Safety and Immunogenicity of a New Meningococcal A Conjugate Vaccine (MenAfriVac™) in a Healthy African Population 2-29 Years of Age

Aldiouma Diallo,[1*#] * Samba Sow[2], Brown Okoko,[3*] Pascal Arduin,[1] Fadima Cheikh Haidara,[2] Milagritos Tapia,[2] Olubukola Idoko,[3] Richard Adegbola,[3] Marie-Pierre Preziosi,[4] Elisa Marchetti,[5] Julie Chaumont,[5] Kader Konde,[10] Helen Findlow,[6] Cheryl Elie,[7] Varsha Parulekar,[8] Brian Plikaytis,[7] Ray Borrow,[6] George Carlone,[7] Prasad Kulkarni,[9] Marc LaForce,[5] and Simonetta Viviani[5]

[#] Presenting author: diallo@ird.sn; * Co-Principal Investigators contributed equally to the research; [1] Institut de Recherche pour le Développement (IRD), Senegal; [2] Centre pour les Vaccins en Développement (CVD), Mali; [3] Medical Research Council Laboratories (MRC), The Gambia ; [4] Meningitis Vaccine Project, Initiative for Vaccine Research, WHO, Switzerland; [5] Meningitis Vaccine Project, PATH, Ferney-Voltaire, France; [6] Vaccine Evaluation Unit, Health Protection Agency, Manchester, UK; [7] Centers for Disease Control and Prevention, Atlanta, GA, USA; [8] iGATE Clinical Research Int., Mumbai, India; [9] Serum Institute of India Ltd, Pune, India; [10] Multi Disease Surveillance Centre, Ouagadougou, Burkina Faso

Background

The Meningitis Vaccine Project (MVP) was created in 2001, funded by a grant from the Bill and Melinda Gates Foundation, as a partnership between WHO and PATH to develop and introduce affordable meningococcal conjugate vaccines to eliminate meningococcal epidemics in sub-Saharan Africa (1,2).

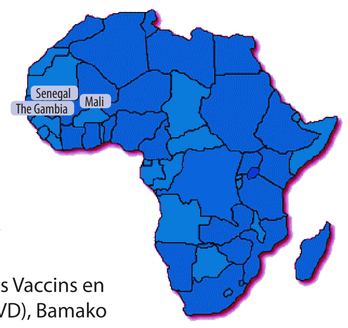
A new conjugate Meningococcal A vaccine (PsA-TT), manufactured by Serum Institute of India Ltd, Pune, India, has been shown to be safe and immunogenic in a clinical Phase I study in India.

A phase I study was completed in India (3) and a pivotal phase II study in African toddlers aged 12-23 months showed that a single dose of PsA-TT vaccine is able to prime immunological memory (4, 5).

Methods

PsA-TT vaccine is currently being tested in a phase II/III clinical study in an African population 2 to 29 years of age at three study sites located in the meningitis belt (6):

- Senegal, Institut de Recherche pour le Développement (IRD) Niakhar Field Station
- The Gambia, Medical Research Council Laboratories (MRC), Basse Field Station
- Mali, Centre pour les Vaccins en Développement (CVD), Bamako



The study was conducted according to ICH/GCP guidelines. Community approval of the study and individual consent were obtained according to country-specific legal requirements and customs. Subjects were randomized in a 2:1 ratio to receive a single injection of either:

- PsA-TT vaccine (MenAfriVac™ , produced by Serum Institute of India Ltd), one dose of 0.5 mL containing 10 µg meningococcal A polysaccharide conjugated to 10-20 µg Tetanus Toxoid, with Al[PO]4 as adjuvant or;
- Licensed meningococcal tetravalent polysaccharide vaccine (GSK Mencevax ACWY®), one dose of 0.5 mL containing 50 µg of each meningococcal polysaccharide ACWY.

Safety was assessed through active daily follow-up for four days following vaccination. All Adverse Events were collected up to four weeks after vaccination and Serious Adverse Events are collected for the entire study duration (one year).

Blood draws were performed just prior to vaccination (baseline), at four weeks, at six months, and one year after vaccination.

