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

Stephen V Liu, MD
Associate Professor of Medicine
Georgetown University Hospital
Washington, DC

RTP
RESEARCH
TO PRACTICE

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.

RTP
RESEARCH
TO PRACTICE

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 Corporation, the parent company of GHI, 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, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati 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.

RTP
RESEARCH
TO PRACTICE

Research To Practice CME Planning Committee Members, Staff and Reviewers

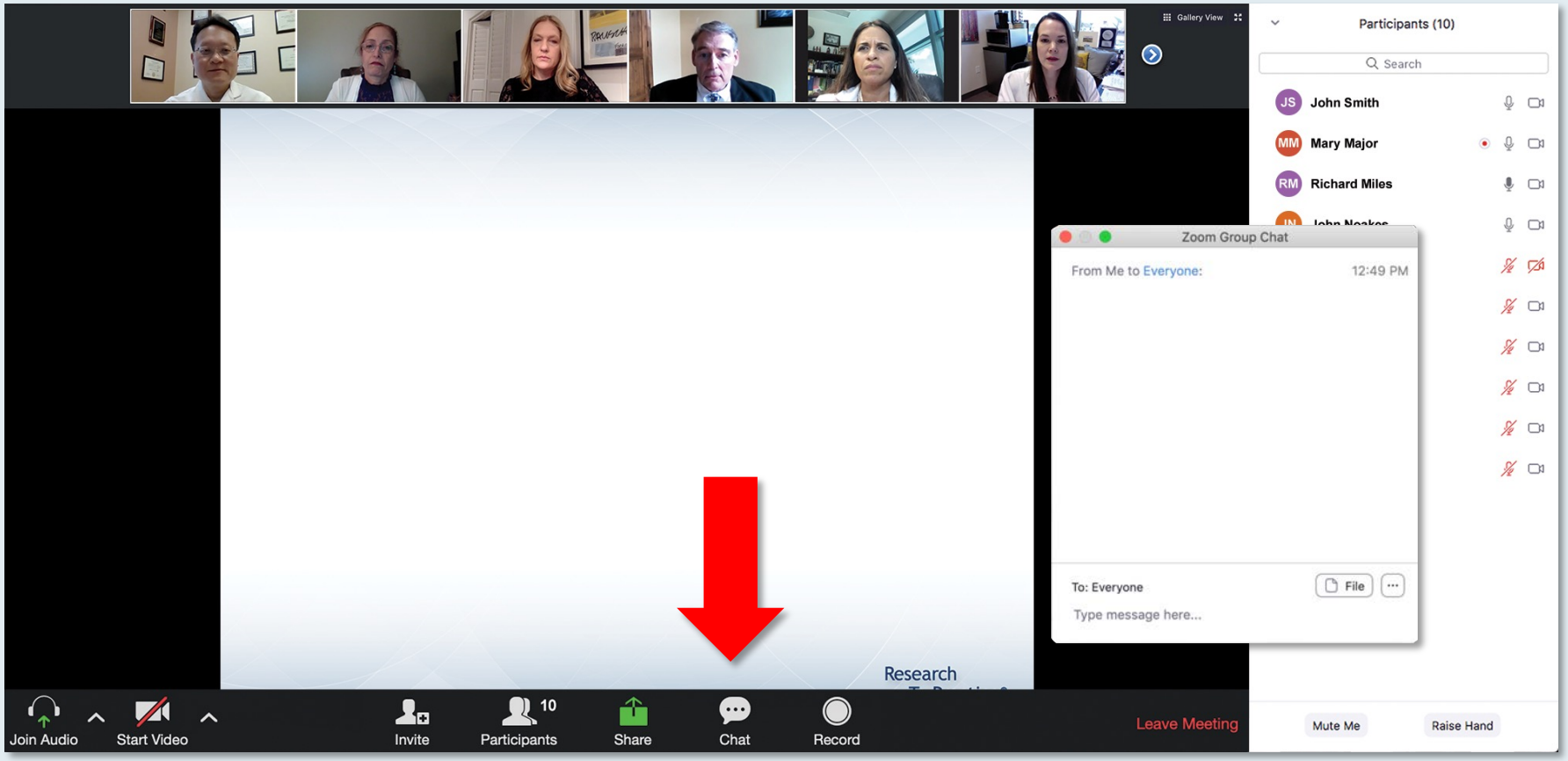
Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Liu — Disclosures

Advisory Committee	Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology, Genentech, a member of the Roche Group, Guardant Health, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Novartis, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Takeda Pharmaceuticals USA Inc, Turning Point Therapeutics Inc
Consulting Agreements	BeiGene Ltd, Blueprint Medicines, Daiichi Sankyo Inc, Elevation Oncology, Genentech, a member of the Roche Group, Janssen Biotech Inc, Lilly, Turning Point Therapeutics Inc
Contracted Research	Alkermes, Bayer HealthCare Pharmaceuticals, Blueprint Medicines, Bristol-Myers Squibb Company, Elevation Oncology, Genentech, a member of the Roche Group, Lilly, Merck, Merus BV, Pfizer Inc, Rain Therapeutics, RAPT Therapeutics, Turning Point Therapeutics Inc
Data and Safety Monitoring Board/Committee	Candel Therapeutics

RTP
RESEARCH TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions

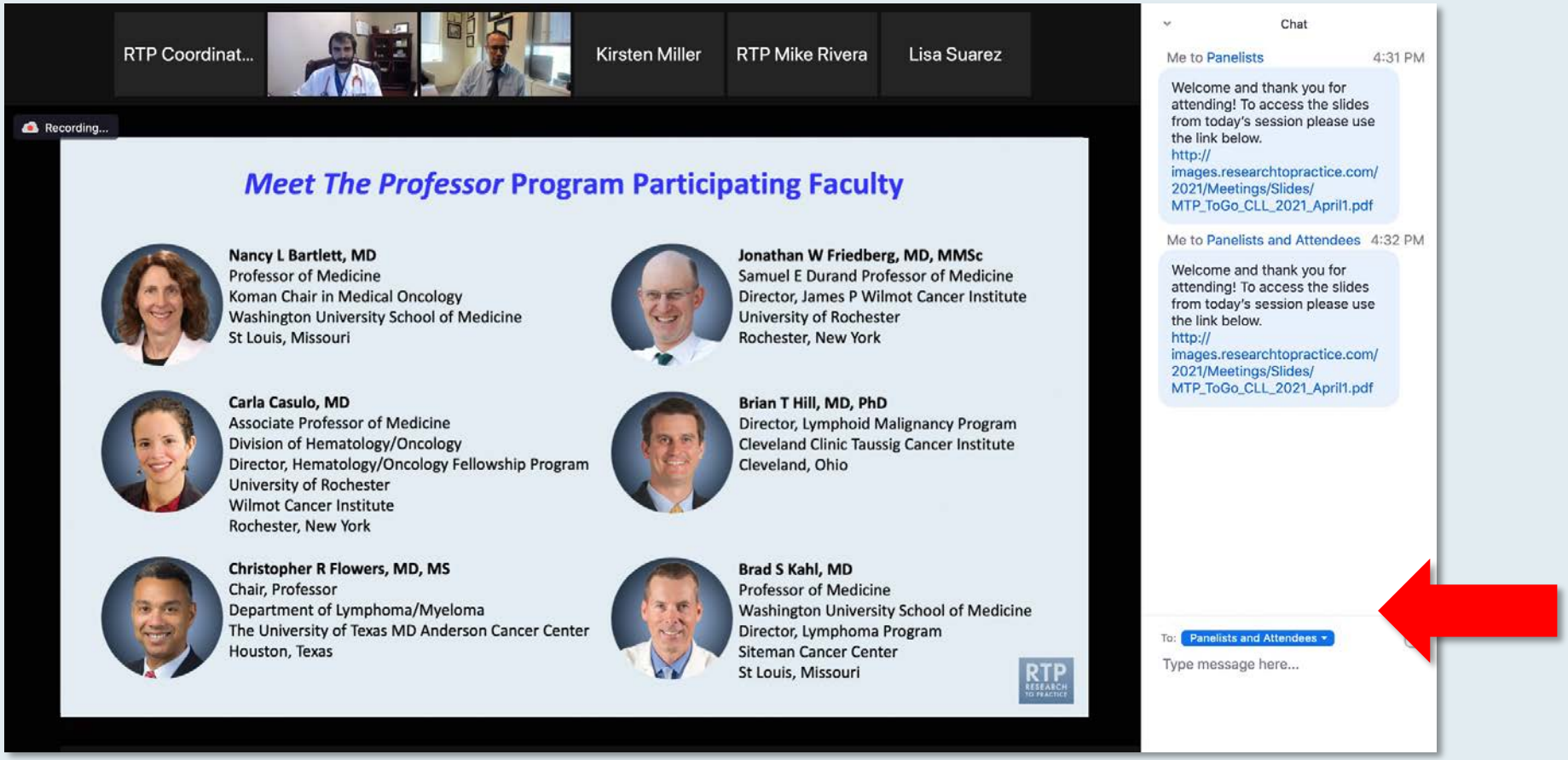


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

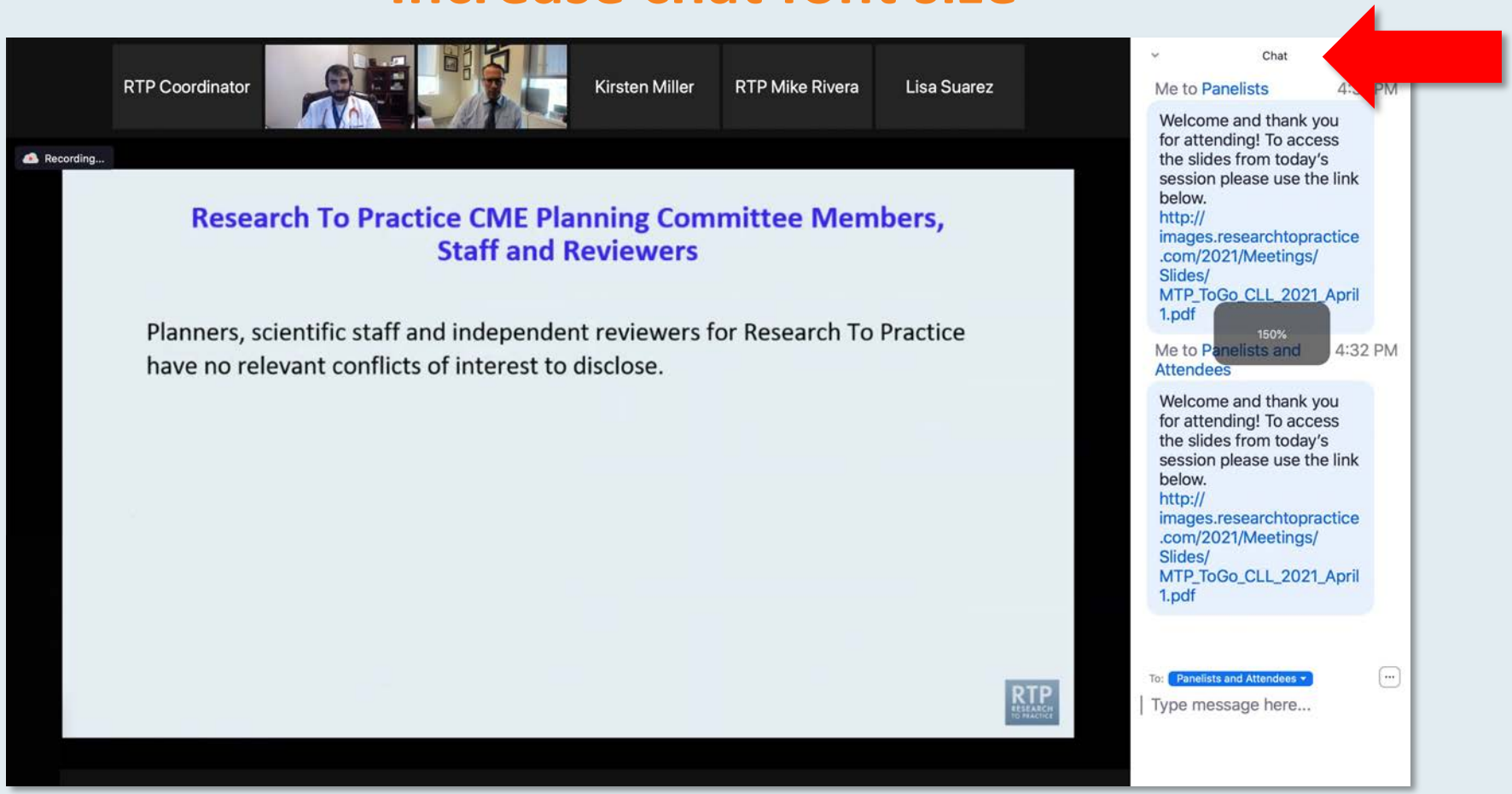


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Increase chat font size



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

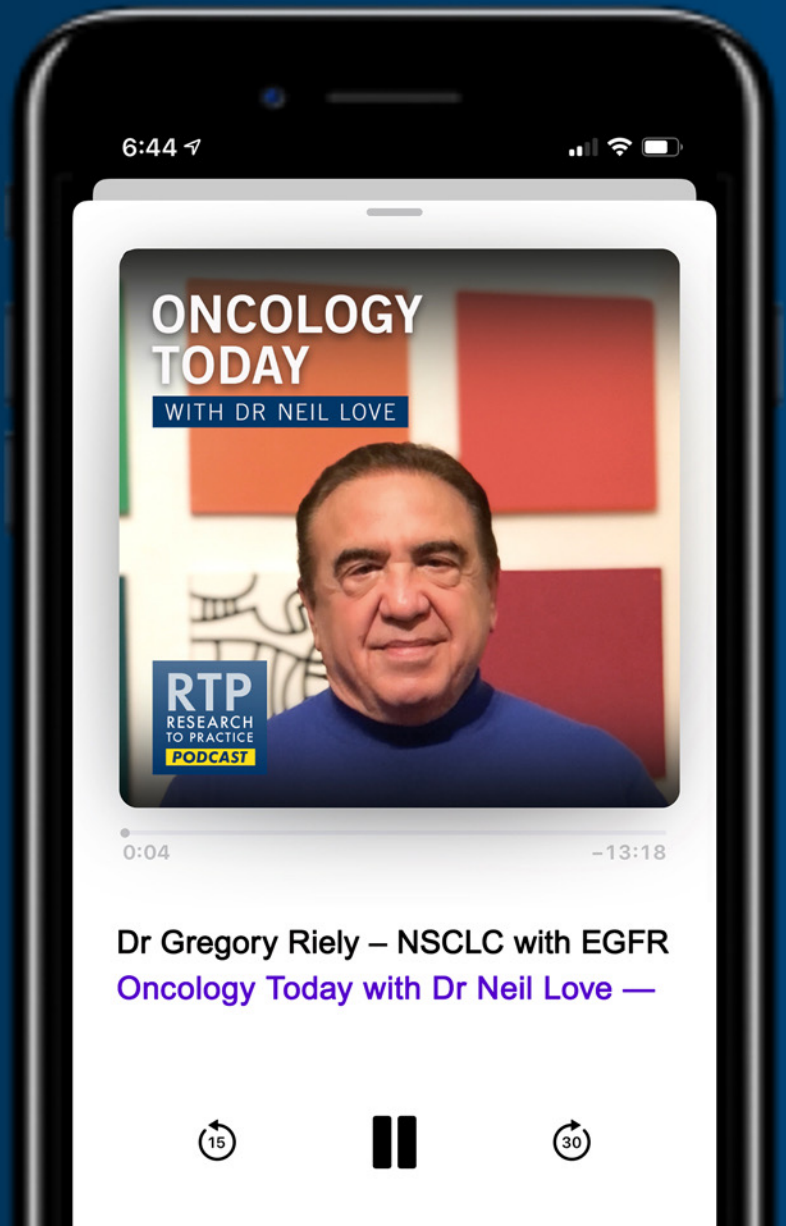
NSCLC with EGFR Exon 20 Insertion Mutations

DR GREGORY RIELY
MEMORIAL SLOAN KETTERING CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Meet The Professor

Optimizing the Management of Hepatobiliary Cancers

Thursday, July 28, 2022
5:00 PM – 6:00 PM ET

Faculty

Robin K Kelley, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

WORLD PREMIERE OF AN ENDURING CME ACTIVITY

Oncology Today: Management of Unresectable Stage III Non-Small Cell Lung Cancer

Monday, August 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Jeffrey Bradley, MD

David R Spigel, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

WORLD PREMIERE OF AN ENDURING CME ACTIVITY

Oncology Today:
The Use of T-DXd in HER2-Low Breast Cancer

Tuesday, August 2, 2022
5:00 PM – 6:00 PM ET

Faculty

Shanu Modi, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Ovarian Cancer

Wednesday, August 3, 2022
5:00 PM – 6:00 PM ET

Faculty

Prof Jonathan A Ledermann

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Recent Advances in Medical Oncology:
A daylong CME hybrid (live/online) event

Saturday, August 6, 2022

9:00 AM – 4:30 PM PT (12:00 PM – 7:30 PM ET)

Bellagio Las Vegas | Las Vegas, Nevada

Faculty

Neeraj Agarwal, MD
Harold J Burstein, MD, PhD
Ibiayi Dagogo-Jack, MD
Rafael Fonseca, MD
Brad S Kahl, MD
Rutika Mehta, MD, MPH
Craig Moskowitz, MD
Joyce O'Shaughnessy, MD
Krina Patel, MD, MSc
Philip A Philip, MD, PhD, FRCP
Suresh S Ramalingam, MD
Sandy Srinivas, MD

Moderator

Neil Love, MD

In Partnership with the American Oncology Network

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Small Cell Lung Cancer

Thursday, August 11, 2022
5:00 PM – 6:00 PM ET

Faculty

Jacob Sands, 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.

RTP
RESEARCH
TO PRACTICE

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

Stephen V Liu, MD
Associate Professor of Medicine
Georgetown University Hospital
Washington, DC

RTP
RESEARCH
TO PRACTICE

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 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
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

RTP
RESEARCH
TO PRACTICE

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

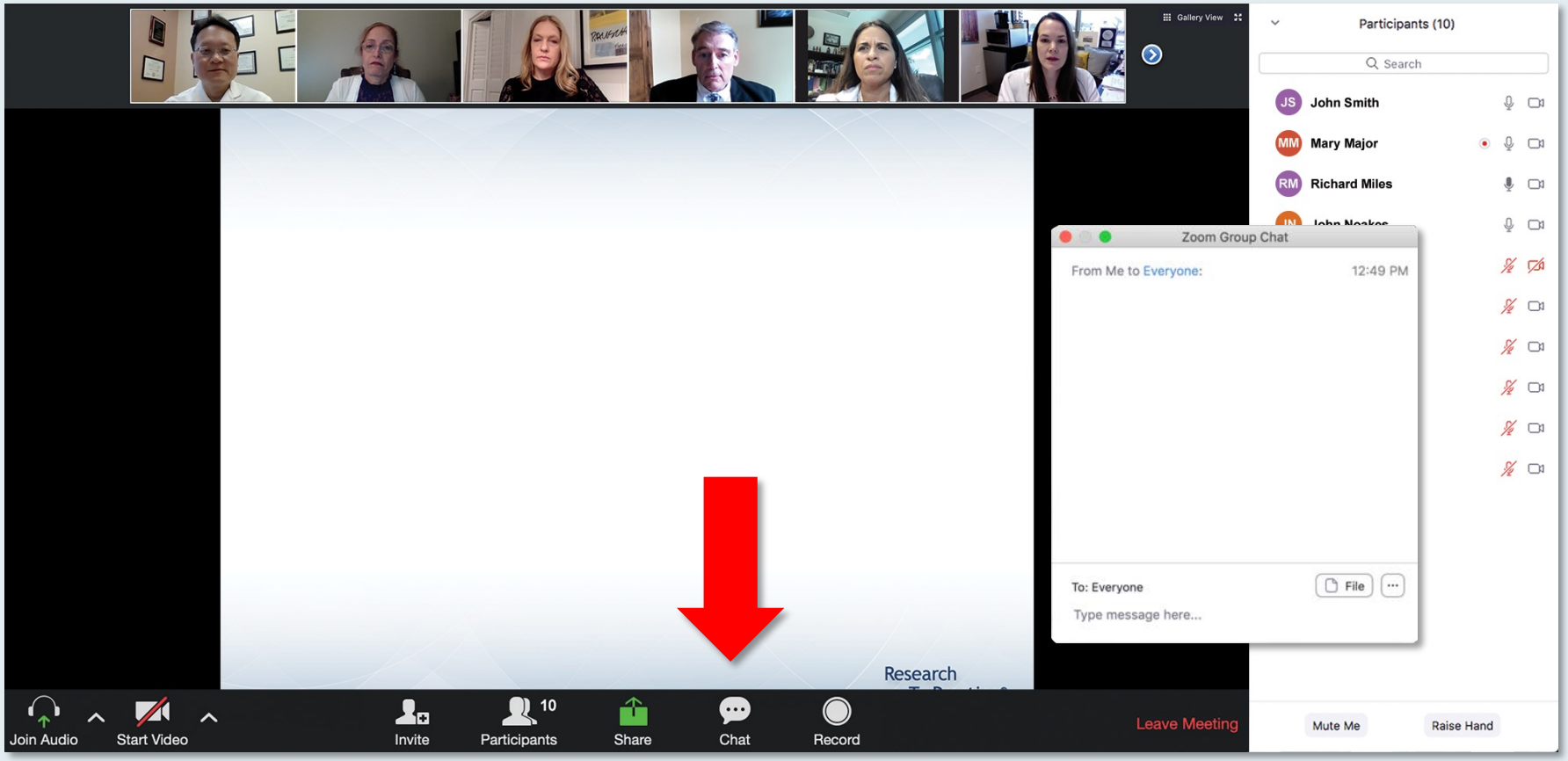
Alexander I Spira, MD, PhD
CEO and Clinical Director, NEXT Virginia
Director, Virginia Cancer Specialists
Research Program
Fairfax, Virginia

Stephen V Liu, MD
Associate Professor of Medicine
Georgetown University Hospital
Washington, DC

MODERATOR
Neil Love, MD
Research To Practice

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions



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

RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

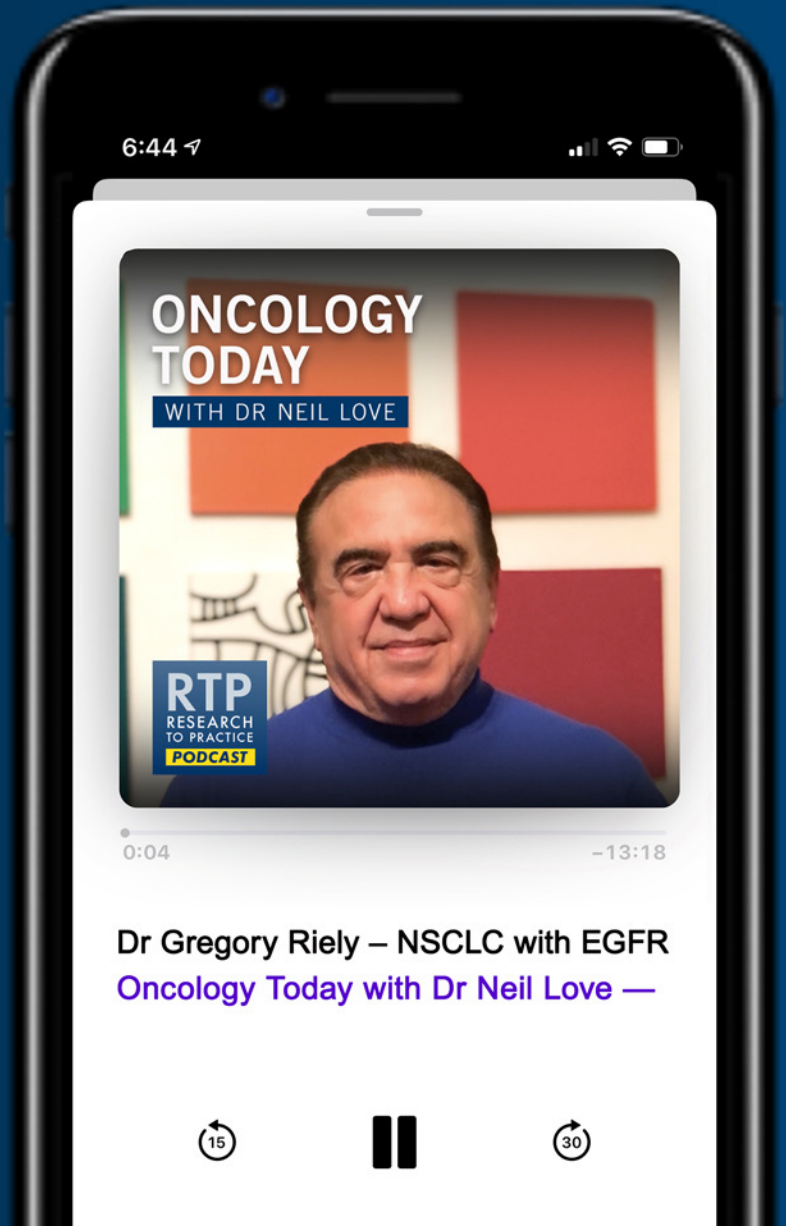
NSCLC with EGFR Exon 20 Insertion Mutations

DR GREGORY RIELY
MEMORIAL SLOAN KETTERING CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Meet The Professor

Optimizing the Management of Hepatobiliary Cancers

Thursday, July 28, 2022
5:00 PM – 6:00 PM ET

Faculty

Robin K Kelley, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

WORLD PREMIERE OF AN ENDURING CME ACTIVITY

Oncology Today: Management of Unresectable Stage III Non-Small Cell Lung Cancer

Monday, August 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Jeffrey Bradley, MD

David R Spigel, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

WORLD PREMIERE OF AN ENDURING CME ACTIVITY

Oncology Today:
The Use of T-DXd in HER2-Low Breast Cancer

Tuesday, August 2, 2022
5:00 PM – 6:00 PM ET

Faculty

Shanu Modi, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Ovarian Cancer

Wednesday, August 3, 2022
5:00 PM – 6:00 PM ET

Faculty

Prof Jonathan A Ledermann

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Recent Advances in Medical Oncology:
A daylong CME hybrid (live/online) event

Saturday, August 6, 2022

9:00 AM – 4:30 PM PT (12:00 PM – 7:30 PM ET)

Bellagio Las Vegas | Las Vegas, Nevada

Faculty

Neeraj Agarwal, MD
Harold J Burstein, MD, PhD
Ibiayi Dagogo-Jack, MD
Rafael Fonseca, MD
Brad S Kahl, MD
Rutika Mehta, MD, MPH
Craig Moskowitz, MD
Joyce O'Shaughnessy, MD
Krina Patel, MD, MSc
Philip A Philip, MD, PhD, FRCP
Suresh S Ramalingam, MD
Sandy Srinivas, MD

Moderator

Neil Love, MD

In Partnership with the American Oncology Network

RTP RESEARCH TO PRACTICE

Recent Advances and Real-World Implications in Medical Oncology

A Daylong Multitumor Educational Symposium
in Partnership with the American Oncology Network

Saturday, August 6, 2022

Breast Cancer

9:05 AM – 10:05 AM PT

Faculty

Harold J Burstein, MD, PhD
Joyce O'Shaughnessy, MD

Genitourinary Cancers

10:05 AM – 11:05 AM PT

Faculty

Neeraj Agarwal, MD
Sandy Srinivas, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Recent Advances and Real-World Implications in Medical Oncology

A Daylong Multitumor Educational Symposium
in Partnership with the American Oncology Network

Saturday, August 6, 2022

Multiple Myeloma

11:20 AM – 12:20 PM PT

Faculty

Rafael Fonseca, MD
Krina Patel, MD, MSc

CLL and Lymphomas

12:55 PM – 1:55 PM PT

Faculty

Brad S Kahl, MD
Craig Moskowitz, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Recent Advances and Real-World Implications in Medical Oncology

A Daylong Multitumor Educational Symposium
in Partnership with the American Oncology Network

Saturday, August 6, 2022

Gastrointestinal Cancers

1:55 PM – 2:55 PM PT

Faculty

Rutika Mehta, MD, MPH
Philip A Philip, MD, PhD, FRCP

Lung Cancer

3:10 PM – 4:10 PM PT

Faculty

Ibiayi Dagogo-Jack, MD
Suresh S Ramalingam, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Small Cell Lung Cancer

Thursday, August 11, 2022
5:00 PM – 6:00 PM ET

Faculty

Jacob Sands, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

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

Stephen V Liu, MD
Associate Professor of Medicine
Georgetown University Hospital
Washington, DC

RTP
RESEARCH
TO PRACTICE

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.

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Liu — Disclosures

Advisory Committee	Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology, Genentech, a member of the Roche Group, Guardant Health, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Novartis, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Takeda Pharmaceuticals USA Inc, Turning Point Therapeutics Inc
Consulting Agreements	BeiGene Ltd, Blueprint Medicines, Daiichi Sankyo Inc, Elevation Oncology, Genentech, a member of the Roche Group, Janssen Biotech Inc, Lilly, Turning Point Therapeutics Inc
Contracted Research	Alkermes, Bayer HealthCare Pharmaceuticals, Blueprint Medicines, Bristol-Myers Squibb Company, Elevation Oncology, Genentech, a member of the Roche Group, Lilly, Merck, Merus BV, Pfizer Inc, Rain Therapeutics, RAPT Therapeutics, Turning Point Therapeutics Inc
Data and Safety Monitoring Board/Committee	Candel Therapeutics

RTP
RESEARCH TO PRACTICE

Gigi Chen, MD
John Muir Health
Pleasant Hill, California

Minesh Dinubhai Patel, MD
Piedmont Cancer Institute
Peachtree City, Georgia

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

Priya Rudolph, MD, PhD
Georgia Cancer Specialists
Athens, Georgia

Adam R Miller, MD
Mass General/North Shore Cancer Center
Danvers, Massachusettes

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

Jiaxin (Jason) Niu, MD, PhD
The University of Texas
MD Anderson Cancer Center
Gilbert, Arizona

RTP
RESEARCH
TO PRACTICE

Meet The Professor with Dr Liu

Introduction: Journal Club with Dr Liu – Part 1

MODULE 1: Case Presentations

MODULE 2: Journal Club with Dr Liu – Part 2

MODULE 3: Appendix of Key Publications

RTP
RESEARCH
TO PRACTICE

Meet The Professor with Dr Liu

Introduction: Journal Club with Dr Liu – Part 1

MODULE 1: Case Presentations

MODULE 2: Journal Club with Dr Liu – Part 2

MODULE 3: Appendix of Key Publications

RTP
RESEARCH
TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 7, 2022 VOL. 387 NO. 1

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer

S. Modi, W. Jacot, T. Yamashita, J. Sohn, M. Vidal, E. Tokunaga, J. Tsurutani, N.T. Ueno, A. Prat, Y.S. Chae, K.S. Lee, N. Niikura, Y.H. Park, B. Xu, X. Wang, M. Gil-Gil, W. Li, J.-Y. Pierga, S.-A. Im, H.C.F. Moore, H.S. Rugo, R. Yerushalmi, F. Zagouri, A. Gombos, S.-B. Kim, Q. Liu, T. Luo, C. Saura, P. Schmid, T. Sun, D. Gambhire, L. Yung, Y. Wang, J. Singh, P. Vitazka, G. Meinhardt, N. Harbeck, and D.A. Cameron, for the DESTINY-Breast04 Trial Investigators*

RTP RESEARCH TO PRACTICE

Clin Lung Cancer 2021;22(6):483-99.

Review Article

Antibody Drug Conjugates in Lung Cancer: State of the Current Therapeutic Landscape and Future Developments

Joshua E. Reuss,[1] Laura Gosa,[2] Stephen V. Liu[1]

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Antibody-Drug Conjugates in Oncology: Recent Research Development

- Brentuximab vedotin (ECHELON-1): Hodgkin lymphoma
- Belantamab mafodotin: Multiple myeloma
- Polatuzumab vedotin: DLBCL
- Sacituzumab govitecan: Breast and bladder cancer
- Enfortumab vedotin: Bladder cancer
- Trastuzumab deruxtecan (T-DXd): Breast cancer (second line, HER2 low), upper GI, colorectal and lung cancer

RTP
RESEARCH
TO PRACTICE

Clin Cancer Res 2022;28(7):1302-12.

