

Meet The Professor

Current and Future Management of Patients with NSCLC and an Actionable Target Beyond EGFR

D Ross Camidge, MD, PhD

Professor of Medicine/Oncology

Joyce Zeff Chair in Lung Cancer Research

University of Colorado, Anschutz Medical Campus

Denver, Colorado

Commercial Support

This activity is supported by educational grants from Amgen Inc, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Elevation Oncology Inc, Genentech, a member of the Roche Group, Novartis, and Turning Point Therapeutics Inc.

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 companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Mersana Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncoceptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

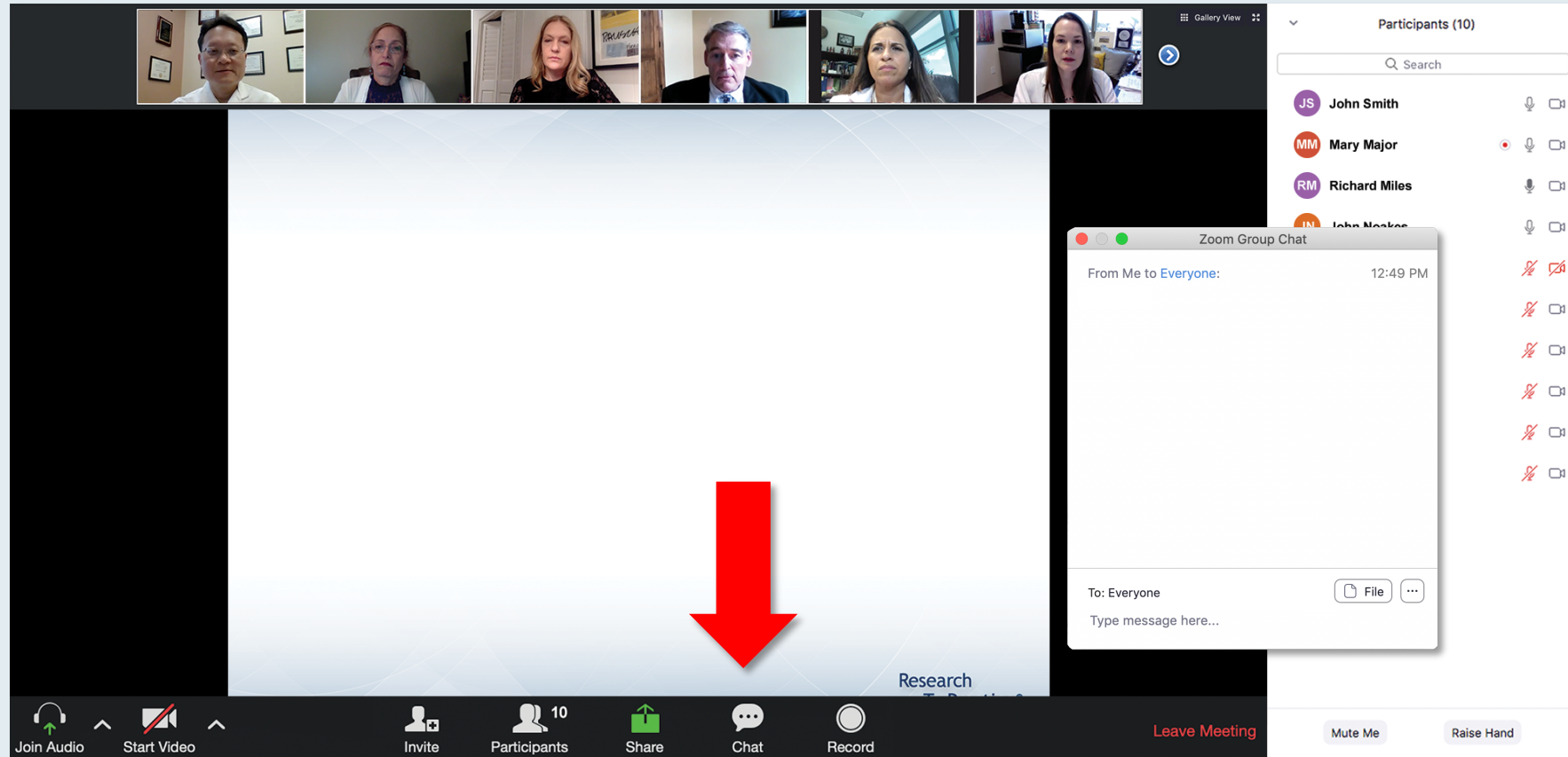
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Dr Camidge — Disclosures

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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.

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

The screenshot shows a Zoom meeting interface. At the top, there are video thumbnails for participants: RTP Coordinat..., Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. A 'Recording...' indicator is visible. The main content is a slide titled 'Meet The Professor Program Participating Faculty' with six faculty members listed:

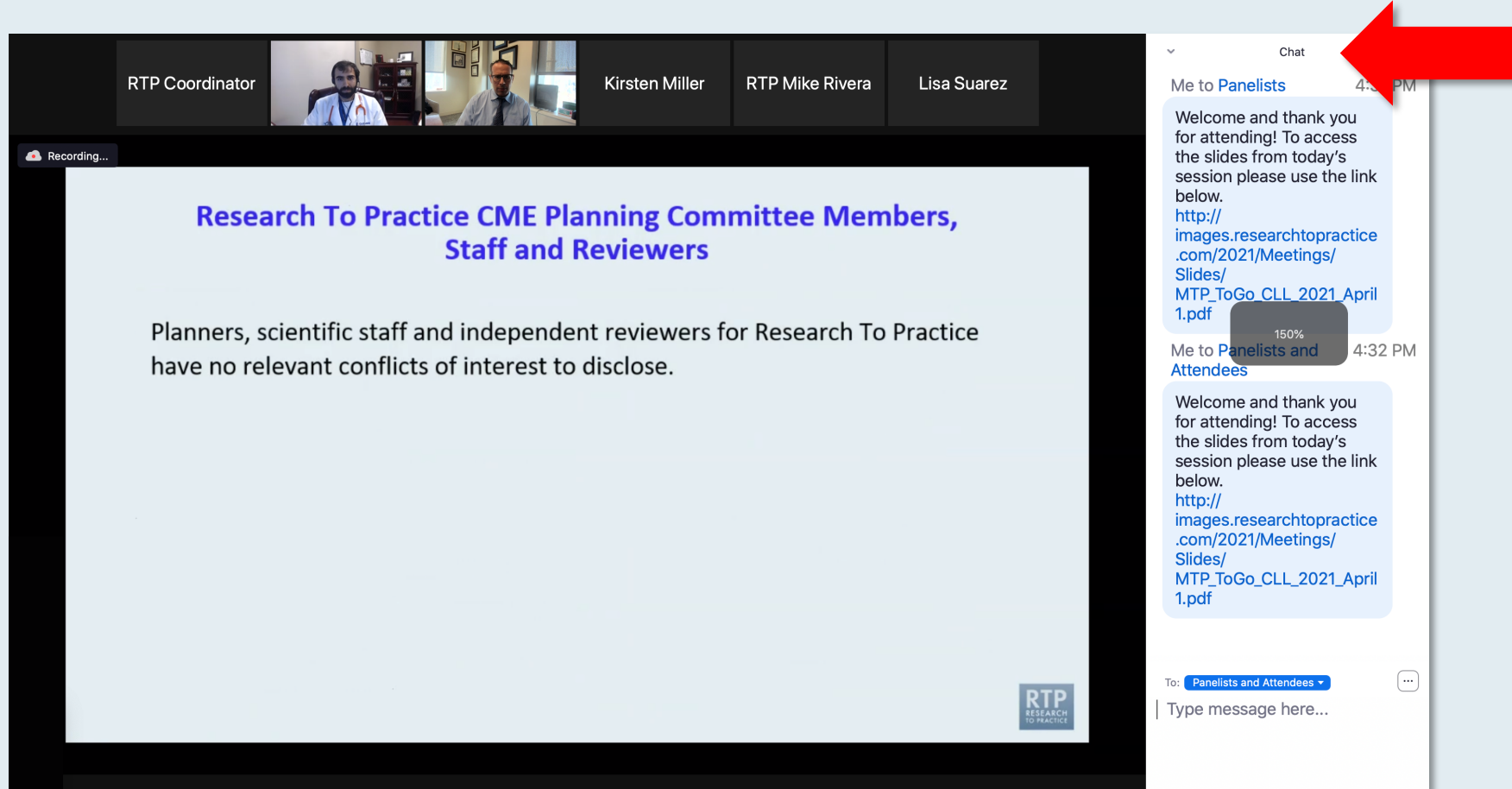
- Nancy L Bartlett, MD**
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- Jonathan W Friedberg, MD, MMSc**
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Director, James P Wilmot Cancer Institute
University of Rochester
Rochester, New York
- Carla Casulo, MD**
Associate Professor of Medicine
Division of Hematology/Oncology
Director, Hematology/Oncology Fellowship Program
University of Rochester
Wilmot Cancer Institute
Rochester, New York
- Brian T Hill, MD, PhD**
Director, Lymphoid Malignancy Program
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio
- Christopher R Flowers, MD, MS**
Chair, Professor
Department of Lymphoma/Myeloma
The University of Texas MD Anderson Cancer Center
Houston, Texas
- Brad S Kahl, MD**
Professor of Medicine
Washington University School of Medicine
Director, Lymphoma Program
Siteman Cancer Center
St Louis, Missouri

The chat window on the right shows two messages from 'Me to Panelists' and 'Me to Panelists and Attendees' at 4:31 PM and 4:32 PM respectively. Each message contains a welcome message and a link to a PDF: http://images.researchtopractice.com/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April1.pdf. A red arrow points to a white line above the chat submission box, indicating how to expand it.

Drag the white line above the submission box up to create more space for your message.

Familiarizing Yourself with the Zoom Interface

Increase chat font size



The screenshot displays a Zoom meeting interface. At the top, there are video thumbnails for participants: RTP Coordinator, Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. The main content area shows a slide titled "Research To Practice CME Planning Committee Members, Staff and Reviewers" with the text: "Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose." A "Recording..." indicator is visible in the top left of the slide area. On the right, the chat window is open, showing two messages from "Me to Panelists" and "Me to Panelists and Attendees". A red arrow points to the font size adjustment icon (a plus sign) in the chat window's header area. The chat messages include a welcome message and a link to a PDF document: http://images.researchtopractice.com/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April_1.pdf. The chat window also shows a "150%" font size indicator and a "Type message here..." input field.

**Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.**

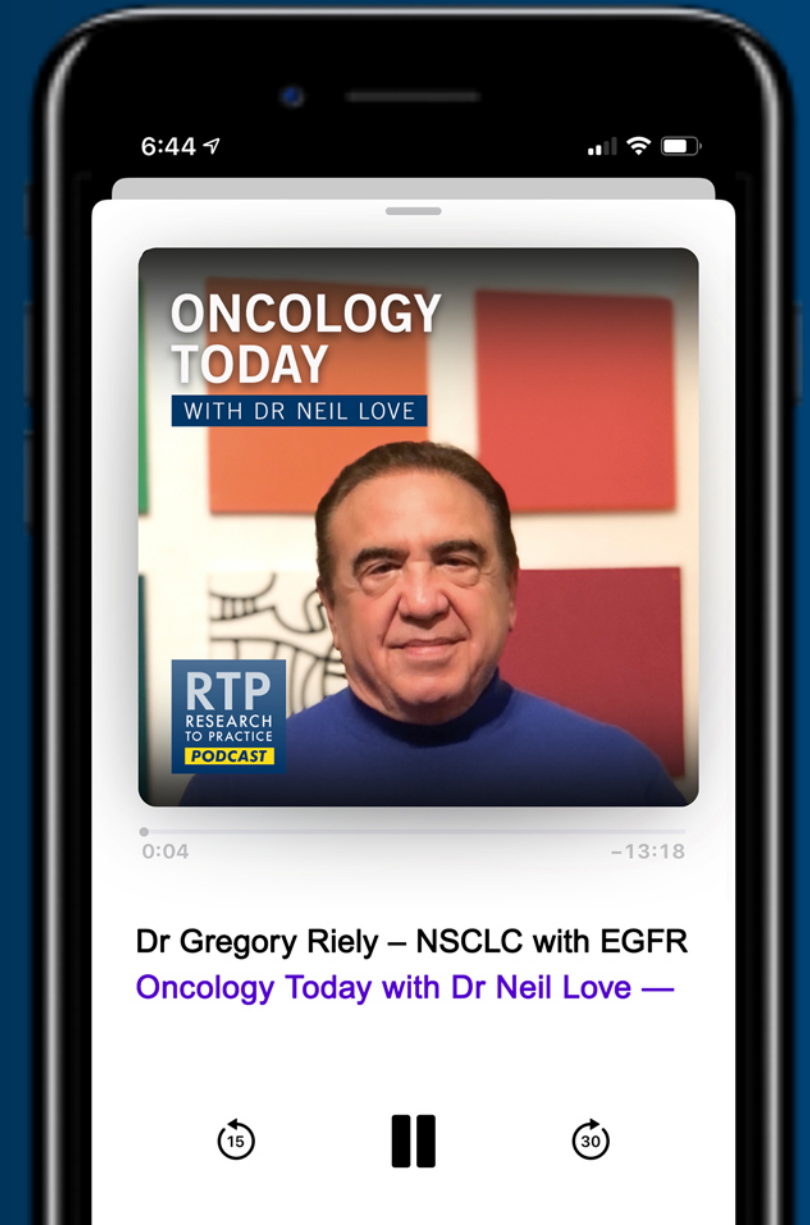
ONCOLOGY TODAY

WITH DR NEIL LOVE

NSCLC with EGFR Exon 20 Insertion Mutations



DR GREGORY RIELY
MEMORIAL SLOAN KETTERING CANCER CENTER



What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

A Complimentary NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Prostate Cancer

Thursday, April 28, 2022

6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty

Kathy D Burns, RN, MSN, AGACNP-BC, OCN

Robert Dreicer, MD, MS

Sandy Srinivas, MD

Ronald Stein, JD, MSN, NP-C, AOCNP

Non-Small Cell Lung Cancer

Thursday, April 28, 2022

6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)

Faculty

Edward B Garon, MD, MS

Kelly EH Goodwin, MSN, RN, ANP-BC

Tara Plues, APRN, MSN

Anne S Tsao, MD, MBA

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Kathleen N Moore, MD, MS

Krishnansu S Tewari, MD

Deborah Wright, MSN, APRN, AGCNS-BC

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Amanda K Wagner, APRN-CNP, AOCNP

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Matthew Gubens, MD, MS

Lowell L Hart, MD

Chaely J Medley, MSN, AGNP

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Faculty to be announced

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Shilpa Gupta, MD

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Sumanta Kumar Pal, MD

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**Optimizing the Management of
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**Thursday, May 5, 2022
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Yelena Y Janjigian, MD

Moderator

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Ashish M Kamat, MD, MBBS

Stephen B Williams, MD, MBA, MS

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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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Christina Baik, MD, MPH
Associate Professor of Medicine
Thoracic, Head and Neck Medical Oncology
University of Washington School of Medicine
Fred Hutchinson Cancer Research Center
Seattle, Washington



Alexander E Drilon, MD
Chief, Early Drug Development Service
Associate Attending Physician
Thoracic Oncology Service
Memorial Sloan Kettering Cancer Center
New York, New York



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Medical Campus
Denver, Colorado



Justin F Gainor, MD
Director, Center for Thoracic Cancers at
Massachusetts General Hospital
Director of Targeted Immunotherapy in the
Henri and Belinda Termeer Center for
Targeted Therapies
Associate Professor of Medicine, Harvard
Medical School
Massachusetts General Hospital
Boston, Massachusetts

Meet The Professor Program Participating Faculty



Melissa Johnson, MD

Director, Lung Cancer Research Program
Associate Director of Drug Development for
the Drug Development Unit in Nashville
Sarah Cannon Research Institute
Nashville, Tennessee



MODERATOR

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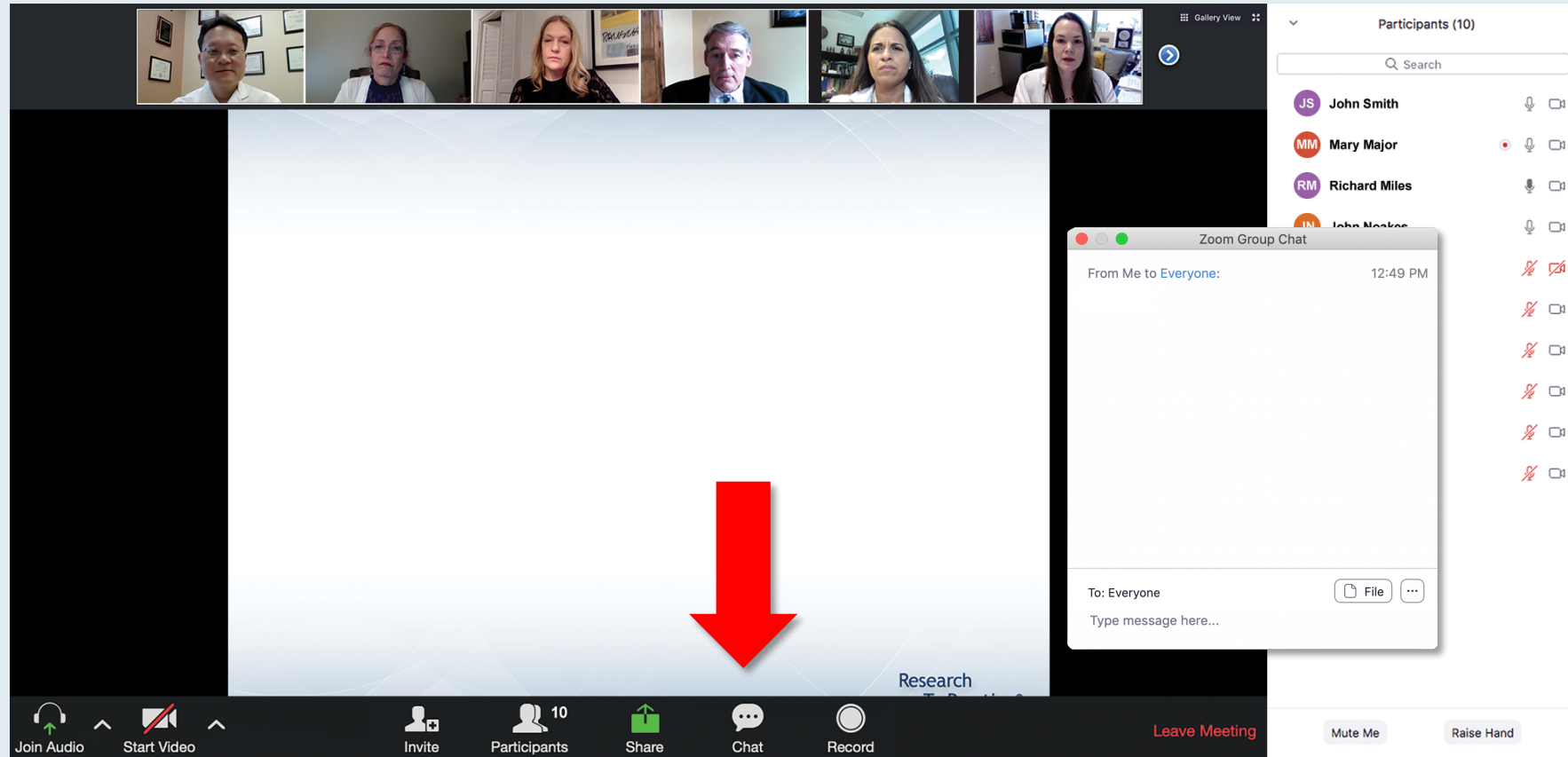
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Virginia Cancer Specialists
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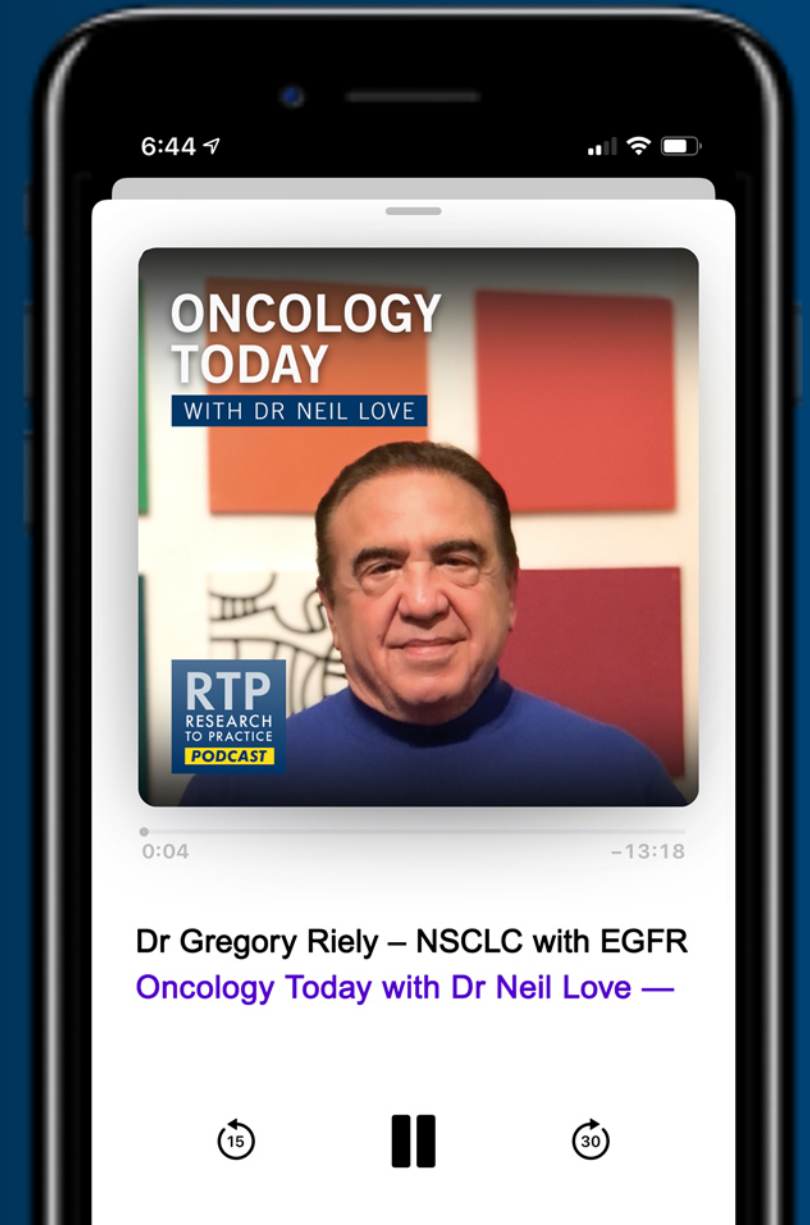
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Spencer Henick Bachow, MD
Lynn Cancer Institute Affiliate
FAU Schmidt College of Medicine Boca
Raton, Florida



Jennifer L Dallas, MD
Novant Health Cancer Institute
Charlotte, North Carolina



Daniel R Carrizosa, MD, MS
Atrium Health Levine Cancer Institute
Charlotte, North Carolina



Sunil Gandhi, MD
Lecanto, Florida



Mamta Choksi, MD
Florida Cancer Specialists
New Port Richey, Florida



Rajni Sinha, MD, MRCP
Piedmont Cancer Institute
Atlanta, Georgia

Meet The Professor with Dr Camidge

Introduction: First-Line Systemic Treatment/Brain Metastases

MODULE 1: ALK Rearrangements

MODULE 2: KRAS G12C Mutations

MODULE 3: MET Exon 14 Skipping Mutations

MODULE 4: HER2 Mutations

MODULE 5: NTRK Fusions

MODULE 6: ROS1 Fusions

MODULE 7: RET Fusions

MODULE 8: BRAF Mutations

MODULE 9: NRG1 Fusions

MODULE 10: Appendix of Key Publications

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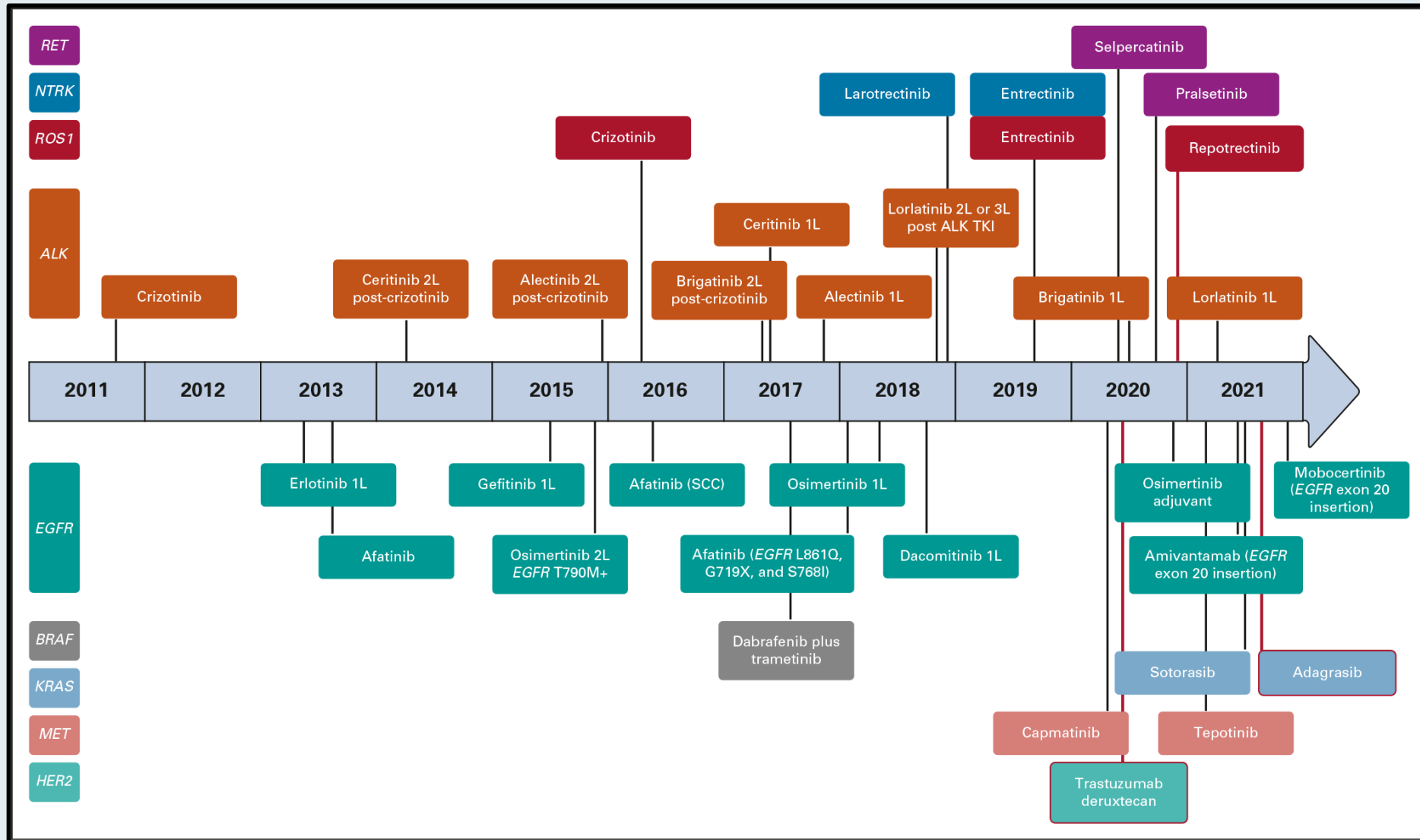
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Timeline of Select FDA-Approved Targeted Therapies for Oncogene-Driven NSCLC






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Abstract CT032

**ANNUAL
MEETING**
2022 *New Orleans*



APRIL 8-13, 2022 • #AACR22

Activity and Safety of Alectinib for *ALK*-Altered Solid Tumors from MyPathway

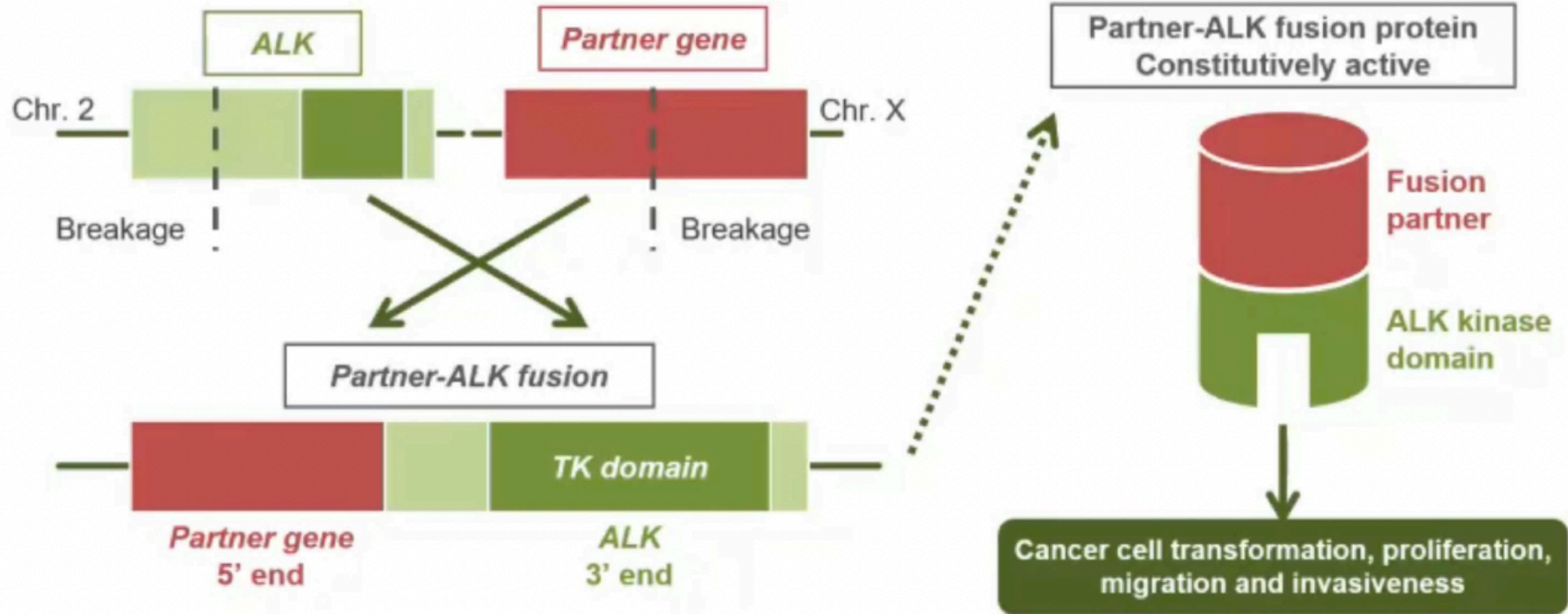
Funda Meric-Bernstam, MD

University of Texas MD Anderson Cancer Center, Houston, TX, USA

Charles Swanton,^{1,2} Claire F. Friedman,^{3,4} Christopher J. Sweeney,⁵ Funda Meric-Bernstam,⁶ David Spigel,^{7,8} Ron Bose,⁹ Howard Burris,^{7,8} Walter C. Darbonne,¹⁰ Julia Malato,¹⁰ Jonathan Levy,¹⁰ Yong Wang,¹⁰ Tania Szado,¹⁰ Katja Schulze,¹⁰ John Hainsworth,^{7,8} Razelle Kurzrock¹¹

