

# CpG Adjuvant Plus HBV Vaccination in HIV Infection Achieves Sustained Seroprotection for Up to 3 Years



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## INTRODUCTION

Hyporesponsiveness to HBV vaccine is well recognized in HIV infected individuals. Immunostimulatory CpG oligodeoxynucleotide motifs are unmethylated cytosine-guanine dinucleotides which act as potent Th1-like adjuvants with many antigens including HBV vaccine in healthy, HIV seronegative adults (*J Clin Immunol* 2004;24:693-701).

## OBJECTIVES

- To assess the safety and tolerability of CpG ODN 7909 as an adjuvant with **Enerix** vaccine in HIV infected adults
- To assess the immunogenicity (kinetics and magnitude of the HBsAg-specific humoral response) to **CpG-Enerix** vaccine compared to **Enerix-B** vaccine alone in HIV positive individuals on effective antiretroviral therapy

## METHODS

### STUDY DESIGN

- Randomized, Double-Blind, Single Site, Placebo Controlled Trial
- Injection 0, 1, 2 months
- Anti-HBs antibody measurement at Baseline, wk 2, 4, 6, 8, 10, and 12 on protocol and month 6, 12, 24, 30, and 36 in follow-up
- Control Group (n=19) received Enerix 40µg (IM)
- Intervention Group (n=19) received Enerix 40µg and CpG 1mg (IM)

### INCLUSION CRITERIA

- HBV susceptible (never vaccinated or vaccinated (3 doses) with anti-HBs titres <10mIU/mL)
- HIV infected
- Aged 18-55 years
- HAAART (defined as 3+ antiretrovirals where at least one is a protease inhibitor or efavirenz) for a minimum of 6 months
- CD4 count ≥ 200 cells / ml
- HIV RNA < 50 copies/ ml for a minimum of 3 months
- Negative serum tier for HBsAg and HBV DNA

### EXCLUSION CRITERIA

- Immunosuppressive conditions
- Liver enzymes (ALT/AST) greater than 3 times normal values
- Receipt of any blood product, or immunoglobulin preparation within two months prior to enrollment or anticipated receipt of these products within the study period
- Pregnant or breastfeeding

## RESULTS

### Demographics

	Enerix-B	Enerix-B +CpG
N	19	19
Age (yrs)	42.9 ± 7.3	41.0 ± 7.4
Race		
Caucasian	17	15
Black	2	2
Other	0	2
Sex		
Male	18	14
Female	1	5
HBV vaccine naïve	9	10

## DISCUSSION

Overall, experimental and control vaccines were well tolerated, without any apparent increase in systemic or local injection site reactions above that expected in a standard vaccine administration trial.

- The addition of CpG 7909 vaccine adjuvant to Enerix-B improved several measures of this vaccines utility in HBV vaccine hyporesponsive individuals:
  - earlier seroconversion
  - earlier seroprotection
  - greater numbers of subjects with anti-HBs titres ≥ 10 and ≥ 100 at time points after week 24 and up to 3 years after vaccination
  - higher anti-HBs titres at each time point
- This was true in both vaccine naïve and prior vaccine failure subjects

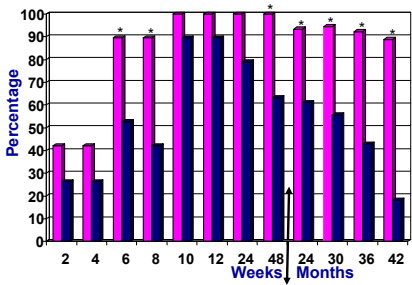
## CONCLUSION

- CpG 7909 is safe and efficacious in achieving rapid, higher, and sustained anti-HBV titres and seroprotecting HIV subjects for up to 36 months.
- CpG 7909 may be beneficial to HBV vaccine hyporesponsive individuals who are at risk for exposure to HBV.

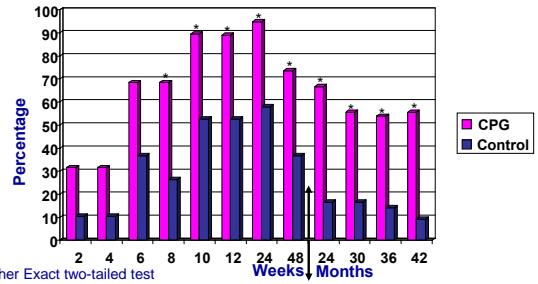
## ACKNOWLEDGMENT

AIDS Programme Committee of the Ontario Ministry of Health  
 Canadian HIV Trials Network

Individuals obtaining and maintaining anti-HBs antibody titres ≥ 10 IU/L

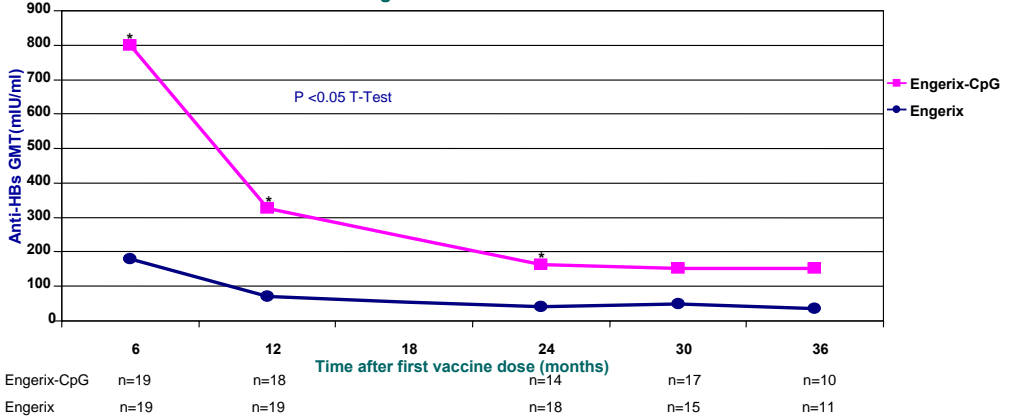


Individuals obtaining and maintaining anti-HBs antibody titres ≥100 IU/L



\* P < 0.05 Fisher Exact two-tailed test

Long term anti-HBs GMT



P < 0.05 T-Test

	6	12	18	24	30	36
Enerix-CpG	n=19	n=18		n=14	n=17	n=10
Enerix	n=19	n=19		n=18	n=15	n=11