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# ALINA: efficacy and safety of adjuvant alectinib versus chemotherapy in patients with early-stage *ALK+* NSCLC

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# Declaration of interests

Benjamin J. Solomon has the following relationships to disclose:

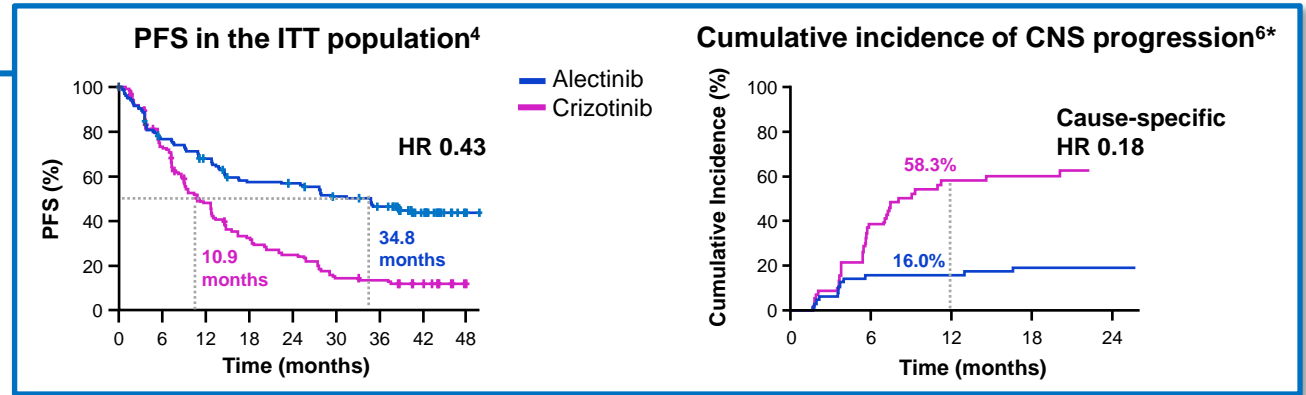
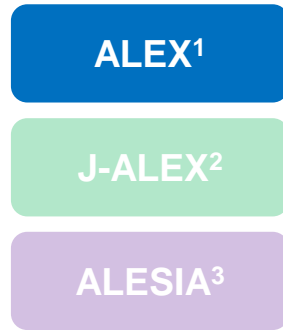
- Advisory board role: Amgen, AstraZeneca, BeiGene, Bristol Myers Squibb, D3 Bio, Janssen, Lilly, Merck, Pfizer, Takeda, Roche/Genentech
- Invited speaker: Amgen, AstraZeneca, Pfizer, Roche/Genentech
- Member of board of directors: International Association for the Study of Lung Cancer, Thoracic Oncology Group of Australasia, Cancer Council of Victoria
- Research grant: Sanofi
- Sponsor/funding: Beigene, Bristol Myers Squibb, Lilly, Novartis, Nuvalent, Roche/Genentech, Pfizer

# The unmet need in resectable *ALK+* NSCLC

- Around 30–40% of patients with NSCLC are diagnosed with resectable disease.<sup>1–4</sup> Despite treatment, the risk of disease recurrence remains high (~45–76%, depending on stage)<sup>5\*</sup>
- *ALK* rearrangements are found in 4–5% of patients with NSCLC; *ALK+* NSCLC is typically:<sup>6–13</sup>
  - Seen in younger patients (median age at diagnosis ~55 years)
  - More common in non-smokers
  - Associated with a high risk of brain metastases (~50–60% of patients over the course of the disease)
- For patients with **resectable *ALK+* NSCLC** the current standard-of-care after surgery is **adjuvant platinum-based chemotherapy**; immunotherapy is not recommended<sup>14</sup>

