

Supplementary Material

Pharmacoeconomic analysis of Brigatinib versus Alectinib in First-Line Treatment of Anaplastic Lymphoma Kinase-Positive Advanced Non-small-cell Lung Cancer in China

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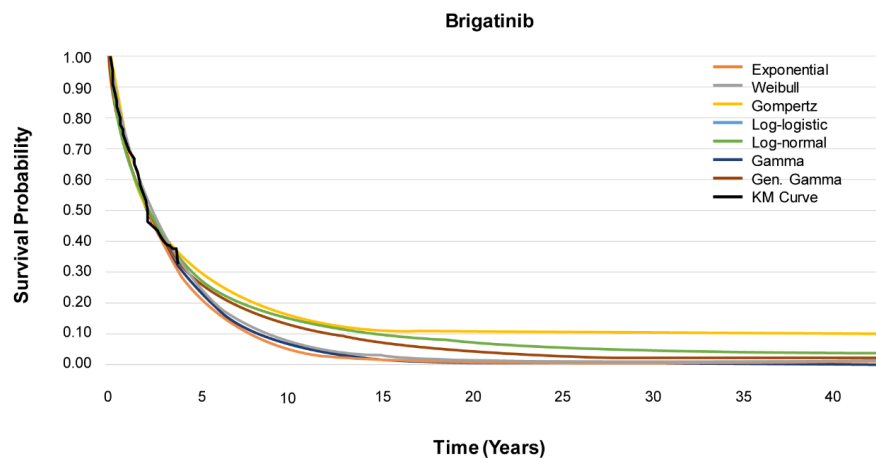
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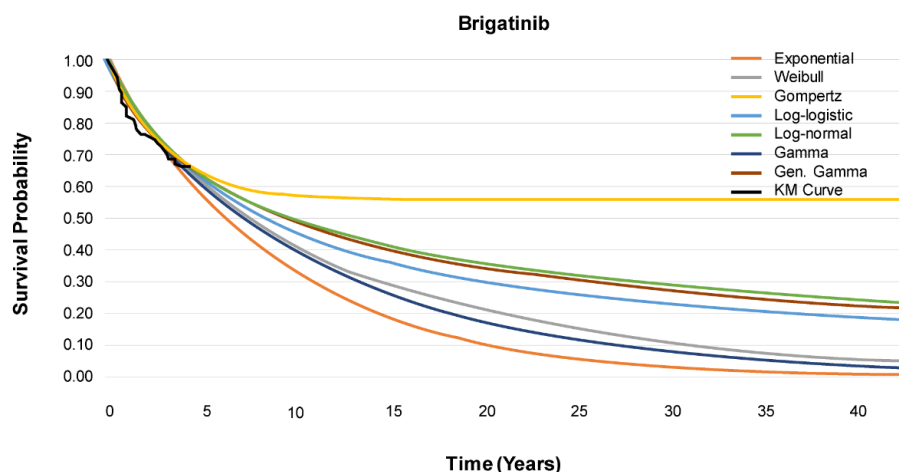
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1. Supplementary Figures



Supplementary Figure 1 Independent review committee assessed progression-free survival of brigatinib in the ALTA-1L trial



Supplementary Figure 2 Independent review Committee assessed overall survival of brigatinib in the ALTA-1L trial

Supplementary Table 1 Consulted clinical experts

Province	Title
Shandong	Chief physician
Shanxi	Chief physician
Beijing	Chief physician
Beijing	Associate chief physician
Beijing	Associate chief physician
Chongqing	Chief physician
Shanghai	Associate chief physician
Shanghai	Attending physician
Hubei	Associate chief physician
Guangdong	Chief physician

Supplementary Table 2 Drug costs

Parameters	Brigatinib		Alectinib	Sources
Dosage	90 mg q.d. (first week)	180 mg q.d. (second week onwards)	600 mg b.i.d.	[1,2]
First cycle cost (USD)	192.54	981.93	1696.53	[3] Calculated
Subsequent cycle cost (USD)	-	1309.24	1696.53	

q.d.: once a day; b.i.d: twice a day; Cycle length: 28 days/4 weeks

Supplementary Table 3 Cost of medical and health resources for patients with NSCLC

Item	Unit Cost (USD)	Sources
Medical oncology outpatient registration fee	5.38	Average value from Clinical Expert Opinion
Laboratory tests (full blood tests, etc.)	78.21	
Imaging examination	106.21	
PET-CT examination	1105.52	
ECG	4.00	

