165

The pharmacokinetics of 882C, a thymidine analogue with potent anti-VZV activity, in healthy volunteers. R.W.Peck, B.C.Weatherley, J.Posner. The Wellcome Foundation Ltd. Beckenham, Kent, UK.

882C (1-(ß-D-arabinofuranosyl)-5-(1-propynyl)uracil) is under investigation for the treatment of varicella zoster virus infections. It has an IC_{50} of 0.6 - 3.8 •M against a range of VZV strains. Initial studies of its pharmacokinetics in man have shown that it has a long elimination half-life of 12 - 14 h and gives plasma concentrations exceeding the IC_{50} for at least 24 h after single oral doses of 50 mg or more[1]. Pharmacokinetics have been further investigated in 15 healthy male volunteers receiving single oral doses of 200 mg on two occasions at least a week apart in the presence and absence of a standard breakfast. Mean C_{max}, AUC and T_{max} were 8.9 •M, 170.4 •M.h and 4.7 h fasting and 7.5 •M, 152.6 •M.h and 5.1 h after food. The reduction in C_{max} after food was statistically significant (95% CI for ratio fed/fasted 0.76 - 0.99) but the change in mean AUC was not (95% CI for ratio 0.81 -1.05). However food reduced the variability in AUC with a reduction in subjects with a high fasting AUC and a rise in those with low fasting values. There was no change in $t_{\bullet}$, CL/f, V_Z/f or CL_R or in the pharmacokinetic parameters of 5-propynyluracil, the main metabolite. These single dose data suggest it should be possible to maintain plasma concentrations of 882C well above the IC_{50} with once or twice daily dosing and without food related restrictions.

1. Peck et al. Tolerability and pharmacokinetics of 882C a novel nucleoside analogue, in healthy male volunteers. Br.J.Clin.Pharm,1992;33(5):568P.

166

Ribavirin in Genital Herpes. Results of a Three-Phase Study. Carvajal F.A.*, Palacio G.M.E., Garibay V.M. *Hospital Civil ISSSTEP, Puebla, Pue. Mexico.

We report results of a 3-phase study of Ribavirin in patients with genital herpes. In phase 1, 30 patients were randomly assigned into 3 groups: A, oral + topical Ribavirin; B, oral Ribavirin + topical placebo; C, oral placebo + topical Ribavirin. Dosage was 6 capsules (200 mg each capsule) + 1 mm thick cream coat for 6 days. In phase 2 patients were divided in 2 groups: Ribavirin or placebo and treated with 2 capsules daily for 12 months. In phase 3, previously Ribavirin patients shifted to intermittent therapy (1200 mg Ribavirin daily/6 days) just in case of a recurrence, and previously placebo patients shifted to continuous therapy (400 mg Ribavirin daily). Both schemes were followed during 12 months.

Objective in phase 1 was to evaluate effectiveness of topical route and oral + topical Ribavirin combined in acute genital herpes. In phase 2 and 3 was to evaluate number of recurrences.

RESULTS: In phase 1 groups behaved A > C ≥ B. In phase 2, two patients with Ribavirin and 8 patients placebo presented a recurrence (p = 0.025*) and in phase 3, the whole intermittent therapy group had at least one recurrence (11 had two, 4 had one) and in group continuous therapy, 7 patients had recurrence (2 had two, 5 had one [p = 0.001*]).

*Fisher's exact test.