

Antiviral compound provides full protection from Ebola virus in nonhuman primates

October 9 2015

Rhesus monkeys were completely protected from the deadly Ebola virus when treated three days after infection with a compound that blocks the virus's ability to replicate. These encouraging preclinical results suggest the compound, known as GS-5734, should be further developed as a potential treatment, according to research findings to be presented tomorrow at the IDWeek conference.

Travis Warren, Ph.D., a principal investigator at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), said the work is a result of the continuing collaboration between USAMRIID and Gilead Sciences of Foster City, Calif. Scientists at the Centers for Disease Control and Prevention (CDC) also contributed by performing initial screening of the Gilead Sciences compound library to find molecules with promising [antiviral activity](#).

The initial work identified the precursor to GS-5734, a small-molecule antiviral agent, which led to the effort by Gilead and USAMRIID to further refine, develop and evaluate the compound. Led by USAMRIID Science Director Sina Bavari, Ph.D., the research team used cell culture and animal models to assess the compound's efficacy against several pathogens, including Ebola [virus](#).

In animal studies, treatment initiated on day 3 post-infection with Ebola virus resulted in 100 percent survival of the monkeys. They also exhibited a substantial reduction in viral load and a marked decrease in the physical signs of disease, including internal bleeding and tissue

damage.

"The compound, which is a novel nucleotide analog prodrug, works by blocking the viral RNA replication process," said Warren. "If the virus can't make copies of itself, the body's immune system has time to take over and fight off the infection."

In cell culture studies, GS-5734 was active against a broad spectrum of viral pathogens. These included Lassa virus, Middle East Respiratory Syndrome (MERS) virus, Marburg virus, and multiple variants of Ebola virus, including the Makona strain causing the most recent outbreak in West Africa.

"This is the first example of a small molecule—which can be easily prepared and made on a large scale—that shows substantive post-exposure protection against Ebola virus in [nonhuman primates](#)," Bavari commented. "In addition to 100 percent survival in treated animals, the profound suppression of viral replication greatly reduced the severe clinical signs of disease."

Taken together, the robust therapeutic efficacy observed in primates and the potential for broad-spectrum antiviral activity suggest that further development of GS-5734 for the treatment of Ebola virus and other viral infections is warranted, Bavari said.

According to Tomas Cihlar, Ph.D., of Gilead Sciences, the company is currently conducting phase I clinical studies of the compound in healthy human volunteers to establish the safety and pharmacokinetic profile.

"We are exploring alternative directions for developing this compound, including potential use of the animal efficacy rule," Cihlar said, referring to a regulatory mechanism under which the U.S. Food and Drug Administration may consider efficacy findings from adequate and well-

controlled animal studies of a drug in cases where it is not feasible or ethical to conduct human trials.

Ebola virus causes severe hemorrhagic fever in humans and nonhuman primates with high mortality rates and continues to emerge in new geographic locations, including West Africa, the site of the largest outbreak to date. Over 28,000 confirmed, probable and suspected cases have been reported in Guinea, Liberia and Sierra Leone, with over 11,000 reported deaths, according to the World Health Organization. Although several clinical trials are currently underway, there are no licensed vaccines or therapies against Ebola virus.

Research on Ebola virus is conducted in Biosafety Level 4 (maximum containment) laboratories, where investigators wear positive-pressure "space suits" and breathe filtered air as they work. USAMRIID is the only organization in the Department of Defense with Biosafety Level 4 capabilities, and its research benefits both military personnel and civilians.

More information: idsa.confex.com/idsa/2015/webprogram/Paper54208.html

Provided by US Army Medical Research Institute of Infectious Diseases

Citation: Antiviral compound provides full protection from Ebola virus in nonhuman primates (2015, October 9) retrieved 17 April 2024 from <https://medicalxpress.com/news/2015-10-antiviral-compound-full-ebola-virus.html>

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