Pentavalent Meningococcal (MenABCWY) Vaccine Is Safe and Well Tolerated With Immunogenicity Noninferior to Coadministered MenB-FHbp and MenACWY-CRM in a Phase 2 Study of Healthy Adolescents and Young Adults

James Peterson,¹ Daniel Drazan,² Hanna Czajka,³ Jason Maguire,⁴ Jean-Louis Pregaldien,⁵ Ilkka Seppa,⁶ Roger Maansson,⁷ Robert O'Neill,⁴ Annaliesa S. Anderson,⁴ Paul Balmer,⁸ Johannes Beeslaar,⁹ John L. Perez^{7*}

¹J. Lewis Research, Salt Lake City, UT, USA; ²General Practice for Children and Adolescents, Jindividual Specialist Medical Practice, Krakow, and Faculty of Medicine, University of Rzeszow, Poland; ⁴Pfizer Vaccine Research and Development, Pearl River, NY, USA; ⁵Pfizer Vaccine Research Center, Tampere, Finland; ⁷Pfizer Vaccine Research and Development, Collegeville, PA, USA; ⁸Pfizer Vaccine Medical Development and Scientific/Clinical Affairs, Collegeville, PA, USA; ⁹Pfizer Vaccine Research and Development, Hurley, UK *Presenting author

BACKGROUND

- Neisseria meningitidis causes invasive meningococcal disease, which can manifest as meningitis and/or septicemia¹ – Incidence in United States in 2018: 0.10 individuals per 100,000 population²
- Highest incidence among infants, young children, adolescents/young adults, and the elderly²
- Serogroups A, B, C, W, and Y are responsible for the majority of invasive meningococcal disease worldwide³
- Quadrivalent serogroup A, C, W, and Y conjugate vaccines and recombinant protein serogroup B vaccines are available
- Current immunization recommendations are complicated owing to differences in target age groups and dosing schedules between vaccines⁴ - A single pentavalent vaccine for serogroups A, B, C, W, and Y would provide a comprehensive, convenient, and simplified option
- Potential to increase adherence and optimize disease prevention
- Investigational pentavalent vaccine, MenABCWY
- MenB-FHbp (factor H binding protein [FHbp]; Trumenba®, bivalent rLP2086; Pfizer Inc, Philadelphia, PA)
- MenACWY-TT (tetanus toxoid conjugate vaccine; Nimenrix®; Pfizer Europe MA EEIG, Brussels, Belgium) • This first-in-human study evaluated the immunogenicity, safety, and tolerability of MenABCWY in healthy adolescents and young adults 10–25 years of age

OBJECTIVES

- To describe the immunogenicity of
- 1 dose of MenABCWY compared with 1 dose of MenACWY-CRM (quadrivalent meningococcal CRM conjugate vaccine; Menveo[®]; GSK Vaccines Srl, Sovicille, Italy) - 2 doses of MenABCWY compared with 1 dose of MenACWY-CRM
- MenABCWY compared with MenB-FHbp 1 month after dose 2
- To confirm immune responses of MenABCWY were noninferior to the immune response of MenACWY-CRM and MenB-FHbp • To describe the safety and tolerability of MenABCWY after doses 1 and 2

METHODS

Study Design and Subjects

- Ongoing phase 2/3, randomized, active-controlled, observer-blinded, multicenter study (United States, Czech Republic, Finland, and Poland; NCT03135834) Randomization 1:2
- MenABCWY (Months 0, 6) and saline placebo (Month 0)
- MenB-FHbp (Months 0, 6) and MenACWY-CRM (Month 0)
- Healthy male and female subjects 10–25 years of age, not pregnant, and MenB vaccine-naive Both MenACWY vaccine-naive and experienced subjects included

Immunogenicity Evaluations

- Immune responses measured with serum bactericidal activity assays using human complement (hSBA) against serogroups A, C, W, and Y test strains and 4 MenB test stra (expressing FHbp A22, A56, B24, and B44 variants)
- Subjects (%) with ≥4-fold rises in titers from baseline and titers ≥ lower limit of quantitation (LLOQ; 1:8) for serogroups A, C, W, and Y test strains, stratified by ACWY experience
- 5 coprimary endpoints for MenB test strains
- The percentage of subjects with ≥4-fold rises in titers from baseline against one of each of the 4 test strains
- The percentage of subjects with a titer ≥LLOQ (1:16 or 1:8, depending on strain) for all 4 test strains combined (composite response)
- Note: correlate of protection is $\geq 1:4^5$ - Geometric mean titers (GMTs) calculated for all serogroups

