Thoracic Malignancies

Best of ASCO 2024

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Disclosures:

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AbbVie, Amgen, Aprea, Astellas, AstraZeneca, Astellas, Beigene, BMS, Checkmate, Elicio, Genmab, Genentech, Gilead, GSK, Immunocore, Inbrx, Incyte, Jacobio, Lilly, Merck, Mirati, Novartis, Pfizer, Poseida, Tempus, Seattle Genetics, and Sophia

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Non-Small Cell Lung Cancer
Stage IV 1st line: 8506

NRG-LU002: *Randomized Phase II/III Trial Of Maintenance Systemic Therapy Versus Local Consolidative Therapy (LCT) Plus Maintenance Systemic Therapy For Limited Metastatic Non-Small Cell Lung Cancer (NSCLC)*

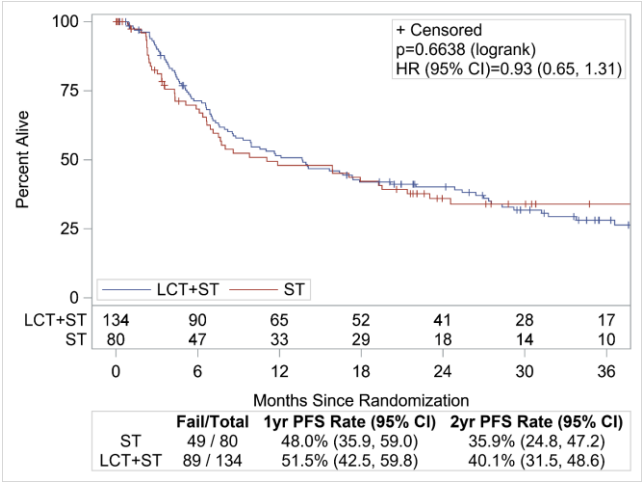
Puneeth Iyengar, MD, PhD, Chen Hu, PhD, Daniel Gomez, MD, Robert Timmerman, MD, Charles Simone, MD, Clifford Robinson, MD, David Gerber, MD, Saiama N Waqar, MBBS, MSCI, Jessica S Donington, MD, Stephen G Swisher, MD, Michael Weldon, MSc, Jackie Wu, PhD, Bryan Faller, MD, Sawsan Rashdan, MD, Kevin L Stephans, MD, Pamela Samson, MD, Kristin A Higgins, MD, Ryan Nowak, MD, Jessica A Lyness, MS, Jeffrey D Bradley, MD

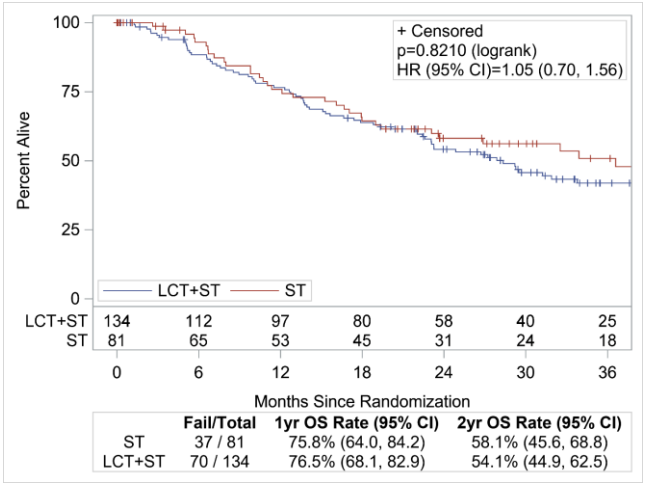
Non-Small Cell Lung Cancer
Stage IV 1st line: NRG-LU002

- NRG-LU002: Randomized phase II/III trial of maintenance systemic therapy versus local consolidative therapy (LCT) plus maintenance systemic therapy for limited metastatic non-small cell lung cancer (NSCLC).

Patients with metastatic NSCLC having completed at least 4 cycles or courses* of first-line/induction systemic therapy Restaging studies reveal no evidence of progression and limited metastatic disease (0-3 discrete extracranial sites), all of which must be amenable to SBRT/ radiation +/- Surgery A minimum of one disease site (metastasis or primary) needs to be present after first-line/induction systemic therapy and treatable with local consolidative therapy	**STRATIFY**	**Histology:** Squamous vs. Non-squamous **Systemic Therapy:** Immunotherapy-containing Induction Regimens vs. Cytotoxic Chemotherapy Only Induction Regimens**	**RANDOMIZE**	**Arm 1**: Maintenance systemic therapy alone** **Arm 2:** SBRT/radiation or SBRT/ radiation and Surgery to all sites of metastases (0-3 discrete sites) and/or irradiation (SBRT or hypofractionated RT) of the primary site followed by maintenance systemic therapy. All Arm 2 patients, even if treated with Surgery, must have one site of disease (metastasis or primary) treated with radiation*** If a metastatic site is best treated with hypofractionated radiation, this will be permitted if SBRT or surgery not indicated *** **As noted in Section 5**

Primary objective of Ph II: PFS
Primary Objective of Ph III: OS

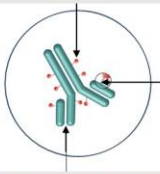




Non-Small Cell Lung Cancer
Stage IV 2nd line: LBA8500

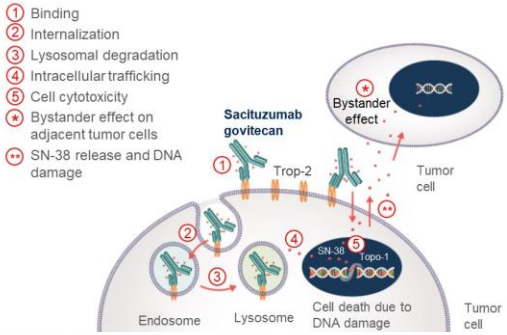
Sacituzumab Govitecan Is a First-in-Class Trop-2–Directed Antibody-Drug Conjugate

SN-38 payload
- SN-38 is more potent than the parent compound, irinotecan (Topo-1 inhibitor)
- SN-38 is rapidly internalized and efficiently released to the tumor with minimized effect on healthy tissues



Linker for SN-38
- pH-sensitive, hydrolyzable linker for SN-38 release in targeted tumor cells and tumor microenvironment, allowing bystander effect
- High drug-to-antibody ratio (7.6:1)[1]

Humanized anti–Trop-2 antibody
- Binds with high (K_D = 0.3 nM) affinity to Trop-2, an epithelial antigen expressed on many solid tumors[2]



EVOKE-01: Global, Randomized, Open-Label, Phase 3 Study

Key eligibility criteria
- Measurable stage IV NSCLC
- ECOG PS 0–1
- Radiographic progression after platinum-based and anti-PD-(L)1–containing regimen[a]
- In addition, patients with known AGAs must have received ≥ 1 approved TKI[b]
  - *EGFR/ALK* test required. Testing of other AGAs recommended[c]
- Previously treated stable brain metastases were included
- No prior treatment with Topo-1 inhibitors, Trop-2–targeted therapies, or docetaxel

N = 603

R 1:1

Sacituzumab govitecan
10 mg/kg on Days 1 and 8 of 21-day cycles[d]

Docetaxel
75 mg/m² on Day 1 of 21-day cycles[d]

End points

Primary
- OS

Secondary
- PFS, ORR, DOR, and DCR by INV per RECIST v1.1
- Safety and tolerability
- QoL using NSCLC-SAQ

Stratified by
- **Histology** (squamous vs nonsquamous)
- **Response to last anti-PD-(L)1–containing regimen** (responsive [best response CR/PR] vs nonresponsive [PD/SD])
- **Received prior targeted therapy for AGA** (yes vs no)

At data cutoff (29 November 2023), the study median follow-up was 12.7 months (range, 6.0–24.0)

Non-Small Cell Lung Cancer
Stage IV 2nd line: EVOKE-01 + TROPION-Lung01

	TROPION-Lung01[14]		EVOKE-01[12]	
	Dual Primary End Point PFS (BIRC), OS		OS	
Primary End Point	Datopotamab-Deruxtecan	Docetaxel	Sacituzumab-Govitecan	Docetaxel
No.	299	305	299	304
Male, %	61	69	65	71
Median age	63	64	66	64
Nonsquamous/squamous, %	78/22	77/23	72/28	74/26
AGAs, %	17	17	6.4	8.2
Prior anti–PD(L)-1, %	88	88	100	100
Prior treatment lines 1/2/3, %	56/36/7	57/33/9	56/34/10	55/33/12
ORR, % (95% CI)	26.4 (21.5 to 31.8)	12.8 (9.3 to 17.1)	13.7 (10.0 to 18.1)	18.1 (13.9 to 22.9)
Median DoR, months (95% CI)	7.1 (5.6 to 10.9)	5.6 (5.4 to 8.1)	6.7 (4.4 to 9.8)	5.8 (4.1 to 8.3)
Median PFS, months (95% CI)	4.4 (4.2 to 5.6)[a]	3.7 (2.9 to 4.2)[a]	4.1 (3.0 to 4.4)[b]	3.9 (3.1 to 4.2)[b]
HR for PFS (95% CI)	0.75 (0.62 to 0.91)[a]	0.92 (0.77 to 1.11)[b]		
HR for PFS in nonsquamous (95% CI)	0.63 (0.51 to 0.78)[a]	0.94 (0.67 to 1.32)[b]		
HR for PFS in squamous (95% CI)	1.38 (0.94 to 2.02)[a]	0.93 (0.75 to 1.15)[b]		
Median OS, months (95% CI)	12.4 (10.8 to 14.8)[c]	11.0 (9.8 to 12.5)[c]	11.1 (9.4 to 12.3)	9.8 (8.1 to 10.6)
HR for OS, (95% CI)	0.90 (0.72 to 1.13)[c]	0.84 (0.68 to 1.04)		
TRAEs leading to treatment discontinuation, %	8	12	6.8	14.2

