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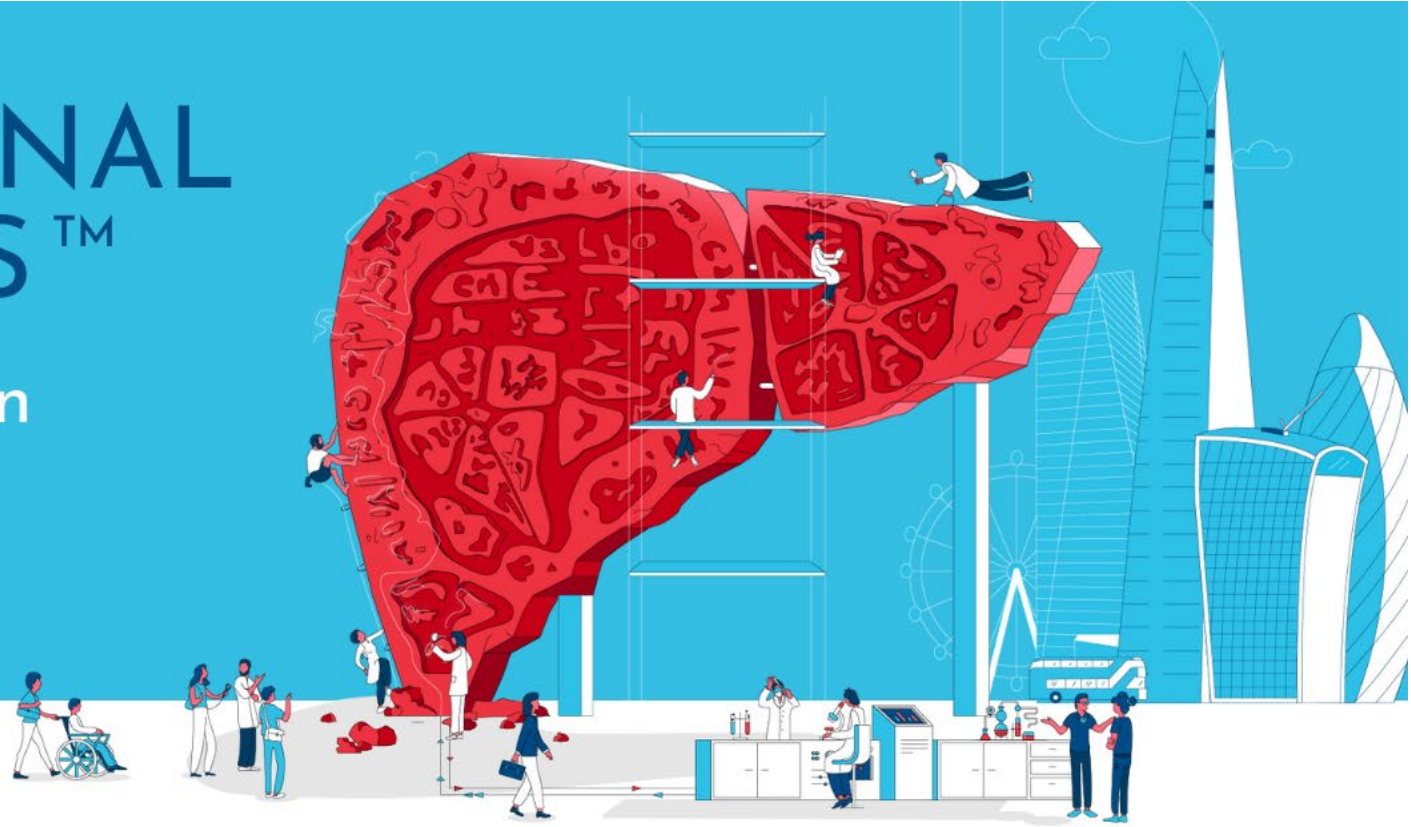

Long-Term Persistence of Anti-HBs Antibodies after Vaccination with a 3-Antigen HBV Vaccine Compared with a Single-Antigen HBV Vaccine

