

EP 12: Real-World Use of ALK Inhibitors in Advanced Non-Small Cell Lung Cancer: A Multicenter Study in Kazakhstan

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INTRODUCTION

ALK-positive non-small cell lung cancer (NSCLC) shows marked sensitivity to ALK tyrosine kinase inhibitors (TKIs), yet real-world data from Central Asia remain limited despite several available drug generations. **In Kazakhstan**, next-generation ALK inhibitors were long difficult to access, which complicated treatment sequencing and delayed timely initiation of therapy.

The Kazakhstan Halkyna Foundation was created in response to this situation, offering patients access to advanced ALK-targeted therapy before such drugs were covered by the state healthcare system. Under its national patient access program, the Foundation supplies alectinib, brigatinib, and lorlatinib free of charge to eligible patients — a step that has allowed real-world treatment patterns and outcomes to be assessed in a wider patient population than would otherwise have been possible. Here we report baseline disease burden, metastatic spread, and treatment sequencing among patients with ALK-positive NSCLC treated in Kazakhstan.

METHODS

A retrospective, multicenter cohort study was conducted at oncology centers across Kazakhstan, enrolling 141 patients with ALK-positive NSCLC treated with **alectinib, brigatinib or lorlatinib** in routine clinical practice. Baseline demographic and clinical characteristics were collected together with disease stage at treatment initiation and patterns of metastatic involvement, with particular attention to central nervous system (CNS) metastases.

Treatment sequencing was also evaluated, including whether patients received more than one line of ALK-targeted therapy.

Patient characteristics were summarized using descriptive statistics, and exploratory subgroup analyses were performed according to baseline CNS involvement.

RESULTS

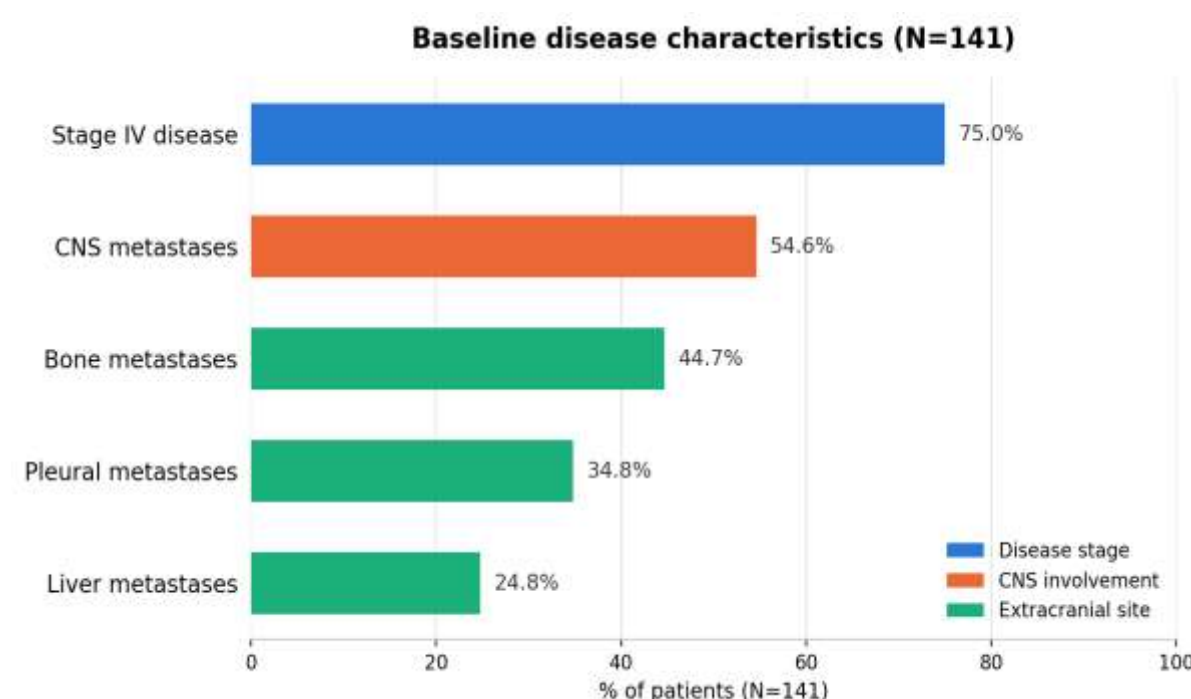


Figure 1. Baseline disease stage, CNS metastases, and extracranial metastatic sites in patients with ALK-positive NSCLC

The majority of patients presented with advanced disease, with **Stage IV in 75.0% (105/141)**. **Baseline CNS** metastases were identified in 54.6% of patients (77/141), followed by **bone (44.7%), pleural (34.8%), and liver metastases (24.8%)** as the most common extracranial sites.

