O1 SURVEILLANCE BIOPSY-DRIVEN STEROID WITHDRAWAL: IMPACT ON KIDNEY TRANSPLANT OUTCOME

A. Bouquegneau, S. Grosch, M. Milicevic, C. Bonvoisin, C. Bovy, J.M. Krzesinski, L. Weekers

4, CHU Liège, Liège, Belgium

Introduction: In a Cochrane group meta-analysis steroid sparing strategy was associated with increased risk of acute rejection and lower long term kidney survival. Therefore our steroid withdrawal (SW) strategy relies on a surveillance biopsy (SB) performed at 3 month. When this SB is normal the steroid are tapered off, but usually kept otherwise. The impact of this strategy in terms of risk of acute rejection, decline of eGFR and transplant survival was analyzed.
Methodology: Retrospective analysis of prospectively collected data since 2007, including 461 kidney transplant performed from 1/1/07 until 30/4/2015. Among those, 373 SB were performed when steroid had been tapered to the lowest level. SB were scored according to BANFF 2013 classification, 287 were deemed adequate and are further analyzed here after.
Results: Histologically, 77% (n = 222) of adequate SB did not show any sign of rejection (No SCR). Among these, SW was possible in 72 % (n = 159) of cases (SW+). Late acute rejection occurred in 15 of these patients (9%). The main reason for keeping steroids (No SW) despite normal SB was the necessity to withdraw antimetabolites.

A subclinical rejection was observed in 65 SB with the following histological findings (n): borderline changes (47), acute cellular changes (10) ranging from Ia to IIb, acute antibody mediate rejection (12) among which 4 mixed rejections. SW was achieved in only 17 of these patients (26%). Late acute rejection was observed in 6 of those cases (35%).

The 5 years graft survival was 97, 76, 77 and 100% for the No SCR/SW+; No SCR/NoSW ; SCR+/No SW and SCR+/SW+ groups, respectively.
Conclusion: SB allows the identification of a population where SW is safe with excellent graft survival and few late rejection.

O2 LONG-TERM OUTCOMES OF 12 RENAL TRANSPLANT RECIPIENTS TREATED WITH ECULIZUMAB TO PREVENT ATYPICAL HEMOLYTIC SYNDROME RECURRENCE

C. Levi[5,6], V. Fremeaux-Bacchi[1,6], J. Zuber[5,6], M. Devriese[1], M. Rabant[4,6], R. Snanoudj[5], A. Scemla[5], L. Amrouche[5,6], A. Mejean[2,6], L. Lamhaut[3], C. Legendre[5,6], R. Sberro-Soussan[5]

[1]Service d'immunologie; [2]Service d'urologie, Hôpital Européen Georges Pompidou. Assistance Publique des Hôpitaux de Paris; [3]Service d'anesthésie et réanimation; [4]Service de pathologie rénale; [5]Service de transplantation rénale adulte, Hôpital Necker. Assistance publique des hôpitaux de Paris; [6]Université Paris Descartes, Paris, France

Atypical hemolytic uremic syndrome (aHUS) is an orphan disease with a high rate of recurrence after kidney transplantation. However, cases reports of successful prevention of post-transplant aHUS recurrence with eculizumab emerged a few years ago. To further delineate its optimal use, we describe the largest series of kidney transplant recipients treated with prophylactic eculizumab.

Twelve renal transplant recipients with aHUS-related end stage renal disease received eculizumab, including ten from day 0 and two at the time of recurrence (days 6 and 25). Clinical and histological features, complement alternative pathway and free eculizumab concentrations were investigated. The median follow-up was 24.6 (4.5 – 68.2) months.

Five patients had previously lost at least one renal transplant from aHUS recurrence. A genetic mutation was identified in nine patients while anti-H antibodies were readily detected in two others. No patient demonstrated biological features of aHUS recurrence under treatment. Three antibody-mediated rejections (ABMRs) occurred despite the lack of detectable C5 activity. ABMR was associated with subclinical TMA in two patients. One patient lost his graft after several complications, including ABMR. Another patient experienced post-transplant C3 glomerulonephritis. The last median serum creatinine was 128.2 ± 40.8 μmol/L.

This study confirms that eculizumab is highly effective in preventing post-transplantation aHUS recurrence, yet may not fully block ABMR pathogenesis

O3 EFFICACY AND TOLERANCE OF AN ASSOCIATION OF EVEROLIMUS AND REDUCED DOSES OF CALCINEURIN INHIBITORS: REAL-LIFE MONOCENTRIC EXPERIENCE

A. Devresse[2], L. Morin[2], L. Amrouche[2], C. Tinel[2], M. Rabant[1], C. Legendre[2], D. Anglicheau[2]

[1]Service d'anatomo-pathologie, Hôpital Necker-Enfants Malades; [2]Service de Néphrologie et Transplantation Adulte, Hôpital Necker-Enfants Malades, Paris, France

This work reports our experience on the efficacy and security profiles of low-dose of calcineurin inhibitors (CNI) associated with everolimus (EVL) in kidney transplantation.

This is a monocentric study including 215 low risk kidney recipients transplanted between 05/2011 and 02/2016 treated with basiliximab, CNI), steroids and EVL (n = 97) or mycophenolic acid (MPA, n = 118). Intent to treat analyses are shown.

Baseline characteristics were similar except for the time of follow-up (485 ± 243 days in the EVL group vs 912 ± 489, $p < 0.01$). Tacrolimus (Tac) blood concentrations were 5.7 ± 1.7 μg/L vs 8.2 ± 2.5 μg/L at M3, 3.5 ± 1.5 μg/L vs 6.6 ± 2 μg/L at M12 in the groups Tac/EVL and Tac/MPA respectively. At M12, incidence of acute rejection (20% vs 20%, $p = 1$) de novo DSA (18% vs 9%, $p = 0.10$), graft loss (2% vs 7%, $p = 0.12$) and death (3% vs 4%, $p = 0.73$) were similar in the EVL and MPA group, respectively. Serum creatinine at M3 (139 ± 48 μmol/L vs 142 ± 61 μmol/L $p = 0.92$) and M12 (132 ± 44 μmol/L vs 146 ± 65 μmol/L $p = 0.21$) were similar. Proteinuria was higher at M3 (0.19 ± 0.21 g/g vs 0.14 ± 0.13 g/g $p = 0.01$) in the EVL group, but similar at M12 (0.13 ± 0.22 g/g vs 0.18 ± 0.28 g/g, $p = 0.73$). Immunosuppressive regimen changes were more frequent (67% vs 53%, $p = 0.04$) in the EVL group, mostly due to side effects. Incidence of surgical complication, anemia after M3, diarrhea, folliculitis, diabetes, BK and CMV viremia were similar in the EVL and MPA groups. Lymphoedema (15% vs 3%, $p < 0.01$) and statin use at M12 (70% vs 52%, $p = 0.02$) were more frequent in the EVL group while leucopenia (14% vs 45%, $p < 0.01$) was less frequent. In seronegative recipients for CMV, incidence of CMV primary infection was reduced (3% vs 33%, $p < 0.01$).

In low risk kidney transplants, initial treatment by CNI/EVL or CNI/MPA have similar efficacy, decreased incidence of CMV primary infection and increased incidence of immunosuppressive regimen changes.

O4 ECULIZUMAB IN C3 GLOMERULOPATHY RECURRENCE AFTER KIDNEY TRANSPLANT

G. Jeantet, D. Bertrand, D. Anglicheau, N. Jourde-Chiche, P. Gatault, E. Cassuto, F. Fakhouri, V. Fremeaux-Bacchi, A.L. Sellier-Leclerc, A. Lionet, M. Rabant, M. Le Quintrec

4, Transplantation rénale-Néphrologie, Montpellier, France

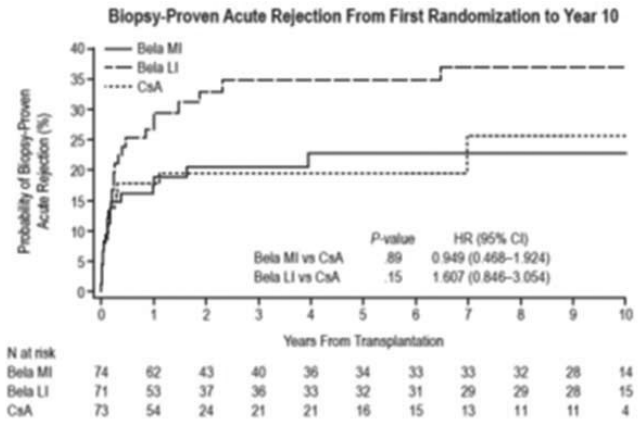
Clinical GC3 recurrence occured in more than 50% after renal transplantation and is the first cause of allograft loss at 5 years post-transplantation. Eculizumab (EC) has been used in severe GC3 on native kidney and in few cases in graft recurrence with mitigate results. The aim of this study was to evaluate EC efficacy in graft GC3 recurrence in french cohort. We retrospectively analyzed patients who received EC for a clinical GC3 graft recurrence. Clinical recurrence was defined by a proteinuria >0.7 g/g and/or increasing serum creatinine > 30% from the baseline. Recurrence had to be proven by graft biopsy and was considered by C3 deposits without associated rejection. Data were collected the day of recurrence, the first day of EC starting and at the last follow up. Partial remission (PR) was defined by stabilization (±25%)or improvement of serum creatinine and proteinuria reduction upper than 50%. Complete remission (CR) is defined by a normalized serum creatinine (basal value) and proteinuria lower than 0.5 g/g. 9 patients received EC for GNC3 recurrence. The mean time of recurrence diagnosis was 44 days. (7 in the first 3 months including 3 in the first month). At diagnosis serum creatinine was 220 μmol/L (range : 114–304 μmol/L) and proteinuria was 0.60 g/g (range : 0–6.2 g/g). In all graft biopsies, C3 deposit was positive. At EC initiation mean proteinuria was 1.9 g/g (range 0.60–3.97 g/g) and mean serum creatinine was 200 μmol/L (range 122–304 μmol/L). After a median follow-up of 14 months, two patients had CR, 3 had PR. 4 patients had no remission and 2 non-responders lost their graft. Median of serum creatinine was 160 μmol/L (range 76–690) and median proteinuria 0.9 g/g. Conclusion : 5/9 patients had a good had a response to EC with improved renal function an proteinuria reduction. EC could be an option for recurrence treatment in selective patients. Complement analysis performed but not yet analyzed may help to select the good responders.

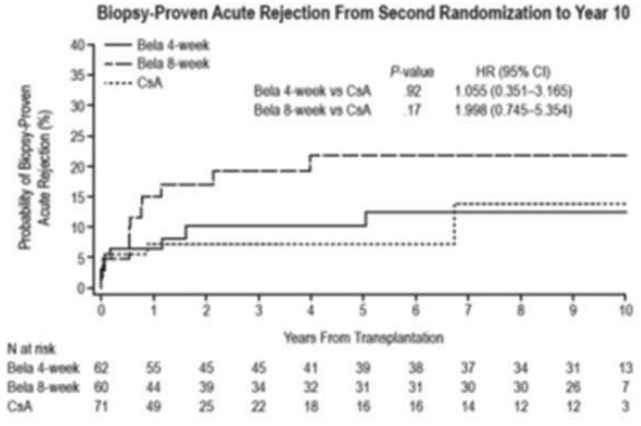
O5 ACUTE REJECTION BY BELATACEPT 4- VS 8-WEEK DOSING: PHASE II STUDY 10-YEAR RESULTS

F. Vicenti[7], G. Blancho[2], A. Durrbach[1], G. Grannas[3], J. Grinyó[4], U. Meier-Kriesche[6], M. Polinsky[6], H. Zhao[6], C.P. Larsen[5]

[1]University Hôpital of Bicêtre, Le Kremlin-Bicêtre; [2]University Hospital of Nantes, Nantes, France; [3]Medizinische Hochschule Hannover, Hannover, Germany; [4]University Hospital of Bellvitge, Barcelona, Spain; [5]Emory University Transplant Center, Atlanta; [6]Bristol-Myers Squibb, Lawrenceville; [7]University of California San Francisco, San Francisco, United States

Background: At 1 year post transplant in IM103-100, bela patients had similar acute rejection (AR) rates and significantly improved renal function vs cyclosporine (CsA) patients. This analysis examined biopsy-proven AR (BPAR) at 10 years post-transplant.
Methods: Patients were randomized to receive bela more intense (MI; n = 74), bela less intense (LI; n = 71), or CsA (n = 73). At 3–6 months post-transplant, bela patients underwent a 2nd randomization to receive bela 5 mg/kg every 4 weeks (n = 62) or 8 weeks (n = 60). All randomized transplanted patients were analyzed through 10 years post-transplant. BPAR was histologically confirmed centrally and compared using Cox regression.
Results: BPAR cumulative event rates from 1st randomization to 10 years post-transplant were 23%, 37%, and 26% for bela MI, LI and CsA, respectively. Hazard ratios (HRs) comparing BPAR did not differ statistically (Fig. 1). BPAR from 2nd randomization to 10 years post-transplant was most common in patients receiving bela 8 weeks; cumulative event rates for BPAR at 10 years post-transplant for bela every 4 weeks, bela every 8 weeks, and CsA were 11%, 22%, and 14%, respectively. One patient (bela every 4 weeks) had grade IIB BPAR. No patient had grade III BPAR. Irrespective of dosing frequency, HRs comparing BPAR in bela and CsA patients did not differ significantly (Fig. 2).





Conclusions: At 10 years post-transplant, BPAR rates were similar between bela and CsA patients, with numerically higher rates in patients receiving bela every 8 weeks vs 4 weeks.

O6 VARIABILITY OF CALCINEURIN INHIBITORS BLOOD LEVELS AND NON-ADHERENCE

S. Belaiche[2,5], B. Décaudin[2,5], S. Dharancy[4,6], S. Gautier[1,7], C. Noel[3,6], P. Odou[2,5], M. Hazzan[3,6]

[1]Département de pharmacologie; [2]Institut de pharmacie; [3]Service de Néphrologie; [4]Service des Maladies de l'appareil digestif et de la Nutrition, CHU Lille; [5]EA 7365 - GRITA - Groupe de Recherche sur les formes Injectables et les Technologies Associées; [6]Inserm U995 - LIRIC - Lille Inflammation Research International Center; [7]Inserm, U1171, Univ Lille, Lille, France

Introduction: Calcineurin inhibitors (CNI) blood level variability raises the question of therapeutic adherence after transplantation. The aim of the present study was to identify factors associated with this variability assessed by the coefficient of variation (CV).
Material & Methods: We followed prospectively a cohort of recipients who received a renal transplantation for more than 1 year. For all patients we recorded: clinical data, data from a constructed clinical pharmacist (CP) interview and data from 6 self-reports measuring: non-adherence (The Compliance Evaluation Test, CET), satisfaction (SatMed-Q), behaviors (The Theory Planed Behavior, TPB), beliefs about medications (BMQ), perception of the illness (Brief IPQ) and social vulnerability (EPICE).
Results: 408 recipients were enrolled (59.3% male, mean age 52 years old). We compared 2 groups according to a CV for CNI blood levels with a cut-off at 30%, which represents the 3rd quartile of the distribution (group 1: CV<30%, n = 302, group 2: CV≥30%, n = 106). In an univariate analysis the distance hospital-home, immunosuppression with cyclosporine or sodic mycophenolate, time since transplantation, discrepancies in the drug regimen between the community pharmacy and the patient declarations (DisMed) were associated with a greater risk of CV≥30%. By contrast, immunosuppression with tacrolimus once daily and 2 items of the TPB questionnaire (past behaviors and intentions) confer a lower risk of CV ≥30%. In multivariate analysis 2 of these factors remain significant: DisMed (2.62 [1.16–6.09]) and the item intention of the TPB questionnaire (0.25 [0.11–0.57]).
Conclusion: These results suggest that a CV ≥30% for CNI blood levels after 1 year post transplantation could be associated with therapeutic non-adherence. The CP interview seems to be an accurate and simple method to detect non-adherence which was not revealed by the self-report questionnaires.

O7 FIRST RENAL TRANSPLANTATION WITH AND WITHOUT STEROIDS IN ELDERLY RECIPIENTS: MULTICENTER OBSERVATIONAL RETROSPECTIVE STUDY

L. Porcène, F. Duthe, L. Ecotière, E. Gand, F. Bridoux, A. Thierry, R. Groupe Spiesser

4, CHU de Poitiers, Poitiers, France

Introduction: Benefits of steroid (Cs) withdrawal in low-risk renal transplant recipients remain debated. In elderly recipient, the impact of an early steroid withdrawal has not been assessed.
Patients and methods: This observational study (11 centers) includes elderly recipients aged 65 or more, receiving a first renal transplant between 2008 and 2014. Cs- group is defined by the absence of Cs at D8 post-transplant, in the absence of preformed DSA; Cs+ group is weaned in the first months post-transplantation or receives a long-term corticosteroid therapy. Data are from the ASTRE database of the Spiesser group.
Results: 278 transplant patients were included: 36 Cs- and 242 Cs+ patients. Mean age of recipients is 71 ± 4 and 70 ± 3 years in Cs- and Cs+ patients, respectively (p = 0.18).

The median follow-up is 30 (35) months: 36 (38) in the Cs- and 27 (34) months in the Cs+ group (p = 0.02). At 30 months, survival of Cs- patients is 94% versus 95% for Cs+ group (p = 0.20); graft survival is 91% in the Cs- group and 95% in the Cs+ group (p = 0.58).

At 3 months, the GFR is lower in the Cs- group compared with the Cs+ group: 36 ± 13 versus 43 ± 15 mL/min/1.73 m² (p < 0.01). At M6, 1 year, 2 years and at the largest decline, GFR did not differ between the two groups.

At 1 year, prevalence of acute rejection is 25% (9/36) in the Cs- group versus 9% (22/242) in the Cs+ group (p < 0.01). Prevalence of de novo DSAs is similar: 19% (7/36) in the Cs- group versus 12% (29/242) in the Cs+ group (p = 0.28). Prevalence of diabetes is 19% (7/36) in Cs- patients versus 25% (39/242) in Cs+ patients (p = 0.47). At two years, we noted 13 major cardiovascular events: 8% (3/36) and 4% (10/242) in the Cs- and in Cs+ group, respectively (p = 0.23).
Discussion: Early steroid withdrawal is associated with a poorer graft function at 3 months post-transplant and an increased number of acute rejections.
Conclusion: Early steroid withdrawal in an elderly population receiving a first renal transplant does not seem relevant.

O8 CLINICAL AND HISTOLOGICAL IMPACT OF A B CELL DEPLETING AGENT IN ABO COMPATIBLE LIVER TRANSPLANTATION WITH PREFORMED DSAS

A. Del Bello[4], V. Dubois[1], J. Dumortier[2], N. Congy-Jolivet[3], N. Kamar[4]
[1]Laboratoire d'immunologie; [2]Service de gastroentérologie, CHU Lyon, Lyon; [3]Laboratoire d'immunologie; [4]Service de Nephrologie-HTA-Transplantation d'Organes, CHU Toulouse, Toulouse, France

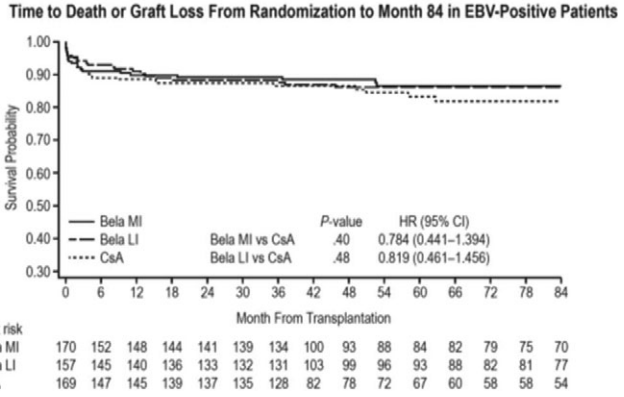
Introduction: The negative impact of preformed anti-HLA donor specific antibodies (pDSAs) in liver transplantation (LT) is clearly established. However, the interest of a B-cell depleting agent for induction is unknown. Here, we proposed to investigate in a retrospective multicenter study the clinical and histological outcomes of Rituximab for induction of patients transplanted with pDSAs.
Patients & method: Between 2004 à 2016, all liver recipients transplanted in participating centers were screened for DSAs at day 0 and after LT (with the Luminex technique, cut-off MFI >1000). All clinical events (infectious, cancer, and death) were reported. All rejection episodes were biopsy proven and graded according to the last Banff classification.
Results: 56/728 liver transplants performed during this period presented pDSAs [17 with anti-class I, 16 with anti-class- II and 17 with anti-class I and II], including 15 with a positive crossmatch (XM+). Rituximab was performed for induction for 17 patients (7 with a XM+), associated with polyclonal antibodies (15 patients) or anti-IL2R (2 patients); 13 patients received an induction by polyclonal antibodies, or anti-IL2R only (11 patients). 9 patients did not received an induction. 15 patients developed at least 1 episode of rejection (5/17 in the Rituximab group and 10/33 in the group without rituximab); 4 patients met the criteria for acute antibody mediated rejection. 1 of the 4 patients was treated by Rituximab at induction (p = ns). The patient's and grafts'survival at 1, 3 and 5 years were 82%, 67% et 50% in the Rituximab group and 91%, 80% et 57% in the group without Rituximab (p = ns). The 5 years post LT infectious complication rate was similar in patient who received or not an induction by rituximab (respectively 40% vs 25%, p = ns).
Conclusions: Rituximab used as an induction treatment for patients with pDSAs could be interesting in LT, without significantly increasing the risk of infectious complications.