Dr. Timo Vesikari

Nordic Research Network Oy, Tampere, Finland

Aino Forstén, Johanna N. Spaans, Vlad Popovic, Francisco Diaz-Mitoma

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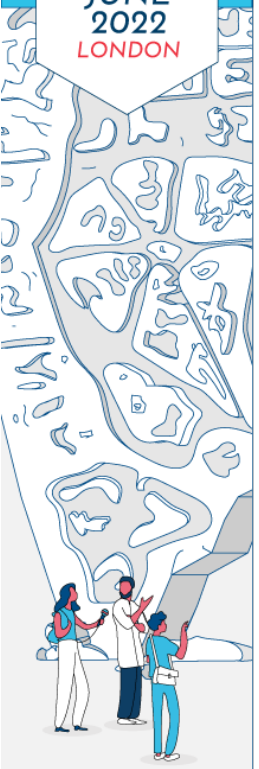


Disclosure Information

Timo Vesikari, MD, PhD (Tampere, Finland)

Nordic Research Network (NRN) Ltd and University of Tampere Vaccine Research Center, Tampere, Finland

Disclosure Information :

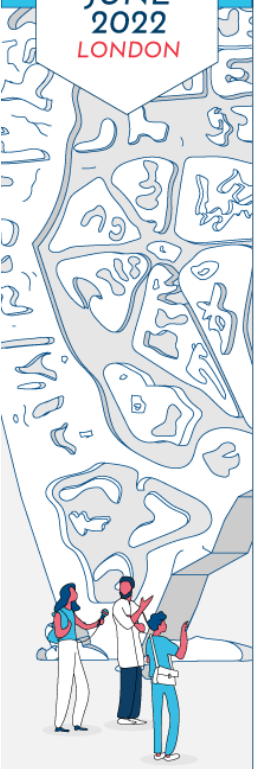
Financial disclosure :

- The presenter of this presentation was a Principal Investigator of this study and Nordic Research Network Oy received financial support for the services performed in conducting the study AT University of Tampere Vaccine Research Center study sites (N=10)

Investigational/unapproved use disclosure:

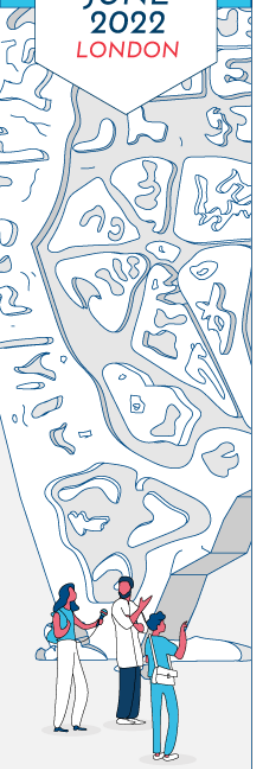
- The presenter will be discussing 3-antigen hepatitis B (HBV) vaccine, PreHevbrio™, PreHevbri™ which is an approved vaccine for use by the U.S. Food and Drug Administration, the European Medicines Agency for use in EU, MHRA for use in UK, and has not been approved in Canada

Study Sponsor : VBI Vaccines Inc.



Hepatitis B Vaccination

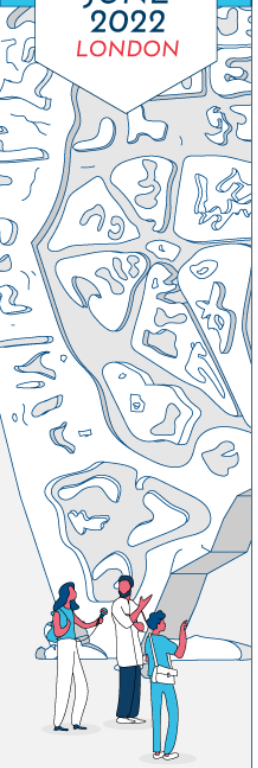
- HBV infection and the associated morbidity and mortality can be effectively prevented with hepatitis B vaccination
- The magnitude of the immune response to HBV vaccination can be measured by **serum levels of anti-HBs; persistence and durability** of anti-HBs titers are believed to be dependent upon the induced peak levels
- Conventional single-antigen yeast-derived HBV vaccines **(1A-HBV)** have reduced immunogenicity in adults; Long-term persistence of anti-HBs in vaccinated adults is unclear



