Remarkably Low Dose of MK-8591 Protects Monkeys Against HIV-Like Virus

Merck’s investigational antiretroviral could one day be dosed only weekly among humans.

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An extraordinarily low weekly dose of Merck’s investigational antiretroviral MK-8591 protected rhesus macaque monkeys against rectal infection with a simian form of HIV known as SHIV. This finding indicates that the drug could one day be dosed only weekly among humans.

Martin Markowitz, MD, a professor at the Aaron Diamond AIDS Research Center in New York City presented findings from a study of eight initially SHIV-negative monkeys at the 2018 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

MK-8591 belongs to a new investigational class of antiretrovirals (ARVs); it is a nucleoside reverse transcriptase translocation inhibitor. A previous study showed that the drug completely protected rhesus macaques against rectal SHIV infection when it was dosed at 3.9 milligrams per kilogram of body weight weekly.

The new study sought to determine the lowest effective dose of MK-8591 for preventing rectal SHIV infection among such animals.

Eight male rhesus macaques were treated with 3.9 mg/kg of MK-8591 weekly for 20 weeks and 1.3 mg/kg of the drug once weekly for six weeks after that. They were exposed to SHIV rectally six days after first receiving the first lower dose of the drug and weekly thereafter until they contracted the virus or had received up to four exposures.

The animals that remained SHIV negative after this treatment phase received no MK-8591 for four weeks before undergoing the same protocol of treatment and weekly exposure to the virus once again, only this time they received 0.43 mg/kg of the drug weekly.

Next, the researchers took any remaining SHIV-negative animals off MK-8591 for 10 weeks and repeated the treatment and exposure protocol at a dose of 0.1 mg/kg.

All eight animals remained SHIV negative after the rectal exposures to the virus conducted while

they received 1.3 and 0.43 mg/kg of MK-8591. During the 0.1 mg/kg treatment phase, two of the animals contracted the virus, one after three exposures and the other after four exposures.

The study authors concluded that MK-8591 completely protects against SHIV infection when dosed at 1.3 and 0.43 mg/kg each week and is partially protective when dosed at 0.1 mg/kg weekly. (The lower dose is associated with a 7.2-fold greater likelihood of SHIV acquisition compared with the higher doses.)

Consequently, the investigators speculated that humans could achieve protection against HIV with a weekly dose of MK-8591 of a mere 250 micrograms (0.25 milligrams) weekly or 10 micromicrograms (0.00000007 mg) daily. By comparison, daily Truvada (tenofovir disoproxil fumarate/emtricitabine) as pre-exposure prophylaxis (PrEP) contains a respective 200 mg and 300 mg of the two ARVs contained in the tablet.

To read the conference abstract, click here.

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