

**HIV Grand Rounds Lecture:**  
**Long-Acting Injectable Cabotegravir for HIV PrEP: What We Know and What We Need To**  
**Know-Raphael Landovitz, MD, MSc**  
Post Lecture Q&A

1. Why does PrEP reach Max protection after a week for anal sex but it takes about 3 weeks for frontal hole sex? I'm just curious about the science behind it, I tried looking for research behind this and I couldn't find a reliable source.

Let's use the term TDF/FTC PrEP because PrEP is not just one medication any longer. TDF/FTC PrEP as onset of protection of about 7 days for all populations and sex acts. See the IAS-USA guidelines published in JAMA in 2018 and again in 2020.

2. It would be interesting to know more about what the blocking/stratification factors were for enrollment, as the design looks to have been successful in balancing background characteristics.

Randomization was stratified by site using permuted blocks of size 8, 10 and 12.

3. CAB is definitely the way to go and shows that it has long plasma concentration. What would be the recommended baseline screening tests to avoid any sero- conversion in resource limited settings (Not South Africa) but in other parts of Sub Saharan Africa? ..... (fun fact question is from Ntula from Zambia)

It was addressed live.

4. What were the methods used for determining TDF/FTC adherence?

Both plasma tenofovir levels and intra-erythrocytic TFV-DP levels in dried bloods spots.

5. Any thoughts about a 3-drug lead in for all PrEP given the potential for infection during lead in and for those already infected in the window?

The Thai group has advocated for this; I find it problematic with regard to complexity and stigma, and would only delay detection further but not abrange the risk of suppressing infection on 2 or 1 drug subsequently.

6. Any thoughts of whether adherence to oral pills in this study would differ from the general population?

That's always a problem; generalizing the motivation of people who enroll in a study to what would be seen in a general population.

7. Any thoughts on long-acting injectable drug for PEP?

Islatravir, the monthly oral pill being studied for PrEP now has animal data that 1 dose for PEP might be an option. CAB has not been studied in that context.

8. HPTN083 showed 4 incident infections despite therapeutic levels of cabotegravir. The suggested viremic escape can occur at higher levels of cabotegravir. Were mutations 148 and 263 associated with these failures? If so this wipes out integrase inhibitors as therapeutic options.

148 was seen in most of the resistant cases. 263 was seen in one. The phenotypes suggest retained susceptibility to DTG, but I would not feel comfortable using it in these cases. The cross class resistance is a concern certainly.

9. CEPA called the pricing of cabotegravir/rilpivirine for treatment of HIV as reasonable, but noted that long acting cabotegravir as PrEP is not cost effective. Any comments?

That's not CEPAC's conclusion. Their conclusion was that it would not be cost effective if priced identically to the current pricing of CAB + RPV combination injectable treatment.

10. Could LAI for PrEP be injected into the arm?

Not currently.

11. How often is the LAI for PrEP injection required?

The first 2 injections are 4 weeks apart, after that 8 weeks between injections.

12. Comment: looking at some of the structural and systemic, cultural barriers adolescents and young person's face when it comes to retaining them on PrEP Tx ... very interesting. this might be a breakthrough in Africa

Agree.

13. If cabotegravir is effective for HIV prevention for 2 months but in women subtherapeutic levels last up to 12 months will this lead to pressure to cause integrase resistance if hiv is caught in the ensuing 10 months.

As was noted in the discussion of 083's "B" cases, we now have 3 cases of infection acquisition during the "tail" that did not result in resistance. While this does not mean it cannot happen, it is reassuring that this was not seen. It's also not just in women that the tail is prolonged.

14. Is E138K also a NNRTI mutation? How about RPV?

138 is an important mutation location both in integrase and reverse transcriptase, but obviously have different implications depending on what gene they reside.

15. This may also reinforce the need for 2-3 drugs to treat HIV. Are you assume that the INSTI resistance was due to CAB use? Should we begin using the more sensitive RNA

test to screen folks for PrEP to ensure HIV-infected persons from get on treatment ASAP?

Circulating integrase resistance is extremely rare and would not be thought to be the source of transmitted resistance. Yes, my hypothesis is that we will need more sensitive diagnostics for long-acting PrEP.

16. Was an HIV RNA quant done at baseline and ALSO missed the diagnosis during window period?

That is correct. Implying that the window period began after the RNA test was obtained.

17. Will you do an analysis to examine how much CAB changed the window period of the tests used to detect HIV?

We have already done this and it is in press at JID.

18. Can adolescents be given this medication?

If the FDA approves for adolescents, yes.

19. How about the pregnant and breastfeeding, can they receive the medication?

That is being studied currently.

20. Any side effects ?

The side effects were reviewed in the talk; injection site reactions were the most common.

21. How long will it take to be effective?

We don't know the answer to this question yet.

22. How long will 1 dose last for protection?

We don't know the answer to this question yet. It is currently administered every 8 weeks.

23. How long will retests be required before the next dose?

Please clarify the question.

24. What will be the route of administration?

It is given as an intramuscular injection in the buttock muscle.