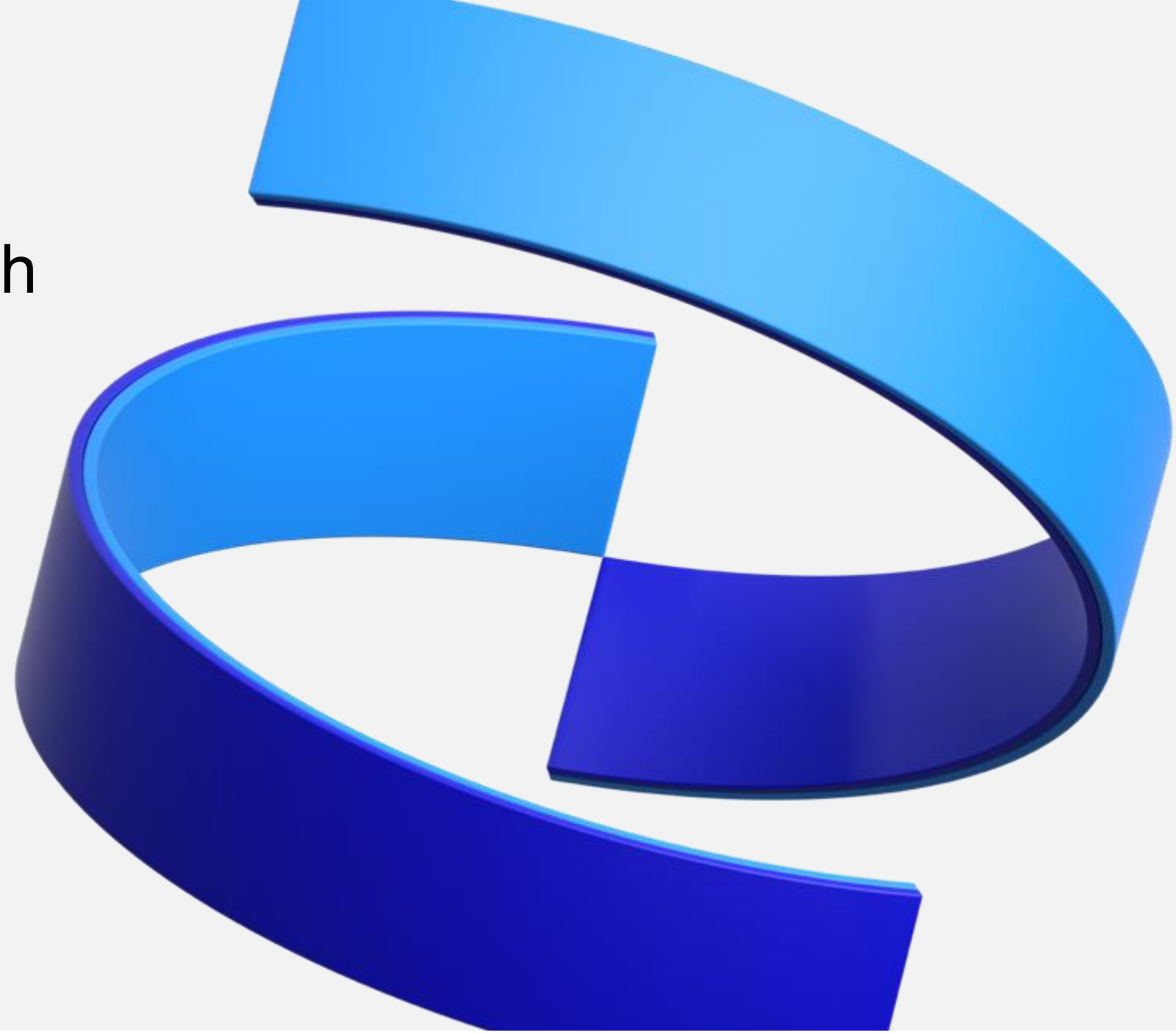
Lorlatinib Versus Crizotinib in Patients With Advanced ALK-Positive Non-Small Cell Lung Cancer: 5-Year Outcomes From the Phase 3 CROWN Study



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EM-DEU-lor-0119

Pfizer

CROWN: Subsequent Treatment and PFS2 (WCLC 2024)

Clinical and molecular characteristics of early progressors (≤12 months) on lorlatinib vs those who remained progression free after 5 years

