Iniciativa científica de:

GECP lung cancer research

Lung Cancer UPDATES

WCLC HIGHLIGHTS

12 - 15 **SEPTIEMBRE** 2026

Seoul, Republic of South Korea



#WCLCUPDATES

Iniciativa científica de:

GECP lung cancer research

Lung Cancer UPDATES

WCLC HIGHLIGHTS

12 - 15 SEPTIEMBRE 2026

Seoul, Republic of South Korea

Cáncer de pulmón no microcítico avanzado con driver

Silvia Sequero Lopez

Hospital Universitario San Cecilio, Granada

CÁNCER DE PULMÓN NO MICROCÍTICO AVANZADO CON DRIVERS

PAPILLON
Ami-chemo in 1L
Ex20ins NSCLC

PAPILLON: Phase 3 Study Design

Key eligibility criteria

- Treatment-naïve,[a] locally advanced or metastatic NSCLC
- Documented *EGFR* Ex20ins
- ECOG PS 0 or 1

Stratification factors

- ECOG PS
- History of brain metastases[b]
- Prior EGFR TKI use[a]

1:1 Randomization (N=308)

Amivantamab-chemotherapy (n=153)

Chemotherapy (n=155)

Crossover to 2L amivantamab monotherapy

- Crossover permitted only after BICR-confirmed disease progression
- Amivantamab monotherapy given Q3W

Primary endpoint: PFS by BICR according to RECIST v1.1[c]

Key secondary endpoint:

- Protocol-specified final overall survival (OS)[c]

Estimated to provide ~56% power to detect a statistically significant difference in OS, with statistical power further attenuated due to crossover

Other prespecified endpoints reported in this presentation:

- IPCW crossover-adjusted OS[d]
- PFS from randomization to second progression event (PFS2)
- Safety
- Patient-reported outcomes (PROs)

Dosing (in 21-day cycles)

Intravenous amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) Q3W starting at Week 7 (first day of Cycle 3)

Chemotherapy on the first day of each cycle:

- **Carboplatin:** AUC5 for the first 4 cycles
- **Pemetrexed:** 500 mg/m^2 until disease progression

Chul Kim

PAPILLON (ClinicalTrials.gov identifier: NCT04538664) enrollment period: December 2020 to November 2022; clinical cut-off: March 20, 2026.

[a]Removed as stratification factor since only 4 participants had prior EGFR TKI use (brief monotherapy with common EGFR TKIs was allowed if lack of response was documented). [b]Participants with brain metastases were eligible if they received definitive treatment and were asymptomatic, clinically stable, and off corticosteroid treatment for ≥2 weeks prior to randomization. [c]Key statistical assumption: 300 participants with 200 events needed for 90% power to detect an HR of 0.625 (estimated PFS of 8 vs 5 months). PFS, ORR, and then OS were included in hierarchical testing. [d]IPCW was a prespecified model for the crossover-adjusted OS analysis. 2L, second-line; AUC, area under the curve; Ex20ins, exon 20 insertion; IPCW, inverse probability of censoring weighting; RECIST, Response Evaluation Criteria in Solid Tumors.

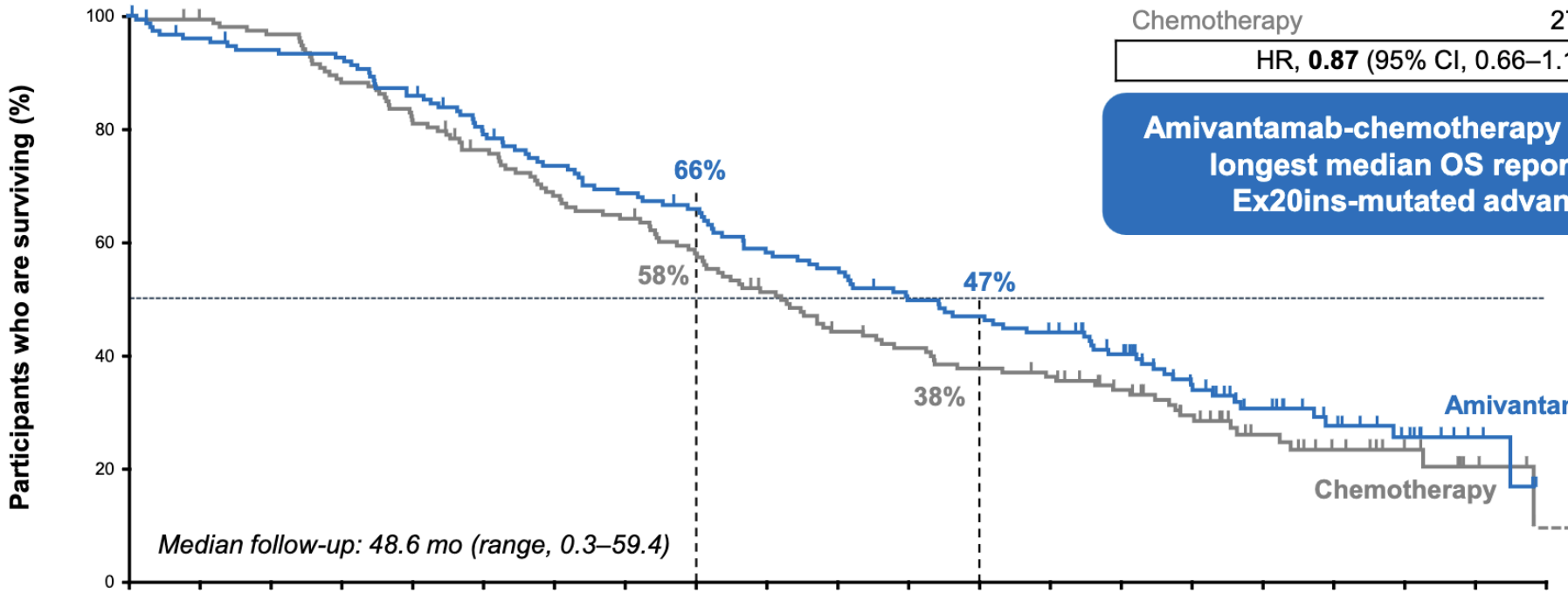
PAPILLON: Final Overall Survival in the ITT Population

PAPILLON
Ami-chemo in 1L Ex20ins NSCLC

	Median OS (95% CI)
Amivantamab-chemotherapy	34.3 mo (27.0–40.8)
Chemotherapy	27.9 mo (24.0–32.4)

HR, **0.87** (95% CI, 0.66–1.14); *P*=0.307

Amivantamab-chemotherapy demonstrated the longest median OS reported to date in Ex20ins-mutated advanced NSCLC



No. at risk																				
Amivantamab-chemotherapy	153	144	140	138	128	118	107	100	95	84	80	71	67	62	52	36	26	18	12	4	0
Chemotherapy	155	153	148	136	127	114	103	96	86	74	63	58	53	50	41	30	20	14	9	4	0

97 of 128 (76%) participants who discontinued due to progressive disease crossed over to amivantamab[a]

Chul Kim

[a]A total of 97 participants (87 participants as part of the crossover cohort plus an additional 10 participants off-protocol) received 2L amivantamab monotherapy out of 128 chemotherapy-randomized participants with BICR-confirmed disease progression. 2L, second-line; Ex20ins, exon 20 insertion.

