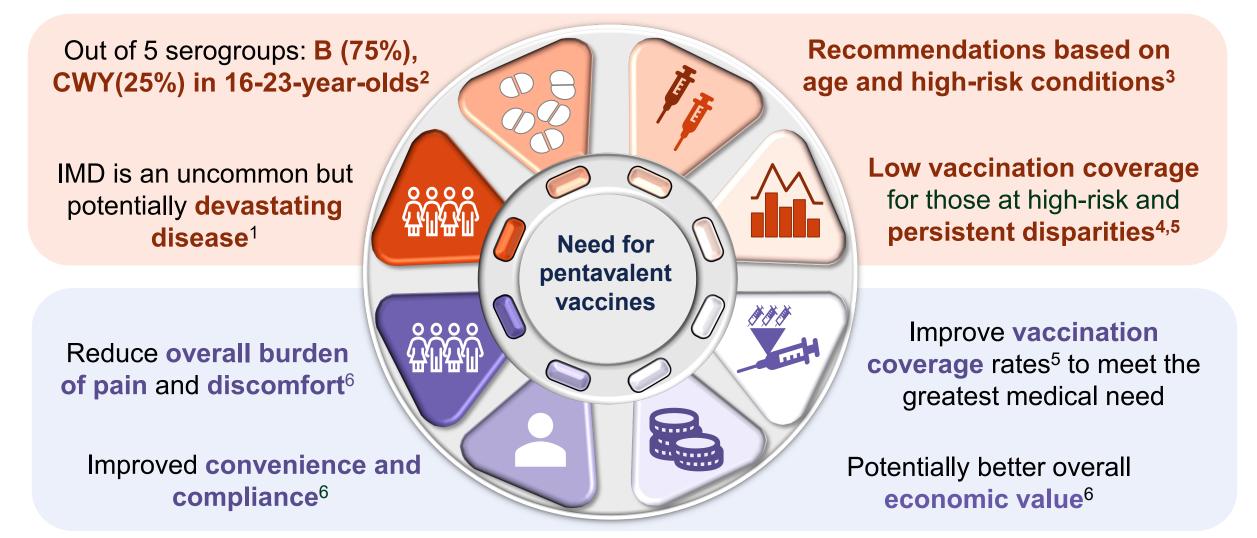


MenABCWY for the prevention of Invasive Meningococcal Disease caused by serogroups A, B, C, W and Y

Wendy Sohn, MD Global Medical Lead Neisseria Vaccines

Concerted Prevention of IMD in Adolescents and Young Adults



1. Mbaeyi S, et al. JAMA Pediatr 2020; 174 (9):843-851; 2. Enhanced Meningococcal Disease Surveillance Reports 2015-2022; 3. CDC Immunization Schedule 2024; 4. Pingali C, et al. MMWR Morb Mortal Wkly Rep 2023; 72(34):912-919; 5. Marshall G, et al. Clin Infect Dis 2022, 75(1):155-158; 6. Kroger A, et al. General Best Practice Guidelines for Immunization. [www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf]. Accessed on February 28th, 2024.

MenABCWY Program Built on Antigenic Components of MenACWY_{CRM} (Menveo) and MenB-4C (Bexsero)

Lyophilized MenACWY _{CRM} (vial)	+	Liquid MenB-4C (prefilled syringe)	=	MenABCWY ¹
MenACWY _{CRM} ² 2010		MenB-4C ³ 2015		Anticipated 2025 ¹
Immunogenicity and Safety in Healthy 2 months-55 year-olds ²		Immunogenicity and Safety in Healthy 10-25 year-olds ³		Immunogenicity and Safety in Healthy 10-25 year-olds
Immunogenicity in high-risk patients ⁴⁻⁶		Immunogenicity in high-risk patients ^{7,8}		
Persistence of immune response after 4-6 years ⁹⁻¹¹		Persistence of immune response after 4-7.5 years ¹²		
Real-world effectiveness ¹³		Real-world effectiveness ¹⁴⁻¹⁶		

1. GSK Press Release April 16, 2024. https://www.gsk.com/en-gb/media/press-releases/gsk-s-5-in-1-meningococcal-abcwy-vaccine-candidate-accepted-for-regulatory-review-by-us-fda/; 2. Prescribing Information for <u>BEXSERO</u>; 4. Isitt C et al, *HIV* Med. 2023; 24(9):979-989; 5. Kimura A et al, *Clinical and Vaccine Immunology*. 2011; 18(3):483-486; 6. Findlow J et al, *Vaccine*. 2015; 33(29):3322-30; 7.Martinon-Torres F et al, *Pediatrics*. 2018; 142(3): e207174250; 8. Robin C et al, *Clin Microbiol Infect*. 2022, 28(12):1609-1614; 9. Tipton et al, *Vaccine*. 2019; 37(42):6171-6179; 10. Baxter et al, *Pediatr Infect Dis J*. 2014; 33(11):1169-1176; 11. Jacobson et al *Pediatr Infect Dis J*. 2013; 32(4):e170-177; 12. Watson PS et al. *Expert Review of Vaccines*. 2019; 18:4, 343-352; 13. Hyoung Im J et al, *Vaccine*. 2020; 38 (730-732); 14. McMillan M et al, *Clin Infect Dis*. 2021; 73(1):e233–7; 15. Wang B et al *Lancet Infect Dis*. 2022; 22:1011–20; 16. Wang B et al. *J Infect*. 2023; 22:S0163–4453