Ahn M, et al. *Ann Oncol* 2023, 34:S1661; Paz-Ares LG, et al. *J Clin Oncol* 2024, 42:2860

Non-Small Cell Lung Cancer With KRAS G12C: LBA 8509

2024 ASCO ANNUAL MEETING

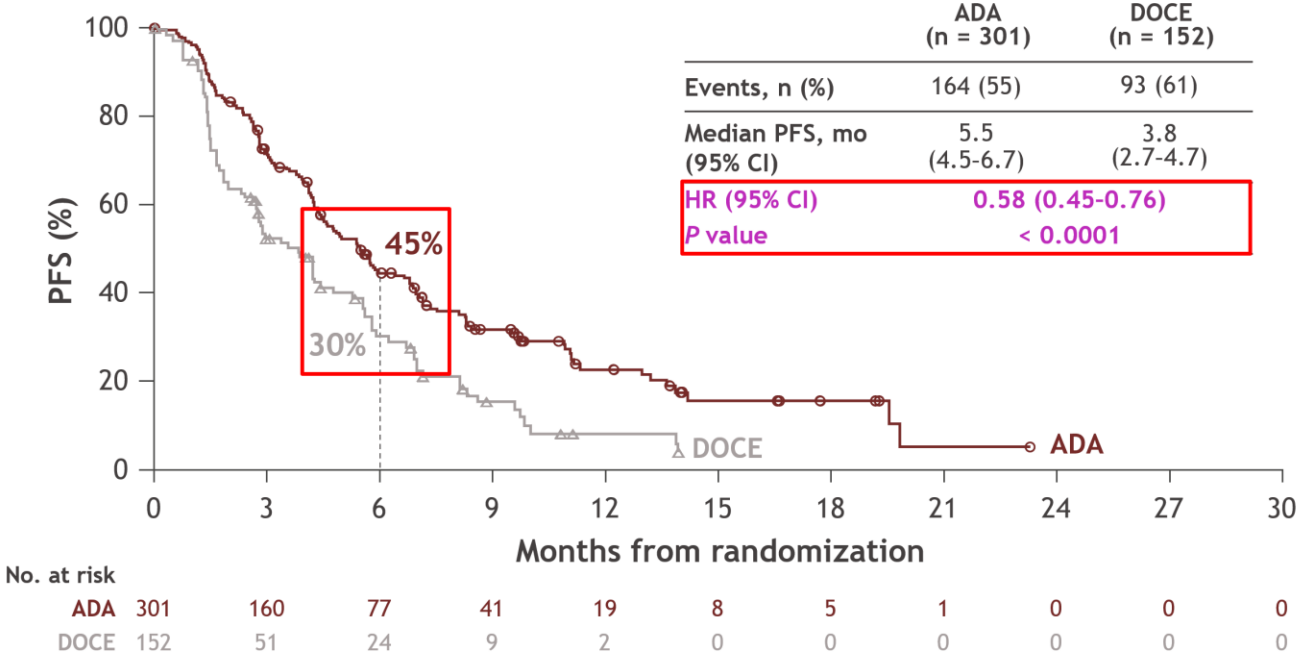
KRYSTAL-12: phase 3 study of adagrasib versus docetaxel in patients with previously treated locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring a *KRAS*^{G12C} mutation

Tony S. K. Mok,[1] Wenxiu Yao,[2] Michaël Duruisseaux,[3-5] Ludovic Doucet,[6] Aitor Azkárate Martínez,[7] Vanesa Gregorc,[8] Oscar Juan-Vidal,[9] Shun Lu,[10] Charlotte De Bondt,[11] Filippo de Marinis,[12] Helena Linardou,[13] Young-Chul Kim,[14] Robert Jotte,[15] Enriqueta Felip,[16] Giuseppe Lo Russo,[17] Martin Reck,[18] Mary F. Michenzie,[19] Wenjing Yang,[19] Julie N. Meade,[19a] Fabrice Barlesi[20]

[1]Chinese University of Hong Kong, Hong Kong Special Administrative Region, China; [2]Sichuan Cancer Hospital & Institute, Chengdu, China; [3]Louis Pradel Hospital, Hospices Civils de Lyon Cancer Institute, Lyon, France; [4]Cancer Research Center of Lyon, UMR INSERM 1052, CNRS 5286, Lyon, France; [5]Université Claude Bernard Lyon 1, Université de Lyon, Lyon, France; [6]Institut de Cancérologie de l'Ouest, Nantes, France; [7]Hospital Universitario Son Espases, Mallorca, Spain; [8]Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Italy; [9]Hospital Universitari i Politècnic La Fe, Valencia, Spain; [10]Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [11]Antwerp University Hospital, University of Antwerp, Antwerp, Belgium; [12]Istituto Europeo di Oncologia, IRCCS, Milan, Italy; [13]Fourth Oncology Department & Comprehensive Clinical Trials Center, Metropolitan Hospital, Athens, Greece; [14]Chonnam National University Medical School and CNU Hwasun Hospital, Hwasun-Gun, Republic of Korea; [15]Rocky Mountain Cancer Center, US Oncology Research, Denver, CO, USA; [16]Vall d'Hebron Institute of Oncology, Vall d'Hebron Barcelona Hospital Campus, Universitat Autonoma de Barcelona, Barcelona, Spain; [17]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [18]Airway Research Center North, German Center for Lung Research, LungenClinic, Grosshansdorf, Germany; [19]Mirati Therapeutics, a Bristol Myers Squibb company, San Diego, CA, USA; [20]Gustave Roussy & Paris Saclay University, Villejuif, France

Non-Small Cell Lung Cancer (NSCLC) With KRAS G12C – KRYSTAL-12

Primary endpoint: PFS[a] per BICR



	ADA (n = 301)	DOCE (n = 152)
Events, n (%)	164 (55)	93 (61)
Median PFS, mo (95% CI)	5.5 (4.5-6.7)	3.8 (2.7-4.7)
HR (95% CI)	0.58 (0.45-0.76)	
P value	< 0.0001	

Median follow-up: 7.2 months.

[a]Time from randomization to the date of disease progression per BICR or death due to any cause, whichever occurs first. For patients who started a subsequent anticancer therapy prior to disease progression or death, PFS was censored at the date of the last tumor assessment prior to the start of the new therapy.

Non-Small Cell Lung Cancer With *EGFR* Alterations – Treatment naïve

	FLAURA	FLAURA 2	MARIPOSA
Design	Osimertinib vs 1st Gen TKI	Chemo + Osimertinib vs Osimertinib	Amivantamab + Lazertinib vs Osi
ORR (%)	80 vs 76	83 vs. 76	86 vs. 85
Median DOR (mo)	17.2 vs 8.5	24.0 vs. 15.3	25.8 vs. 16.8
Median PFS (mo)	18.9 vs 10.2	25.5 vs. 16.7	23.7 vs. 16.6
Median OS	35.8 vs 27.0	Not mature	Int. OS favors Ami + Laz (HR:0.80)
AEs - G≥ 3 (%)	We all know!	54 vs. 11	More skin toxicity
FDA	Approved	Approved (Feb 2024)	Evaluating

Ramalingam SS, et al. NEJM 2020; 382:41; Planchard D, et al. NEJM 2023; 389:1935; Cho BC, et al. Ann Oncol 2023.10.062

Non-Small Cell Lung Cancer With *EGFR* Alterations: Post-Osimertinib

MARIPOSA 2	Ami + Laz + Chemo (n=263)	Ami + Chemo (n=131)	Chemo (n=263)
ORR (%)	63	64	36
Median DOR (mo)	9.4	6.9	5.6
Median PFS (mo)	8.3	6.3	4.2
Median PFS -intracranial (mo)	12.8	12.5	8.3
PFS @ 1-year	54	50	34
Interim OS	0.96 (0.67-1.35	0.77 (0.49-1.21)	

Passaro A, et al. Ann Oncol 2024: 35; 77

Non-Small Cell Lung Cancer With *EGFR* Alterations: Post-Osi - LBA8505

Subcutaneous amivantamab vs intravenous amivantamab, both in combination with lazertinib, in refractory *EGFR*-mutated, advanced non-small cell lung cancer

