High Seroprotection Rates Achieved with Two Doses of Sci-B-Vac, a Third Generation Hepatitis B Vaccine containing PreS1, PreS2 and S Antigens.

F Diaz-Mitoma[1], N Machluf [2], D Anderson [1], J Spaans[1], and A Mazaltov[2]
[1]VBI Vaccines Inc. Ottawa, ON Canada; [2]SciVac, Rehovot, Israel

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INTRODUCTION

- Acute hepatitis B virus (HBV) infection may develop into a chronic disorder leading to a carrier state, chronic hepatitis, cirrhosis, and liver cancer
- Although licensed HBV vaccines are safe and effective in controlling HBV in healthy individuals younger than 40 years of age[1], vaccine efficacy decreases as individuals age, as they develop immuno-compromising conditions or habits (diabetes, smoking, etc.), or if there is non-compliance with the complete required vaccine regimen
- Except for immuno-compromised individuals, it is generally accepted that once an individual is seroprotected, defined as achieved anti-HBs ≥ 10 mIU/mL, they remain protected for the duration of their life[2]
- There has been significant decrease in the incidence rate of acute HBV in the US, Europe and in Asia, however, the prevalence of chronic HBV and the prevalence of HBV carriers have remained constant or have increased[1]
- Europe, more so than the US, faces an increased risk of HBV due to increasing global mobilization and the refugee crisis
- A more potent vaccine that is safe, well-tolerated, and protects individuals faster or with fewer doses may address both public health and compliance needs
- Sci-B-Vac® is a third-generation HBV vaccine that is:
  - The only commercially-available HBV vaccine to contain the Pre-S1, Pre-S2, and S components of HBV surface antigens (HBsAg)
  - Adjuvanted with alum
  - Manufactured in mammalian cells

AIMS

1. To test the ability of Sci-B-Vac® to elicit robust seroprotection rates after two and three vaccinations
2. To compare the safety and immunogenicity of Sci-B-Vac® to Engerix-B® in hepatitis B-naive subjects

METHODS

Seroprotection rates (SPR or anti-HBs of ≥ 10 mIU/mL) were analyzed after administration of the second and third doses of Sci-B-Vac® in three clinical studies:

1. *A Phase 4 study conducted in Israel* : a single-arm, open-label study (n=83 Sci-B-Vac®)
2. *A Phase 3 study conducted in Vietnam* : a single-blind comparative, controlled, and randomized study (n=120 Sci-B-Vac® : n=117 Engerix-B®)
3. *A Phase 3 study conducted in Russia* : a comparative, randomized study (n=47 Sci-B-Vac® : n=47 Engerix-B®)

The three studies were conducted according to good clinical practice with the following designs:

Subject population : Healthy volunteers between 18-45 years of age

Vaccination schedule : 0, 1, and 6 months

Dosage : Sci-B-Vac® contained 10 micrograms of HBs antigen formulated in alum hydroxide, Engerix-B® contained 20 micrograms of HBs antigen

Testing : Blood for hepatitis B antibody testing was collected before and after each immunization. Standard diary cards were collected to determine vaccine reactogenicity and safety. Volunteers were followed for a total of 12 months

RESULTS

Safety and Tolerability :

Both vaccines had similar reactogenicity and safety profiles, with no safety signals detected during subject follow-up

Russia Phase 3 study:

An increase in the levels of AST, ALT, and GGT were noted in 1 subject as manifestations of fatty liver disease. No systemic symptoms in response to vaccine administration were identified. Local symptoms (erythema, itch, pain) emerged at equal rates in both study arms. In total, 16 adverse events were recorded in 9 subjects - Engerix-B® arm 13 adverse events in 7 subjects; Sci-B-Vac® arm 3 adverse events in 2 subjects.

