What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Non-Small Cell Lung Cancer with an EGFR Mutation

Friday, April 26, 2024
12:15 PM – 1:45 PM

Faculty

Marianne J Davies, DNP, ACNP, AOCNP, FAAN
Alexander I Spira, MD, PhD
Jillian Thompson, MSN, ANP-BC, AOCNP
Helena Yu, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Marianne J Davies, DNP, ACNP, AOCNP, FAAN
Program Manager, Care Signature
Oncology Service Line, Yale New Haven Health
Oncology Nurse Practitioner-Senior APP II
Yale Cancer Center
Smilow Cancer Hospital at Yale New Haven
Associate Professor
Yale University School of Nursing
New Haven, Connecticut

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

Jillian Thompson, MSN, ANP-BC, AOCNP
Nurse Practitioner
MedStar Georgetown University Hospital
Lombardi Comprehensive Cancer Center
Washington, DC

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

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

RTP
RESEARCH
TO PRACTICE

Ms Davies — Disclosures

No relevant conflicts of interest to disclose

Dr Spira — Disclosures

Advisory Committees	Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Blueprint Medicines, Bristol Myers Squibb, Daiichi Sankyo Inc, Gritstone bio, Incyte Corporation, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Novartis, Regeneron Pharmaceuticals Inc, Sanofi, Takeda Pharmaceuticals USA Inc
Contracted Research	AbbVie Inc, ADC Therapeutics, AI Therapeutics, Alkermes, Amgen Inc, Arch Therapeutics Inc, ArriVent Biopharma, Astellas, Astex Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Blueprint Medicines, BluPrint Oncology, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, CytomX Therapeutics, Daiichi Sankyo Inc, Gritstone bio, Ignyta Inc, Incyte Corporation, Janssen Biotech Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MacroGenics Inc, Medikine, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Nalo Therapeutics, Novartis, Plexxikon Inc, Regeneron Pharmaceuticals Inc, Revolution Medicines, Roche Laboratories Inc, Rubius Therapeutics, Scorpion Therapeutics, Synthekine, Takeda Pharmaceuticals USA Inc

RTP
RESEARCH
TO PRACTICE

Ms Thompson — Disclosures

Advisory Committees	Janssen Biotech Inc, Mirati Therapeutics Inc
Nonrelevant Financial Relationship	Targeted Oncology

Dr Yu — Disclosures

Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Blueprint Medicines, C4 Therapeutics, Cullinan Oncology, Daiichi Sankyo Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc
Data and Safety Monitoring Board/ Committee	Janssen Biotech Inc
Research Funding to My Institution	AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Blueprint Medicines, Cullinan Oncology, Daiichi Sankyo Inc, Erasca, Janssen Biotech Inc, Novartis, Pfizer Inc

Commercial Support

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

Research To Practice NCPD Planning Committee Members, Staff and Reviewers

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

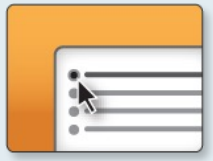
This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

RTP
RESEARCH
TO PRACTICE

Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

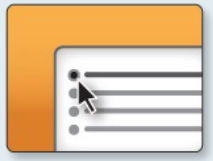
Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

RTP RESEARCH TO PRACTICE

Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



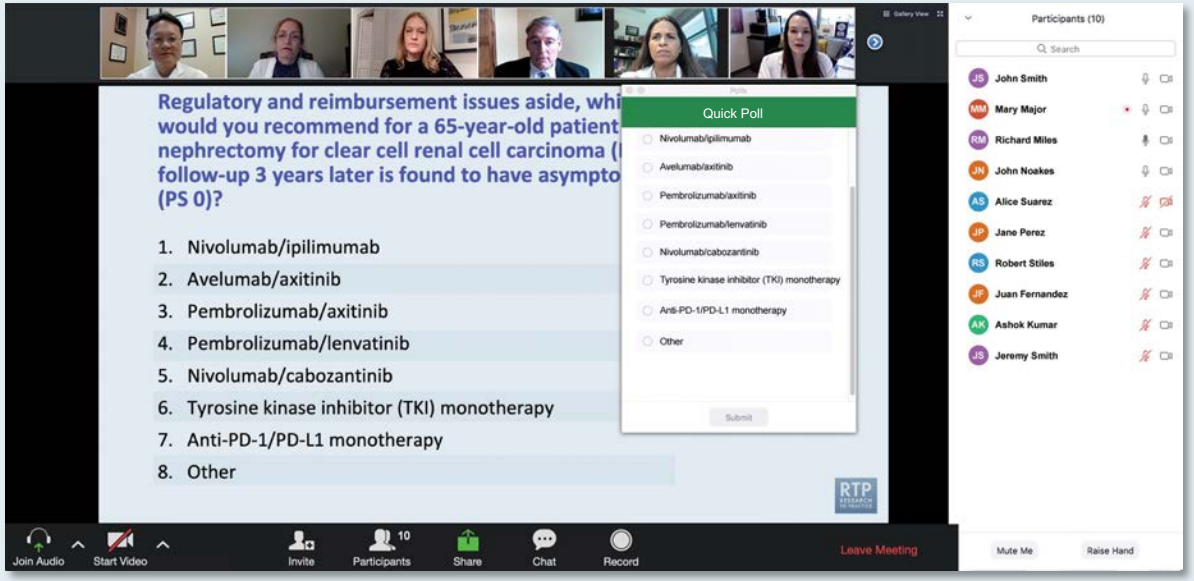
Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

RTP
RESEARCH
TO PRACTICE

Clinicians, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

RTP
RESEARCH
TO PRACTICE

“What I Tell My Patients”
Sixteenth Annual RTP-ONS NCPD Symposium Series

Wednesday April 24	**Hormone Receptor–Positive Breast Cancer** 6:00 PM – 8:00 PM ET
Thursday April 25	**Endometrial Cancer** 6:00 AM – 7:30 AM ET
	Antibody–Drug Conjugates 12:15 PM – 1:45 PM ET
	Chronic Lymphocytic Leukemia and Bispecific Antibodies in Lymphoma 6:00 PM – 8:00 PM ET
Friday April 26	**Head and Neck Cancer** 6:00 AM – 7:30 AM ET
	Non–Small Cell Lung Cancer with an EGFR Mutation 12:15 PM – 1:45 PM ET
	Ovarian Cancer 6:00 PM – 7:30 PM ET
Saturday April 27	**Hepatobiliary Cancers** 6:00 AM – 7:30 AM ET
	Myelofibrosis 12:15 PM – 1:45 PM ET
	Gastroesophageal and Colorectal Cancers 6:00 PM – 8:00 PM ET
Wednesday, May 1	**LIVE WEBINAR — Prostate Cancer** 7:00 PM – 8:00 PM ET

RTP
RESEARCH TO PRACTICE

Consulting Nurse Faculty

Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Kathleen D Burns, RN, MSN, AGACNP-BC, OCN
City of Hope Comprehensive Cancer Center
Duarte, California

Sonia Glennie, ARNP, MSN, OCN
Swedish Cancer Institute Center for Blood Disorders
Seattle, Washington

Amy Goodrich, CRNP
The Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

Jessica Mitchell, APRN, CNP, MPH
Mayo Clinic College of Medicine and Science
Rochester, Minnesota

Tiffany A Richards, PhD, ANP-BC, AOCNP
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC
University of Arkansas for Medical Sciences
Little Rock, Arkansas

Ronald Stein, JD, MSN, NP-C, AOCNP
USC Norris Comprehensive Cancer Center
Los Angeles, California

https://www.ResearchToPractice.com/ONS2024Clips

RTP RESEARCH TO PRACTICE

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Non-Small Cell Lung Cancer with an EGFR Mutation

Friday, April 26, 2024
12:15 PM – 1:45 PM

Faculty

Marianne J Davies, DNP, ACNP, AOCNP, FAAN
Alexander I Spira, MD, PhD
Jillian Thompson, MSN, ANP-BC, AOCNP
Helena Yu, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Agenda

Introduction

Module 1: Localized Non-Small Cell Lung Cancer (NSCLC) with an EGFR Mutation

Module 2: First-Line Therapy for Patients with Metastatic NSCLC and EGFR Mutations

Module 3: Management of Progressive EGFR-Mutated NSCLC

Module 4: Targeting EGFR Exon 20 Insertion Mutations

Agenda

Introduction

Module 1: Localized Non-Small Cell Lung Cancer (NSCLC) with an EGFR Mutation

Module 2: First-Line Therapy for Patients with Metastatic NSCLC and EGFR Mutations

Module 3: Management of Progressive EGFR-Mutated NSCLC

Module 4: Targeting EGFR Exon 20 Insertion Mutations

Consulting Nursing Faculty Comments

Patient education about clinical trial participation

Amy Goodrich, CRNP

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction

Module 1: Localized Non-Small Cell Lung Cancer (NSCLC) with an EGFR Mutation

Module 2: First-Line Therapy for Patients with Metastatic NSCLC and EGFR Mutations

Module 3: Management of Progressive EGFR-Mutated NSCLC

Module 4: Targeting EGFR Exon 20 Insertion Mutations

EGFR Testing in Non-Small Cell Lung Cancer (NSCLC)

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Spectrum of EGFR mutations found in NSCLC; clinical relevance of and similarities and differences among various detectable EGFR mutations**
- **Incidence of targetable EGFR mutations in localized and metastatic disease; optimal timing of EGFR testing**
- **Available platforms to identify EGFR mutations in patients with NSCLC; advantages and limitations of next-generation sequencing versus one-off testing**
- **Reliability of plasma-based assays to document the presence of actionable EGFR mutations; current clinical utility**
- **Role of repeat biomarker testing in the care of patients with progressive NSCLC with an EGFR mutation**

Targetable Oncogenic Drivers

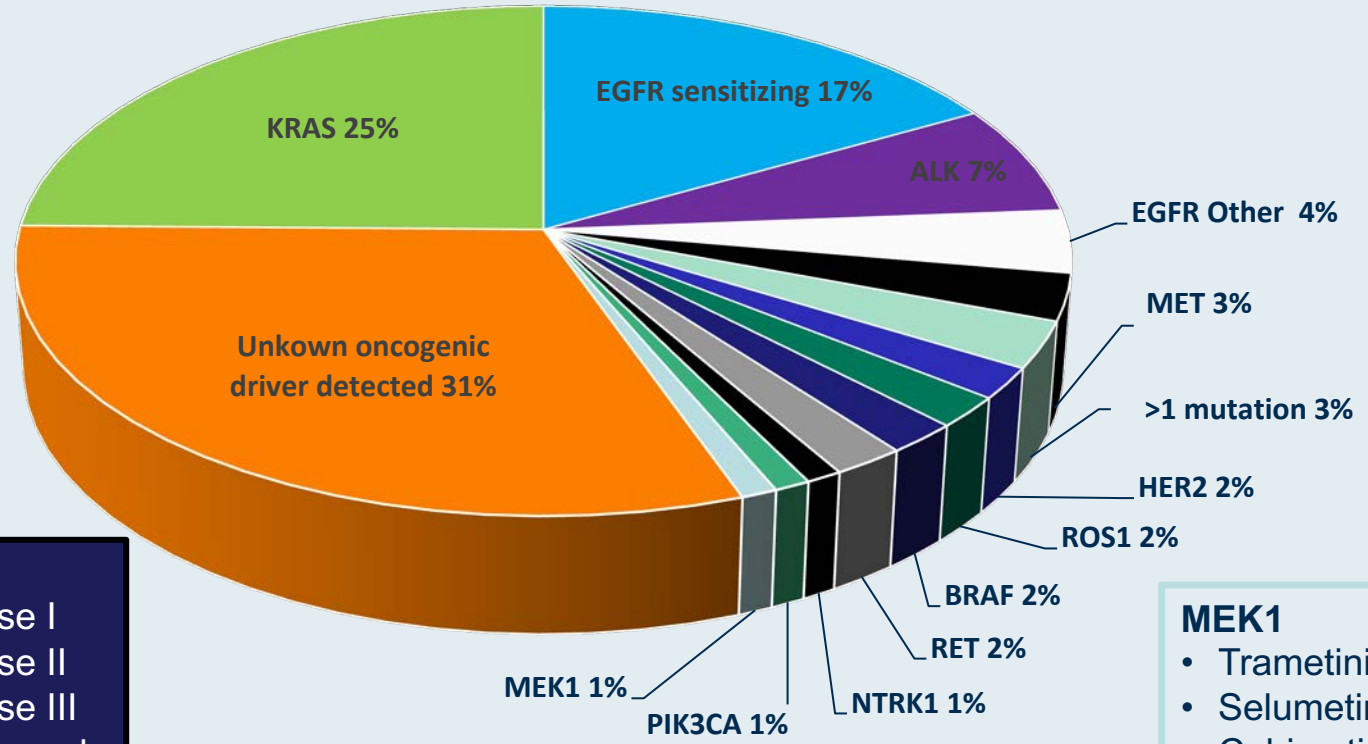
EGFR sensitizing
- Gefitinib[4]
- Erlotinib[4]
- Afatinib[4]
- Osimertinib[4]
- Necitumumab[4]
- Rociletinib[3]

ALK
- Crizotinib[4]
- Alectinib[4]
- Ceritinib[4]
- Lorlatinib[2]
- Brigatinib[2]

MET
- Crizotinib[2]
- Cabozantinib[2]

HER2
- Trastuzumab emtansine[2]
- Afatinib[2]
- Dacomitinib[2]

ROS1
- Crizotinib[4]
- Cabozantinib[2]
- Ceritinib[2]
- Lorlatinib[2]
- DS-6051b[1]



BRAF
- Vemurafenib[2]
- Dabrafenib[2]

RET
- Cabozantinib[2]
- Alectinib[2]
- Apatinib[2]
- Vandetanib[2]
- Ponatinib[2]
- Lenvatinib[2]

KEY
1 - Phase I
2 - Phase II
3 - Phase III
4 - Approved

MEK1
- Trametinib[2]
- Selumetinib[3]
- Cobimetinib[1]

PIK3CA
- LY3023414[2]
- PQR 309[1]

NTRK1
- Entrectinib[2]
- LOXO-101[2]
- Cabozantinib[2]
- DS-6051b[1]

Presented by Frances Shepherd at 2019 ASCO Annual Meeting.

RTP RESEARCH TO PRACTICE

Marianne J Davies, DNP, ACNP, AOCNP, FAAN

What I tell my patients who are never-smokers and are diagnosed with lung cancer and how I explain the significance of EGFR mutations

RTP
RESEARCH
TO PRACTICE

Osimertinib for Localized and Locally Advanced NSCLC with an EGFR Mutation

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Long-term findings, including overall survival outcomes, with adjuvant osimertinib for Stage IB to Stage IIIA NSCLC with an EGFR mutation after complete tumor resection**
- **Protection against central nervous system (CNS) disease recurrence observed with adjuvant osimertinib**
- **Patient selection for and appropriate incorporation of adjuvant osimertinib into routine practice**

Osimertinib for Localized and Locally Advanced NSCLC with an EGFR Mutation

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Choosing between osimertinib and immune checkpoint inhibition for patients eligible for both treatments**
- **Tolerability of osimertinib in the adjuvant setting; appropriate threshold for dose reduction, dose delays or treatment discontinuation for patients with NSCLC receiving adjuvant osimertinib**
- **Ongoing efforts seeking to further define the role of osimertinib in the management of nonmetastatic NSCLC with an EGFR mutation**

Osimertinib

Mechanism of action

- **EGFR tyrosine kinase inhibitor**

Indication in the adjuvant setting

- **After tumor resection for patients with NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test**

Recommended dose

- **80 mg PO once daily, with or without food, until disease recurrence, or unacceptable toxicity, or for up to 3 years**

Osimertinib package insert, 2/2024.