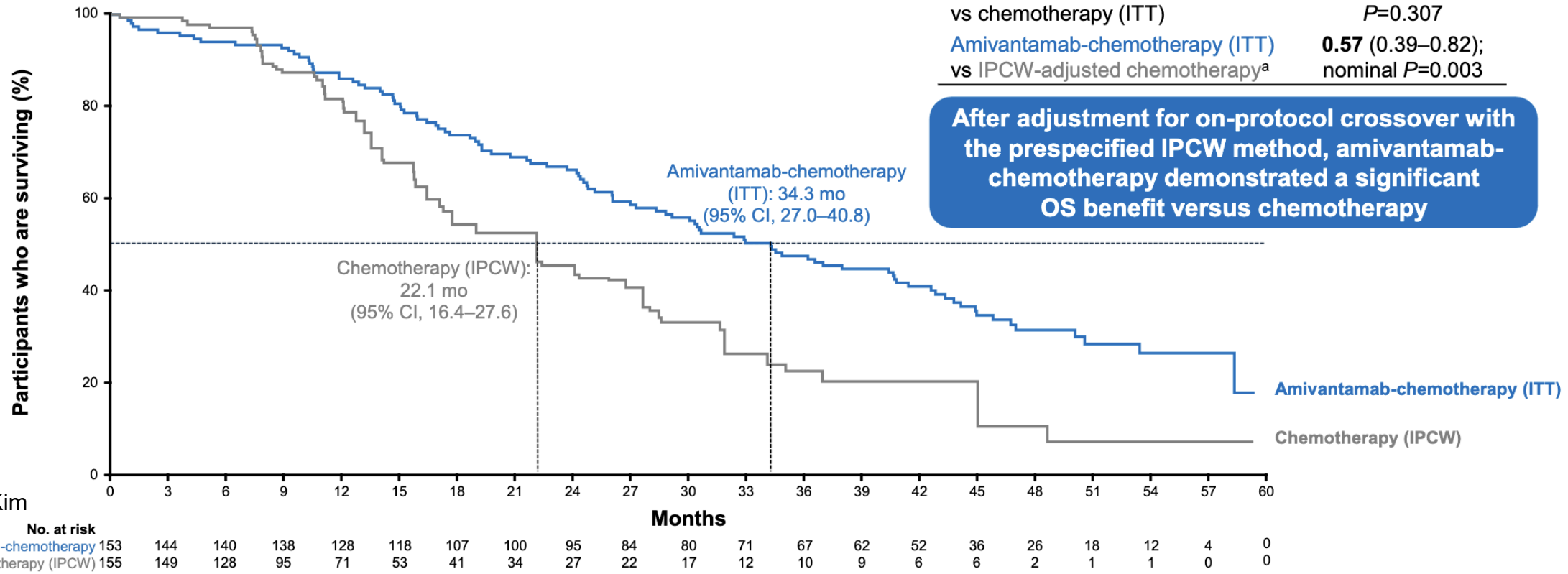
PAPILLON: Crossover-Adjusted Final Overall Survival

Inverse Probability of Censoring Weighting (IPCW)

PAPILLON
Ami-chemo in 1L
Ex20ins NSCLC

	HR (95% CI)
Amivantamab-chemotherapy (ITT) vs chemotherapy (ITT)	**0.87** (0.66–1.14); *P*=0.307
Amivantamab-chemotherapy (ITT) vs IPCW-adjusted chemotherapy[a]	**0.57** (0.39–0.82); nominal *P*=0.003

After adjustment for on-protocol crossover with the prespecified IPCW method, amivantamab-chemotherapy demonstrated a significant OS benefit versus chemotherapy



No. at risk																				
Amivantamab-chemotherapy	153	144	140	138	128	118	107	100	95	84	80	71	67	62	52	36	26	18	12	4	0
Chemotherapy (IPCW)	155	149	128	95	71	53	41	34	27	22	17	12	10	9	6	6	2	1	1	0	0

Chul Kim

[a]Two additional recommended models[1] demonstrated improvement in the OS benefit consistent with IPCW: Two-Stage Estimation (TSE): HR, 0.54 (95% CI, 0.35–0.77) and Rank Preserving Structural Failure Time (RPSFT): HR, 0.71 (95% CI, 0.37–1.36).

1. Question and answer on adjustment for cross-over in estimating effects in oncology trials. European Medicines Agency. Accessed August 18, 2026. https://www.ema.europa.eu/en/documents/scientific-guideline/question-and-answer-adjustment-cross-over-estimating-effects-oncology-trials_en.pdf.

