Poster #826

Safety and Efficacy of Starting Antiretroviral Therapy in the First Week of Life

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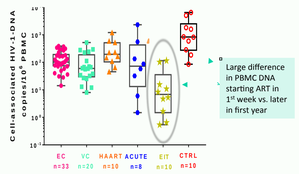
Background

- Antiretroviral therapy (ART) started in the first week of life may limit HIV viral reservoir and improve treatment outcomes

Very low DNA levels in PBMCs from the first EIT children
P. Garcia Broncano, Presentation #2360, CROI 2019



- 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, ≥ 35 weeks gestation, and ≥ 2000g
- Treatment doses of NVP, ZDV, and 3TC started as initial ART, and changed to LPV-r, ZDV, 3TC after 2-5 weeks
  - Switched to LPV-r when > 2 weeks of life and > 40 weeks gestational age equivalent
  - Dosing: **NVP** -- 6mg/kg BID; **ZDV** -- 4 mg/kg BID (0-4 wks), 8mg/kg BID 4-6 wks, then by WHO weight band; **3TC** – 2 mg/kg BID (0-4 wks), 4 mg/kg BID (4-6 wks), 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

Results

Enrollment:

- From April 2015-July 2018, 40 HIV+ infants were enrolled
- Median age at 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/ZDV/3TC was after 2.7 weeks (range 2.1, 5.9 weeks)

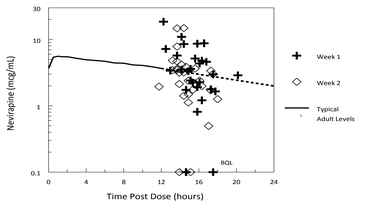
Baseline Maternal Characteristics (N=40)	
Median age	27 (IQR 22, 30)
Median CD4 count	348 cells/mm^3(IQR 222, 567)
Median HIV RNA	4.38 log copies/mL (IQR 2.77, 4.91)
ART regimen in pregnancy	None: 17 (43%) EFV/TDF/FTC: 10 (25%) DTG/TDF/FTC: 11 (28%) Other: 2 (5%)

Baseline Infant Characteristics (N=40)	
Female	28 (70%)
Median gest age at birth	38.5 wks (IQR 36, 40)
Median birthweight	2.9 kg (IQR 2.6, 3.1)
Median baseline HIV RNA	4.05 log copies/mL (IQR 2.79, 4.86)
Median CD4%	50% (IQR 38, 56)

Pharmacokinetics at Weeks 1 and 2:

- Median NVP trough concentration was 3.3 mcg/mL at 1 week and 2.7 mcg/mL at 2 weeks (at a median of 15.6 and 14.5 hours from last dose, respectively) (Figure 1)
- 15 (50%) of 30 infants tested were below therapeutic target of 3.0 mcg/mL at 2 wks (including 2 BLQ, indicating non-adherence)
- *NVP concentrations did not correlate with the magnitude of decline in HIV RNA log copies/mL at either 2 or 4 weeks*

Figure 1: NVP trough concentrations at 1 and 2 weeks



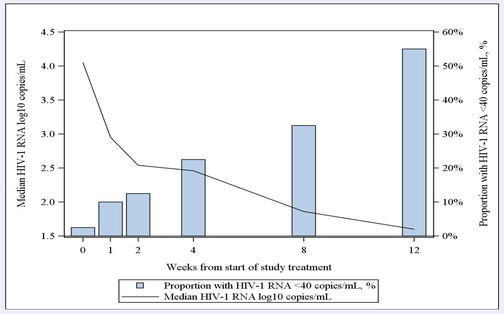
Safety through 12 weeks of ART:

- No deaths or loss to follow-up
- 1 Grade 3 neutropenia
- No modification of ART for toxicity
- 3 Grade 2 rashes (at 3-4 wks of age)
- 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**

Figure 2:
Median HIV RNA log copies/mL and percentage of infants < 40 copies/mL after 0, 1, 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**

Acknowledgements

We thank the EIT Study participants and their families, and the EIT Study team: Maureen Sakoi, Tlhabologo Baitseme, Thelma Ketshabile, Maduo Oabona, Mogomotsi Modikwa, Salome Othusitse, Obakeng Makalane, Rabana Thuto Aeshar, Maipelo Kegakilwe, Nametsegang Tshosa, Dorcus Babuile, Jamie Ramaabya, Simon Mosopa, Muchaneta Bhondai, Kebaiphe Moabi, Tebogo Mokotedi, Boitumelo Tebape, Kesegofetse Agisanang, Masego Rabantetse, Disaro Jack, Tumalano Sekoto, Thabani Ncube, Lorato Esele, Princess Bobo Mapenshi, Comfort Maphorisa, Tshepho Frank, Laura Vaughan, Chloe Aluetta-Young, Morgan Packer, Ria Madison, Mompati Mmalane, Ron Bosch, Max Essex, Timothy Henrich, Mogomotsi Matshaba, Loeto Mazhani, Kenneth McIntosh, Madisa Mine, Chipo Petlo, Kathleen Powis, Xu Yu. We also thank: The Botswana Ministry of Health and Wellness, the Botswana Human Research Development Committee, the Harvard Office of Human Research Administration, the EIT DSMB Members, and the NIH (Judi Miller, Ellen Decarlo, Patrick Jean-Philippe, Sheryl Zwerski). This study was funded by NIH/NIAID (U01AI14235).