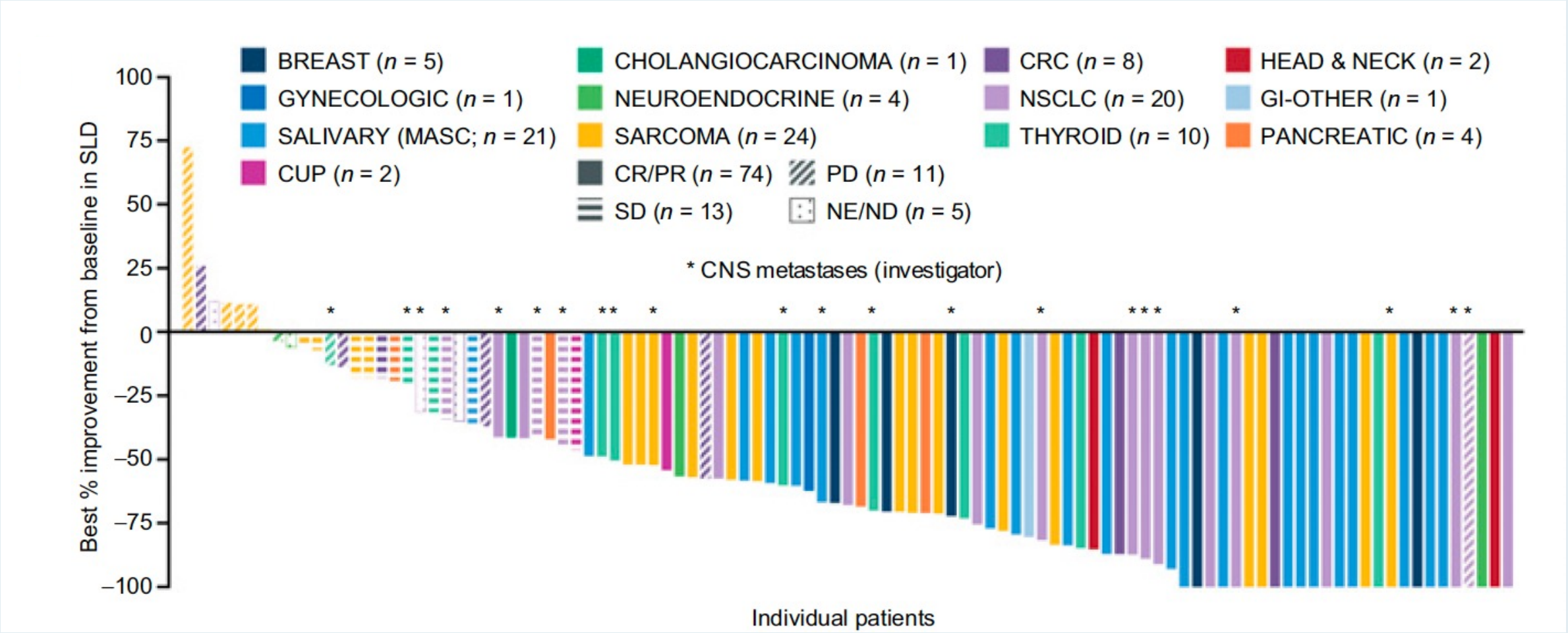
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

Updated Integrated Analysis of the Efficacy and Safety of Entrectinib in Patients With *NTRK* Fusion-Positive Solid Tumors

George D. Demetri[1], Filippo De Braud[2], Alexander Drilon[4], Salvatore Siena[3,5], Manish R. Patel[6], Byoung Chul Cho[7], Stephen V. Liu[8], Myung-Ju Ahn[9], Chao-Hua Chiu[10], Jessica J. Lin[11], Koichi Goto[12], Jeeyun Lee[9], Lyudmila Bazhenova[13], Thomas John[14], Marwan Fakih[15], Sant P. Chawla[16], Rafal Dziadziuszko[17,18], Takashi Seto[19], Sebastian Heinzmann[20], Bethany Pitcher[21], David Chen[22], Timothy R. Wilson[22], and Christian Rolfo[23]

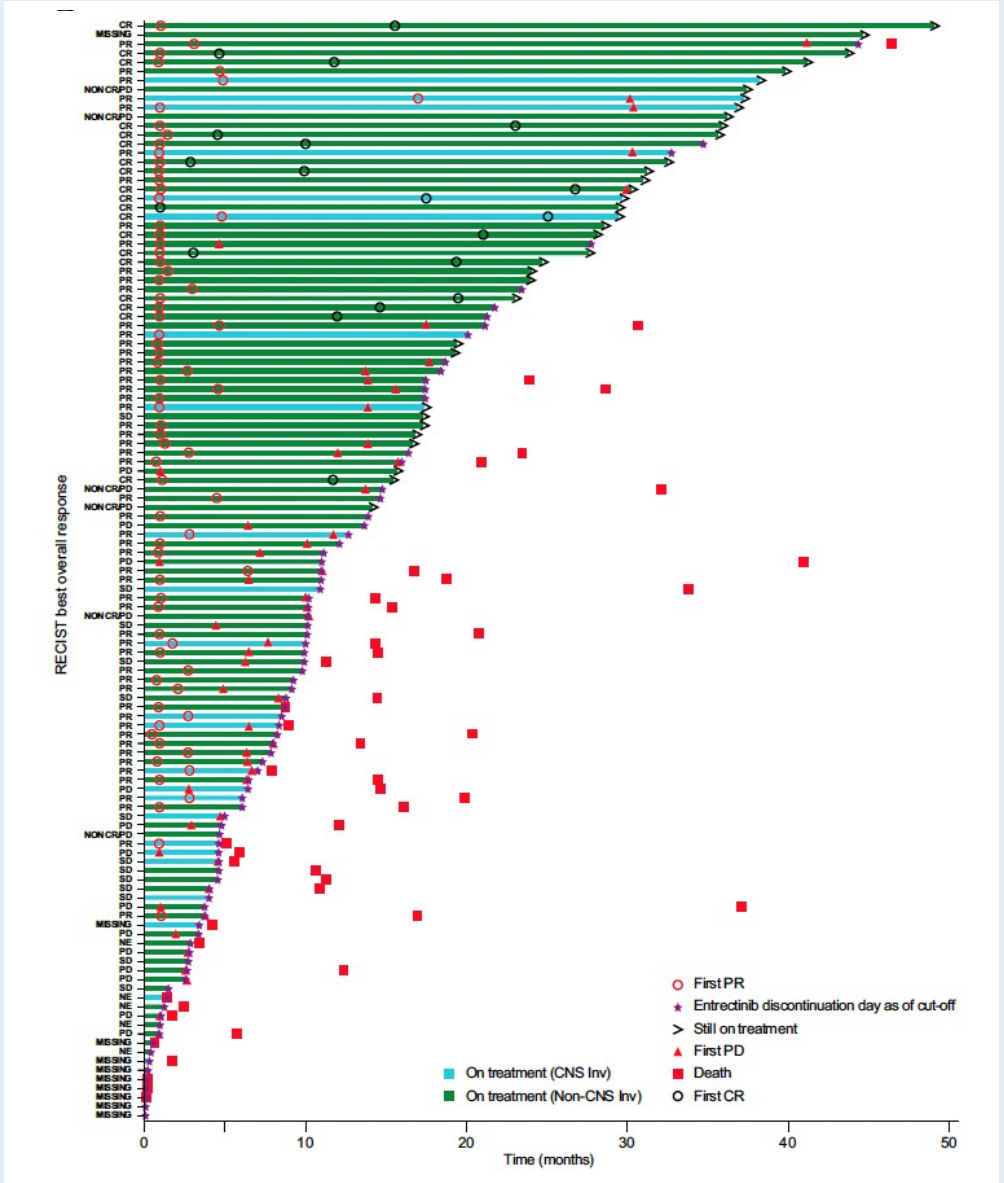
JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Best Individual Patient Responses



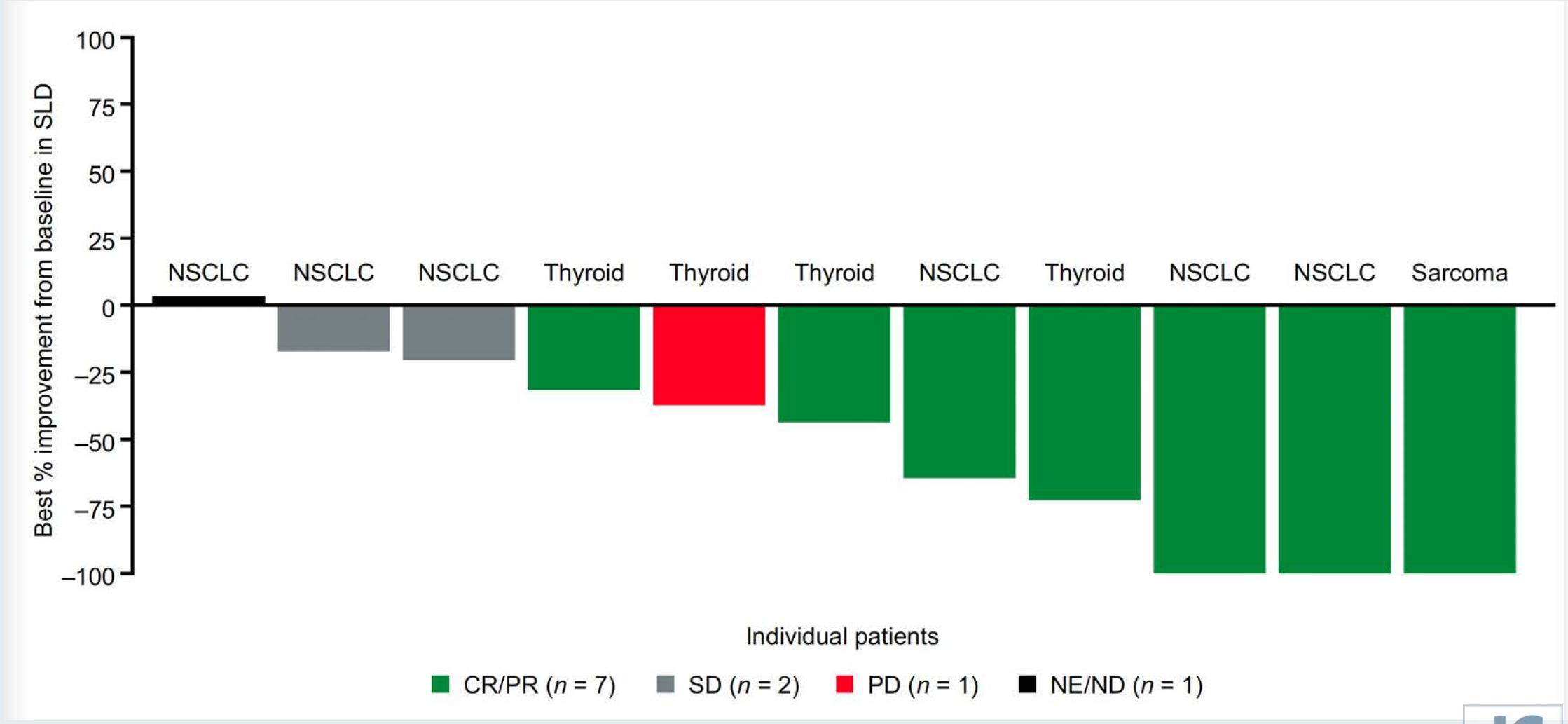
Demetri GD et al. *Clin Cancer Res* 2022;28(7):1302-12.

Time on Entrectinib Treatment



Demetri GD et al. *Clin Cancer Res* 2022;28(7):1302-12.

Best Intracranial Responses to Entrectinib in Patients with Solid Tumors with NTRK Fusions and Measurable CNS Metastases



Demetri GD et al. *Clin Cancer Res* 2022;28(7):1302-12.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Liu

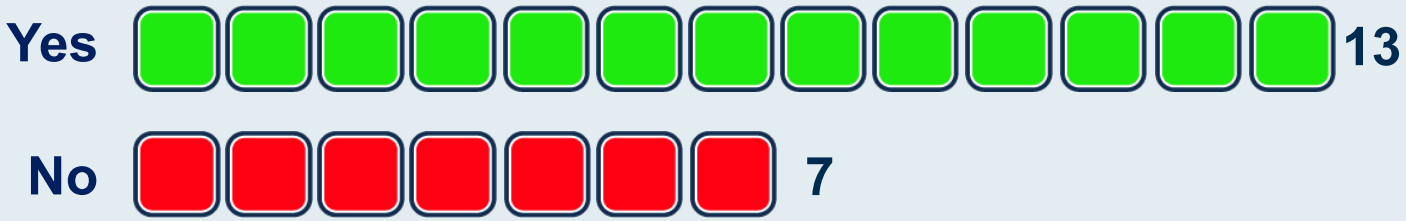
Introduction: Journal Club with Dr Liu

MODULE 1: Case Presentations

- Dr Patel: A 45-year-old woman with metastatic lung adenocarcinoma with a ROS1 fusion
- Dr Miller: A 77-year-old woman with metastatic lung adenocarcinoma with a HER2 mutation
- Dr Kumar: A 62-year-old-woman with RET fusion-driven lung adenocarcinoma
- Dr Kumar: A 70-year-old woman with metastatic adenocarcinoma of the lung with a MET exon 14 mutation
- Dr Rudolph: A 70-year-old woman with recurrent lung adenocarcinoma with a MET T263M mutation
- Dr Chen: A 79-year-old woman with metastatic lung adenocarcinoma with a MET exon 14 mutation
- Dr Sinha: A 78-year-old woman with ALK fusion-driven lung adenocarcinoma
- Dr Miller: A 67-year-old woman with metastatic lung adenocarcinoma and a KRAS G12C mutation
- Dr Niu: A 61-year-old woman with metastatic lung adenocarcinoma and an NRG1 fusion
- Dr Niu: A 52-year-old man with lung adenocarcinoma with both BRAF V600E and IDH1 mutations

RTP RESEARCH TO PRACTICE

A patient with a long smoking history presents with highly symptomatic metastatic nonsquamous NSCLC requiring immediate treatment, and chemotherapy is started while awaiting next-generation sequencing. PD-L1 TPS (tumor proportion score) is 90%. Would you recommend adding an anti-PD-1/PD-L1 antibody as well?



Survey of lung cancer clinical investigators; RTP lung cancer satellite symposium at ASCO 2022.

Case Presentation: A 45-year-old woman with metastatic lung adenocarcinoma with a ROS1 fusion who has a CR with crizotinb – PD-L1 40%

Dr Minesh Patel (Peachtree City, Georgia)

RTP
RESEARCH
TO PRACTICE

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

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, would you generally offer targeted therapy as consolidation treatment to a patient with unresectable Stage IIIB NSCLC (PD-L1 TPS 50%) who has undergone definitive chemoradiation therapy and is found to have a ROS1 rearrangement?

 Dr Baik	No	 Dr Gainor	No
 Dr Camidge	No	 Dr Johnson	No
 Dr Drilon	Yes, entrectinib/crizotinib for 3 years	 Dr Spira	No

RTP RESEARCH TO PRACTICE

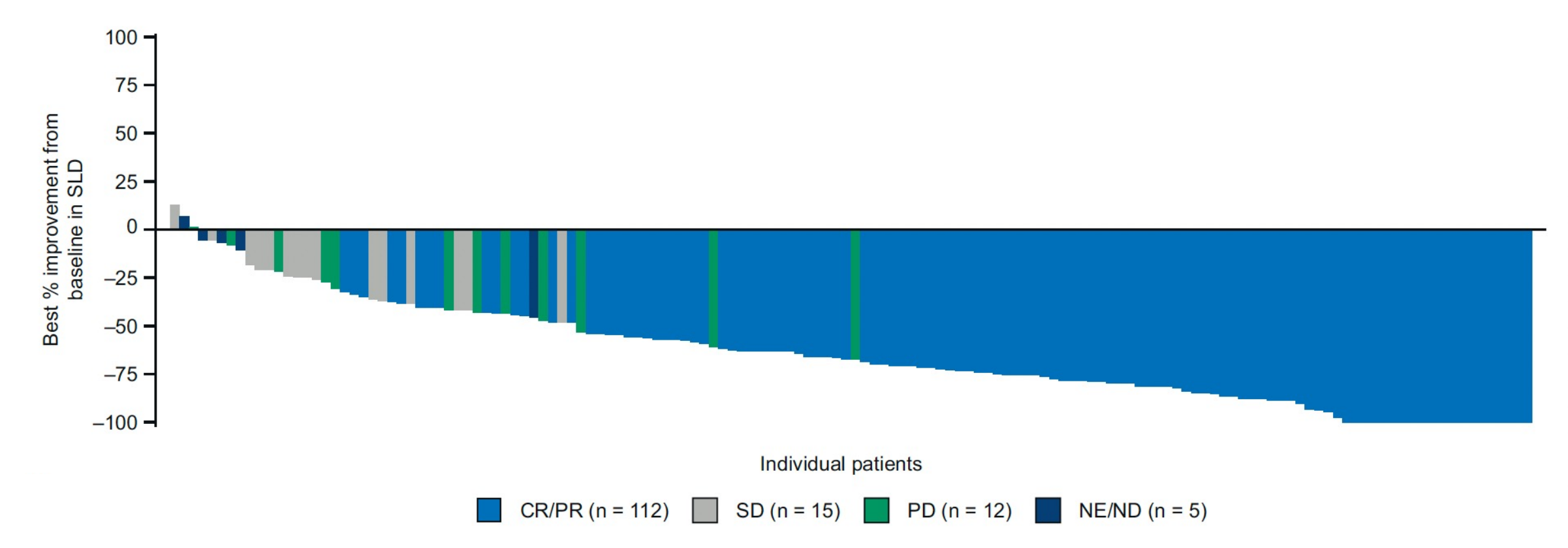
JTO Clin Res Rep 2022;3(6):100332.

ORIGINAL ARTICLE

Long-Term Efficacy and Safety of Entrectinib in *ROS1* Fusion–Positive NSCLC

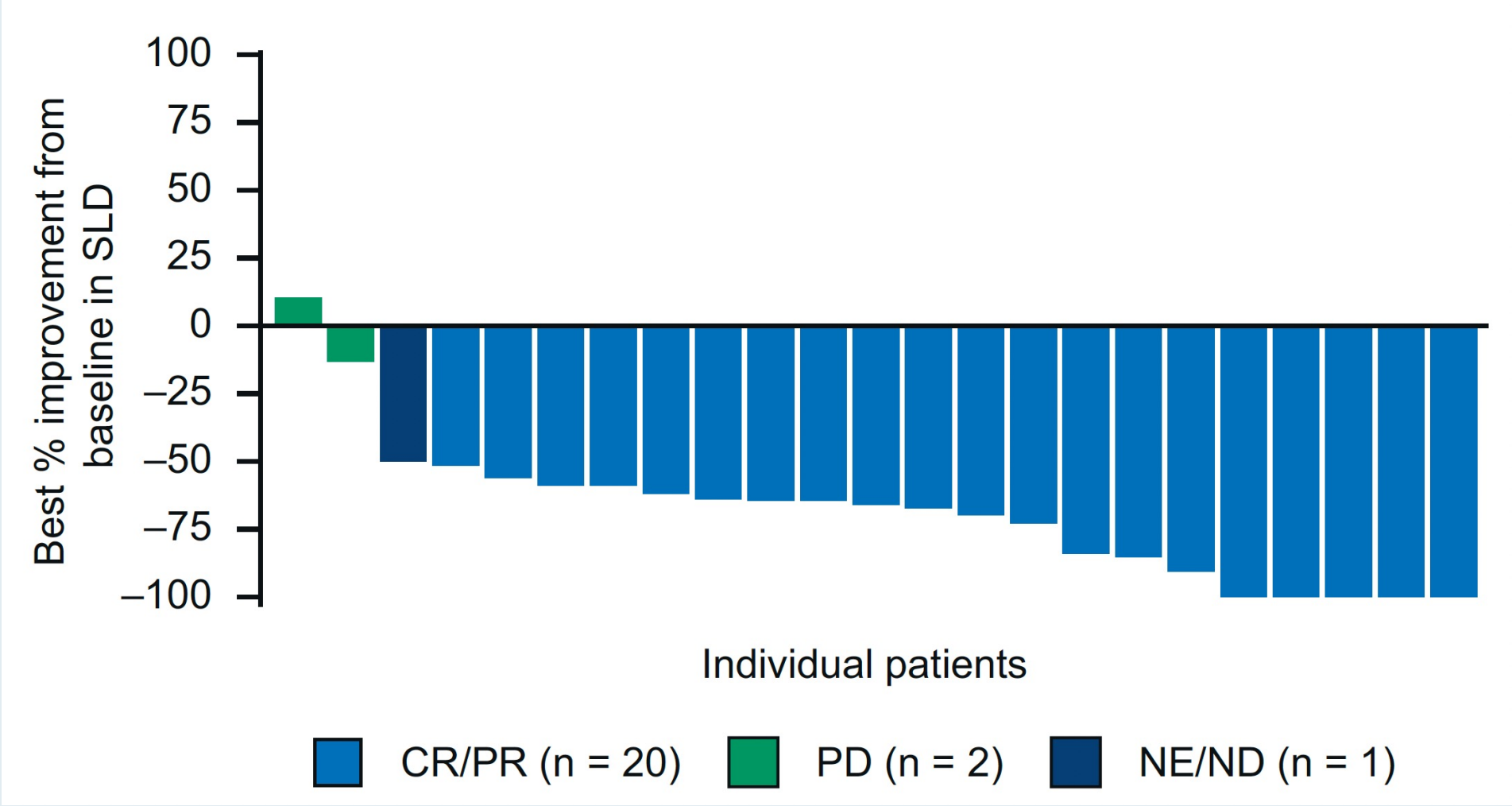
Alexander Drilon, MD,[a] Chao-Hua Chiu, MD,[b] Yun Fan, MD,[c]
Byoung Chul Cho, MD, PhD,[d] Shun Lu, MD, PhD,[e] Myung-Ju Ahn, MD, PhD,[f]
Matthew G. Krebs, MD, PhD,[g] Stephen V. Liu, MD,[h] Thomas John, MD,[i]
Gregory A. Otterson, MD,[j] Daniel S. W. Tan, MD,[k] Tejas Patil, MD,[l]
Rafal Dziadziuszko, MD, PhD,[m] Erminia Massarelli, MD, PhD,[n] Takashi Seto, MD,[o]
Robert C. Doebele, MD, PhD,[l] Bethany Pitcher, MSc,[p] Nino Kurtsikidze, MD,[q]
Sebastian Heinzmann, PhD,[r] Salvatore Siena, MD[r,s,*]

Best Overall Response with Entrectinib



Drilon A et al. *JTO Clin Res Rep* 2022;3(6):100332.

Best Intracranial Responses with Entrectinib in Patients with BICR-Assessed Measurable CNS Metastases at Baseline



BICR = blinded independent central review

Drilon A et al. *JTO Clin Res Rep* 2022;3(6):100332.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

Dr Adam Miller
(Danvers, Massachusetts)

Case Presentation: A 77-year-old woman with metastatic lung adenocarcinoma with a HER2 mutation who has an excellent response to T-DXd but with toxicity (PD-L1 5%)

Dr Minesh Patel
(Peachtree City, Georgia)

Perspectives on the use of T-DXd

RTP
RESEARCH
TO PRACTICE

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?

T-DXd = trastuzumab deruxtecan

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 a HER2 mutation, and which targeted therapy would you generally offer?

 Dr Baik	Second line T-DXd	 Dr Gainor	Second line T-DXd
 Dr Camidge	Second line T-DXd	 Dr Johnson	Second line T-DXd
 Dr Drilon	First line T-DXd	 Dr Spira	First line T-DXd

RTP RESEARCH TO PRACTICE

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/ pemetrexted/ pembrolizumab
 Dr Camidge	Carboplatin/ pemetrexed/ pembrolizumab	 Dr Johnson	Pembrolizumab
 Dr Drilon	Pembrolizumab	 Dr Spira	Carboplatin/ pemetrexted/ pembrolizumab

RTP RESEARCH TO PRACTICE

Original Study

Clin Lung Cancer 2022;23(1):52-9.

The Effects of HER2 Alterations in EGFR Mutant Non-small Cell Lung Cancer

Misako Nagasaka, MD PhD,[1,2] Vijendra Singh,[1] Yasmine Baca,[3] Ammar Sukari,[1] Chul Kim,[4] Hirva Mamdani,[1] Alexander I. Spira,[5] Dipesh Uprety,[1] Gerold Bepler,[1] Edward S. Kim,[6] Luis E. Raez,[7] Sachin Gopalkrishna Pai,[8] Chukwuemeka Ikpeazu,[9] Matthew Oberley,[3] Rebecca Feldman,[3] Joanne Xiu,[3] W. Michael Korn,[3] Antoinette J. Wozniak,[10] Hossein Borghaei,[11] Stephen V. Liu[4]

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Incidence of ERBB Gene Fusions (EGFR, ERBB2, ERBB4) Across Tumor Types

Schubert L et al.

ASCO 2021;Abstract 3091.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Case Presentation: A 62-year-old-woman with RET fusion-driven lung adenocarcinoma who has a CR with selpercatinib after disease progression on local therapy

Dr KS Kumar (Trinity, Florida)

RTP RESEARCH TO PRACTICE

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?

 Dr Baik	Pralsetinib	 Dr Gainor	Pralsetinib
 Dr Camidge	Selpercatinib	 Dr Johnson	Selpercatinib
 Dr Drilon	Selpercatinib	 Dr Spira	Selpercatinib

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, would you generally offer targeted therapy as consolidation treatment to a patient with unresectable Stage IIIB NSCLC (PD-L1 TPS 50%) who has undergone definitive chemoradiation therapy and is found to have a RET fusion?

 Dr Baik	Yes, pralsetinib for 2 years	 Dr Gainor	No
 Dr Camidge	No	 Dr Johnson	No
 Dr Drilon	Yes, selpercatinib for 3 years	 Dr Spira	No

RTP RESEARCH TO PRACTICE

Transl Lung Cancer Res 2022;11(1):111-6.

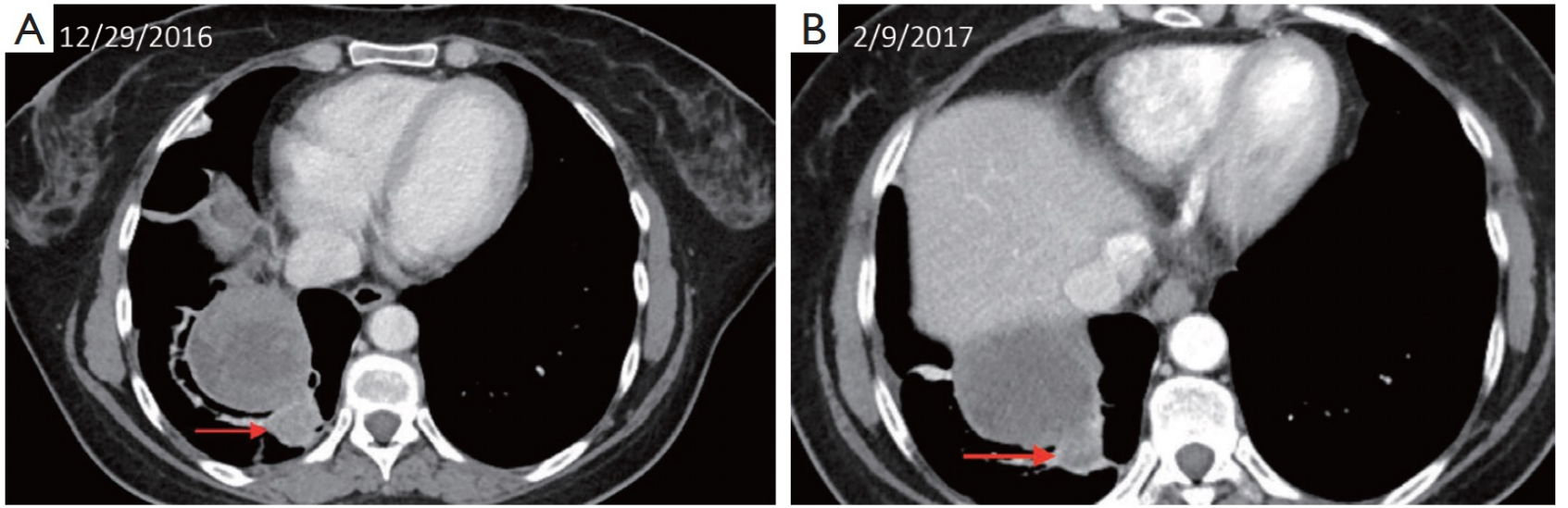
Case Report

Use of on-therapy ctDNA monitoring in a patient with *KIF5B-RET* fusion positive advanced non-small cell lung cancer: a case report

Vincent Yeung[1], Chul Kim[1], Lesli A. Kiedrowski[2], Stephen V. Liu[1], Joshua E. Reuss[1]^

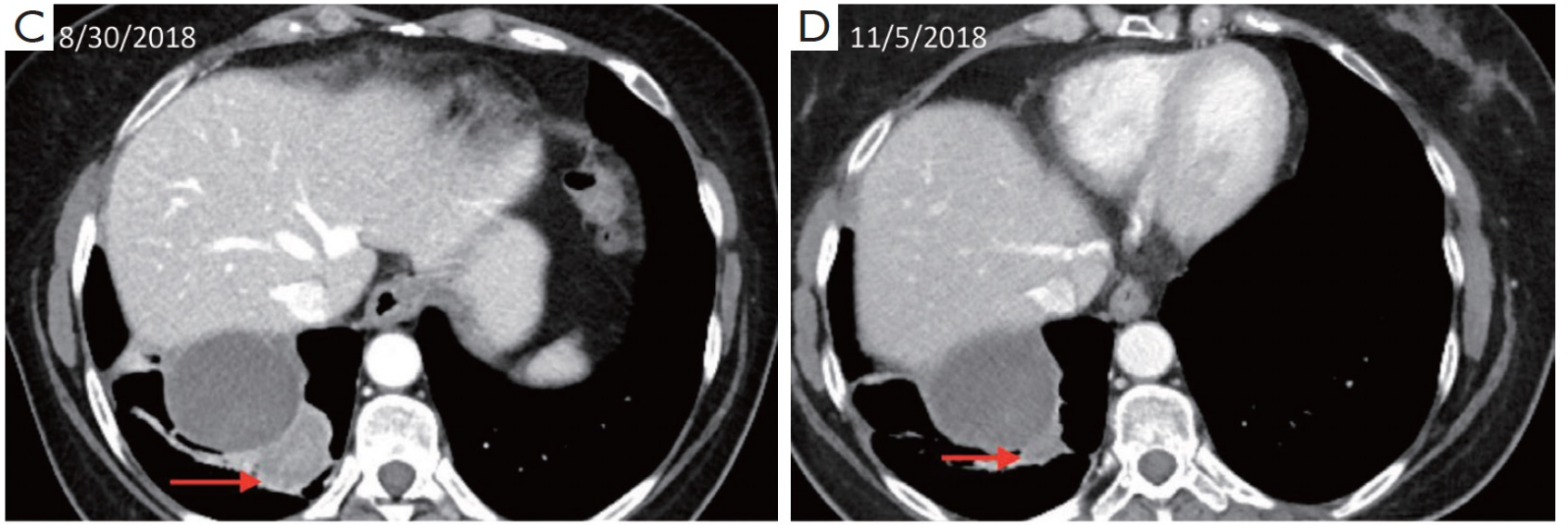
CT Imaging Assessments During Treatment

RLL RET-fusion+ lesion prior to treatment



Follow-up: Stable disease with RXDX-105

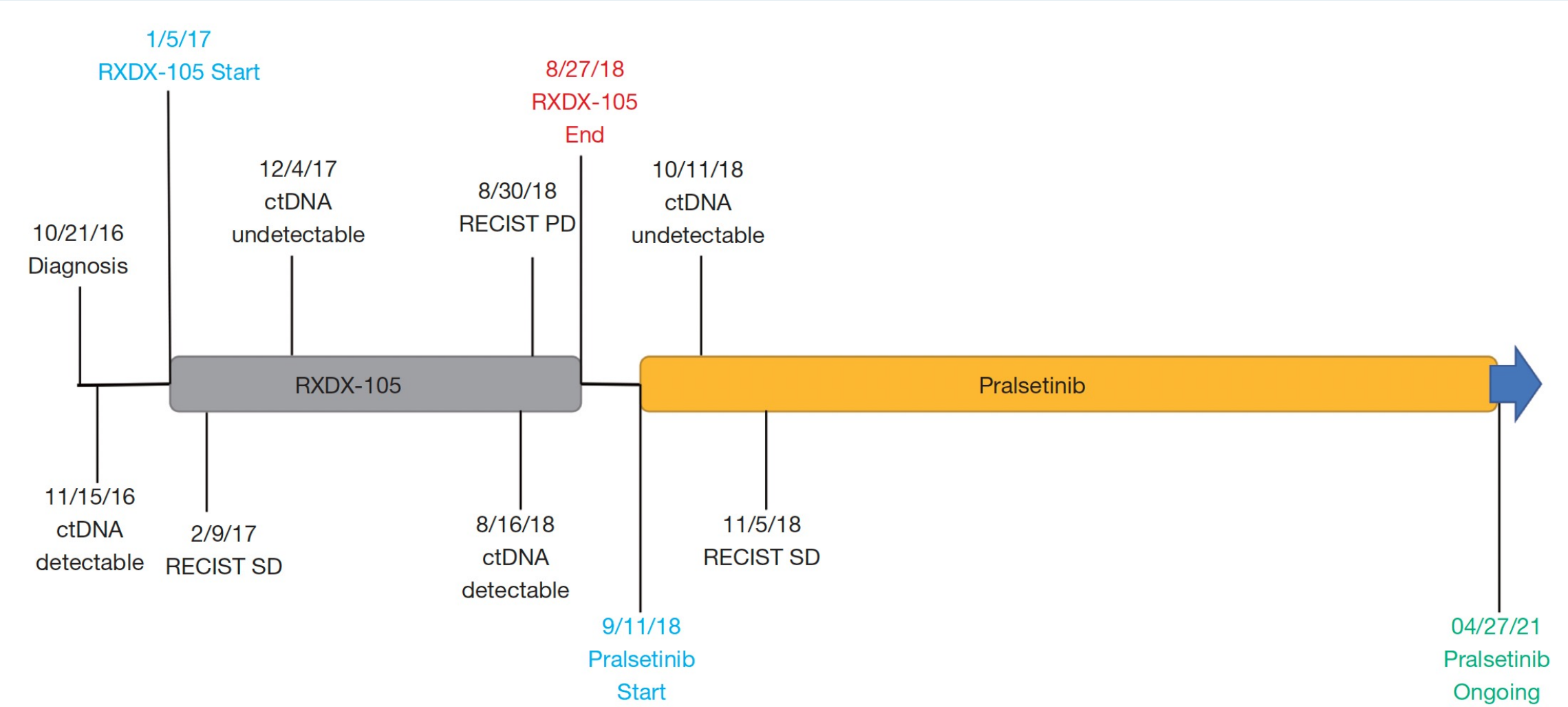
At progression on RXDX-105



Follow-up: Stable disease with pralsetinib

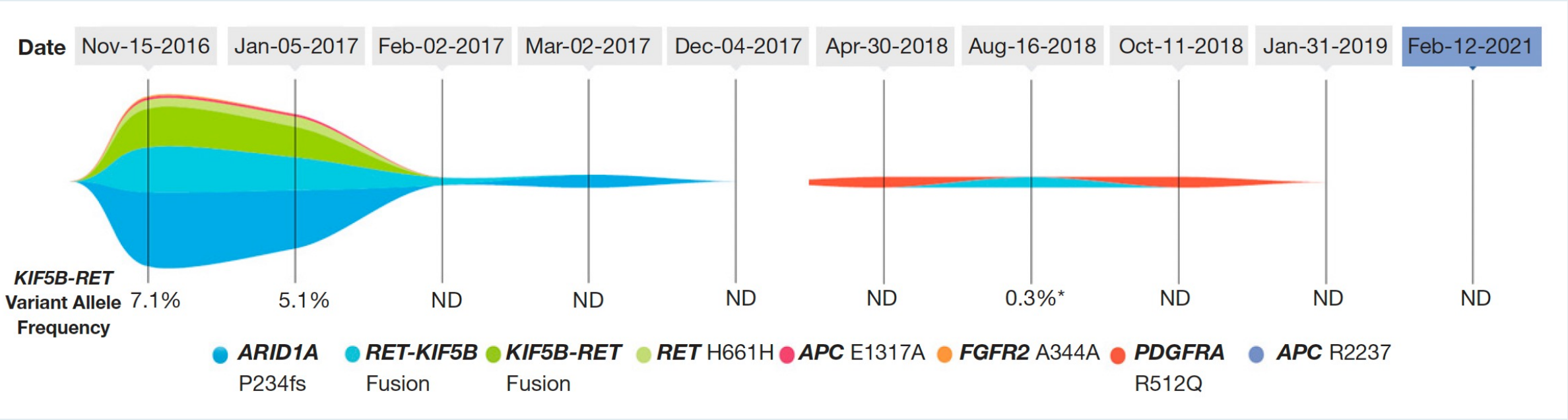
Yeung V et al. *Transl Lung Cancer Res* 2022;11(1):111-6.

