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Short communication

Immunogenicity of the pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV) administered concomitantly with the meningococcal serogroup B (4CMenB) vaccine in infants: A post-hoc analysis in a phase 3b, randomised, controlled trial

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ABSTRACT

Background: No data are currently available on immunogenicity of higher-valent pneumococcal conjugate vaccines when co-administered with a 4-component meningococcal serogroup B vaccine (4CMenB).
Methods: Post-hoc analysis of pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV) immunogenicity when co-administered with 4CMenB (2 + 1 schedule) and/or a CRM-conjugated meningococcal serogroup C vaccine (MenC-CRM) in a trial assessing 4CMenB reduced schedules and co-administration with MenC-CRM (NCT01339923). Infants were randomized to receive 4CMenB and MenC-CRM (Group 1) or MenC-CRM (Group 2) at 3, 5, and 12 months (M) of age. Both groups received PHiD-CV (3 + 1 schedule) as part of the Brazilian national immunisation programme at 3 M, 5 M, 7 M, and 12 M of age. Antibody responses were assessed pre-vaccination, 1 M post-dose 2, pre-booster, and 1 M post-booster.
Results: Anti-pneumococcal antibody responses were in similar ranges in the two study groups.
Conclusions: 4CMenB co-administration did not seem to impact antibody responses to PHiD-CV in infants.

1. Introduction

Pneumonia and invasive disease caused by *Streptococcus pneumoniae* are major causes of mortality in young children worldwide [1]. The World Health Organization (WHO) recommends inclusion of a pneumococcal conjugate vaccine (PCV) in national immunisation programmes (NIPs) [2]. PCV implementation in NIPs started in 2000 with the 7-valent PCV (PCV7), which was later gradually replaced by higher-valent PCVs such as the pneumococcal non-typeable *Haemophilus influenzae* (NTHi) protein D conjugate vaccine (PHiD-CV, *Synflorix*, GSK) in 2009 and the 13-valent PCV (PCV13, *Prevnar 13/Prevenar 13*, Pfizer Inc.) in 2010 [2], both cover-

Abbreviations: WHO, World Health Organization; PCV, pneumococcal conjugate vaccine; PCV7, the 7-valent PCV; PCV13, the 13-valent PCV; NTHi, non-typeable *Haemophilus influenzae*; PHiD-CV, pneumococcal NTHi protein D conjugate vaccine; NIP, national immunisation programme; IMD, invasive meningococcal disease; 4CMenB, meningococcal serogroup B vaccine; MenC-CRM, CRM-conjugated meningococcal serogroup C vaccine; ECL, electrochemiluminescence; GMC, geometric mean concentration.

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ing additional serotypes. These higher-valent PCVs demonstrated effectiveness against pneumonia and invasive pneumococcal disease in young children [3–7]. By the end of 2018, higher-valent PCVs were included in the paediatric NIPs of 135 countries [8].

Meningococcal disease caused by *Neisseria meningitidis* is another vaccine-preventable infectious disease that causes significant morbidity and mortality among infants and young children [9,10]. Invasive meningococcal disease (IMD) epidemiology varies with region and in time. However, nearly all cases are known to be caused by six serogroups (A, B, C, W, X, and Y) [11]. After introduction of meningococcal conjugate vaccines against serogroups A, C, W, and Y in several countries around the world, including European countries, the United States, Canada, Australia, and Brazil, serogroup B became the predominant cause of meningococcal disease in most of these countries [12]. In recent years, there has been an increasing use of multivalent ACWY conjugate vaccines, which replaced the MenC vaccines in several countries with meningococcal immunization programmes. In these countries, MenACWY conjugate vaccines are recommended as part of the routine immunization programmes, not only for adolescents, but also for infants and/or toddlers [13].

