

Impact of Initial CD4+ T Cell Response to Highly Active Antiretroviral Therapy on Subsequent CD4+ T Cell Trends

STARLEY B. SHADE, MPH, PETER W. HUNT, MD, JEFF N. MARTIN, MD, STEVEN G. DEEKS, MD, DONALD I. ABRAMS, MD
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

For more information contact:
Starley B. Shade, MPH
Community Consortium
Positive Health Program
3180 18th Street, Suite 201
San Francisco, CA 94110
tel: 415/476-9554 ext. 26
fax: 415/476-6948
email: sshade@php.ucsf.edu

ABSTRACT

Background: Following initiation of HAART, most patients experience rapid increases in CD4+ T cell count in the first few months (mos) of therapy. It is not known whether the magnitude of this initial rise is associated with subsequent CD4+ T cell response while viral load (VL) is undetectable, or whether it is associated with the subsequent occurrence and magnitude of VL rebound and/or CD4+ T cell changes after VL rebound.

Methods: We examined patients from two clinic-based cohorts who initiated HAART, achieved an undetectable VL (<500 copies/mL), and subsequently experienced virologic failure. We defined rapid first-phase CD4+ T cell rise as a change in CD4+ T cell count of >50 cells/mm³ 2 to 16 weeks after HAART initiation. We censored patients at cessation of therapy or initiation of a successful salvage regimen.

Results: 104 patients met all criteria. Mean age was 41 years and mean pre-HAART CD4+ T cell count was 184 cells/mm³. Median follow-up after virologic failure was 14 mos. Fifty-five patients (53%) had a rapid first-phase CD4+ T cell rise (>50 cells). There were no differences by demographic characteristics, duration of undetectable VL, or first VL after failure between those with and without a rapid first-phase rise. In the first 12 mos after virologic failure, patients with a rapid first-phase rise had greater increases in their log₁₀ VL compared with those without a rapid first-phase rise (1.13 vs. 0.87 log₁₀ copies/mL; p<0.04). The CD4+ T cell counts of those with a rapid first-phase rise remained stable while they were undetectable (4.1 cells/mm³ per year), though those without a rapid first-phase rise gained 15.3 cells/mm³ per year (p<0.03). Similarly, after controlling for log₁₀ VL, the CD4+ T cell counts of those with a rapid first-phase rise remained stable after becoming detectable (6.1 cells/mm³ per year), while those without a rapid first-phase rise gained 23.8 cells/mm³ per year (p<0.001).

Conclusions: Patients who have large initial CD4+ T cell responses to HAART have larger increases in viral load and fewer CD4+ T cell gains after experiencing virologic failure. A large initial CD4+ T cell response may increase the number of targets available for HIV, encourage viral replication, and mute future increases in CD4+ T cell counts. Knowledge of initial CD4+ T cell rise may help clinicians manage patients who experience virologic failure.

BACKGROUND

- Many patients experience rapid increases in CD4+ T cell count after initiating Highly Active Antiretroviral Therapy (HAART).
- We do not know whether CD4+ T cell increase predicts:
 - CD4+ T cell changes while viral load is undetectable;
 - Viral load rebound;
 - Magnitude of viral load rebound; or
 - CD4+ T cell changes after viral load rebound.

METHODS

POPULATION

- Patients from two San Francisco Bay Area clinic-based cohorts
 - SCOPE—Study of the Consequences of the Protease Inhibitor Era
 - VLODB—Community Consortium Viral Load Observational Database
- Eligibility Criteria
 - Patients who initiated their first HAART regimen; then
 - Achieved an undetectable viral load (< 500 copies/mL) within 9 months; and
 - Subsequently experienced virologic failure (>500 copies/mL).
- Patients were defined as having an initial CD4+ T cell response if they had at least a >50 cell/mm³ increase 2 to 16 weeks after HAART initiation.
- Follow-up data were collected every 4 to 6 months, and included:
 - HIV RNA viral load
 - CD4+ T cell count
 - Changes in antiretroviral therapy.
- Patients were followed until cessation of therapy or initiation of a successful salvage regimen.

SAMPLE

- 104 patients met all eligibility criteria.
- Median time from initiation of HAART to viral failure was 3 months.
- Median follow-up after viral failure was 14 months.
- 55 patients (53%) had an initial CD4+ T cell response to initiation of HAART.