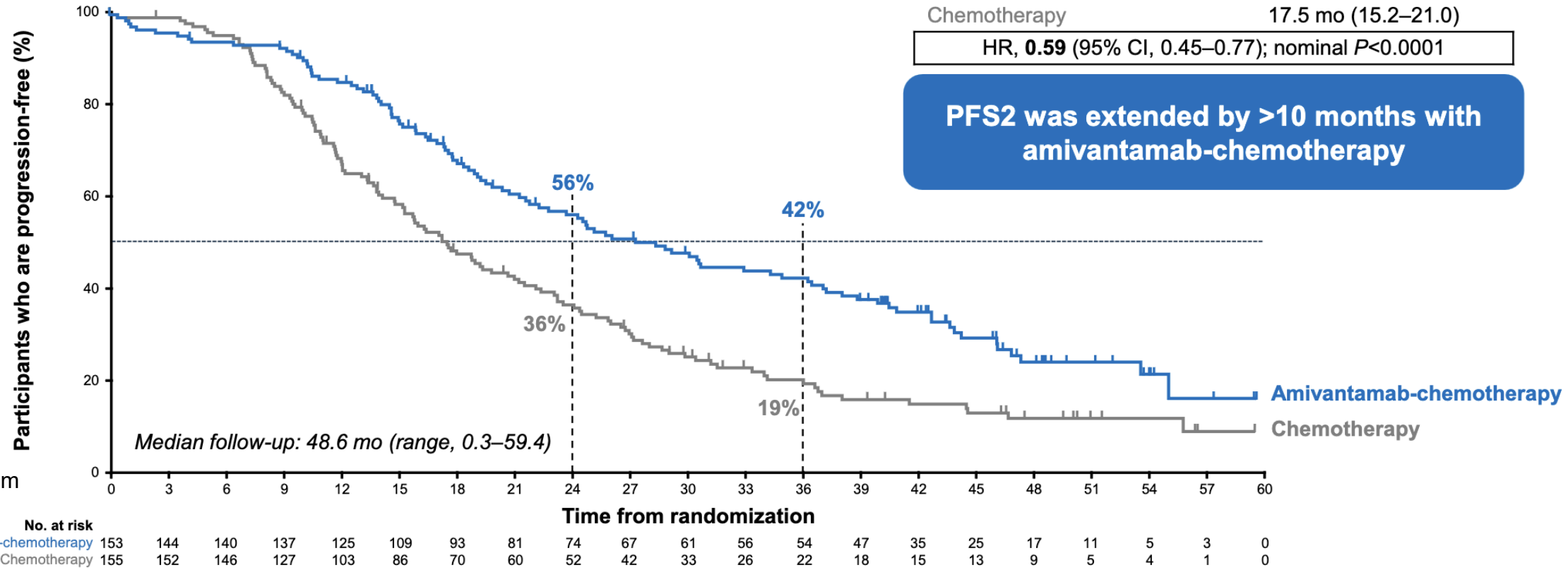
PAPILLON
Ami-chemo in 1L Ex20ins NSCLC

PFS2: PFS From Randomization to Second Progression Event[a]

	Median PFS2 (95% CI)
Amivantamab-chemotherapy	28.3 mo (21.8–36.2)
Chemotherapy	17.5 mo (15.2–21.0)

HR, **0.59** (95% CI, 0.45–0.77); nominal *P*<0.0001

PFS2 was extended by >10 months with amivantamab-chemotherapy



No. at risk																				
Amivantamab-chemotherapy	153	144	140	137	125	109	93	81	74	67	61	56	54	47	35	25	17	11	5	3	0
Chemotherapy	155	152	146	127	103	86	70	60	52	42	33	26	22	18	15	13	9	5	4	1	0

Chul Kim

[a]Consistent with PFS2, time to treatment discontinuation and time to subsequent therapy were extended with amivantamab-chemotherapy versus chemotherapy (14.1 vs 7.6 mo; HR, 0.36; 95% CI, 0.28–0.46; *P*<0.0001 and 16.9 vs 9.9 mo; HR, 0.37; 95% CI, 0.29–0.48; *P*<0.0001, respectively).

REZILIENT 3: 1L Zipalertinib + Chemotherapy vs Chemotherapy

Daniel SW Tan

REZILIENT :**Re**searching **Zi**palertinib **i**n ***EGFR***mt **N**on–Small Cell Lung Cancer **T**umors

Eligibility criteria:

- 1L metastatic NSCLC
- **Local testing** of *EGFR*mt ex20ins for eligibility
- ECOG PS 0 or 1
- **Stable brain metastases permitted**
- Archival tissue available

Safety Lead-in
(N=6)

Zipalertinib (100 mg BID)
+
Pemetrexed/Platinum
(Carboplatin or cisplatin)

Safety lead-in completed:
Combination safe to proceed as assessed by IDMC

Randomized Phase 3 Study (NCT05973773)
(N=280)

R

- **Zipalertinib + Pemetrexed/Platinum** (Carboplatin or cisplatin)
- **Pemetrexed/Platinum** (Carboplatin or cisplatin) → Optional Cross-over → **Zipalertinib**

Stratification factors:

- ECOG PS
- Brain metastases (Yes/No)
- Region (Asia/Non-Asia)

Primary:

- **PFS by BICR**

Secondary

- OS
- PFS (investigator)
- ORR
- DoR
- Safety
- PROs

- 122 clinical sites globally
- Study overseen by IDMC

Primary analysis: at 162 PFS events to detect HR 0.60, 2-sided α: 0.05, 90% power

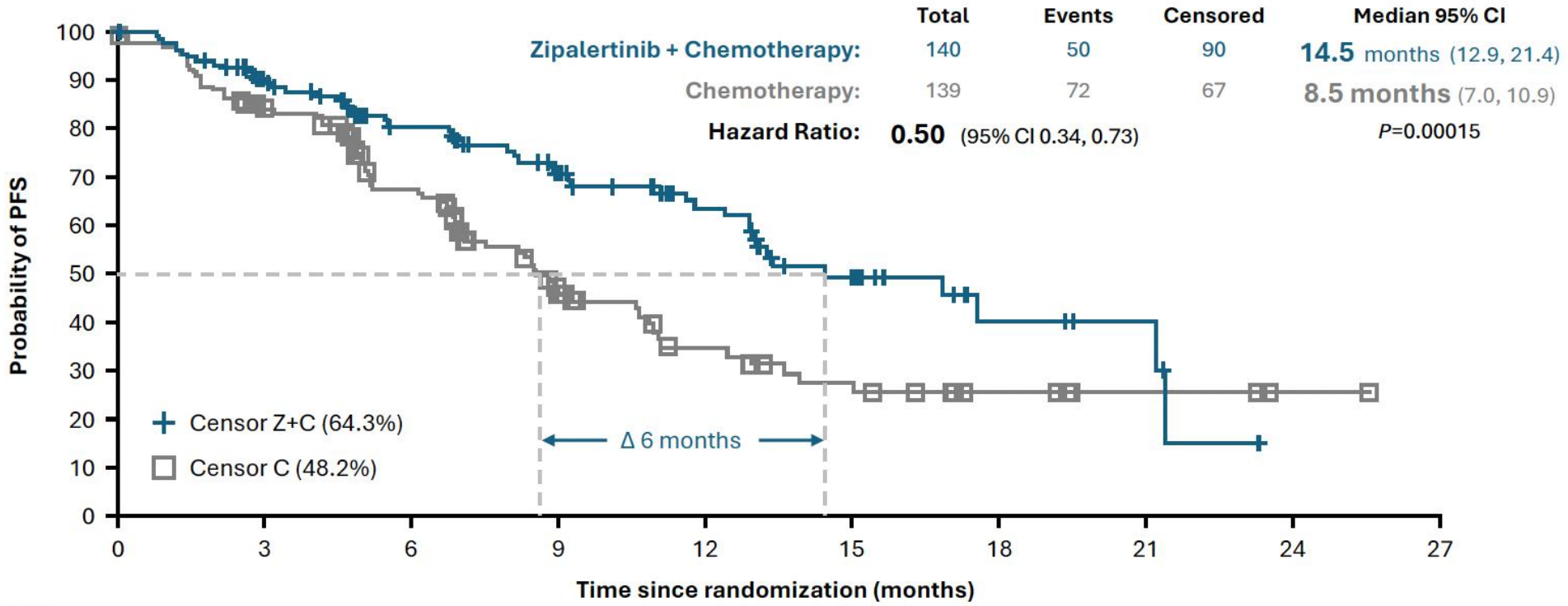
Pre-specified interim analysis:

- At 122 PFS events (data cutoff date May 29, 2026)
- If one-sided P<0.0098, superiority to be claimed

1L, first line; BICR, blinded independent central review; BID, twice daily; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; *EGFR*mt, epidermal growth factor receptor mutant; ex20ins, exon 20 insertions; HR, hazard ratio; IDMC, Independent Data Monitoring Committee; NSCLC, non–small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival, PRO, patient-reported outcome; R, randomization.