A multi-component, protein-based meningococcal serogroup B vaccine (4CMenB) was first licenced in 2013 in Europe for use in persons aged 2 months and above, and has since been approved in several countries worldwide as a 3 + 1 or 2 + 1 regimen [14,15]. Immediately following its introduction in the United Kingdom's NIP, 4CMenB demonstrated a 2-dose vaccine effectiveness of 82.9% (95% confidence interval: 24.1–95.2) against all serogroup B invasive cases in infants [16].

Successful implementation of paediatric vaccines in NIPs relies on a high vaccine uptake, which may be achieved by co-administration with other recommended vaccines for the same age group. Currently no data are available on immunogenicity of higher-valent PCVs when co-administered with 4CMenB.

The pre-defined objectives of our study were to evaluate reduced 4CMenB schedules and catch-up series [15], as well as to assess immunogenicity and safety of 4CMenB and the CRM-conjugated meningococcal serogroup C (MenC-CRM, *Menjugate*, GSK) vaccine when co-administered [17]. The corresponding results have previously been reported, showing that concomitant administration of MenC-CRM and 4CMenB in infants was safe and immunogenic, resulting in non-inferior responses to MenC-CRM and sufficient immune response to 4CMenB after primary and booster vaccination [17]. Moreover, a reduced schedule of 4CMenB in infants and catch-up series in children proved to be safe and immunogenic, having the potential to widen 4CMenB coverage [15].

The study design also provided the opportunity to evaluate immune responses to PHiD-CV, which was administered as part of the NIP in Brazil. In this post-hoc analysis, the objective was to evaluate immunogenicity of PHiD-CV in infants when the first 2 of the 3 primary doses and the booster dose were co-administered with 4CMenB.

2. Methods

A phase 3b open-label study investigated administration of 4CMenB according to reduced schedules in infants or as catch-up series in children [15], and co-administration of 4CMenB and MenC-CRM [17] (NCT01339923). This post-hoc analysis was performed on remaining blood samples from the subset of children who received 4CMenB, PHiD-CV and/or MenC-CRM co-administration [17]. This subset was enrolled between April 2011 and December 2014 at four sites in Brazil.

The protocol of the clinical trial was approved by local institutional review boards and ethics committees prior to the study start. The study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice. Written informed consent was obtained from a parent or guardian of each infant prior to enrolment in the study.

Healthy infants 83–104 days of age were eligible for participation if they had not received any previous MenB, MenC, or pneumococcal vaccine. Detailed exclusion criteria have been presented previously [15,17].

Children included in our analysis were randomised 1:1 using a web-based randomisation system to receive either 4CMenB and MenC-CRM (Group 1) or MenC-CRM (Group 2) at 3, 5, and 12 months of age. MenB was administered in Group 2 at 13 and 15 months of age [17]. Both groups received PHiD-CV (3 + 1 schedule, co-administered with the study vaccines) through the NIP at 3, 5, 7, and 12 months of age (Fig. 1). PHiD-CV and MenC-CRM were administered intramuscularly into the left thigh, with a spacing of at least 2.5 cm between injection sites. 4CMenB was administered into the right thigh. Each 0.5 mL PHiD-CV dose (*Synflorix*, GSK, lot numbers: SPNA189CN, ASPNA410AH) contained 1 μg of each capsular polysaccharide of serotypes 1, 5, 6B, 7F, 9V, 14, and 23F, and 3 μg for serotype 4, each individually conjugated to NTHi protein D, and 3 μg of capsular polysaccharides of serotypes 18C and 19F conjugated to tetanus and diphtheria toxoids, respectively. The composition of 4CMenB and MenC-CRM vaccines was described elsewhere [15,17].

Safety, assessed in the full analysis set, was reported previously [17]. Immunogenicity was assessed from blood samples collected at 3, 6, 12, and 13 months of age in both study groups (pre-vaccination, 1 month post-dose 2, pre-booster vaccination, and 1 month post-booster, respectively). No blood sample was collected after the third primary PHiD-CV dose. Serotype-specific anti-polysaccharide IgG antibody concentrations were measured using a direct binding electrochemiluminescence (ECL) assay [18], which was bridged to the currently recommended WHO reference assay (ELISA) [19,20]. ECL antibody concentration threshold corresponding to 0.35 μg/mL measured by reference ELISA assay was 0.35 μg/mL. While this population-derived IgG antibody threshold value is considered the reference antibody concentration for assessment of vaccine efficacy against invasive pneumococcal disease [21,22], it is important to highlight that achievement of this threshold for a specific serotype does not necessarily predict protection against IPD due to that serotype in an individual person.

