Poster 1034

Pediatric ART Interruptions Transiently Raise HIV DNA Without Large Changes to Long-Term Reservoirs

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Cohort studied

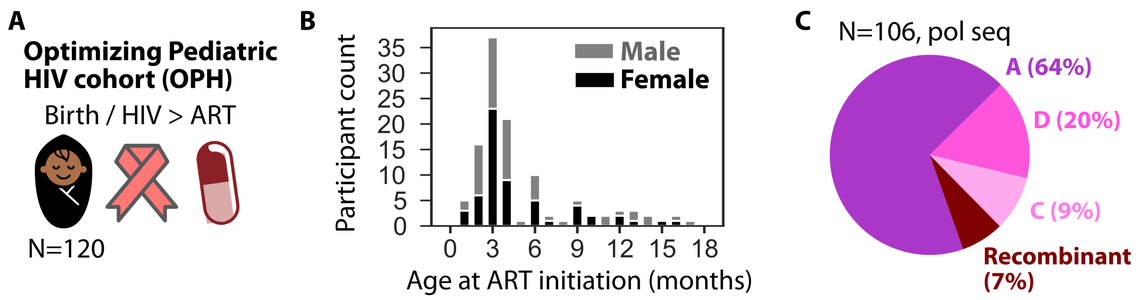


Figure 1. OPH cohort data and study design.
A) Overall cohort comprises 120 Kenyan children who acquired HIV near birth and received early ART.
B) HIV-1 subtype from 106 participants sequenced via pol.
C) Histogram of ART initiation age colored to show balance of male and female children.

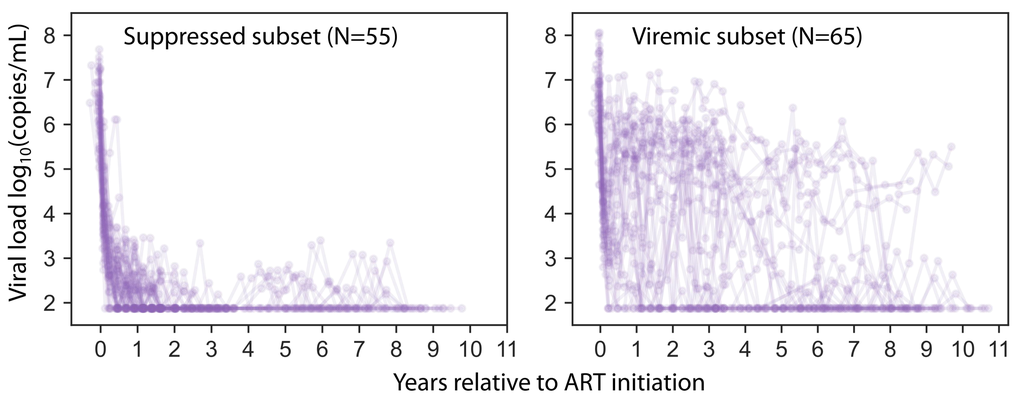
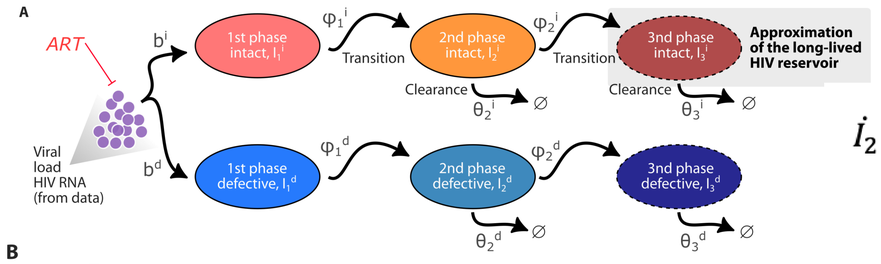


Figure 2. Viral loads for the **suppressed** and **viremic** subsets of OPH participants, stratified based on whether viral load dropped below 1000 copies/mL within the first year of ART and stayed below 3000 copies/mL thereafter.