MenABCWY Program Built on Antigenic Components of MenACWY_{CRM} (Menveo) and MenB-4C (Bexsero)

Lyophilized MenACWY_{CRM} (vial) Liquid MenB-4C (prefilled syringe)

= MenABCWY¹

MenABCWY Proposed Indication²

Vaccine indicated for active immunization to prevent invasive disease caused by Neisseria meningitidis serogroups A, B, C, W, and Y in individuals **10 through 25 years** of age

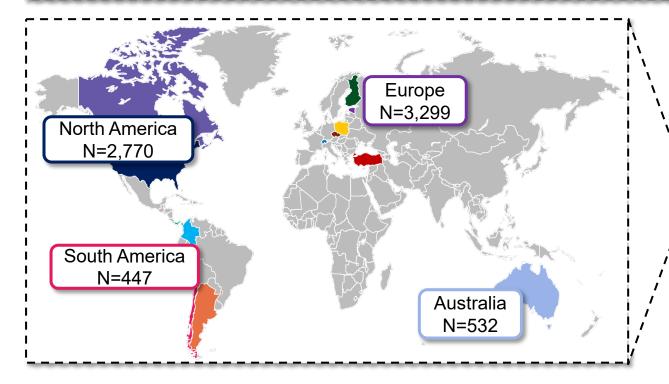
Administer 2 doses (0.5 mL each) intramuscularly at least 6 months apart

1. GSK Press Release April 16, 2024. https://www.gsk.com/en-gb/media/press-releases/gsk-s-5-in-1-meningococcal-abcwy-vaccine-candidate-accepted-for-regulatory-review-by-us-fda/;

^{2.} MenABCWY Candidate Vaccine Draft Prescribing Information, February 2024

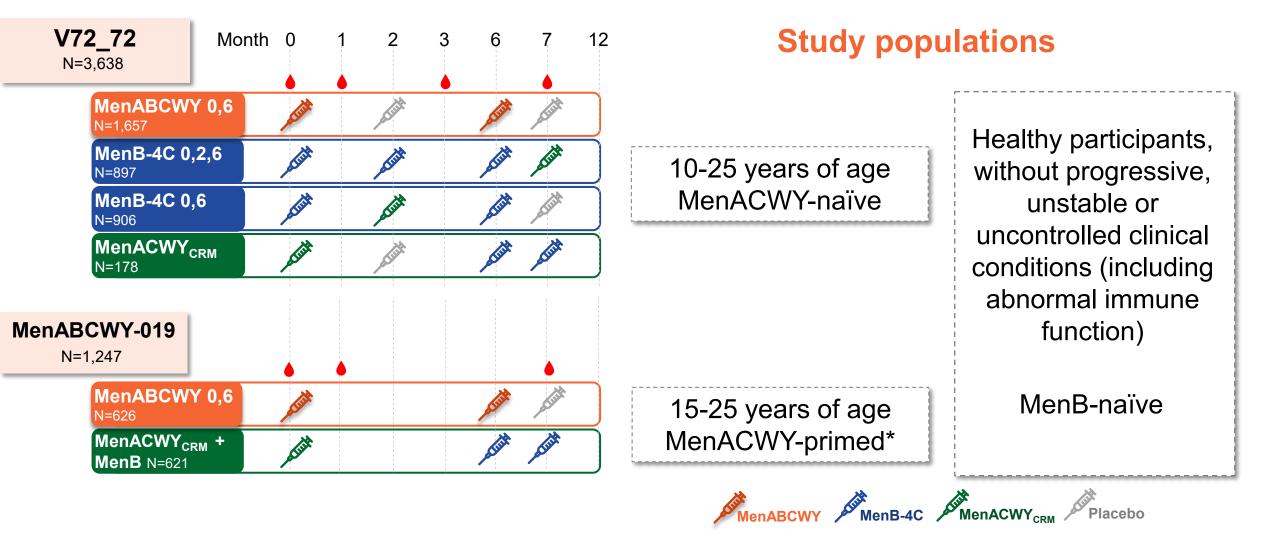
Comprehensive MenABCWY Clinical Development Program *12 Studies, >7,000 Participants, 13 Countries*

