

Varied Patterns of Decay of Intact Human Immunodeficiency Virus Type 1 Proviruses Over 2 Decades of Antiretroviral Therapy

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STUDY BACKGROUND & OBJECTIVES

To perform longitudinal measurements of intact, defective and total proviral DNA in 14 people with HIV over the course of 2 decades of well documented virally suppressive ART.

To determine new pattern of HIV DNA decay over time

Table 1. Decreases in Intact, Defective and Total Proviral DNA From First to Last Time Point

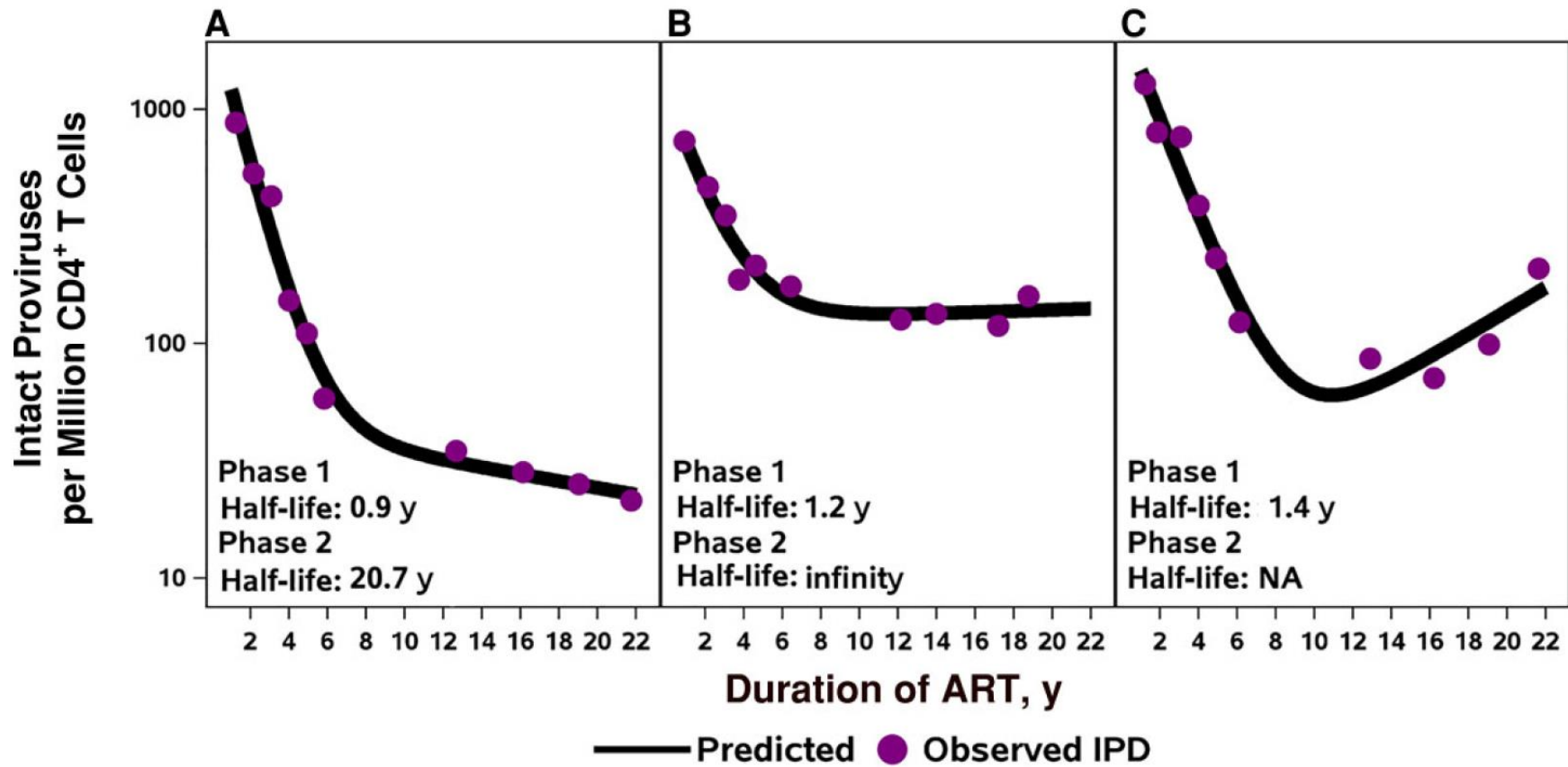
Proviral DNA	Fold Reduction From First to Last Time Point (n = 14) ^a	
	Median (IQR)	Range
Intact^b	13.4 (4.6–46.0)	1.8–91
Defective	0.7 (0.3–1.7)	0.1–4.5
Total	2.7 (1.2–4.9)	0.3–6.7

Abbreviation: IQR, interquartile range.

^aThe first time point was year 1 of antiretroviral therapy (ART); the last time point, years 17–23.

^bFor 2 participants with censored results, the change in intact proviral DNA was calculated using the estimated assay lower limit.

A decay of intact proviruses but not defective proviruses was observed over the course of the study.



Three patterns were observed across 10 participants*:

- Five participants had biphasic decay of IPD levels, **Panel A**
- Three had biphasic decay with a second-phase plateau (slope effectively zero), **Panel B**
- Two showed evidence of increased IPD levels during the second decade of ART, **Panel C**

*Four participants with substantial censored DNA levels or other longitudinal patterns were not included in the modeling.

CONCLUSIONS

The slowing or reversal of intact HIV DNA decay suggests that the mechanisms of infected cell clearance and persistence are different during the first phase of decay (median half-life, 1 year) compared with the second phase (median half-life, >25 years)

If the decay rate during the second phase could be accelerated (like the first phase), it may be possible to achieve HIV remission.

Two participants with late increase in intact provirus were both women, which is consistent with previous reports (PMID: 34612493)

This might be attributable to hormonal and immunologic changes during reproductive aging, which require further investigation.

TAKE HOME MESSAGE

- ▶ HIV lives for a long time in persons
- ▶ There is a slow decay in the amount of HIV living in a person
- ▶ This study shows different patterns of decay.
- ▶ Understanding how HIV gets lower over time may help us develop new ways to make this process go faster to get rid of HIV.