REZILIENT 3: Primary Endpoint PFS by BICR

Daniel SW Tan



Number at risk										
Zipalertinib + chemotherapy	140	109	81	59	40	22	7	4	0	
Chemotherapy	139	102	73	36	20	14	6	3	1	0

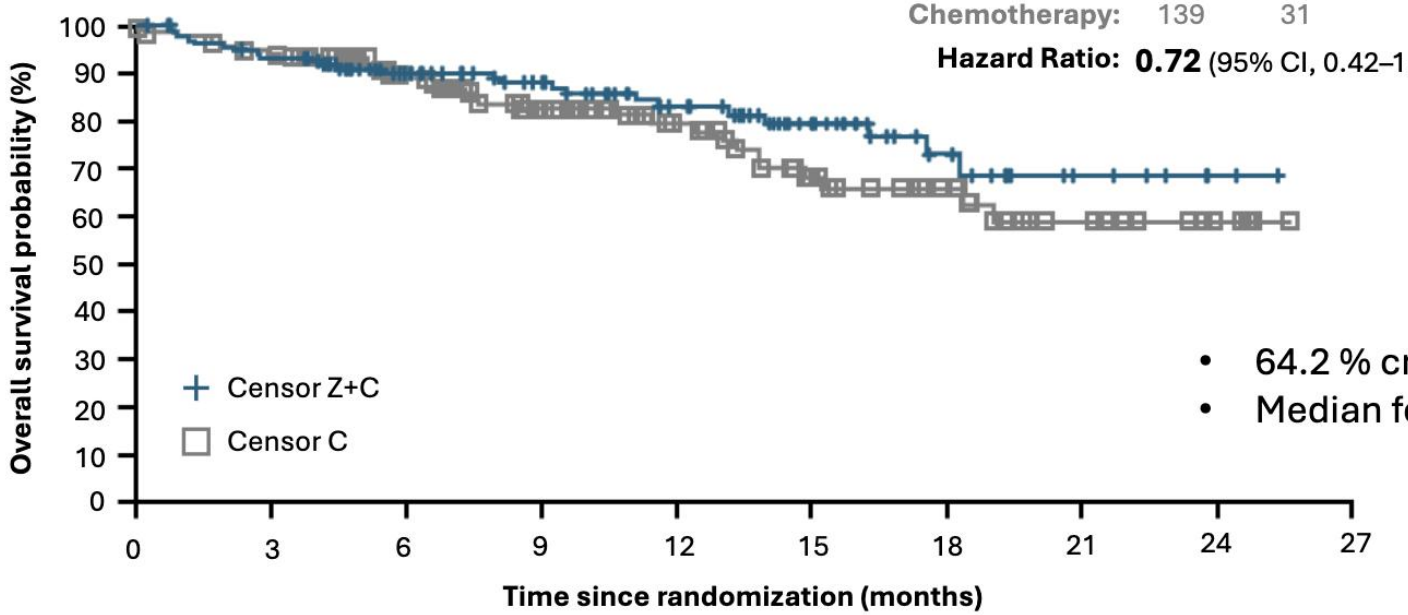
BICR, blinded independent central review; C, chemotherapy; CI, confidence interval; NE, not estimable; PFS, progression-free survival; Z+C, zipalertinib + chemotherapy.

REZILIENT 3: Overall Survival

Daniel SW Tan

	Total	Events	Censored	Median 95% CI
Zipalertinib + chemotherapy:	140	24	116	NE (NE, NE)
Chemotherapy:	139	31	108	NE (18.4, NE)

Hazard Ratio: **0.72** (95% CI, 0.42–1.23) *P*=0.11082



- 64.2 % crossover to zipalertinib[a]
- Median follow-up 10.9 months

Number at risk

Zipalertinib + Chemotherapy	140	127	98	79	56	38	19	8	3	0
Chemotherapy	139	126	97	67	47	31	22	11	4	0

[a]Based on 53 patients with progressive disease, of whom 34 crossed over.
C, chemotherapy; NE, not estimable; Z+C, zipalertinib + chemotherapy.

ARROS-1: A Global First-in-Human Phase 1/2 Clinical Trial of Zidesamtinib in Advanced *ROS1*-Positive NSCLC and Other Solid Tumors (NCT05118789)

PHASE 1

Zidesamtinib dose escalation (25 – 150 mg QD) in ROS1 TKI-pretreated patients with advanced *ROS1*+ solid tumors

PHASE 2: Zidesamtinib 100 mg QD (RP2D)

PATIENT POPULATION	PRIOR ROS1 TKI	PRIOR LINES CHEMO/I-O [a]
ROS1+ NSCLC Cohorts	ROS1 TKI-naive	≤ 1
	1 prior ROS1 TKI [b]	None
		1
	≥ 2 Prior ROS1 TKIs [c]	≤ 1
Any *ROS1*+ Solid Tumor Cohort [d]	Any	Any

PHASE 2 ENDPOINTS

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

Alexander E. Drilon,

[a] Platinum-based chemotherapy with or without immunotherapy. [b] Either crizotinib or entrectinib. [c] With initial TKI of either crizotinib or entrectinib. [d] Exploratory cohort, currently enrolling; includes patients with NSCLC who do not qualify for any of the other cohorts.

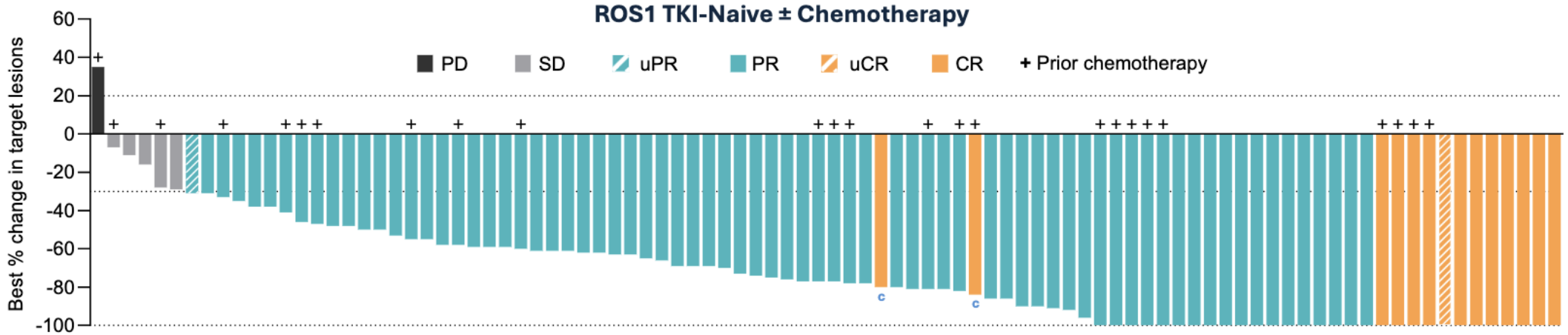
BICR, blinded independent central review; **chemo**, chemotherapy; **DOR**, duration of response; **I-O**, immunotherapy; **NSCLC**, non-small cell lung cancer; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **PK**, pharmacokinetics; **PRO**, patient reported outcome; **QD**, once daily; **ROS1**, c-ros oncogene 1; **RP2D**, recommended phase 2 dose; **TKI**, tyrosine kinase inhibitor; **TTR**, time to response.

