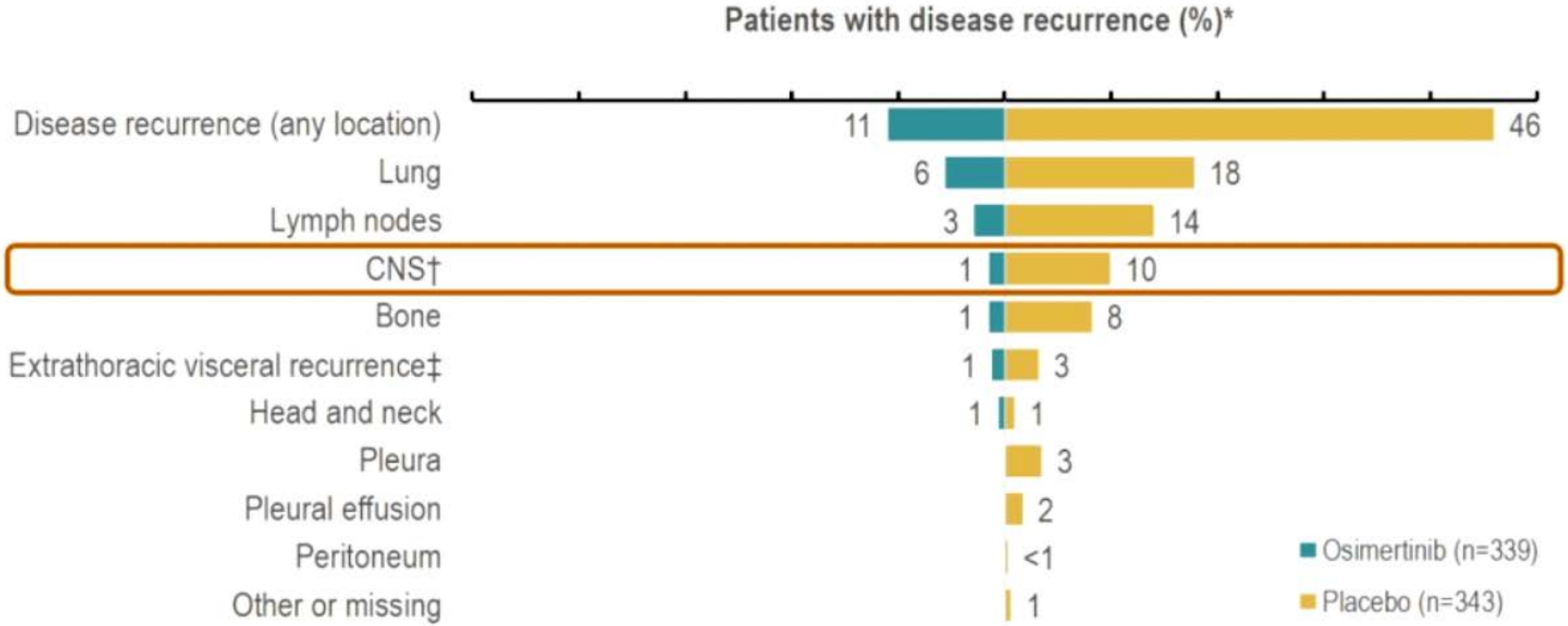
RTP RESEARCH TO PRACTICE

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

Tsuboi M et al.

ESMO 2020;Abstract LBA1.

ADAURA: Sites of Disease Recurrence



Tsuboi M et al. ESMO 2020;Abstract LBA1.

RTP RESEARCH TO PRACTICE

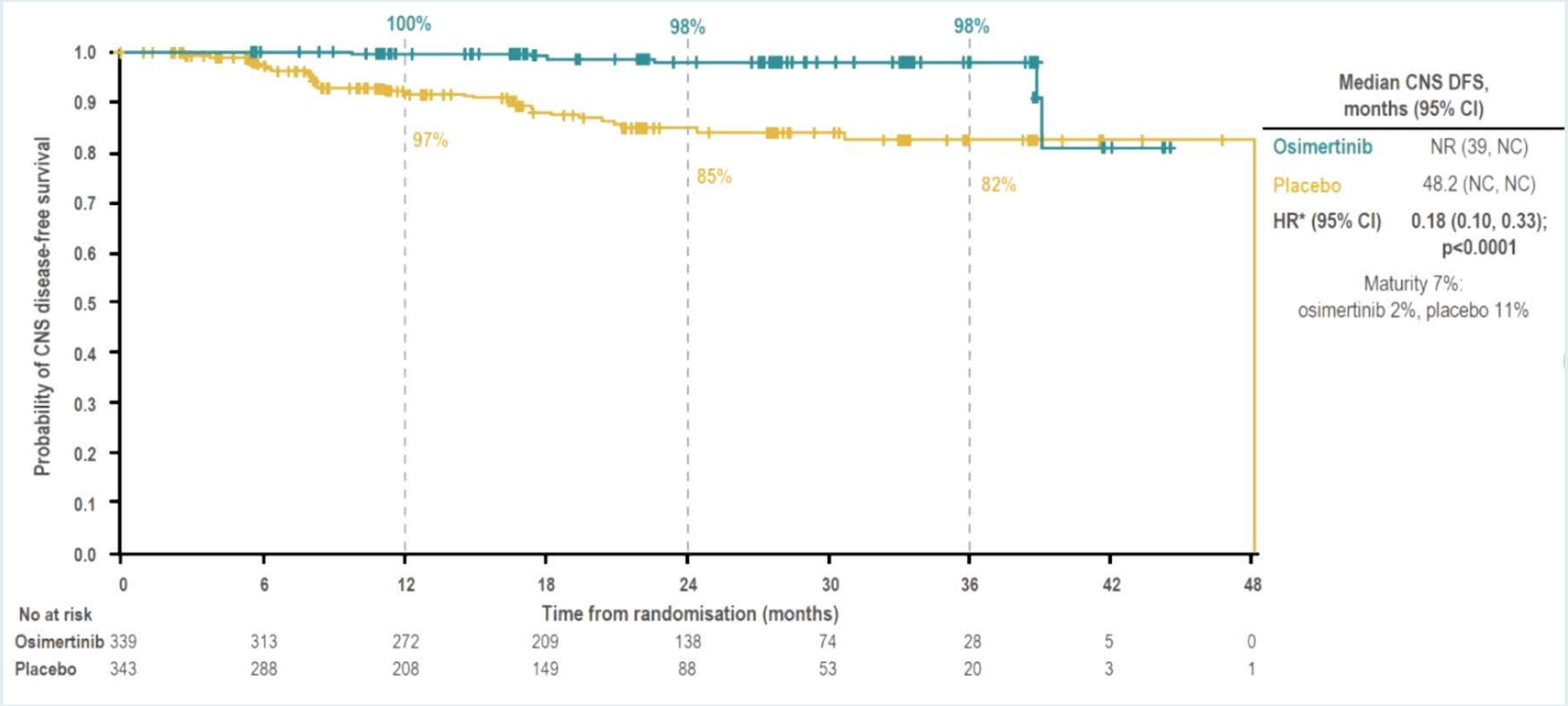
ADAURA: CNS DFS Events

- Overall, 45 patients (osimertinib n=6, placebo n=39) had CNS DFS events

	Overall population	
Patients, n (%)	**Osimertinib n=339**	**Placebo n=343**
CNS DFS events:	6 (2%)	39 (11%)
CNS recurrence	4 (1%)	33 (10%)
Death	2 (1%)	6 (2%)

Tsuboi M et al. ESMO 2020;Abstract LBA1.