O9 LONG-TERM OUTCOMES IN EPSTEIN-BARR VIRUS POSITIVE (EBV+) PATIENTS RECEIVING BELATACEPT (BELA) OR CYCLOSPORINE (CSA) IN BENEFIT-EXT

S. Florman[10], J. Medina Pestana[4], M. Del C Rial[1], L. Rostaing[5], D. Kuypers[3], A. Matas[9], T. Wekerle[2], J. Grinyó[7], U. Meier-Kriesche[8], M. Polinsky[8], H. Zhao[8], A. Durrbach[6]
[1]Instituto de Nefrologia, Buenos Aires, Argentina; [2]Med Univ of Vienna, Vienna, Austria; [3]Univ Hosp Leuven, Leuven, Belgium; [4]Hosp do Rim, Sao Paolo, Brazil; [5]Univ Hospital Grenoble, Grenoble; [6]Univ Hôpital of Bicêtre, Le Kremlin-Bicêtre, France; [7]Univ Hosp Bellvitge, Barcelona, Spain; [8]Bristol-Myers Squibb, Lawrenceville; [9]Univ of Minnesota, Minneapolis; [10]Mount Sinai Med Ctr, New York, United States

At 7 years post transplant in BENEFIT-EXT, bela-treated pts had similar graft survival and improved renal function vs CsA-treated pts. Outcomes in pts who were EBV+ prior to transplant are described. Bela is indicated for use only in EBV+ pts.

Recipients of extended criteria donor kidneys were randomized to bela more intense (MI), bela less intense (LI), or CsA immunosuppression. All randomized, transplanted EBV+ pts were analyzed through 7 years post-transplant. Time to death or graft loss was compared between regimens using Cox regression. GFR was estimated from months 1–84 using a repeated measures model.



Of 543 randomized pts, 496 were EBV+. Of these, 121/170 bela MI, 124/157 bela LI, and 102/169 CsA pts were evaluable for death/graft loss at 7 years. HRs comparing time to death/graft loss were 0.784 for bela MI vs CsA (p = 0.40) and 0.819 for bela LI vs CsA (p = 0.48) (Fig.). Serious AE rates were similar (87%, bela MI; 89%, bela LI; 84%, CsA). Estimated mean GFR increased over 7 years for both bela regimens but declined for CsA (7-year estimated mean GFR: bela MI, 53.5; bela LI, 53.6; CsA, 36.1 mL/min/1.73 m^2). GFR slopes diverged between bela and CsA over time; the interaction of treatment vs time effect from the model favored each bela regimen vs CsA ($p \leq 0.001$). Among bela pts, PTLD occurred in 3 EBV+ and 5 EBV-negative pts by month 84.

Outcomes in the subset of EBV+ pts were consistent with those observed in the ITT population: bela was associated with similar death/graft loss and improved renal function vs CsA.

O10 TRANSPLANTATION OF HEPATOCYTES DIFFERENTIATED FROM SIMIAN INDUCED PLURIPOTENT STEM CELLS (SIPSC) AS PROOF OF CONCEPT FOR AUTOLOGOUS CELL THERAPY OF INHERITED LIVER DISEASES

E. Luce[2], C. Steichen[2], S. Abed[1], P. Leboulch[1], L. Maouche- Chrétien[1], A. Dubart-Kupperschmitt[2]
[1]Inserm U962/CEA/IMETI/STI, Fontenay-Aux-Roses; [2]Inserm UMR_S1193, Villejuif, France

Introduction: Before transplantation of hepatocytes derived from pluripotent stem cells for the treatment of severe hereditary metabolic diseases, the safety and efficacy of this approach must be established in large animal models, such as non-human primate. Our goal is to demonstrate that the simian iPSC (siPSCs) differentiated into hepatocytes (siHeps) can effectively engraft in the liver after autologous transplantation.
Methods: We reprogrammed fibroblasts from a young macaque and characterized the cells obtained by the usual methods. We then established the protocol for differentiation of siPSCs into siHeps together with GFP lentiviral vector labelling for discriminating the transplanted cells from the resident ones after autologous transplantation.
Results: We generated siPSCs and confirmed the normality of their karyotype. After 20 days of differentiation, we get siHeps expressing liver-specific markers such as HNF4α, AFP and ALB. In addition, after lentiviral transduction, more than 85% of them also expressed GFP. Finally, we have established the conditions of freeze / thaw necessary to achieve a siHep bank that allow the recovery of over 95% of viable cells expressing liver markers after thawing. In order to study the *in vivo* functionality of siHep-GFP, we are currently transplanting these cells into an immunodeficient mouse model of liver regeneration.
Conclusion: We have successively generated and characterized siPSCs and have differentiated them into hepatocytes, GFP-labelled after lentiviral transduction, to achieve a siHep-GFP bank. We are currently investigating the ability of these cells to engraft *in vivo*. The final step of the project will be the autologous transplantation of siHep-GFP into the monkey liver. This would represent the first simian model of autologous transplantation of hepatocytes derived from iPSCs.

O11 REGULATION OF LYMPHOCYTES ACTIVITY BY MESENCHYMAL STEM CELLS AND THEIR EXOSOMES

Y. Fan[2], F. Herr[2], A. Vernochet[2], N. Roders[2], A. Durrbach[2,1]
[1]IFRNT, Service de Néphrologie, Hôpital Kremlin-Bicêtre, Le Kremlin-Bicêtre; [2]UMRS 1197, Villejuif, France

Introduction: The mesenchymal stem cells (MSCs) are a powerful cell immunomodulator regulate the function of B, T and NK cells involved in allogeneic reaction. Their immunomodulatory properties depend on cell contacts and factors secreted by MSCs. Exosomes produced by these cells could provide new therapeutic product.
Objective: The objective of this work is to study the effect of exosomes derived from MSC *in vitro* on B, T and NK cells.
Method: MSCs used are isolated from fetal liver. Exosomes were isolated from MSC culture medium by a series of ultracentrifugation.
Results: MSCs inhibit the proliferation of T and B lymphocytes. Unlike MSCs, their exosomes do not inhibit the proliferation of T and B lymphocytes, but they inhibit the proliferation, activation and cytotoxicity (CD107a expression). The FACs analyse show that exosomes have surface expression of TGFβ. Their inhibition on NK cells is altered by presenting anti-TGFβ neutralizing antibody, and when culture NK cells with TGFβ exerce same effect of exosomes.

These results suggest that the immunomodulatory properties of MSCs on NK could depend on TGFβ presented or associated with exosomes.

O12 A SINGLE INFUSION OF THIRD-PARTY MESENCHYMAL STROMAL CELLS AT DAY 3 AFTER LIVER TRANSPLANTATION IS NOT SUFFICIENT TO INDUCE OPERATIVE TOLERANCE

O. Detry[2], M. Vandermeulen[2], M.H. Delbouille[2], J. Somja[1], N. Bletard[1], A. Briquet[3], C. Lechanteur[3], O. Giet[3], E. Baudoux[3], M. Hannon[3], F. Baron[3], Y. Beguin[3]

[1]Service d'Anatomo-Pathologie; [2]Service de Chirurgie & Transplantation; [3]Service d'Hématologie, CHU Liege, Liege, Belgium

Introduction: Mesenchymal stromal cell (MSC) infusion could be a mean to establish donor-specific immunological tolerance in solid organ recipients. The aim of this phase 2 study was test the hypothesis of possible induction of operative tolerance by third-party MSC in liver transplant (LT) recipients.
Methods: 10 stable and low-risk LT recipients under standard immunosuppression (Tac-MMF- low dose steroids) received 1.5–3 $\times$ 10^6/kg third-party MSCs on post-operative day 3 $\pm$ 2. By protocol, progressive weaning of immunosuppression was attempted in patients who did not develop rejection and had normal graft function and month-6 graft biopsy. Tacrolimus was progressively tapered from day 180 to be discontinued by day 270. After day-270 graft biopsy, MMF was progressively tapered and definitely discontinued by day 365 in the absence of rejection.
Results: One patient from the MSC group was excluded from immunosuppression withdrawal attempt due to HCC recurrence, and the 9 others met the necessary criteria. In one patient, tacrolimus and MMF withdrawal was performed without rejection. In two patients, MMF monotherapy was achieved at month 9, but graft rejection occurred during MMF withdrawal and was successfully treated by tacrolimus reintroduction. In 6 patients, the transaminases significantly increased during tacrolimus withdrawal. In these cases, withdrawal was cancelled and liver tests normalised after increase of the tacrolimus dose. No graft was lost due to the withdrawal attempt.
Conclusion: A single post transplant MSC injection is not sufficient to induce operative tolerance after LT.

O13 OUTCOME OF TRANSPLANTED KIDNEYS FROM EXTENDED CRITERIA DONORS PRESERVED ON PERFUSION MACHINES

M. Assem, F. Provot[3], D. Bertrand[4], P.F. Westeel[1], H. Mazouz[1], C. Poulain[1], M. Jaureguy[1], F. Saint[2], D. Guerrot[4], M. Hazzan[3], G. Choukroun[1]

[1]Service de Néphrologie et de Transplantation; [2]Service d'Urologie, CHU Amiens, Amiens; [3]Service de Néphrologie et de Transplantation, CHU Lille, Lille; [4]Service de Néphrologie et de Transplantation, CHU Rouen, Rouen, France

Introduction: Transplantation of kidneys from expanded criteria donors (ECD) has increased in the past years because of the shortage of grafts. Two methods of preservation are available, static cold storage method (PS) or hypothermic machine perfusion (MP). The aim of our study was to compare outcomes of the transplantation depending on the mode of graft preservation.
Methodology: Our study includes all kidney transplantations performed from ECD between 2010 and 2014 in Amiens, Lille and Rouen. Patients were followed until 01/01/2016. We analyzed graft and patient survival, slow recovery (SGF) and delayed renal function (DGF) and changes in glomerular filtration rate (GFR).
Results: Two hundred and ninety-two grafts were on CS and 150 were connected to MP. The use of an MP was independently associated with a decreased risk of occurrence of SGF (OR = 0.28 (0.15–0.53), $p < 0.01$) or DGF (OR = 0.39 (from 0.24 to 0.65), $p < 0.01$). GFR was higher at the end of hospitalization for transplantation and at 1 and 3 months after transplantation (37.0 $\pm$ 20.0, 42.4 $\pm$ 20.9 and 45.3 $\pm$ 22.1 mL/min/1.73 m^2 vs 29.9 $\pm$ 17.8, 35.9 $\pm$ 20 and 40.9 $\pm$ 20.4 mL/min/1.73 m^2 ($p < 0.05$) in the MP group. Hospitalization duration was reduced by an average of 4 days in transplant patients from MP ($p < 0.01$). We observed an increase in the rate of graft artery stenosis in the PS group (10.3 vs 1.3%, $p < 0.01$) and a non-significant trend to an improved graft survival at 1 year in the MP group (86.7 % vs 83.2 %, p = NS).
Conclusion: The use of perfusion machines for kidneys grafts from ECD can limit the consequences of ischemia-reperfusion. This may explain the decrease risk in delayed recovery of graft function and the shorter duration of initial hospitalization. It could also have a beneficial effect on the risk of transplant renal artery stenosis.

O14 THE FINE-TUNING OF CXCL8 PROTECTS KIDNEY AGAINST ISCHEMIA-REPERFUSION INJURY IN MICE LACKING MICRORNA-146A

L. Amrouche[1,2], G. Desbuissons[2], V. Sauvaget[2], A. Benon[2], C. Nguyen[2], C. Legendre[1,2], F. Terzi[2], D. Anglicheau[2,1]

[1]Service de Transplantation rénale adultes, Hôpital Necker; [2]INSERM U1151 - Equipe Terzi, Institut Necker Enfants Malades, Paris, France

Ischemia-reperfusion induced by kidney transplantation leads to the development of tubular injury and interstitial inflammation that need to be controlled to avoid fibrosis development. We hypothesized that microRNAs are involved in the regulation of the balance between lesions and adaptive repair. Using HK2 human proximal tubular epithelial cells, we studied the response to pro-inflammatory cytokines and the regulation of miR-146a. We explored its targets after stimulation by IL-1β. *In vivo* we explored the effect of unilateral renal ischemia-reperfusion injury (IRI) in wild-type (WT) or miR-146a invalidated mice.

In pro-inflammatory conditions, we identified miR-146a to be transcriptionally upregulated by ligands of the interleukin-1-toll-like receptor signaling in HK2 cells. IL-1β treatment induced miR-146a expression through the activation of NF-κB. MiR-146a acted as a negative feedback regulator of this critical pathway by targeting IRAK1, thus decreasing CXCL8/CXCL1 expression by injured tubular cells. *In vivo* in mice, miR-146a was found to be induced in response to renal IRI 7 days after the injury. In human, miR-146a was found to be induced in the renal allograft of patients who experienced acute tubular necrosis early after transplantation as compared to patients with normal allograft biopsy results ($p < 0.05$). Mir-146a levels were also increased in urine samples collected 10 days after renal transplantation in recipients of a deceased donor kidney as compared to recipients of a living donor kidney ($p < 0.01$). Fourteen days after unilateral IRI, *miR-146a*$^{-/-}$ mice had greater tubular injury, inflammatory infiltrate and fibrosis compared with WT mice. Inhibition of the CXCL8/CXCL1 signaling using reparixin, a CXCR2 inhibitor, prevented the development of tubular injury, inflammation and fibrosis after IRI in *miR-146a*$^{-/-}$ mice. These results highlight miR-146a as a key mediator of the renal response to injury by limiting the consequences of inflammation.

O15 EVALUATION OF OUTCOMES IN RENAL TRANSPLANTATION USING MACHINE PERFUSION FOR THE PRESERVATION OF KIDNEYS FROM EXPANDED CRITERIA DONORS

E. Savoye[8], M.A. Macher[8], M. Videcocq[3], P. Gatault[9], M. Hazzan[2], I. Abboud[5], A. Thierry[6], D. Bertrand[7], S. Drouin[4], J. Sayegh[1], O. Bastien[8], O. Huot[8], D. Noury[8], B. Averland[8], P. Guerrini[8], H. Jullian[8], H. Logerot[8], C. Legeai[8], C. Antoine[8]

[1]CHU Anger, Anger; [2]CHU Lille, Lille; [3]CHU Nantes, Nantes; [4]CHU La Pitié Salpétrière APHP; [5]CHU Saint Louis APHP, Paris; [6]CHU Poitier, Poitier; [7]CHU Rouen, Rouen; [8]Agence de la biomédecine, Saint Denis; [9]CHU Tours, Tours, France

The shortage of kidney grafts led to retrieve organs from old donors with one or more co-morbidities, considered as "expanded criteria donors" (ECD). In France, since 2012, the Agency of biomedicine (ABM) has recommended the use of machines perfusion (MP) to preserve kidneys from this donor population to improve kidney preservation and the transplantation outcomes, with the creation of a specific lump sum financing the additional costs of this strategy. This study evaluates the impact of MP vs cold storage (CS), for the period 2011–2014 with kidneys from ECD.

From the ABM database (Cristal), the effect of MP on the delayed graft function (DGF) was analyzed using a multivariate logistic model excluding pre-emptive transplants and primary non functions (PNF). In addition, transplants from the same donor, whose one kidney preserved by MP and the other by CS (population of twins), were analyzed using a mixed model. Co-morbidities of recipients are more frequent and the age of donors and recipients is significantly higher for kidney preserved by MP (n = 801) vs CS (n = 3515). With 16% of DGF for MP vs 29% for CS, MP has a protective effect on the DGF (OR adjusted = 0.45, CI [0.36, 0.56]). In the population of the twins (84 pairs, 168 grafts), we observed 7% of DGF for MP vs 33% for CS and an adjusted OR 0.19 (CI [0.06; 0.58]). The durations of hospitalization and dialysis after transplantation are shorter with fewer sessions of dialysis.

Our results confirm the reduction in the incidence of the DGF of ECD kidneys preserved by machines, with 2.2 times less risk despite a population more at risk in this group, and a lower 5.2 times risk in the population of the kidneys "twins". It remains to assess the impact of the DGF in the long term survival and measure the cost effectiveness of this strategy.

O16 USE OF HYPOTHERMIC MACHINE PERFUSION FOR LIVING DONORS' KIDNEYS

J. Malaise, M. Beaunoyer, M. Lallier, A. Barama, A. Duclos, P. Daloze
Département de Chirurgie, Université de Montréal, Montréal, Canada

Introduction: Hypothermic machine perfusion (MP) has been widely studied in deceased donor kidneys and has been shown to improve kidney graft preservation. Paired exchange programs create a need for donors or kidneys to travel. As some adverse experience occurs, we explore the use of MP using the universal cannula for a short renal artery without an aortic patch.
Methods: From November 2013, 49 kidneys from living donor underwent MP using Belzer's machine perfusion solution. Nine kidneys travelled to a pediatric transplantation center. All kidneys were retrieved by laparoscopic nephrectomy. A Gel-sealed hand-assist access device permitted rapid extraction of the graft.
Results: The mean first ischemic time was 2 min. No delayed graft function or primary nonfunction occurred, and there was no graft loss or patient death. At the start of MP, mean renovascular resistance (RR) was 0.93 ± 0.59 (SD) mmHg/ml/min, mean perfusion flow (PF) was 39 ± 44 mL/min and mean temperature was 7.4 ± 0.8°C. Mean pump time was 2 h 25 min ± 38 min. At the end of machine perfusion, mean RR was 0.28 ± 0.13 mmHg/mL/min, mean PF was 98 ± 52 mL/min and mean temperature was 6.0 ± 0.8° C.

In several grafts, very high renovascular resistances were noted, which is unexpected in living donation. No pre- or intraoperative conditions could explain this phenomenon.
Conclusions: As renovascular resistance at the start of MP was independently associated with primary nonfunction of kidneys retrieved after cardiac death, high values were unexpected for living donor kidneys. The results probably reflect the impact of warm ischemia on the graft. Especially in pediatric kidney transplantation, high renovascular resistance may have a deleterious effect that MP may prevent.

O17 IL-33 CONTRIBUTES TO KIDNEY ISCHEMIA-REPERFUSION-INDUCED INJURY IN MICE

M. Ferhat[3,2], A. Robin[3,1], S. Giraud[3,1], J.M. Goujon[6,2,3], T. Hauet[3,5,2], J.M. Gombert[4,2,3], A. Thierry[7,2,3], A. Herbelin[3,1]
[1]CHU de Poitiers; [2]Faculté de Médecine et de Pharmacie, Université de Poitiers; [3]IRTOMIT INSERM U1082, Poitiers; [4]Laboratoire d'Immunologie, CHU de Poitiers; [5]Laboratoire de Biochimie, CHU de Poitiers; [6]Service d'anatomo-pathologie, CHU de Poitiers; [7]Service de Néphrologie-Hémodialyse-Transplantation rénale, CHU de Poitiers, Poitiers, France

Introduction: Ischemia-reperfusion injury (IRI) is a major cause of acute kidney injury (AKI) which is characterized by leukocyte infiltration and renal tubular injury. We hypothesized that alarmin release by necrotic cells during IRI contributes to tissue damage leading to renal failure. In this study, our objective was to investigate the involvement of the alarmin/cytokine IL-33 in the pathogenesis of renal IRI.
Methods: Ten-to-twelve week-old wild-type (WT) and IL-33-deficient (IL-33$^{Gt/Gt}$) male C57BL/6 mice were subjected to 32 min of unilateral kidney ischemia or a Sham operation. After reperfusion, blood samples were collected and kidneys were harvested to assess kidney function, IL-33 levels by ELISA, leucocyte infiltration by flow cytometry, IL-33 expression by western blot, RTqPCR and immunofluorescence staining.
Results: At steady state, IL-33, which was expressed in the nucleus of peritubular cells, was released from WT kidney tissue shortly after IR. Its local loss was revealed by immunofluorescence staining and confirmed by western-blot, as was a concomitant increase in IL-33 plasma levels. Moreover, transcripts of IL-33 were upregulated in the WT kidney 6 h post-IR. IL-33$^{Gt/Gt}$ mice were less sensitive to kidney damage following IR than their WT counterparts, as attested by both lower creatinine levels and tissue damage. From a mechanistic standpoint, our findings are consistent with the hypothesis of a key role of IL-33 in the recruitment of NKT cells and of neutrophils which are known for their deleterious effect during IR. Indeed, the decreased susceptibility of IL-33$^{Gt/Gt}$ mice to kidney damage was associated with the loss of recruitment of NKT cells and an attenuated neutrophil infiltrate. Remarkably, *HIF1α* was upregulated after IR in WT mice but not in IL-33$^{Gt/Gt}$ mice, thereby suggesting an HIF-1α/IL-33 regulatory circuit.
Conclusion: This study underlines a possible new role of IL-33 as an innate-immune mediator during kidney IR injury.