- > 10 completed Ph1-2 studies: different formulations and administration schedules in ages 9 42 years¹
- 2 completed Ph3 studies: safety and immunogenicity of MenABCWY in MenACWY-naïve and primed 10-25 yrs²⁻³
- ➤ 1 ongoing Phase 2 study: evaluating 2 doses administered 2 or 4 years apart in ages 11 14 years⁴



Vaccine exposed set ¹	N		
MenABCWY (Total)	3,718		
MenABCWY	→ 1,216		
MenB-4C	2,969		
MenACWY _{CRM}	361		
TOTAL receiving ≥ 1 dose of study vaccine	7,048		

Phase 3 Studies Assessed Safety and Immunogenicity of MenABCWY Compared to MenB-4C, MenACWY_{CRM} Administered per CDC Schedule at Study Onset



N for each study arm depicts the exposed set. *MenACWY-primed participants received dose of licensed MenACWY vaccine \geq 4 years prior to study start Clinicaltrials.gov identifier <u>NCT04502693</u>, accessed May 31st, 2024 and Clinicaltrials.gov identifier <u>NCT04707391</u>, accessed May 31st, 2024.

Demographics and Baseline Characteristics of Phase 3 Studies

		V72_72		MenABCWY-019		
		MenABCWY N=1,657	MenB-4C 0-6 N=906	MenACWY_{скм} N=178	MenABCWY N=626	MenACWY_{скм} N=621
Median age	At 1 st vaccination, years (range)	16 (9–26)	16 (9–26)	16 (10–25)	16 (15–25)	16 (15–25)
Age group	10–11 years	320 (19%)	172 (19%)	27 (15%)	0	0
	12–17 years	666 (40%)	368 (41%)	76 (43%)	450 (72%)	441 (71%)
	18–25 years	671 (40%)	366 (40%)	75 (42%)	176 (28%)	180 (29%)
Region	US	491 (30%)	270 (30%)	52 (29%)	366 (59%)	365 (59%)
Sex	Female	933 (56%)	446 (49%)	100 (56%)	343 (55%)	325 (52%)
Race	White	1492 (90%)	791 (87%)	162 (91%)	474 (76%)	467 (75%)
	Asian	71 (4%)	60 (7%)	9 (5%)	22 (4%)	33 (5%)
	Black or African American	59 (4%)	29 (3%)	6 (3%)	94 (15%)	86 (14%)
	Other	35 (2%)	26 (3%)	1 (1%)	36 (6%)	38 (6%)
Ethnicity	Not Hispanic or Latino	1546 (93%)	852 (94%)	172 (97%)	447 (71%)	432 (69%)
	Hispanic or Latino	92 (6%)	41 (5%)	6 (3%)	179 (29%)	192 (31%)
	Not reported	19 (1%)	13 (1%)	0	0	0





Evidence Supporting Safety and Immunogenicity of MenABCWY

Serogroups A C W Y

Serogroup B

Solicited and unsolicited adverse events after each dose of MenABCWY, MenB-4C or MenACWY_{CRM}

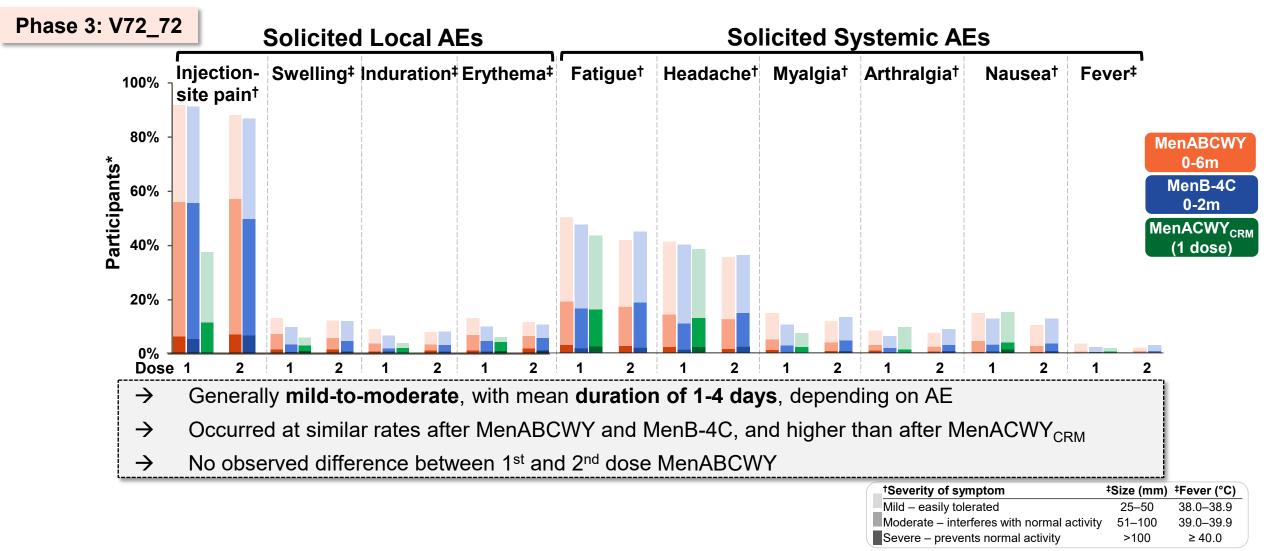
Non-inferiority vs MenACWY_{CRM} in MenACWY-naïve and -primed

