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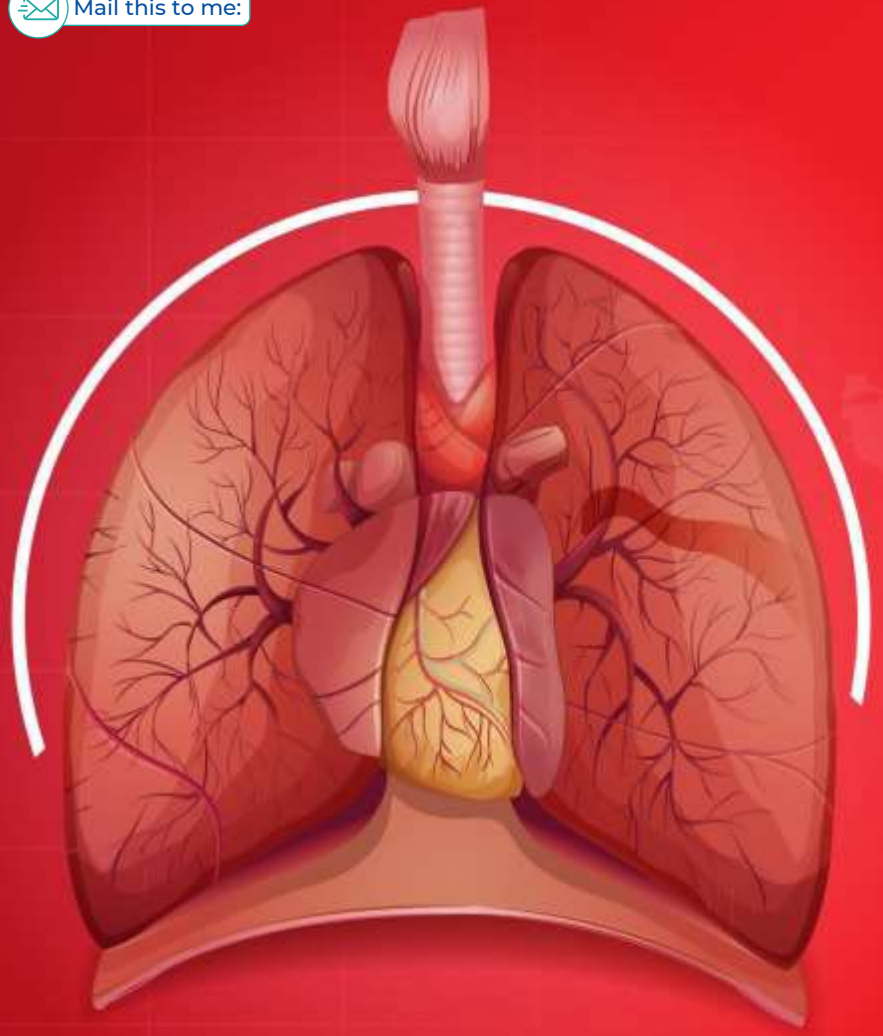

Role of ALECENSA in 1L ALK+ mNSCLC Asian Patients

ALESIA Study

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alectinib 150 mg capsules

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ALESIA

Phase III Study

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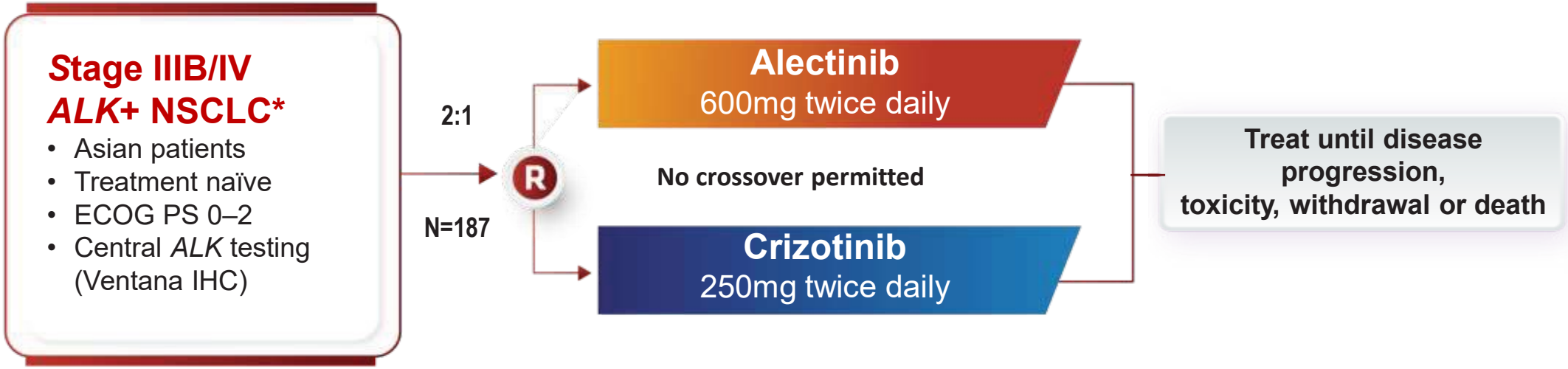
ALESIA: Alectinib vs Crizotinib In Treatment-naïve Asian Patients With Advanced ALK+ NSCLC



