Obstetric and Infant Outcomes Following Maternal Third Trimester Exposure to Tenofovir 1% Vaginal Gel


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Introduction

- Drug safety evaluation in pregnancy: assess potential impact of drug exposure
  - Obstetric (OB) outcomes
  - Infant outcomes

- Evaluated OB and infant outcomes, including infant malformations
  - Registrants enrolled in planned 3rd trimester TFV gel studies
Design

Planned third trimester exposures
- MTN-002
- MTN-008

Unplanned first trimester exposures
- Phase 2B & 3 trials

MTN-016 Pregnancy Registry
Methods

- Restricted to planned 3rd trimester exposure, comparisons using Fisher’s exact test
  - MTN-002: open label, single dose, 1% TFV gel prior to cesarean
  - MTN-008: 2:1 placebo-controlled, 7 daily doses, 1% TFV gel

- Outcomes
  - OB: preterm birth, postpartum hemorrhage, non-reassuring fetal status, chorioamnionitis, gestational diabetes (MTN-008)
  - Infant: any visit with variation from normal physical exam (PE) (MTN-008)
Malformation outcomes

- Two consultant geneticists determined endpoints via independent review of PE data, pregnancy and medication history, genetic screening data, and photo data (MTN-002 & MTN-008)
Results

- **Enrollment into registry**
  - 100% (16/16) of MTN-002 mothers, 25% (n=4) of whom enrolled prior to pregnancy outcome
  - 90% (88/98) of MTN-008 mothers, 97% (n=86) of whom enrolled prior to pregnancy outcome

- **Infant retention at 12 months**
  - 88% (MTN-002) and 80% (MTN-008)

- **Infant malformations**
  - One defect (ear canal) in MTN-002: prevalence (6%) comparable to US background prevalence (3%) for malformations (p=0.51)
  - No defects noted among infants from MTN-008
Obstetric and newborn outcomes following 7-day third trimester exposure to TFV gel

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Placebo (n=30)</th>
<th>1% TFV gel (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-term birth</td>
<td>2%</td>
<td>7%</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>19%</td>
<td>10%</td>
</tr>
<tr>
<td>Non-reassuring fetal status</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>2%</td>
<td>7%</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>0%</td>
<td>3%</td>
</tr>
<tr>
<td>Infant PE findings</td>
<td>24%</td>
<td>27%</td>
</tr>
</tbody>
</table>

p-values:
- Pre-term birth: p=0.27
- Postpartum hemorrhage: p=0.36
- Non-reassuring fetal status: p=1.0
- Chorioamnionitis: p=0.27
- Gestational diabetes: p=0.34
- Infant PE findings: p=1.0
Conclusions

- First report from a novel pregnancy registry
  - Suggests single-dose and 7-day repeat dose TFV 1% gel exposure in 3rd trimester do not impact several important OB/infant outcomes
- Pregnancy registries can provide valuable data for evaluating maternal and infant safety associated with third trimester microbicide use
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