IL-2 May Delay Need for Antiretroviral Treatment

September 19, 2007 By Tim Horn

An intriguing study suggests that periodic injections with interleukin-2 (IL-2) may allow HIV-positive patients to keep their CD4 counts high and postpone their need to begin antiretroviral therapy. Results from the 130-patient French clinical trial were reported yesterday at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Chicago.

IL-2, approved as Proleukin (aldesleukin) in the United States and licensed for the treatment of various cancers, remains an experimental immune-based therapy for HIV. Unlike drugs currently used to treat HIV, IL-2 does not attack the virus but rather boosts the production and activity of several important immune system cells, notably CD4s and CD8s.

While numerous studies have found that IL-2 greatly increases CD4 cell counts in people with HIV—especially those who have relatively healthy levels when starting the drug—researchers have been unable to carve out a niche for the drug in the HIV treatment repertoire.

There have also been concerns that IL-2's ability to increase CD4 cell counts has a drawback. With the CD4 count jump, there is a greater number of cellular targets for HIV to attack, potentially causing viral load to skyrocket. In turn, experts have remained cautious about using IL-2 in the absence of antiretroviral therapy to keep viral load in check.

Jean-Michel Molina, MD, of Saint-Louis Hospital in Paris, and his colleagues conducted a clinical trial to determine if the CD4-boosting effects of IL-2 might delay the need for antiretroviral therapy in HIV-positive patients, while at the same time studying the drug's effect on viral load in the absence of treatment.

Patients were randomized to placebo or intermittent cycles of IL-2: twice-daily subcutaneous injections of IL-2—using a moderate dose of 4 million units (MIU)—for five days, beginning at the start of the study and at weeks 8, 16, and 24, along with two additional cycles between weeks 48 and 80.

During the study's 96-week follow-up period, IL-2 treatment (or placebo) was considered to be a failure if patients developed an HIV-related health problem or their CD4 counts fell below 300—a

typical cutoff for beginning antiretroviral therapy.

At the start of the study, patients' viral loads averaged 75,000 copies and CD4 counts averaged 383 cells. Sixty-six patients underwent the intermittent cycles of IL-2 whereas 64 received placebo.

Approximately 95 percent in the IL-2 group underwent three treatment cycles; 89 percent completed four and 52 percent completed additional cycles after 48 weeks.

Through week 96, 36 percent of patients in the IL-2 group, compared with 61 percent in the placebo group, experienced treatment failure. This difference was highly statistically significant, meaning that it wasn't due to chance. What's more, the time to treatment failure was significantly shorter in the placebo group, meaning that patients who didn't receive IL-2 became candidates for HIV treatment much earlier on in the study.

As for CD4 counts at the end of the 96-week follow-up period, those in the IL-2 group averaged a 51-cell increase over their pre-study levels, compared with a 64-cell decline in the placebo group. Dr. Molina also noted that viral loads increased only slightly in both groups, with no statistically significant differences between them.

Consistent with other studies, side effects of IL-2 were observed in a large number of patients. Approximately 85 percent of the IL-2 recipients experienced weakness (asthenia), 83 percent developed experienced fevers, and 53 percent reported nausea.

Dr. Molina concluded by noting that antiretroviral therapy was delayed by an average of 48 weeks among those who received IL-2. "In antiretroviral-naive patients with 300 to 500 CD4 cells," he and fellow authors state in their published abstract, "IL-2 therapy was able to induce sustained increases in CD4 cells without affecting HIV replication, allowing patients to substantially defer the initiation of antiretroviral therapy."

Source:

Molina J, Levy Y, Hamonic S, et al. **Intermittent interleukin-2 therapy to defer antiretroviral therapy in patients with human immunodeficiency virus infection** [Abstract H-718]. 47th Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, 2007.
