121

ALTERATIONS OF PRODUCTIVE HIV INFECTION LEVELS IN PATIENTS UNDER ANTIVIRAL THERAPY. Dominique, Mathez* ; Sultan, Y.** ; De Belilovsky, C.* ;Paul, D.***; Decker, R.*** ; Leibowitch, J.*. *Hôpital Raymond Poincare, Garches, France, **Hôpital Cochin, Paris, France, ***Abbott Laboratories, North Chicago, Illinois, USA.

Mononuclear cells from HIV-1 sero-positive subjects were thawed, submitted to lethal gamma-irradiation in vitro (45 Gray), and co-cultured at 10^5 and $5x10^5$ (4 replicates each) with PHA-stimulated normal lymphocytes. The frequency of radiation-resistant infectious cells (R-HEV scores) correlated with the detection of p24 antigen in paired sera ($p < 0.001$), and with AIDS-related disease ($p<0.001$) or with CD4-lymphopenia ($p<0.001$). In contrast, R-HEV scores remained consistently low in non-progressor asymptomatics repeatedly monitored over 2-5 years. R-HEV scores significantly declined in blood MNCs of 18/20 patients within 3 months of AZT treatment (300mg x 4/d), and had returned in half of those to pretreatment levels within 6 months under continuous treatment. In 12 patients receiving 500 mg AZT once-a-day, R-HEV scores also declined and then recurred to baseline values in most patients after 6 months. Because radiation-resistant cell-associated infectivity is a measure of productive HIV infection in the patient, the assay system could provide information on drug dosages and regimens in reference to efficacy, as of phase I - II studies.

122

Efficacy of Intranasal R 77975 for the Prevention of Experimentally Induced Rhinovirus Infection and Illness. FG Hayden, K Andries, and PAJ Janssen, University of Virginia School of Medicine, Charlottesville, Virginia, USA and Janssen Research Foundation, Beerse, Belgium.

Rhinoviruses (RV), the most frequent cause of the common cold syndrome, are an important target for antiviral chemoprophylaxis. The pyridazinamine R 77975 is a capsid-binding anti-RV compound with a broad in vitro spectrum (70% of RV serotypes at 0.02 ug/ml). The current study was designed to assess the protective efficacy of intranasal R 77975 against experimentally induced RV infection and illness. Under blinded conditions, susceptible males (serum neut. antibody titers $\leq$ 1:2) were isolated and randomly assigned to treatment with R 77975 (2 mg per dose) or the OH-β-cyclodextrin vehicle as placebo (P) by metered-pump spray (two 0.1 ml sprays per nostril per dose) six times per day for a total of 25 doses. They were inoculated with RV (serotypes Hank's or 39) by nasal drops within 15 minutes following the second and third doses of study drug and monitored with daily symptom recording and nasal washings for virus isolation. Infection, detected by either virus shedding or seroconversion, developed in 12(92%) of 13 P and 7(58%) of 12 R 77975 subjects (p = NS). Virus shedding was detected in 85% of P and 33% of R 77975 subjects ($p = 0.025$). Clinical colds developed in 7(54%) of 13 P and 1(8%) of 12 R 77975 subjects during treatment ($p = 0.04$, efficacy = 85%). The one R 77975 subject reporting a cold did not have laboratory evidence of RV infection. Standardized symptom scores tended ($p=0.1$) to be lower (50% reduction) in the R 77975 group (mean $\pm$ SD, 6 $\pm$ 8) than in P (12 $\pm$ 10), but mucus weights did not differ between the R 77975 (12.6 $\pm$ 10.9) and P (13.0 $\pm$ 9.2) groups. Two of four R 77975 subjects who shed virus after cessation of drug administration developed late-onset cold symptoms, as did two P subjects. The findings indicate that intranasal R 77975 is an effective agent for the prevention of experimentally induced rhinovirus illness. Studies to determine the efficacy of less frequent but longer duration administration are planned.