

Cost-Effectiveness of Venetoclax in Combination with Azacitidine in Unfit Patients with Previously Untreated Acute Myeloid Leukemia in China

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INTRODUCTION

- Acute myeloid leukemia (AML) is an aggressive and fast-growing hematological cancer with a five-year survival rate of approximately 30% [1], of which half of the patients are ineligible for intensive chemotherapy (unfit AML) and have an even lower five-year survival rate of only about 5% [2,3].
- Unfit AML patients are generally offered lower-intensity regimens; however, the efficacy is unsatisfactory. These patients remain afflicted with the disease. Patients are at high risks of infection, dependent on blood transfusions and ICU care, leading to heavy disease burden [2].
- Venetoclax, the first oral BCL-2 inhibitor, has demonstrated significant clinical efficacy and substantially improved patient quality of life, and was recommended by Chinese and international guidelines to treat unfit AML patients [4,5].

OBJECTIVES

The objective of the study was to assess the cost-effectiveness of venetoclax in combination with azacitidine (Ven+AZA) versus azacitidine (AZA) for patients newly diagnosed with unfit AML, from the healthcare perspective in China.

METHODS

- A three-state partitioned survival model (event-free survival (EFS), progressive/relapsed, and death) which is a typical approach in modelling of oncology therapies, was developed. Especially, composite complete remission(CR/CRi) was further introduced as a substate of EFS to better reflect the clinical reality. (Figure 1)
- Based on findings from real-world studies and guidelines of AML in China, the baseline age was set at 60 years old [2, 5]. Considering the life expectancy of Chinese population[6], a 15-year time horizon was used to balance the long-term uncertainty of model stimulation and capture most disease progression.
- Clinical inputs of CR/CRi rate, EFS curves and OS curves were derived from VIALE-A trial Asian subgroup (N=93) to better represent the efficacy in Chinese population. VIALE-A is a multicenter and randomized double-blind pivotal phase 3 trial to compare the efficacy and safety of VEN+AZA and AZA.
 - CR/CRi rate: Ven+AZA 70.49% vs. AZA 28.13%
 - EFS and OS curves: Reconstructed the individual patient-level data and fitted to 6 parametric distributions. The curve that exhibited the best fit per AIC, BIC and visual inspection was selected for use in the model. Exponential distributions were ultimately chosen for EFS and OS curves for both group. (Figure 2)
- Cost inputs involved direct medical costs including the costs of drug and administration, healthcare resource utilization, palliative care and adverse event management. Cost inputs were informed by public prices and literature review. Dose intensity and length of taking drugs were from VIALE-A trial Asian subgroup to correspond to the efficacy data. (Table 1)

- Utility values in the model were dependent on health state and derived from EQ-5D-5L data in VIALE-A using Chinese tariff. AE disutility were obtained from literature. (Table 1)
- Uncertainty analyses were performed, including one-way sensitivity analysis(OWSA), probabilistic sensitivity analysis(PSA) and scenario analysis under different time horizons.

