Long acting injectable cabotegravir: updated efficacy and safety results from HPTN 084


on behalf of the HPTN 084 study team

AIDS 2022, Montreal, abstract #OALBX0108
HPTN 084 is an ongoing Phase 3 randomized, controlled trial that demonstrated the superiority of long-acting injectable cabotegravir (CAB) compared to daily oral TDF/FTC for HIV prevention in individuals assigned female at birth.

- HIV incidence CAB 0.20 vs TDF/FTC 1.85 per 100 py, HR 0.12; 95% CI 0.05 - 0.31

The blinded portion of the trial was stopped at a planned interim review in November 2020.

Participants were subsequently unblinded and continued on their original randomised study regimen pending a protocol amendment to offer open-label CAB.
Methods

• We report on HIV infections detected in the 12-month period following trial unblinding
  – 5 NOV 20 - 5 NOV 21, detected through 31 DEC 21
  – based on site and HPTN Laboratory Center testing.

• We estimated cumulative HIV incidence for the combined primary blinded and 12-month unblinded follow-up period, by study group.

• We report grade 2+ adverse events, injection site reactions, pregnancy incidence and outcomes for the 12-month post-unblinding period only.
HIV incidence: CAB vs TDF/FTC

Blinded period, through Nov 2020

HR 0.12; 95% CI 0.05 - 0.31

36 infections
1942 person years

4 infections
1956 person-years

CAB n=1614

TDF/FTC n=1610

Delany-Moretiwe, Lancet 2022
HIV incidence: CAB vs TDF/FTC

Combined blinded and unblinded period, through Dec 2021

HR 0.11; 95% CI 0.05 - 0.24

<table>
<thead>
<tr>
<th>Incidence rate per 100 PY</th>
<th>CAB n=1613*</th>
<th>TDF/FTC n=1610</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV incidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>56 infections</td>
<td>3292 person years</td>
<td>1,70</td>
</tr>
<tr>
<td>6 infections</td>
<td>3334 person years</td>
<td>0.18</td>
</tr>
</tbody>
</table>

*Excludes 1 baseline infection from the blinded period
Cabotegravir infections: blinded period

A. Before enrollment i.e. baseline
B. No recent CAB exposure
C. Before injections i.e. oral lead-in
D. On time CAB injections
Cabotegravir infections: cumulative

A1 7\% 4.6 3.8 7.7 8.5 7.7
B1 100\% 5 5.9
B2 100\% 5.1 52.2
B3 7\% 16 57
B4 0\% 5 4
C1 0\% 5.7 4.3 8.6 6 15.1 4.9 8.3 16.1
DX 100\% 5.4 5.7 4.3 8.6 6 15.1 4.9 8.3 16.1

A Before enrollment i.e. baseline
B No recent CAB exposure
C Before injections i.e. oral lead in
D On time CAB injections

Step 1: Oral CAB lead-in
Step 2: CAB LA 600 mg IM
Step 2: CAB LA injection > 2 week overdue
Step 3: Open-label TDF/FTC
Step 3: Overdue TDF/FTC dispensation
Annual follow-up

Percent adherence to oral lead-in
CAB LA 600 mg IM
Open-label TDF/FTC dispensed
First HIV positive visit
First site positive visit
Cabotegravir group infections: C1

- No quantifiable CAB during the oral lead-in
- Participant received first injection at first HIV positive visit
- Site-based testing did not detect infection at that visit
- Site detected infection 28 days later, when product was held
- Infection confirmed 4.5 months later
### Safety: Grade 2+ events, unblinded period

