Meet The Professor
Non-Small Cell Lung Cancer with an Actionable Target Beyond EGFR

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

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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.

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

Dr Gainor — Disclosures

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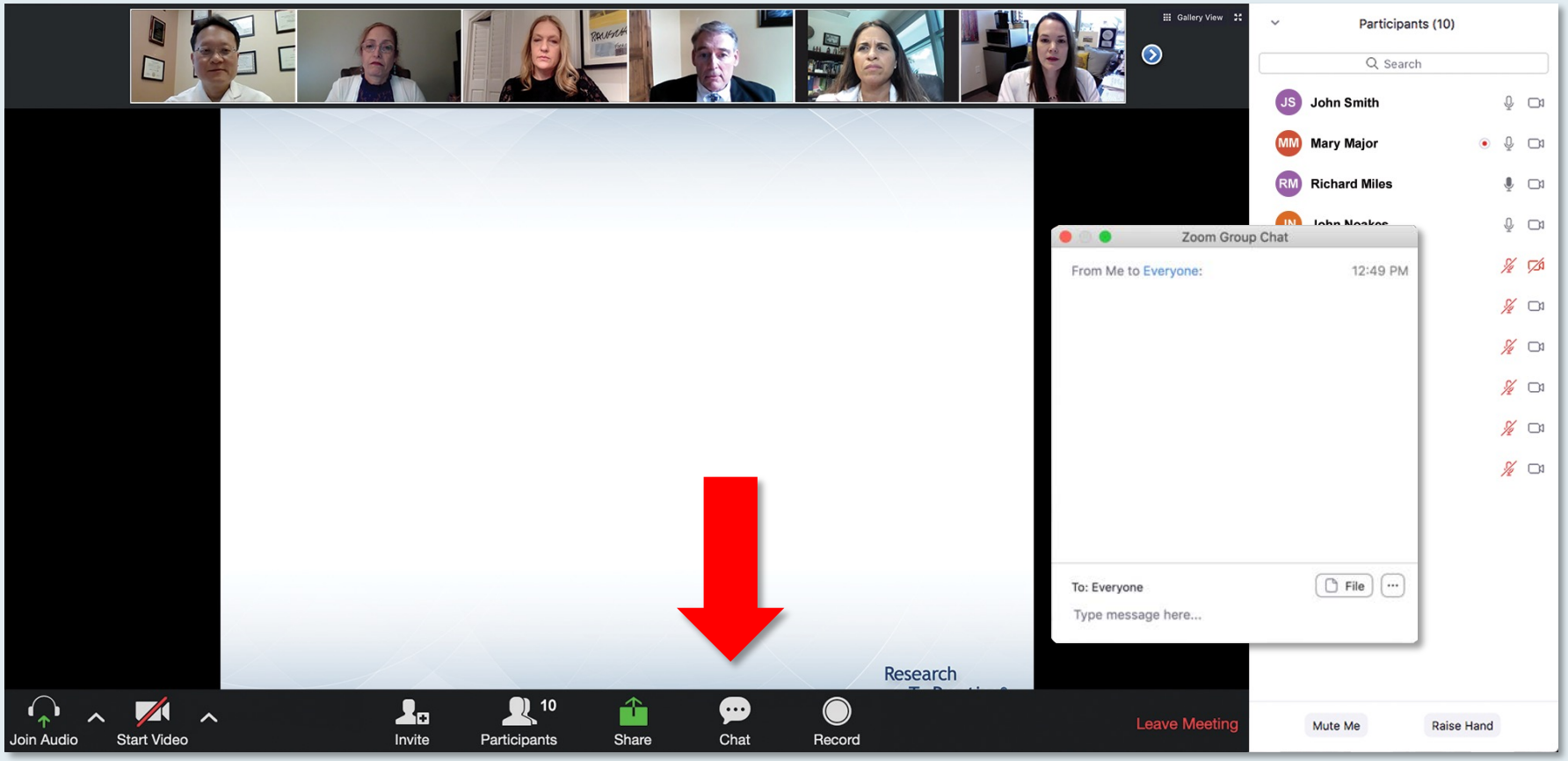
Contracted Research	Adaptimmune, ALX Oncology, Array BioPharma Inc, a subsidiary of Pfizer Inc, Blueprint Medicines, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Jounce Therapeutics, Merck, Moderna, Novartis, Scholar Rock, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company
Employment (Immediate Family Member)	Ironwood Pharmaceuticals

We Encourage Clinicians in Practice to Submit Questions



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

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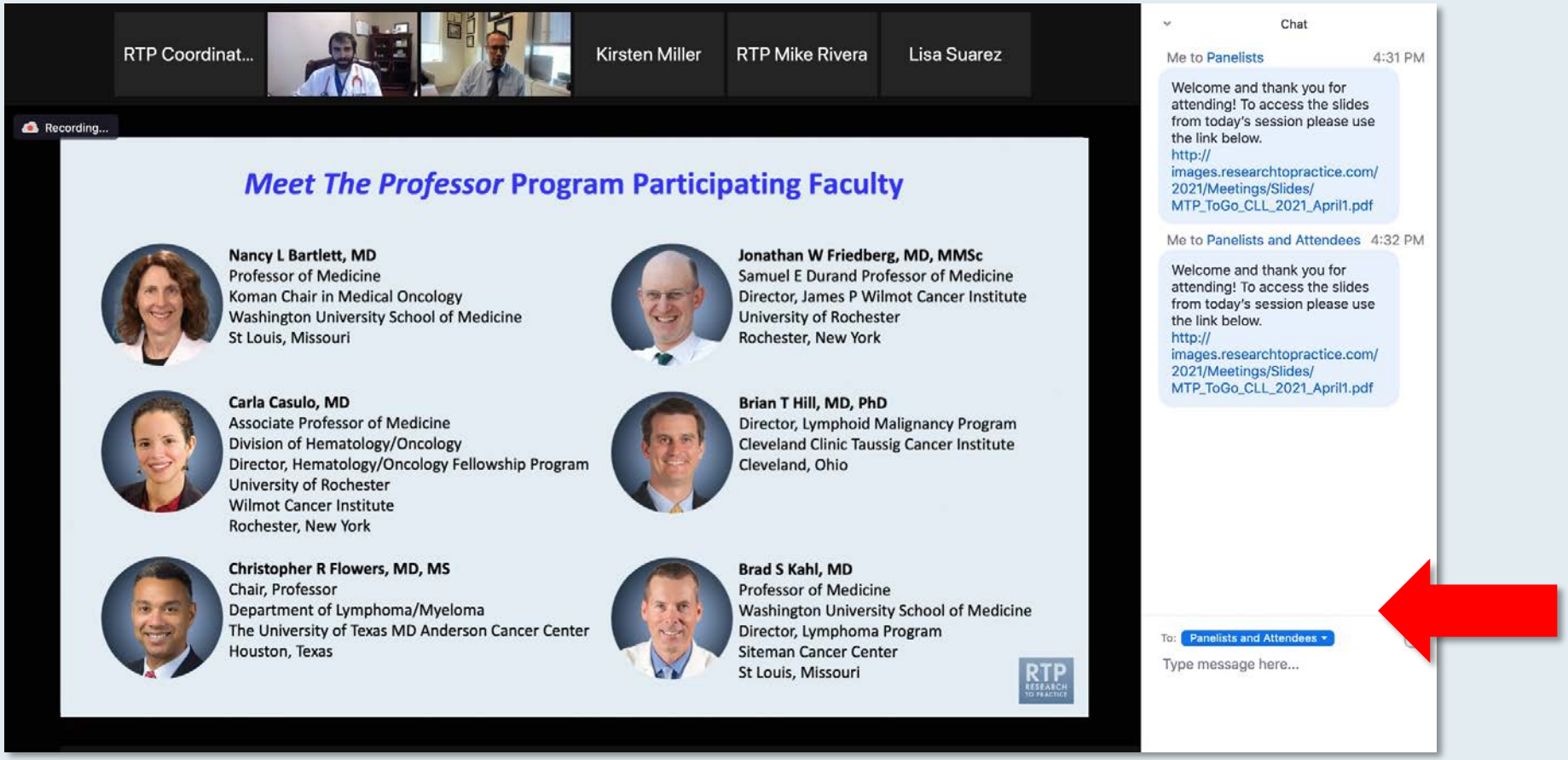
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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Familiarizing Yourself with the Zoom Interface

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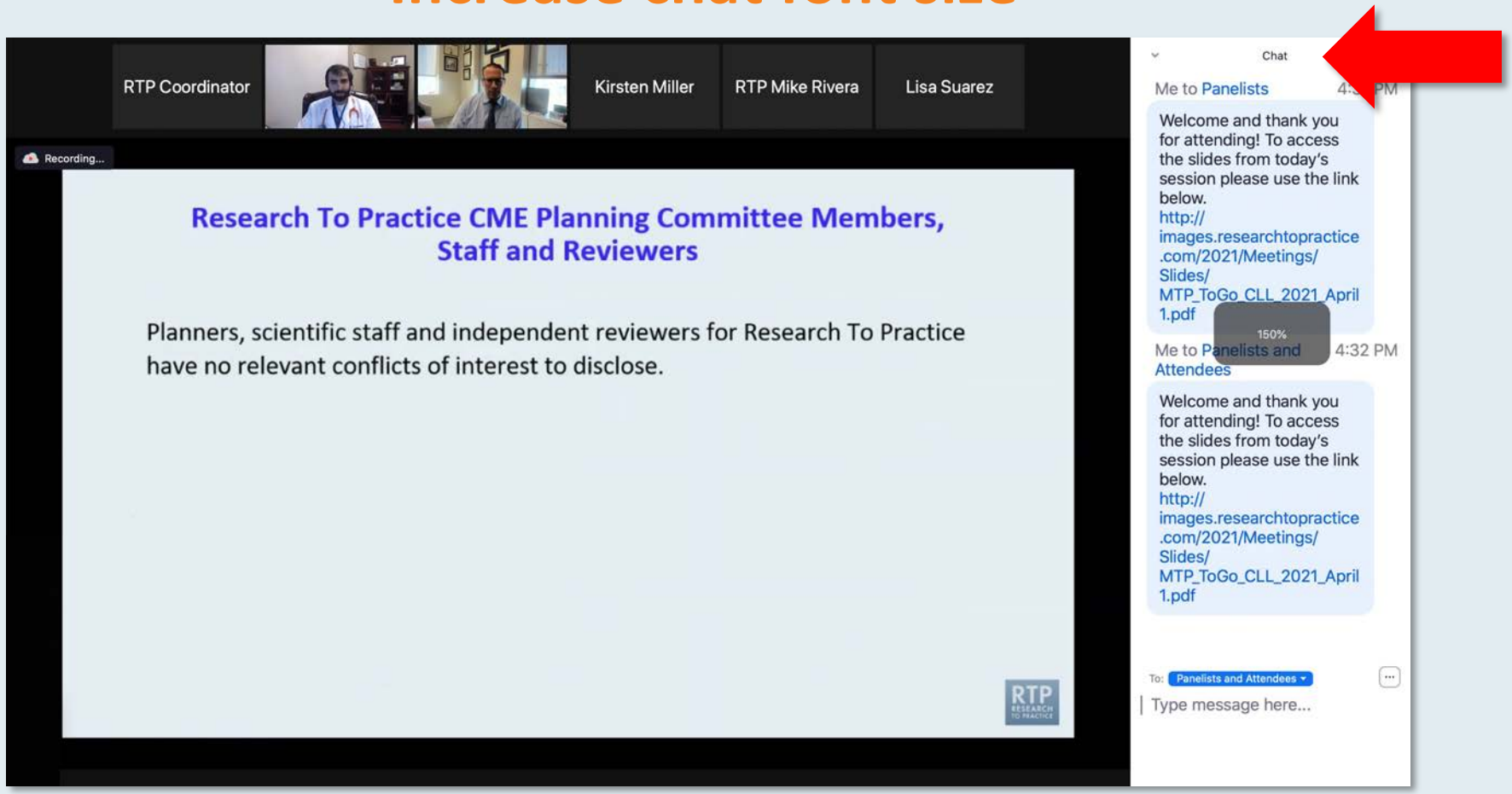

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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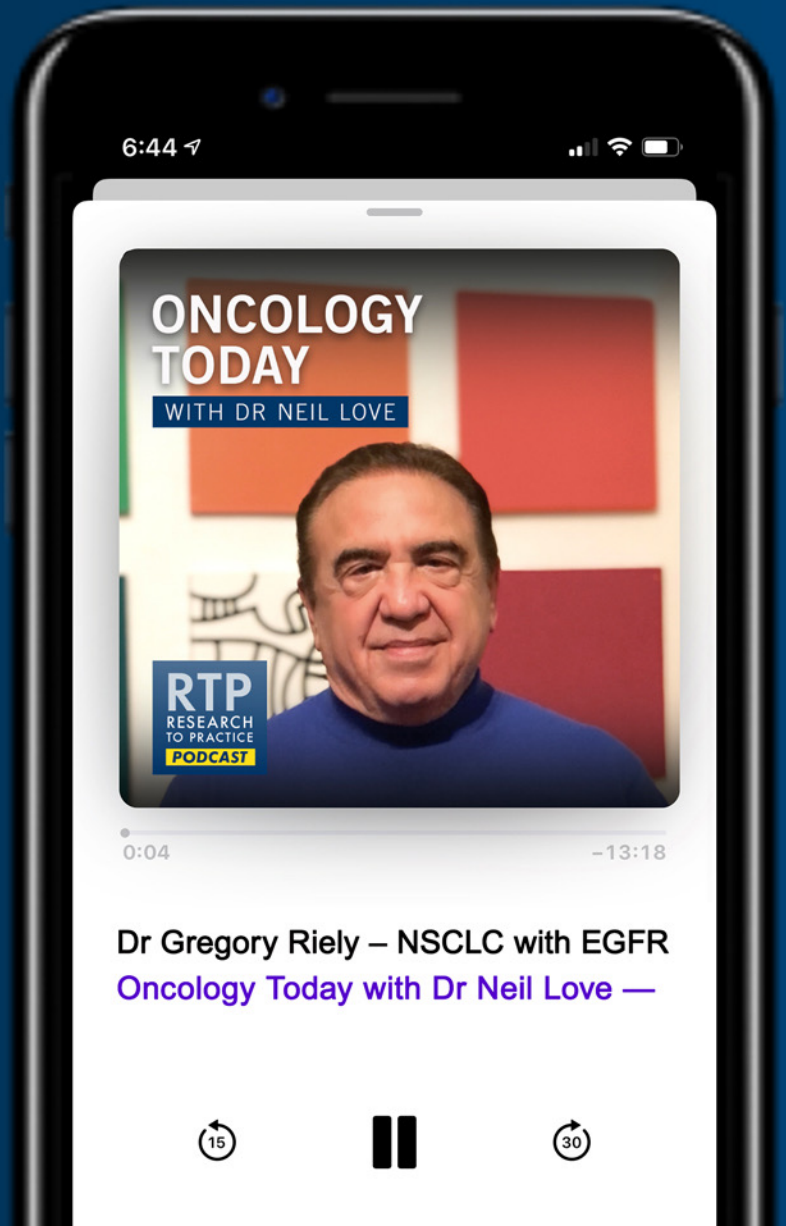

Clinical Investigator Perspectives on the Management of Renal Cell Carcinoma

Thursday, May 19, 2022

5:00 PM – 6:00 PM ET

Faculty

Thomas E Hutson, DO, PharmD
Brian I Rini, MD

Moderator

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Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Tuesday, May 24, 2022
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Faculty

Susan O'Brien, MD

Moderator

Neil Love, MD

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Current and Future Management of Myelofibrosis

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5:00 PM – 6:00 PM ET

Faculty

John Mascarenhas, MD

Moderator

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Optimizing the Management of Gastroesophageal Cancers

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5:00 PM – 6:00 PM ET

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Acute Myeloid Leukemia and Myelodysplastic Syndromes

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Michael R Savona, MD
Eunice S Wang, MD

Prostate Cancer

Saturday, June 4, 2022
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

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Luis Paz-Ares, MD, PhD
Heather Wakelee, MD
Jared Weiss, MD
Helena Yu, MD

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Kristen K Ciombor, MD, MSCI
Eileen M O'Reilly, MD
Philip A Philip, MD, PhD, FRCP
John Strickler, MD
Eric Van Cutsem, MD, PhD

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Joyce F Liu, MD, MPH
Kathleen N Moore, MD, MS

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6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

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Thank you for joining us!

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

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Meet The Professor Program Participating Faculty

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

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

Justin F Gainor, MD
Director, Center for Thoracic Cancers at
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Associate Professor of Medicine, Harvard
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Massachusetts General Hospital
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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

Alexander I Spira, MD, PhD
CEO and Clinical Director, NEXT Virginia
Director, Virginia Cancer Specialists Research Program
Fairfax, Virginia

MODERATOR
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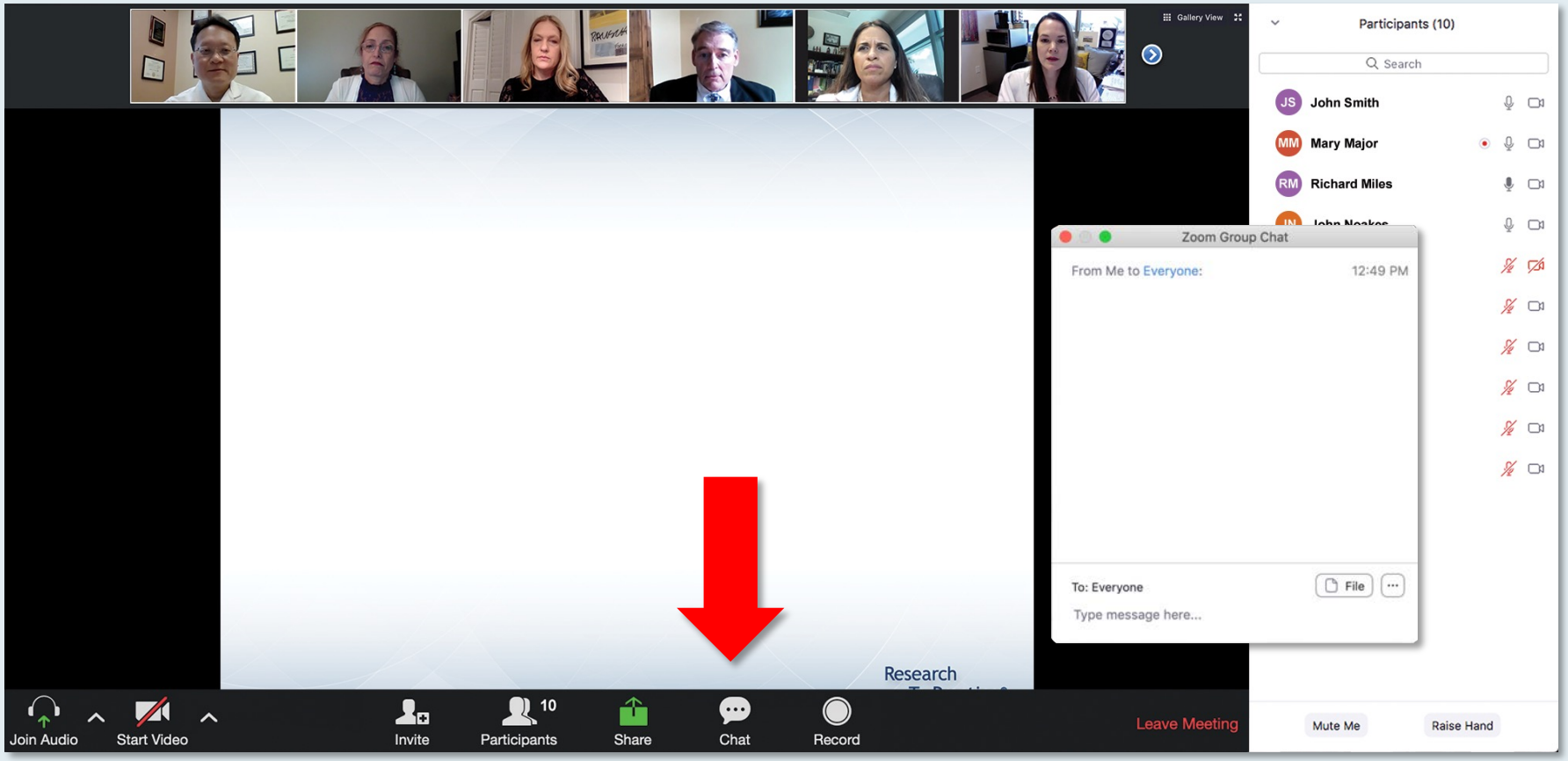

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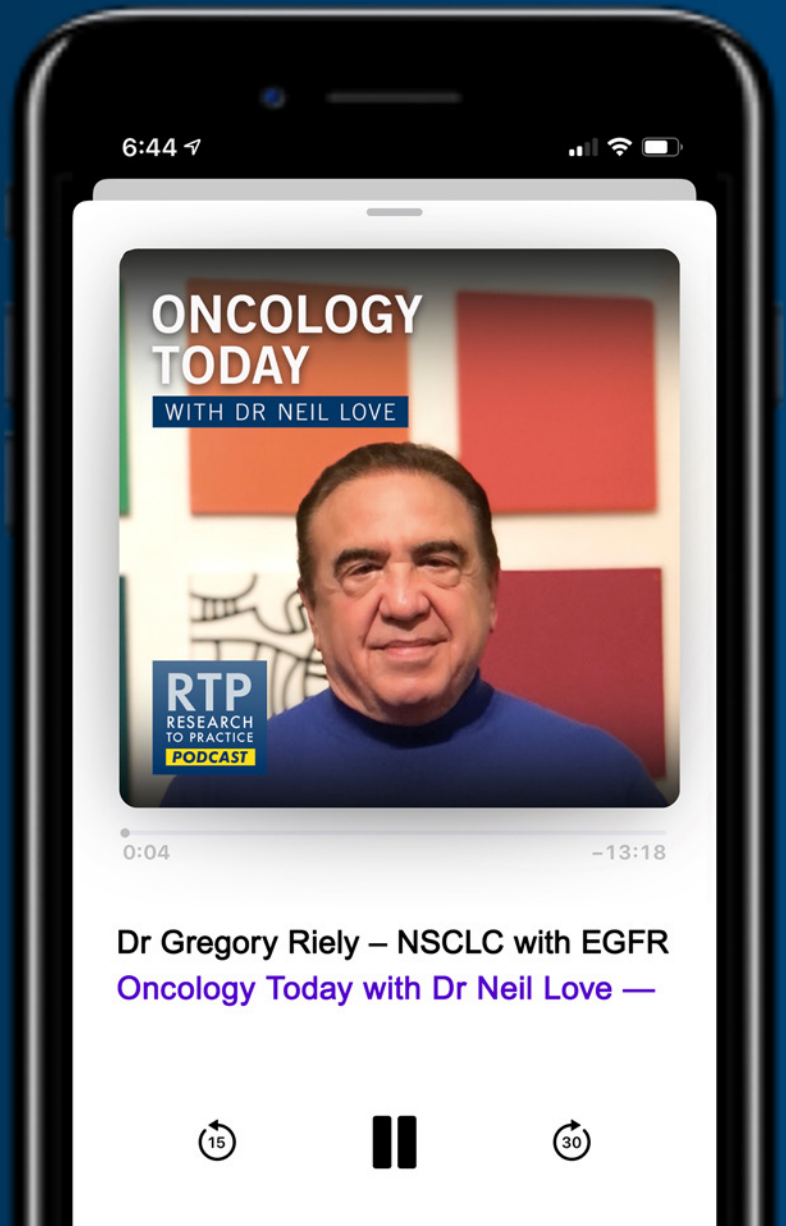

