Randomized multicenter trial of foscarnet versus ganciclovir for preemptive therapy of cytomegalovirus infection after allogeneic stem cell transplantation

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The present study compared foscarnet with ganciclovir for preemptive therapy of cytomegalovirus (CMV) infection after allogeneic blood or marrow stem cell transplantation (SCT). Patients with CMV infection, as detected by weekly antigenemia or polymerase chain reaction (PCR) in blood leukocytes, were randomized to intravenous therapy for 2 weeks with either foscarnet at 60 mg/kg or ganciclovir at 5 mg/kg administered every 12 hours; if CMV infection remained detectable, patients received an additional 2 weeks of intravenous foscarnet at 90 mg/kg or ganciclovir at 6 mg/kg given once daily for 5 days per week, after which therapy was stopped. Primary efficacy endpoint was the occurrence of CMV disease or death from any cause within 180 days after SCT. A total of 213 patients were treated with either foscarnet (n = 110) or ganciclovir (n = 103). Kaplan-Meier estimates of event-free survival within 180 days after SCT were similar in the 2 treatment groups (P = .8). During study treatment, severe neutropenia (< 0.5 × 10⁹/L) occurred in 11 (11%) patients on ganciclovir versus 4 (4%) patients on foscarnet (P = .04), and impaired renal function was observed in 5 (5%) patients on foscarnet versus 2 (2%) patients on ganciclovir (P = .4). Neutropenia or thrombocytopenia required discontinuation of ganciclovir in 6 (6%) patients but in no foscarnet-treated patient (P = .03). After allogeneic SCT, preemptive therapy of CMV infection with foscarnet shows similar efficacy as with ganciclovir, but is associated with a lower proportion of patients who develop severe neutropenia and who require discontinuation of antiviral therapy due to hematotoxicity. (Blood. 2002;99:1159-1164)

Introduction

Cytomegalovirus (CMV) remains a leading cause of infectious complications after allogeneic bone marrow or peripheral blood stem cell transplantation (SCT). In the absence of preventive measures, the incidence of CMV infection is 60% to 70% in the first 3 months after allogeneic SCT when graft donor or patient are CMV seropositive, and one third of patients with evidence of CMV infection develop CMV pneumonia. CMV pneumonia is a serious condition, which, with the best presently available therapy, is associated with a high mortality. Therefore, major emphasis must be placed on the prevention of CMV disease in allograft recipients.

For CMV-seropositive patients or seronegative patients with a seropositive graft donor, 2 main strategies are currently used to prevent CMV disease in the posttransplantation course. Prophylactic drug treatment is aimed at suppressing CMV reactivation, and is given to all patients irrespective of the results of virologic monitoring. Alternatively, preemptive therapy consists of initiating antiviral treatment only when active CMV infection is documented in order to prevent the development of CMV disease. Thus, with the preemptive therapy approach, the use of potentially toxic drugs against CMV, such as ganciclovir and foscarnet, is restricted to patients at highest risk for CMV disease.

The antiviral agents ganciclovir and foscarnet exhibit potent in vitro and in vivo activity against CMV. Prophylactic intravenous ganciclovir in placebo-controlled studies of allograft recipients resulted in marked reduction of CMV disease but was not associated with improved survival. In contrast, preemptive ganciclovir treatment based on positive CMV cultures was associated with both a significantly decreased incidence of CMV disease and better survival after allogeneic SCT when compared with placebo. Newer diagnostic techniques, such as the CMV antigenemia assay or the polymerase chain reaction (PCR) in peripheral blood specimens, permit the detection of CMV infection at an early stage when the systemic viral load is still low. A randomized comparison of PCR and viral cultures for initiation of preemptive ganciclovir therapy after allogeneic SCT showed a significantly shorter time to detection of CMV infection in PCR-monitored patients;
earlier ganciclovir treatment in this group resulted in lower incidence of CMV disease and improved survival.11

However, ganciclovir use is associated with marked toxicity to the bone marrow, and severe neutropenia was reported in up to 35% of patients who received ganciclovir treatment after allogeneic SCT.6,7,9,17 By contrast, the antiviral drug foscarnet appears to lack significant hematotoxicity in allograft recipients.18-20 Thus, foscarnet might be an alternative option for preemptive therapy of CMV infection after SCT. First results suggest that preemptive foscarnet treatment mediates protection from CMV disease in SCT recipients.19,21