¹Francis Crick Institute, London, UK; ²UCL Hospitals, London, UK; ³Memorial Sloan Kettering Cancer Center, New York, NY, USA; ⁴Weill Medical College at Cornell University, New York, NY, USA; ⁵Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; ⁶University of Texas MD Anderson Cancer Center, Houston, TX, USA; ⁷Sarah Cannon Research Institute, Nashville, TN, USA; ⁸Tennessee Oncology, PLLC, Nashville, TN, USA; ⁹Washington University School of Medicine, St. Louis, MO, USA; ¹⁰Genentech, Inc., South San Francisco, CA, USA; ¹¹Medical College of Wisconsin Cancer Center, Milwaukee, WI, USA

Mechanism of ALK Fusions



Partial Responses or Stable Disease Were Observed Across Tumor Types

Patients with <i>ALK</i> rearrangement (n=10)					
Confirmed BOR	PFS (months)	Tumor type	Fusion partner	Additional <i>ALK</i> alteration	Co-mutations*
PR	16.4	Skin (Melanoma)	<i>EMILIN1</i>	—	<i>TERT</i> promoter
PR	8.3	Papillary urothelial carcinoma	<i>DCTN1</i>	Mutation (D1529N)	<i>TP53</i> V272L; <i>KEL</i> R655W; <i>DNMT3A</i> R736H; <i>FAT1</i> T3845M
PR	8.2	Colon adenocarcinoma	<i>DIAPH2</i>	—	<i>TP53</i> H178fs*69, Y163C; <i>FBXW7</i> R465C; <i>ATM</i> Y370fs*1; <i>BRCA</i> R8fs*5
SD >4 mos	13.6	Colon adenocarcinoma	<i>STRN</i>	—	<i>TP53</i> R306*
SD >4 mos	10.1	Uterine leiomyosarcoma	<i>IGFBP5</i>	—	<i>CDKN2A/B</i> loss; <i>CHEK2</i> loss
SD >4 mos	5.5	Pancreatic adenocarcinoma	<i>EML4</i>	—	<i>TP53</i> S241F; <i>KRAS</i> Q61H
PD	2.8	Colon adenocarcinoma	Unknown	—	<i>KRAS</i> G12V; <i>APC</i> Q1291*; <i>TP53</i> R175H
PD	1.7	Esophageal adenocarcinoma	<i>STRN</i>	—	<i>APC</i> loss; <i>CDK12-SRCIN1</i> fusion; <i>ERBB2</i> amp.; <i>TP53</i> C176F
PD	1.7	Uterine serous carcinoma	Unknown	Mutation (E269D)	<i>TP53</i> E221*; <i>KRAS</i> amp.; <i>MYC</i> amp.
Not evaluable	NE	Uterine inflammatory myofibroblastic tumor	<i>IGFBP5</i>	Mutation (C1021R)	<i>DNMT3A</i> K829R

*Co-mutations of known significance identified by tissue report (FoundationMedicine Inc.), or if not available, the molecular report used for patient enrollment BOR, best overall response; PD, progressive disease; PR, partial response; SD, stable disease

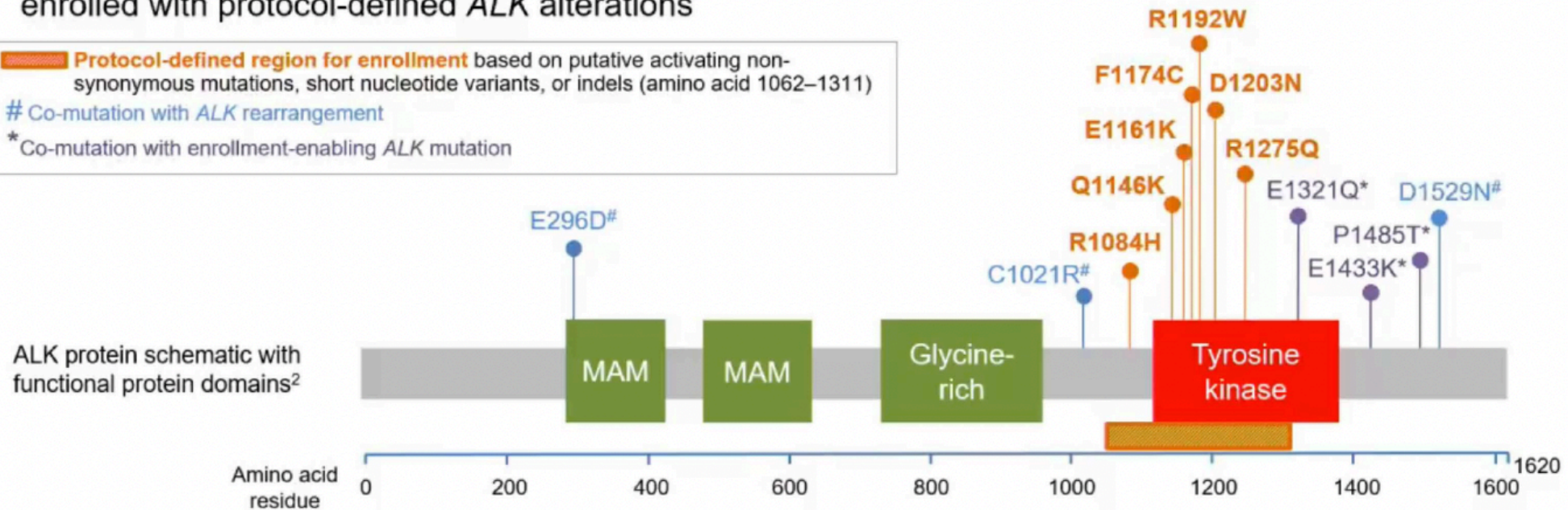
ALK Mutations Enabling Enrollment Were Located in Protocol-Defined Regions Within and Near the Tyrosine Kinase Domain

- Alectinib had been shown to be active on *ALK* activating point mutations like F1174L, R1275Q in cell-line-derived models¹
- Additional *ALK* co-mutations were identified in a subset of patient samples enrolled with protocol-defined *ALK* alterations

Protocol-defined region for enrollment based on putative activating non-synonymous mutations, short nucleotide variants, or indels (amino acid 1062–1311)

Co-mutation with *ALK* rearrangement

* Co-mutation with enrollment-enabling *ALK* mutation



1. Sakamoto, et al Cancer Cell 2011
2. Modified from cBioPortal (<https://www.cbioportal.org/>)

A patient presents with ALK-positive NSCLC, including asymptomatic brain metastases. Would you be likely to include radiation therapy to the brain in the initial treatment?

1. No
2. Yes, if it required whole-brain radiation therapy
3. Yes, if it required stereotactic body radiation therapy
4. Yes

SPECIAL SERIES: THORACIC ONCOLOGY: CURRENT AND FUTURE THERAPY

Managing Central Nervous System Spread of Lung Cancer: The State of the Art

David Chun Cheong Tsui, MD, PhD¹; D. Ross Camidge, MD, PhD¹; and Chad G. Rusthoven, MD²

J Clin Oncol 2022;40(6):642-60.



Brain Metastases in *EGFR*- and *ALK*-Positive NSCLC: Outcomes of Central Nervous System-Penetrant Tyrosine Kinase Inhibitors Alone Versus in Combination With Radiation

Nicholas J. Thomas, BA,^a Nathaniel J. Myall, MD,^b Fangdi Sun, MD,^a Tejas Patil, MD,^c Rao Mushtaq, MD,^c Chandler Yu, BS,^d Sumi Sinha, MD,^d Erqi L. Pollom, MD,^e Seema Nagpal, MD,^f D. Ross Camidge, MD, PhD,^c Chad G. Rusthoven, MD,^g Steve E. Braunstein, MD, PhD,^d Heather A. Wakelee, MD,^b Caroline E. McCoach, MD, PhD^{a,h,*}

Comparing Addition of Radiotherapy in EGFR- and ALK-Positive NSCLC With Brain Metastases: Are We Evaluating the Optimal End Point?

Nardone V et al. *J Thorac Oncol* 2022;17(2):e10-2.

In Response to:
“Comparing Addition of
Radiotherapy in EGFR- and
ALK-Positive NSCLC With
Brain Metastases: Are We
Evaluating the Optimal
Endpoint?”

Thomas NJ et al. *J Thorac Oncol* 2022;17(2):e12-4.

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and an ALK rearrangement?



Dr Baik

Alectinib



Dr Gainor

Lorlatinib



Dr Camidge

Alectinib



Dr Johnson

Alectinib



Dr Drilon

Alectinib



Dr Spira

Alectinib

Regulatory and reimbursement issues aside, would you generally offer targeted treatment prior to attempting local therapy (eg, stereotactic radiosurgery, whole-brain radiation therapy) for an asymptomatic patient with newly diagnosed nonsquamous NSCLC (PD-L1 TPS 50%), brain metastases and an ALK rearrangement?



Dr Baik

Yes, alectinib



Dr Gainor

Yes, lorlatinib



Dr Camidge

Yes, alectinib



Dr Johnson

Yes, alectinib



Dr Drilon

Yes, alectinib



Dr Spira

No

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and a ROS1 rearrangement?



Dr Baik

Entrectinib



Dr Gainor

Crizotinib



Dr Camidge

Entrectinib



Dr Johnson

Entrectinib



Dr Drilon

Entrectinib



Dr Spira

Entrectinib

Regulatory and reimbursement issues aside, would you generally offer targeted treatment prior to attempting local therapy (eg, stereotactic radiosurgery, whole-brain radiation therapy) for an asymptomatic patient with newly diagnosed nonsquamous NSCLC (PD-L1 TPS 50%), brain metastases and a ROS1 rearrangement?



Dr Baik

Yes, entrectinib



Dr Gainor

Yes, entrectinib



Dr Camidge

Yes, entrectinib



Dr Johnson

Yes, entrectinib



Dr Drilon

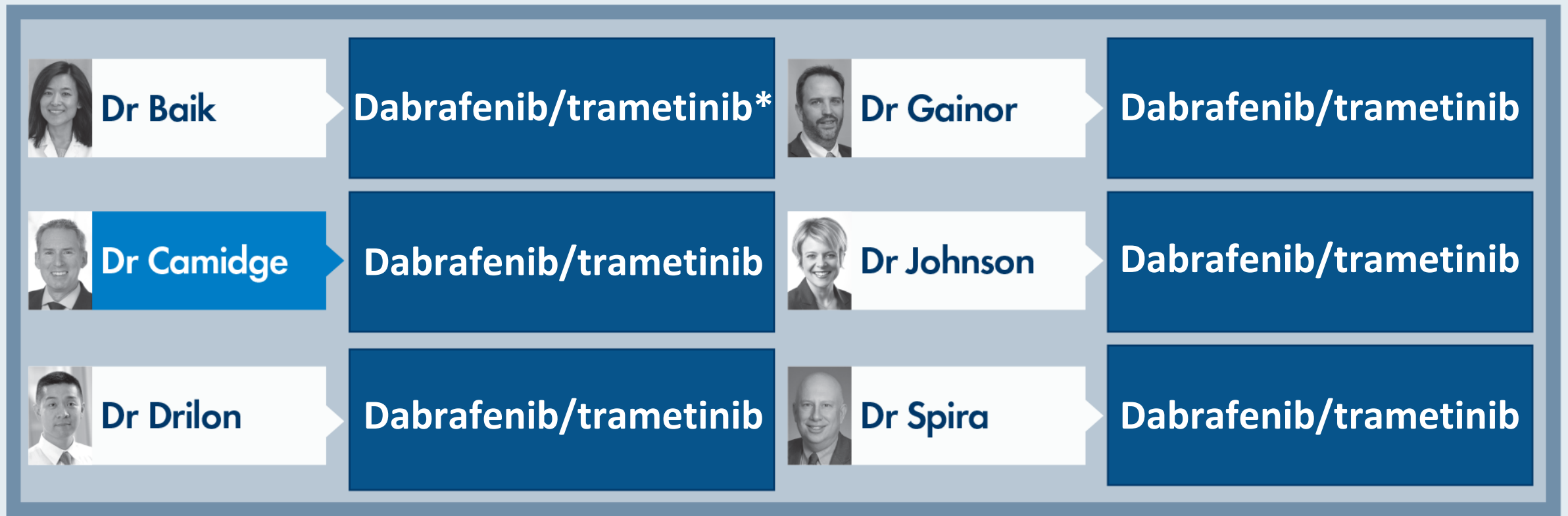
Yes, entrectinib



Dr Spira

No

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and a BRAF V600E mutation?



* If the patient is a nonsmoker or if the patient has a high disease burden and needs a fast tumor response

Regulatory and reimbursement issues aside, would you generally offer targeted treatment prior to attempting local therapy (eg, stereotactic radiosurgery, whole-brain radiation therapy) for an asymptomatic patient with newly diagnosed nonsquamous NSCLC (PD-L1 TPS 50%), brain metastases and a BRAF V600E mutation?



Dr Baik

**Yes, dabrafenib/
trametinib**



Dr Gainor

No



Dr Camidge

**Yes, dabrafenib/
trametinib**



Dr Johnson

No



Dr Drilon

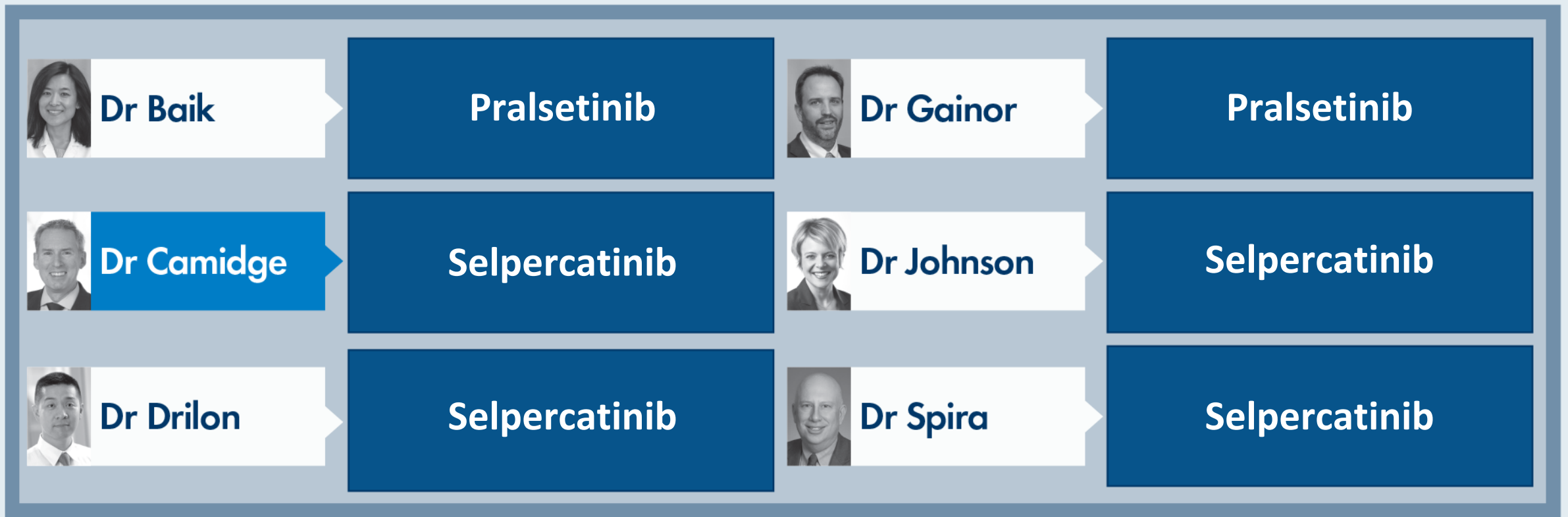
**Yes, dabrafenib/
trametinib**



Dr Spira

No

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and a RET fusion?



Regulatory and reimbursement issues aside, would you generally offer targeted treatment prior to attempting local therapy (eg, stereotactic radiosurgery, whole-brain radiation therapy) for an asymptomatic patient with newly diagnosed nonsquamous NSCLC (PD-L1 TPS 50%), brain metastases and a RET fusion?



Dr Baik

Yes, pralsetinib



Dr Gainor

Yes, selpercatinib



Dr Camidge

Yes, selpercatinib



Dr Johnson

Yes, selpercatinib



Dr Drilon

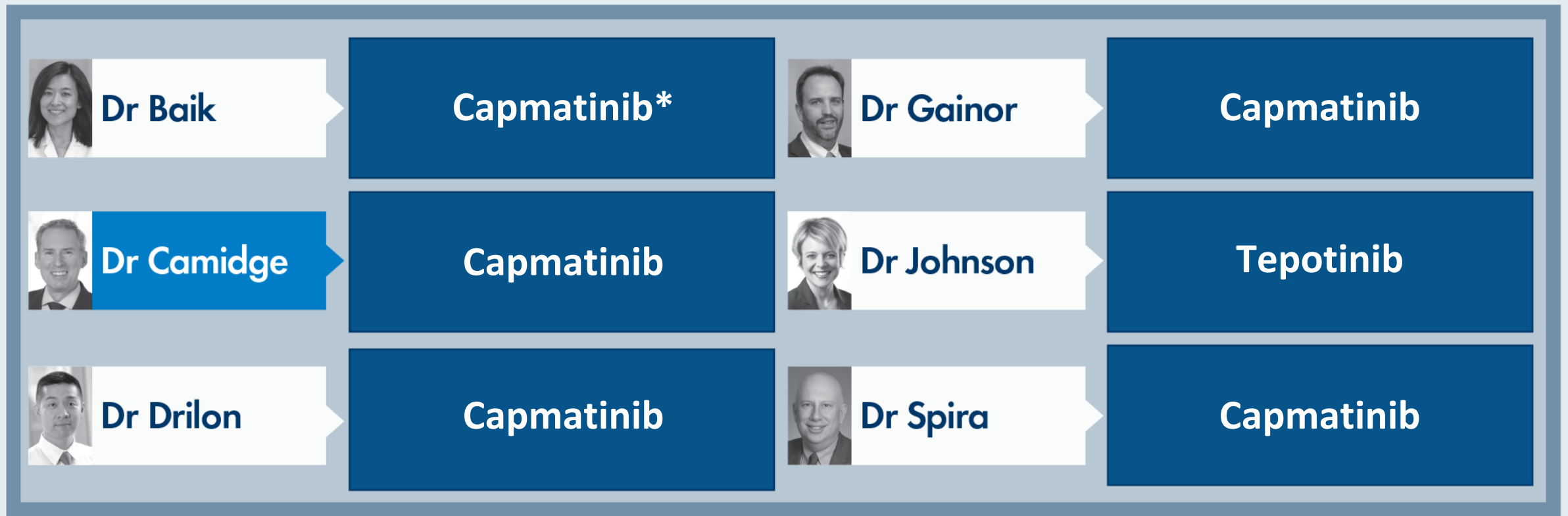
Yes, selpercatinib



Dr Spira

No

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and a MET exon 14 skipping mutation?



* If the patient is a nonsmoker

Regulatory and reimbursement issues aside, would you generally offer targeted treatment prior to attempting local therapy (eg, stereotactic radiosurgery, whole-brain radiation therapy) for an asymptomatic patient with newly diagnosed nonsquamous NSCLC (PD-L1 TPS 50%), brain metastases and a MET exon 14 skipping mutation?



Dr Baik

Yes, capmatinib



Dr Gainor

Yes, capmatinib



Dr Camidge

Yes, capmatinib



Dr Johnson

No



Dr Drilon

Yes, capmatinib



Dr Spira

No

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and a KRAS G12C mutation?



Dr Baik

Carboplatin/
pemetrexed/
pembrolizumab



Dr Gainor

Pembrolizumab



Dr Camidge

Carboplatin/
pemetrexed/
pembrolizumab



Dr Johnson

Pembrolizumab



Dr Drilon

Pembrolizumab



Dr Spira

Carboplatin/
pemetrexed/
pembrolizumab

Regulatory and reimbursement issues aside, would you generally offer targeted treatment prior to attempting local therapy (eg, stereotactic radiosurgery, whole-brain radiation therapy) for an asymptomatic patient with newly diagnosed nonsquamous NSCLC (PD-L1 TPS 50%), brain metastases and a KRAS G12C mutation?



Dr Baik

No



Dr Gainor

No



Dr Camidge

No



Dr Johnson

No



Dr Drilon

Yes, sotorasib



Dr Spira

No

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and an NTRK fusion?



Dr Baik

Larotrectinib



Dr Gainor

Larotrectinib



Dr Camidge

Entrectinib



Dr Johnson

Larotrectinib



Dr Drilon

Larotrectinib



Dr Spira

Larotrectinib

Regulatory and reimbursement issues aside, would you generally offer targeted treatment prior to attempting local therapy (eg, stereotactic radiosurgery, whole-brain radiation therapy) for an asymptomatic patient with newly diagnosed nonsquamous NSCLC (PD-L1 TPS 50%), brain metastases and an NTRK fusion?



Dr Baik

Yes, larotrectinib



Dr Gainor

Yes, entrectinib



Dr Camidge

Yes, entrectinib



Dr Johnson

No



Dr Drilon







Yes, larotrectinib



Dr Spira


No

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and a HER2 mutation?

 Dr Baik	Carboplatin/ pemetrexed	 Dr Gainor	Carboplatin/ pemetrexed/ pembrolizumab
 Dr Camidge	Carboplatin/ pemetrexed/ pembrolizumab	 Dr Johnson	T-DXd
 Dr Drilon	T-DXd	 Dr Spira	T-DXd

T-DXd = trastuzumab deruxtecan

Regulatory and reimbursement issues aside, would you generally offer targeted treatment prior to attempting local therapy (eg, stereotactic radiosurgery, whole-brain radiation therapy) for an asymptomatic patient with newly diagnosed nonsquamous NSCLC (PD-L1 TPS 50%), brain metastases and a HER2 mutation?

 Dr Baik	No	 Dr Gainor	No
 Dr Camidge	No	 Dr Johnson	No
 Dr Drilon	Yes, T-DXd	 Dr Spira	No

T-DXd = trastuzumab deruxtecan

Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and HER2 overexpression?



Dr Baik

Pembrolizumab



Dr Gainor

**Carboplatin/
pemetrexed/
pembrolizumab**



Dr Camidge

**Carboplatin/
pemetrexed/
pembrolizumab**



Dr Johnson

Pembrolizumab



Dr Drilon

Pembrolizumab



Dr Spira

**Carboplatin/
pemetrexed/
pembrolizumab**

Regulatory and reimbursement issues aside, would you generally offer targeted treatment prior to attempting local therapy (eg, stereotactic radiosurgery, whole-brain radiation therapy) for an asymptomatic patient with newly diagnosed nonsquamous NSCLC (PD-L1 TPS 50%), brain metastases and HER2 overexpression?



Dr Baik

No



Dr Gainor

No



Dr Camidge

No



Dr Johnson

No



Dr Drilon

No



Dr Spira

No

Meet The Professor with Dr Camidge

Introduction: First-Line Systemic Treatment/Brain Metastases

MODULE 1: ALK Rearrangements

- Dr Bachow: A 62-year-old woman with squamous NSCLC metastatic to the brain and an ALK rearrangement – PD-L1 TPS 70%
- Dr Gandhi: A 70-year-old man with localized NSCLC with an ALK rearrangement and significant comorbidities

MODULE 2: KRAS G12C Mutations

MODULE 3: MET Exon 14 Skipping Mutations

MODULE 4: HER2 Mutations

MODULE 5: NTRK Fusions

MODULE 6: ROS1 Fusions

MODULE 7: RET Fusions

MODULE 8: BRAF Mutations

MODULE 9: NRG1 Fusions

MODULE 10: Appendix of Key Publications

Case Presentation: A 62-year-old woman with squamous NSCLC metastatic to the brain and an ALK rearrangement – PD-L1 TPS 70%



Dr Spencer Henick Bachow (Boca Raton, Florida)

Case Presentation: A 70-year-old man with localized NSCLC with an ALK rearrangement and significant comorbidities



Dr Sunil Gandhi (Lecanto, Florida)

For a patient with metastatic nonsquamous NSCLC with an ALK rearrangement and a PD-L1 TPS of 50% who receives first-line alectinib with response followed by disease progression, would you recommend repeat mutation testing?



Dr Baik

Yes, tissue biopsy



Dr Gainor

Yes, liquid and tissue biopsy



Dr Camidge

Yes, liquid and tissue biopsy



Dr Johnson

Yes, liquid biopsy



Dr Drilon

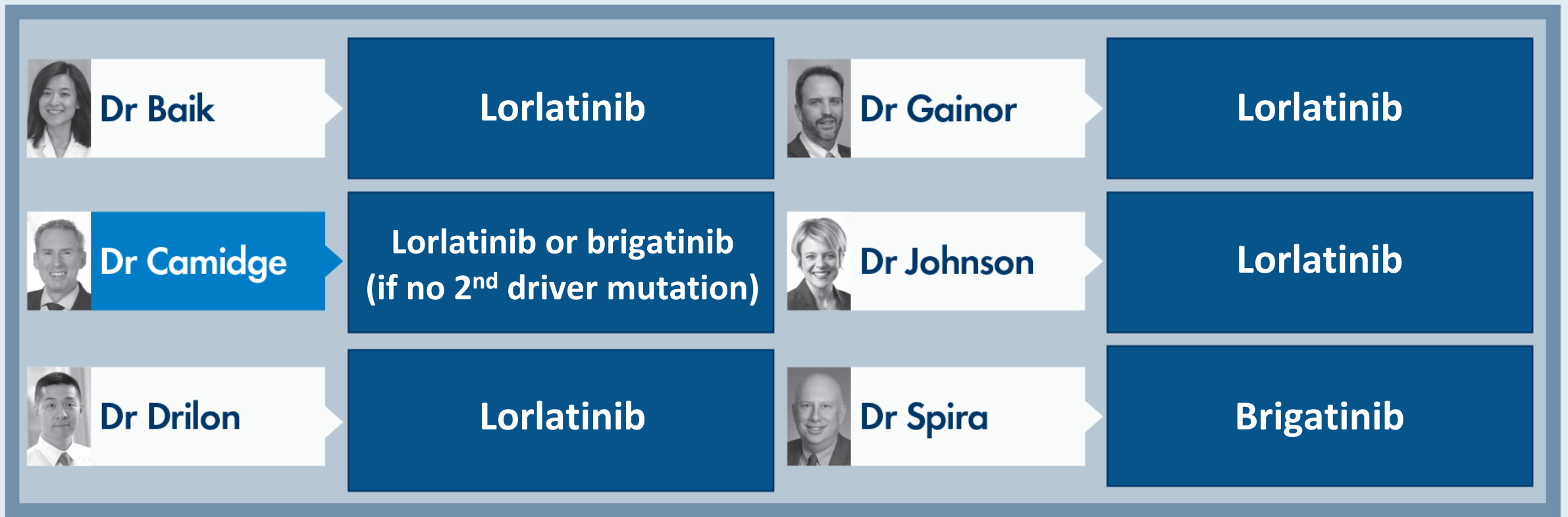
Yes, liquid and tissue biopsy



Dr Spira

Yes, liquid and tissue biopsy

In general, what would be your preferred second-line therapy for a patient with metastatic nonsquamous NSCLC with an ALK rearrangement and a TPS of 50% who experiences disease progression on alectinib?



Key Randomized Trials in Treatment-Naïve Advanced ALK-Rearranged NSCLC

Study	Intervention	Comparator	ORR	CNS ORR
PROFILE 1014	Crizotinib	Platinum/pemetrexed	74% vs 45%	—
PROFILE 1029	Crizotinib	Platinum/pemetrexed	88% vs 46%	—
ASCEND-4	Ceritinib	Platinum/pemetrexed	73% vs 27%	73% vs 27%
ALEX	Alectinib	Crizotinib	83% vs 76%	81% vs 50%
J-ALEX	Alectinib	Crizotinib	92% vs 79%	—
ALESIA	Alectinib	Crizotinib	91% vs 77%	—
ALTA-1L	Brigatinib	Crizotinib	71% vs 60%	78% vs 26%
CROWN	Lorlatinib	Crizotinib	76% vs 58%	82% vs 23%
eXalt3	Ensartinib	Crizotinib	75% vs 67%	64% vs 21%

Tan AC et al. *J Clin Oncol* 2022;40(6):611-25; Soria JC et al. *Lancet* 2017;389(10072):917-29; Peters S et al. *N Engl J Med* 2017;377(9):829-38; Camidge DR et al. *J Thorac Oncol* 2021;16(12):2091-108; Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29; Horn L et al. *JAMA Oncol* 2021;7(11):1617-25; Popat S et al. ESMO 2021;Abstract 1195P.

