Year in Review: EGFR-Mutant Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, January 15, 2025
5:00 PM – 6:00 PM ET

Faculty

Enriqueta Felip, MD, PhD
Helena Yu, MD

Moderator

Neil Love, MD

RTP Year in Review 2025

Faculty

Enriqueta Felip, MD, PhD
Head, Thoracic Oncology Unit
Vall d'Hebron University Hospital
Vall d'Hebron Institute of Oncology (VHIO)
Professor of Medicine, UAB
Barcelona, Spain

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Helena Yu, MD
Medical Oncologist
Associate Attending
Memorial Sloan Kettering Cancer Center
New York, New York

RTP Year in Review 2025

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, and Taiho Oncology Inc.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, ADC Therapeutics, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Clovis Oncology, Coherus BioSciences, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Hologic Inc, 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, Legend Biotech, Lilly, 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, Nuvalent, 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, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.

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Dr Yu — Disclosures

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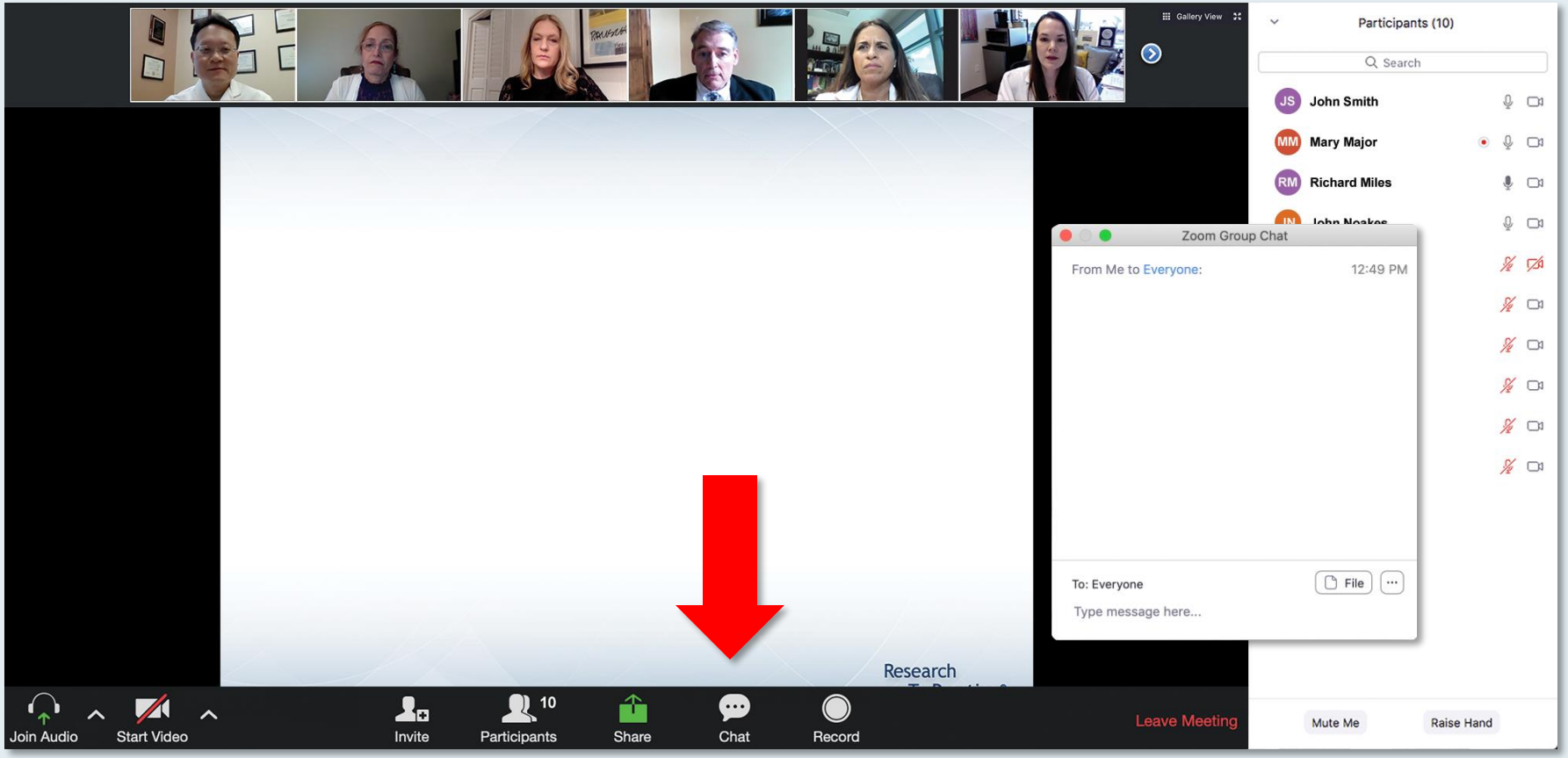
Contracted Research (To Institution)	AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Cullinan Therapeutics, Daiichi Sankyo Inc, Janssen Biotech Inc, Kumquat Biosciences, SystImmune Inc, Taiho Oncology Inc
Data and Safety Monitoring Boards/Committees	Janssen Biotech Inc, Mythic Therapeutics

We Encourage Clinicians in Practice to Submit Questions



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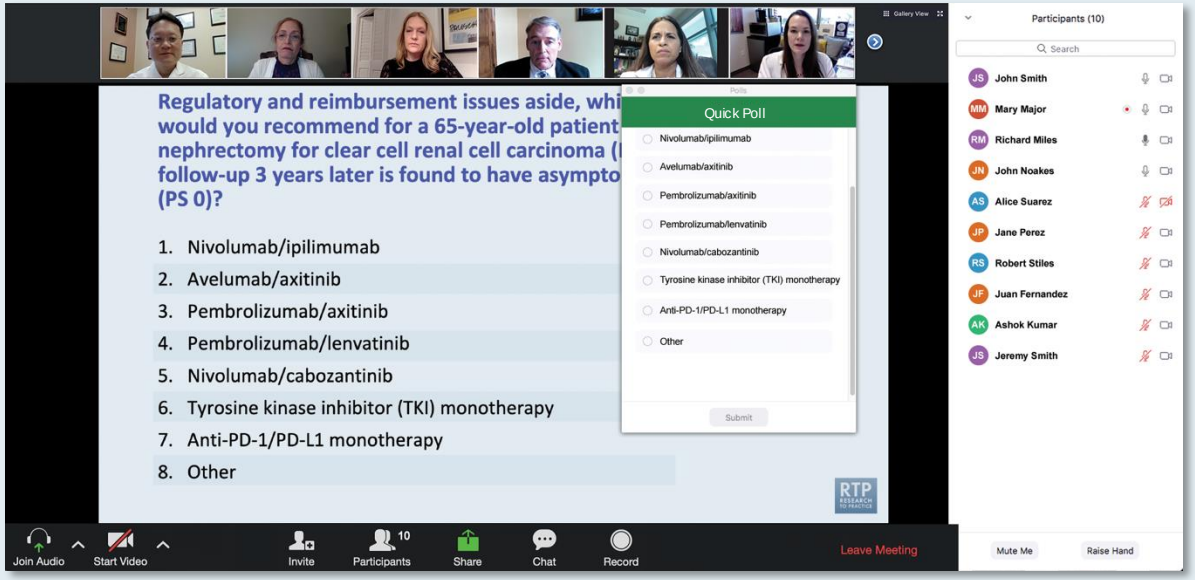

ONCOLOGY TODAY

WITH DR NEIL LOVE

Special Edition — Key Presentations on Lung Cancer from Recent Major Conferences

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GEORGETOWN UNIVERSITY HOSPITAL

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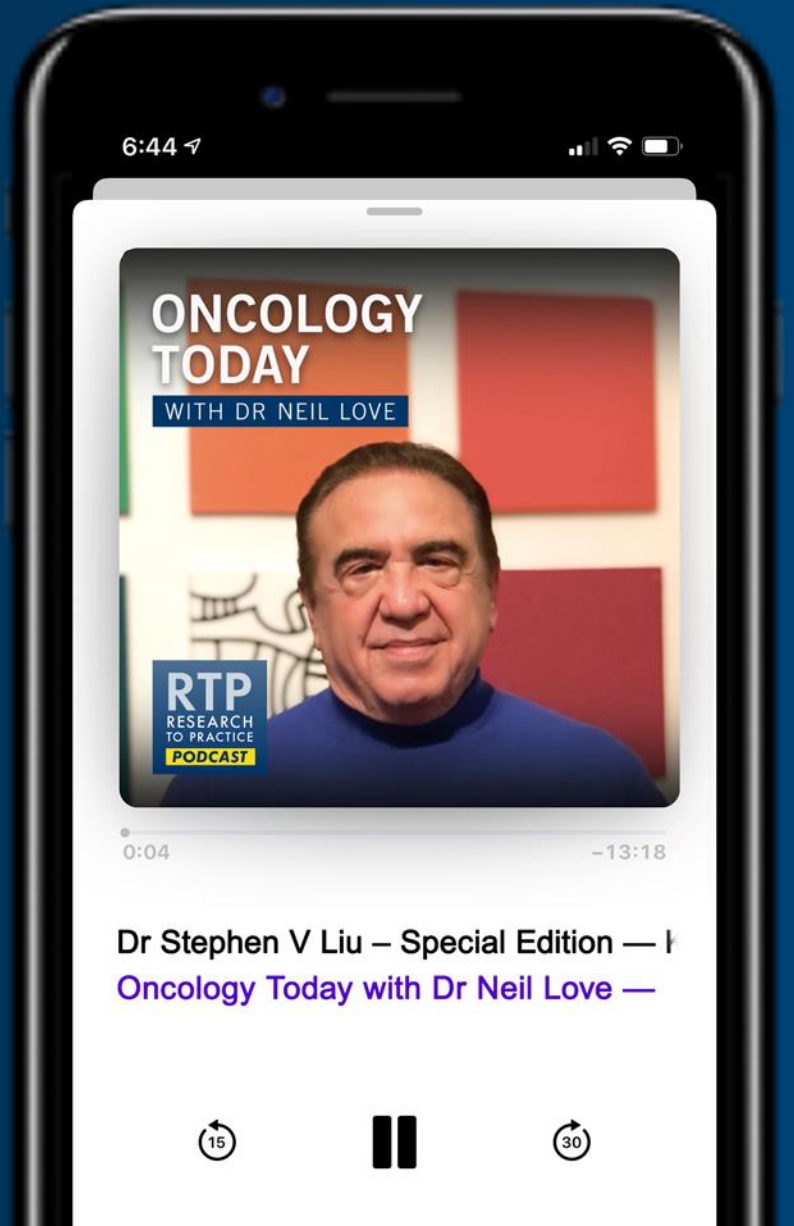

Teaching Cases from Investigators: The Application of Available Research to the Clinical Care of Patients with Hepatocellular Carcinoma

A CME Symposium Held in Conjunction with the 2025 ASCO® Gastrointestinal Cancers Symposium

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6:15 PM – 8:15 PM PT (9:15 PM – 11:15 PM ET)

Faculty

Anthony El-Khoueiry, MD

Aiwu Ruth He, MD, PhD

Richard S Finn, MD

Stacey Stein, MD

Moderator

Stephen “Fred” Divers, MD

RTP RESEARCH TO PRACTICE

What Clinicians Want to Know: Biomarker Assessment and Related Treatment Decision-Making for Patients with Colorectal Cancer

A CME Symposium Held in Conjunction with the 2025 ASCO® Gastrointestinal Cancers Symposium

Friday, January 24, 2025

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

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Arvind Dasari, MD, MS

Van K Morris, MD

Jenny Seligmann, MBChB, PhD

Eric Van Cutsem, MD, PhD

Moderator

Christopher Lieu, MD

RTP RESEARCH TO PRACTICE

Practical Perspectives: Experts Review Actual Cases of Patients with Various Forms of Gastrointestinal Cancer

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Matthew D Galsky, MD

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Tian Zhang, MD, MHS

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AGENDA

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MODULE 1: First-Line Treatment of Metastatic Disease

MODULE 2: Adjuvant and Neoadjuvant Therapy

MODULE 3: EGFR Exon 20 Insertion Mutations

MODULE 4: Antibody-Drug Conjugates

Thank you for joining us!

Information on how to obtain CME, ABIM MOC and ABS credit will be provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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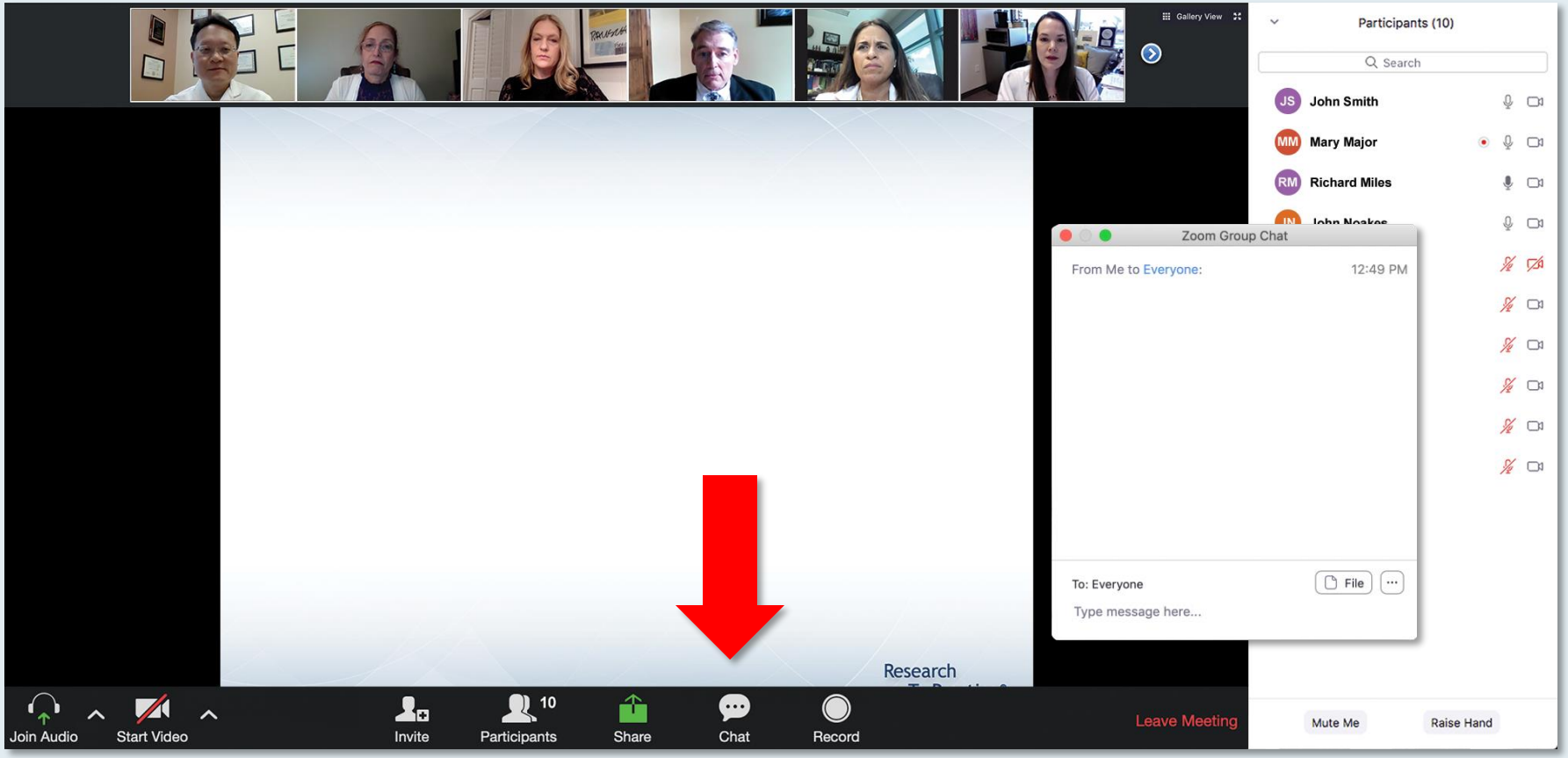

