Cost-Effectiveness of Every Two Month Cabotegravir Long-Acting for PrEP Compared With Daily Oral Tenofovir Disoproxil/Fumarate Emtricitabine as PrEP to Prevent HIV-1 in the UK

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Key Takeaways

- **CAB-LA for PrEP is dominant (cost-saving and improves health outcomes [i.e., reduction in HIV-1 acquisition, improvement in QALYs]) vs. daily oral TDF/FTC and no PrEP for individuals at high-risk of acquiring HIV-1**
- **CAB-LA remained cost-effective or cost-saving in scenario and sensitivity analyses vs. both TDF/FTC and no PrEP**
- **CAB-LA provides an alternative PrEP modality for individuals who are at high risk of acquiring HIV-1**

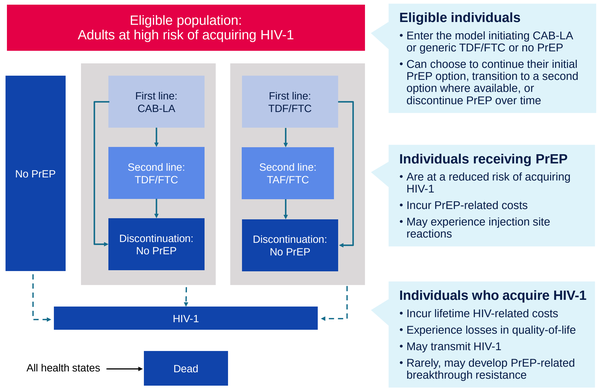
Introduction

- Pre-exposure prophylaxis (PrEP) refers to the use of anti-retroviral therapies (ART) to prevent human immunodeficiency virus (HIV)-1 transmission[1]
  - Cabotegravir long-acting (CAB-LA) is expected to be licensed for use as PrEP in the United Kingdom (UK) or pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in high-risk adults and adolescents, weighing at least 35 kg
  - Oral PrEP has been available in the UK since 2017 through the National Health Service (NHS), with two options currently available, tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) and tenofovir alafenamide (TAF)/FTC[2] with TDF/FTC being the standard of care
  - The superiority of CAB-LA in reducing the risk of HIV-1 acquisition compared with TDF/FTC has been demonstrated in the HIV Prevention Trials Network (HPTN)-083 (men who have sex with men [MSM] and transgender women [TGW]) and HPTN-084 trial populations (cisgender women [CGW])[3,4]
- The objective was to evaluate the cost-effectiveness of CAB-LA for PrEP vs. TDF/FTC as PrEP or no PrEP in the UK from an NHS perspective

Methods

- A previously published Markov model with a 1-month cycle length, lifetime time horizon, and a five-year duration of HIV-1 risk was adapted to the UK NHS setting (**Figure 1**)[5]
- The modelled population included adults aged 18 and older at high-risk of acquiring HIV-1

Figure 1. Model Structure



Model Overview

- The model estimated lifetime costs, quality-adjusted life-years (QALYs), life-years (LYs), and incremental cost-effectiveness ratios (ICERs), with costs and health outcomes discounted at 3.5% annually
- Modelled costs included PrEP-related costs (e.g., drug, administration, monitoring, and injection site reaction [ISR] costs) and lifetime costs associated with HIV-1 (**Table 1**)
  - Administration, visit, and monitoring requirements for CAB-LA were derived from British HIV Association (BHIVA)/British Association for Sexual Health and HIV (BASHH) guidelines, with unit costs taken from the Personal Social Services Research Unit (PSSRU).[6,7] Furthermore, individuals receiving CAB-LA could also experience ISRs
  - Individuals receiving oral PrEP also completed ongoing monitoring visits and tests. Administration costs were not included for oral interventions

Model Overview

- If HIV-1 seroconversion occurred, individuals discontinued use of PrEP and were assumed to receive HIV-1-related care and incurred HIV related costs (i.e., HIV related visits, tests, and ART costs)
- A reduction in life expectancy was assumed for individuals who acquired HIV-1 by application of standardized mortality ratios (SMRs) to general population lifetables
- Furthermore, a utility decrement was applied to individuals who acquired HIV-1

