

INTRODUCTION

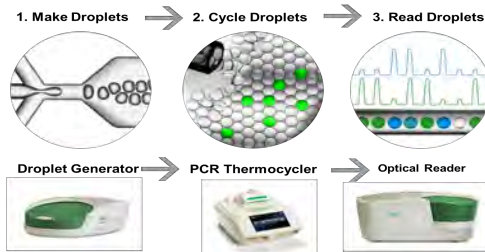
- Cure among HIV-1-infected individuals is precluded due to early establishment of latent HIV-1 reservoirs, primarily in resting memory CD4+ T cells¹⁻³.
- Early combination antiretroviral therapy (cART) restricts the size of the latent reservoir, and affords long-term virologic control in the absence of antiretroviral therapy (HIV-1 remission)⁴.
- Rapid institution of cART at 30 hours of age may have contributed to prolonged HIV-1 remission (27 months instead of ~2 weeks) in the "Mississippi Child" by restricting reservoir size^{5,6}.
- The rapidity with which HIV-1 reservoirs are formed in perinatal infection, and the effects of early cART on the dynamics of decay of HIV-1-infected cells and their transcriptional states are not defined.

OBJECTIVE

Characterize decay of biomarkers of HIV-1 infection under Lopinavir/ritonavir-based ART in perinatally-infected infants during the first two years of life.

- Cellular HIV-1 DNA:** Total HIV-1 DNA (Pol); Episomal HIV-1 DNA (2-LTR circle)
- Cellular HIV-1 RNA:** multiply spliced RNA (Tat/Rev); unspliced RNA (Gag)
- Viral Outgrowth Assay:** Replication competent HIV-1 DNA from resting CD4+ T cells⁷.

METHODS



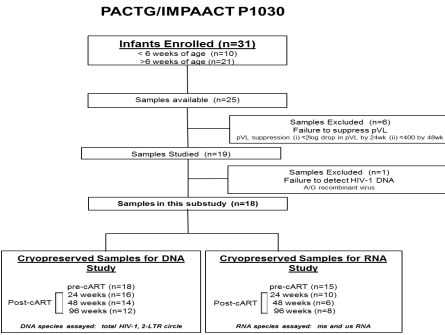
- HIV-1 DNA- normalized to RPP30 (LOD: 2.6 copies/106 cells)
- HIV-1 RNA- normalized to total input RNA (LOD- msRNA- 0.18 copies/ugRNA; usRNA- 0.35 copies/ugRNA)

Adapted from Bio-Rad

Statistical Analysis: Slopes for HIV-1 DNA estimated using linear mixed effects model. Relationships between HIV-1 DNA, RNA, and viral load are summarized by follow-up week using either Pearson (for log-transformed variables) or Spearman correlation coefficients

***p<0.0001; **p<0.01; *p<0.05 indicated statistical significance.

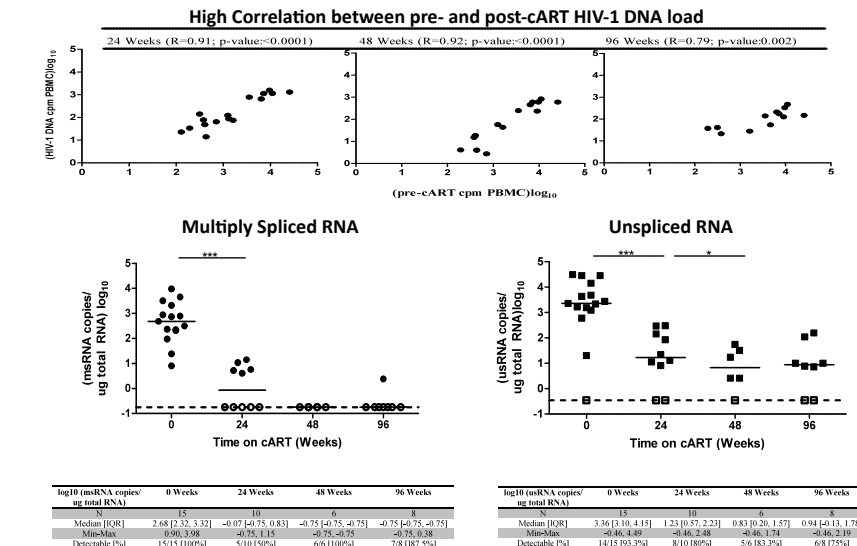
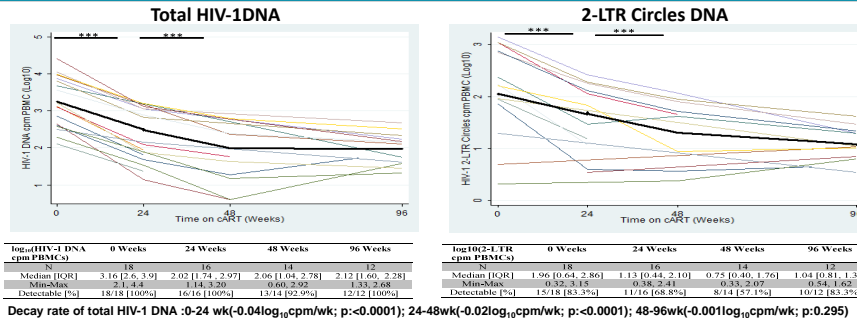
STUDY POPULATION