3A-HBV *vs.* 1A-HBV : Vaccine Design and Function

	3-antigen HBV (3A-HBV)	Single-antigen HBV (1A-HBV)
Viral antigens mimicked:		
S Antigen	✓	✓
Pre-S2	✓	
Pre-S1	✓	
Dose of S Antigen:	10µg	20µg
Adjuvant:	Alum	Alum
Derivation:	Mammalian Cell	rDNA yeast

- Pre-S1 antigen induces key neutralizing antibodies that block virus receptor binding (Rendi-Wagner, 2006; Krawczyk, 2014)
- T cell responses to pre-S1 and pre-S2 antigens can further boost responses to the S antigens, resulting in a greater immune response (Hellström UB et al., 2009).



PROTECT Study

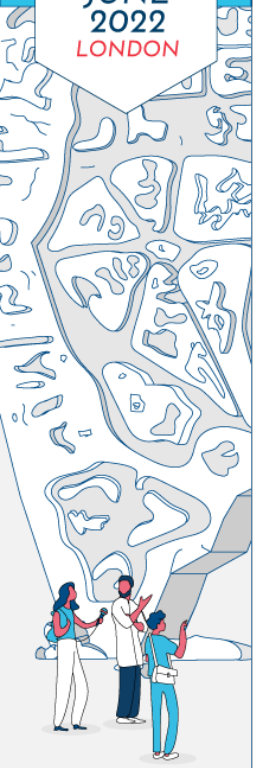
- **PROTECT**: phase 3, randomized, active-controlled, blinded, multi-center study[1] *[NCT03408730]* designed to evaluate the immunogenicity and safety of a 3-antigen HBV vaccine (3A-HBV, PreHevbrio™/PreHevbri™/Sci-B-Vac®) and a single-antigen HBV vaccine (1A-HBV, Engerix-B®)

- Total of **1607 adults**, age18-90 (median age 58.0 years), including those with well-controlled chronic conditions, were enrolled across 28 sites in Europe, U.S. and Canada and randomized at 1:1 ratio to receive a 3-dose course of either **10 µg of 3A-HBV, or 20 µg of 1A-HBV** at days 0, 28, and 168

- **Seroprotection Rate** (SPR, % of subjects achieving anti-HBs ≥ 10 mIU/mL) at Day 196 (4 weeks after the 3rd dose) was[1]:
  - In adults age 18+: **91.4%** for 3A-HBV vs. **76.5%** for 1A-HBV – Diff. 14.9% [95%CI: 11.2%, 18.6%]
  - In adults age 45+: **89.4%** for 3A-HBV vs. **73.1%** for 1A-HBV – Diff. 16.4% [95%CI: 12.2%, 20.7%]

- **Peak anti-HBs titers** (GMC) at Day 196 were **8021.9 mIU/mL** for 3A-HBV and **3787.3 mIU/mL** for 1A-HBV