Key Randomized Trials in Treatment-Naïve Advanced ALK-Rearranged NSCLC (continued)

Study	Intervention	Comparator	Median PFS	PFS Hazard ratio	OS Hazard ratio
PROFILE 1014	Crizotinib	Platinum/pemetrexed	11 vs 7 mo	0.45	0.76
PROFILE 1029	Crizotinib	Platinum/pemetrexed	11 vs 7 mo	0.40	0.90
ASCEND-4	Ceritinib	Platinum/pemetrexed	17 vs 8 mo	0.55	0.73
ALEX	Alectinib	Crizotinib	35 vs 11 mo	0.50	0.67
J-ALEX	Alectinib	Crizotinib	34 vs 10 mo	0.37	0.80
ALESIA	Alectinib	Crizotinib	NR v 11 mo	0.37	0.28
ALTA-1L	Brigatinib	Crizotinib	24 vs 11 mo	0.49	0.92
CROWN	Lorlatinib	Crizotinib	NR vs 9 mo	0.28	0.72
eXalt3	Ensartinib	Crizotinib	26 vs 13 mo	0.52	0.88

Tan AC et al. *J Clin Oncol* 2022;40(6):611-25; Soria JC et al. *Lancet* 2017;389(10072):917-29; Peters S et al. *N Engl J Med* 2017;377(9):829-38; Camidge DR et al. *J Thorac Oncol* 2021;16(12):2091-108; Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29; Horn L et al. *JAMA Oncol* 2021;7(11):1617-25; Popat S et al. ESMO 2021;Abstract 1195P.

Outcomes According to *ALK* Status Determined by Central Immunohistochemistry or Fluorescence In Situ Hybridization in Patients With *ALK*-Positive NSCLC Enrolled in the Phase 3 ALEX Study

Tony Mok, MD,^{a,*} Solange Peters, MD, PhD,^b D. Ross Camidge, MD, PhD,^c Johannes Noé, PhD,^d Shirish Gadgeel, MD,^{e,f} Sai-Hong Ignatius Ou, MD, PhD,^g Dong-Wan Kim, MD,^h Krzysztof Konopa, MD, PhD,ⁱ Emanuela Pozzi, MSc,^d Ting Liu, MD, PhD,^d Isabell R. Loftin, PhD,^j Crystal Williams, MPH,^j Alice T. Shaw, MD, PhD^{k,l}



Contents lists available at [ScienceDirect](#)

Lung Cancer

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



Short communication: The activity of brigatinib in patients with disease progression after next generation anaplastic lymphoma tyrosine kinase inhibitors and an exploratory analysis of circulating tumor DNA

Thomas E. Stinchcombe^{a,*}, Xiaofei Wang^b, Robert C. Doebele^c, Leylah M. Drusbosky^d, David E. Gerber^e, Leora Horn^f, Erin M. Bertino^g, Geoff Liu^h, Liza C. Villaruzⁱ, D. Ross Camidge^c

Brigatinib Versus Crizotinib in ALK Inhibitor-Naive Advanced ALK-Positive NSCLC: Final Results of Phase 3 ALTA-1L Trial

D. Ross Camidge, MD, PhD,^{a,*} Hye Ryun Kim, MD, PhD,^b Myung-Ju Ahn, MD, PhD,^c James C. H. Yang, MD, PhD,^d Ji-Youn Han, MD, PhD,^e Maximilian J. Hochmair, MD,^f Ki Hyeong Lee, MD, PhD,^g Angelo Delmonte, MD, PhD,^h Maria Rosario Garcia Campelo, MD,ⁱ Dong-Wan Kim, MD, PhD,^j Frank Griesinger, MD, PhD,^k Enriqueta Felip, MD, PhD,^l Raffaele Califano, MD,^{m,n} Alexander I. Spira, MD,^o Scott N. Gettinger, MD,^p Marcello Tiseo, MD,^q Huamao M. Lin, PhD,^r Yuyin Liu, PhD,^s Florin Vranceanu, MD, PhD,^t Huifeng Niu, PhD,^u Pingkuan Zhang, MD,^v Sanjay Popat, BSc, PhD, FRC^w

Clin Cancer Res 2022;[Online ahead of print].

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

Circulating Cell-free DNA as a Prognostic Biomarker in Patients with Advanced *ALK*⁺ Non-small Cell Lung Cancer in the Global Phase III ALEX Trial

Rafal Dziadziuszko¹, Solange Peters², Tony Mok³, D. Ross Camidge⁴, Shirish M. Gadgeel⁵, Sai-Hong Ignatius Ou⁶, Krzysztof Konopa¹, Johannes Noé⁷, Malgorzata Nowicka⁷, Walter Bordogna⁷, Peter N. Morcos⁸, Vlatka Smoljanovic⁷, and Alice T. Shaw⁹

Tumor Shrinkage With Combination of Alectinib and Trastuzumab in a Patient With *ALK*-Rearranged Non-small Cell Lung Cancer Harboring *HER2*-Amplification as an Acquired Resistance Mechanism to *ALK* Inhibitor Therapy

David Chun Cheong Tsui,¹ Dara Aisner,² Hala Nijmeh,² Liming Bao,²
Alexander Menter,³ D. Ross Camidge¹

Meet The Professor with Dr Camidge

Introduction: First-Line Systemic Treatment/Brain Metastases

MODULE 1: ALK Rearrangements

MODULE 2: KRAS G12C Mutations

Dr Choksi: A 74-year-old woman and heart transplant recipient with metastatic NSCLC and a KRAS G12C mutation – PD-L1 TPS 20%

MODULE 3: MET Exon 14 Skipping Mutations

MODULE 4: HER2 Mutations

MODULE 5: NTRK Fusions

MODULE 6: ROS1 Fusions

MODULE 7: RET Fusions

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MODULE 9: NRG Fusions

MODULE 10: Appendix of Key Publications

Case Presentation: A 74-year-old woman and heart transplant recipient with metastatic NSCLC and a KRAS G12C mutation – PD-L1 TPS 20%



Dr Mamta Choksi (New Port Richey, Florida)

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

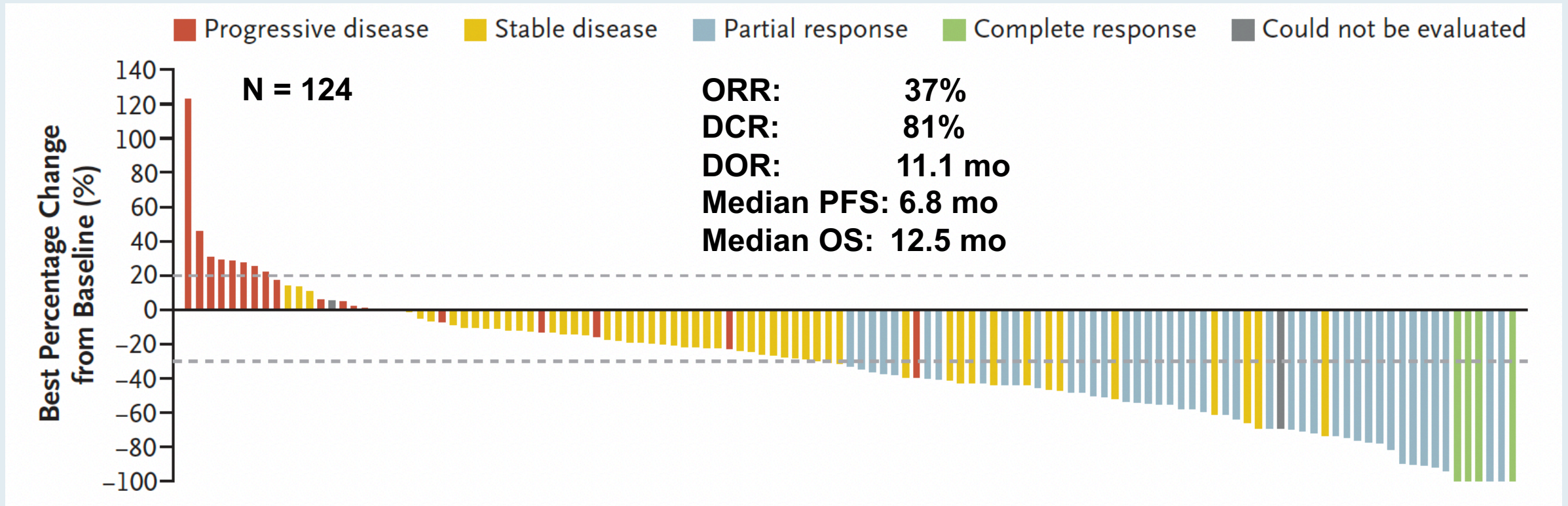
JUNE 24, 2021

VOL. 384 NO. 25

Sotorasib for Lung Cancers with *KRAS* p.G12C Mutation

F. Skoulidis, B.T. Li, G.K. Dy, T.J. Price, G.S. Falchook, J. Wolf, A. Italiano, M. Schuler, H. Borghaei, F. Barlesi, T. Kato, A. Curioni-Fontecedro, A. Sacher, A. Spira, S.S. Ramalingam, T. Takahashi, B. Besse, A. Anderson, A. Ang, Q. Tran, O. Mather, H. Henary, G. Ngarmchamnanrith, G. Friberg, V. Velcheti, and R. Govindan

CodeBreakK 100: Sotorasib for Previously Treated Metastatic NSCLC with KRAS p.G12C Mutation



Long-term Outcomes With Sotorasib in Pre-treated *KRAS* p.G12C Mutated NSCLC: 2-year Analysis of CodeBreakK 100

Presenter: Grace K. Dy¹, MD

¹Roswell Park Comprehensive Cancer Center

On behalf of: Ramaswamy Govindan², Vamsidhar Velcheti³, Gerald S. Falchook⁴, Antoine Italiano⁵, Juergen Wolf⁶, Adrian G. Sacher⁷, Toshiaki Takahashi⁸, Suresh S. Ramalingam⁹, Christophe Doooms¹⁰, Dong-Wan Kim¹¹, Alfredo Addeo¹², Jayesh Desai¹³, Martin Schuler¹⁴, Pascale Tomasini¹⁵, Qui Tran¹⁶, Simon Jones¹⁶, Agnes Ang¹⁶, Abraham Anderson¹⁶, Antreas Hindoyan¹⁶, David S. Hong¹⁷, Bob T. Li¹⁸

²Washington University in St Louis, ³New York University Langone, ⁴Sarah Cannon Research Institute, ⁵Institut Bergonie, ⁶Universitätsklinikum Köln, ⁷Princess Margaret Cancer Centre, ⁸Shizuoka Cancer Center ⁹Winship Cancer Institute, ¹⁰Universitair Ziekenhuis Leuven ¹¹Seoul National University Hospital, ¹²Hopitaux Universitaires de Geneve, ¹³Peter MacCallum Cancer Centre, ¹⁴Universitätsklinikum Essen, ¹⁵Hopital de la Timone, ¹⁶Amgen Inc., ¹⁷MD Anderson Cancer Center, ¹⁸Memorial Sloan Kettering Cancer Center

Efficacy Analysis

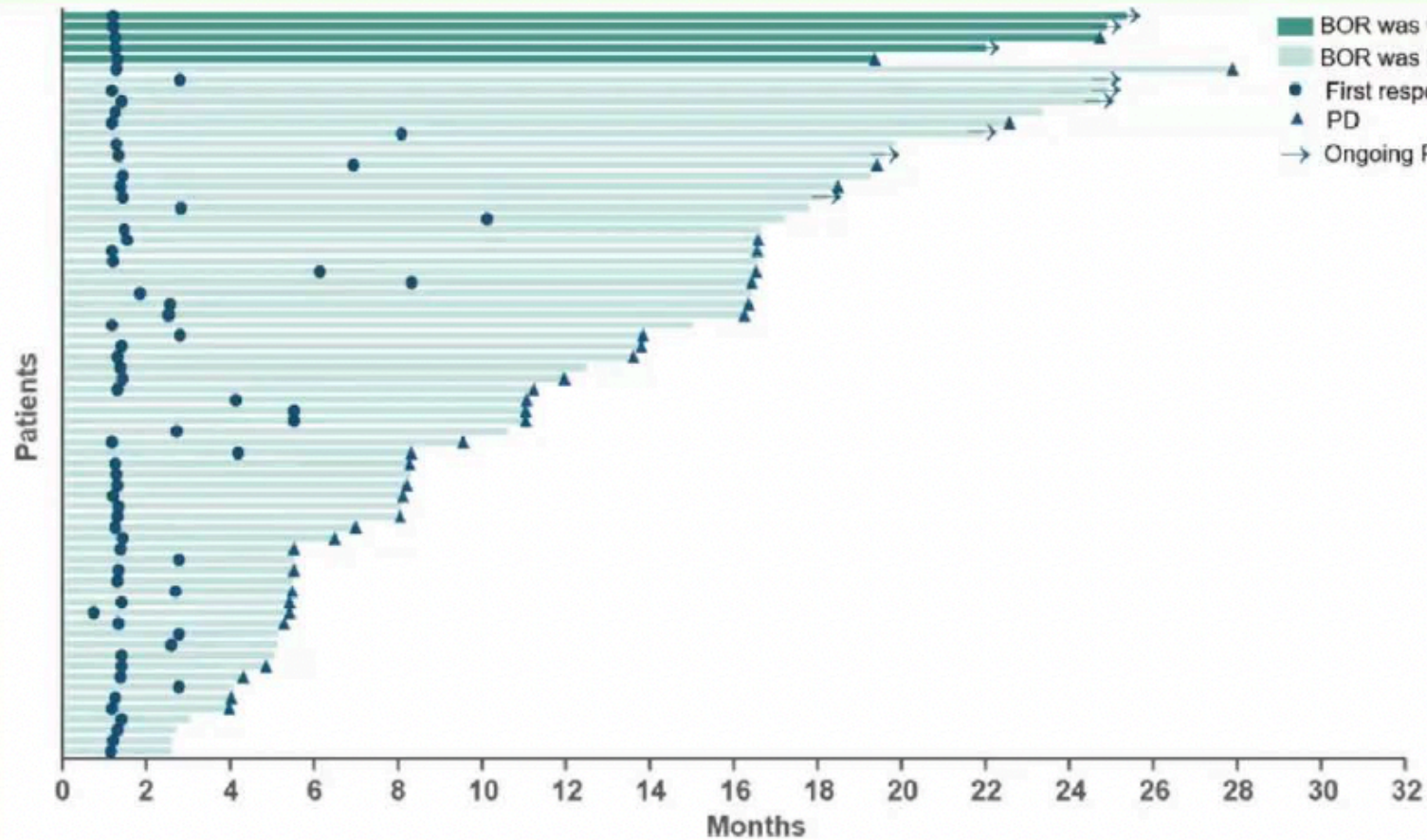
Response by Central Review	Phase 1/2 NSCLC N = 172*
Objective response rate, % (95% CI)	40.7 (33.3, 48.4)
Best overall response, n (%)	
Complete response	5 (2.9)
Partial response	65 (37.8)
Stable disease	74 (43.0)
Progressive disease	23 (13.4)
Not evaluable or missing scan	5 (2.9)
Disease control rate, % (95% CI)	83.7 (77.3, 88.9)
Median progression-free survival, months (95% CI)	6.3 (5.3, 8.2)

CI = Confidence Interval.

95% CIs are based on estimated variance for log-log transformation of the Kaplan-Meier survival Estimate. Follow-up time is summarized by reversing the status indicator for censored and events. Time to response and duration of response are calculated among confirmed responders.

*2 patients are not included in the efficacy set as they did not have measurable lesions at baseline and were ineligible for response assessment.

Durability of Response



**Median time to response:
6 weeks**

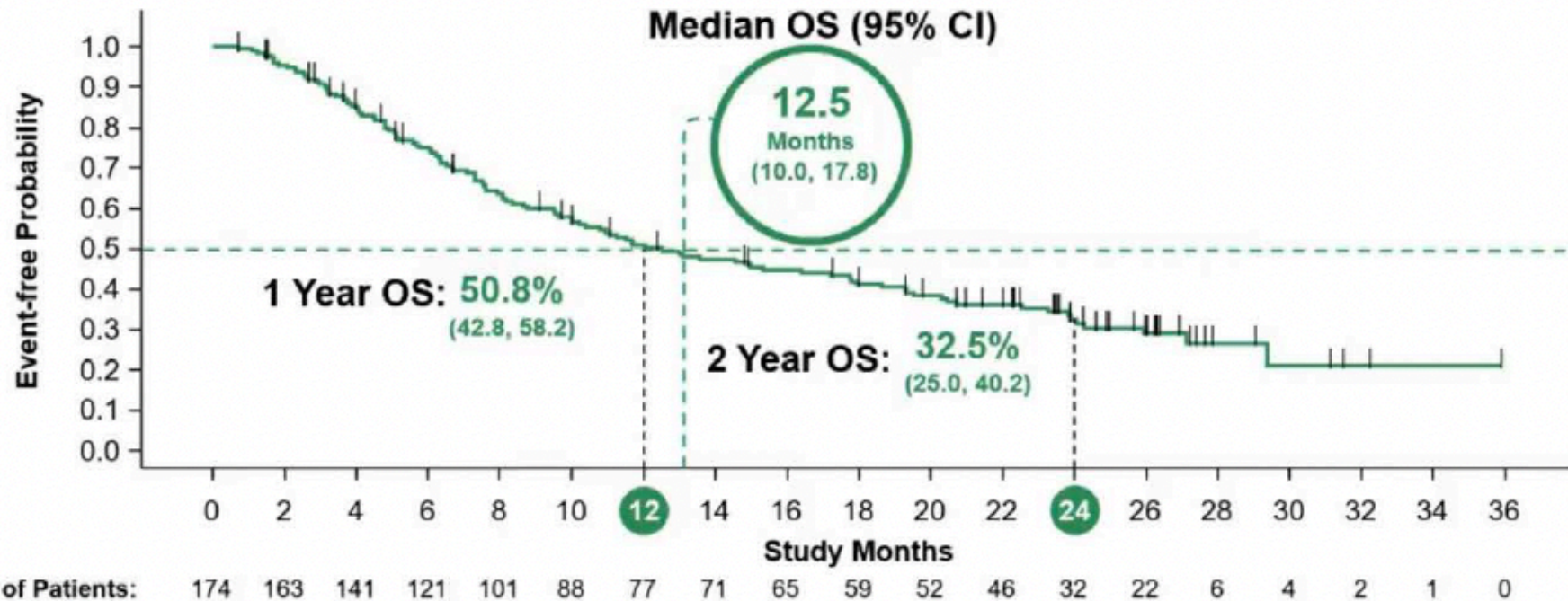
- 70% of patients had a response at their first scan

**Median duration of response: 12.3 months
(95% CI: 7.1, 15.0)**

**50.6% (95% CI: 37.4, 62.4)
of responders remained in response for 12+ months**

BOR, best overall response; CR, complete response; PD, progressive disease; PFS, progression-free survival; PR, partial response.

Overall Survival



2-year overall survival observed in 32.5% of patients

Median follow-up time for OS was 24.9 months

95% CIs are based on estimated variance for log-log transformation of the Kaplan-Meier survival estimate.

Meet The Professor with Dr Camidge

Introduction: First-Line Systemic Treatment/Brain Metastases

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MODULE 3: MET Exon 14 Skipping Mutations

Dr Dallas: A 77-year-old woman with metastatic NSCLC and a MET exon 14 skipping mutation

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MODULE 6: ROS1 Fusions

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Case Presentation: A 77-year-old woman with metastatic NSCLC and a MET exon 14 skipping mutation

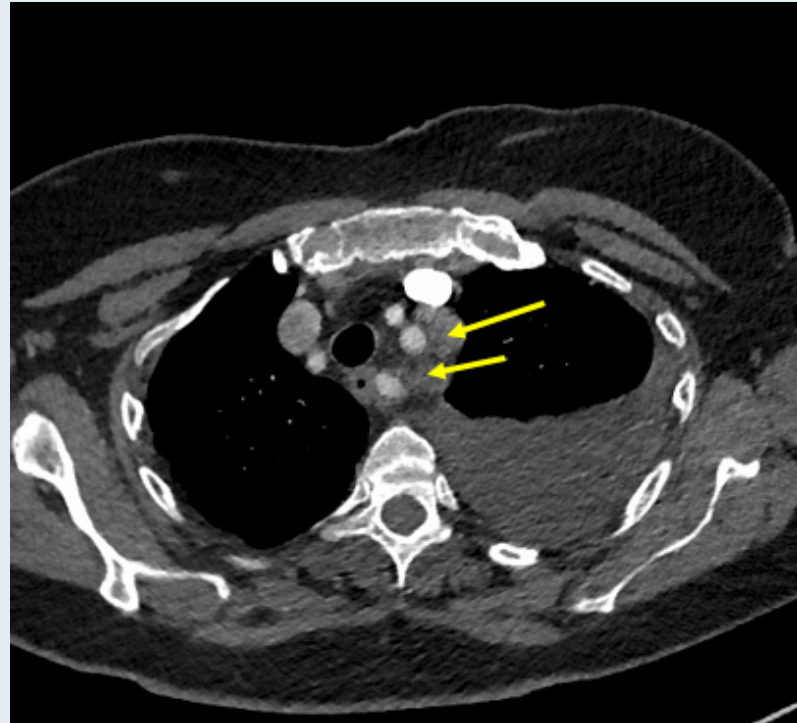


Dr Jennifer L Dallas (Charlotte, North Carolina)

Case Presentation: A 77-year-old woman with metastatic NSCLC and a MET exon 14 skipping mutation (continued)



**Dr Jennifer L Dallas
(Charlotte, North Carolina)**



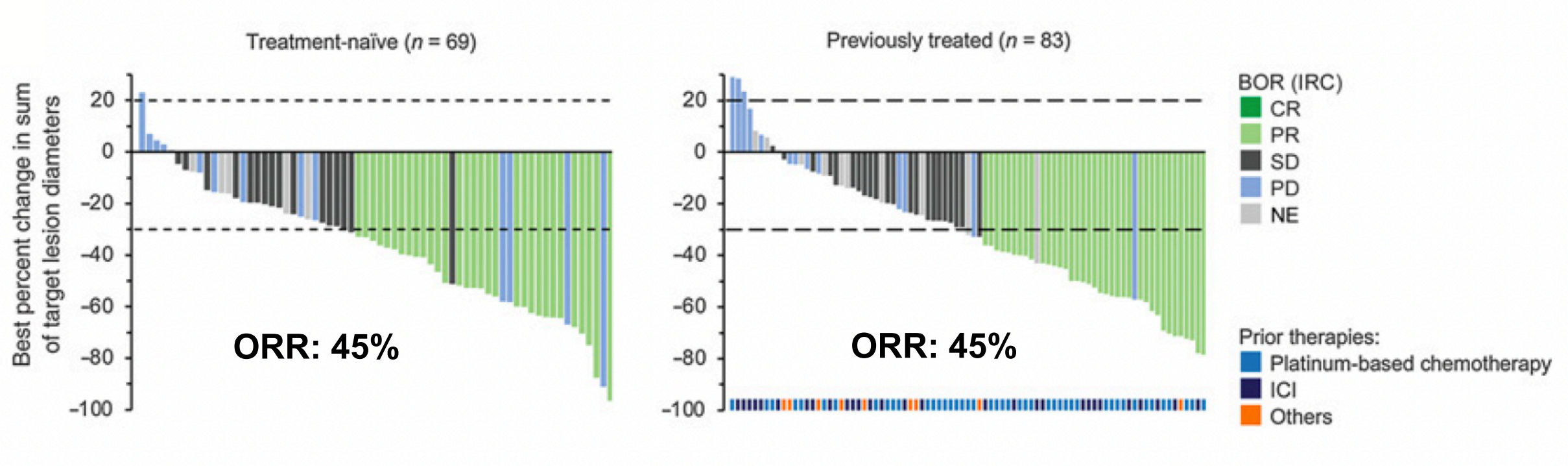
CT chest with PE protocol January 2022 showing superior mediastinal adenopathy, large left pleural effusion

Tepotinib Efficacy and Safety in Patients with *MET* Exon 14 Skipping NSCLC: Outcomes in Patient Subgroups from the VISION Study with Relevance for Clinical Practice

Xiuning Le¹, Hiroshi Sakai², Enriqueta Felip³, Remi Veillon⁴, Marina Chiara Garassino^{5,6}, Jo Raskin⁷, Alexis B. Cortot⁸, Santiago Viteri⁹, Julien Mazieres¹⁰, Egbert F. Smit¹¹, Michael Thomas¹², Wade T. Iams¹³, Byoung Chul Cho¹⁴, Hye Ryun Kim¹⁴, James Chih-Hsin Yang¹⁵, Yuh-Min Chen¹⁶, Jyoti D. Patel¹⁷, Christine M. Bestvina¹⁸, Keunchil Park¹⁹, Frank Griesinger²⁰, Melissa Johnson²¹, Maya Gottfried²², Christian Britschgi²³, John Heymach¹, Elif Sikoglu²⁴, Karin Berghoff²⁵, Karl-Maria Schumacher²⁶, Rolf Bruns²⁷, Gordon Otto²⁶, and Paul K. Paik^{28,29}

***Clin Cancer Res* 2022;28(6):1117-26.**

VISION: Tepotinib in Advanced NSCLC with MET Exon 14 Skipping Mutations



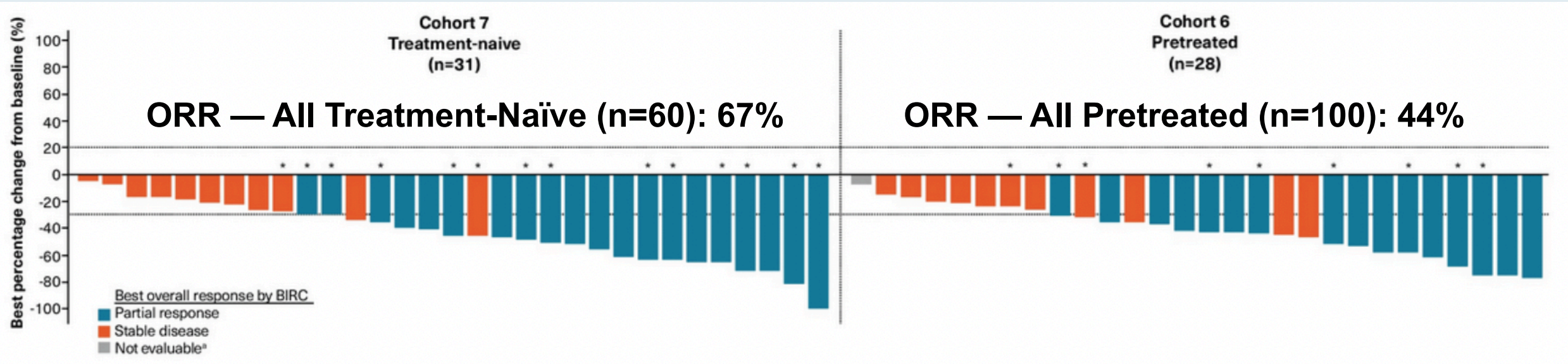
Le X et al. *Clin Cancer Res* 2022;28(6):1117-26.

Capmatinib in *MET* Exon 14-Mutated, Advanced NSCLC: Updated Results from the GEOMETRY mono-1 Study

Wolf J et al.

ASCO 2021;Abstract 9020.

GEOMETRY mono-1: Overall Response Rates (Cohorts 7 and 6)

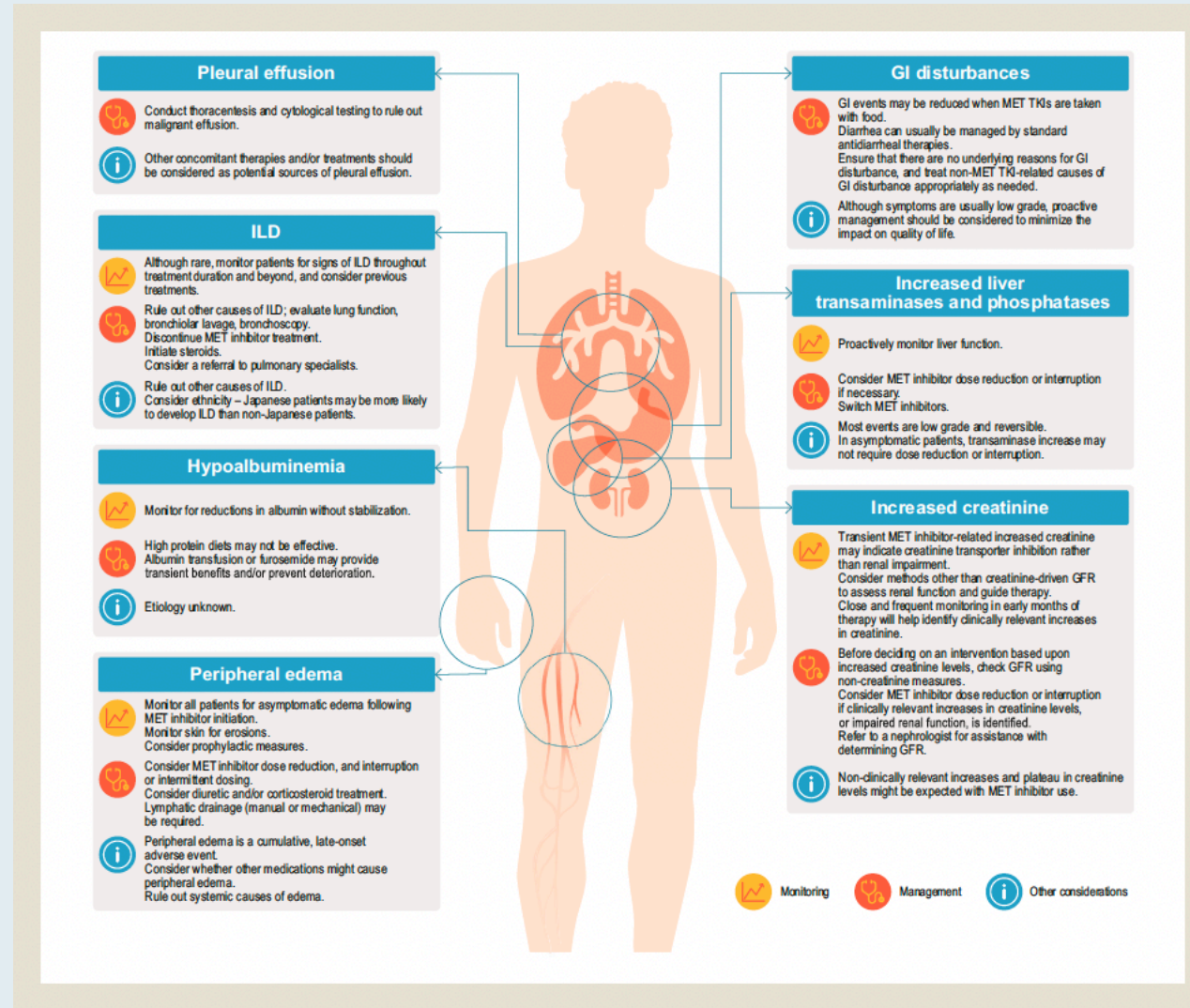


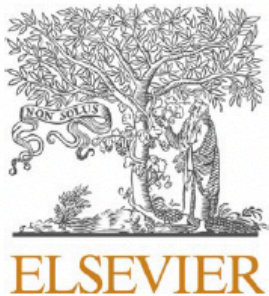
Safety of MET Tyrosine Kinase Inhibitors in Patients With *MET* Exon 14 Skipping Non-small Cell Lung Cancer: A Clinical Review

Alexis Cortot, MD, PhD,¹ Xiuning Le,² Egbert Smit,³ Santiago Viteri,⁴
Terufumi Kato,⁵ Hiroshi Sakai,⁶ Keunchil Park,⁷ D. Ross Camidge,⁸
Karin Berghoff,⁹ Soetkin Vlassak,⁹ Paul K. Paik^{10,11}

Clin Lung Cancer 2022;[Online ahead of print].

