

Temporary Antiretroviral Therapy During Primary HIV-1 Infection Lowers The Viral Set-point: The Prospective, Randomized Primo-SHM Study



Radjin Steingrover^{1,2}, Ingrid Schellens³, Annelies Verbon⁴, Kees Brinkman⁵, Aeilko Zwinderman⁶, Suzanne Jurriaans⁷, Frank Miedema³, Joep Lange¹, Debbie van Baarle³, Jan M. Prins¹



¹Dept. of Internal Medicine, Division of Infectious Diseases, Tropical Medicine and AIDS, and Center for Infection and Immunity Amsterdam (CINIMA), Academic Medical Center; Amsterdam; ²International Antiviral Therapy Evaluation Center; Amsterdam; ³Department of Immunology, University Medical Center, Utrecht; ⁴Dept. of Internal Medicine, Academic Hospital Maastricht; Maastricht; ⁵Dept. of Internal Medicine, Onze Lieve Vrouwe Gasthuis, Amsterdam; ⁶Dept. of Clinical Epidemiology and Biostatistics, Academic Medical Center; Amsterdam; ⁷Dept. of Medical Microbiology, Academic Medical Center; Amsterdam, all in The Netherlands

Introduction

An important question still pending is whether temporary highly active antiretroviral therapy (HAART) during primary HIV infection (PHI) can affect the viral setpoint, through preservation and enhancement of HIV-1 specific cellular immune responses, or through other mechanisms.

