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LUNG CONNECT

ONCOGENE-ADDICTED NSCLC HIGHLIGHTS FROM ASCO 2024

Prof. Nicolas Girard, MD

Institut Curie, Paris, France

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CLINICAL TAKEAWAYS

EGFR:

- **PALOMA-2:** provides evidence for the efficacy and safety of subcutaneous amivantamab + lazertinib and suggests it could be suitable as a first-line option for patients with *EGFR*-mutant advanced NSCLC
- **PALOMA-3:** subcutaneous amivantamab with lazertinib is noninferior to intravenous amivantamab plus lazertinib and has an improved safety profile and greater convenience

ALK:

- **CROWN:** after 5 years of treatment, the median PFS of patients with advanced *ALK*-positive NSCLC treated with lorlatinib has yet to be reached, corresponding with the longest PFS ever reported in advanced NSCLC

KRAS:

- **KRYSTAL-12:** adagrasib demonstrated a statistically significant and clinically meaningful improvement in PFS and ORR over docetaxel in patients with previously treated *KRAS*^{G12C}-mutated NSCLC

HER2:

- **SOHO-01:** in patients with heavily pre-treated *HER2*-mutant NSCLC, treatment with BAY 2927088 resulted in rapid, substantial and durable responses
- **Beamion LUNG-1:** zongertinib was well tolerated and demonstrated promising initial efficacy in pre-treated patients with *HER2*-mutated NSCLC

ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; KRAS, Kirsten rat sarcoma virus; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival

EDUCATIONAL OBJECTIVES

- Understand the clinical trial data and emerging profile of targeted therapies for the treatment of molecularly driven lung cancer

SUBCUTANEOUS AMIVANTAMAB AND LAZERTINIB AS FIRST-LINE TREATMENT IN PATIENTS WITH *EGFR*-MUTATED, ADVANCED NSCLC: RESULTS FROM THE PHASE 2 PALOMA-2 STUDY

Lim S, et al. ASCO 2024. Abstract #LBA8612

SUBCUTANEOUS AMIVANTAMAB VS INTRAVENOUS AMIVANTAMAB, BOTH IN COMBINATION WITH LAZERTINIB, IN REFRACTORY *EGFR*-MUTATED, ADVANCED NSCLC: PRIMARY RESULTS, INCLUDING OVERALL SURVIVAL, FROM THE GLOBAL, PHASE 3, RANDOMISED CONTROLLED PALOMA-3 TRIAL

Leighl N, et al. ASCO 2024. Abstract #LBA8505

EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer

PALOMA-2/-3: BACKGROUND

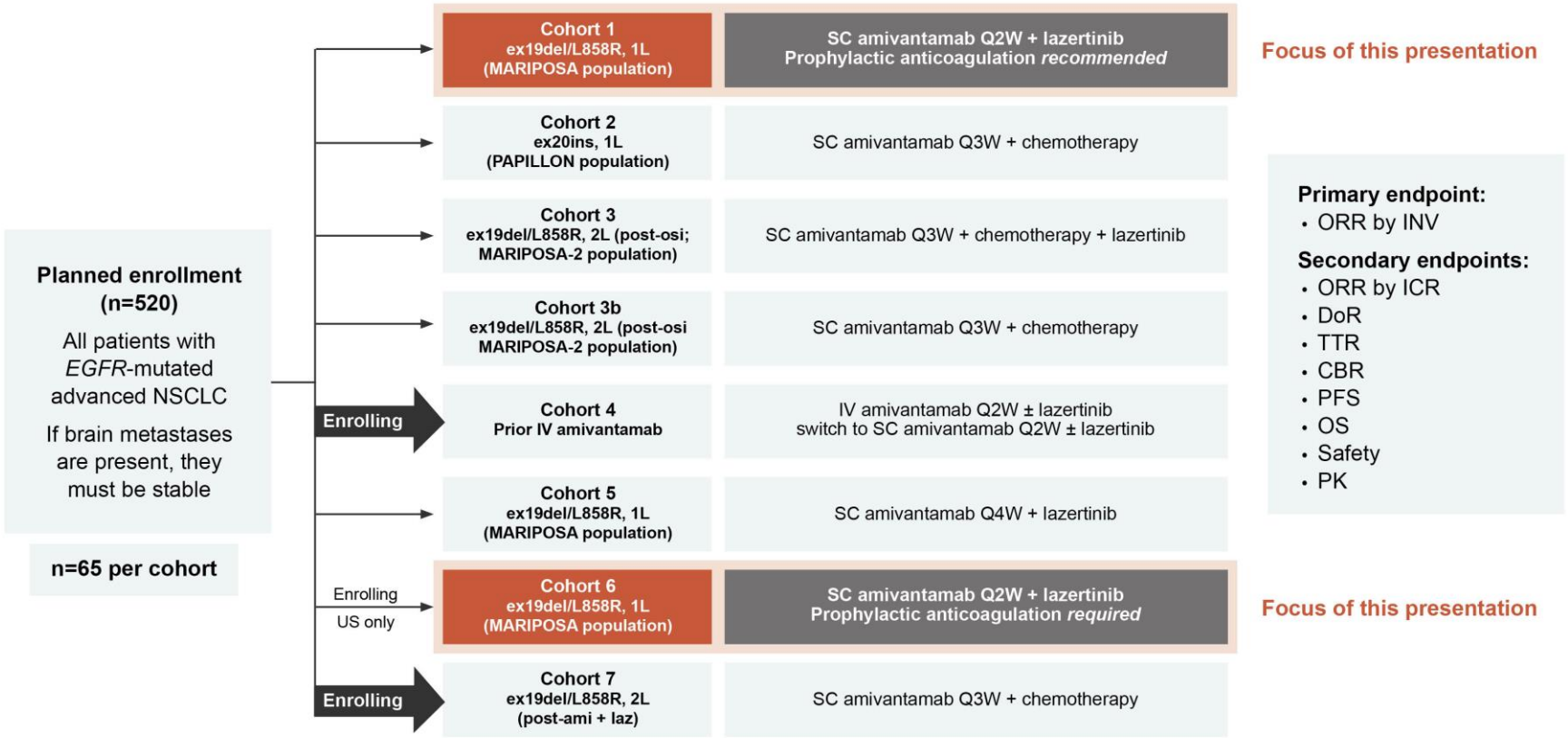
- Amivantamab, an EGFR-MET bispecific antibody with immune cell-directing activity, is approved as an IV formulation for first- and second-line treatment of patients with *EGFR* exon 20 insertion-mutated advanced NSCLC
- First-line amivantamab + lazertinib (3rd generation EGFR TKI) provided clinically meaningful improvements in PFS in *EGFR*-mutated advanced NSCLC patients versus osimertinib in the MARIPOSA study
- A subcutaneous (SC) formulation of amivantamab is being developed to improve patient experience and convenience for healthcare professionals
- The recommended phase 2 dose and dosing schedule was determined in the phase 1 PALOMA study
- The efficacy and safety of the SC formulation is now being evaluated in the PALOMA-2 and PALOMA-3 studies

NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

Lim S, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8612) (ASCO 2024 poster); Leighl N, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8505) (ASCO 2024 oral presentation); Cho BC, et al. Annals of Oncology (2023) 34 (suppl_2): S1254-S1335

PALOMA-2: BACKGROUND AND STUDY DESIGN

- PALOMA-2 is a phase 2 study evaluating the efficacy, safety and PK of first-line SC amivantamab + lazertinib in *EGFR*-mutated advanced NSCLC



1L, first line; 2L, second line; ami, amivantamab; CBR, clinical benefit rate; DoR, duration of response; EGFR, epidermal growth factor receptor; ex19 del, exon 19 deletion; ex20ins, exon 20 insertion; ICR, independent central review; INV, investigator; IV, intravenous; laz, lazertinib; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; osi, osimertinib; PFS, progression-free survival; PK, pharmacokinetics; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks; SC, subcutaneous; TTR, time to response; US, United States

Lim S, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8612) (ASCO 2024 poster)

PALOMA-2: RESULTS

EFFICACY

Responses (confirmed and unconfirmed)

	Cohort 1 (n=68)		Cohort 6 (n=45)[a]		Overall (N=113)	
	INV	ICR	INV	ICR	INV	ICR
ORR (95% CI), %	75 (63-85)	81 (70-89)	80 (65-90)	76 (61-87)	77 (68-84)	79 (70-86)

The median follow-up was 10.0 months for Cohort 1, 6.1 months for Cohort 6, and 8.6 months overall.
[a]Efficacy analyses in Cohort 6 were performed on patients who enrolled on or before July 20, 2023.

- Among the confirmed responders in both cohorts:
  - Median TTR: 1.9 months (range, 1.4-5.3)
  - Median DoR: not estimable

SAFETY

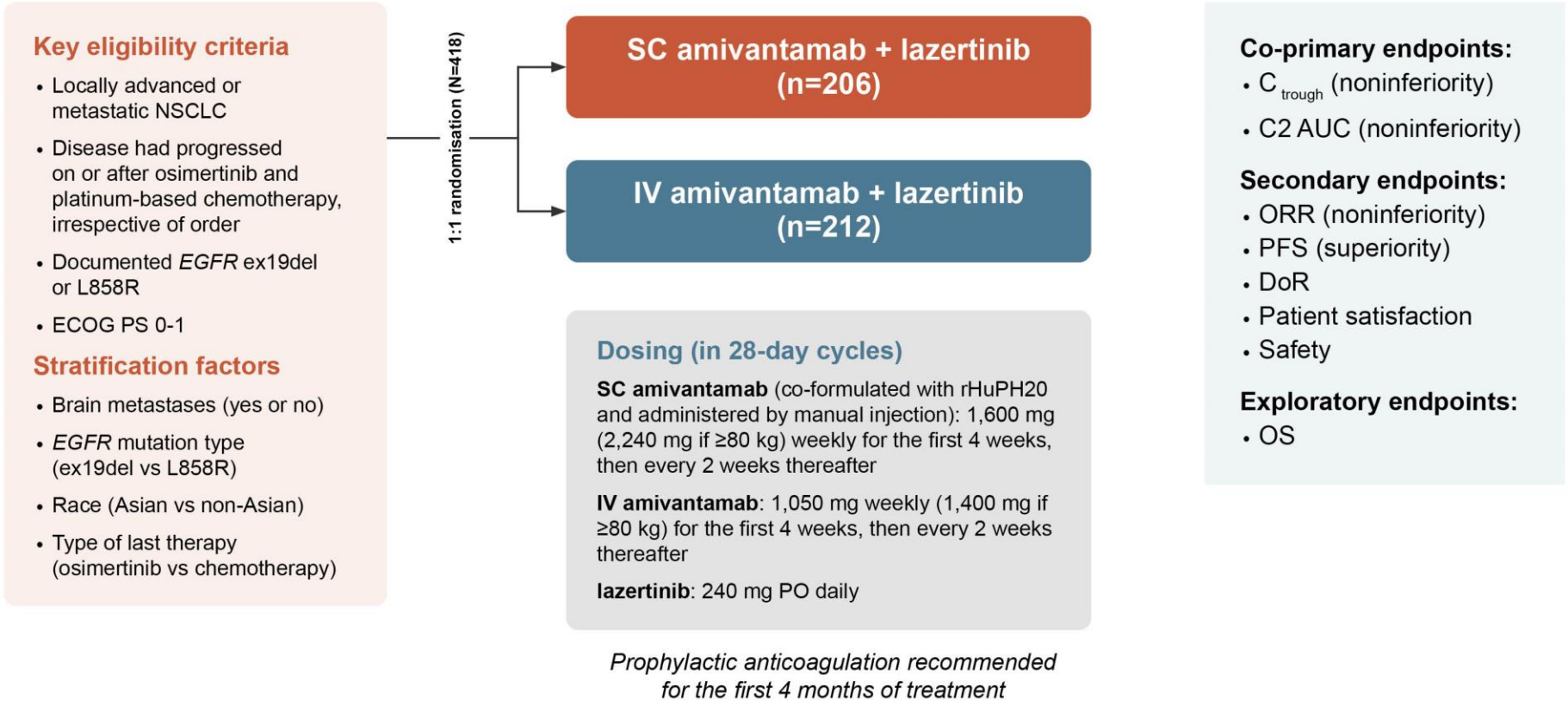
- The safety profile of SC amivantamab + lazertinib was consistent with previous reports of the IV formulation, with no new safety signals identified
- However, markedly lower rates of ARRs and VTE were observed with the SC formulation
- Discontinuation of all agents due to TRAEs occurred in 9% (11/125) of patients

ARR, administration-related reaction; CI, confidence interval; DoR, duration of response; ICR, independent central review; INV, investigator; IV, intravenous; ORR, objective response rate; SC, subcutaneous; TRAE, treatment related adverse event; TTR, time to response; VTE, venous thromboembolism

Lim S, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8612) (ASCO 2024 poster)

PALOMA-3: BACKGROUND AND STUDY DESIGN

- PALOMA-3 (NCT05388669) is a phase 3 study which evaluated SC ami+laz vs IV ami+laz for pharmacokinetics (PK), efficacy, and safety among pts with *EGFR* ex19del or L858R-mutated advanced NSCLC and disease progression on osimertinib and platinum-based chemotherapy



ami, amivantamab; AUC, area under the curve; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; Ex19 del, exon 19 deletion; IV, intravenous; laz, lazertinib; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SC, subcutaneous

Leighl N, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8505) (ASCO 2024 oral presentation)

