Single-Dose PRO 140 Has Lasting Effects

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Researchers once again reported promising results from an early study of PRO 140, an experimental HIV entry inhibitor. As was reviewed at a conference this past summer, and summarized again this week at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy in Chicago, the greatly prolonged antiviral effect may mean simple injectable dosing once every other week.

PRO 140, a laboratory-made antibody that blocks the CCR5 receptor on CD4 cells, is being developed by Progenics Pharmaceuticals, based in Tarrytown, NY. By blocking CCR5, PRO 140 prevents HIV from successfully binding with the surface of CD4s, preventing the virus from infecting healthy cells.

Progenics' clinical trial, conducted at 10 sites in the United States, evaluated three single intravenous doses of PRO 140: 0.5 milligram per kilogram (mg/kg) of body weight, 2.0 mg/kg and 5.0 mg/kg. No other HIV medications were taken in the study.

A total of 39 HIV-positive patients, none of whom had used antiretrovirals in the past, were enrolled. They were all required to have virus using the CCR5 coreceptor (as opposed to HIV that uses the CXCR4 coreceptor). Of the 13 patients in each dosing group, 10 patients received PRO 140 and three received placebo.

Reductions in viral load were the primary focus of the study. Patients who received 5.0 mg/kg of PRO 140 achieved an average maximum viral load drop of 1.83 log, with some patients achieving viral load reductions of 2.5 log.

Ten days after receiving single-dose PRO 140, viral loads dropped by an average of 1.7 log in the 5.0 mg/kg group, compared to average reductions of 1.2 log in the 2.0 mg/kg group, 0.58 log in the 0.5 mg/kg group and 0.39 log in the placebo group.

After two to three weeks, patients who received 5.0 mg/kg PRO 140 still averaged viral loads 1.0 log below pretreatment levels. By day 28 of the study, most patients in the trial saw their viral loads return to pre-treatment levels.

CD4 counts increased, on average, by 129 cells in the 5.0 mg/kg PRO 140 group by day 8. The elevations in all groups persisted for approximately three weeks after the drug was administered.

The authors note that CD4 cells are “maximally coated” with PRO 140 one to two weeks after dosing, a finding that is consistent with the antiviral effect of the drug.

The study also found PRO 140 to be generally well tolerated with no serious drug-related adverse events reported. Two of the 39 patients in the study—one receiving PRO 140 and another receiving placebo—experienced a switch in their HIV tropism, from CCR5-using virus to dual-tropic (CCR5 and CXCR4) virus.

One patient in the study developed antibodies to PRO 140, though it is not yet known if this will have an affect on treatment responses or cause side effects.

The company is reporting that it has developed a subcutaneous injection version of PRO 140—an advantage over an intravenous formulation, which would require a health care professional to administer the drug. The company has plans to explore the subcutaneous formulation in pending clinical trials.

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