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Drug targeting Ebola virus protein VP24 shows promise in monkeys

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An experimental medication that targets a protein in Ebola virus called VP24 protected 75% of a group of monkeys that were studied from Ebola virus infection, according to new research conducted by the U.S. Army, in collaboration with Sarepta Therapeutics, Inc. The study was published this week in *mBio*, the online open-access journal of the American Society for Microbiology

The research compared drugs called phosphorodiamidate morpholino oligomers (PMOs) —- synthetic "antisense" molecules that target the genetic code within Ebola and similar viruses, preventing their ability to reproduce. While previous work by the authors showed that a combination PMO targeting the genes that code for proteins called VP35 and VP24 protected rhesus monkeys from Ebola virus infection, the current study revealed that targeting VP24 alone was sufficient to confer protection from Ebola virus, whereas an agent targeting VP35 alone resulted in no protection.

The majority of monkeys treated with a medication called AVI-7537, which targets VP24, survived infection with Ebola virus and showed substantial reduction of virus in their bloodstreams within eight days of treatment, compared to animals receiving a placebo.

"The study demonstrates that we can protect non-human primates from Ebola virus, using only a single antisense agent," said lead study author Travis K. Warren, PhD, a principal investigator in the Molecular and Translational Sciences Division at the U.S. Army Medical Research

Institute of Infectious Diseases in Fort Detrick, Md.

Response in these animals is generally considered a gold standard to predicting similar response in humans, he said. Many of the products that are being used by doctors to treat patients infected with Ebola virus in West Africa have not been tested in any animal model or in non-human primates, he said. Despite many efforts to develop vaccines and antiviral medicines against filoviruses like Ebola, there are currently no licensed medical countermeasures against these viruses.

During the study, researchers gave Ebola virus-infected rhesus monkeys one of three medications: AVI-7537; AVI-7539, which targets VP35; or a combination treatment that included both AVI-7537 and AVI-7539, called AVI-6002. A fourth group of monkeys received just saline and served as the control group. The animals received these treatments intravenously, once a day for up to 14 days.

Seventy-five percent of animals treated with AVI-7537 and 62 percent of animals receiving the combination treatment, AVI-6002, survived until the end of the study. By contrast, animals receiving saline developed progressive signs of Ebola disease and succumbed within an average of eight days following infection, and animals treated with AVI-7539 succumbed within 10 days of infection.

Additional tests showed that AVI-6002 and AVI-7537 were similar in their ability to reduce viral load, substantially reducing or eliminating infectious virus and viral RNA in the animals' bloodstreams. Animals treated with AVI-6002 and AVI-7537 also had less liver and kidney damage, a common complication of filovirus infection, than those treated with placebo or AVI-7539.

"The work demonstrates that impairment of VP24 alone is enough to protect against Ebola virus infection and that targeting VP24 may lead to

the development of more effective countermeasures against this important viral pathogen," said senior study author Sina Bavari, PhD, Science Director for the U.S. Army Medical Research Institute of Infectious Diseases.

Provided by American Society for Microbiology

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