The Clinical Implications of Key Recent Data Sets in Oncology: A Daylong Multitumor Educational Symposium in Partnership with Florida Cancer Specialists

A CME/MOC- and NCPD-Accredited Event

Saturday, October 22, 2022
7:30 AM – 5:30 PM ET

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FLORIDA CANCER SPECIALISTS & Research Institute

Welcome FCS Members!

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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 premeeting survey before 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.

Complete Your Evaluation: Tap the CME Evaluation button to complete your evaluation electronically to receive credit for your participation.

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

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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 premeeting survey before the meeting.

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

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

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Clinicians in Attendance…

- Please complete the premeeting survey at the beginning of each module.
- A link to the postmeeting survey will be emailed to each participant within 24 hours.

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What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Breast Cancer

A 2-Part CME Satellite Symposium Series Held in Conjunction with the 2022 San Antonio Breast Cancer Symposium®

HER2-Positive Breast Cancer

Wednesday, December 7, 2022

7:15 PM – 9:15 PM CT

ER-Positive Breast Cancer

Thursday, December 8, 2022

7:15 PM – 9:15 PM CT

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Questions and Controversies in the Management of Hematologic Cancers — What Clinicians Want to Know

A 3-Part CME Friday Satellite Symposium and Virtual Event Series

Preceding the 64th ASH Annual Meeting

Chronic Lymphocytic Leukemia

Friday, December 9, 2022

11:30 AM – 1:30 PM CT

Hodgkin and Non-Hodgkin Lymphoma

Friday, December 9, 2022

3:15 PM – 5:15 PM CT

Multiple Myeloma

Friday, December 9, 2022

7:00 PM – 9:00 PM CT

Moderator: Neil Love, MD

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Agenda

Module 1 — Lung Cancer: *Drs Langer and Lovly*

Module 2 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs LaCasce and Smith*

Module 3 — Prostate and Bladder Cancers: *Drs Morgans and Yu*

Module 4 — Renal Cell Carcinoma: *Prof Powles*

Module 5 — Multiple Myeloma: *Dr Usmani*

Module 6 — Hepatobiliary Cancers: *Dr Abou-Alfa*

Agenda

Module 7 — Breast Cancer: *Drs Goetz and Krop*

Module 8 — Endometrial Cancer: *Dr Westin*

Module 9 — Ovarian Cancer and PARP Inhibitors: *Dr O'Malley*

Module 10 — Gastrointestinal Cancers: *Drs Messersmith and Strickler*

Module 11 — Melanoma: *Prof Long*

Lung Cancer Faculty

Corey J Langer, MD
Director of Thoracic Oncology
Abramson Cancer Center
Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

Christine M Lovly, MD, PhD
Associate Professor of Medicine
Division of Hematology and Oncology
Ingram Associate Professor of Cancer Research
Co-Leader, Translational Research and Interventional Oncology Program
Vanderbilt University Medical Center and
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee

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Lung Cancer Agenda

MODULE 1: First line treatment of metastatic NSCLC in patients without targetable mutations

MODULE 2: Neoadjuvant and Adjuvant Treatment of Localized NSCLC

MODULE 3: Targeted Treatment of Metastatic NSCLC

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Lung Cancer Agenda

MODULE 1: First line treatment of metastatic NSCLC in patients without targetable mutations

MODULE 2: Neoadjuvant and Adjuvant Treatment of Localized NSCLC

MODULE 3: Targeted Treatment of Metastatic NSCLC

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Case Presentation: Dr John Heymach

- 55-year-old Asian woman with 10 pack year history of smoking (quit 20y ago), presented with malignant pleural effusion and persistent pulmonary infections.
- Evaluation revealed lung adenocarcinoma, with multiple bone metastases and two small brain metastases
- Profiling revealed KRAS G12D as well as STK11 and KEAP1 mutations

Case Presentation: Dr John Heymach (cont)

- She was initially treated at an outside institution with chemo+pembrolizumab and had disease progression at cycle 3.
- She was enrolled in the Hudson study and received the ATR inhibitor ceralasertib plus durvalumab.
- Minor response lasting more than 6 months.
- Eventually developed PD and was treated with subsequent lines of chemo+bev+atezo (Impower150) and docetaxel
- Died approximately 14 months after diagnosis.

Discussion Questions

First-Line Treatment for Metastatic NSCLC in Patients without Targetable Mutations

Common queries…

- Is anti-PD-1/PD-L1 monotherapy a reasonable consideration for patients with a PD-L1 TPS between 1% and 49%, particularly those who are less fit or have nonvisceral disease?
- Regulatory and reimbursement issues aside, in which situations, if any, do you believe anti-PD-1/anti-CTLA-4 combinations are currently a consideration, and which doublets?
- What is your usual approach to patients with PD-L1-negative tumors?
- Do you believe there is any difference in clinical outcomes with the approved anti-PD-1/PD-L1 antibodies?

Discussion Questions

First-Line Treatment for Metastatic NSCLC in Patients without Targetable Mutations (cont)

- Do you believe patients who have autoimmune complications with immunotherapy are more likely to benefit?
- Do you believe there are currently any clinically meaningful predictors of immunotherapy benefit beyond PD-L1 and TMB?
- In patients with high PD-L1 levels, when do you add chemotherapy to anti-PD-1/PD-L1 antibodies, and how much do you consider the magnitude of the assay result?
- Do you believe the results of the PACIFIC trial warrant consideration of this approach in some patients with classic indications for surgery?
- Can you describe an ideal patient for neoadjuvant chemoimmunotherapy?

Lung Cancer Agenda

MODULE 1: First line treatment of metastatic NSCLC in patients without targetable mutations

MODULE 2: Neoadjuvant and Adjuvant Treatment of Localized NSCLC

MODULE 3: Targeted Treatment of Metastatic NSCLC

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Systemic Management of Resectable and LA- NSCLC:
2022 Update

Corey J. Langer MD, FACP
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Professor of Medicine
Perelman School of Medicine
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The unmet need in resectable NSCLC persists

Most patients who receive adjuvant chemotherapy will experience disease recurrence within 5 years

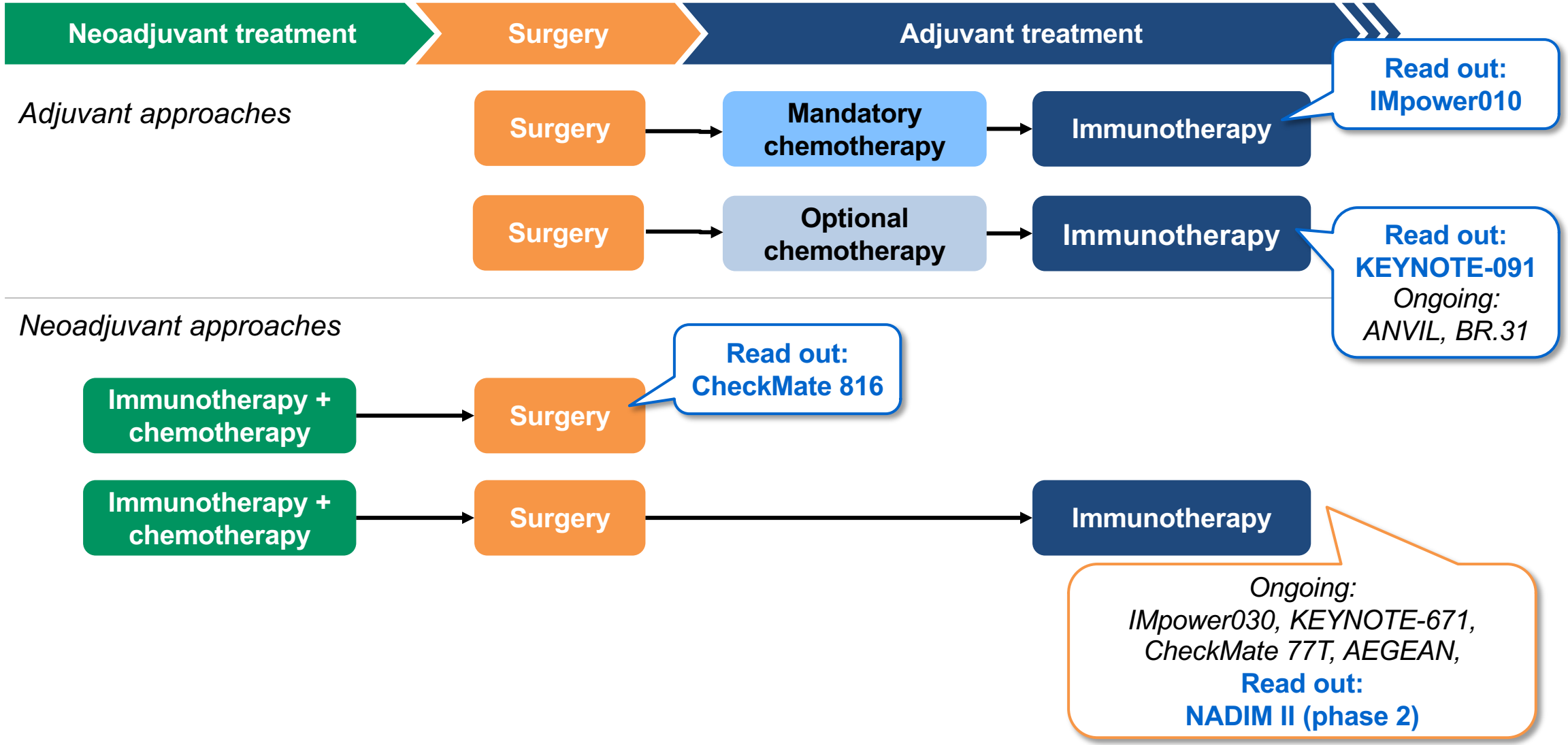
Early stage[1,2]	Regional / locally advanced disease[1,2]	
Stage IB	Stage II	Stage III
		
~45% chance of recurrence or death[a]	~62% chance of recurrence or death[a]	~76% chance of recurrence or death[a]

[a]Median follow-up: 5.2 years, data based on AJCC Staging Manual 6th edition

AJCC, American Joint Committee on Cancer; NSCLC, non-small cell lung cancer

1. Pignon JP, et al. J Clin Oncol 2008;26:3552–59; 2. Edge SB, et al. AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer; 2010

Phase III studies with immunotherapy in resectable NSCLC are taking different approaches



Adjuvant IO Phase III randomized trials
DFS and PD-L1 TPS data - consistent data?

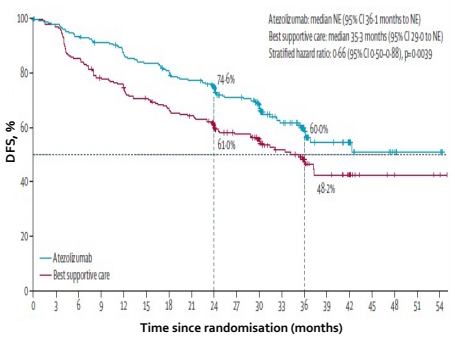
Effect of PD-L1 expression

IMpower010 Stage II/IIIA[1]

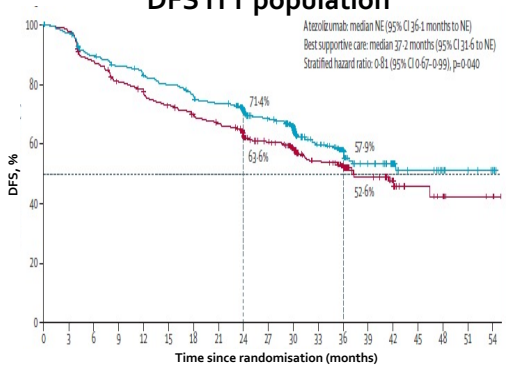
A DFS benefit with atezolizumab vs. BSC was observed in the PD-L1 ≥1% population but not in the ITT population

	HR (95% CI)
PD-L1 TPS ≥1%	0.66 (0.50, 0.88); p=0.0039
ITT population	0.81 (0.67, 0.99); p=0.040

DFS PD-L1 TC ≥1% population



DFS ITT population

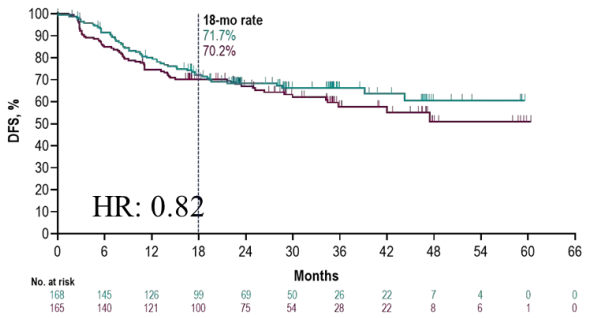


PEARLS/ KEYNOTE 091 Stage IB–IIIA[2]

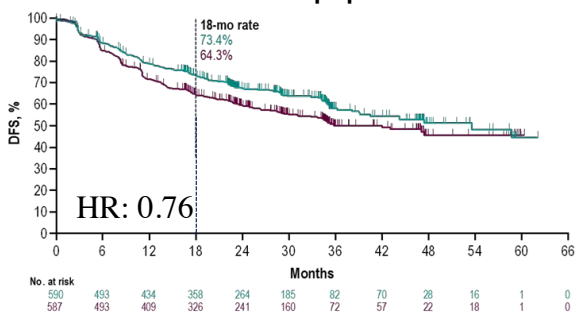
DFS was significantly improved with pembrolizumab in the all-comers population but not in the PD-L1 TPS ≥50% population

	HR (95% CI)
All comers	0.76 (0.63, 0.91); p=0.0014
PD-L1 TPS ≥50%	0.82 (0.57, 1.18); p=0.14

DFS PD-L1 TPS ≥50% population



DFS ITT population

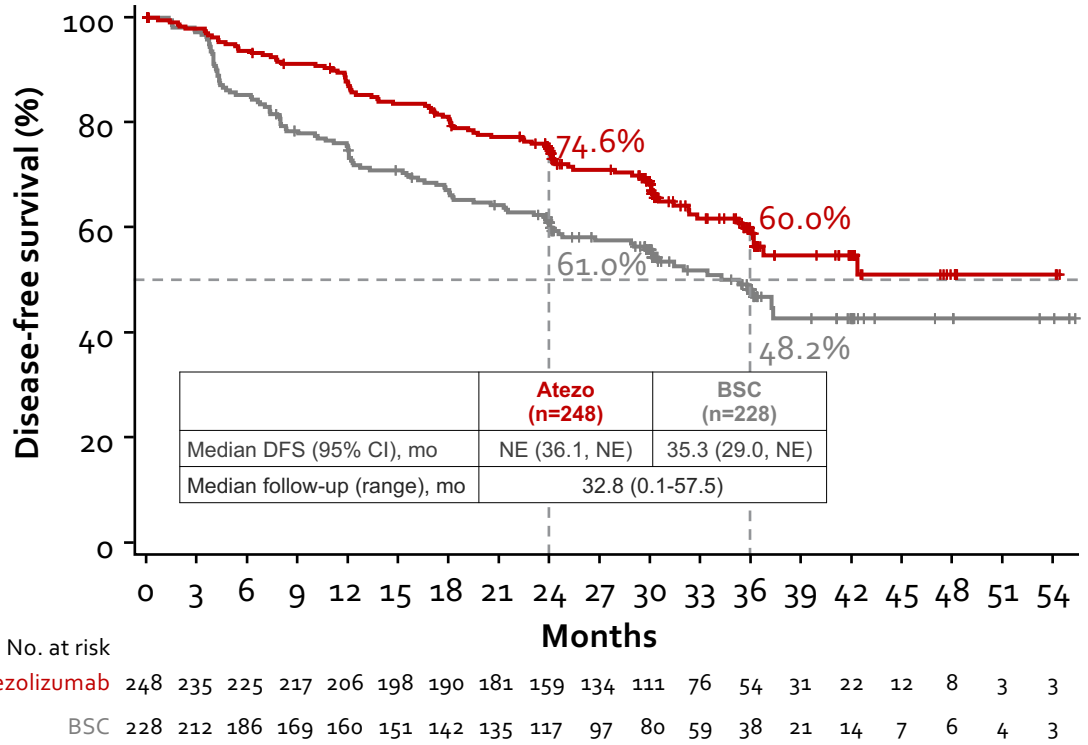


Approvals

PD-L1 ≥1%	PD-L1 ≥50%
	 and other countries

IMpower010: the primary endpoint of improved DFS in patients with PD-L1 TC ≥1%, stage II–IIIA* NSCLC was met

DFS in PD-L1 TC ≥1%, stage II–IIIA, completely resected NSCLC



Primary analysis populations

Population analysed for DFS	n	HR (95% CI)§
PD-L1 TC ≥1%, stage II–IIIA	476	0.66 (0.50, 0.88)
All-randomised, stage II–IIIA	882	0.79 (0.64, 0.96)
ITT (all randomised, stage IB–IIIA)	1005	0.81 (0.67, 0.99)

Endpoint was met at DFS IA

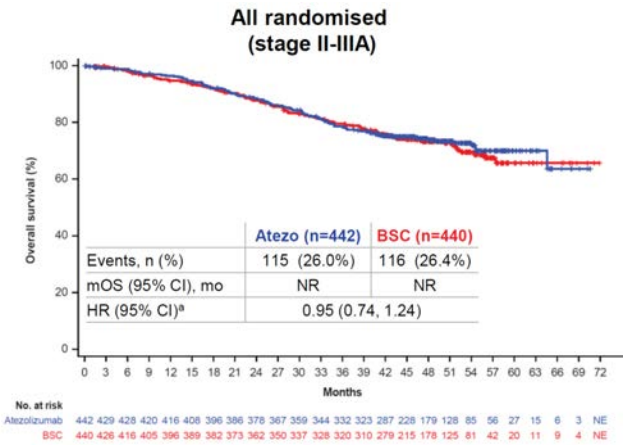
Endpoint was not met at DFS IA, and follow-up is ongoing

***Per TNM 7th edition (select stage II–IIIB per TNM 8th edition)**

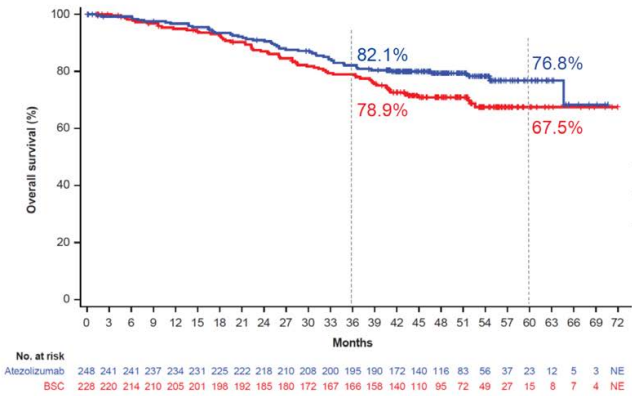
Wakelee, et al. ASCO 2021 (Abs 8500); Felip, et al. Lancet 2021

IMpower010: OS trend of atezolizumab in PD-L1 ≥1% Stage II–IIIA (interim OS analysis)

No OS benefit in the all-randomised Stage II–IIIA



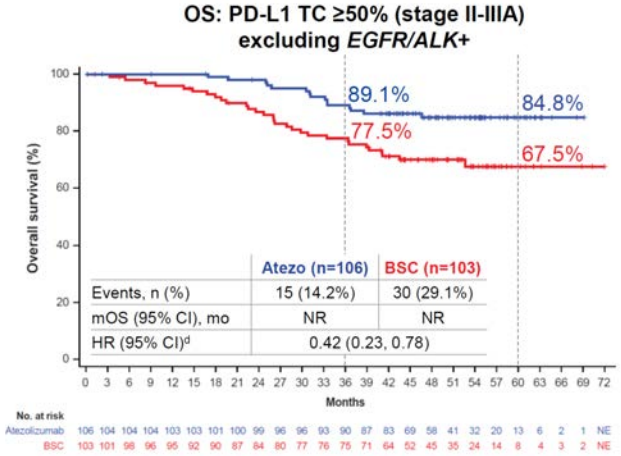
OS interim analysis in PD-L1 TC ≥1% (Stage II–IIIA)



mOS, median overall survival; NR, not reached. [a]By SP263 assay. [b]Stratified.

