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

Susanna Koski,[1] Federico Martinon-Torres,[2] Mika Rämet,[3] Lefteris Zolotas,[4] Ryan Newton,[4] Roger Maansson,[5] Mark Cutler,[6] Paula Peyrani,[7] Jamie Findlow,[8] Paul Balmer,[7] Luis Jodar,[7] William C. Gruber,[6] Annaliesa S. Anderson,[6] Johannes Beeslaar[4]

[1]Helsinki South Vaccine Research Clinic, Tampere University, Tampere and FVR – Finnish Vaccine Research, Helsinki, Finland; [2]Hospital Clínico Universitario de Santiago, Santiago de Compostela, Spain; [3]Faculty of Medicine and Healthy Technology Tampere University, Tampere, and FVR – Finnish Vaccine Research, Tampere, Finland; [4]Vaccine Research and Development, Pfizer Ltd, Hurley, Berkshire, UK; [5]Vaccine Clinical Research and Development, Pfizer Inc, Collegeville, PA, USA; [6]Vaccine Research and Development, Pfizer Inc, Pearl River, NY, USA; [7]Vaccines/Antivirals and Evidence Generation, Pfizer Inc, Collegeville, PA, USA; [8]Vaccines/Antivirals and Evidence Generation, Pfizer

INTRODUCTION

- The combination of rapid, severe clinical course and ever-evolving epidemiology indicates vaccination as the best approach for avoiding adverse outcomes of invasive meningococcal disease (IMD).[1]
- A meningococcal serogroup ACWY tetanus toxoid conjugate vaccine (MenACWY-TT; Nimenrix®; Pfizer Europe MA EEIG, Brussels, Belgium) was first approved in the European Union in 2012 on the basis of safety data and immunogenicity data derived from serum bactericidal antibody (SBA) assays using baby rabbit complement (rSBA) from clinical studies.[2,3]
  - MenACWY-TT has demonstrably reduced meningococcal serogroup W IMD when included in toddler and/or adolescent immunization programs in Chile, England, the Netherlands, and Australia.[4-7]
- The current licensed MenACWY-TT dosing schedule[3] for infants is:
  - ≥6 weeks to <6 months of age: 2 primary doses given 2 months apart, booster at 12 months of age
  - ≥6 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 age 3 months followed by a booster at age 12 months (ie, 1+1 schedule).

METHODS

Study Design

- This phase 3b, single-arm, open-label study (ClinicalTrials.gov, NCT04819113) was conducted at multiple sites in Finland, Poland, and Spain.
- Eligible participants 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 age 12 months.
  - Concomitant administration of routine vaccines was permitted at an anatomical 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[8,9]) 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 vast majority of participants (n=141; 97.2%) included in the safety population were White, 76 (52.4%) were female, and the mean ± SD age at Dose 1 was 94.4±6.1 days.

