1. PROMISE TRIALS

BACKGROUND
PROMISE was a randomized controlled trial conducted in 14 countries around the globe that began in 2010. The aim was to determine the optimal in utero ARV strategy to prevent vertical transmission of HIV and maintain maternal and infant health.

Breastfeeding versions of PROMISE (1077BF) were designed for countries where maternal triple ART during breastfeeding (BF) was not standard when the study began. PROMISE 1077BF was conducted in 7 countries in Africa and India (Figure 1).

FIGURE 1. Breastfeeding Version of PROMISE Study Sites

2. STUDY TREATMENT

BREASTFEEDING VERSION OF PROMISE
To assess the effects of the potential adverse impact of ARV exposure on infant growth, we evaluated the effect of postnatal ARV exposure on somatic growth of HIV-exposed uninfected breastfed infants (HEUs) within the Breastfeeding Version of the PROMISE trial (1077BF).

The 1077BFV trial involved 3 sequential randomizations to address the different ARV strategies (Figure 2) for eligible healthy mother–infant pairs. Infants with birth weight below 2000g were excluded. All infants received standard care nevirapine prophylaxis from birth through week 6 of life.

3. METHODS

GROWTH ASSESSMENTS
Length, weight, and head circumference were measured using standard methods at birth and postpartum. Infant feeding method and infant HIV infection status were monitored throughout follow-up.

STATISTICAL METHODS
We studied the effect of the postpartum randomization on infants’ growth using an intention-to-treat approach and World Health Organisation z-scores at birth, age 10, 26 weeks (primary time point), 74 and 104 weeks:

• Infant growth: BMI, z-score
• Infant feeding method
• Weight for age (WAZ)
• Head circumference-for-age (HCAZ)

4. RESULTS

POSTPARTUM ENROLMENT
Mothers (n=2441) and their infants (n=2444; 13 sets of twins) were randomised within 14 days after delivery:

• Maternal triple ART, n=1127 infants
• Infant Nevirapine prophylaxis, n=1217 infants

This included 128 mothers who entered PROMISE as Late Presenters in labour or soon after delivery. Median follow up was to 104 weeks of age. Ten percent of infants (236) prematurely discontinued study follow-up, 38 due to death (2%).

BASELINE CHARACTERISTICS
Maternal and infant baseline characteristics were comparable between study arms (Table 1).

TABLE 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>Mothers’ (n=2415) Value</td>
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<tr>
<td>Median Age (Q1-Q3)</td>
<td>26.6 years (23.2-30.3)</td>
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<tr>
<td>ARV use in pregnancy:</td>
<td></td>
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<tr>
<td>No ARV use (Late Presenters)</td>
<td>128 (5%)</td>
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<tr>
<td>ZDV/3TC/LPV (TCLVP)</td>
<td>1002 (41%)</td>
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<tr>
<td>ZDV/n pregnancy vs ARV/TFV xVI</td>
<td>1003 (42%)</td>
</tr>
<tr>
<td>Median BMI (Q1-Q3)</td>
<td>24.7 (22.2-27.3)</td>
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<tr>
<td>Median CD4 pre ART (Q1-Q3)</td>
<td>5355 cells/µl (4086-6777)</td>
</tr>
<tr>
<td>Median viral load post delivery (Q1-Q3)</td>
<td>40 (144-1543)</td>
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<tr>
<td>Infants’ (n=2444) Value</td>
<td></td>
</tr>
<tr>
<td>Median weeks of gestation (Q1-Q3)</td>
<td>39 weeks (38-40)</td>
</tr>
<tr>
<td>Median birth weight (Q1-Q3)</td>
<td>2900g (2660-3200)</td>
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</tbody>
</table>

5. CONCLUSIONS

WHAT THESE DATA SHOW
Growth outcomes in breastfed HEUs through age 74 weeks did not differ significantly between infants who received Nevirapine prophylaxis during the period of breastfeeding and those whose mothers received predominantly tenofovir-containing ART.

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The study protocols were approved by all relevant ethics committees. The study was registered with ClinicalTrials.gov under ID NCT00373202.

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