Poster #420

Patterns of Persistent Viremia After 10 Years of Suppressive ART: ACTG A5276s

Sharon A. Riddler*[1], Evgenia Aga[2], Ronald Bosch[2], Joseph Eron[3], Rajesh Gandhi[4], Barbara Bastow[5], Margaret Bedison[1], David Vagratian[1], John Mellors[1], and the AIDS Clinical Trials Group 5276s Study Team

[1]University of Pittsburgh, Pittsburgh, PA, USA; [2]Center for Biostatistics in AIDS Research, Harvard School of Public Health, Boston, MA, USA; [3]University of North Carolina, Chapel Hill, NC, USA; [4]Massachusetts General Hospital, Boston, MA, USA, and [5]Social & Scientific Systems, Inc, Silver Spring, MD, USA

Sharon Riddler, M.D.
University of Pittsburgh
Keystone Building, Suite 510
3520 Fifth Ave
Pittsburgh PA 15213
Telephone: (412) 383-1741
Fax: (412) 383-2900
E-mail: riddler@pitt.edu

BACKGROUND

- Longitudinal data describing patterns of persistent viremia among patients on long-term antiretroviral therapy (ART) with plasma HIV-1 RNA <50 copies/ml is limited.
- We measured plasma viremia with an HIV-1 RNA assay with single-copy sensitivity (SCA) in a cohort of well characterized HIV-infected individuals within the ACTG ALLRT study (AIDS Clinical Trials Group Longitudinal Linked Randomized Trials).

OBJECTIVES

- **Describe the pattern of residual viremia measured by single copy assay (SCA) in subjects on ART with longitudinal follow up for up to 12 years.**
- **Evaluate for evidence of ongoing decay in plasma viremia.**

METHODS

- A5276s subjects with SCA results at year 4 (weeks 192 and 208) meeting the following criteria were identified:
  - Initiation of first ART within the ACTG clinical trials: ACTG 384, A5014, A5095, A5142
  - Available plasma at approximately 7, 10, and 12 years after ART initiation.
- Plasma from each time point was tested with a SCA targeting gag; the limit of detection was dependent on the input plasma volume and varied from 0.4 to 1 copies/ml (c/ml).
- Subjects initiated ART between 1998 and 2004. Plasma samples were tested between 2011 and 2013.
- SCA amplification efficiency was determined from pre-therapy baseline plasma for all subjects with SCA < 1 copy/ml at both year 4 samples. Inefficient amplification was defined as <10% of the value from the Roche HIV-1 Monitor assay v1.0 or v1.5.
- Repeated measures logistic regression model assessed the likelihood of HIV-1 RNA ≥1 copy/ml during follow up.

- Subjects were grouped according to the SCA results from the year 4 samples (at weeks 192 and 208 after ART initiation):
  - **Persistent** (+/+): ≥1 copy/ml at both weeks 192 and 208
  - **Intermittent** (-/+ or +/-): ≥1 copy/ml at either week 192 or 208, and <1 copy/ml at the other week
  - **Negative** (-/-): <1 copy/ml at both weeks 192 and 208

Characteristics of Study Population

	Total N=64	Persistent N=17	Intermittent N=25	Negative N=22
Sex (%)				
Male	81%	88%	84%	73%
Race/Ethnicity (N, %)				
White, non-Hispanic	37 (58%)	13 (76%)	13 (52%)	11 (50%)
Black, non-Hispanic	15 (23%)	3 (18%)	9 (36%)	3 (14%)
Hispanic	10 (16%)	1 (6%)	2 (8%)	7 (32%)
Other	2 (4%)	0 (0%)	1 (4%)	1 (5%)
Pre-ART CD4 cell count (cells/mm^3)				
Median	219	255	196	216
(IQR)	(81, 347)	(97, 316)	(48, 294)	(141, 407)
Pre-ART HIV-1 RNA (log_{10} copies/ml)				
Median	4.7	5.1	4.8	4.5
(IQR)	(4.4, 5.4)	(4.6, 5.5)	(4.4, 5.5)	(4.2, 4.8)
Duration of ART to last SCA (years)				
Median	11.2	10.5	11.0	11.3
(IQR)	(10.4, 12.8)	(9.9, 12.8)	(10.4, 12.8)	(10.8, 12.5)

Longitudinal Outcomes

	Persistent N=17	Intermittent N=25	Negative N=22
SCA ≥ 1 copy/ml (%)			
Year 7 of ART	65%	32%	14%
Year 10 of ART	56%	36%	9%
Median HIV-1 RNA (copies/ml)			
Year 7 of ART	1.5	<1	<1
Year 10 of ART	1.4	<1	<1

