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

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:
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?
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

ClinicalTrials.gov Identifier: NCT02720094

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

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.

**5 weeks**

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

**148 weeks**

- IM CAB q8 wks + daily oral placebo
- 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

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
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)
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
• 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%
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.

The content in this presentation are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, HRSA, HHS, or the U.S. Government.