Clinical Characteristics	Early progressors (n=28)[a]	Nonprogressors (n=45)[a]	Total (n=73)
Age, mean (SD), years	60.5 (12.9)	56.1 (14.0)	57.8 (13.7)
Sex, n (%)			
Male	16 (57)	24 (53)	40 (55)
Female	12 (43)	21 (47)	33 (45)
Race, n (%)[b]			
Asian	15 (54)	28 (62)	43 (59)
White	12 (43)	16 (36)	28 (38)
ECOG performance status, n (%)			
0	11 (39)	23 (51)	34 (47)
1	15 (54)	22 (49)	37 (51)
2	2 (7)	0	2 (3)
Brain metastases at baseline, n (%)			
Yes	6 (21)	10 (22)	16 (22)
No	22 (79)	35 (78)	57 (78)
Tumor burden at baseline, mm			NA
Mean (SD)	84.9 (45.7)	54.7 (34.4)	NA

Molecular profiling, n (%)[c]	Early progressors (n=28)[a]	Nonprogressors (n=45)[a]
Confirmed *ALK* positive	14 (50)	35 (78)
EML4-ALK variant 1	6 (21)	10 (22)
EML4-ALK variant 2	0	5 (11)
EML4-ALK variant 3	5 (18)	11 (24)
EML4-ALK other variant	3 (11)	7 (16)
Other *ALK* fusion	0	2 (4)
Unconfirmed *ALK* positive[d]	14 (50)	10 (22)
***TP53* mutation detected**	16 (57)	10 (22)

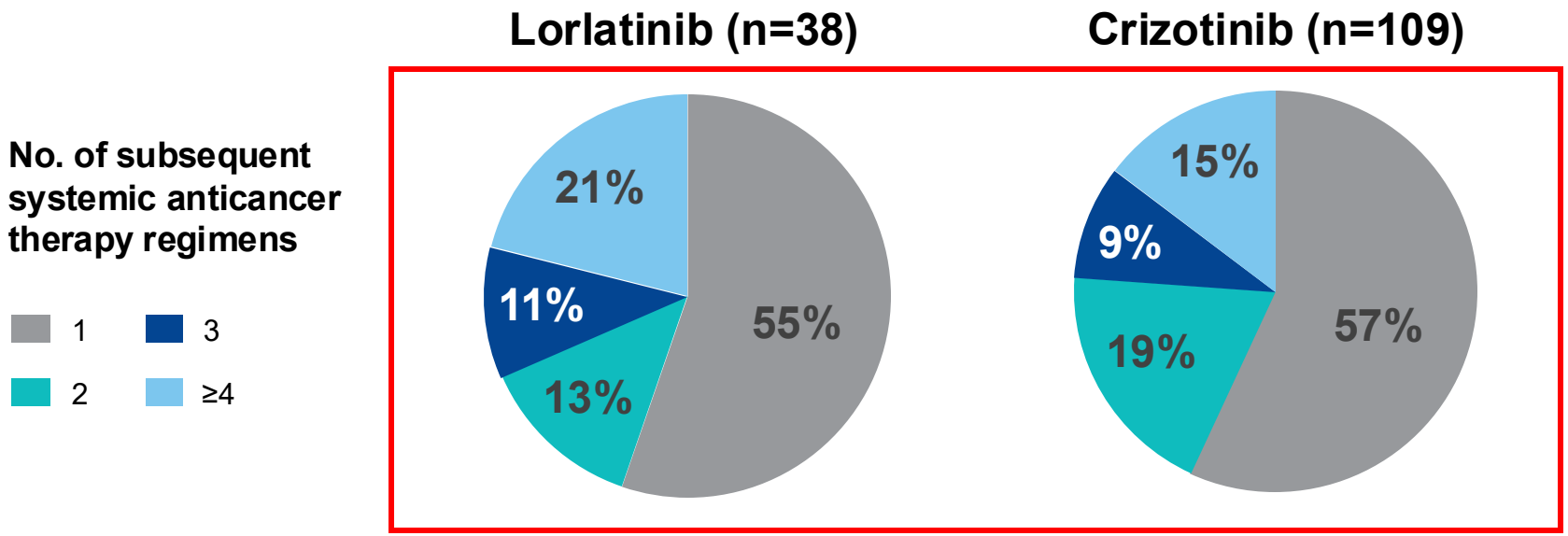
[a]Early progressors are defined as patients with PFS events (PD or death) within 12 months of the start of the study. Nonprogressors are defined as patients who were PFS-free (alive with no documented PD) at 60 months (including patients with PFS events >60 months). [b]There was 1 (4%) patient in the early progressors group and 1 (2%) patient in the nonprogressors group with other or missing race. [c]Based on ctDNA analysis at baseline and/or tumor tissue at screening. Only based on ctDNA analysis for patients in China. [d]ctDNA was either NA, not tested, or tested with no ctDNA detected. Tumor tissue was either NA or testing had failed.

