Switching to New Tenofovir Linked to Rise in BMI and Cardiovascular Risk

This finding from a study of people switching from TDF to TAF for HIV treatment may also have implications for those on PrEP.

October 18, 2019 By Benjamin Ryan

Switching from the older version of tenofovir, tenofovir disoproxil fumarate (TDF), to the new one, tenofovir alafenamide (TAF), is associated with an increase in body mass index (BMI) and atherosclerotic cardiovascular disease risk, the National AIDS Treatment Advocacy Project (NATAP) reports. These findings from a study of people on antiretroviral (ARV) treatment may apply not just to people living with HIV but also to HIV-negative individuals on pre-exposure prophylaxis (PrEP).

TDF, which is sold as the brand-name, stand-alone pill Viread, is included in a number of combination HIV treatment tablets from Gilead Sciences, including Atripla (efavirenz/TDF/emtricitabine), Complera (rilpivirine/TDF/emtricitabine), Stribild (elvitegravir/cobicistat/TDF/emtricitabine) and Truvada (TDF/emtricitabine). TDF is also included in Merck's Delstrigo (doravirine/TDF/lamivudine) and Mylan's Symfi (efavirenz 600 mg/TDF/lamivudine), Symfi Lo, (efavirenz 400 mg/TDF/lamivudine) and Cimduo (TDF/lamivudine).

Truvada is approved both as a component of an HIV treatment regimen and for use as PrEP. Viread is also approved to treat hepatitis B.

TAF, which is sold as the brand-name tablet Vemlidy to treat hepatitis B , is included in Gilead's HIV regimens Biktarvy (bictegravir/TAF/emtricitabine), Genvoya (elvitegravir/cobicistat/TAF/emtricitabine), Odefsey (rilpivirine/TAF/emtricitabine) and Descovy (TAF/emtricitabine) as well as Janssen's Symtuza (darunavir/cobicistat/TAF/emtricitabine).

Descovy was approved as PrEP earlier this month.

Previous studies in both HIV-negative and HIV-positive individuals have indicated that TAF is associated with lower bone and kidney toxicity compared with TDF. However, there has been no evidence that taking Descovy rather than Truvada for PrEP reduces the rates of related clinical

outcomes, including kidney disease and bone fractures—each of which are already rare in the relatively young population that seeks out PrEP.

Presenting their findings at the IDWeek 2019 meeting in Washington, DC, earlier this month, a research team at Thomas Jefferson University in Philadelphia studied 110 people with HIV between ages 40 and 75 who had taken a TDF-containing regimen for at least one year during which their viral load remained below 200. During the study, all participants switched to TAF but made no other changes to their ARV regimen and were observed for one year.

Atherosclerotic cardiovascular disease (ASCVD) involves plaque buildup in the arteries. The study relied on the 2018 American College of Cardiology/American Heart Association guidelines to determine ASCVD risk scores, which estimate the likelihood of a heart attack within 10 years. A risk score of below 5.0% is considered low risk, between 5.0% and 7.4% is borderline risk, 7.5% to 19.9% is intermediate risk and 20.0% or greater is high risk.

The study participants were 50 years old on average. Seventy-three percent were men, 58% were Black, 35% were white, 6% were Latino and 2% were Asian. Four percent were underweight (a BMI under 18.5), 31% were normal weight (a BMI of 18.5 to 24.9), 28% were overweight (a BMI of 25 to 29.9) and 37% were obese (a BMI of 30 or greater). The cohort had been on ARVs for a median of eight years. Forty-nine percent of them took an integrase inhibitor along with TDF, 29% took a non-nucleoside reverse transcriptase inhibitor and 16% took a protease inhibitor.

One year after their switch from TDF to TAF, the group's median weight rose from 185.4 pounds to 190.5 pounds, and the median BMI increased from 28.0 to 28.2. The median total cholesterol increased from 173.8 to 195.0, and the median LDL cholesterol increased from 98.6 to 112.1. The median HDL cholesterol and triglycerides also rose, but these changes were not statistically significant, meaning they may have been driven by chance. There was no change in the ratio of total cholesterol to HDL cholesterol. Finally, the median ASCVD risk score increased from borderline to intermediate risk: from 6.9% to 8.1%.

After adjusting the data to account for female sex, the study authors found that switching from TDF to TAF was associated with a 0.45-point increase in BMI. Adjusting the data for age, female sex, race and the time since HIV diagnosis indicated that the medication switch was associated with a 13% increase in the ASCVD risk score.

The study authors believe that the increase in BMI was not likely a reflection of a "return to health," given that the participants were already on stable HIV treatment regimens at the time they switched to TAF. Although the increase in BMI was small, the uptick could nevertheless be

clinically relevant because even such small shifts on this measure can affect the lifetime risk of diabetes and ASCVD. The 13% increase in ASCVD risk meant that more than half of the participants were now indicated to receive statin treatment.

To read the NATAP report, click here.

To view the IDWeek 2019 program, click here.