Overview of Monitoring and Management Considerations for Key Adverse Events

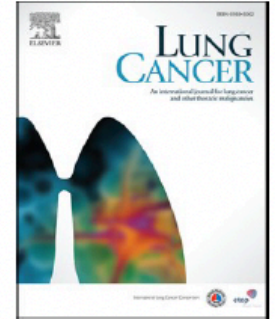




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Lung Cancer

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



Real-world insights into patients with advanced NSCLC and *MET* alterations

Marisa Bittoni^{a,*}, James Chih-Hsin Yang^b, Jin-Yuan Shih^c, Nir Peled^d, Egbert F. Smit^e, D. Ross Camidge^f, Rajeswara Rao Arasada^a, Dina Oksen^g, Emmanuelle Boutmy^g, Christopher Stroh^g, Andreas John^g, David P. Carbone^a, Paul K. Paik^{h,i}

Telisotuzumab vedotin (teliso-v) monotherapy in patients with previously treated c-Met⁺ advanced non-small cell lung cancer

D. Ross Camidge,¹ Fedor Moiseenko,² Irfan Cicin,³ Hidehito Horinouchi,⁴ Elena Filippova,⁵ Jair Bar,⁶ Shun Lu,⁷ Pascale Tomasini,⁸ Christopher Ocampo,⁹ Danielle Sullivan,⁹ David Maag,⁹ Jonathan Goldman¹⁰

¹University of Colorado Cancer Center, Aurora, CO, USA; ²St. Petersburg City Cancer Center, St. Petersburg, Russia; ³Trakya University Medical Center, Edirne, Turkey; ⁴National Cancer Center Hospital, Tokyo, Japan; ⁵Center of Palliative Medicine De Vita, St. Petersburg, Russia; ⁶Sheba Medical Center, Ramat Gan, Israel; ⁷Shanghai Chest Hospital, Shanghai, People's Republic of China; ⁸Aix Marseille Univ, APHM, INSERM, CNRS, CRCM, Hôpital Nord, Multidisciplinary Oncology and Therapeutic Innovations Department, Marseille, France; ⁹AbbVie, Inc., North Chicago, IL, USA; ¹⁰University of California, Los Angeles, CA, USA

Telisotuzumab vedotin monotherapy in patients with previously treated c-Met+ advanced non-small cell lung cancer: Stage 2

Jonathan W. Goldman, MD
David Geffen School of Medicine at UCLA
USA



2021 World Conference on Lung Cancer
SEPTEMBER 8 - 14, 2021 | WORLDWIDE VIRTUAL EVENT

Abstract P47.03



Meet The Professor with Dr Camidge

Introduction: First-Line Systemic Treatment/Brain Metastases

MODULE 1: ALK Rearrangements

MODULE 2: KRAS G12C Mutations

MODULE 3: MET Exon 14 Skipping Mutations

MODULE 4: HER2 Mutations

Dr Sinha: A 67-year-old woman with metastatic NSCLC and a HER2 exon 19 mutation pathogenic variant – PD-L1 TPS 15%

MODULE 5: NTRK Fusions

MODULE 6: ROS1 Fusions

MODULE 7: RET Fusions

MODULE 8: BRAF Mutations

MODULE 9: NRG Fusions

MODULE 10: Appendix of Key Publications

Case Presentation: A 67-year-old woman with metastatic NSCLC and a HER2 exon 19 mutation pathogenic variant – PD-L1 TPS 15%



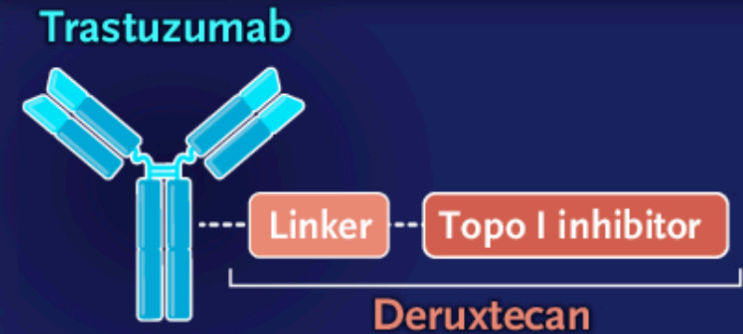
Dr Rajni Sinha (Atlanta, Georgia)

DESTINY-Lung01 Study

MULTICENTER, INTERNATIONAL, PHASE 2 STUDY

91

Adults with metastatic *HER2*-mutant NSCLC refractory to standard treatment (median follow-up, 13 mo)



Confirmed objective response
(assessed by independent central review)

55% (95% CI, 44–65)

Duration of response

9.3 mo

Progression-free survival

8.2 mo

Overall survival

17.8 mo

Grade 3 or higher drug-related adverse events occurred in 46% of patients.

Trastuzumab deruxtecan showed durable anticancer activity.

DESTINY-Lung01: Summary of Adverse Events and AEs of Clinical Interest

Event	N = 91
Discontinued due to AEs	25%
Dose reduction due to AEs	34%
Dose interruption due to AEs	32%
Drug-related interstitial lung disease (ILD)	26% (N = 24)
Grade 1	3 pts
Grade 2	15 pts
Grade 3	4 pts
Grade 5	2 pts
Median time to onset of ILD	141 days
Median duration of ILD	43 days

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Dr Carrizosa: A 30-year-old man with metastatic NSCLC and an NTRK fusion – PD-L1 TPS 10%

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Case Presentation: A 30-year-old man with metastatic NSCLC and an NTRK fusion – PD-L1 TPS 10%



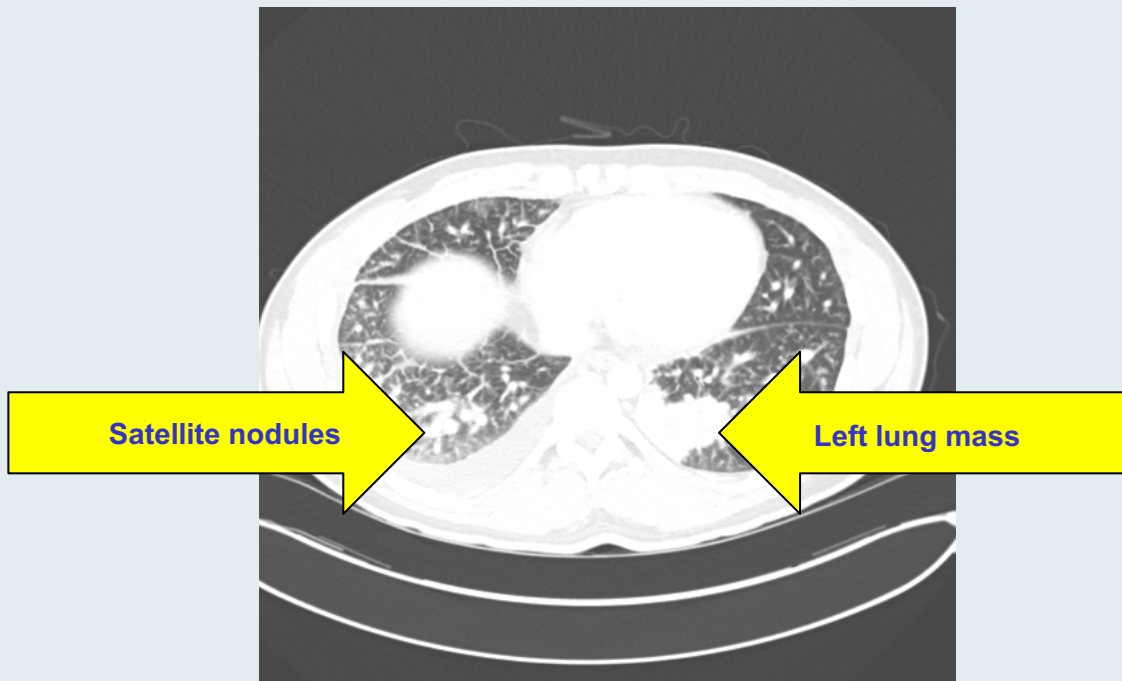
Dr Daniel R Carrizosa (Charlotte, North Carolina)

Case Presentation: A 30-year-old man with metastatic NSCLC and an NTRK fusion – PD-L1 TPS 10% (continued)

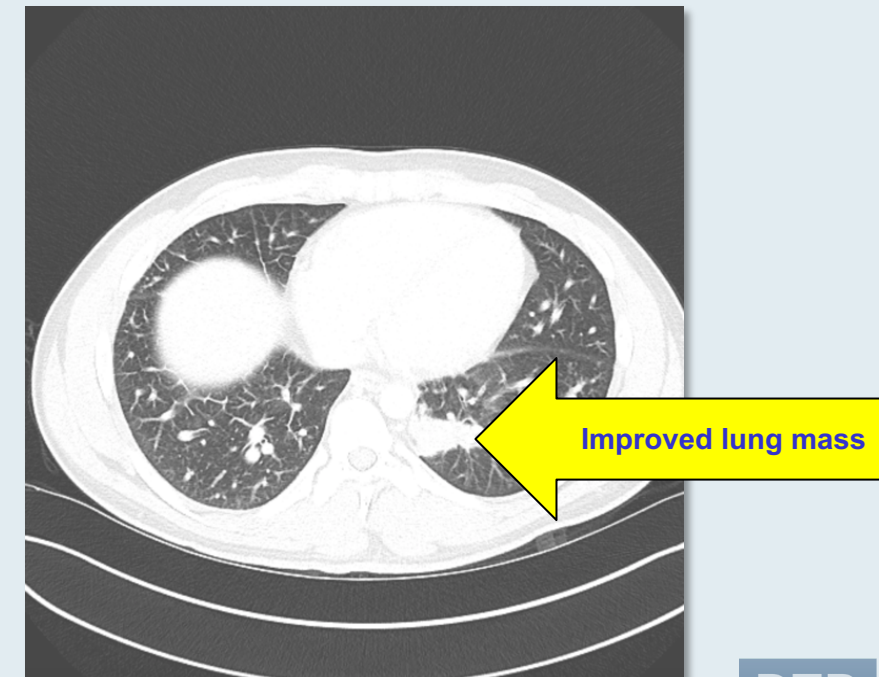


Dr Daniel R Carrizosa
(Charlotte, North Carolina)

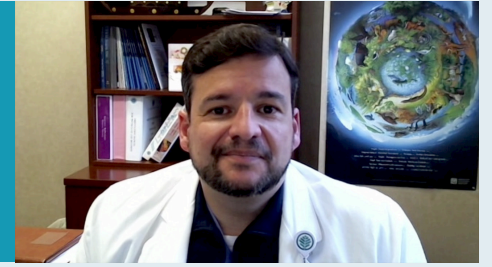
Baseline CT



CT after carboplatin/paclitaxel with
bevacizumab and atezolizumab

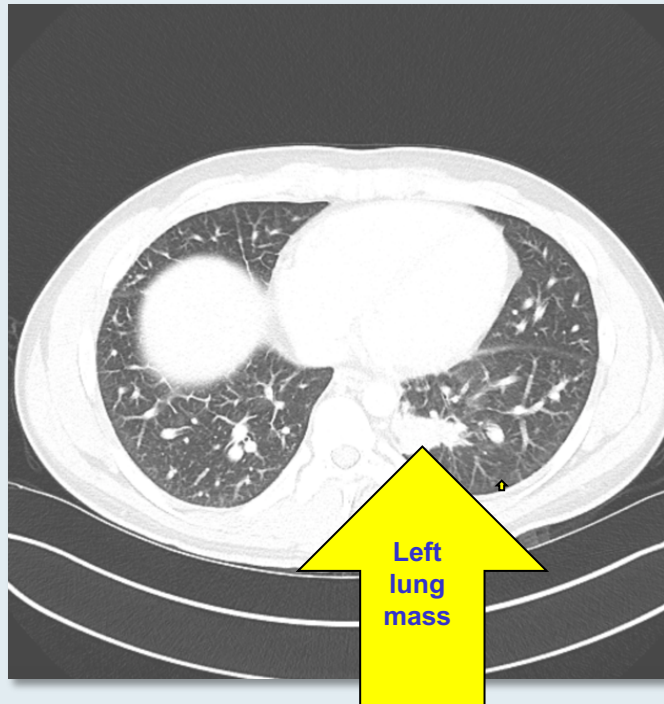


Case Presentation: A 30-year-old man with metastatic NSCLC and an NTRK fusion – PD-L1 TPS 10% (continued)

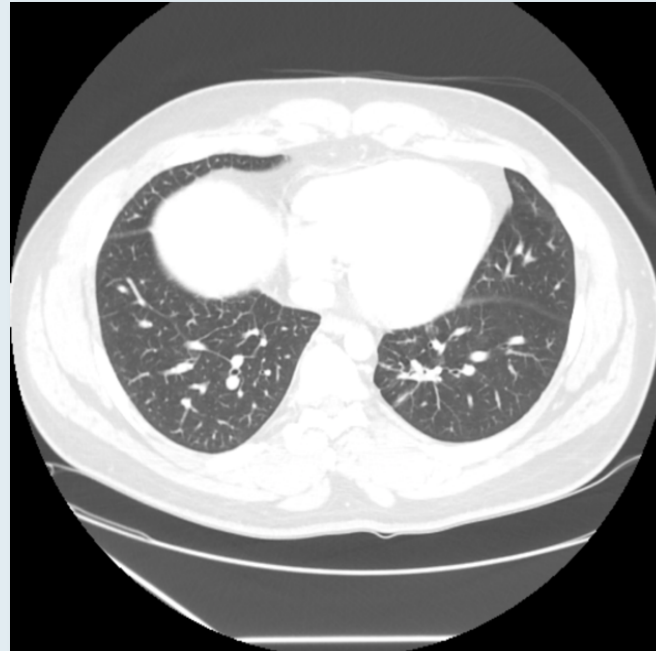


**Dr Daniel R Carrizosa
(Charlotte, North Carolina)**

**CT after carboplatin/paclitaxel with
bevacizumab and atezolizumab**



CT after entrectinib



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Key Trials of ROS1 TKIs for TKI-Naïve NSCLC with ROS1 Fusions

ROS1 TKI	Study	Phase	ORR	Median DoR	Median PFS	Intracranial ORR
Crizotinib	PROFILE 1001	Ib	38/53 (72%)	25 mo	19 mo	—
	OxOnc	II	91/127 (72%)	20 mo	16 mo	—
	EUCROSS	II	21/30 (70%)	19 mo	20 mo	—
	AcSe	II	35/36 (69%)	—	6 mo	—
	METROS	II	17/26 (65%)	21 mo	23 mo	33%
Entrectinib	Drilon et al	I/II	41/53 (77%)	25 mo	19 mo	55%
Ceritinib	Lim et al	II	20/30 (67%)	21 mo	19 mo	29%
Brigatinib	Gettinger et al	I	1/1 (100%)	—	—	—
Lorlatinib	Shaw et al	I/II	13/21 (62%)	25 mo	21 mo	64%
Repotrectinib	Cho et al	I/II	10/11 (91%)	—	—	100%
Taletrectinib	Fujiwara et al	I	6/9 (67%)	—	—	—

Key Trials of ROS1 TKIs for TKI-Pretreated NSCLC with ROS1 Fusions

ROS1 TKI	Study	Phase	ORR
Entrectinib (after crizotinib)	Drilon et al	I/II	0/6 (0%)
Ceritinib (after crizotinib)	Lim et al	II	0/2 (0%)
Brigatinib (after crizotinib)	Gettinger et al	I	0/2 (0%)
Lorlatinib	Shaw et al	I/II	After crizotinib: 14/40 (35%) After ≥2 prior TKIs: 0/6 (0%)
Repotrectinib	Drilon et al	I/II	After 1 prior TKI: 7/18 (39%) After ≥2 prior TKIs: 2/7 (29%)
Taletrectinib (after crizotinib)	Fujiwara et al	I	1/3 (33%)

Abstract 3255

Phase 1/2 TRIDENT-1 Study of Repotrectinib in Patients with *ROS1+* or *NTRK+* Advanced Solid Tumors

Byoung Chul Cho,¹ Robert C. Doebele,² Jessica J. Lin,³ Misako Nagasaka,⁴ Christina Baik,⁵ Anthonie J. van der Wekken,⁶ Vamsidhar Velcheti,⁷ Ki Hyeong Lee,⁸ Stephen V. Liu,⁹ Benjamin Solomon,¹⁰ Steven Kao,¹¹ Matthew G. Krebs,¹² Viola Zhu,¹³ Shanna Stopatschinskaja,¹⁴ D. Ross Camidge,¹⁵ Alexander Drilon¹⁶

¹Yonsei Cancer Center, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; ²University of Colorado Anschutz Medical Campus, Aurora, CO, USA;

³Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; ⁴Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA;

⁵Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, University of Washington School of Medicine, Seattle, WA, USA;

⁶University of Groningen and University Medical Centre Groningen, Groningen, Netherlands; ⁷Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA;

⁸Chungbuk National University Hospital, Cheongju, Republic of Korea; ⁹Georgetown Lombardi Comprehensive Cancer Center, Georgetown University, Washington D.C., USA;

¹⁰Peter MacCallum Cancer Center, Melbourne, Australia; ¹¹The Chris O'Brien Lifecare, Camperdown, Australia;

¹²Division of Cancer Sciences, The University of Manchester and the Christie NHS Foundation Trust, Manchester, UK;

¹³Chao Family Comprehensive Cancer Center, University of California Irvine School of Medicine, Orange, CA, USA; ¹⁴Turning Point Therapeutics Inc., San Diego, CA, USA;

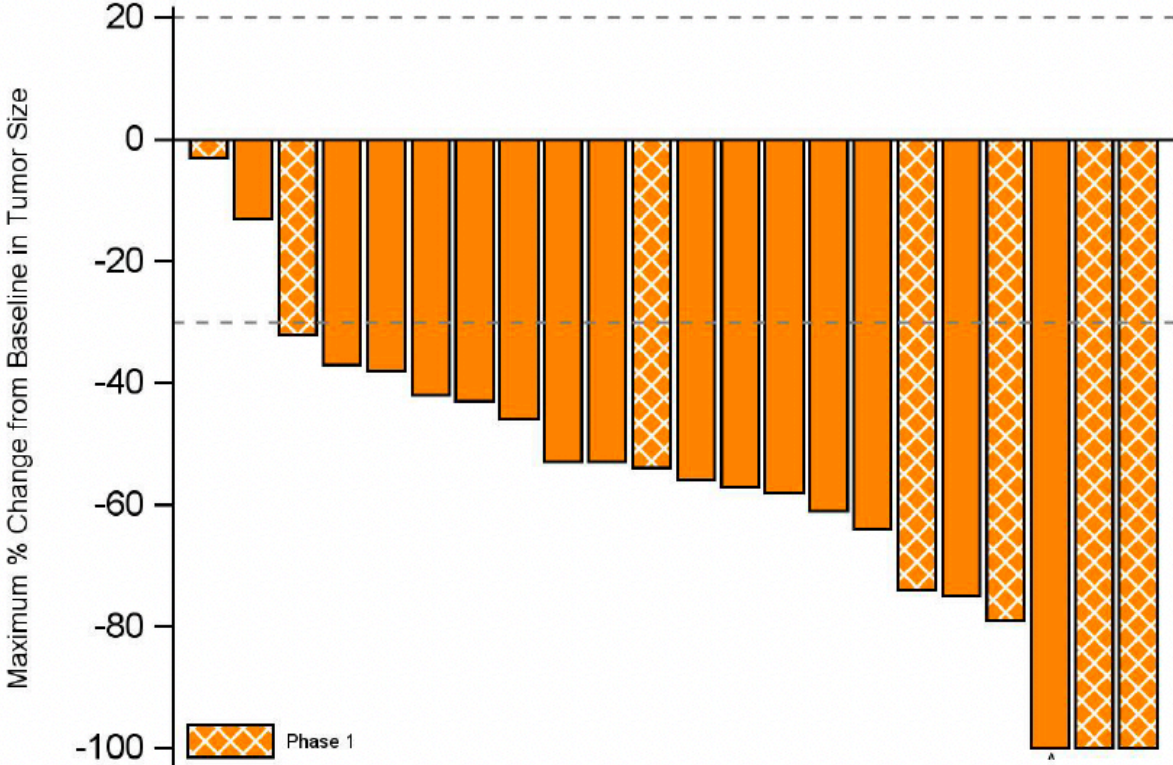
¹⁵Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA



2020 World Conference
on Lung Cancer Singapore

TRIDENT-1: Clinical Activity in TKI-Naïve Advanced NSCLC with ROS1 Fusions

Overall Response (N=22)



^ = Patient previously a confirmed partial response now in unconfirmed CR on treatment.

	Phase 2 N=15	Phase 1+2 N=22
Confirmed ORR, % (95% CI)	93% (68–100)	91% (71–99)

N=22 patients with baseline and at least two post baseline scans

- N=15 Phase 2 patients
- N=7 Phase 1 patients treated at or above the Phase 2 recommended dose

As of 31 December 2020, the 16th patient in Phase 2 has an unconfirmed PR and is on treatment awaiting a second post-baseline confirmatory scan.

AACR-NCI-EORTC Virtual International Conference on

MOLECULAR TARGETS AND CANCER THERAPEUTICS

October 7-10, 2021



Poster #: P224

Update from the Phase 2 registrational trial of repotrectinib in TKI-pretreated patients with *ROS1+* advanced non-small cell lung cancer and with *NTRK+* advanced solid tumors (TRIDENT-1)

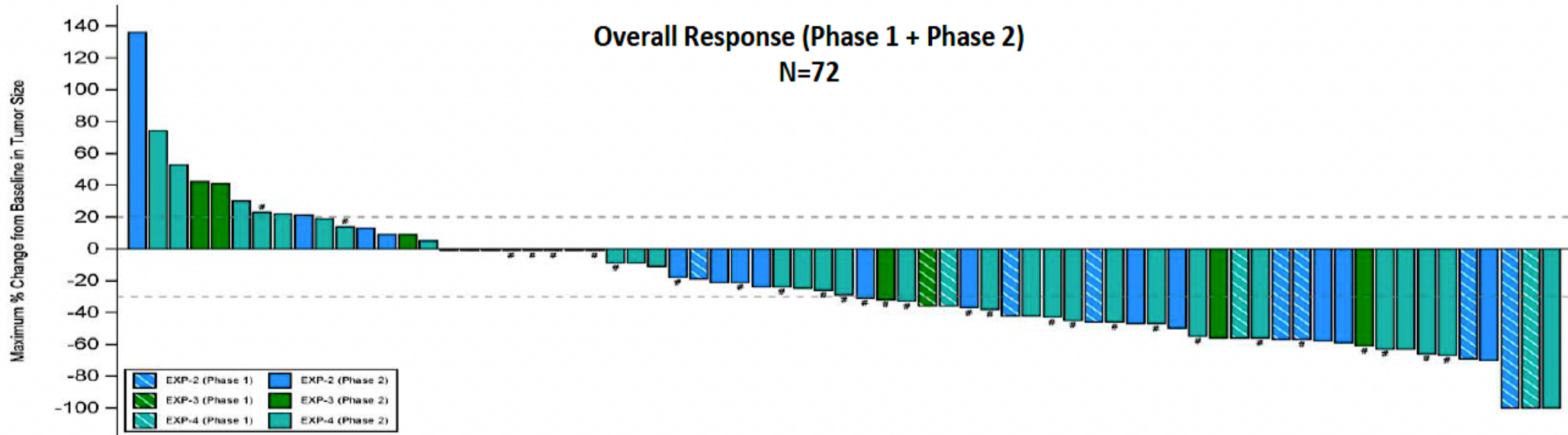
Jessica J. Lin,¹ Byoung Chul Cho,² Christoph Springfeld,³ D. Ross Camidge,⁴ Benjamin Solomon,⁵ Christina Baik,⁶ Vamsidhar Velcheti,⁷ Young-Chul Kim,⁸ Victor Moreno,⁹ Anthonie J. van der Wekken,¹⁰ Enriqueta Felip,¹¹ Dipesh Uprety,¹² Denise Trone,¹³ Shanna Stopatschinskaja,¹³ Alexander Drilon¹⁴

¹Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; ²Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; ³Heidelberg University Hospital, National Center for Tumor Diseases, Department of Medical Oncology, Heidelberg, Germany; ⁴University of Colorado Denver, Anschutz Medical Campus, Aurora, CO, USA; ⁵Peter MacCallum Cancer Center, Melbourne, Australia; ⁶University of Washington School of Medicine, Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; ⁷NYU Perlmutter Cancer Center, New York, NY, USA; ⁸Chonnam National University Medical School, and CNU Hwasun Hospital, Hwasun-gun, Republic of Korea; ⁹Fundación Jiménez Díaz - START Madrid, Madrid, Spain; ¹⁰University of Groningen, University Medical Centre Groningen, Groningen, Netherlands; ¹¹Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; ¹²Karmanos Cancer Institute, Detroit, MI, USA; ¹³Turning Point Therapeutics Inc, San Diego, CA, USA; ¹⁴Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA.

TRIDENT-1: Phase II Study Design

ROS1+ Advanced NSCLC				NTRK+ Advanced Solid Tumors	
EXP-1 ROS1 TKI naïve (N=55)	EXP-2 1 prior ROS1 TKI AND 1 platinum-based chemotherapy (N=60)	EXP-3 2 prior ROS1 TKIs AND No prior chemotherapy (N=40)	EXP-4 1 prior ROS1 TKI AND No prior chemotherapy (N=60)	EXP-5 TRK TKI naïve (N=55)	EXP-6 TRK TKI pretreated (N=40)
	Treated (N=21)	Treated (N=11)	Treated (N=44)	Data from NTRK+ cohorts (EXP-5 and EXP-6) will be presented at LB# 6546 during Plenary Session 2: New Drugs on the Horizon I	
	Efficacy Evaluable (N=16)	Efficacy Evaluable (N=9)	Efficacy Evaluable (N=36)		

TRIDENT-1: Preliminary Efficacy in Patients with TKI-Pretreated Advanced NSCLC with ROS1 Fusions



#Patient remains on treatment
3 patients not displayed due to discontinuing treatment prior to first post-baseline scans.