- **Stratification factors:** ECOG PS (0/1 vs 2) and CNS metastases at baseline (yes vs no)
- **Primary endpoint:** PFS by INV
- **Secondary endpoints:** Time to CNS progression by IRC, ORR by INV, DOR by INV, OS and Safety
- **Median duration of survival follow-up: 61 months Alectinib** vs **51 months Crizotinib**

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Patients were enrolled from China, Thailand and South Korea. *Asymptomatic CNS metastases allowed.
Data cut-off 16 May 2022. ClinicalTrials.gov: NCT02838420. CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; INV, investigator IRC, independent review committee; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival

ALESIA: Baseline Characteristics

		Alectinib (n=125)	Crizotinib (n=62)
Age, years	Median (range)	**51.0** (21–78)	49.0 (28–83)
Gender, %	Male / Female	**51.2 / 48.8**	54.8 / 45.2
ECOG PS, %	0–1 / 2	**96.8 / 3.2**	98.4 / 1.6
Smoking Status, %	Active smoker / Non-smoker / Past smoker	**3.2 / 67.2 / 29.6**	4.8 / 72.6 / 22.6
CNS Metastases by IRC, %	Yes	**35.2**	37.1
CNS Metastases by INV, %	Yes	**33.6**	32.3
Prior brain radiation, %	Yes	**6.4**	8.1

Baseline characteristics were balanced between treatment arms.
Approximately **35%** of patients had CNS metastases at baseline

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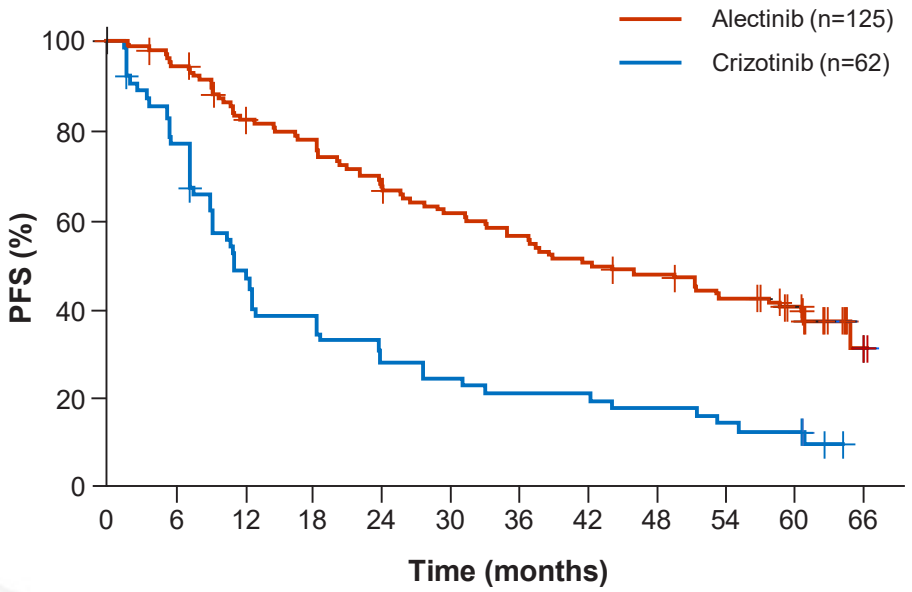
CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; INV, investigator; IRC, independent review committee.
Zhou C, et al. ESMO Asia 2022 (Abs. LBA11).

ALESIA: PFS By INV In The ITT Population



	Alectinib (n=125)	Crizotinib (n=62)
Median PFS, months (95% CI)	**41.6** (33.1 – 58.9)	**11.1** (9.1 – 18.4)
HR (95% CI)	**0.33** (0.23 – 0.49)	

In this updated analysis, a durable PFS benefit of alectinib vs crizotinib was demonstrated; median PFS (INV) **41.6 months with alectinib**[1]

This is consistent with that reported from the global ALEX study where median PFS (INV) was 34.8 months with alectinib and 10.9 months with crizotinib (HR 0.43)[2]

