Welcome

47TH Annual Meeting

PHOENIX

May 17-20, 2026

SCT

SOCIETY FOR CLINICAL TRIALS

David Sackett Trial of the Year Award

- Improves the lot of humankind
- Provides the basis for a substantial, beneficial change in health care.
- Reflects expertise in subject matter, excellence in methodology, and concern for study participants
- Overcame obstacles in implementation
- The presentation of its design, execution, and results is a model of clarity and intellectual soundness

Tribute

CLINICAL TRIALS

Clinical Trials
2015, Vol. 12(5) 540–551

DOI: 10.1177/1740774515597895
ctj.sagepub.com
SAGE

An interview with David Sackett, 2014–2015

Edited by R. Brian Haynes[1] and Steven N Goodman[2]

B-ENHANCEMENT OF HBV VACCINATION IN PERSONS LIVING WITH HIV (BEe-HIVe): Evaluation of HEPLISAV-B®

A Multicenter Trial of the ACTG

Kristen Marks, MD, MS
On behalf of ACTG 5379 (BEe-HIVe) Study Team

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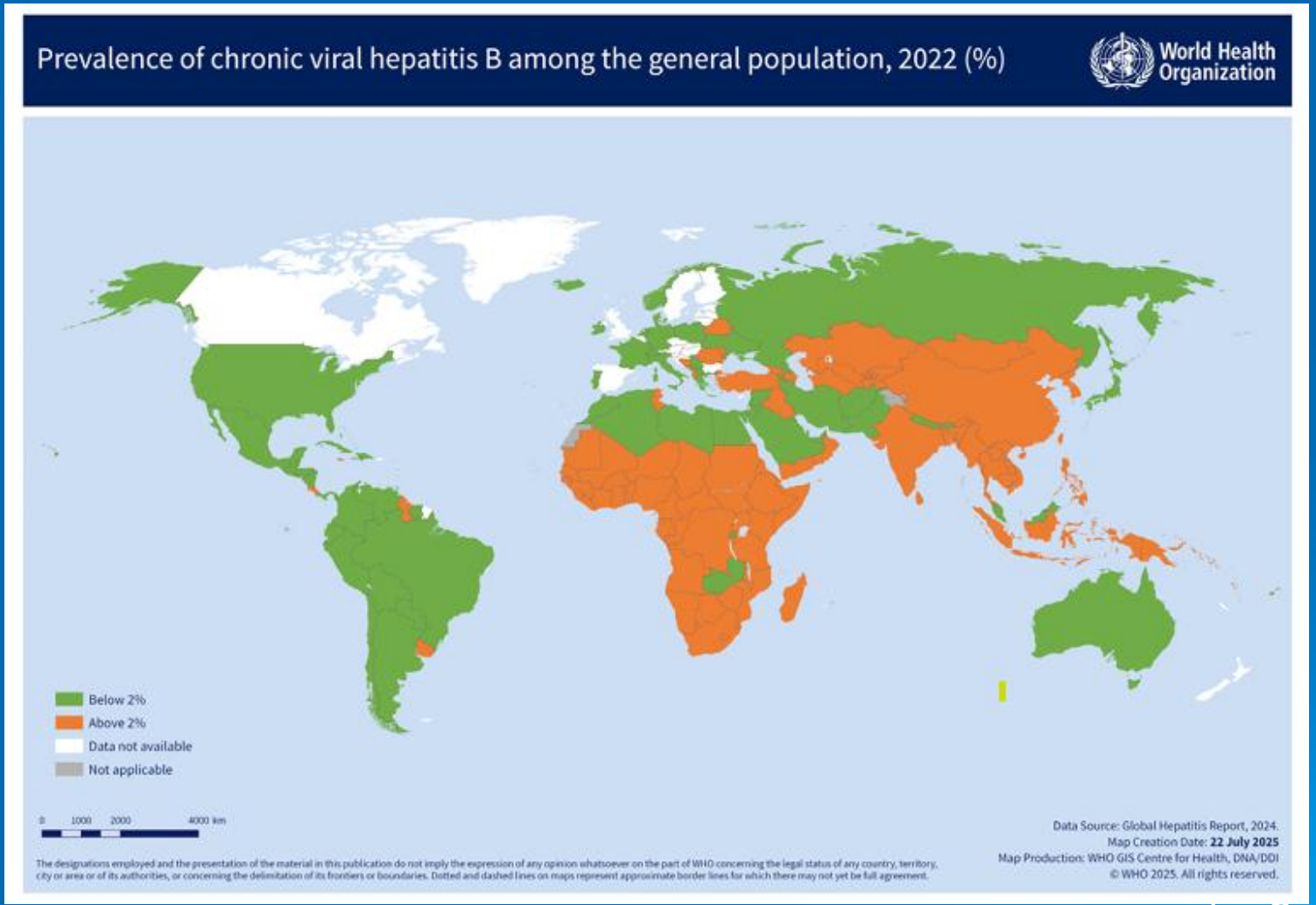
Disclosures

- Research grants: Gilead Sciences, Glaxo Smith Kline
- Data safety monitoring Board: Immorna, Novo Nordisk

- This research was supported by grants UM1 AI068634, UM1 AI068636, and UM1 AI106701 from the National Institute of Allergy and Infectious Diseases.
- Additional funding and support for the study products were provided by Dynavax Technologies.

HBV is the Most Common Bloodborne Infection Worldwide

- 254 million worldwide
- 96 countries have a hepatitis B prevalence above 2%
- These countries are home to approximately 65% of the world's population
- In African and Western Pacific Regions – 5% of population live with chronic hepatitis B



HBV Epidemiology, US (2023)

An estimated **640,000–862,000+** people in the US have chronic HBV infection.

2,214 Acute HBV cases reported

Adjusted estimate of **14,400 new infections**

After a 30% drop (2019-2020), **rates of acute hepatitis B** have remained relatively **stable**

Rates of acute hepatitis B are **highest among adults aged 40–59** years

HBV prevalence is higher in people born outside of US. Highest in **non-Hispanic Asian/Pacific Islander**

CDC 2023 Viral Hepatitis Surveillance Report

Snapshot: Hepatitis B Virus (HBV) Infection

- ✓Vaccine preventable
- ✓Treatment controls but does not cure infection
- ✓Acute illness may be asymptomatic, mild illness, or fulminant hepatitis
- ✓Chronic illness may result in cirrhosis or liver cancer
- ✓Transmitted through contact with infectious blood, semen, or other body fluids and perinatally
- ✓Younger exposure results in chronic infection more often

HBV is a life long, dynamic disease

- Changes over time
- Risk of end stage liver disease and liver cancer increases with ongoing inflammation and viremia in adults
  - Antiviral drugs can decrease fibrosis progression
  - Fibrosis can be reversible with antiviral drugs
- HBV can be controlled but not cured
  - Often indefinite antiviral treatment is required
- Reactivation can occur even in those who achieved immunologic control (lost HBs antigen)

Universal Testing of HBV since 2023

Summary of 2023 HBV screening and testing recommendations

Screen all adults aged 18 years and older at least once in their lifetime using a triple panel test

Screen pregnant people for hepatitis B surface antigen (HBsAg) during each pregnancy regardless of vaccination and history of testing

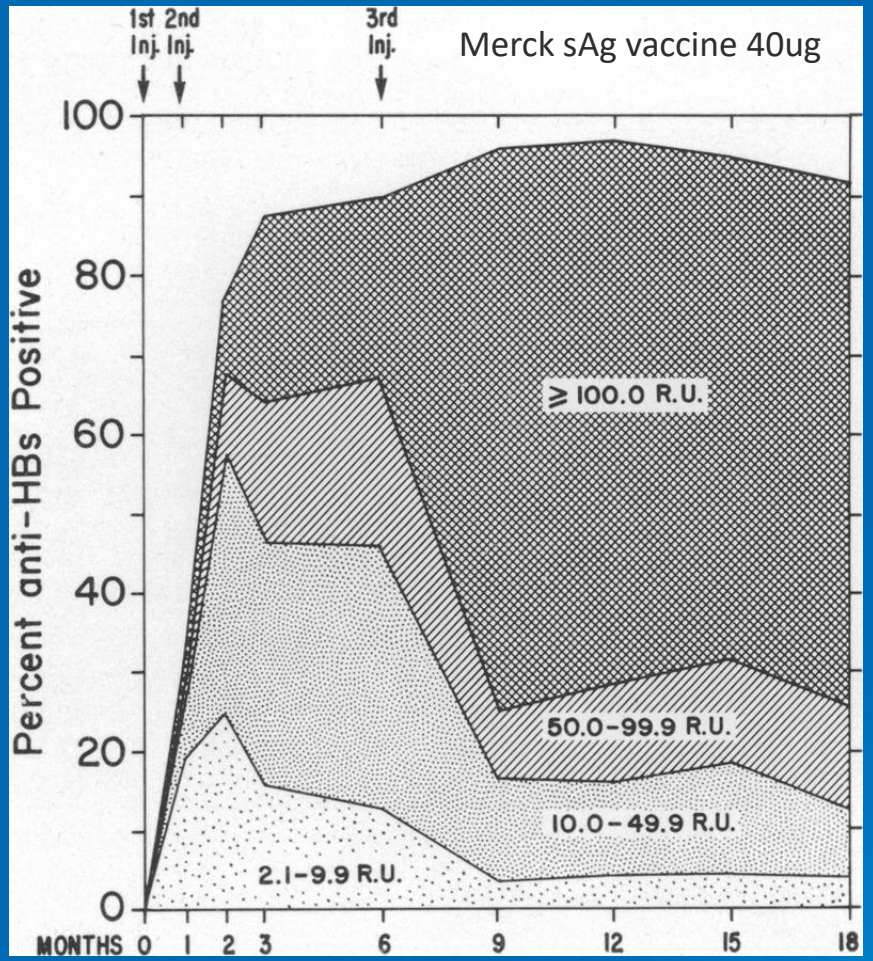
Expand periodic risk-based testing to include people incarcerated, people with a history of sexually transmitted infections or multiple sex partners, and people with hepatitis C virus infection

Test anyone who requests HBV testing regardless of disclosure of risk

Screening and Testing for Hepatitis B Virus Infection: CDC Recommendations — United States, 2023

HBV Vaccine Mechanism of Action and Correlate of Protection

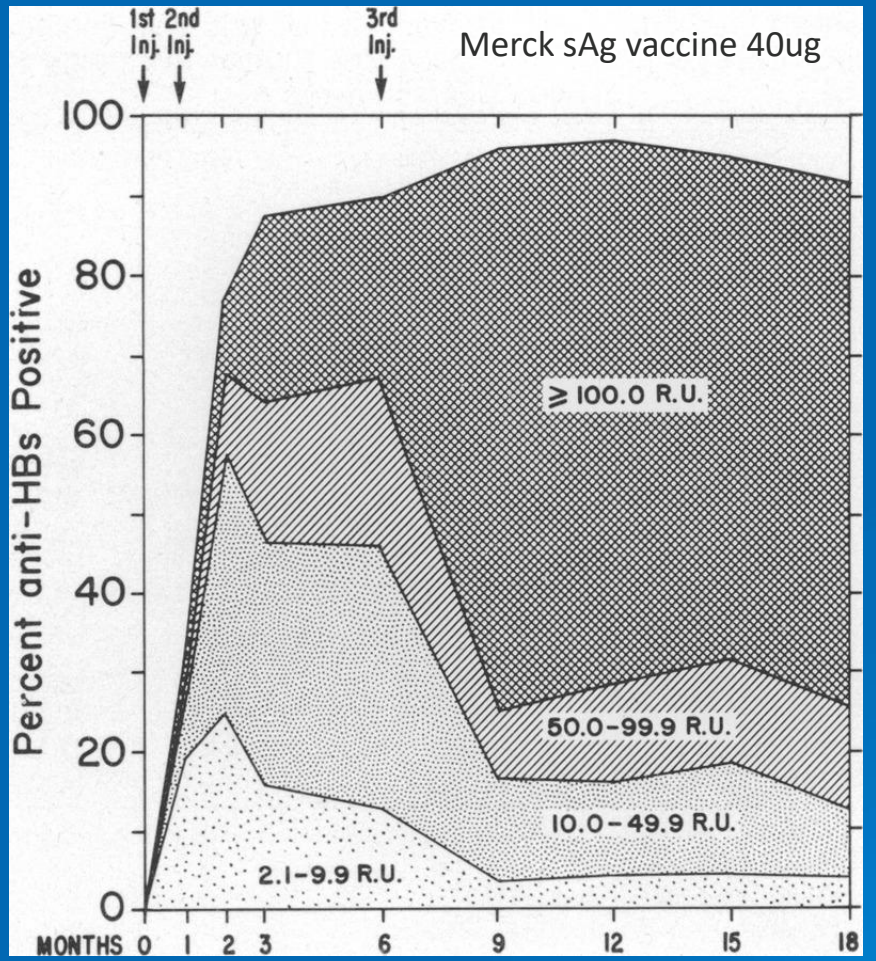
- 1964- “Australia antigen" or hepatitis B surface antigen (HBsAg), discovered by Blumberg
- 1970-3 – experiments using heat inactivated serum to induce immunity
- 1981 – FDA approved sAg vaccine derived from plasma of HBsAg-positive donors (Merck)
- 1986 - DNA recombinant HBsAg vaccines (no blood products)/alum adjuvant
  - Expression of HBsAg in yeast cells
  - HBsAg self assembles into viral-like particles
  - Differ from natural viral particles as lack pre-S and lack glycosalation
  - Safe and over 1 billion doses given



Szmuness W et al. N Engl J Med 1980; 303:833-841.

HBV Vaccine Mechanism of Action and Correlate of Protection

- Correlate of protection - Anti-HBs titer of >10mIU/mL*
  - Also significant correlate in people with HIV**
- Vaccine-induced seroprotection is considered a surrogate for clinical protection



*Szmuness W et al. N Engl J Med 1980; 303:833-841.
**Landrum et al. AIDS. 2010;24(4):545.