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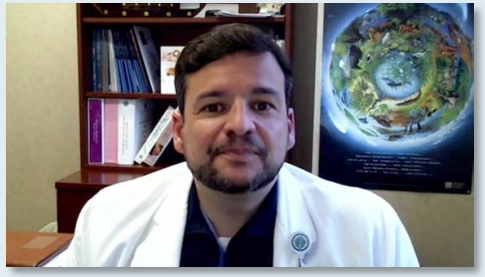
Employment (Immediate Family Member)	Ironwood Pharmaceuticals

Spencer Henick Bachow, MD
Lynn Cancer Institute
Boca Raton, Florida



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

Susannah Friemel, MD
Iowa Cancer Specialists
Bettendorf, Iowa

Ranju Gupta, MD
LVPG Hematology Oncology Associates
Bethlehem, Pennsylvania

Sulfi Ibrahim, MD
Reid Health
Richmond, Indiana

Kapisthalam (KS) Kumar, MD
Florida Cancer Specialists
Trinity, Florida

William R Mitchell, MD
Southern Oncology Specialists
Charlotte, North Carolina

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

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Meet The Professor with Dr Gainor

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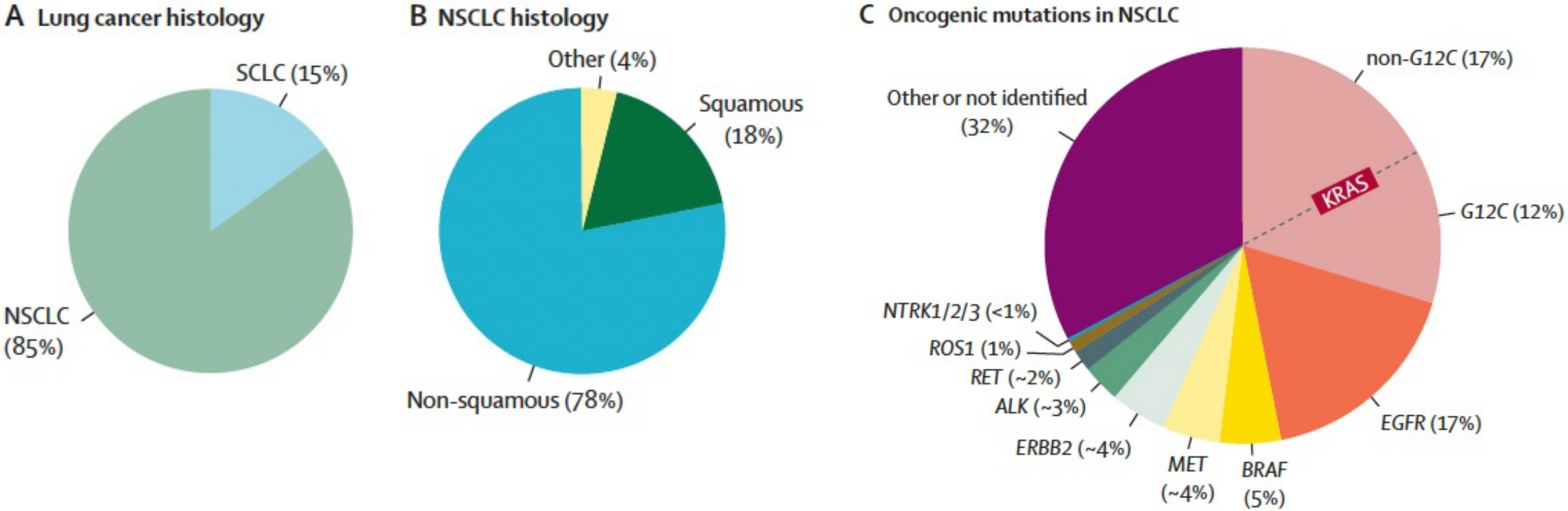
Lancet 2021;398:535-54. Seminar

Lung cancer

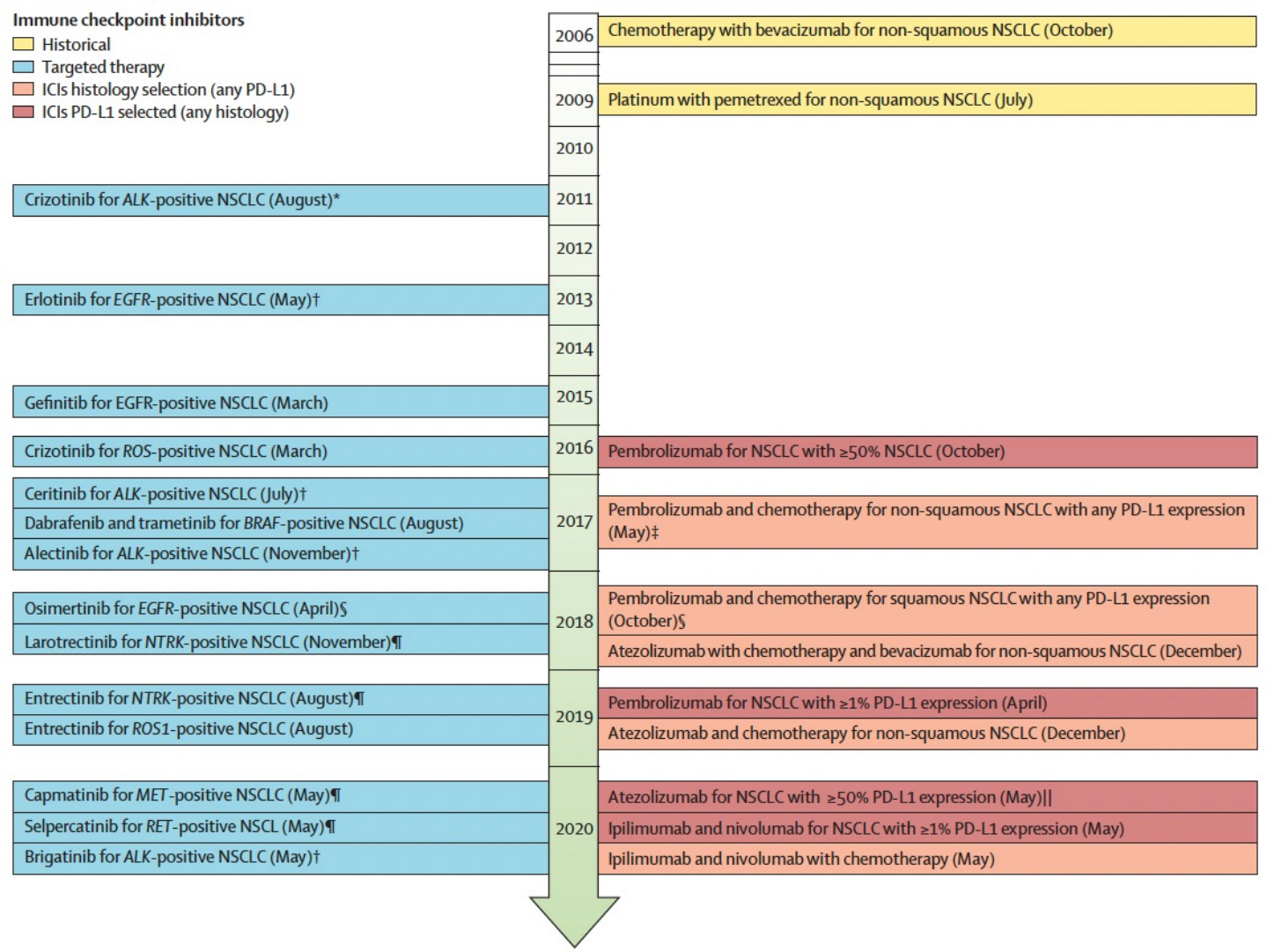
Alesha A Thai, Benjamin J Solomon, Lecia V Sequist, Justin F Gainor, Rebecca S Heist

Lung Cancer Histology



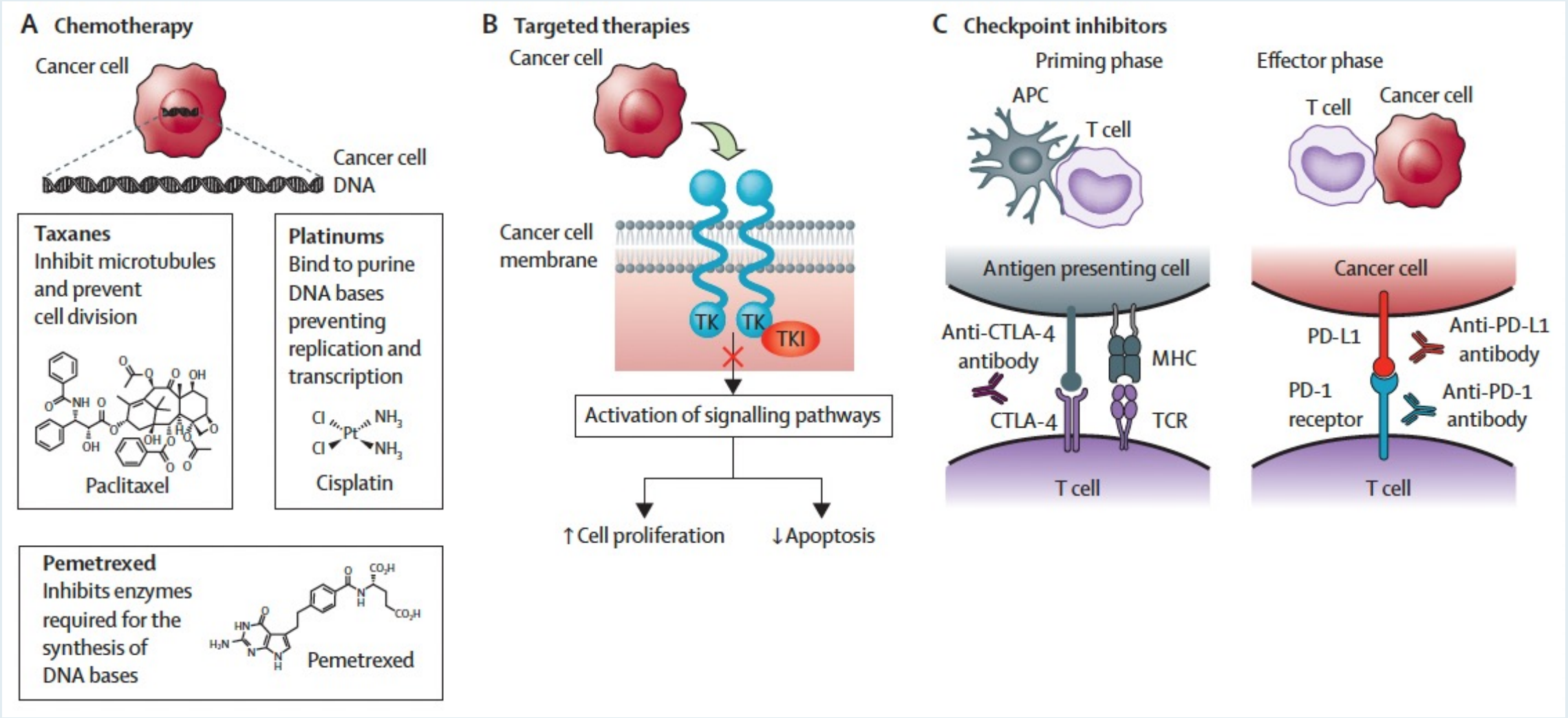
Thai AA et al. *Lancet* 2021;398:535-54.

Timeline of Selected US Food and Drug Administration Drug Approvals for Patients with Treatment-Naïve Metastatic NSCLC



Thai AA et al. *Lancet* 2021;398:535-54.

Mechanisms of Anticancer Therapies



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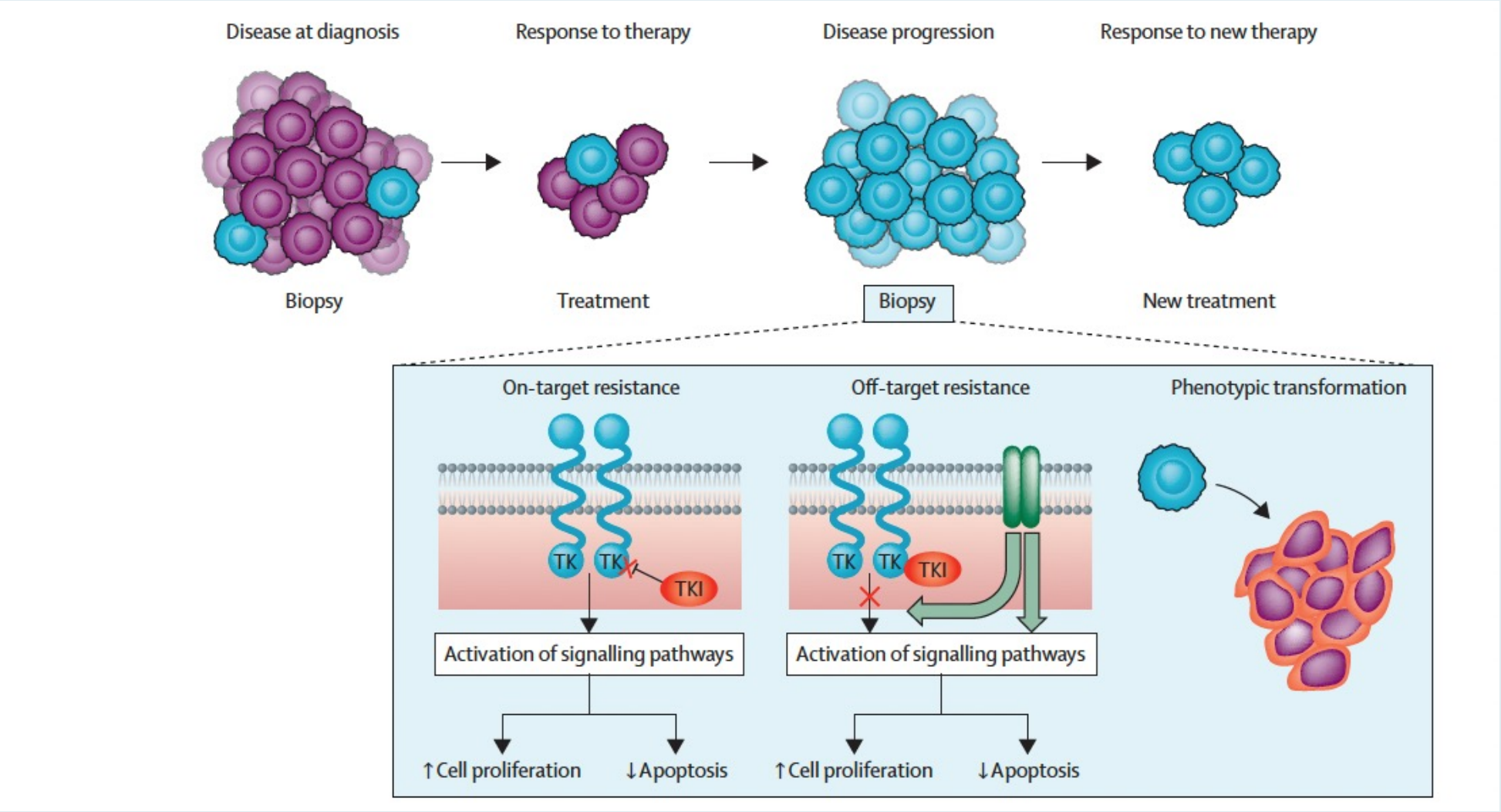
Evolution of Resistance to Targeted Therapies



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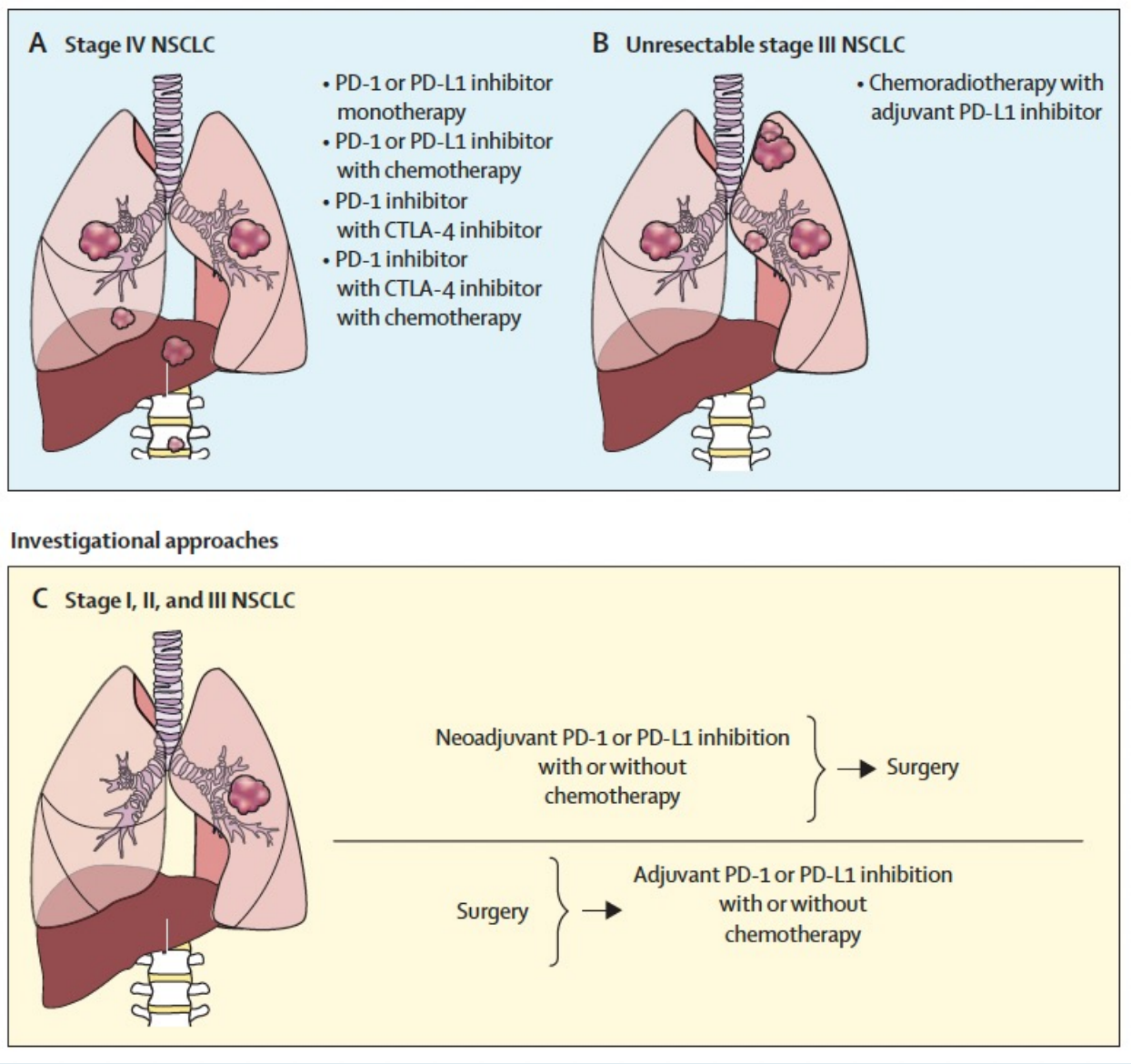
Immunotherapy Treatment Approaches in NSCLC



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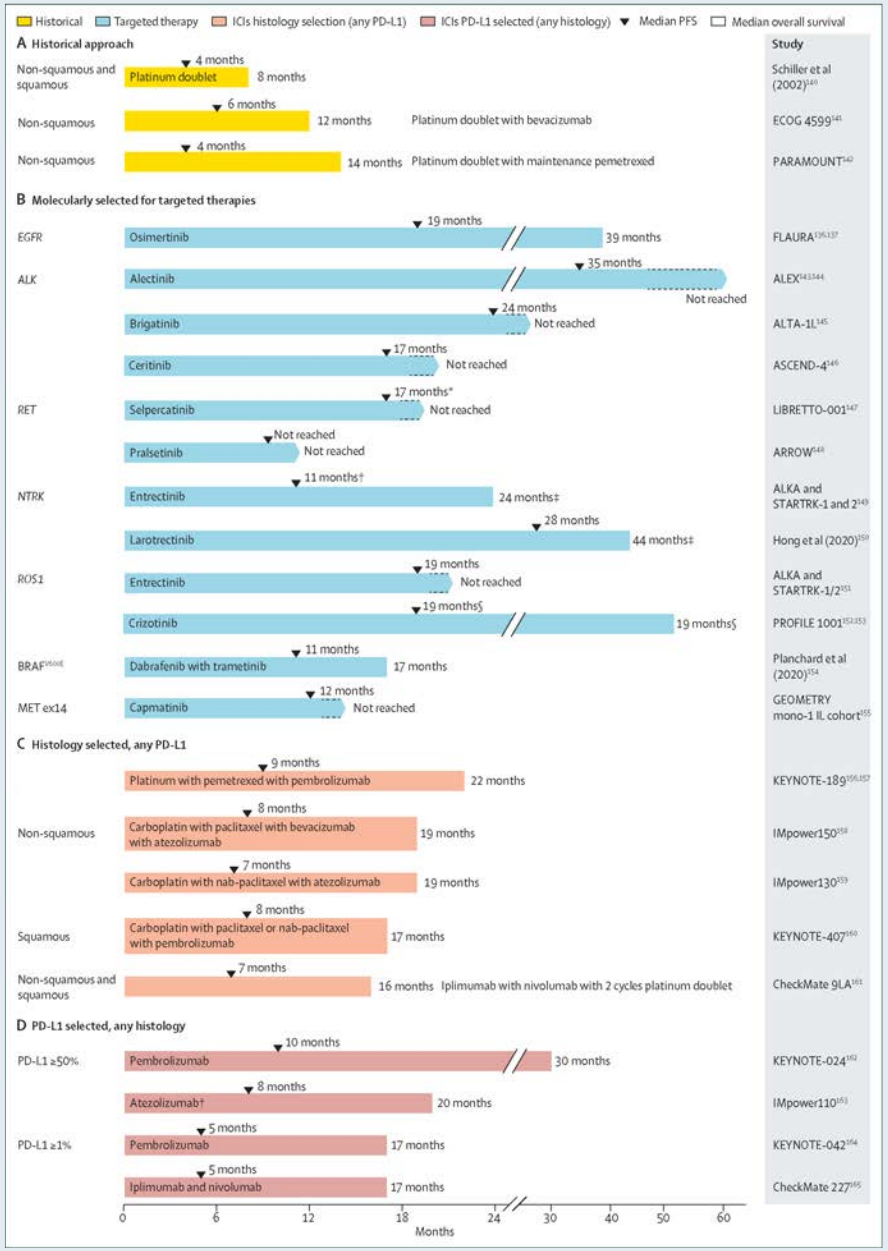
Selected US FDA-Approved Therapies for Up-Front Treatment of Metastatic NSCLC



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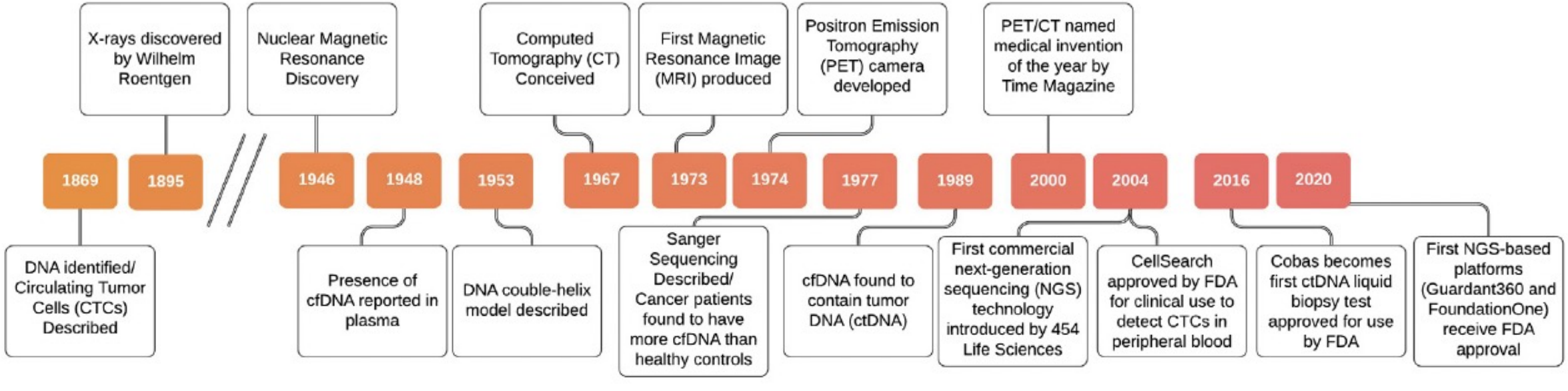
J Am Coll Radiol 2022;19(2 Pt B):336-43.

