Lung Cancer UPDATES
WCLC HIGHLIGHTS
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Iniciativa científica de:
GECP lung cancer research

Cáncer de pulmón no microcítico estadio IV (avanzado) con driver

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Disclosures

- ***Advisory / Consultancy :*** *AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Roche, Takeda, Pfizer, Janseng-Cilag*

- ***Speaker Bureau / Expert testimony****: AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Pfizer, Roche, Takeda, Pierre-Fabre, Regeneron*

- ***Travel / Accommodation / Expenses*** *:Bristol-Myers Squibb, Pfizer, Roche, Takeda, Astra Zeneca*

EGFR mutations

FLAURA 2: Osimertinib with or without Chemotherapy in *EGFR*-Mutated Advanced NSCLC

Study design

Patients with untreated locally advanced / metastatic EGFRm NSCLC

Key inclusion criteria:

- Aged ≥18 years
- Pathologically confirmed non-squamous NSCLC
- Ex19del / L858R (local / central test)
- WHO PS 0 / 1
- Stable CNS metastases were allowed
- Brain scans at baseline (MRI / CT; mandatory)

N=557

R 1:1

Stratified by:

- **Race** (Asian Chinese / Asian non-Chinese / non-Asian)
- **EGFRm test** (local / central)
- **WHO PS** (0 / 1)

Osimertinib 80 mg (QD) + pemetrexed 500 mg/m² + carboplatin AUC5 or cisplatin 75 mg/m² (Q3W for 4 cycles for platinum-based treatments) → **Maintenance osimertinib 80 mg (QD) + pemetrexed 500 mg/m² (Q3W)**

Treatment beyond PD allowed per investigator discretion

Osimertinib 80 mg (QD)

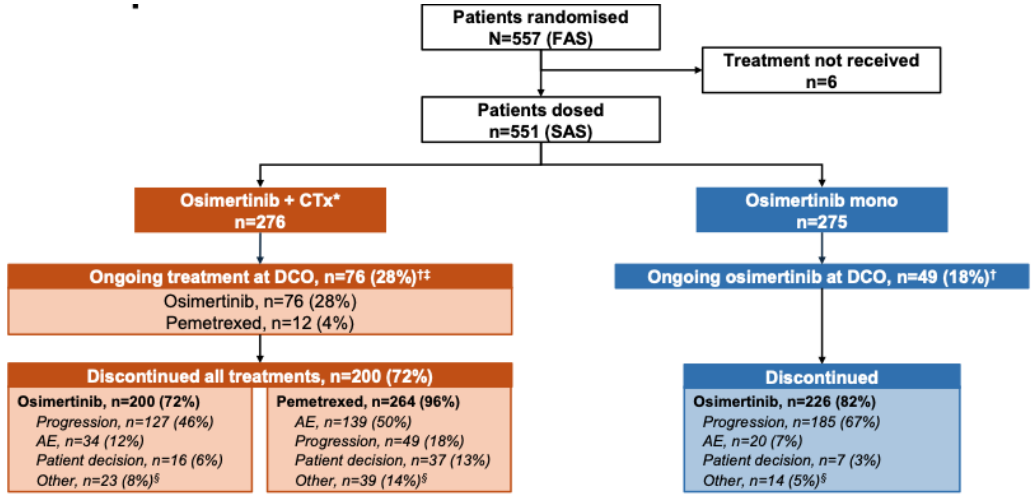
Follow-up:

- RECIST v1.1 assessment at 6 and 12 weeks, then Q12W until RECIST v1.1-defined radiological PD
- Survival follow-up for Q12W until data cut-off for the planned final OS analysis

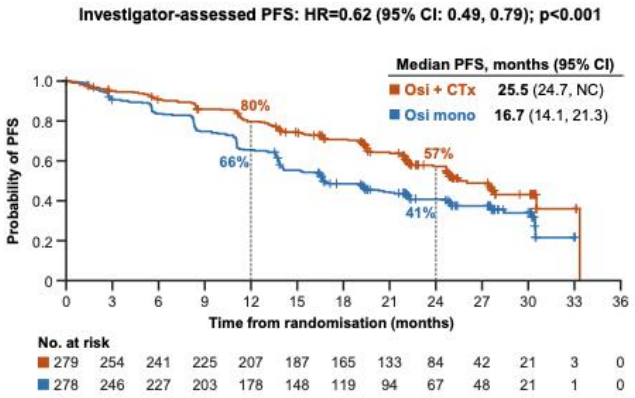
- **Primary endpoint:** Investigator-assessed PFS (RECIST v1.1)[1]
- **Secondary endpoints included:** OS, TFST, DoR, DCR, PFS2, TSST, HRQoL

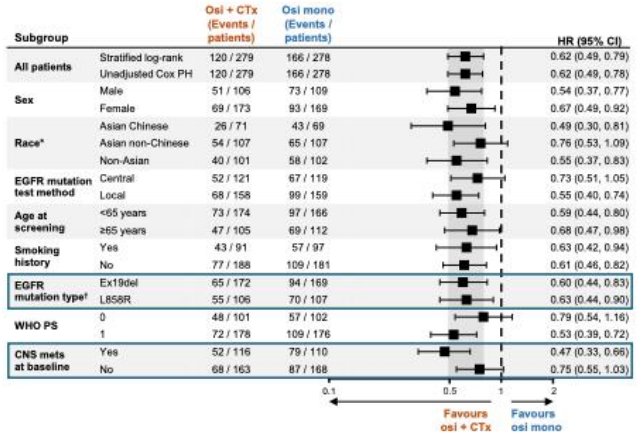
OS was a key secondary endpoint*
Final OS analysis performed at 57% maturity

Patient disposition



Progression Free Survival





Osi + CTx showed a statistically significant and clinically meaningful improvement in PFS versus osi mono; PFS benefit was consistent across predefined subgroups

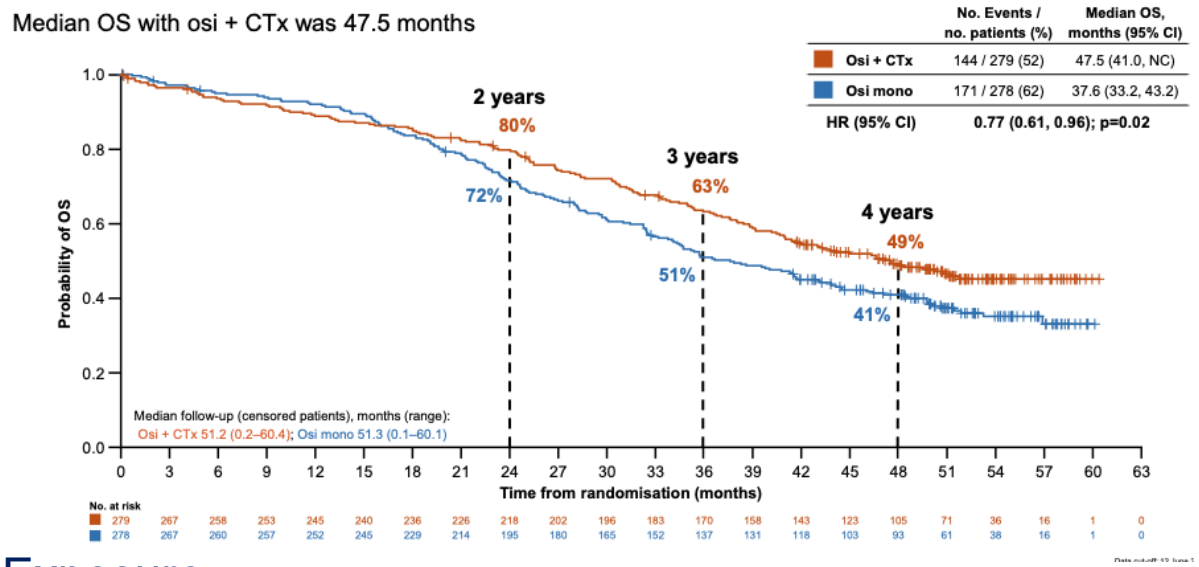
Baseline Characteristics

Characteristic, %*	Osi + CTx (n=279)	Osi mono (n=278)
Sex: male / female	38 / 62	39 / 61
Age: median (range), years	61 (26–83)	62 (30–85)
Race: Asian Chinese / Asian non-Chinese / non-Asian / missing†	25 / 39 / 35 / <1	25 / 38 / 36 / 1
WHO PS: 0 / 1‡	37 / 62	37 / 63
Smoking status: never / current / former	67 / 1 / 31	65 / 1 / 33
Histology: adenocarcinoma / adenosquamous / other	99 / 1 / 1	99 / 0 / 1
EGFR mutation type: Ex19del / L858R§	61 / 38	60 / 38
Locally advanced / metastatic	5 / 95	3 / 97
CNS metastases present at baseline	42	40
Baseline tumour size: median (range), mm	57 (10–284)	57 (11–221)