The NEW ENGLAND JOURNAL of MEDICINE

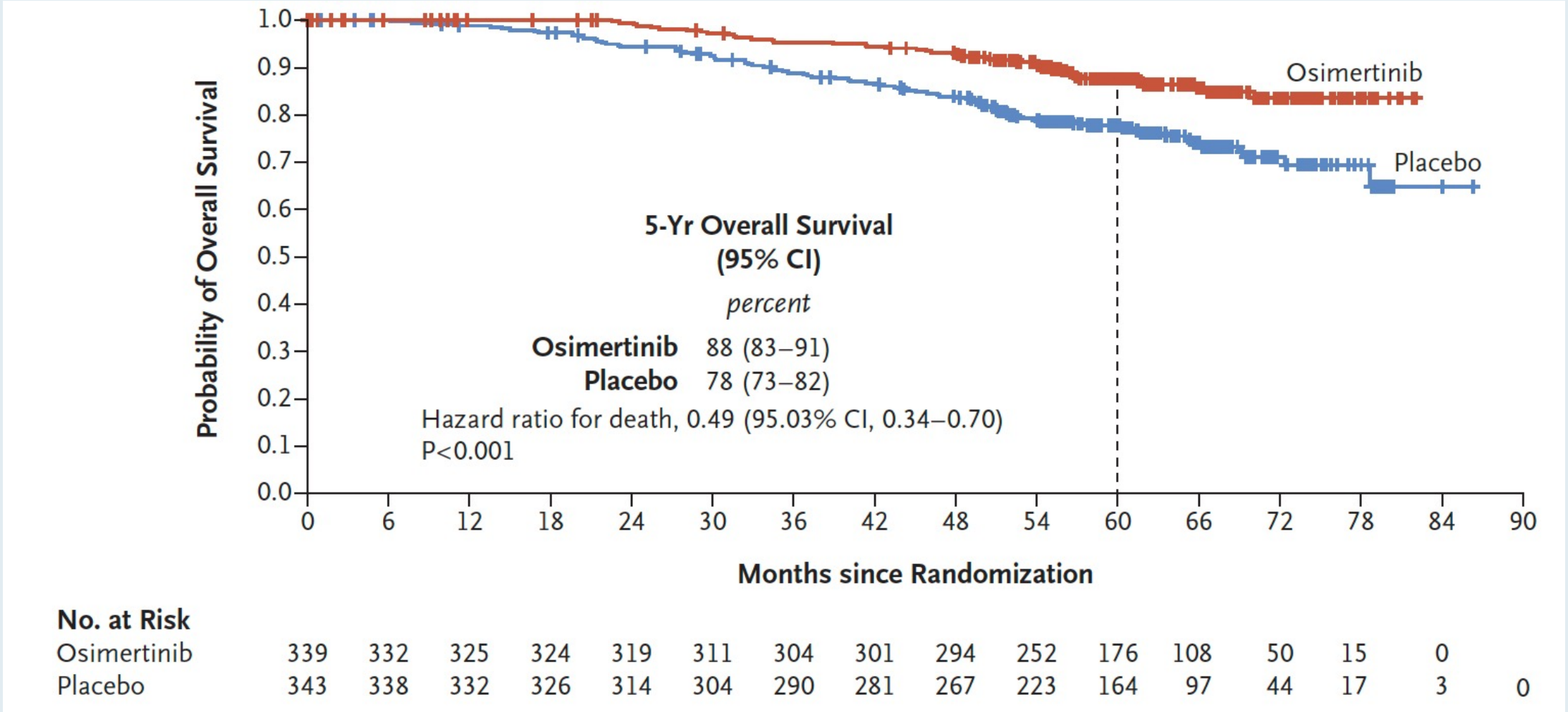
ORIGINAL ARTICLE

Overall Survival with Osimertinib in Resected *EGFR*-Mutated NSCLC

Masahiro Tsuboi, M.D., Roy S. Herbst, M.D., Ph.D., Thomas John, M.B., B.S., Ph.D., Terufumi Kato, M.D., Margarita Majem, M.D., Ph.D., Christian Grohé, M.D., Jie Wang, M.D., Ph.D., Jonathan W. Goldman, M.D., Shun Lu, M.D., Wu-Chou Su, M.D., Filippo de Marinis, M.D., Frances A. Shepherd, M.D., Ki Hyeong Lee, M.D., Ph.D., Nhieu Thi Le, M.D., Arunee Dechaphunkul, M.D., Dariusz Kowalski, M.D., Ph.D., Lynne Poole, M.Sc., Ana Bolanos, M.D., Yuri Rukazenkov, M.D., Ph.D., and Yi-Long Wu, M.D., for the ADAURA Investigators*

2023;389(2):137-47

ADAURA: Overall Survival in Stage IB-IIIA Disease



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

RTP RESEARCH TO PRACTICE

Osimertinib After Chemoradiation Therapy Demonstrated an Efficacy Benefit for Unresectable Stage III NSCLC with an EGFR Mutation in the Phase III LAURA Trial

Press Release – Febuary 19, 2024

"Positive high-level results from the LAURA Phase III trial showed osimertinib demonstrated a statistically significant and highly clinically meaningful improvement in progression-free survival (PFS) for patients with unresectable, Stage III epidermal growth factor receptor-mutated (EGFRm) non-small cell lung cancer (NSCLC) after chemoradiotherapy (CRT) compared to placebo after CRT.

LAURA is a randomised, double-blind, placebo-controlled, multi-centre, global Phase III trial in patients with unresectable, Stage III EGFRm NSCLC whose disease has not progressed following definitive platinum-based 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."

https://www.astrazeneca.com/media-centre/press-releases/2024/tagrisso-improved-pfs-in-stage-iii-lung-cancer.html

RTP RESEARCH TO PRACTICE

Jillian Thompson, MSN, ANP-BC, AOCNP

What I tell my patients who are about to begin osimertinib for localized or locally advanced EGFR-mutant NSCLC; goals of adjuvant therapy

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction

Module 1: Localized Non-Small Cell Lung Cancer (NSCLC) with an EGFR Mutation

Module 2: First-Line Therapy for Patients with Metastatic NSCLC and EGFR Mutations

Module 3: Management of Progressive EGFR-Mutated NSCLC

Module 4: Targeting EGFR Exon 20 Insertion Mutations

Established First-Line Therapy for Metastatic NSCLC with an EGFR Mutation

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Long-term benefit observed with up-front osimertinib monotherapy for patients with metastatic NSCLC with an EGFR mutation**
- **Intracranial response rates and rates of CNS progression documented with up-front osimertinib**
- **Sequencing of osimertinib relative to local therapies, such as stereotactic radiosurgery and whole-brain radiation therapy, for patients with NSCLC with an EGFR mutation and brain metastases**
- **Utility of rechallenge with osimertinib for patients who receive the drug in the adjuvant setting and experience subsequent disease progression**
- **Strategies to prevent and/or ameliorate gastrointestinal, dermatologic and other adverse events (AEs) with osimertinib**

Osimertinib

Mechanism of action

- **EGFR tyrosine kinase inhibitor**

Indication in the first-line metastatic setting

- **For patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test**
- **In combination with pemetrexed and platinum-based chemotherapy, for patients with locally advanced or metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test**

Recommended dose

- **Metastatic NSCLC: 80 mg PO once daily, with or without food, until disease recurrence, or unacceptable toxicity**
- **Locally advanced or metastatic NSCLC: 80 mg PO once daily administered in combination with pemetrexed and platinum-based chemotherapy, with or without food, until disease progression or unacceptable toxicity due to osimertinib**

Osimertinib package insert, 2/2024.

RTP RESEARCH TO PRACTICE

Marianne J Davies, DNP, ACNP, AOCNP, FAAN

What I tell my patients with EGFR-mutant metastatic NSCLC who are about to begin first-line treatment with osimertinib with or without chemotherapy

RTP
RESEARCH
TO PRACTICE

Newly Approved and Promising Investigational Approaches to First-Line Therapy for Metastatic NSCLC with an EGFR Mutation

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Rationale for the evaluation of osimertinib in combination with chemotherapy as first-line treatment for patients with NSCLC with an EGFR mutation**
- **Progression-free survival (PFS) and other key efficacy and safety outcomes observed with first-line osimertinib/chemotherapy compared to osimertinib alone**
- **Recent FDA approval of first-line osimertinib/chemotherapy and selection of optimal candidates for this strategy**

Newly Approved and Promising Investigational Approaches to First-Line Therapy for Metastatic NSCLC with an EGFR Mutation

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Mechanistic similarities and differences between the bispecific antibody amivantamab and EGFR TKIs; rationale for the selection of lazertinib as a therapeutic partner for amivantamab in clinical trials**
- **PFS and other efficacy outcomes observed with first-line amivantamab in combination with lazertinib compared to osimertinib for patients with NSCLC and an EGFR mutation**
- **Potential clinical role of first-line amivantamab/lazertinib**

FDA Approves Osimertinib with Chemotherapy for NSCLC with an EGFR Mutation

Press Release – Febuary 16, 2024

"The Food and Drug Administration approved osimertinib with platinum-based chemotherapy for patients with locally advanced or metastatic non-small cell lung cancer (la/mNSCLC) whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.

Efficacy was evaluated in FLAURA 2 (NCT04035486), an open-label, randomized trial of 557 patients with EGFR exon 19 deletion or exon 21 L858R mutation-positive la/mNSCLC and no prior systemic therapy for advanced disease. Patients were randomized 1:1 to receive either osimertinib with platinum-based chemotherapy or osimertinib monotherapy.

The major efficacy outcome measure was progression free survival (PFS), as assessed by investigator, with overall survival (OS) as a key secondary outcome measure."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-osimertinib-chemotherapy-egfr-mutated-non-small-cell-lung-cancer

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 23, 2023 VOL. 389 NO. 21 1935-48

Osimertinib with or without Chemotherapy in *EGFR*-Mutated Advanced NSCLC

D. Planchard, P.A. Jänne, Y. Cheng, J.C.-H. Yang, N. Yanagitani, S.-W. Kim, S. Sugawara, Y. Yu, Y. Fan, S.L. Geater, K. Laktionov, C.K. Lee, N. Valdiviezo, S. Ahmed, J.-M. Maurel, I. Andrasina, J. Goldman, D. Ghiorghiu, Y. Rukazenkov, A. Todd, and K. Kobayashi, for the FLAURA2 Investigators*

Amivantamab

Mechanism of action

- **Bispecific EGFR-directed and MET receptor-directed antibody**

Indication in the recurrent setting

- **As a single agent for adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy**

Recommended dose as a single agent

- **Administered weekly for 4 weeks, with the initial dose as a split infusion in week 1 on day 1 and day 2, then administer every 2 weeks thereafter, starting at week 5, until disease progression or unacceptable toxicity**
- **Body weight less than 80 kg = 1,050 mg**
- **Body weight greater than or equal to 80 kg = 1,400 mg**

Amivantamab package insert, 3/2024.

RTP RESEARCH TO PRACTICE

Lazertinib

Mechanism of action

- Oral third-generation, irreversible EGFR TKI

Indication

- Investigational

Pivotal clinical data

- Phase III MARIPOSA trial of lazertinib and amivantamab combination therapy versus osimertinib versus lazertinib as first-line therapy for patients with locally advanced or metastatic NSCLC with an EGFR mutation
- Phase III MARIPOSA-2 trial of amivantamab and chemotherapy with and without lazertinib for advanced NSCLC with an EGFR mutation after disease progression on osimertinib

Cho BC et al. ESMO 2023;Abstract LBA14. Passaro A et al. *Ann Oncol* 2024;35(1):77-90.

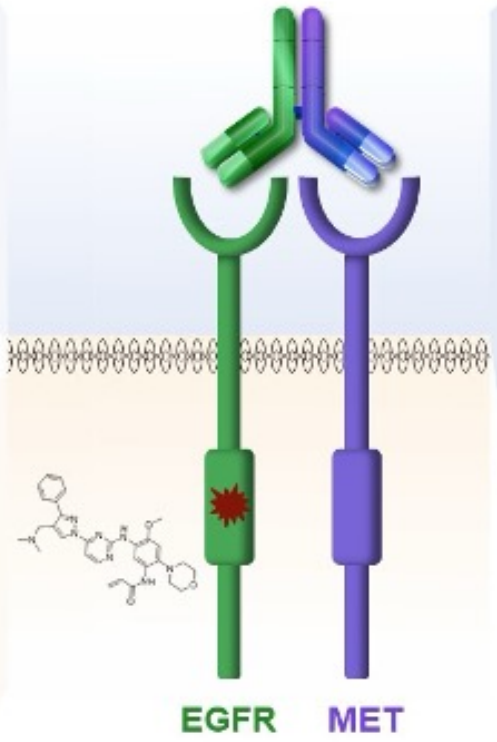
Amivantamab and Lazertinib

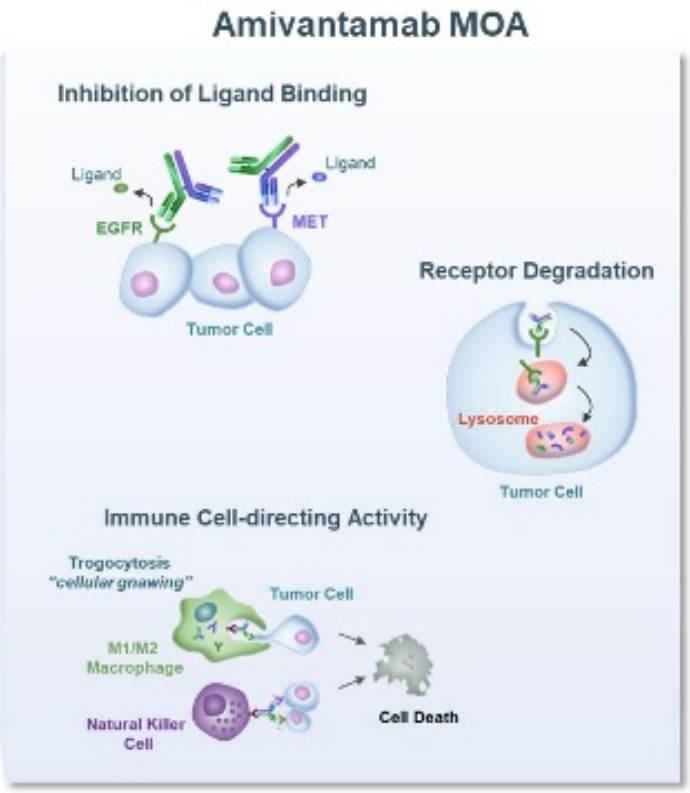
Amivantamab (am-e-van-tuh-mab)

- Fully human bispecific antibody that targets EGFR and MET
- Fc portion has immune cell-directing activity[1]
- Demonstrated clinical activity across diverse EGFRm NSCLC[2-4]
- Granted Breakthrough Therapy Designation for EGFRm Exon20ins NSCLC post-chemotherapy in US and China

Lazertinib (la-zer-tin-ib)

- Potent 3rd-gen TKI with efficacy in activating EGFR mutations, T790M, and CNS disease[5,6]
- Low rates of EGFR-related toxicity such as rash and diarrhea[5]
- Low cardiovascular safety risk[7]
- Safety profile that supports combination with other anti-EGFR molecules





[1]Vijayaraghavan *Mol Cancer Ther* 19:2044; [2]Haura *JCO* 37:9009 (oral); [3]Park JCO 38:9512 (poster); [4]Sabari *JTO* 16:S108 (oral); [5]Ahn *Lancet Oncol* 20:P1681; [6]Kim *JCO* 38:9571 (poster); [7]Haddish-Berhane *JTO* 16:S677 (poster).
BTD, Breakthrough Therapy Designation; CNS, central nervous system; EGFRm, epidermal growth factor receptor mutant; gen, generation; MOA, mechanism of action; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

Bauml JM et al. ASCO 2021;Abstract 9006.

MADRID 2023 ESMO congress

Abstract LBA14

MARIPOSA

Amivantamab Plus Lazertinib Versus Osimertinib as First-line Treatment in *EGFR*-mutated Advanced NSCLC

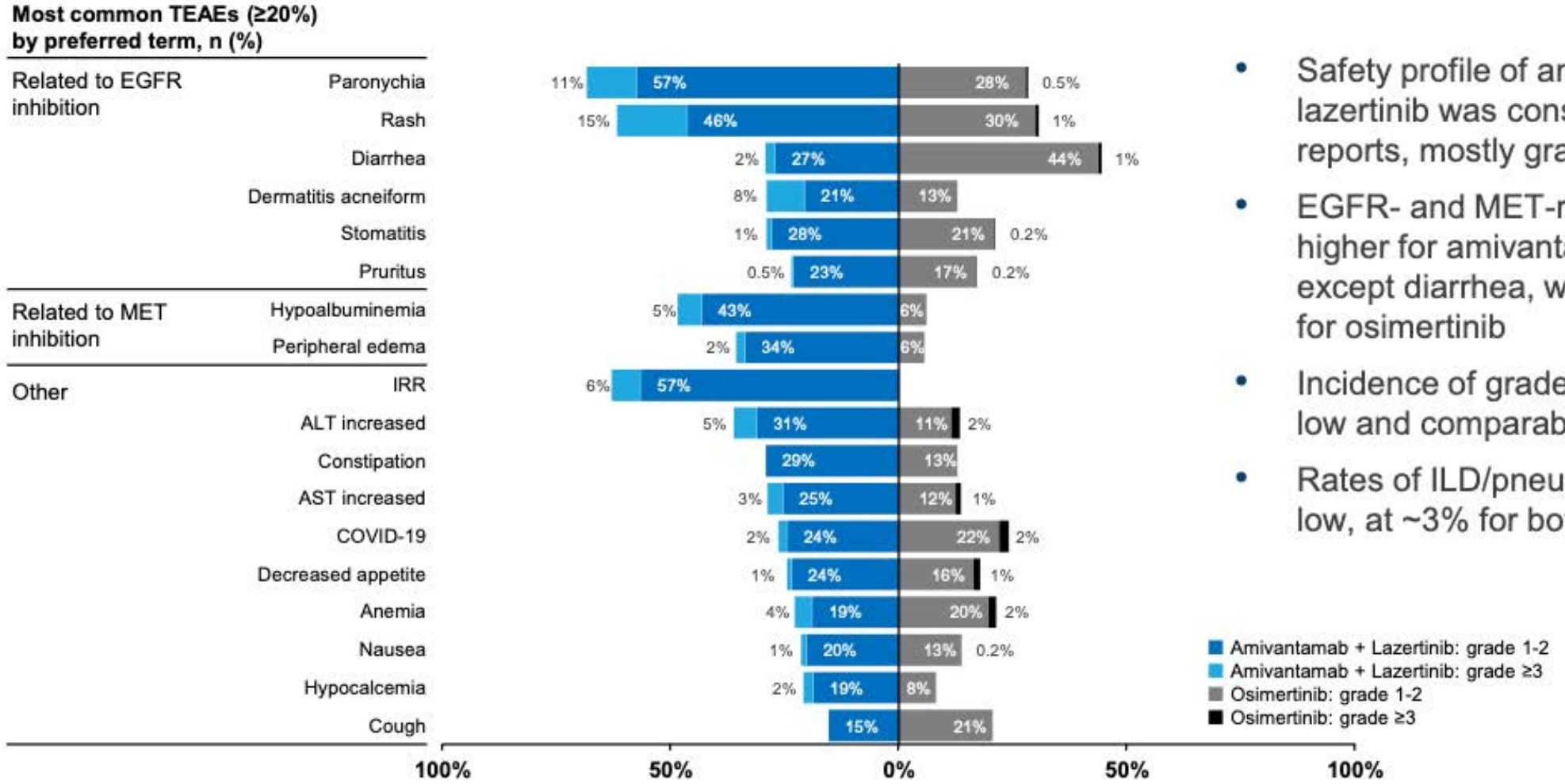
Primary Results from MARIPOSA, a Phase 3, Global, Randomized, Controlled Trial

Byoung Chul Cho,[1] Enriqueta Felip,[2] Alexander I. Spira,[3] Nicolas Girard,[4] Jong-Seok Lee,[5] Se-Hoon Lee,[6] Yuriy Ostapenko,[7] Pongwut Danchaivijitr,[8] Baogang Liu,[9] Adlinda Alip,[10] Ernesto Korbenfeld,[11] Josiane Mourão,[12] Tao Sun,[13] Melissa Martinez,[13] Joshua M. Bauml,[14] S. Martin Shreeve,[15] Seema Sethi,[14] Roland E. Knoblauch,[14] Hidetoshi Hayashi,[16] Shun Lu[17]

[1]Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea [2]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [3]Virginia Cancer Specialists, Fairfax, VA, USA; [4]Institut Curie, Institut du Thorax Curie-Montsouris, Paris, France; [5]National University Bundang Hospital, Seongnam, Republic of Korea; [6]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [7]National Cancer Institute, Kyiv, Ukraine; [8]Siriraj Hospital, Mahidol University, Bangkok, Thailand; [9]Harbin Medical University Cancer Hospital, Heilongjiang, China; [10]University of Malaya Medical Centre, Kuala Lumpur, Malaysia; [11]Hospital Britanico de Buenos Aires, Buenos Aires, Argentina; [12]Barretos Cancer Hospital, Barretos, Brazil; [13]Janssen R&D, Raritan, NJ, USA; [14]Janssen R&D, Spring House, PA, USA; [15]Janssen R&D, San Diego, CA, USA; [16]Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka, Japan; [17]Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China.

