Pre-exposure prophylaxis for HIV in women: daily oral tenofovir, oral tenofovir-emtricitabine, or vaginal tenofovir gel in the VOICE Study (MTN 003)

Marrazzo JM, Ramjee G, Nair G, Palanee T, Mkhize B, Nakabiito C, Taljaard M, Piper J, Gomez K, Chirenje M, for the VOICE Team

Study funding: U.S. NIH NIAID, NICHD & NIMH UM1AI068633; UM1AI068615
The VOICE Study

- Phase 2B, randomized, double-blind, placebo-controlled, five-arm trial of daily use of the following for prevention of HIV acquisition in women:
  - Vaginal tenofovir (TFV) 1% gel (40 mg)
  - Oral tenofovir (TDF, 300 mg)
  - Oral tenofovir / emtricitabine (TDF / FTC; 300 mg / 200 mg)
VOICE Design

5,029 HIV- women

Vaginal sex in prior 3 months
Not pregnant or breastfeeding
Willing to use effective contraception

Randomized to once daily use

Oral TDF  Oral FTC/TDF  Oral Placebo  Vaginal TFV  Vaginal placebo

Monthly visits

Comprehensive HIV prevention counseling, condoms, contraception, pregnancy test, STI evaluation & treatment, provision of study product

1° endpoints: HIV infection, safety
Who were the 5,029 Women in VOICE?

- **UGANDA**: 322 participants
  - Makerere Univ./JHU, Kampala (1 site)

- **ZIMBABWE**: 630 participants
  - UZ-UCSF, Harare (1 site)
  - UZ-UCSF, Chitungwiza (2 sites)

- **SOUTH AFRICA**: 4,077 participants
  - **Durban Area**
    - Medical Research Council (7 sites)
    - CAPRISA eThekwini (1 site)
  - **Johannesburg Area**
    - WRHI (1 site)
    - PHRU Soweto (1 site)
  - **Klerksdorp Area**
    - Aurum Institute (1 site)
## Variation Across Countries

Women in the VOICE study were between 18-45 years old, but most were in their 20’s.

<table>
<thead>
<tr>
<th></th>
<th>South Africa</th>
<th>Uganda</th>
<th>Zim</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Average Age</strong></td>
<td>24.7</td>
<td>28.3</td>
<td>28.1</td>
</tr>
<tr>
<td><strong>Percentage younger than age 25</strong></td>
<td>55%</td>
<td>25%</td>
<td>26%</td>
</tr>
<tr>
<td><strong>Percentage who are married</strong></td>
<td>8%</td>
<td>50%</td>
<td>94%</td>
</tr>
<tr>
<td><strong>Education (≥ secondary school)</strong></td>
<td>54%</td>
<td>3%</td>
<td>60%</td>
</tr>
</tbody>
</table>
Key Findings from VOICE

- No product – tenofovir gel, oral tenofovir or oral Truvada – proven effective in preventing HIV
  - Most participants did not use daily as recommended
- Compared to older, married women, young single women less likely to use products and more likely to get HIV
  - New infections in young women more frequent than expected
  - Nearly 10 of every 100 women got HIV in 1 year at some South African sites
Daily Use Not Acceptable

- Results are disappointing but clear
  - Daily use (gel or tablet) is **not** the right approach for women like those in VOICE (mostly young and unmarried)

- We still need safe and effective HIV prevention methods that young, unmarried women will actually use
Researchers tested blood samples from 773 participants.

- Some blood samples had drug in them.
- Most blood samples that should have had drug in them did not (less than 1 out of 3 women had drug found in their blood).
- This was true for oral tenofovir, Truvada, and tenofovir gel groups.

These results indicate that most women did not use them daily as recommended.

Also, those least likely to use their products, single women under age 25, were also most likely to get HIV.
Incidence of HIV Acquisition

<table>
<thead>
<tr>
<th></th>
<th>South Africa</th>
<th>Uganda / Zimbabwe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age &lt;25 y</strong></td>
<td>8.7 (7.6, 10)</td>
<td>2.6 (1.1, 5.1)</td>
</tr>
<tr>
<td><strong>≥ 25 y</strong></td>
<td>4.7 (3.8, 5.8)</td>
<td>0.8 (0.4, 1.7)</td>
</tr>
<tr>
<td><strong>Married</strong></td>
<td>0.9 (0.2, 2.7)</td>
<td>0.9 (0.4, 1.7)</td>
</tr>
<tr>
<td><strong>Unmarried</strong></td>
<td>7.5 (6.6, 8.4)</td>
<td>2.8 (1.1, 5.7)</td>
</tr>
</tbody>
</table>

