BACKGROUND

• Increased maternal viral load (MVL) and decreased CD4 cells (CD4) have been associated with increased risk of perinatal HIV-1 transmission.

• The PROMISE 1077FB study included three sequential randomizations: antepartum, postpartum, and breastfeeding and maternal health following breastfeeding.

• The PROMISE 1077FB study also included a group of mothers close to or after delivery who were not randomized in the antepartum component but who were eligible for randomization if eligibility criteria were met (late presenters).

• In the postpartum component, mothers of infant (M)-pairs were randomized 4-14 days postpartum and eligible M-pairs were randomized at 6-14 days postpartum to a maternal triple-drug antiretroviral (mART) arm or infant nevirapine (INVP) arm (Figure 1).

METHODS

• The Postpartum Component of PROMISE was conducted in 14 sites in Malawi, Malawi, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe.

• 2,431 mothers with HIV-1 infection and CD4 counts ≥350 cells/mm3 (or above country-specific guidelines) and their HIV-1-uninfected infants were randomized at 6-14 days postpartum to mART (n=1,220) or INVP (n=1,211) between June 2011 and October 2014.

• MVL was analyzed real-time for mothers on ART and batch-tested retrospectively for mothers not receiving ART.

• Infant HIV-1 specimens were collected at entry (7-14 days postpartum) and weeks 6, 14, 26, and 50 postpartum.

• CD4 was measured real-time at entry and weeks 14, 26, and 38, and at postnatal visit.

• Baby HIV-1 NAT specimens were collected and assayed real-time at weeks 1 (entry), 6, every 4 weeks until week 28, then every 12 weeks.

• Infant infection was defined as a positive HIV-1 NAT at any two post-entry timepoints.

• The associations of baseline and time-varying MVL and CD4 with HIV-1 transmission risk were modeled using proportional hazards regression models with randomized treatment arm, where MVL categorized as ≥500 or <500 copies/ml, and adjustment for randomization to the mART arm during the antepartum component of PROMISE.

• For analyses using time-varying MVL and CD4, each treatment arm was analyzed separately because the post-randomization visits showed little overlap between the two arms with respect to MVL and CD4 cell count (Figure 2).

RESULTS

• There were seven infants with HIV-1 infection in each treatment group.

• In the mART arm, the median infant age at first positive HIV-1 NAT test was 38 weeks (range, 13-50 weeks).

• In the INVP arm, the median infant age at first positive HIV-1 NAT test was 26 weeks (range, 6-74 weeks).

• In the mART arm, the median infant at first positive HIV-1 NAT test was not detected to 52,000 copies/ml.

• In the INVP arm, the median infant at first positive HIV-1 NAT test ranged from not detected to 52,000 copies/ml.

CONCLUSIONS

• In the mART arm, time-varying MVL and CD4 were not significantly associated with infant HIV-1 transmission.

• In the mART arm, increased MVL and decreased CD4 during breastfeeding were associated with increased risk of infant HIV-1 infection.

• Two infant transmissions were observed following periods of MVL that were <40 copies/ml.

• These data emphasize the important role of adherence to mART in controlling MVL and preventing infant HIV-1 infection and suggest that INVP should be considered in situations with documented poor maternal ART adherence.

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