Timeline of Clinical Course



Yeung V et al. *Transl Lung Cancer Res* 2022;11(1):111-6.

ctDNA Surveillance



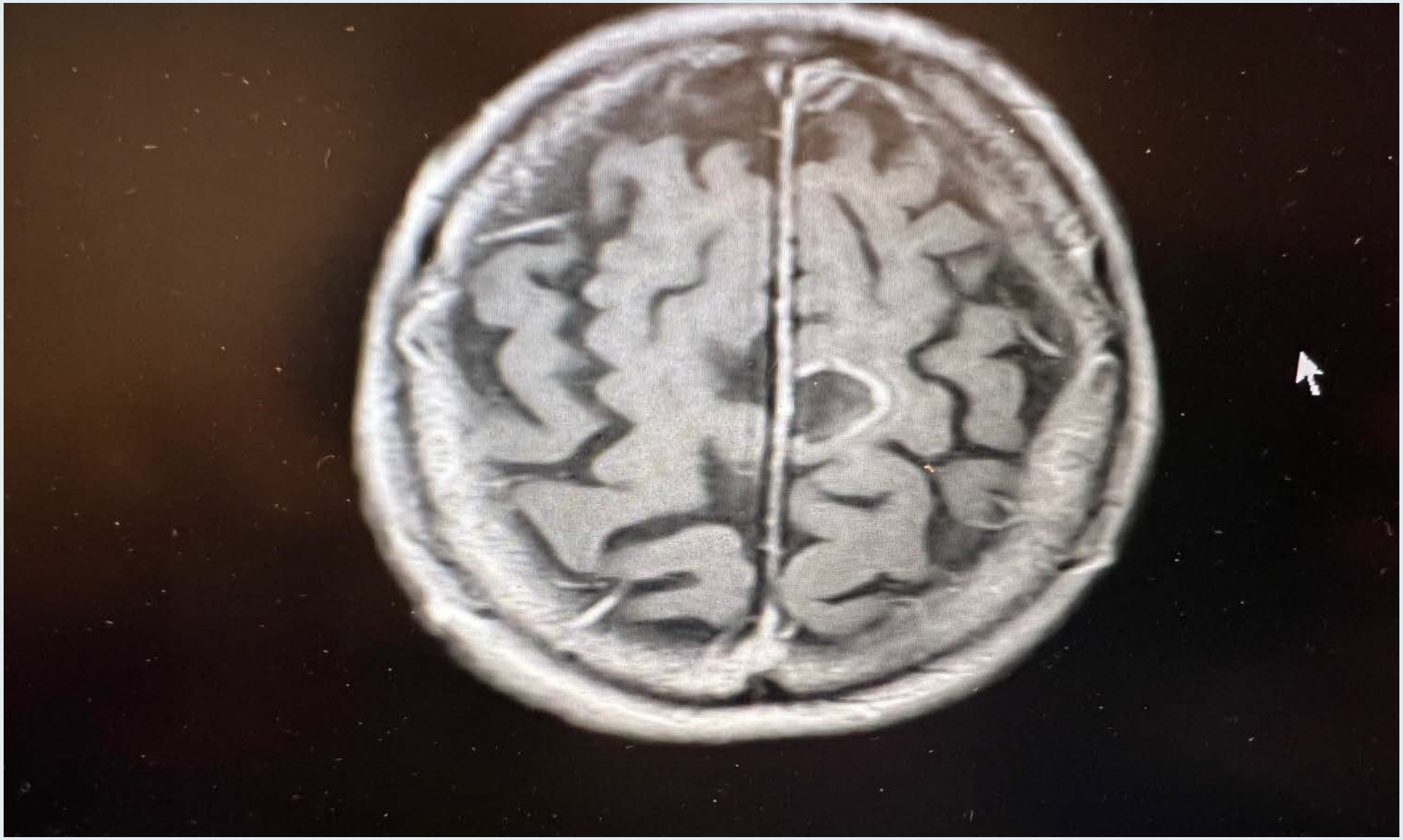
Yeung V et al. *Transl Lung Cancer Res* 2022;11(1):111-6.

Case Presentation: A 70-year-old woman with adenocarcinoma of the lung with brain, bone and lung metastases – PD-L1 30%, MET exon 14 mutation

Dr KS Kumar
(Trinity, Florida)

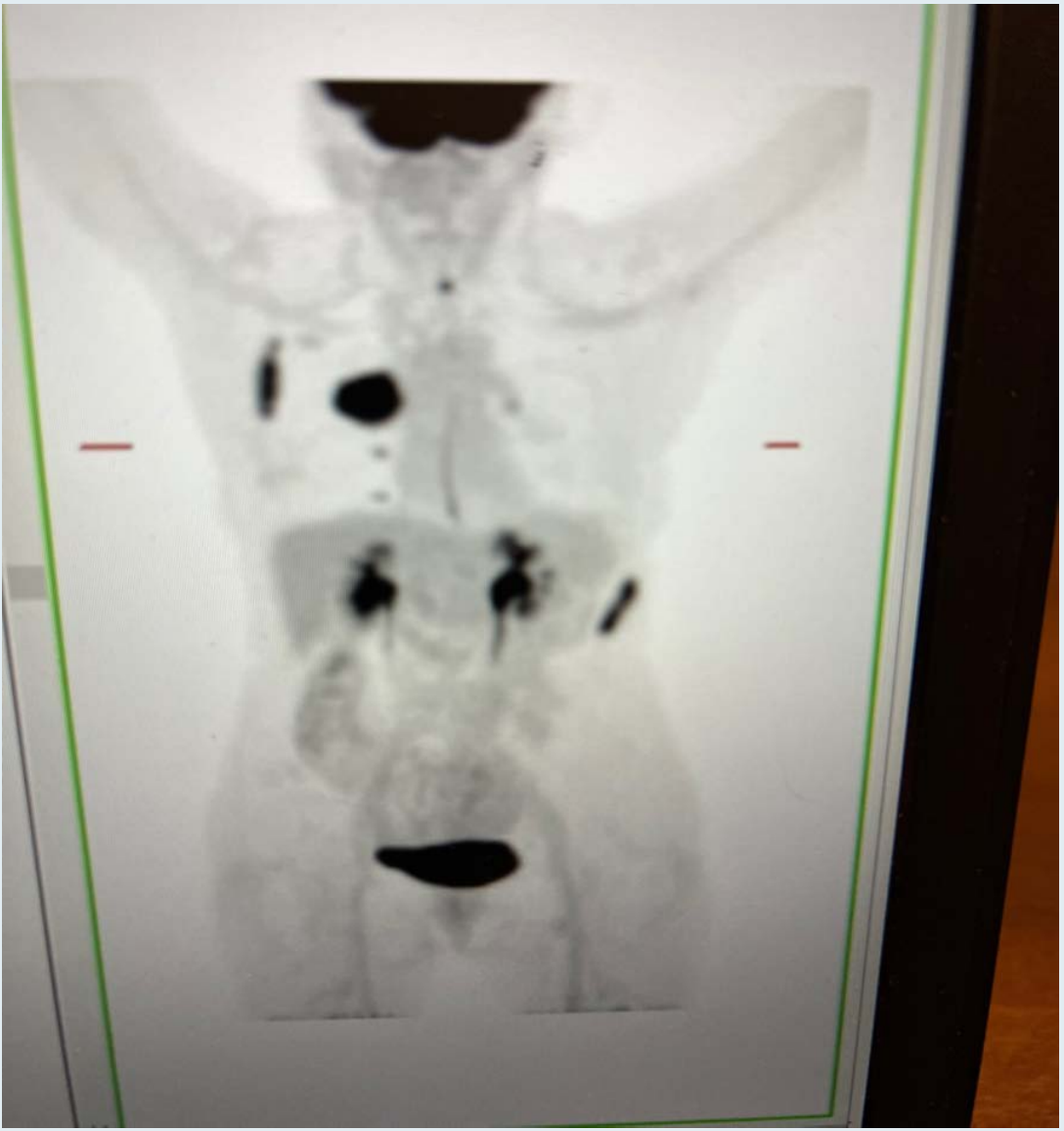
RTP
RESEARCH
TO PRACTICE

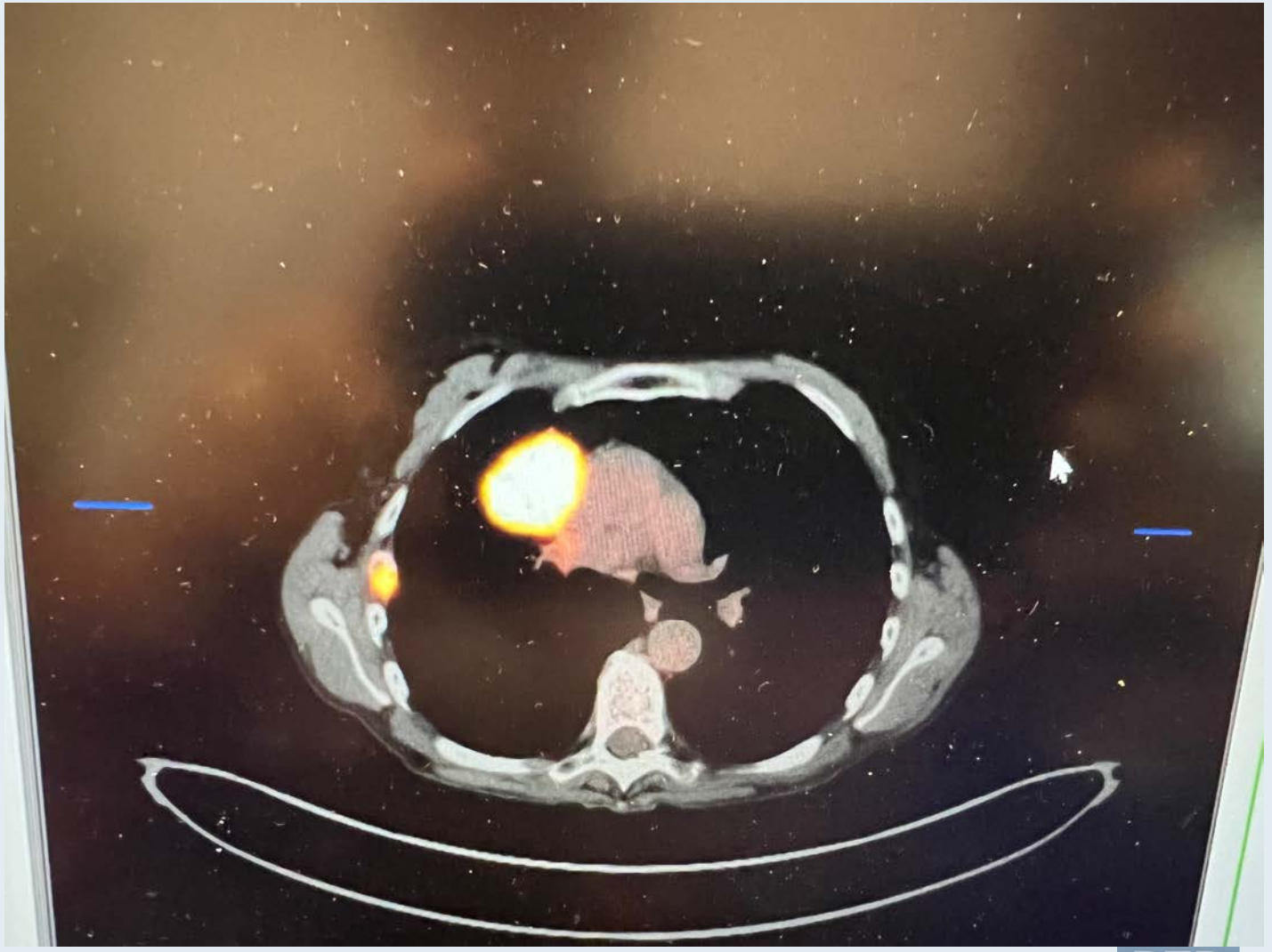
Left Frontal Lobe Mass with Vasogenic Edema



RTP
RESEARCH
TO PRACTICE

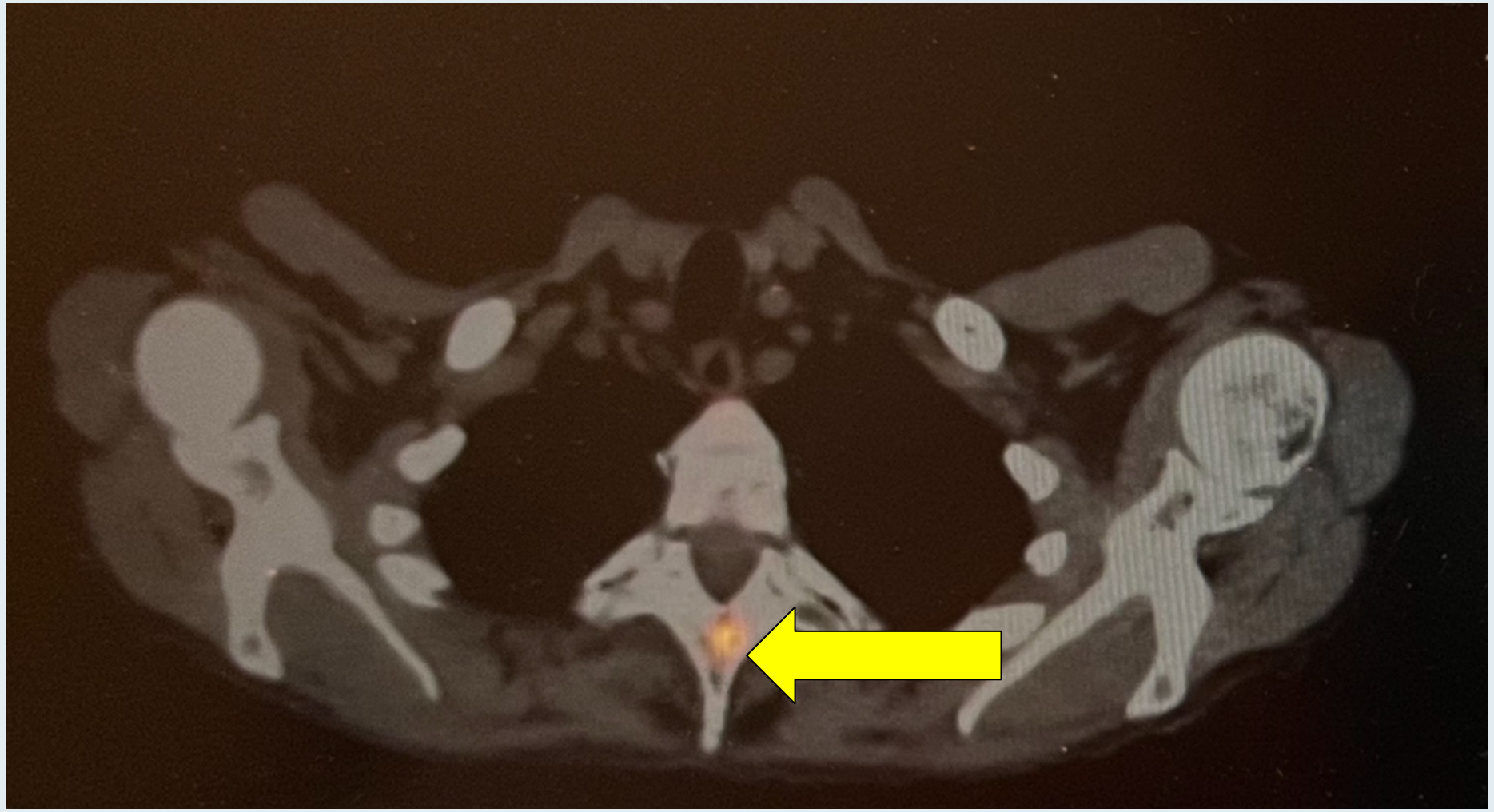
Right Upper Lobe Mass with Bone Mets





RTP
RESEARCH
TO PRACTICE

Thoracic Vertebral Body Mets



Case Presentation: A 70-year-old woman with recurrent lung adenocarcinoma with a MET T263M mutation who is clinically stable on tepotinib

Dr Priya Rudolph (Athens, Georgia)

RTP
RESEARCH
TO PRACTICE

Case Presentation: A 79-year-old woman with metastatic lung adenocarcinoma with a MET exon 14 mutation who has toxicity with capmatinib

Dr Gigi Chen (Pleasant Hill, California)

RTP
RESEARCH
TO PRACTICE

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?

 Dr Baik	Capmatinib*	 Dr Gainor	Capmatinib
 Dr Camidge	Capmatinib	 Dr Johnson	Tepotinib
 Dr Drilon	Capmatinib	 Dr Spira	Capmatinib

* If the patient is a nonsmoker

RTP RESEARCH TO PRACTICE

PRECISION MEDICINE

original reports

Landscape and Clonal Dominance of Co-occurring Genomic Alterations in Non–Small-Cell Lung Cancer Harboring *MET* Exon 14 Skipping

Xiuning Le, MD, PhD[1]; Lingzhi Hong, MD, PhD[1,2]; Chuck Hensel, PhD[3]; Rongrong Chen, PhD[4]; Haley Kemp, MPAS[1]; Niamh Coleman, MBBCh, PhD[5]; Christine A. Ciunci, MD[6]; Stephen V. Liu, MD[7]; Marcelo V. Negrao, MD[1]; Jennifer Yen, PhD[3]; Xuefeng Xia, MD, PhD[4]; Juergen Scheuenpflug, PhD[8]; Christopher Stroh, PhD[8]; Dilafruz Juraeva, PhD[8]; Anne Tsao, MD[1]; David Hong, MD, PhD[5]; Victoria Raymond, MS[3]; Paul Paik, MD[9]; Jianjun Zhang, MD, PhD[1]; and John V. Heymach, MD, PhD[1]

JCO Precis Oncol 2021;5:PO.21.00135.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Case Presentation: A 78-year-old woman with inflammatory arthritis and ALK fusion-driven lung adenocarcinoma with slow progression on alectinib – PD-L1 15%

Dr Rajni Sinha (Atlanta, Georgia)

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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?

 Dr Baik	Lorlatinib	 Dr Gainor	Lorlatinib
 Dr Camidge	Lorlatinib or Brigatinib (if no 2nd driver mutation)	 Dr Johnson	Lorlatinib
 Dr Drilon	Lorlatinib	 Dr Spira	Brigatinib

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

Treatment Patterns and Outcomes in ALK or ROS1 Altered NSCLC: An ATOMIC Registry Study

Marmarelis ME et al.

ASCO 2022;Abstract 9077.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

Case Presentation: A 67-year-old woman with metastatic lung adenocarcinoma and a KRAS G12C mutation – PD-L1 5% – who received sotorasib

Dr Adam Miller (Danvers, Massachusetts)

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 a KRAS G12C mutation, and which targeted therapy would you generally offer?

 Dr Baik	Second line Sotorasib	 Dr Gainor	Second line Sotorasib
 Dr Camidge	Second line Sotorasib	 Dr Johnson	Second line Sotorasib
 Dr Drilon	Second line Sotorasib	 Dr Spira	Second line Sotorasib

RTP RESEARCH TO PRACTICE

AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

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

Presenter: Grace K. Dy[1], MD

[1]Roswell Park Comprehensive Cancer Center

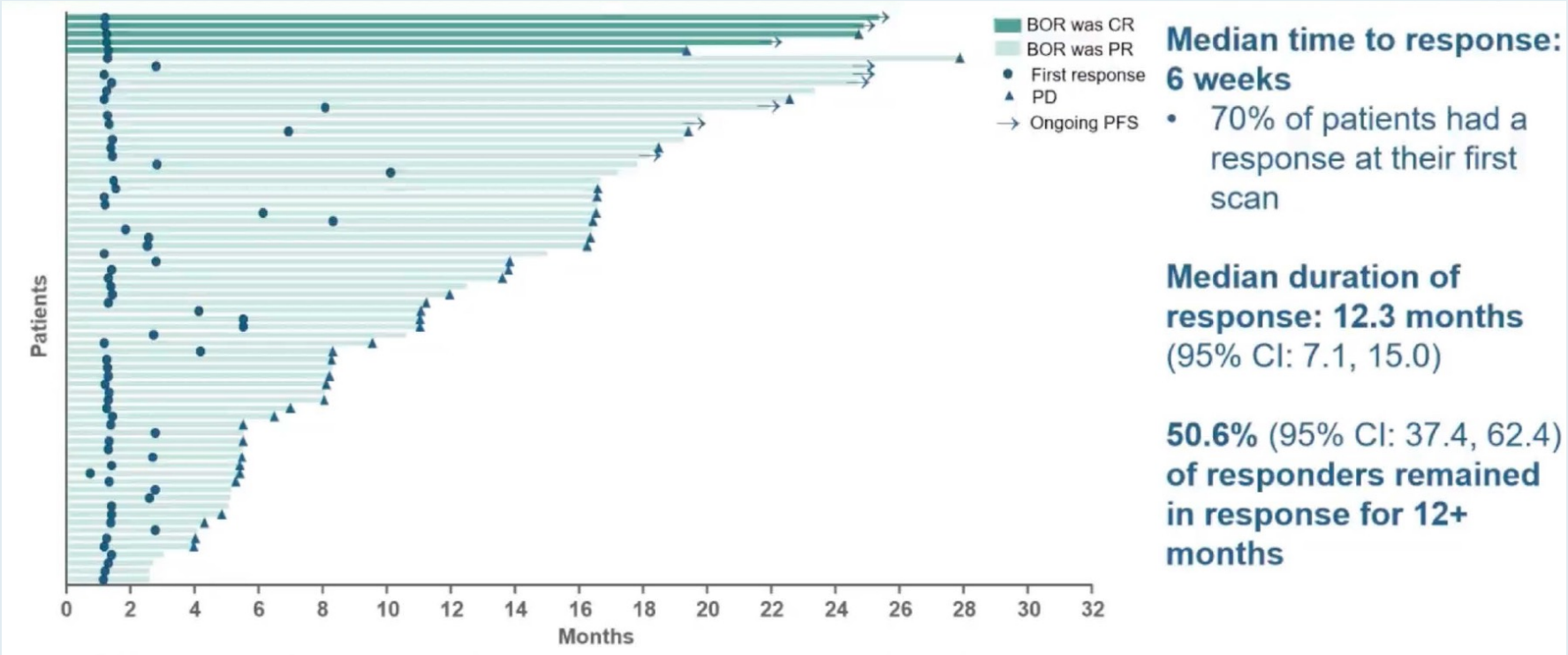
On behalf of: Ramaswamy Govindan[2], Vamsidhar Velcheti[3], Gerald S. Falchook[4], Antoine Italiano[5], Juergen Wolf[6], Adrian G. Sacher[7], Toshiaki Takahashi[8], Suresh S. Ramalingam[9], Christophe Dooms[10], Dong-Wan Kim[11], Alfredo Addeo[12], Jayesh Desai[13], Martin Schuler[14], Pascale Tomasini[15], Qui Tran[16], Simon Jones[16], Agnes Ang[16], Abraham Anderson[16], Antreas Hindoyan[16], David S. Hong[17], Bob T. Li[18]

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

Abstract CT008

RTP RESEARCH TO PRACTICE

CodeBreaK 100: 2-Year Update with Sotorasib for Previously Treated Metastatic NSCLC with KRAS p.G12C Mutation



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)

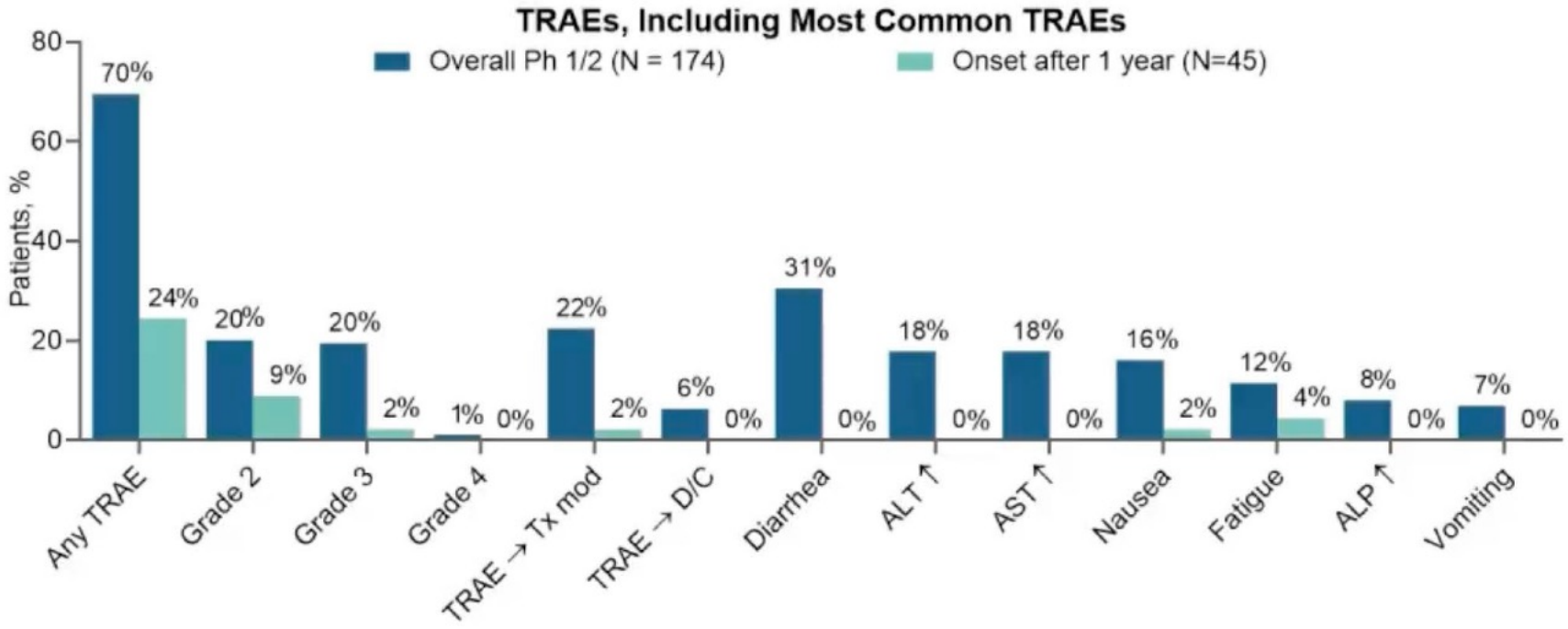
50.6% (95% CI: 37.4, 62.4) **of responders remained in response for 12+ months**

Efficacy Update (N = 172)
ORR: 40.7%
DCR: 83.7%
Median PFS: 6.3 mo
Median OS: 12.5 mo
1-year OS rate: 50.8%

Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

CodeBreaK 100: Treatment-Related Adverse Events



Grade 3 or 4 TRAEs occurred in 21% of patients

- One patient with new onset Grade 3 TRAE after 1 year (hemolytic anemia)

No fatal TRAEs occurred

- No TRAE leading to discontinuation after 1 year

Well-tolerated in the long-term: late-onset TRAEs were mild and manageable

Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

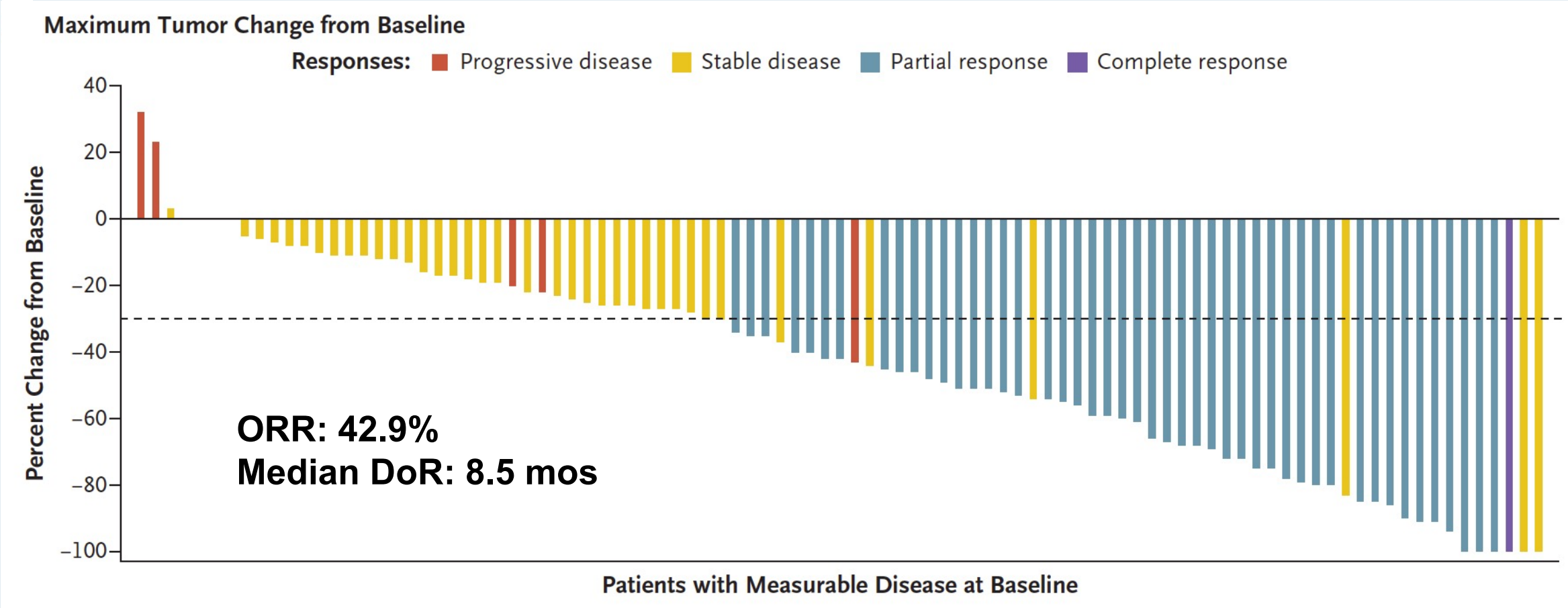
Adagrasib in Non–Small-Cell Lung Cancer Harboring a *KRAS*^{G12C} Mutation

Pasi A. Jänne, M.D., Ph.D., Gregory J. Riely, M.D., Ph.D., Shirish M. Gadgeel, M.D., Rebecca S. Heist, M.D., M.P.H., Sai-Hong I. Ou, M.D., Ph.D., Jose M. Pacheco, M.D., Melissa L. Johnson, M.D., Joshua K. Sabari, M.D., Konstantinos Leventakos, M.D., Ph.D., Edwin Yau, M.D., Ph.D., Lyudmila Bazhenova, M.D., Marcelo V. Negrao, M.D., Nathan A. Pennell, M.D., Ph.D., Jun Zhang, M.D., Ph.D., Kenna Anderes, Ph.D., Hirak Der-Torossian, M.D., Thian Kheoh, Ph.D., Karen Velastegui, B.Sc., Xiaohong Yan, Ph.D., James G. Christensen, Ph.D., Richard C. Chao, M.D., and Alexander I. Spira, M.D., Ph.D.

N Engl J Med 2022;387(2):120-31.

RTP RESEARCH TO PRACTICE

KRYSTAL-1: Response in a Phase II Study of Adagrasib for Advanced or Metastatic NSCLC Harboring a KRAS G12C Mutation



Jänne PA et al. *N Engl J Med* 2022;387(2):120-31.

RTP RESEARCH TO PRACTICE

KRYSTAL-1: Select Treatment-Related Adverse Events with Adagrasib for Advanced or Metastatic NSCLC Harboring a KRAS G12C Mutation

Adverse event (N = 116)	Any grade	Grade ≥3
Diarrhea	70.7%	0.9%
Nausea	69.8%	4.3%
Fatigue	59.5%	6.9%
Vomiting	56.9%	0.9%
Blood creatinine increased	34.5%	0.9%
ALT increased	28.4%	5.2%
AST increased	26.7%	5.2%

Jänne PA et al. *N Engl J Med* 2022;387(2):120-31.

RTP RESEARCH TO PRACTICE

Case Presentation: A 61-year-old woman with metastatic lung adenocarcinoma and an activating NRG1 fusion who is unable to tolerate afatinib

Dr Jason Niu (Gilbert, Arizona)

RTP RESEARCH TO PRACTICE

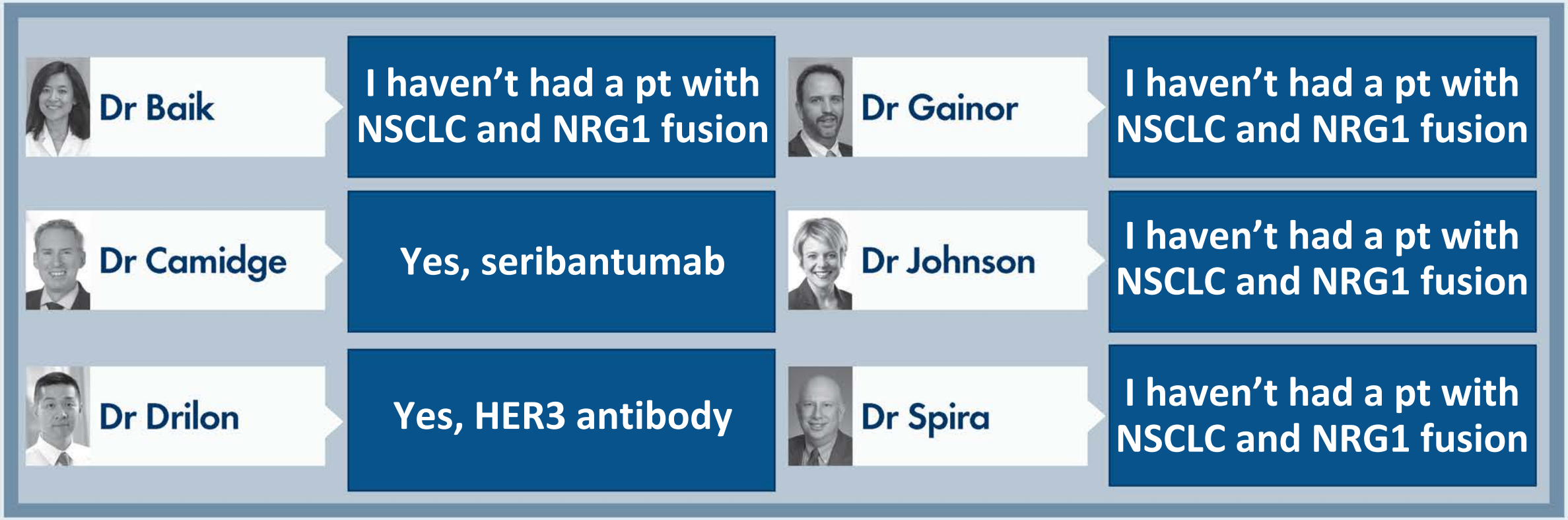
Regulatory and reimbursement issues aside, what would be your preferred first-line therapy for a 65-year-old asymptomatic patient with metastatic NSCLC (PD-L1 TPS 50%) and an NRG1 fusion?

 Dr Baik	Carboplatin/ pemetrexed/ pembrolizumab*	 Dr Gainor	Carboplatin/ pemetrexed/ pembrolizumab
 Dr Camidge	Carboplatin/ pemetrexed/ pembrolizumab	 Dr Johnson	Pembrolizumab
 Dr Drilon	Carboplatin/ pemetrexed/ pembrolizumab	 Dr Spira	Carboplatin/ pemetrexed/ pembrolizumab

* If patient does not have smoking history; pembrolizumab alone if patient has a smoking history

RTP RESEARCH TO PRACTICE

Have any of your patients with advanced NSCLC and an NRG1 fusion responded to targeted therapy?



