Cost of managing brain metastases in patients with ALK-positive advanced NSCLC with first-line ALK tyrosine kinase inhibitors (TKIs) in China

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INTRODUCTION

Patients with ALK-positive advanced non-small cell lung cancer (aNSCLC) have a high occurrence of brain metastases (BM). Approximately 15-35% of patients with ALK-positive aNSCLC will develop BM during the course of the disease[1]. Patients with ALK-positive aNSCLC have high clinical and economic burden compared with those without BM[2,3]. With the increasing permeability of brain penetration effect of second-generation and third-generation ALK-TKIs compared with crizotinib[4,5,6], the risk of brain metastasis progression may be avoided, thereby reducing the management costs.

OBJECTIVES

This study estimates the costs of managing BM in patients with ALK-positive aNSCLC receiving lorlatinib, crizotinib, alectinib, brigatinib and ensartinib as first-line treatment in China.

METHODS

105 clinical experts from tertiary hospitals across 23 regions in China were surveyed by questionnaire on healthcare resources utilization (HCRU) in ALK-positive aNSCLC patients with and without BM. HCRU included surgical resection, radiotherapy, medical visits, hospitalizations, laboratory tests, imaging, and special tests for BM and ALK gene tests. Diagnostic tests and treatment costs were excluded. The costs are derived from expert estimation.

The total annual costs with TKIs were estimated by weighting the yearly costs of managing patients with and without BM using the ITT population and Asian group cumulative incidence rate (CIR) of BM progression in clinical trials (Table 1 and 2). The 12-month cumulative incidence results represent the management costs for the first year of treatment, whilst the 24-month/36-month/48-month cumulative incidence results represent the costs for the second/third/fourth year of treatment. It is assumed that HCRU in patients with and without BM is the same during the subsequent treatment years.

Table 1 : Cumulative incidence of progression of BM in global clinical trials

	CROWN trial		ALEX trial		eXalt3 trial		ALTA trial	
	Lorlatinib N=149	Crizotinib N=142	Alectinib N=152	Crizotinib N=151	Ensartinib N=143	Crizotinib N=143	Brigatinib N=136	Crizotinib N=137
12-month								
ITT population	2.8%[7]	33.2%[7]	9.4%[9]	41.4%[9]	NR	NR	12.0%[13]	22.6%[13]
Without BM at baseline	1.0%[8]	17.8%[8]	4.6%[10]	31.5%[10]	4.2%[12]	23.9%[12]	NR	NR
With BM at baseline	7.4%[8]	72.3%[8]	16.0%[10]	58.3%[10]	NR	NR	NR	NR
24-month								
ITT population	5.0%[8]	45.0%[8]	NR	NR	NR	NR	NR	NR
Without BM at baseline	1.1%[8]	28.8%[8]	7.20%[11]	45.3%[11]	NR	NR	NR	NR
With BM at baseline	18.0%[8]	91.00%[8]	NR	NR	NR	NR	NR	NR
36-month / 48-month								
ITT population	7.8%[14]	72.7%[14]	NR	NR	NR	NR	NR	NR
Without BM at baseline	4.7%[14]	63.6%[14]	NR	NR	NR	NR	NR	NR