Immunogenicity

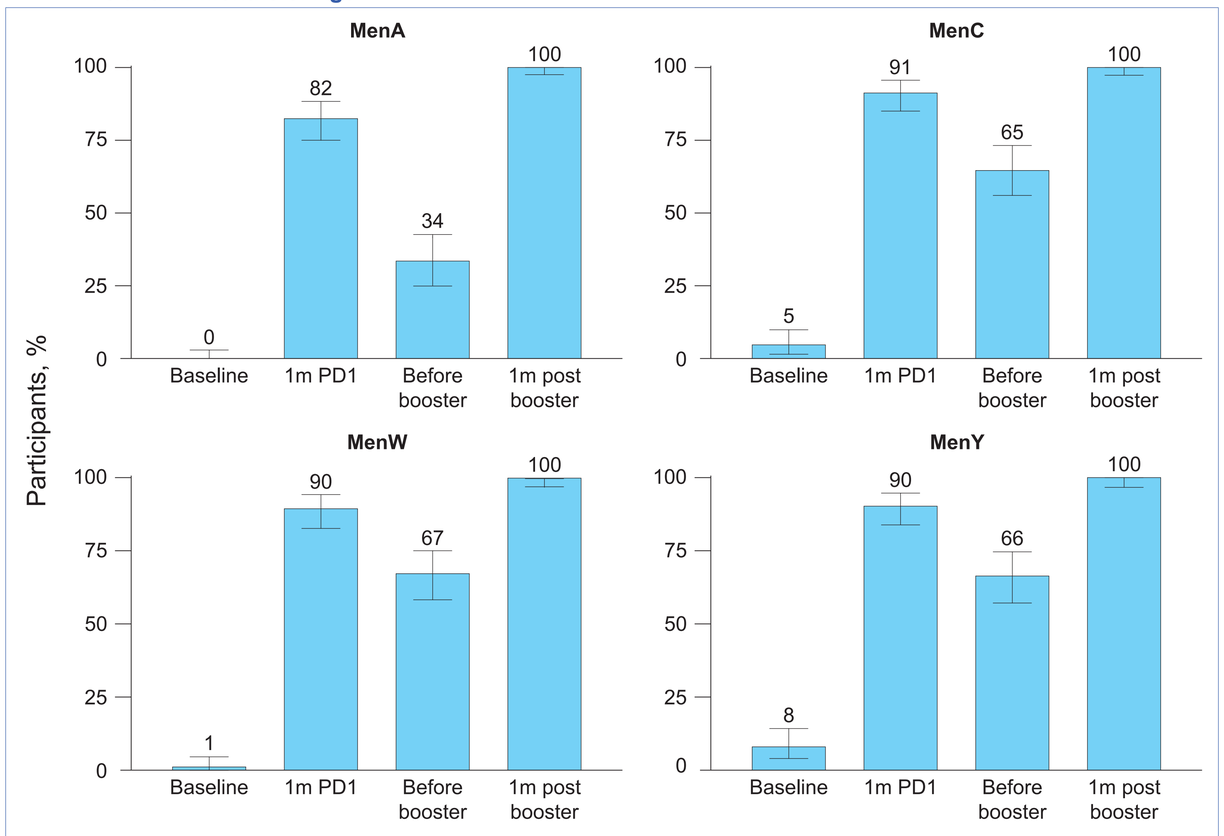
- High percentages of participants had seroprotective rSBA titers after Dose 1 compared with baseline **(Figure 1)**.
  - Substantial percentages of participants retained seroprotective titers at 9 months after Dose 1 (ie, before the booster).
  - All participants (100%) were seroprotected for all 4 serogroups after the booster.
- rSBA GMTs increased substantially after Dose 1 compared with baseline **(Figure 2)**.
  - GMTs then decreased but remained above baseline at 9 months after Dose 1.
  - GMTs after the booster further increased and were higher than those after the primary dose, indicative of anamnestic responses for all 4 serogroups.

Safety

- Local reactions, most commonly injection site pain, were all mild or moderate in severity **(Figure 3)**.
  - Local reactions were reported more frequently after the booster compared with Dose 1.
- Systemic events were predominantly mild or moderate in severity; no Grade 4 events or fevers >40.0°C were reported **(Figure 3)**.
  - Systemic events were reported for 86.9% of participants after Dose 1 and 75.4% of participants after the booster.
- A total of 24.1% of participants reported AEs within 30 days after either dose **(Table 1)**.
  - Reported AEs were most commonly infections and infestations (18.6%).
- Related AEs were infrequent and consistent with reactogenicity events.
- No participants withdrew from the study due to reactogenicity or AEs.
- No related SAEs or deaths were reported.