RTP RESEARCH TO PRACTICE

Lung Cancer 158 (2021) 25–28

Contents lists available at ScienceDirect

Lung Cancer

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

NRG1 fusions: Biology to therapy

Stephen V. Liu *

2022 ASCO ANNUAL MEETING

Abstract 3006

CRESTONE: Initial Efficacy and Safety of Seribantumab in Solid Tumors Harboring NRG1 Fusions

Daniel R. Carrizosa,[1] Mark E. Burkard,[2] Yasir Y. Elamin,[3] Jayesh Desai,[4] Shirish M. Gadgeel,[5] Jessica J. Lin,[6] Saiama N. Waqar,[7] David R. Spigel,[8] Young Kwang Chae,[9] Parneet K. Cheema,[10] Eric B. Haura,[11] Stephen V. Liu,[12] Danny Nguyen,[13] Karen L. Reckamp,[14] Frank Yung-Chin Tsai,[15] Valerie M. Jansen,[16] Alexander Drilon,[17] Sai-Hong Ignatius Ou,[18] D Ross Camidge,[19] Tejas Patil[19]

[1]Levine Cancer Institute/Atrium Health, Charlotte, NC; [2]University of Wisconsin Carbone Cancer Center, Madison, WI; [3]The University of Texas MD Anderson Cancer Center, Houston, TX; [4]Peter MacCallum Cancer Centre, Melbourne, Australia; [5]Henry Ford Cancer Institute/Henry Ford Health System, Detroit, MI; [6]Massachusetts General Hospital, Boston, MA; [7]Washington University School of Medicine, St. Louis, MO; [8]Sarah Cannon Research Institute, Nashville, TN; [9]Northwestern University, Chicago, IL; [10]William Osler Health System, Calgary, Canada; [11]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; [12]Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC; [13]City of Hope, Huntington Beach and Irvine, CA; [14]Cedars-Sinai Medical Center, Los Angeles, CA; [15]HonorHealth, Scottsdale, AZ; [16]Elevation Oncology, Inc. New York, NY; [17]Memorial Sloan Kettering Cancer Center, New York, NY; [18]Chao Family Comprehensive Cancer Center, University of CA-Irvine, Orange, CA; [19]University of Colorado Cancer Center, Aurora, CO

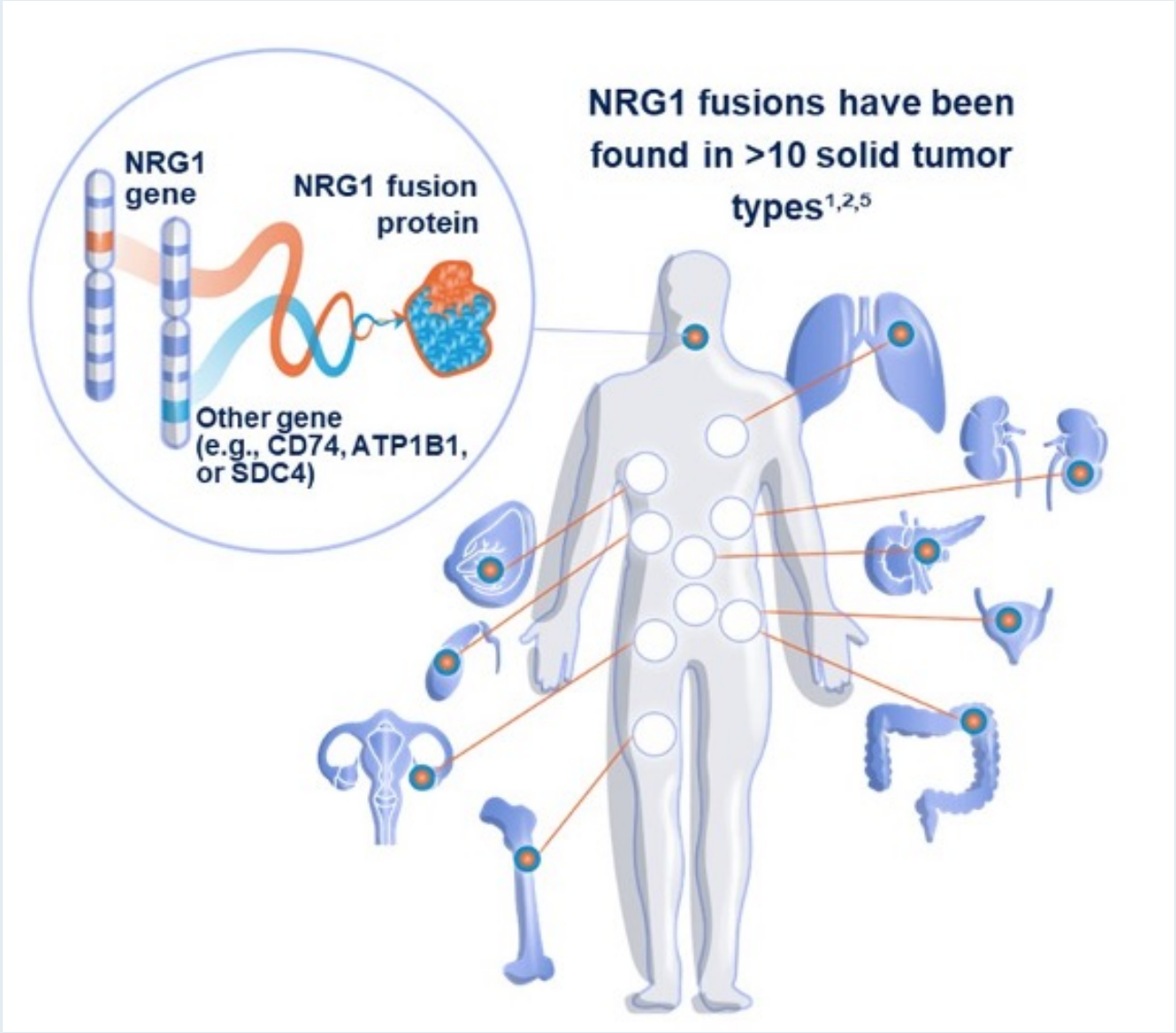
PRESENTED BY:
Daniel R. Carrizosa, MD

Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

NRG1 Gene Fusions in Solid Tumors



Carrizosa DR et al. ASCO 2022;Abstract 3006.

CRESTONE: Safety Summary of Seribantumab Monotherapy

Adverse events reported in ≥15% of patients

	Treatment-emergent AEs (N=35); n (%)				Treatment-related AEs (N = 35); n (%)			
Preferred Term	**Any Grade**	**Grade 1**	**Grade 2**	**Grade ≥ 3†**	**Any Grade**	**Grade 1**	**Grade 2**	**Grade ≥ 3‡**
Patients with ≥1 AE	35 (100)	8 (23)	10 (29)	17 (49)	30 (86)	17 (49)	11 (31)	2 (6)
Diarrhea	17 (49)	11 (31)	4 (11)	2 (6)	14 (40)	10 (29)	3 (9)	1 (3)
Fatigue	14 (40)	7 (20)	7 (20)	0	10 (29)	5 (14)	5 (14)	0
Rash§	11 (31)	9 (26)	2 (6)	0	9 (26)	7 (20)	2 (6)	0
Hypokalemia	10 (29)	6 (17)	3 (9)	1 (3)	3 (9)	3 (9)	0	0
Nausea	10 (29)	7 (20)	1 (3)	2 (6)	6 (17)	5 (14)	1 (3)	0
Abdominal pain‖	8 (23)	4 (11)	2 (6)	2 (6)	3 (9)	1 (3)	2 (6)	0
Decreased appetite	8 (23)	4 (11)	3 (9)	0	3 (9)	1 (3)	2 (6)	0
Headache	8 (23)	7 (20)	1 (3)	0	1 (3)	1 (3)	0	0
Hypomagnesemia	8 (23)	6 (17)	1 (3)	0	2 (6)	2 (6)	0	0
Cough	7 (20)	5 (14)	2 (6)	0	1 (3)	1 (3)	0	0
Anemia^	6 (17)	4 (11)	1 (3)	1 (3)	1 (3)	1 (3)	0	0
Dysuria	6 (17)	6 (17)	0	0	0	0	0	0

- Safety profile of 35 patients with tumors harboring NRG1 fusions who received at least 1 dose of seribantumab in the CRESTONE study
  - One DLT (Grade 2 fatigue resulting in dose reduction by the Investigator in the safety run-in)
  - 27 (77%) patients received the optimized RP2D of seribantumab 3g QW
- Majority (80%) of TRAEs were Grade 1 or 2
- Two (6%) patients received dose reductions for AEs per the Investigator
  - One patient for Grade 1 ALT increase
  - One patient for Grade 2 fatigue
- No patients discontinued seribantumab for AEs

†2 Grade 5 TEAEs (unrelated to seribantumab) of lung infection (n=1 patient) and malignant neoplasm progression (n=1 patient); ‡No Grade 4 or 5 TRAEs reported; 2 Grade 3 TRAEs of diarrhea (n=1 patient) and vomiting (n=1 patient); §Includes preferred term (PT) of rash and maculo-papular rash; ‖Includes PT of abdominal pain, abdominal pain upper, abdominal distention; ^Includes PT of anemia and iron deficiency anemia.

AE, adverse event; ALT, alanine transaminase; DLT, dose-limiting toxicity; TRAE, treatment-related adverse event

Visit cut-off: 18 April 2022

Carrizosa DR et al. ASCO 2022;Abstract 3006.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

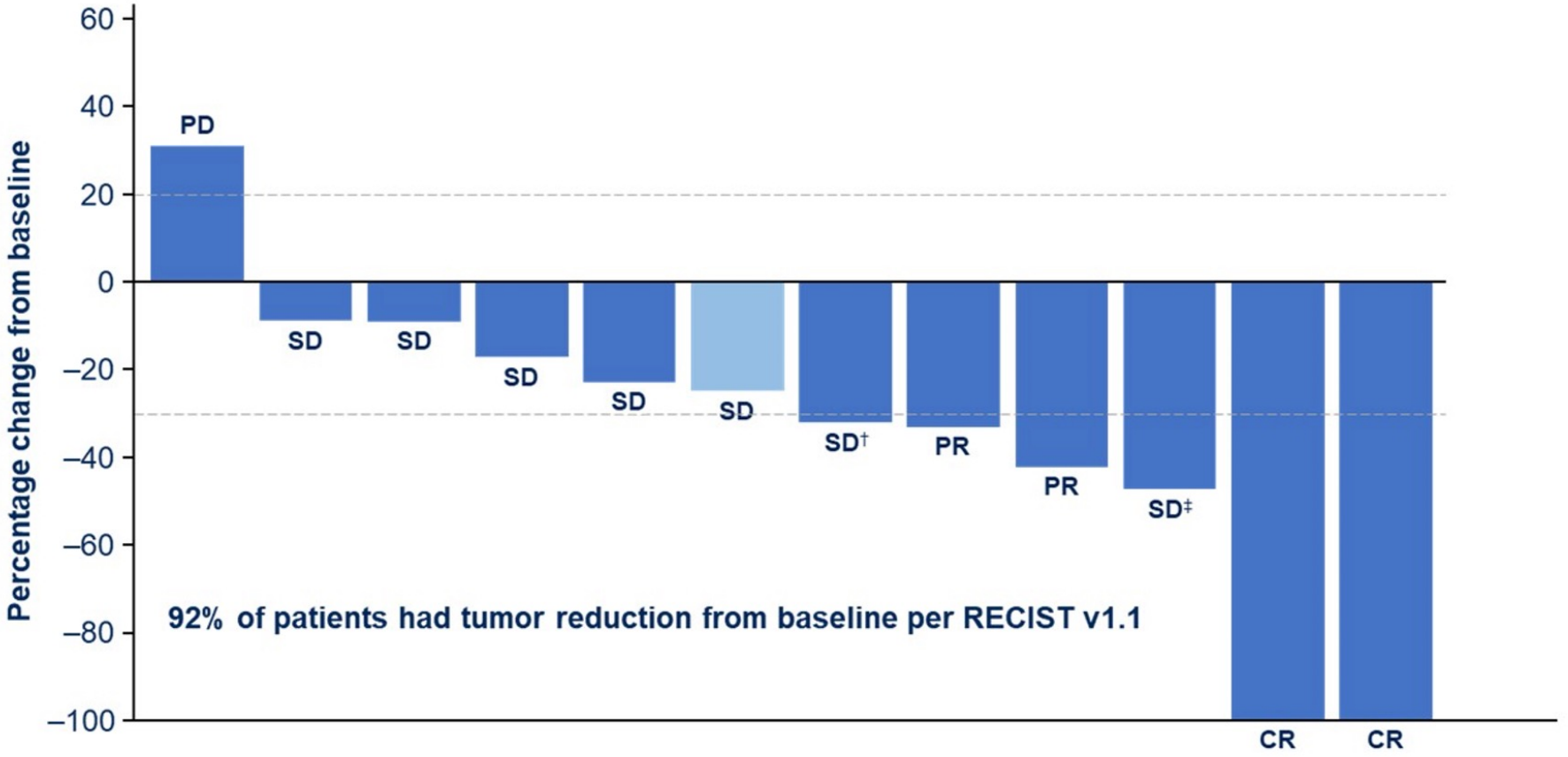
CRESTONE: Clinical Activity of Seribantumab in Tumors Harboring NRG1 Fusions

Investigator-assessed (INV) Response, %	Cohort 1 Primary Efficacy Population† (n=12‡)	Cohort 1 - NSCLC Primary Efficacy Population† (n=11‡)
Objective response rate; n (%)	**4 (33)**	**4 (36)**
Complete response; n (%)	**2 (17)**	**2 (18)**
Partial response; n (%)	**2 (17)**	**2 (18)**
Stable disease; n (%)	7 (58)	6 (55)
Progressive disease; n (%)	1 (8)	1 (9)
Disease control rate; n (%)	11 (92)	10 (91)

Carrizosa DR et al. ASCO 2022;Abstract 3006.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

CRESTONE: Efficacy of Seribantumab for Tumors Harboring NRG1 Fusions

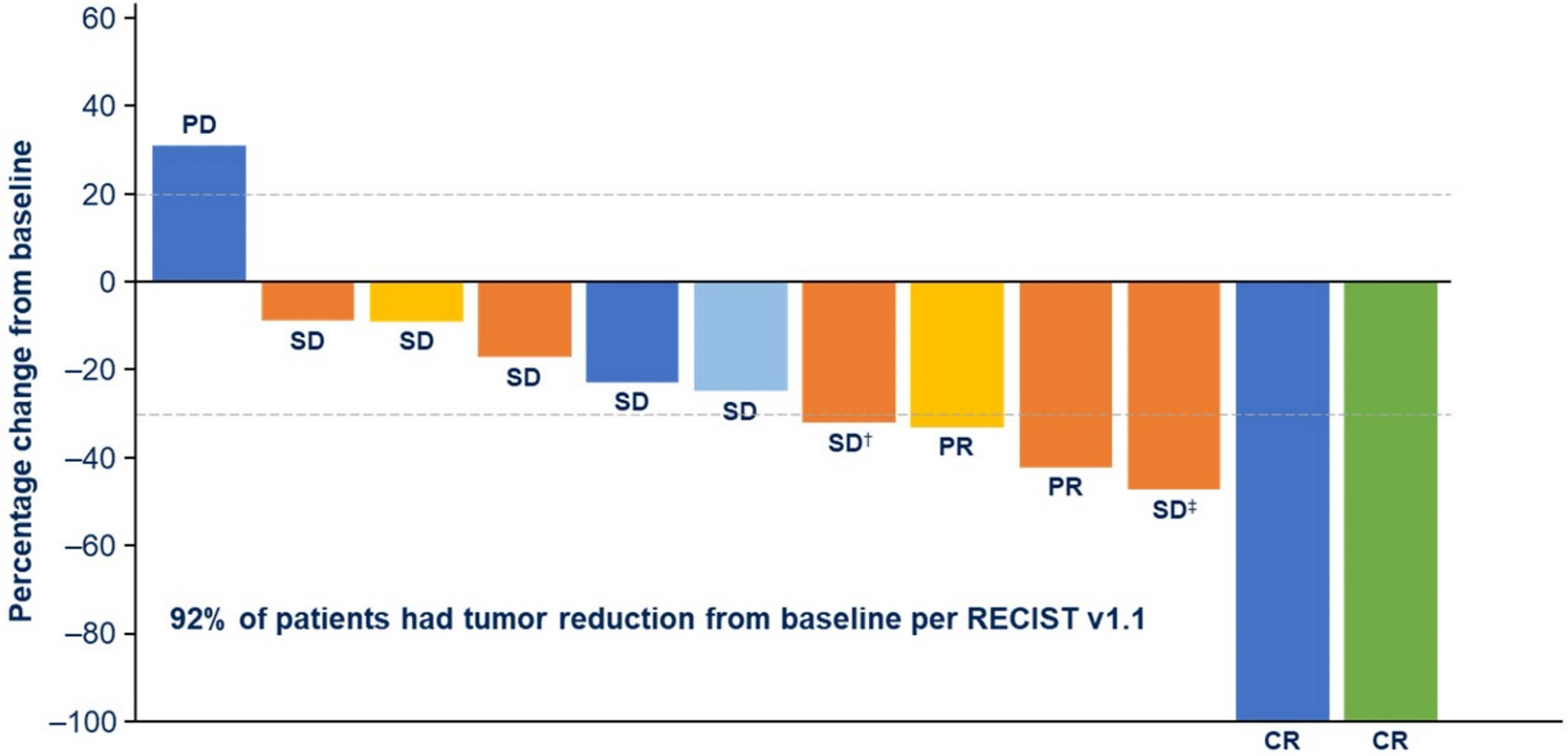


Confirmed INV-ORR	
Overall	33% (4/12)
NSCLC	36% (4/11)

Primary tumor type:
- Lung/NSCLC
- Pancreas

Carrizosa DR et al. ASCO 2022;Abstract 3006.

CRESTONE: Efficacy of Seribantumab for Tumors Harboring NRG1 Fusions Regardless of Fusion Partner



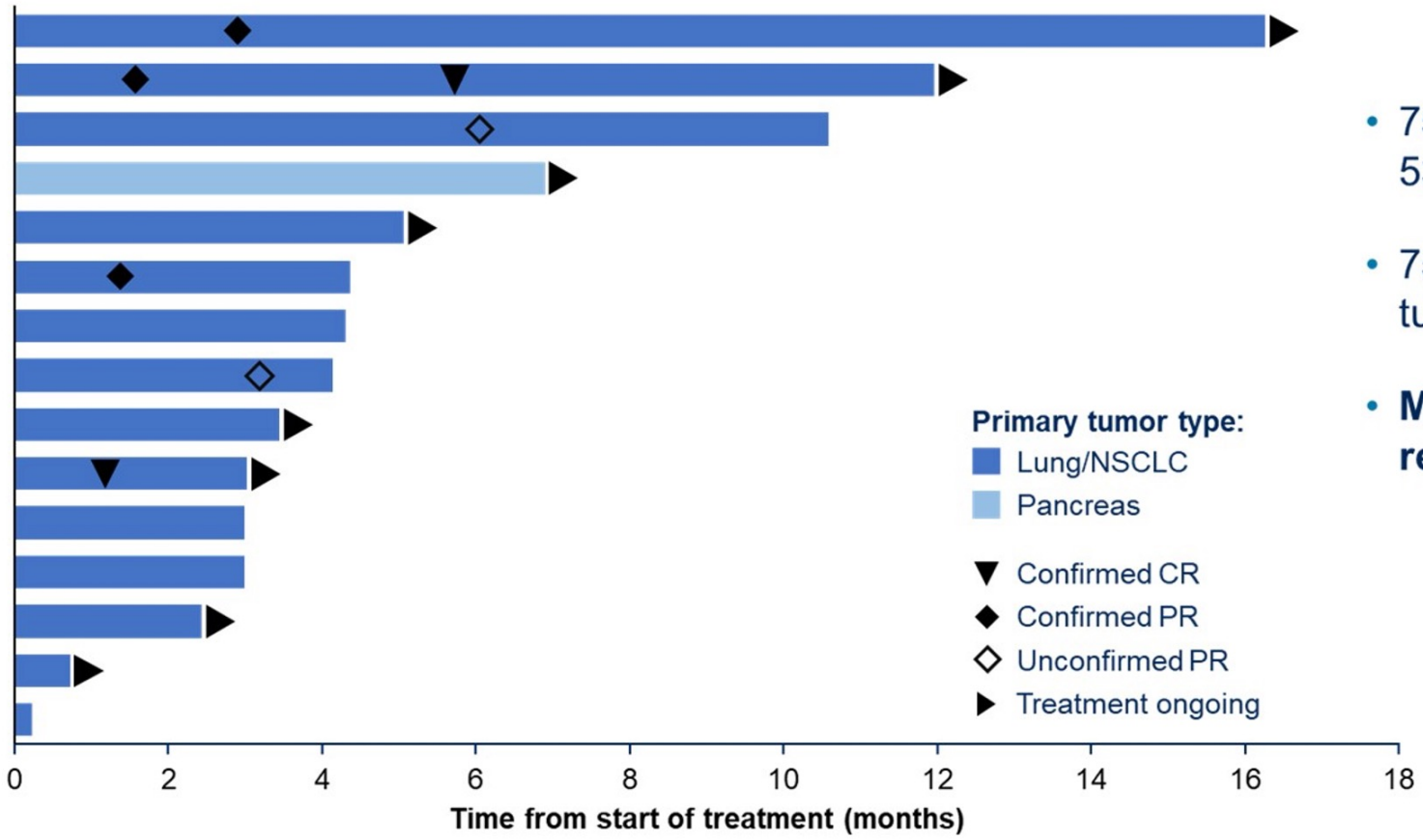
Confirmed INV-ORR	
Overall	33% (4/12)
NSCLC	36% (4/11)

NRG1 fusion partner:

- SLC3A2
- CD74
- SDC4
- ATP1B1
- ITGB1

Carrizosa DR et al. ASCO 2022;Abstract 3006.

CRESTONE: Duration of Seribantumab Therapy for Patients with NRG1 Fusions

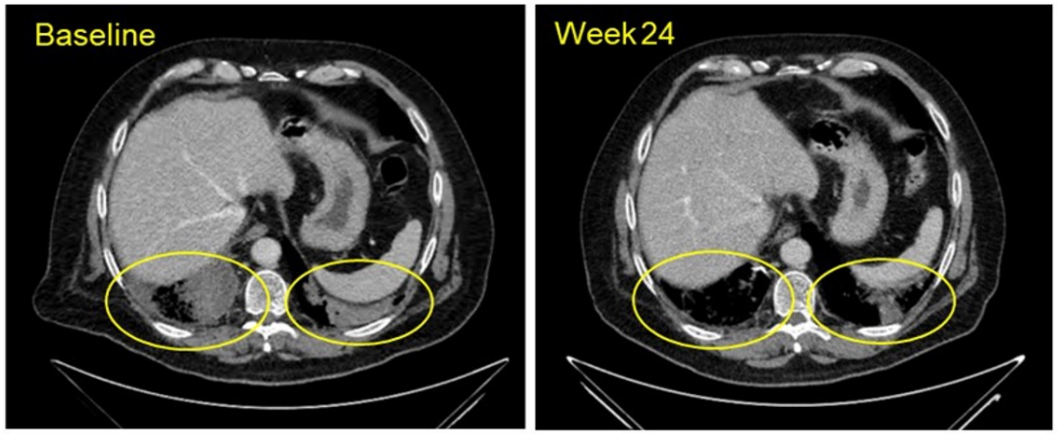


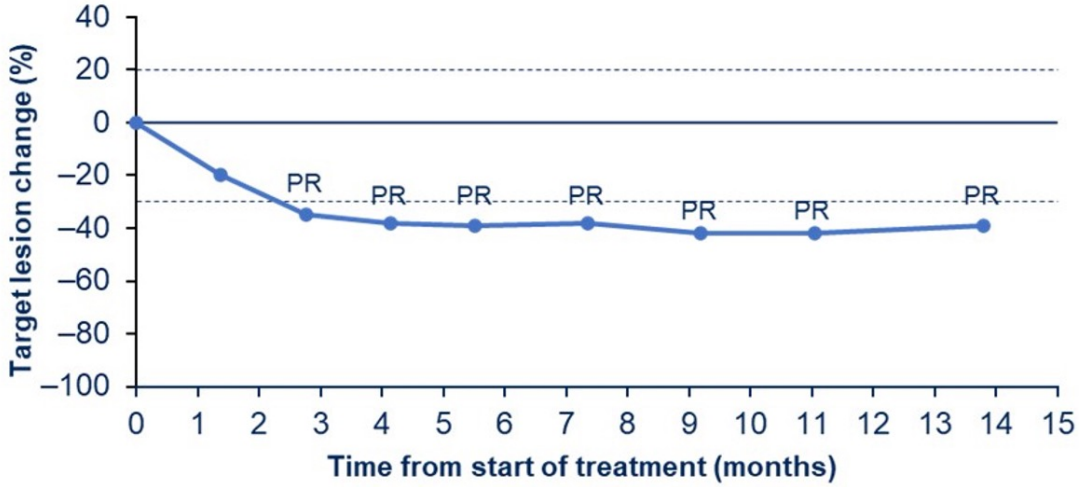
- 75% of **responding** patients and 53% of **all** patients remain on treatment
- 75% of **responses** occurred by first tumor assessment (Week 6 ± 2 weeks)
- **Median DOR has not yet been reached** (range: 1.4–11.5 months)

DoR = duration of response; CR = complete response; PR = partial response

Carrizosa DR et al. ASCO 2022;Abstract 3006.

CRESTONE: A Durable Response in a Patient with CD74-NRG1 NSCLC





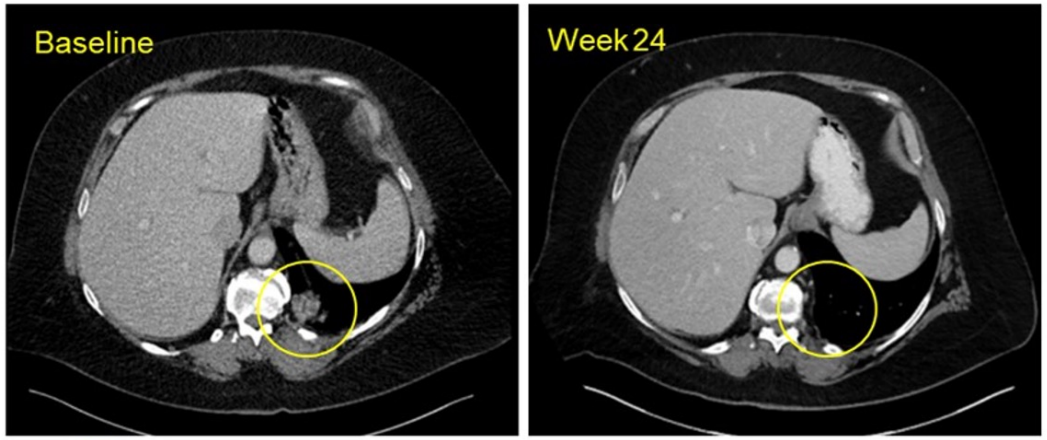
- 70-year-old male with NSCLC adenocarcinoma
- Three prior lines including platinum-based chemotherapy, immunotherapy (IO), and investigational therapy (IO and targeted agent)
- PR (35% tumor reduction) at Week 12; maximum tumor reduction of 42%
- Duration of response 11.5 months (ongoing)
- Seribantumab treatment ongoing for 16.0 months
  - Initiated seribantumab treatment under safety run-in
  - Transitioned to seribantumab 3g QW after induction/consolidation

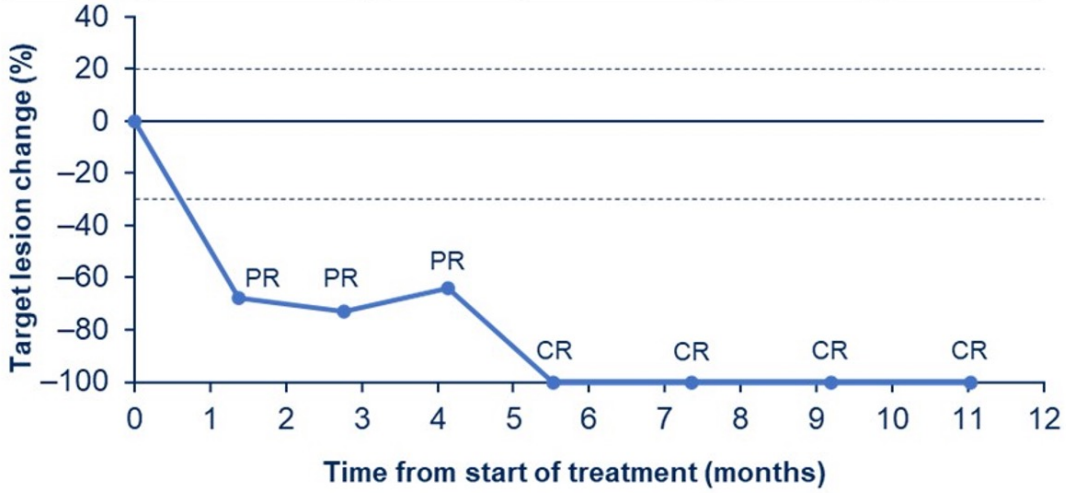
NSCLC = non-small cell lung cancer

Carrizosa DR et al. ASCO 2022;Abstract 3006.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

CRESTONE: A Deep and Durable Response in a Patient with ITGB1-NRG1 NSCLC





- 60-year-old female with NSCLC adenocarcinoma
- Three prior lines including platinum-based chemotherapy and immunotherapy
- PR (68% tumor reduction) at Week 6
- Deepening of response to CR at Week 24
- Duration of response 9.7 months
  - CR ongoing for 5.6 months
- Treatment ongoing for 11.7 months

Carrizosa DR et al. ASCO 2022;Abstract 3006.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

Efficacy of Afatinib in Patients with Advanced/Metastatic Solid Tumors Harboring NRG1 Gene Fusions: A Novel, Prospective Real-World Outcomes Study Based on Single-Patient Protocol Data

Liu SV et al.

ASCO 2022;Abstract TPS3180.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

Case Presentation: A 52-year-old man with lung adenocarcinoma with both BRAF V600E and IDH1 mutations and a mixed response to BRAFi/MEKi therapy – PD-L1 95%

Dr Jason Niu (Gilbert, Arizona)

RTP RESEARCH TO PRACTICE

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?

 Dr Baik	Dabrafenib/trametinib*	 Dr Gainor	Dabrafenib/trametinib
 Dr Camidge	Dabrafenib/trametinib	 Dr Johnson	Dabrafenib/trametinib
 Dr Drilon	Dabrafenib/trametinib	 Dr Spira	Dabrafenib/trametinib

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

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, would you generally offer targeted therapy as consolidation treatment to a patient with unresectable Stage IIIB NSCLC (PD-L1 TPS 50%) who has undergone definitive chemoradiation therapy and is found to have a BRAF V600E mutation?

 Dr Baik	No	 Dr Gainor	No
 Dr Camidge	No	 Dr Johnson	No
 Dr Drilon	Yes, dabrafenib/trametinib for 3 years	 Dr Spira	No

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Liu

Introduction: Journal Club with Dr Liu – Part 1

MODULE 1: Case Presentations

MODULE 2: Journal Club with Dr Liu – Part 2

MODULE 3: Appendix of Key Publications

RTP
RESEARCH
TO PRACTICE

Mol Cancer Ther 2021;20(12):2577-84.

