129

Antiherpesviral Efficacy of Brovavir (BV-araU) in Immuno-Suppressed Mice

H. Machida, K. Ijichi and N. Ashida; Res. Lab., Yamasa Shoyu Co., Ltd.

Brovavir (BV-araU) shows potent *in vitro* antiviral activities against HSV-1 and varicella-zoster virus. It exhibited the most potent activity against VZV among all compounds tested. We have also shown marked efficacies of oral and i.p. treatments with brovavir against HSV-1 encephalitis, and systemic and cutaneous infections with HSV-1. Herpes virus infections are often seen in immuno-compromised patients, and these infections tend to be life-threatening. For clinical application of anti-herpes drugs, therefore, it is important that they are effective even in immuno-suppressed animals. We have studied *in vivo* effect of brovavir against i.p. infection with HSV-1 in immuno-suppressed mice treated with cyclophosphamide (CYP). Oral treatment with brovavir was effective even in immuno-suppressed mice, although a dose of the drug necessary for significant reduction of the mortality was higher than that in CYP-non-treated normal mice. A lot of infective viruses were seen in gastro-intestinal tract of immuno-suppressed mice in contrast to that of the CYP-non-treated normal mice. Brovavir treatment at a dose of 20 mg/kg b.i.d. suppressed viral growth in the organs. Brovavir at a dose of 100 mg/kg b.i.d. was effective in increasing both survival rate and mean survival time of the immuno-suppressed 4-week-old mice, and at doses of 20 and 50 mg/kg, at which brovavir was effective in decreasing the mortality of HSV-1-infected normal mice, led to extension of the mean survival time, but did not reduce the mortality. However, brovavir significantly reduced the mortality of immuno-suppressed 7-week-old mice at these lower doses. Similar potency of brovavir treatment was achieved in the efficacy against cutaneous infection in immuno-suppressed mice. From these findings, brovavir is expected to be beneficial for the clinical use even in the immuno-compromised patients.

130

Bromovinyldeoxyuridine Treatment of Herpes Simplex Virus and Varicella-Zoster Virus Infections: A Review

P.C. Maudgal and E. De Clercq
Ophthalmological Clinic and Rega Institute for Medical Research, Katholieke Universiteit Leuven, Leuven, Belgium

Bromovinyldeoxyuridine (BVDU) has a potent and selective antiviral activity against herpes simplex virus type 1 (HSV-1) and varicella-zoster virus (VZV) infections. Both experimental and clinical data have established BVDU to be a safe and potent compound for the treatment of HSV-1-induced epithelial disease, stromal keratitis, endothelitis and iritis, whether administered as topical eyedrops or orally. Similarly, it has been found to be superior to other antiviral agents when administered orally in the simian varicella-zoster model. Oral treatment with BVDU of herpes zoster in cancer patients led to a rapid healing of the skin lesions. Oral and topical BVDU administration to a limited number of ophthalmic-zoster patients similarly led to a prompt improvement of both the skin and eye lesions. Except for local hypersensitivity reactions to the eyedrops in a small number of patients, no other local or systemic toxic side effects of the drug were observed.