After the second of the 3 primary PHiD-CV doses and the booster PHiD-CV dose, immunogenicity was assessed in the corresponding per protocol set, which included children who correctly received all vaccine doses specified in the protocol up to the considered time point.

The Geometric Mean Concentration (GMC) calculations were performed by taking the anti-log of the mean of the log concentration transformations. Children with missing or non-evaluable measurements were excluded from the GMC calculations.

In this study, the calculated sample size was necessary to demonstrate confirmatory objectives of the study, which were reported elsewhere [17]. As this sample size was considered adequate for our descriptive analysis, no additional sample size calculation was performed.

All presented results are descriptive, and no statistical criteria were used to compare between groups.

3. Results

Of the initially enrolled 251 infants [17], 223 (117 in Group 1 and 106 in Group 2) had sufficient blood volume available and

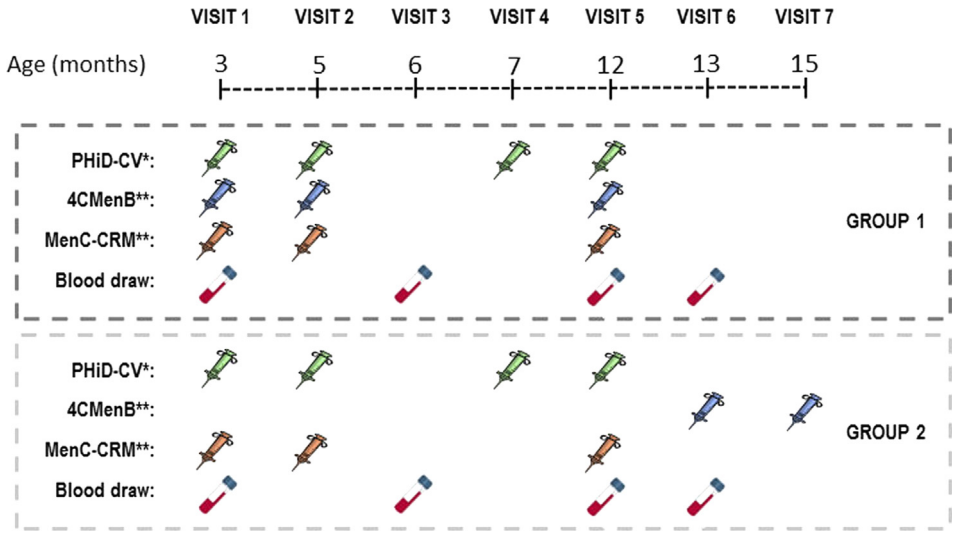

Fig. 1. Study design. PHiD-CV, pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine; 4CMenB, meningococcal serogroup B vaccine; MenC-CRM, CRM-conjugated meningococcal serogroup C vaccine. *administered as part of the national immunisation programme. **study vaccine.

213 (111 in Group 1 and 102 in Group 2) were included in the per protocol set for the analysis of PHiD-CV immunogenicity. Ten children were excluded from the per protocol set for: having received a different treatment than randomized to (5), missing serological data at baseline (4), or having an underlying condition forbidden by the protocol (1). Demographic and other baseline characteristics were balanced between study groups (Table 1).

