Rapid onset of seroprotection in young adults immunized with a 3-antigen hepatitis B virus (HBV) vaccines compared to a single-antigen HBV vaccines

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Introduction

- Hepatitis B (HBV) infection remains a significant public health risk, with an estimated 240-350 million people chronically infected worldwide.
- In the U.S., rates of new HBV infections are highest among individuals age 30-39 years, underscoring the importance of continued adult vaccination against HBV.
- Younger adults who are at risk of HBV infection through exposure in the workplace or home, travel to countries with high HBV prevalence, or through exposure as a result of high-risk behavior, need a highly effective and safe HBV vaccines with a rapid onset of seroprotection.
- Sci-B-Vac® is a 3-antigen HBV vaccine that contains all three HBV surface antigens (HBsAg) – S, pre-S1, and pre-S2 – is adjuvanted with alum, and 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 vaccine.[1,2]
- To date, four (4) Phase 3 and one (1) Phase 4 studies have assessed kinetics of seroprotection rate in adults vaccinated with Sci-B-Vac compared to a single-antigen HBV vaccines, Engerix-B® (GSK).

Study Designs & Objectives

	PROTECT	CONSTANT	38-13-040	SG-005-5	SCIB018
	Phase 3, 2-arm safety and immunogenicity study *[NCT03393754]*	**Phase 3, 4-arm lot-to-lot consistency study** *[NCT03408730]*	**Phase 3 study conducted in Russia** *[NCT04209400]*	**Phase 3 study conducted in Vietnam** *[NCT04531098]*	**Single-arm, Phase 4 study conducted in Israel** *[NCT04179786]*
N size	1,607	2,838	100	402	91
Age Range	18+ years	18-45 years	18-45 years	18-45 years	20-40 years
Sci-B-Vac	10 µg	10 µg	10 µg	10 µg	10 µg
Control Vaccine	20 µg Engerix-B	20 µg Engerix-B	20 µg Engerix-B	20 µg Engerix-B	-
Random.	1:1	1:1:1:1	1:1	1:1:1	-
Dosing	0, 4, 24 weeks	0, 4, 24 weeks	1, 28, 180 days	0, 30, 180 days	0, 1, 6 months
Primary Endpoint(s)	Based on seroprotection rates (SPR) at Day 196: i. Non-inferiority in adults ≥ age 18 ii. Superiority in adults ≥ age 45	Consistency of immune response at Day 196 as measured by GMC of anti-HBs across three consecutive lots of Sci-B-Vac	Seroconversion rates after the 2nd and 3rd vaccination	Demonstration of clinical equivalence of 2 production lots of Sci-B-Vac	Qualify new in-house reference standard for quality control in compliance with the European Pharmacopeia and the Israeli Ministry of Health
Secondary& Exploratory Endpoint(s)	Safety and tolerability, anti-HBs titers, kinetics of immune response	Safety and tolerability, SPR, anti-HBs titers, kinetics of immune response	Seroprotection rates after 2nd and 3rd vaccination, safety and tolerability	Anti-HBs response just prior to and 6 months after 3rd dose, safety and tolerability	Characterize immunological responses, safety and tolerability

Study Participant Disposition

	PROTECT		CONSTANT		38-13-040		SG-005-5			SCIB018
Subjects Screened	2,472		4,452		100		N/A			199
- Screen Failure	*865 (35%)*		*1,614 (36%)*		-		*N/A*			107
Subjects Randomized	1,607 at 28 study sites		2,838 at 35 study sites		100 at 3 study sites		402 at 1 study site			N/A
Clinical Study Arms	Engerix-B® 20 µg	Sci-B-Vac® 10 µg	Engerix-B® 20 µg	Pooled Sci-B-Vac® 10 µg	Engerix-B® 20 µg	Sci-B-Vac® 10 µg	Engerix-B® 20 µg	Sci-B-Vac® 10 µg *[BTG Lot]*	Sci-B-Vac® 10 µg *[SG Lot]*	Sci-B-Vac® 10 µg
Subjects Randomized	811	796	712	2,126	50	50	134	134	134	91
Mean Age	56.6	56.6	33.4	33.5	30.6	28.4	20.6	20.9	20.6	26.2
% of Subjects Age 18-45	154 (19%)	145 (18%)	100%	100%	100%	100%	100%	100%	100%	100%
Gender										
- Male	303 (37%)	315 (40%)	291 (41%)	907 (43%)	18 (36%)	21 (42%)	38 (33%)	38 (34%)	34 (28%)	74 (81%)
- Female	508 (63%)	481 (60%)	421 (59%)	1219 (57%)	32 (64%)	29 (58%)	79 (68%)	74 (66%)	86 (72%)	17 (19%)
Mean BMI	29.1	29.4	25.7	25.9	23.6	24.2	20.0	20.9	20.0	-
Diabetic Status										
- Diabetics	65 (8%)	60 (8%)	-	-	-	-	-	-	-	-
- Non-diabetics	746 (92%)	736 (92%)								
Smoking Status										
- Current smoker	113 (14%)	104 (13%)	136 (19%)	408 (19%)	-	-	6 (5%)	1 (1%)	2 (2%)	25 (38%)
- Former smoker	224 (28%)	203 (26%)	141 (20%)	404 (19%)	-	-	-	-	-	13 (14%)
- Non-smoker	474 (58%)	489 (61%)	435 (61%)	1313 (62%)	-	-	111 (95%)	111 (99%)	118 (98%)	44 (48%)
Country/Region										
- United States	342 (42%)	338 (43%)	188 (26%)	564 (27%)	-	-	-	-	-	-
- Europe	336 (41%)	332 (42%)	493 (69%)	1472 (69%)	-	-	-	-	-	-
- Canada	133 (16%)	126 (16%)	31 (4%)	90 (4%)	-	-	-	-	-	-
- Russia	-	-	-	-	50 (100%)	50 (100%)	-	-	-	-
- Vietnam	-	-	-	-	-	-	134 (100%)	134 (100%)	134 (100%)	-
- Israel	-	-	-	-	-	-	-	-	-	91 (100%)
Withdrew	42 (5%)	40 (5%)	69 (10%)	228 (11%)	3 (6%)	3 (6%)	15 (11%)	18 (13%)	13 (10%)	8 (9%)
Completed Study	769	756	643	1,898	47	47	119	116	121	83

