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Effect of S-28463 in reducing recurrent genital HSV-2 in guinea pigs. D.I. Bernstein*, R.L. Miller†, E. Tepe*, J.C. Mester*, C.J. Harrison‡. *J.N. Gamble Inst. of Med. Res., Cincinnati, OH, †3M Pharm., 3M Company, St. Paul, MN, ‡Creighton Univ. and Univ. of Nebraska Med. Center, Omaha, NE, USA.

Recurrent genital herpes simplex virus (HSV) infections can be suppressed by oral acyclovir but require daily administration of multiple doses. We evaluated S-28463, a more potent analog of the immunomodulator, imiquimod, for its effect on recurrent HSV disease. Guinea pigs (N=67) that developed genital HSV-2 disease were randomized to receive S-28463 or placebo beginning on day 15 P.I.. We compared 0.1 mg/kg given subcutaneously once per day, once every other day, and once per week for 3 weeks. Animals were evaluated daily for spontaneous recurrence from d15-90. Blood was obtained on d15, 22, 29, 35 and 90 to compare interferon levels and immune responses. All regimens reduced the number of recurrent lesion days by over 80% ($p < .001$ vs. control) during the 3 weeks of therapy. Recurrences were lowest in the once per week group. Following discontinuation of drug (d35-90), recurrent lesion days remained significantly reduced in all 3 groups ($p < .005$ vs. control) and were again lowest (65% reduction) in the once per week group. Interferon levels were highest initially, remained consistently elevated only in the once per week group, and appeared to correlate to lymphoproliferative responses. Unlike other traditional antiviral therapies, S-28463 significantly reduced recurrences during treatment and for at least 8 weeks after discontinuation even when given once per week.

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Psychosocial impact of genital herpes in guinea pigs: effect of 0-2B9¼ therapy. D. Bernstein*, N. Bourne†, S. Rosenthal†, L. Stanberry†. *J. N. Gamble Institute of Medical Research, Cincinnati, OH, †Children's Hospital Research Foundation, Cincinnati, OH.

Genital herpes infection only produces severe morbidity and mortality in select, mostly immunocompromised groups. In the majority of infected subjects, the psychosocial implications of the disease equal or outweigh the clinical. We have, therefore, developed an animal model to quantitate the psychosocial implications and allow us to measure the impact of therapy. We chose the guinea pig because the pathogenesis of disease most closely resembles that of humans. The limited expressive language abilities of the animal made evaluation difficult; and we, therefore, limited responses to yes or no questions. Both characterologic and behavioral self-blame were assessed. The scale ranged from "You're o.k., but I'm a filthy animal who deserves to live in a cage the rest of my life" to "I'm o.k., and you should be in this cage." Herpes coping data were plotted by Martin Meir curve for the time to return to baseline. The Earl Kernofsky scale was used to measure the impact on quality of life. Variables that impacted on these scores included age, sex, severity of initial disease, and frequency of recurrences. Antiviral therapy reduced the behavioral, but not the characterologic self-blame score ($p < .01$). We believe this model should be useful for evaluating future antiviral therapies and people should give us a lot of money to continue these studies.