Work Group Considerations Regarding MenABCWY Vaccine and Discussion of Potential Risk Groups for MenB Vaccination

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GSK's MenABCWY Vaccine Clinical Development Program

- Phase 3 studies
  - V72_72: ages 10–25 years, MenACWY-naïve/MenB-naïve, N=3,638
    - 87-91% White*; 3-6% Hispanic or Latino*; 49-56% female
  - MenABCWY-019: ages 15–25 years, MenACWY-primed/MenB-naïve, N=1,247
    - 75-76% White*; 29-31% Hispanic or Latino*; 52-55% female
  - Comparators: MenACWY-CRM, MenB-4C 0,2 mo., MenB-4C 0,6 mo.

- 10 Phase 1 and 2 studies

*Demographics of participants reflect countries in which studies performed

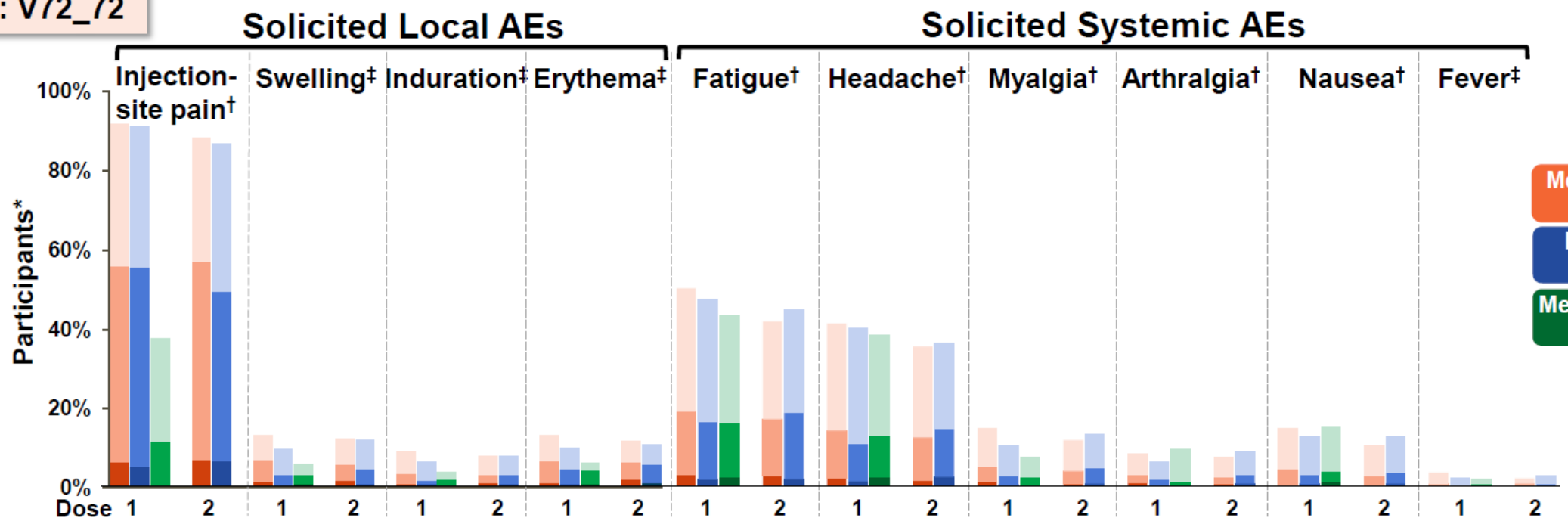
Assessment of Safety

- Phase 3 studies
  - Solicited local and systemic AEs after each dose of MenABCWY, MenACWY, and MenB
- Integrated Safety Analysis (N=7,048)
  - Unsolicited AEs within 30 days of vaccination
  - Related, leading to withdrawal, medically attended, related medically attended, SAEs, deaths

AE, adverse event; SAE, serious adverse event

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

Phase 3: V72_72



- → Generally **mild-to-moderate**, with mean **duration of 1-4 days**, depending on AE
- → Occurred at similar rates after MenABCWY and MenB-4C, and higher than after MenACWY$_{CRM}$
- → No observed difference between 1st and 2nd dose MenABCWY

†Severity of symptom	‡Size (mm)	‡Fever (°C)
Mild – easily tolerated	25–50	38.0–38.9
Moderate – interferes with normal activity	51–100	39.0–39.9
Severe – prevents normal activity	>100	≥ 40.0

AE: adverse event; *Number of participants varies by study vaccination: 1428-1638 for MenABCWY arm, 823-835 for MenB-4C and 178 for MenACWY.
GSK, Data on File 2024N555060

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

Integrated Safety Analysis (Pooled) N =7,048	MenABCWY N=3,718 n (%)	MenB-4C N=2,969 n (%)	MenACWY$_{CRM}$ N=361 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.

Solicited and Unsolicited AE Following Vaccination

- Solicited AE:
  - Local AE: MenABCWY≈MenB and MenABCWY>MenACWY
  - Systemic AE: MenABCWY≈MenB≈MenACWY

- Unsolicited AE:
  - MenABCWY slightly greater than MenB and greater than MenACWY
    - Except for AE leading to withdrawal during the entire study period: MenABCWY≈MenB<MenACWY

AE, adverse event

SAEs and Deaths

- SAE during entire study period: MenABCWY≈MenB>MenACWY (all ≤2%)
  - Related SAE during entire study period: MenABCWY≈MenB>MenACWY (all ≤0.1%)
    - 4 of 5 resolved or partially resolved (seizure*, connective tissue disorder*, neuromyelitis optica*, pyrexia/nausea/vomiting/headache¥)
    - 1 ongoing (ulcerative colitis† with positive family history for Crohn's disease)
- Deaths (all unrelated)
  - MenABCWY recipients (1): suicide
  - MenB recipients (2): drug overdose, poisoning
  - MenACWY recipients (1): suicide

*MenABCWY vaccine recipient, ¥MenACWY recipient, †MenB recipient
SAE, serious adverse event

