**Results:** 134 liver cirrhotic patients in the waiting list were enrolled. Before LT 44%, 12.7% and 13.4% of patients were non adherent to therapy, to outpatient visit and to requested blood tests, respectively. Non adherent patients, compared to patients with good adherence, were younger (mean 52.1 vs 54 ys, p 0.09), unmarried (96.6% vs 71.3%, p 0.06) and with external LOC (66.7% vs 40.5%, p 0.04). 23 out of 134 (17.1%) patients underwent LT during the study period. When univariate and multivariate analysis was performed, being divorced and having a better MELD score were independent risk factors for non adherence to medical prescriptions (OR, 95%CI : OR, 95% CI). At 6 months after LT 15%, 20% and 10% of patients were non adherent to therapy, to outpatient visit and to blood tests, respectively. These patients, compared to patients with good adherence, presented better MELD at time of transplantation (mean 12.7 vs 16.9, p 0.04), were drinking alcohol (33.3% vs 5.9%, p 0.001) and referred >3 side effects of immunosuppression therapy (66.7% vs 23.5%, p. 0.02). At 12 months after LT 60%, 50% and 50% of patients were non adherent to therapy, to outpatient visit and to blood tests, respectively. These patients, compared to patients with good adherence, were younger (mean 55.3 vs 61, p.05), presented better MELD at time of transplantation (mean 13.3 vs 17.5), were drinking alcohol (50% vs 0%, p.001) after liver transplantation and referred >3 side effects of immunosuppression (83.3% vs 50%, p.02). Poor adherence after LT was related with poor adherence before transplant in 50% of the cases.

**Conclusions:** Adherence to medical regimen is poor in patients in the waiting list for LT but also at 12 months after LT. Being divorced and having a better MELD score are independent risk factors for non adherence to medical prescriptions in patients on the waiting list, side effects of immunosuppression seem to be a risk factor of poor adherence after LT, therefore information and education for those patients are badly needed.

---

**708 DE NOVO MALIGNANCY FOLLOWING LIVER TRANSPLANTATION – RETROSPECTIVE ANALYSIS OF 641 LIVER TRANSPLANTATIONS**

C. Graeb1, M. Franki1, M. Angele1, M. Rentsch1, M. Guba1, C. Wimmer1, C.C.J. Bruns1, R. Zachoval2, K-W. Jauch1, F. Loehe1

1Dept. of Surgery, 2Dept. of Medicine

**Introduction:** Development of de novo malignancy following liver transplantation represents a main cause of late mortality. The ongoing improvement of both surgical technique and immunosuppressive regimens has lead to an ongoing increase in long term patient survival. Therefore, the individual patient’s risk for development of various forms of solid organ malignancy has continuously risen. In addition, the patient’s underlying disease, i.e. alcoholic cirrhosis, PSC, or various forms of hepatitis, may add to the patient’s susceptibility to cancer. Here, we analyze both the incidence and potential risk factors in our cohort of liver transplanted patients.

**Method:** Our retrospective analysis was based upon the peri- and postoperative data bases (including the Munich Tumor Registry) of 537 patients in a total 641 liver transplantsations.

**Results:** The cumulative risk for tumor development 20 years after transplantation with a value of 19% lay significantly higher than in an age matched cohort (9%), 49/537 pts. developed a total 74 tumors (excluding pre-existent HCC) during a mean follow up of 9 years. Tumor prevalence increased from 1.3% in the first year to 20% 15 years after transplantation. The median time interval from transplantation to tumor development was 6 years (range 1-17 years). 19 pts. died as a result of malignancy, 30 pts. remain alive following diagnosis. 11/19 patients (57.9%) died within 2 years following transplantation. The most common tumours were basalioma (37%), squamous cell skin cancer SCC (22%), LDP (7%), ENT malignancy (7%) and urethra carcinoma (6%). The relative early development of basaliomata (on average 52 mths) in comparison to SCC (72 mths) was remarkable, as well as the observation that squamous cell cancer (57%) was more common than adenocarcinoma (37%). At the time-point of evaluation, no significant difference was detectable with respect to the form of immunosuppression with comparative numbers of patients treated with cyclosporine monotherapy (32%), CyA-steroids (14%), tacrolimus monotherapy 37% and tacrolimus-steroids (7%). Despite the fact that cyclosporine has been used for a significantly longer time period (124 patient years) than tacrolimus (64 patient years), no difference was evident in overall tumor incidence.

