A Phase II/III Observer-blind, Randomized, Active Controlled Study to Compare the Safety and Immunogenicity of a Meningococcal A Conjugate Vaccine (MenAfriVac™) with Meningococcal ACWY Polysaccharide Vaccine in Healthy Indian Children 2-10 Years of Age

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Background

Meningococcal disease (Group A N. meningitidis) is endemic in India with large, country-wide recurrent outbreaks every 8 to 10 years. Epidemiologic evidence is scarce and limited to outbreak investigations and ad hoc surveillance. Control measures in India are limited to health education, chemoprophylaxis of contact cases, and the provision of multivalent polysaccharide vaccine to high risk groups during epidemics. [1, 2, 3, 4]

The Meningitis Vaccine Project aims to eliminate epidemic meningitis through development, testing and widespread use of meningococcal conjugate vaccines. Through Phase I & II trials, a single dose of a new PsA-TT conjugate vaccine manufactured by Serum Institute of India Ltd. (SIIL) has been shown to be safe and highly immunogenic in Indian adults and African children 1 to 2 years old. [5, 6, 7]

Objectives

To compare immunogenicity and safety of a single dose of PsA-TT vaccine with that of Men PsA component of a licensed ACWY meningococcal vaccine 28 days after vaccination.

Methods

Observer-blind, randomized controlled trial of 340 Indian children (2 to10 year-olds)

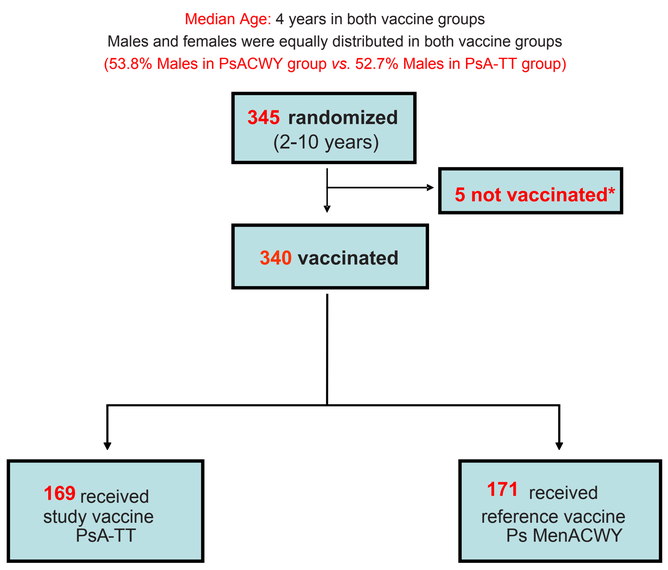
Test vaccine: PsA-TT— 0.5ml dose contains 10 mcg Ps, 10-33 mcg TT; AlPO4 adjuvant

Reference vaccine: GSK Mencevax ACWY® - 0.5 ml contains 50µg Ps A, C, W and Y

Immune response measured by Serum Bactericidal Antibody titers (rSBA) and anti-MenPsA specific IgG (ELISA).

Safety assessed through active daily follow-up for 4 days post-vaccination, and the recording of all AEs for 28 days and SAEs for the duration of the study.

Figure 1: Study profile at four weeks



* 3 excluded due to systolic murmur; 1 excluded due to febrile convulsions; 1 withdrawal of consent before vaccination

Table 1. Overall participant safety profile at 4 weeks post-vaccination

	PsA-TT vaccine (n = 169)			PsACWY vaccine (n = 171)		
	Number	%	(95%CI)	Number	%	(95%CI)
Type of Adverse Event						
Immediate Serious Reaction (within 30 minutes post-vaccination)	0	**0**	(0-2)	0	**0**	(0-2)
Local Reaction (within 4 days post-vaccination)	52	**31***	(24-38)	21	**12***	(8-18)
Systemic Reaction (within 4 days post-vaccination)	44	**26**	(20-33)	35	**21**	(15-27)
Adverse Event (within 28 days post-vaccination)	98	**58**	(50-66)	91	**53**	(45-61)
Serious Adverse Event (within 28 days post-vaccination)	1	**0.6**	(0-3)	0	**0**	(0-2)

* p = 0.00004, trend due to a higher incidence of tenderness reported in PsA-TT *vs.* PsACWY group. One subject reported two tenderness reactions on day 0 and day 2.
Rates of systemic reactions, AEs and SAEs were similar between vaccine groups. All AEs and SAEs were unrelated to the study vaccine.
No deaths were reported.

