Cost-Effectiveness of Cabotegravir (CAB) + Rilpivirine (RPV) Long-Acting (LA) in People Living with HIV (PLHIV) in Austria

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Key Takeaways

- **Cabotegravir + rilpivirine long-acting (CAB + RPV LA), administered by intramuscular injection every 2 months (Q2M) is the first complete LA regimen for HIV maintenance treatment**
- **CAB + RPV LA Q2M is non-inferior to daily oral ART regarding efficacy and tolerability and levels of treatment satisfaction are high [1].**
- **CAB + RPV LA Q2M was demonstrated to generate improved health state utility; elicited through a post-hoc analysis of HRQoL data from ATLAS and FLAIR studies [2].**
- **Current antiretroviral therapy (ART) for people with HIV administered on a daily oral basis remains challenging for some.**
- **In the base case CUA, CAB + RPV LA Q2M was the dominant (less costly, more effective) treatment versus SoC. Results were robust to sensitivity analyses.**
- **CAB+RPV LA Q2M is associated with improvement in QALYs, and lower overall costs compared with SoC and thus could generate savings in the Austrian healthcare system.**

Introduction

Current antiretroviral therapy (ART) has improved health outcomes for people living with HIV (PLHIV) but requires daily oral administration, making adherence to treatment a challenge for some patients. In this regard, Akinwunmi et al. (2021) [3] reported that 65.8% of PLHIV were interested in trying long-acting (LA) therapy and that the majority of patients with unmet need (about 80%-90%) felt that LA therapy would help with the various challenges associated with taking oral ART daily. Vocabria (cabotegravir LA, CAB LA) in combination with Rekambys (rilpivirine LA, RPV LA) (CAB+RPV LA), administered by a healthcare professional via intramuscular (IM) injection every 2 months (Q2M), is the first complete LA regimen for the maintenance treatment of HIV.

Objective

The objective of this analysis was to evaluate the cost-effectiveness of CAB+RPV LA Q2M, prescribed in line with its licence, compared with standard of care (SoC) in Austria.

Methods

A previously published Markov-cohort-state-transition model including a separate viral transmission model [4] was adapted to the Austrian healthcare setting (Table 1). A utility advantage of 0.02 was applied for LA treatment based on a post-hoc analysis of health-related quality of life (HRQoL) data from ATLAS and FLAIR. A reduction in adherence rate of 25.6% was assumed for SoC [5]. Parameters were explored in probabilistic and one-way deterministic sensitivity analyses (PSA & DSA).

Table 1: Further relevant aspects of the methods

Methods	
Type of study	• Cost-effectiveness model (CEM) & cost-utility analysis (CUA)

Type of model	• Deterministic hybrid model using
	  • A decision tree and
	  • A Markov-cohort-state-transition model

Perspective **Time horizon** **Cycle length**	• Austrian healthcare perspective • Lifetime (80 years) • 1 month
Discount rate (annual)	• Cost: 3% • Outcomes: 3%
Population	• PLHIV in Austria • Age: 43 years (mean), gender: 26% female

Intervention (1st line)	• Oral administration („oral lead-in“ phase at least 28 days)
	  • CAB: Vocabria 30mg,once daily [reimbursement price per package (RP/P): 650.90€ (30 tablets)]
	  • RPV: Edurant 25mg, once daily [RP/P: 294.90€ (30 tablets)]
	• Injections IM
	  • Vocabria 600mg, once monthly (for month 2 and month 3) [RP/P: 1,277.15€ (1 vial)]
	  • Rekambys 900mg, once monthly (for month 2 and month 3) [RP/P: 575.95€ (1 vial)]
	  • Vocabria 600mg, once Q2M (starting with month 5 im injection Q2M) [RP/P: 1,277.15€ (1 vial)]
	  • Rekambys 900mg, once Q2M (starting with month 5 im injection Q2M) [RP/P: 575.95€ (1 vial)]