ARROS-1: Objective Response in ROS1 TKI-Naive Patients with NSCLC

Alexander E. Drilon,

Advanced *ROS1*+ NSCLC RECIST v1.1 by BICR	**ROS1 TKI-Naive ± Prior Chemotherapy (n = 94)**
ORR, % (n/N) [a] [95% CI]	**94%** (88/94) [87, 98]
CR, % (n/N) [b]	**15%** (14/94)

[a] Includes 1 single-timepoint PR pending confirmation in ongoing patient.
[b] Includes 1 single-timepoint CR pending confirmation in ongoing patient with prior confirmed PR.

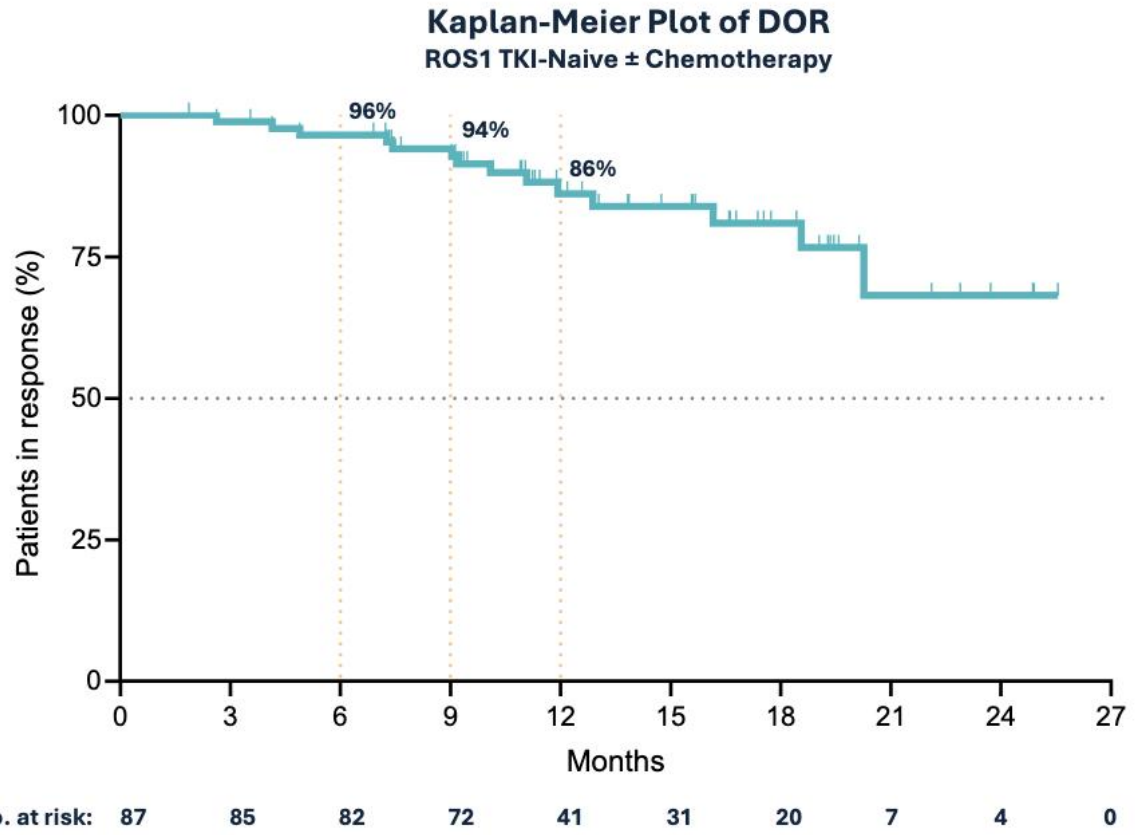


[c] CR with <100% shrinkage due to residual non-pathologic lymph node.
BICR, blinded independent central review; **CR**, complete response; **NSCLC**, non-small cell lung cancer; **ORR**, objective response rate; **PD**, progressive disease; **PR**, partial response; **RECIST**, Response Evaluation Criteria in Solid Tumor; **ROS1**, c-ros oncogene 1; **SD**, stable disease; **TKI**, tyrosine kinase inhibitor; **uCR**, unconfirmed CR (single-timepoint CR pending confirmation in ongoing patient with prior confirmed PR); **uPR**, unconfirmed PR (single-timepoint PR pending confirmation in ongoing patient).

ARROS-1: Duration of Response in ROS1 TKI-Naive Patients with NSCLC

Alexander E. Drilon,

Advanced *ROS1*+ NSCLC Kaplan-Meier Estimate	**ROS1 TKI-Naive ± Prior Chemotherapy n = 87**
% DOR ≥ 6 months [95% CI]	**96%** [89, 99]
% DOR ≥ 9 months [95% CI]	**94%** [86, 97]
% DOR ≥ 12 months [95% CI]	**86%** [75, 92]
Median DOR, months [95% CI]	**NR** [20, NE]