GSK's MenABCWY Immunogenicity of MenABCWY against 110 serogroup B strains

> Immunological noninferiority of MenABCWY vs MenB-4C

Persistence and booster immune response up to 24 months

Solicited Local and Systemic AEs within 7 Days, after Each Vaccination with MenABCWY, MenB-4C or MenACWY_{CRM}



MenABCWY Demonstrated a Well-Tolerated Safety Profile Comparable to MenB-4C

Integrated Safety Analysis (Pooled)	MenABCWY N=3,718	MenB-4C _{N=2,969}	MenACWY _{CRM} N=361	
N =7,048	n (%)	n (%)	n (%)	
Unsolicited AEs (within 30 days of any vaccination)	1,072 (29%)	736 (25%)	47 (13%)	
Related*	256 (7%)	155 (6%)	10 (3%)	
AEs leading to withdrawal	8 (0.2%)	4 (0.1%)	0	
Medically attended AEs [†]	416 (12%)	302 (11%)	8 (4%)	
Related medically attended AEs [†]	22 (0.6%)	15 (0.5%)	0	
SAEs (entire study period)	70 (1.9%)	58 (2%)	5 (1.4%)	
Related*	3 (0.1%)	2 ‡ (0.1%)	0	
Deaths (all unrelated)	1§	2¶	1§	

*Assigned as related by investigator; † Medically attended flags for AEs are not available in studies V102P1, V102_02, V102_02E1 and V102_03. Participants from these studies are not included. Therefore, the denominator is different for the 3 groups (MenABCWY N=3488, MenB N=2861, MenACWY N=213); ‡2 SAEs occurred in the MenB-4C arms of the studies included in the pooled safety analysis: 1 SAE followed a MenB-4C and 1 followed a MenACWY-CRM vaccination; \$Suicide; ¶Deaths by poisoning and drug overdose; AE: adverse event; SAE: serious adverse event GSK, Data on File 2024N555058.

Evidence Supporting Safety and Immunogenicity of MenABCWY

Serogroups A C W Y

Serogroup B

Solicited and unsolicited adverse events after each dose of MenABCWY, MenB-4C or MenACWY_{CRM}

Non-inferiority vs MenACWY_{CRM} in MenACWY-naïve and -primed GSK's MenABCWY Immunogenicity of MenABCWY against 110 serogroup B strains

Immunological noninferiority of MenABCWY vs MenB-4C

Persistence and booster immune response up to 24 months

Assays Used to Infer Meningococcal Vaccine Protection

Traditional hSBA

Vaccine targets

N. meningitidis capsule polysaccharide Highly abundant, conserved antigens¹

hSBA against serogroupspecific polysaccharide capsule reference strain infers protection against all strains in serogroup²

Surrogate of protection:

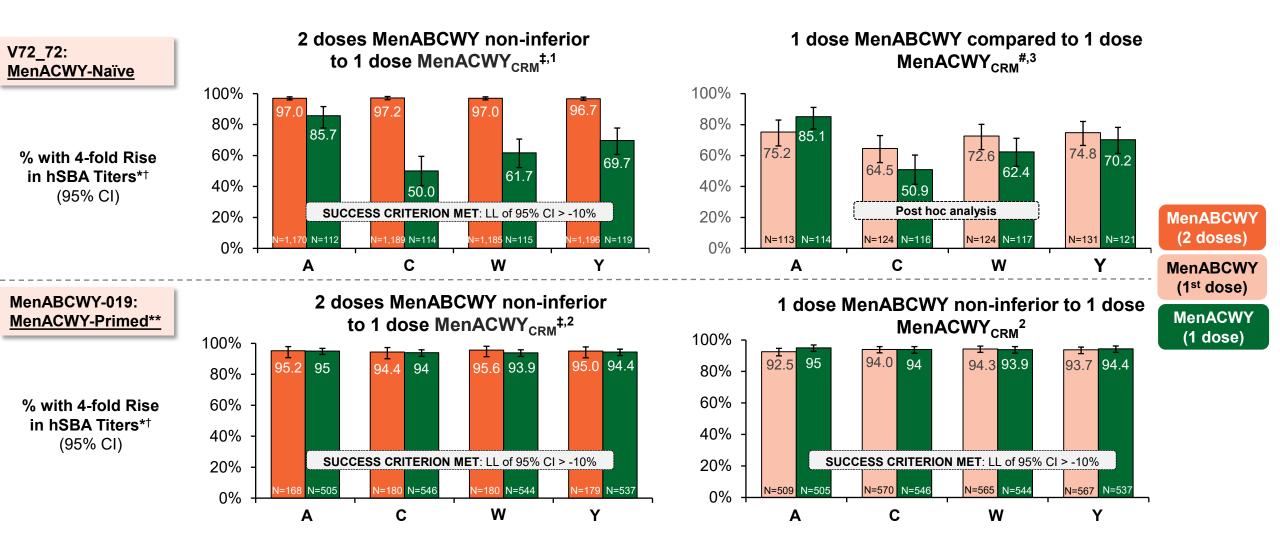
titer ≥4 threshold for protection^{2,3,4,5,6}

