Cost Analysis of Ganciclovir (GCV) and Foscarnet (FOS) in Recipients of Allogeneic Hematopoietic Cell Transplant (aHCT) with Cytomegalovirus (CMV) Viremia

Chen J[2], Kriengkauyiat J[1,2], Ito J[1], Tegtmeier B[1], Dickter J[1], Dadwal S[1]

[1]City of Hope, Division of Infectious Diseases, Duarte, CA; [2]City of Hope, Department of Pharmacy, Duarte, CA

Correspondence to:
Sanjeet Dadwal, M.D.
City of Hope, Division of Infectious Diseases,
1500 E. Duarte Rd., Duarte, CA 91010, USA
Tel: 626-256-4673 ext 62202
Fax: 626-301-8954
Email: sdadwal@coh.org

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Abstract

INTRODUCTION: GCV and FOS are two treatment options for cytomegalovirus (CMV) viremia in recipients of aHCT. Current data does not show that one agent is more effective than the other, but both can lead to severe adverse reactions (myelosuppression with GCV, renal impairment and electrolyte imbalances with FOS). To our knowledge, there are no studies comparing the health care costs between GCV and FOS for the treatment of CMV viremia.
PURPOSE: The primary objective of this study is to compare health care resource use (HCRU) between GCV and FOS in the treatment of CMV viremia.
METHODOLOGY: Retrospective chart review. Inclusion criteria: patients who received GCV or FOS for at least 7 days between April 27, 2014 to December 31, 2015 for CMV viremia that occurred during the first year following aHCT, detectable CMV PCR >1250 IU/ml for haploidentical and cord blood transplants, CMV PCR ≥ 3750 IU/mL for all other aHCT, and a rising CMV PCR in high risk patients (e.g. graft-vs-host disease, high dose corticosteroids, lymphopenia). Exclusion criteria: CMV disease before or with first viremia and concomitant cidofovir use. HCRU included drug, hospitalization and home health, dialysis, and growth factor costs. Drug costs were calculated using the wholesale acquisition costs (WAC), and other health care costs were calculated using reference costs from various databases.
RESULTS: While not statistically significant, patients receiving GCV (n=52) required fewer days of IV therapy compared to those who received FOS (n=13): 21.5 days (3 to 83 days) vs. 27 days (6 to 88 days), p=0.47. Total duration of therapy was longer in the GCV group: 37 days (13 to 164 days) vs. 28 days (6 to 88 days), p=0.12. Hospitalization days for treatment were similar: 9 days (0 to 28 days) vs. 9 days (0 to 31 days), p=0.59. More GCV patients experienced at least a 50% reduction in white blood cell count: 33 patients (64%) vs. 6 patients (46%), p=0.34. However, growth factor utilization was higher in the FOS group: 28 patients (54%) vs. 9 patients (69%), p=0.36. Dialysis use was higher in the FOS group: 1 patient (2%) vs. 3 patients (23%), p<0.05. The total treatment cost was lower in the GCV group: $43,200 vs. $55,700.
CONCLUSION: Health care resource costs trend towards favoring use of GCV over FOS for the treatment of CMV viremia.

Introduction

•Ganciclovir is first-line treatment and foscarnet is an alternative treatment for CMV viremia following hematopoietic stem cell transplantation, but there are no robust studies showing that one agent is more efficacious than the other.
•Because foscarnet can cause renal impairment, electrolyte wasting, and seizures, our institution recommends ganciclovir as the first-line agent for the treatment of CMV viremia
•However, ganciclovir is myelosuppressive, and in our hematology and stem cell transplant patients, physicians may be more cautious about using ganciclovir due to the risk for prolonged marrow suppression and/or graft failure.
•Our policy restricts foscarnet use to patients with marrow failure, progressive pancytopenia, and ganciclovir failure/resistance.
•To our knowledge, there are currently no studies that compare the health care costs and pharmacoeconomic outcomes between ganciclovir and foscarnet for the treatment of CMV viremia.
•To promote more appropriate prescribing of ganciclovir and foscarnet, we designed a study to evaluate the health care costs associated with each agent, including drug costs, hospitalizations, and costs associated with adverse effects and supportive care.
•Because ganciclovir has an oral equivalent (valganciclovir), we believe that the use of foscarnet would require a longer duration of hospitalization and/or a higher rate of home health utilization.
•With respect to side effects, we anticipated that the utilization and cost of filgrastim would be higher in patients who use ganciclovir and was compared to the cost of dialysis in patients who use foscarnet.