One month after the second of the 3 primary PHiD-CV doses, in each study group, for each vaccine serotype, the percentage of infants with antibody concentrations ≥0.35 μg/mL was at least 92.1%, except for serotypes 6B (82.5% in Group 1 and 89.1% in Group 2) and 23F (90.5% in Group 1 and 85.7% in Group 2). The percentages of infants with antibody concentrations ≥0.35 μg/mL were in similar ranges between the two study groups for vaccine-related serotypes 6A (27.0% in Group 1 and 16.1% in Group 2) and 19A (71.4% in Group 1 and 55.4% in Group 2). For each pneumococcal serotype, antibody GMCs were in similar ranges between the two study groups (Table 2).

One month after the PHiD-CV booster dose (3 + 1 schedule), in each study group, for each vaccine serotype, the percentage of toddlers with antibody concentrations ≥0.35 μg/mL was at least 96.8%. The percentages of infants with antibody concentrations ≥0.35 μg/mL were in similar ranges between the two study groups for vaccine-related serotypes 6A (73.4% in Group 1 and 79.1% in Group 2) and 19A (98.4% in Group 1 and 92.9% in Group 2). For each pneumococcal serotype, post-booster antibody GMCs were in similar ranges in these two study groups (Table 2).

4. Discussion

Co-administration of paediatric vaccines may improve vaccine uptake and reduce the number of healthcare visits required for vaccines administration. This analysis showed similar immune responses against vaccine serotypes and vaccine-related pneumococcal serotypes 6A and 19A between children who received PHiD-CV, 4CMenB, and MenC-CRM concomitantly and those who received PHiD-CV and MenC-CRM without 4CMenB. A plain language summary contextualizing the results, relevance, and potential impact of this clinical research is displayed in the Focus on the Patient Section (Fig. 2).

In our study, PHiD-CV was administered according to a 3 + 1 dosing schedule, as included in the NIP in Brazil during the study period [23]. 4CMenB was administered according to a reduced (2 + 1) schedule, which was shown to be immunogenic and having

Table 1
Demographic and other baseline characteristics (per protocol set). Group 1, participants who received the first two primary and booster PHiD-CV doses concomitantly with 4CMenB and MenC-CRM at 3, 5, and 12 months of age and the third primary PHiD-CV dose at 7 months of age; Group 2, participants who received the first two primary and booster PHiD-CV doses concomitantly with MenC-CRM at 3, 5, and 12 months of age, the third primary PHiD-CV dose at 7 months of age, and 4CMenB at 13 and 15 months of age; N, number of infants with sufficient blood volume available included the per protocol set for the analysis of PHiD-CV immunogenicity; PHiD-CV, pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine; 4CMenB, meningococcal serogroup B vaccine; MenC-CRM, CRM-conjugated meningococcal serogroup C vaccine; n (%) = number (percentage) of infants in a given category; SD, standard deviation.

Characteristics	Parameters or Categories	Group 1 N = 111 Value or n (%)	Group 2 N = 102 Value or n (%)
Age at first dose (months)	Mean ± SD	2.96 ± 0.17	2.96 ± 0.15
Sex	Female	69 (62.2%)	47 (46.1%)
	Male	42 (37.8%)	55 (53.9%)
Race	Other	83 (74.8%)	65 (63.7%)
	White	24 (21.6%)	35 (34.3%)
	Black or African American	4 (3.6%)	2 (2.0%)
Weight at first dose (kg)	Mean ± SD	5.99 ± 0.748	6.13 ± 0.838
Height at first dose (cm)	Mean ± SD	59.61 ± 2.289	60.25 ± 2.488
Body Mass Index at first dose (kg/m^2)	Mean ± SD	16.84 ± 1.616	16.84 ± 1.833

Table 2
Anti-pneumococcal IgG antibody concentrations against PHiD-CV serotypes and PHiD-CV-related serotypes 6A and 19A (per protocol set, ECL assay). Group 1, participants who received the first two primary and booster PHiD-CV doses concomitantly with 4CMenB and MenC-CRM at 3, 5, and 12 months of age and the third primary PHiD-CV dose at 7 months of age; Group 2, participants who received the first two primary and booster PHiD-CV doses concomitantly with MenC-CRM at 3, 5, and 12 months of age, the third primary PHiD-CV dose at 7 months of age, and 4CMenB at 13 and 15 months of age; PHiD-CV, pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine; 4CMenB, meningococcal serogroup B vaccine; MenC-CRM, CRM-conjugated meningococcal serogroup C vaccine; M, month; N, number of infants with available results; GMC, geometric mean concentration; CI, confidence interval; ECL, electrochemiluminescence.

