People With X4 Virus Who Failed Selzentry Have Good Long-Term Results

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People who failed treatment on the entry inhibitor Selzentry had good long-term health outcomes after switching their antiretroviral (ARV) regimen, despite having an HIV-strain that has been associated with poorer health. These data were presented September 13 at the 50th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Boston.

Most strains of HIV use a cellular coreceptor known as CCR5 or “R5” to enter and infect CD4 cells. Other strains use a different receptor, CXCR4 or “X4,” while still other strains use both. A number of years ago, scientists observed that the dominant strain of HIV switches from R5 to X4 in people with advanced disease and that people with X4 or mixed virus have lower CD4 cells and more accelerated disease progression than people with only R5 virus..

This phenomenon was a serious concern as the first CCR5 entry inhibitor, Selzentry (maraviroc), was being developed. If Selzentry—by suppressing R5 virus—caused X4 virus to develop or dominate, scientists worried it could lead to much faster disease progression.

To help address this concern, researchers from Pfizer—Selzentry’s maker—analyzed follow-up data from 15 people who had experienced treatment failure while taking Selzentry in the MERIT study. MERIT was designed to compare Selzentry with Sustiva (efavirenz) in people starting ARV therapy for the first time. To be eligible for this analysis, a person needed to have a switch in his or her virus’s coreceptor preference, or “tropism,” after starting treatment.

The average CD4 count of these study participants before staring Selzentry was 220, and the average viral load was 117,000. The average time from starting treatment and having a tropism switch was 85 days, though the average time to treatment failure was 183 days. Average follow-up of the participants after failing on Selzentry was nearly four years. In two of the 15 people, the shift from R5 to X4 virus persisted even after they stopped taking Selzentry.

Unfortunately, only one test was available to measure the tropism of a person’s virus at the time that MERIT was running, and this test wasn’t very sensitive. This meant that a substantial percentage of people initially classified as having only R5 virus and let into the study actually had low levels of X4 virus as well. Based on reanalysis of the 15 study participants using more

sensitive tests that are now available, as many as eight actually had measurable X4 virus during the screening period, and would have been excluded from the study.

Regardless, most of the participants had no negative consequences from their viral tropism switch. Fourteen of the 15 achieved undetectable virus on their subsequent regimen. Also, there were only two serious health problems during the follow-up—secondary syphilis and tuberculosis—and experts determined that neither had any relationship to its ARV therapy.

“With extended follow-up, no adverse clinical consequences were observed following failure-associated emergence of CXCR4-using virus with [Selzentry],” concluded the authors. “Subjects had good immunological outcomes and responded to subsequent therapy.”

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