Effect of *Apretude* on Serum Creatinine When Used for Pre-Exposure Prophylaxis

Summary

- *Apretude* (long-acting cabotegravir, CAB LA) does not inhibit the renal organic cation transporter (OCT) 2 or the multidrug and toxin extrusion transporter (MATE) 1 and therefore is unlikely to inhibit tubular secretion of creatinine.[1]
- In HPTN 083, Grade 2 and Grade 3 incidences of decreased creatinine clearance and increased serum creatinine were reported with similar frequencies in the Apretude (long-acting cabotegravir, CAB LA) and tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) arms.[2]
- In HPTN 084, Grade 2 or higher incidences of decreased creatinine clearance and increased serum creatinine were reported with similar frequencies in the long-acting cabotegravir (CAB LA) and tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) arms.[3]
- 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.

PHARMACOLOGY OF CABOTEGRAVIR

Unlike dolutegravir, CAB does not inhibit OCT2 or MATE1 and therefore is unlikely to inhibit tubular secretion of creatinine.[1]

CLINICAL TRIALS

HPTN 083

HPTN 083 is a randomized, double-blind, double-dummy, phase 2b/3, non-inferiority study designed to assess the safety and efficacy of CAB LA compared to daily oral TDF/FTC for PrEP in HIV-uninfected cisgender men and transgender women who have sex with men.[2]

Eligible participants for the HPTN 083 trial had a creatinine clearance of at least 60 mL/min.[4]

Adverse events specific to serum creatinine increases of creatinine clearance decreases from HPTN 083 are listed in Table 1 below.

Table 1. Increases in Serum Creatinine and Decreases in Creatinine Clearance in HPTN 083[2]

	Overall (N = 4562)	CAB LA Group (n = 2280)	TDF/FTC Group (n = 2282)
Grade 2 or higher			
Decreased creatinine clearance	3257 (71.4)	1588 (69.6)	1669 (73.1)
Increased serum creatinine	810 (17.8)	382 (16.8)	428 (18.8)
Grade 3 or higher			
Decreased creatinine clearance	349 (7.7)	159 (7.0)	190 (8.3)
Increased serum creatinine	156 (3.4)	80 (3.5)	76 (3.3)

DAIDS AE Grading[5]: Serum creatinine - *Grade 2 increase* >1.3 to 1.8 times the ULN -or- increase to 1.3 to <1.5 times participant's baseline, *Grade 3 increase* >1.8 to <3.5 times the ULN -or- increase to 1.5 to <2.0 times participant's baseline; Creatinine clearance – *Grade 2 decrease* <90 to 60 mL/min or mL/min/1.73 m^2 -or- 10 to <30% decrease from participant's baseline, *Grade 3 decrease* <60 to 30 mL/min or mL/min/1.73 m^2 -or-30 to <50% decrease from participant's baseline

CAB LA = long-acting cabotegravir; TDF/FTC = tenofovir/emtricitabine; ULN = upper limit of normal

HPTN 084

HPTN 084 is a double-blind, placebo-controlled, phase 3, superiority trial evaluating the safety and efficacy of long-acting injectable cabotegravir compared to daily oral TDF/FTC for pre-exposure prophylaxis in HIV-uninfected cisgender women.[3]

Eligible participants for the HPTN 084 trial had a creatinine clearance of at least 60 mL/min.[6]

Adverse events specific to serum creatinine increases of creatinine clearance decreases from HPTN 083 are listed in Table 2 below.

Table 2. Increases in Serum Creatinine and Decreases in Creatinine Clearance in HPTN 084[3]

	Overall (N = 3224)	CAB LA Group (n = 1614)	TDF/FTC Group (n = 1610)
Grade 2 or higher			
Decreased creatinine clearance	2359 (73)	1166 (72)	1193 (74)
Increased serum creatinine	664 (21)	337 (21)	327 (20)

DAIDS AE Grading[5]: Serum creatinine - *Grade 2 increase* >1.3 to 1.8 times the ULN -or- increase to 1.3 to <1.5 times participant's baseline, *Grade 3 increase* >1.8 to <3.5 times the ULN -or- increase to 1.5 to <2.0 times participant's baseline; Creatinine clearance – *Grade 2 decrease* <90 to 60 mL/min or mL/min/1.73 m^2 -or- 10 to <30% decrease from participant's baseline, *Grade 3 decrease* <60 to 30 mL/min or mL/min/1.73 m^2 -or-30 to <50% decrease from participant's baseline

CAB LA = long-acting cabotegravir; TDF/FTC = tenofovir/emtricitabine; ULN = upper limit of normal

REFERENCES

1. ViiV Healthcare. Global Data Sheet for Cabotegravir (PrEP). Version 01. July 1, 2021.
2. Landovitz R DD, Clement ME, et al. Cabotegravir for HIV prevention in cisgender men and transgender women. *NEJM*. 2021;385(7):595-609. doi:http://dx.doi.org/10.1056/NEJMoa2101016.
3. Delany-Moretlwe S. Long acting injectable cabotegravir is safe and effective in preventing HIV infection in cisgender women: results from HPTN 084. Presented at HIV Research for Prevention Conference (HIVR4P), January 27-28 and February 3-4, 2021 (Virtual).
4. NCT02720094 (HPTN 083). Available at: https://clinicaltrials.gov/ct2/show/NCT02720094?term=cabotegravir+prep&rank=1. Accessed October 3, 2019.
5. Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases, National Institutes of Health. DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (version 2.1, Jul 2017). Available at: https://rsc.niaid.nih.gov/clinical-research-sites/daids-adverse-event-grading-tables. Accessed on October 1, 2021.
6. NCT03164564 (HPTN 084). Available at: https://clinicaltrials.gov/ct2/show/NCT03164564?term=cabotegravir+prep&rank=3. Accessed October 3, 2019.