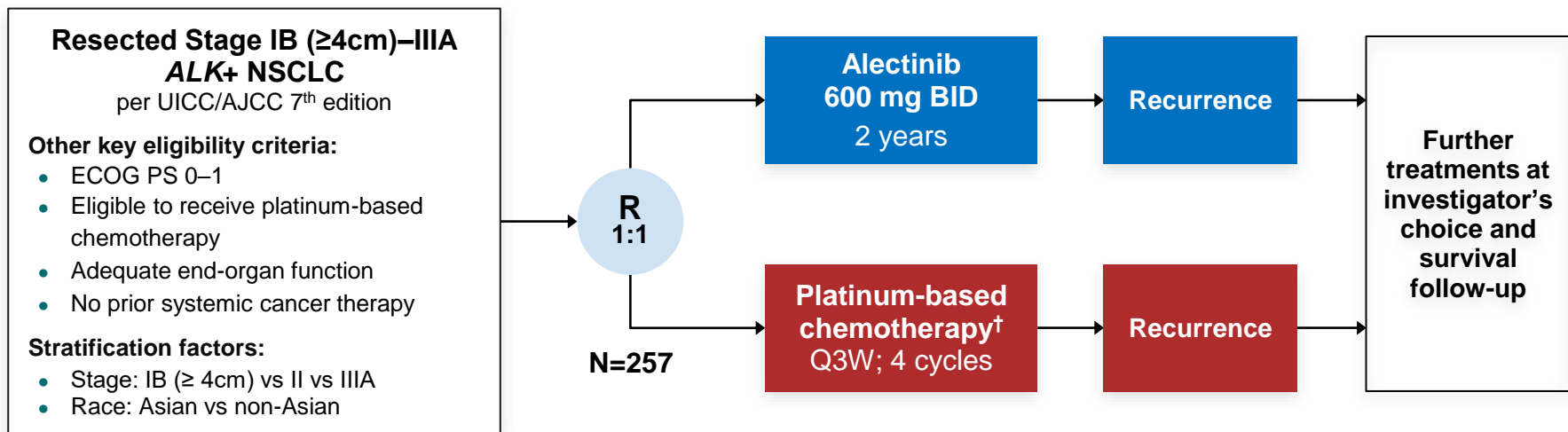
# Alectinib is a potent oral ALK TKI with efficacy in the CNS

- In advanced *ALK*+ NSCLC, three phase III trials have shown statistically significant and clinically meaningful improvements in PFS with alectinib compared with crizotinib,<sup>1-4</sup> as well as high levels of intracranial activity<sup>5-7</sup>



- Long-term treatment with alectinib has been demonstrated to be well tolerated with a well-characterised, manageable safety profile<sup>8</sup>
- Alectinib is a recommended first-line treatment in advanced *ALK*+ NSCLC;<sup>9</sup> as of August 2023, an estimated cumulative total of >92,000 patients have been treated with alectinib in clinical practice<sup>10</sup>

# ALINA study design\*



## Primary endpoint

- DFS per investigator,‡ tested hierarchically:
  - Stage II–IIIA → ITT (Stage IB–IIIA)

## Other endpoints

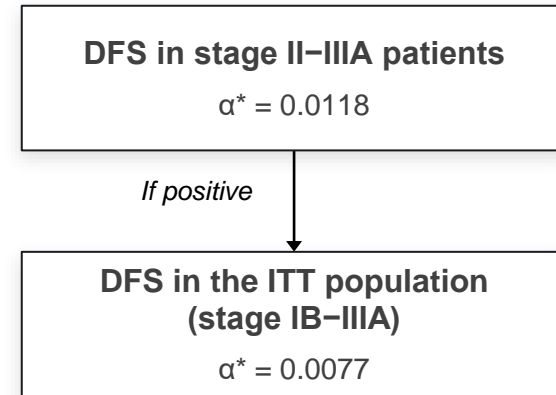
- CNS disease-free survival
- OS
- Safety

*Disease assessments (including brain MRI)<sup>§</sup> were conducted: at baseline, every 12 weeks for year 1–2, every 24 weeks for year 3–5, then annually*

# ALINA statistical analysis plan

- ALINA was designed to demonstrate superiority of alectinib compared with chemotherapy, with 80% power to detect a DFS HR of:
  - 0.55 in the stage II–IIIa subpopulation
  - 0.58 in the ITT population (stage IB–IIIa)
- One interim analysis was pre-planned after ~67% (59) events in the stage II–IIIa subpopulation

