SAFETY AND REACTOGENICITY OF THE BOOSTER DOSE OF 2 INVESTIGATIONAL PROTEIN-BASED PNEUMOCOCCAL VACCINE FORMULATIONS IN TODDLERS: A PHASE II RANDOMIZED TRIAL

INTRODUCTION

- Introduction of pneumococcal conjugate vaccines (PCVs) in national immunization programs substantially reduced the invasive pneumococcal disease (IPD) burden worldwide.1
- However, their success is challenged by the variability in IPD-causing serotypes between geographic regions and serotype replacement,2 which highlights the need to broaden protection beyond capsular polysaccharides included in PCVs.

GSK Vaccines is investigating vaccine formulations containing highly conserved pneumococcal proteins, including pneumolysin (Ply) and pneumococcal histidine-triad protein D (PhtD).

- It has been shown that two investigational vaccine formulations containing Ply toxoid (dPly) and PhtD each at either 10 µg (PCV/dPly/PhtD-10) or 30 µg (PCV/dPly/PhtD-30) combined with polysaccharide conjugates of the pneumococcal non-typeable Haemophilus influenzae protein D conjugate vaccine (PCV5; GSK Vaccines) were well tolerated in adults and toddlers in Europe,3,4 and in infants and children in the USA.5

- A phase II trial (ClinicalTrials.gov: NCT01204658) showed that PCV/dPly/PhtD-10 and PCV/dPly/PhtD-30 formulations had a safety profile comparable to that of PCV5 (primary vaccine) and was immunogenic (secondary objectives) after primary vaccination in European infants.6

Here, we present safety and reactogenicity results following booster vaccination in the same study (secondary objectives). Immunogenicity outcomes are presented in abstract IDWeek 59120.

METHODS

Study design and participants

- In this phase II, multi-center, observer-blinded, controlled trial conducted in the Czech Republic, Germany, Poland and Sweden, infants previously not vaccinated against Streptococcus pneumoniae were randomized to receive either dPly/PhtD-10, dPly/PhtD-30, PCV5 or 13-valent PCV (PCV13, Pfizer) (Figure 1).

- Study vaccines were given in a 3+1 schedule (primary vaccination at ages 2, 3, 4 months and booster dose at 12–15 months) co-administered with diphtheria tetanus, tetanus, and hepatitis B inactivated poliomyelitis Haemophilus influenzae type b inactivated (DTP/HBV/IPV) (GSK Vaccines not licensed in the USA).7

- The study was conducted according to the principles of Good Clinical Practice and the Declaration of Helsinki.

Safety assessment

- Safety reporting intervals are indicated in Figure 1.

- Safety outcomes were evaluated on the total vaccinated cohort (TVC).

Figure 1. Study design and vaccines (ClinicalTrials.gov: NCT01204658).

RESULTS

Demographic characteristics

- Of 576 infants enrolled in the primary vaccination phase, 564 toddlers who received booster vaccination were included in the TVC (Figure 1).

- Demographic characteristics were similar between Table 1.

Table 1. Demographic characteristics (total vaccinated cohort)

<table>
<thead>
<tr>
<th>Category</th>
<th>PCV5 (N=144)</th>
<th>PCV/dPly/PhtD-10 (N=144)</th>
<th>PCV/dPly/PhtD-30 (N=144)</th>
<th>N=140</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>12 ± 0.6</td>
<td>13.2 ± 0.5</td>
<td>12.3 ± 0.6</td>
<td>13.2 ± 0.6</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>64 (46.4%)</td>
<td>66 (47.1%)</td>
<td>66 (47.1%)</td>
<td>64 (46.4%)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>80 (53.6%)</td>
<td>78 (52.9%)</td>
<td>78 (52.9%)</td>
<td>76 (53.6%)</td>
</tr>
<tr>
<td>White - Caucasian / European heritage, n (%)</td>
<td>142 (99.3%)</td>
<td>139 (97.9%)</td>
<td>140 (99.3%)</td>
<td>139 (99.3%)</td>
</tr>
</tbody>
</table>

- Other heritage, n (%) | 2 (1.4%) | 2 (1.4%) | 3 (2.1%) | 0 (0.0%) |

- Solicited adverse events

- The most commonly reported solicited adverse events (AEs) at injection site of pneumococcal vaccines were redness in the PCV/dPly/PhtD-10 and PCV5 formulations (47.9% and 41.0% of toddlers, respectively) and pain in the PCV/dPly/PhtD-10 and PCV13 groups (45.7% and 44.3%, respectively) (Figure 2A).

