

The Total Lymphocyte (TLC) as a Surrogate for CD4 count to Monitor HAART in Resource-Limited Countries

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Background

- ❖ In many resource-limited countries, CD4 count and Plasma Viral Load (PVL) are not feasible for routine clinical use due to a lack of sophisticated laboratory equipment or prohibitively high cost per test.
- ❖ Meanwhile, dramatic price reductions in HAART are increasing access to treatment in these countries.
- ❖ Feasible and inexpensive surrogate markers, such as Total Lymphocyte Count (TLC), are needed if HAART is to be routinely monitored.

Objective

To determine if change in CD4 count correlates with change in TLC in HIV-positive patients on antiretroviral therapy.

Methods I

- ❖ Retrospective review of HIV-positive patients initiating antiretroviral therapy from 1996 through 2000 at The Miriam Hospital Immunology Center, Providence, RI, USA.

Methods II

- ❖ Inclusion criteria from clinical database:
 - CD4 count < 250 cells/mm³ prior to start of a HAART regimen ('Baseline CD4 Count'). This criteria chosen since HAART often initiated at low CD4 counts in resource limited settings.*
 - No antiretroviral therapy in the 3 months prior to starting new regimen.*
 - At least 6 months duration on the new regimen.*
- ❖ CD4 count, PVL, and TLC recorded at each visit.
- ❖ Patients included irrespective of adherence to simulate routine clinical practice.

