

Rapid Clearance of the Inducible HIV-1 Reservoir after Initiation of Antiretroviral Therapy

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BACKGROUND

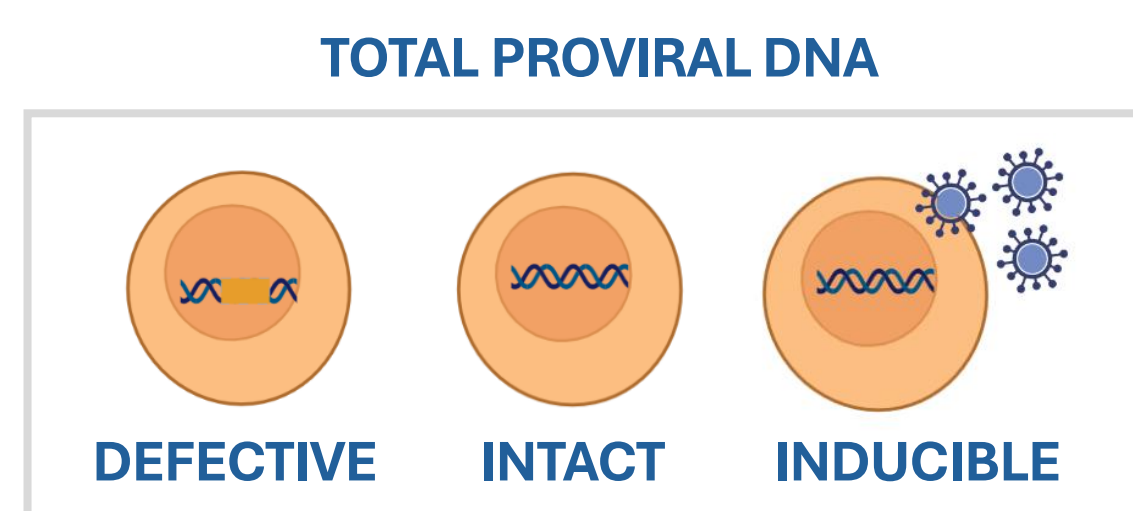
- ✓ The dynamics of the establishment of the intact and defective viral reservoirs after ART initiation have been described by others.
- ✓ The inducible reservoir is a minor fraction, but critical for persistent low-level viremia and for viral recrudescence after ART interruption.
- ✓ Here, we aimed at comparing the dynamics of the establishment of the inducible reservoir upon ART initiation.

STUDY POPULATION & METHODS

- ✓ Study group: 40 participants in the DUALITY study⁽¹⁾, which were people living with HIV (PWH) starting first-line ART with DTG+3TC or DTG+FTC/TAF (n=20 each).

Characteristic	N=40
Age, median (IQR)	31.9 (27.3 - 35.4)
Male at birth, n (%)	40 (100%)
Ethnicity, n (%)	
Caucasian	25 (62.5%)
Hispanic-Latino	14 (35.0%)
Other	1 (2.5%)
Transmission group, n (%)	
Heterosexual	4 (10.0%)
MSM	35 (87.5%)
Unknown	1 (2.5%)
Time since diagnosis of HIV-1 (weeks) median (IQR)	2.1 (1.6 - 2.9)
Plasma viral load (log ₁₀ copies/mL), median (IQR)	4.5 (4.1 - 4.9)
Absolute CD4 ⁺ count (cells/mm ³), median (IQR)	472 (355 - 579)
% CD4 ⁺ , median (IQR)	24.1 (19.8 - 32.8)
Absolute CD8 count (cells/mm ³), median (IQR)	864 (589 - 1084)
% CD8 ⁺ , median (IQR)	47.5 (39.1 - 55.2)
CD4 ⁺ /CD8 ⁺ ratio, median (IQR)	0.5 (0.4 - 0.8)