O18 PREVENTIVE GC7 REDUCES BRAIN DEATH-INDUCED RENAL INJURIES IN A PRECLINICAL PORCINE MODEL

S. Giraud[6,3,7], T. Kerforne[6,2,7], P. Couturier[6,3,8], S. Inal[3,5,6], P. Hannaert[6,4,7], M. Tauc[1], T. Hauet[6,3,7,8,5]
[1]Université de Nice-Sophia Antipolis, LP2M, CNRS-7370, Nice; [2]CHU de Poitiers, Département d'Anesthésie-Réanimation; [3]CHU de Poitiers, Service de Biochimie; [4]CNRS; [5]FHU SUPORT; [6]INSERM U1082; [7]Université de Poitiers, Faculté de médecine et pharmacie, Poitiers; [8]Plateforme Labellisée IBiSA MOPICT GenESI INRA, Surgères, France

Introduction: N1-guanyl-1,7-diaminoheptane (GC7), an inhibitor of eIF5A, exhibits anti-inflammatory features and promotes anoxic/ischemic tolerance. Thus, GC7 pretreatment could be useful in order to protect organs submitted to ischemia before transplantation in heart-beating donors.
Methods: Using a pig brain death donation preclinical model, we carried out the *in vivo* evaluation of GC7 pre-treatment (3 mg/kg iv bolus), after brain death, at the beginning of the 4 h-reanimation, after which one kidney was collected, cold-stored (18-h in UW), and allo-transplantated in a double-nephrectomized recipient. Groups were defined as follows (n = 6 per group): healthy (Control), untreated Brain death (BD) and GC7-treated BD (GC7).
Results: R1. At the end of 4 h-reanimation, GC7 decreased (80–100%, $p < 0.05$) BD-increased markers: (i) eIF5A hypusination, (ii) tissue levels of reactive oxygen species markers (CellRox staining and Aconitase), (iii) tissue levels of nitrotyrosine, and (iv) the mitochondrial-dependent apoptosis pathway (Bax/Bcl-2 proapoptotic *ratio*, Caspase-9). In addition, GC7 increased (2 to 6-fold, $p < 0.05$) the expression of anti-oxidant proteins (SOD2 and HO-1, as well as PGC-1a, Nrf2, and total & p-Sirtuin1 & 3). **R2.** At the end of cold storage, GC7 treatment normalized BD-dependent decrease of SOD2 and HO-1 proteins expression ($p < 0.05$). In addition, GC7 significantly restored the BD-dependent increase of the Bax/Bcl-2 (proapoptotic) *ratio* ($p < 0.05$).
Conclusion: After the reanimation phase, preventively given GC7 proved protective for kidneys against brain death-induced injuries; during the cold storage phase, GC7 appeared to preserve antioxidant defences and to protect mitochondria. Early and long-term, post-transplantation propagation of observed protective effects are currently evaluated.

O19 LONG TERM OUTCOME IN PEDIATRIC RENAL TRANSPLANT: A SINGLE-CENTER EXPERIENCE

S. Dorent-Marcelino, M. Tsimaratos, F. Garaix
Service de Pédiatrie Multidisciplinaire, CHU Timone Enfants, Marseille, France

Introduction: Kidney transplantation is the treatment of end stage renal failure in children (IRCT). The current problem of the IRCT is not patient survival but the quality of life of transplant recipients. One of the challenges of pediatric renal transplantation is also to study long-term outcome after of transplants. Few studies report more than 20 years of follow-up. In this context, we analyzed the evolution of pediatric renal transplants performed in our single center (CHU Timone-Enfants).
Methods: We analyzed 146 pediatric renal transplantations performed between 1974 and 2013. We compared the cohort before 1994 (group 1, 42 grafts), to the 1994–2003'one (group 2, 45 grafts) and the 2004–2013'one (group 3, 59 grafts). Patient survival and graft survival at 1, 5, 10, 15 and 20 years were studied and the characteristics of the rejection, the occurrence of lymphomas and education and social outcome.
Results: The patient survival is at 1, 5, 10 and 20 years of 96%, 93.8%, 91.8% and 90%. No deaths found in group 3. The patient survival is significantly different between group 1 and group 2 and 3. The graft survival is at 1, 5, 10, 15 and 20 years of 90.7%, 80.1%, 70.2%, 64.8% and 56.7%. The graft survival is at 1 year in group 1, 2 and 3 respectively of 83%, 91% and 95% and at 5 years respectively of 61.6%, 86.7% et 86%. 44% of grafts will experience at least one rejection. Six lymphomas (4%) are observed. 67% of children in groups 2 and 3 have a normal education. 61% of adults late in the monitoring of groups 2 and 3 have a employment or training.
Conclusion: The long-term outcome of our cohort is well compared to what is described in the literature. Nevertheless, improving graft survival remains very long term a challenge.

O20 IMPACT OF THE TRANSITION CONSULTATION IN RENAL TRANSPLANTATION

J. Perrin[2], S. Burtey[1], S. Gentile[1,2], F. Garaix[1,2], M. Tsimaratos[1,2]
[1]CHU Conception; [2]CHU Timone, Marseille, France

Introduction: Kidney transplantation is the treatment of choice for end stage renal disease. 80% of transplanted children reach adulthood with a functioning graft. Since therapeutic adherence and therefore renal graft survival are altered during adolescence, the transfer of these patients in adult care carries an increased risk of graft dysfunction. The transfer is defined as moment of switch from paediatrician to the adult medicine specialist. The transition is a program designed to prepare patients to transfer.

Methods: The aim of our study is to evaluate the impact of a transition process for Children with renal transplantation in Timone's childrens Hospital in Marseille. We studied two cohorts of patients: one before and one after the establishment of the transitional consultation (TC). Our main objective was to assess the impact of the TC on biopsy proven acute rejection. Secondary endpoints are reduction in glomerular filtration rate (GFR) two years after the transfer, knowledge of the treatment and creatinine levels. We were also interested in searching for more subjective criteria such as the satisfaction of the transfer and the transition process.
Results: Both groups of patients are comparable. The TC has no impact on the frequency of acute rejection nor on GFR decrease (two years after), knowledge of treatment or creatinine levels. Satisfaction of patients about transfer are similar between the two groups. However, patients who followed the TC say they were better prepared for the transfer, but the difference is not significant (68.8% against 40%, $p = 0.11$).
Conclusion: In this work the TC does not affect the outcome of grafts or patients. The evaluation of our practices raises the question of its maintenance or an improvement of the transition program.

O21 RISK FACTORS FOR EARLY GRAFT FAILURE AND DEATH AFTER KIDNEY TRANSPLANTATION IN RECIPIENTS OLDER THAN 70 YEARS

M. Lemoine[5], D. Titeca[2], T. Lobbedez[3], G. Choukroun[1], B. Hurault De Ligny[3], M. Hazzan[4], D. Guerrot[5], D. Bertrand[5]
[1]Néphrologie, dialyse, transplantation; [2]Réanimation médicale, CHU Amiens, Amiens; [3]Néphrologie, dialyse, transplantation, CHU Caen, Caen; [4]Néphrologie, dialyse, transplantation, CHU Lille, Lille; [5]Néphrologie, dialyse, transplantation, CHU Rouen, Rouen, France

Introduction: The number of patients older than 70 years on the kidney transplant waiting list is rapidly growing. Despite a demonstrated benefit compared to dialysis, mortality, especially the first year of transplant, is high in this population. The aim of this study was to evaluate early death and graft failure and to determine the risk factors associated with these events in this population.
Methods: This multicenter retrospective study included all the patients older than 70 years receiving a kidney transplant between January 2000 and December 2014 in the North-West of France (n = 171). Baseline characteristics and outcomes after transplantation were studied. The Kaplan-Meier method was used to assess patient and graft survival. A Cox regression analysis was used to evaluate risk factors for graft failure and patient death.
Results: The mean recipient age was 73.3 ± 2.5 years. Death-censored graft survival at 1, 3 and 5 years was 82.6%, 78.7% and 75.4% respectively. Patient survival at 1, 3 and 5 years was 90.1%, 82.5% and 68.1% respectively. One year after transplant, 17 patients (9.9%) were dead, mainly from infectious (58.8%) or cardiovascular disease (29.4%). During the first year of transplantation, 96 patients (60%) were hospitalized for an infectious disease and 73 (45.1%) for a cardiovascular event. According to the Cox multivariate analysis, the independent risk factors for death or graft failure during the first year were arrhythmia (OR = 2.26 CI 95% (1.08–4.8)), LVEF under 60% (OR = 2.0 CI 95% (1.03–3.9)), HLA antibodies (OR = 2.1 CI 95% (1.04–4.2), deceased donor from cardiovascular cause (OR = 5.18 CI 95% (1.2–22.2)) and acute rejection (OR = 2.8 CI 95% (1.22–6.3)).
Conclusion: In this study, the one-year graft survival is low, which can be partly explained by the poor graft quality. In kidney transplant recipients older than 70 years, cardiac evaluation and immunosuppression optimization seem to be crucial to improve patients' survival.

O22 EVALUATION OF QUALITY OF LIFE IN A POST-LIVER TRANSPLANTATION PEDIATRIC POPULATION, KIDNEY OR HEART: A PROSPECTIVE STUDY

F. Magali, A. Fabre[1], F. Garaix[1], K. Baumstarck[2], M. Tsimaratos[1]
[1]CHU Timone Pédiatrie multidisciplinaire; [2]Laboratoire de Santé publique, Faculté de médecine marseille, Marseille, France

Introduction: The improvement in treatments using pediatric solid organ transplantation allows nowadays to take into account the quality of life (QOL) as a key element. However, it remains poorly studied. The objective was to evaluate the QOL of children with renal, hepatic and cardiac transplants as well as that of their parents and then to seek influential factors.
Method: We included patients under 18 who benefited from a renal, hepatic or cardiac transplant less than 10 years ago. The children's and adolescents' QOL was measured with the help of the 'Vécu et Santé Perçue de l'Adolescent' questionnaires, adapted to the child's age and that of the parents thanks to the WHOQOL questionnaire. The factors were studied using univariate analysis.
Results: Of the 59 patients included, 45 answered the questionnaires. The children's QOL was inferior to that of the healthy population except for "general well-being" (73.4/100 versus 68.5/100) and "vitality" (83.2/100 versus 81.4/100) and to that of the leukaemia group except for "vitality" (83.2/100 versus 81.6/100). Transplanted adolescents had higher QOL scores than that of the healthy population and of the leukaemia group except for "hobbies" (56.9/100 versus 62.2/100) and "psychological well-being" (72.6/100 versus 74.8/100). In hetero-evaluation, transplanted children and adolescents had quality of life scores higher than that of the leukaemia group, excluding "school work", "friendships" and "hobbies". The parents had lower QOL scores compared with the French average. The gender of the child was not a predicting factor contrary to immunosuppressant treatment, parent's schooling level, and siblings.
Conclusion: The pediatric QOL comes out as satisfactory, the parental one is inferior to the healthy population.

O23 THE IMPACT OF BODY MASS INDEX OR WAIST CIRCUMFERENCE AND ON RENAL TRANSPLANT OUTCOMES

M. Huet, I. Szwarc, M. Lequintrec, G. Mourad, J.E. Serre
34, CHU Montpellier, Montpellier, France

Background: Body mass index (BMI) as a predictor of morbidity and mortality after kidney transplantation is controversial. A high waist circumference (WC) has been recently associated with an increased risk of mortality in renal transplant patients. This study aimed to evaluate the impact of BMI and WC on long term graft and patient survival after renal transplantation.
Methods: We conducted a single-center prospective cohort study included 762 kidney transplant patients who received anthropometric measurements at 3 months of transplantation from January 1996 and December 2010. Patients were divided into 4 groups of BMI according to WHO guidelines and into 4 groups of WC according to the values of quartile. Risk factors affecting graft and patient survival were analyzed using a Cox model with adjustment.
Results: Obesity prevalence (defined by BMI > 30 Kg/m^2 or WC >94 cm for men and >80 cm for women) was respectively 7% and 41% at 3 months. Patients with TT or high BMI were older, had more hypertension, delayed graft function and graft dysfunction at 3 months. During a mean follow-up of 10 years, BMI>30 Kg/m^2 was not a risk factor for mortality or graft loss. However, an elevated WC (>98 cm for men and >80 cm for women) was associated with a high risk of graft loss (HR = 12.7 [3.46–47.09], $p < 0.001$), independently of the BMI and other risk factors.
Conclusions: High BMI had no impact on long-term graft and patient survival but abdominal obesity defined by the WC should be considered as an independent risk factor for long term graft loss. It remains to clarify the pathophysiological mechanisms underlying this association.

O24 PREGNANCY OUTCOMES IN SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANT RECIPIENTS: A NATIONAL FRENCH SURVEY STUDY

G. Normand[6], F. Brunner[6], L. Badet[7], F. Buron[6], M. Caton[5], J. Massardier[5], L. Esposito[1,2], P. Grimbert[1,2], G. Mourad[9], J. Serre[9], S. Caillard[11], G. Karam[10], D. Cantarovich[10], E. Morelon[6,8,4,3], O. Thaunat[6,8,3,4]
[1]Nephrology and Renal Transplantation, Henri Mondor Hospital; [2]INSERM U955, Paris Est University, Créteil; [3]Claude Bernard Lyon 1 University; [4]UMR 5308, CNRS; [5]Hôpital Femme-Mère-Enfants; [6]Service de Transplantation, Néphrologie et Immunologie Clinique; [7]Service d'Urologie, Hospices Civils de Lyon; [8]Unit 1111, INSERM, Lyon; [9]Department of Nephrology, CHU Lapeyronie, Montpellier; [10]Institute of Transplantation Urology and Nephrology, Nantes University Hospital, Nantes; [11]Department of Nephrology-Transplantation, Strasbourg University Hospital, Strasbourg; [12]Department of Nephrology and Organ Transplantation, CHU Rangueil, Toulouse, France

Introduction: Simultaneous pancreas and kidney transplantation (SPK) is currently the best therapeutic option for patients with type 1 diabetes and terminal renal failure. Renal transplantation restores fertility enabling women to pursue pregnancies. However, scarcity of available data on pregnancy outcomes in SPK impedes fair medical counseling.
Methods: Between 2007 and 2015, the medical files of all pregnancies that lasted more than 3 months among recipients of successful SPK in France were retrospectively analyzed.
Results: Twenty-six pregnancies in 22 SPK recipients were identified. Main maternal complications included gestational hypertension (53.8%) and infections (50%). Caesarean section was performed in 73% of cases. Overall fetal survival was 92.6% with a mean gestational age of 34.2 ± 3 weeks. Eleven (40.7%) children presented intra-uterine growth retardation at 2nd trimester ultrasound but birth weight <10th percentile was only observed in 4 cases (16.7%). Endocrine pancreas graft function remained stable during pregnancy. An acute kidney rejection occurred in 2 patients, one of which resulting in graft loss. Kidney and pancreas graft survival was respectively 90.7% and 100% at 2 years.
Conclusion: Pregnancy in SPK is feasible, but patients should be informed of the risks for the fetus, the mother and the grafts. Planning of pregnancy in SPK women is key to allow a personalized multidisciplinary monitoring, which represents the most straightforward approach to optimize outcomes.

O25 CLINICAL OUTCOME OF RECIPIENTS OVER 70 YEARS OF AGE AFTER RENAL TRANSPLANTATION

J. Malaise, A. Barama, A. Duclos, M. Lallier, M. Beaunoyer, P. Daloze
Département de Chirurgie, Université de Montréal, Montréal, Canada

Introduction: There is an increasing rate of older patients initiating dialysis. Therefore, those patients are more often selected than previously for transplantation. However, the survival advantage of transplantation for older recipients remains controversial. And the ethical balance of equity over utility is a major dilemma.
Methods: We reviewed 871 consecutive renal transplantations performed between January 2003 and May 2016.
Results:

	group R < 55	group 55 < R < 60	group 60 < R < 65	group 65 < R < 70	group R > 70
Patients, n	577	109	95	70	20
Recipient age (years)	42	57	63	67	73
Donor age (years)	43	47	48	54	58
Living donor %	25%	12%	12%	14%	25%
Mean Follow up (years)	5.9	5.2	5.2	4.6	2.7
Kidney loss %	10%	5%	7%	7%	5%
Death %	6%	14%	19%	17%	15%
Patient survival rate (%)1, 5, 10 years	99.1, 95.1, 90.0	99.0, 93.2, 73.6	96.8, 86.2, 66.3	98.4, 86.5, 69.8	94.1, 80.7, 40.3
Death Censored Graft survival rate (%)1, 5, 10 years	95.8, 91.5, 85.7	97.2, 95.0, 95.0	98.9, 94.7, 85.2	92.8, 92.8, 92.8	100, 87.5, 87.5

The main cause of graft loss in older recipients remains death with a functioning graft. The patient survival rate is lower in older versus younger kidney recipients, but this difference grows up 5 years after transplantation. Concomitant cardiovascular disease and pre-existing cancer must be screened extensively before listing the patient. The waiting time before transplantation is also an important issue. With time, patients become too sick to be transplanted.

In conclusion, in our experience, an older recipient benefit from renal transplantation. A good selection of recipients is mandatory to avoid futile transplantation. It seems that living donor kidney transplantation is the best option.

O26 LONG-TERM OUTCOME OF ISLET AFTER KIDNEY TRANSPLANTATION COMPARED TO ISLET TRANSPLANTATION ALONE

M. Chetboun[2,1], K. Benomar[4], R. Caiazzo[2,1], K. Le Mapihan[4], C. Noël[3], J. Kerr-Conte[1], F. Pattou[1,2], M.C. Vantyghem[1,4]
[1]University Hospital of Lille, Inserm U1190; [2]University Hospital of Lille, Service de Chirurgie Générale et Endocrinienne; [3]University Hospital of Lille, Service de Néphrologie; [4]University Hospital of Lille, Service d'Endocrinologie, Diabétologie et Métabolismes, Lille, France

Background: Islet transplantation (Tx) is an eligible therapy for brittle Type 1 Diabetic patients (T1D) with hypoglycemia unawareness or previous kidney Tx. The aim of this study was to compare the long-term outcome of allogenic intraportal islet Tx in uremic (Islet After Kidney, IAK) and non-uremic (Islet Tx Alone, ITA) patients treated with the Edmonton immuno-suppressive regimen.
Patients and Methods: 33 T1D (19 ITA, 14 IAK) were enrolled in a single-center phase 2 clinical trial and received a median islet mass of 13.9(11.1–15.8) $\times$ 10^3 IE/kg in 2.7[2.5–2.9] sequential radiological or surgical intra-hepatic infusions over a 3-month period. Patients were followed up for more than 10 years.
Results: 32 T1D patients (97%) achieved insulin-independency with a median duration of 2747(1605–3886) days. Graft function was maintained in 25 patients (14 ITA, 11 IAK), and 11 patients remained off insulin (4 ITA, 7 IAK) at last follow-up (June 2016) with a median follow-up of 3723(2141–4028) days. The Kaplan-Meier estimated (KMe) proportions of graft survival in ITA and IAK were respectively 84 and 85% at 5 years and 72 and 86% at 10 years ($p = 0.54$). The KMe proportions of insulin–independent ITA and IAK were respectively 44 and 49% at 5 years and 19 and 49 at 10 years ($p = 0.47$). The mean daily insulin needs were significantly lower at 10 years (ITA: 0.31 $\pm$ 0.07; IAK: 0.29 $\pm$ 0.11 UI/kg) than at baseline (ITA: 0.61 $\pm$ 0.04/ $p = 0.007$; IAK 0.56 $\pm$ 0.03 UI/kg/$p = 0.03$). Mean estimated glomerular filtration rate remained stable in both groups up to 10 years (ITA: 71 $\pm$ 8; IAK: 55 $\pm$ 8 mL/min/1.73 m^2) compared to baseline (ITA: 82 $\pm$ 3/$p = 0.36$; IAK 56 $\pm$ 3 mL/min/1.73 m^2/$p = 0.56$). The primary graft function was a predictive factor of long-term graft survival and insulin-independency compared to the recipient type.
Conclusions: Long-term outcome of intraportal IAK Tx with EIR is similar to that one of ITA. The 10-year percentage of insulin-independence varies between 19 and 49% with the Edmonton protocol.