We report the results of a prospective randomized multicenter trial in which foscarnet and ganciclovir were compared in the preemptive therapy of CMV infection after allogeneic SCT. In this study, antiviral treatment was initiated upon detection of CMV by antigenemia assay or by PCR in peripheral blood leukocytes, and was given for no longer than 4 weeks. In addition to reducing the likelihood of adverse events, antiviral therapy of shorter duration might be advantageous, because prolonged ganciclovir treatment impairs the reconstitution of CMV-specific CD8+ cytotoxic T-cell responses after SCT, thereby increasing the risk for late CMV disease.22

Patients, materials, and methods

Study design

The study was a prospective randomized open-label comparison of foscarnet and ganciclovir for preemptive therapy of CMV infection carried out at 21 centers of the European Group for Blood and Marrow Transplantation (EBMT) and at 3 transplant centers in the United States. The local institutional ethical committees at each of the 24 participating centers approved the study, which followed good clinical practices guidelines. Written informed consent was obtained from each patient. Recipients of an allogeneic bone marrow or peripheral blood stem cell transplant who were at least 12 years of age were screened once a week for the presence of CMV in peripheral blood specimens (Figure 1). For this screening, the study centers had to select either a CMV antigenemia assay or a PCR for CMV DNA in peripheral blood leukocytes. Each center had to submit the methodology of the CMV detection test used to the steering committee for approval prior to activation of the study. CMV was considered present if CMV antigenemia was detected at least once, or if the PCR for CMV DNA was positive in at least 2 consecutive blood specimens a minimum of 3 days and a maximum of 7 days apart. Patients were eligible for the study if CMV was detected by one of these 2 assays within the first 100 days after SCT. Exclusion criteria were development of CMV disease prior to or concomitant with first detection of CMV in blood; CMV antigenemia or positive PCR for CMV DNA in blood before SCT that did not become negative by the time of engraftment; serum creatinine clearance less than 60 mL/min, neutrophil counts less than 0.5 × 10^9/L, or platelet counts unsustainable more than 25 × 10^9/L at the onset of study drug treatment; therapy with foscarnet or ganciclovir within 3 months before study inclusion; and known allergy to either study medication.

Enrolled patients were stratified by transplantation center to balance possible effects of the CMV detection method selected, and by the type of allograft donor (related versus unrelated) since the incidence of CMV disease might differ between these groups. Within each stratum, patients were randomized to receive either intravenous foscarnet at 60 mg/kg every 12 hours or intravenous ganciclovir at 5 mg/kg every 12 hours for 14 days (induction treatment) (Figure 1). Both drugs were administered as 1-hour infusions, and patients in the foscarnet group received extra hydration with more than or equal to 500 mL of isotonic saline or dextrose 5% both before and during the foscarnet infusion. If CMV was undetectable in peripheral blood by the end of induction treatment, the study drug was discontinued. If CMV was still detectable by antigenemia assay or PCR in blood specimens after induction treatment, patients then received either intravenous foscarnet at 90 mg/kg as 2-hour infusion or intravenous ganciclovir at 6 mg/kg as 1-hour infusion for an additional 14 days (maintenance treatment) (Figure 1); during maintenance treatment, both drugs were administered once a day for 5 days per week, and foscarnet-treated patients received the same extra hydration as during the induction regimen. The dosages of foscarnet and ganciclovir during induction and maintenance treatment were adjusted to decreased renal function according to predetermined guidelines. If CMV was still detectable in blood specimens by the end of the maintenance regimen, the treatment was considered a failure, and patients were treated at the discretion of the investigator. Patients who relapsed with CMV antigenemia or PCR detection in peripheral blood after the end of the induction or maintenance regimens were retreated outside protocol, and use of the same drug as in the study was recommended.

Outcome measures

The primary study endpoint was the proportion of patients with event-free survival within 180 days after SCT. Events were defined as the occurrence of CMV disease or death from any cause. CMV disease was diagnosed by documenting CMV in tissue specimens, or in bronchoalveolar lavage fluid (BAL) when CMV pneumonia was suspected, with associated symptoms and signs as defined at the 4th International CMV Workshop.22 All reported episodes of CMV disease were evaluated in a blinded fashion by an independent endpoint committee, and only episodes ratified by this panel of experts were included in the analyses.