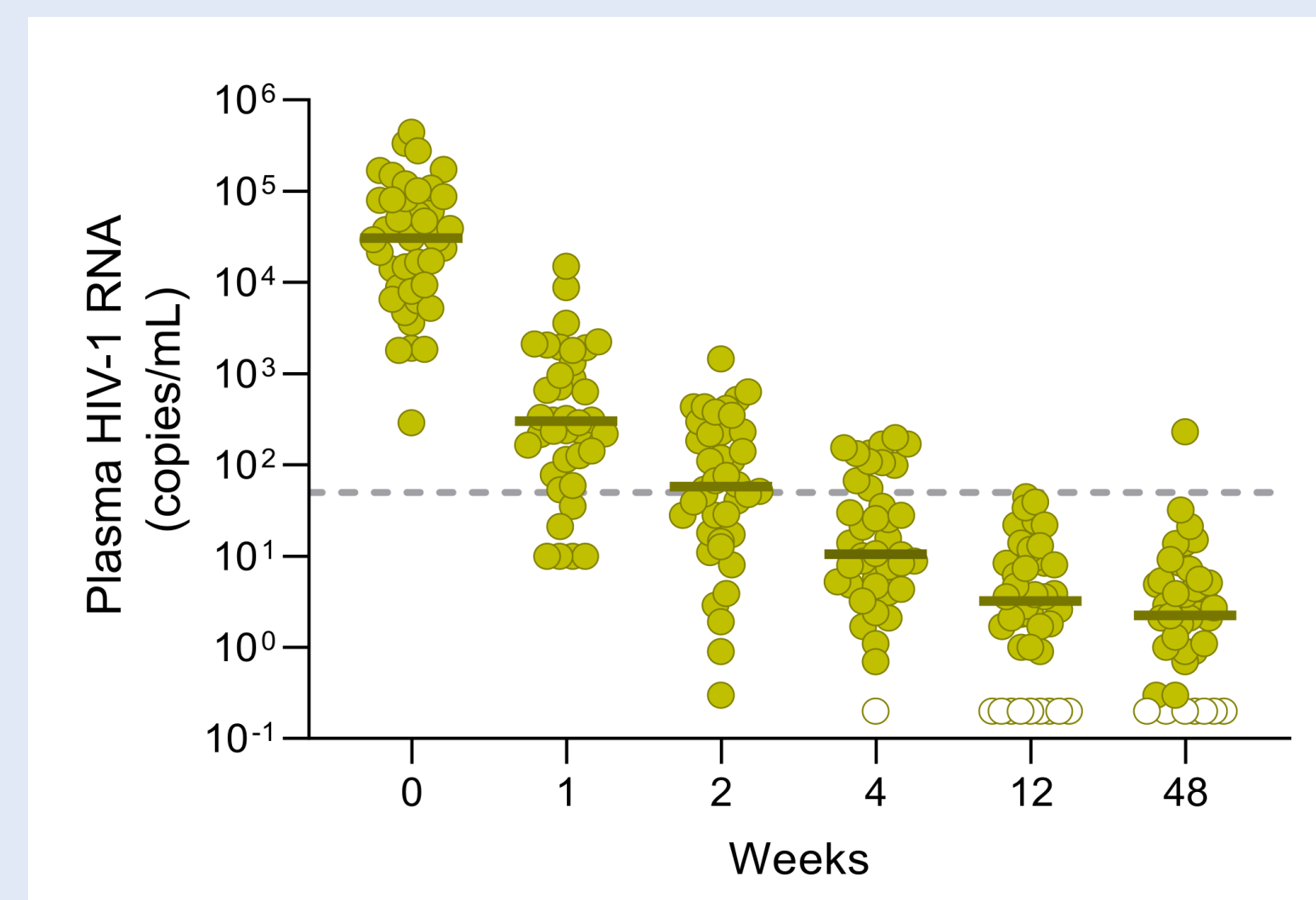
- ✓ The size of the different fractions of the HIV reservoir (total, intact and inducible reservoir) was measured in peripheral CD4⁺ T cells at baseline and weeks 2, 4, 12, 24 and 48.
- ✓ Total proviral HIV-DNA was measured using droplet digital PCR, (LOD=1.4 HIV-1 DNA cps/10⁶ CD4⁺ T cells).
- ✓ Intact and defective proviruses were quantified using the Intact Proviral DNA Assay (IPDA; LOD=2.8 HIV-1 DNA cps/10⁶ CD4⁺ T cells).
- ✓ The inducible reservoir was quantified using the VIP-SPOT assay⁽²⁾ (Viral Protein Spot Assay; average LOD 0.3 HIV-1 antigen producing cell per 10⁶ CD4⁺ T cells).