Table 2. Serogroup A Serum Bactericidal Antibody Titres (rSBA): ≥ 1:128 (percentage with 95% Confidence Interval) at baseline (pre-vaccination) and 28 days post-vaccination

Vaccine	PsA-TT vaccine (n = 169)								PsACWY vaccine (n = 171)							
Timing of Sample	Pre				Post				Pre				Post			
Age group (years)	N	n	%	(95%CI)	N	n	%	(95%CI)	N	n	%	(95%CI)	N	n	%	(95%CI)
2 to 10	169	104	**61.5**	(53.8-68.9)	168	168	**100**	(97.8-100)	171	111	**64.9**	(57.3-72)	170	170	**100**	(97.9-100)

N = total sample size n = number of subjects reaching the threshold

Figure 2. Pre vaccination MenA rSBA Titres: Reverse cumulative distribution curves

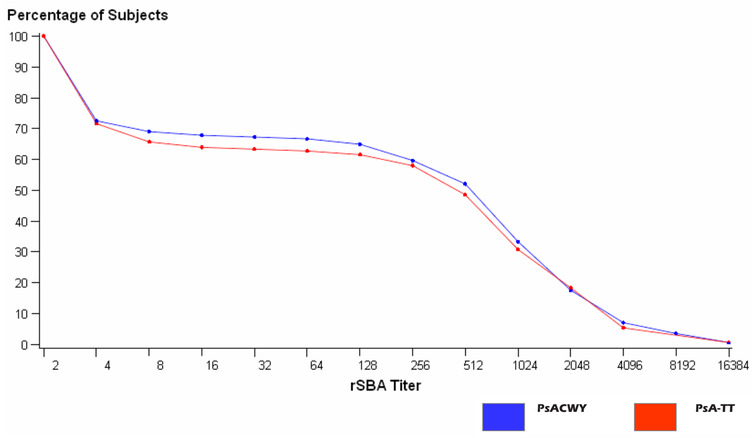


Figure 3. Day 28 Post-Vaccination MenA rSBA Titres: Reverse cumulative distribution curves

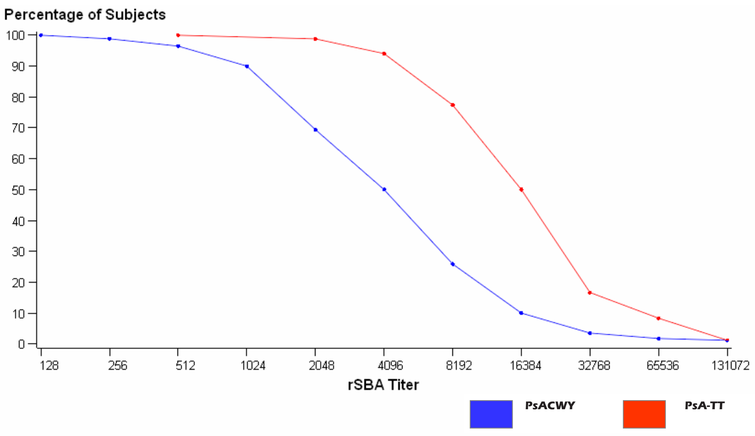


Figure 4. MenA rSBA Geometric Mean Titers (GMT) *Pre- and 28 days post-vaccination*

