

Hepatitis B Vaccines

Heplisav-B

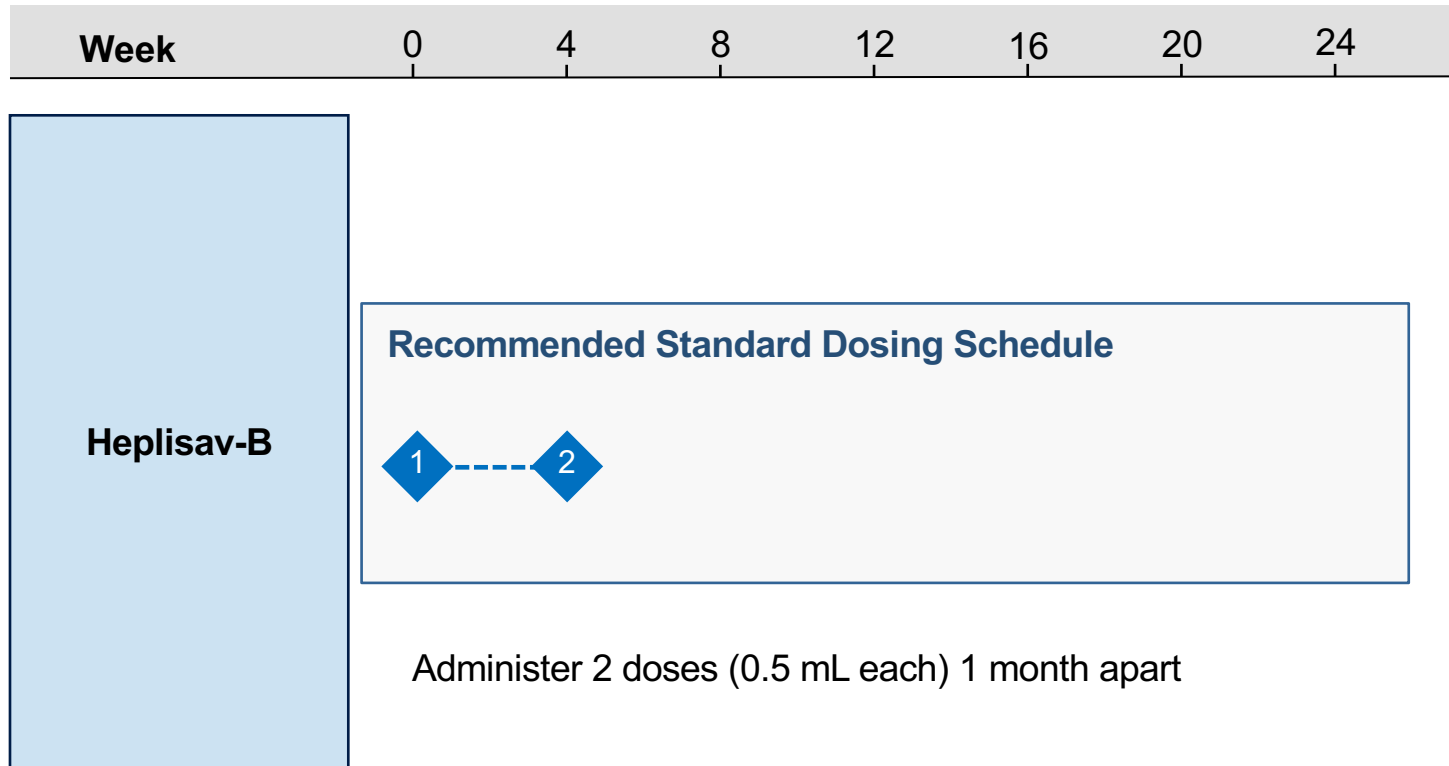
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Last Updated: February 21, 2022

Heplisav-B Vaccine

- **Indication**
 - For the prevention of HBV in adults ≥ 18 years of age
- **Heplisav-B Components (0.5 mL)**
 - 20 μg HBsAg
 - 3,000 μg CpG 1018 adjuvant
- **Dosing**
 - 2 doses (0.5 mL with each dose), given 1 month apart
- **Serious Adverse Events**
 - Reported in 1.5%

Heplisav-B Vaccine: Standard Dosing



Heplisav-B Vaccine: Summary of Key Phase 3 Studies

- HBV-10: Heplisav-B vs Engerix-B in Healthy Adults 18-55 Years of Age
- HBV-16: Heplisav-B vs Engerix-B in Healthy Adults 40-70 Years of Age
- HBV-17: Heplisav-B vs Engerix-B in CKD
- HBV-17 (subgroup): Heplisav-B vs Engerix-B in CKD and DM
- HBV 23: Heplisav-B vs Engerix-B in Adults 18-70 Years of Age
- HBV 23 (subgroup): Heplisav-B vs Engerix-B in Adults 18-70 Years of Age, DM
- HBV 10 & 16: Heplisav-B vs Engerix-B, Ages 18-70 Years of Age, DM, Obese

Hepelisav-B versus Engerix-B in Healthy Adults, Aged 18-55 Years
HBV-10 Trial

Heplisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 18-55 Years HBV-10 Trial: Design

- **Design**

- Phase 3 observer-blinded randomized controlled trial to compare the safety and efficacy of Heplisav-B versus Engerix-B in healthy adults

- **Participants**

- Ages 15-55 years[^]
- HBV vaccine naïve
- Exclusions: HBV*, HIV, pregnancy (or lactation), autoimmune or other clinically significant illness, immunosuppressed

- **Setting**

- Multiple centers in Canada and Germany

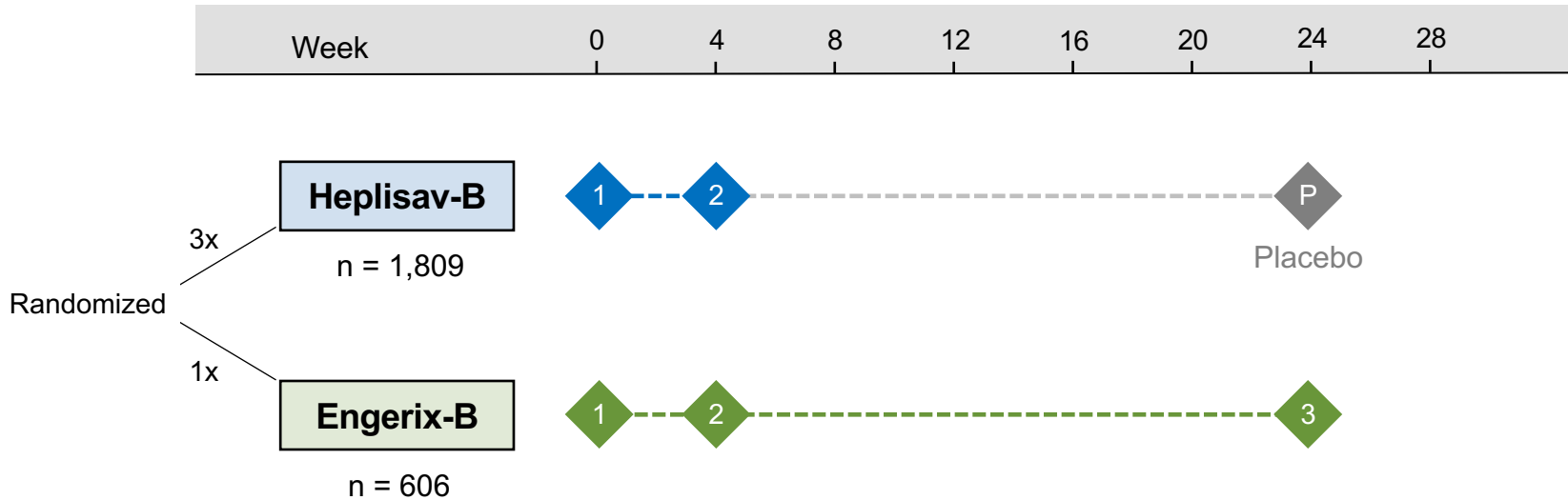
- **Study End-Point**

- Seroprotection = anti-HBs level ≥ 10 mIU/mL

[^]Adolescents age 11-17 years were eligible, but most had previously received HBV vaccine as child as part of universal vaccine program.

^{*}Any positive for HBsAg, anti-HBs, or anti-HB core

Heplisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 18-55 Years HBV-10 Trial: Design



Vaccine Dosing

Heplisav-B: 0.5 mL dose of 3 mg CpG 1018 adjuvant with 20 mcg recombinant HBsAg at weeks 0 and 4, followed by administration of saline placebo at week 24

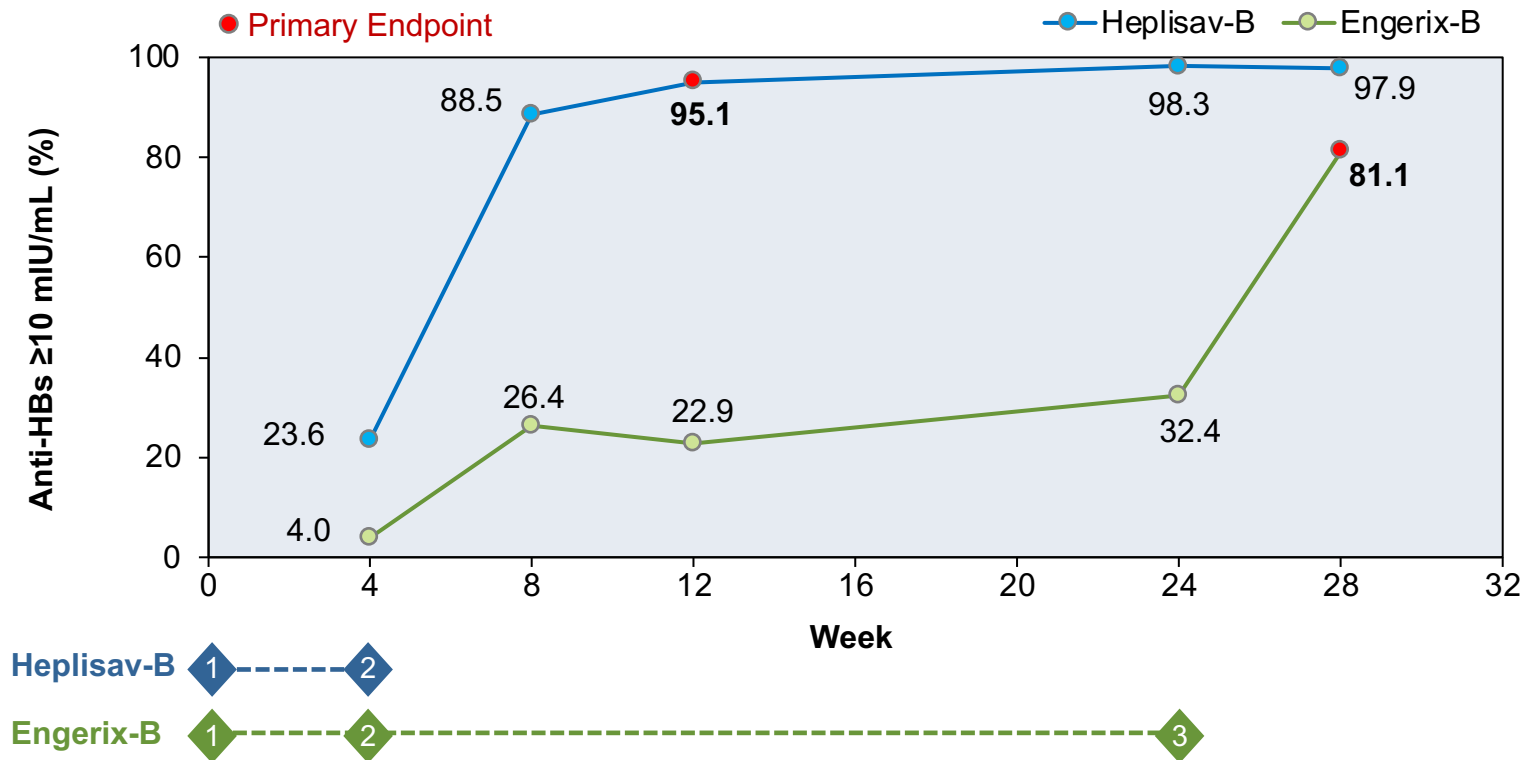
Engerix-B: 1 mL dose of 20 mcg recombinant HBsAg at weeks 0, 4, and 24

Heplisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 18-55 Years HBV-10 Trial: Baseline Characteristics

Baseline Characteristic	Heplisav-B (n = 1,809)	Engerix-B (n = 606)
Age, mean (range), years	40 (18-55)	40 (18-55)
Male, no. (%)	852 (47)	262 (43)
Race, no. (%)		
White	1,690 (93)	556 (92)
Black	39 (2)	20 (3)
Asian	43 (2)	22 (4)
Other	37 (3)	8 (1)
Weight, mean (range), kg	80.3 (43-173)	80.8 (39-179)
Body mass index, kg/m ²	27.4 (15.0-58.1)	27.6 (16.4-63.2)
Smoker, n (%)	654 (36)	224 (37)

Source: Halperin SA, et al. Vaccine. 2012;30:2256-63.

Heplisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 18-55 Years HBV-10 Trial: Results



Source: Halperin SA, et al. Vaccine. 2012;30:2556-63.

Hepelisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 18-55 Years HBV-10 Trial: Conclusions

Conclusions: “A short, two-dose regimen of HBV-ISS induced a superior antibody response than a three-dose regimen of a licensed hepatitis B vaccine and was well tolerated.”

Hepelisav-B vs Engerix-B in Healthy Adults, Aged 40-70 Years
HBV-16 Trial

Heplisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 40-70 Years HBV-16 Trial: Study Design

- **Design**

- Phase 3 randomized observer-blinded controlled trial to compare the safety and efficacy of Heplisav-B versus Engerix B vaccines in healthy adults 40-70 years of age

- **Participants** n = 2,4520

- Ages: 40-70 years
- HBV vaccine naïve
- Exclusions: HBV*, HIV, pregnancy or lactation, autoimmune or other clinically significant illness, immunosuppressed

- **Setting**

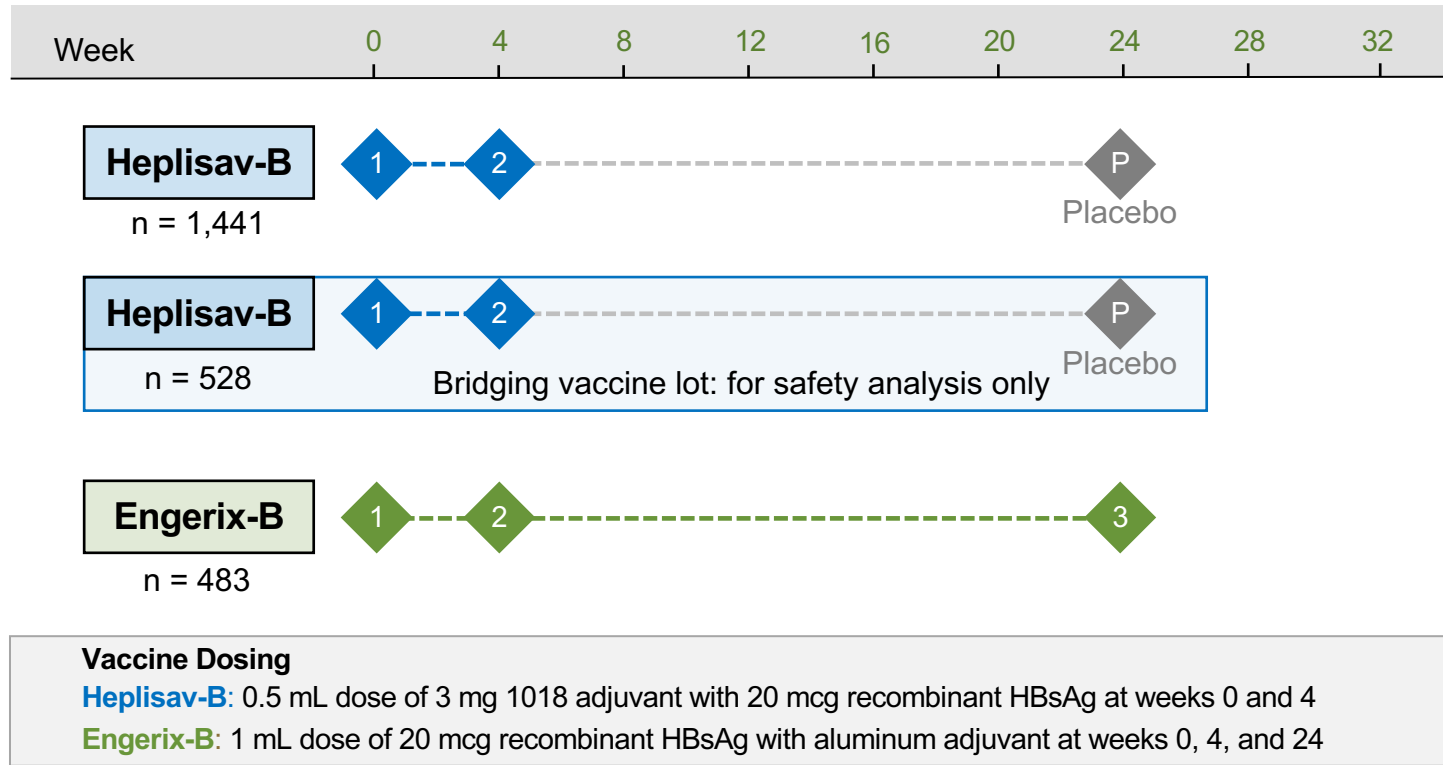
- Multiple centers in United States and Canada

- **Study End-Point**

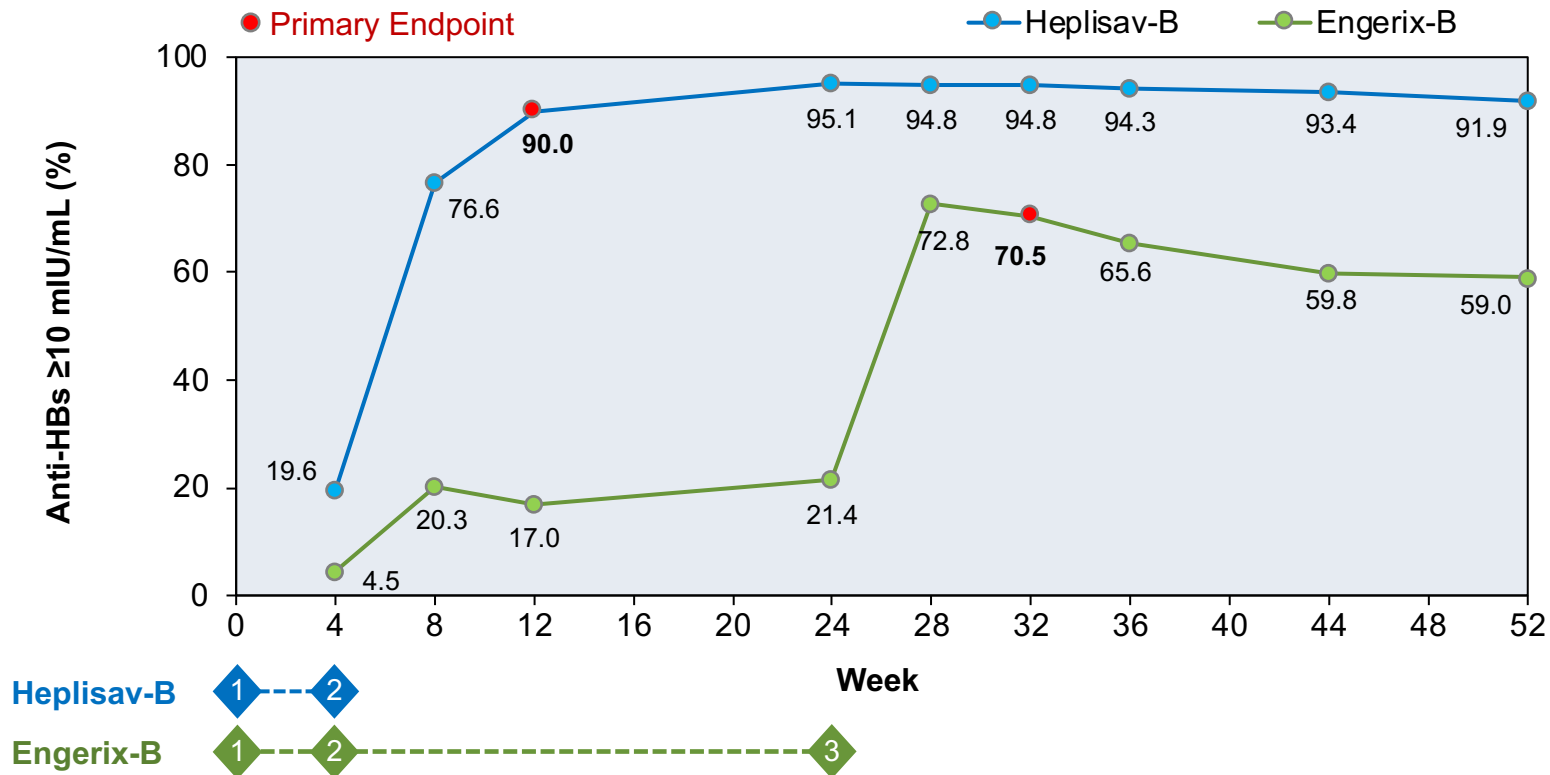
- Seroprotection = anti-HBs level ≥ 10 mIU/mL

*Any positive test for HBsAg, anti-HBs, or anti-HB core

Heplisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 40-70 Years HBV-16 Trial: Design



Heplisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 40-70 Years HBV-16 Trial: Results



Source: Heyward WL, et al. Vaccine. 2013;31:5300-5.

Heplisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 40-70 Years HBV-16 Trial: Adverse Reactions

Adverse Event, no. (%)	Heplisav-B (n = 1,968)	Engerix-B (n = 481)
Local reaction (among n=1953)		
Total	666 (34)	154 (32)
Severe	11 (0.6)	3 (0.6)
Systemic reaction (among n=1953)		
Total	586 (30)	166 (35)
Severe	42 (2)	19 (4)
Any related adverse event (AE)	142 (7)	29 (6)
Any related severe AE (grade 3 or above)	0	1 (0.2)
Any AE leading to study discontinuation	17 (0.9)	2 (0.4)
Death	1 (0.05)	1 (0.2)

Source: Heyward WL, et al. Vaccine. 2013;31:5300-5.

Hepelisav-B Vaccine versus Engerix-B Vaccine in Healthy Adults Aged 40-70 Years HBV-16 Trial: Conclusions

Conclusions: “When compared to the HBsAg-Eng three-dose regimen given at 0, 1, and 6 months, HBsAg-1018 demonstrated superior seroprotection with only two doses at 0 and 1 month. The safety profile of HBsAg-1018 was comparable to that of the licensed vaccine, HBsAg-Eng. HBsAg-1018 would provide a significant public health contribution toward the prevention of hepatitis B infection.”

Hepelisav-B versus Engerix-B in Adults with Chronic Kidney Disease (CKD)
HBV-17 Trial

Heplisav-B Vaccine versus Engerix-B Vaccine in Adults with CKD HBV-17 Trial: Design

- **Design**

- Phase 3 randomized, observer-blinded, active controlled, trial to compare the safety and efficacy of 3 doses of Heplisav-B versus 4 double-doses of Engerix B in adults with chronic kidney disease (CKD)

- **Participants** (n = 521 randomized, 507 analyzed)

- Ages: 18-75 years
- Chronic kidney disease: GFR ≤ 45 mL/min/1.73 m² +/- hemodialysis
- HBV vaccine naïve
- Exclusions: HBV*, HIV, HCV, pregnancy or lactation, autoimmune or other clinically significant illness, immunosuppressed

- **Setting**

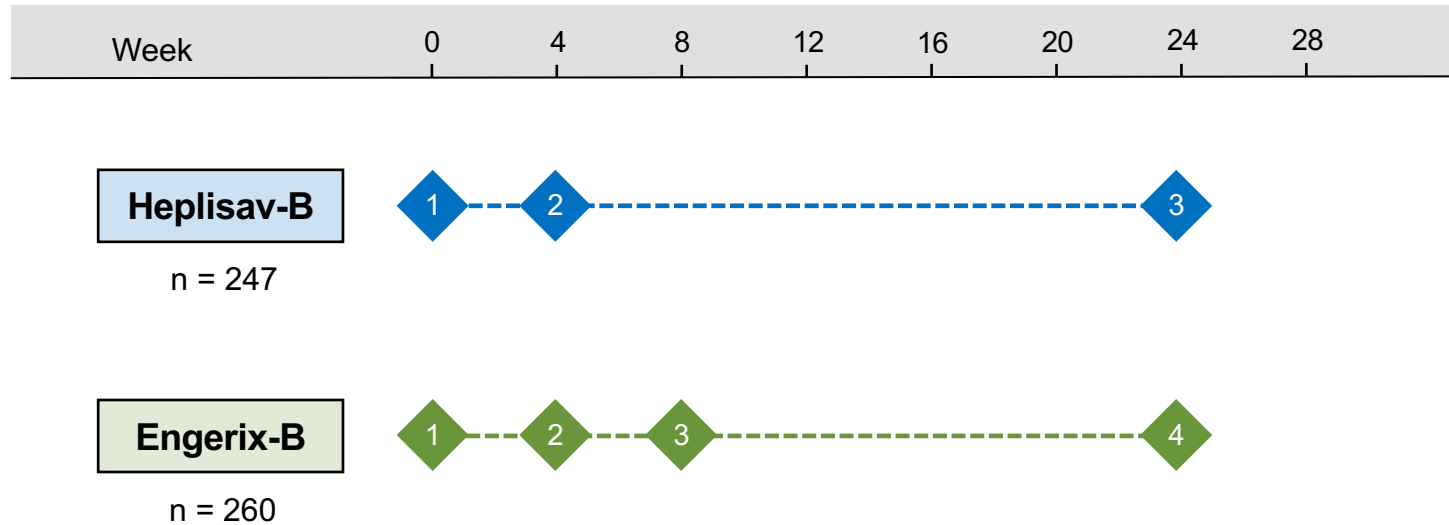
- Multiple centers in United States & Canada

- **Study End-Point**

- Seroprotection = anti-HBs level ≥ 10 mIU/mL

*Any positive for HBsAg, anti-HBs, or anti-HB core

Heplisav-B Vaccine versus Engerix-B Vaccine in Adults with CKD HBV-17 Trial: Design

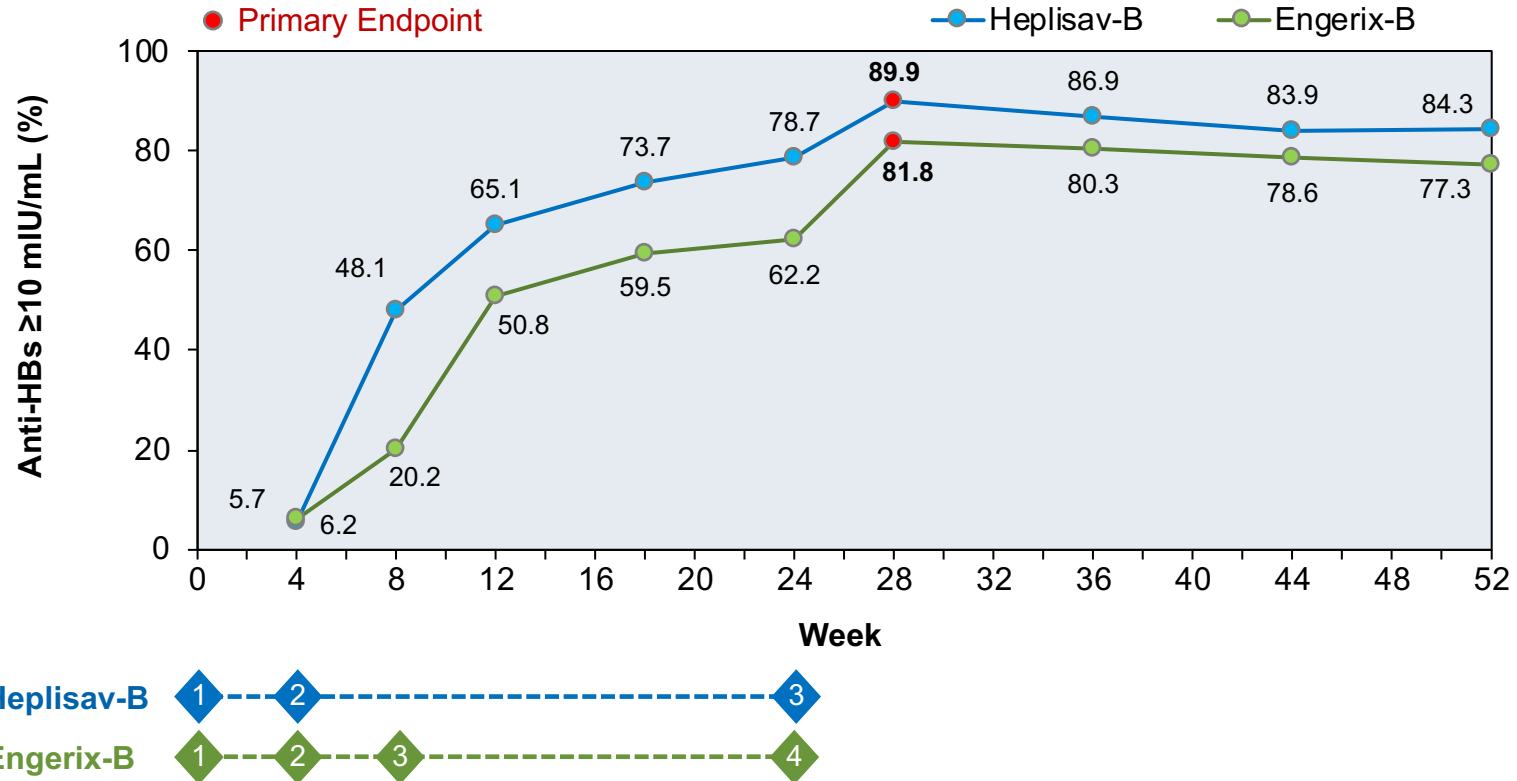


Vaccine Dosing

Heplisav-B: 0.5 mL dose (standard dose = 20 mcg) recombinant HBsAg at weeks 0, 4, and 24

