National University Hospital

High-Dose Intravenous Immunoglobulin for BK Virus DNAemia Protects Against BK Nephropathy But Not Acute Rejection

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Introduction:

- BK virus DNAemia (BKV-D) continues to be a burden for kidney transplant recipients (KTRs)
- There is a lack of approved direct antiviral therapies and the mainstay of treatment is reduction of immunosuppression
- This is associated with a risk of acute rejection (AR)
- We describe our experience of treatment of BKV-D with high-dose IVIG (HDIVIG) in a multi-ethnic cohort of KTRs

Methods:

- Single-centre, retrospective cohort study
- **146 KTRs** transplanted between 1-Apr-2019 and 31-Dec-2023
- BK DNA was screened at monthly intervals post-transplant from months 1-9, then 3-monthly until 24-months post-transplant
- At diagnosis of BKV-D, immunosuppression was reduced by halving of anti-metabolite dose, followed by cessation and then conversion to mTOR-inhibitors(mTORi); reduction of Prednisolone dose if appropriate; less commonly other adjunctive therapy
- **HDIVIG was given at 2g/kg every 4-6 weeks for any ongoing BKV-D > 3 log**
- Allograft biopsy was performed in cases of allograft dysfunction (elevated creatinine / proteinuria)
- Outcomes of KTRs with BKV-D were manually abstracted from case records