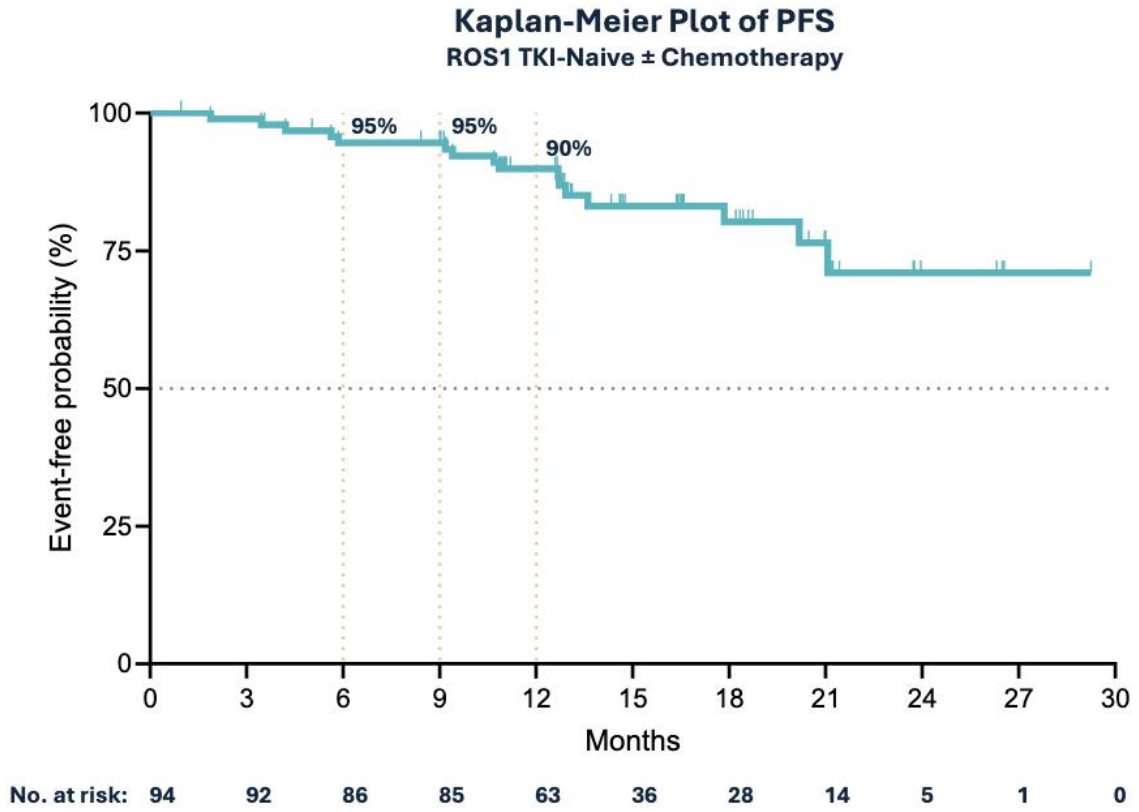


DOR, duration of response; **NE**, not estimable; **NR**, not reached; **NSCLC**, non-small cell lung cancer; **ROS1**, c-ros oncogene 1; **TKI**, tyrosine kinase inhibitor.

ARROS-1: Progression-Free Survival in ROS1 TKI-Naive Patients with NSCLC

Alexander E. Drilon,

Advanced *ROS1*+ NSCLC Kaplan-Meier Estimate	**ROS1 TKI-Naive ± Prior Chemotherapy n = 94**
% PFS ≥ 6 months [95% CI]	**95%** [87, 98]
% PFS ≥ 9 months [95% CI]	**95%** [87, 98]
% PFS ≥ 12 months [95% CI]	**90%** [81, 95]
Median PFS, months [95% CI]	**NR** [NE, NE]



NE, not estimable; NR, not reached; NSCLC, non-small cell lung cancer; PFS, progression-free survival; ROS1, c-ros oncogene 1; TKI, tyrosine kinase inhibitor.

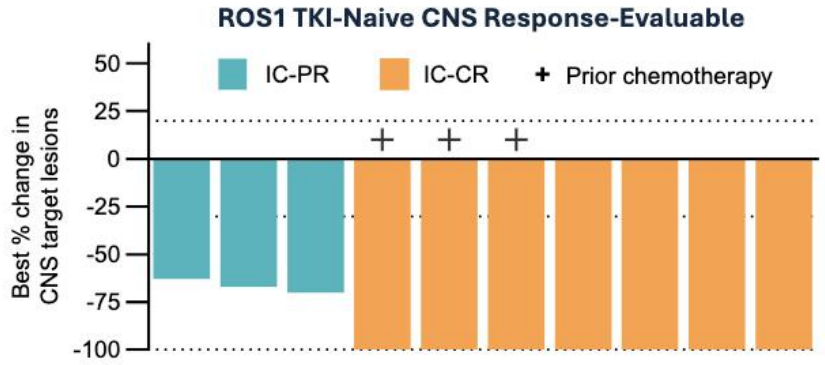
ARROS-1: CNS Activity in ROS1 TKI-Naive Patients with NSCLC

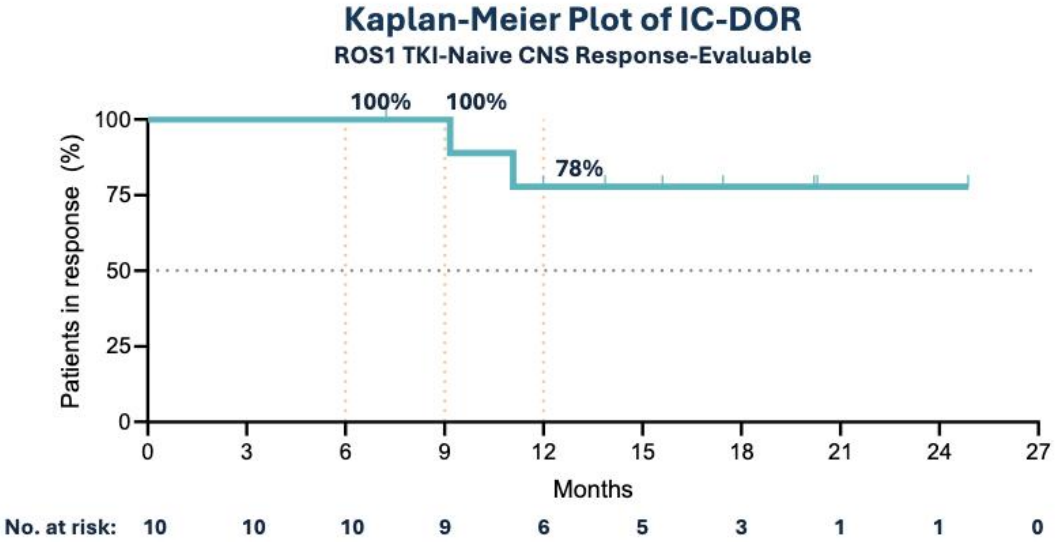
Alexander E. Drilon,

CNS Response-Evaluable Population [a] RECIST v1.1 by BICR	ROS1 TKI-Naive ± Prior Chemotherapy n = 10
IC-ORR, % (n/N) [95% CI]	**100%** (10/10) [69, 100]
IC-CR, % (n/N)	**70%** (7/10)
% IC-DOR ≥ 6 months [b] [95% CI]	**100%** [100, 100]
% IC-DOR ≥ 9 months [b] [95% CI]	**100%** [100, 100]
% IC-DOR ≥ 12 months [b] [95% CI]	**78%** [36, 94]
Median IC-DOR, months [b] [95% CI]	**NR** [9, NE]

[a] Includes patients without brain radiation within 2 months of the first dose of zidesamtinib with measurable (≥5 mm) CNS lesions at baseline by BICR.
[b] Analyses of DOR based on Kaplan-Meier estimates.

