Cost-effectiveness and Public-Health Impact of Cabotegravir Long-Acting Injectable for HIV Pre-exposure Prophylaxis in Canada

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Adenike R. Adelakun,[1] Michael Dolph,[2] Emily Matthews,[2] Alan Oglesby,[3] Kelly Campbell,[4] Ashley Davis,[5] Janine Xu,[1] Isabelle Hardy,[6] Natalya Danchenko,[7] Sarah-Jane Anderson[7]

[1]GlaxoSmithKline Inc., Mississauga, Canada; [2]Cytel Inc., Toronto, Canada; [3]ViiV Healthcare, Durham, USA; [4]RTI Health Solutions, Manchester, UK, [5]RTI Health Solutions, Durham, USA; [6]ViiV Healthcare ULC, Montreal, Canada; [7]ViiV Healthcare, London, UK

Key Takeaways

- **Cabotegravir long-acting (CAB-LA) injectable administered every 2 months is superior to daily tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for HIV-1 pre-exposure prophylaxis (PrEP).**
- **CAB-LA was less costly ($174,847) and more effective (36.86 QALYs) than TDF/FTC ($192,328; 36.67 QALYs) and no PrEP ($261,682; 36.29 QALYs) and prevented more primary and secondary HIV-1 infections than daily oral TDF/FTC and no PrEP.**
- **The number needed to treat (NNT) to prevent one primary HIV infection over the modelled time horizon was 13 for CAB-LA and 19 for TDF/FTC compared with No PrEP.**
- **On average, 37 people need to switch from TDF/FTC to CAB-LA to avoid one additional HIV infection.**
- **CAB-LA as PrEP in Canada offers public health and economic benefits by preventing additional HIV infections and reducing the clinical and economic burden of HIV.**

Introduction

- By the end of 2022, ~65,270 persons were living with HIV in Canada.[1]
- In 2022, 5 people acquired HIV each day in Canada. HIV incidence increased by 24.9% between 2021 and 2022, and 15% between 2020 and 2022.[1,2]
- New HIV acquisition rates differ by exposure categories, sex, and Canadian jurisdictions.[1,2]

- HIV pre-exposure prophylaxis (PrEP) has been demonstrated to prevent HIV acquisition in individuals who do not have HIV but are at increased risk of infection.[3,4]
- 98% of PrEP users in Canada in 2022 were male.[5]
- Despite being available in Canada for 8 years, daily oral PrEP, tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) is underutilized by at risk individuals.[6] High levels of adherence are required for PrEP to be effective.[6]

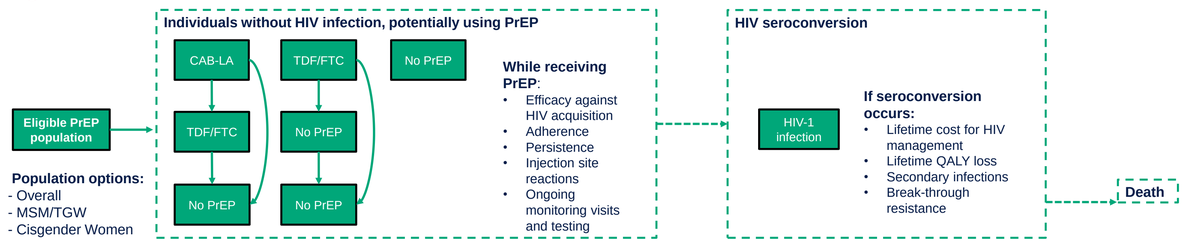
- Cabotegravir long-acting (CAB-LA) injectable, the first long-acting injectable, administered every two months was approved in Canada (May 2024) as PrEP to reduce the risk of sexually acquired HIV-1 infection in at-risk adults and adolescents, including men who have sex with men (MSM), transgender women (TGW), and cisgender women (CGW).
- The HIV Prevention Trials Network (HPTN) 083 (MSM and TGW) and HPTN 084 (CGW) studies demonstrated the superiority of every two months CAB-LA versus the standard of care, TDF/FTC for HIV-1 PrEP. [3,4]

- **Objective:** To estimate the lifetime clinical and economic impact of CAB-LA compared with oral TDF/FTC and no PrEP from a Canadian public payer perspective.