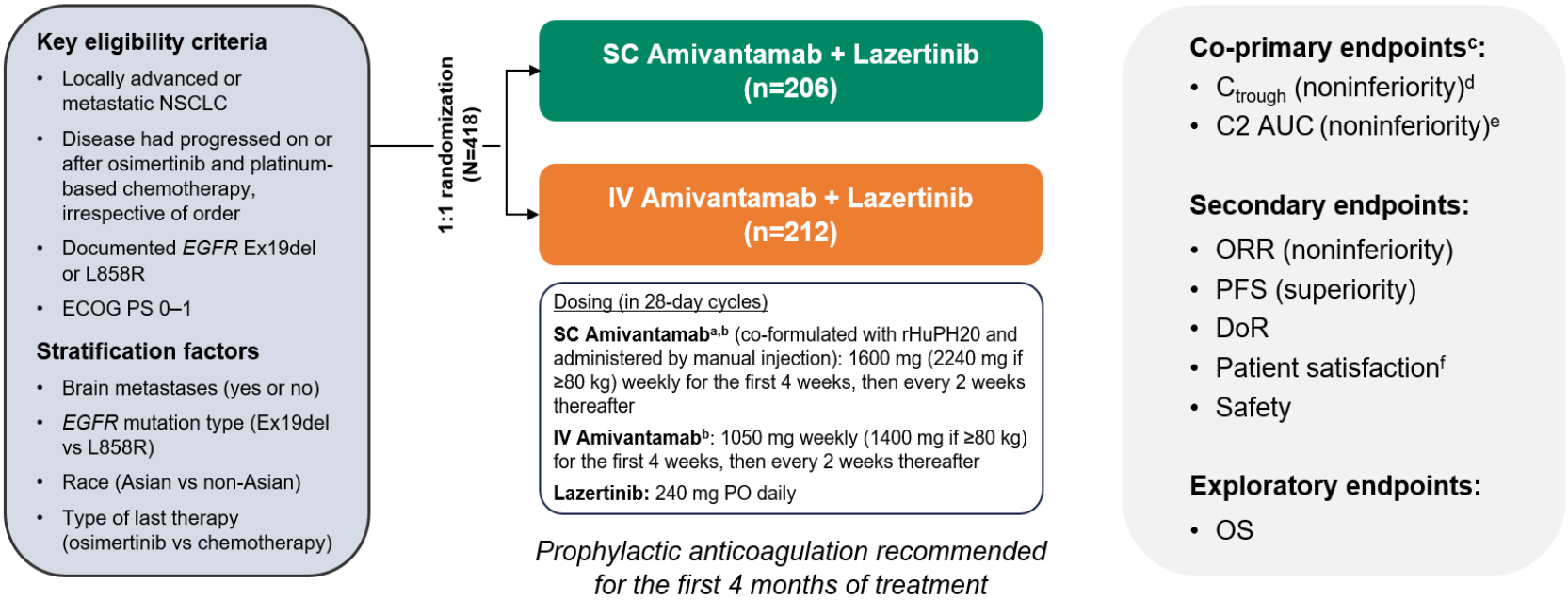
Primary results, including overall survival, from the global, phase 3, randomized controlled PALOMA-3 trial

Natasha B Leighl,[1] Hiroaki Akamatsu,[2] Sun Min Lim,[3] Ying Cheng,[4] Anna R Minchom,[5] Melina E Marmarelis,[6] Rachel E Sanborn,[7] James Chih-Hsin Yang,[8] Baogang Liu,[9] Thomas John,[10] Bartomeu Massutí,[11] Alexander I Spira,[12] John Xie,[13] Debopriya Ghosh,[13] Ali Alhadab,[14] Remy B Verheijen,[15] Mohamed Gamil,[16] Joshua M Bauml,[16] Mahadi Baig,[13] Antonio Passaro[17]

[1]Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Internal Medicine III, Wakayama Medical University, Wakayama, Japan; [3]Division of Medical Oncology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea; [4]Jilin Cancer Hospital, Changchun, China; [5]Drug Development Unit, The Royal Marsden Hospital and The Institute of Cancer Research, Sutton, UK; [6]Division of Hematology and Oncology, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [7]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA; [8]Department of Medical Oncology, National Taiwan University Cancer Center, Taipei, Taiwan; [9]Harbin Medical University Cancer Hospital, Harbin, China; [10]Peter MacCallum Cancer Centre, The University of Melbourne, Melbourne, Australia; [11]Alicante University Dr. Balmis Hospital, ISABIAL, Alicante, Spain; [12]Virginia Cancer Specialists, Fairfax, VA, USA; [13]Janssen Research & Development, Raritan, NJ, USA; [14]Janssen Research & Development, San Diego, CA, USA; [15]Janssen Research & Development, Leiden, The Netherlands; [16]Janssen Research & Development, Spring House, PA, USA; [17]European Institute of Oncology IRCCS, Milano, Italy.

Non-Small Cell Lung Cancer With *EGFR* Alterations: PALOMA-3

PALOMA-3: Phase 3 Study Design



PALOMA-3 (ClinicalTrials.gov Identifier: NCT05388669) enrollment period: August 2022 to October 2023; data cutoff: 03-Jan-2024.

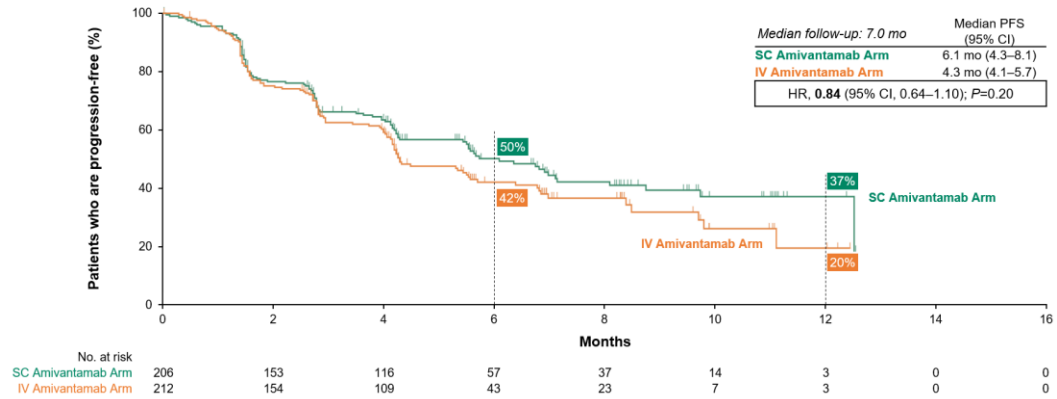
[a]SC amivantamab was co-formulated with rHuPH20 at a concentration of 160 mg/mL. [b]C1 for IV: Days 1 to 2 (Day 2 applies to IV split dose only [350 mg on Day 1 and the remainder on Day 2]), 8, 15, and 22; C1 for SC: Days 1, 8 , 15, and 22; after C1 for all: Days 1 and 15 (28-day cycles). [c]For calculating primary and key secondary outcomes, we estimated that a sample size of 400 patients would provide >95% power for a 1-sided alpha of 0.05 allocated to each of the co-primary endpoints and 80% power with a 1-sided alpha of 0.025 allocated to ORR. A hierarchical testing approach at a 2-sided alpha of 0.05 was used for the co-primary endpoints (noninferiority), followed by ORR (noninferiority) and PFS (superiority), with a combined 2-sided alpha of 0.05. [d]Two definitions of the same endpoint were used as per regional health authority guidance. [e]Measured between C2D1 and C2D15. [f]Assessed by modified TASQ.

AUC, area under the concentration-time curve; C, Cycle; C_{trough}, observed serum concentration of amivantamab at steady state; D, Day; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, Exon 19 deletion; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; rHuPH20, hyaluronidase; SC, subcutaneous; TASQ, Therapy Administration Satisfaction Questionnaire.

Non-Small Cell Lung Cancer With *EGFR* Alterations: PALOMA-3

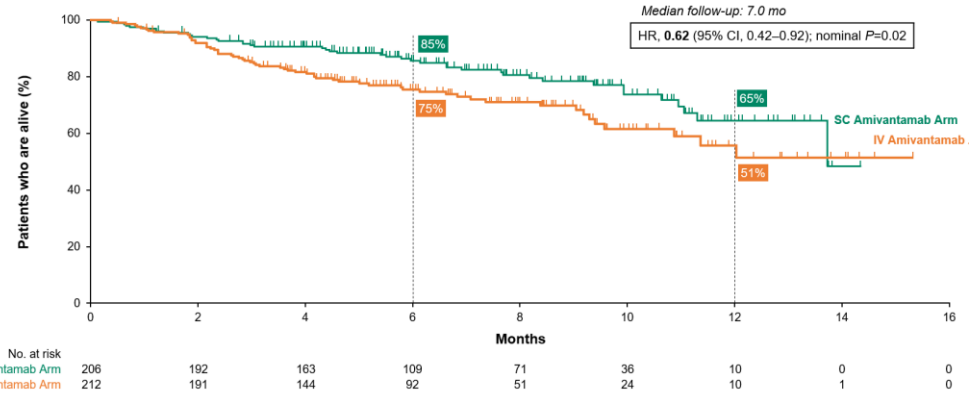
Progression-free Survival

PFS was numerically longer with SC vs IV amivantamab, with an HR of 0.84

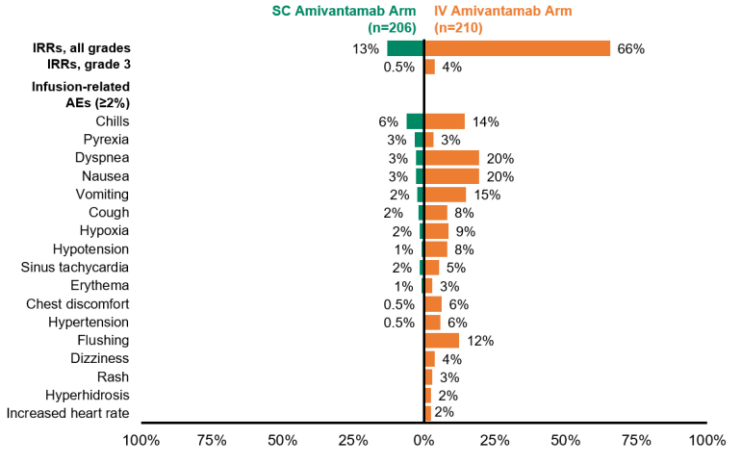


Overall Survival

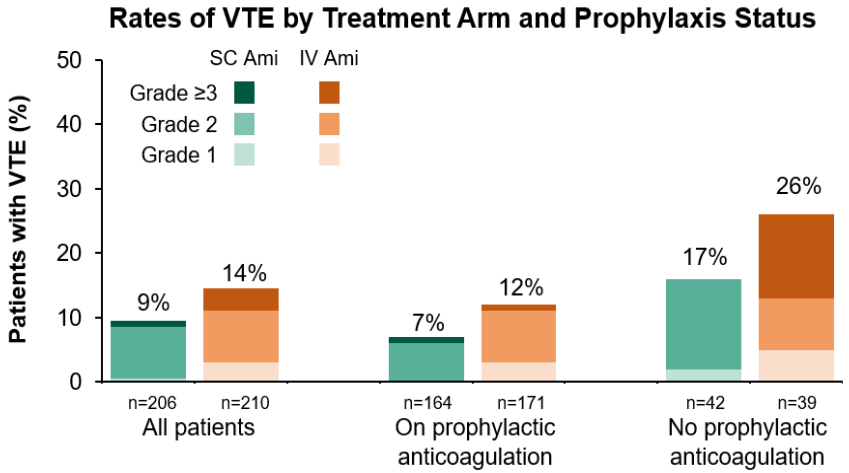
There was an OS benefit associated with SC amivantamab, with an HR of 0.62 compared to the IV amivantamab arm[a]