## DFS testing hierarchy

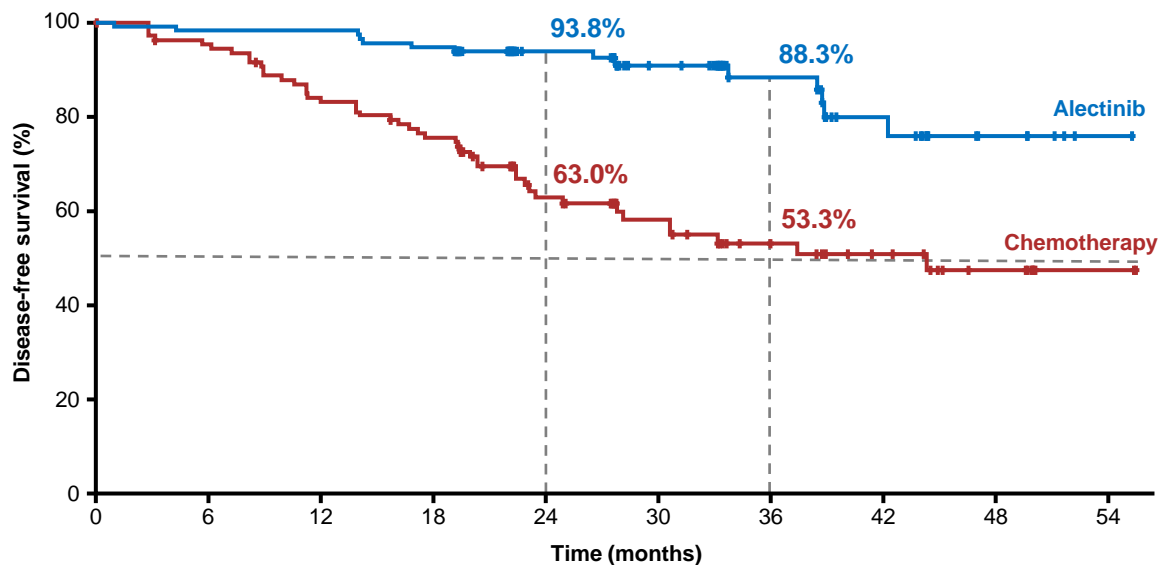


**Here, we report the primary results from  
the pre-specified interim analysis  
(clinical cut-off date: 26 June 2023)**

# Patient demographics and baseline characteristics (ITT)

Characteristic	Alectinib (n=130)	Chemotherapy (n=127)
<b>Median age</b> <65 / ≥65 years, %	54 years 79 / 21	57 years 73 / 27
<b>Sex:</b> female / male, %	58 / 42	46 / 54
<b>Smoking status:</b> never / former / current, %	65 / 32 / 4	55 / 43 / 2
<b>Race:</b> Asian / non-Asian, %	55 / 45	56 / 44
<b>ECOG PS:</b> 0 / 1, %	55 / 45	51 / 49
<b>Stage at diagnosis*:</b> IB / II / IIIA, %	11 / 36 / 53	9 / 35 / 55
<b>Nodal status:</b> N0 / N1 / N2, %	16 / 35 / 49	14 / 34 / 52
<b>Histology:</b> squamous / non-squamous, %	5 / 95	2 / 98
<b>Surgical procedure:</b> Lobectomy / Other‡, %	97 / 3	92 / 8

# Disease-free survival: stage II–III A\*



## No. at risk

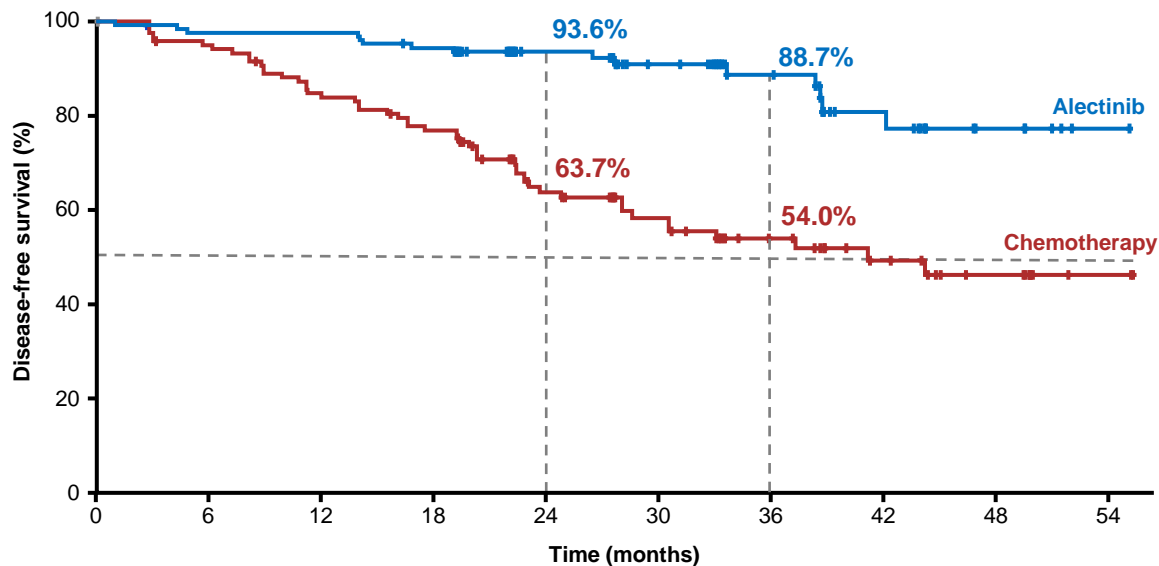
	0	6	12	18	24	30	36	42	48	54
Alectinib	116	111	111	107	67	49	35	21	10	3
Chemo	115	102	88	79	48	35	23	17	10	2