Safety Evaluations

- Reactogenicity assessed for 7 days after each dose by electronic diary
- Local reactions: redness, swelling, injection site pain Systemic events: fever, vomiting, diarrhea, headache, fatigue, chills, muscle pain, joint pain
- Adverse events (AEs) evaluated by severity through 1 month after dose 2
- Serious AEs, medically attended AEs, and newly diagnosed chronic medical conditions evaluated through 6 months after dose 2
- Immediate AEs assessed within 30 minutes after each dose

Statistical Analyses

- Percentages with associated 2-sided Clopper Pearson 95% Cls
- Percentage difference with associated 2-sided 95% CIs, calculated using the Miettinen-Nurminen method
- GMT with 95% CIs for GMTs calculated in log scale with reference to the appropriate t distribution; lower and upper limits exponentiated
- 95% Cls for the GMT ratios (GMRs) calculated using t distribution for the mean difference of logarithmically transformed results and transforming confidence limits back to original units
- Prespecified ACWY noninferiority analyses (MenABCWY vs MenACWY-CRM), post hoc ACWY analyses, and post hoc MenB noninferiority analyses (MenABCWY vs MenB-FHbp; **Table 1**)
- Populations used for immunogenicity analyses
- Serogroups A, C, W, and Y: modified intent-to-treat (mITT) population
- Includes all randomized subjects with ≥1 valid and determinate assay result available at any time point
- Serogroup B: evaluable immunogenicity population Includes all subjects in the mITT population as well as those who are randomized to the group of interest, are eligible, receive investigational products as randomized, have blood drawn for assay testing within the required time frames, have ≥1 valid and determinate assay result after the second vaccination, and have no important protocol deviations

The different populations reflect that the primary immunogenicity objectives relate to MenB, whereas ACWY immunogenicity endpoints are secondary

Table 1. Overview of Noninferiority Ana	lyses	
Endpoint	Serogroup ^a	Noninferiority Criterion
Differences in percentages of subjects achieving ≥4-fold rises in hSBA titers	A, B, C, W, Y	10% margin (ie, if the lower limit of the 95% CI for the difference was greater than –10%)
Differences in composite response ^b	В	10% margin (ie, if the lower limit of the 95% CI for the difference was greater than –10%)
hSBA GMT ratios	A, B, C, W, Y	2-fold margin (ie, if the lower limit of the 95% CI for the GMR was greater than 0.5)
GMT=geometric mean titer; hSBA=serum bactericidal activity assay using human complement; LLOQ=lower limit of a	uantitation; MenB=meningococcal se	erogroup B.

^aAnalyses by MenACWY vaccine experience were performed for serogroups A, C, W, and Y. ^bDefined as hSBA titer \geq LLOQ for all 4 MenB strains.

