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

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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 widely used antiretroviral for HIV infection, but it has been associated with an increased risk of CKD based on findings from cohort studies including the D:A:D study.

- Due to a 91% lower plasma tenofovir level, tenofovir alafenamide (TAF) may provide a safer renal safety profile compared to TDF.

Methods

- Studies TAF 10 and 11 and 2 Phase 3 international, double-blind, 144-week studies in adults naïve to HIV therapy with high and low baseline levels of eight CKD risk factors (age, sex, race, diabetes, hypertension, dyslipidemia, renal impairment, use of nephrotoxic agents) were analyzed.

Mechanism of Action

Tenofovir Disoproxil Fumarate and Tenofovir Alafenamide

- Tenofovir Disoproxil Fumarate
  - In the tubular cell, tenofovir is not metabolized.
  - It is secreted into the urine as a glucuronide.
  - Tubular proteinuria increases on TDF with chronic dosing.

- Tenofovir Alafenamide
  - It is metabolized to tenofovir dihydrogen phosphate within the renal tubule.
  - Tubular proteinuria may decrease on TAF with chronic dosing.

Results

- Studies TAF 10 and 11 and 2 Phase 3 international, double-blind, 144-week studies in adults naïve to HIV therapy with high and low baseline levels of eight CKD risk factors (age, sex, race, diabetes, hypertension, dyslipidemia, renal impairment, use of nephrotoxic agents) were analyzed.

- Changes in Tubular Proteinuria at Week 96
  - 0.4% (1)

- Adults on TAF and TDF maintained high rates of virologic success.

- Changes in Proteinuria and Albuminuria at Week 96
  - 5%

- Low Risk for CKD (≤1 risk factor)

- Medium Risk for CKD

- High Risk for CKD (≥5 risk factors)

- Incidental CKD on TDF

- 12% (107)

- Low Risk for CKD

- Medium Risk for CKD

- High Risk for CKD

- 0 / +2

- CKD defined as post-baseline eGFR <60 mL/min for >3 Months (with BL eGFR ≤35 mL/min or >60 mL/min to ≤60 mL/min).

- Due to a 91% lower plasma tenofovir level, tenofovir alafenamide provides a safer renal safety profile compared to TDF.

- There may be a graded increase in incident CKD with TDF.

- Overall, fewer participants were incident CKD cases with TAF compared to TDF.

- For patients with low baseline eGFR (BL eGFR 30 <60 mL/min), tenofovir alafenamide may be a safer option.

- Continuous renal safety monitoring over 2 years in 2 randomized, double-blind studies (NCT02923005 and NCT02923019) comparing TAF vs TDF demonstrated a single-tubular mechanism, ECF/TAF and ECF/TDF, respectively.

- Renal outcomes by CKD risk category in antiretroviral naïve adults treated with TAF/TDF or TDF/TDF are described.

References

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