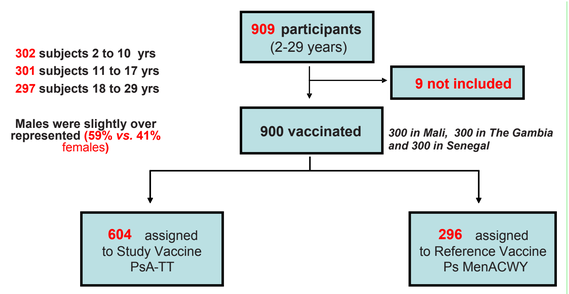
The immune response was evaluated before and four weeks after vaccination:

- Functional activity was measured by an SBA assay using baby rabbit complement and strain F8238, rSBA titers are expressed as the reciprocal of the final serum dilution giving ≥50% killing after 60 min.
- Serogroup A-specific IgG was measured by a standardized ELISA incorporating methylated human serum albumin.

Carriage: To evaluate nasopharyngeal carriage of *Neisseria meningitidis* over a period of one year (NP sample at each blood draw). Results of carriage are presented separately (7).

* **Results at four weeks are presented in this poster, the study is ongoing and data on persistence at six months and one year are currently being collected.**

Figure 1: Subjects study profile at four weeks



Safety Results

Local and systemic reactions were mild or moderate with similar frequency in the two vaccine groups and across the three sites and age groups:

- All local reactions were transient and resolved without sequelae within four days after vaccination. The most reported local reaction was tenderness, with a higher trend (not statistically significant) in the PsA-TT group vs. the PsACWY group. More local reactions were reported at the Senegal and Gambia sites.
- Headache was the most reported systemic reaction in the 11 to 29 year age group (11.2% vs. 10.7%). Fever was equally reported in the two vaccine groups (3% vs. 1.7%), all fevers were < 40 C°.
- More systemic reactions were reported at the Gambia site compared to the two other sites.

Similar rates of AEs were reported in the two study groups, at the three sites, and in the three age groups.

No deaths and no SAEs were reported in the first 28 days after vaccination.

Table 1: Local reactions at injection site at 4 days post-vaccination

		PsA-TT vaccine (N = 604)			PsACWY vaccine (N = 296)		
		n	%	(95%CI)	n	%	(95%CI)
Local reaction							
Tenderness	**All**	30	**5**	(3.4-7.0)	4	**1.4**	(0.4-3.4)
	Intensity 1	29	**4.8**	(3.2-6.8)	4	**1.4**	(0.4-3.4)
	2	1	**0.2**	(0.0-0.9)	0	**0**	(0.0-1.2)
	3	0	**0**	(0.0-0.6)	0	**0**	(0.0-1.2)
Induration	**All**	7	**1.2**	(0.5-2.4)	1	**0.3**	(0.0-1.9)
	Diameter ≤ 5 mm	1	**0.2**	(0.0-0.9)	0	**0**	(0.0-1.2)
	> 5 mm	5	**0.8**	(0.3-1.9)	1	**0.3**	(0.0-1.9)
	≥ 20 mm	1	**0.2**	(0.0-0.9)	0	**0**	(0.0-1.2)
	≥ 50 mm	0	**0**	(0.0-0.6)	0	**0**	(0.0-1.2)
At least one local reaction		34	**5.6**	(3.9-7.8)	5	**1.7**	(0.6-3.9)