RTP RESEARCH TO PRACTICE

MARIPOSA: Safety Profile of Amivantamab with Lazertinib



- 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

Cho BC et al. ESMO 2023;Abstract LBA14.

Common Toxicities Associated with Amivantamab

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Spectrum, frequency and severity of common toxicities with amivantamab, such as dermatologic AEs, fatigue, musculoskeletal pain and stomatitis**
- **Incidence and timing of infusion-related reactions with amivantamab; appropriate premedication and infusion modification strategies**
- **Pathophysiology of ocular toxicities associated with amivantamab, such as keratitis, dry eye, conjunctival redness, blurred vision and uveitis; importance of consultation with ophthalmology for patients experiencing symptoms**

Common Toxicities Associated with Amivantamab

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Other, less frequently occurring side effects with amivantamab, such as interstitial lung disease (ILD)/pneumonitis; recommended approaches for monitoring and management**
- **Effect on the tolerability of amivantamab when administered in combination with other systemic therapies, such as lazertinib and/or chemotherapy**

Jillian Thompson, MSN, ANP-BC, AOCNP

What I tell my patients who are being considered for or enrolling on a clinical trial with amivantamab/lazertinib

RTP
RESEARCH
TO PRACTICE

Consulting Nursing Faculty Comments

Experiencing grief as an oncology provider

Sonia Glennie, ARNP, MSN, OCN

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction

Module 1: Localized Non-Small Cell Lung Cancer (NSCLC) with an EGFR Mutation

Module 2: First-Line Therapy for Patients with Metastatic NSCLC and EGFR Mutations

Module 3: Management of Progressive EGFR-Mutated NSCLC

Module 4: Targeting EGFR Exon 20 Insertion Mutations

The Current and Future Management of Progressive NSCLC with an EGFR Mutation

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Published findings with and ongoing evaluation of osimertinib combined with other agents, such as savolitinib and tepotinib, to overcome common mechanisms of resistance**
- **Recently presented data with amivantamab in combination with chemotherapy with and without lazertinib for patients with NSCLC with an EGFR mutation who experience disease progression on osimertinib**
- **Rationale for targeting HER3 in patients with NSCLC with an EGFR mutation; structural components and mechanism of action of patritumab deruxtecan (HER3-DXd)**

The Current and Future Management of Progressive NSCLC with an EGFR Mutation (Continued)

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Published efficacy and safety findings with HER3-DXd for NSCLC with an EGFR mutation after progression on EGFR TKI therapy and platinum-based chemotherapy**
- **Potential clinical roles of amivantamab/chemotherapy with or without lazertinib and HER3-DXd for progressive NSCLC with an EGFR mutation**

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY
driving innovation in oncology

ORIGINAL ARTICLE

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☆

A. Passaro[1*†], J. Wang[2†], Y. Wang[3], S.-H. Lee[4], B. Melosky[5], J.-Y. Shih[6], J. Wang[7], K. Azuma[8], O. Juan-Vidal[9], M. Cobo[10], E. Felip[11], N. Girard[12,13], A. B. Cortot[14], R. Califano[15], F. Cappuzzo[16], S. Owen[17], S. Popat[18], J.-L. Tan[19], J. Salinas[20], P. Tomasini[21], R. D. Gentzler[22], W. N. William, Jr.[23], K. L. Reckamp[24], T. Takahashi[25], S. Ganguly[26], D. M. Kowalski[27], A. Bearz[28], M. MacKean[29], P. Barala[30], A. B. Bourla[31], A. Girvin[30], J. Greger[30], D. Millington[32], M. Withelder[30], J. Xie[31], T. Sun[31], S. Shah[30], B. Diorio[31], R. E. Knoblauch[30], J. M. Bauml[30], R. G. Campelo[33‡] & B. C. Cho[34‡], for the MARIPOSA-2 Investigators§

2024;35(1):77-90

Patritumab Deruxtecan (HER3-DXd)

Mechanism of action

- **Antibody-drug conjugate directed against HER3**

Indication

- **Investigational**

Key clinical trial

- **HERTHENA-Lung02 Phase III trial of patritumab deruxtecan versus platinum-based chemotherapy in metastatic or locally advanced NSCLC with an EGFR mutation after progression on third-generation EGFR TKI therapy**

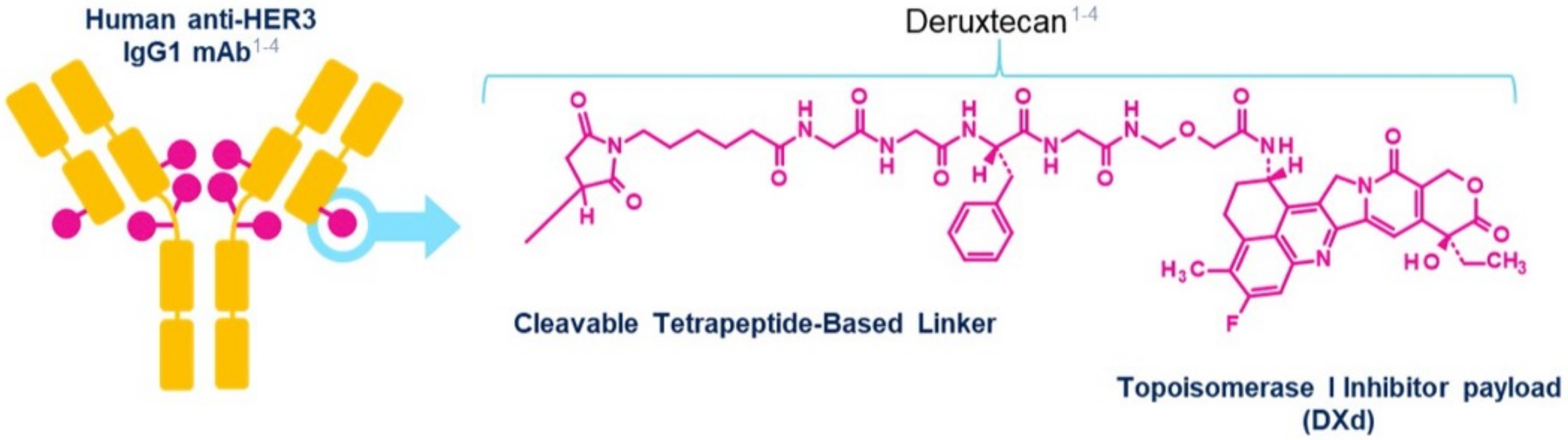
Mok T et al. *Future Oncol* 2024;20(15):969-80.

RTP RESEARCH TO PRACTICE

HER3-DXd Targeting HER3 May Address Multiple EGFR TKI Resistance Mechanisms

HER3-DXd is an antibody-drug conjugate with 3 components:

- A fully human anti-HER3 IgG1 mAb (patritumab), covalently linked to:
- A topoisomerase I inhibitor payload, an exatecan derivative, via
- A tetrapeptide-based cleaver linker



Janne PA et al. ASCO 2021;Abstract 9007.

Tolerability and Other Practical Considerations with HER3-DXd

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Frequency of dose interruptions, dose reductions and treatment discontinuation with HER3-DXd in published clinical trials**
- **Rates of Grade ≥3 cytopenias reported among patients receiving HER3-DXd; optimal monitoring of complete blood counts**
- **Other commonly reported treatment-related AEs observed with HER3-DXd, such as gastrointestinal issues and fatigue**
- **Incidence and severity of ILD reported with HER3-DXd; appropriate monitoring and management**

Marianne J Davies, DNP, ACNP, AOCNP, FAAN

What I tell my patients who are being considered for or are about to enroll on a clinical trial with patritumab deruxtecan

RTP
RESEARCH
TO PRACTICE

Jillian Thompson, MSN, ANP-BC, AOCNP

What I tell my patients with metastatic lung cancer about the importance of clinical trial participation

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction

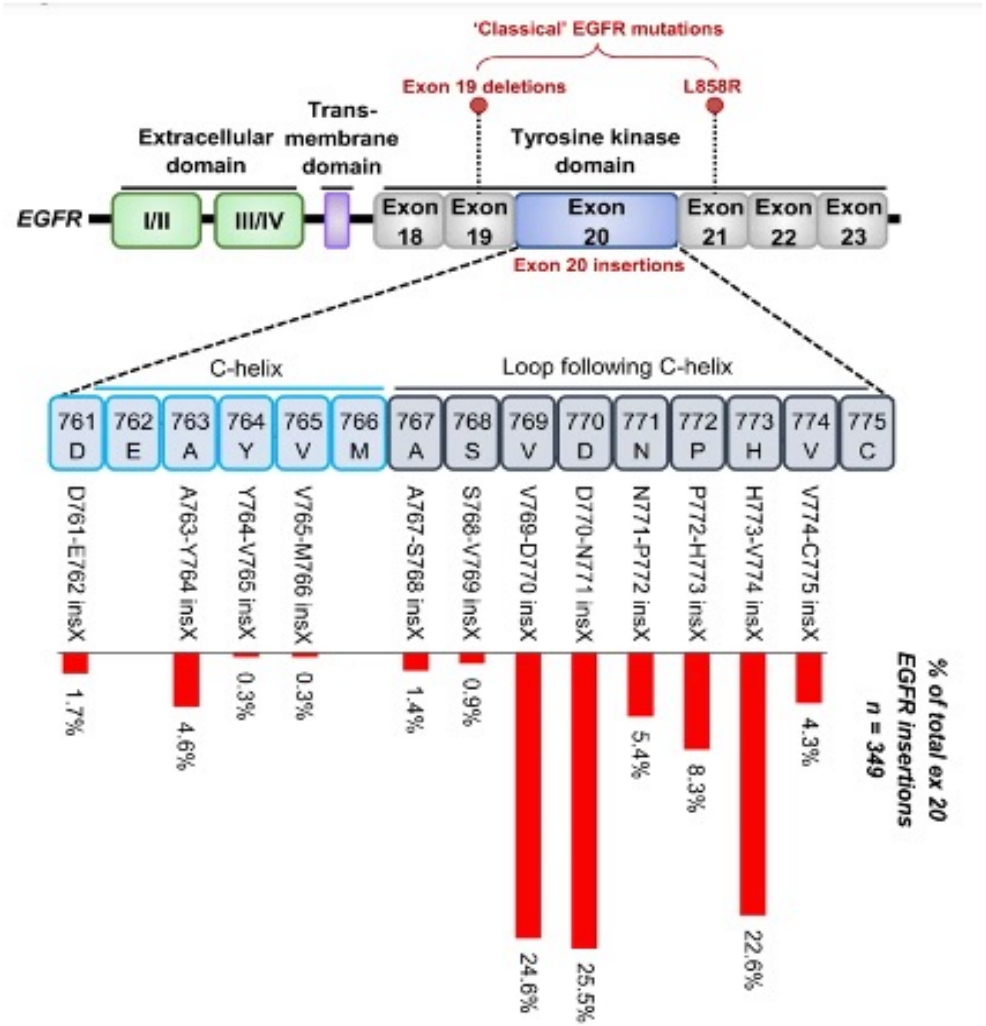
Module 1: Localized Non-Small Cell Lung Cancer (NSCLC) with an EGFR Mutation

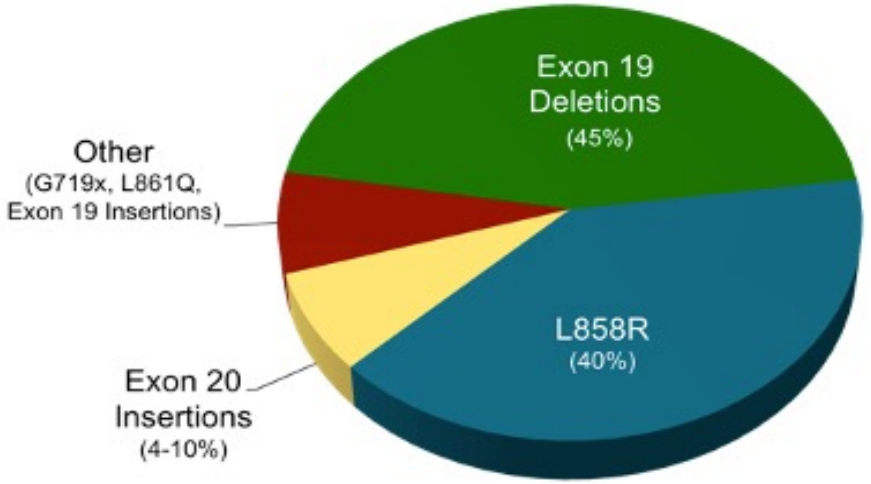
Module 2: First-Line Therapy for Patients with Metastatic NSCLC and EGFR Mutations

Module 3: Management of Progressive EGFR-Mutated NSCLC

Module 4: Targeting EGFR Exon 20 Insertion Mutations

Frequency of EGFR Exon 20 Mutations





Exon 20 NSCLC: US and China				
		Exon 20 Frequency	Total Number of NSCLC Patients/year	
United States	EGFR HER2	2.1% 1.5%	3.6%	7700
China	EGFR HER2	2.4% 3.9%	6.3%	41100

Courtesy of Zofia Piotrowska, MD, MHS

RTP RESEARCH TO PRACTICE

Treatment for Metastatic NSCLC with EGFR Exon 20 Insertion Mutations

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Rationale for the lack of activity with traditional EGFR TKIs in this patient subset; biological basis for the activity of amivantamab**
- **Long-term efficacy and safety data with amivantamab for patients with metastatic NSCLC and EGFR exon 20 insertion mutations who experience progression on or after platinum-based chemotherapy**
- **Key findings with the combination of amivantamab and platinum-based chemotherapy for newly diagnosed advanced NSCLC with EGFR exon 20 insertion mutations**

Treatment for Metastatic NSCLC with EGFR Exon 20 Insertion Mutations (Continued)

Dr Spira
Fairfax, Virginia

Dr Yu
New York, New York

- **Recent FDA approval of amivantamab in combination with chemotherapy as first-line treatment for NSCLC with EGFR exon 20 insertion mutations; implications for therapeutic sequencing**
- **Rationale for the recent voluntary withdrawal of mobocertinib for NSCLC with EGFR exon 20 insertion mutations**

Amivantamab

Mechanism of action

- **Bispecific EGFR-directed and MET receptor-directed antibody**

Indication in the first-line setting

- **In combination with carboplatin and pemetrexed for patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test**

Recommended dose

- **Initial week 1 dose is a split infusion given on day 1 and day 2**
- **Body weight <80 kg: 1,400 mg IV infusion weekly with chemotherapy on weeks 1-4, then 1,750 mg IV infusion q3wk beginning week 7 until progression/toxicity**
- **Body weight ≥80 kg: 1,750 mg IV infusion weekly with chemotherapy on weeks 1-4, then 2,100 mg IV infusion q3wk beginning week 7 until progression/toxicity**

Amivantamab package insert, 3/2024.

RTP RESEARCH TO PRACTICE

FDA Approves Amivantamab for NSCLC with EGFR Exon 20 Insertion Mutations

Press Release – March 1, 2024

"The Food and Drug Administration approved amivantamab-vmjw with carboplatin and pemetrexed for the first-line treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test.

The FDA also granted traditional approval to amivantamab-vmjw for adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy. FDA previously granted accelerated approval for this indication.

