Comparative Antiviral Activities of BV-araU And Acyclovir *In Vitro* And *In Vivo*
H. Machida, Research Laboratories, Yamasa Shoyu Co., Ltd., Choshi, Chiba-ken, Japan

1-β-D-Arabinofuranosyl-*E*-5-(2-bromovinyl)uracil (BV-araU) and acyclovir (ACV) were compared for their *in vitro* and *in vivo* anti-herpesvirus activities. In the plaque reduction assay, both compounds exhibited marked antiviral activity against herpes simplex virus type 1 (HSV-1) in human embryonic lung fibroblasts. Average of 50% plaque depression doses of BV-araU for 5 strains of varicella-zoster virus was 0.4 ng/ml, while the 50% plaque depression dose of ACV was about 1 μg/ml. However, BV-araU showed little effect against herpes simplex virus type 2 and human cytomegalovirus replication. In animal models, treatment with 12.5 (oral route) and 25 (intraperitoneal route; i.p.) mg of BV-araU per kg twice a day for a week caused significant increases in survival rate and in mean survival time in the groups of mice infected either intracerebrally (i.c.) or i.p. with HSV-1 strain WT-51, and most of mice treated with 100 or 200 mg of BV-araU per kg survived. Oral treatments with BV-araU were as effective as or more effective than i.p. treatments in both infection systems. ACV scarcely showed antviral efficacy in reducing final mortality in mice infected i.c. with the virus at a dose up to 200 (oral treatment) and 50 (i.p. treatment) mg/kg twice a day, while ACV demonstrated higher antiviral efficacy than BV-araU against i.p. infection with HSV-1 strain WT-51.

Machida, H. (1986). Antimicrob. Agents Chemother. 29: 524-526.
Machida, H., et al. (1981). Antimicrob. Agents Chemother. 20: 47-52.

Inhibition of in vivo Herpes Simplex Virus Reactivation by Acyclovir. Richard B. Tenser and Wade A. Edris. Penn State University College of Medicine, Hershey, PA, USA

In vivo reactivation of herpes simplex virus (HSV) and inhibition of reactivation by acyclovir (AcV) was studied in a mouse model. HSV-1 infection of spinal dorsal root ganglia (drg) was established by footpad inoculation of virus. 28-49 days post - virus inoculation, latent HSV infection was found in the third lumbar (L-3), L-4, L-5 and L-6 drg in 14%, 50%, 95% and 41%, respectively. For reactivation studies, therefore, we concentrated investigations on the L-5 drg. During the period of latency, HSV reactivation was induced by sciatic neurectomy, and drg latent infection remaining three weeks later was determined. In unoperated and in sham operated control mice, latent L-5 drg infection was present in 90-100%. After sciatic neurectomy, latent infection was present in only 28%, evidence of HSV reactivation and subsequent clearance. After sciatic neurectomy plus AcV treatment, 61% of mice remained latently infected. Following AcV treatment alone, 75% were latently infected. The marked decrease in latency after neurectomy (decrease from 90% to 28%), therefore was minimized by AcV treatment (decrease from 75% to 61%). This result was probably due to AcV inhibition of neurectomy - induced HSV reactivation.