Anti-Viral Efficacy and Induction of an Antibody Response Against Surface Antigen from the TL7 Agonist GS-9620 in the Woodchuck Model of Chronic HBV Infection


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Introduction

• Though antiviral treatments can suppress Hepatitis C virus (HCV) and Hepatitis B virus (HBV) load in chronic infection, durable viral suppression is difficult to achieve in the absence of an effective vaccine. An effective vaccine is needed to prevent hepatitis and to achieve viral eradication.

Background

• GS-9620 is an orally active, selective and potent TLR7 agonist that induced IFN-α and selective upregulation of ISGs in human, non-human primates, and transgenic mice. Treatment induction of antiviral response was evaluated in a chronic woodchuck hepatitis virus (WHV) infection model.

Methods

• The study was conducted collaboratively between Cornell University (Ithaca, NY), Georgetown University Medical Center (Washington, DC), and Gilead Sciences, Foster City, CA. Single dose evaluation of pharmacokinetics (PK) and pharmacodynamics (PD) in uninfected animals was done to determine an active tolerated starting dose for the efficacy study. The efficacy study investigated 4 different dose regimens and was used as an uninfected control group. The experimental design is shown in Table 1. GS-9620 serum concentrations were determined using a LCMES method.

• Serum viral load was determined by slot blot hybridization and samples below the limit of detection (LOD) were considered negative. The study included: 1) pretreatment samples, 2) groups of 36 woodchucks chronically infected with WHV and treated with 5 mg/kg GS-9620 (Groups 1-5), 3) woodchucks chronically infected with WHV treated with 10 mg/kg GS-9620 (Group 6), 4) woodchucks chronically infected with WHV treated with 0.1 mg/kg GS-9620 (Group 7).

Results

• GS-9620 treatment resulted in a dose-dependent reduction in serum WHsAg, WHsAb, and liver viral DNA with a mean reduction in serum viral load of 2.2 logs. Treatment induced dose dependent increases in serum interferon-α (α) and select ISGs

Conclusions

• Four weeks of oral treatment with the TL7 agonist GS-9620 in woodchucks chronically infected with WHV resulted in a sustained, marked reduction in serum levels of viral DNA and WHsAg and in the induction of an anti-WHs antibody response.

References & Acknowledgements

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