Areas for Improvement – HBV prevention through vaccination

- Vaccine uptake/coverage globally – universal immunization
  - Especially newborn birth dose
  - Adults at risk
- Heat stable/freeze stable
- Fewer doses
- Durability
- Indication for all situations (pregnant, infant, etc)
- Surveillance and preparation for vaccine escape mutants
- Better vaccine efficacy for people with HIV, immunocompromised, older persons

HBV & People with HIV

- Increased exposure risks
- Lower likelihood response to conventional vaccine (35-80%, recent metanalysis 65%)
- Immunity wanes faster
- ? Vaccine access is better
- ? Vaccine completion rates better
  - Only 25% of adults complete 3-dose vaccine series*
    - Increases to 45% with use of 2 dose series**
  - Texas clinics study (2011-21): Of 44% vaccine eligible PLWH, 9% received 3 dose within 1 year, 17% any dose***

Predictors of vaccine non-response

- HIV Viremia
- CD4<350
- Older Age
- HCV
- Occult HBV

Farooq and Sherman. Current HIV/AIDS Reports 2019;16:395–403
**Williams et al, MMWR Surveill Summ 2017;66(11):1-28.*
*** Bruxvoort et al. JAMA Network Open; 2020; 3;(11).*
****Garcia et al. Viral Hepat. 2023; 00: 1-3.*

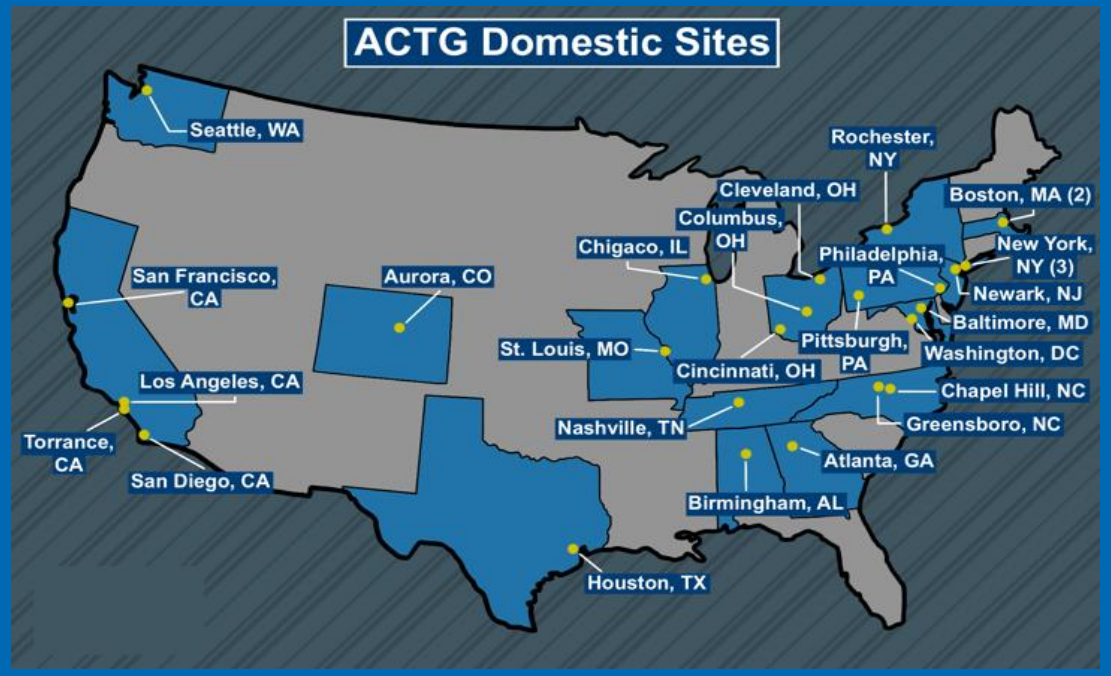
Strategies to Improve Response to Standard HBV Vaccines

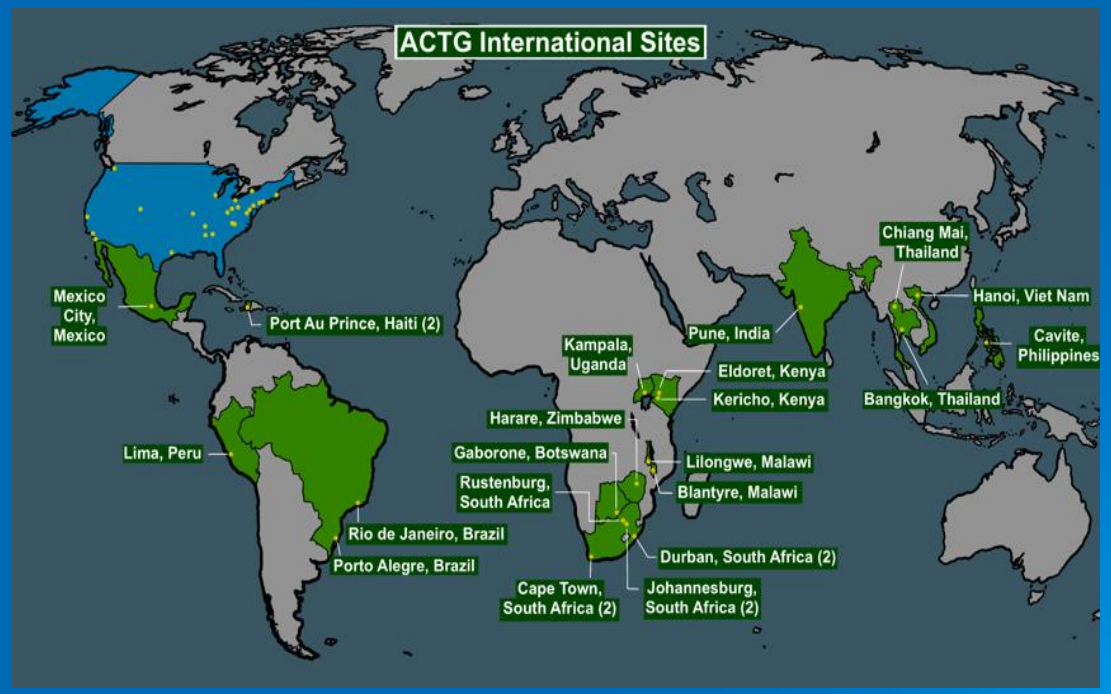
- 4th doses (e.g. 0, 1, 2, 6 mos)
- Higher doses (double dose)
- Accelerated schedule (0, 1, 3 wks) – to improve completion
- For nonresponders: Additional dose or repeat series
- Additional antigens (e.g. addition of pre-S)
- Novel vectors
- Novel adjuvants (e.g. HepB-CpG)

Farooq and Sherman. Current HIV/AIDS Reports 2019;16:395–403
Human Vaccines and Immunotheraputics (2017) 13:1304–1313

About the ACTG

- NIH-funded clinical trials network
- Advancing Clinical Therapeutics Globally, formerly the AIDS Clinical Trials Group
- 53 Core Clinical Research Sites(CRS)
  - 28 Domestic CRSs
  - 25 International CRSs
- 15 Countries (new sites Mexico, Vietnam, Philippines)





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ACTG

Background for BEe-HIVe Study

- Conventional vaccine, which consists of recombinant Hepatitis B surface antigen (HBsAg) and an alum adjuvant, achieves seroprotection (Anti-HBs ≥10 mIU/mL) in 35-80% in people with HIV
  - Predictors of non-response include older age, low CD4 count, HIV viremia
  - ACTG 5220 evaluated the safety and efficacy of adding GM-CSF as an adjuvant to conventional HBV vaccine providing response rate estimate
- HepB-CpG (HEPLISAV-B®) contains recombinant HBsAg (20 mcg) and CpG 1018® adjuvant
  - Adjuvant binds to TLR9 (sensing receptor for innate immune responses) expressed on plasmacytoid dendritic cells and memory B cells
  - In 2017, FDA-approved as 2 dose series for adults 18 years and older

Research

JAMA | Original Investigation

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

The BEe-HIVe Randomized Clinical Trial

Kristen M. Marks, MD; Minhee Kang, PhD; Triin Umbleja, MSc; Andrea Cox, MD, PhD; Karen J. Vigil, MD; Ngan T. Ta, MD, PhD; Ayotunde Omoz-Oarhe, MD; Hugo Perazzo, MD, PhD; Josphat Kosgei, MBChB; Timothy Hatlen, MD; Jennifer Price, MD, PhD; Leolin Katsidzira, DPhil; Khuanchai Supparatpinyo, MD; Kevin Knowles, PhD; Beverly L. Alston-Smith, MD; Parita Rathod, BS; Kenneth E. Sherman, MD, PhD; for the ACTG 5379 (BEe-HIVe) Study Team

JAMA. 2025;333(4):295-306. doi:10.1001/jama.2024.24490

Immunogenicity and Safety of Hepatitis B Virus (HBV) Vaccine With a Toll-Like Receptor 9 Agonist Adjuvant in HBV Vaccine-Naïve People With Human Immunodeficiency Virus

Kristen M. Marks,[1] Minhee Kang,[2] Triin Umbleja,[2] Anchalee Avihingsanon,[3] Patcharaphan Sugandhavesa,[4] Andrea L. Cox,[5] Karen Vigil,[6] Hugo Perazzo,[7] Jennifer C. Price,[8] Leolin Katsidzira,[9] Christina Vernon,[10] Beverly Alston-Smith,[11] and Kenneth E. Sherman[12]; the ACTG 5379 Study Team*

CID 2023:77 (1 August) • BRIEF REPORT

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CLINICAL SCIENCE

Brief Report: Hepatitis B Vaccination Histories in Persons With HIV Needing Revaccination

Kang, Minhee PhD[a]; Umbleja, Triin MSc[a]; Avihingsanon, Anchalee MD, PhD[b]; Cardoso, Sandra W. MD, PhD[c]; Kosgei, Josphat MBChB[d]; Vigil, Karen J. MD[e]; Ngan, Ta Thi Dieu MD, PhD[f]; Chakalisa, Unoda MD, MSc[g]; Caruso, Stephanie MBA[h]; Sherman, Kenneth E. MD, PhD[i]; Marks, Kristen M. MD[j]

Author Information

JAIDS Journal of Acquired Immune Deficiency Syndromes 101(5):p 534-540, May 1, 2026. | *DOI:* 10.1097/QAI.0000000000003828

Research Letter FREE

HepB-CpG Vaccine in People With HIV and Prior Nonresponse to HBV Vaccine

The BEe-HIVe Trial End-of-Study Results

Kristen M. Marks, MD[1]; Minhee Kang, PhD[2]; Triin Umbleja, MSc[2]; Andrea Cox, MD, PhD[3]; Karen J. Vigil, MD[4]; Anchalee Avihingsanon, MD, PhD[5]; Patcharaphan Sugandhavesa, MD[6]; Leolin Katsidzira, MBChB, DPhil[7]; Josphat Kosgei, MBChB[8]; Hugo Perazzo, MD, PhD[9]; Jennifer Price, MD, PhD[10]; Stephanie Caruso, MBA[11]; Kevin Knowles, PhD[11]; Beverly L. Alston-Smith, MD[12]; Parita Rathod, BS[13]; Kenneth E. Sherman, MD, PhD[14,15]; for the ACTG 5379 (BEe-HIVe) Study Team

JAMA September 9, 2025 Volume 334, Number 10

Study Design

- Phase III, prospective, open-label, interventional, two group study conducted at US and non-US sites
- Group B – No prior HBV vaccination (n=73)
  - Participants receive HepB-CpG 3 doses at entry and at weeks 4 and 24.
- Group A – Non-response to conventional vaccine (n=561)
  - Participants randomized 1:1:1 to receive
    - **HepB-CpG 2 doses** at entry and week 4 (n=187)
    - **HepB-CpG 3 doses** at entry and at weeks 4 and 24 (n=
    - **HepB-alum** (Engerix®) 3 doses at entry and at weeks 4
  - Group A stratified by sex at birth and diabetes
- Participants on study for 72 weeks

- Open label design allowed examination of potential differences in the completion of 2- vs. 3-dose series
- Challenges in masking the study products with different injection volume and color

Study Design

Vaccine 55 (2025) 127028

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

An efficient vaccine clinical trial: ACTG A5379 hepatitis B vaccine trial in persons with HIV

Minhee Kang [a,*], Kristen M. Marks [b], Andrea L. Cox [c], Kenneth E. Sherman [d]

