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Cost-utility Analysis of Lorlatinib for the First-line Treatment of Patients with ALK Positive Advanced Non-small Cell Lung Cancer in China

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Background

- Non-small-cell lung cancer (NSCLC) accounts for 80%-85% of lung cancer cases[1,2], which is one of the main causes of cancer-related deaths. 3% to 5% of patients with NSCLC test ALK fusion gene.
- A global multicenter, randomized controlled, open-label, phase III clinical trial (CROWN)[3,4] showed that a potent third-generation ALK inhibitor lorlatinib is more effective than crizotinib in patients with previously untreated ALK-positive advanced NSCLC. There was a statistically significant and clinically significant improvement in progression-free survival (PFS); in terms of central nervous system progression, lorlatinib reduced patients' risk of disease progression or death by 92% % risk of intracranial progression.
- However, the study of economic impact of lorlatinib is limited in China.

Objective

- This study aimed to compare the cost-effectiveness of lorlatinib and alectinib for the first-line treatment of patients with ALK positive advanced NSCLC from the perspective of the Chinese healthcare system.

Methods

Population

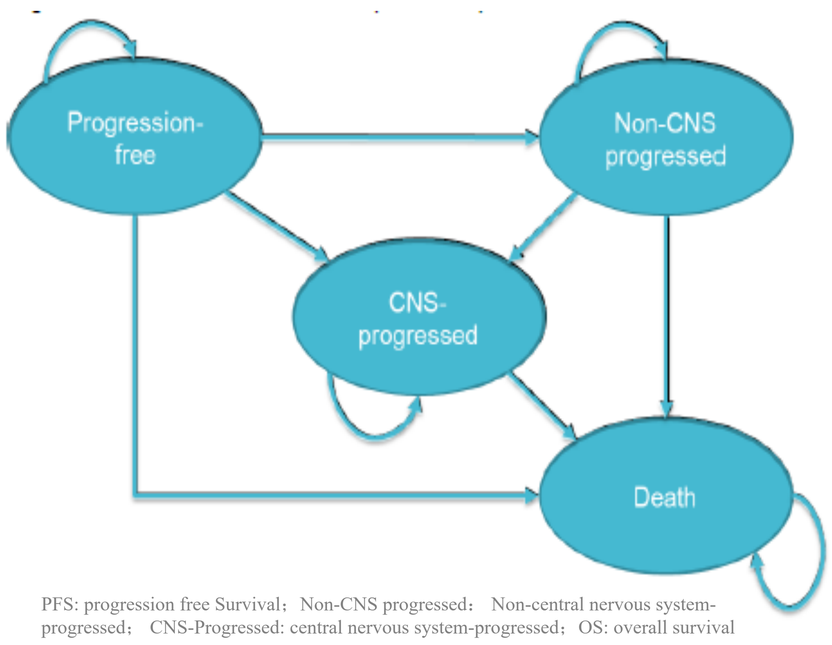
- Previously untreated patients with ALK positive advanced or metastatic NSCLC
- The baseline characteristics of simulated patients were consistent with those of the global multicenter, randomized controlled, open-label, phase III clinical trial of lorlatinib (CROWN trial).

Treatments in the Model

- The first-line treatment in the model
- Intervention: Lorlatinib (dosage: 100 mg/time, once per day)
- Comparator: Alectinib (dosage: 600 mg/time, twice per day)

Model Structure

- A partitioned survival model was developed using PFS and OS.
- A four-state model was used as the base case structure. In the four-state model, the progressed health state was divided into non-CNS progressed disease and CNS-progressed disease. (Figure 1)



PFS: progression free Survival；Non-CNS progressed： Non-central nervous system-progressed； CNS-Progressed: central nervous system-progressed； OS: overall survival

Figure 1. Four-state base case structure (base case)

Model Setting

- Perspective: China healthcare system perspective
- Cycle length: 30 days
- Base case time horizon: lifetime
- Parameters: Clinical trials, published data and expert opinion
- Half-cycle correction was applied for all costs and outcomes
- Discount rate: 5%

