Results from HPTN 083 and 084

Beatriz Grinsztejn MD, Ph.D
INSTITUTO NACIONAL DE INFECTOLOGIA
EVANDRO CHAGAS - FIOCRUZ
Rio de Janeiro, Brazil
HPTN 083 Study Design

**STEP 1**
- Every day for 5 weeks
- **Group A**: CAB
- **Group B**: Screening day and informed consent

**STEP 2**
- Weeks 5 and 9
- **Group A**: TDF/FTC
- **Group B**: CAB

**STEP 3**
- Every 2 months for approximately 3 years
- **Group A**: TDF/FTC
- **Group B**: CAB

**STEP 4**
- Every day for 1 year
- **Group A**: TDF/FTC
- **Group B**: CAB
- OPTIONAL
- Every day for 5 weeks
- **Group A**: TDF/FTC
- **Group B**: CAB
- 2 shots, 4 weeks apart then every 2 months

**STEP 5**
- OPEN LABEL EXTENSION
- **Group A**: TDF/FTC
- **Group B**: TDF/FTC

(20% Intralipid solution)
EFFICACY
HPTN 083 HIV Incidence: CAB vs. TDF/FTC

Combined blinded and unblinded period, through May 2021

HIV Incidence

- **CAB** (n=2244): 25 Infections (0.54), 4660 PY
- **TDF/FTC** (n=2248): 73 Infections (1.59), 4596 PY

Hazard Ratio (95% CI)

- **Favors CAB**
  - Hazard Ratio: 0.34
  - CI: 0.22 to 0.53
- **Favors TDF/FTC**
  - Hazard Ratio: 1.23
  - NI margin: 1.5

Open to Enrollment:
- 12-16-2016

CI, confidence interval
- 4.4 Years

Primary Analysis:
- 05-14-2020

Year 1 Unblinded Analysis:
- 05-14-2021

Landovitz, R. HIV Glasgow 2022.
HPTN 084 HIV Incidence: CAB vs. TDF/FTC

Combined blinded and unblinded period, through Dec 2021

HIV Incidence

<table>
<thead>
<tr>
<th>HIV Incidence Rate/100 PY</th>
<th>CAB</th>
<th>TDF/FTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Infections</td>
<td>0.18</td>
<td>0.05</td>
</tr>
<tr>
<td>56 Infections</td>
<td>1.70</td>
<td>0.11</td>
</tr>
<tr>
<td>3334 PY</td>
<td>3292 PY</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>0.05</th>
<th>0.24</th>
</tr>
</thead>
</table>

Hazard Ratio (95% CI)

- Favors CAB
- Favors TDF/FTC

0.75
1
2

CI, confidence interval

*Excludes 1 baseline infection from the blinded period

Delany-Morelwe, S et al. AIDS 2022. #OALBX0108
Long-acting cabotegravir is very effective at preventing HIV in MSM, TGW, and cisgender women

- 66% reduction in HIV infection when compared to MSM and TGW who were offered TDF/FTC
- 89% reduction in HIV infection when compared to cisgender women who were offered TDF/FTC
### HPTN 083 HIV Incidence by Subgroup CAB vs. TDF/FTC

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>CAB Events/PY (IR%)</th>
<th>TDF/FTC Events/PY (IR%)</th>
<th>HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td>11/2185 (0.50)</td>
<td>33/2114 (1.56)</td>
<td>0.32 (0.16, 0.63)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>2/1016 (0.20)</td>
<td>6/1071 (0.56)</td>
<td>0.33 (0.07, 1.61)</td>
</tr>
<tr>
<td><strong>Cohort</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGW</td>
<td>2/368 (0.54)</td>
<td>7/383 (1.83)</td>
<td>0.29 (0.06, 1.41)</td>
</tr>
<tr>
<td>MSM</td>
<td>11/2829 (0.39)</td>
<td>32/2800 (1.14)</td>
<td>0.34 (0.17, 0.67)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black/African-American</td>
<td>4/686 (0.58)</td>
<td>15/711 (2.11)</td>
<td>0.28 (0.10, 0.83)</td>
</tr>
<tr>
<td>Non-Black/African-American</td>
<td>0/837 (0.00)</td>
<td>5/790 (0.63)</td>
<td>0.09 (0.00, 2.06)</td>
</tr>
<tr>
<td><strong>Region</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>US</td>
<td>4/1523 (0.26)</td>
<td>20/1501 (1.33)</td>
<td>0.19 (0.07, 0.56)</td>
</tr>
<tr>
<td>Latin America</td>
<td>6/1016 (0.59)</td>
<td>11/1007 (1.09)</td>
<td>0.54 (0.20, 1.46)</td>
</tr>
<tr>
<td>Asia</td>
<td>2/569 (0.35)</td>
<td>6/580 (1.03)</td>
<td>0.34 (0.07, 1.66)</td>
</tr>
<tr>
<td>Africa</td>
<td>1/92 (1.08)</td>
<td>2/96 (2.08)</td>
<td>0.52 (0.05, 5.77)</td>
</tr>
</tbody>
</table>

