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Rapid increase in anti-HBsAg titers and higher seroprotection rates in adults immunized with Sci-B-Vac® compared to a monovalent hepatitis B vaccine:

Results from PROTECT – A double-blind, randomized, controlled, phase-3 study

Joanne M. Langley[1*], Timo Vesikari[2], Nathan Segall[3], Brian J Ward[4*], Curtis Cooper[5*], Guillaume Poliquin[6*], Bruce Smith[7], Pierre van Damme[8], Isabel Leroux-Roels[9], Geert Leroux-Roels[10], Nathalie Machluf[11], Johanna Spaans[12], Bebi Yassin-Rajkumar[12], David E. Anderson[12], Vlad Popovic[12], and Francisco Diaz-Mitoma[12]

[1]Departments of Pediatrics and Community Health and Epidemiology, Canadian Center for Vaccinology, Halifax, Nova Scotia B3K 6R8, Canada; [2]Vaccine Research Center, Tampere, Finland; [3]Clinical Research Atlanta, Stockbridge, Georgia, 30281, USA; [4]McGill University Health Centre-Vaccine Study Centre, Montreal, Quebec H9H 4Y6, Canada; [5]Department of Medicine, Ottawa Hospital, Ottawa, Ontario K1H8L6, Canada; [6]University of Manitoba, Winnipeg, Manitoba R3E 3P4, Canada; [7]Department of Mathematics and Statistics, Dalhousie University, Halifax, Nova Scotia B3H 4R2, Canada; [8]University of Antwerp-Center for the Evaluation of Vaccination, Universiteitsplein, Wilrijk, Belgium; [9]Universitair Ziekenhuis Gent, Gent, Belgium; [10]Ghent University Hospital-UZ Gent, Gent, Belgium; [11]SciVac Ltd/VBI, Rehovot 7610303, Israel; [12]VBI Vaccines Inc., Ottawa, Ontario K1V 1C1, Canada;* Canadian Immunization Research Network

INTRODUCTION

- Although licensed Hepatitis B virus (HBV) vaccines are effective in preventing HBV in children and healthy young adults, there is reduced vaccine efficacy in older persons, and those with diabetes, obesity or who smoke cigarettes [1].
- Sci-B-Vac®:
  - A trivalent HBV vaccine that contains S antigen and pre-S1 and pre-S2 components of the HBV surface antigen (HBsAg)
  - Adjuvanted with alum
  - Manufactured in mammalian cells
- Pre-S1 antigen induces key neutralizing antibodies that block virus-receptor binding and T cell response to pre-S1 and pre-S2 antigens could further boost responses to the S antigens, resulting in a more immunogenic response [2,3].

OBJECTIVES

Co-primary objectives:

- Non-inferiority of seroprotection rates (SPRs) (>10 IU/mL) of Sci-B-Vac® vs. Engerix-B® in all participants age ≥ 18 years, 4 weeks after 3rd vaccination (at day 196)
- Superiority of SPR of Sci-B-Vac® vs. Engerix-B® in participants age ≥ 45 years, 4 weeks after 3rd vaccination (at day 196)

Secondary and Exploratory objectives:

- Non-inferiority of SPRs of Sci-B-Vac® after receiving the 2nd vaccination compared with SPR of Engerix-B® after receiving the 3rd vaccination.
- Reactogenicity (day 1-6), adverse events (AEs) at day 1-28 postvaccination and serious AEs, medically significant events or new onset of chronic illness (NOCI) through day 336
- Comparison of Geometric Mean Concentration (GMC) of anti-HBs at day 196

STUDY DESIGN

- Eligibility criteria : (i) ≥ age 18, (ii) any gender, (iii) healthy or controlled chronic condition (e.g. Type 2 Diabetes), (iv) negative serology (HBV, HCV, HIV), and (v) no severe renal impairment
- Age stratification : Age 18-44, 45-64, and 65+
- Vaccination dosages & schedule :
  - Sci-B-Vac® : 10µg, 1mL injection at 0, 4, 24 wks
  - Engerix-B® : 20µg, 1mL injection at 0, 4, 24 wks
- Safety follow-up : 12 months

Clinical Trials Identifier: NCT03393754

RESULTS

Immunogenicity

Figure 1:
Both PROTECT Co-Primary Endpoints Met

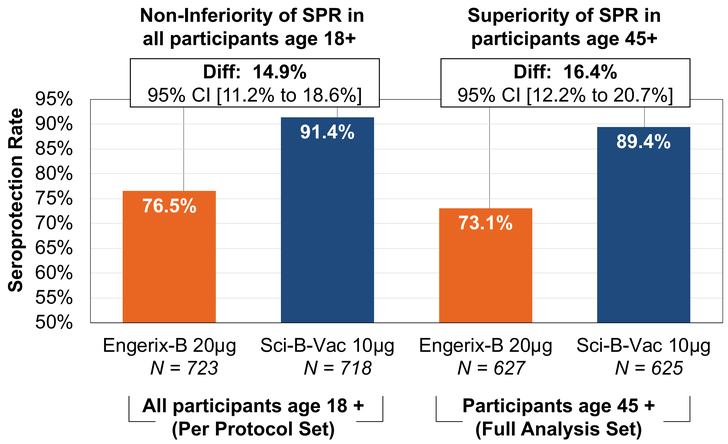


Figure 2:
Higher (5-8x) (GMC) was observed with Sci-B-Vac® after 3rd vaccination, across key subgroups

