CMV Seroconversion during Prolonged Prophylaxis with Valgancyclovir in D+/R- Kidney Transplant Recipients Prevents CMV Disease: Long-time Follow-up

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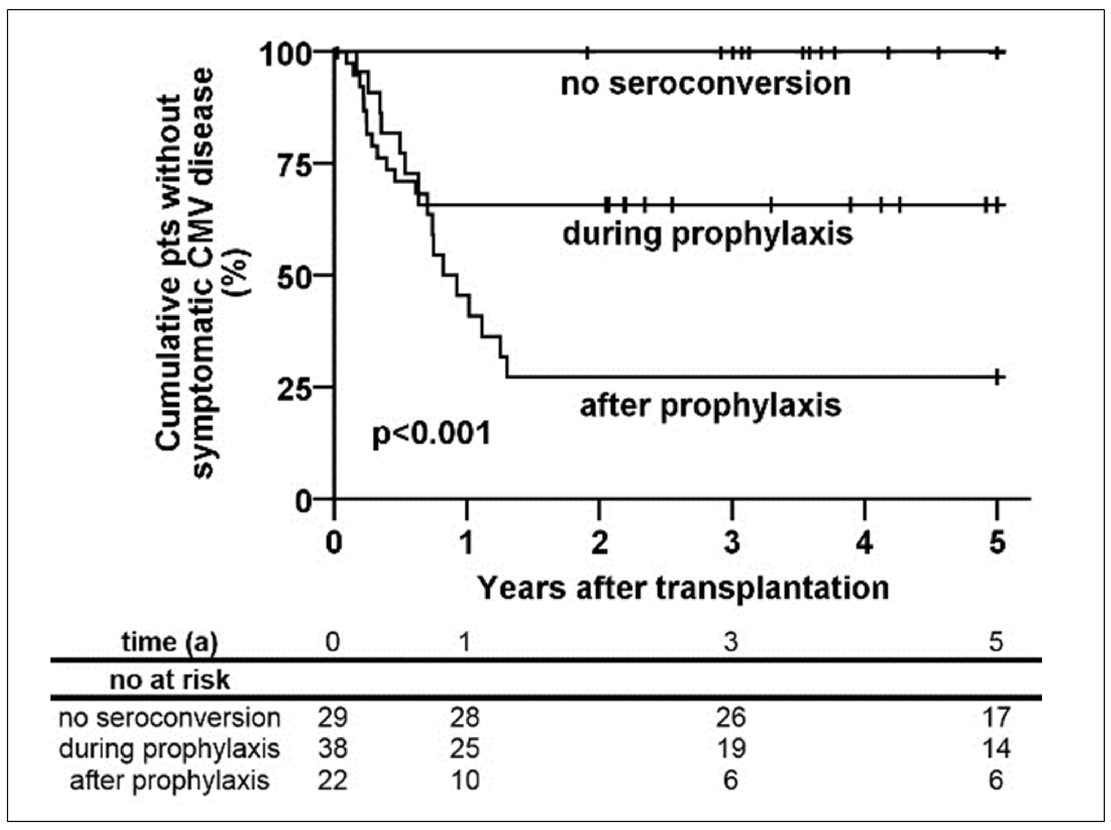
Background: Kidney transplant patients often develop severe clinical manifestations of CMV disease during immunosuppression (1,2). Patients with high-risk CMV constellation (D+/R) are at further elevated risk (3). The incidence and timing of CMV-seroconversion and CMV disease and the influence of prolonged prophylaxis with Valgancyclovir on the clinical course of CMV infection in the long term are not well known.



time (a)	0	1	3	5
no at risk				
no seroconversion	29	28	26	17
during prophylaxis	38	25	19	14
after prophylaxis	22	10	6	6

Fig. 1

Methods: We conducted a retrospective long-term observational study of a well-characterized cohort of 89 consecutive patients with high-risk CMV constellation (D+/R-) who received a kidney transplant between 2003 and 2012. The majority of patients received prolonged Valgancyclovir prophylaxis after transplantation (median 187 (126-261) days). Long-term outcomes over a period of up to 10 years after transplantation were assessed.

Results: During the follow-up (median 62 months) 60 (67%) patients developed CMV seroconversion, only 29 (33%) symptomatic CMV disease. In 43% of the patients seroconversion occurred during prophylaxis with Valgancyclovir (median 154 days after transplantation), 25% showed conversion after the end of prophylaxis with Valgancyclovir (median 320 days after transplantation). The baseline characteristics of the two groups did not differ significantly. Seroconversion during prophylaxis vs. after ending of prophylaxis was associated with significantly less CMV disease (34% vs. 73%, p=0.007), less severe CMV disease (16% vs. 64%, p<0.001) and less organ manifestations (26% vs. 64%, p=0.006) (Table 1). Valgancyclovir resistance occurred in 1 case (1%). In this cohort risk of disease was limited to the first 475 days after transplantation. (Fig. 1)

Conclusions: CMV seroconversion during prolonged prophylaxis with Valgancyclovir occurred after a median of 154 days and was associated with significantly lower incidence of CMV disease, severe CMV disease and CMV complications.

	All (N=89)	seroconversion during prophylaxis (N=38)	conversion after end of prophylaxis (N=22)	p
Age (years) (mean, SD)	52 (14)	53 (12)	52 (16)	0.870
Duration of VGCV-Prophylaxis(days)	187 (126-261)	153 (90-268)	168 (129-254)	0.345
VGCV-dose (mg/d) (median, range)	213 (181-338)	193 (127-303)	274 (186-366)	0.147
Follow-up (months) (median, range)	62 (37-82)	60 (36-79)	69 (35-100)	0.304
Time to seroconversion (d)	200 (117-325)	154 (90-236)	320 (219-497)	<0.001
CMV disease	29 (33%)	13 (34%)	16 (73%)	0.007
Organ involvement	32 (36%)	10 (26%)	14 (64%)	0.006
Severe CMV disease	20 (22%)	6 (16%)	14 (64%)	<0.001
Hospitalization due to CMV disease	18 (20%)	8 (21%)	10 (46%)	0.078
CMV therapy	31 (35%)	14 (37%)	16 (73%)	0.007
Symptomatic reactivation	7 (8%)	3 (8%)	4 (18%)	0.405
Deceased	15 (17%)	4 (11%)	4 (18%)	0.449
Graft loss	10 (11%)	5 (13%)	3 (14%)	1.000

Table 1

(1) Opelz G et al. Am J Transplant. 2004 Jun;4(6):928-36
(2) Kotton CN et al. Transplantation 2013 Aug 27;96(4):333-60
(3) Humar A. et al., Transplantation 2010 Dec 27;90(12):1427-31

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