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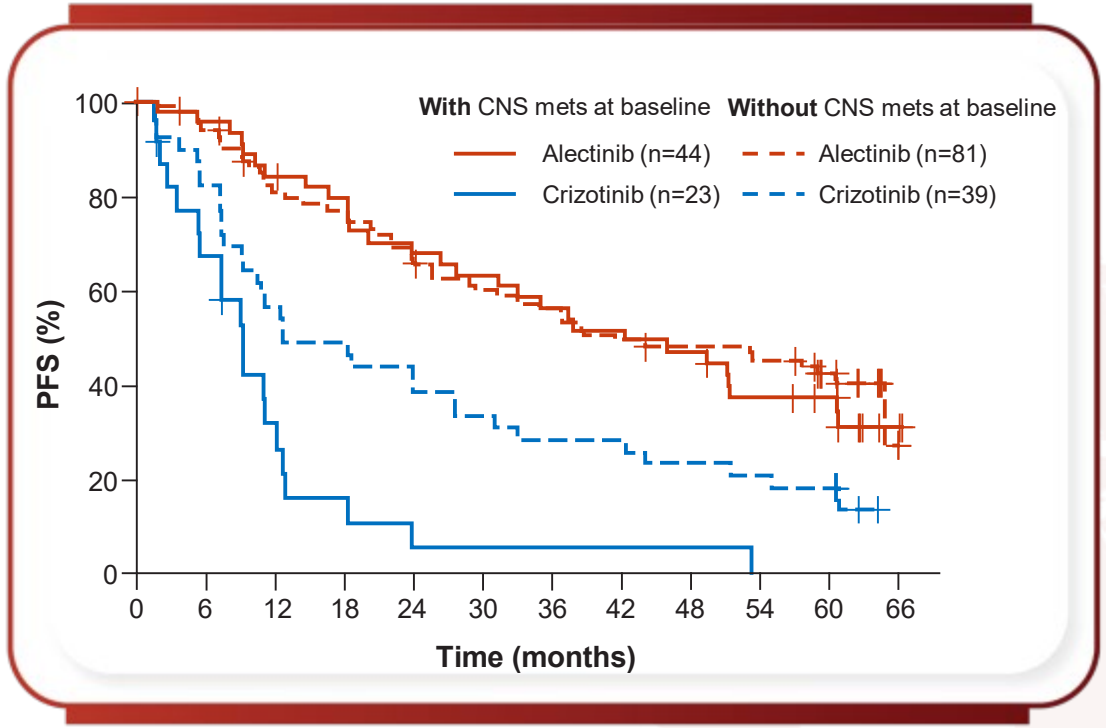
Data cut-off 16 May 2022.
CI, confidence interval; HR, hazard ratio; INV, investigator; ITT, intent-to-treat; PFS, progression-free survival.
[1]Zhou C, et al. ESMO Asia 2022 (Abs. LBA11); [2]Mok T, et al. Ann Oncol 2020.

ALESIA: PFS According To CNS Status At Baseline[1]



	With CNS mets at baseline	
	Alectinib (n=44)	Crizotinib (n=23)
Median PFS, months (95% CI)	42.3 (27.8 – 60.7)	9.2 (5.5 – 12.2)
HR (95% CI)	0.17 (0.09–0.33)	

	Without CNS mets at baseline	
	Alectinib (n=81)	Crizotinib (n=39)
Median PFS, months (95% CI)	41.6 (29.5 – 64.9)	12.7 (9.2 – 27.6)
HR (95% CI)	0.45 (0.29 – 0.71)	

The PFS benefit was observed irrespective of CNS mets at baseline, confirming both **systemic and CNS efficacy of alectinib in Asian patients**[1]

These findings are consistent with that observed in the global ALEX study[2]

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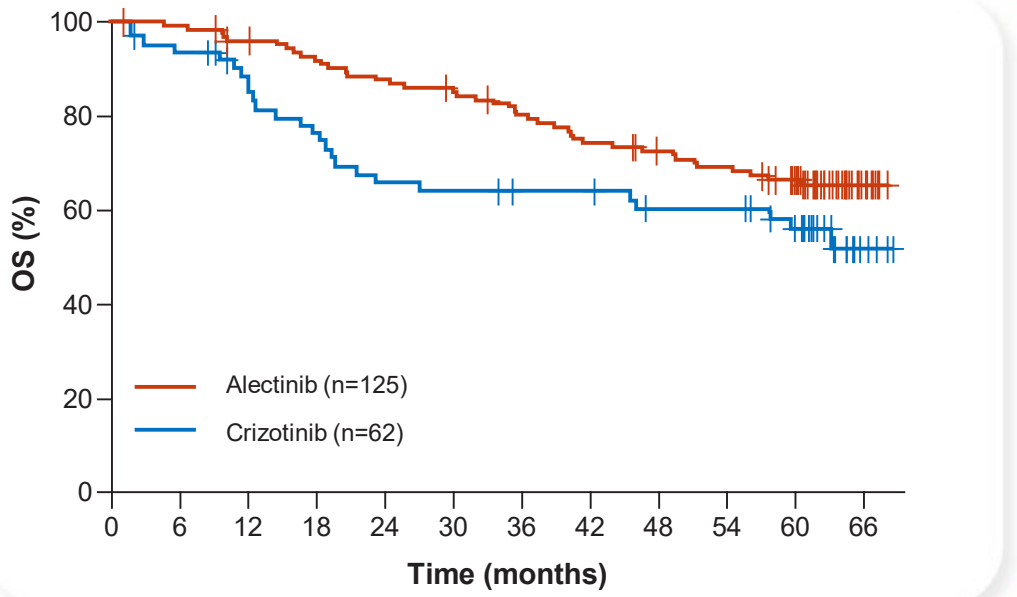
Data cut-off 16 May 2022.
CI, confidence interval; CNS, central nervous system; HR, hazard ratio; mets, metastases; PFS, progression-free survival.
[1]Zhou C, et al. ESMO Asia 2022 (Abs. LBA11); [2]Mok T, et al. Ann Oncol 2020.