Immunogenicity Assessment

- Serogroup A, C, W, Y
  - Seroresponse: 4-fold rise in hSBA titers
- Serogroup B
  - Seroresponse: 4-fold rise in hSBA titers
  - enc-hSBA assay: Assessment of protection against diverse disease-causing serogroup B strains
    - 110 randomly selected strains that represent 95% of U.S. “disease-causing” strains

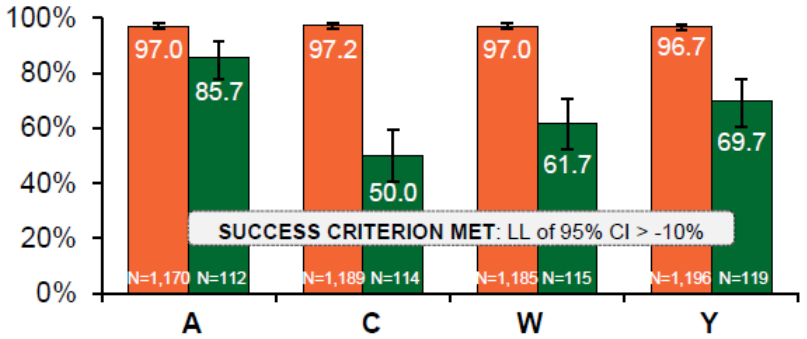
enc-hSBA, endogenous complement hSBA

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

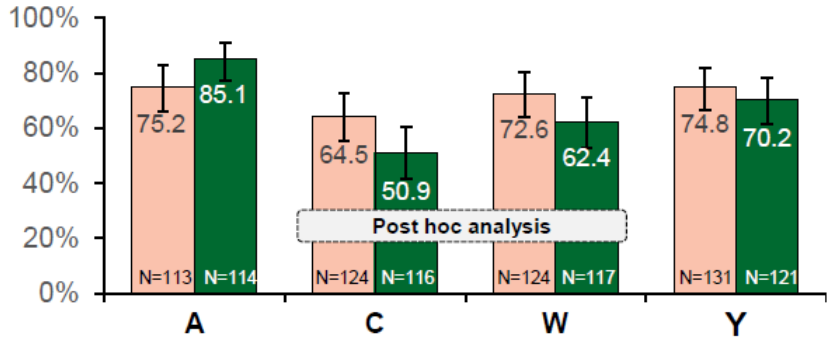
V72_72: MenACWY-Naïve

% with 4-fold Rise in hSBA Titers*† (95% CI)

2 doses MenABCWY non-inferior to 1 dose MenACWY$_{CRM}$‡,1



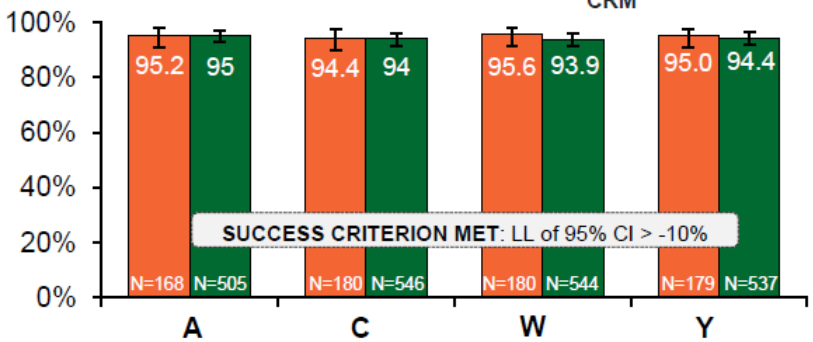
1 dose MenABCWY compared to 1 dose MenACWY$_{CRM}$#,3



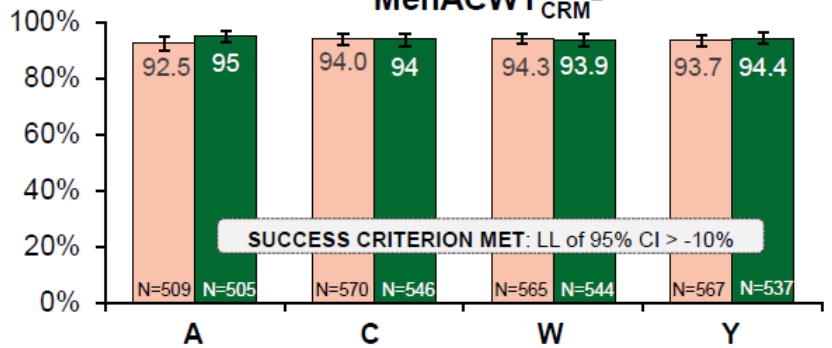
MenABCWY-019: MenACWY-Primed**

% with 4-fold Rise in hSBA Titers*† (95% CI)

2 doses MenABCWY non-inferior to 1 dose MenACWY$_{CRM}$‡,2



1 dose MenABCWY non-inferior to 1 dose MenACWY$_{CRM}$2



MenABCWY (2 doses)

MenABCWY (1st dose)

MenACWY (1 dose)

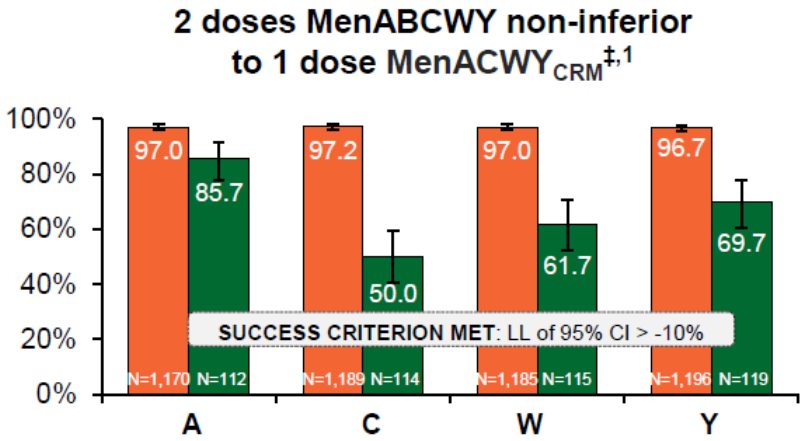
*At 1 month after 1 or 2 doses of MenABCWY or after single MenACWY vaccination; †Defined as a post-vaccination titer ≥4-fold the LOD or ≥LLOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥4-fold the LLOQ if pre-vaccination titer ≥LOD and <LLOQ, and a post-vaccination titer ≥4-fold the pre-vaccination titer if pre-vaccination titer ≥LLOQ. 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.

