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Higher proportion of responders with Hepatitis B (HepB) Antibody (Ab) levels ≥ 100 mIU/mL with the tri-antigenic HepB vaccine, Sci-B-Vac®, compared to Engerix-B®

Results from the Phase 3 double-blind, randomized study comparing immunogenicity and safety (PROTECT)

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Introduction

- Although currently licensed HepB vaccines are effective in preventing Hepatitis B virus (HBV) infection in children and healthy young adults, there is reduced vaccine efficacy in older persons, smokers, and those with immunocompromising co-morbidities, including diabetes and obesity[1]
- While HBsAb levels ≥ 10 mIU/mL are considered a correlate of vaccine-induced protection (seroprotection), research has found that breakthrough infections have occurred in vaccinees whose anti-HBs titres are low, < 100 mIU/mL[2]
- Sci-B-Vac® is a tri-antigenic HepB vaccine that contains all three HBV surface antigens (HBsAg) – S, pre-S1, and pre-S2 – is adjuvanted with alum, and is manufactured in mammalian CHO cells
- The pre-S1 antigen induces key neutralizing antibodies that block virus-receptor binding. T cell response to pre-S1 and pre-S2 antigens could further boost responses to the S antigens, resulting in a more immunogenic response[3,4]
- Two Sci-B-Vac ® phase 3 studies were recently completed in Europe, the U.S., and Canada, including the PROTECT study presented here *[NCT03393754]*

Study Design & Objectives

Study Overview:

PROTECT was designed to assess immunogenicity and safety of Sci-B-Vac® *vs.* Engerix-B®

- 1,607 adults, age 18+, healthy or with controlled chronic condition, negative serology (HBV, HCV, HIV), and no severe renal impairment, were randomized 1:1 to receive:
  - Sci-B-Vac®: 10 µg, 1mL injection at 0, 4, 24 wks; or
  - Engerix-B®: 20µg, 1mL injection at 0, 4, 24 wks
- Safety follow up of 12 months from the 1st vaccination

Study Objectives:

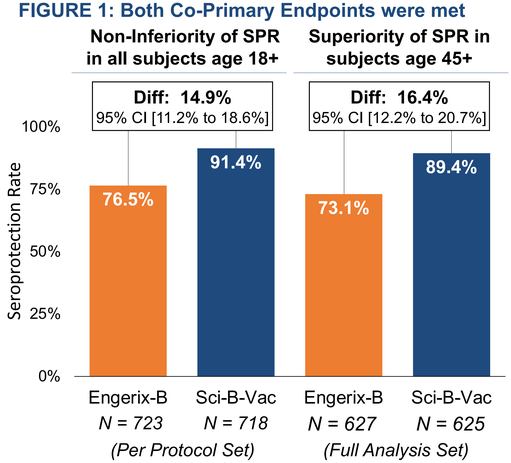
- **Co-Primary:**
  - Non-inferiority of seroprotection rate (SPR) of Sci-B-Vac® *vs.* Engerix-B® in all participants age 18+, 4 weeks after the 3rd vaccination (at day 196)
  - Superiority of SPR of Sci-B-Vac ® *vs.* Engerix-B® in participants age 45+, 4 weeks after the 3rd vaccination (at day 196)
- **Secondary and Exploratory** (not a complete list):
  - Comparison of Geometric Mean Concentration (GMC) of HBsAb at day 196
  - Comparison of HBsAb titers ≥ 100 mIU/mL
  - Reactogenicity, adverse events (AEs), serious AEs (SAEs), medically-significant AEs and new onset of chronic illness (NOCI)

PROTECT Study Subject Disposition

Subjects Screened	2,472	
- Screened Failure	*865 (35%)*	
Subjects Randomized	1,607 at 28 study sites	
Clinical Study Arms	**Engerix-B®**	**Sci-B-Vac®**
Subjects Randomized *(Full Analysis Set)*	811	796
Mean Age	56.6	56.6
Age Segmentation (%)		
- 18-44 years	154 (19%)	145 (18%)
- 45-64 years	361 (45%)	355 (45%)
- 65+ years	296 (37%)	296 (37%)
Gender		
- Male	303 (37%)	315 (40%)
- Female	508 (63%)	481 (60%)
Mean BMI	29.1	29.4
Diabetic Status		
- Diabetic	65 (8%)	60 (8%)
- Non-diabetic	746 (92%)	736 (93%)
Smoking Status		
- Current Smoker	113 (14%)	104 (13%)
- Former Smoker	224 (28%)	203 (26%)
- Non-smoker	474 (58%)	489 (61%)
Country/Region		
- Europe	336 (41%)	332 (42%)
- United States	342 (42%)	338 (43%)
- Canada	133 (16%)	126 (16%)
Withdrew	42 (5.2%)	40 (5.0%)
Completed Study *(All Enrolled Set)*	769	756

Results : Co-Primary Endpoints

FIGURE 1: Both Co-Primary Endpoints were met



- *Non-inferiority :* If the lower bound of the 95% confidence interval (CI) of the difference between the SPR in the Sci-B-Vac arm minus the SPR in the Engerix-B arm is > -5%
- *Statistical superiority :* The lower bound of the same 95% CI is greater than 0%
- *Clinical superiority :* The lower bound of the same 95% CI is > 5%