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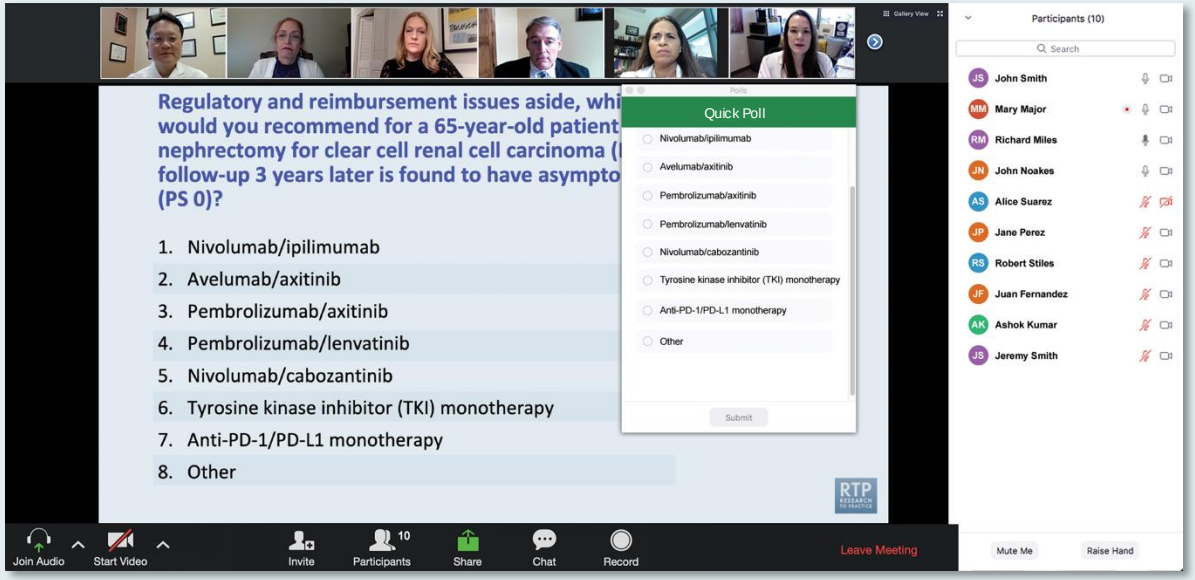

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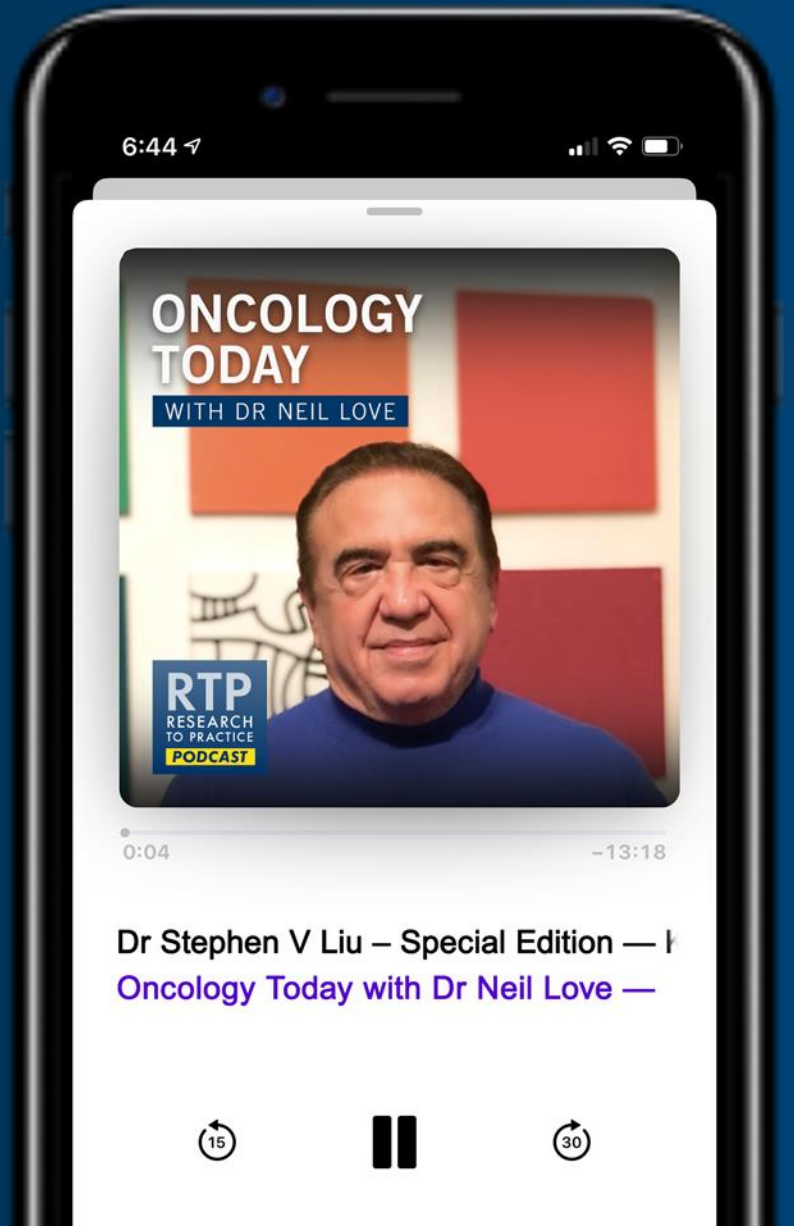

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Research To Practice CME Planning Committee Members, Staff and Reviewers

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Dr Felip — Disclosures

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Nonrelevant Financial Relationships	Medical Trends, Medscape, PeerVoice

Dr Yu — Disclosures

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Data and Safety Monitoring Boards/Committees	Janssen Biotech Inc, Mythic Therapeutics

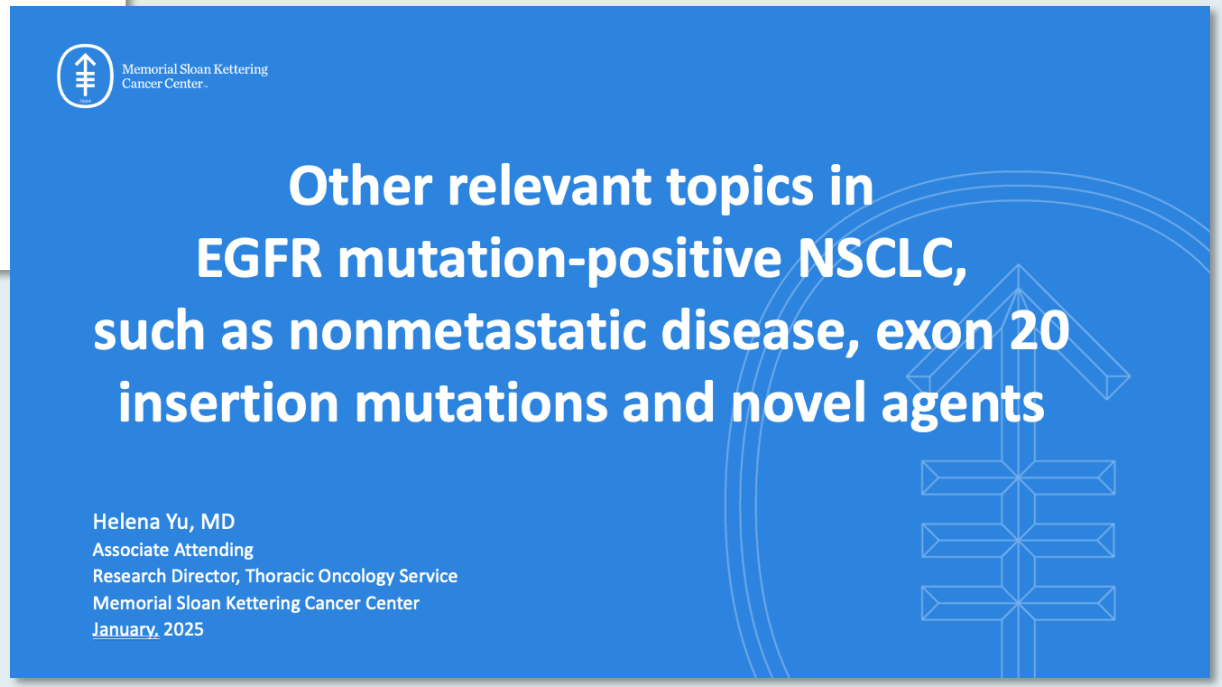
This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

Management of Metastatic EGFR Mutation-Positive NSCLC

Enriqueta Felip

Medical Oncology Service, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron Barcelona Hospital Campus, Universitat Autònoma de Barcelona, Barcelona, Spain

January 15, 2025



Key Data Sets

Enriqueta Felip, MD, PhD

- Valdiviezo N et al. **FLAURA2**: Impact of **Tumor Burden** on Outcomes of **1L Osimertinib** ± **Chemotherapy** in Patients with EGFR-Mutated Advanced NSCLC. WCLC 2024;Abstract MA12.04.
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- Park S et al. Phase II Efficacy and Safety of **80 mg Osimertinib** in Patients with **Leptomeningeal Metastases** Associated with Epidermal Growth Factor Receptor Mutation-Positive Non-Small Cell Lung Cancer **(BLOSSOM)**. *J Clin Oncol* 2024 August 10;42(23):2747-56.

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- Felip E et al. **Amivantamab plus Lazertinib** versus **Osimertinib** in **First-Line** EGFR-Mutant Advanced Non-Small-Cell Lung Cancer with **Biomarkers of High-Risk Disease**: A Secondary Analysis from **MARIPOSA**. *Ann Oncol* 2024 September;35(9):805-16.
- Besse B et al. **Mechanisms** of **Acquired Resistance** to 1L **Amivantamab plus Lazertinib** vs **Osimertinib** in Patients with EGFR-Mutant Advanced NSCLC: An Early Analysis from the **Phase III MARIPOSA** Study. ESMO 2024;Abstract LBA55.
- Popat S et al. **Amivantamab plus Chemotherapy** vs Chemotherapy in EGFR-Mutated, Advanced Non-Small Cell Lung Cancer After **Disease Progression on Osimertinib**: Second Interim Overall Survival from **MARIPOSA-2**. ESMO 2024;Abstract LBA54.

Key Data Sets

Enriqueta Felip, MD, PhD (Continued)

- Leighl NB et al. **Subcutaneous** versus **Intravenous Amivantamab**, Both in Combination with **Lazertinib**, in Refractory Epidermal Growth Factor Receptor-Mutated Non-Small Cell Lung Cancer: Primary Results from the **Phase III PALOMA-3** Study. *J Clin Oncol* 2024 October 20;42(30):3593-605.
- Mok T et al. **Nivolumab** plus Chemotherapy in Epidermal Growth Factor Receptor-Mutated Metastatic Non-Small-Cell Lung Cancer After Disease Progression on Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors: **Final Results of CheckMate 722**. *J Clin Oncol* 2024 April 10;42(11):1252-64.
- Yang JC-H et al. **Phase III KEYNOTE-789** Study of **Pemetrexed and Platinum** with or without **Pembrolizumab** for Tyrosine Kinase Inhibitor-Resistant, *EGFR*-Mutant, Metastatic Nonsquamous Non-Small Cell Lung Cancer. *J Clin Oncol* 2024 December;42(34):4029-39.

Key Data Sets

Helena Yu, MD

- Blakely CM et al. **Neoadjuvant Osimertinib** for the Treatment of **Stage I-IIIA** Epidermal Growth Factor Receptor-Mutated Non-Small Cell Lung Cancer: A Phase II Multicenter Study. *J Clin Oncol* 2024 September 10;42(26):3105-14.
- John T et al. Molecular Residual Disease **(MRD) Analysis** from the **ADAURA** Trial of Adjuvant (Adj) **Osimertinib** in Patients (pts) with Resected EGFR-Mutated (EGFRm) **Stage IB-IIIA** Non-Small Cell Lung Cancer (NSCLC). ASCO 2024;Abstract 8005.
- Lu S et al. **Osimertinib After Chemoradiotherapy** in **Stage III** *EGFR*-Mutated NSCLC. *N Engl J Med* 2024 August 15;391(7):585-97.
- Lu S et al. **Osimertinib** After Definitive **Chemoradiotherapy** in **Unresectable Stage III** Epidermal Growth Factor Receptor-Mutated Non-Small-Cell Lung Cancer: Analyses of **Central Nervous System** Efficacy and **Distant Progression** from the **Phase III LAURA** Study. *Ann Oncol* 2024 December;35(12):1116-25.
- Sands J et al. **Datopotamab Deruxtecan** in Advanced or Metastatic Non-Small Cell Lung Cancer with Actionable Genomic Alterations: Results from the Phase II **TROPION-Lung05 Study**. *J Clin Oncol* 2025 January 6;[Online ahead of print].

