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Development of (-)-β-D-2,6-Diaminopurine Dioxolane as a Potential Antiviral Agent. R. F. Schinazi,[1*] H. M. McClure,[2] F. D. Boudinot,[3] Y. Jxiang,[3] and C. K. Chu.[3] VA Medical Center/Emory University, Decatur, GA 30033;[1] Yerkes Regional Primate Research Center/Emory University, Atlanta, GA 30322;[2] and Department of Med. Chem. and Pharmacognosy, College of Pharmacy, Univ. of Georgia, Athens, GA 30602, USA.[3]

(-)-β-D-2,6-Diaminopurine dioxolane (**DAPD**) is an effective inhibitor of HIV-1, HIV-2, SIV, and HBV *in vitro*. The EC_{50} for DAPD for HBV DNA replication intermediates or HBV virion synthesis inhibition was ~ 0.1 μM, making this purine one of the most potent anti-HBV agents. Complete cessation of viral replication occurred with these compounds at 3 μM. No marked toxicity (≤ 14%) was noted with DAPD when tested up to 300 μM in HBV transfected 2.2.15 cells; in contrast, DDC exhibited 61% inhibition at that concentration. We have systematically evaluated the metabolism of DAPD in human lymphocytes and liver cells. DAPD is rapidly converted intracellularly to the 5'-triphosphate (DAPD-TP) in HepG2 cells. DAPD-TP was the major intracellular metabolite. The compound is not bioconverted to the guanosine analogue by adenosine deaminase. Biochemical and pharmacological characteristics, including pharmacokinetic parameters after intravenous administration of radiolabeled and unlabeled DAPD in rhesus monkeys will be presented. The high *in vitro* therapeutic index, low toxicity profile in various cultures and animals, and simple metabolism suggests that DAPD should be evaluated for treatment of human HBV infection. *(Support: VA, NIH-AI-25899, & RR-00165)*

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A Phase I/II Open-Label Study to Assess the Safety, Pharmacokinetic Profile, and Preliminary Antiviral Effects of OST-577 (a Human Anti-hepatitis B Surface Antigen Monoclonal Antibody) Administered to Patients who are Persistently Hepatitis B Antigen Seropositive. **DP Paar, MD, BM Montgomerie, RN, P Nadler, MD, ER Schiff, MD and RB Pollard, MD. The University of Texas Medical Branch at Galveston, Galveston, TX, USA; Protein Design Labs, Mountain View, CA, USA; the University of Miami, Miami, FL, USA.**

We conducted a phase I/II dose-escalating trial to assess the safety and efficacy of a human monoclonal antibody (OST-577) directed against hepatitis B virus (HBV) surface antigen in 11 participants with chronic HBV infection. Subjects received either 0.5 mg/kg, 1 mg/kg, or 2 mg/kg intravenously on days 0, 1, 3, 7, 14, 21, and 35 and were followed for a total of 158 days. Serum HBV DNA and hepatic transaminases were measures of efficacy. Study data through day 70 are available for 6 subjects. Five responded with a mean reduction in HBV DNA of 75% (2 converted to negative) and in SGOT of 49%; the 6th did not respond. One subject in the 2 mg/kg cohort had chills with infusions. The other had infusion-related rigor, fever, and hypotension necessitating a dose reduction to 1 mg/kg. Investigation of the etiology of these adverse events is underway. These early data indicate that OST-577 leads to a reduction in serum HBV DNA and transaminases in patients with chronic HBV infection. Additional studies are needed to establish its role in the treatment of chronic HBV infection.