Is polyomavirus associated nephropathy more common in kidney transplant recipients exposed to valganciclovir?

– A retrospective single center analysis –

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Objective

BK polyomavirus-associated nephropathy (PVAN) is a frequent complication in the early phase after kidney transplantation(1). The most important known risk factor is the intensity of immunosuppression(1). A recent study suggests that exposure to valganciclovir (VGC) could also be a risk factor(2). Our study aims to confirm or refute this hypothesis.

Methods

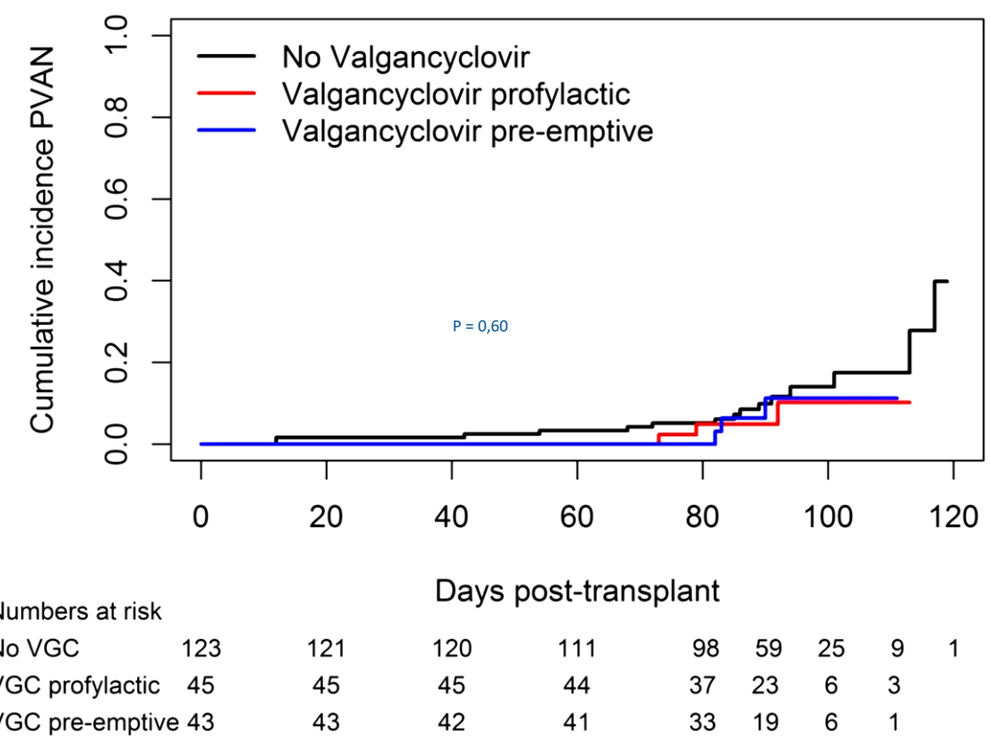
This retrospective single center study includes 211 adults who received a kidney transplant between 2014 and 2019. Cytomegalovirus (CMV) seronegative recipients of a CMV seropositive donor kidney received VGC prophylaxis, whereas CMV seropositive recipients were managed by a pre-emptive CMV strategy. The primary endpoint is the risk of PVAN, defined as detectable polyomavirus DNAemia > 3 log copies/mL or PVAN on renal biopsy in the first 100 days post transplant. To investigate VGC as a potential risk factor for PVAN, we performed a uni- and multivariable Cox regression analysis with VGC treatment and strength of immunosuppressive therapy (standard *versus* reduced dose of mycophenolic acid or steroids) as time-dependent variables.

Results

Eighteen patients (9%) developed polyomavirus DNAemia > 3 log copies/mL during the first 100 days, amongst whom 4 (2%) had biopsy-confirmed PVAN.

The multivariable analysis shows that women have a lower risk of developing PVAN (HR 0.077, p = 0.013), while the risk increases with age (HR 1.04 for every additional year, p = 0.029). We found a trend towards a lower risk of PVAN for patients on reduced immunosuppressive therapy (HR 0.44, p = 0.12). We found no association between VGC use and PVAN (HR 0.99, p = 0.98).

Cumulative incidence PVAN according to VGC-use



Risk factors for PVAN

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	**P value**	**HR** (95% CI)	**P value**
Sex				
Male	Reference		Reference	
Female	0.07 (0.01–0.52)	0.01	0.077 (0.01–0.58)	0.013
Age (year)	1.04 (1.00–1.08)	0.04	1.04 (1.01–1.08)	0.029
Induction therapy				
IL2Ra	Reference			
ATG	0.53 (0.21–1.38)	0.19		
Maintenance therapy				
Tacrolimus	Reference			
Cyclosporin	0.86 (0.31–2.36)	0.77		
Strength of Maintenance therapy				
Standard	Reference		Reference	0.12
Reduced	0.39 (0.14–1.10)	0.075	0.44 (0.15–1.24)	
VGC				
No	Reference		Reference	
Yes	0.90 (0.33–2.50)	0.85	0.99 (0.35–2.78)	0.98
VGC therapy subtype				
None	Reference			
Prophylaxis	0.67 (0.19–2.32)	0.53		
Pre-emptive	1.93 (0.43–8.66)	0.39		
Acute rejection				
No	Reference			
Yes	0.85 (0.11–6.45)	0.88		

Conclusion

Our study is the first to reassess in depth the hypothesis that VGC treatment increases the risk of PVAN, but we could not confirm an effect. The unique strength of this study is the correction for the degree of immunosuppression and the statistical use of time-dependent covariates. This methodological approach can provide a foundation for further studies, needed to confirm our findings.

References

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