Key Data Sets

Helena Yu, MD (Continued)

- Lisberg A et al. **Intracranial** Efficacy of **Datopotamab Deruxtecan (Dato-DXd)** in Patients (pts) with Previously Treated Advanced/Metastatic Non-Small Cell Lung Cancer (a/m NSCLC) with Actionable Genomic Alterations (AGA): Results from **TROPION-Lung05**. ASCO 2024;Abstract 8593.
- Ahn M-J et al. Efficacy and Safety of **Datopotamab Deruxtecan (Dato-DXd)** in Patients (pts) with Previously-Treated EGFR-Mutated **Advanced** Non-Small Cell Lung Cancer (NSCLC): A **Pooled Analysis** of **TROPION-Lung01** and **TROPION-Lung05**. ESMO Asia 2024;Abstract LBA7.
- 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 December 10;41(35):5363-75.
- Yu HA et al. Translational Insights and Overall Survival in the **U31402-A-U102** Study of **Patritumab Deruxtecan (HER3-DXd)** in EGFR-Mutated NSCLC. *Ann Oncol* 2024 May;35(5):437-47.
- Mok T et al. **HERTHENA-Lung02: Phase III** Study of **Patritumab Deruxtecan** in Advanced *EGFR*-Mutated NSCLC After a Third-Generation EGFR TKI. *Future Oncol* 2024 May;20(15):969-80.

Key Data Sets

Helena Yu, MD (Continued)

- Garon EB et al. **Phase 3 TroFuse-004** Study: **Sac-TMT** vs Chemotherapy for Previously Treated **Advanced** NSCLC with EGFR/Other Genomic Alterations. WCLC 2024;Abstract P2.10A.06.
- Leighl NB et al. **Trofuse-009: Phase 3** Study of **Sac-TNT** vs Platinum-Doublet Chemotherapy for Previously Treated EGFR-Mutated **Advanced** NSCLC. WCLC 2024;Abstract P2.10A.07.
- Fang W et al. Updated Efficacy and Safety of **Anti-TROP2 ADC SKB264 (MK-2870)** for Previously Treated Advanced NSCLC in Phase 2 Study. AACR 2024;Abstract CT247.
- Passaro A et al. Safety and Anti-tumour Activity of **Zipalertinib** in NSCLC Patients (pts) with **EGFR Exon 20 Insertion (ex20ins)** Mutations Who Received **Prior Amivantamab**. ESMO 2024;Abstract 1254MO.
- Yu HA et al. **REZILIENT2**: Phase 2 Study of **Zipalertinib** in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) with **Exon 20 Insertions (ex20ins)** and Other Uncommon Epidermal Growth Factor Receptor *(EGFR)* Mutations. ASCO 2024;Abstract TPS8670.
- Yu HA et al. **REZILIENT3**: **Phase 3** Study of **Zipalertinib plus Chemotherapy** in Patients with **Previously Untreated, Advanced** Nonsquamous Non-Small Cell Lung Cancer (NSCLC) Harboring Epidermal Growth Factor Receptor (EGFR) **Exon 20 Insertions (Ex20ins)** Mutations. ASCO 2024;Abstract TPS8671.

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MODULE 1: First-Line Treatment of Metastatic Disease

MODULE 2: Adjuvant and Neoadjuvant Therapy

MODULE 3: EGFR Exon 20 Insertion Mutations

MODULE 4: Antibody-Drug Conjugates

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- Popat S et al. **Amivantamab plus Chemotherapy** vs Chemotherapy in EGFR-Mutated, Advanced Non-Small Cell Lung Cancer After **Disease Progression on Osimertinib**: Second Interim Overall Survival from **MARIPOSA-2**. ESMO 2024;Abstract LBA54.
- Leighl NB et al. **Subcutaneous** versus **Intravenous Amivantamab**, Both in Combination with **Lazertinib**, in Refractory Epidermal Growth Factor Receptor-Mutated Non-Small Cell Lung Cancer: Primary Results from the **Phase III PALOMA-3** Study. *J Clin Oncol* 2024 October 20;42(30):3593-605.

Valdiviezo N et al. FLAURA2: Impact of Tumor Burden on Outcomes of 1L Osimertinib ± CT in Patients with EGFR-mutated Advanced NSCLC. WCLC 2024; Abstract MA12.04

My take home messages

- The mechanisms for the observed clinical benefit with osimertinib+CT combination are not currently known
  - ✓ It is possible that the combination overcomes intratumor heterogeneity

- The PFS benefit appeared to be most pronounced among patients with BM at baseline
  - ✓ Brain scans were performed at screening and at the time of PD in all patients. Patients with brain metastases at screening underwent brain scans at each tumor assessment

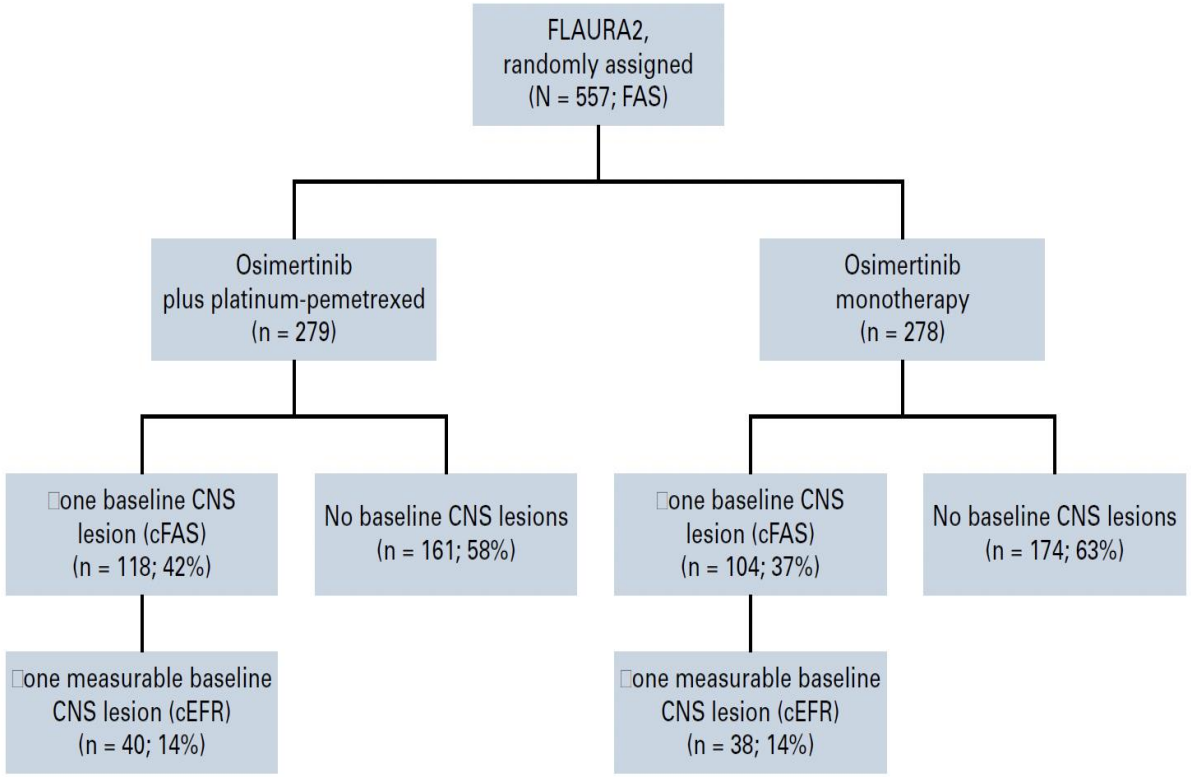
- PFS benefit was observed with osimertinib+CT vs osimertinib alone in patients with high tumor burden

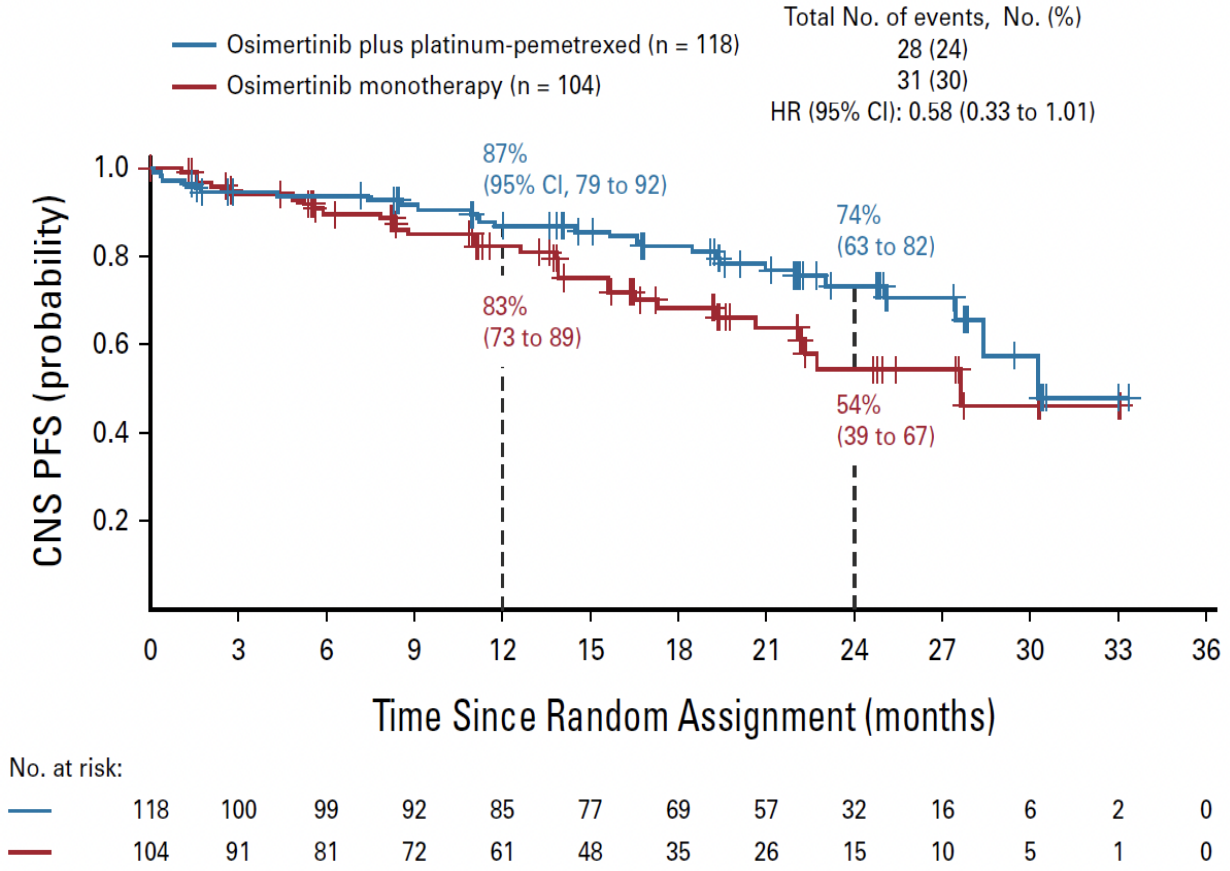
- No PFS differences in patients with intra-thoracic disease (HR 0.97)

Courtesy of Enriqueta Felip, MD, PhD

Jänne PA et al. CNS Efficacy of Osimertinib With or Without CT in EGFR-Mutated Advanced NSCLC. J Clin Oncol. 2024 Mar 1;42(7):808-820

- **FLAURA2: systemic PFS was improved with osimertinib+CT vs osimertinib monotherapy in the subgroup of patients with CNS metastases (mPFS 24.0 vs 13.8 mo; HR 0.47) and those without (27.6 vs 21.0 mo; HR 0.75)**
- **The present study reports CNS efficacy (including CNS PFS) of osimertinib+CT vs osimertinib in patients from FLAURA2**

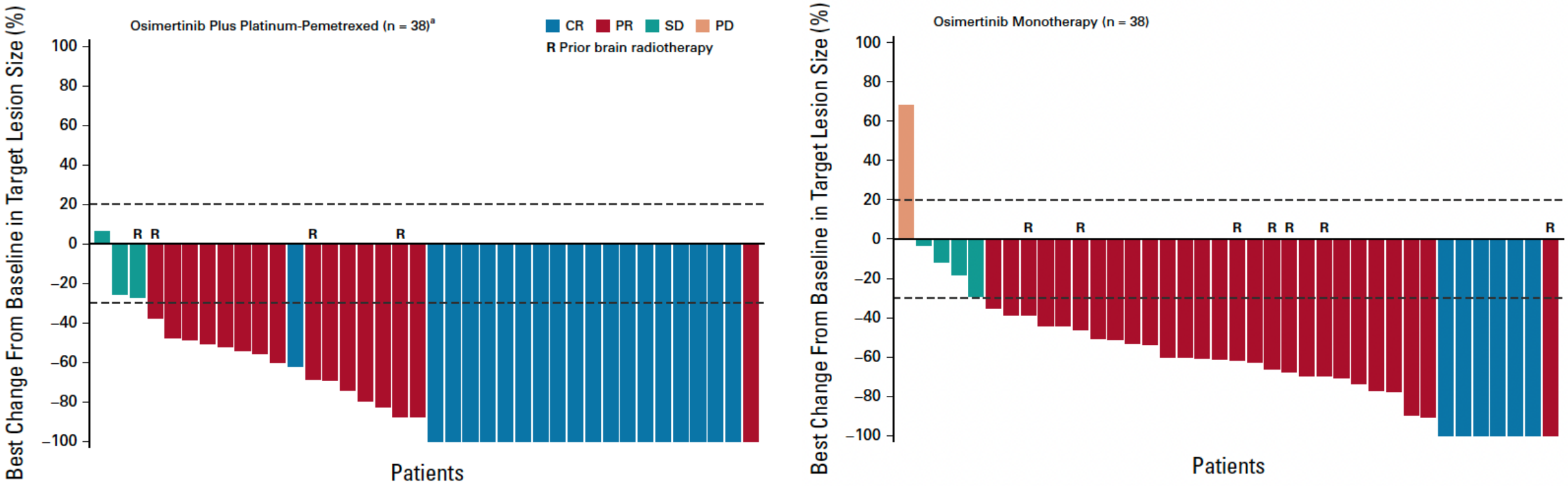




Courtesy of Enriqueta Felip, MD, PhD

CNS PFS in CNS-full analysis set

Jänne PA et al. CNS Efficacy of Osimertinib With or Without CT in EGFR-Mutated Advanced NSCLC. J Clin Oncol. 2024 Mar 1;42(7):808-820



Patients in the combination arm had a greater depth of response compared with those in the monotherapy arm

Courtesy of Enriqueta Felip, MD, PhD

Jänne PA et al. CNS Efficacy of Osimertinib With or Without CT in EGFR-Mutated Advanced NSCLC. J Clin Oncol. 2024 Mar 1;42(7):808-820

My take home messages

- All randomly assigned patients in FLAURA2 had brain scans at baseline (MRI in 84%)
- Scans were assessed by neuroradiologist BIRC
- Among 222 patients with baseline CNS metastases, osimertinib+CT demonstrated a clinically and meaningful improvement in CNS PFS compared with osimertinib monotherapy
- Data support the combination as 1L in patients with EGFR mutations and CNS disease at baseline

Courtesy of Enriqueta Felip, MD, PhD

Park S et al. Phase II Efficacy and Safety of 80 mg Osimertinib in Patients With Leptomeningeal Metastases Associated With EGFR Mutation-Positive NSCLC (BLOSSOM). J Clin Oncol. 2024 Aug 10;42(23):2747-2756

My take home messages

- High efficacy of 80 mg once daily of osimertinib in patients with LMs

- An important limitation (as recognized by the authors in the “Discussion”): the study includes patients initially treated with 1st and 2nd generation EGFR TKI
  - ✓ The present SoC: 3rd generation EGFR TKI

- The study supports the standard osimertinib dose (80 mg) vs double daily dose (160 mg) in patients with CNS disease

Courtesy of Enriqueta Felip, MD, PhD

Positive Topline OS Results from Pivotal Phase III MARIPOSA Study Announced

Press Release: January 7, 2025

"[Today were] announced positive topline results for the gold standard endpoint in cancer treatment of overall survival (OS) from the Phase 3 MARIPOSA study, evaluating amivantamab-vmjw plus lazertinib as a first-line therapy for patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions (ex19del) or L858R substitution mutations. The chemotherapy-free combination regimen met the final pre-specified secondary endpoint of OS and demonstrated clinically meaningful and statistically significant improvement in OS versus the current standard of care osimertinib. Improvement in median OS is expected to exceed one year. Results from the final OS analysis build upon previously reported data from the interim analysis and positive results from the PFS analysis.

