BACKGROUND

More than 1 million HIV-infected women become pregnant and deliver babies annually, and the majority of these women now receive antiretroviral therapy (ART) prophylaxis and are expected to continue lifelong ART after delivery. The benefits of postpartum ART were recently reported from PROMISE 1077HS, however, methodological limitations have hindered consistent results among ART trials. Previous studies have shown high rates of discontinuation and VF among postpartum HAART-naive women. Predictors of poor adherence may have included prior usage of 5HT, antiretroviral treatment, and level of HIV-1 and ART prevention knowledge.

This PROMISE 1077HS study design provides an opportunity to explore predictors of virologic failure among women randomized to continue ART postpartum, including whether self-report about missed doses of ART is an accurate measure of adherence and link to VF.

METHODS

PROMISE 1077HS was an open-label, comparative effectiveness study evaluating two strategies for the management of ART among postpartum women with high CD4 T-cell counts (>350 cells/μL), continuing ART and discontinuing ART and restarting when clinically indicated (Figure 1). The potential ART regimen supplied by the study was Lamivudine/Efavirenz (LVP/EFV) plus fixed dose combination Tenofovir/Emtricitabine (TFDC/TDC) and was chosen because it was the preferred regimen for use in pregnancy according to WHO guidelines at the time the study was designed. Women were required to return within 60 days of delivery.

Participants randomized to the discontinuous ART arm had ART restarted at the time of the following criteria:

1. Developed an AIDS-defining illness Stage 2 illnesses.
2. Had a recorded CD4 T-cell count <500 cells/μL.
3. Developed a non-AIDS criterion illness that required ART.
4. Developed an opportunistic infection requiring ART.
5. Developed an opportunistic infection requiring ART.
6. Developed an opportunistic infection requiring ART.

For women who continued ART, self-reported and self-reported adherence were collected every 12 weeks. For these analyses:

- VF was defined as 2 consecutive visits with
  - a viral load level ≥50 copies/mL, after 24 weeks on ART
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- Self-reported adherence was defined as missing ART for 3 days or more in a single week.

- Predictors of VF and re-suppression were examined using Cox proportional hazard regression, with adherence as a time-varying covariate. Other predictors were variables of interest.

- Exploratory analyses were performed comparing the probability of VF using a list of 40 covariates.

RESULTS

- Of the 627 women randomized to continue ART, 625 had HIV-1 RNA and adherence data, of whom 623 were for ART for at least 24 weeks and were included in the analysis. Complete adherence data were collected for 1,278 weeks of ART.

- Among these women, 1% were recruited by 27 years (CV 25.5%) and median CD4 cell count was 90 (IQR 43–213) and median CD4 CD4 T-cell count 90 (IQR 43–213) (Figure S7).

- Participants were from South America and Caribbean (38%), Barbara (27%), Asia (24%), and the United States (19%).

- Among 1% of all women reported using alcohol in the past year, and 3% reported smoking tobacco in the past year.

- Among 3%, all women reported using antidepressants, antianxiety, and antihypertensive drugs.

- Among 80% of women reported missing ART doses over the prior 4 days. This increased to 11% at 48 weeks and 12% at 56 weeks.

- Of 175 women with VF, 120 had risk data available. Of those, 12% failed to return to their current regimen. VF with resistance to current regimen was then compared in women on non-suppressed (<400 copies/mL) or suppressed (<400 copies/mL) therapy.

- The probability of VF were (see top panel of Figure 2)
  - 0.12 by week 48
  - 0.12 by week 48
  - 0.12 by week 48
  - 0.12 by week 48
  - 0.12 by week 48
  - 0.12 by week 48

- When using a more stringent definition of VF (≥100 copies/mL), the estimated probability increases: 0.16 by week 48, 0.18 by week 56, and 0.19 by week 144 (Figure 2, bottom panel).

- There were differences by group: participants from South America and the Caribbean having the highest estimated probability of VF (Figure 2).

- In univariate regression (Table 2), self-report of any missed ART doses in the prior 4 weeks, younger age, region, and mother's education (pre-entry ART) were predictive of VF.

- At the first multivariable model for VF, significant predictors included missed ART doses within the prior 4 weeks, younger age, shorter duration of pre-entry ART, and region (South America/Caribbean) (Table 2).

- Figure 4 shows the probability of virologic-suppression among the 175 women with VF (both consecutive virologic-suppression, copy/mL levels ≥400 copies/mL).

- Figure 5 shows the median and interquartile range of the distribution of median duration of suppression for all individuals included in the analysis.

- There were no statistically significant predictors of re-suppression, although analyses were limited by small sample size.

CONCLUSIONS

- A simple 4-week ART ART trial could predict clinical failure among women who continued ART in PROMISE 1077HS.

- Regional differences in risk of VF have not been well characterized and require further study in regard to specific racial and ethnic groups.

- Postpartum women who have VF are at high risk for other virologic measures; future research may be needed to further explore this preliminary finding.

- Further research should explore strategies that may successfully support ART adherence for postpartum women.