ADAURA: CNS DFS in Overall Population



Tsuboi M et al. ESMO 2020;Abstract LBA1.

RTP RESEARCH TO PRACTICE

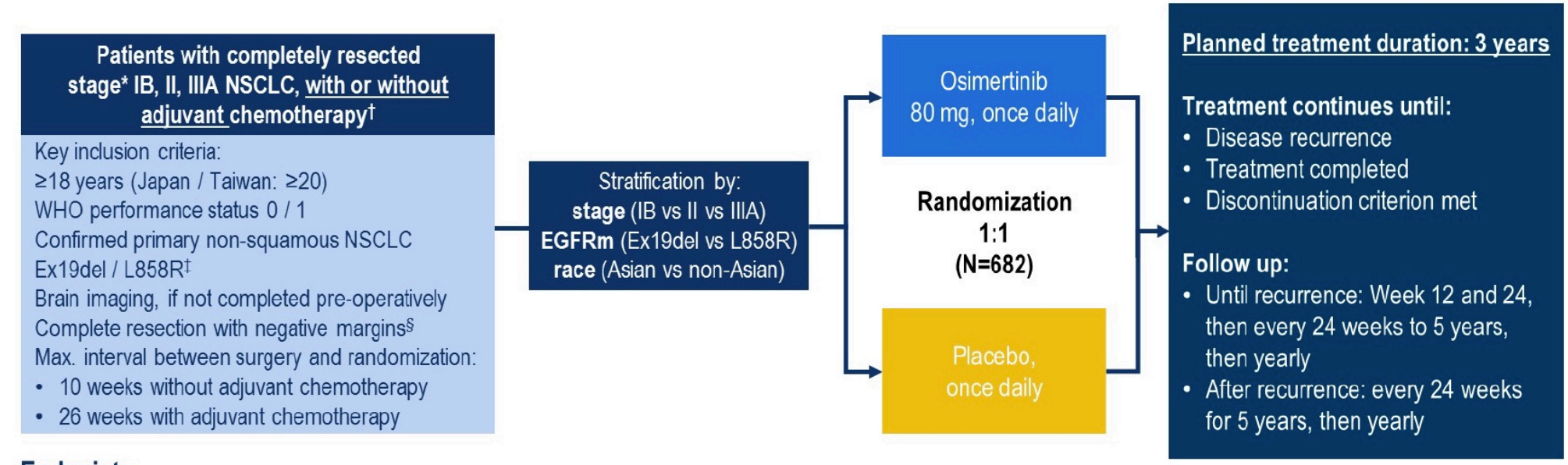
Osimertinib as Adjuvant Therapy in Patients (pts) with Stage IB–IIIA EGFR Mutation Positive (EGFRm) NSCLC After Complete Tumor Resection: ADAURA

Herbst RS et al.
ASCO 2020;Abstract LBA5.

