Maternal Triple Antiretrovirals (mART) and Infant Nevirapine (iNVP) Prophylaxis for the Prevention of Mother-to-Child Transmission (MTCT) of HIV during Breastfeeding (BF)

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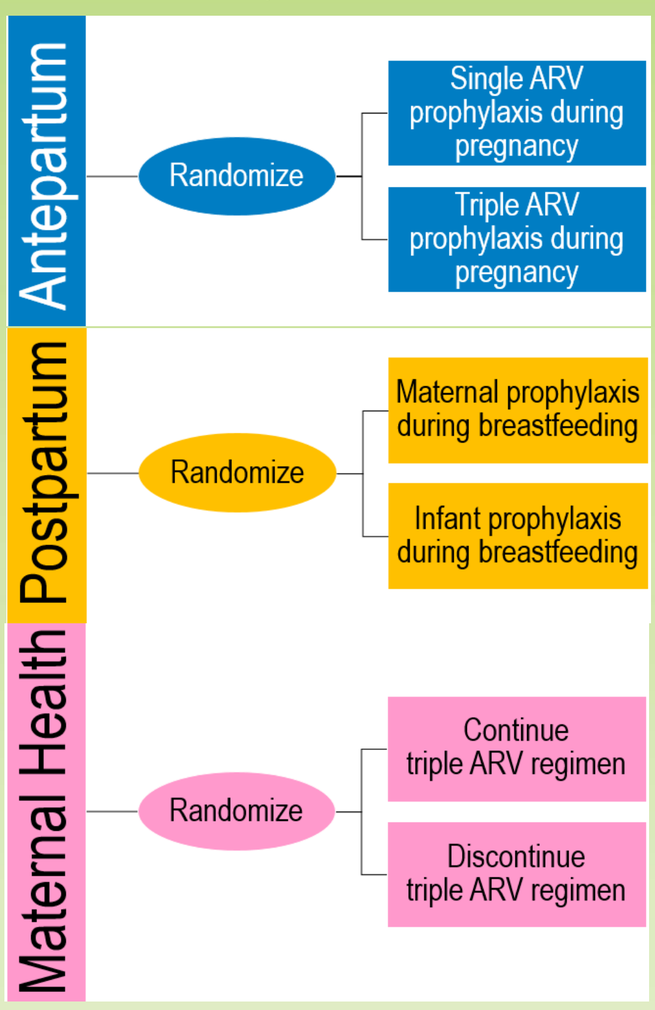
BACKGROUND

Breastfeeding (BF) is crucial to reducing infant morbidity and mortality in developing countries but may result in HIV transmission if the mother is HIV-infected. Prior clinical trials showed that both maternal antitroviral treatment (mART) and infant nevirapine (iNVP) are effective in prevention of perinatal transmission of HIV. PROMISE is the first randomized trial designed to directly compare the efficacy and safety of these two strategies during extended BF into the second year of life. The PROMISE studies included three randomizations: antepartum, postpartum during breastfeeding, and maternal health following breastfeeding, as shown below.

FIGURE 1. PROMISE Study Randomizations



METHODS

The Postpartum Component of PROMISE was conducted in sub-Saharan Africa (13 sites) and India (1 site). HIV-infected women with CD4+ ≥ 350 cells/mm3 (or greater than country-specific guidelines) and their HIV-uninfected newborns were randomized at 6-14 days postpartum to mART or iNVP. Of 2,431 mother-infant pairs enrolled in this component, 1,220 were randomized to mART and 1,211 were randomized to iNVP

Randomized regimens were continued until 18 months postpartum, unless there was cessation of breastfeeding, infant HIV infection, or toxicity.

Kaplan-Meier probabilities and incidence rates per 100 person-years were used in primary analyses of efficacy and safety.

RESULTS

WOMEN WERE ASYMPTOMATIC

Women were asymptomic with median CD4+ cell count of 686 cells/mm^3 and 97% WHO Clinical Stage 1. Women had a median age of 26 years.

