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Efficacy and safety of low-dose ganciclovir preemptive therapy in allogeneic haematopoietic stem cell transplant recipients compared with conventional-dose ganciclovir: a prospective observational study

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Objectives: We performed a prospective observational study comparing the efficacy and safety of low-dose ganciclovir (5 mg/kg/day) as initial preemptive therapy in allogeneic haematopoietic stem cell transplantation (HSCT) recipients with conventional-dose ganciclovir (10 mg/kg/day).

Methods: All adult patients undergoing allogeneic HSCT were enrolled at a transplant centre over a 24 month period. The decision to use low-dose or conventional-dose ganciclovir was at the discretion of each attending haematologist. A logistic regression model with inverse probability of treatment weighting (IPTW) using propensity scores was performed to reduce the effect of the selection bias in assignment for ganciclovir preemptive therapy.

Results: Of the 252 HSCT recipients, 97 (38%) received preemptive ganciclovir therapy. Of these, 53 (55%) and 44 (45%) received low-dose and conventional-dose ganciclovir, respectively. The viral clearance rate was higher in the low-dose ganciclovir group [98% (52/53)] than in the conventional-dose ganciclovir group [86% (38/44), $P=0.04$], while the low-dose ganciclovir group exhibited a longer viral clearance time (median 21.0 days) than the conventional-dose ganciclovir group (median 14.0 days, $P=0.05$). The rate of discontinuation of therapy due to neutropenia or nephrotoxicity was similar in the two groups, although conventional-dose ganciclovir was changed to another regimen more frequently than low-dose ganciclovir. There were three cases of cytomegalovirus (CMV) disease in each group after the initial preemptive therapy. The logistic regression models using propensity scores also revealed that there were no significant differences in viral clearance, secondary episodes of CMV infection, CMV disease and overall mortality between the two groups.

Conclusions: Low-dose ganciclovir appears to be safe, and to be at least as effective as conventional-dose ganciclovir for CMV viraemia in allogeneic HSCT recipients.

Keywords: cytomegalovirus, haematopoietic stem cell transplantation, HSCT

Introduction

Cytomegalovirus (CMV) remains an important complication of allogeneic haematopoietic stem cell transplantation (HSCT).[1–3] CMV diseases such as CMV pneumonia are the cause of substantial mortality, so that preemptive strategies based on various diagnostic tests are the standard treatment to minimize CMV-related morbidity in HSCT recipients.[4] Preemptive therapy is initiated when CMV infection is detected but before CMV-associated symptoms develop, and ganciclovir has been the first-line treatment recently.[3] Ganciclovir has been demonstrated to reduce the risk of CMV infection, but neutropenia occurs in up to 30% of HSCT recipients during ganciclovir therapy.[5,6] It is approximately twice as common in patients receiving conventional-dose ganciclovir (10 mg/kg/day) preemptive therapy as in untreated patients, and is associated with an increased risk of bacterial as well as invasive fungal infection.[5,7,8]

To reduce such ganciclovir-related adverse effects in HSCT recipients, preemptive therapy with low-dose ganciclovir (5 mg/kg once daily) has been suggested.[2,6] However, there have been few direct comparisons of the clinical usefulness of low-dose ganciclovir preemptive therapy with conventional-dose ganciclovir preemptive therapy.[9] We therefore compared the efficacy and safety of low-dose ganciclovir as initial preemptive therapy for CMV reactivation in allogeneic HSCT recipients with conventional-dose ganciclovir.

Patients and methods

Data collection

Between February 2009 and January 2011, all adult patients undergoing allogeneic HSCT at a 2700 bed, tertiary care hospital in Seoul, South Korea, were eligible for this study. Our hospital committee, consisting of infectious diseases specialists and haematologists, approved the use of low-dose ganciclovir therapy at the discretion of the attending haematologists in January 2009. Thus the data for the efficacy and safety of low-dose ganciclovir preemptive therapy compared with conventional-dose ganciclovir preemptive therapy were collected prospectively in the HSCT recipient registry data from February 2009. Patients with positive CMV antigenaemia who were not treated for CMV disease before ganciclovir preemptive therapy were included in the final analysis. Baseline clinical data were obtained from the hospital's electronic database of the HSCT recipient registry.

