Background

- Antiretroviral therapy (ART) started in the first week of life may limit HIV viral reservoir and improve treatment outcomes
- WHO supports early infant diagnosis and recommends ART initiation without delay
- Few antiretrovirals are available during neonatal period
- ZDV, 3TC, NVP, LPV/r (from 2 weeks), RAL
- Little information is available about safety, viral efficacy, and pharmacokinetics (PK) of ART in early infancy

Methods

- The EIT Study (U01AI114235) enrolled HIV-infants < 7 days of age, > 25 gestational age, and ≥ 2000g
- Treatment doses of NVP, ZDV, and 3TC started as initial ART, and changed to LPV+r, ZDV, 3TC after 2 weeks
- Switched to LPV+r when > 2 weeks of life and > 2000g gestational age expected
- Dosing: NVP – 6mg/kg ID; ZDV – 4 mg/kg BID (0-4wks), 8mg/kg BID 4-6wks, then by WHO weight band; 3TC – 2 mg/kg BID (0-4wks), 4mg/kg BID (4-6wks), then by WHO weight band; LPV+r – by WHO weight band
- Study visits and HIV RNA testing at wks 0, 1, 2, 4, 8, 12
- PK testing of NVP trough values at weeks 1 and 2
- Median age of HIV screening was 1 day after birth (range 0, 4 days)
- Median age of enrolled infants at ART initiation was 2 days after birth (range 1, 5)
- Median change from NVP/ZDV/3TC to LPV-r/zidovudine was after 2.7 weeks

Safety through 12 weeks of ART:
- No deaths or loss to follow-up
- 1 Grade 3 neutropenia
- No modification of ART for toxicity
- No Grade 3/4 anemia

Viral Suppression

- Infant plasma HIV RNA declined from a median of 4.05 log copies/mL at baseline (IQR 2.79, 4.86 log copies/mL) to 2.54 log copies/mL at 2 wks (IQR 1.86, 3.21) and <1.60 log copies/mL at 12 wks (IQR <1.60, 1.93 log copies/mL) (Figure 2)
- – HIV RNA response at 12 weeks did not differ by baseline HIV RNA, or other factors
- In the 4-week period following transition to LPV-r-based ART, 9 (22.5%) had transient increases in HIV RNA thought to be adherence-related (spitting out LPV-r)
- After 12 weeks of ART, 22 (55%) had HIV RNA < 40 copies/mL, and only 3 (8%) had HIV RNA > 400 copies/mL

Results

- Baseline Material Characteristics (N=40)
  | Median age | 27 (IQR 22, 30) |
  | Median CD4% | 50% (IQR 38, 56) |
  | Median HIV RNA | 4.38 log copies/mL (IQR 2.74, 6.51) |
  | ART regimen in pregnancy | None: 17 (43%), OSFT/OSFT: 20 (50%), OTSF/OTSF: 11 (28%), Other: 2 (5%) |
- Baseline Infant Characteristics (N=40)
  | Female | 26 (70%) |
  | Median gest age at birth | 38.5 wks (IQR 36, 41) |
  | Median birthweight | 2.9 kg (IQR 2.6, 3.3) |
  | Median baseline HIV RNA | 4.05 log copies/mL |
  | Median CD4% | 50% (IQR 38, 56) |

Figure 1: NVP trough concentrations at 1 and 2 weeks

Figure 2: Median HIV RNA log copies/mL and percentage of infants < 40 copies/mL after 0, 2, 4, 8, and 12 weeks on ART

Conclusions

- NVP, ZDV, 3TC started in the first week of life was safe and effective, even among the 50% of infants with NVP levels below the ideal therapeutic PK target
- All infants were successfully transitioned from NVP to LPV-r at 2-5 weeks. However, poor LPV/r tolerability may have contributed to transient viral increases following this transition in over 20% of infants
- By 12 weeks of life, almost all children (93%) were able to achieve HIV RNA declines to < 400 copies/mL

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