Long-Acting Injectable Cabotegravir: the Future of HIV PrEP?

Brian R. Wood, MD
Associate Professor of Medicine
University of Washington
Mountain West AIDS Education & Training Center

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No conflicts of interest or relationships to disclose. Will be discussing an investigational antiretroviral.

Full HPTN 083 study results not yet available. Will be reviewing data from a preliminary DSMB analysis today.

Outline

• General notes about cabotegravir
• News from the phase 3 PrEP trial (and why it’s a big deal)
• Questions, concerns, and next steps for long-acting PrEP
What is Cabotegravir?
Cabotegravir (CAB)

- Investigational integrase strand transfer inhibitor
- Potential infrequent dosing and parenteral administration
  - Oral half-life: 40 hours
  - Parenteral nanosuspension (IM, SC) half-life: 21-50 days
  - Median time from discontinuation to undetectable plasma level (IM, SC): 43-66 weeks
- Metabolized by UGT1A1 (main pathway) & UGT1A9
  - Minimal CYP metabolism; likely few drug interactions
- Relatively **low** barrier to resistance
Injectable Long-Acting Cabotegravir

Image courtesy of Dr. Raphael Landovitz, UCLA
What is the HPTN 083 Trial and What’s the Big News?
HPTN 083

A Phase 2b/3 Double Blind Safety and Efficacy Study of Injectable Cabotegravir Compared to Daily Oral TDF/FTC, for Pre-Exposure Prophylaxis in HIV-Uninfected Cisgender Men and Transgender Women who have Sex with Men

**Target enrollment:** 4,500 HIV-uninfected cisgender men and transgender women who have sex with men and who are at risk of HIV acquisition

**Primary outcome:** HIV Prevention effectiveness of cabotegravir compared to daily oral TDF/FTC

ClinicalTrials.gov Identifier: NCT02720094

Slide courtesy of Dr. Raphael Landovitz, UCLA
IM CAB Every 2 Months vs Oral Daily FTC/TDF for HIV PrEP
HPTN 083: Study Design

Study Design

• Phase 2b/3, multinational, double blind, double dummy, randomized trial to assess efficacy of long-acting IM cabotegravir (CAB) compared to daily oral FTC/TDF for preventing HIV infection
• Enrolled cisgender MSM and transgender women at high risk for HIV
• Endpoints: incident HIV infections; safety

1:1

Oral CAB daily + daily oral placebo → Oral FTC/TDF daily + daily oral placebo

5 weeks

IM CAB q8 wks + daily oral placebo

148 weeks*

Oral FTC/TDF daily + IM placebo q8 wks

*Followed by 48 weeks oral FTC/TDF daily

Source: https://www.hptn.org
IM CAB Every 2 Months vs Oral Daily FTC/TDF for HIV PrEP
HPTN 083: Study Population

• Participants: 4,565 MSM and transgender women enrolled
  - Average age: 28
  - 66% under age 30
  - 40% under age 25
  - 12% transgender women
  - 50% black/African American at US sites

Source: https://www.hptn.org
IM CAB Every 2 Months vs Oral Daily FTC/TDF for HIV PrEP

HPTN 083: Results

- **38 infections** with Oral FTC/TDF, Incidence 1.21%
- **12 infections** with IM CAB, Incidence 0.38%
- IM CAB has 3x fewer infections compared to Oral FTC/TDF

**Estimated background HIV incidence rate:** 4.5%; **actual overall incidence rate:** 0.79%

- AE’s more frequent with IM CAB: injection site reactions, pyrexia, elevated BP

Source: [https://www.hptn.org](https://www.hptn.org)
Injectable Cabotegravir for HIV PrEP

Outstanding Questions and Concerns

• Necessary oral lead-in? Oral tail?
  - Is “direct to inject” safe?

• Risk of missed doses?
  - Why did the 12 HIV infections in CAB arm occur?
  - Did these individuals acquire integrase resistance?

• Cost, timing of FDA evaluation, clinical logistics

• Comparison to oral FTC/TAF

• Weight change over time
  - CAB had neutral effect on weight in prior small study
Long-Acting HIV PrEP
What’s Next?

• HPTN 084: similar design in cisgender women in Africa
  - Started approximately 1 year after HPTN 083
  - DSMB review: study should continue; review again this year
  - Will assess for superiority of IM CAB vs oral FTC/TDF

• FDA re-assessment of IM CAB/RPV-LA for treatment

• Further work towards other long-acting PrEP agents:
  - Examples: islatravir (NRTTI), GS-6207 (capsid inhibitor)
**Long-Acting HIV PrEP**

**Summary**

- Preliminary analysis demonstrates that IM cabotegravir every 2 months is statistically non-inferior to daily oral FTC/TDF for HIV PrEP
- Potential for enormous benefit: easier adherence, reduced side effects (option with significant renal insufficiency?), reduced stigma and fear of intimate partner violence
- Full analysis and FDA review pending
Poll

• What percentage of persons currently taking oral PrEP do you anticipate would transition to IM PrEP administered in clinic every 2 months?

A) 0-25%
B) 25-50%
C) 50-75%
D) >75%
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