

## **Long-Term Fracture Complications in HIV Patients Treated with Antiretroviral Therapy Combined with Tenofovir Alafenamide: A Database Study**

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### **Introduction**

Antiretroviral therapy (ART) has become widely adopted for the management of HIV patients and resulted that these patients live longer and healthier lives. Nucleoside reverse transcriptase inhibitors (NRTIs) have become common drugs used in combination with ART for the HIV infection treatment and prophylaxis. Tenofovir Alafenamide (TAF), a novel NRTI, acts as a nucleotide analogue and competitively binds to reverse transcriptase, thus halting DNA synthesis. However, TAF exhibits side-effects, which include bone and renal damage. The purpose of this study is to establish the incidence and nature of complications following surgical management of fractures in HIV patients treated with TAF.

### **Methods**

Data retrieval and analysis were performed using the Research Network within TriNetX, a globally federated database, consisting of de-identified patient records from across 102 healthcare organizations. HIV patients who underwent operative treatment of fractures of the lumbar spine and pelvis, tibia, femur, or unspecified lower leg and were treated with TAF or not were analyzed and compared. Both TAF and no-TAF cohorts were 1:1 propensity score matched for demographic factors and comorbidities, yielding n=2,855 patients per group. Outcomes included 5-year postoperative complications such as thrombocytopenia, osteopenia, osteophyte formation, osteoporosis with or without fractures, periprosthetic fractures, osteomyelitis, and sepsis. Risk percentages, risk ratios, 95% confidence intervals (CI), and P values were calculated. Significance was set at  $P < 0.05$ .

### **Results**

Patients taking TAF encountered significantly lower rates of osteoporosis without fractures (13.7% vs. 11.5%; RR 1.188; 95% CI 1.036, 1.363;  $P < .013$ ), osteopenia (12.9% vs. 9.3%; RR 1.389; 95% CI 1.196, 1.612;  $P < .0001$ ), sepsis (15.3% vs. 13.0%; RR 1.181; 95% CI 1.039, 1.343;  $P < .01$ ), thrombocytopenia (12.7% vs. 10.9%; RR 1.174; 95% CI 1.018, 1.354;  $P < .027$ ), osteophytes (6.1% vs. 4.7%; RR 1.299; 95% CI 1.043, 1.617;  $P < .019$ ), and periprosthetic fractures (.4% vs. 0%; RR null; 95% CI .001, .006;  $P < .002$ ). Some outcomes investigated were found to have insignificant results including osteoporosis with fractures (5.1% vs. 4.1%; RR 1.239; 95% CI 0.977, 1.572;  $P < .077$ ) and osteomyelitis (7.4% vs. 6.3%; RR 1.167; 95% CI 0.963, 1.414;  $P < .116$ ).

### **Discussion**

Addition of TAF to ART for HIV patients with fractures is associated with reduced risk of osteoporosis, osteopenia, sepsis, thrombocytopenia, and periprosthetic fractures within a 5-year postoperative follow up compared to HIV patients treated with ART with no TAF.

### **Clinical Significance**

Orthopedic surgeons should consider careful precaution in postoperative care when performing surgical treatment of fractures in HIV patients, specifically those treated with ART without TAF. Further research is needed to establish a causative relationship between TAF and long-term postoperative complications in HIV patients treated for fractures.