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

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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

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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

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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

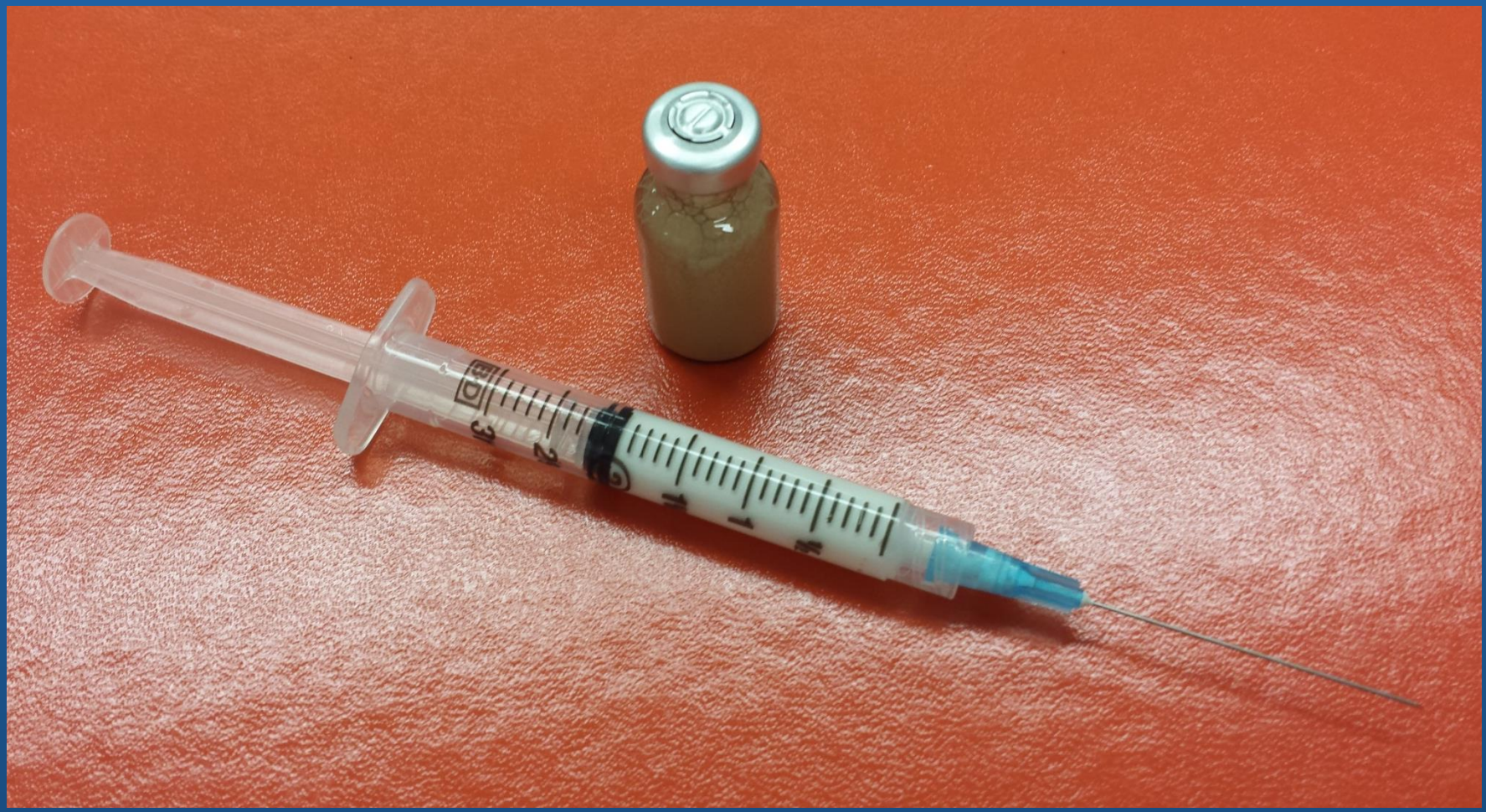

Image courtesy of Dr. Raphael Landovitz, UCLA

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What is the HPTN 083 Trial and What's the Big News?