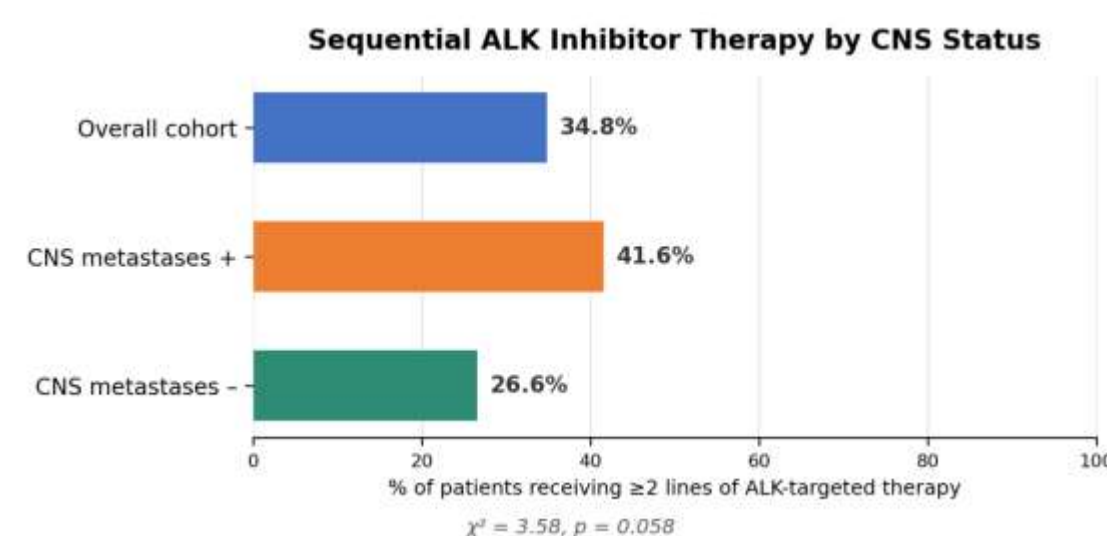


Figure 2. Sequential ALK inhibitor therapy was more frequent in patients with baseline CNS metastases.

Sequential ALK inhibitor therapy was observed in 34.8% of patients overall (49/141) and more frequently among those with baseline CNS metastases (41.6%) than without (26.6%; $\chi^2=3.58, p=0.058$). This difference did not reach statistical significance.

Overall mortality was 7.1% (10/141) at data cutoff, with no significant difference across treatment groups ($p=0.73$). Mortality was numerically higher among patients with CNS metastases compared to those without (9.1% vs 4.7%; $p=0.31$), though this difference did not reach statistical significance. At data cutoff, the majority of patients remained on treatment and **median progression-free survival (PFS) had not been reached**.

DISCUSSION

CNS involvement was present in over half of patients at baseline (54.6%), exceeding rates typically reported in ALK inhibitor clinical trials. This may reflect the high proportion of patients presenting with advanced disease in this real-world setting, together with historically limited access to CNS-penetrant ALK inhibitors.

Patients with baseline CNS metastases showed a trend toward more frequent use of sequential ALK-targeted therapy (41.6% vs 26.6%; $p=0.058$), suggesting a more treatment-intensive and clinically challenging disease trajectory in this subgroup.

This real-world experience was enabled by the Kazakhstan Halkyna Foundation's national access program, which provided alectinib, brigatinib and lorlatinib free of charge to eligible patients. Following implementation of the program, alectinib and lorlatinib were subsequently incorporated into Kazakhstan's publicly funded drug provision framework, supporting sustainable access to these agents beyond the early-access program.

LIMITATIONS

Mortality was assessed at a single data cutoff using the study registry. A separate program report with longer follow-up subsequently indicated a higher mortality rate, likely reflecting differences in follow-up duration and data cutoff timing. A more comprehensive analysis across the Foundation's full drug access program will be presented as an e-poster at ESMO Congress 2026.

CONCLUSION

This real-world multicenter cohort demonstrates a high burden of CNS metastases in ALK-positive NSCLC and frequent use of sequential ALK-targeted therapy. These findings support early initiation of CNS-penetrant agents in similarly resource-limited settings.

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