Conclusions. Surges in MMR administration and heightened community awareness during a measles outbreak can result in a large number of VARs, consuming considerable public health resources. When evaluating the need to suspect measles among patients with febrile rash, clinicians should consider time since MMR administration, clinical presentation, and history of measles exposure. Collecting appropriate specimens for timely virus genotyping could inform appropriate public health action.

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LB-9. Broad-spectrum Investigational Agent GS-5734 for the Treatment of Ebola, MERS Coronavirus and Other Pathogenic Viral Infections with High Outbreak Potential
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Background. Recent viral outbreaks with significant mortality such as Ebola virus (EBOV), SARS-coronavirus (CoV), and MERS-CoV reinforced the need for effective antiviral therapeutics to control future epidemics. GS-5734 is a novel nucleoside analog prodrug in the development for treatment of EBOV, SARS-CoV, and MERS-CoV.

Method. Antiviral activity of GS-5734 has been established in vitro against a wide range of pathogenic RNA virus families, including filoviruses, coronaviruses, and paramyxoviruses (EC50 = 37 to 200 nM) (Warren et al., Nature 2016; Sheahan et al., Sci Transl Med 2017). Herein, we describe the in vivo translation of broad-spectrum activity of GS-5734 in relevant animal disease models for Ebola, Marburg, MERS-CoV, and Nipah.

Result. Therapeutic efficacy against multiple filoviruses with 80–100% survival was observed in rhesus monkeys infected with lethal doses of EBOV (Kikwit/1995 or Makona/2014) or Marburg virus and treated with once daily intravenous (IV) administration of 5 to 10 mg/kg GS-5734 beginning 1 to 3 days post-infection (p.i.). In all rhesus monkey filovirus infection models, GS-5734 significantly reduced systemic viremia and ameliorated severe clinical disease signs and anatomic pathology. In mice infected with MERS-CoV, twice daily subcutaneous administration of 25 mg/kg GS-5734 beginning 1 day p.i. significantly reduced lung viral load and improved respiratory function. In rhesus monkeys, once-daily IV administration of 5 mg/kg GS-5734 initiated 4 days prior to MERS-CoV infection reduced lung viral load, improved clinical disease signs, and ameliorated severe lung pathology. Finally, in African green monkeys infected with a lethal dose of Nipah virus therapeutic once-daily IV administration of 10 mg/kg GS-5734, starting 1 day p.i. resulted in 100% survival to at least day 30 without any major respiratory or CNS symptoms.

Conclusion. GS-5734 is currently being tested in a phase 2 study in male Ebola survivors with persistent viral RNA in semen. Iyoprophilized drug formulation has been developed that can be administered to humans via a 30-minutes IV infusion and does not require cold chain storage. Together, these results support further development of GS-5734 as a broad-spectrum antiviral to treat viral infections with high mortality and significant outbreak potential.

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