PROMISE 1077HS
Adherence Analysis

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A randomized strategy trial conducted among women who received highly active antiretroviral therapy (ART) during pregnancy for purposes of prevention of mother-to-child transmission (PMTCT) of HIV but do not otherwise meet criteria to initiate HAART for their own health
PROMISE 1077HS

• To determine whether continuation of HAART (Arm A) after delivery or other pregnancy outcome reduces morbidity and mortality compared to discontinuation and re-initiation of ART according to current standards of care (Arm B).

• The primary combined endpoint includes death, AIDS-defining illness, and serious non-AIDS-defining cardiovascular, renal, and hepatic events.
Among women who do not meet criteria for ART for their own health, who received a triple ARV (ART) regimen during pregnancy for PMTCT, is long term health better served by continuing or stopping ART postpartum?

1077HS Research Question

Screen

Enroll (n=2000)

R

CONTINUE ART
Follow-up until 84 weeks after last participant randomized

STOP ART
Follow-up until 84 weeks after last participant randomized
Primary Adherence Objective

• “To evaluate rates of self-reported adherence to ART and its association with the primary endpoint and with CD4+ cell count, HIV-1 viral load, and HIV-1 resistance patterns at 1, 2, and 3 years following randomization.”
Adherence Objectives

• To compare adherence among those in the immediate treatment arm to those in the delayed treatment arm
• To compare Quality of Life data between those in the immediate versus delayed ART arms
• To determine which components of the QOL/Adherence/Resource use self report form are most predictive of nonadherence
• To look at geographic differences in adherence
Additional objective

• ~18 months into the study, addition of a detailed adherence questionnaire asking about barriers
1. Side effects make me feel sick
2. Following dietary restrictions is hard (taking medicine with or without food)
3. Needing to share ART with other family members and friends
4. Not understanding how to take the medicine
5. Religious beliefs
6. Traveling away from home
7. Transportation problems getting to the clinic for refills
8. Pills getting lost, damaged, or stolen
9. It is hard to take so many pills
10. I am tired of taking pills every day
11. Remembering to take pills every day
12. I am busy taking care of my baby
13. I am busy doing other things (household work, childcare for older children, working)
14. Other health problems or illnesses get in the way
15. Fear or worry that other people inside of the home will find out I am sick
16. Fear or worry that other people outside of the home will find out I am sick
17. I don’t feel sick so it is hard to take pills every day
18. I don’t think the pills work and prefer other types of alternative treatment
19. I don’t think I need the pills right now because my CD4 T-cell count is high (my immune system is strong)
20. If someone saw me taking my pills, they might start asking questions
21. Of all the choices above, what is the MAIN reason it is difficult to take medication every day? **NOTE:** Choose one of the options checked above that is identified as the main reason and enter number here.
I. Have you disclosed your HIV status to your primary sex partner?

(Check one box)

- Yes
- No
- I do not have a primary sex partner (husband or boyfriend)

J. Have you disclosed your HIV status to any of the following (outside of primary partner)?

(Check one box for each item below)

1. Parent(s)
2. Sibling(s)
3. Children
4. Other relatives
5. One or more friends
6. Religious leader
7. Counselor
8. I have not disclosed my HIV status to anyone
9. Other, specify

NOTE: If you answer ‘Yes’ to this item, use the line below to specify the category (not name) of person to whom you have disclosed your status. (e.g., Teacher.)

Specify [70]:

K. Does difficulty telling people about your HIV status (disclosing your HIV status to family and friends) make taking your HIV medications everyday a challenge?

