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Combined Effects of r Interferon-β and AZT on HIV Replication **In Vitro**. G.J. Williams, Southern Research Institute, Birmingham, AL, C.B. Colby, Triton Biosciences, Inc., Alameda, CA, USA.

The toxic effects of AZT has prompted investigation for the use of AZT with other agents to achieve protection against HIV using nontoxic AZT dosages. The effects of human recombinant interferon beta (rIFN-β) and AZT, alone and in combination, on HIV replication **in vitro** were examined and found to be potentially beneficial. HIV mediaited cytopathic effects (CPE) were determined by tetrazolium dye assay and HIV p24 antigen in culture fluids from infected cells was measured by ELISA. MT-2 cells were infected with the RF-II strain of HIV either by cocultivation with HIV persistently infected H9 producer cells or with cell-free virus preparations. AZT used alone reduced HIV replication in MT-2 cells irrespective of the manner of infection, while low concentrations of rIFN-β used alone were effective only when cell-free virus preparations were used. However, rIFN-β further reduced HIV-mediated CPE as well as HIV p24 antigen synthesis in cultures of MT-2 cells treated with sub-optimal AZT doses, irrespective of the manner of infection. These results and those obtained using other methodologies will be discussed.

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Combination of Acyclovir (ACV) Plus Vidarabine (ara-A) or ACV Plus Interferon (IFN) Against Herpes Simplex Virus Type 1 (HSV-1) and HSV-2 in Cell Cultures. J.C. Overall, Jr., A. Moon, and E.R. Kern. Univ. of Utah Sch. of Med., Salt Lake City, Utah, USA.

Although mortality and morbidity in serious HSV infections have been reduced by treatment with ara-A or ACV, results have not been optimal. We tested combination vs single drug therapy in human foreskin fibroblast (HFF) and mouse embryo fibroblast (MEF) cells using an automated microtiter plate assay. Combination index (CI) values (<1, synergistic; around 1, indifferent; >1, antagonistic) were calculated from a Dose Effect Analysis computer program. The CI values with ACV plus ara-A in HFF cells were quite variable, but, in general, appeared to be additive to synergistic against HSV-1 (mean of 12 CI values 0.90, range 0.41-1.33), and antagonistic against HSV-2 (mean CI 2.17, range 1.18-4.48). The combination of ACV plus ara-A in MEF cells gave variable CI values: generally antagonistic against HSV-1 (mean CI 1.83, range 1.11-2.78) and indifferent against HSV-2 (mean CI 1.10, range 0.77-2.43). The combination of ACV plus recombinant human IFN alpha A in HFF cells was highly synergistic against both HSV-1 (mean CI 0.27, range 0.09-0.46) and HSV-2 (mean CI 0.18, range 0.07-0.32). The combination of ACV plus recombinant IFN alpha A/D In MEF cells was synergistic against both HSV-1 (mean CI 0.61, range 0.37-0.79) and HSV-2 (mean CI 0.34, range 0.17-0.47). These in vitro results suggest that the combination of ACV plus IFN appears more promising than ACV plus ara-A for further evaluations against HSV infections in animal models and in clinical trials.