ALK, anaplastic lymphoma kinase; ctDNA, circulating tumor DNA; ECOG, Eastern Cooperative Oncology Group; EML4, Echinoderm Microtubule-Associated Protein-Like 4; NA, not available; PD, progressive disease; PFS, progression-free survival; SD, standard deviation; *TP53*, tumor protein 53.

Mok. TSK, et al. Presented at: WCLC Annual Meeting; September 7-10th, 2024; San Diego, CA.

Subsequent systemic anticancer therapy

- After 5 years of follow-up, 75 of 149 (50%) patients had discontinued lorlatinib and 135 of 142 (95%) had discontinued crizotinib[a]
- 38 of 149 (26%) patients in the lorlatinib arm and 109 of 147 (74%) in the crizotinib arm had ≥1 subsequent systemic anticancer therapy



[a]After 5 years of follow-up. Among patients who discontinued lorlatinib, only 8 had intracranial progression.
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Details of first subsequent systemic anticancer therapy

	Lorlatinib (n=38)	Crizotinib (n=109)
First subsequent systemic anticancer therapy, n (%)		
ALK TKI	23 (61)	101 (93)
Alectinib	12 (52)	68 (67)
Crizotinib	4 (17)	5 (5)
Ceritinib	3 (13)	3 (3)
Lorlatinib	3 (13)	4 (4)
Brigatinib	1 (4)	21 (21)
Chemotherapy ± anti-angiogenic	13 (34)	4 (4)
Chemotherapy/immunotherapy	1 (3)	0
Chemotherapy/immunotherapy/anti-angiogenic	1 (3)	0
Other[a]	0	4 (4)
DOT on first subsequent systemic anticancer therapy, median (IQR), months	9.3 (2.6-22.6)	14.9 (5.3-38.4)
ALK TKIs as first subsequent therapy[b]	12.5 (2.0-31.7)	15.8 (7.0-39.9)
Non–ALK TKIs as first subsequent therapy[c]	6.7 (2.6-19.7)	1.2 (0.8-2.7)

