INFECTIOUS DISEASES

Efficacy of remdesivir in a rhesus macaque model of MERS-CoV infection

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Remdesivir (GS-5734), a drug developed by Gilead Sciences, is currently under trial for the treatment of COVID-19, the disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Remdesivir, a nucleotide analogue that blocks viral replication, has shown in vitro efficacy against SARS-CoV-2 and in vitro and in vivo efficacy in mice against two coronaviruses responsible for previous respiratory disease outbreaks, SARS-CoV and Middle East Respiratory Syndrome coronavirus (MERS-CoV).

Although most attention is now on pandemic SARS-CoV-2, cases of MERS continue to emerge and the World Health Organization has listed MERS-CoV as a priority pathogen for research and development. Clinical trials for MERS-CoV vaccines are underway, but efforts to identify antiviral treatments and translate them to the clinic are lagging.

In a study published in *PNAS*, investigators from the NIH now report that remdesivir can reduce the severity of the disease in rhesus macaques infected with MERS-CoV; these results provide further evidence of the potential for remdesivir to treat MERS-CoV infections.

In the study, 18 rhesus macaques were randomly assigned to three groups. The control group included three animals treated with vehicle solution 24 h before MERS-CoV inoculation and three animals treated at 12 h post MERS-CoV inoculation. A group of six rhesus macaques was treated prophylactically with remdesivir 24 h before MERS-CoV inoculation, and one group of six animals was treated therapeutically with the drug at 12 h post-inoculation with MERS-CoV. Treatments were then administered daily until 6 d post-inoculation (dpi).

All animals from the control group showed clinical signs of the disease, such as increased respiratory rates, whereas prophylactic and therapeutic treatments respectively prevented or reduced clinical disease.

Analysis of the levels of viral RNA by qRT-PCR at 6 dpi revealed lower viral load in the lungs of treated animals compared with those in the controls. Histological examination showed that therapeutic treatment decreased the severity of lung lesions compared with vehicle-treated animals. The lungs of the prophylactically treated animals were normal.

"Taken together, the data presented here on the efficacy of remdesivir in prophylactic and therapeutic treatment regimens, the difficulty of coronaviruses to acquire resistance to remdesivir, and the availability of human safety data warrant testing of the efficacy of remdesivir treatment in the context of a MERS clinical trial," say the investigators in their report.

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