Mathematical modeling HIV DNA inclusive of viremia – HIV DNA levels can be described by accounting for HIV RNA



$$\dot{I}_2 = \phi_1 I_1 - (\theta_2 + \phi_2) I_2$$
$$\dot{I}_3 = \phi_2 I_2 - \theta_3 I_3$$

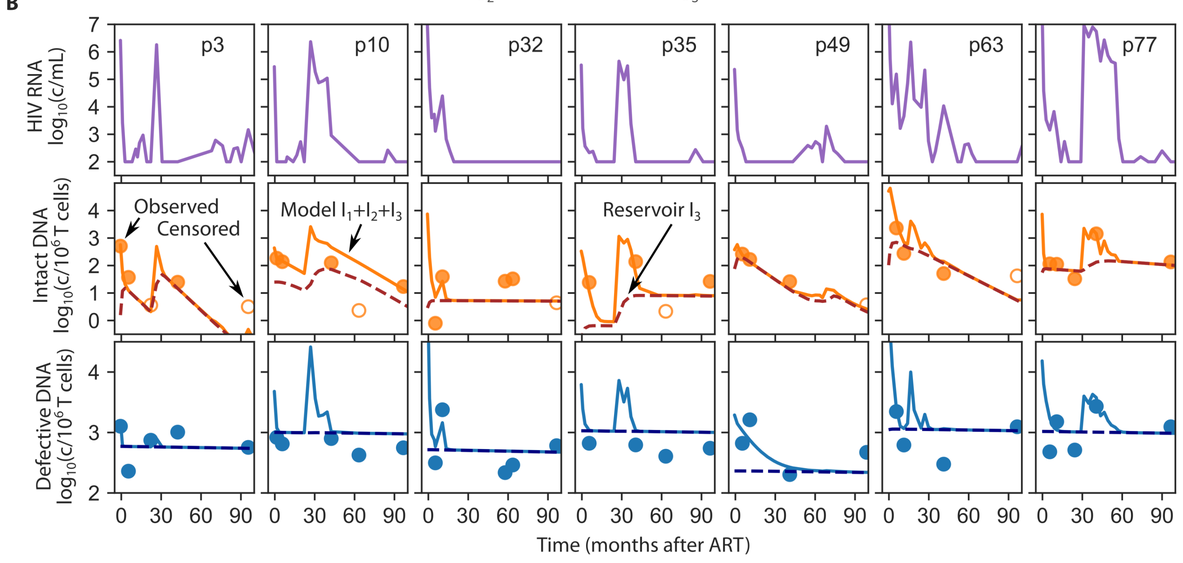


Figure 4. Modeled kinetics including viremia allow comparison with viremic and suppressed subset.
A) Model schematic/equations linking HIV RNA viremia and creation of HIV DNA
B) Seven example model fits where each column shows a participant, and the rows show HIV RNA and observed intact and defective HIV DNA (dots) vs model output of total HIV DNA ($I1+I2+I3$, solid line) and Phase 3 long-lived HIV DNA ($I3$, dashed line) which is intended to approximate the rebound competent HIV reservoir.

Decay rates in the suppressed subset – Differential decay of intact and defective proviruses