Figure 1 Model structure

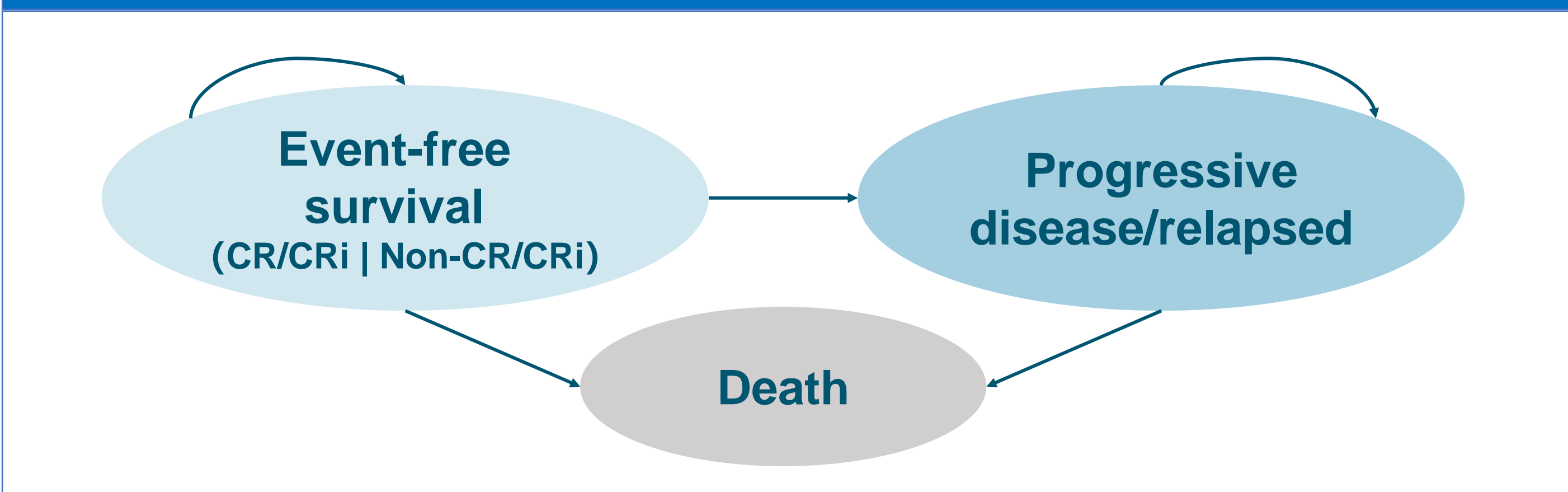


Figure 2 Parametric survival curves

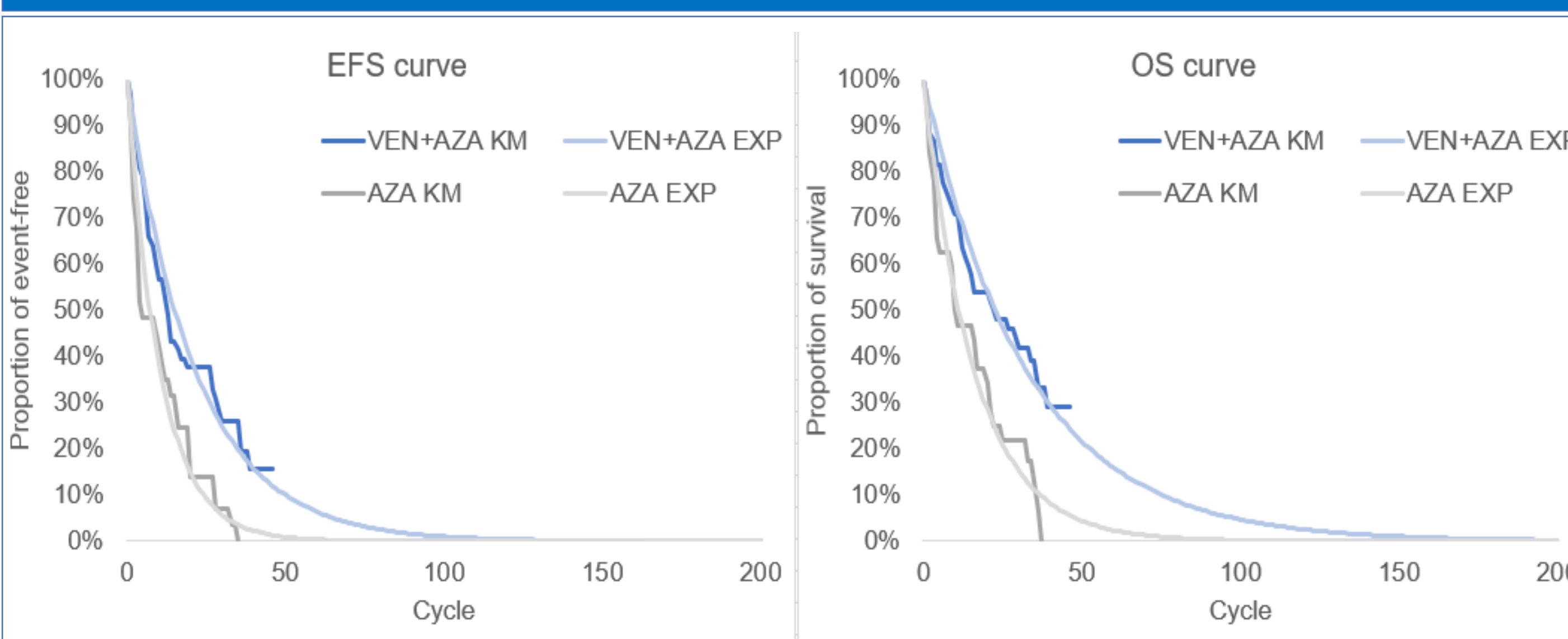


Table 1 Key model inputs (V: VEN+AZA group, A: AZA group)

Drug costs		Price	Dose intensity	DoT	Source
Venetoclax		¥ 117.5 /100mg	66.3%	6 cycles	Public price, VIALE-A Asian group data [7]
Azacitidine		¥ 346 /100mg	V: 97.6% A: 99.5%	V: 6 cycles A: 2.5 cycles	
HRU costs	Group	EFS (CR/CRi)	EFS (Non-CR/CRi)	PD/RL	Source
Lab/radiological test	V	¥1,977	¥2,426	¥2,637	Public price, literature review [2,8,9]
	A	¥2,019	¥2,426	¥2,637	
Outpatient/hospitalization	V	¥583	¥1,024	¥1,654	
	A	¥804	¥1,181	¥1,929	
Red blood transfusion	V	¥66	¥345	¥1,325	
	A	¥265	¥596	¥1,723	
Platelet transfusion	V	¥158	¥824	¥ 3,168	
	A	¥634	¥1,426	¥6,020	
Anti-infective	V	¥1,547	¥4,642	¥15,475	
	A	¥3,095	¥12,380	¥20,117	
ICU care	V	/	/	¥2,056	
	A	/	/	¥3,271	
Utility		0.798	0.786	0.737	VIALE-A data [7]

RESULTS

Base case results

- Over a 15-year horizon, Ven+AZA resulted in 1.7 QALYs gained compared to AZA, which was driven by its improved CR/CRi and survival in Asian population (even numerically superior to the ones in overall population). Meanwhile, Ven+AZA could notably save the costs of blood transfusions, anti-infective therapy, ICU care and palliative care. The ICER result was 20,564 CNY/QALY, which is only a quarter of the willingness-to-pay threshold of 1 times GDP per capita in China in 2023 (89,358 CNY). (Table 2, 3)

Table 2 Base case results

Results	Ven+AZA	AZA	Incremental
Total costs (CNY)	¥ 439,799	¥ 404,896	¥ 34,903
Total QALYs	3.00	1.30	1.70
Total LYs	3.79	1.67	2.12
ICER (CNY/QALY)	/	/	¥ 20,564