Table 1. Model Inputs

Parameter	Value
Population distribution	
Percentage MSM/TGW	96.86%[6]
Percentage CGW	3.14%[6]
Underlying incidence of HIV-1 (MSM/TGW)	5.01 per 100 PY[8]
Underlying incidence of HIV-1 (CGW)	3.47 per 100 PY[8]
Effectiveness of PrEP (relative risk reduction %)	
CAB-LA vs. no PrEP (MSM/TGW; CGW)	91%; 93%[8]
TDF/FTC[a] vs. no PrEP (MSM/TGW; CGW[b])	75%; 46%[8]
Mean age at which individuals initiate PrEP (years)	
MSM/TGW	26[3]
CGW	25[4]
PrEP use characteristics	
Percentage of individuals with detectable tenofovir (MSM/TGW)	86%[3]
Percentage of individuals with detectable tenofovir (CGW)	55.9%[4]
Relative improvement in persistence for CAB-LA vs. TDF/FTC	35%
Percentage of individuals who choose to transition to TAF/FTC each month while receiving TDF/FTC	0.185%[9]
PrEP related costs (GBP)	
CAB-LA annual acquisition costs	£8,379.14 (Year 1)[10] £7,182.12 (Year 2+)[10]
TDF/FTC annual acquisition costs	£416.39[10]
TAF/FTC annual acquisition costs	£4,331.01[10]
Annual administration and visit costs (GBP)	
CAB-LA administration cost	£82.93 (Year 1)[7] £71.08 (Year 2+)[7]
CAB-LA visit costs	£407.43 (Year 1)[7] £349.23 (Year 2+)[7]
TDF/FTC and TAF/FTC visit costs	£349.23 (Year 1)[7] £232.82 (Year 2+)[7]
CAB-LA monitoring costs (MSM/TGW; CGW)	£790.83; £706.89 (Year 1)[10,11,12] £432.54; £357.93 (Year 2+)[10,11,12]
TDF/FTC and TAF/FTC monitoring costs (MSM/TGW; CGW[b])	£790.83; £706.89 (Year 1)[10,11,12] £432.54; £357.93 (Year 2+)[10,11,12]
HIV-1-related costs and health outcomes	
Monthly HIV-1-related care visit costs (GBP)	£154.98[13]
Monthly ART costs (GBP)	£607.82[14]
Annual PrEP-related breakthrough resistance costs (GBP)	£9,430.36[14]
Utility decrement associated with acquiring HIV-1	–0.11[15]
SMR for those who acquire HIV-1 (MSM/TGW; CGW)	1.50; 2.18[16]
Lifetime secondary transmissions associated with each HIV-1 acquisition (MSM/TGW; CGW)	1.38[17]; 0.8[18]

ART, antiretroviral therapy; CAB-LA, cabotegravir long-acting; CGW, cisgender women; HIV, human immunodeficiency virus; MSM, men who have sex with men; PY, person year; PrEP, pre-exposure prophylaxis; TAF/FTC, tenofovir alafenamide/emtricitabine; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine; TGW, transgender women.
[a]The effectiveness of TAF/FTC is assumed to be equivalent to TDF/FTC. [b]TAF/FTC is only available for MSM and TGW subpopulations.

Effectiveness and Incidence Estimates

- The effectiveness of CAB-LA and TDF/FTC were taken from an indirect treatment comparison (ITC) based on the HPTN-083 and -084 trials. This ITC also derived a meta-regression to allow for exploration of TDF/FTC effectiveness at different levels of adherence (a treatment-effect modifier)[8]
  - Underlying incidence of HIV-1 was also estimated using the ITC
  - Adherence to TDF/FTC (measured by detectable tenofovir in plasma concentrations) was taken from the HPTN-083 and -084 trials
- Individuals on CAB-LA were assumed to have improved persistence compared with those on TDF/FTC, reflecting the benefit an additional PrEP modality may have for those in whom oral PrEP is not appropriate

Results

Base Case Analysis

- CAB-LA was the dominant option in the base case analysis vs. TDF/FTC and no PrEP (**Table 2**)
- Lower lifetime costs and improved health outcomes were observed for individuals receiving CAB-LA, driven by the lower number of HIV-1 acquisitions in the CAB-LA arm (**Table 2**)

Probabilistic sensitivity analysis vs. TDF/FTC

- The ICER was most sensitive to changes in the underlying HIV-1 incidence for the MSM/TGW population (**Figure 2**)
- A probabilistic sensitivity analysis demonstrated that CAB-LA was cost-effective compared with generic TDF/FTC in 94% of 1,000 Monte Carlo simulations at a willingness-to-pay (WTP) threshold of £30,000 per QALY

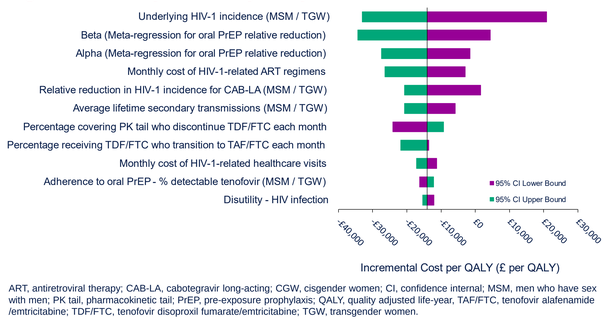
Deterministic scenario analysis

- Several scenario analyses were conducted (**Table 3**). For all scenarios explored, CAB-LA remained cost-effective vs. TDF/FTC at a willingness to pay (WTP) threshold of £20,000 per QALY
  - Alternative improvements in persistence were tested to reflect clinical opinion that CAB-LA may have an improvement of up to 50% compared with TDF/FTC
- The scenario analyses outlined in **Table 3** were also performed for the comparison between CAB-LA and no PrEP; CAB-LA remained the dominant alternative in all scenarios