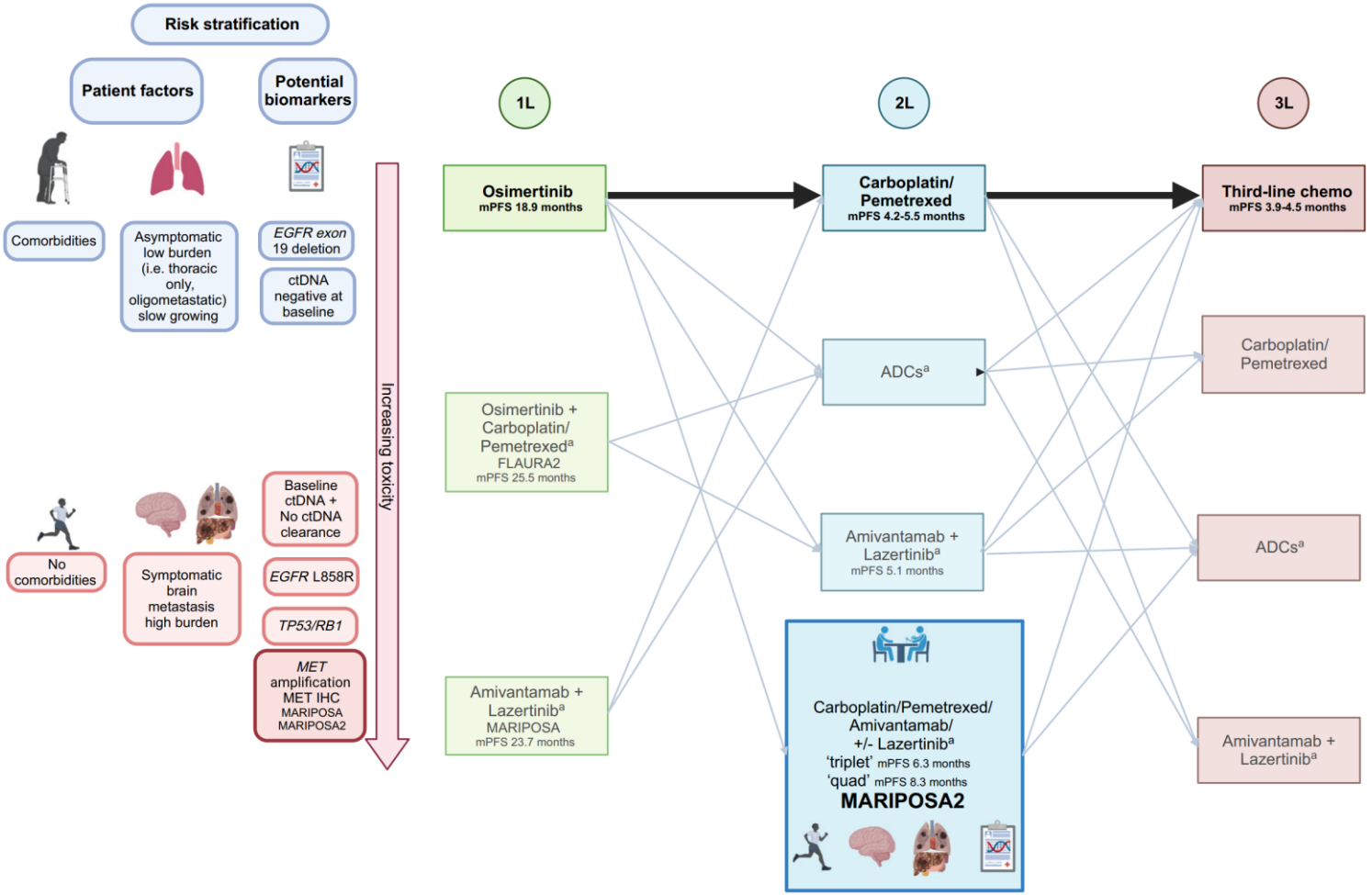
Non-Small Cell Lung Cancer With *EGFR* Alterations: PALOMA-3



- IRRs were observed in 13% of patients in the SC arm vs 66% in the IV arm, representing a 5-fold reduction
  - There were no grade 4 or 5 IRRs
  - Most IRRs occurred during Cycle 1
- IRRs leading to hospitalization were not observed in the SC arm vs 2 events in the IV arm
- No IRR-related discontinuations occurred in the SC arm vs 4 events in the IV arm



Non-Small Cell Lung Cancer With *EGFR* Alterations: Sequencing



Chen MF, et al. Ann Oncol 2024: 35; 4

Non-Small Cell Lung Cancer with *ALK* Fusion: LBA8503

2024 ASCO ANNUAL MEETING

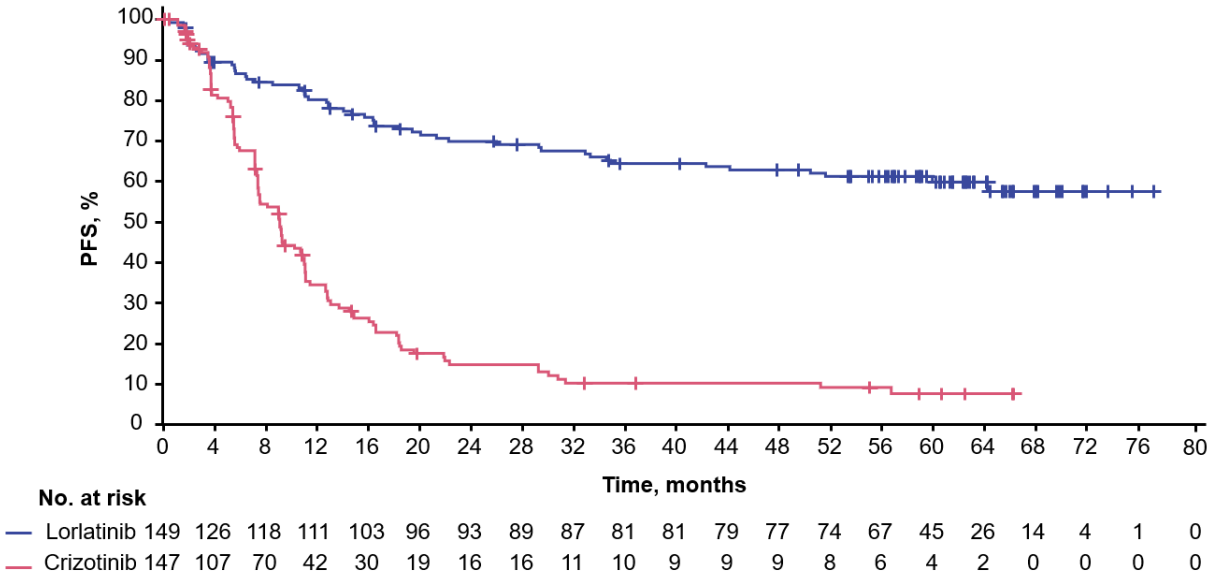
Lorlatinib vs Crizotinib in Treatment-Naive Patients With Advanced *ALK*+ Non-Small Cell Lung Cancer: 5-Year Progression-Free Survival and Safety From the CROWN Study

Benjamin J. Solomon,[1] Geoffrey Liu,[2] Enriqueta Felip,[3] Tony S. K. Mok,[4] Ross A. Soo,[5] Julien Mazieres,[6] Alice T. Shaw,[7] Filippo de Marinis,[8] Yasushi Goto,[9] Yi-Long Wu,[10] Dong-Wan Kim,[11] Jean-François Martini,[12] Rossella Messina,[13] Jolanda Paolini,[13] Anna Polli,[13] Despina Thomaidou,[14] Francesca Toffalorio,[13] Todd M. Bauer[15]

[1]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [2]Princess Margaret Cancer Centre, Toronto, ON, Canada; [3]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [4]State Key Laboratory of Translational Oncology, Chinese University of Hong Kong, Hong Kong; [5]National University Cancer Institute, Singapore; [6]Toulouse University Hospital and Centre de Recherche Cancérologie Toulouse CRCT, INSERM, France; [7]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [8]European Institute of Oncology, IRCCS, Milan, Italy; [9]National Cancer Center Hospital, Tokyo, Japan; [10]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, Guangdong, China; [11]Seoul National University College of Medicine and Seoul National University Hospital, Seoul, South Korea; [12]Pfizer, La Jolla, CA, USA; [13]Pfizer, Milan, Italy; [14]Pfizer, Athens, Greece; [15]Greco-Hainsworth Centers for Research/Tennessee Oncology, Nashville, TN, USA

