Isentress Might Reduce Risk of a "Fatty" Liver From Protease Inhibitors

November 4, 2010

A new laboratory study suggests that the integrase inhibitor Isentress (raltegravir) could prevent the accumulation of excess fat in the liver (steatosis) that results from protease inhibitor (PI) therapy. These data were presented at the 61st Annual Meeting of the American Association for the Study of Liver Diseases, held October 29 to November 2 in Boston.

Several antiretroviral (ARV) drugs used to treat HIV have been implicated in steatosis. These include older drugs such as Zerit (stavudine) and several drugs from the PI class. While steatosis is not immediately harmful, and is usually reversible, it can ultimately lead to lasting health problems if it is not addressed right away. What's more, with HIV drugs, steatosis is intricately tied to other blood fat disorders, including increases in trigylcerides and "bad" types of cholesterol and the risk for developing diabetes, as well as accumulation of fat in the gut. Such disorders can significantly increase a person's risk for developing cardiovascular disease.

Unfortunately, people with HIV who take ARVs must remain on them for life—at least for now—and many don't have the option to stop taking a PI. This means that steatosis must be addressed. However, researchers are getting close to understanding why these HIV drug–induced disruptions in fat metabolism occur, and there have been some hints that Isentress might actually be able to counteract the accumulation of liver fat from PIs.

To test this theory, Min Liang, PhD, from the Virginia Commonwealth University in Richmond, and her colleagues examined the behavior of liver cells in the presence of the various drugs. Previously, Liang's team found that PIs can put stress on a type of cell known as the endoplasmic reticulum (ER), which aids in the healthy formation of other types of cells and structures in the liver. ER stress has been shown to contribute to liver steatosis.

Liang and her colleagues proceeded with their studies based on a hunch that Isentress actually protects against ER stress, and their hunch appears to be correct. When PIs were added to liver cells alone, they caused the accumulation of fat in those cells. When Isentress was added to this mix, however, the cells did not take on additional fat.

Further research will be needed to duplicate these results and to document that these effects can be seen in living animals before extrapolating them to humans. Nevertheless, these do offer hope that people who must take a PI may be able to avoid steatosis—and possibly other fat disorders.

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