Year in Review:
Targeted Therapy for Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, May 8, 2024
5:00 PM – 6:00 PM ET

Faculty

Justin F Gainor, MD
Karen Reckamp, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

Faculty

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

Karen Reckamp, MD, MS
Director, Division of Medical Oncology
Associate Director of Clinical Research
Clinical Professor, Department of Medicine
Cedars-Sinai Cancer
Los Angeles, California

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, and Novartis.

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, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI Biopharma, a Sobi company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, 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, Kronos Bio Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology 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, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks 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.

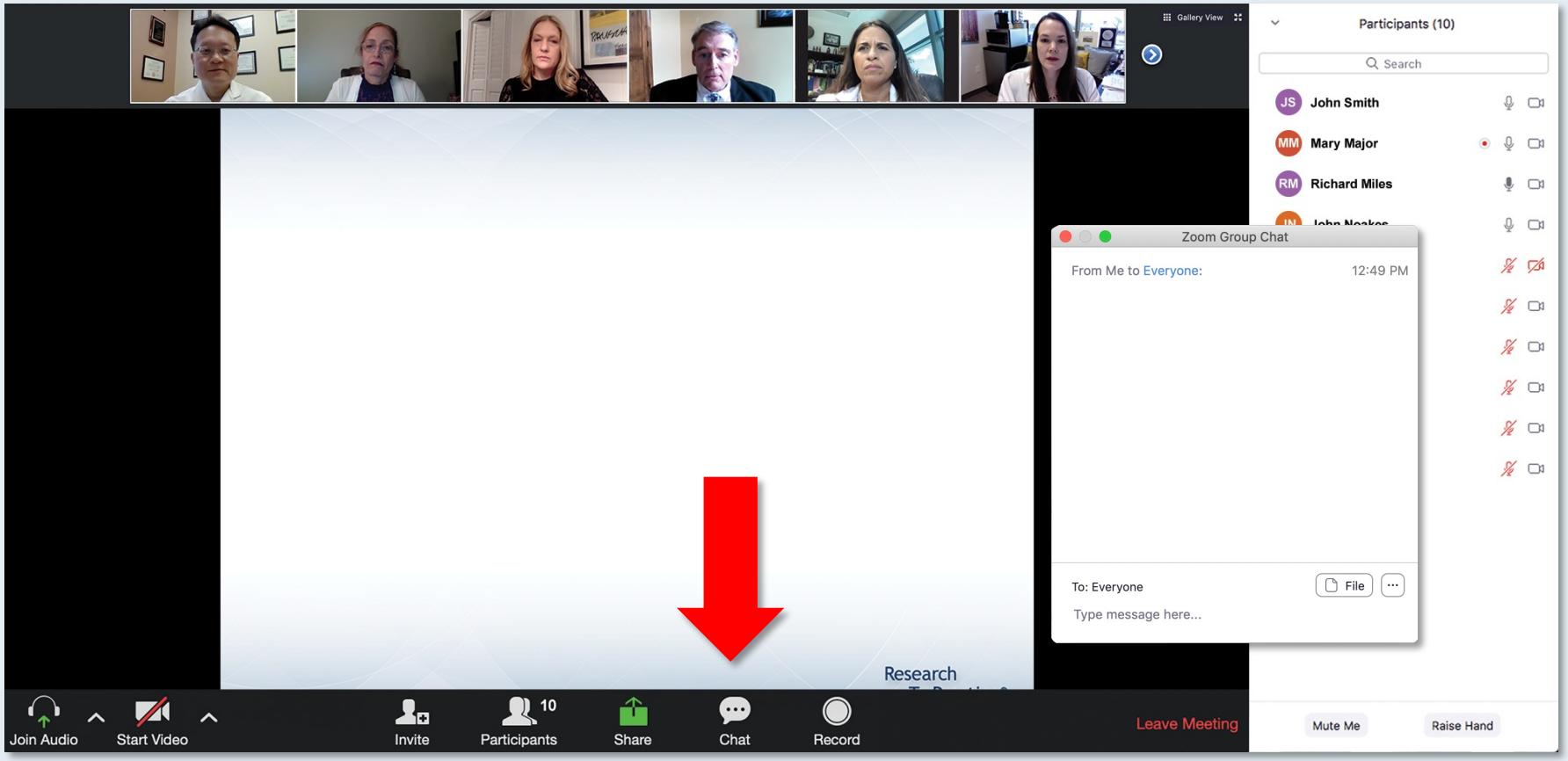
Dr Gainor — Disclosures

Advisory Committees	AI Proteins, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Genentech, a member of the Roche Group, Gilead Sciences Inc, ITeos Therapeutics, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Mariana Oncology, Merck, Merus, Mirati Therapeutics Inc, Moderna, Novartis, Novocure Inc, Nuvalent, Pfizer Inc, Sanofi, Silverback Therapeutics, Takeda Pharmaceuticals USA Inc
Consulting Agreements	Pfizer Inc, Merck, Novartis, Takeda Pharmaceuticals USA Inc
Contracted Research	Adaptimmune, ALX Oncology, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Bristol Myers Squibb, Genentech, a member of the Roche Group, Jounce Therapeutics, Merck, Moderna, NextPoint Therapeutics, Novartis, Palleon Pharmaceuticals

Dr Reckamp — Disclosures

Consulting Agreements	Amgen Inc, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Daiichi Sankyo Inc, EMD Serono Inc, Genentech, a member of the Roche Group, GSK, Janssen Biotech Inc, Lilly, Mirati Therapeutics Inc, Novocure Inc
Contracted Research	Blueprint Medicines, Calithera Biosciences, Daiichi Sankyo Inc, Elevation Oncology, Genentech, a member of the Roche Group, Janssen Biotech Inc

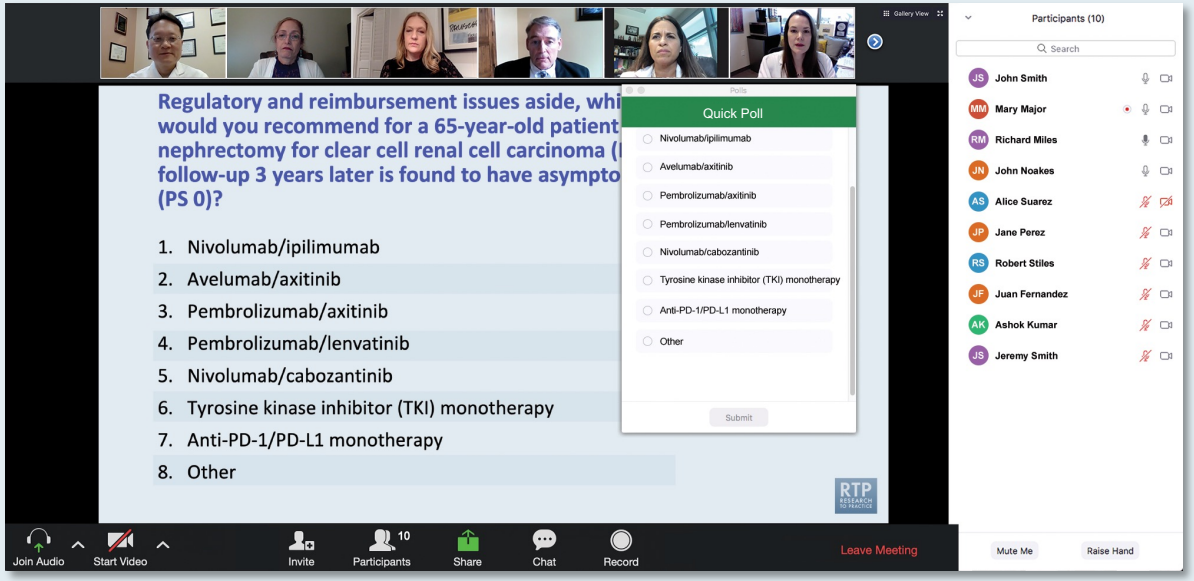
We Encourage Clinicians in Practice to Submit Questions



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

RTP RESEARCH TO PRACTICE

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



ONCOLOGY TODAY

WITH DR NEIL LOVE

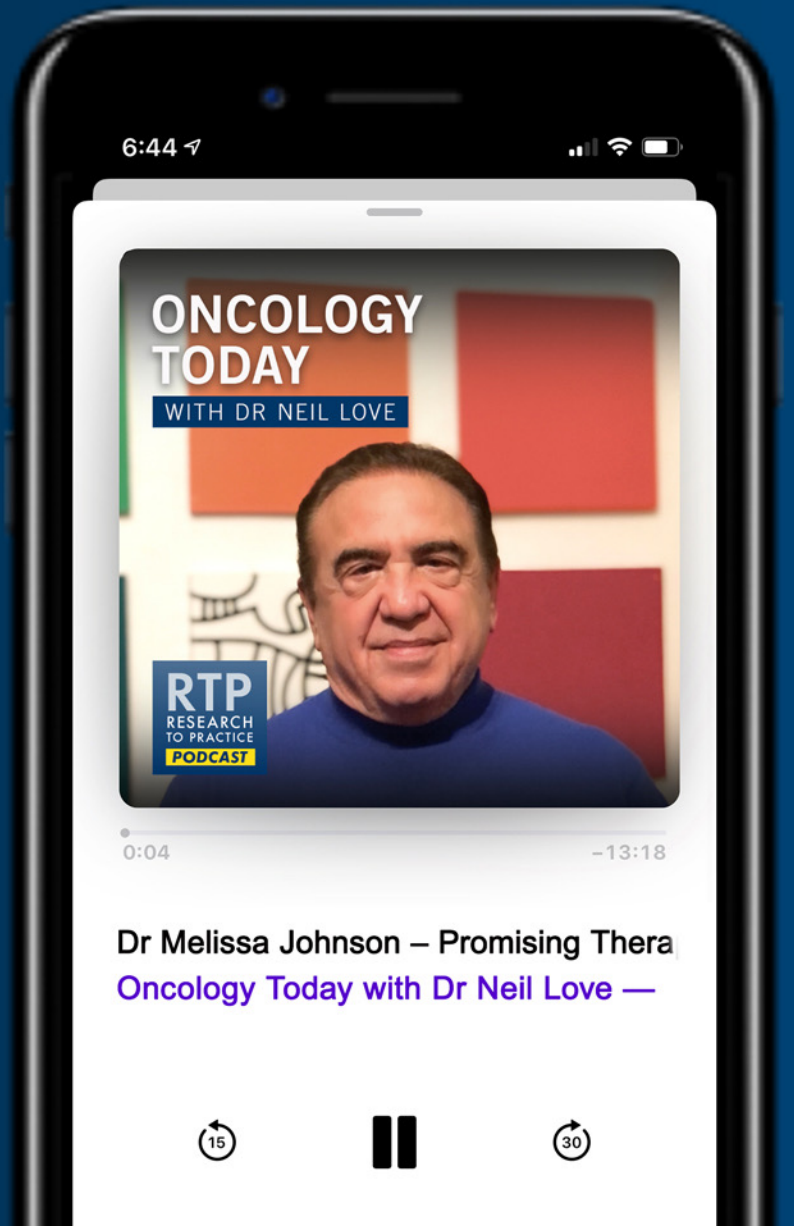
Promising Therapeutic Strategies for Patients with Progressive Metastatic Non-Small Cell Lung Cancer

DR MELISSA JOHNSON
SARAH CANNON RESEARCH INSTITUTE

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Year in Review: Myelofibrosis

A CME/MOC-Accredited Live Webinar

Tuesday, May 14, 2024
5:00 PM – 6:00 PM ET

Faculty

Aaron T Gerds, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

Hepatobiliary Cancers

Friday, May 31, 2024

11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)

Faculty

Robin K (Katie) Kelley, MD

Additional faculty to be announced

Antibody-Drug Conjugates in Lung Cancer

Saturday, June 1, 2024

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

Faculty

Rebecca S Heist, MD, MPH

Luis Paz-Ares, MD, PhD

Jacob Sands, MD

Non-Small Cell Lung Cancer with an EGFR Mutation

Friday, May 31, 2024

6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)

Faculty

Jonathan W Goldman, MD

Joel W Neal, MD, PhD

Zofia Piotrowska, MD, MHS

Joshua K Sabari, MD

Helena Yu, MD

Prostate Cancer

Saturday, June 1, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Neeraj Agarwal, MD, FASCO

Emmanuel S Antonarakis, MD

Andrew J Armstrong, MD, ScM

Tanya B Dorff, MD

Matthew R Smith, MD, PhD

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

Multiple Myeloma

Sunday, June 2, 2024

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

Faculty

To be announced

LIVE WEBCAST

Colorectal Cancer

Monday, June 3, 2024

7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

Faculty

John Strickler, MD

Additional faculty to be announced

Ovarian and Endometrial Cancer

Sunday, June 2, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Floor J Backes, MD
Mansoor Raza Mirza, MD
Ritu Salani, MD, MBA
Angeles Alvarez Secord, MD, MHSc

Metastatic Breast Cancer

Monday, June 3, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Aditya Bardia, MD, MPH
Harold J Burstein, MD, PhD
Professor Giuseppe Curigliano, MD, PhD
Sara A Hurvitz, MD, FACP
Joyce O'Shaughnessy, MD
Hope S Rugo, MD

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

LIVE WEBCAST

Bispecific Antibodies in Lymphoma

Tuesday, June 4, 2024

7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

Faculty

Tycel Phillips, MD

Additional faculty to be announced

Agenda

Introduction: Bringing Research into Practice

Module 1: EGFR Activating Mutations

Module 2: Exon 20 Insertion Mutations

Module 3: MET Exon 14 Alterations

Module 4: HER2 Mutations and Overexpression

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 Year in Review 2024

Year in Review:
Targeted Therapy for Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, May 8, 2024
5:00 PM – 6:00 PM ET

Faculty

Justin F Gainor, MD
Karen Reckamp, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

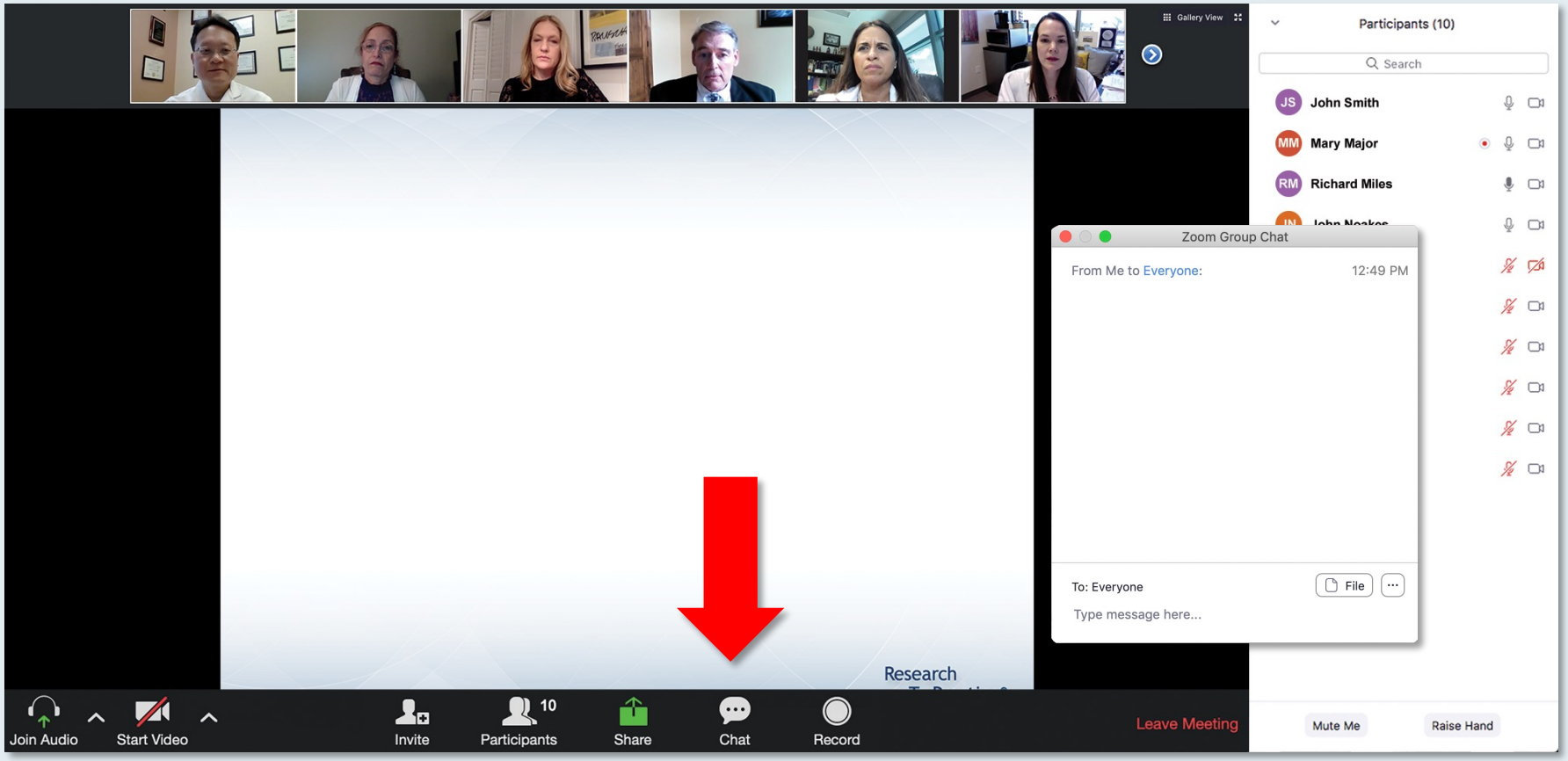
Faculty

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

Karen Reckamp, MD, MS
Director, Division of Medical Oncology
Associate Director of Clinical Research
Clinical Professor, Department of Medicine
Cedars-Sinai Cancer
Los Angeles, California

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

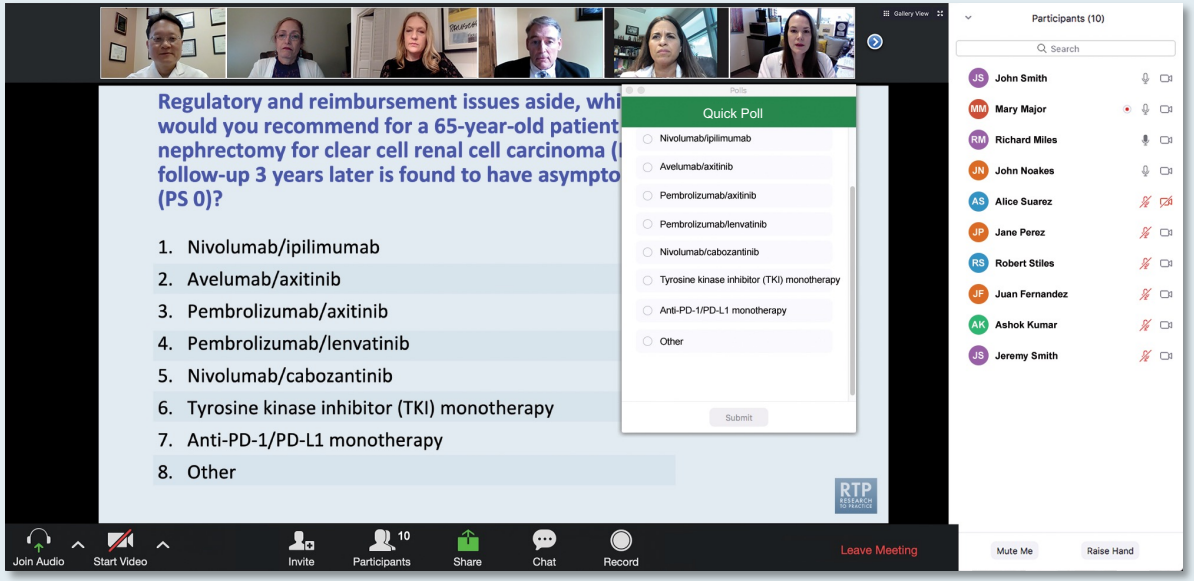
We Encourage Clinicians in Practice to Submit Questions



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

RTP RESEARCH TO PRACTICE

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



ONCOLOGY TODAY

WITH DR NEIL LOVE

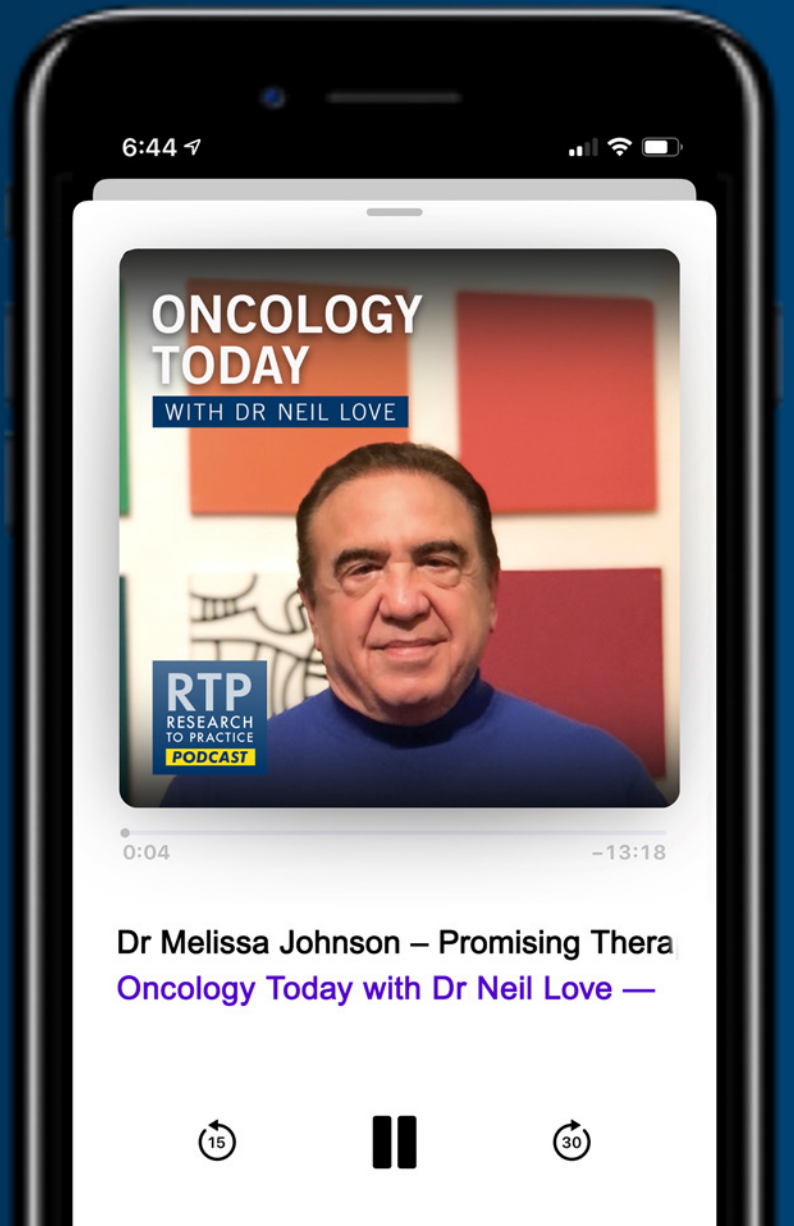
Promising Therapeutic Strategies for Patients with Progressive Metastatic Non-Small Cell Lung Cancer

DR MELISSA JOHNSON
SARAH CANNON RESEARCH INSTITUTE

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Year in Review: Myelofibrosis

A CME/MOC-Accredited Live Webinar

Tuesday, May 14, 2024
5:00 PM – 6:00 PM ET

Faculty

Aaron T Gerds, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

Hepatobiliary Cancers

Friday, May 31, 2024

11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)

Faculty

Robin K (Katie) Kelley, MD

Additional faculty to be announced

Antibody-Drug Conjugates in Lung Cancer

Saturday, June 1, 2024

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

Faculty

Rebecca S Heist, MD, MPH

Luis Paz-Ares, MD, PhD

Jacob Sands, MD

Non-Small Cell Lung Cancer with an EGFR Mutation

Friday, May 31, 2024

6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)

Faculty

Jonathan W Goldman, MD

Joel W Neal, MD, PhD

Zofia Piotrowska, MD, MHS

Joshua K Sabari, MD

Helena Yu, MD

Prostate Cancer

Saturday, June 1, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Neeraj Agarwal, MD, FASCO

Emmanuel S Antonarakis, MD

Andrew J Armstrong, MD, ScM

Tanya B Dorff, MD

Matthew R Smith, MD, PhD

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

Multiple Myeloma

Sunday, June 2, 2024

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

Faculty

To be announced

LIVE WEBCAST

Colorectal Cancer

Monday, June 3, 2024

7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

Faculty

John Strickler, MD

Additional faculty to be announced

Ovarian and Endometrial Cancer

Sunday, June 2, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Floor J Backes, MD
Mansoor Raza Mirza, MD
Ritu Salani, MD, MBA
Angeles Alvarez Secord, MD, MHSc

Metastatic Breast Cancer

Monday, June 3, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Aditya Bardia, MD, MPH
Harold J Burstein, MD, PhD
Professor Giuseppe Curigliano, MD, PhD
Sara A Hurvitz, MD, FACP
Joyce O'Shaughnessy, MD
Hope S Rugo, MD

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

LIVE WEBCAST

Bispecific Antibodies in Lymphoma

Tuesday, June 4, 2024

7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

Faculty

Tycel Phillips, MD

Additional faculty to be announced

Year in Review:
Targeted Therapy for Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, May 8, 2024
5:00 PM – 6:00 PM ET

Faculty

Justin F Gainor, MD
Karen Reckamp, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, and Novartis.