Hazard ratios (95%CI)
### HPTN 084 HIV Incidence by Subgroup CAB vs. TDF/FTC

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>CAB Events/PY (IR%)</th>
<th>TDF/FTC Events/PY (IR%)</th>
<th>HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>4/1956 (0·20%)</td>
<td>36/1942 (1·85%)</td>
<td>0·12 (0·05–0·31)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 years</td>
<td>3/866 (0·35%)</td>
<td>20/851 (2·34%)</td>
<td>0·17 (0·05–0·54)</td>
</tr>
<tr>
<td>≥25 years</td>
<td>1/1090 (0·09%)</td>
<td>16/1091 (1·47%)</td>
<td>0·09 (0·02–0·49)</td>
</tr>
<tr>
<td>Contraceptive Method</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMPA</td>
<td>3/1009 (0·30%)</td>
<td>21/1000 (2·10%)</td>
<td>0·16 (0·05–0·53)</td>
</tr>
<tr>
<td>NET-EN</td>
<td>1/175 (0·57%)</td>
<td>6/182 (3·30%)</td>
<td>0·22 (0·03–1·48)</td>
</tr>
<tr>
<td>Implant</td>
<td>0</td>
<td>8/607 (1·32%)</td>
<td>0·06 (0·00–1·16)</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>1/152 (0·66%)</td>
<td>0·32 (0·01–9·89)</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30 kg/m²</td>
<td>4/1389 (0·29%)</td>
<td>27/1447 (1·87%)</td>
<td>0·16 (0·06–0·45)</td>
</tr>
<tr>
<td>&gt;30 kg/m²</td>
<td>0</td>
<td>9/495 (1·82%)</td>
<td>0·05 (0·00–0·96)</td>
</tr>
</tbody>
</table>

### Hazard ratios (95% CI)

<table>
<thead>
<tr>
<th>Hazard ratios (95% CI)</th>
<th>0.01</th>
<th>0.1</th>
<th>1</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

Long-acting cabotegravir is also very effective at preventing HIV in:

- Young individuals
- Black individuals
- Transgender women
- Individuals from various regions of the world
- Individuals using various contraceptive methods
- Individuals with higher BMIs
SAFETY
HPTN 083: Injection Site Reactions

Cabotegravir
- Mild (Grade 1)
- Moderate (Grade 2)
- Severe (Grade 3)

TDF/FTC
- Mild (Grade 1)
- Moderate (Grade 2)
- Severe (Grade 3)

<table>
<thead>
<tr>
<th>Injection Number</th>
<th>Cabotegravir, n</th>
<th>TDF/FTC, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2117</td>
<td>2081</td>
</tr>
<tr>
<td>2</td>
<td>2117</td>
<td>2081</td>
</tr>
<tr>
<td>3</td>
<td>2037</td>
<td>2014</td>
</tr>
<tr>
<td>4</td>
<td>1938</td>
<td>1940</td>
</tr>
<tr>
<td>5</td>
<td>1872</td>
<td>1869</td>
</tr>
<tr>
<td>6</td>
<td>1761</td>
<td>1760</td>
</tr>
<tr>
<td>7</td>
<td>1620</td>
<td>1606</td>
</tr>
<tr>
<td>8</td>
<td>1464</td>
<td>1463</td>
</tr>
<tr>
<td>9</td>
<td>1360</td>
<td>1355</td>
</tr>
<tr>
<td>10</td>
<td>1200</td>
<td>1193</td>
</tr>
<tr>
<td>11</td>
<td>1034</td>
<td>1037</td>
</tr>
<tr>
<td>12</td>
<td>877</td>
<td>903</td>
</tr>
<tr>
<td>13</td>
<td>744</td>
<td>760</td>
</tr>
<tr>
<td>14</td>
<td>604</td>
<td>596</td>
</tr>
<tr>
<td>15</td>
<td>465</td>
<td>482</td>
</tr>
<tr>
<td>16</td>
<td>372</td>
<td>370</td>
</tr>
<tr>
<td>17</td>
<td>298</td>
<td>288</td>
</tr>
<tr>
<td>18</td>
<td>234</td>
<td>220</td>
</tr>
<tr>
<td>19</td>
<td>168</td>
<td>146</td>
</tr>
<tr>
<td>OVERALL</td>
<td>57.7%</td>
<td>31.2%</td>
</tr>
</tbody>
</table>

Percentage of Participants Reporting an ISR

- Cabotegravir
- TDF/FTC

Landovitz RJ et al. NEJM 2021
21% participants had any ISR
- 32% CAB vs 9% TDF/FTC

4% participants had Grade 2+ ISR
- 7% CAB vs 1% TDF/FTC

Zero discontinuations d/t ISRs
The Bottom Line: Efficacy in specific populations

• Long-acting cabotegravir was safe and well tolerated

• The most common side effect was injection site reaction (ISR)
  o The majority were mild to moderate in severity
  o Reports of ISRs decreased over time
  o Very few ISRs led to the discontinuation of cabotegravir
• Data are still being collected on the safety of cabotegravir during pregnancy and breastfeeding

• To date, data does not suggest there are any safety concerns
FAILURES

HIV Testing Challenges
CAB-LA and HIV testing

CAB-LA suppresses viral replication and delays Ab production

- Rapid tests and Ag/Ab assays often fail to detect infection
- Supplemental Ab tests may be negative/indeterminate for many months
- HIV RNA levels often remain low or undetectable for long periods

Delayed detection of HIV infection

→ Delayed ART initiation
→ Emergence of INSTI resistance
CAB-LA and HIV testing

HPTN 083

Breakthrough infections:

- Very rare, but unexplained
- Total of 6 cases of breakthrough despite on-time injections
- **INSTI resistance:** all 6 cases

HPTN 084

Breakthrough infections:

- Very few infections, no true breakthrough case
- **No INSTI resistance detected**
Predicted effects of introduction of LA CAB PrEP in sub-Saharan Africa

IMPLEMENTATION
Translating evidence into action

Implementation Science

Scientific Evidence

Public Health implementation
Health as a right!

Countries and access to health care

Countries with free and universal health care
Countries with universal but not free health care
Countries with free but not universal healthcare
Countries with neither free nor universal healthcare
Unknown

Obrigada!

Beatriz Grinsztejn  gbeatriz@ini.fiocruz.br

www.fiocruz.br