Discussion of LBA5

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

ADAURA Phase III Trial Schema



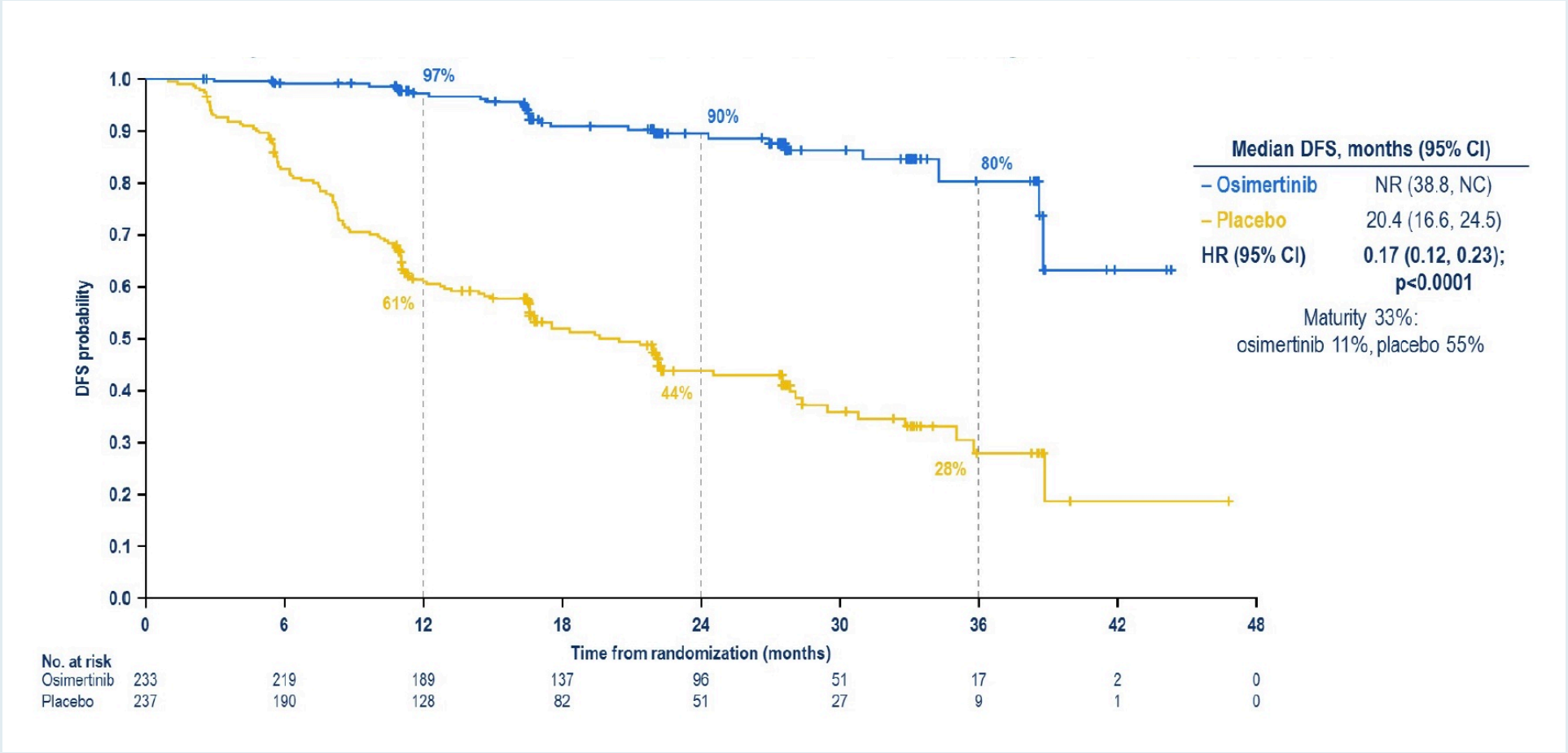
Endpoints

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

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

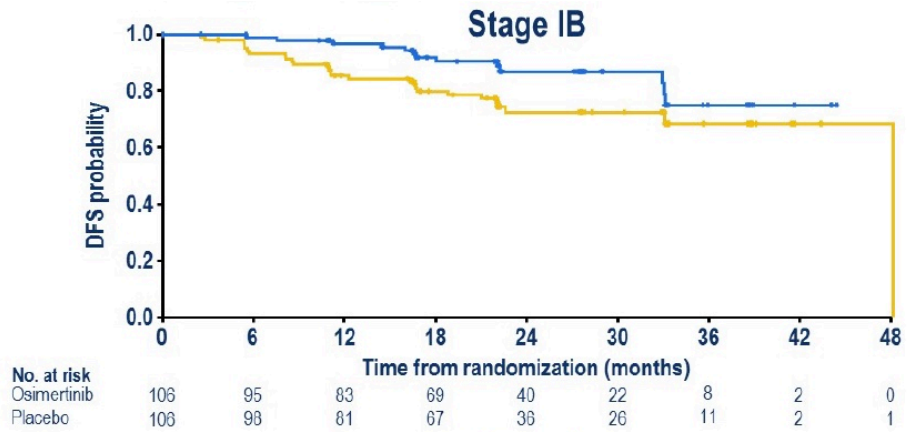
Herbst RS et al. ASCO 2020;Abstract LBA5.

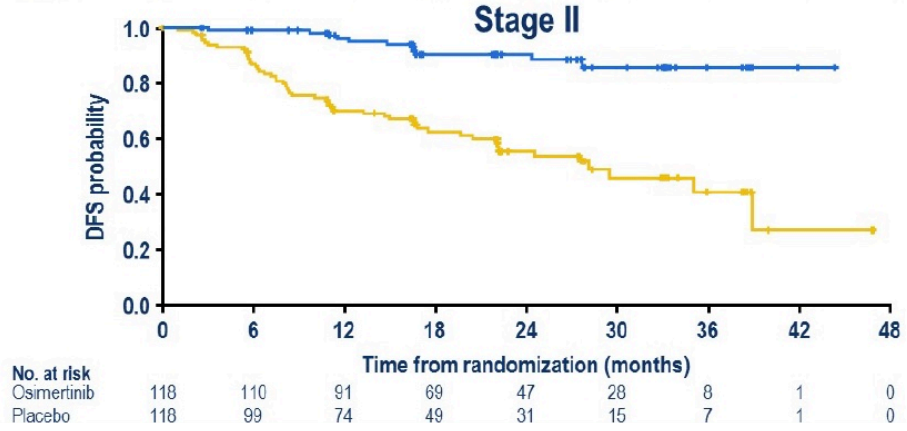
ADAURA Primary Endpoint: Inv-Assessed DFS (Stage II/IIIA)



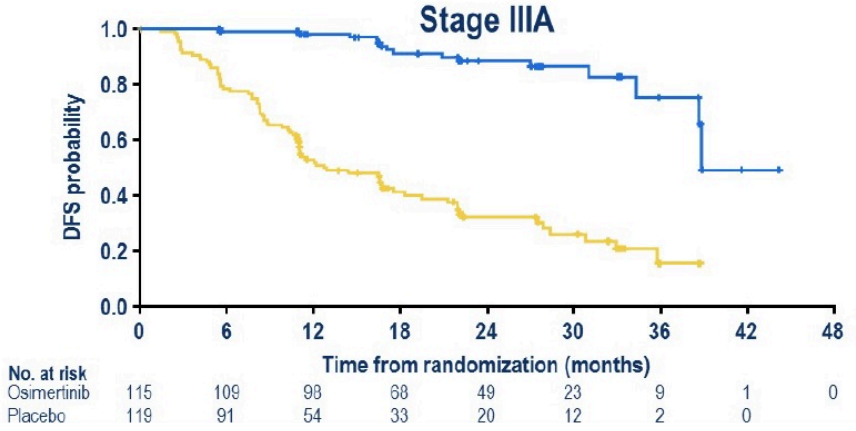
Herbst RS et al. ASCO 2020;Abstract LBA5.