	Time point (3 + 1 schedule)	% of infants with antibody concentrations ≥0.35 μg/mL (95% CI)			Antibody GMC (95% CI), μg/mL		
		N	Group 1	Group 2	N	Group 1	Group 2
Vaccine serotypes							
1	Pre-vaccination	73	2.7 (0.3–9.6)	3.6 (0.4–12.5)	55	0.05 (0.05–0.06)	0.05 (0.04–0.06)
	1 M post-dose 2	63	98.4 (91.5–100.0)	100.0 (93.6–100.0)	56	2.62 (2.07–3.32)	2.46 (2.07–2.93)
	Pre-booster	75	78.7 (67.7–87.3)	78.0 (65.3–87.7)	59	0.62 (0.52–0.74)	0.59 (0.47–0.75)
	1 M post-booster	64	100.0 (94.4–100.0)	97.7 (87.7–99.9)	43	2.89 (2.33–3.60)	2.93 (2.21–3.89)
4	Pre-vaccination	73	0.0 (0.0–4.9)	3.6 (0.4–12.5)	55	0.04 (0.04–0.05)	0.04 (0.04–0.05)
	1 M post-dose 2	63	95.2 (86.7–99.0)	100.0 (93.6–100.0)	56	2.82 (2.12–3.74)	2.52 (2.05–3.09)
	Pre-booster	75	89.3 (80.1–95.3)	84.8 (73.0–92.8)	59	0.88 (0.73–1.07)	0.79 (0.64–0.98)
	1 M post-booster	64	100.0 (94.4–100.0)	100.0 (91.8–100.0)	43	4.77 (3.72–6.11)	3.77 (2.74–5.18)
5	Pre-vaccination	73	2.7 (0.3–9.6)	1.8 (0.1–9.7)	55	0.11 (0.10–0.12)	0.11 (0.10–0.12)
	1 M post-dose 2	63	92.1 (82.4–97.4)	98.2 (90.5–100.0)	56	1.12 (0.90–1.41)	1.12 (0.95–1.32)
	Pre-booster	75	68.0 (56.2–78.3)	72.9 (59.7–83.6)	59	0.48 (0.40–0.57)	0.53 (0.43–0.67)
	1 M post-booster	61	98.4 (91.2–100.0)	97.7 (87.7–99.9)	43	1.62 (1.30–2.02)	1.58 (1.18–2.11)
6B	Pre-vaccination	73	15.1 (7.8–25.4)	16.4 (7.8–28.8)	55	0.11 (0.09–0.14)	0.11 (0.08–0.13)
	1 M post-dose 2	63	82.5 (70.9–91.0)	89.1 (77.8–95.9)	55	1.25 (0.89–1.74)	1.20 (0.88–1.64)
	Pre-booster	75	94.7 (86.9–98.5)	89.8 (79.2–96.2)	59	1.15 (0.95–1.39)	1.06 (0.86–1.30)
	1 M post-booster	64	100.0 (94.4–100.0)	100.0 (91.8–100.0)	43	4.91 (3.97–6.07)	4.29 (3.24–5.67)
7F	Pre-vaccination	73	2.7 (0.3–9.6)	5.5 (1.1–15.1)	55	0.05 (0.04–0.06)	0.06 (0.04–0.07)
	1 M post-dose 2	63	98.4 (91.5–100.0)	100.0 (93.6–100.0)	56	2.41 (1.95–2.97)	2.54 (2.10–3.06)
	Pre-booster	75	97.3 (90.7–99.7)	100.0 (93.9–100.0)	59	1.36 (1.16–1.59)	1.32 (1.10–1.58)
	1 M post-booster	64	100.0 (94.4–100.0)	100.0 (91.8–100.0)	43	5.08 (4.18–6.17)	5.16 (4.08–6.52)
9 V	Pre-vaccination	73	8.2 (3.1–17.0)	3.6 (0.4–12.5)	55	0.09 (0.07–0.11)	0.09 (0.07–0.11)
	1 M post-dose 2	63	93.7 (84.5–98.2)	100.0 (93.6–100.0)	56	1.56 (1.23–1.98)	1.70 (1.41–2.05)
	Pre-booster	75	90.7 (81.7–96.2)	91.5 (81.3–97.2)	59	1.10 (0.90–1.36)	0.95 (0.76–1.19)
