CAB LA FOR HIV PREVENTION IN AFRICAN CISGENDER FEMALE ADOLESCENTS (HPTN 084-01)


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Disclosure: None
To the brave young participants, and their parents/guardians, who agreed to join this study and made it such a success…

THANK YOU!
Background

• Preventing HIV among key populations, especially adolescent girls and young women (AGYW) in Africa and sexual and gender minority youth globally, is critical to controlling the HIV pandemic.

• Despite global guidelines recommending oral PrEP for key youth populations, profound inequalities in PrEP access as well as challenges with adherence and persistence.

• Long-acting cabotegravir (CAB LA) has been found to be highly effective for preventing HIV among cisgender sexual minority men and transgender women (HPTN 083) as well as cisgender women (HPTN 084).

• HPTN 084-01 was a single arm, open label, Phase 2b safety study of CAB LA among African cisgender adolescent females.
Objectives

Primary
• To evaluate the safety, tolerability and acceptability of CAB LA in healthy, HIV uninfected female adolescents aged below 18 years

Secondary
• To examine adherence to, and timeliness of, injections over time among adolescent participants provided CAB LA and information regarding its safety and efficacy
• To examine patterns of sexual risk behavior over time among adolescent participants provided CAB LA and information regarding its safety and efficacy
• To characterize the pharmacokinetics of CAB LA in adolescents
Inclusion Criteria

• Assigned female at birth
• Below 18 years of age
• Body weight ≥ 35 kg (72 lbs)
• Self-reported sexual activity with a male (oral, anal or vaginal) in the past 12 months
• Negative pregnancy test, not breastfeeding, and willing to use a reliable form of long-acting contraception
• In generally good health (including laboratory evidence)
• Willing to provide written informed assent/consent for the study and/or able to obtain written parental/guardian informed consent
**Study Flow**

**Step 1**: Oral CAB 30 mg QD

**Step 2**: IM injections of 3 mL (600mg) administered in the gluteal muscle

**Step 3**: Oral TDF/FTC (300mg/200mg) QD or move to 084 OLE for CAB LA

* This presentation covers Steps 1 & 2

**Study Product**

- **Step 1**: Oral CAB 30 mg QD
- **Step 2**: IM injections of 3 mL (600mg) administered in the gluteal muscle
- **Step 3**: Oral TDF/FTC (300mg/200mg) QD or move to 084 OLE for CAB LA
Study Sites

Uganda (Kampala; MU-JHU Research Collaboration CRS)

Zimbabwe (Harare; Spilhaus CRS)

South Africa (Johannesburg; Ward 21 CRS)

Accrual completed in 9 months - - 3 months ahead of schedule!
69 Participants Screened

55 Participants Enrolled

Reasons for Screen Failure

- Pregnant or BF – 4
- Laboratory – 3
- HIV positive – 1
- Refused LARC – 1
- Not sexually active – 1
- Unwillingness – 2
- Other medical/social reason - 2

55 entered Step 1 (Oral Phase)

53 entered Step 2 (Injection Phase)

52 entered Step 3 (Follow-up Phase)

Step 1 Discontinuations = 2
- 1 Grade 3 increased alanine aminotransferase (not related)
- 1 Grade 3 increased lipase (not related)

Step 2 Discontinuations = 1
- Pregnancy; ultimately entered HPTN 084 OLE

4 chose TDF/FTC

48 chose CAB-LA

95% retention through Step 2
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (range)</td>
<td>16 (12-17) years</td>
</tr>
<tr>
<td>Black African race</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td></td>
</tr>
<tr>
<td>35 to &lt; 50 kg</td>
<td>27%</td>
</tr>
<tr>
<td>≥ 50 kg</td>
<td>73%</td>
</tr>
<tr>
<td><strong>Sexually Transmitted Infections</strong></td>
<td></td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>7%</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>31%</td>
</tr>
<tr>
<td>At least one sex partner living with HIV</td>
<td>25%</td>
</tr>
<tr>
<td>Median episodes vaginal sex past month</td>
<td>2</td>
</tr>
<tr>
<td>Anal sex past month (yes)</td>
<td>5%</td>
</tr>
<tr>
<td>Transactional sex past month (yes)</td>
<td>22%</td>
</tr>
<tr>
<td>Significant depressive symptoms (CES-D-10)</td>
<td>36%</td>
</tr>
</tbody>
</table>
Safety