				Immu	unogen	nicity								
 Demographic characteris 	rics generally similar	across groups		Serogr	Serogroups A, C, W, and Y									
 Majority women (57.4%) Majority White (85.6%) Mean ± SD age at dose 1 was 17.1±4.9 years Randomization MenABCWY + saline, n=544 MenACWY-naive, n=277 MenACWY-experienced, n=276 543 (99.8%) and 486 (89.3%) of subjects received doses 1 and 2, respectively MenB-FHbp + MenACWY-CRM, n=1066 MenACWY-naive, n=544 MenACWY-experienced, n=522 1057 (99.2%) and 946 (88.7%) of subjects received doses 1 and 2, respectively 			MenAC \geq 4-fold - 95% supe • Noninf ACWY - 95% Men - 2-fold but r Serogr • For all - 95%	 MenACWY-CRM dose shown across serogroups for both ACWY-naive and -experienced subjects using ≥4-fold rises in hSBA titers from baseline (Figure 1A; Table 2) 95% CI lower limit for the percentage difference >0 for some serogroups among MenACWY-naive subjects, sugges superior responses with MenABCWY vs MenACWY-CRM Noninferiority of MenABCWY after each dose to MenACWY-CRM as evaluated by GMRs shown across ACWY sero ACWY-naive subjects (Table 3) 95% CI lower limit for GMR >1 in some instances, indicating possibly increased GMTs in the MenABCWY vs the M MenACWY-CRM group 2-fold criteria were met for ACWY-experienced subjects when comparing 1 dose of MenABCWY to 1 dose of Mer but not when response after second dose of MenABCWY was compared with a single dose of MenACWY-CRM Serogroup B For all 5 coprimary endpoints, noninferiority of MenABCWY compared with MenB-FHbp was shown (Figure 1B; Tc – 95% CI lower limit for the percentage difference >0 for some endpoints, suggesting possibly superior responses wit MenABCWY vs the MenABCWY vs MenB-FHbp Noninferiority of MenABCWY to MenB-FHbp based on GMRs was also shown (Table 5) 95% CI lower limit for GMR >1 in some instances, indicating possibly increased GMTs in the MenABCWY vs MenB-FHbp 										
				Men • Noninf – 95%	ABCWY vs I feriority of M CI lower lim	MenB-FHbp enABCWY to Me it for GMR >1 in se	nB-FHbp base ome instances	ed on GMRs was c , indicating possibl	also shown (1 y increased (Table 5) GMTs in the MenAl	3CWY vs the	e MenB-F		
Table 2. Differen	ces in Percen	tages of Subj	ects Achi MenAQ	Men • Noninf – 95% eving ≥4-Fol	ABCWY vs <i>I</i> feriority of Ma CI lower lim	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite	nB-FHbp base ome instances rs for Se	ed on GMRs was c , indicating possibl rogroups A,	also shown (T y increased (C, W, ar MenACW	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b	3CWY vs the	e MenB-F		
Table 2. Differen	ces in Percen	tages of Subj MenABCWY + Saline	ects Achi MenAd + M	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b MenB-FHbp enACWY-CRM	ABCWY vs / feriority of Ma CI lower lim d Rises i	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite	nB-FHbp base ome instances rs for Se	ed on GMRs was c , indicating possible rogroups A, enABCWY + Saline	also shown (T y increased (C, W, ar MenACW	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b MenB-FHbp enACWY-CRM	3CWY vs the	e MenB-F		
Table 2. Differen Serogroup Time Point	ces in Percen %	tages of Subj MenABCWY + Saline (95% CI) ^c	ects Achi MenAa + M	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b MenB-FHbp enACWY-CRM (95% Cl)°	ABCWY vs / feriority of Ma CI lower lim d Rises i	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite ifference (95% Cl)d	nB-FHbp base ome instances rs for Se	ed on GMRs was c , indicating possible rogroups A, enABCWY + Saline (95% CI) ^c	also shown (T y increased (C, W, ar MenACW + Ma %	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b MenB-FHbp enACWY-CRM (95% CI) ^c	3CWY vs the	e MenB-F		
Table 2. Differen Serogroup Time Point A Im PD1	ces in Percen % % 96.9	tages of Subj MenABCWY + Saline (95% CI) ^c	ects Achi MenAa + M	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b MenB-FHbp enACWY-CRM (95% CI) ^c	ABCWY vs / feriority of Ma CI lower lim d Rises i	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite (95% CI)d (-2.1. 3.7)	nB-FHbp base ome instances rs for Se %	ed on GMRs was a , indicating possible rogroups A, enABCWY + Saline (95% CI) ^c	also shown (T y increased (C, W, ar MenACW henACW	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b AenB-FHbp enACWY-CRM (95% CI) ^c (94.9. 98.5)	3CWY vs the %	e MenB-f Differenc (95°		
