7. Two-Dose 4CMenB Vaccination in Adolescents Elicits a Bactericidal Activity against 15 Outbreak-Representative Meningococcal Strains

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Session: P-1. Adolescent Vaccines

Background: Meningococcal outbreaks have often been associated with *N. meningitidis* serogroup B (MenB) in high-income countries. We examined whether antibodies elicited by the 4-component MenB vaccine (4CMenB) in adolescents could induce complement-mediated bacterial killing of a panel of 14 genetically diverse MenB strains representative of outbreaks that occurred from 2001 to 2016 (11 from the US, 2 from the UK, and 1 from France). One *N. meningitidis* serogroup W (MenW) hyperendemic strain (UK, 2011) was also included in the analysis.

Methods: In a previous multicenter study (NCT02212457), adolescents aged 10-18y received 2 4CMenB doses 2 months apart. We tested individual sera collected from a subgroup of 20 US participants at pre-vaccination and 1 month post-second dose in a serum bactericidal assay with human complement (hSBA) against the meningococcal strain panel. Similarly, sera collected from 23 Chilean adolescents aged 11-17y (NCT00661713) were tested in a hSBA against a subset of 4 strains (3 from the US, 1 from the UK).

Results: At baseline, the percentage of US subjects with seroprotective titers (hSBA ≥ 1:4) ranged from 5% to 35%. One month after 4CMenB series completion, 65% to 100% had seroprotective titers (hSBA ≥ 1:4) against 11 out of the 14 MenB tested strains. The seroprotection rate was 45%, 25%, and 15% against the 3 remaining MenB strains. Against MenW, the percentage of adolescents with hSBA titers ≥ 1:4 was 15% at baseline and 95% one month after series completion. No significant changes in the percentage of subjects were observed when analysing hSBA titers ≥ 1:8. Moreover, the subset analysis indicated similar results for US and Chilean subjects for 3 out of 4 strains: the percentage of US vs Chilean subjects with hSBA titers ≥ 1:4 was 100% vs 100%; 80% vs 74%; 45% vs 52%. For the 4th strain, 65% of US subjects vs 91% of Chilean subjects showed a hSBA ≥ 1:4.

Conclusion: 4CMenB elicited bactericidal antibodies against a panel of 14 outbreak-representative MenB strains and 1 MenW hyperendemic strain in US adolescents. No major differences were detected in the bactericidal activity of Chilean subjects vaccinated with 4CMenB when tested against a subset of 4 MenB outbreak strains, suggesting that the immune response to 4CMenB is comparable in adolescents from different geographic areas.

Disclosures: Alessia Biolchi, n/a, GSK (Employee) Sara Tomei, n/a, GSK (Employee) Laura Santini, n/a, GSK (Employee) Rita La Gaetana, n/a, GSK Vaccines (Employee, Shareholder) Elena Mori, n/a, GSK (Employee) Patricia Novy, PhD, GSK (Employee, Shareholder) Rino Rappuoli, PhD, GSK (Employee) Rafik Bekkat-Berkani, M.D, GSK (Employee, Shareholder) Marzia Monica Giuliani, n/a, GSK (Employee, Shareholder) Mariagrazia Pizza, Biological Sciences, PhD, GSK Vaccines (Employee)

8. Higher hepatitis B antibody titres induced in all adults vaccinated with a tri-antigenic hepatitis B (HBV) vaccine, compared to a mono-antigenic HBV vaccine: results from two pivotal phase 3 double-blind, randomized studies (PROTECT and CONSTANT)

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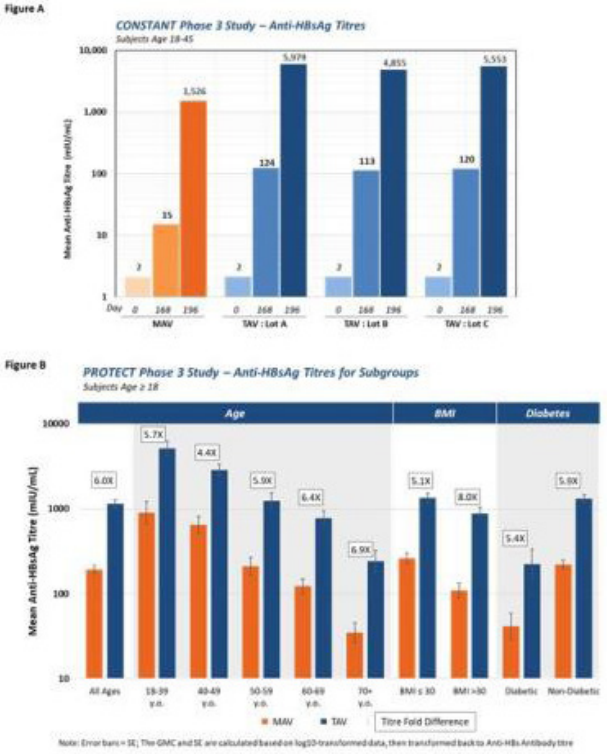
PROTECT and CONSTANT Study Groups

Session: P-2. Adult Vaccines

Background: More than 2 billion individuals worldwide have evidence of past or current hepatitis B virus (HBV) infection, emphasizing the importance of awareness and need for elimination of HBV infection. Effective vaccination, defined as the induction of protective anti-HBs titres, is a key component of those elimination plans. Magnitude of the immune response to HBV vaccines can be measured by serum levels of anti-HBs, whose persistence and durability is believed to be dependent upon the peak antibody levels reached after completion of vaccinations.

CONSTANT and PROTECT: High Hepatitis B antibody titres after vaccination



Methods: In two phase 3, head-to-head studies of immunogenicity and safety of a tri-antigenic HBV vaccine (TAV) containing 10 µg of full-length HBs (pre-S1 + pre-S2 + S antigens) and a mono-antigenic HBV vaccine (MAV) containing 20 µg of small HBs antigen, subjects were vaccinated at months 0, 1 and 6 with safety follow-up for at least 6 months after the 3rd vaccination. PROTECT, which enrolled 1607 adults age ≥18, demonstrated non-inferiority of seroprotection rates (SPR, defined as the % of participants achieving anti-HBs titres ≥10 mIU/mL) of TAV *vs*. MAV in adults age ≥ 18 and superiority of SPR in adults age ≥ 45. CONSTANT, which enrolled 2838 adults age 18–45 demonstrated manufacturing equivalence of 3 lots of TAV. In both studies, anti-HBs titres were measured across timepoints and safety was assessed.

Results: In CONSTANT, at day 168 after two doses, mean anti-HBs titers (mIU/mL) induced across the 3 lots of TAV were > 7.5x those induced with MAV [113–124 *vs*. 15]. At day 196, after the 3rd dose, mean anti-HBs titers induced with TAV remained substantially higher than those induced with MAV [4855–5979 *vs*. 1526] (Fig A). In PROTECT, anti-HBs titers were 6x higher in all subjects ≥ 18 year at day 196 [1148 *vs*. 193] with TAV and 5-8x higher in key subgroups compared to MAV, regardless of age, BMI, or diabetic status (Fig B). Adverse events were well-balanced and consistent with known vaccine safety profiles.

Conclusion: In the two pivotal phase 3 studies, TAV demonstrated its ability to rapidly elicit higher anti-HBs titres compared to MAV, in all study subject populations, reflecting the very strong immune response to TAV, which may be an important predictor of the persistence and durability of seroprotection.

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