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 Menigitis Belt: A Preliminary report


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OBJECTIVES

Primary Objective
To compare the immunogenicity of a single dose of the PA-TT vaccine with that of the Men A component of the PA-CWY vaccine at 30 days after vaccination.

Secondary Objective
To evaluate the safety of a single dose of the PA-TT vaccine after 4 weeks post-vaccination with comparison to a reference vaccine (ACWY135) and a control (PA/TW conjugate vaccine) (MS).

Methods

- Phase I, observer blind, randomized study of a new meningococcal group A conjugate vaccine (PA-TT).
- Test Vaccine: One dose of 0.5 ml contains 10 mg of PA-TT, 10 mg of tetanus, and 50 mg of aluminum phosphate.
- Reference: meningococcal polysaccharide vaccine (ACWY-135) and control (PA/TW conjugate vaccine).
- Study design: 2 arms: 1) control, 2) test vaccine.
- Study was conducted according to GCP and regulatory guidelines.
- Single-dose injection of the test vaccine 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 was assessed using complement-dependent assays.
- The term "specific" immunity was determined by standard ELISA.
- The concentration of anti-Meningococcal IgG antibodies was determined by standard ELISA.

Study Profile for Week 4 Analysis

- 805 children randomized
- 600 vaccinated
- 205 assigned to Study Vaccine (PA-TT)
- 200 assigned to Control Vaccine (ACWY-135)
- 480 vaccinated
- 395 in MI, 21% in The Gambia
- 279 in MI, 52% in The Gambia
- 245 in MI, 40% in The Gambia
- 201 in MI, 20% in The Gambia
- 201 assigned to Study Vaccine (PA-TT)
- 200 assigned to Control Vaccine (ACWY-135)
- 201 assigned to Study Vaccine (PA-TT)
- 200 assigned to Control Vaccine (ACWY-135)
- 201 assigned to Study Vaccine (PA-TT)
- 200 assigned to Control Vaccine (ACWY-135)

Immunogenicity

- SBA: IgA GMT 28 days post vaccination, % of subjects with 4-fold rises pre to post-vaccination in PA-TT group were higher than the RV group (see fig 3.4).
- In the ITT analysis, SBA 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 PA-TT than ACWY-135 group (group 7).

Results

Safety

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

Conclusions

- In African toddlers the PA-TT vaccine induced 20-fold higher bactericidal antibodies than the currently 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.