Yes, Sustiva Is Linked to an Increased Risk of Suicidal Behaviors

This finding comes from an analysis of the global START study, which proved in 2015 that starting HIV treatment early is best.

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A new analysis of the global START trial has found that beginning treatment with a regimen including Sustiva (efavirenz) is associated with an increased risk of suicidal behaviors. This finding is particularly reliable compared with those of other studies that have examined the drug's link with suicide because it comes from a randomized controlled trial, which allowed the study's authors to better control for variables that might have otherwise clouded their findings.

Sustiva (efavirenz) is included in the single-tablet regimen Atripla (efavirenz/tenofovir disoproxil fumarate/emtricitabine). The antiretroviral (ARV) has fallen out of favor in the United States because of its troublesome side effects, which include nightmares. Among all the single-tablet regimens manufactured by Gilead Sciences that include tenofovir disoproxil fumarate, Atripla is the only one that the company did not revise by swapping in tenofovir alafenamide, the updated, safer version of tenofovir.

The randomized controlled START trial, published in 2015, included 4,684 HIV-positive individuals from around the world who had not yet started ARV treatment and had a CD4 count above 500. A total of 271 (5.8 percent) of them had a psychiatric diagnosis. The participants were randomly assigned to begin ARVs immediately or to begin on a deferred basis, waiting until their CD4 count dropped to 350 or below, until they developed AIDS or other serious illnesses or until they met qualifications for starting treatment according to local guidelines.

Findings from this new analysis were published in Clinical Infectious Diseases.

The trial prespecified that 3,515 of the participants (75 percent) would receive Sustiva as part of their ARV regimen when they began treatment. Forty percent of those with a psychiatric diagnosis were prespecified to receive Sustiva, compared with 77 percent of those without such a diagnosis. Among those prespecified to receive Sustiva, 3.1 percent had a preexisting psychiatric diagnosis, compared with 13.9 percent of those prespecified for other ARVs. A respective 5.2 percent and 16.8 percent of each group used psychotropic medications.

Twenty-eight members of the immediate treatment group and 25 members of the deferred

treatment group reported suicidal behaviors during an average follow-up of 3.2 years. This translated to rates of 0.39 and 0.34 per 100 cumulative years of follow-up, respectively. This meant that, overall, there was no statistically significant difference in the rate of suicidal behaviors between the two groups, meaning any apparent difference might have been driven by chance.

The researchers looked at the rate of suicidal behaviors among those randomized to start treatment immediately, looking at the entire study period, and compared that rate among those in the deferred treatment arm only among the period before those individuals started ARVs.

Among those prespecified to receive Sustiva, 18 participants in the immediate treatment group reported suicidal behavior, for a rate of 0.36 per 100 cumulative years. (The researchers excluded from their analysis one individual in this group who reported suicidal behavior but who did not actually end up taking Sustiva.) By comparison, four individuals in the deferred treatment arm who were prespecified to take Sustiva reported suicidal behaviors during the period before they started treatment, for a rate of 0.10 per 100 cumulative years.

The study authors calculated that taking Sustiva was associated with a 3.31-fold greater risk of suicidal behaviors.

By comparison, among those prespecified to receive regimens that did not include Sustiva, the rate of suicidal behaviors was higher, at a respective 0.56 and 0.66 per 100 cumulative years in the immediate and deferred treatment arms. (Which makes sense, since this group had a higher rate of psychiatric diagnoses.) But the difference between these rates was not statistically significant.

Among the 109 participants who had a prior psychiatric diagnosis and were prespecified to receive Sustiva, none in the deferred group reported suicidal behavior during the period before they started treatment, compared with six of those in the immediate treatment arm after they'd started Sustiva (for a rate of 2.7 per 100 cumulative years).

The strongest predictor of suicidal behavior among those in the immediate treatment group was a prior psychiatric diagnosis, which was associated with a 12.5-fold increased risk of such behavior among those prespecified to receive Sustiva and a 9.3-fold increased risk among those prespecified to receive other ARVs. However, whether they were prespecified to receive Sustiva or other ARVs did not affect this increased risk in a way that was statistically significant.

Among those prespecified to receive Sustiva, heavy alcohol use was associated with a 4.6-fold increased risk of suicidal behavior and recreational drug use was associated with a 2.6-fold increased risk, while each relative addition of 10 years of age decreased the risk by 49 percent.

To read the study abstract, click here.

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