Non-Small Cell Lung Cancer with *ALK* Fusion: CROWN Study

At 60.2 Months of Median Follow-Up, Median PFS by Investigator Was Still Not Reached With Lorlatinib



	Lorlatinib (n=149)	Crizotinib (n=147)
Events, n	55	115
PFS, median (95% CI), months	NR (64.3-NR)	9.1 (7.4-10.9)
HR (95% CI)	**0.19 (0.13-0.27)**	

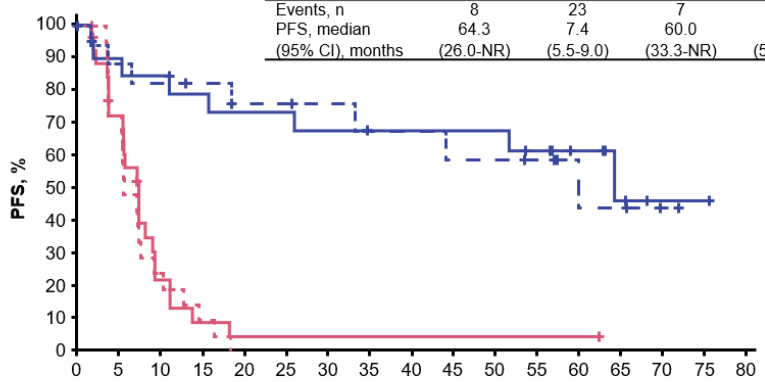
HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival.

Non-Small Cell Lung Cancer with *ALK* Fusion – CROWN Study

Lorlatinib Treatment Benefited Patients With Poor Prognostic Biomarkers

PFS by *EML4::ALK* Fusion Variant

	Variant 1		Variant 3a/b	
	Lorlatinib (n=20)	Crizotinib (n=26)	Lorlatinib (n=18)	Crizotinib (n=23)
Events, n	8	23	7	21
PFS, median (95% CI), months	64.3 (26.0-NR)	7.4 (5.5-9.0)	60.0 (33.3-NR)	5.6 (5.3-7.6)



***EML4::ALK* variant 1**
No. at risk

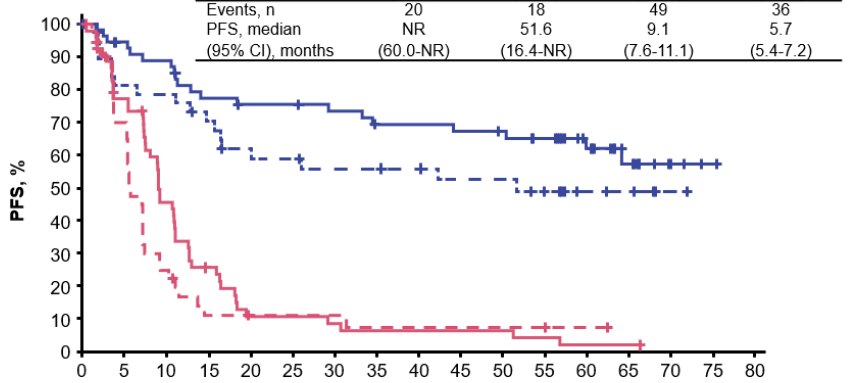
Lorlatinib	20	17	16	14	13	13	12	11	11	11	11	9	6	3	1	1	0
Crizotinib	26	18	5	2	1	1	1	1	1	1	1	1	1	0	0	0	0

***EML4::ALK* variant 3**
No. at risk

Lorlatinib	18	15	14	13	11	11	9	8	8	7	7	6	3	3	1	0	-
Crizotinib	23	15	5	2	0	0	0	0	0	0	0	0	0	0	0	0	-

PFS by *TP53* Status

	Lorlatinib		Crizotinib	
	TP53 mut (-) (n=56)	*TP53* mut (+) (n=41)	*TP53* mut (-) (n=58)	*TP53* mut (+) (n=42)
Events, n	20	18	49	36
PFS, median (95% CI), months	NR (60.0-NR)	51.6 (16.4-NR)	9.1 (7.6-11.1)	5.7 (5.4-7.2)



Lorlatinib
No. at risk

TP53 mut (-)	56	50	47	40	38	38	36	33	33	32	31	28	20	12	4	1	0
TP53 mut (+)	41	30	29	25	21	20	18	18	17	15	15	12	6	4	1	0	0

Crizotinib
No. at risk

TP53 mut (-)	58	40	23	12	5	5	4	3	3	3	3	2	1	1	0	-	-
TP53 mut (+)	42	28	10	4	3	3	3	2	2	2	2	2	1	0	0	-	-

ctDNA, circulating tumor DNA; mut, mutation; NR, not reached; PFS, progression-free survival. Based on ctDNA from plasma collected at screening.

Non-Small Cell Lung Cancer (NSCLC) With *EGFR* Alterations: LBA4

2024 ASCO® ANNUAL MEETING

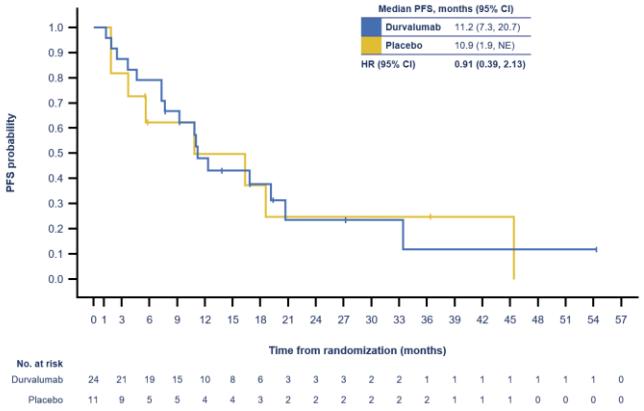
Osimertinib after definitive chemoradiotherapy in patients with unresectable stage III epidermal growth factor receptor-mutated (EGFRm) NSCLC: primary results of the Phase 3 LAURA study

Suresh S. Ramalingam,[1] Terufumi Kato, Xiaorong Dong, Myung-Ju Ahn, Le-Van Quang, Nopadol Soparattanapaisarn, Takako Inoue, Chih-Liang Wang, Meijuan Huang, James Chih-Hsin Yang, Manuel Cobo, Mustafa Özgüroğlu, Ignacio Casarini, Dang-Van Khiem, Virote Sriuranpong, Eduardo Cronemberger, Xiangning Huang, Toon van der Gronde, Dana Ghiorghiu, Shun Lu

[1]Emory University School of Medicine, Winship Cancer Institute, Atlanta, GA, USA

Non-Small Cell Lung Cancer With *EGFR* Alterations: LAURA Study

PACIFIC EGFRm *post-hoc* subgroup analysis



LAURA Phase 3 double-blind study design

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

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

Osimertinib 80 mg, once daily

Randomization 2:1 (N=216)

Stratification by:
Concurrent vs sequential CRT
Stage IIIA vs stage IIIB/IIIC
China vs non-China

Placebo, once daily

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

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

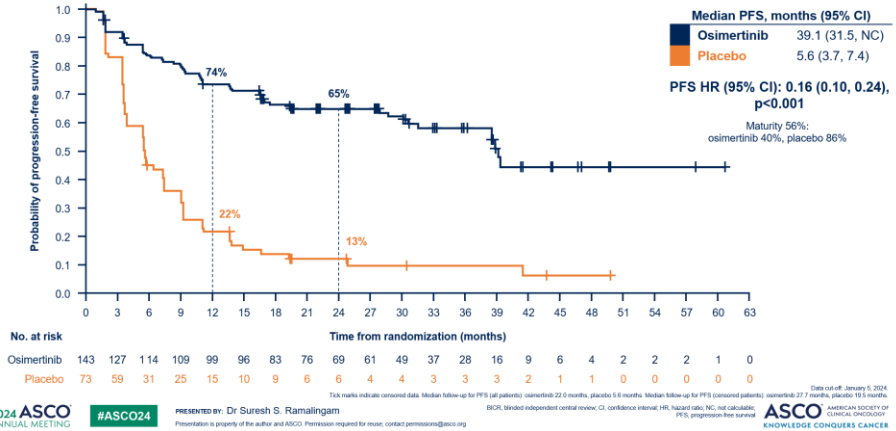
Tumor assessments:
- Chest CT / MRI and brain MRI
- At baseline, every 8 weeks to Week 48, then every 12 weeks until BICR-assessed progression

Endpoints
- **Primary endpoint:** PFS assessed by BICR per RECIST v1.1 (sensitivity analysis: PFS by investigator assessment)
- **Secondary endpoints included:** OS, CNS PFS, safety