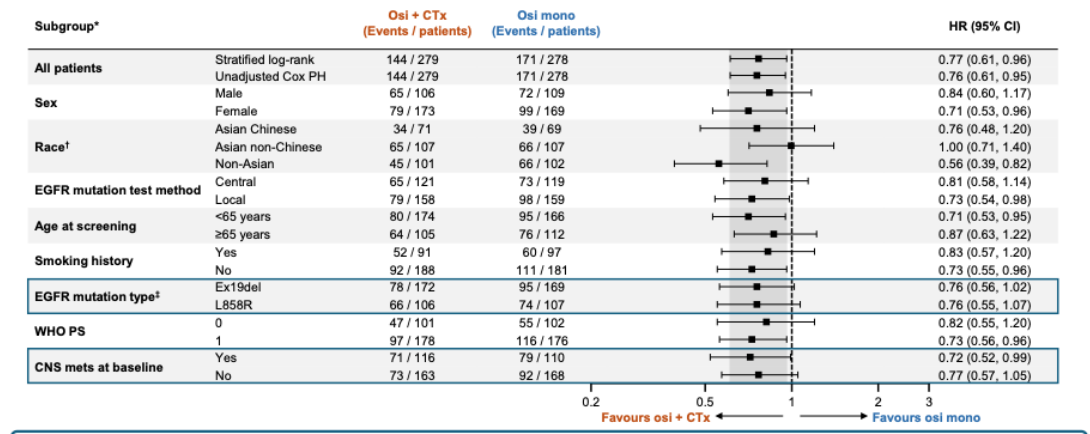
EGFR mutations

FLAURA 2: Osimertinib with or without Chemotherapy in *EGFR*-Mutated Advanced NSCLC

Overall Survival

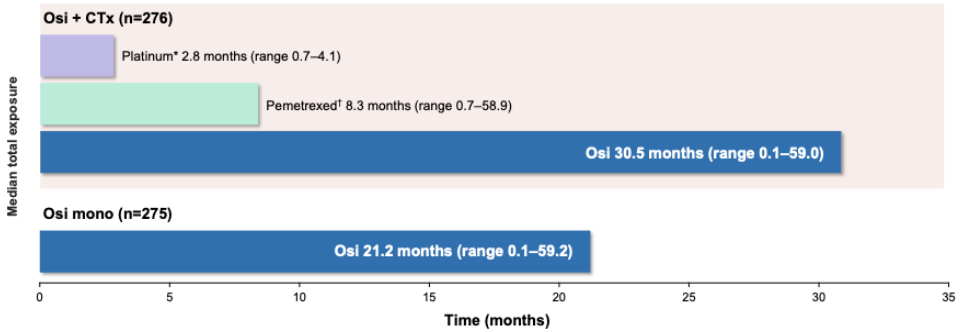


OS subgroup analysis



OS benefit was consistent across predefined subgroups

Exposure

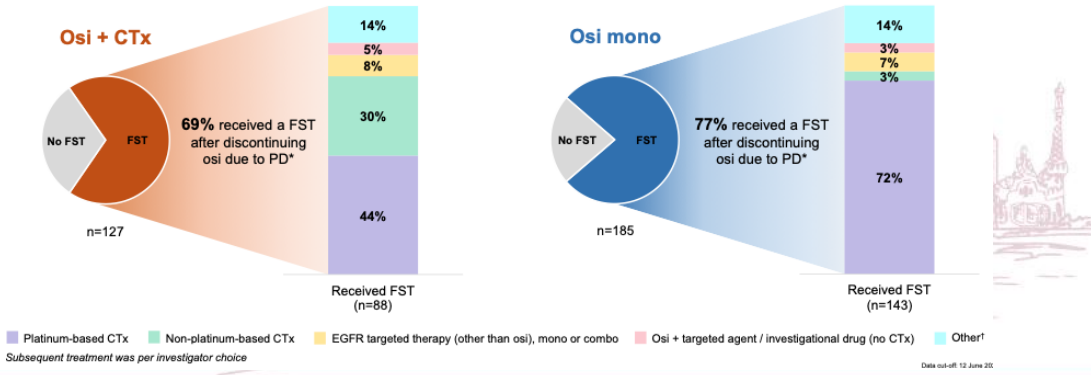


The osi + CTx arm had a long CTx-free period – median exposure to osi vs pem was 30.5 vs 8.3 months

First Subsequent Treatment

CTx was the most common FST (74%) after osi + CTx – 44% of FSTs were rechallenge with platinum CTx

OS benefit with osi + CTx was observed despite SoC CTx being the most common FST after osi mono



EGFR mutations

FLAURA vs FLAURA 2 vs MARIPOSA trial

	Osimertinib	Osimertinib-Pemetrexed-carboplatin	Amivantamab-Lazertinib
Study	FLAURA	FLAURA2	MARIPOSA
Efficacy	PFS 18.9 m **OS 38.6 m v 31.8 m**	PFS 25.5 m **Δ 9.9 m** **OS 47.5 m v 37.6 m (HR 0.77)**	PFS 23.7 m **Δ12 m+** **OS Not reached v 36.7 m (HR 0.75)**
Side effects (all grades)	Diarrhoea 42% Rash 22% Paronychia 27% Neutropenia 4% Neutrophil count decreased 7% Anaemia 11%	Diarrhoea 46% Rash 30% Paronychia 26% Neutropenia 25% Neutrophil count decreased 24% Anaemia 48% (G3 20%) Creatinine increase 14%	Diarrhoea 32% Rash 64% Paronychia 69% Infusion related reaction 65% Peripheral edema 38% Venous thromboembolism 40% Anaemia 27%
Supportive care	Emollient cream, steroid creams	Emollient cream, steroid creams Cytopenias/ mouthwashes	Emollient cream, steroid creams Prophylactic antibiotics, anticoagulation
Schedule	Daily oral tablet Visit every 2-3 months	Daily oral tablet, Iv Infusion once every 3 weeks	Daily oral tablet, Infusion/ subcut once per week for first 4 weeks; once every 2 weeks thereafter
Financial	$	$$	$$$$

David Planchard et al WCLC 2025 , Soria JC et al N Engl J Med. 2018, Cho BC et al N Engl J Med. 2024

EGFR mutations

HARMONi: Ivonescimab vs Placebo Plus Chemo, Phase 3 in Patients with EGFR+ NSCLC Progressed with 3rd gen EGFR-TKI

Study design

Key Eligibility Criteria

Locally advanced or metastatic NSCLC:

- EGFR sensitizing mutation+
- Progressed on 3rd gen EGFR-TKI
- ECOG 0 or 1
- Any PD-L1 expression

Stratification factor by geographic region:

- Brain metastases (yes or no)

R 1:1

N=438

Ivonescimab + Chemotherapy (N = 219)

Placebo + Chemotherapy (N = 219)

Ivonescimab: 20 mg/kg Q3W

Chemotherapy:

- Carboplatin: AUC5 Q3W x 4 cycles (21 day/cycle)
- Pemetrexed: 500 mg/m² Q3W

Endpoints:

Primary

- OS, PFS by IRRC per RECIST 1.1

Secondary

- ORR by IRRC, DoR, safety and tolerability

Planned Efficacy Analyses

- PFS primary (at ~231 events) & OS interim analyses
- OS final analysis (at ~261 events)

