

Monday April 11

Oral Session II
Preclinical Pharmacology and Evaluation
of Antiviral Agents

Anti-Viral Therapy in Woodchucks During the Late Acute Phase of Woodchuck Hepatitis Virus (WHV) Infection. PJ Cote, BE Korba, B Tennant, B Baldwin, RH Purcell, and JL Gerin. Division of Molecular Virology and Immunology, Rockville, Md; Cornell Veterinary School, Ithaca, NY; Laboratory of Viral Diseases, NIH, Bethesda, Md.

Colony-bred woodchucks inoculated at birth with standard WHV inocula develop high rates of chronic infection (65 to 75%); essentially all such carriers develop primary hepatocellular carcinoma within three years. Thus, the woodchuck/WHV system may represent a predictive model for therapy of hepadnavirus-induced disease. We describe here a placebo-controlled study of ARA-AMP in combination with immune response modifiers during the late acute phase of WHV infection (5 months post inoculation); preliminary studies in adult chronic carriers showed that ARA-AMP (15 mg/kg/day, 2 weeks) was well tolerated and caused a transient depression (> 90%) in serum WHV DNA levels during treatment. The same ARA-AMP treatment of 20 neonatal woodchucks at the late acute phase of infection (5 months of age) caused a significant decrease in serum WHV DNA levels compared to controls. However, even with superimposed immunotherapy using a WHV vaccine (50 ug) and IL-2 (100,000 IU/kg, 5 days), there was no significant difference as of 7 months post infection in seroconversion rate to anti-surface antibodies between the untreated (n=19) and treated (n=20) groups. Thus, short-term therapy during the late acute phase of WHV infection did not appear to interdict the progression to the chronicity. However, the model appears to be useful in the in vivo evaluation of various anti-viral strategies for chronic hepadnavirus infection and disease.