| | Historical Ctrl (n=14) | ILRT Rx (n=13) | P value |
|---|---|---|---|
| Serum Creatinine at time of diagnosis (mean ± SE) | 2.5 ± 0.23 | 2.3 ± 0.22 | 0.6 |
| Graft Loss at 6 months post diagnosis (%) | 29% | 7.7% | 0.32 |
| Graft Loss at last follow-up (%) | 50% | 7.7% | 0.03 |
| BKV viremia clearance (%) | n/a | 82% | |

Our gene expression profiles suggest that renal allografts with enhanced inflammation at the time of diagnosis of BKV nephritis diagnosis are at increased risk for renal allograft loss. Our data also suggest that management of BKV nephritis using a combination approach of IVIG, leflunomide and reduced tacrolimus is associated with improved outcomes.

## 227 IMPACT OF RABBIT ANTI-THYMOCYTE GLOBULIN INDUCTION THERAPY ON REACTIVATION OF BK VIRUS IN RENAL TRANSPLANT RECIPIENTS

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Reactivation of Polyoma BK virus has been recognized as an important cause of kidney allograft nephropathy and loss. BK nephropathy (BKN) has been associated with potent immunosuppression regimens. The impact of rabbit anti-thymocyte globulin (RATG) induction on BK viremia (BKV) and BK nephropathy has not been well defined. RATG has been associated with increased viral activation such as EBV. At our institution, all kidney recipients are maintained on triple immunosuppression including tacrolimus, mycophenolate and prednisone unless contraindicating complications require a change. Prior to January 2007, no induction therapy was used and thereafter RATG was used. Trough tacrolimus targets were not changed. Throughout our experience, we have prospectively monitored for BKV. We now report the results of a retrospective analysis of the impact of RATG on BKN and BKV (primary end-points). BKV was monitored via serum BKV PCR at post transplant months 1, 2, 3, 4, 5, 6, 9, and 12. In addition, CMV and EBV PCR were performed based on clinical indications. Those with positive viremia had reductions in immunosuppression. Evidence of renal dysfunction with positive BK viremia led to renal biopsy. BKN was diagnosed by histological and immunohistochemical changes. Univariate analysis included Student¡¦s t-test, Mann Whitney test, Fisher¡¦s exact test, and log-rank test (p value <0.05 was significant). Stepwise (forward step likelihood ratio method) Cox regression model was performed to assess predictive factors for BK viremia. Between January 2006 and December 2007, 275 isolated kidney transplantations were analyzed (40 were excluded for clinical indications that warranted changes). In total, 110 kidney recipients received no induction (Group I) while 135 pts had RATG (Group II). There were no differences between donor and patient demographics except for follow-up (I: 571,,b148 days vs. II: 246,,b102; p<0.01). Data was censored at one year follow up. Patient (I: 97% vs. II: 99%; p=0.78) and graft survival (I: 95% vs. II: 99%; p=0.63) were similar. Though one year actuarial incidence of BKV was similar (I: 19% vs. II: 29%; p=0.11). BKV developed earlier in RATG cohort (I: 163¡Ó22 vs. II: 108¡Ó 74 days; p=0.03). There was no difference in the BK log viral copies/mL (I: 3.8¡Ó0.8 vs. II: 4.0¡Ó0.8; p=0.11). Although BK nephropathy was more prevalent in Group I (I: 7.2% vs. II: 0.7%; p=0.01). no grafts were lost to BKN. There was no difference in CMV (I: 23% vs. II: 12%; p=0.08) nor EBV infection (I: 3.6% vs. II: 6.2%; p=0.24). Multivariate analysis revealed that only age (HR: 1.05 95%CI: 1.02-1.07; p=0.001) and induction therapy (HR: 2.2; 95%CI: 1.2-4.1; p=0.01) were predictors of BKV. The preliminary data suggest RATG leads to increased BK virus reactivation; despite no evidence of changes in CMV or EBV infection. However aggressive BK PCR monitoring could curtail the progression of earlier BKV to BK nephropathy. Long-term follow-up is on going in order to determine aggregate BK viremia and nephropathy.

