HEPATITIS B ONLINE

Hepatitis B Vaccines

PreHevbrio (3-Antigen) HBV Vaccine

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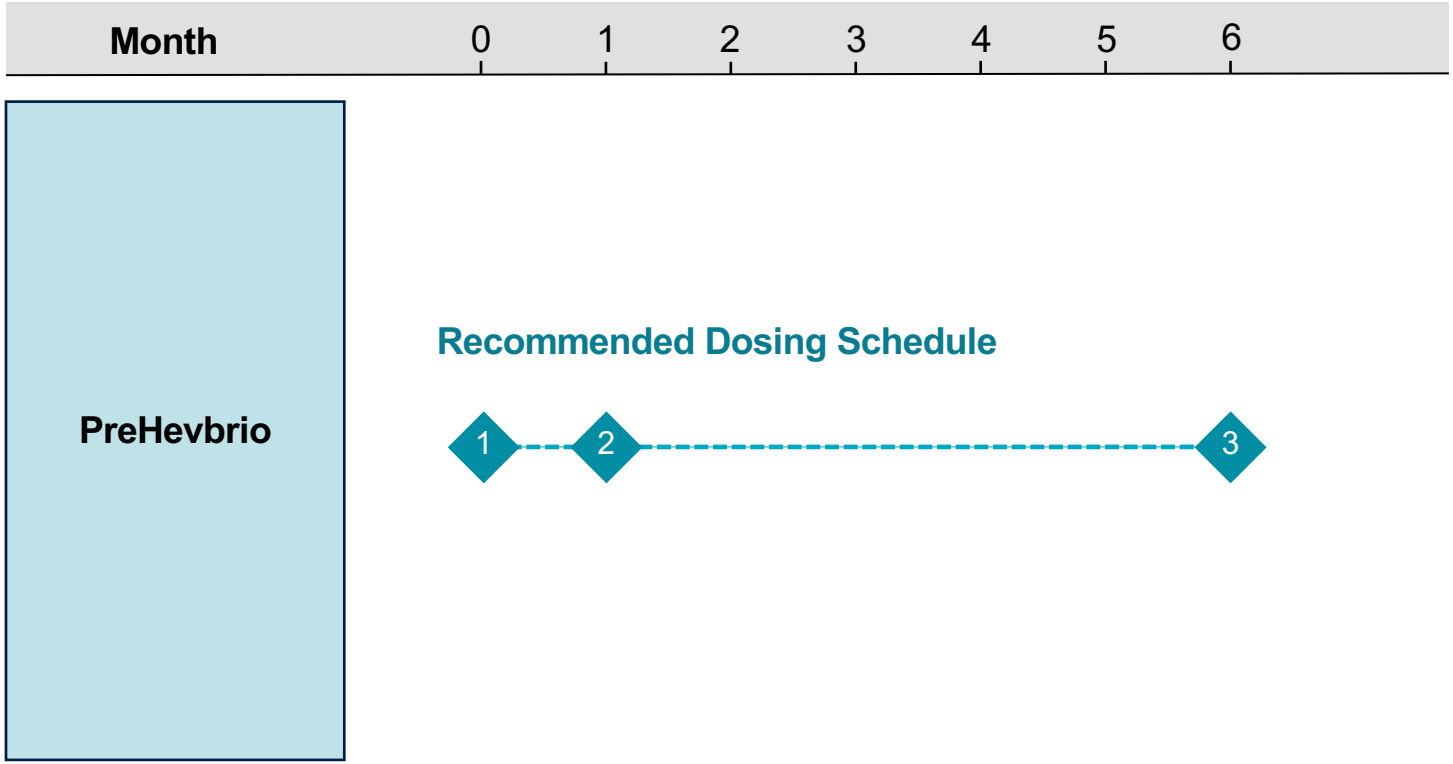
PreHevBrio (3-Antigen) HBV Vaccine

- **Indication**
  - For the prevention of HBV in adults ≥18 years of age
- **Components**
  - 10 µg HBs Antigens
  - 500 µg Aluminum hydroxide
- **Dosing**
  - 3 doses (1.0 mL with each dose), given at 0, 1, and 6-months.
- **Serious Adverse Events** (within 6 months of vaccination)
  - Reported in 2.5%

PreHevbrio: Standard Dosing Schedule



PreHevbrio Hepatitis B Vaccine: Summary of Key Phase 3 Trials

- PROTECT: PreHevbrio versus Engerix-B in Adults ≥18 years of age
- CONSTANT: 4-arm lot-to-lot study of PreHevbrio versus Engerix-B in adults 18-45 years of age