hSBA, human serum bactericidal assay

1. CDC, 2022. About meningococcal vaccines. https://www.cdc.gov/vaccines/vpd/mening/hcp/about-vaccine.html; 2. Donald RGK et al. Hum Vaccin Immunother. 2017;13:255–265; 3. Balmer P et al. Postgrad Med. 2020;132:184–191;

4. Goldschneider I, et al. J Exp Med. 1969;129(6):1307-1348; 5. Bröker M et al. Vaccine. 2009;27:5574–5580; 6.Ferlito et al. Clin Exp Immunol. 2018;194(3): 361-370; 6. Muzzi A et al. MSphere. 2022;e00385223

MenABCWY Non-Inferior to MenACWY_{CRM} in MenACWY-Naïve and MenACWY-Primed Participants



*At 1 month after 1 or 2 doses of MenABCWY or after single MenACWY vaccination; [†]Defined as a post-vaccination titer ≥4-fold the LOD or ≥LLOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥4-fold the pre-vaccination titer ≥4-fold the pre-vaccination titer ≥LOD and <LLOQ, and a post-vaccination titer ≥4-fold the pre-vaccination titer ≥LOQ. LOD: 4 for MenA, MenC, MenW, and MenY. LLOQ = 12 for MenA; 8 for MenC; 8 for MenW; 10 for MenY, except for the post-hoc analysis for which LLOQs were 8 for MenA and 11 for MenC; *Licensure criteria agreed with CBER; #full set analysis; **Primed participants had received a dose of MenACWY vaccine at least 4 years prior. CI – confidence interval, hSBA - human serum bactericidal assay, LOD – limit of detection; LLOQ – lower limit of quantitation 1. Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024; 2. Clinicaltrials.gov identifier NCT04707391, accessed May 31st, 2024; 3. GSK, Data on File 2024N555056.

Assays Used to Infer Meningococcal Vaccine Protection

Vaccine targets

MenACWY Vaccines *N. meningitidis* capsule polysaccharide

Highly abundant, conserved antigens¹

Traditional hSBA

hSBA against serogroupspecific polysaccharide capsule reference strain infers protection against all strains in serogroup²

hSBA does not assess

vaccine induced immune

response against many

diverse strains expressing

more than 1 antigen⁴

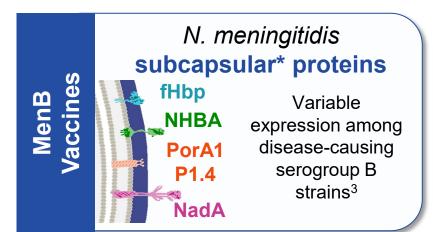
enc-hSBA

14

GSK developed enc-hSBA⁵ to test against multiple serogroup B strains

110 strains randomly selected from 2000-2008 IMD cases, that continue to represent 95% of US disease causing serogroup B strains⁵ collected up to 2017

hSBA, human serum bactericidal activity; enc-hSBA, endogenous complements human serum bactericidal activity, Men, meningococcal serogroup; fHbp – factor H binding protein; NHBA – Neisserial Heparin Binding Antigen; NadA – Neisseria Adhesin A; PorA1 P1.4 – porin A1 P1.4. *A MenB capsular vaccine was poorly immunogenic due to structural similarity between the capsule and human tissue⁵ 1.CDC, 2022. About meningococcal vaccines. <u>https://www.cdc.gov/vaccines/vpd/mening/hcp/about-vaccine.html</u>; 2. Donald RGK *et al. Hum Vaccin Immunother*. 2017;13:255–265; 3. Balmer P *et al. Postgrad Med.* 2020;132:184–191; 4. Kleinschmidt A *et al. NPJ Vaccines*. 2021;6:29; 5. Muzzi A et al. *MSphere*. 2022;e00385223



