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Safety of Didanosine plus Stavudine Combination Therapy in HIV-infected Subjects in a Pilot Randomized Double-blinded Trial. R Pollard, D Hardy, D Peterson, J Pottage, N Hellmann, J Skovronski, L Reynolds, V Rutkiewicz, S Ogorzalek, C McLaren, L Dunkle. University of Texas Medical Branch, Galveston, TX; University of California, Los Angeles Medical Center, Los Angeles, CA; University of Texas, Southwestern Medical Center, Dallas, TX; Rush Medical College, Chicago, IL; Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT.

Combination antiretroviral therapy may produce a greater immunologic and antiviral effect than monotherapy in the treatment of HIV infection. This trial is the first study of the long-term safety and antiviral activity of didanosine (Videx®) and stavudine (Zerit®) combination therapy in the treatment of HIV infection. A total of 75 subjects (15 per dose group) with previously-untreated HIV infection and CD4 cell counts of 200-500/mm^3 will be randomized to receive 52 weeks of therapy with one of the following didanosine+stavudine combination regimens: 200mg+40mg, 200mg+20mg, 100mg+40mg, 100mg+20mg, or 100mg+10mg (each dose administered bid; doses are adjusted for weight < 60 kg). As of November 21, 1994, 39 subjects were treated with study therapy for a median of 13 weeks (0.1 to 44 weeks). At baseline the subjects have a median age of 30 and a CD4 cell count of 325/mm^3. Two subjects have discontinued therapy due to adverse events (one subject with grade 3 neutropenia and one with skin rash). Two subjects required dose reduction for liver transaminase elevations > 5 times upper limit of normal (grade 3) but have tolerated therapy at the reduced dose. No subject has experienced peripheral neuropathy requiring dose modification; one subject developed a Bell's palsy on therapy but has subsequently tolerated resumption of therapy. No elevations of amylase or lipase > 1.4 times upper limit of normal (grade 2-4) have occurred. These preliminary data suggest that didanosine+stavudine combination therapy can be safely administered at several dose combinations for at least 13 weeks. The relationship of adverse events to dose will be evaluated by an external DSMB.

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Oral brivudin versus intravenous acyclovir in the treatment of herpes zoster in immunocompromised patients: a randomized double-blind trial

P. Wutzler, E. De Clercq*, K. Wutke, and I. Färber
Institute for Antiviral Chemotherapy, Friedrich-Schiller University of Jena, Germany;
*Rega Institute for Medical Research, Katholieke Universiteit Leuven, Belgium

In patients that are profoundly immunocompromised by the underlying disease and/or chemotherapy or radiotherapy, herpes zoster is more common than in the general population. Under immunocompromised conditions the course of varicella-zoster virus (VZV) infections can become extremely serious due to the development of visceral dissemination. In addition, immunocompromised patients are at high risk to progression of cutaneous rash and delayed healing of lesions. The results of a randomized double-blind trial comparing oral brivudin and intravenous acyclovir for the treatment of herpes zoster in adult patients with malignant disease are presented here.

The efficacy of oral brivudin versus intravenous acyclovir was compared in a randomized multicentered study under double-blind conditions using the double-dummy technique. A total of 48 patients with a herpes zoster rash less than 72 hours in duration were entered in the study. Brivudin was given as one 125-mg tablet every six hours. Acyclovir was infused over one hour at a dose of 10 mg/kg every eigth hours. Treatment was continued for five days. There was no significant difference between the treatment groups when analysed in terms of new lesion formation, increase in area of rash within the primary dermatome, cutaneous dissemination and affection of mucous membranes or visceral organs. Both treatment regimes were also equally effective in the time to full crusting of lesions. Oral brivudin and intravenous acyclovir were well tolerated by most patients. There was no necessity to interrupt the treatment in any case. Being as effective as intravenous acyclovir in the treatment of herpes zoster, oral brivudin offers the potential for outpatient therapy of herpes zoster in immunocompromised patients.