FPI: Jan 2022 (overall)
LPI Asia: Nov 2022
LPI NA & EU (and overall): Oct 2024

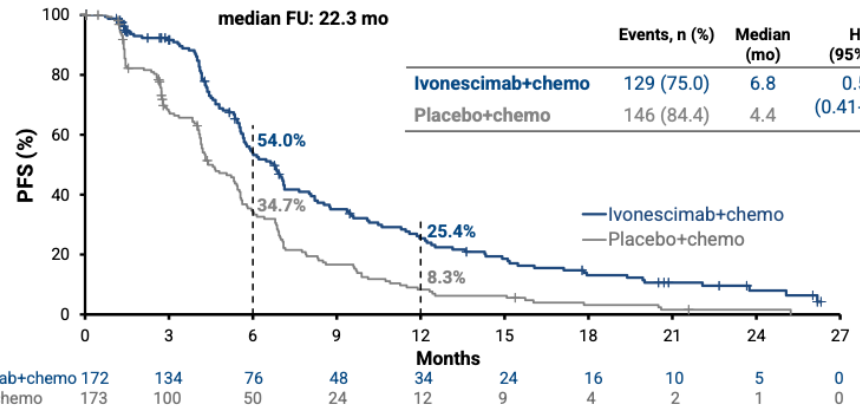
DoR=duration of response; ECOG=eastern cooperative oncology group; EGFR= Epidermal growth factor receptor; EU=Europe; FPI=first patient in; IRRC= independent radiology review committee; LPI=last patient in; mets=metastases; NA=North America; ORR=overall response rate; OS=overall survival; NSCLC=non-small cell lung cancer; TKI=tyrosine kinase inhibitor; PD-L1 = programmed cell death ligand; PFS=progression-free survival; Q3W=every 3 weeks; RECIST=response evaluation criteria in solid tumors.

Note: Positive outcomes were reported from the single-region (Asia) study HARMONi-A, with PFS as the primary endpoint.

Baseline characteristics

Characteristic, n (%)	Ivonescimab+chemo (N=219)	Placebo+chemo (N=219)
Age – Median (range)	62 (32-84)	60 (36-84)
≥65 yr	83 (37.9)	88 (40.2)
Female	130 (59.4)	127 (58.0)
Region – NA & Europe	83 (37.9)	82 (37.4)
Asia	136 (62.1)	137 (62.6)
Race – Asian	153 (69.9)	153 (69.9)
White	51 (23.3)	54 (24.7)
ECOG - 1	162 (74.0)	157 (71.7)
Smoking - Never	143 (65.3)	155 (70.8)
Stage - IV	215 (98.2)	214 (97.7)
Brain metastasis	54 (24.7)	54 (24.7)
Liver metastasis	32 (14.6)	23 (10.5)
Prior line of systemic cancer therapy (median)	1.0	1.0
Prior EGFR-TKI		
1st/2nd generation	95 (43.4)	92 (42.0)
3rd generation	219 (100)	218 (99.5)
4th generation	1 (0.5)	0
EGFR Mutation		
19del	131 (59.8)	118 (53.9)
L858R	74 (33.8)	90 (41.1)
Non-19del/L858R*	15 (6.8)	11 (5.0)

Progression Free Survival

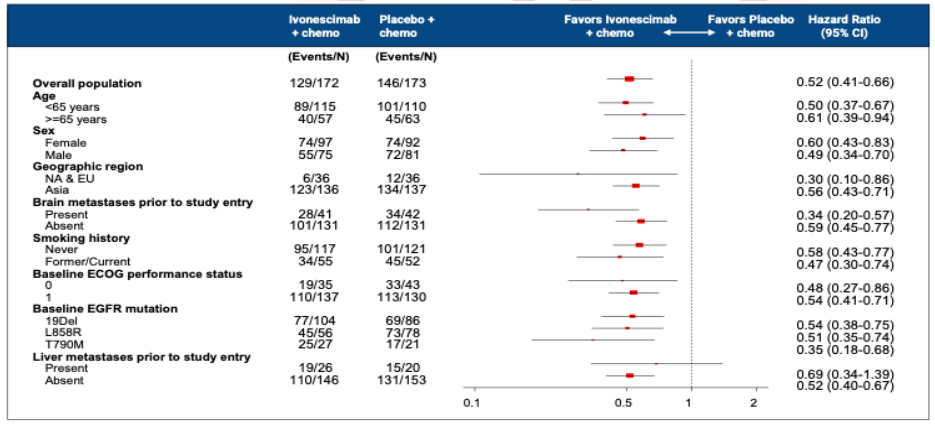


	Events, n (%)	Median (mo)	HR (95% CI)	*P* Value
Ivonescimab+chemo	129 (75.0)	6.8	0.52 (0.41-0.66)	<0.0001
Placebo+chemo	146 (84.4)	4.4		

No. at risk										
Ivonescimab+chemo	172	134	76	48	34	24	16	10	5	0
Placebo+chemo	173	100	50	24	12	9	4	2	1	0

Consistent PFS benefit by investigator: HR = 0.58 (95% CI: 0.45-0.73)

Subgroup analysis

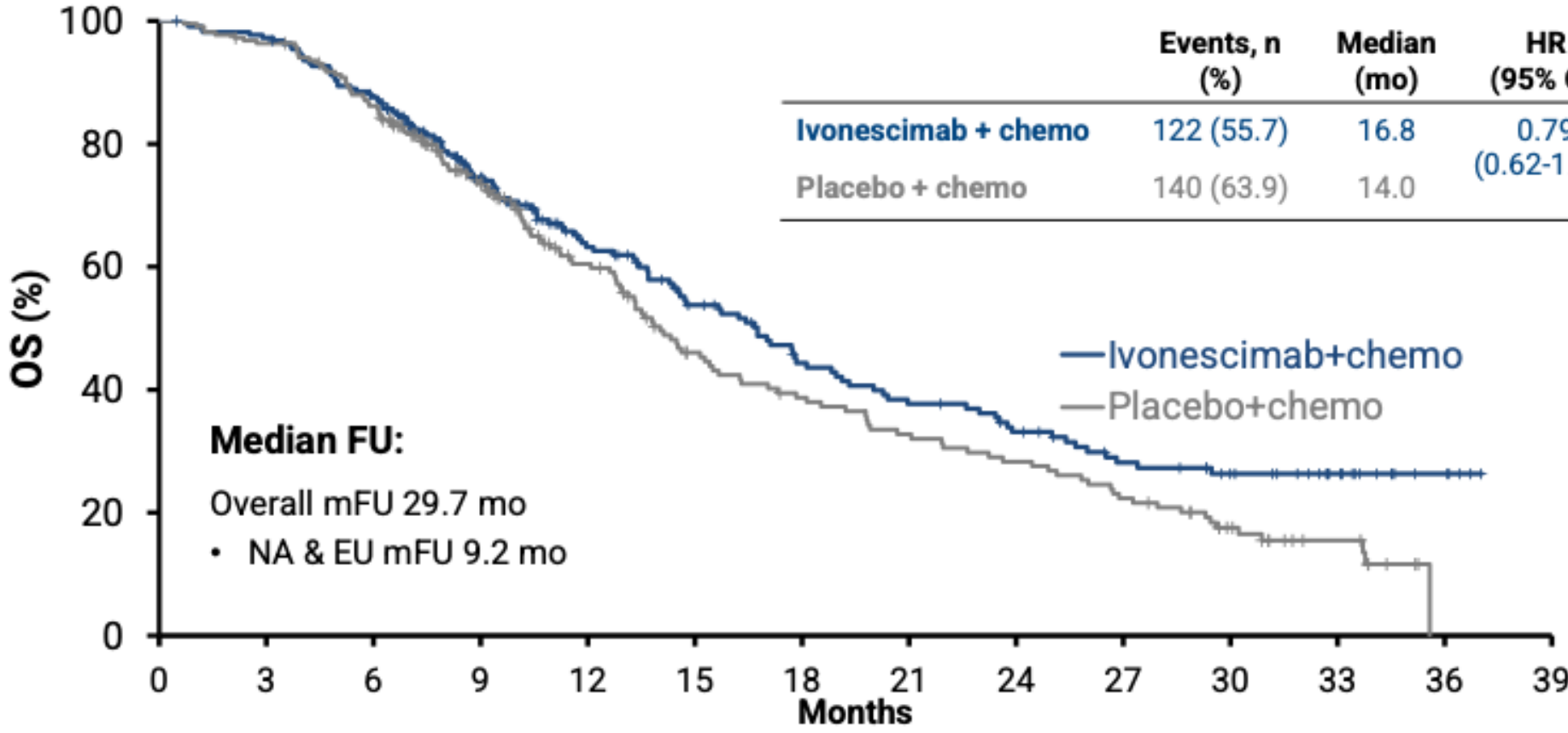


EGFR mutations

HARMONi: Ivonescimab vs Placebo Plus Chemo, Phase 3 in Patients with EGFR+ NSCLC Progressed with 3rd gen EGFR-TKI

