OUTCOMES OF NEONATES WITH RAPID HIV TREATMENT IN US: TREATING INFANTS EARLY STUDY

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BACKGROUND

- Little is known about the outcomes of perinatally-infected infants in clinical (non-research) settings following early intensive initiation and treatment with antiretroviral therapy (ART).
- The Treating Infants Early Study (TIES) is an observational cohort study that aims to describe the management, efficacy and safety of ART initiated before 6 weeks of life among infants with HIV in communities throughout the USA.

METHODS

- Infants and mothers were referred for enrollment by their providers.
- Informed consent was obtained by phone or in person, with paper or electronic documentation.
- Infant eligibility criteria included HIV diagnosis (=2 nucleic acid tests [NAT]), age < 2 years at enrollment, and ART initiation at < 6 weeks of life. Their mothers were also offered brief enrollment, which included a one-time blood draw and history.
- Maternal, birth and ART history, and clinical outcomes were abstracted from medical records, collected periodically during follow up.
- Antiretroviral (ARV) initiation was defined as the first day of 3 drugs at treatment dosing
- Descriptive statistics were applied for this analysis.
- Blood specimens were collected into a BD Vacutainer® CPT™ Mononuclear Cell Preparation Tube-Sodium Citrate opportunistically, when blood was drawn for clinical indications; samples were shipped overnight at room temperature to a central lab; peripheral blood mononuclear cells and plasma were separated, aliquotted, frozen and stored.

RESULTS

Enrolment

- Among 38 infants screened from Dec. 2015 to Sept. 2018, 15 enrolled, providing median (range) follow-up of 19 (1-32) months; one infant was excluded from analysis due to prior research participation.
- 10 of their mothers enrolled.
- Consent was obtained by phone for 13 (electronic signature once, written 12 times), and in person twice.

RESULTS

Maternal Characteristics (n=11)	Value
Age at delivery (years)˜	24 (15, 36)
Diagnosis	
Perinatal	*1*
Prior to pregnancy	*1*
During pregnancy	*4*
Intrapartum	*4*
On ARV during pregnancy	6
Substance Use near delivery	3
CD4 count (cells/mm^3)^*	477 (163, 2,291)
HIV-1 RNA [Log$_{10}$(copies/ml)]*	4.1 (1.3, 4.80)

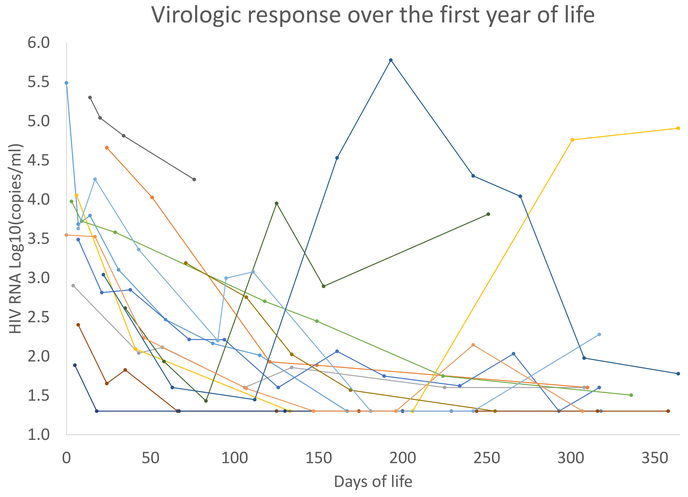
*Values are ˜median (range) on n; ^ available from 8 *< 14 days prior to delivery*

Infant Characteristics (n=14)	Value
Female*	9
Birth Weight (kg)	2725 (1100, 3915)
Gestational Age (weeks)	37 (28, 40)
CD4 %^	46 (10,66)
CD4 count (cells/mm^3)^	2,390 (231, 4,190)
HIV-1 RNA [Log$_{10}$(copies/ml)]^	3.7(1.9, 5.5)
ARV Regimen prior to diagnosis	
ZDV alone	2
ZDV+NVP(prophylactic dosing)*	6
ZDV+3TC+NVP (prophylactic dosing)*	4
ZDV+3TC+NVP (treatment dosing)	2
Age at first + HIV NAT	4 (0-17)
Age at ART start (days)	8.5 (0-36)
ARV regimen upon diagnosis	
ZDV+3TC+NVP (treatment dosing)	12
ZDV+3TC+LPV/r	2
State of residence	FL (4), DC (3), TX (2), NJ, MO, GA, CA, OR

*Values are median (range) or n, ^ Closest to birth.*NVP dosed as per HPTN 0404 to target prophylactic exposures*

VIROLOGY

- There was a wide range of baseline plasma HIV RNA levels and initial responses
- Virologic suppression (RNA < the lower limit of detection) was achieved in 11/14 infants after a median (range) of 143 (13-469) days of ART
- One infant had virologic rebound (> 200 c/ml, at 295 days)
- Ten remained suppressed throughout follow up; one had very early and prolonged suppression, from day 66 through day 958 of life in once case)



SAFETY AND TOLERABILITY

- Anemia was commonly reported during follow up in 8 (53%) infants, and neutropenia in 5 (33%)
- ART was never interrupted due to perception of drug toxicity but 2 regimens were changed based on birth HIV genotypes

DISCUSION AND CONCLUSIONS

- Response to ART likely related to host/viral factors, but also adherence challenges
- Heterogeneity in baseline HIV RNA levels is likely multifactorial, potentially reflecting the duration of infection (i.e. earlier or later in utero), transplacental passage of maternal ARV, and other maternal/infant/viral factors
- Most infants with HIV in this cohort had initiated ART before 9 days of age, underscoring the urgent need for potent and safe ART options in the neonatal period.
- With rapid and durable virologic suppression, some perinatally-infected infants treated in community settings might have low reservoir levels and could be good candidates for future studies of remission strategies.

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