Due to the impact of these data on patient care, these OS results will be presented at an upcoming major medical meeting, and will be shared with global health authorities. Amivantamab combined with lazertinib is approved in the United States and Europe for the first-line treatment of patients with EGFR-mutated NSCLC based on the MARIPOSA Phase 3 study."

https://finance.yahoo.com/news/rybrevant-amivantamab-vmjw-plus-lazcluze-130000654.html?guccounter=2

Gadgeel S et al. Amivantamab Plus Lazertinib vs Osimertinib in First-line EGFR-mutant Advanced NSCLC: Longer Follow-up of the MARIPOSA Study. WCLC 2024; Abstract OA02.03

My take home messages

- After longer follow-up (median: 31.1 months), data continue to favor 1L amivantamab+lazertinib over osimertinib with a promising OS trend (HR, 0.77) in patients with EGFR-mutant advanced NSCLC
- OS curves separate early and widen over time, favoring amivantamab+lazertinib
- *Press release:* positive and clinically meaningful OS benefit with the combination
- A clear scientific rationale: “proactively address mechanisms of resistance to osimertinib blocking EGFR and MET”
- High incidence of EGFR- and MET-related AEs; toxicity management is relevant
- The data support the combination as 1L in patients with EGFR mutations

Courtesy of Enriqueta Felip, MD, PhD

Nguyen D et al. Amivantamab Plus Lazertinib vs Osimertinib in First-Line, EGFR-Mutant Advanced NSCLC: Patient-relevant Outcomes from MARIPOSA. WCLC 2024; Abstract MA12.07

My take home messages

- Amivantamab + lazertinib combination therapy delayed symptomatic progression compared to osimertinib
  - ✓ Symptomatic progression is a patient-relevant endpoint

- QoL was maintained in both treatment arms
  - ✓ The increased adverse events from amivantamab+ lazertinib did not meaningfully impact patients' health-related QoL

Courtesy of Enriqueta Felip, MD, PhD

Felip E et al. Amivantamab plus lazertinib vs osimertinib in 1L EGFR-mutant advanced NSCLC with biomarkers of high-risk disease: a secondary analysis from MARIPOSA. Ann Oncol. 2024 Sep;35(9):805-816

My take home messages

- Approx 50% of patients had TP53 co-mutations (detected by ctDNA NGS); 70% of patients had detectable EGFR mutations by ddPCR

- Amivantamab+lazertinib significantly improved median PFS vs osimertinib in high-risk subgroups with:
  - ✓ History of brain metastases (HR, **0.69**; *P*=0.010)
  - ✓ Baseline liver metastases (HR, **0.58**; *P*=0.017)
  - ✓ *TP53* co-mutations (HR, **0.65**; *P*=0.003)
  - ✓ Detectable baseline *EGFR*m ctDNA[b] (HR, **0.68**; *P*=0.002)
  - ✓ Without *EGFR*m ctDNA[b] clearance at Week 9 (HR, **0.49**; *P*=0.015)

- Amivantamab+lazertinib effectively overcomes the effect of these negative prognostic factors

- Among the corresponding subgroups without high-risk features, amivantamab+lazertinib showed a numerical PFS benefit over osimertinib

Courtesy of Enriqueta Felip, MD, PhD

Besse B et al. Mechanisms of acquired resistance to 1L amivantamab plus lazertinib vs osimertinib in patients with EGFR-mutant advanced NSCLC: An early analysis from the phase III MARIPOSA study. ESMO 2024; Abstract LBA55

My take home messages

- Using ctDNA NGS analysis, amivantamab+lazertinib reduced the incidence of MET amplifications and EGFR resistance mutation vs osimertinib
- Low rate (0.9%) of TP53/RB1 loss (associated with SCLC transformation)
- Confirm the scientific rationale: proactively address mechanisms of resistance to osimertinib blocking EGFR and MET

Courtesy of Enriqueta Felip, MD, PhD

Popat S et al. Amivantamab plus CT vs CT in EGFR-mutated, advanced NSCLC after disease progression on osimertinib: Second interim overall survival from MARIPOSA-2. ESMO 2024;Abstract LBA54

My take home messages

- At the 2nd interim analysis (median follow-up 18.1 mo), promising OS trend favoring amivantamab+CT in the post-osimertinib setting (OS HR 0.73)

- Amivantamab+CT vs CT was associated with improvement in:
  - ✓Time to symptomatic progression
  - ✓Time to treatment discontinuation
  - ✓Time to subsequent therapy
  - ✓PFS2

- An increasing number of treatment regimens will be available in this scenario: targeted combinations, ADC, CT+bispecifics antibody

Courtesy of Enriqueta Felip, MD, PhD

Leighl NB et al. Subcutaneous vs Intravenous Amivantamab, Both in Combination With Lazertinib, in Refractory EGFR-Mutated NSCLC: Primary Results From Phase III PALOMA-3 Study. J Clin Oncol. 2024 Oct 20;42(30):3593-3605

My take home messages

Adapted from Dr Jessica Lin's Discussion at ASCO 2024

- sc amivantamab demonstrated PK non-inferiority
- sc amivantamab demonstrated advantage in safety
  - ✓ Reduced rates of IRR and VTE
- sc amivantamab demonstrated non-inferior efficacy
  - ✓ Intriguing signal for improved efficacy (needs further investigation)

- The impact of sc administration on lymphatic absorption and immune stimulation is unknown but may also play a role in the OS results (????)
- The sc formulation of amivantamab in combination with lazertinib may become a treatment option in the future

Courtesy of Enriqueta Felip, MD, PhD

RARITAN, N.J., December 16, 2024 – The manufacturer today announced the U.S. Food and Drug Administration (FDA) has issued a Complete Response Letter (CRL) for the Biologics License Application (BLA) for a fixed combination of amivantamab and recombinant human hyaluronidase for subcutaneous administration (SC amivantamab) in patients with non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) mutations.

The CRL is related to observations as part of a standard pre-approval inspection at a manufacturing facility. The CRL is unrelated to the product formulation, or the efficacy and safety data submitted in the regulatory application, and the FDA has not requested any additional clinical studies. The currently approved intravenous (IV) formulation of amivantamab-vmjw is not impacted by the CRL.

AGENDA

Year in Review: EGFR-Mutant Non-Small Cell Lung Cancer

MODULE 1: First-Line Treatment of Metastatic Disease

MODULE 2: Adjuvant and Neoadjuvant Therapy

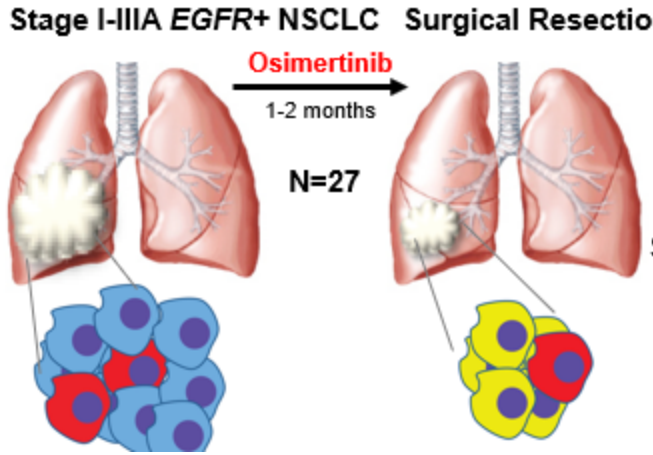
MODULE 3: EGFR Exon 20 Insertion Mutations

MODULE 4: Antibody-Drug Conjugates

(Neo)adjuvant or Consolidation Therapy

- Blakely CM et al. **Neoadjuvant Osimertinib** for the Treatment of **Stage I-IIIA** Epidermal Growth Factor Receptor-Mutated Non-Small Cell Lung Cancer: A Phase II Multicenter Study. *J Clin Oncol* 2024 September 10;42(26):3105-14.
- John T et al. Molecular Residual Disease **(MRD) Analysis** from the **ADAURA** Trial of Adjuvant (Adj) **Osimertinib** in Patients (pts) with Resected EGFR-Mutated (EGFRm) **Stage IB-IIIA** Non-Small Cell Lung Cancer (NSCLC). ASCO 2024;Abstract 8005.
- Lu S et al. **Osimertinib After Chemoradiotherapy** in **Stage III** EGFR-Mutated NSCLC. *N Engl J Med* 2024 August 15;391(7):585-97.
- Lu S et al. **Osimertinib** After Definitive **Chemoradiotherapy** in **Unresectable Stage III** Epidermal Growth Factor Receptor-Mutated Non-Small-Cell Lung Cancer: Analyses of **Central Nervous System** Efficacy and **Distant Progression** from the **Phase III LAURA** Study. *Ann Oncol* 2024 December;35(12):1116-25.

Neoadjuvant osimertinib for early stage



Primary Endpoint:
Major Pathologic Response (MPR) Rate
(Powered to detect MPR ~ 50%)

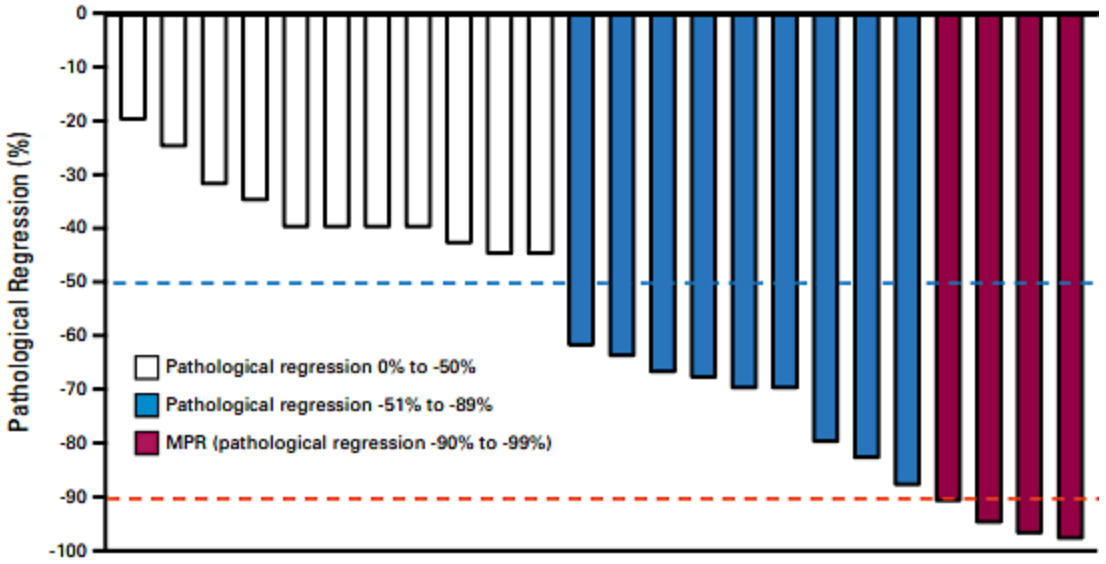
Secondary Endpoints:

Safety:
Surgical Complications
Unresectability Rate

Efficacy:
Lymph Node Downstaging
Pathological Response Rate
pCR Rate
5-year DFS/OS

Exploratory Endpoint:
Identify mechanisms underlying disease persistence

Primary Endpoint:
Major Pathologic Response Rate = 15%



Courtesy of Helena Yu, MD

Characteristic	All (N=27)
Age at Diagnosis (yrs)	66.5
Sex, N (%)	
Female	22 (81.5)
Male	5 (18.5)
Race/Ethnicity, N (%)	
White	15 (55.6)
Asian	11 (40.7)
Hispanic	1 (3.7)
Clinical Stage, N (%)	
IA	5 (18.5)
IB	3 (11.1)
IIA	3 (11.1)
IIB	7 (25.9)
IIIA	9 (33.3)
EGFR Mutation, N (%)	
L858R	16 (59.3)
Exon 19 deletion	11 (40.7)

Variable	No. (%)
Surgery	24 (88.9)
R0	23 (85.2)
R1	1 (3.7)
Not resected	3 (11.1)
Pathological response in resected tumors	
pCR (0% viable tumor)	0 (0)
MPR (≤10% viable tumor)	4 (16.7)
11%-49% viable tumor	9 (37.5)
<50% viable tumor	13 (54.2)
≥50% residual viable tumor	11 (45.8)

