undergoing first liver transplantation; comparison of Tacrolimus once daily to twice daily; The primary outcome was the patient adherence to the medication regime. Secondary outcomes were as follows: safety (measured as rate of medication complications), graft survival and pharmacokinetics. Taking clinical heterogeneity in trial participants and treatments into account, a random-effect model was chosen for the meta-analyses.

**Results:** Change of the immunosuppression regime showed improved adherence of patients according to individual criteria and the Basel Assessment of Adherence Scale to Immunosuppressives. There was no statistically significant increase in Serious Adverse Events (SAEs) or rejection.

**Conclusion:** Based on validated adherence evaluation and SAEs the change in Tacrolimus-based immunosuppression is safe and promotes adherence in liver transplant patients.

#### PLB049 PRESERVATION OF RENAL FUNCTION WITH EARLY USE OF MTOR INHIBITOR OR LATE CHANGE IN IMMUNOSUPPRESSION IN LIVER TRANSPLANTATION

Maria Lúcia Zanotelli, Mariana Pranke, Alfeu Fleck Jr, Guillermo Kiss, Marcos Mucenic, Eduardo Schlindwein, Ian Leipnitz, Mario Meine, Juliano Martini, Ajácio Brandão, Cláudio Marroni, Guido Cantisani Irmandade Santa Casa De Misericórdia De Porto Alegre - Porto Alegre - Rio Grande Do Sul - Brasil, Brazil

**Introduction:** Early use of everolimus (EVR) associated with reduced calcineurin inhibitor (CI) in liver transplantation (LTx) has been shown to be effective in preventing acute cellular rejection (ACR) with reduced nephrotoxicity caused by chronic use or high doses of CI. The objective of this study was to compare the benefit of early ( $\leq$ 30 days post-LTx), intermediate (>30 days and  $\leq$ 180 days) and late (> 180 days) use of EVR in preserving renal function (RF) in the LTx patients.

**Methods/Materials:** A prospective study of 98 patients submitted to LTx with hepatocellular carcinoma and / or acute renal injury (GRF <60 ml/min), as measured by the Cockcroft-Gault formula on days 1 (1st day EVR), 30, 90, 180, 360. The initial dose of EVR was 0.75 mg or 1.0 mg bid with a serum level (SL) adjusted between 3–6 ng/ml (the same for reduced dose tacrolimus). For the evaluation of efficacy, the presence of ACR confirmed by biopsy was considered.

**Results:** Comparing the three groups, it was observed that GRF remained stable, with no difference over time (p = 0.620). In the early group, the GRF profile of the patients with SL adjusted TAC, showed a tendency to improve the RF. In patients with SL TAC> 6 ng/ml, despite the stability of RF, there was a tendency for GRF to drop (p = 0.034). Regardless of the group, no patient had biopsy-confirmed ACR from the onset of EVR.

**Conclusion:** Stability of RF throughout the sample was observed over the follow-up period regardless of the lower GRF in those patients who started EVR late. There was a trend for improvement of GRF in those patients treated early with adjusted SL TAC, without impairing efficacy. These results are promising for further studies with a larger number of patients and longer follow-up.

| PLB050 | CONCANAV  |
|--------|-----------|
|        | CYTOTOXIC |
|        | POTENTIAL |
|        | RECURRENC |

CONCANAVALIN-A STIMULATED CD8 + CD40L+ T-CYTOTOXIC LYMPHOCYTES AND DONOR AGE AS POTENTIAL SURROGATE BIOMARKER FOR HCV RECURRENCE RISK IN LIVER TRANSPLANTATION

Francisco Boix, Jorge Eguia, Gema Gonzalez-Martinez, Rafael Alfaro, Jose A. Galian, Jose A. Pons, Santiago Llorente, Maria R Moya-Quiles, Alfredo Minguela, Francisco Sanchez-Bueno, <u>Manuel Muro</u> Clinical University Hospital Virgen De La Arrixaca, Spain

Introduction: Currently, liver transplant (LT) is a well-established treatment for patients with chronic HCV-related cirrhosis. Upon LT, HCV infection recurs virtually in every recipient. Progression of chronic HCV is more aggressive after LT with a probability of developing graft cirrhosis estimated in 30% at 5 years. This life-treating condition requires a major effort searching for quick and reliable biomarkers capable of predict HCV recurrence.