RESULTS

SAMPLE CHARACTERISTICS (N=104)

Male	97%
Age, mean (±sd)	41 (±8)
Pre-HAART CD4, mean (±sd)	184 (±178)
Pre-HAART log ₁₀ VL, mean (±sd)	3.3 (±1.0)

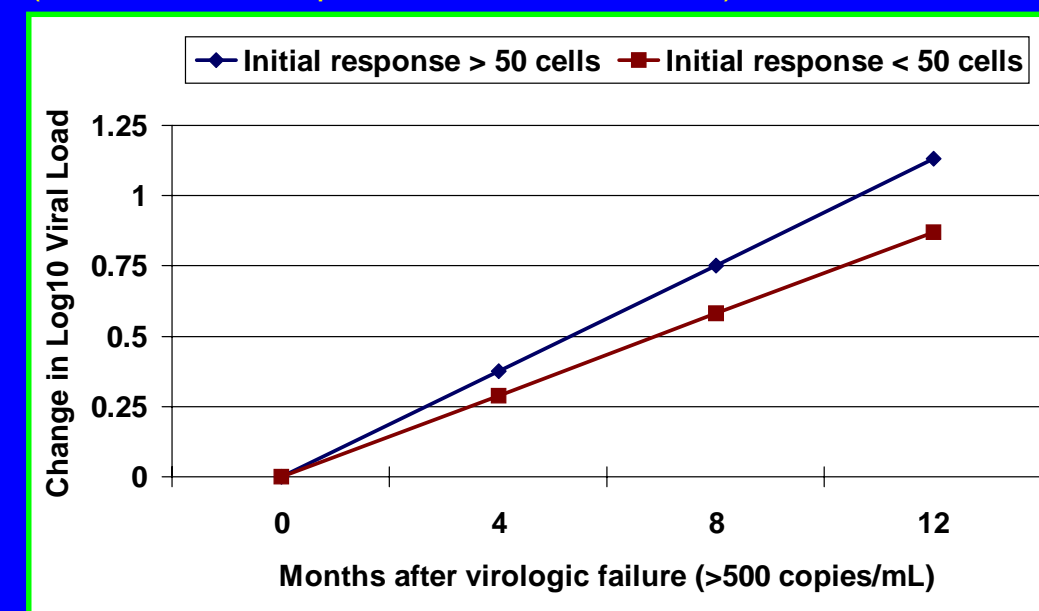
- There were no differences between those with and without an initial CD4+ T cell response by:
 - Demographic characteristics;
 - Baseline clinical characteristics;
 - Duration of undetectable viral load; or
 - First viral load after virologic failure.

CHANGE IN VIRAL LOAD AND CD4+ T CELL COUNT BY INITIAL CD4+ T CELL RESPONSE (Repeated Measures Analysis)¹

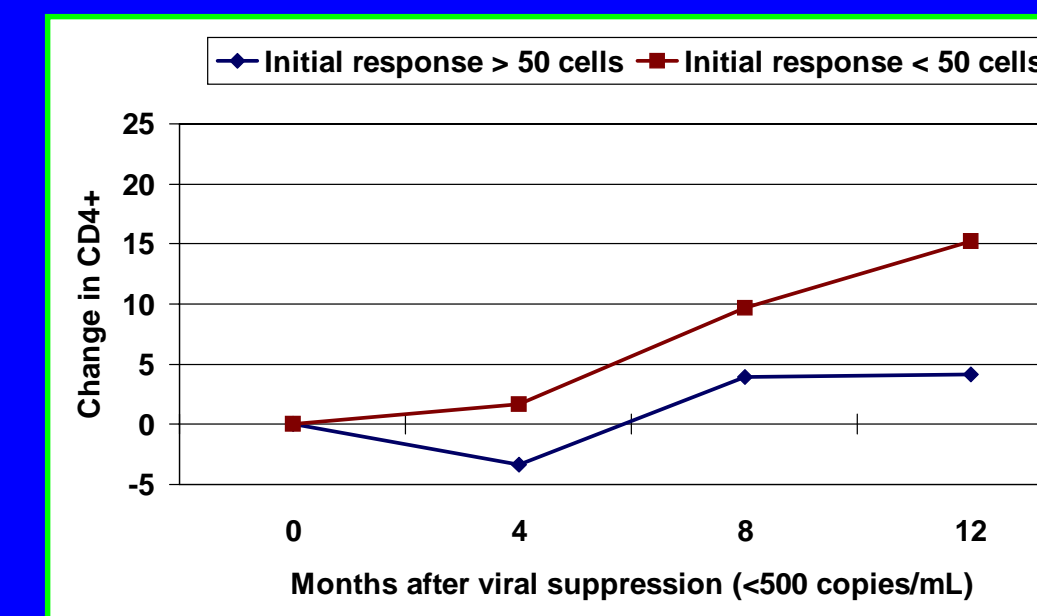
	CD4+ T Cell Rise > 50 cells/mm ³		
	YES	NO	p≤
12 month change in log₁₀ viral load After virologic failure	1.13	0.87	0.04
12 month change in CD4+ T cell count While VL undetectable	4.1	15.3	0.03
After virologic failure	6.1	23.8	0.001

