Results of the CAPRISA 004 trial of tenofovir gel

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# HIV prevalence in pregnant women in rural Vulindlela (2005-2008)

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>HIV Prev (%) (N=1237)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤16</td>
<td>10.6</td>
</tr>
<tr>
<td>17-18</td>
<td>21.3</td>
</tr>
<tr>
<td>19-20</td>
<td>33.0</td>
</tr>
<tr>
<td>21-22</td>
<td>44.3</td>
</tr>
<tr>
<td>23-24</td>
<td>51.1</td>
</tr>
</tbody>
</table>
CAPRISA 004 assessed the safety and effectiveness of tenofovir gel

- BAT 24 coitally-related gel use
  - Insert 1 gel up to 12 hours **Before** sex,
  - insert 1 gel as soon as possible within 12 hours **After** sex,
  - no more than **Two** doses in **24** hours
Double-blinded, randomized placebo-controlled proof-of-concept trial

Enrolled Eligible: 889

Tenofovir: 445

- 15 lost to follow up
- 8 terminated early

Retention: 94.8%

Completed study: 422

Placebo: 444

- 10 lost to follow up
- 12 terminated early
- 1 died

Completed study: 421
Effectiveness of tenofovir gel in preventing HIV infection

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td># HIV infections</td>
<td>38</td>
<td>60</td>
</tr>
<tr>
<td>Women-years (# women)</td>
<td>680.6 (445)</td>
<td>660.7 (444)</td>
</tr>
<tr>
<td>HIV incidence</td>
<td>5.6</td>
<td>9.1</td>
</tr>
</tbody>
</table>

(HIV incidence per 100 women-years)

Incidence rate ratio: 0.61 (CI: 0.4 to 0.94);  p = 0.017

39% lower HIV incidence in tenofovir gel group
Impact of adherence on effectiveness of tenofovir gel

<table>
<thead>
<tr>
<th></th>
<th># HIV</th>
<th>N</th>
<th>TFV</th>
<th>Placebo</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High adherers</strong> (&gt;80% gel adherence)</td>
<td>36</td>
<td>336</td>
<td>4.2</td>
<td>9.3</td>
<td>54%</td>
</tr>
<tr>
<td><strong>Intermediate adherers</strong> (50-80% adherence)</td>
<td>20</td>
<td>181</td>
<td>6.3</td>
<td>10.0</td>
<td>38%</td>
</tr>
<tr>
<td><strong>Low adherers</strong> (&lt;50% gel adherence)</td>
<td>41</td>
<td>367</td>
<td>6.2</td>
<td>8.6</td>
<td>28%</td>
</tr>
</tbody>
</table>
HSV-2 status at enrolment and study exit

Enrolled in HIV trial: 889 (CAPRISA 004)

At risk for HSV-2: 434

Tenofovir: 208

Placebo: 226

Completed study: 202

Completed study: 224

1 missing 454 HSV-2 positive

3 missing 3 equivocal exit results

1 missing 1 equivocal exit result
## Impact of tenofovir gel on HSV-2 incidence

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir gel n=202*</th>
<th>Placebo gel n=224*</th>
</tr>
</thead>
<tbody>
<tr>
<td># HSV-2 infections</td>
<td>29</td>
<td>58</td>
</tr>
<tr>
<td>Women-years of follow-up</td>
<td>292.3</td>
<td>287.3</td>
</tr>
<tr>
<td>HSV-2 incidence per 100wy (95% CI)</td>
<td>9.9 (6.6, 14.2)</td>
<td>20.2 (15.3, 26.1)</td>
</tr>
</tbody>
</table>

*Note: Excludes equivocal HSV-2 results at study exit

\[
\text{IRR} = 0.49 \quad (\text{CI}: 0.30, 0.78); \quad p = 0.003
\]

51% protection against HSV-2 by tenofovir gel (CI: 22%-70%)
Summary of the findings

• Proof of concept that tenofovir gel can prevent HIV infection in women
  ▪ 50% less HIV after 1 year of tenofovir gel use (p=0.007)
  ▪ 39% protection after 30 months of gel use (p=0.017)
  ▪ 54% effective in women using gel consistently (p=0.025)

• Proof of concept that tenofovir gel can prevent HSV-2 infection in women
  ▪ 51% reduction in HSV-2 (p=0.003)

• Safety
  ▪ No substantive safety concerns
  ▪ No tenofovir resistance identified
  ▪ No evidence of behavioral disinhibition
Comparison of HIV effectiveness: HIVNET 012 and CAPRISA 004

HIVNET 012 - nevirapine

CAPRISA 004 tenofovir gel

Study

PMTCT - HIVNET 012

Tenofovir gel - CAP 004

Tenofovir gel – high adherence
Tenofovir gel – medium adherence
Tenofovir gel – low adherence

Efficacy
Conclusions

1. Women, and young women in particular, bear the brunt of the HIV epidemic in Africa

2. Tenofovir gel potentially adds a new approach to HIV prevention as the first that can be used and controlled by women. It could help empower women to take control of their own risk of HIV infection.

3. The CAPRISA 004 study is the first step - additional studies are urgently needed to confirm and extend the findings of the CAPRISA 004 trial

4. Once confirmed and implemented, tenofovir gel has the potential to alter the HIV epidemic. It is estimated that this gel could prevent 1.3 million new HIV infections and over 800,000 deaths in South Africa alone.
Acknowledgements

- **Trial Oversight Committee:**
  - **CAPRISA:** Q Abdool Karim, SS Abdool Karim
  - **FHI:** W Cates, L Dorflinger, and D Taylor
  - **USAID:** L Claypool, J Manning, J Spieler
  - **CONRAD:** H Gabelnick
  - **LIFElab (TIA):** B Okole, C Montague
  - **Gilead Sciences:** J Rooney

- **DSMB members:** K Mayer (Chair), E Bukusi, K Dickson, C Lombard & S Self. Independent DSMB statistician: M Chen

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- **Study monitors:** S Combes, C. Katz, L McNeil & A Troxler, FHI

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