	Atezo (n=248)	BSC (n=228)
Events, n (%)	52 (21.0%)	64 (28.1%)
mOS (95% CI), mo	NR	NR
HR (95% CI)[-]	0.71 (0.49, 1.03)	

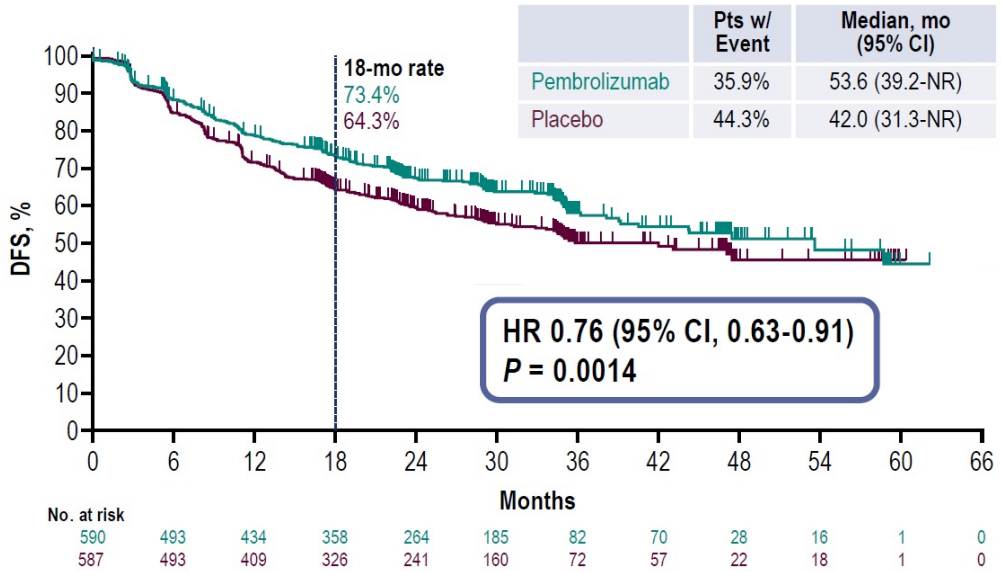
Clinically meaningful OS trend in PD-L1 ≥50%



Wakelee H, et al. Presented at WCLC 2022 (Abstract PL03.09)

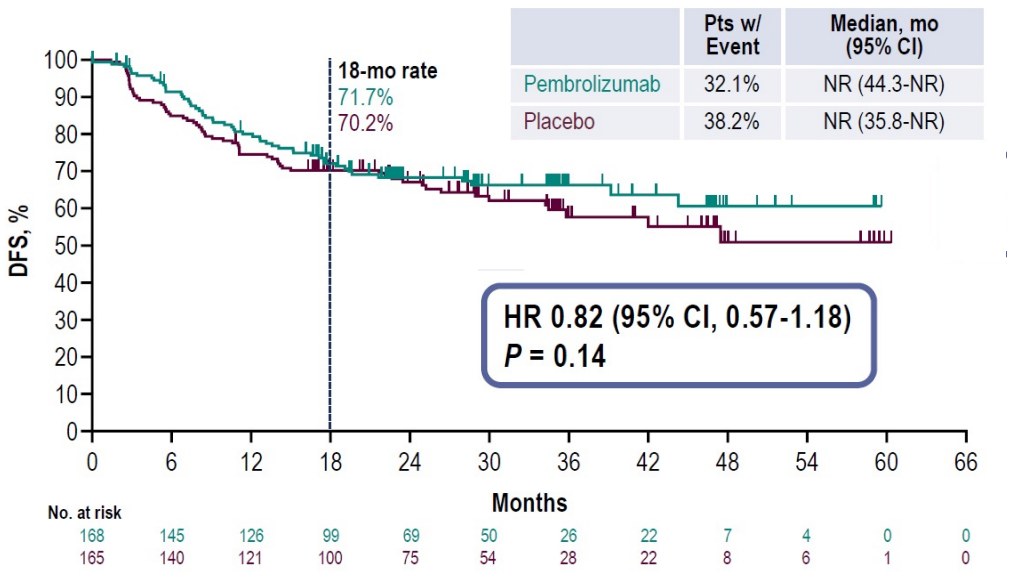
KEYNOTE-091: one dual primary endpoint of a DFS benefit in the overall population was met

DFS in the overall population (PD-L1 unselected, stage IB–III, completely resected NSCLC



	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	35.9%	53.6 (39.2-NR)
Placebo	44.3%	42.0 (31.3-NR)

DFS in PD-L1 TPS ≥50%, stage IB–III, completely resected NSCLC*



	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	32.1%	NR (44.3-NR)
Placebo	38.2%	NR (35.8-NR)

OS data are not yet mature

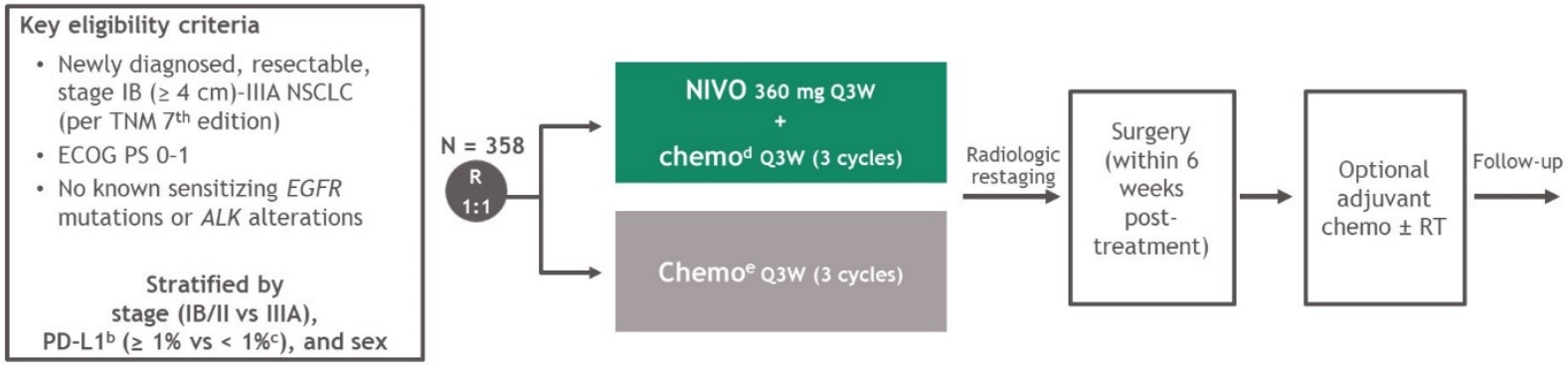
Data cut-off: 20 September, 2021; response assessed per RECIST v1.1 by investigator review

*At the interim analysis, this dual primary endpoint did not meet statistical significance

Paz-Ares, et al. ESMO Plenary 2022 (Abs VP3-2022)

Neoadjuvant nivolumab: CheckMate 816 and NADIM II

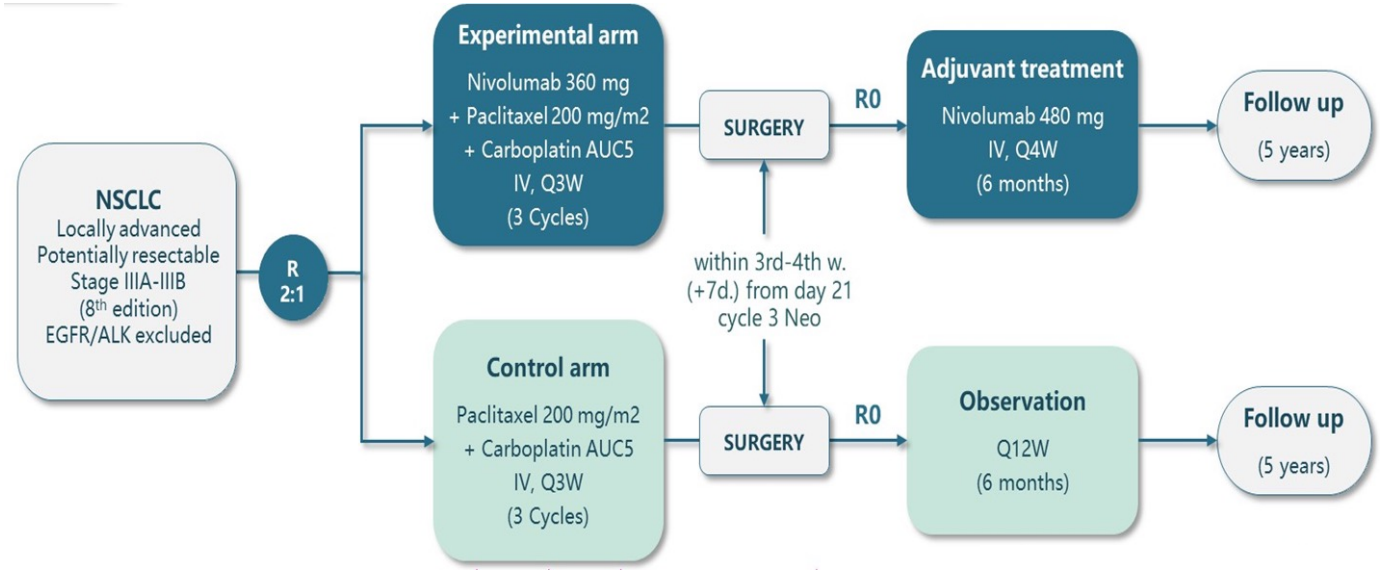
CheckMate 816



Primary endpoints:

- pCR by BICR
- EFS by BICR

NADIM II

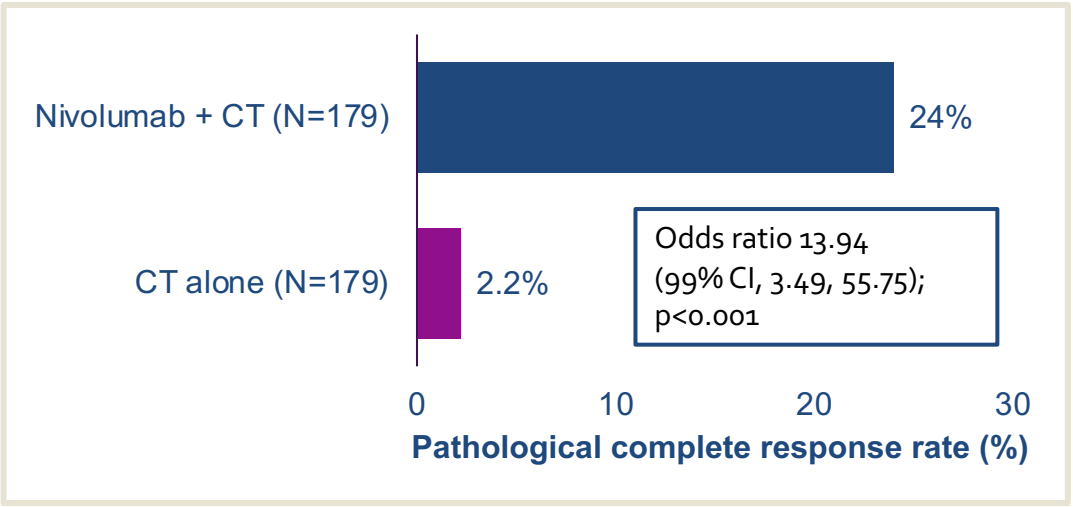


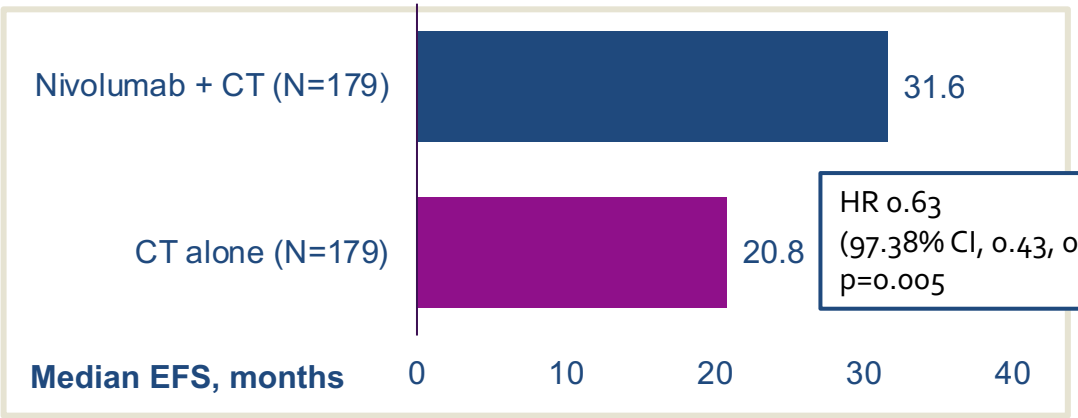
Primary endpoint:

- pCR

Neoadjuvant nivolumab: Odds ratio and EFS

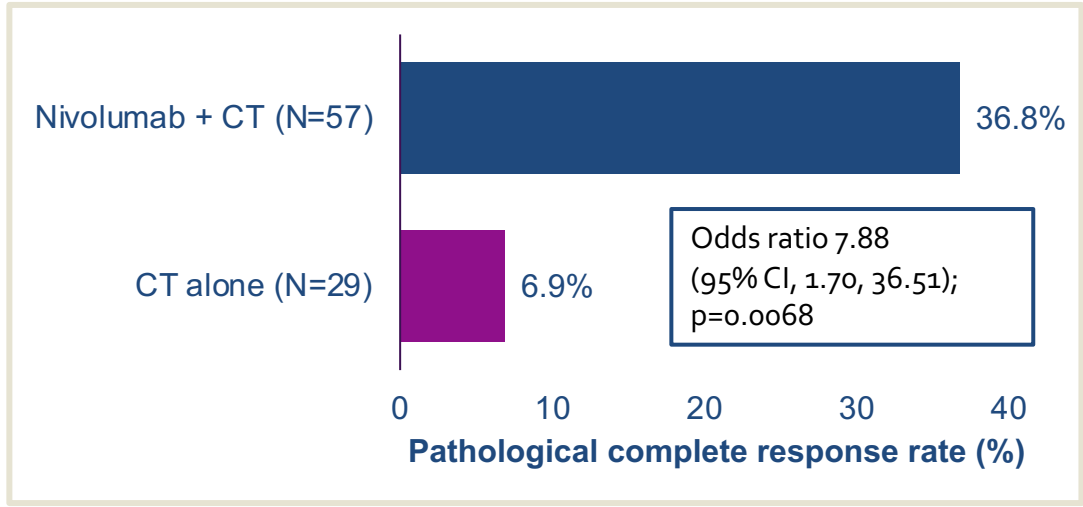
CheckMate 816[1]

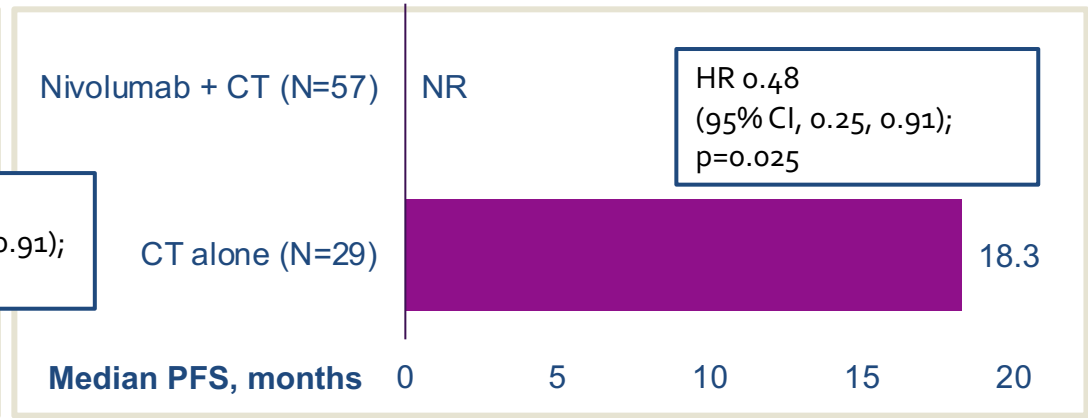




mOS: NR (HR 0.57)

NADIM II[2]



