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203. Activity of Cefepime in Combination with Taniborbactam (formerly VNRX-5133) Against *Pseudomonas aeruginosa* from a Global 2018-2020 Surveillance Collection

Meredith Hackel, PhD MPH[1]; Mark G G. Wise, PhD[2]; Daniel F. Sahm, PhD[1]; [1]IHMA, Inc., Schaumburg, Illinois; [2]IHMA, Schaumburg, Illinois

Session: O-40. What's New in Antimicrobial Resistance

Background. Taniborbactam is a novel cyclic boronate-based broad-spectrum β-lactamase inhibitor (BLI) with potent and selective inhibitory activity against both serine- and metallo-β-lactamases (MBLs). Taniborbactam restores the activity of cefepime (FEP) against many multidrug resistant organisms, including cephalosporin- and carbapenem-resistant Enterobacterales and *Pseudomonas aeruginosa* (PA). We evaluated the *in vitro* activity of the investigational combination cefepime-taniborbactam and comparators against clinical isolates of PA collected during a 2018-2020 surveillance.

Methods. MICs of FEP with taniborbactam fixed at 4 μg/mL (FTB) and comparators were determined against 3,219 PA collected from 221 sites in 52 countries in 2018-2020. Resistant phenotypes were based on 2021 CLSI breakpoints. Acquired β-lactamase (BL) genes were identified via PCR/Sanger sequencing or whole-genome sequencing (WGS) for 516 isolates with meropenem (MEM) MIC ≥8 μg/mL, and for 94 randomly selected isolates with FEP or ceftazidime MIC ≥16 μg/mL. 186 isolates with FTB MIC ≥16 μg/mL, 16 with FTB MIC=8 μg/mL and one with FTB MIC=4 μg/mL were subjected to WGS.

Results. Overall, 28.7%, 26.2% and 20.3% of PA isolates were nonsusceptible (NS) to piperacillin-tazobactam (TZP), MEM or FEP, respectively (Table). FTB demonstrated potent activity ($MIC_{50/90}$, 2/8 μg/mL; 94.2% inhibited at ≤8 μg/mL) against PA overall and inhibited between 63.4% (ceftazidime-avibactam [CZA] NS) and 82.1% (TZP NS) of isolates in the NS subsets compared to 0% to 69.1% S for comparators. Against the 111 strains carrying VIM or NDM MBL genes, 67.6% had FTB MICs ≤8 μg/mL, with 11.7% having FTB MICs of 16 μg/mL. Plausible explanations for elevated FTB MICs included IMP MBL genes, penicillin binding protein 3 variations, and/or possible efflux pump up-regulation.

Results.

Resistance Phenotype/Genotype	N (%)	Percent susceptible					
		FTB[a]	FEP	CZA	CT	MEV[b]	TZP
P. aeruginosa, all	3219 (100%)	94.2	79.7	90.7	89.1	87.2	71.3
FEP NS	654 (20.3%)	71.6	0	56.1	50.5	53.1	5.8
MEM NS	842 (26.2%)	81.0	44.2	67.0	63.9	51.1	30.5
CZA NS	298 (9.3%)	63.4	3.7	0	16.1	24.5	4.0
CT NS	350 (10.9%)	68.0	7.4	28.6	0	35.4	6.3
MEV NS[b]	412 (12.8%)	70.2	25.5	45.4	45.2	0	9.7
TZP NS	925 (28.7%)	82.1	33.4	69.1	64.5	59.8	0
MBL-positive (VIM or NDM)	111 (13.7%)[c]	67.6	3.6	2.7	0.9	8.1	2.7

FTB, cefepime-taniborbactam; FEP, cefepime; CZA, ceftazidime-avibactam; CT, ceftolozane-tazobactam; MEM, meropenem; MEV, meropenem-vaborbactam; TZP, piperacillin-tazobactam; MBL, metallo-β-lactamase; NS, nonsusceptible based on 2021 CLSI breakpoints

[a] corresponds to a provisional susceptible breakpoint of ≤8 μg/mL

[b] as there is no CLSI breakpoint, susceptibility is based on EUCAST susceptible breakpoint of ≤8 μg/mL