	EXP-2		EXP-3		EXP-4	
	Phase 2 (N=16)	Phase 1 + 2 (N=23)	Phase 2 (N=9)	Phase 1 + 2 (N=10)	Phase 2 (N=36)	Phase 1 + 2 (N=39)
Confirmed ORR (cORR) (95% CI)	31% (11 - 59)	39% (20 - 61)	33% (7 - 70)	30% (7 - 65)	31%* (16 - 48)	33%* (19 - 50)
Duration of Response (range in months)	1.8+ - 9.2 n=5	1.8+ - 11.1 n=9	1.9+ - 12.9+ n=3	1.9+ - 12.9+ n=3	1.7+ - 15.0+ n=11	0.8+ - 15.0+ n=13

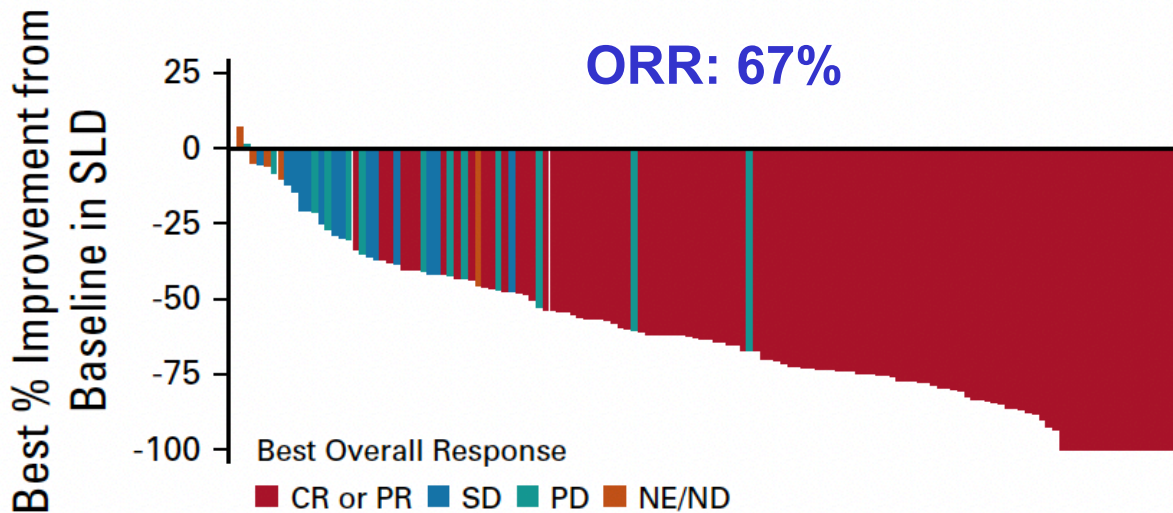
Updated Integrated Analysis of the Efficacy and Safety of Entrectinib in Locally Advanced or Metastatic *ROS1* Fusion–Positive Non–Small-Cell Lung Cancer

Rafal Dziadziuszko, MD, PhD¹; Matthew G. Krebs, MD, PhD²; Filippo De Braud, MD^{3,4}; Salvatore Siena, MD^{3,5}; Alexander Drilon, MD⁶; Robert C. Doebele, MD, PhD⁷; Manish R. Patel, DO⁸; Byoung Chul Cho, MD, PhD⁹; Stephen V. Liu, MD¹⁰; Myung-Ju Ahn, MD, PhD¹¹; Chao-Hua Chiu, MD¹²; Anna F. Farago, MD, PhD¹³; Chia-Chi Lin, MD¹⁴; Christos S. Karapetis, MBBS, MMedSc¹⁵; Yu-Chung Li, MD¹⁶; Bann-mo Day, PhD¹⁷; David Chen, PharmD¹⁷; Timothy R. Wilson, PhD¹⁷; and Fabrice Barlesi, MD, PhD^{18,19}

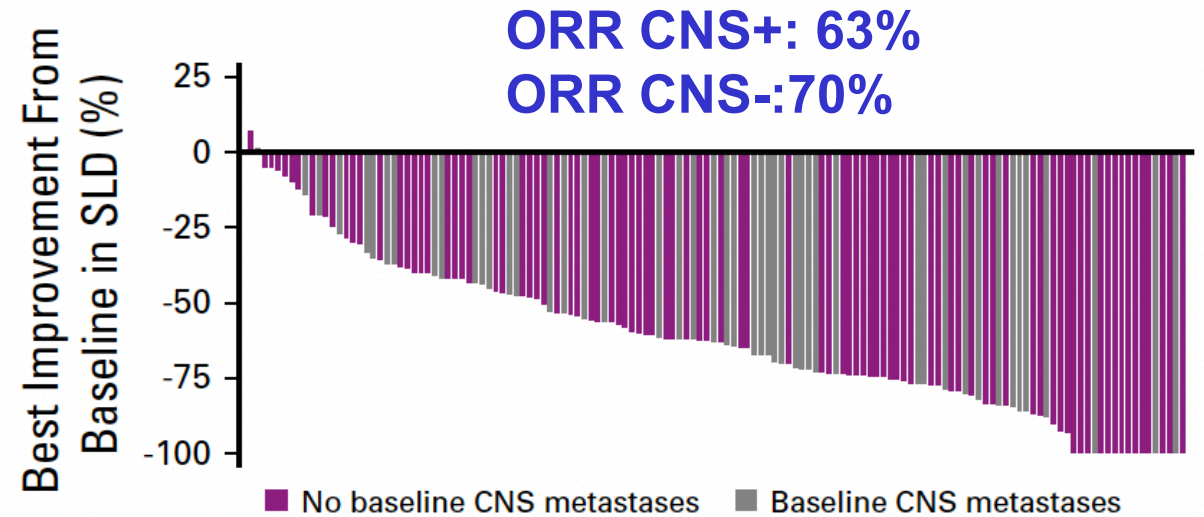
J Clin Oncol 2021;39(11):1253-63.

Integrated Analysis of ALKA-372-001, STARTRK-1, STARTRK-2, and STARTRK-NG

Efficacy Evaluable Population (N = 161)



Patients with (n = 56) and without (n = 105) CNS Metastases at Baseline




ORR = objective response rate

Future Oncol 2022;[Online ahead of print].

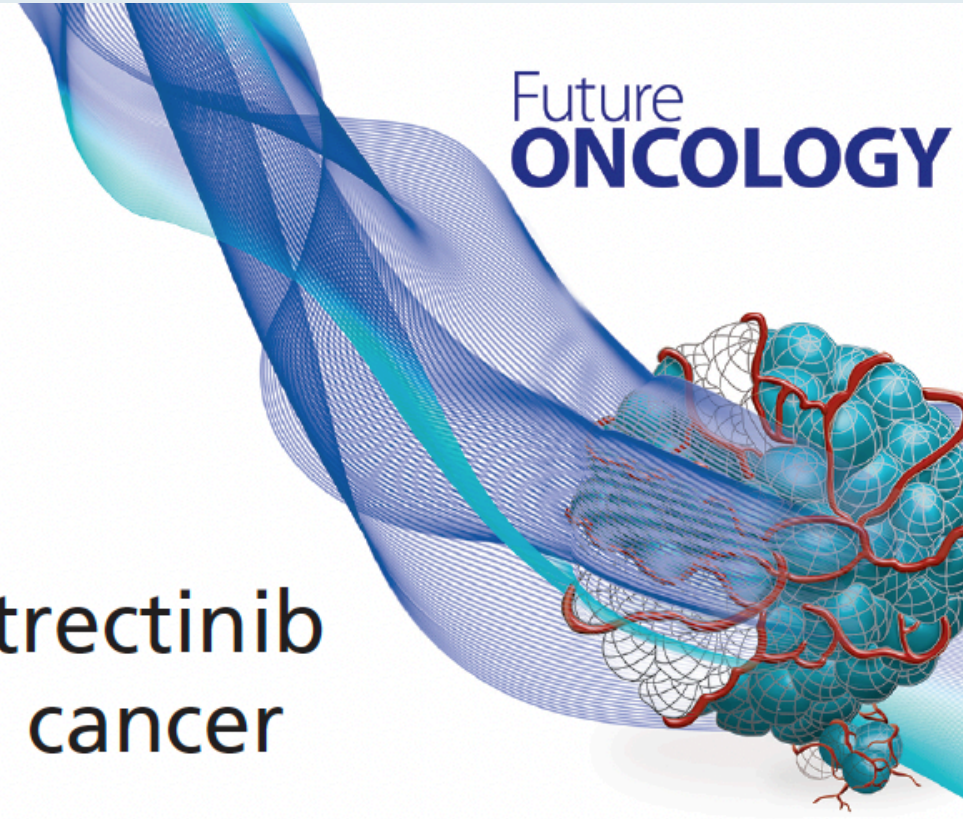
Research Article

For reprint orders, please contact: reprints@futuremedicine.com

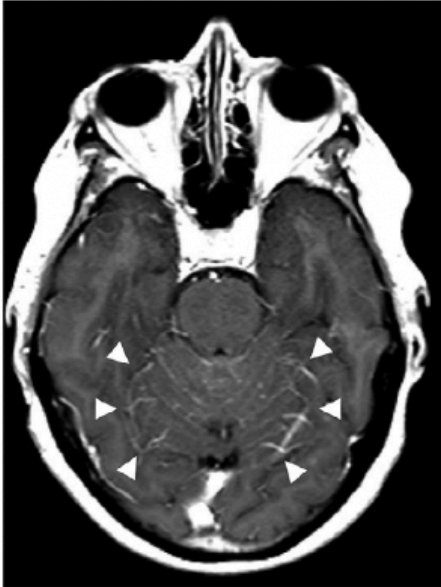
Effectiveness of crizotinib versus entrectinib in *ROS1*-positive non-small-cell lung cancer using clinical and real-world data

Gabriel Tremblay^{*,1} , Michael Groff¹, Laura Iadeluca², Patrick Daniele¹, Keith Wilner², Robin Wiltshire², Lauren Bartolome², Tiziana Usari², Joseph C Cappelleri² & D Ross Camidge³

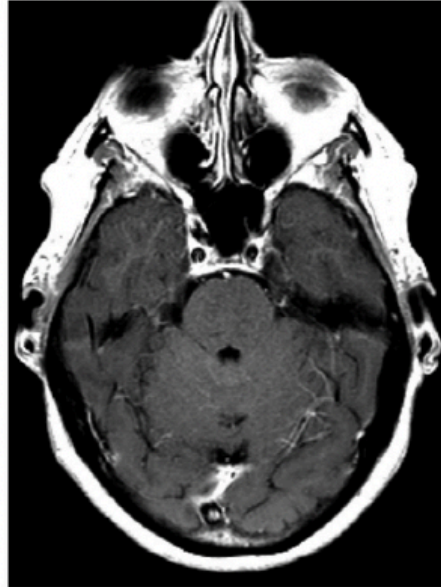
Future
ONCOLOGY



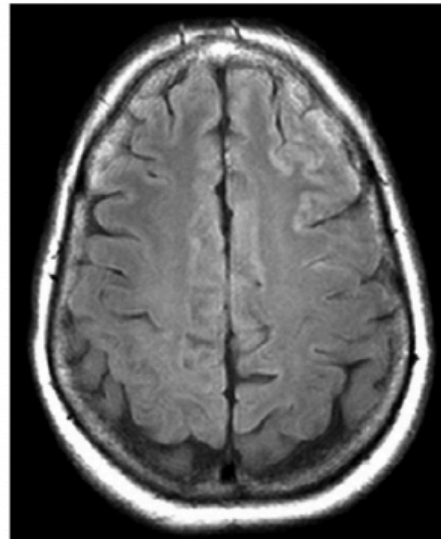
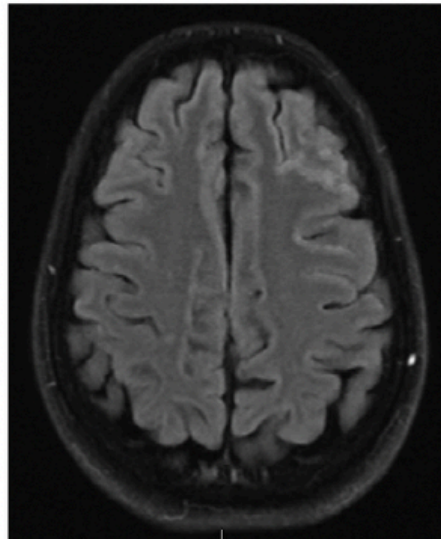
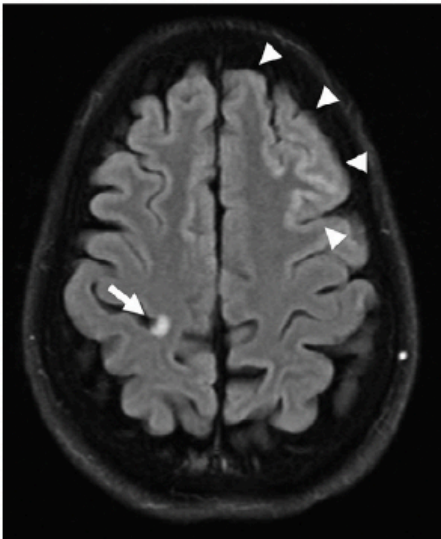
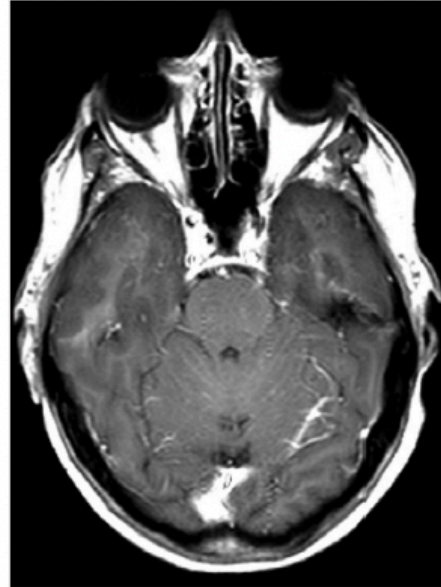
Progression on pralsetinib



6 weeks on selpercatinib



10 weeks on selpercatinib



T1-weighted postgadolinium
(top row)

Postcontrast T2-weighted
FLAIR (bottom row) MRI

Arrow heads highlight
leptomeningeal enhancement.
Arrow highlights brain metastasis
which was treated with SRS

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Pralsetinib for *RET* fusion-positive non-small-cell lung cancer (ARROW): a multi-cohort, open-label, phase 1/2 study



Justin F Gainor, Giuseppe Curigliano, Dong-Wan Kim, Dae Ho Lee, Benjamin Besse, Christina S Baik, Robert C Doebele, Philippe A Cassier, Gilberto Lopes, Daniel SW Tan, Elena Garralda, Luis G Paz-Ares, Byoung Chul Cho, Shirish M Gadgil, Michael Thomas, Stephen V Liu, Matthew H Taylor, Aaron S Mansfield, Viola W Zhu, Corinne Clifford, Hui Zhang, Michael Palmer, Jennifer Green, Christopher D Turner, Vivek Subbiah

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AUGUST 27, 2020

VOL. 383 NO. 9

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

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

Pivotal Studies of Selpercatinib and Pralsetinib for Advanced NSCLC with RET Fusion

	Selpercatinib ¹	Pralesetinib ²
Pivotal study	LIBRETTO-001 Phase I/II (N = 105)	ARROW Phase I/II (N = 233)
FDA approval	May 8, 2020	September 4, 2020
Setting	Previous platinum-based chemotherapy and previously untreated	Previous platinum-based chemotherapy and previously untreated
ORR	64%	61%
Median duration of response	17.5 months	Not reached
Common Grade ≥3 adverse events	Hypertension (14%) Increased ALT (12%) and AST (10%) Hyponatremia (6%) Lymphopenia (6%)	Neutropenia (18%) Hypertension (11%) Anemia (10%) Decreased WBC (6%)

¹ Drilon A et al. *N Engl J Med* 2020;383(9):813-24. ² Gainor JF et al. *Lancet Oncol* 2021;22(7):959-69.

Clin Lung Cancer 2021;23(1):e5–8.

Case Report

Central Nervous System Response to Selpercartinib in Patient With *RET*-rearranged Non-small Cell Lung Cancer After Developing Leptomeningeal Disease on Pralsetinib

David Chun Cheong Tsui,¹ Brian D. Kavanagh,² Justin M. Honce,³
Candice Rossi,¹ Tejas Patil,¹ D. Ross Camidge¹

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ORIGINAL ARTICLE

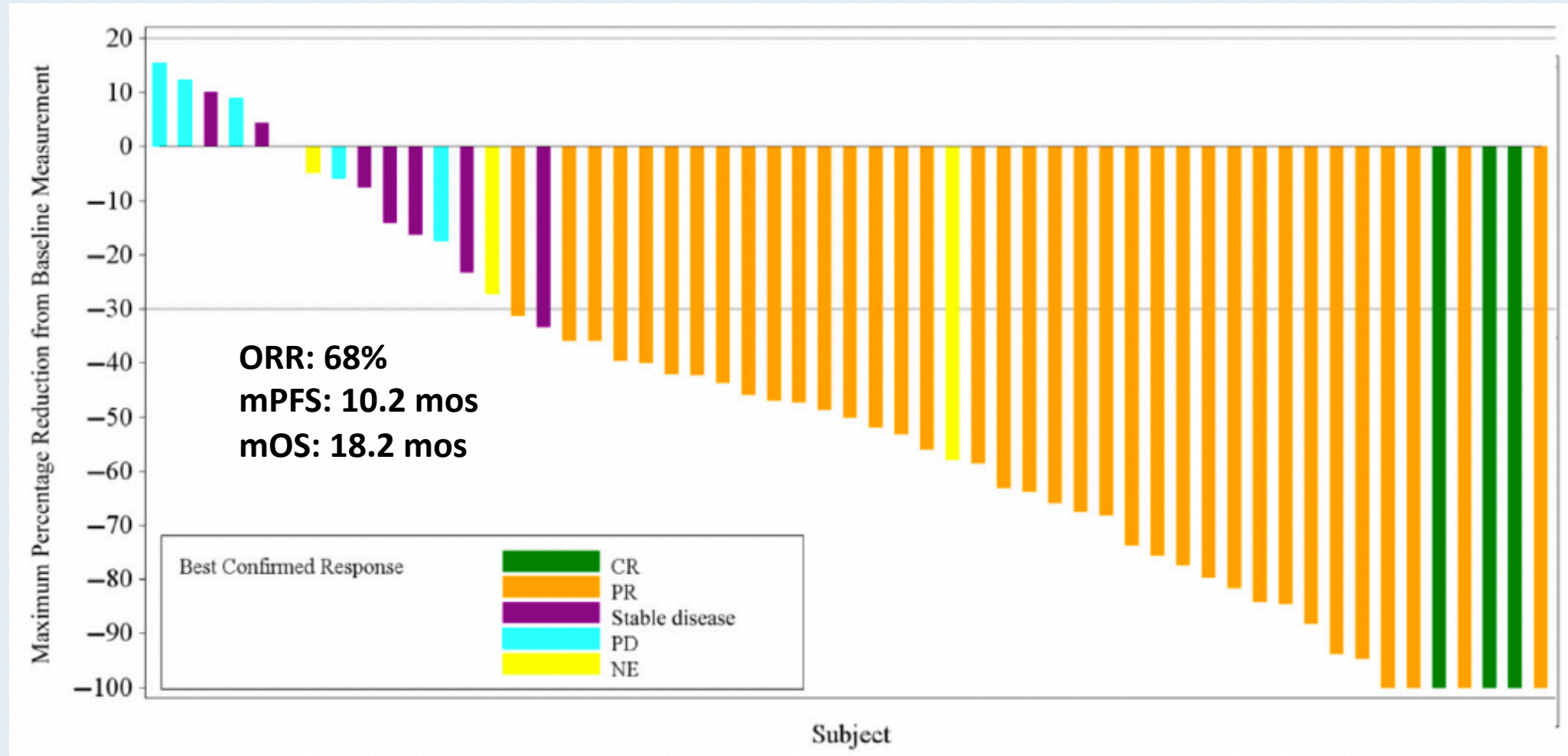


Phase 2 Study of Dabrafenib Plus Trametinib in Patients With *BRAF* V600E-Mutant Metastatic NSCLC: Updated 5-Year Survival Rates and Genomic Analysis

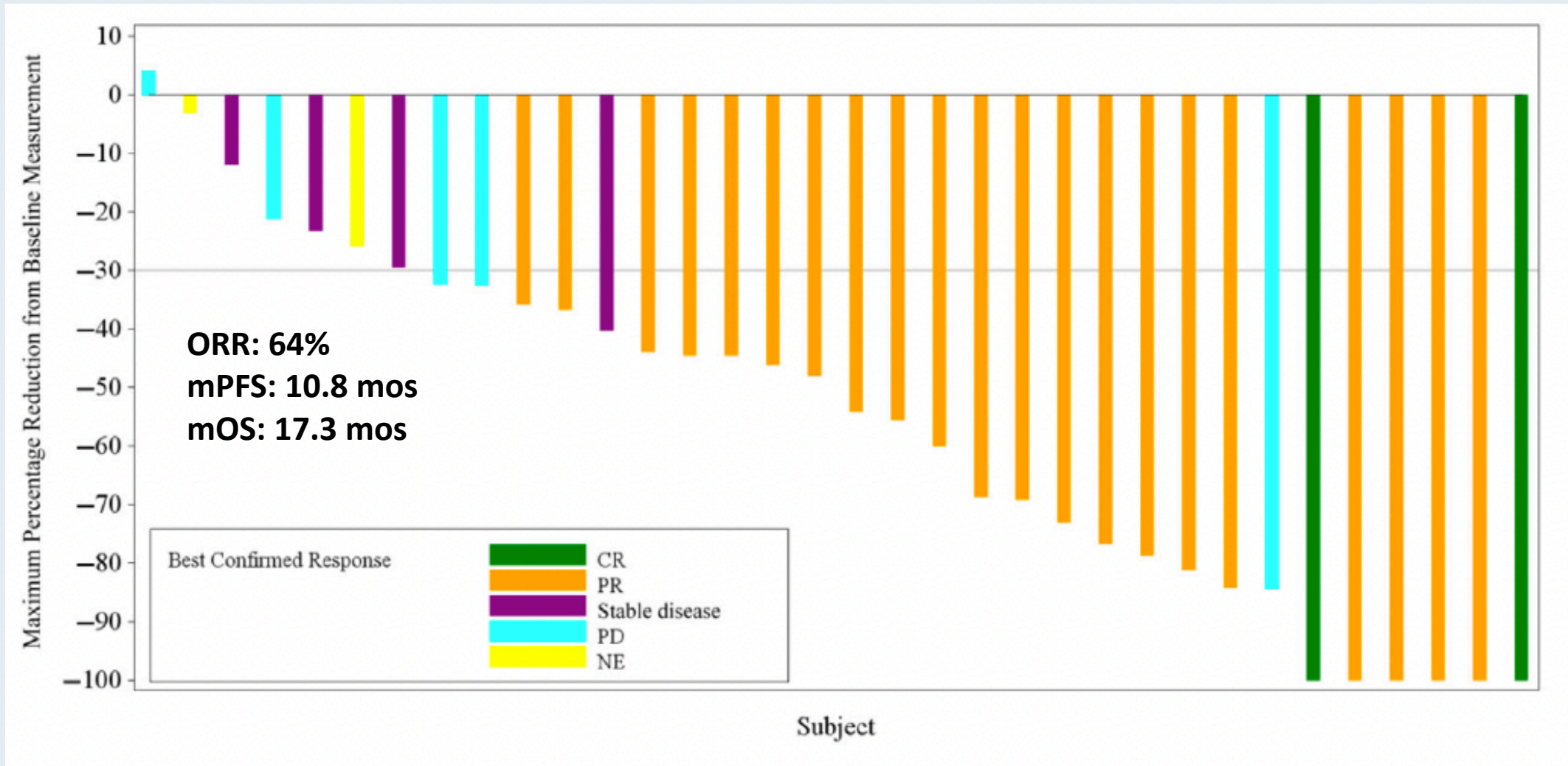
David Planchard, MD,^a Benjamin Besse, MD,^a Harry J. M. Groen, MD,^b Sayed M. S. Hashemi, MD,^c Julien Mazieres, MD,^d Tae Min Kim, MD, PhD,^e Elisabeth Quoix, MD, PhD,^f Pierre-Jean Souquet, MD,^g Fabrice Barlesi, MD, PhD,^{a,h} Christina Baik, MD, MPH,ⁱ Liza C. Villaruz, MD,^j Ronan J. Kelly, MD,^k Shirong Zhang, PhD,^l Monique Tan, MD,^l Eduard Gasal, MD,^l Libero Santarpia, MD, PhD,^m Bruce E. Johnson, MD^{n,*}

Five-Year Update: Phase II Study of Dabrafenib/Trametinib for BRAF V600E-Mutant Metastatic NSCLC

Pre-Treated Patients (N = 57)



Five-Year Update: Phase II Study of Dabrafenib/Trametinib for BRAF V600E-Mutant Metastatic NSCLC Treatment-Naïve Patients (N = 36)



Five-Year Update: Phase II Study of Dabrafenib/Trametinib for BRAF V600E-Mutant Metastatic NSCLC

Outcomes According to Genomic Alterations Detected by NGS

Cohort	Genetic Alterations	Cohort	Best Response	PFS, mo	OS, mo
Dabrafenib plus trametinib (cohort B; ORR, 68.4%; mPFS, 10.2 mo; mOS, 18.2 mo)	<i>BRAF</i> V600E+ <i>IDH1</i> R132C	B	CR	6.9	40.7
	<i>BRAF</i> V600E+ <i>KRAS</i> G13C	B	PR	58.1	58.1
	<i>BRAF</i> V600E+ <i>IDH1</i> R132L ^{a,b}	B	PR	32.4	32.4
	<i>BRAF</i> V600E+ <i>PIK3CA</i> E542K ^c	B	PR	16.7	55.2
	<i>BRAF</i> V600E+ <i>cMET</i> ex14 skipping	B	PR	10.2	18.2
	<i>BRAF</i> V600E+ <i>PIK3CA</i> E545K ^c	B	NE	1.4	3.8
	<i>BRAF</i> V600E+ <i>PIK3CA</i> E545K ^c	B	PD	1.4	3.1
	<i>cMET</i> T1010I ^d	B	PR	27.6	59.4
	<i>JAK3</i> S493C ^d	B	PR	5.6	10.3
	<i>KRAS</i> G12V ^d	B	PD	2.9	4.4
Dabrafenib plus trametinib (cohort C; ORR, 63.9%; mPFS, 10.8 mo; mOS, 17.3 mo)	<i>BRAF</i> V600E+ <i>mTORT</i> 1977K ^c	C	PR	7.0	7.0
	<i>BRAF</i> V600E+ <i>IDH1</i> R132C	C	PR	10.4	17.3
	<i>BRAF</i> V600E+ <i>IDH1</i> R132L	C	PR	5.5	8.2
	<i>BRAF</i> V600E+ <i>BRAF</i> G466V	C	Stable disease	19.4	40.2
	<i>ALK</i> fusion ^{d,e}	C	Stable disease	13.8	40.9 ^f
	<i>JAK3</i> S493C ^d	C	PR	19.3	51.2 ^f

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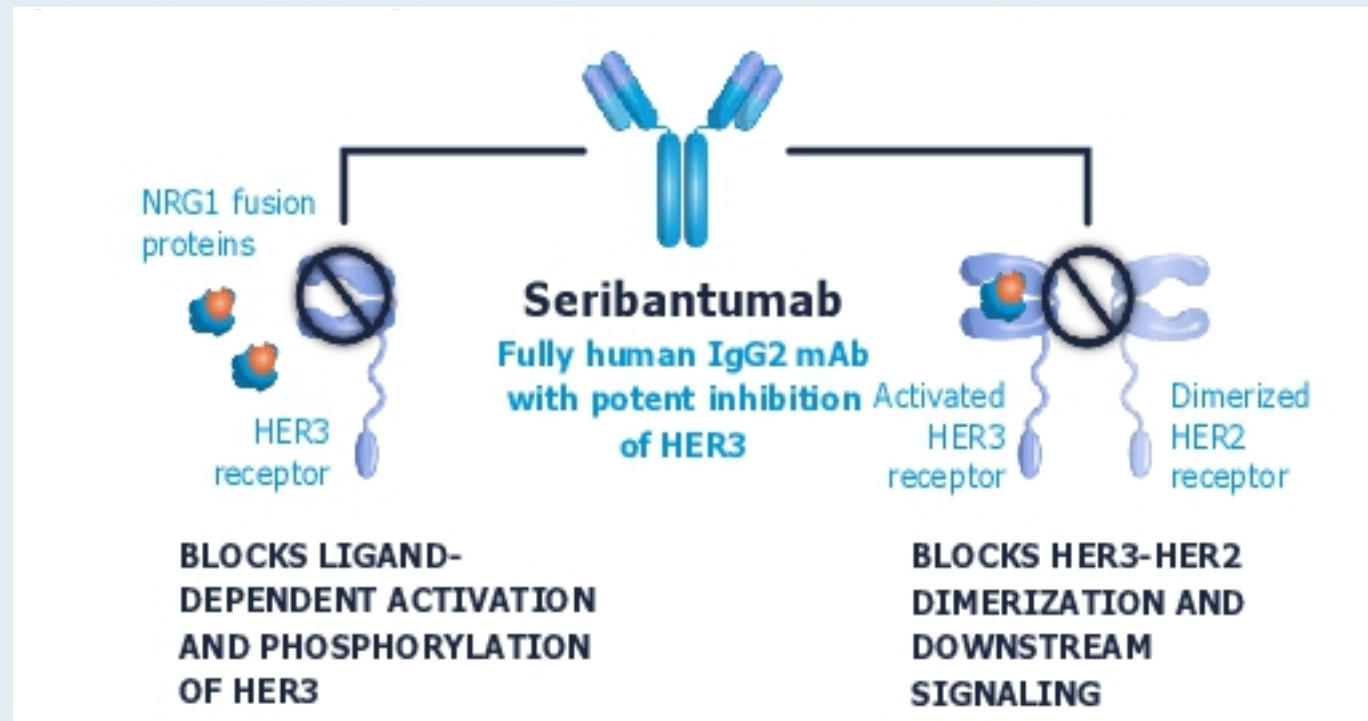
MODULE 8: BRAF Mutations

MODULE 9: NRG1 Fusions

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Neuregulin-1 (NRG1) Gene Fusions and Seribantumab Mechanism of Action

- NRG1 gene fusions are rare oncogenic drivers found in 0.2% of solid tumors including lung, colorectal, breast and ovarian
- NRG1 fusion proteins predominantly retain an active EGF-like domain, which drives tumorigenesis and proliferation through aberrant HER3 activation
- Seribantumab is a fully human monoclonal antibody against HER3



Investigational New Drugs (2021) 39:1604–1612
<https://doi.org/10.1007/s10637-021-01145-y>

PHASE I STUDIES

Phase 1 dose escalation study of seribantumab (MM-121), an anti-HER3 monoclonal antibody, in patients with advanced solid tumors

Crystal S. Denlinger¹  · Vicki L. Keedy² · Victor Moyo³ · Gavin MacBeath³ · Geoffrey I. Shapiro⁴

Best Overall Response with and Recommended Phase II Dose of Seribantumab in Advanced Solid Tumors

Best response	Dose escalation (n = 25)	Dose expansion (n = 18)
Overall response	0	0
Complete response	0	0
Partial response	0	0
Stable disease	6 (24%)	7 (39%)
Progressive disease	11 (44%)	8 (44%)

- Most adverse events were transient and mild to moderate (Grade 1 or 2) in severity
- The maximum tolerated dose was not reached in the dose escalation portion, and the 40 mg/kg loading dose followed by 20 mg/kg weekly maintenance dose was considered well tolerated and chosen for the dose expansion portion of the study

CRESTONE: Ongoing Phase II Study of of Seribantumab in Patients With Neuregulin-1 (NRG1) Fusion-Positive Advanced Solid Tumors

Trial Identifier: NCT04383210 (Open)

Advanced solid tumor with an NRG1 gene fusion
Disease progression on or unresponsive to at least one prior standard therapy appropriate for their tumor type and stage of disease
No further available curative therapy options
No prior pan-ERBB or any ERBB/HER2/HER3 directed therapy (Cohort 1 only)

Primary Endpoint: Objective response rate

Seribantumab
1-h IV infusion at various doses once weekly, every 2 weeks and every 3 weeks, during the induction, consolidation and maintenance dosing phases, respectively

Patient Cohorts:

Cohort 1: A minimum of 55 adult advanced solid tumor patients harboring NRG1 gene fusions, who have received prior standard treatment, excluding prior ERBB-directed therapy.

