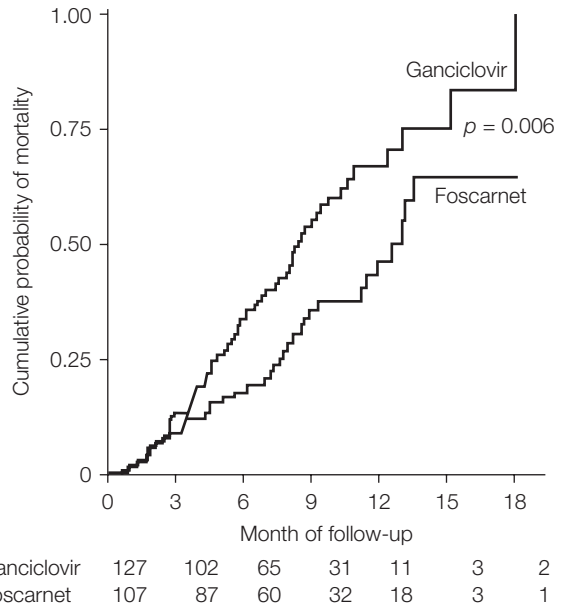

Figure 219.4. Cumulative probability of mortality among patients assigned to foscarnet or ganciclovir treatment for CMV retinitis. Mortality was significantly higher in the ganciclovir group ($p = 0.006$ by the log-rank test). The numbers of patients at risk at each time point are shown at the bottom of the figure. (Reproduced with permission from Anonymous (1992).)

patients receiving present-day, highly effective combination antiretroviral therapy.

Practical disadvantages associated with foscarnet therapy are that the drug must be given daily for maintenance therapy, whereas ganciclovir may be given only five or even three times per week (Hall *et al.*, 1991), and intravenous ganciclovir can be avoided by using oral maintenance valganciclovir, which has efficacy equivalent to intravenous ganciclovir. The toxicity profiles of these two drugs differ: neutropenia is common with ganciclovir, whereas foscarnet very rarely causes significant neutropenia (Clinigen Healthcare, 2014); foscarnet causes renal damage but ganciclovir does not. However, dose-limiting toxicity is more likely with foscarnet than with ganciclovir, and patients must be more closely monitored than with ganciclovir or valganciclovir.

Combination therapy using ganciclovir and foscarnet has been found to be of benefit in patients with clinically resistant CMV retinitis in a number of open, uncontrolled studies in adults and children (Coker *et al.*, 1991; Butler *et al.*, 1992; Dieterich *et al.*, 1993a; Flores-Aguilar *et al.*, 1993; Kupperman *et al.*, 1993; Weinberg *et al.*, 1994), as well as in a randomized multicenter controlled trial of patients with persistently active or relapsed CMV retinitis in which combination therapy was superior to either ganciclovir or foscarnet monotherapy in delaying time to progression as assessed by fundus photography (Anonymous, 1996). CMV replication also appears to be well controlled in patients receiving either combination or alternating therapy with ganciclovir and foscarnet when cumulative weekly doses of each drug are lower than standard monotherapy maintenance regimens, although this has not yet been tested in a large, multicenter randomized controlled trial (Jacobson *et al.*, 1994; Peters *et al.*, 1994). Induction and maintenance regimens for foscarnet have varied (see section 4a, Adults). Quality of life is less with combination therapy than with monotherapy, although some patients are opting for one drug to be given by intravenous administration and the other drug to be received by intravitreal administration (see section 7d, Treatment of aciclovir-resistant HSV and VZV infections).

GASTROINTESTINAL DISEASE

Besides the retina, gastrointestinal disease is the most frequent site of CMV infection in patients with AIDS, with the colon and esophagus being the most commonly involved sites. Gastrointestinal CMV infections respond well to foscarnet therapy. Reported response rates are as high as 90% and relapses after induction therapy are substantially less common than with retinitis (maintenance therapy was seldom used, even in patients not receiving antiretroviral therapy) (Nelson *et al.*, 1991; Blanshard, 1992; Dieterich *et al.*, 1993b; Colebunders *et al.*, 1994; Wilcox *et al.*, 1995; Dieterich *et al.*, 1997). Response to therapy usually occurs within 2–3 weeks of initiating therapy (Reusser *et al.*, 1992). Treatment of patients with acute CMV hepatitis resulted in clinical and biochemical resolution of their disease within 3 weeks of therapy. Only a transient response was observed in patients in this same study who received foscarnet treatment for sclerosing cholangitis (Blanshard, 1992).

In an open-label comparative study, HIV-infected patients with symptomatic CMV gastrointestinal disease (and not receiving combination, potent antiretroviral therapy) were randomized to receive ganciclovir ($n = 22$) or foscarnet ($n = 26$). Responses were assessed clinically, endoscopically, histologically, and by enumeration of CMV inclusions in biopsies. The complete or good clinical response rates, and the response rates based on reduction in CMV inclusions on biopsy, were the same in both groups (73%), and endoscopically determined response rates were also statistically equivalent (85% and 83%, respectively). In this study, maintenance therapy did not appear to prevent progression of disease to a significant extent, as the time to progression was 16 weeks in those receiving maintenance therapy compared with 13 weeks in those not so treated (Blanshard *et al.*, 1995).

Another open-label study comparing ganciclovir with foscarnet treatment for CMV gastrointestinal disease in 29 HIV-infected patients also showed equivalent efficacy of the two drugs based on reduction in CMV viremia (100% in the ganciclovir group vs. 93% in the foscarnet group), loss of CMV in intestinal mucosa (92% vs. 83%, respectively) and clinical response (87% vs. 93%) (Gerna *et al.*, 1997).

Parente and Bianchi Porro (1998) conducted a randomized, controlled trial comparing foscarnet with ganciclovir therapy for HIV-infected patients with CMV esophagitis. A total of 23 patients with newly diagnosed esophagitis were randomized to receive foscarnet ($n = 11$) or ganciclovir ($n = 10$). The two groups were well matched for age, gender, CD4 counts, duration of AIDS, and severity of symptoms. Marked endoscopic improvement occurred in an equivalent proportion of subjects (73% of those treated with foscarnet and