[a]Includes investigational drug, cabozantinib, and osimertinib. [b]N numbers are 23 for lorlatinib and 101 for crizotinib. [c]N numbers are 15 for lorlatinib and 8 for crizotinib.
ALK, anaplastic lymphoma kinase; DOT, duration of treatment; IQR, interquartile range; TKI, tyrosine kinase inhibitor.
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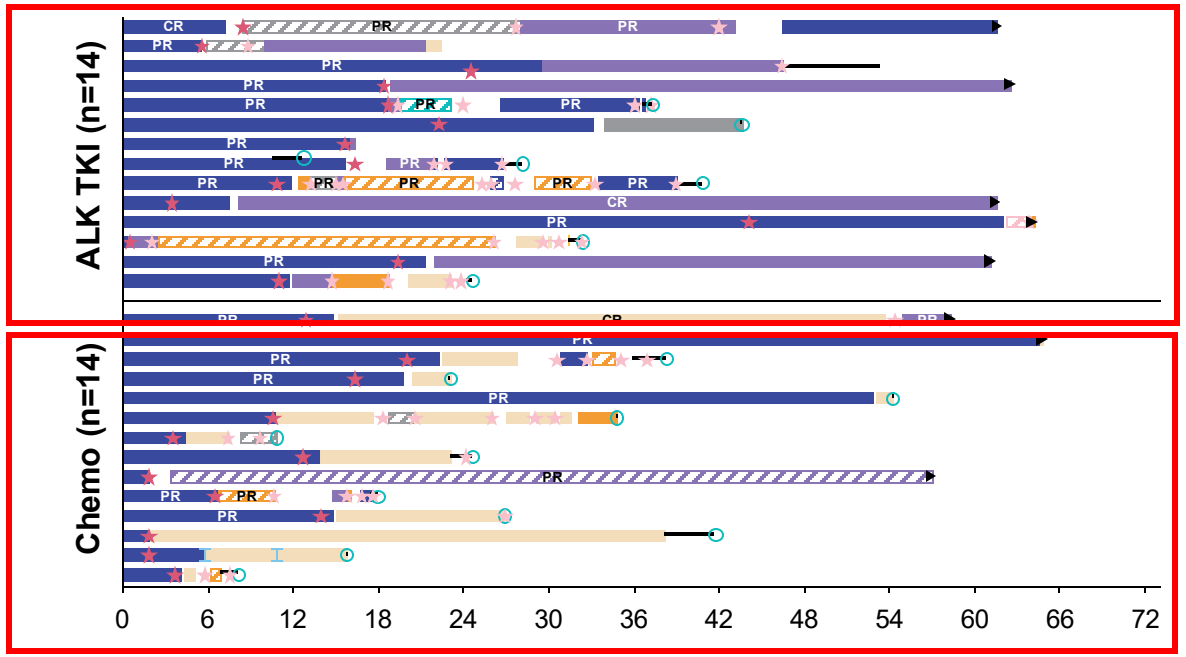
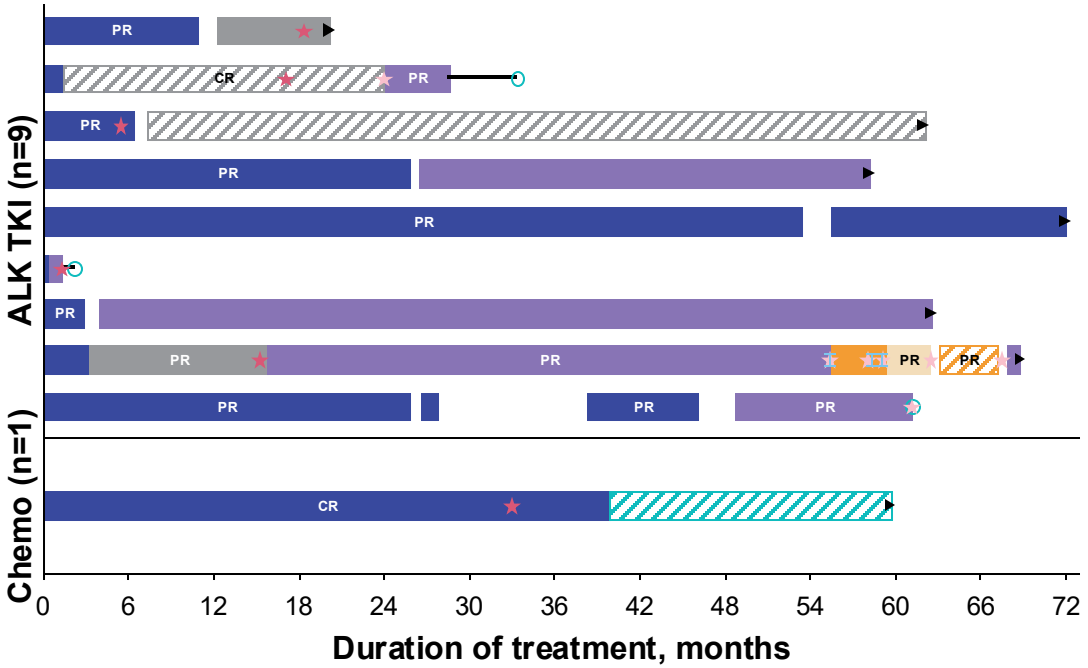
Duration of treatment for subsequent therapies post lorlatinib

Discontinued due to PD or global deterioration of health status



Discontinued due to AE or other reasons



Alectinib | Brigatinib | Ceritinib | Chemo/anti-angiogenic | Chemo/anti-angiogenic/immuno | Chemo/immuno | Crizotinib | Death | INV PD | Lorlatinib | No follow-up therapy | Other | Overlap | PD | Single-agent immuno | Single-agent or doublet chemo | Treatment ongoing

- ALK TKIs and chemo were used as subsequent lines of treatment in patients who discontinued lorlatinib due to PD or other reasons
- Outcomes of subsequent treatment varied, and responses were observed in patients irrespective of prior lorlatinib DOT or response

AE, adverse event; ALK, anaplastic lymphoma kinase; chemo, chemotherapy; CR, complete response; DOT, duration of treatment; Immuno, immunotherapy; INV PD, investigator-determined progressive disease; PD, progressive disease based on the follow-up anticancer therapy case report form; PR, partial response; TKI, tyrosine kinase inhibitor.