Preemptive therapy

Allogeneic HSCT recipients were prospectively monitored for CMV antigenaemia pre-HSCT and once weekly from day 21 to day 100 post-HSCT. Samples of heparinized blood (10 mL) were processed and 2×10^5 cells were stained after fixation to monitor antigenaemia (Light Diagnostics, Chemicon International Inc., CA, USA).[10] CMV antigenaemia of $\geq$5 cells per 200 000 cells in high-risk patients and $\geq$20 cells per 200 000 cells in low-risk patients were indications for preemptive therapy. High-risk patients were defined as those receiving anti-thymoglobulin in the preoperative regimen, those with grade 3–4 acute graft-versus-host disease (GVHD) or those receiving more than 0.5 mg/kg methylprednisolone. The decision to perform low-dose ganciclovir (5 mg/kg/day) or conventional-dose ganciclovir (5 mg/kg twice daily) was at the discretion of each attending haematologist. Intravenous ganciclovir was given daily for at least 2 weeks (the induction period) or until patients were negative for CMV antigenaemia. If the CMV cleared within the induction period, maintenance therapy was omitted. If the CMV antigenaemia persisted, a maintenance dose of ganciclovir (5 mg/kg/day) was given 5 days/week until the antigenaemia was negative. Escalation of the dose of ganciclovir was considered if the antigenaemia increased or if CMV disease was suspected. In cases of bone marrow failure, we considered changing the regimen to foscarnet (90 mg/kg twice daily).

Definitions

The total duration of antigenaemia clearance was defined as the date of initial preemptive therapy minus the viral clearance date. CMV-related pneumonia was defined as fulfilment of all the relevant criteria, namely symptoms and radiographic and histologic proof of CMV infection by lung biopsy or bronchoalveolar lavage.[11] CMV gastroenteritis was defined as detection of CMV in biopsy specimens by virus isolation, immunohistochemical analysis or *in situ* hybridization, accompanied by gastrointestinal symptoms.[3] The minimum requirements for CMV syndrome were the presence of fever (>38°C) for at least 2 days within a 4 day period, the presence of neutropenia or thrombocytopenia, and detection of CMV in blood or biopsy specimens.[12,13] Neutropenia was defined as an absolute neutrophil count of $<1\times10^9$/L.[11] The primary analysis was performed on the intention-to-treat population, including all patients who received preemptive ganciclovir therapy due to CMV infection. We also carried out a per-protocol analysis involving those patients who received daily low-dose or conventional-dose ganciclovir preemptive therapy for at least 2 weeks or until they were negative for CMV antigenaemia without switching to the alternative dose regimen.

Statistical analysis

Categorical variables were compared using Fisher's exact test or Pearson's χ^2 test, as appropriate, and continuous variables were compared using the Mann–Whitney *U*-test or Student's *t*-test. To reduce the effect of selection bias in the assignment of patients to ganciclovir preemptive therapy in this observational study, we performed a rigorous adjustment of differences in baseline characteristics by propensity score analysis. Propensity scores were estimated without regard to outcomes, using multiple logistic regression analysis.[14] All pre-specified covariables, which are listed in Table 1, were included in the logistic regression models for low-dose ganciclovir therapy versus conventional-dose ganciclovir therapy with forward stepwise selection in the final model. The final model included age, kinds of preemptive therapy, occurrence of acute GVHD, grading acute GVHD, initial creatinine clearance and the use of steroids. Model discrimination was assessed with *c*-statistics ($c=0.849$),[15] and model calibration with Hosmer–Lemeshow statistics ($P=0.920$). The effect of low-dose ganciclovir preemptive therapy on various outcome measures was analysed by performing a logistic regression analysis with covariable adjustment using the propensity score. In addition, we carried out logistic regression analysis with inverse probability of treatment weighting (IPTW) using the propensity score.[16] All tests of significance were two-tailed and $P\leq0.05$ was considered significant. All statistical analyses were performed with SAS software, version 9.1 (SAS Institute Inc., Cary, NC, USA). Additionally, to show the non-inferiority of low-dose ganciclovir therapy in viral clearance, secondary episode of CMV infection, CMV disease and overall mortality, non-inferiority analysis was performed with PASS software (NCSS, Kaysville, UT, USA) (Table S1, available as Supplementary data at *JAC* Online). A non-inferiority margin of 6 percentage points was chosen for the absolute difference in outcome.[17] When the significance level was fixed at 0.025, we estimated that the study would retain 80% power to show non-inferiority of low-dose preemptive therapy.