<u>enc-hSBA</u>: Immune Response Against Diverse Serogroup B Strains in MenABCWY vs MenB-4C Arms

Immunological Vaccine Effectiveness (IVE)

Test-Based

Responder-Based

 $IVE = (1 - relative risk) \times 100$

Relative risk defined as the percentage of tests without bactericidal activity in the group receiving MenB-containing vaccine compared to controls

→ informs on breadth of MenB vaccine strain coverage at a population level

Percentage of participants whose sera killed ≥70% of strains tested[†]

→ percentage of participants achieving broad protection against serogroup B strains

*relative risk = ratio between % of tests lacking bactericidal activity against 110-strain panel in group receiving MenB-containing vaccine and control (MenACWY vaccine); [†]Target number of strains tested for each participant was 35 strains out of the 110 strains panel. MenB: meningococcal serogroup B; enc-hSBA: endogenous complement serum bactericidal activity; IVE: immunological vaccine effectiveness Welsch et al, *Vaccine*. 2018;36(15): 5309-5317; Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024

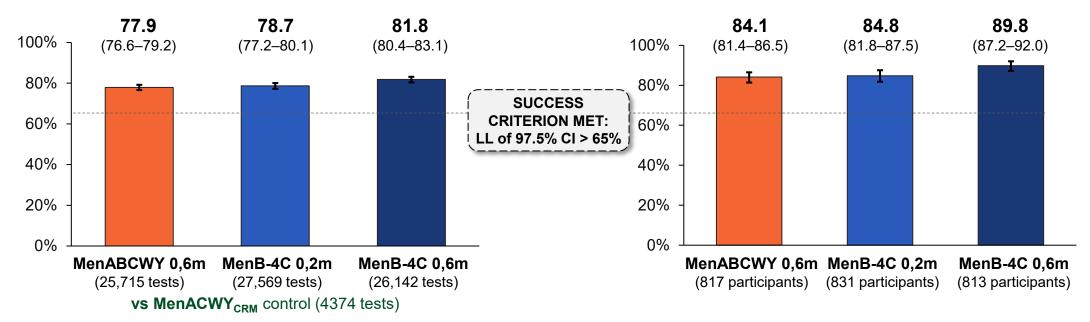
<u>enc-hSBA</u>: Immune Response against Diverse Serogroup B Strains after 2 doses of MenABCWY or MenB-4C

Test-Based IVE

Informs breadth of MenB vaccine strain coverage at a population level

Responder-Based IVE

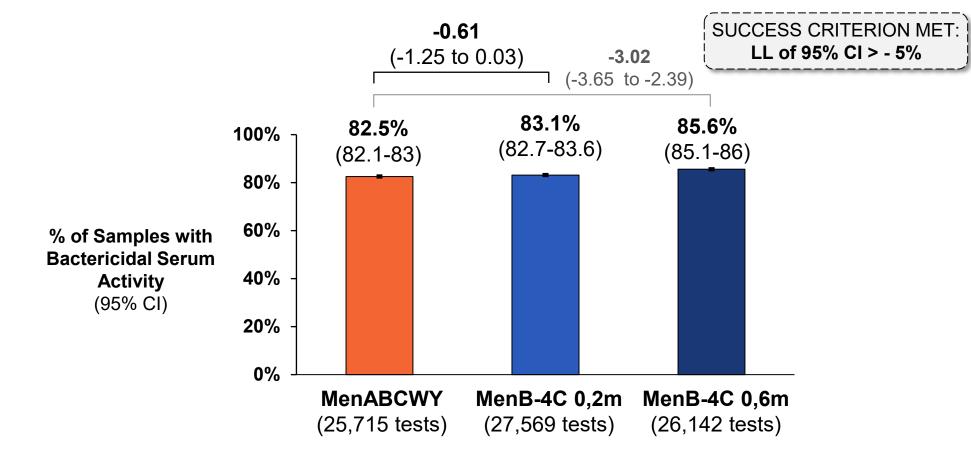
→ % participants achieving broad protection against serogroup B strains



MenABCWY achieved breadth of bactericidal effect against a diverse and broad panel of serogroup B strains, similar to MenB-4C 2-dose administered 2 or 6 months apart

The 3 MenB-4C schedules were hierarchically tested for IVE in the order: MenB-4C 0-2-6m → MenB-4C 0-2m. The 0-2m schedule was the last schedule to meet the predefined success criterion (LL of 95% Cl > 65%) and was hence chosen as the comparator for the MenABCWY 0-6m schedule for all subsequent statistical analyses. LL, lower limit; IVE: immunological vaccine effectiveness Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024