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 Gainor — Disclosures

Advisory Committees	AI Proteins, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Genentech, a member of the Roche Group, Gilead Sciences Inc, ITeos Therapeutics, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Mariana Oncology, Merck, Merus, Mirati Therapeutics Inc, Moderna, Novartis, Novocure Inc, Nuvalent, Pfizer Inc, Sanofi, Silverback Therapeutics, Takeda Pharmaceuticals USA Inc
Consulting Agreements	Pfizer Inc, Merck, Novartis, Takeda Pharmaceuticals USA Inc
Contracted Research	Adaptimmune, ALX Oncology, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Bristol Myers Squibb, Genentech, a member of the Roche Group, Jounce Therapeutics, Merck, Moderna, NextPoint Therapeutics, Novartis, Palleon Pharmaceuticals

Dr Reckamp — Disclosures

Consulting Agreements	Amgen Inc, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Daiichi Sankyo Inc, EMD Serono Inc, Genentech, a member of the Roche Group, GSK, Janssen Biotech Inc, Lilly, Mirati Therapeutics Inc, Novocure Inc
Contracted Research	Blueprint Medicines, Calithera Biosciences, Daiichi Sankyo Inc, Elevation Oncology, Genentech, a member of the Roche Group, Janssen Biotech Inc

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

Management of Non-small Cell Lung Cancer (NSCLC) with *EGFR* Mutation

Karen Reckamp, MD, MS
Professor of Medicine
Division Director, Medical Oncology
Cedars-Sinai
Los Angeles, CA

Cedars Sinai Cancer

cedars-sinai.org

Targeted Therapy in NSCLC

Justin F. Gainor, M.D.
Director, Center for Thoracic Cancer Program
Massachusetts General Hospital
Associate Professor
Harvard Medical School

MGH 1811 MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

Key Data Sets

Karen Reckamp, MD, MS

- Tsuboi M et al. **Overall survival** with **osimertinib** in **resected EGFR-mutated** NSCLC. *N Engl J Med* 2023;389(2):137-47.
- John T et al. Three-year safety, tolerability, and health-related quality of life outcomes of **adjuvant osimertinib** in patients **with resected Stage IB to IIIA EGFR-mutated** NSCLC: Updated analysis from the **phase 3 ADAURA** trial. *J Thorac Oncol* 2023;18(9):1209-21.
- Planchard D et al. **Osimertinib** with or without **chemotherapy** in **EGFR-mutated advanced** NSCLC. *N Engl J Med* 2023;389(21):1935-48.
- Jänne PA et al. **CNS efficacy** of **osimertinib** with or without **chemotherapy** in epidermal growth factor receptor-mutated **advanced** non-small-cell lung cancer. *J Clin Oncol* 2024;42(7):808-20.
- Cho BC et al. **Amivantamab plus lazertinib** vs **osimertinib** as **first-line** treatment in patients with **EGFR-mutated, advanced** non-small cell lung cancer (NSCLC): **Primary results** from **MARIPOSA**, a **phase III**, global, randomized, controlled trial. ESMO 2023;Abstract LBA14.

Key Data Sets

Karen Reckamp, MD, MS (continued)

- Passaro A et al. **Amivantamab** plus **chemotherapy** with and without **lazertinib** in **EGFR-mutant advanced** NSCLC after disease progression on osimertinib: **Primary results** from the **phase III MARIPOSA-2** study. *Ann Oncol* 2024;35(1):77-90.
- Yu HA et al. **HERTHENA-Lung01**, a phase II trial of **patritumab deruxtecan (HER3-DXd)** in epidermal growth factor receptor-mutated non-small-cell lung cancer after epidermal growth factor receptor tyrosine kinase inhibitor therapy and platinum-based chemotherapy. *J Clin Oncol* 2023;41(35):5363-75.
- Johnson ML et al. **Intracranial efficacy** of **HER3-DXd** in patients with **previously treated advanced EGFR-mutated** NSCLC: Results from **HERTHENA-Lung01**. ESMO 2023;Abstract 1319MO.
- Zhou C et al. **Amivantamab** plus **chemotherapy** in NSCLC with **EGFR exon 20 insertions**. *N Engl J Med* 2023;389(22):2039-51.
- Paz-Ares L et al. **TROPION-Lung05: Datopotamab deruxtecan (Dato-DXd)** in previously treated non-small cell lung cancer (NSCLC) with **actionable genomic alterations** (AGAs). ESMO 2023;Abstract 1314MO.

Key Data Sets

Justin F Gainor, MD

- Solomon BJ et al. **ALINA**: Efficacy and safety of **adjuvant alectinib** versus chemotherapy in patients with **early-stage ALK+** non-small cell lung cancer (NSCLC). ESMO 2023;Abstract LBA2.
- Goto K et al. **Trastuzumab deruxtecan** in patients with **HER2-mutant metastatic** non-small-cell lung cancer: **Primary results** from the randomized, phase II **DESTINY-Lung02** trial. *J Clin Oncol* 2023;41(31):4852-63.
- Li BT et al. **Trastuzumab deruxtecan (T-DXd)** in patients (pts) with **HER2 (ERBB2)-mutant** (HER2m) **metastatic** non–small cell lung cancer (NSCLC) with and without brain metastases (BMs): **Pooled analyses** from **DESTINY-Lung01** and **DESTINY-Lung02**. ESMO 2023;Abstract 1321MO
- Smit EF et al. **Trastuzumab deruxtecan** in patients with **metastatic** non-small-cell lung cancer (**DESTINY-Lung01**): **Primary results** of the HER2-overexpressing cohorts from a single-arm, phase 2 trial. *Lancet Oncol* 2024;25(4):439-54.
- Drilon A et al. Long-term efficacy and safety of **entrectinib** in **ROS1 fusion-positive** NSCLC. *JTO Clin Res Rep* 2022;3(6):100332.

Key Data Sets

Justin F Gainor, MD (continued)

- Drilon A et al. **Repotrectinib** in **ROS1 fusion-positive** non-small-cell lung cancer. *N Engl J Med* 2024;390(2):118-31.
- Zhou C et al. **First-line selpercatinib** or chemotherapy and pembrolizumab in **RET fusion-positive** NSCLC. *N Engl J Med* 2023;389(20):1839-50.
- Wolf J et al. Patient-reported outcomes in **capmatinib**-treated patients **with METex14-mutated advanced** NSCLC: Results from the **GEOMETRY mono-1** study. *Eur J Cancer* 2023;183:98-108.
- Mazieres J et al. **Tepotinib** treatment in patients with **MET exon 14-skipping** non-small cell lung cancer: Long-term follow-up of the **VISION** phase 2 nonrandomized clinical trial. *JAMA Oncol* 2023;9(9):1260-6.
- de Langen AJ et al. **Sotorasib** versus docetaxel for previously treated non-small-cell lung cancer with **KRASG12C mutation**: A randomised, open-label, **phase 3** trial. *Lancet* 2023;401(10378):733-46.
- Garassino MC et al. **KRYSTAL-7**: Efficacy and safety of **adagrasib** with pembrolizumab in patients with **treatment-naïve, advanced** non-small cell lung cancer (NSCLC) harboring a **KRASG12C mutation**. ESMO 2023;Abstract LBA65.

Agenda

Introduction: Bringing Research into Practice

Module 1: EGFR Activating Mutations

Module 2: Exon 20 Insertion Mutations

Module 3: MET Exon 14 Alterations

Module 4: HER2 Mutations and Overexpression

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction: Bringing Research into Practice

Module 1: EGFR Activating Mutations

Module 2: Exon 20 Insertion Mutations

Module 3: MET Exon 14 Alterations

Module 4: HER2 Mutations and Overexpression

ASCO Plenary Session: Sunday, June 2, 2024

Prospective randomized multicenter phase III trial comparing perioperative chemotherapy (FLOT protocol) to neoadjuvant chemoradiation (CROSS protocol) in patients with adenocarcinoma of the esophagus (ESOPEC trial).
Abstract: LBA1. Presenter: Jens Hoeppner, MD

Neoadjuvant nivolumab plus ipilimumab versus adjuvant nivolumab in macroscopic, resectable stage III melanoma: The phase 3 NADINA trial.
Abstract: LBA2. Presenter: Christian U Blank, MD, PhD

Comparative effectiveness trial of early palliative care delivered via telehealth versus in person among patients with advanced lung cancer.
Abstract: LBA3. Presenter: Joseph A Greer, PhD

Osimertinib (osi) after definitive chemoradiotherapy (CRT) in patients (pts) with unresectable stage (stg) III epidermal growth factor receptor-mutated (EGFRm) NSCLC: Primary results of the phase 3 LAURA study.
Abstract: LBA4. Presenter: Suresh S Ramalingam, MD

ADRIATIC: Durvalumab (D) as consolidation treatment (tx) for patients (pts) with limited-stage small-cell lung cancer (LS-SCLC).
Abstract: LBA5. Presenter: David R Spigel, MD

ASCO Plenary Series Program

Tuesday, April 30, 2024
3:00 PM – 4:00 PM (EST)

Melissa Lynne Johnson, MD—Chair
Sarah Cannon Research Institute
Welcome and Introduction

Stephen V. Liu, MD
Georgetown University
Unmet Needs in Lung Cancer: KRAS as a Target (and Why It Has Been So Difficult)

Yuankai Shi, MD, PhD
National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College
ABSTRACT 468214: A pivotal phase 2 single-arm study of glecirasib (JAB-21822) in patients with NSCLC harboring KRAS G12C mutation.

Julia K. Rotow, MD
Dana-Farber Cancer Institute
Discussion of Abstract 468214

Panel Question and Answer with Drs. Liu, Shi, and Rotow, Moderated by Dr. Johnson

FDA Grants Accelerated Approval to Fam-Trastuzumab-Deruxtecan-Nxki for Unresectable or Metastatic HER2-Positive Solid Tumors

Press Release – April 5, 2024

"…the Food and Drug Administration granted accelerated approval to fam-trastuzumab deruxtecan-nxki for adult patients with unresectable or metastatic HER2-positive (IHC3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.

Efficacy was evaluated in 192 adult patients with previously treated unresectable or metastatic HER2-positive (IHC 3+) solid tumors who were enrolled in one of three multicenter trials: DESTINY-PanTumor02 (NCT04482309), DESTINY-Lung01 (NCT03505710), and DESTINY-CRC02 (NCT04744831).

The major efficacy outcome measure in all three trials was confirmed objective response rate (ORR), and an additional efficacy outcome was duration of response (DOR). All outcomes were assessed by independent central review (ICR) based on RECIST v1.1. In DESTINY-PanTumor02, ORR was 51.4% (95% CI: 41.7, 61.0) and median DOR was 19.4 months (range 1.3, 27.9+). In DESTINY-Lung01, ORR was 52.9% (95% CI: 27.8, 77.0) and median DOR was 6.9 months (range 4.0, 11.7+). In DESTINY-CRC02, ORR was 46.9% (95% CI: 34.3, 59.8), and DOR was 5.5 months (range 1.3+, 9.7+)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-fam-trastuzumab-deruxtecan-nxki-unresectable-or-metastatic-her2

Evolving Trends in Targeted Therapy for NSCLC

- Adjuvant/neoadjuvant treatment (role of chemotherapy)
- After chemotherapy/radiation therapy for locally advanced NSCLC
- First-line treatment of metastatic disease
  - Versus chemotherapy
  - CNS activity
- Second-line treatment of metastatic disease

Agenda

Introduction: Bringing Research into Practice

Module 1: EGFR Activating Mutations

Module 2: Exon 20 Insertion Mutations

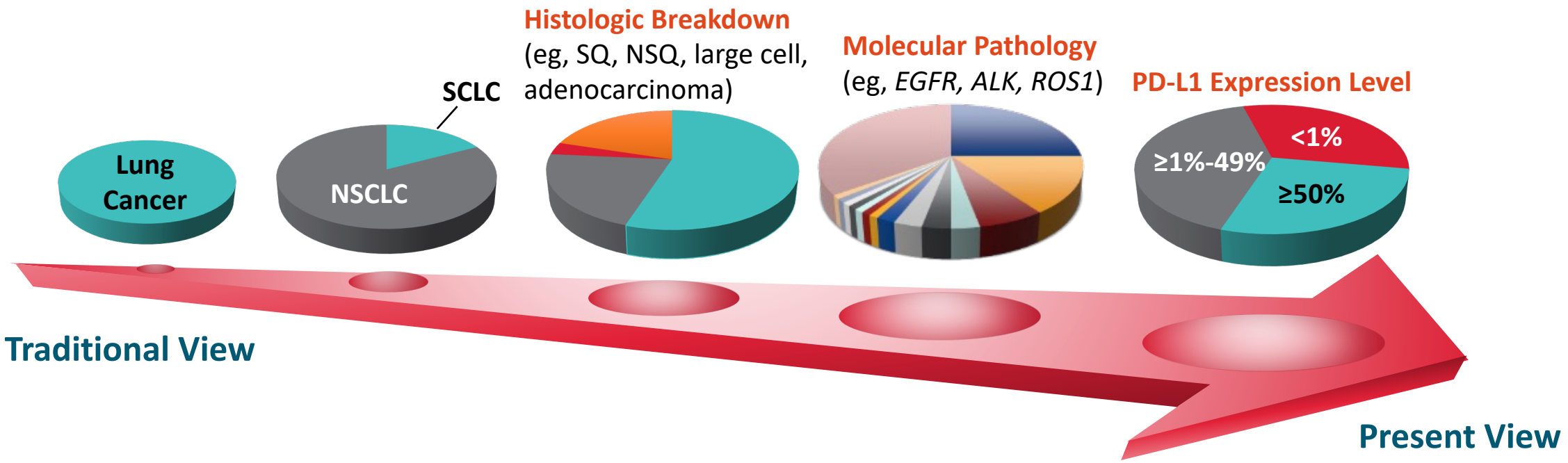
Module 3: MET Exon 14 Alterations

Module 4: HER2 Mutations and Overexpression

RTP RESEARCH TO PRACTICE

Evolution of Therapy in Lung Cancer

Not 1 disease, but many

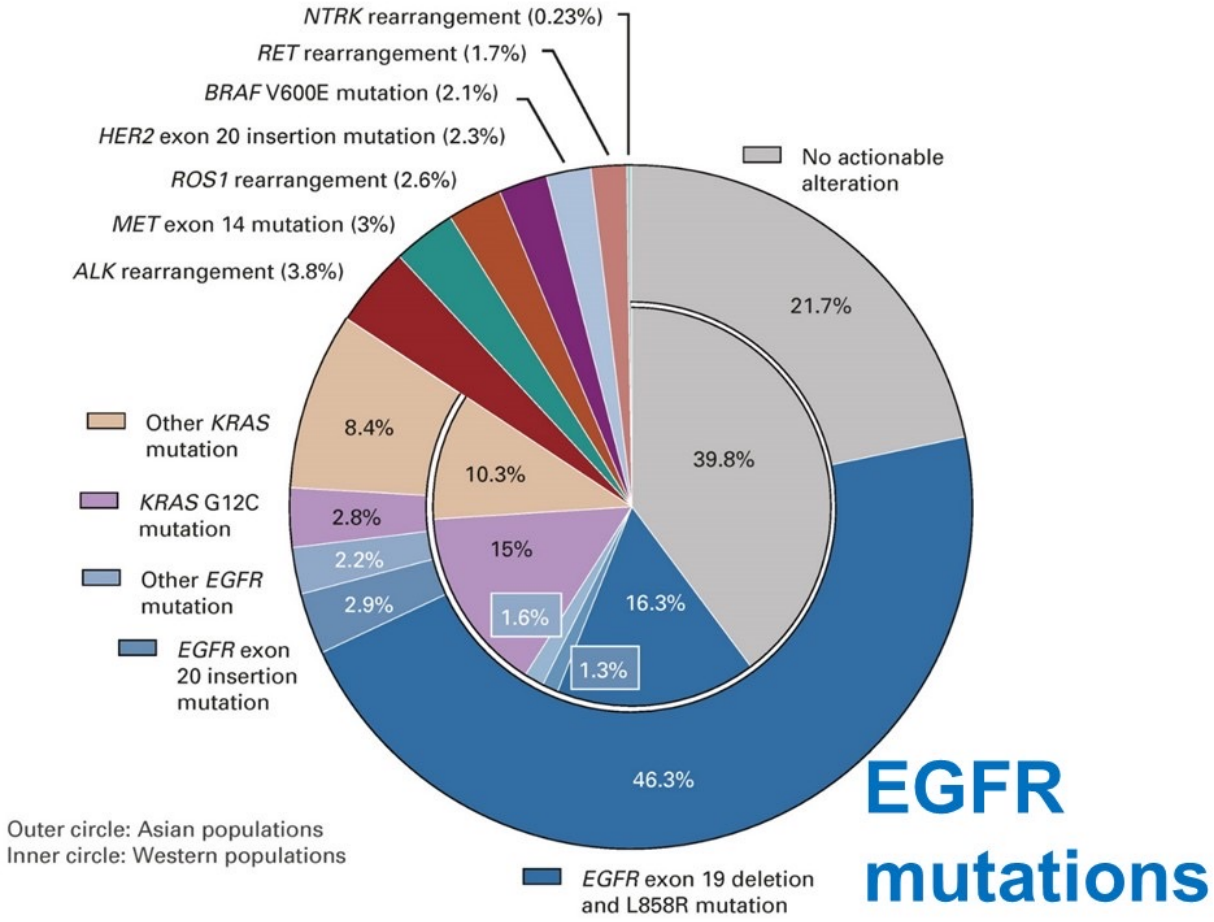


Cedars Sinai Cancer

Cooper. Pathology. 2011;43:103. Langer. JCO. 2010;28:5311. Galon. Immunity. 2013;39:11. Pao. Lancet Oncol. 2011;12:175. Krigsfeld. AACR 2017. Abstr CT143.

Courtesy of Karen Reckamp, MD, MS

Oncogenic drivers in NSCLC



EGFR mutations

EGFR mutations are found in 15-40% of tumors from patients with advanced NSCLC – similar frequency in early-stage disease.

Third Generation EGFR Tyrosine Kinase Inhibitor (TKI) osimertinib improved survival compared to first generation TKIs *eg* gefitinib or erlotinib

Tan JCO 2022; Soo ASCO 2023

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Osimertinib as Adjuvant or Consolidation Therapy

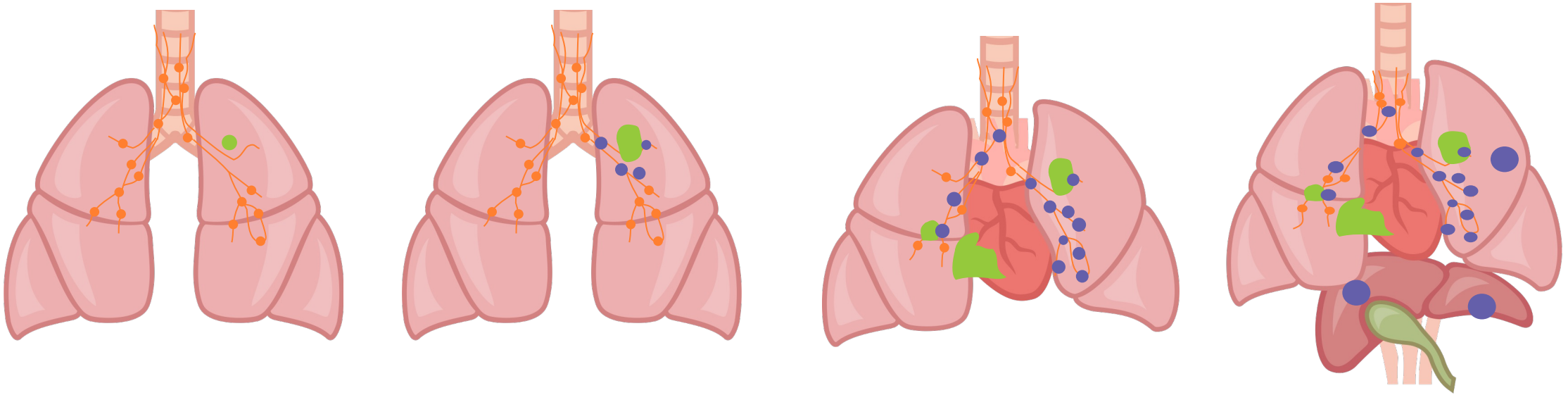
- Tsuboi M et al. **Overall survival** with **osimertinib** in **resected EGFR-mutated** NSCLC. *N Engl J Med* 2023;389(2):137-47.
- John T et al. Three-year safety, tolerability, and health-related quality of life outcomes of **adjuvant osimertinib** in patients **with resected Stage IB to IIIA EGFR-mutated** NSCLC: Updated analysis from the **phase 3 ADAURA** trial. *J Thorac Oncol* 2023;18(9):1209-21.

Moving Targeted Therapy Earlier in the Disease Course

December 18, 2020—Approval of adjuvant osimertinib

April 18, 2024—Approval of adjuvant alectinib

February 19, 2024—Press release, consolidation osimertinib improves PFS



Stage I **Stage II** **Stage III** **Stage IV**

Tumors Nonmetastatic lymph nodes Regional/local metastatic lymph nodes/distant metastases

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

ADAURA Phase III study design

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
≥18 years (Japan / Taiwan: ≥20)
WHO performance status 0 / 1
Confirmed primary non-squamous NSCLC Ex19del / L858R‡
Brain imaging, if not completed pre-operatively
Complete resection with negative margins§
Maximum interval between surgery and randomization:
- 10 weeks without adjuvant chemotherapy
- 26 weeks with adjuvant chemotherapy

Stratification by:
Stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
Race (Asian vs non-Asian)

Randomization 1:1 (N=682)

Osimertinib 80 mg, once daily

Placebo, once daily

Planned treatment duration: 3 years

Treatment continued until:
- Disease recurrence
- Treatment completion
- Discontinuation criterion met

Follow-up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

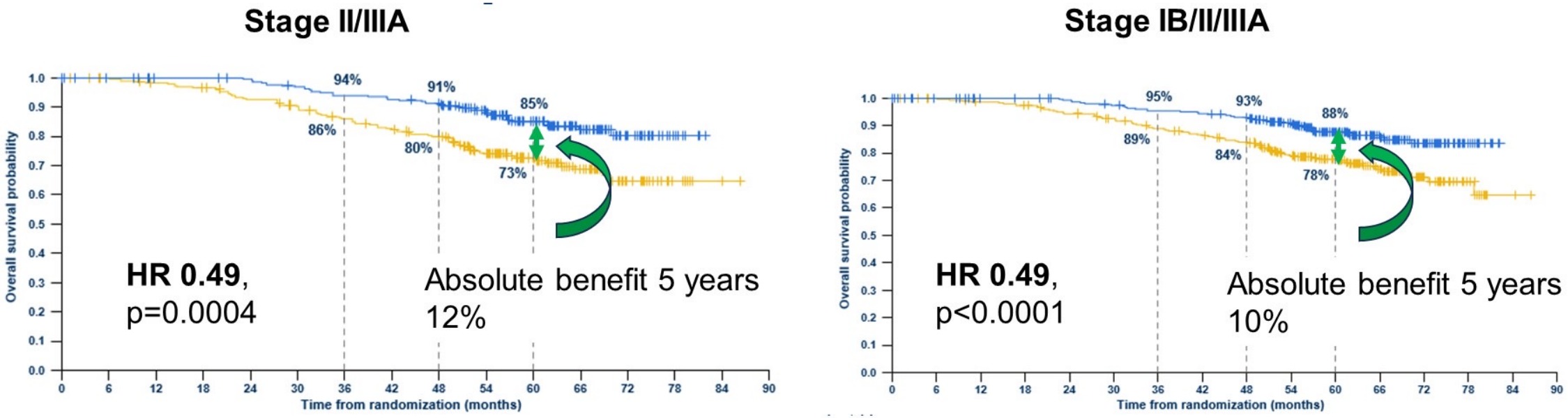
Endpoints
- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Herbst RS et al. ASCO 2023;
Tsuboi M et al. N Engl J Med 2023;389(2):137-47.

ADAURA—Osimertinib improves Overall Survival in resected *EGFR* mutation positive NSCLC



- **Early but Protocol pre-specified final analysis** with 21% maturity and ~60 months median follow up

- **Subsequent treatment:** More patients in placebo arm received EGFR TKIs (88% vs 76%)

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Herbst RS et al. ASCO 2023;
Tsuboi M et al. N Engl J Med 2023;389(2):137-47.

