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ORIGINAL RESEARCH

Post-Marketing Surveillance Observational Study of Quadrivalent Meningococcal Diphtheria Toxoid Conjugate Vaccine (MenACWY-DT, MCV4/Menactra®) in the Republic of Korea, 2014–2019

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ABSTRACT

Background: Invasive meningococcal disease is a notifiable disease in the Republic of Korea. The meningococcal (groups A, C, Y, and W) polysaccharide diphtheria toxoid conjugate vaccine (MenACWY-DT, Menactra®) was licensed in the Republic of Korea in 2014. This post-marketing surveillance (PMS) observational study aims to assess the safety of MenACWY-DT administration of routine clinical care to individuals aged 9–23 months as a two-dose series at least 3 months apart and to individuals 2–55 years as a single dose.

Methods: The PMS observational study (NCT02864927) included participants aged 9 months to 55 years and who were given MenACWY-DT during routine healthcare visits. The study participants were followed-up for up to 30 days following vaccination (additional time was allowed for the visit or phone call to be conducted). Study outcomes included solicited and unsolicited adverse reactions, unexpected adverse events, and serious adverse events (SAEs).

Results: A total of 640 participants 9–23 months of age and 671 participants 2–55 years of age were eligible for safety analysis. Overall, AEs were reported by 35.3% of participants aged < 2 years and 45% of participants aged 2–55 years. Solicited adverse reactions were reported by 21.4% and 17.4% of participants aged < 2 years and 2–55 years, respectively. Unsolicited adverse reactions were reported by 26.1% and 37.9%, respectively. No vaccine-related SAEs occurred during the study. The AEs reported in Korean population were consistent with the known safety profile of MenACWY-DT, and most were of grade 1–2 in severity.

Conclusions: This study did not detect any unanticipated or new safety findings of concern with MenACWY-DT in either of the study age groups, and provides reassurance that MenACWY-DT can be used as part of routine immunization care for the prevention of invasive meningococcal disease.

Trial Registration: ClinicalTrials.gov Identifier, NCT02864927

Keywords: Adverse reactions or events; Menactra®; MenACWY-DT; MCV4; Meningococcal infections; Meningococcal vaccine; Safety; Vaccines

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Key Summary Points

Post-marketing surveillance (PMS) of MenACWY-DT (Menactra®) provides the safety profile of this vaccine in a real-life setting.

No safety concerns identified with MenACWY-DT in the Korean population.

MenACWY-DT is safe to use in children, adolescents and adults of age 9 months to 55 years.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.13353113.

INTRODUCTION

Meningococcal disease is caused by the Gram-negative aerobic diplococcus *Neisseria meningitidis*. The serogroups A, B, C, W, and Y account for over 90% of meningococcal disease cases worldwide [1, 2]. The prevalence of the meningococcal disease varies across different countries, ranging from 0.16 to 1.65 cases/100,000 individuals in well-developed countries to over 300 cases/100,000 individuals in the sub-Saharan meningitis belt [3]. The greatest burden of meningococcal disease occurs in children under 5 years of age. Incidence peaks are also seen among adolescents and young adults [2, 4]. According to global disability-adjusted life years (DALY) estimation, the burden of all-age meningitis (of all causes) was 20.4 million DALYs [17.8–23.4] in 2017 [5].

Invasive meningococcal disease (IMD) may present as acute sepsis or meningitis. Meningococcal meningitis combined with septic shock is responsible for a higher mortality [3]. The burden of IMD in the Republic of Korea was reported to be relatively low with an annual incidence of 0.05 cases per 100,000 persons [6]. High incidence rates were noted in Korean children < 5 years of age with approximately 1.35 cases per 100,000 persons [6]. Serogroup B and C are the most common meningococcal carriage isolates among Korean adolescents, although serogroup distributions are consistently changing [7]. There were outbreaks caused by serogroup W in 2011 in military recruits which led to required meningococcal vaccination of all recruits in 2012 [8]. IMD remains an under-reported disease in Korea because of the limitations in culture surveillance methods and limited epidemiological studies [8–10]. The lack of herd protection is also thought to be a risk factor for the outbreaks in the Republic of Korea [9]. Vaccination is considered the best strategy to prevent IMD. Availability of novel vaccines, including the meningococcal polysaccharide-conjugate vaccines to serogroups A, C, W, and Y (MenACWY), by conjugating the polysaccharide antigen to a carrier protein, reduced the nasopharyngeal carriage and offered broader protection against a higher number of serogroups [2].

The meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Menactra®) was approved by the U.S. Food and Drug Administration in 2005 [11]. A product license for Menactra® was approved in the Republic of Korea by the Ministry of Food and Drug Safety (MFDS) in November 2014, for active immunization to prevent IMD caused by *Neisseria meningitidis* for individuals aged 11–55 years. Age indication was later expanded to include adults and children 9 months to 55 years of age in June 2015. Results from a randomized, phase 3 clinical trial in Korea confirmed that a single dose of MenACWY-DT induced an immune response with a seroconversion rate of > 60% for all four serogroups, and was well-tolerated in Korean adolescents and adults [12]. While several studies have investigated the safety of MenACWY-DT administered routinely to adolescents and adults [4, 13, 14], there are limited data on the safety of MenACWY-DT in the Korean population. We monitored the safety of

MenACWY-DT routinely administered in a post-licensure safety surveillance study across children 9- to 23-month-olds who are given two series at least 3 months apart, and in adults and children aged 2–55 years when given as a single dose.

METHODS

Study Design and Participants

According to the MFDS regulations, an open, multi-center, prospective, observational study was performed within 4 years after the MenACWY-DT (Menactra®) product license approval in the Republic of Korea (ClinicalTrials.gov Identifier: NCT02864927) in children aged 9–23 months old across 25 institutions, from July 2016 to June 2019, and in the population aged 2–55 years across 13 institutions from June 2016 to July 2018. The study protocol and amendments were approved by the institutional ethics committee or institutional review board (IRB) of Wonju Severance Christian Hospital. The IRB approval number for this study is CR115100-102. The study was performed according to local and national regulations and was consistent with the standards established by the Declaration of Helsinki and compliant with the International Council for Harmonization guidelines for Good Clinical Practice and MFDS regulations (basic standard for the re-examination of a new drug). An informed consent form was signed after vaccination by each participant, or the participant's parents or legally acceptable representatives, before enrolment in the study.

Participants were enrolled after vaccination as per routine clinical practice. Children aged 9–23 months old who received two doses of MenACWY-DT at least 3 months apart were eligible. Participants 2–55 years of age who received one dose of MenACWY-DT during a routine healthcare visit were eligible. Enrolled subjects were followed after one dose of MenACWY-DT (first or second dose for subjects from 9 to 23 months) whatever their age (and therefore vaccination schedule) at enrolment. The main exclusion criteria were previous (in the 4 weeks before enrolment) or planned participation in another clinical study.

Safety Evaluation

Participants and/or caregivers were given a diary card to record safety information about their daily temperature, daily measurement or intensity grade of all solicited injection site and systemic reactions, and the action taken to treat any solicited reactions, for the 7 days after vaccination (day 0–day 7) until resolution. Information about any other medical events, including serious adverse events (SAEs) that may occur between the vaccination and the next visit, and if any treatment was provided, was also recorded (day 0–day 30). Unexpected adverse events (AEs) defined as an unsolicited AE, the nature or severity of which was not consistent with the applicable product information (Korean product information leaflet), were also reported. The safety data were collected at visit 2 [30 (+7) days after visit 1 (day 0)]. In cases where the participant could not attend visit 2, the safety information was obtained over the telephone within 42 days from visit 1. Women participants who became pregnant during the study participation were asked to report their pregnancies. They were to be followed-up until the childbirth in order to obtain information about the outcome, including spontaneous abortions, fetal death, stillbirth, and congenital anomalies, if any were reported.

