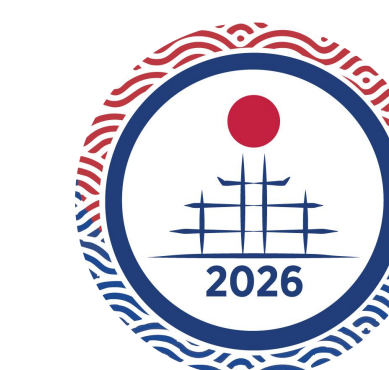




# Poster #: EP12.10: Efficacy and Safety of Ensartinib Combined With Anlotinib in Lorlatinib-Resistant ALK-Positive NSCLC: An Exploratory Analysis

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## INTRODUCTION

Second and third generation ALK tyrosine kinase inhibitors (TKIs) have substantially improved progression-free survival (PFS) in advanced ALK positive non-small cell lung cancer (NSCLC). However, acquired resistance, especially to lorlatinib, remains a major clinical challenge with no established standard of care. This retrospective exploratory study evaluated the efficacy and safety of ensartinib combined with anlotinib in patients with lorlatinib resistant ALK positive NSCLC.

## METHODS

Eligible patients were aged  $\geq 18$  years with histologically confirmed stage IIIB-IV ALK positive NSCLC and documented disease progression on lorlatinib. Prior to lorlatinib, patients could have received up to two non-ensartinib ALK-TKIs. The primary endpoints were objective response rate (ORR) and disease control rate (DCR); Safety was assessed by treatment-related adverse events (TRAEs).

## KEYWORDS

Lorlatinib resistance; Ensartinib; Anlotinib; ALK positive;

## CONCLUSION

Ensartinib combined with anlotinib demonstrates promising antitumor activity and favorable tolerability in heavily pretreated lorlatinib resistant ALK positive NSCLC. These preliminary findings support further validation in larger prospective cohorts with extended follow up.

## RESULTS

Between July 2016 and January 2025, seven patients were enrolled (median age 58 years, range 38-80; 85.7% female; 100% adenocarcinoma). TP53 mutation and brain metastases were each present in 2 patients (28.6%); 5 patients (71.4%) had an ECOG performance status of 1 (**Table 1**).

No complete responses were observed. Three patients (42.9%) achieved partial response, with an ORR of 42.9% (95% CI: 9.9%-81.6%) and DCR of 85.7% (95% CI: 42.1%-99.6%) (**Table 2**). Tumor responses of the 7 patients were presented in **Figure1**. TRAEs occurred in 4 patients (57.1%), including liver dysfunction, anemia, and decreased appetite (each 14.3%). One patient (14.3%) experienced a grade  $\geq 3$  skin reaction leading to dose reduction; No permanent discontinuations due to AEs were reported (**Table 3**).

Table 1. Baseline Clinical Characteristics

| Patient Characteristic  | Total (N=7) |
|-------------------------|-------------|
| Age <65                 | 5 (71.4%)   |
| Female                  | 6 (85.7%)   |
| Adenocarcinoma          | 7 (100%)    |
| ALK Positive            | 7 (100%)    |
| Combined other mutation |             |
| Yes                     | 2 (28.6%)   |
| No                      | 4 (57.1%)   |
| Unknown                 | 1 (14.3%)   |
| IVA                     | 4 (57.1%)   |
| IVB                     | 3 (42.9%)   |
| Brain Metastases        | 2 (28.6%)   |
| ECOG PS                 |             |
| 1                       | 5 (71.4%)   |
| 2                       | 2 (28.6%)   |
| <Third lines            | 1 (14.3%)   |
| $\geq$ Third lines      | 6 (85.7%)   |

Table 2. Objective tumor responses

| Overall Objective Response | Total (N=7)    |
|----------------------------|----------------|
| CR                         | 0              |
| PR                         | 3 (42.9%)      |
| SD                         | 3 (42.9%)      |
| PD                         | 0              |
| NE                         | 1 (14.3%)      |
| ORR (CR+PR)                | 3 (42.9%)      |
| 95%CI                      | (9.9%, 81.6%)  |
| DCR (CR+PR+SD)             | 6 (85.7%)      |
| 95%CI                      | (42.1%, 99.6%) |