Overall Survival

	Events, n (%)	Median (mo)	HR (95% CI)	*P* Value
Ivonescimab + chemo	122 (55.7)	16.8	0.79 (0.62-1.01)	0.0570
Placebo + chemo	140 (63.9)	14.0		

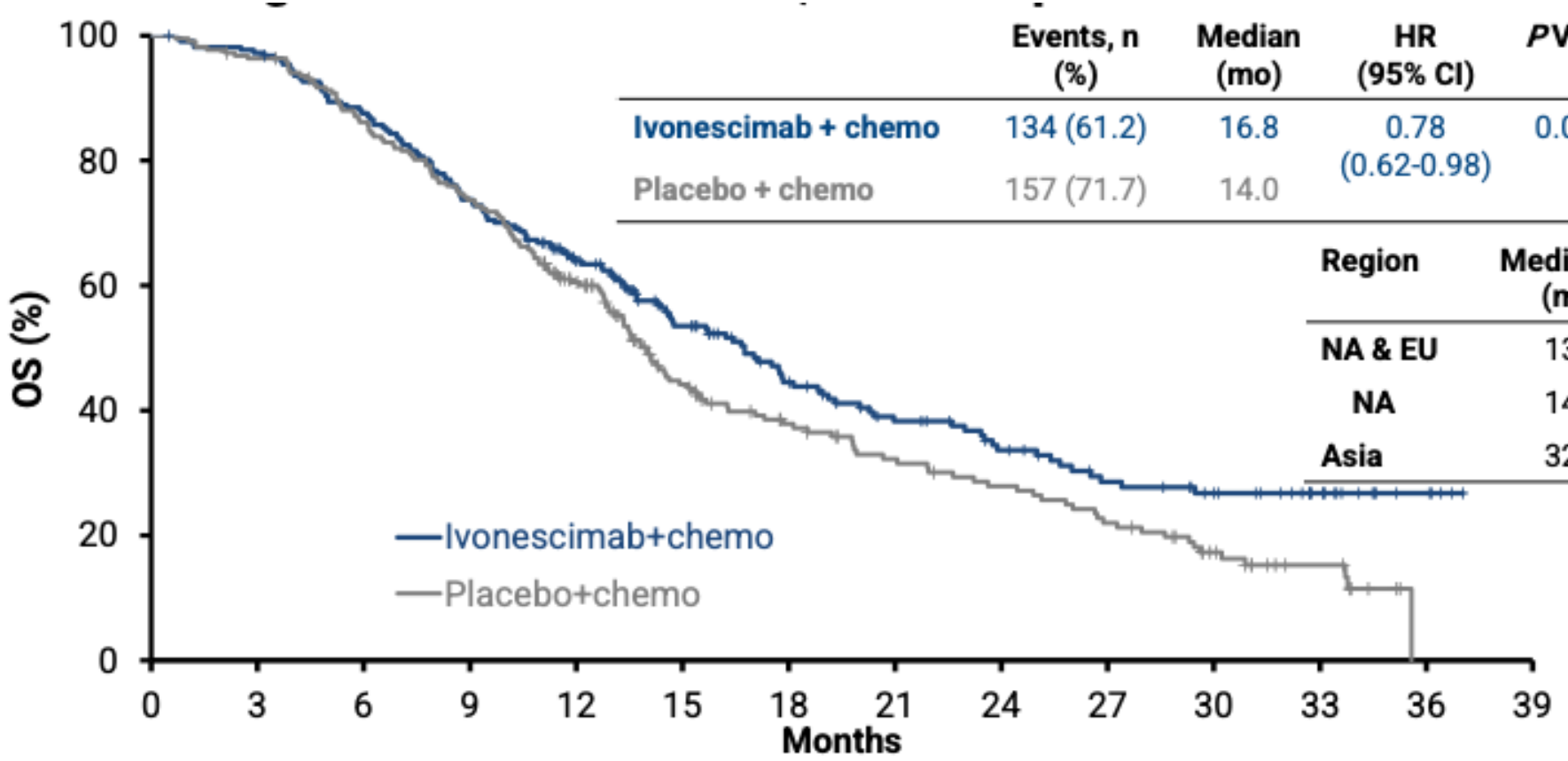


No. at risk														
Ivonescimab+chemo	219	212	189	137	98	77	60	51	43	33	26	16	5	0
Placebo+chemo	219	210	186	132	92	63	52	44	38	30	18	9	0	

EGFR mutations

HARMONi: Ivonescimab vs Placebo Plus Chemo, Phase 3 in Patients with EGFR+ NSCLC Progressed with 3rd gen EGFR-TKI

Overall Survival: Long Term Follow-up



	Events, n (%)	Median (mo)	HR (95% CI)	*P* Value
Ivonescimab + chemo	134 (61.2)	16.8	0.78 (0.62-0.98)	0.0332
Placebo + chemo	157 (71.7)	14.0		

Region	Median FU (mo)	Median OS (mo)
NA & EU	13.7	17.0 vs. 14.0
NA	14.6	NR vs. 14.0
Asia	32.7	16.7 vs. 14.0

Data cutoff
NA&EU: Sep 2025
Asia: Apr 2025

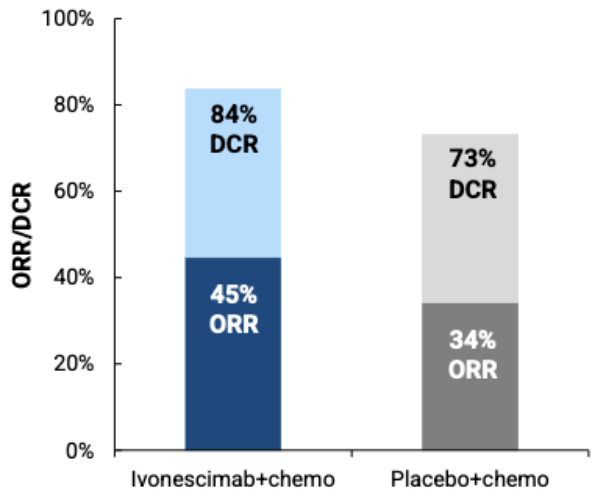
No. at risk

Ivonescimab+chemo	219	212	190	160	127	92	68	53	43	33	26	16	5	0
Placebo+chemo	219	210	186	159	119	74	56	45	38	30	18	9	0	

EGFR mutations

HARMONi: Ivonescimab vs Placebo Plus Chemo, Phase 3 in Patients with EGFR+ NSCLC Progressed with 3rd gen EGFR-TKI