	1 M post-booster	64	100.0 (94.4–100.0)	100.0 (91.8–100.0)	43	4.43 (3.49–5.62)	4.62 (3.47–6.16)
14	Pre-vaccination	73	56.2 (44.1–67.8)	60.0 (45.9–73.0)	55	0.45 (0.34–0.60)	0.49 (0.35–0.68)
	1 M post-dose 2	63	96.8 (89.0–99.6)	98.2 (90.5–100.0)	56	4.63 (3.40–6.29)	5.69 (4.50–7.19)
	Pre-booster	75	100.0 (95.2–100.0)	100.0 (93.9–100.0)	59	2.75 (2.21–3.42)	2.77 (2.19–3.49)
	1 M post-booster	64	100.0 (94.4–100.0)	100.0 (91.8–100.0)	43	9.99 (8.17–12.21)	10.25 (7.93–13.25)
18C	Pre-vaccination	73	6.9 (2.3–15.3)	9.1 (3.0–20.0)	55	0.09 (0.07–0.10)	0.09 (0.08–0.11)
	1 M post-dose 2	63	98.4 (91.5–100.0)	100.0 (93.6–100.0)	56	10.63 (7.58–14.92)	8.96 (6.69–11.99)
	Pre-booster	75	100.0 (95.2–100.0)	100.0 (93.9–100.0)	59	3.38 (2.68–4.25)	4.57 (3.50–5.96)
	1 M post-booster	64	100.0 (94.4–100.0)	100.0 (91.8–100.0)	43	19.37 (15.47–24.26)	24.15 (18.71–31.17)
19F	Pre-vaccination	73	19.2 (10.9–30.1)	21.8 (11.8–35.0)	55	0.16 (0.13–0.20)	0.18 (0.14–0.22)
	1 M post-dose 2	63	98.4 (91.5–100.0)	100.0 (93.6–100.0)	56	7.49 (5.70–9.84)	7.98 (6.24–10.22)
	Pre-booster	75	100.0 (95.2–100.0)	100.0 (93.9–100.0)	59	3.52 (2.94–4.21)	4.30 (3.42–5.40)
	1 M post-booster	64	100.0 (94.4–100.0)	100.0 (91.8–100.0)	43	12.70 (10.21–15.79)	13.94 (10.53–18.46)
23F	Pre-vaccination	73	11.0 (4.9–20.5)	7.3 (2.0–17.6)	55	0.10 (0.08–0.13)	0.08 (0.06–0.11)
	1 M post-dose 2	63	90.5 (80.4–96.4)	85.7 (73.8–93.6)	56	1.18 (0.91–1.52)	1.12 (0.90–1.40)
	Pre-booster	75	60.0 (48.0–71.2)	69.0 (55.5–80.5)	58	0.46 (0.38–0.56)	0.49 (0.40–0.60)
	1 M post-booster	63	96.8 (89.0–99.6)	100.0 (91.8–100.0)	43	2.16 (1.75–2.67)	2.27 (1.79–2.87)
Vaccine-related serotypes							
6A	Pre-vaccination	73	13.7 (6.8–23.8)	7.3 (2.0–17.6)	55	0.10 (0.08–0.13)	0.09 (0.08–0.12)
	1 M post-dose 2	63	27.0 (16.6–39.7)	16.1 (7.6–28.3)	56	0.18 (0.14–0.23)	0.16 (0.12–0.20)
	Pre-booster	75	36.0 (25.2–47.9)	39.0 (26.6–52.6)	59	0.25 (0.20–0.32)	0.24 (0.19–0.32)
	1 M post-booster	64	73.4 (60.9–83.7)	79.1 (64.0–90.0)	43	0.85 (0.65–1.12)	0.90 (0.62–1.32)
19A	Pre-vaccination	73	34.3 (23.5–46.3)	21.8 (11.8–35.0)	55	0.22 (0.17–0.27)	0.19 (0.15–0.24)
	1 M post-dose 2	63	71.4 (58.7–82.1)	55.4 (41.5–68.7)	56	0.57 (0.45–0.74)	0.47 (0.32–0.67)
	Pre-booster	74	78.4 (67.3–87.1)	78.0 (65.3–87.7)	59	0.83 (0.63–1.08)	0.85 (0.61–1.18)
	1 M post-booster	64	98.4 (91.6–100.0)	92.9 (80.5–98.5)	42	2.92 (2.23–3.83)	2.91 (1.93–4.39)

