shown to inhibit reactivation of virus from latently infected murine trigeminal ganglia cocultured on Vero cells. Here we report that IV treatment with a nanoparticle formulation of mCF_3PG also suppresses reactivation of latent ocular infection in mice. Further development of mCF_3PG, however, is restricted by its low water solubility and lack of oral bioavailability (in mice). We synthesized and studied the 6-deoxy analog of mCF_3PG – 2-((3-(trifluoromethyl)phenyl)amino)purine (GLS361B, Sacrovir™) – as a possible prodrug. Sacrovir™ has higher water solubility than mCF_3PG and is converted to mCF_3PG by human liver cytosol. Sacrovir™ has modest oral absorption in mice but is converted rapidly into mCF_3PG and a second oxidized metabolite. It is oxidized to the same metabolites after IP injection into guinea pigs. Further studies to enhance the oral bioavailability of Sacrovir™ and to determine its ADME properties in different species are underway.

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Anti-HBV Activities of Novel 2′,3′-C-substituted beta-L-nucleoside Analogues

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Hepatitis B virus (HBV) infection is a medical challenge of global proportions. Today there are some 300 million people chronically infected with the virus and about 1 million patients die from HBV-related liver diseases each year. Nucleoside/nucleotide HBV pol inhibitors have been used widely for the treatment of HBV infection. Due to the persistence of the HBV infection, a prolonged treatment of years are often required, which puts a high demand on the safety profile of a successful therapy. Besides, the development of resistance has been observed with the current therapies, which is fueled by the high rate of viral replication and the low fidelity of the viral polymerase. There remains a strong need for new, potent and safe pharmaceutical agents to treat HBV, and particularly the new therapeutics that are useful in treating the resistant HBV infections. A series of novel 2′,3′-C-substituted beta-L-nucleosides have been synthesized and evaluated. The lead compound showed a good anti-HBV activity and safety property. The further studies on those 2′ and 3′-modified beta-L-nucleosides are on-going.

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