MenACWY-TT Long-Term Antibody Persistence Following Adolescent Vaccination and Evaluation of a Booster Dose: A Review of Clinical Data

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BACKGROUND

- Meningococcal disease is a major global health concern, with mortality rates of 10%–15%; long-term sequelae, including severe neurologic, visual, and hearing impairments, occur in 10%–20% of survivors.[1]
  - *Neisseria meningitidis* serogroups A, B, C, W, and Y are responsible for most cases of invasive meningococcal disease (IMD).[2]
- A peak in carriage and IMD occurs during adolescence and young adulthood.[2-4]
- In the United States, preventative vaccination with a quadrivalent meningococcal (MenACWY) conjugate vaccine is recommended at 11–12 years of age, with a booster dose at 16 years of age.[5]
- A MenACWY tetanus toxoid conjugate vaccine (MenACWY-TT; Nimenrix®, Pfizer Ltd, Kent, UK) was first licensed in 2012 and is currently available in the European Union and 50 other countries, although it is not currently licensed in the United States.[6]
- Immune responses following vaccination with MenACWY conjugate vaccines have been reported to decline over a period of several years.[2,7]

OBJECTIVE

- The long-term persistence of MenACWY-TT immune responses in adolescents as well as the safety and immunogenicity of a booster dose given 10 years after primary vaccination are reviewed.

METHODS

Study Design

- Two primary studies—a phase 2 study (Study 1; NCT00356369) conducted in Saudi Arabia and the Philippines, and a phase 3 study (Study 2; NCT00464815) conducted in India, the Philippines, and Taiwan—included adolescents 11–17 years of age (Study 1 included subjects 11–55 years of age) who were given a single dose of MenACWY-TT or MenACWY polysaccharide vaccine (MenACWY-PS).[8-12]
  - Study 1 (NCT00356369) also included 5 year persistence data.
- The extension studies (NCT01934140 for Study 1; NCT03189745 for Study 2) enrolled subjects in the Philippines who had completed vaccination with MenACWY-TT or MenACWY-PS in the primary studies.[13,14]
  - These studies evaluated immune responses up to 10 years after the primary vaccination and the safety and immunogenicity of a MenACWY-TT booster dose, given at Year 10 to all participants regardless of the vaccine received in the primary study.

Immunogenicity

- The percentage of subjects with serum bactericidal assay (SBA) titers ≥1:8 using rabbit complement (rSBA) for all serogroups (A, C, W, Y) and rSBA geometric mean titers (GMTs) are described for primary, persistence, and booster studies.
- Antibody responses at 1 month, 5 years, and 10 years after primary vaccination and at 1 month after booster vaccination are reported.

Safety

- Reactogenicity events occurring ≤4 days after administration of the booster dose, including solicited local events (pain, redness, swelling) and solicited general events (fatigue, fever, gastrointestinal symptoms, headache), are described.
  - Adverse events (AEs) occurring within 30 days after the booster dose and serious AEs (SAEs) occurring within 6 months after the booster dose were also recorded.

Analyses

- rSBA responses (rSBA titers ≥1:8) were calculated for each serogroup with exact 2-sided 95% CIs using the Clopper-Pearson method.
- For GMTs, 95% CIs were calculated as back transformation of CIs based on the Student *t* distributions for the mean logarithm of titers.
- Safety analyses were descriptive in nature.

RESULTS

Population

- Across the 2 studies, 411 subjects were evaluated 10 years after primary vaccination and 406 were evaluated 1 month after MenACWY-TT booster dosing **(Table 1)**.

Table 1. Demographics

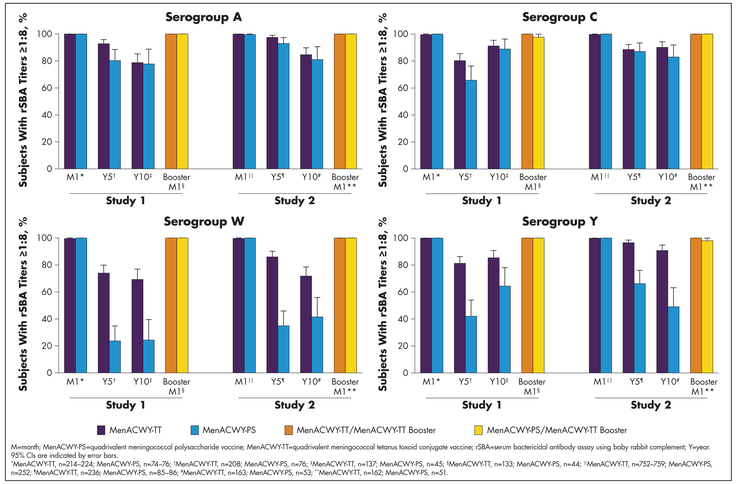
Demographic	Study 1*		Study 2	
	MenACWY-TT n=133	MenACWY-PS n=44	MenACWY-TT n=170	MenACWY-PS n=59
Men, n (%)	76 (57)	21 (48)	90 (53)	36 (61)
Race				
Asian – South East Asian heritage, n (%)	133 (100)	44 (100)	170 (100)	59 (100)
Age at booster vaccination, y				
Mean ± SD	23.9±1.7	24.0±1.9	24.2±1.9	24.0±2.0
Median (range)	24.0 (21–28)	24.0 (21–28)	24.0 (21–27)	24.0 (21–28)

MenACWY-PS=quadrivalent meningococcal polysaccharide vaccine; MenACWY-TT=quadrivalent meningococcal tetanus toxoid conjugate vaccine.
*Includes only those subjects aged 11–17 years at time of primary vaccination.

