

A Randomized, Observer-Blinded, Phase I study to Assess the Safety and Immunogenicity of Vi-DT Conjugate Vaccine compared to Vi-Polysaccharide (Typhim Vi®, Sanofi Pasteur) Typhoid Vaccine in Healthy Filipino Adults and Children.

**Authors:** Samuel Teshome<sup>1</sup>, Mario Rosario Capeding<sup>2</sup>, Yang Hee Kim<sup>1</sup>, Jiwook Park<sup>1</sup>, Ju Yeon Park<sup>1</sup>, Deok Ryun Kim<sup>1</sup>, Yun Chon<sup>1</sup>, Sue Kyoung Jo<sup>1</sup>, JaeSeung Yang<sup>1</sup>, Sushant Sahastrabuddhe<sup>1</sup>, Jean-Louis Excler<sup>1</sup>

*<sup>1</sup>International Vaccine Institute, Seoul, South Korea <sup>2</sup>Research Institute of Tropical Medicine, Manila, the Philippines*

**Background:** Vaccination with Vi- polysaccharide vaccine has been shown to protect individuals from typhoid fever but their use is hampered by several limitations: T-cell independent immune response mechanism with no development of immune memory; less effective and immunogenic in children <2 years of age; no boosting effect following vaccination and shorter duration of protection requiring revaccination every 3 years. With the initial know-how from US NIH, IVI developed a new typhoid conjugate vaccine (Vi-DT), Vi- polysaccharide conjugated to diphtheria toxoid (DT). The technology was transferred to SK Chemicals, Republic of Korea, in August 2013.

**Methods:** This is a Phase I randomized, observer-blinded study to assess the safety and immunogenicity of Vi-DT conjugate vaccine compared to Vi-Polysaccharide vaccine. Healthy male and female participants aged 2-45 years were enrolled stratified into 18-45, 6-17, and 2-5 years age de-escalation study. The study was conducted at the Research Institute for Tropical Medicine (RITM), Manila, The Philippines. A total of 144 participants were randomized between Test (Vi-DT) and Comparator (VI Polysaccharide) vaccines administered at 0 and 4 weeks. Since the comparator vaccine is administered as a single dose, the second dose administered was a flu vaccine to keep the blinding. The Primary objective is to evaluate the safety of 25 µg of Vi-DT typhoid conjugate vaccine, while the secondary objectives are to assess the immunogenicity of 25 µg of Vi-DT typhoid conjugate vaccine and to compare the safety and immunogenicity of Vi-DT with Vi- Polysaccharide typhoid vaccine.

**Results:** 48 participants in each age cohort for a total of 144 participants were randomized and enrolled to Vi-DT vs Typhim-Vi + Vaxigrip (comparator) group. Blinded safety data was generated for each cohort and submitted for review and approval to safety monitoring committee and institutional review boards. Approval by the safety monitoring committee and institutional review boards was required for age de-escalation enrollment. No severe adverse event was reported. The vaccines were safe and generally well tolerated with mild to moderate solicited adverse events. The immunogenicity results will be presented.

**Conclusions:** The Vi-DT vaccine deserves further evaluation in humans in particular in younger children less than 2 years of age. This typhoid vaccine will be an important addition to existing typhoid fever control and prevention methods.

(Funded by Bill and Melinda Gates Foundation)