Selzentry Comparable to Sustiva After 96 Weeks in Treatment Naives

July 21, 2009 By Tim Horn

Selzentry (Celsentri; maraviroc) is comparable to Sustiva (efavirenz) in HIV-positive patients starting antiretroviral (ARV) treatment for the first time, according to 96-week data from a reanalysis of a study that originally suggested that Selzentry was less effective than the standard-of-care non-nucleoside reverse transcriptase inhibitor (NNRTI). The latest review of the data, relying on a new enhanced-sensitivity tropism assay, was reported Tuesday, July 21, at the Fifth International AIDS Society (IAS) Conference on HIV Pathogenesis, Treatment and Prevention in Cape Town.

Selzentry, manufactured by Pfizer, has already been proved safe and effective in clinical trials involving treatment-experienced patients.

Pfizer's MERIT study, originally reported by Michael Saag, MD, of the University of Alabama at Birmingham, during the last IAS conference, held two years ago in Sydney, was the first to test the CCR5-blocking entry inhibitor in patients beginning HIV therapy for the first time. The study randomized treatment-naive patients to either Selzentry, using a 300 mg dose taken once or twice a day, or Sustiva, both used with Combivir (zidovudine plus lamivudine).

Sixteen weeks into the study, the once-daily Selzentry arm was discontinued because of inferior viral load responses.

Upon entering the study, patients had to have a pretreatment viral load above 2,000 and were required to have CCR5-tropic HIV—a strain of virus that targets CCR5 on the surface of CD4 cells as opposed to CXCR4, which typically arises in patients in more advanced stages of infection and usually renders Selzentry ineffective. Patients were screened for the study using an older version of Monogram Bioscience's Trofile assay, which can only detect CXCR4-using virus if it makes up more than 10 percent of the blood sample tested. Monogram's newer assay can detect CXCR4-using virus that makes up as little as 0.3 percent of the tested blood sample.

The average viral load and CD4 count at entry was 4.87 log and 250 cells, respectively. The average age was 37 years; roughly 71 percent of the study participants were male.

According to Saag's original presentation, based on data using the older Trofile assay, 69.3 percent of those in the Sustiva group, compared to 65.3 percent in the Selzentry group, had viral

loads below 50 copies after 48 weeks. Saag reported that this 4.2 percent difference was just large enough to suggest that Selzentry is inferior to Sustiva in terms of reducing viral load to undetectable.

In the original reanalysis of the 48-week study data—dubbed MERIT ES (extra sensitive)—reported at the 2008 joint meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and Infectious Disease Society of America (IDSA), Saag and his colleagues used the new ultra-sensitive Trofile assay to retest blood samples of those who enrolled in the study.

In the reanalysis using the new tropism assay, 15 percent of the patients enrolled in the study were found to have a dual/mixed population of CCR5- and CXCR4-using HIV at the start of the study. They were then removed from the reanalysis, given that they technically shouldn't have entered the study in the first place. At ICAAC and again at this year's IAS conference, Saag's team reported comparisons between Selzentry and Sustiva in a more pure population of patients with CCR5-using HIV.

Fifty-eight percent of patients in the Selzentry group, compared with 62 percent of patients in the Sustiva group, had viral loads below 50 copies after 48 weeks, according to the 96-week analysis. Results also show that, at the end of almost two years, a similar number of patients taking Selzentry remained on therapy compared to those taking Sustiva: 66.9 percent and 66 percent, respectively.

For patients with high viral loads upon entering the study—above 100,000 copies/mL—a similar number of patients taking Selzentry maintained undetectable viral load compared with those taking Sustiva—roughly 56 percent in both groups.

CD4 cell count gains were significantly greater in the Selzentry group compared with the Sustiva group after 96 weeks. Among those taking Selzentry for two years, CD4s were 212 cells above their pre-treatment levels, compared with a 171-cell gain in the Sustiva group.

At 96 weeks, similar to 48 weeks, the most common adverse effects reported by patients taking Selzentry were nausea, headache, fatigue and dizziness. Among those taking Sustiva, the most commonly reported adverse effects were nausea, headache, diarrhea, dizziness, vomiting and abnormal dreams.

Pfizer has indicated to AIDSmeds.com that, in light of these more encouraging findings, discussions with regulatory agencies—such as the U.S. Food and Drug Administration—are ongoing regarding the possible approval of Selzentry for HIV-positive people starting therapy for the first time.