- No product related SAEs
- No product discontinuations due to AEs
- No incident HIV infections
- No events of weight gain, hepatotoxicity, hypersensitivity, rash, seizures or pancreatitis

<table>
<thead>
<tr>
<th>AESI in Steps 1&amp;2</th>
<th># of pts</th>
<th>Severity (# of pts)</th>
<th>Detail</th>
</tr>
</thead>
</table>
| CrCl decreased   | 41       | Grade 2 – 39  
Grade 3 – 2   | Resolved without intervention |
| Blood glucose increased | 22 | Grade 1 – 21  
Grade 2 – 1 | Resolved without intervention |
| Blood creatinine increased | 9  | Grade 1 – 1  
Grade 2 – 6  
Grade 3 – 2 | Resolved without intervention |
| Neuropsychiatric events | 3  | Grade 1 – 1  
Grade 2 – 1  
Grade 4 – 1 | Depressive symptoms  
Anxiety (stress)  
Suicidal behavior/attempt  
**All resolved with counseling** |
| Rhabdomyolysis   | 1        | Grade 2           | Myalgia resolved |
Tolerability – Injection Site Reactions (ISR)

- No participants (n=53) discontinued early due to intolerability
- Most common ISR was injection site pain followed by induration and swelling

**Percentage of Participants Reporting any ISR by Week and Grade**

<table>
<thead>
<tr>
<th>Week</th>
<th>Any ISR</th>
<th>Grade 2 ISR</th>
<th>Grade 3 ISR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 5</td>
<td>17%</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>Week 9</td>
<td>8%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Week 17</td>
<td>2%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Week 25</td>
<td>2%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Week 33</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Adherence

Oral CAB Adherence (pill count)

-Week 2: 20% 100%, 60% 90-99%, 20% 80-89%
-Week 4: 30% 100%, 70% 90-99%, 10% 80-89%

Injection Adherence

-Week 5: 53 (n=53) On Time
-Week 9: 52 (n=53) On Time
-Week 17: 53 (n=53) On Time
-Week 25: 52 (n=53) On Time
-Week 33: 50 (n=53) On Time

Percentage of pills taken:
100% 90-99% 80-89% 75-79% <75%
### Acceptability – Week 17 (after 3 injections)

#### What do you like about an injectable method?

<table>
<thead>
<tr>
<th>Feature</th>
<th>Favorability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protects against HIV</td>
<td>54.7%</td>
</tr>
<tr>
<td>Easier to use than other methods</td>
<td>41.5%</td>
</tr>
<tr>
<td>Longer-term protection than other methods</td>
<td>22.6%</td>
</tr>
<tr>
<td>Can be used discreetly</td>
<td>18.9%</td>
</tr>
<tr>
<td>Administered by healthcare professional</td>
<td>9.4%</td>
</tr>
<tr>
<td>Doesn’t interrupt sex</td>
<td>9.4%</td>
</tr>
<tr>
<td>Nothing</td>
<td>7.5%</td>
</tr>
</tbody>
</table>

#### What concerns do you have about an injectable method?

<table>
<thead>
<tr>
<th>Concern</th>
<th>Favorability</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>35.8%</td>
</tr>
<tr>
<td>May be painful</td>
<td>28.3%</td>
</tr>
<tr>
<td>May cause harmful side effects</td>
<td>18.9%</td>
</tr>
<tr>
<td>Once injected, it cannot be reversed</td>
<td>13.2%</td>
</tr>
<tr>
<td>May not protect against HIV</td>
<td>11.3%</td>
</tr>
<tr>
<td>Cannot be used discreetly</td>
<td>5.7%</td>
</tr>
<tr>
<td>May not be affordable</td>
<td>1.9%</td>
</tr>
</tbody>
</table>
Conclusions