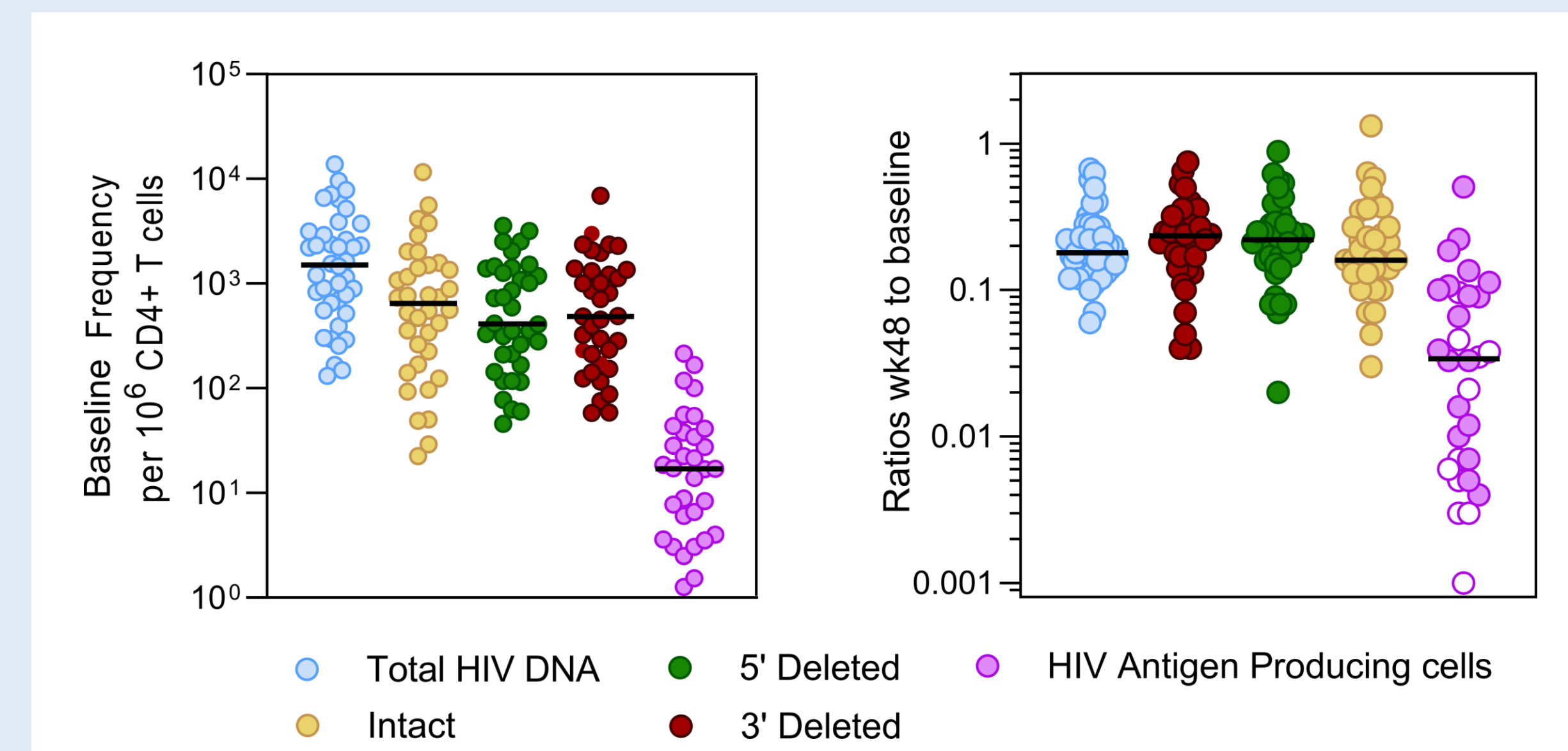
RESULTS

1. Plasma viral load during the study.

Hybrid data from standard and ultra-sensitive assays (LOD=3.3 cps/ml).