PALOMA-3: RESULTS

EFFICACY

	SC amivantamab arm (n=206)	IV amivantamab arm (n=212)
ORR (95% CI), %		
All responders	30 (24-37)	33 (26-39)
	Relative risk, 0.92 (95% CI, 0.70-1.23); p=0.001	
Confirmed responders	27 (21-33)	27 (21-33)
	Relative risk, 0.99 (95% CI, 0.72-1.36); p>0.001	
Best response, n (%)		
CR	1 (0.5)	1 (0.5)
PR	61 (30)	68 (32)
SD	93 (45)	81 (38)
PD	37 (18)	42 (20)
Not evaluate	14 (7)	20 (9)
DCR (95% CI), %	75 (69-81)	71 (64-77)
Median TTR (range), mo	1.5 (1.2-6.9)	1.5 (1.2-9.9)
Median DoR (95% CI), mo	11.2 (6.1-NE)	8.3 (5.4-NE)
Median PFS, (95% CI), mo	6.1 (4.3-8.1)	4.3 (4.1-5.7)
HR (95% CI)	0.84 (0.64-1.10); p=0.20	
Median OS (95% CI), mo	NA	NA
HR (95% CI)	0.62 (0.42-0.92); p=0.017	

SAFETY

- TEAEs were consistent between arms
- AEs leading to death were uncommon and similar between arms
- Treatment discontinuations: 9% in SC arm and 12% in IV arm
- IRRs were ~5-fold lower in the SC arm: 13% vs 66% for IV
- Prophylactic anticoagulants were administered to 80% of patients in the SC arm and 81% for IV
- Among all study patients, VTE was reported by 9% in the SC arm vs 14% for IV.
- Across both arms, VTE incidence was 10% for pts who received prophylactic anticoagulants vs 21% for pts who did not

AE, adverse event; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; HR, hazard ratio; IRR, infusion-related reaction; IV, intravenous; mo, months; NE, not evaluable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; pts, patients; SC, subcutaneous; SD, stable disease; TEAE, treatment emergent adverse event; TTR, time to response; VTE, venous thromboembolism

Leighl N, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8505) (ASCO 2024 oral presentation)

PALOMA-2/-3: SUMMARY

- **PALOMA-2:** SC amivantamab + lazertinib showed meaningful efficacy in 1L *EGFR*-mutated NSCLC with an ORR comparable to that of the IV formulation
  - The safety profile was as previously observed for the IV formulation, with the exception of VTE and ARR, which were markedly lower
- **PALOMA-3:** SC amivantamab demonstrated noninferior PK and ORR compared to IV
  - Unexpectedly, DoR, PFS, and OS were longer in the SC arm vs IV, suggesting that the route of administration or formulation may affect outcomes
  - The safety profile was improved for SC amivantamab, with lower IRR and VTE rates

Clinical perspective

PALOMA-2

- This study provides evidence for the efficacy and safety of SC amivantamab + lazertinib and suggests it could be suitable as a first-line option for patients with *EGFR*-mutant advanced NSCLC

PALOMA-3

- Subcutaneous amivantamab with lazertinib is noninferior to the intravenous combination and has an improved safety profile and greater convenience

1L, first-line; ARR, administration related reaction; DoR, duration of response; EGFR, epidermal growth factor receptor; IRR, infusion-related reaction; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; SC, subcutaneous; VTE, venous thromboembolism

Lim S, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8612) (ASCO 2024 poster); Leighl N, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8505) (ASCO 2024 oral presentation)

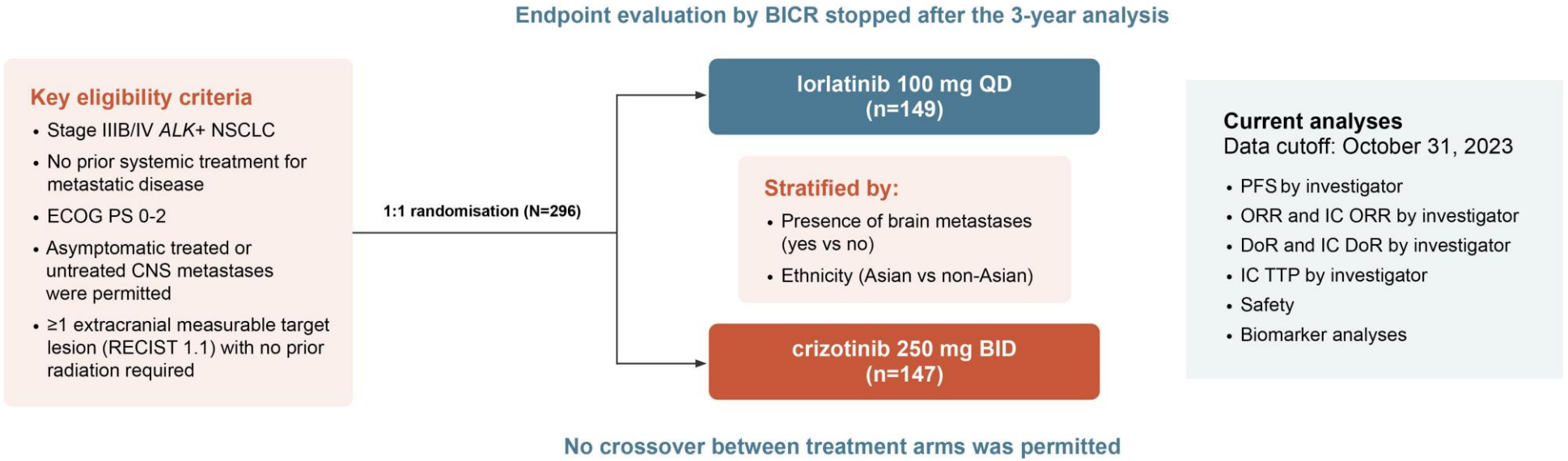
LORLATINIB VS CRIZOTINIB IN TREATMENT-NAÏVE PATIENTS WITH ADVANCED *ALK*+ NSCLC: 5-YEAR PROGRESSION-FREE SURVIVAL AND SAFETY FROM THE CROWN STUDY

Solomon B, et al. ASCO 2024. Abstract #LBA8503

ALK, anaplastic lymphoma kinase; NSCLC, non-small cell lung cancer

CROWN: BACKGROUND AND STUDY DESIGN

- Lorlatinib, a brain-penetrant, 3rd-generation ALK TKI, demonstrated improved PFS and intracranial activity vs crizotinib in the phase 3 CROWN study in previously untreated patients with advanced ALK+ NSCLC
- In a previous analysis at 3-years follow-up, median PFS by BICR was still not reached
- Long-term efficacy and safety outcomes from the CROWN study after 5 years of follow-up was reported at ASCO 2024