Model Inputs

Efficacy

- Parametric survival curves were fit to endpoints from CROWN to inform efficacy in the model to estimate likely outcomes beyond the observed duration of the clinical trial. [3,4]
- The best fitting curve was identified based on the goodness-of-fit criterion. (Figure 2)

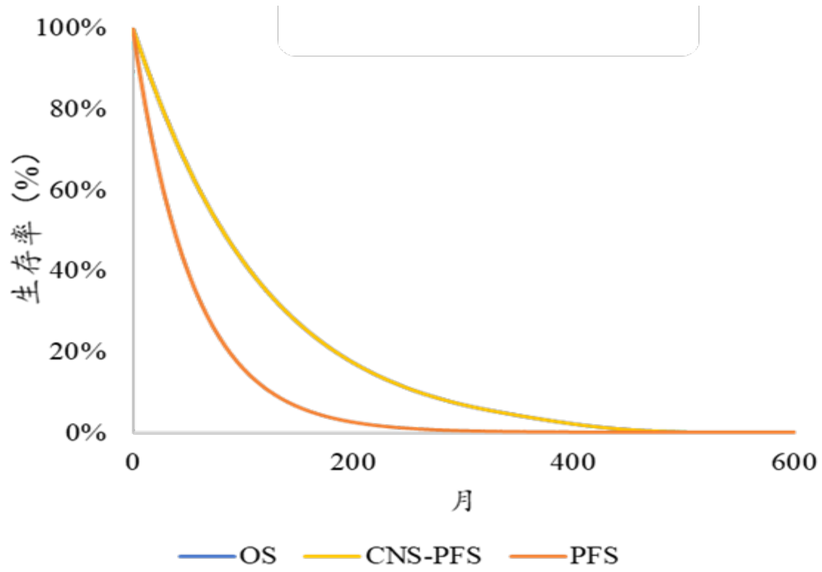


Figure 2. Survival curves for lorlatinib

Due to the lack of head-to-head comparison between lorlatinib and alectinib, a network meta-analysis was conducted using the two pivotal clinical trial of lorlatinib (CROWN trial) and alectinib (ALEX trial) [5]. HRs were applied to baseline crizotinib OS and PFS curves to predict outcomes for each comparator. (Table 1).

Table 1. Results of network meta-analysis

Endpoints	Hazard ratio（HR）
PFS	Alectinib vs. Crizotinib：0.33（95%CI：0.13-0.74）
PFS	Alectinib vs. Lorlatinib：1.21（95%CI：0.21-6.42）
OS	Alectinib vs. Crizotinib：0.93（95%CI：0.5-1.72）
OS	Alectinib vs. Lorlatinib：1.29（95%CI：0.52-3.21）

Costs

From the perspective of China healthcare system perspective, this study included direct medical costs, referring to the first-line treatment costs, later-line treatment costs, follow-up examination costs, additional treatment costs for patients with brain metastases, adverse event treatment costs, and death costs. (Table 2)

Table 2. Costs (RMB)

Costs (RMB)	Lorlatinib	Alectinib
Drug costs	¥681,480.15	¥566,389.87
Later-line treatment costs	¥65,829.70	¥75,971.75
Management costs	¥91,511.66	¥81,574.46
Death costs	¥9,117.60	¥10,193.60
AE costs	¥53.21	¥52.56
Total costs	**¥847,992**	**¥734,182**

Utility

This study modelled CROWN utility values by incorporating stratification factors of Health state, treatment status, treatment arm. And the resulting utility value in the basic analysis was 0.85 and 0.74 for the progression-free state and progressed state, respectively.

The model also used the absolute utility value 0.52 reported by Roughley et al.[6] to represent the CNS-progressed health state.

