

# Safety and immunogenicity of a parenteral trivalent P2-VP8 subunit rotavirus vaccine

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## Background and aims

A P[8] monovalent parenteral subunit rotavirus vaccine (P2-VP8-P[8]) was well-tolerated and immunogenic, but elicited limited responses against heterotypic rotavirus strains. We expanded valency to include the three most common P types and evaluated safety and immunogenicity of this trivalent formulation (P2-VP8-P[4],[6],[8]) in South African adults, toddlers and infants.

## Methods

A multi-site, double-blind, randomised, placebo-controlled trial was conducted from February 2016–December 2017. Two dose-levels were assessed in healthy adults and toddlers; thereafter three dose-levels were assessed in term infants  $\geq 6$  and  $< 8$  weeks (three injections four weeks apart). Primary safety endpoints included local and systemic reactions within seven days and adverse events within 28 days after each injection. Primary immunogenicity endpoints, among infants receiving all study injections per protocol, compared serum anti-P2-VP8 IgA and IgG, and neutralising antibody responses in sera four weeks after the final injection, in each vaccine group to placebo. Rotarix<sup>®</sup> was administered after completion of study vaccinations, and its faecal shedding was assessed by ELISA in a subset of infants.

## Results

Thirty adults, 30 toddlers and 557 infants were assessed for safety, with no significant differences observed between vaccine/placebo groups in the proportions with local reactions, systemic reactions or adverse events. The proportions of infants with anti-P2-VP8 IgG seroresponses to all three antigens (P[4], P[6] and P[8]) were significantly higher in the 15 $\mu$ g, 30 $\mu$ g and 90 $\mu$ g groups (99, 99 and 100%, respectively) compared to placebo (9%;  $p < 0.0001$ ). Although significantly higher than in placebo recipients, the proportions of infants with anti-P2-VP8 IgA seroresponses to each individual antigen were modest (20–34%) across all three active dose groups. The proportions of infants with neutralising antibody seroresponses to rotaviruses representing all three types (P[4], P[6] and P[8]) in the vaccine were 8, 50, 61 and 62%, respectively, in the placebo, 15 $\mu$ g, 30 $\mu$ g and 90 $\mu$ g groups: significantly higher than placebo recipients ( $p < 0.0001$ ). There was a 41% reduction in PCR-confirmed Rotarix shedding in the 90 $\mu$ g group compared to placebo (95% CI: 0.1–65,  $p = 0.0346$ ).

## Conclusion

The trivalent P2-VP8 vaccine was well-tolerated, with promising anti-P2-VP8 IgG and neutralising antibody responses across the three vaccine P-types.