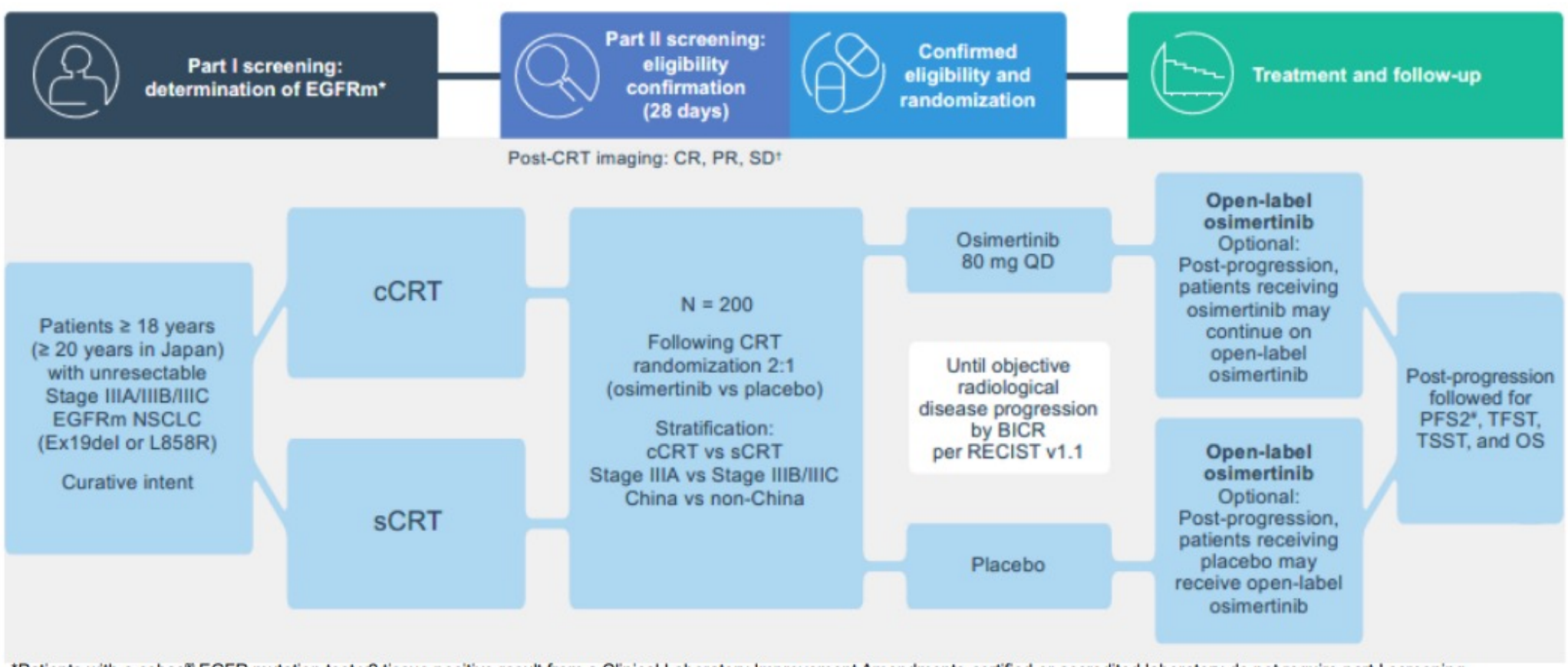
Questions remain after ADAURA

- **How can perioperative targeted therapy be optimized?**
  - What is the optimal duration?
  - Is chemotherapy necessary?
- **What is the optimal timing for TKI therapy?**
  - Neoadjuvant/adjuvant/both
- **Which patients benefit?**
  - Stage IA or locally advanced
  - All EGFR mutations or only Exon 19del/L858R
- **Can detection of MRD identify patients to intensify or de-intensify therapy?**
- **What are the mechanisms of resistance?**
  - What are the best therapies after relapse?

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

LAURA—Consolidation osimertinib in unresectable stage III NSCLC, NCT03521154



- Osimertinib demonstrated a statistically significant improvement in PFS for patients with unresectable, Stage III EGFRm NSCLC after CRT compared to placebo after CRT.
- Overall survival (OS) data showed a favourable trend for osimertinib, although data were not mature at the time of this analysis. The trial will continue to assess OS as a secondary endpoint.

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

LAURA—Consolidation osimertinib in unresectable stage III NSCLC, NCT03521154

Osimertinib demonstrated overwhelming efficacy benefit for patients with unresectable, Stage III EGFR-mutated lung cancer in LAURA Phase III trial

Osimertinib demonstrated a statistically significant improvement in PFS for patients with unresectable, Stage III EGFRm NSCLC after CRT compared to placebo after CRT.

Overall survival (OS) data showed a favourable trend for osimertinib, although data were not mature at the time of this analysis. The trial will continue to assess OS as a secondary endpoint.

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Evolving Treatment Landscape for *EGFR* mutant NSCLC

- Increased options for frontline therapy that improve efficacy with osimertinib and chemotherapy and amivantamab and lazertinib
- Paradigm for subsequent therapy is shifting with amivantamab and chemotherapy, patritumab deruxtecan and possibly datopotamab deruxtecan with differing mechanisms of action
- Adjuvant osimertinib improves OS for resected *EGFR* mutated NSCLC and should be used for most patients in this setting
- Consolidation osimertinib improves PFS for patients following CRT, await full results
- Biomarker testing should be done in the perioperative setting for the greatest benefit for all patients
- Biomarkers for patient selection will be essential

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

First-Line Therapy for Metastatic NSCLC with EGFR Activating Mutations

- Planchard D et al. **Osimertinib** with or without **chemotherapy** in **EGFR-mutated advanced** NSCLC. *N Engl J Med* 2023;389(21):1935-48.
- Jänne PA et al. **CNS efficacy** of **osimertinib** with or without **chemotherapy** in epidermal growth factor receptor-mutated **advanced** non-small-cell lung cancer. *J Clin Oncol* 2024;42(7):808-20.
- Cho BC et al. **Amivantamab plus lazertinib** vs **osimertinib** as **first-line** treatment in patients with **EGFR-mutated, advanced** non-small cell lung cancer (NSCLC): **Primary results** from **MARIPOSA**, a **phase III**, global, randomized, controlled trial. ESMO 2023;Abstract LBA14.

FLAURA2 Phase III—osimertinib +/- chemotherapy

Pts with untreated locally advanced / metastatic EGFRm NSCLC

Key inclusion criteria:

- Aged ≥18 years (Japan: ≥20 years)
- Pathologically confirmed non-squamous NSCLC
- Ex19del / L858R (local / central test)
- WHO PS 0 / 1
- No prior systemic therapy for advanced NSCLC

Osimertinib 80 mg (QD) + pemetrexed 500 mg/m² + carboplatin AUC5 or cisplatin 75 mg/m² (Q3W for 4 cycles), followed by maintenance osimertinib 80 mg (QD) + pemetrexed (Q3W)*
n=279

Randomisation 1:1 (N=557)

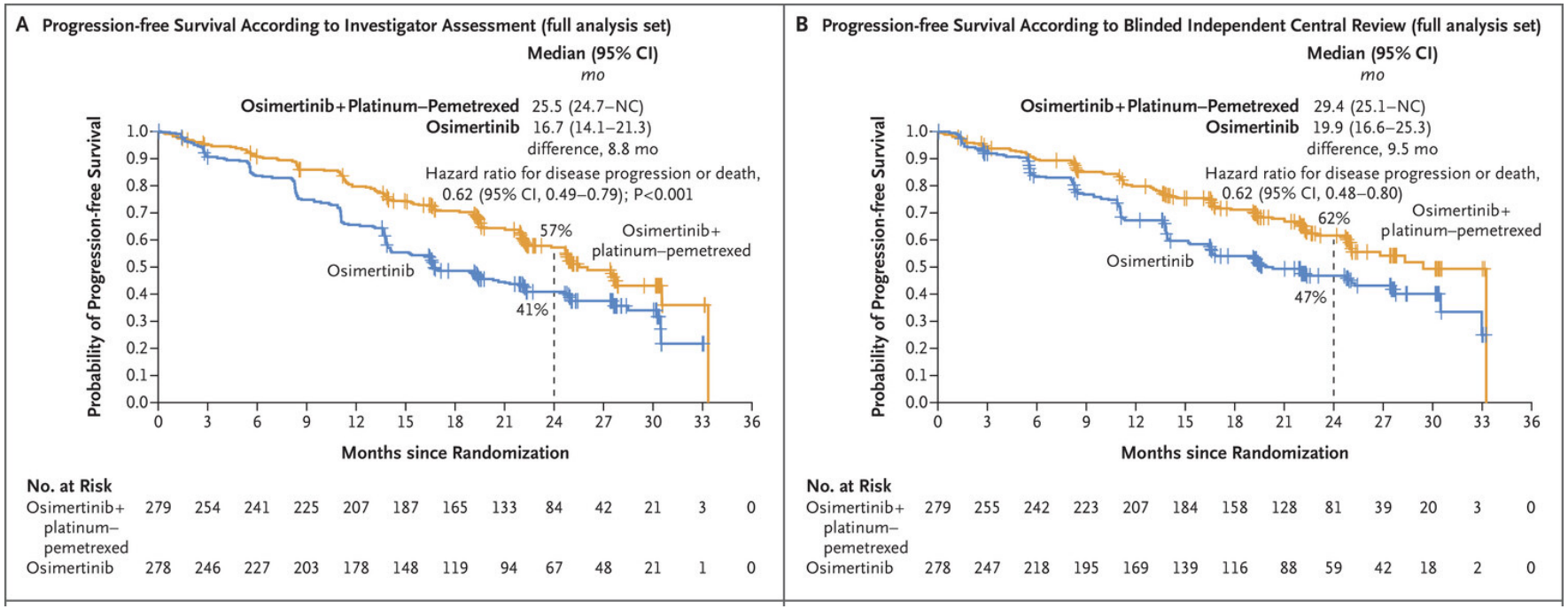
Osimertinib 80 mg (QD)
n=278

Primary endpoint:

- PFS by investigator assessment per RECIST 1.1†‡

Key secondary endpoints:

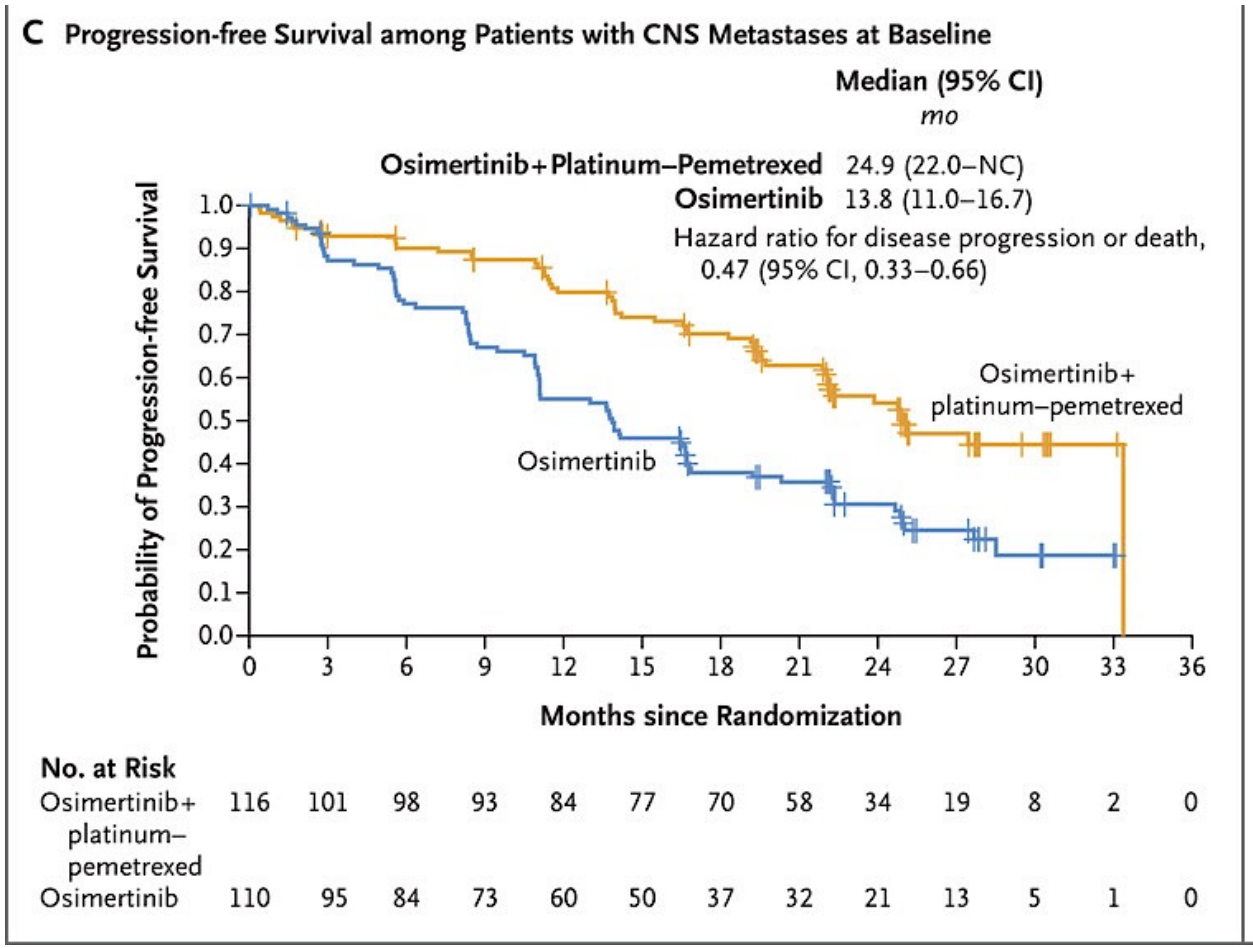
- OS, ORR, DoR, DCR, HRQoL, safety (AEs by CTCAE v5), PFS2†

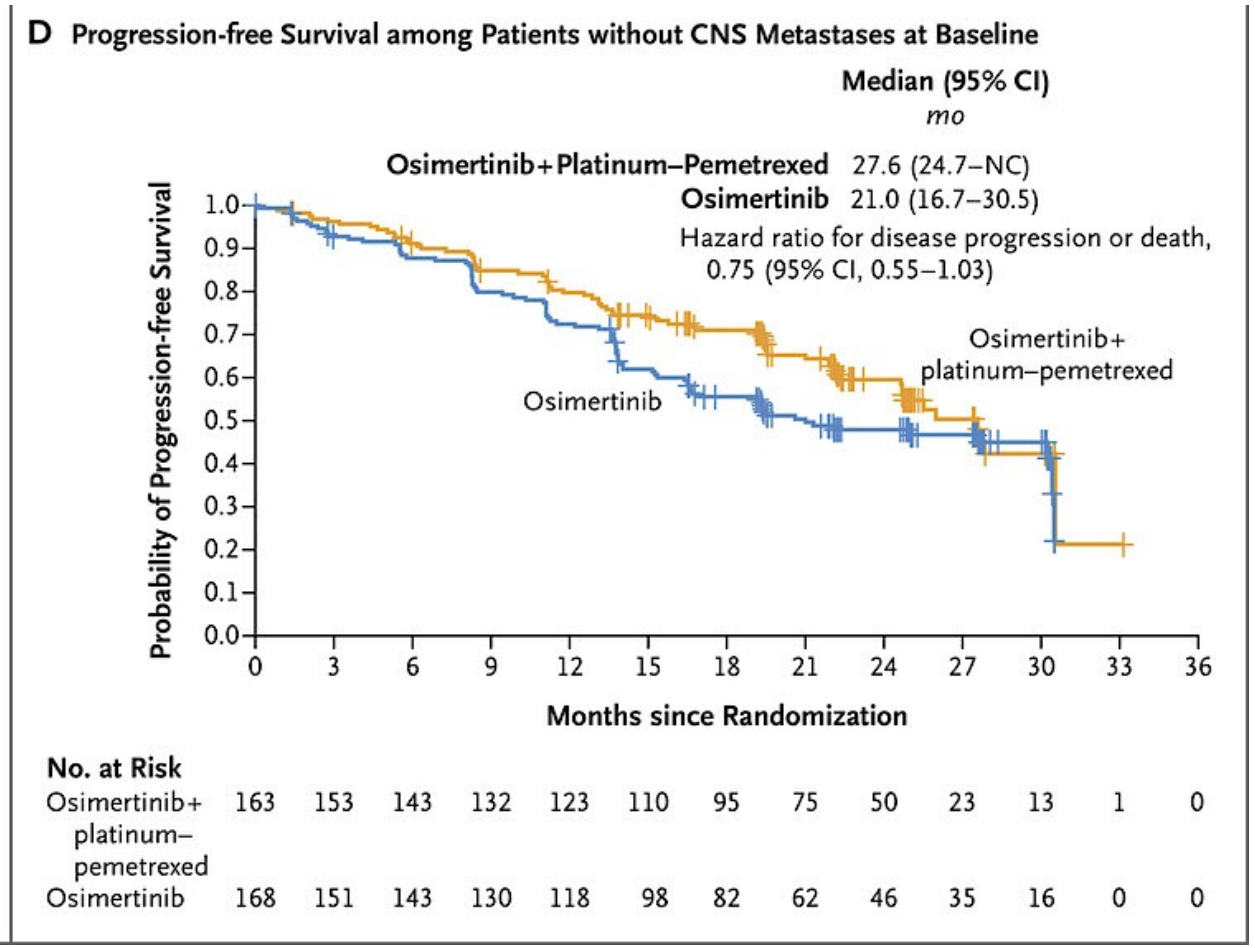


Courtesy of Karen Reckamp, MD, MS

Planchard et al. ESMO Open 2021;6:100271; Jänne PA et al. WCLC 2023; Planchard D et al. N Engl J Med 2023;389(21):1935-48.

FLAURA2—PFS with CNS metastases

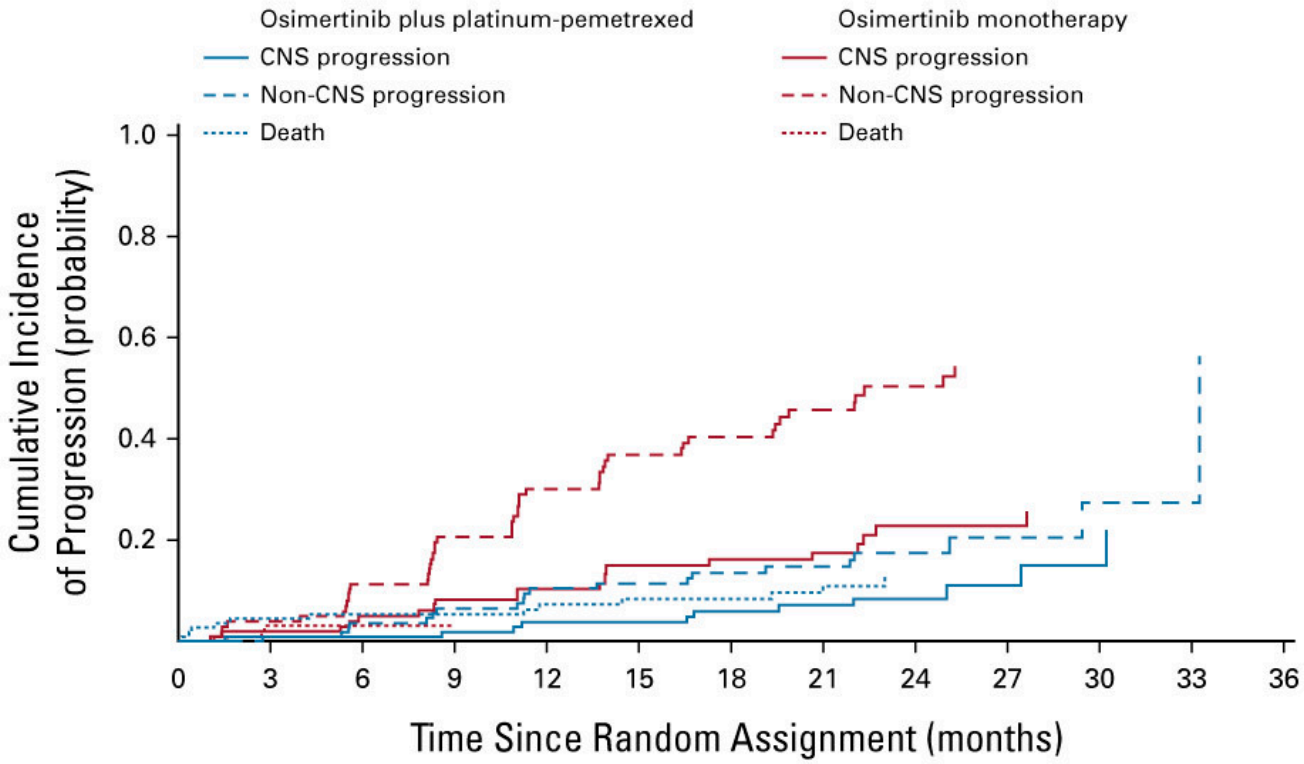


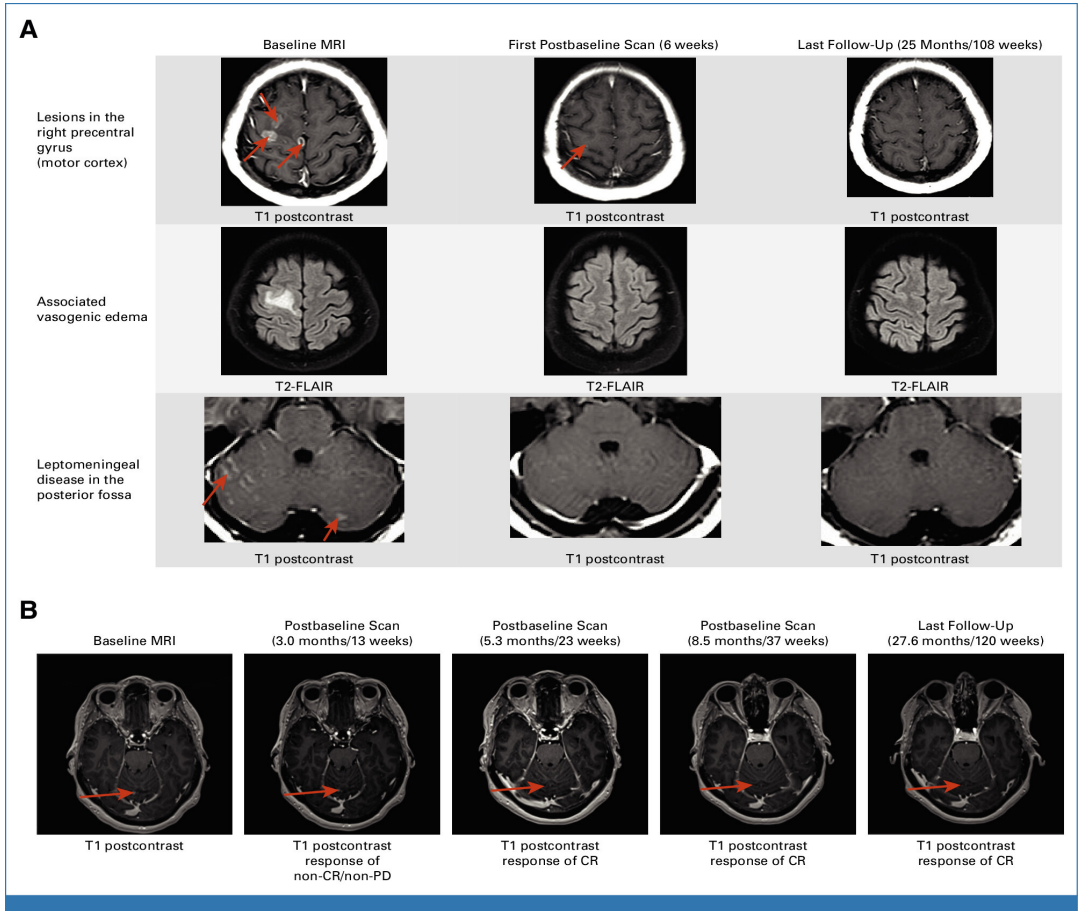


Courtesy of Karen Reckamp, MD, MS

Jänne PA et al. WCLC 2023. Planchard D et al. N Engl J Med 2023;389(21):1935-48.

FLAURA2—Lower Risk of CNS Progression





The estimated probability of observing CNS progression at 24 months was 9% (95% CI 4, 16) with osimertinib and the addition of CTx vs 23% (95% CI 14, 33) with osimertinib monotherapy

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Planchard D et al. ESMO 2023; Jänne PA et al. J Clin Oncol 2024;42(7):808-20.

