Vaccine Update: Hep B Vaccine in People with HIV

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No conflicts of interest or relationship to disclose

Disclaimer

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Hepatitis B Vaccines

- HepB-CpG (Heplisav-B)
- Energix-B
- Recombivax HB
- Twinrix

- PreHevbrio no longer available in the US

JAMA | Original Investigation

HepB-CpG vs HepB-Alum Vaccine in People With HIV and Prior Vaccine Nonresponse

The BEe-HIVe Randomized Clinical Trial

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Background:

- HBV is leading cause of liver-related mortality worldwide
- People with HIV have lower rates of seroprotection from recombinant Hep B vaccines (34-93%)

What's different about HepB-CpG?

- Recombinant vaccine with TLR-9 agonist to stimulate response to vaccine
- In vaccine-naïve people with HIV, 100% seroprotection with 3 doses of HepB-CpG

Source: *JAMA*. doi:10.1001/jama.2024.24490

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Aim:

Determine whether HepB-CpG improves response for HepB among people with HIV who are non responders to conventional vaccines

Objectives:

Compare seroprotection response of 2 doses of HepB-CpG vaccine vs 3 does of HepB-alum vaccine (noninferiority study)

Compare seroprotection response of 3 doses of HepB-CpG vaccine vs 3 doses of HepB-alum vaccine (superiority study)

Study Design:

Phase 3 open-label, RCT in people with HIV who had previously received HBV vaccine

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Participants:

Adults 18 and over on ART (CD4 count $\geq$100 and HIV VL < 1000) with prior HepB vaccination and without evidence of seroprotection or infection post vaccination

Definition of prior HepB vaccine response or infection – HepsAg positive, HepB cAb, HepBsAb $\geq$ 10 at any time

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Intervention:

2 doses of HepB-CpG at 1 and 4 weeks

3 doses HepB-CpG at 0, 4, and 24 weeks

Vs

3 doses of HepB-alum 20ug at 0, 4, 24 weeks

Outcomes:

Primary outcome: efficacy – HBsAb $\geq$ 10 at 12 weeks after initiation of 2 dose series or at 28 weeks after initiation of 3 dose series

Secondary outcomes: seroprotection at study visits, and level of HBsAb titer

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Table. Baseline Characteristics of the Participants

	HepB-CpG vaccine		3 Doses of HepB-alum vaccine (n = 186)
	2 Doses (n = 187)	3 Doses (n = 188)	
Age, y			
Median (IQR)	46 (27-57)	45 (33-55)	47 (32-58)
Group, No. (%)			
18-39	72 (39)	69 (37)	65 (35)
40-49	30 (16)	45 (24)	42 (23)
50-59	58 (31)	53 (28)	43 (23)
≥60	27 (14)	21 (11)	36 (19)
Sex assigned at birth, No. (%)[a]			
Female	67 (36)	68 (36)	67 (36)
Male	120 (64)	120 (64)	119 (64)
Gender identity, No. (%)[b]			
Cisgender	184 (98)	181 (97)	180 (97)
Transgender spectrum	3 (2)	6 (3)	5 (3)
Race, No. (%)[c]			
American Indian or Alaska Native	1 (1)	2 (1)	1 (1)
Asian	29 (16)	35 (19)	33 (18)
Black or African American	84 (45)	76 (40)	74 (40)
White	63 (34)	62 (33)	72 (39)
Multiple	2 (1)	1 (1)	2 (1)
Other	2 (1)	4 (2)	1 (1)
Unknown	6 (3)	8 (4)	3 (2)
Ethnicity, No. (%)[c]			
Hispanic or Latino	39 (21)	42 (22)	40 (22)
Not Hispanic or Latino	148 (79)	145 (77)	144 (77)
Unknown	0	1 (1)	2 (1)
Injection drug use, No. (%)			
Current	0	0	0
Former	5 (3)	10 (5)	11 (6)
Never	182 (97)	178 (95)	175 (94)
Smoking status, No. (%)[d]			
Current	36 (19)	48 (26)	42 (23)
Former	41 (22)	36 (19)	39 (21)
Never	109 (59)	103 (55)	103 (56)
Diabetes, No. (%)[a]	25 (13)	23 (12)	26 (14)
Body mass index[e]			
Median (IQR)	26.8 (22.6-30.2)	26.6 (22.9-31.2)	26.0 (22.5-30.2)
Category, No. (%)[e]			
<18.5	9 (5)	7 (4)	7 (4)
18.5-<25	64 (34)	74 (39)	75 (41)
25-<30	61 (33)	49 (26)	53 (29)
≥30	53 (28)	58 (31)	50 (27)