No CNS progression events observed among the 78 ROS1 TKI-naive patients who entered the study without brain metastases at baseline per BICR





BICR, blinded independent central review; CNS, central nervous system; IC-CR, intracranial complete response; IC-DOR, intracranial duration of response; IC-ORR, intracranial objective response rate; IC-PR, intracranial partial response; NE, not estimable; NR, not reached; NSCLC, non-small cell lung cancer; RECIST, Response Evaluation Criteria in Solid Tumor; ROS1, c-ros oncogene 1; TKI, tyrosine kinase inhibitor.

DESTINY-Lung04 trial design

Isamu Okamoto

A randomized, open-label, multicenter, Phase 3 trial (NCT05048797)

Patients

- Unresectable locally advanced or metastatic nonsquamous NSCLC
- Treatment naïve for advanced disease
- *HER2* exon 19 or 20 mutation by central/local test
- ECOG PS 0 or 1
- Asymptomatic/stable/treated brain metastases permitted
- ≥1 measurable lesion per RECIST 1.1

R 1:1

N=454

T-DXd* n=227

Pembro† + platinum chemo‡ + pemetrexed§ n=227

Endpoints

Primary¶
- PFS (BICR)

Secondary
- OS‖
- ORR and DOR (BICR)
- PFS2 (investigator)
- Safety and tolerability

Stratification factors

- Presence/history of brain metastases (yes vs no)
- Smoking history status (ever vs never)

- Data cutoff for final PFS analysis / first OS interim analysis: **June 9, 2026**
  - Formal hypothesis testing for OS will be performed at second interim and final analyses only
- Median (range) duration of follow up: **21.6 months (0.4–51.1) with T-DXd** vs **20.4 months (0.1–52.0) with pembro + chemo**

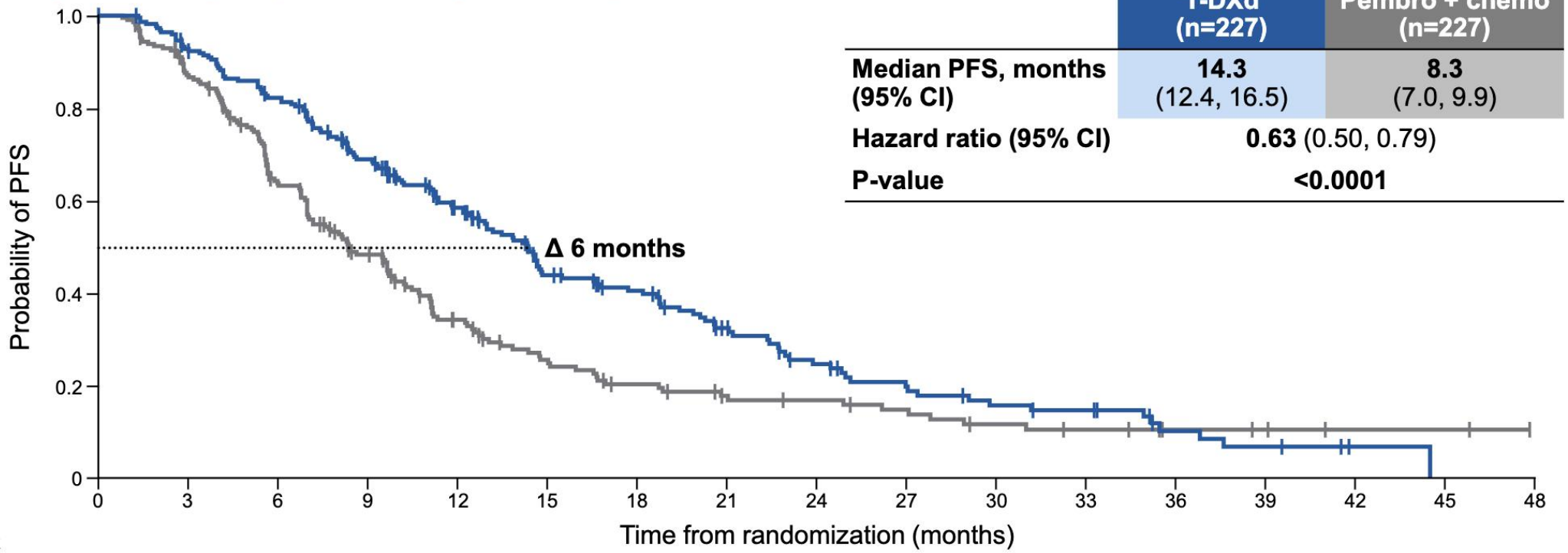
PFS, ORR, and DOR all per RECIST 1.1. Participants with objective radiological CNS disease progression per RECIST 1.1 could continue with their assigned trial treatment if, in the investigator's opinion, they continued to receive clinical benefit and were without any discontinuation criteria. Treatment crossover was not permitted

*5.4 mg/kg IV Q3W until disease progression, unacceptable toxicity, or other discontinuation criteria; †200 mg IV Q3W until disease progression, unacceptable toxicity, or other discontinuation criteria; ‡investigator choice of cisplatin (75 mg/m^2) or carboplatin (AUC 5) IV Q3W for up to four cycles; §500 mg/m^2 IV Q3W until disease progression, unacceptable toxicity, or other discontinuation criteria; ¶for the final PFS analysis, ~306 events provided 90% power to detect a hazard ratio of 0.69 with a two-sided significance level of 5%; ‖the first OS interim analysis was conducted at the time of final PFS analysis; no formal hypothesis testing was planned

PFS (BICR): primary endpoint

Isamu Okamoto

	T-DXd (n=227)	Pembro + chemo (n=227)
Median PFS, months (95% CI)	**14.3** (12.4, 16.5)	**8.3** (7.0, 9.9)
Hazard ratio (95% CI)	**0.63** (0.50, 0.79)	
P-value	**<0.0001**	