PreHevbrio versus Engerix-B in Healthy Adults

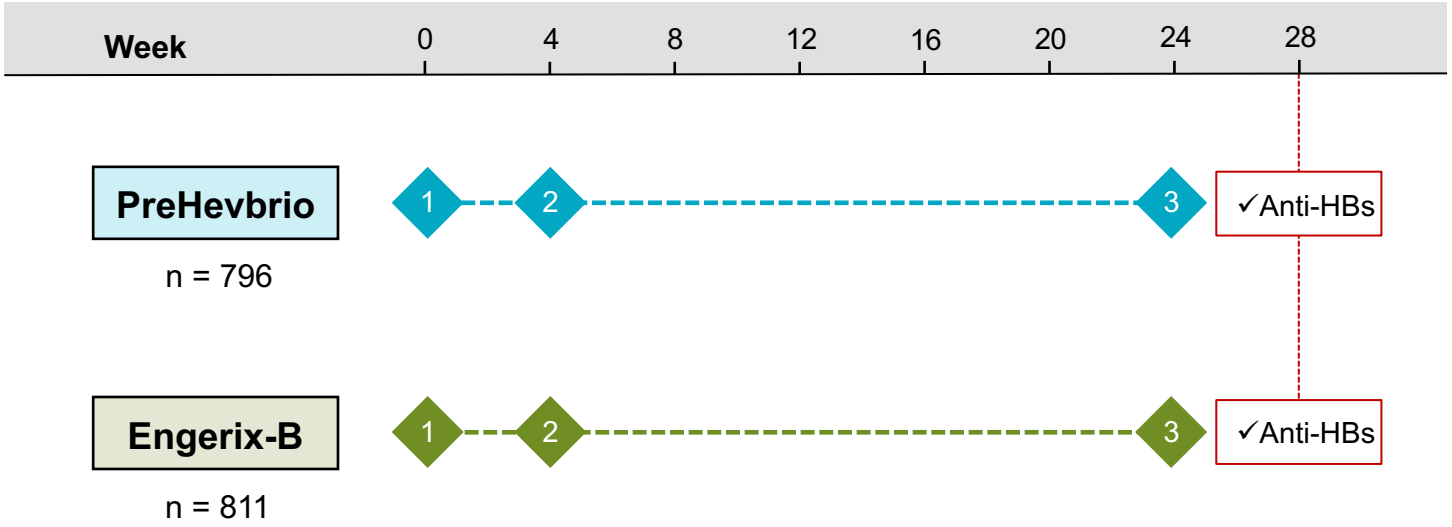
PROTECT Trial

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults
PROTECT Trial: Design

- **Design**
  - Phase 3, double-blind, randomized controlled trial, conducted at multiple sites in the USA, Finland, Canada, and Belgium that compared the safety and immunogenicity of PreHevbrio verus Engerix-B hepatitis B vaccines
- **Participants (n = 1,607)**
  - Ages: ≥18 years
  - HBV vaccine naïve
  - Exclusions: current or past HBV infection; HIV; HCV; pregnancy; receipt of any live attenuated vaccine within 4 weeks of enrollment; receipt of inactivated vaccine within 2 weeks of enrollment; and uncontrolled comorbidities
- **Primary End Point**
  - Anti-HBs seroprotection rate 4 weeks after 3rd dose of PreHevbrio or Engerix-B

Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults
PROTECT Trial: Design



Vaccine Dosing

PreHevbrio: 1.0 mL dose of 10 µg HBs antigens at weeks 0, 4, and 24

Engerix-B: 1 mL dose of 20 µg recombinant HBsAg at weeks 0, 4, and 24

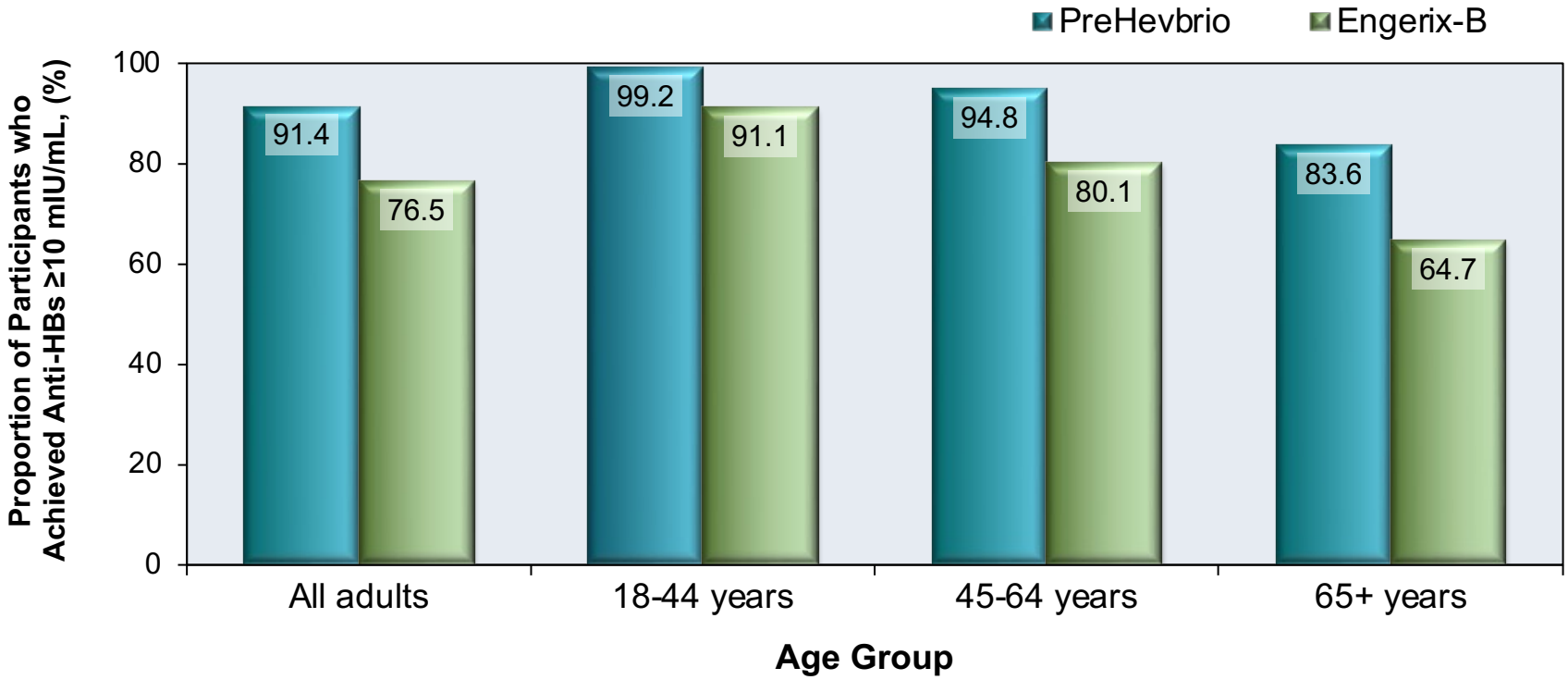
Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults
PROTECT Trial: Baseline Characteristics

Baseline Characteristic	PreHevbrio (n = 796)	Engerix-B (n = 811)
Age, mean (range), years	56.6 (18-86)	56.6 (18-90)
Male, no. (%)	315 (39.6)	303 (37.4)
Race, no. (%)		
White	715 (89.8)	730 (90.0)
Black/African American	66 (8.3)	65 (8.0)
Asian, Pacific Islander, Native Hawaiian, AI/AN	15 (1.8)	16 (2.0)
Current smoker, no. (%)	104 (13.1)	113 (13.9)
Type 2 diabetes, no. (%)	60 (7.5)	65 (8.0)
Country or region		
USA	338 (42.5)	342 (42.2)
Canada	126 (15.8)	133 (16.4)
Europe	332 (41.7)	336 (41.4)

