

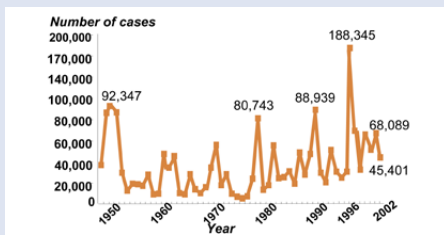
A PHASE I, DOUBLE BLIND, RANDOMIZED STUDY TO EVALUATE A NEW MENINGOCOCCAL GROUP A CONJUGATE VACCINE IN HEALTHY INDIAN ADULTS

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Background

The annual incidence of disease during meningococcal group A epidemics in sub-Saharan Africa can exceed 1000 per 100,000 population:



A vaccine that confers durable protective immunity after 1 dose, induces herd immunity and is affordable for widespread use in Africa is required. <http://www.meningvax.org/jillo-meningbelt-cycle.htm>

Primary objective

- To evaluate safety of a single injection of a new meningococcal group A conjugate vaccine (PsA-TT) during 4 weeks post-vaccination, with comparison to a reference vaccine (Ps/A/C) and to a control vaccine (TT).

Secondary objectives

- To assess the week 4 immune responses in terms of serum bactericidal antibody (SBA) activity and serogroup A IgG responses.
- To determine the persistence of responses at weeks 24 and 48 (antibody persistence testing is ongoing).

Methods

- Phase I, double blind, randomized study of a new meningococcal group A conjugate vaccine (PsA-TT).
- Test vaccine: One dose of 0.5 mL contains 10 µg Ps, 10-20 µg TT, and adjuvant, AIPO₄.
- Reference vaccine: meningococcal polysaccharide A+C vaccine (Ps/A/C)
- Control vaccine: Tetanus Toxoid-adsorbed vaccine (TT).
- Single intramuscular injection of 1 of the 3 vaccines was administered to a total of 74 healthy Indian adults ranging from 18 to 35 years of age (PsA-TT n = 24, Ps/A/C n = 25, TT n = 25).
- Blood samples were collected pre- and 4 weeks post-vaccination.
- Safety was assessed using well established criteria and metrics.
- Functional activity measured by the SBA assay using complement preserved baby rabbit serum and strain F8238. SBA titers are expressed as the reciprocal of the final serum dilution giving ≥ 50% killing after 60 min.
- Serogroup A-specific IgG measured by standardised ELISA incorporating methylated human serum albumin. The calibration factor of the standard CDC1992 serum for serogroup A was 91.8 µg/mL.

- The concentration of anti-tetanus IgG antibodies was determined by standardised ELISA relative to the 1st International Tetanus reference serum (26/488).

Results

Safety

- In the three vaccine groups local solicited reactions were similar, mild and transient.
- The most reported local solicited reactions were pain, redness and swelling (Figure 1).
- All local solicited reactions resolved within two days.
- Systemic solicited reactions were also mild, transient and resolved without sequelae (Figure 2) and all resolved within 3 days from onset.
- The number of subjects with at least one solicited reaction was similar among the recipients of the three vaccine groups: PsA-TT 75%, Ps/A/C 68% and TT 76%.
- The number of subjects who reported at least one non-solicited reaction was similar in the three vaccine groups: PsA-TT 38%, Ps/A/C 32% and TT 40%.
- All non-solicited reactions were unrelated to vaccination.
- No serious adverse events were reported.

Figure 1. Overview of local solicited adverse events (AEs) 7 days post-vaccination

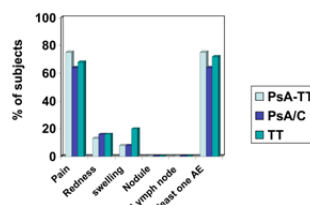
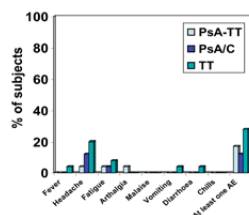


Figure 2. Overview of systemic solicited adverse events (AEs) 7 days post-vaccination



Immunogenicity

- SBA: rSBA GMT post-vaccination and ≥ 4 fold rises pre to post-vaccination for the PsA-TT group were the same or higher (not statistically significant) than the Ps/A/C group. Both the PsA-TT and Ps/A/C groups had significantly higher rSBA GMTs post-vaccination than the TT group. (Figures 3, 4; Table 1).
- ELISA: Serogroup A-specific IgG GMCs were higher for PsA-TT than Ps/A/C (P < 0.05) whilst both were higher than the TT controls (Figure 5).
- Post-vaccination, the % of subjects with tetanus toxoid (TT) ELISA concentrations ≥ 0.1 IU/mL was 96% for PsA-TT and 100%

for both PsA/C and TT. The TT GMC was significantly higher for PsA-TT and TT than PsA/C post-vaccination (Figure 6).

Figure 3. Serogroup A rSBA GMTs before and 4 weeks post-immunisation

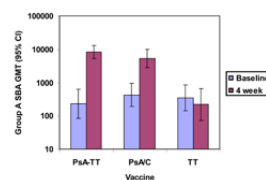


Table 1. Four-fold or greater rise in rSBA antibody titre baseline to week 4

Vaccine	N	≥ 4-Fold rises	
		N	% [95% CIs]
PsA-TT	24	20	83 [63; 95]
Ps/A/C	25	18	72 [51; 88]
TT	25	3	12 [3; 31]

Figure 4. Percentage of subjects with rSBA titres of < 8, 8 to 64 or ≥ 128 for baseline and 4 weeks following vaccination with PsA-TT, Ps/A/C or TT

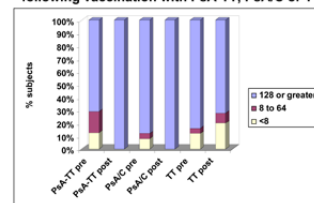


Figure 5. Serogroup A-specific IgG GMCs before and 4 weeks post-immunisation

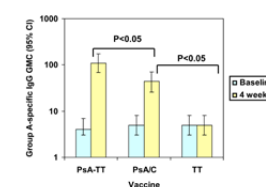
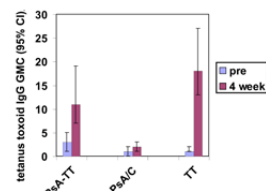


Figure 6. Tetanus toxoid IgG GMCs before and 4 weeks post-immunisation



Conclusions

- The group A conjugate vaccine, PsA-TT, was safe and immunogenic in Indian adults.
 - PsA-TT induced higher SBA and ELISA antibody levels than the licensed Ps/A/C polysaccharide vaccine, with statistically significant differences between the serogroup A-specific GMCs.
 - PsA-TT boosts tetanus responses.
- Progression to phase II studies has commenced.