• It is feasible to enroll sexually-active adolescents into biomedical HIV prevention trials, with parental/guardian consent

• Interest in a long-acting HIV prevention product was high among cisgender AGYW under the age of 18

• Adherence to the injection visits was exceptional

• CAB LA was found to be safe and tolerable, with no discontinuations of product due to adverse events

• Participants found CAB LA to be acceptable and expressed interest in future use

• Most participants (92%) chose to continue CAB LA over TDF/FTC when given a choice
A BIG THANK YOU to all of the HPTN 084-01 participants, their families, and the communities that support them for their commitment to the study and to the site staff for their dedication to study implementation!

**Acknowledgments**

**Sponsor**

- Overall support for the HIV Prevention Trials Network (HPTN) is provided by the National Institute of Allergy and Infectious Diseases (NIAID), Office of the Director (OD), National Institutes of Health (NIH), National Institute on Drug Abuse (NIDA), and the National Institute of Mental Health (NIMH) and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) under Award Numbers UM1AI068619-15 (HPTN Leadership and Operations Center), UM1AI068617-15 (HPTN Statistical and Data Management Center), and UM1AI068613-15 (HPTN Laboratory Center).
- HPTN 084-01 is also co-funded by the Bill & Melinda Gates Foundation (BMGF) and support is provided by Viiv Healthcare.
- The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

**DAIDS**

- Adeola Adeyeye
- Hans Spiegel
- Carl Dieffenbach
- Sheryl Zwerski
- Melissa Kin
- Katie Shin
- Irene Rwakazina
- Usma Sharma
- Judi Miller
- Roberta Black

**Pharmaceutical Support**

- Viiv Healthcare

**HIV Prevention Trials Network (HPTN)**

- Laboratory Center (Johns Hopkins University)
- Statistical Center for HIV/AIDS Research and Prevention (SCHARP), Fred Hutchinson Cancer Research Center
- Leadership and Operations Center, FHI 360
- HPTN Leadership

**HPTN Leadership**

- Myron Cohen
- Wafaa El-Sadr
- Deborah Donnell
- Sue Eshleman
- Nirupama Sista
- Kathy Hinson
- Beth Farrell

**Additional Support**

- Bill & Melinda Gates Foundation
Acknowledgments

Leadership & Operations (LOC)
• Erica Hamilton
• Scott Rose
• Amber Babinec
• Gabriela Salinas-Jimenez
• Tanette Headen

Study Team
• Marcus Bryan
• Rhonda White
• Molly Dyer

Community Team
• Laura Long
• Sam Alvarado
• Eric Miller
• Kevin Bokoch

Communications Team
• Julie Ngo
• Lynda Emel
• James Hughes
• Sahar Zangeneh
• Brett Hanscom
• Jennifer Schille

Finance Team
• Sarah Stone
• Gloria Pherribo
• Priti Patel

HPTN Lab Center (LC)
• Mark Marzinke
• Estelle Piwowar-Manning
• Yaw Agyei
• Ethel Weld

HPTN Statistical & Data Management Center (SDMC)
• Aida Asmelesh (Clinical Monitoring Committee)
• Kate MacQueen (HPTN Ethics Working Group)
• Linda-Gail Bekker (Protocol Team Member)
• Raphael J. Landovitz (Protocol Team Member)

Sites (Investigator of Record/PI, Sub-Investigators, Study Coordinators)
Ward 21 CRS (South Africa):
• Sinead Delaney-Moretwe
• Carrie-Anne Mathew
• Elizabeth Helena Roos
• Ishana Naidoo

MU-JHU CRS (Uganda):
• Brenda Gati Mirembe
• Clemensia Nakabiito
• Betty Kamira

Spilhaus CRS (Zimbabwe):
• Nyaradzo Mgodi
• Bekezela Siziba
• Eunice Tahuringana

Our Community Educators & Recruiters and CAB Members

Bill & Melinda Gates Foundation
• Lut Van Damme

VIIV Healthcare
• Cindy McCoig
• Alex Rinehart

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