ALESIA: OS In The ITT population



	Alectinib (n=44)	Crizotinib (n=23)
Patients with event, n (%)	**41** (32.8)	**26** (41.9)
Median OS, months (95% CI)	**NE** (NE – NE)	**NE** (45.5 – NE)
HR (95% CI)	**0.60** (0.37–0.99)	
5-year OS rate, % (95% CI)	**66.4** (57.9 – 74.9)	**56.0** (43.0 – 69.1)
Patients remaining at risk, n	**69**	**25**

After 5 years of follow-up, OS data remain immature. A clinically meaningful improvement in 5-year survival with alectinib vs crizotinib was demonstrated **(alectinib 66.4% vs 56.0% for crizotinib)**[1*]

A clinically meaningful improvement in 5-year survival was observed in the global ALEX study **(alectinib 62.5% vs 45.5% for crizotinib)**[2*]

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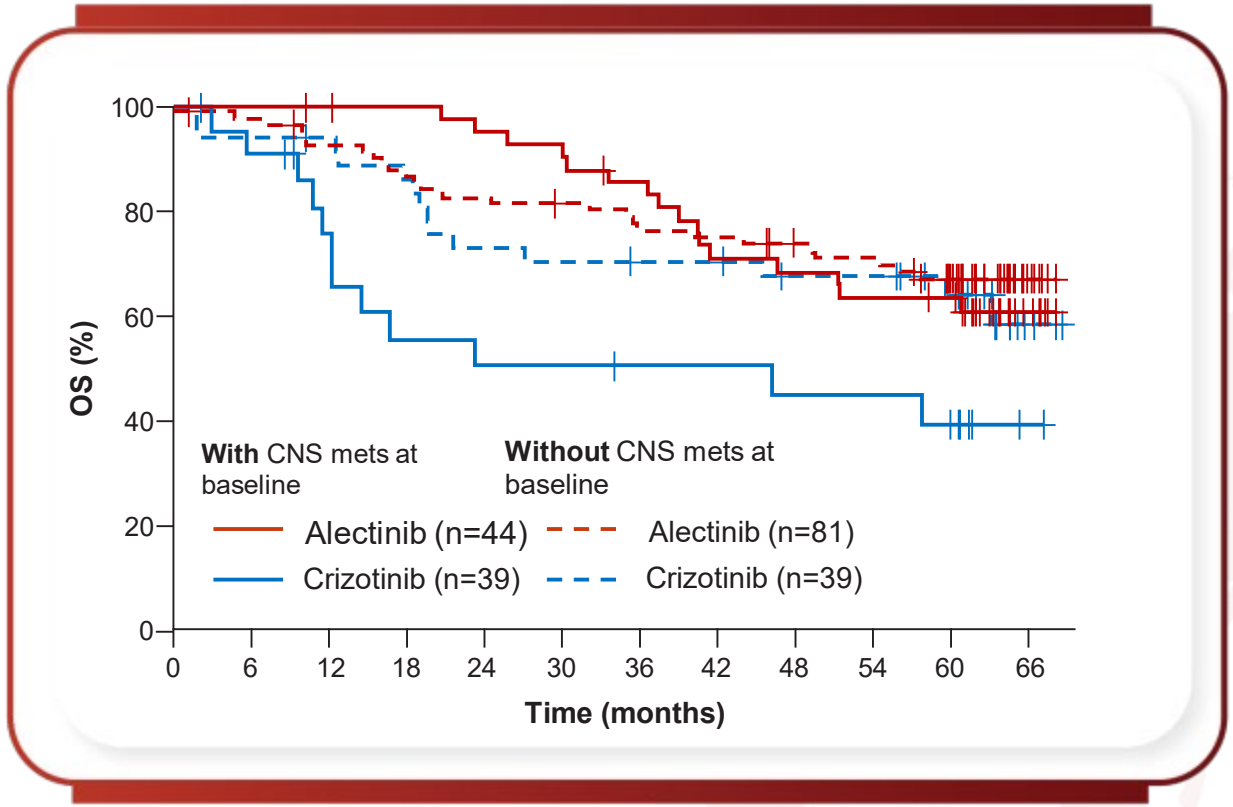
Data cut-off 16 May 2022. *Crossover was not permitted before PD in ALESIA or ALEX;4 †Crossover was permitted after study drug discontinuation in J-ALEX..
BID, twice daily; CI, confidence interval; HR, hazard ratio; INV, investigator; ITT, intent-to-treat; NE, not evaluable; OS, overall survival; PD, progressive disease.
[1]Zhou C, et al. ESMO Asia 2022 (Abs. LBA11); [2]Mok T, et al. Ann Oncol 2020; [3]Hotta K, et al. ESMO Open 2022; [4]Mok T, et al. Ann Oncol 2020.

