Why Do Some Newer HIV Drugs Cause Weight Gain?

Future research should examine how particular combinations of antiretrovirals contribute to weight gain, according to one expert.

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Some of the newer antiretrovirals (ARVs), in particular integrase inhibitors, have been associated with weight gain, aidsmap reports. Given this concerning finding, researchers should set their sights on understanding which particular combinations of ARVs are the biggest drivers of weight gain among people with HIV.

That is according to an address given by Andrew Hill, PhD, of the University of Liverpool at the 17th European AIDS Conference in Basel, Switzerland, this month.

To some degree, the weight gain seen after individuals start ARVs is a result of the "return to health" effect among individuals who started with a compromised immune system. However, it is clear that this is not the only factor, given how weight gain can differ based on which ARVs individuals take.

The integrase inhibitors dolutegravir and bictegravir are associated with the greatest weight gains. Dolutegravir is sold as a stand-alone pill under the brand name Tivicay and is included in Juluca, Dovato and Triumeq. Bictegravir is included in Biktarvy and is not approved as a stand-alone tablet.

Tenofovir disoproxil fumarate (TDF) and efavirenz have each been tied to weight loss in various studies. TDF, which is sold as a stand-alone pill under the brand name Viread (which is also approved as a treatment for hepatitis B virus, or HBV), is included in Atripla, Complera, Delstrigo, Stribild, Symfi, Symfi Lo, Temixys and Truvada. Truvada is approved for use as pre-exposure prophylaxis (PrEP) against HIV. Efavirenz is sold as the stand-alone pill Sustiva and is included in Atripla, Symfi and Symfi Lo.

Research has consistently indicated that TDF-containing regimens are associated with less weight gain compared with regimens containing Ziagen (abacavir) or the newer version of TDF, tenofovir alafenamide (TAF). Abacavir is included in Triumeq, Epzicom and Trizivir.

TAF, which is sold as a stand-alone treatment for HBV under the brand name Vemlidy, is included

in Biktarvy, Genvoya, Odefsey, Symtuza and Descovy. Descovy is also approved for use as PrEP.

Research suggests that TDF reduces the weight-gaining effects of other ARVs. For example, in the GEMINI clinical trials of the two-drug regimen Dovato, participants who did not receive TDF gained more weight than individuals who took Dovato plus TDF.

In the ADVANCE trial, weight gain was not explained by better tolerability of dolutegravir or TAF.

In studies of TAF as a treatment for HBV, as well as those looking at the drug as HIV treatment, the ARV was associated with higher rates of elevated sugar in the urine and LDL cholesterol in the blood. This suggests that the drug is affecting metabolic pathways, which may help explain its link to weight gain.

Within the non-nucleoside reverse transcriptase inhibitors class of ARVs, rilpivirine is tied to greater weight gain than efavirenz. Rilpivirine is sold as the stand-alone pill Edurant and is included in Complera, Juluca, Odefsey and the investigational long-acting injectable treatment Cabenuva, which is currently awaiting a decision from the Food and Drug Administration.

When drugs associated with weight gain are used together, there are additive effects. The greatest amount of weight gain was seen in the ADVANCE trial among individuals receiving TAF, emtricitabine and dolutegravir—for example, Descovy plus Tivicay.

The greatest weight gain has been seen among women and African Americans, who, unfortunately, are underrepresented in clinical trials. Hill called for greater recruitment of Black women in particular to future studies.

For a complete listing of the contents of ARV combination tablets, click here.

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