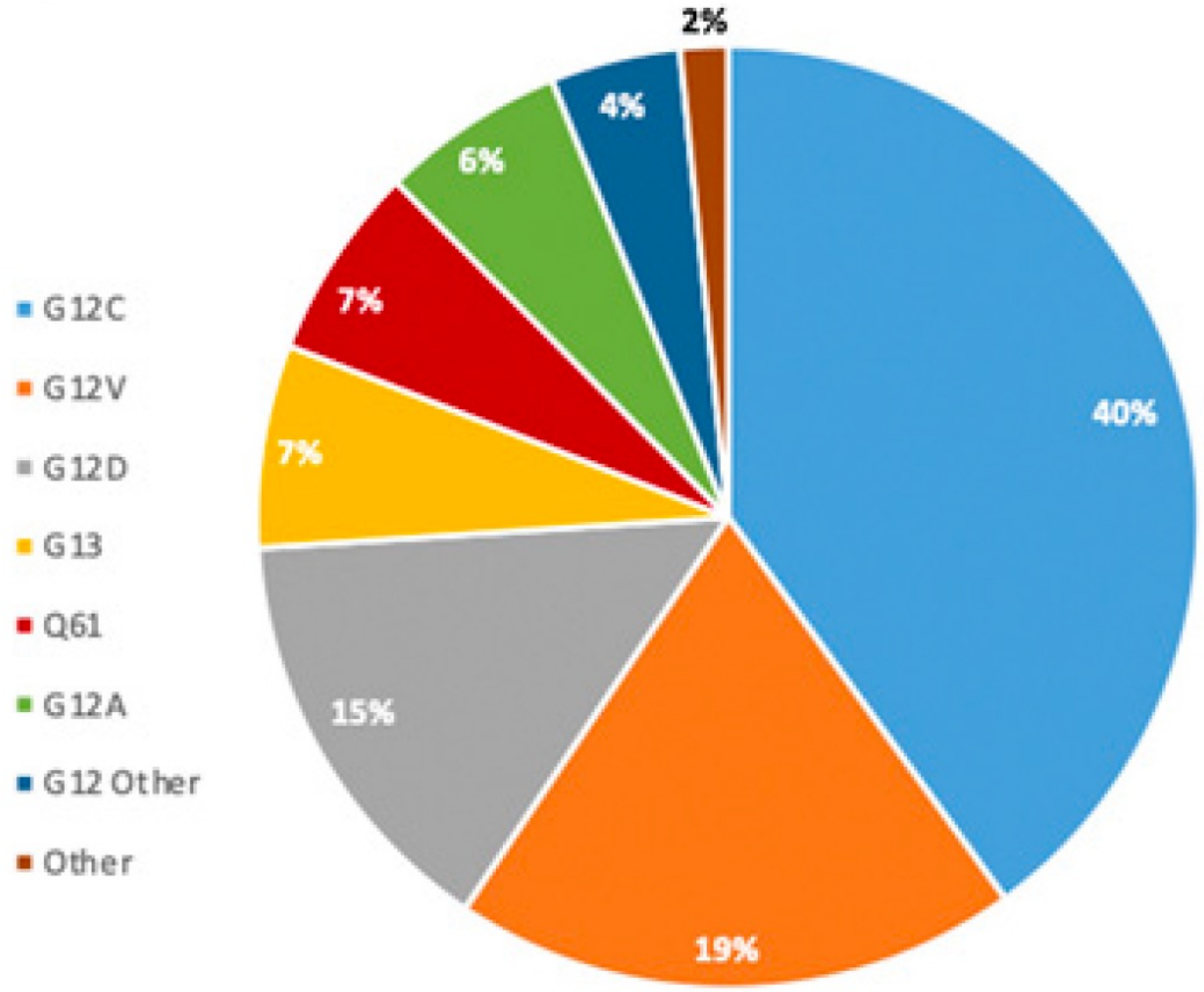
MOLECULAR CANCER THERAPEUTICS | COMPANION DIAGNOSTIC, PHARMACOGENOMIC, AND CANCER BIOMARKERS

Characterization of KRAS Mutation Subtypes in Non–small Cell Lung Cancer

Julia Judd[1], Nagla Abdel Karim[2], Hina Khan[3], Abdul Rafeh Naqash[4,5], Yasmine Baca[6], Joanne Xiu[6], Ari M. VanderWalde[7], Hirva Mamdani[8], Luis E. Raez[9], Misako Nagasaka[8], Sachin Gopalkrishna Pai[10], Mark A. Socinski[11], Jorge J. Nieva[12], Chul Kim[13], Antoinette J. Wozniak[14], Chukwuemeka Ikpeazu[15], Gilberto de Lima Lopes Jr[15], Alexander I. Spira[16], W. Michael Korn[6], Edward S. Kim[17], Stephen V. Liu[13], and Hossein Borghaei[1]

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

KRAS Mutational Distribution in All NSCLC

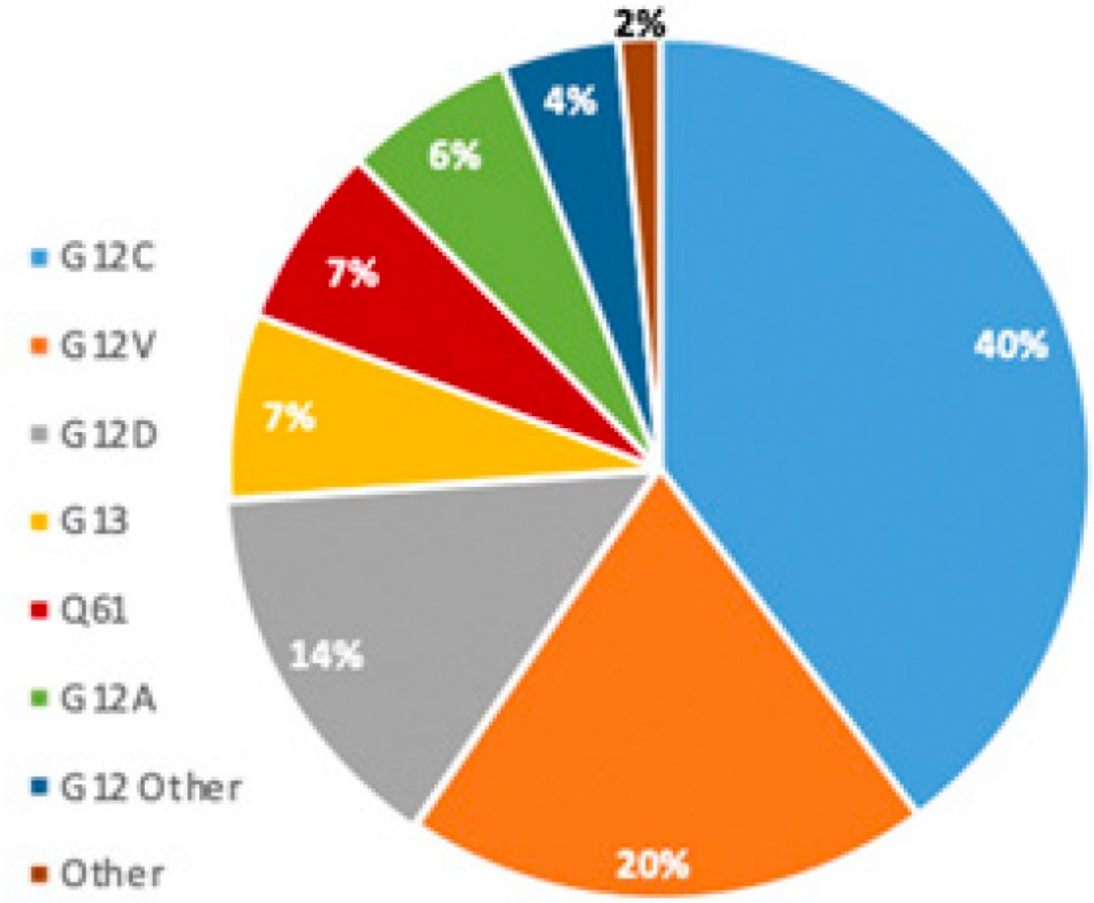


KRAS Categories	N
G12C	1,882
G12V	915
G12D	684
G13	327
Q61	313
G12A	298
G12 Other	210
Other	77
Total	4,706

Judd J et al. *Mol Cancer Ther* 2021;20(12):2577-84.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

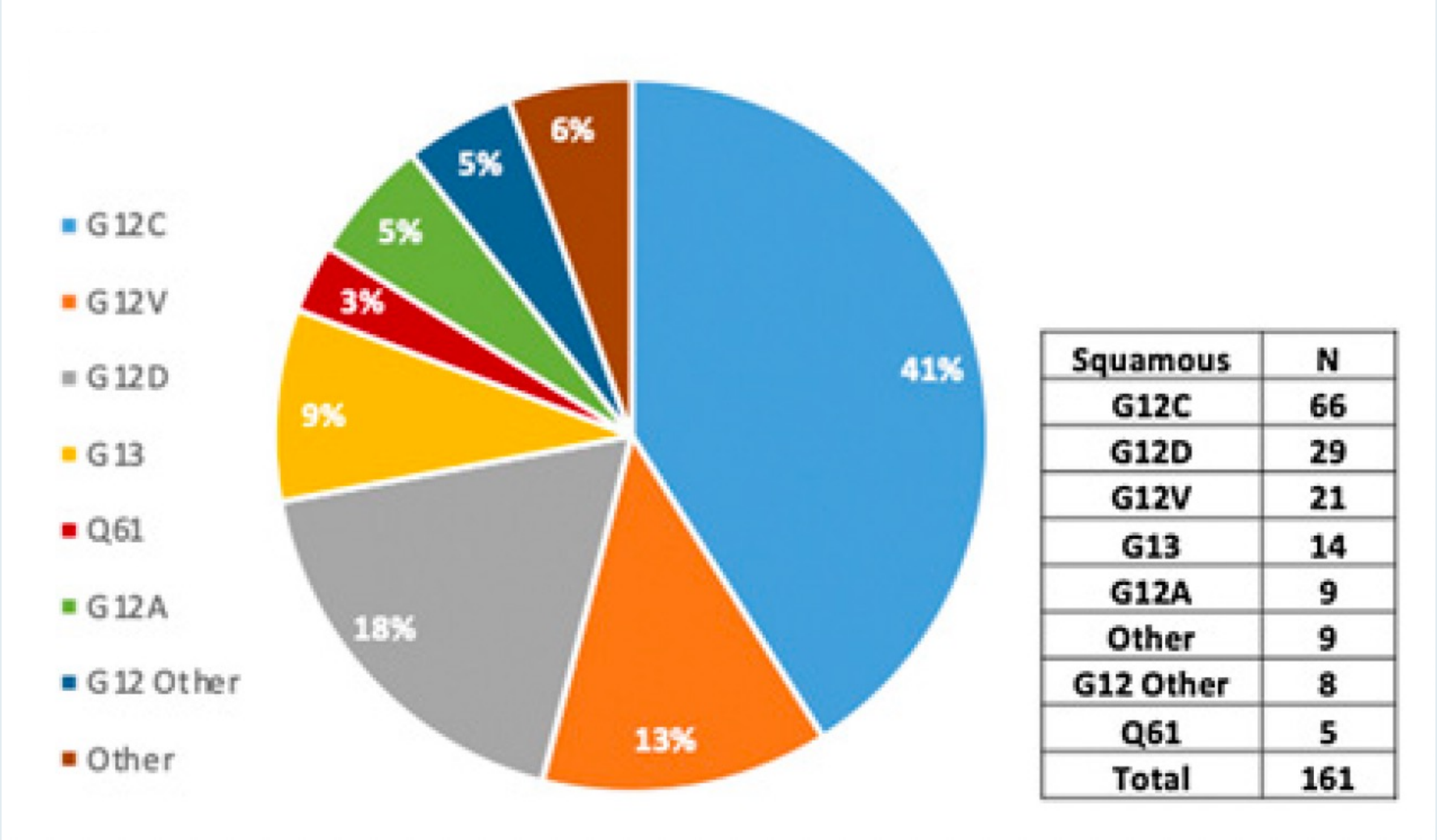
KRAS Mutational Distribution in Adenocarcinoma NSCLC



Adenocarcinoma	N
G12C	1,548
G12V	768
G12D	557
G13	269
Q61	267
G12A	249
G12 Other	171
Other	60
Total	3,889

Judd J et al. *Mol Cancer Ther* 2021;20(12):2577-84.

KRAS Mutational Distribution in Squamous Cell NSCLC



Squamous	N
G12C	66
G12D	29
G12V	21
G13	14
G12A	9
Other	9
G12 Other	8
Q61	5
Total	161

Judd J et al. *Mol Cancer Ther* 2021;20(12):2577-84.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

A First-in-Human Study of AO-176, a Highly Differentiated Anti-CD47 Antibody, in Patients with Advanced Solid Tumors

Burris HA et al.

ASCO 2021;Abstract 2516.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Liu

Introduction: Journal Club with Dr Liu – Part 1

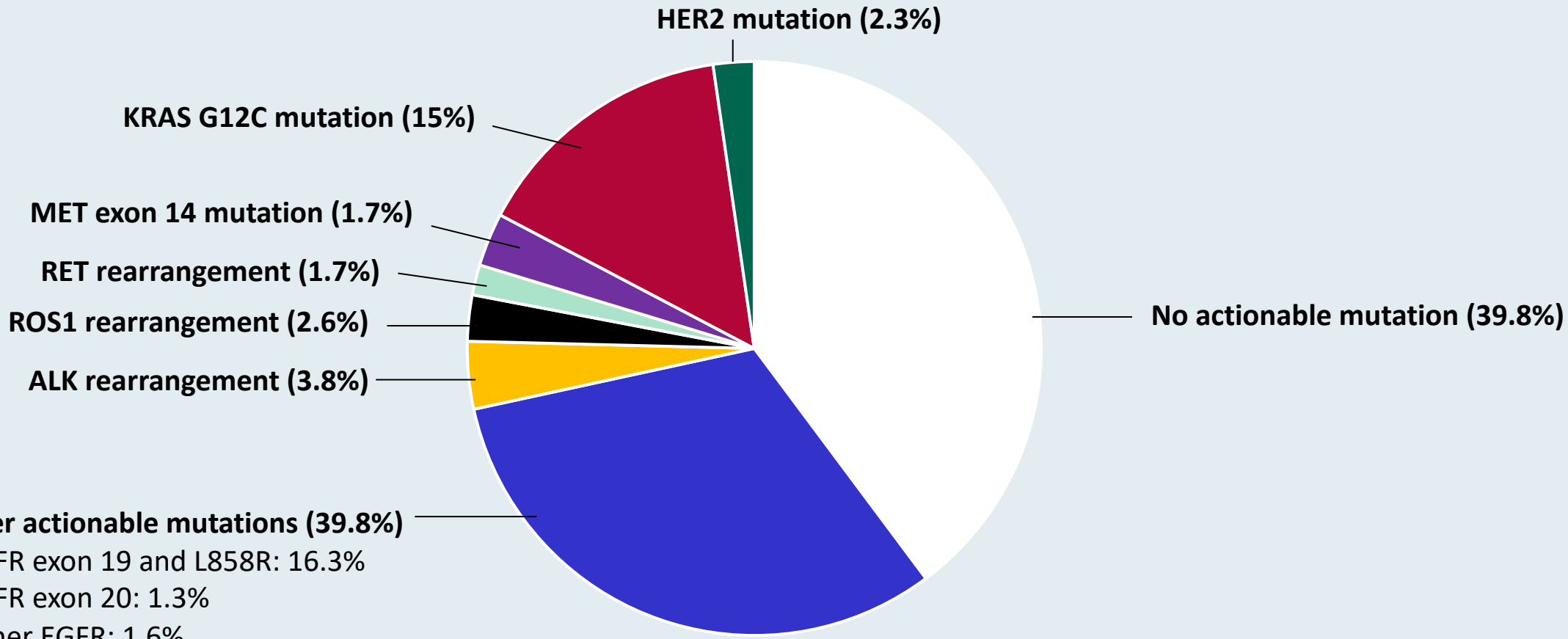
MODULE 1: Case Presentations

MODULE 2: Journal Club with Dr Liu – Part 2

MODULE 3: Appendix of Key Publications

RTP
RESEARCH
TO PRACTICE

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

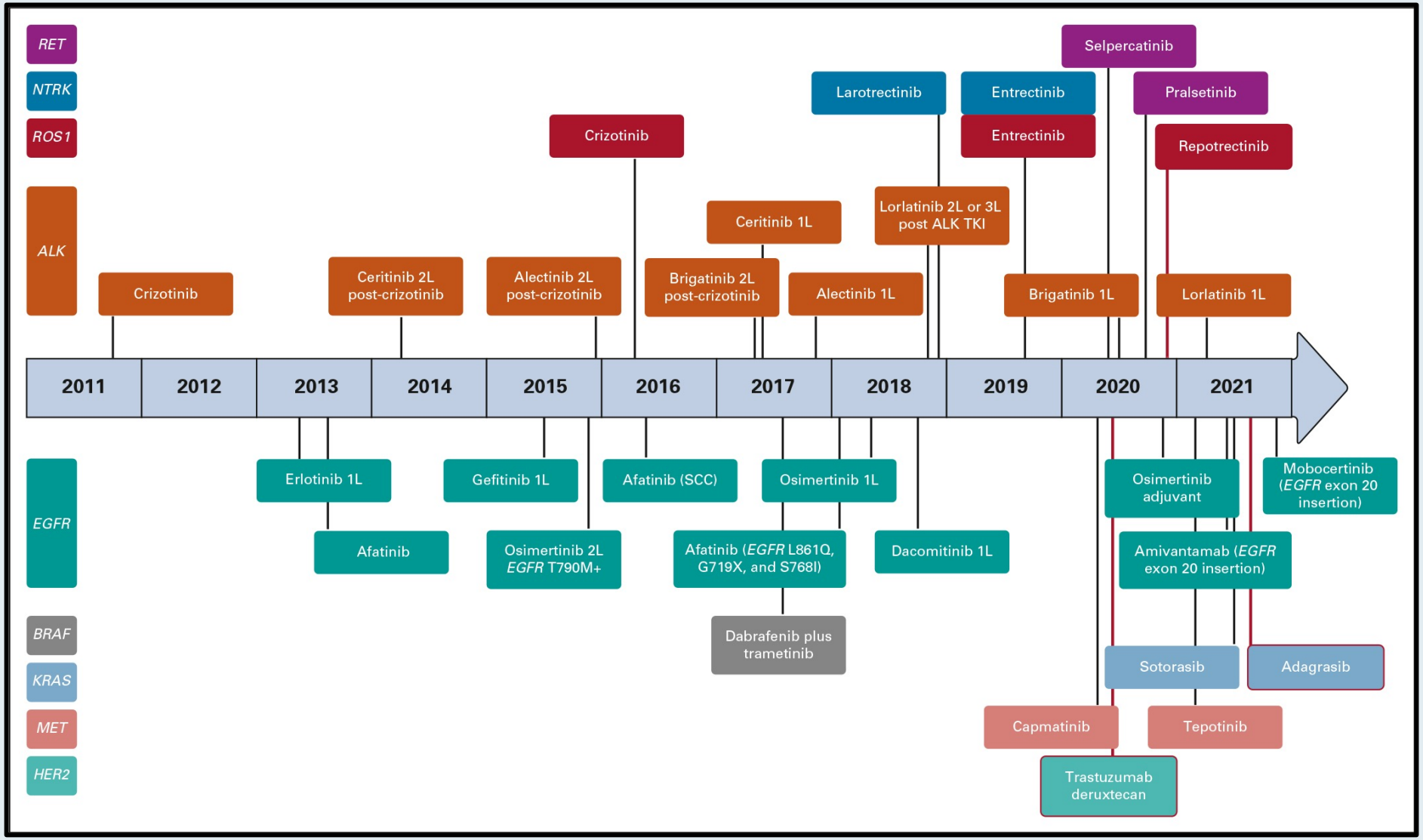


Other actionable mutations (39.8%)
--EGFR exon 19 and L858R: 16.3%
--EGFR exon 20: 1.3%
--Other EGFR: 1.6%
--Other KRAS: 10.3%
--BRAF V600E: 2.1%
--NTRK rearrangement: 0.23%

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

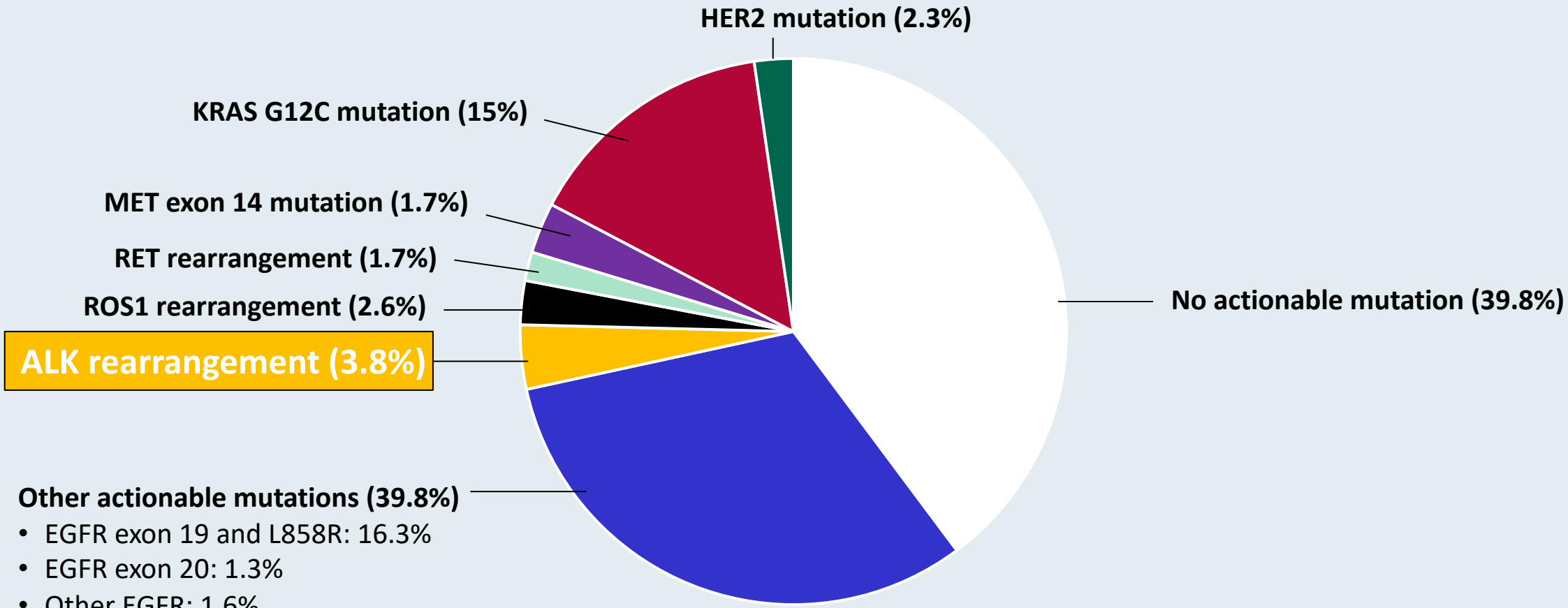


Tan AC et al. *J Clin Oncol* 2022;40(6):611-25.

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%
- 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

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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

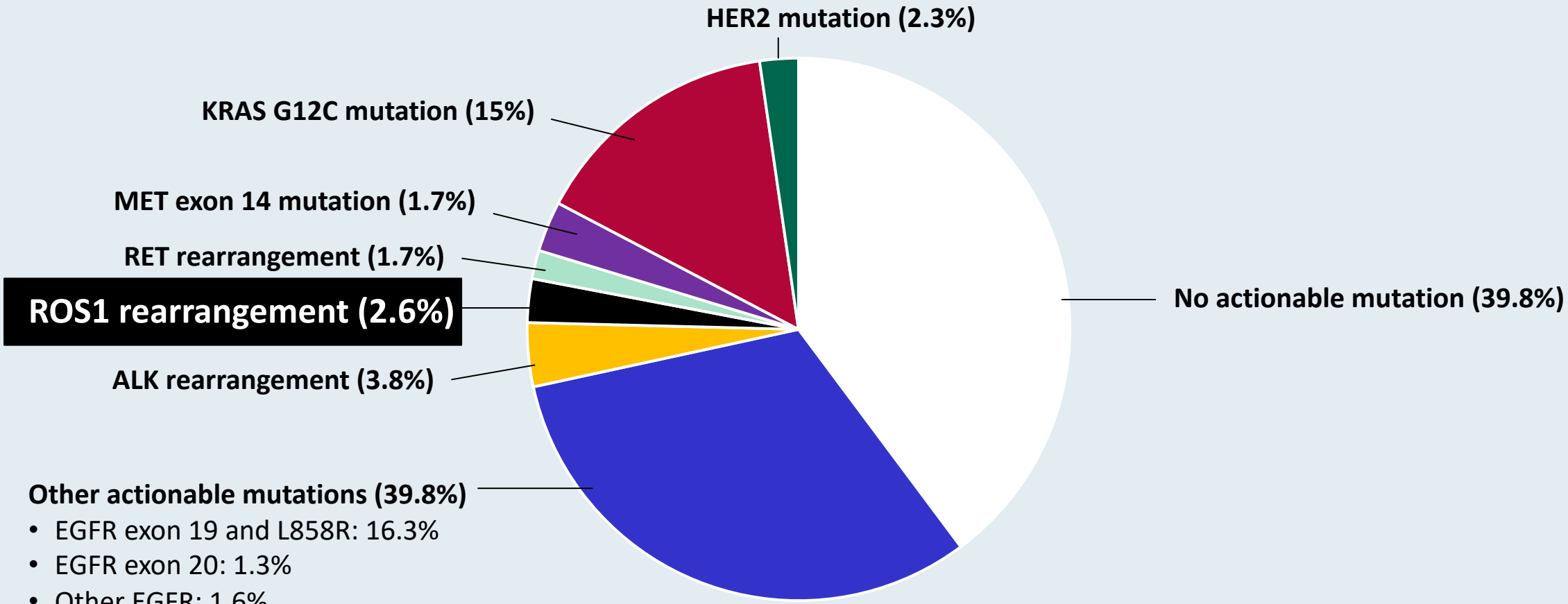
Common and Unique Adverse Effects of ALK TKIs

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.

RTP RESEARCH TO PRACTICE

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(6):611-25.

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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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

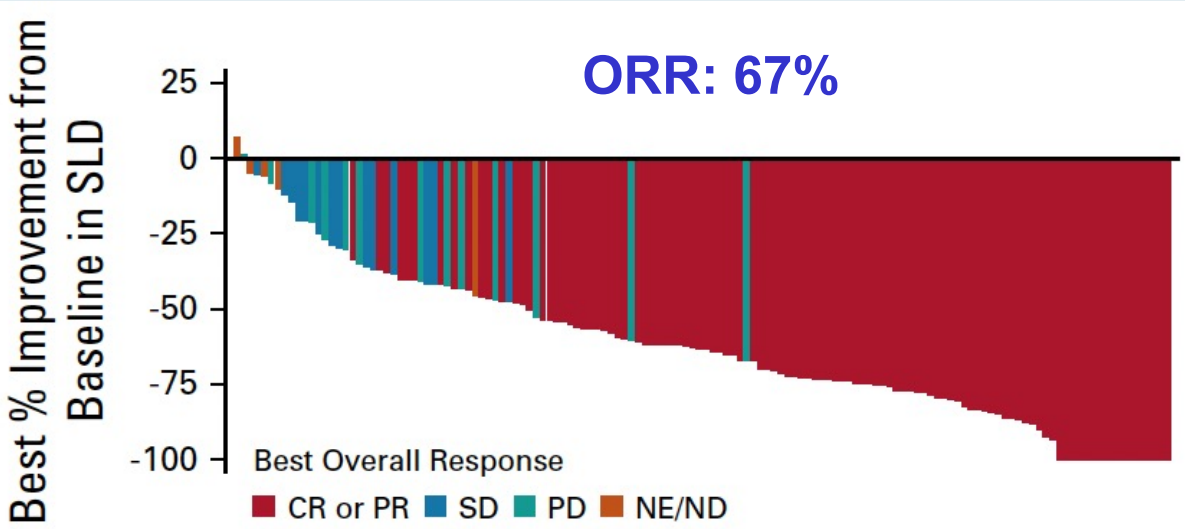
Rafal Dziadziuszko, MD, PhD[1]; Matthew G. Krebs, MD, PhD[2]; Filippo De Braud, MD[3,4]; Salvatore Siena, MD[3,5]; Alexander Drilon, MD[6]; Robert C. Doebele, MD, PhD[7]; Manish R. Patel, DO[8]; Byoung Chul Cho, MD, PhD[9]; Stephen V. Liu, MD[10]; Myung-Ju Ahn, MD, PhD[11]; Chao-Hua Chiu, MD[12]; Anna 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.

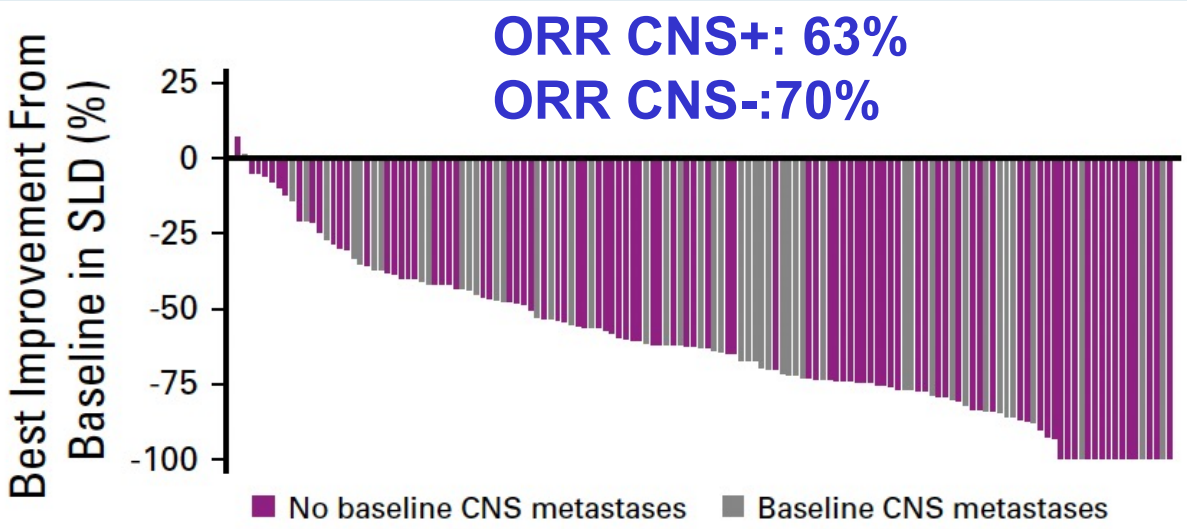
RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

Abstract LBA9023

EFFICACY AND SAFETY OF ENTRECTINIB IN PATIENTS WITH *ROS1*-POSITIVE (*ROS1*+) ADVANCED/METASTATIC NSCLC FOR THE BLOOD FIRST ASSAY SCREENING TRIAL (BFAST)

Solange Peters,[1] Shirish M. Gadgeel,[2] Tony Mok,[3] Ernest Nadal,[4] Saadettin Kilickap,[5] Maurice Pérol,[6] Jacques Cadranel,[7] Shunichi Sugawara,[8] Chao-Hua Chiu,[9] Mor Moskovitz,[10] Chong-Jen Yu,[11] Tomohiro Tanaka,[12] Rhea Nersesian,[13] Sarah M. Shagan,[13] Margaret Maclennan,[14] Michael Mathisen,[13] Vijay Bhagawati-Prasad,[15] Venice Archer,[15] Rafal Dziadziuszko[16]

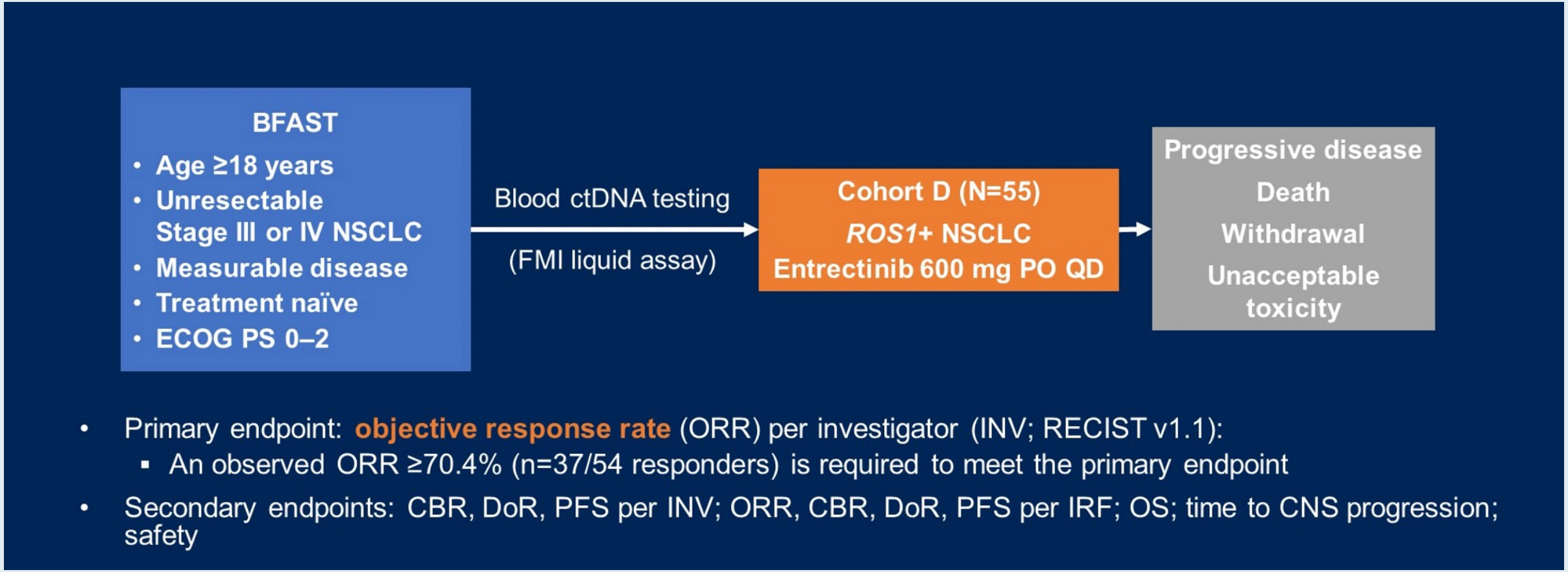
[1]Lausanne University Hospital, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; [2]Henry Ford Cancer Institute/Henry Ford Health System, Detroit, Michigan; [3]State Laboratory of Translational Oncology, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, Hong Kong SAR; [4]Thoracic Oncology Unit, Department of Medical Oncology, Catalan Institute of Oncology (ICO), L'Hospitalet de Llobregat, Barcelona, Spain; [5]Istinye University Faculty of Medicine, Department of Medical Oncology, Instanbul, Turkey; [6]Department of Medical Oncology, Centre Léon Bérard, Lyon, France; [7]Department of Pneumology and Thoracic Oncology, APHP, Hôpital Tenon and GRC04 Theranoscan Sorbonne Université, Paris, France; [8]Department of Pulmonary Medicine, Sendai Kousei Hospital, Sendai, Japan; [9]Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; [10]Thoracic Cancer Service, Rambam Health Care Campus, Haifa, Israel; [11]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; [12]Chugai Pharmaceutical Co. Ltd, Tokyo, Japan; [13]Genentech Inc., South San Francisco, California; [14]Syneos Health, Edinburgh, UK; [15]Roche Products Ltd, Welwyn Garden City, UK; [16]Department of Oncology and Radiotherapy and Early Clinical Trials Unit, Medical University of Gdansk, Gdansk, Poland

Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.

ASCO® AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

RTP RESEARCH TO PRACTICE

BFAST Study Design



- Primary endpoint: **objective response rate** (ORR) per investigator (INV; RECIST v1.1):
  - An observed ORR ≥70.4% (n=37/54 responders) is required to meet the primary endpoint
- Secondary endpoints: CBR, DoR, PFS per INV; ORR, CBR, DoR, PFS per IRF; OS; time to CNS progression; safety

Peters S et al. ASCO 2022;Abstract LBA9023.

