National Cancer Institute
Office of Cancer Communications

UPDATE

IV INTERNATIONAL CONFERENCE ON AIDS
JUNE 12-16, 1988, STOCKHOLM, SWEDEN

TITLE ..... Pharmacokinetics and Long-Term Therapy of AIDS and ARC with AZT and Acyclovir

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OF PRESENTATION

STOCKHOLM--Scientists reported today that the drug combination AZT and acyclovir may be useful as a treatment for AIDS and AIDS-related complex (ARC). The therapy can induce some clinical and laboratory improvements in patients. However, it is not clear whether the combination is better than AZT alone, Robert Yarchoan, M.D., of the U.S. National Cancer Institute (NCI) said at the 4th International Conference on AIDS in Stockholm.

AZT prolongs the lives of many AIDS patients and is available by prescription for the majority of patients. Acyclovir is used to treat herpesvirus infections. In the laboratory, acyclovir has little activity against human immunodeficiency virus (HIV), the cause of AIDS. It can, however, potentiate the anti-HIV activity of AZT in cell cultures without increasing the toxicity of AZT.

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Scientists are trying to develop effective AIDS therapies that combine agents that have different toxicities. This can reduce the total amount of each drug received, and, thus, possibly lessen toxicities. AZT can cause dose-limiting bone marrow suppression. Acyclovir generally causes little toxicity when used in the treatment of herpesviruses.

Dr. Yarchoan reported on 5 AIDS and 5 ARC patients who received the drug combination for up to 1 1/3 years. The study was conducted by Dr. Yarchoan, Dr. Samuel Broder, and colleagues at NCI, Bethesda, Md., in collaboration with Wellcome Research Laboratories, Research Triangle Park, N.C.

Seven patients have now received the therapy for 12 to 65 weeks, he said, indicating that the regimen can be tolerated for more than a year. However, three of these patients had to have their doses reduced because of blood toxicities.

The standard regimen consisted of 100 mg of AZT--one-half of the present recommended dose for AZT alone--and 800 mg of acyclovir orally every four hours. This is a much higher dose of acyclovir than is generally used to treat herpesvirus.

Two patients had to withdraw from the study when they developed opportunistic infections after the first week. A third patient withdrew in the 17th week of therapy because of severe anemia, and later died of AIDS-associated complications.

The seven patients who continued to receive the therapy had increases in the numbers and functioning of their T cells, important measures of immune repair. However, Dr. Yarchoan said, some patients showed declining T cells even after months of therapy. (T cells are immune system white blood cells that are severely depleted in patients with AIDS and advanced ARC.)

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Two patients with HIV in their blood when they entered the study had no detectable virus after receiving therapy.

Herpesviruses may be cofactors that stimulate activation of HIV, Dr. Yarchoan said. Because of this, it is possible that acyclovir may indirectly help prevent activation of HIV by suppressing herpesviruses.

The scientists will continue to treat and follow the patients' progress.

Today's presentation updates findings published when the patients had been treated for up to 27 weeks. Those findings appeared in the April 1988 Annals of Internal Medicine.*

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*Surbone A, Yarchoan R, McAtee N et al: Treatment of the acquired immunodeficiency syndrome (AIDS) and AIDS-related complex with a regimen of 3'-azido-2',3'-dideoxythymidine (azidothymidine or zidovudine) and Acyclovir: A pilot study. Annals of Int Med 108:534-540, 1988.