Blakely J Clin Oncol. 2024

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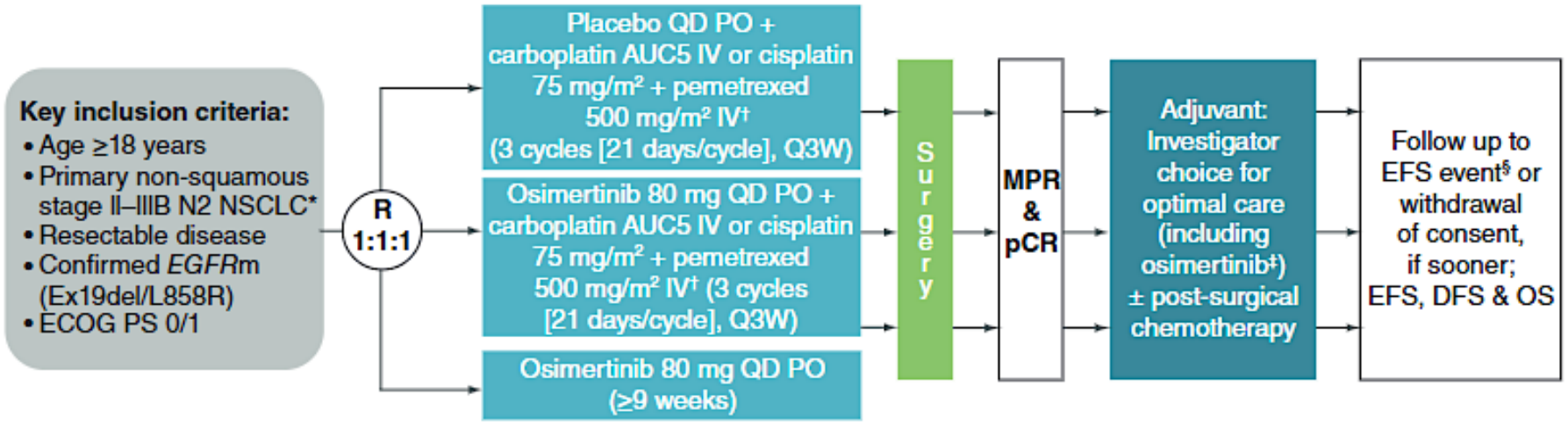
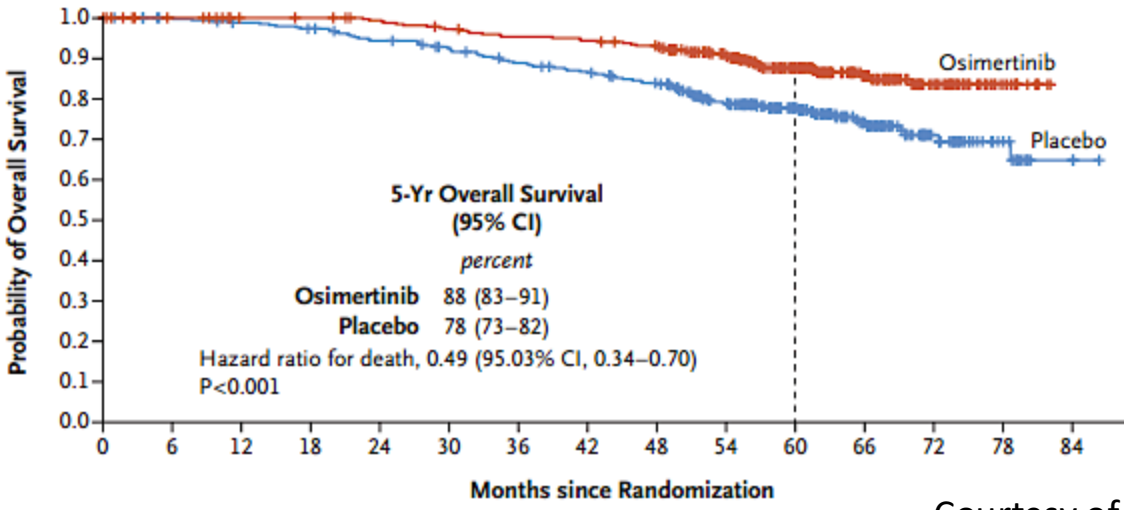
Neoadjuvant osimertinib for early stage

NeoADAURA study schema



OS benefit of adjuvant osimertinib

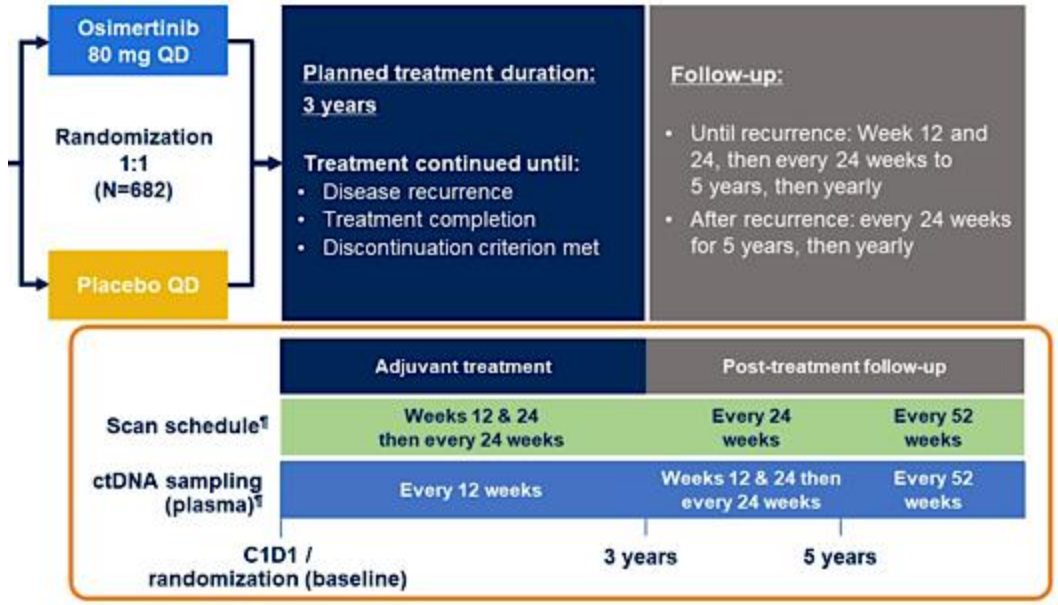


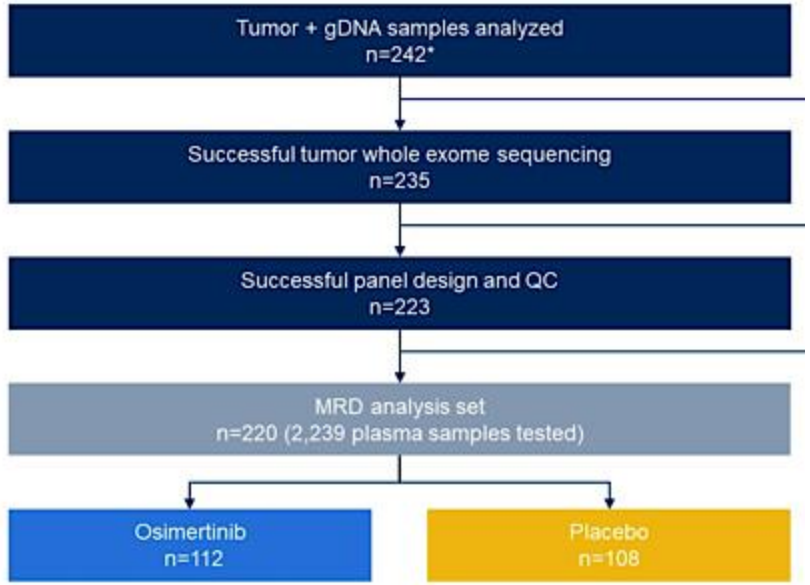
- Lower than expected MPR and PCR rate
- Possibly due to short treatment time (1-2 mo?)
- Clear survival benefit of adjuvant osimertinib
- Chemotherapy may be important for initial cytoreduction
- Await NeoADAURA results

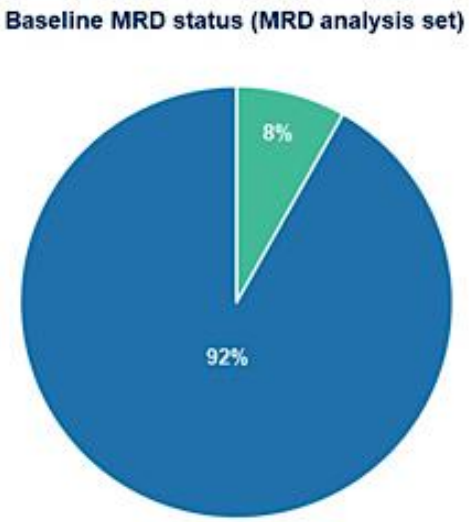
Courtesy of Helena Yu, MD

Blakely J Clin Oncol. 2024

ADAURA MRD Analysis

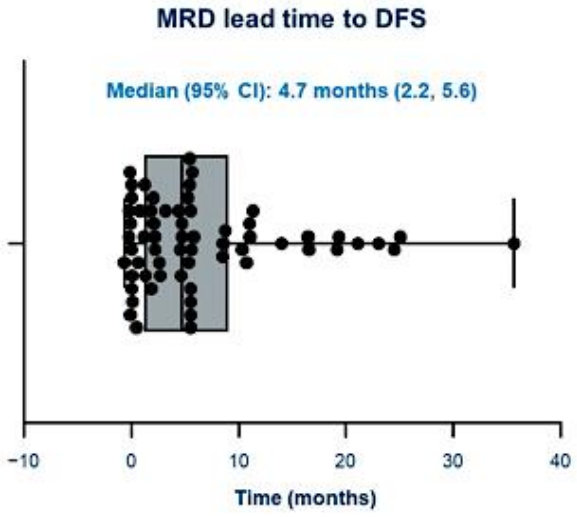


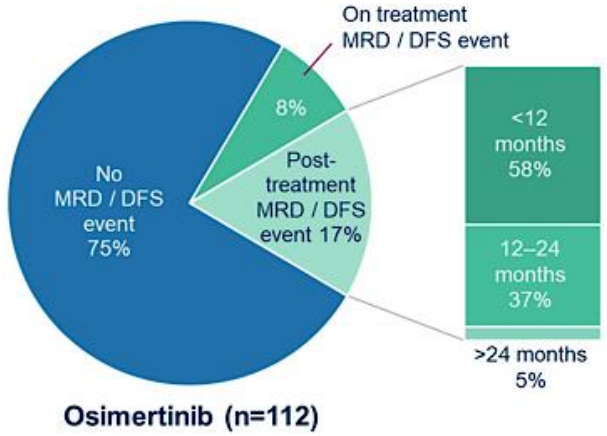


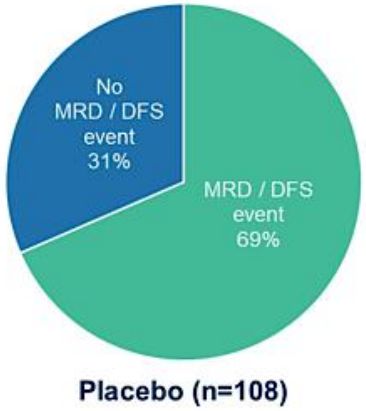


75% (84 / 112) patients receiving osimertinib maintained a DFS and MRD event-free status* during treatment and in post-treatment follow-up†

- Most MRD or DFS events* occurred post-osimertinib; 58% (11 / 19) occurred within 12 months post-osimertinib







- Tumor-informed MRD testing feasible, with lead time of 4.7mo
- DFS/MRD events often happened post-osimertinib in osi arm

Courtesy of Helena Yu, MD

John ASCO 2024; Abstract 800

LAURA: Osimertinib after chemoradiation

Patients with locally advanced, unresectable stage III* EGFRm NSCLC with no progression during / following definitive CRT† treatment

Key inclusion criteria:
- ≥18 years (Japan: ≥20)
- WHO PS 0 / 1
- Confirmed locally advanced, unresectable stage III* NSCLC
- Ex19del / L858R‡
- Maximum interval between last dose of CRT and randomisation: 6 weeks

Osimertinib 80 mg, once daily

Randomisation 2:1
(N=216)

Stratification by:
cCRT vs sCRT
Stage IIIA vs stage IIIB / IIIC
China vs non-China

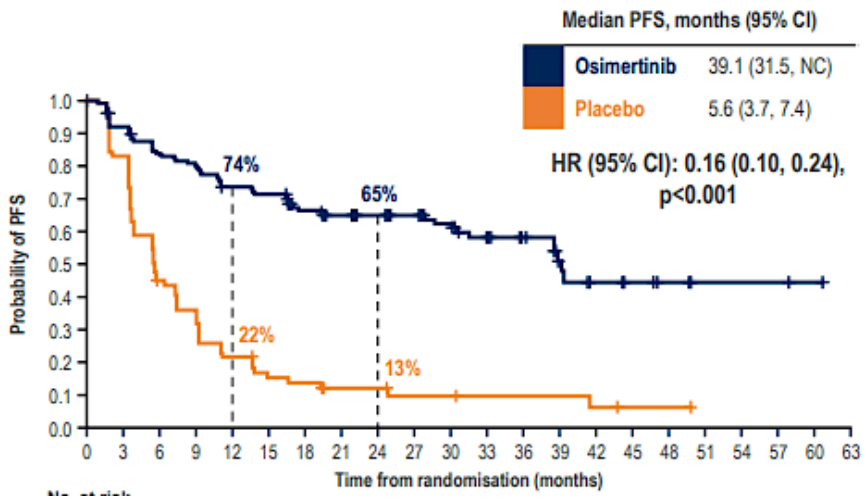
Placebo, once daily

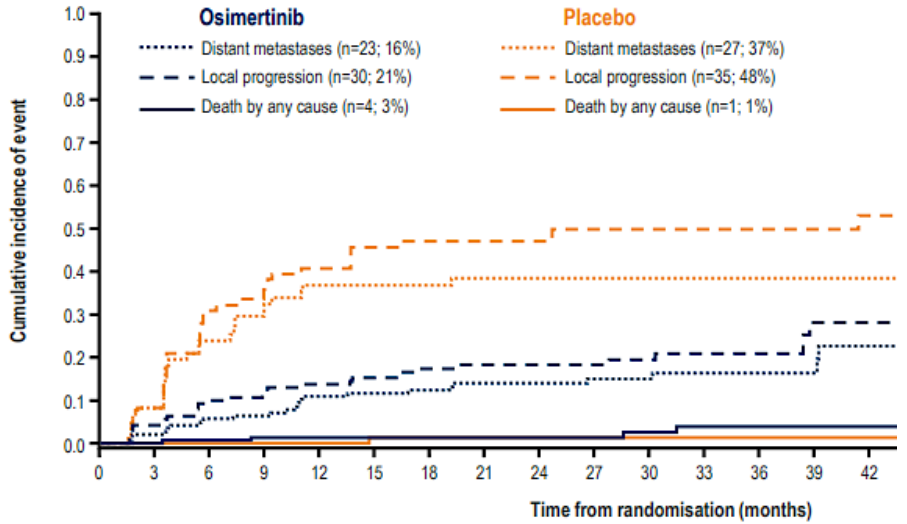
Treatment duration until BICR-assessed progression (per RECIST v1.1), toxicity, or other discontinuation criteria

Open-label osimertinib after progression offered to both treatment arms§

Primary Endpoint: PFS by BICR

PFS by BICR assessment[4]





Progression events by BICR assessment (LAURA)[9]

	Osimertinib (n=143)	Placebo (n=73)
Events, n (%)	57 (40)	63 (86)
Distant metastases*	23 (16)	27 (37)
Local progression*	30 (21)	35 (48)
Death in absence of distant metastases or local progression	4 (3)	1 (1)
Censored, n (%)	86 (60)	10 (14)

	Osimertinib (n=143)	Placebo (n=73)
Total CNS PFS events, n (%)†	29 (20)	30 (41)
CNS RECIST progression‡	18 (13)	26 (36)
Death in absence of CNS progression	11 (8)	4 (5)
Censored patients, n (%)	114 (80)	43 (59)
Median CNS PFS, months (95% CI)	**NR (NC, NC)**	**14.9 (7.4, NC)**

HR: 0.17 (0.09, 0.32), p<0.001 (nominal)

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Courtesy of Helena Yu, MD

Lu Ann Oncol 2024; Lu N Engl J Med 2024

Take home: LAURA: Osimertinib after chemoradiation

- Adjuvant osimertinib after chemoradiation led to improved time to metastatic disease and CNS progression
- High-risk group ~10% has baseline CNS metastases, ~50% no PET scan
- INDEFINITE osimertinib until progression. Should this be standard of care in resected disease as well? Or is this just replicated osimertinib in (micro) metastatic disease?

