Cost-effectiveness of long-acting cabotegravir plus long-acting rilpivirine for the treatment of HIV-1 in Taiwan

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Getting ahead of HIV together

Introduction

- Cabotegravir and rilpivirine long-acting (CAB LA + RPV LA) is the first complete long-acting injectable therapy for the treatment of HIV-1. CAB LA + RPV LA has demonstrated non-inferiority to conventional daily oral regimens in virologically suppressed People Living with HIV (PLHIV).
- As directly observed therapy administered every 2 months, it has the potential to address challenges associated with oral therapy including suboptimal adherence.

Objectives

- This study aims to assess the cost-effectiveness of introducing CAB LA + RPV LA for treatment experienced PLHIV in Taiwan who are on a stable antiretroviral regimen, currently virologically suppressed, and who have not shown prior virological failure due to drug resistance to INSTI/INIs.

Methods

- A hybrid decision tree and Markov cohort state transition model was used to evaluate the costs and outcomes associated with CAB LA + RPV LA and a pooled oral comparator including Biktarvy, Triumeq, Juluca, Odefsey and Dovato. Schematics depicting the treatment pathways modelled and the within-treatment-line health states are presented in Figure 1.
- Data from the ATLAS/ATLAS-2M/FLAIR clinical trials were used to inform regimen efficacy. The effectiveness of oral regimens was adjusted to reflect adherence based on a published study.[1] Health states were defined using viral load and CD4+ cell count, with death an absorbing state. 4 therapy lines were included, with discontinuation due to tolerability, virologic or other reasons.
- Cost data was specific to Taiwan, based on a National Health Insurance Research Database costing study, published literature and input from clinical experts.[2] Administration costs of CAB LA + RPV LA reflect the assumption that the injection will be administered by a physician. Oral therapies are associated with a pharmaceutical service fee for general outpatient prescription.
- The analysis accounts for three benefits of CAB LA + RPV LA: adherence benefits (with a 5% difference in adherence based on local data), the potential to further reduce onwards viral transmission, and higher health state utility values (HSUV) versus oral therapy from the post-hoc analysis of trials. The difference in HSUV for CAB+RPV LA versus daily oral is shown in Table 1.

Figure 1. CAB LA + RPV LA model structure: treatment pathway and within therapy health states

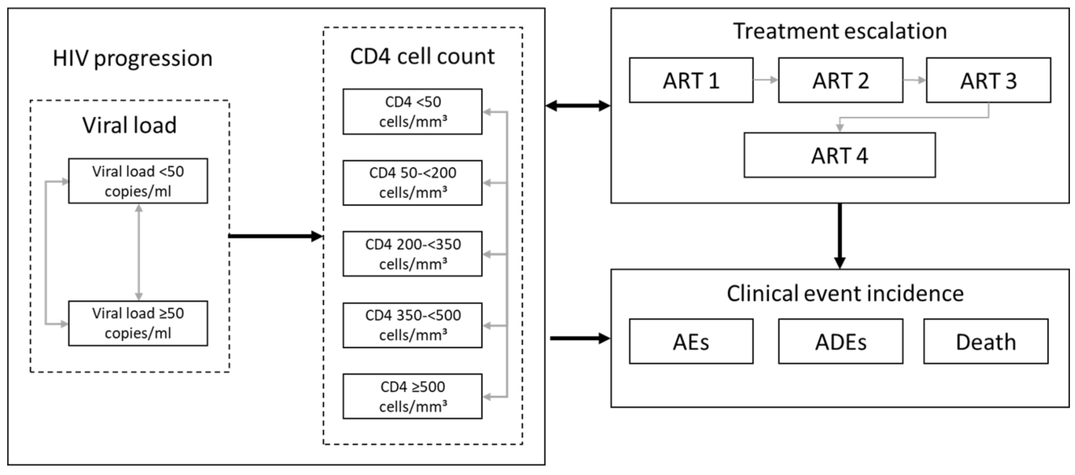


Table 1. Calculated treatment disutility based on ATLAS/ATLAS-2M//FLAIR data

	Treatment	Adjusted Mean (95% CI)	Adjusted Difference (CAB +RPV - Current ART)	P-value (CAB +RPV - Current ART)
Baseline	CAB + RPV (n=556)	0.83 (0.82, 0.84)	0.00 (-0.01 – 0.02)	0.533
	current ART (n=561)	0.83 (0.82, 0.84)		
Week 24	CAB + RPV (n= 535)	0.84 (0.82, 0.85)	0.02 (0.00 – 0.04)	0.024
	current ART (n=546)	0.82 (0.81, 0.83)		
Week 48	CAB + RPV (n=500)	0.84 (0.83, 0.85)	0.02 (0.00 – 0.03)	0.030
	current ART (n=548)	0.82 (0.81, 0.83)		