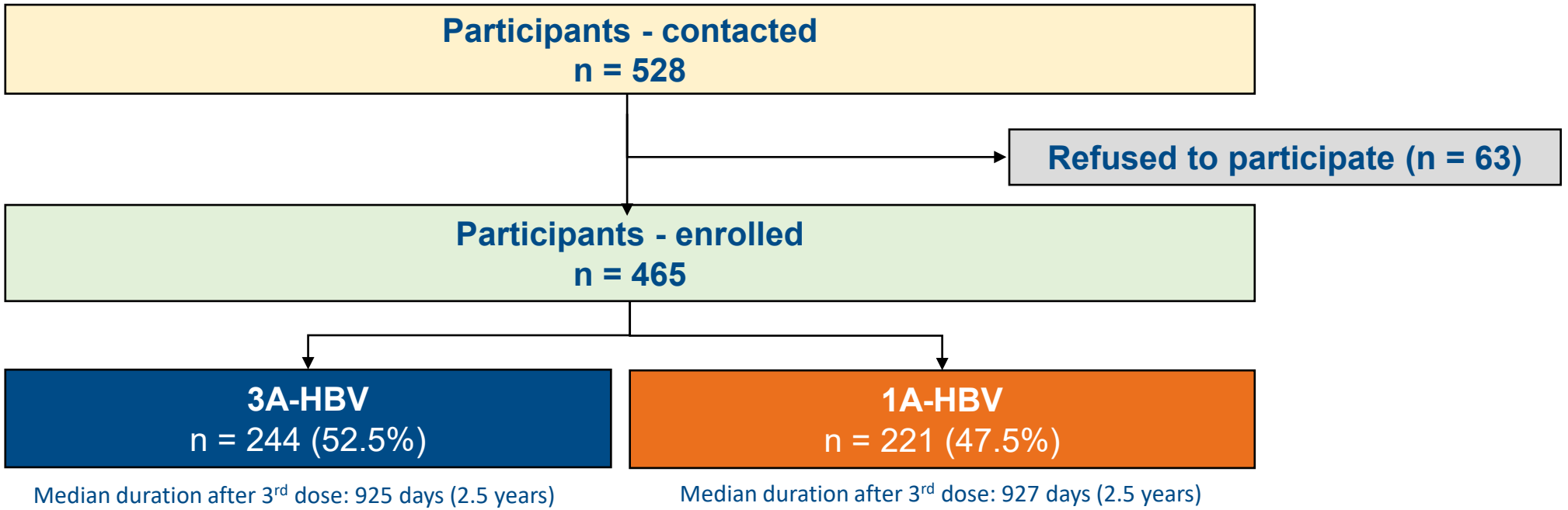
[1]Vesikari T et al. Immunogenicity and safety of a tri-antigenic versus a mono-antigenic hepatitis B vaccine in adults (PROTECT): a randomised, double-blind, phase 3 trial. Lancet Infect Dis, Published online May 11, 2021 https://doi.org/10.1016/S1473-3099(20)30780-5



PROTECT Follow-Up Study in Finland

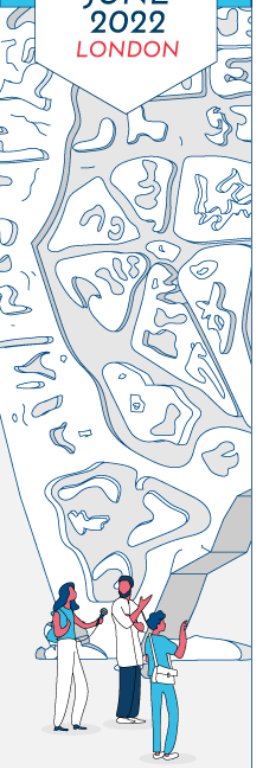
- 465 participants from 5 PROTECT clinical sites in Finland who all received 3 doses of study vaccines (3A-HBV or 1A-HBV) and achieved anti-HBs ≥ 10 mIU/mL by Day 196 (4 weeks after the 3rd dose
- **Study objectives**:
  - To determine anti-HBs titers at 2.5 years after the completion of vaccination
  - To determine the proportion of participants who retained anti-HBs ≥ 10 mIU/mL at 2.5 years following completion of the vaccination series
  - To determine the proportion of participants who retained anti-HBs ≥ 100 mIU/mL for 2.5 years after the completion of vaccination

PROTECT Follow-Up Study in Finland



Immunogenicity testing

- Frozen samples were sent to the same central laboratory for testing using the **same validated anti-HBs quantitative assay** [VITROS 5600, Ortho-Clinical Diagnostics, NJ, USA] as in the PROTECT study