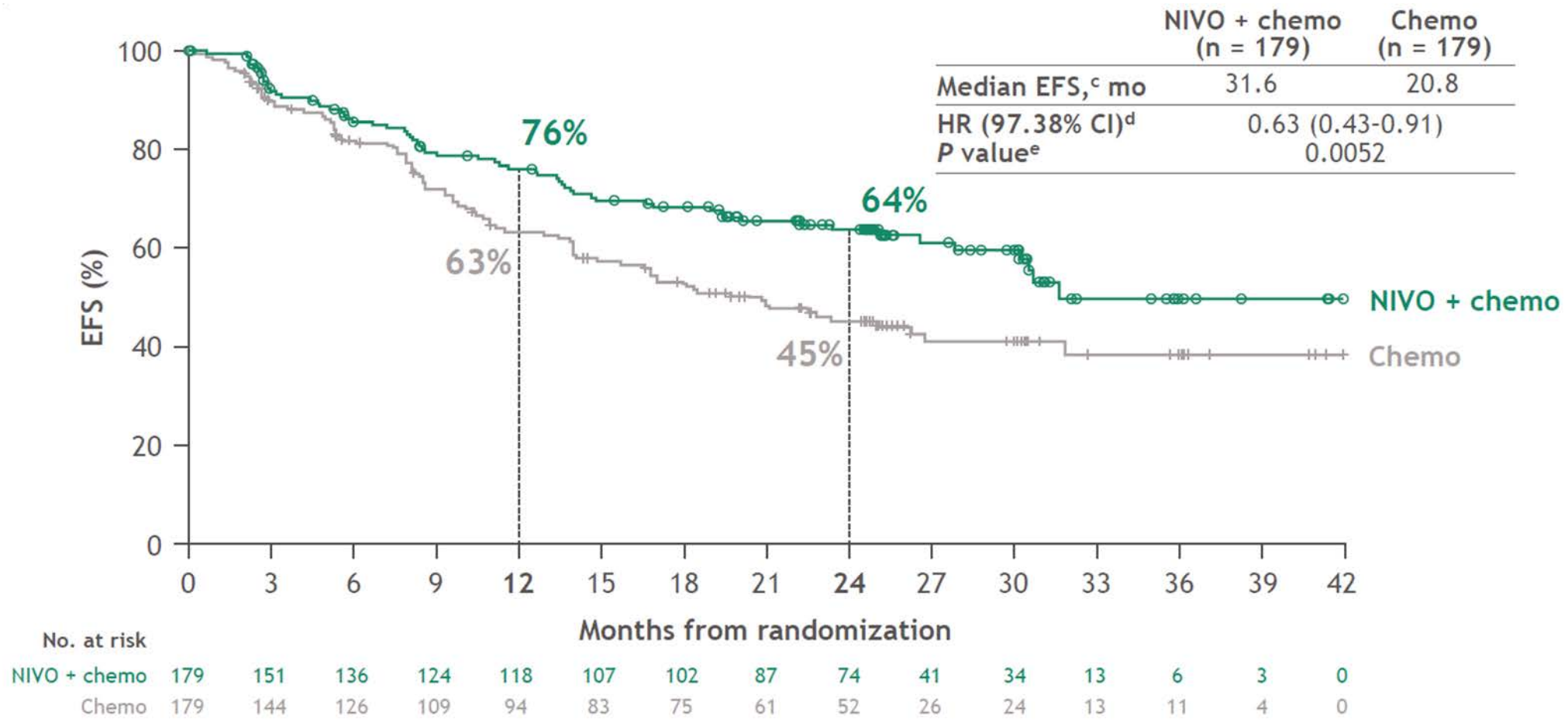


mOS: NR (HR 0.40)

CI, confidence interval; CT, chemotherapy; EFS, event-free survival; HR, hazard ratio; NR, not reached

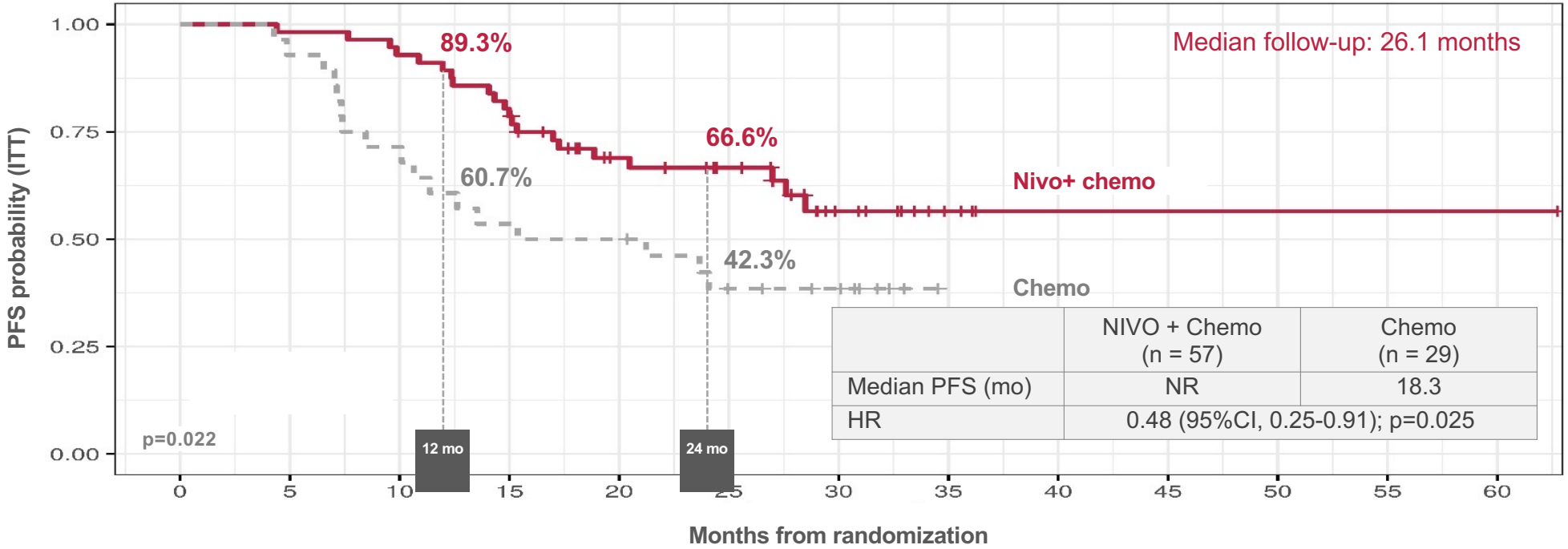
1. Forde PM, et al. N Engl J Med 2018;378:1976–86; 2. Provencio M, et al. Presented at ASCO 2022 (Abstract 8501)

CheckMate 816: neoadjuvant nivolumab + chemotherapy improved EFS compared with chemotherapy alone



Girard, et al. AACR 2022 (Abs CT012)
Forde, et al. N Engl J Med 2022

NADIM II: SECONDARY ENDPOINTS – Progression-free survival

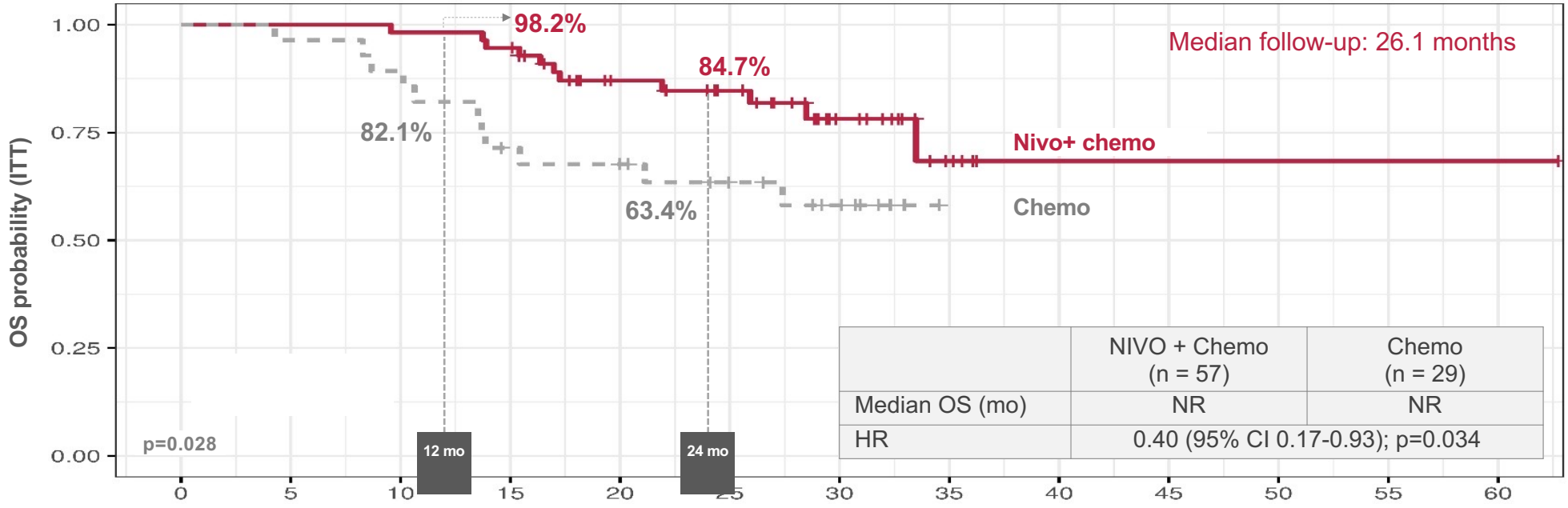


	NIVO + Chemo (n = 57)	Chemo (n = 29)
Median PFS (mo)	NR	18.3
HR	0.48 (95%CI, 0.25-0.91); p=0.025	

Number at risk													
Nivo + chemo	56	55	52	44	30	24	11	4	1	1	1	1	1
Chemo	28	26	20	15	14	9	7	0	0	0	0	0	0

Progression-free survival was defined as the time from randomization to any of the following events: progression of disease, recurrence disease, or death due to any cause. Progression/recurrence will have determined by RECIST 1.1

NADIM II: SECONDARY ENDPOINTS – Overall survival



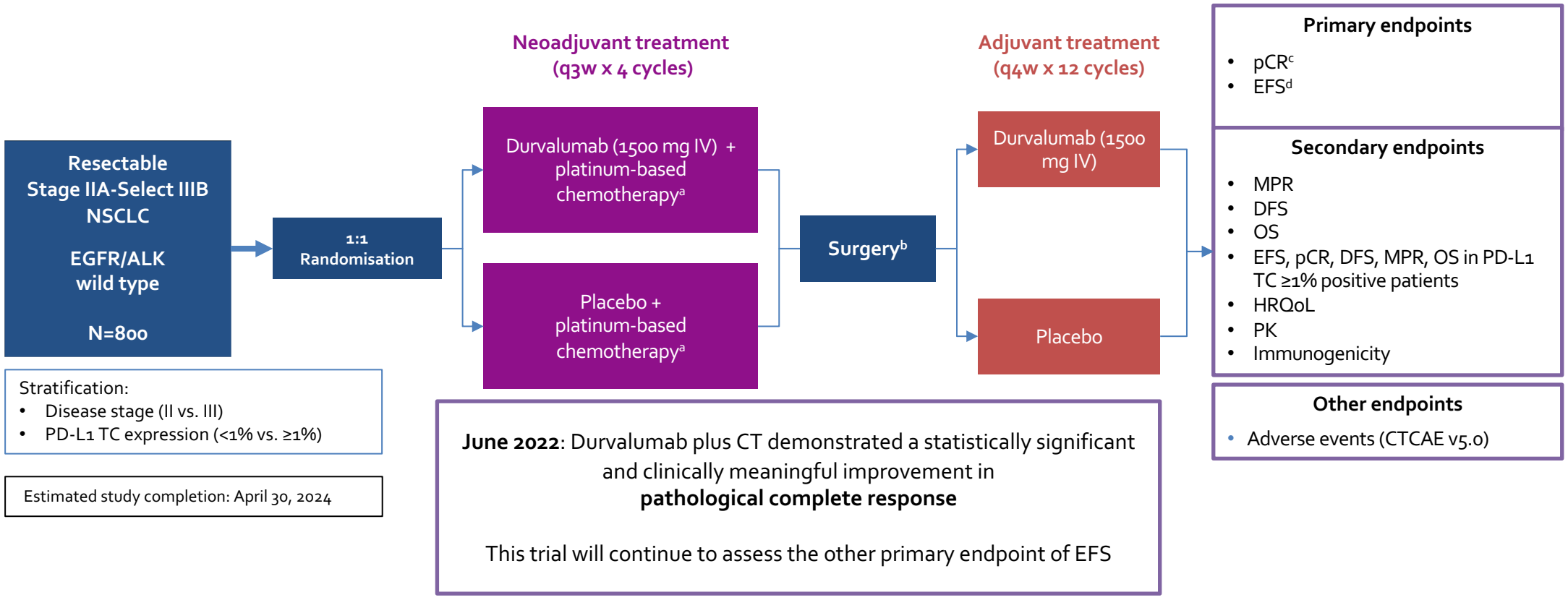
	NIVO + Chemo (n = 57)	Chemo (n = 29)
Median OS (mo)	NR	NR
HR	0.40 (95% CI 0.17-0.93); p=0.034	

Number at risk													
Nivo + chemo	56	56	55	53	37	31	15	5	1	1	1	1	1
Chemo	28	27	25	19	17	13	9	0	0	0	0	0	0

Overall survival was defined as the time from randomization to death. OS was censored on the last date a participant was known to be alive

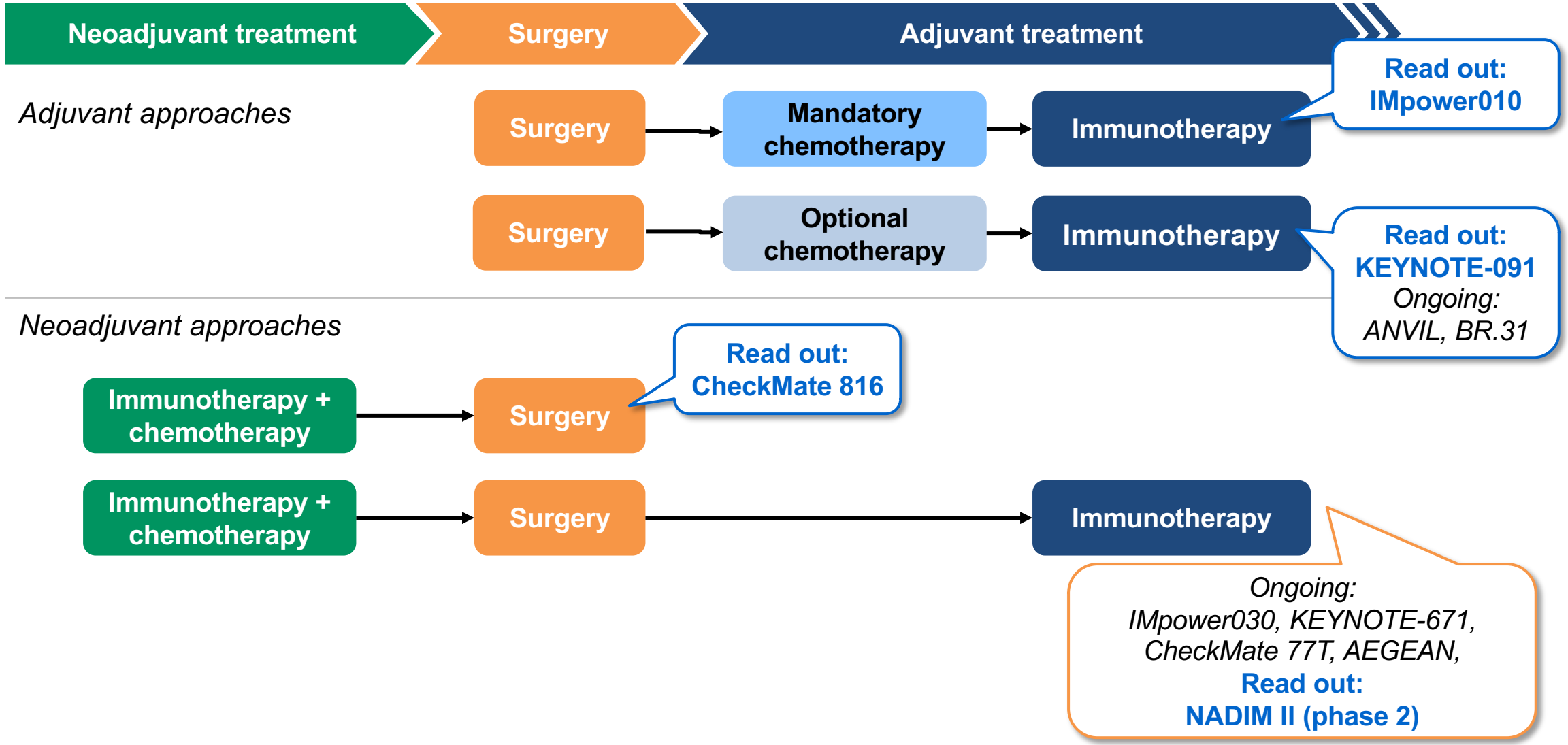
AEGEAN: further positive results with a perioperative regimen

Phase III, placebo-controlled, double-blind, randomised, multicenter study[1,2]



1. Study NCT03800134. ClinicalTrials.gov; 2. Heymach JV, et al. Clin Lung Cancer 2022;23(3):247–51

Several phase III studies with immunotherapy in resectable NSCLC will read soon…



Arguments for Neoadjuvant Immune Checkpoint Inhibition Followed by Surgical Resection

Higher antigen load and release from dying cells in untreated tumors

- ✓ Better priming of immune system

Fit host immune system, intact nodal stations

No significant clonal evolution

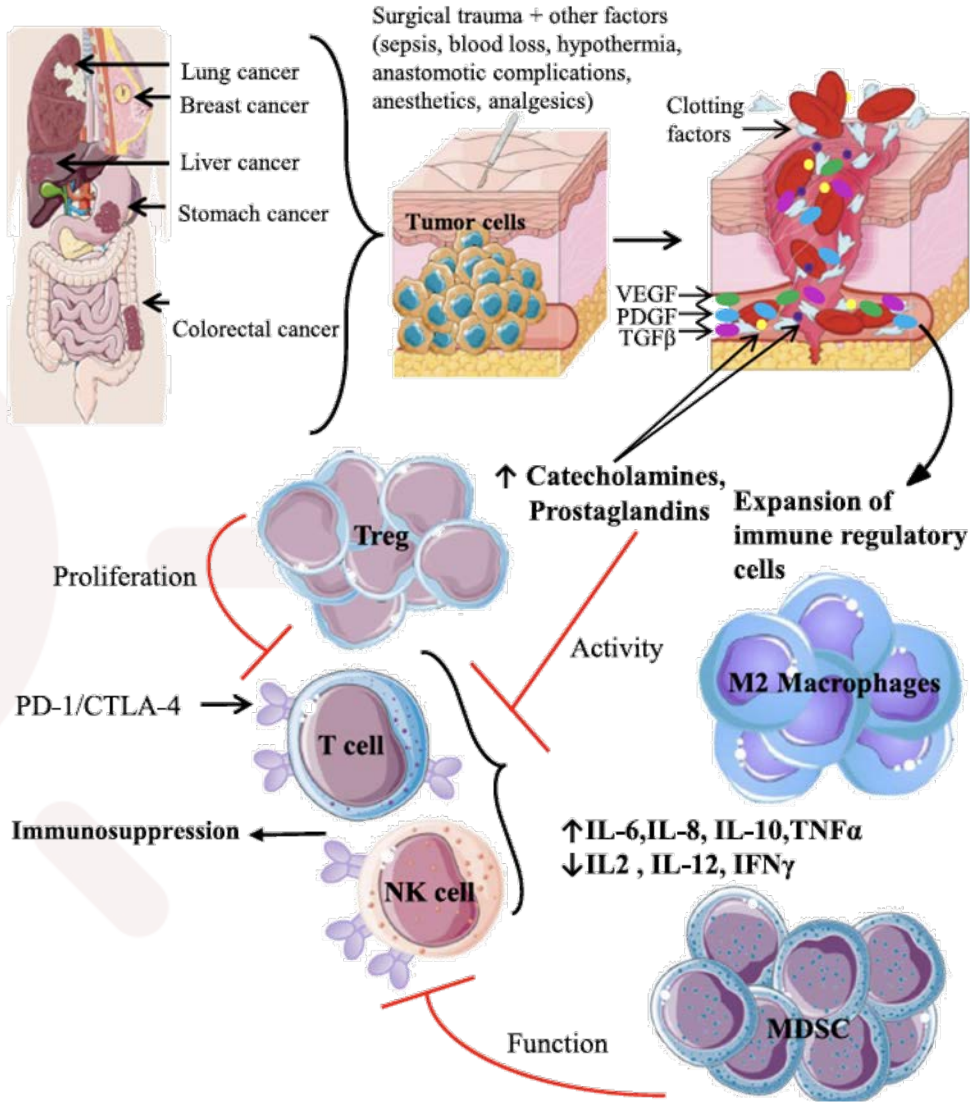
- ✓ Tumor less heterogeneous

Opportunity to accurately study the effects of IO

- ✓ Access to pre and post tissue

Ability to access efficacy of the therapy

Shorten timeframe to completion of trials (early surrogate for survival?)