ART: antiretroviral therapy, CAB: cabotegravir, CI: confidence interval, RPV: rilpivirine

Results

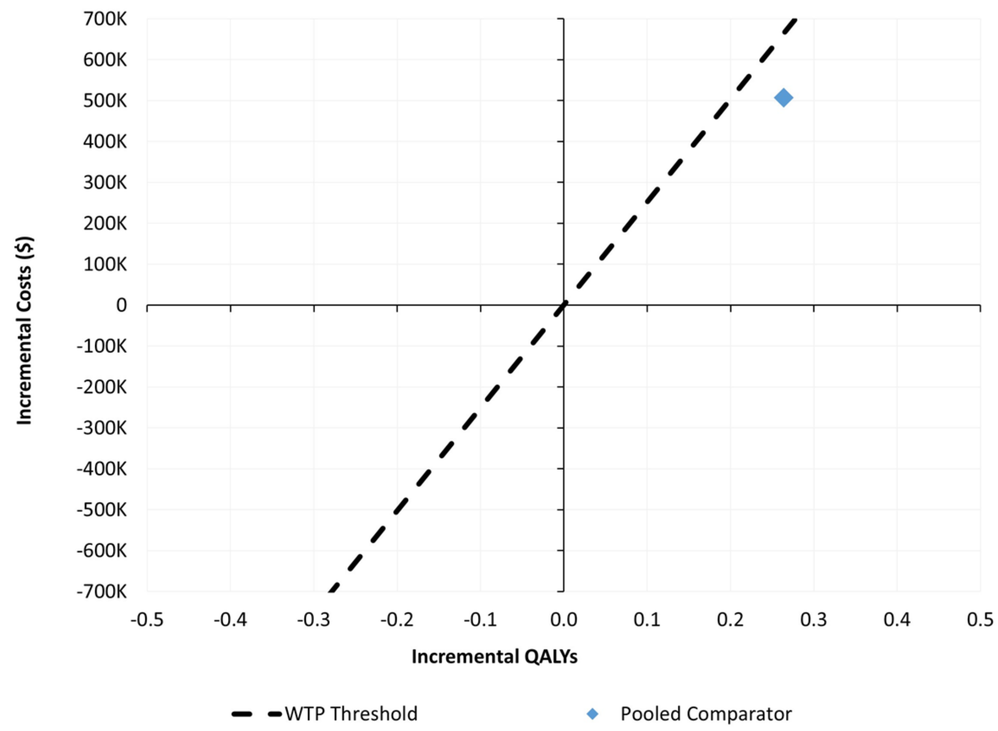
Base case analysis

- The base-case scenario presented here reflects a monthly cost of CAB LA + RPV LA of NT$18,553.00 (per injection cost of NT$37,106.00 in Taiwan) with the analysis conducted from the payer's perspective. Costs and outcomes are discounted at a rate of 3%. The discounted patient-level results under the reference case scenario are shown in Table 2, which presents the total discounted lifetime quality adjusted life years (QALYs), life years (LYs) and costs for CAB LA + RPV LA and the pooled oral comparator. The incremental cost-effectiveness ratio (ICER) gives the additional cost per additional QALY of CAB LA + RPV LA relative to the pooled oral comparator.
- Treatment with CAB LA + RPV LA is associated with a QALY gain of 0.264 versus the oral comparator. CAB LA + RPV LA is also associated with a small increase in costs relative to the pooled oral treatment arm (NT$507,137.71). The ICER of CAB LA + RPV LA was NT$1,920,437.12, which is below the three times GDP WTP threshold of NT$2,515,623.00 in Taiwan. As a result, CAB LA + RPV LA is cost-effective in this analysis (Figure 3).