ALESIA: OS According To CNS Status At Baseline



	With CNS mets at baseline	
	Alectinib (n=44)	Crizotinib (n=23)
Patients with event, n (%)	**16** (36.4)	**12** (52.2)
Median OS, months (95% CI)	**NE** (51.4 – NE)	**46.2** (12.2 – NE)
HR (95% CI)	**0.40** (0.19–0.85)	
5-year OS rate, % (95% CI)	**63.6** (48.9 – 78.3)	**39.3** (17.4 – 61.2)
Patients remaining at risk, n	**25**	**6**
	Without CNS mets at baseline	
	Alectinib (n=81)	**Crizotinib** (n=39)
Patients with event, n (%)	**25** (30.9)	**14** (35.9)
Median OS, months (95% CI)	**NE** (NE – NE)	**NE** (59.8 – NE)
HR (95% CI)	**0.81** (0.42–1.55)	
5-year OS rate, % (95% CI)	**67.8** (57.4 – 78.2)	**64.9** (49.3 – 80.4)
Patients remaining at risk, n	**44**	**19**

OS data remain immature.
The OS benefit of alectinib vs crizotinib was observed, irrespective of CNS mets at baseline[1*]

Data cut-off 16 May 2022.*Crossover was not permitted before PD in ALESIA
CI, confidence interval; CNS, central nervous system; HR, hazard ratio; mets, metastases; NE, not evaluable
OS, overall survival.; PD, progressive disease
Zhou C, et al. ESMO Asia 2022 (Abs. LBA11).

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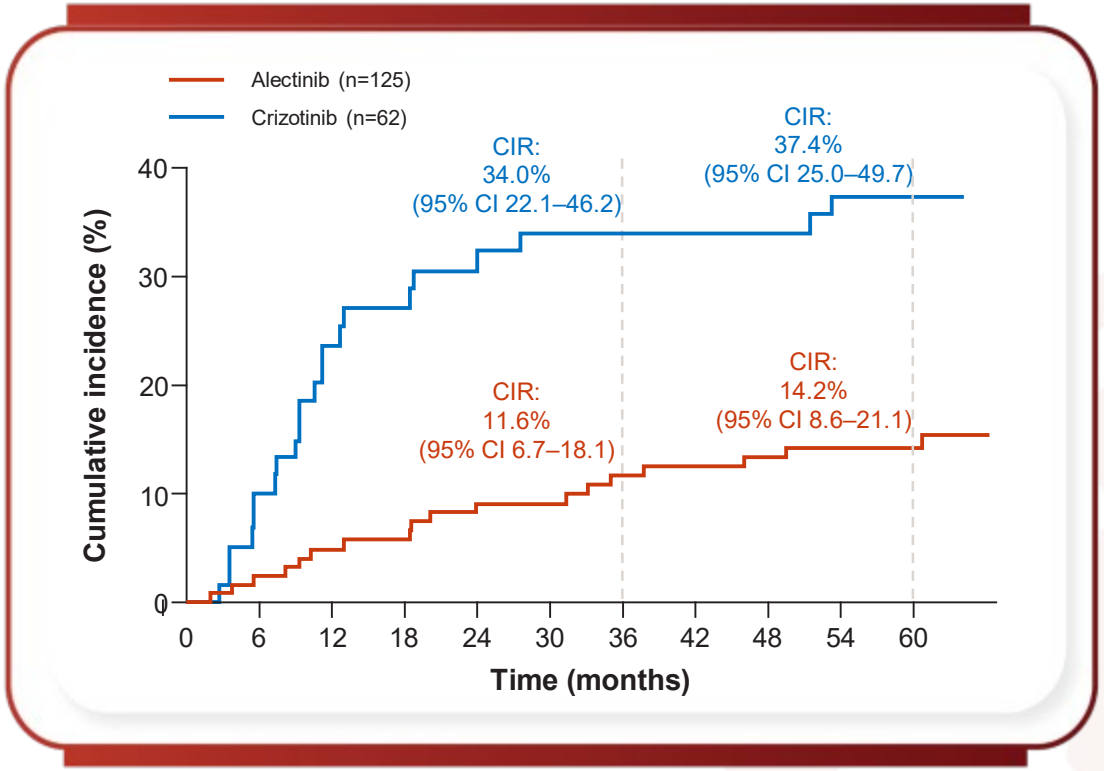
ALESIA: Time To CNS Progression In The ITT Population[1*]