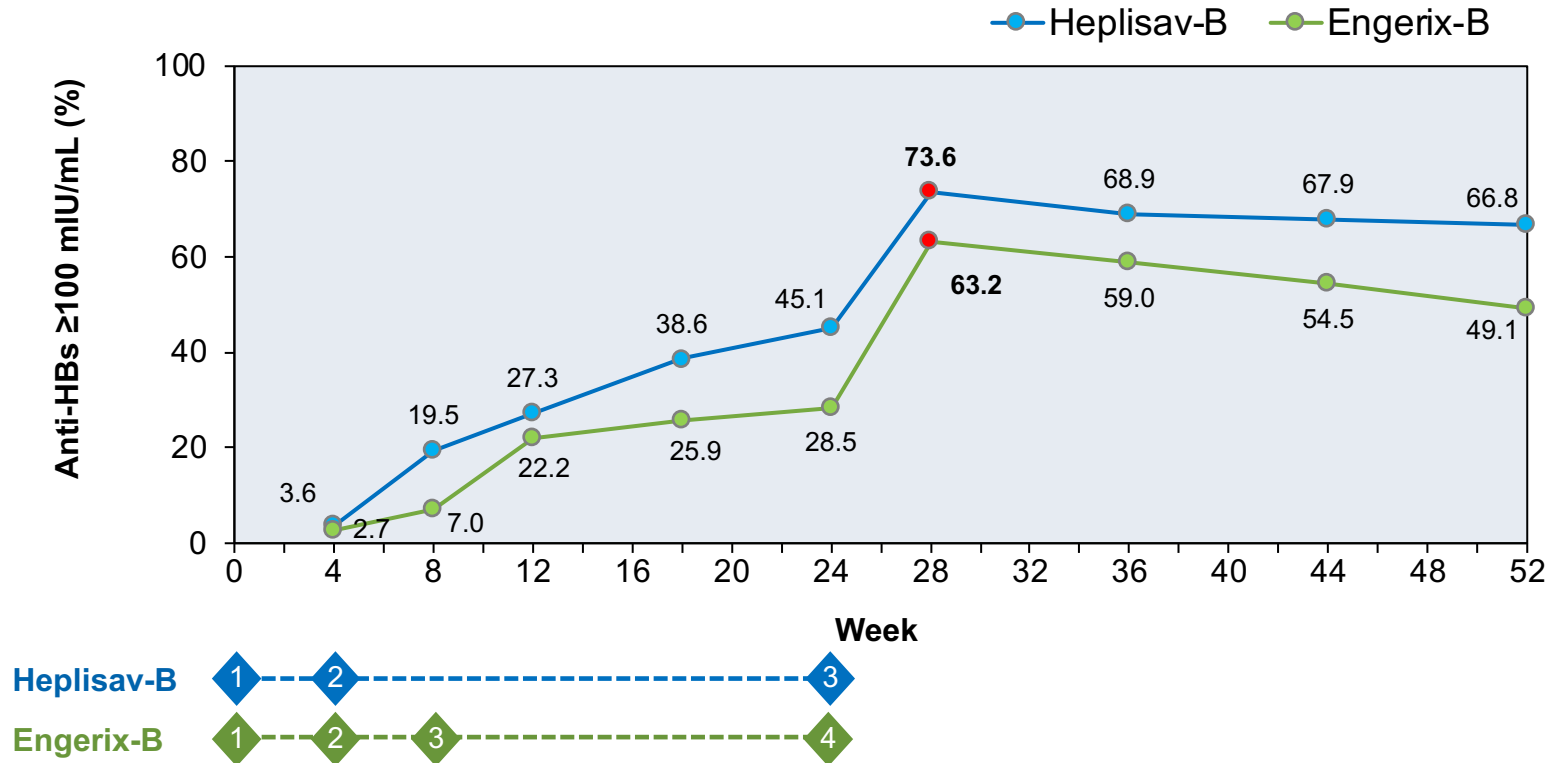
Engerix-B: 1 mL dose (double dose = 40 mcg) recombinant HBsAg at weeks 0, 4, 8, and 24

Heplisav-B Vaccine versus Engerix-B Vaccine in Adults with CKD HBV-17 Trial: Results (anti-HBs ≥ 10 mIU/mL)



Source: Janssen RS, et al. Vaccine. 2013;31:5306-13.

Heplisav-B Vaccine versus Engerix-B Vaccine in Adults with CKD HBV-17 Trial: Results (anti-HBs ≥ 100 mIU/mL)



Source: Janssen RS, et al. Vaccine. 2013;31:5306-13.

Hepatitis B Vaccine versus Engerix-B Vaccine in Adults with CKD HBV-17 Trial: Conclusions

Conclusions: “In chronic kidney disease patients, 3 doses of HBsAg-1018 induced significantly higher seroprotection, earlier seroprotection, and more durable seroprotection than 4 double doses of HBsAg-Eng.”

Hepelisav-B versus Engerix-B in Adults with Chronic Kidney Disease (CKD)
HBV-17: Diabetes Mellitus Subgroup Analysis

Heplisav-B versus Engerix-B in Adults with CKD HBV-17 DM Subgroup Analysis: Design

- **Background**

- Phase 3 randomized, observer-blinded, active controlled, conducted in multiple centers in United States and Canada trial to compare the safety and efficacy of 3 doses of Heplisav-B versus 4 double-doses of Engerix B in adults with chronic kidney disease (CKD)

- **Participants**

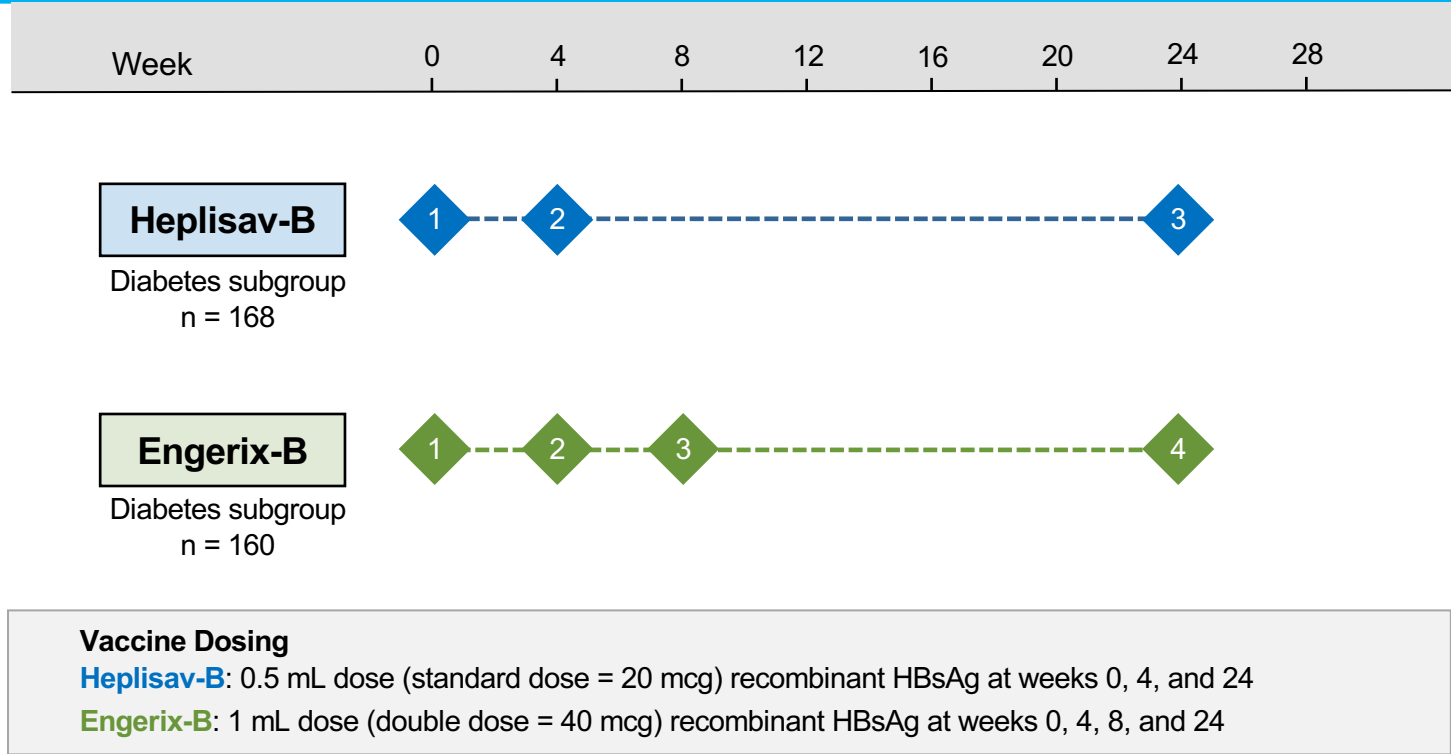
- n = 328 randomized (n = 326 analyzed in modified intent-to-treat (mITT))
- Ages: 18-75 years
- Chronic kidney disease: GFR ≤ 45 mL/min/1.73 m² +/- hemodialysis
- Type 2 diabetes mellitus
- HBV vaccine naïve
- Exclusions: HBV*, HIV, HCV, pregnancy or lactation, autoimmune or other clinically significant illness, immunosuppressed

- **Study End Point**

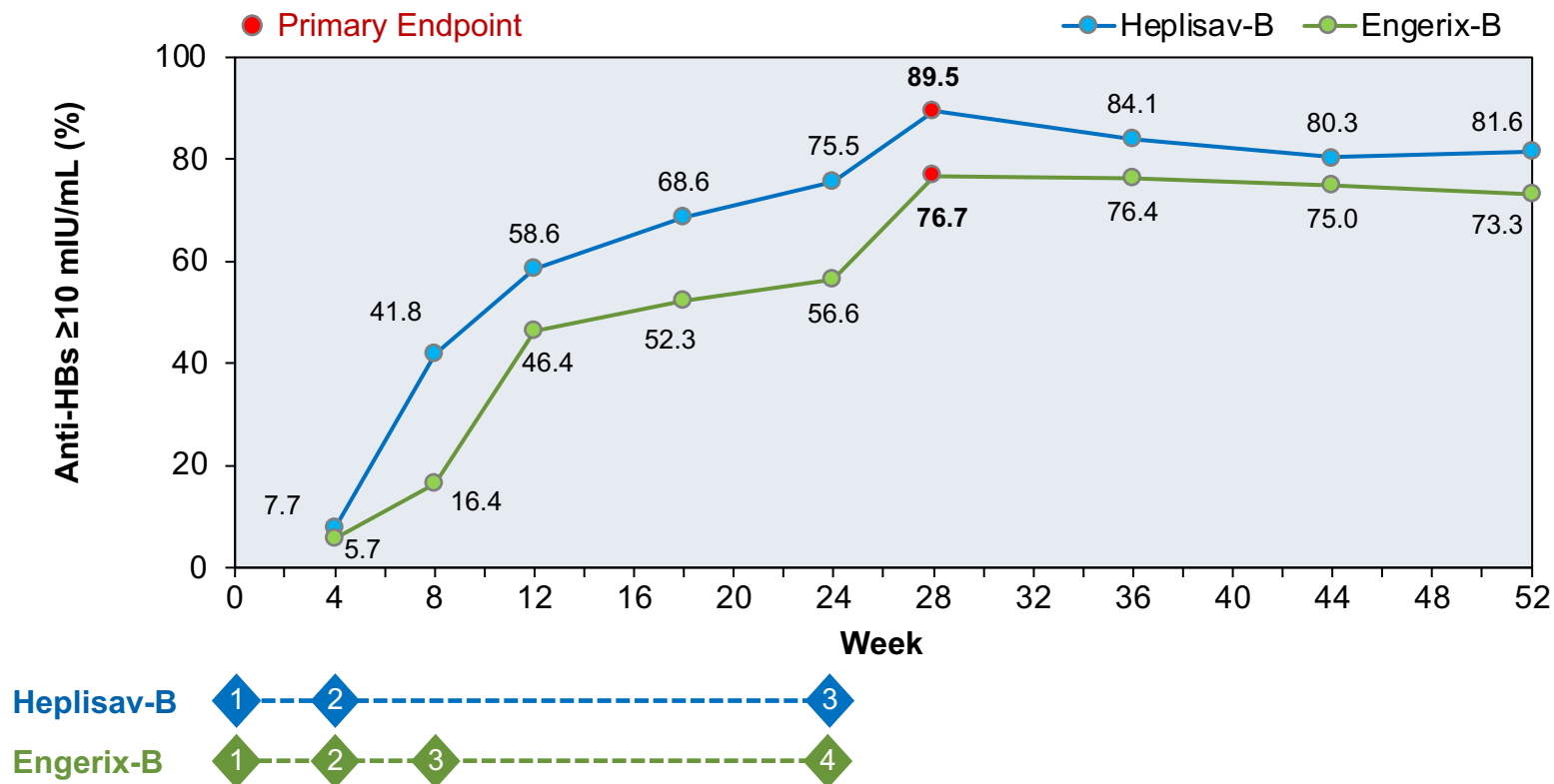
- Seroprotection = anti-HBs antibody level ≥ 10 mIU/mL

*Any positive for HBsAg, anti-HBs, or anti-HB core

Hepelisav-B versus Engerix-B in Adults with CKD HBV-17 DM Subgroup Analysis: Design



Hepelisav-B versus Engerix-B in Adults with CKD HBV-17 DM Subgroup Analysis: Results



Source: Janssen JM, et al. Vaccine. 2015;3:833-7.