Table 2. Discounted patient-level cost-effectiveness results

Treatment	Total QALYs	Total LYs	Total Costs	Cost / QALY
CAB LA + RPV LA	12.030	16.266	NT$8,053,375.77	-
Pooled comparator	11.766	16.171	NT$7,546,238.06	
Incremental	0.264	0.094	NT$507,137.71	NT$1,920,437.12

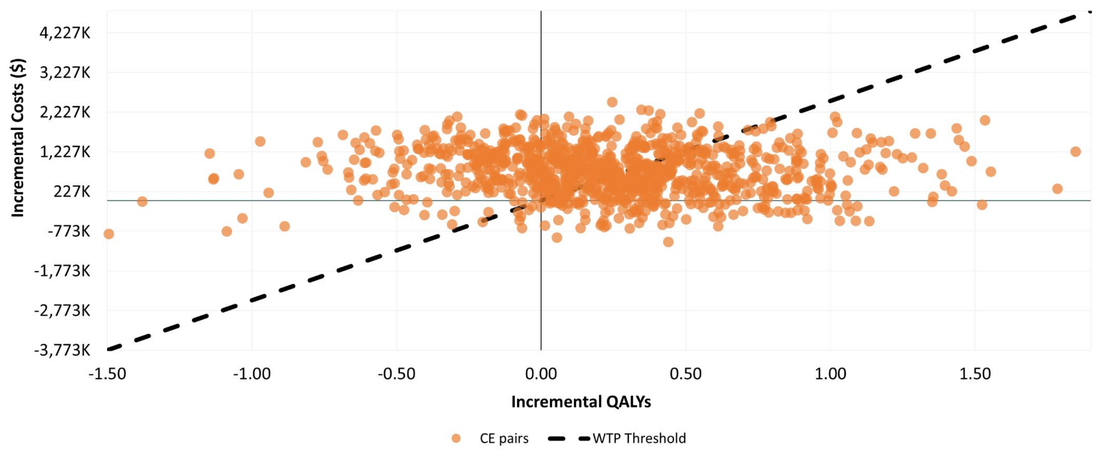
Figure 2. Cost-effectiveness plane for CAB LA + RPV LA versus pooled oral comparator



Deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA)

- Deterministic sensitivity analyses were undertaken to explore how uncertainty in the individual input parameters used in the transmission component of the model influenced the results of the study. For the disease transmission components of the model, DSA indicated that the ICER is most sensitive to the lifetime QALYs expected in those who are newly infected and in the general population, as this determines the implications for population health of onward transmissions. In addition, behavioral parameters in MSM are also influential, as the majority of transmission in the population is in this group. A PSA was used to assess how second-order uncertainty in the model parameters impacts upon the results of the study. The model was run 1,000 times, and each time all parameters associated with a probability distribution are sampled randomly from their respective probability distribution. The results of the 1,000 runs are presented in Figure 3.
- DSA for the cohort of patients treated with CAB LA + RPV LA indicated that treatment adherence and the utility advantage for CAB LA + RPV LA were influential. However, PSA demonstrated that results are robust, with mean incremental QALYs and incremental cost comparable to deterministic analysis for the treated population.
- Crucially, this PSA does not include the disease transmission component of the model and as result outputs are not directly comparable to the base case analysis, however we are able to explore the impact of uncertainty associated with the inputs describing the treated population.

Figure 3. Scatter plot for probabilistic sensitivity analysis of CAB LA + RPV LA versus pooled oral comparator



Conclusion

- The results of this economic analysis suggest that CAB LA + RPV LA is cost-effective in the Taiwanese setting versus a pooled basket of oral comparators. The ICER for treatment with CAB LA + RPV LA compared with the oral comparator was NT$1,920,437.12, which is justifiable at the three times GDP threshold in Taiwan.
- CAB LA + RPV LA can provide an alternative treatment choice for PLHIV, particularly for those who would benefit from, or prefer, treatment in the form of injections administered every 2 months (Q2M) rather than taking daily oral ARTs.

References: 1. Ross EL, Weinstein MC, Schackman BR, et al. The clinical role and cost-effectiveness of long-acting antiretroviral therapy. Clin Infect Dis. 2015;60(7):1102-10.
2. Anderson SJ, Hsu CY, Ou HT, et al. Cost-Effectiveness of Juluca for Human Immunodeficiency Virus Infection Treatment in Virologically Suppressed Adults in Taiwan.

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