Conclusion. FTB demonstrated potent in vitro activity against PA with different resistance profiles, including NS to FEP, MEM, and TZP, and to the BI/BLI combinations CZA, ceftolozane-tazobactam, and meropenem-vaborbactam. FTB was the most active agent tested against PA harboring VIM and NDM MBs. These findings support the continued development of FTB as a potential new treatment option for challenging infections due to MDR PA.

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01. Serum Bacterial Activity Against Circulating and Reference Strains of Meningococcal Serogroup B in the United States: A Review of Meningococcal Serogroup B (MebN) Vaccines in Adolescents and Young Adults

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Session: P-01. Adolescent Vaccines

Background. US adolescents and young adults are at particular risk of invasive meningococcal disease (IMD). In 2018, meningococcal serogroup B was responsible for 36% of IMD cases in the US overall and for 66% of cases in adolescents and young adults. This age group is at high risk of IMD during outbreaks, which result in significant response-related costs. MenB vaccine efficacy against IMD relies on its ability to provide broad protection against diverse disease-causing strains. MenB-FHbp (Trumeno) and MenB-4C (Bexsero) are MenB vaccines licensed in the US as 2-dose series with an interval of 6 mo or 1 mo, respectively, recommended in healthy adolescents and young adults. We review available data on vaccine coverage of serogroup B strains.

Methods. A literature review identified relevant information from peer-reviewed publications, congress presentations, and ClinicalTrials.gov. Previously presented but unpublished data from 2 phase 3 studies were included.

Results. After 2 MenB-FHbp doses, percentages of adolescents and young adults achieving serum bactericidal assay activity using human complement (hSBA) titers ≥ 1:8 were 79%–99% for 4 heterologous representative test strains and 71%–97% for 10 additional strains, confirming cross-protection against a diverse strain panel (Figure 1; unpublished data). These 14 heterologous strains collectively represent ~80% of disease-causing strains in the US and Europe. In a published study with limited sample size, ~5% of subjects had hSBA titers ≥ 1:8 against strains from 4 US college outbreaks after 2 MenB-FHbp doses. After 2 MenB-4C doses, percentages of 10–25-year-olds achieving hSBA titers ≥ 1:8 against 3 reference strains homologous to the vaccine antigen were 82%–93% (published data); 15%–100% of adolescents achieved hSBA titers ≥ 1:8 against a panel of 14 strains (unpublished data). Of college students who received 2 MenB-4C doses, 53%–93% achieved hSBA titers ≥ 1:8 against 5 US outbreak strains (4/5 strains had antigenic similarity to MenB-4C; published data).

Conclusion. MenB-FHbp and MenB-4C protect against various serogroup B strains. As for the breadth of coverage provided by these vaccines, available data show that MenB-FHbp elicits robust immune responses to a wide variety of disease-causing strains prevalent in the US (Figure 2).

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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 gonorrhea, 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, serogroup B Neisseria heparin binding antigen (NHBA) peptide 2, Neisserial adhesin A (NadA) variant 3; and PorA (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.

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 is mainly in serogroup W. At the genome level, Ng and Nm share up to 90% homology. Most of the outer membrane vesicle antigens, like PiqP, OmpB (BamA), NspA, MtrE, MetQ, LbpA, PorB, FerA, 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 protocomic characterizations of IMD and gonorrhea strains will provide information on the molecular basis of the underlying broad strain coverage, while informing decisions regarding prevention and immunization strategies.

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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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Session: P-01. Adolescent Vaccines

Background. Booster doses of meningococcal conjugate vaccines may in principle be effective in reducing gonococcal infections in adolescents. Research on future genomic and proteomic characterizations of IMD and gonorrhea strains will provide information on the molecular basis of the underlying broad strain coverage, while informing decisions regarding prevention and immunization strategies.

Methods. A phase III modified double-blind, randomized study (NCT04386429) 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 proportion of individuals with hSBA titers ≥ 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 (2.5 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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04. Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) Administered in Meningococcal Vaccine-Naïve Participants Across a Broad Age Range (2 Years and Older) in Japan

Hitoshi Kikuchi, MD; Mandeep S. Dhingra, MD

Session: P-01. Adolescent Vaccines

Background. MenACYW-TT [MenQuad®] 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 (MenACYW-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 ≥ 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 (2.5 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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