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02. Beyond B Antigen Coverage: The Potential of the 4CMenB Vaccine for Cross-protection Against Pathogenic *Neisseria* Infections

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Session: P-01. Adolescent Vaccines

Background. Two human pathogenic *Neisseria* species exist: *N. meningitidis* (*Nm*) and *N. gonorrhoeae* (*Ng*). Although causing disparate clinical syndromes, invasive meningococcal disease (IMD) and gonorrhoea, they are genetically similar and share key protein antigens. The 4CMenB vaccine, licensed against meningococcal B disease, comprises 4 antigenic components (factor H binding protein (fHbp), variant 1.1, subfamily B; *Neisseria* heparin binding antigen (NHBA) peptide 2; *Neisseria* adhesin A (NadA) variant 3; and Porin A (PorA) P1.4), and potentially protects against non-B invasive meningococcal and gonococcal strains. In this review, we summarize the similarities between these antigens and those in *Nm* serogroups A, C, W, X and Y and *Ng*.

Methods. Published data in humans were analyzed to conduct a narrative literature review of the potential extent of meningococcal vaccine-induced protection against non-B meningococcal strains and *Ng*. Techniques applied to indirectly measure this effect are based on genotype-phenotype modelling, strain coverage, bactericidal killing and direct impact on disease reduction.

Results. Data were identified from countries in America, Europe, Africa and Oceania. The genes encoding for fHbp and NHBA are also present in strains belonging to the five non-B serogroups, while NadA is present in several strains of serogroups C, W and Y, and PorA P1.4 mainly in serogroup W. At the genome level, *Ng* and *Nm* share up to 90% homology. Most of the outer membrane vesicle antigens, like PilQ, Omp85 (BamA), NspA, MtrE, MetQ, LbpA, PorB, FetA, OpcA and NHBA, are highly conserved in *Ng*. In addition, a synergistic effect might enhance immunogenicity against non-B serogroups as shown against serogroup B.

Conclusion. 4CMenB components are present and conserved in several *Ng* and *Nm* strains. Recent results demonstrate that 4CMenB reduces MenW disease incidence in infants and might generate cross-protection against other non-B serogroups. In addition, 4CMenB has been proven to be effective in reducing gonococcal infections in adolescents. Research on future genomic and proteomic characterizations of IMD and gonorrhoea strains will provide information on the molecular basis of the underlying broad strain coverage, while informing decisions regarding prevention and immunization programmes.

Disclosures. Yara Ruiz Garcia, MSc, PhD, GSK group of companies (Employee) Woo-Yun Sohn, MD, GSK group of companies (Employee, Shareholder) Mariagrazia Pizza, Biological Sciences, PhD, GSK group of companies (Employee, Shareholder) Rafik Bekkat-Berkani, M.D., GSK group of companies (Employee, Shareholder)

03. Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) Administered as a Booster Dose in Adults and Adolescents Vaccinated Against Meningococcal Disease 3 - 6 Years Earlier

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Background. Booster doses of meningococcal conjugate vaccines may induce long-term protection against invasive meningococcal disease. MenACYW-TT [MenQuadfi] is a quadrivalent meningococcal conjugate vaccine, licensed for use in ages 2 years and older in USA. The vaccine is also licensed in ages 12 months and older in EU and other countries.

Methods. A phase IIIb study (NCT04084769) was conducted to evaluate the persistence of immune response in adults and adolescents primed 3-6 years earlier with either MenACYW-TT or MCV4-CRM (Menveo) and, safety and immunogenicity of MenACYW-TT when administered as a booster dose with or without concomitant administration with MenB vaccines (Bexsero and Trumenba). Serum bactericidal assays with human complement (hSBA) and baby rabbit complement (rSBA) were used to measure antibodies against vaccine serogroups at baseline (Day 0 [D0]), D06 (in a subset) and 30 days post-vaccination (D30). Safety data were collected up to 6 months post-vaccination.

Results. At D0, the GMTs were higher in subjects primed with MenACYW-TT vs MCV4-CRM for serogroups C, Y and W, and were comparable for serogroup A. At D0, all hSBA GMTs were higher than those observed pre-priming dose, suggesting persistence of immunity. Sufficiency of hSBA seroresponse (>75%) was demonstrated

following administration of MenACYW-TT booster dose regardless of the priming vaccine administered 3-6 years earlier. Vaccine seroresponse in a subset of participants at D06 ranged from 77.8% (95%CI 62.9%; 88.8%) for serogroup A to 97.8% (88.5%; 99.9%) for serogroup W suggesting a quick onset of immune response post-booster. Post-vaccination (D30) hSBA GMTs were comparable for serogroups A, Y and W regardless of the nature of the priming vaccine and were higher for serogroup C in subjects primed with MenACYW-TT vaccine. The MenACYW-TT booster dose was well-tolerated and had similar safety profiles regardless of the priming vaccine. The safety profiles were comparable regardless of the MenB vaccine co-administered with MenACYW-TT vaccine.

Conclusion. MenACYW-TT used as priming vaccine was able to demonstrate persistence of immune response 3-6 years later. MenACYW-TT elicits robust booster responses in adults and adolescents primed with MenACYW-TT or MCV4-CRM

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04. Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) Administered in Meningococcal Vaccine-Naive Participants Across a Broad Age Range (2-55 Years) in Japan

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Session: P-01. Adolescent Vaccines

Background. MenACYW-TT [MenQuadfi] is a quadrivalent meningococcal conjugate vaccine, licensed for use in ages 2 years and older in USA. The vaccine is also licensed in ages 12 months and older in EU and certain other countries. We evaluated the safety and immunogenicity of MenACYW-TT compared to a licensed quadrivalent conjugate meningococcal vaccine (MenACWY-DT [Menactra]) in Japanese children, adolescents and adults (2-55 years of age).

Methods. A phase III modified double-blind, randomized study (NCT04368429) to evaluate the immunogenicity and safety of a single dose of MenACYW-TT versus MenACWY-DT was conducted in 360 participants (ratio 1:1) between ages 2 and 55 years in Japan. Serum bactericidal assays with human complement (hSBA) were used to measure antibodies against vaccine serogroups at baseline (Day 0) and 30 days post-vaccination (D30). Safety data were collected up to 30 days post-vaccination.

Results. Non-inferiority of immune responses for all four serogroups, based on percentages of participants achieving hSBA vaccine seroresponse as primary endpoint, was demonstrated for MenACYW-TT compared to MenACWY-DT at Day 30 in comparison to baseline: 85.6% vs 65.4% for serogroup A, 96.6% vs 62.6% for serogroup C, 87.4% vs 49.2% for serogroup W, and 97.7% vs 63.5% for serogroup Y. The proportions of individuals with hSBA titers $\geq 1:8$ following MenACYW-TT administration were higher than those after MenACWY-DT administration for serogroups C (98.9% vs 81.0%), W (99.4% vs 91.1%) and Y (100% vs 89.4%) and comparable for serogroup A (96.6% vs 92.7%). The hSBA GMTs were higher following administration of MenACYW-TT for all four serogroups. Immunogenicity results in participants 10 to 17 years of age and ≥ 18 years of age were comparable to those in the whole population (2-55 years). The safety profiles of MenACYW-TT and MenACWY-DT were comparable. There were no immediate adverse events (AEs), no AEs leading to study discontinuation, and no vaccine-related serious adverse events reported in the study.

Conclusion. MenACYW-TT vaccine was well tolerated and demonstrated a non-inferior immune response compared to that for the licensed MenACWY-DT vaccine when administered as a single dose to meningococcal vaccine-naïve children, adolescents, and adults in Japan.

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