	Alectinib (n=125)	Crizotinib (n=62)
CNS progression without prior systemic progression		
Patients with events, n (%)	**18** (14.4)	**22** (35.5)
Cause-specific HR (95% CI)	**0.16** (0.08–0.32)	
Estimated cumulative incidence, % (95% CI)		
At 36 months	**11.6** (6.7 - 18.1)	**34.0** (22.1 - 46.2)
At 60 months	**14.2** (8.6 - 21.1)	**37.4** (25.0 - 49.7)

Treatment of Asian patients with alectinib delayed the time to CNS progression, resulting in an **84% reduction in the risk of CNS progression with alectinib** compared with crizotinib[1]

These findings are consistent with that observed in the global ALEX study (cause-specific HR 0.16)[2]

*Derived from investigators' assessment. CNS PD = CNS Target Lesion PD per RECIST version 1.1, appearance of new CNS lesion(s), and/or unequivocal PD of Non-Target CNS lesion(s).
Data cut-off 16 May 2022.
CI, confidence interval; CIR, cumulative incidence rate; CNS, central nervous system; HR, hazard ratio; ITT, intent-to-treat; PD, progressive disease.
[1]Zhou C, et al. ESMO Asia 2022 (Abs. LBA11); [2]Peters S, et al. N Engl J Med 2017.

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ALESIA: Post-Progression Therapy

	Alectinib (n=125)	Crizotinib (n=62)
Patients with PD, n	**68**	**48**
Anti-cancer therapy after PD, n (%)	**42** (61.8)	**38** (79.2)
ALK inhibitor, n (%)	**25** (36.8)	**28** (58.3)
Alectinib	**5** (7.4)	**14** (29.2)
Lorlatinib	8 (11.8)	6 (12.5)
Brigatinib	6 (8.8)	7 (14.6)
Crizotinib	7 (10.3)	2 (4.2)
Ceritinib	3 (4.4)	4 (8.3)
Ensartinib	2 (2.9)	1 (2.1)
Investigational drug	1 (1.5)	0
Chemotherapy, n (%)	24 (35.3)	**15** (31.3)
Anti-VEGF therapies, n (%)	**9** (13.2)	**3** (6.3)
Immunotherapy, n (%)	**3** (4.4)	**2** (4.2)
Other therapies, n (%)	**6** (8.8)	**7** (14.6)

Crossover between treatment arms was not permitted during the study
Approximately **30%** of patients in the crizotinib arm received alectinib following disease progression[1]

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Data cut-off 16 May 2022. ALK, anaplastic lymphoma kinase; PD, progressive disease; VEGF, vascular endothelial growth factor.
Zhou C, et al. ESMO Asia 2022 (Abs. LBA11).

ALESIA: Safety Overview[1]

Events, n (%)	Alectinib (n=125)	Crizotinib (n=62)
Patients with ≥1 event		
All grade AEs	125 (100)	62 (100)
Serious AEs	35 (28.0)	18 (29.0)
Grade ≥3 AEs	60 (48.0)	34 (54.8)
Fatal AEs	5 (4.0)*	3 (4.8)
AEs leading to treatment discontinuation	14 (11.2)	9 (14.5)
AEs leading to dose reduction	33 (26.4)	17 (27.4)
AEs leading to dose interruption	33 (26.4)	19 (30.6)

Grade ≥3 AEs with ≥3% difference in frequency between treatment arms, n (%)	Alectinib (n=125)	Crizotinib (n=62)
Weight increased	11 (8.8)	1 (1.6)
Blood creatine phosphokinase increased	8 (6.4)	2 (3.2)
ALT increased	3 (2.4)	4 (6.5)
Nausea	1 (0.8)	3 (4.8)
Neutrophil count decreased	0	9 (14.5)
ECG QT prolonged	0	3 (4.8)
White blood cell count decreased	0	3 (4.8)
Decreased appetite	0	3 (4.8)
Hyponatraemia	0	3 (4.8)
Interstitial lung disease	0	3 (4.8)
Vomiting	0	3 (4.8)
Bradycardia	0	2 (3.2)
Hepatic function abnormal	0	2 (3.2)

With a median treatment duration more than three-times longer for alectinib (42.3 months) compared to crizotinib (12.6 months), alectinib had a more favourable safety profile[1]

Consistent with the safety profile observed in the global ALEX study, no new safety signals were detected[2]

*Three additional fatal events occurred during the longer follow-up: one was due to COVID-19 pneumonia, and the other two were reported as 'death' and not related to alectinib treatment.
Data cut-off 16 May 2022.
AE, adverse event; ALT, alanine aminotransferase; ECG, electrocardiogram; CI, confidence interval; HR, hazard ratio; INV, investigator; ITT, intent-to-treat; NE, not evaluable; OS, overall survival.
[1]Zhou C, et al. ESMO Asia 2022 (Abs. LBA11); [2]Mok T, et al. Ann Oncol 2020.

