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Pharmacoepidemiology of Cytomegalovirus Prophylaxis in a Large Retrospective Cohort of Kidney Transplant Recipients with Medicare Part D Coverage

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Abstract

We assembled a cohort of 21,117 kidney transplant patients from July 2006 to June 2011 with Medicare Part D coverage using US Renal Database System (USRDS) data to determine real-world use of cytomegalovirus (CMV) prophylaxis. CMV prophylaxis was defined as filled prescriptions for daily oral valganciclovir (900 mg), ganciclovir (3 g) or valganciclovir (6–8 g) within 28 days of transplant. Multilevel logistic regression analyses were performed to determine factors associated with CMV prophylaxis. CMV prophylaxis (97% valganciclovir) was identified in 61% of kidney transplant recipients (median duration, 64 days); 71% of seronegative recipients of kidneys from seropositive donors (D+/R–); 63% of R+ patients; 60% of patients with unknown serostatus; and 34% of D–/R– patients. Variability in usage of prophylaxis among transplant centers was greater than variability within transplant centers. One in four transplant centers prescribed CMV prophylaxis to > 60% of their D–/R– patients. CMV donor/recipient serostatus, lymphocyte-depleting agents for induction and mycophenolate for maintenance were associated with CMV prophylaxis. CMV prophylaxis was commonly used among kidney transplant recipients. Routine prescription of CMV prophylaxis to D–/R– patients may have occurred in

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DISCLAIMER

The data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the US government.

AUTHOR CONTRIBUTIONS

Carlos A. Q. Santos – Participated in research design, performance of research, data analysis and writing of the paper.

Daniel C. Brennan – Participated in research design, performance of research, data analysis and writing of the paper.

Mohammed J. Saeed – Participated in research design, performance of research, data analysis and writing of the paper.

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some transplant centers. Limiting unnecessary use of CMV prophylaxis may decrease healthcare costs and drug-related harms.

Keywords

cytomegalovirus; kidney transplant; pharmacoepidemiology

INTRODUCTION

Uncontrolled cytomegalovirus (CMV) infection and disease among kidney transplant recipients is a preventable cause of allograft failure and death (1). CMV infection can be asymptomatic, or manifest as CMV syndrome or tissue-invasive disease (2;3). Different CMV prevention strategies have been studied for CMV-seronegative recipients of kidneys from CMV-seropositive donors (D+/R-) and CMV-seropositive patients (R+), and include administering prophylactic antiviral medications for 3 to 6 months post-transplant (4–7), and preemptive treatment after detecting viral replication in blood (6;8–10). Both prophylactic and preemptive treatment can markedly improve post-transplant outcomes by reducing CMV-associated morbidity and death (11;12). Consensus guidelines on CMV prevention in solid-organ transplant recipients first published in 2010 recommended either strategy for D+/R- and R+ patients, but favored prophylaxis for D+/R- patients (13). No CMV prevention strategy was recommended for D-/R- patients given their very low risk of CMV disease (14).

Real-world use of CMV prophylaxis across US transplant centers is unknown. CMV prevention practices are not tracked by the United Network for Organ Sharing (UNOS), and no surveys or pharmacoepidemiologic studies of CMV prevention practices used by kidney transplant centers have been published. Surveys of adult liver and lung transplant programs showed differences in CMV prevention strategies, antiviral medication choice and length of therapy (15;16). With over 200 US transplant centers performing more than 17,000 kidney transplants per year (17), significant variability in real-world use of CMV prophylaxis may exist, and CMV prophylaxis may be overprescribed.

To determine the pharmacoepidemiology of CMV prophylaxis after kidney transplantation as it is used in clinical practice, we assembled a large cohort of kidney transplant patients from July 2006 to June 2011 with Medicare Part D coverage using the US Renal Database System (USRDS) Standard Analysis Files, and identified filled prescriptions for CMV prophylaxis stratified according to CMV donor/recipient serostatus, transplant center and fiscal year of transplant. Determining filled prescriptions for CMV prophylaxis in kidney transplant recipients at the population level can provide insight regarding its utilization as new evidence regarding CMV prevention strategies are published (4–10), and identify factors associated with its use.

METHODS

Data sources

We used the following USRDS Standard Analysis Files: Core and Transplant datasets; Institutional (2006 to 2011), Physician/Supplier (2006 to 2011) and Part D (2006 to 2011) ESRD Medicare Payment Data. The Core dataset contains demographic, insurance, facility and death information; the Transplant dataset contains information regarding kidney transplantation from the United Network of Organ Sharing (UNOS); the Medicare Institutional dataset contains inpatient hospital administrative claims; the Medicare Physician/Supplier dataset contains outpatient physician administrative claims; and the Medicare Part D dataset contains medication claims in the outpatient setting.