**Conclusion:** The more potent immunosuppressant tacrolimus seems to be related to a higher incidence of postoperative malignancy. In our analysis, the primary indication (alcoholic cirrhosis, PSC, and viral hepatitis) for liver transplantation was not related to a higher incidence for malignancy. The cumulative tumor incidence following liver transplantation makes a continuous surveillance of transplanted pts. necessary.

---

**709 PREEMPTIVE VS. PROPHYLACTIC APPROACH TO CYTOMEGALOVIRUS IN LIVER TRANSPLANTATION**

G. Smallwood1, K. Kempton1, A. Sieber1, C. Fasola1, T. Heffron1

1Emory University School of Medicine, 2Emory University Hospital

Cytomegalovirus (CMV) continues to be source of increased morbidity and mortality in the solid organ transplantation. Currently valganciclovir is FDA approved for CMV prevention in both heart transplant and kidney transplantation. In the pivotal PV16000 registration trial, liver transplant recipients, receiving valganciclovir, had an increase in tissue invasive CMV disease. Although not approved, many transplant centers use valganciclovir for CMV prophylaxis due to easier patient compliance.

**Aim:** To compare the frequency of CMV viremia as determined by polymerase chain reaction (PCR) between liver transplant patients being followed with a preemptive strategy and treatment compared to patients taking valganciclovir for 100 days as prophylaxis.

**Methods:** This is an IRB approved review of patients being followed for CMV. Patients were routinely followed by weekly, serial blood draws for CMV by polymerase chain reaction (PCR). Based on time transplanted, patients may have received valganciclovir prophylaxis of 900mg daily or only monitored. At time of seroconversion, patients were started on ganciclovir IV 5mg/kg Q12H and continued to be followed by PCR to monitor treatment. All patients received the same immunosuppression protocol which included daclizumab induction. Outcomes were determined by rate of CMV viremia.

**Results:** Patients (n =119) receiving prophylactic valganciclovir was similar in race, gender, and age to the patients being followed preemptively (n=131). CMV viremia within the first 3 months of transplant were similar between groups [31.3%/41(131) vs. 26.8%/32(119); p=0.488]. Pre-emptive patients seroconverted earlier [52.2%/37.9 days vs. 120.9 ± 91.3 days; p<0.001] but had overall lower rates of conversion compared to the prophylactic group [35.1%/46(131) vs. 49.6%/49.6%; p = 0.022]. The prophylactic group had similar rates of viremia while on drug vs off drug [32/119 vs 27/119; p=0.4350). High-risk (-/-) had similar rates of viremia (75% vs. 70.4%; p=0.843). Patients taking valganciclovir had increased risk to develop viremia[RR 0.527 to 0.951;p=0.02] with decreased viremia free survival.

**Conclusions:** Use of prophylactic valganciclovir in liver transplant does not prevent CMV viremia and break through viremia is not uncommon. Additional multicenter work should be done with this agent in liver transplant.

---

**710 STEROID IMMUNOSUPPRESSION INDUCES CHANGES IN THE GLUCOCORTICOID RECEPTOR**

J. Hutchinson1,2, Y. Chen1,2, V. Pravica1,2

1University of Southern California, 2National Institute of Transplantation

**Introduction:** Initial high dose steroid treatment of transplant recipients induces changes in the cytoplasmatic glucocorticoid receptor (cGR) that may affect the mode of action of the drug. The cGR consists of functionally distinct isoforms of the GR and chaperone molecules, including FK binding protein 5 (FKBP5), that modulate GR signaling. Normal sensitivity to steroids requires expression of appropriate GR isoforms and the collaboration with FKBP5. Gene transactivation requires the GR-a isoform and is inhibited by excessive expression of the hGR-b isoform. Over expression of FKBP5 can attenuate steroid sensitivity by restraining translocation of the GR from cytoplasm to nucleus. We investigated the effect of bolus glucocorticoid (GC) treatment on the structure of the eGR complex by measuring the levels of GR isoform expression and FKBP5 transcription.