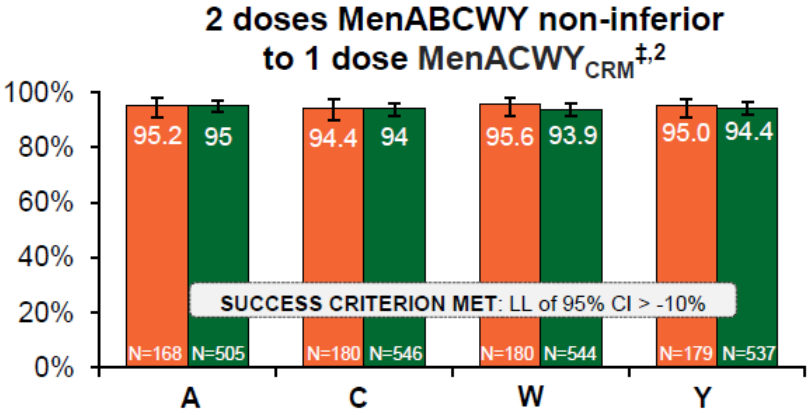
Presentation by GSK at ACIP, June 2024

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

V72_72: MenACWY-Naïve



MenABCWY-019: MenACWY-Primed**



- 2 doses MenABCWY non-inferior to 1 dose MenACWY
  - MenACWY-naïve and primed recipients

*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 LLOQ if pre-vaccination titer ≥LOD and <LLOQ, and a post-vaccination titer ≥4-fold the pre-vaccination titer if pre-vaccination titer ≥LLOQ. 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

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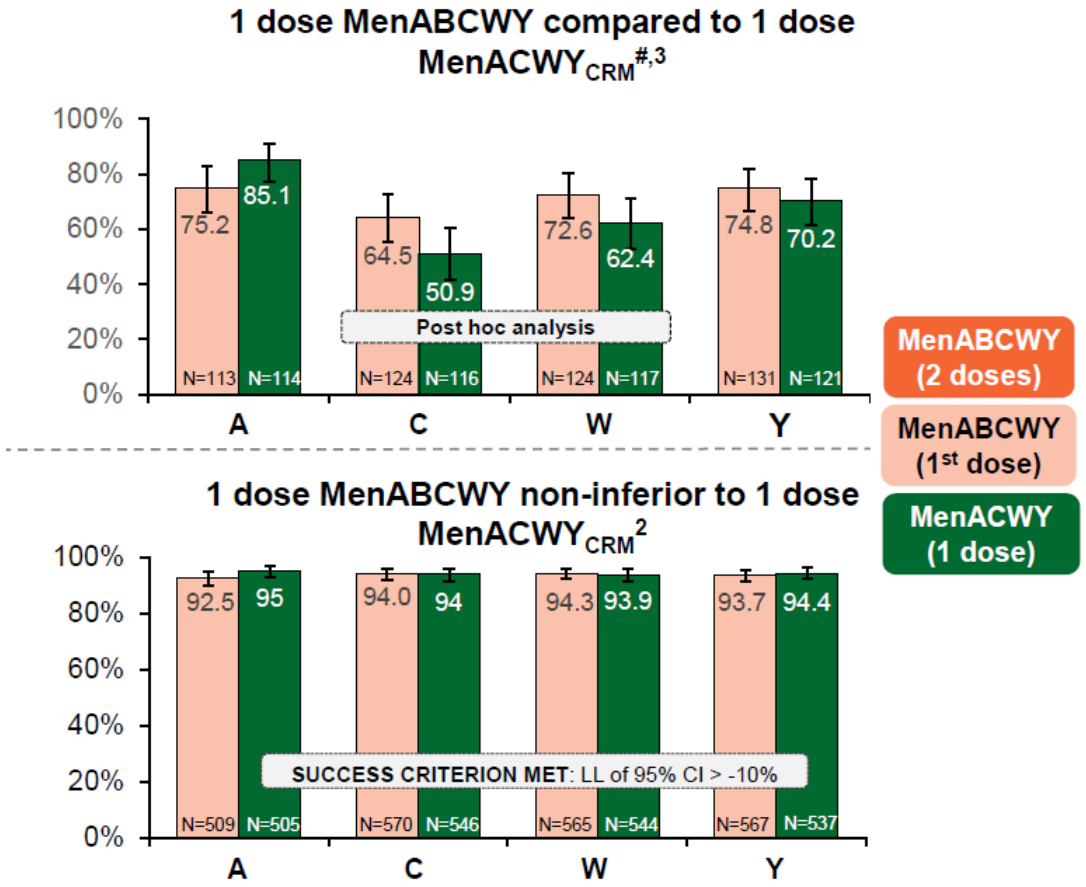
MenABCWY Non-Inferior to MenACWY$_{CRM}$ in MenACWY-Naïve and MenACWY-Primed Participants

- 1 dose MenABCWY non-inferior to 1 dose MenACWY in MenACWY-primed recipients
  - Naïve recipients: ad hoc analysis; confidence intervals overlap for all 4 serogroups
    - Responses greater for MenABCWY recipients compared to MenACWY recipients
      - Except for serogroup A (rare in U.S.)