RTP RESEARCH TO PRACTICE

BFAST: Entrectinib Efficacy Consistent with Tissue-Based Trials

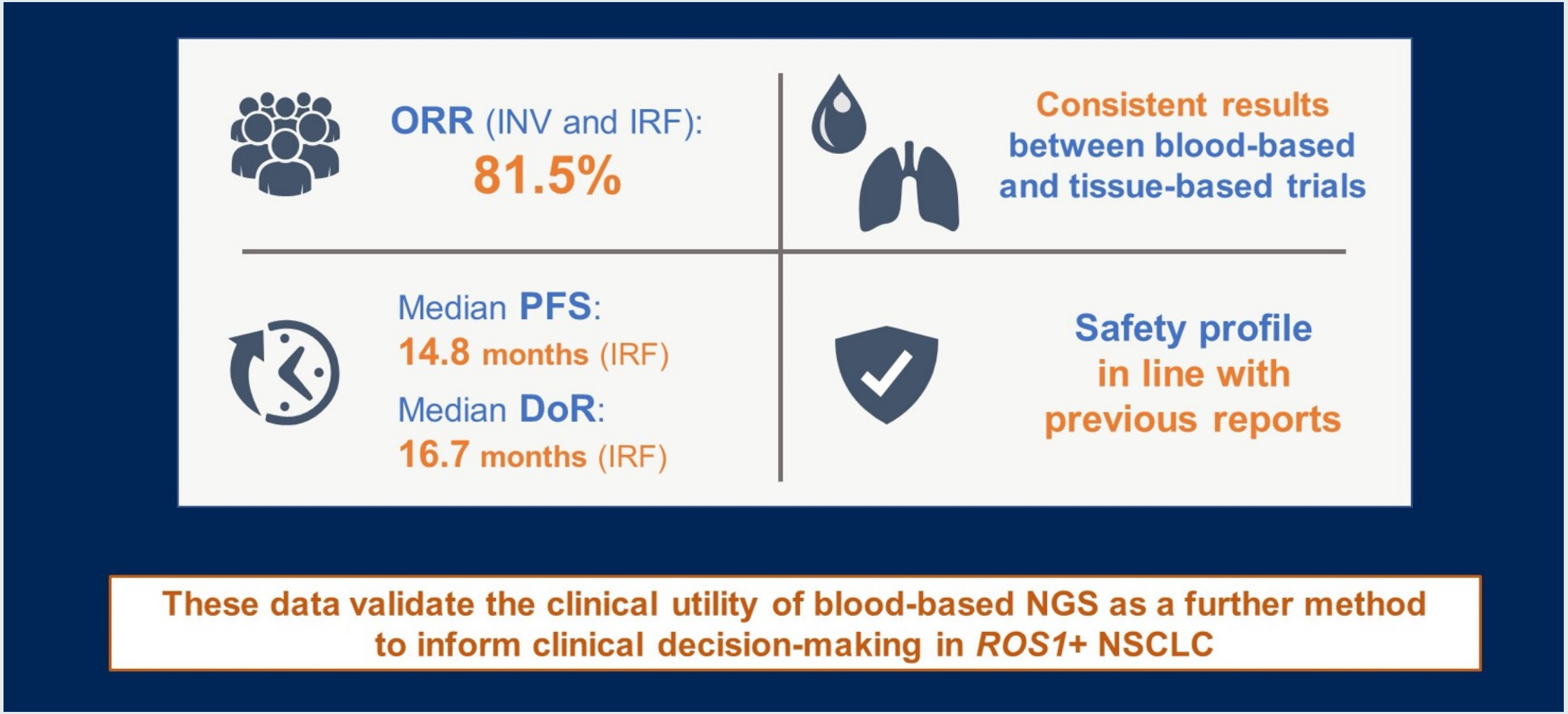
- **BFAST met its primary endpoint in the *ROS1*+ NSCLC arm**
  - Confirmed ORR: 81.5% per INV and IRF
- **Responses were durable** in this cohort:
  - Median PFS per INV: 12.9 months
  - Median DoR per INV: 13.0 months
  - Median time to CNS PD was not reached
- OS data were immature, with only 20 events reported
- **No new safety signals** were identified

BFAST *ROS1*+ NSCLC arm (N=54)		
	INV assessment	**IRF assessment**
ORR, n (%) [95% CI]	**44 (81.5)** [68.6–90.8]	**44 (81.5)** [68.6–90.8]
Complete response (CR)	2 (3.7)	3 (5.6)
Partial response (PR)	42 (77.8)	41 (75.9)
CBR*, n (%) [95% CI]	47 (87.0) [75.1–94.6]	44 (81.5) [68.6–90.8]
Median PFS, months (95% CI)	**12.9** (8.7–18.5)	**14.8** (7.2–24.0)
12-month event-free rate, %	50.7	52.4
Median DoR, months (95% CI)	**13.0** (6.3–18.4)	**16.7** (5.6–24.0)
12-month event-free rate, %	53.2	57.3
Median time to CNS PD, months (95% CI)	**NE** (NE)	**NE** (NE)
12-month event-free rate, %	83.5	86.4
OS	*Immature*	
Patients with event, n (%)	20 (36)	

Peters S et al. ASCO 2022;Abstract LBA9023.

RTP RESEARCH TO PRACTICE

BFAST Summary



Peters S et al. ASCO 2022;Abstract LBA9023.

RTP RESEARCH TO PRACTICE

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

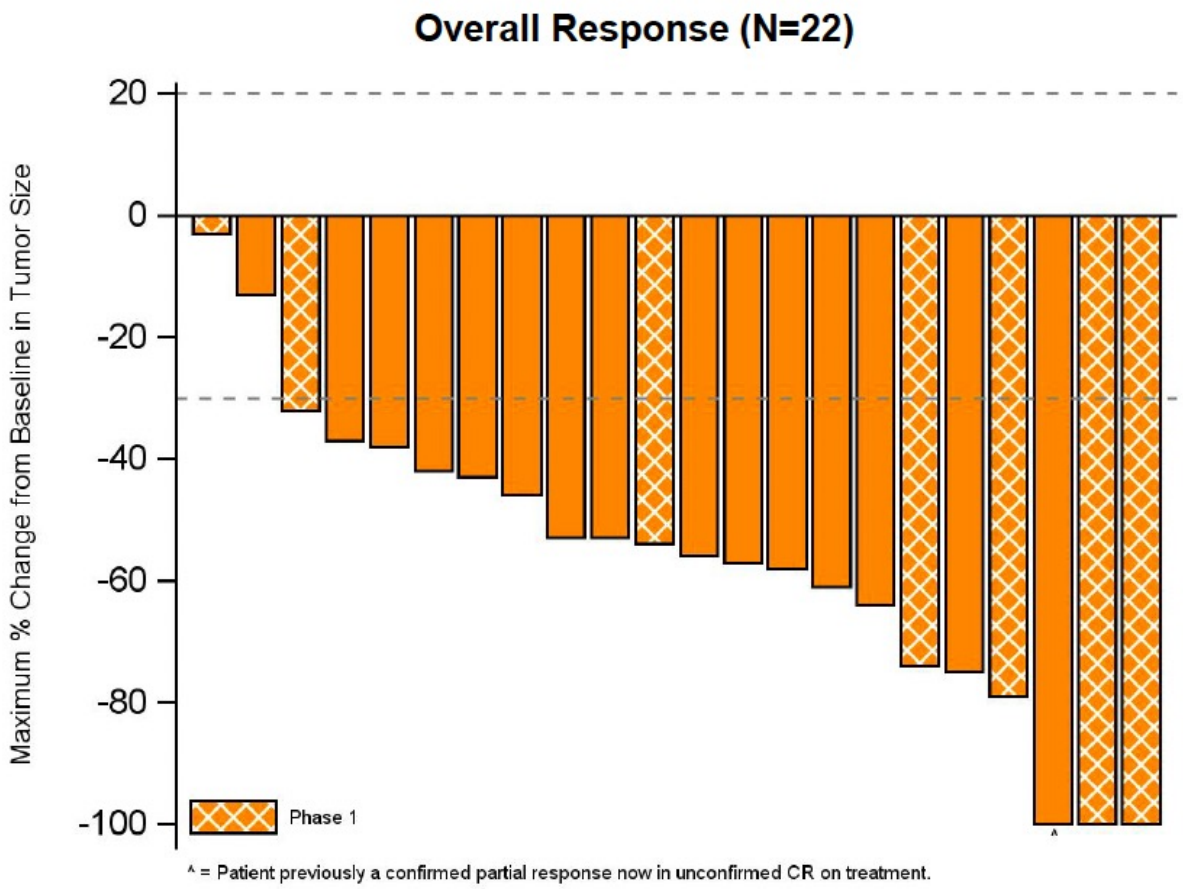
Phase 1/2 TRIDENT-1 Study of Repotrectinib in Patients with *ROS1*+ or *NTRK*+ Advanced Solid Tumors

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

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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

AACR American Association for Cancer Research FINDING CURES TOGETHER
NIH NATIONAL CANCER INSTITUTE
EORTC European Organisation for Research and Treatment of Cancer The future of cancer therapy

Poster #: P224

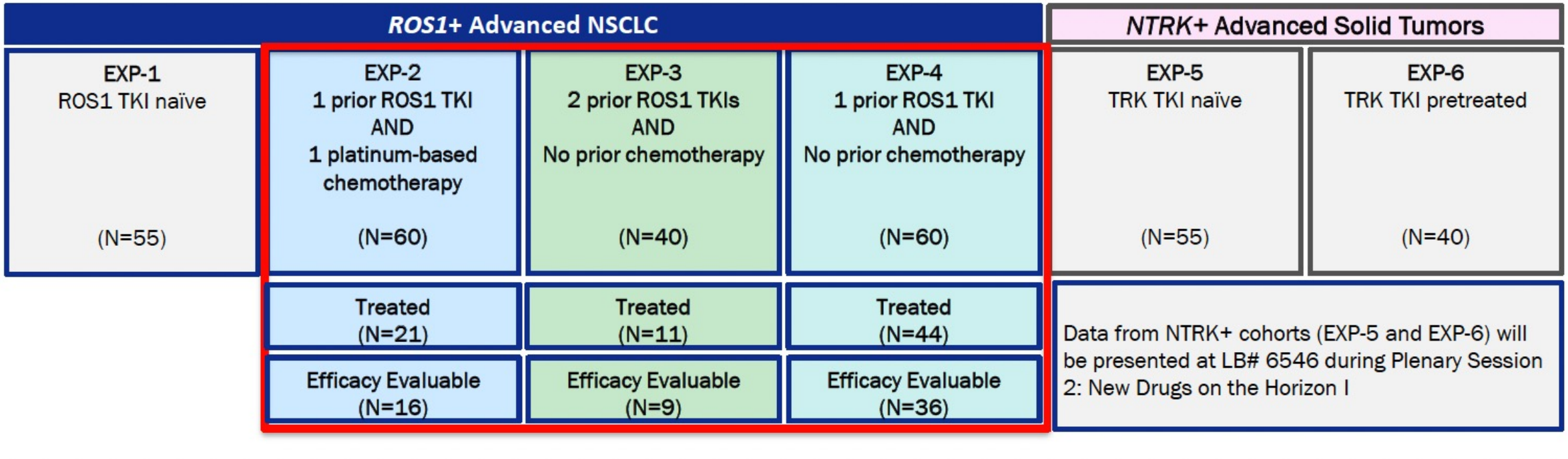
Update from the Phase 2 registrational trial of repotrectinib in TKI-pretreated patients with *ROS1+* advanced non-small cell lung cancer and with *NTRK+* advanced solid tumors (TRIDENT-1)

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.

RTP RESEARCH TO PRACTICE

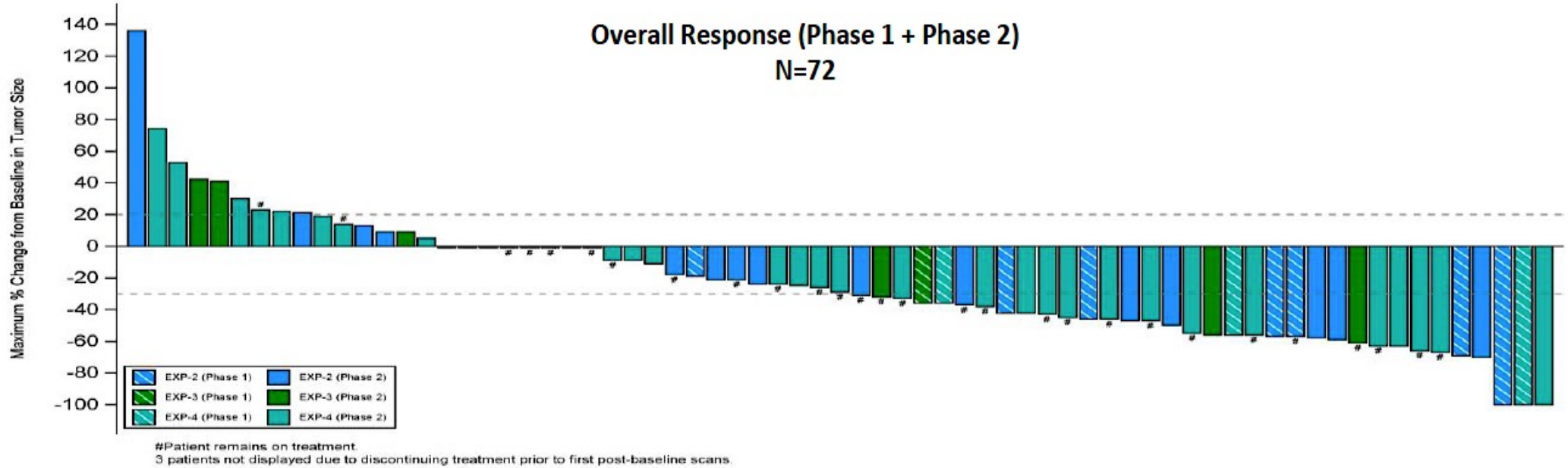
TRIDENT-1: A Phase II Study Design



Lin JJ et al. AACR 2021;Abstract 224.

RTP RESEARCH TO PRACTICE

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

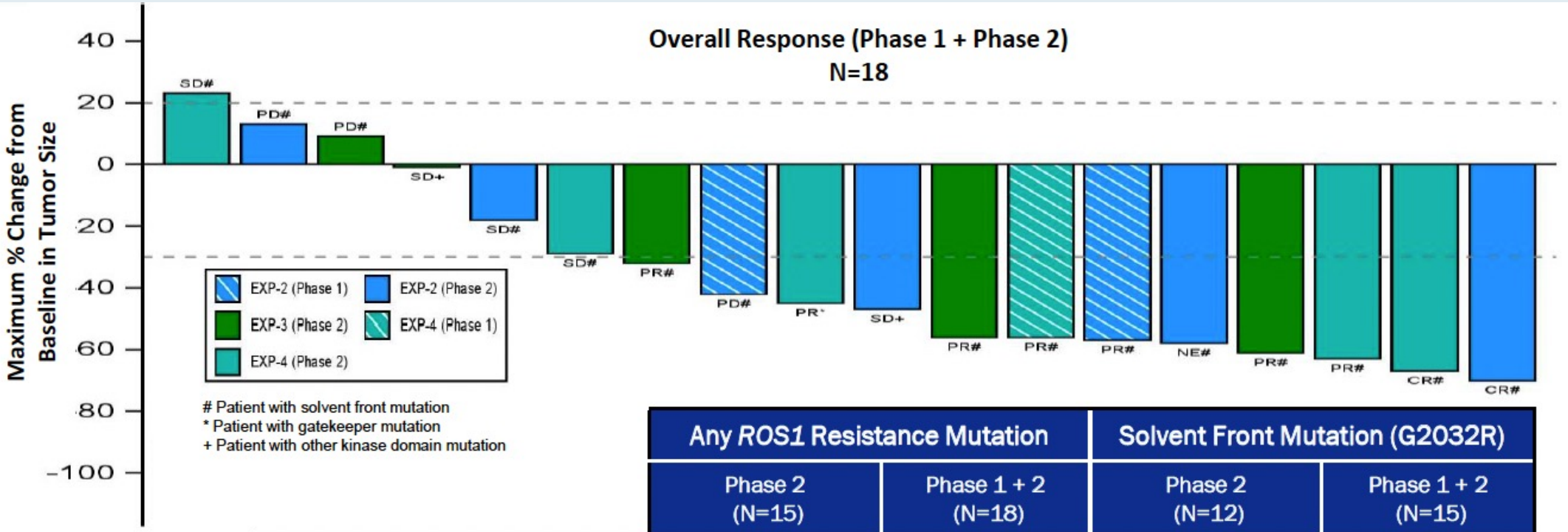


	EXP-2		EXP-3		EXP-4	
	Phase 2 (N=16)	Phase 1 + 2 (N=23)	Phase 2 (N=9)	Phase 1 + 2 (N=10)	Phase 2 (N=36)	Phase 1 + 2 (N=39)
Confirmed ORR (cORR) (95% CI)	**31%** (11 – 59)	**39%** (20 – 61)	**33%** (7 – 70)	**30%** (7 – 65)	**31%*** (16 – 48)	**33%*** (19 – 50)
Duration of Response (range in months)	1.8+ – 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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

Updated Efficacy and Safety of Larotrectinib in Patients with Tropomyosin Receptor Kinase (TRK) Fusion Lung Cancer

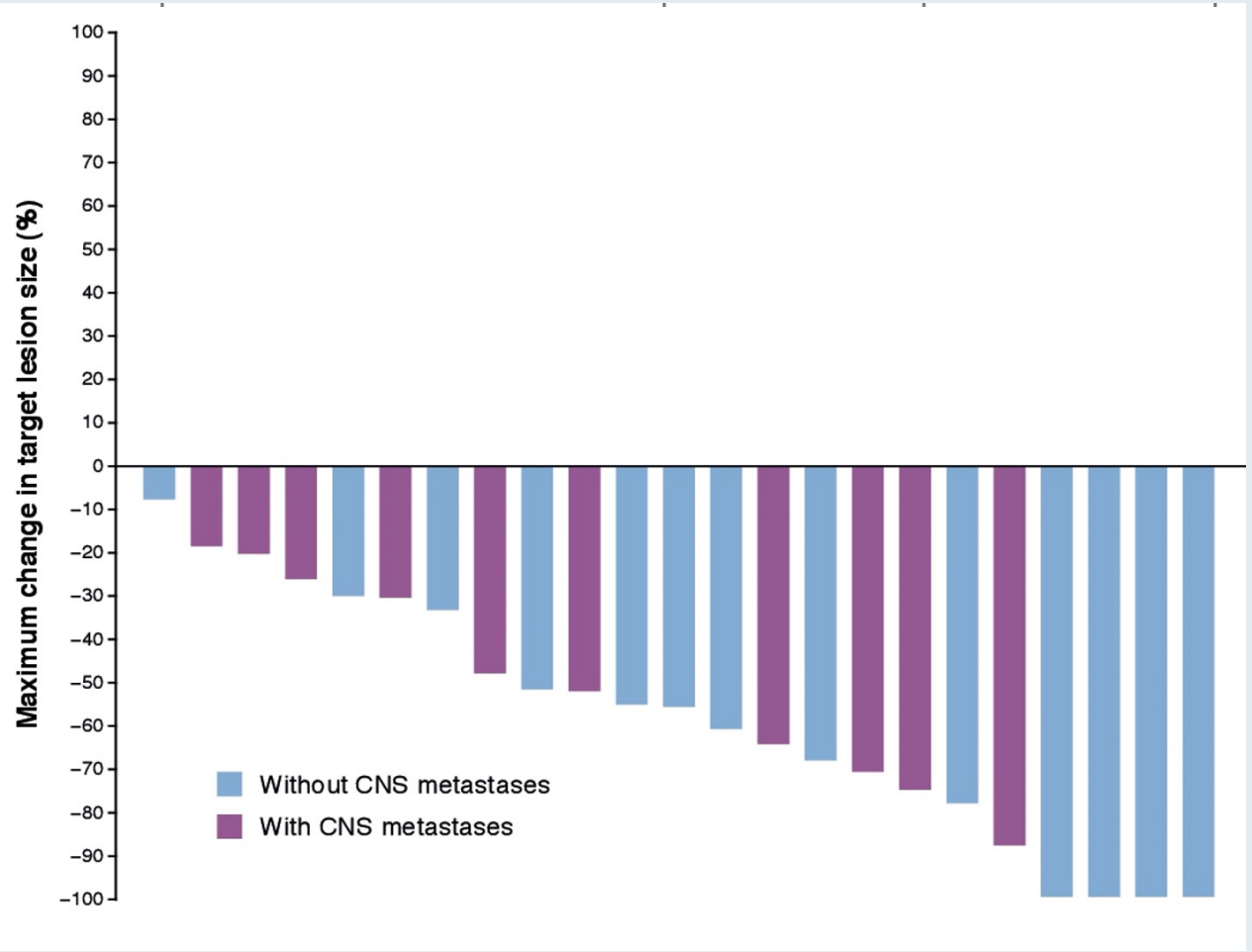
Peters S et al.

ASCO 2022;Abstract LBA9024.

RTP
RESEARCH
TO PRACTICE

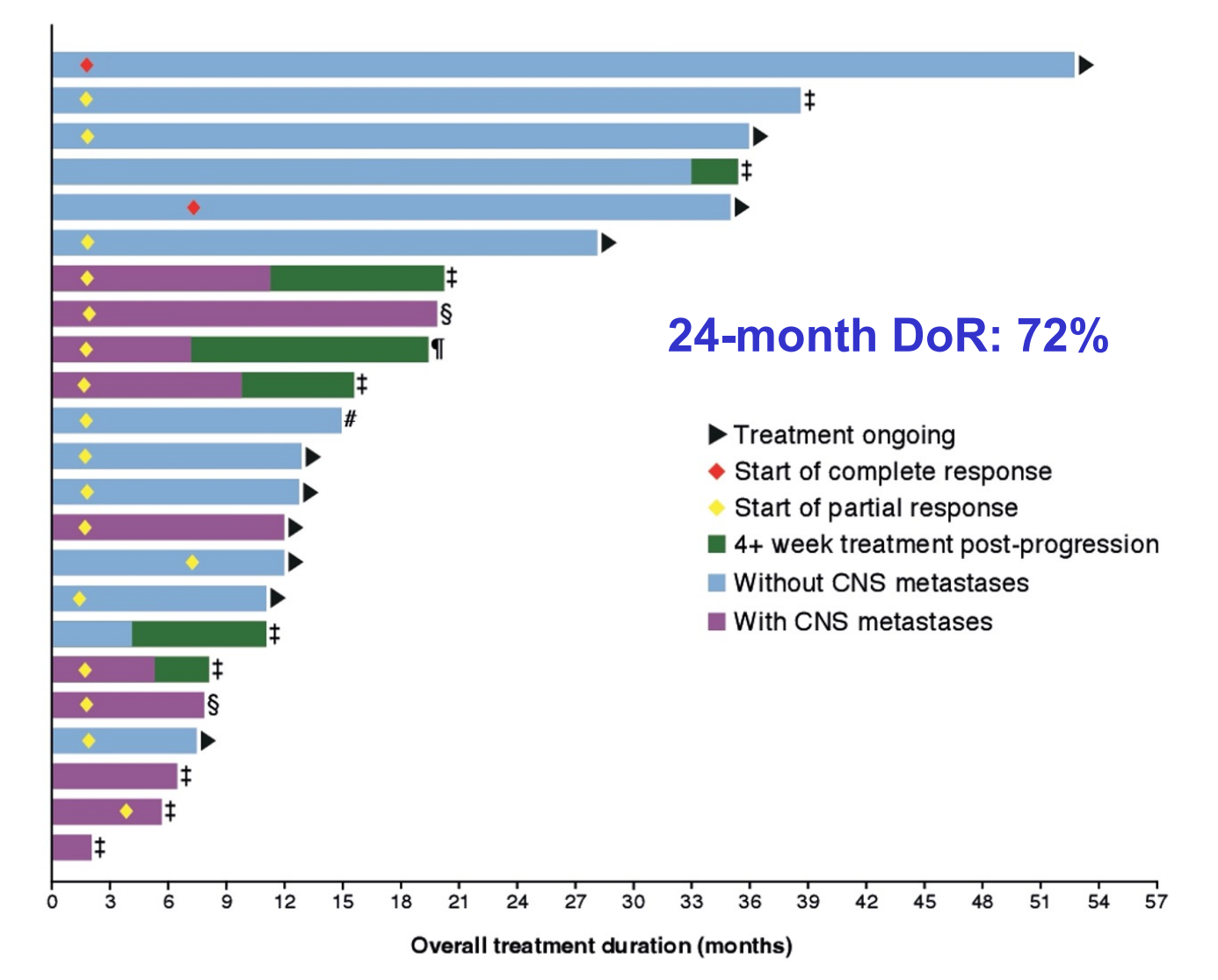
Response to Larotrectinib

	All patients (N=26)	Patients with CNS metastases (n=12)
Evaluable patients, n	23	10
ORR, % (95% CI)	83 (61–95)	80 (44–97)
Best overall response, n (%)		
Complete response	2 (9)	0
Partial response	17 (74)	8 (80)
Stable disease	4 (17)	2 (20)
Progressive disease	0	0



Peters S et al. ASCO 2022;Abstract LBA9024.

Larotrectinib Duration of Response

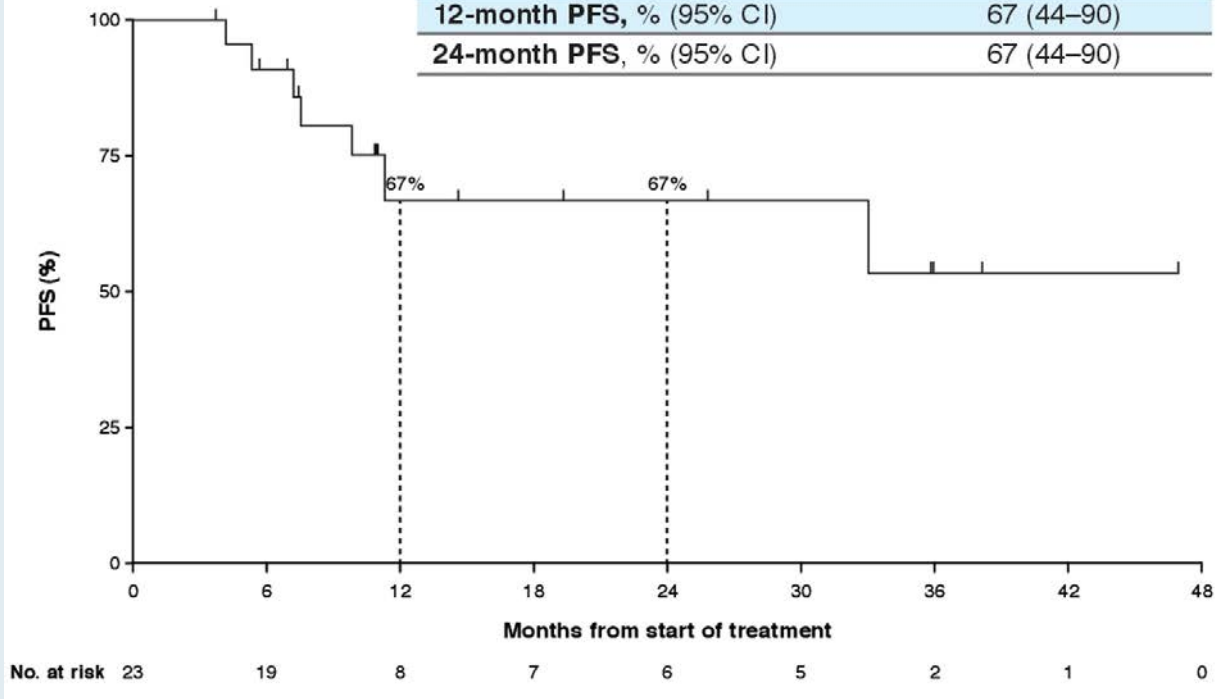


Peters S et al. ASCO 2022;Abstract LBA9024.

Survival Analyses with Larotrectinib

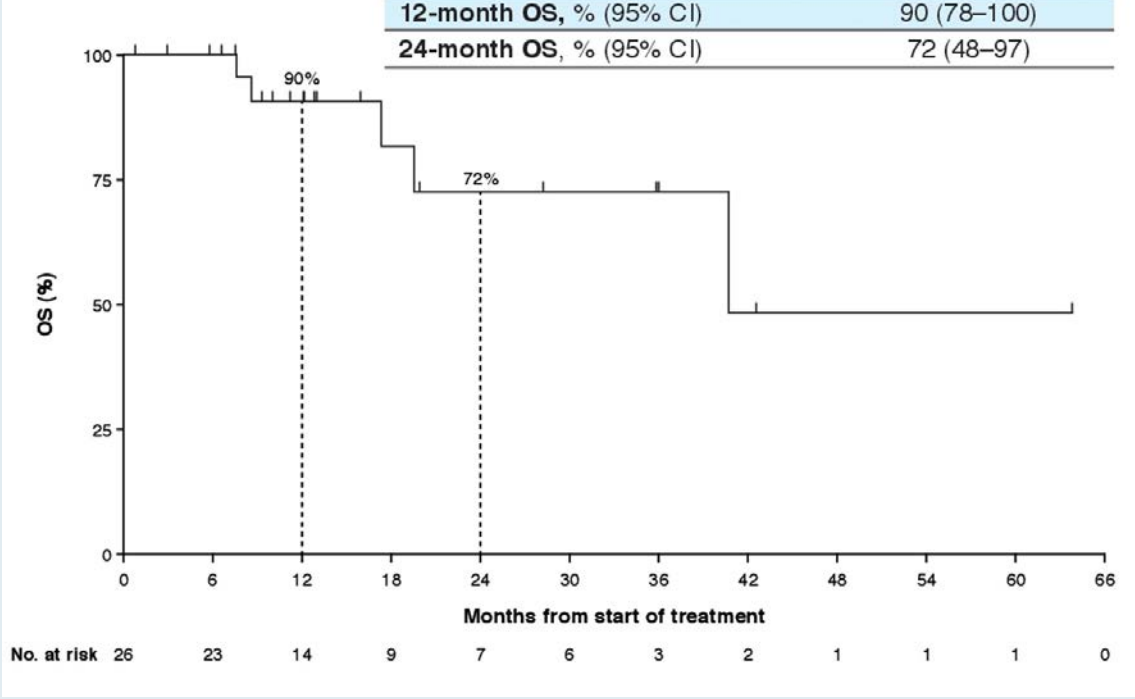
PFS

Median PFS, months (95% CI)	Not reached (9.9–NE)
Median follow-up, months	14.6
12-month PFS, % (95% CI)	67 (44–90)
24-month PFS, % (95% CI)	67 (44–90)



OS

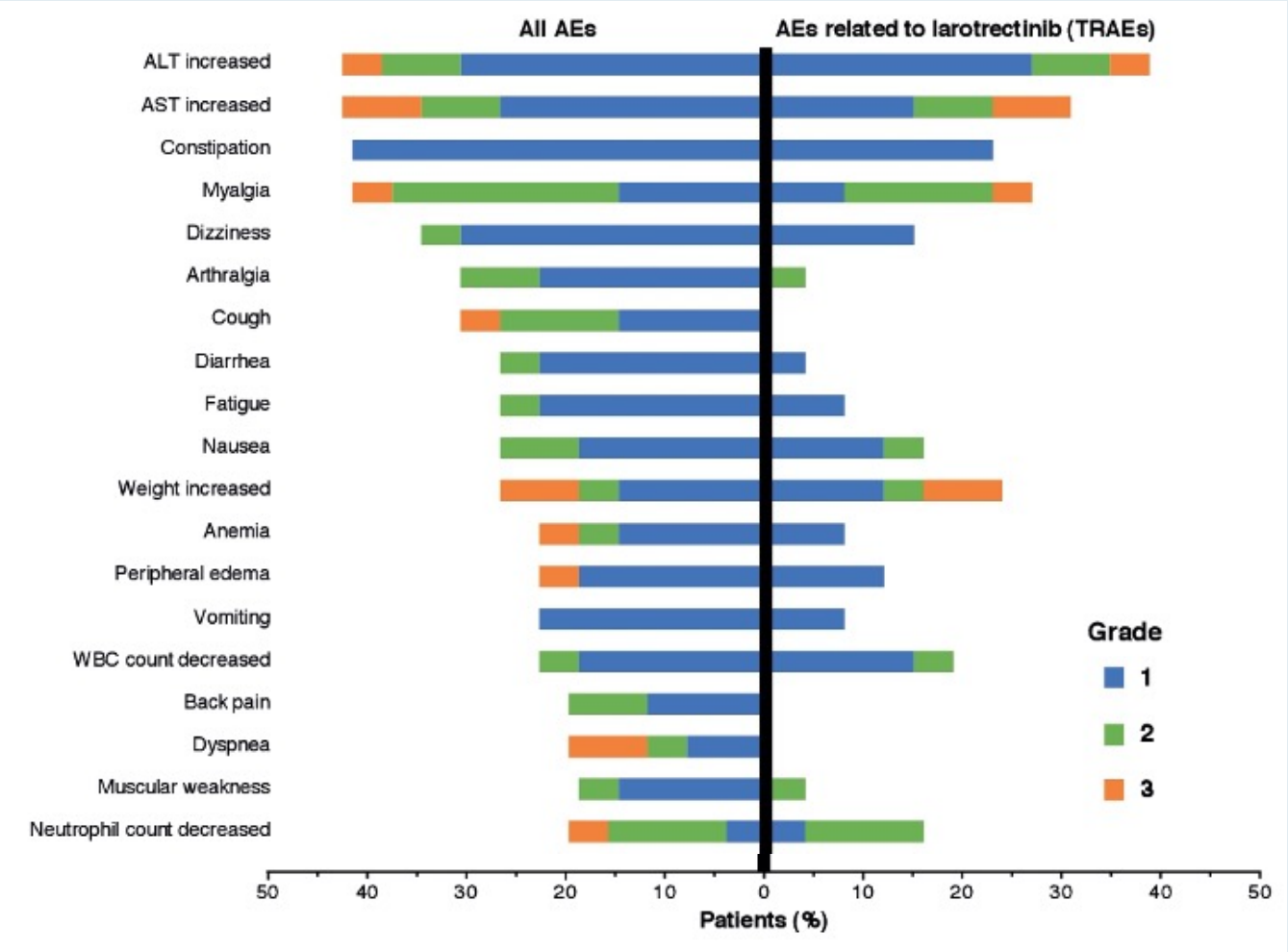
Median OS, months (95% CI)	40.7 (19.4–NE)
Median follow-up, months	12.9
12-month OS, % (95% CI)	90 (78–100)
24-month OS, % (95% CI)	72 (48–97)



Peters S et al. ASCO 2022;Abstract LBA9024.

RTP RESEARCH TO PRACTICE

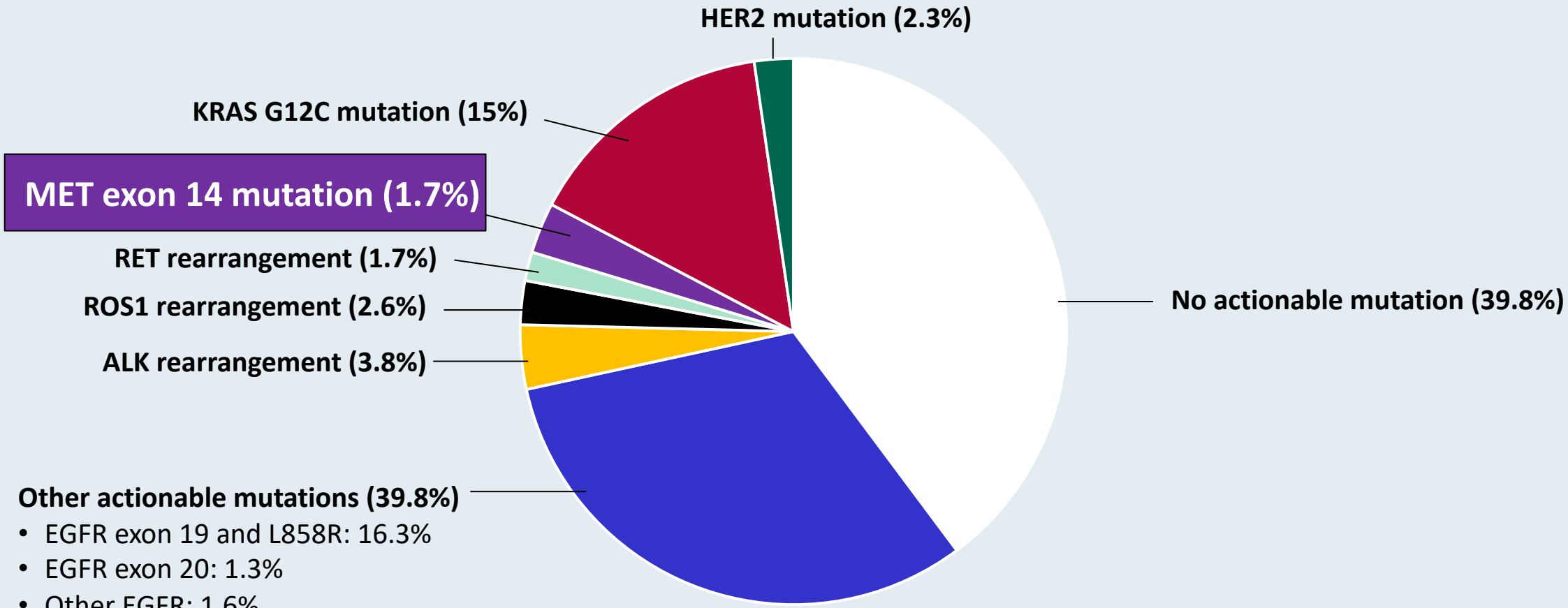
Safety Profile with Larotrectinib



Peters S et al. ASCO 2022;Abstract LBA9024.