Immunotherapy in NSCLC

ESMO VIRTUAL PLENARY

EORTC European Organisation for Research and Treatment of Cancer
The future of cancer therapy

etop
Information | Research

Pembrolizumab Versus Placebo For Early-Stage NSCLC Following Complete Resection and Adjuvant Chemotherapy When Indicated: Randomized, Triple-Blind, Phase 3 EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 Study

L. Paz-Ares,[1*] M. O'Brien,[2*] M. Mauer,[3] U. Dafni,[4] K. Oselin,[5] L. Havel,[6] E. Esteban,[7] D. Isla,[8] A. Martinez-Marti,[9] M. Faehling,[10] M. Tsuboi,[11] J.S. Lee,[12] K. Nakagawa,[13] J. Yang,[14] S.M. Keller,[14] N. Jha,[3] S. Marreaud,[3] R. Stahel,[15] S. Peters,[16**] B. Besse[17**] on behalf of the PEARLS/KEYNOTE-091 Investigators

[1]Hospital Universitario 12 de Octubre, CNIO, Ciberonc & Universidad Complutense, Madrid, Spain; [2]Royal Marsden Hospital, London, UK; [3]European Organisation for Research and Treatment of Cancer, Headquarters Brussels, Belgium; [4]National and Kapodistrian University of Athens and Frontier Science Foundation Hellas; [5]North Estonia Medical Centre, Tallinn, Estonia; [6]Charles University and Thomayer Hospital, Prague, Czech Republic; [7]Hospital Universitario Central de Asturias, Oviedo, Spain; [8]University Hospital Lozano Blesa, IIS Aragon, Zaragoza, Spain; [9]Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; [10]Klinikum Esslingen, Esslingen, Germany; [11]National Cancer Center Hospital East, Kashiwa, Japan; [12]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea; [13]Kindai University Faculty of Medicine, Osaka, Japan; [14]Merck & Co., Inc., Kenilworth, NJ, USA; [15]European Thoracic Oncology Platform, Bern, Switzerland; [16]Lausanne University Hospital, Lausanne, Switzerland; [17]Institut Gustave Roussy, Villejuif, France
*Drs. Paz-Ares and O'Brien contributed equally to this presentation. **Drs. Peters and Besse contributed equally to this presentation.

ESMO

Abstract VP3-2022

RTP RESEARCH TO PRACTICE

PEARLS/KEYNOTE-091: Author Summary and Conclusions

- Pembrolizumab provided statistically significant, clinically meaningful DFS improvement versus placebo in the overall population
  - Median DFS of 53.6 months with pembrolizumab vs 42.0 months with placebo (HR, 0.76)
  - Generally consistent DFS benefit in participants with PD-L1 TPS <1%, 1-49%, and ≥50%
  - OS data are immature
  - DFS in the PD-L1-defined populations and OS will be tested at future analyses according to the analysis plan
- Pembrolizumab safety profile as expected
- **Data suggest pembrolizumab has the potential to be a new adjuvant treatment option for patients with stage IB (T ≥4 cm) to IIIA NSCLC following complete resection and adjuvant chemotherapy when recommended, regardless of PD-L1 expression**

TPS = tumor proportion score

Paz-Ares L et al. ESMO Virtual Plenary Sessions 2022;Abstract VP3-2022.

FDA-Approved Immunotherapy Combination Options for First-Line Therapy

Combination regimen	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab (q3wk or q6wk) + platinum and pemetrexed[1]	8/20/18	KEYNOTE-189	Nonsquamous	0.56
Pembrolizumab (q3wk or q6wk) + carboplatin, paclitaxel or *nab* paclitaxel[2]	10/30/18	KEYNOTE-407	Squamous	0.71
Atezolizumab (q3wk) + carboplatin and paclitaxel and bevacizumab[3]	12/6/18	IMpower150	Nonsquamous	0.80
Atezolizumab (q3wk) + carboplatin and *nab* paclitaxel[4]	12/3/19	IMpower130	Nonsquamous	0.79
Nivolumab (q2wk) + ipilimumab[5]	5/15/20	CheckMate 227	PD-L1 TPS ≥1, EGFR and/or ALK wt	0.76
Nivolumab (q3wk) + ipilimumab and chemotherapy[6]	5/26/20	CheckMate 9LA	EGFR and/or ALK wt	0.72

[1] Rodriguez-Abreu. *Ann Oncol* 2021. [2] Paz-Ares. *J Thorac Oncol* 2020. [3] Socinski *J Thorac Oncol* 2021. [4] West. *Lancet Oncol* 2019.
[5] Paz-Ares. ASCO 2021;Abstract 9016. [6] Reck. ASCO 2021;Abstract 9000.

FDA-Approved Single-Agent Immunotherapy Options for First-Line Therapy

Monotherapy	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab[1,2] (q3wk or q6wk)	4/11/19 10/24/16	KEYNOTE-042 KEYNOTE-024	PD-L1 TPS ≥1%	0.63
Atezolizumab[3] (q2wk, q3wk or q4wk)	5/18/20	IMpower110	PD-L1 TPS ≥50, EGFR and/or ALK wt	0.59
Cemiplimab[4] (q3wk)	2/22/21	EMPOWER-Lung 1 (Study 1624)	PD-L1 TPS ≥50, EGFR and/or ALK and/or ROS1 wt	0.57

[1] Mok. *Lancet* 2019. [2] Reck. *J Clin Oncol* 2019. [3] Herbst. *N Engl J Med* 2020. [4] Sezer. *Lancet* 2021.

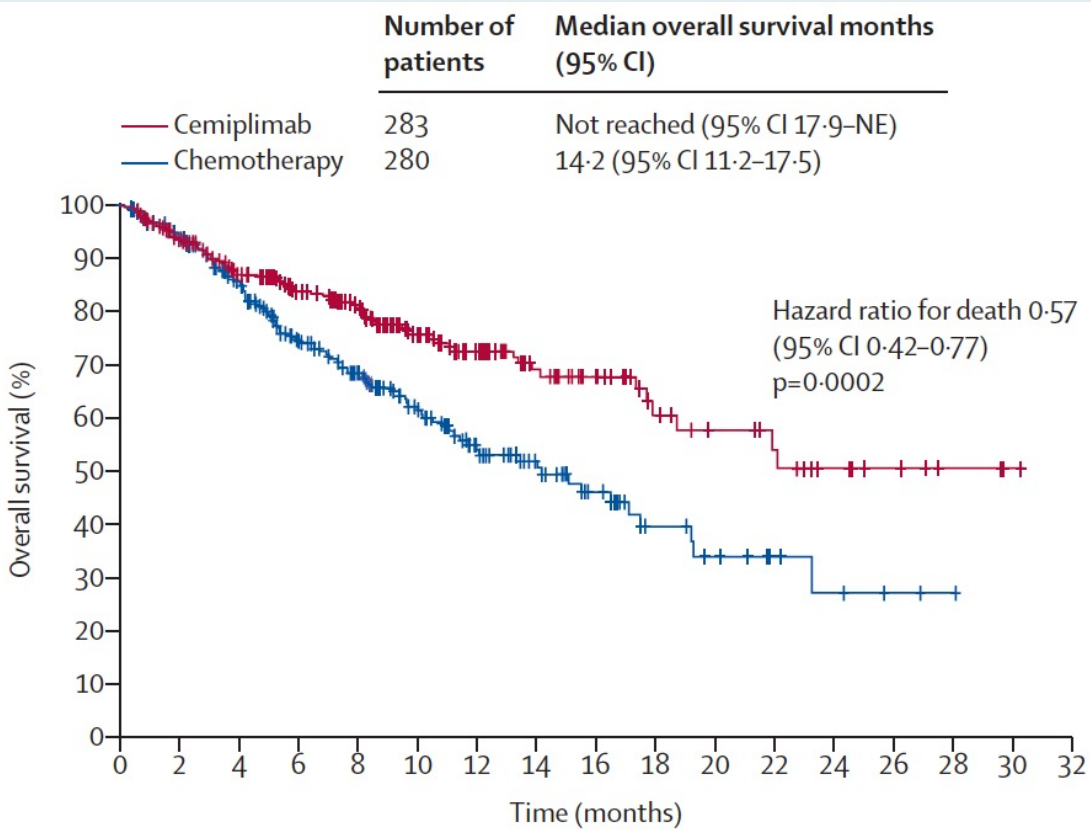
Lancet 2021;397(10274):592-604.

Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial

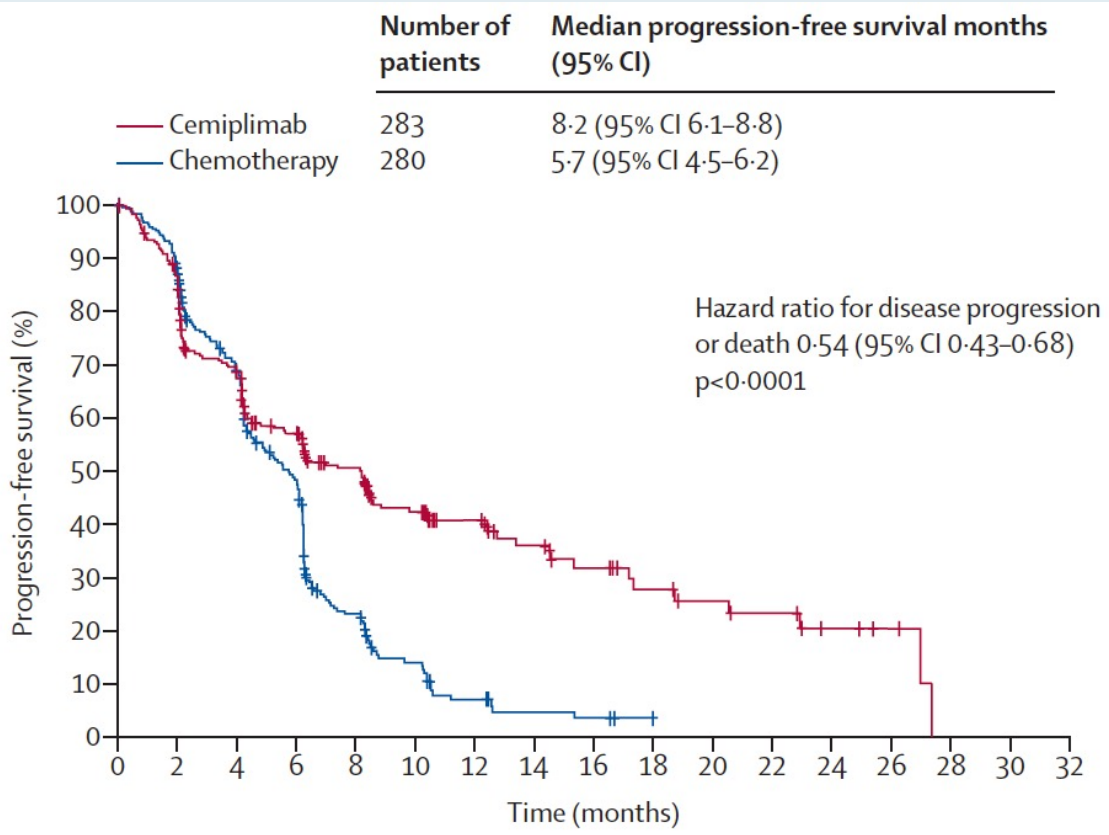
Ahmet Sezer, Saadettin Kilickap, Mahmut Gümüş, Igor Bondarenko, Mustafa Özgüroğlu, Miranda Gogishvili, Haci M Turk, Irfan Cicin, Dmitry Bentsion, Oleg Gladkov, Philip Clingan, Virote Sriuranpong, Naiyer Rizvi, Bo Gao, Siyu Li, Sue Lee, Kristina McGuire, Chieh-I Chen, Tamta Makharadze, Semra Paydas, Marina Nechaeva, Frank Seebach, David M Weinreich, George D Yancopoulos, Giuseppe Gullo, Israel Lowy, Petra Rietschel

EMPOWER-Lung 1: A Phase III Trial of Cemiplimab Monotherapy for First-Line Treatment of NSCLC with PD-L1 ≥50%

Overall Survival



Progression-Free Survival



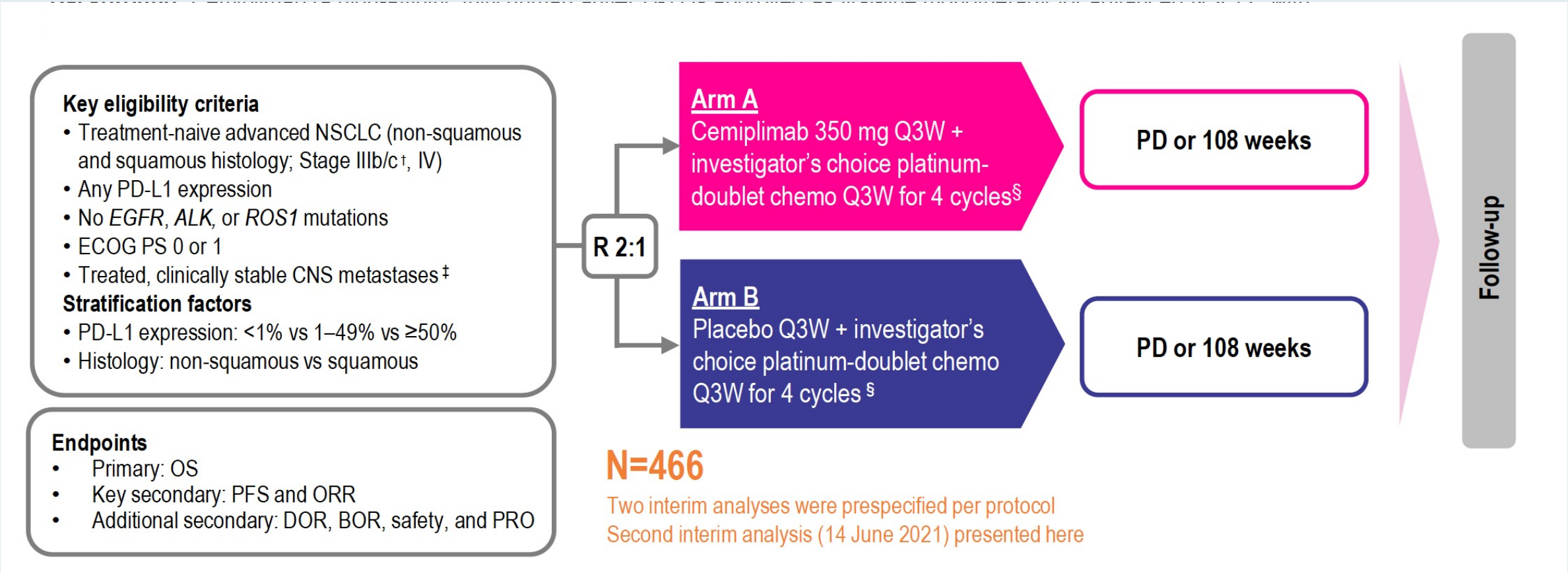
Sezer A et al. *Lancet* 2021;397(10274):592-604.

Cemiplimab plus chemotherapy versus chemotherapy alone in non-small cell lung cancer: a randomized, controlled, double-blind phase 3 trial

Miranda Gogishvili[1], Tamar Melkadze[2], Tamta Makharadze[3], Davit Giorgadze[4], Mikhail Dvorkin[5], Konstantin Penkov[6], Konstantin Laktionov[7], Gia Nemsadze[8], Marina Nechaeva[9], Irina Rozhkova[10], Ewa Kalinka[11], Christian Gessner[12,13], Brizio Moreno-Jaime[14], Rodolfo Passalacqua[15], Siyu Li[16], Kristina McGuire[16], Manika Kaul[16], Anne Paccaly[16], Ruben G. W. Quek[16], Bo Gao[16], Frank Seebach[16], David M. Weinreich[16], George D. Yancopoulos[16], Israel Lowy[16], Giuseppe Gullo[16] and Petra Rietschel[16]

Nat Med 2022 Aug 25;[Online ahead of print].