Methods

- A decision-analytic Markov model was used to evaluate the treatment pathway and capture the expected clinically important differences in costs and outcomes between patients receiving every two months CAB-LA versus daily oral TDF/FTC or no PrEP.
- The model is an adaptation of the recently published cost-effectiveness analysis performed for the US context, and has a similar underlying structure, but has been further adapted to allow for incorporation of the results of an Indirect Treatment Comparison (ITC) study.[7,8]
- In base case, modelled individuals initiated a PrEP option (CAB-LA or TDF/FTC) or no PrEP upon model entry and continued to receive their initially assigned PrEP option until discontinuation, HIV acquisition, or death.
- Number needed to treat (NNT) was estimated for PrEP compared with no PrEP and for CAB-LA compared with TDF/FTC.
- An ITC including the HPTN 083 and 084 studies provided an estimate of the effectiveness of CAB-LA vs. no PrEP based on the observed effectiveness of CAB-LA vs. TDF/FTC and the predicted effectiveness of TDF/FTC vs. no PrEP. [8]
- While receiving PrEP, individuals were at a lower risk of acquiring HIV-1 infection than those not receiving PrEP, with protection levels dependent on their selected PrEP option, PrEP adherence and persistence.
- Individuals who acquired HIV-1 infection discontinued use of PrEP and subsequently received HIV-related care, including multiclass antiretroviral (ARV) treatment regimens, ongoing monitoring, and other related care, for the remainder of their lifetimes.
- Secondary HIV seroconversions related to onward transmission were also estimated in the model.
- The model adopts a Canadian public payer perspective over a lifetime horizon while discounting costs and outcomes at 1.5% as per the Canada's Drug Agency (CDA-AMC) guidelines.

Figure 1. Model Structure



MSM: men who have sex with men; TGW: transgender women; CGW: cisgender women; PrEP: pre-exposure prophylaxis; CAB-LA: cabotegravir long-acting injectable; TDF/FTC: tenofovir disoproxil fumarate/emtricitabine; QALY: quality adjusted life years
Note: The PrEP option tenofovir alafenamide/emtricitabine (TAF/FTC) was not included in the base case analyses because it is not publicly covered for PrEP in Canada. It is only available for MSM and TGW subpopulations

Inputs and Assumptions

- Values obtained from publicly available sources and validated by Canadian HCPs, **Table 1**.

Table 1. Model Characteristics

Parameter	Value
Population distribution	
MSM and TGW, CGW[5]	98.0%, 2.0%
Mean age (years)	
MSM and TGW (HPTN 083), CGW (HPTN 084)[3,4]	26, 25
HIV incidence assumptions (events/100 person years)	
HIV incidence without PrEP – MSM/TGW[9]	4.3
HIV incidence without PrEP – CGW[9]	3.1
ITC summary results[8]	
Base case % effectiveness of TDF/FTC vs no PrEP	
MSM and TGW (HPTN 083)	75.1%
CGW (HPTN 084)	46.3%
Base case % effectiveness of CAB-LA vs no PrEP	
MSM and TGW (HPTN 083)	91.1%
CGW (HPTN 084)	92.5%
PrEP use characteristics[3,4,10]	
Adherence reported (detectable tenofovir)	
MSM and TGW (HPTN 083)	86.0%
CGW (HPTN 084)	55.9%
CAB-LA PrEP persistence	
% remaining on CAB-LA at 6 months, 12 months	84.2%, 68.9%
% remaining on oral PrEP at 6 months, 12 months	70.2%, 57.4%
Percentage of individuals initiating TDF/FTC to cover pharmacokinetic (PK) tail after discontinuing CAB-LA	50.0%
Percentage of individuals covering PK tail who discontinue TDF/FTC each month	20.0%
Injection site reaction incidence (CAB-LA)[3,4]	
Moderate (MSM and TGW, CGW)	48.0%, 12.0%
Severe (MSM and TGW, CGW)	2.9%, 0.1%
Breakthrough resistance incidence (INSTI, NRTI)[3]	
CAB-LA	0.16%, 0.00%[a]
TDF/FTC	0.00%, 0.19%
Average lifetime transmissions with each HIV infection (spillover effect)	0.8[b]
SMR for all-cause mortality in HIV positive individuals (MSM and TGW, CGW)	1.07, 1.13[c]

CGW: cisgender women; FTC: emtricitabine; HPTN: HIV Prevention Trials Network; MSM: men who have sex with men; PrEP: pre-exposure prophylaxis; TDF: tenofovir disoproxil fumarate; TGW: transgender women; ITC: indirect treatment comparison; NRTI: nucleoside reverse transcriptase inhibitor; INSTI: integrase strand transfer inhibitors; SMR: standardized mortality ratio.
[a] CGW are assumed to have similar breakthrough resistance as MSM/TGW from HPTN 083; [b] input from HCPs [c] calculated based on life expectancy in Trickey et al. (2023).