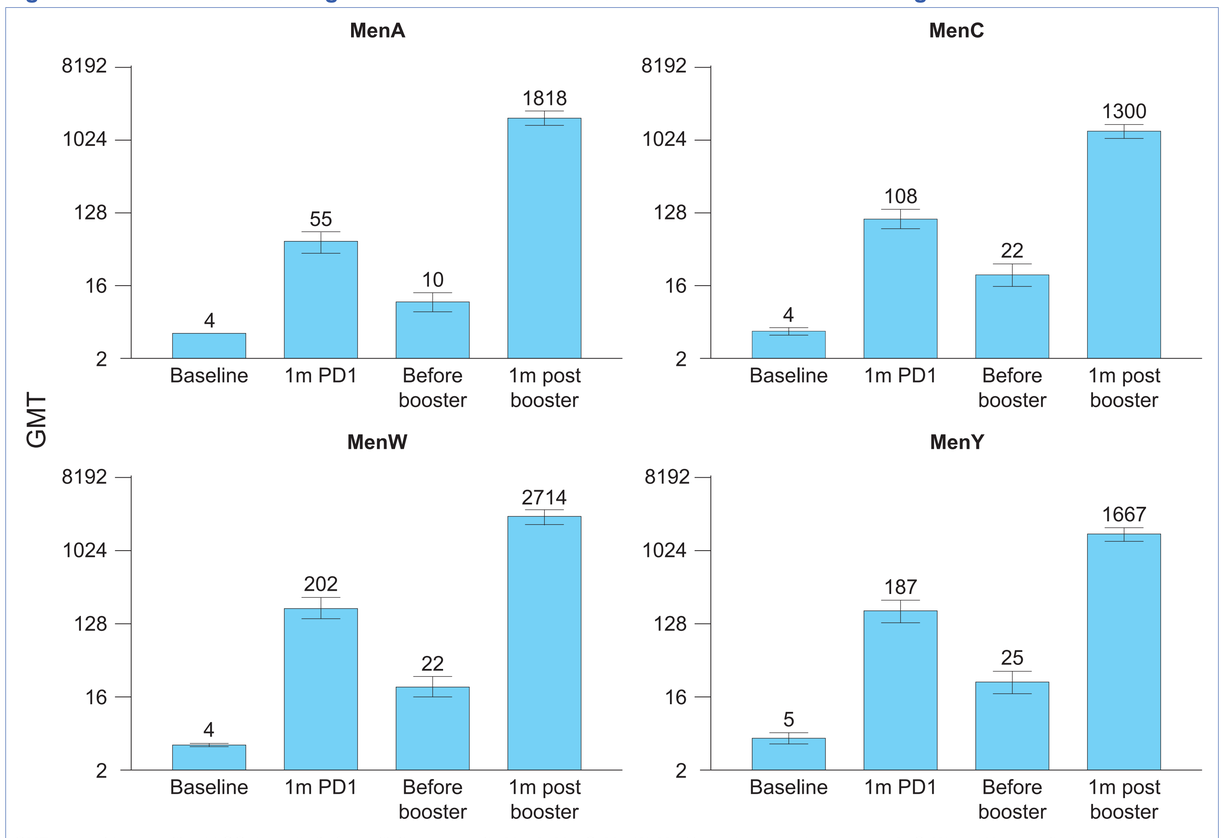
RESULTS (continued)

