Cabotegravir for HIV PrEP

Oral Cabotegravir (Optional)

Oral Cabotegravir
30 mg
INSTI

Cabotegravir Injectable (IM)

Cabotegravir (200 mg/mL)
600 mg (3 mL)
INSTI

December 2021: FDA approved as HIV PrEP for at-risk adults and adolescents weighing ≥35 kilograms (77 pounds)

Source: Cabotegravir Prescribing Information.
Cabotegravir Dosing with Renal or Hepatic Impairment

**Dosing with Renal Insufficiency**
- Mild (CrCl ≥60 to <90 mL/min): no adjustment
- Moderate (CrCl ≥30 to <60 mL/min): no adjustment
- Severe (CrCl 15 to <30 mL/min) or ESRD (<15 mL/min): increased monitoring for adverse effects is recommended
- Dialysis: not expected to alter cabotegravir levels

**Dosing with Hepatic Impairment**
- Mild-to-Moderate (Child A or B): no dose adjustment
- Severe (Child C): unknown

Source: Cabotegravir Prescribing Information.
Cabotegravir for HIV PrEP: Prescribing Information

**Lead-In**

[OPTIONAL]

- ≥28 days
- 1 Month
- 2 Months
- 2 Months
- 2 Months
- 2 Months...

**Cabotegravir Injections**

- Cabotegravir 30 mg daily
- Cabotegravir 600 mg (3 mL) IM

Source: Based on Cabotegravir Prescribing Information. Illustration: David H. Spach, MD
Cabotegravir for HIV PrEP: Tail Phase Recommendations

- Consider alternative forms of PrEP after stopping cabotegravir if at continuing risk of acquiring HIV-1
- Start within 2 months of the final cabotegravir injection

Source: Based on Cabotegravir Prescribing Information. Illustration: David H. Spach, MD
If PrEP indicated, prescribe TDF-FTC or TAF-FTC within 8 weeks of stopping cabotegravir

• Continue follow-up visits quarterly for 12 months
Cabotegravir Baseline Laboratory Monitoring

- **Baseline Laboratory Tests Indicated Prior to Starting Cabotegravir:**
  - HIV RNA (within 1 week prior to initiation visit)
  - HIV-1/2 antigen-antibody assay
  - STI testing (syphilis, gonorrhea, chlamydia)

- **Baseline Laboratory Tests NOT Indicated Prior to Starting Cabotegravir:**
  - Serum creatinine (eCrCl)
  - Hepatitis B serology (HBsAg, anti-HBs, anti-HBc)*
  - Lipid panels
  - Liver function tests

*Note: if person has not previously received HBV immunization, obtaining hepatitis B serologic testing should be done as general health management to determine if hepatitis B vaccine series indicated and to screen for active hepatitis B infection..
2021 CDC PrEP Guidelines
Cabotegravir for HIV PrEP: Monitoring on Cabotegravir

Cabotegravir Injections

- Month 1: HIV Ag/Ab, HIV RNA
- Month 3: HIV Ag/Ab, HIV RNA, STI Screen*
- Month 5: HIV Ag/Ab, HIV RNA
- Month 7: HIV Ag/Ab, HIV RNA, STI Screen^*
- Month 9: HIV Ag/Ab, HIV RNA

* Bacterial STI screening for men who have sex with men and transgender women who have sex with men (every 4 months)
^ Bacterial STI screening for heterosexually active women and men (syphilis, gonorrhea, chlamydia every 6 months)

Source: CDC Preexposure Prophylaxis for the Prevention of HIV Infection in the U.S.– 2021 Update Clinical Practice Guideline
Cabotegravir (long-acting injectable) for HIV PrEP
Summary of Key Phase 3 Studies

• HPTN 083: Cabotegravir versus TDF-FTC for MSM and TGW
• HPTN 084: Cabotegravir versus TDF-FTC for Cisgender women

Abbreviations: HPTN = HIV Prevention Trials Network; TDF-FTC = tenofovir DF-emtricitabine; MSM = men who have sex with men; TGW = transgender women
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)

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

**Step 1**
- Oral CAB 30 mg Daily
- Oral CAB Placebo Daily

**Step 2**
- IM CAB 600 mg Weeks 5, 9, and every 8 weeks thereafter
- Oral TDF-FTC Placebo Daily

**Step 3**
- Oral TDF-FTC Placebo Daily
- Oral TDF-FTC Daily
- IM CAB Placebo Weekly 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*