Limitations

- As a cohort-level Markov model not a dynamic transmission model, the impacts associated with reduced onward transmission (i.e., secondary seroconversions) had to be estimated
  - However, the structure used in this analysis was aligned with previous health technology assessment (HTA) submissions for TDF/FTC. Furthermore, the transparency of a Markov model may be preferred by HTA bodies
- Impacts associated with disease progression of HIV-1 were not modelled as the focus of this analysis was to model the prevention of HIV-1, rather than HIV-1 progression
- Long-term data for adherence and persistence of CAB-LA were not available at the time of this analysis; therefore, expert clinical opinion was considered to inform assumptions related to persistence in the model
  - Despite the paucity of data available for persistence of CAB-LA from HPTN-083 and -084, a recent real-world study reported significant persistence for users of CAB-LA in a large community-based clinic network in the US, with discontinuations primarily attributed to insurance coverage gaps or side effects.[19,20] Improved persistence of CAB-LA vs. oral PrEP is also consistent with clinical expert opinion

Figure 2. One-way Sensitivity Analysis vs. TDF/FTC



ART, antiretroviral therapy; CAB-LA, cabotegravir long-acting; CGW, cisgender women; CI, confidence internal; MSM, men who have sex with men; PK tail, pharmacokinetic tail; PrEP, pre-exposure prophylaxis; QALY, quality adjusted life-year, TAF/FTC, tenofovir alafenamide /emtricitabine; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine; TGW, transgender women.

Table 2. Base Case Analysis

	CAB-LA vs. TDF/FTC		CAB-LA vs. no PrEP		Incremental difference	
	CAB-LA	TDF/FTC	CAB-LA	No PrEP	vs. TDF/FTC	vs. No PrEP
Total costs (GBP)	£76,026	£80,293	£76,026	£109,357	–£4,268	–£33,331
Total QALYS	25.48	25.18	27.32	26.60	0.30	0.72
Total LYs	29.56	29.53	31.67	31.58	0.04	0.08
Total HIV-1 acquisitions	0.25	0.35	0.25	0.49	–0.1	–0.24
ICER: Cost/QALY gained (GBP)					**–£14,081** **CAB-LA is dominant**	**–£46,310** **CAB-LA is dominant**

CAB-LA, cabotegravir long-acting; GBP, Great British pound; HIV, human immunodeficiency virus; LY, life year; PrEP, pre-exposure prophylaxis; QALY, quality-adjusted life-year; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine.

Table 3. Scenario Analysis vs. TDF/FTC

Scenario	Incremental costs	Incremental QALY	ICER	Interpretation
Scenario 1: Population is MSM/TGW only	–£4,374.79	0.30	**–£14,402**	**CAB-LA is dominant**
Scenario 2: Population is CGW only	£158.76	0.27	**£590**[a]	**CAB-LA is cost-effective**[b]
Scenario 3: The duration of HIV-1 risk is 1 year	£814.34	0.10	**£8,435**[a]	**CAB-LA is cost-effective**[b]
Scenario 4: The duration of HIV-1 risk is 10 years	–£1,452.14	0.29	**–£5,001**	**CAB-LA is dominant**
Scenario 5: Relative improvement in persistence of 20% for CAB-LA vs. TDF/FTC	–£1,942.62	0.25	**–£7,763**	**CAB-LA is dominant**
Scenario 6: Relative improvement in persistence of 50% for CAB-LA vs. TDF/FTC	–£9,645.78	0.42	**–£22,755**	**CAB-LA is dominant**
Scenario 7: Inclusion of RNA testing (£50 per test included for each visit)[21]	–£4,086.24	0.30	**–£13,483**	**CAB-LA is dominant**

CAB-LA, cabotegravir long-acting; CGW, cisgender women; HIV, human immunodeficiency virus; ICER, incremental cost-effectiveness ratio; MSM, men who have sex with men; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine; TGW, transgender women.
[a]The ICER is located in quadrant 1 of the cost-effectiveness plane, where CAB-LA is more costly and more effective. [b]Based on a WTP threshold of £20,000 per QALY.

Conclusions

- This analysis demonstrates that CAB-LA is dominant vs. daily oral TDF/TFC and no PrEP among eligible individuals in the UK
- For the modelled populations at high-risk of HIV-1, CAB-LA is cost-saving and provides a greater QALY gain and reduction in HIV-1 acquisitions compared with daily oral TDF/FTC and no PrEP
- CAB-LA may be an important tool to reduce new HIV-1 transmissions in the UK with cost savings compared with generic daily oral TDF/FTC
- Furthermore, CAB-LA is an option for individuals who may have not considered PrEP use to date because they are unable or unwilling to take oral PrEP

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