Immunosuppressive drugs predispose the kidney transplant recipient to reactivation of cytomegalovirus (CMV) infections. Prophylaxis given to these patients is very important for the prevention of opportunistic CMV infections.

The objective of this study was to evaluate the short term and standard-dose valganciclovir prophylaxis for CMV infections in living donor kidney transplantation.

Methods. This study is retrospective one. Between April 2014 and April 2019 100 patients after living donor kidney transplantation with results CMV PCR-DNA and prophylactic treatment were studied retrospectively at Medipol University Medical Faculty Organ Transplantation Department, Istanbul, Turkey.

Results. The mean age was 38.3±15.6 years. 68 (68%) patients were males and 32 (32%) patients were females. All patients were treated with 900 mg daily and 90 days valganciclovir prophylaxis. Mean follow-up was 29.1±15 months. There were not detected CMV infections during the follow-up period.

Conclusions: Short term and standard-dose valganciclovir prophylaxis appears to be successful prevention CMV infections in living donor kidney transplantation.

Keywords. Living donor kidney transplantation, CMV infections, valganciclovir, prophylaxis.

Conflict of interest statement: all the authors declared no competing interests.

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Introduction. Cytomegalovirus (CMV) infection significantly increases recipient morbidity and mortality after kidney transplantation [1]. The most important risk factor is high dose immunosuppression and anti-thymocyte globulin (ATG) induction for CMV infections [2]. Approximately 60% of the adult population has been exposed to CMV and are potential carriers of infection [3, 4].

In current scientific literature, the standard dose and duration of valganciclovir (VGV) for the CMV prophylaxis is 900 mg once daily for 6 months [5]. VGV mainly is used in the treatment of high-risk patients (preoperative donor CMV (+)/recipient CMV (-) and in induction with ATG) [6].

The aim of this study was to evaluate the short term and standard-dose valganciclovir prophylaxis for CMV infections in living donor kidney transplantation.

Material and Methods. Between April 2014 and April 2019 100 patients after living donor kidney transplantation with results CMV PCR-DNA and prophylactic treatment were studied retrospectively at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey.

Results. Mean age was 38.3 ± 15.6 years, 68 (68%) patients were males and 32 (32%) patients were females. The mean body mass index was 25.2 ± 5.6 kg/m². The 27 (27%) patients were done preemptive transplantation. The indications for kidney transplantation were; 37 (37%) patients had unknown cause of end-stage renal failure, 32 (32%) had diabetes mellitus, 14 (14%)...
had hypertension, 12 (12%) had chronic glomerulonephritis, 3 (3%) patient had polycystic kidney disease and 2 (2%) other causes (Alport syndrome, vesicoureteral reflux, etc.). In all these donors and recipients, preoperative CMV IgM was (-), CMV was IgG (+). During the first year of transplantation, the acute rejection rate constituted 9% (9 patients).

All patients were treated with ATG induction. Mean ATG dosages per kilogram were 1.57 ± 0.17 mg/kg. Mean cumulative ATG dosages per patient were 370 ± 140 mg.

Mean follow-up was 29.1 ± 15 months. During follow-up period four graft loss due to humoral rejection happened and 5 patients died. Graft survival rates for 1 and 5 years were 98% and 96%, respectively. Patient survival rates for 1 and 5 years were 98% and 95%, respectively. Five patients died with cardiovascular disease.

In our cohort, there was not detected CMV infection in follow up. Table 1 shows a comparison of our results with literature results.

Discussion. Viral infections are an important cause of graft dysfunction after kidney transplantation [7]. CMV infection may reduce graft survival and patient survival [8]. It is the most important viral agent that requires prophylaxis after renal transplantation. CMV infection is a serious condition that may occur especially during the first few months after kidney transplantation. The cytopathic effect of cytomegalovirus on glomerular cells was first described by Richardson et al. [9]. CMV can cause glomerular vasculopathy, tubulointerstitial nephritis (rich in plasma cells), and graft dysfunction [10]. CMV conditions 20% of cause symptomatic disease [11, 12]. CMV 10-60% can be seen in patients not receiving prophylaxis [13, 14].

The immunosuppressive dose is the most important risk factor for the CMV infections [15, 16]. Especially, the risks increase in patients using high dose immunosuppressive and ATG induction (acute rejection etc.) [17]. Also, the other risk factors are a preoperative CMV IgM-IgG of donors and recipients. [18]. In our study, all these preoperative donors and recipients CMV IgM was (-), CMV IgG was (+). The first year of transplantation, the acute rejection rate was 9% (9 patients). All patients were treated with ATG induction. Mean ATG dosages per kilogram were 1.57 ± 0.17 mg.

CMV PCR-DNA and transplant kidney biopsies are used as the gold standard diagnostics of CMV disease [19]. Pathological finding (Owl-Eye Inclusions) are pathognomonic [20]. In our study, CMV PCR-DNA was assessed and trucut transplant kidney biopsy was performed in 9 patients with increased creatinine values. CMV-PCR<1000 copies/mL was not found anything in trucut transplant kidney biopsy for CMV infections.

Prophylaxis is very important for prevention the CMV infections. Intravenous Ganciclovir or oral VGV is used for CMV prophylaxis [21]. VGV is using low and high dose (450 mg/day and 900 mg/day) or short term and long term (3 months or 6 months) [22-24]. In our clinic, we use only VGV. Our standard protocol is a high dose (900 mg/day) and short term (90 days) prophylaxis in all patients.

Using high dose and long term (900 mg/day – 6 months) of VGV reduces frequency of CMV infection, but leukocytopenia and thrombocytopenia are potential severe side effects of this prophylaxis [25, 26]. CMV replication induces a state of immunosuppression. CMV infection was significantly associated with bacterial, fungal, and parasitic infections [27]. In our study, leukopenia, thrombocytopenia, bacterial, fungal, and parasitic infections associated with CMV prophylaxis were not detected.

In our study, during the follow-up period CMV infection was not detected. Of course, in addition to valganciclovir effectiveness two factors can contribute in this result: first is low dose ATG induction, second is donor and recipient CMV IgG (+).

Conclusions. Short-term standard-dose valganciclovir prophylaxis appears to be successful prevention CMV infections in living donor kidney transplantation. However, physicians must take into account ATG induction dose and preoperative CMV IgM and IgG positivity.

### Table 1

|                      | Dose of Valganciclovir (mg/kg/day) | Duration of Prophylaxis (day) | CMV Infection (n/%) | ATG Induction (n/%) | Acute Rejection (n/%) |
|----------------------|-----------------------------------|-----------------------------|--------------------|-------------------|---------------------|
| Halim et al [22]     | 900 mg/kg/day                     | 180 days                    | 1 (1%)             | 50 (51%)          | 24 (24.5%)          |
| Gabardi et al [23]   | 900 mg/kg/day                     | 180 days                    | 26 (24.3%)         | 77 (72%)          | 14 (13%)            |
| Stevens et al [24]   | 900 mg/kg/day                     | 180 days                    | 12 (26.7%)         | 5 (1.5)           | 4 (8.9%)            |
| Our Study            | 900 mg/kg/day                     | 90 days                     | -                  | 100 (100%)        | 9 (9%)              |
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