Current and Nadir CD4+ Counts Are Associated with Heplisav-B Seroprotection Rates in People with HIV

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Background

- People with HIV (PWH) are at an increased risk of developing chronic HBV from acute infection, and HIV-HBV coinfection is associated with higher rates of liver-specific and all-cause mortality
- Responses to existing HBV vaccines range between 20-70% in the literature despite more frequent dosing or higher-dosed vaccines
- Predictors of responsiveness to HBV vaccines historically have included younger age, current antiretroviral therapy (ART) use, viral load, and current and nadir CD4+ counts
- Heplisav-B, which includes an immunostimulatory adjuvant, was FDA-approved in 2017 as a two-dose HBV vaccine in adults >18
- In healthy adults, Heplisav-B induced seroprotection in 90-95% compared to 70-80% with Engerix
- No data exists in PWH, and rates of seroprotection and predictors of responsiveness are unknown in this setting

Methods

- **Study Design**
  - Setting: quaternary care center HIV clinic
  - Study design: retrospective cohort study
  - Inclusion criteria: PWH ages 18 years and older without current seroprotection (defined as most recent hepatitis surface antibody [anti-HBs] <10 mIU/mL)
  - Exclusion criteria: participants without follow-up titers after immunization
  - Primary outcome: seroprotection rate (SPR), defined as proportion of participants with anti-HBs ≥10 mIU/mL at any point following the first vaccination
- **Statistical Analysis**
  - Median (IQR) and proportions were reported
  - Fisher's exact test was used to compare categorical variables
  - Mann-Whitney U and Kruskal-Wallis tests were used to test difference in continuous variables between 2 or 3 or more groups, respectively
  - Trend analysis related to current and nadir CD4+ T-cell count was performed via the Cochran-Armitage test

Results

The seroprotection rate in PWH with Heplisav-B was 81%, and 86% when excluding significant non-HIV immunosuppression – the highest published SPR for HBV vaccination in PWH.

Study Snapshot

52/64 (81%) of PWH developed seroprotection

48/56 (86%) of PWH without significant non-HIV immunosuppression* developed seroprotection

**Asplenia, metastatic cancer, active chemotherapy, decompensated cirrhosis*

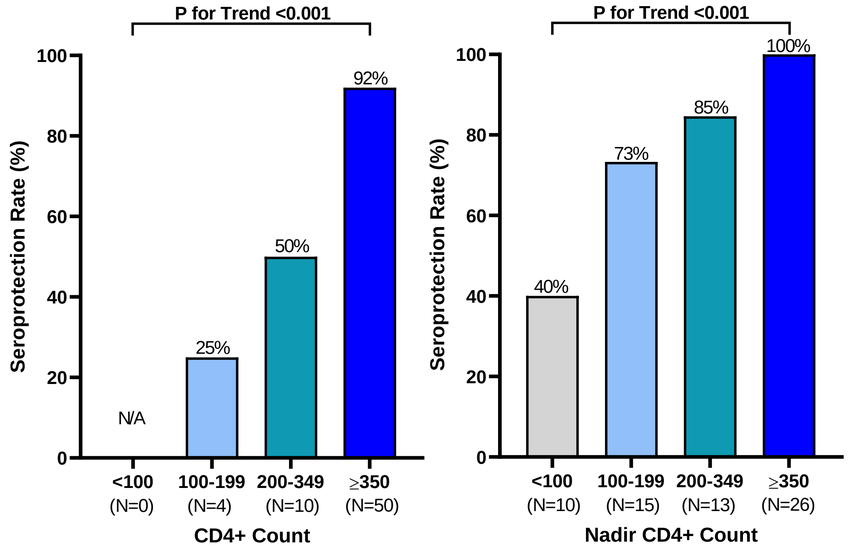
Lack of seroprotection was associated with significant non-HIV immunosuppression

No SPR differences in time between doses or from final dose to antibody measurement

There were no differences in SPR based on:
- Race, ethnicity, gender
- Chronic medical conditions
- Prior HBV immunization
- Prior anti-HBs or anti-HBc positivity

No significant changes in HIV viral load before and after immunization (median time to measurement, 12 weeks [IQR 9-25 weeks])

Current and Nadir CD4+ Counts Are Associated with SPR



Baseline Characteristics

Characteristics	Non-Responder (N = 12)	Responder (N = 52)	P Value
Age, y	61 [57-66]	57 [43-62]	0.06
Male (%)	75%	83%	0.68
Race/Ethnicity			
White / Non-Hispanic	50%	35%	
White / Hispanic	25%	21%	
African-American	8%	19%	0.94
Asian	8%	11%	
Other	8%	14%	
BMI	25 [23-34]	27 [24-30]	1.00
CKD III-V	0%	6%	1.00
Diabetes Mellitus	17%	19%	1.00
Current Smoking	25%	19%	0.70
Non-HIV Immunosuppression	33%	8%	0.03
Any prior HBV vaccine	67%	67%	1.00
Anti-HBs ever +	17%	10%	0.61
Anti-HBc ever +	25%	31%	1.00
Viral Load <40 pre-vaccine	100%	88%	1.00
CD4	273 [197 – 461]	660 [420 – 1,006]	<0.001
Nadir CD4	121 [52 – 180]	363 [174 – 525]	<0.001

Limitations

- Results derived from retrospective single-center experience without direct comparison to other HBV vaccines
- Small sample size precluded multivariate analysis
- Small number of female and viremic participants may limit generalizability
- Safety data on adverse reactions was not systematically collected

Conclusions / Implications

- Heplisav-B was associated with high rates of seroprotection, exceeding the SPR of prior HBV vaccines in PWH
- SPR in PWH without significant non-HIV immunosuppression may be comparable to that seen with Heplisav-B in healthy adults
- SPR was associated with current and nadir CD4+ T-cell counts
- Further work is needed to optimize seroprotection in those with lower current and nadir CD4+ counts and other non-responders
- Heplisav-B should be considered first-line for HBV vaccination in PWH