Median survival follow up: alectinib, 27.9 months; chemotherapy, 27.8 months

	Alectinib (N=116)	Chemotherapy (N=115)
Patients with event	14 (12%)	45 (39%)
Death	0	1
Recurrence	14	44
Median DFS, months (95% CI)	Not reached	44.4 (27.8, NE)
<b>DFS HR</b> (95% CI)	<b>0.24</b> (0.13, 0.45) p†<0.0001	



# Disease-free survival: ITT (stage IB–IIIA)\*



## No. at risk

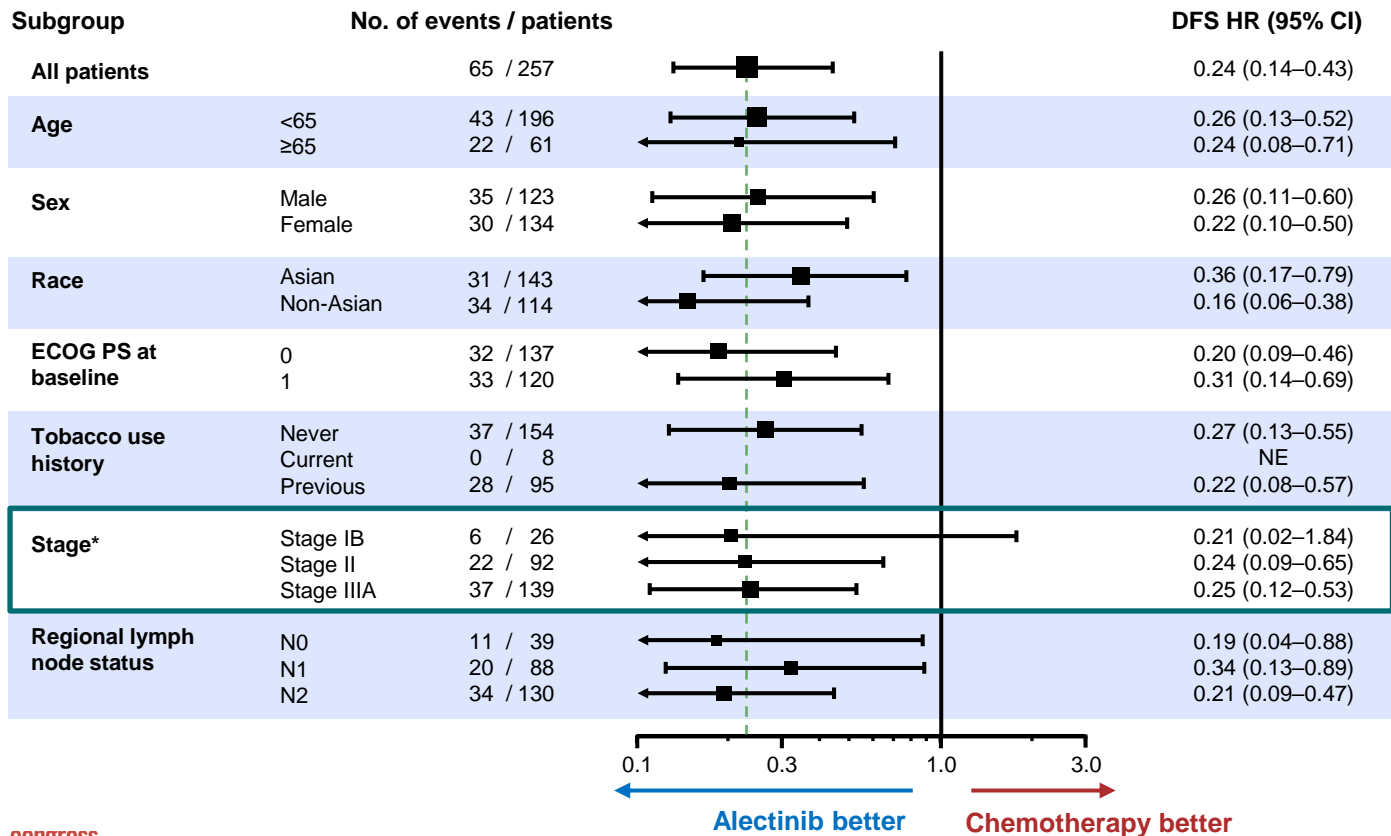
	0	6	12	18	24	30	36	42	48	54
Alectinib	130	123	123	118	74	55	39	22	10	3
Chemo	127	112	98	89	55	41	27	18	11	2