Study design and patient population

We performed a retrospective cohort study of patients ≥ 18 years of age who underwent kidney transplantation from July 1, 2006 to June 30, 2011 identified from the Transplant dataset (n=83,309) (Figure 1). We chose the cohort inception dates to have 6 months of pre-existing data to determine comorbidities, and at least 6 months of follow-up data. We excluded patients with no Medicare Part A, B or D coverage, no UNOS information, no inpatient coding for kidney transplantation (ICD-9-CM procedure code 55.69) within 14 days of the USRDS-reported transplant date, patients for whom the index kidney transplant was not the first and only solid-organ transplant and patients transplanted in Puerto Rico. We censored patients at the time of subsequent solid-organ transplantation (ICD-9-CM procedure codes 55.69, 50.59, 50.51, 37.51, 33.50–33.52, 33.6, 52.80–52.83, 46.97), end of Medicare Part A, B or D coverage, death or December 31, 2011, whichever came first. We excluded patients who were censored ≥ 180 days after kidney transplantation since we wanted to determine the usage of CMV prophylaxis after transplantation. The final study population consisted of 21,117 kidney transplant recipients. This study was approved by the Institutional Review Board of Washington University in St. Louis.

Patient characteristics

Demographic and clinical characteristics of the study population were determined at the time of transplantation. The type of transplant, induction and maintenance immunosuppressive therapy, CMV donor/recipient serostatus, human leukocyte antigen (HLA) A, B and DR matching and primary diagnoses leading to kidney transplant were determined using the Transplant dataset. The fiscal year of transplant was defined as spanning July 1 and June 30 of the following year. Other comorbidities were identified using the Elixhauser classification with Klabunde modification, requiring 1 or more inpatient or 2 or more physician/supplier claims coded with the relevant ICD-9-CM diagnosis codes ≥ 30 days apart (18;19).

Transplant center characteristics

The number of kidney transplants performed per year at a transplant center was determined using the Transplant dataset (n=83,309). Hospitals were categorized as small (1 to 25 transplants/year), medium (26 to 80 transplants/year) or large (> 80 transplants/year)

transplant centers by mean annual kidney transplant volume. Transplant centers were also categorized according to US census bureau regions and divisions (20). We could not determine whether transplant centers were teaching hospitals since the USRDS prohibits linking transplant center data to American Hospital Association Annual Survey data.

CMV prophylaxis

Anti-CMV medications filled in the outpatient setting were determined using the Part D dataset. CMV prophylaxis was defined as filled prescriptions for valganciclovir 900 mg orally per day, ganciclovir 3 g orally per day or valacyclovir 6–8 g orally per day within 28 days of transplantation (4–10). The duration of CMV prophylaxis was computed by summing the length of each prescription in days as long as the gap between prescriptions was 15 days. We stratified our study population according to CMV donor/recipient serostatus, transplant center and fiscal year of transplant and determined the proportion of patients in each group that used CMV prophylaxis.

Statistical analysis

Descriptive statistics were used to describe the demographic and clinical characteristics of the study population. Chi-square tests were performed to determine if CMV prophylaxis and valganciclovir use were different across CMV donor/recipient serostatus groups. Cochran-Armitage trend tests were performed to determine if CMV prophylaxis and valganciclovir use increased across fiscal years of transplant. Kruskal-Wallis tests were performed to determine if durations of CMV prophylaxis were different across CMV donor/recipient serostatus groups and fiscal years of transplant. Multilevel logistic regression analyses with varying intercepts by transplant center were performed to identify patient-level and transplant center-level factors associated with CMV prophylaxis, while taking into account differences in baseline probabilities of usage of CMV prophylaxis across transplant centers (21). Variables were specified by selecting clinically meaningful factors that could potentially be associated with CMV prophylaxis. Multicollinearity was assessed during multiple steps in the variable selection process by performing condition number testing (22). Patient-level variables included demographic data (age, sex, race and ethnicity), transplant information (type of transplant, lymphocyte-depleting agents for induction, mycophenolate for maintenance immunosuppression, CMV donor/recipient serostatus, HLA matching) and selected comorbidities (diabetes mellitus, arthritis/collagen vascular disease). Transplant center-level variables included the size of the transplant center by mean annual kidney transplant volume and US census bureau division. Interactions between the use of lymphocyte-depleting agents for induction and CMV donor/recipient serostatus were assessed, given the potential for effect modification of serostatus by use of lymphocyte-depleting agents. Starting with a hierarchically well-formulated initial model containing patient-level and transplant center-level variables, and interactions between lymphocyte-depleting agents for induction and CMV donor/recipient serostatus, we performed hierarchical backward elimination in a series of multilevel logistic regression models to arrive at a penultimate model, followed by assessment of confounding and consideration of precision to arrive at the final model (23). Statistical significance was set at a p-value of 0.05. All analyses were performed using SAS version 9.2 (Cary, North Carolina).