Comparator (1st, 2nd, 3rd line)	• SoC (weighted SoC)
	  • Biktarvy 275mg (~ 29.18%), (emtricitabin, tenofoviralafenamid, bictegravir) [RP/P: 730.15€ (30 tablets)]
	  • Triumeq 950mg (~ 17.55%), (abacavir, lamivudin, dolutegravir) [RP/P: 762.35€ (30 tablets)]
	  • Dovato 350mg (~ 9.94%), (lamivudin, dolutegravir) [RP/P: 682.30€ (30 tablets)]
	  • Odefsey 250mg (~ 13.22%), (emtricitabin, rilpivirine, tenofoviralafenamid) [RP/P: 834.05€ (30 tablets)]
	  • Tivicay 50mg + Descovy 210mg (~ 20.17%), (dolutegravir, emtricitabin, tenofoviralafenamid) Tivicay [RP/P: 588.30€ (30 tablets)] + Descovy [RP/P: 564.95€ (30 tablets)]
	  • Genvoya 510mg (~ 9.94%), (elvitegravir, emtricitabin, cobicistat, tenofoviralafenamid) [RP/P: 930.95€ (30 tablets)]

4th line ARTs	• 4L ART 1
	  • Darunavir Accord 600mg [RP/P: 176.05€ (60 tablets)], Ritonavir Accord 100mg [RP/P: 24.15€ (30 tablets)], Isentress (raltegravir) 400mg [RP/P: 850.55€ (60 tablets)], Intelence (etravirin) 200mg [RP/P: 456.70€ (60 tablets)]
	• 4L ART 2
	  • Darunavir Accord 600mg [RP/P: 176.05€ (60 tablets)], Ritonavir Accord 100mg [RP/P: 24.15€ (30 tablets)], Celsentri (maraviroc) 300mg [RP/P: 880.20€ (60 tablets)], Intelence (etravirin) 200mg [RP/P: 456.70€ (60 tablets)]
	• 4L ART 3
	  • Darunavir Accord 600mg [RP/P: 176.05€ (60 tablets)], Ritonavir Accord 100mg [RP/P: 24.15€ (30 tablets)], Celsentri (maraviroc) 300mg [RP/P: 880.20€ (60 tablets)], Tivicay (dolutegravir) 50mg [RP/P: 588.30€ (30 tablets)]

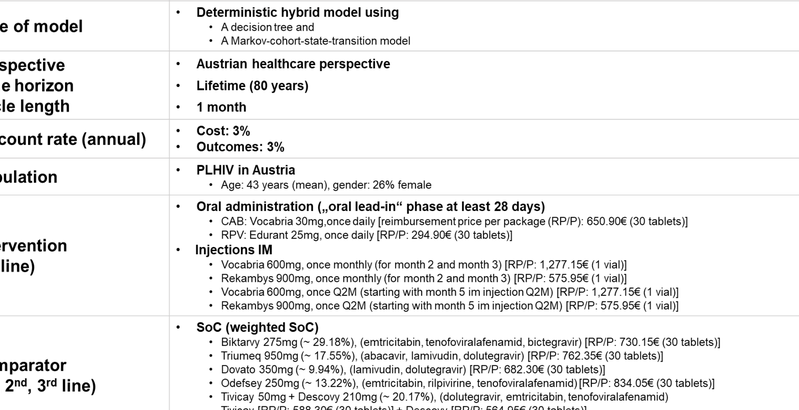
Outcomes	• Life years (LYs); quality-adjusted life-years (QALYs) • Total costs; incremental cost-effectiveness ratio (ICER) & incremental cost-utility ratio (ICUR)

Source: developed by IPF

Model description

- The model includes the health states HIV progression (viral load [VL]), CD4 cell count and death (Figure 1).
- PLHIV are at risk of developing AIDS-defining events (ADEs) and treatment-related adverse events (AEs) (Figure 1).
- The CEM contained a maximum of four ART lines (Figure 1).