Secondary endpoints included the time to development of CMV disease; the rates of patients with persistently positive blood specimens for CMV after completion of induction or maintenance treatment, and of patients who required retreatment after discontinuation of the study drug; the occurrence of herpes simplex virus infection, varicella-zoster virus infection, and major nonviral infections (defined as pneumonia, bloodstream infection, symptomatic urinary tract infection, or infection of the central nervous system due to bacterial, fungal, or protozoal organisms and requiring therapy) within 100 days and 180 days following SCT; the utilization of hematopoietic growth factors in the first 100 days after SCT; the occurrence of renal impairment defined as serum creatinine increase more than or equal to 100% or creatinine clearance decrease more than or equal to 50% from baseline values, and the rates of neutropenia less than 0.5 × 10^9/L during induction and maintenance treatment. Safety was monitored by hematologic and chemical evaluations and urinary analyses, and adverse events were reported.

Statistical analyses

The study was designed to have a power of 80% to detect a difference of at least 15% in event-free survival within 180 days after SCT between the 2 treatment groups. We assumed that both study drugs would result in event-free survival rates of 85%. A one-sided group sequential test was used at an overall significance level of 0.05 to assess the non inferiority of
One interim analysis of the primary efficacy variable and safety was performed when the first 110 patients had completed 180 days of follow-up using the O’Brien-Fleming method.24 The evaluation of the results was done by an independent data and safety monitoring board. Using predetermined guidelines for stopping the trial, the board did not recommend early termination or alteration of the study. Because of this interim analysis, the P value required for significance in the primary efficacy analysis was .047.

Kaplan-Meier analysis was used to estimate event-free survival in the first 180 days after SCT.25 The log-rank test was used to compare the probabilities of event-free survival in both treatment groups. Additional evaluation of the primary endpoint was done by logistic regression analysis to assess the influence of the following variables: study drug (foscarnet versus ganciclovir), type of allograft donor (related versus unrelated), source of stem cell graft (bone marrow versus peripheral blood), type of CMV detection test (antigenemia versus PCR). The Fisher exact test was used to compare proportions in the study groups. A one-sided test was only used for the noninferiority evaluation of foscarnet versus ganciclovir, whereas all additional tests were done 2-sided. Analyses of safety and of primary and secondary endpoints was done on an all-patients-treated basis.

Results

Between January 1996 and March 1998, 218 patients were enrolled in the study: 112 were assigned to receive foscarnet and 106 to receive ganciclovir. Five patients were excluded from analyses: in the foscarnet group, 2 patients never received study medication because of severe neutropenia (n = 1) and patient withdrawal (n = 1); in the ganciclovir group, 3 patients were excluded because of low platelet counts before onset of study treatment (n = 1), foscarnet treatment within the past 3 months (n = 1), and lost patient’s records (n = 1). The characteristics of the 213 evaluable patients were well balanced at baseline (except in terms of sex, with more male patients in the foscarnet group) (Table 1).

The median (range) time of follow-up after SCT was similar in the 2 study groups, and was 183 (172-241) days for patients assigned to foscarnet and 184 (175-219) days for patients assigned to ganciclovir. The median (range) time from SCT to randomized treatment start was 43 (19-104) days in the foscarnet group versus 51 (11-101) days in the ganciclovir group (P = .09). The median (range) duration of exposure to randomized study drug was 16 (3-33) days among foscarnet-treated patients and 16 (2-33) days among patients who received ganciclovir. The proportion of patients who completed induction or maintenance treatment without premature discontinuation or switch of study drug was similar in the 2 groups: during the induction regimen, it was 95% in the foscarnet group versus 85% in the ganciclovir group; during maintenance treatment, it was 73% in the foscarnet group versus 82% in the ganciclovir group. The proportion of patients who discontinued treatment prematurely because of an adverse effect was 2% in the foscarnet group versus 5% in the ganciclovir group during induction treatment, and 0% in the foscarnet group versus 3% in the ganciclovir group during the maintenance regimen.

CMV disease and mortality

During the first 180 days after allogeneic SCT, the Kaplan-Meier estimates of event-free survival in both treatment groups were similar (P = .6) (Figure 2). The probability of event-free survival by day 180 after SCT was 66% for patients assigned to receive foscarnet and 73% for patients assigned to receive ganciclovir. The analysis of the primary efficacy endpoint in a logistic regression model adjusted for study drug, allograft donor type, source of stem cell graft, and CMV detection test used showed no significant influence of these parameters on event-free survival within 180 days after SCT (Table 2).