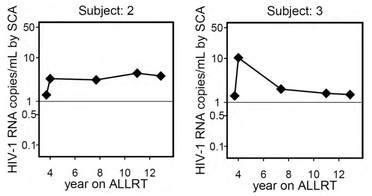
Results and Conclusions

- **Subjects with persistent viremia during year 4 generally had viremia ≥ 1 c/ml at years 7 and 10 (65% and 56%, respectively); by contrast, subjects with undetectable viremia during year 4 rarely had viremia ≥ 1 c/ml at years 7 and 10 (14% and 9%, respectively) (Longitudinal Outcomes Table).**
- **In the subset of N=27 subjects with SCA ≥ 1 c/ml at week 192 of ART, with a total of 111 subsequent SCA measurements, there was no evidence of a decline in the probability of SCA ≥ 1 c/ml over time (p=0.55). The median HIV-1 RNA in these 27 subjects was 1.9, 1.5, and 1.3 copies/ml at year 4, 7, and 10, respectively.**
- **The level of residual viremia measured after approximately 4 years of suppressive ART remains stable for up to 11 years of follow up with no evidence of further decay.**
- **The factors that determine the pattern of persistent viremia are under investigation (see Poster #425LB).**

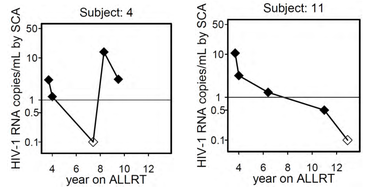
Patterns of Longitudinal Viremia by SCA

Persistent : N=17
(SCA ≥ 1 copy/ml at both weeks 192 and 208)

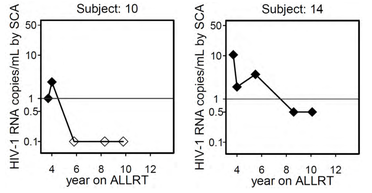
5 (29%) had all subsequent SCA ≥ 1 c/ml



9 (53%) had a single SCA < 1 c/ml

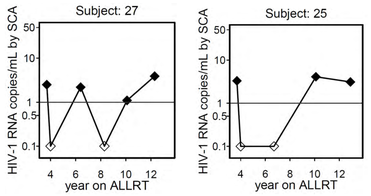


3 (18%) had more than 1 SCA < 1 c/ml

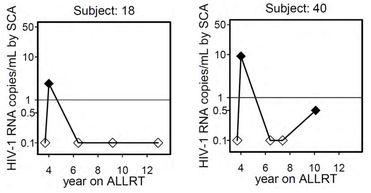


Intermittent: N=25
(SCA ≥1 copy/ml at either week 192 or 208, and <1 copy/ml at the other week)

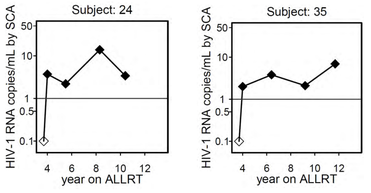
15 (60%) had both ≥ 1 and < 1 c/ml



8 (32%) had all subsequent SCA < 1 c/ml

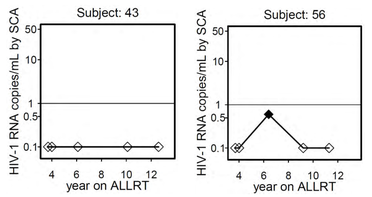


2 (8%) had all subsequent SCA ≥ 1 c/ml

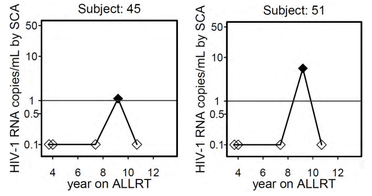


Negative: N=22
(SCA <1 copy/ml at both weeks 192 and 208)

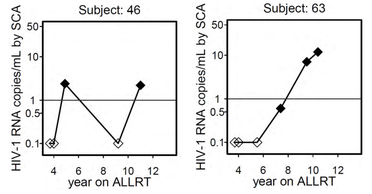
13 (59%) had all subsequent SCA < 1 c/ml



7 (32%) had one subsequent SCA ≥ 1 c/ml



2 (9%) had 2 subsequent SCA ≥ 1 c/ml



Undetected HIV-1 RNA levels by SCA were set to 0.1 copies/ml. The undetected values are represented in the figures with an open symbol. Values less than 1 copy but detectable are indicated by a closed symbol.

ACKNOWLEDGEMENTS:
The A5276s Team wishes to thank the Study Volunteers, Study Staff at participating ACTG Sites, and the ALLRT Protocol Team.
This clinical trial was supported by NIH grants AI-68636 and AI-68634.