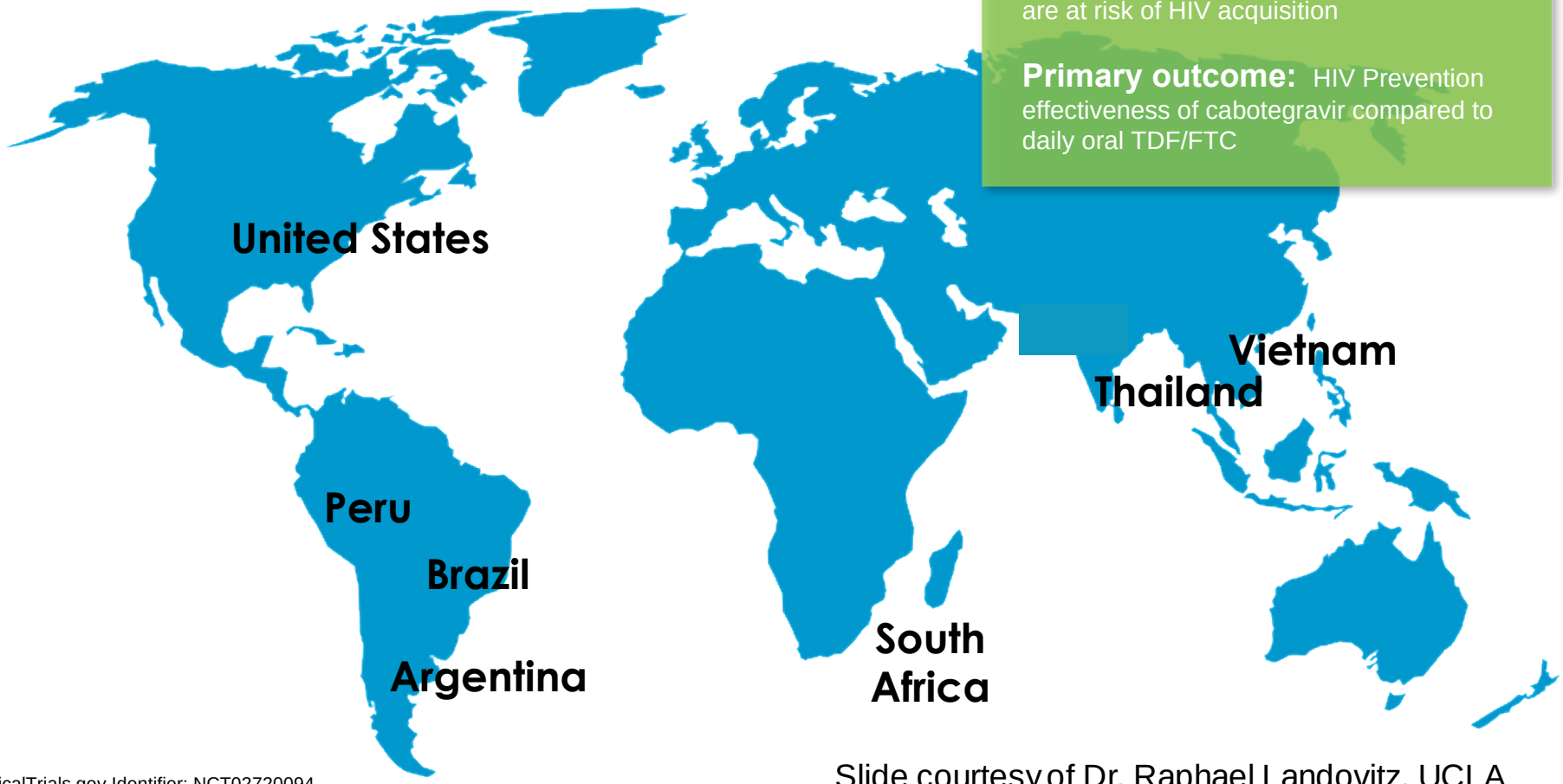
HPTN 083

HPTN
HIV Prevention
Trials Network

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

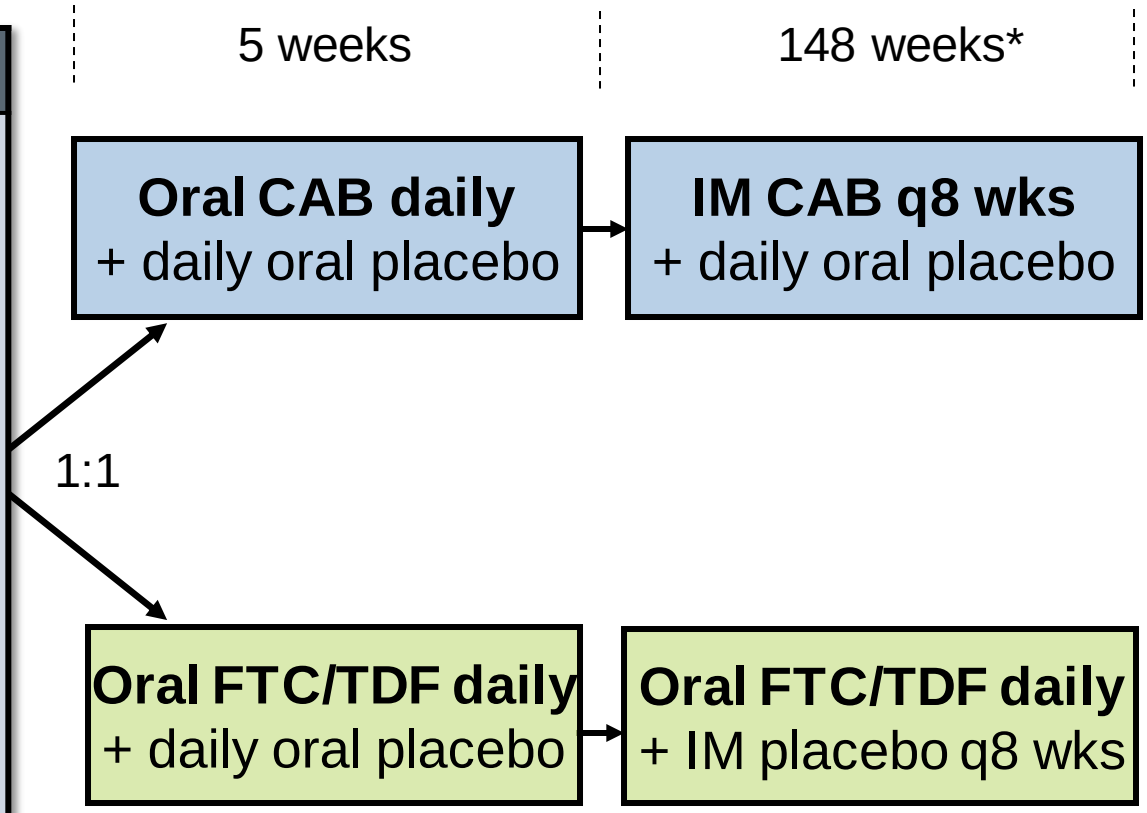
Slide courtesy of Dr. Raphael Landovitz, UCLA

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



*Followed by 48 weeks oral FTC/TDF daily

Source: https://www.hptn.org

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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