ORIGINAL ARTICLE ■ *Clinical Practice Management*

Liquid Biopsy, Diagnostic Imaging, and Future Synergies

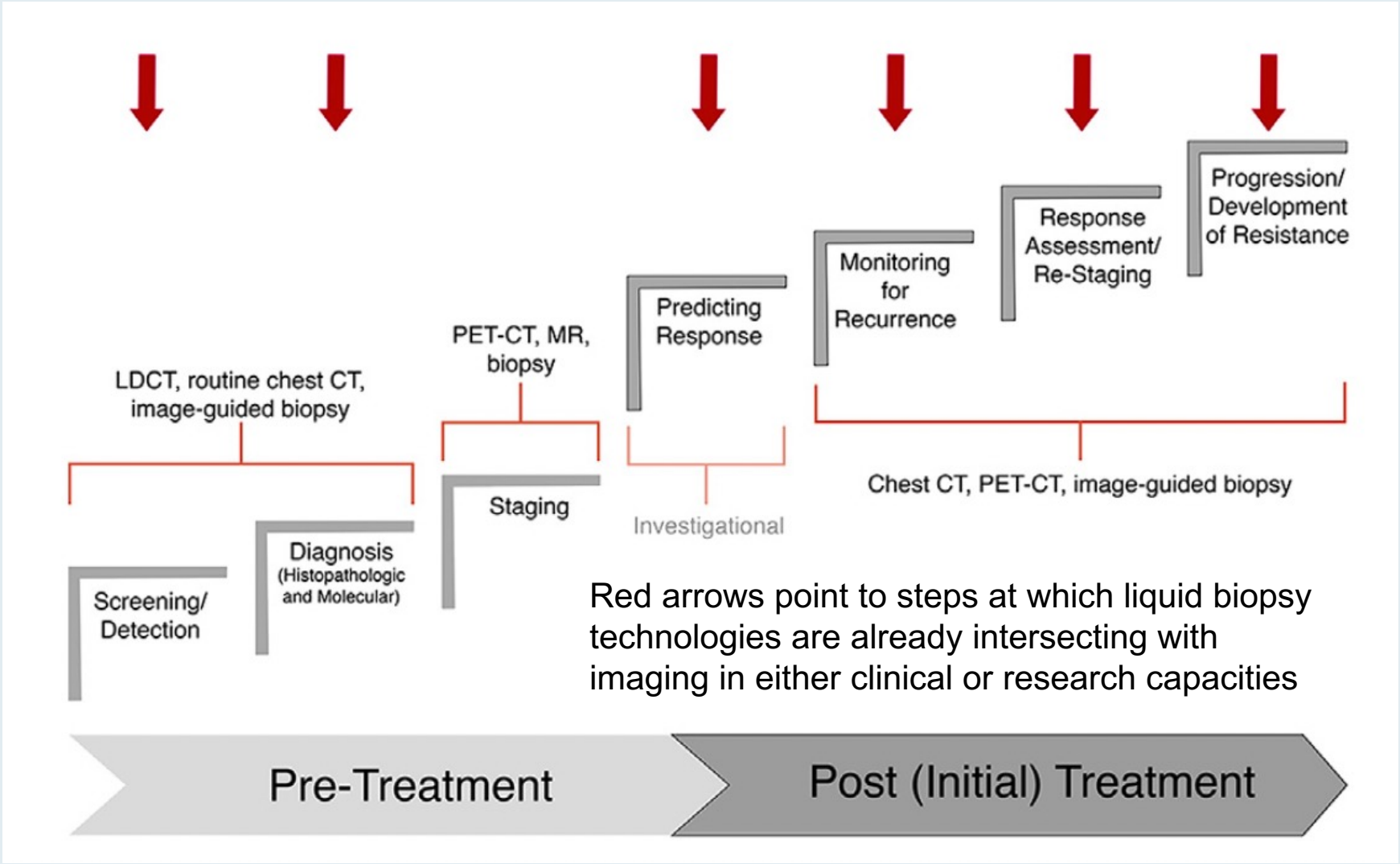
Milena Petranovic, MD[a,b,c], Sana Raoof, MD, PhD[d], Subba R. Digumarthy, MD[a,b,e], Amita Sharma, MBBS[a,b,f], Jo-Anne O. Shepard, MD[a,b,g], Justin F. Gainor, MD[b,h,i], Pari V. Pandharipande, MD, MPH[a,b,j,k]

Timeline of Notable Events in the Separate Evolution of Radiology and Liquid Biopsy



Petranovic M et al. *J Am Coll Radiol* 2022;19(2 Pt B):336-43.

Opportunities for Cancer Control in NSCLC



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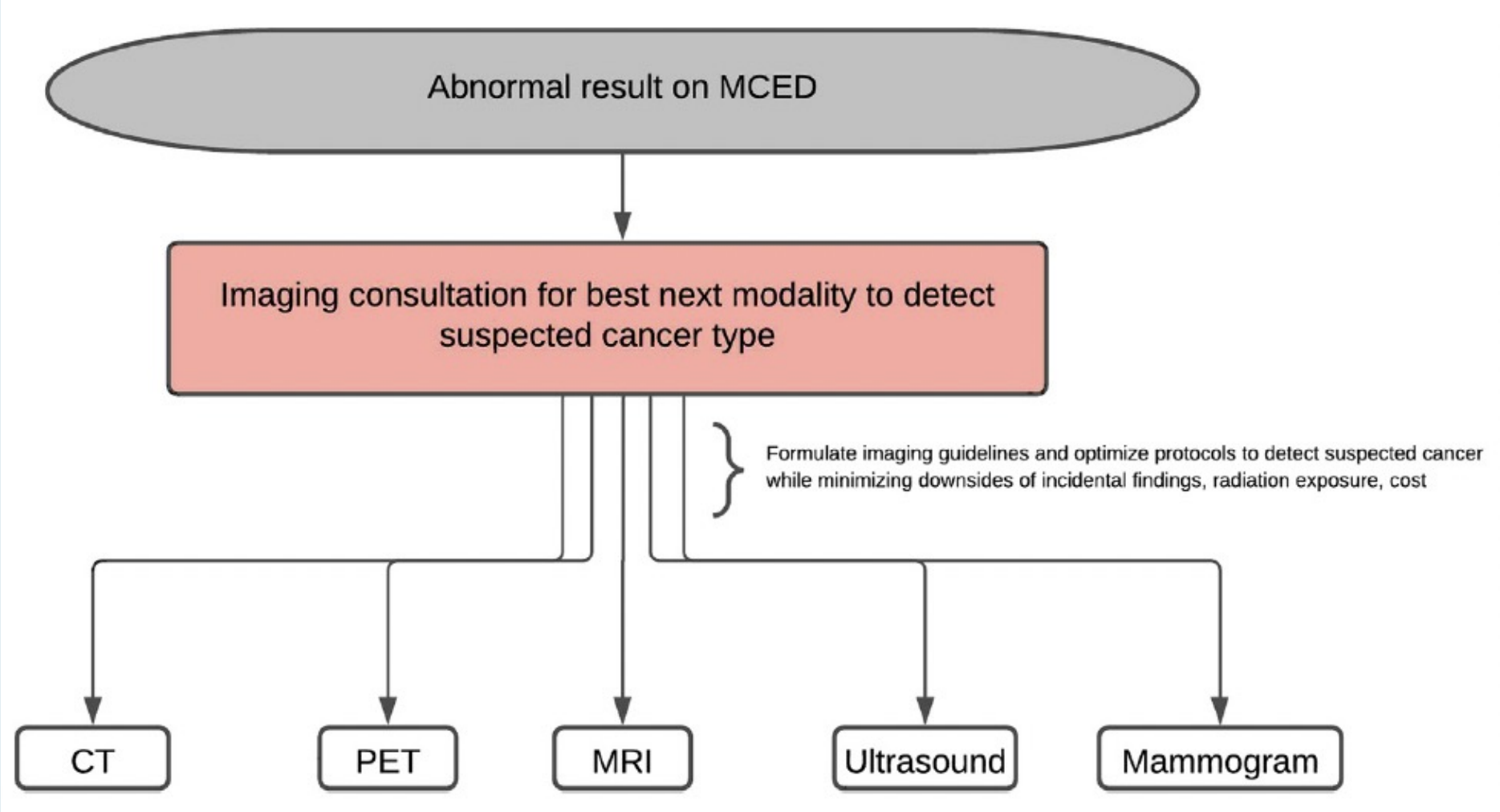
Workflow Algorithm in Setting of Abnormal Multicancer Early Detection (MCED) Results Obtained Before Imaging



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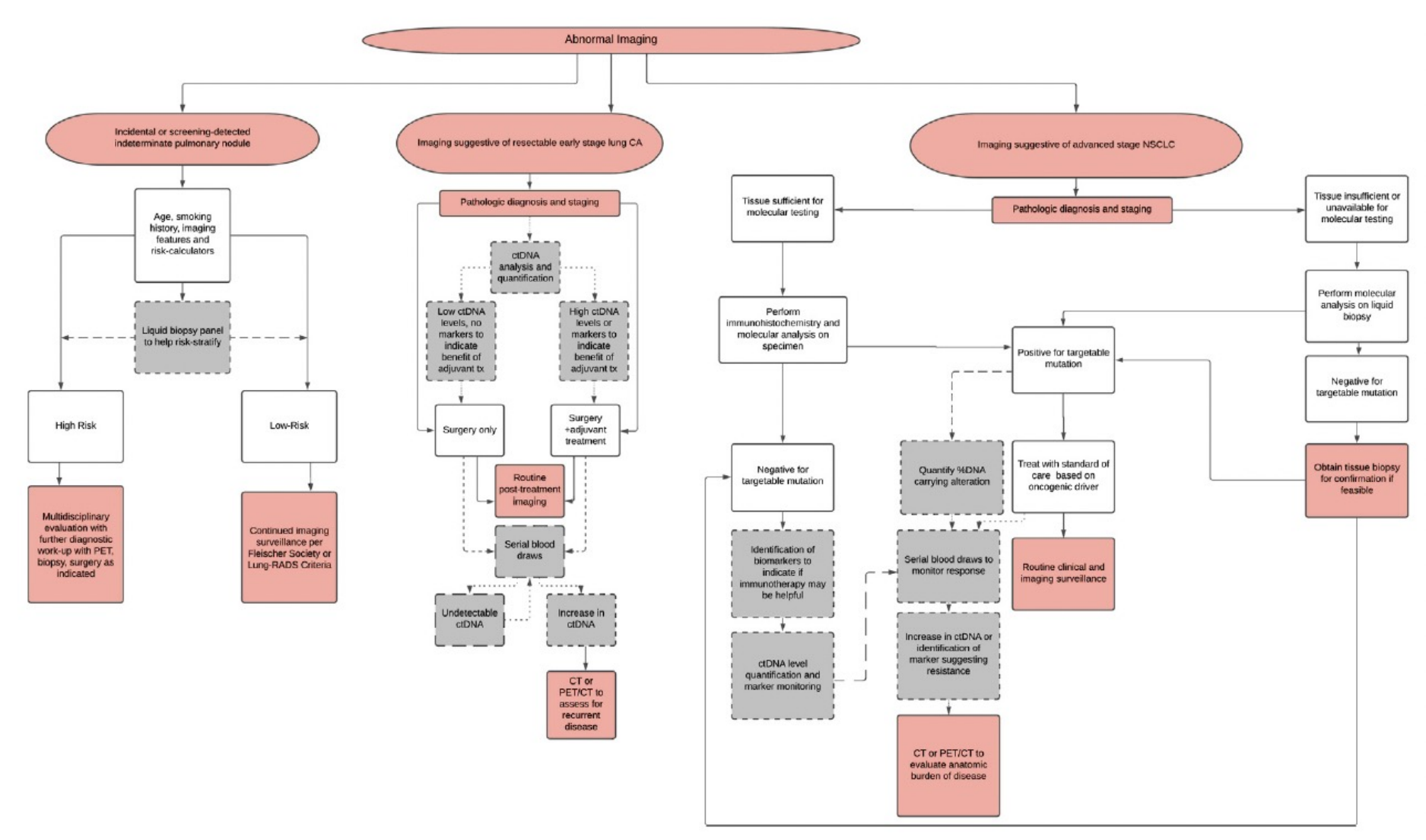
Possible Future Algorithms in the Care of Suspected NSCLC Subsequent to Initial Imaging



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Non-Small Cell Lung Cancer Actionable Mutations Beyond EGFR

ALK Rearrangements

ROS1 Fusions

BRAF Mutations

RET Fusions

MET Exon 14 Skipping Mutations

KRAS G12C Mutations

HER2 Mutations

NTRK Fusions

NRG1 Fusions

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer an immune checkpoint inhibitor (alone or in combination with chemotherapy) to a patient with metastatic nonsquamous NSCLC and an ALK rearrangement, and would level of PD-L1 expression have any bearing on this decision?

 Dr Baik	Beyond third line; No	 Dr Gainor	I would not recommend ICI in any line; No
 Dr Camidge	Beyond third line; No	 Dr Johnson	Beyond third line; No
 Dr Drilon	Beyond third line; Yes	 Dr Spira	Second line; No

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Regulatory and reimbursement issues aside, in which line of therapy would you generally offer an immune checkpoint inhibitor (alone or in combination with chemotherapy) to a patient with metastatic nonsquamous NSCLC and a ROS1 rearrangement, and would level of PD-L1 expression have any bearing on this decision?

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 Dr Drilon	Beyond third line; Yes	 Dr Spira	Second line; No

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer an immune checkpoint inhibitor (alone or in combination with chemotherapy) to a patient with metastatic nonsquamous NSCLC and a BRAF V600E mutation, and would level of PD-L1 expression have any bearing on this decision?

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer an immune checkpoint inhibitor (alone or in combination with chemotherapy) to a patient with metastatic nonsquamous NSCLC and a RET fusion, and would level of PD-L1 expression have any bearing on this decision?

 Dr Baik	Beyond third line; No	 Dr Gainor	I generally don't use ICIs in these pts; No
 Dr Camidge	Beyond third line; No	 Dr Johnson	Second line; No
 Dr Drilon	Beyond third line; Yes	 Dr Spira	Second line; No

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer an immune checkpoint inhibitor (alone or in combination with chemotherapy) to a patient with metastatic nonsquamous NSCLC and a MET exon 14 skipping mutation, and would level of PD-L1 expression have any bearing on this decision?

 Dr Baik	First line*; No	 Dr Gainor	Second line; No
 Dr Camidge	Beyond third-line; No	 Dr Johnson	Second line; No
 Dr Drilon	Second line; Yes	 Dr Spira	Second line; No

* In patients with smoking history with or without high tumor mutation burden

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer an immune checkpoint inhibitor (alone or in combination with chemotherapy) to a patient with metastatic nonsquamous NSCLC and a KRAS G12C mutation, and would level of PD-L1 expression have any bearing on this decision?

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer an immune checkpoint inhibitor (alone or in combination with chemotherapy) to a patient with metastatic nonsquamous NSCLC and a HER2 mutation, and would level of PD-L1 expression have any bearing on this decision?

 Dr Baik	Beyond third line; No	 Dr Gainor	First line; No
 Dr Camidge	First line; No	 Dr Johnson	Second line; No
 Dr Drilon	Second line; Yes	 Dr Spira	Second line; No

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer an immune checkpoint inhibitor (alone or in combination with chemotherapy) to a patient with metastatic nonsquamous NSCLC and HER2 overexpression, and would level of PD-L1 expression have any bearing on this decision?

 Dr Baik	First line; Yes	 Dr Gainor	First line; No
 Dr Camidge	First line; No	 Dr Johnson	Second line; No
 Dr Drilon	First line; Yes	 Dr Spira	First line; No

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer an immune checkpoint inhibitor (alone or in combination with chemotherapy) to a patient with metastatic nonsquamous NSCLC and and NTRK fusion, and would level of PD-L1 expression have any bearing on this decision?

 Dr Baik	Beyond third line; No	 Dr Gainor	Second line; No
 Dr Camidge	Beyond third line; No	 Dr Johnson	Second line; No
 Dr Drilon	Beyond third line; Yes	 Dr Spira	Second line; No

RTP
RESEARCH
TO PRACTICE

Meet The Professor with Dr Gainor

Introduction

MODULE 1: Immunotherapy in Patients with Targetable Mutations

MODULE 2: Case Presentations

- Dr Kumar: An 81-year-old man with recurrent, localized spindle cell carcinoma of the lung – PD-L1: 40%
- Dr Gupta: A 58-year-old woman with MSS adenocarcinoma of the lung with an NRG1 fusion
- Dr Morganstein: A 58-year-old woman with metastatic PD-L1-negative adenocarcinoma of the lung and a RET KF5B fusion
- Dr Friemel: A 70-year-old woman with Stage IIB adenocarcinoma of the lung and an ALK rearrangement – PD-L1: 5%
- Dr Carrizosa: A 52-year-old woman with metastatic NSCLC and an ALK (2p23) rearrangement – PD-L1 TPS: 50% and a 65-year-old man with metastatic adenocarcinoma of the lung, involving the brain, and an ALK rearrangement – PD-L1: 20%
- Dr Bachow: A 69-year-old man with metastatic adenocarcinoma of the lung and a HER2 V659D mutation
- Dr Mitchell: A 58-year-old woman with metastatic BRAF V600E-mutant adenocarcinoma of the lung – PD-L1 TPS: 80%
- Dr Ibrahim: A 67-year-old man with metastatic squamous cell carcinoma of the lung and an IDH1 mutation

MODULE 3: KRAS G12C Mutations

MODULE 4: ROS1 and NTRK Fusions

MODULE 5: Journal Club with Dr Gainor

MODULE 6: Appendix of Key Publications

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Case Presentation: An 81-year-old man with recurrent, localized spindle cell carcinoma of the lung – PD-L1: 40%

Dr KS Kumar (Trinity, Florida)

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TO PRACTICE

J Thorac Oncol 2021;16(5):850-9.

A Phase II Study of Capmatinib in Patients with MET-Altered Lung Cancer Previously Treated with a MET Inhibitor

Ibiayi Dagogo-Jack[1,2], Philicia Moonsamy[3], Justin F. Gainor[1,2], Jochen K. Lennerz[4], Zofia Piotrowska[1,2], Jessica J. Lin[1,2], Inga T. Lennes[1,2], Lecia V. Sequist[1,2], Alice T. Shaw[1,2,5], Kelly Goodwin[1], Sara E. Stevens[1], Andrew Do[1], Subba R. Digumarthy[6], Kristin Price[7], Alona Muzikansky[2], Aaron N. Hata[1,2], Rebecca S. Heist[1,2,‡]

Case Presentation: A 58-year-old woman with MSS (microsatellite-stable) adenocarcinoma of the lung with an NRG1 fusion

Dr Ranju Gupta (Bethlehem, Pennsylvania)

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TO PRACTICE

Case Presentation: A 58-year-old woman with metastatic PD-L1-negative adenocarcinoma of the lung and a RET KF5B fusion

Dr Neil Morganstein (Summit, New Jersey)

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Clin Cancer Res. 2021 August 01; 27(15): 4160–4167. doi:10.1158/1078-0432.CCR-21-0800.

Intracranial efficacy of selpercatinib in *RET* fusion-positive non-small cell lung cancers on the LIBRETTO-001 trial

Vivek Subbiah[1], Justin F. Gainor[2], Geoffrey R. Oxnard[3], Daniel S.W. Tan[4], Dwight H. Owen[5], Byoung Chul Cho[6], Herbert H.F. Loong[7], Caroline E. McCoach[8], Jared Weiss[9], Yu Jung Kim[10], Lyudmila Bazhenova[11], Keunchil Park[12], Haruko Daga[13], Benjamin Besse[14], Oliver Gautschi[15], Christian Rolfo[16], Edward Y. Zhu[17], Jennifer F. Kherani[17], Xin Huang[17], Suhyun Kang[18], Alexander Drilon[19]

BJC British Journal of Cancer

Br J Cancer 2021;124(11):1757-8.