Study Outcomes

Primary endpoints included were the occurrence of solicited adverse reactions within 7 days of vaccination, unsolicited AEs (spontaneously reported events) recorded for 30 days after vaccination, and SAEs occurring throughout the study.

The causality assessment between solicited reactions and serious/non-serious unsolicited systemic AEs and vaccination were assessed by the investigator as certain (a clinical event occurring in a plausible time relationship to drug administration), probable/likely (a clinical

event with a reasonable time sequence to administration of the drug), possible (a clinical event with a reasonable time sequence to administration of the drug, but which could also be explained by concurrent disease or other drugs), unlikely (a clinical event with a temporal relationship to drug administration), conditional/unclassified (a clinical event for which more data are essential for a proper assessment), or unassessable/unclassified (an adverse reaction that cannot be judged because of insufficient information). The grades of severity included grade 1 (mild, regarded as having no interference with activity), grade 2 (moderate, regarded as having some interference with activity), and grade 3 (severe, regarded as significant and preventing daily activity). Safety analysis by subpopulations including gender, age, vaccination history (any vaccination within the last 4 weeks), prior medical history (prior to enrolment, obtained verbally about the participant, with the help of parents in the case of children and adolescents), concomitant disease (any disease noted at the time of vaccine administration), and concomitant medication (any medication or vaccination being taken at the time of MenACWY-DT vaccination and during the course of the study) were performed.

Statistical Analyses

No statistical hypotheses were tested, and all evaluations were descriptive in nature. A maximum of 1438 eligible/enrolled participants were planned to be recruited to ensure at least 600 evaluable participants were available in each age group (9–23 months and 2–55 years) for the safety assessments.

The safety analysis set included all those who received a dose of MenACWY-DT regardless of their vaccination schedule and who were followed-up for safety evaluation. Safety surveillance in participants aged 9–23 months was considered only for one of the doses (1st or 2nd shot) administered. Summary statistics were presented for AEs (MedDRA preferred term), maximum intensity, action taken, time of onset, days of occurrence, and relationship to the vaccine. The 95% confidence intervals (CIs) were calculated using the exact binomial distribution according to the Clopper–Pearson method for proportions and the normal approximation for quantitative data. All statistical analyses were carried out with SAS Software v.9.2 or above (Cary, NC, USA).

RESULTS

Of the 648 (9–23 months of age) and 707 (2–55 years of age) participants enrolled, 640 (98.8%) and 671 (94.9%), respectively, were eligible for safety analysis. The main reasons for exclusion in both age groups were lost to follow-up (5 and 23 participants, respectively) and not meeting the inclusion criteria (2 participants in each). Demographics and baseline characteristics are presented in Table 1. Overall, AEs were reported by 35.3% of participants aged < 2 years and 45% of participants aged 2–55 years. Solicited adverse reactions were reported by 21.4% and 17.4% of participants aged < 2 years and 2–55 years, respectively. Unsolicited adverse reactions were reported by 26.1% and 37.9%, respectively. One participant reported one SAE during the follow-up period (Table 2). No women enrolled became pregnant during the study.

Solicited Adverse Reactions

Solicited injection site reactions and systemic reactions were reported in 12.3% and 9.1% of participants < 2 years and 10.3% and 7.2% of participants aged 2–55 years, respectively. The most common solicited reactions in participants < 2 years were injection site erythema (7.2%) and pyrexia (4.4%) and ,in ages 2–55 years of age, injection site pain (9.2%) and myalgia (5.4%). Most solicited reactions began within 3 days post-vaccination, resolved within 1–3 days, and were grade 1 in intensity in both populations (Table 3). In participants aged < 2 years, for solicited reactions, comparison of the rates of injection site reactions/systemic reactions by prior vaccination versus no vaccination history was 22.1% versus 15.1% ($P = 0.0414$). Comparison of rates in patients taking versus not taking concomitant