Immunogenicity

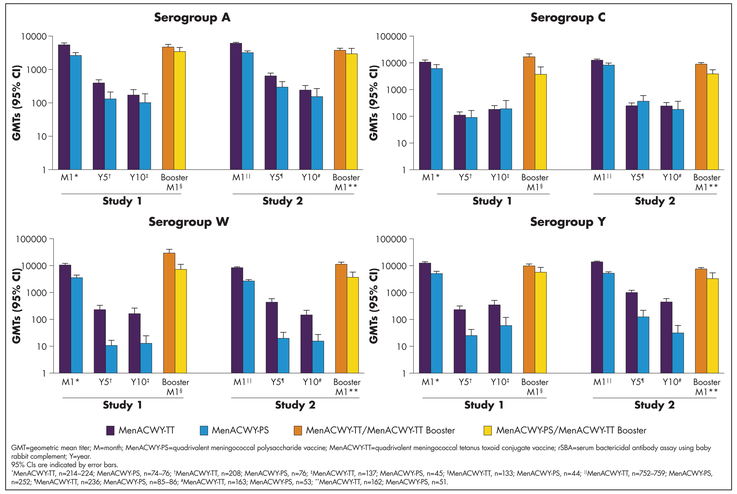
- Across serogroups, the percentages of subjects with rSBA titers ≥1:8 through 10 years after primary vaccination ranged from 69.3%–91.2% in the MenACWY-TT group compared with 24.4%–88.9% in the MenACWY-PS group, across both studies **(Figure 1)**.
  - 10 years after primary vaccination, GMTs ranged from 146.0–446.9 in the MenACWY-TT group compared with 12.9–191.0 in the MenACWY-PS group, across both studies **(Figure 2)**.
- One month after a MenACWY-TT booster dose, 100% of subjects had rSBA titers ≥1:8 in the MenACWY-TT group; corresponding percentages in the MenACWY-PS group were 97.7%–100% **(Figure 1)**.
  - GMTs at 1 month after a MenACWY-TT booster dose were markedly higher than prebooster values: 3760.1–29,371.0 in the MenACWY-TT group and 2956.0–7222.0 in the MenACWY-PS group **(Figure 2)**.

Figure 1. Immune Response to MenACWY-TT Across Clinical Studies and Time Points



M=month; MenACWY-PS=quadrivalent meningococcal polysaccharide vaccine; MenACWY-TT=quadrivalent meningococcal tetanus toxoid conjugate vaccine; rSBA=serum bactericidal antibody assay using baby rabbit complement; Y=year. 95% CIs are indicated by error bars.
†MenACWY-TT, n=214–224; MenACWY-PS, n=74–76; ‡MenACWY-TT, n=208; MenACWY-PS, n=76; §MenACWY-TT, n=137; MenACWY-PS, n=45; ‖MenACWY-TT, n=133; MenACWY-PS, n=44; ¶MenACWY-TT, n=752–759; MenACWY-PS, n=252; #MenACWY-TT, n=236; MenACWY-PS, n=85–86; **MenACWY-TT, n=163; MenACWY-PS, n=53; ††MenACWY-TT, n=162; MenACWY-PS, n=51.

Figure 2. MenACWY-TT rSBA GMTs Across Clinical Studies and Time Points



GMT=geometric mean titer; M=month; MenACWY-PS=quadrivalent meningococcal polysaccharide vaccine; MenACWY-TT=quadrivalent meningococcal tetanus toxoid conjugate vaccine; rSBA=serum bactericidal antibody assay using baby rabbit complement; Y=year.
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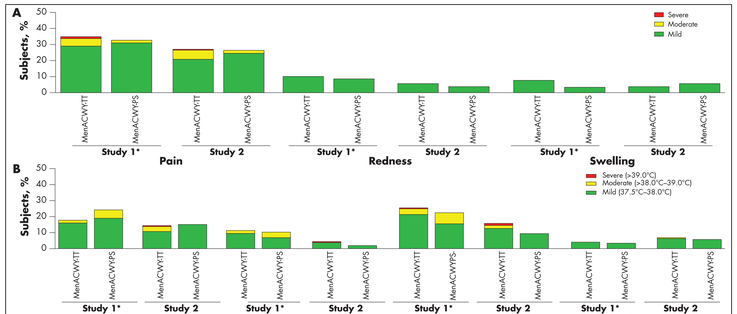
Safety

- Both local and general reactogenicity events after MenACWY-TT booster vaccination were largely mild to moderate in severity **(Figure 3A** and **3B)**.
  - Pain at the injection site was the most commonly reported local event across both studies; headache and fatigue were the most commonly reported general events **(Figure 3A** and **3B)**.
  - Safety data for Study 1 includes all subjects (aged 11–55 years at the time of primary vaccination).

Figure 3. Percentages of Subjects Experiencing Local Reactions (A) and Systemic Events (B) After MenACWY-TT Booster Across Clinical Studies



MenACWY-PS=quadrivalent meningococcal polysaccharide vaccine; MenACWY-TT=quadrivalent meningococcal tetanus toxoid conjugate vaccine.
*Data from all study participants, 11–55 years at time of primary vaccination.

CONCLUSIONS

- **Immune responses were generally higher or similar among adolescents receiving primary vaccination with MenACWY-TT compared with MenACWY-PS for all serogroups, and these responses persisted through 10 years after primary vaccination, suggesting that MenACWY-TT may help prevent IMD throughout the lengthy risk period in this age group.**
- **Additionally, a MenACWY-TT booster dose administered 10 years after primary vaccination resulted in robust immune responses and may further extend protection from IMD regardless of the primary vaccine received.**

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DISCLOSURES

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