COMMENT

An early look at selective RET inhibitor resistance: new challenges and opportunities

Jessica J. Lin[1] and Justin F. Gainor[1]

Ann Oncol 2020;31(12):1725-33.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Mechanisms of resistance to selective RET tyrosine kinase inhibitors in *RET* fusion-positive non-small-cell lung cancer

J. J. Lin[1,2], S. V. Liu[3], C. E. McCoach[4], V. W. Zhu[5], A. C. Tan[6], S. Yoda[1,2], J. Peterson[1,2], A. Do[1,2], K. Prutisto-Chang[1,2], I. Dagogo-Jack[1,2], L. V. Sequist[1,2], L. J. Wirth[1,2], J. K. Lennerz[2,7], A. N. Hata[1,2], M. Mino-Kenudson[2,7], V. Nardi[2,7], S.-H. I. Ou[5], D. S.-W. Tan[6] & J. F. Gainor[1,2*]

A First-in-Human Phase 1 Study of the Next-Generation RET Inhibitor LOXO-260 in RET Inhibitor Refractory Patients with RET-Altered Cancers (Trial in Progress)

Pennell NA et al.

ASCO 2022;Abstract TPS8595.

Chylothorax and Chylous Ascites During RET Tyrosine Kinase Inhibitor Therapy

Kalchiem-Dekel O et al.

ASCO 2022;Abstract 9080.

Case Presentation: A 70-year-old woman with Stage IIB adenocarcinoma of the lung and an ALK rearrangement – PD-L1: 5%

Dr Susannah Friemel (Bettendorf, Iowa)

RTP RESEARCH TO PRACTICE

Dr Daniel Carrizosa
(Charlotte, North Carolina)

A 52-year-old woman with metastatic NSCLC and an ALK (2p23) rearrangement – PD-L1 TPS: 50%

A 65-year-old man with metastatic adenocarcinoma of the lung, involving the brain, and an ALK rearrangement – PD-L1: 20%

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Case Presentation: A 69-year-old man with metastatic adenocarcinoma of the lung and a HER2 V659D mutation

Dr Spencer Bachow (Boca Raton, Florida)

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RESEARCH
TO PRACTICE

Case Presentation: A 58-year-old woman with metastatic BRAF V600E-mutant adenocarcinoma of the lung – PD-L1 TPS: 80%

Dr William Mitchell (Charlotte, North Carolina)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 67-year-old man with metastatic squamous cell carcinoma of the lung and an IDH1 mutation

Dr Sulfi Ibrahim (Richmond, Indiana)

Case Presentation: A 67-year-old man with metastatic squamous cell carcinoma of the lung and an IDH1 mutation

DETECTED ALTERATION(S) / BIOMARKER(S)	% CFDNA OR AMPLIFICATION	ASSOCIATED FDA-APPROVED THERAPIES	CLINICAL TRIAL AVAILABILITY
ALK T1151M	0.5%	Alectinib, Brigatinib, Lorlatinib Ceritinib, Crizotinib	Yes
PIK3CA E545K	10.0%	Alpelisib	Yes
TP53 Y220H	0.9%	None	Yes
TP53 T150fs	20.3%	None	Yes
NFE2L2 S301L	22.2%	None (VUS)[$]	No (VUS)[$]
KEAP1 R272G	20.8%	None (VUS)[$]	No (VUS)[$]
FBXW7 G329W	10.9%	None (VUS)[$]	No (VUS)[$]
NOTCH1 E242K	0.2%	None (VUS)[$]	No (VUS)[$]
ATM G2695R	0.2%	None (VUS)[$]	No (VUS)[$]
SMO R421Q	0.2%	None (VUS)[$]	No (VUS)[$]
ERBB2 (HER2) R103Q	0.1%	None (VUS)[$]	No (VUS)[$]
EGFR R252C	0.1%	None (VUS)[$]	No (VUS)[$]

CONTACT US

Biomarker Findings

Blood Tumor Mutational Burden - 6 Muts/Mb
Microsatellite status - MSI-High Not Detected
Tumor Fraction - 39%

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

FBXW7 R479P
IDH1 R132C
PIK3CA E545K
AKT2 amplification
CCND1 amplification
KRAS amplification
MDM2 amplification
FGF19 amplification
FGF3 amplification
FGF4 amplification
SF3B1 H662Q
TP53 R306*

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Gainor

Clinicopathologic Characteristics and Outcomes for Patients with KRAS G12D-Mutant Non-Small Cell Lung Cancer (NSCLC)

Cooper AJ et al.

ASCO 2022;Abstract e21024.

Cancers (Basel) 2021;13(14):3572.

cancers

MDPI

Article

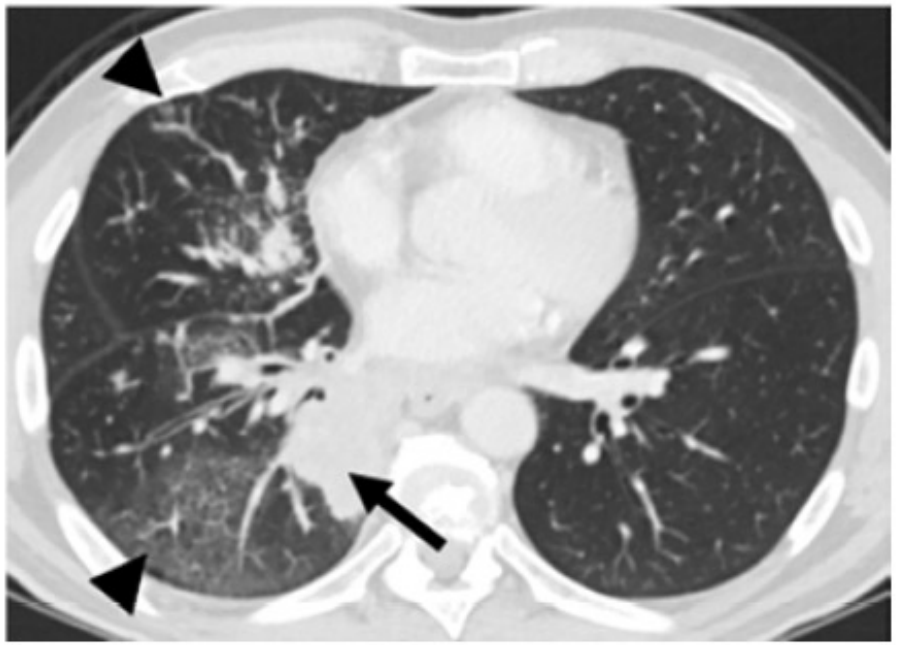
Clinical and Imaging Features of Non-Small Cell Lung Cancer with G12C KRAS Mutation

Markus Y. Wu [1], Eric W. Zhang [1], Matthew R. Strickland [2], Dexter P. Mendoza [1], Lev Lipkin [3], Jochen K. Lennerz [3], Justin F. Gainor [2], Rebecca S. Heist [2] and Subba R. Digumarthy [1,*]

JC JOURNAL CLUB

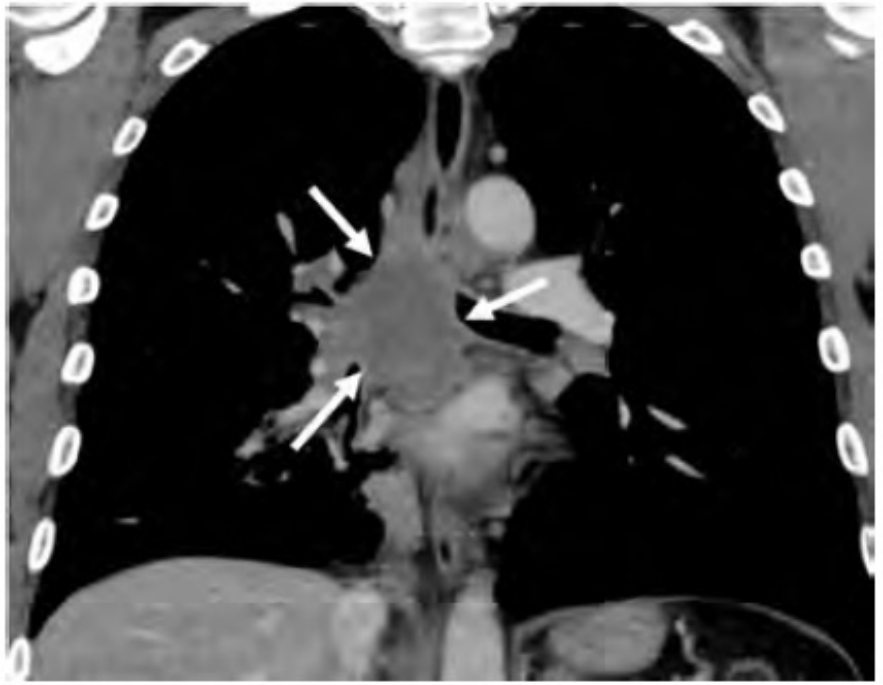
RTP RESEARCH TO PRACTICE

Representative Imaging Features in a 64-Year-Old Man, a Prior Smoker, with NSCLC and a KRAS G12C Mutation



(A)

Pretreatment CT images show a solid mass in the right lower lobe (A, black arrow) and associated septal and peribronchial thickening consistent with lymphangitic carcinomatosis (A, black arrowheads).

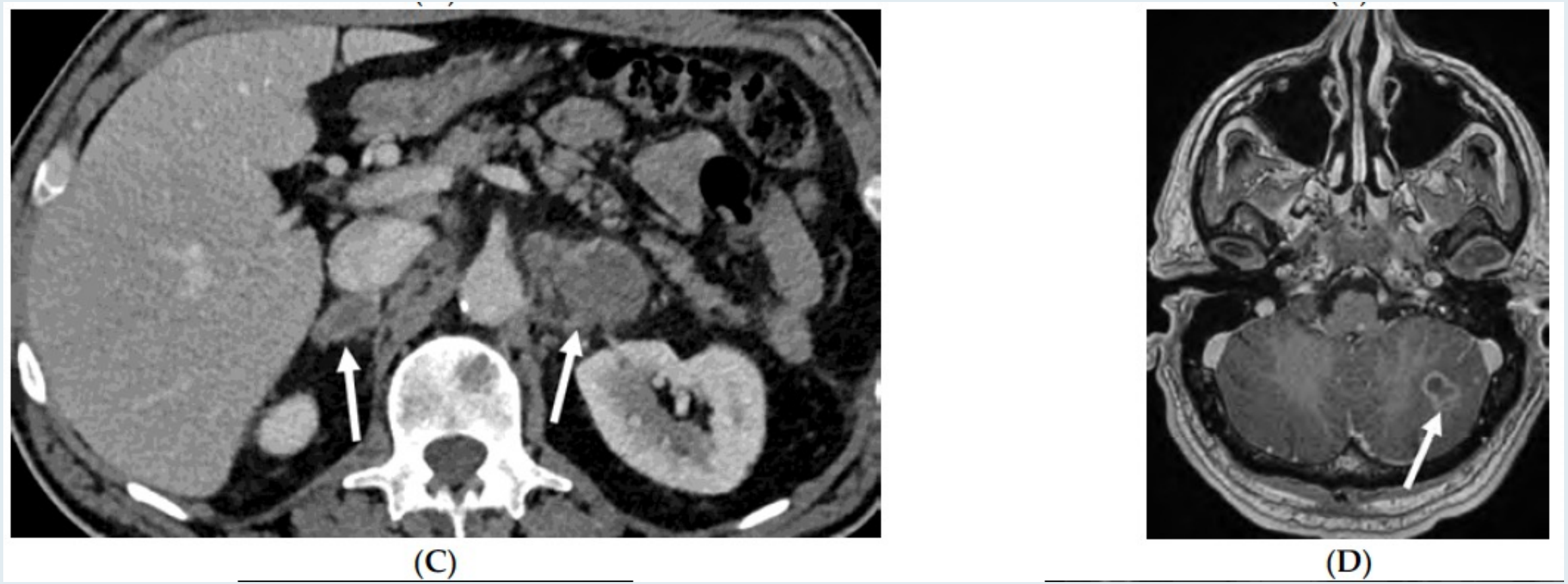


(B)

There was extensive mediastinal and hilar lymphadenopathy (B, white arrows)

Wu MY et al. *Cancers (Basel)* 2021;13(14):3572.

Representative Imaging Features in a 64-Year-Old Man, a Prior Smoker, with NSCLC and a KRAS G12C Mutation

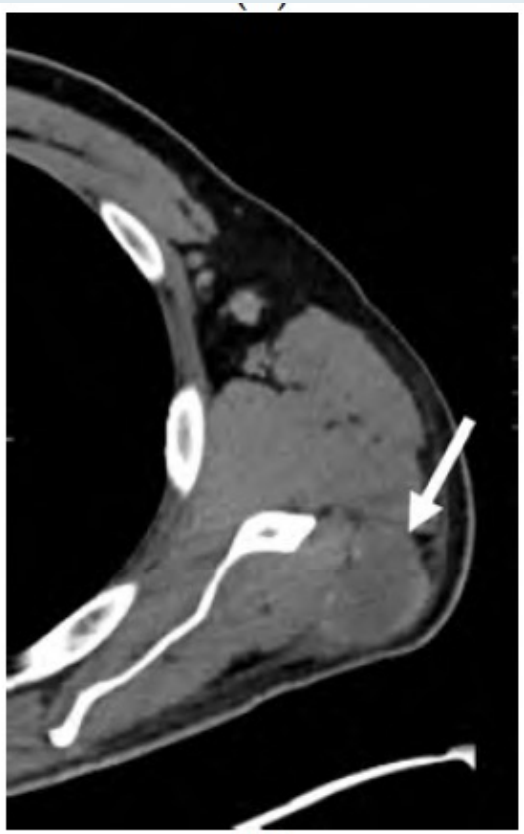


Bilateral adrenal metastases (C, white arrows)

Brain metastasis (D, white arrow)

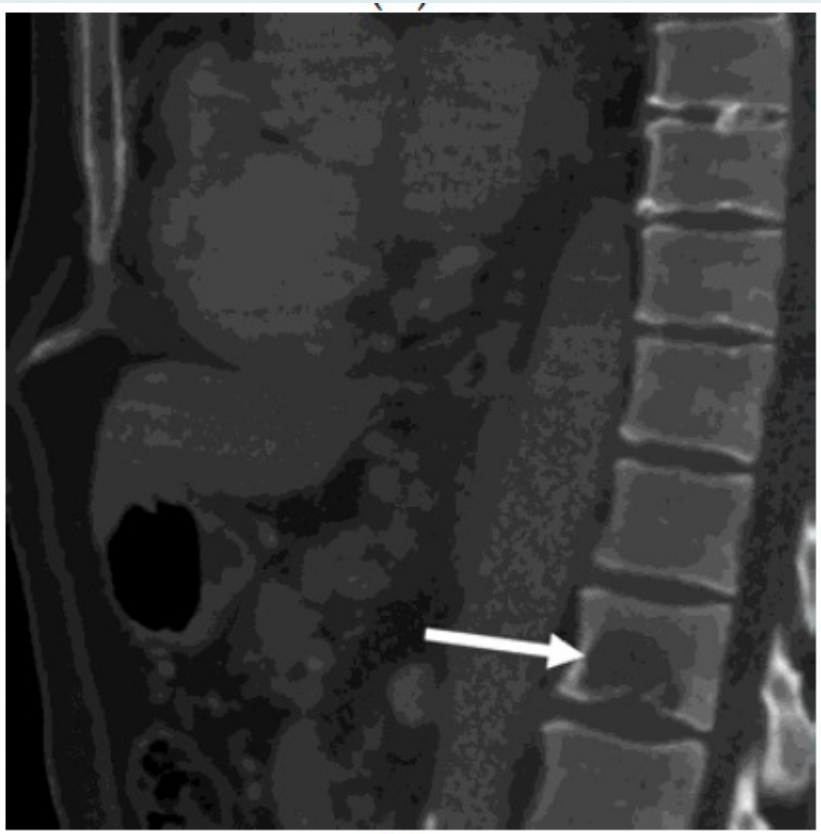
Wu MY et al. *Cancers (Basel)* 2021;13(14):3572.

Representative Imaging Features in a 64-Year-Old Man, a Prior Smoker, with NSCLC and a KRAS G12C Mutation



(E)

Soft tissue metastasis (E, white arrow)



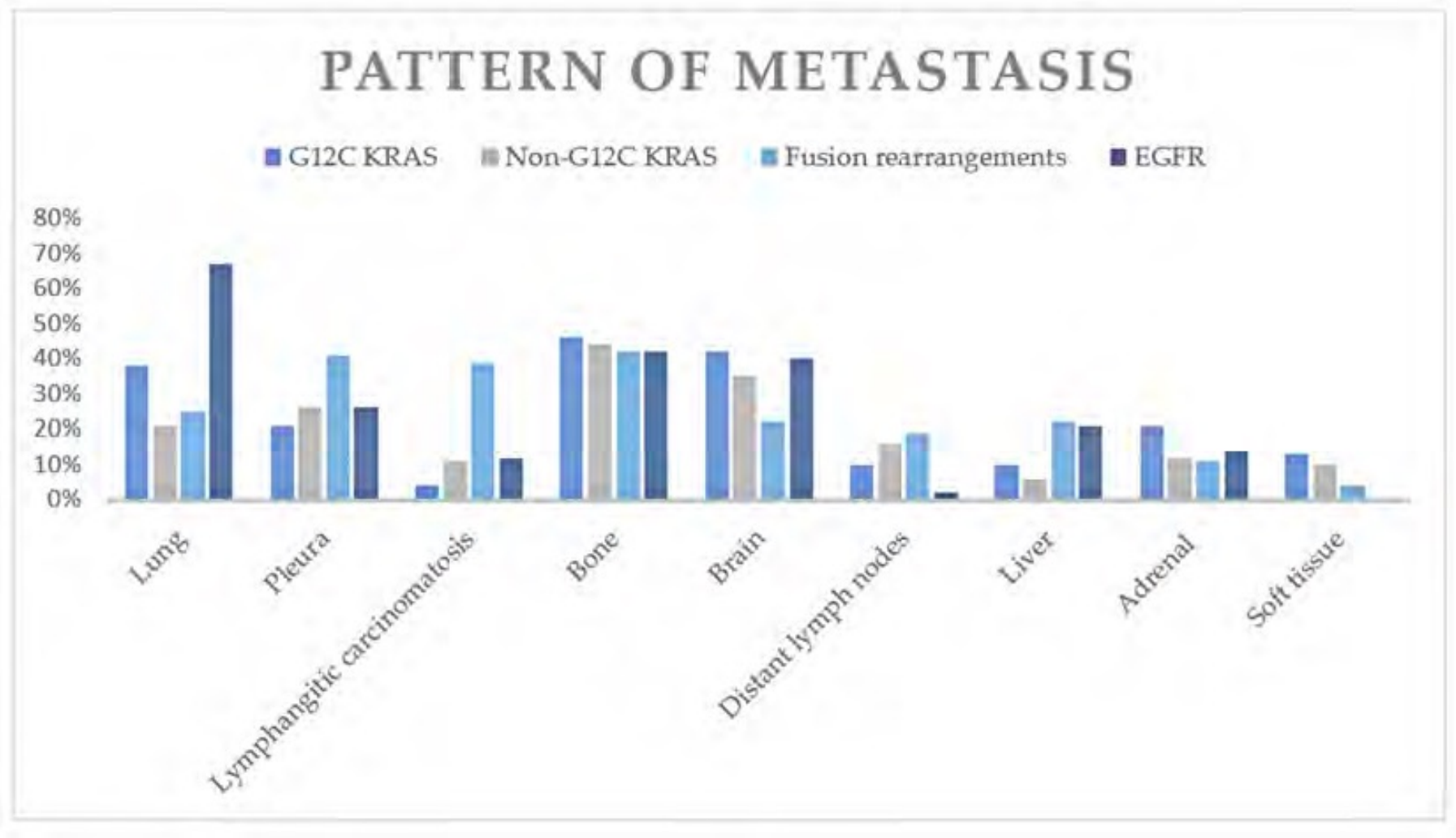
(F)

A lytic osseous metastasis of the first lumbar vertebral body (F, white arrow)

Wu MY et al. *Cancers (Basel)* 2021;13(14):3572.

RTP RESEARCH TO PRACTICE

Frequency of Various Metastatic Sites in NSCLC with KRAS G12C Mutation and with Other Genetic Alterations



Wu MY et al. *Cancers (Basel)* 2021;13(14):3572.

RTP RESEARCH TO PRACTICE

Cancer Discov 2021;11(8):1913-22.

