Safety and Immunogenicity of a New Meningococcal A Conjugate Vaccine (MenAfriVac™) in a Healthy African Population 2-29 Years of Age

Background

The Meningitis Vaccine Project (MVP) was created in 2001, funded by a grant from the Bill and Melinda Gates Foundation, as a partnership between WHO and INMDH to develop and introduce affordable meningococcal conjugate vaccines to eliminate meningococcal epidemics in sub-Saharan Africa (1,2). A new conjugate Meningococcal A vaccine (PsA-TT), manufactured by Serum Institute of India Ltd, Pune, India, has been shown to be safe and immunogenic in a clinical Phase I study in India. A phase II study was completed in India (2) and an initial phase I study in African toddlers aged 2.23 months showed that an single dose of PsA-TT vaccine is able to prime immunological memory (4,5).

Methods

PsA-TT vaccine is currently being tested in a phase II/II clinical study in an African population 2 to 29 years of age at three study sites: located in the meningitis belt (6):

- Senegal, Institut de Recherche pour le Développement (IRD), Niakhar Field Station
- The Gambia, Medical Research Council Laboratories (MRC), Banjul Field Station
- Mal, Centre pour les Vaccins en Développement (CVD), Bamako

The study was conducted according to ICH/GCP guidelines. Community approval of the study and individual consent were obtained according to country-specific legal requirements and customs. Subjects were randomized in a 1:1 ratio to receive a single injection of either:

- PsA-TT vaccine (MenAfriVac™, produced by Serum Institute of India Ltd), one dose of 0.5 mL containing 10 µg meningococcal A polysaccharide conjugated to 10-20 µg Titeran Tussol, with AS01 as adjuvant;
- Licensed meningococcal tetavalent polysaccharide vaccine (GSK Menace ACWY), one dose of 0.5 mL containing 50 µg of each meningococcal polysaccharide ACWY.

Safety was assessed through active daily follow-up for four days following vaccination. All Adverse Events were collected up to four weeks after vaccination and Serious Adverse Events are collected for the entire study duration (1 year). Blood drawn were performed just prior to vaccination (baseline), at four weeks, at six months, and one year after vaccination.

The immune response was evaluated before and four weeks after vaccination:

- Functional activity was measured by an SBA assay using baby rabbit complement and strain F8238. SBA titers are expressed as the reciprocal of the final serum dilution giving ≥30% killing after 60 min.
- Serogroup A-specific IgG was measured by a standardized ELISA using purified meningococcal serogroup A polysaccharide.
- Carriage: To evaluate nasopharyngeal carriage of Neisseria meningitidis over a period of one year (NP sample at each blood draw), nasal swabs were collected separately (7).

- Results at four weeks are presented in this poster, the study is ongoing and data on persistence at six months and one year are currently being collected.

Safety Results

Local and systemic reactions were mild or moderate with similar frequency in the two vaccine groups and across the three sites and age groups:

- All local reactions were transient and resolved without sequelae within four days after vaccination. The most reported local reaction was tenderness, with a higher trend (not statistically significant) in the PsA-TT group than in the PsACWY group. More local reactions were reported at the Senegal and Gambia sites.
- Headache was the most reported systemic reaction in the 1.1 to 29 year age group (11.2% vs. 10.7%). Fever was equally reported in the two vaccine groups (1% vs. 1.7%), all fevers were ≤ 40°C.
- More systemic reactions were reported at the Gambia site compared to the other two sites. Similar rates of AEs were reported in the two study groups, at the three sites, and in the three age groups. No deaths and no SAEs were reported in the first 28 days after vaccination.

Results: Immune response as measured by ELISA

Group A-specific IgG ≥ 4-fold rise to post-vaccination in the PsA-TT group were significantly higher than in the PsACWY group in all age groups. MenA SBA GMT post-vaccination in the PsA-TT group are significantly higher than in the PsACWY group in all age groups.

The proportion of subjects with MenA IgG ≥ 1:128 at baseline and after vaccination was similar in both the PsA-TT and the PsACWY group.

Table 1: Local reactions at injection site at 4 days post-vaccination

<table>
<thead>
<tr>
<th>Reaction</th>
<th>PsA-TT (N=604)</th>
<th>PsACWY (N=99)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>0 (0-0.2%)</td>
<td>0 (0-0.2%)</td>
<td></td>
</tr>
<tr>
<td>Irritability</td>
<td>0 (0-0.2%)</td>
<td>0 (0-0.2%)</td>
<td></td>
</tr>
<tr>
<td>Loss of Appetite</td>
<td>0 (0-0.2%)</td>
<td>0 (0-0.2%)</td>
<td></td>
</tr>
<tr>
<td>At Least One Systemic Reaction</td>
<td>28 (4.6%)</td>
<td>2 (2.0%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>4 (0.7%)</td>
<td>0 (0-0.2%)</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>17 (2.8%)</td>
<td>1 (1.0%)</td>
<td></td>
</tr>
</tbody>
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