CpG-adjuvanted Hepatitis B vaccination improves seroprotection rates in Veterans with HIV

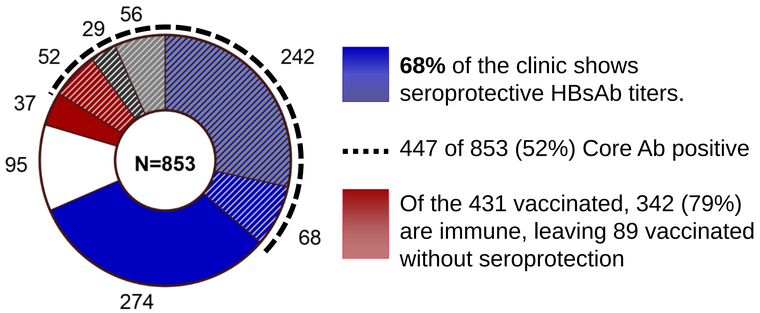
Meagan Deming, MD, PhD[1,2], Shyam Kottilil, MD, PhD[1], Eleanor Wilson, MD, MHS[1,3]

[1]Institute of Human Virology, [2]Center for Vaccine Development and Global Health, University of Maryland Medical Center, [3]VA Maryland Health Care System, Baltimore, Maryland

725 W. Lombard Street, N156
Baltimore, MD 21201
mdeming(at)ihv.umaryland.edu
410-706-8333 (office)
844-732-1275 (fax)

BACKGROUND:

- Hepatitis B virus (HBV) infections remain a global health issue with complications including liver cirrhosis and hepatocellular carcinoma. Individuals co-infected with Human Immunodeficiency Virus (HIV) and HBV have increased liver-related morbidity and mortality compared to those with HBV mono-infection.
- Vaccination is a potent intervention to prevent HBV infection, but certain critical populations including people living with HIV are less likely to achieve seroprotection after vaccination. Seroprotection (antibody to hepatitis B surface antigen titer ≥ 10 IU/mL) was historically poor, with trial rates ranging from **34 to 88%** and **improving with immunologic reconstitution and viral suppression**.
- Seroprotection rates (SPR) over the past two decades have dramatically improved with an improved immunologic status in this Veteran Infectious Disease clinic population. However, a subset of patients remain HBV vaccine nonresponders despite re-vaccination attempts, suspected to reflect intrinsic immunologic anergy.



- **We hypothesized that Veterans with HIV who were nonresponders to prior HBV vaccines may yet respond to a more immunogenic vaccine**.
- The CpG-adjuvanted Hepatitis B vaccine, Heplisav-B, has shown increased seroprotection rates in other classically difficult to vaccinate groups (including the elderly and those with diabetes), but has not yet been studied in individuals with HIV.

Heplisav-B is immunogenic in prior nonresponders to HBV vaccines, including persons with HIV.

Table 1: Participant characteristics

Participants enrolled	18
Male (%)	17 (94%)
Day 60 available	10 (56%)
Median age	65 (range 44-83)
HIV Positive (%)	17 (94%)
viral load	ND or <40 (n=16), 71 (n=1)
median CD4	610 cells/mm3 (range 242 to 1263); 32% (range 16 to 51)
HBcAb positive	8 (44%)
HCV Ab positive	10 (56%); 2 (11%) RNA positive

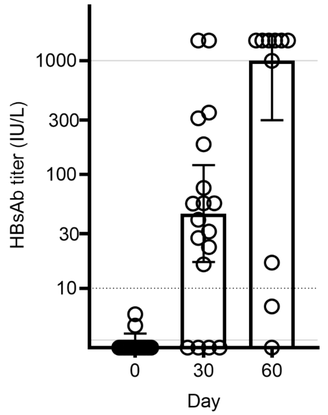


Fig 1: HBsAb titers after vaccination

METHODS:

Veterans who had records of prior alum-adjuvanted HBV vaccination series without subsequent seroprotection were re-vaccinated with Heplisav-B on day 0 and day 30.

- HBsAb collected days 0, 30, and 60
- Serum cytokines assessed pre-vaccination on day 0 and at 1 day
- No exclusions for HBcAb, HIV, or HCV positivity

RESULTS:

- Most participants (14 of 18) achieved seroprotective titers after a single dose of Heplisav-B, with a geometric mean titer of 45 IU/L (95% CI 17 to 121).
- At day 60, 30 days after the second dose, 8 of the 10 had seroresponded, and 6 had titers above the limit of quantification (>1000 IU/L).

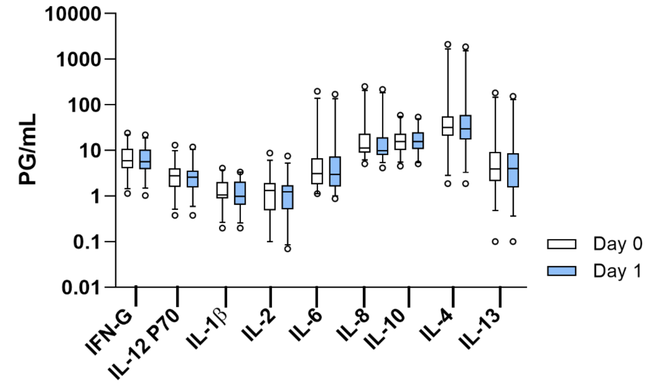


Fig 2: Cytokine responses at 1 day after vaccination.
Day 1 cytokine responses show no significant change compared to day 0 (vaccination).

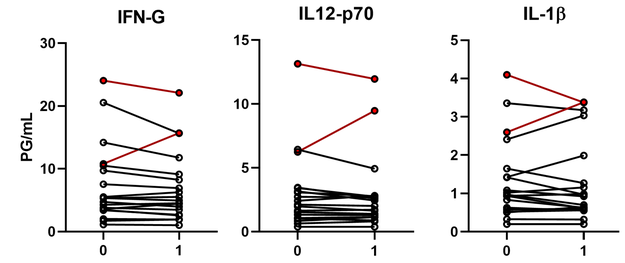


Fig 3: Day 0 and 1 cytokine levels are not predictive of vaccine response. The two individuals who did not have seroprotective HBsAb titers are shown in red. Other cytokines assayed showed similar lack of correlation with vaccine responsiveness.

CONCLUSIONS:

Despite prior alum-adjuvanted HBV vaccine series, a subset of the Veterans remained nonimmune to HBV. On re-vaccination, **Heplisav-B is immunogenic in persons with HIV**.

ACKNOWLEDGEMENTS

This work was supported by NIH grant T32AI007524. MD and EW were supported by an investigator-initiated grant from Dynavax, which had no role in the design of the study, analysis, or interpretation of the data.

This material is the result of work supported with resources and the use of facilities at the VA Maryland Health Care System, Baltimore, Maryland. The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government.