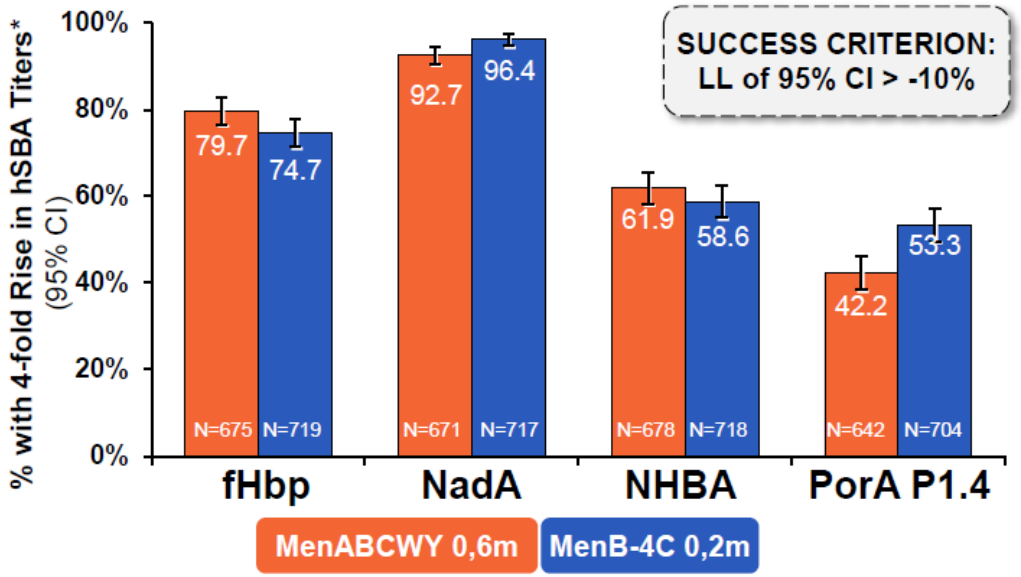
ichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥4-fold the LLOQ if pre-vaccination titer ≥LOD and <LLOQ, and
; 8 for MenC; 8 for MenW; 10 for MenY, except for the post-hoc analysis for which LLOQs were 8 for MenA and 11 for MenC;
ifidence interval, hSBA - human serum bactericidal assay, LOD – limit of detection; LLOQ – lower limit of quantitation
ata on File 2024N555056.

Presentation by GSK at ACIP, June 2024

hSBA: MenABCWY Immune Response Against Serogroup B Reference Strains

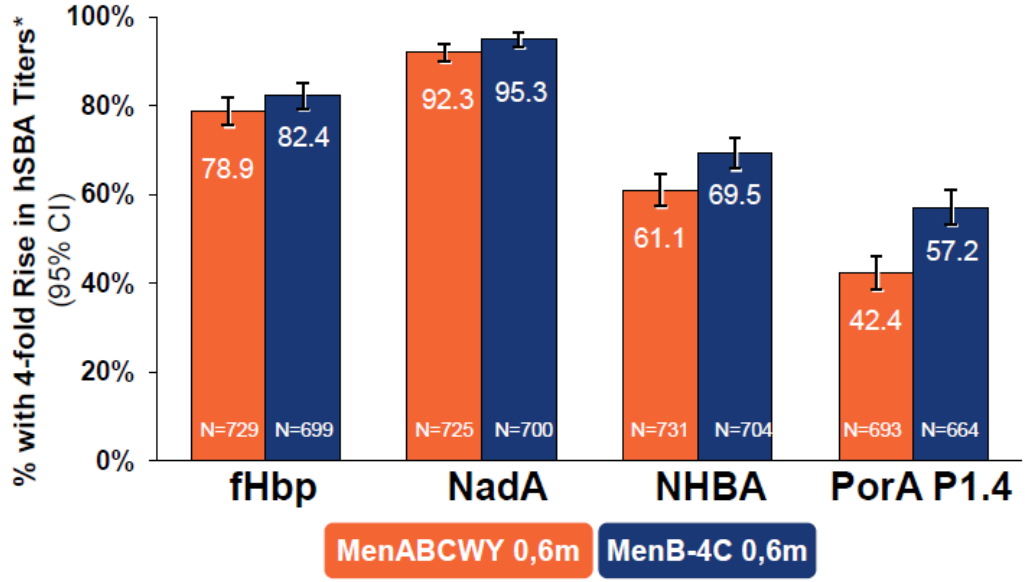
MenABCWY 0,6m vs MenB-4C 0,2 m

Group difference: (95%CI)	5.02 (0.6 to 9.4)	–3.68 (–6.2 to –1.3)	3.31 (–1.8 to 8.4)	–11.06 (–16.3 to –5.7)



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

Group difference: (95%CI)	-3.53 (-7.6 to 0.6)	–3.01 (–5.6 to –0.5)	-8.31 (–13.2 to -3.4)	–14.80 (–20.0 to –9.5)



- 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 2nd MenABCWY or 2nd 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 LOD or ≥LLOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥4-fold the LLOQ if pre-vaccination titer ≥LOD and <LLOQ, and a post-vaccination titer ≥4-fold the pre-vaccination titer if pre-vaccination titer ≥LLOQ. LOD – limit of detection; LLOQ – lower limit of quantitation; LOD: fHbp: 3; NadA: 6; NHBA: 4; PorA P1.4: 4. LLOQ: fHbp: 5; NadA: 15; NHBA: 4; PorA P1.4: 6. fHbp, factor H binding protein; hSBA, human serum bactericidal assay; LL, lower limit; LOD – limit of detection; LLOQ – lower limit of quantitation; NadA, *Neisseria* adhesin A; NHBA, Neisserial heparin-binding antigen; Por A P1.4, porin A