Hepelisav-B versus Engerix-B in Adults with CKD HBV-17 DM Subgroup Analysis: Conclusions

Conclusions: “HBsAg-1018 induced significantly higher seroprotection than HBsAg-Eng in CKD patients with diabetes.”

Hepalisav-B versus Engerix-B in Adults 18-70 Years of Age
HBV-23 Trial

Hepatitis B versus Engerix-B in Adults 18-70 Years of Age HBV-23 Trial: Study Design

- **Background**

- Phase 3 observer-blinded active-controlled randomized trial to assess the immunogenicity of Hepatitis B (HBsAg-1018) vaccine versus Engerix-B vaccine in adults 18-70 years of age, with or without diabetes.

- **Participants**

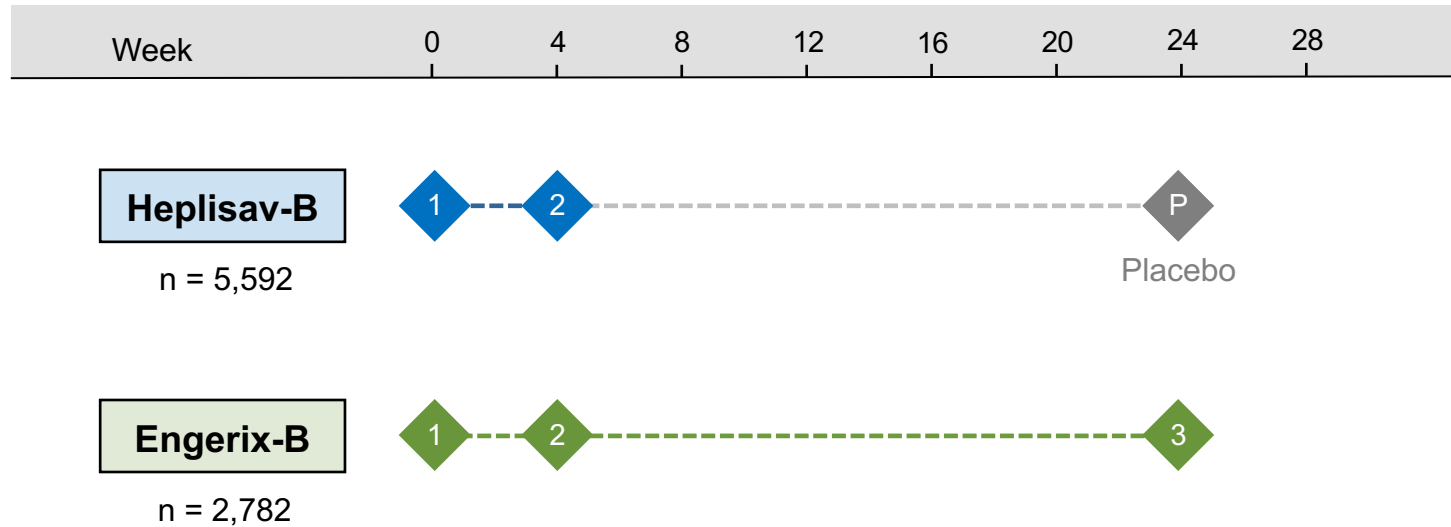
- n = 8,374 persons, including 961 with type 2 diabetes mellitus
- Ages: 18-70 years
- HBV vaccine naïve
- Exclusions: HBV, HIV, pregnancy or lactation, chronic steroid use, autoimmune condition

- **Study End Point**

- Seroprotection = anti-HBs antibody level ≥ 10 mIU/mL

*Any positive for HBsAg, anti-HBs, or anti-HB core

Hepelisav-B versus Engerix-B in Adults 18-70 Years of Age HBV-23 Trial: Study Design



Vaccine Dosing

Hepelisav-B: 0.5 mL dose of 3 mg 1018 adjuvant with 20 mcg recombinant HBsAg at weeks 0 and 4, followed by administration of saline placebo at week 24

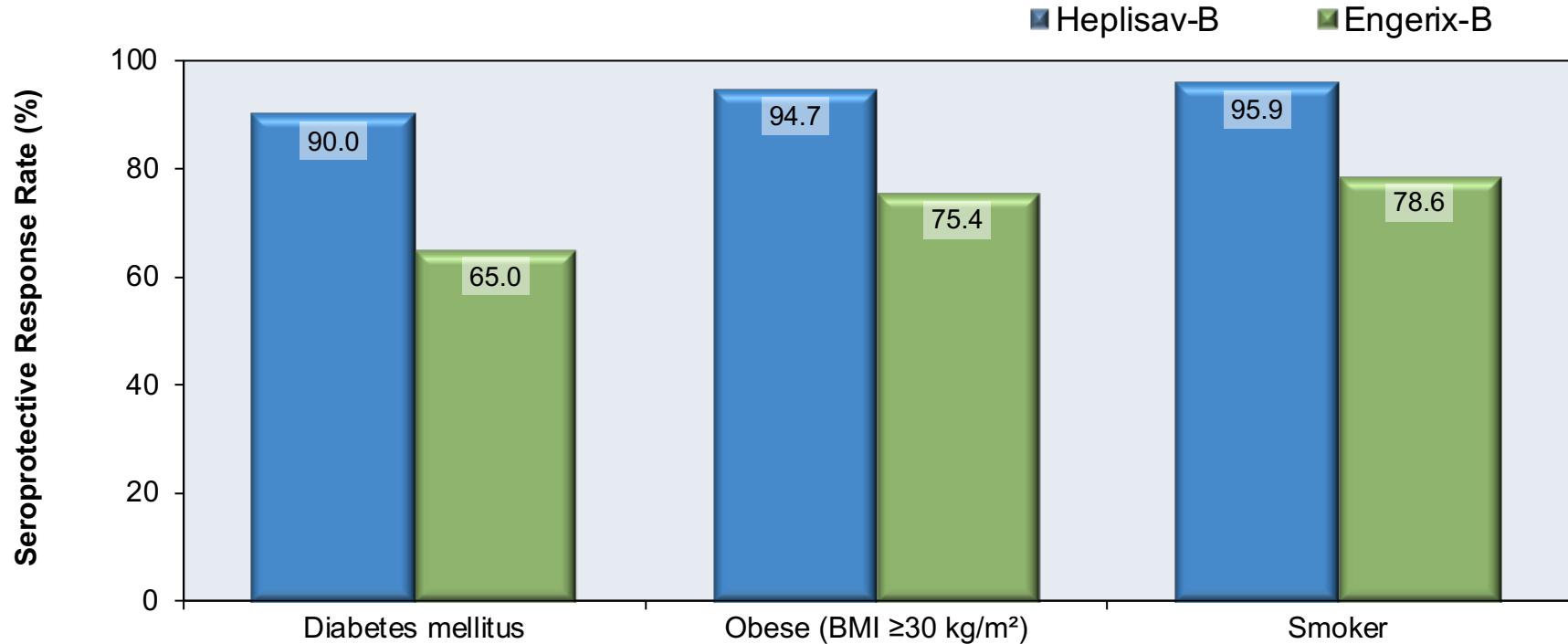
Engerix-B: 1 mL dose of 20 mcg recombinant HBsAg with aluminum adjuvant at weeks 0, 4, and 24

Hepatitis B versus Engerix-B in Adults 18-70 Years of Age HBV-23 Trial: Baseline Characteristics

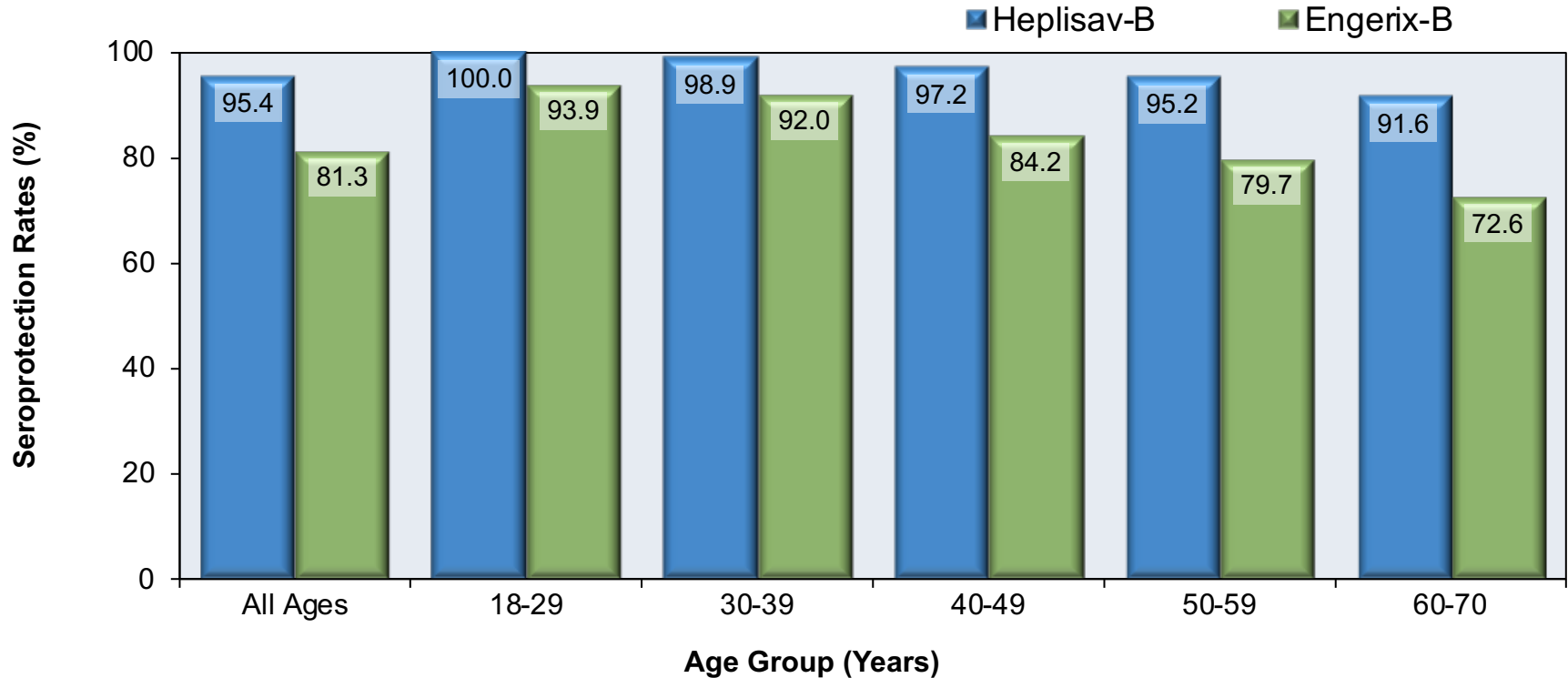
Baseline Characteristic	Hepatitis B (n = 5,592)	Engerix-B (n = 2,782)
Age, mean (SD), years	50.4 (11.7)	50.4 (11.7)
Male, no. (%)	2845 (51)	1391 (50)
Race, no. (%)		
White	3972 (71)	2007 (72)
Black	1462 (26)	697 (25)
Asian	57 (1)	38 (1.4)
American Indian/Alaskan Native	60 (1)	24 (1)
Other	41 (1)	16 (0.6)
Body mass index (BMI), mean (SD), kg/m ²	31 (7.5)	31 (7.6)
BMI ≥30 kg/m ² , n (%)	2728 (49)	1286 (46)
Smoker, n (%)	1844 (33)	909 (33)
Diabetes type 2, n (%)	763 (13.6)	381 (13.7)