Table 1 Demographics of participants

Characteristic	Participants aged 9–23 months ($n = 640$)	Participants aged 2–55 years ($n = 671$)
Gender	340 (53.1):300 (46.9)	305 (45.5):366 (54.6)
Male, *n* (%): female, *n* (%)		
Age, median (range)	12 months (9–23)	3 years (2–55)
Vaccination history within 4 weeks prior to the date of study vaccine administration, *n* (%)	217 (33.9)	74 (11)
Study vaccine administration		
Injection dose, *n* (%)		
1st dose	575 (89.8)	670 (99.9)
2nd dose	65 (10.2)	1 (0.2)
Injection side, *n* (%)		
Right	162 (25.3)	93 (13.9)
Left	478 (74.7)	578 (86.1)
Injection site, *n* (%)		
Upper arm	273 (42.7)	621 (92.6)
Thigh	367 (57.3)	50 (7.5)
Other	0	0

Table 2 Overall incidence of adverse reactions and events reported

	Participants aged 9–23 months ($n = 640$)			Participants aged 2–55 years ($n = 671$)		
	Participants with AEs, *n* (%)	Number of AEs	95% CI	Participants with AEs, n (%)	Number of AEs	95% CI
Solicited reactions						
Injection site reactions	79 (12.3)	111	9.9–15.2	69 (10.3)	108	8.1–12.8
Systemic reactions	58 (9.1)	115	7–11.6	48 (7.2)	86	5.3–9.4
Unsolicited AEs						
Injection site	1 (0.2)	1	0–0.9	3 (0.5)	3	0.1–1.3
Systemic	166 (25.9)	311	22.6–29.5	251 (37.4)	400	33.7–41.2
Serious AEs	1 (0.2)	1	–	0	0	–

AEs adverse events, *CI* confidence interval

Table 3 Overall incidence of solicited adverse reactions

	Participants aged 9–23 months (n = 640)						Participants aged 2–55 years (n = 671)					
	Participants with ARs, n (%)	Number of ARs	95% CI	Severity			Participants with ARs, n (%)	Number of ARs	95% CI	Severity		
				Grade 1, n (%)	Grade 2, n (%)	Grade 3, n (%)				Grade 1, n (%)	Grade 2, n (%)	Grade 3, n (%)
Injection site reactions	79 (12.3)	111	9.9–15.2	35 (5.5)	12 (1.9)	3 (0.5)	69 (10.3)	108	8.1–12.8	59 (8.8)	16 (2.4)	10 (1.5)
Injection site erythema	46 (7.2)	46	5.3–9.5	12 (1.9)	7 (1.1)	3 (0.5)	22 (3.3)	22	2.1–4.9	9 (1.3)	6 (0.9)	7 (1)
Injection site pain	33 (5.2)	33	3.6–7.2	24 (3.8)	8 (1.3)	0	62 (9.2)	62	7.2–11.7	51 (7.6)	10 (1.5)	1 (0.2)
Injection site swelling	32 (5)	32	3.4–7.0	10 (1.6)	3 (0.5)	1 (0.2)	24 (3.6)	24	2.3–5.3	16 (2.4)	3 (0.5)	5 (0.8)
Systemic reactions	58 (9.1)	115	7.0–11.6	44 (6.9)	18 (2.8)	7 (1.1)	48 (7.2)	86	5.3–9.4	38 (5.7)	13 (1.9)	3 (0.5)
Crying	14 (2.2)	14	1.2–3.6	10 (1.6)	1 (0.2)	3 (0.5)	–	–	–	–	–	–
Decreased appetite	24 (3.8)	24	2.4–5.5	22 (3.4)	2 (0.3)	0	–	–	–	–	–	–
Irritability	21 (3.3)	21	2.0–5.0	10 (1.6)	8 (1.3)	3 (0.5)	–	–	–	–	–	–
Pyrexia	28 (4.4)	28	2.9–6.3	15 (2.3)	7 (1.1)	1 (0.2)	7 (1)	7	0.4–2.1	4 (0.6)	1 (0.2)	1 (0.2)
Somnolence	20 (3.1)	20	1.9–4.8	14 (2.2)	4 (0.6)	2 (0.3)	–	–	–	–	–	–
Vomiting	8 (1.3)	8	0.5–2.5	4 (0.6)	2 (0.3)	2 (0.3)	–	–	–	–	–	–
Headache	–	–	–	–	–	–	18 (2.7)	18	1.6–4.2	15 (2.2)	3 (0.5)	0
Malaise	–	–	–	–	–	–	25 (3.7)	25	2.4–5.5	19 (2.8)	5 (0.8)	1 (0.2)
Myalgia	–	–	–	–	–	–	36 (5.4)	36	3.8–7.4	26 (3.9)	7 (1)	3 (0.5)

