Elevated Tenofovir Exposure via Intensive Pharmacokinetic Monitoring is Associated with Progressive Kidney Function Decline

Sanjiv M. Baxi, MS, MD, MPH, RD1, Rebecca Scherzer, PhD2, Ruth Greenblatt, MD3, Howard Minkoff, MD3, Kathryn Anastos, MD4, Mardge Cohen, MD3, Mary A. Young, MD5, Monica Gandhi, MD, MPH2, and Michael G. Shlipak, MD, MPH2, for the Women’s Interagency HIV Study (WIHS)

1Department of Medicine, University of California, San Francisco, San Francisco, California, USA, and School of Public Health, University of California, Berkeley, California, USA, and Department of Medicine, Veterans Affairs Hospital, San Francisco, California, USA, and 2Department of Clinical Pharmacy, University of California, San Francisco, San Francisco, California, USA, 3Division of Infectious Diseases, State University of New York, Downstate Medical Center, Brooklyn, New York, USA, and 4Departments of Medicine and Obstetrics and Gynecology and Women’s Health, Albert Einstein College of Medicine, Bronx, New York, USA, and 5CORE Center/ Division of Infectious Diseases, John H. Stricker Jr. Hospital of Cook County, Chicago, Illinois, USA, and 6Department of Medicine, Georgetown University Medical Center

BACKGROUND

- Tenofovir disoproxil fumarate (TDF) is commonly used in HIV treatment and prevention.
- Acute toxicity is of concern, but longitudinal use of TDF is associated with decline in kidney function over time.
- Factors associated with elevated TFV blood levels are not well known, and drug concentration monitoring for tenofovir (TFV)-associated kidney disease is rarely performed.
- We hypothesized that greater TFV blood levels would be associated with reduced eGFR and faster eGFR decline in HIV-infected women.
- We performed 24 intensive pharmacokinetic (PK) evaluations of TDF in a cohort of HIV-infected women and evaluated the relationship between areas-under-the-time-concentration curves (AUC) with serially measured renal function over the succeeding 7 years.

MATERIALS AND METHODS

- Study population: The Women’s Interagency HIV Study (WIHS) is a multicenter, prospective cohort of HIV-infected women and evaluated the association with decline in kidney function over time in a real-life cohort of HIV-infected women.
- Differences in eGFR trajectories were most pronounced in the initial follow-up period and higher baseline TFV AUC was associated with worse eGFR levels and changes, even after controlling for traditional and HIV-related characteristics.
- Assessing tenofovir drug exposure in HIV prevention and treatment settings may be important in predicting and potentially averting nephropathy on tenofovir-based regimens.

RESULTS

- Figure 1: Higher Baseline TFV AUC is Associated with Reduced eGFRcr (ml/min/1.73 m²) at Baseline in Women Living with HIV.
- Figure 2: Higher baseline TFV AUC associated with lower eGFR (ml/min/1.73 m²) over 7 years of follow-up.
- Figure 3: Higher baseline TFV AUC is associated with sustained reductions in eGFR (ml/min/1.73 m²) over 7 years of follow-up.

CONCLUSION

- Higher tenofovir exposure (as measured in intensive PK studies) is strongly associated with decline in kidney function over time in a real-life cohort of HIV-infected women.

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