Efficacy was evaluated in PAPILLON (NCT04538664), a randomized, open-label multicenter trial of 308 patients with EGFR exon 20 insertion mutations. Patients were randomized 1:1 to receive amivantamab-vmjw with carboplatin and pemetrexed or carboplatin and pemetrexed."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-amivantamab-vmjw-egfr-exon-20-insertion-mutated-non-small-cell-lung-cancer-indications

2023;389:2039-51

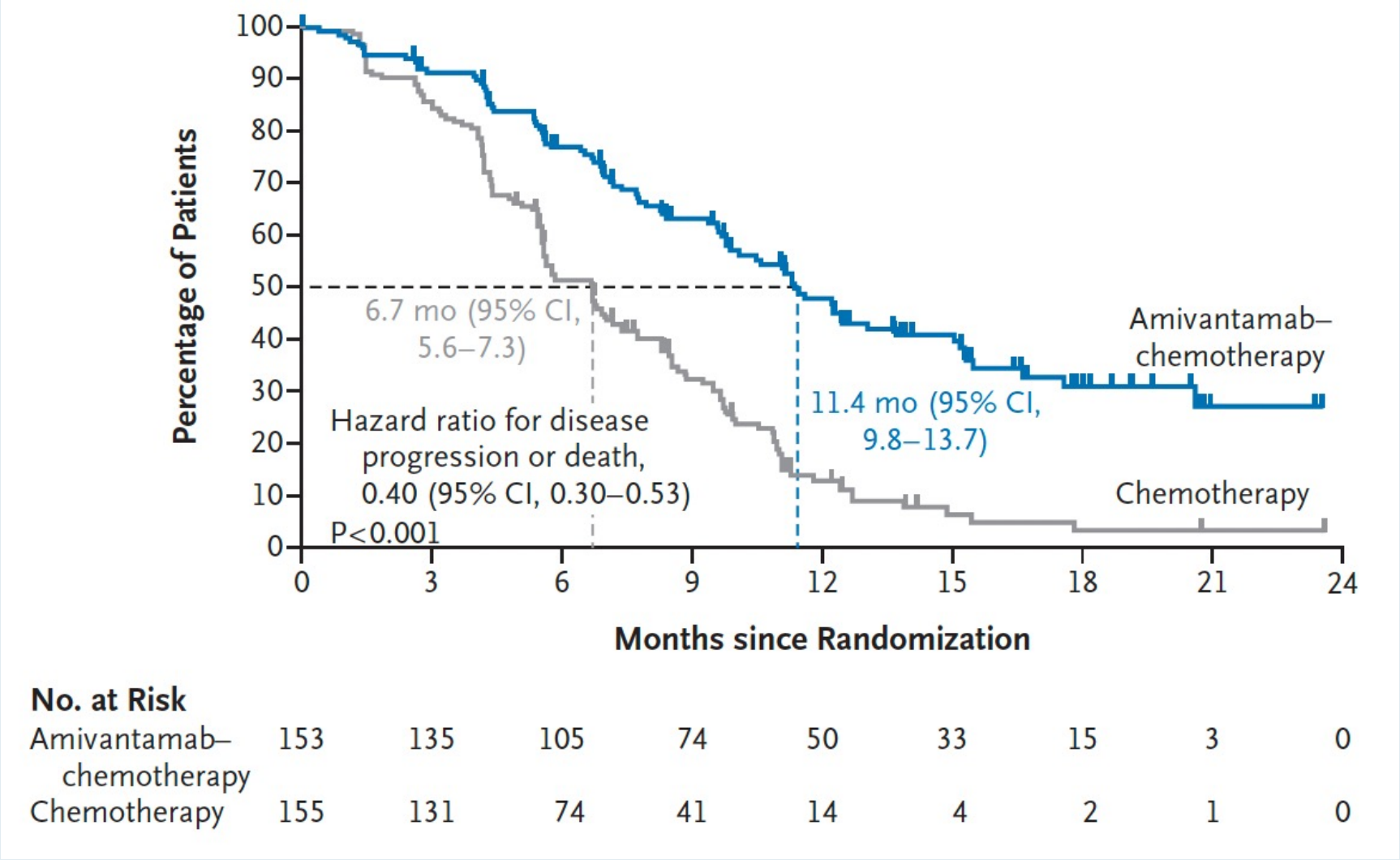
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Amivantamab plus Chemotherapy in NSCLC with *EGFR* Exon 20 Insertions

C. Zhou, K.-J. Tang, B.C. Cho, B. Liu, L. Paz-Ares, S. Cheng, S. Kitazono, M. Thiagarajan, J.W. Goldman, J.K. Sabari, R.E. Sanborn, A.S. Mansfield, J.-Y. Hung, M. Boyer, S. Popat, J. Mourão Dias, E. Felip, M. Majem, M. Gumus, S. Kim, A. Ono, J. Xie, A. Bhattacharya, T. Agrawal, S.M. Shreeve, R.E. Knoblauch, K. Park, and N. Girard, for the PAPILLON Investigators*

PAPILLON Trial Primary Endpoint: PFS by Blinded Independent Central Review



Zhou C et al. *N Engl J Med* 2023;389:2039-51.

PAPILLON: Select Adverse Events

Adverse event	Amivantamab-chemotherapy (n = 151)		Chemotherapy (N = 155)	
	All grades	Grade ≥3	All grades	Grade ≥3
Neutropenia	59%	33%	45%	23%
Anemia	50%	11%	55%	12%
Leukopenia	38%	11%	32%	3%
Rash	54%	11%	8%	0
Thrombocytopenia	36%	10%	30%	10%

- 7% of patients discontinued amivantamab due to drug-related adverse reactions

Zhou C et al. *N Engl J Med* 2023;389:2039-51.

APPENDIX

Osimertinib for Localized and Locally Advanced NSCLC with an EGFR Mutation

RTP
RESEARCH
TO PRACTICE

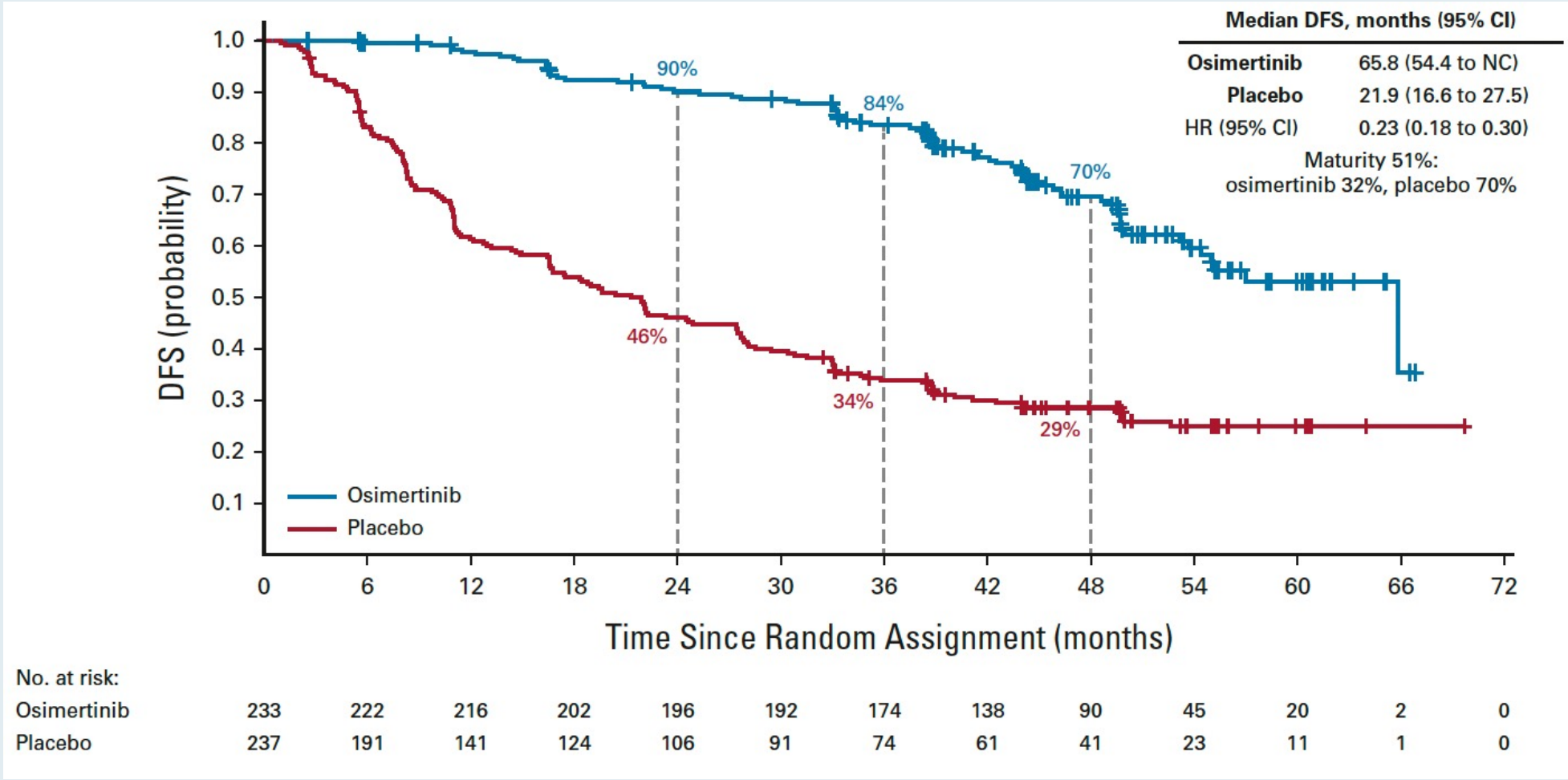
J Clin Oncol 2023;41(10):1830-40

clinical trial updates

Adjuvant Osimertinib for Resected EGFR-Mutated Stage IB-IIIA Non–Small-Cell Lung Cancer: Updated Results From the Phase III Randomized ADAURA Trial

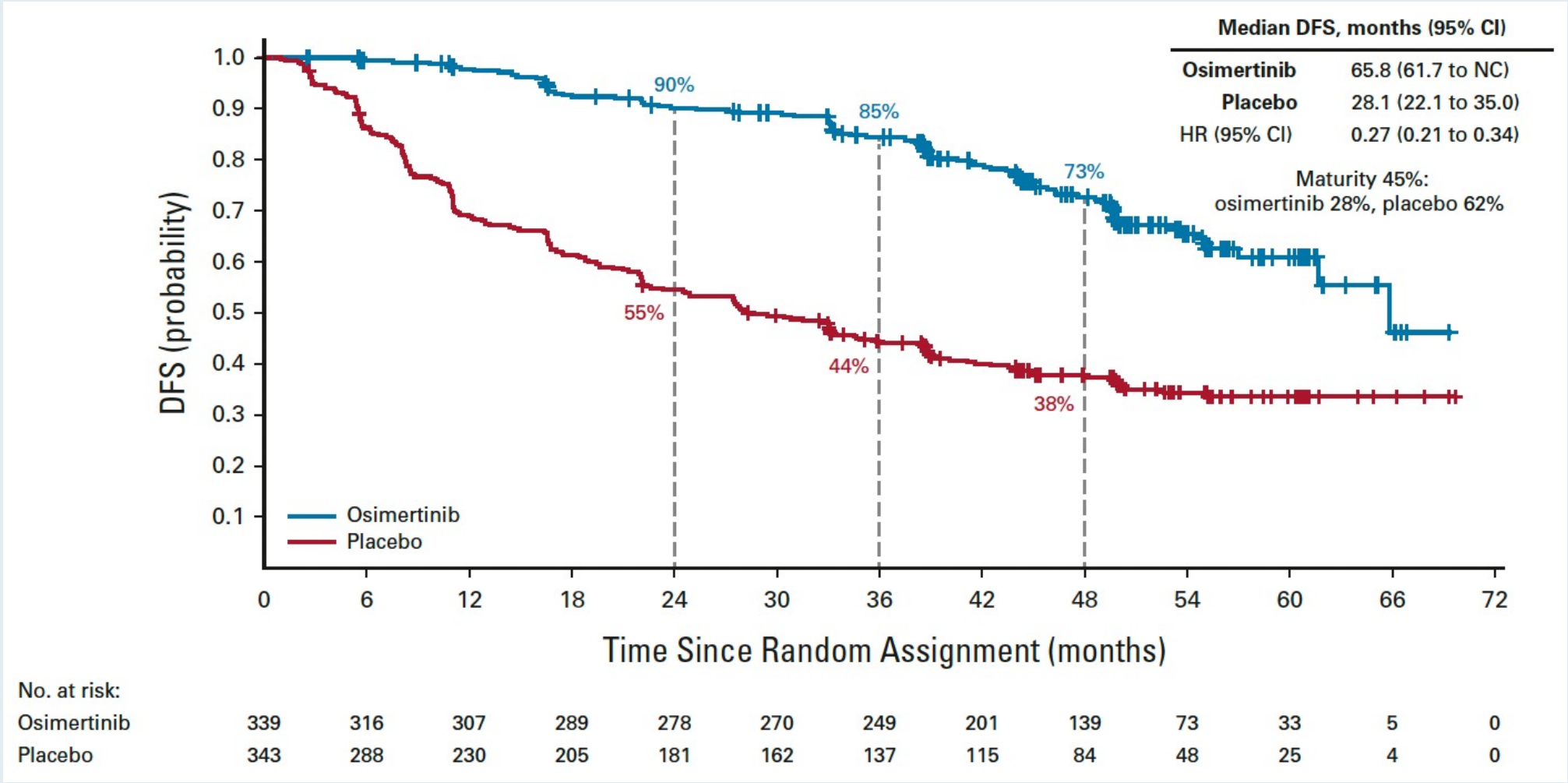
Roy S. Herbst, MD, PhD[1]; Yi-Long Wu, MD[2]; Thomas John, PhD[3]; Christian Grohe, MD[4]; Margarita Majem, MD, PhD[5]; Jie Wang, MD, PhD[6]; Terufumi Kato, MD[7]; Jonathan W. Goldman, MD[8]; Konstantin Laktionov, PhD[9]; Sang-We Kim, MD, PhD[10]; Chong-Jen Yu, MD, PhD[11,12]; Huu Vinh Vu, MD, PhD[13]; Shun Lu, MD[14]; Kye Young Lee, MD, PhD[15]; Guzel Mukhametshina, MD[16]; Charuwan Akewanlop, MD[17]; Filippo de Marinis, MD[18]; Laura Bonanno, MD[19]; Manuel Domine, MD, PhD[20]; Frances A. Shepherd, MD[21]; Damien Urban, MBBS[22,23]; Xiangning Huang, PhD[24]; Ana Bolanos, MD[25]; Marta Stachowiak, MPharm[26]; and Masahiro Tsuboi, MD, PhD[27]

ADAURA Updated Results: Disease-Free Survival (DFS) in Stage II/IIIA Disease



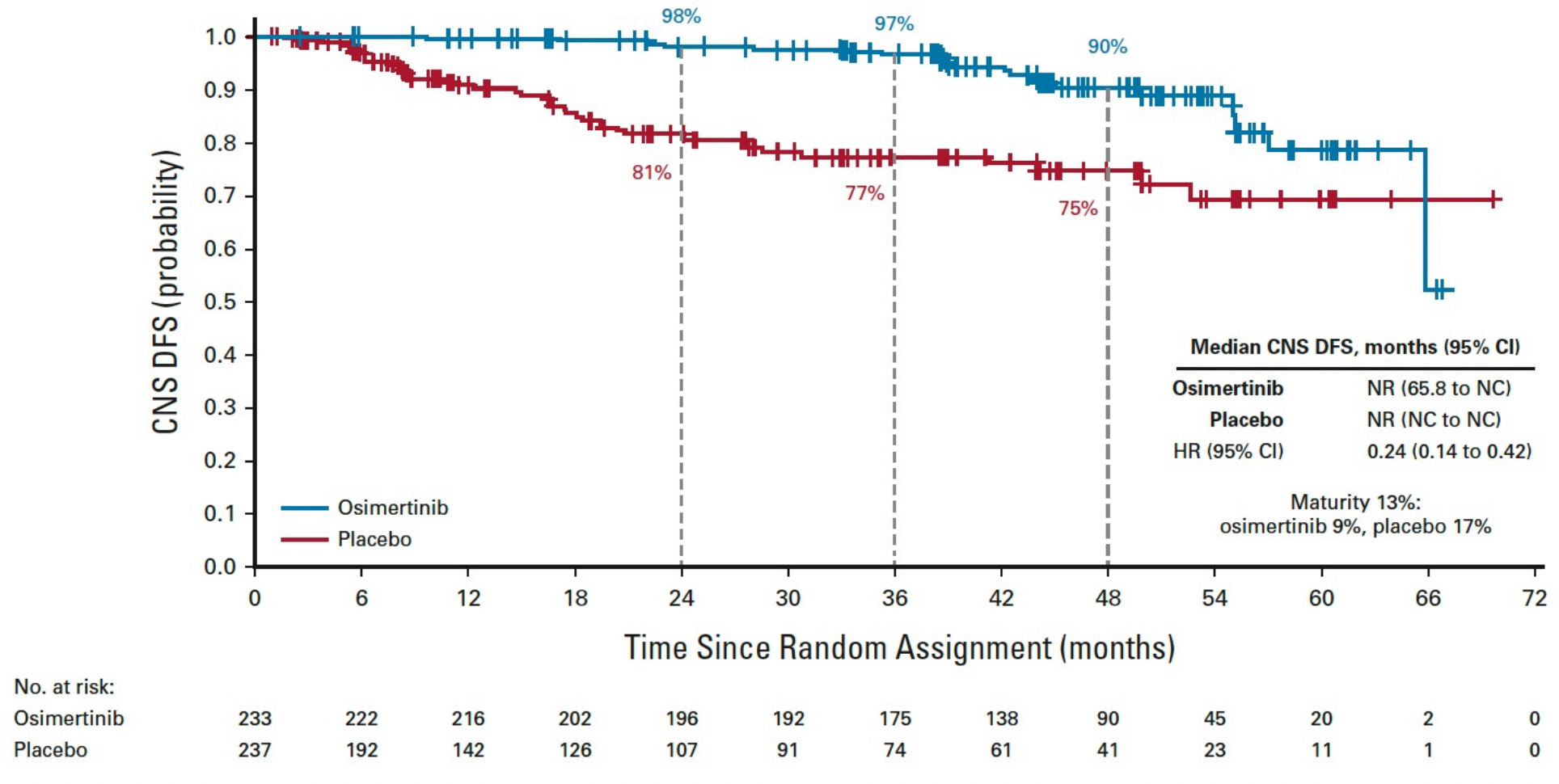
Herbst RS et al. *J Clin Oncol* 2023;41(10):1830-40.