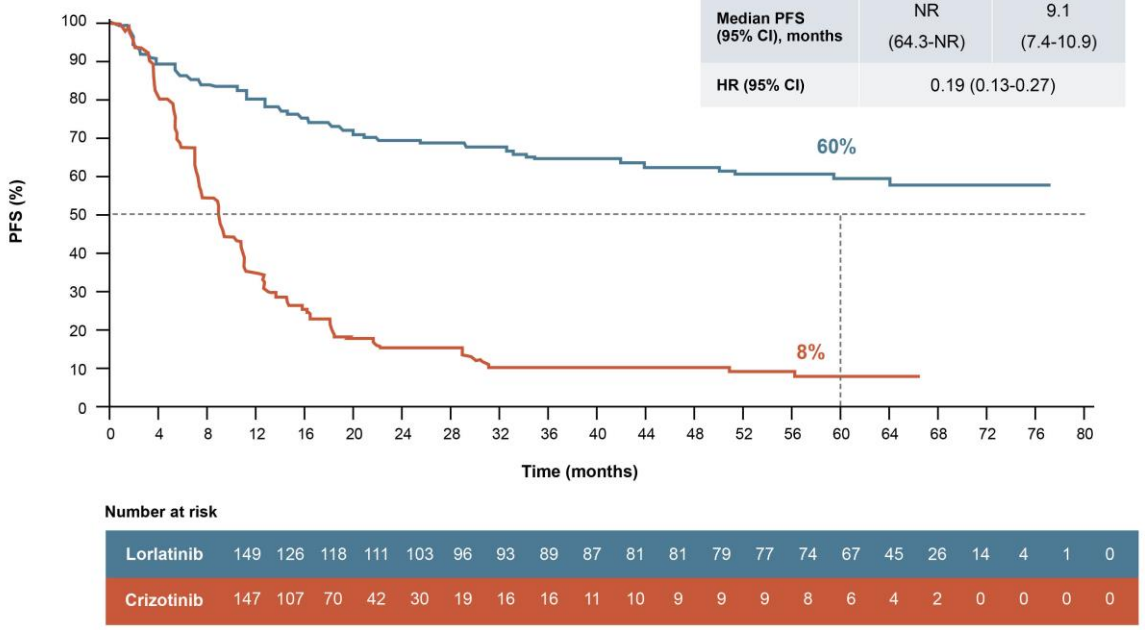
ALK, anaplastic lymphoma kinase; BICR, blinded independent central review; BID, twice daily; CNS, central nervous system; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; IC, intracranial; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; PS, performance status; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumours; TKI, tyrosine kinase inhibitor; TTP, time to tumour progression

Solomon B, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8503) (ASCO 2024 oral presentation); Solomon B, et al. J Clin Oncol 2024: https://doi.org/10.1200/JCO.24.005

CROWN: RESULTS

- Median follow-up for PFS: 60.2 months in the lorlatinib and 55.1 months in the crizotinib arm

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



Number at risk

Lorlatinib	149	126	118	111	103	96	93	89	87	81	81	79	77	74	67	45	26	14	4	1	0
Crizotinib	147	107	70	42	30	19	16	16	11	10	9	9	9	8	6	4	2	0	0	0	0

	With Baseline Brain Metastases		Without Baseline Brain Metastases	
	Lorlatinib (n=35)	Crizotinib (n=38)	Lorlatinib (n=114)	Crizotinib (n=109)
PFS				
Median (95% CI), months	NR (32.9-NR)	6.0 (3.7-7.6)	NR (64.3-NR)	10.8 (9.0-12.8)
HR (95% CI)	0.08 (0.04-0.19)		0.24 (0.16-0.36)	
5-year PFS (95% CI), %	53 (35-68)	Not estimable	63 (52-71)	10 (5-19)
Time to IC progression				
Median (95% CI), months	NR (NR-NR)	7.2 (3.7-11.0)	NR (NR-NR)	23.9 (16.4-30.8)
HR (95% CI)	0.03 (0.01-0.13)		0.05 (0.02-0.13)	

- **Grade 3/4 AEs:** 77% of pts with lorlatinib, 57% of pts with crizotinib
- TRAEs led to treatment discontinuation in 5% and 6% of pts in the lorlatinib and crizotinib arms, respectively
- **Safety profile** was **consistent with** that observed in **prior analyses**
- **No new *ALK* mutations detected** in ctDNA collected at the end of lorlatinib treatment (n = 31)

AE, adverse events; ALK, anaplastic lymphoma kinase; CI, confidence interval; ctDNA, circulating tumour DNA; HR, hazard ratio; IC, intracranial; NR, not reached; PFS, progression-free survival; TRAE, treatment related adverse event;

Solomon B, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8503) (ASCO 2024 oral presentation); Solomon B, et al. J Clin Oncol 2024: https://doi.org/10.1200/JCO.24.005

CROWN: SUMMARY

- After 5 years of follow up, median PFS in the lorlatinib arm has yet to be reached with 60% of patients being progression-free
- 92% of patients were intracranial progression-free
- No new safety signals emerged
- These results correspond to the longest PFS ever reported in advanced NSCLC and together with the absence of new safety signals, indicate an unprecedented improvement in outcomes for pts with advanced *ALK*+ NSCLC

Clinical perspective

- This is the longest PFS reported in *ALK*+ NSCLC, and of any targeted therapy in lung cancer to date
- The benefit of lorlatinib is not confined to patients with brain metastases
- These results represent an unprecedented outcome for patients with advanced *ALK*+ NSCLC and set a new benchmark for targeted therapies in cancer

ALK, anaplastic lymphoma kinase; NSCLC, non-small cell lung cancer; PFS, progression-free survival

Solomon B, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8503) (ASCO 2024 oral presentation); Solomon B, et al. J Clin Oncol 2024: https://doi.org/10.1200/JCO.24.005

