First HIV Gene Therapy Proves Safe With Hint of Effectiveness

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A clinical trial exploring a gene therapy called OZ1 in people with HIV proves that it can be done safely, according to a study published February 15 in *Nature Medicine* and reported by *ScienceDaily*. While the treatment did not seem to have any discernible effect on viral load, CD4 cells among OZ1 recipients remained higher than those in the placebo group for two years of follow-up.

Despite the promise of gene therapy for many diseases, it does carry the risk that modified genes can have dangerous and unintended effects on the body. Side effects in an early gene therapy experiment in children several years ago brought the field to a screeching halt. Gene therapy experiments in people with HIV were restarted within the past few years, and until now none had reported both safety and efficacy results.

To determine the safety and effectiveness of a gene therapy called OZ1, Ronald Mistuyasu, MD, from the University of California in Los Angeles and his colleagues randomized 74 HIV-positive patients to receive either the gene therapy or a placebo. All of the patients had stem cells removed and reinfused. Roughly half of the study volunteers received cells that had been modified with the OZ1 molecule; the rest received unmodified cells. All patients had been taking antiretroviral therapy, and all stopped taking their drugs after being reinfused with their own stem cells. Mitsuyasu's team tracked the patients' CD4 counts and virus levels after the infusion of cells.

Though there was no significant difference in viral loads between the placebo and OZ1 recipients, there were also no differences in safety or side effects. There were, however, hints that the OZ1 did prompt an antiviral response, with those receiving the gene-modified cells having consistently higher CD4 counts throughout 100 weeks of follow-up.

"Part of the reason that we didn't see a larger effect is that the persistence of the anti-HIV gene in the patients' blood was not as long as we would have liked," Mistuyasu said. "We need to find better ways to get the genes into the patients and maintain them."

He recommends further research to determine whether using other gene delivery mechanisms or possibly treating people first with drugs that kills off native stem cells—to make room for the new cells—will be more effective.