ADAURA Updated DFS Results in the Overall Population (Stage IB-IIIA Disease)



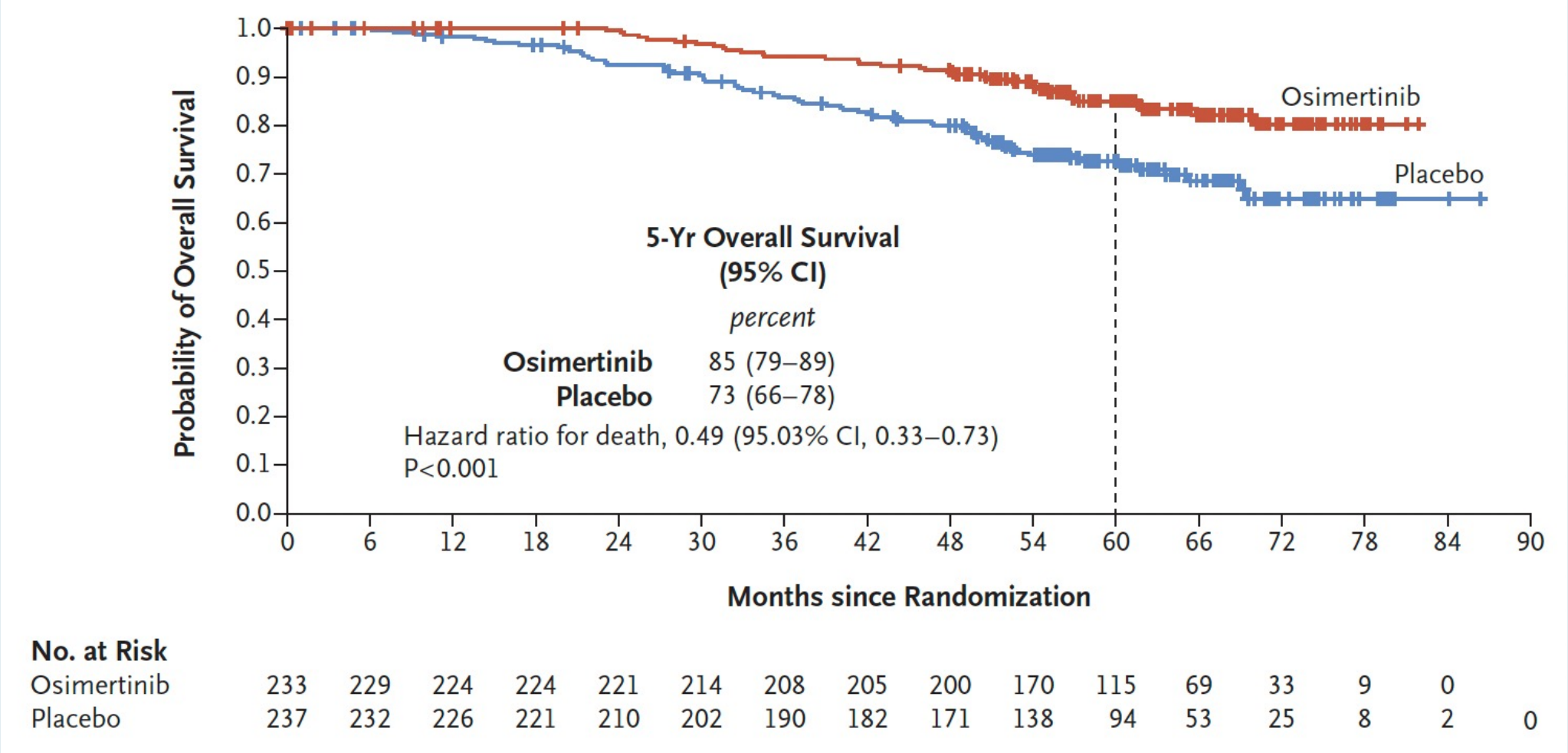
Herbst RS et al. *J Clin Oncol* 2023;41(10):1830-40.

ADAURA Trial: CNS Disease-Free Survival per Investigator Assessment in Stage II-IIIA Disease



Herbst RS et al. *J Clin Oncol* 2023;41(10):1830-40.

ADAURA: Overall Survival in Stage II/IIIA Disease



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

ADAURA: Most Common All-Causality Adverse Events in ≥10% of Patients in Both Treatment Groups

	Osimertinib (n = 337)				Placebo (n = 343)			
Most Common All-Causality AE[d]	Any Grade	Grade 1	Grade 2	Grade 3	Any Grade	Grade 1	Grade 2	Grade 3
Diarrhea	159 (47)	114 (34)	36 (11)	9 (3)	70 (20)	55 (16)	14 (4)	1 (< 1)
Paronychia	92 (27)	33 (10)	56 (17)	3 (1)	5 (1)	2 (1)	3 (1)	0
Dry skin	84 (25)	79 (23)	4 (1)	1 (< 1)	23 (7)	19 (6)	4 (1)	0
Pruritus	70 (21)	52 (15)	18 (5)	0	30 (9)	28 (8)	2 (1)	0
Cough	66 (20)	45 (13)	21 (6)	0	61 (18)	44 (13)	17 (5)	0
Stomatitis	59 (18)	35 (10)	18 (5)	6 (2)	15 (4)	11 (3)	4 (1)	0
Upper respiratory tract infection	53 (16)	29 (9)	22 (7)	2 (1)	37 (11)	19 (6)	18 (5)	0
Nasopharyngitis	50 (15)	31 (9)	19 (6)	0	36 (10)	25 (7)	11 (3)	0
Decreased appetite	48 (14)	33 (10)	13 (4)	2 (1)	13 (4)	9 (3)	4 (1)	0
Dermatitis acneiform	41 (12)	31 (9)	10 (3)	0	16 (5)	12 (3)	4 (1)	0
Mouth ulceration	39 (12)	32 (9)	7 (2)	0	10 (3)	7 (2)	3 (1)	0
Weight decreased	35 (10)	19 (6)	14 (4)	2 (1)	9 (3)	7 (2)	2 (1)	0
Nausea	34 (10)	28 (8)	5 (1)	1 (< 1)	20 (6)	15 (4)	5 (1)	0
Rash	33 (10)	24 (7)	9 (3)	0	12 (3)	10 (3)	2 (1)	0
Arthralgia	23 (7)	18 (5)	5 (1)	0	37 (11)	32 (9)	5 (1)	0
Headache	26 (8)	24 (7)	2 (1)	0	34 (10)	27 (8)	7 (2)	0

Herbst RS et al. *J Clin Oncol* 2023;41(10):1830-40.

First-Line Therapy for Metastatic NSCLC with an EGFR Mutation

2020;382:41-50

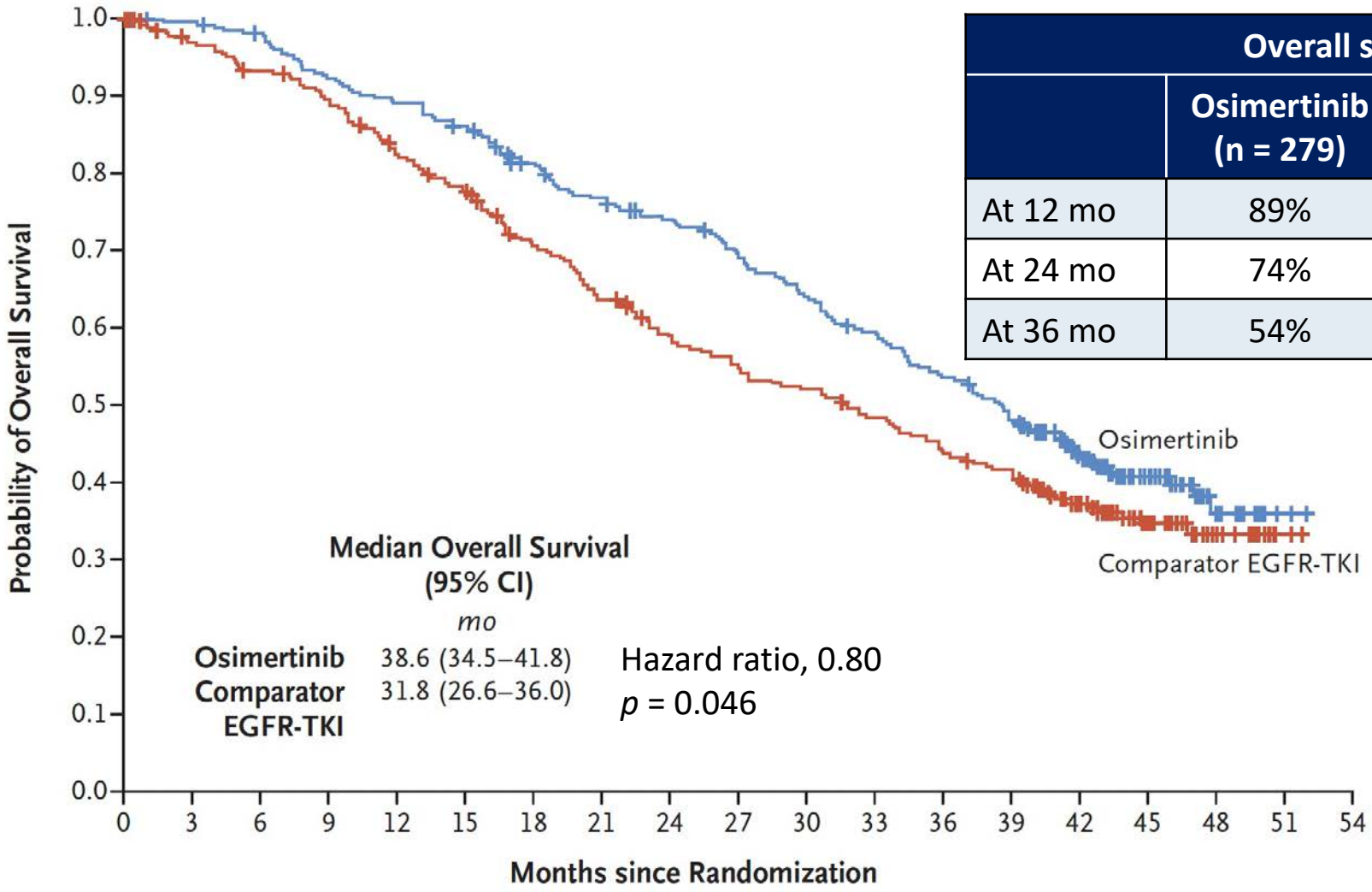
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Overall Survival with Osimertinib in Untreated, *EGFR*-Mutated Advanced NSCLC

S.S. Ramalingam, J. Vansteenkiste, D. Planchard, B.C. Cho, J.E. Gray, Y. Ohe, C. Zhou, T. Reungwetwattana, Y. Cheng, B. Chewaskulyong, R. Shah, M. Cobo, K.H. Lee, P. Cheema, M. Tiseo, T. John, M.-C. Lin, F. Imamura, T. Kurata, A. Todd, R. Hodge, M. Saggese, Y. Rukazenkov, and J.-C. Soria, for the FLAURA Investigators*

FLAURA Trial: Overall Survival



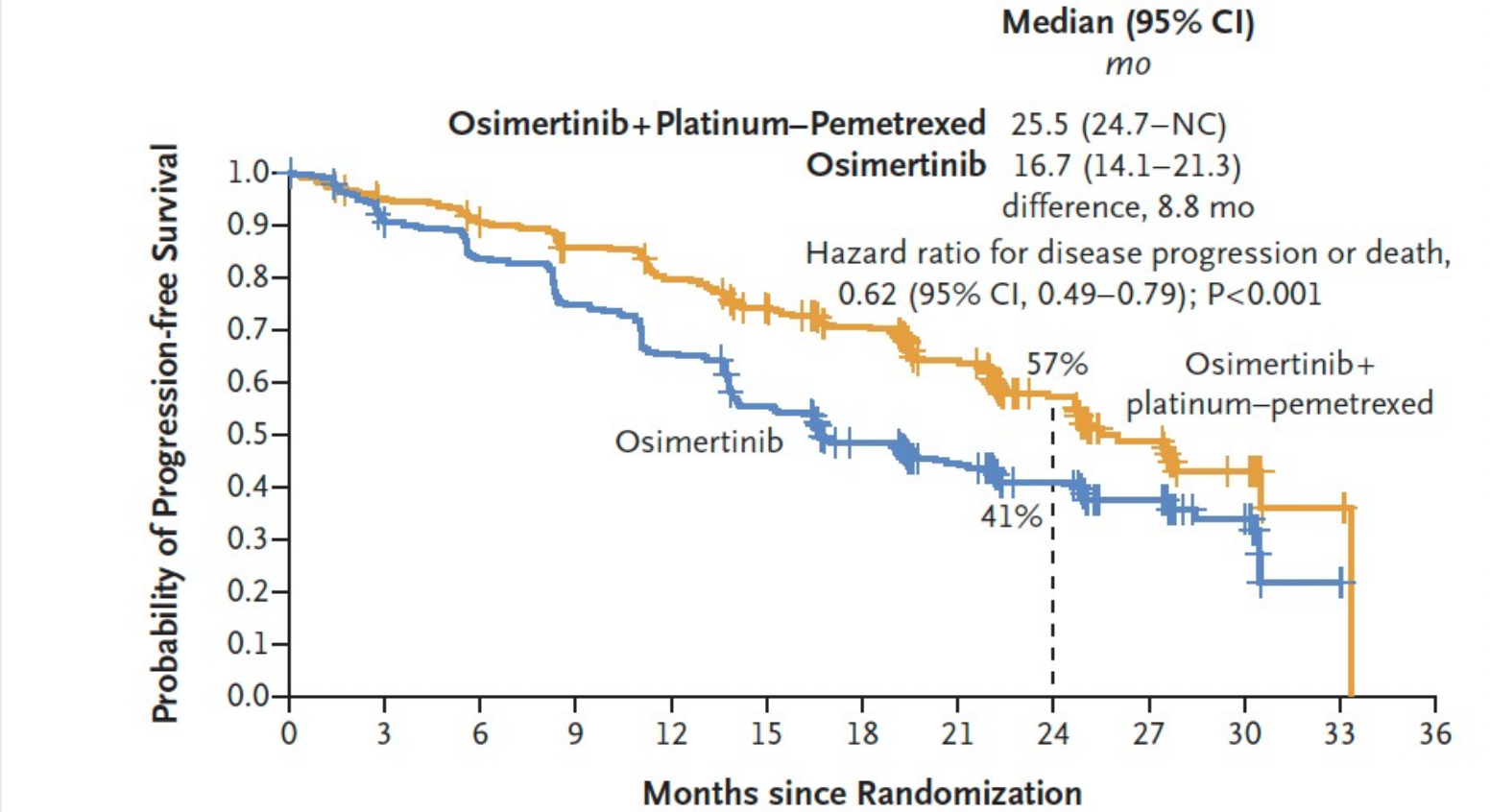
Overall survival		
	Osimertinib (n = 279)	Comparator EGFR TKI (n = 277)
At 12 mo	89%	83%
At 24 mo	74%	59%
At 36 mo	54%	44%

TKI = tyrosine kinase inhibitor

Ramalingam SS et al. *N Engl J Med* 2020;382:41-50.

