Use of Long-Acting Cabotegravir as Pre-Exposure Prophylaxis in Children and Adolescents

Summary

- The efficacy and safety of long-acting cabotegravir (CAB LA) for pre-exposure prophylaxis (PrEP) in children and adolescents have not been established.
- Pharmacokinetics
  - Limited data are available in virologically suppressed adolescents, aged 12 to <18 years, weighing at least 35 kg from the Week 16 analysis of the MOCHA (IMPAACT 2017) study
  - Population pharmacokinetic analyses revealed no clinically relevant differences in exposure between the HIV-1 infected adolescent and HIV-1 infected and uninfected adult participants from the cabotegravir development program
  - No dosage adjustment is needed for adolescents weighing ≥35 kg.
- HPTN 084-1 is a single arm, open label, phase 2b safety substudy of HPTN 084 in cisgender adolescent females.
  - There were no discontinuations in participants receiving CAB LA due to adverse events or serious adverse events.
  - Adverse events of special interest (AESI) included decreases in creatinine clearance (n=41), increases in blood glucose (n=22) and increases in serum creatinine (n=9). Most AESI were Grades 1 or 2.
  - There were no HIV infections reported.
- Substudies of HPTN 083 and HPTN 084 are ongoing to assess the safety, tolerability, and acceptability of CAB LA for PrEP in adolescent males and females, respectively.
- Important Safety Information and Boxed Warning can be found in the Prescribing Information and can also be accessed from the Our HIV Medicines section of viivhealthcare.com/us.

To access additional scientific information related to ViiV Healthcare medicines, visit the ViiV US Medical Portal at viivhcmedinfo.com.

The efficacy and safety of long-acting CAB LA for PrEP in children and adolescents have not been established.

Pharmacokinetics

The pharmacokinetics and safety of CAB LA for the treatment of HIV-1 infection are being assessed in an ongoing phase 1/2 multicenter, open-label, non-comparative study [the MOCHA study (IMPAACT 2017)].[1] Virologically suppressed adolescents, aged 12 to <18 years, weighing at least 35 kg were enrolled and received either oral cabotegravir 30 mg once-daily for 1 month followed by CAB LA, or oral rilpivirine 25 mg once-daily for 1 month followed by RPV LA injections, administered monthly x3 doses while continuing background cART.

Limited data are available from the Week 16 analysis. Eight adolescents who received CAB LA were included.[1]

At baseline, the median age of participants was 14.5 years, the median weight was 57.2 kg, 25% were female, 100% were non-white, no participants had a $CD4^+$ T-cell count less than 350 cells/mm^3.[1]

Data from MOCHA were used to model the pharmacokinetics of CAB LA when administered every-2-months (see Table 1 below).

Table 1. Predicted Pharmacokinetic Parameters Following Oral Cabotegravir and Initiation and Every-2-Month Administration of CAB LA in Adolescent Participants Aged 12 to <18 years (≥35 kg)[1]

Dosing Phase	Dosage Regimen	Geometric Mean (5th, 95th Percentile)[a]		
		$AUC_{(0\text{-}tau)}$[b] (µg•h/mL)	C_{max} (µg/mL)	C_{tau} (µg/mL)
Oral lead-in[c]	30 mg once daily	193 (106, 346)	14.4 (8.02,25.5)	5.79 (2.48,12.6)
Initial injection[d]	600 mg IM Initial Dose	2123 (881, 4938)	11.2 (5.63,21.5)	1.84 (0.64,4.52)
Every 2-month injection[e]	600 mg IM Every 2-month	4871 (2827, 8232)	7.23 (3.76,14.1)	2.01 (0.64,4.73)

[a] Pharmacokinetic (PK) parameter values were based on population PK model simulations in a virtual HIV-1 infected adolescent population weighing 35-156 kg.

[b] tau is dosing interval: 24 hours for oral administration; 1 month for the initial injection, 2 months for every 2 months for IM injections of extended-release injectable suspension.

[c] Oral lead-in pharmacokinetic parameter values represent steady-state.

[d] Initial injection C_{max} values primarily reflect oral dosing because the initial injection was administered on the same day as the last oral dose; however, the $AUC_{(0\text{-}tau)}$ and C_{tau} values reflect the initial injection.