Supplementary Table 4 Utilization of health resources before progression

In the first cycle*					Sources
	Item	Frequency/month	Patient ratio[#]	USD/month	
Clinic	Medical oncology clinic	0.70	100%	3.77	Average value from Clinical Expert Opinion
Inspection	Laboratory tests (whole blood cells, etc.)	0.50	100%	39.10	
	PET-CT	1.00	80%	884.41	
				Cost per month	927.28
				Cost per cycle	853.02
During the follow-up period					
	Item	Frequency/month	Patient ratio	USD/month	
Clinic	Medical oncology clinic	0.70	100%	3.77	Average value from Clinical Expert Opinion
	Laboratory tests (whole blood cells, etc.)	0.40	100%	31.28	
Inspection	Imaging examinations (MRI, CT, X-ray)	0.40	100%	42.48	
	Electrocardiograms	0.35	100%	1.40	
				Cost per month	78.93
				Cost per cycle	72.61

* The cost of the first cycle includes the PET-CT examination at the own expense of some patients

The proportion of patients undergoing the item

Per month: 30.5 days; Cycle length : 28 days/4 weeks

Supplementary Table 5 Utilization of health resources after progression

	Item	Frequency/month	Patient ratio [#]	USD/month	Sources
Clinic	Medical oncology clinic	1.00	100%	5.38	Average value from Clinical Expert Opinion
	Laboratory tests (whole blood cells, etc.)	0.50	100%	39.10	
Inspection	Imaging examinations	0.50	100%	53.10	
	Electrocardiograms	0.50	100%	2.00	
				Cost per month	
				Cost per cycle	
				99.59	
				91.61	

Per month: 30.5 days; Cycle length : 28 days/4 weeks

Supplementary Table 6 Adverse events treatment cost

	Cost per event (USD)	Sources
Adverse reactions		
Skin adverse reactions such as rash and itching	14.14	Average value from Clinical Expert Opinion
Gastrointestinal adverse reactions such as diarrhea, nausea, vomiting, abdominal pain, and constipation	16.03	

Fatigue, edema and other systemic damage	22.53
Hepatobiliary damage such as elevated transaminases	59.34
Anemia	77.79
Kidney damage such as elevated serum creatinine	61.30
Pneumonia and other respiratory damage	126.59
Q-T prolongation and bradycardia	40.92
Hypertension	50.62
Musculoskeletal disorders such as myalgia	14.25
High blood sugar	28.74
Hypercholesterolemia	45.24
Hypophosphatemia	17.01
Elevated blood creatine kinase	30.65
Elevated amylase and lipase	71.72
Lymphocytes, neutropenia	120.97
Visual impairment	27.13

Supplementary Table 7 Subsequent treatment after progression

Parameters	Lorlatinib	Sources
Dosage	100 mg q.d.	[4]
Cycle cost (USD)	1672.39	[3] Calculated

Supplementary Table 8 Parameters changes in the one-way sensitivity analysis

Parameter	Base-case value	Changes	Sources
Brigatinib cycle cost (USD)	1309.24	± 20% of the base-case value	Assumption
Alectinib cycle cost (USD)	1696.53	± 20% of the base-case value	
Utilization of health resources before progression -first cycle (USD)	853.02	± 20% of the base-case value	
Utilization of health resources before progression - follow-up (USD)/cycle	72.61	± 20% of the base-case value	
Health resource utilization cost after progression (USD)/cycle	91.61	± 20% of the base-case value	
Concomitant treatment cost of brigatinib(USD)/cycle	20.97	± 20% of the base-case value	
Concomitant treatment cost of alectinib(USD)/cycle	20.97	± 20% of the base-case value	
Treatment cost after progression of brigatinib (USD)/cycle	1672.39	± 20% of the base-case value	
Treatment cost after progression of alectinib (USD)/cycle	1672.39	± 20% of the base-case value	
Adverse events (AEs) cost of brigatinib(USD)/cycle	2.73	± 20% of the base-case value	
Adverse events (AEs) cost of alectinib (USD)/cycle	0.77	± 20% of the base-case value	
Hospice cost (USD)	1801.33	± 20% of the base-case value	

