PRO 140 Has Long-Lasting Activity Against HIV

October 28, 2008 By Tim Horn

Positive early results from a Phase II clinical trial of intravenous (IV) PRO 140, an experimental HIV entry inhibitor, were reported October 26 at the 2008 joint meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the Infectious Disease Society of America (IDSA). Separately, Progenics Pharmaceuticals announced this week encouraging results from a study evaluating a much more user-friendly subcutaneous (SC) formulation of PRO 140.

PRO 140 is a laboratory-made antibody that binds to a protein on the CCR5 membrane of CD4 cells. Once PRO 140 does this, HIV cannot successfully bind with the surface of CD4s; thus the virus is prevented from infecting healthy cells.

While Pfizer's Selzentry (maraviroc) works differently from PRO 140, both drugs target CCR5 and are considered HIV entry inhibitors.

The Phase II study reported at ICAAC/IDSA by Jeffrey Jacobson, MD, of Drexel University College of Medicine in Philadelphia evaluated IV PRO 140 in HIV-positive patients who had not taken any antiretrovirals (ARVs) for at least three months before enrollment. Using tropism testing, all study volunteers were required to have HIV that uses the CCR5 co-receptor to enter CD4 cells; patients with virus that uses another co-receptor called CXCR4 were excluded.

The 31 patients enrolled were monitored for 58 days following a single-dose infusion of placebo or one of two doses of PRO 140 (either 5 or 10 milligrams per kilogram [mg/kg] of body weight). The average viral load upon study entry was 35,000 copies; the average CD4 count at the start of the study was 403 cells.

The interim analysis reported by Dr. Jacobson involved the first 15 patients treated in the study, with five patients randomized to each of the three groups.

In the 5 mg/kg group, the average maximum viral load drop was 1.9 log—very similar to the results of a Phase Ib study reported in July 2007. In the 10 mg/kg group, the average maximum viral load drop was 2.17 log. These reductions in viral load, compared with a 0.5 log drop in the placebo group, were statistically significant, meaning that the differences were too large to have occurred by chance.

As was seen in earlier studies, PRO 140 continued to work against HIV long after single-infusion therapy. In the 10 mg/kg group, for example, viral loads remained an average of 1.55 log below their pre-treatment levels.

IV administration of PRO 140 was “generally well tolerated” compared with placebo infusions. According to Jacobson, there were no serious drug-related side effects.

Progenics has developed an SC injection version of PRO 140. According to the company, a recently completed proof-of-concept study reports that five patients who used once-weekly injections of the drug, at a dose of 324 mg, experienced a maximum average viral load reductions of 1.77 log.

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