Naidoo J, et al. JTO 2023, 18(5): 657

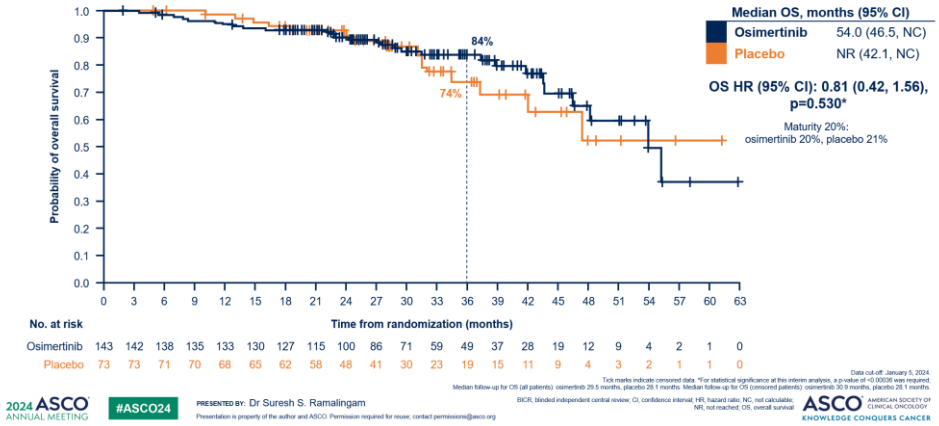
Non-Small Cell Lung Cancer With *EGFR* Alterations: LAURA Study

Progression-free survival by BICR



Interim analysis of overall survival

- In the placebo arm, 81% of patients with BICR-confirmed progression crossed over to osimertinib



Small Cell Lung Cancer (SCLC) Consolidation in Limited-Stage – LBA5

2024 ASCO ANNUAL MEETING

ADRIATIC: durvalumab as consolidation treatment for patients with limited-stage small-cell lung cancer (LS-SCLC)

David R. Spigel, Ying Cheng, Byoung Chul Cho, Konstantin Laktionov, Jian Fang, Yuanbin Chen, Yoshitaka Zenke, Ki Hyeong Lee, Qiming Wang, Alejandro Navarro, Reyes Bernabe, Eva Buchmeier, John Wen-Cheng Chang, Isamu Okamoto, Sema Sezgin Goksu, Andrzej Badzio, Bethany Gill, Hema Gowda, Haiyi Jiang, Suresh Senan

Small Cell Lung Cancer (SCLC) Consolidation in Limited-Stage – ADRIATIC

ADRIATIC study design

Phase 3, randomized, double-blind, placebo-controlled, multicenter, international study (NCT03703297)

- Stage I–III LS-SCLC (stage I/II inoperable)
- WHO PS 0 or 1
- Had not progressed following cCRT*
- PCI* permitted before randomization

N=730

R‡

Durvalumab
1500 mg Q4W
N=264

Placebo
Q4W
N=266

Durvalumab + tremelimumab
D 1500 mg Q4W + T 75 mg Q4W for 4 doses, followed by D 1500 mg Q4W
N=200

cCRT components
- Four cycles of platinum and etoposide (three permitted†)
- RT: 60–66 Gy QD over 6 weeks or 45 Gy BID over 3 weeks
- RT must commence no later than end of cycle 2 of CT

Stratified by:
Disease stage (I/II vs III)
PCI (yes vs no)

Treatment until investigator-determined progression or intolerable toxicity, or for a **maximum of 24 months**

Dual primary endpoints:
- Durvalumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

Key secondary endpoints:
- Durvalumab + tremelimumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

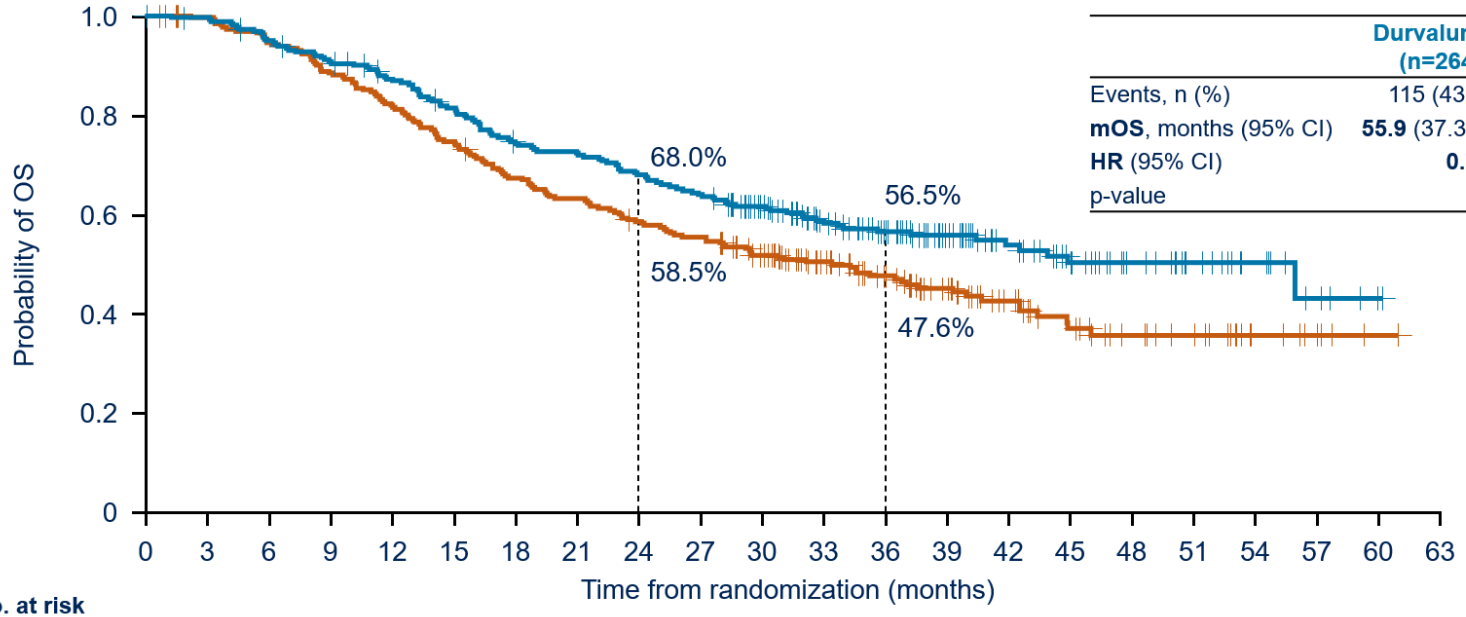
Other secondary endpoints:
- OS/PFS landmarks
- Safety

*cCRT and PCI treatment, if received per local standard of care, must have been completed within 1–42 days prior to randomization.
†If disease control was achieved and no additional benefit was expected with an additional cycle of chemotherapy, in the opinion of the investigator.
‡The first 600 patients were randomized in a 1:1:1 ratio to the 3 treatment arms; subsequent patients were randomized 1:1 to either durvalumab or placebo.

Small Cell Lung Cancer (SCLC) Consolidation in Limited-Stage – ADRIATIC

Overall survival (dual primary endpoint)

- Median duration of follow up in censored patients: 37.2 months (range 0.1–60.9)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

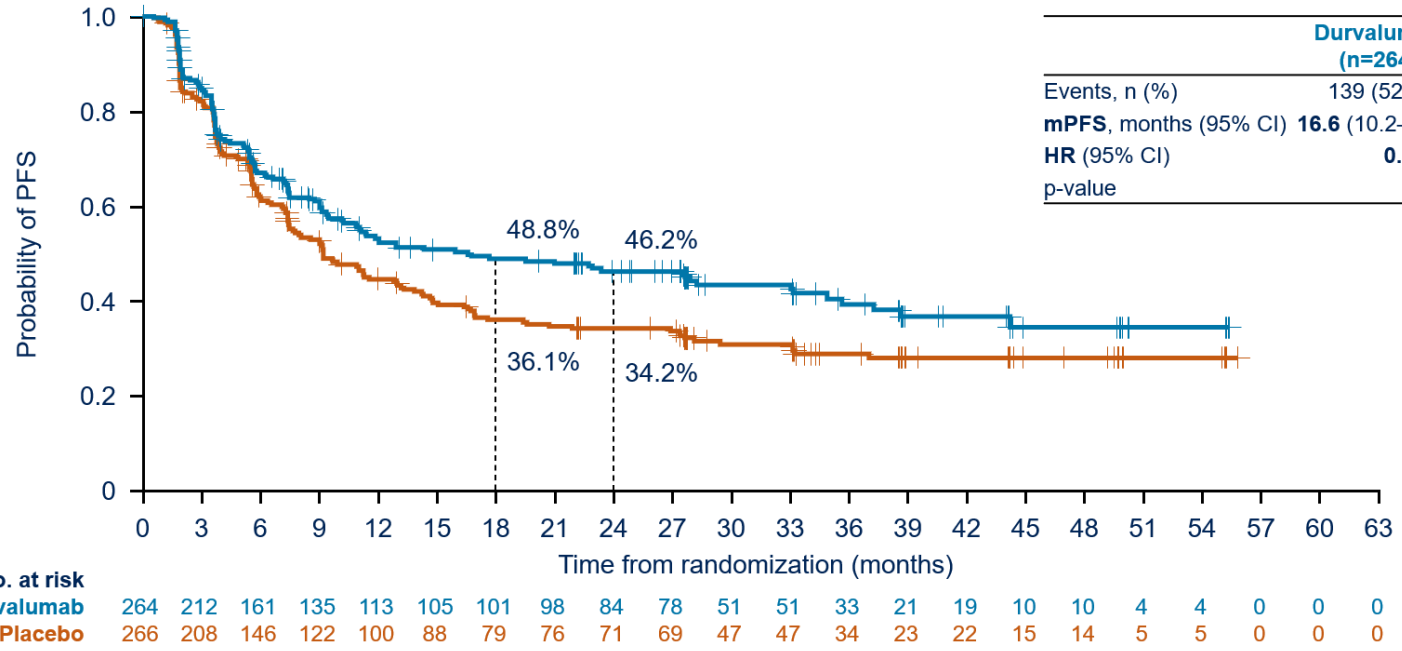
No. at risk																					
Durvalumab	264	261	248	236	223	207	189	183	172	162	141	110	90	68	51	39	27	19	11	5	1	0
Placebo	266	260	247	231	214	195	175	164	151	143	123	97	80	62	44	31	23	19	8	5	1	0

OS was analyzed using a stratified log-rank test adjusted for receipt of PCI (yes vs no). The significance level for testing OS at this interim analysis was 0.01679 (2-sided) at the overall 4.5% level, allowing for strong alpha control across interim and final analysis timepoints.