Table 2. Differen Serogroup Time Point A 1m PD1 1m PD2°	ces in Percen % % 96.9 97.0	tages of Subj MenABCWY + Saline (95% CI) ^c (94.1, 98.7) (93.9, 98.8)	ects Achi MenAa MenAa 1 1 1 1 1 1 1 1 1 1 1 1 1	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b MenB-FHbp enACWY-CRM (95% CI)° (93.7, 97.4)	ABCWY vs / feriority of Ma CI lower lim d Rises i b b b c l c l c l c l c l c l c l c l c	MenB-FHbp enABCWY to Me it for GMR >1 in se ifference (95% CI) ^d (-2.1, 3.7) (-2.2, 3.8)	nB-FHbp base ome instances rs for Se % %	ed on GMRs was c s, indicating possible cogroups A, enABCWY + Saline (95% CI) ^c (92.7, 98.4) (92.5, 98.5)	also shown (T y increased (C, W, ar MenACW * MenACW 97.0	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b AenB-FHbp enACWY-CRM (95% CI) ^c (94.9, 98.5)	3CWY vs the % -0.8 -0.8	e MenB-F Difference (95° (-4. (-4.		
Table 2. Differen Serogroup Time Point A Im PD1 Im PD2e C	ces in Percen % % 96.9 97.0	tages of Subj MenABCWY + Saline (95% CI) ^c (94.1, 98.7) (93.9, 98.8)	ects Achi MenAa MenAa 1 1 1 1 1 1 1 1 1 1 1 1 1	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b MenB-FHbp enACWY-CRM (95% CI)° (93.7, 97.4)	ABCWY vs / feriority of Ma CI lower lim d Rises i % 1.1 1.1	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite (95% CI) ^d (-2.1, 3.7) (-2.2, 3.8)	nB-FHbp base ome instances rs for Se % 96.2 96.3	ed on GMRs was a , indicating possible rogroups A, enABCWY + Saline (95% CI) ^c (92.7, 98.4) (92.5, 98.5)	also shown (T y increased (C, W, ar MenACW / MenACW / MenACW / MenACW	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b MenB-FHbp enACWY-CRM (95% Cl) ^c (94.9, 98.5) –	3CWY vs the % -0.8 -0.8	e MenB-F Differenc (95° (-4. (-4.		
Table 2. Differen Serogroup Time Point A Im PD1 Im PD2° C Im PD1	ces in Percen % % 96.9 97.0 75.5	tages of Subj MenABCWY + Saline (95% CI)° (94.1, 98.7) (93.9, 98.8) (69.8, 80.6)	ects Achi MenA	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b MenB-FHbp enACWY-CRM (95% CI) ^c (93.7, 97.4) –	ABCWY vs / feriority of Ma o CI lower lim d Rises i % 1.1 1.1 5.5	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite (95% CI) ^d (-2.1, 3.7) (-2.2, 3.8) (-1.3, 11.9)	nB-FHbp base ome instances rs for Se % 96.2 96.3 93.4	ed on GMRs was c indicating possible rogroups A, enABCWY + Saline (95% CI) ^c (92.7, 98.4) (92.5, 98.5) (89.6, 96.1)	also shown (T y increased (C, W, ar MenACW / MenACW / MenACW / MenACW / MenACW	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b MenB-FHbp enACWY-CRM (95% Cl) ^c (94.9, 98.5) – (93.6, 97.4)	3CWY vs the % -0.8 -0.8 -2.4	e MenB-f Difference (95' (-4. (-4.		
Table 2. Differen Serogroup Time Point A Im PD1 Im PD2e C Im PD2e Im PD2e	ces in Percen ////////////////////////////////////	tages of Subj MenABCWY + Saline (95% CI) ^c (94.1, 98.7) (93.9, 98.8) (69.8, 80.6) (93.2, 98.5)	ects Achi MenA	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b AenB-FHbp enACWY-CRM (95% Cl) ^c (93.7, 97.4) – (65.8, 74.0) –	ABCWY vs / feriority of Ma CI lower lim d Rises i % 1.1 1.1 1.1 5.5 26.5	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite (95% CI) ^d (-2.1, 3.7) (-2.2, 3.8) (-1.3, 11.9) (21.6, 31.1)	nB-FHbp base ome instances rs for Se % % 96.2 96.3 93.4 94.8	ed on GMRs was c , indicating possible rogroups A, enABCWY + Saline (95% CI) ^c (92.7, 98.4) (92.5, 98.5) (89.6, 96.1) (91.1, 97.3)	also shown (T y increased (C, W, ar MenACW / MenACW / MenACW / MenACW / MenACW / MenACW	Gable 5) GMTs in the MenAl nd Y Y-Experienced ^b AenB-FHbp enACWY-CRM (95% CI) ^c (94.9, 98.5) – (93.6, 97.4) –	3CWY vs the % 7% -0.8 -0.8 -0.8 -0.8	e MenB-I Difference (95 (-4) (-4) (-4)		
