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Markers for Sustained Viral Suppression and HIV Reservoir in Very Early Treated HIV-infected Children in Botswana

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Background

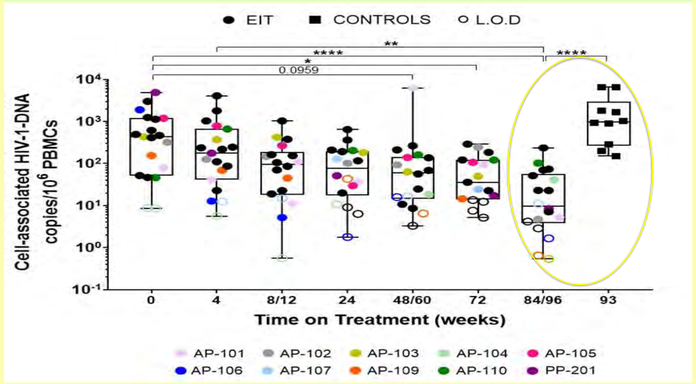
- Markers for sustained viral suppression over time are not available for HIV infection
- The unique nature of very early infant treatment raises the possibility of using the basic HIV screening tests as longitudinal markers for viral reservoir quantification and for treatment success
- We evaluated whether HIV serology was a useful marker for sustained RNA suppression or low cell-associated HIV reservoir among HIV-infected children treated very early in life

Methods

- The Early Infant Treatment Study (EIT) started antiretroviral treatment (ART) for HIV-infected children at < 7 days of age
- Quantitative HIV DNA was evaluated every 1-3 months in PBMCs, and at 84 weeks with repeat qualitative whole blood DNA PCR testing and dual enzyme immunosorbent assay (EIA)
- HIV RNA evaluation occurred every 1-3 months and at 84 weeks post treatment initiation
- Children starting ART at age 30-365 days in the Botswana ART program and sampled at 24-36 months of age served as controls (Figure 1).
- Comparisons of HIV serology, RNA suppression or low cell-associated HIV reservoir among HIV-infected children treated very early in life were by Wilcoxon Rank Sum testing

Figure 1

Among the first 17 EIT children: median PBMC DNA reservoir significantly lower than 10 control children (10.9 vs. 981.4 copies/million cells)



Results

- 30 of 40 HIV+ children in the EIT study reached 84 weeks by the time of this analysis (Table 1 and Table 2)
  - o 14/30 (47%) had sustained RNA < 40 copies/mL from 24 to 84 wks
    - *12/14 (86%) had negative 84 week EIA, 2/14 (14%) indeterminate*
    - *10/14 (71%) had negative 84 week whole blood qualitative DNA PCR, 0 indeterminate*
  - o 16/30 (53%) had RNA > 40 copies/mL at least once from 24 to 84 wks
    - *5/16 (31%) had negative 84 week EIA, 1/16 (6%) indeterminate*
    - *4/16 (25%) had negative 84 week whole blood qualitative DNA PCR, 1 (6%) indeterminate*
- In total, the 84 week EIA was negative for 17/30 (57%) and whole blood qualitative DNA PCR had reverted to negative for 14/30 (47%)
  - EIA and qualitative PCR concordant for 73% of interpretable tests
  - *Nearly half of very early treated children can no longer be diagnosed by conventional testing by 84 weeks*
- Cell-associated DNA from PBMCs differed from plasma results
  - No association between the PBMC reservoir and the EIA test result at 84 weeks (p=0.63) in this first group of EIT children tested

Table 1: Plasma HIV RNA by Week of ART, and Week 84/96 Serostatus by EIA, Whole Blood Qualitative DNA, and PBMC DNA

	Plasma HIV RNA by ART week								Week 84 EIA Antibody	Week 84 Qualitative DNA	Week 84/96 PBMC DNA (copies/million cells)
	0	4	12	24	36	60	84	96			
A	1661	53	<40	<40	<40	<40	<40	<40	-	-	5.3
B	17244	186	<40	11182	52	<40	<40	634	+	-	4.7
C	1636	408	<40	<40	<200	3648	<40	<40	+	+	0.5
D	1111950	1413	42	860	<40	98	49993	69	+	+	15.6
E	1375	161	72	<40	<40	<40	<40	33727	+/-	+	115.0
F	>10000000	191	<40	<40	<40	<40	<40	<40	-	-	1.7
G	<40	<40	<40	<40	<40	<40	<40	<40	-	-	10.9
H	60247	307	50	164	46	<40	<40	<40	-	-	0.6
I	3145	533	<40	<40	<40	<40	<40	<40	-	-	102.3
J	1005	561	42	<40	<40	<40	<40	<40	+/-	-	2.9
K	272	6591	<40	735	55	106	339	1128	+	+	51.4
L	1314	<40	<40	<40	<40	<40	319	<40	+	+	4.2
M	23686	<40	<40	<40	<40	<40	<40	<40	-	+	7.1
N	20291	12315	145164	1595770	133084	<40	7114	65	+	+	70.2
O	<200	<40	<40	<40	<40	<40	<40	<40	-	-	23.0
P	12984	<40	<40	<40	<40	<40	<40	<40	-	-	22.8
Q	315020	1051	97	300	166	<40	<40	<40	-	+	73.3
R	79	66	77	<40	<40	<40	<40	<40	-	+	236.2
S	11677	<40	<40	<40	<40	<40	<40	<40	-	-	--
T	224127	388	163	<40	<40	<40	<40	<40	-	+	--
U	143616	46	<40	<40	3966	<40	<40	<40	+	-	--
V	8548	487	<40	<40	<40	<40	<40	<40	-	-	--
W	33502	628	<40	76	<40	<40	<40	<40	-	+/-	--
X	1837	118	166	5019	15325	23868	69549	2671	+	+	--
Y	88885	456	45	<40	<40	28822	358491	36044	+	+	--
Z	2279	<40	<40	<40	<40	<40	<40	--	-	-	--
AA	31708	350	<40	<40	89356	<40	<40	--	+/-	+	--
BB	114	105	<40	40	52	<40	<40	--	-	+	--
CC	276	743	310	255	31341	<40	<40	--	+	+	--
DD	292	41	59	<40	<40	364	<40	--	-	-	--

Table 2: Predictive value of 84 Week Serology and Whole Blood Qualitative DNA for Sustained Plasma Suppression from 24-84 weeks

Negative HIV Serology	71% with sustained suppression
Positive HIV Serology	100% with at least one rebound
Negative Qualitative HIV DNA	71% with sustained suppression
Positive Qualitative HIV DNA	73% with at least one rebound

Conclusions

- **HIV serostatus and whole blood qualitative DNA at 84 weeks were useful markers for sustained RNA suppression (but not for PBMC reservoir) among early-treated children**
- **Very low viral reservoirs continue to be noted among early-treated children**

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