Table 2: Systemic reactions at 4 days post-vaccination

	PsA-TT vaccine (N =604)			PsACWY vaccine (N =296)		
	n	%	(95%CI)	n	%	95%CI)
Systemic Reactions – ALL (2 to 29 year olds)						
Fever	18	3.0	(1.8-4.7)	5	1.7	(0.6-3.9)
Vomiting	8	1.3	(0.6-2.6)	5	1.7	(0.6-3.9)
Diarrhoea	6	1	(0.4-2.1)	2	0.7	(0.1-2.4)
At Least One Systemic Reaction	**18**	**3.0**	**(1.8-4.7)**	**5**	**1.7**	**(0.6-3.9)**
Systemic Reactions - 2 to10 year olds						
Lethargy	3	1.5	(0.3-4.3)	2	2	(0.2-7.1)
Irritability	0	0	(0.0-1.8)	1	1	(0.0-5.5)
Loss of Appetite	1	0.5	(0.0-2.7)	1	1	(0.0-5.5)
At Least One Systemic Reaction	**7**	**3.4**	**(1.4-7)**	**2**	**2**	**(0.2-7.1)**
Systemic Reactions - 11 to 29 year olds						
Headache	45	11.2	(8.3-14.7)	21	10.7	(6.7-15.8)
Fatigue	6	1.5	(0.6-3.2)	10	5.1	(2.5-9.1)
Myalgia	3	0.7	(0.2-2.2)	3	1.5	(0.3-4.4)
Arthralgia	2	0.5	(0.1-1.8)	3	1.5	(0.3-4.4)
At Least One Systemic Reaction	**11**	**2.7**	**(1.4-4.9)**	**3**	**1.5**	**(0.3-4.4)**

Table 3: Overall participants' safety profile four weeks after vaccination

	Mali Site						Senegal Site						The Gambia Site					
	PsA-TT vaccine (N=201)			PsACWY vaccine (N=99)			PsA-TT vaccine (N=202)			PsACWY vaccine (N=98)			PsA-TT vaccine (N=201)			PsACWY vaccine (N=99)		
	n	%	(95%CI)	n	%	(95%CI)	n	%	(95% CI)	n	%	(95%CI)	n	%	(95% CI)	n	%	(95%CI)
Type of Adverse Event																		
Local Reaction (within 4 days post vaccination)	1	**0.5**	(0-2.7)	1	**1.0**	(0-5.5)	17	**8.4**	(5.0 - 13.1)	3	**3.1**	(0.6-8.7)	16	**8.0**	(4.6-12.6)	1	**1.0**	(0.0-5.5)
Systemic Reaction (within 4 days post vaccination)	0	**0**	(0-1.8)	0	**0**	(0-3.7)	13	**6.4**	(3.5 - 10.8)	3	**3.1**	(0.6-8.7)	5	**2.5**	(0.8-5.7)	2	**2.0**	(0.2-7.1)
Adverse Event (within 28 days post vaccination)Δ	14	**7**	(3.9-11.4)	7	**7.1**	(2.9-14)	16	**7.9**	(4.6 12.5)	8	**8.2**	(3.6-15.5)	26	**12.9**	(8.6-18.4)	13	**13.1**	(7.2-21.4)

Results: Immune response as measured by rSBA

MenA rSBA ≥ 4-fold rises from pre- to post-vaccination in the PsA-TT group are significantly higher than in the PsACWY group in all age groups.

MenA rSBA GMT post-vaccination in the PsA-TT group are significantly higher than in the PsACWY group in all age groups.

The proportion of subjects with MenA rSBA ≥ 1:128 at baseline and after vaccination was similar in both the PsA-TT and the PsACWY group.

Figure 2: MenA Serum rSBA ≥ 4-fold rise by age group at 28 days post-vaccination

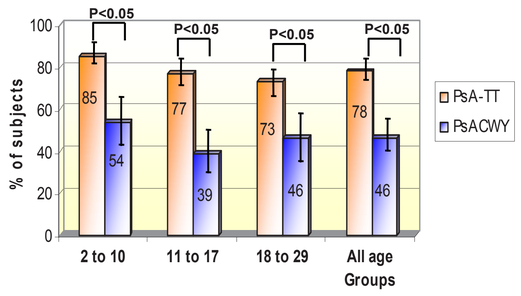
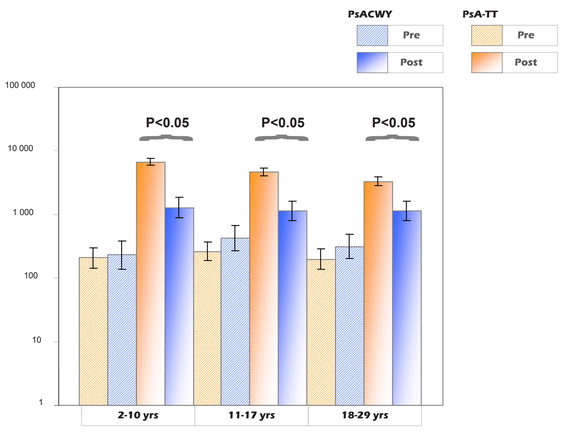


