Study Finds Tobira's New HIV Med TBR-652 Safe and Tolerable

May 18, 2011

An experimental antiretroviral (ARV) drug by Tobira Therapeutics, TBR-652, was found to be both safe and tolerable in a study published in the June 1 issue of the *Journal of Acquired Immune Deficiency Syndromes*.

TBR-652 is a type of drug known as a CCR5 antagonist. In the same family as the drug Selzentry (maraviroc), CCR5 antagonists bind to the CCR5 receptor that serves as a sort of doorknob that HIV uses to get into CD4 cells. Though these types of drugs are quite potent, they do not work in people who have virus that uses another receptor to enter cells, called CXCR4.

Until recently, tropism tests—which tell what receptors a person's HIV uses—have not been very sensitive. They misclassified people's virus in up to 10 percent of cases. This led doctors to be unsure of the best way to prescribe a CCR5 antagonist. More recently, much more sensitive tropism tests have become available, however, generating renewed interest in this class of drug.

As reported at last year's International AIDS Conference (IAC), TBR-652 was found to be quite potent at higher doses in a 10-day study performed in people who'd never taken ARVs before. At the 50, 75 and 150 milligram (mg) doses, people's virus plummeted by nearly 100-fold, which is in the range of some of the most potent ARVs currently available and similar to the reductions in HIV levels found with Selzentry.

TBR-652 also binds to a second cell receptor, potentially giving it additional properties that might prove beneficial to people with HIV. That cell receptor, CCR2, is associated with increased cellular inflammation and is implicated in diseases ranging from atherosclerosis and insulin-resistance to rheumatoid arthritis. Given that increased inflammation has been tied to heart attacks and other health problems in people with HIV, TBR-652's potential to reduce inflammation has piqued the interest of researchers.

In the 10-day study, reported in part at IAC, TBR-652 did significantly affect the inflammatory protein MCP-1. In those taking the 50 mg and 150 mg doses, MCP-1 levels rose, indicating less inflammation. In addition, TBR-652 appeared to lower high-sensitivity C-reactive protein (hsCRP), which indicates additional anti-inflammatory effects. Reductions in hsCRP did not reach a statistically significant level, however, meaning that the reductions could have occurred by chance.

In this new report of the same study, Jacob Lalezari, MD, from Quest Clinical Research in San Francisco, and his colleagues report on the safety and tolerability of TBR-652. They found that 10 days on the drug produced no serious side effects, regardless of the dose. Most of the side effects found were of mild to moderate intensity.

The predominant side effect was stomach problems—including nausea, diarrhea and stomach pain—although several of these also occurred in people who received a placebo. Two people taking TBR-652 required a prescription to manage their stomach pain or nausea.

Headache and abnormal dreams also occurred in a couple of individuals, predominantly at the highest dose of 150 mg. The primary laboratory abnormalities were generally attributable, at least partly, to other causes and were of mild to moderate severity.

The authors state that, “TBR-652 warrants further investigation as a potent, oral, un-boosted, once-daily CCR5 receptor antagonist to be used in combination HIV-treatment regimens, especially in treatment-naive patients.”

“The effect of CCR2 antagonism on hsCRP, IL-6 and other biomarkers of inflammation will be further investigated,” they continue, “with the hopes of clarifying their usefulness in predicting inflammatory processes and reducing the risk of inflammatory disease.”

The authors further add that researchers are carrying out studies on drug interactions with other ARVs so that they can begin a Phase II study.

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