ADAURA: DFS by Stage



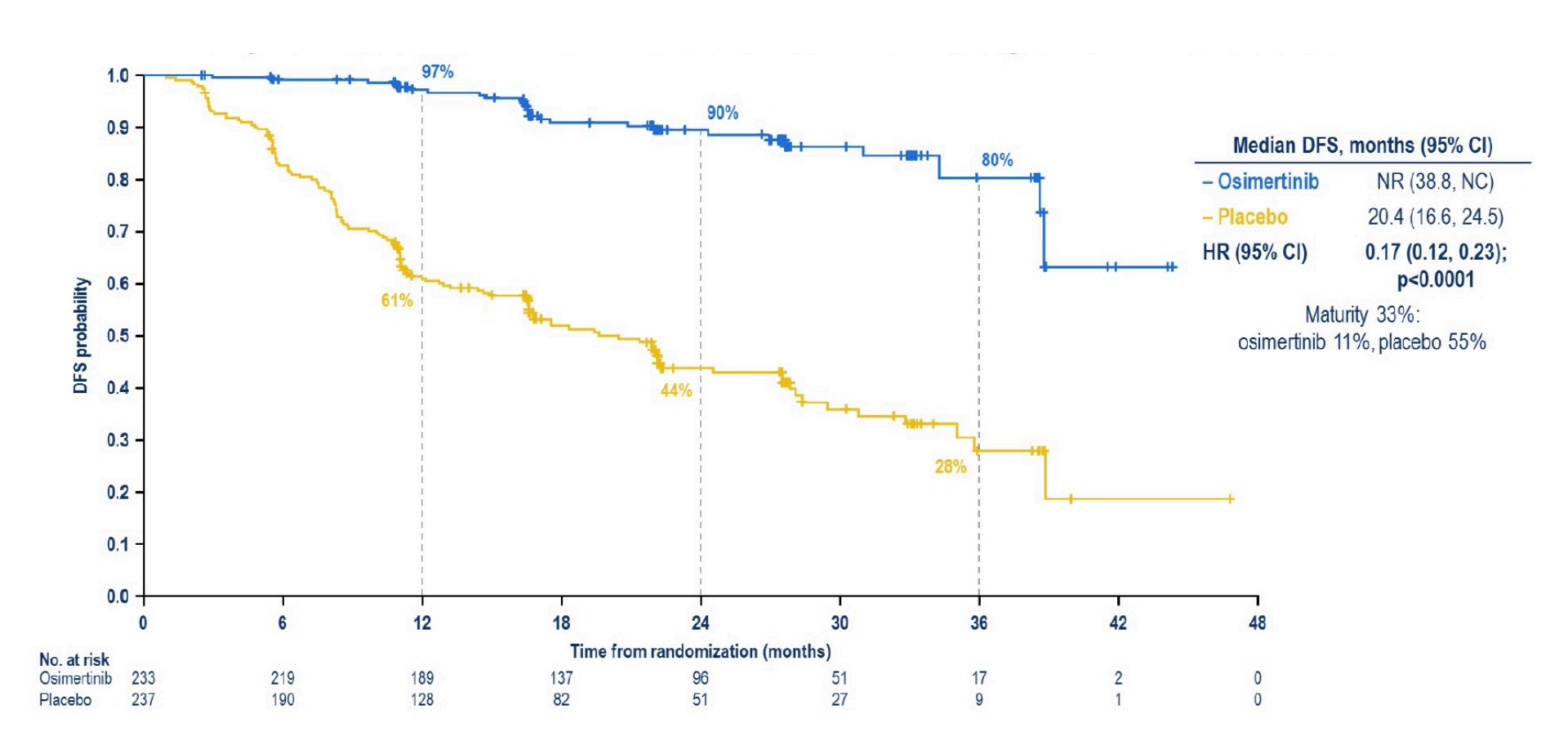


	Stage IB	Stage II	Stage IIIA
2 year DFS rate, % (95% CI)			
– Osimertinib	87 (77, 93)	91 (82, 95)	88 (79, 94)
– Placebo	73 (62, 81)	56 (45, 65)	32 (23, 42)
Overall HR (95% CI)	0.50 (0.25, 0.96)	0.17 (0.08, 0.31)	0.12 (0.07, 0.20)



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.

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)."

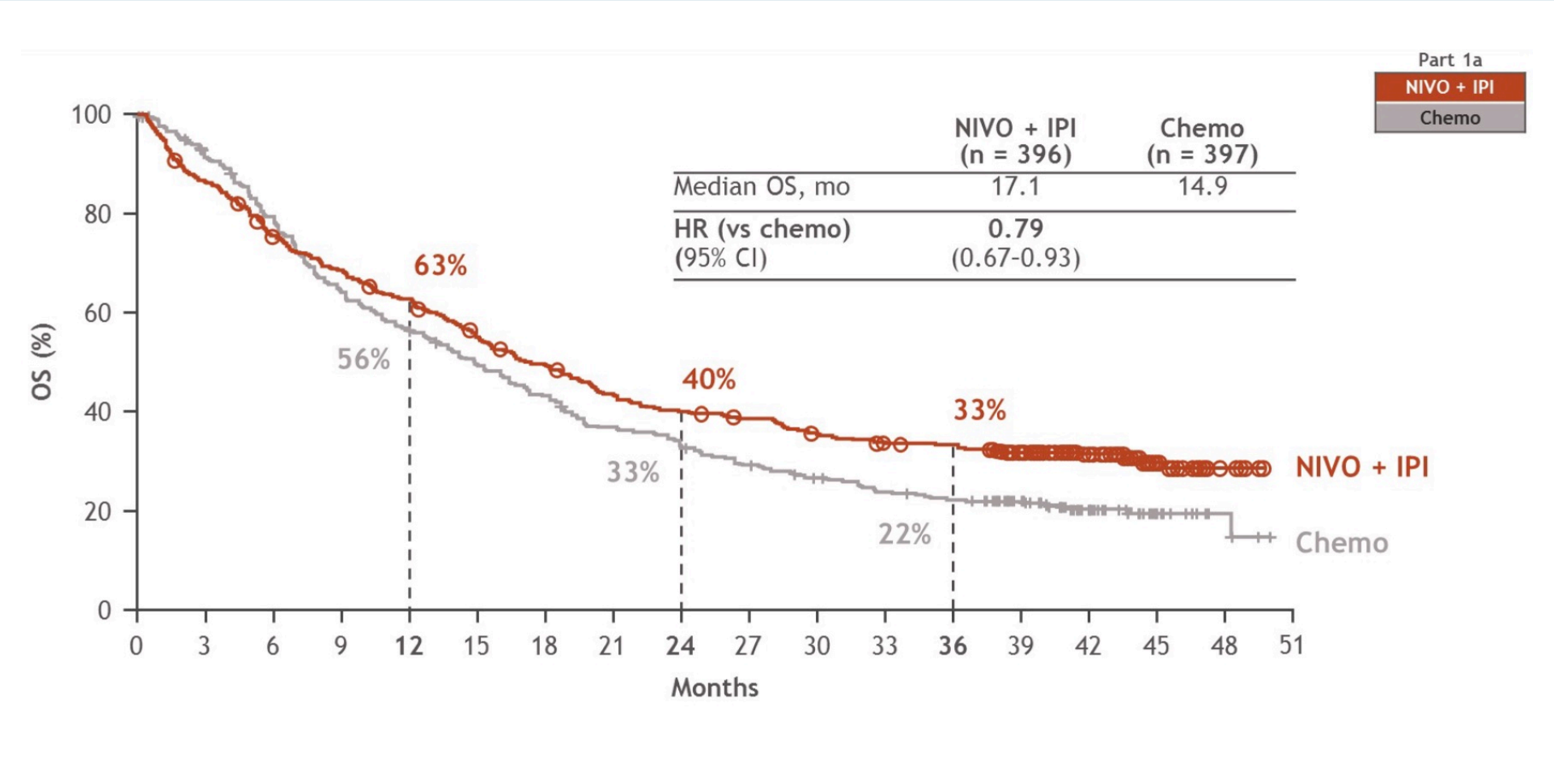
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-nivolumab-plus-ipilimumab-first-line-mnsclc-pd-l1-tumor-expression-1

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.