O27 EVALUATION OF PROFESSIONAL PRACTICES (EPP) IN RENAL PEDIATRIC TRANSPLANTATION IN FRANCE IN 2015

F. Garaix[5,4], E. Berard[8], M. Charbit[9,5], S. Decramer[14,5], O. Dunan[12], A. Fischbach[13], J. Harambat[1], M.A. Macher[10,5], E. Merieau[15,5], D. Morin[6], R. Novo[2,5], B. Ranchin[3], I. Vrillon[7], T. Ulinski[11], G. Roussey[5]
[1]CHU Bordeaux, Bordeaux; [2]CHU Lille, Lille; [3]CHU Lyon, Lyon; [4]CHU Marseille; [5]Groupe transplantation SNP, Marseille; [6]CHU Montpellier, Montpellier; [7]CHU Nancy, Nancy; [8]CHU Nice, Nice; [9]CHU Necker; [10]CHU RDB; [11]CHU Trousseau, Paris; [12]CHU Réunion, Reunion; [13]CHU Strasbourg, Strasbourg; [14]CHU Toulouse, Toulouse; [15]CHU Tours, Tours, France

Introduction: The SNP transplant committee decided to make an EPP in pediatric kidney transplant in France.
Material and method: A questionnaire was sent to 14 pediatric transplant centers. It included 96 questions about 10 main themes. He was declarative and filled by one member/team.
Results: All centers responded. They average realized 92 transplants per year (cumulative) (2 to 15/year/center), 14 with living donor/year (15%), and followed a cohort of 648 children. All teams use a lower weight limit for grafting (about 11 kg). 3 centers transfers small chidren. All teams inform parents about living donors, 92% characterize parent's HLA and 77% exclude their antigens. Less than 3 teams accept donors <10 kg or <2 years and/or in block kidneys. We found 2.3 HLA compatibility (0.7 B, 1 DR, 0.5 DQ). No team excludes donor because of an CMV's mismatch and just one for an EBV's mismatch. 85% of the activity is realized in pediatric units and by pediatric surgeons. 3 teams don't wait for the résult of the crossmatch. A pediatric's nephrologist is present at time of declamping in 77% of centers. Anticoagulation is systematic in 62% of centers. Sequential quadruple immunosuppression is used by all : 100% of induction (92% of basiliximab), 100% of steroids are done before graft then relay by CNI (85% tacrolimus) and antimetabolite (92% of MMF) for all. 54% stopped steroids before J7 postoperative and 3 teams keep steroids for long term. The ImTOR are not yet used outside protocols. 85% of grafts are systematically biopsied (83% in M3). 62% of the teams have a therapeutic education program (half of the centers has a specific nurse for these programs).
Conclusion: This analysis of practices is a first step that will allow the group to work with the results from cristal to look for indicators that optimize the survival long-term graft.

O28 RESCUE ALLOCATION FOR LIVER TRANSPLANTATION IN A CONTEXT OF ORGAN SHORTAGE: RESULTS OF A FRENCH CENTER FROM 2011 TO 2015

G. Giretti[3,2], L. Barbier[3,2], P. Bucur[3,2], F. Marques[3,2], J.M. Perarnau[3,2], M. Ferrandière[3,2], A.C. Tellier[3,2], V. Kerouredan[3,2], C. Silvain[1,2], E. Salamé[3,2]
[1]Hopital de Poitiers, Poitiers; [2]FHU SUPORT; [3]3, Hôpital Trousseau, Tours, France

Introduction: In France, liver grafts that have been refused by five teams are considered for rescue allocation, with the choice of the recipient being at the team's discretion. While this system allows using otherwise discarded grafts in a context of organ shortage, outcomes and potential benefits need to be assessed.
Methods: Between 2011 and 2015, outcomes of rescue allocation grafts ($n = 33$) were compared to standard allocation grafts ($n = 321$) in a single French center.
Results: Liver grafts in the rescue allocation group were older (62.9 vs 53.9 years, $p = 0.007$) and had a higher donor risk index (1.86 vs 1.61, $p = 0.010$). Recipients in this group had a lower MELD score (13.8 vs 21.6, $p < 0.001$) and had mostly HCC (67.0% vs 40.4%, $p = 0.010$). There were higher rates of early and delayed hepatic artery thrombosis (15.2% vs 3.1%, $p = 0.001$) and retransplantation (18.2% vs 4.7%, $p = 0.002$) in the rescue allocation group. Patient survival was not different between groups, but graft survival was impaired (95% vs 82% at 1 year and 94% vs 74% at 3 years, $p = 0.001$).
Conclusion: Our results show that discarded liver grafts can be allocated through a rescue procedure to low-MELD patients. Hepatic artery thrombosis and retransplantation are more frequent and account for impaired graft survival. This allocation procedure seems nevertheless to benefit low-MELD hepato-cellular carcinoma patients, who would otherwise have a prolonged time on the waiting list and a high risk of drop out. This strategy enables utilization of otherwise discarded grafts in the context of organ shortage.

O29 ESTIMATION OF END STAGE RENAL DISEASE RISK AMONG DONORS

F. Gaillard[3], S. Baron[1], C. Fournier[3], M.O. Timsit[2], C. Legendre[3], M. Courbebaisse[1]
[1]Service de physiologie, Hopital Européen Georges Pompidou; [2]Service d'urologie, hopital Européen Georges Pompidou; [3]Transplantation rénale, Hopital Necker, Paris, France

Introduction: Kidney donation is associated with an increased risk of end-stage renal disease (ESRD). In order to standardize donor acceptance criteria, a multi-parameter evaluation was recently developed to calculate ESRD risk prior to donation. However the ESRD risk threshold at which a donor could be accepted remains to be determined.
Methods: We compared ESRD risk among donors and non-donors with two calculators in two cohorts. This first cohort consists of 338 potential donors, among them 27 were not accepted as donors due to medical contraindication. ESRD risk was compared between donors and non donors. The second cohort consists of 63 donors with a 5 years follow up post donation. We calculated their ESRD risk at donation and 5 years after donation.
Results: Subjects not accepted as donors due to medical cause (n = 27) had a significantly higher 15-year ESRD risk compared to donors (n = 288) with both calculators (0.25 vs 0.14 $p < 0.001$ for that developed by Grams *et al.* and 2.21 vs 1.43 p = 0.002 for that developed by Ibrahim *et al.*). In analysis of another group of 63 donors with a 5-year follow-up after donation, we found a significant correlation between pre-donation and post-donation 15-year ESRD risk and also post-donation lifetime ESRD risk (r^2=0.32 $p < 0.0001$ and r^2=0.16, $p < 0.001$, respectively) with the calculator developed by Grams *et al.* Five years after donation, 15-year and lifetime ESRD risks increased by 3 fold (range 0.78 to 9) and by 2 fold (range 0.4 to 8), respectively, compared to the pre-donation risks.
Conclusion: ESRD risk calculators found a significantly higher ESRD risk in non donors than in donors. However there was no clear ESRD risk threshold between to differentiate the two groups. In conclusion, ESRD risk calculators could be used to decline donation early but cannot yet be used alone to accept donation.

O30 RENAL TRANSPLANTATION USING A MAASTRICHT CATEGORY III NON-HEARTBEATING DONOR. ONE YEAR SINGLE CENTER EXPERIENCE

S. Drouin, M. Raux, J. Tourret, G. Lebreton, G. Coffin, J. Cohen, N. Arzouk, S. Ourahma, J. Parra, B. Riou, P. Leprince, B. Barrou
4, Hôpital Pitié Salpêtriere, Paris, France

Introduction: The extension to Maastricht category III non-heartbeating donor (who died after limitation of life sustaining therapy (LST)) started in France in 2015. Seven organ extractions from Maastricht III donors have been realized in our center followed by seven renal transplantations
Patients et methods: We prospectively collected data from donors and recipients. The limitation of LST has been made in intensive care unit, the normothermic regional perfusion was established by specialized team and donor was secondarily transferred in the operative room by an ambulance.
Results: The mean age of donors was 45 ± 11 years, 5 were men (71%) and the mean creatinine before death was 52 ± 24 mmol/L. The duration between limitation of LST and cardiac arrest was 17 ± 5 min, the mean functional warm ischemic time (mean blood pressure < 45 mmHg) was 19 ± 2 min and the duration between normothermic regional perfusion and clamping was 135 ± 20 min.

The mean age of recipients was 45 years ± 9, 6 were men (86%), the duration of dialysis was 36 ± 24 months and the duration on waiting list was 32 ± 22 months. The mean incompatible graft rate was 23 % ± 22. The cold ischemic time was 10 ± 3 years. After transplantation, no patient presents delayed graft function. One patient required dialysis immediately after the surgery because an hyperkaliemia.

Mean creatinines were 126, 124, 137 et 133 mmol/L à J8, M1, M3 et M6 respectively.
Conclusion: Transplantation with Maastricht III category donors seems to be a safe and feasible procedure when achieved by trained teams. It seems easier to develop than procedure for Maastricht II category donor. Short term results for renal transplantation are very satisfactory, as those found in literature. Nevertheless, a cohort and a longer follow up are necessary.

O31 LONG-TERM EVALUATION OF RENAL TRANSPLANT PATIENTS WITH SEVERE PERIPHERAL ARTERY DISEASE WITH OR WITHOUT VASCULAR AORTOBIFEMORAL BYPASS

J. Oniszczuk[1], L. Guy[1], P. Gatault[5], P. Grimbert[2], L. Frimat[3], E. Rosset[1], D. Bertrand[4], C. Garrouste[1], A.E. Heng[1]
[1]63, CHU G. Montpied, Clermont-Ferrand; [2]94, CHU H. Mondor, Créteil; [3]54, CHU Nancy-Brabois, Nancy; [4]76, CHU Bois Guillaume, Rouen; [5]37, CHU H.Bretonneau, Tours, France

Introduction: Elderly patients represent a growing population of chronic kidney disease and end-stage renal disease and are associated with more and more comorbid diseases. Thus, population on the transplant waiting list and graft donors have poorer vascular quality. In this study, we aimed to compare outcomes and follow-up of renal transplant recipients with severe peripheral arterial disease on aortobifemoral bypass (RTP) compared to a population (PAD) but without any prosthesis.
Methodology: We identified 33 RTP patients and 33 PAD patients stage 3 or 4 between 01/2004 and 03/2016 throughout 5 French transplant centers.
Results: Patient survival at 5 years is 88.9% (57.9–97.5) in the RTP group and 90.6 % (73.5–98.5, p = 0.72) in the PAD group. Graft survival at 5 years is 78.8% (60.6–89.3) in the RTP group and 96.9% (77.9–98.5) in the PAD group (p = 0.08). RTP and PAD recipients have similar eDFG at 5 years: respectively 43.34 mL/min/1.73 m^2 (31–50) and 30 mL/min/1.73 m^2 (30–30, p = 0.93. In comparison with the PAD group, we noted in the RTP group: (i) a higher rate of delayed graft function of 72.7% vs 51.5 % (p = 0.08), (ii) and a non-significant higher rate of surgical revision after initial post renal transplantation hospitalization (42.4% vs 24.2%, p = 0.12), (iii) a higher rate of acute rejection at 12 months (34% vs 13%, p = 0.08) (iv) a similar mean number of cardiovascular events (1.21 vs 1.37, p = 0.70) between the groups , (v) a significant high rate of serious bacterial infections (1.27 vs 0.63, p = 0.04).
Discussion: Kidney transplantation on vascular bypass is associated with good patient survival and good graft survival. However, we noted a non-significant higher rate of DFG, acute rejection and serious bacterial infections. Complementary further larger studies are necessary to confirm these data.

O32 DOES HANGING DONORS BE REALLY MARGINAL FOR LUNG TRANSPLANTATION?

R. Renard, T. Le Houerou, P. Puyo, P. Bonnette, M. Glorion, S. Abou Taam, A. Roux, M. Le Guen, A. Chapelier, E. Sage
Chirurgie Thoracique et Transplantation Pulmonaire, Hôpital Foch, Suresnes, France

Background: Success of lung transplantation (LTx) depends on several factors, including the selection of the donor. Hanging donors are mostly excluded, based on pulmonary edema, barotrauma and hypoxia. However there is no evidence of higher LTx morbidity-mortality with lungs providing by suicidal hanging.
Methods: All lung transplantation performed at Foch hospital between January 2010 and July 2015 were analyzed outcomes of LTx to compare hanging donors (Hanging group) with donors having other cause of death (Control group).
Results: During this period 299 LT were performed and divided in 2 groups: Hanging group (N = 20) and Control group (N = 279). Donor characteristics did not differ in age, sex, time on mechanical ventilation before retrieval, PO2/FIO2 ratio, smoking history, chest Xray or bronchial secretion. Recipient diagnoses did not differ significantly between the both groups. Primary graft dysfunction (PGD) at 72 h was no statistically significant between Hanging group ((PGD 0–1 70%, PGD 2 20% and PGD 3 10%)) and Control group (PGD 0–1 61%, PGD 2 23% and PGD 3 16%). Median of post-operative mechanical ventilation duration (1 [range, 0–84] vs 1 [range, 0–435] days), intensive care unit stays (7 [range, 2–66] vs 7 [range, 2–91] days), and total hospital lengths of stay (31 [range, 20–84] vs 32 [range, 12–410] days) did not differ significantly between the two groups. The percentage predicted forced expiratory volume in 1 s at 6 months and 12 months were comparable in both groups (6 months, Hanging 72.3 ± 35.1% vs Control 73.3 ± 20.5%, p = 0.65; 12 months, Hanging 65.5 ± 31.2% vs Control 78.5 ± 20.2%, p = 0.26). No statistically significant differences were found on the survival between Hanging group and the Control group with respectively at 1 year (83% and 85%) and 2 years (75% and 80%) (p = 0.76).
Conclusion: The LT outcomes are not different between hanging donors and the others cause of death. Hanging donors should be considered as conventional donors.

O33 IMPACT OF THE ECMO ON RENAL DELAYED FUNCTION AND PATIENT SURVIVAL IN SIMULTANEOUS HEART-KIDNEY TRANSPLANTATION

J. Serre[1], S. Varnous[4], G. Lebreton[4], G. Hekimian[3], J. Amour[2], S. Ouldamar[3], S. Drouin[1], J. Tourret[1], G. Coutance[4], S. Ourahma[1], P. Leprince[4], B. Barrou[1], N. Arzouk[1]

[1]Département d'urologie néphrologie et transplantation rénale; [2]Service d'anesthésie et réanimation; [3]Service de chirurgie cardiaque et thoracique, Hôpital de la Pitié Salpétrière; [4]Service de réanimation, Hôpital de la pitié Salpétrière, Paris, France

Combined heart-kidney transplant improves survival in patients compared with only heart transplant in patients who are on dialysis before transplantation and in patients with reduced preoperative GFR who are at high risk for new onset dialysis postoperatively.

The impact of the use of "the extracorporeal membrane oxygenation" (ECMO) was studied in pre-transplantation, but still never in post-transplantation like a factor, which can improve DGF or survival.

Since 2012, the veno-arterial ECMO was installed in a systematic way in per operational of combined heart-kidney transplant.

In this study, we evaluate after combined heart–kidney transplantation the benefit of the femoral veno-arterial ECMO on renal delayed graft function (DGF) and survival grafts and patients.

Thirty recipients between 2002 and February 2016 were included in this study. 17 patients profited from an ECMO systematically in per-transplantation since 2012 in a consecutive way whereas it was not it among 13 other patients.

The 2 groups were comparable for the age, the stage of kidney injury (preemptive transplantation/dialysis), gravity of the cardiac status (intubation, use of dobutamine, use to the ECMO or assistance, antecedent of sternotomy) and the characteristics of the donors.

The Incidence of the DGF is not significantly different between the two groups with 47.06% in the group with ECMO versus 53.85% in the group without ECMO, Whereas the early survival at 3 month was significantly improved with use of the ECMO with 94.1% (16/17) in the group with ECMO vs 61.5% (8/13) in the group without ECMO ($p = 0.0271$).

There was no difference between the 2 groups for renal/cardiac function and acute rejection.

We conclude that the ECMO significantly improves early survival of the patients undergoing combined heart-kidney transplant, but its place in the prevention of renal DGF remains to be defined in larger group.

O34 LIVER TRANSPLANTATION FROM TYPE 3 DONOR AFTER CIRCULATORY DEATH AND REGIONAL NORMOTHERMIC CIRCULATION. FIRST RESULTS OF A FRENCH CENTER

E. Savier[1,6], G. Rousseau[1], F. Perdigao[1], D. Eyraud[2], H. Brisson[3], L. Puybasset[4], B. Riou[5], O. Langeron[3], J.C. Vaillant[1], O. Scatton[1]

[1]Chirurgie digestive et Hépato-bilio-pancréatique, Transplantation hépatique, CHU Pitié-Salpêtrière, APHP, UPMC Univ. Paris 06; [2]Département d'anesthésie-réanimation, CHU Pitié-Salpêtrière, APHP, UPMC Univ. Paris 06; [3]Réanimation chirurgicale polyvalente, CHU Pitié-Salpêtrière, APHP, UPMC Univ. Paris 06; [4]Réanimation neurochirurgicale, CHU Pitié-Salpêtrière, APHP, UPMC Univ. Paris 06; [5]Service d'accueil des urgences, CHU Pitié-Salpêtrière, APHP, UPMC Univ. Paris 06, Paris; [6]Inserm U1082. Irtomit, Poitiers, France

Introduction: Liver transplantations (LT) from type 3 donor after circulatory death (DCD3) are authorized since 1 year according to a prospective protocol of evaluation of the *Agence de la Biomédecine*. A normothermic regional circulation was applied for any LT.

Methodology: Comparison of 8 DCD3 LT to 25 control LT selected according to DCD3 selection's criteria, i.e., LT from a donor died by encephalic death, liver alone, not split, 1st LT, MELD≤ 18 (protocol≤ 25), donor≤ 60 years, receiver≤ 65 years, cold ischemia≤ 9 hours (protocol≤ 8 h) in SCOT 15 (protocol: any solution). The 2 groups were not significantly (NS) different for all these selection criteria. T-test. mean ± SEM.

Results: The functional warm ischemia was 19.6 ± 1.2 minutes in the DCD3 group. A cardiac arrest was noted 6 times (24%) in the control group. No primary non-function was observed, nor a loss of graft before day 90 (median follow up of DCD3: 7.5 months). In group DCD3 the early allograft dysfunction (EAD according to Salvalaggio) was absent 6 times (75%) and moderate twice (25%) and in the control group these rates of EAD were: absence 56%, light: 20%, moderate: 20%, severe: 4%. During the first week following LT, in the DCD3 group versus (vs.) the control group, the peak of AST at day 0 was of 1688 ± 405 IU/L vs 2100 ± 390 IU/L (NS), peak of ALT at day 0: 1419 ± 366 IU/L vs 1070 ± 190 IU/L (NS), factor V at day 2: 93 ± 11% vs 84 ± 7% (NS), mean of creatinin during the first week (W0): 103 ± 28 μM vs 71 ± 5 μM (NS), mean of total bilirubin during W1: 29 ± 8 μM vs 52 ± 15 μM (NS), mean of gGT during W1: 374 ± 62 IU/L vs 257 ± 23 IU/L ($p = 0.037$), respectively.

Conclusion: The first results of LT from DCD3 are comparable with those of control LT, even if some biological anomalies are suggestive of more significant ischemia-reperfusion injury.

O35 REAL-TIME IMAGING WITH THE O-ARM OF LUNG PARENCHYMA DURING EX-VIVO LUNG RECONDITIONING

J. De Wolf, M. Glorion, P. Puyo, P. Bonnette, A. Roux, M. Le Guen, F. Parquin, A. Chapelier, E. Sage

2, Foch Hospital, Suresnes, France

Introduction: Ex vivo lung perfusion (EVLP) has been developed as a method to reassess and repair damaged lungs. However, evaluation of the lung during procedure is limited to a combination of physiological variables as gas exchange, pulmonary mechanics (stable peak inspiratory pressure and dynamic compliance), and pulmonary vascular resistance.

The aim of this study is to analyse the feasibility and utility of a scan via the O-Arm (Medtronic, Inc., Minneapolis, MN, USA) imaging to help the evaluation of the lung during ex vivo lung reconditioning (EVLR) procedure in Operating Room.

Methods: We evaluated three consecutive extended-criteria brain-death donor lungs during EVLR. For functional evaluation, the following variables were assessed: partial pressure of arterial oxygen (Pao2), pulmonary vascular resistance (PVR), and lung compliance (LC) every hour. For parenchyma evaluation, the lungs underwent a scan via the O-Arm, a fluoroscopic device capable of providing three-dimensional images through the use of cone-beam technology at 1 and 4 h.

