Older Tenofovir May Not Be Tied to Fracture Risk After All

Gilead has based its entire HIV drug portfolio on updating tenofovir, ostensibly to make it safer for bones and kidneys.

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A new analysis from French researchers calls into question whether Gilead Sciences' mainstay antiretroviral (ARV) tenofovir disoproxil fumarate (TDF) is associated with bone fracture, as has long been presumed, aidsmap reports.

Research had found that TDF, which is marketed as an individual tablet under the brand name Viread, is associated with kidney and bone toxicities, including a decline in bone mineral density. In recent years, Gilead has released an updated version of TDF, tenofovir alafenamide (TAF), which is associated with improved markers of kidney and bone health.

Whether taking TAF over TDF reduces the risk of bone fracture, however, is a matter of debate. Some researchers have argued that the clinical benefit of switching from TDF to TAF is realized only when both drugs are taken with a so-called boosting agent, either Tybost (cobicistat) or Norvir (ritonavir).

The only TDF-inclusive combination tablet that Gilead has not updated with a TAF-inclusive version is Atripla (efavirenz/tenofovir disoproxil fumarate/emtricitabine). Otherwise, TDF-inclusive combination tablets and their TAF-inclusive counterparts include: Complera (rilpivirine/tenofovir disoproxil fumarate/emtricitabine) and Odefsey (emtricitabine/rilpivirine/tenofovir alafenamide); Stribild (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate) and Genvoya (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide); and Truvada (tenofovir disoproxil fumarate/emtricitabine) and Descovy (emtricitabine/tenofovir alafenamide).

During the coming years, the TDF-inclusive combination tablets will lose their patent protection, opening the door for cheaper generics.

TAF is also included in Gilead's Biktarvy (bictegravir/emtricitabine/tenofovir alafenamide), Merck's Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate) and Janssen's Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide).

TDF is included in Mylan Pharmaceuticals' Symfi (efavirenz 600 mg/lamivudine/tenofovir disoproxil

fumarate) and Symfi Lo (efavirenz 400 mg/lamivudine/tenofovir disoproxil fumarate).

Gilead markets TAF as an individual tablet for the treatment of hepatitis B virus (HBV) under the brand name Vemlidy.

Descovy is currently under investigation in a Phase III trial that is comparing its safety and efficacy with that of Truvada for use as pre-exposure prophylaxis (PrEP) against HIV.

Publishing their findings in the Journal of Acquired Immune Deficiency Syndromes, researchers studied a population of 254 people enrolled in the French Hospital Database on HIV prior to starting ARVs who experienced a low-impact fracture between 2000 and 2010. The study authors matched these individuals according to age and sex with 376 HIV-positive people enrolled in the database before starting treatment for the virus who had not experienced a fracture.

When they received their first fracture diagnosis, 49 percent of the cohort members had taken TDF, for a median of 2.5 years, and 82 percent had taken a protease inhibitor, for a median of 4.3 years.

The investigators took into account a host of factors that might have influenced fracture risk among the study group and found that neither TDF nor protease inhibitor exposure was associated with fracture risk.

To read a POZ feature article that questions the benefit of TAF over TDF, click here.

To read the study abstract, click here.

To read the aidsmap article, click here.

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