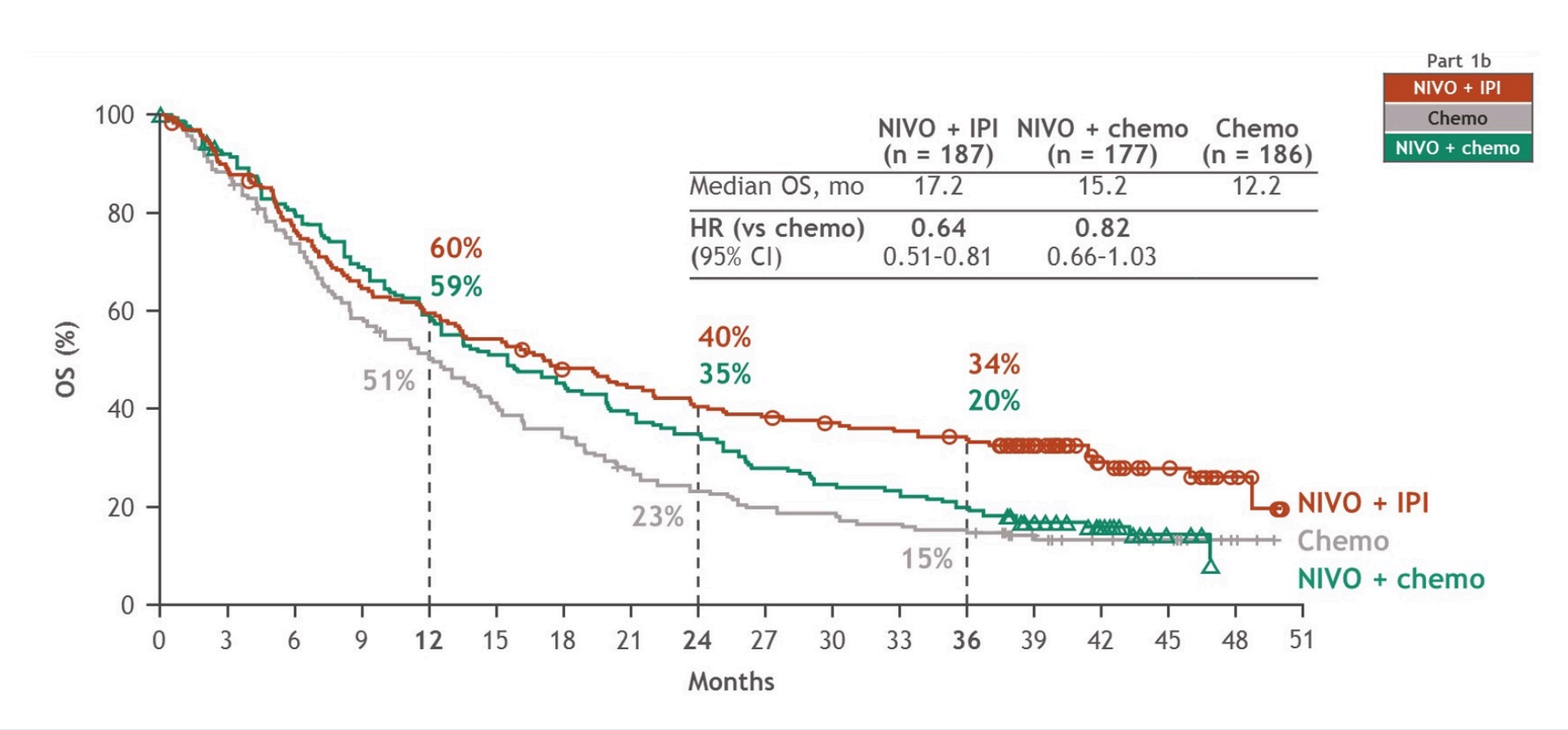
ASCO 2020;Abstract 9500.

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.

RTP RESEARCH TO PRACTICE

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)."

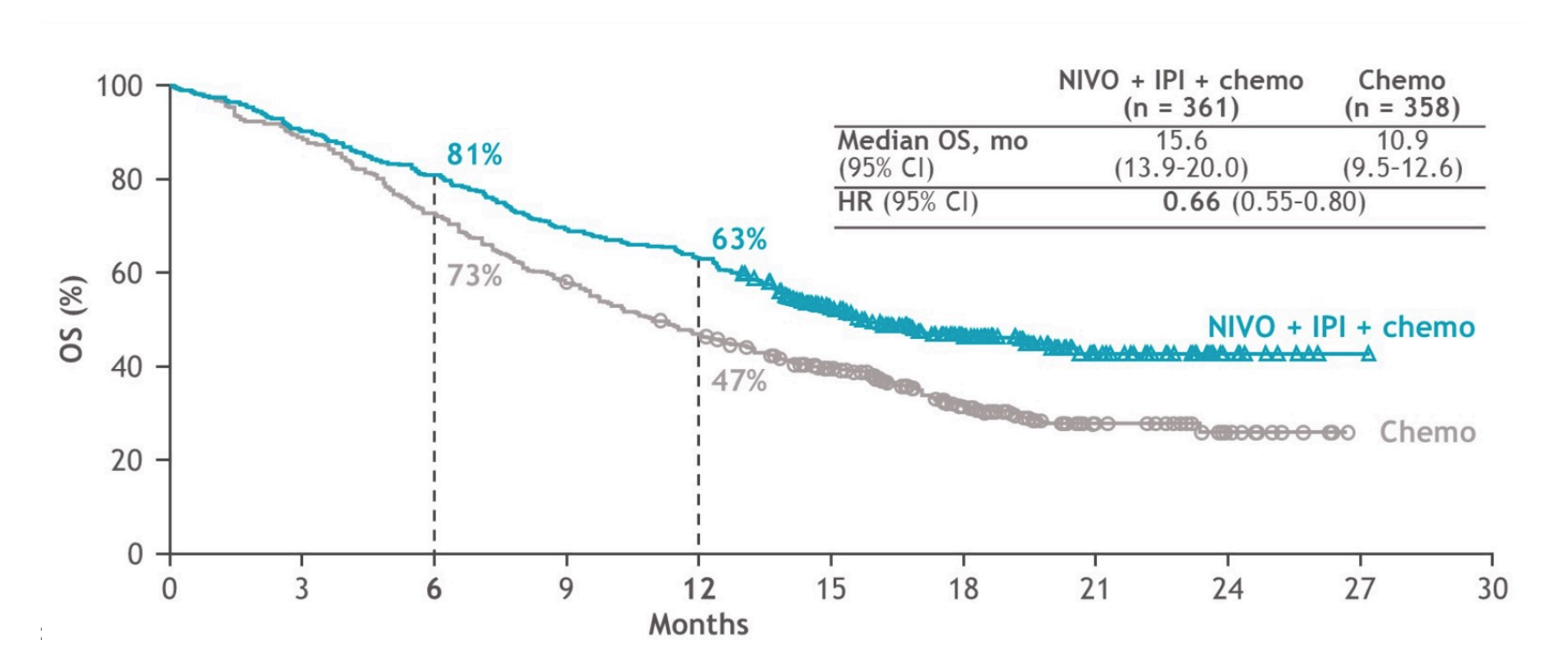
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-nivolumab-plus-ipilimumab-and-chemotherapy-first-line-treatment-metastatic-nsclc