In each group, 5 patients developed CMV disease (Table 3). CMV disease occurred in 7 patients before and in 3 patients after day 100 after SCT (on days 137, 168, and 177 after SCT, respectively). Death from CMV disease occurred in 2 ganciclovir-treated patients who developed CMV pneumonia. The other 8 patients survived the episode of CMV disease.

The overall mortality rates within 180 days after SCT were 26%

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Table 1. Baseline characteristics of the 213 patients after allogeneic SCT who received preemptive treatment of CMV infection with either foscarnet or ganciclovir

<table>
<thead>
<tr>
<th>Variable</th>
<th>Foscarnet</th>
<th>Ganciclovir</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>39 (12-58)</td>
<td>40 (14-61)</td>
<td>.5</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>73/37</td>
<td>53/50</td>
<td>.02</td>
</tr>
<tr>
<td>Source of stem cell graft</td>
<td>Bone marrow</td>
<td>72</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>Peripheral blood</td>
<td>38</td>
<td>43*</td>
</tr>
<tr>
<td>Type of transplant</td>
<td>Related</td>
<td>77</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td>Unrelated</td>
<td>33</td>
<td>30</td>
</tr>
<tr>
<td>CMV serology before SCT</td>
<td>Recipient (pos/neg)</td>
<td>87/23</td>
<td>81/21†</td>
</tr>
<tr>
<td></td>
<td>Donor (pos/neg)</td>
<td>65/44†</td>
<td>61/41†</td>
</tr>
</tbody>
</table>

SCT indicates stem cell transplantation; CMV, cytomegalovirus.
*One cord blood graft.
†One serology result each unavailable.

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Table 2. Multivariate analysis of the effects of study drug, type of allograft donor, source of stem cell graft, and type of CMV detection test used on the primary efficacy endpoint (occurrence of CMV disease or death from any cause) in the first 180 days after allogeneic SCT

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>Confidence interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foscarnet vs ganciclovir</td>
<td>0.74</td>
<td>0.40-1.34</td>
<td>.32</td>
</tr>
<tr>
<td>Unrelated vs related graft donor</td>
<td>0.88</td>
<td>0.43-1.80</td>
<td>.73</td>
</tr>
<tr>
<td>Bone marrow vs peripheral blood SCT</td>
<td>0.96</td>
<td>0.48-1.91</td>
<td>.92</td>
</tr>
<tr>
<td>PCR for CMV vs CMV antigenemia</td>
<td>1.60</td>
<td>0.84-3.03</td>
<td>.14</td>
</tr>
</tbody>
</table>

CMV indicates cytomegalovirus; SCT, stem cell transplantation; PCR, polymerase chain reaction.
in the foscarnet group and 22% in the ganciclovir group, respectively (Table 3).

**CMV detection in blood after completion of treatment**

After completion of the induction regimen, CMV was still detectable in peripheral blood specimens by antigenemia or PCR in 29% of patients treated with foscarnet and in 34% of patients who received ganciclovir (P = .4). By the end of maintenance treatment the respective figures were 10% and 13% (P = .2). Within 180 days after SCT, the proportion of patients who required retreatment for CMV infection after completion of the study drug regimens was 43% in the foscarnet group versus 28% in the ganciclovir group (P = .06). The median interval between discontinuation of study drug and retreatment of CMV infection was 27 days for patients who received foscarnet and 38 days for ganciclovir-treated patients.

**Other herpesvirus infections and major nonviral infections**

The rates of herpes simplex virus infection within 100 days and within 180 days after SCT were 8% and 13%, respectively, among patients assigned to foscarnet, and 9% and 14%, respectively, in patients receiving ganciclovir. For varicella-zoster virus infection, the corresponding figures were 5% and 10% in the foscarnet group, and 3% and 12% in the ganciclovir group. The proportion of patients who developed major nonviral infections within 100 days and within 180 days following SCT were 26% and 35%, respectively, in the foscarnet group versus 28% and 33%, respectively, in the ganciclovir group. There was no significant difference between treatment groups for the rates of infections due to herpes simplex virus or varicella-zoster virus, or of major nonviral infections during the time periods analyzed.