TAKE HOME: Osimertinib is standard of care after definitive therapy for all locally advanced EGFR-mutant lung cancers

Courtesy of Helena Yu, MD

Lu Ann Oncol 2024; Lu N Engl J Med 2024

AGENDA

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Zipalertinib for Patients with EGFR Exon 20 Insertion Mutations

- Passaro A et al. Safety and Anti-tumour Activity of **Zipalertinib** in NSCLC Patients (pts) with **EGFR Exon 20 Insertion (ex20ins)** Mutations Who Received **Prior Amivantamab**. ESMO 2024;Abstract 1254MO.
- Yu HA et al. **REZILIENT2**: Phase 2 Study of **Zipalertinib** in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) with **Exon 20 Insertions (ex20ins)** and Other Uncommon Epidermal Growth Factor Receptor *(EGFR)* Mutations. ASCO 2024;Abstract TPS8670.
- Yu HA et al. **REZILIENT3**: **Phase 3** Study of **Zipalertinib plus Chemotherapy** in Patients with **Previously Untreated, Advanced** Nonsquamous Non-Small Cell Lung Cancer (NSCLC) Harboring Epidermal Growth Factor Receptor (EGFR) **Exon 20 Insertions (Ex20ins)** Mutations. ASCO 2024;Abstract TPS8671.

Zipalertinib after amivantamab

Key eligibility criteria

- Locally advanced or metastatic NSCLC
- Documented *EGFR* exon 20 insertion
- *Progressed on or after amivantamab*
- ECOG PS 0 or 1
- Stable/asymptomatic brain metastases allowed

Zipalertinib
100 mg BID oral[a]

Primary endpoint:

- ORR and DOR per RECIST v1.

Secondary endpoints:

- Safety
- PFS
- DCR

Statistics, n (%) [95% CI]	Ami only (n=18)	Ami + other ex20ins (n=12)	Total (N=30)
Confirmed ORR	9 (50.0) [26.0–74.0]	3 (25.0) [5.5–57.2]	12 (40.0) [22.7–59.4]
CR	1 (5.6) [0.1–27.3]	0	1 (3.3) [0.1–17.2]
PR	8 (44.4) [21.5–69.2]	3 (25.0) [5.5–57.2]	11 (36.7) [19.9–56.1]
SD	7 (38.9) [17.3–64.3]	8 (66.7) [34.9–90.1]	15 (50.0) [31.3–68.7]
DCR (CR+PR+SD)	16 (88.9) [65.3–98.6]	11 (91.7) [61.5–99.8]	27 (90.0) [73.5–97.9]

- It was previously unknown whether there was cross-resistance between EGFR exon 20 directed antibodies versus tyrosine kinase inhibitors
- Zipalertinib appears to be effective after amivantamab with an ORR of 50%
- Zipalertinib is less effective (ORR 25%) after a different TKI (Poziotinib, mobocertinib, BLU-451)
- Assessment of sequencing of TKI and antibody are needed

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Courtesy of Helena Yu, MD

Passaro ESMO 2024; Abstract 1254MO

Ongoing zipalertinib trials

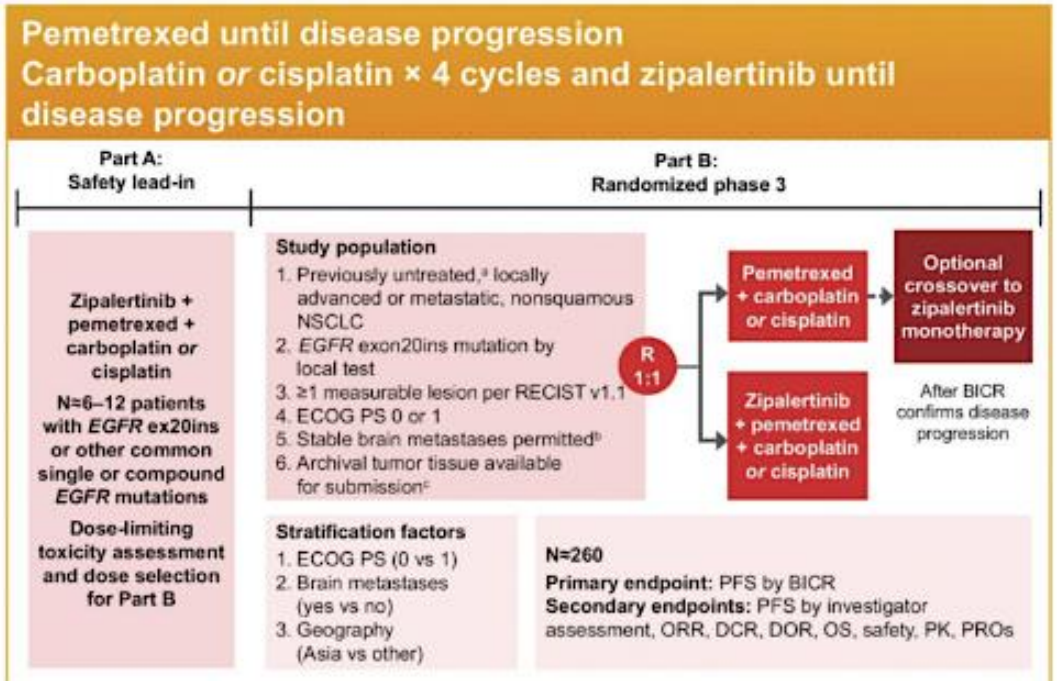
REZILIENT2: Zipalertinib in CNS, 1L, after other exon20 + uncommon mtns[1]

Zipalertinib 100 mg orally twice daily

Cohort A[a]	Cohort B[a]	Cohort C	Cohort D[a]
Patients with *EGFR* ex20ins mutations who have progressed on or after first-line platinum-based chemotherapy and prior therapy targeting ex20ins mutations (administered together or separately) for advanced disease	Patients with *EGFR* ex20ins mutations who have not received prior treatment for advanced disease	Patients with ex20ins, other uncommon single or compound *EGFR* mutations, and active brain metastases (including LMD) and who may or may not have received prior treatment for advanced disease	Patients harboring other, uncommon, non-ex20ins, single or compound *EGFR* mutations who have progressed on or after standard systemic therapy

Primary	• Investigator-assessed ORR per RECIST v1.1
Secondary	• DCR, DOR, PFS • OS • Intracranial efficacy (ORR, DOR, DCR) per RANO-BM (Cohort C) • Safety and tolerability • PK
Exploratory	• Population PK parameters and association with safety and efficacy • *EGFR* mutations/biomarkers from tumor samples and ctDNA

REZILIENT3: Phase 3 of 1L Zipalertinib + chemo vs chemo[2]



- REZILIENT2 will assess zipa in atypical EGFR, CNS disease and after other exon 20 treatments
- REZILIENT3 is a registrational study to assess zipa + chemo as 1L treatment (similar to amivantamab + chemo)

Courtesy of Helena Yu, MD

1:Yu ASCO 2024;Abstract TPS8670
2:Yu ASCO 2024; Abstract TPS8671

AGENDA

Year in Review: EGFR-Mutant Non-Small Cell Lung Cancer

MODULE 1: First-Line Treatment of Metastatic Disease

MODULE 2: Adjuvant and Neoadjuvant Therapy

MODULE 3: EGFR Exon 20 Insertion Mutations

MODULE 4: Antibody-Drug Conjugates

Anti-PD-1 Immunotherapy in Combination with Chemotherapy for Tyrosine Kinase Inhibitor (TKI)-Resistant Metastatic NSCLC

- Mok T et al. **Nivolumab** plus Chemotherapy in Epidermal Growth Factor Receptor-Mutated Metastatic Non-Small-Cell Lung Cancer After Disease Progression on Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors: **Final Results of CheckMate 722**. *J Clin Oncol* 2024 April 10;42(11):1252-64.
- Yang JC-H et al. **Phase III KEYNOTE-789** Study of **Pemetrexed and Platinum** with or without **Pembrolizumab** for Tyrosine Kinase Inhibitor-Resistant, *EGFR*-Mutant, Metastatic Nonsquamous Non-Small Cell Lung Cancer. *J Clin Oncol* 2024 December;42(34):4029-39.

Anti-PD-1 Immunotherapy in Combination with Chemotherapy for Tyrosine Kinase Inhibitor-Resistant, EGFR-Mutant Metastatic NSCLC

Outcome	KEYNOTE-789[1]		CheckMate 722[2]	
	Pembrolizumab + chemotherapy (n = 245)	Placebo + chemotherapy (n = 247)	Nivolumab + chemotherapy (n = 144)	Chemotherapy (n = 150)
Median progression-free survival (Hazard ratio; p-value)	5.6 mo	5.5 mo	5.6 mo	5.4 mo
	0.80 (0.0122)		0.75 (0.0528)	
Median overall survival (Hazard ratio; p-value)	15.9 mo	14.7 mo	19.4 mo	15.9 mo
	0.84 (0.0362)		0.82 (not reported)	
Overall response rate	29.0%	27.1%	31%	27%
Median duration of response	6.3 mo	5.6 mo	6.7 mo	5.6 mo

[1] Yang JC et al. *J Clin Oncol* 2024 Dec;42(34):4029-39;
[2] Mok T et al. *J Clin Oncol* 2024 Apr 10;42(11):1252-64.

Courtesy of Enriqueta Felip, MD, PhD

Antibody-Drug Conjugates for Advanced Disease

- Sands J et al. **Datopotamab Deruxtecan** in Advanced or Metastatic Non-Small Cell Lung Cancer with Actionable Genomic Alterations: Results from the Phase II **TROPION-Lung05 Study**. *J Clin Oncol* 2025 January 6;[Online ahead of print].
- Lisberg A et al. **Intracranial** Efficacy of **Datopotamab Deruxtecan (Dato-DXd)** in Patients (pts) with Previously Treated Advanced/Metastatic Non-Small Cell Lung Cancer (a/m NSCLC) with Actionable Genomic Alterations (AGA): Results from **TROPION-Lung05**. ASCO 2024;Abstract 8593
- Ahn M-J et al. Efficacy and Safety of **Datopotamab Deruxtecan (Dato-DXd)** in Patients (pts) with Previously-Treated EGFR-Mutated **Advanced** Non-Small Cell Lung Cancer (NSCLC): A **Pooled Analysis** of **TROPION-Lung01** and **TROPION-Lung05**. ESMO Asia 2024;Abstract LBA7.
- 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 December 10;41(35):5363-75.
- Yu HA et al. Translational Insights and Overall Survival in the **U31402-A-U102** Study of **Patritumab Deruxtecan (HER3-DXd)** in EGFR-Mutated NSCLC. *Ann Oncol* 2024 May;35(5):437-47.

Antibody-Drug Conjugates for Advanced Disease (Continued)

- Mok T et al. **HERTHENA-Lung02: Phase III** Study of **Patritumab Deruxtecan** in Advanced EGFR-Mutated NSCLC After a Third-Generation EGFR TKI. *Future Oncol* 2024 May;20(15):969-80.
- Garon EB et al. **Phase 3 TroFuse-004** Study: **Sac-TMT** vs Chemotherapy for Previously Treated **Advanced** NSCLC with EGFR/Other Genomic Alterations. WCLC 2024;Abstract P2.10A.06.
- Leighl NB et al. **Trofuse-009: Phase 3** Study of **Sac-TNT** vs Platinum-Doublet Chemotherapy for Previously Treated EGFR-Mutated **Advanced** NSCLC. WCLC 2024;Abstract P2.10A.07.
- Fang W et al. Updated Efficacy and Safety of **Anti-TROP2 ADC SKB264 (MK-2870)** for Previously Treated Advanced NSCLC in Phase 2 Study. AACR 2024;Abstract CT247.

