



# Higher hepatitis B antibody titers induced in all adults vaccinated with a 3-antigen hepatitis B (HBV) vaccine, compared to a single-antigen HBV vaccine: Results from two pivotal phase 3 double-blind, randomized studies (PROTECT and CONSTANT)

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## Introduction

- More than 2 billion individuals worldwide have evidence of past or current hepatitis B virus (HBV) infection.
- With no available cure for such an infectious disease, vaccination remains the most important intervention in the prevention of HBV infection and associated diseases and complications.
- The magnitude of the immune response to HBV vaccines can be measured by serum levels of anti-HBs, persistence and durability of which is believed to be dependent upon peak levels induced.
- Sci-B-Vac<sup>®</sup> 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.<sup>1,2</sup>
- Two Sci-B-Vac<sup>®</sup> phase 3 studies – PROTECT and CONSTANT – were recently completed in the U.S., Europe, and Canada.

## Study Design & Objectives

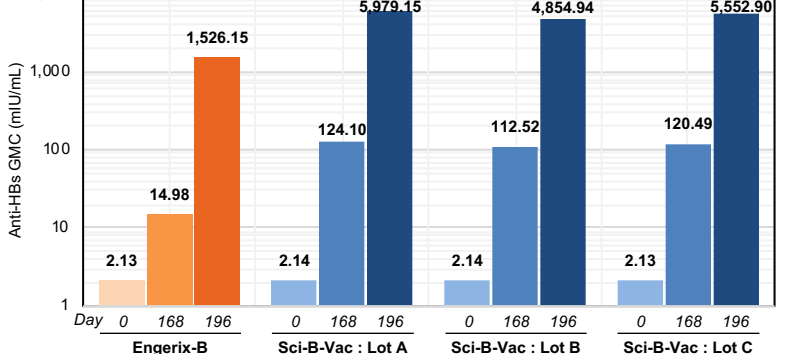
	PROTECT	CONSTANT
	<b>2-arm safety and immunogenicity study</b> [NCT03393754]	<b>4-arm lot-to-lot consistency study</b> [NCT03408730]
<b>N size</b>	1,607	2,838
<b>Age Range</b>	18+ years	18-45 years
<b>Sci-B-Vac</b>	10 µg	10 µg
<b>Control Vaccine</b>	20 µg Engerix-B <sup>®</sup> (GSK)	20 µg Engerix-B <sup>®</sup> (GSK)
<b>Random.</b>	1:1	1:1:1:1
<b>Dosing</b>	0, 4, 24 weeks	0, 4, 24 weeks
	Based on seroprotection rates (SPR):	Consistency of immune response as measured by GMC of anti-HBs across three consecutive lots of Sci-B-Vac
<b>Primary Endpoint(s) (at Day 196)</b>	i. Non-inferiority in adults ≥ age 18 ii. Superiority in adults ≥ age 45	
<b>Secondary &amp; Exploratory Endpoint(s)</b>	Safety and tolerability, anti-HBs titers, kinetics of immune response	Safety and tolerability, SPR, anti-HBs titers, kinetics of immune response

## Study Participant Disposition

	PROTECT		CONSTANT			
<b>Subjects Screened</b>	2,472		4,452			
- Screen Failure	865 (35%)		1,614 (36%)			
<b>Subjects Randomized</b>	1,607 at 28 study sites		2,838 at 37 study sites			
<b>Clinical Study Arms</b>	Engerix-B <sup>®</sup> 20 µg	Sci-B-Vac <sup>®</sup> 10 µg	Engerix-B <sup>®</sup> 20 µg	Lot A Sci-B-Vac <sup>®</sup> 10 µg	Lot B Sci-B-Vac <sup>®</sup> 10 µg	Lot C Sci-B-Vac <sup>®</sup> 10 µg
<b>Subjects Randomized</b>	811	796	712	711	709	706
<b>Mean Age</b>	56.6	56.6	33.4	33.8	32.9	33.9
<b>Age Segmentation</b>			100% age 18-45 years			
- 18-44 years	154 (19%)	145 (18%)				
- 45-64 years	361 (45%)	355 (45%)				
- 65+ years	296 (37%)	296 (37%)				
<b>Gender</b>						
- Male	303 (37%)	315 (40%)	291 (41%)	303 (43%)	313 (44%)	291 (41%)
- Female	508 (63%)	481 (60%)	421 (59%)	408 (57%)	396 (56%)	415 (59%)
<b>Mean BMI</b>	29.1	29.4	25.7	25.9	25.8	26.0
<b>Diabetic Status</b>			N/A			
- Diabetics	65 (8%)	60 (8%)				
- Non-diabetics	746 (92%)	736 (92%)				
<b>Smoking Status</b>						
- Current smoker	113 (14%)	104 (13%)	136 (19%)	139 (20%)	143 (20%)	126 (18%)
- Former smoker	224 (28%)	203 (26%)	141 (20%)	137 (19%)	131 (19%)	136 (19%)
- Non-smoker	474 (58%)	489 (61%)	435 (61%)	435 (61%)	435 (61%)	443 (63%)
<b>Country/Region</b>						
- United States	342 (42%)	338 (43%)	188 (26%)	191 (27%)	187 (26%)	186 (26%)
- Europe	336 (41%)	332 (42%)	493 (69%)	489 (69%)	493 (70%)	490 (70%)
- Canada	133 (16%)	126 (16%)	31 (4%)	31 (4%)	29 (4%)	30 (4%)
- Other	42 (5.2%)	40 (5.0%)	69 (9.7%)	75 (10.5%)	72 (10.2%)	81 (11.5%)
<b>Withdrew</b>			643	636	637	625
<b>Completed Study</b>	769	756				

