INTRODUCTION

• Cure among HIV-1-infected individuals is precluded due to early establishment of latent HIV-1 reservoirs, primarily in resting memory CD4+ T cells[1,2].

• 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 cells 7.

METHODS

STUDY POPULATION

RESULTS

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

<table>
<thead>
<tr>
<th>Time (Weeks)</th>
<th>pVL (Log10)</th>
<th>Total HIV-1 DNA (Log10)</th>
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<tbody>
<tr>
<td>20</td>
<td>-0.021</td>
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<tr>
<td>48</td>
<td>0.066</td>
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<tr>
<td>96</td>
<td>0.295</td>
<td>-0.208</td>
</tr>
</tbody>
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Correlation of HIV-1 RNA (us) and Total DNA

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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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REFERENCES