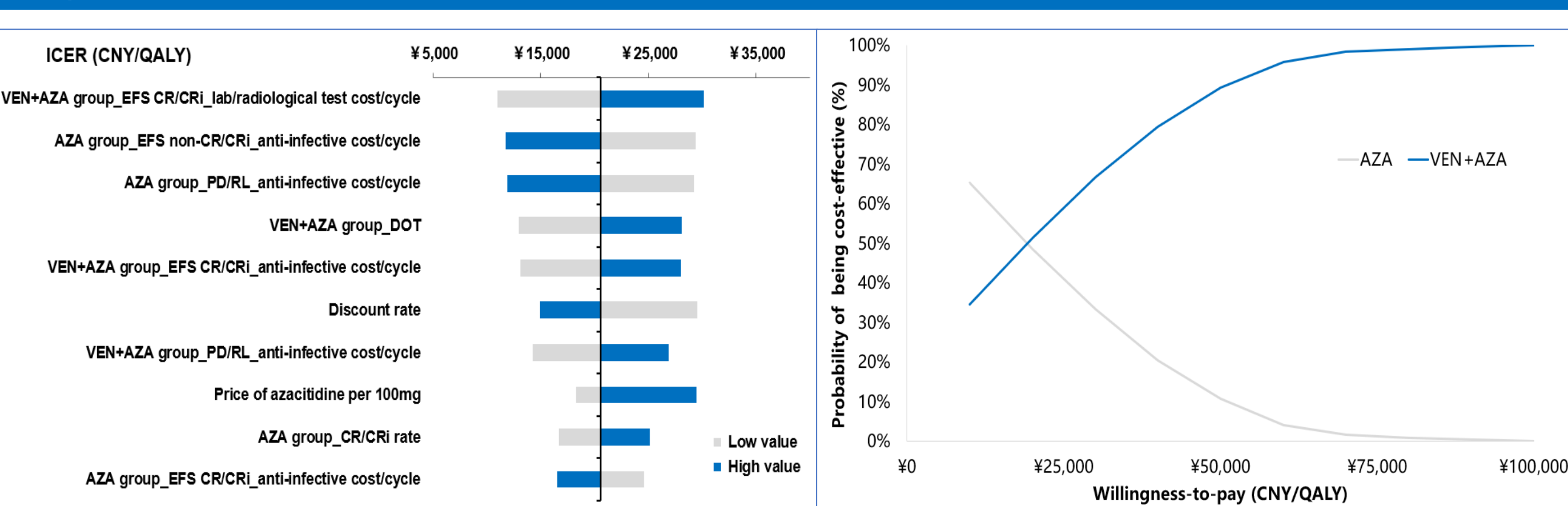
Table 3 Costs by item

Item	Ven+AZA	AZA	Incremental
Drug and administration	¥64,732	¥7,514	¥57,218
HRU costs	¥337,119	¥351,660	¥14,541
Lab/radiological test	¥110,472	¥56,988	¥53,484
Blood transfusion (red blood, platelet)	¥32,588	¥55,676	¥23,089
Outpatient/hospitalization	¥35,388	¥24,775	¥10,613
Anti-infective	¥150,903	¥200,462	¥49,560
ICU care	¥7,769	¥13,758	¥5,989
AE costs	¥3,818	¥2,743	¥1,075
Palliative care	¥34,130	¥42,979	¥8,849

Uncertainty analyses results

- OWSA shown that costs of lab/radiological test in EFS (CR/CRi) in Ven+AZA group, anti-infective costs in EFS (non-CR/CRi) in AZA group, etc., had the greatest impact of the result. (Figure 3)
- PSA demonstrated the robustness of the results, with 83% of simulations confirming the cost-effectiveness of Ven+AZA at 0.5 times GDP per capita in China in 2023 and almost 100% cost-effectiveness at 1 times GDP per capita. (Figure 3)
- From 5 years to lifetime, ICER ranged from dominant to 29,264 CNY, suggesting that VEN+AZA had a favorable economic profile.

Figure 3 Results of sensitivity analyses



CONCLUSIONS

The study suggests that venetoclax in combination with azacitidine is a cost-effective regimen for newly diagnosed unfit AML patients in China.

Reference
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Disclosure
Yuxia Wu, He Xu, Xinran Zhao, Guanqi Hong, Jun Liu are current employees of IQVIA, which received funds from AbbVie Inc. Yang Yi is a postdoctoral fellow at School of Public Health, Fudan University and was responsible for directing this study. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in of financial conflict with the subject.