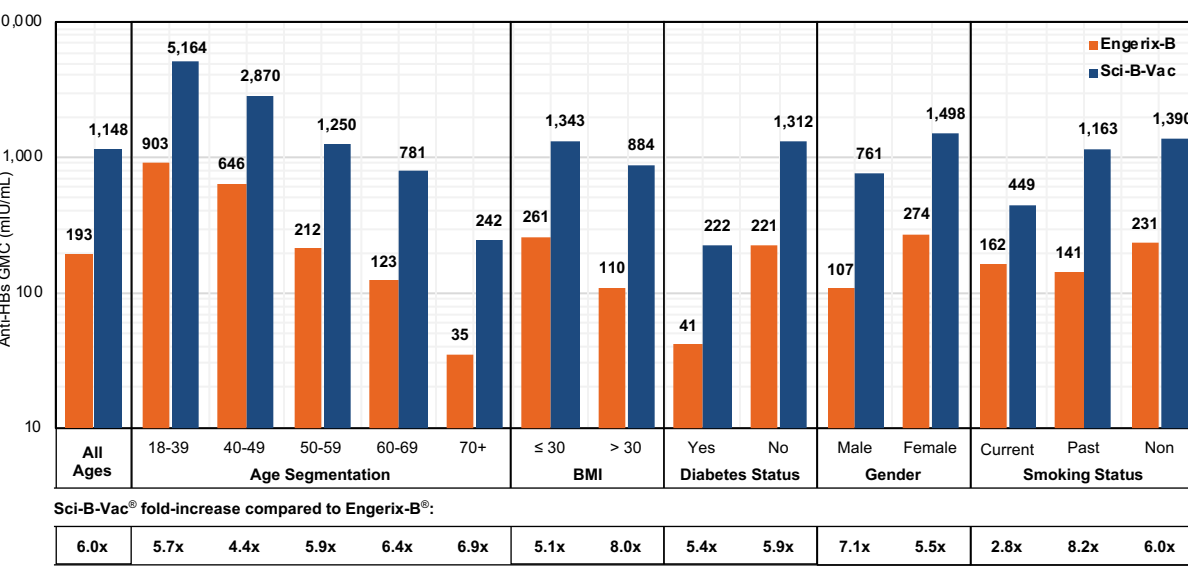
## Results : CONSTANT

FIGURE 1: Geometric Mean Concentrations (GMC) of anti-HBs induced across the 3 lots of Sci-B-Vac<sup>®</sup> were > 7.5x higher after two doses [Day 168], and remained substantially higher after the third dose [Day 196], compared to those induced by Engerix-B<sup>®</sup> at the same time points



## Results : PROTECT

FIGURE 2: GMC of anti-HBs for Sci-B-Vac<sup>®</sup> were 6x higher in all participants age ≥ 18 years and 4-8x higher in key subgroups, regardless of age, BMI, gender, or diabetic status, at Day 196 compared to Engerix-B<sup>®</sup>



## Conclusions

- Sci-B-Vac<sup>®</sup> continued to demonstrate its ability to safely and rapidly elicit robust immune responses in adults, as illustrated in the results of these two pivotal Phase 3 studies
- In PROTECT, 4-8x higher anti-HBs GMC was maintained for patients who received Sci-B-Vac<sup>®</sup> compared to Engerix-B<sup>®</sup>, regardless of age, BMI, or diabetic status
- In healthy 18-45 year-olds in CONSTANT, after two doses, at day 168, Sci-B-Vac<sup>®</sup> elicited a mean anti-HBs GMC, across the pooled lots, of 119 mIU/mL, > 7.5x higher anti-HBs titers compared to Engerix-B<sup>®</sup>
- Higher injection site-related reactogenicities were noted with Sci-B-Vac<sup>®</sup> compared to Engerix-B<sup>®</sup> in PROTECT and CONSTANT, mostly of mild or moderate severity, which resolved without intervention in 2-3 days
- No major safety signals were observed – adverse events were well-balanced and consistent with the known safety profile of Sci-B-Vac<sup>®</sup>

## Acknowledgements

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## References

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

## Disclosure

Dr. Langley was the Principal Investigator of this study and her institution received financial support for the services performed for conducting the studies.

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