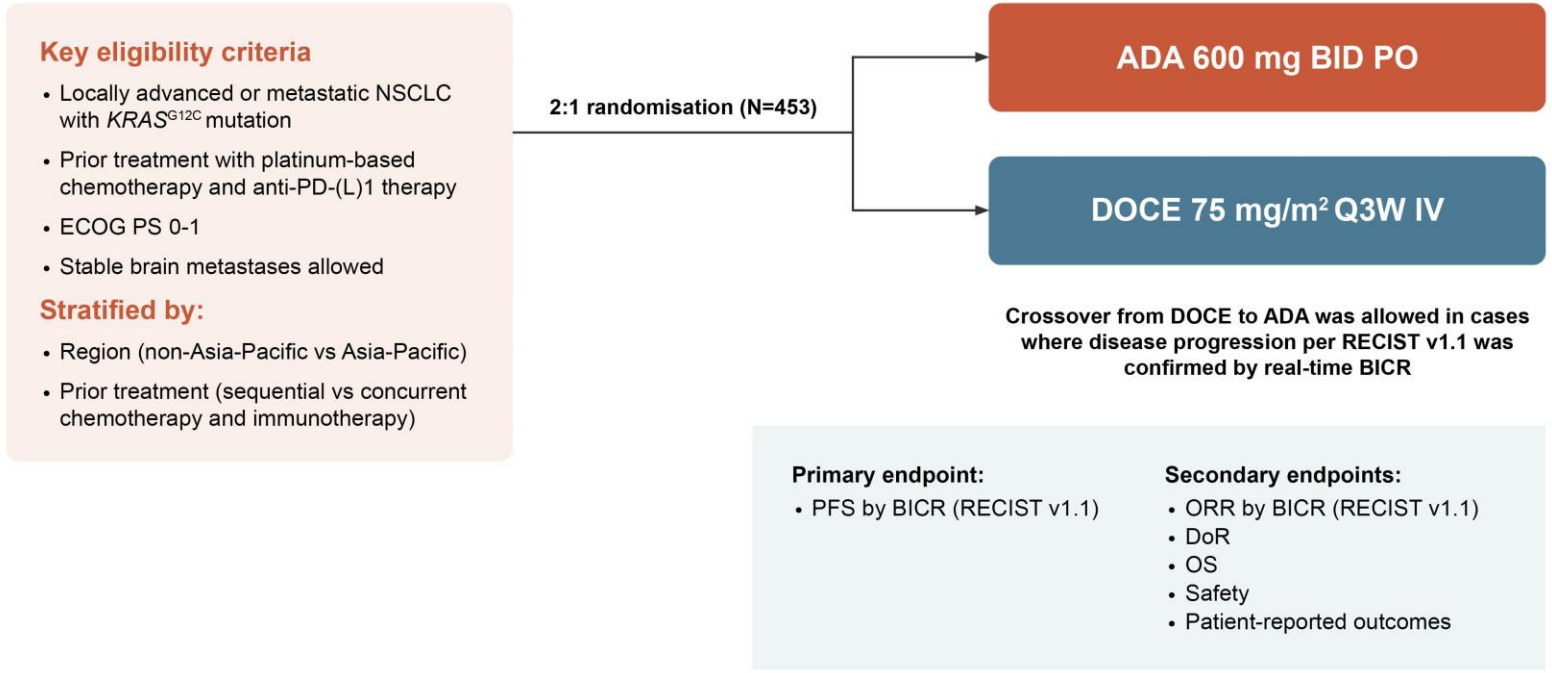
KRYSTAL-12: PHASE 3 STUDY OF ADAGRASIB VERSUS DOCETAXEL IN PATIENTS WITH PREVIOUSLY TREATED ADVANCED/METASTATIC NSCLC HARBOURING A *KRAS*^{G12C} MUTATION

Mok T, et al. ASCO 2024. Abstract #LBA8509

KRAS, Kirsten rat sarcoma virus; NSCLC, non-small cell lung cancer

KRYSTAL-12: BACKGROUND AND STUDY DESIGN

- Adagrasib (ADA), a potent covalent inhibitor of KRAS^{G12C}, demonstrated deep and durable responses with promising PFS and OS in patients with previously treated KRAS^{G12C}-mutated NSCLC in the phase 1/2 KRYSTAL-1 trial
- KRYSTAL-12 (NCT04685135) is a randomised, open-label phase 3 trial of ADA compared with docetaxel (DOCE) in patients with KRAS^{G12C}-mutated locally advanced or metastatic NSCLC who had previously received a platinum-based chemotherapy, concurrently or sequentially with anti-PD-(L)1 therapy. The primary analysis was reported at ASCO 2024

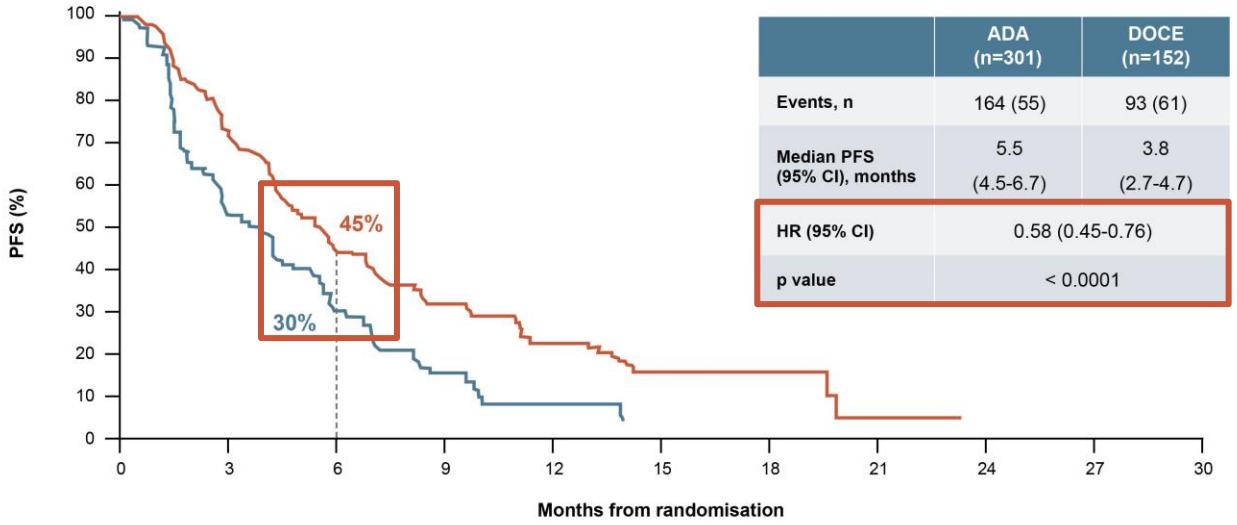


AE, adverse event; BICR, blinded independent central review; BID, twice daily; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; KRAS, Kirsten rat sarcoma virus; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PO, by mouth; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours

Mok T, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8509) (ASCO 2024 oral presentation)

KRYSTAL-12: RESULTS

PFS (BICR)



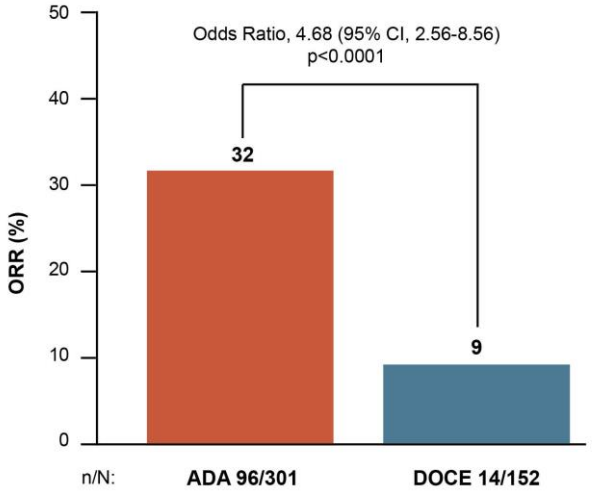
	ADA (n=301)	DOCE (n=152)
Events, n	164 (55)	93 (61)
Median PFS (95% CI), months	5.5 (4.5-6.7)	3.8 (2.7-4.7)
HR (95% CI)	0.58 (0.45-0.76)	
p value	< 0.0001	

