

Comparison of early serologic response of early syphilis to treatment with a single-dose benzathine penicillin G between HIV-positive and HIV-negative patients: a cohort study

Chia-Jui Yang^{1,2}, Wen-Chun Liu³, Lan-Shin Chang³, Cheng-Hsin Wu³, Yi-Ching Su³, Chien-Ching Hung³

¹Department of Internal Medicine, Far Eastern Memorial Hospital, New Taipei City, Taiwan

²School of Medicine, National Yang-Ming University, Taipei, Taiwan

³Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

Correspondence: yangcj@ntu.edu.tw

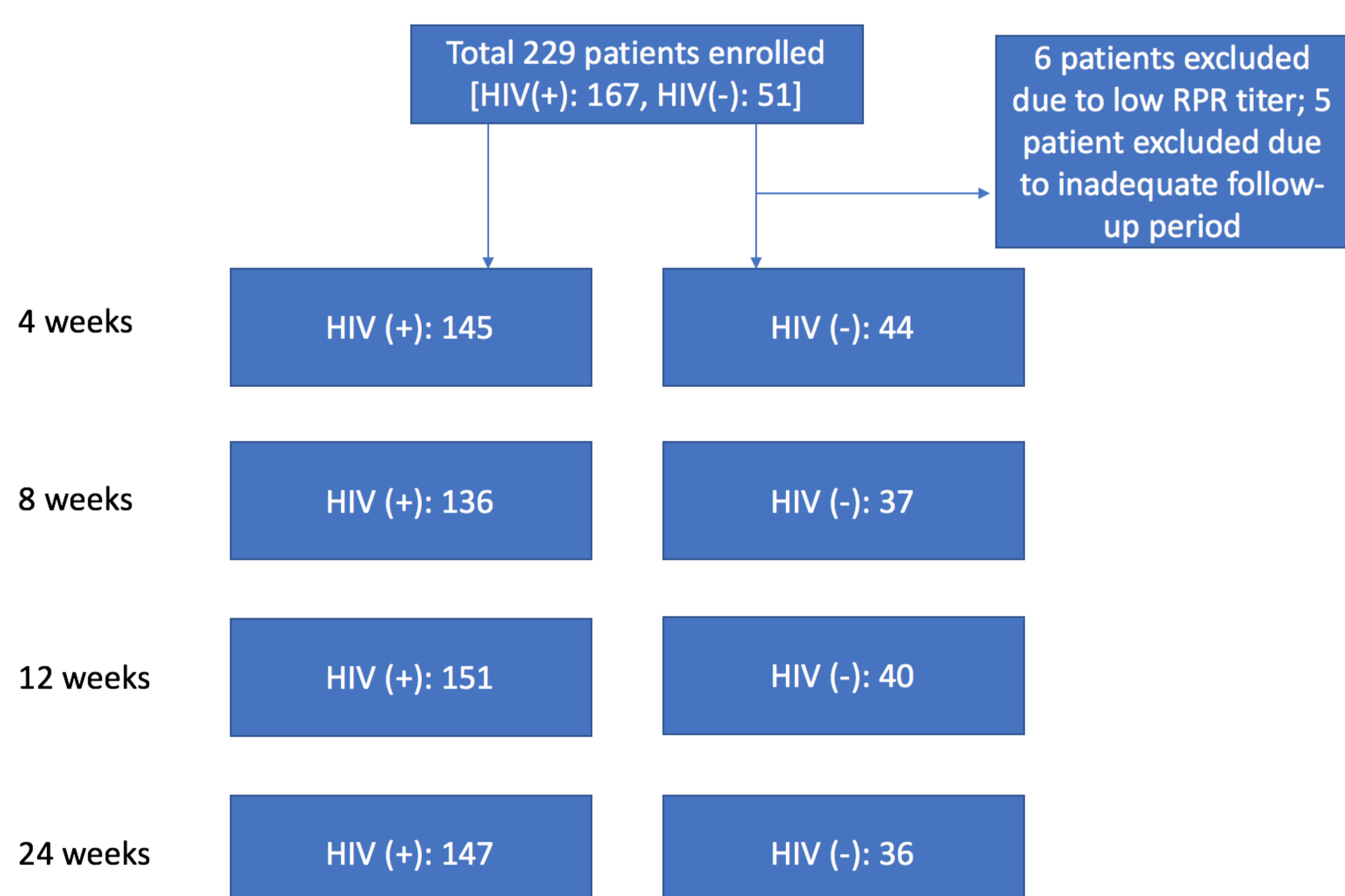
Background

1. Serologic response of early syphilis to treatment has been reportedly poorer in HIV-positive patients compared with HIV-negative patients; however, the interpretation of the published data is limited by the differences in study design, subjects with different stages of syphilis included, definition used for serologic response, treatment administered, and follow-up frequency and duration.
2. We aimed to compare the early serologic response of early syphilis to benzathine penicillin G (BPG) during the monthly follow-up for 3 consecutive months between HIV-positive and HIV-negative patients.

Materials and Methods

1. Subjects: Patients aged >20 years with early syphilis (primary, secondary, early latent) and RPR titers ≥ 4
2. Exclusion: RPR titers <4; concurrent antibiotic therapy at baseline or during the follow-up
3. Study design: single-center, prospective observational study in northern Taiwan
4. Treatment: a single-dose 2.4 MU benzathine penicillin G
5. Follow-up: RPR titer every 4 weeks for 12 weeks, followed by every 12 weeks thereafter.
