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Rapid ART in blood donors with Acute and Recent HIV clade C infection in South Africa

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BACKGROUND

- Blood donations in South Africa are tested in parallel for HIV antibody (Ab) and RNA using individual-donation nucleic acid testing (ID-NAT), allowing annual detection of ~60 Acute (RNA+/Ab-) and >400 Recent (RNA+/Ab+/LAg recent) HIV infections.
- **We hypothesized that initiation of antiretroviral therapy (ART) in earlier Fiebig stages would correlate with smaller HIV reservoir size.**

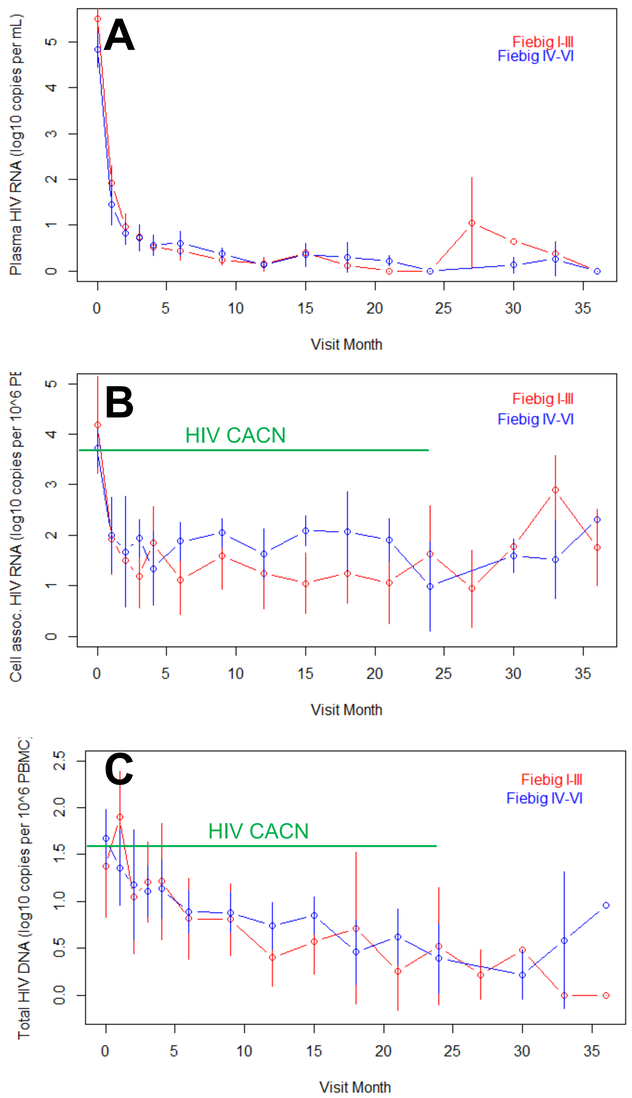
METHODS

- A prospective cohort study enrolled Acute and Recent HIV infected blood donors from 2015-2017.
- HIV Ab (Abbott Prism), RNA (Grifols ID-NAT) and recency of infection < 195 days (Sedia limiting-antigen avidity (LAg)) were measured on index donation and enrolment samples.
- Donors were referred rapidly to an academic research network for ART with RAL/TDF/FTC X 6 months followed by EFV/TDF/FTC.
- A comparator group of untreated Acute and Recent HIV infected blood donors was enrolled (HIV unTx)
- We measured plasma RNA using the single copy Aptima HIV-1 Quant Assay (Hologic) with 5 replicates, cell-associated HIV RNA by qRT-PCR and total HIV DNA by real-time nested PCR.
- We described data using medians and interquartile range (IQR) and compared HIV reservoir size between treatment initiation in Fiebig I-III vs. IV-VI using negative binomial regression.

Table 1. Baseline characteristics of the study population, by Fiebig stage. Numeric values are medians (interquartile range)

Variable		Fiebig I-III (N=18)	Fiebig IV-VI (N=45)	HIV unTx (N=100)
Age		34	28	26
Female (n, %)		13 (72)	32 (71)	75 (75)
Enrollment Delay* (days)		7 (3)	25 (17)	N/A
Duration of follow-up (months)		28 (16)	21 (7)	N/A
Poor Compliance (n, %)		3 (17%)	9 (20%)	N/A
HIV Genotype	C	16	36	-
	02_AG	0	1	-
	No Amp/Missing	2	8	-
Plasma HIV RNA # (log10 copies/mL)		6.06 (1.43)	4.85 (1.72)	3.95 (1.18)
HIV caRNA # (log10 copies/10^6PBMC)		3.83 (3.00)	3.68 (1.61)	3.72 (1.71)
HIV DNA # (log10 copies/10^6 PBMC)		1.68 (2.12)	1.81 (1.59)	1.51 (1.39)
CD4 count # (cells/uL)		459 (371)	484 (290)	-

* From date of blood donation



Figures. (A) Plasma RNA; **(B)** cell-associated RNA; and **(C)** and cell-associated total DNA by week on ART and Fiebig stage at enrollment.

RESULTS

- Cohort enrolment included 18 Fiebig I-III (7 day treatment delay) and 45 Fiebig IV-VI (25 day delay); 70% female Genotype: Clade C (62), 02_AG (1) (**Table 1**).
- Reservoir measurements after median followups of 28 and 21 months (**Figures A,B,C and Table 2**) showed:
  - A. Single copy Plasma RNA at enrollment was ~1 $\log_{10}$ higher in Fiebig I-III than IV-VI but after treatment did not differ by month, Fiebig group, age or sex.
  - B. Cell-assoc RNA did not differ by Fiebig stage at enrollment but declined by 0.28 $\log_{10}$ with each month of treatment, was significantly lower in Fiebig I-III vs. Fiebig IV-VI and borderline lower in females.
  - C. Cell assoc total DNA also did not differ by Fiebig stage at enrollment but declined by 0.18 $\log_{10}$ with each month of treatment and was borderline higher with older age and borderline lower in females.

Table 2. Multivariable negative binomial of HIV reservoir parameters.

Variable	Estimate	p value
$\log_{10}$ Plasma RNA		
Months on Rx	-0.66	0.55
Fiebig I-III vs IV-VI	-15.41	0.35
Age	+0.37	0.49
Female vs Male	-17.10	0.14
Poor Compliance	+0.23	0.99
Months * Fiebig group	+0.52	0.70
$\log_{10}$ Cell-Assoc. RNA		
Months on Rx	-0.28	0.001
Fiebig I-III vs IV-VI	-3.31	0.008
Female vs Male	-1.43	0.10
Poor Compliance	+1.18	0.29
Month * Fiebig	+0.24	0.01
$\log_{10}$ Cell-Assoc. DNA		
Months on Rx	-0.18	<0.0001
Fiebig I-III vs IV-VI	-0.22	0.70
Age	+0.04	0.11
Female vs Male	-1.05	0.06

CONCLUSIONS

- **Among HIV Clade C-infected donors initiated on ART within 195 days of infection, we observed a small impact of Fiebig I-III treatment on long-term reservoir as measured by lower cell-associated RNA expression.**
- **Borderline lower cell-associated RNA and total DNA in women than in men irrespective of Fiebig stage at treatment initiation.**
- **This study demonstrated that, in a high HIV incidence setting, a partnership between a national blood service and an academic research network can establish early treatment cohorts for subsequent HIV Cure research initiatives.**

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