Cohort 2: Up to 10 adult advanced solid tumor patients harboring NRG1 gene fusions, who have received prior standard treatment, including prior ERBB-directed therapy

Cohort 3: Up to 10 adult advanced solid tumor patients harboring NRG1 gene fusions lacking an EGF-like domain, who have received prior standard treatment, which may have included prior ERBB-directed therapy

Clinicopathologic Features and Response to Therapy of *NRG1* Fusion–Driven Lung Cancers: The eNRGy1 Global Multicenter Registry

Alexander Drilon, MD¹; Michael Duruisseaux, MD^{2,3,4}; Ji-Youn Han, MD, PhD⁵; Masaaki Ito, MD, PhD^{6,7,8}; Christina Falcon, MPH¹; Soo-Ryum Yang, MD¹; Yonina R. Murciano-Goroff, MD, DPhil⁹; Haiquan Chen, MD, PhD^{10,11}; Morihito Okada, PhD⁸; Miguel Angel Molina, PhD¹²; Marie Wislez, MD, PhD^{13,14}; Philippe Brun, MD¹⁵; Clarisse Dupont, MD²; Eva Branden, PhD^{16,17}; Giulio Rossi, MD, PhD^{18,19}; Alexa Schrock, PhD²⁰; Siraj Ali, MD, PhD²⁰; Valérie Gounant, MD²¹; Fanny Magne, MD²²; Torsten Gerriet Blum, MD²³; Alison M. Schram, MD⁹; Isabelle Monnet, MD²⁴; Jin-Yuan Shih, MD, PhD²⁵; Joshua Sabari, MD²⁶; Maurice Pérol, MD²⁷; Viola W. Zhu, MD²⁸; Misako Nagasaka, MD^{29,30}; Robert Doebele, MD, PhD³¹; D. Ross Camidge, MD, PhD³¹; Maria Arcila, MD¹; Sai-Hong Ignatius Ou, MD, PhD³²; Denis Moro-Sibilot, MD³³; Rafael Rosell, MD, PhD³⁴; Lucia Anna Muscarella, PhD³⁵; Stephen V. Liu, MD³⁶; and Jacques Cadranel, MD³⁷

J Clin Oncol 2021;39(25):2791-802.

Meet The Professor with Dr Camidge

Introduction: First-Line Systemic Treatment/Brain Metastases

MODULE 1: ALK Rearrangements

MODULE 2: KRAS G12C Mutations

MODULE 3: MET Exon 14 Skipping Mutations

MODULE 4: HER2 Mutations

MODULE 5: NTRK Fusions

MODULE 6: ROS1 Fusions

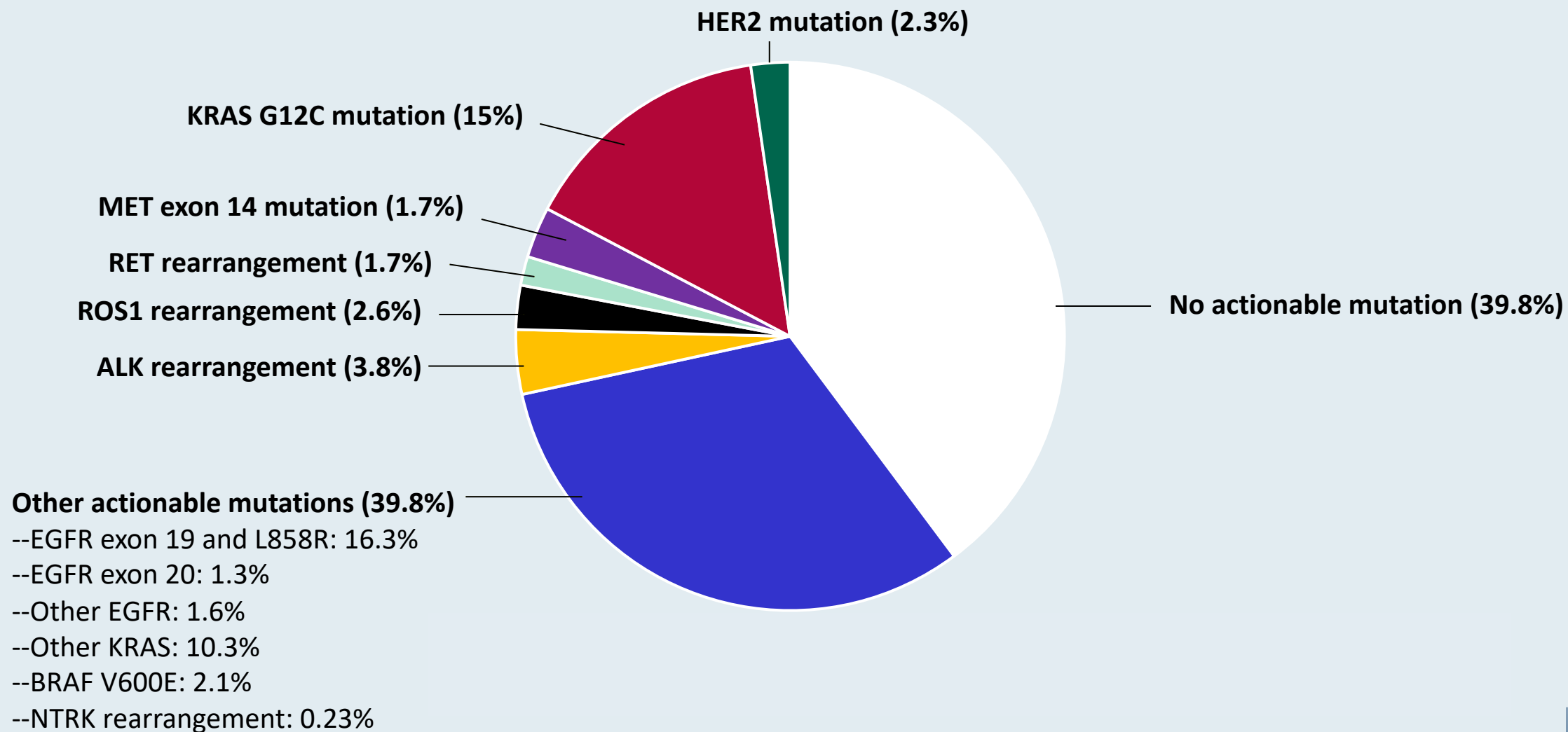
MODULE 7: RET Fusions

MODULE 8: BRAF Mutations

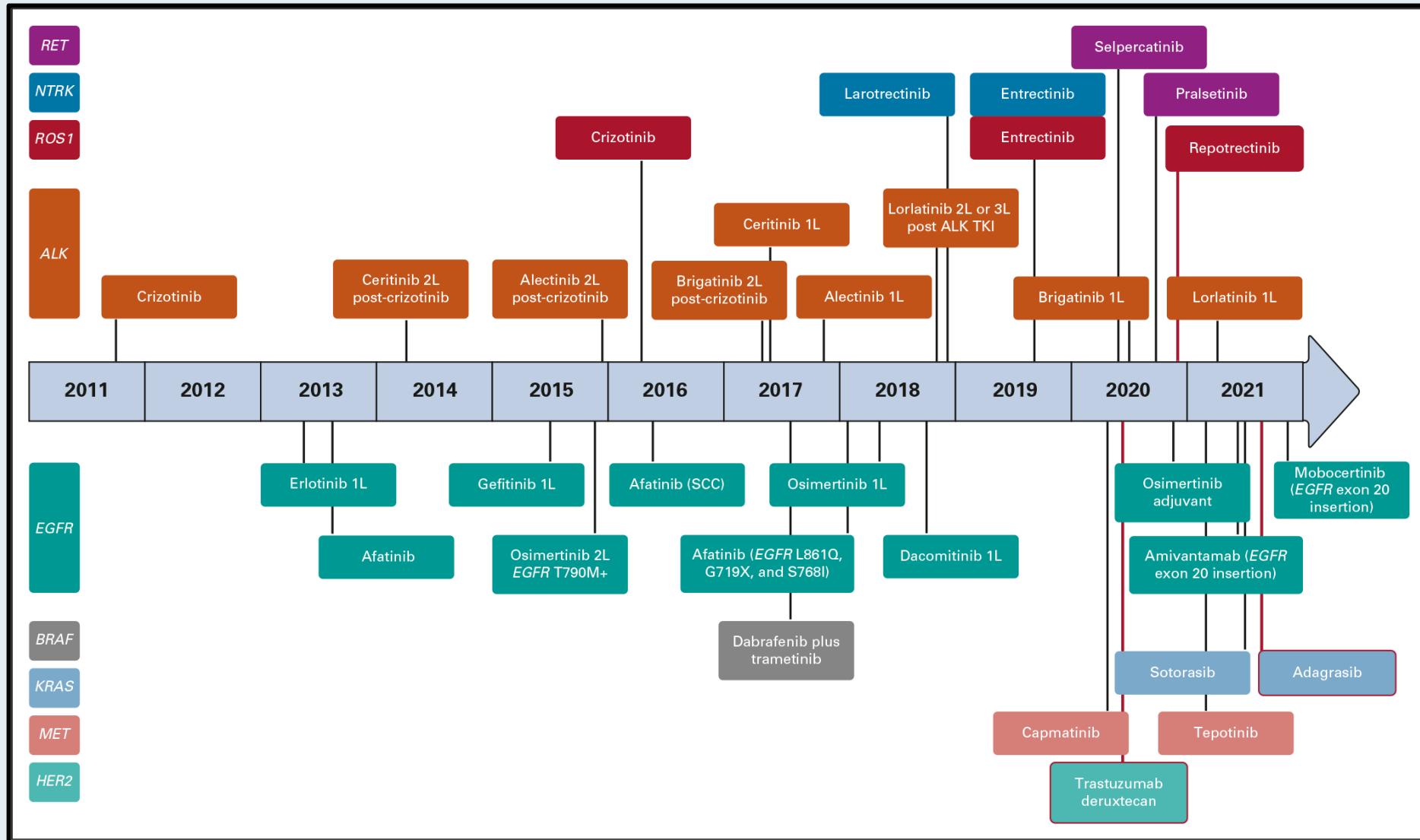
MODULE 9: NRG Fusions

MODULE 10: Appendix of Key Publications

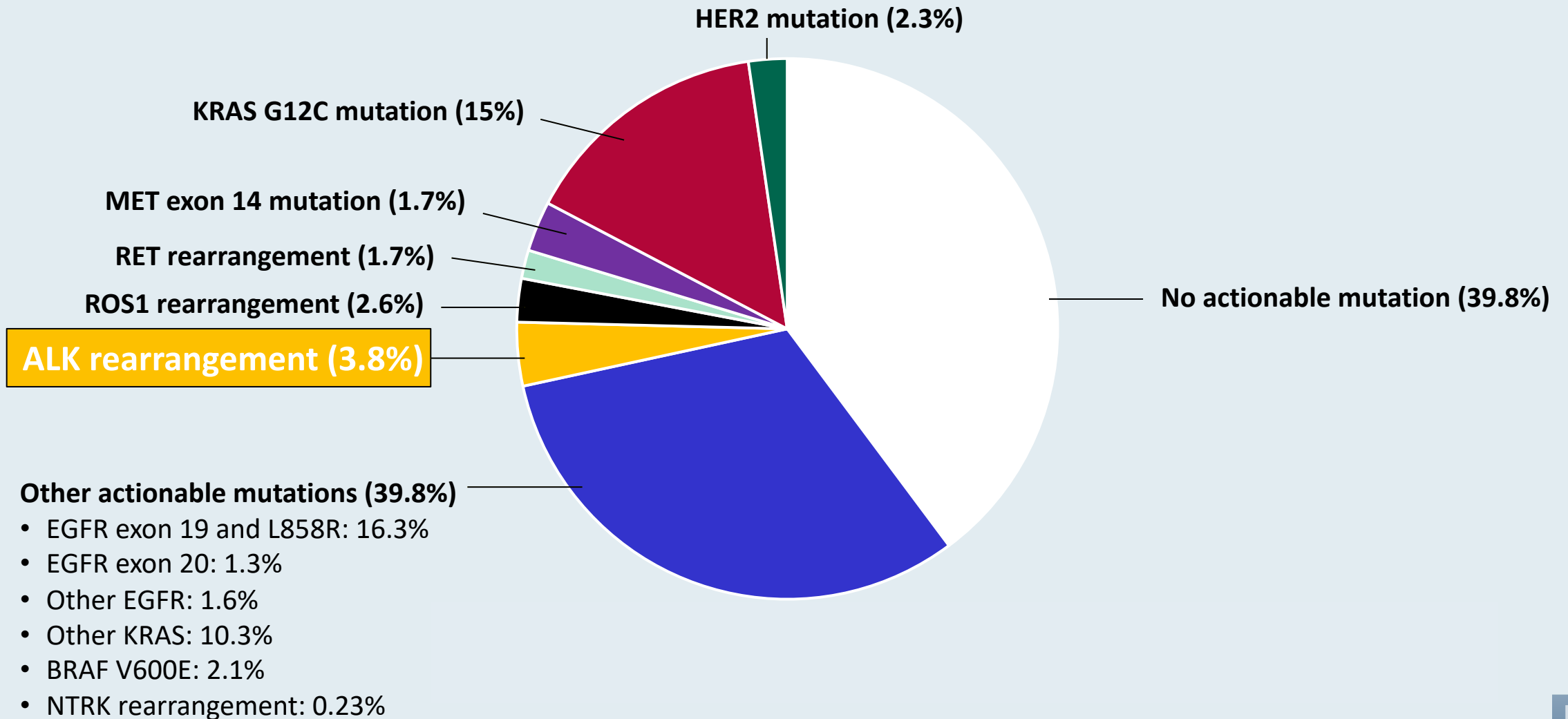
Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung



Timeline of Select FDA-Approved Targeted Therapies for Oncogene-Driven NSCLC



Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung



Key Randomized Trials in Treatment-Naïve Advanced ALK-Rearranged NSCLC

Study	Intervention	Comparator	ORR	CNS ORR
PROFILE 1014	Crizotinib	Platinum/pemetrexed	74% vs 45%	—
PROFILE 1029	Crizotinib	Platinum/pemetrexed	88% vs 46%	—
ASCEND-4	Ceritinib	Platinum/pemetrexed	73% vs 27%	73% vs 27%
ALEX	Alectinib	Crizotinib	83% vs 76%	81% vs 50%
J-ALEX	Alectinib	Crizotinib	92% vs 79%	—
ALESIA	Alectinib	Crizotinib	91% vs 77%	—
ALTA-1L	Brigatinib	Crizotinib	71% vs 60%	78% vs 26%
CROWN	Lorlatinib	Crizotinib	76% vs 58%	82% vs 23%
eXalt3	Ensartinib	Crizotinib	75% vs 67%	64% vs 21%

Tan AC et al. *J Clin Oncol* 2022;40(6):611-25; Soria JC et al. *Lancet* 2017;389(10072):917-29; Peters S et al. *N Engl J Med* 2017;377(9):829-38; Camidge DR et al. *J Thorac Oncol* 2021;16(12):2091-108; Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29; Horn L et al. *JAMA Oncol* 2021;7(11):1617-25; Popat S et al. ESMO 2021;Abstract 1195P.

Key Randomized Trials in Treatment-Naïve Advanced ALK-Rearranged NSCLC (continued)

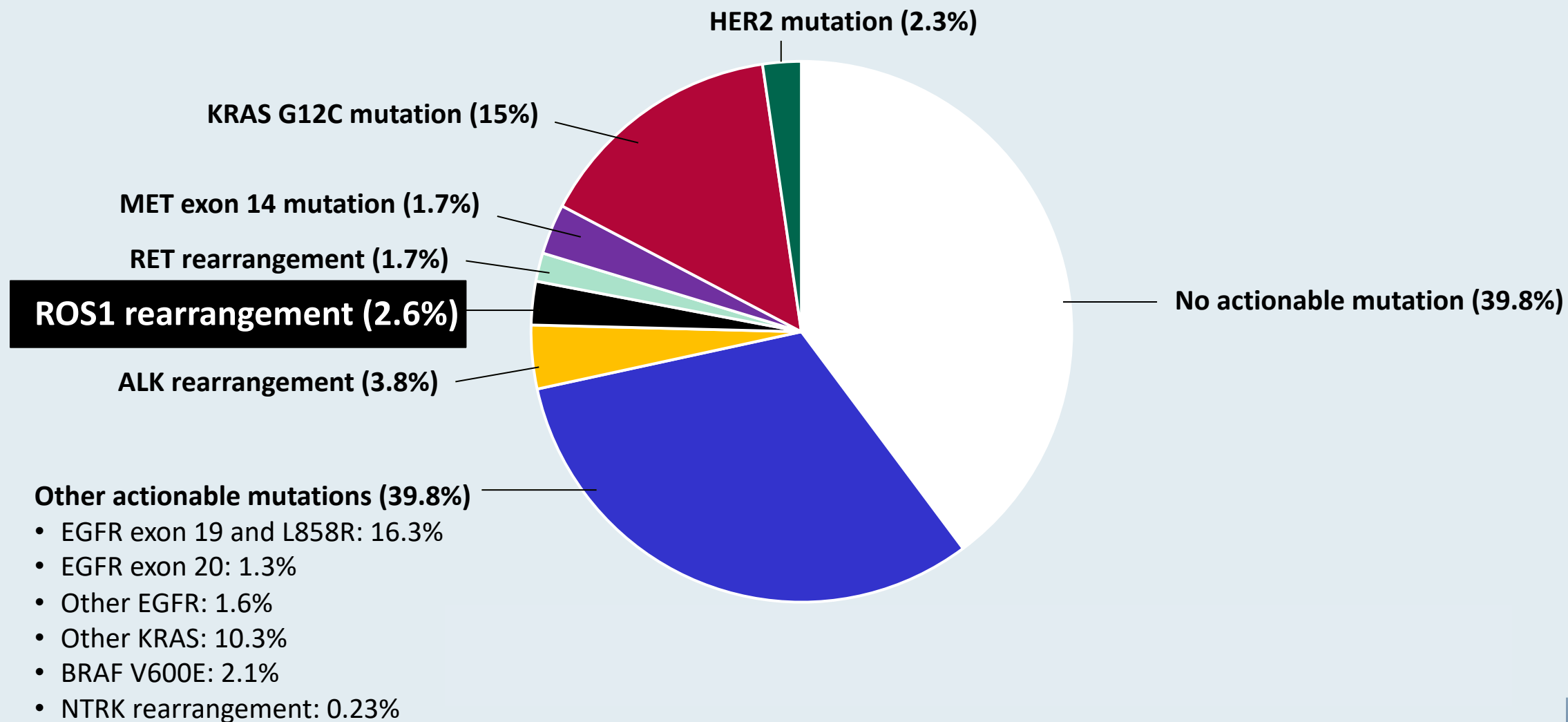
Study	Intervention	Comparator	Median PFS	PFS Hazard ratio	OS Hazard ratio
PROFILE 1014	Crizotinib	Platinum/pemetrexed	11 vs 7 mo	0.45	0.76
PROFILE 1029	Crizotinib	Platinum/pemetrexed	11 vs 7 mo	0.40	0.90
ASCEND-4	Ceritinib	Platinum/pemetrexed	17 vs 8 mo	0.55	0.73
ALEX	Alectinib	Crizotinib	35 vs 11 mo	0.50	0.67
J-ALEX	Alectinib	Crizotinib	34 vs 10 mo	0.37	0.80
ALESIA	Alectinib	Crizotinib	NR v 11 mo	0.37	0.28
ALTA-1L	Brigatinib	Crizotinib	24 vs 11 mo	0.49	0.92
CROWN	Lorlatinib	Crizotinib	NR vs 9 mo	0.28	0.72
eXalt3	Ensartinib	Crizotinib	26 vs 13 mo	0.52	0.88

Tan AC et al. *J Clin Oncol* 2022;40(6):611-25; Soria JC et al. *Lancet* 2017;389(10072):917-29; Peters S et al. *N Engl J Med* 2017;377(9):829-38; Camidge DR et al. *J Thorac Oncol* 2021;16(12):2091-108; Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29; Horn L et al. *JAMA Oncol* 2021;7(11):1617-25; Popat S et al. ESMO 2021;Abstract 1195P.

Common and Unique Adverse Effects of ALK TKIs

ALK TKI	Most common adverse effects
Crizotinib	Vision disorders, nausea, diarrhea, vomiting, edema, constipation, elevated transaminases, fatigue, decreased appetite, upper respiratory infection, dizziness and neuropathy
Ceritinib	Diarrhea, nausea, vomiting, fatigue, abdominal pain, decreased appetite and weight loss
Alectinib	Constipation, fatigue, edema, myalgia and anemia
Brigatinib	Diarrhea, fatigue, nausea, rash, cough, myalgia, headache, hypertension, vomiting and dyspnea
Lorlatinib	Hypercholesterolemia, hypertriglyceridemia, edema, peripheral neuropathy, weight gain, cognitive effects, fatigue, dyspnea, arthralgia and diarrhea
Ensartinib	Rash, nausea, pruritus and vomiting

Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung



Key Trials of ROS1 TKIs for TKI-Naïve NSCLC with ROS1 Fusions

ROS1 TKI	Study	Phase	ORR	Median DoR	Median PFS	Intracranial ORR
Crizotinib	PROFILE 1001	Ib	38/53 (72%)	25 mo	19 mo	—
	OxOnc	II	91/127 (72%)	20 mo	16 mo	—
	EUCROSS	II	21/30 (70%)	19 mo	20 mo	—
	AcSe	II	35/36 (69%)	—	6 mo	—
	METROS	II	17/26 (65%)	21 mo	23 mo	33%
Entrectinib	Drilon et al	I/II	41/53 (77%)	25 mo	19 mo	55%
Ceritinib	Lim et al	II	20/30 (67%)	21 mo	19 mo	29%
Brigatinib	Gettinger et al	I	1/1 (100%)	—	—	—
Lorlatinib	Shaw et al	I/II	13/21 (62%)	25 mo	21 mo	64%
Repotrectinib	Cho et al	I/II	10/11 (91%)	—	—	100%
Taletrectinib	Fujiwara et al	I	6/9 (67%)	—	—	—

Key Trials of ROS1 TKIs for TKI-Pretreated NSCLC with ROS1 Fusions

ROS1 TKI	Study	Phase	ORR
Entrectinib (after crizotinib)	Drilon et al	I/II	0/6 (0%)
Ceritinib (after crizotinib)	Lim et al	II	0/2 (0%)
Brigatinib (after crizotinib)	Gettinger et al	I	0/2 (0%)
Lorlatinib	Shaw et al	I/II	After crizotinib: 14/40 (35%) After ≥2 prior TKIs: 0/6 (0%)
Repotrectinib	Drilon et al	I/II	After 1 prior TKI: 7/18 (39%) After ≥2 prior TKIs: 2/7 (29%)
Taletrectinib (after crizotinib)	Fujiwara et al	I	1/3 (33%)

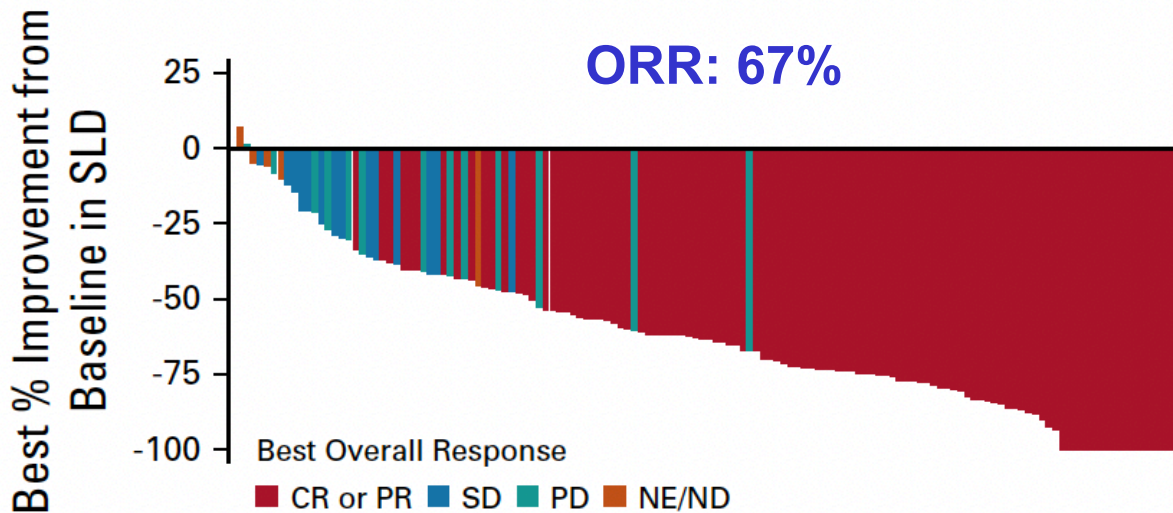
Updated Integrated Analysis of the Efficacy and Safety of Entrectinib in Locally Advanced or Metastatic *ROS1* Fusion–Positive Non–Small-Cell Lung Cancer

Rafal Dziadziuszko, MD, PhD¹; Matthew G. Krebs, MD, PhD²; Filippo De Braud, MD^{3,4}; Salvatore Siena, MD^{3,5}; Alexander Drilon, MD⁶; Robert C. Doebele, MD, PhD⁷; Manish R. Patel, DO⁸; Byoung Chul Cho, MD, PhD⁹; Stephen V. Liu, MD¹⁰; Myung-Ju Ahn, MD, PhD¹¹; Chao-Hua Chiu, MD¹²; Anna F. Farago, MD, PhD¹³; Chia-Chi Lin, MD¹⁴; Christos S. Karapetis, MBBS, MMedSc¹⁵; Yu-Chung Li, MD¹⁶; Bann-mo Day, PhD¹⁷; David Chen, PharmD¹⁷; Timothy R. Wilson, PhD¹⁷; and Fabrice Barlesi, MD, PhD^{18,19}

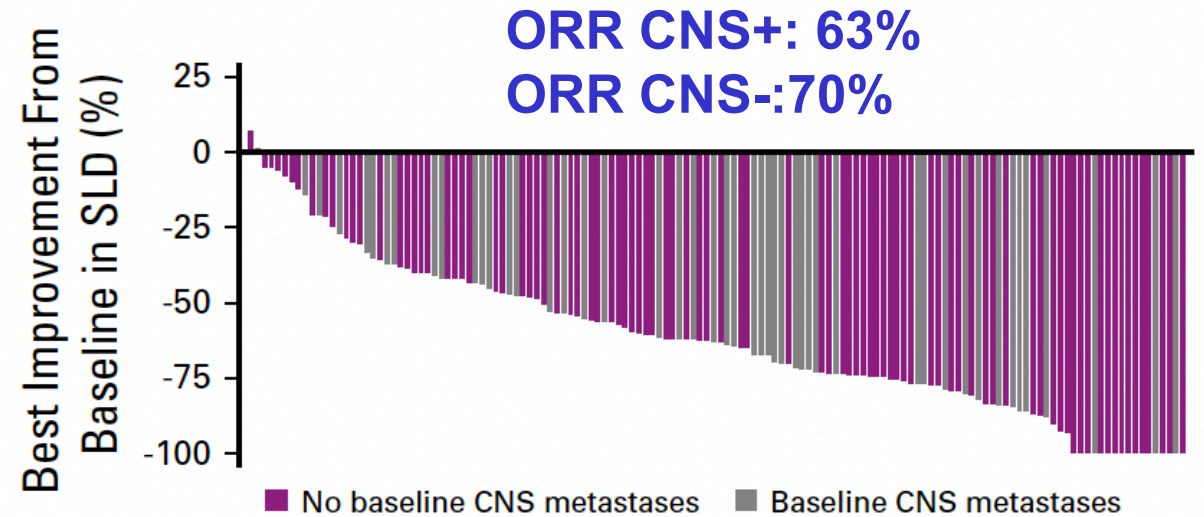
J Clin Oncol 2021;39(11):1253-63.

Integrated Analysis of ALKA-372-001, STARTRK-1, STARTRK-2, and STARTRK-NG

Efficacy Evaluable Population (N = 161)



Patients with (n = 56) and without (n = 105) CNS Metastases at Baseline



ORR = objective response rate

Entrectinib Duration of Response and Survival Analyses

Efficacy	NSCLC with ROS1 fusions		
	Efficacy evaluable (N = 161)	Baseline CNS metastases (n = 56)	No baseline CNS metastases (n = 105)
Median DoR	15.7 mo	14.9 mo	24.6 mo
12-month DoR	63%	62%	63%
Median PFS	15.7 mo	11.8 mo	19.0 mo
12-month PFS	55%	47%	60%
Median OS	NE	28.3 mo	NE
12-month OS	81%	75%	84%

Select Treatment-Related Adverse Events

Adverse events	NSCLC with ROS1 fusions safety evaluable population (N = 210)	
	Any grade	Grade ≥3
Dysgeusia	43%	<1%
Dizziness	35%	<1%
Constipation	31%	0
Fatigue	30%	<1%
Diarrhea	27%	3%
Weight increase	29%	8%
AST increase	12%	2%
ALT increase	11%	3%

Repotrectinib Granted FDA Breakthrough Therapy Designation for Metastatic NSCLC with ROS1 Fusions

Press Release – December 8, 2020

“...repotrectinib has been granted breakthrough therapy designation by the Food and Drug Administration (FDA) for the treatment of patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC) who have not been treated with a ROS1 tyrosine kinase inhibitor (TKI-naïve).

The breakthrough therapy designation for repotrectinib was supported by the initial data from TKI-naïve ROS1-positive NSCLC patients enrolled in the Phase 1 and Phase 2 portions of the TRIDENT-1 study, which is currently evaluating patients in multiple potentially registrational cohorts.”