Clinical acquired resistance to KRAS^{G12C} inhibition through a novel KRAS switch-II pocket mutation and polyclonal alterations converging on RAS-MAPK reactivation

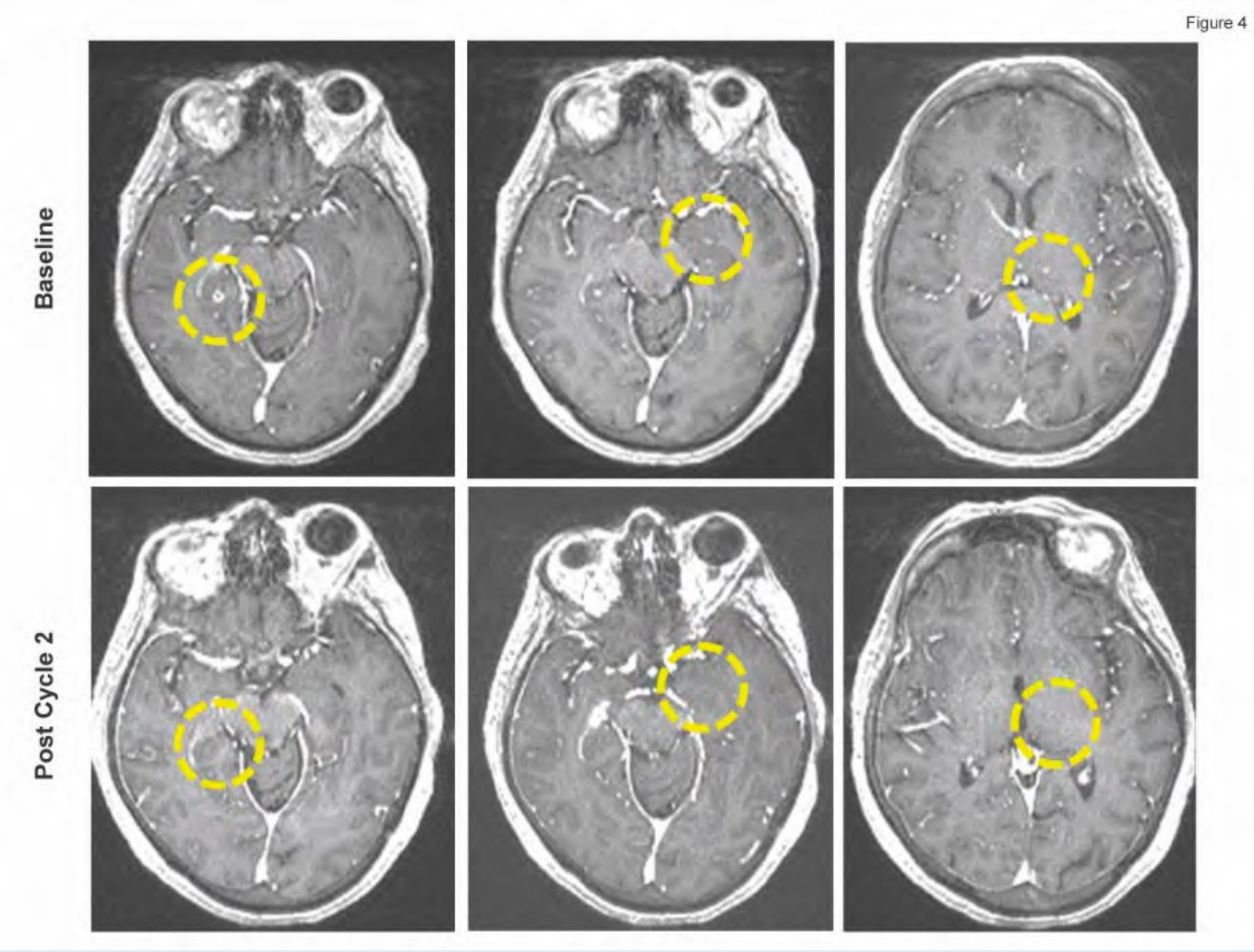
Noritaka Tanaka[1,*], Jessica J. Lin[1,*], Chendi Li[1,*], Meagan B. Ryan[1], Junbing Zhang[1], Lesli A. Kiedrowski[2], Alexa G. Michel[1], Mohammed U. Syed[1], Katerina A. Fella[1], Mustafa Sakhi[1], Islam Baiev[1], Dejan Juric[1], Justin F. Gainor[1], Samuel J. Klempner[1], Jochen K. Lennerz[3], Giulia Siravegna[1], Liron Bar-Peled[1], Aaron N. Hata[1,#], Rebecca S. Heist[1,#], Ryan B. Corcoran[1,#]

Activity of Adagrasib (MRTX849) in Brain Metastases: Preclinical Models and Clinical Data From Patients With KRAS^{G12C}-Mutant Non–Small Cell Lung Cancer

Joshua K. Sabari[1*], Vamsidhar Velcheti[1*], Kazuhide Shimizu[2,3*], Matthew R. Strickland[2,4*], Rebecca S. Heist[2], Mohini Singh[2], Naema Nayyar[2], Anita Giobbie-Hurder[4], Subba R. Digumarthy[2], Justin F. Gainor[2], Anant P. Rajan[2], Edwin Nieblas-Bedolla[2], Aaron C. Burns[5], Jill Hallin[5], Peter Olson[5], James G. Christensen[5], Sylvia C. Kurz[1†], Priscilla K. Brastianos[2†], Hiroaki Wakimoto[2†]

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

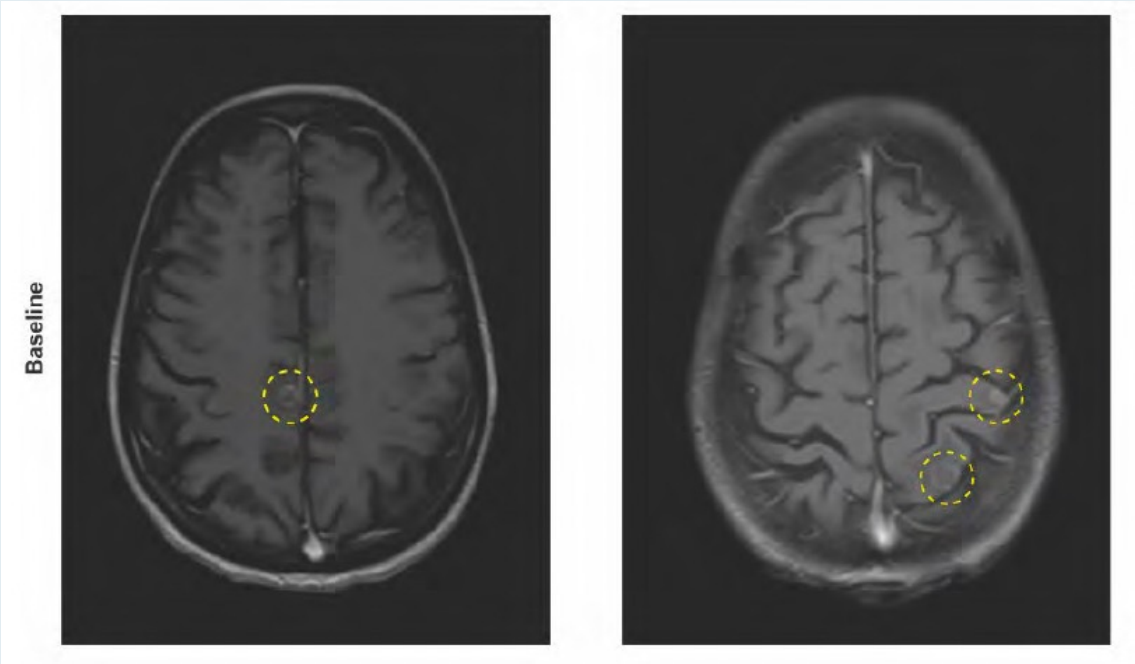
A 67-year-old woman with Stage IIIA adenocarcinoma of the lung who received adagrasib

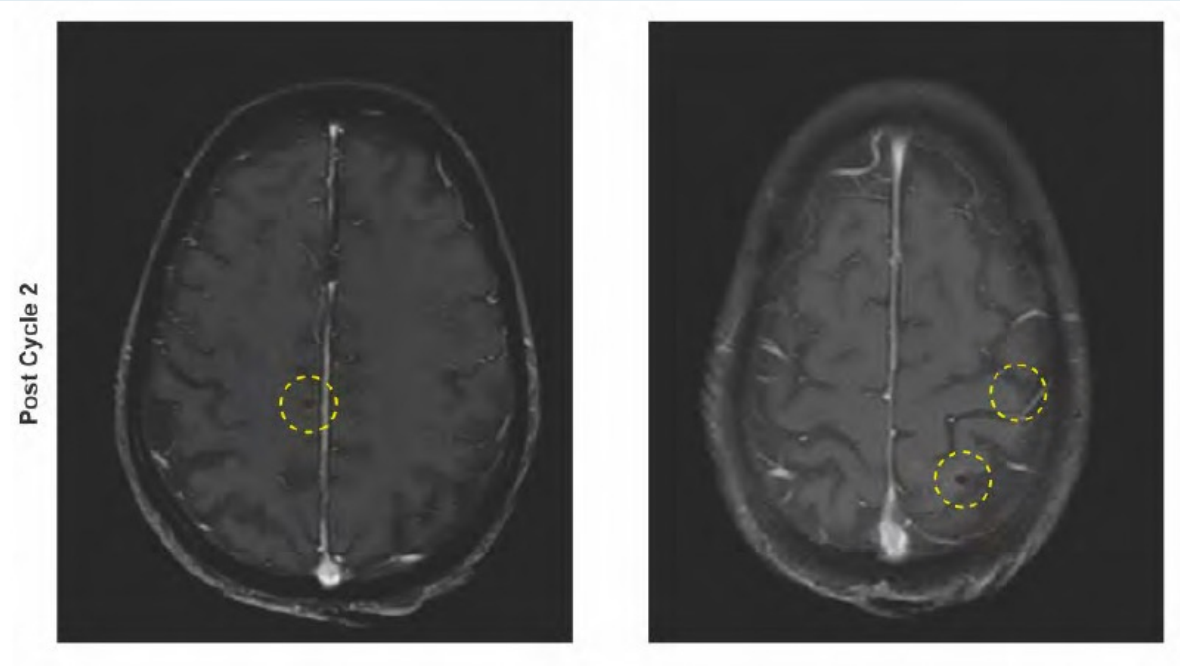


Sabari JK et al. *Clin Cancer Res* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

A 66-year-old man with metastatic NSCLC and brain metastases, who received adagrasib





Sabari JK et al. *Clin Cancer Res* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Gainor

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer targeted treatment to a patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and a ROS 1 rearrangement, and which targeted therapy would you generally offer?

 Dr Baik	First line Entrectinib	 Dr Gainor	First line Crizotinib
 Dr Camidge	First line Entrectinib	 Dr Johnson	First line Entrectinib
 Dr Drilon	First line Entrectinib	 Dr Spira	First line Entrectinib

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer targeted treatment to a patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) and an NTRK fusion, and which targeted therapy would you generally offer?

 Dr Baik	First line Larotrectinib	 Dr Gainor	First line Larotrectinib
 Dr Camidge	First line Entrectinib	 Dr Johnson	First line Larotrectinib
 Dr Drilon	First line Larotrectinib	 Dr Spira	First line Larotrectinib

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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%)	—	—	—

Drilon A et al. *Nat Rev Clin Oncol* 2021;18(1):35-55.

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%)

Drilon A et al. *Nat Rev Clin Oncol* 2021;18(1):35-55.

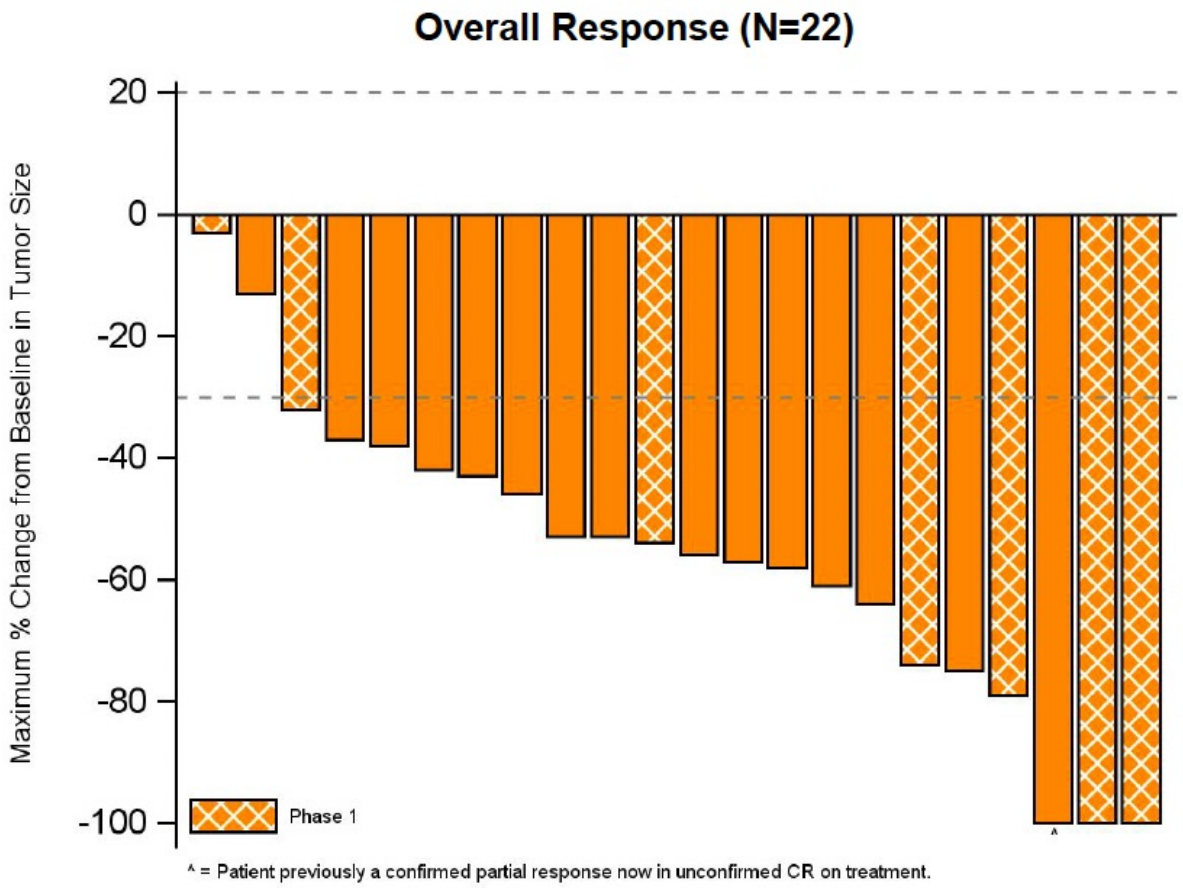
Abstract 3255

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 Drilon[16]

[1]Yonsei Cancer Center, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; [2]University of Colorado Anschutz Medical Campus, Aurora, CO, USA; [3]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; [4]Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA; [5]Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, University of Washington School of Medicine, Seattle, WA, USA; [6]University of Groningen and University Medical Centre Groningen, Groningen, Netherlands; [7]Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA; [8]Chungbuk National University Hospital, Cheongju, Republic of Korea; [9]Georgetown Lombardi Comprehensive Cancer Center, Georgetown University, Washington D.C., USA; [10]Peter MacCallum Cancer Center, Melbourne, Australia; [11]The Chris O'Brien Lifehouse, Camperdown, Australia; [12]Division of Cancer Sciences, The University of Manchester and the Christie NHS Foundation Trust, Manchester, UK; [13]Chao Family Comprehensive Cancer Center, University of California Irvine School of Medicine, Orange, CA, USA; [14]Turning Point Therapeutics Inc., San Diego, CA, USA; [15]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA

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



	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.

Cho BC et al. WCLC 2020;Abstract 3255.

AACR-NCI-EORTC Virtual International Conference on
MOLECULAR TARGETS AND CANCER THERAPEUTICS
October 7-10, 2021

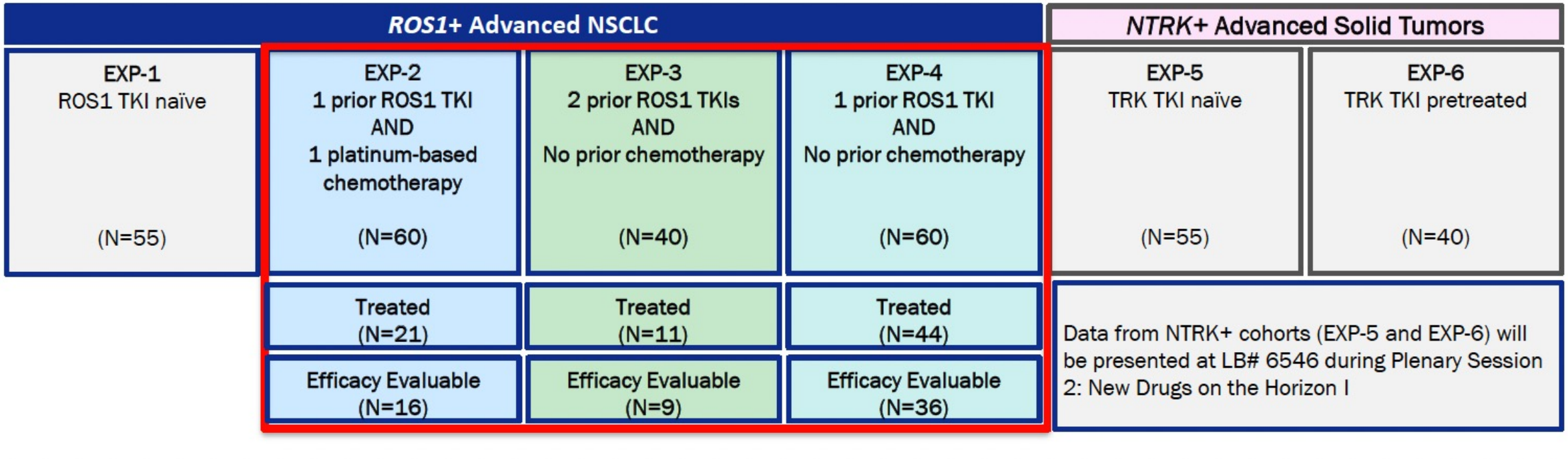
Poster #: P224

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 Drilon[14]

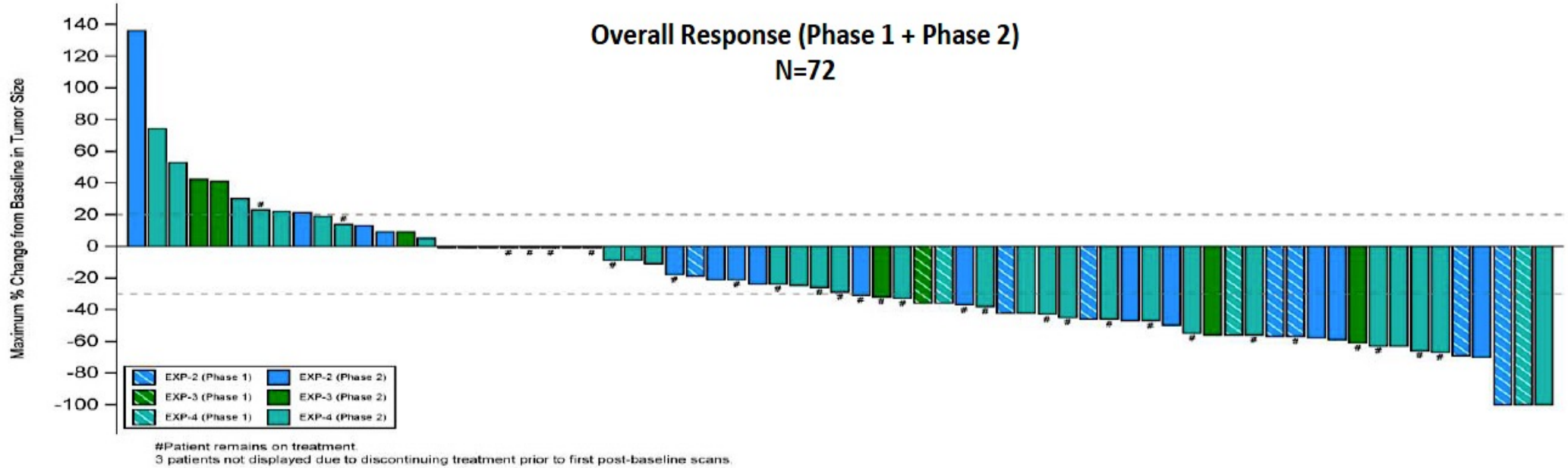
[1]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; [2]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [3]Heidelberg University Hospital, National Center for Tumor Diseases, Department of Medical Oncology, Heidelberg, Germany; [4]University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

TRIDENT-1: Phase II Study Design



Lin JJ et al. AACR 2021;Abstract 224.

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



	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

Lin JJ et al. AACR 2021;Abstract 224.

original reports

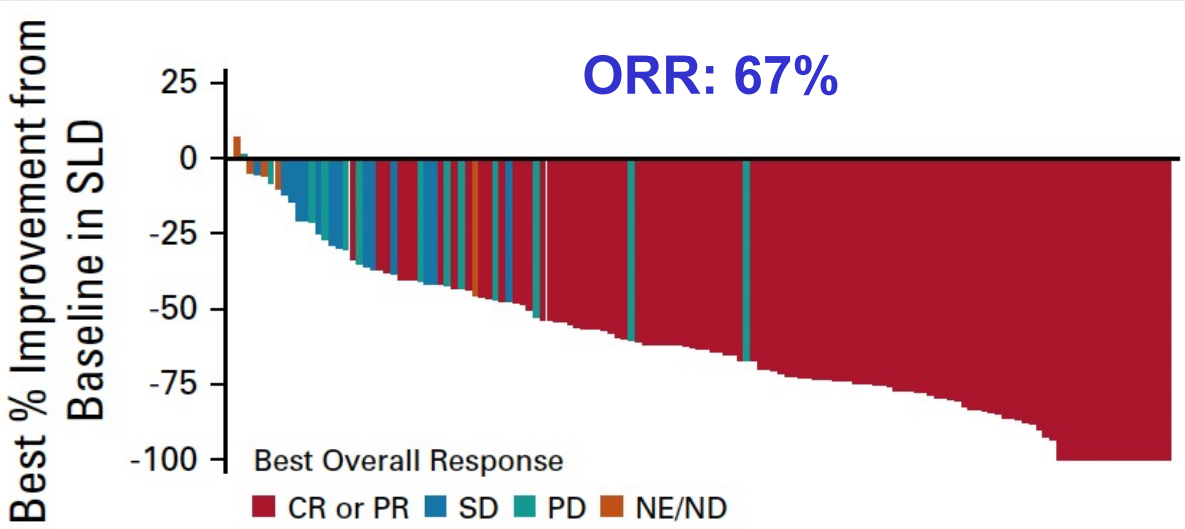
Updated Integrated Analysis of the Efficacy and Safety of Entrectinib in Locally Advanced or Metastatic *ROS1* Fusion–Positive Non–Small-Cell Lung Cancer

Rafal Dziadziuszko, MD, PhD[1]; Matthew G. Krebs, MD, PhD[2]; Filippo De Braud, MD[3,4]; Salvatore Siena, MD[3,5]; Alexander Drilon, MD[6]; Robert C. Doebele, MD, PhD[7]; Manish R. Patel, DO[8]; Byoung Chul Cho, MD, PhD[9]; Stephen V. Liu, MD[10]; Myung-Ju Ahn, MD, PhD[11]; Chao-Hua Chiu, MD[12]; Anna F. Farago, MD, PhD[13]; Chia-Chi Lin, MD[14]; Christos S. Karapetis, MBBS, MMedSc[15]; Yu-Chung Li, MD[16]; Bann-mo Day, PhD[17]; David Chen, PharmD[17]; Timothy R. Wilson, PhD[17]; and Fabrice Barlesi, MD, PhD[18,19]

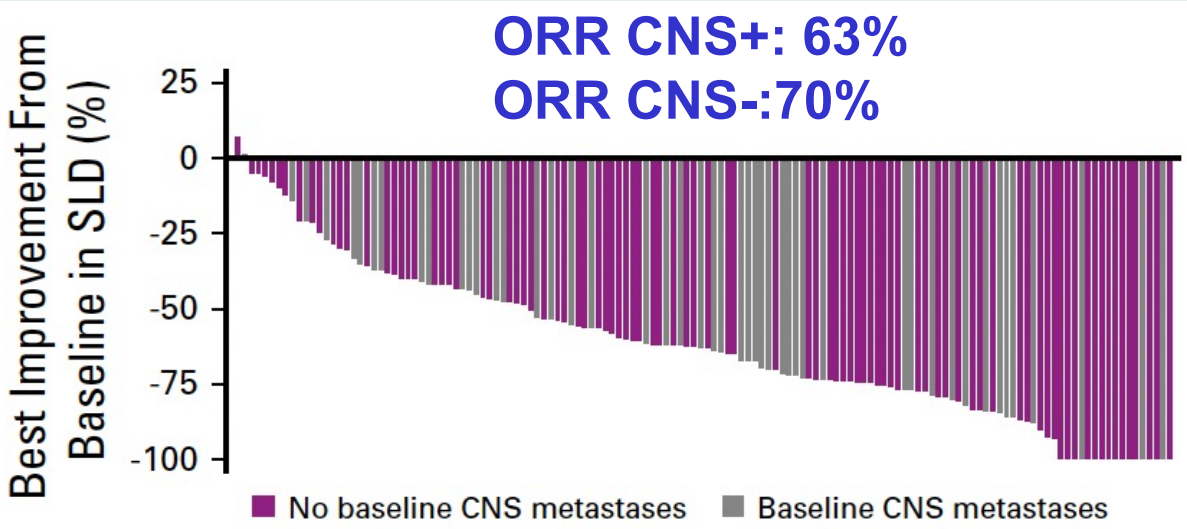
J Clin Oncol 2021;39(11):1253-63.