Results

Study population

Ninety-seven (38%) patients received preemptive ganciclovir therapy due to CMV infection and 2 patients (0.8%) with CMV disease were excluded. Of these 97 patients, 53 (55%) received low-dose ganciclovir as preemptive therapy, and the remaining 44 (45%) received conventional-dose ganciclovir. Baseline clinical characteristics are shown in Table 1. The low-dose ganciclovir group was similar to the conventional-dose group in terms of median age, initial diagnosis, source of haematopoietic progenitor cells and CMV serostatus in donors and recipients. There was no significant difference in the initial mean CMV antigenaemia titre between the two groups (median 32 cells per 200 000 cells versus 13 cells per 200 000 cells, $P=0.92$). However, fewer patients who received low-dose ganciclovir experienced acute GVHD during the first 100 days after HSCT than did those

Table 1. Baseline clinical characteristics of the HSCT recipients receiving low-dose and conventional-dose ganciclovir therapy

	Low-dose ganciclovir ($n=53$)	Conventional-dose ganciclovir ($n=44$)	*P* value
Age (years), median (range)	41 (16–70)	46 (17–63)	0.30
Male gender	32 (60)	25 (57)	0.72
Diagnosis			0.45
acute myeloid leukaemia	25 (47)	20 (46)	
acute lymphoblastic leukaemia	13 (25)	7 (16)	
chronic myeloid leukaemia	1 (2)	0 (0)	
aplastic anaemia	6 (11)	5 (11)	
myelodysplastic syndrome	4 (8)	7 (16)	
non-Hodgkin's lymphoma	4 (8)	2 (5)	
paroxysmal nocturnal haemoglobinuria	0 (0)	3 (7)	
Type of transplant			0.37
allogeneic, sibling	18 (34)	15 (34)	
allogeneic, family donor other than sibling	21 (40)	12 (27)	
allogeneic unrelated	14 (26)	17 (39)	
Stem cell source			0.56
bone marrow	6 (11)	7 (16)	
peripheral blood	47 (89)	37 (84)	
CMV serostatus			>0.99
recipient+/donor+	52 (98)	43 (98)	
recipient+/donor−	1 (2)	1 (2)	
High-risk patients for CMV disease[a]	49 (92)	36 (82)	0.11
anti-thymoglobulin use	49 (92)	36 (82)	
methylprednisolone use	5 (9)	1 (2)	
grade 3–4 acute GVHD	6 (11)	19 (43)	
Cut-off value			0.11
>5 cells per 200 000 cells	49 (92)	36 (82)	
>20 cells per 200 000 cells	4 (8)	8 (18)	
Initial CMV antigen titre, median (IQR)	32 (10–104)	13 (3–49)	0.92
Absolute neutrophil count before ganciclovir therapy (1×10^9/L), median (IQR)	2.85 (1.57–5.95)	3.40 (2.09–6.59)	0.94
Haemoglobin level before ganciclovir therapy (g/dL), median (IQR)	9.9 (9.0–11.1)	10.2 (8.9–11.5)	0.99
Platelet count before ganciclovir therapy ($\times10^3$/mm^3), median (IQR)	127 (44–178)	98 (27–171)	0.22
Creatinine clearance before ganciclovir therapy (mL/min/1.73 m^2), median (IQR)	60.0 (59.0–90.0)	60.0 (58.5–90.0)	0.58
GVHD prophylaxis			0.77
cyclosporine	5 (9)	6 (14)	
cyclosporine/methotrexate	47 (89)	37 (84)	
others	1 (2)	1 (2)	
Patients experiencing GVHD during first 100 days	17 (32)	29 (66)	0.001
Grade of GVHD			0.11
1	2 (12)	2 (7)	
2	9 (53)	8 (28)	
3	3 (18)	10 (35)	
4	3 (18)	9 (31)	

Continued

Table 1. *Continued*

	Low-dose ganciclovir ($n=53$)	Conventional-dose ganciclovir ($n=44$)	*P* value
Regimen for GVHD treatment			0.66
corticosteroid/cyclosporine	13 (76)	21 (73)	
corticosteroid/tacrolimus	2 (12)	3 (10)	
corticosteroid/cyclosporine/azathioprine	2 (12)	3 (10)	
corticosteroid/cyclosporine/mycophenolate	0	2 (7)	
Initial episode of viraemia after transplantation, median days (IQR)	36.0 (27.5–47.0)	35.0 (24.3–46.0)	0.94

Data are presented as number (%), unless otherwise specified.
[a]High-risk patients for CMV disease were defined as those receiving anti-thymoglobulin in the pre-operative regimen, those with grade 3–4 acute GVHD or those receiving >0.5 mg/kg methylprednisolone.

who received conventional-dose ganciclovir [32% (17/53) versus 66% (29/44), $P=0.001$]. The overall proportions of patients with each grade of acute GVHD did not differ between the two groups ($P=0.11$).

