

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

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June 4, 2020

Disclosures

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.

See press release and webinar:

<https://www.hptn.org/news-and-events/announcements/cab-la-proves-be-highly-effective-prevention-hiv-acquisition>

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

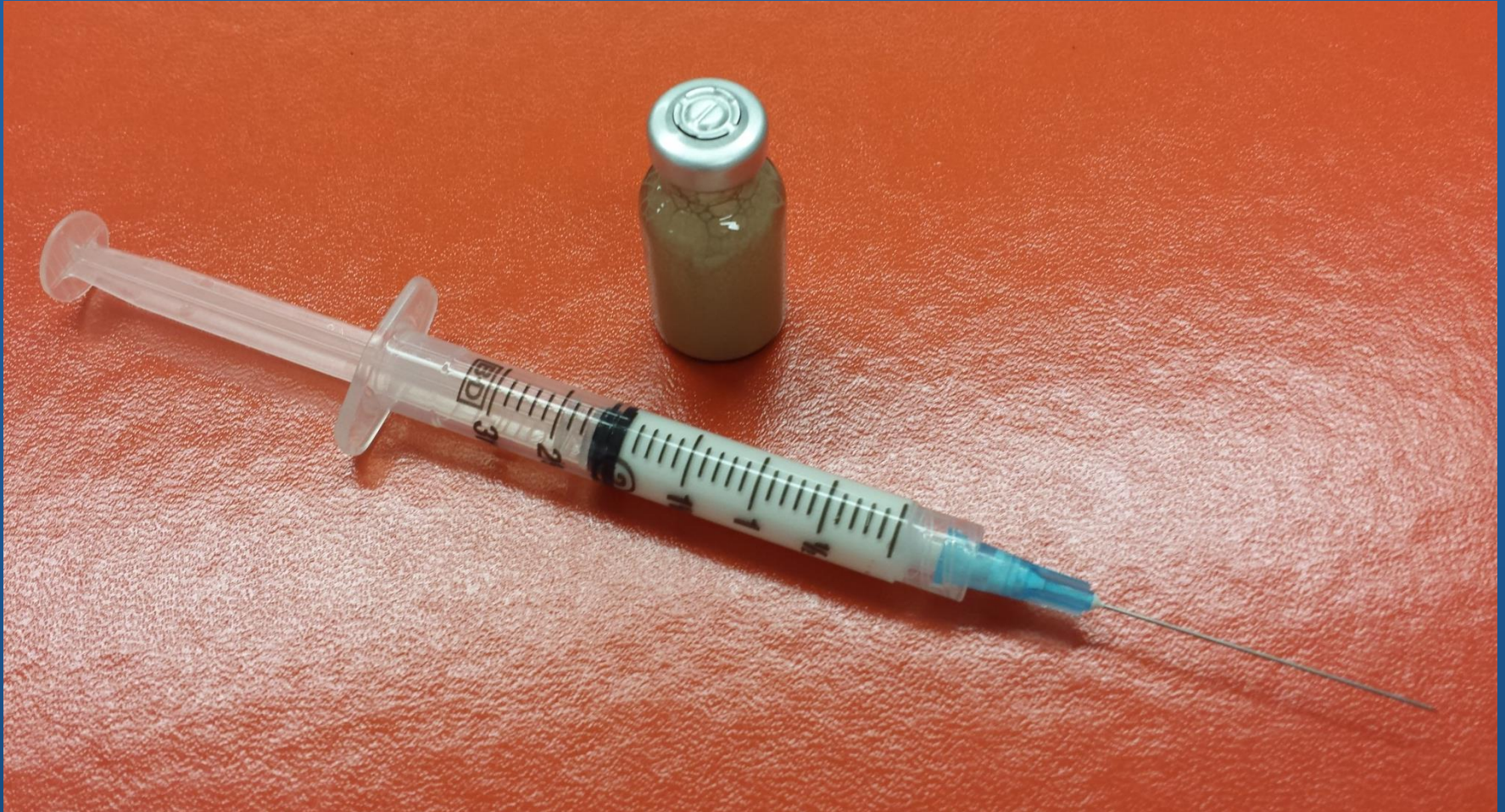


Image courtesy of Dr. Raphael Landovitz, UCLA

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

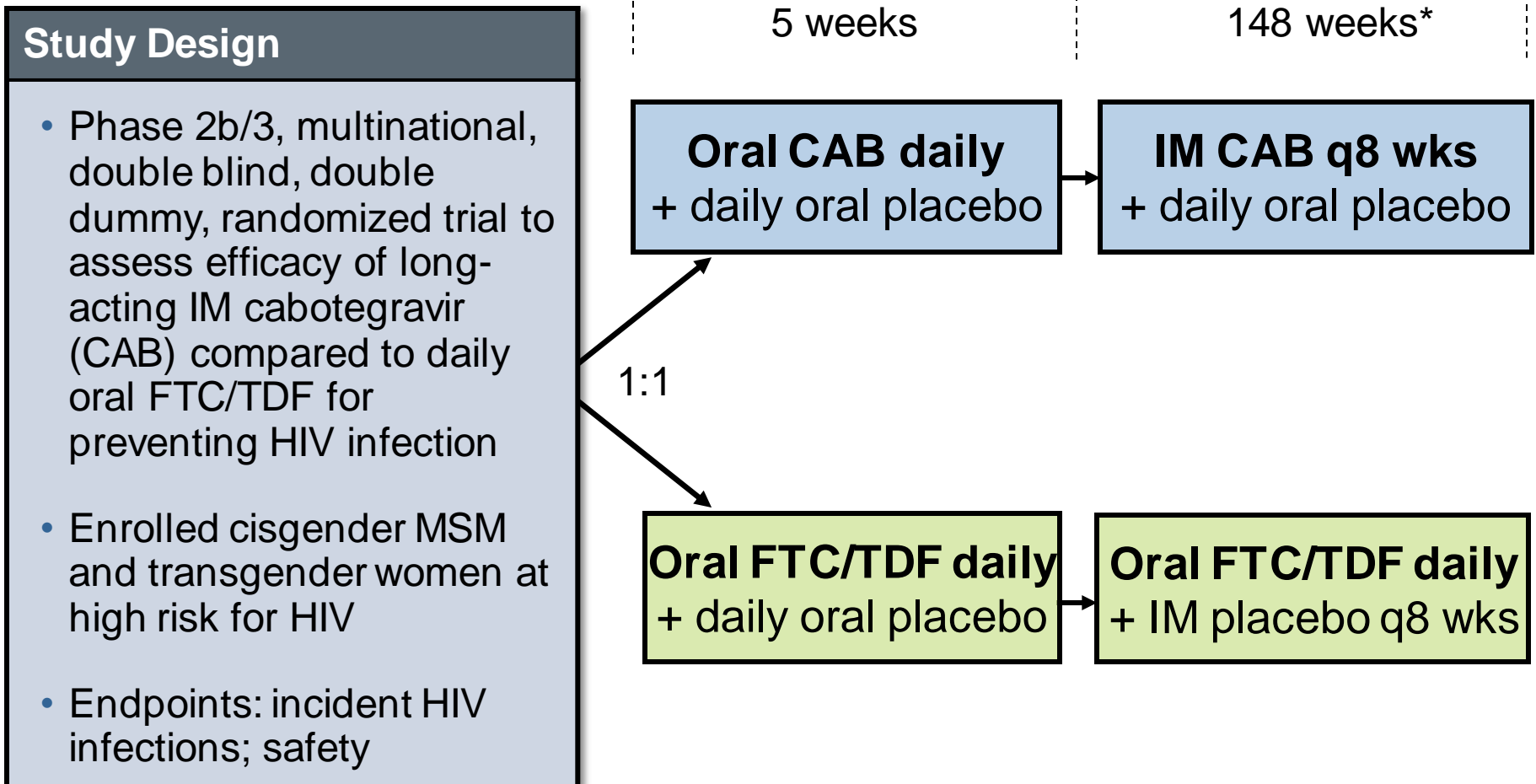
Target enrollment: 4,500 HIV-uninfected cisgender men and transgender women who have sex with men and who are at risk of HIV acquisition

