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Comparative effects of famciclovir and valaciclovir on cutaneous and neurological HSV-1 infection in normal and immunocompromised mice. A.M.Thackray and H.J. Field, University of Cambridge, Madingley Road, Cambridge, CB3 OES, UK.

A model simulating chronic HSV infection in the immunocompromised host was established in mice. Immunosuppression was induced using cyclosporin-A; the immunological effects were restricted to T-cell function, but resulted in prolonged virus replication at cutaneous and neurological sites following inoculation of the ear pinna with HSV-1. The model was used to evaluate the effects of famciclovir (FCV) and valaciclovir (VACV), which are oral prodrugs of penciclovir (PCV) and acyclovir (ACV) respectively, on viral pathogenesis. Oral administration of either of the agents resulted in almost identical blood concentrations of PCV and ACV respectively, both of which had very similar activity against HSV-1 in murine cells. Mice were treated orally with FCV or VACV at 50 mg/kg per dose commencing either 1 or 5 days after infection. The responses to chemotherapy (measured by clinical signs, weight gain, inflammation of the ear, and virus titres in skin and brain), all indicated that FCV was superior to VACV. With FCV treatment, infectious virus was completely eradicated from the skin and brainstem, even when the start of therapy was delayed until 5 days after infection. No recurrence of infectious virus was observed following termination of FCV therapy. In contrast, there was a reproducible recurrence of virus replication in both the skin and brainstem on cessation of VACV therapy, even after 10 days of treatment. Similar studies were carried out in mice that received no immunosuppressive treatment. Taken together , these results demonstrate that FCV and VACV have markedly different effects on the pathogenesis of HSV-1 in normal and immunosuppressed mice. We suggest that these data have important implications for the treatment of HSV infections in man.

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Comparison of the Antiviral Efficacy of Acyclovir and Penciclovir in Topically Treated HSV-Infected HRS/J Mice. D. W. Selleseth. Wellcome Research Laboratories, Research Triangle Park, North Carolina, U.S.A.

The zosteriform and orofacial HSV mouse models were used to compare efficacy of topical acyclovir (ZOVIRAX®, ACV) to that of penciclovir (PEN). HRS/J mice were inoculated either on the snout or dorsal flank with HSV-1 (SC-16, wild-type HSV) and treated topically b.i.d. with either 5% ACV or 5% PEN in modified aqueous cream (MAC-P). Treatments were started on either day 2 or 3 post-inoculation (PI) and the mice were scored daily for lesion severity. In both cases 5% ACV was superior to 5% PEN in reducing lesion severity and duration. In a subsequent experiment, HSV-infected HRS/J mice were treated topically b.i.d. with 5% ACV or 5% PEN in MAC-P starting treatment three days PI and continuing until day five PI. The snout skins of the euthanized mice were excised, homogenized, and analyzed for tissue virus titers. The skins treated with 5% PEN had > 2 logs more plaque-forming units per gram of tissue than the snout skins treated with 5% ACV. 5% ACV in MAC-P was significantly superior ($p<0.01$) to 5% PEN in MAC-P in this experiment.