Objectives

•The primary objective of this study was to compare health care resource use (HCRU) between ganciclovir and foscarnet in the treatment of CMV viremia.
•The secondary objective was to evaluate different clinical outcomes (including CMV viral load kinetics, end-organ disease, and mortality as a function of antiviral use) along with side effects and complications arising from the use of either ganciclovir or foscarnet.

Methods

• **Study design:** retrospective chart review of patients at COH
• **Study period:** April 27, 2014 to December 31, 2015.
• **Patient selection:** medical charts were reviewed for patients who developed CMV viremia up to 365 days after a hematopoietic stem cell transplant
• **Data collection:** patient information: patient's age, gender, underlying malignancy, type of transplant, myeloablative conditioning regimen, CMV serostatus, and graft-versus-host disease (GVHD); healthcare resource use: drug costs, hospitalization days, growth factor utilization, home infusion visits, and dialysis
•**Data Analysis:** the chi-squared test was used for dichotomous and categorical variables. Continuous variables were analyzed using the student's t-test. P-values of <0.05 were considered statistically significant. The chi-squared test was performed using an online calculator (Social Science Statistics), and the student's t-test was performed using Microsoft Excel.
•**Definitions/Criteria:**
Inclusion criteria: use of either ganciclovir (n=68) or foscarnet (n=37) for at least 7 days, positive CMV PCR warranting treatment according to institutional policy
Exclusion criteria: the presence of viral disease before or with the first viremia and the utilization of cidofovir concomitantly with ganciclovir or foscarnet
Definitions: CMV viremia thresholds for initiating treatment are defined as follows:
1) any detectable CMV PCR (1250 IU/mL) for haploidentical or cord blood transplants,
2) CMV PCR ≥ 3750 IU/mL for all other hematopoietic stem cells transplants,
3) a rising CMV PCR in high risk patients (high risk criteria include but are not limited to the following: GVHD (acute grade II-IV), high dose corticosteroid therapy (≥1 mg/kg daily), prior anti-thymocyte globulin use, use of clofarabine, lymphopenia, or use of a T-cell depleting regimen).
4) Healthcare Costs:
Drug wholesale acquisition costs (WAC): ganciclovir 500 mg vial-$97.27, foscarnet 6 gram vial-$431.90, valganciclovir 450 mg tablet (generic)-$51.52, and filgrastim 300 mcg vial-$305.96
Hospitalization costs per inpatient day in a non-profit hospital in California[2]: $3,752
Home infusion therapy cost per day[3]: $200
Hemodialysis per person per year cost[4]: $87,945

Results

Figure 1: Patient Selection

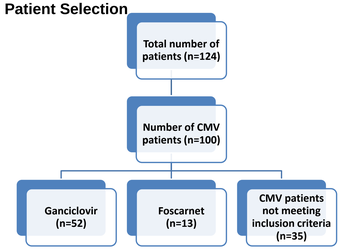


Figure 2: CMV Viral Load Kinetics

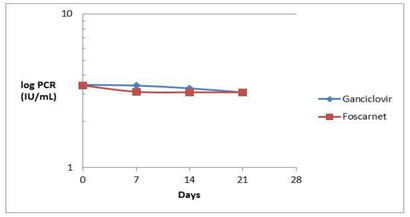


Table 2: CMV Outcomes at 1 Year Follow-Up

	Ganciclovir (n=52)	Foscarnet (n=13)	P value
Recurrence of Viremia	9 patients (16%)	4 patients (31%)	0.27
Viral Disease	2 patients (4%)	0 patients (0%)	1
Death	16 patients (28%)	5 patients (38%)	0.74
Death with Positive Viremia	7 patients (13%)	1 patients (8%)	1