Number at risk

ADA	301	160	77	41	19	8	5	1	0	0	0
DOCE	152	51	24	9	2	0	0	0	0	0	0

Median follow-up: 7.2 months

TUMOUR REPONSE (BICR)



Tumor response	ADA (n=301)	DOCE (n=152)
DCR, n (%)	236 (78)	89 (59)
Median DoR (95% CI), mo	8.3 (6.1-10.4)	5.4 (2.9-8.5)
Remaining in response at 6 mo, %	64	39

SAFETY

- TRAEs were reported in 94% of pts treated with ADA and 86% with DOCE; grade ≥3 TRAEs occurred in 47% and 46% of pts, respectively
- TRAEs led to discontinuation of ADA in 8% of pts and DOCE in 14%

ADA, adagrasib; BICR, blinded central independent review; CI, confidence interval; CR, complete response; DCR, disease control rate; DOCE, docetaxel; DoR, duration of response; HR, hazard ratio; mo, months; ORR, objective response rate; PFS, progression-free survival; PR, partial response; pts, patients; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease; TRAE, treatment-related adverse event

Mok T, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8509) (ASCO 2024 oral presentation)

KRYSTAL-12: SUMMARY

- In KRYSTAL-12, ADA demonstrated a statistically significant and clinically meaningful improvement in PFS and ORR over DOCE in patients with previously treated KRAS^{G12C}-mutated NSCLC
- The safety profile of ADA was consistent with previous reports and with no new safety signals
- These results further support ADA as an efficacious treatment option for pts with previously treated KRAS^{G12C}-mutated locally advanced or metastatic NSCLC

Clinical perspective

- Adagrasib has shown improved efficacy compared with the standard of practice of docetaxel, so the study is likely to be practice changing
- Adagrasib is generally well-tolerated but there are some concerns about liver toxicity and GI side effects
- The study supports early NGS testing rather than individual gene testing

ADA, adagrasib; DOCE, docetaxel; GI, gastrointestinal; KRAS, Kirsten rat sarcoma virus; NGS, next generation sequencing; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival

Mok T, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8509) (ASCO 2024 oral presentation)

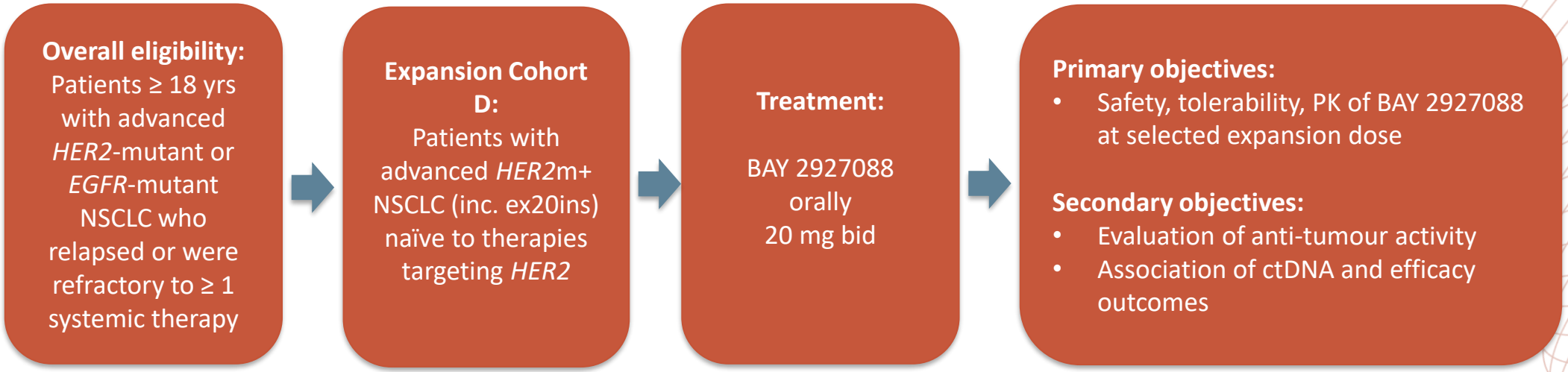
SAFETY AND ANTI-TUMOUR ACTIVITY OF BAY 2927088 IN PATIENTS WITH *HER2*-MUTANT NSCLC: RESULTS FROM AN EXPANSION COHORT OF THE SOHO-01 PHASE 1/2 STUDY

Girard N, et al. ASCO 2024. Abstract #LBA8598

HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer

SOHO-01: BACKGROUND AND STUDY DESIGN

- *HER2* mutations have been reported in approximately 2-4% of patients with NSCLC, with exon 20 insertions being the most common
- BAY 2927088 is an oral, reversible tyrosine kinase inhibitor that potently inhibits *HER2* and mutant *EGFR* in preclinical models
- Encouraging objective responses were observed in patients with NSCLC harbouring a *HER2* activating mutation treated with BAY 2927088 in the dose-escalation/backfill part of the Phase 1/2 SOHO-01 trial (NCT05099172)
- The FDA has granted Breakthrough Therapy designation for BAY 2927088 for previously-treated patients with advanced NSCLC and activating *HER2* mutations. Here we report the safety, anti-tumour activity, and longitudinal ctDNA data in a cohort of patients treated with BAY 2927088 from the expansion part of this trial



bid, twice daily; ctDNA, circulating tumour DNA; EGFR(m+), epidermal growth factor receptor (mutation positive); ex20ins, exon 20 insertion; FDA, Food and Drug Administration; HER2(m+), human epidermal growth factor receptor 2 (mutation positive); NSCLC, non-small cell lung cancer; PK, pharmacokinetics; yrs, years

Girard N, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8598) (ASCO 2024 poster)

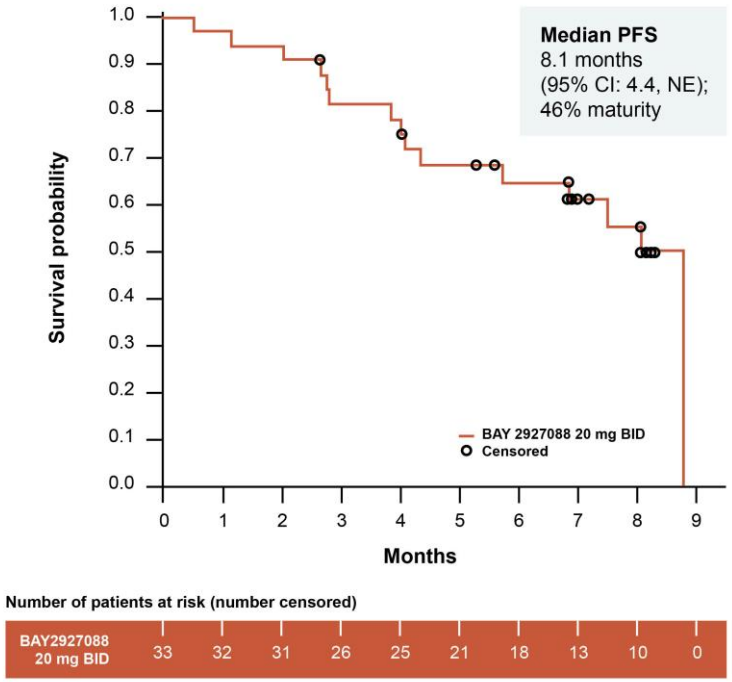
SOHO-01: RESULTS

- Median duration of treatment was 7.1 months (range 0.2-9.2). 34 patients were treated (33 evaluable for efficacy; treatment was ongoing in 17 pts (50%) at data cut-off
- Responses were rapid (median TTR: 5.7 weeks) and durable (median DoR: NR)

