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Pharmacoeconomic Analysis of Brigatinib Versus Alectinib in Chinese Patients with *ALK*-Positive Non-Small Cell Lung Cancer

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INTRODUCTION

- Lung cancer is the prime reason of cancer-related morbidity and mortality in China, of which non-small cell lung cancer (NSCLC) accounts for 85% of all cases.[1]
- Prognosis of NSCLC remains poor and 3%-7% of patients are detected to have tumorigenic rearrangements in *ALK*.[2]
- To target these *ALK* mutations, ALK TKIs are established as the standard of care globally.[2]
- Moreover, Guidelines of Chinese Society of Clinical Oncology recommend TKIs for advanced *ALK*-positive NSCLC patients.[1]
- Alectinib and brigatinib are TKIs with stronger inhibition and higher blood-brain barrier permeability and demonstrated efficacy and safety.[3,4]
- Although alectinib and brigatinib are used to treat patients with *ALK*-positive, advanced NSCLC in China, economic evaluation studies comparing the two need to be explored.

STUDY OBJECTIVE

To perform the pharmacoeconomic analysis of brigatinib and alectinib as first-line treatment in patients with *ALK*-positive NSCLC from a Chinese healthcare system perspective.

METHODS

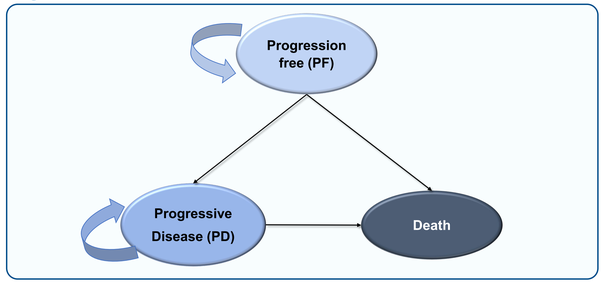
Model construction

- The study was performed from China's healthcare system perspective.
- Cost-minimization analysis (CMA) and cost-effectiveness analysis (CEA) were conducted.
- The model description is presented in **Table 1.**

Table 1: Model characteristics

Model characters	Description
Target population	*ALK*-positive, locally advanced or metastatic (stage IIIB/IV) NSCLC patients
Intervention	Brigatinib
Comparator	Alectinib
Structure	Partitioned survival model included three health states **(Figure 1)**
Cycle	28 days
Time horizon	30 years
Annual discount rate	5%

Figure 1: Model structure



Clinical data

- The data for brigatinib and alectinib were based on the final ALTA-1L and ALEX trials, respectively.
- Due to lack of head-to-head trials, indirect treatment comparison (ITC) data was used to compare brigatinib with alectinib.[5,6]

Cost-minimization and cost-effectiveness analysis

- Cost-minimization analysis was performed to compare the total costs of brigatinib and alectinib, as the health benefits of brigatinib and alectinib were comparable based on ITC results. [5,6]
- Cost-effectiveness analyses for the comparison were conducted using point estimates from ITC as a scenario analysis.
- ITC based on aggregated data were highly vulnerable to systematic variation (bias) resulting from imbalances in effect modifier distributions. Matching-adjusted indirect comparison (MAIC) approach used ALTA-1 brigatinib individual patient data (IPD) and re-weighted the IPD to balance the baseline characteristics of patients in ALEX trial. [5] When a common comparator is available, a population-adjusted anchored indirect comparison was recommended.[7]
- The ALTA-1L clinical trial allowed crossover from the crizotinib arm to brigatinib upon progression, while it was not specified in the ALEX protocol, so the treatment crossover adjustments were considered. [6]
- The anchored MAIC PFS HR 0.98 (0.62, 1.54) [5] and OS HR 0.911 (0.501, 1.165) [6] were used in this CEA scenario.

Costs

- The drug costs of brigatinib and alectinib used the latest price from China.[8]
- Considering that the patient's disease state worsens after disease progression, the model assumed that healthcare resource utilization differs in PF and PD states.
- This study calculated AE management costs (AEs grades ≥3).
- Concomitant treatment mainly included hepatoprotective drugs, that increase white blood cells, thymosin, and antiallergic drugs.
- Subsequent treatment considered platinum-based double-drug chemotherapy; palliative care cost was also considered in this study.
- Costs data were derived from published literature[9] or surveys by clinical experts in 7 provinces of China.

Health state utilities

- The utility value of PFS state in the model was 0.856, and the utility value of PD state was 0.768.[10]
- Disutility of AEs was considered.[11]

Sensitivity analysis and other scenarios

- One-way sensitivity analyses were conducted in CMA.
- Results using HRs from ITC generated by different sources will also been calculated as supplemental CEA scenarios.

RESULTS

Cost-minimization and cost-effectiveness analysis

- In the cost-minimization analysis, brigatinib was cost-saving at USD -24,574 as compared with alectinib **(Table 2)**.
- With respect to cost-effectiveness, brigatinib achieved additional 0.29 QALYs and was less costly (USD -22,710) in comparison with alectinib **(Table 2).**

Table 2: Results of cost minimization and cost-effectiveness analysis

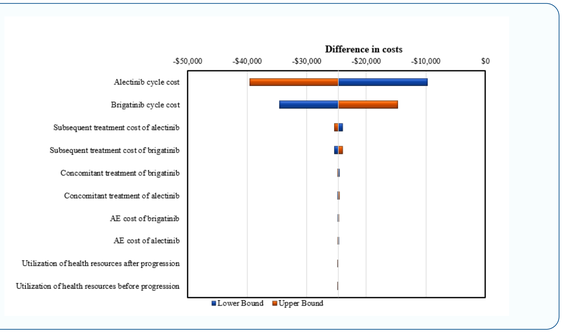
Intervention	Total cost (USD)	Total QALYs	Incremental cost (USD)	Incremental QALYs	ICER (USD/QALY)
Cost minimization analysis					
Brigatinib	62,084	4.82	-	-	-
Alectinib	86,658	4.82	-24,574	-	Brigatinib is cost-saving
Cost-effectiveness analysis-using anchored MAIC data					
Brigatinib	62,084	4.82	-	-	-
Alectinib	84,794	4.54	-22,710	0.29	Brigatinib is dominant

Sensitivity analysis and other scenarios

Sensitivity analysis revealed drug costs to be the most influential factor to ICER **(Figure 2).**

In the supplemental CEA scenarios, when using different HRs, the total costs of brigatinib were lower but the QALYs will be higher or lower versus alectinib.

Figure 2: One-way sensitivity analyses tornado diagram-CMA



CONCLUSIONS

The result of cost-minimization analysis suggested that brigatinib was cost-saving compared to alectinib for the treatment of patients with *ALK*-positive advanced NSCLC in China.

The result of cost-effectiveness analysis using specific HRs showed that brigatinib was economically dominant (more QALYs gains and less costly). It may vary due to different ITC data.

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Disclosures

Gu C and Zhang YJ are employees of Takeda (China). Zhang YJ holds Takeda stocks.

Abbreviations:

ALK, anaplastic lymphoma kinase; ICER, incremental cost-effectiveness ratio; MAIC, matching-adjusted indirect comparison; NSCLC, non-small cell lung cancer; PFS, progression free survival; QALYs, quality-adjusted life-years; TKIs, tyrosine kinase inhibitors; WTP, willingness-to-pay

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