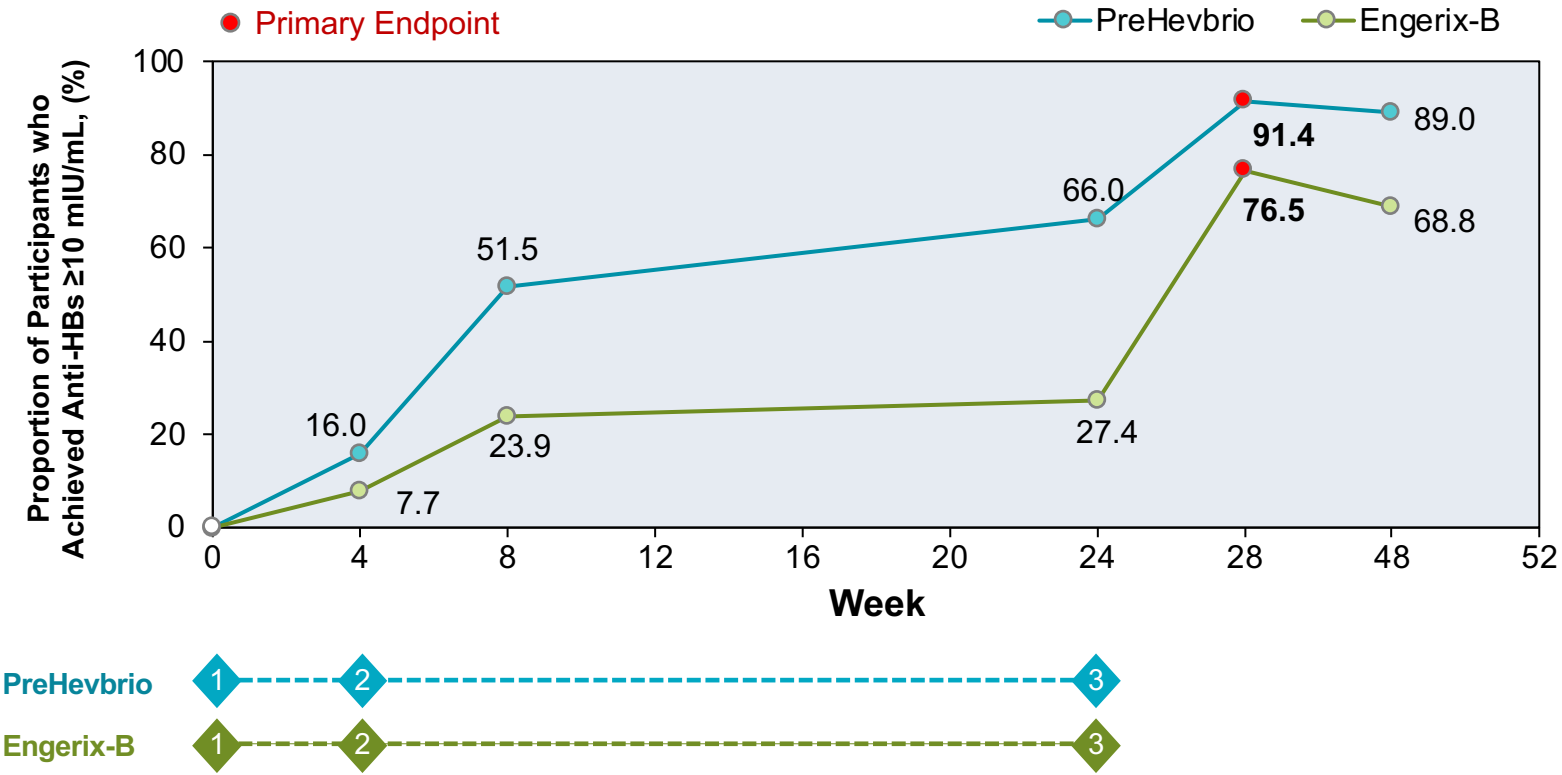
Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults
PROTECT Trial: Week 28 Results (anti-HBs ≥10 mIU/mL), by Age Group



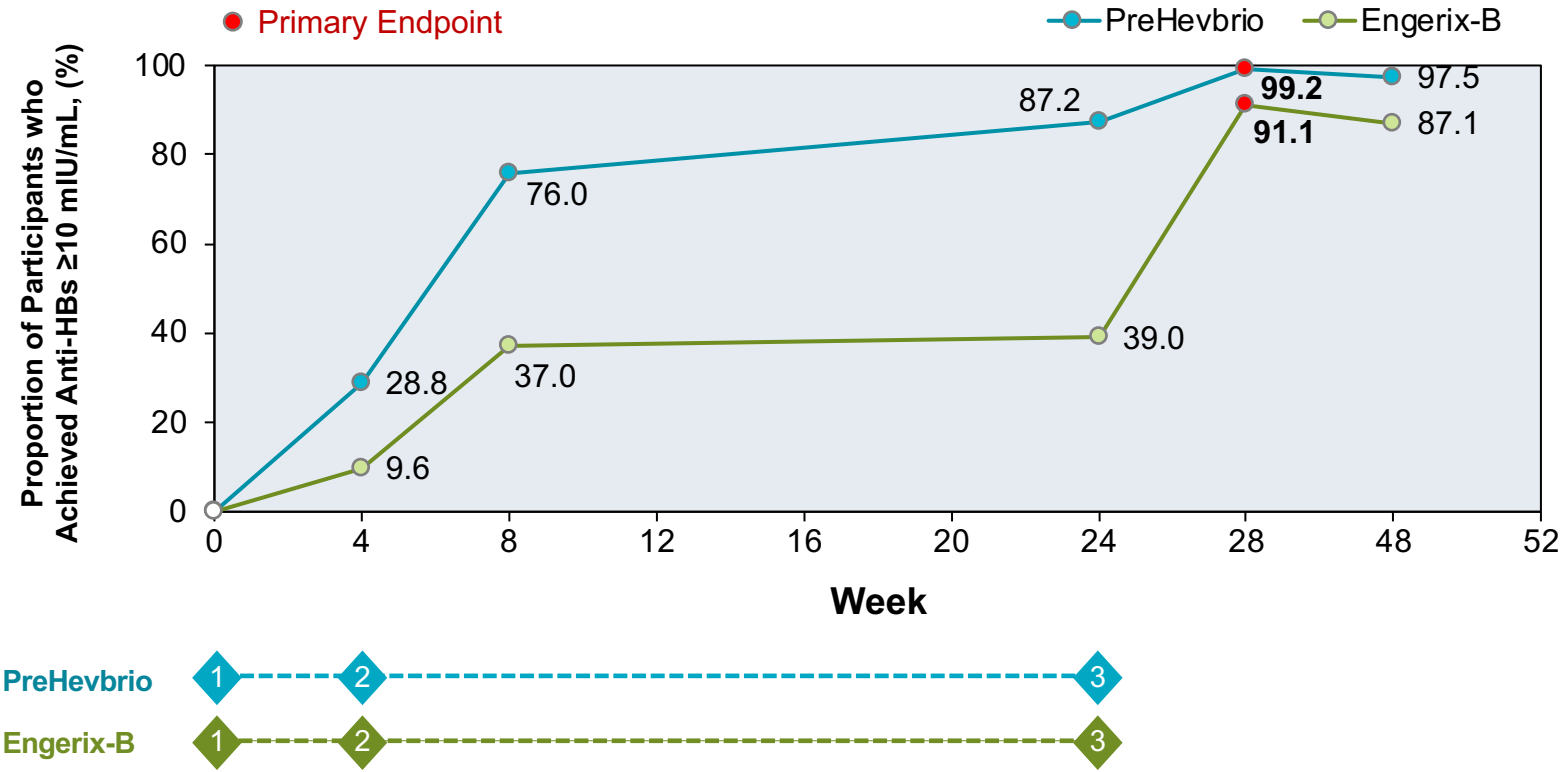
Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults Aged ≥18 Years
PROTECT Trial: Results