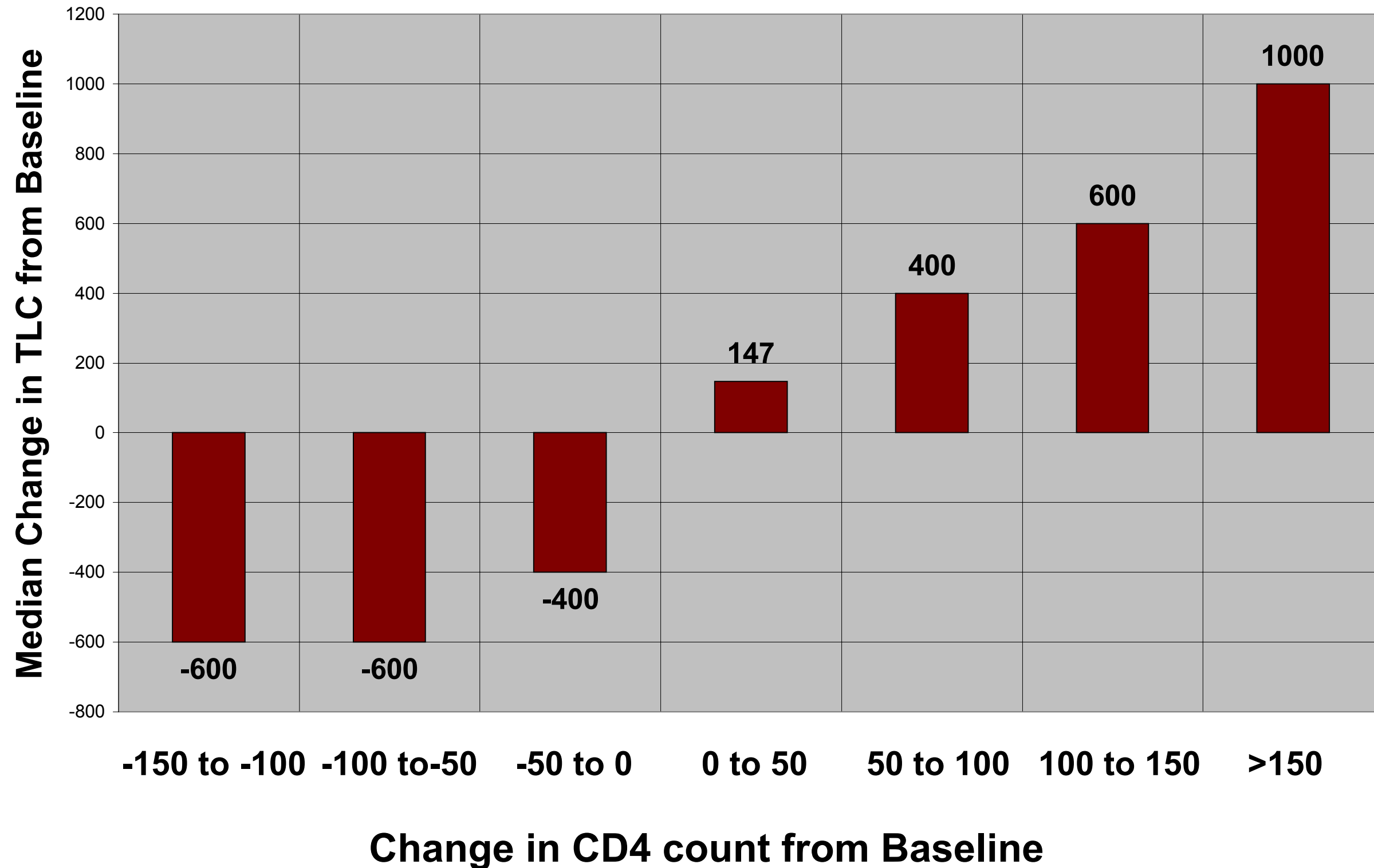
Results

❖ 109 patients met eligibility criteria for this study.

Table: Change in TLC from baseline stratified by the change in CD4 Count from baseline over all visits (cells/mm³).

CD4 Count Change From Baseline	N (Visits)	TLC Change from Baseline		
		Median	Minimum	Maximum
> 150	249	1000	-600	3200
100 to 150	120	600	-400	1700
50 to 100	152	400	-1300	1800
0 to 50	136	147	-1300	2220
-50 to 0	62	-400	-1430	400
-100 to -50	15	-600	-714	600
-150 to -100	10	-600	-1900	-270

Median change in TLC from baseline stratified by change in CD4 count from baseline over all visits (cells/mm³).



Results

Table: Change in TLC (cells/mm³) from baseline stratified by the change in PVL (copies/ml in log₁₀ scale) from baseline over all visits.

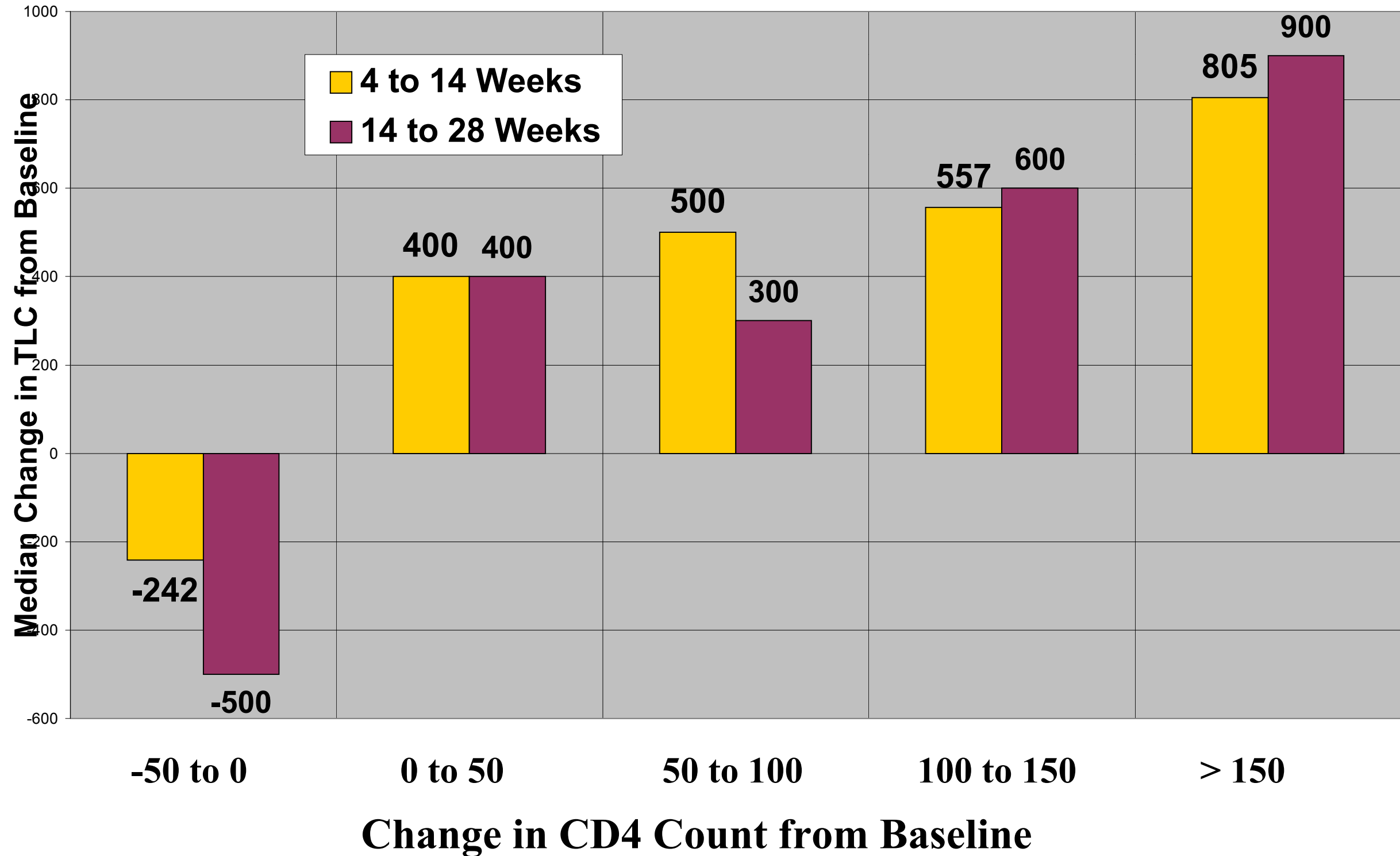
PVL Change from Baseline (log)	N (Visits)	TLC Change from Baseline		
		Median	Minimum	Maximum
Detectable to Undetectable	390	600	-1210	2760
> -2	27	770	-700	2400
-2 to -1	66	445	-1900	2200
-1 to -0.5	30	200	-1300	2558
-0.5 to 0	42	200	-1430	1625
Undetectable to detectable	5	-500	-610	-300
0 to 0.5	30	0	-900	700
0.5 to 1	8	-75	-700	520