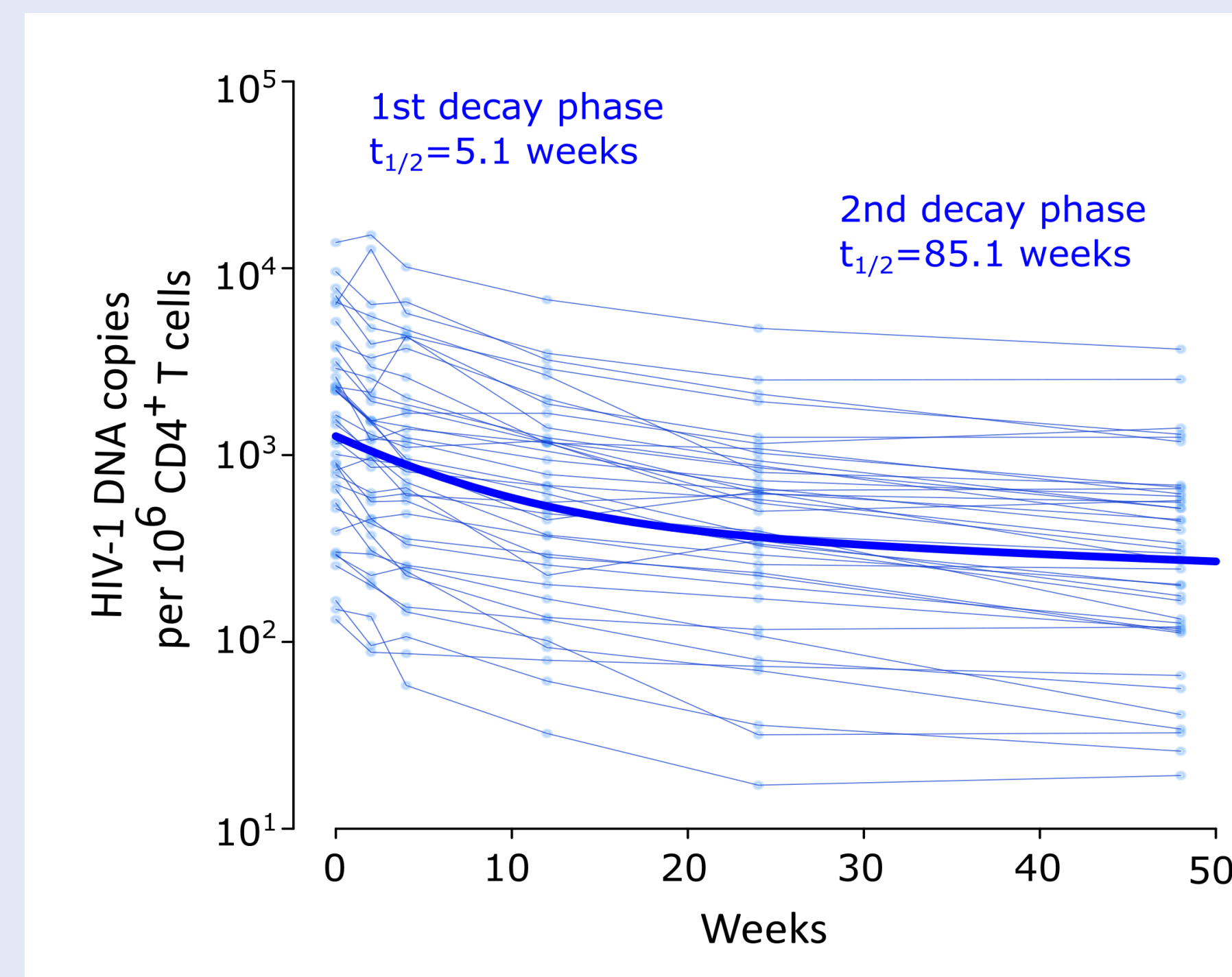
2. Relative size of the diverse fractions of the HIV reservoir and total magnitude of decay within 48 weeks.