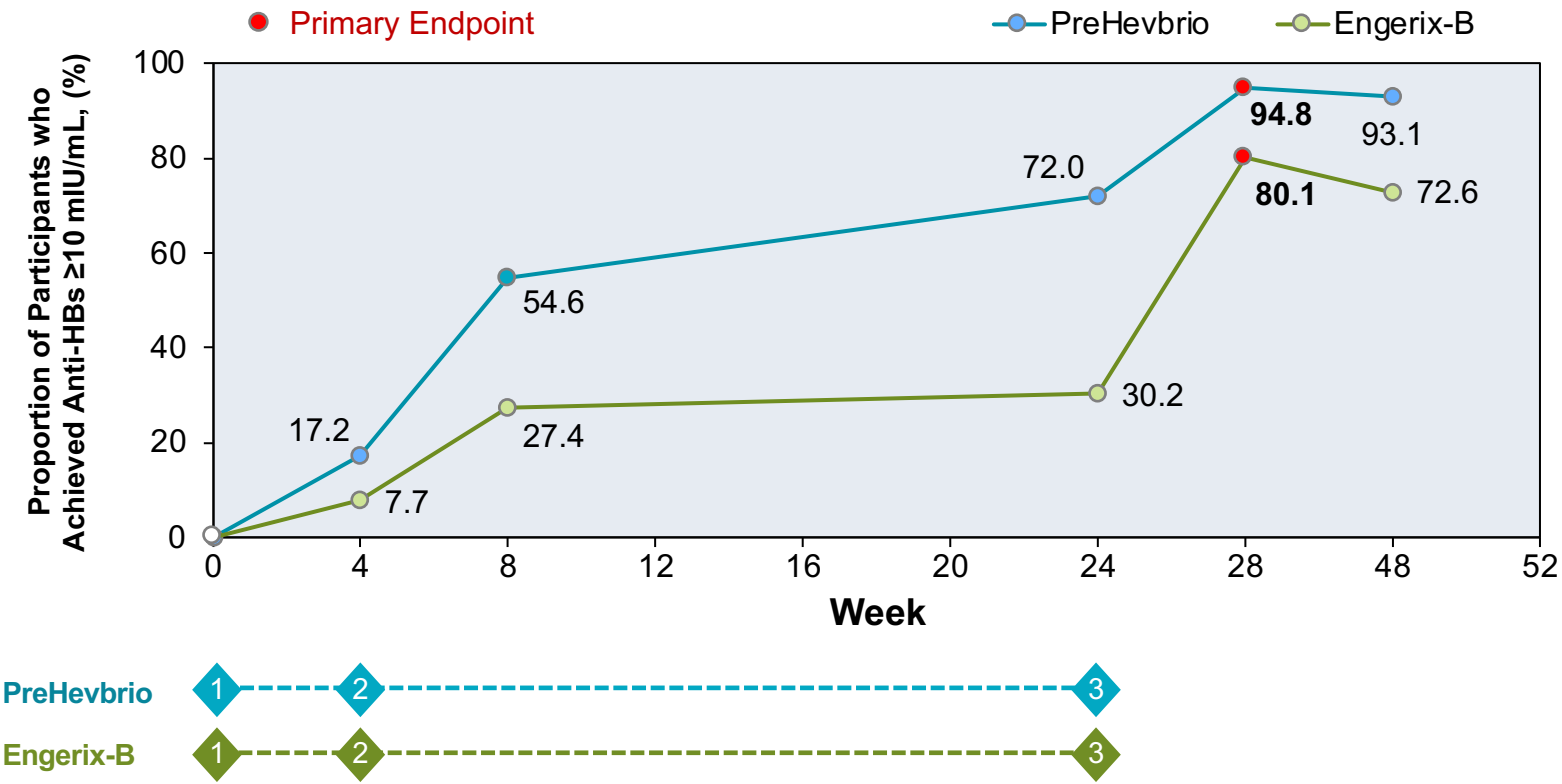
Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults Aged **18-44 Years** PROTECT Trial: Results



