Abstract Identifier : 420

A 3-antigen prophylactic hepatitis B virus vaccine confers rapid onset of protection in young adults, age 18-45, compared to a single-antigen hepatitis B virus vaccine

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INTRODUCTION

- Vaccination rates against Hepatitis B Virus (HBV), a leading cause of liver cirrhosis and hepatocellular carcinoma, remain low in adults.
- The European Centre for Disease Prevention and Control cites adults age 25-34 as the age group most affected by both acute and chronic HBV infections, accounting for 30% of reported cases by 30 EU/EEA Member States in 2017, followed by adults age 35-44 years.
- 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 vaccine with a rapid onset of seroprotection.
- 3A-HBV is a 3-antigen HBV vaccine that contains the three distinct 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]

STUDY DESIGNS & OBJECTIVES

	PROTECT Phase 3 (Europe, US, Canada) *[NCT03393754]*	CONSTANT Phase 3 (Europe, US, Canada) *[NCT03408730]*	SG-005-5 Phase 3 (Vietnam) *[NCT04531098]*	38-13-040 Phase 3 (Russia) *[NCT04209400]*	SCIB018 Phase 4 (Israel) *[NCT04179786]*
N size	1,607	2,838	402	100	91
Age Range	18+ years	18-45 years	18-45 years	18-45 years	20-40 years
3A-HBV	10 µg	10 µg	10 µg	10 µg	10 µg
Control Vaccine	20 µg 1A-HBV	20 µg 1A-HBV	20 µg 1A-HBV	20 µg 1A-HBV	-
Random.	1:1	1:1:1:1	1:1:1	1:1	-
Dosing	0, 4, 24 weeks	0, 4, 24 weeks	0, 30, 180 days	1, 28, 180 days	0, 1, 6 months
Primary Endpoint(s)	Based on SPRs 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 3A-HBV	Demonstration of clinical equivalence of 2 production lots of 3A-HBV	Seroconversion rates after the 2nd and 3rd vaccination	Qualify new in-house reference standard 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	Anti-HBs response just prior to and 6 months after 3rd dose, safety and tolerability	SPRs after 2nd and 3rd vaccination, safety and tolerability	Characterize immunological responses, safety and tolerability

STUDY PARTICIPANT DISPOSITION

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

RESULTS : Seroprotection Rates (SPR; % with anti-HBs titres ≥ 10 mIU/mL) in Adults Age 18-45 Years

Figure 1 : PROTECT

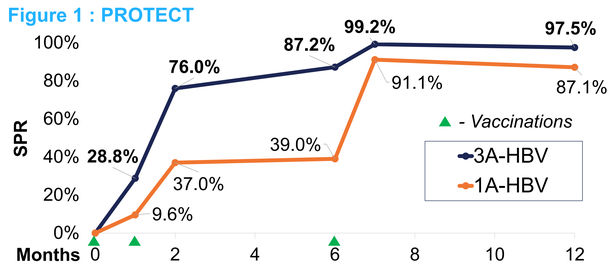


Figure 2 : CONSTANT

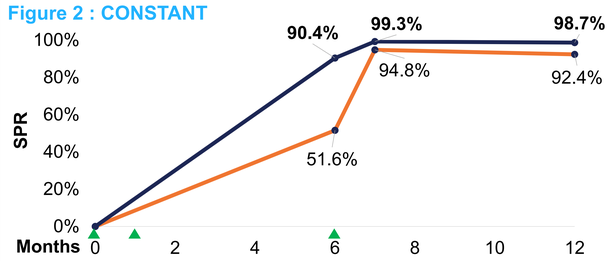


Figure 3 : SG-005-5

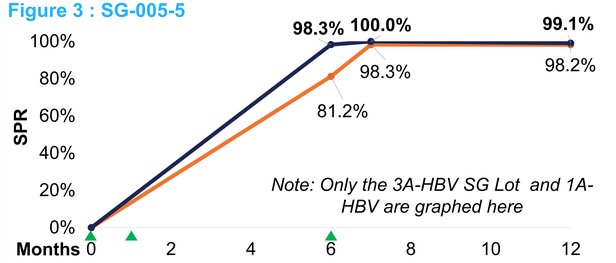


Figure 4 : 38-13-040

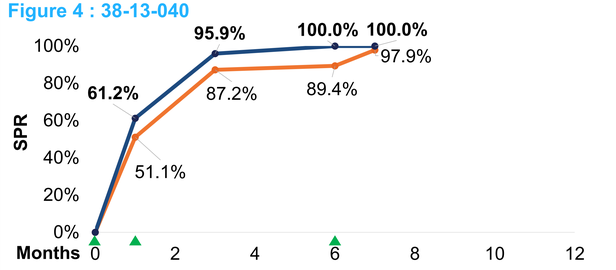
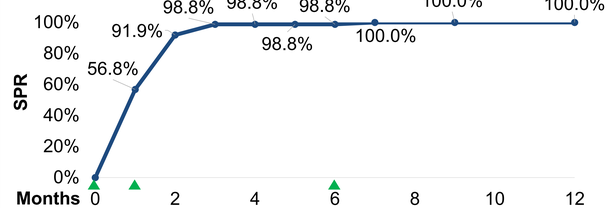


Figure 5 : SCIB018



CONCLUSIONS

- In all 5 studies, 3A-HBV demonstrated its ability to rapidly induce high SPRs in adults age 18-45, a population in which HBV infection rates are the highest.
- Vaccination with 3A-HBV. achieved SPRs of 87.2-100.0% after 2 doses (Month 6) *vs.* 39.0-89.4% with 1A-HBV.
- SPRs increased to 99.2%+ after the 3rd dose of 3A-HBV *vs.* 91.1-98.3% with 1A-HBV.
- No major safety signals were observed, and adverse events were well-balanced and consistent with the known safety profiles of both vaccines.
- 3A-HBV had higher rates of mild or moderate injection site pain and tenderness, and myalgia compared to 1A-HBV.

REFERENCES

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

ACKNOWLEDGEMENTS

We thank all clinicians, nurses, and volunteers who contributed to these studies. The contribution of scientists and technologists at VBI Vaccines Inc. is greatly appreciated.

DISCLOSURE

Drs. Timo Vesikari and Joanne M. Langley were the Principal Investigators of these studies and their institutions received financial support for the services performed for conducting the studies.

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