Health Technology Assessment of New Long-Acting, Directly-Observed HIV Treatments in Canada: Impact of Real-World Adherence to Daily Oral Therapy on Treatment, Transmission and Cost-Effectiveness

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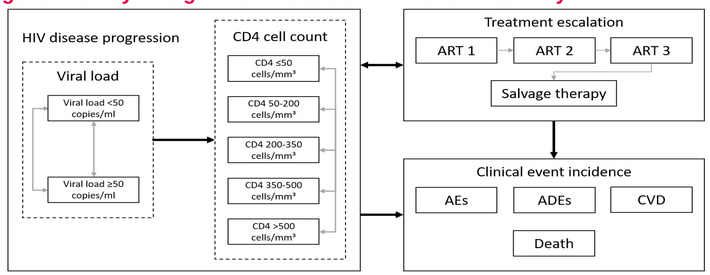
Introduction

- Current antiretroviral therapy (ART) has dramatically improved outcomes for people living with HIV, yet adherence to daily oral ART remains a challenge [1-3]
- Poor ART adherence is a major determinant of poor patient outcomes including virologic failure, HIV drug resistance, disease progression and transmission [4]
- New long-acting (LA) ART administered by health care professionals eliminates the need to adhere to daily oral dosing and may improve clinical outcomes
- In Canada, economic evaluation of health technologies is a required component of health technology assessment, that is used to inform reimbursement decisions
- However, incorporation of adherence into health economic modelling is not yet standard despite its potential impact on patient outcomes and healthcare costs
- **Objective:** To evaluate the cost-effectiveness associated with improved adherence achieved via a novel, directly-observed LA injectable (cabotegravir + rilpivirine; CAB+RPV LA) versus daily oral ART, which is current standard of care (SoC)

Methods

- A published decision-tree and Markov cohort state-transition model was adapted to model the impact of adherence with a scenario analysis testing HIV transmission [5,6]
- The cost-utility analysis was conducted from a public payer perspective in a probabilistic base-case analysis over a lifetime time horizon
- The target population included all adult patients with virologically suppressed HIV-1
- Baseline characteristics, efficacy and safety data were pooled from ATLAS, FLAIR [7,8]
- Health states were defined by therapy line and HIV disease progression (**Figure 1**)
- All treatment costs and costs from fee schedules were reported in 2019 Canadian dollars with Ontario costs used as a proxy for national costs
- The total costs, life-years, and quality-adjusted life-years (QALYs) of CAB+RPV LA and SoC were estimated and compared using the Incremental Cost-Effectiveness Ratio

Figure 1. Study Design: Health States & Treatment Pathway



ART, antiretroviral therapy; CVD, cardiovascular disease; AE, adverse event; ADE, AIDS-defining event.

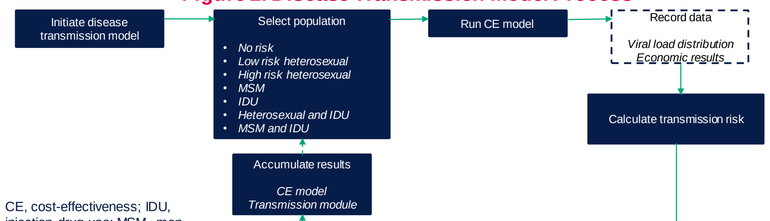
Treatment Adherence

- Viral suppression in the SoC arm was adjusted to reflect published adherence data with reductions derived from Samji et al. [9]
  - 24.4% of patients had ≥1 treatment interruptions over 2.4 years; median=0.8 years to resumption
  - Therefore, 24.4% had 66.7% adherence (1 - 0.8 years / 2.4 years)
- A weighted average adherence rate for the SoC arm was calculated
  - Reduction in adherence to SoC = 100% - [(24.4% x 66.7%) + (75.6% x 100%)] = 8.1%
- With a 91.9% adherence rate, viral suppression in the SoC arm was estimated at 87.8% using efficacy adjustments from Ross et al. [10]
  - Viral suppression = 1.01111*Adherence - 0.05056 = 1.01111*91.88% - 0.05056 = 87.8%
- The model assumed no drug wastage occurred due to suboptimal adherence
- CAB+RPV LA efficacy was not adjusted due to administration being directly-observed

Disease Transmission

- In a scenario analysis, the impact of adherence on onwards HIV transmission was modelled to estimate the number of onwards infections **(Figure 2)**

Figure 2. Disease Transmission Model Process



CE, cost-effectiveness; IDU, injection drug use; MSM, men who have sex with men.