Vietnam Phase 3 study:

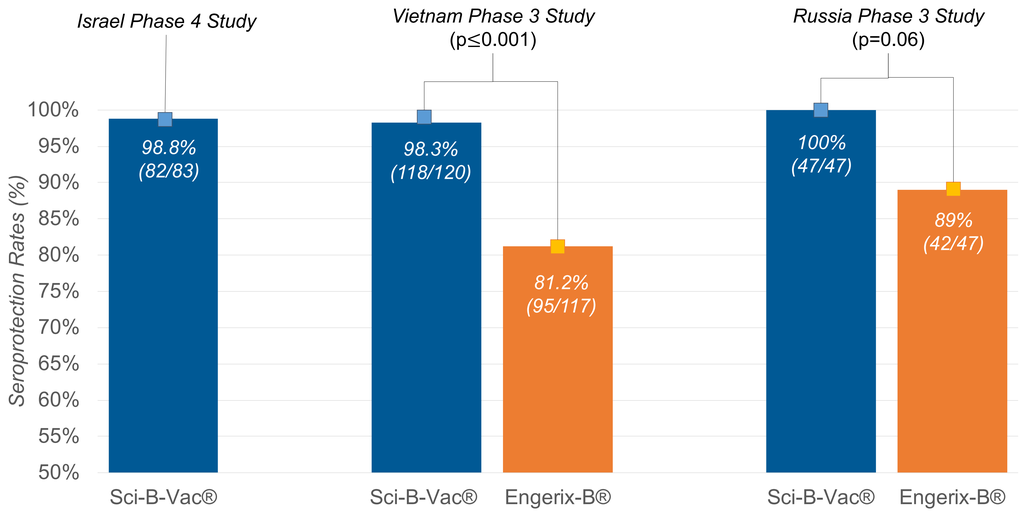
54% of subjects receiving Sci-B-Vac® and 35% of subjects receiving Engerix-B® experienced reactogenicity events. The most common were injection site pain, followed by myalgia, fatigue, and malaise. A total of 5 severe adverse events occurred in this study, 4 in the Engerix-B® arm and 1 in the Sci-B-Vac® arm, but only 1 was related to the study vaccine – syncope in the subject in the Sci-B-Vac® study arm.

Immunogenicity :

Seroprotection Rates (SPR) and anti-HBs titers (GMC)

Studies		Month 2-post 2nd dose SPR% (GMC)	Month 6-post 2nd dose SPR% (GMC)	Month 7-post 3rd dose SPR% (GMC)	Month 12 SPR% (GMC)
Israel Phase 4	Sci-B-Vac®	91% (358)	98.8% (300)	100% (6,799)	100% (2,281)
Vietnam Phase 3	Sci-B-Vac®	-	98.3% (328)	100% (12,158)	99% (3,188)
	Engerix-B®	-	81.2% (44)	98% (4,124)	98% (991)
Russia Phase 3	Sci-B-Vac®	-	100%	100%	100%
	Engerix-B®	-	89%	97.8%	97.8%

Seroprotection Rates (SPR%) after Two Immunizations, at Day 180:



The column graph above demonstrates the seroprotection rates in the three different clinical studies. The statistical comparison of the Engerix-B® and Sci-B-Vac® arms after two vaccinations demonstrated a significant difference in the phase 3 Vietnamese Study using Fisher's Exact Test

CONCLUSIONS

- Three separate clinical studies demonstrated that Sci-B-Vac® has an acceptable safety profile and that most individuals under the age of 45 achieve seroprotection after two doses of Sci-B-Vac®
- The Phase 4 study demonstrated that after one dose of Sci-B-Vac®, half of the subjects were seroprotected, and after two doses and more than 90% of subjects were protected.
- The geometric mean concentrations achieved with Sci-B-Vac® were 3-4 fold higher than those achieved with Engerix-B®

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The Phase 3 study in Russia:
- Dr. Yelena Vladimirovna Esaulenko – State Budgetary Healthcare Institution

REFERENCES

1. Whitford K et al. **Long-term Impact of Infant Immunization on Hepatitis B Prevalence: A Systematic Review and Meta-analysis** *Bulletin of the World Health Organization* 2018;96:484-497

2. McMahon B et al. **Antibody Levels and Protection after Hepatitis B Vaccine:Results of a 22 year Follow-Up Study and Response to a Booster Dose.** J Infect Dis 2009;9:1390-1396

CONTACT INFORMATION

Dr. Francisco Diaz-Mitoma fdiazmitoma@vbivaccines.com

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