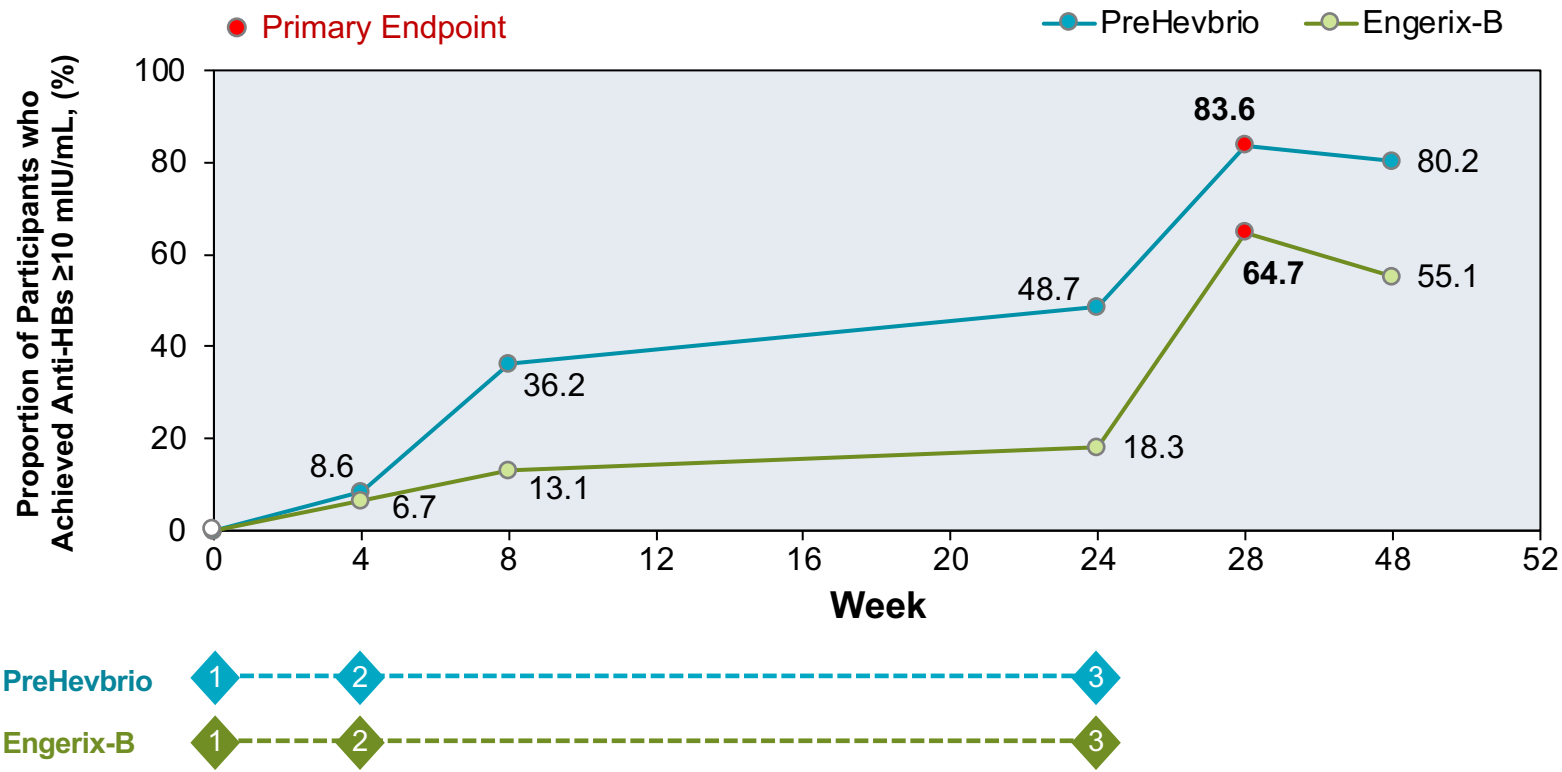
Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults Aged **45-64 Years** PROTECT Trial: Results



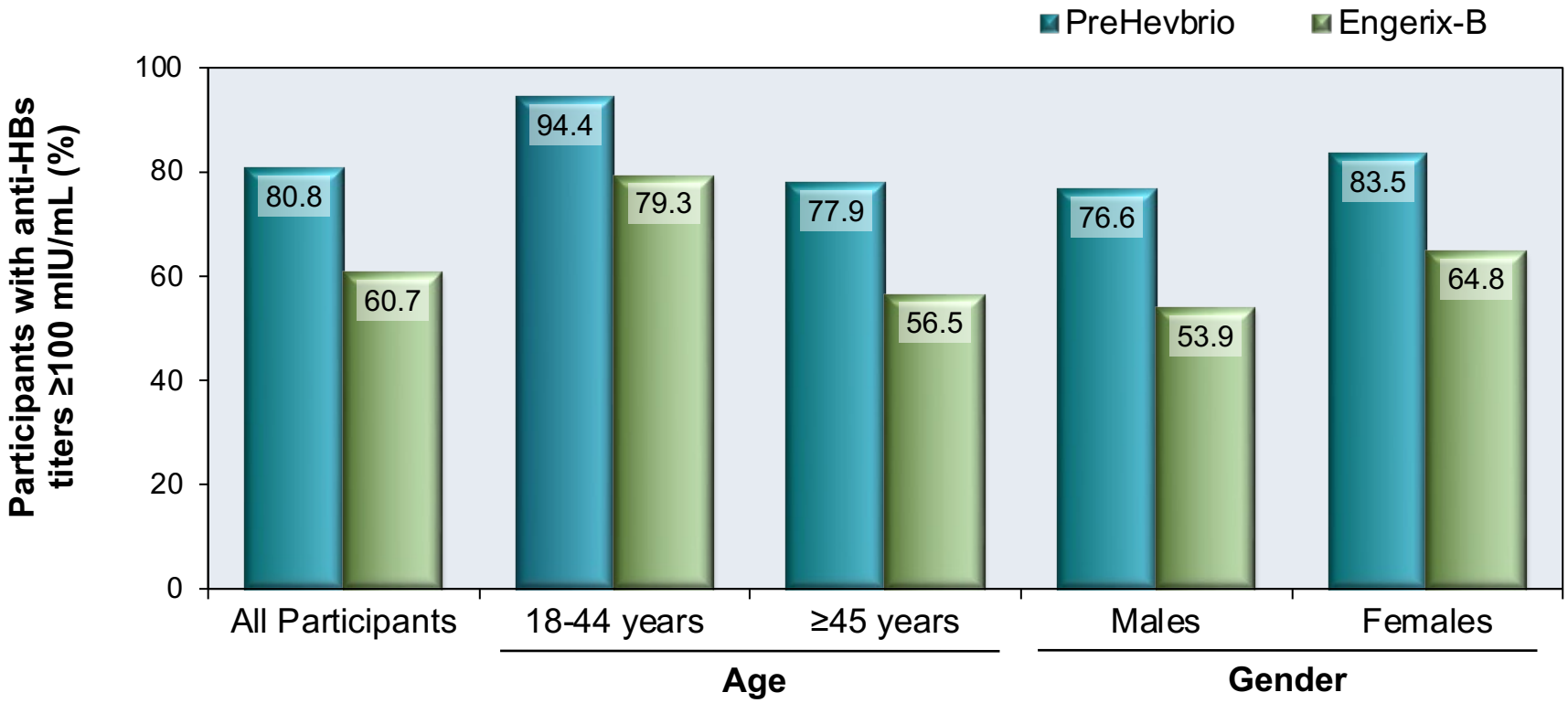
Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults Aged ≥**65 Years** PROTECT Trial: Results