Datopotamab deruxtecan

TROPION-Lung05

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

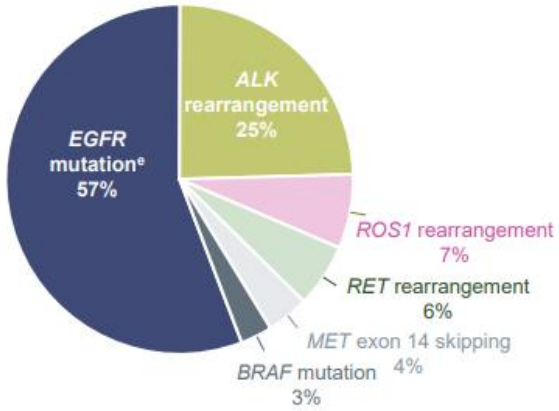
Treatment

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

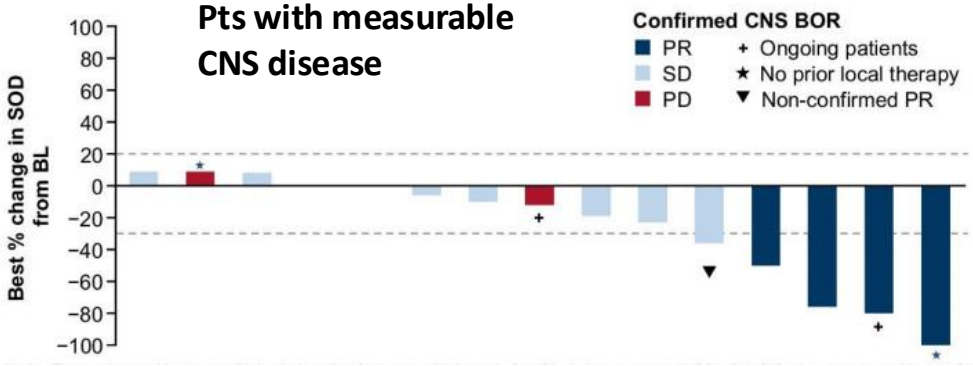


Response per BICR	All treated patients (N=137)
ORR confirmed, n (%) [95% CI][a]	49 (35.8) [27.8-44.4]
Median DOR (95% CI), months	7.0 (4.2-9.8)
DCR confirmed, n (%) [95% CI][a]	108 (78.8) [71.0-85.3]
Median PFS, (95% CI), months[b]	5.4 (4.7-7.0)

	With BL brain mets (N=53)	Without BL brain mets (N=84)
ORR,[b] n (%) [95% CI][c]	15 (28) [17–42]	34 (40) [30–52]
CR	0	4 (5)
PR	15 (28)	30 (36)
SD	21 (40)	35 (42)
Non-CR/Non-PD	2 (4)	1 (1)
PD	10 (19)	9 (11)
NE	5 (9)	5 (6)
DCR,[d] n (%) [95% CI][c]	38 (72) [58–83]	70 (83) [74–91]
CBR,[e] n (%) [95% CI][c]	21 (40) [27–54]	43 (51) [40–62]
PFS,[f] median, [95% CI]	5.4 [3.1–7.0]	5.6 [4.9–8.3]

IC ORR,[d] n (%) [95% CI][e]	4 (22) [6–48]
IC DCR,[f] n (%) [95% CI][e]	13 (72) [47–90]

Pts with measurable CNS disease



72% of pts with brain mets had prior local treatment

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Courtesy of Helena Yu, MD

Sands J Clin Oncol 2025;Lisberg ASCO 2024;Abstract 8593

Datopotamab deruxtecan

EGFR+ NSCLC from TL1 and TL5

TROPION-Lung05 (Phase II study)

- Presence of ≥1 actionable genomic alteration (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
  - ≥1 line of targeted therapy
  - 1–2 prior cytotoxic agent–containing therapies including Pt-CT in the metastatic setting
  - Radiographic disease progression after most recent therapy

→ **Dato-DXd** 6 mg/kg Q3W[a] **(N=137)**

TROPION-Lung01 (Phase III study)

- In those with actionable genomic alterations (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
  - 1–2 prior approved targeted therapies + Pt-CT, and ≤1 anti–PD-(L)1 mAb
  - No prior docetaxel

R 1:1

→ **Dato-DXd** 6 mg/kg Q3W[b] **(N=299)**

→ **Docetaxel** 75 mg/m² Q3W[b] **(N=305)**

***EGFR*m Pool: N=117**

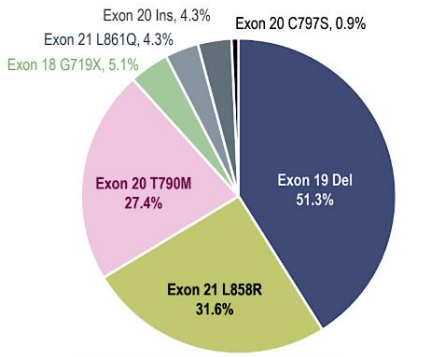
TROPION-Lung05 (n=78)

TROPION-Lung01 (n=39)

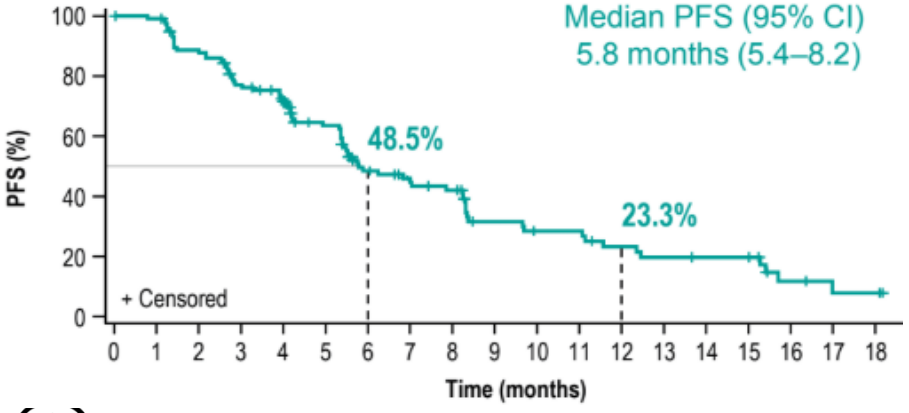
Endpoints:

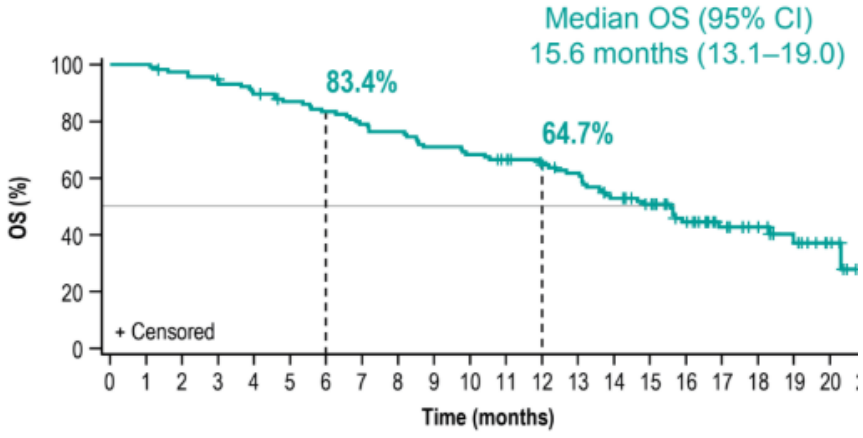
- ORR per BICR
- BOR per BICR
- DCR per BICR
- DOR per BICR
- PFS per BICR
- OS
- Safety

Characteristic	*EGFR*m Pool (N=117)
Median age (range), years	63 (36–81)
Sex, female, n (%)	73 (62.4)
Race, n (%)	
Asian	81 (69.2)
White	27 (23.1)
Black or African American	1 (0.9)
Other/missing	8 (6.8)
ECOG PS, n (%)	
0	39 (33.3)
1	78 (66.7)
Smoker[a], n (%)	55 (47.0)
Nonsquamous histology[b], n (%)	115 (98.3)
Brain metastasis at study entry, n (%)	36 (30.8)
Median lines systemic therapy (range)[c]	3 (1–5)
Prior osimertinib[d], n (%)	96 (82.1)
First line	47 (40.2)
Second line	34 (29.1)



AESIs[a], n (%)	
Stomatitis/oral mucositis	81 (69)
Grade 3[b]	11 (9)
Ocular surface events	38 (32)
Grade 3[b]	3 (3)
Adjudicated drug-related ILD	5 (4)
Grade 3[b]	1 (1)





Response	*EGFR*m Pool (N=117)
Confirmed ORR,[a] n (%) [95% CI]	50 (**42.7**) [33.6–52.2]
BOR, n (%)	
CR	5 (**4.3**)
PR	45 (**38.5**)
SD	48 (41.0)
Non-CR/Non-PD	3 (2.6)
PD	12 (10.3)
NE	4 (3.4)
Median DOR, months (95% CI)	**7.0** (4.2–9.8)
DCR,[b] n (%) [95% CI]	101 (**86.3**) [78.7–92.0]

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Ahn ESMO Asia; Abstract LBA7

Courtesy of Helena Yu, MD

Datopotamab deruxtecan

Press release:

PUBLISHED
12 November 2024

Datopotamab deruxtecan new BLA submitted for accelerated approval in the US for patients with previously treated advanced EGFR-mutated non-small cell lung cancer

The companies have voluntarily withdrawn the BLA in the US for datopotamab deruxtecan for patients with advanced or metastatic nonsquamous NSCLC based on the TROPION-Lung01 Phase III trial.

The decision to submit a new BLA for *EGFR*-mutated NSCLC and withdraw the previously submitted BLA for nonsquamous NSCLC was informed by feedback from the US Food and Drug Administration (FDA).

Recruiting

Phase III, Open-label Study of First-line Osimertinib With or Without Datopotamab Deruxtecan for EGFRm Locally Advanced or Metastatic Non-small Cell Lung Cancer (TROPION-Lung14)

ClinicalTrials.gov ID NCT06350097

Sponsor AstraZeneca

Recruiting

A Study to Investigate the Efficacy and Safety of Dato-DXd With or Without Osimertinib Compared With Platinum Based Doublet Chemotherapy in Participants With EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer (TROPION-Lung15)

ClinicalTrials.gov ID NCT06417814

- Biomarker for antibody drug conjugates may be driver oncogene – datopotamab and patritumab both seeking approval in EGFR+ lung cancer
- ADCs initially thought too bulky and therefore with limited CNS penetration, but CNS efficacy is present
- Efforts to combine ADCs with osimertinib are ongoing

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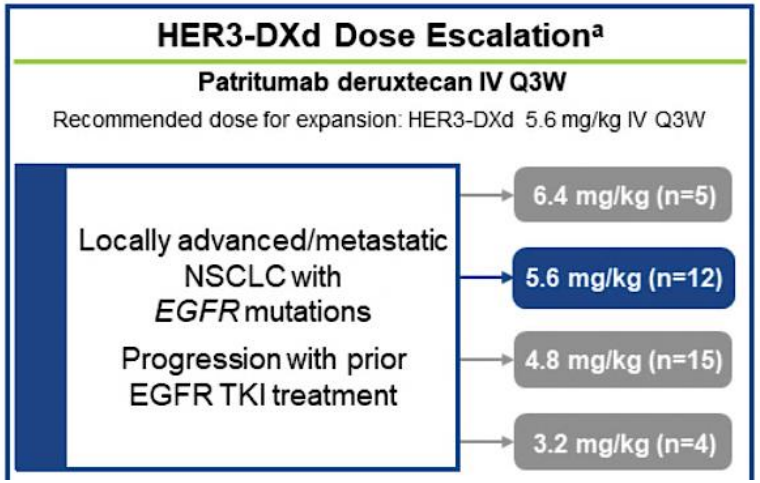
Courtesy of Helena Yu, MD

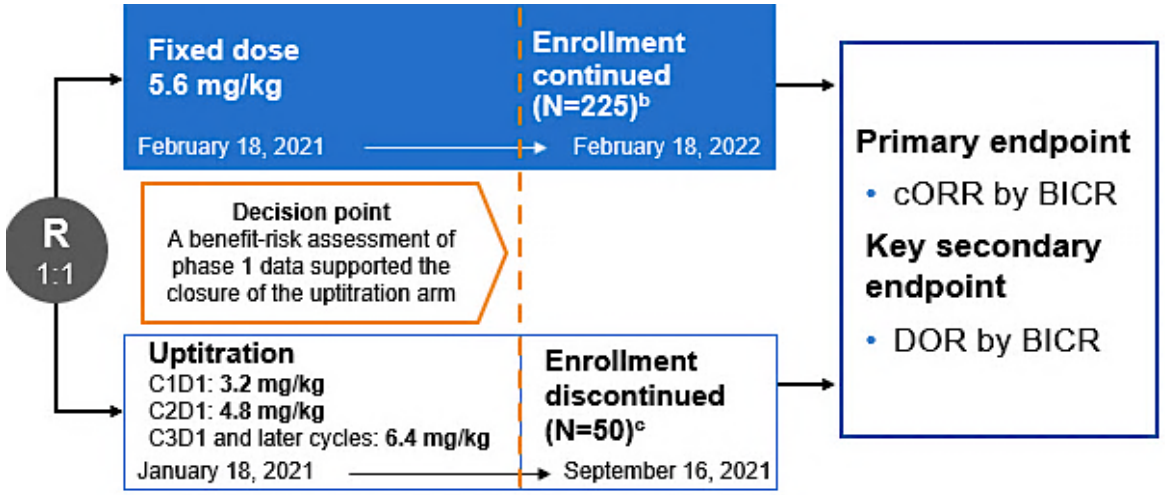
Ahn ESMO Asia; Abstract LBA7

Patritumab deruxtecan

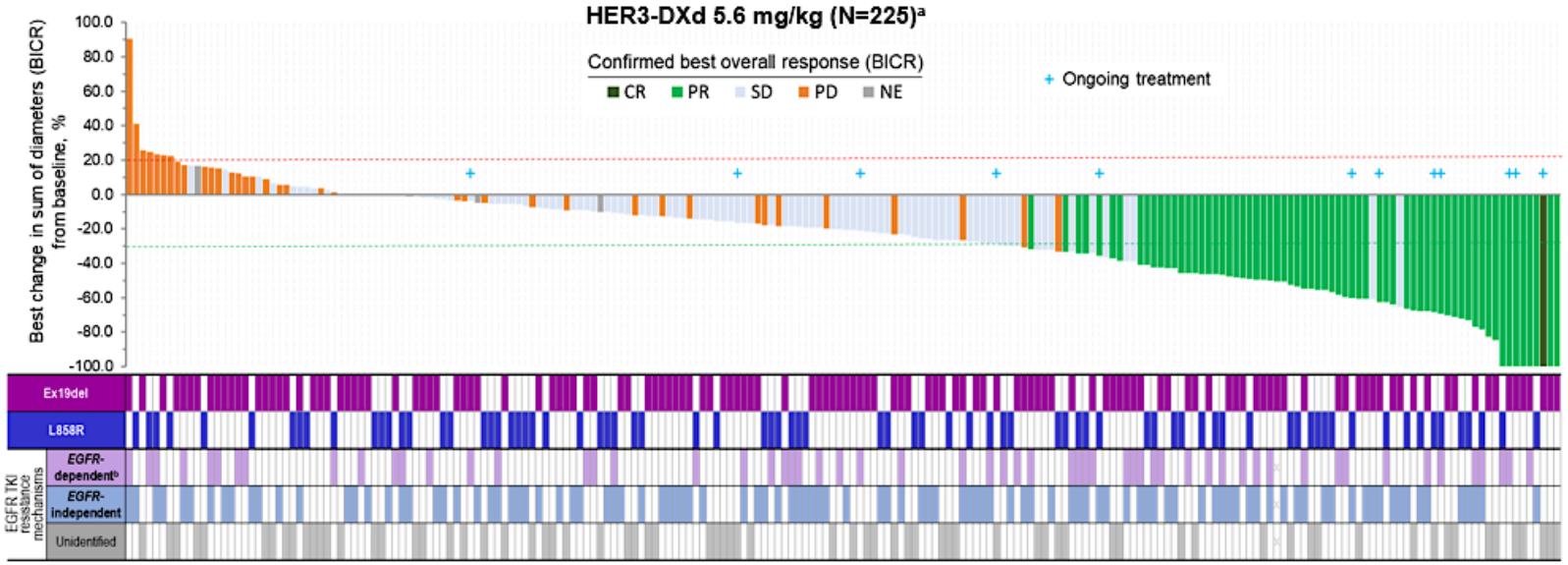
Phase 1 Dose escalation



HERTHENA-Lung01 Registrational phase 2



Confirmed responses and survival		Prior EGFR TKI (any) and PBC (N=225)	Subset with prior 3G EGFR TKI and PBC (n=209)
cORR (95% CI), %		**29.8 (23.9-36.2)**	**29.2 (23.1-35.9)**
Best overall response (BICR), n (%)	CR	1 (0.4)	1 (0.5)
	PR	66 (29.3)	60 (28.7)
	SD[a]	99 (44.0)	91 (43.5)
	PD	43 (19.1)	41 (19.6)
	NE[b]	16 (7.1)	16 (7.7)
DCR (95% CI), %		73.8 (67.5-79.4)	72.7 (66.2-78.6)
DOR, median (95% CI), mo		6.4 (4.9-7.8)	6.4 (5.2-7.8)
PFS, median (95% CI), mo		5.5 (5.1-5.9)	5.5 (5.1-6.4)
OS, median (95% CI), mo		11.9 (11.2-13.1)	11.9 (10.9-13.1)

