HALF-DOSE VALGANCICLOVIR PROPHYLAXIS IS SAFE AND COST-EFFECTIVE IN CMV SEROPOSITIVE RENAL TRANSPLANT RECIPIENTS

Yiyun Shi[2], R.Rogers[1], K.Vieira[1], B.Merhi[1], A.Osband[3], G.Bayliss[4], R.Gohh[4], P.Morrissey[3], D.Farmakiotis[1]

[1]Division of Infectious Diseases, [2]Department of Internal Medicine, [3]Department of Surgery, [4]Department of Nephrology, The Warren Alpert Medical School of Brown University, Providence, RI

Contact information: Dimitrios Farmakiotis, dimitrios.farmakiotis@lifespan.org, work phone: (401) 444 3869

October 21-25 • Philadelphia, PA • www.idweek.org

IDWeek 2020™ Advancing Science, Improving Care

Background

Observational studies and experimental models suggest that half dose valganciclovir(VGV) (450mg/d for normal renal function) prophylaxis is as effective as full dose (900mg/d) in preventing CMV infection in kidney transplant recipients (KTR). However, this practice is not supported by current guidelines, due to lack of high-quality evidence, and for fear of selecting resistance, mainly in high-risk, i.e. donor CMV seropositive/recipient negative (D+/R-) KTR . Full dose VGV may be associated with more neutropenia and BK viremia. Our center adopted half dose VGV for seropositive (R+) KTR recipient since Jan/2018. (1-2)

Materials/methods

- Retrospectively collected data from electronic medical record
- Inclusion criteria: all R+ KTR transplanted between 1/1/2014 and 12/31/2018, data are censored at 1-year post transplant, at graft loss, or death.
- Primary endpoints: CMV Viremia, BK viremia, Graft loss, Death.
- Primary analysis: We used log-rank and Gray's tests to compare cumulative incidence of outcomes, after adjustment by propensity score for differences in baseline characteristics , using R 3.6.3.

Results

- 106 R+ KTR received full-dose and 35 half-dose VGV in enrolled consecutively.
- Anti-thymocyte globulin (ATG) induction was associated with significantly higher cumulative incidence of both early (P=0.017) and any (P=0.02) CMV viremia, compared to basiliximab induction (Fig. 1)

Results(cont'd)

- After adjusting for gender and induction regimen, we noted a signal for higher cumulative incidence of any (P=0.044), but not early (P=0.598) CMV viremia in the full-dose VGV group (Fig. 2).
- There were no significant differences (P >0.1) in incidence of neutropenia, BK viremia, graft loss or death between the two groups.
- Cost savings were estimated at $2630 per CMV R+ KTR (Table 1).

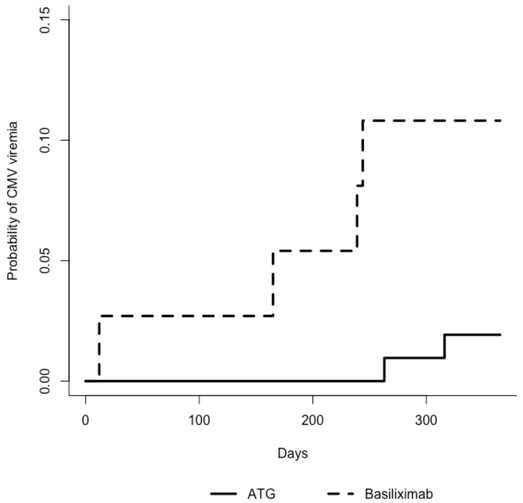

Figure 1. Probability of CMV viremia in KTR who received ATG vs. basiliximab induction

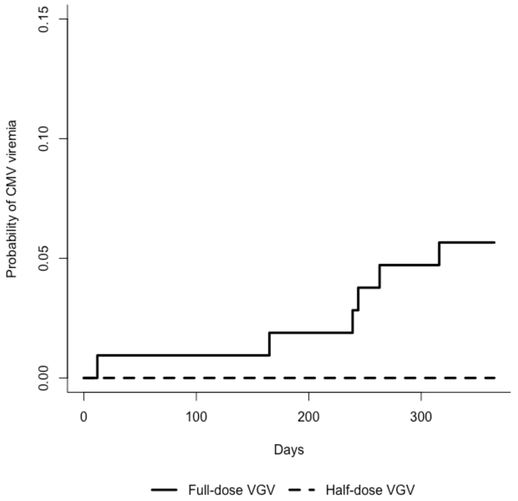

Figure 2. Probability of CMV viremia in KTR who received full-dose vs. half-dose VGV prophylaxis

References

1. Kotton CN, Kumar D, Caliendo AM, Huprikar S, Chou S, Danziger-Isakov L, et al. The Third International Consensus Guidelines on the Management of Cytomegalovirus in Solid-organ Transplantation. Transplantation. 2018;102(6):900-31.
2. Hwang S, Lee J, Lee S, Kim J, Kim M-J, Song J. Effect of low-dose vs standard-dose valganciclovir in the prevention of cytomegalovirus disease in kidney transplantation recipients: a systemic review and meta-analysis. Elsevier; 2018:2473-2478.

	Full-dose VGV n=106	Half-dose VGV n=35	P-value[1]	P-value[2]
Early CMV viremia	2 (1.9)	0 (0)	1.000	0.598[a]
CMV viremia	6 (5.7)	0 (0)	0.336	0.044[b]
BKV viremia	24 (22.6)	8 (22.9)	0.978	0.878[c]
Graft loss	7 (6.6)	3 (8.6)	0.709	0.899[d]
Death	4 (3.8)	1 (2.9)	0.799	0.800[e]
ANC nadir (per µL: median, IQR)	2.7 (1.5-3.7)	2.4 (1.3-3.2)	0.167	
Neutropenia (ANC<1,500/µL)	23 (21.7)	10 (28.6)	0.490	
Estimated cost per patient	$5348	$2718		

ANC: Absolute Neutrophil Count
IQR: Interquartile (25th-75th percentile) range
1: Univariate analyses by Mann-Whitney, χ2 or Fisher's exact test
2: Time-to-event analyses by Gray's or log-rank test
a: Adjusted for gender, induction regimen
b: Adjusted for gender, induction regimen, donor CMV status
c: Adjusted for age
d: Adjusted for donor CMV status
e: Adjusted for induction regimen

Table 1. Comparison of outcomes and cost between the two anti-CMV prophylaxis groups. Data are presented as n (%), unless otherwise indicated.

Conclusions

- In our pilot series, half-dose VGV was at least as effective as full-dose VGV in preventing CMV viremia in R+ KTR, and less costly.
- If larger scale studies verify generalizability of these results, half-dose VGV may be considered as standard of care for R+ KTR.
- In KTR, the antimetabolite probably contributes to CMV viremia.