MARIPOSA—Phase 3 Study Design

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858R
- ECOG PS 0 or 1

Stratification Factors

- *EGFR* mutation type (Ex19del or L858R)
- Asian race (yes or no)
- History of brain metastases[a] (yes or no)

Serial brain MRIs were required for all patients[a]

2:2:1 Randomization (N=1074)

Amivantamab + Lazertinib
(n=429; open-label)

Osimertinib
(n=429; blinded)

Lazertinib
(n=216; blinded)

Dosing (in 28-day cycles)
Amivantamab: 1050 mg (1400 mg if ≥80 kg) weekly for the first 4 weeks, then every 2 weeks
Lazertinib: 240 mg daily
Osimertinib: 80 mg daily

Primary endpoint of progression-free survival (PFS)[b] by BICR per RECIST v1.1:

- **Amivantamab + lazertinib** vs **osimertinib**

Secondary endpoints of amivantamab + lazertinib vs osimertinib:

- Overall survival (OS)[b]
- Objective response rate (ORR)
- Duration of response (DoR)
- PFS after first subsequent therapy (PFS2)
- Symptomatic PFS[c]
- Intracranial PFS[c]
- Safety

Lazertinib monotherapy arm was included to assess the contribution of components

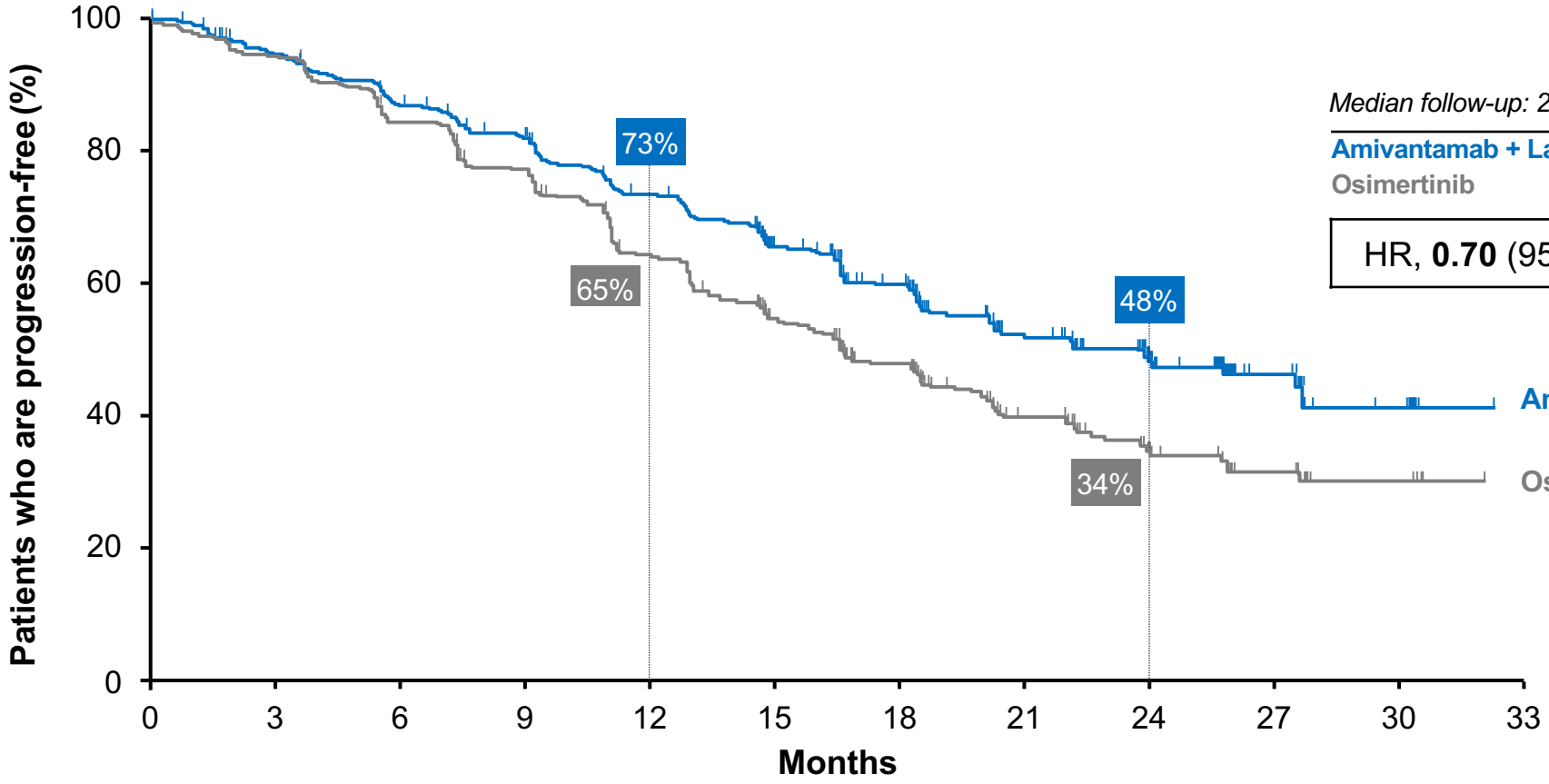
Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Cho BC et al ESMO 2023

MARIPOSA—Progression-free survival

Amivantamab + lazertinib reduced the risk of progression or death by 30% and improved median PFS by 7.1 months



Median follow-up: 22.0 months	**Median PFS (95% CI)**
Amivantamab + Lazertinib	23.7 mo (19.1–27.7)
Osimertinib	16.6 mo (14.8–18.5)

HR, **0.70** (95% CI, 0.58–0.85); *P*<0.001

No. at risk											
Amivantamab + Lazertinib	429	391	357	332	291	244	194	106	60	33	8	0
Osimertinib	429	404	358	325	266	205	160	90	48	28	10	0

[a]At time of the prespecified final PFS analysis, there were a total of 444 PFS events in the amivantamab + lazertinib and osimertinib arms combined.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; mo, months; PFS, progression-free survival.

Cedars Sinai Cancer

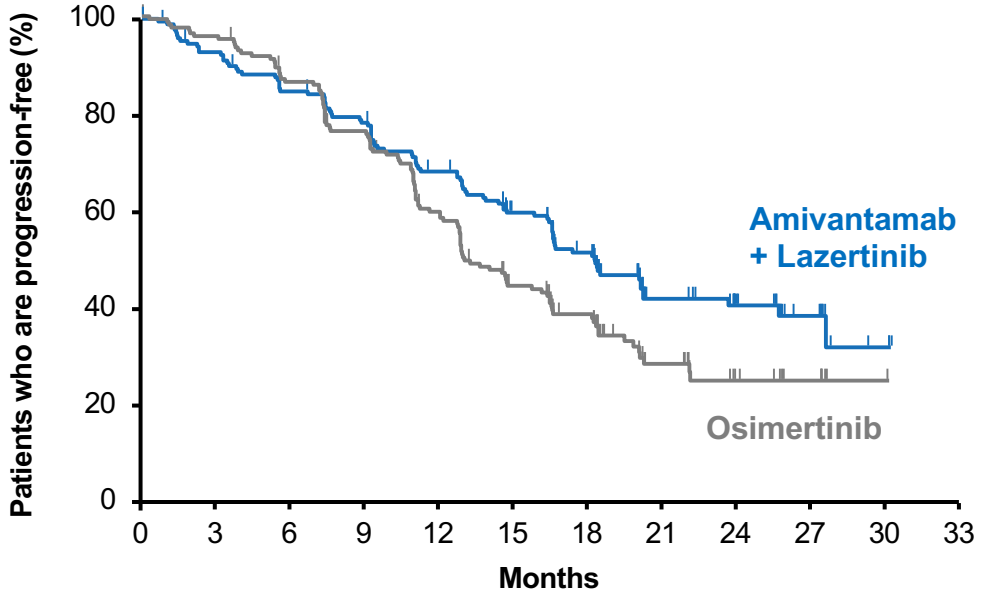
Courtesy of Karen Reckamp, MD, MS

Cho BC et al ESMO 2023

MARIPOSA—PFS Benefit With or Without Brain Metastases

With History of Brain Metastases	Median PFS (95% CI)
Amivantamab + Lazertinib	18.3 mo (16.6–23.7)
Osimertinib	13.0 mo (12.2–16.4)

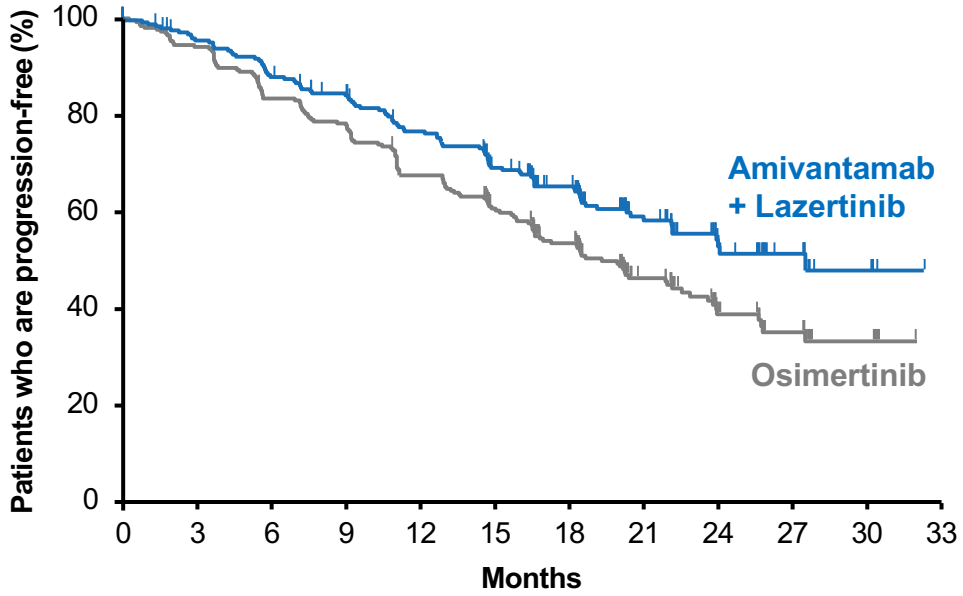
HR, **0.69** (95% CI, 0.53–0.92)



No. at risk												
Amivantamab + Lazertinib	178	162	146	134	115	92	71	34	24	12	3	0
Osimertinib	172	164	146	126	95	64	47	21	11	6	1	0

Without History of Brain Metastases	Median PFS (95% CI)
Amivantamab + Lazertinib	27.5 mo (22.1–NE)
Osimertinib	19.9 mo (16.6–22.9)

HR, **0.69** (95% CI, 0.53–0.89)



No. at risk												
Amivantamab + Lazertinib	251	229	211	198	176	152	123	72	36	21	5	0
Osimertinib	257	240	212	199	171	141	113	69	37	22	9	0

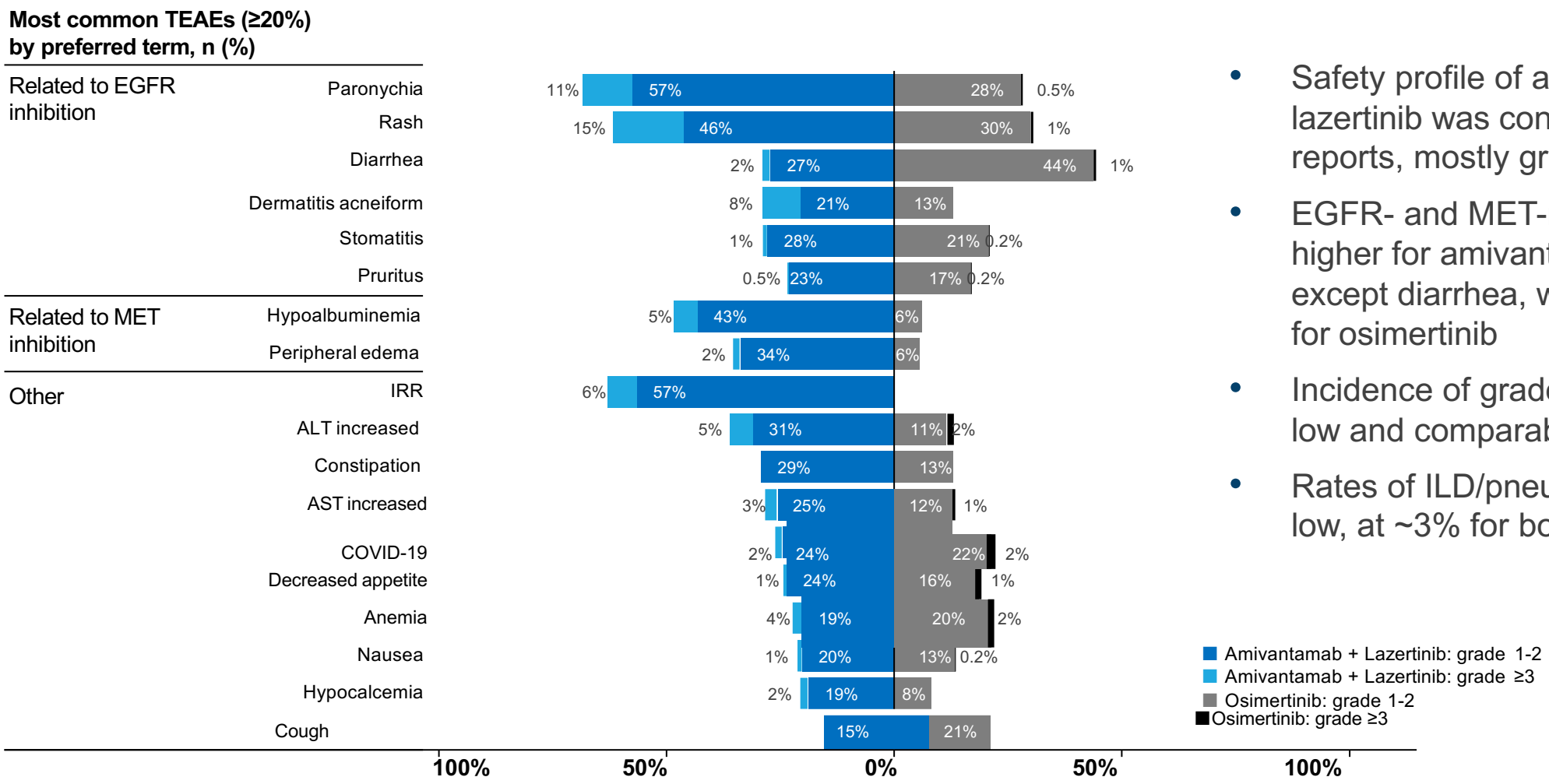
Cedars Sinai Cancer

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; mo, months; NE, not estimable; PFS, progression-free survival.

Courtesy of Karen Reckamp, MD, MS

Cho BC et al ESMO 2023

MARIPOSA—Safety Profile



- Safety profile of amivantamab + lazertinib was consistent with prior reports, mostly grades 1-2
- EGFR- and MET-related AEs were higher for amivantamab + lazertinib except diarrhea, which was higher for osimertinib
- Incidence of grade 4-5 AEs was low and comparable between arms
- Rates of ILD/pneumonitis remained low, at ~3% for both arms

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; EGFR, epidermal growth factor receptor; ILD, interstitial lung disease (includes pneumonitis); IRR, infusion-related reaction; TEAE, treatment-emergent AE.

Cedars Sinai Cancer

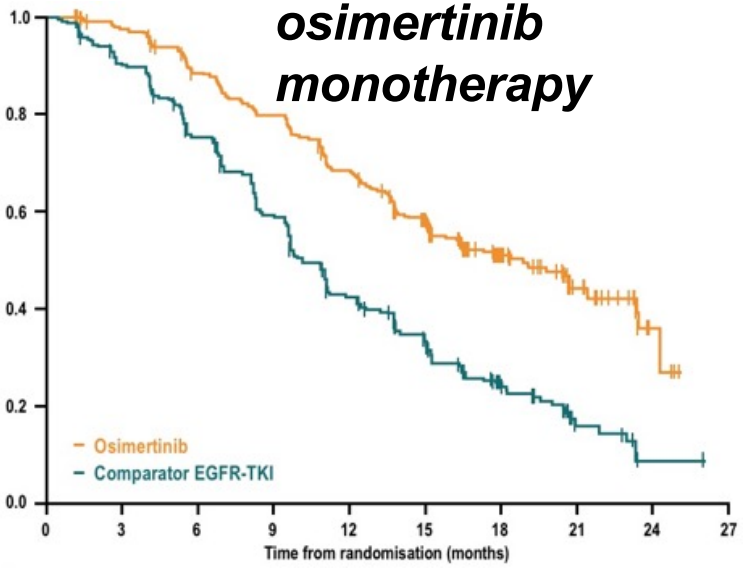
Courtesy of Karen Reckamp, MD, MS

Cho BC et al ESMO 2023

Considering options for frontline treatment of advanced *EGFR*+ NSCLC

FLAURA

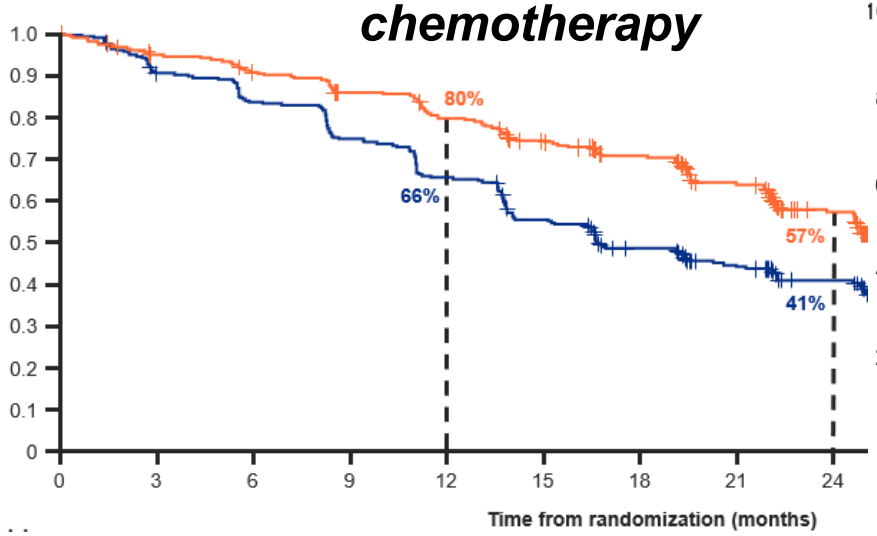
osimertinib monotherapy



Progression-free survival
Osimertinib 18.9 mo
1st gen TKI 10.2 mo

FLAURA2

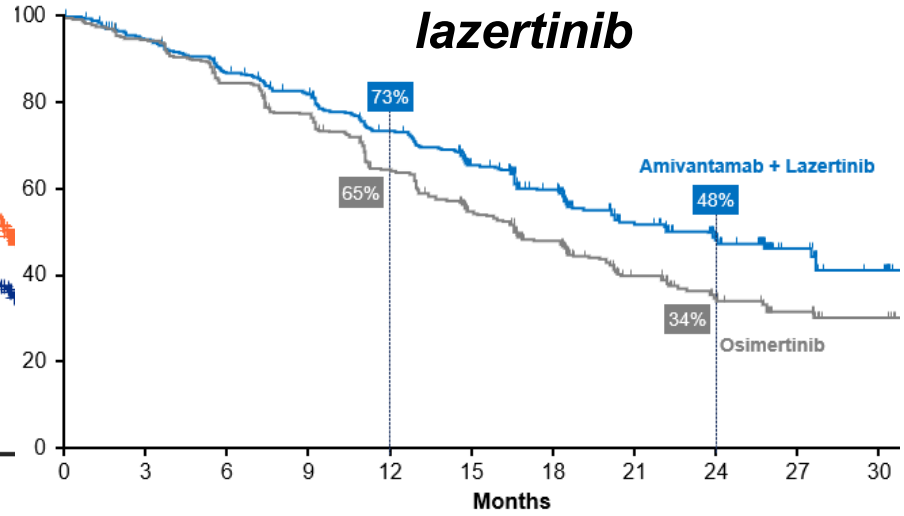
osimertinib + chemotherapy



Progression-free survival
Osi+chemo 25.5 mo
Osimertinib 16.7 mo

MARIPOSA

amivantamab + lazertinib



Progression-free survival
Ami+Laz 23.7 mo
Osimertinib 16.6 mo

- Multiple options for front line, improvement in PFS without detriment in OS
- Increased cost and toxicity compared to osimertinib alone
- Selection of patients will be important (brain mets, disease burden, ctDNA…)

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Advanced NSCLC with an EGFR Mutation After Disease Progression on Osimertinib

- Passaro A et al. **Amivantamab** plus **chemotherapy** with and without **lazertinib** in **EGFR-mutant advanced** NSCLC after disease progression on osimertinib: **Primary results** from the **phase III MARIPOSA-2** study. *Ann Oncol* 2024;35(1):77-90.

MARIPOSA-2—Phase 3 Study Design

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Documented *EGFR* Ex19del or L858R
- *Progressed on or after osimertinib monotherapy (as most recent line)*
- ECOG PS 0 or 1
- Stable brain metastases were allowed; radiation/definitive therapy was not required (untreated)

Stratification Factors

- Osimertinib line of therapy (1st vs 2nd)
- Asian race (yes or no)
- History of brain metastases (yes or no)

2:2:1 Randomization (N=657)

Serial brain MRIs were required for all patients[a]

Amivantamab-Lazertinib-Chemotherapy (n=263)

Chemotherapy (n=263)

Amivantamab-Chemotherapy (n=131)

Dosing (in 21-day cycles)

Amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) every 3 weeks starting at Cycle 3 (week 7)

Lazertinib: 240 mg daily starting after completion of carboplatin[b]

Chemotherapy administered at the beginning of every cycle:

- **Carboplatin:** AUC5 for the first 4 cycles
- **Pemetrexed:** 500 mg/m^2 until disease progression

Dual primary endpoint of PFS[c] by BICR per RECIST v1.1:

- **Amivantamab-Lazertinib-Chemotherapy** vs **Chemotherapy**
- **Amivantamab-Chemotherapy** vs **Chemotherapy**

Secondary endpoints:

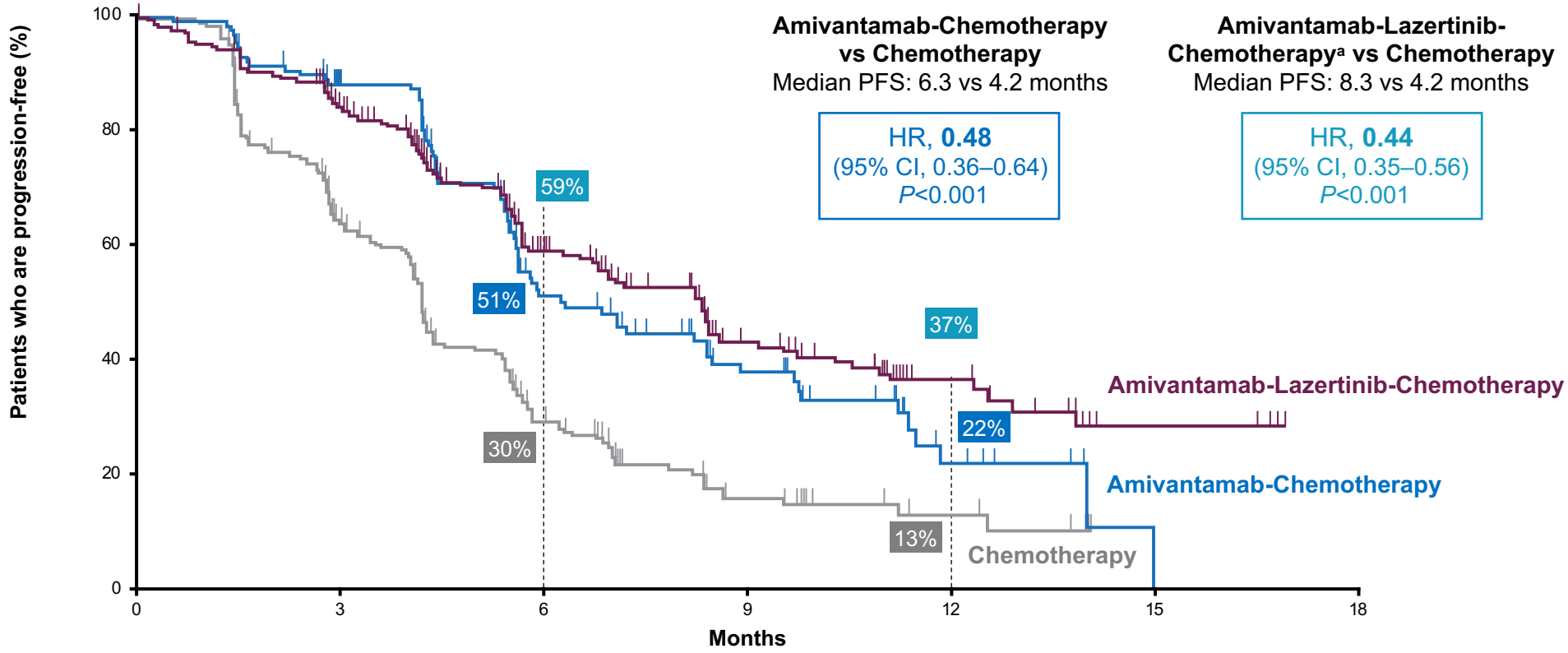
- Objective response rate (ORR)[c]
- Duration of response (DoR)
- Overall survival (OS)[c]
- Intracranial PFS
- Time to subsequent therapy[d]
- PFS after first subsequent therapy (PFS2)[d]
- Symptomatic PFS[d]
- Safety

Courtesy of Karen Reckamp, MD, MS

Passaro A et al. ESMO 2023. Passaro A et al. Ann Oncol 2024;35(1):77-90.

MARIPOSA-2—Progression-free Survival

At a median follow-up of 8.7 months, amivantamab-chemotherapy and amivantamab-lazertinib-chemotherapy reduced the risk of progression or death by 52% and 56%, respectively



No. at risk							
Amivantamab-Chemotherapy	131	99	49	27	7	0	0
Amivantamab-Lazertinib-Chemotherapy	263	194	104	52	21	4	0
Chemotherapy	263	135	49	17	6	0	0

Consistent PFS benefit by investigator: HR, 0.41 (8.2 vs 4.2 mo; *P*<0.001[b]) & HR, 0.38 (8.3 vs 4.2 mo; *P*<0.001[b])

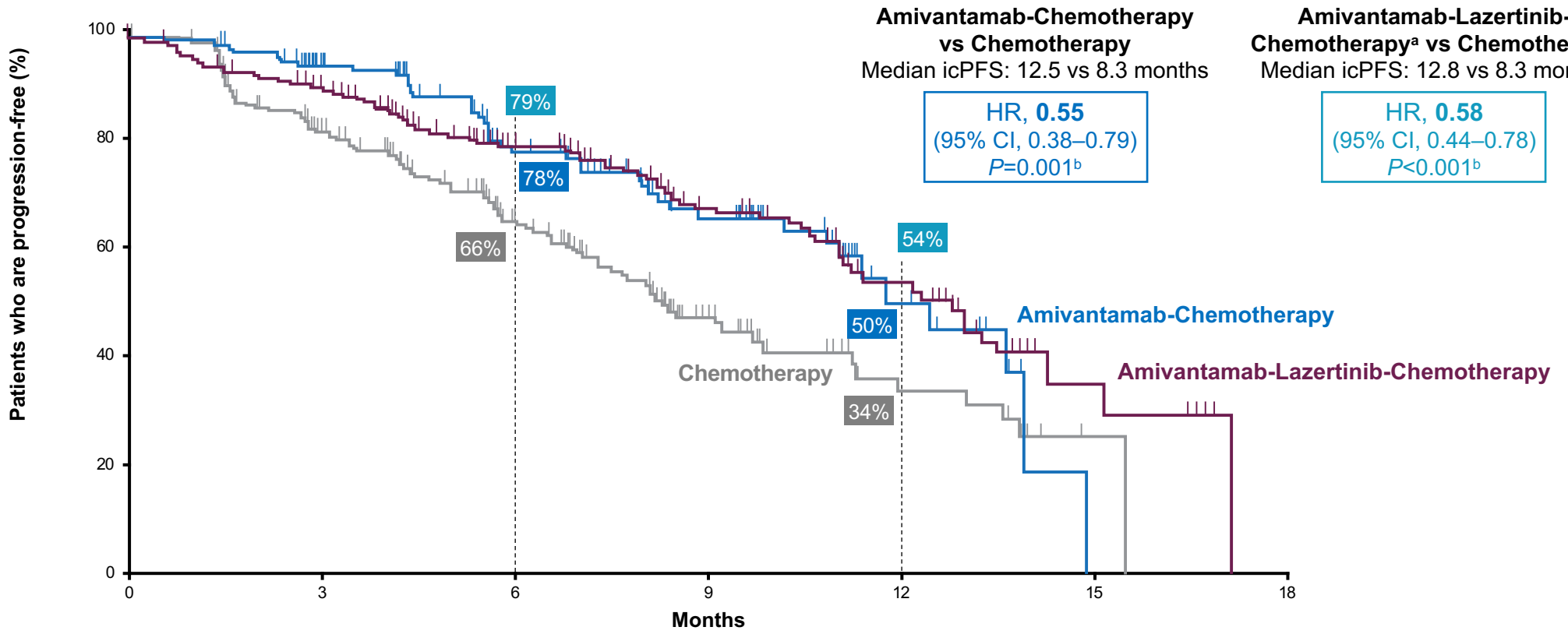
[a]Amivantamab-lazertinib-chemotherapy arm includes all patients regardless of the dosing regimen received. [b]Nominal *P*-value; endpoint not part of hierarchical hypothesis testing.
BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

Courtesy of Karen Reckamp, MD, MS

Passaro A et al. ESMO 2023. Passaro A et al. Ann Oncol 2024;35(1):77-90.