Grade 1 (mild) regarded as having no interference with activity), grade 2 (moderate) regarded as having some interference with activity), and grade 3 (severe) regarded as significant and preventing daily activity

ARs adverse reactions, *CI* confidence interval

medication/vaccinations was 21.3% versus 15.2% ($P = 0.0440$), while for the 2–55 years age group, differences in the rates of injection site reactions/systemic reactions by age were 29.7% in participants aged ≥ 20 to < 30 years, 28.6% in those aged ≥ 40 to ≤ 55 years, and 21.7% in those aged ≥ 10 to < 20 years ($P = 0.0008$). Comparison of rates with prior vaccination versus no vaccination history was 4.1% versus 13.1% ($P = 0.0248$), in patients with past medical history 60% versus 11.7% ($P = 0.0142$) without past medical history, and in patients with concomitant disease 40% versus 11.4% ($P = 0.0053$) without concomitant disease.

Unsolicited Adverse Events

Unsolicited injection site reactions and systemic reactions were reported in 0.2% and 25.9% of participants < 2 years and 0.5% and 37.4% of participants aged 2–55 years, respectively. The most commonly reported unsolicited injection site reactions were injection site induration, reported in 0.2% of participants aged < 2 years, and injection site prutitus, reported by 0.3% of participants aged 2–55 years. Nasopharyngitis was the most commonly reported unsolicited systemic event observed in both age groups (reported by 9.2% of participants < 2 years and 20.4% of participants 2–55 years) followed by bronchitis (reported by 5.3% of participants < 2 years and 5.1% of participants 2–55 years) and rhinitis (reported by 4.5% of participants < 2 years and 5.5% of participants 2–55 years). When assessed for causality, 25.8% and 0.3% were classified as unlikely (nasopharyngitis, 9.2%; bronchitis, 5.3%; rhinitis, 4.5%) and possible (rash, 0.2% and tonsillitis, 0.2%) unsolicited AEs, respectively, in age group < 2 years. The corresponding percentages in 2–55 years age group were 37.3% and 0.2%. None of the reported unsolicited systemic events were classified as certain, probable/likely, conditional/unclassified, or unassessable/unclassifiable in both the age groups. Most unsolicited AEs were of grade 1 in intensity (Table 4).

In participants < 2 years, the differences in the rates of unsolicited events by gender (male versus female) was 22.4% versus 30% ($P = 0.0276$), by prior vaccination versus no vaccination history was 32.7% versus 22.5% ($P = 0.0051$), with versus without concomitant disease was 47.6% versus 25.2% ($P = 0.0212$), and comparison in patients taking versus not taking concomitant medication/vaccinations was 56% versus 3.0% ($P < 0.0001$). Similarly, in participants 2–55 years, the rates of unsolicited events by age included 42.6% in participants aged ≥ 2 to < 10 years, 9.6% in ≥ 10 to ≤ 20 years, and 12.5% in ≥ 20 to < 30 years of age ($P < 0.0001$). Differences in the rates by prior vaccination versus no vaccination history was 58.1% versus 35.2% ($P = 0.0001$), and comparison of patients taking versus not taking concomitant medications was 70.2% versus 2.5% ($P < 0.0001$).

