Low-Level HIV-1 Viremia on ART is Stable Over 6 Months

Leah D Brandt[1], Deborah K McMahon[1], Joshua C Cyktor[1] Amanda J. Saylor[1], William Louth[1], Dianna L. Hoeth[1], Asma Naqvi[1], Karen Harrington[2], Jana L. Jacobs[1], Elias K Halvas[1], Sharon A Riddler[1], John W. Mellors[1]

[1]The University of Pittsburgh, Pittsburgh, PA, USA, [2]Hologic Incorporated, San Diego, CA USA

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BACKGROUND

- Antiretroviral therapy (ART) effectively suppresses plasma HIV-1 RNA to below the limits of detection by clinical assays (20-40 copies(cp)/mL).
- **Low-level viremia (LLV)**, plasma HIV-1 RNA <20-40 cp/mL, can be detected by highly sensitive, **single-copy assays (SCAs) in most people with HIV-1 on long-term ART**.
- Insight is needed about the longitudinal stability of LLV to determine whether changes in LLV result from assay or biologic variation and **if LLV can be used as a stable marker of the proviral expression.**

QUESTIONS AND OBJECTIVE

Q1: *What is the biologic variation of LLV?*

Q2: *Are there patterns of LLV between males and females?*

Q3: *Can LLV be used as a biomarker of change in the expressed HIV-1 reservoir in interventional studies designed to eliminate virus-producing cells?*

WE CONDUCTED A LONGITUDINAL STUDY TO ASSESS THE STABILITY OF LLV BY SCA OVER 6 MONTHS IN PEOPLE WITH HIV-1 ON LONG-TERM ART.

METHODS

We enrolled 20 long-term, ART-suppressed (>5 years) participants (**Table 1**).

- Plasma samples were collected weekly for one month and every 4 weeks or monthly until week 24 (**Figure 1**).
- LLV was measured from 5mL plasma by a multi-replicate adaptation of the Hologic Panther automated SCA platform (Jacobs, *J Clin Micro* 2019) over 10 sampling timepoints.

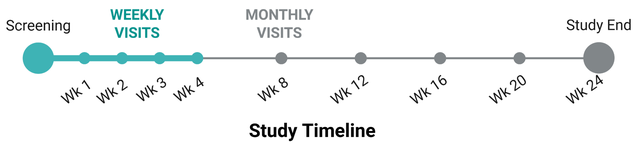


Figure 1. Study schema and timeline of participant plasma collection.

Low-level HIV-1 viremia on long-term ART (>10 years) is consistently detectable and stable over 6 months, with no sex-based differences observed.

Table 1. Study participant characteristics for 16 individuals who have completed analyses.

Sex	Donor ID	Age at entry	Race	Years on ART	ART regimen on study[A]
Males (n = 11)	LLV-08	54	Black	16	BIC/TAF/FTC
	LLV-22	63	Black	23	FTC/RPV/TAF
	LLV-09	56	Caucasian	>10	DTG/3TC
	LLV-25	70	Caucasian	>10	DTG/FTC/TAF
	LLV-28	65	Black	18	DTG/3TC
	LLV-29	62	Caucasian	>10	FTC/TAF/DOR
	LLV-02	66	Black	18	ABC/DTG/3TC
	LLV-47	62	Caucasian	38	ATV/FTC/TAF/RAL
	LLV-58	34	Black	15	BIC/TAF/FTC
	LLV-54	43	Caucasian	22	DTG/3TC
	LLV-34	61	Caucasian	32	DRVr/DTG
Females (n = 5)	LLV-11	57	Black	>10	BIC/TAF/FTC
	LLV-49	58	Black	19	ABC/DTG/3TC
	LLV-26	68	Black	>10	FTC/TAF/DOR
	LLV-17	66	Black	30	ABC/DTG/3TC
	LLV-39	55	Black	30	BIC/TAF/FTC

[A] BIC, bictegravir; TAF, tenofovir alafenamide; FTC, emtricitabine; RPV, rilpivirine; DTG, dolutegravir; 3TC, lamivudine; DOR, doravirine; ABC, abacavir; ATV, atazanavir; RAL, raltegravir; DRVr, darunavir/ritonavir

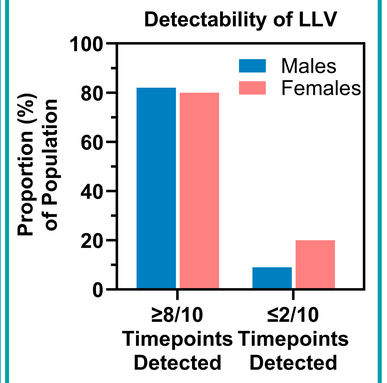


Figure 3. Proportion of males and females with ≥8/10 or ≤2/10 timepoints with detectable LLV.