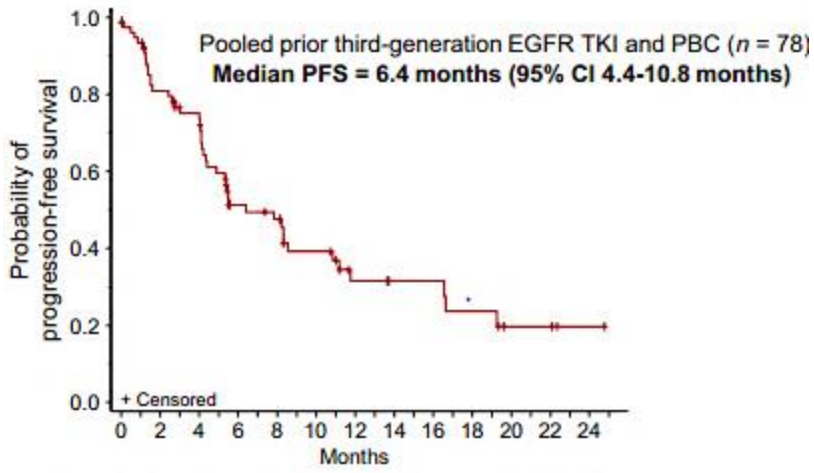


Courtesy of Helena Yu, MD

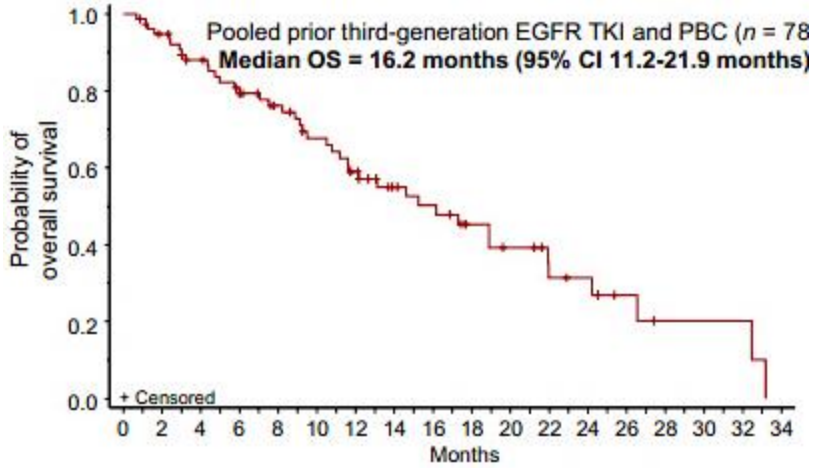
Yu J Clin Oncol 2023

Patritumab deruxtecan

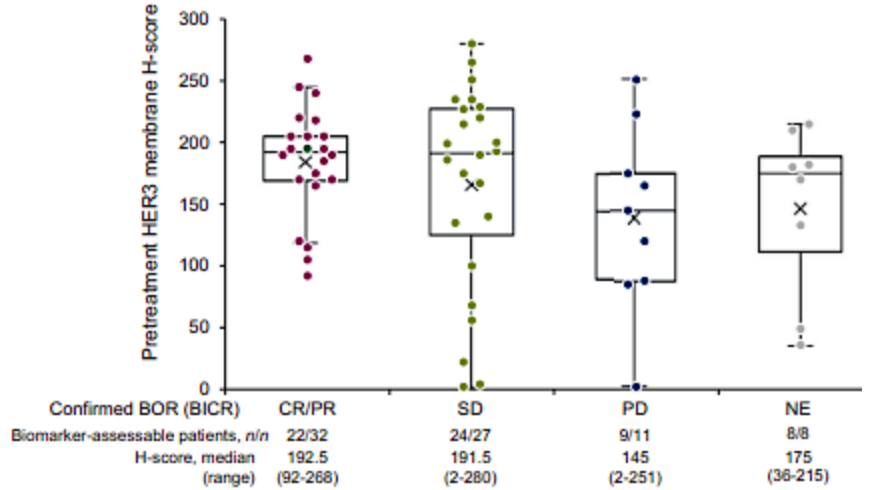
PFS



OS



HER3 expression and response



- Consistent updated PFS and OS
- No new safety signals
- Slightly higher ORR in pts with EGFR-independent resistance (30 vs 48%)
- Acquired resistance mutations included a HER3 frameshift mutation, TOP1 mutation
- HER3 expression did not select for response

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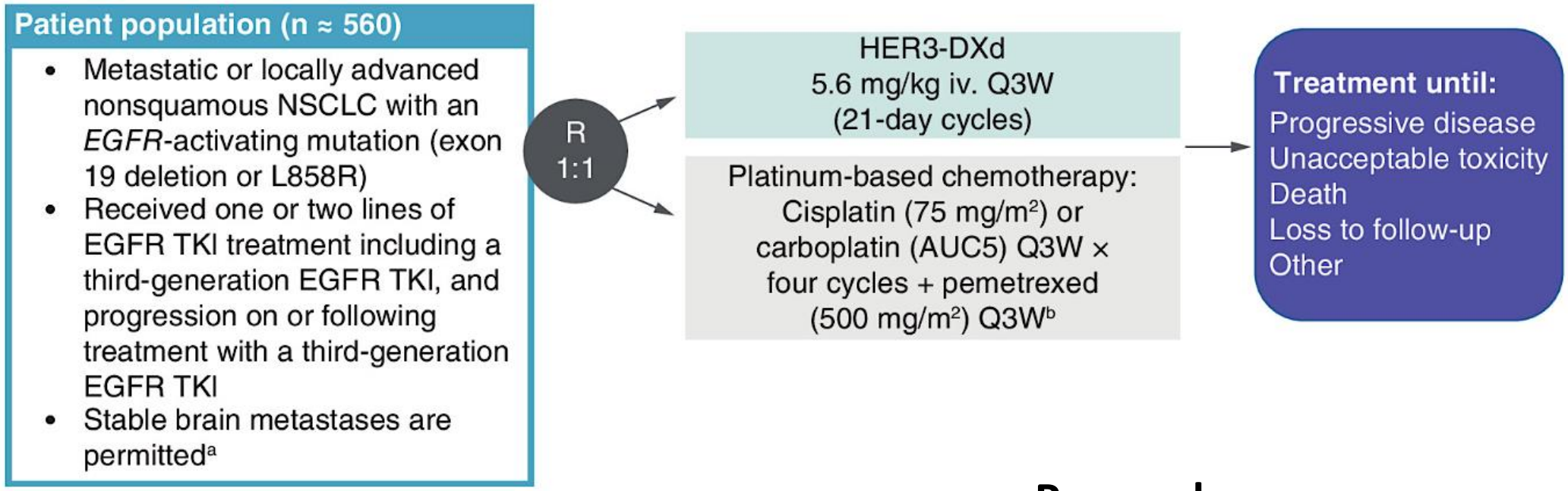
Courtesy of Helena Yu, MD

Yu Ann Oncol 2024

Patritumab deruxtecan



Primary endpoint: Progression-free survival by BICR

Press release:

June 26, 2024 7:45 pm ET

Patritumab Deruxtecan BLA Submission Receives Complete Response Letter from FDA Due to Inspection Findings at Third-Party Manufacturer

Press release:

September 17, 2024 6:00 am ET

Patritumab Deruxtecan Demonstrated Statistically Significant Improvement in Progression-Free Survival Versus Doublet Chemotherapy in Patients with Locally Advanced or Metastatic EGFR-Mutated Non-Small Cell Lung Cancer in HERTHENA-Lung02 Phase 3 Trial

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Courtesy of Helena Yu, MD

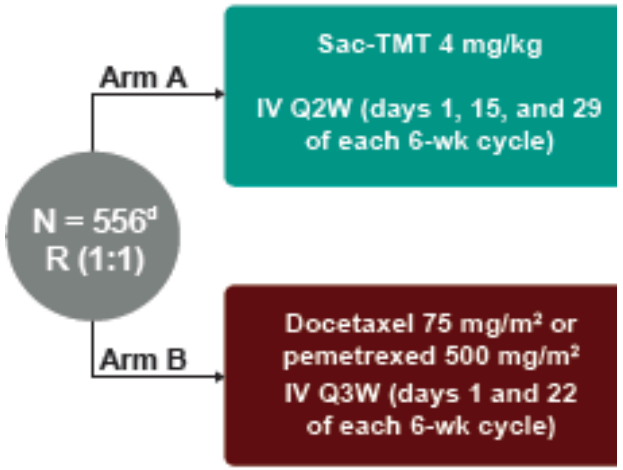
Mok Fut Med 2023

Sacituzumab tirumotecan

TroFuse-004[1]

Study Population

- Age ≥18 y
- Histologically/cytologically documented advanced[a] or metastatic nonsquamous NSCLC
- Presence of exon 19del or exon 21 L858R *EGFR*m or other genomic alterations[b]
- Documented disease progression following 1 or 2 prior lines of TKIs[c] plus 1 platinum-based chemotherapy ± anti–PD-(L)1 after progression on or after TKI
- Measurable disease per RECIST version 1.1
- ECOG PS 0 or 1



AGA: EGFR, ALK, ROS1, BRAF, NTRK, MET, RET

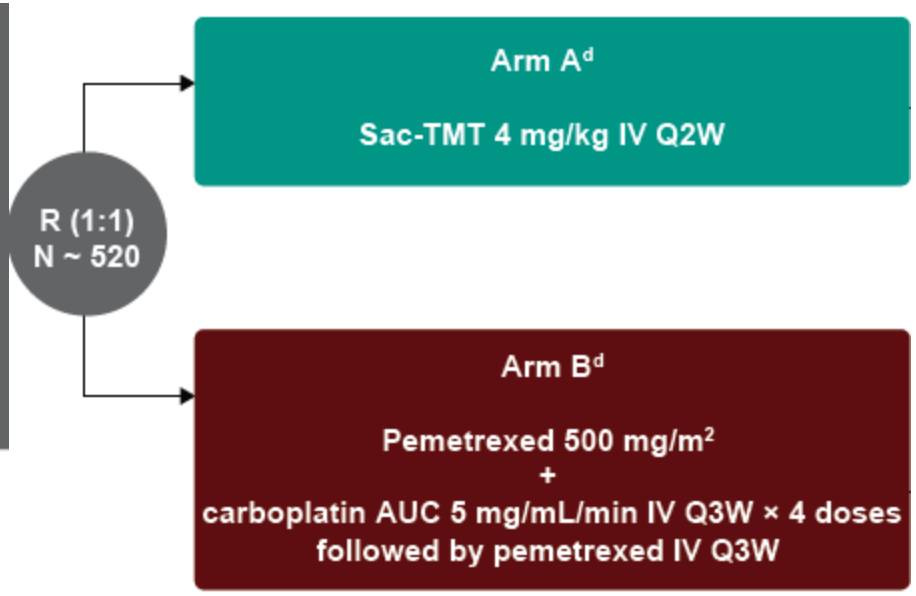
Primary endpoints: PFS and OS

Stratify by: brain mets, TROP2 expression, prior EGFR TKI

TroFuse-009[2]

Study Population

- Age ≥18 y
- Histologically/cytologically documented advanced[a] or metastatic nonsquamous NSCLC
- Presence of *EGFR* mutation (exon 19del, L858R G719X, S768I, or L861Q)
- Radiographic disease progression following
- EGFR TKI therapy[b]
- Measurable disease per RECIST version 1.1
- ECOG PS 0 or 1[c]



Primary endpoints: PFS and OS

Stratify by: brain mets, TROP2 expression, prior EGFR TKI

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Courtesy of Helena Yu, MD

1:Garon WCLC 2024;Abstract P2.10A.06.
2:Leighl WCLC 2024;Abstract P2.10A.07.

Sacituzumab tirumotecan

Press release: December 3, 2024 6:45 am ET

FDA Grants Breakthrough Therapy Designation to Sacituzumab Tirumotecan (sac-TMT) for the Treatment of Certain Patients With Previously Treated Advanced or Metastatic Nonsquamous Non-Small Cell Lung Cancer With EGFR Mutations

	Overall (N=43)	EGFR mutant (N=22)
ORR*, %	43.6%	60.0%
Median DoR, mo (95%CI)	9.3 (3.7, 10.3)	8.7 (3.7, 10.3)
Median PFS, mo (95% CI)	7.2 (5.4, 11.3)	11.5 (5.7, 12.9)
Median OS, mo (95% CI)	22.6 (13.1, NE)	22.7 (19.7, NE)
12-mo OS rate, % (95% CI)	69.0% (52.7, 80.7)	81.0% (56.9, 92.4)
18-mo OS rate, % (95% CI)	56.5% (40.1, 70.0)	76.2% (51.9, 89.3)

- Several ADCs are looking at the AGA space as an entry point (enhanced efficacy in this population)
- Other studies are focused on combination therapies with immunotherapy for larger NSCLC populations
- Need biomarkers to select appropriate ADC for a pt
- We will hopefully have several ADC options for EGFR+ NSCLC in the near future

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Courtesy of Helena Yu, MD

Fang AACR 2024;Abstract CT247

Teaching Cases from Investigators: The Application of Available Research to the Clinical Care of Patients with Hepatocellular Carcinoma

A CME Symposium Held in Conjunction with the 2025 ASCO® Gastrointestinal Cancers Symposium

Thursday, January 23, 2025

6:15 PM – 8:15 PM PT (9:15 PM – 11:15 PM ET)

Faculty

Anthony El-Khoueiry, MD

Aiwu Ruth He, MD, PhD

Richard S Finn, MD

Stacey Stein, MD

Moderator

Stephen “Fred” Divers, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP Year in Review 2025