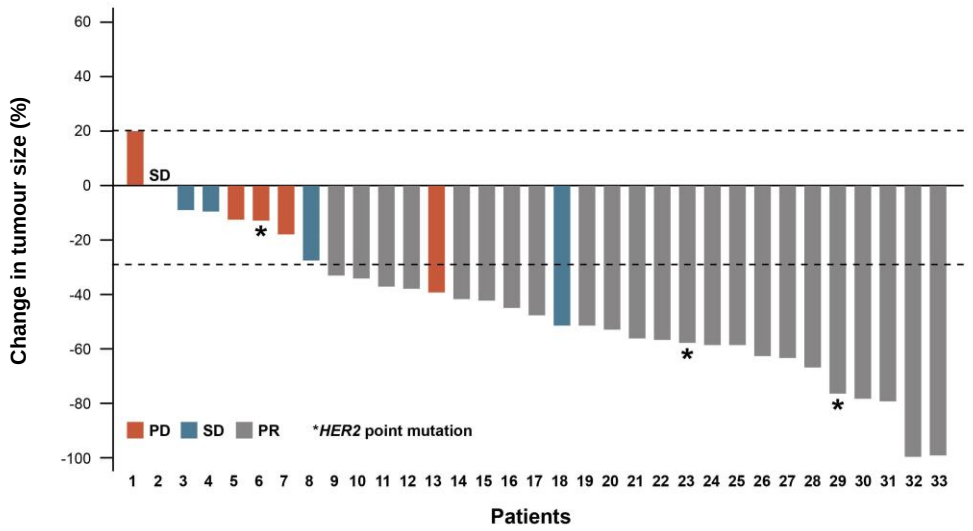
BEST OVERALL RESPONSE PER RECIST V1.1[7]

n (%)	Total (*n*=33)
Best overall response	
Complete response	0
Partial response	23 (70)
Stable disease	5 (15)
Progressive disease	5 (15)
Objective response rate[a] 95% CI	23 (70) 51.3, 84.4
Disease control rate[b] 95% CI	27 (82) 64.5, 93.0

[a] Patients with unconfirmed CR or PR when data were not available for the ongoing patients at the time of analysis or confirmed CR or PR for the others; [b] Patients with stable disease for at least 12 weeks or with either unconfirmed CR or PR when data were not available for the ongoing patients at the time of anaylsis or confirmed CR or confirmed PR for the others



WATERFALL PLOT OF BEST PERCENT CHANGE IN TARGET LESION SIZE FROM BASELINE (EFFICACY ANALYSIS SET)



- Ten patients had a dose reduction, eight had dose interruptions, and three discontinued study treatment due to a drug-related adverse event. Most common AEs were diarrhoea (85%; mainly grade 1-2) and rash (47%; grade 1-2).

AE, adverse event; bid, twice daily; CI, confidence interval; CR, complete response; DoR, duration of response; NE, not estimable; NR, not reached; PD, partial disease; PR, partial response; pts, patients; SD, stable disease TTR, time to response

Girard N, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8598) (ASCO 2024 poster)

SOHO-01: SUMMARY

- BAY 2927088 led to rapid, substantial, and durable responses in patients with pretreated *HER2*-mutant NSCLC
- The safety profile was consistent with previously reported data
- Changes in ctDNA levels may be an early indicator of clinical benefit
- These data support the further clinical development of BAY 2927088 in pts with *HER2*-mutant NSCLC

ctDNA, circulating tumour DNA; HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer; pts, patients

Girard N, et al. J Clin Oncol 2024;42(suppl 17; abstr LBA8598) (ASCO 2024 poster)

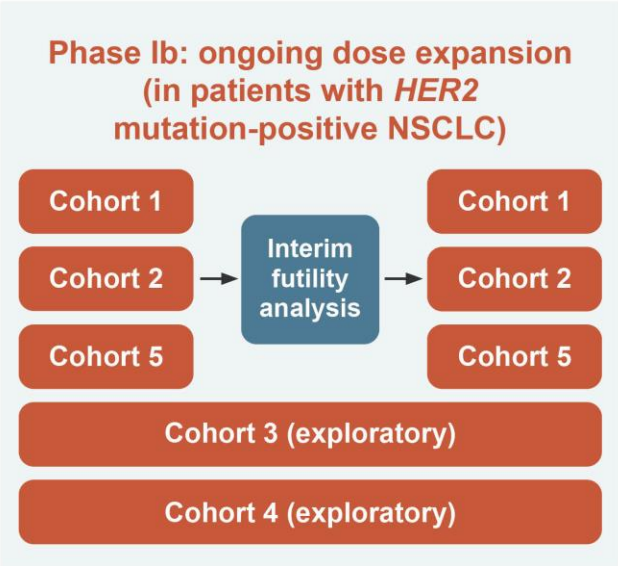
PHASE 1A/1B TRIAL OF ZONGERTINIB (BI 1810631), A HER2-SPECIFIC TKI, IN PATIENTS WITH HER2 ABERRATION-POSITIVE SOLID TUMOURS: UPDATED PHASE 1A DATA FROM BEAMION LUNG-1, INCLUDING PROGRESSION-FREE SURVIVAL DATA

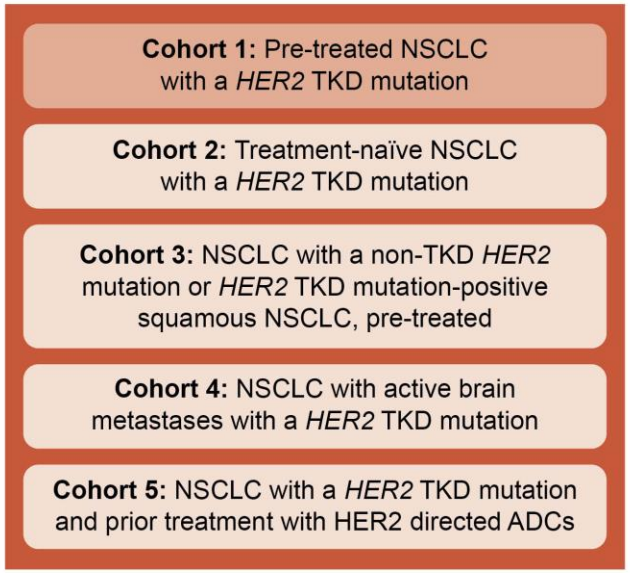
Heymach J, et al. ASCO 2024. Abstract #8514