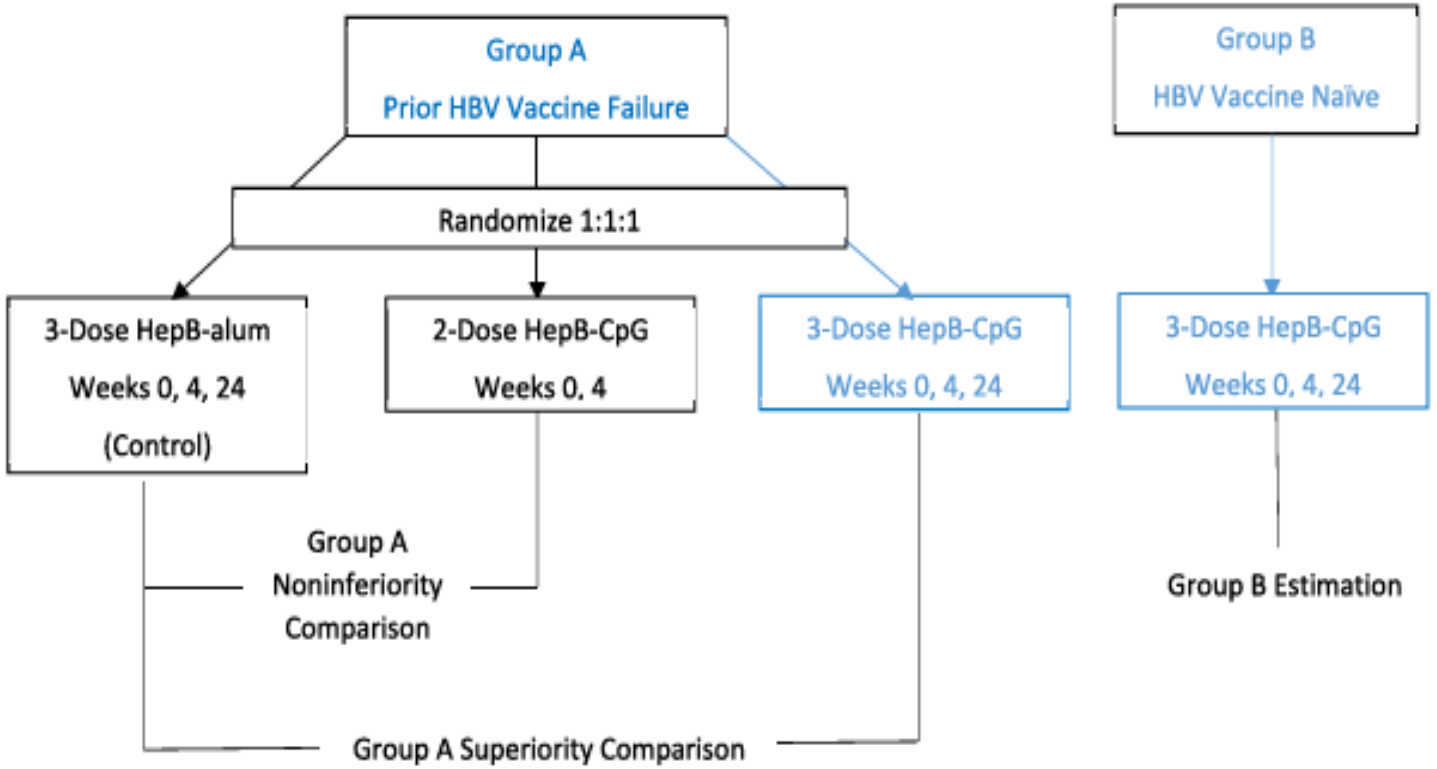


Fig. 1. A5379 study design. Groups A and B are populations defined by the prior vaccine status, and studying them under one protocol exhibits a basket trial design feature (in blue) of studying multiple subgroups receiving the same intervention (3-dose HepB-CpG vaccine series). Within Group A are multiple comparisons of multiple vaccines (HepB-CpG and HepB-alum as control) and dose frequencies (2- or 3-doses), and the control arm is shared for the multiple comparisons. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

- Master protocol
- Enrolled groups simultaneously and at same sites
- Reduced cost

- Efficient design addresses multiplicity in statistical testing and interim data monitoring
- Laboratory-based immunogenicity endpoint

Study Population

- People with HIV who did not respond to prior HBV vaccination (Group A)
- People with HIV with no known history of HBV vaccination (Group B)
  - FDA mandated

- Aimed for at least 30% participants of female sex at birth in each study group
- Aimed for at least 30% participants enrolled at international sites

Vaccine dosing

- HepB-CpG administered IM as 0.5 mL dose (contains 20 mcg of HBsAg and 3000 mcg CpG 1018® adjuvant)
- HepB-alum administered as 1.0 ml dose (contains 20 mcg of HBsAg)

- Keeping HBsAg dose consistent allowed conclusions about adjuvant's effect in PWH

Primary Objectives – Vaccine Naive

- To determine the week 28 SPR of a 3-dose regimen of HepB-CpG
- To describe safety

- Same vaccine and schedule were followed for the participants assigned to 3-dose HepB-CpG in Groups A and B allowing comparison as a secondary objective

Immunogenicity and Safety of Hepatitis B vaccine with a Toll-like Receptor 9 Agonist Adjuvant (HEPLISAV-B) in HBV Vaccine-naive People with HIV

Marks et al., 2023 | *Clinical Infectious Diseases*

IDSA Infectious Diseases Society of America

BACKGROUND: ACTG 5379 sought to evaluate whether a TLR-9 adjuvanted vaccine, HepB-CpG, could improve seroprotective humoral responses for HBV in people with HIV.

Single-am evaluation of vaccine-naïve PWH

ACTG 5379 is an ongoing, prospective, open-label study to evaluate immunogenicity of HepB-CpG in people with HIV

75 HepB vaccine naïve people with HIV were enrolled between December 2020 and August 2021 at 13 international sites

- ✓ People with HIV age 18-70
- ✓ CD4 ≥100 cells/mm3 and HIV-1 RNA <1000 copies/mL
- ✗ Positive (reactive) for HBsAg, anti-HBs or anti-HBc at any time
- ✗ Prior vaccination for hepatits B

n = 68
(Primary analysis set)

HepB-CpG intramuscularly at Weeks 0, 4, and 24,

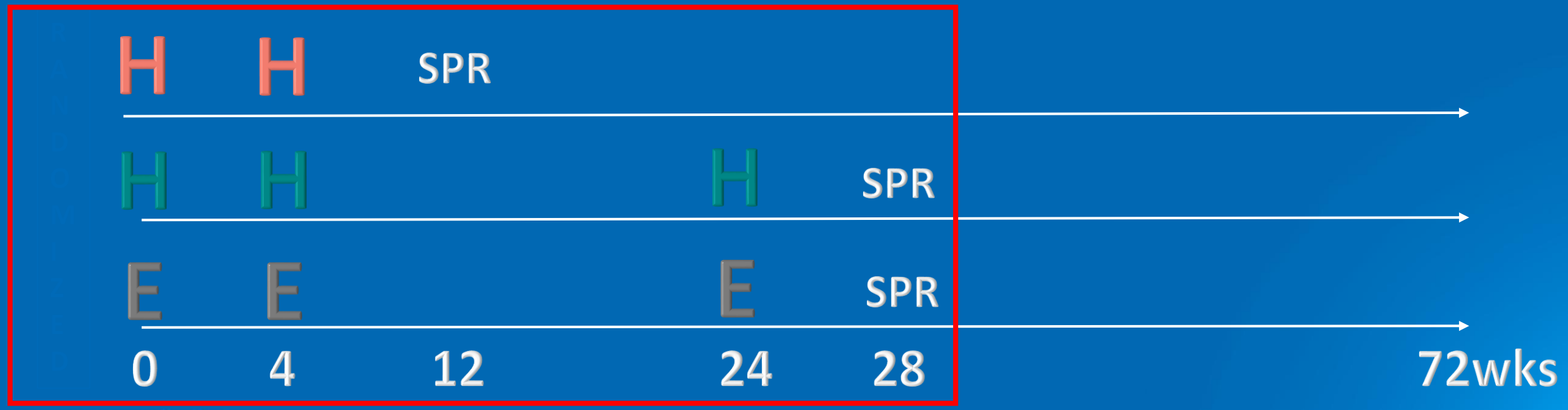
Proportion of participants achieving seroprotection (Anti-HBs ≥10 mIU/mL 4 weeks after vaccination series)

100.0%
(95% CI: 94.7%, 100%)

In this international, multicenter open-label study (ACTG A5379) of HepB-CpG vaccine in people with HIV without prior Hepatitis B Virus (HBV) vaccination, all 68 participants achieved HBV seroprotective titers after the 3-dose series in the primary analysis. No unexpected safety issues were observed.

Primary Objectives – Non-responders

- To compare the seroprotection response (SPR) of 2-dose HepB-CpG to 3-dose HepB-alum (non-inferiority)
- To compare SPR of 3-dose HepB-CpG to 3-dose HepB-alum (superiority)
- To describe safety



Prior Non-responders

Key Inclusion Criteria

- Documentation of HBV vaccination
- Serum HBsAb level <10 mIU/mL or "negative" within 45 days of study entry
- 18-70 years old
- On ART for >56 days prior to entry
- CD4+ cell count >100 cells/mm3
- HIV-1 RNA <1000 copies/mL
- Hemoglobin A1c <9.0%
- If childbearing potential, agree to use contraception

Key Exclusion Criteria

- Serum HBsAb level ≥10 mIU/mL at any time
- Infection or prior exposure to HBV defined as HBsAg or HBcAb positive
- History of [illegible] decompen
- Chronic ki[illegible] G5
- Cancer di[illegible] chemothe
- Various im[illegible] conditions
- Breastfee[illegible]
- Allowed lower CD4 counts and detectable HIV RNA to allow people recently initiated on treatment

Statistical Considerations

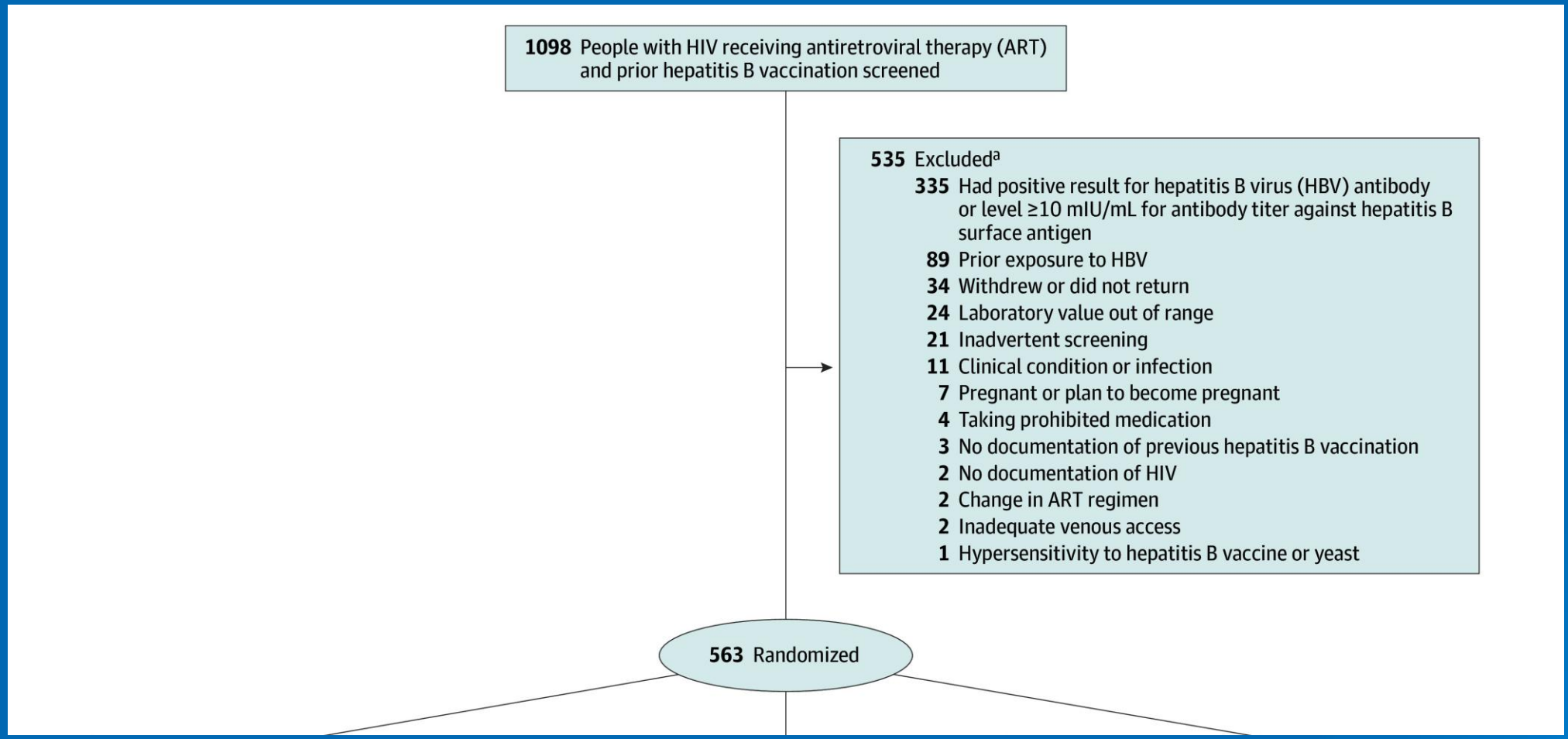
- Primary SPR Endpoint Seroprotection response (SPR) defined as anti-HBs ≥10 mIU/mL at Week 28 in 3-dose arm and Week 12 in 2-dose arm
  - Anti-HBs Ab quantification range 5-1000 mIU/m
- Primary Analysis
  - Noninferiority comparison between 2-dose HepB-CpG and 3-dose HepB-alum
  - Superiority comparison between 3-dose HepB-CpG and 3-dose HepB-alum
  - Bonferroni correction for the two primary analyses
- Analysis Method: Difference in SPR proportions with a 2-sided 97.5% CI
  - Newcombe method, stratified by sex at birth and screening diabetes status
  - Primary Analysis Set: Participants with SPR result within window
  - Sensitivity Analysis: Imputation for a missed SPR result when prior and post missed result are concordant