To our knowledge the present study is the first randomized clinical trial to test the hypothesis that temporary early HAART can affect the viral setpoint established 36 weeks after a single treatment interruption (TI).

Methods

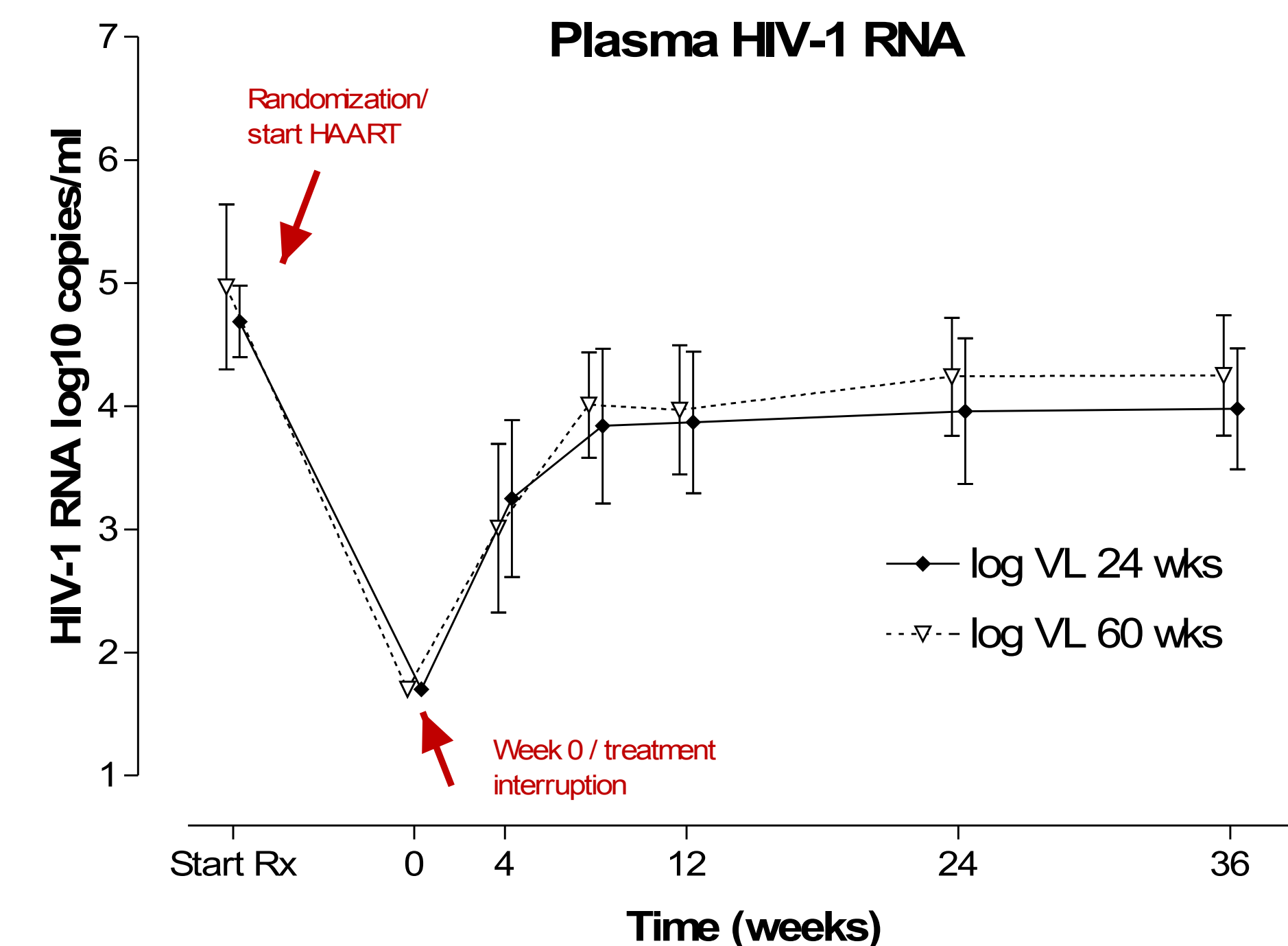
- The Primo-SHM study is a multicenter, semi-factorial, open-label, randomized clinical trial that compares a course of early HAART (24 or 60 weeks), with untreated patients. This design allows for 2 pairwise comparisons: between subjects that were randomized to 24 or 60 weeks of treatment, and between untreated and treated patients, (for subjects that are randomized over three arms).
- HAART consists of lamivudine/zidovudine, efavirenz and lopinavir boosted with ritonavir. Lopinavir is discontinued when the pVL drops below the lower level of quantification (LLQ) of the assay (50 copies/ml).
- The inclusion criteria required laboratory evidence of PHI defined as:
 - a negative or indeterminate western blot in combination with a positive p24 antigen or HIV-1 RNA test result
 - a negative HIV screening within the previous 180 days
- The predefined endpoint was the viral setpoint during steady state viraemia at 36 weeks after seroconversion or TI.