6. Serologic response: a decline of RPR titre by >4-fold at each time point compared with baseline.
7. Serologic failure: an increase of RPR titre by ≥ 4 -fold during follow up after ever achieving a decline of the titre.

Consort Diagram



Results

1. Between January 2015 and June 2018, 167 HIV-positive and 51 HIV-negative patients were included; all were MSM.
2. Compared with HIV-positive patients, HIV-uninfected patients had more cases of secondary syphilis (49.0% vs. 29.9%, $p=0.018$), less early latent syphilis (43.1% vs. 62.9%, $p=0.015$), less prior syphilis (19.6% vs. 69.5%, $p<0.001$) (Table 1)
3. HIV-negative patients had faster serologic response than HIV-positive patients: 63.6 vs 36.6% ($p=0.002$), 94.6% vs 69.9%, ($p=0.001$), 95.0% vs 81.5% ($p=0.048$), and 97.2% vs 85.7% ($p=0.083$) at week 4, week 8, week 12, and week 24, respectively. (Figure 1)
4. In multivariate analysis to examine the factors associated with 12-week serologic response, the response was associated with prior syphilis (adjusted AOR, 0.22; 95% CI, 0.08-0.61) and per 1-log₂ increase of RPR titer at baseline (AOR, 1.01; 95% CI, 1.00-1.01, $p=0.008$) (Table 2).

Table 1. Characteristics of patients with early syphilis

	HIV-positive (n=167)	HIV-negative (n=51)	P-value
Age, mean (SD), years	36.7 (8.4)	30.6 (7.1)	<0.001
Stage of syphilis, n (%)			
Primary	12 (7.2)	8 (15.7)	0.093
Secondary	50 (29.9)	25 (49.0)	0.018
Primary + Secondary	0 (0)	4 (7.8)	-
Early latent	105 (62.9)	22 (43.1)	0.015
HBsAg (+), n (%)	24 (14.4)	2 (3.9)	1.0
Anti-HCV (+), n (%)	15 (13.0)	2 (3.9)	0.744
Prior syphilis, n (%)	116 (69.5)	10 (19.6)	<0.001
CD4 cell counts, cells/uL	384 (130-1601)	-	
HIV RNA, copies/ml	36779 (<20-313000)	-	
cART, n (%)	145 (86.8)	-	-

