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Immunogenicity and safety of a quadrivalent meningococcal polysaccharide CRM conjugate vaccine in infants and toddlers☆

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SUMMARY

Objectives: This phase III study assessed the safety and immunogenicity of MenACWY-CRM, a quadrivalent meningococcal conjugate vaccine, administered with routine vaccines starting at 2 months of age.

Methods: Healthy infants received MenACWY-CRM in a two- or three-dose primary infant series plus a single toddler dose. In addition, a two-dose toddler catch-up series was evaluated. Immune responses to MenACWY-CRM were assessed for serum bactericidal activity with human complement (hSBA). Reactogenicity and safety results were collected systematically.

Results: After a full infant/toddler series or two-dose toddler catch-up series, MenACWY-CRM elicited immune responses against the four serogroups in 94–100% of subjects. Noninferiority of the two- versus three-dose MenACWY-CRM infant dosing regimen was established for geometric mean titers for all serogroups. Following the three-dose infant primary series, 89–98% of subjects achieved an hSBA $\geq$8 across all serogroups. Immune responses to concomitant routine vaccines given with MenACWY-CRM were noninferior to responses to routine vaccines alone, except for pertactin after the two-dose infant series. Noninferiority criteria were met for all concomitant antigens after the three-dose infant series.

Conclusions: MenACWY-CRM vaccination regimens in infants and toddlers were immunogenic and well tolerated. No clinically meaningful effects of concomitant administration with routine infant and toddler vaccines were observed.

1. Introduction

Neisseria meningitidis is a leading cause of bacterial meningitis and sepsis that can result in permanent disability or death within hours in otherwise healthy individuals.[1,2] Meningococcal disease occurs globally and is characterized by an epidemiology with fluctuations in the incidence and occurrence of outbreaks and epidemics.[3,4] Six immunologically distinct serogroups (A, B, C, W-135, X, and Y) are associated with significant pathogenic potential for invasive disease.[5] The varied epidemiology of meningococcal disease, its propensity to cause outbreaks, the severity of disease and associated high case fatality rate, and its associated societal impact constitute a uniquely challenging global health concern.

MenACWY-CRM (Menveo®; Novartis Vaccines and Diagnostics) is a polysaccharide–CRM_{197} conjugate vaccine directed against serogroups A, C, W-135, and Y.[6] In early phase studies, MenACWY-CRM was well tolerated and highly immunogenic in infants, a group at high risk for meningococcal disease.[7,8] Results from the US study groups of a large phase III MenACWY-CRM infant study illustrated robust immunogenicity and good tolerability.[9] This report describes results from the Latin American study groups of the same study, in which infants received MenACWY-CRM from 2 months of age. Specific objectives were to assess the safety and immunogenicity of three- and four-dose

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Table 1
Vaccinations and serum samples, per group, per time point

Cohort	Group	Procedure	Age (months)									
			2	4	6	7	12	13	15	16	17	18
Immunogenicity	LA1A	MenACWY-CRM	X		X		X					
		Routine vaccines	X	X	X		X					
		Serum sample	X			X	X	X				
	LA1B	MenACWY-CRM	X		X			X				
		Routine vaccines	X	X	X		X					
		Serum sample	X			X	X	X				
	LA2	MenACWY-CRM					X		X			
		Routine vaccines	X	X	X		X					
		Serum sample	X			X	X	X				
	LA3A	MenACWY-CRM	X	X	X					X		
		Routine vaccines	X	X	X					X		
		Serum sample	X			X				X	X	
	LA3B	MenACWY-CRM	X	X	X						X	
		Routine vaccines	X	X	X					X		
		Serum sample	X			X				X	X	
	LA4	MenACWY-CRM					X		X			
		Routine vaccines	X	X	X		X		X[a]			
		Serum sample	X			X	X			X		
Safety only	LA5	MenACWY-CRM	X	X	X		X					
		Routine vaccines	X	X	X		X					
	LA6A	MenACWY-CRM					X		X			
		Routine vaccines	X	X	X		X					
	LA6B	MenACWY-CRM						X	X			
		Routine vaccines	X	X	X		X					
	LA6C	MenACWY-CRM										X
		Routine vaccines	X	X	X		X					

DTaP, diphtheria, tetanus, and acellular pertussis; Hib, *Haemophilus influenzae* type b.
[a] MenACWY-CRM concomitant with DTaP and Hib.