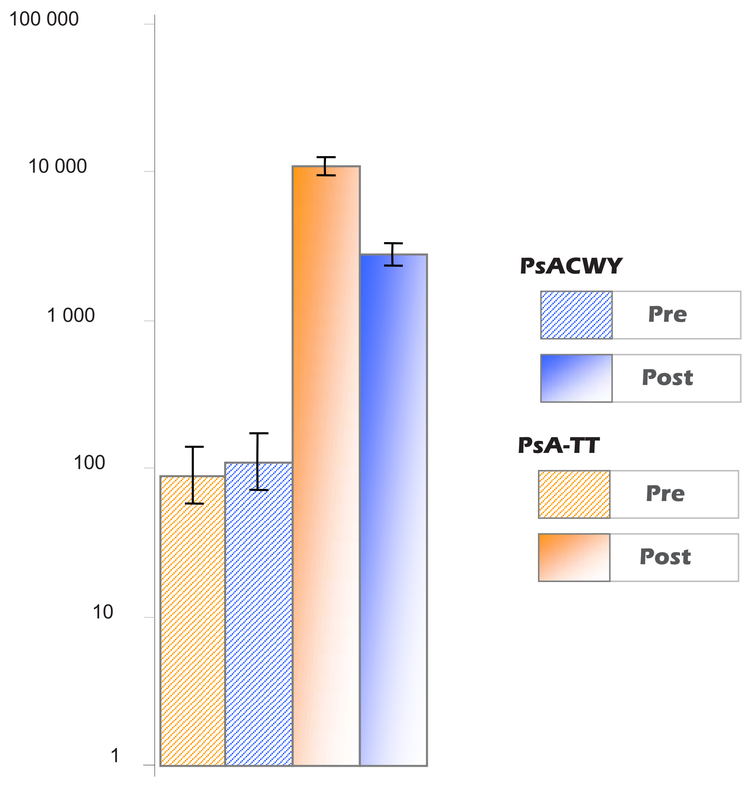
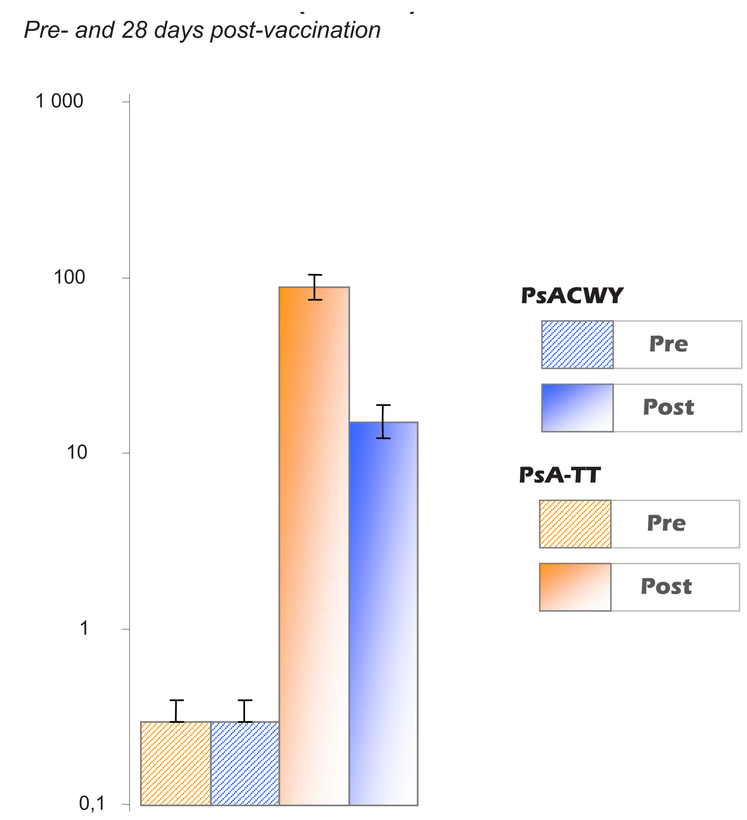


Figure 5. MenA IgG (ELISA) Geometric Mean Concentrations (GMC) *Pre- and 28 days post-vaccination*



Findings

Fourfold increase in rSBA titers are higher in the PsA-TT group (95.2% compared to 78.2% in the PsACWY group). This demonstrates non-inferiority of the PsA-TT vaccine to the PsACWY vaccine.

Significantly higher rSBA GMTs are observed in the PsA-TT group (11209 compared to 2838 in the PsACWY group). Similarly, anti-MenPsA IgG GMCs are significantly higher in the PsA-TT group (89.1 compared to 15.3 in the PsACWY group).

The percentage of subjects with a 4-fold increase in IgG ELISA is 100% in the PsA-TT group and 97.6% in the PsACWY group (at 28 days compared to baseline). The percentage of subjects with ≥ 2 µg/ml in IgG ELISA is 100% in the PsA-TT group and 91.2% in the PsACWY group (at 28 days).

The safety profile is similar in both groups except for tenderness (30% in the PsA-TT group compared to 12% in the PsACWY group).

Conclusions

The new PsA-TT conjugate vaccine is highly immunogenic and is as safe and well tolerated as a licensed and widely used Ps vaccine.

References

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