RTP RESEARCH TO PRACTICE

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(6):611-25.

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

Abstract 9008

Amivantamab in NSCLC patients with MET exon 14 skipping mutation: Updated results from the CHRYSALIS study

Matthew G. Krebs,[1] Alexander I. Spira,[2] Byoung Chul Cho,[3] Benjamin Besse,[4] Jonathan W. Goldman,[5] Pasi A. Jänne,[6] Zhiyong Ma,[7] Aaron S. Mansfield,[8] Anna Minchom,[9] Sai-Hong Ignatius Ou,[10] Ravi Salgia,[11] Zhijie Wang,[12] Casilda Llacer Perez,[13] Grace Gao,[14] Joshua C. Curtin,[14] Amy Roshak,[14] Robert W. Schnepp,[14] Meena Thayu,[14] Roland E. Knoblauch,[14] Chee Khoon Lee[15]

[1]Division of Cancer Sciences, The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [2]Virginia Cancer Specialists Research Institute, US Oncology Research, Fairfax VA; [3]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [4]Institut Gustave Roussy, Villejuif, France; [5]David Geffen School of Medicine at UCLA, Los Angeles, CA; [6]Dana Farber Cancer Institute, Boston, MA; [7]Henan Cancer Hospital, Zhengzhou, China; [8]Mayo Clinic, Rochester, MN; [9]Drug Development Unit, Royal Marsden/Institute of Cancer Research, Sutton, UK; [10]University of California Irvine, Orange, CA; [11]City of Hope, Duarte, CA; [12]Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China; [13]Medical Oncology Intercenter Unit, Regional and Virgen de la Victoria University Hospitals, IBIMA, Málaga, Spain; [14]Janssen R&D, Spring House, PA; [15]St George Hospital, Kogarah, Australia

Copies of this slide deck obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from ASCO® or the author of this slides.

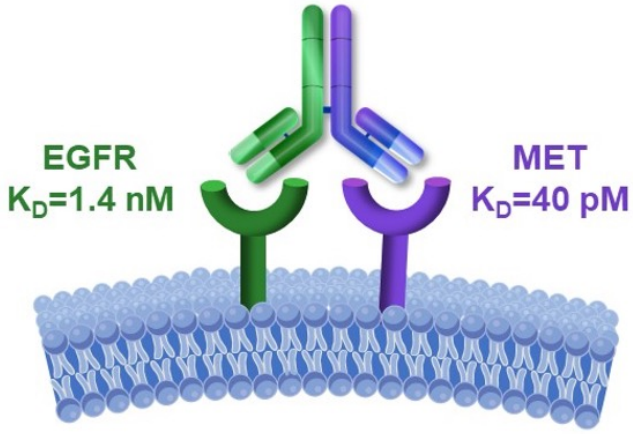
Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.

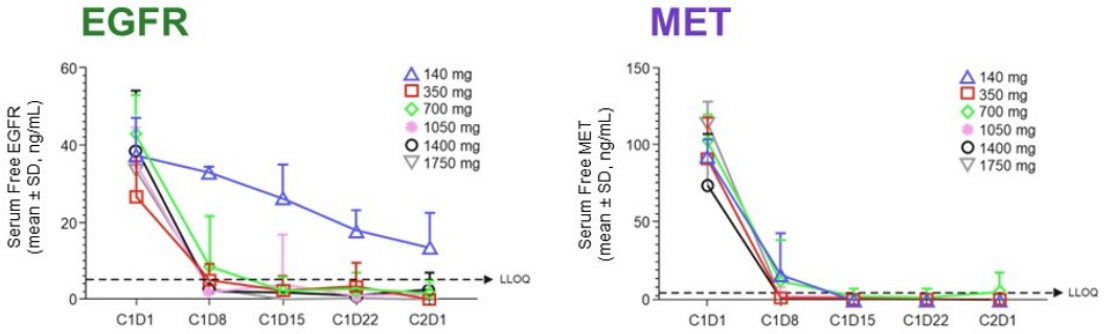
ASCO® AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

RTP RESEARCH TO PRACTICE

Amivantamab: EGFR-MET Bispecific Antibody

- Demonstrated monotherapy activity in EGFR ex20ins NSCLC following progression on platinum-based chemotherapy (ORR, 40%; DOR, 11.1 months)[1]
- Demonstrated activity in TKI-resistant EGFRm NSCLC with MET amplification[2,3]
- Has higher affinity for MET (40 pM) than EGFR (1.4 nM)
- Depletion of free soluble target proteins, suggesting total body target engagement, occurs at ≥140 mg for sMET and ≥350 mg for sEGFR
- Evaluation in primary MET-driven tumors is ongoing





C, cycle; D, day; DOR, duration of response; EGFR, epidermal growth factor receptor; EGFRm, EGFR-mutated; ex20ins, exon 20 insertion mutations; K_D, dissociation constant; LLOQ, lower limit of quantification; NSCLC, non-small cell lung cancer; ORR, overall response rate; SD, standard deviation; sEGFR, soluble EGFR; sMET, soluble MET; TKI, tyrosine kinase inhibitor.

1. Park K, et al. *J Clin Oncol*. 2021;39(30):3391-3402. 2. Haura EB, et al. Presented at: ASCO; May 31-June 4, 2019. 9009 (oral). 3. Bauml J, et al. Presented at: ASCO; June 4-8, 2021. 9006 (oral).

Krebs MG et al. ASCO 2022;Abstract 9008.

RTP RESEARCH TO PRACTICE

CHRYSALIS Phase I Study Design

Part 1: Dose Escalation

140–1750 mg

Objective: Establish RP2D

RP2D

Amivantamab
1050 mg (<80 kg)
1400 mg (≥80 kg)

Intravenous dosing
C1 QW, C2+ Q2W

Part 2: Dose Expansion

MET-2 Cohort: *METex14* n=55[a]
(up to 100 planned)

Objective: Safety and efficacy at the RP2D

Eligibility

- Metastatic or unresectable/advanced NSCLC
- Failed or ineligible for standard of care therapy

Eligibility for METex14 Cohort

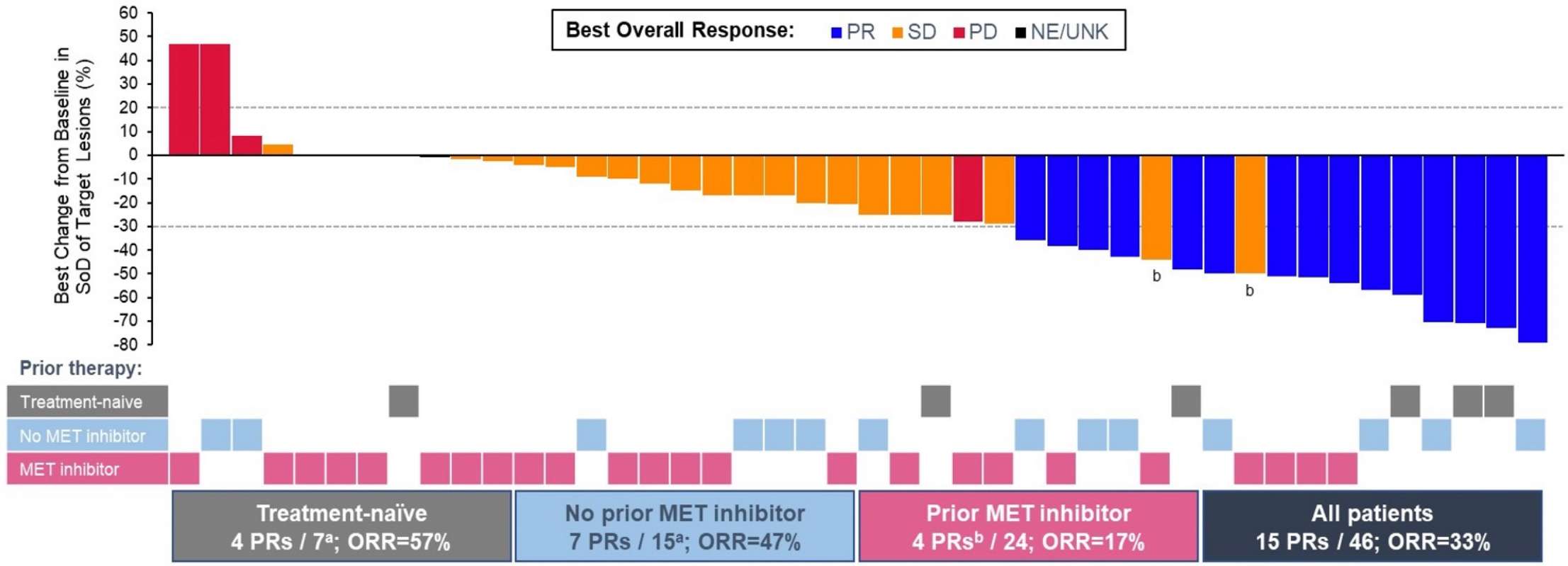
- Measurable disease
- Primary METex14 mutation by NGS of tumor or ctDNA

Krebs MG et al. ASCO 2022;Abstract 9008.

RTP RESEARCH TO PRACTICE

CHRYSALIS: Antitumor Activity of Amivantamab

- A total of 46 patients were efficacy evaluable

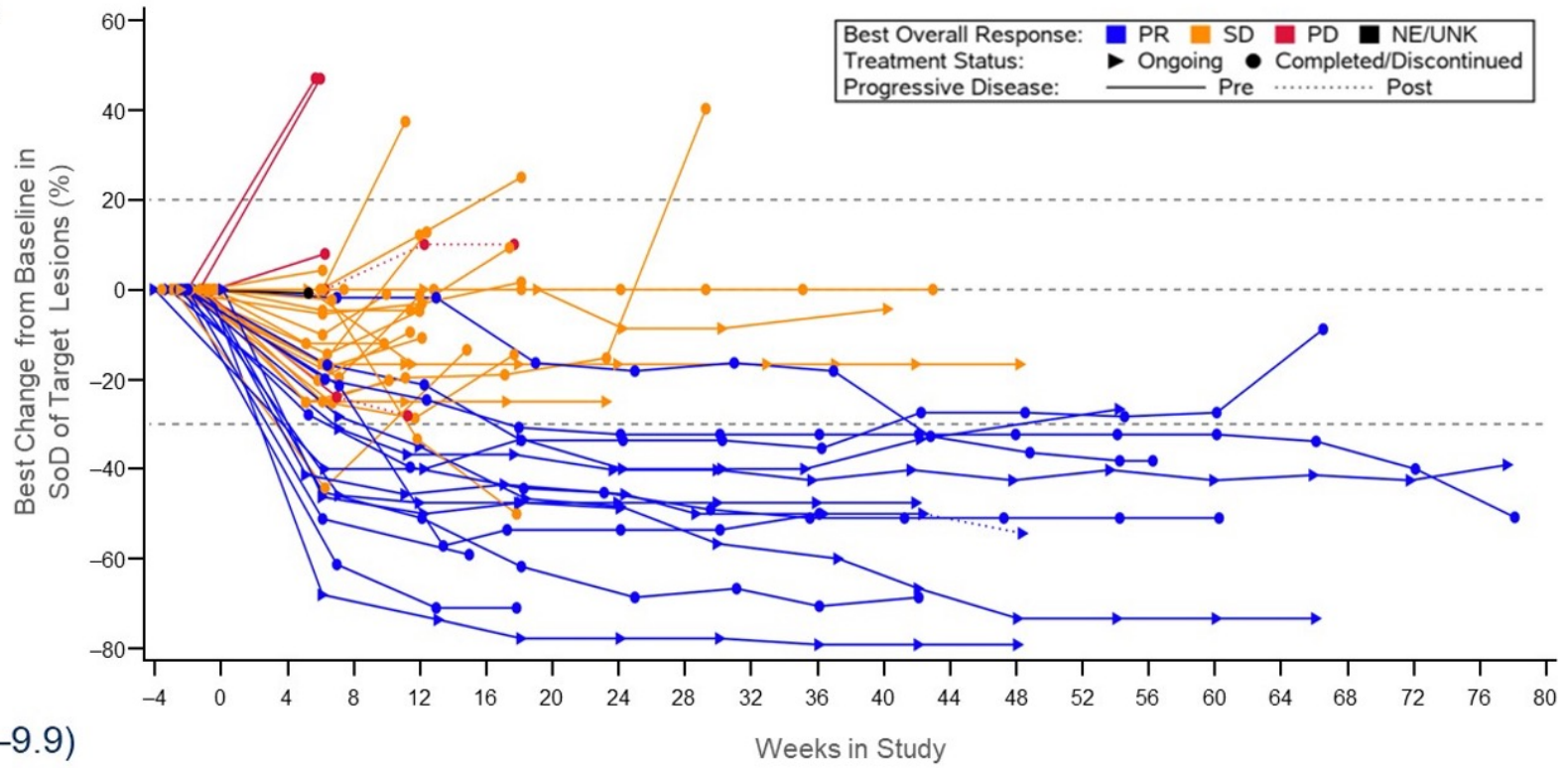


Krebs MG et al. ASCO 2022;Abstract 9008.

RTP RESEARCH TO PRACTICE

CHRYSALIS: Durability of Response to Amivantamab

- Median duration of response is not estimable
  - 11/15 patients who responded are ongoing
  - 10 patients (67% of responders) with response duration ≥6 months
- Clinical benefit rate=59%[a]
  - Treatment-naïve: 71%
  - No prior MET: 53%
  - Prior MET: 58%
- Median PFS=6.7 mo (95% CI 2.9–15.3)
  - Treatment-naïve: NE (95% CI 2.6–NE)
  - No prior MET: 8.3 mo (95% CI 1.5–15.3)
  - Prior MET: 4.2 mo (95% CI 2.9–NE)
- Median time to response=1.6 mo (range, 1.2–9.9)



Krebs MG et al. ASCO 2022;Abstract 9008.

RTP RESEARCH TO PRACTICE

CHRYSALIS: Safety Profile

TEAE (≥15%) by Preferred Term, n (%)	RP2D (n=425) Median follow-up 11.8 months		METex14 Subset (n=55) Median follow up 5.1 months	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Infusion related reaction	283 (67)	11 (3)	38 (69)	3 (5)
Rash	155 (36)	8 (2)	17 (31)	1 (2)
Dermatitis acneiform	155 (36)	4 (1)	22 (40)	0
Paronychia	193 (45)	7 (2)	21 (38)	0
Fatigue	93 (22)	8 (2)	17 (31)	2 (4)
Hypoalbuminemia	135 (32)	10 (2)	15 (27)	1 (2)
Stomatitis	91 (21)	2 (0.5)	15 (27)	0
Decreased appetite	76 (18)	2 (0.5)	12 (22)	0
Dyspnea	96 (23)	21 (5)	12 (22)	4 (7)
Peripheral edema	104 (24)	4 (1)	11 (20)	0
Pruritus	79 (19)	0	12 (22)	0
Nausea	104 (24)	2 (0.5)	11 (20)	0
Constipation	105 (25)	0	10 (18)	0
Hypomagnesemia	41 (10)	0	9 (16)	0
Aspartate aminotransferase increased	64 (15)	5 (1)	9 (16)	1 (2)
Alanine aminotransferase increased	72 (17)	10 (2)	8 (15)	1 (2)
Cough	78 (18)	0	3 (5)	0

- Treatment modifications due to toxicity (n=425): interruptions in 21%, reductions in 12%, and discontinuations in 5% of patients
  - Rates of pneumonitis/ILD was 4%
  - Cumulative grouped rash-related AEs[a] occurred in 322 (76%) patients, with 16 grade ≥3 (4%)
- Safety profile for METex14 subset is consistent with the larger CHRYSALIS safety population, with majority of events grade 1-2
- No new safety signals found

Krebs MG et al. ASCO 2022;Abstract 9008.

RTP RESEARCH TO PRACTICE

Tepotinib and Capmatinib Receive FDA Approval for the Treatment of Advanced NSCLC with MET Exon 14 Skipping Mutations

Tepotinib Press Release – February 3, 2021

The FDA granted accelerated approval to tepotinib for adult patients with metastatic 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.

Capmatinib Press Release – May 6, 2020

The FDA granted accelerated approval to for adult patients with metastatic NSCLC whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping. Efficacy was demonstrated in the GEOMETRY mono-1 trial (NCT02414139), a multicenter, non-randomized, open-label, multicohort study enrolling 97 patients with metastatic NSCLC with confirmed MET exon 14 skipping. Patients received capmatinib 400 mg orally twice 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. https://wayback.archive-it.org/7993/20201222063225/https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-capmatinib-metastatic-non-small-cell-lung-cancer

RTP RESEARCH TO PRACTICE

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

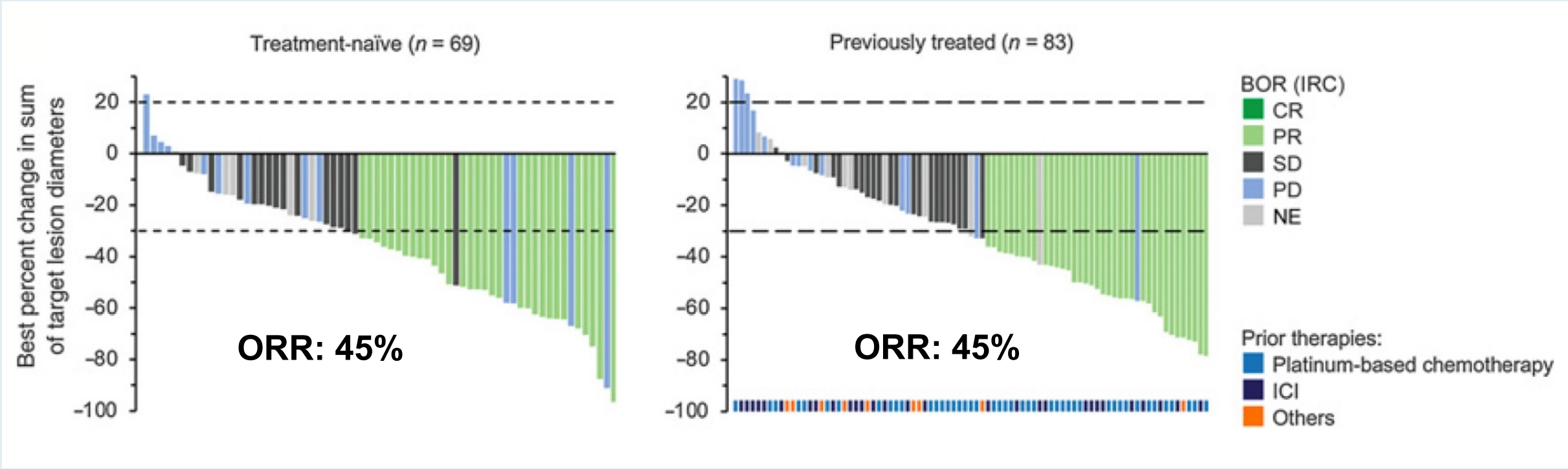
Tepotinib Efficacy and Safety in Patients with *MET* Exon 14 Skipping NSCLC: Outcomes in Patient Subgroups from the VISION Study with Relevance for Clinical Practice

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.**

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

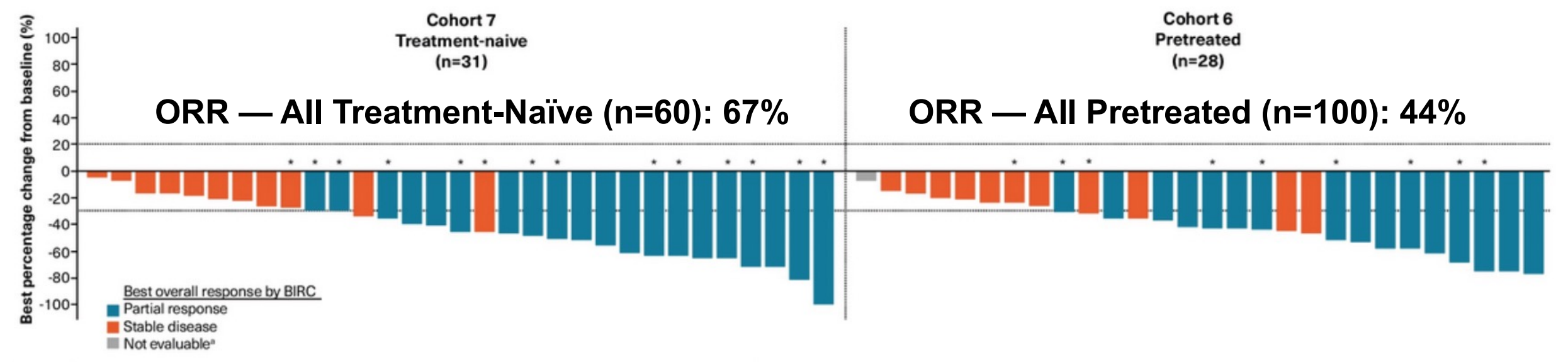
Capmatinib in *MET* Exon 14-Mutated, Advanced NSCLC: Updated Results from the GEOMETRY mono-1 Study

Wolf J et al.

ASCO 2021;Abstract 9020.

RTP
RESEARCH
TO PRACTICE

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



Wolf J et al. ASCO 2021;Abstract 9020.

RTP RESEARCH TO PRACTICE

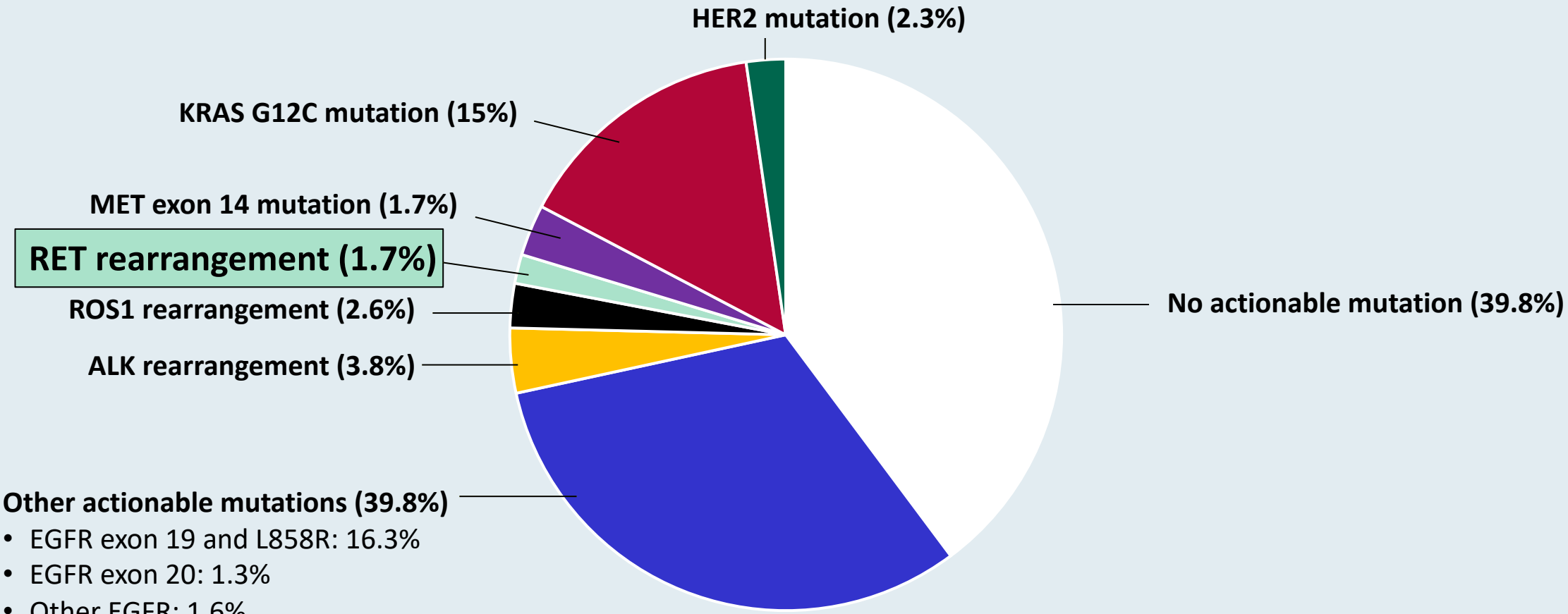
GEOMETRY mono-1: Most Common Adverse Events (Cohorts 7 and 6)

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.

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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%	Prior platinum-based chemo: 61% Treatment-naïve: 70%
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

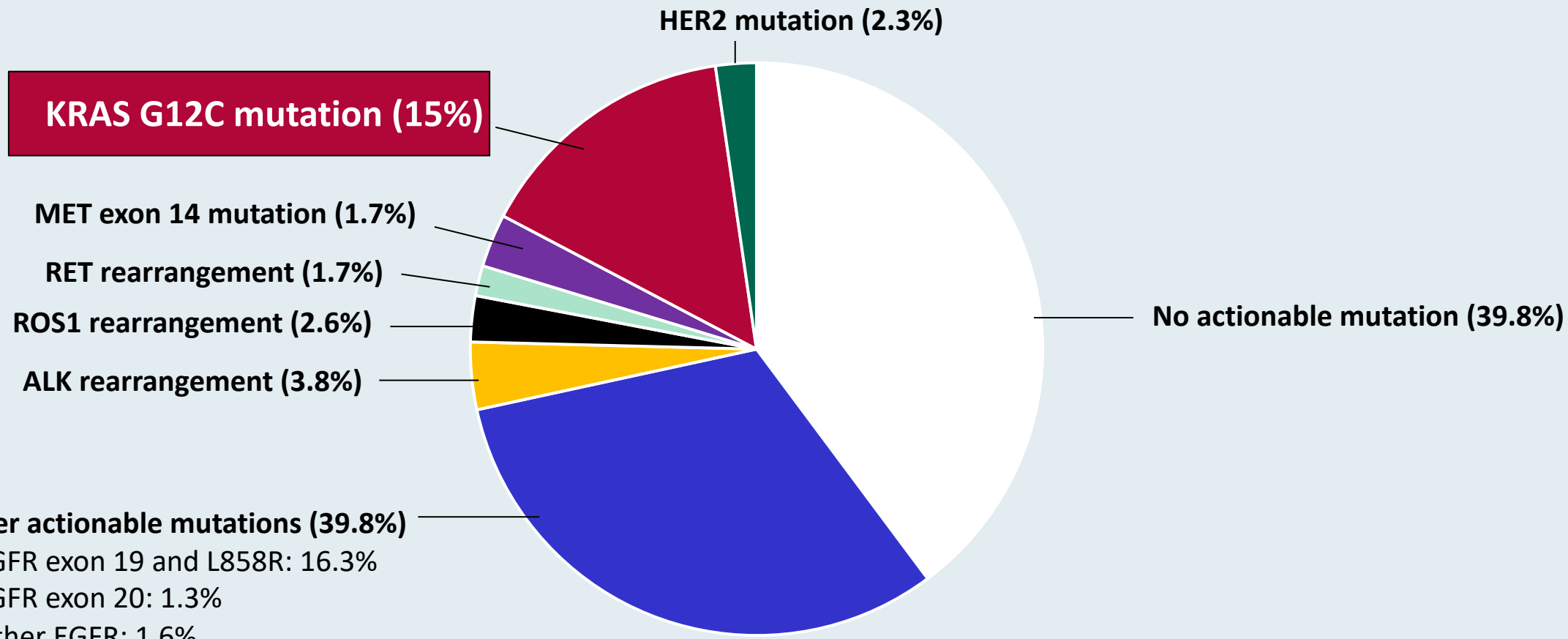
Ongoing Phase III Trials of Selpercatinib or Pralsetinib for NSCLC with RET Fusion

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.

RTP RESEARCH TO PRACTICE

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

AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

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

Presenter: Grace K. Dy[1], MD

[1]Roswell Park Comprehensive Cancer Center

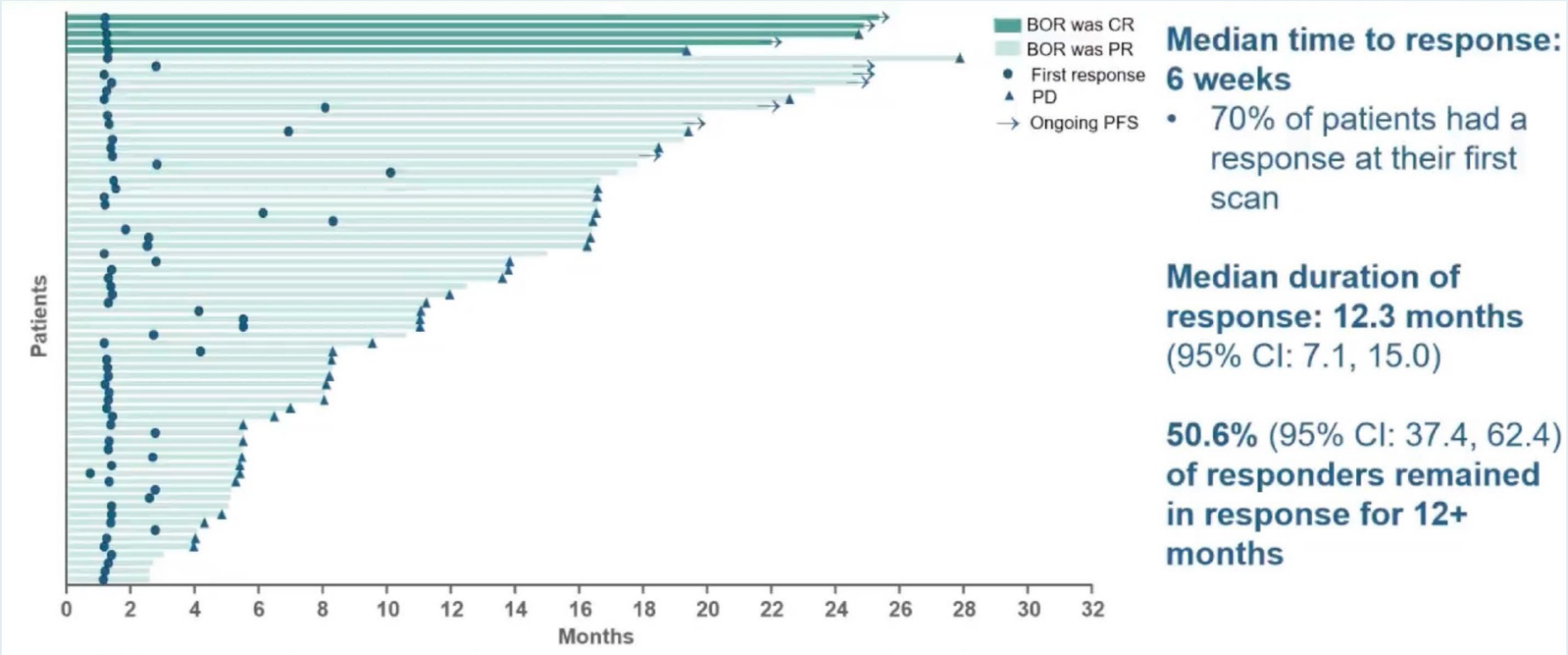
On behalf of: Ramaswamy Govindan[2], Vamsidhar Velcheti[3], Gerald S. Falchook[4], Antoine Italiano[5], Juergen Wolf[6], Adrian G. Sacher[7], Toshiaki Takahashi[8], Suresh S. Ramalingam[9], Christophe Dooms[10], Dong-Wan Kim[11], Alfredo Addeo[12], Jayesh Desai[13], Martin Schuler[14], Pascale Tomasini[15], Qui Tran[16], Simon Jones[16], Agnes Ang[16], Abraham Anderson[16], Antreas Hindoyan[16], David S. Hong[17], Bob T. Li[18]

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

Abstract CT008

RTP RESEARCH TO PRACTICE

CodeBreaK 100: 2-Year Update with Sotorasib for Previously Treated Metastatic NSCLC with KRAS p.G12C Mutation



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)

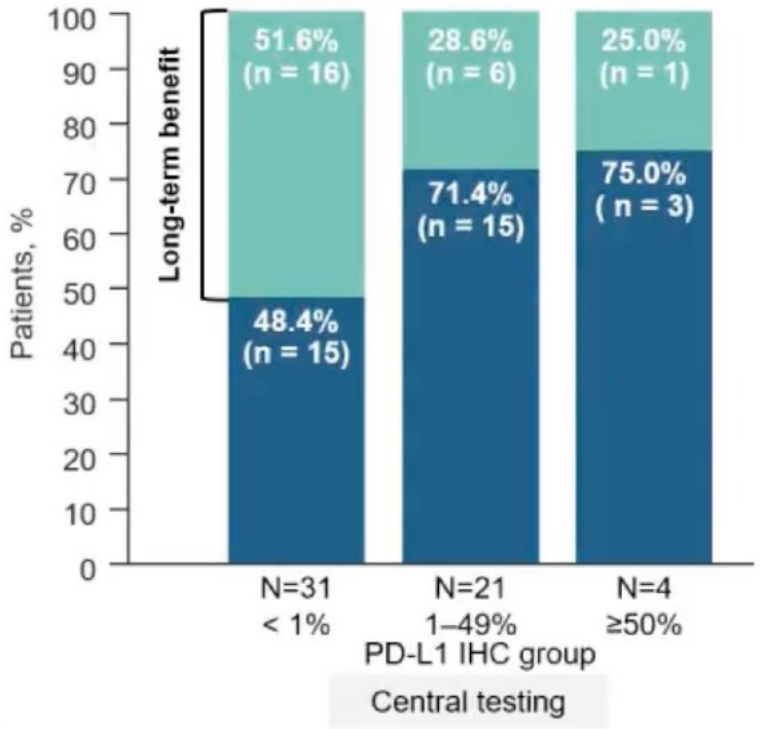
50.6% (95% CI: 37.4, 62.4) **of responders remained in response for 12+ months**