Source: Jackson S, et al. Vaccine. 2018;36:668-74.

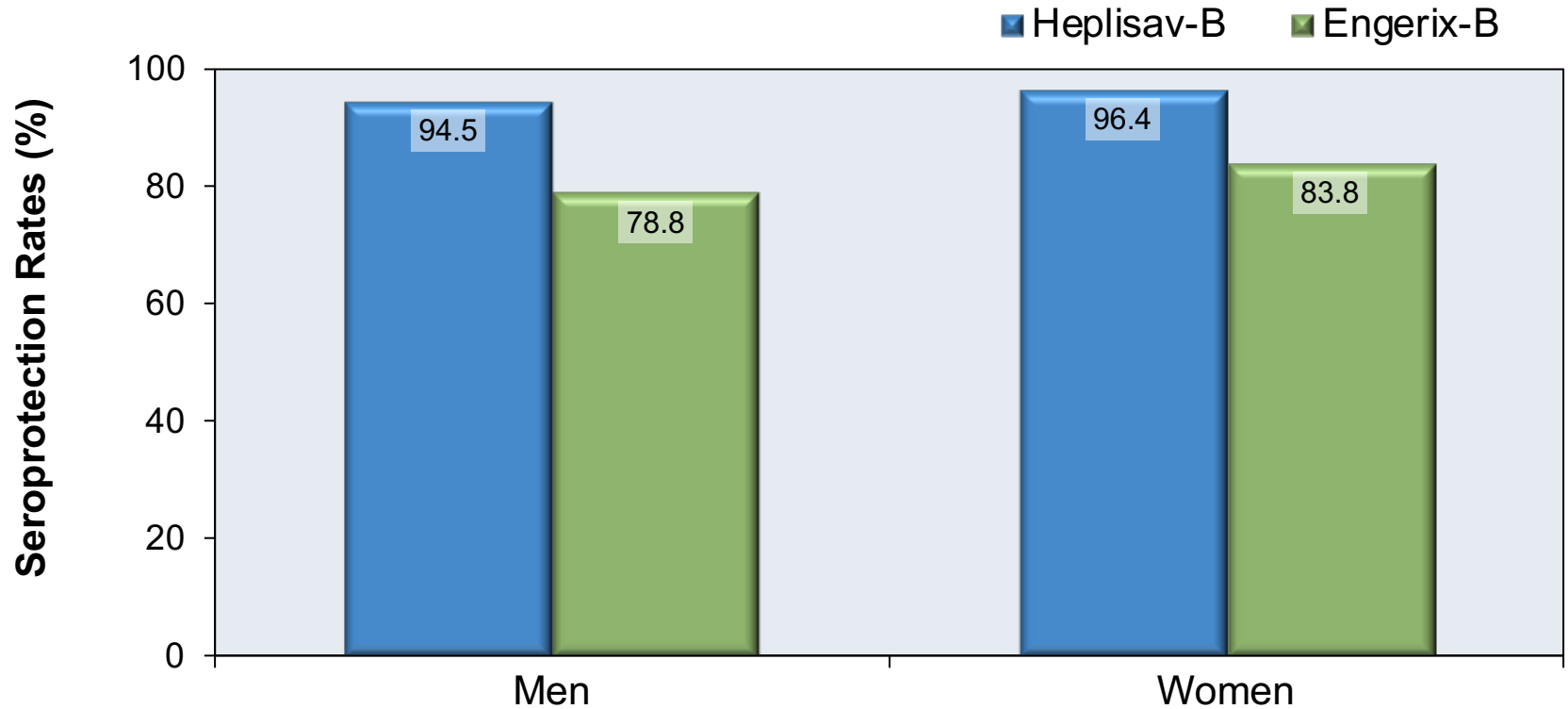
Heplisav-B versus Engerix-B in Adults 18-70 Years of Age HBV-23 Trial: Results, by Key Subgroups



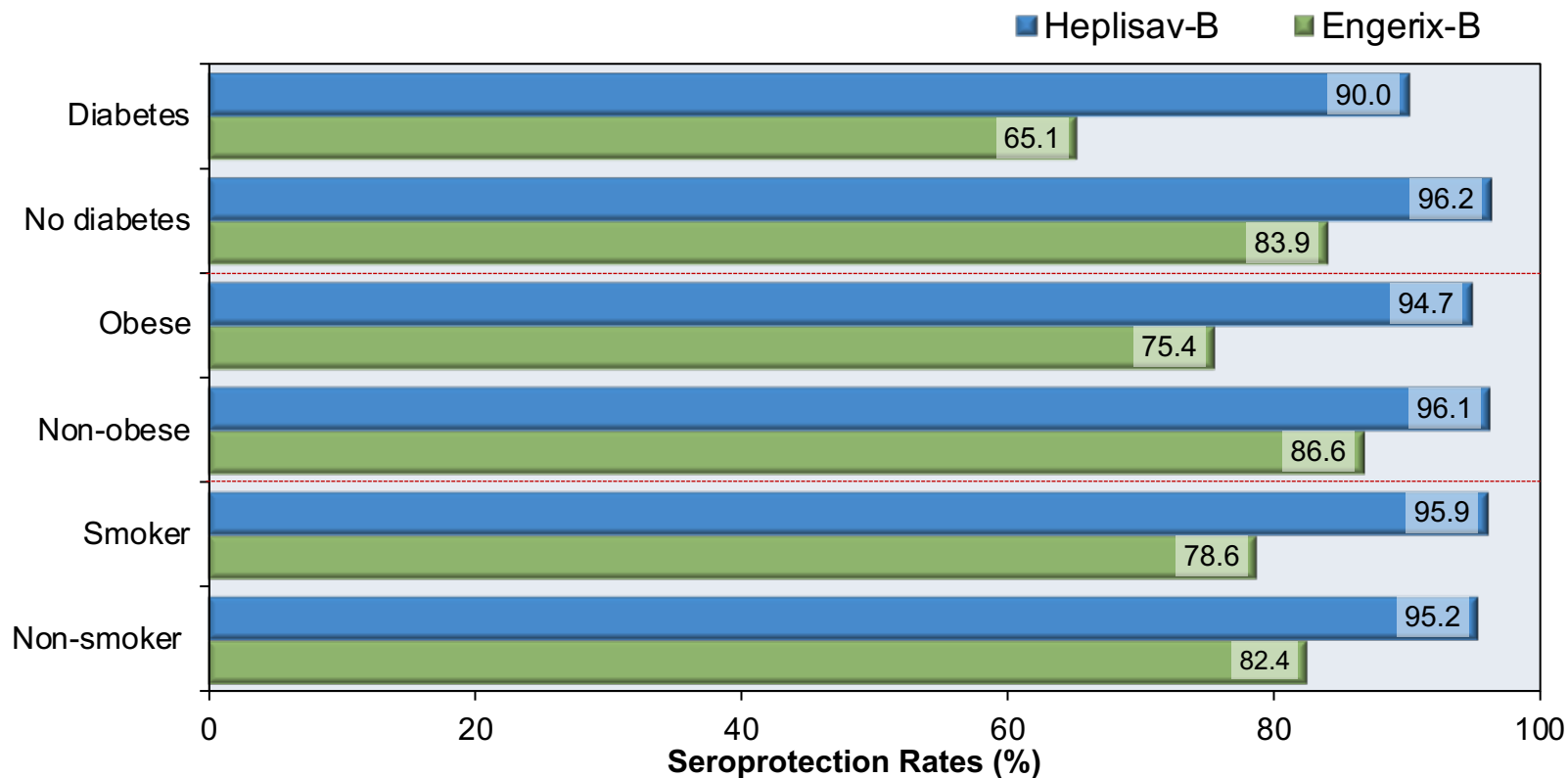
Hepatitis B versus Engerix-B in Adults 18-70 Years of Age HBV-23 Trial: Results, by Age Group



HepB versus EngB in Adults 18-70 Years of Age HBV-23 Trial: Results, by Gender



Hepatitis B versus Engerix-B in Adults 18-70 Years of Age HBV-23 Trial: Results, by Comorbidities



Source: Jackson S, et al. *Vaccine*. 2018;36:668-74.

HepHisav-B versus Engerix-B in Adults 18-70 Years of Age HBV-23 Trial: Conclusions

Conclusions: “Two doses of HBsAg-1018, administered over 4 weeks, induced significantly higher seroprotection rates than three doses of HBsAg-Eng, given over 24 weeks, in adults with factors known to reduce the immune response to hepatitis B vaccines as well as in those without those factors. With fewer doses in a shorter time, and greater immunogenicity, HBsAg-1018 has the potential to significantly improve protection against hepatitis B in adults at risk for hepatitis B infection.”

