Renal Safety of TAF vs TDF and ABC in a Pooled Analysis of 26 Phase 2/3 Clinical Trials

Introduction

- Tenofovir alafenamide (TAF) is a novel tenofovir (TFV) prodrug associated with 91% lower plasma TFV levels compared with the marketed prodrug tenofovir disoproxil fumarate (TDF).
- Higher plasma TFV levels have been associated with nephrotoxicity.
- For patients being switched to TAF from TDF, TFV associated renal toxicity may be prolonged post-switch by 4 weeks due to TFV associated renal injury.
- Compared with TDF, TAF showed improved renal safety across multiple renal markers in both treatment-naïve and treatment-experienced participants.
- These potentially novel findings favoring renal safety for TAF vs ABC were identified with the consistent with the individual trials and favored renal outcomes.

Methods

- Our objective was to conduct a large, integrated analysis of individuals from 26 TAF clinical trials.
- As expected, the pooled biomarker analysis was consistent with the individual trials and favored renal outcomes of TAF vs TDF.
- Other 322 (5%) 126 (4%) 18 (2%) 466 (5%)
- Treatment-experienced adults (n=2) – 3TC, lamivudine; AE, adverse event; ATV, atazanavir; B, BIC, bictegravir; β2 M, beta-2 microglobulin; C, COBI, cobicistat; DRV, darunavir; EFV, efavirenz; ELV, elvitegravir; eGFR CG, estimated glomerular filtration rate by Cockcroft-Gault; F, FTC, emtricitabine; OL, open label; P, PRINCE, prasugrel; R, Raltegravir; TDF, tenofovir disoproxil fumarate; TAF, tenofovir alafenamide; TDF-FF, tenofovir alafenamide 2 mg/FTC 200 mg.

Results

- There were no cases of PRT, or fatal events (n=0).
- Treatment-naïve and virologically suppressed participants had consistent with the individual trials and favored renal outcomes of TAF vs TDF.
- Pooled analysis has demonstrated that TAF is associated with consistent with the individual trials and favored renal outcomes of TAF vs TDF.
- As expected, the pooled biomarker analysis was consistent with the individual trials and favored renal safety of TAF vs TDF.
- TAF’s clinical renal safety profile (with statistically significant favorable renal biomarkers) is likely similar to ABC.
- Long-term safety of TAF, TDF and ABC-containing regimens will continue to be monitored.

Conclusions

- This pooled analysis of 26 studies with >12,000 py of TAF exposure provided the statistical power to demonstrate a clear clinical renal safety advantage of TAF over TDF, consistent with biomarker differences in individual clinical trials.
- PLH initiating or switching to TAF did not experience PRT and had significantly lower rates of renal discontinuations, compared with those on TDF.
- As expected, the pooled biomarker analysis was consistent with the individual trials and favored renal safety of TAF vs TDF.

Acknowledgments

- Supported by the National Institute of Allergy and Infectious Diseases, the National Cancer Institute, the National Heart, Lung, and Blood Institute, the National Institute of Stevens-Johnson Syndrome, and the National Institute of Drug Abuse, and the National Institute of Mental Health.

References

- The study was supported by Gilead Sciences, Inc. and the National Institutes of Health, National Heart, Lung, and Blood Institute, National Institute of Allergy and Infectious Diseases, National Institute of Mental Health, National Cancer Institute, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Drug Abuse, National Institute of Environmental Health Sciences, National Institute of General Medical Sciences, and National Institute of Nursing Research.