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

Dziadziuszko R et al. *J Clin Oncol* 2021;39(11):1253-63.

Meet The Professor with Dr Gainor

Clinical Characteristics and Molecular Features of Non-Small Cell Lung Cancers (NSCLCs) Following Disease Progression on Immune Checkpoint Inhibitors (ICIs)

Gainor JF et al.

ASCO 2022;Abstract e21178.

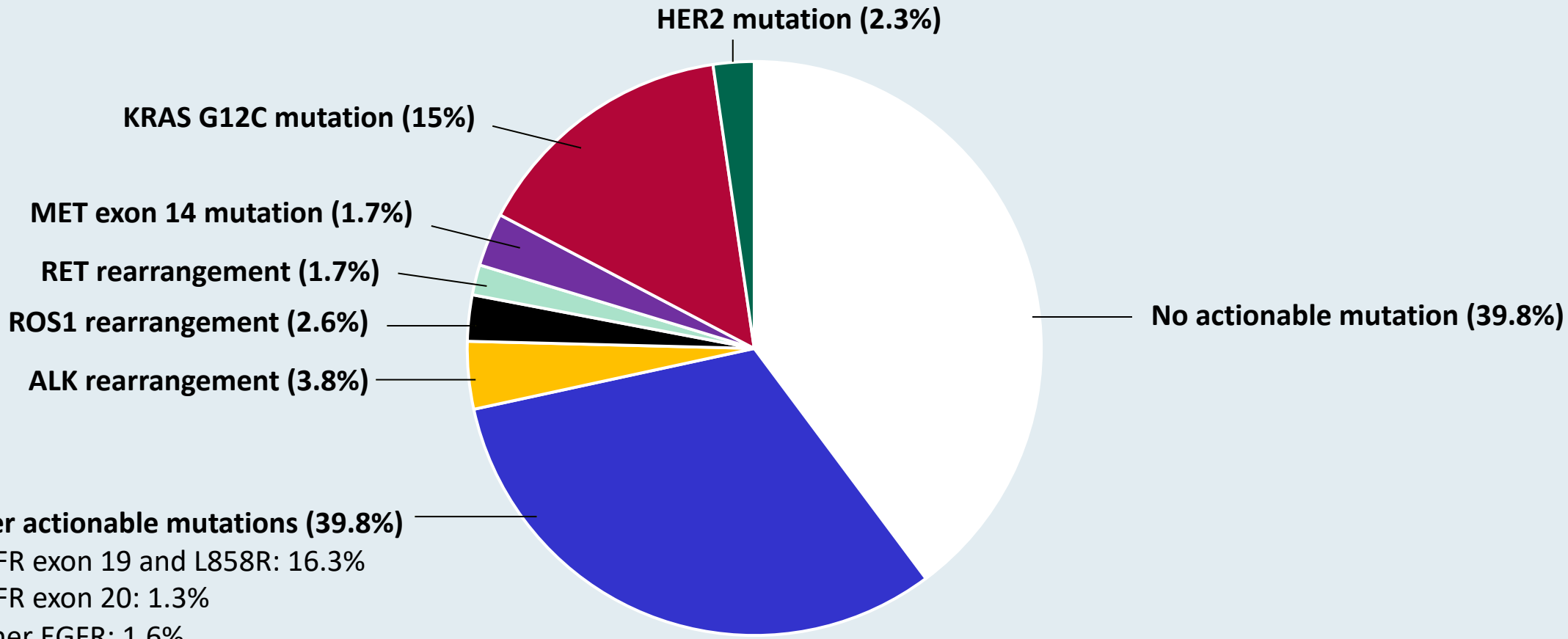
BRIEF COMMUNICATION
https://doi.org/10.1038/s43018-021-00198-5
Nat Cancer 2021;2(5):498-502.
nature cancer

Palbociclib demonstrates intracranial activity in progressive brain metastases harboring cyclin-dependent kinase pathway alterations

Priscilla K. Brastianos[1,4]✉, Albert E. Kim[1,4], Nancy Wang[1], Eudocia Q. Lee[2], Jennifer Ligibel[2], Justine V. Cohen[1,3], Ugonma N. Chukwueke[2], Maura Mahar[1], Kevin Oh[1], Michael D. White[1], Helen A. Shih[1], Deborah Forst[1], Justin F. Gainor[1], Rebecca S. Heist[1], Elizabeth R. Gerstner[1], Tracy T. Batchelor[1], Donald Lawrence[1], David P. Ryan[1], A. John Iafrate[1], Anita Giobbie-Hurder[2], Sandro Santagata[2], Scott L. Carter[2], Daniel P. Cahill[1,5] and Ryan J. Sullivan[1,5]

Meet The Professor with Dr Gainor

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

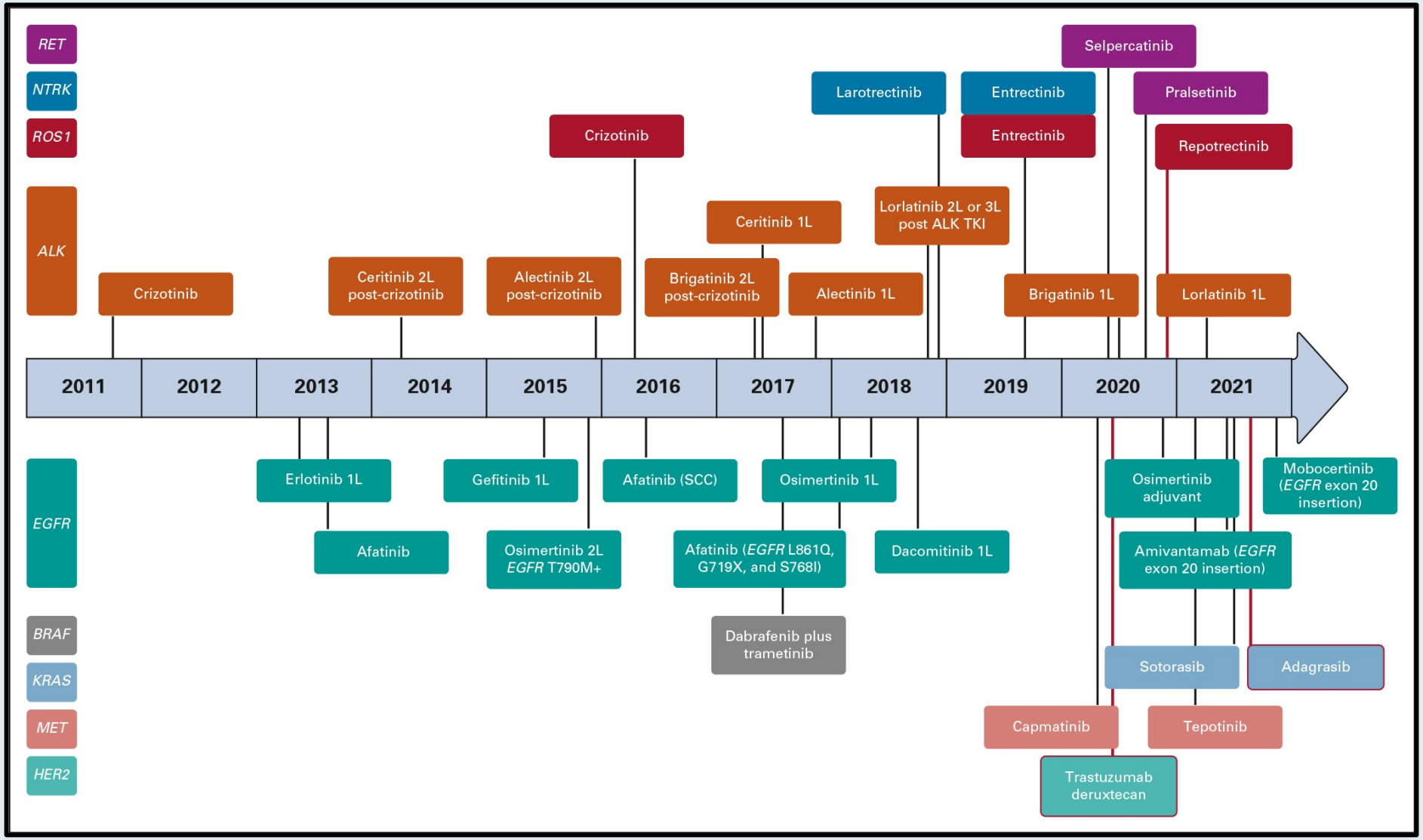


Other actionable mutations (39.8%)
--EGFR exon 19 and L858R: 16.3%
--EGFR exon 20: 1.3%
--Other EGFR: 1.6%
--Other KRAS: 10.3%
--BRAF V600E: 2.1%
--NTRK rearrangement: 0.23%

Derived from Tan AC et al. *J Clin Oncol* 2022;40(6):611-25.

RTP RESEARCH TO PRACTICE

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

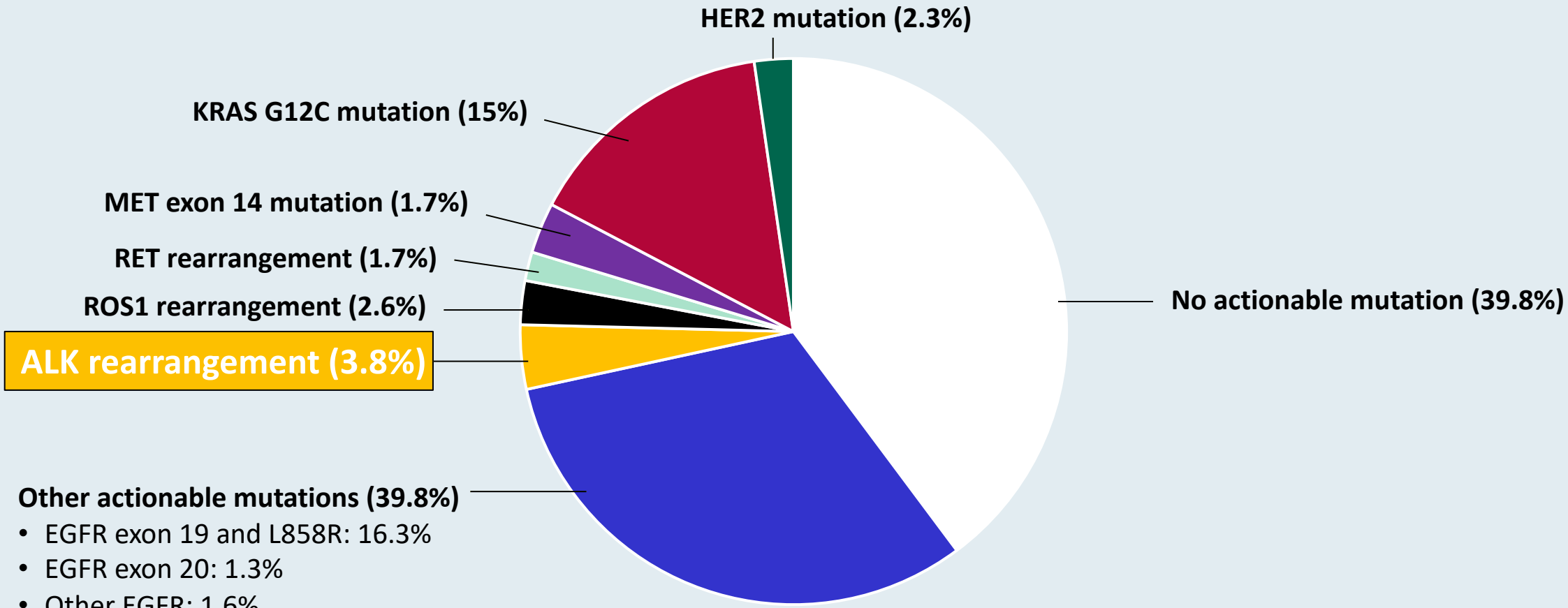


Tan AC et al. *J Clin Oncol* 2022;40(6):611-25.

Note: Red line indicates Breakthrough Therapy designation

RTP RESEARCH TO PRACTICE

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



- EGFR exon 19 and L858R: 16.3%
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Derived from Tan AC et al. *J Clin Oncol* 2022;40(6):611-25.

RTP RESEARCH TO PRACTICE

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

Crizotinib PI, rev 1/2021; Ceritinib PI, rev 3/2019; Alectinib PI, rev 1/2021; Brigatinib PI, rev 5/2020; Lorlatinib PI, rev 3/2021
Xia B et al. *Transl Lung Cancer Res* 2020;9(6):2521-253; Gristina V et al. *Pharmaceuticals* 2020;13(12):474.

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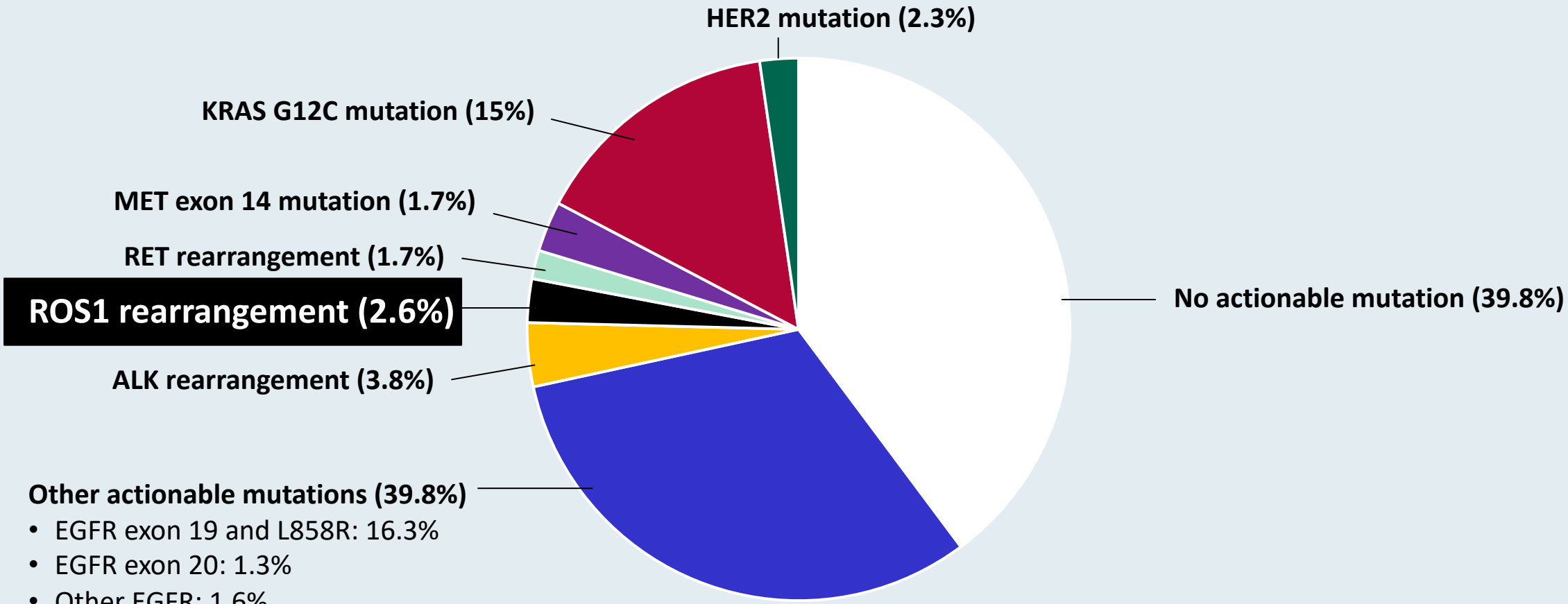

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RTP RESEARCH TO PRACTICE

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%)	—	—	—

Drilon A et al. *Nat Rev Clin Oncol* 2021;18(1):35-55.

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%)

Drilon A et al. *Nat Rev Clin Oncol* 2021;18(1):35-55.

original reports

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, PhD[1]; Matthew G. Krebs, MD, PhD[2]; Filippo De Braud, MD[3,4]; Salvatore Siena, MD[3,5]; Alexander Drilon, MD[6]; Robert C. Doebele, MD, PhD[7]; Manish R. Patel, DO[8]; Byoung Chul Cho, MD, PhD[9]; Stephen V. Liu, MD[10]; Myung-Ju Ahn, MD, PhD[11]; Chao-Hua Chiu, MD[12]; Anna F. Farago, MD, PhD[13]; Chia-Chi Lin, MD[14]; Christos S. Karapetis, MBBS, MMedSc[15]; Yu-Chung Li, MD[16]; Bann-mo Day, PhD[17]; David Chen, PharmD[17]; Timothy R. Wilson, PhD[17]; and Fabrice Barlesi, MD, PhD[18,19]

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

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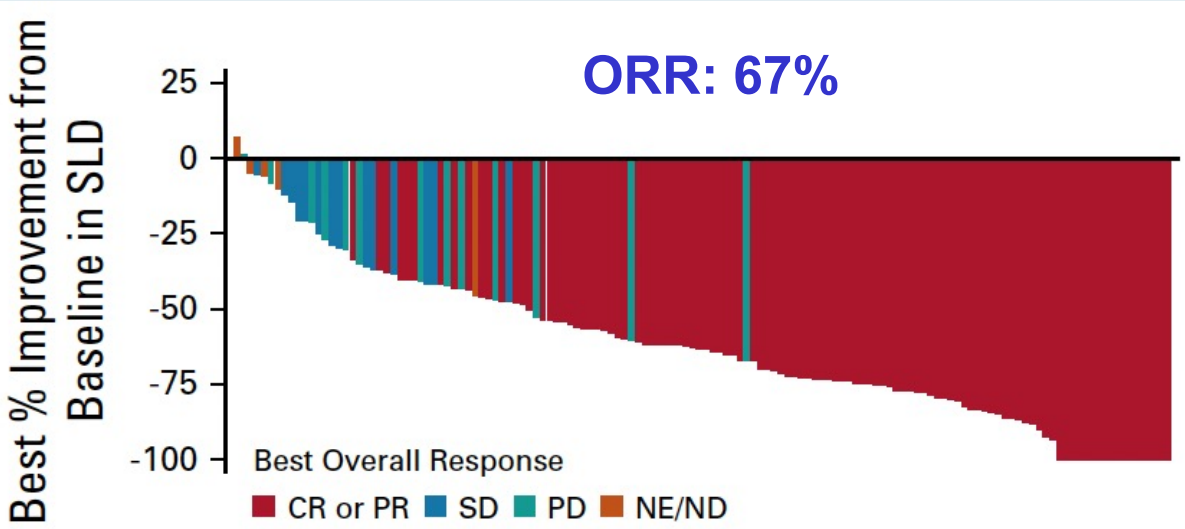
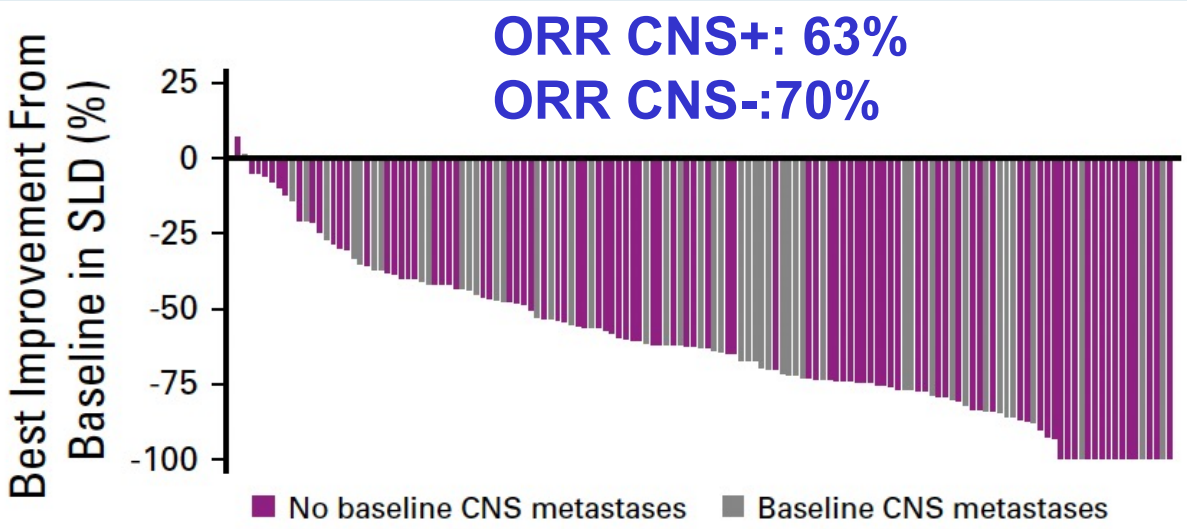


Patients with (n = 56) and without (n = 105) CNS Metastases at Baseline



ORR = objective response rate

Dziadziuszko R et al. *J Clin Oncol* 2021;39(11):1253-63.

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%

Dziadziuszko R et al. *J Clin Oncol* 2021;39(11):1253-63.

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%

Dziadziuszko R et al. *J Clin Oncol* 2021;39(11):1253-63.