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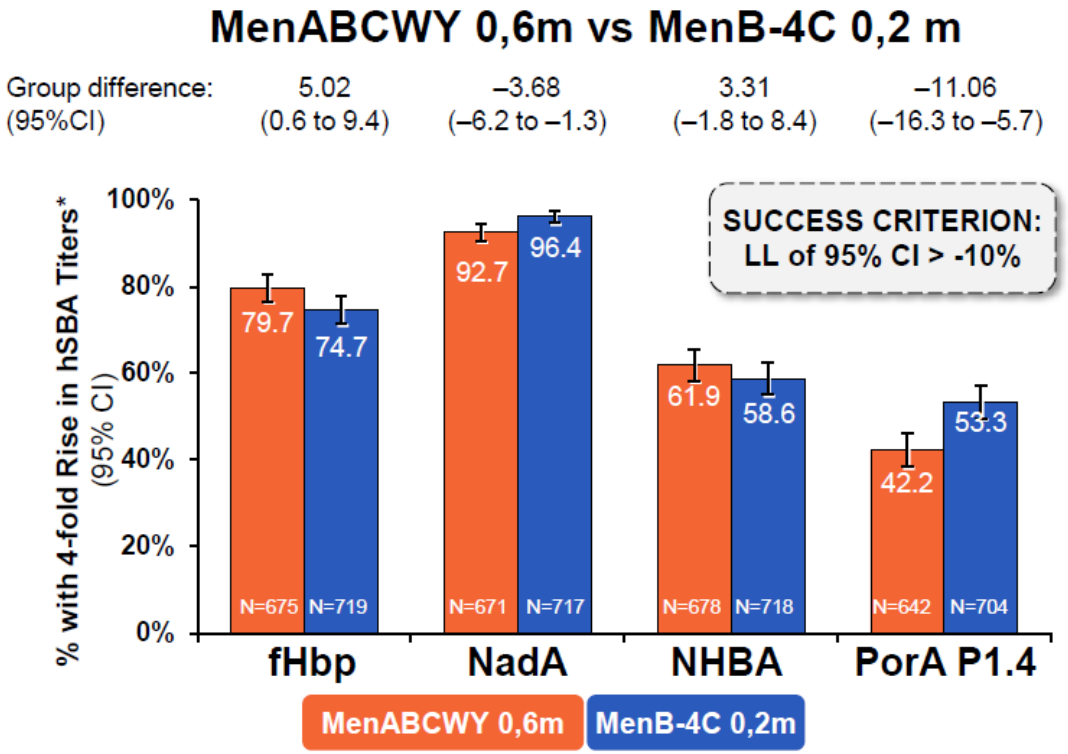
hSBA: MenABCWY Immune Response Against Serogroup B Reference Strains



- MenABCWY vs. MenB 0,2:
  - Success criterion met for 3 of 4 strains (fHbp, NadA, NHBA)

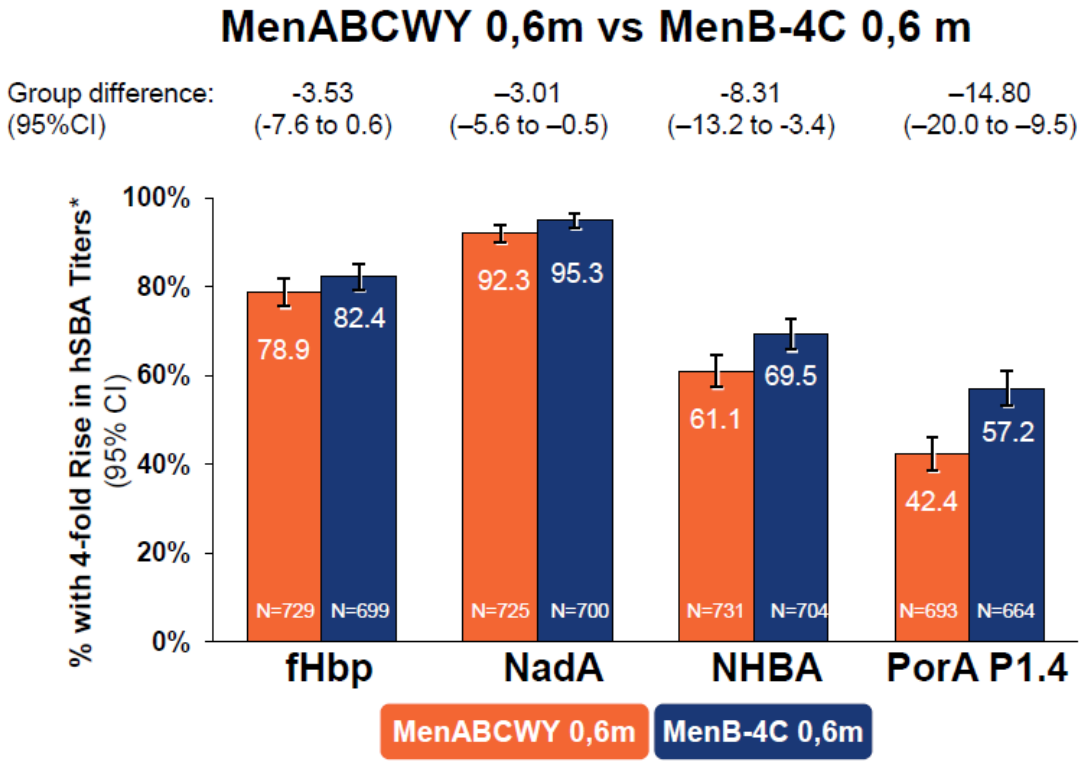
- Secondary endpoint not met because success criterion not met for all 4 strains
- MenABCWY elicited comparable immune responses for 3 reference strains vs MenB-4C 0,2 and 2 reference strains vs MenB-4C 0,6m.

*At 1 month after 2nd MenABCWY or 2nd 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 LOD or ≥LLOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥4-fold the LLOQ if pre-vaccination titer ≥LOD and <LLOQ, and a post-vaccination titer ≥4-fold the pre-vaccination titer if pre-vaccination titer ≥LLOQ. LOD – limit of detection; LLOQ – lower limit of quantitation; LOD: fHbp: 3; NadA: 6; NHBA: 4; PorA P1.4: 4. LLOQ: fHbp: 5; NadA: 15; NHBA: 4; PorA P1.4: 6. fHbp, factor H binding protein; hSBA, human serum bactericidal assay; LL, lower limit; LOD – limit of detection; LLOQ – lower limit of quantitation; NadA, *Neisseria* adhesin A; NHBA, Neisserial heparin-binding antigen; Por A P1.4, porin A

Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024

hSBA: MenABCWY Immune Response Against Serogroup B Reference Strains

- MenABCWY vs. MenB 0,6:
  - Success criterion met for 2 of 4 strains (fHbp, NadA)