RESULTS

Patient characteristics

Our study population consisted of 21,117 kidney transplant recipients from 228 transplant centers (Table 1). The median age was 52 years, and 40% were female. Fifty-seven percent of patients were white and 19% were Hispanic. Seventy-six percent of patients underwent deceased donor kidney transplantation. Sixty percent of patients received induction with lymphocyte-depleting agents, and commonly prescribed maintenance immunosuppressive medications were mycophenolate, tacrolimus and steroids. CMV donor/recipient serostatus was D+/R– in 16% of patients; R+ in 69%; D–/R– in 12%; and unknown in 3%. HLA A, B and DR matching was 2 in 71% of patients. The most common primary diagnoses leading to kidney transplant were hypertensive nephrosclerosis and type 2 diabetes mellitus. Diabetes mellitus was identified in 39% of patients; congestive heart failure in 11%; chronic pulmonary disorders in 9%; and arthritis or collagen vascular disease in 5%.

Transplant center characteristics

The median number of kidney transplants performed per year at the 228 transplant centers was 43 (Table 2). Sixty-two hospitals were small, 106 were medium and 60 were large transplant centers by volume. Transplant centers were spread over a wide geographic range.

CMV prophylaxis

CMV prophylaxis (97% valganciclovir) was used in 61% of kidney transplant recipients; 71% of D+/R– patients; 63% of R+ patients; 60% of patients with unknown serostatus; and 34% of D–/R– patients (Table 3). D+/R– patients and patients with unknown serostatus had longer durations of CMV prophylaxis than R+ and D–/R– patients. The proportion of patients who filled prescriptions for CMV prophylaxis and valganciclovir increased slightly over time, whereas the duration of CMV prophylaxis remained the same (median: 64 days) (Table 4). The proportion of patients on CMV prophylaxis varied by transplant center (Figure 2). Many transplant centers prescribed CMV prophylaxis to most of their patients, whereas others used it less frequently. The proportion of patients with D+/R–, R+, unknown and D–/R– serostatus on CMV prophylaxis also varied by transplant center (Figure 3A–D). Twenty-six percent of transplant centers had more than 60% of D–/R– patients on prophylaxis, whereas 37% had less than 10% of D–/R– patients on prophylaxis.

Factors associated with CMV prophylaxis are shown in Figure 4A–B. In multivariate analysis, patient-level factors associated with CMV prophylaxis were female sex (OR 1.09); lymphocyte-depleting agents for induction (OR 1.68); mycophenolate for maintenance (OR 1.53); D+/R– serostatus (OR 6.08), R+ serostatus (OR 3.88) and unknown serostatus (OR 3.07), compared to D–/R– serostatus; and collagen vascular disease (OR 1.23) (Figure 4A). Of 228 transplant centers, 51 were more likely than average to have patients on prophylaxis and 44 were less likely than average to have patients on prophylaxis (Figure 4B). Variability among transplant centers (variance = 1.13) was greater than variability within transplant centers after accounting for patient-level factors (residual = 0.99). Patient-level factors associated with CMV prophylaxis among D–/R– kidney transplant recipients were non-

white race (OR 1.39), lymphocyte-depleting agents for induction (OR 1.64) and HLA A, B, DR match 2 (OR 1.25) after accounting for transplant center-level effects.

DISCUSSION

We assembled a large cohort of kidney transplant recipients from July 2006 to June 2011 with Medicare Part D coverage using USRDS data and identified filled prescriptions for CMV prophylaxis. We found that CMV prophylaxis (mostly valganciclovir) was commonly used in kidney transplant recipients. Multiple randomized controlled trials published from 2004 to 2010 demonstrated the efficacy and safety of valganciclovir or ganciclovir prophylaxis in preventing CMV disease among D+/R- and R+ kidney transplant recipients (4;6-8). One study published in 2008 showed that ganciclovir prophylaxis was associated with increased long-term allograft survival compared to preemptive therapy with valganciclovir (6). These trials, along with the relative ease of administering CMV prophylaxis compared to preemptive therapy (24), may have led transplant physicians to commonly prescribe CMV prophylaxis.