Results : Rapid Onset of Seroprotection (anti-HBs ≥ 10 mIU/mL) in Adults Age 18-45 Years

Figure 1 : PROTECT

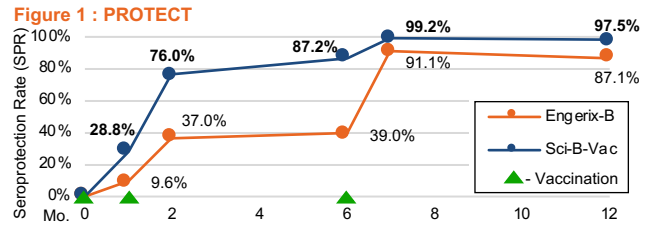


Figure 2 : CONSTANT

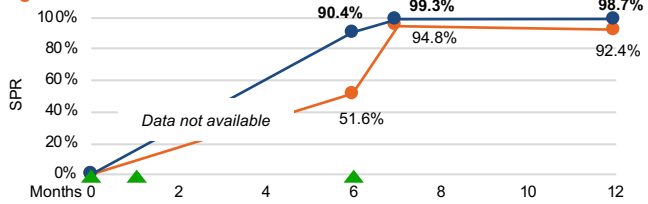


Figure 3 : 38-13-040

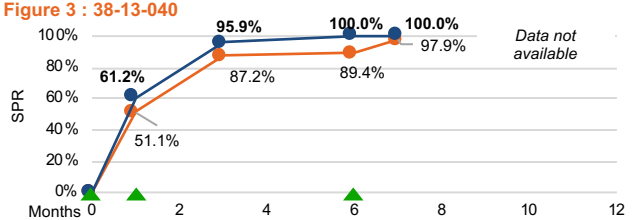


Figure 4 : SG-005-5

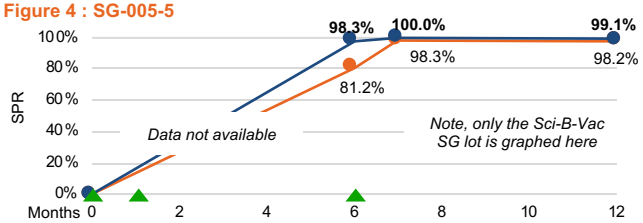
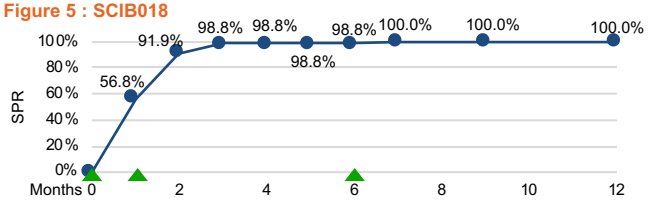


Figure 5 : SCIB018



Conclusions

- In all 5 studies, Sci-B-Vac demonstrated its ability to rapidly induce high rates of seroprotection in adults age 18-45, a population in which HBV infection rates are the highest.
- Vaccination with Sci-B-Vac achieved SPRs of 87.2-100.0% after 2 doses, by month 6, vs. 39.0-89.4% with Engerix-B.
- These seroprotection rates increased to 99.2%+ after the 3rd dose, vs. 91.1-98.3% with Engerix-B
- Data from two of the controlled studies show that Sci-B-Vac induced SPRs of 76.0-95.9% by month 3, after 2 doses, compared to 37.0-87.2% with Engerix-B
- No major safety signals were observed, and adverse events were well-balanced and consistent with the known vaccine safety profiles
- Sci-B-Vac had higher rates of mild or moderate injection site pain and tenderness, and myalgia compared to Engerix B

References

1. Heermann KH *et al., J Virol.* 1984;52(2):396-402
2. Milich DR *et al. Science.* 1985;228(4704):1195-1199.

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Disclosure

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