	Alectinib (N=130)	Chemotherapy (N=127)
Patients with event	15 (12%)	50 (39%)
Death	0	1
Recurrence	15	49
Median DFS, months (95% CI)	Not reached	41.3 (28.5, NE)
DFS HR (95% CI)	<b>0.24</b> (0.13, 0.43) p <sup>†</sup> <0.0001	

At the data cutoff date, **OS data were immature** with only 6 (2.3%) OS events reported<sup>‡</sup>

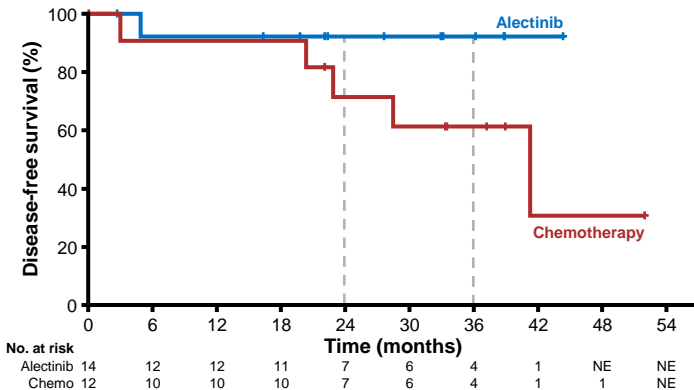
Median survival follow up: alectinib, 27.8 months; chemotherapy, 28.4 months

# Disease-free survival subgroup analysis (ITT)



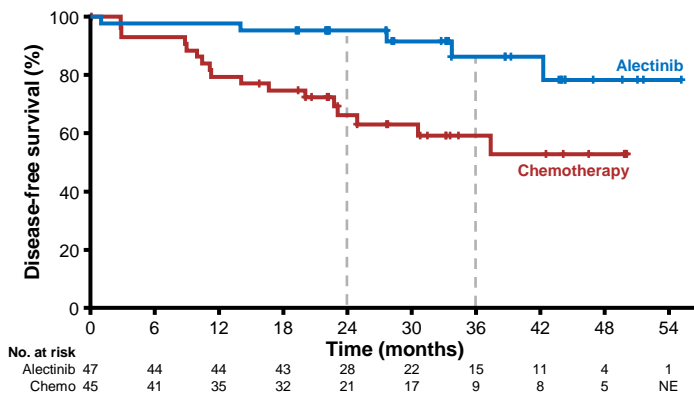
# Disease-free survival by stage\*

## Stage IB

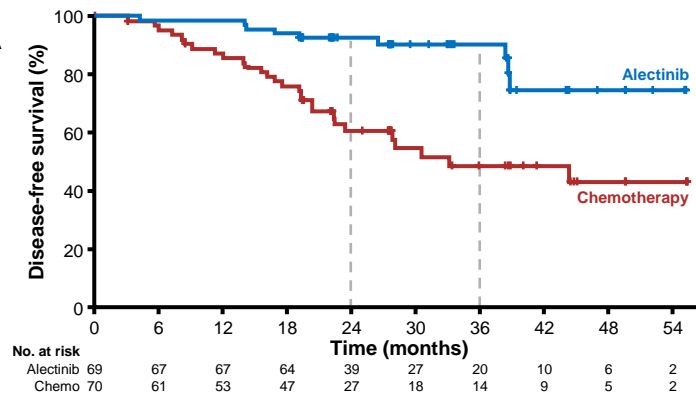


2-year DFS rate, % (95% CI)	Stage IB (n=26)	Stage II (n=92)	Stage IIIA (n=139)
<b>Alectinib</b>	<b>92.3</b> (77.8, 100.0)	<b>95.6</b> (89.5, 100.0)	<b>92.7</b> (86.4, 98.9)
<b>Chemotherapy</b>	<b>71.6</b> (44.2, 99.0)	<b>66.3</b> (51.7, 81.0)	<b>60.7</b> (47.9, 73.5)
<b>HR<sup>†</sup></b> (95% CI)	<b>0.21</b> (0.02, 1.84)	<b>0.24</b> (0.09, 0.65)	<b>0.25</b> (0.12, 0.53)