Table 2. Differen Serogroup Time Point A Im PD1 Im PD2° C Im PD1 Im PD2° W	ces in Percen % % % 96.9 97.0 75.5 96.5	tages of Subj MenABCWY + Saline (95% CI) ^c (93.9, 98.8) (93.9, 98.8) (69.8, 80.6) (93.2, 98.5)	Control MenAd MenAd MenAd % MenAd %	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b MenB-FHbp enACWY-CRM (95% Cl) ^c (93.7, 97.4) – (65.8, 74.0) –	ABCWY vs / feriority of Ma CI lower lim d Rises i % 1.1 1.1 1.1 5.5 26.5	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite (95% CI) ^d (-2.1, 3.7) (-2.2, 3.8) (-1.3, 11.9) (21.6, 31.1)	nB-FHbp base ome instances rs for Se 96.2 96.3 93.4 93.4 94.8	ed on GMRs was c , indicating possible rogroups A, enABCWY + Saline (95% CI) ^c (92.7, 98.4) (92.5, 98.5) (89.6, 96.1) (91.1, 97.3)	also shown (T y increased (C, W, ar MenACW / MenACW / MenACW / MenACW / MenACW / MenACW	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b AenB-FHbp enACWY-CRM (95% CI) ^c (94.9, 98.5) – (93.6, 97.4) –	3CWY vs the % 7% -0.8 -0.8 -0.8	e MenB- Differen (95 (-4 (-4		
Table 2. Differen Serogroup Time Point A Im PD1 Im PD2° C Im PD2° W Im PD1 Im PD2° W Im PD1 Im PD2°	ces in Percen % % % % % 96.9 97.0 75.5 96.5 86.6	tages of Subj MenABCWY + Saline (95% CI) ^c (93.9, 98.8) (93.9, 98.8) (69.8, 80.6) (93.2, 98.5) (81.8, 90.5)	Control MenAd MenAd MenAd % MenAd %	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b AenB-FHbp enACWY-CRM (95% CI) ^c (93.7, 97.4) – (65.8, 74.0) – (71.9, 79.6)	ABCWY vs / feriority of Ma CI lower lim d Rises i % 1.1 1.1 1.1 5.5 26.5 26.5	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite (95% CI) ^d (-2.1, 3.7) (-2.2, 3.8) (-1.3, 11.9) (21.6, 31.1) (4.9, 16.1)	nB-FHbp base ome instances rs for Se % % % % % % 96.2 93.4 94.8 96.2 96.2	ed on GMRs was c , indicating possible rogroups A, enABCWY + Saline (95% CI) ^c (92.7, 98.4) (92.5, 98.5) (89.6, 96.1) (91.1, 97.3) (92.7, 98.4)	also shown (T y increased (C, W, ar MenACW / MenACW / MenACW / MenACW / MenACW / MenACW	Gable 5) GMTs in the MenAl nd Y Y-Experienced ^b AenB-FHbp enACWY-CRM (95% CI) ^c (94.9, 98.5) – (93.6, 97.4) – (94.9, 98.5)	3CWY vs the % 	e MenB-! Differen (95 (-4 (-4 (-4		
Table 2. Differen Serogroup Time Point A Im PD1 Im PD2° C Im PD2° W Im PD2° W Im PD1 Im PD2°	ces in Percen % % % 96.9 97.0 97.0 75.5 96.5 96.5 96.6 97.4	tages of Subj MenABCWY + Saline (95% CI)° (94.1, 98.7) (93.9, 98.8) (69.8, 80.6) (93.2, 98.5) (81.8, 90.5) (94.4, 99.0)	Cts Achi MenA % % % 95.8 95.8 70.0 70.0 70.0 75.9 75.9	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b MenB-FHbp enACWY-CRM (95% CI) ^c (93.7, 97.4) – (65.8, 74.0) – (71.9, 79.6) –	ABCWY vs / feriority of Ma CI lower lim d Rises i % 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1.	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite (95% Cl) ^d (-2.1, 3.7) (-2.2, 3.8) (-1.3, 11.9) (21.6, 31.1) (4.9, 16.1) (17.1, 25.8)	nB-FHbp base ome instances rs for Se % % % % % % % % % %	ed on GMRs was c , indicating possible rogroups A, enABCWY + Saline (95% CI) ^c (92.7, 98.4) (92.5, 98.5) (89.6, 96.1) (91.1, 97.3) (91.1, 97.8)	also shown (T y increased C C, W, ar MenACW % 97.0 97.0 97.0 97.0	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b AenB-FHbp enACWY-CRM (95% CI) ^c (94.9, 98.5) – (93.6, 97.4) – (94.9, 98.5) –	3CWY vs the % -0.8 -0.8 -0.8 -0.8 -0.8 -0.8 -0.8 -0.8	e MenB- Differen (95 (-4 (-4 (-4 (-4 (-4		
Table 2. Differen Serogroup Time Point A Im PD1 Im PD2° C Im PD10 Im PD2° W Im PD2° W Im PD10 Im PD2° Y Im PD10 Im PD10	ces in Percen % % % % 96.9 97.0 97.0 75.5 96.5 86.6 97.4 86.0	tages of Subj MenABCWY + Saline (95% CI) ^c (94.1, 98.7) (93.9, 98.8) (93.9, 98.8) (69.8, 80.6) (93.2, 98.5) (81.8, 90.5) (94.4, 99.0)	Cts Achi MenA %	Men • Noninf – 95% eving ≥4-Fol CWY-Naive ^b MenB-FHbp enACWY-CRM (93.7, 97.4) (65.8, 74.0) (71.9, 79.6) 	ABCWY vs / feriority of Ma o CI lower lim d Rises i % 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1	MenB-FHbp enABCWY to Me it for GMR >1 in se in hSBA Tite (95% CI) ^d (-2.1, 3.7) (-2.2, 3.8) (-1.3, 11.9) (21.6, 31.1) (17.1, 25.8) (8.1, 19.7)	nB-FHbp base ome instances rs for Se % % % % % % % % % %	ed on GMRs was c indicating possible rogroups A, enABCWY + Saline (95% CI) ^c (92.7, 98.4) (92.5, 98.5) (89.6, 96.1) (91.1, 97.3) (91.1, 97.8)	also shown (T y increased (C, W, ar MenACW % 97.0 97.0 - 97.0 - 97.0 -	Table 5) GMTs in the MenAl nd Y Y-Experienced ^b MenB-FHbp enACWY-CRM (95% CI) ^c (94.9, 98.5) – (93.6, 97.4) – (94.9, 98.5) – (94.9, 98.5) – (94.9, 98.5) – (94.9, 98.5) – (94.9, 98.5) – (91.9, 96.6)	BCWY vs the % % -0.8 -0.8 -0.8 -0.8 -0.8 -0.8 -0.8 -0.8 -0.8 -0.8 -0.8	e MenB-I Differend (95 (-4 (-4 (-4 (-4 (-4		