Figure 1: Model design



Source: HEOR Ltd. 2021

Clinical Data

- Results of an anchored Bucher's frequentist adjusted indirect treatment comparison (ITC) including pooled ATLAS + FLAIR and ATLAS-2M, comparing CAB+RPV LA with SoC, was used [6].

Resource use and costs

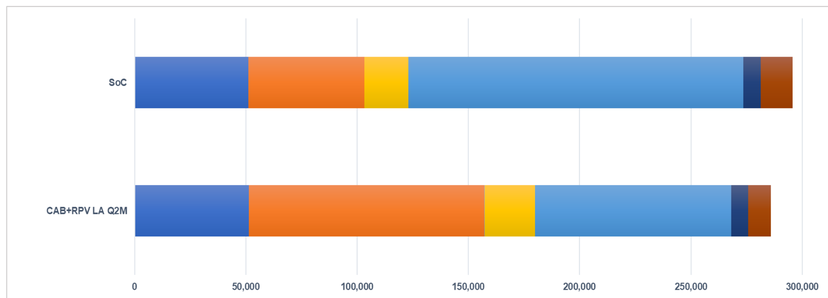
- For all drugs included in table 1, the reimbursement prices were taken from the official Austrian classified index of goods [7].
- Cost parameters: administration & outpatient [8], inpatient & end-of-life (EoL) [9] & AE costs [7, 8, 9].

Results

Costs

Figure 2 depicts the total costs (€) of CAB+RPV LA Q2M and SoC subcategorized according to each cost component. The comparison of CAB+RPV LA Q2M and SoC reveals cost savings for CAB+RPV LA Q2M regarding the cost components "costs of 4L ARTs", "EoL costs" and "additional costs for disease transmission (DTx)". Whereas all other cost parameters are associated with higher costs for CAB+RPV LA Q2M compared with SoC.

Figure 2: Cost components of CAB LA+RPV LA Q2M and SoC



	CAB+RPV LA Q2M	SoC
Health state costs	51,381	51,120
1st line therapy costs	105,726	52,114
1st line admin costs	139	0
Subsequent line costs	22,674	19,857
Adverse Events costs	57	0
Costs of 4L ARTs	88,115	150,531
End of Life costs	7,573	7,718
Additional costs for DTx	10,216	14,366

Source: developed by IPF

Effectiveness of CAB+RPV LA Q2M

Table 2 summarises how the improvement in adherence and utility associated with the administration of CAB+RPV LA Q2M has an impact on clinically relevant outcomes; through:

- patients remaining on CAB+RPV LA for longer, and
- a lower number of HIV transmissions associated with CAB+RPV LA Q2M (Table 2). Subsequently, the QALY loss due to the onward transmission of HIV is also lower compared with SoC.

Furthermore, PLHIV receiving CAB+RPV LA we demonstrated to remain virological suppressed for longer and spent less time virologically unsuppressed, "VL ≥ 50 copies/ml" (Table 2 & Figure 3).

Table 2: Effectiveness of prescribing CAB+RPV LA Q2M

Parameter	CAB+RPV LA Q2M	SoC	Effectiveness of CAB+RPV LA Q2M (Difference)
Administration of ART 1 (in months)	149.15	105.78	43.37
Total QALY lost due to DTx	-0.16	-0.22	0.06
Number of DTx	0.05	0.07	-0.02
VL < 50 copies/ml (in months)	316.37	303.59	12.78
VL ≥ 50 copies/ml (in months)	15.22	20.55	-5.33

ART 1: first line ART of the CEM **Source: IPF calculations**

Cost-effectiveness results

Average lifetime cost per patient in the CAB+RPV LA Q2M group was 285,881€ whilst for those receiving SoC was 295,706€. Prescribing CAB+RPV LA Q2M was associated with 9,825€ cost saving. CAB+RPV LA Q2M generated 13.08 QALYs versus 12.60 QALYs for SoC. Thus, in the base case analysis, CAB+RPV LA Q2M was the dominant treatment (Table 3).

