Preventing Pregnancy in an HIV Prevention Trial: Lessons Learned from the VOICE Study

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Overview

- Introduction
- Strategies to prevent pregnancy in VOICE
- Baseline pregnancy related factors and contraceptive use
- Predictors of pregnancy
- Lessons learnt
Introduction

- Preventing pregnancy in HIV prevention trials is vital:
  - Safety of study product on pregnancy not established
  - To avoid the impact that time of study product will have on the power to detect an effective intervention
- Reported incidence ranges from 64/100 to 4/100 person years (P/Y)
Introduction

- SSA – an important region for HIV prevention trials due to increased incidence amongst young women
- High fertility rates secondary to:
  - Cultural norms and expectations
  - Gender dynamics
- Women not empowered to make decisions regarding reproductive health
VOICE (MTN 003)

- A randomized, double-blinded, placebo-controlled trial of daily oral tenofovir, oral tenofovir-emtricitabine, and 1% vaginal tenofovir gel for HIV-1 prevention.
- 360 women, between the ages of 18-45 were enrolled at CAPRISA eThekwini CRS
- Average period of follow up: 13 months (range 0-22 months)
- Women who agreed to use an effective method of contraception and had no pregnancy intention at enrolment were eligible
Contraceptive Services

- Baseline and monthly contraceptive counselling: to assess contraceptive needs/pregnancy intention
- Pregnancy testing conducted at screening, enrolment and at monthly follow up visits
- Accessibility: Hormonal contraception (injectable –DMPA/NET-EN and combined oral contraceptives –COCs) provided on site
- Referrals facilitated for IUCD insertion and tubal ligation to public sector facilities
Monitoring of Contraceptive Use

- Contraceptive log and “Follow up Family Planning” CRF used to track contraceptive use
- Documentation of DOH accessed services- signed FP card
- Urine pregnancy testing conducted at every monthly follow up visit
Pregnancy Screening Failures

- 772 screened/412 screening failures
- 42 (5.5%) of 772 women were ineligible due to pregnancy related factors

Diagram:
- (23) 55%
- (12) 29%
- (6) 14%
- (1) 2%

Legend:
- not on effective method at B/L
- last pregnancy outcome ≤ 42 days
- pregnant at screening
- pregnancy intention within next 24 months
More than two thirds of women opted for injectable contraceptives

277 (77%) reported condom use at the time of enrolment
Pregnancy Incidence & Outcomes

- 358 women followed up/ 35 pregnancies/ 36 outcomes
- Pregnancy incidence 9.7/100 PY (95% CI: 6.7, 13.5)
- 25% opted for termination of pregnancy
Contraception and Pregnancy

- COCs:
  - Baseline: 74% (26/35)
  - At conception: 83% (29/35)
- Injectable:
  - Baseline: 26% (9/35)
  - At conception: 8.5% (3/35)

A pie chart shows the switch from injectable contraception:
- 44% (4) COCs
- 33% (3) COCs/IUD
- 11% (1) switch reported after conception
- 11% (1) COCs/stopped
## Pregnancy Incidence

<table>
<thead>
<tr>
<th></th>
<th>All arms</th>
<th>TDF</th>
<th>FTC/ TDF</th>
<th>Oral placebo</th>
<th>Tenofovir 1% gel</th>
<th>Gel placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence rate (100 PY)</td>
<td>9.7</td>
<td>5.4</td>
<td>11.7</td>
<td>4.5</td>
<td>17.2</td>
<td>10.3</td>
</tr>
<tr>
<td>95% CI</td>
<td>[6.7,13.5]</td>
<td>[1.1,15.8]</td>
<td>[1.2,11.6]</td>
<td>[1.2,11.6]</td>
<td>[8.6,30.8]</td>
<td>[4.1,21.2]</td>
</tr>
</tbody>
</table>

P value testing comparison between the Tenofovir and gel placebo arms = 0.31
46% of pregnancies occurred during the first 6 months. 37% of total pregnancies occurred within first 3 months.

Pregnancy incidence increased slightly at month 24 because of pregnancies reported at study end visit.

Table: Pregnancy Incidence Rates at 6 month intervals

<table>
<thead>
<tr>
<th>Follow up time in months</th>
<th>6 months</th>
<th>12 months</th>
<th>18 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative pregnancies</td>
<td>16</td>
<td>27</td>
<td>33</td>
<td>35</td>
</tr>
<tr>
<td>Incidence rate (per 100 PY)</td>
<td>9.3</td>
<td>8.8</td>
<td>9.2</td>
<td>9.7</td>
</tr>
</tbody>
</table>
The following were not conclusive risk factors for pregnancy in this data set:

- Randomization arm
- Younger age
- Level of education
- Income source
- Marital status, having/living with primary partner
Summary

Risk factors for pregnancy:
- Not having living children at baseline (p 0.049)
- COCs as a method of contraception (p<0.001)

Limitations of this analysis:
- No accurate measure of contraceptive use at study end: missing data for contraceptive use within 3 months of study exit
Lessons Learnt

- Counselling around reasons for ineligibility must be discrete
- Active promotion of IUCD as a contraceptive method/on site provision of IUCD insertion
- In depth discussion around pregnancy intention taking into account social and cultural factors
- Addressing contraceptive related adverse events
- Addressing timing of contraceptive switching
- Importance of study in HIV prevention field and the effect of pregnancy/time of study product
Acknowledgements

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