Small Cell Lung Cancer (SCLC) Consolidation in Limited-Stage – ADRIATIC

Progression-free survival* (dual primary endpoint)

- Median duration of follow up in censored patients: 27.6 months (range 0.0–55.8)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	139 (52.7)	169 (63.5)
mPFS, months (95% CI)	**16.6** (10.2–28.2)	**9.2** (7.4–12.9)
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

No. at risk																						
Durvalumab	264	212	161	135	113	105	101	98	84	78	51	51	33	21	19	10	10	4	4	0	0	0
Placebo	266	208	146	122	100	88	79	76	71	69	47	47	34	23	22	15	14	5	5	0	0	0

*By BICR per RECIST v1.1.

PFS was analyzed using a stratified log-rank test adjusted for disease stage (I/II vs III) and receipt of PCI (yes vs no). The significance level for testing PFS at this interim analysis was 0.00184 (2-sided) at the 0.5% level, and 0.02805 (2-sided) at the overall 5% level. Statistical significance for PFS was achieved through the recycling multiple testing procedure framework and testing at the 5% (2-sided) alpha level (adjusted for an interim and final analysis).

Small Cell Lung Cancer (SCLC)
DLL3- Bispecific Antibody – 8015

DeLLphi-301: Tarlatamab phase 2 trial in small cell lung cancer (SCLC)—Efficacy and safety analyzed by presence of brain metastases

Anne-Marie C. Dingemans,[1] Myung-Ju Ahn,[2] Fiona Blackhall,[3] Martin Reck,[4] Horst-Dieter Hummel,[5] Suresh S. Ramalingam,[6] Melissa L. Johnson,[7] Hiroaki Akamatsu,[8] Jürgen Wolf,[9] Jacob Sands,[10] Taofeek K.Owonikoko,[11] Hossein Borghaei,[12] Sujoy Mukherjee,[13] Shuang Huang,[13] Pablo Martinez,[13] Luis Paz-Ares[14]

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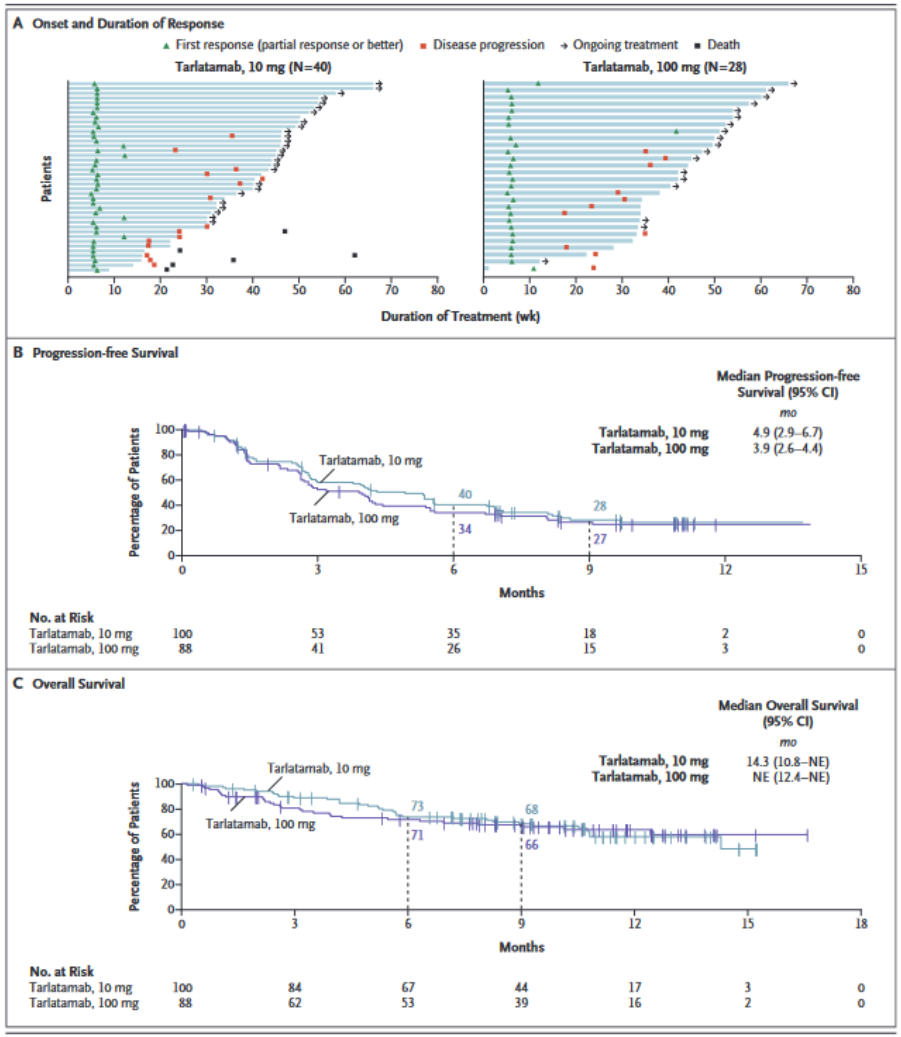
Small Cell Lung Cancer (SCLC)
DLL3- Bispecific Antibody – DeLLphi-301



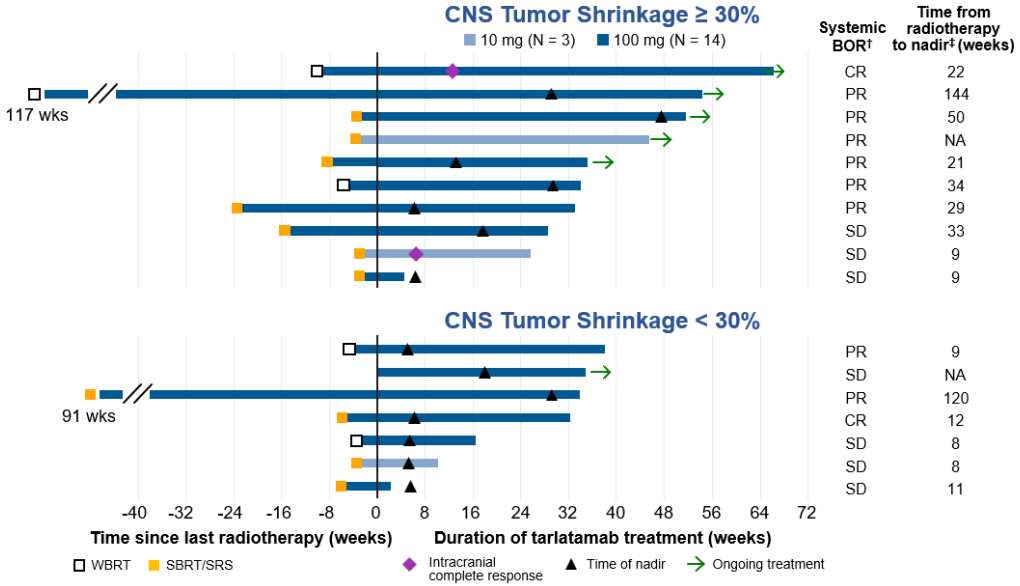
Ahn MJ, et al. NEJM 2023

Small Cell Lung Cancer (SCLC)
DLL3- Bispecific Antibody – DeLLphi-301

Intracranial Activity*

Tarlatamab 10 mg (n = 3) or 100 mg (n = 14) Q2W with baseline CNS lesion ≥ 10 mm

- **mRANO BM§ analyses (N = 17)**
  - CNS tumor shrinkage ≥ 30% in 10 of 17 patients (59%)
  - Intracranial disease control in 94% (16 of 17) patients (95% CI, 71.3–99.9)
  - Median duration of intracranial disease control was NE (range, 2.6–13.9+ months)
  - CNS disease progression per modified RANO-BM occurred in 3 of 17 patients (18%)



CNS tumor shrinkage was observed in patients with previously treated brain metastases

*The CNS measurable analysis set included patients who had ≥ 2 brain scans (baseline and post-baseline) and were identified per modified RANO-BM by BICR as having ≥ 1 brain lesion ≥ 10 mm at baseline. †Systemic BOR was determined using RECIST v1.1 by BICR. ‡Minimum percentage change from baseline (smallest SLD) before disease progression. Median follow-up: 11.8 months. §mRANO BM represents RANO BM criteria with the following modifications: (1) corticosteroid data and clinical status were not incorporated into imaging reads; (2) diffusion weighted imaging MRI sequences were not required but were made available to the independent reviewer if received. **BICR**, blinded independent central review; **BOR**, best overall response; **CNS**, central nervous system; **CR**, complete response; **mRANO BM**, modified response assessment in neuro-oncology criteria for brain metastases; **MRI**, magnetic resonance imaging; **NA**, not available; **NE**, not estimable; **PR**, partial response; **RECIST**, Response Evaluation Criteria in Solid Tumors; **RT,** radiotherapy; **SBRT**, stereotactic body radiation therapy; **SD**, stable disease; **SLD**, sum of longest diameter; **SRS**, stereotactic radiosurgery; **WBRT**, whole brain radiation therapy.

