Cost-Effectiveness Analysis of Acalabrutinib for Patients with Relapse and Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma

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BACKGROUND

- Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL) are characterized by distinct immunophenotype and represent clonal proliferative tumors of mature B lymphocytes.
- Most CLL/SLL cases are challenging to cure, with 30% to 40% of patients experiencing disease progression or relapse within 1 year.
- Acalabrutinib is a second-generation bruton tyrosine kinase (BTK) inhibitor that offers greater target inhibition and fewer side effects.
- In the ASCEND trial, acalabrutinib monotherapy demonstrated a sustained survival benefit compared to rituximab plus Idelalisib (IdR) or bendamustine (BR).

OBJECTIVE

- The aim of the study is to evaluate the cost-effectiveness of acalabrutinib compared to zanubrutinib for R/R CLL/SLL patients from the perspective of Chinese healthcare system.

METHODS

- In this study, a cost-effectiveness analysis method was used to simulate the medical costs and health outcomes of patients with R/R CLL/SLL treated with acalabrutinib and zanubrutinib regimen based on the partitioned survival model.

Study population

- The target population of this study was previously R/R CLL/SLL patients.
- The baseline characteristics of the simulated patients were derived from a matched adjusted indirect comparison study, which matched the baseline characteristics of the patient populations in the acalabrutinib ASCEND trial and the zanubrutinib ALPINE trial.

Intervention and control groups

- The intervention group was acalabrutinib. The usage and dosage were 100mg twice daily until disease progression or intolerance.
- The control group is zanubrutinib. The usage and dosage were 160mg twice daily until disease progression or intolerance.

Model structure

- A three-state partitioned survival model was performed to simulate R/R CLL/SLL patients, including progression-free survival (PFS), disease progression (PD), and Death.
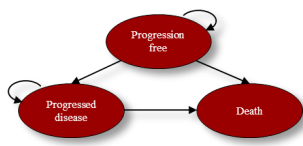

Model settings

- This study was conducted from the perspective of Chinese healthcare system.
- The cycle period was one month (30 days), simulated until the cohort of patients reached 100 years of age, and adjusted using a half-cycle correction.
- Both costs and health outcomes were discounted at a rate of 5%.

Clinical data

- The efficacy data for acalabrutinib were obtained from the ASCEND trial, while data for zanubrutinib were obtained from the ALPINE trial.
- The hazard ratio (HR) of PFS and OS were derived from an existing matching-adjusted indirect comparison (MAIC) study for acalabrutinib and zanubrutinib.

Treatment regimen	PFS		OS	
	HR	SE.	HR	SE.
Acalabrutinib	0.9016	0.17	0.5552	0.19
Zanubrutinib	1.0000	0.01	1.0000	0.01

- Exponential, Weibull, Gompertz, Loglogistic, Lognormal and Generalized Gamma survival distribution formula were used to fit the PFS and OS curve for both patients groups, respectively.
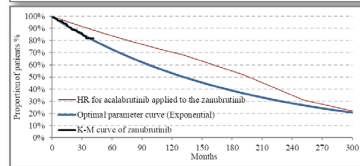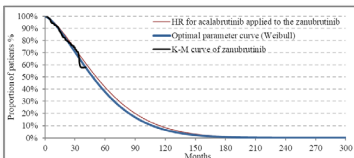
- All common grade 3 or higher adverse events (AEs) in the ASCEND and ALPINE trials were considered.

Costs

- Only direct medical costs were included in the study from the perspective of Chinese healthcare system.
- The direct medical costs considered in this research model primarily encompass first-line treatment costs, second-line treatment costs, follow-up examination costs, adverse event management costs, and end-of-life treatment costs.
- The cost data for all drugs and medical resource utilizations were obtained from the average provincial and municipal bid prices and clinical expert surveys.

Utility values

- This study utilized health-related quality of life data collected from participants in the ASCEND trial, measured using the EuroQol five dimension scale (EQ-5D) scale.
- After processing the individual data of the patient population, the utility values for PFS and PD status were 0.808 and 0.791, respectively.
- The disutility values associated with AEs were derived from published literature.

Health state	Utility value	SE.
PFS	0.808	0.012
PD	0.791	0.026

| Adverse events	Disutility value
Atrial fibrillation	-0.470
Hypertension	-0.131
Hemorrhage	-0.020

RESULTS

- The base-case analysis results indicated that the incremental cost-effectiveness ratio (ICER) was 70,807 China Yuan (CNY) per quality-adjusted life year (QALY) gained.

Base-case	Acalabrutinib	Zanubrutinib	incremental	ICER
Total costs	750,365	650,603	149,635	70,807
Total QALYs	8.33	6.93	1.41	

- The one-way sensitivity analysis (OWSA) results indicated the most significantly parameters influencing the ICER were the HR of PFS, the price of acalabrutinib and the price of zanubrutinib.
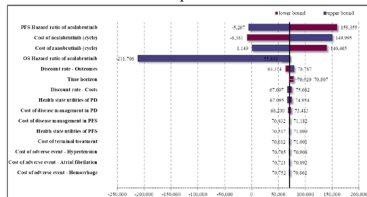
- The probabilistic sensitivity analysis (PSA) results indicated the proportion of acalabrutinib being the more cost-effective strategy compared with zanubrutinib was 87.80% when the willingness to pay (WTP) threshold was set at 3 times the gross domestic product (GDP) per capita.
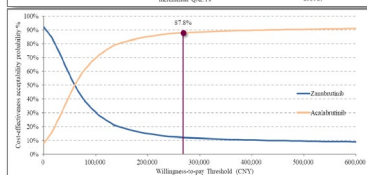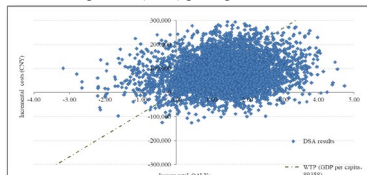
CONCLUSIONS

- Acalabrutinib provides enhanced and precise inhibition of the BTK target, leading to a significant improvement in patient survival outcomes.
- Our study suggests that acalabrutinib is a cost-effective choice compared to zanubrutinib for the treatment of R/R CLL/SLL from the perspective of the Chinese healthcare system.

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