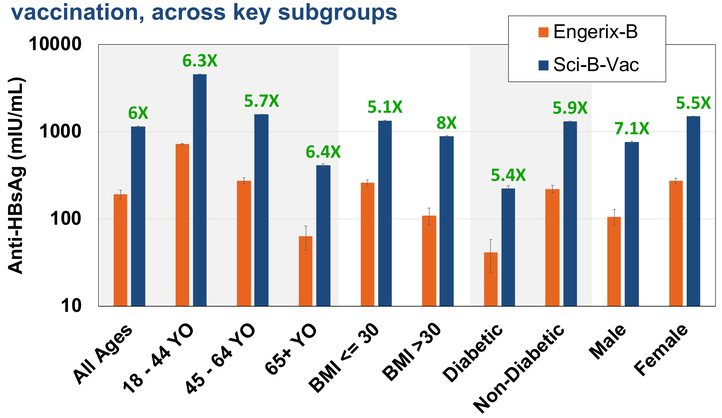
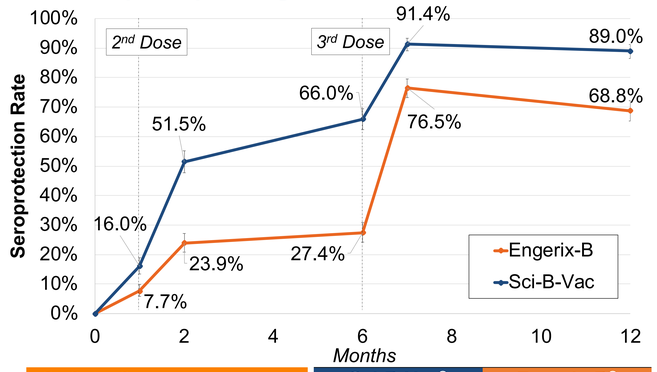


Figure 3:
SPRs for Sci-B-Vac® show a rapid increase in anti-HBsAg titers in all participants age 18+



Safety & Tolerability

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

- Percentage of systemic AEs (headache, fatigue, nausea and diarrhea) were comparable between Sci-B-Vac® and Engerix-B®; however myalgia was more common in Sci-B-Vac® (34.7% *vs* 24.3%)
- Percentage of subjects with ≥ 1 unsolicited AE within 28 days of vaccination was comparable between Sci-B-Vac® (46.4%) and Engerix-B® (48.0%)
- Percentage of participants with ≥ 1 serious AE was comparable − Sci-B-Vac® (4.0%) and Engerix-B® (2.6%)
- Percentage of participants with at least one NOCI was comparable − Sci-B-Vac® (3.3%) and Engerix-B® (3.7%)
- Percentage of participants with at least one medically attended AE was comparable − Sci-B-Vac® (25.4%) and Engerix-B® (28.5%)

PROTECT Study Participant Disposition

SCREENED: **2,472**
Screening Failure: 868 (35%)
RANDOMIZED: **1,607**
28 clinical study sites in U.S., Europe, and Canada

	Sci-B-Vac®	Engerix-B®
FULL ANALYSIS SET:	**796**	**811**
Age:		
• 18-44	145 (18%)	154 (19%)
• 45-64	355 (45%)	361 (45%)
• 65+	296 (37%)	296 (37%)
Gender:		
• Male	315 (40%)	303 (37%)
• Female	481 (60%)	508 (63%)
Other Variables:		
• Avg. BMI (kg/m²)	29.4 (13.5-56.3)	29.1 (11.3-63.5)
• % Type 2 Diabetes	7.5%	8.0%
• % Current Smokers	13.1%	13.9%
Geography:		
• United States	255	205
• Canada	116	99
• Europe	285	249
Withdrew	**40 (5.0%)**	**42 (5.2%)**
Completed (%)	**95.2%**	**96.8%**
PER PROTOCOL SET	**756**	**769**

CONCLUSIONS

- SPR of Sci-B-Vac® was non-inferior to Engerix-B® in adults ≥18 years and superior in adults ≥ 45 years.
- Sci-B-Vac® demonstrated more rapid increase in seroprotection after the 1st and 2nd vaccinations; however it did not meet the secondary objective of non-inferiority of SPRs of Sci-B-Vac® after the 2nd vaccination compared with SPR of Engerix-B® after the 3rd vaccination.
- Sci-B-Vac® induced 5-8x higher antibody GMC compared to Engerix-B®.
- Higher rates of injection site pain, tenderness, and myalgia per injection were noted with Sci-B-Vac® compared to Engerix-B®; however, AEs were mostly mild-to-moderate in intensity. No safety signals were observed, and safety and tolerability were consistent with the known profile of Sci-B-Vac®.

DISCLOSURE

Dr. Langley was the Principal Investigator of this study and her institution received financial support for the services performed for conducting the study at her study center(s)

ACKNOWLEDGEMENTS

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CONTACT INFORMATION

Dr. Joanne Langley joanne.langley@dal.ca
Dr. Francisco Diaz-Mitoma fdiazmitoma@vbivaccines.com

VBI VACCINES