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Thrice-weekly maintenance therapy for cytomegalovirus retinitis in patients with acquired immunodeficiency syndrome (AIDS)

To the Editors:

Cytomegalovirus (CMV) retinitis is the most common localization of CMV disease in patients with acquired immunodeficiency syndrome (AIDS) and is, in fact, the most frequent ocular opportunistic infection, often leading to a partial or total loss of vision [1]. Induction treatment for CMV disease is relatively well standardized (2 to 3 weeks of daily intravenous ganciclovir or foscarnet) and able to control the progression of the retinitis in approximately 60 to 80% of cases [2,3]. Without maintenance therapy, the relapse rate approaches 100% within 3 to 6 weeks. Even with maintenance therapy with ganciclovir (5 mg/kg/day) or foscarnet (120 mg/kg/day) daily for 5 days/week, 50% of patients relapse after a median time of 8 to 16 weeks [4,5]. It has been suggested that doubling the dose of ganciclovir (to 10 mg/kg/day), but with thrice-weekly administration, may be as effective as the standard dosage of 5 days/week [6,7]. To follow is our report of the results of an open, prospective, clinical study of maintenance therapy, using the thrice-weekly approach, for CMV retinitis in AIDS patients.

A total of 69 human immunodeficiency virus (HIV)-infected adults diagnosed with CMV disease between May 1988 and December 1993 were eligible for inclusion in the study. Those who had CMV retinitis (n = 57), with or without other localizations, were given at least 2 weeks of intensive induction therapy with either intravenous ganciclovir (5 mg/kg every 12 h), foscarnet (60 mg/kg every 8 h) or both. Of these 57 patients, 33 successfully completed the induction treatment, gave their consent to receive intravenous maintenance therapy thrice weekly and were included in the study. Maintenance therapy was started with either ganciclovir (10 mg/kg/day) or foscarnet (100 mg/kg/day) or both, every Monday, Wednesday and Friday, for a mean period of 19 (range 6 to 78) weeks. The crude relapse rate was 51% (17/33) and the crude mortality rate was 66% (22/33). Altogether, 27 patients received ganciclovir (14 relapses, 18 deaths), four received foscarnet (two relapses, two deaths), and two patients received both (one relapse, two deaths). The time to relapse of CMV retinitis, time to death or relapse and time to death are shown in Figure 1. The median time to relapse was 18 weeks, the median survival time free of CMV retinitis was 14 weeks and the median survival time was 34 weeks. Neutropenia occurred in eight patients (24%), seven receiving ganciclovir and one receiving foscarnet, and anemia occurred in two patients (6%), both of whom were receiving ganciclovir. No changes in therapy were required. The neutropenia was controlled using granulocyte colony-stimulating factor and the anemia with blood transfusion when required.

Treatment with either drug improved median survival time from the time of CMV diagnosis to 6 to 8 months to almost 1 year in those responding to anti-CMV treatment. Maintenance therapy is mandatory to delay relapse and progression to blindness. The median time to relapse has been reported to range from 2 to 4 weeks without maintenance therapy and from 8 to 19 weeks with daily or 5 days/week maintenance therapy [4,5]. Both ganciclovir and foscarnet appear to be equally effective in preventing relapses, although in at least one study, foscarnet significantly increased survival time (by around 4 months) compared with ganciclovir [4]. Hall and colleagues [6] and Garweg and coworkers [7] have reported that a total weekly dose of 30 mg/kg of ganciclovir, distributed in three, five or seven doses, has similar efficacy in preventing relapses. Our results are in agreement with these studies and emphasize that the thrice-weekly approach does not appear to be worse in terms of survival. Ganciclovir therapy is often complicated by severe neutropenia, thereby requiring temporary or permanent discontinuation or modification of dosage in at least 25% of patients. In our study, eight (24%) of 29 patients developed moderate neutropenia that did not require discontinuation of therapy. Thus, the toxicity rate was similar to that seen with standard therapy (5 mg/kg/day for 5 days/week).

At present, oral ganciclovir is being evaluated as

maintenance therapy for CMV retinitis and the preliminary results are promising, with similar efficacy to that of standard regimens of intravenous ganciclovir delivered 5 or 7 days/week. As the number of AIDS patients with CMV retinitis is increasing, more patients will need maintenance therapy. A thrice-weekly approach is clearly more comfortable for the patients and less time-consuming. Our study indicates that this hypothesis should be further tested in a prospective randomized trial.

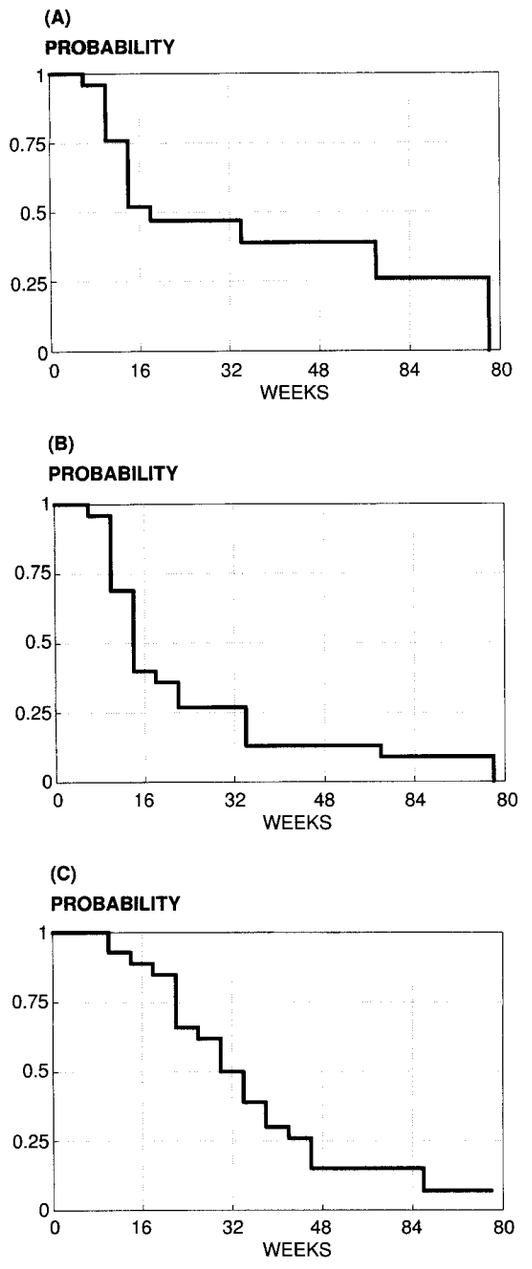

Figure 1 Survival and control of CMV retinitis in 33 study patients receiving thrice-weekly maintenance ganciclovir or foscarnet therapy: (**A**) Time without retinitis progression (17 patients progressed, 16 censored; median 18 weeks); (**B**) Time of survival free of retinitis (25 patients died or relapsed, 8 censored; median 14 weeks); (**C**) Time of survival from diagnosis of retinitis (22 patients died, 11 censored; median 34 weeks).

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Infection caused by *Ochrobactrum anthropi*

To the Editors:

Ochrobactrum anthropi (formerly Centers for Disease Control group Vd), *Alcaligenes xylosoxidans* subspecies *xylosoxidans*, and *Agrobacterium radiobacter* belong to the former genus *Achromobacter* [1]. These pathogens are glucose-non-fermentative, non-fastidious, oxidase-positive, motile (by peritrichous flagella) gram-negative