Results: Among the 3 pairs of donors lungs, 2 were transplanted because they recovered physiological function with PaO2/FiO2 ratio more than 400 mmHg, stability of other functional parameters (PVR and LC) and lung attenuation of ground-glass opacification in scan. However, one pair of lungs was not transplanted because of the deterioration of the pulmonary vascular resistance, the peak inspiratory pressure, and dynamic compliance. This pulmonary functional impairment was associated with the emergence of a massive pulmonary oedema on the per-procedure O-Arm scan.

Discussion: The use of a high-performance real-time imaging system, such as O-Arm, to evaluate lung grafts from extended-criteria donors during EVLR show an additional argues to select and increase the lung transplants pool.

O36 IMPACT OF DONOR DISSEMINATED INTRAVASCULAR COAGULATION ON KIDNEY ALLOGRAFT RECIPIENTS? A MULTICENTRIC RETROSPECTIVE STUDY

C. Garrouste[3], J. Baudenon[3], I. Etienne[6], P. Gatault[7], B. Pereira[2], A. Thierry[5], J. Oniszczuk[3], J. Sayegh[1], D. Anglicheau[4], A.E. Heng[3]

[1]Service de Néphrologie, CHU Angers, Angers; [2]Biostatistique, CHU Gabriel Montpied; [3]4, Service de Néphrologie CHU Gabriel Montpied, Clermont-Ferrand; [4]Service de Néphrologie, CHU Necker, Paris; [5]Service de Néphrologie, CHU Poitiers, Poitiers; [6]Service de Néphrologie, CHU Rouen, Rouen; [7]Service de Néphrologie, CHU Tours, Tours, France

Introduction: Diagnosis of disseminated intravascular coagulation was frequent (DIC) in intensive care unit. In 2013, only 19 of 1504 brain death kidney donors had DIC in France. The aim of this study was to evaluate the impact of donor DIC on kidney transplantation (KT).

Methods: We identified 169 kidney recipients with DIC + brain death donors between 01/1996 and 12/2012 in 6 French transplant centers. They were matched to 338 recipients with DIC- donors according to (i) age and sex of the donor, (ii) expanded criteria donor or not (iii) graft year (iv) and center.

Results: DIC+ donors had more frequently oliguria (21.2 vs 11.2% $p = 0.004$) and creatinine > 133 μmoL/L (41.1 vs 10.3% $p = 0.001$), during resuscitation. They received more often amines (95.8 vs 73.3% $p = 0.001$), blood and platelets infusion ($p = 0.001$). After KT, delayed graft function was observed in 28.1% of DIC and + 22.8% of DIC- (NS). The average hospital stay was similar between patients KT with DIC+ 17.3j and DIC- 16.4j (NS). Renal survival in DIC+ group at 1, 5 and 10 years were 94.5, 89.3 and 73.9% and in DIC- group of 96.2, 90.8 and 81.3% (NS). The median eGFR were not different between DIC + and DIC-at M3 (45.9 vs 48.1 mL/min), M60 (42.0 vs 43.1 mL/min) and M120 (35.3 vs 37.4 mL/min) (NS). In DIC+ recipient, SAL induction was associated with a better eGFR outcome between M3 (44.8 mL/min) and M12 (48.5 mL/min) in comparison with anti IL2R inductions(48.3 and 46.7 mL/min respectively) $p = 0.04$ while a delayed introduction anticalcineurin seems not impacted on eGFR evolution.

Discussion: While DIC + donors presented more frequently kidney damage (tubular necrosis, glomerular thrombi), DIC of the donor does not affect graft survival or long-term graft function in KT recipients.

O37 IL-6 PRODUCTION BY MONOCYTES IS ASSOCIATED WITH GRAFT FUNCTION DECLINE IN PATIENTS WITH BORDERLINE CHANGES SUSPICIOUS FOR ACUTE T CELL-MEDIATED REJECTION

O. Désy[1], S. Béland[1], P. Vallin[1], J. Riopel[1], E. Latulippe[1], N. Najafian[2], A. Chandraker[2], M. Agharazii[1], I. Houde[1], I. Batal[2], S.A. De Serres[1]
[1]4, CHU de Québec - Université laval, Québec, Canada; [2]Brigham and Woman's Hospital and Harvard Medical School, Boston, United States

Background and Hypothesis: The borderline changes suspicious for acute T-cell-mediated rejection (BL) is a diagnostic category currently questioned for its relevance. The undetermined clinical significance of this diagnosis leads to heterogeneous therapeutic management. Based on previous observations, we hypothesized that measuring IL-6 secretion by peripheral blood mononuclear cells (PBMCs) in patients with BL identifies those with ongoing graft damage.
Methods: From a cohort of 105 patients with concurrent biopsy and PBMC collection, we studied 28 patients with BL, in the absence of ABMR. The primary outcome was the change in eGFR at 6 months. We measured IL-6 levels secretion in PBMC culture supernatants. We then conducted phenotypic and functional characterization of patients IL-6 secreting cells by flow cytometry, followed by characterization of mouse dendritic cells (DCs).
Results: The primary outcome was strongly associated with IL-6 levels (clinically meaningful decline of 5.0 $\pm$ 1.5 mL/min for each increase in log10 IL-6; $p = 0.004$). These results were consistent after adjustment for baseline eGFR and antirejection treatment ($p = 0.003$). 3-month PBMC sample were available in 19 patients and demonstrated that the secretion of IL-6 was stable over time. Phenotyping revealed that the main source of IL-6 was $CD14^+CD16^-CCR2^+HLADR^+CD86^+CD11c^+$ monocytes. In an independent cohort, we found a significant correlation between IL-6 secretion and interstitial DC density in the biopsy. In mice, we then observed that kidney DCs share features with macrophages and function as effector cells secreting IL-6. Kidney DCs showed a lower capacity for proliferation of CFSE-labeled $CD8^+$ and $CD4^+$ T cells and a lower production of IL-2 in MLR supernatants, compared with splenic DCs.
Conclusions: These data suggest that IL-6 is a potential marker of active rejection in patients with BL, is produced by monocytes in the blood, and correlates with DCs in the allograft.

O38 A NEW DIAGNOSTIC SCORE OF INTRAVASCULAR ACTIVATED MONONUCLEAR CELLS IN ANTIBODY-MEDIATED REJECTION IN HEART TRANSPLANTATION

M. Racapé[6,5], I. Zouhry[5], A. Loupy[5], J. Reeves[1], C. Toquet[2], P. Rouvier[4], A. François[7], S. Varnous[4], A. Gay[7], S. Pattier[2], R. Guillemain[3], P. Halloran[1], P. Bruneval[3], J. Duong Van Huyen[5]
[1]ATAGC, Edmonton, Canada; [2]Hôpital Laennec, Nantes; [3]Hôpital Européen Georges Pompidou; [4]Hôpital La Pitié-Salpetrière; [5]Hôpital Necker - Enfants Malades; [6]PARCC INSERM U970, Paris; [7]Hôpital Charles Nicolle, Rouen, France

Background: The ISHLT classification defines Intravascular Activated Mononuclear Cells (IAMC) as one of the histopathologic features of Antibody-Mediated Rejection (pAMR) in heart transplantation. However, no accurate grading of IAMC correlating with pAMR diagnosis has been proposed. The aim of this study was to develop a score to grade the extent and the pattern of the IAMC in endomyocardial biopsies (EMB) with AMR.
Methods: This case-control study included heart transplant patients from five French referral centers with biopsy-proven AMR (pAMR1-3) ($n = 64$) and a matched control group of 44 patients without rejection (pAMR0). IAMC on EMBs was graded blind of pAMR grades by two skilled pathologists according to the percentage of the area with IAMC in capillaries and to the maximum number of IAMC in the most affected capillary on a 0 to 3 scale and a positivity defined by a grade ≥ 1. The score was compared to the gene expression profile in EMBs by microarray using the ABMR molecular score and pathogenesis-based transcripts reflecting endothelial activation (ENDAT), DSA (DSAST), macrophage burden (QCMAT), gamma-interferon response (GRIT) and NK-cell burden (NKB) (http://atagc.med.ualberta.ca).
Results: 100% of control EMBs were graded as IAMC score 0. All pAMR1(I+) EMBs and none of the pAMR1(H+) and pAMR2-3 were graded as IAMC score 0. The highest IAMC score 3 was mainly distributed in pAMR2-3 (Fischer's exact = 0.000). Increase in the IAMC score was associated with an increase in the proportion of C4d and CD68 (macrophage marker) positive EMBs, and a higher proportion of DSA positive at EMB. It was also associated with an increase in the expression of ENDAT, DSAST, GRIT, NKB and QCMAT transcripts (All Kruskal-Wallis<0.001).
Conclusion: The IAMC score is associated with molecular activation in grafted myocardial tissue. The IAMC score could help pathologists for AMR diagnosis, emphasizing the value of IAMC in AMR detection.

O39 ANTI-DONOR HLA ANTIBODY RESPONSE AFTER PANCREATIC ISLET GRAFTING: CHARACTERISTICS, RISK FACTORS AND IMPACT ON GRAFT FUNCTION

E. Pouliquen[5], P. Baltzinger[10], A. Lemle[10], C. Chen[7], A. Parissiadis[9], S. Borot[1], L. Frimat[8], S. Girerd[8], T. Berney[2], S. Lablanche[3], P.Y. Benhamou[3], E. Morelon[5], L. Badet[6], V. Dubois[9], L. Kessler[10], O. Thaunat[5]
[1]Service d'Endocrinologie-Métabolisme et Diabétologie-Nutrition, Centre Hospitalier Universitaire Jean Minjoz, Besançon; [2]Departement of Surgery, Islet Isolation, and Transplantation Center, Geneva University Hospitals, Geneve; [3]Département d'Endocrinologie, Pôle DigiDune, Hôpital Universitaire de Grenoble, Grenoble; [4]Laboratoire d' histocompatibilité, Etablissement Français du Sang; [5]service de transplantation et d'immunologie clinique; [6]Service d'urologie et de chirurgie de la transplantation, Hôpital Edouard Herriot; [7]INSERM U1111, Université de Lyon, Lyon; [8]Service de Néphrologie, Centre Hospitalier Universitaire de Nancy, Nancy; [9]Laboratoire d' histocompatibilité, Etablissement Français du Sang; [10]Service d'Endocrinologie Diabète et Maladies Métaboliques, Hôpitaux Universitaires de Strasbourg, Strasbourg, France

Introduction: Pancreatic islet grafting restores endogenous insulin production in type 1 diabetic patients but long-term outcomes remains disappointing. In solid organ transplantation, donor-specific anti-HLA antibodies (DSA) are the first cause of organ failure. This retrospective multicentric study aimed at providing in-depth characterization of DSA response after pancreatic islet grafting, identifying the risk factor for DSA generation and determining the impact of DSA on graft function.
Material & methods: 42 pancreatic islet graft recipients from the GRAGIL consortium (Groupe Rhin-Rhône-Alpes-Genève pour la Greffe d'Ilots de Langerhans) were enrolled. Sera analyses were centralized and performed using the same highly sensitive solid phase assay platform (Immucor). Screening of sera for anti-HLA antibody was performed for each patient, before grafting and every year thereafter until the loss of graft function. In case of positivity, the specificities of antibodies were determined (single antigen kit) as well as their ability to activate the complement cascade (C3d binding assay).
Results: Prevalence of DSA was 25% at 3 years post-grafting. The risk of sensitization increased steeply after immunosuppressive drugs withdrawal. DSA repertoire diversity correlated with the number of HLA and eplet mismatches. DSA titer was significantly lower from what observed in solid organ transplantation. No detected DSA bound the complement fraction C3d. Importantly, DSA did not increase the attrition rate of pancreatic islets graft.
Conclusion: In contrast with solid organ transplantation, DSA did not seem to impact negatively pancreatic islet graft survival. This might be due to the low DSA titers, specific features of IgG limiting their ability to activate the complement, and/or the lack of allogenic endothelial targets in pancreatic islet grafts.

O40 COMPLEMENT MARKERS IN IMMUNOADSORPTION COMBINED WITH MEMBRANE FILTRATION

L. Rostaing
4, CHU de Grenoble, GRENOBLE CEDEX 09, France

Introduction: In HLA incompatible transplantation [donor-specific alloantibody (DSA)] pretransplant desensitization is mandatory in order to eliminate the DSA that might fix complement (C). In a randomized crossover design we demonstrated that combined membrane filtration (MF) with immunoadsorption (IA) is significantly associated with more immunoglobulins and C1q component elimination than regular IA (Eskadary F, NDT 2014).

C system (CS) plays a major role in graft rejection; activation of the CS is mediated by classical, alternative and lectin pathways that converge in terminal complement complex, C5b-9. Classical complement pathway is believed to play an important role as an effector of rejection. Higher mannan binding lectin (MBL) levels have been associated with more C-mediated damage resulting in severe form of rejection.
Methods: In order to evaluate the impact of IA+MF vs IA on global C functional activity, in a crossover study (14 patients) the soluble C5b-9 and MBL antigen levels were measured in by ELISA, in order to investigate the depletion efficiency of both strategies.
Results: The addition of MF to IA was associated with a significant reduction of C5b-9 (mean: 38%) as compared to IA alone (mean: 16%). Preliminary data on lectin pathway show that MBL depletion was more pronounced upon combined treatment IA+MF (mean: 44%) as compared to IA alone (mean: 13%).
Conclusion: C activation and increases the removal of MBL. These effects could represent an efficient mechanism to prevent graft rejection in incompatible transplantation.

O41 MOLECULAR PATTERNS IN URINE ASSOCIATED WITH SUBCLINICAL INJURY IN THE RENAL ALLOGRAFT

P. Galichon[5,4,3], Y.C. Xu-Dubois[4], D. Buob[5,4], S. Benbouzid[2], K. Dahan[3], N. Ouali[3], A. Hertig[5,4,3], I. Brocheriou[5,4], E. Rondeau[5,4,3]

[1]Service d'hospitalisation de Jour de Néphrologie, Hôpital Tenon; [2]Service d'Urologie, Hôpital Tenon; [3]Urgences Néphrologiques et Transplantation Rénale, Hôpital Tenon, Assistance Publique – Hôpitaux de Paris; [4]UMR_S1155, INSERM; [5]Université Pierre et Marie Curie, Sorbonne Universités, Paris, France

Background: Subclinical pathological features, such as partial epithelial mesenchymal transition of the renal allograft (renal pEMT) and inflammation on the 3-month surveillance biopsy are associated with a poor prognosis, but it is unclear whether surveillance biopsies are beneficial. Non-invasive biomarkers are wanted, and urinary pellet RNA quantification has yielded promising results on selected candidate genes although normalization issues remain problematic.
Methods: We used immunohistochemistry of vimentin and b catenin to assess renal pEMT in a group of 26 stable transplanted patients with simultaneous renal allograft biopsy and urine sample. We performed a mRNA microarray study using different normalization methods on the urinary cell pellet to evaluate the feasibility of the detection of renal pEMT using urinary cell pellet mRNA quantification. We then characterized the urinary molecular patterns associated with renal pEMT.
Results: We found that, when using a novel method of normalization by Upk1a mRNA, renal pEMT of the renal allograft was associated in urine with differential expression of genes belonging to predefined gene sets of kidney-expressed genes and epithelial mesenchymal transition genes. An unbiased pathway analysis revealed that the immune response was the main biological process associated with pEMT, in keeping with the known association of pEMT with intragraft inflammation. In urine from patients with pristine biopsies, pEMT was not associated with inflammation, but with reduced metabolic functions.
Conclusions: We show that pEMT translates into specific UPK1a-normalized mRNA patterns in urine and use genome-wide analyses to characterize underlying molecular patterns, i.e. increased inflammation and decreased metabolic functions.

O42 MOLECULAR CORRELATES OF ENDOTHELIAL MTOR ACTIVATION IN HEART TRANSPLANT RECIPIENTS

M. Racapé[6,5], A. Loupy[5,6], J. Reeves[1], C. Toquet[2], P. Rouvier[4], A. François[7], S. Varnous[4], A. Gay[7], S. Pattier[2], R. Guillemain[3], P. Halloran[1], P. Bruneval[3], J. Duong Van Huyen[5,6]

[1]ATAGC, Edmonton, Canada; [2]Hôpital Laennec, Nantes; [3]Hôpital Européen Georges Pompidou; [4]Hôpital La Pitié-Salpetrière; [5]4, Hôpital Necker - Enfants Malades; [6]PARCC INSERM U970, Paris; [7]Hôpital Charles Nicolle, Rouen, France

Background: The detection of phosphorylated effectors of the mTOR pathway such as phosphorylated-S6RP in endothelial cells by immunohistochemistry (IHC) has been associated with Antibody-Mediated allograft Rejection (AMR). The aim of this study was to evaluate the molecular phenotype related to the endothelial detection of pS6RP in heart transplant recipients.
Methods: This case-control study included 41 heart transplant patients from four French referral centers with biopsy proven antibody-mediated rejection (pAMR+) and a matched control group of 30 patients without rejection (pAMR0) based on the updated ISHLT classification. From these patients, 94 endomyocardial biopsies (EMB) had adequate material for microarray analysis and endothelial expression analysis of pS6RP by IHC. We also determined the allograft gene expression profile using the ABMR molecular score in addition to pathogenesis-based transcripts reflecting endothelial activation (DSAST and ENDAT), macrophage burden (QCMAT), gamma-interferon response (GRIT) and NK-cell burden (NKB) (http://atagc.med.ualberta.ca).
Results: Among the 94 EMBs included in the main analyses, 50 were pAMR+ (53.2%) and 44 (46.8%) were pAMR0 normal EMBs. Endothelial expression of pS6RP was observed in 27/50 (54%) of pAMR+ biopsies and 12 out of 44 normal biopsies (27.3%, Fischer's exact: $p = 0.012$). As compared with biopsies without pS6RP labeling, biopsies with pS6RP staining showed increased expression of DSAST (Mann-Whitney: $p < 0.0001$), ENDAT ($p = 0.0009$), QCMAT ($p = 0.0046$), NKB ($p = 0.0001$), GRIT ($p = 0.0008$) and increased ABMR molecular score reflecting AMR injury ($p = 0.0001$).
Conclusion: Endothelial activation of mTOR pathway is associated with AMR and increased expression in transcripts reflecting endothelial activation, macrophage burden, microcirculation and NK burden. Our results suggest the importance of the mTOR pathway activation in AMR injury and the potential interest of using mTOR inhibitors in this setting.

O43 ASSOCIATION BETWEEN MATRIX-GLA PROTEIN AND AORTIC STIFFNESS IN KIDNEY TRANSPLANT

M. Dinic[3], M. Maillard[3], P. Delanaye[2], J.M. Krzesinski[2], A. Saint Remy[2], E. Cavalier[1], C. Mariat[3]

[1]Head, Department of Clinical Chemistry University of Liège, CHU Sart-Tilman; [2]Nephrology Department University of Liege, University Hospital Sart Tilman, Liège, Belgium; [3]Service de néphrologie, dialyse, transplantation CHU Nord, Saint Etienne, France

Introduction: Excessive aortic stiffness due to vascular calcifications is observed in kidney transplant recipients and is considered as a robust predictor of cardiovascular and renal events. Matrix-gla-protein (MGP) is an inhibitor of vascular calcifications. In kidney transplant, an association between MGP and all-cause mortality and transplant failure was suggested. The aim of our study is to assess the association between MGP and aortic stiffness in kidney transplant
Material and Methods: We studied the association between inactive MGP levels (dephosphorylated and uncarboxylated: dp-ucMGP), vascular calcifications (Kauppila score) and aortic stiffness (pulse wave velocity, PWV) in prevalent kidney transplant recipients. The analysis of association was performed with uni and multivariate linear regression including traditional and non-traditional cardiovascular risk factors and graft function parameters.
Results: We analyzed 126 patients in two independent centers. The mean age of this cohort was 55.4 ± 13.6 years and the mean time since transplantation was 8.3 ± 7.7 years. In univariate analysis, a significant association was observed between MGP and pulse wave velocity ($p = 0.017$). In multivariate analysis, we showed that the factors independently associated with PWV were age ($p < 0.001$), diabetes mellitus ($p < 0.001$), eGFR ($p = 0.042$) and MGP ($p = 0.048$). No association was found between MGP and the Kauppila score.
Discussion: The absence of correlation between MGP and vascular calcifications may be explained by the lack of sensibility of the Kauppila score.
Conclusion: Our data suggest the existence of a significant and independent association between MGP level and elevated aortic stiffness in kidney transplant recipients. More studies need to be conducted to assess the possible role of MGP as a marker of the cardiovascular risk in kidney transplant.