Willingness-To-Pay Threshold

- According to the recommendations from the "China Pharmacoeconomics Evaluation Guide 2020", three times the gross domestic product per capita (GDP, 85,698 RMB in 2022) was used as the willingness-to-pay threshold to evaluate the outcomes.

Results

Base Case Results

In the base case analysis, compared with alectinib, lorlatinib gained 1.38 incremental quality-adjusted life years (QALYs) (5.28 vs. 3.90), and ¥ 113,810 incremental cost (¥ 847,992 vs. ¥ 734,182). The incremental cost-effectiveness ratio (ICER) was ¥82,824/QALY, which is less than one times per capita GDP (¥85,698, in 2022) in China. Lorlatinib is a more cost-effective treatment option. (Table 3-1, Table 3-2, Figure 3)

Table 3-1. Cost effectiveness analysis results

Treatments	Total Costs	Total LYs	Total QALYs
Alectinib	¥734,182.24	4.93	3.90
Lorlatinib	¥847,992.32	6.57	5.28

Table 3-2. Incremental Results

Treatments	Incremental Costs	Incremental LYs	Incremental QALYs	ICER (¥ per QALY)
Alectinib				
Lorlatinib	¥113,810	1.64	1.37	¥82,824.78

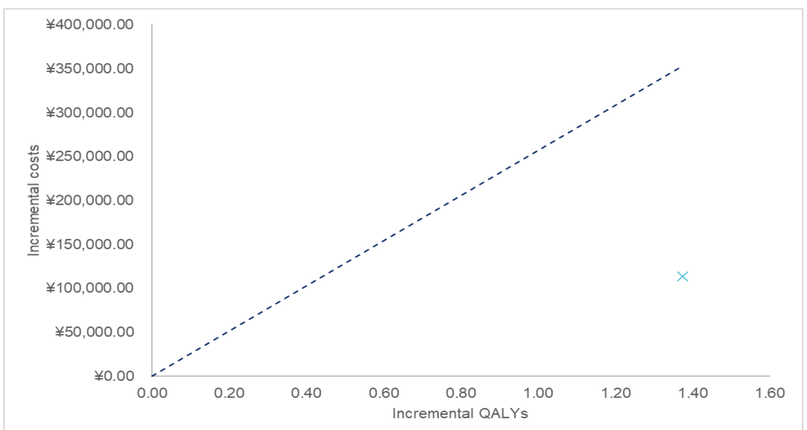


Figure 3. Cost-effectiveness plane

Sensitivity Analysis

One-way Sensitivity Analysis

The one-way sensitivity analysis (OWSA) showed that the top three parameters that had the greatest impact on the results were the OS HR between alectinib and crizotinib, PFS HR between alectinib and crizotinib and the drug price of alectinib. (Figure 4)

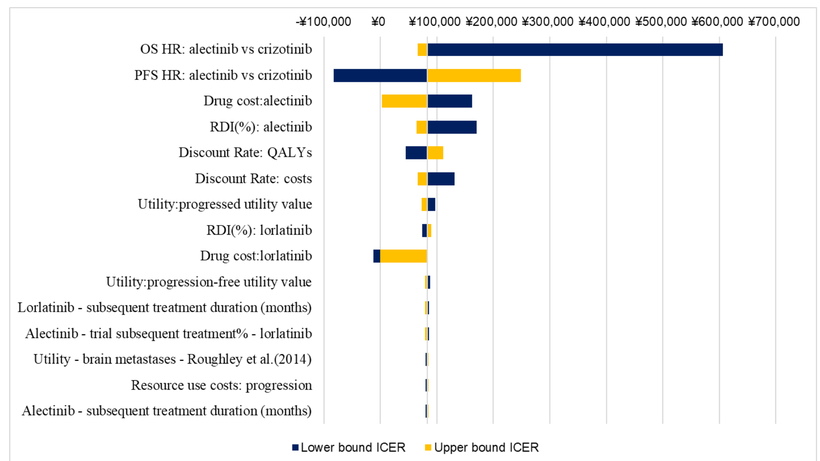


Figure 4. OWSA– Lorlatinib vs. Alectinib

Probabilistic Sensitivity Analysis

The probabilistic sensitivity analysis (PSA) was based on 10,000 probabilistic iterations, which confirmed that results had approximately stabilized before 10,000 iterations.