CMV prophylaxis was more commonly used in D+/R- patients than other kidney transplant recipients, and D+/R- patients received CMV prophylaxis for longer periods of time. D+/R- patients are at the highest risk of developing CMV disease (25) as a result of primary infection in the absence of effective anti-CMV T-cell immunity (26;27). Even with prophylaxis, D+/R- patients can develop CMV disease upon its cessation (28-31). A prospective cohort study published in 2006 (5) and a randomized controlled trial published in 2010 (7) showed that increasing the duration of CMV prophylaxis from approximately 100 to 200 days further decreased the incidence of CMV disease in kidney transplant recipients. These studies may have resulted in the use of longer durations of CMV prophylaxis in D+/R- patients.

Surprisingly, many D-/R- patients received CMV prophylaxis for durations similar to R+ patients. None of the CMV prophylaxis trials included D-/R- patients given their very low risk of CMV disease (4;6-8). In a prospective study of 20 D-/R- patients who did not receive CMV prophylaxis, 1 patient (5%) developed CMV disease 9 months post-transplant (8). Because of its timing, it could not have been prevented even with the administration of CMV prophylaxis for 3 to 6 months. In another prospective study of 79 D-/R- patients, 1 patient (1.3%) developed CMV disease at an unspecified time (31). Given these data, consensus guidelines on CMV prevention published in 2010 and 2013 recommended against the routine use of CMV prophylaxis in D-/R- patients (13;24). Our results suggest however, that CMV prophylaxis may have been routinely prescribed to D-/R- patients in one in four transplant centers from July 2006 to June 2011. Valganciclovir is expensive, with drug costs of approximately \$11,000 to \$15,000 for a 90-day supply dosed at 900 mg per day (8). Moreover, valganciclovir can be harmful, with 52% of patients developing drug-related adverse events such as leukopenia, neutropenia and diarrhea (4;7). Prescription of CMV prophylaxis to D-/R- patients should not be performed routinely since it is unnecessary, costly and potentially harmful at the individual and population level.

CMV donor/recipient serostatus, lymphocyte-depleting agents for induction and mycophenolate for maintenance immunosuppression were associated with CMV prophylaxis, likely reflecting decisions by transplant physicians to administer prophylaxis to patients at higher risk of CMV disease (25;26;31–34). Variability in use of CMV prophylaxis was greater among transplant centers than within transplant centers, with many hospitals that were more likely than average to prescribe prophylaxis, and a nearly equal number that were less likely than average to prescribe prophylaxis. No transplant center-level factors were identified by our analysis, suggesting that the primary driver for CMV prophylaxis use beyond patient-level factors is at the level of the transplant center. Surgeons, nephrologists and infectious disease specialists are likely the primary decision makers at the transplant center-level with regards to CMV and other infection prevention practices, and should be the target population for efforts to optimize utilization of CMV prophylaxis and other infection prevention resources.

The strengths of our study are the large size of the study population, use of prescription claims to determine real-world utilization of CMV prophylaxis, and use of multilevel modeling to more accurately measure patient-level and transplant center-level factors associated with CMV prophylaxis.

A limitation of our study is the inability to validate our main finding that 34% of D–/R– patients received CMV prophylaxis, and that one in four transplant centers prescribed CMV prophylaxis to > 60% of their patients. We cannot compare our transplant center’s protocol with prescriptions for CMV prophylaxis for patients from our transplant center in USRDS data since the USRDS data use agreement prohibits publishing or disclosing data that identify individual providers or facilities. However, we believe this finding to be accurate given that electronic pharmacy records are considered the gold standard of drug dispensing information, since pharmacies are only reimbursed by insurers upon the provision of detailed complete claims (35), and the high quality of records submitted to UNOS regarding CMV donor/recipient serostatus (25). Moreover, while no surveys of CMV prevention practices in kidney transplant centers have been published, a survey of 110 US and Canadian liver transplant centers indicate that CMV prophylaxis was routinely prescribed to D–/R– patients in 49% of hospitals (15), indicating that routine prescription of CMV prophylaxis to patients at minimal risk of CMV disease occurs in many transplant centers in real-world practice.

