ALINA: efficacy and safety of adjuvant alectinib versus chemotherapy in patients with early-stage *ALK*+ non-small cell lung cancer (NSCLC)

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BACKGROUND

- Around 30–40% of patients with non-small cell lung cancer (NSCLC) are diagnosed with resectable disease.[1–4] Despite treatment, the risk of disease recurrence remains high (~45–76%, depending on stage)[5]*
- Anaplastic lymphoma kinase (*ALK*) rearrangements are found in 4–5% of patients with NSCLC; *ALK*+ NSCLC is typically:[6–13]
  - 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 stage IB–IIIA *ALK*+ NSCLC**, the current standard-of-care after surgery is **adjuvant platinum-based chemotherapy**; immunotherapy is not recommended[14]
- In advanced *ALK*+ NSCLC, alectinib is a preferred first-line treatment[14]

*Based on 5-year disease-free survival (DFS) event rates reported by Pignon et al. J Clin Oncol 2008.

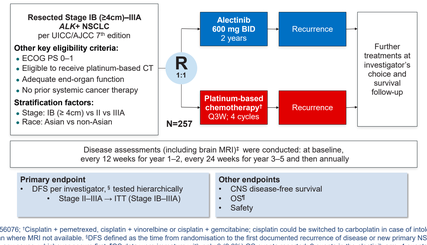
OBJECTIVES

- To describe the results from a prespecified interim analysis of the phase III, open-label, randomised **ALINA** trial (NTC03456076), assessing the efficacy and safety of adjuvant alectinib versus chemotherapy in patients with completely resected *ALK*+ NSCLC

METHODS

- The study design of the ALINA trial is presented in Figure 1
- Data cut-off (DCO) for the interim analysis was 26 June 2023

Figure 1. ALINA study design*



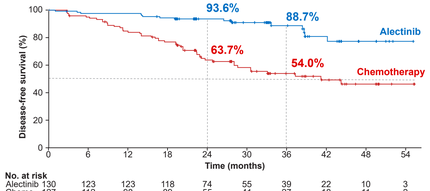
*Superiority trial, NCT03456076; †Cisplatin + pemetrexed, cisplatin + vinorelbine or cisplatin + gemcitabine; cisplatin could be switched to carboplatin in case of intolerability. ‡Assessment by computer tomography scan where MRI not available. §DFS defined as the time from randomisation to the first documented recurrence of disease or new primary NSCLC as determined by the investigator, or death from any cause, whichever occurs first. ¶OS data were immature with only 6 (2.3%) OS events reported; 2 events in the alectinib arm, 4 events in the chemotherapy arm; one additional patient in the chemotherapy arm died but was censored due to incomplete date of death recorded.

ALK+, anaplastic lymphoma kinase positive; AJCC, American Joint Committee on Cancer; BID, twice daily; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group Performance Status; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; OS, overall survival; UICC, Union for International Cancer Control; Q3W, every three weeks.

RESULTS: Efficacy

- 257 patients were randomised to receive alectinib (n=130) or chemotherapy (n=127)
- Baseline characteristics were well balanced between therapy arms (data not shown)
- The median survival follow-up period at DCO was 27.8 and 28.4 months in the alectinib and chemotherapy arms, respectively
- A significant DFS benefit was observed with alectinib vs chemotherapy
  - Stage II–IIIA (HR 0.24; 95% CI: 0.13–0.45)
  - ITT populations (HR 0.24; 95% CI: 0.13–0.43; Figure 2)
- The DFS benefit was maintained across all subgroups (Figure 3)
- The alectinib arm demonstrated improved CNS-DFS benefit in the ITT population compared with the chemotherapy arm (Figure 4)
  - ~ 4% (5/139) vs ~14% (18/127) of patients experienced events in the alectinib and chemotherapy arms, respectively
- In both alectinib and chemotherapy arms, most patients did not experience disease recurrence in CNS-DFS, with a higher proportion in the alectinib arm (Figure 5)
  - The most frequent type of disease recurrence was local/regional
- Distant recurrence mostly occurred in the brain, with ~3% (4/130) affected in the alectinib arm and ~11% (14/127) affected in the chemotherapy arm (Table 1)