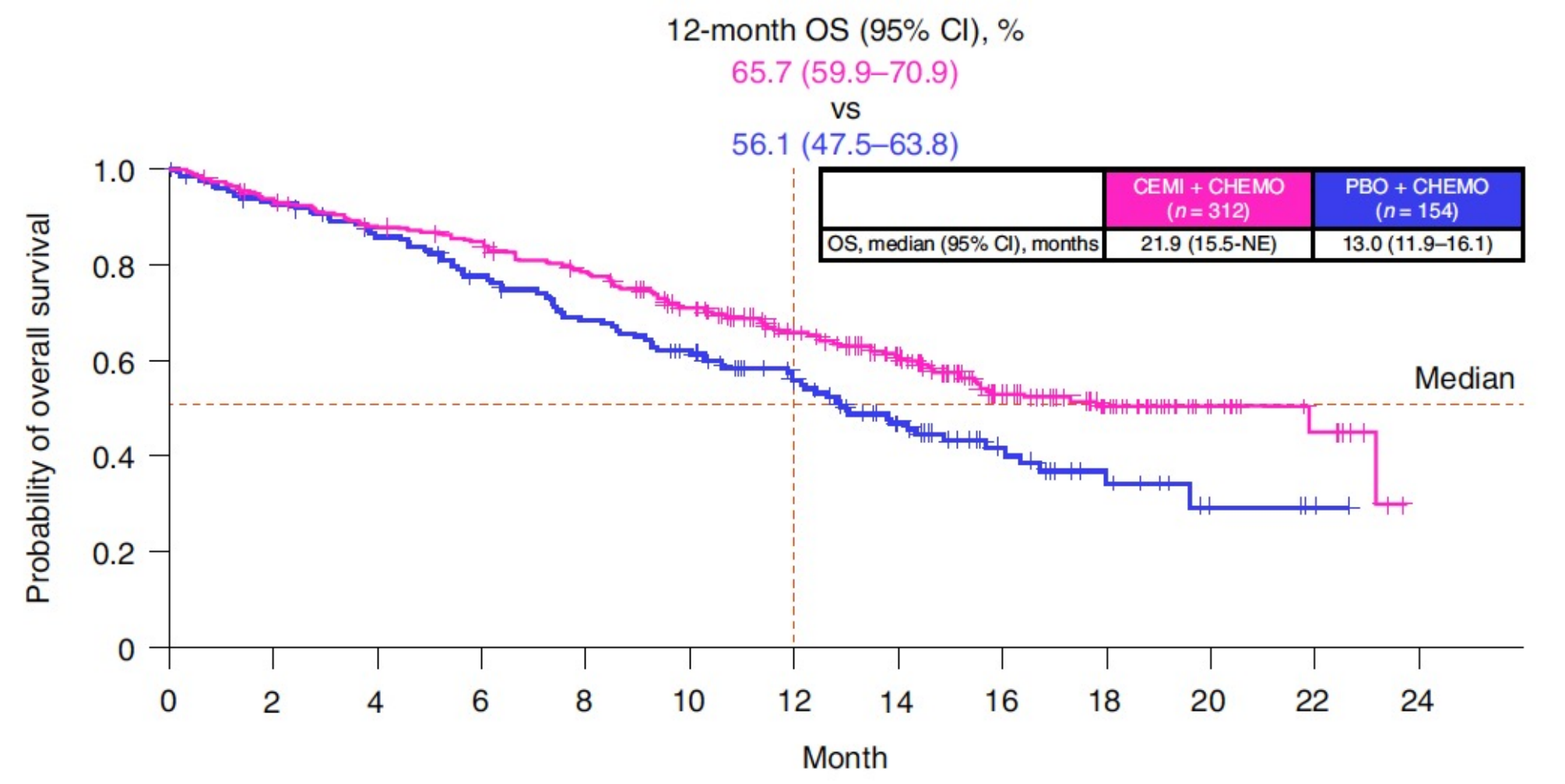
EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC



BOR = best overall response; PRO = patient-reported outcome

Gogishvili M et al. ESMO 2021;Abstract LBA51.

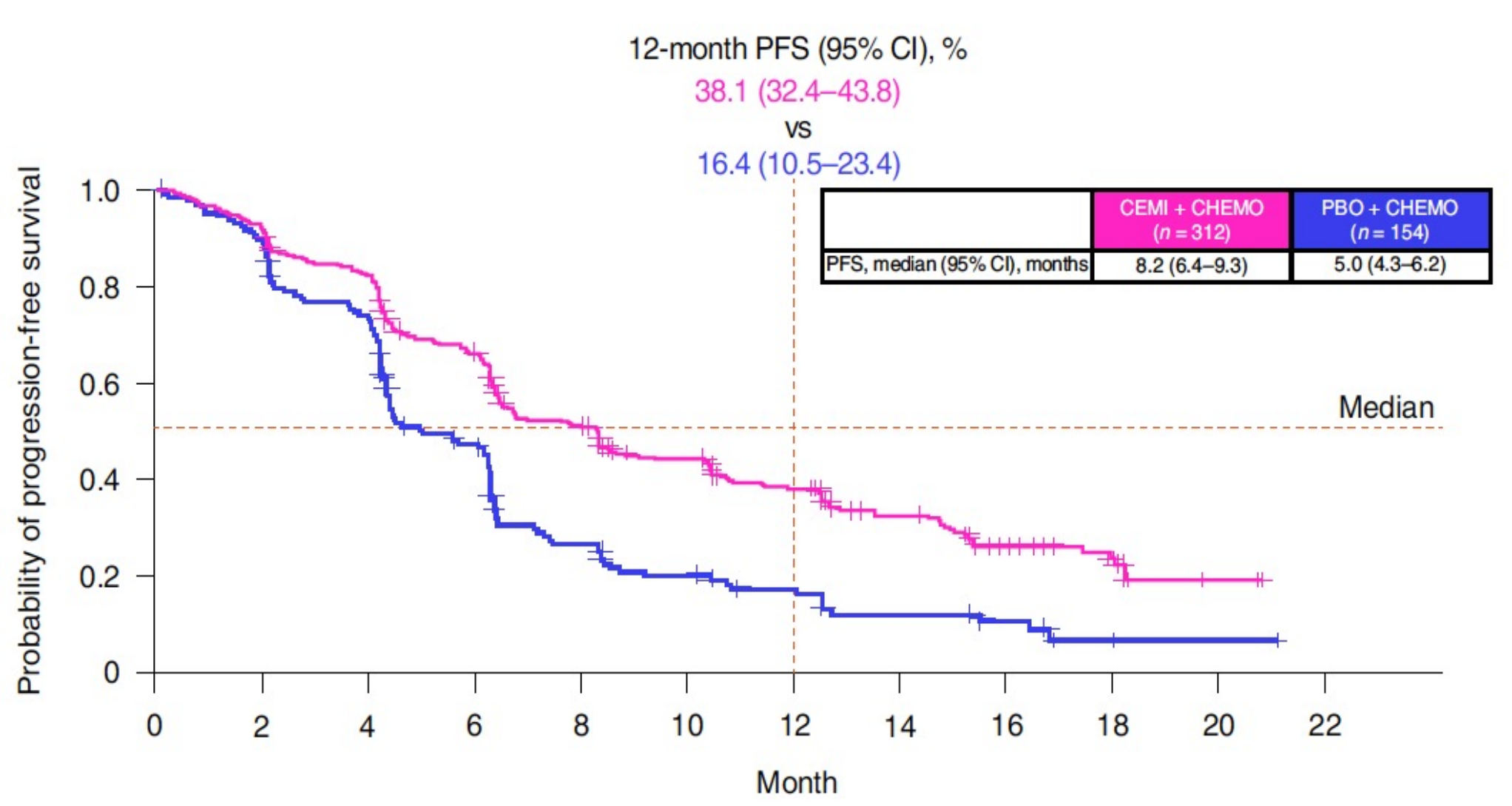
EMPOWER-Lung 3: Overall Survival with First-Line Cemiplimab and Platinum-Doublet Chemotherapy for Advanced NSCLC



Gogishvili M et al. *Nat Med* 2022 Aug 25;[Online ahead of print].

RTP RESEARCH TO PRACTICE

EMPOWER-Lung 3: Progression-Free Survival with First-Line Cemiplimab and Platinum-Doublet Chemotherapy for Advanced NSCLC



Gogishvili M et al. *Nat Med* 2022 Aug 25;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Discussion Questions

First-Line Treatment for Metastatic NSCLC in Patients without Targetable Mutations

Common queries…

- Is anti-PD-1/PD-L1 monotherapy a reasonable consideration for patients with a PD-L1 TPS between 1% and 49%, particularly those who are less fit or have nonvisceral disease?
- Regulatory and reimbursement issues aside, in which situations, if any, do you believe anti-PD-1/anti-CTLA-4 combinations are currently a consideration, and which doublets?
- What is your usual approach to patients with PD-L1-negative tumors?
- Do you believe there is any difference in clinical outcomes with the approved anti-PD-1/PD-L1 antibodies?

Discussion Questions

First-Line Treatment for Metastatic NSCLC in Patients without Targetable Mutations (cont)

- Do you believe patients who have autoimmune complications with immunotherapy are more likely to benefit?
- Do you believe there are currently any clinically meaningful predictors of immunotherapy benefit beyond PD-L1 and TMB?
- In patients with high PD-L1 levels, when do you add chemotherapy to anti-PD-1/PD-L1 antibodies, and how much do you consider the magnitude of the assay result?
- Do you believe the results of the PACIFIC trial warrant consideration of this approach in some patients with classic indications for surgery?
- Can you describe an ideal patient for neoadjuvant chemoimmunotherapy?

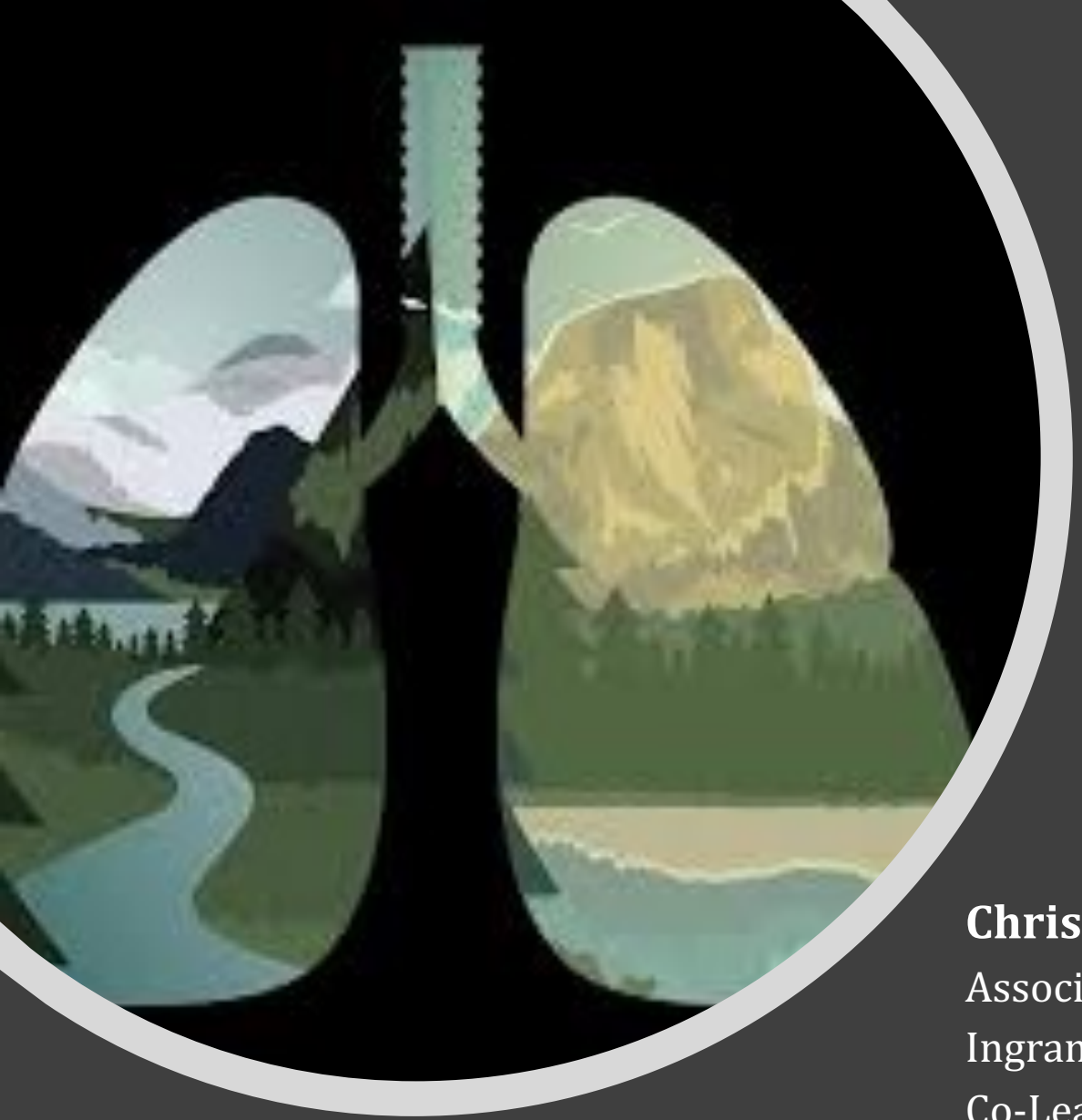
Lung Cancer Agenda

MODULE 1: First line treatment of metastatic NSCLC in patients without targetable mutations

MODULE 2: Neoadjuvant and Adjuvant Treatment of Localized NSCLC

MODULE 3: Targeted Treatment of Metastatic NSCLC

RTP RESEARCH TO PRACTICE



Updates on management of EGFR-mutant and HER2-mutant lung cancer

Christine M. Lovly, MD, PhD
Associate Professor of Medicine, Division of Hematology and Oncology
Ingram Associate Professor of Cancer Research
Co-Leader, Translational Research and Interventional Oncology Program
Vanderbilt University and Vanderbilt Ingram Cancer Center
Nashville, TN

@Christine_Lovly

OBJECTIVES

- Discuss therapeutic strategies for patients with metastatic **EGFR-mutant lung cancer** that experience disease progression on 1st line osimertinib

- Review options for management of metastatic NSCLC harboring **EGFR exon 20 insertion mutations**

- Outline emerging strategies for management of **HER2-mutant** NSCLC

Distinguishing between *EGFR* mutations in NSCLC

"EGFR mutation positive" is not enough detail

SENSITIZING

Common EGFR Mutations

Exon 19 Deletions (~45%)

Most commonly between AA L747 and E749:
E746_A750del, L747_P753insS, L747_T751del, L747_A750insP, E746-S752insV, etc.

L858R point mutation (exon 21), (~40%)

Approved Therapies:
- **Osimertinib (preferred, 1L)**
- Erlotinib, Gefitinib, Afatinib, Dacomitinib

Atypical EGFR Mutations

L861Q, G719X, S768I, etc

Others (TKI sensitivity varies)

Approved Therapies:
- **Afatinib**
- (Osimertinib may also have some activity)

RESISTANT to standard EGFR TKIs

Exon 20 Insertions (AA 761-775)

A767_V769dup

S768_D770dupSVD

V769_D770insASV

D770_N771ins…

D770_P772dup

N771_H773dup

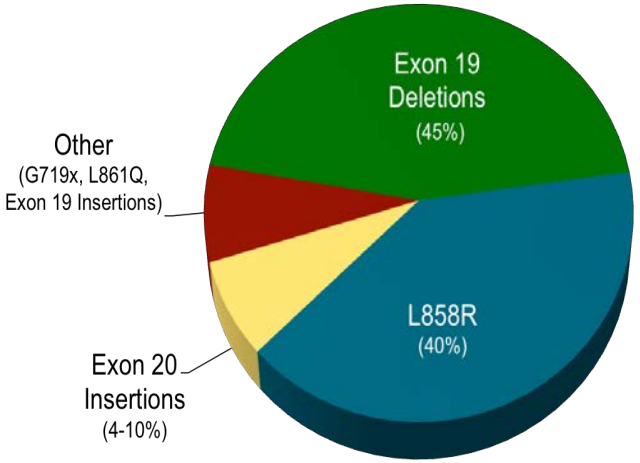
N771_P772ins…

P772_H773dupPH

V774ins

Others…

Approved Therapies:
- **Mobocertinib (2L, post-platinum)**
- **Amivantamab (2L, post-platinum)**



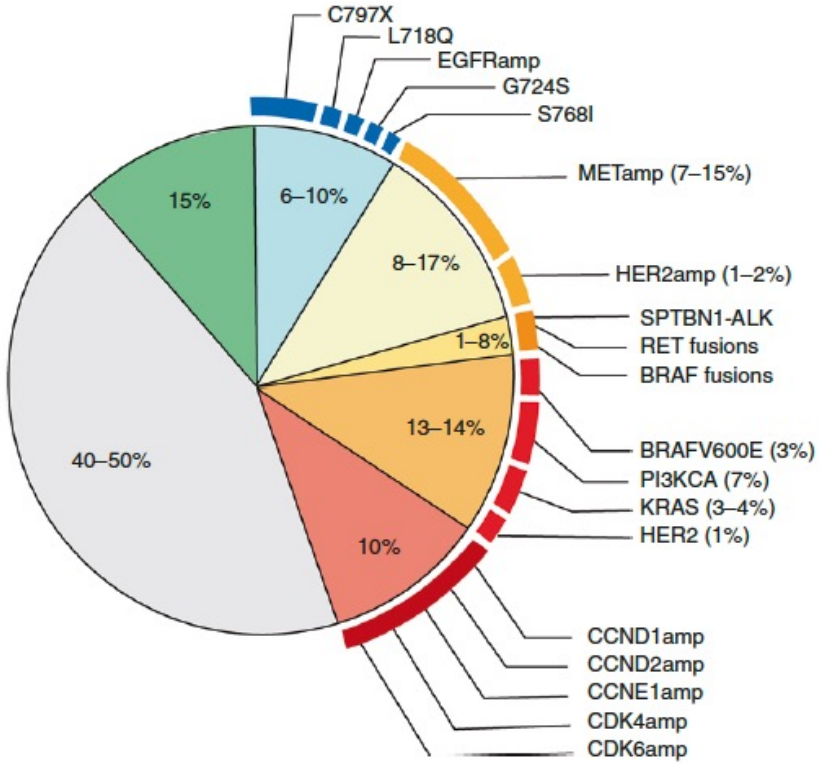
Yasuda H et al. *Lancet Oncol.* 2012;13(1):e23-e31.
Yasuda H et al. *Sci Transl Med.* 2013;5(2216):216ra177.

For EGFR-mutant NSCLC patients, disease progression on osimertinib is now a major challenge

1st line Osimertinib
mPFS 18.9 mos

2nd line therapies after 1st line osimertinib?

Selecting optimal post-Osimertinib therapies requires an understanding of resistance mechanisms and effective strategies to target these mechanisms



- **On-target resistance**
  - *EGFR* C797S, G724S, etc.
  - 5-10%
- **Histologic Transformation**
  - SCLC, squamous, and other histologies
  - Tissue biopsy is critical in the evaluation of osimertinib resistance
  - Up to 15%
- **Bypass pathway activation**
  - most notably *MET* amplification
  - up to 15% pts
- **50-60% of patients don't have a targetable resistance mechanism**

Schoenfeld AJ et al. *Clin Cancer Res.* 2020;26(11):2654-2663.
Leonetti A et al. *Br J Cancer.* 2019;121(9):725-737.