RTP RESEARCH TO PRACTICE

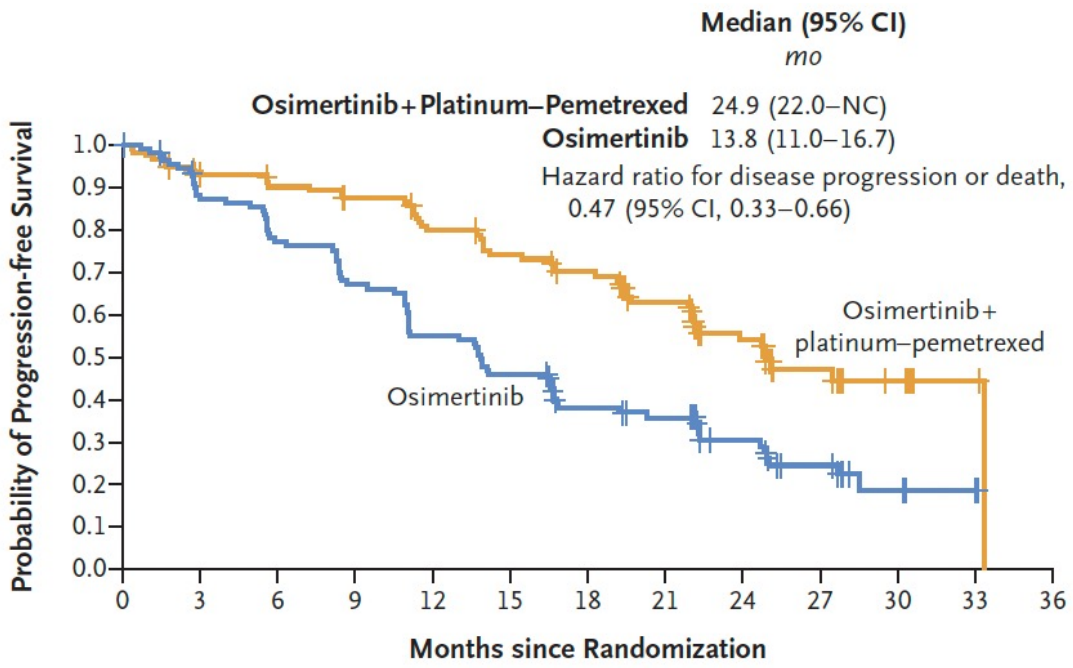
FLAURA2 Primary Endpoint: Investigator-Assessed PFS



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

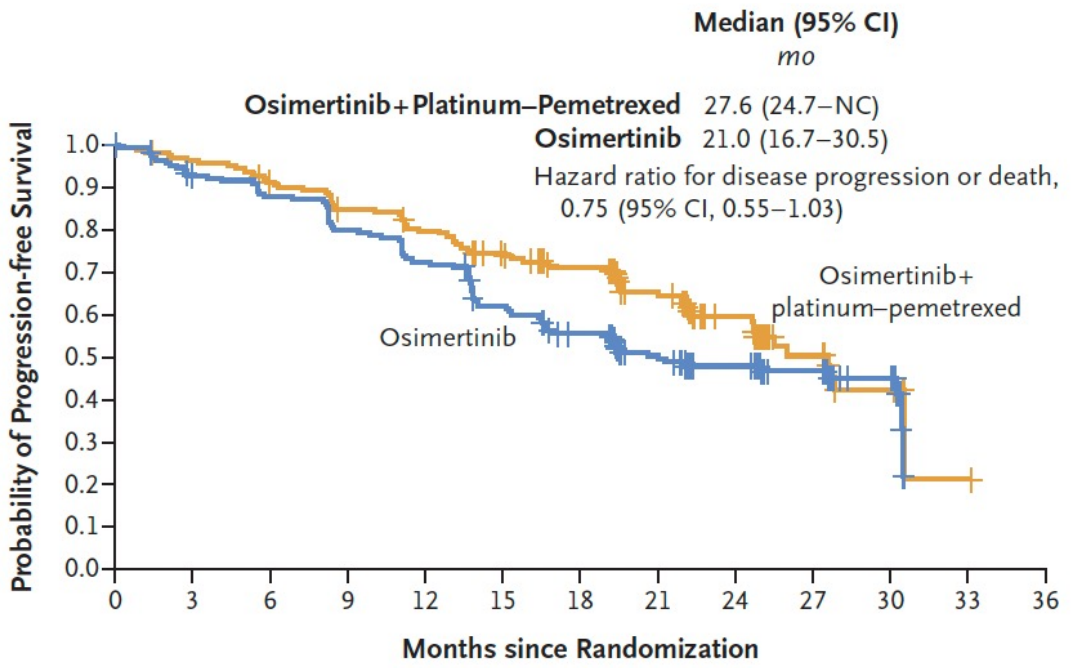
FLAURA2 Trial: PFS for Patients with and without CNS Metastases at Baseline

With CNS Metastases at Baseline



No. at Risk													
Osimertinib+ platinum–pemetrexed	116	101	98	93	84	77	70	58	34	19	8	2	0
Osimertinib	110	95	84	73	60	50	37	32	21	13	5	1	0

Without CNS Metastases at Baseline



No. at Risk													
Osimertinib+ platinum–pemetrexed	163	153	143	132	123	110	95	75	50	23	13	1	0
Osimertinib	168	151	143	130	118	98	82	62	46	35	16	0	0

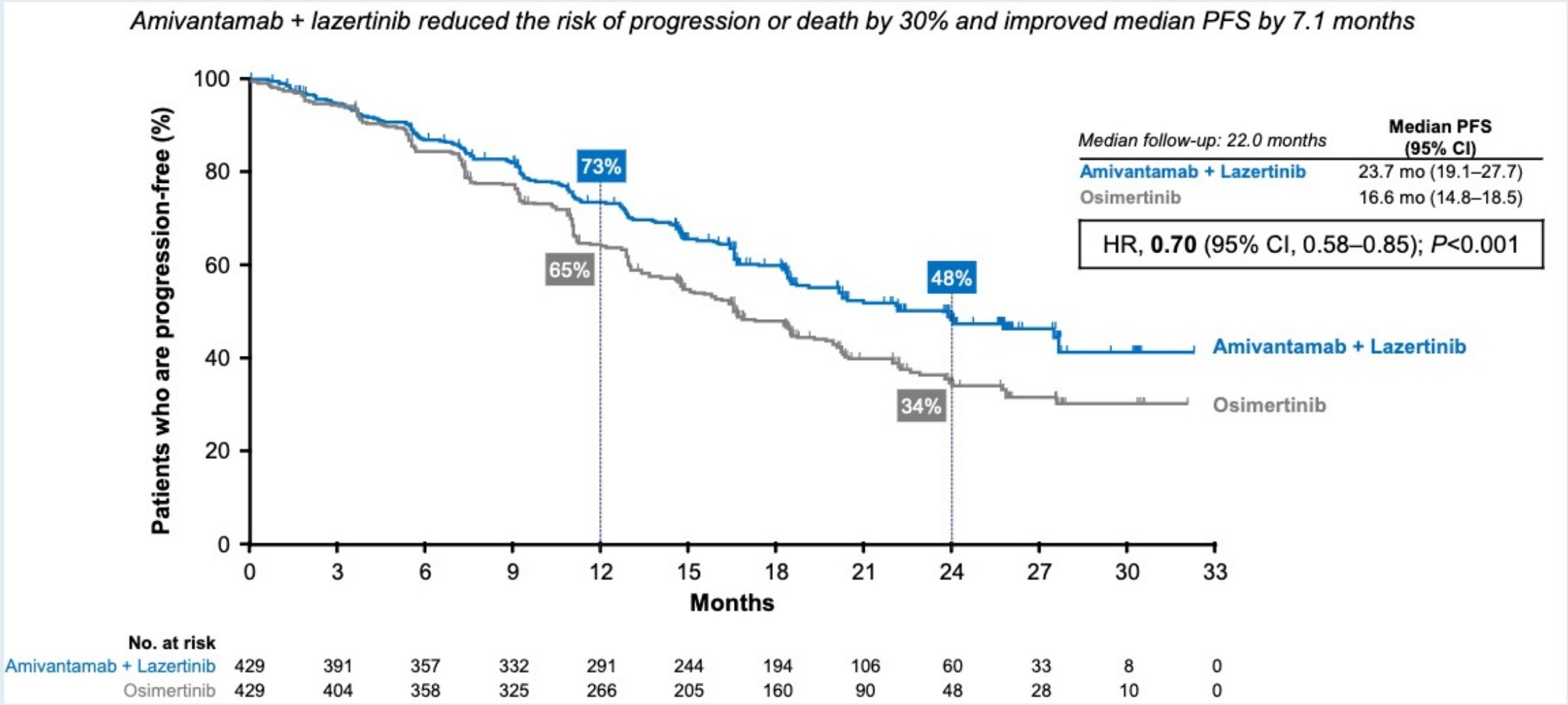
Planchard D et al. *N Engl J Med* 2023;389:1935-48.

FLAURA2: Adverse Events (≥15% of Patients)

Event	Osimertinib + Platinum–Pemetrexed (N=276)					Osimertinib Monotherapy (N=275)				
	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4
Anemia	128 (46)	30 (11)	43 (16)	55 (20)	0	22 (8)	15 (5)	6 (2)	1 (<1)	0
Diarrhea	120 (43)	83 (30)	29 (11)	8 (3)	0	112 (41)	89 (32)	22 (8)	1 (<1)	0
Nausea	119 (43)	81 (29)	34 (12)	4 (1)	0	28 (10)	22 (8)	6 (2)	0	0
Decreased appetite	85 (31)	49 (18)	28 (10)	8 (3)	0	26 (9)	18 (7)	6 (2)	2 (1)	0
Constipation	81 (29)	60 (22)	20 (7)	1 (<1)	0	28 (10)	23 (8)	5 (2)	0	0
Rash	77 (28)	55 (20)	21 (8)	1 (<1)	0	57 (21)	46 (17)	11 (4)	0	0
Fatigue	76 (28)	45 (16)	23 (8)	8 (3)	0	26 (9)	24 (9)	1 (<1)	1 (<1)	0
Vomiting	73 (26)	50 (18)	20 (7)	3 (1)	0	17 (6)	13 (5)	4 (1)	0	0
Stomatitis	68 (25)	40 (14)	27 (10)	1 (<1)	0	50 (18)	32 (12)	17 (6)	1 (<1)	0
Neutropenia	68 (25)	4 (1)	27 (10)	30 (11)	7 (3)	9 (3)	3 (1)	4 (1)	2 (1)	0
Paronychia	65 (24)	28 (10)	35 (13)	2 (1)	0	73 (27)	37 (13)	35 (13)	1 (<1)	0
Neutrophil count decrease	62 (22)	5 (2)	26 (9)	25 (9)	6 (2)	16 (6)	6 (2)	8 (3)	2 (1)	0
Covid-19†	57 (21)	23 (8)	31 (11)	2 (1)	0	39 (14)	18 (7)	21 (8)	0	0
ALT increase	56 (20)	36 (13)	16 (6)	4 (1)	0	21 (8)	17 (6)	3 (1)	1 (<1)	0
Platelet count decrease	51 (18)	19 (7)	11 (4)	18 (7)	3 (1)	19 (7)	18 (7)	1 (<1)	0	0
Thrombocytopenia	51 (18)	19 (7)	13 (5)	16 (6)	3 (1)	12 (4)	6 (2)	3 (1)	3 (1)	0
Dry skin	50 (18)	43 (16)	7 (3)	0	0	66 (24)	62 (23)	4 (1)	0	0
AST increase	48 (17)	42 (15)	5 (2)	1 (<1)	0	13 (5)	12 (4)	0	1 (<1)	0
Blood creatinine increase	46 (17)	33 (12)	13 (5)	0	0	12 (4)	10 (4)	2 (1)	0	0
White-cell count decrease	44 (16)	7 (3)	28 (10)	8 (3)	1 (<1)	18 (7)	9 (3)	8 (3)	1 (<1)	0
Peripheral edema	42 (15)	33 (12)	9 (3)	0	0	12 (4)	9 (3)	3 (1)	0	0

Planchard D et al. *N Engl J Med* 2023;389:1935-48.

MARIPOSA Primary Endpoint: PFS by Blinded Independent Central Review

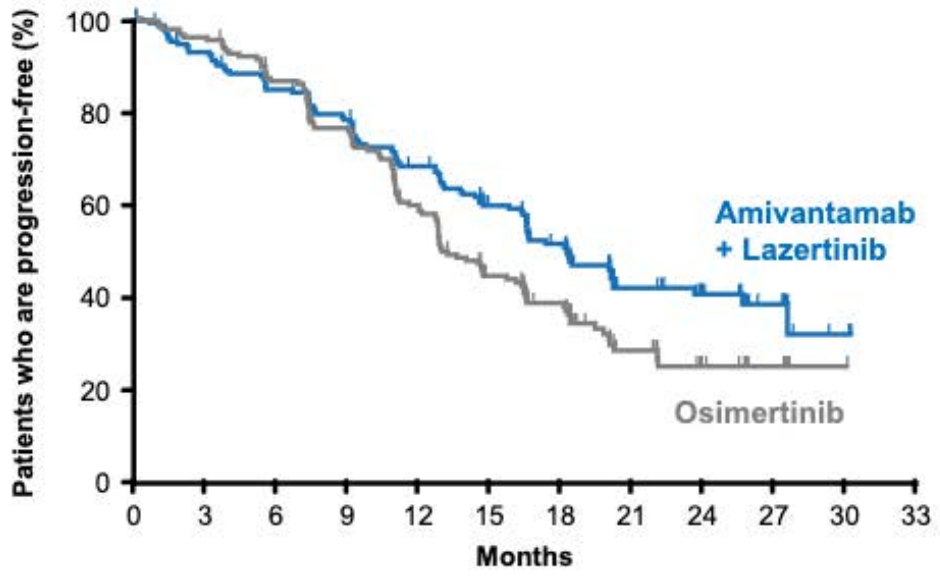


Cho BC et al. ESMO 2023;Abstract LBA14.

MARIPOSA: PFS for Patients with and 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)

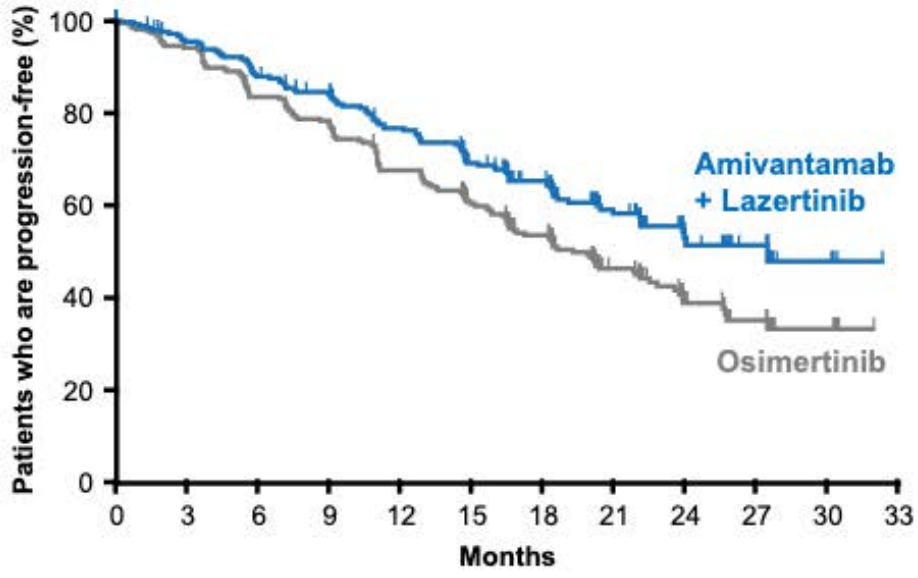
HR, **0.69** (95% CI, 0.53–0.92)



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)



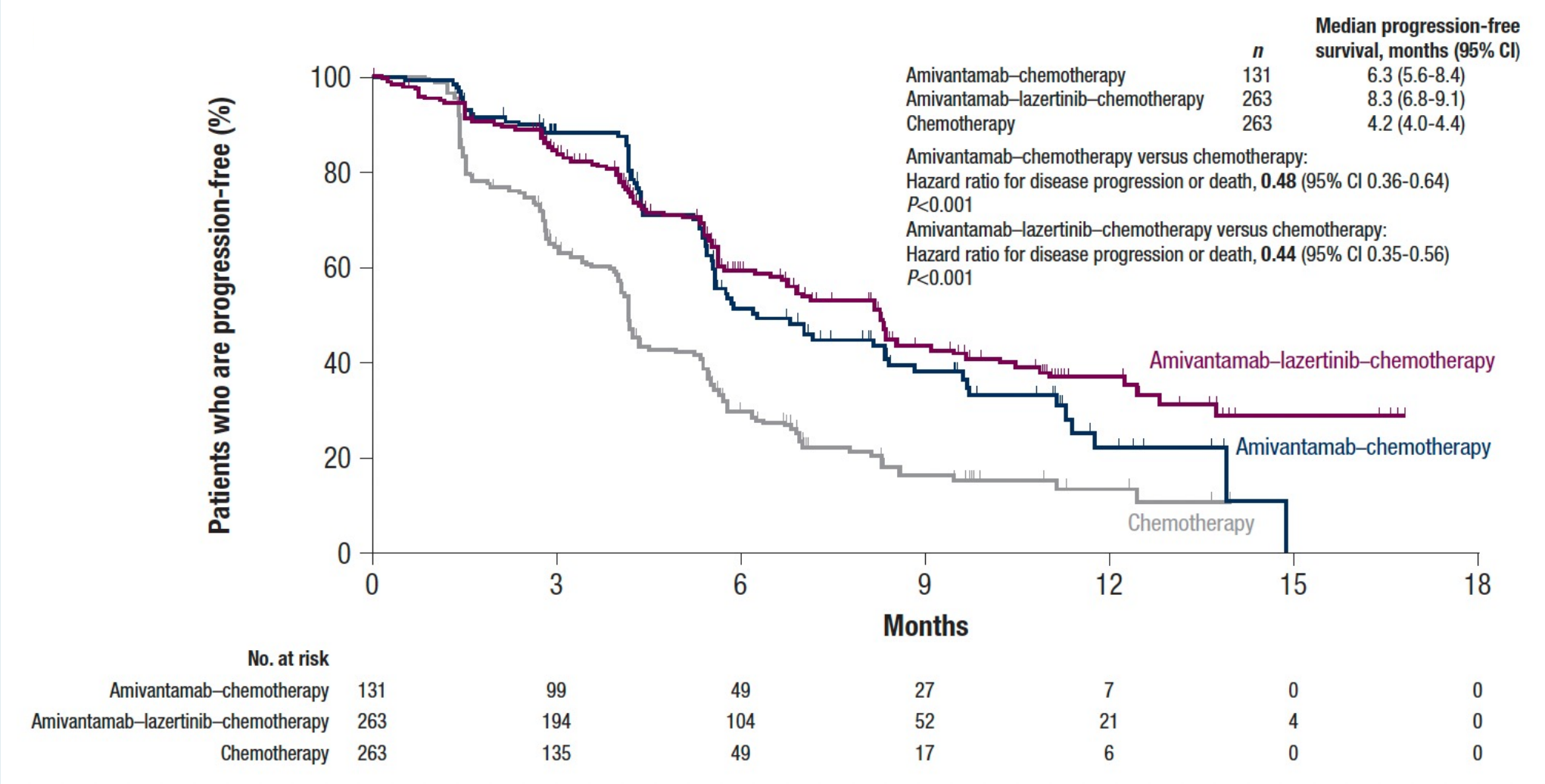
No. at risk												
Amivantamab + Lazertinib	251	229	211	198	176	152	123	72	36	21	5	0
Osimertinib	257	240	212	199	171	141	113	69	37	22	9	0

Cho BC et al. ESMO 2023;Abstract LBA14.

