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Alpha Interferon in Combination with AZT and Activated Lymphocytes for the Prevention and Treatment of FeLV-Induced Immunodeficiency Syndrome (FeLV-FAIDS) N.S. Zeidner, M.H. Myles, C.K. Mathiason-Dubard, E.A. Hoover. Department of Pathology, Colorado State University, Ft. Collins, CO., U.S.A.

AZT inhibited replication of an immunodeficiency inducing strain of feline leukemia virus *in vitro* at concentrations of 0.5-0.005 µg/ml. A 30% synergistic antiviral effect was achieved *in vitro* when AZT was combined with alpha interferon (IFNα) at concentrations between 500-1000 units/ml. When activated, immune lymphocytes were transferred onto FeLV infected targets *in vitro* antiviral activity was demonstrated at Effector:Target ratios as low as 5:1. This antiviral activity could be enhanced another 20% when cells were transferred in combination with AZT plus IFNα at dosages of IFNα which only minimally inhibited FeLV-FAIDS replication. Prophylactic antiviral therapy utilizing AZT and IFNα enabled cats to resist *de novo* infection with FeLV-FAIDS. Although antigenemia remained undetectable in AZT treated cats throughout an 80 day period post inoculation, latent FeLV-FAIDS was detectable by *in vitro* culture of bone marrow progenitor cells. Serial analysis of p27, neutralizing antibody and quantification of latent, reactivatable virus indicated that only those animals receiving AZT plus IFNα could completely resist *de novo* virus challenge. Utilization of either IFNα alone or in combination with AZT to treat asymptomatic, peristent viremia resulted in a significant reduction in circulating viral antigen as early as 14 days post treatment. Depending on whether high or low dosage IFNα was used, cats became refractory to therapy with IFNα at either 3 or 7 weeks after the start of treatment. At these time points animals developed antibodies to IFNα that were neutralizing, specific for exogenous IFNα and dose dependent in terms of the duration and intensity of this response. AZT used alone had no effect on circulating virus load. We are currently exploring the use of low dosage IFNα in combination with adoptive transfer of activated lymphocytes to treat early, persistent retrovirus infection in the FeLV-FAIDS model.

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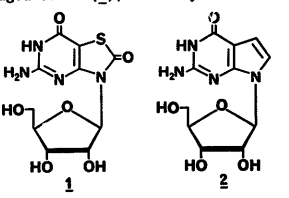
7-Deazaguanosine, A New Immune Enhancer Active Against RNA Viral Infections in Mice. **R.K. Robins**, D.F. Smee, H.A. Alaghamandan, A. Jin, W.B. Jolley, K. Ramasamy, and G.R. Revankar. ICN Nucleic Acid Research Institute, Costa Mesa, California 92626, U.S.A.

A novel immunopotentiating nucleoside, 7-thia-8-oxoguanosine (**1**), prepared in our laboratory, has recently been reported to give significant protection to mice infected i.p. with a number of RNA viruses (Antimicrob. Agents Chemother., 33, 1487, 1989). 7-Deazaguanosine (**2**), first synthesized by Robins, Tolman and Townsend (J. Heterocycl. Chem., 13, 1363, 1976), has recently been studied in our laboratory as an immunopotentiating agent which is similar in some respects to **1**. 7-Deazaguanosine is inactive as an antiviral agent or antitumor agent in various cell culture systems. However, **2** in i.p. treatments (50-200 mg/kg) 24 and 18 hrs prior to virus inoculation offered excellent protection of mice from death induced by Semliki Forest or San Angelo virus infection. Significant survivor increase was also evident in mice treated with Banzi or Encephalomyocarditis (EMC) virus infection. In contrast to **1**, **2** showed oral activity at 100 mg/kg against several of these viral infections. Although **2** is similar to **1** in the activation of host natural killer cells, **2** differs from **1** in the activation of host T-cells and in the lack of B-cell activation and proliferation that is characteristic of 7-thia-8-oxoguanosine, **1**.



1 **2**