Abstract 3255

Phase 1/2 TRIDENT-1 Study of Repotrectinib in Patients with *ROS1+* or *NTRK+* Advanced Solid Tumors

Byoung Chul Cho,¹ Robert C. Doebele,² Jessica J. Lin,³ Misako Nagasaka,⁴ Christina Baik,⁵ Anthonie J. van der Wekken,⁶ Vamsidhar Velcheti,⁷ Ki Hyeong Lee,⁸ Stephen V. Liu,⁹ Benjamin Solomon,¹⁰ Steven Kao,¹¹ Matthew G. Krebs,¹² Viola Zhu,¹³ Shanna Stopatschinskaja,¹⁴ D. Ross Camidge,¹⁵ Alexander Drilon¹⁶

¹Yonsei Cancer Center, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; ²University of Colorado Anschutz Medical Campus, Aurora, CO, USA;

³Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; ⁴Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA;

⁵Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, University of Washington School of Medicine, Seattle, WA, USA;

⁶University of Groningen and University Medical Centre Groningen, Groningen, Netherlands; ⁷Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA;

⁸Chungbuk National University Hospital, Cheongju, Republic of Korea; ⁹Georgetown Lombardi Comprehensive Cancer Center, Georgetown University, Washington D.C., USA;

¹⁰Peter MacCallum Cancer Center, Melbourne, Australia; ¹¹The Chris O'Brien Lifehouse, Camperdown, Australia;

¹²Division of Cancer Sciences, The University of Manchester and the Christie NHS Foundation Trust, Manchester, UK;

¹³Chao Family Comprehensive Cancer Center, University of California Irvine School of Medicine, Orange, CA, USA; ¹⁴Turning Point Therapeutics Inc., San Diego, CA, USA;

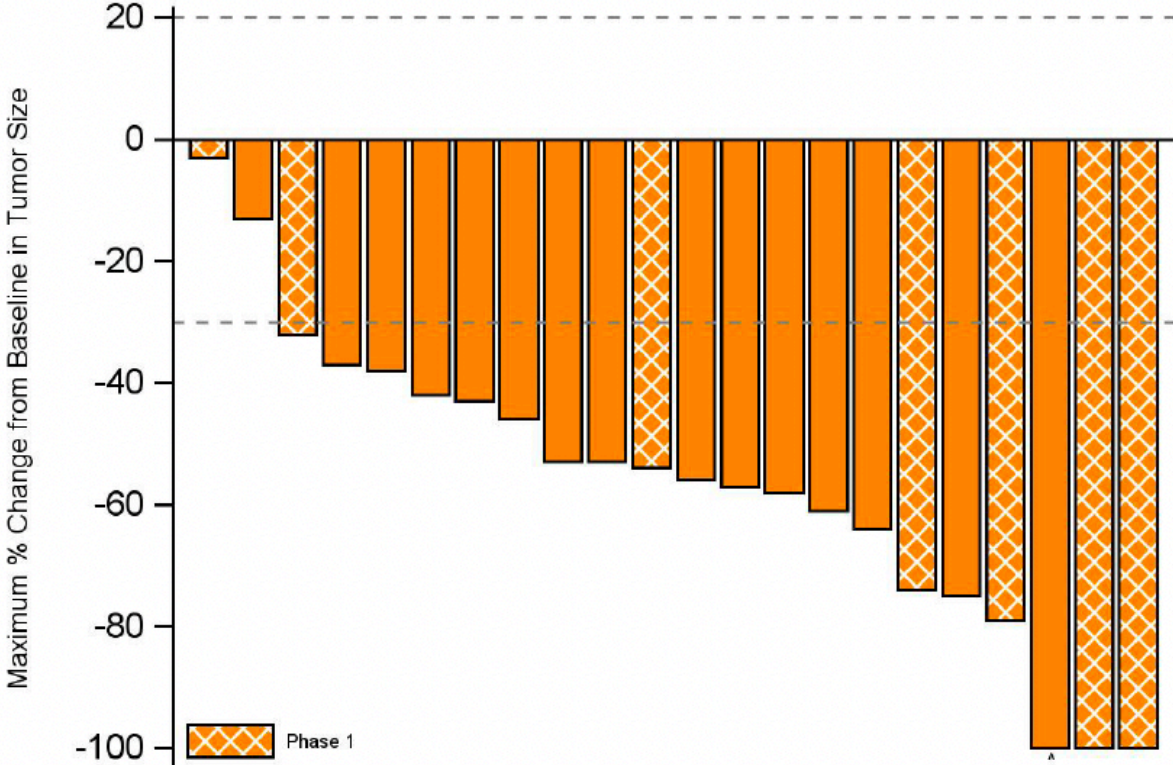
¹⁵Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA



2020 World Conference
on Lung Cancer Singapore

TRIDENT-1: Clinical Activity in TKI-Naïve Advanced NSCLC with ROS1 Fusions

Overall Response (N=22)



^ = Patient previously a confirmed partial response now in unconfirmed CR on treatment.

	Phase 2 N=15	Phase 1+2 N=22
Confirmed ORR, % (95% CI)	93% (68–100)	91% (71–99)

N=22 patients with baseline and at least two post baseline scans

- N=15 Phase 2 patients
- N=7 Phase 1 patients treated at or above the Phase 2 recommended dose

As of 31 December 2020, the 16th patient in Phase 2 has an unconfirmed PR and is on treatment awaiting a second post-baseline confirmatory scan.

AACR-NCI-EORTC Virtual International Conference on

MOLECULAR TARGETS AND CANCER THERAPEUTICS

October 7-10, 2021



Poster #: P224

Update from the Phase 2 registrational trial of repotrectinib in TKI-pretreated patients with *ROS1+* advanced non-small cell lung cancer and with *NTRK+* advanced solid tumors (TRIDENT-1)

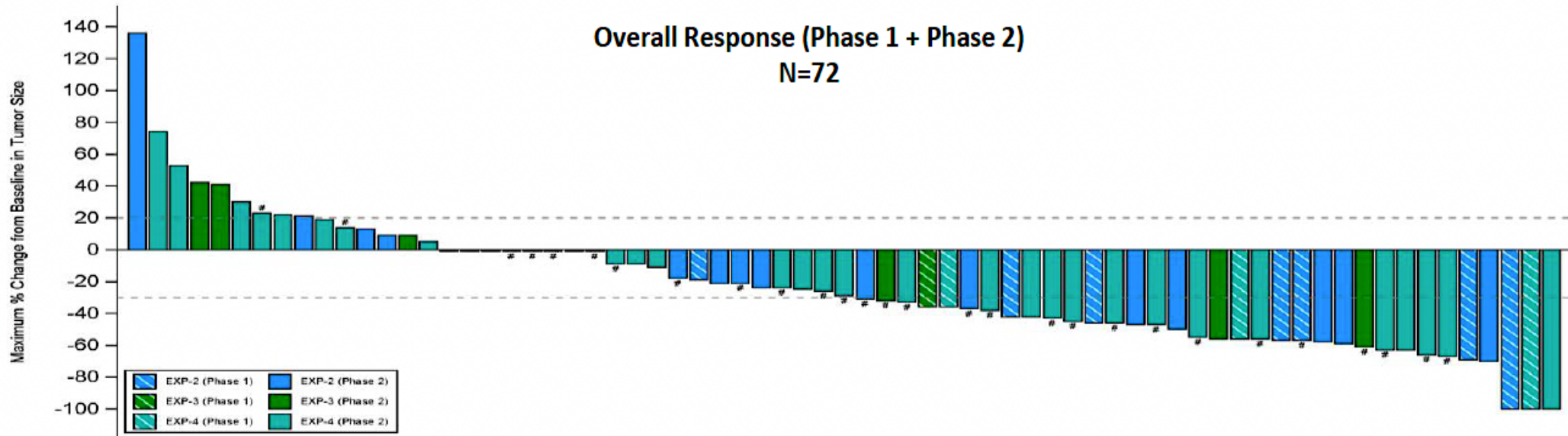
Jessica J. Lin,¹ Byoung Chul Cho,² Christoph Springfeld,³ D. Ross Camidge,⁴ Benjamin Solomon,⁵ Christina Baik,⁶ Vamsidhar Velcheti,⁷ Young-Chul Kim,⁸ Victor Moreno,⁹ Anthonie J. van der Wekken,¹⁰ Enriqueta Felip,¹¹ Dipesh Uprety,¹² Denise Trone,¹³ Shanna Stopatschinskaja,¹³ Alexander Drilon¹⁴

¹Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; ²Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; ³Heidelberg University Hospital, National Center for Tumor Diseases, Department of Medical Oncology, Heidelberg, Germany; ⁴University of Colorado Denver, Anschutz Medical Campus, Aurora, CO, USA; ⁵Peter MacCallum Cancer Center, Melbourne, Australia; ⁶University of Washington School of Medicine, Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; ⁷NYU Perlmutter Cancer Center, New York, NY, USA; ⁸Chonnam National University Medical School, and CNU Hwasun Hospital, Hwasun-gun, Republic of Korea; ⁹Fundación Jiménez Díaz - START Madrid, Madrid, Spain; ¹⁰University of Groningen, University Medical Centre Groningen, Groningen, Netherlands; ¹¹Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; ¹²Karmanos Cancer Institute, Detroit, MI, USA; ¹³Turning Point Therapeutics Inc, San Diego, CA, USA; ¹⁴Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA.

TRIDENT-1: Phase II Study Design

ROS1+ Advanced NSCLC				NTRK+ Advanced Solid Tumors	
EXP-1 ROS1 TKI naïve (N=55)	EXP-2 1 prior ROS1 TKI AND 1 platinum-based chemotherapy (N=60)	EXP-3 2 prior ROS1 TKIs AND No prior chemotherapy (N=40)	EXP-4 1 prior ROS1 TKI AND No prior chemotherapy (N=60)	EXP-5 TRK TKI naïve (N=55)	EXP-6 TRK TKI pretreated (N=40)
	Treated (N=21)	Treated (N=11)	Treated (N=44)	Data from NTRK+ cohorts (EXP-5 and EXP-6) will be presented at LB# 6546 during Plenary Session 2: New Drugs on the Horizon I	
	Efficacy Evaluable (N=16)	Efficacy Evaluable (N=9)	Efficacy Evaluable (N=36)		

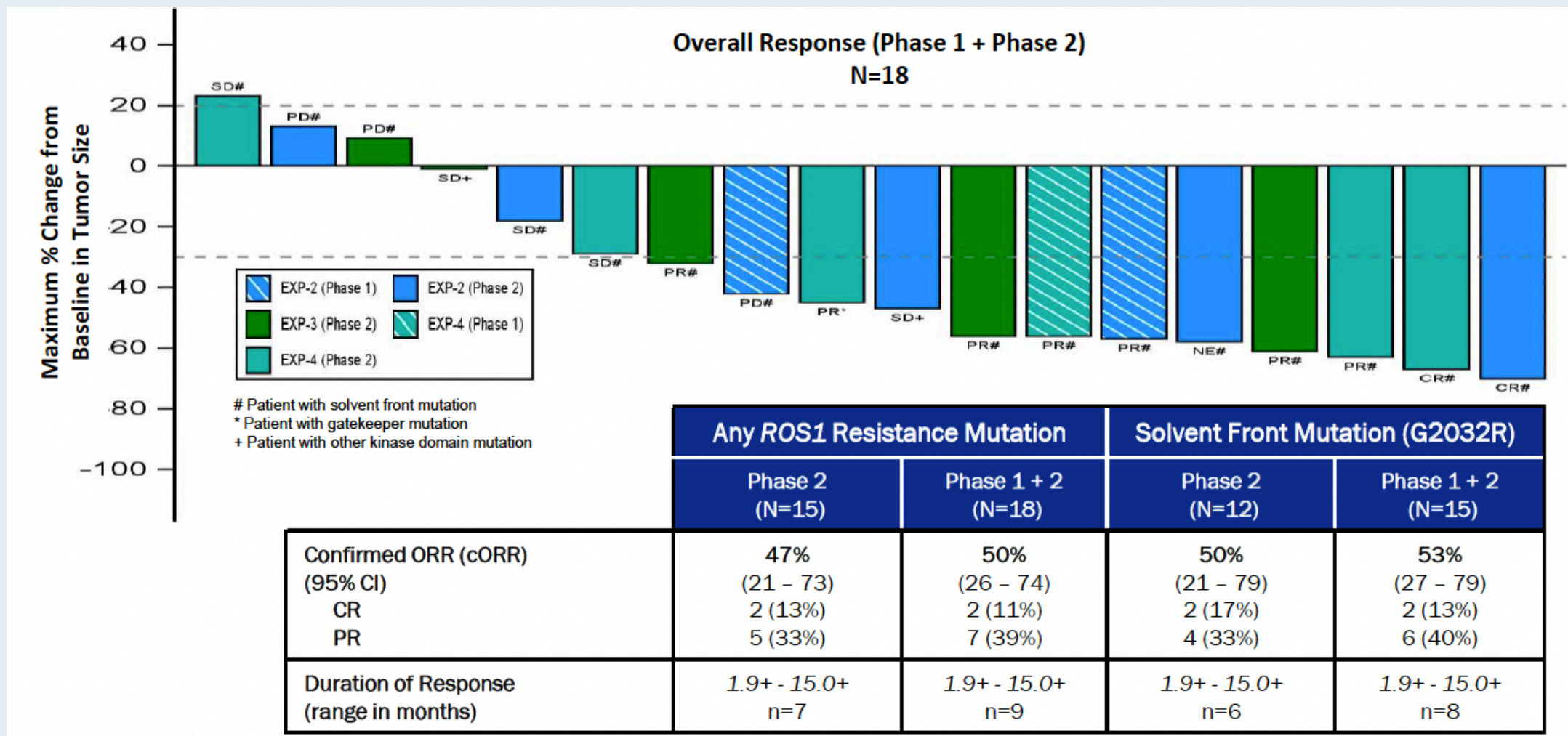
TRIDENT-1: Preliminary Efficacy in Patients with TKI-Pretreated Advanced NSCLC with ROS1 Fusions



#Patient remains on treatment
3 patients not displayed due to discontinuing treatment prior to first post-baseline scans.

	EXP-2		EXP-3		EXP-4	
	Phase 2 (N=16)	Phase 1 + 2 (N=23)	Phase 2 (N=9)	Phase 1 + 2 (N=10)	Phase 2 (N=36)	Phase 1 + 2 (N=39)
Confirmed ORR (cORR) (95% CI)	31% (11 - 59)	39% (20 - 61)	33% (7 - 70)	30% (7 - 65)	31%* (16 - 48)	33%* (19 - 50)
Duration of Response (range in months)	1.8+ - 9.2 n=5	1.8+ - 11.1 n=9	1.9+ - 12.9+ n=3	1.9+ - 12.9+ n=3	1.7+ - 15.0+ n=11	0.8+ - 15.0+ n=13

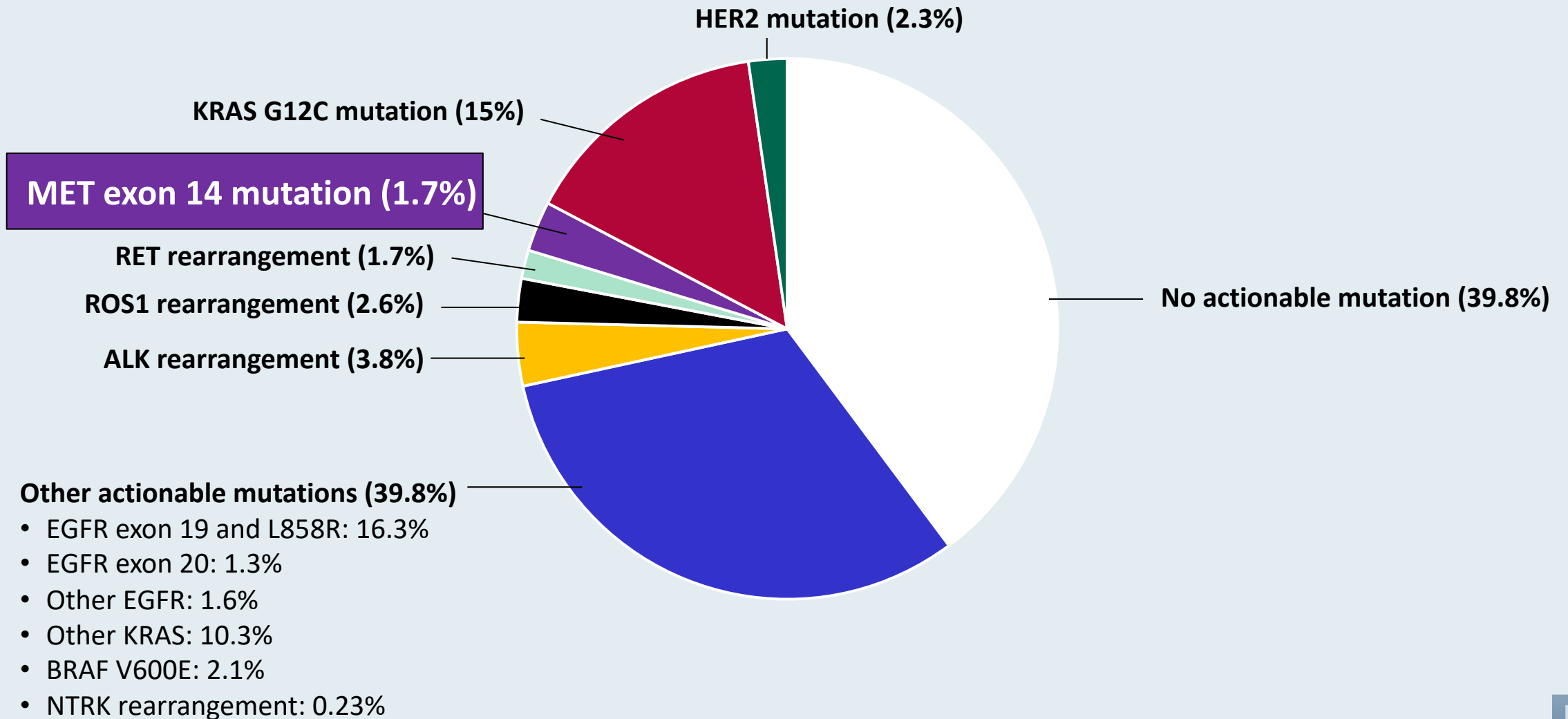
TRIDENT-1: Preliminary Efficacy in Patients with TKI-Pretreated Advanced NSCLC with ROS1 Fusions and Baseline ROS1 Resistance Mutations



TRIDENT-1: Treatment-Emergent Adverse Events (N = 301)

Adverse event	Any grade	Grade 3/4
Dizziness	60%	2%
Dysgeusia	44%	<1%
Constipation	34%	<1%
Paraesthesia	29%	1%
Dyspnea	28%	6%
Anemia	27%	8%
Fatigue	24%	2%
Nausea	21%	1%
	Rate	
Drug discontinuation due to TEAEs	11%	
Drug dose reduction due to TEAEs	17%	

Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung



FDA Grants Accelerated Approval to Tepotinib for Metastatic NSCLC

Press Release – February 3, 2021

“The Food and Drug Administration granted accelerated approval to tepotinib for adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (MET) exon 14 skipping alterations.

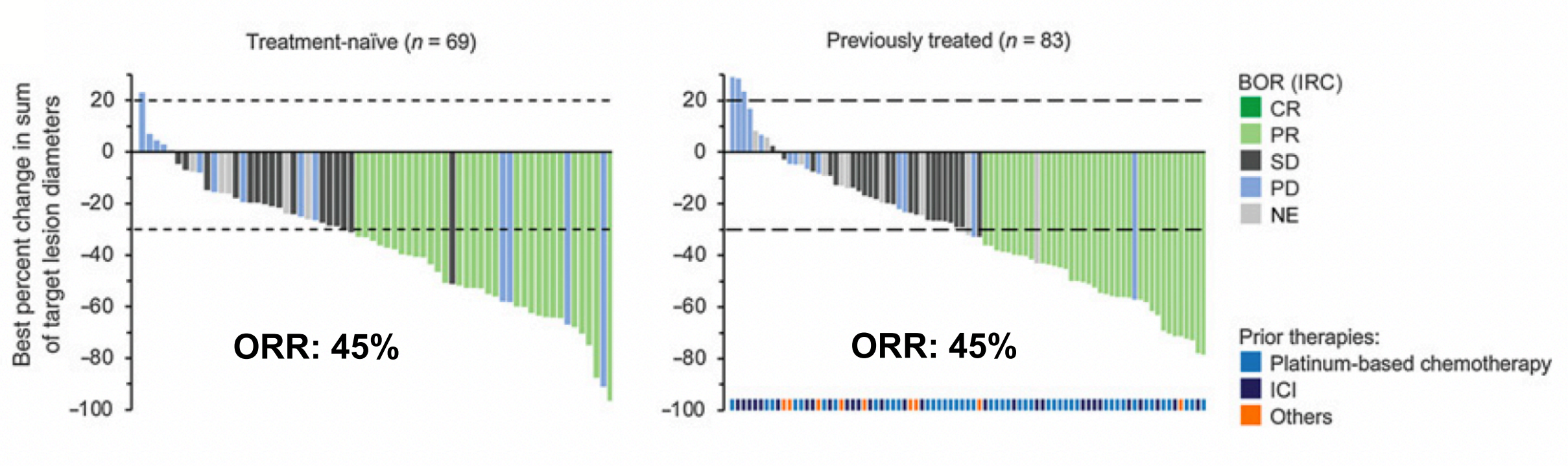
Efficacy was demonstrated in the VISION trial (NCT02864992), a multicenter, non-randomized, open-label, multicohort study enrolling 152 patients with advanced or metastatic NSCLC with MET exon 14 skipping alterations. Patients received tepotinib 450 mg orally once daily until disease progression or unacceptable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

Tepotinib Efficacy and Safety in Patients with *MET* Exon 14 Skipping NSCLC: Outcomes in Patient Subgroups from the VISION Study with Relevance for Clinical Practice

Xiuning Le¹, Hiroshi Sakai², Enriqueta Felip³, Remi Veillon⁴, Marina Chiara Garassino^{5,6}, Jo Raskin⁷, Alexis B. Cortot⁸, Santiago Viteri⁹, Julien Mazieres¹⁰, Egbert F. Smit¹¹, Michael Thomas¹², Wade T. Iams¹³, Byoung Chul Cho¹⁴, Hye Ryun Kim¹⁴, James Chih-Hsin Yang¹⁵, Yuh-Min Chen¹⁶, Jyoti D. Patel¹⁷, Christine M. Bestvina¹⁸, Keunchil Park¹⁹, Frank Griesinger²⁰, Melissa Johnson²¹, Maya Gottfried²², Christian Britschgi²³, John Heymach¹, Elif Sikoglu²⁴, Karin Berghoff²⁵, Karl-Maria Schumacher²⁶, Rolf Bruns²⁷, Gordon Otto²⁶, and Paul K. Paik^{28,29}

***Clin Cancer Res* 2022;28(6):1117-26.**

VISION: Tepotinib in Advanced NSCLC with MET Exon 14 Skipping Mutations



VISION: Treatment-Related Adverse Events with Tepotinib

Adverse events	Cohorts A + C (N = 255)	
	Any grade	Grade 3/4
Peripheral edema	54%	8%
Nausea	20%	<1%
Diarrhea	20%	<1%
Blood creatinine increase	18%	<1%
Hypoalbuminemia	15%	2%
ALT increase	9%	2%
Decreased appetite	8%	<1%
Amylase increase	8%	2%

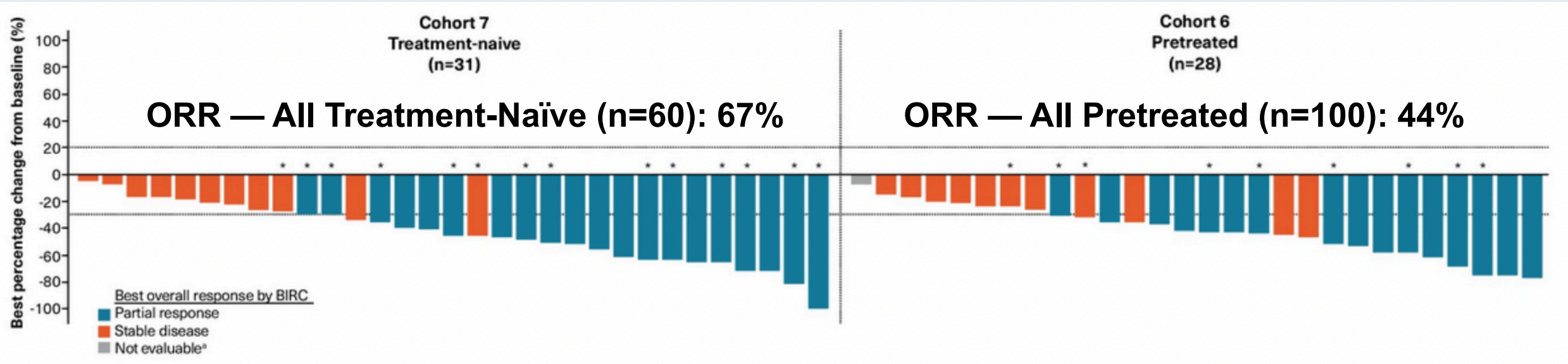
6 confirmed ILD-like events were reported

Capmatinib in *MET* Exon 14-Mutated, Advanced NSCLC: Updated Results from the GEOMETRY mono-1 Study

Wolf J et al.

ASCO 2021;Abstract 9020.

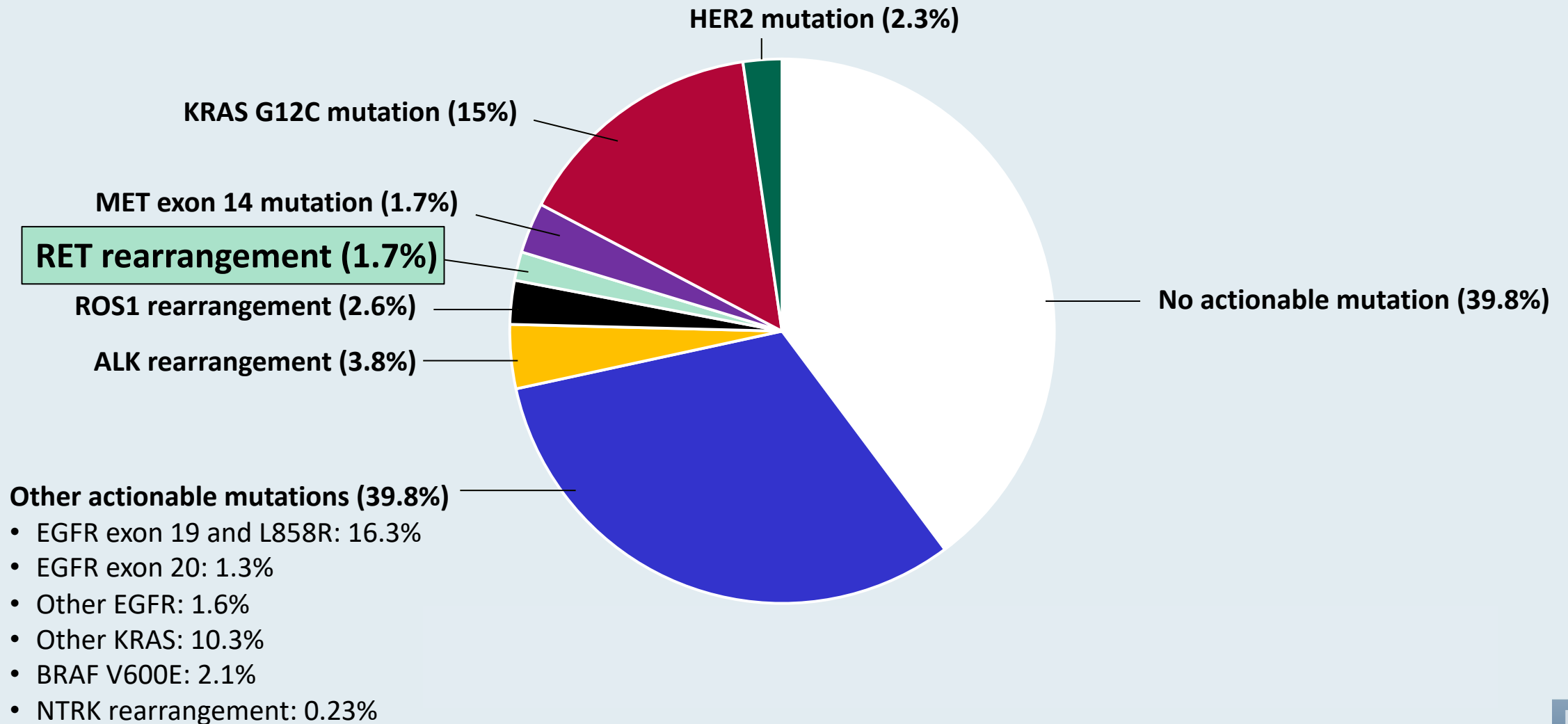
GEOMETRY mono-1: Overall Response Rates (Cohorts 7 and 6)



GEOMETRY mono-1: Most Common Adverse Events (Cohorts 7 and 6)

Adverse event	Cohort 7 — Treatment naïve N = 32		Cohort 6 — Second line N = 31	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Peripheral edema	72%	13%	71%	13%
Nausea	44%	0	32%	3%
Vomiting	15%	3%	26%	0
Increase blood creatinine	31%	0	29%	0
Dyspnea	6%	3%	10%	0
Fatigue	19%	0	29%	0
Decreased appetite	16%	3%	16%	0

Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung



Pralsetinib for *RET* fusion-positive non-small-cell lung cancer (ARROW): a multi-cohort, open-label, phase 1/2 study



Justin F Gainor, Giuseppe Curigliano, Dong-Wan Kim, Dae Ho Lee, Benjamin Besse, Christina S Baik, Robert C Doebele, Philippe A Cassier, Gilberto Lopes, Daniel SW Tan, Elena Garralda, Luis G Paz-Ares, Byoung Chul Cho, Shirish M Gadgil, Michael Thomas, Stephen V Liu, Matthew H Taylor, Aaron S Mansfield, Viola W Zhu, Corinne Clifford, Hui Zhang, Michael Palmer, Jennifer Green, Christopher D Turner, Vivek Subbiah