A5379

Accrual Dec 2020-Feb 2023

41 sites /10 countries

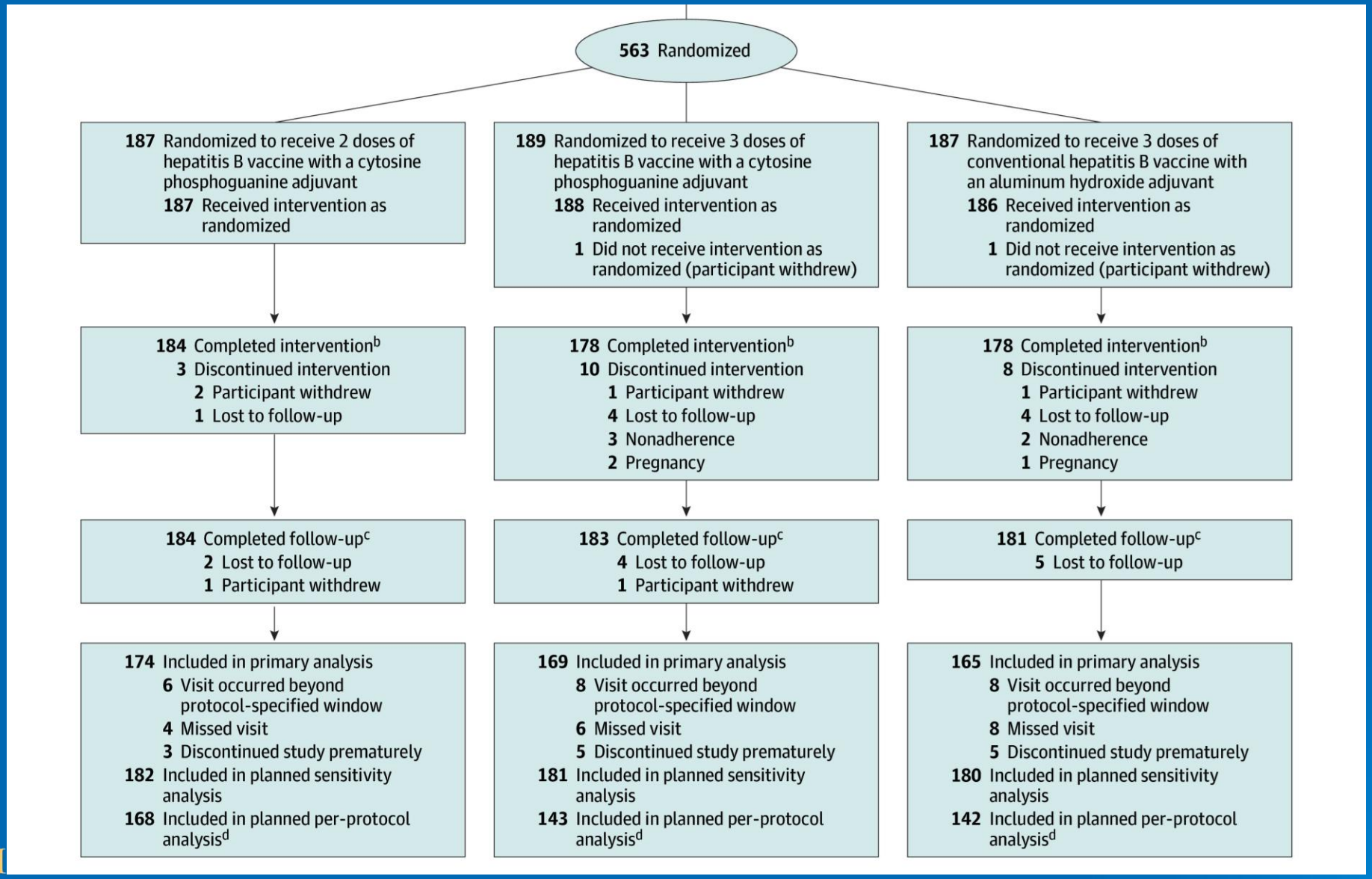
Screen failures: HBV immunity/exposure



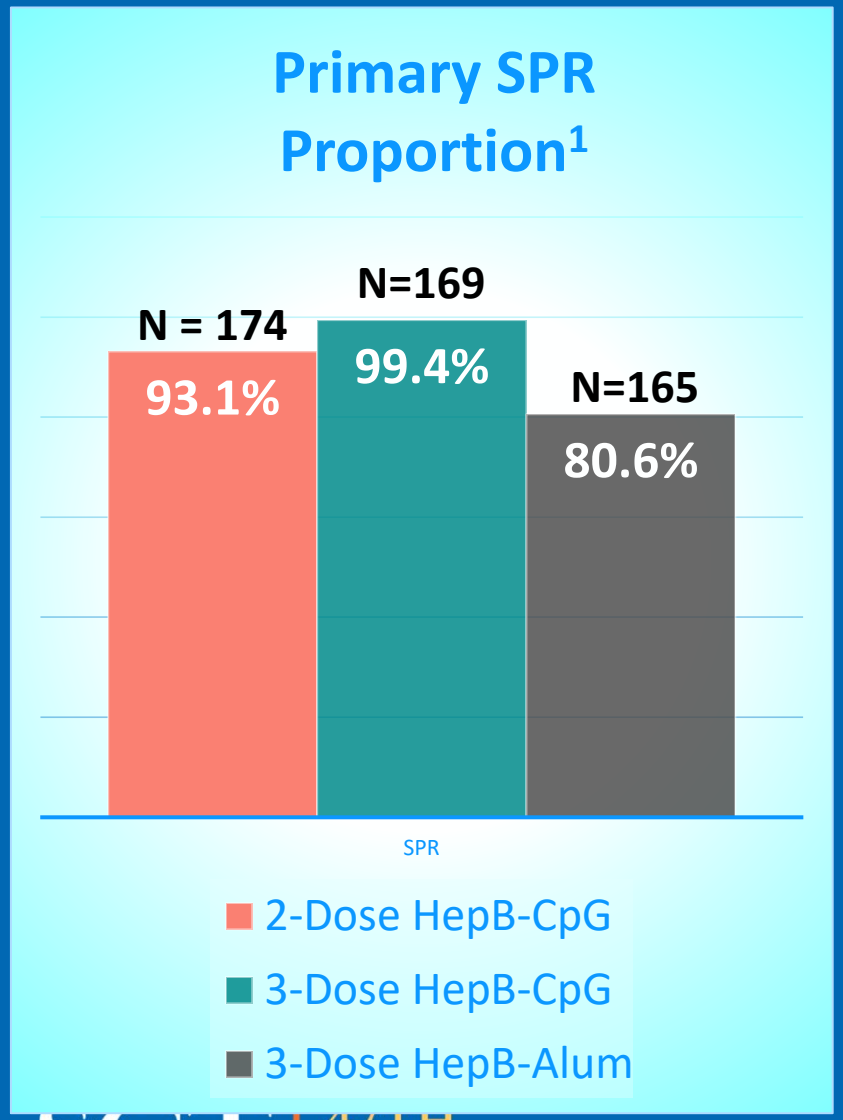
Baseline Characteristics

		HepB-CpG (2-dose) (N=187)	HepB-CpG (3-dose) (N=188)	HepB-alum (3-dose) (N=186)
Age (years)	Median (Q1, Q3)	46 (27, 57)	45 (33, 55)	47 (32, 58)
Sex at birth	Female	36%	36%	36%
Gender Identity	Transgender spectrum	2%	3%	3%
Race	Black	45%	40%	40%
	White	34%	33%	39%
	Asian	16%	19%	18%
Ethnicity	Hispanic or Latino	21%	22%	22%
Country	non-US	45%	46%	42%
IVD user	Former	3%	5%	6%
Smoking status	Current	19%	26%	23%
Nadir CD4 (cells/mm^3)	Median (Q1, Q3)	293 (97, 467)	287 (136, 508)	241 (95, 467)
CD4 Count (cells/mm^3)	Median (Q1, Q3)	609 (434, 859)	650 (511, 862)	647 (477, 854)
HIV-1 RNA (copies/mL)	<40	94%	94%	94%
Diabetes status	Diabetes	13%	12%	14%
BMI (kg/m^2)	Median (Q1, Q3)	26.8 (22.6, 30.2)	26.6 (22.9, 31.2)	26.0 (22.5, 30.2)

96% completed vaccine series



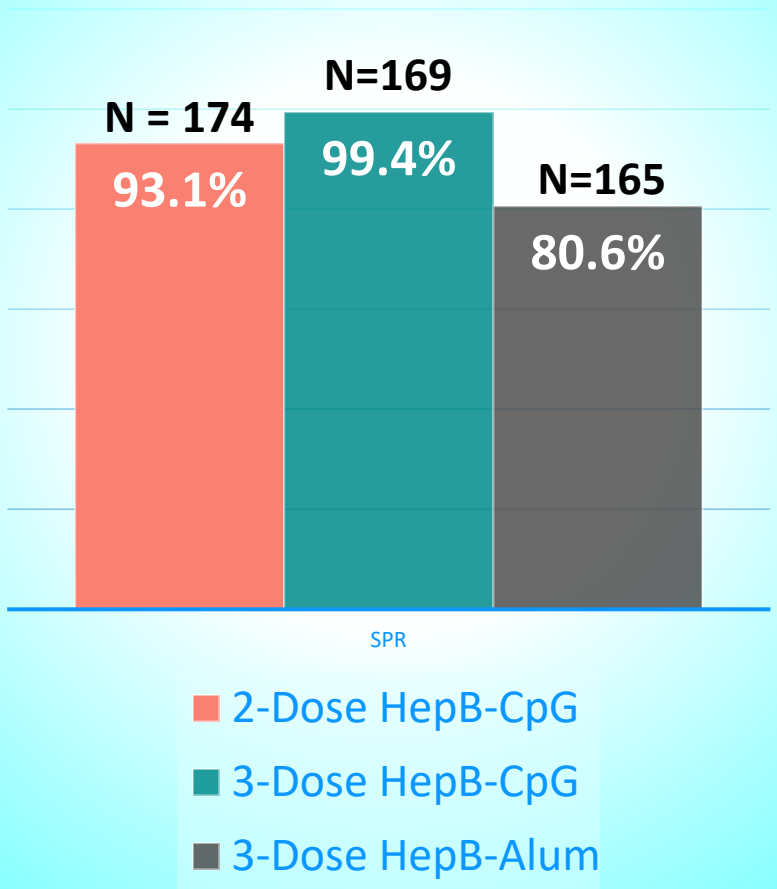
Primary Results



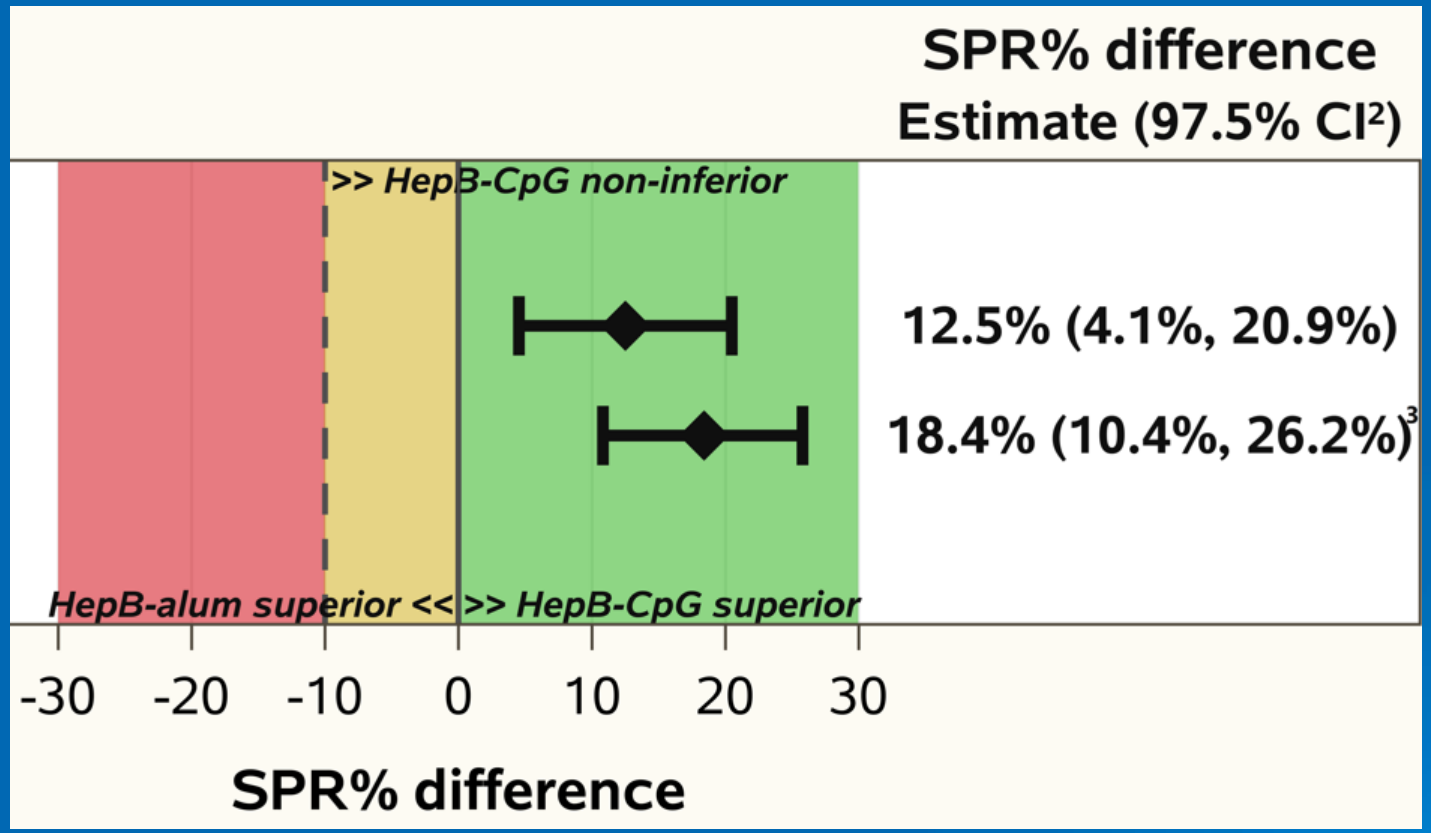
A sensitivity analysis that included participants with imputed results showed SPR:
92.3% (n=182), **99.4%** (n=181), and **77.8%** (n=180).