Figure 3: Renal Function During Therapy

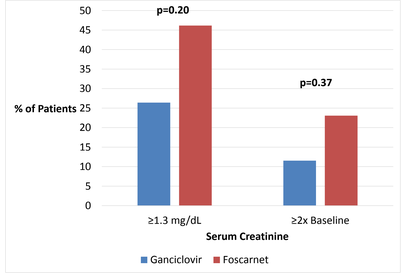


Table 1: Patient Demographics and Characteristics

	Ganciclovir (n=52)	Foscarnet (n=13)	P value
Median Age	55.5 (9 to 73)	53 (22 to 66)	0.06
Male	36 (64%)	21 (72%)	0.48
Underlying Condition			0.43
Leukemias	34 (65%)	6 (46%)	
Myelodysplastic Syndrome	5 (10%)	1 (8%)	
Lymphomas	4 (8%)	3 (23%)	
Multiple Myeloma	1 (2%)	0 (0%)	
Other	8 (15%)	3 (23%)	
Type of Transplant			0.32
Matched Related Donor	7 (14%)	4 (31%)	
Matched Unrelated Donor	21 (40%)	3 (23%)	
Haploidentical	17 (32%)	3 (23%)	
Cord	7 (14%)	3 (23%)	
Myeloablative Conditioning	23 (44%)	8 (62%)	0.36
CMV Serostatus (Donor/Recipient)			1
+/+	28 (54%)	7 (54%)	
+/-	0 (0%)	0 (0%)	
-/+	24 (46%)	5 (38%)	
-/-	0 (0%)	0 (0%)	
Acute GVHD	31 (60%)	7 (54%)	0.76
Chronic GVHD	8 (15%)	2 (15%)	1

Figure 4: Neutropenia During Therapy

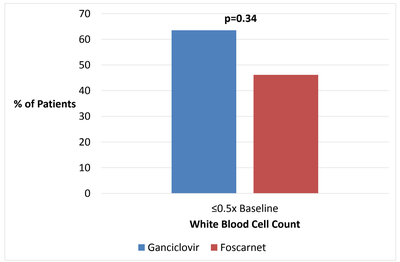


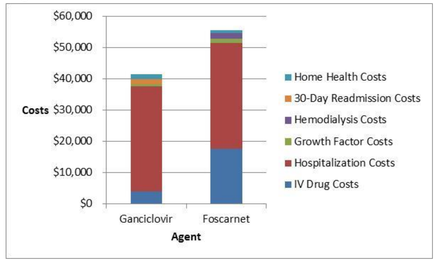
Table 3: Adverse Effects Leading to Therapy Adjustment

	Ganciclovir (n=52)	Foscarnet (n=13)	P Value
Filgrastim Use			
# of Patients (%)	28 (54%)	9 (69%)	0.36
Median # of Doses (Range)	1 (0 to 23)	2 (0 to 25)	0.33
Dialysis			
# of Patients(%)	0 (0%)	3 (23%)	<0.05
Median # of Days (Range)	-	36 (1 to 79)	-
Total # of Days	-	116	-
# of Days per Patient	-	8.9	-

Table 4: Treatment-Related Data

	Ganciclovir (n=52)	Foscarnet (n=13)	P Value
Days of IV Therapy	21.5 (3 to 83)	27 (6 to 88)	0.47
Total Days of Therapy	37 (13 to 164)	28 (6 to 88)	0.12
Hospitalization Days	9 (0 to 28)	9 (0 to 31)	0.59
30-Day Readmissions	2 patients (4%)	0 patients (0%)	1
Total # of Readmit Days	22 days	0 days	-
# of Home Health Patients	12 patients (23%)	4 patients (31%)	0.72
Median # of Home Health Visits	32 visits (7 to 78)	15.5 visits (10 to 18)	-
Total # of Home Health Visits	436 visits	59 visits	-

Figure 5: Health Care Costs



Conclusion

•After accounting for efficacy and safety, ganciclovir may prove to be a more cost-effective agent for the treatment of CMV viremia.
•Growth factor, home health and dialysis costs were unable to be precisely quantified, but they have the potential to have a large impact on treatment costs and should be incorporated into clinical decision making.
•The time to clearance of CMV viremia was similar between ganciclovir and foscarnet.
•No significant differences in the development of recurrent viremia, end-organ disease, or mortality between ganciclovir or foscarnet.
•Clinically, the choice of ganciclovir or foscarnet should be based on patient's individual risk of myelosuppression or renal dysfunction.

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