Gilead's HIV Capsid Inhibitor Might Need Dosing Only Every 6 Months

Studies indicate that there is a very low likelihood that people with HIV have preexisting resistance to the medication.

November 8, 2019 By Benjamin Ryan

Gilead Sciences' experimental capsid inhibitor antiretroviral (ARV), GS-6207, may require dosing only every six months. Additionally, research indicates that there is a very low likelihood that people with HIV will have preexisting resistance to the medication.

Researchers presented a series of studies about GS-6207 at the 17th European AIDS Conference (EACS) in Basel, Switzerland.

In a Phase I study, 40 HIV-negative people were randomized into five groups of eight who received either injections under the skin of GS-6207 at doses of 30, 100, 300 or 450 milligrams or a placebo injection. The study found that the drug was safe and well tolerated. The most common adverse health events were injection site reddening and irritation (47% experienced this) and injection site pain (38%). These effects were mild and resolved within a few days.

An analysis of the participants' metabolism of GS-6207 found that the injection provided prolonged exposure in the body to the drug, which remained detectable for at least 32 weeks. This finding suggests that the drug could perhaps be dosed as seldom as every six months.

In an ongoing, double-blind, placebo-controlled proof-of-concept Phase Ib study, people with HIV who had never taken an experimental capsid inhibitor as part of another study (there are currently no approved drugs from this class) were randomized to receive a single dose of 20, 50, 150 or 450 mg of GS-6207 (six people per dosing group in each of the study's overall cohorts) or a placebo injection (two people per dosing group per cohort).

Ten days after the injection, the reduction in viral load was greater in all the treatment groups compared with the placebo groups and ranged from an average of a 25-fold to a 158-fold reduction, depending on the dosing.

In this study, GS-6207 was also generally safe and well tolerated. The most common adverse health events were injection site pain (41% experienced this) and injection site redness and irritation (28%)—reactions that, again, were all mild and resolved within a few days.

Researchers also analyzed a database of blood samples from 1,500 people with HIV, including 500 people who had not yet taken ARVs; 500 people who had taken ARVs but had not taken protease inhibitors; and 500 people who had taken ARVs and had experienced virologic failure on a protease inhibitor, including both those who did and did not have resistance to that class of drugs. The investigators screened these samples for a series of viral mutations that are associated with resistance to capsid inhibitors. None of the samples had these mutations, which suggests a very low likelihood—perhaps less than 1 in 1,500—that people in the HIV population have preexisting resistance to this drug class.

Lastly, a study looked at isolates of HIV from 51 people that had a naturally occurring variation known as a gag polymorphism that could be associated with a loss of GS-6207's potency in suppressing the virus. The isolates were taken from 15 people who had not been treated with ARVs and 36 people who had. The capsid inhibitor proved highly potent against these individuals' virus in the lab experiments. The drug was not affected by the presence of gag polymorphism or viral mutations associated with protease inhibitor resistance.

Gilead is on the cusp of beginning enrollment into two new clinical trials of GS-6207 given in combination with other ARVs in people with HIV. This includes a Phase II/III study including people who have taken many ARVs and have multidrug resistant virus as well as a Phase II study including people starting HIV treatment for the first time. Participants in these trials will take an oral version of GS-6207 for two weeks and then receive injections of the drug every six months.

To read a press release about the studies, click here.

For information about the new studies beginning enrollment, click here for the study in people who have taken many ARVs, and click here for the study in people starting HIV treatment for the first time.
