TAF ACHIEVES ADEQUATE INTRACELLULAR TENOFOVIR-DP CONCENTRATIONS WITH RIFAMPICIN BASED TB THERAPY

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BACKGROUND

- Co-administration of rifampicin with tenofovir alafenamide fumarate (TAF) reduces plasma tenofovir and intracellular tenofovir diphosphate (TFV-DP) concentrations.
- Standard-dose TAF, with rifampicin, provided higher TFV-DP concentrations than tenofovir disoproxil fumarate (TDF) in a healthy volunteer study. This study assessed the combination of TAF containing ART and rifampicin-based therapy in people with HIV associated tuberculosis (TB).

METHODS

- We conducted an open-label, three-period sequential pharmacokinetic study in virologically suppressed participants with HIV-1, on TDF-based ART during the maintenance phase of rifampicin-containing TB therapy.
- Steady-state TFV-DP and plasma tenofovir concentrations were measured across three treatment periods:
  1) TDF 300 mg daily + rifampicin (TDF + RIF)
  2) TAF 25 mg daily + rifampicin (TAF + RIF)
  3) TDF one month post-completion of TB therapy (TDF only).
- Twenty-four-hour area under the concentration-time curves (AUC_{0-24h}) and geometric mean ratios (GMRs) with 95% confidence intervals (95% CI) were calculated.

RESULTS

- Eighteen participants were enrolled with a median age of 41 years (56% male).
- All participants completed TB therapy.
- TFV-DP concentrations were five-fold higher during TAF + RIF administration when compared with the TDF + RIF, and TDF only treatment periods (Figure 1; Figure 2).
- Plasma tenofovir concentrations were 93% lower with TAF + RIF administration when compared with TDF administration, with and without rifampicin (GMR 0.07 [0.06, 0.09]).

Standard-dose TAF achieved higher intracellular tenofovir diphosphate (TFV-DP) concentrations compared with TDF in patients with HIV-associated, rifampicin-sensitive tuberculosis.

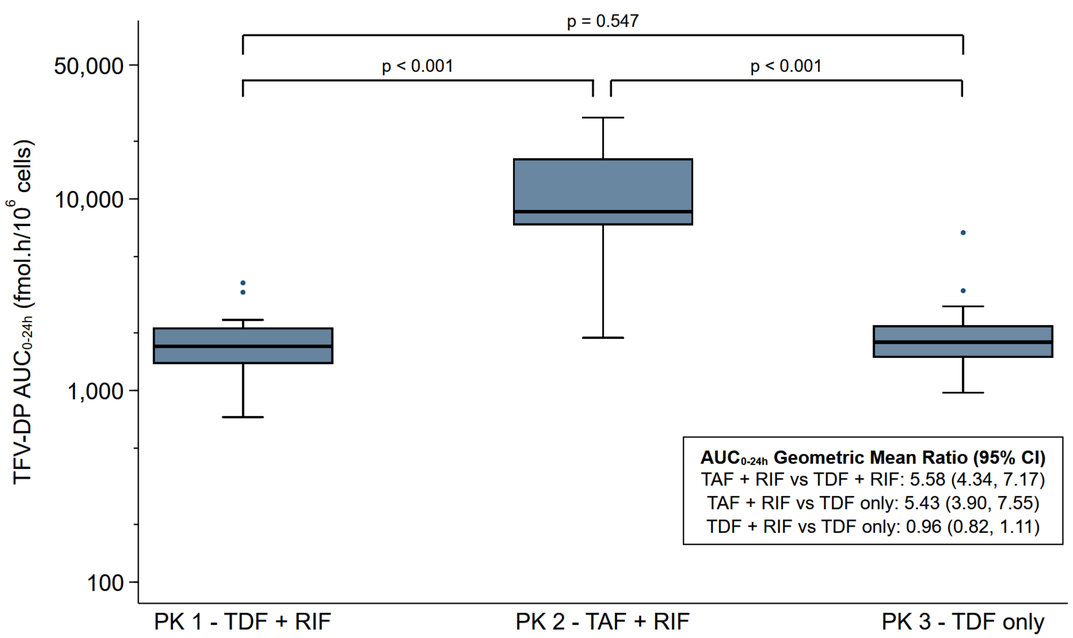


Figure 1: Intracellular Tenofovir Diphosphate 24-Hour Area Under the Concentration-Time Curve by Treatment Period

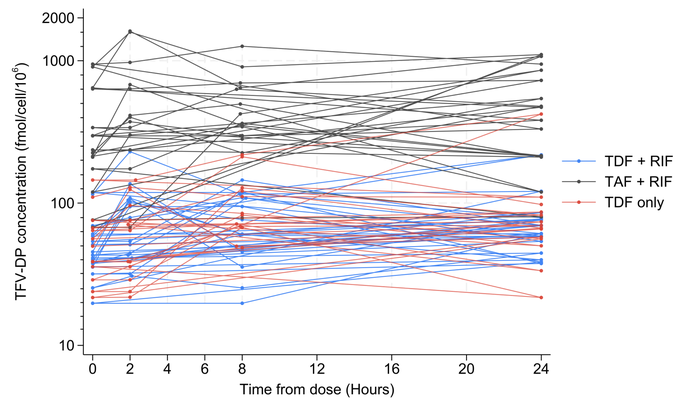


Figure 2: Intracellular Tenofovir Diphosphate Concentration-Time Profiles

- Treatment was well tolerated; No serious adverse events, deaths, or adverse events requiring study discontinuation were reported.

CONCLUSIONS

- Co-administration of TAF-containing ART and rifampicin-based TB therapy was associated with higher TFV-DP concentrations than TDF-containing ART, supporting this combination in the management of HIV-associated TB.
- These findings have important implications for treatment guidelines and clinical practice.
- Further research is needed to assess the long-term outcomes of TB therapy with this treatment regimen.

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