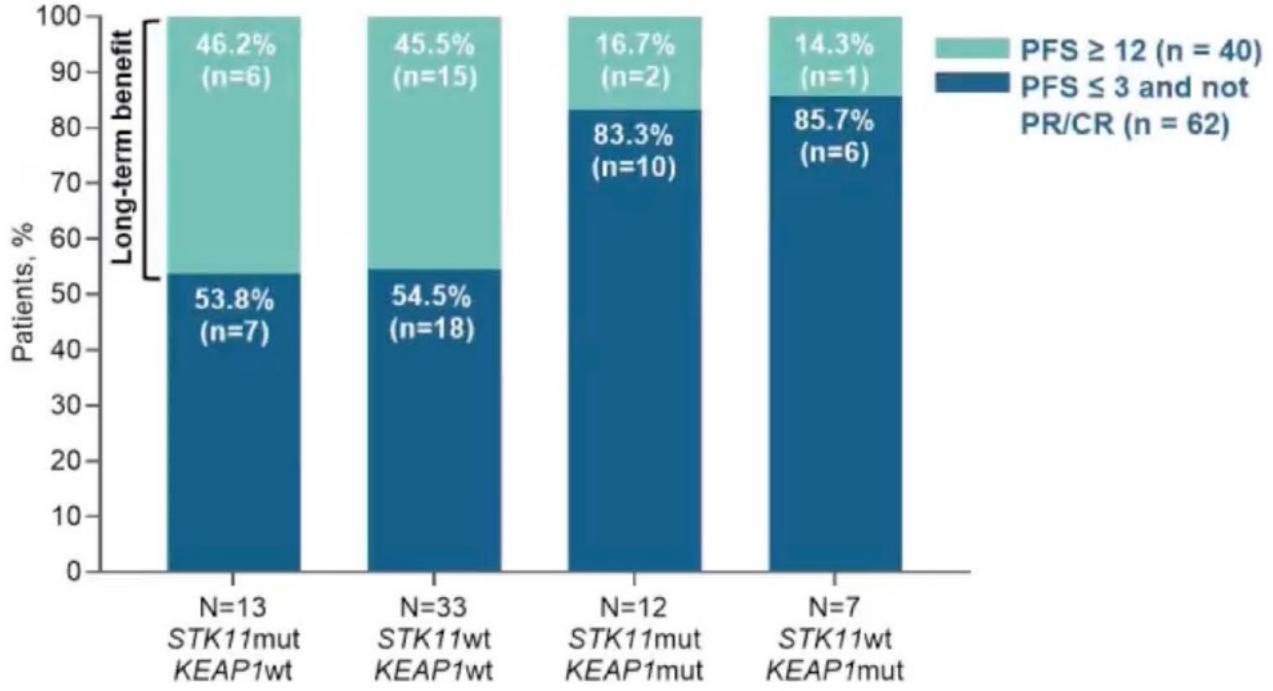
Efficacy Update (N = 172)
ORR: 40.7%
DCR: 83.7%
Median PFS: 6.3 mo
Median OS: 12.5 mo
1-year OS rate: 50.8%

Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

CodeBreaK 100: Exploratory Biomarker Analyses



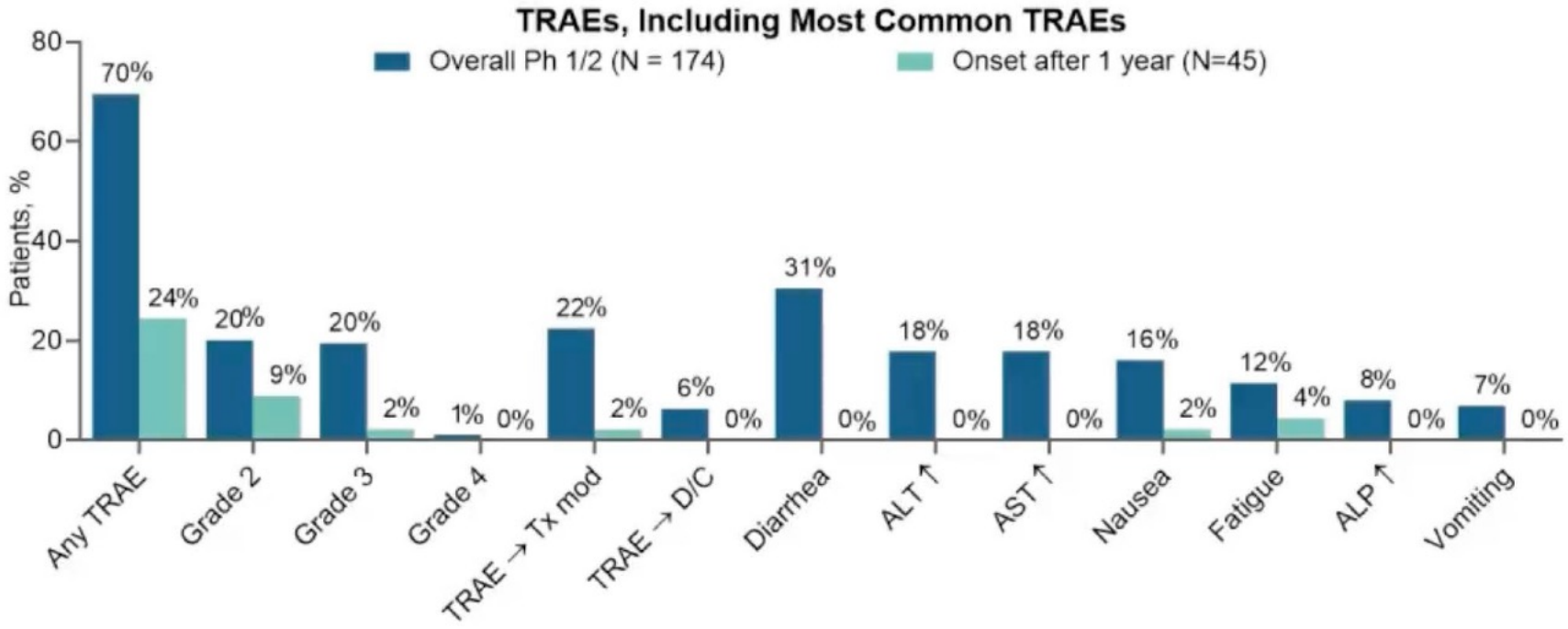


Prolonged clinical benefit was observed across PD-L1 expression, including tumors with low PD-L1 expression and *STK11* co-mutations

Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

CodeBreaK 100: Treatment-Related Adverse Events



Grade 3 or 4 TRAEs occurred in 21% of patients

- One patient with new onset Grade 3 TRAE after 1 year (hemolytic anemia)

No fatal TRAEs occurred

- No TRAE leading to discontinuation after 1 year

Well-tolerated in the long-term: late-onset TRAEs were mild and manageable

Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

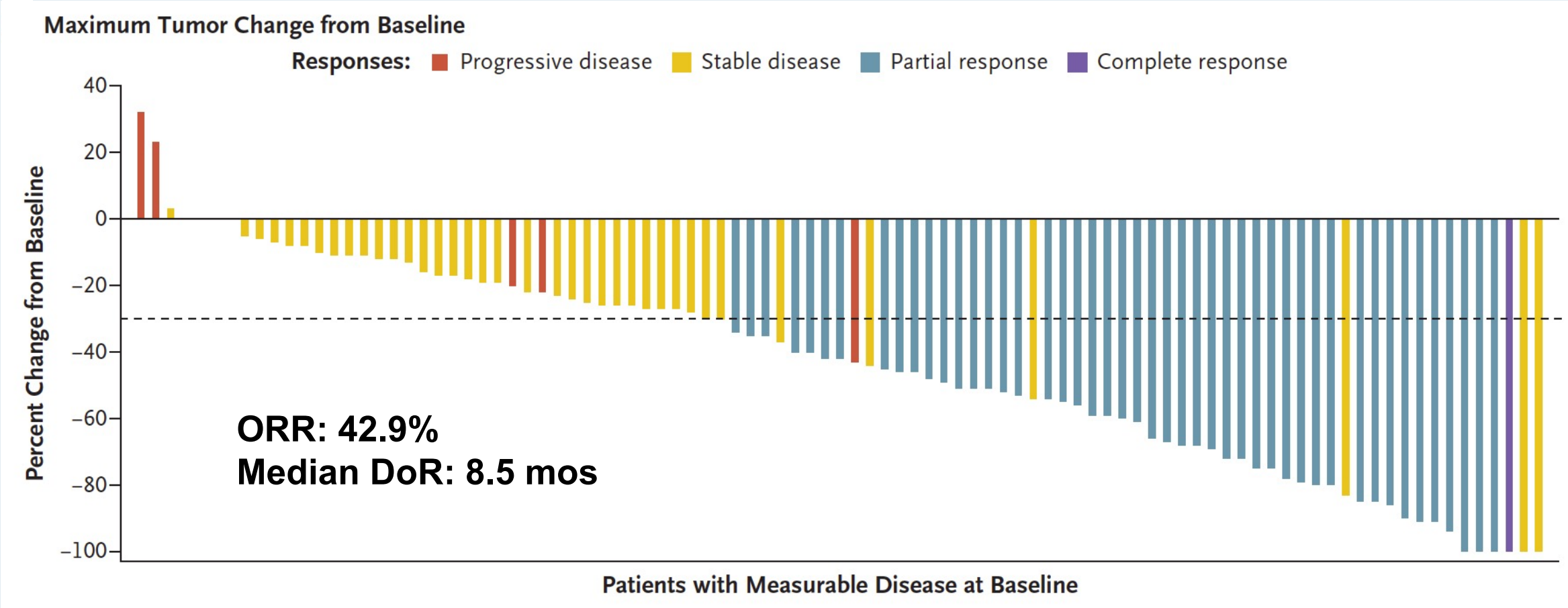
Adagrasib in Non–Small-Cell Lung Cancer Harboring a *KRAS*^{G12C} Mutation

Pasi A. Jänne, M.D., Ph.D., Gregory J. Riely, M.D., Ph.D., Shirish M. Gadgeel, M.D., Rebecca S. Heist, M.D., M.P.H., Sai-Hong I. Ou, M.D., Ph.D., Jose M. Pacheco, M.D., Melissa L. Johnson, M.D., Joshua K. Sabari, M.D., Konstantinos Leventakos, M.D., Ph.D., Edwin Yau, M.D., Ph.D., Lyudmila Bazhenova, M.D., Marcelo V. Negrao, M.D., Nathan A. Pennell, M.D., Ph.D., Jun Zhang, M.D., Ph.D., Kenna Anderes, Ph.D., Hirak Der-Torossian, M.D., Thian Kheoh, Ph.D., Karen Velastegui, B.Sc., Xiaohong Yan, Ph.D., James G. Christensen, Ph.D., Richard C. Chao, M.D., and Alexander I. Spira, M.D., Ph.D.

N Engl J Med 2022;387(2):120-31.

RTP RESEARCH TO PRACTICE

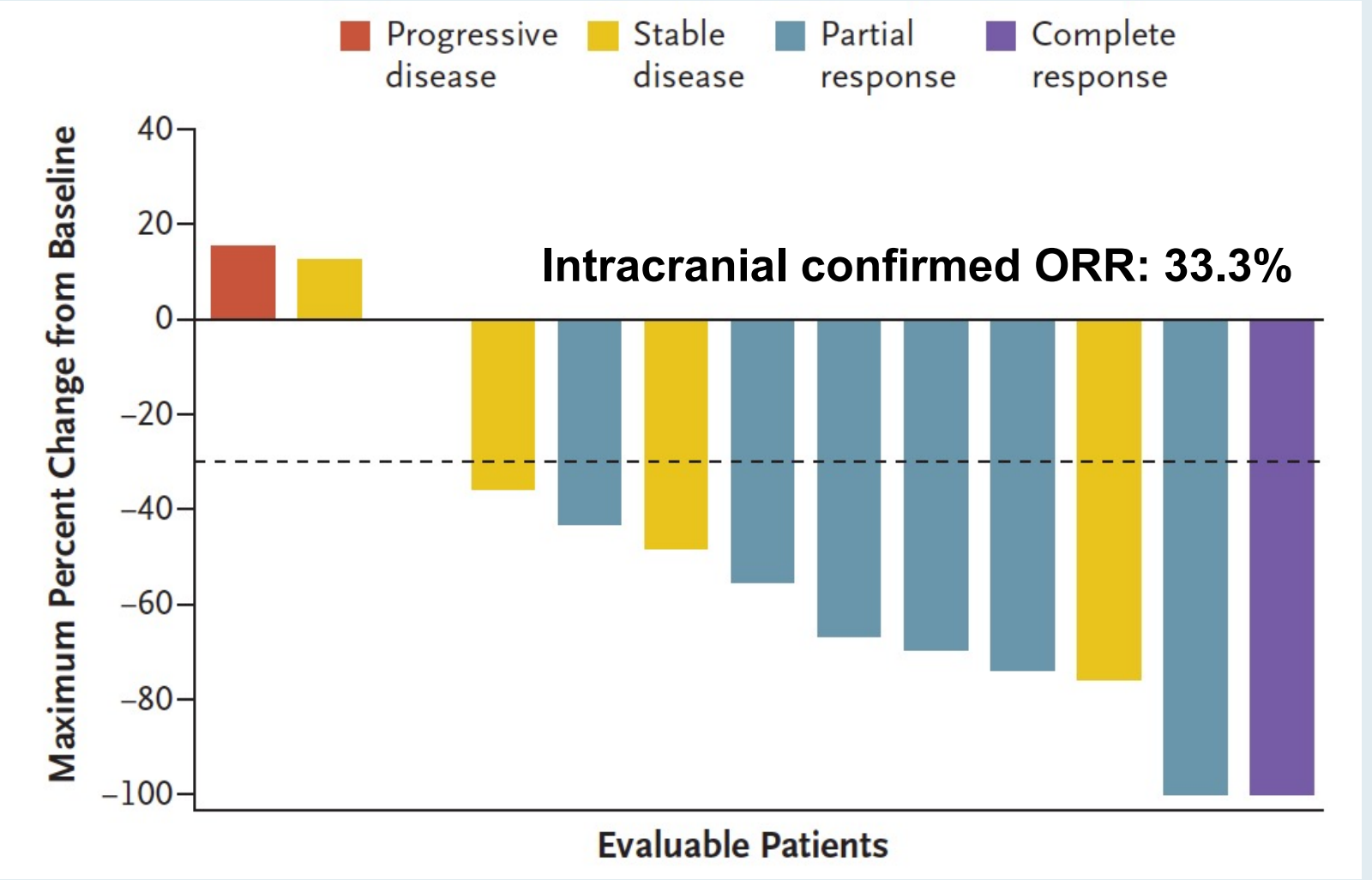
KRYSTAL-1: Response in a Phase II Study of Adagrasib for Advanced or Metastatic NSCLC Harboring a KRAS G12C Mutation



Jänne PA et al. *N Engl J Med* 2022;387(2):120-31.

RTP RESEARCH TO PRACTICE

KRYSTAL-1: Intracranial Responses with Adagrasib for Advanced or Metastatic NSCLC Harboring a KRAS G12C Mutation



Jänne PA et al. *N Engl J Med* 2022;387(2):120-31.

RTP RESEARCH TO PRACTICE

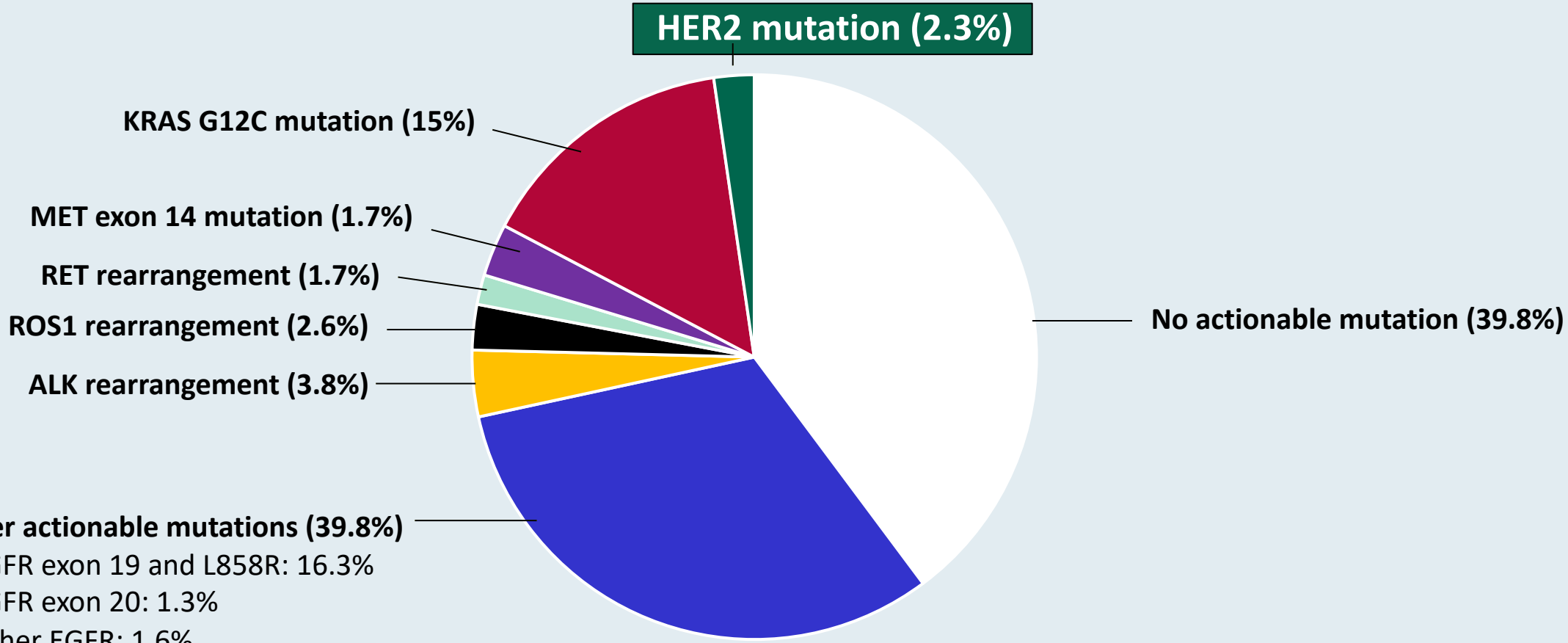
KRYSTAL-1: Select Treatment-Related Adverse Events with Adagrasib for Advanced or Metastatic NSCLC Harboring a KRAS G12C Mutation

Adverse event (N = 116)	Any grade	Grade ≥3
Diarrhea	70.7%	0.9%
Nausea	69.8%	4.3%
Fatigue	59.5%	6.9%
Vomiting	56.9%	0.9%
Blood creatinine increased	34.5%	0.9%
ALT increased	28.4%	5.2%
AST increased	26.7%	5.2%

Jänne PA et al. *N Engl J Med* 2022;387(2):120-31.

RTP RESEARCH TO PRACTICE

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;40:611-25.

RTP RESEARCH TO PRACTICE

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

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

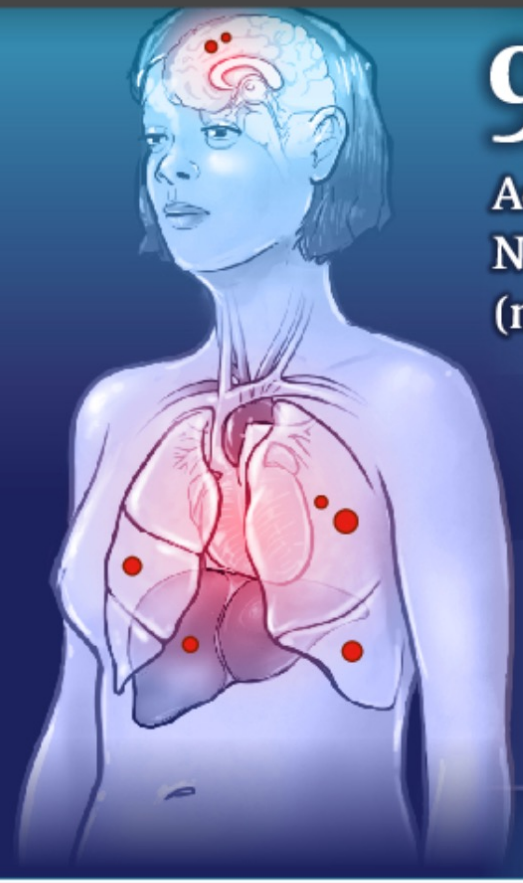
Trastuzumab Deruxtecan in *HER2*-Mutant Non–Small-Cell Lung Cancer

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*

RTP RESEARCH TO PRACTICE

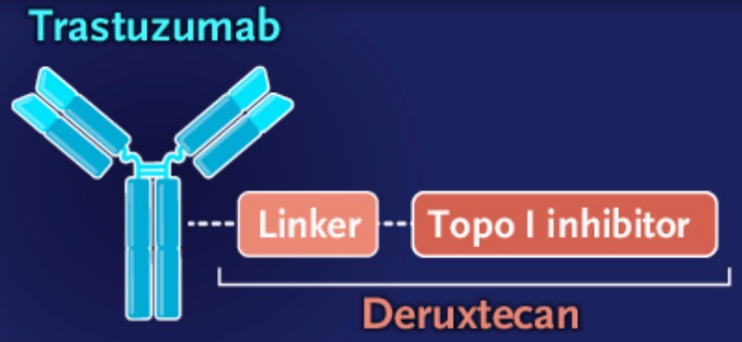
DESTINY-Lung01 Study

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.

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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.

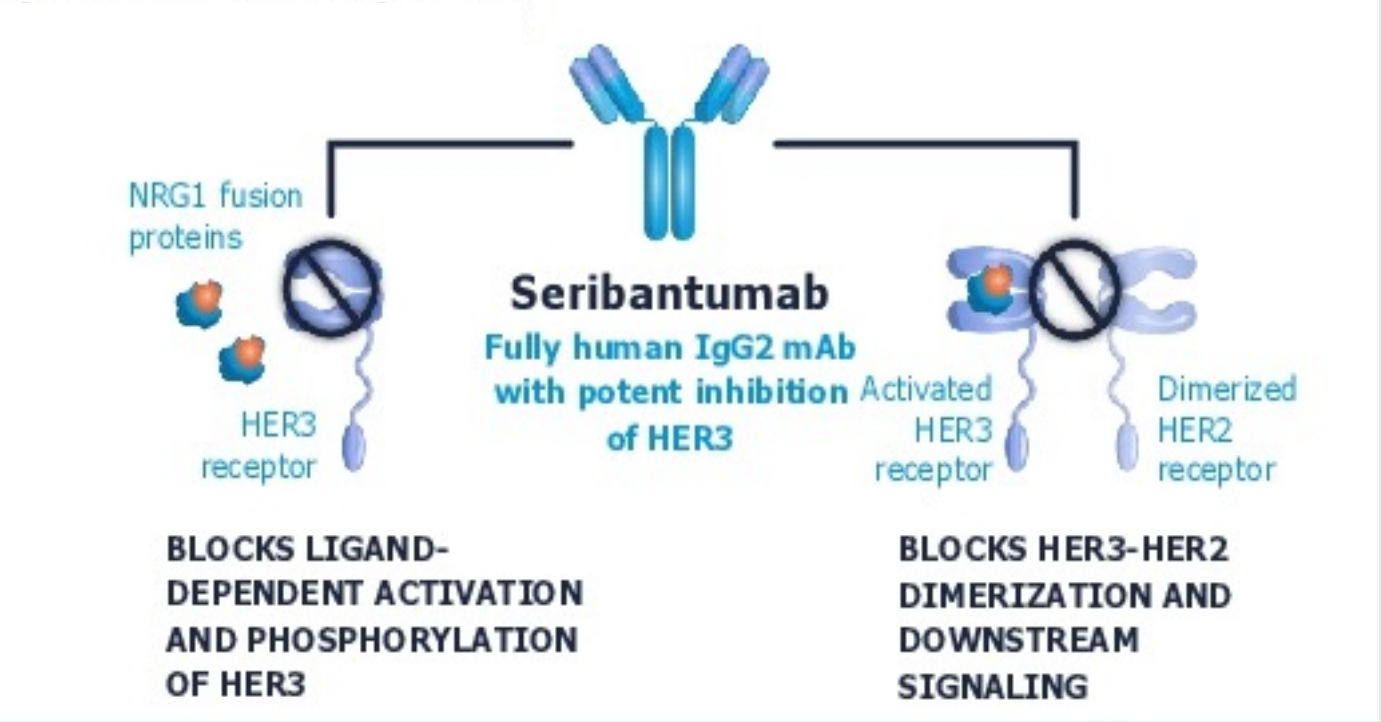
RTP RESEARCH TO PRACTICE

Other Potential Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung

RTP
RESEARCH
TO PRACTICE

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. Gastrointestinal Cancers Symposium 2021;Abstract TPS449.

RTP RESEARCH TO PRACTICE

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]

RTP RESEARCH TO PRACTICE

Best Overall Response with and Recommended Phase II Dose of Seribantumab for 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.

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

Abstract 3006

CRESTONE: Initial Efficacy and Safety of Seribantumab in Solid Tumors Harboring NRG1 Fusions

Daniel R. Carrizosa,[1] Mark E. Burkard,[2] Yasir Y. Elamin,[3] Jayesh Desai,[4] Shirish M. Gadgeel,[5] Jessica J. Lin,[6] Saiama N. Waqar,[7] David R. Spigel,[8] Young Kwang Chae,[9] Parneet K. Cheema,[10] Eric B. Haura,[11] Stephen V. Liu,[12] Danny Nguyen,[13] Karen L. Reckamp,[14] Frank Yung-Chin Tsai,[15] Valerie M. Jansen,[16] Alexander Drilon,[17] Sai-Hong Ignatius Ou,[18] D Ross Camidge,[19] Tejas Patil[19]

[1]Levine Cancer Institute/Atrium Health, Charlotte, NC; [2]University of Wisconsin Carbone Cancer Center, Madison, WI; [3]The University of Texas MD Anderson Cancer Center, Houston, TX; [4]Peter MacCallum Cancer Centre, Melbourne, Australia; [5]Henry Ford Cancer Institute/Henry Ford Health System, Detroit, MI; [6]Massachusetts General Hospital, Boston, MA; [7]Washington University School of Medicine, St. Louis, MO; [8]Sarah Cannon Research Institute, Nashville, TN; [9]Northwestern University, Chicago, IL; [10]William Osler Health System, Calgary, Canada; [11]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; [12]Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC; [13]City of Hope, Huntington Beach and Irvine, CA; [14]Cedars-Sinai Medical Center, Los Angeles, CA; [15]HonorHealth, Scottsdale, AZ; [16]Elevation Oncology, Inc. New York, NY; [17]Memorial Sloan Kettering Cancer Center, New York, NY; [18]Chao Family Comprehensive Cancer Center, University of CA-Irvine, Orange, CA; [19]University of Colorado Cancer Center, Aurora, CO

RTP RESEARCH TO PRACTICE

CRESTONE: An Ongoing Phase II Study of Seribantumab in Patients with Advanced Solid Tumors with NRG1 Fusions

Trial identifier: NCT04383210 (open)

Advanced solid tumor with an NRG1 gene fusion

Disease progression on or unresponsive to at least 1 prior standard therapy appropriate for 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

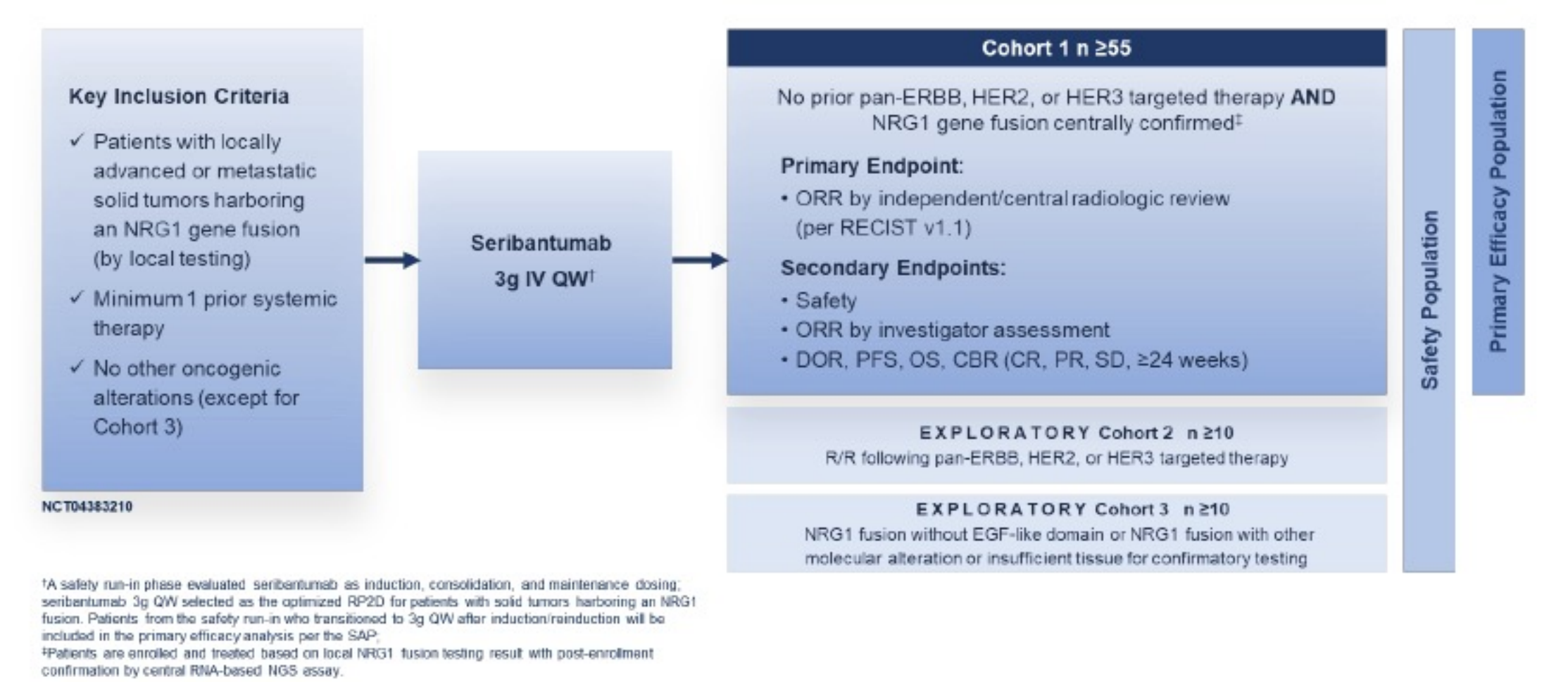
Seribantumab
1-h IV infusion at various doses once weekly, every 2 weeks and every 3 weeks, during the induction, consolidation and maintenance dosing phases, respectively

Patient Cohorts:
Cohort 1: A minimum of 55 adults with advanced solid tumors harboring NRG1 gene fusions who have received prior standard treatment, excluding prior ERBB-directed therapy
Cohort 2: Up to 10 adults with advanced solid tumors harboring NRG1 gene fusions who have received prior standard treatment, including prior ERBB-directed therapy
Cohort 3: Up to 10 adults with advanced solid tumors 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.

RTP RESEARCH TO PRACTICE

CRESTONE: A Phase II Study of Seribantumab for Patients with Advanced Solid Tumors Harboring NRG1 Fusions

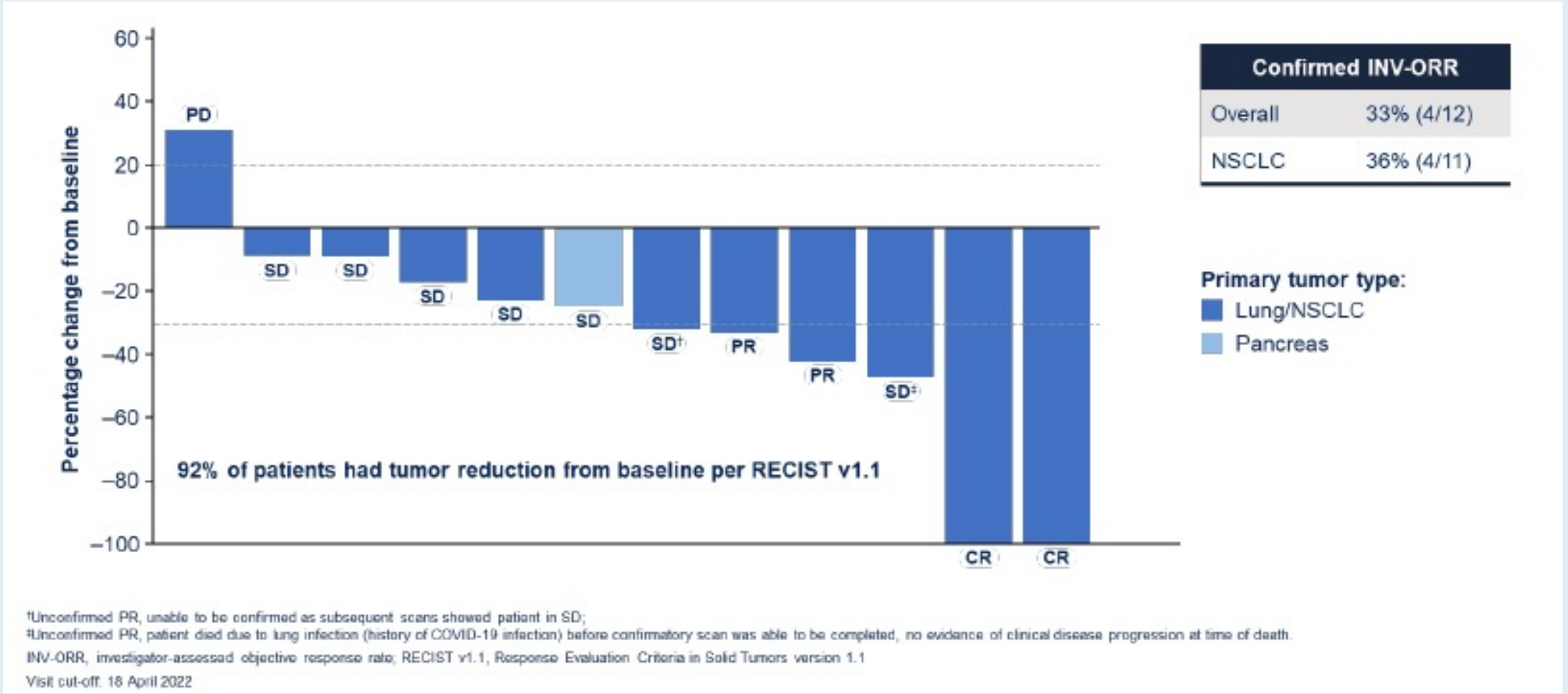


QW = once weekly; ORR = objective response rate; DOR = duration of response; PFS = progression-free survival; OS = overall survival; CBR = clinical benefit rate; CR = complete response; PR = partial response; SD = stable disease

Carrizosa DR et al. ASCO 2022;Abstract 3006.

RTP RESEARCH TO PRACTICE

CRESTONE: Efficacy of Seribantumab for Patients with Advanced Solid Tumors Harboring NRG1 Fusions



PD = progressive disease; SD = stable disease; PR = partial response; CR = complete response

- Median DoR has not been reached

Carrizosa DR et al. ASCO 2022;Abstract 3006.

CRESTONE: Select Treatment-Related Adverse Events with Seribantumab in Patients with Advanced Solid Tumors Harboring NRG1 Fusions

Treatment-related adverse event (N = 35)	Any grade	Grade ≥3
Patients with ≥1 AE	30 (86%)	2 (6%)
Diarrhea	14 (40%)	1 (3%)
Fatigue	10 (29%)	0
Rash	9 (26%)	0
Hypokalemia	3 (9%)	0

Carrizosa DR et al. ASCO 2022;Abstract 3006.

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Hepatobiliary Cancers

Thursday, July 28, 2022
5:00 PM – 6:00 PM ET

Faculty

Robin K Kelley, 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.

RTP
RESEARCH
TO PRACTICE