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Summary and Conclusions: 5 Year Update From the Phase III ALESIA Study

With at least 5 years of follow-up, **ALECENSA 1L 600mg BID continues to demonstrate clinical benefit**
to Asian patients with advanced *ALK*+ NSCLC[1]

- Median PFS of **41.6 months for alectinib** vs 11.1 months for crizotinib
- **PFS benefit irrespective of CNS metastases** at baseline
- **ALECENSA delayed the time to CNS progression**
- **Clinically meaningful increase in 5-year survival rate** (alectinib 66.4% vs 56.0% for crizotinib)

With a three-times longer treatment duration compared to crizotinib, the safety profile of alectinib was more favourable than the safety profile of crizotinib. No new safety signals were observed[1,2]

The data from ALESIA in Asian patients[1,2] are consistent with that observed in the global ALEX study[3] and add to the building wealth of evidence supporting alectinib as the standard-of-care treatment for patients with advanced *ALK*+ NSCLC

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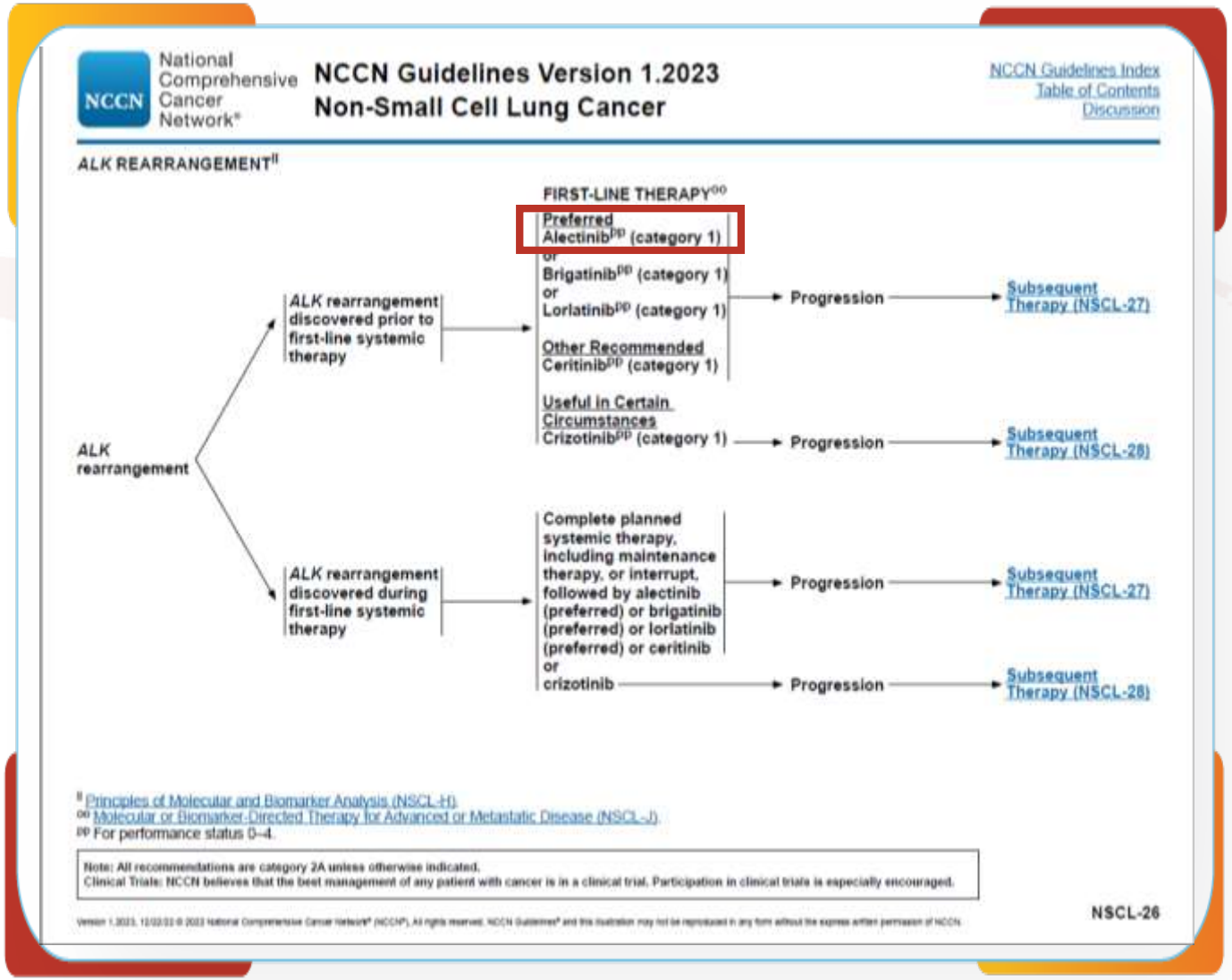
ALK, anaplastic lymphoma kinase; BID, twice daily; CNS, central nervous system; NSCLC, non-small cell lung cancer; PFS, progression-free survival