## 228 THE IMPACT OF CLINICAL POLYOMAVIRUS DISEASE ON GRAFT SRUVIVAL OF PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS – AN ANALYSIS OF OPTN/UNOS DATABASE

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**Background:** Polyomavirus-associated nephropathy often precedes renal allograft dysfunction in adult renal transplant recipients. The OPTN/UNOS began collecting information regarding polyomavirus test results using follow-up forms since June 30, 2004. The aim of this study is to evaluate the impact of clinical polyomavirus disease (PVD) on graft survival after pediatric kidney transplantation.

**Methods:** From Jan 2004 to Dec 2006, a total of 2,065 pediatric kidney alone transplants (age 2-20 yrs) with functioning graft at 6 months were identified the OPTN/UNOS data as of Aug 20, 2007. Graft survival rates were compared for the following 3 groups: PVD group – Patients who had developed PVD (n=57); no PVD group – Patients who had PV test and hadn't developed PVD (nPVD) (n=272); and Control group – Patients who had not performed PV test on followup record (nPVT) (n=1,736). Univariate and multivariate Cox regression analyses were performed to identify risk factors of graft loss.

**Results:** Overall graft survival rates of PVD group were not significantly different from those of control group (nPVT group, log-rank P=0.25) and nPVD group (log-rank P=0.97). In multivariate analysis, both nPVD (RR=1.55 vs nPVT, P=0.31) and PVD (RR=1.00 vs nPVT, P=0.99) were not significant risk factors of graft loss after adjusting for age, race, and rejection treatment within 6 months (Table). Pediatric patients may have a lower rate of graft loss because they are able to mount a more vigorous immune defense against BK virus than adult kidney transplant recipients.

**Conclusions:** Clinical polyomavirus (BK virus) disease may not be as significant a risk for pediatric kidney survival as it is for adult recipients. Larger prospective studies are needed to understand the impact of BK virus infection, replication, and disease on pediatric kidney transplant outcome.

Table. Results of univariate and multivariate Cox regression analyses

| | Unadjusted RR (95%CI) | P value | Adjusted RR (95% CI) | P value |
|---|---|---|---|---|
| Recip Age 15-20 vs 2-14 | 1.47 (1.00-2.16) | 0.050 | 1.48 (1.01-2.19) | 0.046 |
| Recip Black vs others | 2.15 (1.43-3.22) | <0.001 | 2.10 (1.40-3.15) | <0.001 |
| Rejection in 6 mon vs none | 3.28 (2.11-5.01) | <0.001 | 3.17 (2.04-4.94) | <0.001 |
| CPVD nPVT (control) | 1.0 | | 1.0 | |
| nPVD | 1.89 (0.82-4.32) | 0.13 | 1.55 (0.67-3.56) | 0.31 |
| PVD | 0.99 (0.54-1.82) | 0.98 | 1.00 (0.54-1.83) | 0.99 |

## 229 MYCOPHENOLATE HAS ANTIVIRAL PROPERTIES IN BK VIRUS INFECTED VERO CELLS

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We previously reported mycophenolic acid (MPA) reliably reduces BK virus (BKV) copy count in Vero cells (Green monkey kidney cell origin) with infection from various BKV strains. Subsequently we explored potential mechanisms including anti-metabolite effects and molecular markers of mRNA production.

Vero cells were infected with BKV (NCCR rearranged VJ strain) by a 2 hr incubation with 6.5 X 105 BKV copies, washed, then cultured for 1, 7, 14, 21, 28, and 35 days. Culture media with MPA (0, 2 and 8 mg/l) was exchanged weekly. We quantified cellular protein and determined BK viral copy numbers in both cell fractions and SN at all time points. RNA was extracted and reverse transcribed for subsequent quantititative mRNA analysis for Transforming Growth Factor Beta (TGFß). Collagen 1A1, Alpha Smooth Muscle actin (α;SMA). and Heat Shock Protein 47 (HSP) relative to Ribosomal Polymerase II (RPII) which we have shown remains stable in its expression in chronic Vero cell culture ± BKV infection. Quantification of BKV replication and mRNA was by quantitative real time PCR using the Roche Lightcycler 2.0.

MPA (2 and 8 mg/l) reduced BKV copy count greater than 1 log fold in both SN and cells after day 14. There was reduction of protein amount by 50 – 75% in chronic MPA exposed Vero cells consistent with an anti-metabolite effect