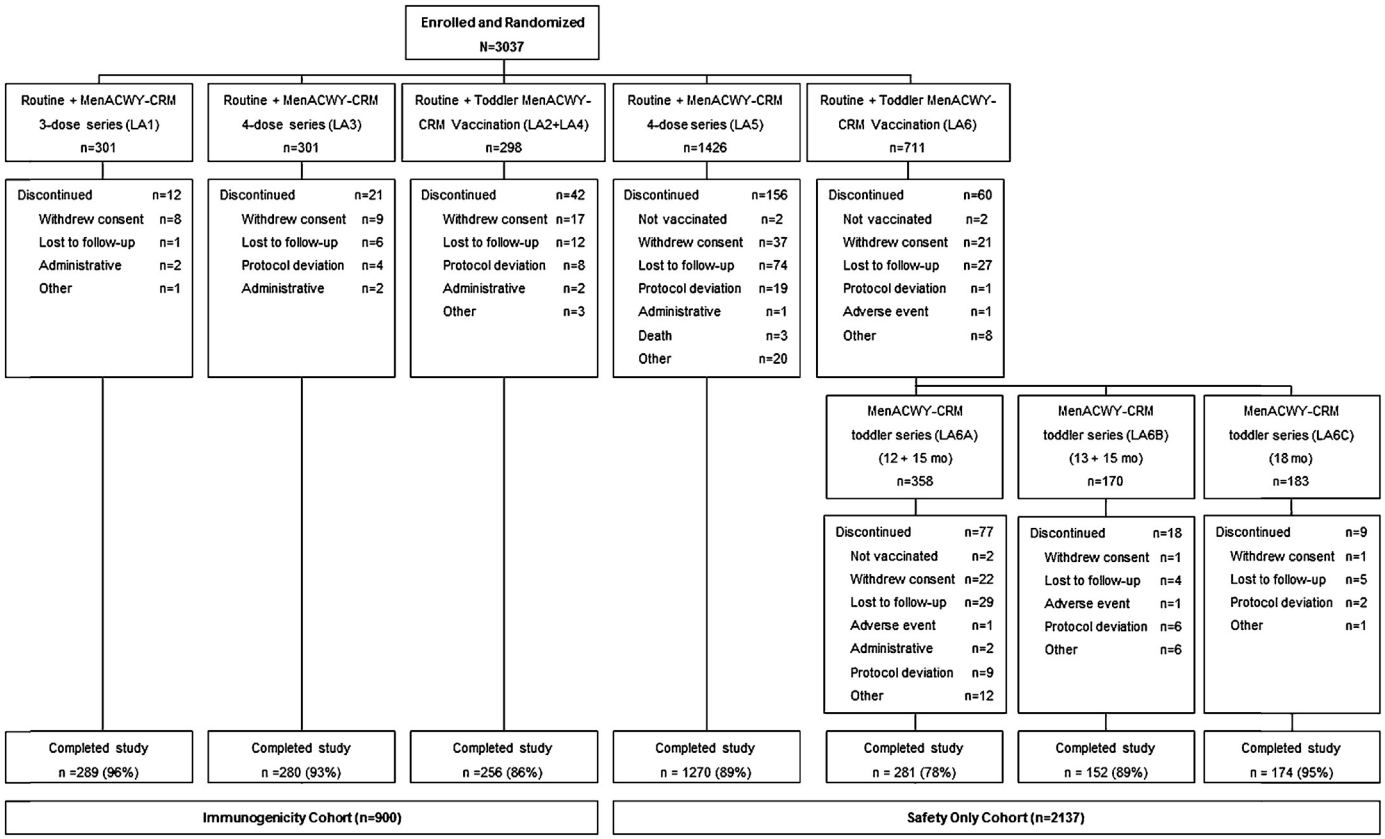

Figure 1. Subject disposition and vaccination schedule. The MenACWY-CRM three-dose series was given at 2, 6, and 12 or 13 months (LA1); the MenACWY-CRM four-dose series was given at 2, 4, 6, and 16 or 17 months (LA3) or at 2, 4, 6, and 12 months (LA5); routine vaccinations only were given before 12 months of age for LA6. Toddler series MenACWY-CRM doses were given at (12 or 13) + 15 months or at 18 months as indicated in the subgroups of LA6. All groups received routine infant vaccinations (DTaP, IPV, Hib, HBV, rotavirus, and PCV7) at months 2, 4, and 6. LA1, LA2, LA4, LA5, and LA6 received concomitant vaccines (MMRV, PCV7, and HAV) at month 12. LA3 received concomitant vaccines (DTaP and Hib) at month 16. (DTaP, diphtheria, tetanus, and acellular pertussis vaccine; HAV, hepatitis A vaccine; HBV, hepatitis B vaccine; Hib, *Haemophilus influenzae* type b vaccine; IPV, inactivated poliovirus vaccine; MMRV, measles, mumps, rubella, varicella vaccine; PCV7, pneumococcal conjugate vaccine; LA, Latin America.).