[1]Zhou C, et al. ESMO Asia 2022 (Abs. LBA11); [2]Zhou C, et al. Lancet Respir Med 2019; [3]Mok T, et al. Ann Oncol 2020.

Clinical Guidelines For 1L Treatment Of *ALK*+ NSCLC



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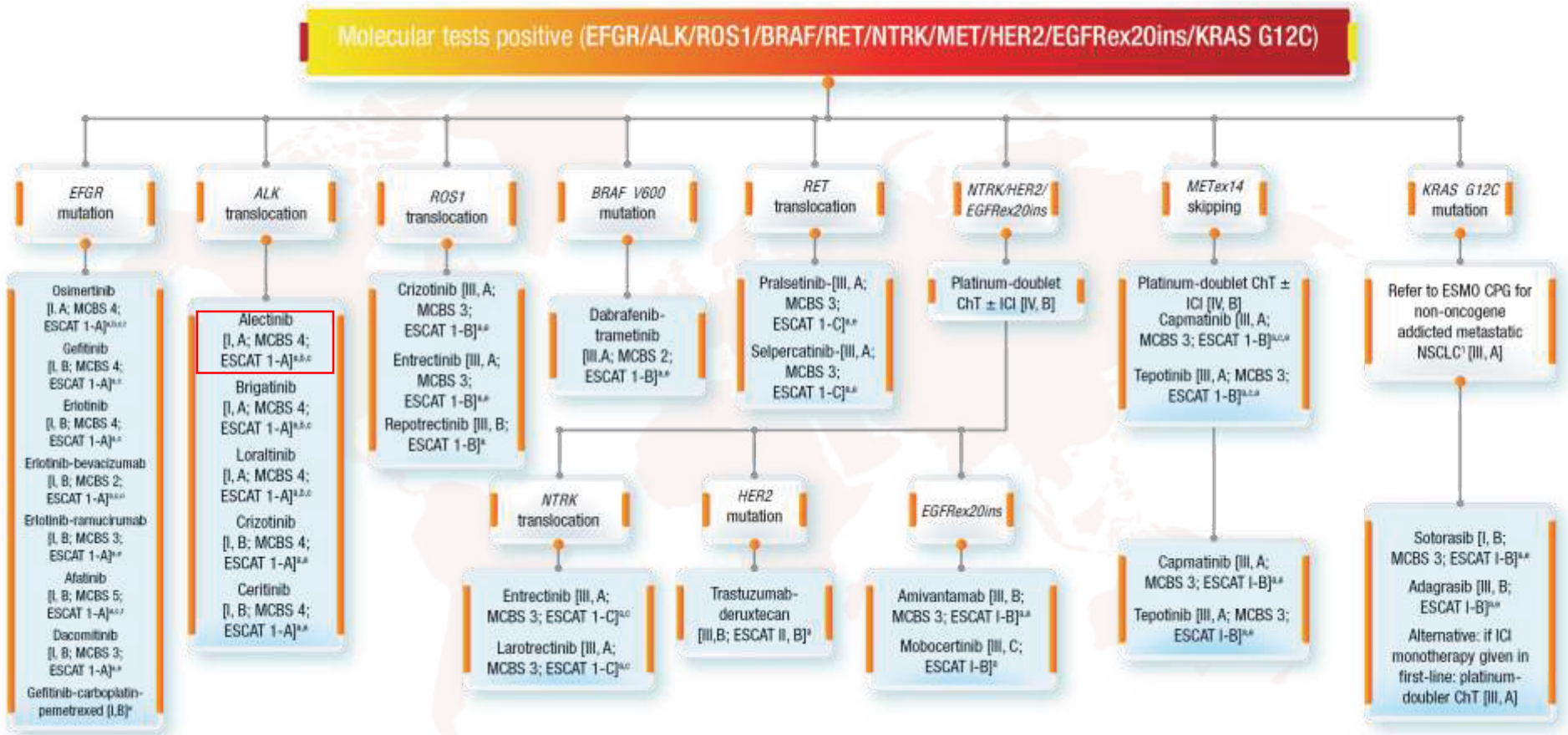
1. NCCN NSCLC guidelines. V1. 2023; 2. Planchard, et al. Ann Oncol 2019

ESMO Guidelines



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