Patient Characteristics (N=18)

Gender	
Female	9/18 (50%)
Pre-cART age (months)	
Median (IQR)	2.04 (1.35, 2.78)
Min, Max	0.99, 5.39
Pre-cART Plasma HIV-1 RNA (log ₁₀ copies/ml)	
Median (IQR)	5.77 (5.40, 6.27)
Min, Max	3.72, 6.88
Race	
White non-Hispanic	0 (0%)
Black non-Hispanic	12 (66.7%)
Hispanic	6 (33.3%)
Pre-cART CD4+ T cell percent	
Median (IQR)	34.50% (29.0, 41)
Min, Max	11.0, 49.0
Prophylactic Regimen	
None	4 (22.6%)
Zidovudine	10 (55.6%)
Zidovudine + Nevirapine	3 (16.7)
Zidovudine + Lamivudine	0 (0%)
Zidovudine + Lamivudine + Nevirapine	1 (5.6%)
Nucleoside Reverse Transcriptase Inhibitors	
Zidovudine + Lamivudine	10 (55.6%)
Stavudine + Lamivudine	7 (38.9%)
Stavudine + Abacavir	1 (5.6%)
Zidovudine + Didanosine	0 (0%)

RESULTS



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Correlation of Total HIV-1 DNA and Viral Outgrowth Assay (VOA) and Q-VOA

HIV-1 DNA and Q-VOA	24 Weeks	48 Weeks	96 Weeks
N	11	8	6
Spearman's (ρ)	0.628	0.539	0.44
P-value (p)	0.240	0.281	0.381
DNA A1/1/PM	66.0 [14.81, 240.15]	169.79 [52.19, 375.08]	148.33 [66.36, 273.61]
Min-Max	7.06, 641.60	8.65, 751.55	33.59, 933.3

Ratio of HIV-1 RNA(us) and Total DNA

usRNA/total HIV-1DNA	0 Weeks	24 Weeks	48 Weeks	96 Weeks
N	14	8	5	6
Median [IQR]	18.24 [6.25, 36.60]	2.26 [0.37, 3.57]	0.68 [0.15, 1.07]	2.46 [0.73, 4.55]
Min-Max	0.05, 70.14	0.06, 15.44	0.03, 1.30	0.59, 8.1

Correlation of HIV-1 RNA with pVL and Total DNA

msRNA	Correlation with Plasma Viral Load (pVL)		
	Time on cART (N)	Spearman's (ρ)	P-value
msRNA	0	0.27	0.33
usRNA	0	0.59	0.02

Correlation with HIV-1 DNA			
	0	15	0.73
msRNA	0	15	0.73
usRNA	0	15	0.68
msRNA	24	10	0.72
usRNA	24	10	0.58
usRNA	48	6	0.38
usRNA	96	8	0.73

CONCLUSIONS

- Rapid establishment of a large pool of HIV-1 infected cells within two months of life in perinatal infection.
- Pre-ART infected cell frequencies influence time to undetectable viral load and eventual reservoir size.
- HIV-1 DNA was in excess of replication competent genomes at all time points tested.
- HIV-1 infected cells decrease in a biphasic manner in the first year of life with cART but stabilizes for an additional year.
- Preferential clearance of transcriptionally active cells with cART, though unspliced RNA detected through 96-weeks.
- Findings have implications for refining cART for infants, including with immunotherapeutic approaches, towards long-term remission

ACKNOWLEDGEMENTS



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