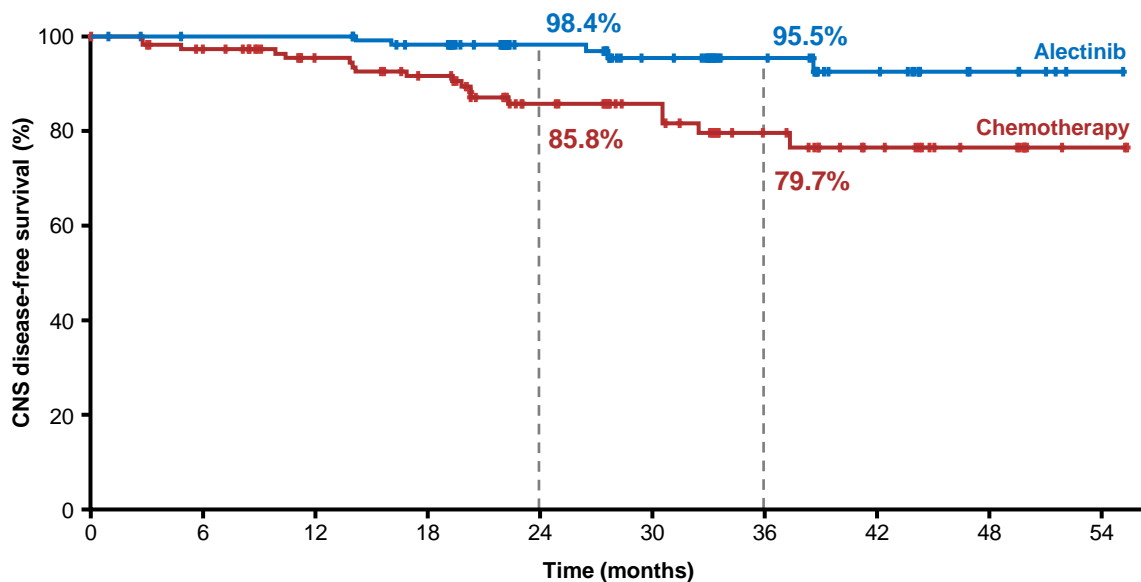
## Stage II



## Stage IIIA



# CNS disease-free survival in the ITT population



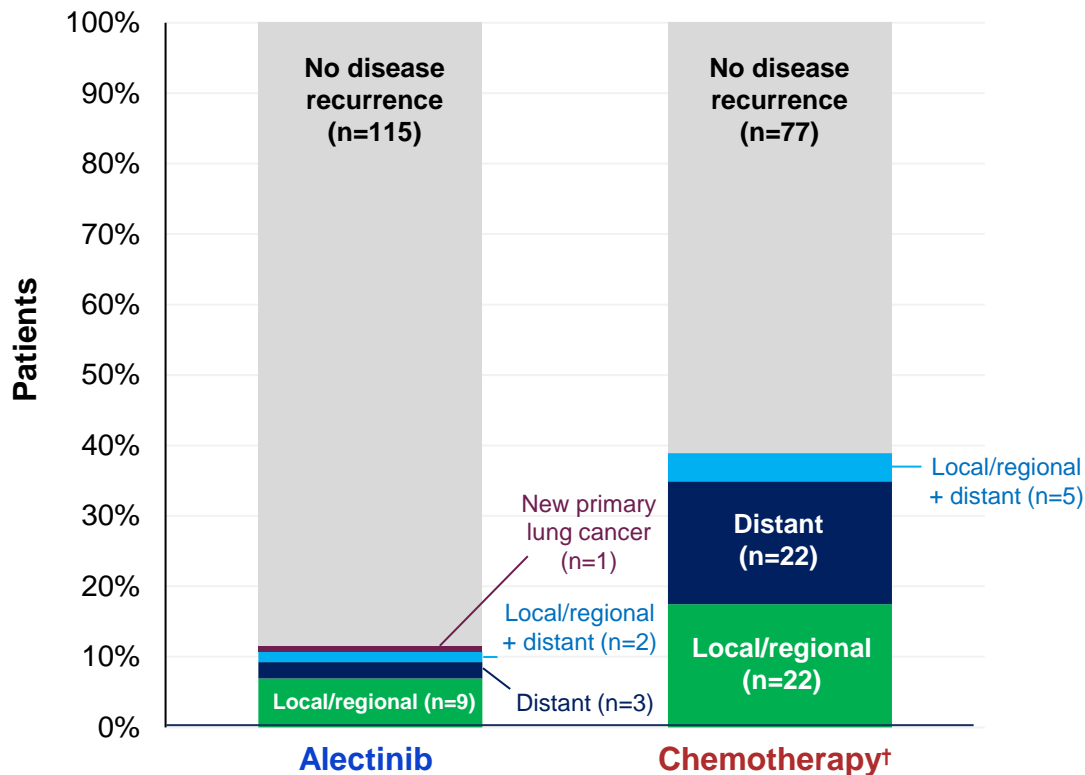
	Alectinib (N=130)	Chemotherapy (N=127)
Patients with event	5	18
Death	1	4
Brain recurrence	4	14
<b>CNS-DFS HR*</b> (95% CI)	<b>0.22</b> (0.08, 0.58)	

