Feasibility of Subcutaneous Entecavir Implants for Chronic Hepatitis B Treatment

Abstract

Patient compliance in the treatment of chronic infectious diseases is critical in preventing disease progression but often hampered by the burden of a lifelong pill regimen. Entecavir (ETV) is a first-line antiviral agent for the treatment of chronic hepatitis B administered as a once-daily oral pill or solution. The aim of our work was to evaluate the feasibility of long-acting implantable formulations of ETV to reduce the compliance burden on patients. To this end, we engineered hot melt extrudates and coated tablets for sustained ETV release in the subcutaneous (SC) space.

A variety of pharmacokinetic release profiles were achieved in rats by tuning the rate-controlling properties within a given modality. While 6-month SC delivery of ETV was demonstrated, local inflammation and necrotic tissue were observed proximal to the implant. Although SC ETV was not well tolerated at high input rates, the demonstrated implant longevity was a substantial increase over previous efforts reported in the literature. The modalities employed herein may have applicability to other therapeutic agents for long-acting hepatitis B treatment.

References