Management of Progressive NSCLC with an EGFR Mutation

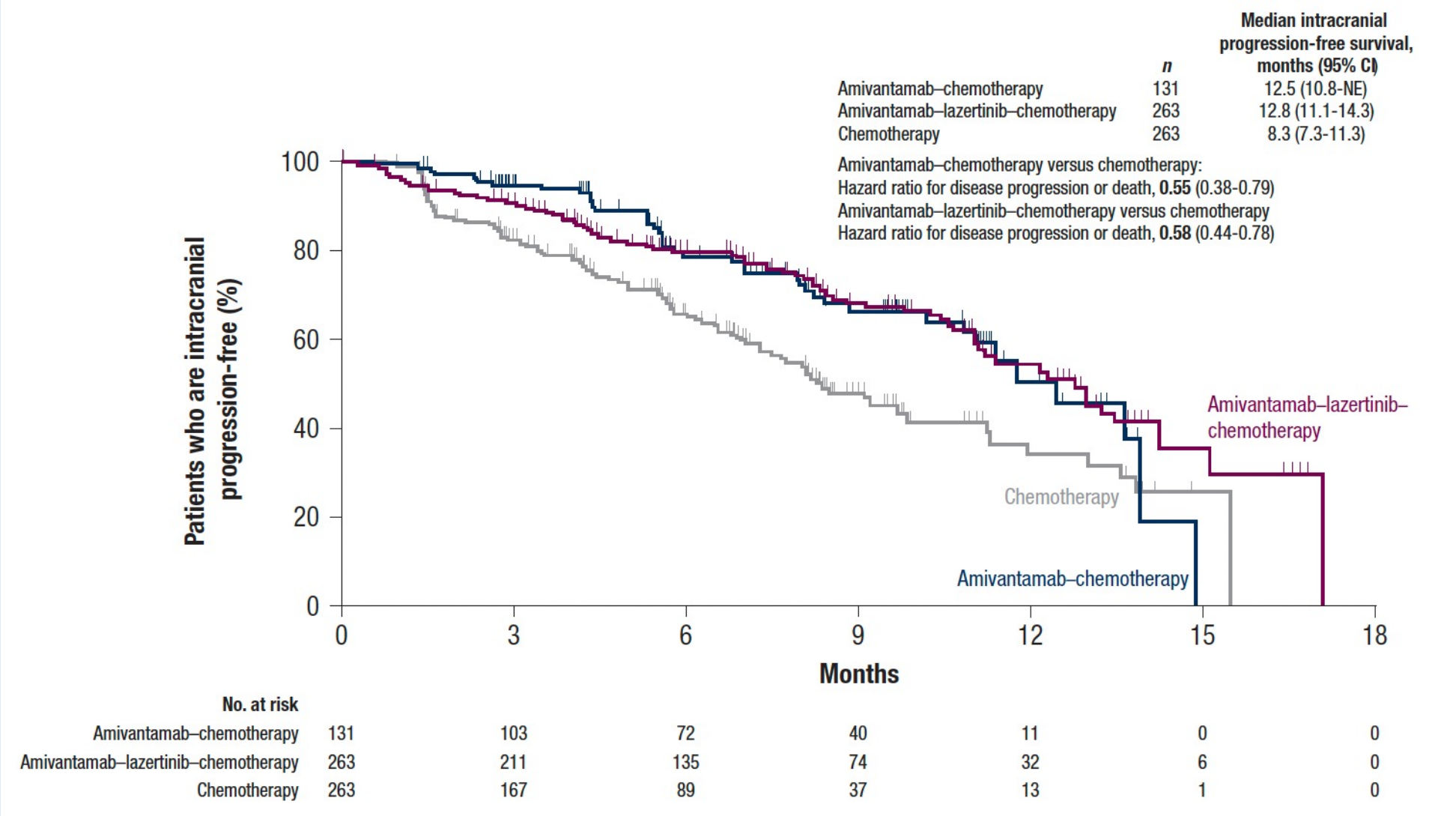
RTP
RESEARCH
TO PRACTICE

MARIPOSA-2 Primary Endpoint: PFS



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

MARIPOSA-2: Intracranial PFS for All Randomized Patients



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

MARIPOSA-2 Trial: Safety Profile

Table 3. Treatment-emergent adverse events

Event, *n* (%)	Chemotherapy (*n* = 243)		Amivantamab–chemotherapy (*n* = 130)		Amivantamab–lazertinib–chemotherapy (*n* = 263)	
Any event	227 (93)		130 (100)		263 (100)	
Grade ≥3	117 (48)		94 (72)		242 (92)	
Any serious event	49 (20)		42 (32)		137 (52)	
Any event resulting in death	3 (1)		3 (2)		14 (5)	
Any event leading to:						
Interruptions of any study agent	81 (33)		84 (65)		202 (77)	
Reductions of any study agent	37 (15)		53 (41)		171 (65)	
Discontinuations of any study agent	9 (4)		24 (18)		90 (34)	
Adverse events[a]	All	Grade ≥3	All	Grade ≥3	All	Grade ≥3
Neutropenia[b]	101 (42)	52 (21)	74 (57)	59 (45)	181 (69)	144 (55)
Thrombocytopenia[b]	72 (30)	22 (9)	57 (44)	19 (15)	158 (60)	96 (37)
Infusion-related reaction	1 (0.4)	0	76 (58)	7 (5)	148 (56)	9 (3)
Anemia	97 (40)	23 (9)	51 (39)	15 (12)	141 (54)	48 (18)
Paronychia	1 (0.4)	0	48 (37)	3 (2)	133 (51)	11 (4)
Nausea	90 (37)	2 (1)	58 (45)	1 (1)	131 (50)	16 (6)
Rash	12 (5)	0	56 (43)	8 (6)	126 (48)	17 (6)
Stomatitis	21 (9)	0	41 (32)	1 (1)	120 (46)	24 (9)
Leukopenia	68 (28)	23 (9)	37 (28)	26 (20)	106 (40)	71 (27)
Hypoalbuminemia	21 (9)	1 (0.4)	29 (22)	3 (2)	104 (40)	12 (5)
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)
Peripheral edema	15 (6)	0	42 (32)	2 (2)	85 (32)	1 (0.4)
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)
Diarrhea	16 (7)	1 (0.4)	18 (14)	1 (1)	68 (26)	10 (4)
Asthenia	40 (16)	5 (2)	34 (26)	1 (1)	67 (25)	14 (5)
Dermatitis acneiform	7 (3)	0	26 (20)	5 (4)	62 (24)	17 (6)
Alanine aminotransferase increased	67 (28)	10 (4)	26 (20)	7 (5)	55 (21)	14 (5)
Hypokalemia	15 (6)	6 (2)	24 (18)	6 (5)	55 (21)	16 (6)
COVID-19	25 (10)	0	27 (21)	2 (2)	44 (17)	0
Hypocalcemia	9 (4)	0	16 (12)	1 (1)	44 (17)	3 (1)
Aspartate aminotransferase increased	57 (23)	0	19 (15)	1 (1)	43 (16)	7 (3)
Hyponatremia	16 (7)	2 (1)	13 (10)	5 (4)	42 (16)	10 (4)
Pruritus	17 (7)	0	20 (15)	0	30 (11)	0
Adverse events of special interest	All	Grade ≥3	All	Grade ≥3	All	Grade ≥3
Rash[c]	30 (12)	0	92 (71)	13 (10)	197 (75)	40 (15)
Venous thromboembolism[d]	11 (5)	7 (3)	13 (10)	3 (2)	58 (22)	17 (6)
Interstitial lung disease[e]	0	0	2 (2)	1 (1)	7 (3)	5 (2)

Passaro A et al. *Ann Oncol* 2023;389:2039-51.

RTP RESEARCH TO PRACTICE

2023 ASCO ANNUAL MEETING

Abstract 9021

Tepotinib + osimertinib for *EGFR* mutant NSCLC with *MET* amplification after first-line osimertinib

Daniel Shao-Weng Tan[1] (daniel.tan.s.w@singhealth.com.sg; @danieltanmd / Twitter), Tae Min Kim[2], Valentina Guarneri[3], Pei Jye Voon[4], Boon Khaw Lim[5], Marie Wislez[6], Cheng Huang[7], Chong Kin Liam[5], Julien Mazieres[8], Lye Mun Tho[9], Hidetoshi Hayashi[10], Nhung Nguyen[11], Puey Ling Chia[12], Filippo de Marinis[13], Xiuning Le[14], Pongwut Danchaivijitr[15], Niki Karachaliou[16], Sabine Brutlach[17], Svenja Adrian[16], Barbara Ellers-Lenz[18], Yi-Long Wu[19]

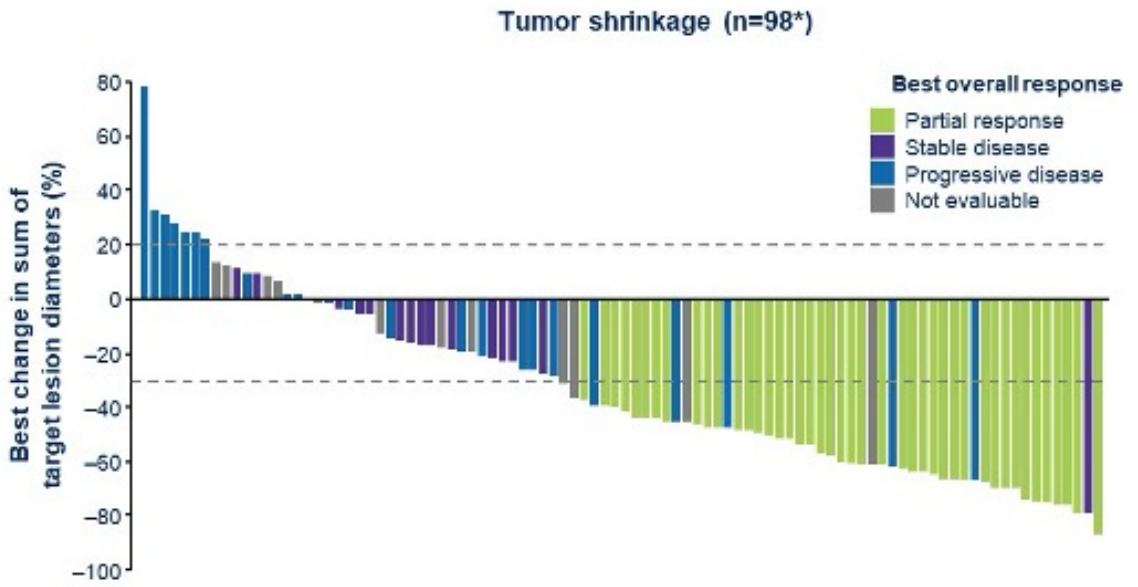
[1]Division of Medical Oncology, National Cancer Centre, Singapore; [2]Seoul National University Cancer Research Institute, Seoul, Republic of Korea; Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea; [3]Department of Surgery, Oncology and Gastroenterology, University of Padova, Oncology 2, IOV - Istituto Oncologico Veneto IRCCS -IOV, Padova, Italy; [4]Hospital Umum Sarawak, Kuching, Sarawak, Malaysia; [5]Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; [6]Thoracic Oncology Unit, Service de Pneumologie, Hôpital Cochin, APHP, Université Paris Cité, France; [7]Department of Thoracic Oncology, Fujian Cancer Hospital, Fuzhou, China; [8]CHU de Toulouse, Pneumology Departement, Paul Sabatier University, Toulouse, France; [9]Department of Oncology, Pantai Hospital Kuala Lumpur, Kuala Lumpur, Malaysia; [10]Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka-Sayama, Osaka, Japan; [11]National Lung Hospital, Hanoi, Viet Nam; [12]Department of Medical Oncology, Tan Tock Seng Hospital, Singapore, [13]Thoracic Oncology Division, European Institute of Oncology (IEO), IRCCS, Milan, Italy, [14]Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [15]Division of Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand; [16]Global Clinical Development, the healthcare business of Merck KGaA, Darmstadt, Germany; [17]Global Development Operations, the healthcare business of Merck KGaA, Darmstadt, Germany; [18]Department of Biostatistics, the healthcare business of Merck KGaA, Darmstadt, Germany; [19]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China

RTP RESEARCH TO PRACTICE

INSIGHT 2 Trial: Objective Response with Tepotinib and Osimertinib in Patients with TBx FISH-Positive MET Amplification

- Of 98 patients with **TBx FISH⁺** *MET*amp (primary analysis set), BOR was PR in 43 patients, for an ORR of 43.9% (95% CI: 33.9, 54.3)
- As the data matures, six additional PRs have been confirmed

		TBx FISH⁺ (n=98)
BOR, n (%)	PR	43 (43.9)
	SD	15 (15.3)
	PD	23 (23.5)
	NE	17 (17.3)
ORR	% (95% CI)	**43.9** (33.9, 54.3)
DOR	Median, months (95% CI)	**9.7** (5.6, ne)
	Events, n (%)	11 (25.6)
PFS	Median, months (95% CI)	**5.4** (4.2, 7.1)
	Events, n (%)	51 (52.0)
OS	Median, months (95% CI)	**ne** (11.1, ne)
	Events, n (%)	23 (23.5)



*Four patients were excluded due to baseline/post-baseline measurement not being available.

BOR, best overall response; CI, confidence interval; DOR, duration of response; FISH, fluorescent in situ hybridization; MET, mesenchymal–epithelial transition factor; *MET*amp, *MET* amplification; ne, not evaluable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; TBx, tissue biopsy.

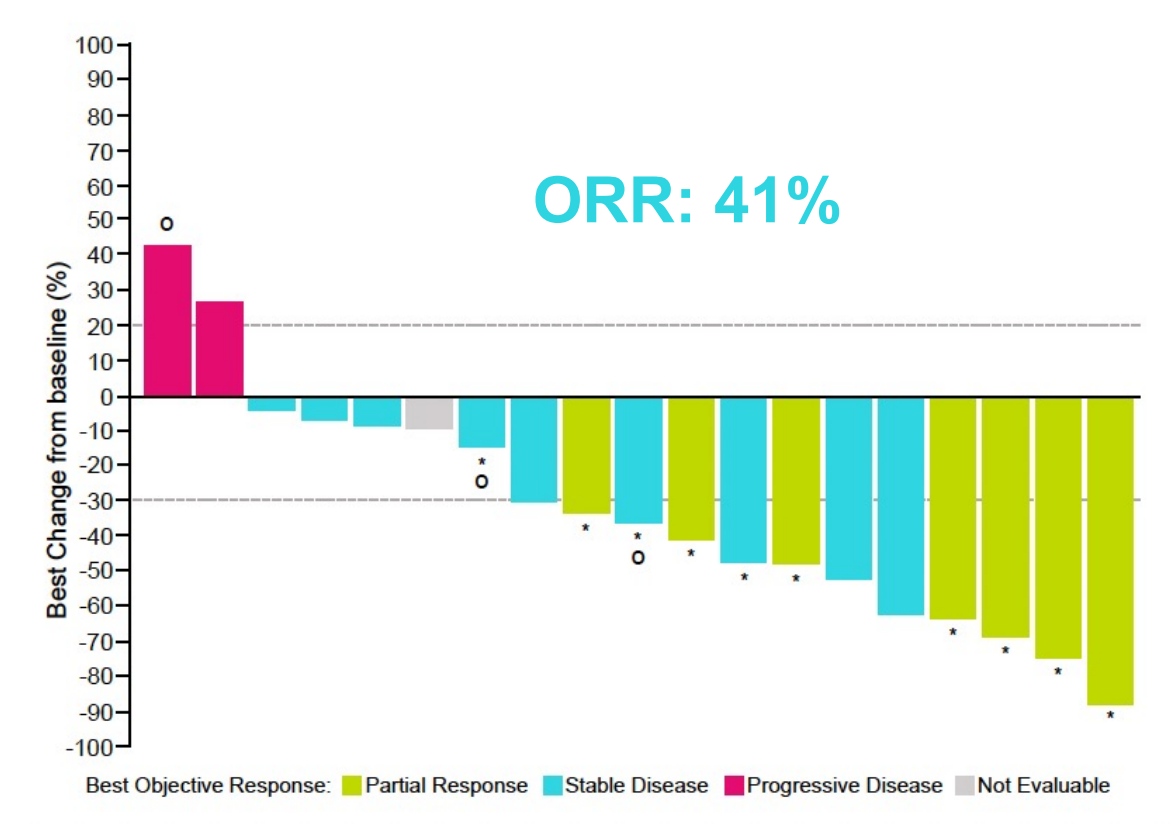
Tan DS-W et al. ASCO 2023;Abstract 9021.

