

diagnosis of rejection or HCV recurrence or both was made based on standard histologic or clinical criteria.

**Results:** Biopsies of non-transplanted HCV patients, 2/15 (13.3%) were positive for C4d. Of the 25 transplant recipients with HCV (group 2), 15 had HCV recurrence only, of which 3 (20%) stained positively for C4d. Ten patients in the HCV group were diagnosed with rejection (with or without HCV recurrence) of which 4 (40%) were positive for C4d stain ( $p=0.38$ ). Of the transplant recipients with non-viral etiologies and rejection (group 3), 20/28 (77%) stained for C4d. Baseline demographic data were similar between groups. Use of dual vs single maintenance immunosuppression was not different between the C4d+ and negative groups. The C4d+ groups had significantly more steroid use at the time of biopsy. Interferon use pre-transplant was not different between the C4d+ and negative groups ( $p=0.66$ ).

**Conclusion:** C4d staining was strongly associated with rejection in all transplant patients. However, in the cohort of HCV+ recipients, C4d staining did not reliably differentiate between rejection and HCV recurrence.

**Abstract# 1369 Poster Board #Session: P213-III Use of Enteric Coated Mycophenolate Sodium as Part of an Immunosuppressive Regimen in Liver Transplant Patients Suffering from Intestinal Intolerance And/or Poor Quality of Life Related to the Use Mycophenolate Mofetil, Catalin Doria,<sup>1</sup> Carlo B. Ramirez,<sup>1</sup> Adam M. Frank,<sup>1</sup> Silvia Vaccino,<sup>1</sup> Natalie Fraser,<sup>1</sup> Ignazio R. Marino,<sup>1</sup> Thomas Jefferson University, Philadelphia, PA.**

**Purpose:** Post-transplant gastrointestinal (GI) side-effects can impair a patient's quality of life (QoL). This study investigates the improvement in GI side-effects and related QoL changes in recipients of liver transplantation (OLT) after converting patients (pts) from mycophenolate mofetil (MMF) to enteric-coated mycophenolate sodium (EC-MPS). Methods: Thirty-four patients who underwent OLT and suffered from GI intolerance were included in this study. All infectious causes of GI intolerance were excluded. Most common described symptoms included: diarrhea, cramping abdominal pain, and nausea. QoL assessed by the Gastrointestinal Quality of Life Index was evaluated before conversion and at months 3, 6 and 12 post-conversion. Patients were converted from MMF to EC-MPS on an equimolar basis at a mean time of 680 days post-OLT (range 19-4708). Baseline immunosuppression of one calcineurin inhibitor, MMF, with or without steroids was the same for all patients. Paired t-test was used to assess differences in mean score changes over time. Results: Mean follow-up was 277 days post-conversion. No rejection episodes, deaths or graft loss were seen during the study period. Conversion from MMF to EC-MPS for GI intolerance post-OLT shows statistically significant improvement in GI-related QoL at 3, 6, and 12 months when compared to baseline assessments ( $p<0.05$  for total mean score).

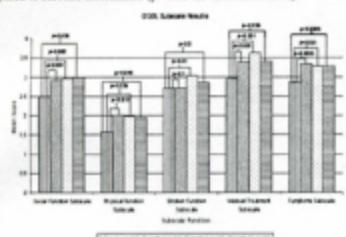


Figure 1 illustrates the mean scores for the 5 subscales (social, physical, emotion, medical treatment and symptoms) evaluated by the Gastro Intestinal Quality of Life Index. The emotion subscale did not present a significant improvement.

**Conclusion:** Our study shows, objectively and prospectively, that pts after OLT who are stable on MMF and develop GI intolerance can be safely converted to EC-MPS with ensuing improvement of the GI side-effects.

**Abstract# 1370 Poster Board #Session: P214-III High Risk of Proteinuria and Lack of Improvement of Kidney Function Following Sirolimus Conversion in Liver Transplant Recipients. Hanif M. Wadei,<sup>1</sup> Martin Mai,<sup>1</sup> Nassim Alsaad,<sup>1</sup> Barry G. Rosset,<sup>1</sup> Thomas A. Gonwa,<sup>1</sup> Transplantation, Mayo Clinic, Jacksonville, FL.**

The effect of sirolimus (SRL) conversion on renal function in liver transplant recipients previously maintained on calcineurin inhibitors is controversial. **Methods:** 61 consecutive liver transplant recipients converted from tacrolimus to SRL were included. Recipients with less than 30-days exposure to SRL, on SRL/tacrolimus combination and anti-thrombin transplant recipients were excluded. Reasons for conversion were worsening renal function ( $n=48$ ), neutropenia ( $n=7$ ) and others ( $n=6$ ). Serum creatinine and 24-hr urine for protein and creatinine clearance were obtained at baseline, at 1-year and at last follow-up from rapamycin initiation. **Results:** Mean pre-conversion creatinine clearance was  $52 \pm 26 \text{ mL/min}$  and follow-up period was  $2.8 \pm 1.4 \text{ years}$ . Overall, kidney function

did not improve following SRL conversion regardless of the cause of SRL initiation.