an acceptable safety profile in the same population [15]. The first 2 primary doses of PHiD-CV were co-administered with the 2 primary 4CMenB doses. The booster doses of the 2 vaccines were also co-administered. MenC-CRM was administered concomitantly with PHiD-CV in both study groups, and PHiD-CV has previously been shown to be immunogenic when co-administered with MenC-CRM [24].

Previously published results from our study show that co-administration of 4CMenB does not appear to impact immune responses to MenC-CRM [17]. Furthermore, this post-hoc analysis suggests that 4CMenB co-administration doesn't impact immune responses to PHiD-CV either.

The results of this post-hoc analysis should be interpreted in light of its strengths and limitations. Although PHiD-CV immunogenicity was not a pre-defined study objective, the possibility of evaluating this was foreseen in the protocol. Due to the study design, no blood samples were taken 1 month after the third primary PHiD-CV dose. Hence, immune responses after the primary vaccination were assessed after the second rather than after the third primary PHiD-CV dose, as it is usually done. Therefore, care

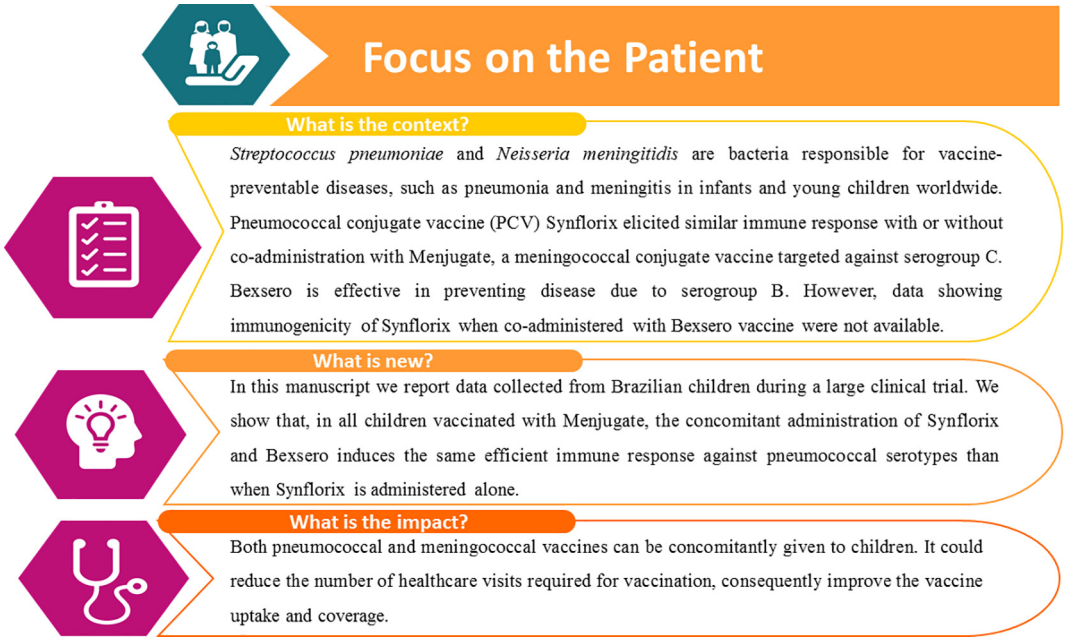

Fig. 2. Focus on the patient.

should be taken when comparing anti-pneumococcal antibody GMCs after the second dose of primary vaccination with results of other studies evaluating immunogenicity of a 3-dose primary PHiD-CV series. The PHiD-CV universal mass vaccination schedule in Brazil was changed in 2016 from 3 + 1 to 2 + 1 [25,26]. This study evaluated immune responses 1 month after the second primary dose, and thus, these results provide valuable information for the 2 + 1 vaccination schedule recently introduced in Brazil, while post booster results reflect the immunogenicity following 3-dose priming.

5. Conclusion

This post-hoc analysis showed that PHiD-CV was immunogenic for the 10 vaccine serotypes and vaccine-related serotypes 6A and 19A when administered concomitantly with 4CMenB and MenC-CRM or with MenC-CRM alone. Anti-pneumococcal antibody GMCs were in similar ranges between the two study groups after the second of the three primary doses and after the booster dose. Co-administration of PHiD-CV doses with 4CMenB doses could improve vaccine uptake and could reduce the number of healthcare visits required for vaccine administration and, therefore, could reduce healthcare resource utilisation.

6. Trademark statement

Bexsero, Menjugate, and Synflorix are trademarks of the GSK group of companies. Prevnar 13 and Prevenar 13 are trademarks of Pfizer Inc.