Results : GMC and % of Subjects with HBsAb titers ≥ 100 mIU/mL

FIGURE 2 : Higher proportion of subjects vaccinated with Sci-B-Vac®, regardless of demographics, achieved HBsAb titers ≥ 100 mIU/mL compared to those vaccinated with Engerix-B®, 4 weeks after the 3rd vaccination (day 196)

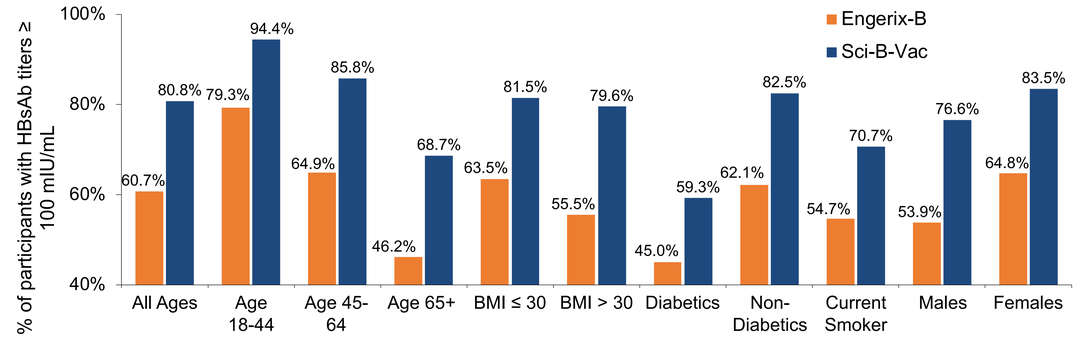


TABLE 1: Higher GMC of HBsAb titers were observed in patients vaccinated with Sci-B-Vac® compared to those vaccinated with Engerix-B®, regardless of demographics, 4 weeks after the 3rd vaccination (day 196)

GMC *mIU/mL*	All Ages	Age 18-44	Age 45-64	Age 65+	BMI ≤ 30	BMI > 30	Diabetics	Non-Diabetics	Current Smokers	Males	Females
Engerix-B®	192.6	720.6	276.5	63.7	260.9	109.9	41.3	221.5	161.9	106.6	273.5
Sci-B-Vac®	1148.3	4570.6	1577.4	410.2	1343.0	884.1	222.4	1312.3	449.5	761.1	1498.3
GMC Ratio	***6.0X***	***6.3X***	***5.7X***	***6.4X***	***5.1X***	***8.0X***	***5.4X***	***5.9X***	***2.8X***	***7.1X***	***5.5X***

Results : Safety & Tolerability

TABLE 2 : The most common AEs were local reactogenicity symptoms, mostly of mild-to-moderate severity, which resolved without intervention within 2-3 days – there was no increase of reactogenicity with subsequent dosing

		Sci-B-Vac® (N=796)	Engerix-B® (N=811)
Local AEs – Injection Site			
Pain	Mild or Moderate	502 (63.1%)	293 (36.1%)
	Severe+	1 (0.1%)	1 (0.1%)
Tenderness	Mild or Moderate	376 (47.2%)	279 (34.4%)
	Severe+	8 (0.9%)	3 (0.4%)
Itchiness	Mild or Moderate	75 (9.4%)	54 (6.6%)
	Severe+	1 (0.4%)	2 (0.2%)
Redness	Mild or Moderate	16 (2.1%)	8 (1.0%)
	Severe+	0 (0.0%)	0 (0.0%)
Swelling	Mild or Moderate	16 (2.0%)	8 (1.0%)
	Severe+	0 (0.0%)	3 (0.4%)

- Systemic AEs within 7 days of vaccination (headache, fatigue, nausea and diarrhea) were comparable between Sci-B-Vac ® and Engerix-B ® except for myalgia which was more common in Sci-B-Vac® (34.7% *vs* 24.3%)
- Unsolicited AEs within 28 days of vaccination were comparable between Sci-B-Vac® (46.4%) and Engerix-B® (48.0%)
- SAEs during the study were comparable between Sci-B-Vac® (4.0%) and Engerix-B® (2.6%)
- Medically-attended AEs during the study were comparable between Sci-B-Vac® (25.4%) and Engerix-B® (28.5%)
- NOCI during the study was comparable − Sci-B-Vac® (3.3%) and Engerix-B® (3.7%)

Conclusions

- PROTECT study met both co-primary endpoints – SPR for Sci-B-Vac® was non-inferior to Engerix-B ® in adults age ≥18 years and superior in adults age ≥45 years
- Sci-B-Vac® induced a more robust immune response as measured by both SPR and GMC of HBsAb titers, compared to Engerix-B®, reducing the proportion of non- or low-responders
- Both vaccines were well tolerated with >95% completion of the 3-dose course of vaccination
- Sci-B-Vac® had higher rates of mild or moderate injection site pain and tenderness, and myalgia compared to Engerix-B®
- No new or unexpected safety signals were observed, and safety and tolerability were consistent with the known profile of Sci-B-Vac®

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Disclosure

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