Results

- When modelling sub-optimal adherence of oral ARTs, disaggregated costs indicate that while first line therapy costs are lower in the oral ART, salvage therapy costs are substantially higher compared to the CAB+RPV LA arm (Table 1).
- Lower QALYs were generated when modelling sub-optimal adherence of oral ARTs vs. 100% adherence (Table 2).
- Higher health state costs associated with CAB+RPV LA vs. oral ARTs are explained by greater LYs CAB+RPV LA arm.
- The scenario analysis modeling disease transmission yielded 3 cases of HIV averted per 1,000 patients due to the increased adherence on a LA regime.

References:

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Table 1. Disaggregated Costs for CAB+RPV LA vs. Oral ARTs +/- Adherence

Treatment Arm	Health State	Disaggregated Absolute Costs ($) 1st Line Therapy	1st Line Admin	Subsequent Lines	Salvage Therapy	Other*
Accounting for suboptimal adherence to daily oral dosing – 91.9% Adherence in Oral ART Arm						
CAB+RPV LA	73,060.10	181,301.85	0	36,109.46	291,093.32	65,999.08
Oral ARTs	72,991.15	154,789.08	0	32,616.90	321,214.32	65,672.43
Without accounting for suboptimal adherence to daily oral dosing – 100% Adherence in Oral ART Arm						
CAB+RPV LA	73,303.97	181,301.85	0	57,350.43	287,992.67	68,554.97
Oral ARTs	73,303.62	184,711.06	0	56,877.21	286,755.83	68,396.74

ART: antiretroviral therapy; *Other: adverse events, adverse drug events, cardiovascular disease, renal impairment, societal and death.

Table 2. Total LYs, QALYs, and Costs, CAB+RPV LA vs. Oral ARTs +/- Adherence

Treatment Arm	Total LYs	Total QALYs	Total Costs
Accounting for suboptimal adherence to daily oral dosing – 91.9% Adherence in Oral ART Arm			
CAB+RPV LA	24.357	18.105	$647,563.82
Oral ARTs	24.231	18.003	$647,283.87
Without accounting for suboptimal adherence to daily oral dosing – 100% Adherence in Oral ART Arm			
CAB+RPV LA	24.568	18.247	$668,503.90
Oral ARTs	24.580	18.256	$670,044.46

ART: antiretroviral therapy; LYs: life-years; QALYs: quality-adjusted life-years.

Discussion

- CAB+RPV LA removes the need to adhere to daily dosing and subsequently reduce onward transmission vs oral SoC, leading to QALY gains and improved health outcomes for patients.
- As a result of optimized adherence, model estimates of treatment with CAB+RPV LA demonstrate cost savings vs oral ARTs in the salvage lines of therapy, likely due to more time spent in the (more costly) salvage lines for the oral ART arm.
- Results from modelling sub-optimal adherence of oral ARTs highlighted potential long-term impacts of being non-adherent to HIV regimens, both in costs and in QALYs.
- With Canadian health technology assessment agencies, payers and policy-makers turning to economic evaluation for guidance on reimbursement decisions, the current standard in health economic modelling, excluding considerations of adherence to medication may not appropriately account for true costs to the health care system.
- Particularly in HIV, adherence should be an important consideration in health economic modelling in order to appropriately reflect the real-world costs and outcomes associated with different modes and frequency of administration.

Conclusions

Modeling the cost-effectiveness of oral ARTs in a world where daily dosing is the only treatment option does not require consideration of how adherence could impact outcomes and costs. With the availability of new long-acting HIV regimens, that avoid the daily reminder of HIV, optimized adherence to treatment becomes an important parameter to consider in order to yield more accurate estimates of costs to the healthcare system and outcomes for patients.

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