Treatment Options after First-Line Osimertinib

General Principles

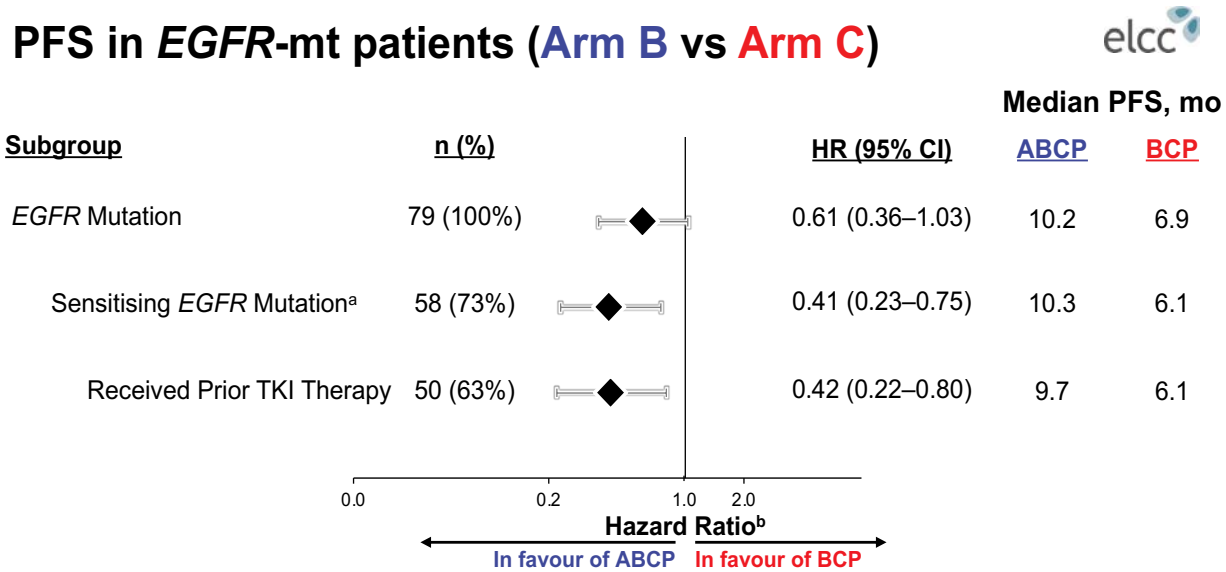
- Platinum-pemetrexed remains the standard of care after 1st line Osimertinib.
- Consider treatment options directed at resistance mechanisms when available
  - Histology-specific chemotherapy
- Enroll patients on clinical trials

To continue Osimertinib or not with chemotherapy?

- Role of continued Osimertinib with carboplatin/pemetrexed is unknown.
  - Carbo/Pem/Osi vs. Carbo/Pem/Placebo being evaluated (COMPEL; NCT04765059)
- Chemo + Osi is generally well tolerated, with more myelosuppression
  - White M, Piotrowska Z, *Clinical Lung Cancer* 2021.
- Consider continuing Osimertinib with carboplatin/pemetrexed for patients with CNS disease which remains controlled on osimertinib.

Role of Immunotherapy After Osimertinib?

- The efficacy of single-agent anti-PD1/PD-L1 inhibitors among EGFR+ NSCLC is low (ORR ~3-12%)[1]
- KEYNOTE-189 *excluded* pts with sensitizing EGFR mutations.
- ImPower150 (Carbo/Pac/Bev/Atezo) is an option. Patients with EGFR-mutant tumors had improvement in PFS/OS with ABCP vs. BCP (small numbers).
- Osi *should not* be given concurrently with IO (↑ pneumonitis risk).



- The addition of atezolizumab to bevacizumab and chemotherapy increased PFS benefit across all *EGFR*-mut patient subgroups, especially those who have received prior TKI

[a] Defined as exon 19 deletions or L858R mutations. [b] Unstratified HR.
Data cutoff 22 Jan 2018.

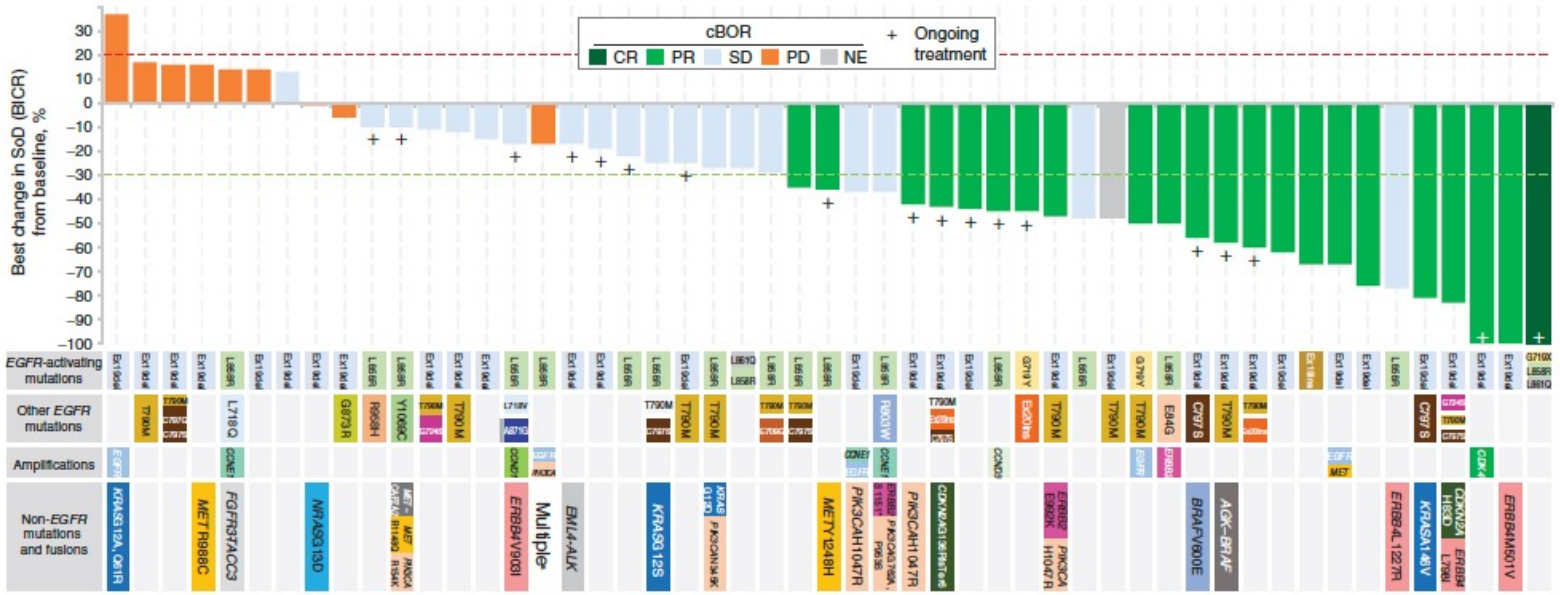
EUROPEAN LUNG CANCER CONFERENCE 2019
Reck et al. IMpower150 in *EGFR*-mt pts

1. Gainor, et all, CCR 2016; 2. Reck, ELCC 2019

Patritumab Deruxtecan
(HER3-DXd; HER3 Antibody-Drug Conjugate)

- HER3 is expressed in most NSCLC tumors.
- Patritumab Deruxtecan (HER3-DXd) is an antibody drug conjugate with a topoisomerase I inhibitor payload.
- HER3 mutation is not a known mechanism of resistance to EGFR TKI in *EGFR*m NSCLC.
- Reference: Janne et al. ASCO 2021

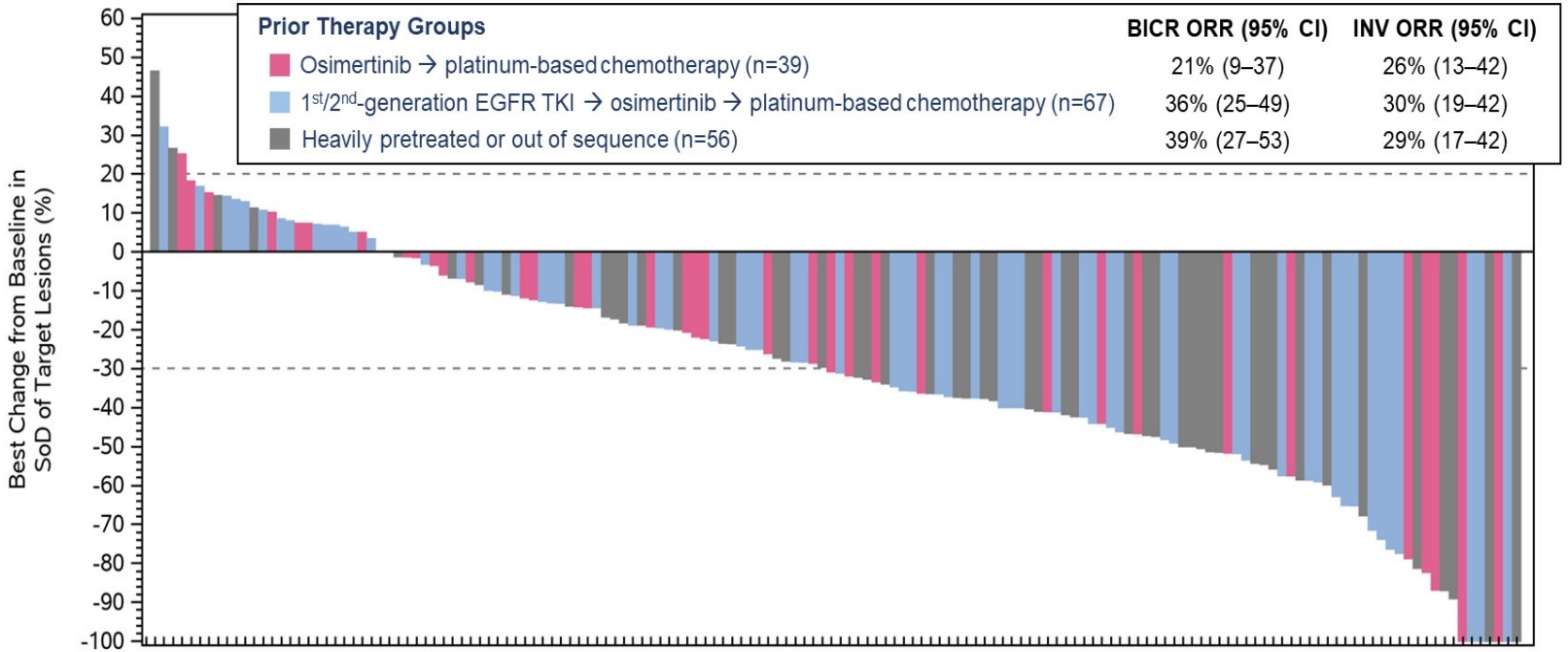
	All (n=57)	Prior PBC + Osi (n=44)
Confirmed ORR (BICR)	39%	39%
mDOR, mo (range)	6.9 (3.1-NE)	7.0 (3.1-NE)
mPFS, mo (range	8.2 (4.4-8.3)	8.2 (4.0-NE)



Responses observed regardless of osimertinib resistance mechanism.

Amivantamab + Lazertinib

Amivantamab (bispecific MET/EGFR antibody) + Lazertinib (3rd gen EGFR TKI)



- 10 efficacy-evaluable patients did not have any evaluable post-baseline target lesion measurements

BICR-assessed Response	n=162
ORR	33% (95% CI, 26–41)
Median DOR	9.6 mo (95% CI, 7.0–NE)
Best response, n (%)	
Complete response	2 (1)
Partial response	52 (32)
Unconfirmed partial response	1 (0.6)
Stable disease	69 (43)
Progressive disease	28 (17)
NE	10 (6)
Clinical benefit rate[a]	57% (95% CI, 49–65)

Investigator-assessed ORR=28% (95% CI, 22–36)
Investigator-assessed median DOR=8.4 mo (95% CI, 5.6–NE)

Median follow-up=10.0 mo (range, 0.3–20.2)
Median progression free survival=5.1 mo (95% CI, 4.2–6.9)
Median overall survival=14.8 mo (95% CI, 12.1–NE)

Amivantamab + Lazertinib – Biomarker Selection?

- ORR 47% (8/17) in patients with identified EGFR/MET mechanism of resistance
- ORR 29% (8/28) in patients without an identified EGFR/MET mechanism of resistance

Shu C, ASCO 2022
Chul B et al. ASCO 2021

Summary: therapeutic strategies after progression on 1st line osimertinib

- The therapeutic approach to patients who progress on osimertinib should be guided by 1) sites of progression (consider local therapy for oligoprogressive disease) and 2) resistance mechanisms, if possible.

- Tissue biopsy should be considered, particularly for patients with baseline EGFR/TP53/Rb1 mutations who are at increased risk of SCLC transformation.

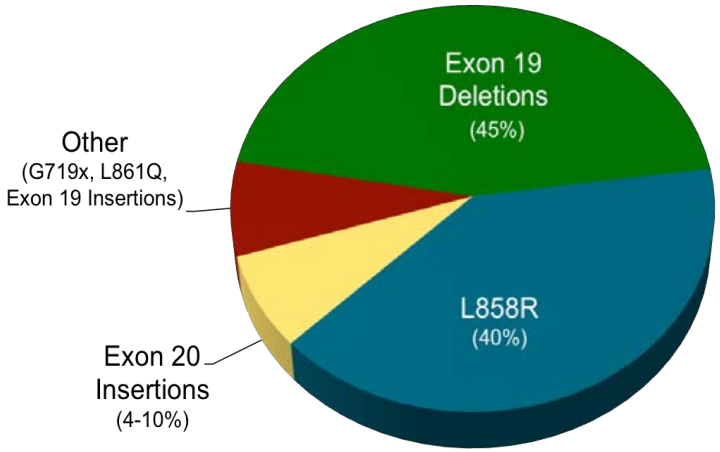
- Outside of clinical trials, I use **platinum doublet chemotherapy +/- osimertinib.**
  - In particular, consider continuing osimertinib with chemotherapy (e.g., carbo/pem/osi) for patients with CNS disease controlled with Osimertinib.

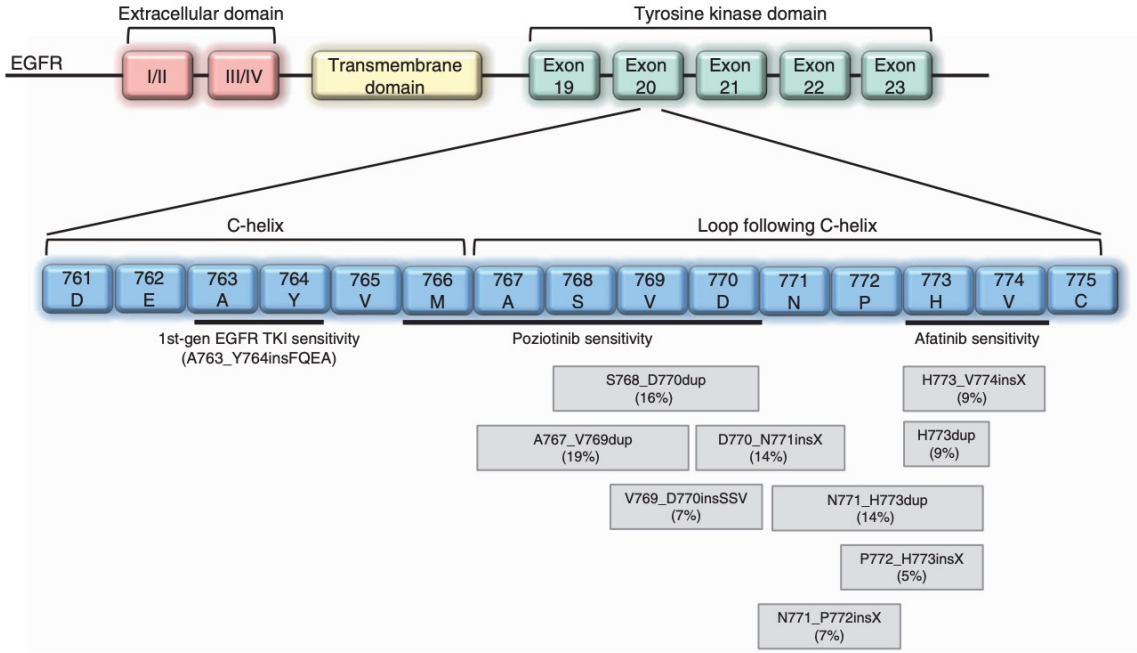
- Numerous agents in development: HER3-DxD, Amivantamab + Lazertinib, "4th generation" EGFR TKIs.

- Also look for "risk adapted" clinical trials based on ctDNA clearance.

EGFR Exon 20 Insertion Mutations

- Like other mutations, can be detected with NGS
- More commonly seen in specific populations
  - Female sex
  - Never smokers
  - Adenocarcinoma histology
- Like EGFR del19/L858R, poor responses to immunotherapy
- Unlike EGFR del19/L858R, poor responses to standard TKIs
- Standard treatment is currently 1st line platinum doublet chemotherapy





Vyse et al. Signal Transduction and Targeted Therapy. 2019
Yasuda, et al. Lancet Oncol, 2011; Yasuda, et al. Science Trans Med, 2014
Heymach J, WCLC 2018, Meador CB, Sequist LV, Piotrowska Z, Cancer Discov 2021.