Unexpected Adverse Events

The most frequently reported unexpected AEs in participants aged < 2 years were nasopharyngitis (9.2%), bronchitis (5.3%), and rhinitis (4.5%), and in age group 2–55 years were nasopharyngitis (20.4%), rhinitis (5.5%), and bronchitis (5.1%). None of the AEs reported led to discontinuation of participants from either of the two groups. When the causal relationship between unexpected systemic events and vaccination was evaluated, most of the unexpected AEs were classified as unlikely (< 2 years, 24.7%; 2–55 years, 36.7%). None of the unexpected systemic events were classified as certain, probable/likely, possible, conditional/unclassified, or unassessable/unclassifiable.

Adverse Events in Children and Adolescents

The rate of any AEs among 604 children and adolescents aged 2–18 years was 46.9%. Solicited injection site reactions were reported by 9.5% and systemic events by 5.8%. The rate of unsolicited injection site reactions was 0.5% and that of unsolicited systemic events was 40.7%. Injection site pain (8.3%) and myalgia (4.6%) were the most common solicited AEs

Table 4 Unsolicited adverse events which occurred with a frequency of at least 0.5% in either of the study participants

	Participants aged 9–23 months ($n = 640$)			Participants aged 2–55 years ($n = 671$)		
	Participants with AEs, *n* (%)	Number of AEs	95% CI	Participants with AEs, *n* (%)	Number of AEs	95% CI
Injection site events	1 (0.2)	1	0–0.9	3 (0.5)	3	0.1–1.3
Systemic reactions	166 (25.9)	311	22.6–29.5	251 (37.4)	400	33.7–41.2
Eye discharge	3 (0.5)	3	0.1–1.4	–	–	–
Constipation	2 (0.3)	2	0–1.1	5 (0.8)	5	0.2–1.7
Diarrhoea	6 (0.9)	6	0.3–2	1 (0.2)	1	0–0.8
Enteritis	6 (0.9)	6	0.3–2	10 (1.5)	10	0.7–2.7
Pyrexia	11 (1.7)	11	0.9–3.1	3 (0.5)	3	0.1–1.3
Bronchitis	34 (5.3)	36	3.7–7.3	34 (5.1)	37	3.5–7
Conjunctivitis	4 (0.6)	4	0.2–1.6	5 (0.8)	5	0.2–1.7
Gastroenteritis	6 (0.9)	6	0.3–2	3 (0.5)	3	0.1–1.3
Impetigo	3 (0.5)	3	0.1–1.4	4 (0.6)	4	0.2–1.5
Influenza	3 (0.5)	3	0.1–1.4	–	–	–
Nasopharyngitis	59 (9.2)	63	7.1–11.7	137 (20.4)	147	17.4–23.7
Otitis media	11 (1.7)	12	0.9–3.1	4 (0.6)	4	0.2–1.5
Pharyngitis	5 (0.8)	6	0.3–1.8	–	–	–
Rhinitis	29 (4.5)	30	3.1–6.4	37 (5.5)	47	3.9–7.5
Sinusitis	7 (1.1)	7	0.4–2.2	2 (0.3)	3	0–1.1
Tonsillitis	6 (0.9)	6	0.3–2	2 (0.3)	3	0–1.1
Upper respiratory tract infection	5 (0.8)	5	0.3–1.8	–	–	–
Arthropod bite	3 (0.5)	3	0.1–1.4	–	–	–
Asthma	5 (0.8)	5	0.3–1.8	4 (0.6)	4	0.2–1.5
Cough	13 (2)	14	1.1–3.5	7 (1)	9	0.4–2.1
Nasal congestion	3 (0.5)	3	0.1–1.4	1 (0.2)	1	0–0.8
Productive cough	4 (0.6)	4	0.2–1.6	2 (0.3)	2	0–1.1
Rhinitis allergic	12 (1.9)	12	1–3.3	11 (1.6)	11	0.8–2.9
Rhinorrhoea	14 (2.2)	15	1.2–3.6	9 (1.3)	12	0.6–2.5
Sneezing	3 (0.5)	3	0.1–1.4	1 (0.2)	1	0–0.8
Upper respiratory tract inflammation	6 (0.9)	6	0.3–2	32 (4.8)	33	3.3–6.7
Dermatitis atopic	3 (0.5)	3	0.1–1.4	–	–	–

