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Safety and immunogenicity of a synthetic carbohydrate-based conjugate vaccine against bacillary dysentery assessed in a phase-I study in healthy adult volunteers

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Glycoconjugates incorporating detoxified LPS from *Shigella flexneri* 2a or *Shigella sonnei*, the two main strains responsible for the endemic form of bacillary dysentery, have been shown to be safe and immunogenic in healthy volunteers. Phase III trials have demonstrated the protective capacity of a *S. sonnei* detoxified LPS-conjugate against *S. sonnei* infection in young adults and children older than 2 years of age. The search for a highly immunogenic *S. flexneri* 2a vaccine, able to generate protective immunity in children below 2 years of age and to get rid of the issues related to LPS detoxification, we have rationally designed SF2a-TT15, a tetanus toxoid (TT) conjugate encompassing a synthetic pentadecasaccharide hapten corresponding to three repeating units of the LPS O-antigen from *S. flexneri* 2a. In preclinical studies, SF2a-TT15 has been shown to induce anti-LPS bactericidal antibodies. We will detail the results of a first-in-human, single-blinded, observer-masked randomized, dose escalation (2 different doses of the sugar component), placebo-controlled study in healthy Israeli volunteers. In summary, the vaccine candidate is safe and its immunogenicity is very promising. These findings support further evaluation for safety, immunogenicity and protective efficacy in additional settings. The results will be put in the global context of the current development of *Shigella* subunit vaccines.

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