Figure 1. Early serologic response rate among HIV (+) and HIV (-) patients

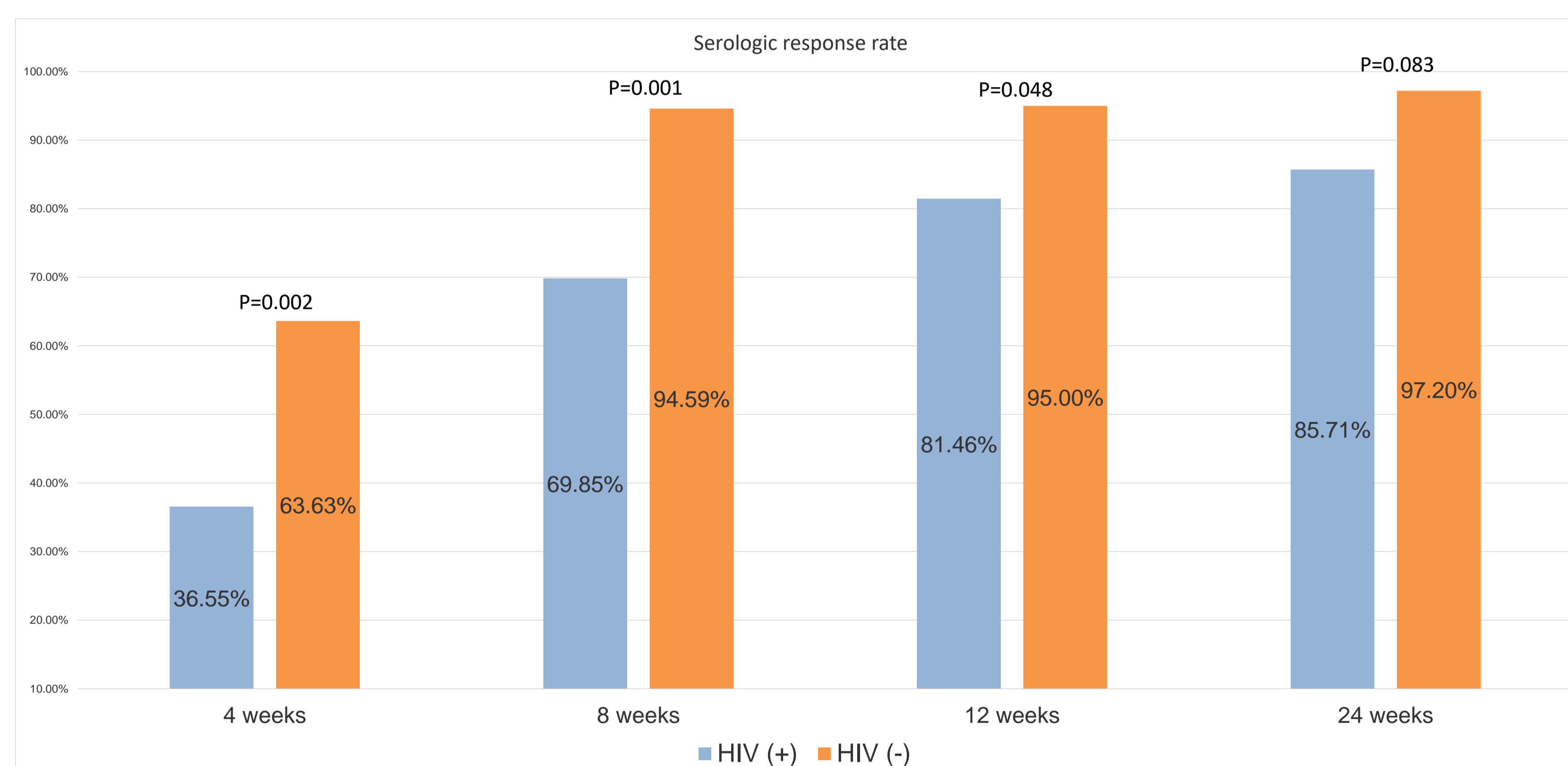


Table 2. Multivariate analysis of factors associated with serologic response at wk 12

	Adjusted odds ratio	P value
Early latent syphilis	0.40 (0.12-1.34)	0.14
RPR titer increase per 1-log ₂	1.01 (1.00-1.01)	0.008
Prior syphilis	0.22 (0.08-0.61)	0.004

Conclusions

1. HIV-negative patients had better early serologic response of early syphilis to BPG than HIV-positive patients during the first 12 weeks of follow-up.
2. The better early serologic response observed in HIV-negative patients than HIV-positive patients is likely related to factors other than HIV infection
3. Prior syphilis infection was associated with a poorer response while a higher RPR titre was associated with a better response to BPG.