

A Population Pharmacokinetic Model Based on HPTN 077 of Long-acting Injectable Cabotegravir for HIV PrEP

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Abstract

Background Cabotegravir delivered as a long-acting intramuscular injection has shown superior efficacy to oral tenofovir-emtricitabine as pre-exposure prophylaxis (PrEP) for HIV. Cabotegravir pharmacokinetics (PK), like those of other long-acting depot preparations, exhibit variability between individuals and between injection occasions. **Aim** To describe the population pharmacokinetics of long-acting cabotegravir (CAB-LA). **Methods** Using available PK measurements from 133 participants in the HIV Prevention Trials Network (HPTN) 077 trial, we analyzed CAB-LA PK data using nonlinear mixed-effects modeling to develop a population PK model. **Results** A two-compartment model with first order absorption best described the CAB-LA PK. The analysis identified between-occasional variability (BOV, i.e., differences in PK within one individual from one injection to the next) as a significant covariate affecting the absorption rate. Sex and body weight were identified as significant covariates influencing the absorption rate and apparent clearance of CAB-LA after intramuscular injection at various doses and frequencies. **Conclusion** The public availability of this model will facilitate and enable a wide variety of future clinically relevant simulations to inform the optimal use of CAB-LA.

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