EFFECTIVENESS, IMMUNOGENICITY AND SAFETY OF A PENTAVALENT MENINGOCOCCAL ABCWY VACCINE IN ADOLESCENTS AND YOUNG ADULTS: RESULTS FROM A PHASE 3, RANDOMIZED, CONTROLLED CLINICAL STUDY
Conflict of Interest

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• **Disclosures:** TN declares research contracts with payments to his institution, with Moderna, SanofiPasteur, GSK, Iliad Biotechnologies, Dynavax, Seqirus, Janssen and MSD. TN also declares personal payments from GSK, Seqirus, MSD, SanofiPasteur, AstraZeneca, Moderna, BioNet and Pfizer for vaccine science advisory boards. TN also participated in Data Safety Monitoring Boards for which he received personal payment from Seqirus, Clover, Moderna, Emergent, Serum Institute of India, SK Bioscience Korea, Emergent Biosolutions and Novavax. PS declares having a clinical research relationship with GSK but without receiving extra compensation. He also declares having clinical research relationships with numerous pharmaceutical entities. PS has received consulting fees from GSK in the past for participating in advisory boards and has also received support from GSK for travel expenses related to attending advisory meetings. AW, CB and DT are employed by GSK. CB and DT hold shares in GSK. The authors declare no other financial and non-financial relationships and activities.

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<th>Name / Company</th>
<th>Honoraria / Expense</th>
<th>Consulting / Advisory Board</th>
<th>Funded Research</th>
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Phase 3, randomized, controlled, observer-blind clinical study of MenABCWY vaccine

GSK MenABCWY vaccine contains the antigenic components of licensed vaccines MenACWY-CRM and 4CMenB

Phase 2/2b studies showed the MenABCWY vaccine was immunogenic with a clinically acceptable safety profile in adolescents and young adults

This Phase 3 study assessed the safety, immunogenicity and immunologically-defined vaccine effectiveness (immunological VE) of MenABCWY against a panel of 110 diverse meningococcal serogroup B (MenB) strains

4CMenB, 4-component meningococcal serogroup B vaccine; Men, meningococcal serogroup; VE, vaccine effectiveness


#ESPID2023
espidmeeting.org
Demonstration of immunological vaccine effectiveness with endogenous complement hSBA (enc-hSBA)

- 4CMenB licensure was based on immunogenicity results generated by hSBA against 4 indicator strains\(^1\); VE was demonstrated in the field\(^2\)

- In Phase 3 study of MenABCWY vaccine (with 4CMenB antigenic components), a novel method was adopted as a proxy for VE demonstration in the field

- Enc-hSBA allows testing in physiological conditions (using vaccinee’s own complement) against a large panel of MenB strains

Demonstration of immunological VE

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4CMenB, 4-component meningococcal serogroup B vaccine; enc-hSBA, endogenous complement hSBA; hSBA, human serum bactericidal antibody assay; Men, meningococcal serogroup; VE, vaccine effectiveness

Enc-hSBA characteristics vs classical hSBA

### Main features\(^1\)\(^-\)\(^4\)
- Quantitative method, enables the measurement of exact antibody titre providing 50\% killing of the indicator strains (4-fold rise / GMTs / GMRs / ≥LLOQs)
- Assesses individual contribution of each vaccine antigen to bacterial killing
- Allows testing against limited number of strains
- Requires selection of seronegative exogenous complement for each indicator strain

### MenB vaccine assessment in Phase 3 clinical trial

#### Enc-hSBA\(^2\)
- Active endogenous complement present in vaccinee’s serum
- Panel of 110 MenB strains

#### Main features\(^2\)\(^,\)\(^5\)
- Binary response: positive or negative bactericidal killing of 110 MenB strains at 1:4 dilution
- Allows assessment of synergistic effects against multiple vaccine antigens
- Allows testing against a broad panel of 110 MenB strains
- Enables evaluation of immunological vaccine effectiveness in conditions as close as possible to real-world settings

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Immunological VE by enc-hSBA: Test-based and Responder-based approaches

**Test-based VE**

- **Reduction in risk of MenB infection** in MenABCWY group vs control group, using formula:
  
  \[ 1 - (\text{relative risk}) \times 100\% \]

- **Relative risk**: MenABCWY group vs control group ratio in percentages of samples without bactericidal serum activity against MenB strain panel

- Indicative of the **breadth of MenABCWY vaccine strain coverage** at population level

**Responder-based VE**

- **Proportion of vaccinated individuals** whose sera kills ≥70% of tested MenB strains in MenABCWY group

- Indicative of the **percentage of participants who achieve broad protection** against MenB strains at an individual level
Primary objectives:

- **Demonstrate:**
  - Test-based & responder-based immunological VE using enc-hSBA against panel of 110 diverse MenB strains
  - Non-inferiority of immunological effectiveness of MenABCWY vs 4CMenB
  - Immunological non-inferiority of 2-dose MenABCWY vs 1-dose MenACWY-CRM in MenACWY vaccine-naïve individuals
  - Safety

Study design and MenABCWY primary objectives

Randomisation:
- 5:5:3:3:3:1
- N(total)=3,651
- Adolescents & young adults

NCT04502693

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<tr>
<td>4CMenB 0-6M</td>
<td>(N=908)</td>
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<tr>
<td>MenABCWY 0-6M</td>
<td>Pooled (N=1,666)</td>
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<tr>
<td>ABCWY-1</td>
<td>(N=552)</td>
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<td>ABCWY-2</td>
<td>(N=557)</td>
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<td>ABCWY-3</td>
<td>(N=557)</td>
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<tr>
<td>MenACWY-CRM</td>
<td>0M</td>
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B, blood sample; enc-hSBA, endogenous complement human serum bactericidal antibody assay; M, study month; Men, meningococcal serogroup; N, number of participants; V, study visit; VE, vaccine effectiveness

