Management of the Pharmacokinetic Tail of Long-Acting Cabotegravir When Used as Pre-Exposure Prophylaxis

Summary

- Cabotegravir remains detectable in the systemic circulation after discontinuation of long-acting cabotegravir (CAB LA) for up to a year or longer (the "pharmacokinetic (PK) tail").
  - The PK tail starts 2 months after the last dose of CAB LA.
- In HPTN 083, there were 16 incident HIV infections during the PK tail.
  - An integrase strand-transfer inhibitor (INSTI) resistance associated mutation (RAM) was detected in 1 case where CAB LA was restarted in the setting of unrecognized HIV infection.
- In HPTN 084, there was 1 incident HIV infection during the PK tail.
- If CAB LA is to be discontinued but the person remains at risk of HIV acquisition, alternative pre-exposure prophylaxis (PrEP) should be prescribed no later than 2 months after the last dose.
- Important Safety Information and Boxed Warning can be found in the Prescribing Information and can also be accessed from Our HIV Medicines.

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The PK tail of CAB LA is best described as persistent plasma concentrations following discontinuation of the medicine. As time goes on, these concentrations can become sub-inhibitory and may lead to the emergence of viral resistance. The PK tail starts 2 months after the last dose of CAB LA.

PK data indicate that cabotegravir may remain detectable in the systemic circulation for up to a year or longer after discontinuation.[1,2] In phase 2 studies conducted in HIV-uninfected participants, plasma concentrations were quantifiable 44-52 weeks after discontinuation in men and for 67 weeks in women.

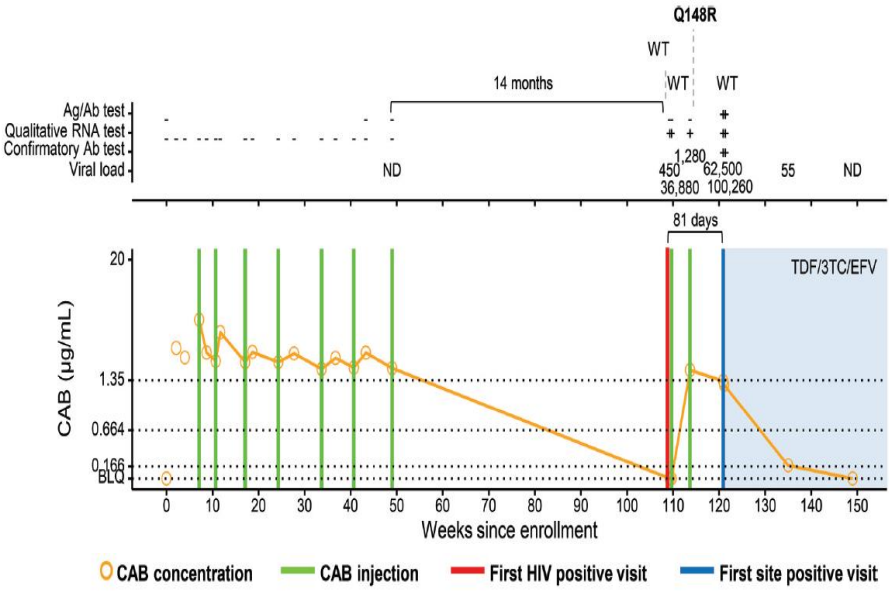
HPTN 083

In HPTN 083, there were 16 incident infections during the PK tail (cases B1, B3-B4, B9-16, BR1-BR2, Dx1-Dx3):[3,4]

- The approximate number of weeks between discontinuation and the first detection of HIV infection ranged from 14 to 135.
  - 14 of the incident infections (Cases B3-B4, B9-B11, B13-B16, BR1-BR2, Dx1-Dx3) occurred between approximately 14 and 60 weeks after the discontinuation of CAB LA.
  - 2 of the incident infections (Cases B1 and B12) occurred approximately 122 and 135 weeks after discontinuation. In both cases cabotegravir plasma concentrations detectable but <1x the protein-adjusted IC90.
- An INSTI RAM was detected in 1 case (BR1; see Figure 1 below).
  - This incident infection was not initially detected by the site (antigen/antibody test); it was detected by the central study laboratory retrospectively (HIV-1 RNA test; viral load 450 copies/mL; no INSTI RAMs on genotype) 56 weeks after the last dose of CAB LA.
  - At the time of detection, the cabotegravir concentration was below the limit of quantification (<0.025 µg/mL).

- Because of the negative antigen/antibody test performed by the site, this participant was restarted on CAB LA for PrEP and received the 2 initiation injections 28 days apart.
- Q148R was detected retrospectively 31 days after the first detection of HIV.
- The site did not detect HIV infection until 81 days after the CAB LA was restarted.
- This participant was treated with efavirenz/tenofovir disoproxil fumarate/lamivudine

Figure 1. Time Course of HIV Infection: Case BR1[5]



For more information about HPTN 083 please click here. For more information about INSTI resistance amongst the incident infections in HPTN 083 please click here.

HPTN 084

In HPTN 084, there was 1 incident HIV infection during the PK tail (case Dx):[6,7]

- The infection occurred 16 weeks after the discontinuation of CAB LA.
  - Cabotegravir plasma concentrations were detectable but <1x the protein-adjusted IC90.
  - No INSTI RAMs were detected.

For more information about HPTN 084 click here.

PrEP After Discontinuation of CAB LA

If CAB LA is to be discontinued but the person remains at risk of HIV acquisition, alternative PrEP should be prescribed no later than 2 months after the last dose.

This information is scientific and non-promotional in nature and is not intended for further distribution.

This information is not intended to offer recommendations for using this product in a manner inconsistent with its approved labeling. Please consult the Prescribing Information. 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.

Selection of references follows principles of evidence-based medicine and, therefore,

references may not be all inclusive.

REFERENCES[2]

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