**Objectives:** Based on these instances, our group evaluated CD8 + CD154 + T-cytotoxic (Tc) cells in a *de novo* cohort of LT recipients as measures of the risk of post-LT HCV recurrence, using polychromatic flow cytometry over the first year post-LT. **Material and Methods:** Thirty Caucasian *de novo* LT recipients were con-

**Material and Methods:** Thirty Caucasian *de novo* LT recipients were consecutively recruited from the University Clinical Hospital 'Virgen de la Arrixaca' in Murcia Region in the Southeast of Spain. A peripheral blood sample was taken at baseline as well as at different time points over the first year post-LT (7 and 15 days, 1st, 2nd, 3rd, 6th and 12th months). Whole peripheral blood samples were cultured with Concanavalin-A (Con-A) in a humidified 5% CO2 incubator at 37°C for 72 h. Upon cell culture, samples were subsequently stained with MoAb for its assessment by Flow Cytometry. Eleven (36.7%) LT recipients (LTr) developed HCV recurrence (HCVr) during the follow-up period. **Results:** Donor age, but not other demographic characteristics, showed significant differences among LTr with and without HCVr. CD8 + CD154 + Tc cells were significantly increased among HCVr study group at 90, 180 and 365 days post-LT. Furthermore, we found that a percentage of CD8 + CD154 + Tc cells>0.68% (p < 0.001) along the long-term was able to stratify LTr at high risk of HCVr. CD8 + CD154 + Tc cells [HR = 3.28, 95% CI 2.1–5.2, p < 0.001] for a percentage (%) >0.68% had a significant impact on HCVr. In the univariate Cox regression model of LTr, older donor and CD

PLB051

## DO MESENCHYMAL STROMAL CELLS PROMOTE HLA SPECIFIC ANTIBODIES FORMATION AFTER INFUSION IN LIVER TRANSPLANT RECIPIENTS?

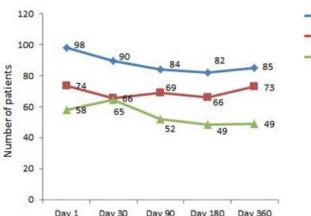
<u>Morgan Vandermeulen</u>, Gianni Maggipinto, François Jouret, Yves Beguin, Olivier Detry

University Hospital Of Liege, Belgium

**Background:** Mesenchymal stromal cells (MSC) immunogenicity is debated. We recently published a prospective, controlled, phase I study evaluating a single administration of third-party MSC in 10 liver transplant recipients (LTR). Here, we focus on the development of antibodies (Ab) against MSC-donor HLA (MscDSA) in LTR following MSC infusion. **Methods:** The LTR under standard immunosuppression received 3rd-party

**Methods:** Ten LTR under standard immunosuppression received 3rd-party unrelated MSC on postoperative day 3, and were prospectively compared to 10 control LTR. Recipients and donor of either liver or MSC were genotyped for HLA A/B/C/DR/DQ. Recipients were tested for HLA Ab before and 1, 3 and 6 months after transplant by Luminex<sup>®</sup>. Ab were considered as positive in case of MFL>1500 and in accordance with the manufacturer's recommendations.

**Results:** In MSC-treated group, 2 patients showed pre-transplant <sub>MSC</sub>DSA. During follow-up, <sub>MSC</sub>DSA were detected in 6 additional patients who had received multiple red blood cell allo-transfusions before and/or rapidly after transplant. These patients also developed Ab against various MSC-unrelated





HLA. Two patients did not develop any  $_{\rm MSC}$ DSA throughout the follow-up, and one of them did not receive any allo-transfusion. MFI of detected  $_{\rm MSC}$ DSA were not significantly different from MFI of other detected HLA Ab. In control group, 3 patients were sensitized pre-transplant, and 6 patients developed *de novo* multiple HLA Ab. Four of these had received multiple allo-transplant, the detection of  $_{\rm MSC}$ DSA is most likely caused by allo-transfusions rather than related to MSC infusion. Further studies are required to confirm that MSC are "immune privileged".