## No. at risk

	0	6	12	18	24	30	36	42	48	54
Alectinib	130	124	124	118	74	55	39	22	10	3
Chemo	127	113	98	90	57	43	27	18	11	2

Median survival follow up: alectinib, 27.8 months; chemotherapy, 28.4 months

# Sites of disease recurrence (ITT)



Site(s) of distant recurrence*	Alectinib (n=130)	Chemotherapy (n=127)
Brain	4	14
Bone	1	8
Adrenal gland	0	3
Lymph node	0	2
Kidney	0	1
Peritoneum	0	1
Other	1	0

# Post-recurrence subsequent therapy

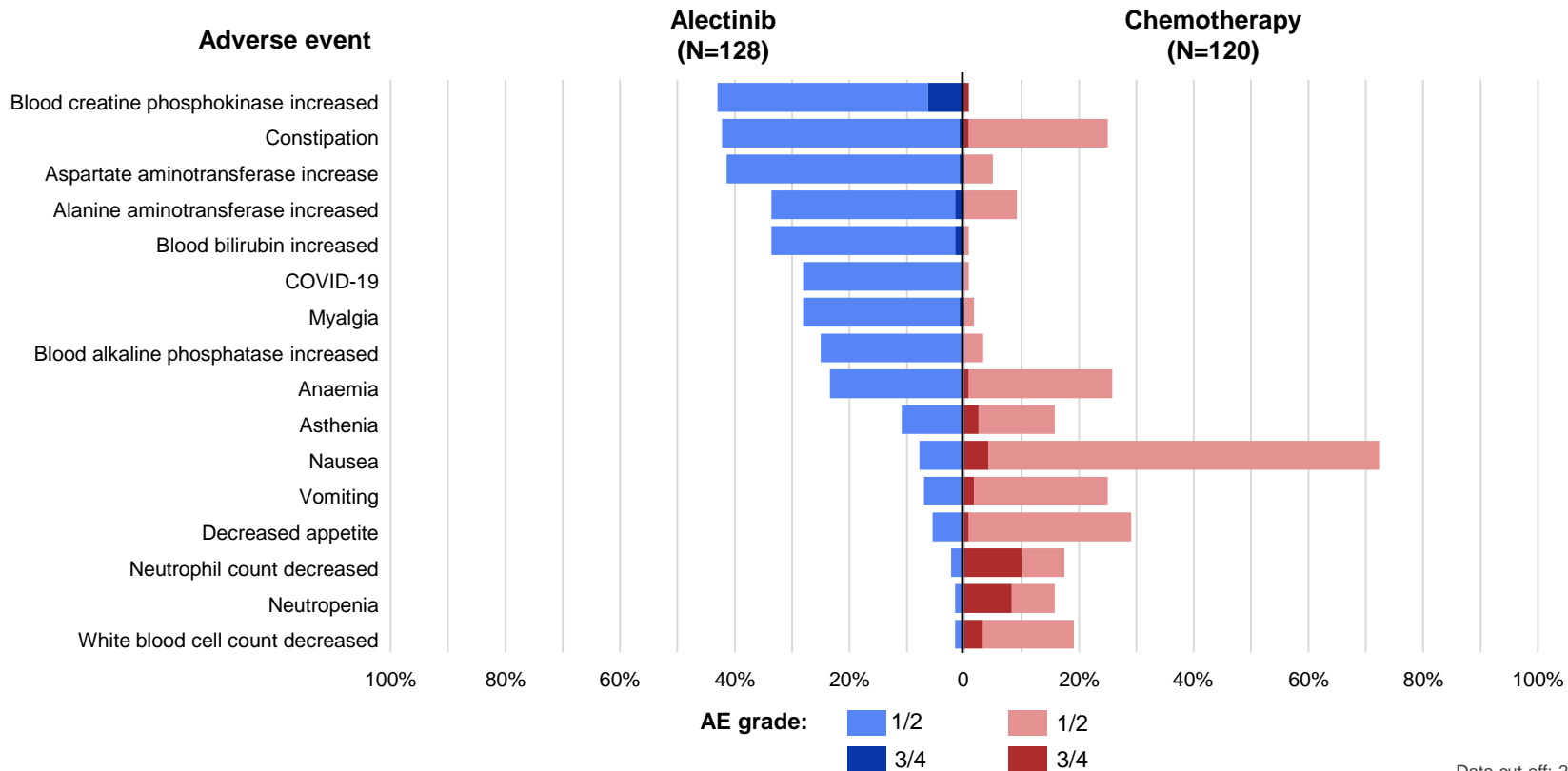
Number of patients with disease recurrence, n (%)	Alectinib (n=15)	Chemotherapy (n=49)
<b>Patients with any subsequent therapy</b>	13 (87)	43 (88)
<b>Systemic therapy</b>	13 (87)	38 (78)
ALK TKI	7 (47)	37 (76)
Alectinib	4 (27)	29 (59)
Brigatinib	4 (27)	4 (8)
Crizotinib	0	4 (8)
Lorlatinib	0	2 (4)
Ceritinib	0	1 (2)
Chemotherapy	6 (40)	2 (4)
Immunotherapy	1 (7)	1 (2)
Other anti-cancer therapy	1 (7)	1 (2)
<b>Radiotherapy</b>	5 (33)	9 (18)
<b>Surgery</b>	1 (7)	3 (6)