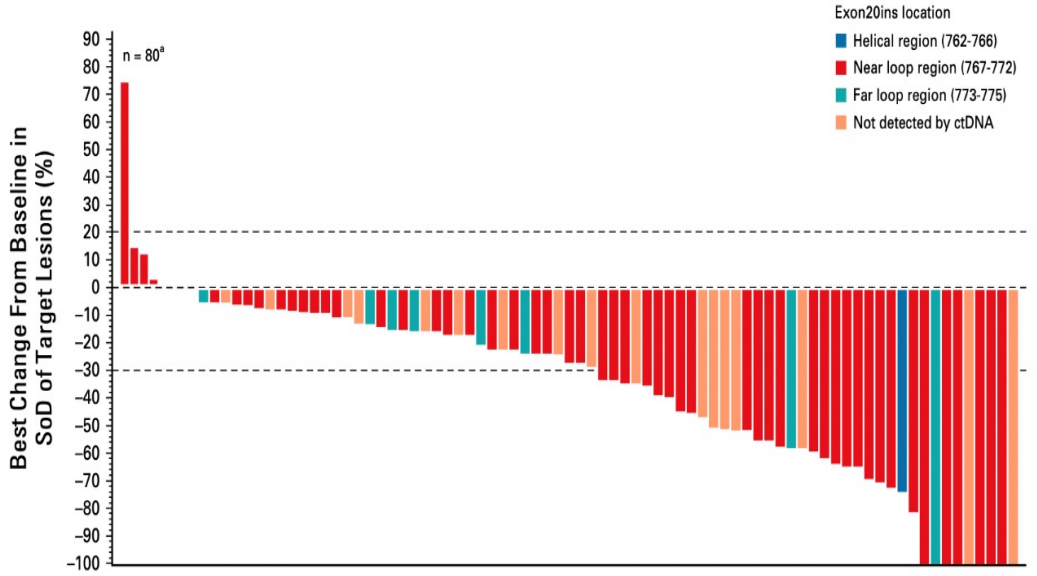
Amivantamab for patients with metastatic lung cancer harboring EGFR exon 20 insertions

Study Population:
- 81 patients
- All with prior platinum-based chemotherapy

Efficacy:
- Confirmed ORR 40%
- mPFS: 8.3 mos; mDOR: 11.1 mos

Toxicity:
- Infusion related reactions (66% Any Grade, 3% Grade > 3) - most commonly on C1D1
- Derm: Rash (86% Any Grade, 4% Grade > 3), Paronychia (45%)
- MET-related: Hypoalbuminemia (27%), Edema (18%)
- Dose Reduction: 13% | Dose discontinuation: 10%

→ **FDA accelerated approval May 21, 2021**



AE (≥15% of Treatment-emergent AEs), n (%)	Safety Population (N=114)			
	Treatment-emergent AE		Treatment-related AE	
	Total	Grade ≥3	Total	Grade ≥3
EGFR-related				
Rash[a]	98 (86)	4 (4)	98 (86)	4 (4)
Paronychia	51 (45)	1 (1)	48 (42)	1 (1)
Stomatitis	24 (21)	0	21 (18)	0
Pruritus	19 (17)	0	19 (17)	0
MET-related				
Hypoalbuminemia	31 (27)	3 (3)	17 (15)	2 (2)
Peripheral edema	21 (18)	0	11 (10)	0
Other				
Infusion related reaction	75 (66)	3 (3)	75 (66)	3 (3)
Constipation	27 (24)	0	7 (6)	0
Nausea	22 (19)	0	13 (11)	0
Dyspnea	22 (19)	2 (2)	6 (5)	0
Fatigue	21 (18)	2 (2)	14 (12)	1 (1)
Increased ALT	17 (15)	1 (1)	14 (12)	1 (1)

Park K et al. *J Clin Oncol.* 2021;39:3391-3402.
Sabari, WCLC 2020

Mobocertinib for patients with metastatic lung cancer harboring EGFR exon 20 insertions

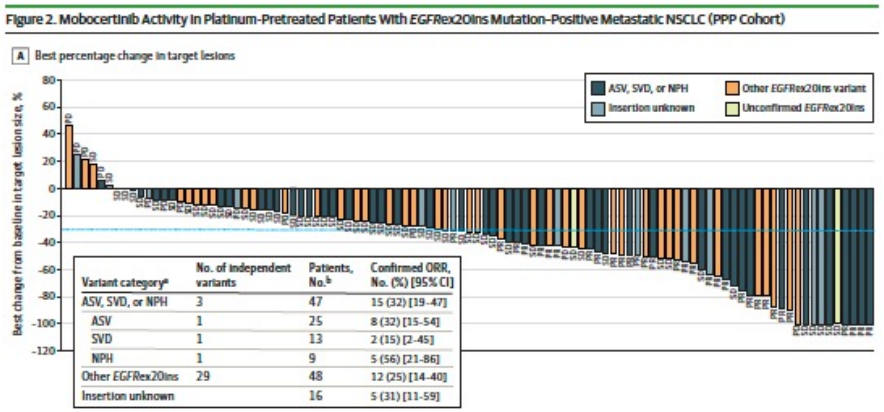
Mobocertinib- Oral, irreversible EGFR TKI (160mg daily)

Study Population:
- 114 patients
- All with prior platinum-based chemotherapy

Efficacy:
- ORR 28% (BIRC)
- mPFS: 7.3 mos; mDOR: 17.5 mos

Toxicity:
- GI: Diarrhea (91% Any Grade, 21% Grade > 3), Decreased Appetite (35%), Nausea (34%)
- Derm: Rash (45% Any Grade, 0% Grade > 3), Paronychia (38%)
- Cardiac: QTc prolongation (11% Any Grade, 3% Grade > 3), one treatment-related death due to cardiac failure
- Dose reduction: 25% | Treatment Discontinuation: 17%

→ **FDA accelerated approval Sept 15, 2021**



	Any Grade	Grade ≥ 3
Diarrhea	**91%**	**21%**
Rash	45%	0%
Paronychia	38%	<1
Anorexia	35%	<1%
Nausea	34%	4%
Dry Skin	31%	0
Vomiting	30%	3%
Cr Increase	25%	2%
Stomatitis	24%	4%

Zhou C et al. *JAMA Oncol.* 2021.

Emerging Drugs for EGFR Exon 20 insertion mutations

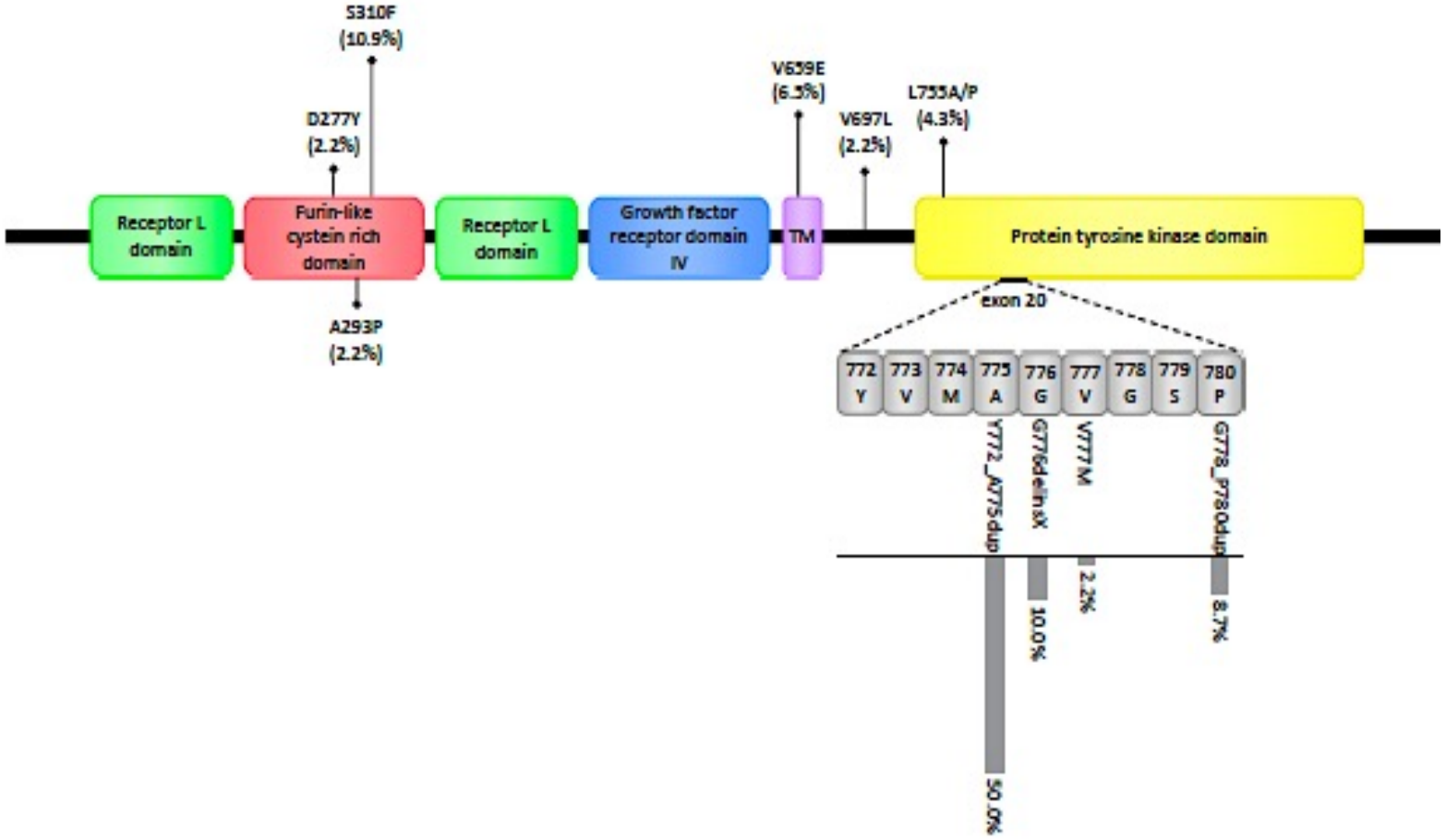
Drug	NCT	Most Recent REF	Notes
Sunvozertinib (DZD9008)	NCT03974022	Janne P, ASCO 2022	Confirmed ORR 37.5 % in overall population presented to date
CLN-081	NCT04036682	Yu HA, ASCO 2022	Confirmed PR 38.4% in overall population presented to date
BDTX-189	NCT04209465	Schram AM, ASCO 2020	*Clinical Development Halted*
BLU-451	NCT05241873	Spira AI, ASCO 2022	CNS Activity Predicted
ORIC-114	NCT05315700	Juntilla MR, AACR 2021	CNS Activity Predicted
HS-10376	NCT05435274		

REF: Clinicaltrials.gov search for “EGFR exon 20” (accessed July 1, 2022) – not an exhaustive list

HER2 mutations in NSCLC

- HER2 mutations occur in 1-3% of NSCLC
  - Exon 20 insertions most common
  - YVMA variant: most common HER2 ex20 insertion variant
  - Point mutations in the tyrosine kinase, transmembrane and extracellular domains also present at lower frequencies.

- HER2 mutations have little to no overlap with gene amplification or protein expression



Jebbink M, et al, Cancer Treatment Rev 2020.
Yu X, et al. Frontiers in Oncol 2022.
Arcila ME, et al. Clin Cancer Re, 2012.
Mazieres J, Annals Oncol, 2016.
Pillai RN, et al. Cancer 2017.

EGFR/HER2 TKIs for HER2-mutant NSCLC

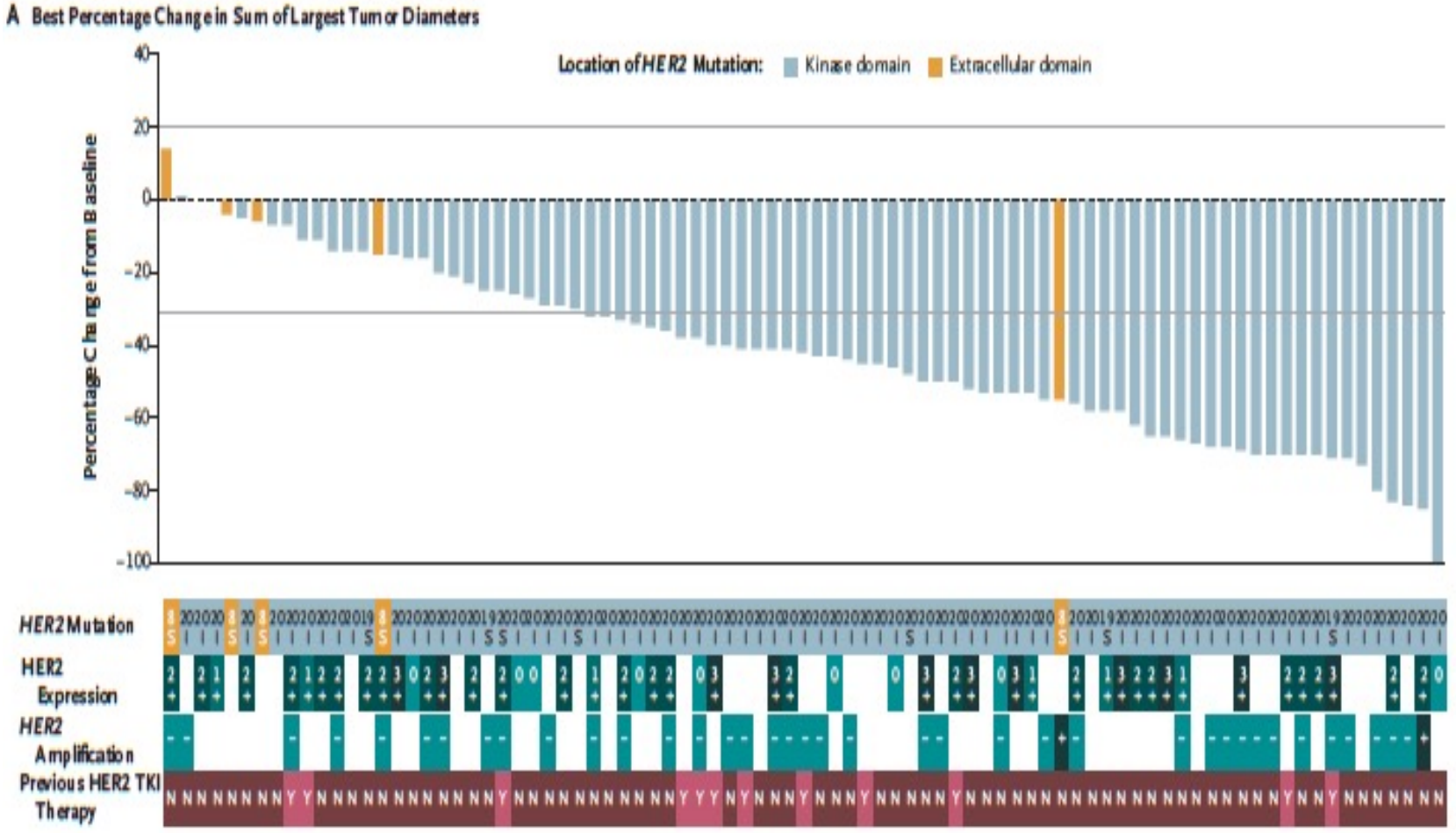
Drug	Target Pop	N	ORR	mPFS	Toxicities
Afatinib[1]	HER2^{mt}	13	8%	16 weeks	Diarrhea, vomiting, rash, paronychia, fatigue, mucositis
Afatinib[2]	HER2^{mt}	27	13%	3 mo	Diarrhea/GI toxicity, skin rash.
Neratinib[3]	HER2^{mt}	26	4%	5.5 mo	Diarrhea (74%), Nausea (43%), Vomiting (41%)
Dacomitinib[4]	HER2^{mt}	26	12%	3 mo	Diarrhea (90%), rash (73%)
Mobocertinib[5]	HER2^{mt}	5	1/5 (20%)		83% Diarrhea, 50% Anorexia
Pyrotinib[6]	HER2^{mt}	60	30%	6.9 mo	92% Diarrhea; 30% Creatinine increase
Poziotinib[7]	HER2^{mt}, Pretreated	90	28%	5.5 mo	49% Gr 3 Rash; 25.6 % Gr 3 Diarrhea
Poziotinib[8]	HER2^{mt}, First-line	48	44%	5.6 mo	49% Gr 3 Rash; 25.6 % Gr 3 Diarrhea

1. Dziadziuszko R, JTO 2019; 2. Lai WCV et al, European Journal of Cancer 2018; 3. Hyman DM, Nature 2018; 4. Kris MG et al. Ann Onc. 2015; 5. Zhou C et al. J Clin Oncol. 2020; 6. Neal JW et al. WCLC 2018. Abstract P1.13-44, 7. Zhou C, JCO 2020, 7. Le X, JCO 2022; 8. Cornelisson R, ESMO 2021

Slide kindly shared by Zofia Piotrowska, MD, MHS

Trastuzumab Deruxtecan (T-DXd) in HER2-mutant NSCLC

DESTINY-Lung01: Single arm, phase 2 study of T-DXd 6.4mg/kg IV q21 days in patients who were "refractory to standard treatment"



	Outcome (95% CI) N=91
ORR	55% (44-65)
mDOR	9.3 mos (5.7-14.7)
mPFS	8.2 mos (6.0-11.9)
mOS	17.8 mos (13.8-22.1)

→ Responses were observed across HER2 mutation sub-types as well as in patients with no detectable HER2 expression or *HER2* gene amplification.

Li BT, NEJM 2022

Trastuzumab Deruxtecan (T-DXd) in HER2-mutant NSCLC

Table 3. Most Common Investigator-Reported Drug-Related Adverse Events in the Study Population (91 Patients).

Event	Grade 1–2	Grade 3	Grade 4	Grade 5	Overall
	number of patients (percent)				
Drug-related adverse event	46 (51)	37 (41)	4 (4)	1 (1)*	88 (97)
Drug-related adverse events with ≥20% incidence					
Nausea	58 (64)	8 (9)	0	0	66 (73)
Fatigue†	42 (46)	6 (7)	0	0	48 (53)
Alopecia	42 (46)	0	0	0	42 (46)
Vomiting	33 (36)	3 (3)	0	0	36 (40)
Neutropenia‡	15 (16)	14 (15)	3 (3)	0	32 (35)
Anemia§	21 (23)	9 (10)	0	0	30 (33)
Diarrhea	26 (29)	2 (2)	1 (1)	0	29 (32)
Decreased appetite	27 (30)	0	0	0	27 (30)
Leukopenia¶	17 (19)	4 (4)	0	0	21 (23)
Constipation	20 (22)	0	0	0	20 (22)

- **Pneumonitis (ILD)**
  - **Adjudicated drug-related ILD occurred in 24/91 patients (26%)**
  - Grade 1: 3 patients
  - Grade 2: 15 patients
  - Grade 3: 4 patients
  - Grade 5: 2 patients
  - Median duration of onset of ILD – 141 days (range, 14-462)
  - 21 patients required corticosteroids

<u>August 11, 2022: US FDA approved T-DXd (5.4mg/kg) for HER-mutant NSCLC after one prior line of therapy.</u>

- Based on phase DESTINY-Lung02 trial (NCT04644237)
- Interim reports shown at ESMO 2022 meeting, reference: Goto K et. al. Ann Oncol. 2022;33(suppl_7):S808-S869.
- RR similar between 6.4mg and 5.4mg doses, but higher rates of ILD at the 6.4mg dose.

Unanswered Questions for HER2-mutant NSCLC

- What is the optimal first-line therapy for HER2-mutant NSCLC?
  - Should we use chemo alone, or chemo + IO?
  - Is the efficacy of T-DXd sufficient for first-line use?

- How can we minimize (and manage) ADC-related toxicities, particularly ILD with T-DXd?

- Is there a role for HER2—targeting TKIs (poziotinib, pyrotinib), or are their toxicity profiles prohibitive?

- How should currently available therapies be sequenced? Is there a role for combinations?

- Management of CNS Metastases in HER2mutant tumors?