## PLB052 IMPACT OF DONOR-RECIPIENT GENETIC RELATIONSHIP ON OUTCOME OF LIVING DONOR LIVER TRANSPLANTATION. A SINGLE CENTER EXPERIENCE

Mahmoud Mohamed Abdelwahab Ali Gastrointestinal Surgery Center, Egypt

**Introduction:** Living donor liver transplantation (LDLT) is a valuable option for expanding donor pool, especially in localities where deceased organ harvesting is not allowed. In addition, rejection rates were found to be lower in LDLT, which is attributed to the fact that LDLT is usually performed between relatives. However, the impact of genetic relation on the outcome of LDLT hasn't been studied. In this study, we examined the difference in rejection rates between LDLT from genetically related (GR) donors and genetically unrelated (GUR) donors.

**Patients and Methods:** All cases that underwent LDLT during the period from May 2004 till May 2014 were included in the study. The study group was divided into 2 groups; LDLT from GR donors and LDLT from GUR donors.

**Results:** Three-hundred and eight patients were included in the study; 214 from GR donors and 94 from GUR donors. HLA typing wasn't included in the workup for matching donors and recipients. GUR donors were wives (36; 11.7%), sons in law (7; 2.3%), brothers in law (12; 3.9%), sisters in law (1; 0.3%) and unrelated (38; 12.3%). The incidence of acute rejection in GR group was 17.4%, and in GUR group was 26.3% (p-value = 0.07). However, there was a significant difference in the incidence of chronic rejection between the 2 groups; 7% in GR group and 14.7% in GUR group (p-value = 0.03). In terms of overall survival, there was no significant difference between both groups.

**Conclusion:** LDLT from GUR donors is not associated with higher incidence of ACR. However, CR was significantly lower when grafts are procured from GR donors. HLA matching may be recommended before LDLT from GUR donors.

## PLB053 RESULTS OF BILIARY COMPLICATIONS WITH THE USE OF LIVER GRAFTS FROM 70 TO 94 YEARS

Oscar Caso Maestro, Carlos Miguel Muñoz Arce, Iago Justo Alonso, Alberto Marcacuzco Quinto, Carlos Jiménez Romero

Hospital Universitario 12 De Octubre, Spain

**Introduction:** The incorporation of the use of grafts from marginal donors, elderly donors, as a good source of production, under a very careful prior selection of the organ currently its use is limited for fear of obtaining poor results, being a challenge despite the results observed so far.

**Methods:** A retrospective, longitudinal, comparative and unicentric study of patients transplanted with hepatic grafts aged 70 to 94 years who developed biliary complications and those who did not present them.

biliary complications and those who did not present them. **Results:** From January 1994 to June 2016, 212 liver transplants were performed with donors aged 70 to 94 years. A total of 16 patients (7.54%) developed biliary complications: 2 ischemic cholangiopathies (12.5%), 11 stenoses (68.75%) and 3 fistulas (18.75%). Donors with similar characteristics, with Males 10 (62.5%) vs 77 (39.3%), AHT 12 (75%) vs 110 (56.1%), CRA 2 (12.5%) vs 12 (6 (50%), vasoactive drugs 8 (50%) vs 151 (77%), prothrombin activity 87 (24) vs. 75 (27) (p = 0.04). Similar characteristics of the etiology, AHT 1 (6.2%) vs 40 (20.4%), low platelets in the complications group (p = 0.01) Bile duct choledocho-choledochostomy was performed without T-Tube 12 (75%) Vs 184 (93.9%) (p = 0.02), immunosuppression with tacrolimus and steroids, both groups comparable for times of cold and hot ischemia. We can highlight that the development of biliary complications is associated with a higher rate of medical, infectious, vascular, cardiovascular and respiratory complications, post-transplant reoperations 3 (19%) vs 19 (10%), retransplantation 2 (12.5%) vs 10 (5.1%).

**Conclusions:** The rate of bile complications in liver transplants with grafts older than 70 years was similar to the described with the use of younger donors. The development of billary complications is associated with a greater development of medical, infectious, vascular, cardiovascular and respiratory complications, being more frequent the need for post-transplant reoperations and re-transplants in this study group.

# PLB054

### PREDISPOSING FACTORS FOR THE DEVELOPMENT OF ARTERIAL COMPLICATIONS WITH THE USE OF LIVER GRAFTS ≥70 YEARS

<u>Carlos Miguel Muñoz Arce</u>, Oscar Caso Maestro, Iago Justo Alonso, Alberto Marcacuzco Quinto, María García-Conde, Carlos Jiménez Romero, Alejandro Manrique Municio, Félix Cambra Molero, Sheila Adriana Araya Chavarría, Jorge Calvo Pulido, Alvaro García Sesma

Hospital Universitario 12 De Octubre, Spain

**Introduction:** The use of liver grafts from elderly donors has shown good results in recent years, a problem when considering the use of this type of grafts is the condition or arterial changes typical of aging.