Kidney function before and after sirolimus initiation in 61 liver transplant recipients			
	Pre-conversion	Last follow-up	P
5-creatinine (mg/dL)	1.7	1.7	0.9
24-hr creatinine clearance (mL/min)	52	51	0.7
24-hr urinary protein (mg/day)	154	414	0.07

Proteinuria  $>500 \text{ mg/day}$  developed in 21 (34%) recipients of whom 7 had proteinuria  $>1 \text{ g}$ . Proteinuria developed mainly in those converted to SRL due to renal dysfunction (20/21 patients). Low creatinine clearance ( $41 \pm 13 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ) and high urinary protein excretion ( $210 \pm 52 \text{ mg}/\text{d}$  vs  $85 \pm 45 \text{ mg}/\text{d}$ ,  $P=0.03$ ) prior to conversion predicted the development of proteinuria. Age at transplant, serum creatinine at transplantation, duration from transplant to SRL initiation, post-transplant diabetes or hypertension did not affect the risk of proteinuria. Kidney function loss from 1-year to last follow-up was more pronounced in recipients with  $>1 \text{ g}$  proteinuria ( $-16 \pm 16 \text{ mL}/\text{min}$  vs  $-2 \pm 14 \text{ mL}/\text{min}$ ,  $P=0.02$ ). **Conclusions:** 1) Conversion to SRL does not improve but may stabilize kidney function in liver transplant recipients. 2) SRL induced proteinuria is common and is associated with poor baseline creatinine clearance and high urinary protein excretion rate. 3) Proteinuria  $>1 \text{ g}$  is detrimental and is associated with precipitous deterioration in kidney function.

**Abstract# 1371 Poster Board #Session: P215-III Persistent Lymphopenia after Anti-Thymocyte Globulin Induction Is Associated with Decreased Long Term Survival in Liver Transplant Recipients.**

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**Introduction:** Anti-dynoycte globulin (ATG) induction is associated with higher graft survival, as well as freedom from acute cellular rejection (ACR) after liver transplantation.

**Purpose:** To determine whether prolonged (165 days) lymphopenia after ATG induction contributes to inferior long term results after liver transplantation.

**Methods:** 378 primary adult liver transplants were performed between 1990 and 2006, with anti-dynoycte globulin for induction. Re-transplants and multi-organ recipients were excluded from the study population. 21 patients died during the first three postoperative months. Of the remaining 357 recipients, 266 were followed-up for more than one year. Patient survival, graft survival censored for patient death, acute cellular rejection incidence and primary disease recurrence were retrospectively analyzed.

**Results:** Persistent lymphopenia correlates inversely with survival [ $B = -0.620$ ,  $p = 0.034$ ,  $\text{Exp}(B) = 0.538$ , 95% CI  $\text{Exp}(B) = 0.303$ -0.956]. The 10-year survival was 77%, 69% and 50% for recipients whose one-year post-transplant lymphocyte count was  $>1200/\text{mm}^3$ ,  $500$ - $1200/\text{mm}^3$  and  $<500/\text{mm}^3$  respectively. This correlation was still present when patient primary disease was inserted into the model. Incidence of ACR was 0.23, 0.38 and 0.45 for the same patient cohorts. That was a statistically significant difference ( $p = 0.05$ ).

**Conclusion:** After induction with ATG, lymphocyte depletion that persists for more than one postoperative year is associated with inferior long-term survival. To what degree this reflects the mechanism of action of ATG remains to be studied. Further investigations, including immunophenotyping and functional assays, should confirm the benefit of avoiding persistent lymphopenia in liver transplant recipients.

**Abstract# 1372 Poster Board #Session: P216-III Everolimus Is Effective in Maintenance Liver Transplant Patients: A Multicenter, Randomized Trial.** Paolo de Simone,<sup>1</sup> Frederik Nevens,<sup>2</sup> Herald Metzelaar,<sup>3</sup> Martina Sterneck,<sup>4</sup> Jérôme Dumortier,<sup>5</sup> Lionel Roestraet,<sup>6</sup> Emiliano Girosi,<sup>7</sup> Evaristo Vare,<sup>8</sup> Liver Transplantation, Azienzo Ospedale Universitario Pisano, Pisa, Italy; <sup>7</sup>UZ Gasthuisberg, Leuven, Belgium; <sup>8</sup>Erasmus Medical Center, Rotterdam, Netherlands; <sup>5</sup>Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany; <sup>6</sup>Hôpital Edouard Herriot, Lyon, France; <sup>4</sup>CHU Rangueil, Lyon, France; <sup>1</sup>Hôpital Cantonal, Genève, Switzerland; <sup>3</sup>Hôpital Clinique Universitaire Santiago de Compostela, Santiago de Compostela, Spain.

**Introduction:** The proliferation signal inhibitor (PSI) everolimus with reduction or discontinuation of calcineurin inhibitor (CNI) may improve deteriorating renal function in liver transplant patients, which is an important unmet medical need. **Methods:** RESCUE was a 6-month, multicenter, randomized, open-label study in maintenance liver transplant recipients (12-60 months post-tx) with CNI-related renal impairment (baseline creatinine clearance [CrCl]  $<60 \text{ mL}/\text{min}$  and  $<20 \text{ mL}/\text{min}$ ). Patients continued standard-dose CNI/cyclosporine or tacrolimus + MPA + steroids (controls) or switched to reduced-dose CNI + everolimus + steroids. **Results:** 145 patients were randomized (everolimus 72, controls 73). Demographics were similar between cohorts. Biopsy-proven acute rejection occurred in 1.4% of patients in each group, with graft losses. At month 6, 80% of everolimus patients had discontinued CNI. The primary endpoint (CrCl/min difference in CrCl at month 6) was not achieved. Mean change in CrCl from baseline was  $1.0 \pm 10.3 \text{ mL}/\text{min}$  with everolimus and  $2.3 \pm 7.8 \text{ mL}/\text{min}$  in controls, a difference