Clinical outcomes in low-dose and conventional-dose ganciclovir groups

The first CMV antigenaemia was detected a median of 36.0 (IQR 27.5–47.0) days after HSCT in the low-dose ganciclovir group and 35.0 (IQR 24.3–46.0) days in the conventional-dose group (Table 1). There was no significant difference in successful viral clearance between the low-dose ganciclovir group [98% (52/53)] and the conventional-dose ganciclovir group [86% (38/44), $P=0.04$] (Table 2). However, low-dose ganciclovir required a longer time for viral clearance (median 21.0 days) than conventional-dose ganciclovir (median 14.0 days, $P=0.05$). There was no significant difference in the total duration of preemptive therapy between low-dose ganciclovir (median 15.0 days) and conventional-dose ganciclovir (median 13.0 days, $P=0.50$).

Of the 97 patients who received preemptive therapy, 23 (24%) experienced a secondary episode of CMV infection after completion of the initial preemptive therapy. The frequency of secondary episodes was higher in the conventional-dose ganciclovir group [34% (15/44)] than in the low-dose ganciclovir group [15% (8/53), $P=0.03$]. The times of onset of the secondary occurrence of antigenaemia after transplantation were similar in the two groups (87.0 days versus 87.3 days, respectively, $P=0.82$). There were three cases of CMV disease in each group after the initial preemptive therapy (one colitis, one pneumonia and one CMV syndrome in the low-dose ganciclovir group versus two colitis and one CMV syndrome in the conventional-dose ganciclovir group). The overall transplant-related mortality was not significantly different in the two groups ($P=0.08$). There was no death due to CMV disease in either group. The results of the per-protocol analysis also revealed that there were no significant differences between the two groups in successful viral clearance and CMV disease after completion of the initial ganciclovir preemptive therapy (Tables S2 and S3, available as Supplementary data at *JAC* Online).

Risk stratifying analysis using propensity scores to reduce the effect of selection bias in assignment for ganciclovir preemptive therapy

The propensity scores were estimated using multiple logistic regression analysis. All pre-specified covariates listed in Table 1 were included. In addition, we performed covariable adjustment analysis using the propensity score and logistic regression analysis with IPTW using the propensity score, to reduce the effect of potential confounding factors and selection bias. These additional analyses showed that there were no significant differences in viral clearance, secondary episodes of CMV infection, CMV disease, and overall mortality between the two groups (Table 3).

Adverse drug reactions in the low-dose and conventional-dose ganciclovir groups

Eleven (21%) patients developed neutropenia in the low-dose ganciclovir group and 13 (30%) in the conventional-dose ganciclovir group ($P=0.32$) (Table 2). The initial neutrophil counts and the lowest absolute counts during ganciclovir therapy did not differ significantly (2.59×10^9/L versus 2.68×10^9/L, $P=0.90$). Median creatinine clearances (IQR) prior to starting ganciclovir were 60.0 mL/min/1.73 m^2 (59.0–90.0) in the low-dose group and 69.5 mL/min/1.73 m^2 (58.8–90.0) in the conventional-dose group ($P=0.58$). Five (9%) of the 53 patients in the low-dose group and 5 (11%) of the 44 patients in the conventional-dose group ($P>0.99$) exhibited a >25% decline in creatinine clearance. However, a change of regimen during preemptive ganciclovir therapy was more common in the conventional-dose ganciclovir group [29% (13/44), with 12 dose-reduced and 1 switched to foscarnet] than in the low-dose ganciclovir group [8% (4/53), 4 dose-increased, $P=0.01$].

