Cabotegravir Maintains Protective Efficacy in the Setting of Bacterial STIs: HPTN 083

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Background

• Bacterial sexually transmitted infections (STIs) facilitate HIV transmission and acquisition
• Mucosal inflammation and genital ulcers can lower the barrier to HIV infection
• It is important to determine whether STIs diminish efficacy of each pre-exposure prophylaxis (PrEP) agent
Background

- Prior studies: STIs do not attenuate the protection offered by tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for HIV PrEP
- No such evaluations have been conducted for long-acting injectable cabotegravir (CAB-LA)
Background


Background
Methods

• Secondary analysis using data from HPTN 083 blinded period
• Serologic testing for syphilis and NAAT for rectal and urethral gonorrhea and chlamydia every 6 months, and with reported symptoms or exposures
• New syphilis infections were centrally adjudicated, as was date of first HIV diagnosis
Methods

- Two analyses were conducted:
  - Association between baseline characteristics and STI incidence
  - CAB-LA maintenance of efficacy in the setting of bacterial STIs
- STI Incidence analysis: excluded those without follow-up STI testing
- Efficacy analysis: included those with baseline STI testing but without follow-up STI testing
Methods: STI Incidence Analysis

• Incident STI infections per 100 person-years (PY), calculated from enrollment to last STI testing.
• Rates were calculated by demographic characteristic:
  • Age, race, ethnicity, gender cohort, education, treatment arm, drug use, alcohol use, region, condom usage, partner number, marital status, and baseline STI.
• Poisson regression to model the association between baseline factors and STI incidence.
Methods: Maintenance of Efficacy

• Cox proportional hazards modeling with STI status as a time-varying covariate
  • Potential interactions between STI status and the relative efficacy of CAB-LA vs. TDF/FTC
• Each time interval between STI tests was classified as “STI-positive” or “STI-negative”

We conducted a base case analysis and two sensitivity analyses
Methods: Maintenance of Efficacy

For the base case analysis, we considered intervals before and after each positive STI test as STI-positive
Methods: Maintenance of Efficacy

Sensitivity Analysis #1: Dichotomized participants as ever/never having an incident STI

Methods: Maintenance of Efficacy

Sensitivity Analysis #2: Carried STI positive status backwards to the last STI negative test

Results: STI incidence

Among 3859 participants, STIs were diagnosed in 1562 (40.5%), with multiple STIs reported for 691 (17.9%).

79% of STI diagnoses occurred in 25% of pts.

Overall STI Incidence and 95% Confidence Interval
- Overall: 50.7% (48.9, 52.6)
- CAB: 49.9% (47.3, 52.6)
- TDF/FTC: 51.6% (48.9, 54.3)

Results: STI Incidence Rates, n= 3859 participants

<table>
<thead>
<tr>
<th></th>
<th># Positive Tests</th>
<th>IR (per 100 PY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any STI</td>
<td>2819</td>
<td>50.7</td>
</tr>
<tr>
<td>Syphilis</td>
<td>923</td>
<td>16.7</td>
</tr>
<tr>
<td>Urogenital Gonorrhea</td>
<td>134</td>
<td>2.4</td>
</tr>
<tr>
<td>Urogenital Chlamydia</td>
<td>249</td>
<td>4.5</td>
</tr>
<tr>
<td>Rectal Gonorrhea</td>
<td>600</td>
<td>11.0</td>
</tr>
<tr>
<td>Rectal Chlamydia</td>
<td>913</td>
<td>16.7</td>
</tr>
</tbody>
</table>

Results: STI Incidence Rate by Subgroup

Results: STI Incidence Rate by Subgroup

Region
- United States: 41.5
- Latin America: 63.9
- Asia: 49.9
- Africa: 75

Age
- <30: 56.4
- ≥30: 40

Race, US
- Black: 50.1
- non-Black: 34.4

Ethnicity
- Hispanic/Latino: 57.4
- Not Hispanic/Latino: 47.1

Marital Status
- Married/Legal Partnership: 39.3
- Live with partner: 57.1
- Married/Legal Partnership: 49.2
- Have partner: 38.9

Baseline STI(s)
- No: 43.1
- Yes: 83.9

Education
- None: 57.1
- Primary: 65.8
- Secondary: 58.1
- Technical: 53.9
- College+: 48.1

Results: STI incidence

In the final multivariable model: only age, race, and baseline STI status were statistically significant at p<0.05

<table>
<thead>
<tr>
<th>Age (&lt;30: Ref.)</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>0.77 (0.70, 0.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>40-49</td>
<td>0.76 (0.65, 0.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>50-59</td>
<td>0.71 (0.58, 0.92)</td>
<td>0.009</td>
</tr>
<tr>
<td>60+</td>
<td>0.93 (0.48, 1.81)</td>
<td>0.84</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Region Specific Race</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia vs Africa</td>
<td>1.62 (0.39, 0.99)</td>
<td>0.43</td>
</tr>
<tr>
<td>US Black vs non-Black</td>
<td>1.37 (1.21, 1.55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA Black/Mixed vs Non-Black/Mixed/Native</td>
<td>1.26 (1.08, 1.46)</td>
<td>0.003</td>
</tr>
<tr>
<td>LA Native vs Non-Black/Mixed/Native</td>
<td>0.65 (0.56, 0.76)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Baseline STI status (No: Ref.)</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2.00 (1.653, 2.418)</td>
<td>&lt;0.001</td>
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</table>
Results: Maintenance of Efficacy

**BASE CASE MODEL**

- **p-value: 0.75**

<table>
<thead>
<tr>
<th></th>
<th>STI Absent</th>
<th>STI Present</th>
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<tbody>
<tr>
<td><strong>CAB</strong></td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>TDF/FTC</td>
<td>0.31 (0.13, 0.71)</td>
<td>0.37 (0.15, 0.95)</td>
</tr>
</tbody>
</table>

Results: Sensitivity Analyses

**BASE CASE MODEL**

- **p-value:** 0.75

**SENSITIVITY ANALYSIS #1**

- **p-value:** 0.90

**SENSITIVITY ANALYSIS #2**

- **p-value:** 0.48

Conclusions

- STI rates were high and concentrated among participants
- Factors associated with STIs were consistent with those reported in the literature, and not associated with study arm
- CAB-LA maintained robust protective efficacy in the setting of bacterial STIs

- These data may be helpful in guiding implementation of new biomedical STI prevention strategies
- CAB-LA maintained protective efficacy, and future PrEP agents should be similarly evaluated
- Continued innovation in STI prevention is critically needed

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Community Educators and Recruiters
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Our 43 sites in 7 countries

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