Table. Baseline Characteristics of the Participants (continued)

	HepB-CpG vaccine		3 Doses of HepB-alum vaccine (n = 186)
	2 Doses (n = 187)	3 Doses (n = 188)	
Time since HIV diagnosis, median (IQR), y[f]	13.0 (8.0-19.8)	14.1 (8.1-20.1)	12.4 (6.9-20.0)
Nadir CD4 cell count, median (IQR), cells/μL[g]	293 (97-467)	287 (136-508)	241 (95-467)
Current antiretroviral therapy regimen duration ≥1 y, No. (%)	136 (73)	142 (76)	136 (73)
CD4 cell count, cells/μL			
Median (IQR)	609 (434-859)	650 (511-862)	647 (477-854)
Category, No. (%)			
<200	6 (3)	3 (2)	6 (3)
200-<350	19 (10)	13 (7)	11 (6)
350-<500	35 (19)	28 (15)	34 (18)
≥500	127 (68)	144 (77)	135 (73)
HIV RNA <40 copies/mL, No. (%)[h]	175 (94)	176 (94)	175 (94)
Time since previous hepatitis B vaccination, No. (%), y			
0-<5	62 (33)	69 (37)	71 (38)
5-<10	38 (20)	43 (23)	41 (22)
≥10	87 (47)	76 (40)	74 (40)
Previous doses of hepatitis B vaccine, No. (%)			
1-2	50 (27)	39 (21)	37 (20)
3	100 (53)	102 (54)	100 (54)
4-5	22 (12)	28 (15)	24 (13)
≥6	15 (8)	19 (10)	25 (13)

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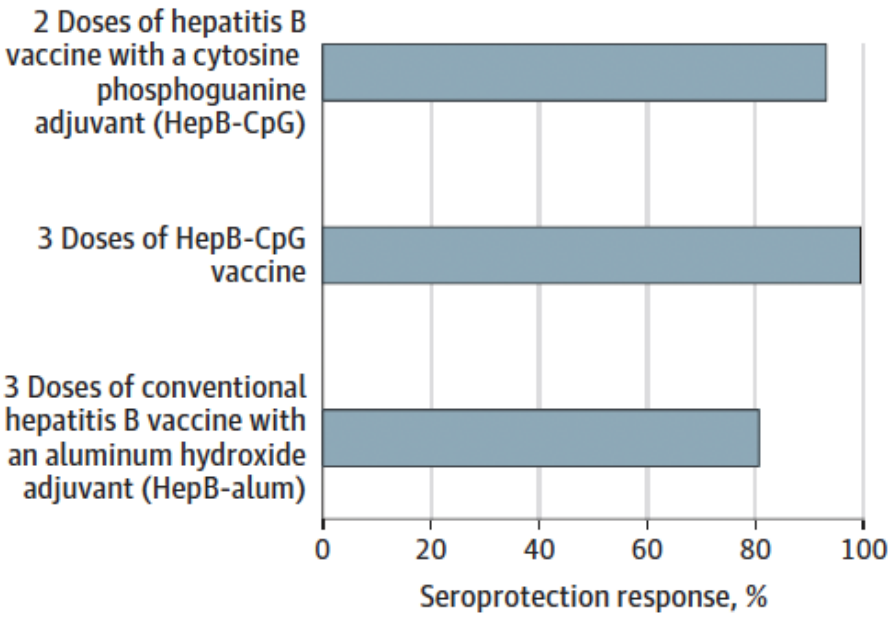
Figure 2. Efficacy Analysis for the Primary Outcome of Seroprotection Response to the Hepatitis B Vaccine

