

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

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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 eThekweni (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.

	South Africa	Uganda	Zim
Average Age	24.7	28.3	28.1
Percentage younger than age 25	55%	25%	26%
Percentage who are married	8%	50%	94%
Education (\geq secondary school)	54%	3%	60%

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

Amount of Drug in Blood

- 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

	South Africa	Uganda / Zimbabwe
Age <25 y	8.7 (7.6, 10)	2.6 (1.1, 5.1)
≥ 25 y	4.7 (3.8, 5.8)	0.8 (0.4, 1.7)
Married	0.9 (0.2, 2.7)	0.9 (0.4, 1.7)
Unmarried	7.5 (6.6, 8.4)	2.8 (1.1, 5.7)

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, Yuktेशwar Sookrajh, Shahnaaz Kadwa, Vimla Naicker, Linda Zako, Arendevi Pather, Nicola Coumi, Sarita Naidoo, Sharika Gappoo, Vijayanand Guddera, Shayhana Ganesh, Gonasagrie Nair, Kalendri Naidoo
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- 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

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