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



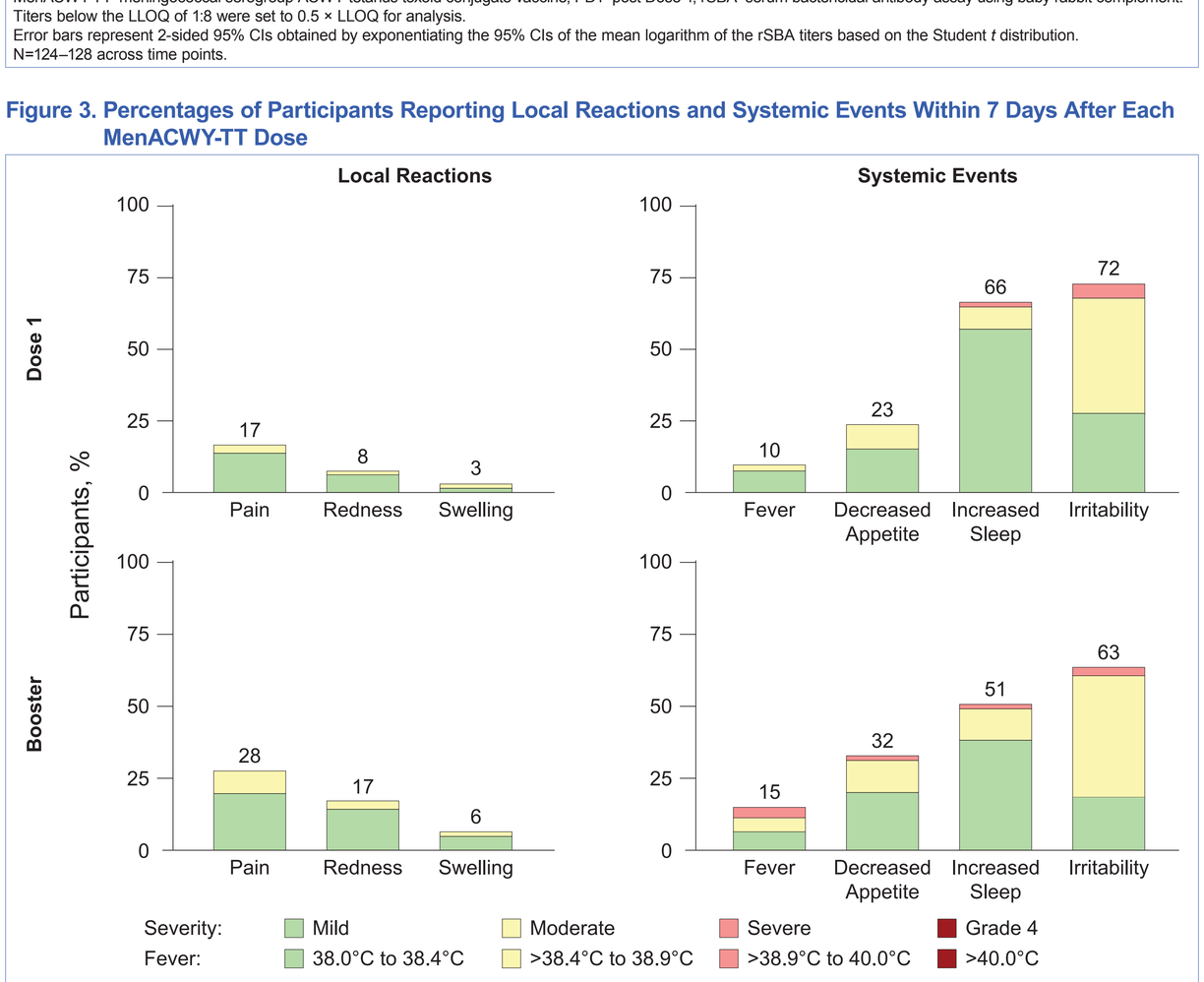
m=month; MenA, MenC, MenW, MenY=meningococcal serogroups A, C, W, and Y, respectively; MenACWY-TT=meningococcal serogroup ACWY tetanus toxoid conjugate vaccine; PD1=post Dose 1; rSBA=serum bactericidal antibody assay using baby rabbit complement.
Seroprotective rSBA titers defined as titers ≥1:8.
Error bars represent 2-sided 95% CIs obtained using the Clopper-Pearson method.
N=124–128 across time points.

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



GMT=geometric mean titer; LLOQ=lower limit of quantitation; m=month; MenA, MenC, MenW, MenY=meningococcal serogroups A, C, W, and Y, respectively; MenACWY-TT=meningococcal serogroup ACWY tetanus toxoid conjugate vaccine; PD1=post Dose 1; rSBA=serum bactericidal antibody assay using baby rabbit complement.
Titers below the LLOQ of 1:8 were set to 0.5 × LLOQ for analysis.
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* distribution.
N=124–128 across time points.

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



MenACWY-TT=meningococcal serogroup ACWY tetanus toxoid conjugate vaccine.
N=142–145 across time points.

RESULTS (continued)

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

AE Type	MenACWY-TT (N=145), n (%)
Any AE	35 (24.1)
Related	1 (0.7)
Serious AE	4 (2.8)
Related	0 (0.0)
Severe AE	1 (0.7)
Related	0 (0.0)
NDCMC	0 (0.0)

AE=adverse event; MenACWY-TT=meningococcal serogroup ACWY tetanus toxoid conjugate vaccine; NDCMC=newly diagnosed chronic medical condition.

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.[10,11]**
- **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]),[12,13] could be an alternative MenACWY-TT vaccination schedule for this age group.**

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Disclosures

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For more information please contact:
Lefteris Zolotas, MD
Vaccine Research and Development
Pfizer Ltd
Hurley, Berkshire, UK
Email: Lefteris.zolotas@pfizer.com

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