Primary Results

Primary SPR Proportion[1]

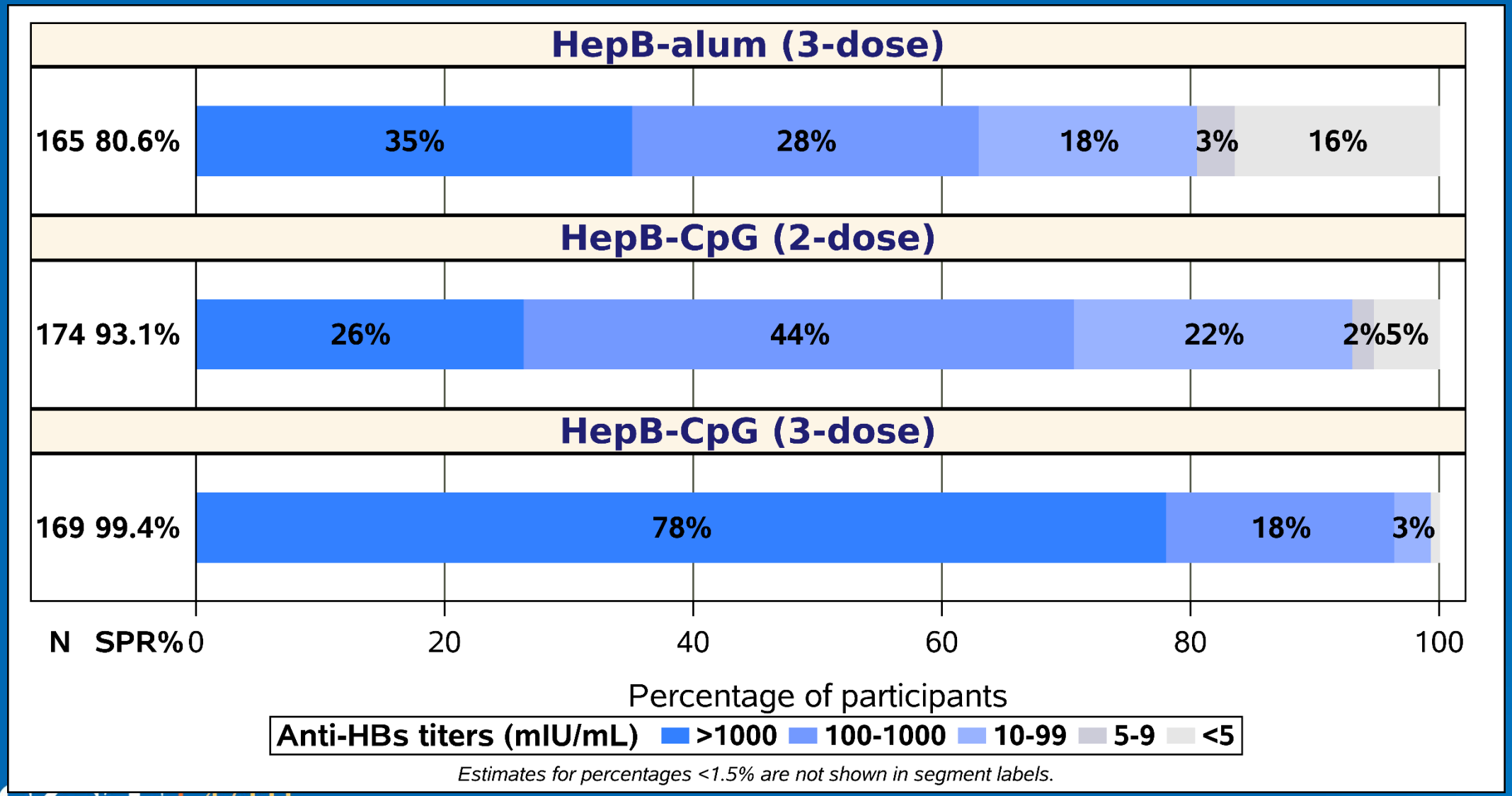


HepB-CpG SPR Comparison to HepB-Alum



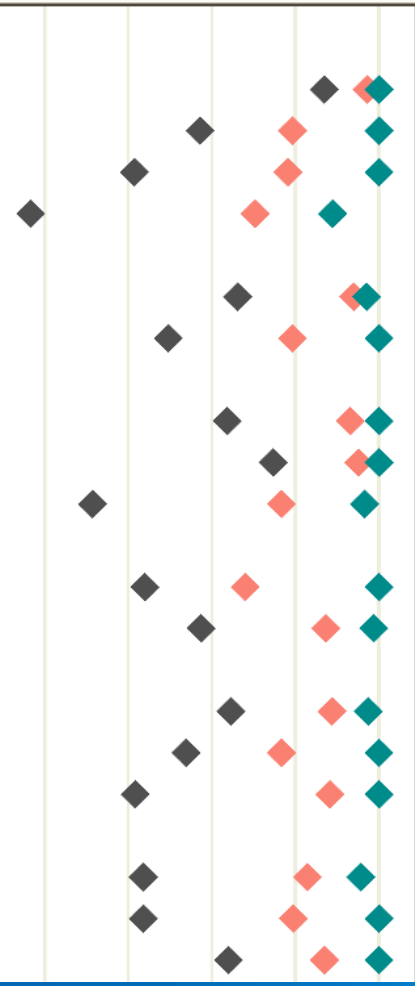
[1] N denotes the number of participant in the Analysis Set
[2] 97.5% Newcombe CI
[3] Repeated CI adjusted for group sequential monitoring

Distribution of Anti-HBs titers*



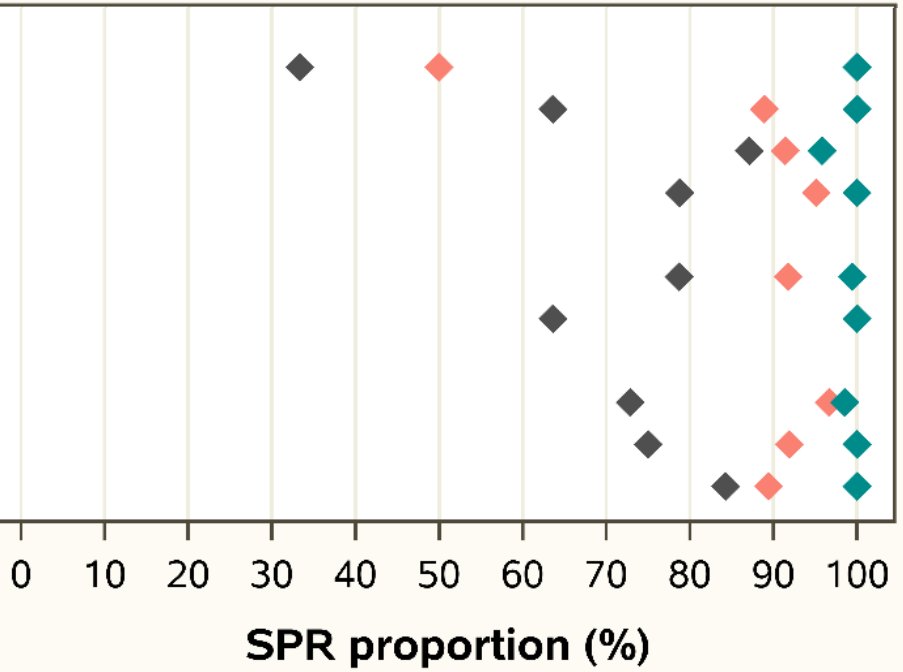
SPR Proportions within Subgroups

	HepB-alum (3-dose) N (SPR%)	HepB-CpG (2-dose) N (SPR%)	HepB-CpG (3-dose) N (SPR%)
Age (years)			
18 - 39	68 (93%)	71 (99%)	68 (100%)
40 - 49	42 (79%)	29 (90%)	42 (100%)
50 - 59	53 (71%)	55 (89%)	53 (100%)
60+	18 (58%)	27 (85%)	18 (94%)
Sex at birth			
Female	68 (83%)	66 (97%)	68 (99%)
Male	113 (75%)	116 (90%)	113 (100%)
Race			
Asian	35 (82%)	29 (97%)	35 (100%)
Black	74 (87%)	82 (98%)	74 (100%)
White	58 (66%)	60 (88%)	58 (98%)
Diabetes status			
Diabetes	22 (72%)	25 (84%)	22 (100%)
No Diabetes	159 (79%)	157 (94%)	159 (99%)
BMI (kg/m²)			
<25	78 (82%)	71 (94%)	78 (99%)
25 - <30	46 (77%)	60 (88%)	46 (100%)
30+	57 (71%)	51 (94%)	57 (100%)
Smoking status			
Current	46 (72%)	35 (91%)	46 (98%)
Former	33 (72%)	39 (90%)	33 (100%)
Never	101 (82%)	107 (93%)	101 (100%)



SPR Proportions within Subgroups

	HepB-alum (3-dose) N (SPR%)	HepB-CpG (2-dose) N (SPR%)	HepB-CpG (3-dose) N (SPR%)
CD4 count (cells/mm³)			
<200	3 (33%)	6 (50%)	3 (100%)
200 - <350	12 (64%)	18 (89%)	12 (100%)
350 - <500	24 (87%)	35 (91%)	24 (96%)
500+	142 (79%)	123 (95%)	142 (100%)
HIV-1 RNA (copies/mL)			
<40	169 (79%)	170 (92%)	169 (99%)
40+	12 (64%)	12 (100%)	12 (100%)
Years since HBV vaccination			
0 - <5	67 (73%)	60 (97%)	67 (99%)
5 - <10	40 (75%)	37 (92%)	40 (100%)
10+	74 (84%)	85 (89%)	74 (100%)



N is the total number of participants at a factor level, SPR% the proportion of N who achieved SPR after imputations for missing data.

Final regression model identified Hep-CpG, younger age higher CD4, and Black race (which varied by region) to be predictive of primary SPR.

Guidelines change: HepB-CpG preferred

HOME > NEWS > Update to the Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV

Update to the Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV

Date: December 16, 2024

Source ClinicalInfo

The *Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV* have been updated.

Hepatitis B Virus

- Recommended Heplisav-B as the preferred vaccine for all people with HIV, including those who are vaccine naive or prior vaccine nonresponders.

https://clinicalinfo.hiv.gov/en/news/update-guidelines-prevention-and-treatment-opportunistic-infections-adults-and-adolescents-5

Now that we can achieve higher anti-HBs titers – should we?

- Guidelines still target HBsAb>=10 mIU/ml
- Titers post vaccination <100 mIU/mL risk for waning of Anti-HBs <10 mIU/mL with conventional vaccine
- When titer <10 mIU/mL exposure to HBV could result in:
  - Acute HBV infection
  - Anamnestic response
- For PWH, dropping <10 mIU/mL increases risk for HBV infection
  - Those who get infected more likely to become chronic if titer <10 mIU/mL
- Could just give 3rd dose to those who need it
  - Retesting not available everywhere
  - Retesting is ecommended in US but not often rigorously implemented

Long-acting ART: Paradigm shifting

- LA-ART offer improved adherence and efficacy as treatment and PrEP
  - No current LA-ART with anti-HBV activity
- Increasing numbers of people being switched off tenofovir
- In clinical trials new infection and HBV reactivation both occur in PWH not on tenofovir, including in people with “prior” anti-HBs
  - Will become more apparent as LA-ART used in high HBV prevalence areas

- Without TDF as the backbone of HIV treatment and prevention, a more rigorous approach to HBV testing and prevention is needed

Research Letter

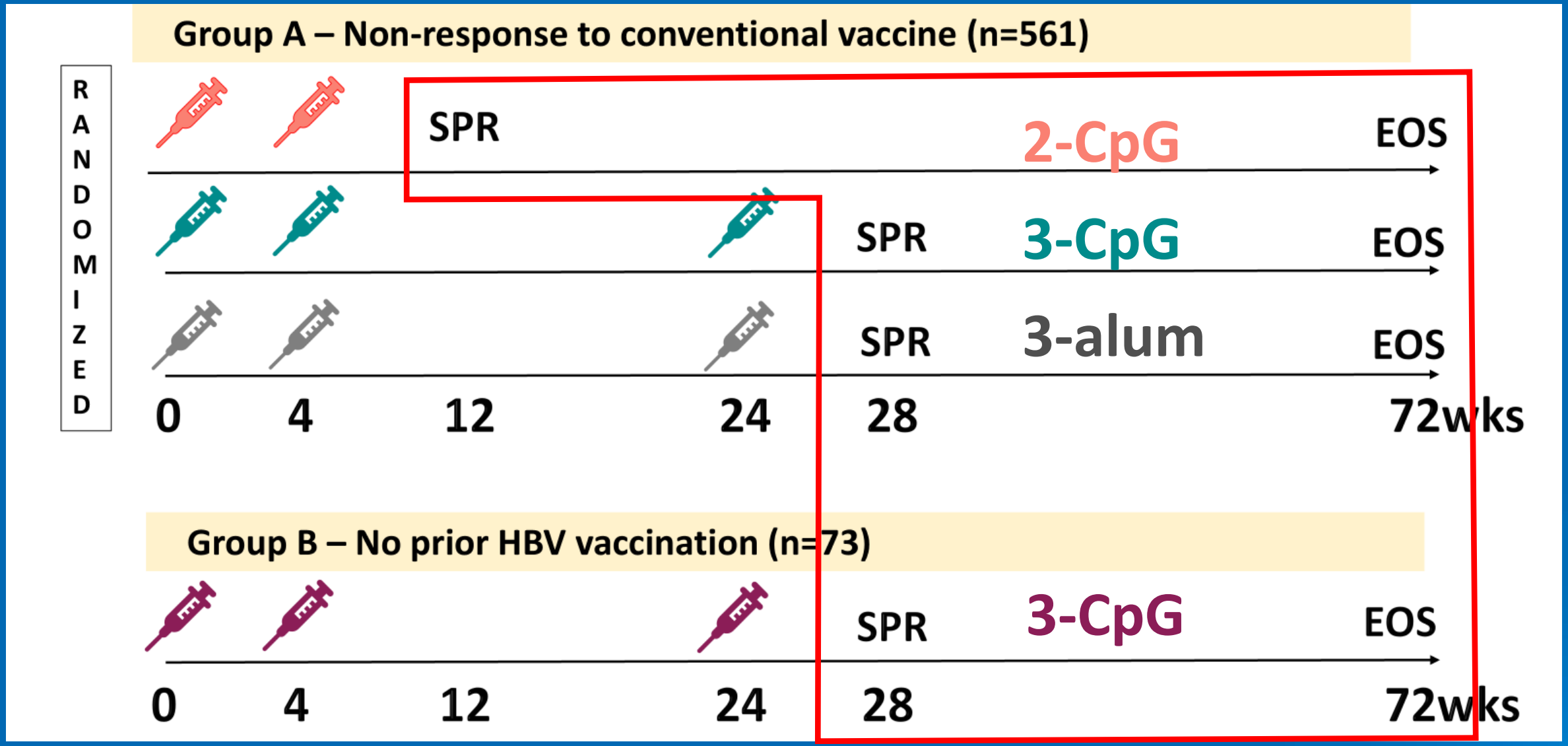
FREE

HepB-CpG Vaccine in People With HIV and Prior Nonresponse to HBV Vaccine

The BEe-HIVe Trial End-of-Study Results

Kristen M. Marks, MD[1]; Minhee Kang, PhD[2]; Triin Umbleja, MSc[2]; Andrea Cox, MD, PhD[3]; Karen J. Vigil, MD[4]; Anchalee Avihingsanon, MD, PhD[5]; Patcharaphan Sugandhavesa, MD[6]; Leolin Katsidzira, MBChB, DPhil[7]; Josphat Kosgei, MBChB[8]; Hugo Perazzo, MD, PhD[9]; Jennifer Price, MD, PhD[10]; Stephanie Caruso, MBA[11]; Kevin Knowles, PhD[11]; Beverly L. Alston-Smith, MD[12]; Parita Rathod, BS[13]; Kenneth E. Sherman, MD, PhD[14,15]; for the ACTG 5379 (BEe-HIVe) Study Team

