A Randomized Double-Blinded Placebo-Controlled Study to Determine Efficacy of Immunoglobulin Therapy to Treat BK Viremia in Renal Transplant Recipients

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INTRODUCTION

This was a multicenter prospective double-blinded randomized placebo-controlled proof-of-concept study conducted at three transplant institutions to assess the efficacy of intravenous immunoglobulin (IVIG) therapy in treatment of BK viremia.

METHODS

Renal transplant recipients with BK virus plasma PCR greater than 1,000 copies/mL

Randomization

Normal saline infusions with immunosuppression reduction

IVIG (1g/kg) monthly for two months with immunosuppression reduction

Patients followed up at 1, 2, 3, 6, and 12 months post-enrollment.

OUTCOME

Resolution of BK viremia by 3 months post-enrollment

LIMITATIONS

Baseline differences in degree of viremia, NK cell response, and DGF are noted and may reflect small sample size. A larger study is necessary to detect differences in treatment effect.

IVIG and immunosuppression reduction may not be more effective than immunosuppression reduction alone in treating BK viremia.

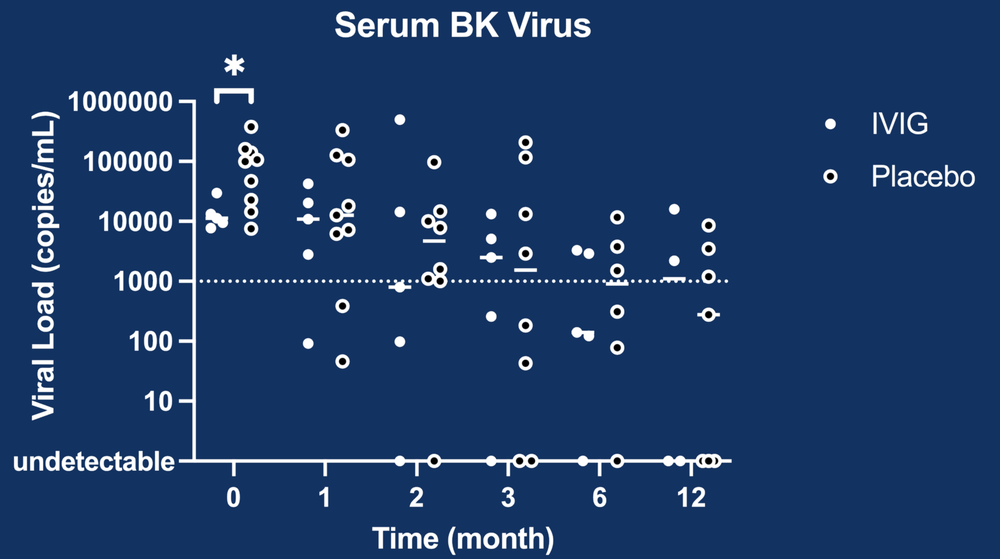

Figure 1. Serum BK Virus. Viral loads were higher in the placebo group than the IVIG group at enrollment, but not significantly different between the two groups at any of the follow-up time points. The dotted line represents threshold of viremia clearance at less than 1000 copies/mL. * p = 0.04. Bar – median (Mann-Whitney between group comparisons).

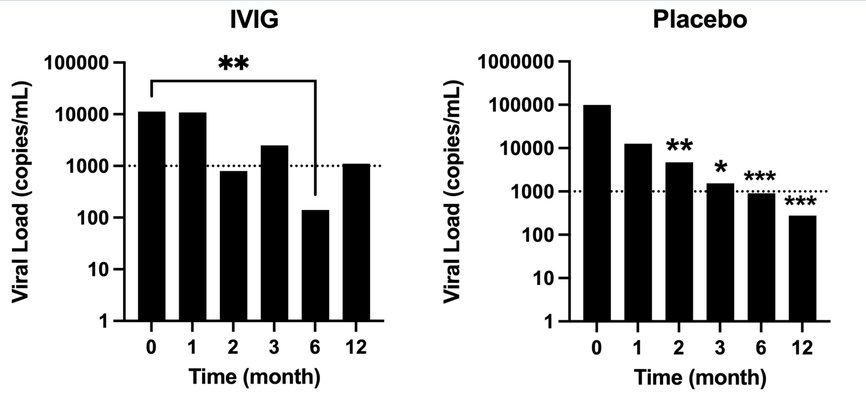

Figure 2. Serum BK Virus. a) Median serum BK viral loads of the IVIG group decreased at the 6 months follow-up time point (** p = 0.008). **b)** Median serum BK viral loads of the placebo group continued to decrease at each follow-up timepoint (* p = 0.04; ** p = 0.006; *** p = 0.0008, 0.0003). The dotted line represents threshold of viremia clearance at less than 1000 copies/mL.

	All (n = 14)	IVIG (n = 5)	Control (n = 9)	p
Age at Transplant	56.6	53.4	58.3	0.38
Female	6 (42.9%)	3 (60%)	3 (33.3%)	0.58
White	9 (69.2%)	3 (60%)	6 (66.7%)	0.99
Prior Transplant	3 (21.4%)	1 (20%)	2 (22.2%)	0.99
Deceased Donor	8 (61.5%)	2 (40%)	6 (66.7%)	0.29
High Risk CMV	2 (22.2%)	0 (0%)	2 (33.3)	0.5
DGF	5 (41.7%)	0 (0%)	5 (71.4%)	0.03*
Time to BKV	6.11	3	7.7	0.19

Table 1. Baseline Demographics. More controls were diagnosed with delayed graft function. Age at transplant in years, and time to BK viremia in months. DGF: delayed graft function.

	IVIG		Placebo	
	n	%	n	%
0				
PV I	5	100	7	77.8
PV II	4	80	6	66.7
PV III	3	60	5	55.6
PV IV	4	80	5	55.6
3				
PV I	5	100	8	88.9
PV II	3	60	7	77.8
PV III	5	100	7	77.8
PV IV	4	80	7	77.8
12				
PV I	4	80	6	66.7
PV II	4	80	6	66.7
PV III	4	80	4	44.4
PV IV	4	80	6	66.7

Table 2. Neutralization. Subjects with neutralizing levels of antibody to BK strains I-IV, as assayed with pseudoviruses, at baseline, 3, and 12 months. Neutralization defined as luminescence < log 10 of negative control. PV: pseudovirus.

ADDITIONAL RESULTS

Subjects' T- and NK-cell responses to BK pseudoviruses were assayed, without significant differences in CD4+ and CD8+ T-cell responses between IVIG and placebo groups as measured by overall and IFNγ+/IL2+/TNFa+ responses. However, the IVIG group had a higher CD107a+ NK-cell response at baseline.