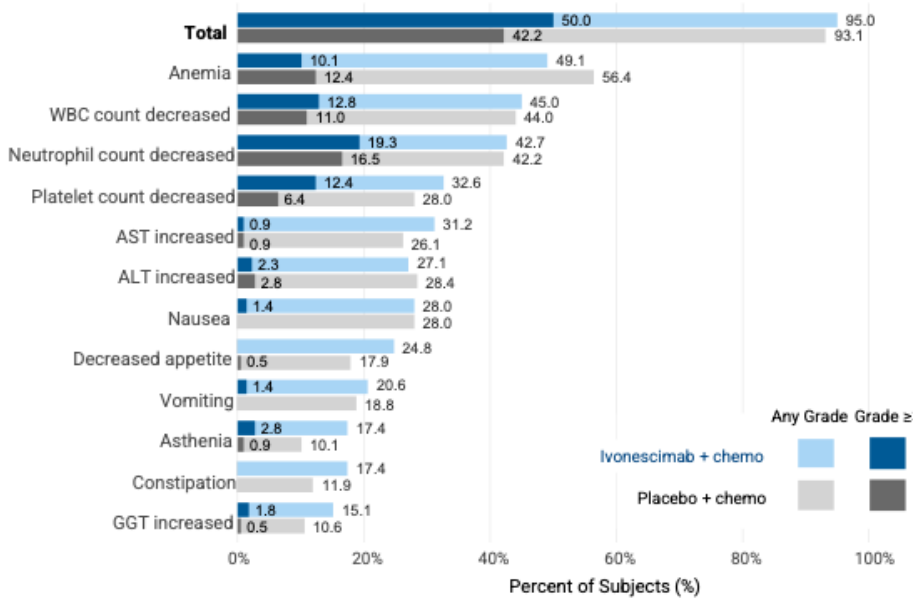
Overall Response Rate



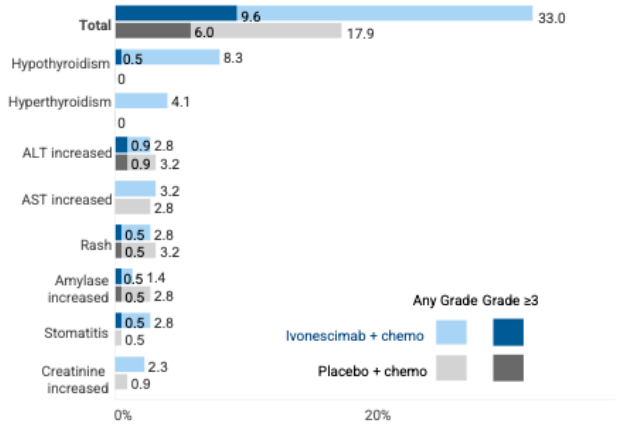
Duration of Response

DoR (mo)	Ivonescimab + chemo	Placebo + chemo
n	98	75
Median (95% CI)	**7.6** (5.5-10.6)	**4.2** (2.9-4.7)

Treatment Related Adverse Events

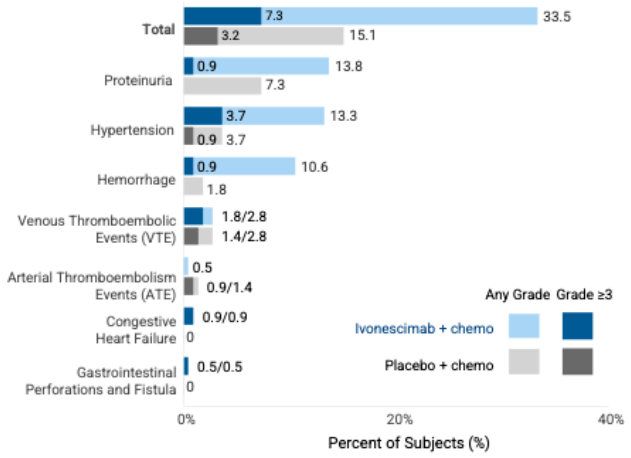


irAE.



Pneumonitis/ILD, Ivo arm vs Pbo arm:
2.8% (1.4% Grade ≥3) vs **1.8%** (1.4% Grade ≥3)

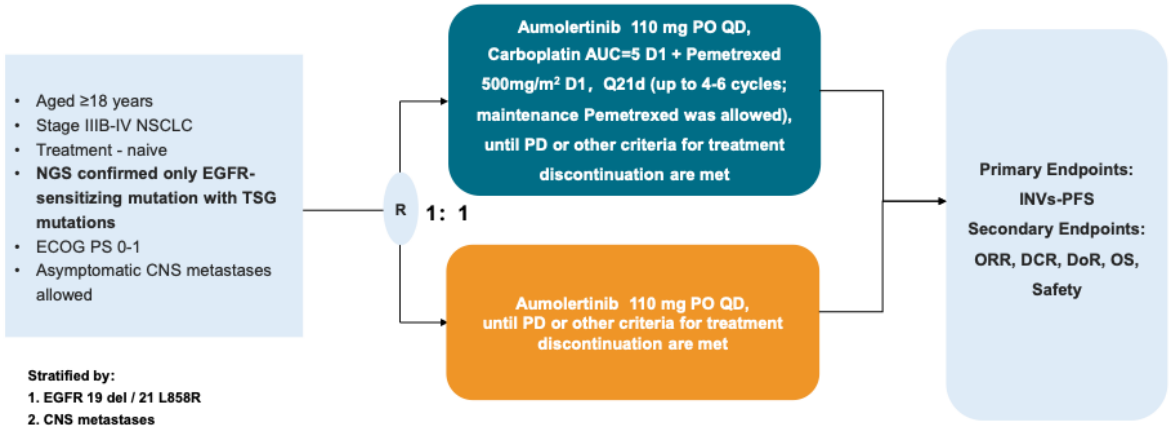
VEGF-related AE



EGFR mutations

Aumolertinib plus ChT for NSCLC with EGFR and Concomitant Tumor Suppressor Genes (ACROSS 2):Phase III study

Study design

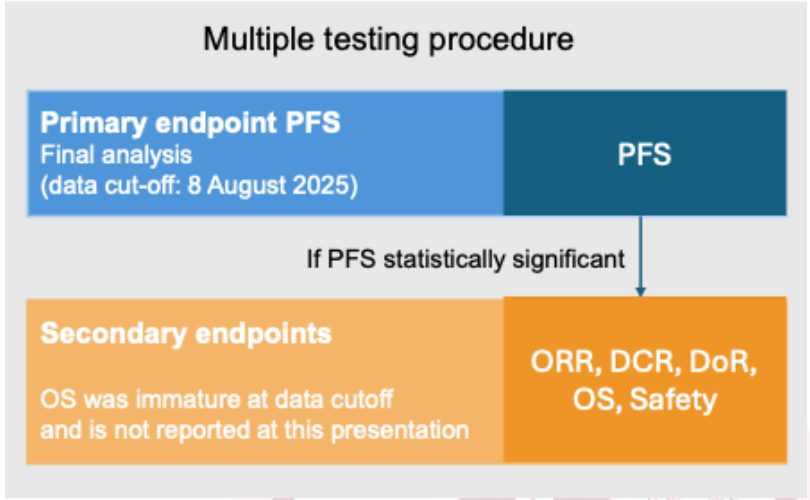


TSGs including :TP53, RB1, APC, PTEN, BRCA2, BRCA1, CHEK2, ATM, CHEK1, PALB2, RAD51C

Baseline characteristics

Characteristic	Aumolertinib + Carboplatin–Pemetrexed (N = 54)	Aumolertinib Monotherapy (N = 64)
Median age (range) - yr	55.5 (33 -73)	59 (33 -75)
Sex - no. (%)		
Male	23 (42.6)	23 (35.9)
Female	31 (57.4)	41 (64.1)
ECOG performance-status score - no. (%)		
0	28 (51.9)	20 (31.3)
1	26 (48.1)	44 (68.7)
Histologic characteristics - no. (%)		
Adenocarcinoma	54 (98.1)	63 (98.4)
Other	0 (1.9)	1 (1.6)
EGFR mutation at randomization - no. (%)		
Exon 19 deletion	25 (46.3)	32 (50)
L858R mutation	29 (53.7)	32 (50)
Disease extent at trial entry - no. (%)		
Locally advanced	2 (3.7)	2 (3.1)
Metastatic	52 (96.3)	62 (96.9)
CNS metastases - no. (%)		
Yes	21 (38.9)	23 (35.9)
No	33 (61.1)	41 (64.1)