MARIPOSA-2—Intracranial PFS

Amivantamab-chemotherapy and amivantamab-lazertinib-chemotherapy reduced the risk of intracranial progression or death by 45% and 42%, respectively



No. at risk							
Amivantamab-Chemotherapy	131	103	72	40	11	0	0
Amivantamab-Lazertinib-Chemotherapy	263	211	135	74	32	6	0
Chemotherapy	263	167	89	37	13	1	0

[a]Amivantamab-lazertinib-chemotherapy arm includes all patients regardless of the dosing regimen received. [b]Nominal *P*-value; endpoint not part of hierarchical hypothesis testing.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; icPFS, intracranial progression-free survival.

Courtesy of Karen Reckamp, MD, MS

Passaro A et al. ESMO 2023. Passaro A et al. Ann Oncol 2024;35(1):77-90.

MARIPOSA-2—Safety Profile

Most common TEAEs (≥25%) by preferred term, n (%)	Chemotherapy (n=243)		Amivantamab-Chemotherapy (n=130)		Amivantamab-Lazertinib-Chemotherapy[a] (n=263)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Associated with EGFR inhibition						
Paronychia	1 (0.4)	0	48 (37)	3 (2)	133 (51)	11 (4)
Rash	12 (5)	0	56 (43)	8 (6)	126 (48)	17 (6)
Stomatitis	21 (9)	0	41 (32)	1 (1)	120 (46)	24 (9)
Diarrhea	16 (7)	1 (0.4)	18 (14)	1 (1)	68 (26)	10 (4)
Associated with MET inhibition						
Hypoalbuminemia	21 (9)	1 (0.4)	29 (22)	3 (2)	104 (40)	12 (5)
Peripheral edema	15 (6)	0	42 (32)	2 (2)	85 (32)	1 (0.4)
Associated with Chemotherapy						
Neutropenia	101 (42)	52 (21)	74 (57)	59 (45)	181 (69)	144 (55)
Thrombocytopenia	72 (30)	22 (9)	57 (44)	19 (15)	158 (60)	96 (37)
Anemia	97 (40)	23 (9)	51 (39)	15 (12)	141 (54)	48 (18)
Leukopenia	68 (28)	23 (9)	37 (28)	26 (20)	106 (40)	71 (27)
Other						
Infusion-related reaction	1 (0.4)	0	76 (58)	7 (5)	148 (56)	9 (3)
Nausea	90 (37)	2 (1)	58 (45)	1 (1)	131 (50)	16 (6)
Constipation	72 (30)	0	50 (38)	1 (1)	96 (37)	3 (1)
Decreased appetite	51 (21)	3 (1)	40 (31)	0	85 (32)	7 (3)
Vomiting	42 (17)	1 (0.4)	32 (25)	1 (1)	76 (29)	10 (4)
Fatigue	47 (19)	4 (2)	36 (28)	4 (3)	69 (26)	15 (6)
Asthenia	40 (16)	5 (2)	34 (26)	1 (1)	67 (25)	14 (5)
Alanine aminotransferase increased	67 (28)	10 (4)	26 (20)	7 (5)	55 (21)	14 (5)
AESIs by grouped term, n (%)						
Rash[b]	30 (12)	0	92 (71)	13 (10)	197 (75)	40 (15)
VTE[c]	11 (5)	7 (3)	13 (10)	3 (2)	58 (22)	17 (6)
ILD	0	0	2 (2)	1 (1)	7 (3)	5 (2)

- Amivantamab-containing arms had higher rates of EGFR- and MET-related AEs
- Neutropenia and thrombocytopenia:
  - Mostly occurred during cycle 1
  - Low rates of febrile neutropenia (2%, 2%, and 8%)
  - Low rates of grade 3-4 bleeding[d] (0%, 1%, and 3%)
- VTE highest in amivantamab-lazertinib-chemotherapy arm
  - No grade 5 events
  - Rates of discontinuation due to VTE were low (0%, 1%, and 0.4%)
- Incidence of ILD was low in all arms (<3%)

[a]Amivantamab-lazertinib-chemotherapy arm includes all patients regardless of the dosing regimen received. [b]Grouping includes the following preferred terms: rash, dermatitis acneiform, rash maculo-papular, erythema, acne, rash pruritic, rash erythematous, rash macular, drug eruption, folliculitis, dermatitis, skin lesion, rash pustular, papule, rash follicular, exfoliative rash, pustule, rash papular, skin exfoliation. [c]Grouping includes the following preferred terms: pulmonary embolism, deep vein thrombosis, embolism, renal vein thrombosis, venous thrombosis limb, venous thrombosis, embolism venous, jugular vein thrombosis, superficial vein thrombosis, thrombophlebitis, thrombosis. [d]Identified by the standardized MedDRA query for "Haemorrhage Terms (Excl Laboratory Terms)".

AE, adverse event; AESI, AE of special interest; EGFR, epidermal growth factor receptor; ILD, interstitial lung disease (includes pneumonitis); TEAE, treatment-emergent AE; VTE, venous thromboembolism.

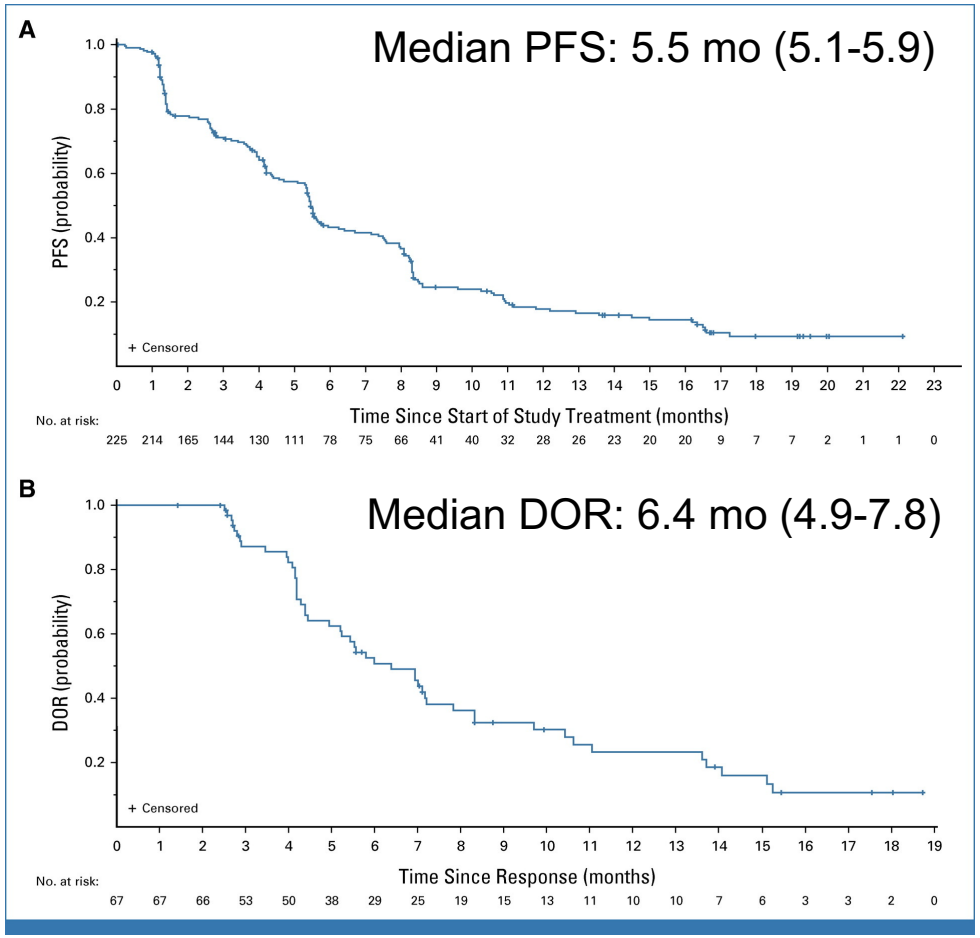
Courtesy of Karen Reckamp, MD, MS

Passaro A et al. ESMO 2023. Passaro A et al. Ann Oncol 2024;35(1):77-90.

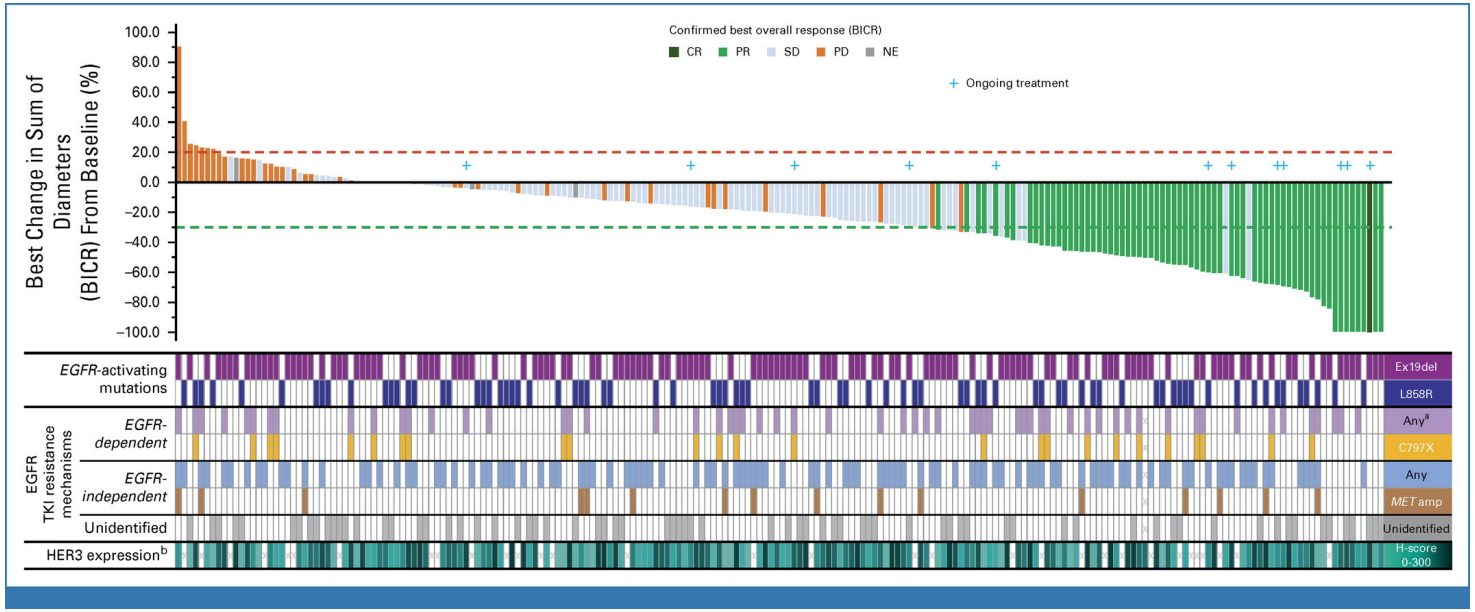
Antibody-Drug Conjugates for Advanced NSCLC

- Yu HA et al. **HERTHENA-Lung01**, a phase II trial of **patritumab deruxtecan (HER3-DXd)** in epidermal growth factor receptor-mutated non-small-cell lung cancer after epidermal growth factor receptor tyrosine kinase inhibitor therapy and platinum-based chemotherapy. *J Clin Oncol* 2023;41(35):5363-75.
- Johnson ML et al. **Intracranial efficacy** of **HER3-DXd** in patients with **previously treated advanced EGFR-mutated** NSCLC: Results from **HERTHENA-Lung01**. ESMO 2023;Abstract 1319MO.
- Paz-Ares L et al. **TROPION-Lung05: Datopotamab deruxtecan (Dato-DXd)** in previously treated non-small cell lung cancer (NSCLC) with **actionable genomic alterations** (AGAs). ESMO 2023;Abstract 1314MO.

HERTHENA-Lung01—Patritumab deruxtecan in *EGFR* mutant NSCLC



ORR: 29.8% (23.9-36.2)



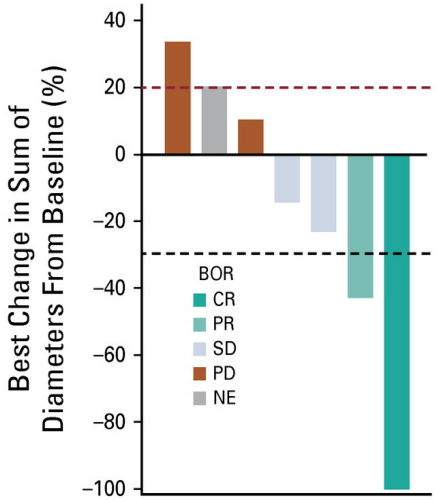
Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Yu HA et al. J Clin Oncol 2023 415363-5375.

HERTHENA-Lung01—CNS outcomes

A

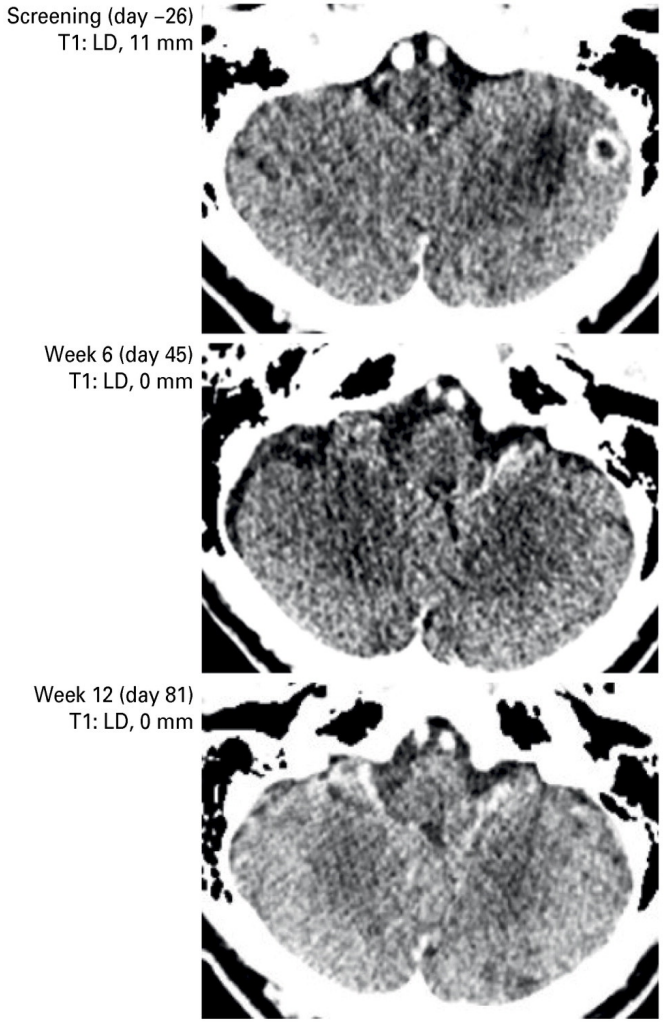


Intracranial ORR by CNS BICR	PD	NE	PD	SD	SD	PR	CR
ORR by BICR	PD	NE	PD	SD	SD	SD	PR

B

Result	Patients with brain metastasis at baseline (n = 30)
cORR, No. (%) (95% CI)[a]	10 (33.3) (17.3-52.8)
CR, No. (%)	9 (30.0)[b]
PR, No. (%)	1 (3.3)
SD or non-CR/non-PD, No. (%)	13 (43.3)
PD, No. (%)	4 (13.3)
NE, No. (%)	3 (10.0)
Duration of response, months, median (95% CI)	8.4 (5.8-9.2)

C



Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

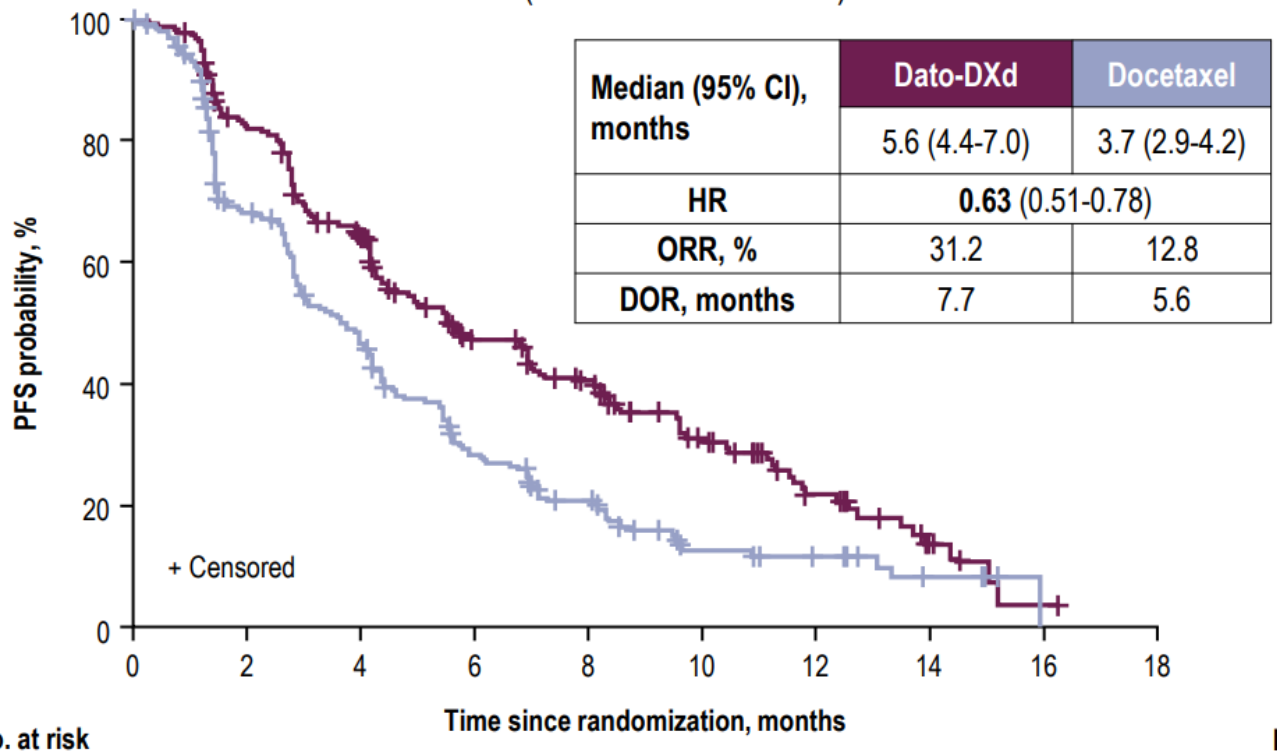
Yu HA et al. J Clin Oncol 2023 415363-5375.
Johnson ML et al. ESMO 2023;Abstract 1319MO.

TROPION-Lung01—PFS by Histology

Non-squamous

(with and without AGAs)

Median (95% CI), months	Dato-DXd	Docetaxel
	5.6 (4.4-7.0)	3.7 (2.9-4.2)
HR	**0.63** (0.51-0.78)	
ORR, %	31.2	12.8
DOR, months	7.7	5.6

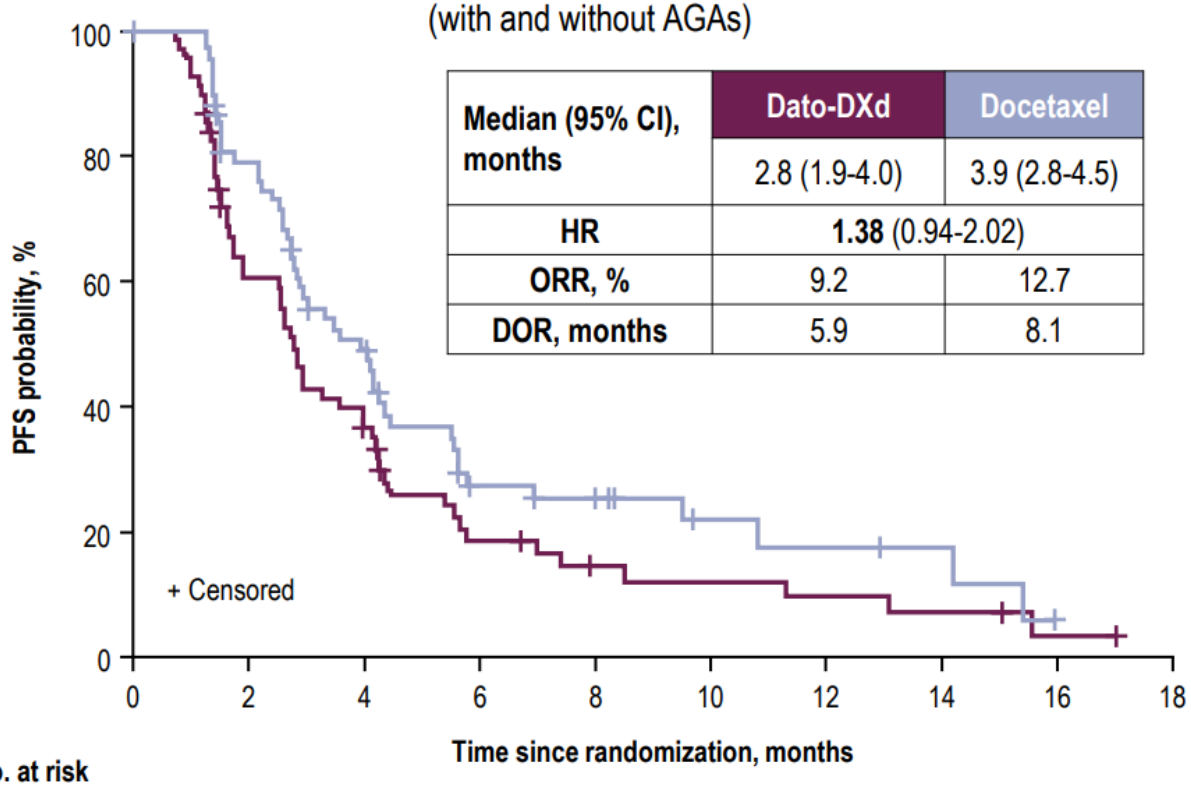


No. at risk										
Dato-DXd	229	178	134	86	68	41	20	7	1	0
Docetaxel	232	135	90	50	32	14	10	4	0	0

Squamous

(with and without AGAs)

Median (95% CI), months	Dato-DXd	Docetaxel
	2.8 (1.9-4.0)	3.9 (2.8-4.5)
HR	**1.38** (0.94-2.02)	
ORR, %	9.2	12.7
DOR, months	5.9	8.1



No. at risk										
Dato-DXd	70	38	22	10	6	5	4	3	1	0
Docetaxel	73	51	30	13	10	5	4	3	0	0

PFS HR for non-squamous without AGAs: 0.71 (0.56, 0.91)

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Lisberg A et al. ESMO 2023

TROPION-Lung05—Datopotamab deruxtecan (Dato-DXd) in NSCLC with actionable genomic alterations

Screening

Key inclusion criteria

- Stage IIIB, IIIC, or IV NSCLC
- Presence of ≥1 actionable genomic alteration (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
- ECOG PS of 0 or 1
- ≥1 line of targeted therapy
- 1 or 2 prior cytotoxic agent–containing therapies including platinum-based therapy in the metastatic setting
- Radiographic disease progression after targeted therapy

Treatment

Dato-DXd
6 mg/kg
Q3W

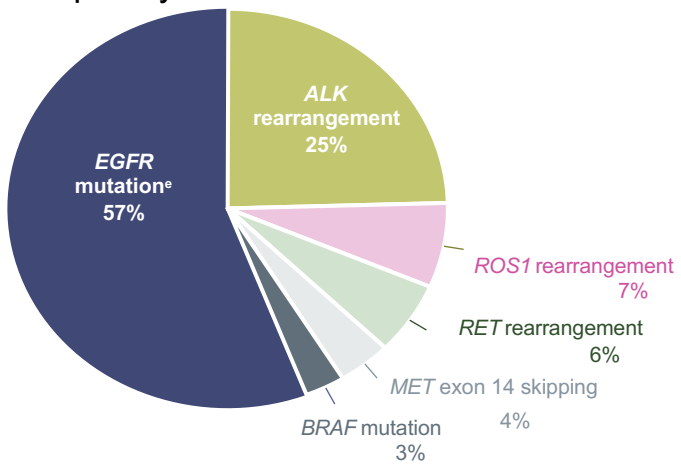
Endpoints[a]

Primary: ORR by BICR

Secondary:

- By BICR and investigator: DOR, DCR, CBR, PFS, TTR
- By investigator: ORR
- OS, safety, PK, immunogenicity

Relative Frequency of Genomic Alterations[b-d]



Courtesy of Karen Reckamp, MD, MS

Paz-Ares L et al. ESMO 2023;Abstract 1314MO.