				M	enACWY-I	Naive ^a			MenACWY-Experienced ^a								
Serogroup Time Point		MenABC	WY + Saline		Men + MenA	B-FHbp CWY-CRM				MenAB	CWY + Saline		Me + Men	nB-FHbp ACWY-CRM			
	n ^b	GMT	(95% CI) ^c	n ^b	GMT	(95% CI) ^c	Ratio ^d	(95% CI)⁰	n ^b	GMT	(95% CI) ^c	n ^b	GMT	(95% CI) [.]	Ratio ^d	(95% CI) ^e	
A																	
1m PD1	264	215.8	(184.6, 252.4)	510	203.2	(178.7, 231.0)	1.06	(0.86, 1.31)	218	568.6	(492.9, 656.0)	411	916.1	(809.1, 1037.3)	0.62	(0.51, 0.76	
1m PD2 ^f	232	151.3	(134.1, 170.7)	-	_	_	0.74	(0.61, 0.92)	191	337.3	(291.7, 390.0)	_	_	_	0.37	(0.30, 0.45	
С																	
1m PD1	262	111.5	(87.2, 142.6)	509	81.4	(68.1, 97.4)	1.37	(1.01, 1.86)	264	814.9	(689.4, 963.2)	506	827.0	(722.5, 946.6)	0.99	(0.79, 1.23)	
1m PD2	231	229.1	(194.7, 269.5)	-	_	_	2.81	(2.11, 3.75)	237	498.7	(429.1, 579.6)	_	_	_	0.6	(0.48, 0.75	
W																	
1m PD1	264	98.4	(80.7, 120.0)	512	71.2	(61.5, 82.4)	1.38	(1.08, 1.77)	219	1214.9	(1032.0, 1430.1)	414	1176.7	(1017.9, 1360.2)	1.03	(0.82, 1.30	
1m PD2 ^f	233	274.1	(242.7, 309.7)	-	_	_	3.85	(3.05, 4.85)	191	570.9	(484.3, 673.0)	_	_	_	0.49	(0.38, 0.62	
Y																	
1m PD1	263	141.9	(118.8, 169.4)	510	96.6	(83.9, 111.2)	1.47	(1.16, 1.85)	218	1174.0	(990.3, 1391.9)	413	1000.2	(872.1, 1147.1)	1.17	(0.94, 1.47)	
1m PD2 ^f	233	301.5	(266.6, 341.0)		_	_	3.12	(2.49, 3.90)	191	558.6	(470.0, 663.9)		_	_	0.56	(0.44, 0.70	