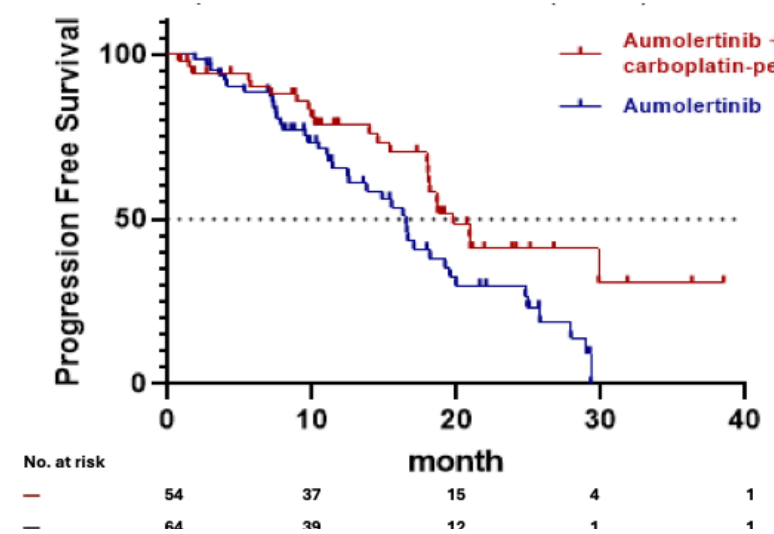
Stadistical design



EGFR mutations

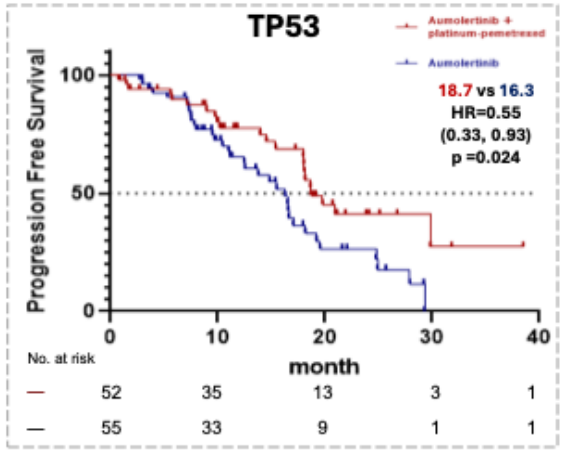
Aumolertinib plus ChT for NSCLC with EGFR and Concomitant Tumor Suppressor Genes (ACROSS 2):Phase III study

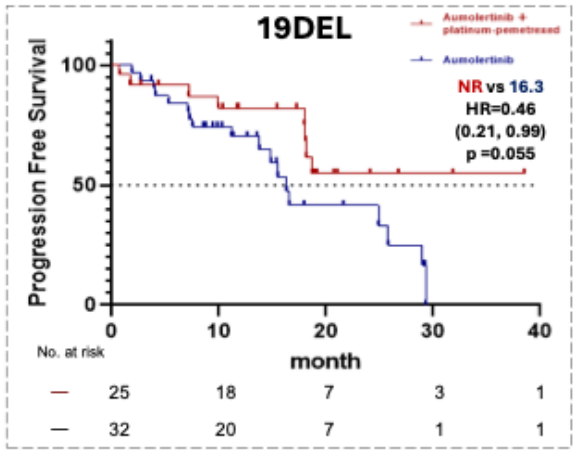
Progression Free Survival

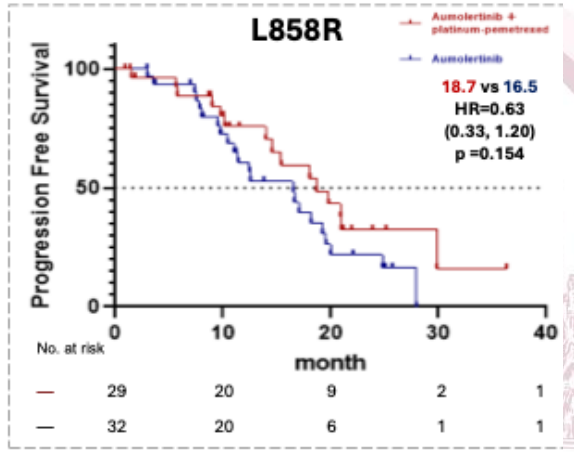


Median PFS, months	
Aumolertinib + Carboplatin–Pemetrexed	19.8
Aumolertinib Monotherapy	16.5
HR (95% CI)	0.55 (0.34, 0.91)
Log-rank P value	0.021

Median follow-up of PFS: 25.3 months; 63 (53.4%) events occurred. OS was immature







Median PFS, months

ORR in combination group and monotherapy group was 70.4% vs 67.2%, and DCR was 92.6% vs 98.4%, respectively.

ROS1rearrangements

Pivotal ARROS-1 Efficacy and Safety Data: Zidesamtinib in TKI Pretreated Patients with Advanced/Metastatic ROS1+ NSCLC

Study Design

ZIDESAMTINIB DESIGN GOALS:

- ROS1 Activity
- \+
- ROS1 Mutant Activity
- \+
- Brain Penetrance
- \+
- Avoiding TRK

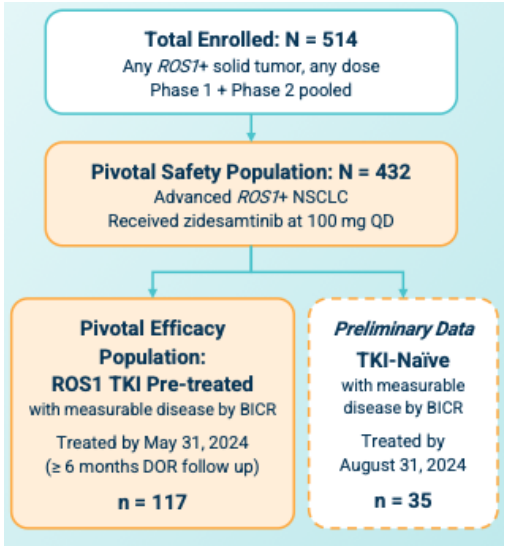
PHASE 1: Zidesamtinib dose escalation (25 – 150 mg QD) in ROS1 TKI pre-treated patients with advanced *ROS1+* solid tumors

PHASE 2: Zidesamtinib 100 mg QD (RP2D)

ARROS-1 PHASE 2 PATIENT POPULATION	PRIOR ROS1 TKI	PRIOR CHEMO/I-O
ROS1+ NSCLC	ROS1 TKI-naïve [a]	≤ 1
	1 prior ROS1 TKI [b]	None
		1 [c]
	≥ 2 Prior ROS1 TKIs [d]	≤ 1
Any *ROS1+* Solid Tumor [e]	Any	Any

PHASE 2 OBJECTIVES

- **Primary:** ORR by blinded independent central review (BICR)
- **Secondary:** Additional efficacy measures (DOR, TTR, CBR, PFS, OS), intracranial activity, overall safety and tolerability, confirmation of PK profile, PROs



Objective Resonse rate

Advanced *ROS1+* NSCLC RECIST 1.1 by BICR	Any prior ROS1 TKI (range 1 – 4) ± chemotherapy	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy
ORR, % (n/N) [95% CI]	**44%** (51/117) [34, 53]	**51%** (28/55) [a] [37, 65]
CR, % (n/N)	1% (1/117)	2% (1/55)

[a] Prior crizotinib only ± chemotherapy: ORR = 68% (19/28). Prior entrectinib only ± chemotherapy: ORR = 33% (9/27).