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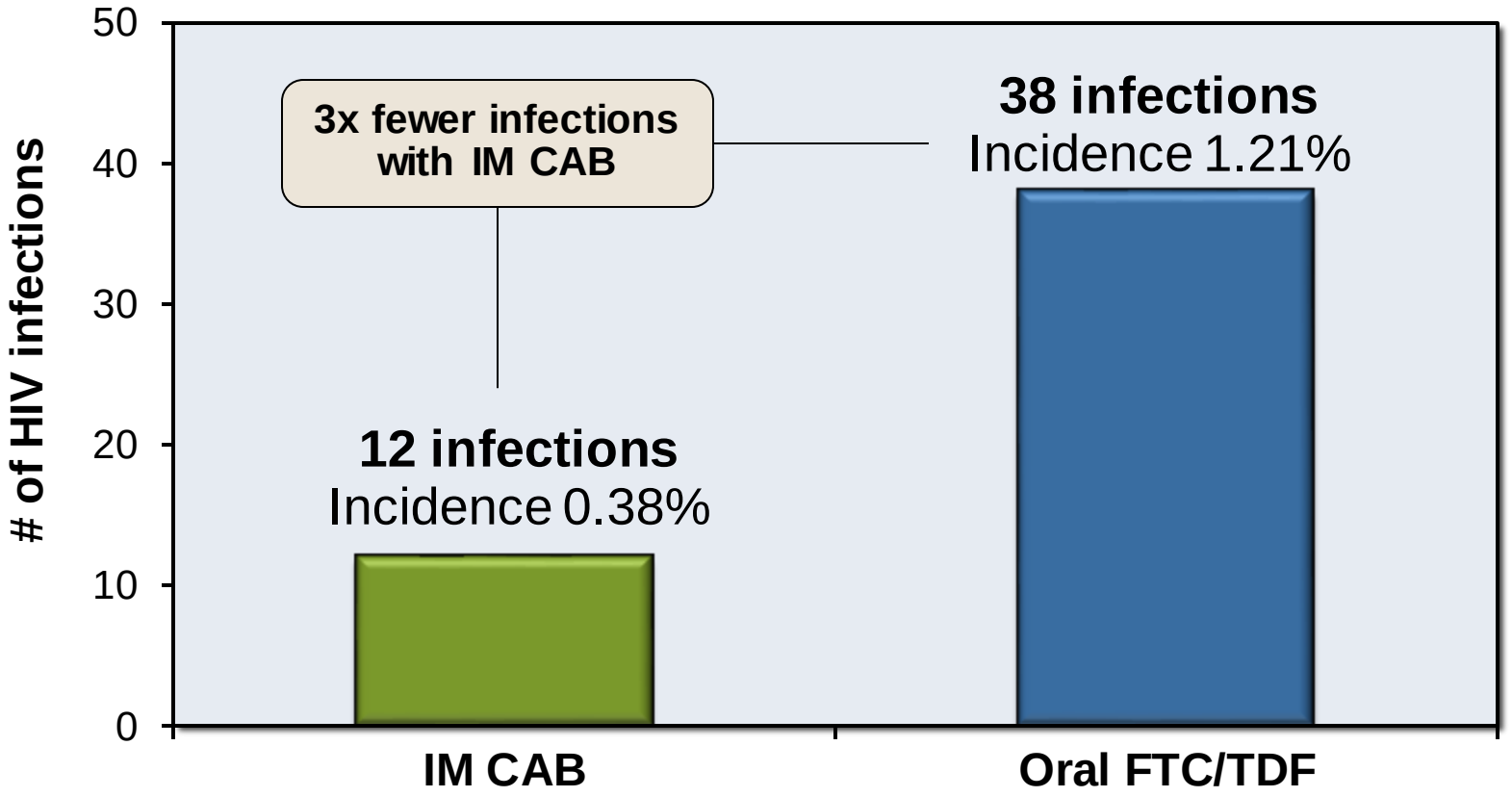
IM CAB Every 2 Months vs Oral Daily FTC/TDF for HIV PrEP
HPTN 083: Results



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

Source: https://www.hptn.org

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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

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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)

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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

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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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AETC AIDS Education & Training Center Program Mountain West