IM Cabotegravir versus TDF-FTC for HIV PrEP for MSM and TGW

HPTN 083
IM Cabotegravir versus TDF-FTC for HIV PrEP for MSM and TGW

HPTN 083: Study Design

• **Background**: Phase 2b/3, double-blind, randomized, multinational trial to assess efficacy of long-acting IM cabotegravir (CAB) compared to daily oral tenofovir DF-emtricitabine (TDF-FTC) for HIV PrEP for men who have sex with men (MSM) and transgender women

• **Setting**
  - 43 global sites

• **Inclusion Criteria**
  - Adult (≥18 years) cisgender MSM and transgender women who have sex with men
  - Substantial HIV risk*
  - Negative HIV serologic test at enrollment and negative HIV RNA ≤14 days before trial entry
  - Generally good health and CrCl 60 mL/min
  - HBsAg negative and HCV antibody negative
  - No contraindications to gluteal injections
  - No injection drug use within 90 days of trial entry

*Condomless receptive anal intercourse; >5 sex partners, stimulant use, rectal/urethral STI or syphilis ≤6 months; SexPro Score <16 (U.S. only)

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Step 1
- Oral TDF-FTC Placebo Daily
- Oral TDF-FTC Placebo Daily
- Oral TDF-FTC Placebo Daily

Oral CAB 30 mg Daily

Step 2
- Oral TDF-FTC Placebo Daily
- Oral TDF-FTC Placebo Daily
- Oral TDF-FTC Placebo Daily

IM CAB 600 mg
- Weeks 5, 9, and every 8 weeks thereafter

Step 3
- Oral TDF-FTC Daily
- Oral TDF-FTC Daily
- Oral TDF-FTC Daily

Oral CAB Placebo Daily
- Weeks 5, 9, and every 8 weeks thereafter

Participants Randomized
n = 4,570

**HPTN 083: Selected Baseline Demographics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 4,566)</th>
<th>Cabotegravir (n = 2,282)</th>
<th>TDF-FTC (n = 2,284)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisgender MSM, n (%)</td>
<td>3,992 (87.4)</td>
<td>2,013 (88.2)</td>
<td>1,979 (86.6)</td>
</tr>
<tr>
<td>Transgender women, n (%)</td>
<td>570 (12.5)</td>
<td>266 (11.7)</td>
<td>304 (13.3)</td>
</tr>
<tr>
<td>Median age (IQR), years, n (%)</td>
<td>26 (22-32)</td>
<td>26 (22-32)</td>
<td>26 (22-32)</td>
</tr>
<tr>
<td>Black race, United States, n (%)</td>
<td>845 (49.8)</td>
<td>411 (48.4)</td>
<td>434 (51.1)</td>
</tr>
<tr>
<td>Geographic region, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States, n (%)</td>
<td>1,698 (37.2)</td>
<td>849 (37.2)</td>
<td>849 (37.2)</td>
</tr>
<tr>
<td>Latin America, n (%)</td>
<td>1,964 (43.0)</td>
<td>980 (42.9)</td>
<td>984 (43.2)</td>
</tr>
<tr>
<td>Asia, n (%)</td>
<td>752 (16.5)</td>
<td>375 (16.5)</td>
<td>377 (16.5)</td>
</tr>
<tr>
<td>Africa, n (%)</td>
<td>152 (3.3)</td>
<td>78 (3.4)</td>
<td>74 (3.2)</td>
</tr>
</tbody>
</table>

*Abbreviations: MSM = men who have sex with men; IQR = interquartile range

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HPTN 083: Results

Number of HIV Infections (After Enrollment)

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Risk Reduction in HIV Infections (After Enrollment)

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Cumulative HIV Incidence (After Enrollment)

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HPTN 083: Results

• When did incident HIV infections occur in CAB arm?
  – 3 during oral lead-in
  – 5 after “prolonged hiatus” from IM CAB
  – 5 during continuous CAB administration

• Were drug levels adequate in TDF-FTC arm?
  – Random sample of 372 participants:
    • 87% detectable plasma tenofovir level
    • 75% levels correlated with high-level protection
    • ≈70% levels suggestive of >4 doses/week (by dried blood spot)

IM Cabotegravir versus TDF-FTC for HIV PrEP for MSM and TGW
HPTN 083: Cabotegravir Injection Site Reactions

• **Type and Severity of Injection-Site Reactions**
  – Most common: pain and tenderness
  – 2.4% chose to discontinue study due to injection reaction

• **Onset**
  – Reactions typically began 1 day after injection

• **Duration**
  – Reactions typically lasted 3-4 days after injection

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HPTN 083: Cabotegravir Injection Site Reactions

IM Cabotegravir versus TDF-FTC for HIV PrEP for MSM and TGW
HPTN 083: Results: Resistance with Cabotegravir

• INSTI Resistance in Cabotegravir Group
  – 1 at baseline; 4 with incident HIV infections
  – No resistance documented after last injection during “tail phase”

IM Cabotegravir versus TDF-FTC for HIV PrEP for MSM and TGW
HPTN 083: Weight Gain

**Conclusions**: Long-acting cabotegravir was superior to daily oral Tenofovir DF–emtricitabine in preventing HIV infection among men who have sex with men and transgender women.

The National HIV Curriculum is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $1,332,044 with 0% financed with non-governmental sources. The contents 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. For more information, please visit HRSA.gov. This project is led by the University of Washington’s Infectious Diseases Education and Assessment (IDEA) Program.