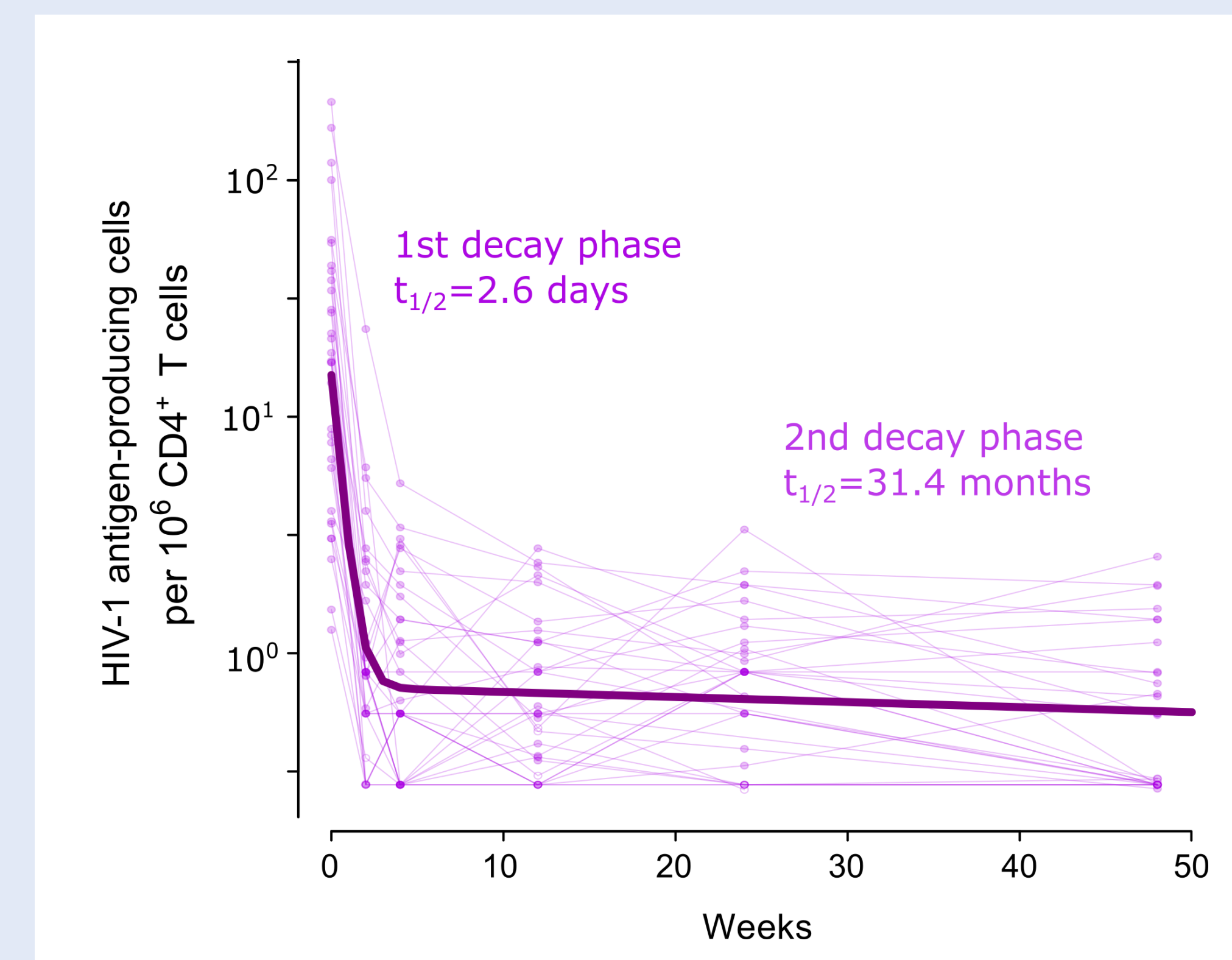
Open circles represent 1/2 LOD when values were undetectable.

3. Decay dynamics of total proviral DNA.

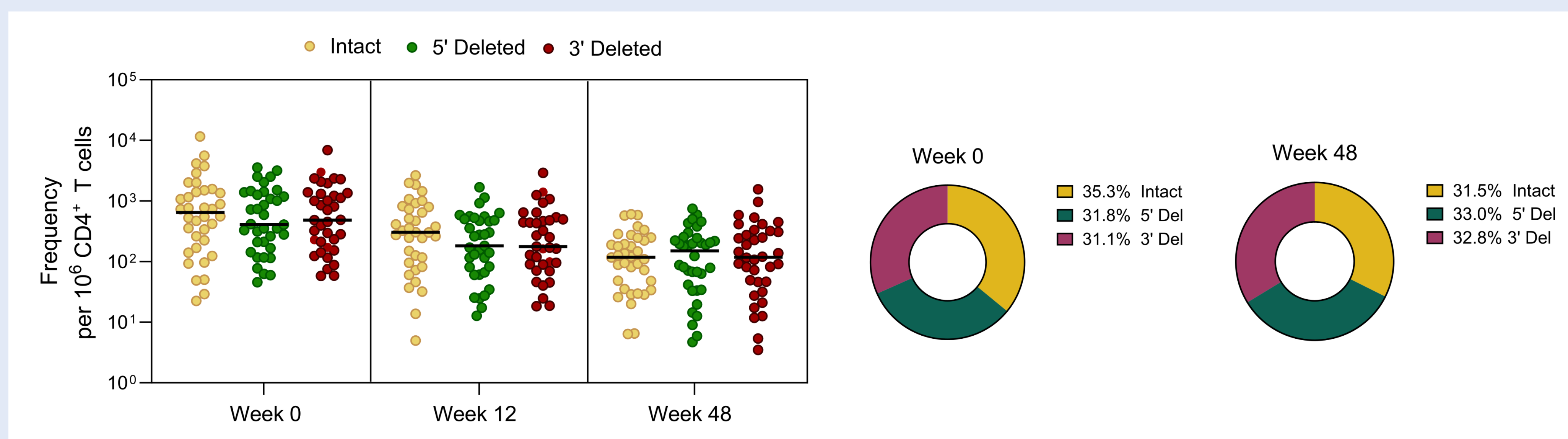
Biphasic decay dynamics fitted using non-linear mixed-effect models.