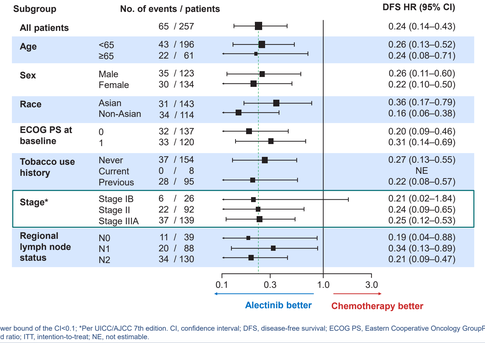
Figure 2. Disease-free survival: ITT (Stage IB–IIIA)*



	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)	**0.24** (0.13; 0.43); p†<0.0001	

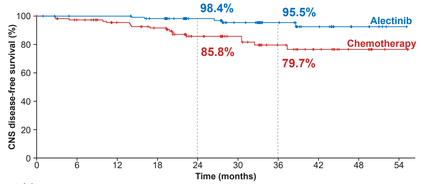
Time from last patient into data cut off was ~18 months. *Per UICC/AJCC 7th edition. †Stratified log rank. DFS defined as the time from randomisation to the first documented recurrence of disease or new primary NSCLC as determined by the investigator, or death from any cause, whichever occurs first.
CI, confidence interval; DFS, disease-free survival; HR, hazard ratio; ITT, intention-to-treat; NE, not estimable.

Figure 3. Disease-free survival subgroup analysis (ITT)



Arrows indicate lower bound of the CI<0.1; *Per UICC/AJCC 7th edition. CI, confidence interval; DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology GroupPerformance Status; HR, hazard ratio; ITT, intention-to-treat; NE, not estimable.

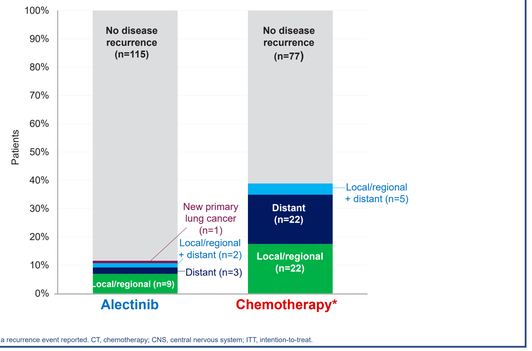
Figure 4. CNS disease-free survival: ITT



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

*Stratified analysis with race and stage as stratification factors. CNS-DFS defined as time from randomisation to the first documented recurrence of disease in the CNS or death from any cause.
CI, confidence interval; CNS, central nervous system; DFS, disease-free survival; HR, hazard ratio; ITT, intention-to-treat.

Figure 5. Sites of disease recurrence: ITT



*One patient died without a recurrence event reported. CT, chemotherapy; CNS, central nervous system; ITT, intention-to-treat.

Table 1. Site(s) of distant recurrence

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

*At disease assessment where first recurrence detected; patients may have multiple sites of disease recurrence counted.

RESULTS: Safety

- AT DCO, 20.3% of patients in the alectinib arms were ongoing treatment
- Similar proportions of patients with adverse events (AEs) were reported in the alectinib and chemotherapy arms (Table 2)
- No unexpected safety finding were observed

Table 2. Safety summary

	Alectinib (N=128)	Chemotherapy (N=120)
Median treatment duration	23.9 months	2.1 months
Patients with any AEs, %	98	93
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

Multiple occurrences of the same AE in one individual are counted only once in each category. AE, adverse event.

CONCLUSIONS

- **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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DISCLOSURES

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