Methods: Retrospective, longitudinal and comparative study of all recipients with hepatic grafts ≥70 years who developed arterial complications and those who didn't present them.

**Results:** From 1994–2016, 212 liver transplants were performed with donors ≥70 years. A total of 14 patients (6.6%) developed vascular complications: 5 stenosis (35.71%) and 9 thrombosis (64.28%). Donors with similar characteristics, regarding longer ICU stay 39 (73) vs 25 (24) h, as well as hypotension 5 (35.7%) vs 55 (27.8%) and use of vasoactive drugs 11 (78.6%) vs 148 (74.7%), similar analytical parameters between both groups without clinically relevant differences. Receptor with a mean of 60 (9.55) years, the characteristics were similar between both groups except for a lower rate of HCV 1 (7.1%) vs 72 (36.4%) (p = 0.01), DM 4 (28.6%) vs 35 (17.7%), previous abdominal surgeries 3 (21.4%) vs 22 (11.1%) and a lower platelet count 71 000 (56 500) (P = 0.04). We couldn't analyze the characteristics of the arterial anastomosis as it is a retrospective study and we lack this information. Bile duct choledochochocholedochostomy was performed without T-Tube, immunosuppression with tacrolimus and steroids in both groups. We can highlight that the development of arterial complications is associated with a higher rate of biliary complications, medical complications and post-transplant renal failure, which resulted in a longer stay in the ICU.

**Conclusions:** The rate of vascular complications in liver transplants with grafts older than 70 years was similar to that described with the use of younger donors. The development of vascular complications is associated with a longer stay in the ICU and a higher rate of development of medical complications, biliary and acute renal transplant post-transplant.

PLB055

#### FIRST CASE OF LIVER RETRANSPLANTATION USING DCD (DONOR AFTER CARDIAC DEATH) MAASTRICHT TYPF II

lago Justo, María García-Conde, Anisa Nutu, Pilar Del Pozo, Óscar Caso, Alberto Marcacuzco, Alejandro Manrique, Jorge Calvo, Félix Cambra,

Álvaro García-Sesma, Carlos Jiménez

Hospital Universitario 12 De Octubre, Spain

**Background:** The scarcity of organs for liver transplantation (LT) is even more dramatic in liver retransplantation (LRT). Occasionally, in life threatening situations such as primary graft failure, we have to consider new sources for LRT. The safe employ of grafts from DCD type II from our team's experience, by far the longest in the world, allowed us to consider these grafts as an adequate option for liver retransplantation, despite the increased rate of long-term biliary complications, and the possibility of a new graft failure.

Methods/Materials: We present a case report of LRT in a 37- year-old man with hepatic HCV cirrhosis plus HCC, MELD score 17; Child B8; performed in our institution.

**Results:** The patient underwent a first LT from right hepatic split graft, from a 32-year-old brain death donor after 11 h of cold ischemia, and 45 min of warm ischemia. Transfusion requirements were 1 unit of PRBC and 2 FFP units. There were no incidents.

After 24 h the patient presented with deteriorating liver function tests and renal failure, requiring renal replacement therapy and respiratory support. A CT scan was performed that showed hepatic artery thrombosis and multiple liver abscesses. He was placed on code 0 for retransplantation and for 3 days he progressively deteriorated until we were offered a DCD type 2 graft from a 35 years old female with 5 min of cardiac arrest, ECC up to 3 I, no alteration of liver enzymes and no macroscopic disease, with less than 5% macrosteatosis. Retransplantation was performed with no complications, 3 RBC and 1 FFP

Retransplantation was performed with no complications, 3 RBC and 1 FFP were transfused. Postoperative course was uneventful except for initial renal dysfunction, solved by the 3rd day. Patient was discharged on the 8th day on MMF and low-dose Tacrolimus. After 3 months the liver is doing well, without evidence of either biliary or arterial disease.

**Conclusion:** To our knowledge, this is the first case of LRT using DCD type II grafts, which could be considered an acceptable source for liver retransplantation