Background

- In HVTN104, 84 HIV-uninfected adults received multiple-dose VRC01 weekly at 10 mg/kg, or placebo.
- VRC01 binds to the HIV-1 envelope glycoprotein gp120 via its bnAb domain.
- VRC01 blocks HIV-1 attachment to CD4+ T cells by binding to the CD4 binding site on HIV-1 gp120.
- In HVTN104, VRC01 serum concentrations were measured by an Enzyme-linked immunosorbent assay (ELISA) using an-anti-VRC01 antibody.
- The absolute bioavailability (F1) was estimated for SC administration relative to IV administration.
- Two-compartment disposition model with first-order elimination from the central compartment.
- In HVTN104 and HVTN016, population pharmacokinetic (popPK) modeling and simulation provided key techniques for guiding the characterization of vital kinetics of VRC01.

Methods

- VRC01 Serum Concentrations were measured by an enzyme-linked immunosorbent assay (ELISA) using anti-VRC01 antibody.
- Nonlinear mixed-effects models were used to fit the popPK model.
- Covariates (age, gender, body weight, body mass index, creatinine clearance, albumin concentration, smoking status, gender, body mass index, and white blood cell count) were considered in the model.
- The resulting popPK model with a random effects formulation of 28% coefficient of variation for random effect estimates, calculated at a 90% confidence interval between subject effects.

Results

- In HVTN104, VRC01 serum concentrations were measured in 21 healthy adults who received VRC01 5 mg/kg SC every 2 weeks or placebo.
- In HVTN105 and HVTN016, population pharmacokinetic (popPK) modeling and simulation provided key techniques for guiding the characterization of vital kinetics of VRC01.
- In HVTN104, VRC01 BNabs were measured in 54 HIV-infected adults with severe disease and were associated with a median serum trough of 400 mcg/mL.
- In HVTN104, 10 mg/kg SC was administered every 2 weeks, with an IV loading dose of 30 mg/kg.
- The final popPK model with a random effects formulation of 28% coefficient of variation for random effect estimates, calculated at a 90% confidence interval between subject effects.

Conclusions

- For the first time, a robust popPK model of VRC01 was constructed and evaluated.
- Standard guidelines for VRC01 characterization.
- Pharmacokinetics were estimated on an internal database of IV 9E21.
- VRC01 was tested in weight-dependent dosing regimens.
- The resulting model was used in the clinical evaluation of various dose regimens of VRC01 to determine the future efficacy trials.
- In HVTN105 and HVTN016, population pharmacokinetic (popPK) modeling and simulation provided key techniques for guiding the characterization of vital kinetics of VRC01.
- The developed popPK modeling and simulation process and results provide key techniques for guiding the characterization of vital kinetics of VRC01.