4CMenB MULTICOMPONENT MENINGOCOCCAL VACCINE DEVELOPED FOR SEROGROUP B MENINGOCOCCI ELICITS CROSS-REACTIVE IMMUNITY AGAINST SEROGROUPS C, W AND Y

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BACKGROUND AND AIM

- Invasive meningococcal disease (IMD) is mostly caused by Neisseria meningitidis serogroups: A, B, C, W, Y, and X and has the highest incidence in infants and adolescents.
- The multicomponent meningococcal serogroup B vaccine (4CMenB, Bexsero, GSK) is designed for broad coverage against MenB strains and currently indicated for active immunisation against IMD caused by MenB.
- However, genes encoding the 4CMenB vaccine antigens are also expressed and conserved in strains belonging to other meningococcal serogroups.²

Areantibodies raised by4CMenB immunisation able to kill non-MenB strains?

AIM OF THE STUDY: Infant sera taken after 4CMenB immunisation were tested for the ability to induce complement-mediated bactericidal killing of non-MenB strains.

MATERIALS AND METHODS

IMD isolates were collected from different countries to ensure that the tested panels are representative of circulating strains and for accuracy of estimation of vaccination impact on non-MenB strains were classified by serogroup, multilocus sequence typing (MLST) and antigen sequence typing.

4CMenB antigens are conserved across serogroups.

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>4CMenB Antigens Presence</th>
<th>MenC Peptides</th>
<th>MenW Peptides</th>
<th>MenY Peptides</th>
</tr>
</thead>
<tbody>
<tr>
<td>MenC</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>MenW</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>MenY</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Control group for this analysis: (age: 2 months old)

4CMenB vaccination schedule

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>number of infants</th>
<th>4CMenB vaccine</th>
<th>Link to clinical sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Strains representative of different clonal complexes and antigens 5% were randomly selected and tested using serum bactericidal activity assay using human complement (hSBA).

RESULTS

- The majority of 147 non-MenB strains were killed by bactericidal activity of sera from 4CMenB vaccinated infants in Euro-3 and Brazilian panels.

CONCLUSIONS

- 4CMenB antigens are present in non-MenB meningococcal strains, with varying sequence relatedness and expression level.
- This is the first example in which an epidemiologically representative large panel of 147 non-MenB strains have been tested against sera raised by 4CMenB vaccination in infants, the population most impacted by IMD.
- 109 out of the 147 representative non-MenB strains were killed in hSBA by infant sera, resulting in an overall coverage of 74% for non-B strains.
- This dataset has important implications for vaccine choice and clinical practice, as it supports and expands on earlier findings of 4CMenB vaccination cross-immunity against prevalent IMD-causing non-MenB serogroups C, W and Y.

REFERENCES


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Trademark statement: Bexsero is a trademark of the GSK group of companies.

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Pre-injection

N=180

NCT00657709

N=20–40

NCT00944034

NCT00847145

Pooled sera were tested in hSBA against MenCWY strains, representative of the overall strain panel.

Bactericidal activity of the infant sera against non-MenB strains showed that 74.1% of tested strains were killed by infant sera post-dose 4.

The percentages of Euro-3 non-MenB strains killed by infant post-injection sera was 72% (hSBA titres >4).

The percentages of Brazilian non-MenB strains killed by infant post-injection sera was 85% (hSBA titres >4).

Killing mainly mediated by: NHBA, fHbp 1 and/or NadA NHBA alone or in synergy NHBA alone or in synergy

Pre-vaccination Post, after vaccination with 4 doses of 4CMenB, N: number of strains killed in hSBA by the 4CMenB elicted immune sera.