JAMA September 9, 2025 Volume 334, Number 10

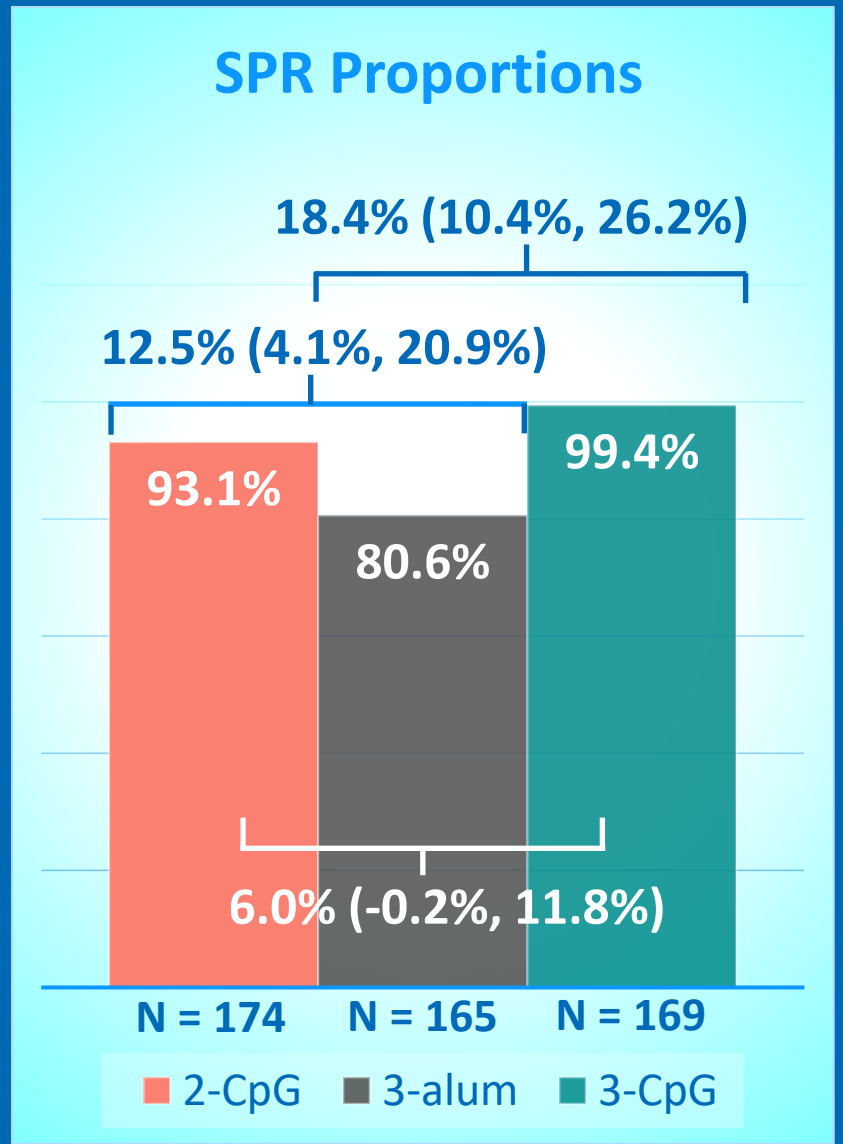

Group A – Non-response to conventional vaccine (n=561)
RANDOMIZED
SPR
2-CpG
EOS
SPR
3-CpG
EOS
SPR
3-alum
EOS
0
4
12
24
28
72wks
Group B – No prior HBV vaccination (n=73)
SPR
3-CpG
EOS
0
4
12
24
28
72wks

Durability Study Objective

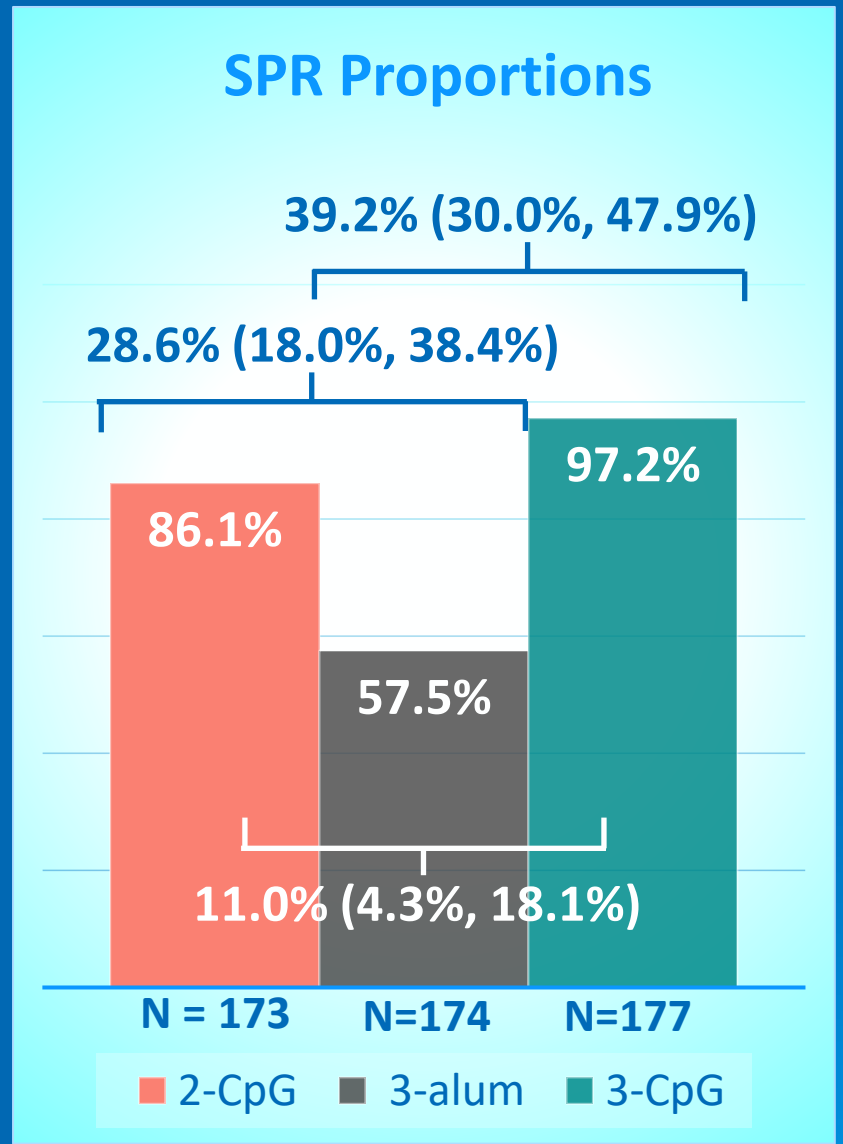
- To assess the end of study (durability) endpoint at the final visit Wk 72 (48 wks after 3-dose, 68 wks after 2-dose) regardless of visit window
  - Seroprotection response (SPR) defined as anti-HBs ≥ 10 mIU/Ml
  - Group A: Estimation of difference in the end of study SPR proportions between study arms with a 2-sided 97.5% CI
    - Newcombe method, stratified by sex at birth and screening diabetes status
  - Group B: Estimation of the end of study SPR proportion with a 2-sided 95% CI
    - Wilson method
  - Consistent with the primary vaccine response analysis approaches

Group A Durability

Primary Results

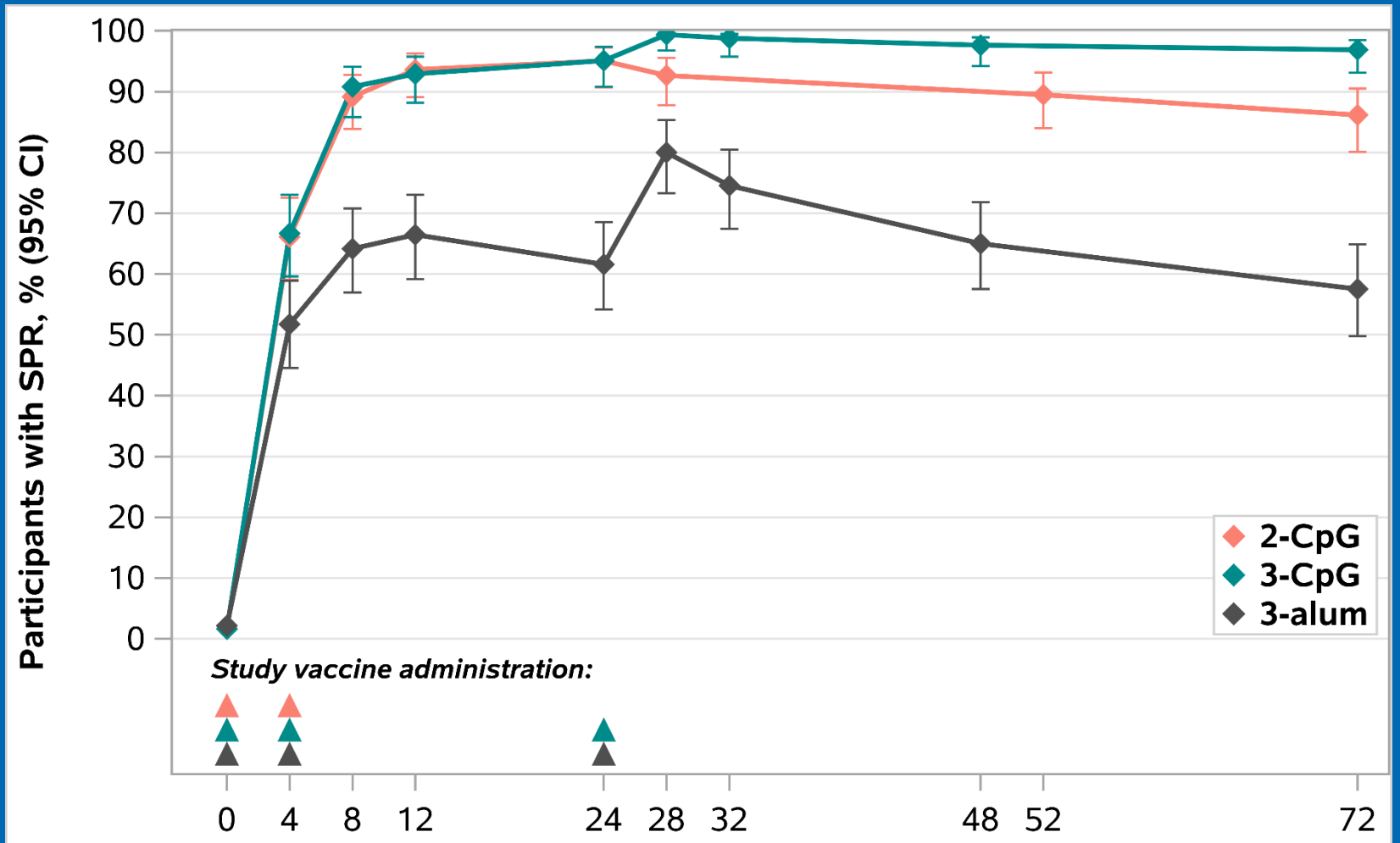


End of Study Results



SCT

Group A: Proportion with Anti-HBs ≥ 10 at Study Visits



End of study Anti-HBs ≥ 10
97.2% of 3-CpG (n=177)
86.1% of 2-CpG (n=173)

57.5% of 3-alum (n=174)