<u>enc-hSBA</u>: Noninferiority of Immune Response against Diverse Serogroup B Strains in MenABCWY vs MenB-4C



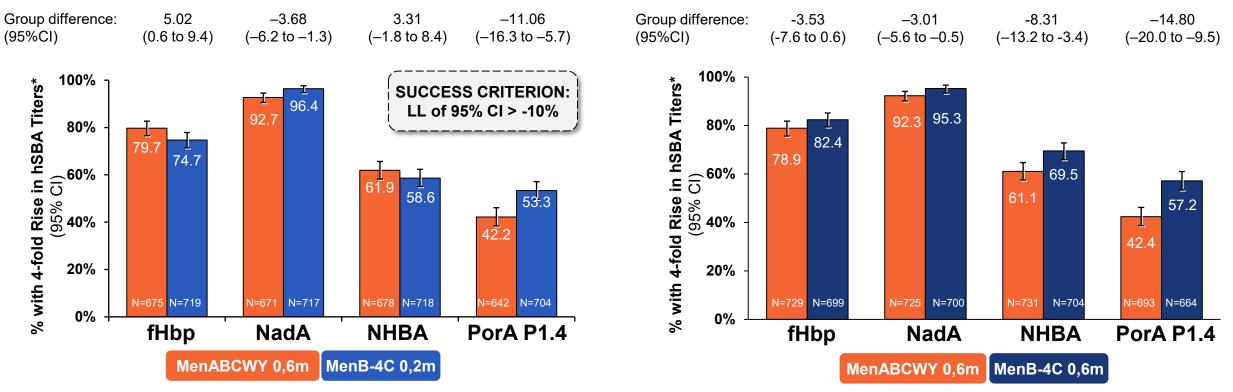
MenABCWY was noninferior to MenB-4C, based on bactericidal effects against diverse strains assessed by enc-hSBA assay

*The 3 MenB-4C schedules were hierarchically tested for IVE in the order: MenB-4C 0-2-6m → MenB-4C 0-2m. The 0-2m schedule was the last schedule to meet the predefined success criterion (LL of 97.5% CI > 65%) and was hence chosen as the comparator for the MenABCWY 0-6m schedule for all subsequent statistical analyses. LL, lower limit Clinicaltrials.gov identifier <u>NCT04502693</u>, accessed May 31st, 2024

<u>hSBA</u>: MenABCWY Immune Response Against Serogroup B Reference Strains

MenABCWY 0,6m vs MenB-4C 0,2 m

MenABCWY 0,6m vs MenB-4C 0,6 m



- Secondary endpoint not met because success criterion not met for all 4 strains
- MenABCWY elicited comparable immune responses for 3 reference strains vs MenB-4C 0,2 and 2 reference strains vs MenB-4C 0,6m.

^{*}At 1 month after 2^{nd} MenABCWY or 2^{nd} MenB-4C vaccination, relative to baseline. 4-fold rise in hSBA titer for each strain was defined as a post-vaccination titer ≥ 4 -fold the LOQ or \geq LOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥ 4 -fold the pre-vaccination titer ≥ 4 -fold the LOQ or \geq LOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥ 4 -fold the pre-vaccination titer ≥ 4 -fold the pre-vaccina

Evidence Supporting Safety and Immunogenicity of MenABCWY

Serogroups A C W Y

Serogroup B

Solicited and unsolicited adverse events after each dose of MenABCWY, MenB-4C or MenACWY_{CRM}

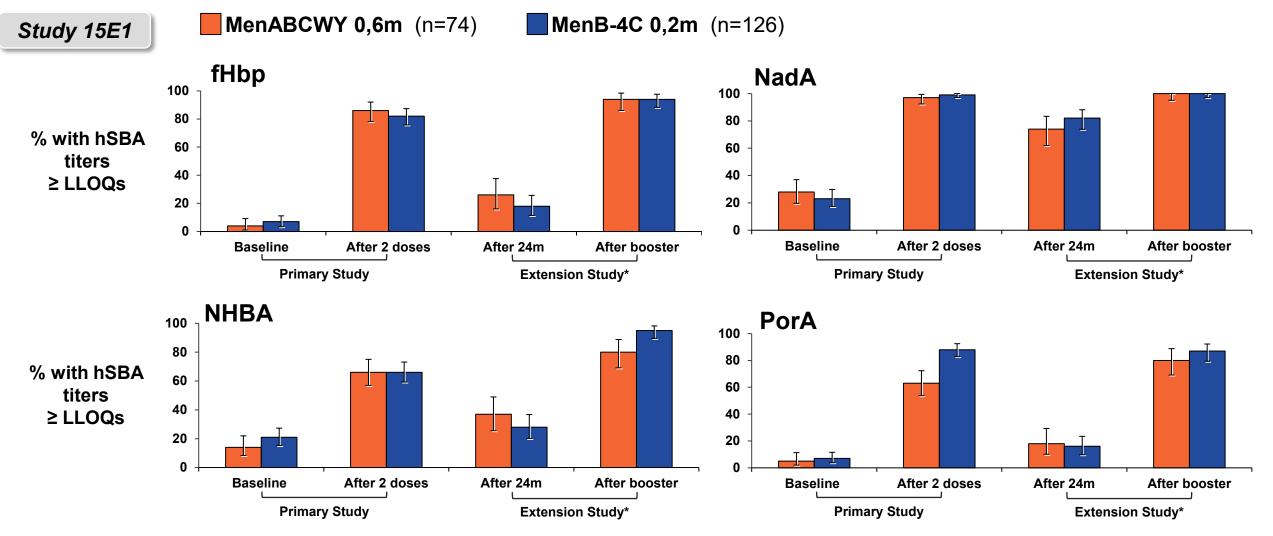
Non-inferiority vs MenACWY_{CRM} in MenACWY-naïve and -primed