Responses were also observed in patients previously treated with:

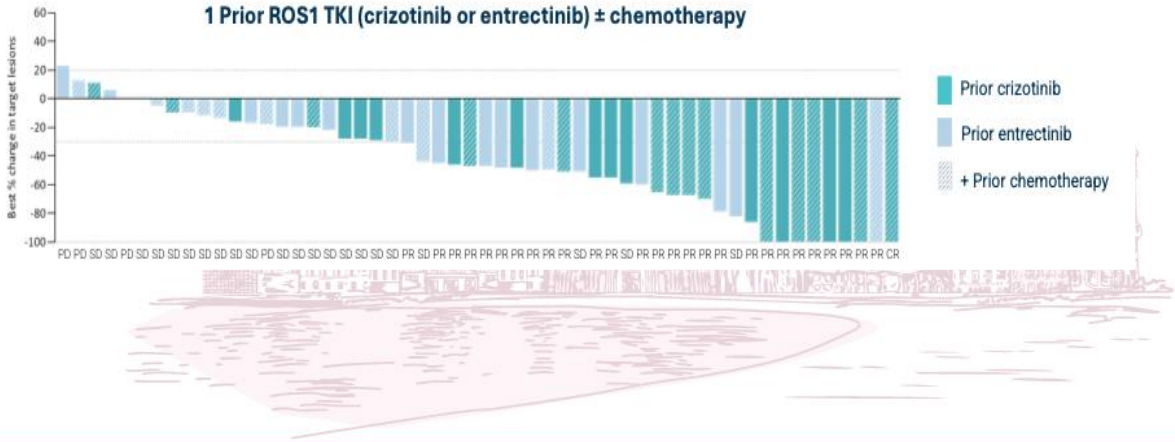
- **≥2 prior ROS1 TKIs ± chemotherapy**: ORR = 38% (22/58; 95% CI: [26, 52])
- **Prior repotrectinib: ORR = 47% (8/17),** DOR range 3.5 to 17.2 months
- **Prior taletrectinib: ORR = 43% (3/7),** DOR range 5.2 to 7.0+ months

Baseline Characteristics

Patient Characteristic	ROS1 TKI Pre-Treated [a] Pivotal Efficacy Population N = 117
Age, median (range)	57 (31 – 83)
Female	66 (56%)
Never smoker	80 (68%)
Geographic Region	
Asia Pacific	30 (26%)
Europe	38 (32%)
North America	49 (42%)
ECOG PS	
0	45 (38%)
1	72 (62%)
Active CNS disease [b]	57 (49%)
Secondary *ROS1* mutation [c]	42 (36%)
G2032R	26 (22%)

Treatment History	ROS1 TKI Pre-Treated [a] Pivotal Efficacy Population N = 117
Prior anticancer therapy, median (range)	2 (1 – 11)
Prior chemotherapy	62 (53%)
Prior ROS1 TKIs ± chemotherapy	
1 prior (crizotinib or entrectinib)	**55 (47%)**
Crizotinib	*28/55 (51%)*
Entrectinib	*27/55 (49%)*
1 prior (repotrectinib or taletrectinib)	4 (3%)
≥2 prior	**58 (50%)**
Lorlatinib, repotrectinib, or taletrectinib	***54/58 (93%)***
Lorlatinib	*43/58 (74%)*
Repotrectinib	*15/58 (26%)*
Taletrectinib	*5/58 (9%)*

Objective Resonse rate



ROS1rearrangements

Pivotal ARROS-1 Efficacy and Safety Data: Zidesamtinib in TKI Pretreated Patients with Advanced/Metastatic ROS1+ NSCLC

Duration of response

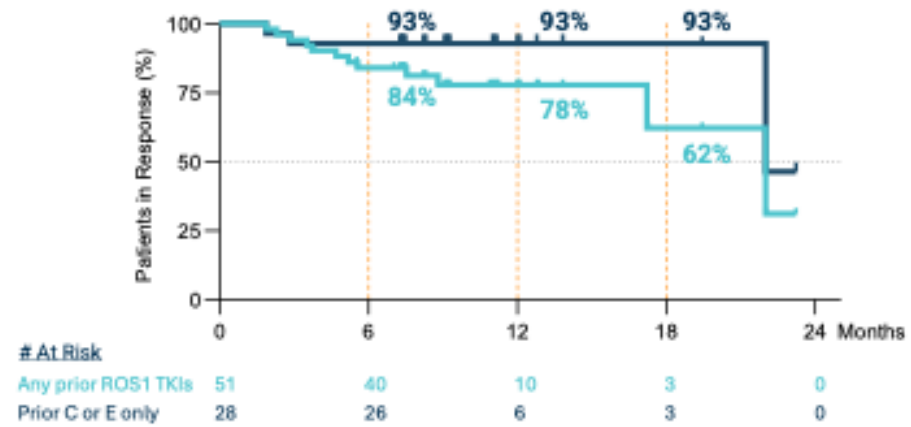
Progression Free Survival

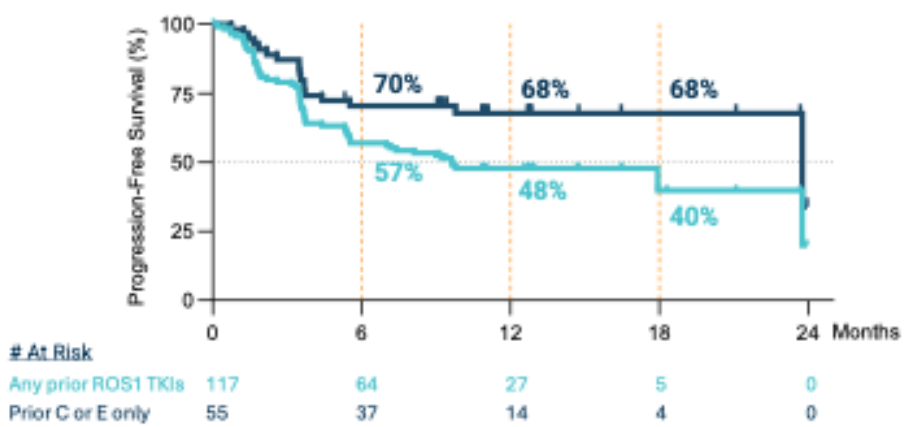
Advanced *ROS1*+ NSCLC Kaplan-Meier Estimate	Duration of Response		Progression-Free Survival	
	Any prior ROS1 TKIs (range 1-4) ± chemotherapy [a]	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy [b]	Any prior ROS1 TKIs (range 1-4) ± chemotherapy [a]	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy [b]
% ≥ 6 months [95% CI]	**84%** [71, 92]	**93%** [74, 98]	**57%** [47, 66]	**70%** [56, 81]
% ≥ 12 months [95% CI]	**78%** [62, 88]	**93%** [74, 98]	**48%** [38, 57]	**68%** [53, 79]
% ≥ 18 months [95% CI]	**62%** [28, 84]	**93%** [74, 98]	**40%** [24, 55]	**68%** [53, 79]

Data cut-off: March 21, 2025

[a] Any prior ROS1 TKI: Emerging median DOR of 22 months [95% CI: 17, NE] continues to mature. Median PFS was 9.7 [5.5, NE] months with median follow-up of 11.1 months (range 0.2-25.6).

[b] 1 prior ROS1 TKI (crizotinib [C] or entrectinib [E]): Emerging median DOR of 22 months [95% CI: 22, NE] and median PFS of 23.8 months [95% CI: 23.8, NE] continue to mature; median follow-up was 11.8 months (range 1.2-25.6).





- In patients that received prior crizotinib only, there were no progression events among responders (DOR range: 7.3+ to 23.2+ months). PFS rate was 89% (95% CI: 70, 96) at 6, 12, and 18 months with median not reached.

- In patients that received ≥2 prior ROS1 TKIs ± chemotherapy, DOR rate was 71% (95% CI: 46, 86) at 6 months and 56% (95% CI: 29, 76) at 12 months.