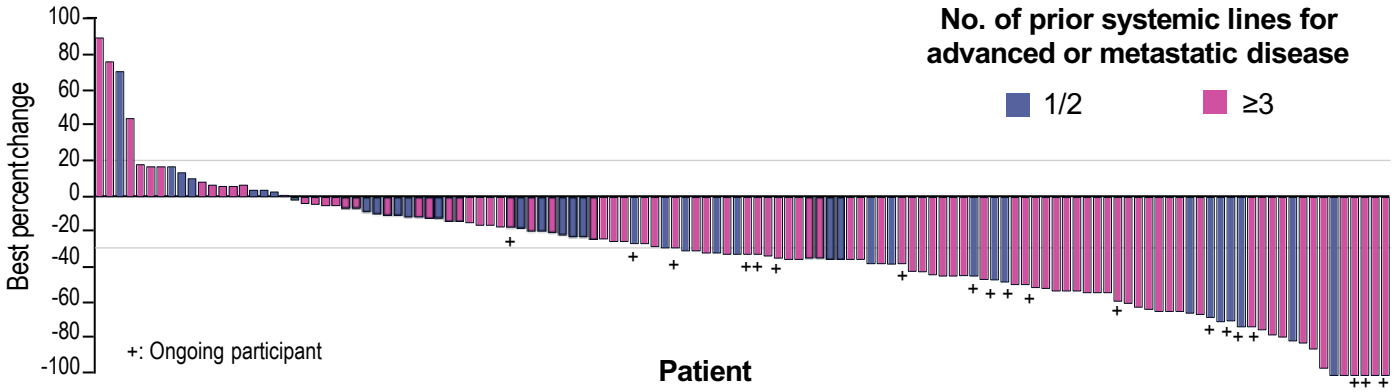
TROPION-Lung05—Efficacy Summary

Response per BICR	All treated patients (N=137)	Patients with *EGFR* mutations (N=78)	Patients with *ALK* rearrangement (N=34)
ORR confirmed, n (%) [95% CI][a]	49 (35.8) [27.8-44.4]	34 (43.6) [32.4-55.3]	8 (23.5) [10.7-41.2]
Median DOR (95% CI), months	7.0 (4.2-9.8)	7.0 (4.2-10.2)	7.0 (2.8-8.4)
DCR confirmed, n (%) [95% CI][a]	108 (78.8) [71.0-85.3]	64 (82.1) [71.7-89.8]	25 (73.5) [55.6-87.1]
Median PFS, (95% CI), months[b]	5.4 (4.7-7.0)	5.8 (5.4-8.3)	4.3 (2.6-6.9)

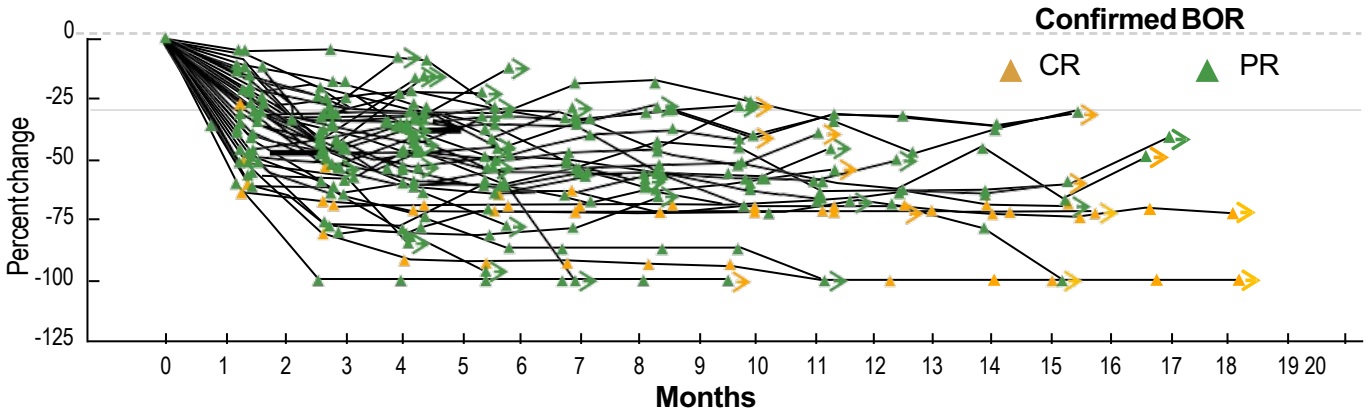
BOR: In the overall population (N=137), 4 patients (3%) achieved a CR and 45 (33%) achieved a PR

***EGFR* subset:** Among patients with sensitizing or T790M mutations (N=68), the ORR was 49.1% in those previously treated with osimertinib

Best Percent Change From Baseline in Sum of Diameters of Target Lesions



Percent Change From Baseline in Sum of Diameters of Target Lesions in Patients With Confirmed CR/PR[c]



BICR, blinded independent central review; BOR, best overall response; CR, complete response; DCR, disease control rate; DOR, duration of response; ORR, objective response rate; PFS, progression-free survival; PR, partial response.

[a]The 2-sided 95% CIs are based on the Clopper-Pearson exact binomial method. [b]Median PFS and PFS probabilities are based on the Kaplan-Meier method. [c]Per BICR.

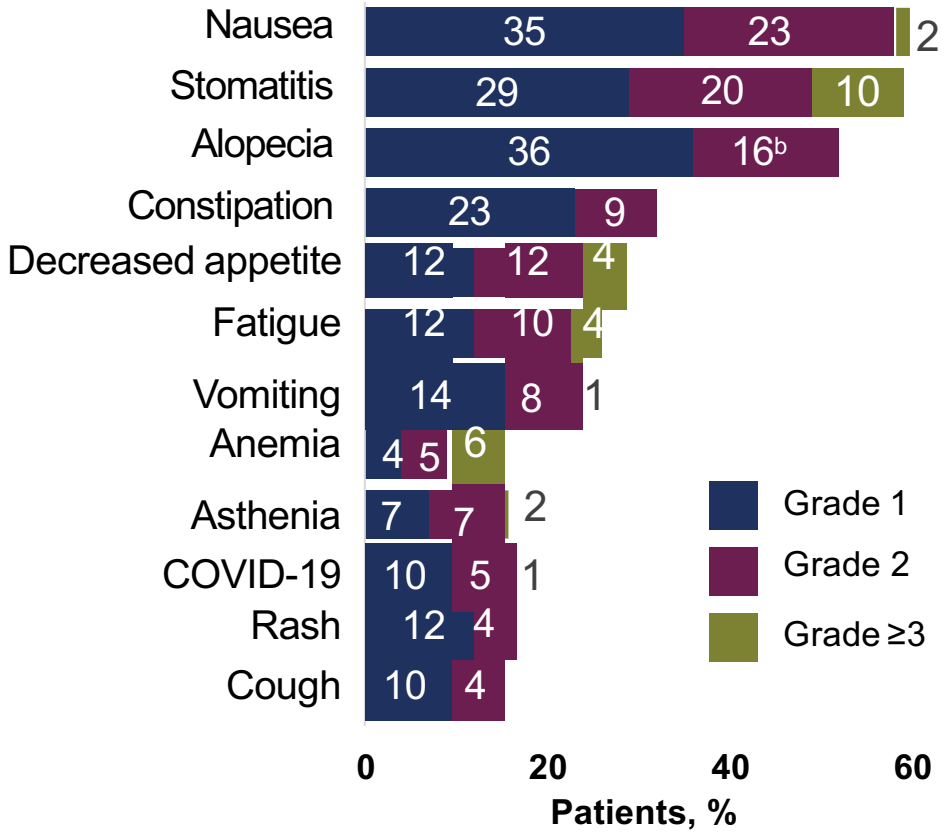
Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Paz-Ares L et al. ESMO 2023;Abstract 1314MO.

TROPION-Lung05—Safety Summary

TEAEs Occurring in ≥15% of Patients; All Grades (N=137)[a]



- 137 patients (100%) experienced **TEAEs** (grade ≥3, 47%)
  - 129 (94%) experienced **treatment-related TEAEs** (grade ≥3, 29%)
  - 34 (25%) experienced **serious AEs** (grade ≥3, 5%)
- 30 (22%), 13 (10%), and 2 (2%) patients experienced TEAEs associated with **dose reduction, dose withdrawal, and death**,[c] respectively

AESI Incidence by Grade[d]

n (%)	Total	Grade 1	Grade 2	Grade ≥3
Oral mucositis/stomatitis	90 (66)	45 (33)	30 (22)	15 (11)
Ocular surface toxicity[e]	36 (26)	26 (19)	7 (5)	3 (2)[f]
IRR	22 (16)	15 (11)	7 (5)	0
Adjudicated drug-related ILD	5 (4)	1 (1)	3 (2)	1 (1)[g]

AE, adverse event; AESI, adverse event of special interest; CTCAE, Common Terminology Criteria for Adverse Events; ILD, interstitial lung disease; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event.
[a]Due to rounding, summed rates may not reflect total percentage of TEAEs. [b]Includes an event reported as grade 3 incorrectly per CTCAE grades. [c]Two deaths were associated with disease progression, unrelated to study drug by investigator. [d]AESIs listed in this slide include all preferred terms defined by the medical concept. [e]Dry eye was the most commonly reported ocular surface toxicity (n=15 [11%]). [f]Patients with grade 3 ocular surface toxicity had corneal disorder, cornea verticillata, and punctate keratitis. [g]One case of ILD was reported as a grade 3 event by investigator, and the patient died due to disease progression per investigator. The same event was adjudicated as a grade 5 event.

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Paz-Ares L et al. ESMO 2023;Abstract 1314MO.

Options for subsequent treatment of advanced *EGFR*+ NSCLC

- Emerging options to treat osimertinib resistance
- Chemotherapy with amivantamab improves PFS over chemotherapy with less toxicity than chemotherapy with amivantamab and lazertinib with CNS benefit
- Patritumab deruxtecan demonstrates responses with ~5.5 mo PFS in heavily pretreated patients with 30% CR in the brain
- Datopotamab deruxtecan shows early efficacy in patients with actionable genomic alterations with ORR in EGFR mutant NSCLC ~43%
- Toxicities differ across therapies and should be considered
- Consideration for potential sequencing of therapies with differing MOA

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Agenda

Introduction: Bringing Research into Practice

Module 1: EGFR Activating Mutations

Module 2: Exon 20 Insertion Mutations

Module 3: MET Exon 14 Alterations

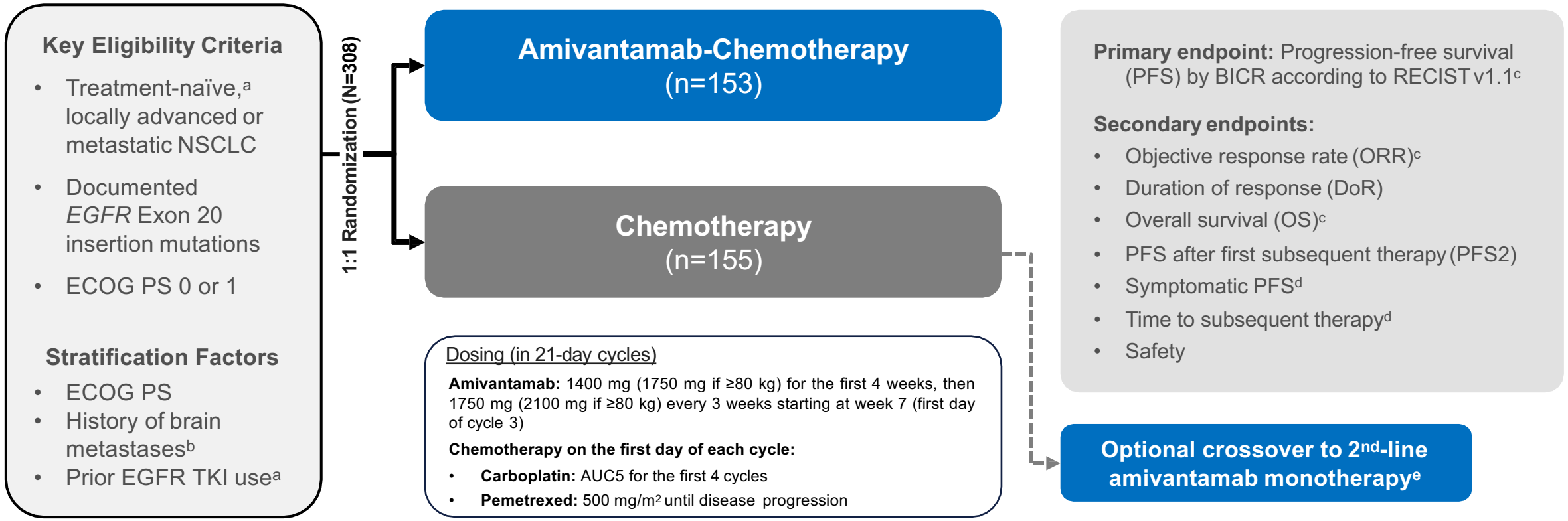
Module 4: HER2 Mutations and Overexpression

RTP
RESEARCH
TO PRACTICE

EGFR Exon 20 Insertion Mutations

- Zhou C et al. **Amivantamab** plus **chemotherapy** in NSCLC with **EGFR exon 20 insertions**. *N Engl J Med* 2023;389(22):2039-51.

PAPILLON—Phase 3 Study Design



PAPILLON (ClinicalTrials.gov Identifier: NCT04538664) enrollment period: December 2020 to November 2022; data cut-off: 3-May-2023.

[a]Removed as stratification factor since only 4 patients had prior EGFR TKI use (brief monotherapy with common EGFR TKIs was allowed if lack of response was documented).
[b]Patients with brain metastases were eligible if they received definitive treatment and were asymptomatic, clinically stable, and off corticosteroid treatment for ≥2 weeks prior to randomization.
[c]Key statistical assumption: 300 patients with 200 events needed for 90% power to detect an HR of 0.625 (estimated PFS of 8 vs 5 months). PFS, ORR, and then OS were included in hierarchical testing.
[d]These secondary endpoints (time to subsequent therapy and symptomatic progression-free survival) will be presented at a future congress.
[e]Crossover was only allowed after BICR confirmation of disease progression; amivantamab monotherapy on Q3W dosing per main study.

AUC, area under the curve; BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HR, hazard ratio; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor.

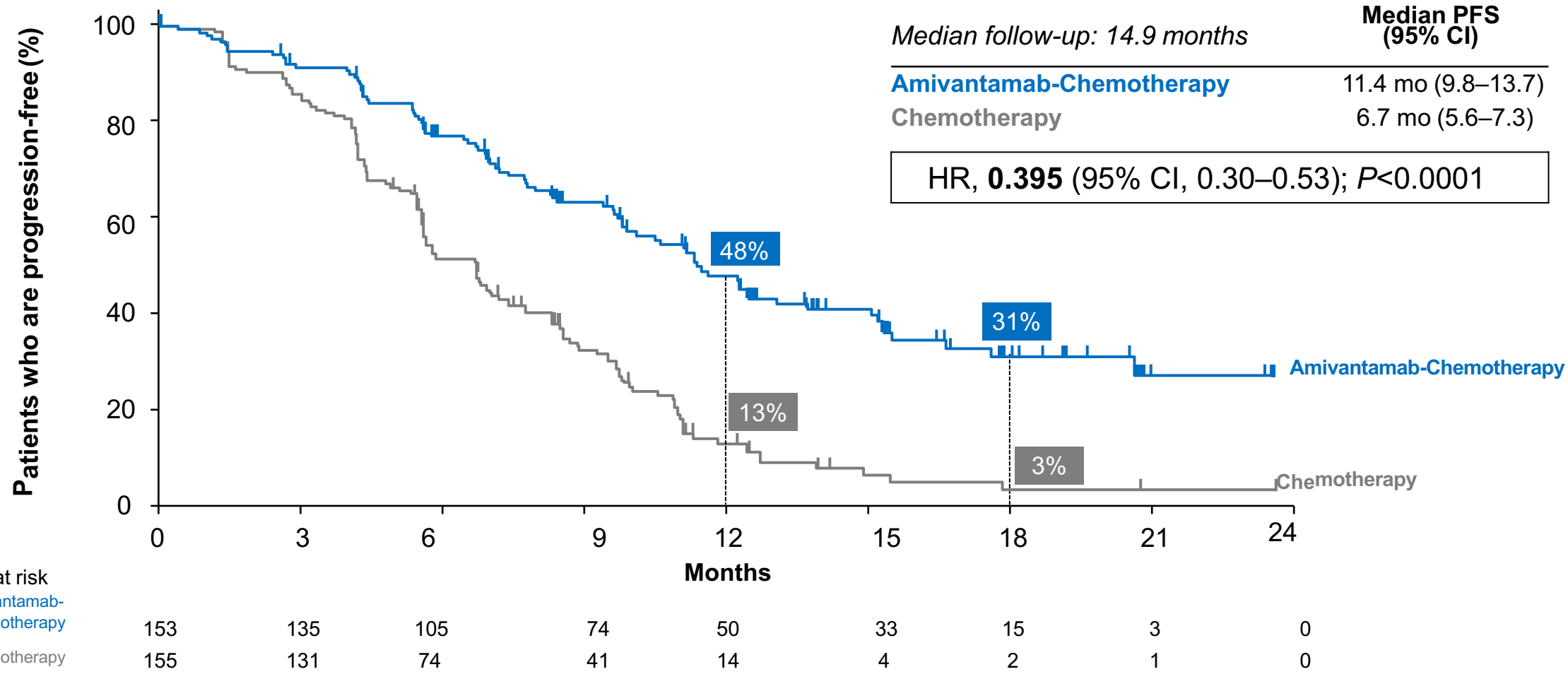
Cedars Sinai Cancer

Girard N et al ESMO 2023; Zhou C et al. N Engl J Med 2023;389(22):2039-51.

Courtesy of Karen Reckamp, MD, MS

PAPILLON—Progression-free Survival

Amivantamab-chemotherapy reduced risk of progression or death by 60%



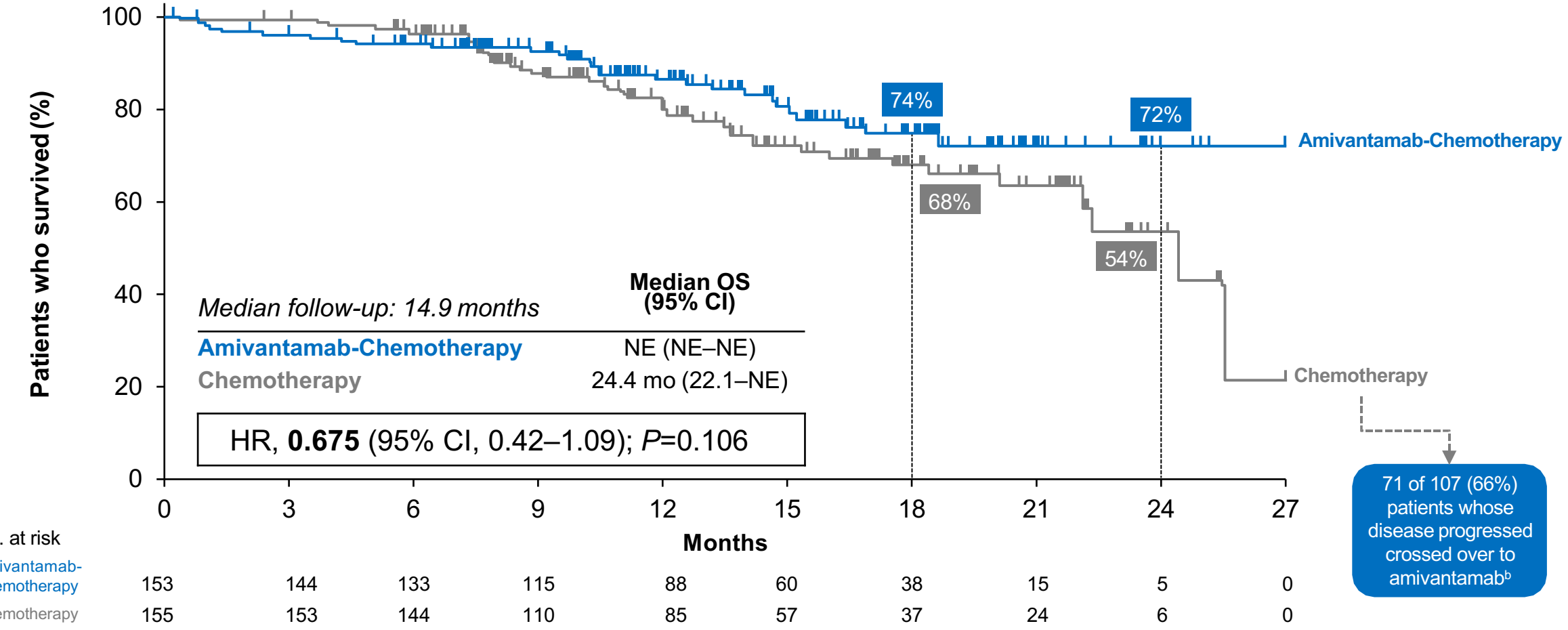
Consistent PFS benefit by investigator: 12.9 vs 6.9 mo (HR, 0.38; 95% CI, 0.29–0.51; *P*<0.0001[a])

Courtesy of Karen Reckamp, MD, MS

Girard N et al ESMO 2023; Zhou C et al. N Engl J Med 2023;389(22):2039-51.

PAPILLON—Interim Overall Survival

Amivantamab-chemotherapy shows trend in reducing risk of death by over 30%



[a]There were 70 deaths in the study at the time of the prespecified interim OS analysis, which represents 23% of all randomized patients and 33% of the ~210 projected deaths for the final OS analysis. [b]A total of 71 patients (65 patients as part of the crossover arm plus an additional 6 patients off-protocol) received second-line amivantamab monotherapy out of 107 chemotherapy-randomized patients with disease progression.

CI, confidence interval; HR, hazard ratio; mo, months; NE, not estimable; OS, overall survival.

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Girard N et al ESMO 2023;
Zhou C et al. N Engl J Med 2023;389(22):2039-51.

PAPILLON—Safety Profile

Most common AEs of any cause by preferred term (≥20%), n (%)	Amivantamab-Chemotherapy (n=151)		Chemotherapy (n=155)	
	All grades	Grade ≥3	All grades	Grade ≥3
Associated with EGFR inhibition				
Paronychia	85 (56)	10 (7)	0	0
Rash	81 (54)	17 (11)	12 (8)	0
Dermatitis acneiform	47 (31)	6 (4)	5 (3)	0
Stomatitis	38 (25)	2 (1)	9 (6)	0
Diarrhea	31 (21)	5 (3)	20 (13)	2 (1)
Associated with MET inhibition				
Hypoalbuminemia	62 (41)	6 (4)	15 (10)	0
Peripheral edema	45 (30)	2 (1)	16 (10)	0
Other				
Neutropenia	89 (59)	50 (33)	70 (45)	35 (23)
Anemia	76 (50)	16 (11)	85 (55)	19 (12)
Infusion-related reaction	63 (42)	2 (1)	2 (1)	0
Constipation	60 (40)	0	47 (30)	1 (1)
Leukopenia	57 (38)	17 (11)	50 (32)	5 (3)
Nausea	55 (36)	1 (1)	65 (42)	0
Thrombocytopenia	55 (36)	15 (10)	46 (30)	16 (10)
Decreased appetite	54 (36)	4 (3)	43 (28)	2 (1)
Alanine aminotransferase increased	50 (33)	6 (4)	56 (36)	2 (1)
Aspartate aminotransferase increased	47 (31)	1 (1)	51 (33)	1 (1)
COVID-19	36 (24)	3 (2)	21 (14)	1 (1)
Hypokalemia	32 (21)	13 (9)	13 (8)	2 (1)
Vomiting	32 (21)	5 (3)	29 (19)	1 (1)

- EGFR- and MET-related AEs were increased with amivantamab-chemotherapy, primarily grade 1-2
- Chemotherapy-associated hematologic and GI toxicities were comparable except for neutropenia
- Neutropenia was transient; majority of events were not serious, with low rates of discontinuations
- Pneumonitis was reported in 4 (3%) patients in the amivantamab-chemotherapy arm

AE, adverse event; EGFR, epidermal growth factor receptor; GI, gastrointestinal.

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Girard N et al ESMO 2023;
Zhou C et al. N Engl J Med 2023;389(22):2039-51.

