Renal Safety of Tenofovir Alafenamide in Patients at High Risk of Kidney Disease

Dawn Wohl1, Anders Thalme1, Robert Finlayson1, Shinichii Oka1, Thai Nguyen1, Susan Guo1, Andrew Cheng1, Moupalai Das1, Marshall Fordyce1
1University of North Carolina at Chapel Hill, USA; 2Karolinska University Hospital, Stockholm, Sweden; 3Taylor Square Private Clinic, NSW, Australia; 4National Center for Global Health and Medicine Hospital, Tokyo, Japan; 5Gilead Sciences, Inc., Foster City, CA, USA

Background
- Risk factors for chronic kidney disease (CKD) in HIV patients include older age, Black race, female sex, diabetes, hypertension, dyslipidemia, renal impairment, and use of nephrotoxic agents.
- Tenofovir disoproxil fumarate (TDF) is a widely used antiretroviral for HIV infection that has been associated with an increased risk of AKI based on findings from cohort studies including the D:A:D study.
- Due to a 9% lower plasma tenofovir (TFV) level, tenofovir alafenamide (TAF) relative to TDF has demonstrated a significantly better renal safety profile and no discontinuations due to renal adverse events through 2 years in 2 randomized, double-blind studies (GS-US-220-2044 and GS-US-220-2111) comparing TAF to TDF. Both regimens are co-formulated as a single-tablet regimen, E/C/F/TAF and E/C/F/TDF, respectively.
- Renal outcomes by CKD risk category in antiretroviral-naive adults treated with E/C/F/TAF or E/C/F/TDF are described.

Methods
- Studies 711 and 111 were phase 3 international, double-blind, 16-week studies in which antiretroviral-naive HIV-1 infected adults aged ≥18 years were randomized 1:1 to a fixed-dose, single-tablet regimen of elvitegravir, cobicistat, and emtricitabine with TFV-DARLIT or TFV-D4T active daily.
- Primary endpoints:
  - Proportion of subjects with HIV-1 RNA < 40 copies/mL at 48 weeks.
  - Changes in goiter (NCKD creatinine case).
  - Decreased GFR and Fanconi (NCKD creatinine case).
- Study outcomes by CKD risk category included renal outcomes. The renal safety study was a randomized, controlled trial comparing TAF to TDF for up to 2 years. The renal outcomes were assessed using the Kidney Disease: Improving Global Outcomes (KDIGO) CKD risk score.
- Additional analyses included changes in quantitative biomarkers (eGFR and creatinine) and proteinuria (UACR in mg/dL) to evaluate renal safety of TAF relative to TDF in patients at high risk of kidney disease.

Results
- Analysis #1 by Number of CKD Risk Factors
  - Baseline Risk Factors for CKD by Number of Risk Factors
  - Baseline Risk Factors for CKD by D:A:D Risk Score

- Analysis #2 by D:A:D Risk Score
  - Efficacy by D:A:D Risk Score
  - Changes in eGFR by D:A:D Risk Score
  - Changes in Proteinuria and Albuminuria by Week 96

Renal Outcomes by Baseline CKD Risk
- Changes (%) in Proteinuria and Albuminuria at Week 96
- Changes (%) in Tubular Proteinuria at Week 96

Conclusions
- Antiretroviral-naive adults with both high and low risk for CKD treated with TAF had more favorable renal outcomes compared to those treated with TDF.
  - Incident CKD through 2 years was 0.1% TAF vs 1.6% TDF.
  - Incident CKD on TDF was observed in all CKD risk groups.
  - There may be a greater grade in incident CKD on TDF (1%, 2%, and 5%, respectively) with increasing CKD risk.
  - Treatment discontinuations due to renal AEs and changes in eGFR were lower with TAF vs TDF.

References
- We extend our thanks to the patients, their partners and families, and all participating Study 104 & 111 investigators.

Acknowledgements
- The findings and conclusions reported in this presentation do not necessarily represent those of the U.S. Department of Health and Human Services or any of its agencies.