

Cidofovir Reported to Have Activity Against Poxvirus Infection in Primates

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Researchers from the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) have disclosed that Gilead Sciences' antiviral drug cidofovir prevented death and disease associated with poxvirus infection in animals. In primates infected with monkeypox, cidofovir treatment reduced respiratory symptoms, fever and pox-like skin lesions and decreased mortality associated with the viral infection.

These data were presented this week in Atlanta, Georgia by Dr. John W. Huggins, Chief, Department of Viral Therapeutics, Virology Division of USAMRIID, at The International Conference on Emerging Infectious Diseases. The conference is organized by the U.S. Centers for Disease Control and Prevention (CDC), the Council of State and Territorial Epidemiologists, the American Society for Microbiology (ASM) and the CDC Foundation. The conference is designed to encourage the exchange of scientific and public health information on global emerging infectious disease issues and highlight scientific activities that address these threats.

"This is the first time we have data in primates that confirm a drug's potential activity against orthopoxvirus infections," Dr. Huggins said. "The disease observed in primates infected with monkeypox is clinically similar to what occurs in humans, so we are quite encouraged by cidofovir's activity in this model. Our next step will be to conduct additional studies to better define the utility of cidofovir for the potential treatment of poxvirus infection in humans."

Ongoing Threat of Monkeypox in Africa

Poxvirus infections in humans historically caused significant disease and death until the advent of efficient poxvirus vaccines in the early 1800's. The public health threat of poxvirus has recently resurfaced with the observation of increased cases of monkeypox infection in humans. For example, research teams from the World Health Organization (WHO) report that from February 1996 to October 1997, more than 400 cases of human monkeypox were confirmed in the Democratic Republic of the Congo (formerly known as Zaire).

Monkeypox infection in humans is associated with signs and symptoms similar to smallpox, including the development of pox-like skin lesions (pustular rash), fever and respiratory symptoms, with subsequent lung hemorrhage and pneumonia. In severe cases, the associated respiratory illness may lead to death.

Monkeypox typically has been transmitted to humans via contact with infected primates or ground squirrels. Recently, however, person-to-person contact has increased and is now the apparent route of transmission in approximately 75 percent of observed cases in the Democratic Republic of the Congo.

Based upon the increase in reported cases, scientific research teams at USAMRIID accelerated efforts to identify experimental or marketed compounds with antiviral activity against poxviruses. Previously, researchers demonstrated that poxviruses contain a DNA polymerase necessary for viral replication and which is similar to the DNA polymerase of herpesviruses. This finding led to the screening of anti-herpes agents for the potential treatment of poxvirus infections.

Among the viral polymerase inhibitors tested in laboratory assays (in vitro), cidofovir was found to have potent and broad-spectrum anti-poxvirus activity. Based upon these data, the team of researchers at USAMRIID designed and conducted the in vivo experiments presented at this week's conference that confirm the poxvirus activity of cidofovir in animals. In these controlled studies, cidofovir was co-administered with oral probenecid and hydration to minimize the potential for nephrotoxicity, the dose-limiting side effect of this therapy.

The U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), located at Ft. Detrick, Maryland, is a leader in evaluating potential agents for the prevention and treatment of emerging viral diseases that must be studied in its high-hazard biocontainment laboratories.

Gilead Sciences is an independent biopharmaceutical company that seeks to provide accelerated solutions for patients and the

people who care for them. The Company discovers, develops, and commercializes proprietary therapeutics for important viral diseases, including a currently marketed product for the treatment of CMV retinitis, a sight-threatening viral infection in patients with AIDS. In addition, the Company is developing products to treat diseases caused by HIV, hepatitis B virus and influenza virus. Gilead common stock is traded on The Nasdaq Stock Market under the symbol GILD.