Our study has other limitations. The study population consisted only of patients with Medicare Part D coverage. Insurance coverage and co-pays for anti-CMV medications differ among Medicare Part D, Medicaid and private insurance providers, and can influence the prescription of CMV prophylaxis to kidney transplant recipients. CMV prevention practices for patients with Medicaid or private insurance may therefore be different. Moreover, we cannot determine actual Part D coverage for CMV prophylaxis since USRDS data does not have the specific Part D plan for each patient in the study population, or the formularies of each individual Part D plan. Demographic data, clinical characteristics and transplant-related information were derived from USRDS and UNOS data, which were not primarily collected for research and therefore may have errors or missing information. Given the high quality of records submitted to UNOS however, and the low proportion of patients in the study

population with missing CMV donor/recipient serostatus, we believe the information on CMV serostatus that we used in this study to be accurate. Moreover, the proportions of D+/R−, R+ and D−/R− patients in this study are similar to those reported in single-center studies (8;31). Donor CMV serologies may have changed or been provided later by the Organ Procurement Organization (OPO). Interestingly, the median duration of prophylaxis prescribed to D−/R− patients was 58 days, with an interquartile range of 30 to 91 days. It is possible that the lower limit of the interquartile range (30 days) reflects D−/R− patients who were prescribed a one-month supply of CMV prophylaxis that was not refilled after the donor serostatus was provided by the OPO. It still constitutes overuse however, since CMV prophylaxis would not have been prescribed if important information were communicated by OPOs in a timely manner. USRDS data does not have information on the glomerular filtration rate of kidney transplant recipients. We therefore could not determine whether the prescribed dose of anti-CMV medications is appropriate for their kidney function. Comorbidities and repeat solid-organ transplantation were identified using ICD-9-CM codes which may not be perfectly accurate. Transplant center-level factors could not be fully investigated given data use agreement restrictions in identifying hospitals and determining their characteristics. Laboratory monitoring for CMV replication and subsequent preemptive treatment was not identified in this analysis. Despite these limitations, our study provides insight into how CMV prophylaxis was utilized in a large study population from multiple transplant centers over time, identifies an opportunity to decrease CMV prophylaxis among D−/R− patients, and sets the stage for comparative effectiveness studies of different CMV prevention strategies in improving transplant outcomes using USRDS data.

In summary, we showed that CMV prophylaxis was commonly used in US kidney transplant recipients with Medicare Part D coverage, and was associated with CMV donor/recipient serostatus, induction with lymphocyte-depleting agents and mycophenolate for maintenance immunosuppression. Some transplant centers may routinely prescribe CMV prophylaxis to D−/R− patients. Decreasing unnecessary use of CMV prophylaxis can decrease healthcare costs and limit drug-related harms.

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Figure 1.

Cohort inception of 21,117 kidney transplant recipients with Medicare Part D coverage.

Figure 2.

Proportion of kidney transplant recipients who were prescribed CMV prophylaxis stratified according to transplant center. Dashed line indicates the mean proportion for the population. Bubbles signify relative sizes of transplant centers by volume. Colors signify US census bureau divisions.

1 2 3 4 5 6 7 8 9

Figure 3.

Proportion of kidney transplant recipients who were prescribed CMV prophylaxis classified according D+/R- (A), R+ (B), unknown (C) and D-/R- (D) serostatus and stratified by transplant center. Dashed lines indicate the mean proportion for the population. Bubbles signify relative sizes of transplant centers by volume. Colors signify US census bureau divisions.

1 2 3 4 5 6 7 8 9

Figure 4. Patient-level (A) and transplant center-level (B) effects for prescription of CMV prophylaxis among kidney transplant recipients. Blue circles represent point estimates, and red bars indicate 95% confidence intervals.

Table 1

Demographic and clinical characteristics of 21,117 kidney transplant recipients at the time of organ transplantation

Variables	All recipients
Age, years	
Mean $\pm$ SD	50.94 $\pm$ 14.27
Median (interquartile range)	52 (41 – 63)
Female sex (%)	40.42
Race (%)	
White	57.16
Black	34.26
Asian	5.98
Other	2.60
Hispanic (%)	18.83
Type of kidney transplant (%)	
Deceased donor	75.83
Living related	15.10
Living unrelated	9.07
Fiscal year of kidney transplant	
2006	19.70
2007	19.48
2008	20.35
2009	19.86
2010	20.61
Induction immunosuppressive therapy (%)	
Thymoglobulin	46.23
Basiliximab	18.81
Alemtuzumab	12.34
Daclizumab	7.73
Atgam	1.29
Sirolimus	1.21
Rituximab	0.65
OKT3	0.25
Everolimus	0.05
Initial maintenance immunosuppressive therapy (%)	
Mycophenolate	92.04
Tacrolimus	87.43
Steroids	66.51
Cyclosporine	7.46
Sirolimus	3.58
Azathioprine	0.47
Everolimus	0.33