Results

Table: Change in TLC from baseline stratified by *time period* and change in CD4 from baseline (cells/mm³).

CD4 Count Change From Baseline	N (patients)	TLC Change from Baseline		
		Median	Minimum	Maximum
<i>At 4 to 14 Weeks</i>				
>150	18	805	0	2000
100 to 150	10	557	100	1700
50 to 100	19	500	-500	900
0 to 50	21	400	-400	1000
-50 to 0	7	-242	-800	200
<i>At 14 to 28 Weeks</i>				
> 150	21	900	0	1900
100 to 150	13	600	-10	1483
50 to 100	23	300	-300	1000
0 to 50	17	400	-1200	2220
-50 to 0	8	-500	-770	200

Median change in TLC from baseline stratified by time period and change in CD4 count from baseline (cells/mm³).



Discussion

- ❖ Previous studies have shown that TLC is a low cost and useful tool for monitoring HIV progression and triggering OI prophylaxis in resource-poor settings.
- ❖ In many resource-limited countries, the costs of CD4 count are so high relative to the reduced prices of antiretroviral drugs that routine monitoring of therapy would often be more expensive than the supply of the drugs themselves.

Table: Annual cost in India of various monitoring schema to an individual patient or a Government-financed clinic.

Monitoring Scheme (Three lab evaluations/year)	Annual Cost (U.S. Dollars)	
	Individual Patient (fee for service-private provider)	Public Clinic (500 patients) (government financed free-care)
TLC only	\$2.40	\$1200
One CD4 count, two TLCs	\$31.60	\$15,800
CD4 count only	\$90.00	\$45,000

Limitations

- ❖ This was a study of patients from the United States. Further study of TLC response to HAART in resource-limited countries is needed.
- ❖ Due to eligibility criteria of CD4 count < 250 and no HAART in the 3 months prior to starting regimen (to simulate the typical use of HAART in resource-limited countries), number of patients included in this study are relatively small.
- ❖ Fewer patients in PVL analysis since baseline PVL were not available for a subset of patients starting HAART in 1996-7.

Conclusion

- ❖ Among patients in a clinical setting initiating a HAART regimen with a CD4 count less than 250 cells/mm³, the change in TLC correlates well with the change in CD4 count and change in PVL.
- ❖ Further prospective study of TLC changes in patients on HAART is needed in resource-limited countries.