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

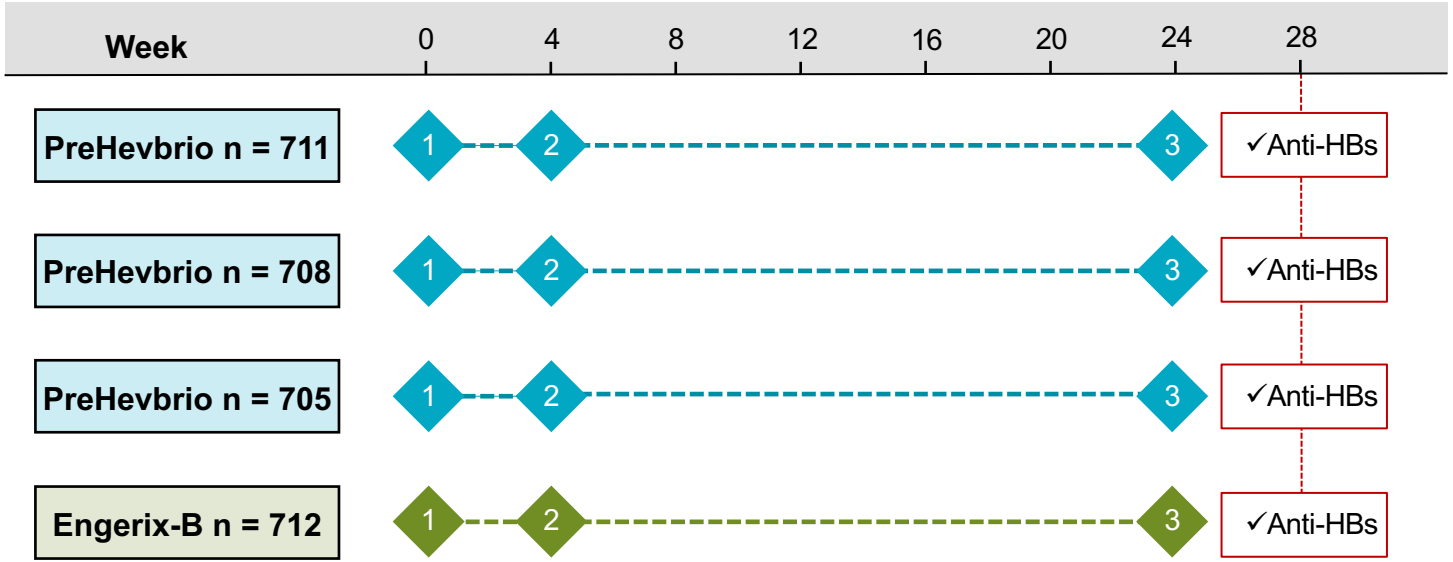
CONSTANT Trial

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

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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.

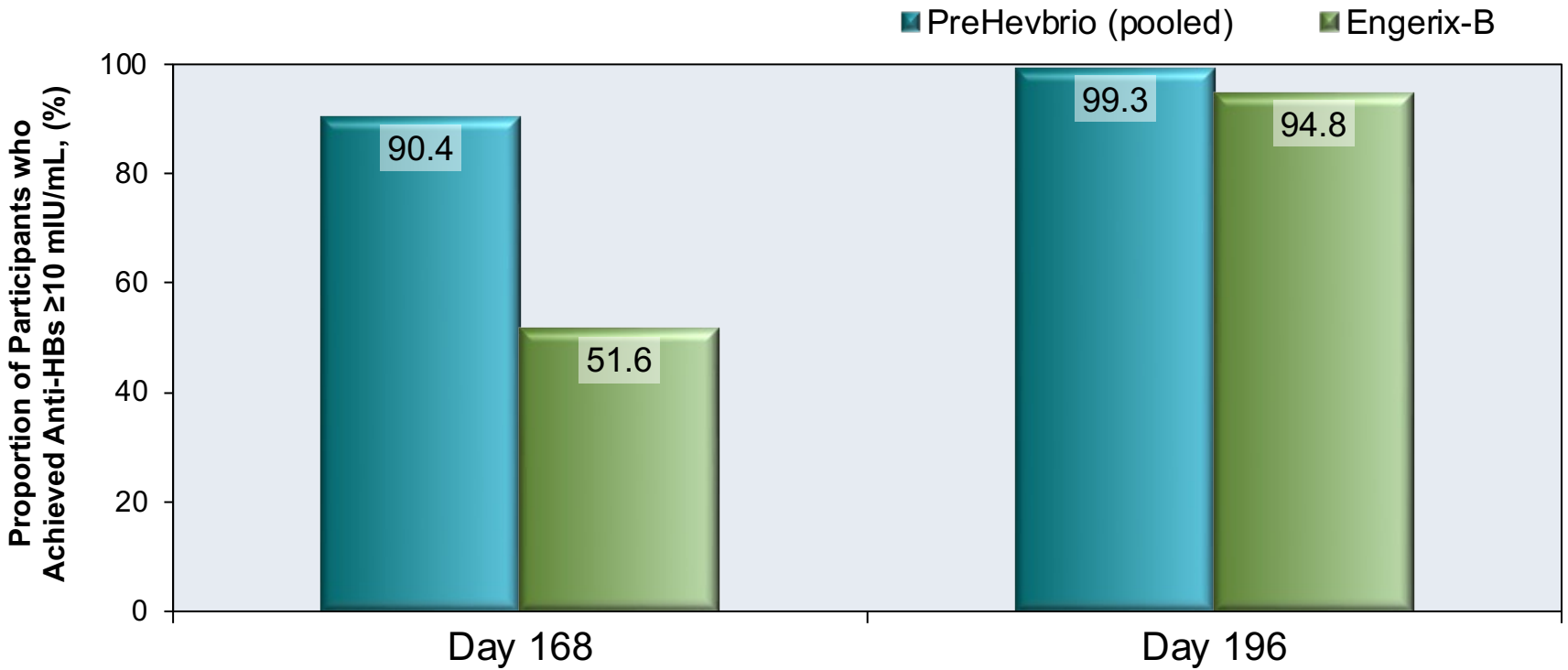
PreHevbrio Vaccine vs Engerix-B Vaccine in Healthy Adults Age 18-45 years CONSTANT Trial: Results