INFANT CHARACTERISTICS

Infant's median gestational age and birthweight were 39 weeks and 2.9 kg, respectively.

OTHER BASELINE CHARACTERISTICS

Baseline characteristics were comparable by study arm. Median duration of breastfeeding was 15 months and not significantly different by study arm (p=0.85). Kaplan-Meier estimates of perinatal transmission of HIV are shown in Figures **2 &3** below; **there were no statistically significant differences between the two arms**. Infant 12-month survival rate was extremely high (98.9%) and did not differ significantly by arm (**Figures 4 & 5**). Incidence rates of maternal and infant safety outcomes did not differ significantly by regimen (Table 1).

FIGURE 2. Results: Time to Perinatal Transmission (Primary Analysis)

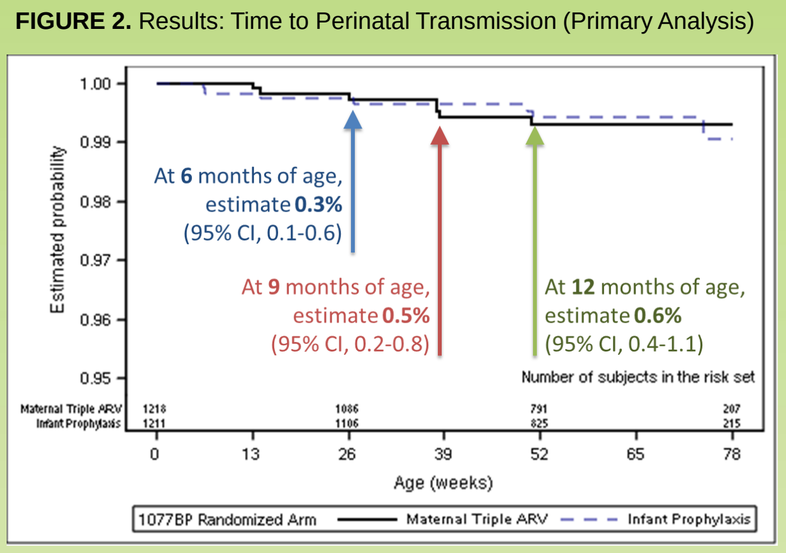


FIGURE 3. Time to Perinatal Transmission (Sensitivity Analysis)

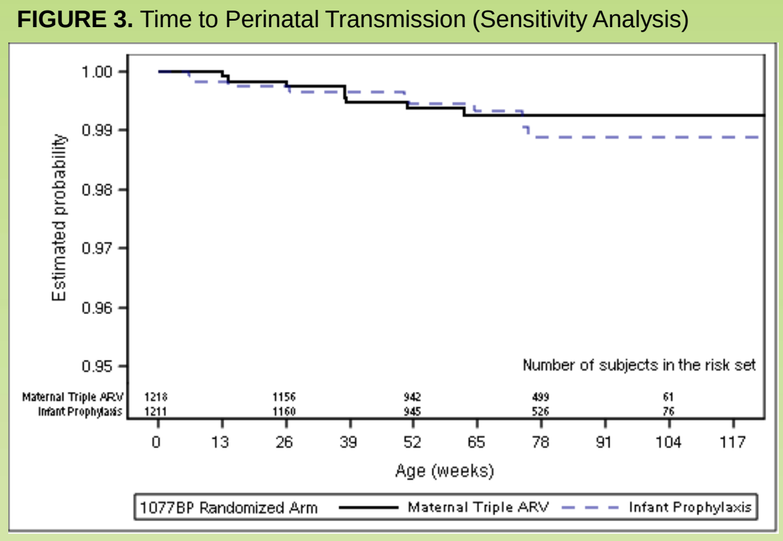


FIGURE 4. Time to Infant Death (Primay Analysis)