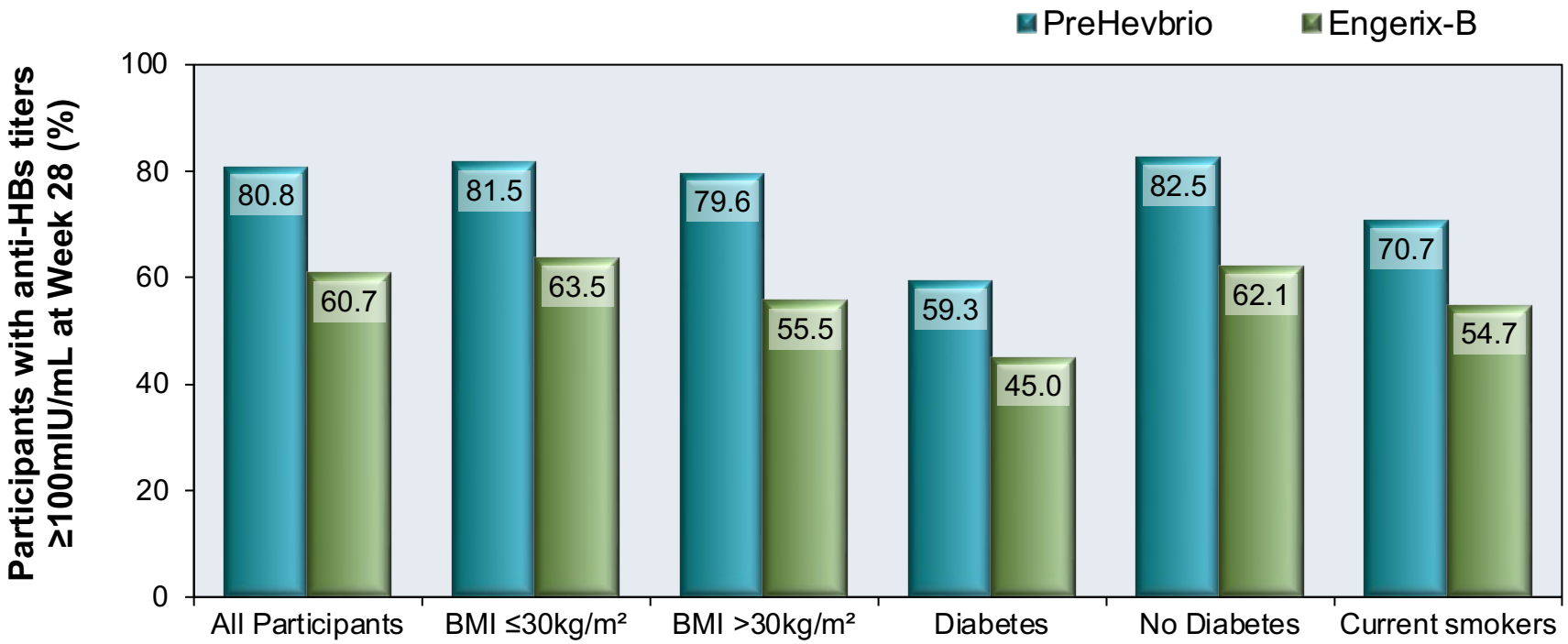
Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults
PROTECT Trial: Results (anti-HBs ≥100 mIU/mL), by Age and Gender



Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults
PROTECT Trial: Results (anti-HBs ≥100 mIU/mL), by BMI, Diabetes, and Smoking



Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio Vaccine vs Engerix-B Vaccine in Adults ≥**18 years** PROTECT Trial: Results

Conclusions: “PreHevbrio was non-inferior to Engerix-B and induced higher seroprotection in adults aged 18 years of age and older after three doses of vaccine.”

Source: Vesikari T, et al. Lancet Infect Dis. 2021;21:1271-81.

PreHevbrio versus Engerix-B in Healthy Adults, Age 18-45

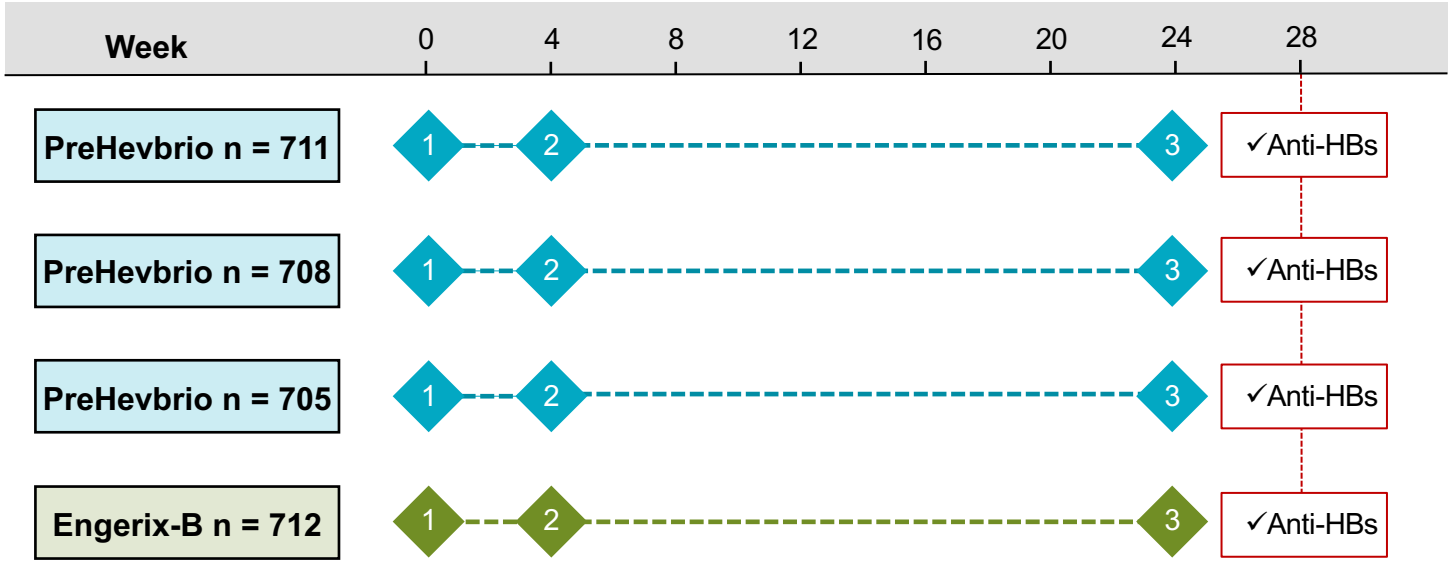
CONSTANT Trial

PreHevbrio Vaccine vs Engerix-B Vaccine in Healthy Adults Age 18-45 years
CONSTANT Trial: Study Design

