Integrase Inhibitors Not Linked to Heart Problems in Swiss Study

People starting on integrase inhibitors were no more likely to have heart attacks, strokes or cardiovascular procedures.

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People who started HIV treatment using an integrase inhibitor were no more likely to experience cardiovascular events, such as heart attacks and strokes, than those who used other classes of antiretroviral medications, according to study findings presented at the 30th Conference on Retroviruses and Opportunistic Infections (CROI).

Commenting on the study, Paul Sax, MD, of Brigham and Women's Hospital in Boston, called the findings "reassuring," as this class of drugs is now critical to HIV treatment worldwide.

Integrase inhibitors have become a mainstay of modern antiretroviral therapy. This drug class includes raltegravir (Isentress), dolutegravir (Tivicay; also in the Triumeq, Juluca and Dovato combination pills), bictegravir (in Biktarvy), elvitegravir (in Stribild and Genvoya) and cabotegravir (in Cabenuva). U.S. treatment guidelines recommend Biktarvy and dolutegravir-based regimens for most people starting HIV treatment.

Previous research has produced mixed evidence about the impact of integrase inhibitors on heart health. One large study, recently published in The Lancet, saw a higher rate of early-onset cardiovascular disease during the first two years after starting integrase inhibitors, but some people in that study had previously used other drug classes. Another study found that integrase inhibitor use was associated with a lower risk for cardiovascular disease. Several studies have shown that people who are initially treated with or switch to integrase inhibitors, especially dolutegravir, are more likely to gain weight, a risk factor for cardiovascular problems. But other studies have not seen this effect. A study presented at CROI found that weight gain among people starting integrase inhibitors was modest and leveled off after two years. Overall, studies have not seen notable weight changes in people taking cabotegravir.

Bernard Surial, MD, of the University Hospital of Bern, and colleagues assessed the impact of integrase inhibitors versus other antiretrovirals on cardiovascular events—myocardial infarction, stroke or receiving an invasive cardiovascular procedure, such as angioplasty or coronary artery bypass surgery—among people starting treatment for the first time.

The analysis included 5,362 people in the Swiss HIV Cohort Study who started initial treatment after May 2008, when the first integrase inhibitor became available in Switzerland. Of these, 1,837 (34%) started on an integrase inhibitor and 3,525 (66%) started on drugs from other antiretroviral classes. Half used dolutegravir, while the rest were roughly evenly divided between bictegravir, elvitegravir and raltegravir. Among those starting on other drug classes, about half used boosted protease inhibitors, and about 40% used NNRTIs. Over the course of the study, the proportion of people starting on an integrase inhibitor rose from zero in mid-2008 to 96% in 2021, while the proportion starting on other drug classes fell from 100% to just 4%.

The median age was approximately 38 years. People who started on integrase inhibitors were more likely to be men (84% versus 76%), less likely to be of African origin (11% versus 18%) and had a higher lowest-ever CD4 count (330 versus 278). The median body mass index in both groups was in the high normal range. History of cardiovascular disease (1.5%), high blood pressure (10%), diabetes (about 2%), smoking status (nearly half) and use of lipid-lowering medications (less than 3%) were similar in both groups. However, people in the integrase inhibitor group were more likely to also take abacavir (Ziagen; also part of the Triumeq coformulation along with dolutegravir), at 23% versus 12%. They also were much more likely to use the newer tenofovir alafenamide (part of the Descovy, Biktarvy, Genvoya and Odefsey coformulations), at 40% versus 1%.

The participants were followed until their first cardiovascular event, death or their last study visit. A total of 116 cardiovascular events occurred over a median five years of follow-up. After adjusting for demographics, HIV-related factors and cardiovascular risk factors, the risk differences between people taking integrase inhibitors versus other antiretrovirals was -0.2% after one year, -0.2% after two years, -0.6% after five years and -0.5% after eight years. This means people taking integrase inhibitors had a slightly lower likelihood of cardiovascular events, though these differences were not statistically significant.

Based on these findings, the researchers concluded, there was “no difference [in] cardiovascular disease events between treatment-naive individuals starting [integrase inhibitors] and those starting other antiretroviral therapy.”

Surial said further studies are needed to look at cardiovascular risk among treatment-experienced people who switch to integrase inhibitors from other drug classes. He stressed the importance of controlling for comorbidities to guard against so-called channeling bias, which can occur if certain drugs are preferentially prescribed for people at greater risk for cardiovascular problems.

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