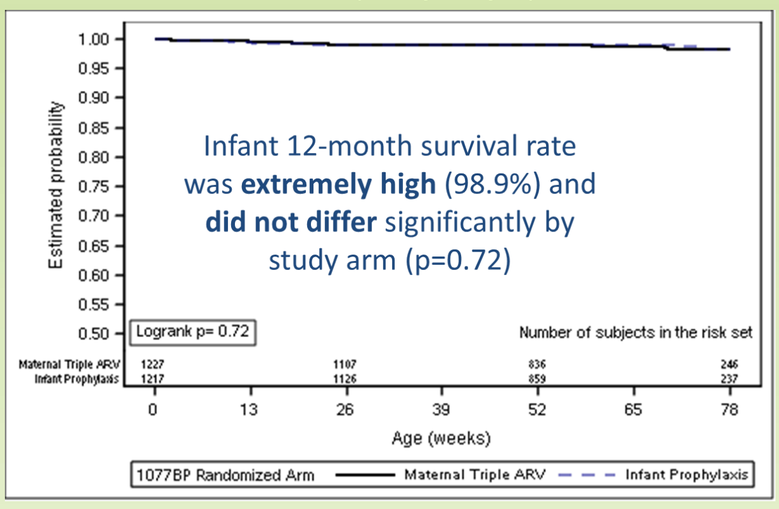


FIGURE 5. Time to Infant Death (Sensitivity Analysis)

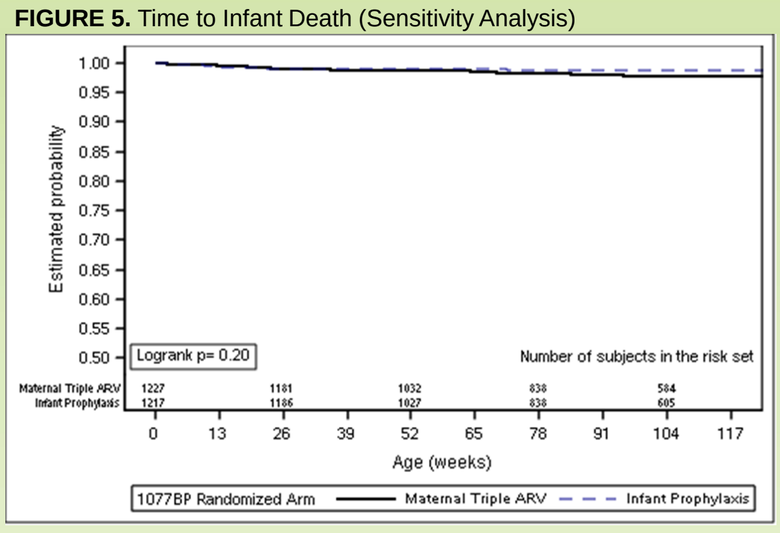


TABLE 1. Maternal and Infant Safety Outcomes

Outcome	mARV (n=1220) Rate (95% CI)	iNVP (n=1211) Rate (95% CI)	p-value, K-M log-rank test
Composite maternal safety endpoint (Grade 3/4 signs/symptoms; Grade 2-4 lab events; or maternal death)	14.8 (12.7-17.3)	14.6 (12.5-16.9)	0.99
Composite severe maternal safety endpoint (i.e., excludes Grade 2 Lab events)	5.1 (4.3-6.1)	5.6 (4.8-6.6)	0.61
Composite infant safety endpoint (Grade 3/4 signs/symptoms; Grade 3/4 lab event; or infant death)	44.1 (39.2-49.5)	43.5 (38.7-48.8)	0.95

CONCLUSIONS

Both maternal ART and infant NVP were safe, associated with very low postnatal perinatal transmission rates during extended breastfeeding, and high infant survival rates.

For mothers who either do not adhere to or tolerate ART, daily infant NVP throughout breastfeeding offers a safe and effective PMTCT alternative during breastfeeding.

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