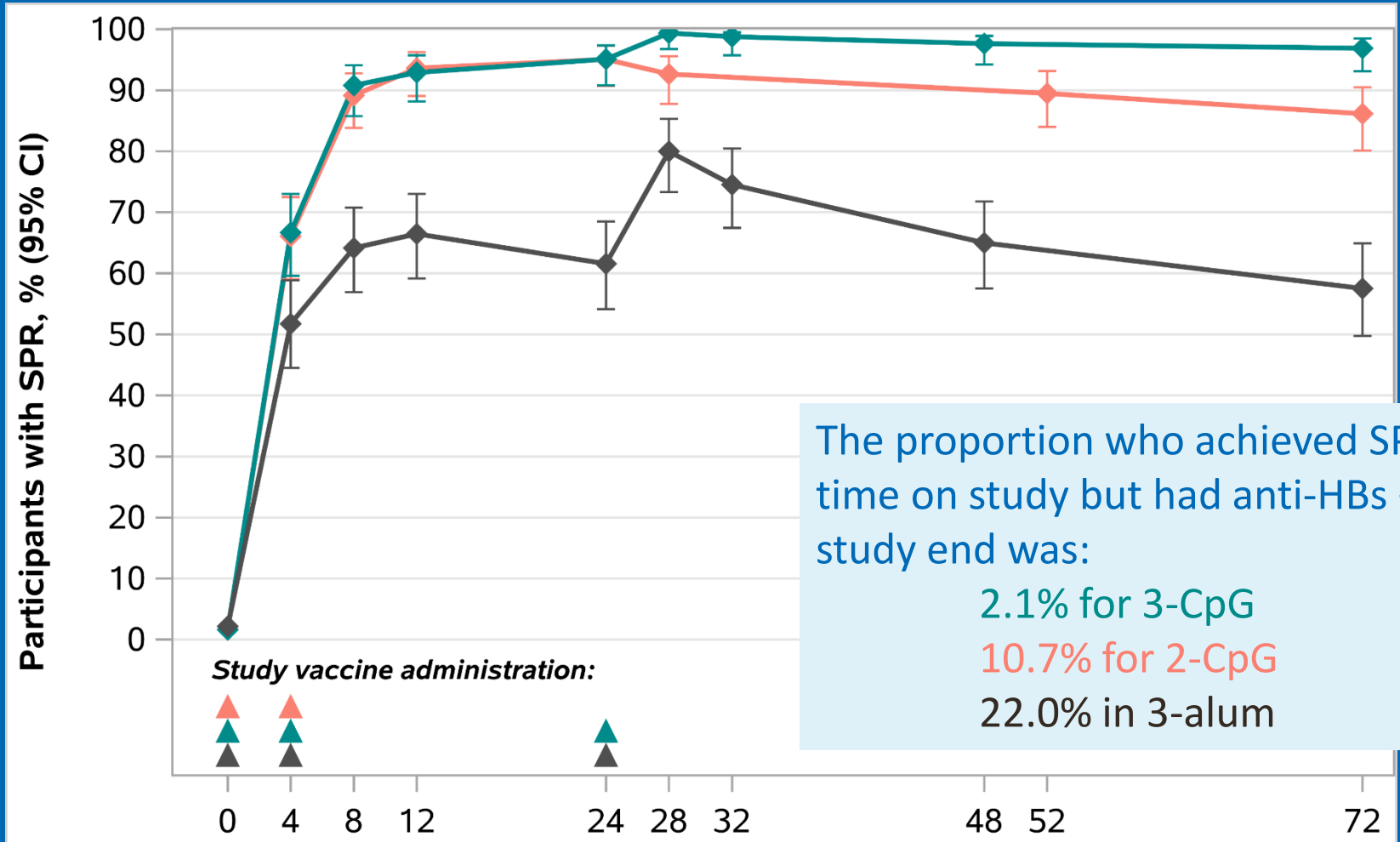
Number of participants:

2-CpG	185 177 175 172	162 163 NA	NA 162	159
3-CpG	188 177 174 169	163 162 161	168 NA	161
3-alum	186 174 173 167	164 160 161	160 NA	153

SCI ANNUAL MEETING

[1]*Study weeks according to the protocol-specified visit windows; visit schedules differed between the 2-dose and 3-dose arms.*

Group A: Proportion with Anti-HBs ≥ 10 at Study Visits



End of study Anti-HBs ≥ 10
97.2% of 3-CpG (n=177)
86.1% of 2-CpG (n=173)

57.5% of 3-alum (n=174)

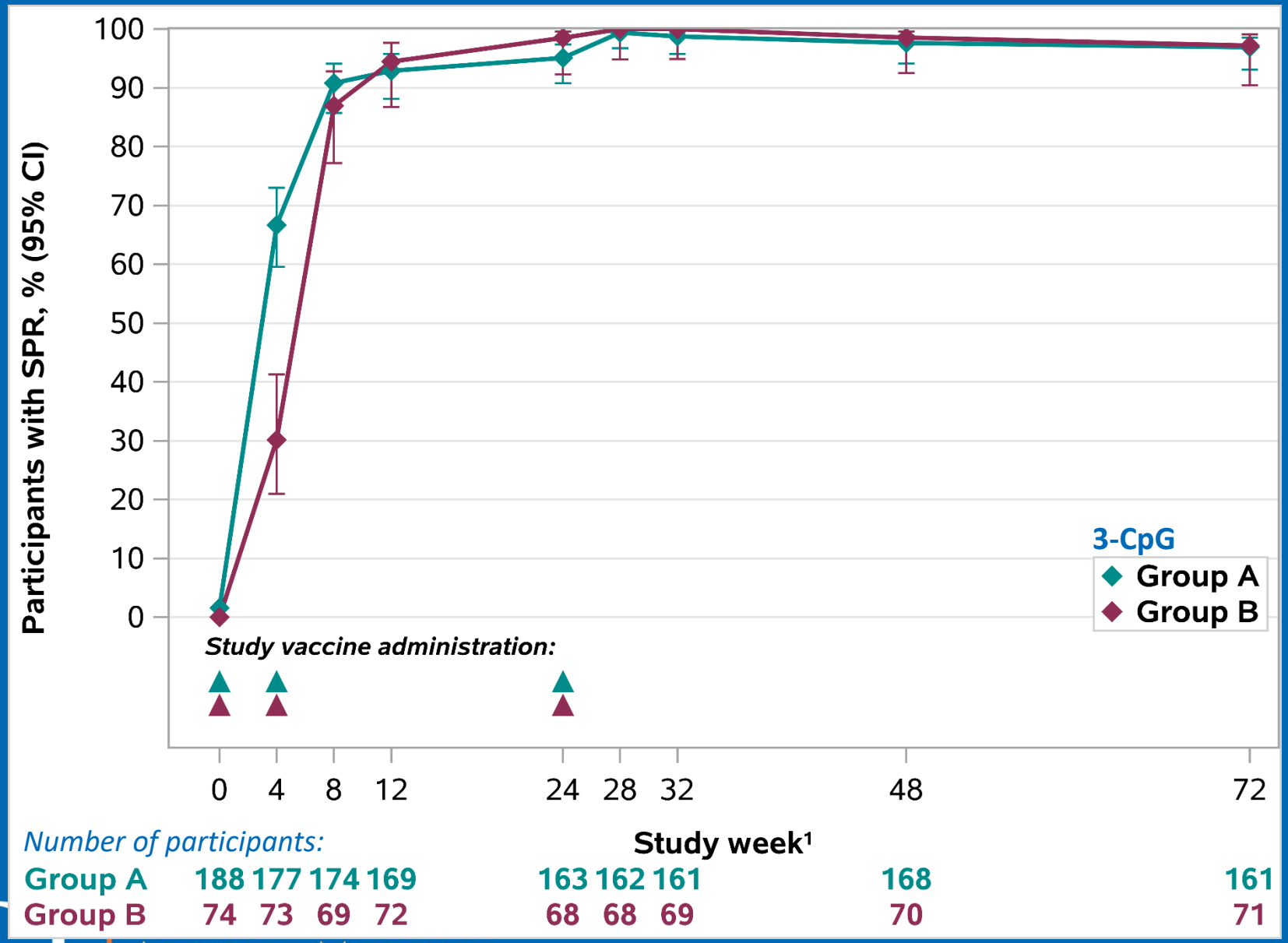
The proportion who achieved SPR at any time on study but had anti-HBs <10 by study end was:

2.1% for 3-CpG
10.7% for 2-CpG
22.0% in 3-alum

and 3-dose arms.

ACTG

Group B: Proportion with Anti-HBs ≥ 10 at Study Visits



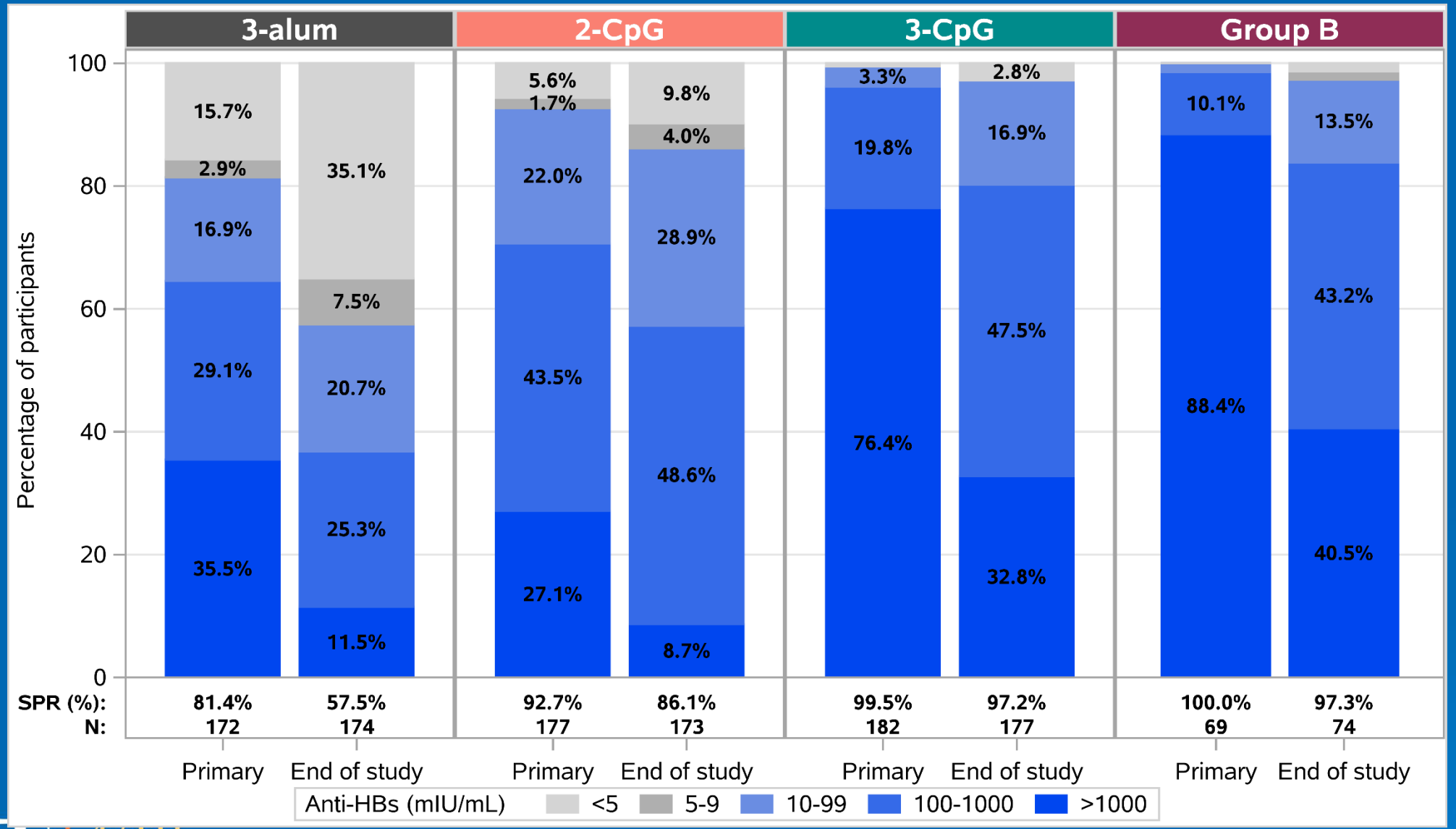
End of study anti-HBs ≥10
97.3% 3-CpG (n=74)

For comparison,
97.2% in Grp A 3-CpG (n=177)

Group B Durability

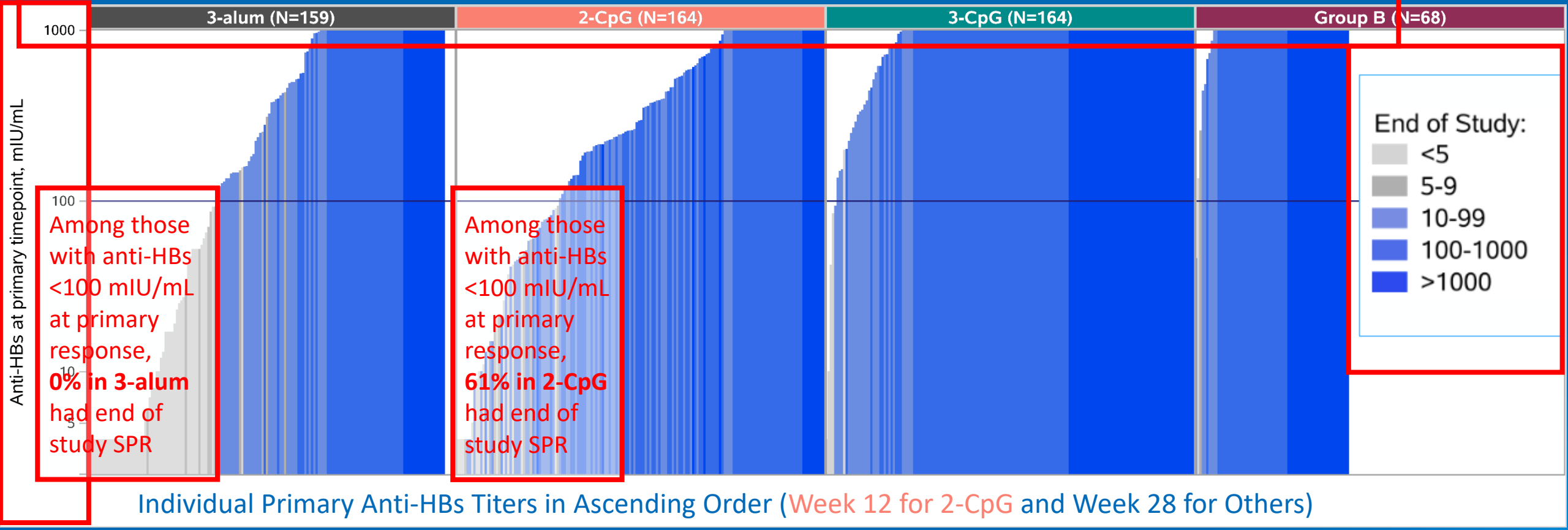
- Primary SPR proportion 100% (CI: 94.7%, 100%)
- End of study SPR proportion 97.3% (CI: 90.7%, 99.3%)

Group A & B: Distribution of Anti-HBs titers*



Primary Anti-HBs Titers and Durability

Among those with anti-HBs >1000 mIU/mL at primary response, **100% in all arms** had end of study SPR



Higher primary anti-HBs titers were more likely to lead to SPR at EOS (≥10 mIU/mL, in blue).

