Tenofovir Alafenamide (TAF) for HIV Prevention in IV Drug Users

Authors: Katy Garrett, Brian Maas, Mackenzie Cottrell, Heather Prince, Craig Sykes, Amanda Schauer, Nicole White, Julie Dumond, Angela Kashuba

Affiliations: UNC, Chapel Hill, NC

Objectives: No medical intervention is FDA-approved for prevention of HIV transmission by IV drug use. TAF is a tenofovir (TFV) prodrug that achieves high concentrations of the active moiety, TFV diphosphate (-dp), in peripheral blood mononuclear cells (PBMCs). We modeled the efficacy of TAF-based PrEP using TFVdp concentrations in PBMCs.

Methods: 24 healthy women given a single oral dose of 5, 10, or 25 mg TAF (n=8/arm) each had 9 plasma and 8 PBMC samples collected over a 14-day period and analyzed for TAF, TFVdp, and dATP using LC-MS/MS. Modeling and simulations were performed in NONMEM7.3 (ICON) using Laplacian estimation with interaction (M3 method for BQL data). Based on the developed model, TFVdp concentrations were simulated across steady-state (1-7 doses/wk) and event-driven (starting 24 or 2h prior to exposure) scenarios. dATP concentrations were simulated using a normal distribution. The TFVdp:dATP ratios were then combined with previously-measured emtricitabine data (FTCtp:dCTP) in a synergistic Emax model with an EC90 target (1,2).

Results: A one-compartment TAF plasma model with transit and PBMC compartments linked via first-order processes best described the data. Inter-individual and residual variability were described using an exponential model and proportional and additive error model, respectively. The TFVdp:dATP ratio at steady-state consistent with 1, 2, and 3+ doses/week of TAF 25mg is predicted to protect 16, 91, and >98% of IVDUs, respectively. Event-driven dosing provides protection for >95% of the population for at least 6 days. When combined with emtricitabine, 2 doses/wk is expected to protect 100% of the population; event driven dosing protects 100% up to 7 days post-exposure.

Conclusion: This simulation predicts >90% protection with 2+ TAF doses/wk alone and 100% when combined with emtricitabine, requiring fewer doses/wk than another TFV prodrug. Results from this analysis could be used to design PrEP studies of TAF for IVDU.


Figure 1: Simulated protected effect based on tenofovir diphosphate (TFVdp):dATP and/or emtricitabine triphosphate (FTCtp):dCTP above target EC90 at steady-state taking 1-7 doses per week. TAF: tenofovir alafenamide, FTC: emtricitabine.