A Phase 3B, Open-Label Study to Evaluate the Safety and Immunogenicity of MenACWY-TT Vaccine in Healthy Infants Given at 3 and 12 Months of Age

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INTRODUCTION

• The combination of rapid, severe clinical course and ever-worsening epidemiology indicates vaccination as the best approach for avoiding adverse outcomes of invasive meningococcal disease (MD).

• A meningococcal serogroup ACWY tetanus toxoid conjugate vaccine (MenACWY-TT; Nimenrix®; Pfizer Europe MA EESP, Brussels, Belgium) was first approved in the European Union in 2012 on the basis of safety data and immunogenicity data derived from serum bactericidal assay (SBA) studies using baby rabbit complement (rSBA) from clinical studies.1,2

• MenACWY-TT has demonstrated reduced meningococcal serogroup W135 when included in toddler and adolescent immunization programs in China, England, the Netherlands, and Australia.3

The current licensed MenACWY-TT dosage schedule4 for infants is:– 16 weeks to <6 months of age: 2 primary doses given 2 months apart, booster at 12 months of age
– 16 months of age: a single primary dose, booster at 12 months of age

The current study aimed to evaluate safety and immunogenicity of an alternative dosing schedule that has not previously been evaluated in infants, consisting of a single primary MenACWY-TT dose administered at 3 months followed by a booster at age 12 months (n = 114 scheduled).

METHODS

Study Design

• This phase 3b, single-arm, open-label study (ClinicalTrials.gov, NCT04189913) was conducted at multiple sites in Finland, Poland, Spain.

• Eligible infants were infants 3 months of age who were born at ≥36 weeks gestation.

• Enrolled participants received MenACWY-TT Dose 1 at age 3 months and a booster at 12 months of age.

• Concomitant administration of routine vaccines was permitted at an unscheduled site other than the site of MenACWY-TT administration.

Immunogenicity Endpoints

Here, we report primary immunogenicity endpoints, which included percentages of participants with seroprotective titers (ie, titers ≥1:8) measured in rSBA and rSBA-geometric mean titers (GMTs) for each serogroup before vaccination, 1 month after Dose 1, before the booster, and 1 month after the booster.

Safety Endpoints

Safety endpoints included the percentages of participants reporting local reactions and systemic events within 7 days; immediate adverse events (AEs); within 30 minutes; and AEs, serious AEs (SAEs), and newly diagnosed chronic medical conditions within 30 days of receiving the booster (primary endpoints) or Dose 1 (secondary endpoints).

RESULTS

Participants

• Of the 149 infants enrolled, 147 and 143 received Dose 1 and the booster, respectively, and 143 (96.0%) completed the study.

• The majority of participants (n=141; 97.2%) included in the safety population were White, 73 (52.4%) were female, and all participants were born at ≥36 weeks gestation.

Immunogenicity

• High percentages of participants had seroprotective rSBA titers after Dose 1 compared with baseline (Figure 1).

• Substantial percentages of participants retained seroprotective titers at 9 months after Dose 1 (ie, before the booster).

• All participants (100%) were seroprotected for all 4 serogroups after the booster.

rSBA GMTs increased substantially after Dose 1 compared with baseline GMTs at ages 3 and 12 months (n=124–128 across time points). Error bars represent 2-sided 95% CIs obtained by exponentiating the 95% CIs of the mean logarithm of the rSBA titers based on the Student t-test.

MenACWY=meningococcal serogroup ACWY tetanus toxoid conjugate vaccine; PD1=post Dose 1; rSBA=serum bactericidal antibody assay using baby rabbit complement.

Figure 1. Percentages of Participants With Seroprotective rSBA Titers Following MenACWY-TT Administration at 3 and 12 Months of Age

Table 1. AEs Within 30 Days After Any MenACWY-TT Dose

AE Type
MenACWY-TT (N=143), n (%) AE
Any AE
35 (24.1)
Related
1 (0.7)
Serious AE
4 (2.8)
Severe AE
0 (0.0)

RESULTS (continued)

Figure 2. rSBA GMTs Following MenACWY-TT Administration at 3 and 12 Months of Age

Table 2. Percentages of Participants Reporting Local Reactions and Systemic Events Within 7 Days After Each MenACWY-TT Dose

Systemic Events

Severity

MenACWY=meningococcal serogroup ACWY tetanus toxoid conjugate vaccine; Nimenrix=MenACWY-TT; PD1=post Dose 1; rSBA=serum bactericidal antibody assay using baby rabbit complement.

Figure 3. Percentages of Participants Reporting Local Reactions and Systemic Events Within 7 Days After Each MenACWY-TT Dose

CONCLUSIONS

• MenACWY-TT administered at 3 and 12 months of age induced seroprotective rSBA titers in a high percentage of participants after Dose 1 and all participants after the booster.

• Analysis of rSBA GMTs indicated substantial increases in immune responses after Dose 1 compared with baseline and robust, anamnestic immune responses after the booster.

• This 1+1 MenACWY-TT schedule was safe and well tolerated, with a safety profile that was consistent with established MenACWY-TT dosing schedules in infants.2,4

• These findings indicate that a 1+1 schedule in infants <6 months of age, which is already being used in some countries or regions (eg, Malta, Galicia [Spain]),2,4 could be an alternative MenACWY-TT vaccination schedule for this age group.

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