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."

https://www.biospace.com/article/releases/turning-point-therapeutics-granted-fda-breakthrough-therapy-designation-for-repotrectinib-treatment-in-patients-with-ros1-positive-metastatic-non-small-cell-lung-cancer-/

RTP RESEARCH TO PRACTICE

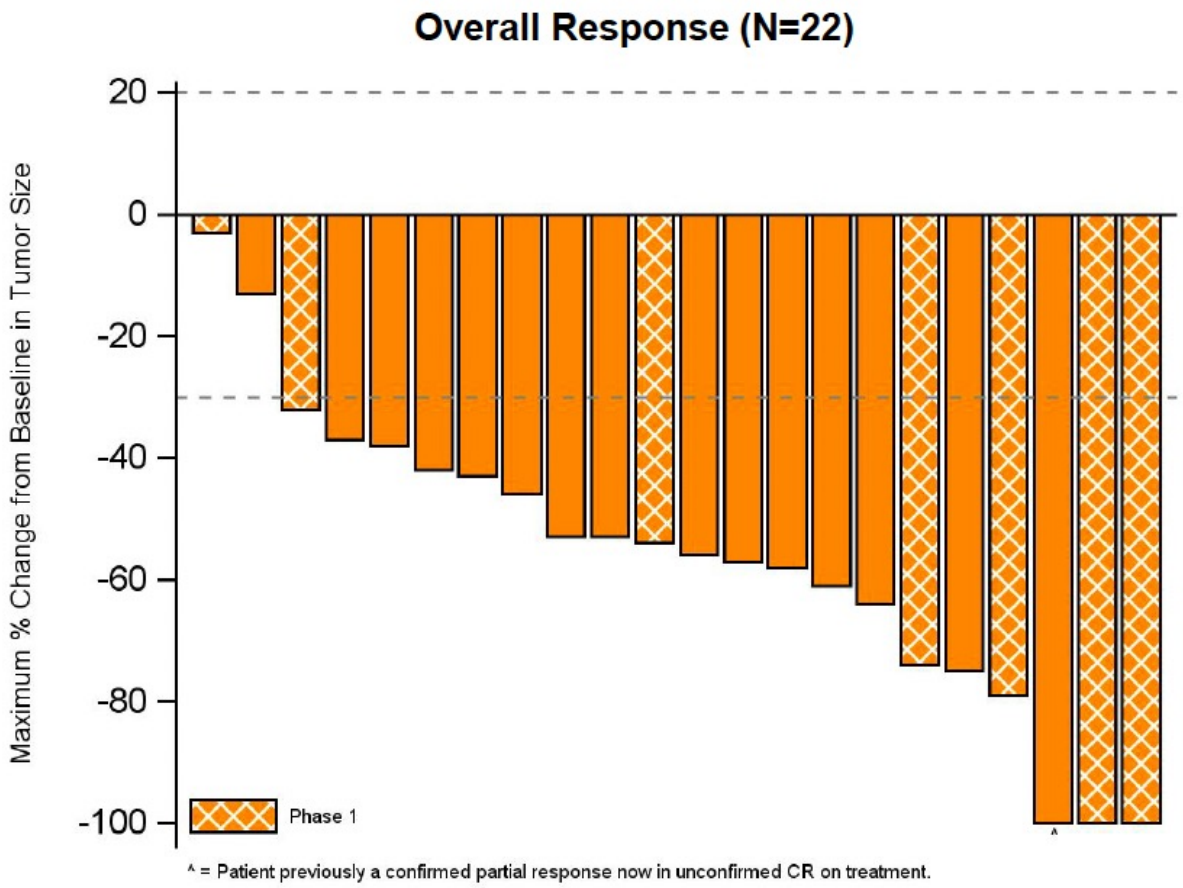
Abstract 3255

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 Drilon[16]

[1]Yonsei Cancer Center, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; [2]University of Colorado Anschutz Medical Campus, Aurora, CO, USA; [3]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; [4]Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA; [5]Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, University of Washington School of Medicine, Seattle, WA, USA; [6]University of Groningen and University Medical Centre Groningen, Groningen, Netherlands; [7]Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA; [8]Chungbuk National University Hospital, Cheongju, Republic of Korea; [9]Georgetown Lombardi Comprehensive Cancer Center, Georgetown University, Washington D.C., USA; [10]Peter MacCallum Cancer Center, Melbourne, Australia; [11]The Chris O'Brien Lifehouse, Camperdown, Australia; [12]Division of Cancer Sciences, The University of Manchester and the Christie NHS Foundation Trust, Manchester, UK; [13]Chao Family Comprehensive Cancer Center, University of California Irvine School of Medicine, Orange, CA, USA; [14]Turning Point Therapeutics Inc., San Diego, CA, USA; [15]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA

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



	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.

Cho BC et al. WCLC 2020;Abstract 3255.

AACR-NCI-EORTC Virtual International Conference on
MOLECULAR TARGETS AND CANCER THERAPEUTICS
October 7-10, 2021

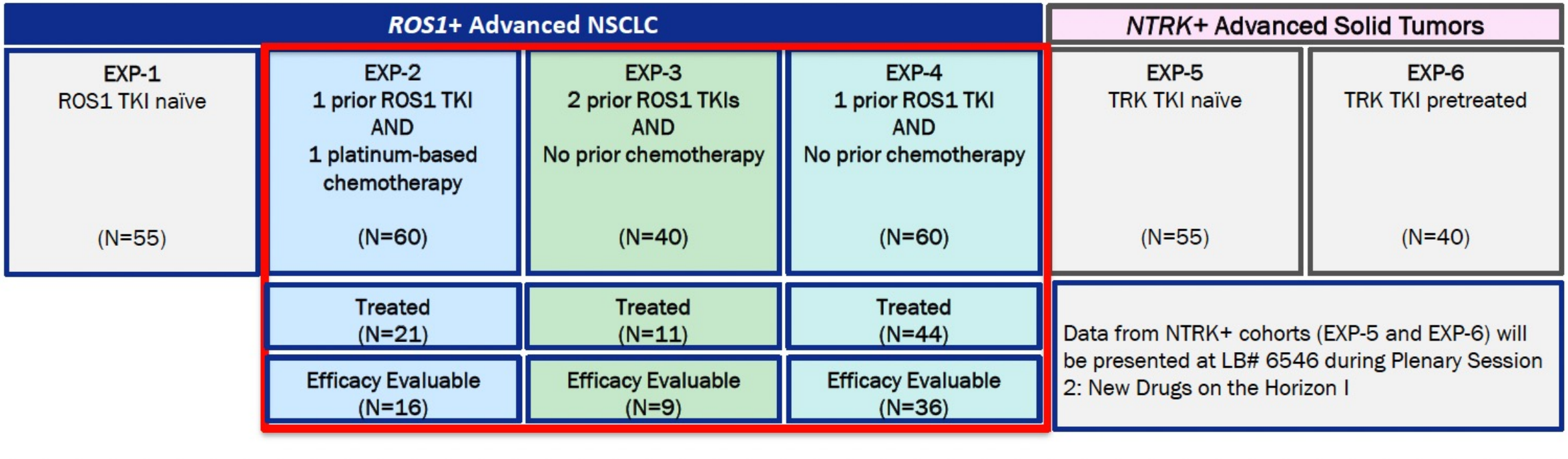
Poster #: P224

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 Drilon[14]

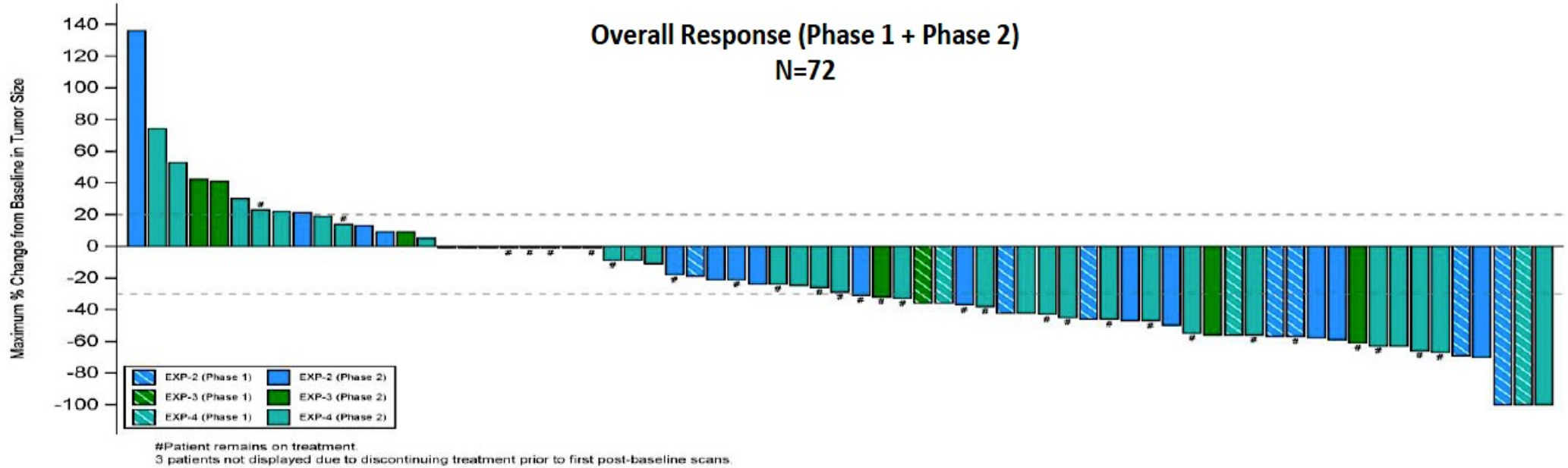
[1]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; [2]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [3]Heidelberg University Hospital, National Center for Tumor Diseases, Department of Medical Oncology, Heidelberg, Germany; [4]University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

TRIDENT-1: Phase II Study Design



Lin JJ et al. AACR 2021;Abstract 224.

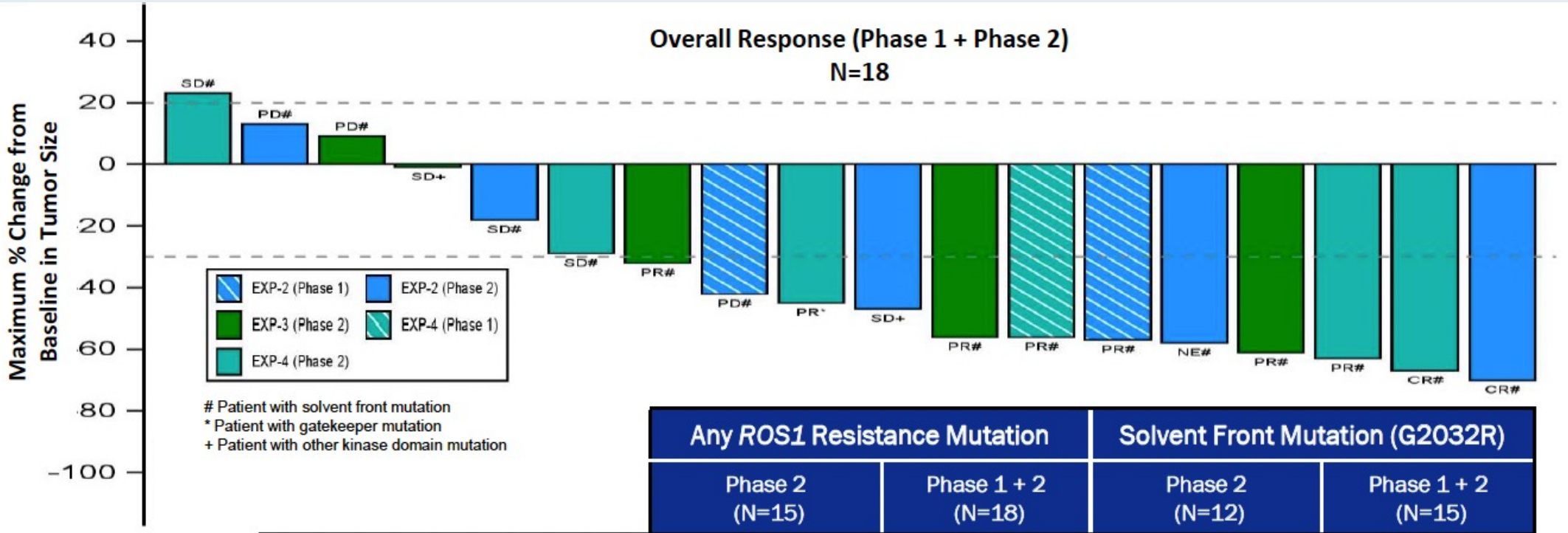
TRIDENT-1: Preliminary Efficacy in Patients with TKI-Pretreated Advanced NSCLC with ROS1 Fusions



	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

Lin JJ et al. AACR 2021;Abstract 224.

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



	Any *ROS1* Resistance Mutation		Solvent Front Mutation (G2032R)	
	Phase 2 (N=15)	Phase 1 + 2 (N=18)	Phase 2 (N=12)	Phase 1 + 2 (N=15)
Confirmed ORR (cORR) (95% CI) CR PR	47% (21 – 73) 2 (13%) 5 (33%)	50% (26 – 74) 2 (11%) 7 (39%)	50% (21 – 79) 2 (17%) 4 (33%)	53% (27 – 79) 2 (13%) 6 (40%)
Duration of Response (range in months)	*1.9+ - 15.0+* n=7	*1.9+ - 15.0+* n=9	*1.9+ - 15.0+* n=6	*1.9+ - 15.0+* n=8

Lin JJ et al. AACR 2021;Abstract 224.

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%	

Lin JJ et al. AACR 2021;Abstract 224.

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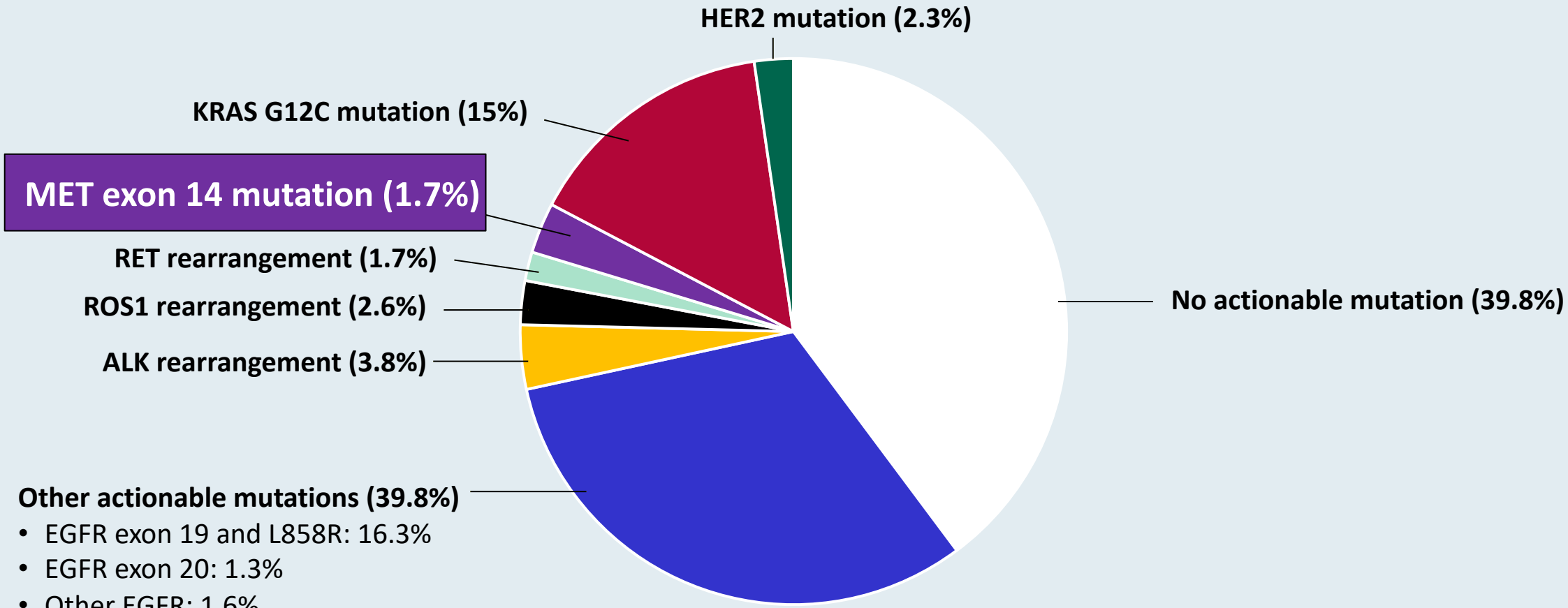

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Derived from Tan AC et al. *J Clin Oncol* 2022;40(6):611-25.

RTP RESEARCH TO PRACTICE

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."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-tepotinib-metastatic-non-small-cell-lung-cancer

RTP RESEARCH TO PRACTICE

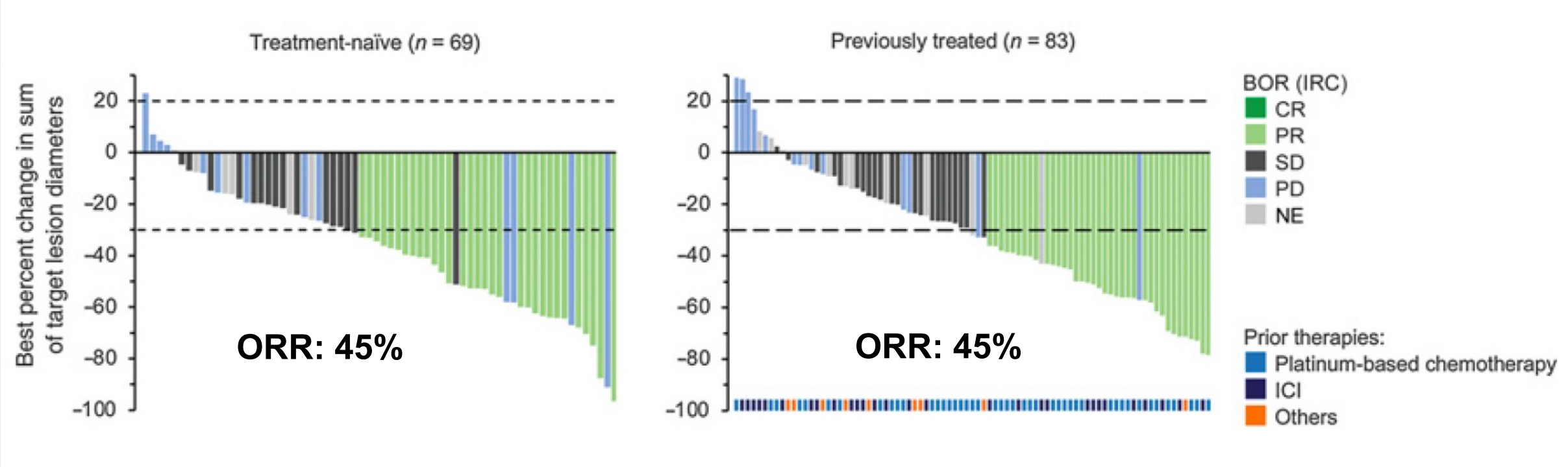
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

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 Le[1], Hiroshi Sakai[2], Enriqueta Felip[3], Remi Veillon[4], Marina Chiara Garassino[5,6], Jo Raskin[7], Alexis B. Cortot[8], Santiago Viteri[9], Julien Mazieres[10], Egbert F. Smit[11], Michael Thomas[12], Wade T. Iams[13], Byoung Chul Cho[14], Hye Ryun Kim[14], James Chih-Hsin Yang[15], Yuh-Min Chen[16], Jyoti D. Patel[17], Christine M. Bestvina[18], Keunchil Park[19], Frank Griesinger[20], Melissa Johnson[21], Maya Gottfried[22], Christian Britschgi[23], John Heymach[1], Elif Sikoglu[24], Karin Berghoff[25], Karl-Maria Schumacher[26], Rolf Bruns[27], Gordon Otto[26], 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.

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

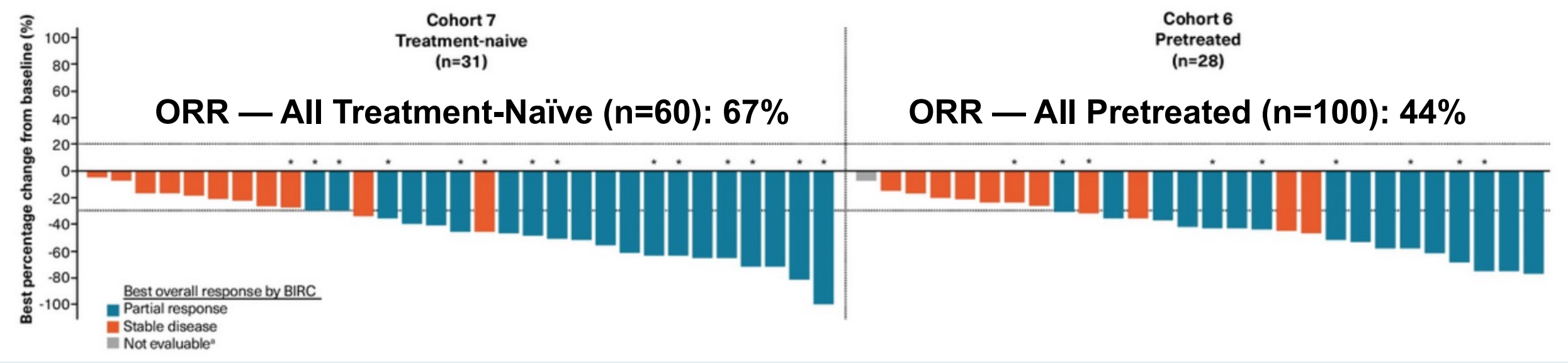
Le X et al. *Clin Cancer Res* 2022;28(6):1117-26.

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)



Wolf J et al. ASCO 2021;Abstract 9020.

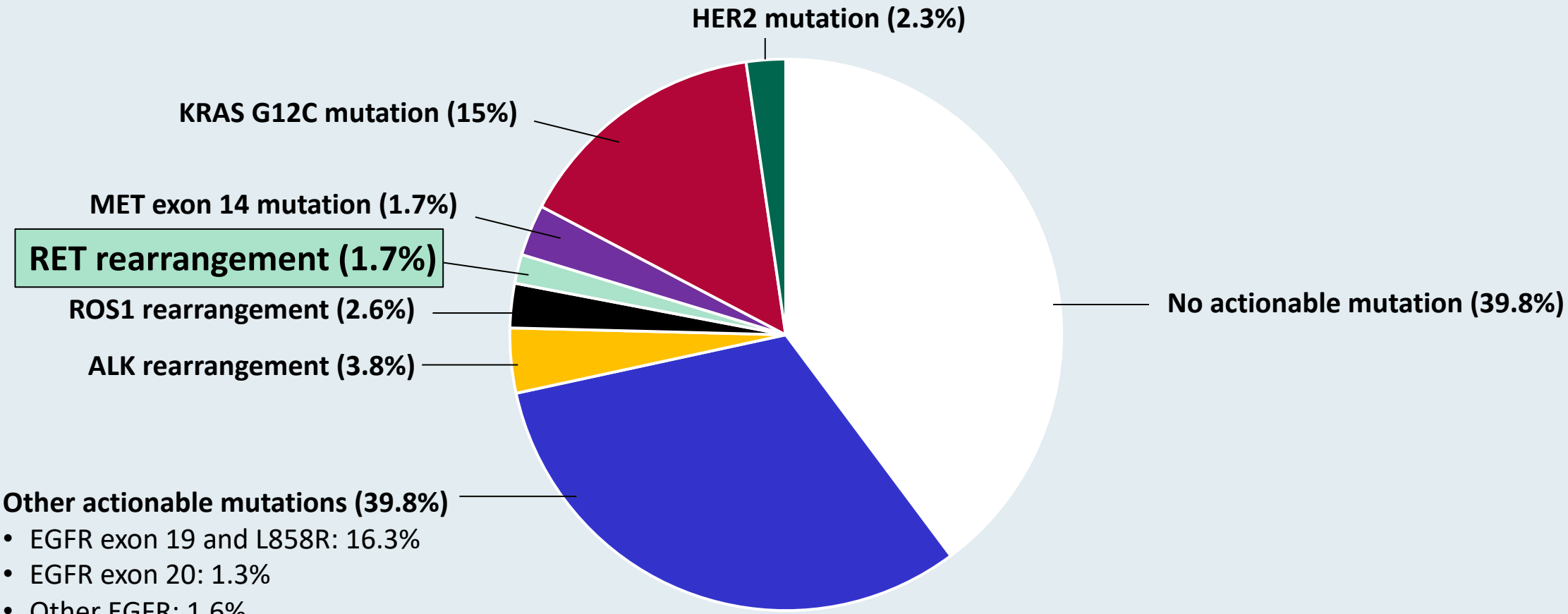
RTP RESEARCH TO PRACTICE

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

Wolf J et al. ASCO 2021;Abstract 9020.

