ASSOCIATION OF MATERNAL TDF-BASED ART WITH BONE MINERAL CONTENT IN BREASTFED INFANTS

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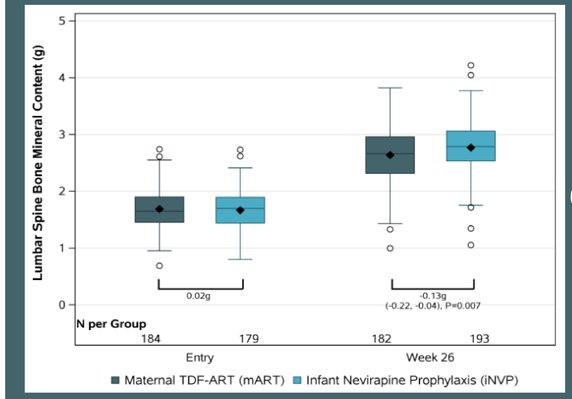
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BACKGROUND

- Tenofovir disoproxil fumarate (TDF) is an important agent for antiretroviral treatment (ART) and prevention of HIV in breastfeeding women, but information about the impact of postpartum use on infant bone and renal safety is limited.
- The IMPAACT PROMISE P1084s substudy [NCT01066858] assessed these outcomes in a subset of mother-infant pairs randomized to either maternal TDF-based ART [TDF/FTC+LPV/r] (mART) or infant nevirapine prophylaxis [no maternal ART] (iNVP) during breastfeeding.

METHODS

- Healthy pairs with normal maternal renal function and no antenatal exposure to maternal TDF who were randomized in PROMISE 1:1 to mART or iNVP at 6-14 days postpartum were eligible for the P1084s substudy.
- Most pairs were enrolled in P1084s on randomization day and followed through Week 74.
- Infant lumbar spine bone mineral content (LS-BMC) was assessed at entry and Week 26 by dual energy x-ray absorptiometry, read centrally by blinded investigators.
- Infant creatinine clearance (CrCl) was calculated using the revised Schwartz equation at entry and Weeks 10, 26, and 74.
- Student t-tests compared mean LS-BMC and CrCl at Week 26 and mean change from entry between arms. All differences are presented as mART – iNVP.



Mean lumbar spine bone mineral content at Week 26 was lower in infants exposed to postnatal TDF containing maternal ART vs. infant nevirapine prophylaxis.

Figure 2: Infant Entry and Week 26 Lumbar Spine Bone Mineral Content by Study Arm

RESULTS

- 400 pairs were enrolled; 2 mART pairs excluded because the mothers did not initiate TDF-based ART.
- At entry [Figure 1], mean (standard deviation (sd)) infant LS-BMC was 1.68g (0.35) and CrCl was 64.2mL/min per 1.73 m^2 (24.6).
- At Week 26, 98% pairs were breastfeeding and 96% were on their assigned antiretroviral strategy.
- Mean (sd) Week 26 LS-BMC was 2.64g (0.48) for mART and 2.77g (0.44) for iNVP; mean difference (95% confidence interval (CI)) -0.13g (-0.22, -0.04), P=0.007, n = 375/398 (94%) [Figure 2]. Mean absolute (-0.14g (-0.23,-0.06)) and percent change (-10.88% (-18.53, -3.23)) in LS-BMC from entry was smaller for mART than iNVP. Similar results were observed in *post hoc* analyses of bone mineral density.
- At Week 26, mean (sd) CrCl was 130.0mL/min per 1.73 m^2 (34.9) for mART vs. 126.1mL/min per 1.73 m^2 (30.0) for iNVP; mean difference (95% CI) 3.8 (-3.0, 10.7), P=0.27, n = 349/398 (88%).

Characteristic at entry	Statstic	mART	iNVP	Total
Sex [N=398]	Male/Female	100/100	100/98	200/198
LS-BMC (g) [N=364]	Median (25^{th}, 75^{th})	1.65 (1.45, 1.90)	1.69 (1.44, 1.89)	1.67 (1.45, 1.90)
Calculated CrCl (mL/min per 1.73 m2) [N=357]	Median (25th, 75th)	62.0 (49.8, 77.8)	57.8 (48.6, 68.8)	59.0 (49.6, 72.7)
Calcium at entry (mg/dL) [N=367]	Median (25^{th}, 75^{th})	10.20 (9.76, 10.68)	10.20 (9.60, 10.68)	10.20 (9.70, 10.68)
Phosphate at entry (mg/dL)[N=377]	Median (25^{th}, 75^{th})	6.20 (5.60, 6.80)	6.30 (5.60, 6.90)	6.20 (5.60, 6.87)

Figure 1: Infant Baseline Characteristics

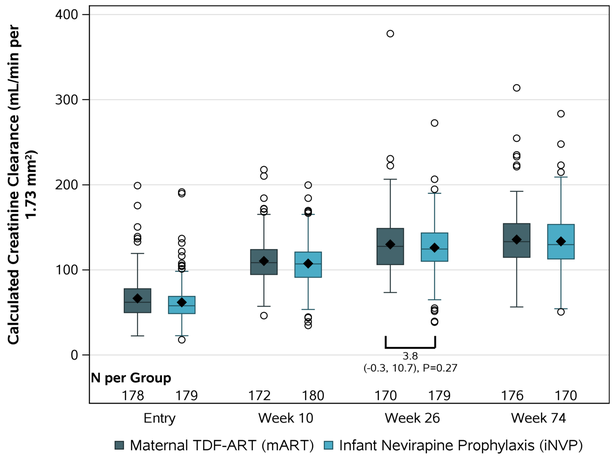


Figure 3: Infant Calculated Creatinine Clearance from Entry, Excluding Outliers

On average, CrCL increased from entry across all visits in both study arms. Renal safety was reassuring in both arms.

CONCLUSIONS

- Although the mean LS-BMC at Week 26 was lower in breastfeeding infants with TDF containing mART compared with iNVP, the difference was less than a half sd (~0.23g), thus clinical relevance is unlikely.
- No infant renal safety concerns were observed

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