GRADE Table 01. Efficacy of a single-dose MenA conjugate vaccination in immunocompetent children (9 to 24 months of age) against serogroup A meningococcal disease

Population : Immunocompetent children aged 9–24 months
Intervention: Single-dose MenA conjugate vaccine (5 µg dosage)
Comparison: No MenA vaccination
Outcome : Serogroup A meningococcal disease

What is the scientific evidence concerning the efficacy of a single dose of MenA conjugate vaccine (versus no Men A vaccination) against serogroup A meningococcal disease in immunocompetent children aged 9–24 months?				
			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		2[1]/ RCT	4
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	None serious[2]	0
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**4**
Summary of Findings	**Statement on quality of evidence**			We are very confident that the true effect lies close to the estimated effect on health outcome.
	Conclusion			We are very confident that the administration of a single dose of MenA conjugate vaccine in children aged 9–24 months prevents serogroup A meningococcal disease.

[1] Two double blind, randomized, controlled clinical studies were conducted – a phase II dose ranging study (PsA-TT-004) in 1200 healthy infants and toddlers in Ghana and a phase III study (PsA-TT-007) in 1500 healthy infants and young children in Mali. Both studies examined various dosages and schedules of MenA conjugate vaccine co-administered with other vaccines routinely administered in this age range. The PsA-TT-004 study included a group of infants given a single MenAfriVac 10µg dose at 9 months of age. The antibody titres (GMTs) of this group at 28 days post-vaccination were lower than those of infants vaccinated in a 2-dose schedule of MenAfriVac 5µg at 14 weeks and 9 months of age, 2845.72 vs. 5048.63, respectively, but GMTs were similar at age 36 months. However, the GMT of controls was 3.25 at 28 days post-vaccination. The PsA-TT-007 included a group given one dose of MenAfriVac 10µg at 9 months of age and another group given one dose of MenAfriVac 5µg at 9 months of age. 97.2% of vaccinees who received MenAfriVac 5µg at 9 months of age seroconverted 28 days after vaccination. A 1-dose schedule with MenAfriVac 10µg or MenAfriVac 5µg was non-inferior to a 2-dose schedule of MenAfriVac 10µg when a seroconversion endpoint was used. One dose of MenAfriVac 5µg at 9 months was non-inferior to one dose of MenAfriVac 10µg at 9 months based on seroconversion after 7 months: 95.8% vs. 96.9%, respectively. Similar GMTs were observed in the two groups 7 months after one dose after adjusting for baseline titre, sex, and visit.

[2] In the two clinical trials, PsA-TT-004 and PsA-TT-007, immunogenicity was measured instead of clinical endpoints. As the efficacy of MenAfriVac is well-established, the evaluation of efficacy in these trials was based on non-inferiority to bactericidal antibody levels induced by MenAfriVac. Serum capsular bactericidal antibodies correlate to protection and can be considered a valid surrogate marker of protection. Therefore, it was decided not to downgrade.

Reference List

1. PsA-TT-004 In Meningitis Vaccine Project and Partners. *Results from the MenA conjugate vaccine (PsA-TT) randomized controlled trials in infants and young children: Executive summary.* Geneva, World Health Organization, 2014 (http://www.who.int/immunization/sage/meetings/2014/october/3_MenA_vaccine_trials_SAGE_01Oct2014.pdf?ua=1, accessed November 2014).
2. PsA-TT-007 In Meningitis Vaccine Project and Partners. *Results from the MenA conjugate vaccine (PsA-TT) randomized controlled trials in infants and young children: Executive summary.* Geneva, World Health Organization, 2014 (http://www.who.int/immunization/sage/meetings/2014/october/3_MenA_vaccine_trials_SAGE_01Oct2014.pdf?ua=1, accessed November 2014).
3. Data to be published: Meningitis Vaccine Project. Protocol No. PsA-TT-004. Final version 1- 30 October 2007-Amendment 1- 15 May 2008- Amendment 2- 23 September 2010.
4. Data to be published: Meningitis Vaccine Project. Protocol No. PsA-TT-007. Final version 1- 20 October 2011-Amendment 1-8 December 2011.