- **Design**
  - Phase 3, double-blind, randomized (1:1:1:1) controlled trial conducted in multiple centers in USA, Canada, Europe that assessed lot-to-lot consistency and immunogenicity of three consecutive PreHevbrio vaccine lots compared with one Engerix B vaccine lot in healthy adults
- **Subjects**
  - Participants: n = 2,838
  - Ages: 18-45 years
  - HBV vaccine naïve
  - Exclusions: current or past HBV, HIV, HCV, immunosuppressed, pregnant or breastfeeding, live attenuated vaccine within prior 4 weeks; inactivated vaccine within prior 2 weeks; blood products / immunoglobulins within 90 days; eGFR <60 mL/min; BMP ≥35; HTN, diabetes mellitus, cancer
- **Primary End-Point**
  - Manufacturing equivalence of 3 independent consecutive lots, in terms of immunogenicity
  - Immunogenicity measured by the geometric mean concentration (GMC) of anti-HBs concentrations 4 weeks after the third injection (day 196)

Source: Vesikari T, et. al. JAMA Network Open. 2021;4:e2128652.

PreHevbrio Vaccine vs Engerix-B Vaccine in Healthy Adults Age 18-45 years
CONSTANT Trial: Design



Vaccine Dosing

PreHevbrio: 1.0 mL dose of 10 µg HBs antigens with aluminum adjuvant at weeks 0, 4, and 24

Engerix-B: 1 mL dose of 20 µg recombinant HBsAg with aluminum adjuvant at weeks 0, 4, and 24

Note: Each PreHevbrio arm represents an independent and different lot of vaccine

Source: Vesikari T, et. al. JAMA Network Open. 2021;4:e2128652.

PreHevbrio Vaccine vs Engerix-B Vaccine in Healthy Adults Age 18-45 years
CONSTANT Trial: Baseline Characteristics

Baseline Characteristic	PreHevbrio (all) (n = 2,124)	Engerix-B (n = 712)
Age, mean (SD), years	33.5 (7.97)	33.4 (8.10)
Male, no. (%)	907 (42.7)	291 (40.9)
Race, no. (%)		
White	1941 (91.4)	654 (91.9)
Asian	37 (1.7)	9 (1.3)
Black or African American	123 (5.8)	38 (5.3)
American Indian or Alaska Native	6 (0.3)	2 (0.3)
Current smoker, no. (%)	406 (19.1)	136 (19.1)
BMI, mean (SD)	25.9 (4.12)	25.7 (4.10)

Source: Vesikari T, et. al. JAMA Network Open. 2021;4:e2128652.

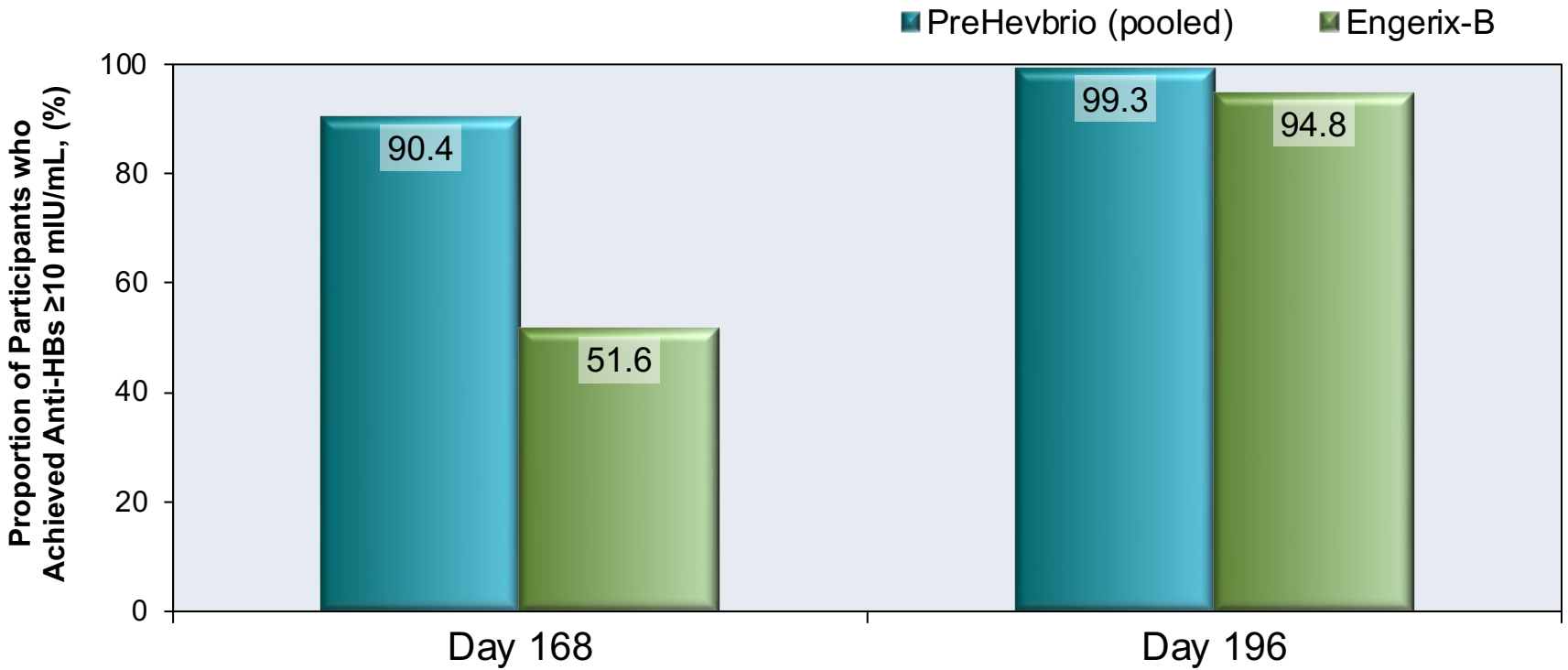
PreHevbrio Vaccine vs Engerix-B Vaccine in Healthy Adults Age 18-45 years CONSTANT Trial: Results