Discussion

Although previous studies have shown that preemptive therapy with ganciclovir is helpful in preventing CMV disease, its toxicity remains of considerable concern, particularly the incidence of neutropenia.[3] Therefore low-dose ganciclovir has been suggested for preemptive therapy in allogeneic HSCT recipients.[2,6,11,18,19] In the present study we found that there were

Table 2. Comparison of outcomes and adverse drug reactions in the low-dose and conventional-dose ganciclovir groups

	Low-dose ganciclovir ($n=53$)	Conventional-dose ganciclovir ($n=44$)	*P* value
Total duration of ganciclovir use (days), median (IQR)	15.0 (8.0–20.0)	13.0 (8.0–18.8)	0.50
Total duration of antigenaemia clearance (days), median (IQR)	21.0 (10.5–21.0)	14.0 (7.0–21.0)	0.05
Paradoxical increase in CMV antigenaemia during the first week[a]	14 (26)	9 (21)	0.49
Discontinuation of preemptive therapy	1 (2)	7 (16)	0.08
discontinuation due to neutropenia	1 (2)	6 (14)	
discontinuation due to nephrotoxicity	0	1 (2)	
Regimen change			0.01
dose escalation	4 (8)	NA	
dose reduction	NA	12 (27)	
change to foscarnet	0	1 (2)	
Neutropenia after ganciclovir therapy[b] (absolute neutrophil count, 1×10^9/L)	2.59±3.55	2.68±3.37	0.90
Creatinine clearance after ganciclovir therapy (mL/min/1.73 m^2), median (IQR)	60.0 (57.0–76.0)	60.0 (53.8–76.8)	0.80
Decreased creatinine clearance after ganciclovir therapy[c] (mL/min/1.73 m^2)	4.38±9.88	5.43±10.00	0.60
Viral clearance	52 (98)	38 (86)	0.04
Secondary episode of CMV infection	8 (15)	15 (34)	0.03
Onset of secondary episode after transplantation, median days (IQR)	73.5 (59.5–78.8)	70.0 (52.5–91.0)	0.82
CMV disease	3 (6)	3 (7)	0.81
pneumonia	1	0	
gastroenteritis	1	2	
CMV syndrome	1	1	
Overall mortality	16 (30)	21 (48)	0.08
CMV-related mortality	0	0	>0.99

Data are presented as number (%), unless otherwise specified. NA, not applicable.
[a]Paradoxical increase in CMV antigenaemia during the first week was defined if the CMV antigenaemia level increased compared with the baseline CMV antigenaemia level during the first week of antiviral therapy.
[b]Differences in absolute neutrophil count between initial and lowest level.
[c]Differences in creatinine clearance between initial and lowest level.

no significant differences between the conventional-dose and low-dose groups in successful viral clearance and CMV disease after completion of the initial preemptive therapy, and that patients who received conventional ganciclovir therapy were more frequently switched to another regimen than those who received low-dose therapy.

Previous studies[6,11,18,19] suggested that low-dose ganciclovir preemptive therapy might be a safe and effective strategy after allogeneic HSCT in clinically stable patients, but this conclusion was not based on direct comparison of low-dose ganciclovir therapy with conventional-dose ganciclovir therapy. Tomonari *et al*.[2] found that a preemptive strategy using ganciclovir 5 mg/kg/day was effective after unrelated cord blood transplantation. However, these workers compared the efficacy of low-dose therapy with that of a historical cohort of patients whom they had treated with conventional-dose therapy.[20] Recently Kim *et al*.[9] published a randomized trial with a relatively small number of patients ($n=68$) comparing low-dose ganciclovir therapy with conventional-dose ganciclovir therapy. They found that the rate of failure was significantly higher in the low-dose group than in the conventional-dose group, although the time required for viral clearance and incidence of CMV disease were similar with low-dose ganciclovir and conventional-dose ganciclovir. In contrast to their findings, we showed that patients who received conventional ganciclovir therapy were more frequently switched to another regimen than those who received low-dose ganciclovir therapy. The reason for this discrepancy is not clear. Possible explanations are differences between the

Table 3. Comparison of outcomes by multiple logistic regression analysis and IPTW

	Model	Adjusted OR (95% CI)[a]	*P* value
Viral clearance	crude	8.21 (0.95–71.04)	0.04
	PS-adjusted multiple logistic	7.89 (0.69–89.65)	0.10
	IPTW	7.03 (0.35–143.15)	0.21
Secondary episode of CMV infection	crude	0.34 (0.13–0.91)	0.03
	PS-adjusted multiple logistic	0.71 (0.21–2.44)	0.59
	IPTW	0.63 (0.23–1.74)	0.74
CMV disease	crude	0.82 (0.16–4.28)	0.81
	PS-adjusted multiple logistic	2.63 (0.28–24.95)	0.40
	IPTW	3.37 (0.33–33.93)	0.30
Overall mortality	crude	0.47 (0.21–1.09)	0.08
	PS-adjusted multiple logistic	0.59 (0.21–1.69)	0.34
	IPTW	0.51 (0.21–1.24)	0.14

PS, propensity score.
[a]Low-dose ganciclovir preemptive therapy was compared with conventional-dose ganciclovir therapy (reference).

induction regimens (i.e. a 1 week induction regimen in the previous study[9] and an induction regimen of at least 2 weeks in our study) and different thresholds of ganciclovir dose increase during the paradoxical increase in CMV antigenaemia, or of ganciclovir dose decrease during the course of neutropenia. We suggest that more prospective clinical studies using the same length of induction regimen and pre-defined dose-changing criteria are needed to resolve this clinical issue.