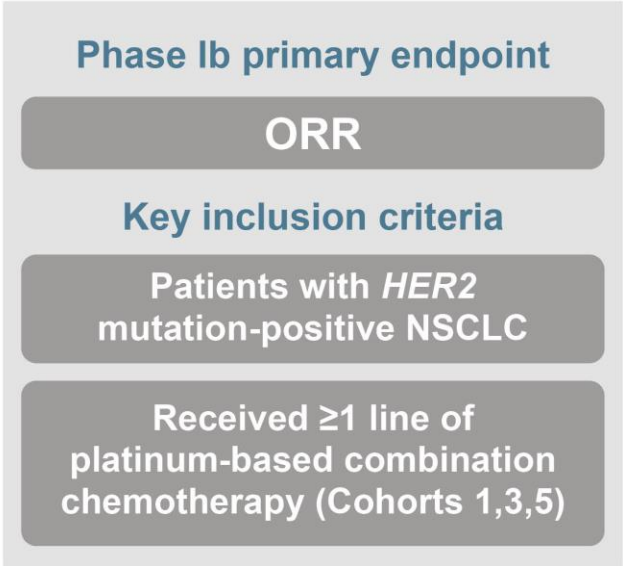
HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer

BEAMION LUNG-1: BACKGROUND AND STUDY DESIGN

- **Zongertinib, a novel HER2-specific TKI**, binds selectively and covalently to the HER2 tyrosine kinase domain while sparing wild-type epidermal growth factor receptor
- **Beamion LUNG-1** (NCT04886804), a Phase 1a/1b, first-in-human, open-label trial, is evaluating the safety and efficacy of zongertinib in patients with HER2 aberration-positive solid tumours (Phase 1a) and *HER2* mutation-positive(m+) NSCLC (Phase 1b). **Here we report the findings from Phase 1b Cohort 1**





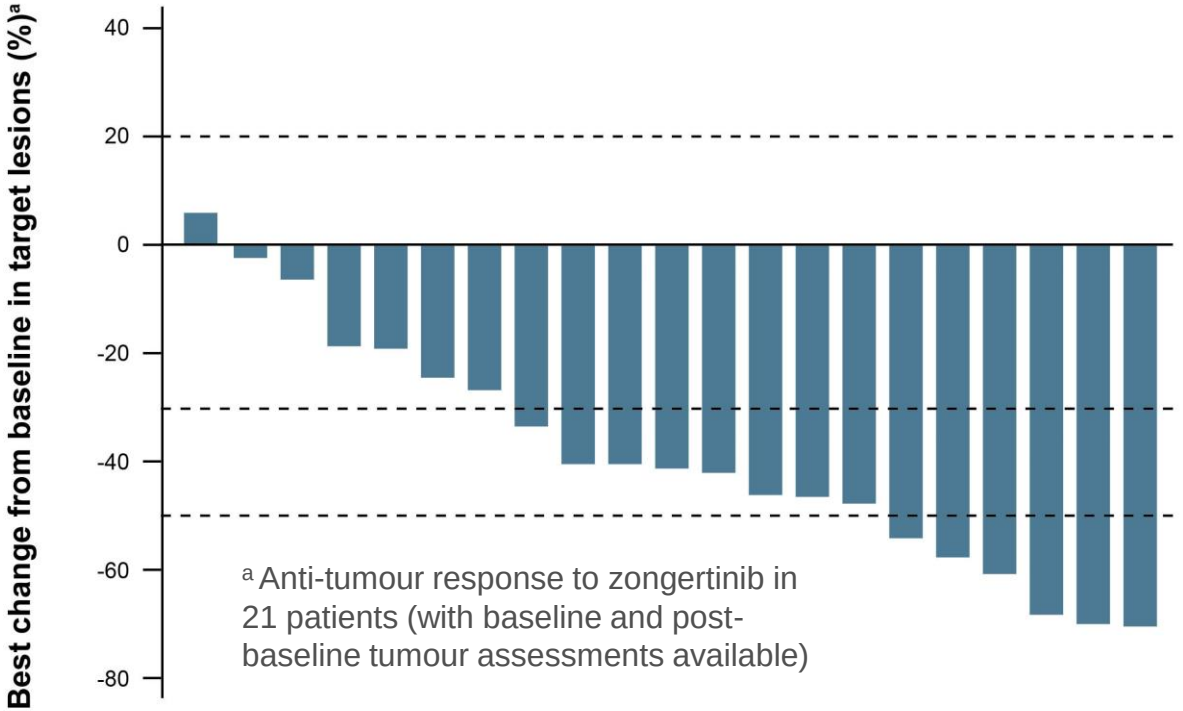


ADC, antibody drug conjugate; HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer; ORR, objective response rate; TKD, tyrosine kinase domain; TKI, tyrosine kinase inhibitor

Heymach J, et al. J Clin Oncol 2024;42(suppl 16; abstr 8514) (ASCO 2024 oral presentation)

BEAMION LUNG-1: RESULTS (PHASE 1B, COHORT 1)

- In a prespecified interim analysis of Phase 1b (July 31, 2023), 42 pts were treated in Cohort 1 (pretreated *HER2*m+ NSCLC randomised to 120/240 mg QD).
- TRAEs (all/G3/G4/G5): 67/5/5/0%, most commonly diarrhoea (G1/G2/G≥3; 24/5/0%)
- Serious TRAEs: 5% (n=2; G4 decreased neutrophils, G4 immune thrombocytopenia).



[a] Anti-tumour response to zongertinib in 21 patients (with baseline and post-baseline tumour assessments available)

	Pre-treated *HER2*m+ NSCLC[a]
Efficacy (N=23)	
ORR, %	74
DCR, %	91
Safety (N=42)	
Any TRAEs, %	67
G≥3 TRAEs, %	10

[a] Excluding patients treated with ADCs; No AEs led to treatment discontinuation

AE, adverse event; DCR, disease control rate; G, grade; HER2m+, human epidermal growth factor receptor 2 mutation-positive; NSCLC, non-small cell lung cancer; ORR, objective response rate; pts, patients; QD, once daily; TRAE, treatment-related adverse event

Heymach J, et al. J Clin Oncol 2024;42(suppl 16; abstr 8514) (ASCO 2024 oral presentation)

BEAMION LUNG-1: SUMMARY

- The first futility analysis in Cohort 1 was passed
- Zongertinib was well-tolerated and demonstrated promising initial efficacy in pre-treated patients with *HER2*-mutated NSCLC

HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer

Heymach J, et al. J Clin Oncol 2024;42(suppl 16; abstr 8514) (ASCO 2024 oral presentation)

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