[e] Pharmacokinetic parameter values represent steady state.

CAB LA = long-acting cabotegravir; $AUC_{(0\text{-}tau)}$ = area under the concentration versus time curve from time 0 to the end of the dosing interval; C_{max} = maximum concentration; C_{tau} = concentration at the end of the dosing interval

Population pharmacokinetic analyses revealed no clinically relevant differences in exposure between the HIV-1 infected adolescent and HIV-1 infected and uninfected adult participants from the cabotegravir development program, therefore, no dosage adjustment is needed for adolescents weighing ≥35 kg.[1]

HPTN 084-1[2]

HPTN 084-1 is a single arm, open label, phase 2b substudy of HPTN 084 evaluating CAB LA for PrEP among people assigned female at birth who were <18 years of age and weighing ≥35 kg.

After a 5 week oral lead-in participants received CAB LA 600 mg (3 mL) intramuscularly every 2 months, after receiving 2 injections one month apart, for 29 weeks.

Results

Fifty-five participants received the OLI with 2 discontinuations adverse events not related to CAB LA. Baseline demographics and characteristics can be found in Table 2 below.

Table 2. Baseline Demographics and Characteristics of Subjects in HPTN 084-1

Characteristic	Result
Mean Age (range)	16 (12-17) years
Black African race	100%
Weight	
<50 kg	27%
≥50 kg	73%
Gonorrhea	7%
Chlamydia	31%
# HIV+ sex partners 1+	26%
Median episodes vaginal sex past month	2
Anal sex past month (yes)	5%
Transactional sex past month (yes)	22%

Safety

There were no discontinuations due to adverse events or serious adverse events. Adverse events of special interest can be found in Table 3 below.

Table 3. AESI Reported During the OLI or with CAB LA

AESI with OLI or CAB LA	N	Outcome
CrCl decreased	41	Resolved without intervention
Grade 2	39	
Grade 3	2	
Blood glucose increased	22	Resolved without intervention
Grade 1	21	
Grade 2	1	
Serum creatinine increased	9	Resolved without intervention
Grade 1	1	
Grade 2	6	
Grade 3	2	
Neuropsychiatric events	3	Resolved with counseling
Grade 1	1	
Grade 2	1	
Grade 4	1	
Rhabdomyolysis	1	Myalgia resolved
Grade 2	1	

AESI = adverse event of special interest; OLI = oral lead-in; CAB LA = long-acting cabotegravir; CrCl = creatinine clearance

There were no reports of weight gain, hepatotoxicity, hypersensitivity, rash, seizures, or pancreatitis.

Injection site reactions (ISRs) were reported infrequently and most occurred with the first or second injections. The most common ISR was pain and most were Grades 1 or 2. There were no discontinuations due to ISRs.

Participants were 100% adherent to CAB LA whereas adherence during the OLI was approximately 20% at Week 2 and approximately 10 at Week 4.

Ongoing Studies

Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV Among Adolescent Males - A Sub-study of HPTN 083.[3]

Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV Among Adolescent Females - A Sub-study of HPTN 084.[4]

Some information contained in this response is outside the approved Prescribing Information. This product is not approved for the use described. This response is not intended to offer recommendations for administering this product in a manner inconsistent with its approved labeling.

In order for ViiV Healthcare to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 877–844–8872. Please consult the attached Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

REFERENCES

1. ViiV Healthcare. Global Data Sheet for Cabotegravir (PrEP). Version 02. October 27, 2021.
2. Hosek S, Hamilton E, Ngo J, et al. CAB LA for HIV prevention in African cisgender female adolescents (HPTN 084-1). Presented at the 30th Conference on Retroviruses and Opportunistic Infections (CROI), February 19-22, 2023, Seattle, WA, USA.
3. NCT04692077 (HPTN 083 substudy in adolescent males). Available at: https://clinicaltrials.gov/ct2/show/NCT04692077?term=hptn+083&draw=2&rank=1. Accessed January 6, 2021.
4. NCT04824131 (HPTN 084 substudy in adolescent females). Available at: https://clinicaltrials.gov/ct2/show/NCT04824131?term=hptn+084&draw=2&rank=1. Accessed January 6, 2021.