GMC of HBV surface antibodies at Day 196	PreHevbrio **Lot A** (n = 620)	PreHevbrio **Lot B** (n = 622)	PreHevbrio **Lot C** (n = 627)
GMC, mean (SD)	5883.9 (5.4)	4824.1 (6.3)	5506.0 (6.0)
Mean adjusted GMC (SE) [95% CI]	5882.3 (1.1) [5112.4-6768.0]	4821.7 (1.1) [4190.1-5548.4]	5570.0 (1.1) [4844.6-6403.7]
Adjusted GMC ratio (95% CI) Lot A vs. Lot B= 0.82 (0.67-1.00) Lot A vs. Lot C = 0.95 (0.78-1.15) Lot B vs. Lot C = 1.16 (0.95-1.41)			

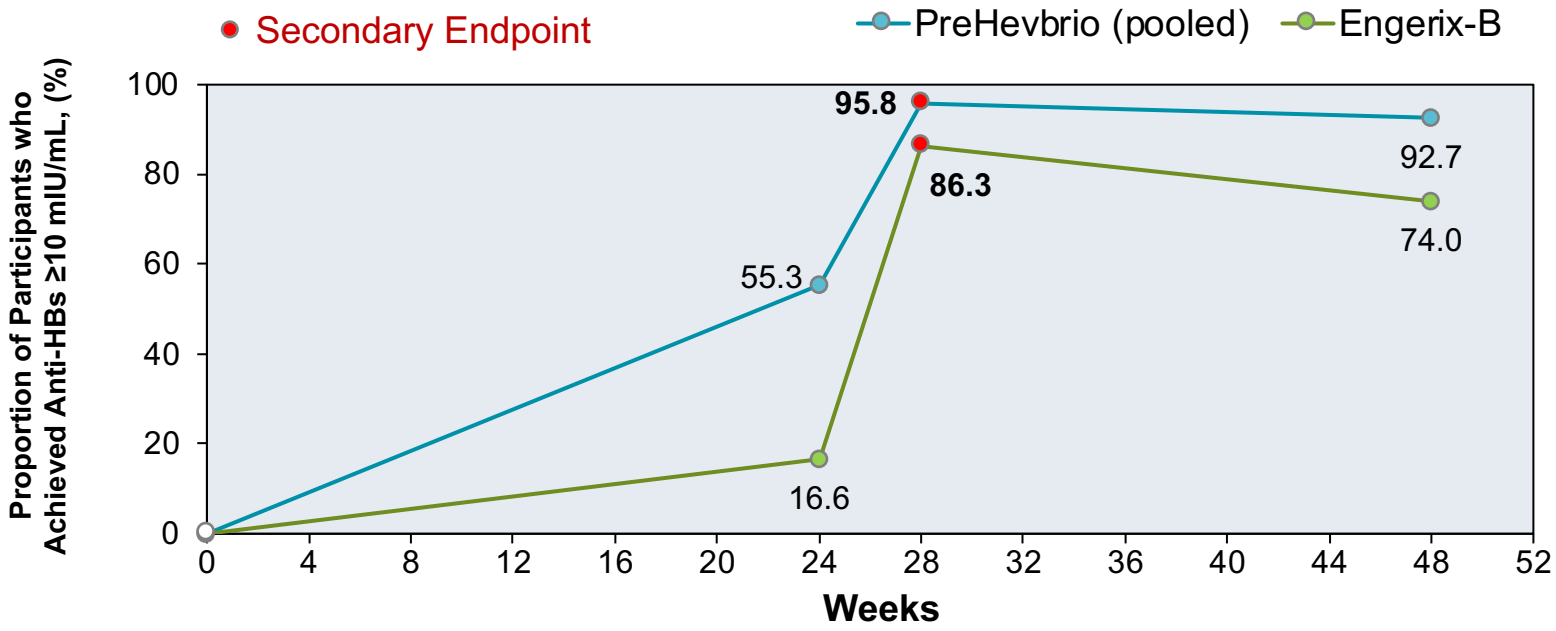
Abbreviations: Geometric mean concentration; SD = standard deviation; SE = standard error; CI= confidence intervals

Source: Vesikari T, et. al. JAMA Network Open. 2021;4:e2128652.

PreHevbrio Vaccine vs Engerix-B Vaccine in Healthy Adults Age 18-45 years
CONSTANT Trial: Results



PreHevbrio Vaccine vs Engerix-B Vaccine in Healthy Adults Age 18-45 years
CONSTANT Trial: Results



Source: Vesikari T, et. al. JAMA Network Open. 2021;4:e2128652.

PreHevbrio Vaccine vs Engerix-B Vaccine in Healthy Adults Age 18-45 years
CONSTANT Trial: Adverse Reactions

Adverse Event (AE), no. (%)	PreHevbrio (n = 2,124)	Engerix-B (n = 712)
Any local reaction n (%)	1805 (85.0)	469 (65.9)
Systemic reaction, any, n (%)	1445 (68.0)	428 (60.1)
Serious AE (Grade 3 or 4), n (%) Participants with ≥1 unsolicited serious AE Vaccine-Related serious AE	42 (2.0) 0 (0)	3 (0.4) 0 (0)

Most common reactions: pain and tenderness (local); headache, fatigue, myalgia (systemic)

Source: Vesikari T, et. al. JAMA Network Open. 2021;4:e2128652.

PreHevbrio Vaccine vs Engerix-B Vaccine in Healthy Adults Age 18-45 years
CONSTANT Trial: Conclusions

Conclusions: “Among persons aged 18 to 45 years, consistently higher antibody concentrations and seroprotection rates were found among those vaccinated with PreHevbrio (all 3 lots) when compared to Engerix-B, after 2 and 3 doses.”

Source: Vesikari T, et. al. JAMA Network Open. 2021;4:e2128652.

Acknowledgments

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HEPATITIS C ONLINE

HEPATITIS B ONLINE

IDEA INFECTIOUS DISEASES EDUCATION & ASSESSMENT