Expanding Precision Medicine in NSCLC

NCCN guidelines for NSCLC, 05/2022

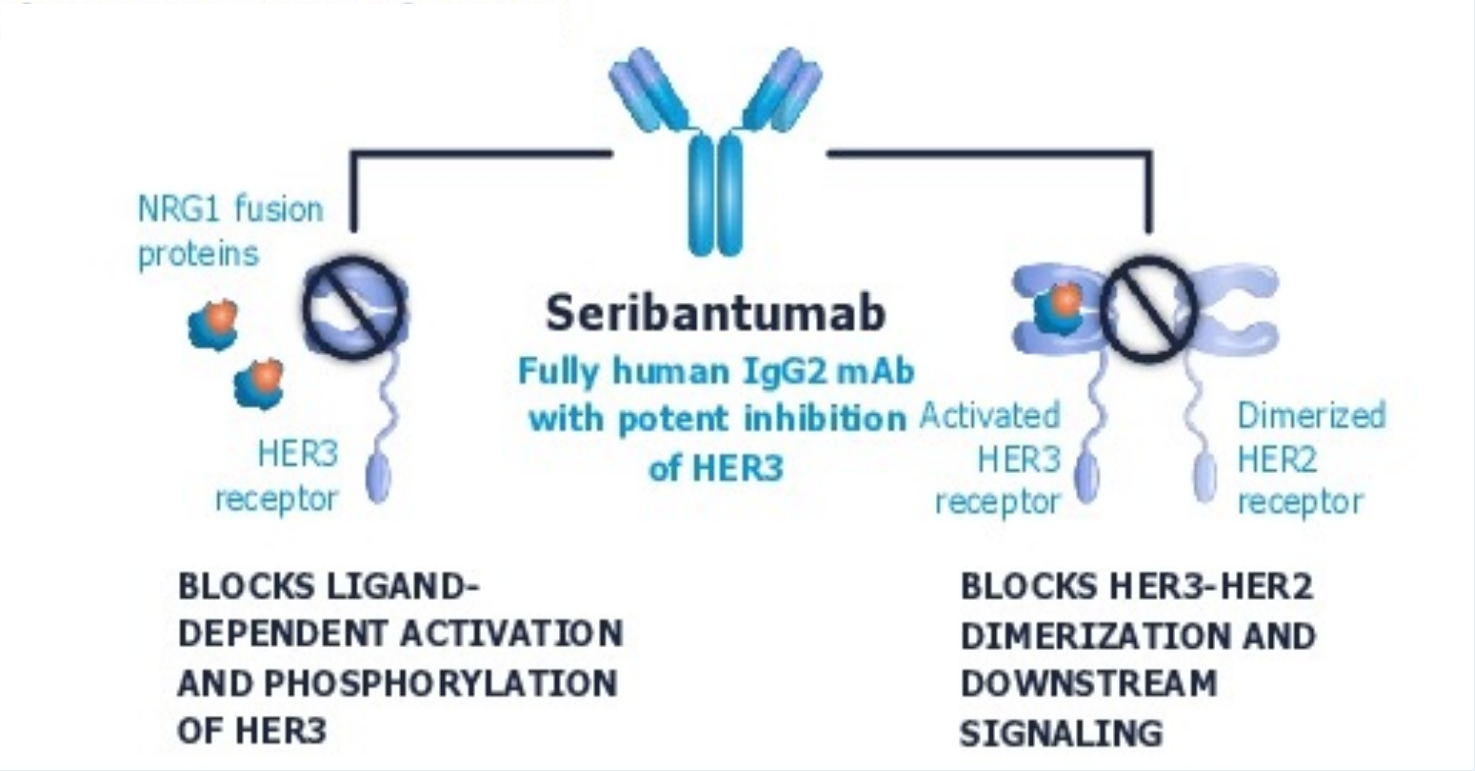
TESTING RESULTS[ll,mm]	
EGFR exon 19 **deletion or** ***L858R*** **mutation positive**	NSCL-20
EGFR S768I, L861Q, **and/or** ***G719X*** **mutation positive**	NSCL-23
EGFR exon 20 **insertion mutation positive**	NSCL-24
KRAS G12C **mutation positive**	NSCL-25
ALK **rearrangement positive**	NSCL-26
ROS1 **rearrangement positive**	NSCL-29
BRAF **V600E mutation positive**	NSCL-31
NTRK1/2/3 **gene fusion positive**	NSCL-32
METex14 **skipping mutation positive**	NSCL-33
RET **rearrangement positive**	NSCL-34
ERBB2 (HER2) **mutation positive**	NSCL-35
PD-L1 ≥50% and negative for actionable molecular biomarkers above	NSCL-36
PD-L1 ≥1%–49% and negative for actionable molecular biomarkers above	NSCL-37
PD-L1 <1% and negative for actionable molecular biomarkers above	NSCL-38

Broad molecular testing of all patients is key for identifying the best treatment strategies for patients with NSCLC.

Other Potential Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung

Neuregulin-1 (NRG1) Gene Fusions and Seribantumab Mechanism of Action

- NRG1 gene fusions are rare oncogenic drivers found in 0.2% of solid tumors including lung, colorectal, breast and ovarian
- NRG1 fusion proteins predominantly retain an active EGF-like domain, which drives tumorigenesis and proliferation through aberrant HER3 activation
- Seribantumab is a fully human monoclonal antibody against HER3



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

2022 ASCO® ANNUAL MEETING

Abstract 3006

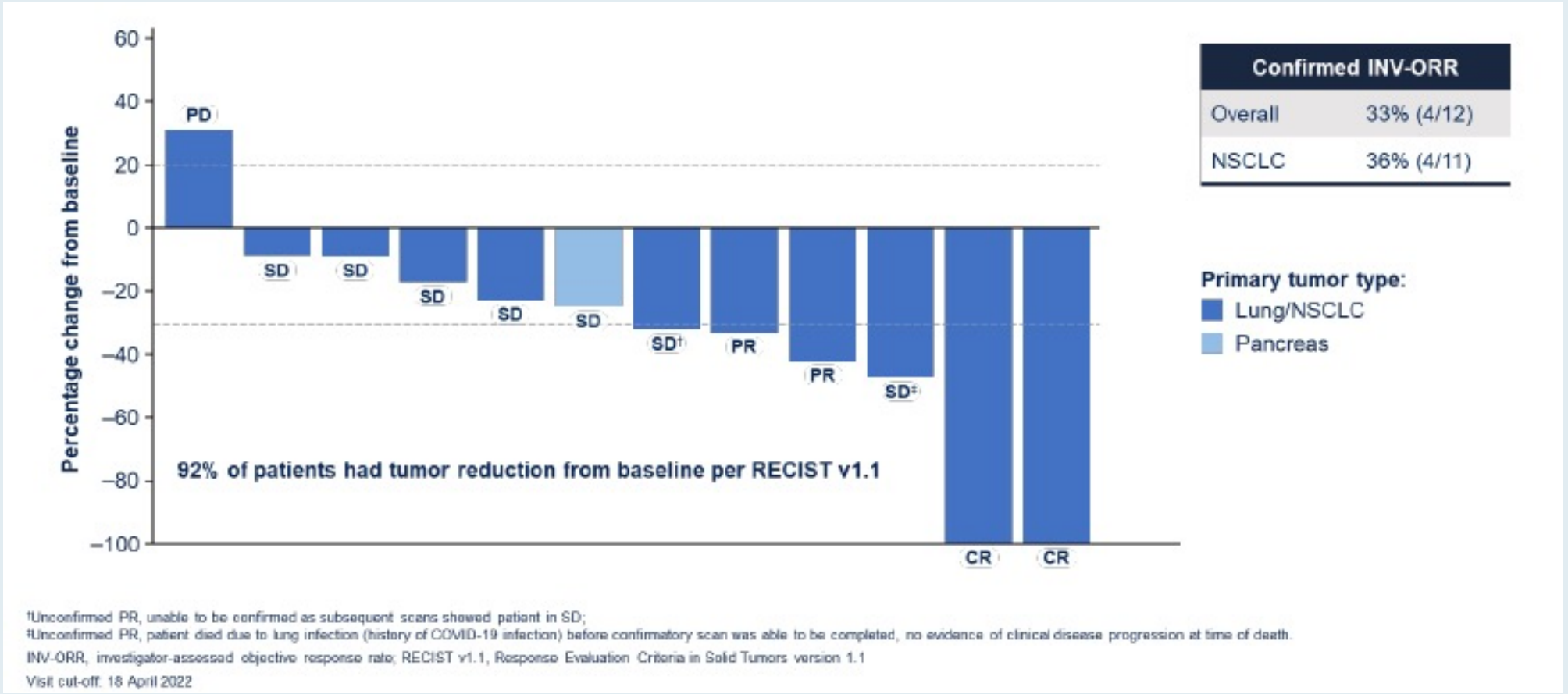
CRESTONE: Initial Efficacy and Safety of Seribantumab in Solid Tumors Harboring NRG1 Fusions

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

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

RTP RESEARCH TO PRACTICE

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

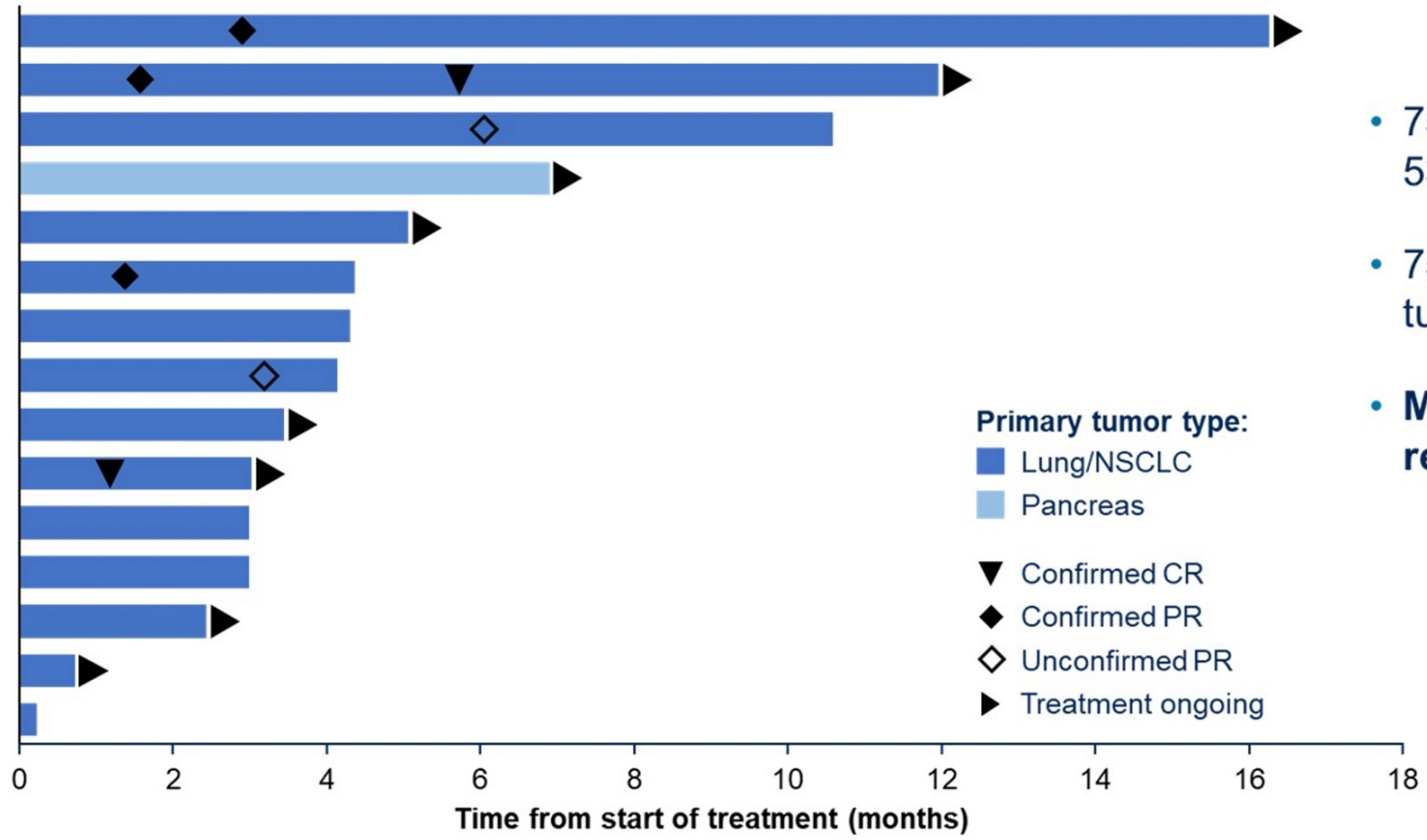


PD = progressive disease; SD = stable disease; PR = partial response; CR = complete response

- Median DoR has not been reached

Carrizosa DR et al. ASCO 2022;Abstract 3006.

CRESTONE: Duration of Seribantumab Therapy for Patients with NRG1 Fusions



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

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

Carrizosa DR et al. ASCO 2022;Abstract 3006.

PARIS 2022 ESMO congress

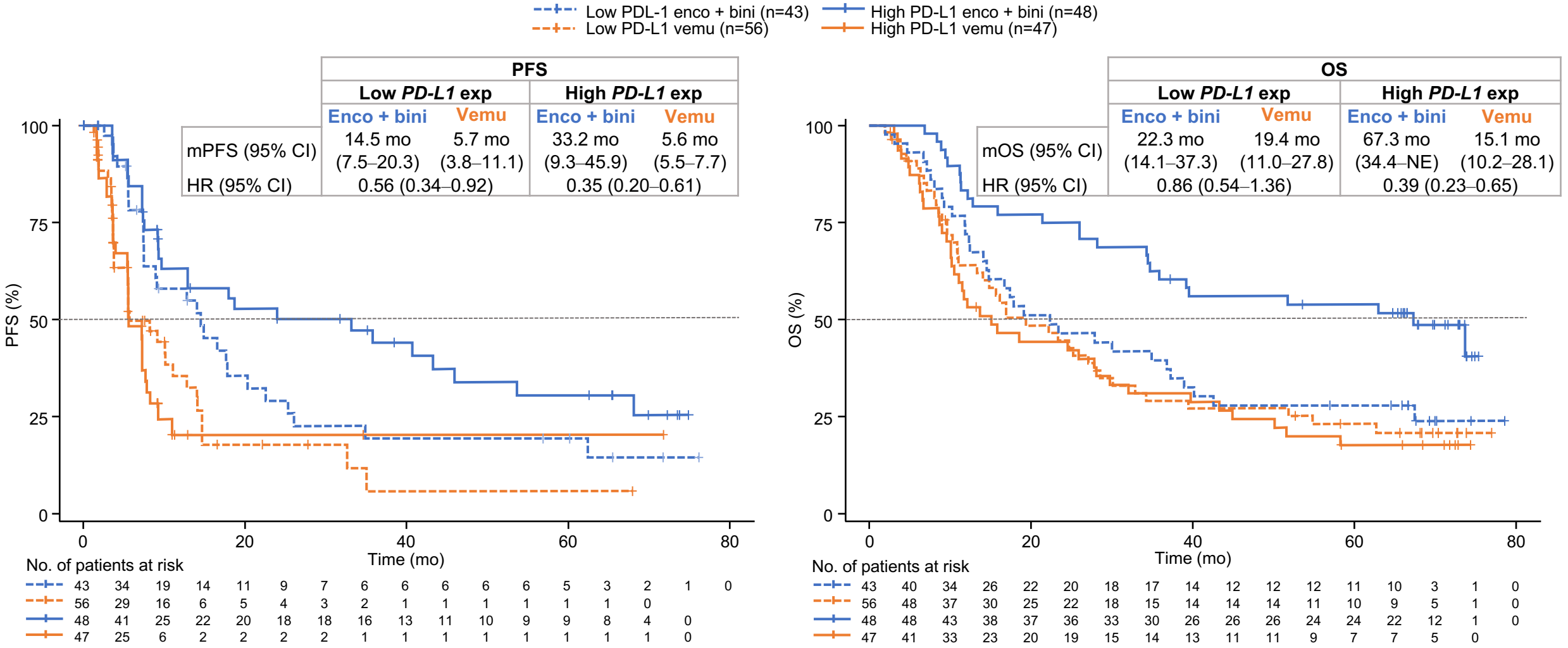
Tumor Biomarker Analysis From COLUMBUS Part 1: Encorafenib + Binimetinib for *BRAF* V600E/K-Mutant Advanced or Metastatic Melanoma

Reinhard Dummer,[1] Nuzhat Pathan,[2] Shibing Deng,[3] Caroline Robert,[4] Ana Arance,[5] Jan Willem B. de Groot,[6] Claus Garbe,[7] Helen J. Gogas,[8] Ralf Gutzmer,[9] Ivana Krajsová,[10] Gabriella Liszkay,[11] Carmen Loquai,[12] Mario Mandala,[13] Dirk Schadendorf,[14] Naoya Yamazaki,[15] Alessandra di Pietro,[16] Tao Xie,[3] Paolo A. Ascierto,[17] Keith Flaherty[18]

[1]University Hospital Zurich, Zurich, Switzerland; [2]Pfizer, Inc, La Jolla, CA, USA; [3]Pfizer, Inc, San Diego, CA, USA; [4]Gustave Roussy and Paris-Saclay University, Villejuif, France; [5]Hospital Clinic of Barcelona, Barcelona, Spain; [6]Isala Oncology Center, Zwolle, Netherlands; [7]University Hospital Tubingen, Tubingen, Germany; [8]National and Kapodistrian University of Athens, Athens, Greece; [9]Johannes Wesling Medical Center, Ruhr University Bochum Campus Minden, Minden, Germany; [10]University Hospital Prague, Prague, Czech Republic; [11]National Institute of Oncology, Budapest, Hungary; [12]University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany; [13]University of Perugia, Perugia, Italy; [14]University Hospital Essen, West German Cancer Center and German Cancer Consortium, Partner Site Essen, Essen, Germany; [15]National Cancer Center Hospital, Tokyo, Japan; [16]Pfizer, Inc, Milan, Italy; [17]Istituto Nazionale Tumori IRCCS Fondazione Pascale, Napoli, Italy; [18]Massachusetts General Hospital, Boston, MA, USA

NCT01909453

PFS and OS by *PD-L1* Gene Expression



There was a larger treatment effect of encorafenib + binimetinib vs vemurafenib on PFS and OS in the high *PD-L1* expression[a] group compared with the low *PD-L1* expression group

COLUMBUS part 1 tumor biomarker analysis (data cutoff: Sep 15, 2020).

[a]High *PD-L1* expression was defined as above median expression.

bini, binimetinib; enco, encorafenib; exp, expression; vemu, vemurafenib.

Discussion Questions

Themes in Targeted Treatment

- Predictors of benefit
- Criteria for use of first-line targeted treatment in metastatic disease
- Durvalumab versus targeted treatment for locally advanced disease
- Brain metastases
- Benefit of immunotherapy
- Toxicity with recent immunotherapy; treatment of the acutely ill patient

Thank you for joining us!

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

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