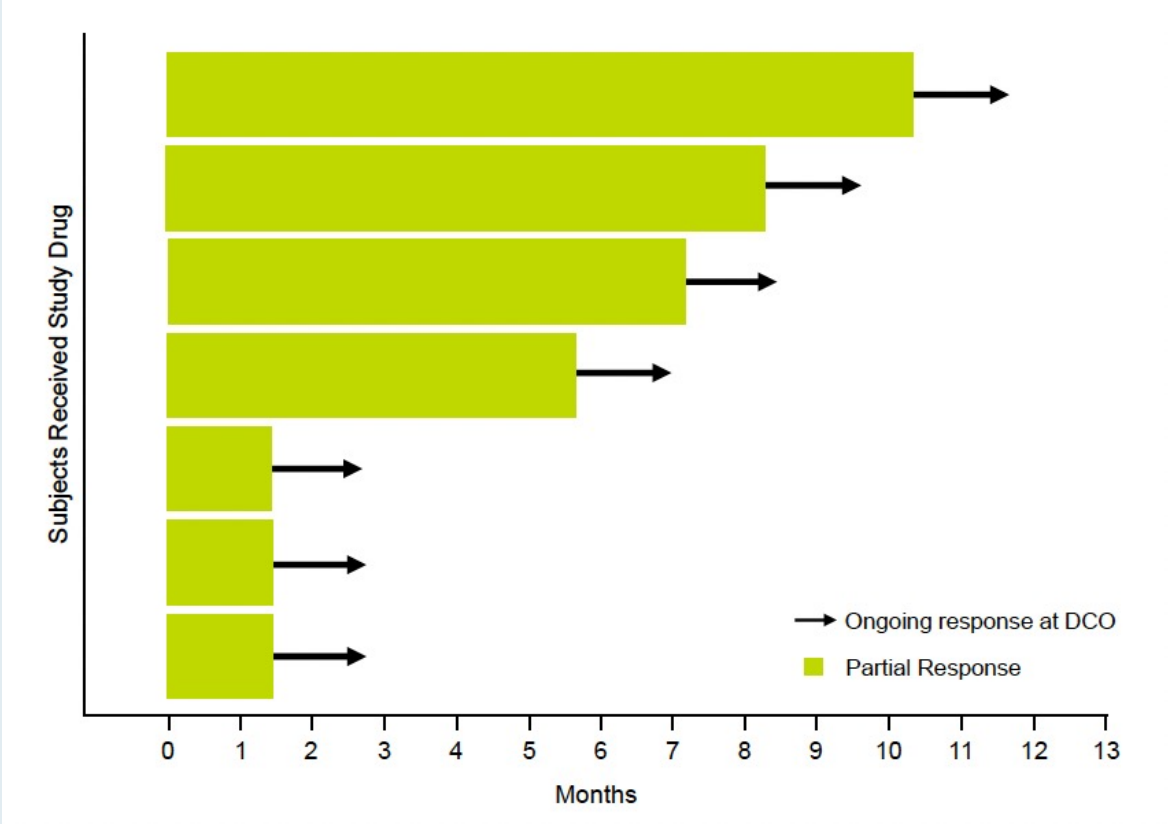
ORCHARD Osimertinib + Savolitinib Interim Analysis: A Biomarker-Directed Phase II Platform Study in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) Whose Disease Has Progressed on First-Line (1L) Osimertinib

Yu HA et al.

ESMO 2021;Abstract 1239P.

ORCHARD: Response and Duration of Response with Osimertinib and Savolitinib for Advanced NSCLC





ORR = objective response rate; DCO = data cutoff

Yu HA et al. ESMO 2021;Abstract 1239P.

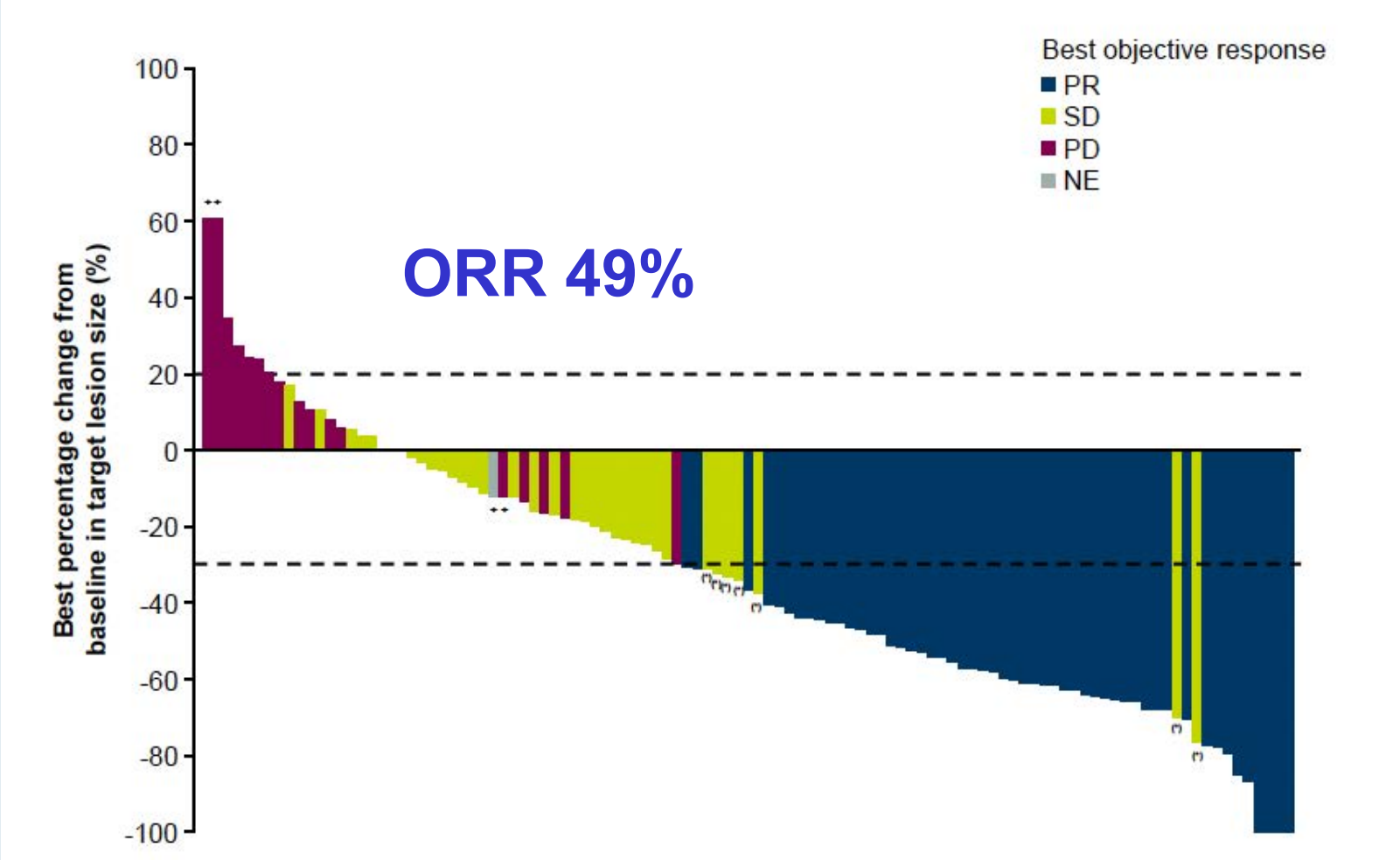
RTP RESEARCH TO PRACTICE

MET Biomarker-Based Preliminary Efficacy Analysis in SAVANNAH: Savolitinib + Osimertinib in EGFRm NSCLC Post-Osimertinib

Ahn M-J et al.

WCLC 2022;Abstract EP08.02-140.

SAVANNAH Trial: Response with Osimertinib and Savolitinib in Patients with Advanced NSCLC and MET Overexpresion



Ahn M-J et al. WCLC 2022;Abstract EP08.-12-140.

RTP RESEARCH TO PRACTICE

Proposed Mechanism of Action for HER3-DXd

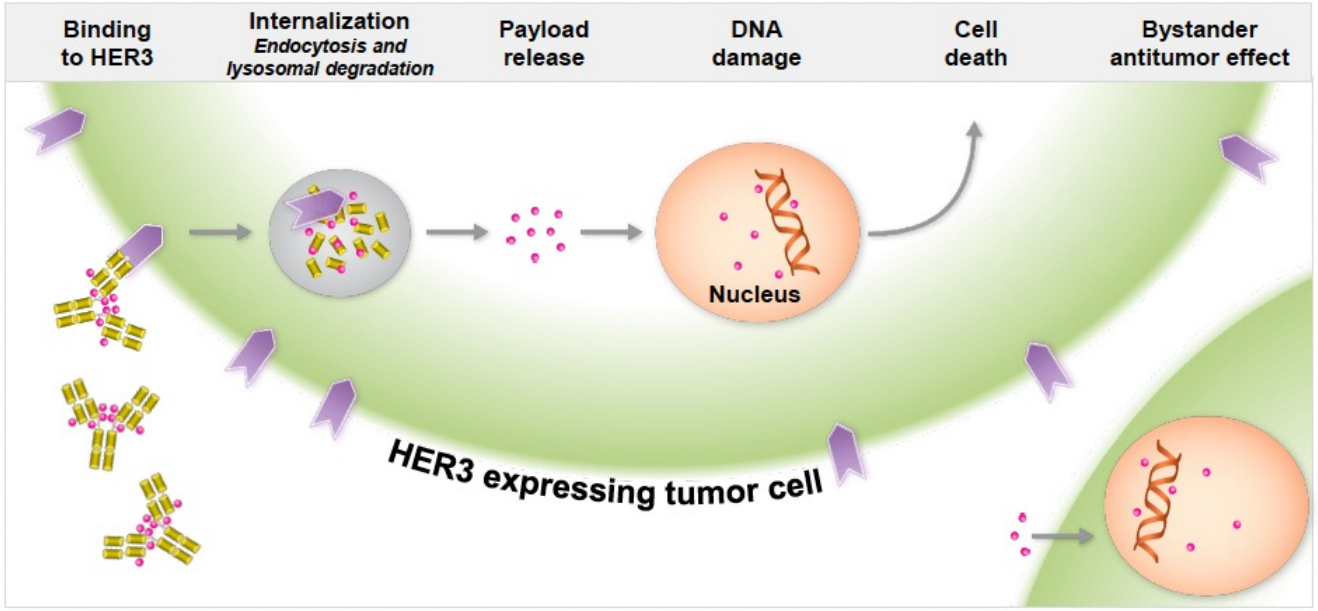
The mAb component of HER3-DXd selectively binds to HER3 on the tumor cell surface[4]

HER3-DXd is internalized by the tumor cell, and intracellular lysosomal enzymes (cathepsins) upregulated in tumor cells cleave the tetrapeptide-based linker.[4,6,10,11]

The topoisomerase I inhibitor payload is released into the cytoplasm of the cell[5,12]

The released payload enters the cell nucleus and damages the tumor cell's DNA. The DNA damage caused by the payload results in tumor cell death[4,6,11,13]

The payload is cell membrane permeable, which enables a bystander antitumor effect resulting in elimination of both HER3 expressing and surrounding tumor cells[5,9]



Steuer CE et al. ASCO 2022;Abstract 9017.

Targeting EGFR Exon 20 Insertion Mutations

RTP
RESEARCH
TO PRACTICE

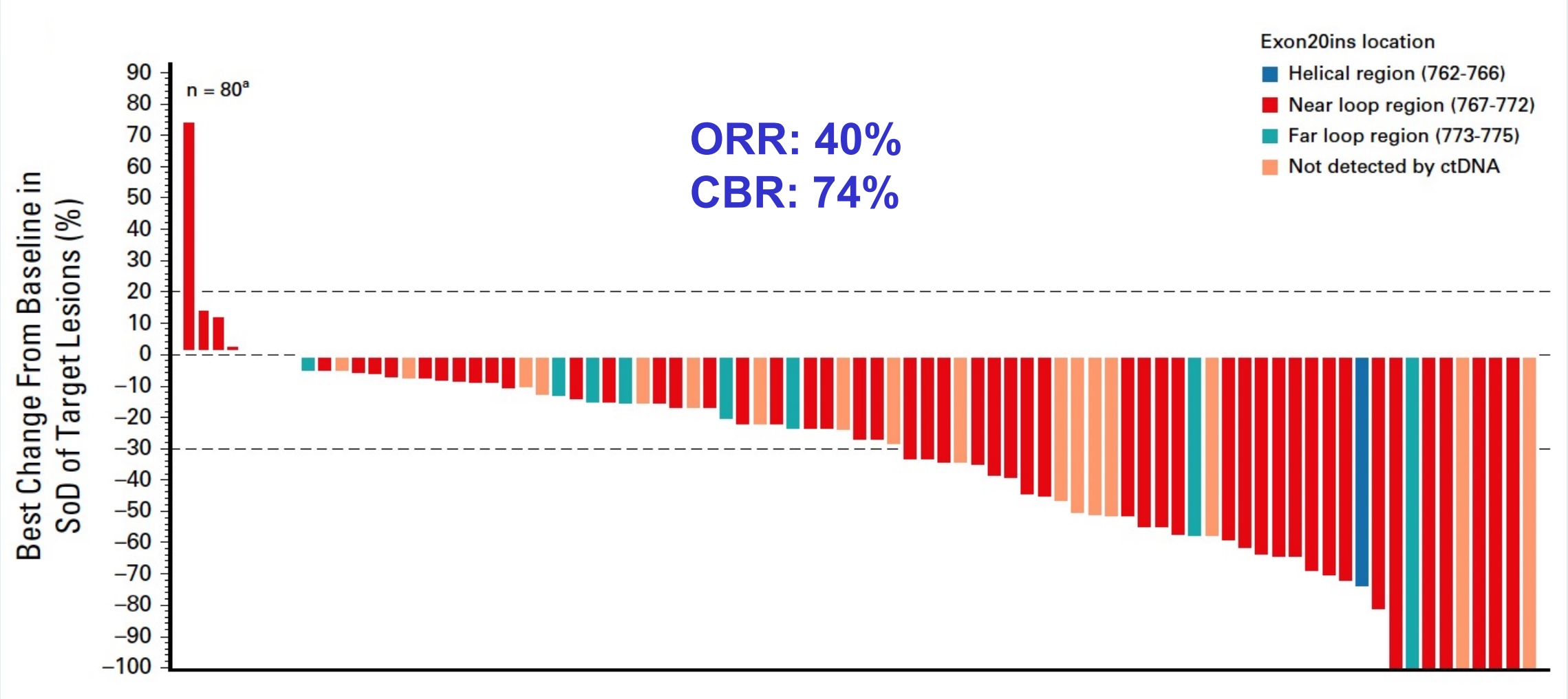
original reports

Amivantamab in EGFR Exon 20 Insertion–Mutated Non–Small-Cell Lung Cancer Progressing on Platinum Chemotherapy: Initial Results From the CHRYSALIS Phase I Study

Keunchil Park, MD, PhD[1]; Eric B. Haura, MD[2]; Natasha B. Leighl, MD[3]; Paul Mitchell, MD[4]; Catherine A. Shu, MD[5]; Nicolas Girard, MD, PhD[6]; Santiago Viteri, MD[7]; Ji-Youn Han, MD, PhD[8]; Sang-We Kim, MD, PhD[9]; Chee Khoon Lee, MD[10]; Joshua K. Sabari, MD[11]; Alexander I. Spira, MD, PhD[12]; Tsung-Ying Yang, MD, PhD[13]; Dong-Wan Kim, MD, PhD[14]; Ki Hyeong Lee, MD, PhD[15]; Rachel E. Sanborn, MD[16]; José Trigo, MD[17]; Koichi Goto, MD, PhD[18]; Jong-Seok Lee, MD, PhD[19]; James Chih-Hsin Yang, MD, PhD[20]; Ramaswamy Govindan, MD[21]; Joshua M. Bauml, MD[22]; Pilar Garrido, MD, PhD[23]; Matthew G. Krebs, MD, PhD[24]; Karen L. Reckamp, MD[25]; John Xie, PhD[26]; Joshua C. Curtin, PhD[26]; Nahor Haddish-Berhane, PhD[26]; Amy Roshak, BS[26]; Dawn Millington, MS[26]; Patricia Lorenzini, MS[26]; Meena Thayu, MD[26]; Roland E. Knoblauch, MD, PhD[26]; and Byoung Chul Cho, MD, PhD[27]

J Clin Oncol 2021;39:3391-402

CHRYSALIS: Tumor Reduction and Response



ORR = overall response rate; CBR = clinical benefit rate

Park K et al. *J Clin Oncol* 2021;39:3391-402.

RTP RESEARCH TO PRACTICE

CHRYSALIS: Summary of Adverse Events (AEs) and Most Common AEs

Event	Safety Population (n = 114), No. (%)	Patients Treated at the RP2D (n = 258), No. (%)
Any AE	113 (99)	257 (100)
Grade ≥ 3 AE	40 (35)	101 (39)
Serious AE	34 (30)	79 (31)
AE leading to death	8 (7)	13 (5)
AE leading to discontinuation	11 (10)	17 (7)
AE leading to dose reduction	15 (13)	26 (10)
AE leading to dose interruption[a]	40 (35)	88 (34)

Most Common AEs in the Safety Population

Adverse Events	Any Grade	Grade ≥3
Rash	86%	4%
Infusion-related reactions	66%	3%
Paronychia	45%	1%

Park K et al. *J Clin Oncol* 2021;39:3391-402.

RTP RESEARCH TO PRACTICE

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Non-Small Cell Lung Cancer with an EGFR Mutation

Friday, April 26, 2024
12:15 PM – 1:45 PM

Faculty

Marianne J Davies, DNP, ACNP, AOCNP, FAAN
Alexander I Spira, MD, PhD
Jillian Thompson, MSN, ANP-BC, AOCNP
Helena Yu, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Ovarian Cancer

Friday, April 26, 2024
6:00 PM – 7:30 PM

Faculty

Courtney Arn, CNP
Floor J Backes, MD
Kathleen N Moore, MD, MS
Jaclyn Shaver, MS, APRN, CNP, WHNP

Moderator

Neil Love, 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 up to 5 minutes after the meeting ends.

To Claim NCPD Credit

In-person attendees: Please refer to the program syllabus for the NCPD credit link or QR code.

Virtual attendees: The NCPD credit link is posted in the chat room.

NCPD/ONCC credit information will be emailed to each participant within 1 to 2 business days.

RTP
RESEARCH
TO PRACTICE