A Primary outcome of seroprotection response to the hepatitis B vaccine



B Difference in primary outcome of seroprotection response to the hepatitis B vaccine

	Difference in seroprotection response, % (97.5% CI)
2 Doses of HepB-CpG vaccine vs 3 doses of HepB-alum vaccine	12.5 (4.1-20.9)
3 Doses of Hep-CpG vaccine vs 3 doses of HepB-alum vaccine	18.4 (10.4-26.2)

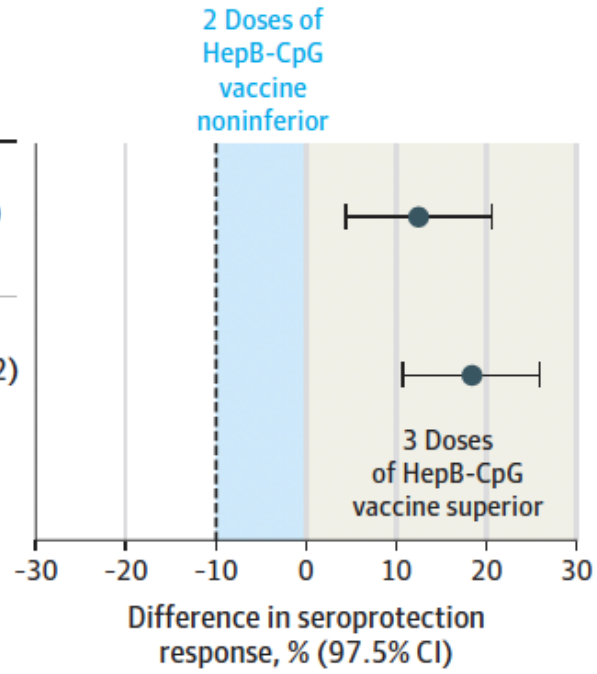


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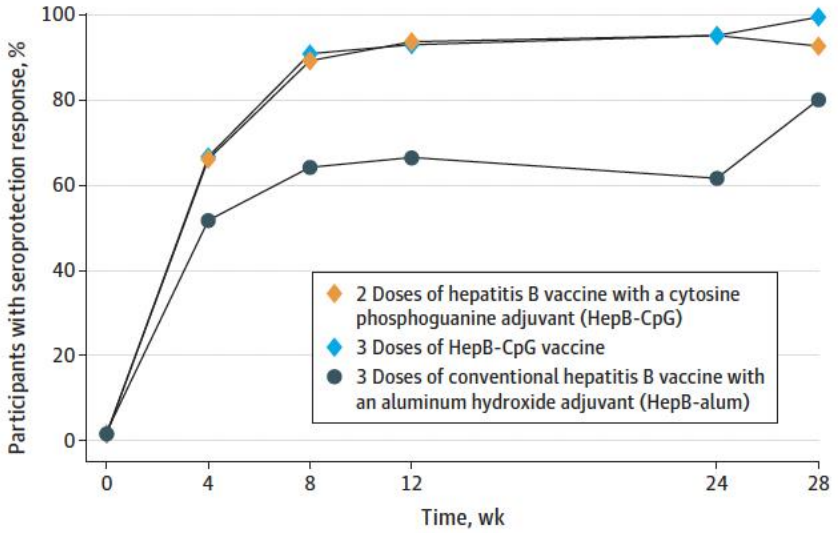
Figure 3. Seroprotection Response to the Hepatitis B Vaccine by Scheduled Study Weeks



No. of participants						
2 Doses of HepB-CpG vaccine	185	177	175	172	162	162
3 Doses of HepB-CpG vaccine	188	177	174	169	162	162
3 Doses of HepB-alum vaccine	186	174	173	167	164	160