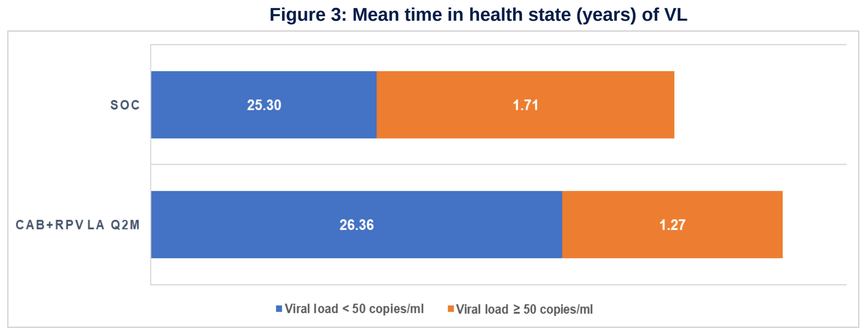
Table 3: CEM and CUA results after DTx

CEM & CUA (base case)			
	CAB+RPV LA Q2M	**SoC**	**Incremental**
Total costs (€) before DTx	**275,664.98**	**281,340.28**	**-5,675.30**
Additional total costs (€) due to DTx	10,215.65	14,365.53	-4,149.88
Total costs (€) after DTx	**285,880.63**	**295,705.81**	**-9,825.19**
Total LYs before DTx	**17.90**	**17.61**	**0.29**
Total LY lost due to DTx	-0.13	-0.18	0.05
Total LYs after DTx	**17.77**	**17.43**	**0.34**
ICER per LY (€) after DTx Δ Total costs / Δ Total LY		**DOMINANT**	
Total QALYs before DTx	**13.24**	**12.83**	**0.41**
Total QALY lost due to DTx	-0.16	-0.22	0.06
Total QALYs after DTx	**13.08**	**12.60**	**0.48**
ICUR per QALY (€) after DTx Δ Total costs / Δ Total QALY		**DOMINANT**	

Source: IPF calculations **DOMINANT: more effective and less costly** **DTx: disease transmission**

The following figure 3 depicts the mean time period spent in years in the different VL defined health states for CAB+RPV LA Q2M versus SoC.

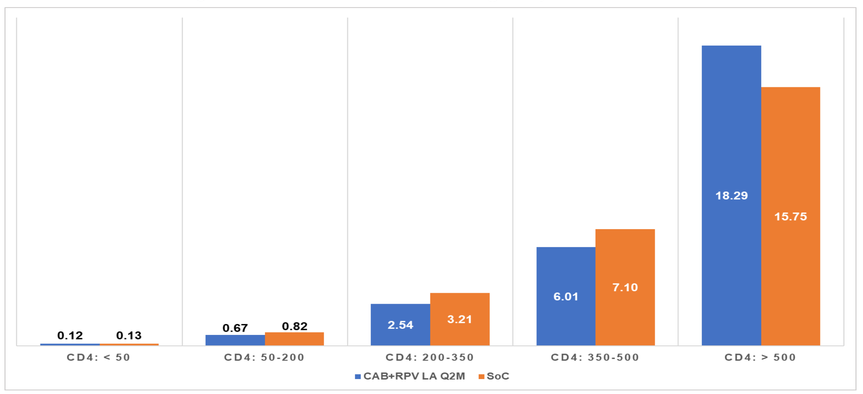
Figure 3: Mean time in health state (years) of VL



Source: developed by IPF

PLHIV treated with CAB+RPV LA Q2M lasted longer in the health state "CD4: > 500" compared with SoC (Figure 4). CD4 cells are associated with the functioning of the immune system regarding the body´s self defenses. The fewer CD4 cells, the more susceptible the body is to certain infections. If there are fewer than 200 CD4 cells, there is a high risk of developing ADEs.