- No large swelling reactions (>50 mm diameter) were reported at the injection sites of either of the investigational vaccines. Large swelling reactions were reported for the other vaccines: 4 at DTPA-HBV/IPV/Hib injection site (2 in the PCV/dPly/PhtD-10, 1 in the PCV5 and 1 in the PCV13 groups) at PCV-1 site and at PCV1 site; all were resolved.

- Pain was the most frequently reported solicited general AE in all groups (range: 59.6%–65.0% of toddlers) (Figure 2B).

- Solicited general AEs considered by the investigator as vaccination-related were reported for a maximum of 36.5% in the PCV/dPly/PhtD-10 group and 27.7% in the PCV13 group.

Figure 2A. Percentage of toddlers with reported solicited adverse events (AEs) at each injection site (A) and solicited general AEs (B) (Days 0–6, total vaccinated cohort).

Figure 2B. Solicited general AEs

<table>
<thead>
<tr>
<th>Category</th>
<th>PCV5 (N=144)</th>
<th>PCV/dPly/PhtD-10 (N=144)</th>
<th>PCV/dPly/PhtD-30 (N=144)</th>
<th>N=140</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain, % (95% CI)</td>
<td>100 (100; 100)</td>
<td>100 (100; 100)</td>
<td>100 (100; 100)</td>
<td>100 (100; 100)</td>
</tr>
<tr>
<td>Swelling, % (95% CI)</td>
<td>0 (0.0; 2.6)</td>
<td>0.0 (0.0; 2.6)</td>
<td>0.0 (0.0; 2.6)</td>
<td>0.0 (0.0; 2.6)</td>
</tr>
<tr>
<td>Redness, % (95% CI)</td>
<td>53.8 (46.4; 61.2)</td>
<td>53.6 (46.3; 61.0)</td>
<td>53.6 (46.3; 61.0)</td>
<td>53.6 (46.3; 61.0)</td>
</tr>
<tr>
<td>Itching, % (95% CI)</td>
<td>9.7 (5.4; 14.1)</td>
<td>0.0 (0.0; 0.7)</td>
<td>0.0 (0.0; 0.7)</td>
<td>0.0 (0.0; 0.7)</td>
</tr>
</tbody>
</table>

No safety concerns were raised.

REFERENCES

6. Odutola et al. VSSD 2016 (abstract O44)
7. Odutola et al. ISPPD 2016 (abstract 724)

DISCLOSURES

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- Prymula reports grants from the GSK group of companies during the conduct of the study and grants from the GSK group of companies, Novartis, Sanofi Pasteur during the submitted work, L. Samborn was principal investigator in clinical trials sponsored by the GSK group of companies, reports grants from the GSK group of companies during the conduct of the study, and received honoraria as speaker from Sanofi Pasteur, Pfizer and Novartis outside the submitted work, S.A. Silfverdal reports grants and personal fees from the GSK group of companies for the conduct of the study, and grants to his institution from Pfizer, Merck and Sanofi Pasteur for the conduct of other studies, J. Albrecht reports grants from the GSK group of companies during the conduct of the study, L. Albrecht reports personal fees for participation in conferences and honoraria as speaker from Pfizer, Merck and GSK group of companies outside the submitted work, M. Tavakoli and D. Borys are advised by the GSK group of companies and receive personal fees from the GSK group of companies, Y. Song works for GSK Pharma & Science as a consultant for the GSK group of companies.

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