O44 HLA-E*01:01 AND HLA-E*01:03 ARE CORRELATED TO POOR SURVIVAL AND INCREASED CHRONIC REJECTION CLAD IN LUNG TRANSPLANTATION

J. Di Cristofaro[5], M. Pelardy[1], A. Loundou[3], A. Basire[1], C. Gomez[2], J. Chiaroni[1], P. Thomas[4], M. Reynaud-Gaubert[2], C. Picard[1,5]

[1]Laboratoire Immunogénétique, Établissement Français du Sang Alpes Méditerranée; [2]Service de Pneumologie et Transplantation Pulmonaire, CHU Nord Faculté de Médecine, URMITE - CNRS-UMR 6236 Aix Marseille Université; [3]Département de santé publique -EA 3279, Assistance Publique-Hopitaux Marseille [AP-HM], Aix-Marseille Université; [4]Service de Chirurgie Thoracique et Transplantation Pulmonaire, CHU Nord Faculté de Médecine, URMITE - CNRS-UMR 6236, Aix Marseille Université; [5]Aix-Marseille Université, CNRS, EFS, ADES UMR 7268, Marseille, France

Lung transplantation (LTx) is a valid therapeutic option for selected patients with end-stage lung disease. HLA-E seems to play a major role in the immune response to different viral infections and to affect transplantation outcome, in hematopoietic stem cell transplantation for example. Two non-synonymous alleles, HLA-E*01:01 and HLA-E*01:03, have functional differences, involving relative peptide affinity, cell surface expression, and potential lytic activity of NK cells.

The aim of this retrospective study was to determine the impact of these two alleles for LTx recipients on anti-HLA allo-immunization risk, overall survival and chronic rejection (CLAD). HLA-E was genotyped in 119 recipients who underwent LTx from 1998 to 2010 in a single transplantation center.

In univariate analysis, both HLA-E homozygous states were associated with impaired overall survival compared to heterozygous HLA-E alleles ($p = 0.01$). In multivariate analysis, HLA-E*01:03 allele showed increased CLAD occurrence when compared to homozygous HLA-E*01:01 status (HR: 3.563 (CI 95%, 1.016–12), $p = 0.047$). HLA-E allele did not affect pathogen infection or the production of de novo DSA.

This retrospective study shows an uninvestigated, deleterious association of HLA-E alleles in LTx and requires verification using a larger cohort.

O45 ANTIBODY MEDIATED REJECTION IN COMBINED LIVER-KIDNEY TRANSPLANTATION

A. Del Bello[6], O. Bestard[1], J. Visentin[2], N. Congy-Jolivet[5], L. Couzi[3], M. Neau[4], F. Jambon[3], N. Kamar[6]

[1]Departement de Nephrologie, Centre hospitalier de Barcelone, Barcelone; [2]laboratoire d'immunologie; [3]Service de Nephrologie; [4]Service d'hépatologie, CHU de Bordeaux, Bordeaux; [5]laboratoire d'imunologie, CHU de Toulouse; [6]4, CHU Toulouse Rangueil, Toulouse, France

Introduction: Successful kidney transplantation (Tx) despite a positive crossmatch is well known after combined liver-kidney transplantation (CLKT). However, several data have showed a harmful impact of anti-HLA DSAs on liver transplants. In this retrospective multicentric study, we aimed to investigate the incidence and consequences of preformed DSAs on liver and renal allografts in CLKT.
Patients & Methods: Among 76 consecutive CLKT performed in the 3 centers, 50 were tested for DSAs with the Luminex SA (cut-off 1 000) at Tx. All rejection episodes were reevaluated according to the last Banff classification for liver and kidney Tx. Kidney and liver tests were evaluated 1, 3, 6, 12, 23 and 60 months after Tx, and at last follow-up.
Results: 6 Tx presented preformed DSAs(12%), including 5 patients with a positive crossmatch at Tx. The patients' (and liver allografts', no liver retransplantation were performed) survival at 1, 2 et 5 years was 67%, 67%, 50% and 88%, 86%, 76% respectively in the groups with or without DSAs (p = ns). The kidney graft's survival at 1 and 2 years was 67%, 67%, and 91%, 91%, in the groups with or without DSAs (p = ns). 5 years post-CLKT, the kidney grafts'survival was 50% in patients with DSAs and 83% in the group without DSAs (p = 0.02). At last follow-up, renal functions were similar in both groups (50 ± 14 mL/min/1.73 m² in the DSA- group at 43 [1–243] months post-CLKT, and 52 ± 24 mL/min/1.73 m² in the DSA+ group at 29[3–80] months post-CLKT(p = ns)). The incidences of kidney and liver acute antibody mediated rejection were at 17% in the DSAs positive group. In the DSA positive and negative group, the rates of acute liver and kidney T-cell mediated rejection were 0% and 7% and 0% et 4% (p = ns).
Conclusions: Preformed DSAs are associated with a poorer survival of kidney transplants at 5 years post CLKT while it does not seem to have a harmful impact on liver-transplants. However, the kidney function was similar at last follow-up in both groups.

O46 ACCESS TO KIDNEY TRANSPLANTATION THANKS TO COLLABORATION BETWEEN FRENCH REFERENCE CENTER FOR OBESITY AND KIDNEY TRANSPLANTATION DEPARTMENT IN THE UNIVERSITY HOSPITAL OF BORDEAUX

A. Lagrave[3], S. Cambos[3], E. Pupier[3], M. Monsaingeon-Henry[3], K. Moreau[1], L. Couzi[1,2], P. Merville[1], B. Gatta-Cherifi[3]

[1]Service de Néphrologie, Transplantation, Dialyse, Hôpital Pellegrin, CHU de Bordeaux; [2]CNRS-UMR 5164 Immuno ConcEpT, Université de Bordeaux, Bordeaux; [3]Service d'Endocrinologie, Diabétologie, Nutrition et Maladies Métaboliques, Hôpital Haut-Lévêque, CHU de Bordeaux, Pessac, France

Introduction: Kidney transplantation (KT) is the preferred therapeutic option for end stage renal disease. Obesity in patients with chronic kidney disease may preclude access to kidney transplantation. A partnership was developed between Regional Reference Center For Obesity (RCO) and Kidney Transplantation Department in the University Hospital of Bordeaux (France). Access to transplantation for these obese patients was studied.
Methodology: Data of patients referred to RCO due to temporary contraindication were gathered between 11/2010 and 02/2016. Obesity severity and its complications were collected. Patients were enrolled in a multidisciplinary weight management program. Outcomes of body weight (BW) loss and KT list status were studied at the end point.
Results: Twenty-nine patients were referred. Two patients didn't enter the program. Of 29 patients, 68.9% were female. Mean age was 54.17 ± 11.4 years. Baseline mean BMI was 39.7 ± 5.6 kg/m² [31.6–52.3]. At baseline, 81.5 % of cohort was on dialysis, 81.5% suffered from hypertension and 59.3% from type 2 diabetes. Mean follow-up time was 19.9 ± 16 months [2–52]. Final weight lost was 6.1 ± 7.9% of initial BW and final BMI reached 37.5 ± 5.7 kg/m².

Contraindication to KT was removed for 13 patients (48.8%) among whom 8 were transplanted, with a final mean BMI 34.8 kg/m². In order to enable the surgery, 3 patients had plastic surgery and 2 patients bariatric surgery. Three patients died. Regarding patients who can't be registered on the waiting list at the moment due to their weight, 5 quitted the program, one is permanently contraindicated, 8 are still part of the programme. For the 2 patients who didn't come, contraindication is still there.
Conclusion: A multidisciplinary BW loss program allowed half of the patients to access to the waiting list for KT.

O47 KIDNEY TRANSPLANTATION AFTER BONE MARROW ALLOGRAFT

M.J. Ziliotis[2], L. Frimat[7], M. Büchler[10], P. Malvezzi[4], S. Caillard-Ohlmann[9], B. Dussol[6], M. Hazzan[5], A.E. Heng[3], R. Peffault De La Tour[8], D. Ducloux[2], E. Deconninck[1], C. Courivaud[2]

[1]Hématologie-Greffe de Moelle; [2]Néphrologie-Dialyse-Transplantation, CHU, Besançon; [3]Néphrologie-Dialyse-Transplantation, CHU, Clermont-Ferrand; [4]Néphrologie - Dialyse -Transplantation, CHU, Grenoble; [5]Néphrologie-Dialyse-Transplantation, CHU, Lille; [6]Néphrologie - Dialyse - Transplantation, CHU, Marseille; [7]Néphrologie-Dialyse-Transplantation, CHU, Nancy; [8]Hématologie-Greffe de Moelle, Hopital St-Louis, Paris; [9]Néphrologie - Dialyse - Transplantation, CHU, Strasbourg; [10]Néphrologie - Dialyse - Transplantation, CHU, Tours, France

Introduction: Kidney insufficiency is a frequent complication after bone marrow allograft, leading to dialysis or kidney graft. The outcome of patients undergoing kidney transplantation after a bone marrow graft is poorly known.
Patients and Methods: A french multicentric retrospective study. All kidney transplant recipients engrafted between 2000 and 2014 with a previous history of bone marrow allograft were enrolled.
Results: Our study identified 19 patients, among which 2 underwent each 2 bone marrow allograft. Sex ratio M/F was 12/7. The mean age at time of bone marrow graft was 27 ± 16 years. The main indication was acute leukemia (13/19). One patient was on dialysis at time of the graft, 3 the following year (1 kidney biopsy/3: ATN) and 12 after one year, in a mean time lapse of 11 ± 6 years. Before kidney transplantation, 2 patients developed a cancer. The mean age of transplantation was 39 ± 13 years. Three patients didn't get any immunosuppression (same donor for kidney and bone marrow), 6 got an induction by antithymocyte globulins and 9 by anti-CD 25. Maintenance immunosuppression included for all patients steroids and CNI, mycophenolate mofetil for 13 and sirolimus for 2. Mean follow-up was 8 ± 4 years, with a high rate of severe infections (10/19) and cancer (6/19), causing 3 deaths.
Conclusion: A history of bone marrow allograft increases the risk of severe infection and neoplasia after kidney transplantation. Nevertheless, the survival rate in this selected population seems satisfying. The numerous infectious and neoplastic complications call for immunosuppressive protocols weighing the history of bone marrow allograft. Further investigations are required.

O48 INTERNATIONAL REGISTRY ON HAND AND COMPOSITE TISSUE TRANSPLANTATION

P. Petruzzo[1,2], M. Lanzetta[3], J.M. Dubernard[1]

[1]Service d'urologie et chirurgie de la transplantation, Hospices Civils de Lyon, Lyon, France; [2]University of Cagliary, Department of surgery, Cagliary; [3]Italian Institute of Hand Surgery, Monza, Italy

Introduction: Since 2002 the International Registry on Hand and Composite Tissue Transplantation includes hand and face allotransplantations.
Methods: Since 1998, 89 upper extremity transplantations (UET) (25 unilateral and 32 bilateral) have been reported, for a total of 57 patients.

Since 2005 28 cases of partial or complete face transplantations (FT) have been reported.

In UET and FT the immunosuppressive therapy included tacrolimus, mycophenolate mofetil, sirolimus and steroids; polyclonal or monoclonal antibodies were used for induction. Follow-up ranges from 4 months to 17 years for UET and from 15 months to 10 years for FT.
Results: Patient survival rate in UET regardless follow-up length was 94.8%, while graft survival was 81.8%. Patient survival rate in face transplantation regardless of follow-up length was 85.7% while graft survival was 92.9%.

Acute rejection (AR) occurred in 78.2% of UET recipients and 10.9% of them developed signs of chronic rejection and/or graft vasculopathy, which led to graft lost in four cases. AR occurred in 63.8% of face recipients while 2 cases of chronic rejection were reported with graft loss of one of them. Complications included, as in solid organ transplantation, opportunistic infections, metabolic complications and malignancies.

Hand-grafted patients developed protective sensibility, 90% of them tactile sensibility and 80% also a partial discriminative sensibility Motor recovery enabled patients to perform most daily activities. Face-grafted patients improved their aesthetic aspect and they were able to perform some activities, which were impossible before the transplantation, such as eating, drinking and speaking that allowed them to live a normal social life.
Conclusions: Hand and face transplantations are successful procedures, however careful evaluation before and after transplantation is indispensable as well as patients' compliance. Indeed, non-compliance to the treatment was the cause of late graft loss.

O49 KINETIC AFP SCORE ANALYSIS IN PATIENTS AWAITING LIVER TRANSPLANTATION (LT) FOR HEPATOCELLULAR CARCINOMA (HCC): A RISK FACTOR FOR MICROVASCULAR INVASION AND RECURRENCE

A. Herrero[2], L. Boivineau[3], J. Ursic-Bedoya[3], N. Molinari[1], B. Guiu[5], J. Ramos[4], E. Assenat[3], S. Faure[3], M. Bismuth[3], F. Panaro[2], F. Navarro[2], G.P. Pageaux[3]
[1]Statistiques, Centre hospitalier Universitaire; [2]Surgery, Liver Transplant Unit, Saint Eloi Universitary Hospital; [3]Hepatology; [4]Histopathology; [5]Radiology, Liver Transplant Unit, Saint Eloi University Hospital, Montpellier, France

Introduction: In France, the use of AFP score in LT indications for HCC reduces the recurrence risk around 10%. The main objective of the study was to evaluate the impact of the kinetics AFP score (delta AFP score) on the microvascular invasion (MVI). Secondary objectives were to analyze the overall survival (OS) and the disease-free survival (DFS) according to the delta AFP score.
Methods: Monocentric study of 169 transplanted for HCC between 2007 and 2015 with an AFP score ≤2 the last quarter preceding LT. The delta AFP score was calculated from the evaluation of the AFP score every 3 months, taking into account the waiting time on list and pre-transplant therapies. The patients were classified into 3 groups: stability; progression ($\Delta \geq +1$); regression ($\Delta \geq -1$). MVI was analyzed on the explant. OS and DFS were evaluated at 1, 3 and 5 years post-LT.
Results: According to the delta AFP score, there were 58% of the patients in the stable group, 23% in the progression group and 19% in the regression group. After histological analysis of the liver explants, 17% of patients had MVI. The presence of MVI was significantly associated with delta AFP score: 10% in the stability group, 50% in the progression group, 7% in the regression group ($p < 0.0001$). In multivariate analysis, only the progression of the delta AFP score was an independent risk factor for MVI ($p < 0.001$, OR = 7.5 [2.8–19.6]). Tumor recurrence after LT was present in 9 patients (5%). Five- year OS and DFS were significantly lower in the progression group compared to the stability and regression groups: OS = 38% vs 92% and 68% p = 0.01, DFS = 82% vs 97% and 91%, p = 0.02.
Conclusion: In selected patients with AFP score ≤2, the progression of AFP score during the waiting period predicts MVI and the risk of recurrence. Delta AFP score becomes a relevant preoperative prognostic factor of tumor aggressiveness. These results should be confirmed by external validation cohorts.

O50 INTRODUCING THE NOTION OF UNACCEPTABLE ANTIGENS IN LIVER TRANSPLANTATION: IMPACT ON THE TRANSPLANT ACCESSIBILITY

A. Del Bello[2], N. Congy-Jolivet[3], B. Audry[1], C. Antoine[1], N. Kamar[2]
[1]Agence de la Biomédecine, Paris; [2]Departement de Nephrologie et de Transplantation d'Organes; [3]Laboratoire d'Immunologie, CHU TOULOUSE, Toulouse, France

Background: The negative impact of anti-HLA donor specific antibodies (DSAs) in liver transplantation is now clearly demonstrated. However, strategies to reduce the risk of acute and chronic antibody mediated rejection have not yet been evaluated. In this study, we investigated the consequences associated with the introduction of unacceptable antigens on transplantation access for liver transplant candidates.
Patients & Method: Between 02/08 et 01/16, all liver transplant candidates followed in our center were screened for anti-HLA antibodies (Ab) (with the Luminex technique, MFI cut-off >1,000) every 3–6 months.
Results: 483 patients were included in this study. 99 of them were sensitized [58 presented anti-class I Ab, 28 presented anti-class II Ab, 13 presented anti-class I and II Ab]. 38 patients presented at least one Ab with a MFI >5,000, and 19 patients at least one Ab with a MFI > 10,000. 38/326 patients were transplanted with DSAs [21 with anti-class I, 13 with anti-class II and 4 with anti-class I and II], including 7 positive crossmatches.

Considering as unacceptable antigens, those for which patients have Ab with MFI > 5,000 (36 patients), the incompatible graft rate was <20%, between 20–50%, 50–85%, and >85% respectively in 19, 19, 36, and 25% of patients.

With a MFI cut-off > à 10,000 (17 patients), the incompatible graft rate was <20%, between 20–50%, 50–85%, and >85% respectively 29, 17, 23, and 29% of patients.

Considering only anti-HLA class- II Ab with a MFI > 10,000 (14 patients), the incompatible graft rate was <20%, between 20–50%, 50–85%, and >85% respectively 50, 14, 21, and 14% of patients.
Conclusion: Considering for unacceptable antigens, only those for which patients have anti-HLA class-II Ab with a MFI >10, 000 (i.e. patient with the highest risk for immunological complications) could reduce the risk for Ab associated complications, without affecting the transplantation access of a majority of liver transplant candidates.

O51 LIVER MALIGNANCIES IN CHILDREN: SINGLE CENTER RESULTS OF LIVER TRANSPLANTATION IN 56 PATIENTS

A. Pire, C. De Magnée, B. D'hondt, M. Janssen, R. Reding
3, Cliniques universitaires Saint Luc, Bruxelles, Belgium

Introduction: This works reviews the single center experience of liver transplantation (LT) for pediatric liver malignancies (LM), particularly hepatoblastoma (HB) and hepatocellular carcinoma (HCC), performed since 32 years.
Patients and Methods: Between 1984 and 2015, 56 children received liver graft for a hepatic malignant tumor, 14 by a cadaveric graft and 42 by a living donor graft. Pretext-IV HB was the indication for LT in 36 patients (median age: 2.2 years; range: 0.6–14.3 years), unresectable HCC in 14 (6.1 years; 0.7–22.4 years), vascular tumor in 5 (2.8 years; 0.8–12.9 years), and rhabdomyosarcoma in one case (5.6 years).
Results: In the HB group, 32/36 (88.9%) became long-term disease-free survivors, 20 of them beyond 5 years post-LT. Four children died in the HB group, three from tumor recurrence (8.3%). In the HCC subgroup, 10/14 (71.4%) became long-term disease-free survivors, 6 of them beyond 5 years post-LT. Four children died in the HCC group. Among the five vascular tumors, two became long-term disease-free survivors after living donor LT, whereas the three remaining cases died after post-mortem donation. The child transplanted for rhabdomyosarcoma died at 2.5 months post-LT from lymphoproliferative disease.
Conclusions: In the past 20 years, oncological LT became a key player in the therapeutic approach towards LM in children. Considering HB, pre-transplant chemotherapy, according to SIOPEL successive protocols, followed by total hepatectomy and LT achieved cancer cure in more than 85% of the cases, provided the tumor is chemosensitive and no inappropriate attempt at partial hepatectomy is proposed for Pretext-IV tumors. Considering HCC, it's still debatable whether Milan criteria for LT indication as applied in adults are also usable in children, where HCC are developed mostly on pre-existing liver disease and accordingly more easily detectable in the early phase of evolution.

O52 IMPACT OF NOVO CANCER AFTER LIVER TRANSPLANTATION IN FRANCE

O. Séréé[3,2], M. Altieri[2,1,6], R. De Mil[2], P.H. Segol[1], E. Salame[9,6], E. Guillaume[2], S. Dharancy[4], G.P. Pageaux[7,6], F. Saliba[8], J. Dumortier[5,6], G. Launoy[2]
[1]CHU Caen; [2]Cancer et prévention, INSERM U1086, Caen; [3]Réseau Régional de Cancérologie, OncoBasseNormandie, Hérouville Saint Clair; [4]CHRU Claude Huriez, Lille; [5]CHU Edouard Herriot; [6]Groupe de recherche Français en greffe du foie (GReF2), Lyon; [7]CHU Saint Eloi, Montpellier; [8]CHU Paul Brousse – APHP, Paris; [9]CHRU Trousseau, Tours, France

Introduction: De novo cancers represent one of the major delayed complications and cause of death after liver transplantation. There is an increased incidence of de novo cancers in liver transplant recipients, but there is little data in France to allow the assessment of the magnitude increased risk in the general population.
Methods: The incidence of cancer among all first liver transplant patients between 1993 and 2012, the data is from the comprehensive register of the Biomedicine Agency, was compared to those of the French population using a standardized incidence ratio (SIR: Standardized Incidence Ratio). The observed incidence of cancer was compared to the expected incidence in the French population by age, sex, and calendar period.
Results: Of 11464 liver transplant patients (77,320 person-years of follow-up), 1,688 malignant tumors were diagnosed (14.7%). The SIR for all neoplasms after liver transplantation was 2.87 [CI 95%, 2.74–3.02]. The cancers with the highest incidence were mainly larynx cancer (SIR, 20.76 [CI 95%, 10.73–36.26]) and esophageal cancer (SIR, 4.80, [CI 95 %, 3.63–6.23]). There is a stronger on-incidence in women compared to men, mainly for cancers of the larynx (SIR, 20.76 [CI 95%, 10.73–36.26]), esophagus (SIR, 12.20 [CI 95%, 6.09–21.82]) and lip-mouth-pharynx locations (SIR, 4.70 [IC 95%, 2.69–7.63]) . The SIR of cancer for both sexes increased by 2.51 [IC 95%, 2.35–2.67] for 1993–2002 to 3.55 [IC 95%, 3.30–3.82] for 2003–2012.
Conclusion: Liver Transplant Recipients have an increased risk of cancer compared with the general population, regardless of age, gender, and the time of transplantation with a higher increase among women. Between the periods 1993–2002 and 2003–2012 the likely increased risk related to improved medical care and better targeted screening.