Figure 4: Mean time in health state (years) of CD4 cell count



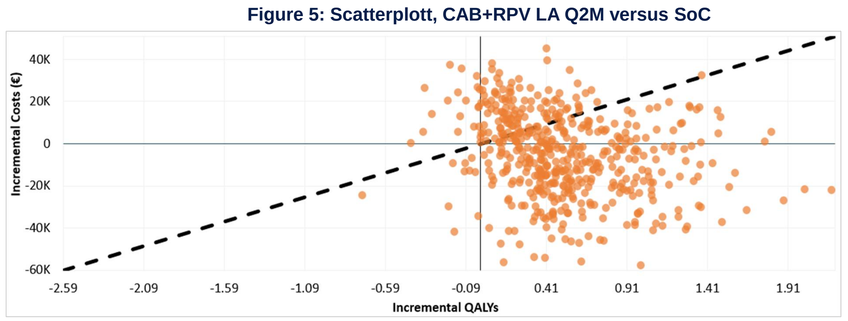
Source: developed by IPF

Sensitivity analyses

PSA and one-way DSA were carried out to examine the robustness of the model. The Monte-Carlo PSA results of 500 second-order simulations plotting incremental costs versus incremental QALYs (Figure 5).

The acceptability curve revealed that in case of a willingness to pay of about 23,000€ (acc. £20,000 NICE threshold) CAB+RPV LA Q2M was a cost-effective strategy versus SoC in around 75% of the simulations.

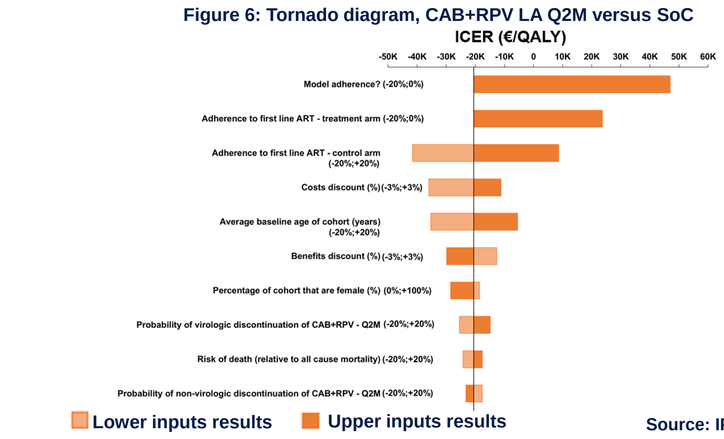
Figure 5: Scatterplott, CAB+RPV LA Q2M versus SoC



Source: IPF calculations

The tornado diagram of the DSA illustrates the effect of variations of CAB LA+RPV LA Q2M versus SoC on base case results. Figure 6 depicts the range of possible ICERs. The highest impact comes from the variations of "model adherence", "adherence to first line ART-treatment arm" and "adherence to first line ART-control arm".

Figure 6: Tornado diagram, CAB+RPV LA Q2M versus SoC



Source: IPF calculations

Strengths & Limitations

A strength of the CEM is the detailed view onto viral DTx by using a separate viral DTx model.

A limitation is that the model does not capture potential utility improvements associated with the various advantages of CAB+RPV LA Q2M, such as freedom from concerns related to daily oral ART.

A further limitation is that the reduction in adherence rate for SoC is based on a publication from 2011 [5]. However, this publication was submitted and approved by NICE (National Institute for Health and Care Excellence) [1].

Since this CEM was conducted in 2021, the reimbursement price for the intervention is now lower. Therefore, the results are anticipated to be even more favorable than what is presented here.

Conclusion

CAB+RPV LA Q2M is associated with improvement in QALYs, and lower overall costs compared with SoC and thus could generate savings in the Austrian healthcare system.

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