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Results: Immunological VE endpoints

Test-based VE

<table>
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<tr>
<th>Percentages of samples without bactericidal serum activity</th>
<th>Relative risk (95% CI)</th>
<th>MenABCWY VE (95% CI)</th>
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<tr>
<td>MenABCWY (N=25,715)</td>
<td>MenACWY (N=4,374)</td>
<td></td>
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<tr>
<td>17.4%</td>
<td>79.0%</td>
<td>0.22 (0.21; 0.23)</td>
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Responder-based VE

| MenABCWY VE (N=817) |                      | 84.1% | 95%CI: 81.4; 86.5 |

Test-based VE and responder-based VE demonstrated with lower limit of 2-sided 95% CI >65%

Cl, confidence interval; Men, meningococcal serogroup; N, number of samples (Test-based VE) or participants (Responder-based VE); VE, vaccine effectiveness
Results: Non-inferiority analysis of effectiveness of MenABCWY vs 4CMenB

Percentages of samples with bactericidal serum activity by enc-hSBA against MenB strain panel after MenABCWY vs 4CMenB*

- MenABCWY N=25,715
  - 82.5%

- 4CMenB N=27,569
  - 83.1%

Group difference (95%CI)
- -0.61
- (-1.25; 0.03)

Effectiveness non-inferiority demonstrated with lower limit of 2-sided 95%CI for group difference above -5%

* 0-2 months schedule
CI, confidence interval; enc-hSBA, endogenous complement human serum bactericidal antibody assay; Men, meningococcal serogroup; N, number of samples

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Results: Immunological non-inferiority analysis of 2-dose MenABCWY vs 1-dose MenACWY*

Percentages of MenACWY vaccine-naïve participants with 4-fold rise in hSBA titres against serogroups A, C, W, Y post-vaccination

<table>
<thead>
<tr>
<th>Group</th>
<th>MenA</th>
<th>MenC</th>
<th>MenW</th>
<th>MenY</th>
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<tbody>
<tr>
<td>N</td>
<td>1,170</td>
<td>1,189</td>
<td>1,185</td>
<td>1,196</td>
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<tr>
<td>MenABCWY</td>
<td>97.0%</td>
<td>97.2%</td>
<td>97.0%</td>
<td>96.7%</td>
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<tr>
<td>MenACWY</td>
<td>85.7%</td>
<td>50.0%</td>
<td>61.7%</td>
<td>69.7%</td>
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* Provisional, subject to FDA review
CI, confidence interval; hSBA, human serum bactericidal antibody; Men, meningococcal serogroup; N, number of participants

Immunological non-inferiority demonstrated with lower limit of 2-sided 95% CI for group difference above -10%
# Results: MenABCWY safety vs 4CMenB and MenACWY

Participants reporting solicited AEs within 7 days after vaccination / unsolicited AEs during study period

<table>
<thead>
<tr>
<th></th>
<th>MenABCWY, n (%)</th>
<th>4CMenB 0-2-6, n (%)</th>
<th>4CMenB 0-6, n (%)</th>
<th>MenACWY, n (%)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>N=1648*</td>
<td>N=893*</td>
<td>N=900</td>
<td>N=178</td>
</tr>
<tr>
<td>Solicited AEs</td>
<td>1,586 (96.1%)</td>
<td>864 (97.1%)</td>
<td>862 (95.8%)</td>
<td>166 (93.3%)</td>
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<tr>
<td>Unsolicited AEs</td>
<td>678 (41.1%)</td>
<td>349 (39.1%)</td>
<td>384 (42.7%)</td>
<td>69 (38.8%)</td>
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<td>Related unsolicited AEs</td>
<td>105 (6.4%)</td>
<td>66 (7.4%)</td>
<td>56 (6.2%)</td>
<td>10 (5.6%)</td>
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<tr>
<td>Serious AEs</td>
<td>25 (1.5%)</td>
<td>20 (2.2%)</td>
<td>22 (2.4%)</td>
<td>5 (2.8%)</td>
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<tr>
<td>Related serious AEs</td>
<td>1 (0.1%)</td>
<td>0</td>
<td>2 (0.2%)</td>
<td>0</td>
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<tr>
<td>Medically-attended unsolicited AEs</td>
<td>479 (29.1%)</td>
<td>238 (26.7%)</td>
<td>288 (32.0%)</td>
<td>44 (24.7%)</td>
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<tr>
<td>Unsolicited AE leading to withdrawal</td>
<td>4 (0.2%)</td>
<td>6 (0.7%)</td>
<td>4 (0.4%)</td>
<td>1 (0.6%)</td>
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<tr>
<td>Unsolicited AE of special interest</td>
<td>6 (0.4%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
<td>0</td>
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<tr>
<td>Deaths</td>
<td>0</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
<td>0</td>
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*N=1650 and N=890 for solicited AEs for MenABCWY group and 4CMenB 0-2-6 group, respectively. AE, adverse event; Men, meningococcal serogroup; N, number of participants with safety data available; n, number of participants in each AE category.
Conclusions

MenABCWY immunological VE was demonstrated against a panel of 110 diverse MenB strains: Test-based and responder-based endpoints met success criteria.

Two MenABCWY doses are non-inferior to 2 doses of 4CMenB and 1 MenACWY dose in 10–25 year-old individuals.

MenABCWY safety profile is consistent with that of 4CMenB.
QUINTET study group & Acknowledgements

• QUINTET study group members:

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