EGFR Exon 20 NSCLC

- Amivantamab remains the targeted therapy option
- Frontline amivantamab with chemotherapy improves PFS over chemotherapy alone with trend toward improved OS
- Novel drugs with an improved therapeutic window are needed
- Drugs with improved CNS activity are necessary

Cedars Sinai Cancer

Courtesy of Karen Reckamp, MD, MS

Agenda

Introduction: Bringing Research into Practice

Module 1: EGFR Activating Mutations

Module 2: Exon 20 Insertion Mutations

Module 3: MET Exon 14 Alterations

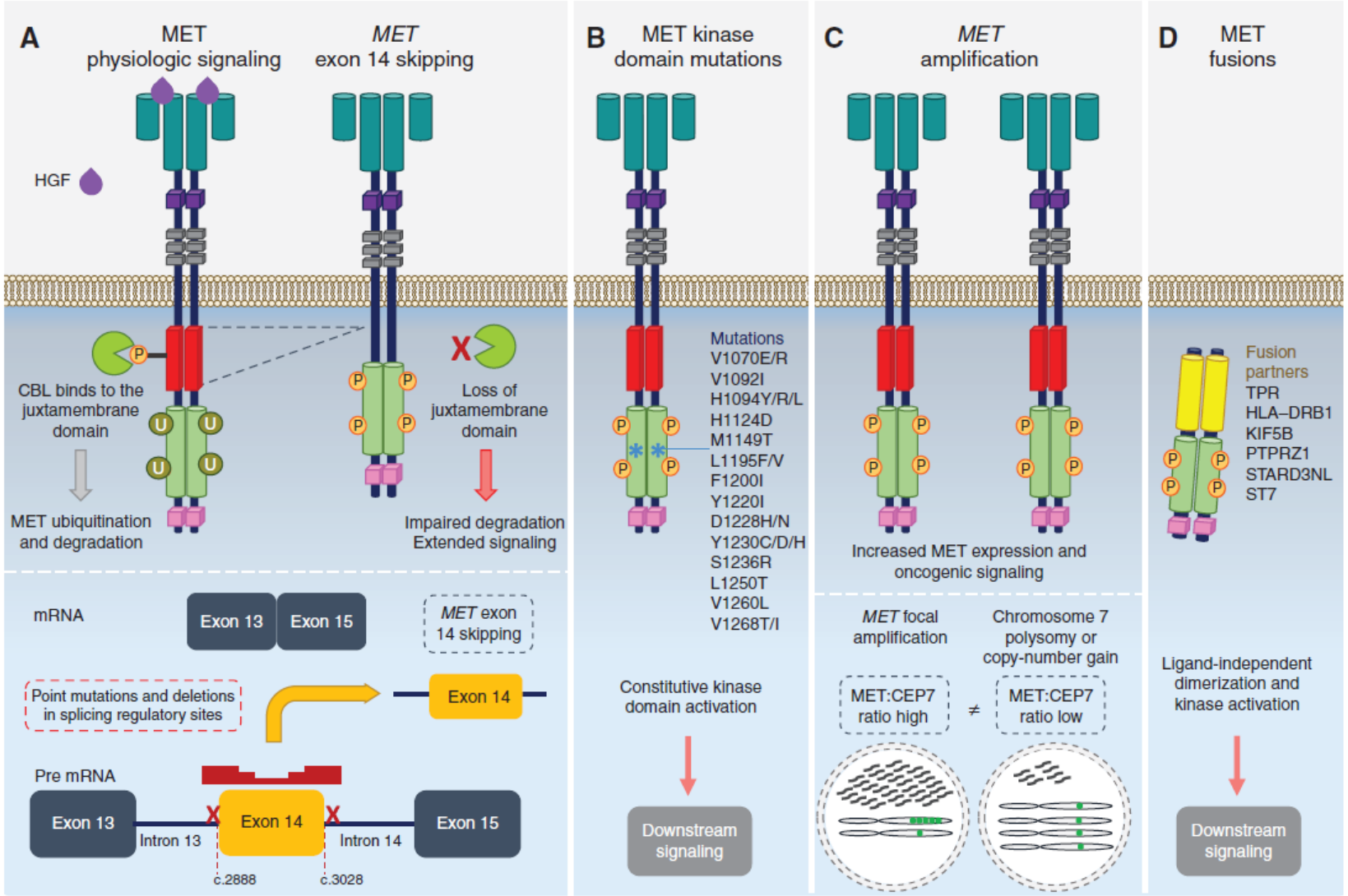
Module 4: HER2 Mutations and Overexpression

RTP RESEARCH TO PRACTICE

MET Exon 14 Alterations

- Wolf J et al. Patient-reported outcomes in **capmatinib**-treated patients **with METex14-mutated advanced** NSCLC: Results from the **GEOMETRY mono-1** study. *Eur J Cancer* 2023;183:98-108.
- Mazieres J et al. **Tepotinib** treatment in patients with **MET exon 14-skipping** non-small cell lung cancer: Long-term follow-up of the **VISION** phase 2 nonrandomized clinical trial. *JAMA Oncol* 2023;9(9):1260-6.

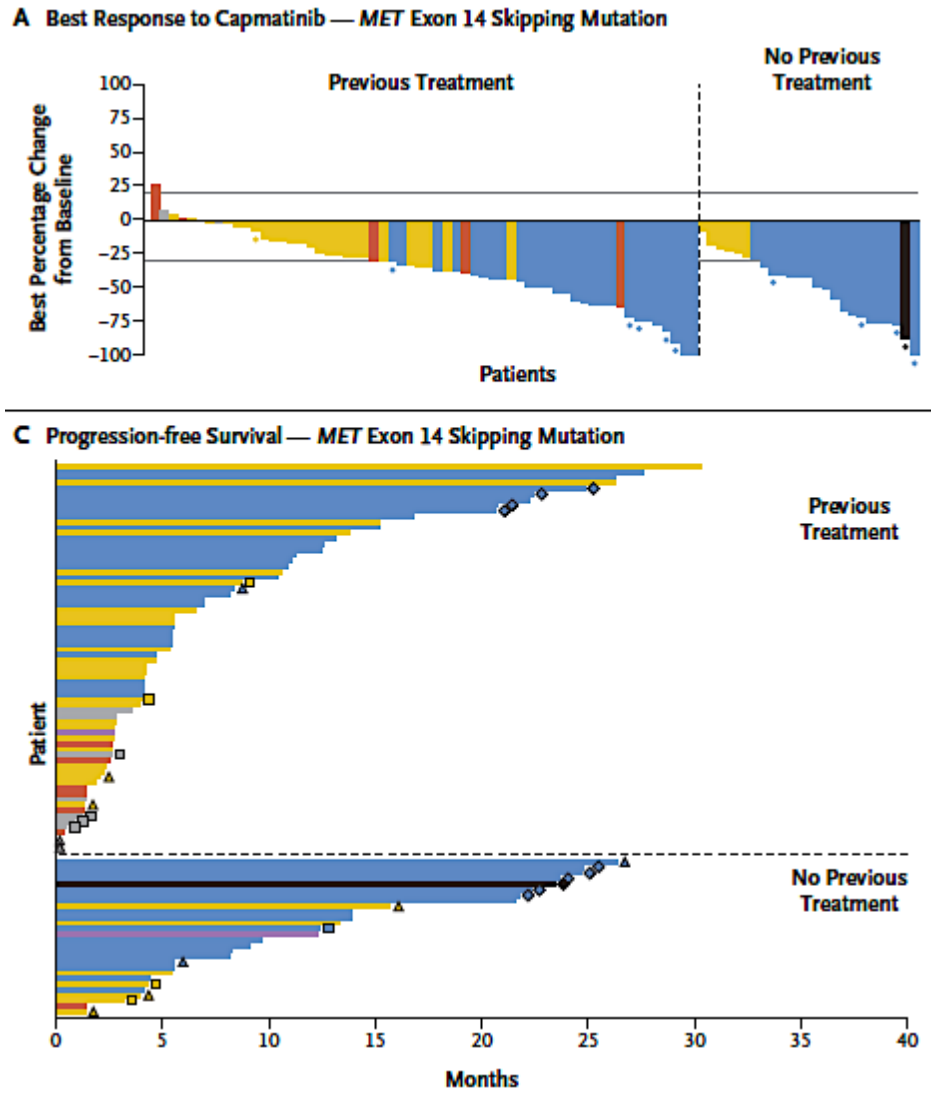
MET as a Driver in NSCLC

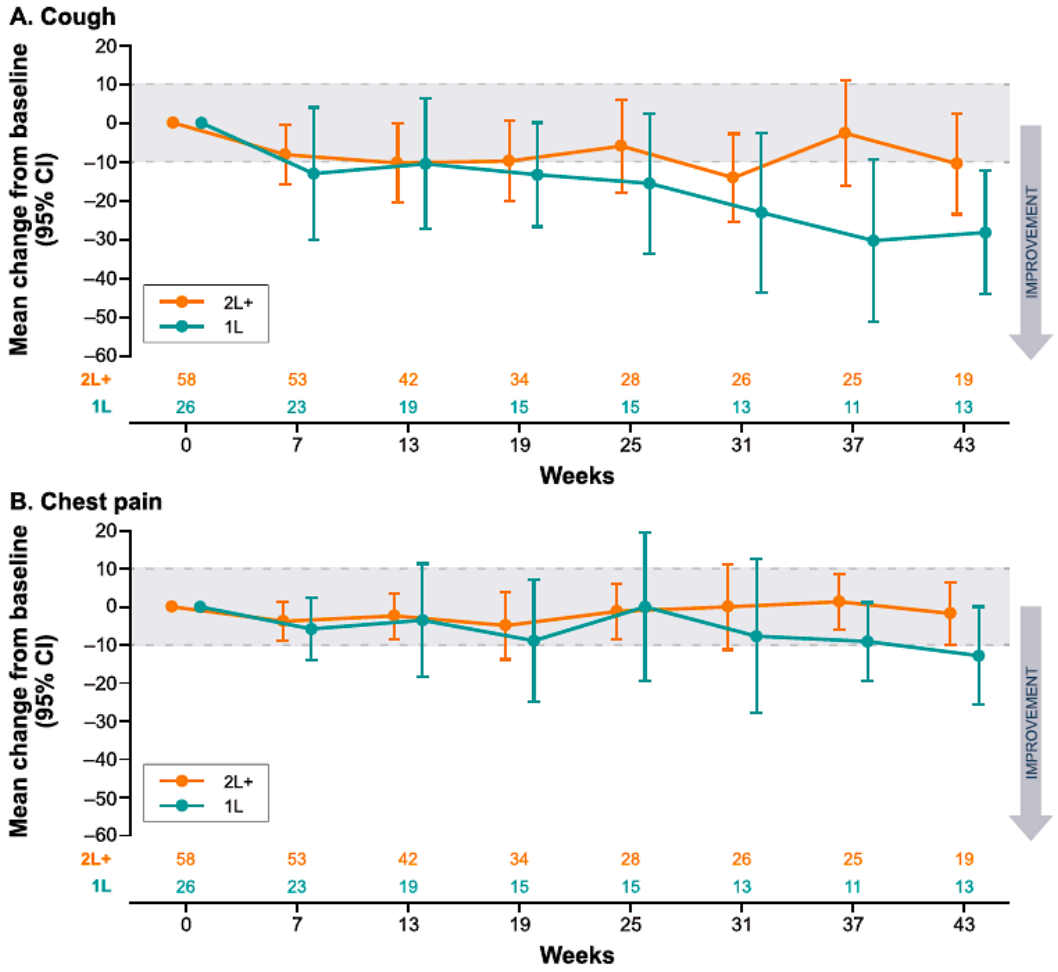


Recondo G, et al. Cancer Discovery 2020

Courtesy of Justin F Gainor, MD

MET Exon 14 Skipping: Capmatinib



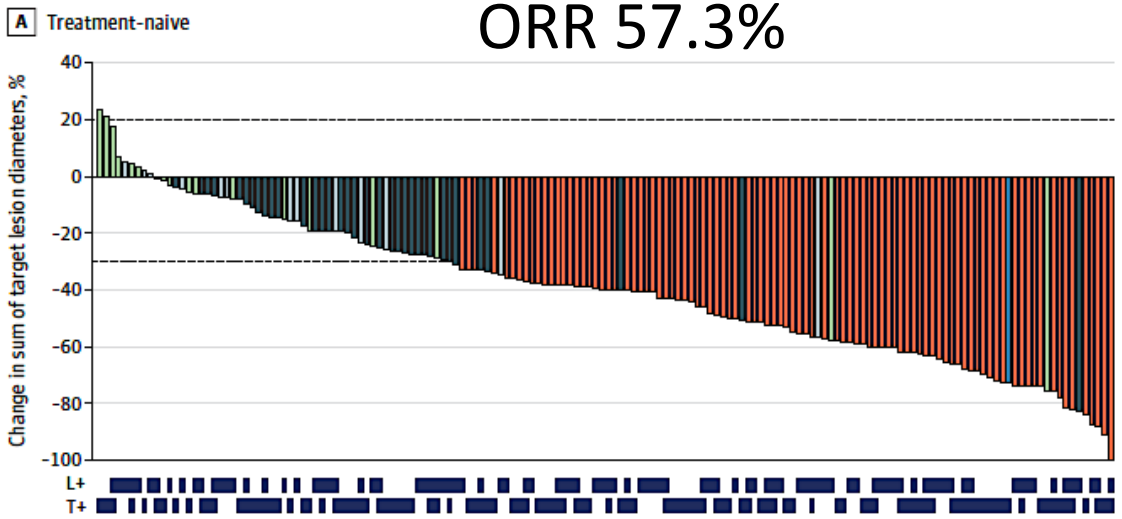


Wolf J, et al. NEJM 2020; Wolf J, et al. E J Cancer 2023

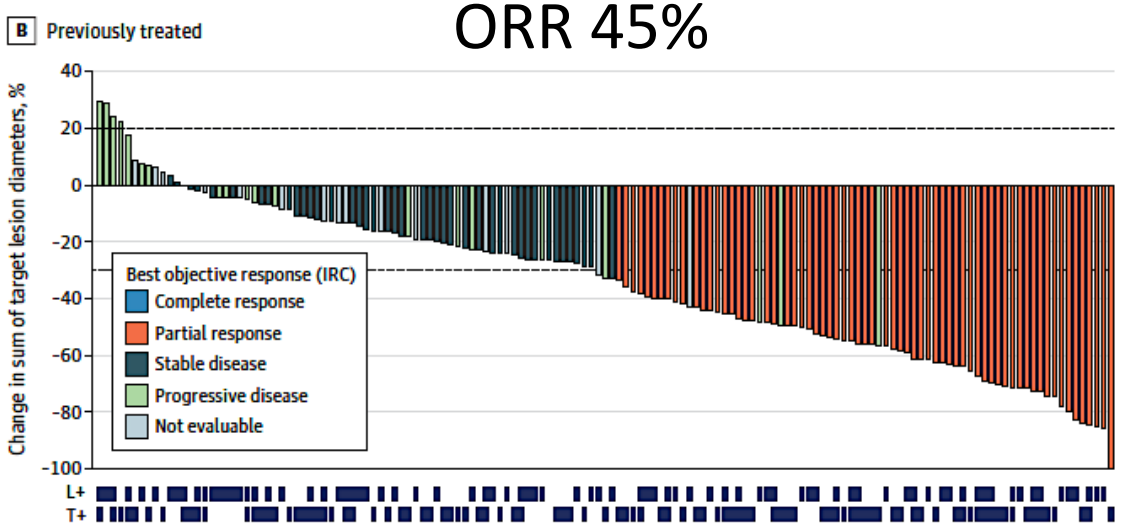
Courtesy of Justin F Gainor, MD

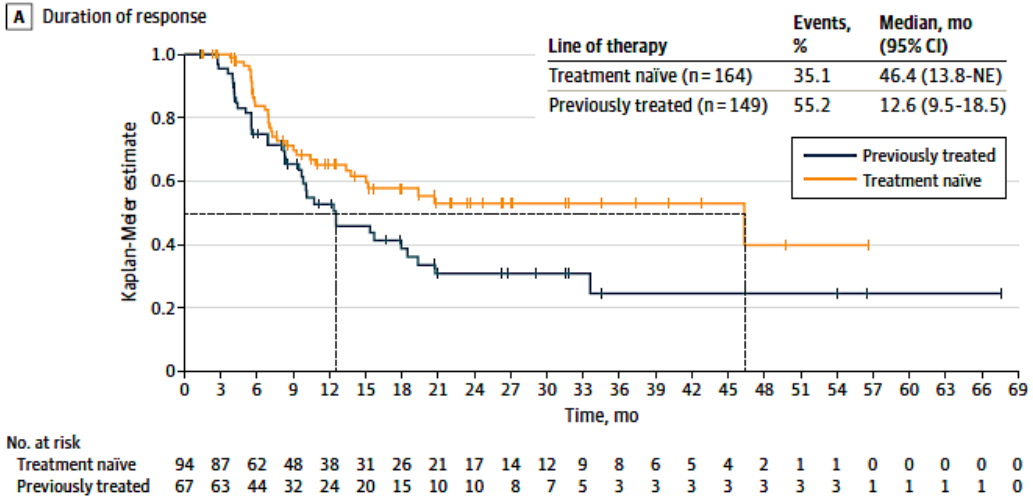
MET Exon 14 Skipping: Tepotinib

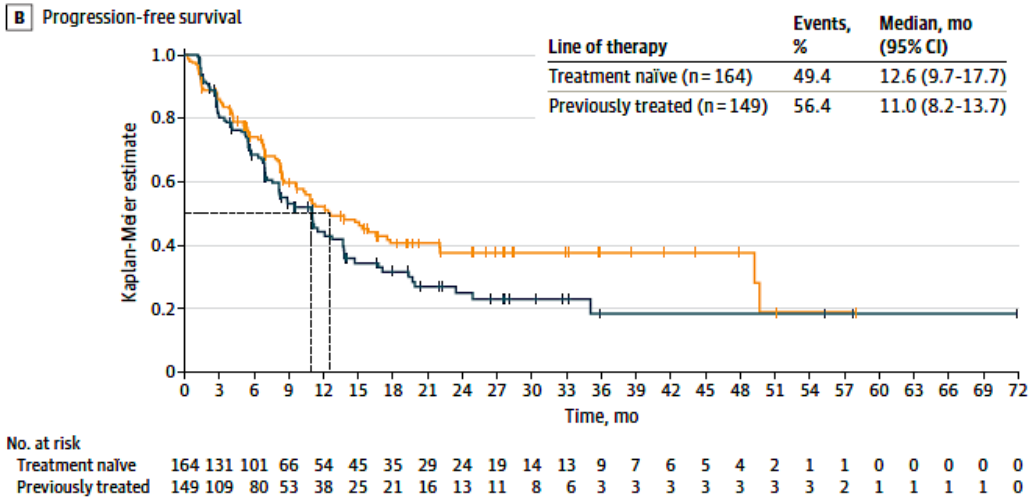
ORR 57.3%



ORR 45%







Mazieres J, et al. JAMA Oncology 2023

Courtesy of Justin F Gainor, MD

MET Exon 14 Skipping: My Take

- Capmatinib and tepotinib are both FDA approved for management of NSCLC with MET exon 14 skipping alterations
- I recommend upfront MET TKI for patients with MET ex 14 skipping
- With long-term follow-up, both capmatinib and tepotinib continue to show significant anti-tumor activity in patients with MET ex 14 skipping
- Clinicians should be aware of long-term, cumulative toxicities, such as peripheral edema

Courtesy of Justin F Gainor, MD

Agenda

Introduction: Bringing Research into Practice

Module 1: EGFR Activating Mutations

Module 2: Exon 20 Insertion Mutations

Module 3: MET Exon 14 Alterations

Module 4: HER2 Mutations and Overexpression

RTP RESEARCH TO PRACTICE

HER2 Mutations and Overexpression

- Goto K et al. **Trastuzumab deruxtecan** in patients with **HER2-mutant metastatic** non-small-cell lung cancer: **Primary results** from the randomized, phase II **DESTINY-Lung02** trial. *J Clin Oncol* 2023;41(31):4852-63.
- Li BT et al. **Trastuzumab deruxtecan (T-DXd)** in patients (pts) with **HER2 (ERBB2)-mutant** (HER2m) **metastatic** non–small cell lung cancer (NSCLC) with and without brain metastases (BMs): **Pooled analyses** from **DESTINY-Lung01** and **DESTINY-Lung02**. ESMO 2023;Abstract 1321MO
- Smit EF et al. **Trastuzumab deruxtecan** in patients with **metastatic** non-small-cell lung cancer (**DESTINY-Lung01**): **Primary results** of the HER2-overexpressing cohorts from a single-arm, phase 2 trial. *Lancet Oncol* 2024;25(4):439-54.

FDA Grants Accelerated Approval to Fam-Trastuzumab-Deruxtecan-Nxki for Unresectable or Metastatic HER2-Positive Solid Tumors

Press Release – April 5, 2024

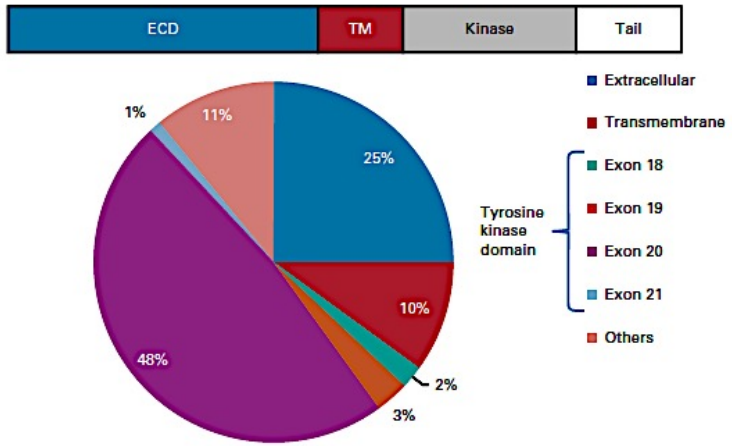
"…the Food and Drug Administration granted accelerated approval to fam-trastuzumab deruxtecan-nxki for adult patients with unresectable or metastatic HER2-positive (IHC3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.

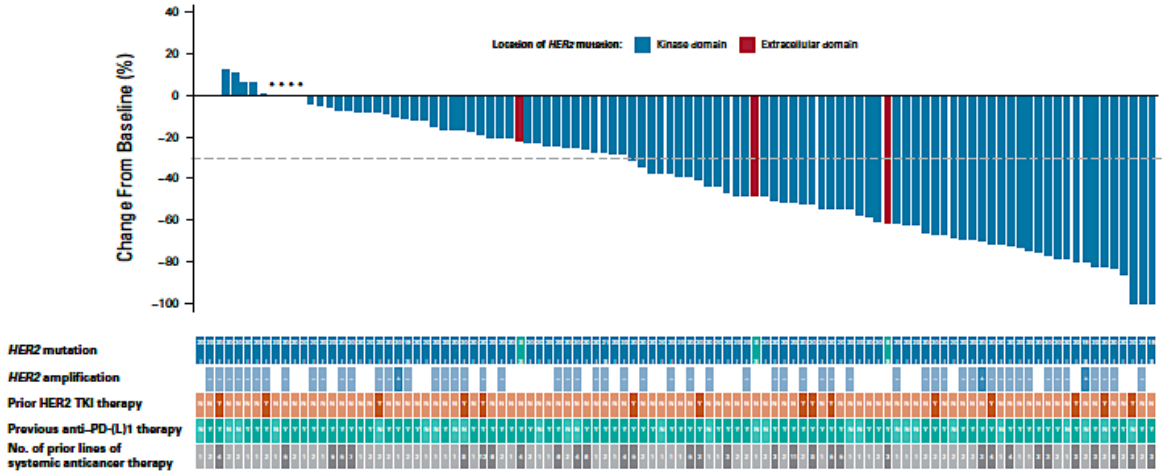
Efficacy was evaluated in 192 adult patients with previously treated unresectable or metastatic HER2-positive (IHC 3+) solid tumors who were enrolled in one of three multicenter trials: DESTINY-PanTumor02 (NCT04482309), DESTINY-Lung01 (NCT03505710), and DESTINY-CRC02 (NCT04744831).

The major efficacy outcome measure in all three trials was confirmed objective response rate (ORR), and an additional efficacy outcome was duration of response (DOR). All outcomes were assessed by independent central review (ICR) based on RECIST v1.1. In DESTINY-PanTumor02, ORR was 51.4% (95% CI: 41.7, 61.0) and median DOR was 19.4 months (range 1.3, 27.9+). In DESTINY-Lung01, ORR was 52.9% (95% CI: 27.8, 77.0) and median DOR was 6.9 months (range 4.0, 11.7+). In DESTINY-CRC02, ORR was 46.9% (95% CI: 34.3, 59.8), and DOR was 5.5 months (range 1.3+, 9.7+)."