- 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 2nd MenABCWY or 2nd 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 LOD or ≥LLOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥4-fold the LLOQ if pre-vaccination titer ≥LOD and <LLOQ, and a post-vaccination titer ≥4-fold the pre-vaccination titer if pre-vaccination titer ≥LLOQ. LOD – limit of detection; LLOQ – lower limit of quantitation; LOD: fHbp: 3; NadA: 6; NHBA: 4; PorA P1.4: 4. LLOQ: fHbp: 5; NadA: 15; NHBA: 4; PorA P1.4: 6. fHbp, factor H binding protein; hSBA, human serum bactericidal assay; LL, lower limit; LOD – limit of detection; LLOQ – lower limit of quantitation; NadA, *Neisseria* adhesin A; NHBA, Neisserial heparin-binding antigen; Por A P1.4, porin A

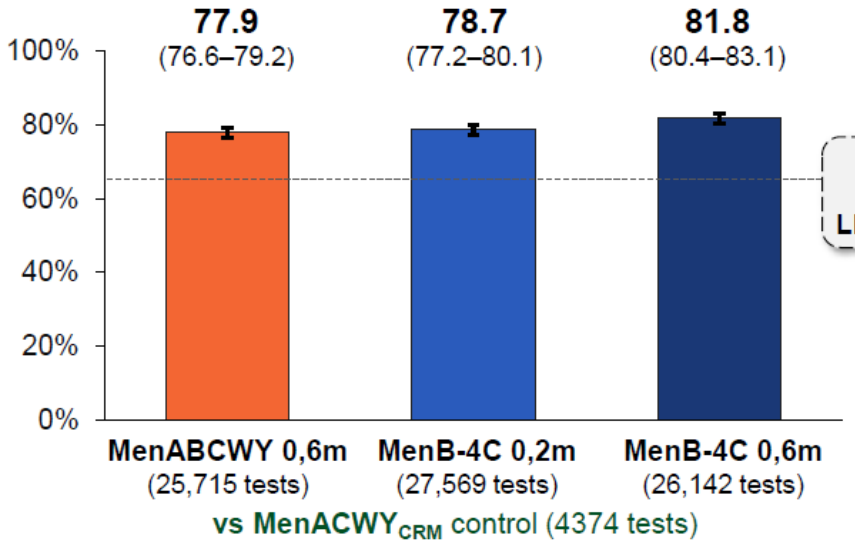
Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024

Presentation by GSK at ACIP, June 2024

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

Test-Based IVE

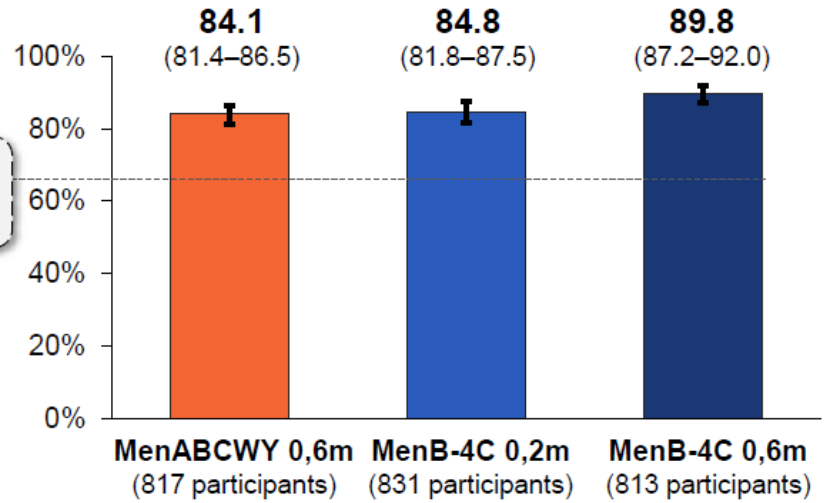
→ Informs breadth of MenB vaccine strain coverage at a population level



SUCCESS CRITERION MET: LL of 97.5% CI > 65%

Responder-Based IVE

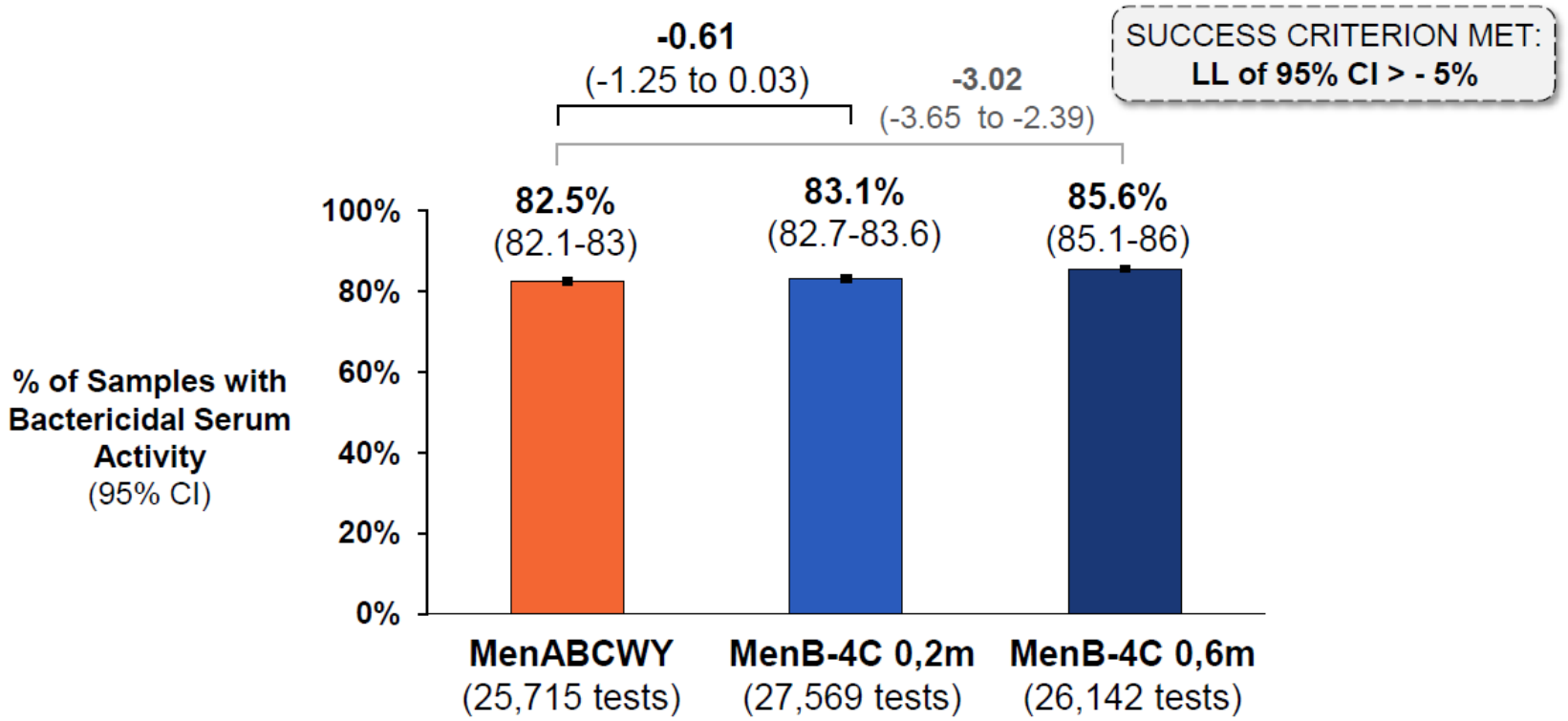
→ % participants achieving broad protection against serogroup B strains