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



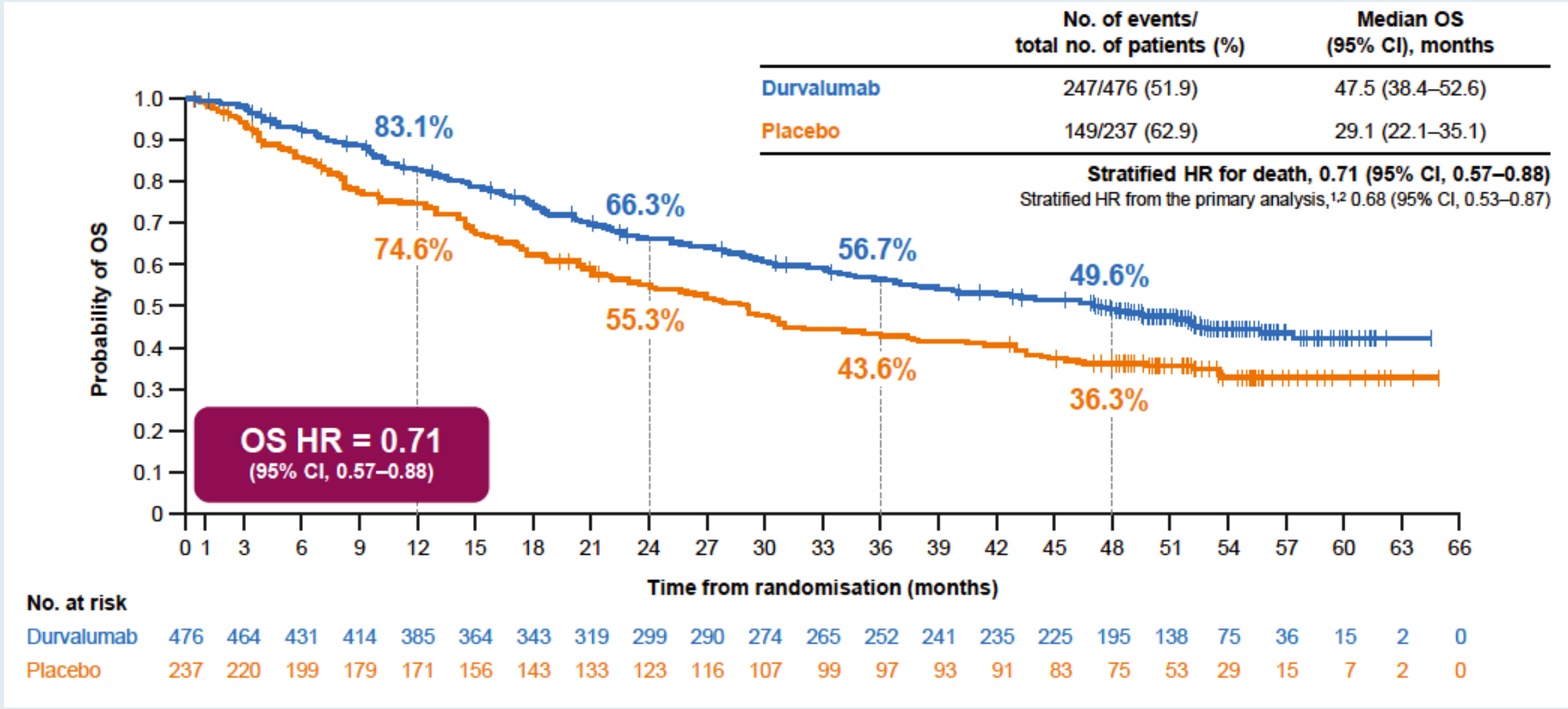
Reck M et al. ASCO 2020;Abstract 9501.

Durvalumab After Chemoradiotherapy in Stage III NSCLC: 4-Year Survival Update from the Phase III PACIFIC Trial

Faivre-Finn C et al.

ESMO 2020;Abstract LBA49.

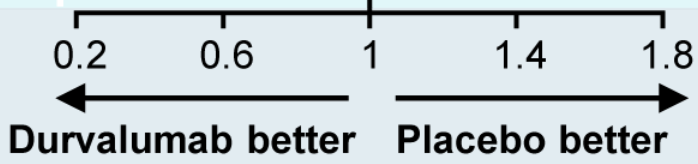
PACIFIC: 4-Year Overall Survival – Intent-To-Treat Population

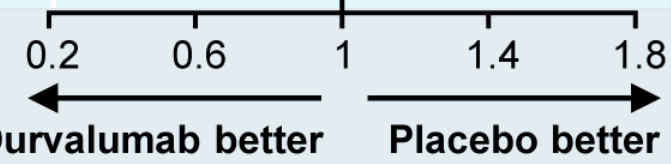


Faivre-Finn C et al. ESMO 2020;Abstract LBA49.

PACIFIC: Updated Outcomes by EGFR Status

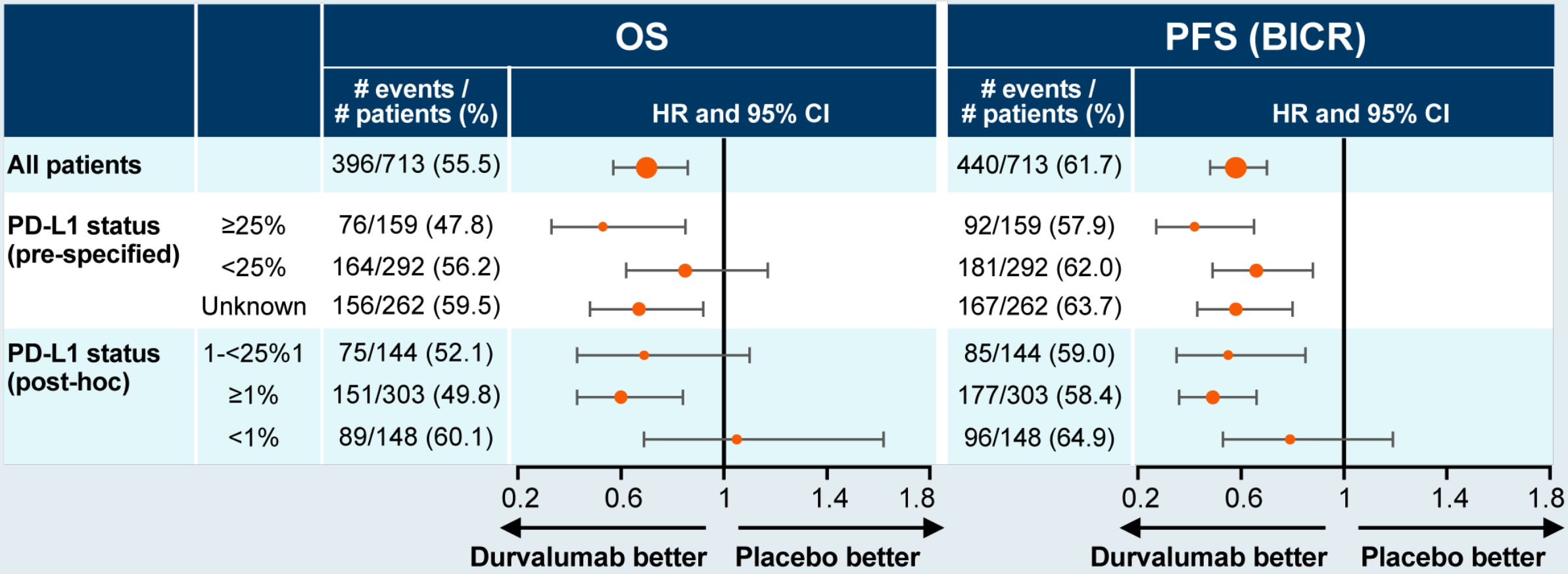
		OS		PFS (BICR)	
		# events / # patients (%)	HR and 95% CI	# events / # patients (%)	HR and 95% CI
***EGFR* mutation**	Positive	24/43 (55.8)		32/43 (74.4)	
	Negative	261/482 (54.1)		290/482 (60.2)	
	Unknown	111/188 (59.0)		118/188 (62.8)	