Incidence per 100-person-years (95% C.I)
Quality of the Study

- Most women came to their study visits and completed study procedures.
- Most women stayed in VOICE until they were scheduled to be finished coming to visits (good participant retention).
- Completion of study procedures and good retention are important for the quality of a study.
Product Safety

- No safety concerns were identified for any of the study products tested in the VOICE Study

- Based on findings from various types of exams
  - Physical exam
  - Pelvic exam
  - Laboratory test results
  - Other health outcomes
Results of Sub-Studies

- VOICE had three sub-studies:
  - VOICE-B – Effects of oral products on bone health
  - VOICE-C – Community factors and beliefs that can influence adherence
  - VOICE-D – Individual behaviors and attitudes about HIV risk and impact on adherence

- Results being analyzed separately
  - Final results of VOICE-C and -D expected mid-2013
  - Results of VOICE-B will be later in 2013 - participants are being followed until August 2013
Conclusions

- Incidence of HIV substantially higher than anticipated
- No study drug significantly reduced risk of HIV acquisition
- Adherence to study products was low, especially among younger, unmarried women
- Results consistent with Fem-PrEP
  - Consider PrEP agents / delivery systems that are long acting and require minimal daily adherence
- Understanding HIV risk perception and biomedical, social and cultural determinants of adherence in this high-risk population urgently needed
VOICE Study Team

- Protocol Co-Chairs: Mike Chirenje, Jeanne Marrazzo
  - Durban, S. Africa: Gita Ramjee, Marwah Jenneker, Yukteshwar Sookrajh, Shahnaaz Kadwa, Vimla Naicker, Linda Zako, Arendevi Pather, Nicola Coumi, Sarita Naidoo, Sharika Gappoo, Vijayanand Guddera, Shayhana Ganesh, Gonasagrie Nair, Kalendri Naidoo
  - Johannesburg, S. Africa: Thesla Palanee, Godpower Akpomiemie, Baningi Mkhize, Wilma Pelser, Ithabeleng Morojele
  - Klerksdorp, S. Africa: Marthinette Taljaard, Ronel Brown, Kathy Mngadi, Pearl Selepe
  - Kampala, Uganda: Clemensia Nakabiito, Flavia Matovu, Kenneth Kintu
  - Harare, Zimbabwe: Nyaradzo Mgodi, Tsitsi Magure, Margaret Mlingo, Petina Musara

- SCHARP: Barbra Richardson, Cliff Kelly, Benoit Masse, Karen Patterson, Missy Cianciola, Molly Swenson, James Dai, Holly Gundacker, Janne Abullarade, Jennifer Schille, Craig Silva, Della Wilson, Stacie Kentop, Jenny Tseng, Martha Doyle, Hongli Li, Jami Moksness, Joleen Borgerding, Sharavi Gandham, Kate Bader, Lynda McVarish

- FHI360: Kailazarid Gomez, Kristine Torjesen, Lisa Levy, Katie Schwartz, Ashley Mayo, Vivian Bragg, Ayana Moore, Katherine Richards, Stephanie Horn, Rhonda White

- MTN Network Lab: Ted Livant, Lorna Rabe, Yaw Agwei, Charlene Dezzutti, Urvi Parikh, Craig Hendrix, John Mellors

- NIH: Jeanna Piper, Roberta Black, Scharla Estep, Usha Sharma, Sheryl Zwerski (NIAID); Heather Watts (NICHD); Cynthia Grossman, Andrew Forsyth (NIMH)

- MTN core: Sharon Hillier, Ian McGowan, Lisa Noguchi, Ariane van der Straten, Barbara Mensch, Ross Cranston, Katie Bunge, Devika Singh, Sharon Riddler, Ken Ho, Cindy Jacobson, Lisa Rossi

- Gilead (oral study drug): Jim Rooney, Howard Jaffe, Rebecca Guzman and Farideh Said

- CONRAD (vaginal study drug): Jill Schwartz; Henry Gabelnick, Gustavo Doncel, David Friend
DISCUSSION

To ask a question

- Unmute your line by pressing *7 and ask it on the line (remute your line by pressing *6)
- Enter it into the chat box in ReadyTalk
- Email your question to avac@avac.org

For more information: www.avac.org/voice; www.prepwatch.org

Webinar recording will be available at www.avac.org/meetingreports