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Activity of famciclovir and penciclovir in HSV-infected animals: a review. D. Sutton, R.J. Ashton, T.H. Bacon, and M.R. Boyd. SmithKline Beecham Pharmaceuticals, Epsom, Surrey, UK.

Penciclovir (PCV) is a potent and highly selective antiherpesvirus agent. Both PCV and its oral form, famciclovir (FCV), are in clinical trials against herpes zoster, genital herpes and herpes labialis. The activity of PCV and FCV against HSV-1 and HSV-2 infections in animals is reviewed. PCV showed potent activity in a variety of cutaneous, genital and systemic HSV infections in mice when administered by the subcutaneous, intravenous or oral routes. The benefit of the greater bioavailabilty of PCV following oral administration of FCV was demonstrated by the greater activity of FCV against a cutaneous HSV-1 infection in mice. In addition, topical PCV was highly effective against a cutaneous HSV-1 infection in guinea pigs. The relative antiviral potencies in mouse cells and pharmacokinetic properties in mice suggested that acyclovir (ACV) would be more efficacious than either penciclovir or famciclovir against HSV infections in mice. However, PCV and FCV in general, were at least as effective as ACV against cutaneous, genital and intranasal infections. Moreover, in mice infected intraperitoneally with HSV-1, both systemically administered PCV or orally administered FCV, even when dosed less frequently, were more active than equivalent treatment with ACV. This is consistent with the high stability of intracellular PCV-triphosphate within herpesvirus-infected cells and the prolonged activity of PCV in cell culture. In addition, there is good evidence to suggest that virus replication within the central nervous system is reduced following treatment with either PCV or FCV. The excellent pharmacokinetic properties of FCV in man together with the prolonged activity of PCV suggest that FCV will be effective in clinical use both at a lower dose and a reduced dosage frequency than ACV.

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A Double-Blind, Placebo (PLB)-Controlled Trial of the Effect of Chronically Administered Oral Famciclovir (FCV; BRL 42810) on Sperm Production in Men with Recurrent Genital Herpes (RGH) Infection. S.L. Sacks, A.M. Bishop, R. Fox, and G.C.Y. Lee, *Division of Infectious Diseases, and Department of Obstetrics and Gynaecology, The University of British Columbia Faculty of Medicine, Vancouver, B.C., Canada.*

FCV is the oral formulation of penciclovir, a new antiviral agent with excellent activities against herpes simplex, varicella zoster, and hepatitis B viruses. As previously observed with preclinical acyclovir studies, reversible, dose-dependent testicular toxicities have been observed following prolonged, high-dose administration of FCV to both rats and dogs. To demonstrate long-term human safety, we performed biweekly semen analyses in men with RGH randomized to treatment with FCV 250 mg po bid for 18 weeks or placebo in a double-blind study. Eight-week pre- and post-treatment periods of biweekly semen analyses were also conducted. Additional safety studies included blood and urine sampling every 4th week. Semen samples were analyzed according to World Health Organization (1987) and British Andrology Society (1989) Guidelines. The primary semen safety parameters were sperm count and concentration. Minimal RGH frequency rates were not required, although frequencies were followed by patient reports. Efficacy analyses were not planned for this study. Of the 79 men enrolled in Vancouver, 12 received no treatment after baseline followup. Of the remainder, 34 were randomized to receive FCV and 33 to PLB. The mean proportions of normal sperm were 71.4%/71.0% for FCV/PLB during baseline and 72.1% for both groups during treatment. Post-treatment proportions were 71.0%/70.7%. No significant effects of treatment were found upon proportions of dead, motile, or normal sperm or any other semen parameter. In summary, FCV 250 mg bid for 18 weeks is well-tolerated in men with RGH and was shown to have had no significant effects on any of the sperm parameters measured.