Hepelisav-B versus Engerix-B in Adults 60-70 Years of Age
HBV-23 (Diabetes Mellitus Subgroup Analysis)

Heplisav-B Vaccine versus Engerix-B Vaccine in Adults 60-70 Years of Age HBV-23 DM Subgroup Analysis: Study Design

- **Background**

- To assess the immunogenicity of Heplisav-B (HBsAg-1018) vaccine versus alum-adjuvanted Engerix-B vaccine in adults 60-70 years of age with type 2 diabetes mellitus in a pre-specified subgroup analysis of HBV-23

- **Participants**

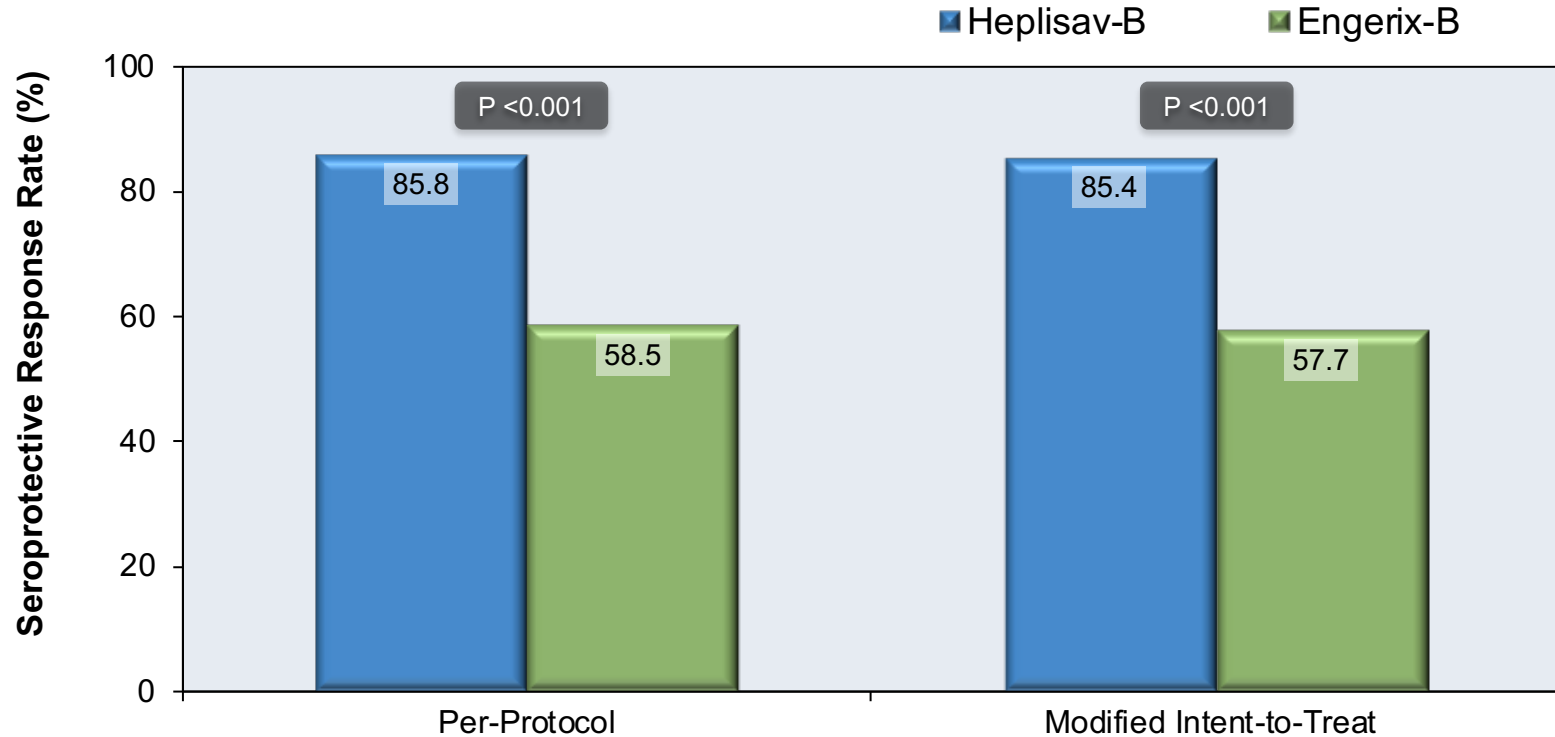
- n = 480 persons with type 2 diabetes mellitus
- Ages: 60-70 years
- HBV vaccine naïve
- Exclusions: HBV*, HIV, pregnancy (or lactation), chronic steroid use, autoimmune condition

- **Study Primary End-Point**

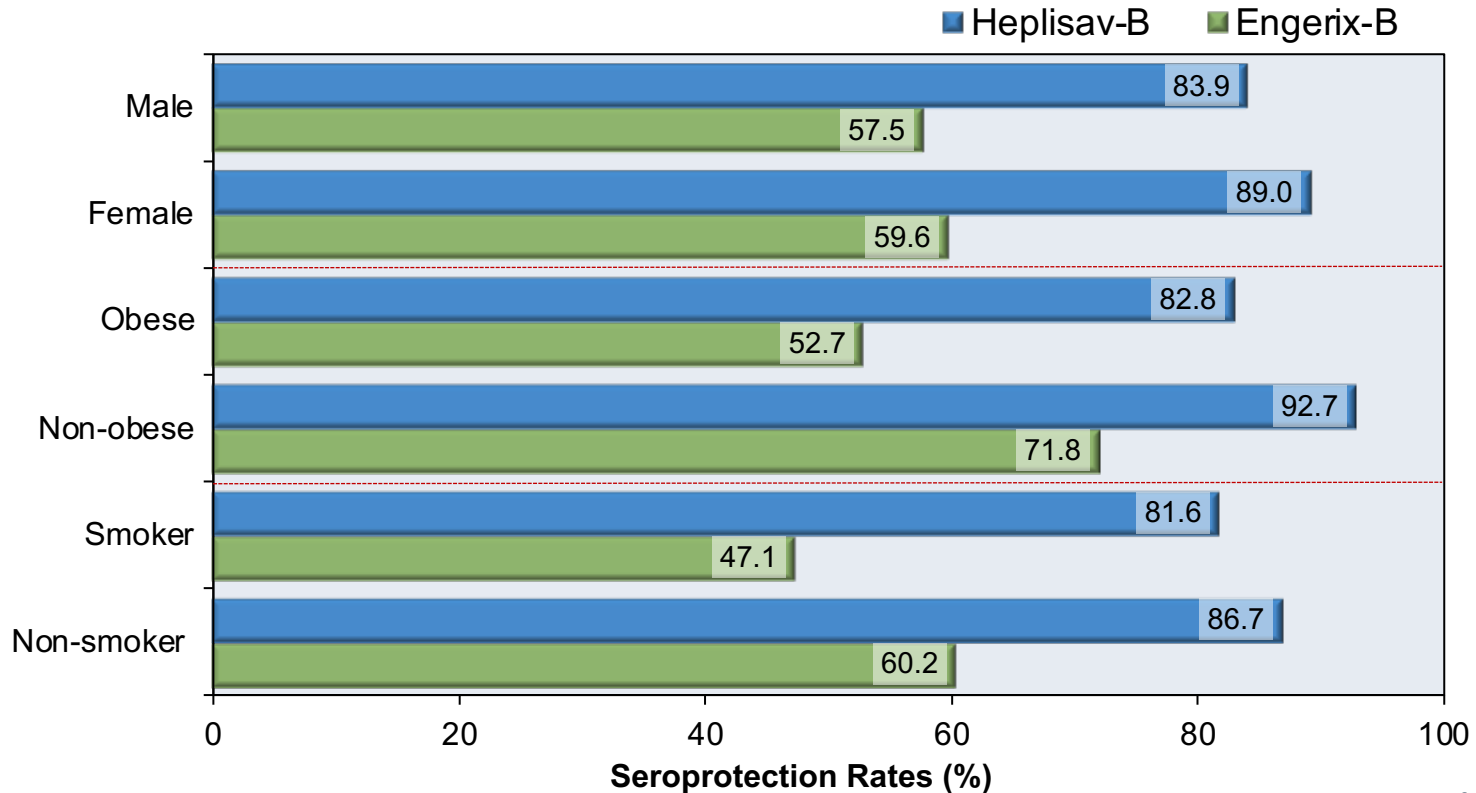
- Seroprotection = anti-HBs antibody level ≥ 10 mIU/mL

*Any positive for HBsAg, anti-HBs, or anti-HB core

Hepelisav-B Vaccine versus Engerix-B Vaccine in Adults 60-70 Years of Age HBV-23 DM Subgroup Analysis: Results



Heplisav-B Vaccine versus Engerix-B Vaccine in Adults 60-70 Years of Age HBV-23 DM Subgroup Analysis: Subpopulations



Source: Hyer RN, Janssen RS. *Vaccine*. 2019;37:5854-61.

Hepelisav-B Vaccine versus Engerix-B Vaccine in Adults 60-70 Years of Age HBV-23 DM Subgroup Analysis: Conclusions

Conclusions: “Two doses of HBsAg/CpG 1018 provides a higher level of seroprotection against HBV than does a 3-dose vaccine (HBsAg/alum) with a similar safety profile in patients aged 60-70 years with type 2 diabetes mellitus.”

HBV-10 and HBV-16 (Combined Analysis)
Immunogenicity of Heplisav-B in Healthy Adults

Heplisav-B versus Engerix-B Vaccine in Healthy Adults—Combined Analysis HBV-10 and HBV-16: Study Design

- **Background**

- Combined post-hoc analysis of two phase 3 randomized controlled trials of Heplisav-B versus Engerix-B to explore immunogenicity or seroprotective responses stratified by patient characteristics

- **Participants**

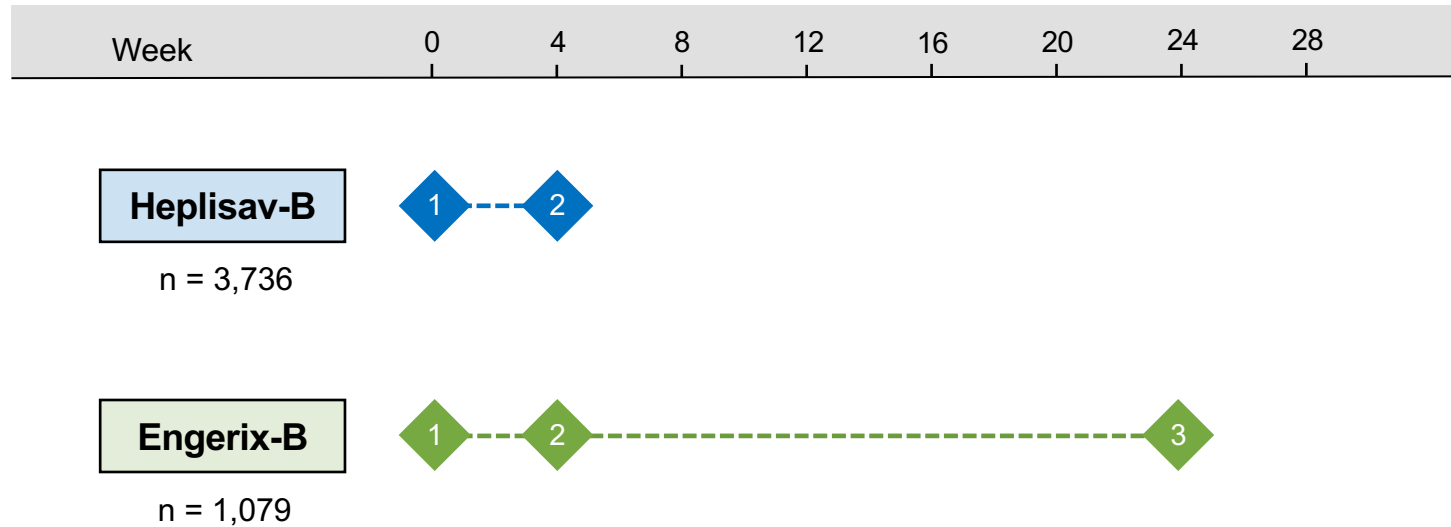
- Trial HBV-10; n = 2,415 participants, aged 18-55 years¹
- Trial HBV-16; n = 2,452 participants, aged 40-70 years²
- HBV infection and vaccine naïve
- Exclusions: HBV, HIV, pregnancy or lactation, autoimmune or other clinically significant illness, immunosuppressed