Figure 4. Level of Antibody Against Hepatitis B Surface Antigen at Primary Time Point

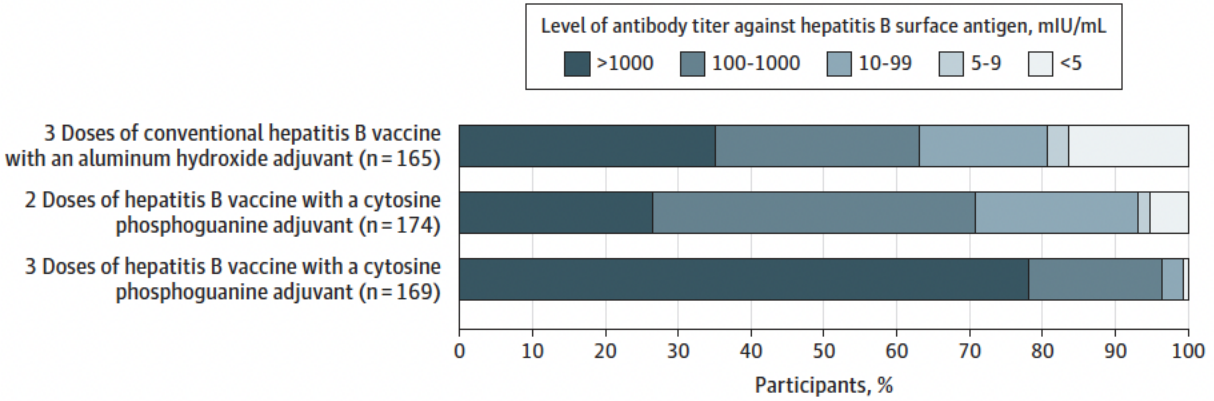


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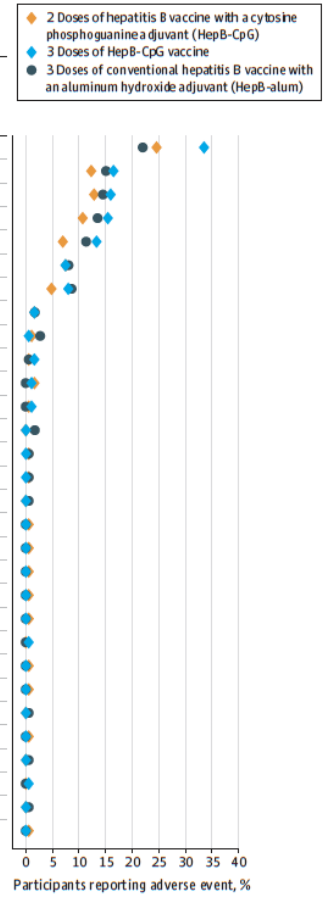
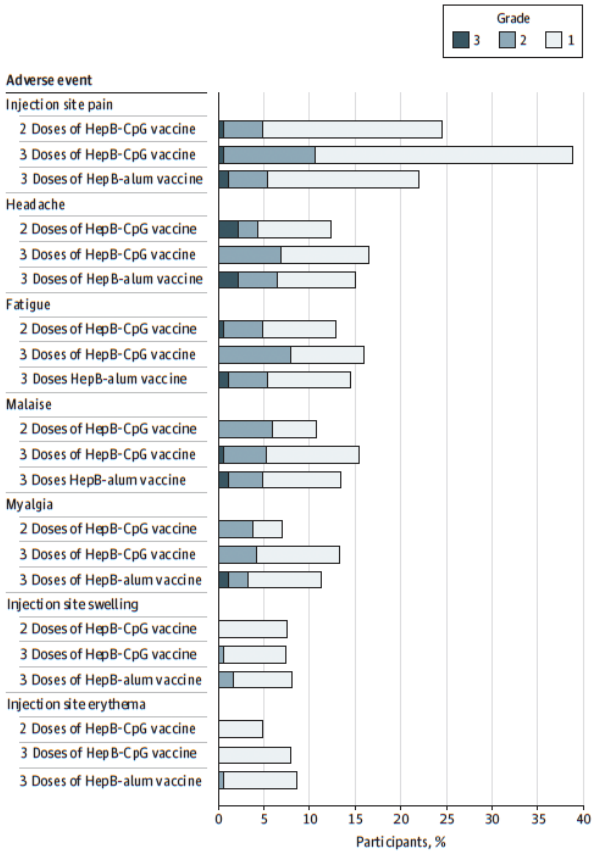
Figure 5. Adverse Events Related to the Hepatitis B Vaccine