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)
  - PDL1 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.

Characteristics of the First 615 Patients Enrolled in Pacific R: A Study of the First Real-World Data on Unresectable Stage III NSCLC Patients Treated with Durvalumab After Chemoradiotherapy

Girard N et al.

ESMO 2020;Abstract 1242P.

Pacific R: Biomarker Status

Biomarker evaluated	Tested, n (%)	Positive, n (%)	Inconclusive, n (%)
PD-L1 expression	442 (71.9)	324 (73.3)	27 (6.1)
EGFR mutation	262 (42.8)	19 (7.3)	7 (2.7)
ALK translocation	256 (41.9)	6 (2.3)	12 (4.7)
BRAF mutation	164 (26.8)	14 (8.5)	5 (3.0)
KRAS mutation	180 (29.5)	44 (24.4)	6 (3.3)

Girard N et al. ESMO 2020;Abstract 1242P.

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

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

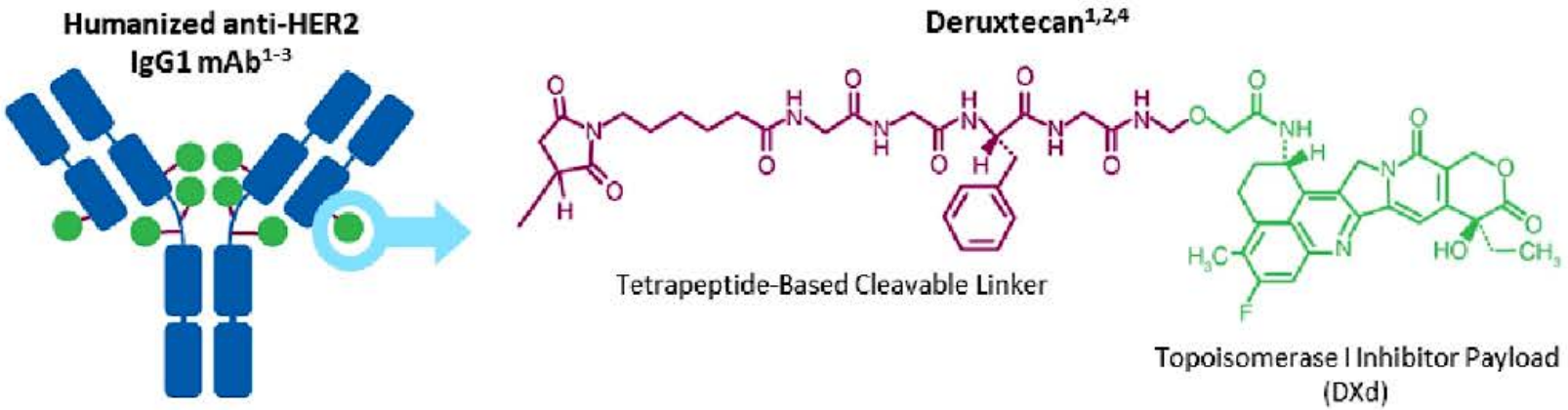
Smit EF et al.

ASCO 2020;Abstract 9504.

Antibody-Drug Conjugate
Trastuzumab Deruxtecan

T-DXd is an ADC with 3 components:

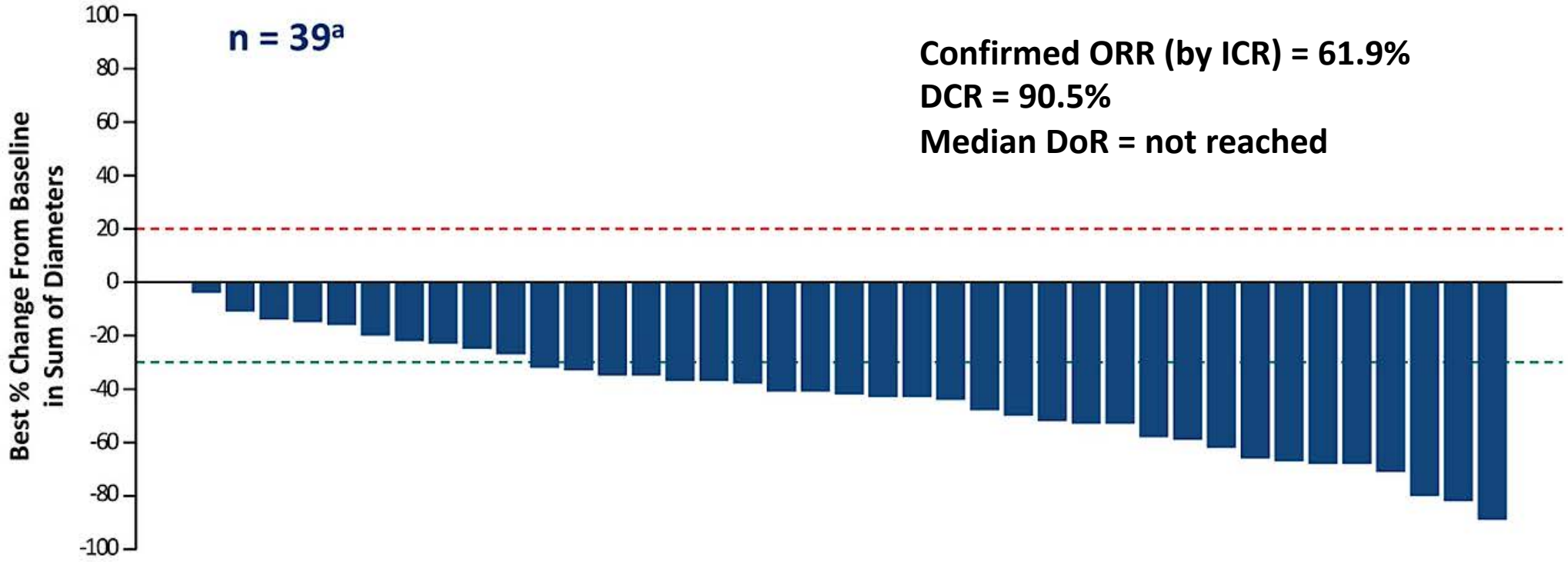
- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