Results: baseline characteristics

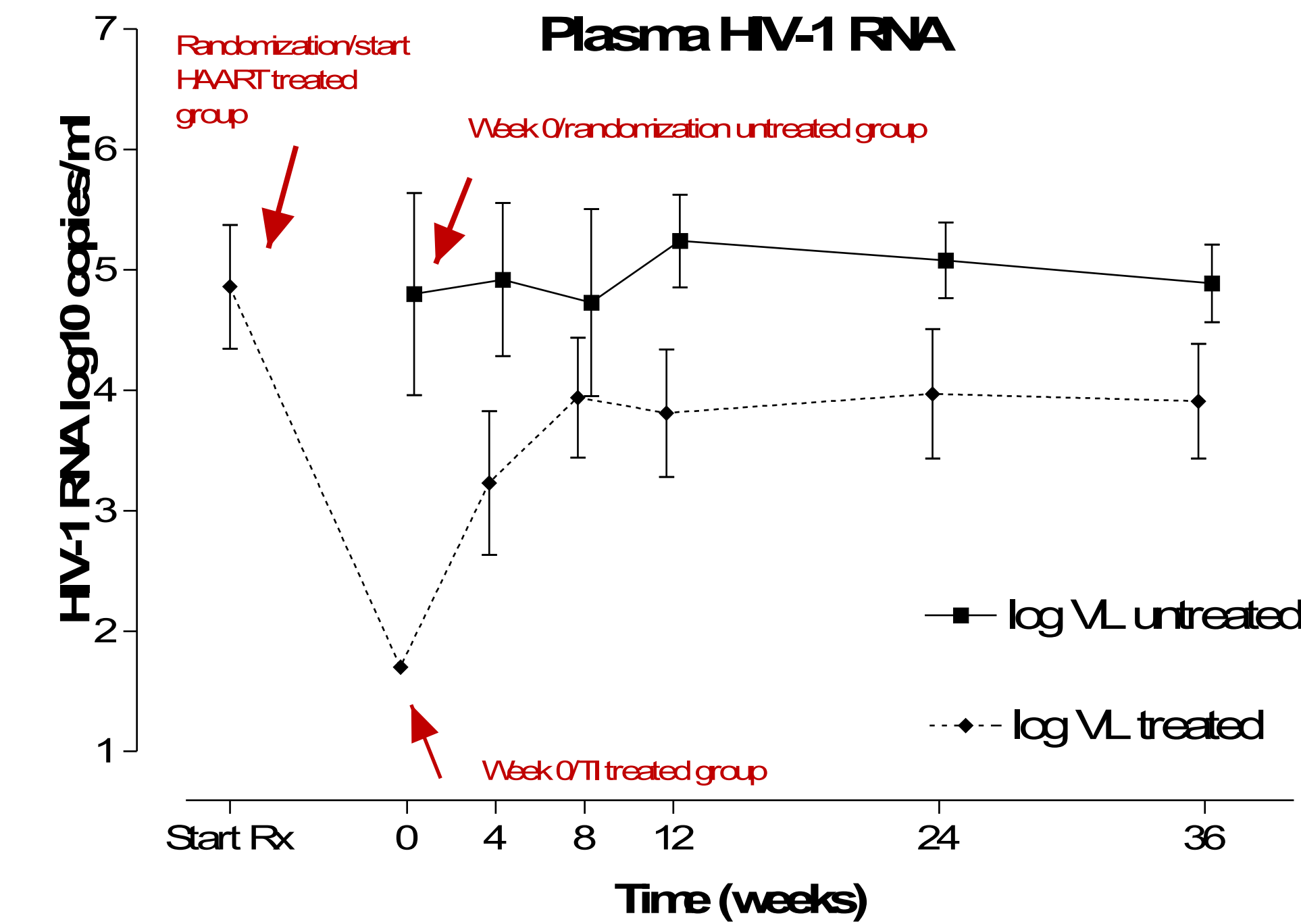
	Comparison 1		Comparison 2	
	24 weeks	60 weeks	Untreated	Early HAART (3-way rand.)
n	19	18	11	20
PHI type				
• negative WB	4 (21%)	3 (17%)	2 (18%)	5 (25%)
• ind. WB	12 (63%)	12 (67%)	7 (64%)	11 (55%)
• SI < 180 days	3 (16%)	3 (17%)	2 (18%)	4 (20%)
Plasma HIV-1 RNA at BL (10log copies/ml)	4.7 (4.4-5.0)	5.0 (4.3-5.6)	4.8 (4.0-5.6)	4.8 (4.3-5.4)
CD4+ T cells at BL (cells/ μ l)	688 (589-787)	453 (338-568)	433 (317-549)	562 (440-685)
Weeks from SC to BL	5.2 (2.9-7.6)	3.6 (1.7-5.6)	4.2 (2.8-5.8)	4.9 (2.4-7.3)

Data are number and percentages, mean values with 95% confidence intervals

Results: 24 vs. 60 weeks



Results: treated vs. untreated



Results

All treated patients had a pVL < 50 copies/ml at the time of TI.

There was no significant difference between 24 and 60 weeks of treatment in pVL 36 weeks after TI (3.6 (3.0-4.3) vs. 4.3 (3.8-4.8), $p > 0.05$), but the viral setpoint was lower in early treated patients compared to untreated subjects: 4.0 (3.5-4.4) and 4.9 (4.7-5.2) ¹⁰log c/ml, respectively, $p < 0.005$. CD4+ T cells at endpoint were 349 (260-438) cells/ μ l in untreated patients vs. 581 (445-718) in treated patients, $p = 0.005$. Independent predictors of the pVL at endpoint were baseline pVL ($p < 0.005$) and early treatment with HAART ($p < 0.05$).

At endpoint, no differences were found between the groups in proliferative capacity of Gag-specific CD4+ and CD8+ T cells, lymphocyte activation and maturation markers, or PD-1 expression.

Conclusions

Both 24 and 60 weeks of HAART during PHI lower the plasma HIV-RNA setpoint after treatment interruption compared to no early treatment.

Correspondence

R. Steingrover, MD
Academic Medical Center, Room T0-111, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands
E: r.steingrover@amc.uva.nl