ROS1rearrangements

Pivotal ARROS-1 Efficacy and Safety Data: Zidesamtinib in TKI Pretreated Patients with Advanced/Metastatic ROS1+ NSCLC

G2032R Resistance Mutation and CNS Subgroups

***ROS1* G2032R Resistance Mutation**		
Advanced *ROS1+* NSCLC Analysis by BICR	**Any prior ROS1 TKI ± chemotherapy**	**1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy** [a]
ORR, % (n/N) [95% CI]	**54%** (14/26) [33, 73]	**83%** (5/6) [36, 100]
% DOR ≥ 6 months [95% CI] [b]	**79%** [47, 93]	**80%** [c] [20, 97]
% DOR ≥ 12 months [95% CI] [b]	**60%** [28, 81]	**80%** [c] [20, 97]

Responses were also observed in patients with:

- ROS1 G2032R mutation following ≥2 prior ROS1 TKIs ± chemotherapy, including lorlatinib or repotrectinib
- Other ROS1 resistance mutations, including G1957A, L1982V, S1986F, F2004C/V, G2032K, and D2033N

[a] Patients received zidesamtinib as their first TKI designed with activity against ROS1 G2032R.
[b] Analyses of DOR based on Kaplan-Meier estimates.
[c] One progression event among responders.

Measurable CNS lesions by BICR at baseline		
Advanced *ROS1+* NSCLC Analysis by BICR	**Any prior ROS1 TKI ± chemotherapy**	**Prior crizotinib only ± chemotherapy**
IC-ORR, % (n/N) [95% CI]	**48%** (27/56) [a] [35, 62]	**85%** (11/13) [55, 98]
IC-CR, % (n/N)	**20%** (11/56)	**54%** (7/13)
% IC-DOR ≥ 6 months [95% CI] [b]	**79%** [56, 91]	**91%** [c] [51, 99]
% IC-DOR ≥ 12 months [95% CI] [b]	**71%** [46, 87]	**91%** [c] [51, 99]

- CNS responses also observed in patients who had received ≥1 prior brain-penetrant TKI, including prior entrectinib, lorlatinib, repotrectinib, or taletrectinib: IC-ORR: 37% (16/43 [a]; [95% CI 23, 53]), including 4 IC-CRs
- No CNS progression was observed among patients who entered the study without brain metastases at baseline per BICR

[a] Includes 2 unconfirmed intracranial partial responses (PR).
[b] Analyses of DOR based on Kaplan-Meier estimates.
[c] One CNS progression event among CNS responders (n=11).

ROS1rearrangements

Pivotal ARROS-1 Efficacy and Safety Data: Zidesamtinib in TKI Pretreated Patients with Advanced/Metastatic ROS1+ NSCLC

Safety in Advanced ROS1 + NSCLC

All Treatment-Emergent Adverse Events (TEAEs) in ≥15% of Patients Treated with Zidesamtinib 100 mg QD (N = 432) [a]

Preferred or grouped term	Any Grade	Grade ≥ 3
Peripheral edema [b]	36%	0.7%
Constipation	17%	0%
Blood CPK increased	16%	3.5%
Fatigue [c]	16%	0.7%
Dyspnea [d]	15%	3.0%

[a] Patients received at least 1 dose of zidesamtinib at 100 mg QD with median duration of exposure of 5 months (range: 0, 32).

[b] Includes terms peripheral edema, peripheral swelling, edema, generalized edema.

[c] Includes terms fatigue, asthenia, malaise.

[d] Includes terms dyspnea, dyspnea exertional, orthopnea

Dose reduction due to TEAEs: 10% (43/432)

- Most common (>2 patients): peripheral edema (n=8), blood CPK increased (n=4), peripheral sensory neuropathy (n=4), arthralgia (n=3), paresthesia (n=3)

Discontinuation due to TEAE: 2% (10/432)

- Most common (>2 patients): pneumonia (n=3)

The only treatment-related adverse event in ≥15% of patients was peripheral edema [b] (29%)

MTAP-delection: a new target?

BMS-986504 in patients with homozygous MTAP-deletion: clinical results in patients with NSCLC enrolled in CA240-0007

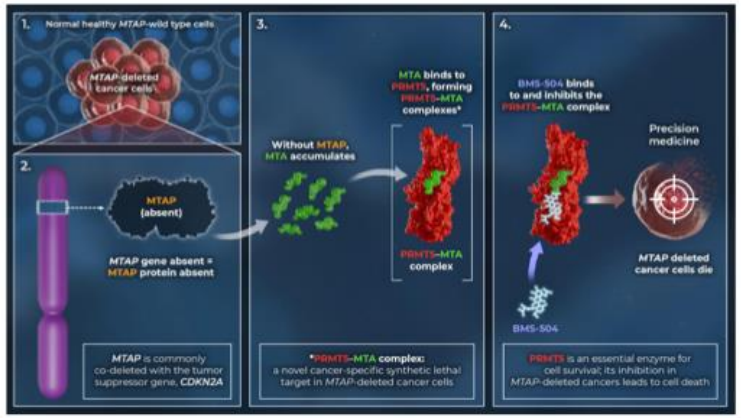
Safety in Advanced ROS1 + NSCLC

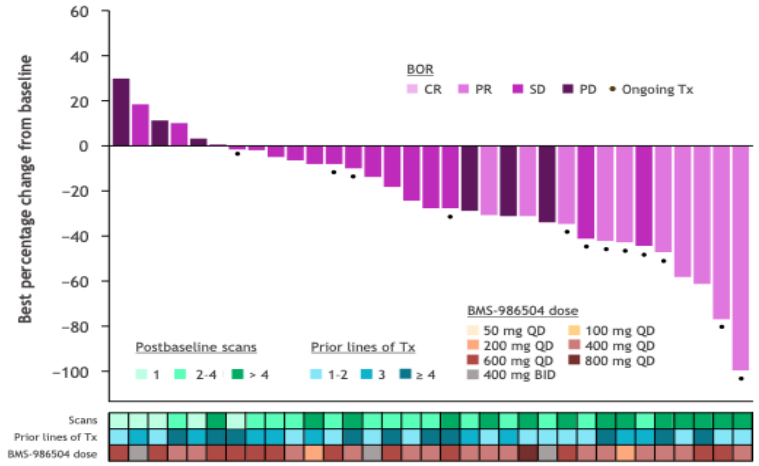
Homozygous *MTAP*-del occurs in 10%–15% of all cancers, with NSCLC comprising up to 27% of this population,1–5 making it a potentially useful therapeutic target

• CA240-0007 is a first-in-human phase 1 study of BMS-986504 (MRTX1719) in patients with advanced solid tumors with homozygous *MTAP*-del

—BMS-986504 was found to be well tolerated and demonstrated antitumor activity across doses and multiple tumors, including NSCLC7
• Here, we report updated efficacy from the dose escalation and expansion phases of CA240-0007 in patients with NSCLC and safety in patients across multiple tumor types

BMS-986504 mechanism of action





• For patients with NSCLC treated at 400 mg QD or 600 mg QD, the ORR was 29% (8/28)

• Responses were observed regardless of age, ECOG PS, or smoking

	NSCLC (n = 35)	NSQ (n = 32)	SQ (n = 3)	*TP53*-positive (n = 17)[b]
ORR,[c] n (%)	10 (29)	9 (28)	1 (33)	7 (41)
CR	0	0	0	0
PR	10 (29)	9 (28)	1 (33)	7 (41)
SD	18 (51)	17 (53)	1 (33)	6 (35)
PD	7 (20)	6 (19)	1 (33)	4 (24)
DCR,[d] n (%)	28 (80)	26 (81)	2 (67)	13 (76)
Median TTR, mo (range)	4.3 (2.8-7.1)	4.1 (2.8-7.1)	4.4 (4.4-4.4)	4.1 (2.8-7.1)

• An additional 2 patients with NSQ NSCLC had ongoing unconfirmed

To wrap up

1. In patients with EGFR mutations, combinations of chemotherapy plus osimertinib, as well as amivantamab plus lazertinib plus osimertinib, are new first-line standards of care.

2. Ivonescimab combined with chemotherapy may be an option in EGFR-mutated patients after progression on TKI therapy; confirmatory studies are needed

3. The coexistence of tumor suppressor gene alterations and EGFR mutations benefits from chemotherapy plus TKI, though the predictive or prognostic value remains uncertain.

4. Zidesamtinib is emerging as a potential option after progression on first-line therapy in patients with ROS1+ NSCLC.

5. MTAP deletion could represent a new therapeutic target in advanced lung cancer