¹ Models adjusted for viral load and CD4+ T cell count.

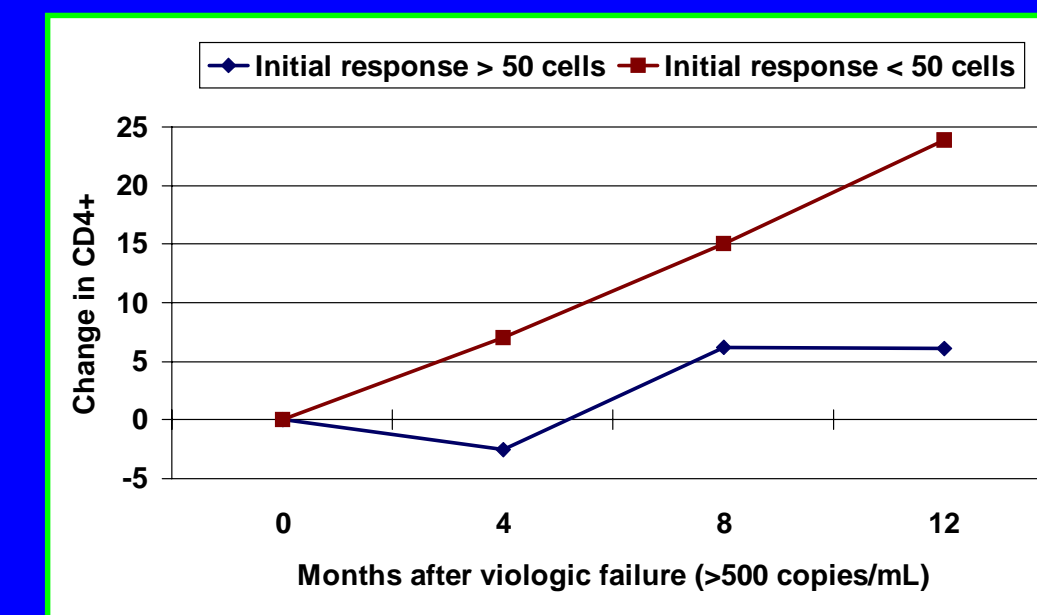
CHANGE IN LOG₁₀ VIRAL LOAD AFTER VIROLOGIC FAILURE (Illustration of Repeated Measures Model)



CHANGE IN CD4+ T CELL COUNT WHILE VIRAL LOAD IS UNDETECTABLE (Illustration of Repeated Measures Model)

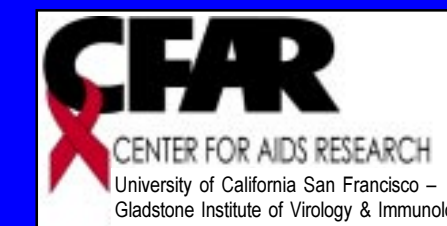


CHANGE IN CD4+ T CELL COUNT AFTER VIROLOGIC FAILURE (Illustration of Repeated Measures Model)



CONCLUSIONS

- Patients who have large initial CD4+ T cell responses to HAART have larger increases in viral load and fewer gains in CD4+ T cell count during viral suppression and after virologic failure.
- A large initial CD4+ T cell response may:
 - increase the number of targets for HIV;
 - encourage viral replication; and
 - mute future increases in CD4+ T cell counts.
- Knowledge of initial CD4+ T cell response may help clinicians manage patients who experience virologic failure.



University of California
San Francisco

