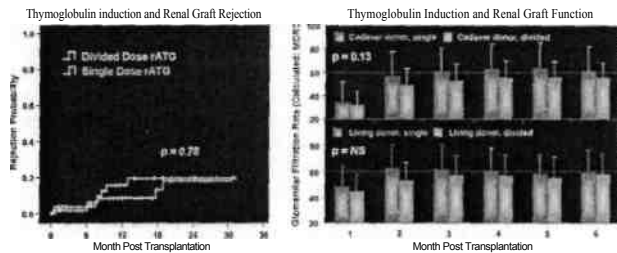


KIDNEY IMMUNOSUPPRESSION: INDUCTION THERAPY

NLDs treated with S-rATG was identical to LDs(mean GFR> 60). In conclusion the two dosing regiments of rATG were equivalent in safety and efficacy with improved renal function in S-rATG treated NLDs. The implication of this for improved long-term graft survival for NLDs is significant.



Abstract# 1450

Prolonged Lymphopenia after Anti-Thymocyte Globulin Induction Is Not Associated with Increased Graft Survival in Renal Transplant Recipients. Dionisios Vrochides,¹ Peter Metrakos,¹ Marcelo Cantarovich,¹ Jean Tchervenkov,¹ Douglas Keith,¹ Miriam Fernandez,¹ Steven Paraskevas.¹ *Departments of Surgery and Medicine, Multi-Organ Transplant Program, McGill University¹ Health Centre, Montreal, QC, Canada.*

Introduction: Anti-thymocyte globulin (ATG) induction is associated with higher graft survival, as well as freedom from acute cellular rejection (ACR) after renal transplantation. ATG may induce prolonged (more than 30 days) lymphopenia. **Purpose:** To determine whether prolonged lymphopenia after ATG induction contributes to superior long term results after renal transplantation.

Methods: A total of 415 primary adult kidney transplants were performed between 1990 and 2004, with anti-thymocyte globulin for induction. Re-transplants and multi-organ recipients were excluded from the study population. Recipients with normal graft function comprised group 1 and those with slow or delayed graft function (S/DGF) comprised group 2. In both groups, recipients with an average value of < 200 lymphocytes/mm³ for the first 30 postoperative days comprised the cohorts of prolonged lymphopenia (group 1a and 2a), whereas the rest comprised the non-lymphodepleted cohorts (group 1b and 2b). Graft survival censored for patient death, patient survival, calculated GFR, ACR and CMV infection rates were retrospectively analyzed. **Results:** S/DGF was observed in 36.4% (n=151) of patients. Prolonged lymphopenia was achieved in 53.4% (n=141) and 68.8% (n=104) of recipients with normal (group 1a) and slow/delayed (group 2a) postoperative graft function respectively. For both the normal and the S/DGF groups, there were no differences in mean actuarial graft and patient survival for the lymphopenic and the non-lymphopenic cohorts (tables 1 and 2). There was no positive correlation of persistent lymphodepletion with the calculated GFR at 7, 30, 180 and 365 days post-transplant. Incidence of ACR was similar between the non-depleted and the depleted groups. CMV incidence was similar between the two groups.

Conclusions: Lymphocyte depletion that persists for more than one postoperative month after induction with ATG is not associated with improved long-term results. That might mean that the efficacy of ATG does not depend on decreasing the total lymphocyte count but rather on eliminating specific lymphocyte subpopulations.

Group 1 (normal function)		Group 2 (S/DGF)	
1a (+LD)	1b (-LD)	2a (+LD)	2b (-LD)
12.9(11.9, 13.9)	12.7(11.4,14.0)	9.5(8.1,10.8)	7.6(6.3,9.0)

Actuarial graft survival p = .769

Abstract# 1451

Differential Effects of Thymoglobulin (Thymo) Depletion and Basiliximab Induction in Sensitized Patients Undergoing Renal Transplantation. Benjamin Philosophe,¹ Heather Hurley,² Kayhree Butler,¹ Eugene Schweitzer,¹ Luis Campos,¹ Matthew Cooper,¹ Rolf Barth,¹ Stephen Bartlett.¹ *Surgery, University of Maryland School of Medicine, Baltimore, MD; ²Pharmacy, University of Maryland School of Medicine, Baltimore, MD.*

Thymo depletion is typically used in high risk renal transplants. Our center has recently adopted a broader use of Thymo enabling us to compare outcomes between unsensitized and highly sensitized patient groups, and to compare Thymo to basiliximab in these two different populations.