(Check one box)

- No, not at all
- Yes, but rarely
- Yes, sometimes
- Yes, much or most of the time
- Yes, all the time
Adherence Objectives

• Among those with evidence of virologic failure (VL > 1,000 copies) due to nonadherence, to characterize most common barriers
• To determine whether barriers vary between those who are adherent and those with episodes of virologic failure
• To determine whether barriers vary by geographic region
PROMISE General Overview: Sequential Randomized 2x2 Factorial Trial

~8,000 women who don’t need treatment for own health (CD4 >350)

AP 14wk-term  IP  PP for Duration BF  After Weaning

Infant uninfected at birth

Maternal Health

Antepartum

Postpartum

Randomize

Triple drug prophylaxis  Triple drug prophylaxis

Randomize

AZT  AZT + SD NVP (7 d TRV)

Randomize

Infant daily NVP

Infant NVP x 6 wks

Triple drug prophylaxis

Continue Triple Drugs

Stop All ARVs

Mother

Mother
### Antepartum Randomization: BF Settings

(For countries where non-triple ARV AP regimens are used for PMTCT)

<table>
<thead>
<tr>
<th>Antepartum</th>
<th>Intrapartum</th>
<th>Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal ZDV</td>
<td>Maternal ZDV + sdNVP + TRV</td>
<td>Maternal TRV for 1 wk (7-12 days)</td>
</tr>
<tr>
<td>Maternal TRV for 1 wk (7-12 days)</td>
<td>Infant daily NVP through 6 weeks</td>
<td>Maternal TRV for 1 wk (7-12 days)</td>
</tr>
<tr>
<td>Maternal Triple ARV Prophylaxis</td>
<td>Maternal Triple ARV Prophylaxis</td>
<td>Infant daily NVP through 6 weeks</td>
</tr>
</tbody>
</table>

**Randomize**

At ≥ 14 wks gestation

Next Potential Randomization

BF M-I pair eligible for Postpartum Component
PROMISE 1077BF/FF

Postpartum Randomization: BF Settings

Populations to be Enrolled

Mother-Infant Pairs from Antepartum Component

Mother-Infant Pairs from Late Presenters Registration
- M-I pairs presenting in labor
- M-I pairs presenting within 72 hours postpartum

Week 1 Visit (Day 7-12 PP)

Maternal Triple ARV Prophylaxis
through BF cessation or 18 mos postpartum, whichever comes first plus Infant NVP through 6 weeks of age

Next Potential Randomization

Mother eligible for Maternal Health Component

Infant eligible for Infant Health Component

Infant NVP Prophylaxis
through BF cessation or 18 mos postpartum, whichever comes first
PROMISE 1077BF/FF

- Maternal triple ARV prophylaxis in Antepartum and Postpartum Components
- Maternal ZDV/sdNVP prophylaxis in Antepartum Component & Maternal triple ARV prophylaxis in Postpartum Component
- Late Presenter (no AP prophylaxis) & Maternal triple ARV prophylaxis in Postpartum Component
- Maternal triple ARV prophylaxis in Antepartum Component & not enrolled in Postpartum Component
- Maternal ZDV/sdNVP prophylaxis in Antepartum Component & Infant NVP prophylaxis in Postpartum Component
- Maternal triple ARV prophylaxis in Antepartum Component & Infant NVP prophylaxis in Postpartum Component

After BF exclusion:
- Mother Continues Triple ARV Regimen
- OR
- Mother Discontinues Triple ARV Regimen

Mother continues in Observational Follow-up
1077BF/FF Adherence Objectives

• Antepartum: To evaluate adherence to maternal ARV regimens
• Postpartum: To evaluate adherence to maternal and/or infant ARV regimens
• Maternal Health: To evaluate rates of self-reported adherence and its association with the primary endpoint, CD4 count, viral load, and resistance patterns 1, 2, and 3 years following randomization
• To compare quality of life between study arms at 1, 2, and 3 years

• Additional questions on barriers not added to BF/FF
Additional opportunities BF/FF

• To compare adherence in those in the maternal health arm among those who continue after cessation of breastfeeding versus those who d/c and restart later for maternal health
  – Are factors associated with nonadherence different by region (comparison using 1077HS)
Additional opportunities BF/FF

• To evaluate adherence at different stages (what factors predict high versus low adherence? What factors are associated with specific patterns of adherence: high on all, low on all, mixed)
  – Pregnancy
  – Postpartum up to 3 or 6 months
  – After cessation of breastfeeding among those who continue for maternal health
DISCUSSION