As stated in the cost-effectiveness plane (figure.4), the PSA showed that most of the incremental cost-effectiveness scatter points of lorlatinib compared with alectinib were in the first quadrant, and lorlatinib has a high probability being cost-effective compared with alectinib. (Figure 5)

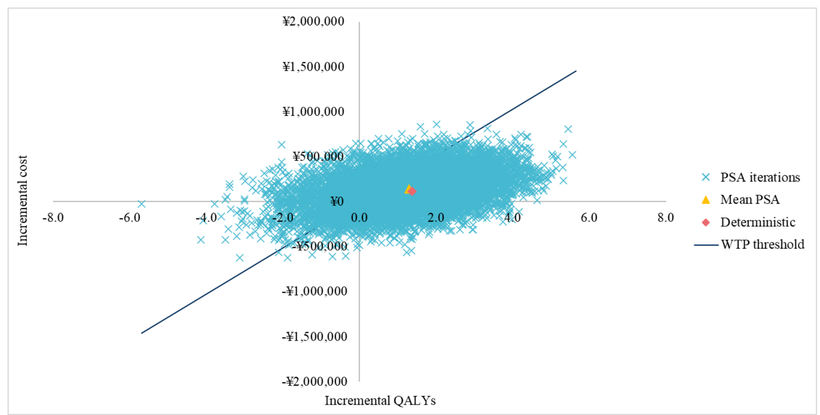


Figure 5. Cost-effectiveness plane – Lorlatinib vs. Alectinib

The setting of willingness-to-pay threshold represents the estimates prepared to pay for the health benefit. The acceptability curve expressed as the ICER in relation to value of WTP shows the acceptance level of two different treatment options at the WTP.

The results showed that as WTP increased, the possibility of lorlatinib being cost-effective increased. When WTP was about 3 times GDP per capita, the possibility of lorlatinib being cost-effective was nearly 80%. (Figure 6)

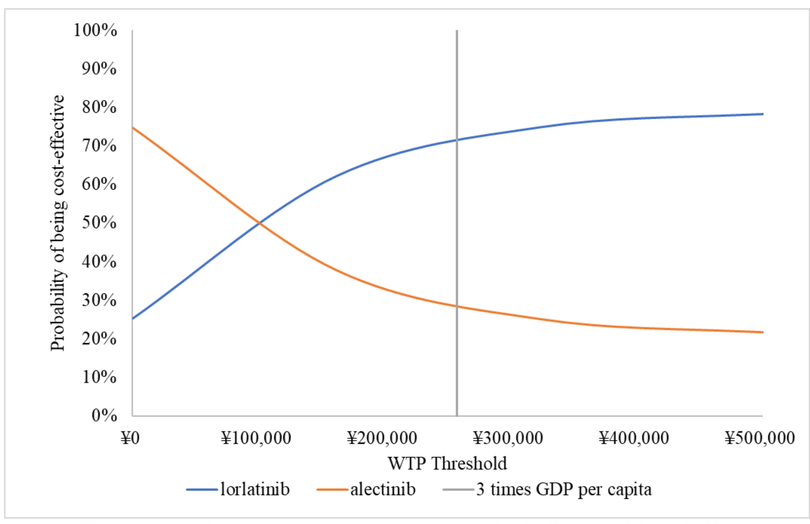


Figure 6. Acceptance curve – Lorlatinib vs. Alectinib

Conclusion

- This study found that for the first-line treatment of patients with ALK+ advanced NSCLC in China, at the current price, the ICER of lorlatinib compared with alectinib is less than 1 times GDP per capita. Lorlatinib is more cost-effective in China

Reference

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