PHARMACOKINETIC-PHARMACODYNAMIC (PK-PD) OF EMTRICITABINE/TENOFOVIR ALAFENAMIDE (F/TAF) DEMONSTRATED WIDE EXPOSURE RANGE ASSOCIATED WITH CLINICAL SAFETY

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Background: Tenofovir alafenamide (TAF) is a novel prodrug of tenofovir (TFV) that has been co-formulated with emtricitabine (F) into a fixed-dose combination tablet (F/TAF) as an N(t)RTI backbone. We conducted a randomized, double-blind, active-controlled study in virologically-suppressed HIV-1 infected patients receiving tenofovir disoproxil fumarate (TDF)-containing regimens to evaluate the efficacy and safety of switching from F/TDF to F/TAF vs continuing F/TDF while remaining on the same third agent. Study drugs were taken without regard to food.

Methods: Patients were randomized 1:1 to switch to F/TAF or continue F/TDF while remaining on the same third agent. The TAF and TFV PK area under the curve over dosing interval (AUC_{tau}) and maximum concentration (C_{max}) were estimated via population PK analysis. The safety endpoints for PK-PD analysis were selected: gastrointestinal (GI) adverse event (diarrhea, nausea, vomiting, abdominal pain), change in hip and spine bone mineral density (BMD), and change in selected lipid parameters. Subjects were grouped into quartile subgroups based on TAF and TFV exposures for evaluation of exposure-safety trends.

Results: 663 patients were randomized and treated (F/TAF 333 vs F/TDF 330). Drug-related serious adverse events were rare (0 vs 0.3%). Drug discontinuation due to adverse events (AEs) was low (2.1% vs 0.9%). In F/TAF-treated patients, TAF and TFV PK exposures were available for 292 and 328 subjects, respectively. No trends in GI AEs were observed across wide range of TAF exposures. Similarly, no trends with TFV exposures were noted. The changes in BMD (hip and spine) and fasting lipids at Week 48 were comparable across TAF and TFV exposure quartiles, with no trends noted.

Conclusion: These data demonstrate that TAF is well tolerated with no trends of safety signal across wide ranges of TAF exposures in virologically suppressed HIV-1 infected patients.

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