# Safety summary

	Alectinib (n=128)	Chemotherapy (n=120)
<b>Median treatment duration</b>	<b>23.9 months</b>	<b>2.1 months</b>
<b>Patients with any AEs, %</b>	<b>98</b>	<b>93</b>
Grade 3/4 AEs	30	31
Grade 5 AEs	0	0
Serious AEs	13	8
Treatment-related serious AEs	2	7
AEs leading to dose reduction	26	10
AEs leading to dose interruption	27	18
AEs leading to treatment withdrawal	5	13

At data cut off, **20.3%** of patients in the alectinib arm were ongoing treatment

# AEs occurring in $\geq 15\%$ of patients





# Other key trials of alectinib in stage I–III NSCLC are ongoing

## NAUTIKA1

USA  
NCT04302025

Phase II study in **resectable stage IB–IIIA NSCLC**, which includes a cohort of patients receiving **perioperative alectinib** (neoadjuvant and adjuvant) + adjuvant chemotherapy<sup>1</sup>

## ALNEO

Italy  
NCT05015010

Phase II study of **perioperative alectinib** in patients with **resectable stage III, ALK+ NSCLC**<sup>2</sup>

## HORIZON-01

International  
NCT05170204

Phase III, open-label, randomised cohort of patients with **unresectable stage III, ALK+ NSCLC** receiving **alectinib** vs durvalumab following chemoradiotherapy<sup>3</sup>

# Summary

- ALINA is the first and only positive phase III trial of an ALK inhibitor in resected, stage IB–IIIA NSCLC
- Treatment with adjuvant alectinib resulted in a statistically significant and clinically meaningful improvement in DFS compared with chemotherapy (HR 0.24; 95% CI 0.13, 0.43;  $p < 0.0001$ )
  - The DFS benefit was seen consistently across subgroups
- An improvement in CNS-DFS was observed (HR 0.22; 95% CI 0.08, 0.58)
- Adjuvant alectinib was tolerable and in line with the known safety profile of alectinib

**Adjuvant alectinib represents an important new treatment strategy  
for patients with resected, stage IB–IIIA, ALK+ NSCLC**

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