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



IM CAB Every 2 Months vs Oral Daily FTC/TDF for HIV PrEP

HPTN 083: Study Design

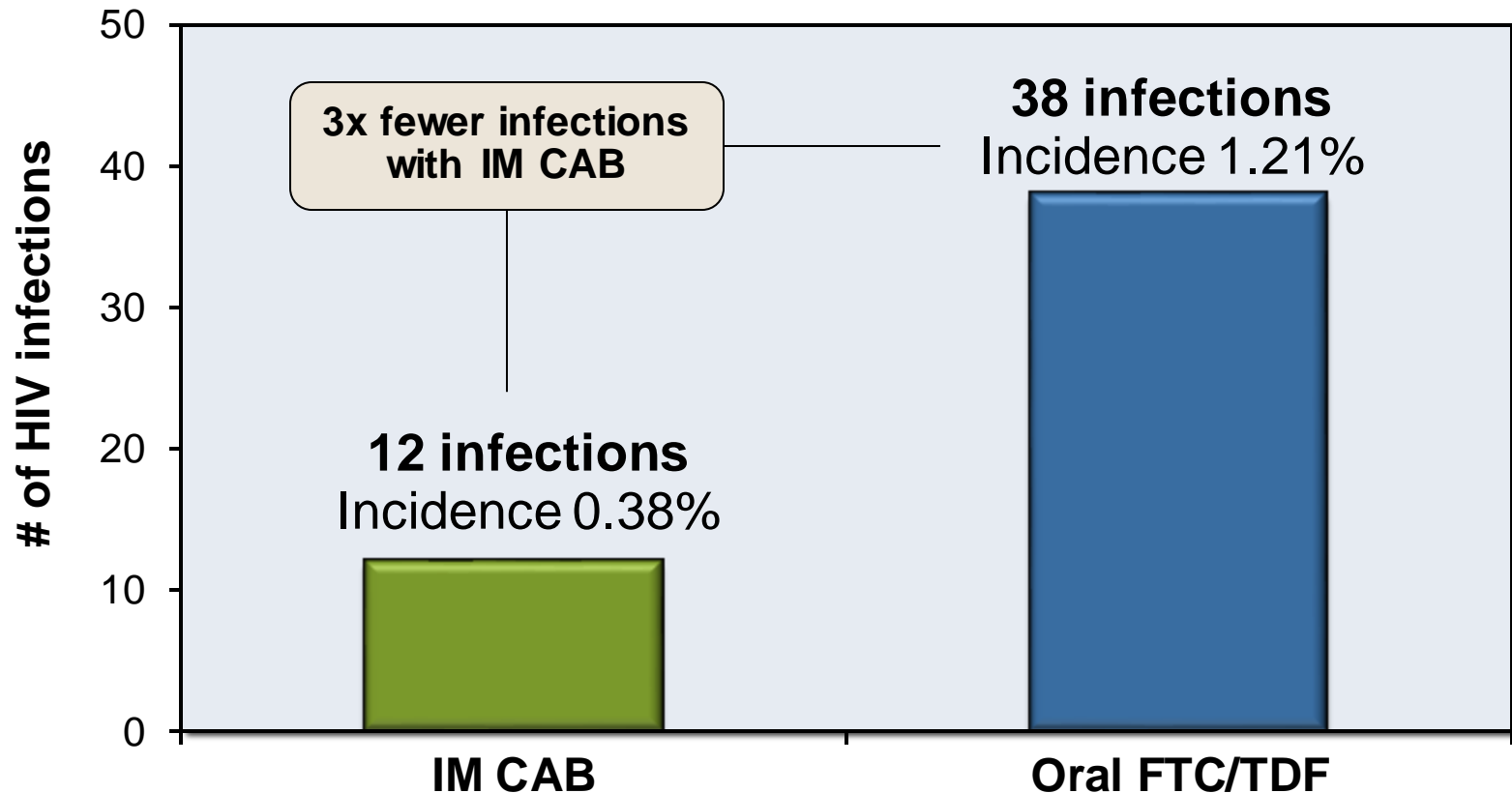


*Followed by 48 weeks oral FTC/TDF daily

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

IM CAB Every 2 Months vs Oral Daily FTC/TDF for HIV PrEP HPTN 083: Results



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

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%

Acknowledgment

The Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling \$3,059,557 and as part of another award totaling \$400,000 with 0% financed with non-governmental sources.

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