Table 2 : Cumulative incidence of progression of BM in Asian group

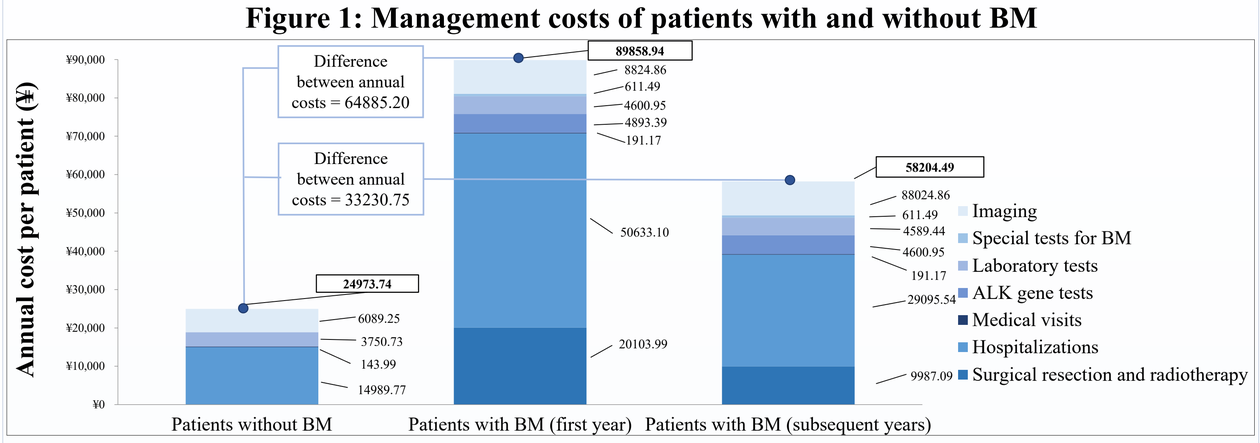
	CROWN trial		J-ALEX/ALESIA		eXalt3 trial		ALTA trial	
	Lorlatinib N=65	Crizotinib N=65	Alectinib N=103/125	Crizotinib N=104/62	Ensartinib NR	Crizotinib NR	Brigatinib NR	Crizotinib NR
12-month								
ITT population	0.8%[15]	40.5%[15]	5.9%[16]	16.8%[16]	NR	NR	NR	NR
Without BM at baseline	0%[15]	28.9%[15]	NR	NR	NR	NR	NR	NR
With BM at baseline	0%[15]	68.0%[15]	NR	NR	NR	NR	NR	NR
24-month								
ITT population	1.6%[15]	65.4%[15]	NR	NR	NR	NR	NR	NR
Without BM at baseline	0%[15]	48.9%[15]	NR	NR	NR	NR	NR	NR
With BM at baseline	NR	NR	NR	NR	NR	NR	NR	NR
36-month / 48-month								
ITT population	2.0%[15]	73.1%[15]	11.6%[17]	34.0%[17]	NR	NR	NR	NR
Without BM at baseline	0%[15]	60.9%[15]	9.1%[17]	23.1%[17]	NR	NR	NR	NR

Key: BM, brain metastases; ITT, intention-to-treat; NR, not report.

RESULTS

In the first year after diagnosis, the annual management cost was ￥24,974 per patient-year without BM and ￥89,859 with BM, resulting in cost savings of ￥64,885 (Figure 1). In the subsequent treatment years, the cost savings is ￥33,231. The biggest driver is hospitalization cost.

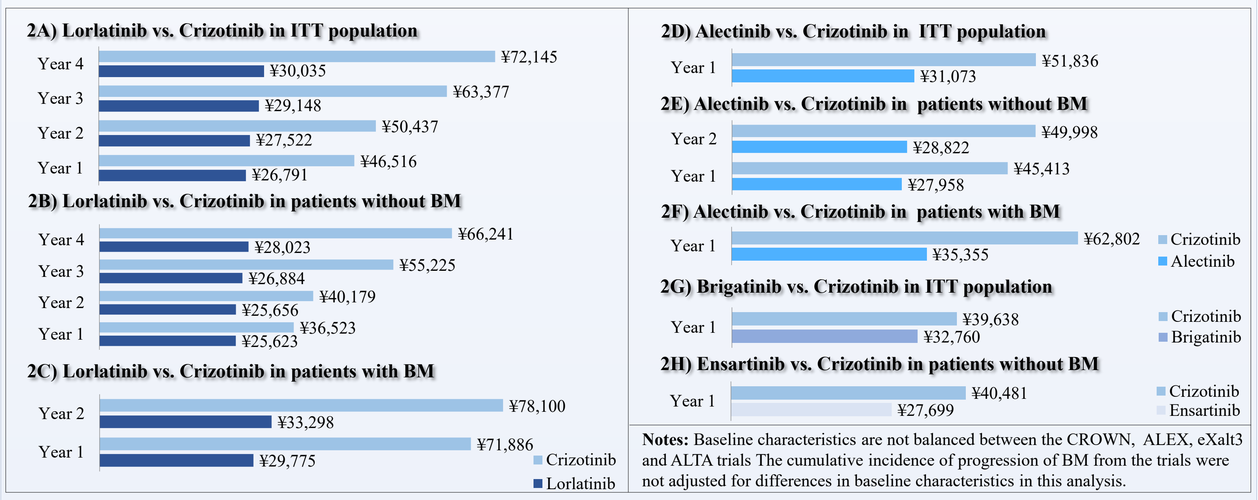
Figure 1: Management costs of patients with and without BM



