Treatment of Genital HSV2 with R-837. C.J. HARRISON[1]*, L.JENSKI[2], R.L. MILLER[3], D.I. BERNSTEIN[4]. Child Hosp Res Fdn[1] and J.N. Gamble Inst Med Res[4], Cincinnati; IUPU[2], Indianapolis; and Riker Labs[3], St. Paul, MN.

Intravaginal R-837 administered bid for 5d prevented acute and recurrent HSV-2 disease when begun 12h post infection (PI) despite R-837's lack of *in vitro* anti-herpes activity. Dosing q.d. starting at 36h PI decreased lesion days per animal in acute disease (2.4 vs 8.3 days) and in recurrent disease (3.1 vs 8.6 days). Both R-837 regimens decreased viral shedding. 20/24 R-837 recipients developed HSV ELISA antibody and peripheral blood mononuclear cell (PBMC) proliferative response to HSV2. B.I.D recipients with <36h HSV2 vaginal replication did not. Plasma IFN was elevated in both R-837 groups (peak on day 3). On day 28 and 42, generation of IL-1, IL-2 and high affinity IL-2 receptors by *in vitro* HSV2 stimulated PBMC from R-837 recipients with minimal genital disease were ≥ that from controls with 4+ genital disease. PGE_2 production from HSV-2 stimulated PBMC was decreased during acute disease by R837 treatment. Latent HSV-2 was recovered from the DRG of 93% of placebo, but from 10% of q.d. and no b.i.d. R-837 recipients. R-837 is a biological response modifier inducing increased cytokines, decreased PGE_2, an in vivo acute antiviral effect, and decreased HSV latency.

Effects of a Series of Immunomodulators on Experimental Phlebovirus Infections. R. W. Sidwell, J. H. Huffman, B. B. Barnett, M. Kende and D. Y. Pifat. Utah State University, Logan, Utah, USA and U.S. Army Medical Research Institute for Infectious Diseases, Fort Detrick, Frederick, Maryland, USA.

Phlebovirus infections are recognized as major diseases of man, with principal viruses being Rift Valley fever (RVFV) and sandfly fever (SFV). A related human phlebovirus isolate from Panama is the Punta Toro virus (PTV), which induces a lethal hepatotropic disease in C57BL/6 mice which is similar to the human disease caused by RVFV and SFV. The PTV infection induced by subcutaneous inoculation into 3-4 week-old mice was used in an extensive study of known immunomodulating agents. These agents included ampligen (poly I•poly C 12u), AM-3, 2-amino-5-bromo-6-phenyl-4(3H)-pyrimidinone (ABPP), 2-amino-5-iodo-6-phenyl-4(3H)-pyrimidinone, 2-amino-5-bromo-6-methyl-4(3H)-pyrimidinone, inosiplex, mannozym, oxamisole, streptonigrin, and neurotropin. All agents were effective against the infection except inosiplex, streptonigrin and neurotropin. Those substances considered highly active were ampligen, AM-3, mannozym and ABPP, with significant inhibition of death and hepatic disease when treatment was initiated 1 to 4 days after virus inoculation. Studies were run to compare treatment routes and schedules for each positive immunomodulator.