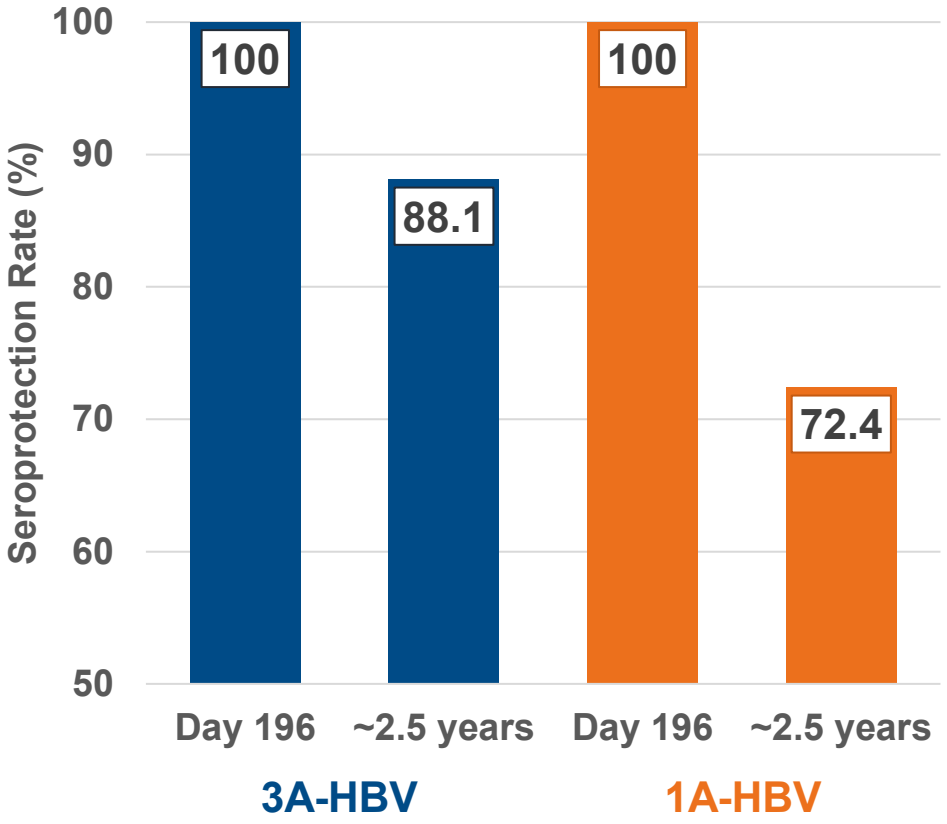


Baseline Characteristics of Follow-Up Study Participants in Finland
(at Enrollment to PROTECT)

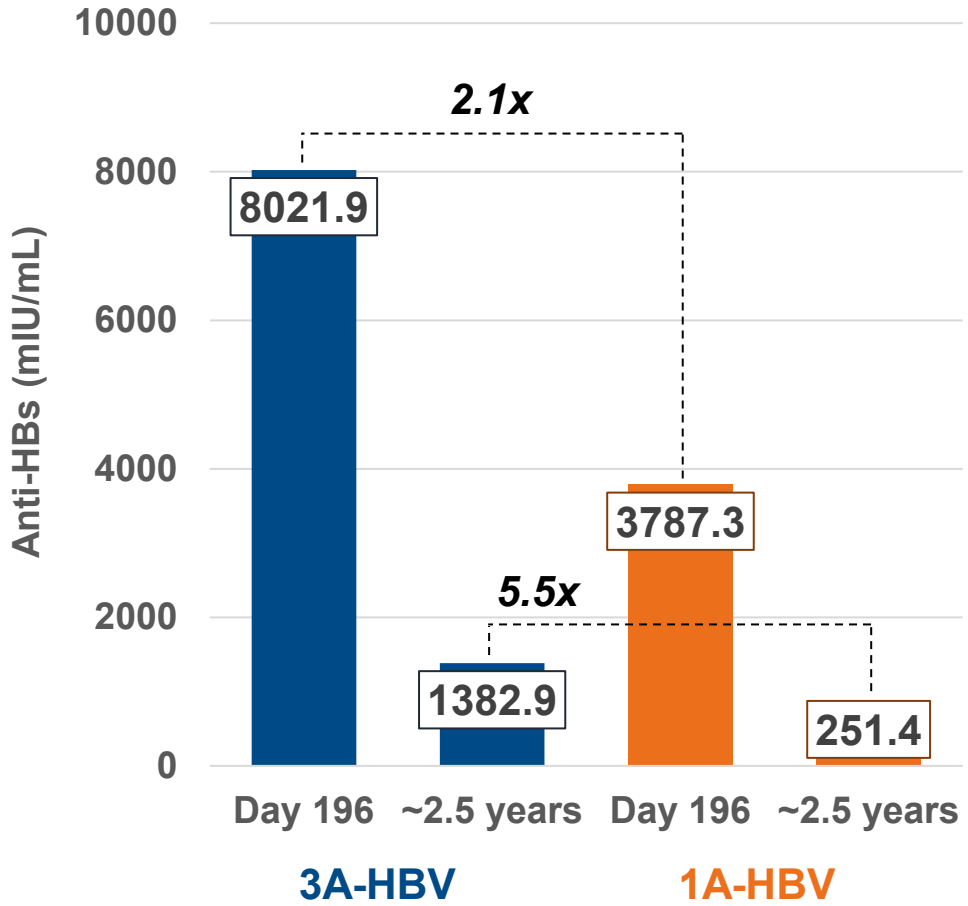
Study Vaccine	3A-HBV 10 µg	1A-HBV 20 µg
Number of subjects	244	221
Median Age (years)	59	59
Age18-44 years	52 (21.3%)	48 (21.7%)
Age 45-64 years	93 (38.1%)	84 (38.0%)
Age 65+ years	99 (40.6%)	89 (47.3%)
Male	94 (38.5%)	58 (35.3%)
Female	150 (61.5%)	143(64.7%)
Mean BMI	27.9 kg/m^2	26.6 kg/m^2
Diabetes - Yes	13 (5.3%)	5 (2.3%)
Diabetes - No	231 (94.7%)	216 (97.7%)
Smoking - Current	29 (11.9%)	29 (13.1%)
Smoking - Former	71 (29.1%)	77 (34.8%)
Non-Smoker	144 (59.0%)	115 (52.0%)