Results

Base-case Results

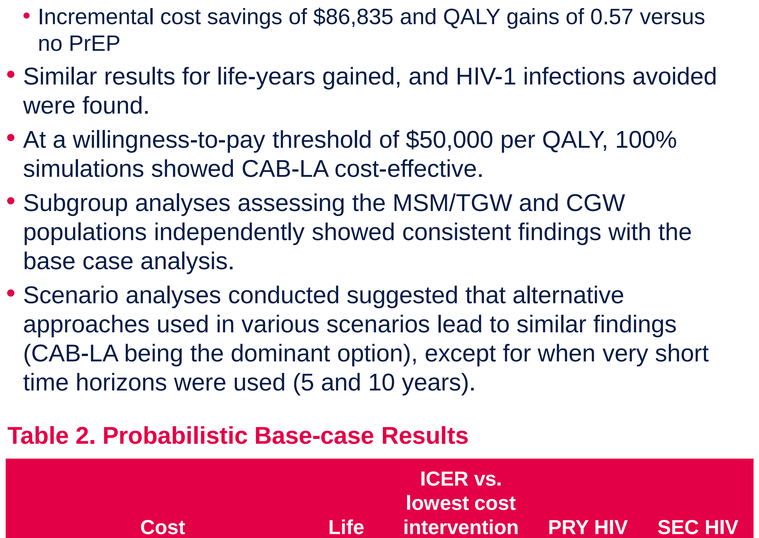
- CAB-LA was less costly ($174,847) and more effective (36.86 QALYs) than TDF/FTC ($192,328; 36.67 QALYs) and no PrEP ($261,682; 36.29 QALYs), **Table 2**.
  - Incremental cost savings of $17,481 and QALY gains of 0.20 versus TDF/FTC
  - Incremental cost savings of $86,835 and QALY gains of 0.57 versus no PrEP
- Similar results for life-years gained, and HIV-1 infections avoided were found.
- At a willingness-to-pay threshold of $50,000 per QALY, 100% simulations showed CAB-LA cost-effective.
- Subgroup analyses assessing the MSM/TGW and CGW populations independently showed consistent findings with the base case analysis.
- Scenario analyses conducted suggested that alternative approaches used in various scenarios lead to similar findings (CAB-LA being the dominant option), except for when very short time horizons were used (5 and 10 years).

Table 2. Probabilistic Base-case Results

	Cost (CAD)	QALYs	Life Years	ICER vs. lowest cost intervention ($/QALY)	PRY HIV infection	SEC HIV infection
CAB-LA	$174,847	36.86	43.24	-	0.10	0.08
TDF/FTC	$192,328	36.67	43.23	CAB-LA is dominant	0.13	0.10
No PrEP	$261,682	36.29	43.22	CAB-LA is dominant	0.18	0.15

CAB-LA: cabotegravir long-acting injectable; TDF: tenofovir disoproxil fumarate; FTC: emtricitabine; HIV: human immunodeficiency virus; PrEP: pre-exposure prophylaxis; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life-year; PRY: primary; SEC: secondary; CAD: Canadian dollar.

Figure 2. Cost-effectiveness Frontier

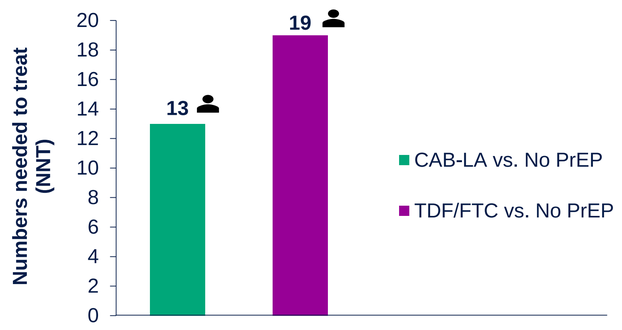


CAB-LA: cabotegravir long-acting injectable; TDF: tenofovir disoproxil fumarate; FTC: emtricitabine; PrEP: pre-exposure prophylaxis; CAD: Canadian dollar; QALY: quality-adjusted life-year.

Numbers Needed to Treat

- The NNT indicates how many patients need to be treated with a particular therapy to prevent one additional event compared with the standard of care.
- The NNT to prevent one primary HIV infection over the modelled time horizon was 13 for CAB-LA and 19 for TDF/FTC compared with No PrEP.
- The NNT for CAB-LA against TDF/FTC was 37. This means that on average, 37 people need to switch from TDF/FTC to CAB-LA to avoid one additional HIV infection.

Figure 3. NNT to Prevent One New HIV-1 Infection



Discussion

- CAB-LA received a positive reimbursement recommendation (with conditions) from the pan-Canadian health technology assessment body, CDA-AMC.[11]
- CDA-AMC reanalyzed the base-case cost-effectiveness model by including treatment administration costs, removing spillover effects, changing the source of baseline HIV incidence rate to the values estimated from the submitted ITC (higher), and assuming 100% oral PrEP adherence.[11]
- The reanalysis of the result by CDA-AMC showed CAB-LA was more costly and more effective compared to TDF-FTC, resulting in an ICER of $29,283 (incremental costs: $2,778; incremental QALYs: 0.09).[11]

Conclusions

- CAB-LA is cost-effective compared to TDF/FTC and no PrEP.
- Overall, compared to TDF/FTC and no PrEP, the results indicate the introduction of CAB-LA as PrEP in Canada would result in substantial public health and monetary benefits by preventing additional HIV infections and reducing the clinical and economic burden of HIV.

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Presenting author: Adenike Adelakun; adenike.r.adelakun@gsk.com