**Use of hematopoietic growth factors**

In the first 100 days after SCT, 28% of patients in the ganciclovir group and 19% in the foscarnet group required hematopoietic growth factors (P = .1). When only patients were considered who received exclusively the originally assigned study drug during this time period, hematopoietic growth factors were given to 25% of ganciclovir-treated patients versus 8% of foscarnet-treated patients (P = .007).

**Safety**

During induction and maintenance therapy, severe neutropenia (< 0.5 x 10^9/L) occurred in 11 (11%) patients in the ganciclovir group versus 4 (4%) patients in the foscarnet group (P = .04). Neutropenia or thrombocytopenia required discontinuation of ganciclovir treatment in 6 (6%) patients but in no foscarnet-treated patient (P = .03). Impaired renal function as defined was observed in 5 (5%) patients receiving foscarnet versus 2 (2%) patients given ganciclovir (P = .4). The rates of serum electrolyte abnormalities were significantly more common in the foscarnet group than in the ganciclovir group: they were 22% versus 4% for hypocalcemia (P < .001), 18% versus 6% for hypomagnesaemia (P = .006), 17% versus 6% for hypokalaemia (P = .01), and 6% versus 0% for hypophosphataemia (P = .01). No patient showed clinical symptoms or signs attributable to changes in serum calcium, magnesium, potassium, or phosphorus levels, but all were supplemented by intravenous infusions when serum levels were low.

**Discussion**

The current study shows that foscarnet can be used with similar efficacy as intravenous ganciclovir for the preemptive therapy of CMV infection after allogeneic bone marrow or peripheral blood SCT. Furthermore, preemptive treatment with foscarnet did not raise safety concerns and was associated with significantly less serious hematotoxicity than with ganciclovir.

Allograft recipients are at particularly high risk for severe CMV disease during the phase of profound combined immunodeficiency, which usually lasts 3 to 4 months after SCT.1,2,22,26 The introduction of prophylactic or preemptive antiviral drug treatment during this early posttransplantation period resulted in a marked reduction of the incidence of CMV pneumonia from approximately 15% to 20%, to 0% to 5%.3,6,7,9,10,12 The incidence of CMV pneumonia and other CMV disease manifestations in our trial was in the range of those in previous reports, and was similar in the 2 treatment groups. CMV pneumonia was diagnosed in a total of 5 patients (2%), and was fatal in the 2 patients who were part of the ganciclovir group.

Preemptive therapy in this study was initiated within the first 100 posttransplantation days, but patients were evaluated up to day 180 after SCT. Prolonged follow-up of patients is required in view of reports on the occurrence of late CMV disease (beyond 100 days posttransplantation) and of death from any cause within 180 days after SCT (primary endpoint). In addition, a multivariate analysis including the variables study drug, type of transplant donor, source of stem cell graft, and CMV detection method used for initiation of preemptive therapy revealed no significant influence of these factors on the primary endpoint.

The length of preemptive therapy of CMV infection selected for this trial was a maximum of 4 weeks in order to reduce the risk for adverse events, late CMV disease, and antiviral drug resistance. Previous data indicated that preemptive treatment based on sensitive CMV assays permitted initiation of therapy at an early stage of CMV infection, and treatment longer than 4 weeks was thus rarely necessary.13 Furthermore, the risk for late CMV disease increases with the duration of prior antiviral drug therapy.29 Foscarnet and ganciclovir are potent inhibitors of CMV replication, and extended use of these agents is thought to impair the reconstitution of posttransplantation CMV-specific cellular immunity, which plays an important role in mediating protection from CMV infection and CMV disease.22,26,30

Patients in both treatment groups received a median of 16 days of study drugs. The proportion of patients who had persistently
positive blood specimens for CMV after the induction and maintenance regimens was similar in the 2 groups, and maintenance treatment was necessary in about one third of patients in both groups. Nevertheless, approximately 10% of patients had detectable CMV in blood after the end of maintenance therapy, and a substantial proportion of patients required retreatment during the study period. Thus, selected patients may need prolonged antiviral drug treatment in spite of the increased risk of late CMV disease. Determination of therapy duration might be facilitated by the introduction of quantitative assays that enable monitoring of the kinetics of systemic CMV load. 27,31,32

There was a trend toward a higher proportion of patients requiring retreatment in the foscarnet group compared with the ganciclovir group (43% versus 28%). This trend may be explained in part by the dose of foscarnet selected for our trial, which was two thirds of the dose recommended for the therapy of established CMV disease. 15 The lower dose of foscarnet was chosen because earlier pilot studies suggested that it was efficacious in preventing CMV disease after SCT. 18,19 Despite the necessity of more frequent retreatment in the foscarnet group, the incidence of CMV disease was not higher than in the ganciclovir group. The lower foscarnet dose thus permitted to reduce the risk of toxicity without jeopardizing the efficacy of preemptive foscarnet treatment.

