An HIV drug you only take twice a year?

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Scientists are reporting an early step toward an HIV drug that could potentially be taken only a couple of times per year.

A single injection of the experimental drug, called lenacapavir, was able to lower blood levels of HIV in a small group of patients. And it was capable of maintaining active levels in the blood for more than six months.

It all raises the possibility of one day having an HIV treatment that only needs to be taken twice a year.

The current treatment regimens for HIV—combinations of oral drugs often called "cocktails"—generally work quite well, said study co-author Dr. Martin Rhee.

"But patients often say that over time, taking daily pills can be a burden," said Rhee, director of clinical research for Gilead Sciences, Inc.—which is developing lenacapavir.

So the hope is that longer-acting HIV medications could "free people from daily pills," Rhee said.

Beyond that, he noted, longer-acting drugs could potentially offer a simpler way to prevent HIV in high-risk people: Right now, that's done with a daily pill regimen known as PrEP (pre-exposure prophylaxis).

However, much more work remains ahead. The new study, published July 1 in the journal *Nature*, offers a "proof of principle" that a dosing interval of every six months is possible, Rhee said.

The researchers found that in 40 healthy people, lenacapavir appeared safe and could remain active in the body for more than six months. And in 32 people with previously untreated HIV, a single injection reduced viral levels in the blood within nine days.

It's encouraging that the drug is "amenable to dosing every six months," said Dr. Rajesh Gandhi, an infectious disease physician at Massachusetts General Hospital, in Boston.

Gandhi, who is also chair-elect of the HIV Medicine Association, agreed there is a need for longer-acting HIV drugs.

The catch is that HIV is not treated with one drug alone—to keep the virus suppressed and limit the chances of it becoming resistant to medication.

So, for any twice-a-year regimen to become a reality, Gandhi explained, two long-acting drugs would have to be paired.

"So the question is, what do you partner this drug with?" he said.

Rhee said Gilead is working on such a partner. More immediately, the researchers will study the effects of lenacapavir, taken every six months, in HIV patients who've tried many standard drugs and are resistant to them.

Other longer-acting drugs for HIV are further along—though the doses are more frequent than

twice a year.

Researchers are studying a combination of two injection drugs—cabotegravir and rilpivirine—that is given monthly. The hope is to keep HIV suppressed in patients who've gotten the virus down to very low levels with standard oral drugs.

Meanwhile, cabotegravir is also being tested for preventing HIV in high-risk people, according to the U.S. National Institutes of Health. In those trials, injections are given every two months.

But while infrequent doses would be convenient and—hopefully—make adherence easier, there are safety questions. If people have side effects from the drug, for example, does that mean they are stuck with them for six months?

To help avoid that, Gandhi said, studies have been using a "lead-in" phase: Patients first take oral versions of the long-acting drugs, to make sure they can tolerate them.

But another concern, Gandhi said, is what could happen if patients miss or delay an injection: As levels of the drug wane in the body, the virus could come roaring back, and possibly develop resistance to the medication.

Rhee agreed that is an issue that will face all long-acting HIV medications under development.

Still, the progress toward new options is encouraging, according to Gandhi. People with HIV should know that scientists are still working on new treatments, he said—including ways to potentially cure it.

"We're still committed to finding a cure," Gandhi said.

More information: John O. Link et al. Clinical targeting of HIV capsid protein with a long-acting small molecule, *Nature* (2020). DOI: 10.1038/s41586-020-2443-1 , www.nature.com/articles/s41586-020-2443-1