As shown in Figure 2, applying the 12-month CIR of BM progression in global clinical trials, the annual cost per patient treated with 1L lorlatinib was ￥26,791 vs. ￥46,516 per patient treated with crizotinib in ITT population. When looking at subgroups, it was ￥25,623 per patient treated with lorlatinib in those without BM, and ￥29,775 in those with BM. Compared with crizotinib, the management cost savings increased year by year in the second to fourth year of treatment for patients receiving 1L lorlatinib. Patients without BM had 2.3/4.9/8.3 times increased in cumulative cost savings at 24/36/48 months of loratinib treatment compared to cumulative cost savings at 12 months.

In year 1, the annual management cost per patient treated with alectinib was ￥31,073, and was ￥32,760 per patient treated with brigatinib in the ITT population. The annual management cost per patient in those without BM was ￥27,958 in alectinib treated patients, and ￥27,699 in ensartinib treated patients in year 1. No data on CIR of BM progression beyond 12 months were available for brigatinib and ensartinib (Figure 2).

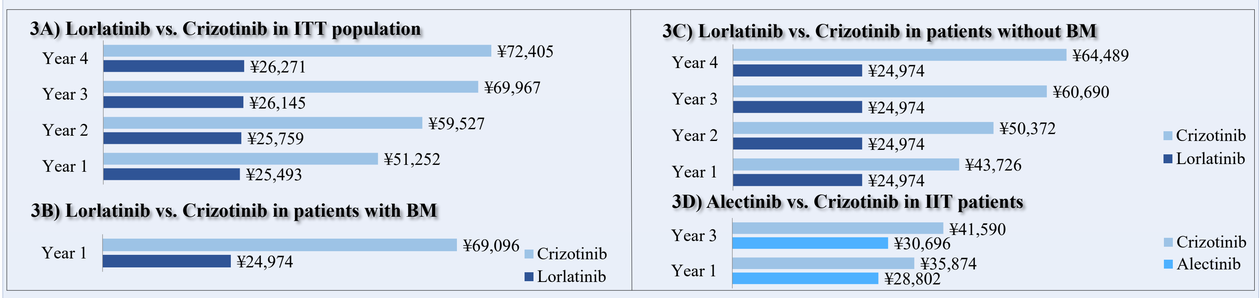
Figure 2: Management costs of patients with 1L ALK-TKIs based on global clinical trials (per patient per year)



Notes: Baseline characteristics are not balanced between the CROWN, ALEX, eXalt3 and ALTA trials The cumulative incidence of progression of BM from the trials were not adjusted for differences in baseline characteristics in this analysis.

As shown in Figure 3, using the CIR of BM progression in the Asian group yielded similar results compared with the global clinical trials. Lorlatinib and alectinib reduce management costs compared with crizotinib. No data on CIR of BM progression in the Asian group were available for brigatinib and ensartinib.

Figure 3: Management costs of patients receiving 1L ALK-TKIs based on Asian group (per patient per year)



CONCLUSIONS

Due to the lower CIR of BM progression with lorlatinib, significant savings in annual BM management costs were observed from year 1 to 4 in patients who received first-line lorlatinib in China, and are biggest in patients without BM, consistent with the known BM protective effect of lorlatinib.

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