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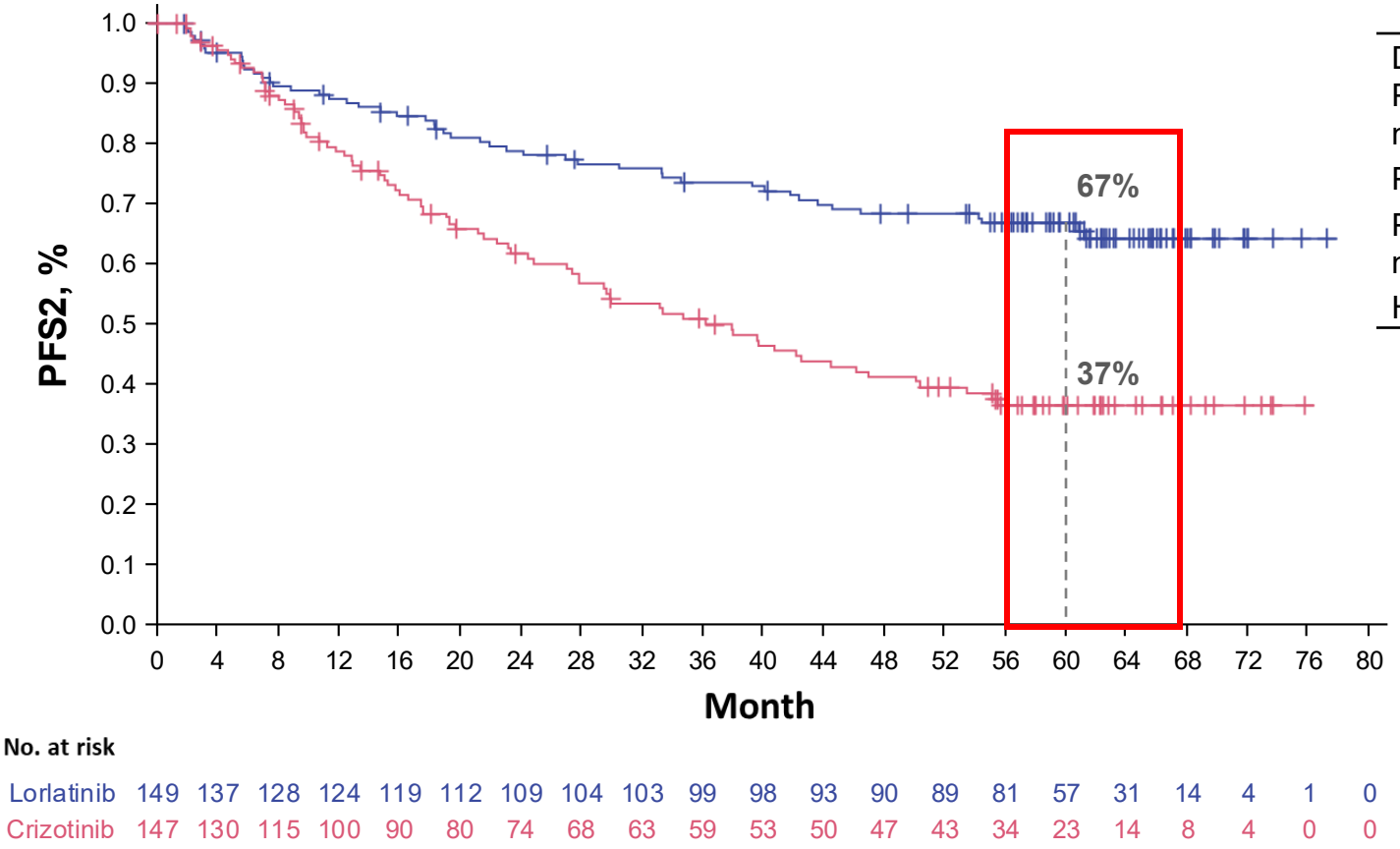
PFS2 was longer in patients who received lorlatinib vs crizotinib as the study treatment



	Lorlatinib (N=149)	Crizotinib (N=147)
Duration of follow-up for PFS2, median (95% CI), months	61.4 (59.2-62.5)	58.4 (56.8-61.9)
PFS2 events, n (%)	48 (32)	78 (53)
PFS2, median (95% CI), months	NR (NR-NR)	37.9 (27.4-50.1)
HR (95% CI)	0.43 (0.30-0.62)	

CI, confidence interval; HR, hazard ratio; NR, not reached; PFS2, time from randomization to the date of disease progression with first subsequent systemic anticancer therapy or death.

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