Longer Term Safety of Tenofovir Alafenamide in Renal Impairment

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Introduction
- Tenofovir disoproxil fumarate (TDF) has been associated with clinically significant renal and bone toxicity.1
- Tenofovir alafenamide (TAF) is a novel prodrug of tenofovir (TFV) that results in 91% lower renal tubular function (quantified proteinuria).•
- Switching to E/C/F/TAF in HIV-1–infected patients with a creatinine clearance (estimated glomerular filtration rate by Cockcroft-Gault equation [eGFR]) of 30–69 mL/min was shown to be effective and safe through 48 weeks.2

Objectives
- To evaluate the 2-year (96-week) safety and efficacy of a single-tablet, once-daily regimen of E/C/F/TAF in HIV-1–infected patients with mild–moderate renal impairment.

Methods

Study Design

- Phase 3, 144-week, multicenter, open-label study (Study 112; NCT01818596).
- Virologically suppressed adults with stable eGFR (30–69 mL/min) switched from TDF or non-TDF–containing regimens to open-label E/C/F/TAF.
- Week-96 efficacy and safety data are described, including tests of renal function and bone mineral density (BMD).

Key Inclusion Criteria
- CD4 cell count ≥50 cells/μL
- ANC ≥1500 cells/μL
- Estimated GFR: Changes Over Time
- No chronic hepatitis B or C virus infection
- HIV-1–infected patients: HIV-1 RNA<50 copies/mL, for ≥6 months
- 10% (23/242) virologic data were not available
- At Week 96, switching to E/C/F/TAF maintained viral suppression, and 2% (5/242) had virologic failure
- 13 patients discontinued due to adverse events (AEs)
- 5 (2%) for decreased eGFR
- 12 patients (5%) discontinued study drug for AEs
- These data support the safety and efficacy of once-daily E/C/F/TAF in HIV-1–infected patients with mild–moderate renal impairment

Results (continued)

Retinal Biomarkers: Changes From Baseline to Week 96

BMD: Changes From Baseline

Virologic Outcomes at Week 96
- 38% of patients (214/562) maintained HIV-1 RNA<50 copies/mL at Week 96.
- In 10% (23/242), virologic data were not available.
- 13 patients discontinued due to adverse events (AEs).
- 10% discontinued due to other reasons (lost to follow-up, noncompliance, protocol violations) and last available HIV-1 RNA<50 copies/mL.
- 2% (5/242) had virologic failure.
- 96% (235/242) had undetectable HIV-1 RNA<50 copies/mL at Week 96.

Safety Summary
- Upper respiratory tract infection (14%), diarrhea (13%), and arthralgia (12%) were the most common AEs.
- AEs, grades, and frequencies were similar in patients with baseline eGFR<60 mL/min.
- No patients discontinued study drug for AEs.
- 7 patients were treated for non-AEs.
- No patients had renal disease progression (2 of these had poorly controlled hypertension).

Conclusions
- This is the first study of a single-tablet antiretroviral regimen in patients with eGFR of 30–69 mL/min.
- At Week 96, switching to E/C/F/TAF maintained viral suppression, and was associated with stable eGFR, reductions in proteasome, and improvements in proximal renal tubular function, and hip and spine BMD.
- These data support the safety and efficacy of once-daily E/C/F/TAF in HIV+ patients with eGFR of 30–69 mL/min without dose adjustment.

References

Acknowledgements
The authors gratefully acknowledge the investigators, study staff, and all participating patients.

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