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AUGUST 27, 2020

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

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

Pivotal Studies of Selpercatinib and Pralsetinib for Advanced NSCLC with RET Fusion

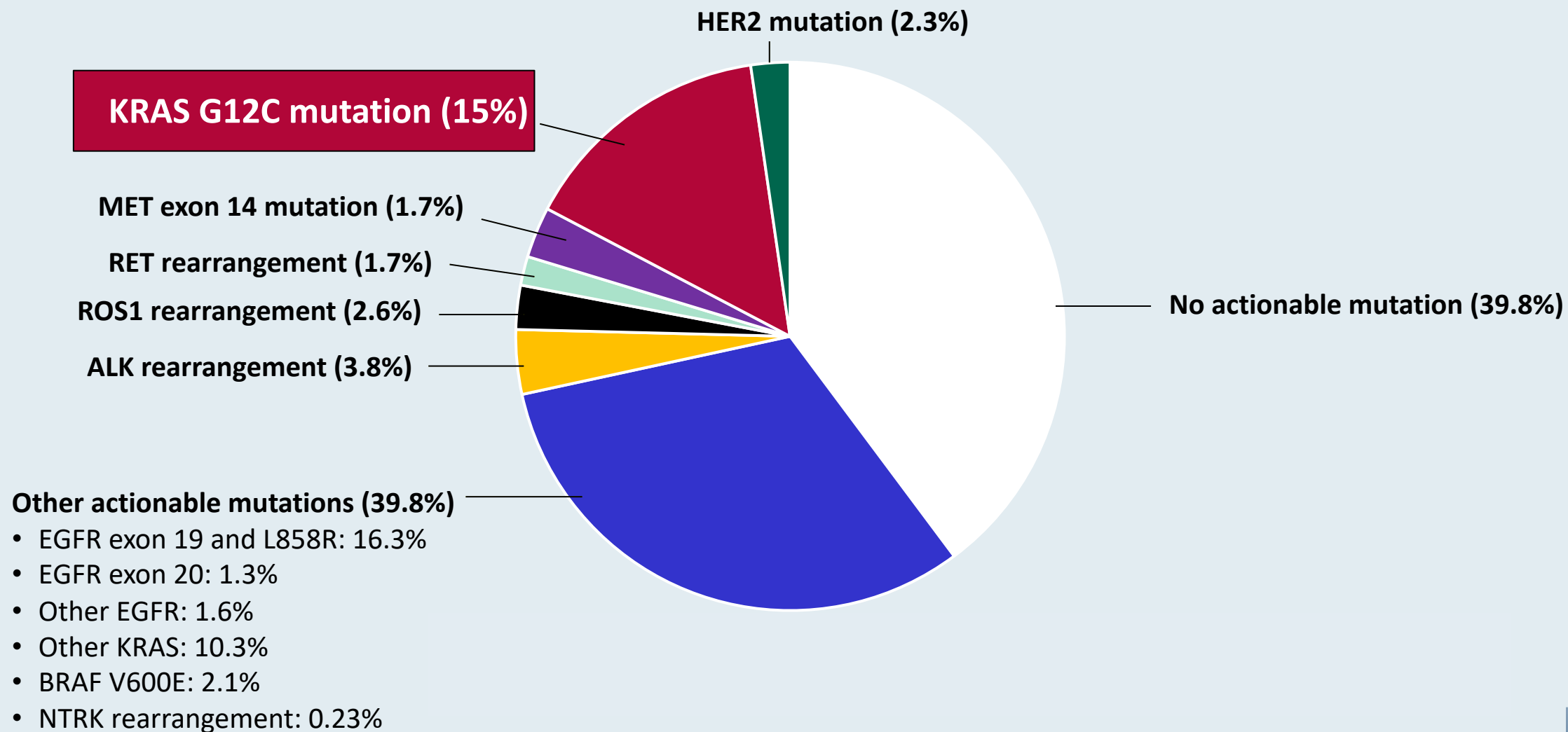
	Selpercatinib ¹	Pralesetinib ²
Pivotal study	LIBRETTO-001 Phase I/II (N = 105)	ARROW Phase I/II (N = 233)
FDA approval	May 8, 2020	September 4, 2020
Setting	Previous platinum-based chemotherapy and previously untreated	Previous platinum-based chemotherapy and previously untreated
ORR	64%	61%
Median duration of response	17.5 months	Not reached
Common Grade ≥3 adverse events	Hypertension (14%) Increased ALT (12%) and AST (10%) Hyponatremia (6%) Lymphopenia (6%)	Neutropenia (18%) Hypertension (11%) Anemia (10%) Decreased WBC (6%)

¹ Drilon A et al. *N Engl J Med* 2020;383(9):813-24. ² Gainor JF et al. *Lancet Oncol* 2021;22(7):959-69.

Ongoing Phase III Trials of Selpercatinib or Pralsetinib for NSCLC with RET Fusion

Trial identifier	Setting	Treatment arms
LIBRETTO-431 (NCT04194944)	Untreated Stage IIIB-IIIC or Stage IV non-squamous NSCLC that is not suitable for radical surgery or radiation therapy	<ul style="list-style-type: none"> • Selpercatinib • Pemetrexed and platinum with or without pembrolizumab
LIBRETTO-432 (NCT04819100)	Stage IB, II or IIIA NSCLC after definitive locoregional therapy	<ul style="list-style-type: none"> • Selpercatinib • Placebo
AcceleRET-Lung (NCT04222972)	Locally advanced or metastatic NSCLC that has not been treated with systemic anticancer therapy for metastatic disease	<ul style="list-style-type: none"> • Pralsetinib • Platinum-based chemotherapy (with or without pembrolizumab)
NCT05170204	Unresectable Stage III NSCLC	<u>Cohort A3</u> <ul style="list-style-type: none"> • Pralsetinib • Durvalumab

Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung



FDA Grants Accelerated Approval to Sotorasib for NSCLC with KRAS G12C Mutation

Press Release – May 28, 2021

“The Food and Drug Administration granted accelerated approval to sotorasib, a RAS GTPase family inhibitor, for adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.

FDA also approved the QIAGEN theascreen® KRAS RGQ PCR kit (tissue) and the Guardant360® CDx (plasma) as companion diagnostics for sotorasib. If no mutation is detected in a plasma specimen, the tumor tissue should be tested.

Approval was based on CodeBreakK 100, a multicenter, single-arm, open label clinical trial (NCT03600883) which included patients with locally advanced or metastatic NSCLC with KRAS G12C mutations. Efficacy was evaluated in 124 patients whose disease had progressed on or after at least one prior systemic therapy. Patients received sotorasib 960 mg orally daily until disease progression or unacceptable toxicity.”

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

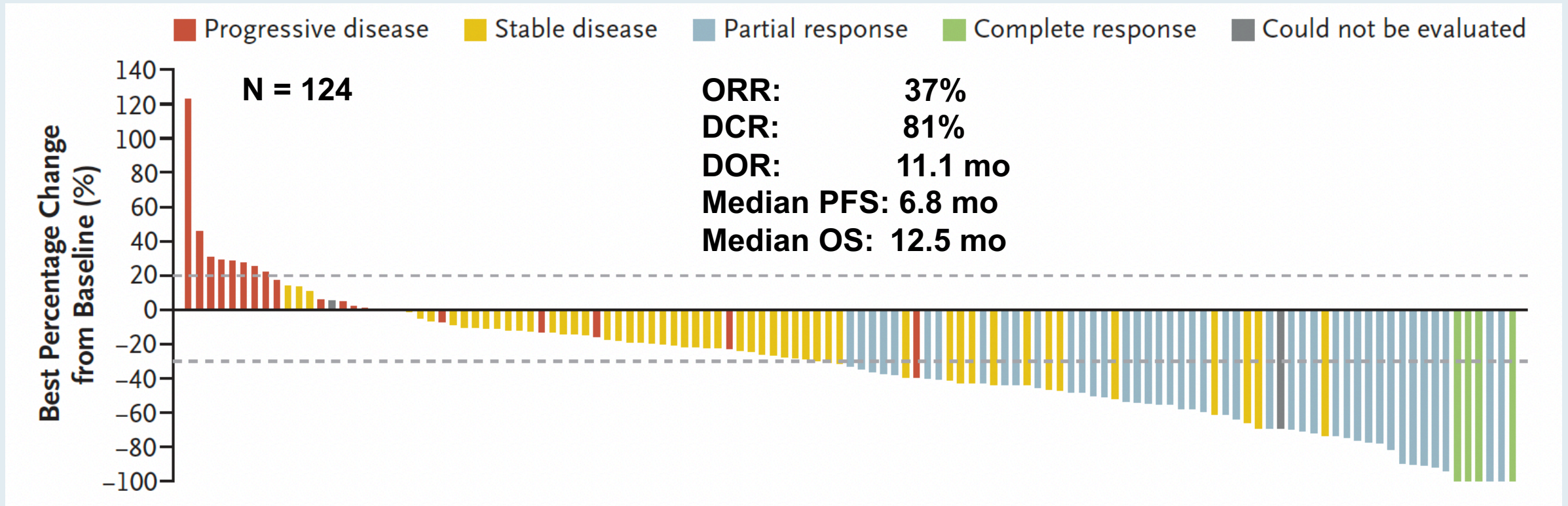
JUNE 24, 2021

VOL. 384 NO. 25

Sotorasib for Lung Cancers with *KRAS* p.G12C Mutation

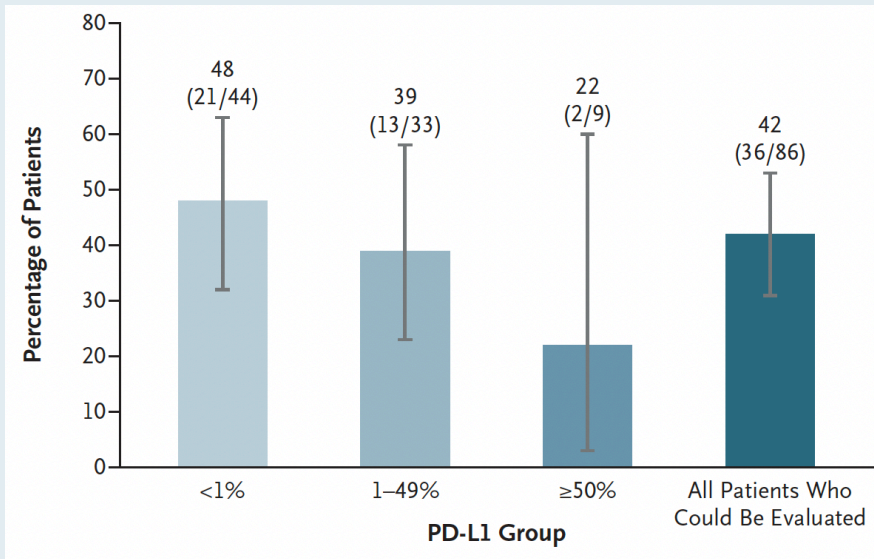
F. Skoulidis, B.T. Li, G.K. Dy, T.J. Price, G.S. Falchook, J. Wolf, A. Italiano, M. Schuler, H. Borghaei, F. Barlesi, T. Kato, A. Curioni-Fontecedro, A. Sacher, A. Spira, S.S. Ramalingam, T. Takahashi, B. Besse, A. Anderson, A. Ang, Q. Tran, O. Mather, H. Henary, G. Ngarmchamnanrith, G. Friberg, V. Velcheti, and R. Govindan

CodeBreakK 100: Sotorasib for Previously Treated Metastatic NSCLC with KRAS p.G12C Mutation

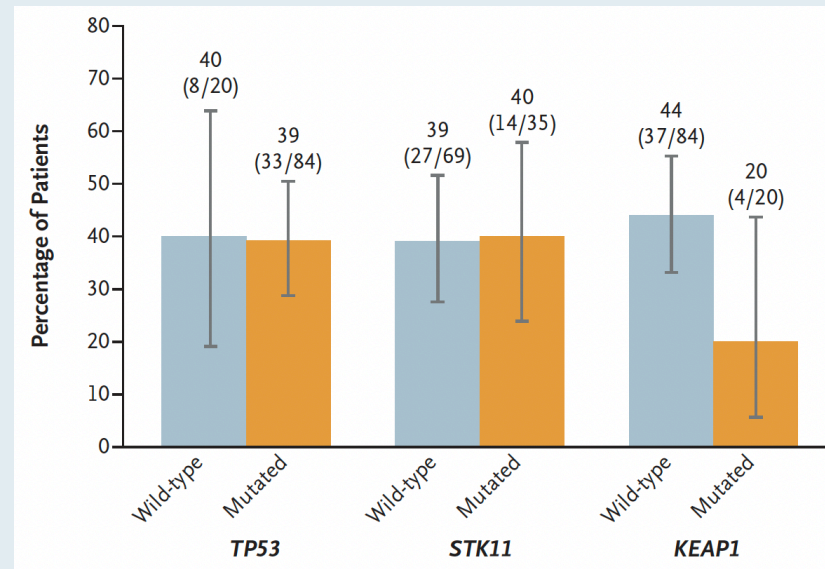


CodeBreakK 100: Exploratory Biomarker Analyses

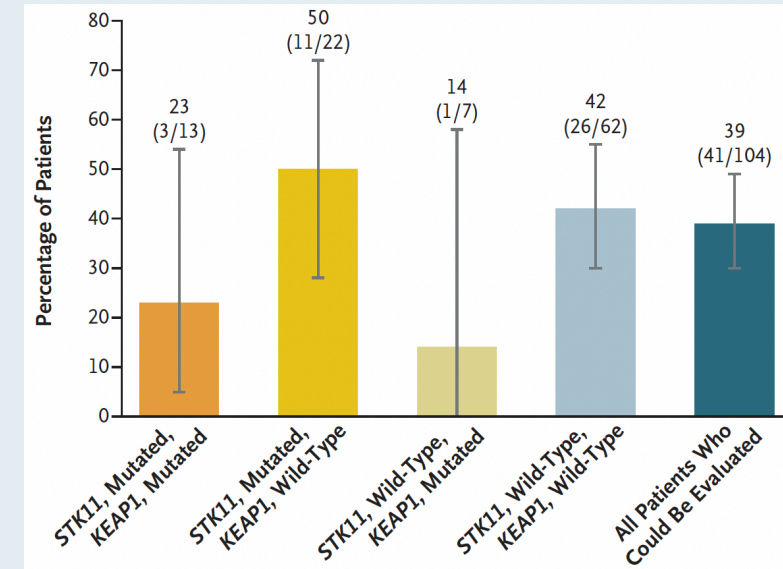
Response According to PD-L1 Expression Level



Response According to Co-occurring Mutations in TP53, STK11 and KEAP1



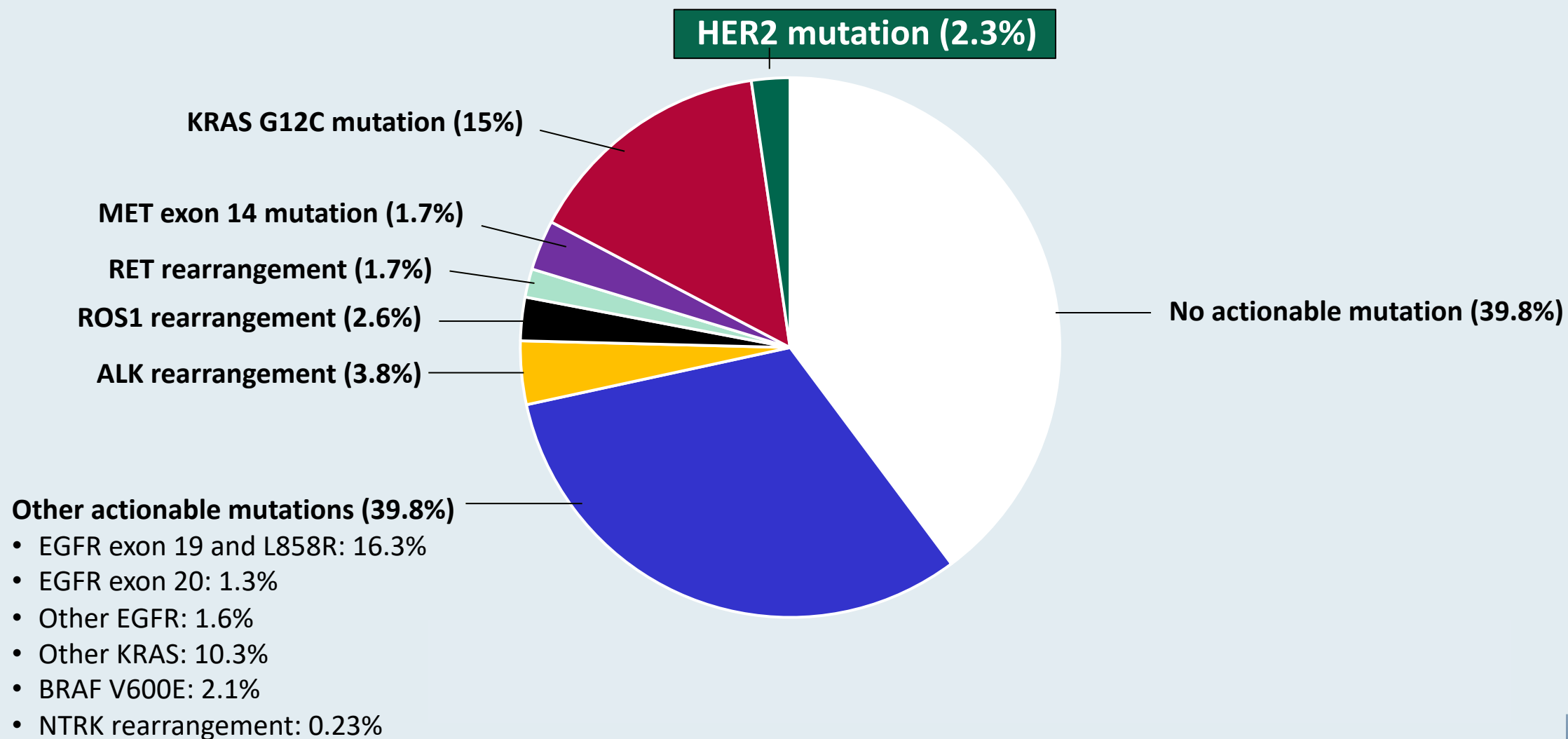
Response According to Mutational Status in Both STK11 and KEAP1



CodeBreakK 100: Adverse Events

Adverse event	Any grade	Grade ≥ 3
Discontinuation due to AE	7%	4%
Dose modification due to AE	22%	16%
Diarrhea	32%	4%
Nausea	19%	0
ALT increase	15%	6%
AST increase	15%	6%
Fatigue	11%	0
Vomiting	8%	0

Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung



N Engl J Med 2022;386(3):241-51.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in *HER2*-Mutant Non–Small-Cell Lung Cancer

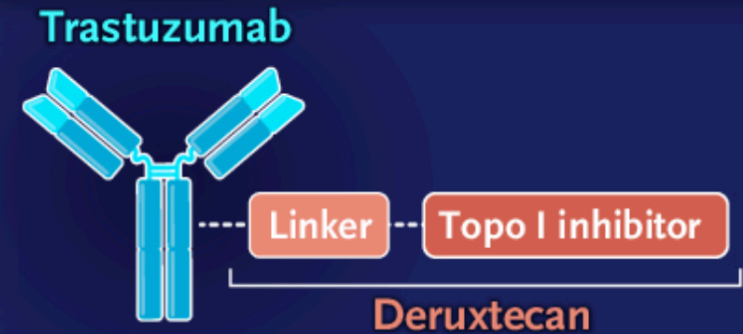
Bob T. Li, M.D., Ph.D., M.P.H., Egbert F. Smit, M.D., Ph.D.,
Yasushi Goto, M.D., Ph.D., Kazuhiko Nakagawa, M.D., Hibiki Udagawa, M.D.,
Julien Mazières, M.D., Misako Nagasaka, M.D., Ph.D., Lyudmila Bazhenova, M.D.,
Andreas N. Saltos, M.D., Enriqueta Felip, M.D., Ph.D., Jose M. Pacheco, M.D.,
Maurice Pérol, M.D., Luis Paz-Ares, M.D., Kapil Saxena, M.D., Ryota Shiga, B.Sc.,
Yingkai Cheng, M.D., Ph.D., Suddhasatta Acharyya, Ph.D., Patrik Vitazka, M.D., Ph.D.,
Javad Shahidi, M.D., David Planchard, M.D., Ph.D., and Pasi A. Jänne, M.D., Ph.D.,
for the DESTINY-Lung01 Trial Investigators*

DESTINY-Lung01 Study

MULTICENTER, INTERNATIONAL, PHASE 2 STUDY

91

Adults with metastatic *HER2*-mutant NSCLC refractory to standard treatment (median follow-up, 13 mo)



Confirmed objective response
(assessed by independent central review)

55% (95% CI, 44–65)

Duration of response

9.3 mo

Progression-free survival

8.2 mo

Overall survival

17.8 mo

Grade 3 or higher drug-related adverse events occurred in 46% of patients.

Trastuzumab deruxtecan showed durable anticancer activity.

DESTINY-Lung01: Summary of Adverse Events and AEs of Clinical Interest

Event	N = 91
Discontinued due to AEs	25%
Dose reduction due to AEs	34%
Dose interruption due to AEs	32%
Drug-related interstitial lung disease (ILD)	26% (N = 24)
Grade 1	3 pts
Grade 2	15 pts
Grade 3	4 pts
Grade 5	2 pts
Median time to onset of ILD	141 days
Median duration of ILD	43 days

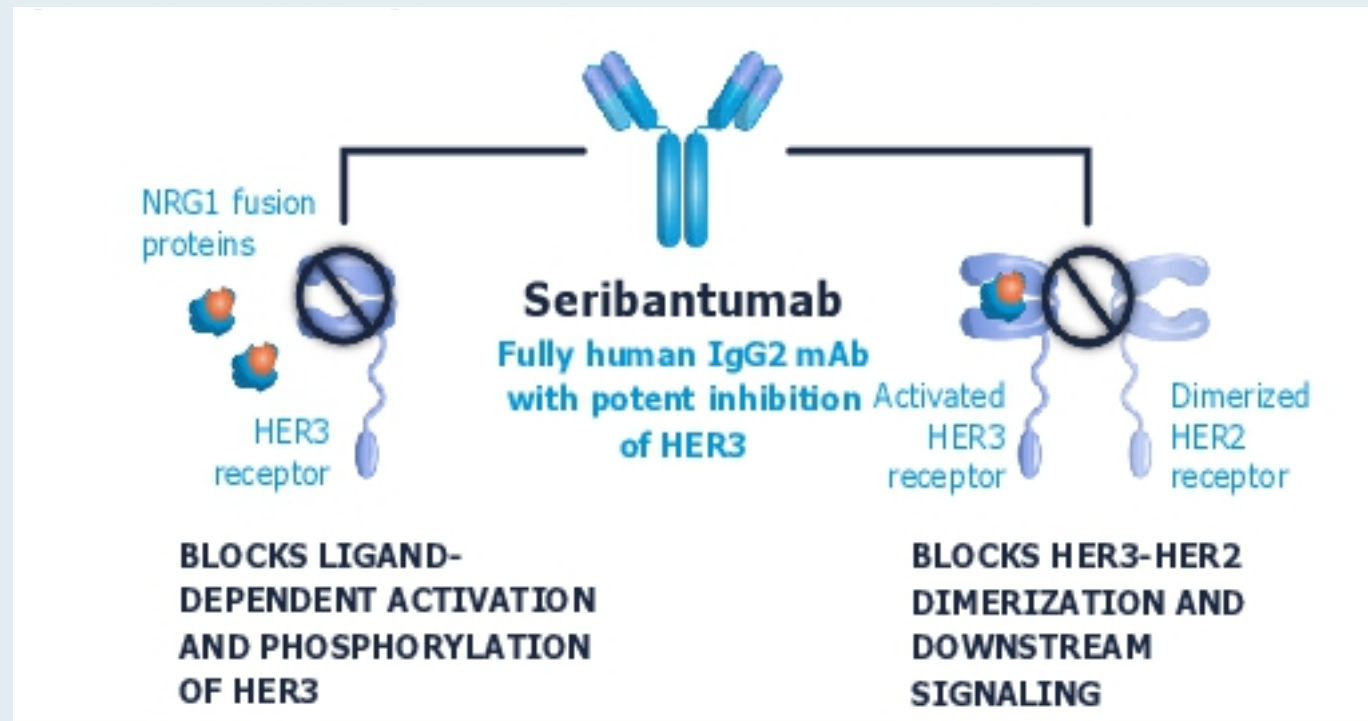
DESTINY-Lung01: Common Adverse Events (N = 91)

Event	Any grade	Grade ≥ 3
Nausea	73%	9%
Fatigue	53%	7%
Alopecia	46%	0
Vomiting	40%	3%
Neutropenia	35%	18%
Anemia	33%	10%
Diarrhea	32%	3%
Decreased appetite	30%	0
Leukopenia	23%	4%
Constipation	22%	0

Other Potential Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung

Neuregulin-1 (NRG1) Gene Fusions and Seribantumab Mechanism of Action


- NRG1 gene fusions are rare oncogenic drivers found in 0.2% of solid tumors including lung, colorectal, breast and ovarian
- NRG1 fusion proteins predominantly retain an active EGF-like domain, which drives tumorigenesis and proliferation through aberrant HER3 activation
- Seribantumab is a fully human monoclonal antibody against HER3



Investigational New Drugs (2021) 39:1604–1612
<https://doi.org/10.1007/s10637-021-01145-y>

PHASE I STUDIES

Phase 1 dose escalation study of seribantumab (MM-121), an anti-HER3 monoclonal antibody, in patients with advanced solid tumors

Crystal S. Denlinger¹  · Vicki L. Keedy² · Victor Moyo³ · Gavin MacBeath³ · Geoffrey I. Shapiro⁴

Best Overall Response with and Recommended Phase II Dose of Seribantumab in Advanced Solid Tumors

Best response	Dose escalation (n = 25)	Dose expansion (n = 18)
Overall response	0	0
Complete response	0	0
Partial response	0	0
Stable disease	6 (24%)	7 (39%)
Progressive disease	11 (44%)	8 (44%)

- Most adverse events were transient and mild to moderate (Grade 1 or 2) in severity
- The maximum tolerated dose was not reached in the dose escalation portion, and the 40 mg/kg loading dose followed by 20 mg/kg weekly maintenance dose was considered well tolerated and chosen for the dose expansion portion of the study

CRESTONE: Ongoing Phase II Study of of Seribantumab in Patients With Neuregulin-1 (NRG1) Fusion-Positive Advanced Solid Tumors

Trial Identifier: NCT04383210 (Open)

Advanced solid tumor with an NRG1 gene fusion
Disease progression on or unresponsive to at least one prior standard therapy appropriate for their tumor type and stage of disease
No further available curative therapy options
No prior pan-ERBB or any ERBB/HER2/HER3 directed therapy (Cohort 1 only)

Primary Endpoint: Objective response rate

Seribantumab
1-h IV infusion at various doses once weekly, every 2 weeks and every 3 weeks, during the induction, consolidation and maintenance dosing phases, respectively

Patient Cohorts:

Cohort 1: A minimum of 55 adult advanced solid tumor patients harboring NRG1 gene fusions, who have received prior standard treatment, excluding prior ERBB-directed therapy.

Cohort 2: Up to 10 adult advanced solid tumor patients harboring NRG1 gene fusions, who have received prior standard treatment, including prior ERBB-directed therapy

Cohort 3: Up to 10 adult advanced solid tumor patients harboring NRG1 gene fusions lacking an EGF-like domain, who have received prior standard treatment, which may have included prior ERBB-directed therapy

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

A Complimentary NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Prostate Cancer

Thursday, April 28, 2022

6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty

Kathy D Burns, RN, MSN, AGACNP-BC, OCN

Robert Dreicer, MD, MS

Sandy Srinivas, MD

Ronald Stein, JD, MSN, NP-C, AOCNP

Non-Small Cell Lung Cancer

Thursday, April 28, 2022

6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)

Faculty

Edward B Garon, MD, MS

Kelly EH Goodwin, MSN, RN, ANP-BC

Tara Plues, APRN, MSN

Anne S Tsao, MD, MBA

Ovarian Cancer

Thursday, April 28, 2022

12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty

Jennifer Filipi, MSN, NP

Kathleen N Moore, MD, MS

Krishnansu S Tewari, MD

Deborah Wright, MSN, APRN, AGCNS-BC

Hepatobiliary Cancers

Thursday, April 28, 2022

8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)

Faculty

Richard S Finn, MD

Amanda K Wagner, APRN-CNP, AOCNP

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

A Complimentary NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Small Cell Lung Cancer

Friday, April 29, 2022

6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty

Marianne J Davies, DNP, MSN, RN, APRN

Matthew Gubens, MD, MS

Lowell L Hart, MD

Chaely J Medley, MSN, AGNP

Breast Cancer

Friday, April 29, 2022

6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)

Faculty

Jamie Carroll, APRN, MSN, CNP

Sara A Hurvitz, MD

Kelly Leonard, MSN, FNP-BC

Hope S Rugo, MD

Chronic Lymphocytic Leukemia

Friday, April 29, 2022

12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty

Lesley Camille Ballance, MSN, FNP-BC

Amy Goodrich, CRNP

Anthony R Mato, MD, MSCE

Susan O'Brien, MD

Acute Myeloid Leukemia and Myelodysplastic Syndromes

Friday, April 29, 2022

8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)

Faculty

Ilene Galinsky, NP

Eunice S Wang, MD

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

A Complimentary NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Cervical and Endometrial Cancer

Saturday, April 30, 2022

6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty

Paula J Anastasia, MN, RN, AOCN

Robert L Coleman, MD

David M O'Malley, MD

Jaclyn Shaver, MS, APRN, CNP, WHNP

Bladder Cancer

Saturday, April 30, 2022

12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty

Monica Averia, MSN, AOCNP, NP-C

Shilpa Gupta, MD

Brenda Martone, MSN, NP-BC, AOCNP

Sumanta Kumar Pal, MD

Thank you for joining us!

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