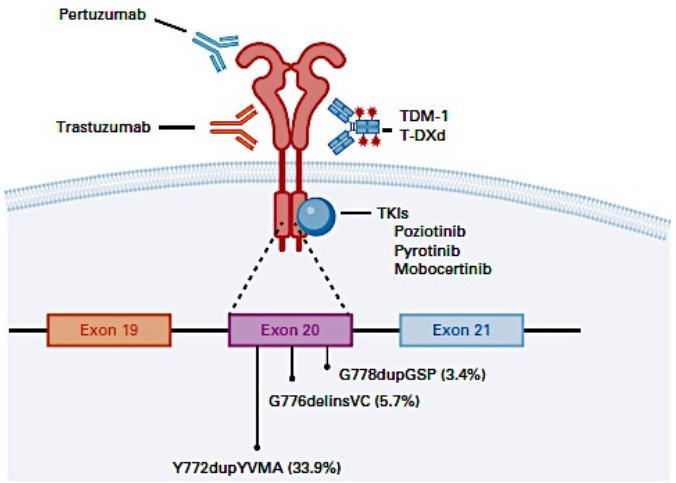
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-fam-trastuzumab-deruxtecan-nxki-unresectable-or-metastatic-her2

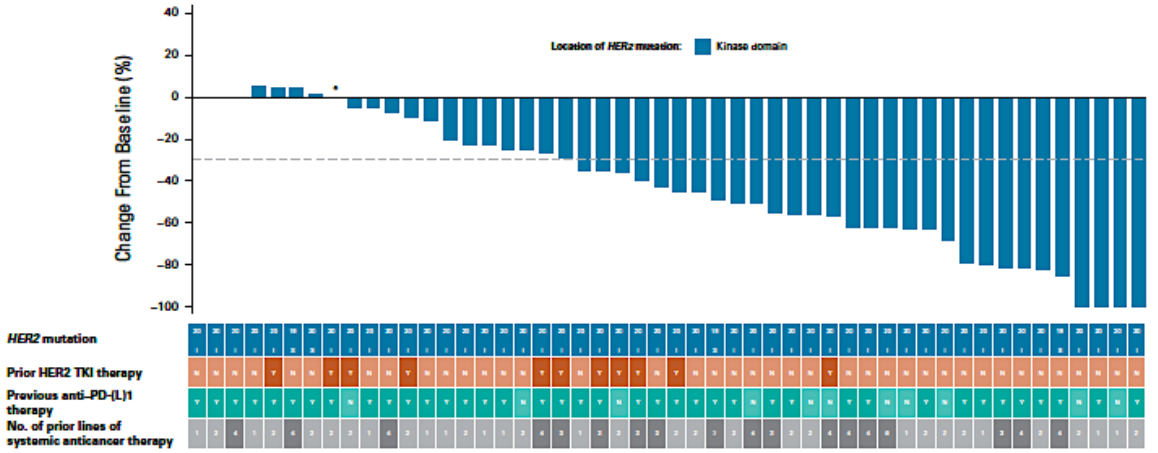
HER2 Mutations





5.4 mg/kg Dose	
ORR	49%
mPFS	9.9 mo
DOR	16.8



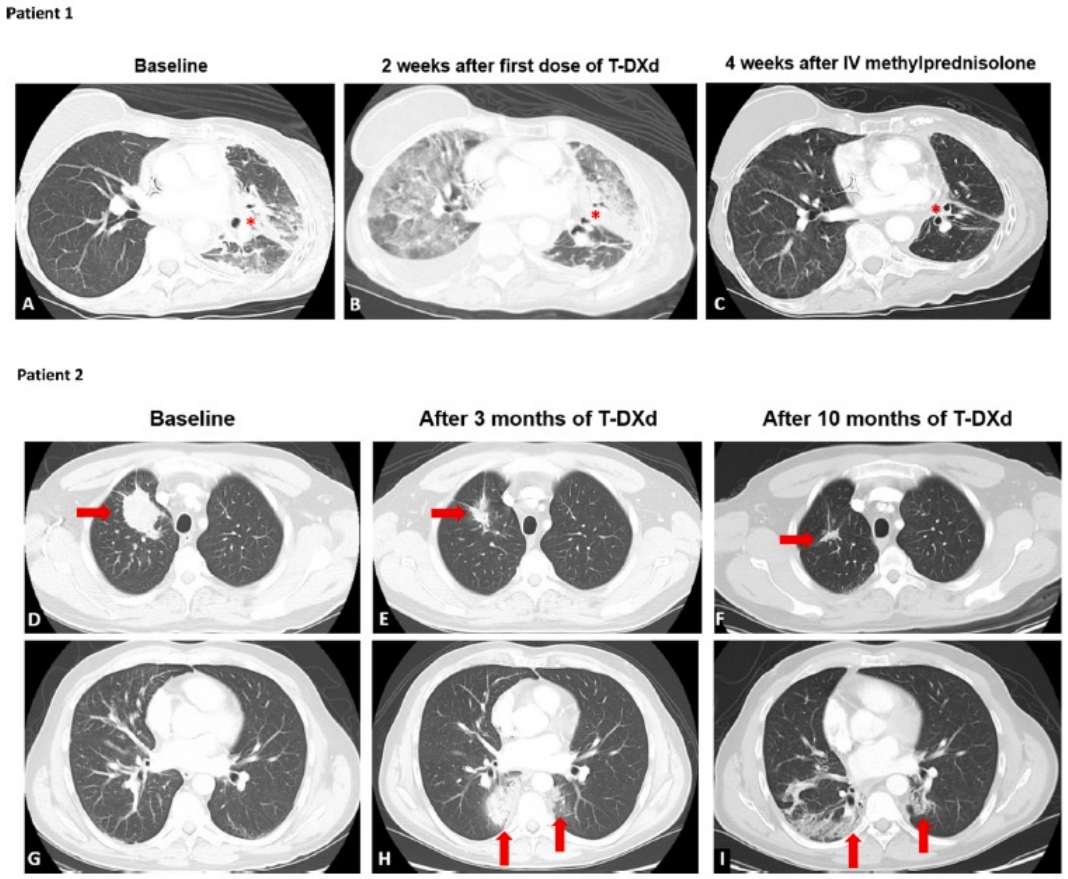


6.4 mg/kg Dose	
ORR	56%
mPFS	15.4 mo
DOR	NE

Cooper A, Gainor JF, J Clin Oncol 2022; Goto K, et al. J Clin Oncol 2023

Courtesy of Justin F Gainor, MD

HER2 Mutations



Adjudicated Drug-Related ILD in Patients With Prior Anti–PD-(L)1 Therapy	T-DXd 5.4 mg/kg Once Every 3 Weeks (n = 74), No. (%)	T-DXd 6.4 mg/kg Once Every 3 Weeks (n = 39), No. (%)
Grade 1	4 (5.4)	2 (5.1)
Grade 2	5 (6.8)	9 (23.1)
Grade 3	1 (1.4)	0
Grade 4	0	0
Grade 5	1 (1.4)	0
Total	11 (14.9)	11 (28.2)

Adjudicated Drug-Related ILD in Patients Without Prior Anti–PD-(L)1 Therapy	T-DXd 5.4 mg/kg Once Every 3 Weeks (n = 27), No. (%)	T-DXd 6.4 mg/kg Once Every 3 Weeks (n = 11), No. (%)
Grade 1	0	2 (18.2)
Grade 2	2 (7.4)	0
Grade 3	0	0
Grade 4	0	0
Grade 5	0	1 (9.1)
Total	2 (7.4)	3 (27.3)

Goto K, et al. J Clin Oncol 2023; Swain SM, et al. Cancer Treatment Reviews 2022

Courtesy of Justin F Gainor, MD

HER2 Mutations

Exploratory Pooled Brain Metastases Analyses: DESTINY-Lung01[1,2] and DESTINY-Lung02[3]

DESTINY-Lung01[a]
- Unresectable/metastatic nonsquamous NSCLC
- Relapsed from or is refractory to standard treatment
- Measurable disease by RECIST v1.1
- ECOG PS of 0 or 1
- Locally reported *HER2*m (Cohort 2)
- Asymptomatic BM allowed[c]

DESTINY-Lung02[b]
- Metastatic *HER2*m NSCLC
- ≥1 prior anticancer therapy (2L+), including platinum-based chemotherapy
- Measurable disease per RECIST v1.1
- ECOG PS of 0 or 1
- Locally reported *HER2*m
- Asymptomatic BM allowed[c]

Cohort 1: HER2-OE (IHC 3+ or IHC 2+) T-DXd 6.4 mg/kg Q3W N = 49

Cohort 1a: HER2-OE (IHC 3+ or IHC 2+) T-DXd 5.4 mg/kg Q3W N = 41

Cohort 2: *HER2*m T-DXd 6.4 mg/kg Q3W N = 42

Cohort 2 expansion: *HER2*m T-DXd 6.4 mg/kg Q3W N = 49

R 2:1

T-DXd 5.4 mg/kg Q3W n = 102

T-DXd 6.4 mg/kg Q3W n = 50

T-DXd 5.4 mg/kg DL-02 BM (n = 32) Non-BM (n = 70)

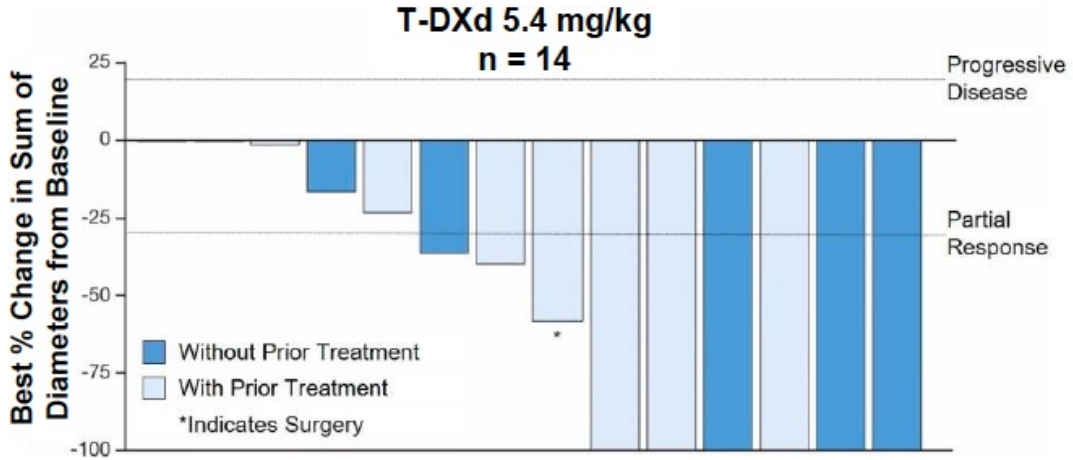
Pooled T-DXd 6.4 mg/kg DL-01 *HER2*m/DL-02 BM (n = 54) Non-BM (n = 87)

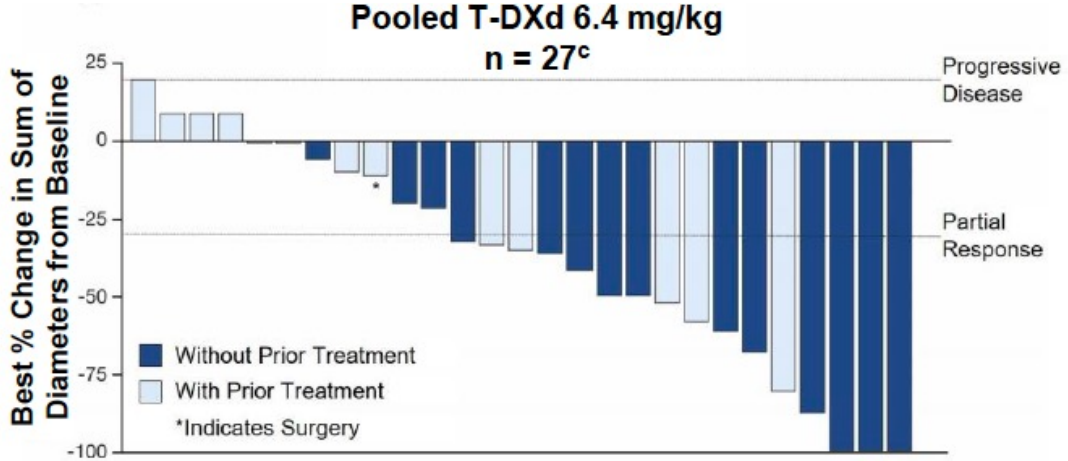
Endpoints

In patients with and without baseline BM:
- Systemic cORR per BICR
- Systemic DoR per BICR
- Sites of progression per BICR
- TEAEs

In patients with measurable baseline BM:[d]
- IC-cORR per BICR
- IC-DCR per BICR
- IC-DoR per BICR

	T-DXd 5.4 mg/kg DL-02 BM n = 14	Pooled T-DXd 6.4 mg/kg DL-01 *HER2*m/DL-02 BM n = 30
IC-cORR, n (%)[a]	**7 (50.0)**	**9 (30.0)**
95% CI[b]	23.0-77.0	14.7-49.4
CR	3 (21.4)	0
PR	4 (28.6)	9 (30.0)
SD	6 (42.9)	13 (43.3)
PD	1 (7.1)	4 (13.3)
NE[c]	0	2 (6.7)
Missing	0	2 (6.7)
IC-DCR, n (%)[a]	**13 (92.9)**	**22 (73.3)**
95% CI[b]	66.1-99.8	54.1-87.7
IC-DoR, months[d]		
Median, (95% CI)[e]	9.5 (3.6-NE)	4.4 (2.9-10.2)





Planchard D, et al. ESMO 2023

Courtesy of Justin F Gainor, MD

HER2 Mutations: My Take

- Trastuzumab deruxtecan (5.4 mg/kg) is a SOC agent for HER2-mutant NSCLC
- Anti-tumor activity across various HER2 mutation types and prior therapy
- CNS anti-tumor activity observed with promising intra-cranial response rates, though limited number of patients and time to intracranial progression is noteworthy (prior BM treatment 2.6-2.8 months; no prior BM treatment 5.6 months – NE).
- My general approach is to still use platinum-doublet +/- anti-PD-1 in first-line, followed by trastuzumab deruxtecan in 2nd line.

Courtesy of Justin F Gainor, MD

HER2 Overexpression

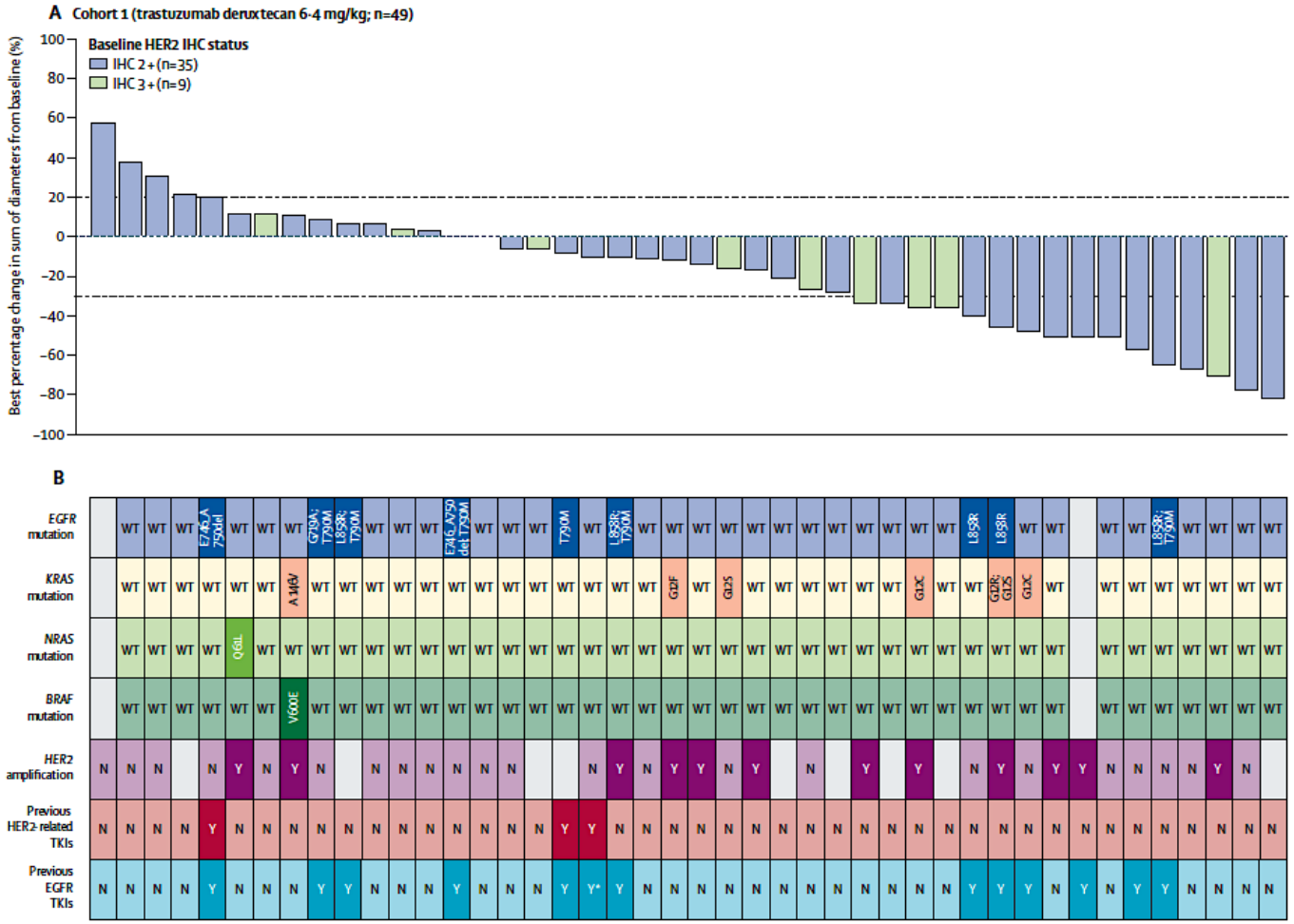
	Cohort 1 (6·4 mg/kg; N=49)	Cohort 1A (5·4 mg/kg; N=41)
(Continued from previous page)		
Number of previous lines of therapy	3 (2–4)	3 (2–4)
HER2 amplification, by FISH	13/38 (34%)	9/37 (24%)
HER2 IHC 2+	10/13 (77%)	0/9
HER2 IHC 3+	3/13 (23%)	9/9 (100%)

Data are median (IQR), n (%), or n/N (%). FISH=fluorescence in situ hybridisation. IHC=immunohistochemistry. *Prior pneumonectomy includes both partial and complete lung resections, and patients who underwent lung surgery for localised disease. †Renal function was defined according to baseline creatinine clearance (calculated with the Cockcroft–Gault equation[33]) ≥90 mL/min (normal), ≥60 and <90 mL/min (mild impairment), ≥30 and <60 mL/min (moderate impairment), and ≥15 and <30 mL/min (severe impairment).[34,35]

Table 1: **Baseline characteristics**

	Cohort 1 (6·4 mg/kg; N=49)	Cohort 1A (5·4 mg/kg; N=41)
Confirmed objective response rate, n (%; 95% CI)	13 (26·5%; 15·0–41·1)	14 (34·1%; 20·1–50·6)
Response outcomes, n (%)		
Complete response	0	2 (5%)
Partial response	13 (27%)	12 (29%)
Stable disease	21 (43%)	18 (44%)
Progressive disease	11 (22%)	4 (10%)
Not evaluable	4 (8%)	5 (12%)
Disease control rate, n (%; 95% CI)	34 (69·4%; 54·6–81·8)	32 (78·0%; 62·4–89·4)
Duration of response, months, median (95% CI)	5·8 (4·3–not evaluable)	6·2 (4·2–9·8)

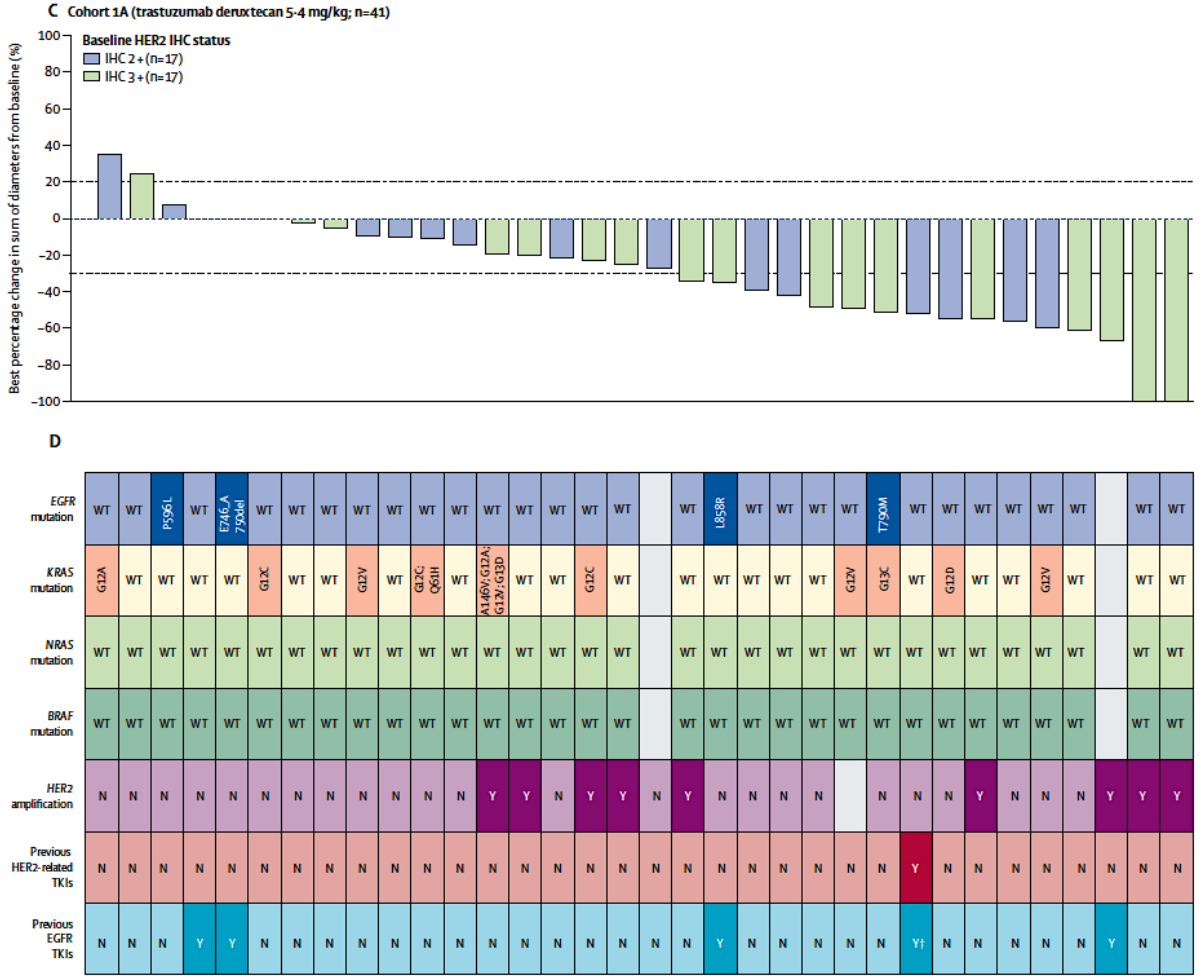
Table 2: **Summary of efficacy by independent central review**

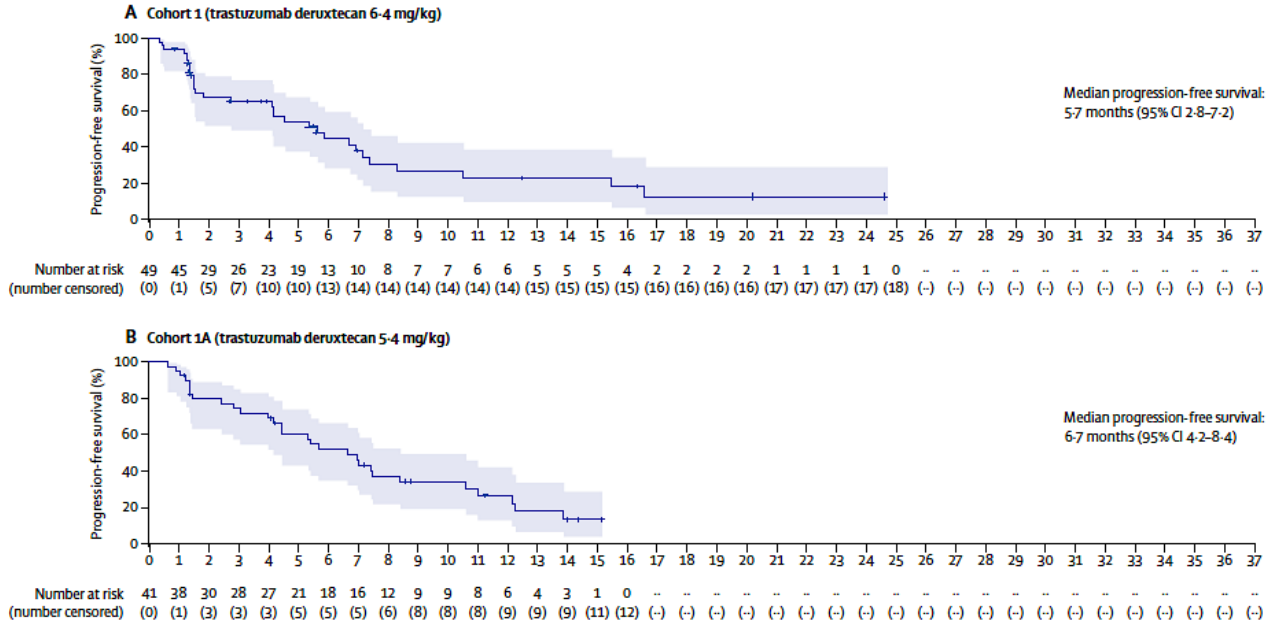


Smit E, et al. Lancet Oncol 2024

Courtesy of Justin F Gainor, MD

HER2 Overexpression





HER2 IHC 3+
ORR 52.9%; mDOR 6.9 months

Smit E, et al. Lancet Oncol 2024

Courtesy of Justin F Gainor, MD

HER2 Overexpression: My Take

- We now need to be testing for HER2 overexpression in NSCLC
- Trastuzumab deruxtecan gained FDA approval for HER2 IHC 3+ solid tumors (i.e., pan-tumor) as of April 2024
- We need more data on the clinicopathologic characteristics of NSCLCs with HER2 overexpression
- I would consider trastuzumab deruxtecan as a new SOC after chemo-IO for NSCLCs with HER2 IHC 3+
- Need more data on HER2 IHC 2+ and how best to position T-DXd

Courtesy of Justin F Gainor, MD

Year in Review: Myelofibrosis

A CME/MOC-Accredited Live Webinar

Tuesday, May 14, 2024
5:00 PM – 6:00 PM ET

Faculty

Aaron T Gerds, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

Thank you for joining us!

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

RTP Year in Review 2024