Figure 3: MenA Serum rSBA GMTs by age group Pre-vaccination and 28 days post-vaccination



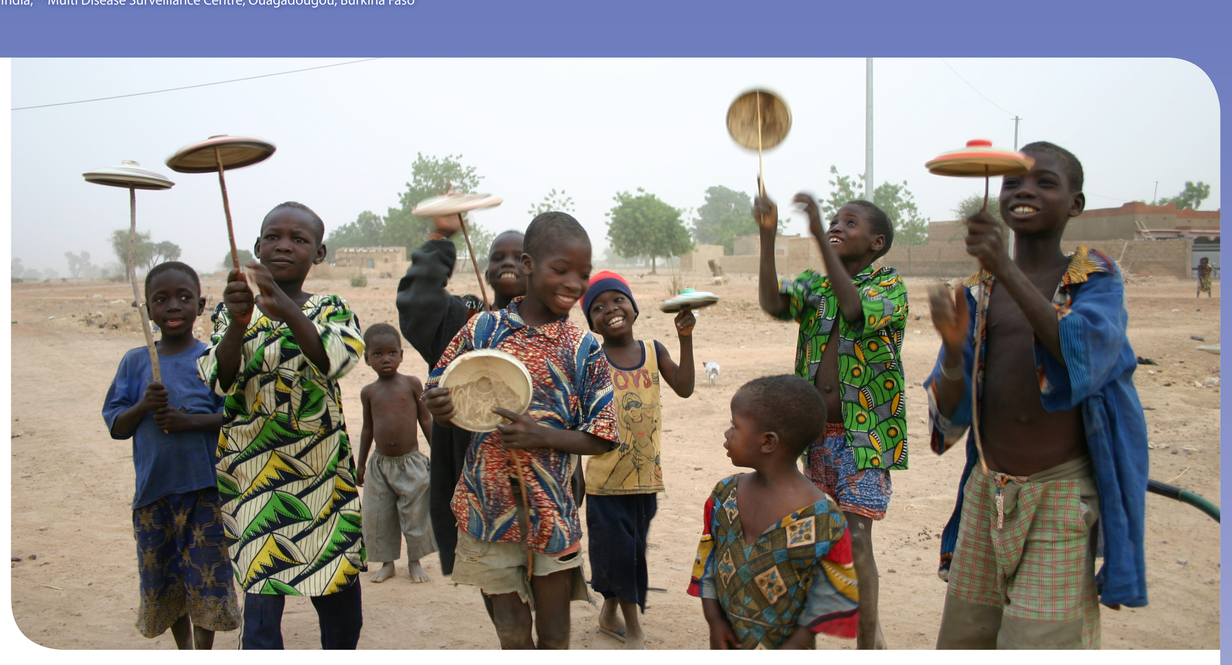
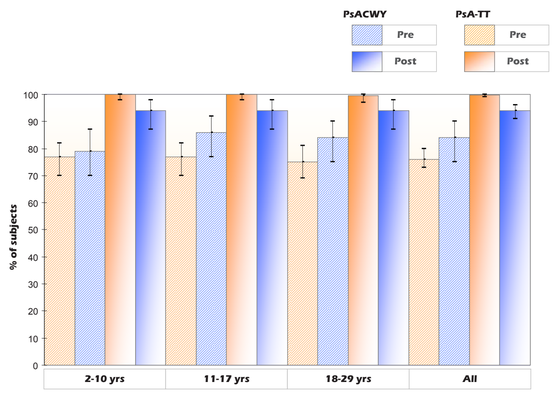


Figure 4: MenA Serum rSBA Titers ≥ 1:128 by age group Pre-vaccination and 28 days post-vaccination



Results: Immune response as measured by ELISA

Group A specific IgG ≥ 4-fold rises pre- to post-vaccination in the PsA-TT group were significantly higher than in the PsACWY group in all age groups.