Although preemptive therapy of CMV infection in our trial was of limited duration, late disease (beyond day 100 after SCT) occurred in 3 of the 10 patients diagnosed with CMV disease. Extended virologic surveillance with repeated courses of preemptive anti-CMV treatment might therefore be required for patients with persistent profound immunosuppression.

Up to one-third of patients who receive prophylactic or preemptive ganciclovir following allogeneic SCT develop severe neutropenia. 6,7,9,17 Furthermore, neutropenia in ganciclovir recipients was shown to be an independent risk factor of mortality. 17 During preemptive therapy, neutropenia less than 0.5 × 10⁹/L among our patients was significantly more frequent in the ganciclovir group (11%) than in the foscarnet group (4%). Moreover, hematologic toxicity required discontinuation of treatment significantly more often in patients receiving ganciclovir (6%) than in patients assigned to foscarnet (0%).

The rate of severe neutropenia in our ganciclovir group appears lower than that in earlier reports on prophylactic or preemptive ganciclovir treatment after SCT. 6,7,9,17 This difference might be related to both a shorter duration of ganciclovir therapy and a more frequent use of hematopoietic growth factors in our trial.

The use of foscarnet is generally associated with renal toxicity. 13 In an earlier study of SCT recipients, intravenous foscarnet was given intermittently but without extra hydration, and resulted in transient renal dysfunction in 50% of allograft recipients. 18 A pilot trial evaluating the foscarnet regimen used in this study showed only mild serum creatinine increases in 14% of patients after allogeneic SCT, and no patient required discontinuation of foscarnet. 19 Similar results were reported by others. 33 All patients in our foscarnet group received intravenous extra hydration both before and during the foscarnet infusions, and dosages of foscarnet were adjusted to decreased serum creatinine clearance. Impaired renal function was documented in 5% of patients who were treated with foscarnet versus 2% of patients receiving ganciclovir, which was not a statistically significant difference. No patient had foscarnet discontinued because of renal impairment. Preemptive foscarnet therapy, however, was associated with more frequent electrolyte disturbances. Serum electrolytes were closely monitored during foscarnet treatment, and low electrolyte levels were corrected by supplementation. Clinical symptoms or signs attributable to changes in serum electrolyte levels were not reported. Thus, foscarnet-related renal toxicity in allograft recipients is limited with the regimen used in this study, and electrolyte disturbances, though common, are not associated with clinical complications if recognized and corrected rapidly.

Both foscarnet and ganciclovir have potent activity against herpes simplex virus and varicella-zoster virus. 13,14 and the rates of infections due to these viruses were similar in the 2 study groups. The incidence of major nonviral infections was also not different between the foscarnet and ganciclovir groups, although severe neutropenia developed more frequently in patients on ganciclovir therapy. The trend toward more common use of hematopoietic growth factors in ganciclovir recipients might explain in part the similar rates of major nonviral infections in the 2 study groups.

In conclusion, our data indicate that the use of foscarnet for preemptive therapy of CMV infection in allograft recipients did not raise safety concerns if patients receive intravenous extra hydration and are monitored for serum electrolyte changes. The efficacy of preemptive foscarnet and ganciclovir treatment is similar, but ganciclovir is associated with a significantly higher rate of severe neutropenia. Future studies need to address the optimal duration of preemptive therapy of CMV infection and its effect on late CMV disease after SCT.

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References

10. Schmidt GM, Horak DA, Niland JC, et al. Randomized, controlled trial of prophylactic ganciclovir for cytomegalovirus pulmonary infection in...
Appendix

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Randomized multicenter trial of foscarnet versus ganciclovir for preemptive therapy of cytomegalovirus infection after allogeneic stem cell transplantation: Presented in part at the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 1999 (abstract H144).

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