Supplementary Table 9 Scenario analyses – cost-effectiveness vs. alectinib

	PFS-HR	OS-HR	ΔQALY	ΔCOST	ICER
CEA scenarios					
Anchored MAIC_IRC_PFS, Anchored MAIC_OS, RPSFTM, re-censoring, treatment crossover adjustments	0.98(0.62, 1.54)	0.911(0.501, 1.656)	0.29	-\$12,792	Brigatinib is dominant
Anchored MAIC_IRC_PFS, Anchored MAIC_OS, RPSFTM, without re-censoring, treatment crossover adjustments	0.98(0.62, 1.54)	0.985(0.559, 1.734)	0.05	-\$13,042	Brigatinib is dominant
Anchored MAIC_IRC_PFS, Anchored MAIC_OS, without treatment crossover adjustments	0.98(0.62, 1.54)	1.11(0.63, 1.96)	-0.32	-\$13,442	41,430*#
Anchored MAIC_IRC_PFS, Unanchored MAIC_OS, without treatment crossover adjustments	0.98(0.62, 1.54)	0.90(0.59, 1.38)	0.32	-\$12,754	Brigatinib is dominant
Anchored MAIC_IRC_PFS, Bucher_OS, without treatment crossover adjustments	0.98(0.62, 1.54)	1.20(0.69, 2.11)	-0.57	-\$13,714	23,937*
Unanchored MAIC_IRC_PFS, Anchored MAIC_OS, RPSFTM, re-censoring, treatment crossover adjustments	0.95(0.67, 1.35)	0.911(0.501, 1.656)	0.29	-\$11,220	Brigatinib is dominant
Unanchored MAIC_IRC_PFS, Anchored MAIC_OS, RPSFTM, without re-censoring, treatment crossover adjustments	0.95(0.67, 1.35)	0.985(0.559, 1.734)	0.05	-\$11,469	Brigatinib is dominant
Unanchored MAIC_IRC_PFS, Anchored MAIC_OS, without treatment crossover adjustments	0.95(0.67, 1.35)	1.11(0.63, 1.96)	-0.32	-\$11,868	37,305*#
Unanchored MAIC_IRC_PFS, Unanchored MAIC_OS, without treatment crossover adjustments	0.95(0.67, 1.35)	0.90(0.59, 1.38)	0.33	-\$11,182	Brigatinib is dominant
Unanchored MAIC_IRC_PFS, Bucher_OS, without treatment crossover adjustments	0.95(0.67, 1.35)	1.20(0.69, 2.11)	-0.57	-\$12,139	21,425*

Bucher_IRC_PFS, Anchored MAIC_OS, RPSFTM, re-censoring, treatment crossover adjustments	0.96(0.61, 1.52)	0.911(0.501, 1.656)	0.29	-\$11,745	Brigatinib is dominant
Bucher_IRC_PFS, Anchored MAIC_OS, RPSFTM, without re-censoring, treatment crossover adjustments	0.96(0.61, 1.52)	0.985(0.559, 1.734)	0.05	-\$11,994	Brigatinib is dominant
Bucher_IRC_PFS, Anchored MAIC_OS, without treatment crossover adjustments	0.96(0.61, 1.52)	1.11(0.63, 1.96)	-0.32	-\$12,394	38,702*#
Bucher_IRC_PFS, Unanchored MAIC_OS, without treatment crossover adjustments	0.96(0.61, 1.52)	0.90(0.59, 1.38)	0.33	-\$11,707	Brigatinib is dominant
Bucher_IRC_PFS, Bucher_OS, without treatment crossover adjustments	0.96(0.61, 1.52)	1.20(0.69, 2.11)	-0.57	-\$12,666	22,271*

* ICER of alectinib vs. brigatinib because brigatinib resulted in less QALYs but was cheaper in these scenarios.

Alectinib would not be cost-effective vs. brigatinib under the willing-to-pay threshold (\$36,976, equivalent to three times the per capita gross domestic product of China in 2023)

Abbreviations: CEA= Cost-Effectiveness Analysis; MAIC= Matching-Adjusted Indirect Comparison; PFS= Progression-free survival; OS= Overall Survival; HR= Hazard ratio; IRC= independent review committee; RPSFTM= rank-preserving structural failure time models; QAIY= Quality-Adjusted Life Year; ICER= Incremental Cost-Effectiveness Ratio

References

1. Brigatinib Tablets Instructions [Internet]. Global Drug Database of YAOZH; 2022 [cited 2023 Dec 12]. Available from: <https://zy.yaozh.com/instruct/sms20230927/lxy202308032.pdf>
2. Alectinib Hydrochloride Capsules Instructions [Internet]. Global Drug Database of YAOZH; 2022 [cited 2023 Dec 12]. Available from: <https://zy.yaozh.com/instruct/sms20221219/xy202211021441.pdf>
3. <https://www.yaozh.com/>
4. <https://labeling.pfizer.com/ShowLabeling.aspx?id=17117>