No. at risk

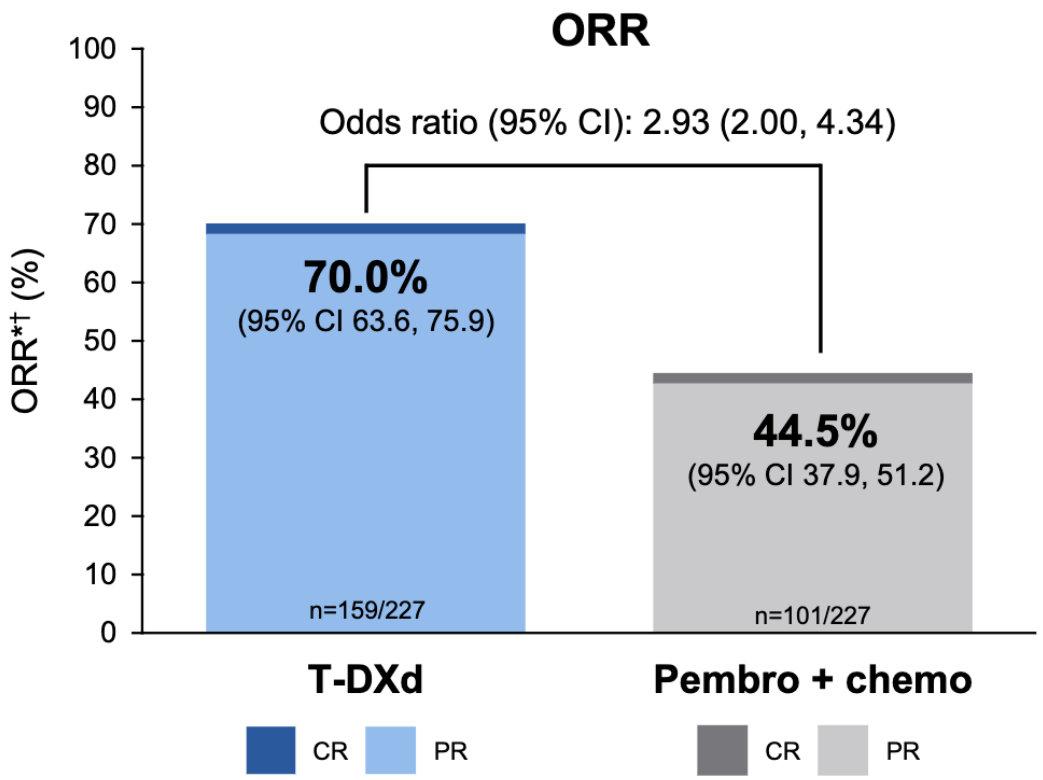
T-DXd	227	203	178	141	104	69	58	37	27	19	15	13	6	4	1	0	0
Pembro + chemo	227	180	123	86	50	33	25	18	17	13	10	8	5	3	2	2	0

T-DXd monotherapy demonstrated a statistically significant and clinically meaningful PFS improvement vs standard-of-care pembro + doublet chemo

PFS per RECIST 1.1; at data cutoff, there were 307 BICR-assessed PFS events

Secondary efficacy endpoints

Isamu Okamoto



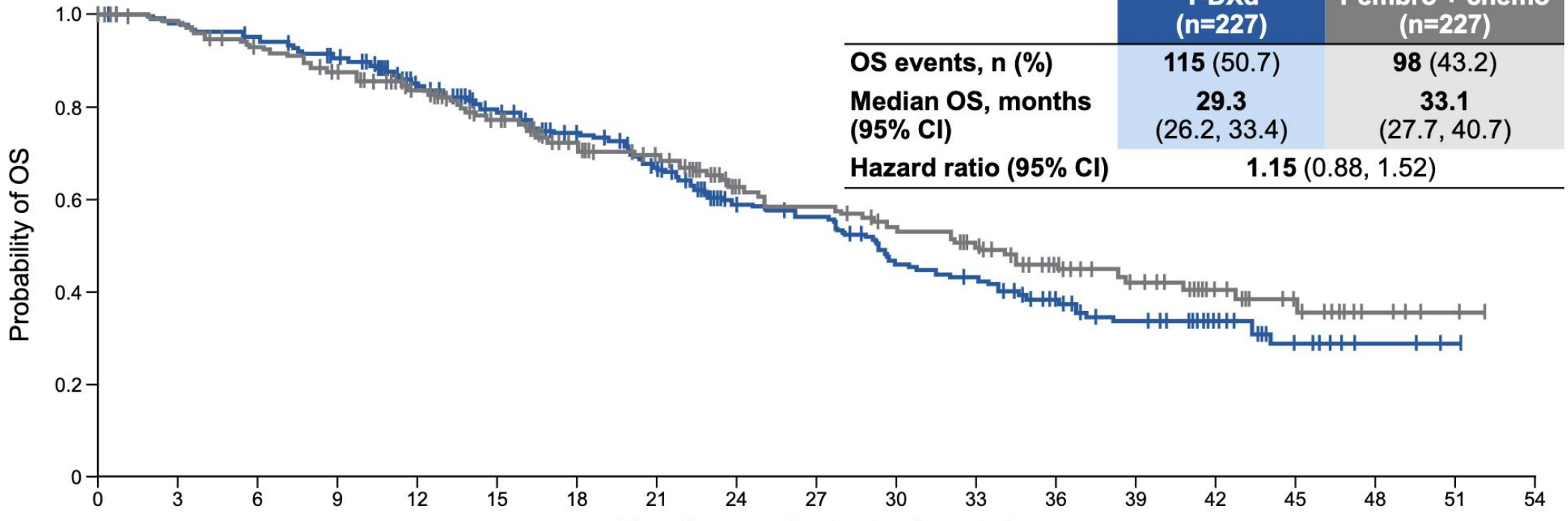
	T-DXd (n=227)	Pembro + chemo (n=227)
Best overall response,*† n (%)		
Complete response	4 (1.8)	4 (1.8)
Partial response	155 (68.3)	97 (42.7)
Stable disease	61 (26.9)	98 (43.2)
Progressive disease‡	4 (1.8)	15 (6.6)
Non-evaluable‡	3 (1.3)	13 (5.7)
Median DOR,* months (95% CI)	13.4 (10.4, 17.2)	9.7 (7.0, 11.1)
Median PFS2,§ months (95% CI)	22.7 (20.3, 26.3)	17.3 (15.6, 21.8)
Hazard ratio (95% CI)	0.80 (0.62, 1.02)	

*By BICR per RECIST 1.1; †includes unconfirmed responses; ‡for patients who died with no evaluable RECIST assessments, best overall response was assigned as either progressive disease (if the death occurred ≤13 weeks after randomization) or non-evaluable (if the death occurred >13 weeks after randomization); §PFS2 was determined by investigator per RECIST 1.1 according to local standard clinical practice as the time from randomization to second progression (earliest progression event following first subsequent therapy) or death

Overall survival*

Isamu Okamoto

	T-DXd (n=227)	Pembro + chemo (n=227)
OS events, n (%)	**115** (50.7)	**98** (43.2)
Median OS, months (95% CI)	**29.3** (26.2, 33.4)	**33.1** (27.7, 40.7)
Hazard ratio (95% CI)	**1.15** (0.88, 1.52)	



No. at risk																		
T-DXd	227	222	214	201	176	157	136	117	85	79	63	58	40	31	22	8	3	1	0
Pembro + chemo	227	213	198	184	164	142	123	110	85	79	69	62	43	31	20	14	5	2	0

No OS benefit was observed with T-DXd; subsequent treatments may have impacted results

At data cutoff, overall data maturity for OS was 46.9%. Median follow up was 21.6 months (range 0.4–51.1) in the T-DXd arm and 20.4 months (range 0.1–52.0) in the pembro + chemo arm

*This administrative OS interim analysis was performed with a two-sided alpha-spend of 0.0001. **Formal hypothesis testing will be performed at the second interim analysis and final analysis**


Gracias