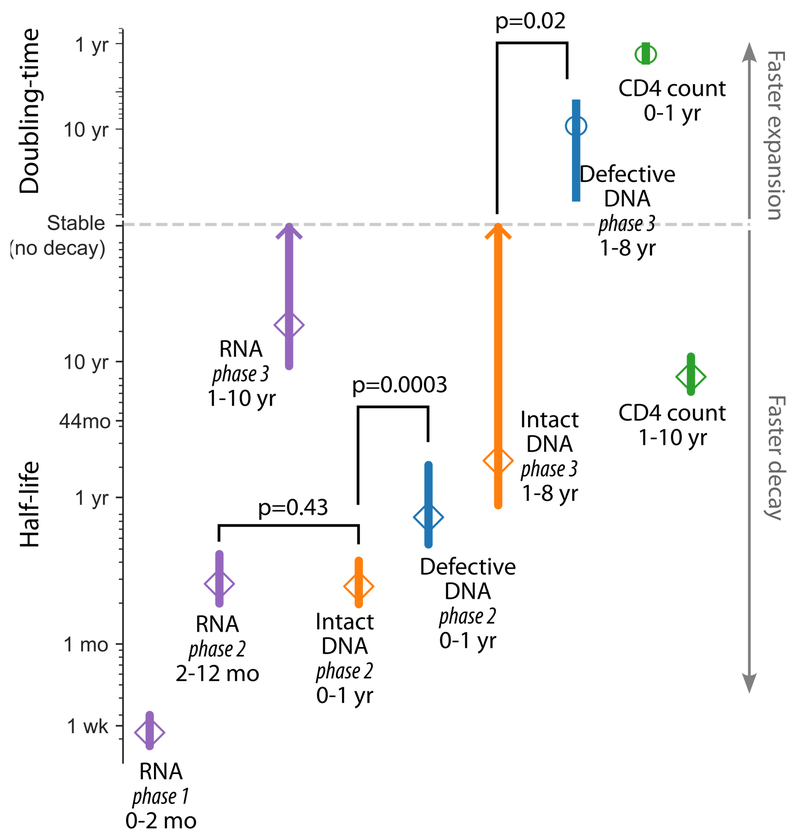


Figure 3. Estimated population means (dots) and 95% confidence intervals (CI, lines) for each data type. Phases were defined as the first 0-2 months, 2-12 months for HIV RNA and 0-1 year for HIV DNA, and 1-8 years on ART. Axes are split by no decay (or very stable kinetics) such that half-lives and doubling times can be presented. Arrows on CI indicate overlap with no decay. Comparisons indicate 1-sided Z-test.

Comparing HIV DNA decay rates in suppressed and viremic subsets – Similar long term reservoir kinetics despite viremia

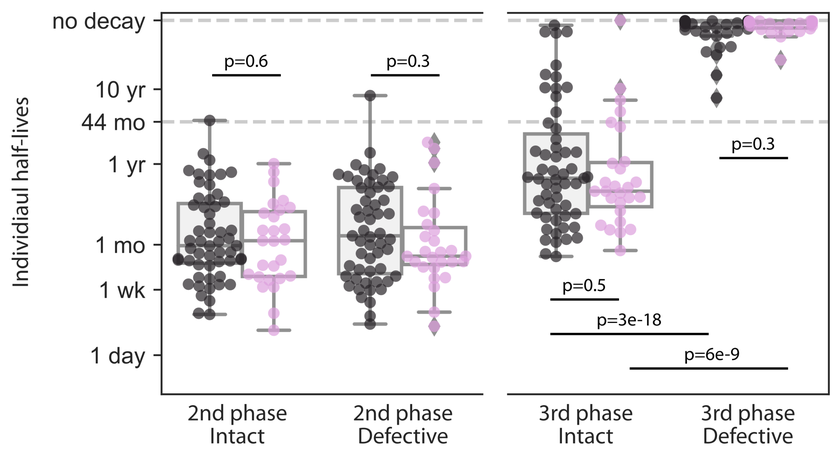


Figure 5. Box plots of individual half-life estimates for intact and defective HIV DNA for Phase 2 and Phase 3 split by suppressed (N=55) and viremic (N=27) participants. P-values indicate one-sided Mann-Whitney U-Test.

Conclusions

- Cross-subtype IPDA worked on 5 virus subtypes for 120 children from Nairobi
- Differential decay of intact and defective proviruses in this pediatric cohort observed for two phases (0-1 year and 1-8 years on ART)
- Modeling could describe HIV DNA whilst accounting for HIV viremia in children who did not achieve perfect suppression and had transient viremia
- **Long-term estimated decay rates in suppressed and viremic participants were not significantly different, suggesting that transient viremia does not strongly raise reservoirs and/or alter long-term dynamics**

We gratefully recognize the study participants, as well as the clinical and administrative teams from the Optimizing Pediatric HIV (OPH) Cohort. Funding was provided by the NIH R01s HD023412 & HD094718 to DL and GJS, K25 AI155224 and R01 AI186721-01 to DBR. LBC is supported by UM1AI164565. DBR is extremely grateful for the support of the University of Washington/Fred Hutch Center for AIDS Research (CFAR, P30 AI027757) through a New Investigator Award and a Supplement that initiated and funded this project. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript