Cost-effectiveness of Maribavir for Post-transplant Refractory (With or Without Resistance) Cytomegalovirus Infection in China

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Background

- Cytomegalovirus (CMV) is a prevalent human herpes virus and poses a significant risk of severe disease, graft rejection, and organ dysfunction in immunocompromised patients, particularly those who have undergone hematopoietic stem cell transplant (HSCT) or solid organ transplants (SOT).[1-3]
- Maribavir (MBV) is an oral antiviral that selectively inhibits the UL97 protein kinase and its substrates, marking it as the first and only approved therapy with this mechanism of action.[4]
- The National Medical Products Administration (NMPA) of China has approved MBV for treating adult patients with post-transplant CMV infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir or foscarnet. .
- Currently, there is insufficient evidence regarding the cost-effectiveness of MBV for treating R/R CMV infection in China following the National Reimbursement Drug List (NRDL) negotiation.

Objective

- To evaluate the cost-effectiveness of MBV compared with investigator-assigned therapy (IAT; valganciclovir/ganciclovir, foscarnet, or cidofovir) for patients in the post-transplant refractory (with or without resistance) CMV infection from the perspective of the Chinese healthcare system.

Methods

Model Design

- This study utilized Microsoft® Excel to develop a decision tree and Markov model (**Figure.1**) to calculate the incremental cost-effectiveness ratio (ICER) of MBV versus IAT in adult patients with refractory CMV infection post-HSCT or SOT

Patient Population

- Patients with R/R CMV infection following HSCT or SOT transplant (starting age: 38.7 for HSCT[5], 41.0 for SOT[6]).

Decision tree model

- The decision tree model allocated patients to MBV or IAT at the primary decision node.
- Patients subsequently proceeded through distinct pathways via chance nodes determined by disease progression patterns. Each pathway was defined by the occurrence of four sequential clinical events: 1) positive CMV viremia detection, 2) progression to CMV disease, 3) complication development, and 4) death.
- Both treatment regimens consisted of 28 mutually exclusive pathways within 1-year time horizon (**Figure.1**).

Markov model

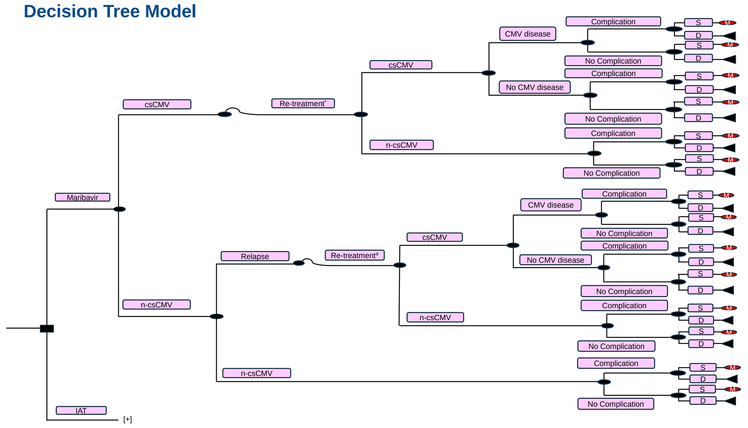
- At the end of the decision tree model, patients achieved two states: a survival state and a death state. Survived patients entered the Markov model, and deceased patients entered the death absorption state.
- Number of patients enrolled in the Markov model between the two regimens were different resulting in different health outcomes and resource consumption.
- The Markov model utilized a 1-year cycle and assumed a lifetime horizon of 50 years (**Figure.1**).

Model assumptions

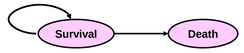
- Patients without viral clearance with MBV or IAT received up to one additional antiviral therapy.
- In the event of treatment failure within the MBV cohort, a subsequent switch to the IAT regimen was assumed.
- In the IAT group, 18.8% of patients were expected to switch to MBV after treatment failure[7], while the remaining 81.2% of patients were expected to continue treatment with the IAT regimen.

Figure.1 Model structure

Decision Tree Model



Markov model



Abbreviations: S: Survival; D: death; csCMV, CMV viremia positive; n-csCMV, CMV viremia negative; IAT, investigator assigned treatment
*Treatment failure with previous regimens required additional therapy; #Patients with CMV recurrence required additional therapy

Parameter inputs

- Results from the SOLSTICE trial informed the foundational characteristics and transition probabilities between csCMV and n-csCMV states[7]. Rates of CMV disease and complications for both CMV-infected and non-CMV-infected conditions were sourced from observational studies. Health state utilities were derived from patients with R/R CMV via a vignette-based time trade-off methodology[8].
- The model included costs for drug acquisition and administration, outpatient and inpatient services, retreatment, adverse event management, complications, terminal care, and disease follow-up. These were compiled from the Yaozhi database, literature, and expert consultations, with MBV's price reflecting the scenario post-negotiation for the NRDL. Costs and outcomes were annually discounted at a rate of 5%.

Base case analysis

- A hypothetical cohort of 1,000 patients was utilized to estimate the average costs and quality-adjusted life years (QALY) for each treatment option. The incremental cost-effectiveness ratio (ICER) was subsequently calculated to assess the cost-effectiveness of MBV, using a willingness-to-pay threshold equivalent to one times the GDP per capita.

Sensitivity analysis

- One-way sensitivity analyses and probabilistic sensitivity analyses assessed the uncertainty of base-case results.

Results

Base case analysis

- MBV increased total costs by **RMB 9,870 (USD 1,385)** and provided an additional **0.277 QALYs** compared to the IAT regimen, resulting in an ICER of **RMB 35,652(USD 5,002)/QALY**. This value remained below the willingness-to-pay threshold (1.0×per capita gross domestic product [GDP] in China), indicating MBV is cost-effective (**Table 1**).

Table 1. Base case results

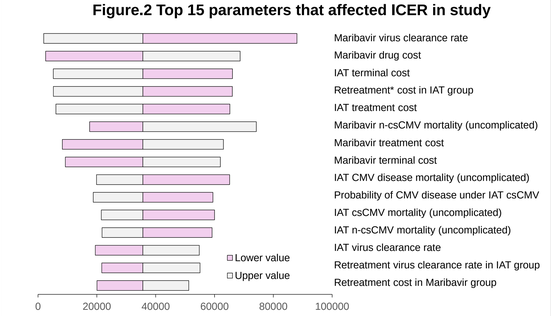
Treatment Options	Total Cost (RMB)	QALYS	Incremental analysis		ICER (RMB/QALY)
			Incremental cost （RMB）	Incremental QALYs	
IAT	359,343	5.401	-	-	
Maribavir	369,213	5.677	9,870	0.277	35,652

Abbreviations: QALYs, quality-adjusted life years; ICER, incremental cost-effectiveness ratio

One-way sensitivity analysis

- One-way sensitivity analysis identified MBV clearance rates, drug costs, and IAT terminal costs as key impact factors of the results as shown in **Figure.2.**

Figure.2 Top 15 parameters that affected ICER in study

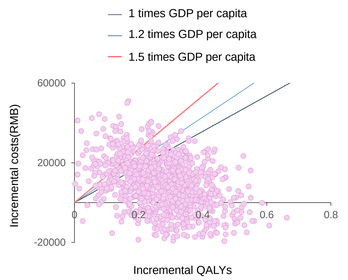


*Retreatment means treatment failure with previous regimens required additional therapy

Probabilistic sensitivity analysis

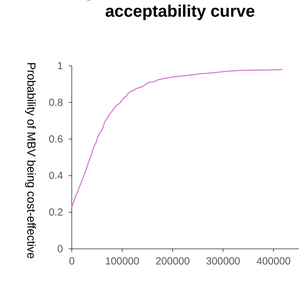
- Probability sensitivity analysis showed that MBV cost-effectiveness probabilities were 78.4%, 83.3%, and 88.1% at willingness-to-pay thresholds of 1, 1.2, and 1.5 times the per capita GDP (RMB 89,358, RMB 107,230, and RMB 134,037), respectively (**Figures 3 and 4**).

Figure.3 Scatter Plot



Abbreviations: QALYs, quality-adjusted life years

Figure. 4 Cost-effectiveness acceptability curve



Conclusion

- Compared to the IAT regimen, the MBV regimen gained 0.277 additional QALYs at an incremental cost of RMB 9,870 (USD 1,385) , resulting in an ICER of RMB 35,652(USD 5,002)/QALY. As this is below one time China's per capita GDP, MBV is a cost-effective treatment option for post-transplant patients with R/R CMV in China, particularly after its inclusion in the NRDL.
- These findings support its use in clinical practice and provide evidence for resource allocation decisions to optimize health outcomes for this patient population.

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Conflicts of interest

- Yanan Sheng is an employee of Takeda (China) International Trading Company and hold the Takeda stock. The remaining authors declare no conflicts of interest.

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This poster is intended for healthcare professionals and health economists .