Variables	All recipients
CMV donor/recipient serostatus (%)	
D+/R-	15.67
R+	68.80
D-/R-	12.11
Unknown	3.41
HLA A, B, DR match (%)	
0	19.68
1	31.42
2	20.23
3	15.35
4	5.55
5	3.64
6	3.05
Primary diagnoses (%)	
Hypertensive nephrosclerosis	28.46
Type 2 diabetes mellitus	22.09
Polycystic kidney disease	6.02
Focal glomerular sclerosis	5.65
Type 1 diabetes mellitus	5.15
Systemic lupus erythematosus	3.59
IgA nephropathy	3.34
Malignant hypertension	1.70
Wegener's granulomatosis	0.66
Goodpasture's syndrome	0.39
Other comorbidities (%)	
Diabetes mellitus	38.84
Congestive heart failure	11.05
Obesity	8.69
Coagulopathy	8.47
Chronic pulmonary disorders	7.82
Peripheral vascular disorders	7.62
Hypothyroidism	7.31
Neurologic disorders	5.76
Arthritis, collagen vascular disease	5.42
Depression	5.17
Valvular heart disease	4.90
Liver disease	4.03
Pulmonary circulation disorders	2.47
Psychoses	2.21

Table 2

Hospital characteristics of 228 transplant centers.

Variables	All hospitals
Number of kidney transplants performed per year	
Mean $\pm$ SD	61.09 $\pm$ 55.29
Median (range)	43 (1 – 283)
Transplant center size by mean number of kidney transplants performed per year (%)	
Small (1 to 25)	62 (27.19)
Medium (26 to 80)	106 (46.49)
Large (> 80)	60 (26.32)
Census bureau regions and divisions	
Northeast	
New England (1)	15 (6.58)
Middle Atlantic (2)	33 (14.47)
Midwest	
East North Central (3)	31 (13.60)
West North Central (4)	20 (8.77)
South	
South Atlantic (5)	33 (14.47)
East South Central (6)	14 (6.14)
West South Central (7)	37 (16.23)
West	
Mountain (8)	14 (6.14)
Pacific (9)	31 (13.60)

Prescription of CMV prophylaxis stratified according to CMV donor/recipient serostatus in the cohort of 21,117 kidney transplant recipients.

Table 3

	All n = 21,117	D+/R- n = 3,310	R+ n = 14,528	Unknown n = 721	D-/R- n = 2,558	p-value
Prophylaxis (%)	12,841 (60.81)	2,364 (71.42)	9,182 (63.20)	429 (59.50)	866 (33.85)	<0.001
Antiviral						
Valganciclovir (%)	12,411 (96.65)	2,304 (97.46)	8,842 (96.30)	421 (98.14)	844 (97.46)	0.005
Ganciclovir (%)	429 (3.34)	59 (2.50)	340 (3.70)	8 (1.86)	22 (2.54)	
Valacyclovir (%)	1 (0.01)	1 (0.04)	0 (0.00)	0 (0.00)	0 (0.00)	
Duration (days)						
Mean	73	79	72	78	70	<0.001
Median	64	62	65	70	58	
25 – 75 percentile	30 – 92	30 – 99	30 – 91	30 – 94	30 – 91	

Prescription of CMV prophylaxis stratified according to fiscal year of transplant in the cohort of 21,117 kidney transplant recipients.

Table 4

	2006 n = 4,159	2007 n = 4,113	2008 n = 4,298	2009 n = 4,194	2010 n = 4,353	p-value
Prophylaxis (%)	2,470 (59.39)	2,474 (60.15)	2,597 (60.42)	2,612 (62.28)	2,688 (61.75)	0.004
Antiviral						
Valganciclovir (%)	2,327 (94.21)	2,340 (94.58)	2,452 (94.42)	2,605 (99.70)	2,687 (99.96)	<0.001
Ganciclovir (%)	143 (5.79)	134 (5.42)	145 (5.58)	7 (0.27)	0 (0.00)	
Valacyclovir (%)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.04)	
Duration (days)						
Mean	74	74	72	73	74	0.394
Median	63	65	63	63	66	
Interquartile range	30 – 92	30 – 93	30 – 91	30 – 91	30 – 92	