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

Number of HIV Infections (After Enrollment)

<table>
<thead>
<tr>
<th></th>
<th>Number of HIV Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM Cabotegravir</td>
<td>13</td>
</tr>
<tr>
<td>Oral Tenofovir DF-Emtricitabine</td>
<td>39</td>
</tr>
</tbody>
</table>

P = 0.0005

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

HPTN 083: Results

Risk Reduction in HIV Infections (After Enrollment)

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

Cumulative HIV Incidence (After Enrollment)

• 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)
**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

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

HPTN 083: Cabotegravir Injection Site Reactions

Participants with ISRs (%)

Cabotegravir Injections

• 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

<table>
<thead>
<tr>
<th>Time Period</th>
<th>IM Cabotegravir</th>
<th>Oral Tenofovir DF-Emtricitabine</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks 0-105</td>
<td>1.23</td>
<td>0.37</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Weeks 0-40</td>
<td>1.26</td>
<td>-0.50</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Weeks 40-105</td>
<td>1.11</td>
<td>1.19</td>
<td>0.93</td>
</tr>
</tbody>
</table>

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.
IM Cabotegravir vs. TDF-FTC for PrEP in Cisgender Women

HPTN 084
IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Study Design

• **Background**: Phase 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 cisgender women (assigned female sex at birth)

• **Setting**
  – 20 sites in 7 countries in Sub-Saharan Africa

• **Inclusion Criteria**
  – Cisgender women (assigned female sex at birth) 18-45 years of age
  – Sexually active (e.g. vaginal sex on ≥2 separate days in the 30 days prior to screening)
  – HBsAg-negative and willing to receive hepatitis B vaccination
  – HCV antibody negative
  – No contraindications to gluteal injections
  – Creatinine clearance of greater than or equal to 60 mL/min
  – ALT <2 x upper limit of normal (ULN) and total bilirubin ≤ 2.5 x ULN
  – Excluded if pregnant or breastfeeding

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Study Design

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Cabotegravir (n = 1,614)</th>
<th>TDF-FTC (n = 1,610)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Age &lt;25 years, n (%)</td>
<td>814 (50.4%)</td>
<td>816 (50.7%)</td>
</tr>
<tr>
<td>Black/African race, n (%)</td>
<td>1,569 (97.2%)</td>
<td>1,554 (96.5%)</td>
</tr>
<tr>
<td>Sexual activity in past month (reported)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;2 sex partners, n (%)</td>
<td>878/1,609 (54.5%)</td>
<td>877/1,609 (54.8%)</td>
</tr>
<tr>
<td>Transactional sex, n (%)</td>
<td>658/1,609 (40.9%)</td>
<td>655/1,600 (40.9%)</td>
</tr>
<tr>
<td>Partner HIV(+) or unknown, n (%)</td>
<td>542/1,609 (33.7%)</td>
<td>558/1,600 (34.9%)</td>
</tr>
<tr>
<td>Anal sex, n (%)</td>
<td>90/1,609 (5.6%)</td>
<td>95/1,600 (5.9%)</td>
</tr>
</tbody>
</table>

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Results

Number of HIV Infections: Risk Reduction

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Results

Number of HIV Infections

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Results

Number of HIV Infections: Risk Reduction

IM Cabotegravir versus TDF-FTC for PrEP in Cisgender Women
HPTN 084: Results

HIV Incidence

<table>
<thead>
<tr>
<th>HIV Incidence (per 100 person years)</th>
<th>IM Cabotegravir</th>
<th>Oral Tenofovir DF-Emtricitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.20</td>
<td>4/1956</td>
<td>36/1942</td>
</tr>
</tbody>
</table>

P < 0.0001

**Interpretation**: Although both products for HIV prevention were generally safe, well tolerated, and effective, cabotegravir was superior to TDF-FTC in preventing HIV infection in women.
IM Cabotegravir Tail-Phase Safety, Tolerability, and Pharmacokinetics

HPTN 077
Cabotegravir Levels After Last Dose of Cabotegravir

Patients with Detectable Plasma Cabotegravir (%)

Weeks after Last Cabotegravir Injection

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