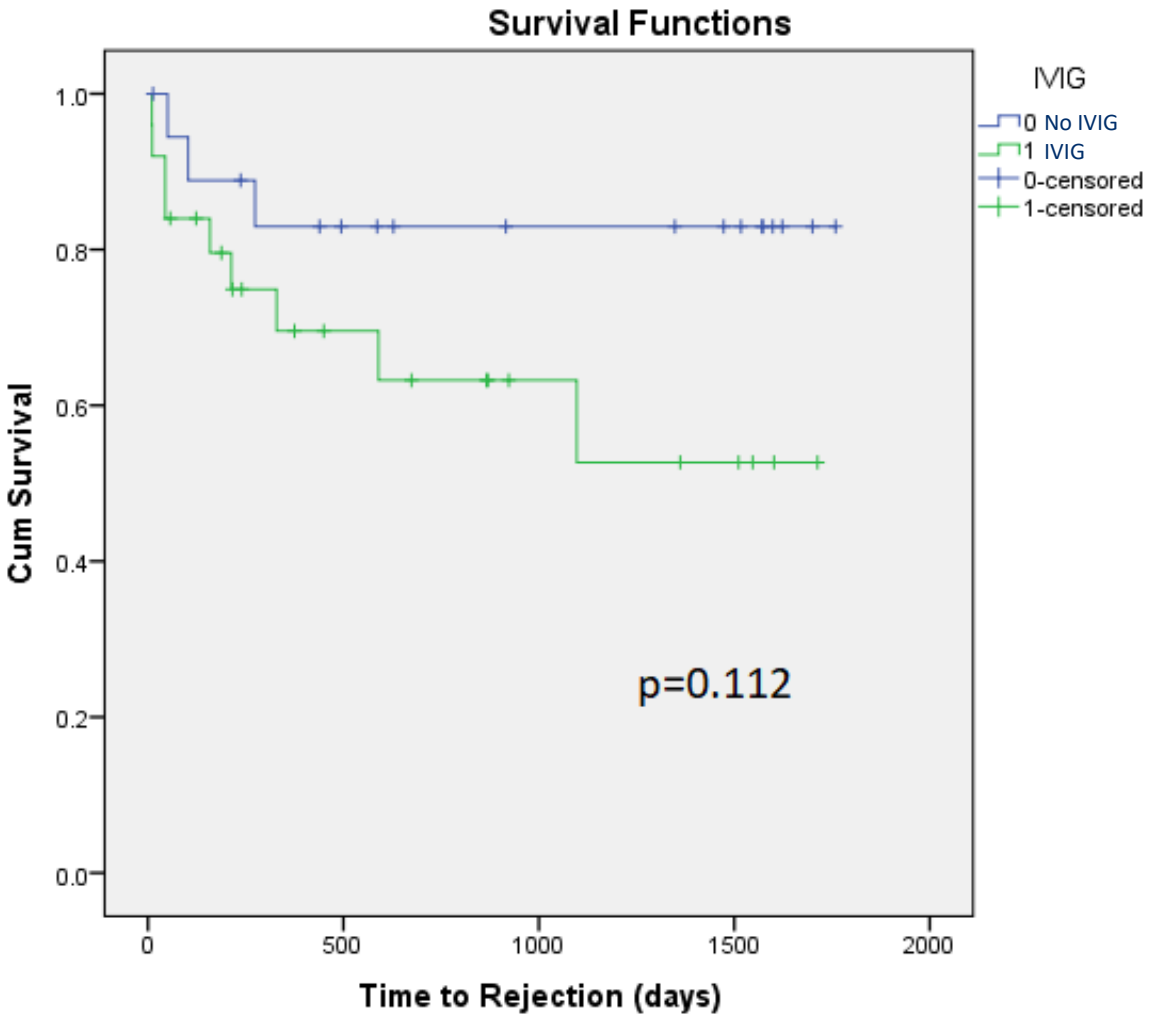
Results

- 44 cases (30%) developed BKV-D
- No significant differences in demographics, induction or maintenance immunosuppression in KTRs who developed BKV-D vs those who did not
- Median time to BKV-D was 93 days post-transplant (range 26 – 644 days)
- Median time to peak BKV-D was 125 days post-transplant (range 28 – 665 days)
- Median follow up time was 2.19 yrs overall

n (%) or median	No BKV-D n=102 (70%)	BKV-D n=44(30%)	p-value
Age (yrs)	48.7	51.1	0.389
Male gender	52 (51%)	19 (43%)	0.247
Ethnicity			0.455
-Chinese	70 (69%)	29 (66%)	
-Malay	14 (14%)	5 (11%)	
-Indian	15 (15%)	6 (14%)	
-Other	3 (3%)	4 (9%)	
Aetiology of ESKD			0.785
-Chronic glomerulonephritis	59 (58%)	24 (55%)	
-Diabetic kidney disease	24 (24%)	12 (27%)	
-Adult polycystic kidney disease	9 (9%)	4 (9%)	
-Hypertension	3 (3%)	0 (0%)	
-Others	7 (7%)	4 (9%)	
Living donor kidney transplant	65 (64%)	27 (61%)	0.456
ABO-incompatible transplant / Rituximab desensitisation	6 (5.9%)	2 (4.5%)	0.547
Leucocyte depleting induction	15 (14.7%)	3 (6.8%)	0.145
Plasma exchange	7 (6.9%)	1 (2.3%)	0.245
Maintenance immunosuppression			0.804
- Tac / MPA	34 (33.3%)	16 (36.4%)	
- CyA / MPA	58 (57%)	25 (56.8%)	

Results

- Antimetabolite was stopped in 19 (43%); mTORi was commenced in 9 (20%); 4 patients received leflunomide; 2 patients had cessation of calcineurin inhibitor
- 25 KTRs (56%) received HDIVIG – these patients had higher peak BKV-D (4.54 log vs 2.98 log, p<0.05) and 9/25 had mTORi conversion (vs 0/19 who did not receive IVIG)
- **93% of BKV-D cases resolved**, at a median of 68 days (range 16 – 636) after initial detection
- Median peak DNAemia was higher in cases without resolution (4.97 log vs 3.72 log, p=NS)
- There were no cases of biopsy-proven BK nephropathy at median follow up of 3.27 years post-transplant
- **10 KTRs (23%) developed rejection within 1 year of BKV-D, 7 of whom developed AR within 6 months (median 44 days);** 7/10 were associated with de-novo donor specific antibody development and antibody mediated rejection
- In the cohort without BKV-D, 10% developed AR within 1 year post-transplant (p=0.05)
- 1 case of graft loss was noted during the study period, 1 year after BKV-D resolution, attributed to AR from immunosuppression non-compliance



Summary and Conclusion

- BKV-D development is not predicted by baseline demographic characteristics, type of transplant or immunosuppression regimen
- HD-IVIG treatment in those with BKV log >3 resulted in resolution of BKV-D in the majority of cases
- Immunosuppression reduction for BKV-D was associated with 23% risk of acute rejection within 1 year, compared to 10% risk in the first year in those without BKV-D
- HD-IVIG may not protect against the occurrence of acute rejection in these patients