SPR and Anti-HBs Titers ~2.5 years After 3rd Dose of HBV Vaccines

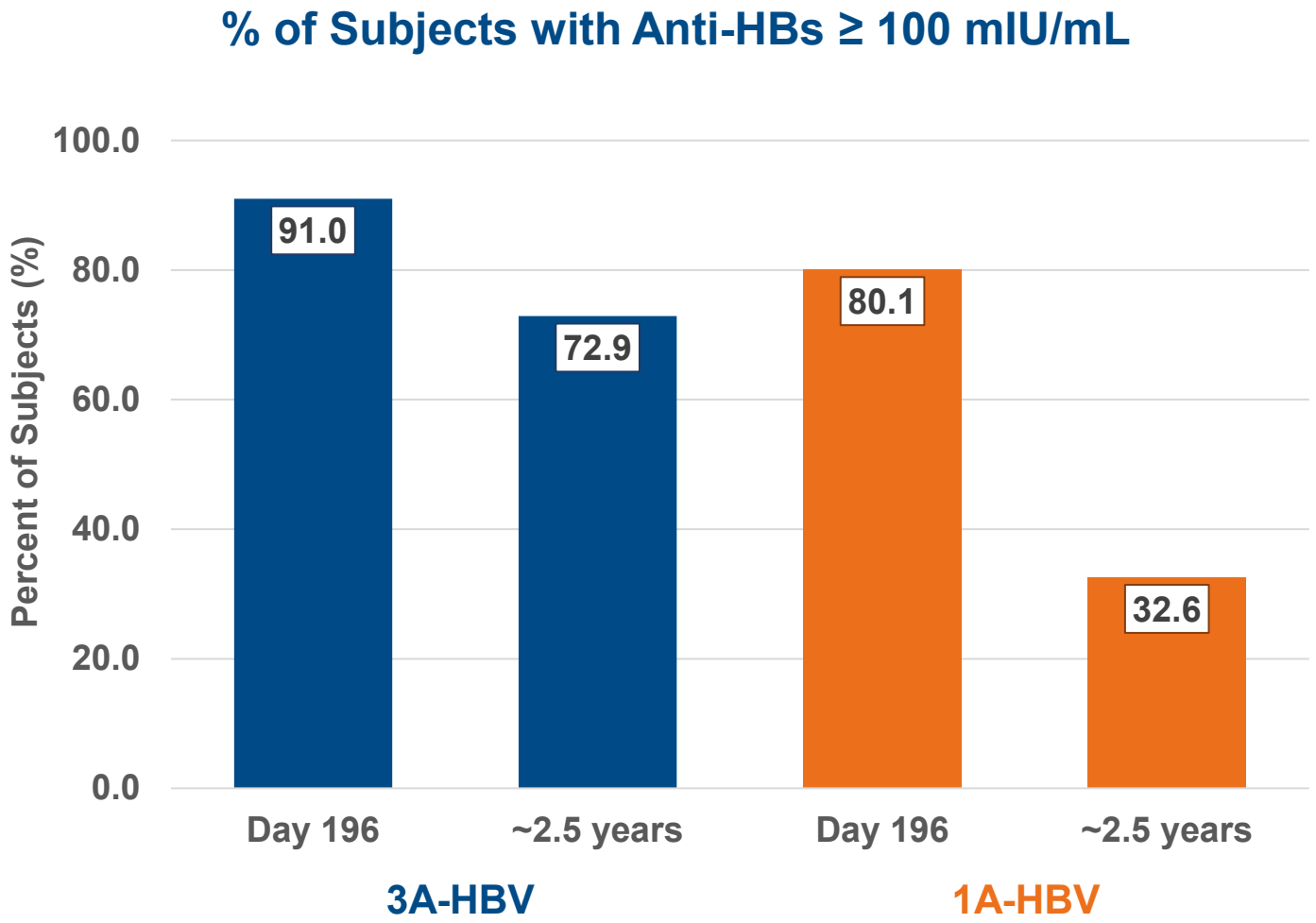
SPR, % of Subjects with Anti-HBs >10 mIU/mL