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



- EGFR exon 19 and L858R: 16.3%
- EGFR exon 20: 1.3%
- Other EGFR: 1.6%
- Other KRAS: 10.3%
- BRAF V600E: 2.1%
- NTRK rearrangement: 0.23%

Derived from Tan AC et al. *J Clin Oncol* 2022;40:611-625.

RTP RESEARCH TO PRACTICE

Lancet Oncol 2021;22(7):959-69.

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 S W Tan, Elena Garralda, Luis G Paz-Ares, Byoung Chul Cho, Shirish M Gadgeel, 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

The NEW ENGLAND JOURNAL of MEDICINE

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

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

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

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.

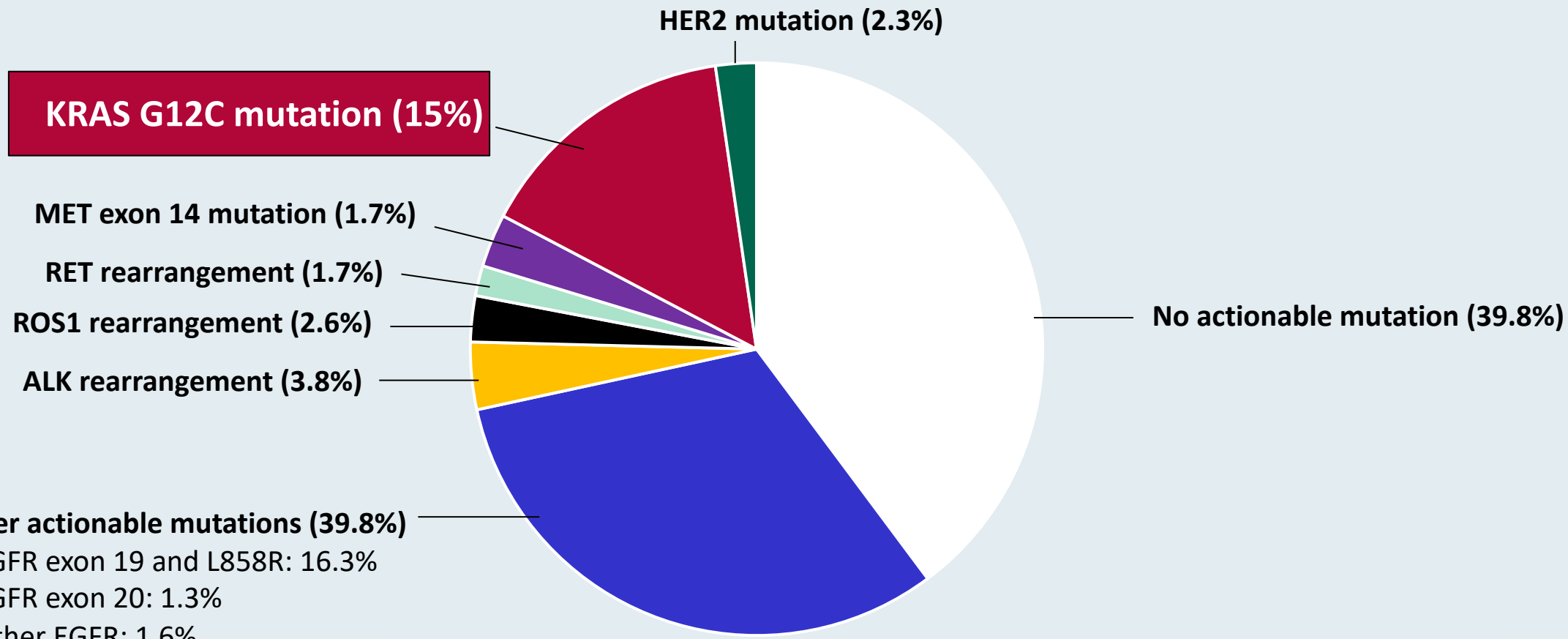
RTP RESEARCH TO PRACTICE

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	• Selpercatinib • Pemetrexed and platinum with or without pembrolizumab
LIBRETTO-432 (NCT04819100)	Stage IB, II or IIIA NSCLC after definitive locoregional therapy	• Selpercatinib • Placebo
AcceleRET-Lung (NCT04222972)	Locally advanced or metastatic NSCLC that has not been treated with systemic anticancer therapy for metastatic disease	• Pralsetinib • Platinum-based chemotherapy (with or without pembrolizumab)
NCT05170204	Unresectable Stage III NSCLC	<u>Cohort A3</u> • Pralsetinib • Durvalumab

www.clinicaltrials.gov; Accessed March 2022.

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



Other actionable mutations (39.8%)

- EGFR exon 19 and L858R: 16.3%
- EGFR exon 20: 1.3%
- Other EGFR: 1.6%
- Other KRAS: 10.3%
- BRAF V600E: 2.1%
- NTRK rearrangement: 0.23%

Derived from Tan AC et al. *J Clin Oncol* 2022;40(6):611-25.

RTP RESEARCH TO PRACTICE

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 therascreen® 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 CodeBreaK 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."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-sotorasib-kras-g12c-mutated-nsclc

RTP RESEARCH TO PRACTICE

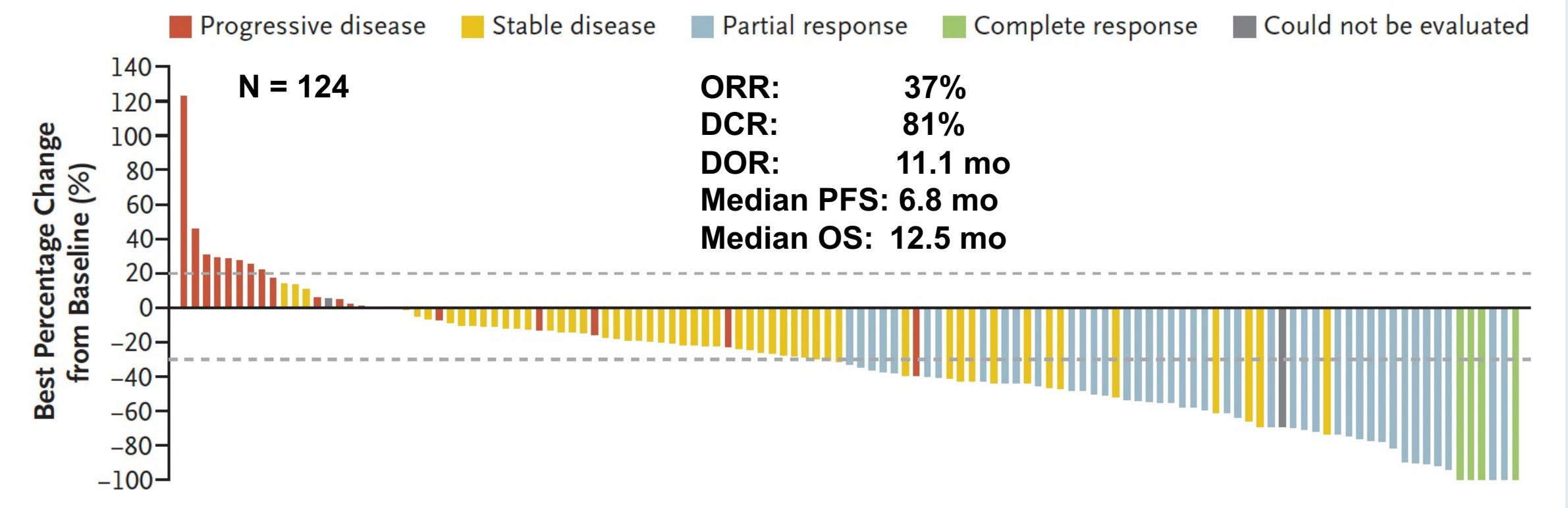
The NEW ENGLAND JOURNAL of MEDICINE

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

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

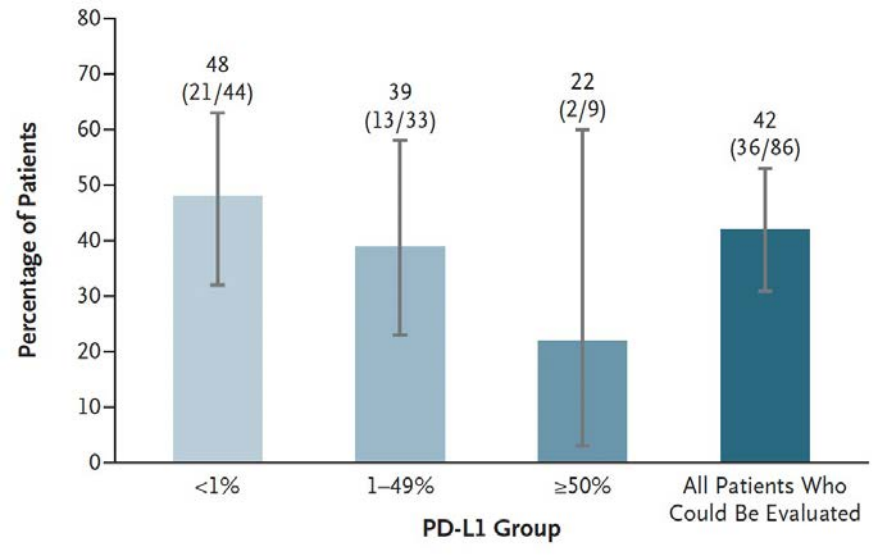


Skoulidis F et al. *N Engl J Med* 2021;384(25):2371-81.

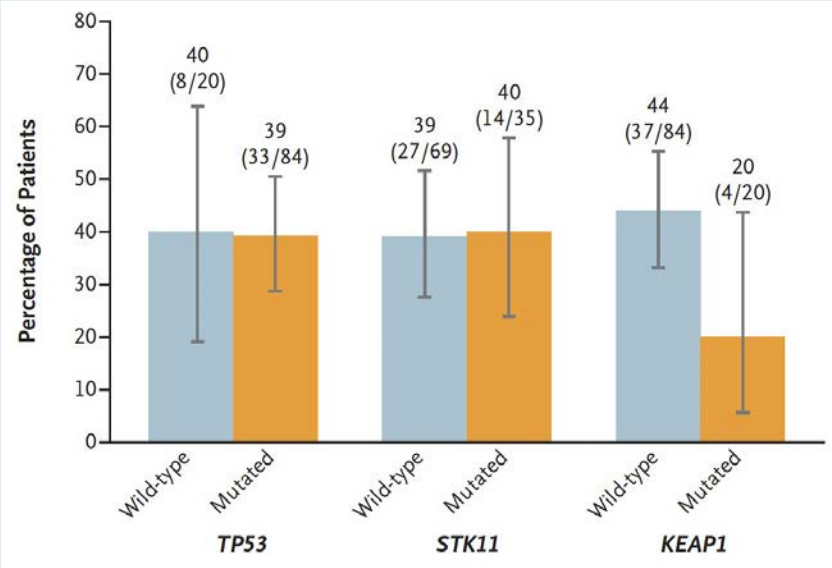
RTP RESEARCH TO PRACTICE

CodeBreaK 100: Exploratory Biomarker Analyses

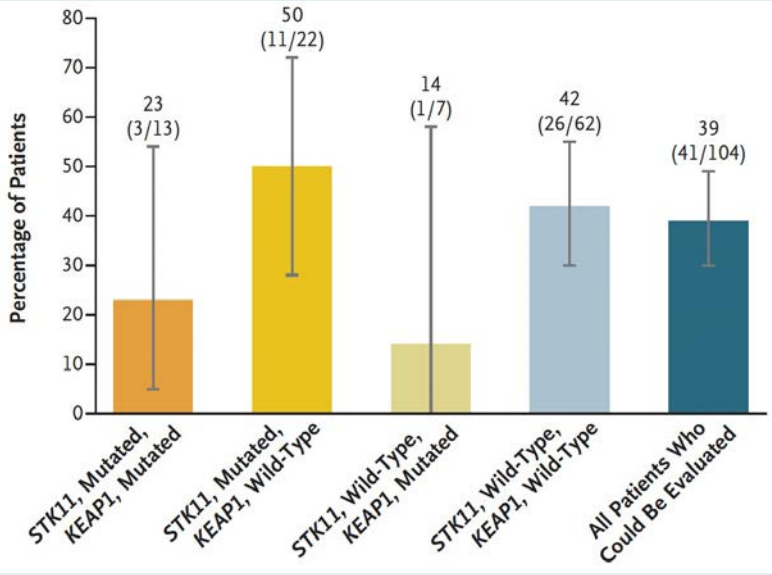
Response According to PD-L1 Expression Level



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



Response According to Mutational Status in Both STK11 and KEAP1



Skoulidis F et al. *N Engl J Med* 2021;384(25):2371-81.

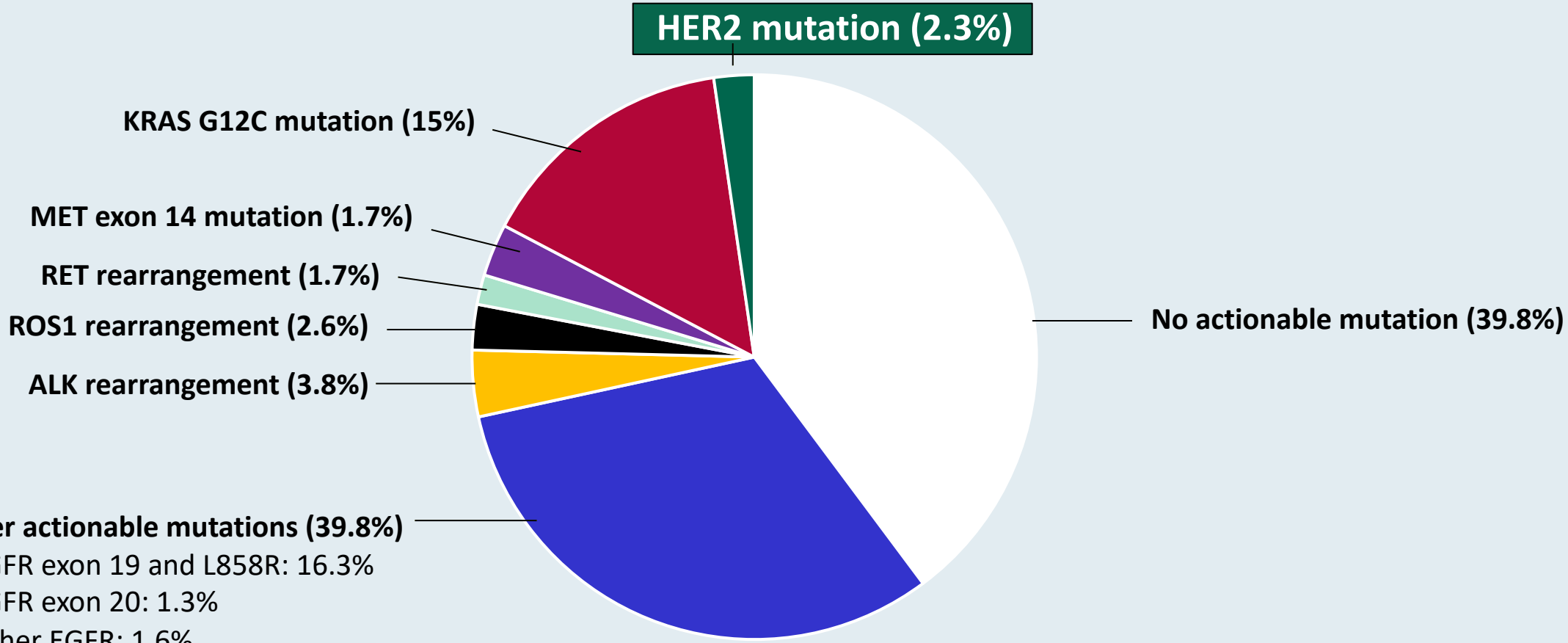
RTP RESEARCH TO PRACTICE

CodeBreaK 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

Skoulidis F et al. *N Engl J Med* 2021;384(25):2371-81.

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



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- BRAF V600E: 2.1%
- NTRK rearrangement: 0.23%

Derived from Tan AC et al. *J Clin Oncol* 2022;40:611-25.

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

The NEW ENGLAND JOURNAL of MEDICINE

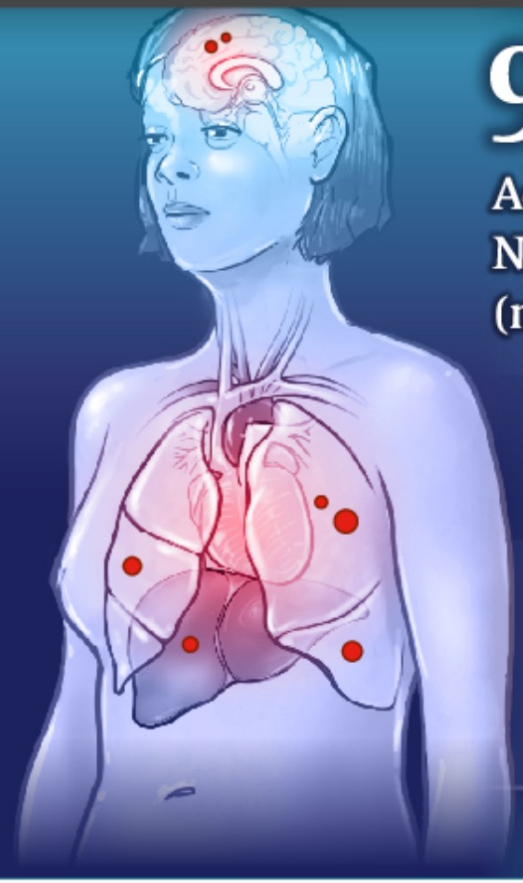
ORIGINAL ARTICLE

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*

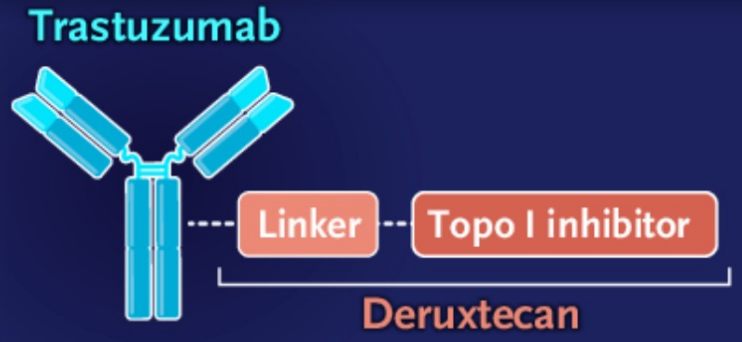
DESTINY-Lung01 Study

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.

Li BT et al. *N Engl J Med* 2022;386(3):241-51.

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

Li BT et al. *N Engl J Med* 2022;386(3):241-51.

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

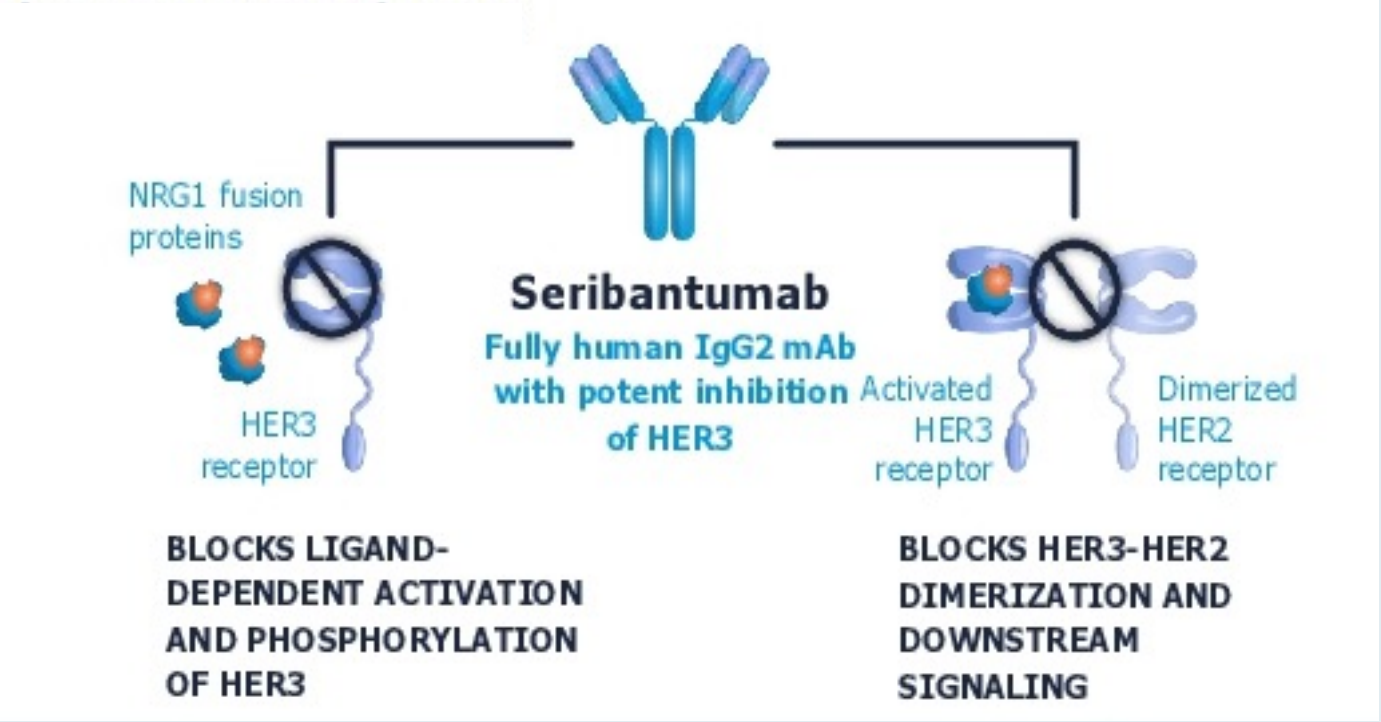
Event	Any grade	Grade ≥3
Nausea	73%	9%
Fatigue	53%	7%
Alopecia	46%	0
Vomiting	40%	3%
Neutropenia	35%	18%
Anemia	33%	10%
Diarrhea	32%	3%
Decreased appetite	30%	0
Leukopenia	23%	4%
Constipation	22%	0

Li BT et al. *N Engl J Med* 2022;386(3):241-51.

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



Bendell JC et al. 2021 Gastrointestinal Cancers Symposium;Abstract TPS449.

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. Denlinger[1] · Vicki L. Keedy[2] · Victor Moyo[3] · Gavin MacBeath[3] · Geoffrey I. Shapiro[4]

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

Denlinger CS et al. Invest New Drugs 2021;39(6):1604-12.

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)

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

Primary Endpoint: Objective response rate

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

www.clinicaltrials.gov; Accessed April 2022.

Clinical Investigator Perspectives on the Management of Renal Cell Carcinoma

Thursday, May 19, 2022

5:00 PM – 6:00 PM ET

Faculty

Thomas E Hutson, DO, PharmD
Brian I Rini, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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

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