A All adverse events related to study vaccines

Adverse event	Reported adverse event, No. (%)		
	2 Doses of HepB-CpG vaccine (n = 187)	3 Doses of HepB-CpG vaccine (n = 188)	3 Doses of HepB-alum vaccine (n = 186)
Injection site pain	46 (25)	73 (39)	41 (22)
Headache	23 (12)	31 (16)	28 (15)
Fatigue	24 (13)	30 (16)	27 (15)
Malaise	20 (11)	29 (15)	25 (13)
Myalgia	13 (7)	25 (13)	21 (11)
Injection site swelling	14 (7)	14 (7)	15 (8)
Injection site erythema	9 (5)	15 (8)	16 (9)
Pyrexia	3 (2)	3 (2)	3 (2)
Pain	2 (1)	1 (1)	5 (3)
Hypothermia	1 (1)	3 (2)	1 (1)
Rash	3 (2)	2 (1)	0
Dizziness	1 (1)	2 (1)	0
Pain in extremity	0	0	3 (2)
Hypertension	1 (1)	0	1 (1)
Peripheral swelling	1 (1)	0	1 (1)
Arthralgia	0	0	1 (1)
Chronic fatigue syndrome	1 (1)	0	0
Cold sweat	1 (1)	0	0
Dermatitis atopic	1 (1)	0	0
Diarrhea	1 (1)	0	0
Feeling hot	1 (1)	0	0
Hemoglobin decreased	0	1 (1)	0
Hyperhidrosis	1 (1)	0	0
Nausea	1 (1)	0	0
Neck pain	0	0	1 (1)
Neutrophil count decreased	1 (1)	0	0
Oropharyngeal pain	0	0	1 (1)
Palpitations	0	1 (1)	0
Upper respiratory tract infection	0	0	1 (1)
Vertigo	1 (1)	0	0



B Adverse events reported by ≥5% of participants



The adverse event terms are MedDRA preferred terms (version 26.1). An adverse event receiving grade 1 was mild; grade 2, moderate; grade 3, severe; and grade 4, potentially life-threatening. The grading system is from the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (version 2.1).

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Take Home Points:

HepB-CpG either 2 or 3 doses led to better seroprotection response compared to HepB-Alum

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OI Guidelines Recommendation

Heplisav-B is now the preferred vaccine for previously unvaccinated individuals, dosed at 0 and 4 weeks (AII)

If Heplisav-B is not available, then double-dose Engerix-B or double-dose Recombivax HB x 3 doses should be given (ACIP does not include this as a recommendation for people with HIV)

Heplisav-B is FDA approved for individuals 18+ years

OI Guidelines Recommendation

Heplisav-B is now the preferred vaccine for previous non-responders, dosed at 0 and 4 weeks (AII), with consideration of 3rd dose at 24 weeks (BIII)

If failed 2 dose series of Heplisav-B, then 3rd dose at 24 weeks after 1st dose (BIII)

OI Guidelines Recommendation – other nuances

Some experts would check anti-HBs annually and give a booster dose if levels fall below 10 mIU/mL, particularly if a person has ongoing risk factors for acquiring HBV and is not receiving tenofovir **(CIII)**

Risk factors for waning immunity – low CD4 counts, initial low titer immediately post completion of vaccination series

Questions?

Acknowledgment

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