O53 INDICATIONS OF SIMULTANEOUS LIVER-KIDNEY TRANSPLANTATION: EXPERIENCE OF A SINGLE CENTER

A. Grunenwald[1], P. Provot[1], F.R. Pruvot[3], S. Dharancy[4], N. Declerck[2], G. Lebuffe[2], M. Hazzan[1], C. Noel[1]

[1]Service de Néphrologie, CHRU de Lille, Chru De Lille; [2]Service d'Anesthésie-Réanimation, Hôpital Claude Huriez, CHRU de Lille; [3]Service de Chirurgie Digestive et Transplantation, Hôpital Claude Huriez, CHRU de Lille; [4]Servie Gastro-entérologie et Hépatologie, CHRU de Lille, Lille, France

MELD score has induced a significant increase of simultaneous liver-kidney transplantations (SLKT). However, it is well established that some patients recover their native renal function after liver transplantation alone (LTA) or SLKT, raising the question of the indication of SLKT, especially when renal failure occurs during the course of liver disease. We performed a retrospective, monocentric, descriptive study with regards to hepatic and renal epidemiological data of all consecutive adult SLKT between 1989 and 2015. We compared 2 groups of patients according to the physician who initially discussed the indication of combined transplantation: hepatologist (group H) or nephrologist (group N). 47 patients all transplanted by the same surgical team were included. 23 were initially in charge of a hepatologist and developed renal failure in the course of their liver disease. 24 were initially in charge of a nephrologist when liver disease was discovered. Age was 48.3 $\pm$ 13.7 in the group H and 44.8 $\pm$ 13.7 years in the group N (NS). Donors were significantly younger than recipients but there was no difference between the 2 groups (32.3 $\pm$ 10.5 in the group H and 36.1 $\pm$ 16.4 years in the group N). In the entire cohort, patient survival was 74.5% and 60% and renal survival (death censored) was 85.7% and 75.7% at 5 and 10 years, respectively. However renal survival, death uncensored, was 51.3% at 10 years, showing that an important proportion of patients died with a functioning kidney. Survival rates and renal function were similar in the 2 groups, although a higher proportion of patients in the group H received a preemptive kidney transplantation (73.9% vs 0%, $p < 0.001$). In the context of organ shortage, the use of kidney from young deceased donor to older recipients remains questionable, especially if some of them died with a functioning kidney or recovered their native renal function. A more accurate process to select candidates for SLK is needed to avoid futile transplantations.

O54 INTEREST OF NEO- ADJUVANT SORAFENIB FOR PATIENTS AWAITING LIVER TRANSPLANT FOR HEPATOCELLULAR CARCINOMA

H. Lubret[3], G. Lassailly[3], O. Goria[5], M. Azahaf[4], V. Gnemmi[1], H. Montialoux[5], S. Cattan[3], E. Boleslawski[2], S. Millet[2], S. Truant[2], F.R. Pruvot[2], P. Mathurin[3], S. Dharancy[3]

[1]Anatomo-pathologie; [2]Chirurgie Digestive; [3]Hépatologie; [4]Radiologie, Lille; [5]Hepatologie Rouen, Rouen, France

Introduction: The benefit of neo-adjuvant sorafenib (So) to keep pts with evolutive hepatocellular carcinoma (HCC) on liver transplant (LT) waiting list is unknown. The aims were to analyze: 1) the rate of drop out for HCC progression, 2) The tolerance of So, 3) the radiological response mRECIST, 4) The morbidity after LT and 5) post-LT HCC recurrence rate.
Methodology: All pts registered on waiting LT list between June 2010 and December 2014 for HCC and treated with So were identified. So tolerance was examined at each visit. Radiological evaluation was performed every 3 months. Postoperative morbidity was recorded. A biannual screening for recurrent HCC by thoraco-abdominal CT was performed.
Results: Among 139 pts were enrolled on TH waiting list for HCC, 32 pts were treated with So. All the pts except one had AFP score <3. So was used to avoid drop out from the waiting list for HCC progression in the majority of cases. 1) 11 pts were transplanted after a waiting period of 12.5 months; 2) The main side effects were diarrhea motor and hands foot syndrome; 3) In pts transplanted, the mRECIST response found stability or partial response in 73% of cases 4) 3 pts underwent further surgery and 3 pts presented early biliary strictures, 5) 3 pts presented recurrent HCC after mean time of follow up of 31 months. 3 years recurrence free survival was at 47%.
Conclusion: The use of neoadjuvant So allowed to transplant only one third of pts. Radiological response mRECIST under-estimated the histological analysis of native livers. Post-LT morbidity seemed high. In a context of graft scarcity, a 3 years recurrence free under 50% discourage this strategy awaiting liver transplant with current allocation system for HCC.

O55 COMPARISON BETWEEN C1Q AND C3D COMPLEMENT-BINDING ABILITY IN SERA OF KIDNEY TRANSPLANT RECIPIENTS WITH DSA

S. Caillard[2], A. Parissiadis[1], G. Gautier Vargas[2], J. Olagne[2], A. Essaydi[1], N. Froelich[1], B. Moulin[2]

[1]Laboratoire d'histocompatibilité, Etablissement Français du sang; [2]Service de Néphrologie et Transplantation, Hôpitaux Universitaires, Strasbourg, France

Recent studies have suggested that complement fixing HLA Ab play an important role in transplantation. The aim of the study was to compare the ability of DSA to bind C1q and C3d and to investigate the correlation between IgG fluorescence intensity (IgG MFI) value in standard SAB and the positivity of C1q and C3d respectively.
Patients and methods: Sera obtained at the time of the biopsy in kidney allograft recipients with DSA who underwent biopsy for cause were screened by SA (normalized MFI for One Lambda, kits LS1A04, LS2A01 One Lambda, and BCM IgG value for Immucor kits LSA1, LSA2), and retested with C1q (MFI cutoff >300, One Lambda) and C3d (Immucor). Allograft biopsies were reclassified according to Banff 2013 and c4d staining was performed using immunofluorescence.
Results: 81 patients had 134 DSA specificities (28 class I and 106 class II). Among them, 49 had one DSA, 21 had 2 DSA, 6 had 3 DSA, 5 had 4 DSA and 1 had 5 DSA. Among the 134 DSA, 53 were c1q positive (40%), 52 were c3d positive (39%). The concordance between c1q and c3d positivity was 90%: 46 DSA were c1q+/c3d+, 75 DSA were c1q−/c3d−, 7 DSA were c1q+/c3d− (B35, Cw4, DQA1*05:01, DQ5, DQ5, DQ6 and DQ7) and 6 DSA were c1q−/c3d+ (DR4, DR7, DR9, DR15, DQ7, DPB1*03:01). Concordance between c1q/c3d positivity and c4d staining was 55% (14 cases c1q+/c3d+/c4d+ and 31 cases c1q−/c3d−/c4d−). We observed a high concordance between MFI value and C1q/C3d reactivities: MFI > 10,000/C1q+: 92%; MFI > 10,000/C3d+: 100%; MFI < 5000/c1q−:94%, MFI < 5000/c3d−: 100%. Five-year graft survival was not significantly associated to DSA ability to fix c1q ($p = 0.16$), c3d ($p = 0.29$), nor c4d staining ($p = 0.08$).
Conclusion: In our experience, DSA ability to fix complement is evaluated similarly by c1q and c3d positivities and strongly correlate with DSA MFI values.

O56 PHENOTYPIC STUDY OF KIDNEY TRANSPLANT PATIENTS PRESENTING *DE NOVO* DSA: A FRENCH MULTICENTER COHORT OF 96 CASES

L. Lanfranco[3], A. Grall[3], S. Ohlmann[11], C. Presne[1], B. Hurault De Ligny[4], F. Villemain[2], E. Heng[5], J. Rerolle[6], G. Touchard[8], R. Snanoudj[7], I. Etienne[10], O. Toupance[9], M. Buchler[12], P. Gatault[12], D. Bertrand[10], Y. Le Meur[3]

[1]CHU Amiens, Amiens; [2]CHU d'Angers, Angers; [3]CHU cavale blanche, Brest; [4]CHU Caen, Caen; [5]CHU G. Montpied, Clermont-Ferrand; [6]CHU de Limoges, Limoges; [7]APHP Necker, Paris; [8]CHU de Poitiers, Poitiers; [9]CHU de Reims, Reims; [10]CHU de rouen, Rouen; [11]CHU Strasbourg, Strasbourg; [12]CHU de Tours, Tours, France

Introduction: Development of *de novo* donor-specific anti-HLA antibodies (DSA) is a crucial event after kidney transplantation. Time to onset of *de novo* DSA and their impact on graft outcome are highly variable. We studied clinical and histological phenotype of kidney transplant patients with *de novo* DSA.
Method: This was a national multicenter cohort study using the ASTRE database and concerning 13 French centers. We included renal transplant patients with *de novo* DSA with or without degradation of renal function. Biopsies were performed at the time of DSA discovery.
Results: We reported 96 cases. The median time to onset of DSA was 5.2 years (0.02–17.97). Development of DSA occurred after the first year post transplantation for 74% of patients. The mean of MFI of the highest ranked DSA was 7444 (+/- 5227.8). Fifteen patients (15,6%) had class 1 DSA alone, 70 (72.9%) had class 2 DSA alone and 11 had both classes. Seventy-five percent of patients with class 2 DSA had an anti-DQ. In multivariate analysis neither post-transplant period, nor the type of DSA, nor the intensity of the MFI were predictive of the severity of the kidney damages on biopsy or renal function decline. Thirty-seven patients received a treatment, which was variable. This illustrates the heterogeneity of practices. After a follow-up of 2.1 $\pm$ 0.8 years, only the presence of transplant glomerulopathy (TG) was significantly associated with graft loss (28.9% vs 2.3%; $p = 0.001$). The presence of TG is associated with a longer DSA exposure (1.3 $\pm$ 1.9 vs 2.9 $\pm$ 3.9 years; $p = 0.016$). A TG score> 1.5 predicted graft loss with a sensitivity of 83.3% and 73.1% of specificity (AUC = 0.813; $p = 0.001$).
Conclusion: Development of *de novo* DSA is associated with different histological, clinical and immunological phenotypes. Transplant glomerulopathy when graft was exposed to de novo DSA is associated with graft loss.

O57 KIDNEY ALLOGRAFT HISTOLOGIC EVOLUTION AFTER TREATMENT OF ANTIBODY-MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

M. Joly[2], J. Olagne[2], A. Parissiadis[1], G. Gautier Vargas[2], N. Cognard[2], C. Muller[2], P. Perrin[2], L. Braun[2], F. Heibel[2], A. Essayidi[1], B. Moulin[2], S. Caillard[2]
[1]Laboratoire d'histocompatibilité, Etablissement Français du sang; [2]Service de Néphrologie et Transplantation, Hôpitaux Universitaires, Strasbourg, France

Antibody-mediated rejection (ABMR) is the main cause of graft loss. Despite a better understanding of its pathogenicity, the treatment is not consensual and prognosis factors need to be defined. The aim of our study was to describe histologic evolution after ABMR therapy.

In this retrospective, monocentric study, all ABMR diagnosed between 01/01/11 and 30/06/15, treated and then controlled by a second biopsy were included. All biopsies were scored according to Banff 2013 classification.

A total of 50 rejections (45 acute and 5 chronic) were diagnosed in 42 patients. ABMR occurred after a median post transplantation delay of 17.9 months [0.3–267.5]. Treatment included corticosteroids for 90% of patients, IVIg for 92%, plasmapheresis for 42% and Rituximab for 68% of patients. Acute histologic lesions significantly decreased between diagnosis and control biopsies (after a mean time of 5 ± 3.2 months): g: 2.18 ± 0.87–1.80 ± 1.07 ($p = 0.013$); ptc: 1.98 ± 1.19–1.44 ± 1.25 ($p = 0.004$), t: 1.08 ± 0.99–0.68 ± 0.84 ($p = 0.012$), i: 1.42 ± 1.03–1.00 ± 0.93 ($p = 0.015$) and c4d: 1.82 ± 1.40–0.67 ± 1.11 ($p < 0.001$). Chronic lesions increased: cg: 0.34 ± 0.72–0.68 ± 1.10, $p = 0.016$ and cv : 0.62 ± 0.90–1.06 ± 0.91, $p = 0.002$. No significant change in IF/TA score was observed. DSA titers significantly decreased after treatment and renal function remained stable between diagnosis and control times. At the end of follow-up, 8 patients lost their graft after a median time of 20 months [10–57 months]; 2 patients died (from infectious causes).

Despite an improvement of histologic parameters and a decreasing of DSA titers, renal function is not significantly improved at medium-term. The risk/benefit ratio of therapy has to be precisely evaluated for patients with ABMR.

O58 REFINEMENT OF HISTOLOGICAL CRITERIA OF ACUTE HUMORAL REJECTION IN SMALL BOWEL TRANSPLANTATION

M. Rabant[1], M. Racapé[1,3], O. Aubert[3], J. Bruneau[1], P. Barbet[1], L.M. Petit[1], F. Lacaille[1], O. Goulet[1], C. Chardot[1], J.L. Taupin[2], D. Canioni[1], J. Duong Van Huyen[1]
[1]4, Hôpital Necker – Enfants Malades; [2]Hôpital Saint Louis; [3]PARCC INSERM U970, Paris, France

Background: Diagnosis criteria of acute humoral rejection in small bowel transplantation (SBT) are not clearly defined, although the presence of preformed or *de novo* DSA has been reported to be deleterious for SBT survival.
Methods: We retrospectively studied all intestinal biopsies obtained in the first year of transplantation from our cohort of SBT patients (n = 23) between May, 2009 and November, 2014. We systematically looked for C4d staining, semi-quantitatively assessed according to the Banff 2007 classification, and for signs of cellular rejection (apoptosis), vascular lesions (capillaritis, thrombosis, hemorrhage congestion), oedema of the chorion, lamina propria inflammation and mucous ulcerations. Identification of anti-HLA DSAs and their ability to fix C1q was performed by Luminex Single Antigen.
Results: We assessed 345 biopsies (17 ± 6 biopsies per patient) from these 23 patients. Among these patients, 3 did not develop DSAs. From the remaining 20 DSA+ patients, 7 (35%) had a C1q-binding DSA. 78 biopsies (22.6%) were C4d+ (grade≥2). Multivariate logistic regression analysis revealed that 3 histological parameters were independently and significatively associated with the presence of C4d on the biopsy: capillaritis (OR 2.883, $p = 0.003$), mucosal ulceration (OR 3.429, $p = 0.003$) and presence of apoptosis (OR 1.957, $p = 0.036$). Patients with less than 15% of C4d+ biopsies had a better graft survival (86% at 2 years) compared to patients with 15–30% of C4d+ biopsies (53% at 2 years) and to patients with more than 30% of C4d+ biopsies (18% at 2 years, log-rank test $p = 0.0015$).
Conclusion: The presence of C4d positive biopsies (grade≥2) in the first year of SBT is significantly associated with capillaritis, ulceration and apoptosis, as well as a worse graft survival at 2 years. These histological signs are relevant for acute humoral rejection diagnosis in SBT.

O59 2015 NATIONAL EXTERNAL PROFICIENCY TESTING: EVALUATION OF ACCEPTABLE AND UNACCEPTABLE HLA SPECIFICITIES ASSIGNMENT BY FRENCH LABORATORIES IN THE NATIONAL ORGAN TRANSPLANT ALLOCATION PROGRAM

C. Gautreau[1], P. Loiseau[1], A. Guyard[2], M. Deschênes[2]
[1]Laboratoire d'Immunologie et d'Histocompatibilité, Hôpital Saint Louis, APHP, Paris; [2]Agence nationale de sécurité du médicament et des produits de santé, Saint Denis, France

Introduction: In France, the determination of acceptable and unacceptable HLA specificities (HLA-Sp) by Luminex Single Antigen assay (LSA) allows virtual crossmatching and kidney organ allocation. Highly sensitized patients can benefit from a national priority through an acceptable mismatch program. LSA is not considered a standardized quantitative assay and unacceptable HLA-Sp identification is based on locally-determined cutoffs. Following national recommendations, acceptable HLA-Sp must exhibit MFI below 500. The aim of the study was to evaluate the uniformity between laboratories for HLA-Sp assignment in the national organ allocation program.
Methodology: Four sera were sent to laboratories participating to the national EPT. Laboratories reported the reagent provider, acceptable or unacceptable HLA-Sp results for HLA-A, B, DR, DQ and MFI cutoff. According to the recommendations from the European Federation of Immunogenetics, an agreement is considered reached if an HLA-Sp is identified by more than 75% of laboratories.
Results: Twenty five HLA laboratories participated to the survey. Cutoffs ranged from 500 to 2000 whatever the reagent used (One Lambda or Immucor). For each serum, 64 Class I and 25 Class II HLA-Sp were analyzed. Considering the 4 sera, acceptable and unacceptable reported HLA-Sp altogether, laboratories reached the 75% consensus in 91% (71.9–100%) of Class I HLA-Sp and 95% (84–100%) of Class II HLA-Sp.
Conclusion: This study aimed to evaluate the level of consensus in the assignment of acceptable and unacceptable HLA specificities by French histocompatibility testing laboratories. Depending on the tested serum, 72% to 100% of HLA–Sp reached the 75% consensus despite the diversity of chosen reagents and MFI cutoffs.

O60 IMPACT OF TOXICITY MECHANISM OF HLA DONOR SPECIFIC ANTIBODIES AND POLYMORPHISMS IN HOST INNATE IMMUNOREGULATORY GENES ON MORTALITY AND DEVELOPMENT OF CHRONIC REJECTION (CLAD) IN LUNG TRANSPLANTATION: DELETERIOUS EFFECT OF FCGR2A CD32 [131R/R] POLYMORPHISM

A. Basire[1], M. Reynaud-Gaubert[2], J. Di Cristofaro[3], A. Loundou[4], P. Paule[5,6], M. Pelardy[1], L.U.C. Lyonnet[5], C. Frassati[1], C. Gomez[2], P. Thomas[7], C. Picard[1,3]
[1]1. 1. Laboratoire Immunogénétique, Établissement Français du Sang Alpes Méditerranée; [2]Service de Pneumologie et Transplantation Pulmonaire, CHU Nord Faculté de Médecine, URMITE – CNRS-UMR 6236 Aix Marseille Université; [3]UMR 7268 ADÉS Aix-Marseille Université /EFS /CNRS; [4]Département de santé publique -EA 3279, Assistance Publique-Hopitaux Marseille AP-HM, Aix-Marseille Université; [5]Laboratoire d'hématologie, Assistance Publique-Hopitaux Marseille AP-HM; [6]UMR-1076, Aix Marseille Université AMU, INSERM; [7]Service de Chirurgie Thoracique et Transplantation Pulmonaire, CHU Nord Faculté de Médecine, URMITE – CNRS-UMR 6236, Aix Marseille Université, Marseille, France

We investigated the impact of mechanisms of toxicities of HLA Donor specific antibodies and polymorphisms in host innate immunoregulatory genes on the mortality and the development of chronic rejection (CLAD) in 176 Lung transplantation (LTx) recipients. Complement-binding antibodies were detected retrospectively for patients with de novo DSA at M1 and M3 after LTx, using the C1q and C3d luminex assays. CD16 engagement were assessed within PBMC effector cells by flow cytometry analysis of the decrease of MFI CD16 at the surface of CD3-CD56 NK cell subsets exposed to allogeneic target cells in presence of DSA. The single-nucleotide polymorphisms (SNPs) of CD32 [131H/R], and CD16 [158F/V], genes encoding the Fc gamma receptor (FcgR), were genotyped by SNAP SHOT method. During the study period, 39 LTx recipients developed CLAD (including 8 patients (20%) with RAS and 31 (80 %) with Bronchiolitis Obliterans) and median overall survival was 35 (+/- 30) months. DSA were detected in 31% of LTx at M1 and 18% at M3. DSA at M3 were associated to lower survival ($p = 0.02$) and CLAD occurrence ($p = 0.01$). C1q bind 48% and 33% of DSA at M1 and M3, respectively. C1q binding DSA at M1 and M3 were not correlated to MFI DSA intensity and clinical occurrence. CD16 polymorphisms were not associated to clinical occurrence and CD16 engagement was independent to C1q binding and MFI DSA intensity. In contrast, in univariate analysis, FCGR2A [131R/R] were associated to lower survival ($p = 0.002$) and chronic rejection occurrence ($p = 0.05$) but not with infectious risk in first year ($p = 0.88$). Cox proportional hazard regression showed a worse prognosis in LTx recipients with FCGR2A

[131R/R] (OR = 1.2, 95% CI 1 to 10.2, p = 0.05).
Finally, these data show that immunologic characteristics of DSA in LTx are different to these of DSA in other organ transplantation. They should be confirmed by another larger LTx cohort.

