Experimental Drug Ciapavir Spurs Reactivation of Latent HIV

The investigational drug showed promise as a component of a “shock and kill” HIV cure approach in a mouse study.

June 30, 2020 By Benjamin Ryan

Experiments in mice have led researchers to conclude that the experimental drug ciapavir shows promise as a component of a “shock and kill” approach to curing HIV because it causes resting HIV-infected cells to begin replicating again, but without driving substantial immune activity.

Even when HIV is well treated with antiretrovirals (ARVs), it remains hidden in what’s known as the viral reservoir, which is composed in large part of long-living immune cells infected with the virus that are in a latent, or nonreplicating, state. Because ARVs can only attack the virus when cells are actively multiplying, this leaves the latently infected cells protected from HIV treatment’s effects.

“Shock and kill” is one of a handful of main avenues the ever-expanding HIV cure research field has taken. It involves prompting, or shocking, latently infected cells to reactivate as well as a method of killing off those cells.

Thus far, researchers have struggled to come up with a particularly promising “shock” treatment.

For the new paper, which was published in Cell Reports Medicine, investigators injected ciapavir into HIV-infected mice engineered to have a human immune system. Levels of HIV rose in the animals’ blood and bone marrow, indicating to the study authors that ciapavir had succeeded in reactivating latently infected cells.

What’s more, the treatment led to only minimum immune activation.

Substantial activation of the immune system can be harmful, even fatal.

“What scientists have found with other ‘shock’ approaches is that they can be too hot and over activate the immune system or too cold and don’t wake up the virus,” Sumit Chanda, PhD, director of the immunity and pathogenesis program at the Cancer Center at Sanford Burnham Prebys in La Jolla, California, and the study’s lead corresponding and co–senior author, said in a press release. “Our research identifies a drug that works in the ‘Goldilocks’ zone—it reawakens the virus without activating the immune system. Our work also provides further evidence that this drug class, called

Smac mimetics, is a promising approach to reactivating latent HIV."

Ciapavir has already undergone safety testing in humans in clinical trials for use as a cancer treatment.

For its use as a component of an HIV cure therapy, investigators will next study ciapavir in monkeys while also conducting additional studies to determine the drug's safety in humans.

"Ciapavir is the first Smac mimetic specifically optimized for an HIV cure, so it is significantly more potent for HIV than other molecules in this class," said Nicholas Cosford, PhD, deputy director of the Cancer Center at Sanford Burnham Prebys and co–senior author of the study. "As a result, ciapavir may be effective when used on its own instead of in combination with a second drug, as our previous research showed, and potentially at lower doses."

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

To read the study abstract, click here.

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