ALK Positive Lung Cancer (UK)
A patient-focused charity that
Supports Empowers Advocates

Lorlatinib

Extracts from a paper published in European Journal of Cancer in March 2022

The study was hosted by the French Collaborative Thoracic Intergroup. The purpose of the study was to gather real-world evidence regarding treatment sequences and outcomes for patients who had received Lorlatinib. Data was collected on 208 patients with advanced or metastatic ALK+ NSCLC who had been treated between October 2015 and June 2019 under the French Expanded Access Programme and who met the predefined inclusion criteria.

The demographics were similar to our UK group –

56% female; 69% never smokers; 87% diagnosed at Stage IV.

28% had brain metastases at the time of their initial diagnosis as NSCLC and, at the start of the Lorlatinib treatment, 77% had brain mets.

78% had previously been treated with chemotherapy and 94% with a 1st or 2nd generation TKI.

Most patients had received several lines of treatment prior to Lorlatinib which was delivered as

2nd line in 4% of patients

3rd line in 17% of patients

4th line in 30% of patients

5th line in 49% of patients

Patients were heavily pretreated - 79% of them had previously received at least three lines of systemic treatment and 46% also had been treated with brain radiation therapy.

Results

("Median" is the value that separates the lower half from the higher half of a data set)

1. The Disease Control Rate (partial or complete response or stable) was 86%

2. Treatment was stopped due to adverse reactions in 14% of patients.

3. The median progression-free survival, ie the time between starting Lorlatinib and evidence of progression, was 9.9 months. This means that 50% had progression before 9.9 months and 50% after 9.9 months.

4. The median overall survival (OS) from starting on Lorlatinib was 32.9 months, ie 50% lived longer that 32.9 months after starting on Lorlatinib.

5. The median overall survival since initial diagnosis of NSCLC was 97.3 months.

6. Of the patients with brain mets at the start of their Lorlatinib treatment, the partial/complete response rate was 56%. The median duration of the response was 16.7 month.

The median OS of over 8 years for this group is not an indication of the mean OS of all ALK+ patients as some patients would not have survived long enough to have been prescribed Lorlatinib and others would not have met the inclusion criteria.

As with all clinical trials and many studies, patients must meet inclusion criteria and the results of these trials and studies may not be replicated in the real world.

The report states

"We found a decrease in the Lorlatinib efficacy with the number of lines of previous ALK-TKIs received; this was also observed in the phase II clinical trial and in a real-life study. In our study, for instance, the PFS decreased from 11.7 months to 5.8 months depending on whether patients had received two or more previous ALK-TKIs. These results suggest a benefit of using Lorlatinib early in the patient's management and highlight the need for further analysis of treatment sequences. However, the question of where to place Lorlatinib in the treatment sequence has recently become more complex, with the results of the phase 3 CROWN trial showing the superiority first-line setting of Lorlatinib over Crizotinib in terms of PFS. In the absence of a direct comparison of first-line Lorlatinib with second-generation ALK-TKIs, it is difficult to provide a definitive answer."

A copy of the full report is available on request.