Mesothelioma LBA8002

2024 ASCO ANNUAL MEETING

ETOP 13-18 BEAT-meso

A randomized phase III study of Bevacizumab (B) and standard Chemotherapy (C) with or without Atezolizumab (A), as first-line treatment for advanced pleural mesothelioma

Sanjay Popat, Enriqueta Felip, Urania Dafni, Anthony Pope, Susana Cedres Perez, Riyaz N.H. Shah, Filippo de Marinis, Laura Cove Smith, Reyes Bernabe Caro, Martin Früh, Kristiaan Nackaerts, Laurent Greillier, Amina Scherz, Bartomeu Massuti, Saemi Schaer, Spasenija Savic Prince, Heidi Roschitzki-Voser, Barbara Ruepp, Solange Peters, Rolf A. Stahel, for the ETOP 13-18 BEAT-meso Collaborators

Mesothelioma: ETOP BEAT-meso

ETOP BEAT-meso: Study Design

Open-label, randomised two-arm, multicentre, phase III trial

Protocol amendment (v3.1): Primary endpoint **PFS & OS → OS only**
Sample size from **320 → 400 patients**

Key eligibility criteria

- ECOG PS 0-1
- Histologically confirmed advanced malignant pleural mesothelioma
- Not amenable for radical surgery
- Evaluable/measurable disease assessed by mRECIST v1.1

R* 1:1

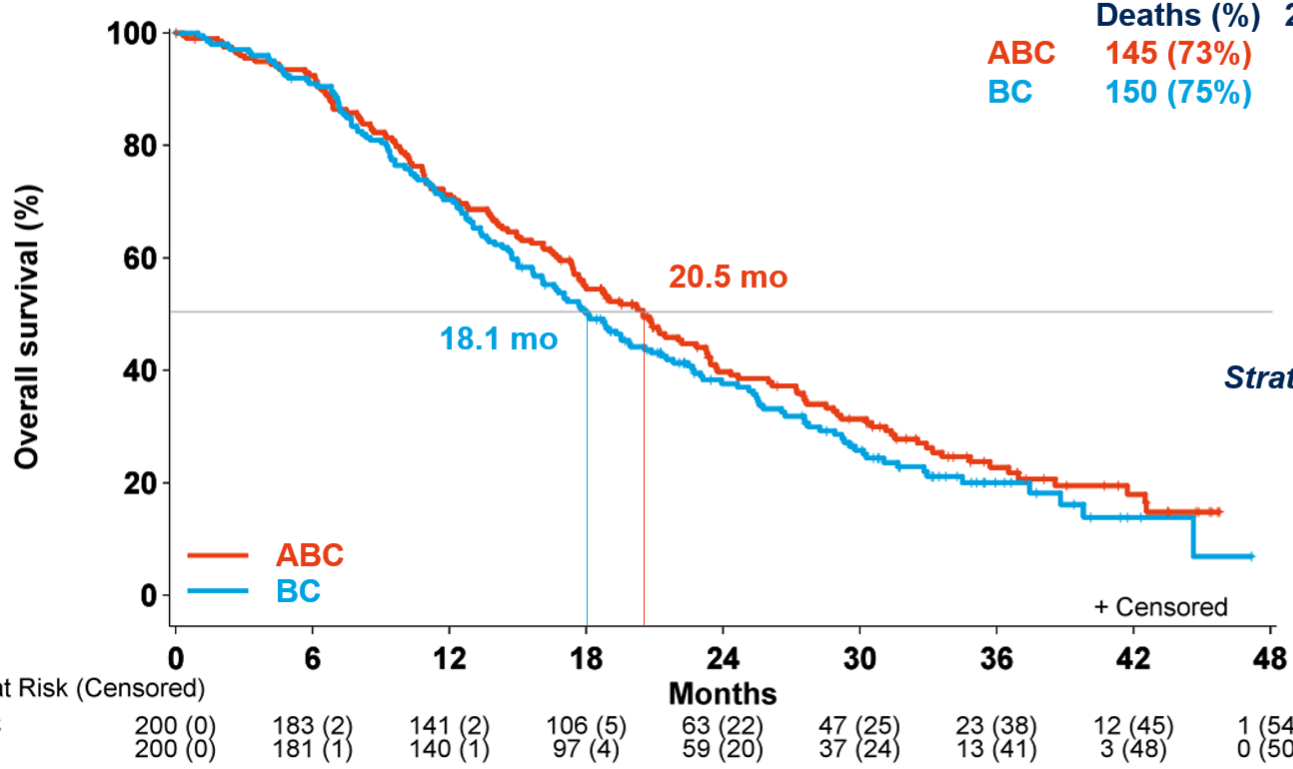
ABC (n=200)
Atezolizumab: 1200mg Q3W
Bevacizumab: 15mg/kg Q3W
} until PD or unacceptable toxicity
Chemotherapy (4 - 6 cycles):
Carboplatin AUC 5 + Pemetrexed 500mg/m^2 Q3W

BC (n=200)
Bevacizumab: 15mg/kg Q3W until PD or unacceptable toxicity
Chemotherapy (4 - 6 cycles):
Carboplatin AUC 5 + Pemetrexed 500mg/m^2 Q3W

*__Stratified by__: Histology (Epithelioid vs Not) & Stage (IV vs Other)

Mesothelioma: ETOP BEAT-meso

ETOP BEAT-meso: Primary endpoint - OS



	Deaths (%)	2-yr OS% (95% CI)
ABC	145 (73%)	40% (33%-47%)
BC	150 (75%)	38% (31%-45%)

HR (95% CI):
0.84 (0.66 – 1.06)
Log-rank p=0.14

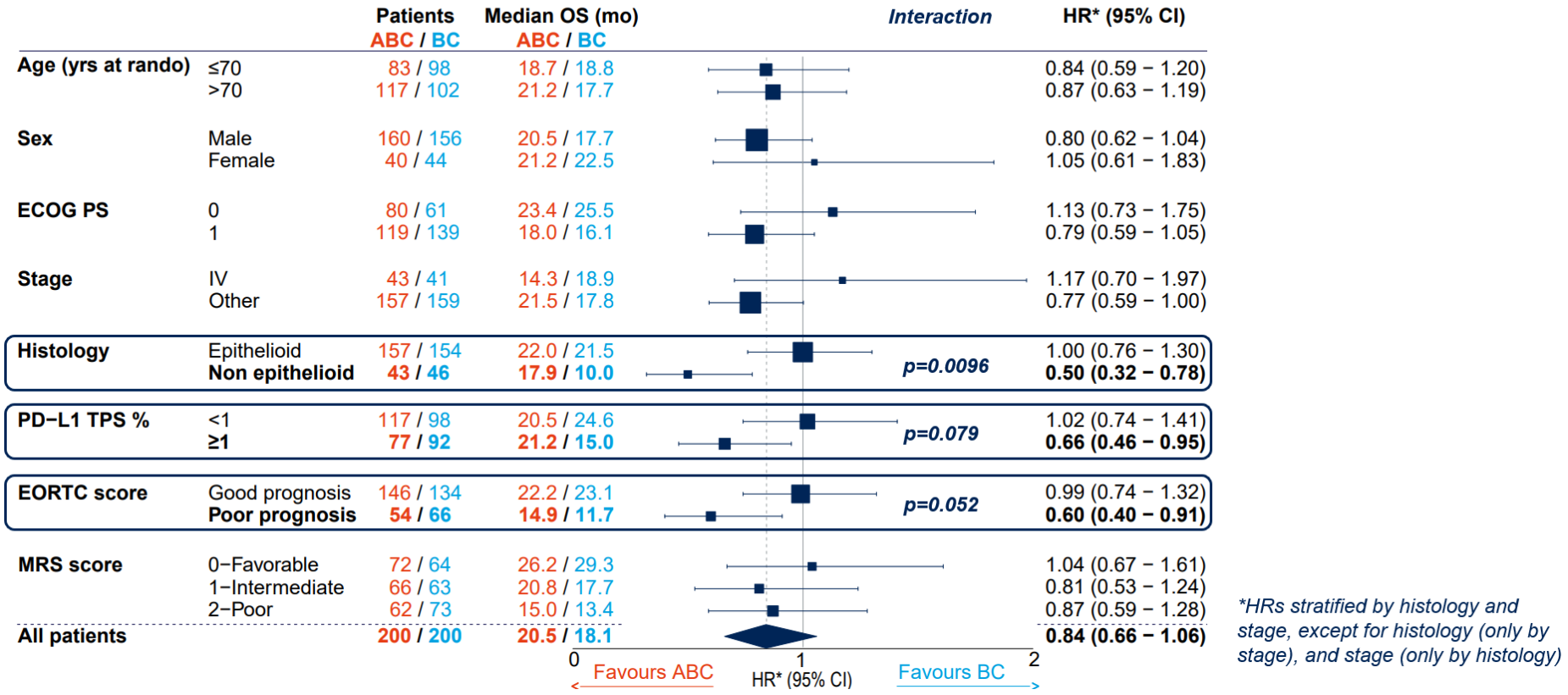
Stratified by histology & stage

Interim for efficacy (previously performed):

Boundary for OS not crossed

Mesothelioma: ETOP BEAT-meso

ETOP BEAT-meso: OS for subgroups of clinical interest



*HRs stratified by histology and stage, except for histology (only by stage), and stage (only by histology)

Questions?

Thank you

→ **Muhammad-furqan@uiowa.edu**