A retrospective analysis of 527 renal transplant recipients (67% CRT, 49% AA) between 2004 and 2006 was performed. 353 unsensitized (peak PRA <20), and 98 sensitized recipients (peak PRA >40%) were analyzed. The 2 year cumulative rejection rate was higher for basiliximab compared to Thymo in the unsensitized patients (21% vs. 6% respectively, p=0.031), but similar in the sensitized patients for both agents (25% for basiliximab, 31% for Thymo, p=n.s.). In the sensitized patients, all the rejections in the basiliximab group were cellular, whereas 12 of the 21 rejections in the Thymo group were antibody mediated (6) or combined cellular and antibody mediated (6). For sensitized patients, graft survival was lower following Thymo depletion at 2 years compared to basiliximab (76% vs.100%, p=0.007). Rejection had no impact on graft

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survival in basiliximab treated patients. In this group, graft survival at 2 years in that rejected at least once was identical to ones that did not have any rejection (both). However, in patients treated with Thymo, rejection had a significant in graft survival regardless of sensitization. Patients without rejection had a 2 year survival of 94%, whereas cellular rejection resulted in a 2 year graft survival (p<0.0001). One-year graft survival for patients that experienced antibody rejection or both antibody and cellular rejection was 63% and 25% respectively. Rejection occurs less frequently with Thymo depletion in unsensitized patients is no better than basiliximab in sensitized patients undergoing renal transplant. In this group, Thymo depletion antibody mediated reject basiliximab induction, and the injections in Thymo depleted patients are more and more likely to result in a graft loss. This may be due to a more rapid recon of T memory cells following depletion in previously sensitized patients which c well with murine data.

Abstract# 1452

Four-Year Outcomes Comparing Thymoglobulin and Basiliximab in Combination with Sirolimus and Reduced-Dose Cyclosporin High Versus Low Risk Immune Responders. Richard J, Knight Schoenberg, Ronald H. Kerman, Hemangshu Podder, Stephan Katz, T. Van Buren, Barry D. *Kahan, Surgery, University of Texas Medical Houston, TX.*

Aim: To determine the effect of thymoglobulin versus basiliximab antibody induction on renal allograft outcomes at 4 years post-transplantation for recipients versus low risk of acute rejection.

Methods: A retrospective single-center review of 276 deceased donor renal recipients who received either basiliximab (n=156) or thymoglobulin in combination with sirolimus and prednisone, followed by delayed introduction of doses of cyclosporine. Recipients were stratified as either high-immune response namely African-Americans, retransplant patients or recipients with a pre-tr PRA>30%. All other recipients were considered low immune responders. Graft acute rejection rate, and graft function were compared between groups. **Results:** With a median follow-up of 21 months (range 1-81 months) thymoglobulin treated high immune responders (group 1) exhibited a 19% incidence of acute rejection versus 28% for basiliximab-treated low-immune responders (group 2, p=0.001). 4 year actuarial graft survival for group 1 was 70% versus 73% group 2 (p=0.001). Serum creatinine values at 4 years were 1.7±0.6 versus 1.6±0.8 mg/dl for group 1 and 2 respectively (p=0.15). Exposures to sirolimus and CsA at 3, 12, 24, and 48 months equivalent between the 2 groups.

Conclusion: A strategy combining thymoglobulin with sirolimus for high-risk recipients resulted in a lower risk of acute rejection and equivalent 4-year graft survival to a basiliximab treated low-immune risk recipient group.

Abstract# 1453

Rabbit ATG Dose: Risk Factor for Opportunistic Infection in Transplant Recipients? G. Guerra,¹ T. R. Srinivas,¹ J. D. Schold Gregg,¹ P. R. Patton,¹ A. I. Reed,¹ C. M. Bucci,¹ S. Hurley,¹ J. Griesche.¹ *University of Florida, Gainesville.*

Opportunistic infections (OI) complicate renal transplantation; immunosuppression, especially antibody induction may contribute to port (PTx) OI. We have used rabbit antithymocyte globulin (RATG) induction in renal transplant recipients (RTxR) at our institution. In late 2005 we lowered the dose of Rabbit ATG (RATG) doses from 5 to 3. To date, the relationship between RATG induction and PTx OI is not well defined. We hypothesized that RATG induction is associated with increased PTx OI risk. To test this hypothesis we analyzed all RTxR transplanted between 2002-06 at our center on RATG induced immunosuppression. We analyzed 100 patients who developed PTx OI (CMV, Nocardia, PCP, Systemic Mycoses, Cryptosporidiosis, PJP, Toxoplasmosis, etc.). RTxR received RATG 1.0 mg/kg/day or 1.5 mg/kg/day for 3-10 days (3 days for DGF; 1.5 mg/kg/day dose in high risk RTxR) and were divided into 3 groups by mg/kg RATG dose (<4.65 - low dose group; 4.65-5.82 - intermediate dose group; > 5.82 -high dose group). We analyzed time to overall PTx OI as infections at 6-months post-transplantation in multivariate analysis adjusting for recipient age, recipient race, transplant type and HLA-A-B-C mismatch. Overall, 6-month infection rates were 31%, 50%, and 55% for low, intermediate and high dose groups, respectively (p=0.008, p for trend = 0.002). In univariate analyses, infection rates were higher with higher RATG dose (log-rank p=0.03 p for trend = 0.01). In multivariate analysis, infection rates were 25%, 30%, and 41% for low, intermediate and high dose groups, respectively (p=0.03 for linear trend). Higher RATG dose was also significantly associated with time to any PTx infection (log-rank p = 0.002, p for trend = 0.001). Adjusted hazard ratios (AHR) of PTx OI was 1.5 (MI), 2.0 (intermediate), and 2.2 (high) for low, intermediate and high dose groups, respectively (p=0.001, p=0.001, p=0.001).

Higher dose RATG induction is associated with higher infection rates. Benefit evaluations of different doses of Thymo are not established by prospective studies in the high level group.