\*NE: Not evaluable

Figure1. Tumors response status

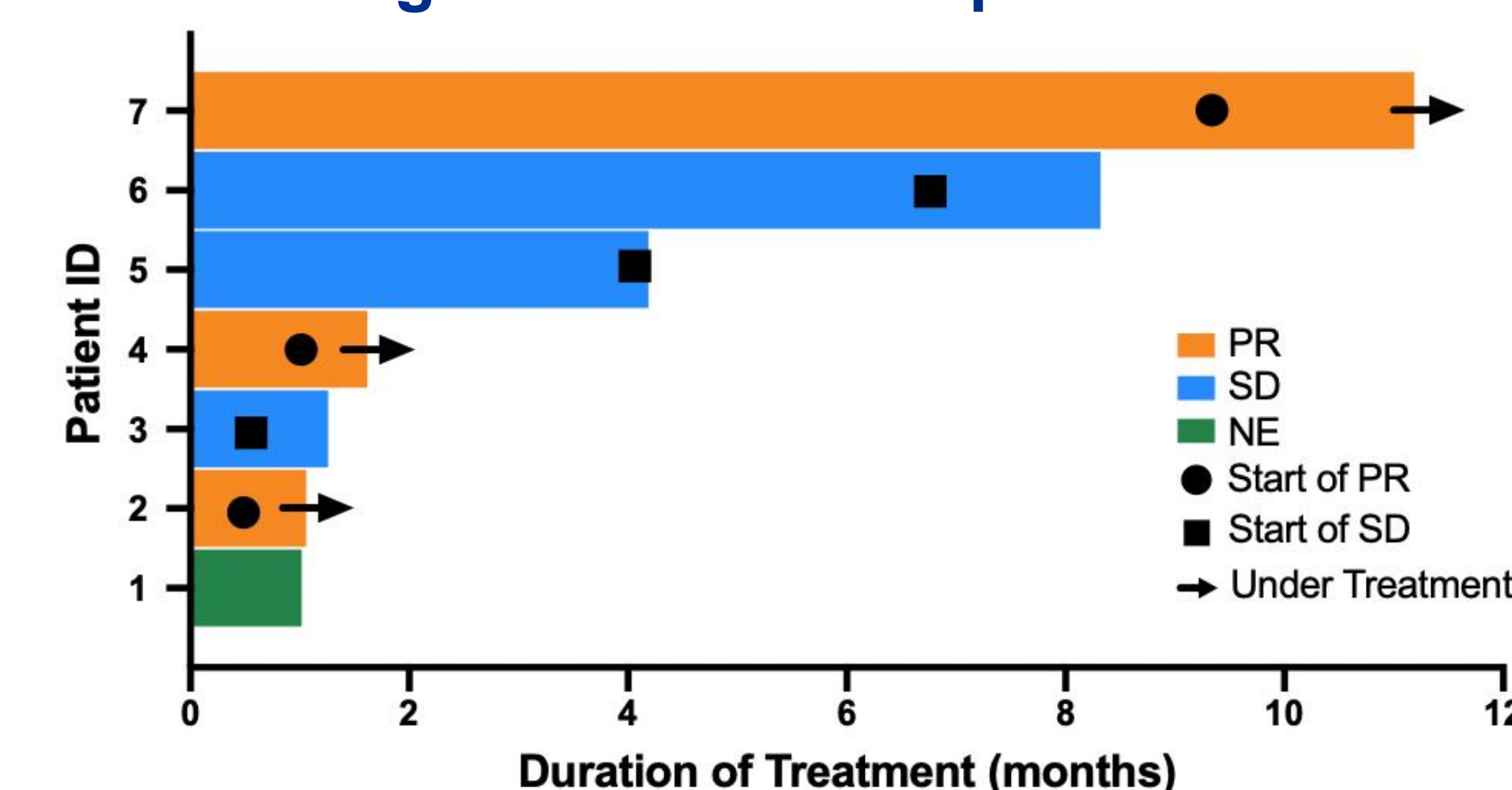


Table 3. Safety profile

| Safety                          | Total (N=7) |
|---------------------------------|-------------|
| Any grade of AE                 | 4 (57.1%)   |
| AEs of grade $\geq 3$           | 1 (14.3%)   |
| SAE                             | 1 (14.3%)   |
| AE-related treatment suspension | 1 (14.3%)   |
| AE-related dose reductions      | 1 (14.3%)   |
| AE-related treatment switch     | 0           |