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 0-6m→MenB-4C 0-2m. The 0-2m schedule was the last schedule to meet the predefined success criterion (LL of 95% CI > 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

enc-hSBA: 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 0-6m→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
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Presentation by GSK at ACIP, June 2024

Immunogenicity for Serogroup B: enc-hSBA

- Success criterion met
  - Compared to MenB 0,2 and MenB 0,6
  - Test-based and responder-based IVE

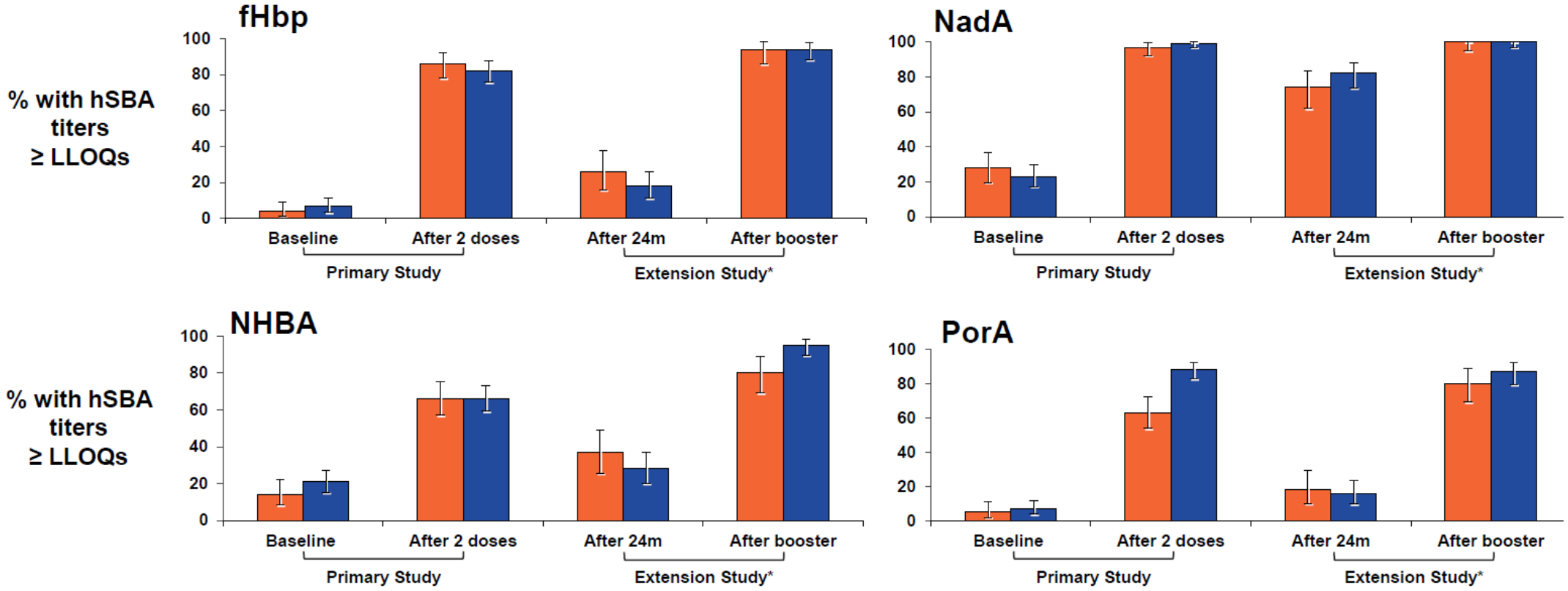
- Response slightly higher for MenB vs. MenABCWY
  - Slightly higher for MenB 0,6 vs. MenB 0,2

IVE, immunological vaccine effectiveness

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

Study 15E1

MenABCWY 0,6m (n=74) **MenB-4C 0,2m** (n=126)



*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

Presentation by GSK at ACIP, June 20

Persistence and Booster Response

- MenB
  - After 24 months, titers waned substantially for B strains fHbp, NHBA, and PorA
  - Robust booster response elicited
  - Confidence intervals overlapped (MenABCWY and MenB 0,2)

- MenACWY
  - After 24 months, titers waned substantially for serogroup A; variable waning noted for other serogroups
  - Robust booster response elicited

Summary

- Favorable safety profile
  - Similar to MenB (more adverse events for MenABCWY than MenACWY)