GSK's MenABCWY Immunogenicity of MenABCWY against 110 serogroup B strains

> Immunological noninferiority of MenABCWY vs MenB-4C

Persistence and booster immune response up to 24 months

Persistence After 24 months and Booster Response of MenABCWY Demonstrated Against Serogroup B Reference Strains



*For follow-on group: blood draws were done at baseline and 5 days after booster dose. For the Matched Naive group: blood draws were baseline (prevaccination), 1 month after 1st dose and 5 days after 2nd dose. fHbp, factor H binding protein; hSBA, serum bactericidal assay using human complement; LLOQ, lower limit of quantitation; NadA, Neisseria adhesin A; NHBA, Neisseria heparin binding antigen; PorA, porin A. The LLOQs were 8.0 (fHbp), 8.6 (NadA), 8.9 (NHBA), 8.2 (PorA). Vesikari T et al. *Hum Vaccin Immunother*. 2021;17(11):4689-4700

MenABCWY Summary

 \rightarrow Combines two well-established vaccines licensed in the US - MenB-4C, MenACWY_{CRM}

→ Clinical program demonstrated safety and immunogenicity in adolescents and young adults

→ Tested against a broad panel of 110 serogroup B strains, representing 95% of US serogroup B disease-causing strains

 \rightarrow Demonstrated persistence of immune response up to 24 months

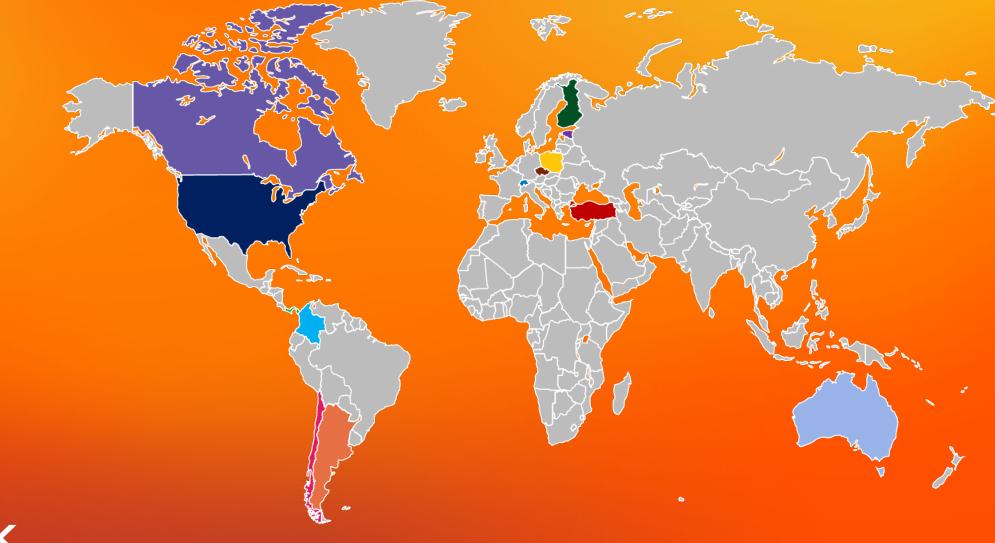
Summary of Data for Policy Considerations

2 doses of MenABCWY can protect against serogroups A,B,C W,Y

- → Achieves broad coverage against strains causing endemic and outbreak disease, to meet the current and evolving US epidemiology
- → Offers the opportunity to improve vaccination coverage in adolescents and young adults
- → Represents the evolution of IMD as **one vaccine-preventable disease**

MenABCWY allows for prevention of IMD with one vaccine

Investigators, study site personnel, study participants, and their families



Thank you!