^bNumber of subjects with valid and determinate assay results. ^cBack transformations of CIs based on Student t distribution for the mean logarithm of assay results. ^dNoninferiority criterion based on a 2-fold margin.

^eBack transformations of CIs based on Student t distribution for the mean difference of the logarithms of the measures. ^fRatios at this timepoint were calculated between 1m PD2 for the MenABCWY groups and 1m PD1 for the MenB-FHbp + MenACWY-CRM groups.

Table 4. Diff ≥4- Ser	eren Fold ogro	ces i Rise up B	n Pe s in ł at 1	rcentage nSBA Tite Month	es of ersª Afte	Sub and r Do	jects Com se 2	Achievi posite R	ng espo	onses ^b for		
	MenABCWY + Saline + MenACWY-CR							bp ſ-CRM	Difference			
Strain (Variant)	n°	n ^d	%	(95% CI) ^e	n°	n ^d	%	(95% CI)°	%	(95% CI) ^f		
PMB80 (A22)	422	320	75.8	(71.5, 79.8)	827	610	73.8	(70.6, 76.7)	2.1	(–3.1, 7.0)		
PMB2001 (A56)	418	396	94.7	(92.1, 96.7)	823	782	95.0	(93.3, 96.4)	-0.3	(-3.2, 2.2)		
PMB2948 (B24)	422	321	76.1	(71.7, 80.1)	835	563	67.4	(64.1, 70.6)	8.6	(3.4, 13.7)		
PMB2707 (B44)	432	396	91.7	(88.6, 94.1)	850	734	86.4	(83.9, 88.6)	5.3	(1.7, 8.7)		
Composite response ^b	418	334	79.9	(75.7, 83.6)	814	605	74.3	(71.2, 77.3)	5.6	(0.6, 10.3)		
hSBA=serum bactericidal activity a quadrivalent meningococcal CRM °The 4-fold rise in titers was defined (ie, 1:16 for PMB80, 1:8 for PMB2	issay using hi conjugate va d as follows: 001, PMB294	uman comple ccine; MenB for subjects v 48, and PMB	ment; LLOQ= =meningococ vith a baselin 2707), a resp	elower limit of quantitati cal serogroup B; MenB e hSBA titer <1:4, a res ponse was defined as a	on; MenAB -FHbp=Trum ponse was in hSBA titer	CWY=penta nenba®, bivo defined as o ≥4 times th	valent serog Ilent rLP2086 In hSBA titer e LLOQ; for	roups A, B, C, W, Y vac 5. ≥1:16; for subjects with subjects with a baseline	ccine; MenA a baseline h hSBA titer ≥	CWY-CRM=Menveo®, SBA titer ≥1:4 and <lloq ≥LLOQ, a response was</lloq 		

defined as an hSBA titer ≥4 times the baseline titer. ^bThe composite response was defined as hSBA titer ≥LLOQ for all 4 MenB strain. ^cNumber of subjects in the specified group. ^dNumber of subjects in the specified categories Calculated using the Clopper Pearson method

^tCalculated using the Miettinen-Nurminen methods for the difference in percentages. Noninferiority at the 10% margin was achieved if the lower limit of this 95% CI was greater than -10%.

Table 5. hS	BA G	MT Ra	tio for Ser	ogrou	p B a	t 1 Month	After	Dose 2
		MenAl + Sa	BCWY line		MenB- MenAC	FHbp WY-CRM		
Strain (Variant)	nª	GMT	(95% CI) ^ь	n°	GMT	(95% CI) ⁵	Ratio ^c	(95% CI) ^d
PMB80 (A22)	433	51.0	(46.7, 55.7)	852	49.3	(46.2, 52.6)	1.03	(0.93, 1.16)
PMB2001 (A56)	435	152.3	(138.5, 167.5)	854	139.5	(130.6, 149.1)	1.09	(0.97, 1.22)
PMB2948 (B24)	426	26.6	(23.9, 29.7)	842	21.2	(19.6, 22.9)	1.26	(1.10, 1.44)
PMB2707 (B44)	436	43.3	(39.1, 47.9)	853	37.8	(35.1, 40.8)	1.14	(1.01, 1.30)
GMT=geometric mean titer; hSl quadrivalent meningococcal Cl	BA=serum bacte RM conjugate vo	ricidal activity as accine; MenB-FH	- ssay using human complement bp=Trumenba®, bivalent rLP20	; MenABCWY= 86.	- oentavalent sero	groups A, B, C, W, Y vaccine	; MenACWY-CR	M=Menveo®,

^aNumber ot subjects in the specified group. ^bBack transformations of confidence levels based on Student t distribution for the mean logarithm of assay results. ^cNoninferiority criterion was based on a 2-fold margin. ^dBack transformations of the CI based on Student t distribution for the mean difference of the logarithms of the measures



- Local reactions and systemic events within 7 days after any dose similar between groups and mostly mild to moderate in severity (Figure 2)
- Injection site pain most commonly reported local reaction
- MenABCWY + saline, n=506; 9.8% severe MenB-FHbp + MenACWY-CRM, n=957; 8.8% severe
- Median time to onset of local reactions 1–2 days after each dose across groups
- Median duration of local reactions 1–2 days after each dose across groups - Most commonly reported systemic events
- Fatique
- MenABCWY + saline: n=343; 5.7% severe – MenB-FHbp + MenACWY-CRM: n=659; 5.0% severe
- Headache
- MenABCWY + saline: n=322; 3.9% severe – MenB-FHbp + MenACWY-CRM: n=624; 3.9% severe

