Validation of a live attenuated rotavirus vaccine as a human infection challenge model in Zambia

Roma Chilengi, Masuzyo Chirwa, Nsofwa Sukwa, Natasha Laban, Caroline Chisenga, Michelo Simuyandi, Nicholas Grassly and Samuel Bosomprah.

Background

Human Infection Challenge (HIC) models offer an opportunity to study pathogenesis and vaccine immunogenicity mechanisms and, have historically been employed to accelerate vaccine development, particularly in human-restricted pathogens. While HIC models can be controversial especially in the context of LMIC, there are scientific and ethical merits of considering the unique opportunity this methodology offers.

We proposed to explore us of Rotarix™, a live attenuated monovalent vaccine routinely administered to Zambian children, as a challenge agent for evaluating candidate rotavirus vaccines.

Methods

A cohort of 22 health Zambian infants has been recruited, baseline examination and sampling done prior to administration of the first dose of RV at 6 weeks of age. The second dose of RV was administered four weeks later accordingly to routine schedule but considered as challenge dose. Saliva, stool and serum was collected on days 0,1,3 and 7 following each RV dose and exited from the cohort at 14 weeks age following examination and collection of a serum sample for testing vaccine seroconversion (computed as a four-fold increase from baseline). Vaccine shedding will be determined by Rotarix specific NSP2 PCR, ELISA will be used to assess rotavirus specific IgA and IgG in both serum and saliva. We will then explore correlations between the various potential immune surrogate markers and faecal shedding for the second vaccine dose.

Results

The study is still ongoing, but we expect to generate the following results before June 2019:

(i)Baseline clinical and socio-demographic characteristics of the cohort including any evidence of pre-vaccination titres of rotavirus specific IgA and IgG; (ii) Concordance between antibody responses induced by the vaccine in serum and levels in oral secretions following immunization; and (iii)relationship between faecal shedding of vaccine strain in stool and antibody levels in serum and oral secretions at the time of vaccination and post-vaccination.

Conclusion

If validated, our challenge model will be a powerful tool for supporting vaccine efficacy evaluation as well as evaluation of potential corelates of protection. Such a model will help generate accurate estimates of vaccine efficacy data from target population contexts.