**Methods:** Peripheral blood mononuclear cells (PBMCs) were obtained before renal transplantation and immediately after the initial methylprednisolone treatment. Gene expressions of the GR-a, -b, -P isoforms and FKBP5 were quantified by the simplex TaqMan relative quantification assay (Applied Biosystems).

**Results:** Increased expression of FKBP5 (17.67±14.01 fold, mean±SD),
Oral Abstracts

Thursday 14 August 2008

711 STEROID AVOIDANCE AFTER RENAL TRANSPLANTATION: RESULTS OF A PROSPECTIVE AND RANDOMIZED TRIAL USING FRESENIUS ATG

D. Cantarovich, L. Rostaing, G. Mourad

for the FRANCIA study group. Nantes University Hospital, Nantes, France

Background: Steroid withdrawal after renal transplantation (Tx) is associated with an increased incidence of acute rejection. We investigated the potential effective role of Fresenius ATG in completely avoiding steroids from the day of Tx.

Aim: sedemedized and multicenter trial was designed in order to evaluate the tolerability and efficacy of a sequential treatment based on Fresenius rabbit anti-T lymphocyte serum (ATG), mycophenolate mofetil (MMF) and cyclosporin (CsA), with and without concomitant corticosteroids (Cs), after a first cadaveric renal Tx.

Patients and immunosuppression: This investigator origin protocol was conducted in 6 french centers and included 204 patients. Central randomization was done according to recipient’s age (> or <50 yrs) and cold ischemia time (CIT; > or <24 hrs). Retransplants were not included. Three patients did not received ATG and were excluded from analysis. Results included 201 patients, 99 in the steroid group (66% men; mean age 48 yrs, range 18-73) and 102 in the steroid avoidance group (71% men; mean age 48, range 19-69). ATG was given at 9 mg/kg the day of surgery, followed by 4 doses of 3 mg/kg on days 1, 3, 5 and 7. MMF was started the day of surgery at 1g/bid. CsA was given at 9 mg/kg the day of surgery, followed by 4 doses of 3 mg/kg on days 1, 3, 5 and 7. MMF was started the day of surgery at 1g/bid. CsA was started on postoperative day 5 at 8 mg/kg, and doses were adjusted according to standard C0 trough levels. 500 mg of Cs were given in all patients during surgery, followed by standard maintenance doses in the steroid group and no Cs at all in the steroid avoidance one.

Results: All patients were followed for at least one year. Mean CIT was similar in both groups: (23 vs 22 hrs). Clinical tolerance of ATG was excellent in both groups: the entire 5-day ATG course was given to 98% of patients in the steroid group (one interruption on day 1 due to thrombocytopenia) and 96% in the steroid avoidance one. The number of severe side-effects did not differ in both groups (42 vs 46%). Four malignancies were observed: 3 in the steroid group and 1 in the steroid avoidance one. CMV infections were 3% in the steroid group and 1% in the steroid avoidance one. Acute rejection (all histologically confirmed) did not differ during the first year: 14% in the steroid group and 22% in the steroid avoidance one; rejection onset was significantly lower in the steroid avoidance group (median 14 days) as compared to the steroid group (median 49 days). Steroid-resistant rejections were not statistically different: 5% in the steroid group and 2% in the steroid avoidance group. One-year patient and graft survival was 99 and 96% in the steroid group and 97 and 94% in the steroid avoidance one.

Conclusion: This study demonstrates that Cs avoidance is possible and safe, with excellent one-year results, in recipients of primary cadaver renal Tx under an immunosuppressive regimen including Fresenius ATG, MMF and CsA.