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

Smit EF et al. ASCO 2020;Abstract 9504.

DESTINY-Lung01: Efficacy

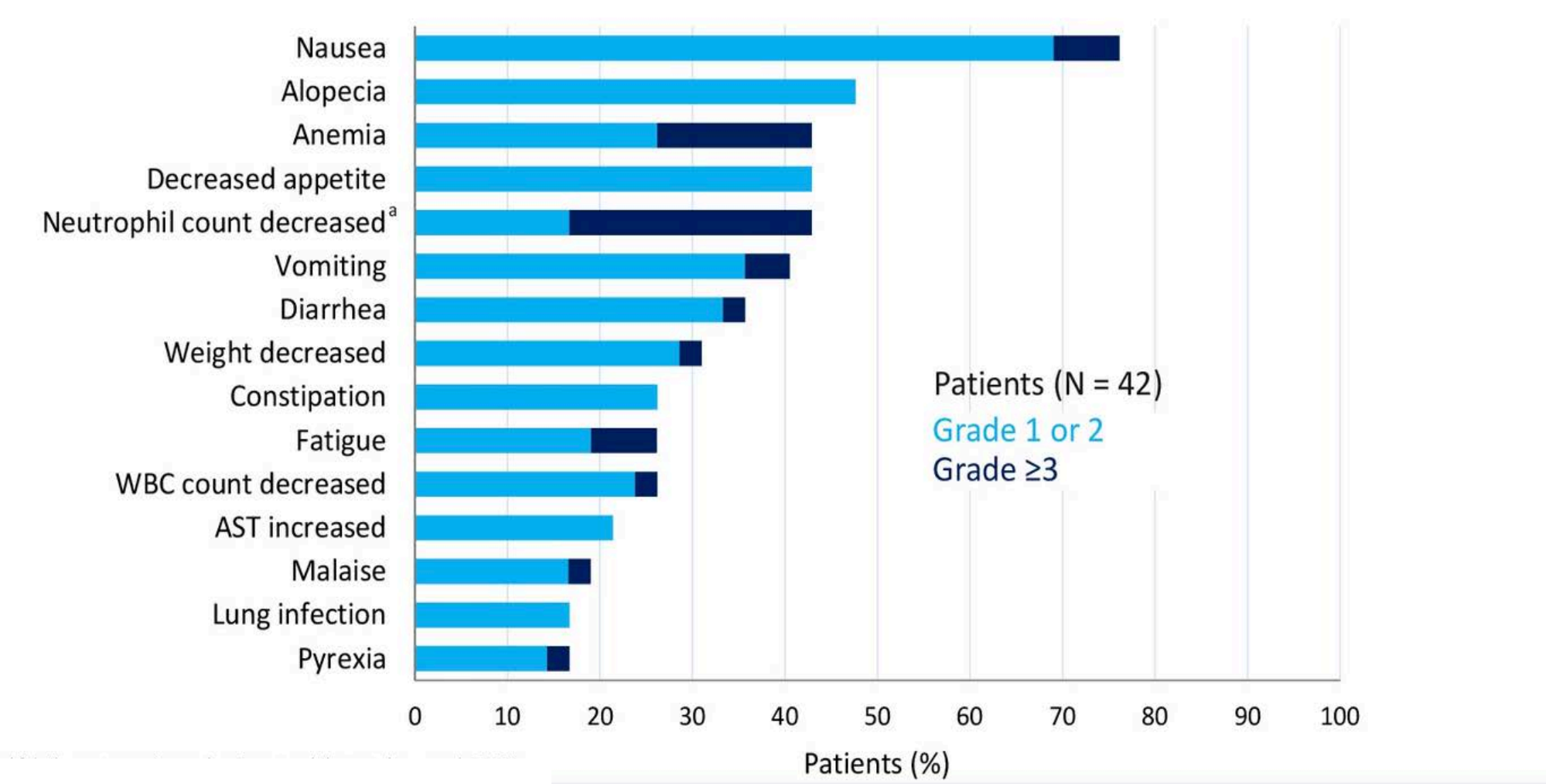


Based on independent central review. Baseline is last measurement taken before enrollment. Shown is best (minimum) percent change from baseline in the sum of diameters for all target lesions.
[a] One patient was missing a baseline assessment and 2 additional patients were missing post-baseline assessments.

- Median PFS = 14.0 months

Smit EF et al. ASCO 2020;Abstract 9504.

DESTINY-Lung01: Treatment-Emergent AEs



Smit EF et al. ASCO 2020;Abstract 9504.

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

	All Patients (N = 42)					
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial lung disease	0[a]	5 (11.9)	0	0	0	5 (11.9)

- Median time to onset of investigator-reported ILD was at 86 days (range, 41-255 days)
- 4 patients had drug withdrawn and 1 had drug interrupted
- All patients received steroid treatment
- 2 patients recovered, 1 recovered with sequelae, 1 was recovering, and 1 had not recovered by data-cutoff
- No grade 5 ILD was observed in this cohort

Smit EF et al. ASCO 2020;Abstract 9504.

Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Hematologic Cancers

A 4-Part Friday Satellite Symposia Live Webinar Series Preceding the 62nd ASH Annual Meeting

Friday, December 4, 2020

Multiple Myeloma
8:30 AM – 10:00 AM Pacific Time
(11:30 AM – 1:00 PM ET)

Chronic Lymphocytic Leukemia
12:00 PM – 1:30 PM Pacific Time
(3:00 PM – 4:30 PM ET)

Acute Myeloid Leukemia
3:00 PM – 4:30 PM Pacific Time
(6:00 PM – 7:30 PM ET)

Hodgkin and Non-Hodgkin Lymphoma
7:00 PM – 8:30 PM Pacific Time
(10:00 PM – 11:30 PM ET)

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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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