Since the preemptive strategy was introduced, the incidence of CMV diseases during the first 3 months following ganciclovir therapy has decreased from 30% to 5% in seropositive recipients, but neutropenia remains one of the most feared complications.[21] Non-randomized studies aiming to solve this problem using pre-transplantation induction courses of ganciclovir have been reported.[22,23] However, since high rates of CMV disease were observed, this approach may not be altogether safe in high-risk patients.[1,22,23] Previous studies showed that low-dose ganciclovir preemptive therapy had tolerable haematological toxicity profiles.[2,6,19] Our data also demonstrate that low-dose ganciclovir therapy has ganciclovir-related toxicity at least no worse than conventional-dose ganciclovir and retains the ability to prevent CMV disease.[2] Thus our findings should be of use in helping physicians to employ toxicity-reducing preemptive ganciclovir therapy or dose de-escalating strategies in the context of the considerable concern about ganciclovir-related neutropenia.

The present study has potential limitations. First, we used a CMV antigenaemia assay that is less sensitive than the quantitative PCR for CMV.[24] Therefore we could not detect the emergence of ganciclovir-resistant infections during the ganciclovir preemptive therapy. In addition some workers may be concerned that low-dose ganciclovir can lead to the emergence of ganciclovir-resistant mutant strains. However, previous studies have not revealed any emergence of ganciclovir-resistant infection during low-dose ganciclovir therapy.[6,11] Since CMV PCR is not covered by the Korea National Health Insurance, our hospital routinely performed CMV antigenaemia assays. Therefore our data may provide useful information for resource-limited settings such as ours. Second, our study was not a randomized trial but a prospective observational study, so that selection bias (i.e. unequal chances of receiving low-dose versus conventional-dose ganciclovir therapy) does not permit any firm conclusion. Although there were no statistically significant differences in CMV antigenaemia threshold, baseline neutrophil count, or proportion of patients at high risk for CMV diseases between the low-dose ganciclovir therapy and conventional-dose ganciclovir therapy groups (Table 1), patients who were susceptible to bone marrow suppression by ganciclovir therapy (i.e. high grade of GVHD and had previous histories of GVHD) were more common among those who received conventional-dose ganciclovir therapy than among those who received low-dose ganciclovir. Thus such uncontrolled confounders may have influenced the outcome of low-dose ganciclovir therapy. However, we tried to overcome this limitation by using risk stratification models using the propensity score to adjust for potential differences between low-dose and conventional-dose ganciclovir therapy. These additional analyses showed that there were no significant differences in viral clearance, secondary episodes of CMV infection, CMV disease or overall mortality between the two groups. However, we still cannot rule out the possibility that some unmeasured confounding factors may have affected our results. Third, this study could be regarded as a non-inferiority test of low-dose ganciclovir therapy compared with conventional-dose ganciclovir therapy. In that case, the null hypothesis is 'inferiority'. Although preemptive therapy with low-dose ganciclovir was shown to be non-inferior to conventional-dose ganciclovir therapy in terms of viral clearance, secondary episode of CMV disease and overall mortality, we could not reject the null hypothesis that low-dose ganciclovir was inferior in CMV disease compared with conventional-dose ganciclovir because of low study power (Table S1). So our study results should be cautiously interpreted because the nature of this study is preliminary and non-randomized. However, observational studies like ours will be needed to answer important policy questions and to help in the design of appropriate randomized trials that can provide more conclusive data.

In conclusion, our data suggest that low-dose ganciclovir is as safe and at least as effective as conventional-dose ganciclovir for preemptive therapy against CMV viraemia in allogeneic HSCT recipients.

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Transparency declarations

None to declare.

Supplementary data

Tables S1, S2 and S3 are available as Supplementary data at *JAC* Online (http://jac.oxfordjournals.org/).

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