Figure 2. (A) Local Reactions and (B) Systemic Events Reported Within 7 Days After Any Dose



MenABCWY=pentavalent serogroups A, B, C, W, Y vaccine; MenACWY-CRM=Menveo[®], quadrivalent meningococcal CRM conjugate vaccine; MenB-FHbp=Trumenba[®], bivalent rLP2086. *At the MenABCWY/MenB-FHbp injection site.

lable 6. Summary of Adverse Events	
Adverse Event	nª
Occurred during 30 d after any dose	
	512

		MenA	BCWY + S	Saline	MenB-FHbp + MenACWY-CRM					
dverse Event	n°	n ^b	%	Events n ^c	n ^b	nc	%	Events n		
ccurred during 30 d after any dose										
All AEs	543	124	22.8	188	1057	255	24.1	376		
Related	543	20	3.7	43	1057	44	4.2	73		
Severe	543	5	0.9	7	1057	17	1.6	19		
ccurred 1 mo after dose 2 through 6 mo										
All SAEs	478	3	0.6	4	950	5	0.5	6		
Related	478	0	0.0	0	950	0	0.0	0		
All MAEs	478	78	16.3	122	950	158	16.6	247		
Related	478	0	0.0	0	950	0	0.0	0		
All NDCMCs	478	1	0.2	1	950	3	0.3	3		
Related	478	0	0.0	0	950	0	0.0	0		

^aNumber of subjects in the specified group. ^bNumber of subjects in the specified category Total number of occurrences of the event specified; subjects could be represented more than once



or more information please contact: John L. Perez MD, MBA, MA Pfizer Inc accine Research and Development 500 Arcola Road Collegeville, PA, USA 19426 Email: john.perez@pfizer.com

- Median day of onset for most systemic events 2 days after each dose across

– Median duration of systemic events 1–2 days after each dose across groups - No local reactions or systemic events led to study withdrawal Subjects (%) reporting AEs up to 30 days after any dose similar between groups

(Table 6) Most related AEs were reactogenicity events

 Subjects (%) reporting AEs up to 6 months after dose 2 similar between groups (Table 6)

No immediate AEs in the MenABCWY group

 No clinically meaningful differences between the ACWY-naive and -experienced participants for all safety outcomes



CONCLUSIONS

- MenABCWY immune responses as assessed by 4-fold rises were robust and noninferior to **MenB-FHbp and MenACWY-CRM** in individuals 10-25 years of age, regardless of prior ACWY exposure
- MenABCWY was well tolerated with an acceptable safety profile
- Profiles between ACWY-naive and -experienced subjects were comparable
- A single, comprehensive vaccine protecting against A, B, C, W and Y disease-causing serogroups may simplify immunization schedules of existing meningococcal vaccines and increase convenience, potentially leading to higher vaccination rates
- The favorable benefit-risk profile of MenABCWY supports further clinical development

REFERENCES

- . Pace D and Pollard AJ. Vaccine. 2012;30(suppl 2):B3-B9. 2. National Center for Immunization and Respiratory Diseases. Enhanced Meningococcal Disease Surveillance Report, 2018. Atlanta, GA: Centers for Disease Control and Prevention; 2018. CS283195.
- 3. Purmohamad A, et al. *Microb Pathog*. 2019;134:103571. 4. Centers for Disease Control and Prevention. Recommended child and
- adolescent immunization schedule for ages 18 years or younger, United 🗸 States 2020. Available at: https://www.cdc.gov/vaccines/schedules/ downloads/child/0-18yrs-child-combined-schedule.pdf. Accessed August 17, 2020.
- 5. Goldschneider I, et al. J Exp Med. 1969;129(6):1307-1326.

FUNDING AND ACKNOWLEDGMENTS

This study was supported by Pfizer Inc. Medical writing support was provided by Kate Russin, PhD, of ICON plc (North Wales, PA, USA) and was funded by Pfizer Inc.

DISCLOSURES

James Peterson, Daniel Drazan, Hanna Czajka, and Ilkka Seppa are investigators in Pfizer clinical studies. Jason Maguire, Jean-Louis Pregaldien, Roger Maansson, Robert O'Neill, Annaliesa S. Anderson, Paul Balmer, Johannes Beeslaar, and John L. Perez are current employees of Pfizer Inc and may hold stock or stock options.