VOICE Overview

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MTN-003 (VOICE) Summary

- Description: *Phase 2B Study of Tenofovir 1% Gel, Tenofovir Tablet and Truvada Tablet for the Prevention of HIV Infection in Women*
- Designed to Estimate:
  - Effectiveness of tenofovir gel compared with placebo
  - Effectiveness of oral tenofovir and oral Truvada compared with placebo
- Examine extended safety of the products
- **Secondary aims include:** adherence/behavioral, drug resistance, PK, delayed seroconversion
Behavioral Aims

- To evaluate:
  a) Adherence to daily product regimens
  b) Change in sexual behavior, condom use and vaginal practices
Locations & Procedures

- 3 Countries: Uganda, Zimbabwe, South Africa
- 15 sites
- 5 arm trial
- Study duration: 12 - 36 months on study product
- Monthly visits
Adherence in biomedical trials tends to be lower than desired:

- Self-report tends to produce high estimates of adherence (with FTF interview or ACASI)
- Clinic based product counts tend to be high
- But, drug detection suggests adherence is lower than any of these indicators
Adherence is Critical

- Differential effectiveness in as treated analyses suggest adherence is critical ... & lower than desired
- Partners PrEP:
  - 81% adherence 75%
- CAPRISA 004
  - Overall end study effectiveness: 39%
    - >80% Adherence 54%
    - 50-80% Adherence 38%
    - <50% Adherence 28%
- iPrEx
  - Overall end study effectiveness: 44%
    - >=90% Adherence 68%
    - 50-90% Adherence 34%
    - <50% Adherence 16%
VOICE: Post-DSMBs (Sept & Nov 2011)

- DSMB futility results: 3 arms discontinued early (N=3000)
- 2 arms continued (Truvada/placebo) until completion (N=2000)
VOICE Behavioral Components

- Behavioral & Adherence Assessments
  - CRFs
  - ACASI
  - Product counts

- Adherence Support Program
  - ASP
  - VASP (6/2011)
### Mode of Administration: Behavioral Questions in VOICE

<table>
<thead>
<tr>
<th>Behavioral questions</th>
<th>CRF (FTF interview)</th>
<th>ACASI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FREQUENCY</strong></td>
<td>Monthly + Quarterly</td>
<td>Quarterly/Annually</td>
</tr>
<tr>
<td>Vaginal sex</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Condom use</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Anal sex</td>
<td></td>
<td>●</td>
</tr>
<tr>
<td>Vaginal practices</td>
<td></td>
<td>●</td>
</tr>
<tr>
<td>Product use</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Adherence rating scale</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>
Anal Sex Questions

In the past 3 months how many times have you had anal sex? By anal sex we mean when a man puts his penis inside your anus.

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7 or more times</th>
</tr>
</thead>
</table>

Repeat | Question
Product Use Calendar Question

6 days ago (Tuesday), did you insert gel?

Yesterday: Yes
2 days ago: Yes
3 days ago: Yes
4 days ago: Yes
5 days ago: Yes
8 days ago: Yes

Repeat Question

Previous Next
<table>
<thead>
<tr>
<th>Original Adherence Counseling Approach (ASP)</th>
<th>New Adherence Counseling Approach (VASP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Used product count from pharmacists to inform the counseling session; reconciled product count and self-reported adherence.</td>
<td>• Counselors will <strong>NOT</strong> review product count prior to counseling session or probe about discrepancies in product count versus self report.</td>
</tr>
<tr>
<td>• Asked the participant how often she had been able to use the product and then based counseling on reported level of adherence.</td>
<td>• Counseling will focus on participant’s experiences using the product, and what makes using product easier or harder, regardless of how much she used it.</td>
</tr>
<tr>
<td>• Adherence plan/strategies based on overcoming <strong>barriers</strong> to product use.</td>
<td>• Adherence plan/strategies based on addressing <strong>adherence-related needs</strong>.</td>
</tr>
<tr>
<td>• Used reported adherence to determine the focus of the session (i.e. page 2 of the counseling worksheet options).</td>
<td>• All sessions will follow the same 8 steps, regardless of how much the participant has been using the study product.</td>
</tr>
<tr>
<td>• Reinforcement of product use instructions (10 key messages) by the <strong>adherence counselor</strong>.</td>
<td>• Product use instructions (10 key messages) removed from the counseling session.</td>
</tr>
<tr>
<td>• Positive reinforcement of good adherence.</td>
<td>• Maintain a neutral counseling approach.</td>
</tr>
<tr>
<td>• Goals focused on perfect adherence.</td>
<td>• Goals focused on making product use manageable.</td>
</tr>
</tbody>
</table>
## VOICE Adherence Support Program (VASP)

<table>
<thead>
<tr>
<th>Step</th>
<th>Process</th>
</tr>
</thead>
</table>
| 1    | **WELCOME**  
|      | Greet/Rapport; Thank participant; Check-in |
| 2    | **FRAME**  
|      | Explain purpose of discussion; Seek permission to continue discussion. |
| 3    | **EXPLORE**  
|      | Explore product use experiences (facilitators/challenges); Discuss efforts on strategies from last session. |
| 4    | **SUMMARIZE**  
|      | Summarize Context/Experiences |
| 5    | **IDENTIFY NEEDS**  
|      | Explore needs for adherence given experiences; What would make it easier? |
| 6    | **STRATEGIZE**  
|      | Explore how participant could increase ease/comfort/efficacy. |
| 7    | **NEGOTIATE**  
|      | Agree on a goal identified by the participant. |
| 8    | **CLOSE**  
|      | Summarize; Thank participant, Document |
VOICE Timeline

9/09 Study start

6/11 VASP implemented

6/11 accrual ends (n=5029)

9/11 oral TDF stopped

11/11 vaginal gel stopped

8/12 Study ends (Truvada+placebo)