Table 4 continued

	Participants aged 9–23 months ($n = 640$)			Participants aged 2–55 years ($n = 671$)		
	Participants with AEs, *n* (%)	Number of AEs	95% CI	Participants with AEs, *n* (%)	Number of AEs	95% CI
Dermatitis	3 (0.5)	3	0.1–1.4	–	–	–
Dermatitis allergic	–	–	–	11 (1.6)	11	0.8–2.9
Rash	5 (0.8)	5	0.3–1.8	2 (0.3)	2	0–1.1
Urticaria	3 (0.5)	3	0.1–1.4	4 (0.6)	5	0.2–1.5

AEs adverse events

reported. Injection site pruritus (0.3%), nasopharyngitis (22.7%), rhinitis (6.1%), and bronchitis (5.6%) were the most common unsolicited AEs reported.

Serious Adverse Events

Only one SAE, considered unrelated to vaccination, was reported during this study. A 15-month-old male was admitted to the hospital due to a common cold (nasopharyngitis) 20 days after receiving the first dose of MenACWY-DT. This study participant was treated and recovered.

DISCUSSION

This study evaluated the safety of MenACWY-DT in children 9–23 months of age, and older children, adolescents, and adults aged 2–55 years. This is the first study to assess the safety of MenACWY-DT in the Republic of Korea after its approval in 2014 and in accordance with the MFDS regulations. The vaccine was well tolerated. There were no unanticipated or new safety findings of concern identified with MenACWY-DT in either of the study populations. Most of the local and systemic reactions were transient and of grades 1–2 in intensity. Nasopharyngitis, which was considered unrelated to vaccination and resolved upon treatment, was the only serious AE reported in a participant aged < 2 years old, while no serious AEs were reported among the 2- to 55-year-old group. No deaths occurred during the study, and no participants discontinued the study due to an AE or adverse reaction. Safety analysis by subpopulations showed differences which were statistically significant; however, they may not be clinically relevant considering the small sample size of the study population. The safety profile of MenACWY-DT in the subpopulation aged 2–18 years was generally comparable to the age group of 2–55 years.

The results reported were consistent with pre-licensure studies for the more common AEs, such as injection site and systemic reactions [12]. The safety profile of MenACWY-DT appears to be similar to that observed in clinical studies and post-licensure studies undertaken in other regions [13–18]. However, it should be noted that the results of this study represent lower rates of AEs compared to those reported in prospective randomized clinical trials.

Post-licensure vaccine safety surveillance is an essential component of any vaccination program and has important implications for informing national immunization policies. Although pre-licensure human clinical studies evaluate vaccine safety, these usually have a limited sample size and only assess otherwise healthy individuals. Therefore, rare AEs, and AEs only occurring in a unique subpopulation may not be detected until a vaccine is widely used in the general population [19]. A limitation of this study is the sample size, which is not large enough to detect extremely rare or uncommon events.

CONCLUSION

In conclusion, the post-marketing safety surveillance of the MenACWY-DT vaccine in the Korean population aged < 2 years and 2–55 years did not reveal any unexpected safety findings of concern. It reaffirms the safety of MenACWY-DT and provides reassurance for the use of the MenACWY-DT as part of routine immunization care for the prevention of meningococcal disease in the Republic of Korea.

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Compliance with Ethics Guidelines. The study protocol and amendments were approved by the institutional ethics committee or institutional review board (IRB) of Wonju Severance Christian Hospital. The IRB approval number for this study is CR115100-102. The study was performed according to local and national regulations and was consistent with the standards established by the Declaration of Helsinki and compliant with the International Council for Harmonization guidelines for Good Clinical Practice and MFDS regulations (basic standard for the re-examination of a new drug). An informed consent form was signed after vaccination by each participant, or participant's parents, or legally acceptable representatives before enrolment into the study.

Data Availability. The datasets generated during and/or analysed during the current study are not publicly available as the data sets are in Korean language but are available from the corresponding author on reasonable request.

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