[c] percent based on total of 813 molecularly characterized isolates

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

Disclosures. **Meredith Hackel, PhD MPH**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **Mark G G. Wise, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **Daniel F. Sahm, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor)

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

Tamera Coyne-Beasley, MD, MPH[1]; Joseph Bocchini, MD[2]; Alejandro Cane, M.D.[3]; Cindy Burman, PharmD[3]; Maria J. Tort, PhD[3]; Jessica Presa, MD[4]; [1]University of Alabama at Birhmingham, Birmingham, Alabama; [2]Willis-Knighton Health System, Shreveport, Louisiana; [3]Pfizer Inc, Buenos Aires, Buenos Aires, Argentina; [4]Pfizer, Inc., Collegeville, Pennsylvania

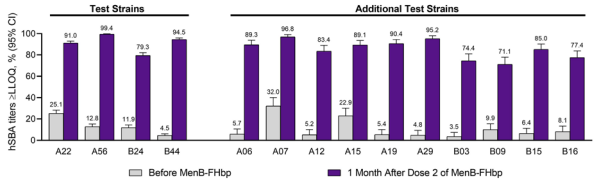
Session: P-01. Adolescent Vaccines

Background. US adolescents and young adults are at particular risk of invasive meningococcal disease (IMD). In 2018, menincococcal 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 (Trumenba) 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 phase 2/3 studies were included.

Results. After 2 MenB-FHbp doses, percentages of adolescents and young adults achieving serum bactericidal activity assay 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, 44%–78% 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 ≥1:5 against 3 reference strains homologous to the vaccine antigen were 82%–93% (published data); 15%–100% of adolescents achieved hSBA titers ≥1:4 against a panel of 14 strains (unpublished data). Of college students who received 2 MenB-4C doses, 53%–93% achieved hSBA titers ≥1:4 against 5 US outbreak strains (4/5 strains had antigenic similarity to MenB-4C; published data).

Figure 1. Adolescents and young adults with hSBA titers ≥LOQ for serogroup B strains before and 1 month after dose 2 of MenB-FHbp.



hSBA=serum bactericidal activity assay using human complement; LLOQ=lower limit of quantitation. hSBA LLOQs are 1:16 for strains A06, A12, A19, and A22 and 1:8 for strains A07, A15, A29, A56, B03, B09, B15, B16, B24, B44. Results are for the evaluable immunogenicity population for 4 test strains (n=829–861) and 10 additional strains (n=150–172).

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**).

Figure 2. Summary of MenB-FHbp and MenB-4C characteristics and available data.

Characteristic/data availability	MenB-FHbp	MenB-4C
Approved by the FDA	✓	✓
Contains protein antigens	✓	✓
Evaluation of immunogenicity	✓	✓
Evaluation of safety	✓	✓
Phase 3 data from the US	✓	–
Evaluation of immune response against heterologous strains	✓	–
Evaluation of immune response against varying levels of antigen expression	✓	–

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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, subfamily B; Neisseria heparin binding antigen (NHBA) peptide 2; Neisserial 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 gonorrhea strains will provide information on the molecular basis of the underlying broad strain coverage, while informing decisions regarding prevention and immunization programmes.

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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 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

Disclosures. **Betzana Zambrano, MD**, **Sanofi Pasteur** (Employee) **Germán Áñez, MD**, **Sanofi Pasteur** (Other Financial or Material Support, Former employee) **Sue Jiayuan, MSc**, **Sanofi Pasteur** (Independent Contractor) **Judy Pan, PhD**, **Sanofi Pasteur** (Employee) **Habiba Arroum, MD**, **Sanofi Pasteur** (Employee) **Kucku Varghese, PhD**, **Sanofi Pasteur** (Employee) **Emilia Jordanov, MD**, **Sanofi Pasteur** (Employee, Shareholder) **Mandeep S. Dhingra, MD**, **Sanofi Pasteur** (Employee, Shareholder)

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 $\geq$ 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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