Post-vaccination, Group A-specific IgG GMCs were significantly higher in PsA-TT than in PsACWY recipients in all age groups.

Post-vaccination, the percentage of subjects with MenA IgG ELISA concentrations ≥ 2 µg/mL is significantly higher in the PsA-TT than in the PsACWY group- 100% (CI 99-100) vs. 88% (CI 84-92).

Baseline titers increased with age in the three sites.

Figure 5: MenA Serum IgG ≥ 4-fold rise by age group 28 days post-vaccination

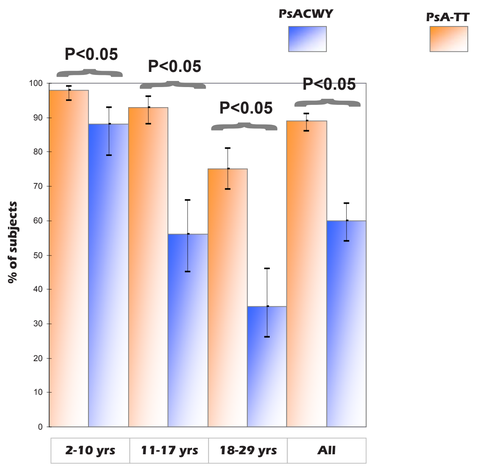


Figure 6: MenA Serum IgG GMCs by age group Pre-vaccination and 28 days post-vaccination

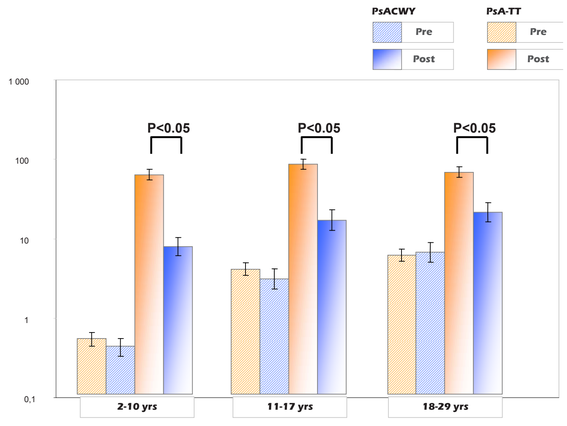
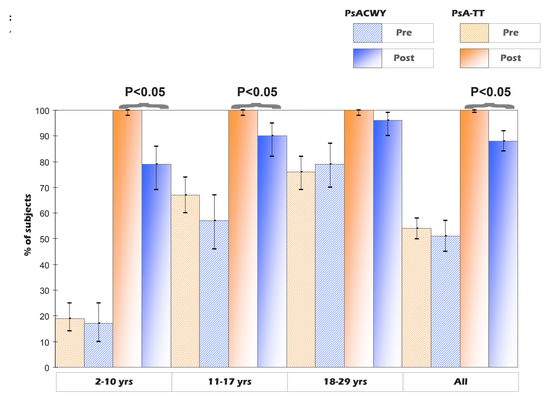


Figure 7: MenA Serum IgG ≥ 2 µg/mL by age group Pre-vaccination and 28 days post-vaccination



Conclusions

The new meningococcal A conjugate vaccine (PsA-TT) was as safe as a licensed tetravalent polysaccharide vaccine in 2 to 29 year-old subjects residing in countries of the African meningitis belt.

Four weeks after vaccination, the PsA-TT vaccine consistently induced higher immune responses with respect to the MenA component of the licensed tetravalent polysaccharide vaccine, as measured by rSBA and IgG ELISA.

Baseline MenA antibody titres were high with both rSBA and ELISA, with an age trend observed only with IgG ELISA.

These findings confirm the higher immunogenicity profile of MenAfriVac™ as compared to the MenA component of a licensed Ps vaccine previously demonstrated in clinical phase I (India) and phase II (Mali & the Gambia) (3-5).

These results further support the large scale introduction of MenAfriVac™ in the 2 to 29 year-old population of the African meningitis belt to eliminate epidemic meningitis.

Acknowledgements

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