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Authors' contributions

DT and FMT designed the study. EDMJ, EJFL, FMT, LYW and MAS performed the study and collected the study data. AW performed the statistical analysis. AW, AH, DB, DT, EDMJ, FMT and MAS analysed and interpreted the data. All authors reviewed and approved the current manuscript.

Potential conflicts of interest

DB, DT, AH are employees of the GSK group of companies. AW is working for Plus100 B.V. on behalf of the GSK groups of companies for biostatistics support. The institution of FMT received clinical trial fees from the GSK group of companies during the conduct of this study, and received personal fees/non-financial support/-grants/other from Ablynx, Janssen, the GSK group of companies, Regeneron, Medimmune, Pfizer, MSD, Roche, Novavax, Astra Zeneca, Novartis and Sanofi-Pasteur. EDMJ received a grant from the GSK group of companies for the conduct of this study. MAS received a grant from the GSK group of companies for the conduct of this study and is a member of advisory boards for the GSK group of companies and received grant and personal fees from Pfizer and Sanofi-Pasteur for research, consulting and advisory boards. LYW received a grant from the GSK group of companies for this study and others along with personal fees from Pfizer for lectures and advisory boards. EJFL have no conflicts of interest to declare.

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Data sharing statement

The product that is studied in this clinical study, together with the rights to the data and results generated, have been transferred to GSK by Novartis. The results summary for this study (*eg: Novartis study V72_28 – NCT#* 01339923) is available on the Novartis Clinical Trials Results website and can be accessed at https://www.novctrd.com/. For interventional studies that evaluate GSK medicines, anonymized patient-level data are made available to independent researchers, subject to review by an independent panel, at www.clinicalstudydatarequest.com within six months of publication. To protect the privacy of patients and individuals involved in our studies, GSK does not publicly disclose patient-level data. Patient level data for this study will be made available on www.clinicalstudydatarequest.com upon request, subject to any pre-existing rights and obligations and/or consents required under the relevant agreements governing or related to these studies.

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