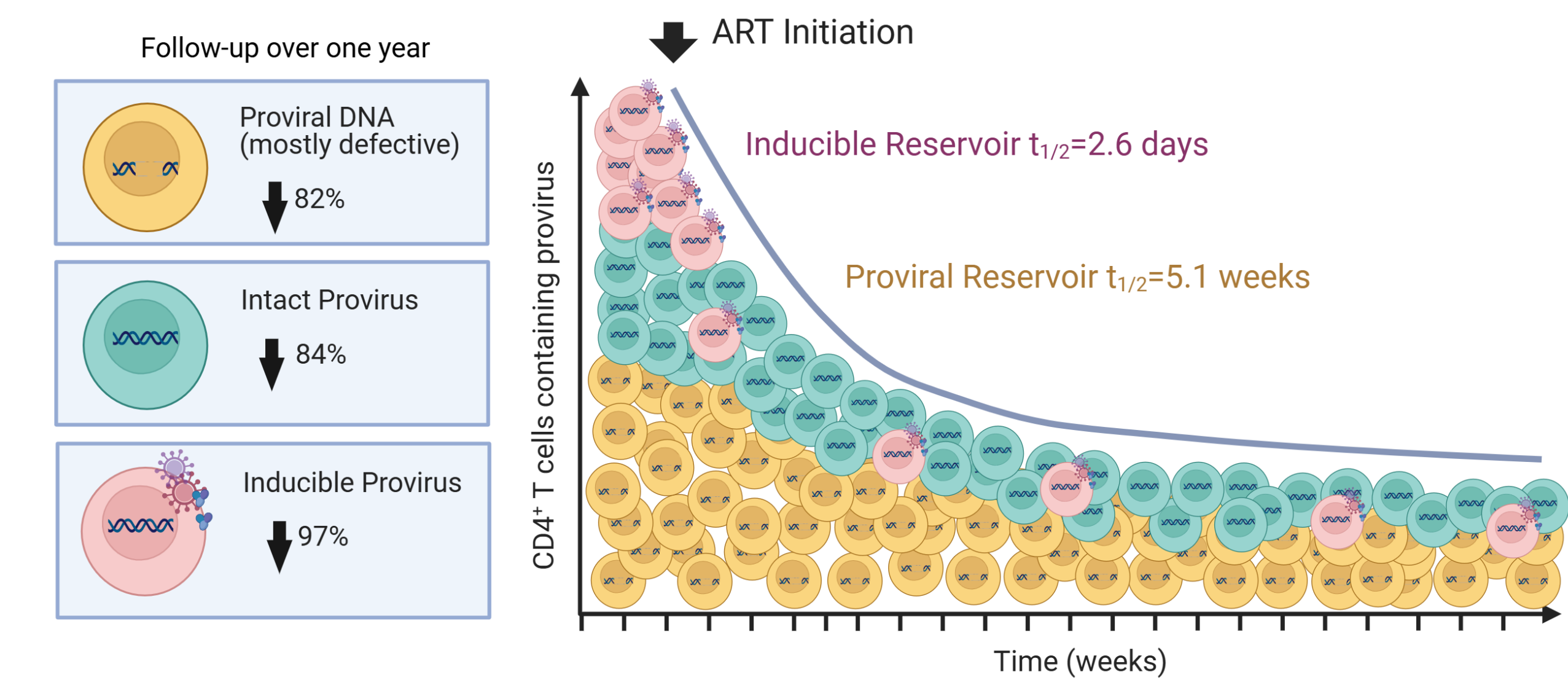
5. Decay dynamics of the inducible reservoir.



4. Evolution in the proportion of intact and defective HIV-1 proviruses.



SUMMARY & CONCLUSIONS



- ✓ The decay of the inducible reservoir is greater and faster than that of total and intact HIV-1 DNA.
- ✓ The inducible fraction of the reservoir is particularly susceptible, or the selective pressure is especially effective at reducing it, during the first days after ART initiation.
- ✓ Therapeutic interventions aimed at impacting the viral reservoir by boosting the immune response targeting the inducible fraction should be implemented at the time of, or immediately before, this window of opportunity.

*Summary Illustration created in <https://BioRender.com>

Further information

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DUALITY study (EudraCT: 2019-002733-10)

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