A Phase II, Randomized Study to Evaluate the Safety and Immunogenicity of a New Meningococcal Group A Conjugate Vaccine in Healthy African Toddlers Residing in the Meningitis Belt: A Preliminary report

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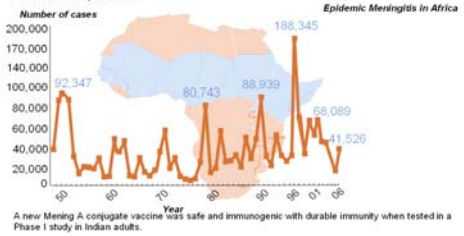
Background

- Recurrent severe epidemics of meningococcal disease strike the meningitis belt extending from Senegal to Ethiopia where annual incidences can reach 1/100. A vaccine that is induces long-lasting protection and herd immunity is needed.



- A new Mening A conjugate vaccine was safe and immunogenic with durable immunity when tested in a Phase I study in Indian adults.

OBJECTIVES

Primary Objective

To compare the immunogenicity of a single dose of the PsA-TT vaccine with that of the Men A component of the PsACYW vaccine at 28 days after vaccination.

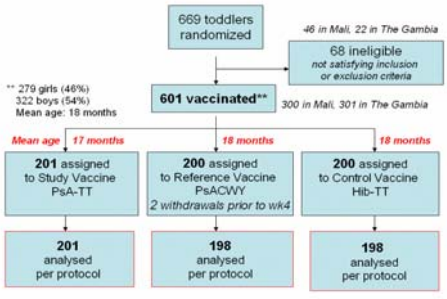
Secondary Objective

To evaluate the safety of a single dose of the PsA-TT vaccine during 4 weeks post immunization, with comparison to a reference vaccine (ACYW135) and a control (PRP-TT conjugate vaccine (Hib).

Methods

- Phase II, observer blind, randomized study of a new meningococcal group A conjugate vaccine (PsA-TT)
- Test Vaccine: One dose of 0.5ml contains 10 ug ps, 10-20 ug TT, adjuvant, ALPO4,
- Reference: mening polysaccharide ACYW135
- Control: Hib vaccine
- Study was conducted according to GCP and regulatory guidelines
- Single IM injection of 1 of the 2 vaccines was administered to a total of 601 healthy African children 12-23 months of age ( )
- Blood samples were collected pre- and 4 weeks post vaccination
- Safety was assessed using well established criteria
- Functional activity measured by the SBA assay using complement preserved baby rabbit serum. SBA titres are expressed as the reciprocal of the final serum dilution giving => 50% killing after 60 mins.
- Serogroup A-specific IgG measured by standardized ELISA
- The Consideration of antitetanus IgG antibodies was determined by standardized ELISA.

Study Profile for Week 4 Analysis



Overall Participant Safety Profile at 4 weeks Post-Immunization

Type of Adverse Events	PsA-TT n/N	%	PsACWY n/N	%	Hib-TT n/N	%
Immediate Reactions (within 2 hours post-immunization)	0/201	0	0/200	0	0/200	0
Local Reactions (within 4 days post-immunization)	27/201	13	10/200	5*	19/200	10
Systemic Reactions (within 4 days post-immunization)	35/201	17	31/200	16	31/200	16
Adverse Events (within 28 days post-immunization)	77/201	38	66/200	33	59/200	30
Serious Adverse Events** (up to 194 days = 7 months post-immunization)	1/201	0.5	3/200	1.5	0/200	0.5

* Fig 1

P = 0.005 (more indurations reported in PsA-TT vs PSACYW group in site 1-Mali)
** All SAEs were unrelated to the study vaccines*

Systemic Reactions at 4 days Post-Immunization

Systemic Reactions	PsA-TT n/201	%	PsACWY n/200	%	Hib-TT n/200	%
Fever	10	5	6	3	6	3
Lethargy	8	4	7	4	4	2
Irritability	5	3	5	3	3	2
Vomiting	3	2	7	4	4	2
Diarrhoea	20	10	21	11	20	10
Loss of Appetite	7	4	12	6	4	2
At least one Reaction	35	17	31	16	31	16

Fig. 2

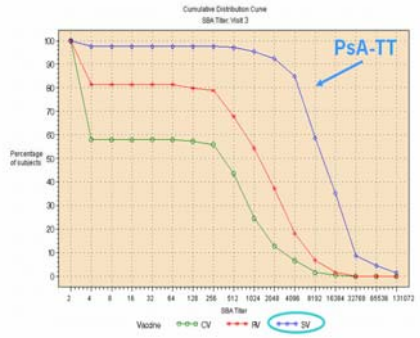
Immunogenicity

- **SBA:** rSBA GMT 28 days post vaccination, % of subjects with 4-fold rises pre to post-vaccination for PsA-TT group were higher the RV group (see fig 3,4).
- In the ITT analysis rSBA GMT post vaccination and antibody rises were higher for study vaccine group than RV (figs 5)
- Similar finding was observed in site-specific ITT analysis
- ELISA: The serogroup A-specific IgG GMCs were higher for PsA-TT than ACYW135 group (group 7)

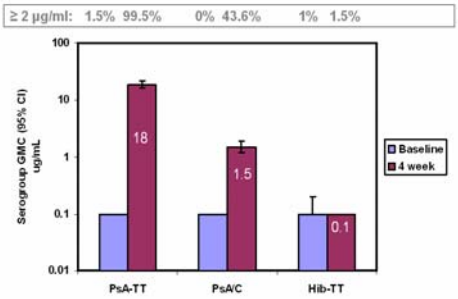
≥ 4-fold rise in serogroup A rSBA titre from week 0 to 4

Vaccine	N	4-Fold Responders N	%	[95% Confidence Limit]
PsA-TT	201	190	96	[92; 98]
PsACWY	200	123	64	[57; 71]
Hib-TT	200	69	36	[29; 43]

Week 4 Men A rSBA Titres
Reverse Cumulative Distribution Curves



Serogroup A-specific IgG Geometric Mean Concentrations (µg/mL)

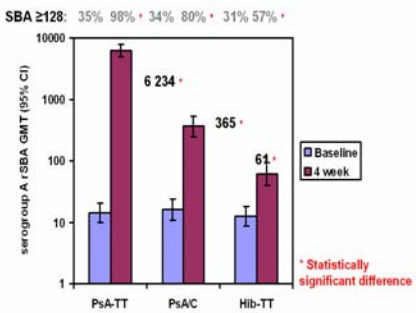


Results

Safety

- Solicited Local reactions were mild and transient in all the three vaccines.
- The most reported reactions were tenderness and indurations.
- There were more indurations reported in the study vaccine group than in the reference vaccine (RV) at Mali site. They were mostly mild.
- The number of subjects with at least one solicited systemic reaction was similar in all the group (see figure 1). Reactions were also mild.
- The number of subjects who reported at least one unsolicited reactions were the same in all the vaccine groups.
- Four cases of serious adverse events reported up to 7 months post immunisation were unrelated to vaccination. Three of these were in RV group.

Men A rSBA GMTs and percentage of subjects with SBA ≥128 4 Weeks after Vaccination



Conclusions

- In African toddlers the PsA-TT vaccine induced 20-fold higher bactericidal antibodies than the current licensed tetravalent polysaccharide vaccine
- No safety issues to date
- This is a huge step towards the development and widespread use of an affordable Men A conjugate vaccine for Sub-Saharan Africa