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)			

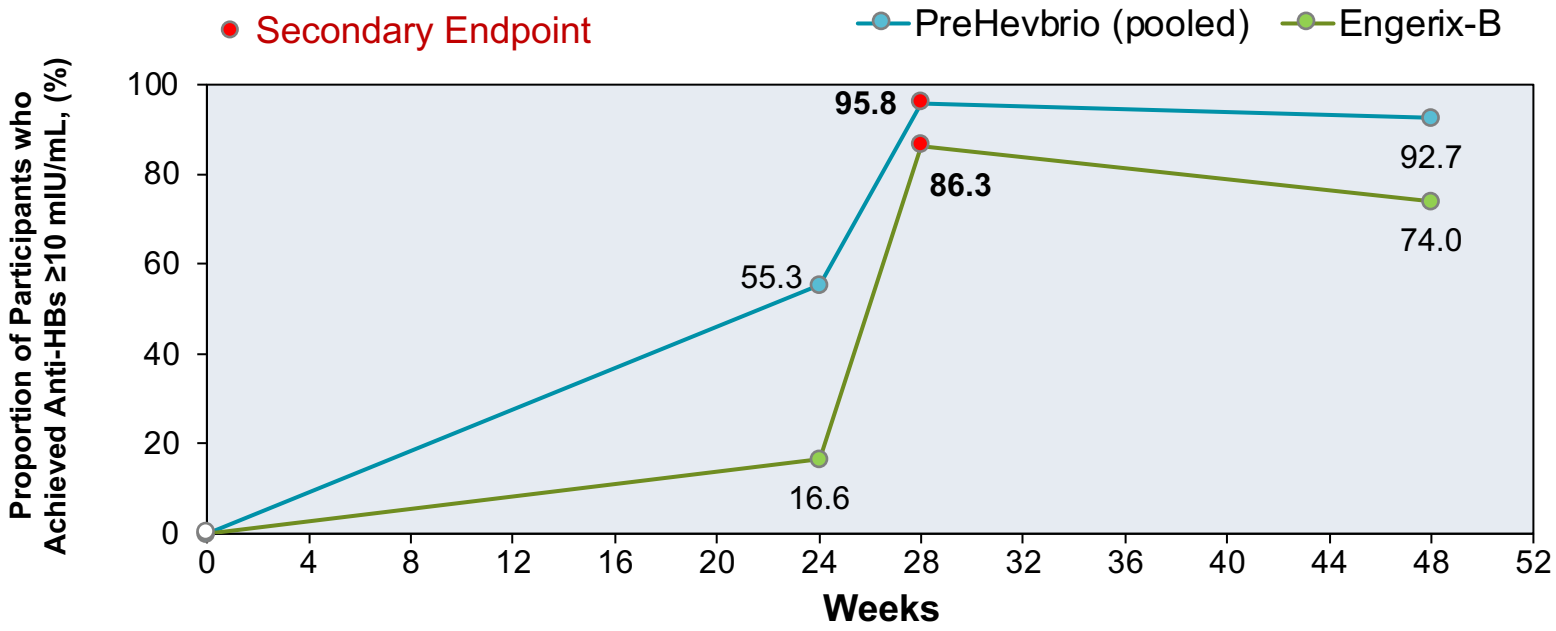
Abbreviations: Geometric mean concentration; SD = standard deviation; SE = standard error; CI= confidence intervals

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.