<table>
<thead>
<tr>
<th>Event</th>
<th>Total (n=2865)</th>
<th>CAB (n=1440)</th>
<th>TDF/FTC (n=1425)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Any Grade 2+ events</td>
<td>2391</td>
<td>1194</td>
<td>1197</td>
</tr>
<tr>
<td>Creatinine clearance decreased</td>
<td>1146</td>
<td>562</td>
<td>584</td>
</tr>
<tr>
<td>Chlamydia infection</td>
<td>453</td>
<td>225</td>
<td>228</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>385</td>
<td>211</td>
<td>174</td>
</tr>
<tr>
<td>Creatinine increased</td>
<td>338</td>
<td>168</td>
<td>170</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>258</td>
<td>140</td>
<td>118</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>213</td>
<td>115</td>
<td>98</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>184</td>
<td>89</td>
<td>95</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>165</td>
<td>94</td>
<td>71</td>
</tr>
<tr>
<td>Headache</td>
<td>164</td>
<td>91</td>
<td>73</td>
</tr>
<tr>
<td>Vulvovaginal candidiasis</td>
<td>157</td>
<td>78</td>
<td>79</td>
</tr>
<tr>
<td>Back pain</td>
<td>154</td>
<td>75</td>
<td>79</td>
</tr>
<tr>
<td>Blood glucose decreased</td>
<td>140</td>
<td>71</td>
<td>69</td>
</tr>
<tr>
<td>Abnormal uterine bleeding</td>
<td>123</td>
<td>59</td>
<td>64</td>
</tr>
<tr>
<td>Any SAE/EAE</td>
<td>48</td>
<td>26</td>
<td>22</td>
</tr>
<tr>
<td>Deaths</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>ISR - Grade 2+ (n=1318)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events reported at frequency ≥ 5%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

80% of Grade 2+ adverse events considered **unrelated** to study products, both arms
Pregnancy incidence: CAB vs TDF/FTC

<table>
<thead>
<tr>
<th></th>
<th>Blinded period</th>
<th>Unblinded period</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAB n=1614</td>
<td>1,5</td>
<td>2,6</td>
</tr>
<tr>
<td>TDF/FTC n=1610</td>
<td>1</td>
<td>3,8</td>
</tr>
<tr>
<td>Total n=3224</td>
<td>1,3</td>
<td>3,2</td>
</tr>
</tbody>
</table>

Cumulative confirmed pregnancies
- CAB: 63
- TDF/FTC: 69
- Total: 132

Cumulative person-years
- CAB: 3239.1
- TDF/FTC: 3238.3
- Total: 6477.3
## Cumulative pregnancy outcomes

<table>
<thead>
<tr>
<th></th>
<th>Total n=132</th>
<th>CAB n=63</th>
<th>TDF/FTC n=69</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>57</td>
<td>23</td>
<td>34</td>
</tr>
<tr>
<td>Known pregnancy outcomes*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live births</td>
<td>61</td>
<td>31</td>
<td>30</td>
</tr>
<tr>
<td>Pregnancy loss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;=37 weeks</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20-36 weeks</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>&lt;20 weeks**</td>
<td>13</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*includes multiple births  
**includes ectopic pregnancy, elective and spontaneous abortion
Conclusions

• CAB continues to be superior to TDF/FTC in preventing HIV infection in individuals assigned female at birth
  – 89% lower risk of HIV in CAB vs. TDF/FTC group
  – No new safety concerns identified
  – Open-label CAB offered to all in the HPTN 084 open-label extension

• Three additional CAB group infections were identified
  – All associated with poor/absent product use
  – no on-injection breakthrough infections observed

• Pregnancy incidence increased in the unblinded period
  – Confirms importance of ongoing evaluation of CAB safety and pharmacology in pregnancy during the HPTN 084 open-label extension

• CAB access should be a priority for populations with greatest need
Sponsor
• U.S. National Institute of Allergy and Infectious Diseases (NIAID), all components of the U.S. National Institutes of Health (NIH)

Additional funding support
• ViiV Healthcare
• Bill & Melinda Gates Foundation
• National Institutes of Mental Health

Pharmaceutical support
• Gilead Sciences
• ViiV Healthcare

HIV Prevention Trials Network
• Leadership and Operations Centre, FHI360
• Laboratory Centre (Johns Hopkins)
• Statistical Center for HIV/AIDS Research and Prevention, Fred Hutchinson Cancer Research Center
• HPTN Leadership

HPTN 084 Study team
• 20 sites in 7 countries in sub-Saharan Africa
• Community advisory boards and partners

… and our study participants!