- Immunogenicity against serogroups A, C, W, Y
  - MenABCWY non-inferior to MenACWY in most study groups
  - Comparison of 1 dose MenABCWY vs. 1 dose MenACWY in naïve recipients not powered for noninferiority; results favorable for all serogroups except A

- Immunogenicity against serogroup B strains
  - MenABCWY non-inferior to MenB based on IVE
  - MenABCWY non-inferior to MenB 0,2 for 3 strains and MenB 0,6 for 2 strains

- Persistence and booster response
  - After 24 months, titers waned substantially for serogroup A and for 3 B strains
  - Robust booster response elicited

IVE, immunologic vaccine effectiveness

Additional Work Group Reflections

- Concern about drop in protection at 2 years for serogroup B strains
- PorA indicator strain is important because it is not really PorA alone but rather represents the full outer membrane vesicle component of the vaccine
  - Response to this indicator strain has bearing on cross-protection

Potential Risk Groups for MenB Vaccination

Schedule Options Under Consideration

Option	ACWY Dose#1	ACWY Dose#2	B Dose#1	B Dose#2
Current recomm.	11–12 yrs	16 yrs	16 yrs – 23 years (preferred 16–18 yrs) SCDM	
1	11–12 yrs	16 yrs	16 yrs	17–18 yrs
2	11–12 yrs	16 yrs	16 yrs risk-based	17–18 yrs risk-based
3	No dose	16 yrs	16 yrs risk-based	17–18 yrs risk-based
4	15 yrs	17–18 yrs	17–18 yrs	17–18 yrs
5 (ACIP)	No dose	16 yrs	16 yrs	17–18 yrs

Proposed recommendations are for routine vaccination unless specified as "risk-based"; option numbers do not represent ordering of preference

SCDM, shared clinical decision-making

Identify Risk Groups for MenB Vaccination

- Based on congregate living settings among adolescents
  - Recommendations will not address military/non-civilian populations as per the ACIP charter

Potential Risk Groups for MenB Vaccination

- College students (4-year students, 1st year students, on-campus residence)
- Boarding schools
- Congregate foster care
- Correctional or detention facilities
- Homeless or emergency shelters
- Institutions for persons with developmental disabilities
- Psychiatric institutions
- Residential treatment centers
- Religious academies
- Wilderness programs, summer camps
- Seasonal worker housing (including agricultural workers)
- College preparatory experiences
- Hotels, motels, and hostels

Duration of Congregate Living Risk Should Exceed Time to Complete Vaccine Series

- College students (4-year students, 1st year students, on-campus residence)
- Boarding schools
- Congregate foster care
- Correctional or ~~detention~~ facilities
- ~~Homeless or emergency shelters~~
- Institutions for persons with developmental disabilities
- Psychiatric institutions
- ~~Residential treatment centers~~
- Religious academies
- ~~Wilderness programs, summer camps~~
- ~~Seasonal worker housing (including agricultural workers)~~
- ~~College preparatory experiences~~
- ~~Hotels, motels, and hostels~~

Factors Associated with Increased Serogroup B Risk among College Students

- 4-year college students had a **5.2**-fold (95% CI: 3.6-7.7) higher risk of serogroup B disease than non-undergraduates aged 18-24 years
  - Risk among 2-year college students was comparable to non-undergraduates (RR 1.0, 95% CI 0.4-2.1)
- First-year students were at **3.8**-fold (95% CI: 2.4-6.0) higher risk of serogroup B disease than non-first-year students
- On-campus residents were at **2.9**-fold (95% CI: 1.8-4.6) higher risk of serogroup B disease than off-campus residents
- Students participating in Greek life were at **9.8**-fold (95% CI: 4.6-21.2) higher risk of serogroup B disease than other students during outbreaks

Weil LW, Crowe SJ, Rubis AB, Soeters HM, Meyer SA, Hariri S, McNamara LA. Risk Factors for Serogroup B Meningococcal Disease Among College Students, *Open Forum Infectious Diseases. 2023;* https://doi.org/10.1093/ofid/ofad607

College Students

- Work Group prefers to include all college students
  - Simplifies recommendations
  - College plans may change
  - Equity considerations

Number of Students at U.S. Colleges and Boarding Schools

- Number of 18 year-olds (in 2020): 4,159,857
- Recent high school completers* in 2022: 2,987,000
  - Percentage of recent high school completers enrolled in college: 62.0%
    - 2-year college: 16.9%
    - 4-year college or university: 45.1%

- >35,000 students enrolled in U.S. boarding schools
  - Older students, many may be likely to attend college

*Includes those who completed a GED or other high school equivalency credential
GED, General Educational Development

Bridged-Race Population Estimates 1990-2020 Results Form (cdc.gov)
Number of recent high school completers and percent enrolled in college, by sex and level of institution: 1960 through 2022
Why Kids Go to Boarding School (usnews.com)

Public Foster Care System

- Continuum of foster care
  - Includes children through 18–21 years (varies by state)
  - Foster family home, group home, residential program
  - May or may not include congregate care settings

- Public foster care system served 570,000 children in 2022
  - 369,000 children in care on September 30, 2022

- Federal law requires children to be placed in least restrictive, most family-like setting
  - Number placed in congregate care decreasing
  - Those in congregate foster care typically spend ~8 months

Children's Bureau, Administration for Children and Families, U.S. Department of Health and Human Services Trends in Foster Care and Adoption: FY 2013 – 2022 | The Administration for Children and Families (hhs.gov)

Inclusive Language

- Work Group prefers to add inclusive language to risk-groups
  - Such that any adolescent who desires protection may receive MenB vaccine
    - Includes those who are unsure of their future plans, which may inform congregate living risk

Proposed Language

- Risk group includes adolescents planning to attend college and adolescents in a congregate living setting (e.g., congregate foster care, boarding school, correctional facility, etc.) who are anticipated to remain in this setting long enough to complete the MenB vaccine series
- Any adolescent who desires protection may receive MenB vaccine, even if they are unsure of their future plans which may inform congregate living risk