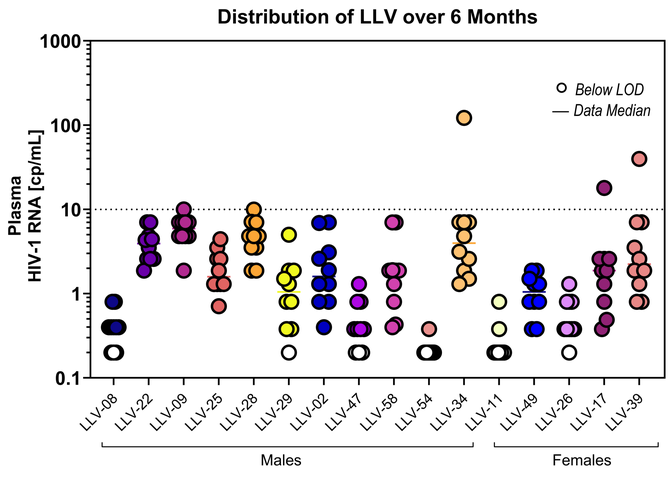


Figure 2. Distribution of LLV across all 10 timepoints in each participant. Data below the limit of detection (LOD) are indicated as open circles (O) and are reported as half the lowest interpolated value of detectable LLV. The dashed horizontal line represents 10 cp/mL.

RESULTS

- We analyzed LLV from 16 participants (**Table 1**).
- LLV was detected in 136/160 (85%) samples evaluated (**Figure 2**).
- 157/160 samples were ≤10 cp/mL, and two samples were >20 cp/mL (**Figure 2**).
- 9 males & 4 females had detectable LLV in ≥8 timepoints (**Figure 3**).
- Slopes of longitudinal LLV from the study population (**Figure 4**) and each participant (not shown) were not significantly different from zero (p=0.30 by linear mixed effects modeling).

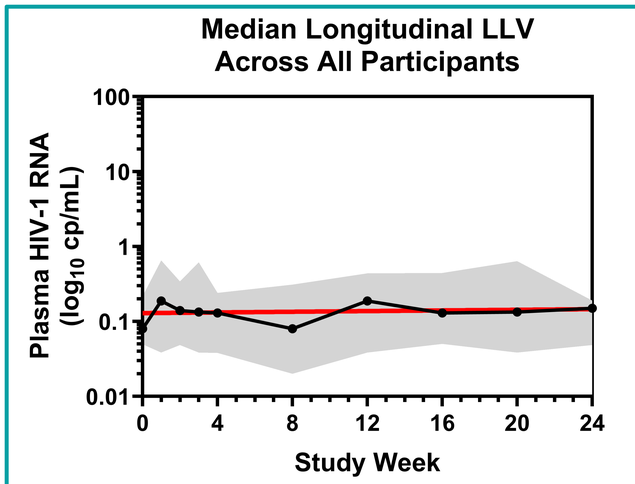


Figure 4. Median plasma LLV over 24 weeks (**black** circles, ●) in 16 participants. The shaded region (▒) indicates interquartile range (25-75%) of LLV at each timepoint. Linear regression of median datapoints is indicated by the red line (—).

CONCLUSIONS

- LLV on long-term ART is stable over 6 months by sensitive, high-throughput automated SCA.
- LLV was ≤10 cp/mL in 98% of samples evaluated.
- There were no differences in patterns of LLV or the proportion of LLV detectability between women and men.
- These findings support the measurement of LLV by high-throughput automated SCA as an initial screening tool to assess the efficacy of therapeutic interventions for their ability to clear virus-producing cells.

PLAIN LANGUAGE SUMMARY

In people on long-term HIV-1 treatment, very low levels of virus (LLV) detected with highly sensitive assays remained stable over six months. This stability—seen in both women and men—suggests that LLV could serve as a simple marker of response to new therapies designed to eliminate virus-producing cells.

ADDITIONAL INFORMATION

Contact information: Leah D. Brandt, PhD; ldb43@pitt.edu

Acknowledgements: We are grateful to the study participants and study team at the University of Pittsburgh.

Funding: CFAR: Rustbelt Center for AIDS Research (P30 AI036219), the Merck Investigators Studies Program (102757), and Hologic Inc. for donating Panther kit reagents.