Anti-HBs Titers



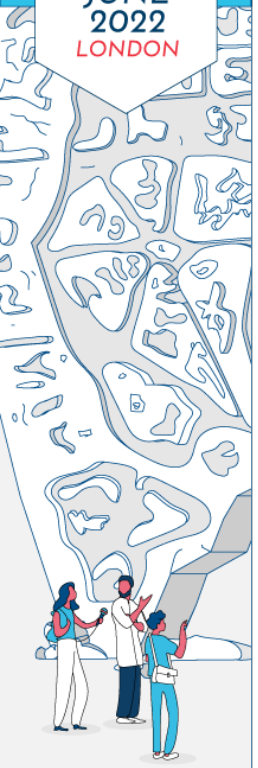
Anti-HBs ≥ 100 mIU/mL ~2.5 years After 3rd Dose of HBV Vaccines



Seroprotection Rates Across Key Subgroups ~2.5 Years of Follow-Up

	SPR (n/N)	
	3A-HBV	1A-HBV
Age 18-44 years	**96.2%** (50/52)	**81.3%** (39/48)
Age 45-64 years	**90.3%** (84/93)	**75.0**% (63/84)
Age ≥65 years	**81.8%** (81/99)	**65.2%** (58/89)
BMI ≤30	**88.9%** (152/171)	**73.1%** (128/175)
BMI >30	**86.3%** (63/73)	**69.6%** (32/46)
Male	**86.2%** (81/94)	**66.7%** (52/78)
Female	**89.3%** (134/150)	**75.5%** (108/143)
Current smoker	**75.9%** (22/29)	**65.5%** (19/29)
Former smoker	**91.6%** (65/71)	**71.1%** (55/77)
Non-smoker	**88.9%** (128/144)	**74.8%** (86/115)

N: Total number of subjects
n: Subjects retained SPR (anti-HBs ≥10 mIU/mL)



Conclusions

After primary immunization of adults 3A-HBV at 10μg vs 1A-HBV at 20μg

- higher seroprotection rate
- higher anti-HBsAb titer

After 2.5 years of follow-up of seroconverters

Seroprotection was lost in 27.6% of 1A-HBV recipients vs. only 11.9% of 3A-HBV recipients

After 2.5 years of follow-up of seroconverters

Mean HBsAb titer was 5x higher in 3A-HBV vs. 1A-HBV recipients

The greater immunogenicity of 3A-HBV vs. 1A-HBV vaccine is even more pronounced upon long term follow-up

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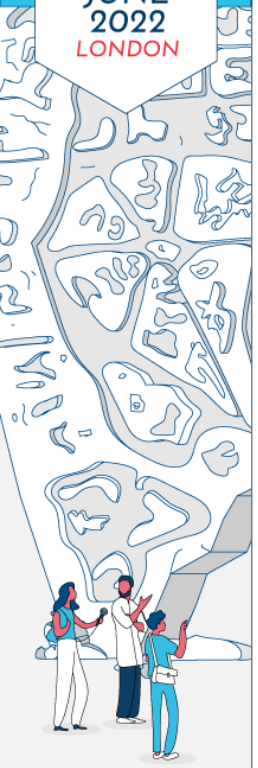

THANK YOU!