Table. End-of-Study (EOS) Seroprotection Response (SPR) by Primary Antihepatitis B Surface (Anti-HBs) Titer Among the Participants Who Had Primary SPR Outcome[a]

	2-Dose HepB-CpG		3-Dose HepB-CpG		3-Dose HepB-alum	
	No.	EOS SPR, No. (%)	No.	EOS SPR, No. (%)	No.	EOS SPR, No. (%)
Total	154	140 (91)	163	159 (98)	128	95 (74)
By anti-HBs titer at the time of primary response, mIU/mL						
10-99	36	22 (61)	4	1 (25)	27	0
100-1000	73	73 (100)	29	28 (97)	46	40 (87)
>1000	45	45 (100)	130	130 (100)	55	55 (100)

[a] The summary is limited to participants with primary SPR outcome who had anti-HBs results available at the end of study. Primary outcome was at week 12 for 2-dose hepatitis B vaccine with a cytosine phosphoguanine adjuvant (hepB-CpG) and at week 28 for 3-dose hepB-CpG and 3-dose hepatitis B vaccine with an aluminum hydroxide adjuvant (hepB-alum).

Marks et al, JAMA 2025

Safety

Post vaccination AEs (Grade 2 or higher within 4 wks of vaccination) were experienced by 33% of 2-dose HepB-CpG, 45% of 3-dose HepB-CpG and 43% of 3-dose HepB-alum participants

- Gr 2/3 AEs that occurred in 5% or more of participants by study arm:

Injection Site Pain	5%	11%	5%
Fatigue	5%	9%	6%
Headache	7%	7%	8%
Malaise	6%	6%	5%
Myalgia	5%	6%	4%

One or more AEs related to vaccines were experienced by 33%, 46% and 36%, respectively, mostly Gr 1 and 2. Vaccination site pain, fatigue, headache, malaise and myalgia were most frequent

- Grade 3 in 3%, 1% and 4% and no deaths related to study vaccine
  - 2 deaths unrelated to vaccines: TB (Wk43, 2-CpG) & cardiac arrest (Wk36, 3-CpG)

Limitations

- Some predictors of non-response not well-represented
  - Low CD4
  - HIV viremia
- Many participants with titers above Anti-HBs upper limit of quantification (1000 mIU/mL)

- Surrogate endpoint so absolute risk reduction is not addressed in this study
- Answers which vaccine strategy is better

BEe-HIVe Conclusions

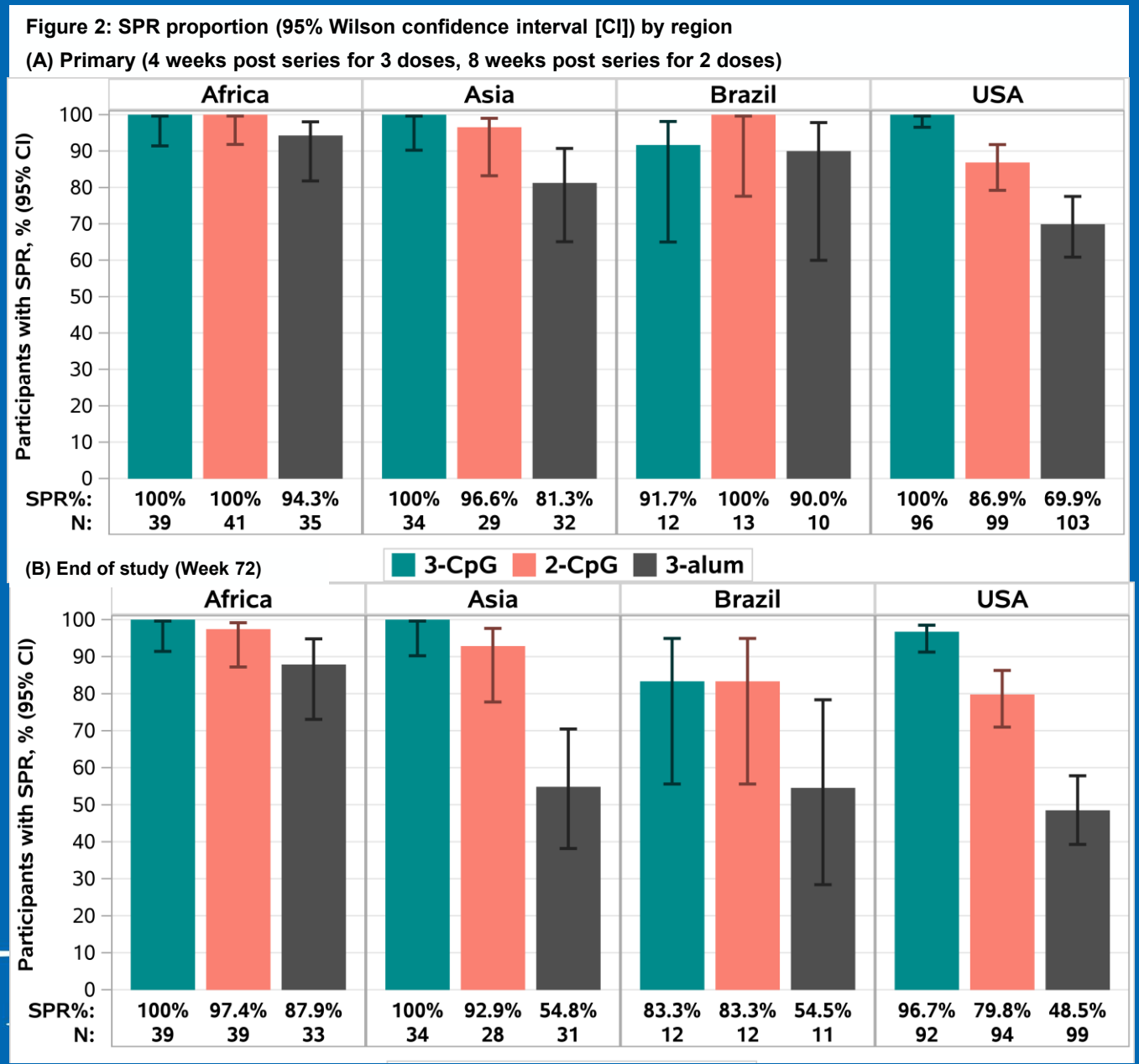
In this study of PWH, HepB-CpG achieved durable seroprotection in both vaccine-naïve and prior vaccine non-response groups.

In those with non-response to conventional HBV vaccine, both 2 and 3 doses of HepB-CpG achieved superior SPR compared to 3 doses of HepB-alum

- Three doses of HepB-CpG achieved a higher proportion with titers >1000mIU/ml compared to two doses, and to 3 doses of HepB-alum
- High titer response after the series led to durability of SPR at end of study
- Higher end of study seroprotection was achieved with HepB-CpG over HepB-alum, and 3 doses of HepB-CpG over 2 doses

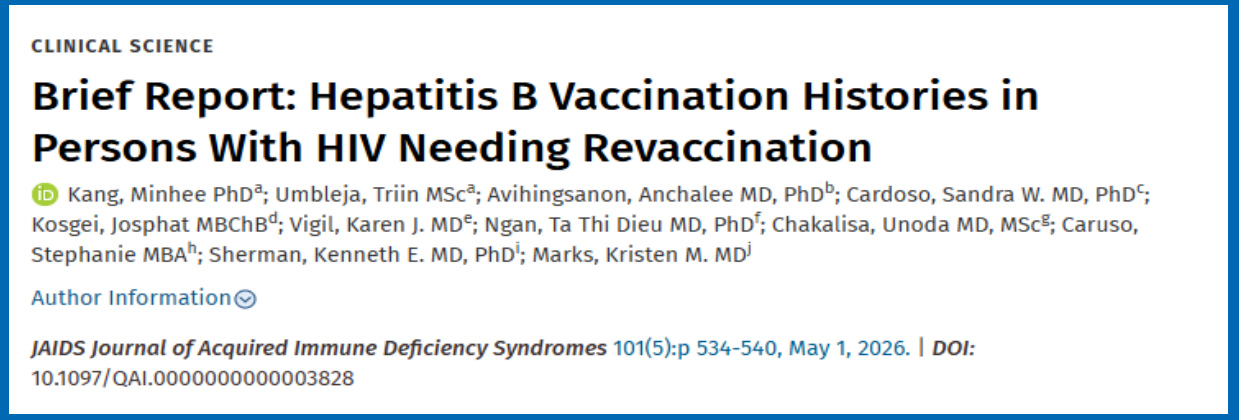
No unexpected safety issues or deaths

Regional Analysis



- HepB-CpG consistently achieved higher SPR than HepB-alum across regions.
- Participant age and timing of initial HBV vaccination likely contribute to regional SPR differences.

Marks et al, CROI abstract 2026



CLINICAL SCIENCE

Brief Report: Hepatitis B Vaccination Histories in Persons With HIV Needing Revaccination

Kang, Minhee PhD[a]; Umbleja, Triin MSc[a]; Avihingsanon, Anchalee MD, PhD[b]; Cardoso, Sandra W. MD, PhD[c]; Kosgei, Josphat MBChB[d]; Vigil, Karen J. MD[e]; Ngan, Ta Thi Dieu MD, PhD[f]; Chakalisa, Unoda MD, MSc[g]; Caruso, Stephanie MBA[h]; Sherman, Kenneth E. MD, PhD[i]; Marks, Kristen M. MD[j]

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JAIDS Journal of Acquired Immune Deficiency Syndromes 101(5):p 534-540, May 1, 2026. | **DOI:** 10.1097/QAI.0000000000003828

- Age at first HBV vaccination varied across regions (p<0.0001)
  - The first vaccination age was as infants (<1 yr) for 50% in Africa, compared to 19%, 14% and 4% in Asia, Brazil, and USA, respectively.
- Prior HBV vaccine doses ranged from 1 to 12
  - 3 doses in 54%, 1–2 doses in 22%, and ≥4 doses in 24%.
- Notably, none in Africa had received ≥4 doses, compared to 4% in Asia, 43% in Brazil, and 36% in USA (p<0.0001).
- Important if to implement HepB-CpG in HBV endemic areas

BEe-HIVe through a Sackett Lens

- ✓Clinically important question
- ✓Right population
- ✓Meaningful outcome
- ✓Rigorous but pragmatic methods
- ✓Results that change practice
- ✓Transparent communication of benefit

Future Areas of Research

- Most cost-effective approach to use of HepB-CpG vaccine
- Long term durability of HepB-CpG
- Optimal HBsAb target
- Use of HepB-CpG in people who were previously exposed to HBV or HBV vaccine with waned immunity (HBsAb <10 mIU/ml)
- HepB-CpG implementation in HBV endemic areas (with different testing and vaccination challenges)

A5379 Sites

- Houston AIDS Research Team CRS (31473)
- Hanoi Medical University CRS (32482)
- Gaborone CRS (12701)
- Chiang Mai University HIV Treatment (CMU HIV Treatment) CRS (31784)
- Harbor-UCLA CRS (603)
- Thai Red Cross AIDS Research Centre (TRC-ARC) CRS (31802)
- Wits Helen Joseph Hospital CRS (Wits HJH CRS) (11101)
- Kenya Medical Research Inst./Walter Reed Project CRS (KEMRI/WRP) (12501
- Greensboro CRS (3203)
- Instituto de Pesquisa Clinica Evandro Chagas (IPEC) CRS (12101)
- Penn Therapeutics, CRS (6201)
- University of Rochester Adult HIV Therapeutic Network CRS (31787)
- Case Clinical Research Site (2501)
- Hospital Nossa Senhora da Conceicao CRS (12201)
- Cincinnati Clinical Research Site (2401)
- UCSF HIV/AIDS CRS (801)
- Blantyre CRS (30301)
- Joint Clinical Research Centre (JCRC)/Kampala CRS (12401)
- Vanderbilt Therapeutics (VT) CRS (3652)
- Brigham and Women's Hospital Therapeutics CRS (107)
- Ohio State University CRS (2301)
- Weill Cornell Uptown CRS (7803)
- Whitman-Walker Institute, Inc. CRS (31791)
- Soweto ACTG CRS (12301)
- Massachusetts General Hospital CRS (MGH CRS) (101)
- Weill Cornell Chelsea CRS (7804)
- Johns Hopkins University CRS (201)
- Northwestern University CRS (2701)
- University of Washington Positive Research CRS (1401)
- University of Pittsburgh CRS (1001)
- UCSD Antiviral Research Center CRS (701)
- Chapel Hill CRS (3201)
- Alabama CRS (31788)
- De La Salle Health Science Institute (31981)
- UCLA CARE Center CRS (601)
- New Jersey Medical School Clinical Research Center CRS (31786)
- Durban International Clinical Research Site CRS (11201)
- Washington University Therapeutics (WT) CRS (2101)
- The Ponce de Leon Center CRS (5802)
- Columbia P&S CRS (30329)
- University of Colorado Hospital CRS (6101)

Thank you to the A5379 study participants

ACTG NIH NIAID

Weill Cornell Medicine
Cornell Clinical Trials Unit

DYNAVAX

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