- **Study End-Point**

- Seroprotection = anti-HBs level ≥ 10 IU/L
- Peak seroprotection analysis: Heplisav-B (week 24); Engerix-B (week 28)

*Any positive for HBsAg, anti-HBs, or anti-HB core

Heplisav-B versus Engerix-B Vaccine in Healthy Adults—Combined Analysis HBV-10 and HBV-16: Study Design



Vaccine Dosing

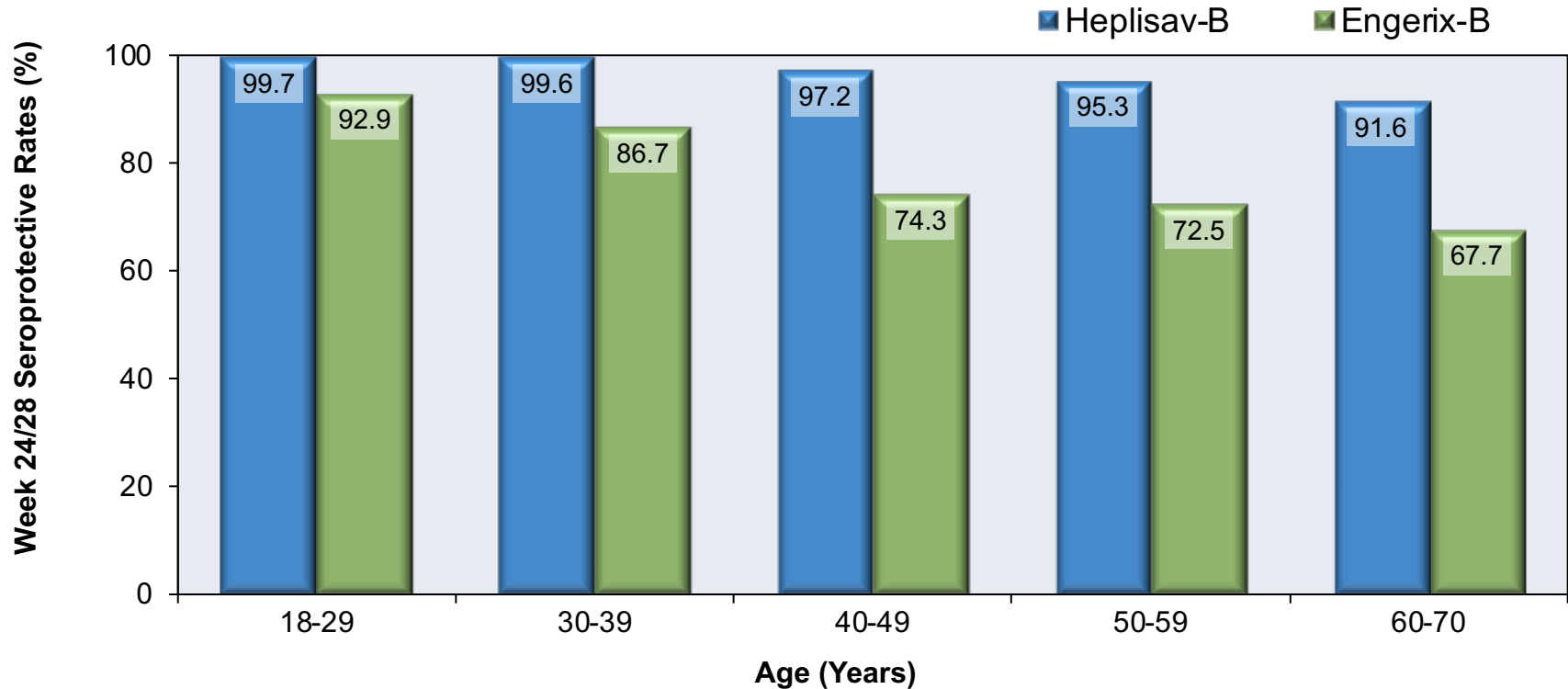
Heplisav-B: 0.5 mL dose of 3 mg 1018 adjuvant with 20 mcg recombinant HBsAg at weeks 0 and 4, followed by administration of saline placebo at week 24

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

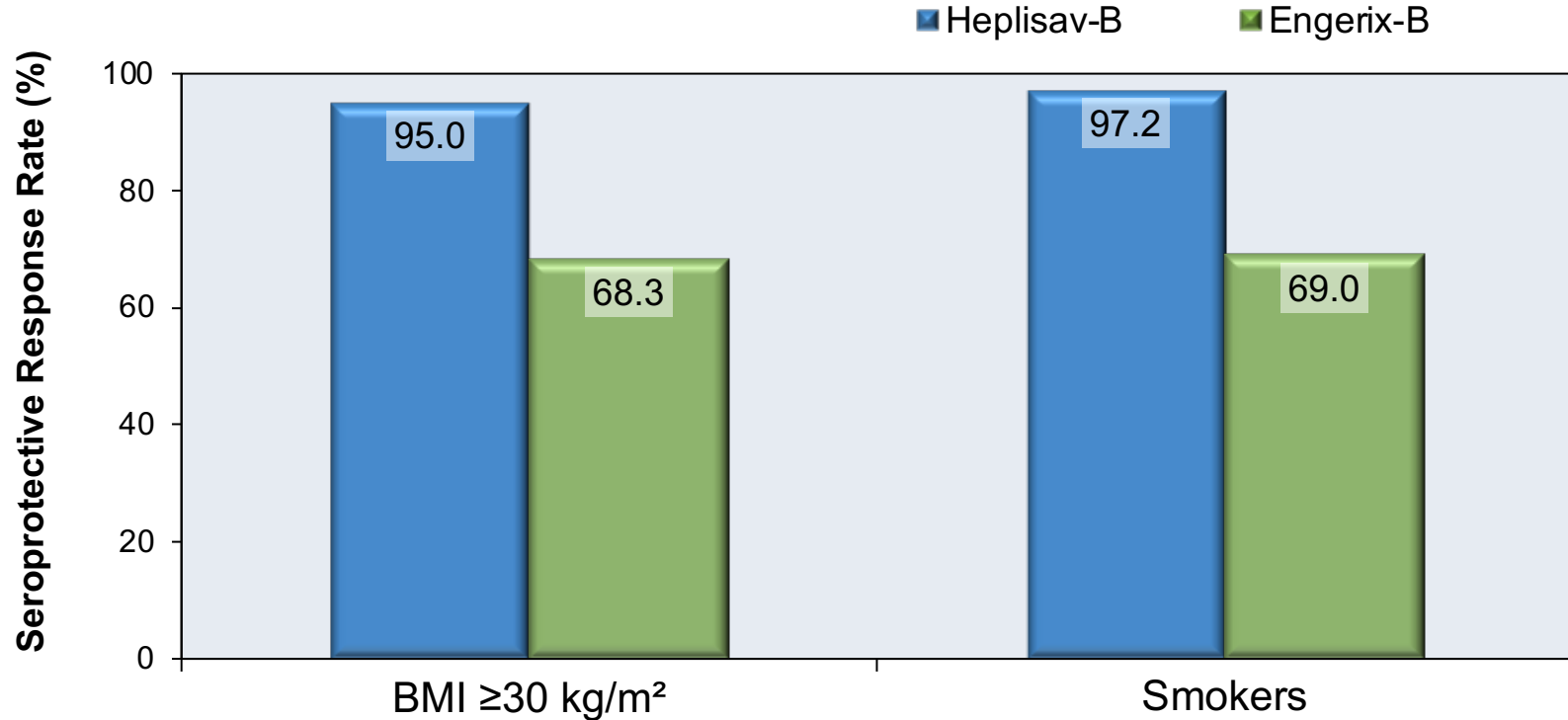
Heplisav-B versus Engerix-B Vaccine in Healthy Adults—Combined Analysis HBV-10 and HBV-16: Baseline Characteristics

Baseline Characteristic	Heplisav-B (n = 3,736)	Engerix-B (n = 1,079)
Age, mean (SD), years	47 (11)	46 (11)
Male, no. (%)	1775 (48)	495 (46)
Race, no. (%)		
White	3282 (88)	951 (88)
Black	327 (9)	86 (8)
Asian	66 (2)	26 (2.5)
Other	61 (1)	16 (1.5)
Body mass index, mean (SD), kg/m ²	29 (6.2)	29 (6.4)
Smoker, n (%)	1067 (29)	336 (31)

Heplisav-B versus Engerix-B Vaccine in Healthy Adults—Combined Analysis HBV-10 and HBV-16: Seroprotection, by Age Group



Heplisav-B versus Engerix-B Vaccine in Healthy Adults—Combined Analysis HBV-10 and HBV-16: Response in Subgroups



Hepelisav-B versus Engerix-B Vaccine in Healthy Adults—Combined Analysis HBV-10 and HBV-16: Conclusions

Conclusions: “Two doses of HBsAg-1018, administered over 4 weeks, induced significantly higher seroprotection rates than three doses of HBsAg-Eng, given over 24 weeks, in adults with factors known to reduce the immune response to hepatitis B vaccines as well as in those without those factors. With fewer doses in a shorter time, and greater immunogenicity, HBsAg-1018 has the potential to significantly improve protection against hepatitis B in adults at risk for hepatitis B infection.”

This slide deck is from the University of Washington's
Hepatitis B Online and *Hepatitis C Online* projects.

Hepatitis B Online

www.hepatitisB.uw.edu

Hepatitis C Online

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This project is funded by the Centers for Disease Control and Prevention (CDC)
Cooperative Agreement (CDC-RFA- PS21-2105)