O61 REGULATORY T LYMPHOCYTES PROFILE AS A POSSIBLE PREDICTIVE BIOMARKER OF THE BRONCHIOLITIS OBLITERANS SYNDROME AFTER LUNG TRANSPLANTATION IN HUMANS

M. Durand[1,3], P. Lacoste[2,3], C. Brosseau[1,2], E. Durand[2], J. Loy[2], P.J. Royer[2], A. Magnan[2], S. Brouard[1]
[1]CRTI – ITUN – INSERM UMR 1064; [2]UMR INSERM 1087 CNRS 6291, Institut du Thorax; [3]Université de Nantes, Nantes, France

Although immunosuppressive drugs dramatically improve acute rejection management in the last decades, the irreversible chronic allograft dysfunction (CLAD) remains a therapeutic challenge for the long-term graft survival in lung transplantation (TP). For Bronchiolitis Obliterans Syndrome (BOS), the main form of CLAD, both immune mechanisms involved and predictive biomarkers have to be better defined. The COLT (Cohort in Lung TP), initiated in order to understand the physiopathology of CLAD, gave us the opportunity to follow the immune profile of the patients from the TP to the BOS occurrence.

The lymphocyte profile of 5 stable (STA) and 5 BOS patients was investigated before TP, 1–6 months after TP, 6 months before BOS and at the BOS diagnosis. PBMCs were analysed by flow-cytometry with the "classical" T-cells markers: CD3, CD4, CD25, CD45RA, and FoxP3. CXCR3, CCR6, CD39, CD73 CD15s and PD1 were also added to go deeper in the helper (Th) and regulatory T cells (Tregs) subsets.

Monitoring doesn't show any significant difference between patients who will report a BOS in the 4 years and STA in the proportions of common CD4 and CD8 T cells subsets. We highlight an increase in $FoxP3^+$ Tregs proportion 1–6 months post-TP in BOS compared to STA (0.85% and 3.36% in STA and BOS respectively, $p < 0.005$). We validated this profile on 33 STA and 25 BOS patients (1.61% and 3.18% in STA and BOS respectively, $p < 0.001$). Then, the analysis of the Tregs subsets denotes mainly memory Tregs ($CD45RA^-$ and $CD39^+$) are responsible for the Tregs increase found in BOS patients. Finally, we show that unlike Acute Rejection, the BOS survival is significantly increased in patients with a low proportion of Tregs 1–6 months post-TP (41% and 75% in $_{hi}$Tregs and $_{low}$Tregs respectively, $p < 0.01$).

In conclusion, we lead to identify Regulatory T cells as new potential predictive biomarkers of the BOS including both phenotypical and functional modalities in humans.

O62 KIDNEY TRANSPLANT TOLERANT PATIENTS DISPLAY B CELLS WITH GZMB REGULATORY B CELLS THAT MAY BE EXPAND IN VITRO

M. Chesneau[2,1], S. Le Bot[1,2], A. Chenouard[1,2,3], P. Guerif[1], M. Giral[1,3,2], S. Brouard[1,2,3]
[1]CHU; [2]4, INSERM UMR 1064; [3]université de Nantes, Nantes, France

Introduction: Whereas a B cell transcriptional profile has been recorded for operationally tolerant kidney recipients, their role in this process of tolerance has not been reported yet. We analyzed the phenotype of B cells from operationally tolerant patients, healthy volunteers and kidney-transplant recipients with stable graft function and their suppressive functions on T cell response.
Methods: Suppressive properties of autologous B cells were tested on proliferation, apoptosis and type I pro-inflammatory cytokine production by effector $CD4^+CD25^-$ T cells after anti-CD3/anti-CD28 stimulation. Mechanisms of suppression were studied in transwell co-culture and usage of inhibitors (anti IL-10, anti TGF-b and anti GzmB). Regulatory B cells were then expanded using different stimulation pathways and their suppressive properties was tested after expansion in vitro.
Results: We report that tolerant recipients harbor a higher number of B cells expressing GzmB and able to inhibit $CD4^+CD25^-$ effector T cell proliferation in a dose dependent manner. This effect needs B cells to interact with their T cell targets and acts through a dose dependant GzmB pathway. Interestingly, we showed that it is possible in vitro to expand by 10 fold the proportion of these $GzmB^+$ B cells depending on IL-21 activation, BCR stimulation and low stimulation by CD40L and ODN. In vitro expanded GzmB+ regulatory B cells still keep a regulatory function on $CD4^+CD25^-$ effector T cell proliferation after 3 days of expansions.
Conclusion: These data provide novel insights into the characterization of B cell–mediated immune-regulation in tolerance in clinic and may constitute a useful therapeutic tool in solid organ transplantation and autoimmune diseases.

O63 FOLLICULAR HELPER T CELLS EXPRESSION IN RENAL TRANSPLANTED RECIPIENTS TREATED WITH BELATACEPT (CTLA4-IG)

C. Leibler[1,2], A. Thiolat[1], C. Pilon[1], J. Cohen[1], P. Grimbert[1,2]
[1]Equipe 21, INSERM U955; [2]Hôpital Henri Mondor, Service de Transplantation rénale et Néphrologie, Créteil, France

Recent clinical results have demonstrated that kidney recipients treated with Belatacept displayed better graft survival and a lower incidence of de novo DSA when compared to control patients treated with CNI. Folicular Helper T cells are specialized cells responsible for plasma-cells induction. The aim of the study was to determine if CTLA4-Ig could modulate TFH expression.

We conducted a comparative flow-cytometry analysis of circulating TFH (cTFH), defined by the markers CD3 + CD4 + CD45RA-CXCR5 + , in kidney transplanted patients with stable graft function. The patients were divided in 3 groups and were compared to healthy blood donors : (A) Naive patients (with absence of HLA sensitization before the transplantation) treated with CTLA4-Ig for 10 years (n = 6), (B) Naive patients treated with CNI for 10 years (n = 10) and (C) Sensitized patients (with presence of DSA with MFI <3000 before kidney transplantation) treated with CTLA4-Ig for 1 year (n = 8).

The mean frequencies of memory T lymphocytes and cTFH among T cells were significantly lower in the naive patients treated with CTLA4-Ig as compared to the CNI group (p = 0.025 et 0.0025). The decrease in expression was observed in all the 3 cTFH subgroups (cTFH 1.2 and 17). Moreover, whereas global memory T cells frequencies were higher in the sensitized group of patients treated with CTLA4-Ig in comparison to naive patients treated with CTLA4-Ig, cTFH expression among memory T cells was similar in both groups.

Our results suggest that CTLA4-Ig impairs memory T cells development in naive but not sensitized patients. Moreover, CTLA4-Ig decreases cTFH expression, even in patients with pre-formed memory T cells. This mechanism could be involved in the lower level of DSA secretion observed in CTLA4-Ig treated patients.

O64 CTLA4-IG AND B-CELLS: A DIRECT IMPACT?

C. Leibler[1,2], A. Thiolat[1], C. Pilon[1], J. Cohen[1], P. Grimbert[1,2]
[1]Equipe 21, INSERM U955; [2]Hôpital Henri Mondor, Service de Transplantation rénale et Néphrologie, Créteil, France

Kidney recipients treated with Belatacept (CTLA4-Ig) have a lower incidence of de novo DSA and displayed a different distribution of B-cells subpopulations when compared to control patients treated with CNI, suggesting a specific drug's regulatory effect on B-cells biology. Since, B-cells express CTLA4 ligands at their surface (CD80 and CD86 molecules), the aim of this study was to determine whether CTLA4-Ig had a direct impact on B-cells functionality.

Firstly, we characterized in blood sample of kidney transplanted patients the distribution of CD80–CD86 expression according to B-cell subsets. By designing several models of in vitro activation, we analyzed the impact of CTLA4-Ig on cultured B-cells. We assessed their proliferation (by CFSE), mortality (by 7AAD), plasma-cells differentiation (by cytometry analysis) and immunoglobulin (Ig) production (by luminex assay) at day 5 and 10 of the experiments.

The distribution of CD80 and CD86 varied according to the maturation stage of B-cells subsets but their expression was significantly decreased in kidney recipients treated with CTLA4-Ig. We demonstrated that, in vitro, CTLA4-Ig blocked IgG production and particularly IgG3 (p = 0.03) whereas there was only a slight decrease in plasmablasts frequencies (Fold decrease = 10%) and no impairment of B-cells survival and proliferation.

Our results suggest that CTLA4-Ig may directly impair functions of terminally differentiated B-cells (plasmablasts) by decreasing Ig production without acting on other B-cells function (mortality, maturation, proliferation).

O65 A NEW POPULATION OF $IFNG^+IL10^+IL34^+$ SECRETING HUMAN $CD8^+CD45RC^{LOW}$ TREGS EFFICIENTLY INHIBITS ANTI-DONOR IMMUNE RESPONSE IN TRANSPLANTATION

S. Bézie, L. Boucault, V. Daguin, I. Anegon, C. Guillonneau
INSERM UMR1064, Nantes, France

Introduction: We previously reported the suppressive properties of rat $CD8^+CD45RC^{low}$ T cells. To date, human counterparts have never been studied for their relevance as regulatory cells.
Materials and Methods: Cell populations were sorted from PBMCs from healthy volunteers by FACS Aria. Cytokine secretion assay detection kits were used to sort IFNg and/or IL10 secreting Treg subpopulations. Tregs were cultured in vitro with syngeneic $CD4^+CD25^-$T cells and allogeneic APCs to analyze their suppressive function. $CD8^+CD45RC^{low}$Tregs were expanded for 14 days with cytokines and allogeneic stimulation. PBMCs with or without expanded Tregs were infused into NSG mice models of GVH and allograft.
Results: Compared to $CD45RC^{high}$ subset, $CD45RC^{low}$ cells expressed higher levels of PD1, CD122, Foxp3, GITR and HLADR, as well as IL34, IL10, TGFb1 and IFNg. We demonstrated that $IFNg^+IL10^+$ secreting

$CD8^+CD45RC^{low}$ T cells inhibited more efficiently allogeneic responses in vitro than classical $CD4^+CD25^{hi}CD127^-$ Tregs. We confirmed the involvement of IL10, IFNg and IL34 cytokines in Tregs suppressive function by adding blocking antibodies to the co-culture assay. We identified their mechanisms of action as mediated by IL-2 deprivation, and preferential contact with pDCs, but not cytotoxicity. Finally, we observed that these Tregs can be efficiently expanded, until 1055 (±131) fold in 14 days. Following expansion, Tregs were enriched in $Foxp3^+$ $IL34^+$ $IL10^+$ and $IFNg^+$ cells and possessed a strong suppressive function. Indeed, transfer of expanded Tregs significantly delayed in a dose dependant manner GVH development and allogeneic skin graft rejection in humanized mice infused with human PBMCs.
Conclusions: We identified and characterized a new natural regulatory T cell population efficiently inhibiting anti-donor immune response.

O66 A COMPOSITE SCORE ASSOCIATED WITH CLINICAL OPERATIONAL TOLERANCE IN KIDNEY TRANSPLANT RECIPIENTS

R. Danger[4,5], M. Chesneau[4,5], C. Paul[4,5], P. Guérif[4,5], M. Durand[4,5], K.A. Newell[8], L.A. Turka[10], S. Kanaparthi[9], J.P. Soulillou[4,5], M. Sykes[11], R. Houlgatte[1,2], M. Giral[4,5,3,6], G. Ramstein[7], S. Brouard[4,5,3]
[1]DRCI, CHU de Nancy; [2]INSERM UMR 954, Nancy; [3]CIC Biotherapy; [4]Institute of Transplantation, Urology and Nephrology ITUN, CHU de Nantes; [5]INSERM UMR1064; [6]Faculté de Médecine, Université de Nantes; [7]LINA DUKe, UMR 6241, Université de Nantes, Ecole des Mines de Nantes & CNRS, Nantes, France; [8]Department of Surgery, Emory University, Atlanta, Georgia; [9]Immune Tolerance Network, Bethesda, Maryland; [10]Center for Transplantation Sciences, Department of Surgery, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; [11]Columbia Center for Translational Immunology, Columbia University Medical Center, New York, New York, United States

Introduction: New challenges in renal transplantation include using biological information to devise a useful clinical test for discerning high- and low-risk patients for individual therapy and ascertaining the best combination and appropriate dosages of drugs.
Method: Based on a 20-gene signature from a microarray meta-analysis mostly centered on B cells, we applied a sparse methodology and selected significant variables to identify a minimal and robust combination of six genes and two demographic parameters associated with operational tolerance.
Results: This composite score of operational tolerance (cSoT) is able to discriminate operationally tolerant patients with an AUC of 0.97 (95% CI = 0.94–1.00). The cSoT is not influenced by immunosuppressive treatment, induction therapy, or post-transplant lymphoproliferative disorder history of patients. The cSoT is predictive of *de novo* appearance of anti-HLA antibodies in tolerant patients ($p = 0.0009$) and tolerance loss ($p = 0.025$). It was validated by quantitative PCR (AUC = 0.86, 95% CI = 0.66–1.00) and demonstrated specificity toward a model of tolerance induction.
Conclusion: This score would not only allow clinicians to identify candidate patients for immunosuppression minimization protocols but may prevent under- or over-immunosuppression by improving follow-up of patients across their transplant life, thus paving the way for individual therapy.

O67 BKV REPLICATION IN KIDNEY TRANSPLANT RECIPIENTS: TOWARDS AN EARLIER MARKER?

M. Solis[3,4], A. Velay[3,4], R. Porcher[1], P. Domingo-Calap[4], E. Soulier[4], M. Joly[2,4], M. Meddeb[3], W. Kack-Kack[3,4], B. Moulin[2,4], S. Bahram[4], F. Stoll-Keller[3,4], H. Barth[3,4], S. Caillard[2,4], S. Fafi-Kremer[3,4]
[1]Centre d'Epidémiologie Clinique CRESS, UMR1153, Université Paris Descartes, Paris; [2]Département de Néphrologie – Transplantation; [3]Laboratoire de Virologie, Hôpitaux Universitaires de Strasbourg; [4]Université de Strasbourg, Inserm UMR S1109, LabEx Transplantex, Fédération de Médecine Translationnelle de Strasbourg FMTS, Strasbourg, France

Introduction: BK virus-associated nephropathy (BKVN) is the most frequent BKV-associated disease after renal transplantation. BKV viremia has shown a high positive predictive value for the development of BKVN, allowing preemptive immunosuppressive therapy adaptation. However, the delayed nature and incomplete success of this preemptive strategy underscore the need for prognostic markers of BKV replication. In this study, we aimed to develop a new marker that predicts BKV replication.
Material and methods: Five hundred and thirty samples were prospectively collected from 168 KTR on the day of transplantation and at additional time points post-transplantation. BKV DNA load was quantified using a commercial qPCR. BKV strains of KTR displaying viruria and/or viremia were genotyped by sequencing analysis. Anti-BKV neutralizing antibodies (Nabs) titers were measured using the BKV pseudovirus system (Pastrana et al, J Virol 2013).
Results: BKV viruria was detected in 52 KTR and BKV viremia was observed in 28 patients, among them 13 developed BKVN. In BKV-replicating KTR, BKV genotype I, genotype II and genotype IV strains were identified in 45, 1 and 6 patients, respectively. Anti-BKV Nabs were positive in 97.6% of KTR before transplantation. The risk of developing viruria was higher for patients with lower Nabs titers before transplantation against their subsequently-replicating genotype (HR (95% CI) = 0.44 (0.25–0.76; $p = 0.003$). The replicating BKV is acknowledged to be of donor origin. Indeed, donor/recipient mismatches in regard to genotypic neutralization profiles and replicating strains were found to follow disease severity ($p < 0.05$).
Conclusion: Determination of anti-BKV Nabs titer in donors and recipients before transplantation may represent a valuable prognostic marker of BKV replication and allow for better-suited induction and maintenance immunosuppressive therapy as well as adapted viral monitoring.

O68 EFFECTIVENESS AND SAFETY OF AN IMMUNOSUPPRESSION REDUCTION PROTOCOL FOR THE TREATMENT OF BK VIREMIA IN KIDNEY TRANSPLANT RECIPIENTS

D. Hebmann[1], K. Moreau[1], I. Garrigue[2], L. Couzi[1,3], P. Merville[1,3], B. Taton[1,4]
[1]Unité de transplantation rénale, Hôpital pellegrin; [2]Laboratoire de virologie, Hopital Pellegrin; [3]CNRS-UMR 5164 Immuno ConcEpT, Bordeaux; [4]Institut de mathématiques UMR CNRS 5251, Université de Bordeaux, Talence, France

Objective: To evaluate the efficiency of an immunosuppression reduction protocol as a treatment of BK virus viremia in kidney transplant recipients.
Methods: This exhaustive retrospective study included all the patients who presented a BK viremia over 1000 copies/mL between 2012 and 2016 in our center. All of them followed a 2-stage immunosuppression reduction protocol. Stage 1: switch to cyclosporine (C0 target: 50—100 ng/mL in low immunological risk patients, 80—120 ng/mL in others) and corticosteroids removal or reduction. Stage 2, if viremia persisted after 12 weeks: cyclosporinemia C0 target decreased to 50—80 ng/mL, mycophenolate mofetil replaced by everolimus (C0 target: 3—8 ng/mL). Follow-up was 9 months from the beginning of stage 1. The associations of induction treatment, history of rejection or CMV infection, delay from transplantation to diagnosis and from diagnosis to treatment, initial viral load, with viral response (12-week undetectable viremia period) were assessed as response hazard-ratios (RHR) in multivariate Cox models.
Results: Of 49 patients were diagnosed with BK viremia and treated accordingly. Viral response was obtained in 42 (86%) of them (35 during stage 1, 7 during stage 2) within a mean delay of 276 ± 158 days. Three patients presented rejection (1 borderline, 2 acute cellular rejections). One responder (2.4%) and one non-responder (14.3%) lost their graft on BKv nephropathy and rejection. In multivariate analysis, viral response was associated with a lower viral load at the time of diagnosis (RHR: 2.26 per decade decrease, $p = 0.019$), and a shorter delay between time of diagnosis and reduction of immunosuppression (RHR: 3.6 for a diagnosis-to-treatment delay shorter that 17 days vs more, $p = 0.0061$).
Conclusion: Reduction of immunosuppression was effective in treating BK viremia, with an acceptable immunologic risk. Early diagnosis and reduction of immunosuppression were strongly associated with viral response.

O69 IMPACT OF LEFLUNOMIDE THERAPY ON *BK VIRUS* NEPHROPATHY IN KIDNEY TRANSPLANT RECIPIENT: A RETROSPECTIVE MULTICENTRIC STUDY

N. Keller[3], S. Duquennoy[1], A. Conrad[2], E. Morelon[2], B. Moulin[3], N. Bouvier[1], S. Fafi Kremer[4], S. Caillard[3], B. Hurault De Ligny[1]
[1]Service de néphrologie-dialyse-transplantation rénale, Hôpital de la Côte de Nacre, Caen; [2]Service de transplantation, néphrologie et immunologie, Hôpital Edouard-Herriot, Lyon; [3]Service de Néphrologie Transplantation; [4]Service de Virologie, Hôpitaux Universitaires, Strasbourg, France

Background: BK virus nephropathy (BKVN) is a major issue in kidney transplant recipient and may lead to graft failure. There is no specific treatment and the impact of Leflunomide, an antiviral and immunosuppressive drug, has not been clearly evaluated yet. We report the results of a retrospective study exploring the impact of Leflunomide on patients with BKVN.
Methods: A retrospective and multicentric (Lyon, Caen and Strasbourg) study was performed in patients with biopsy-proven or presumed BKVN between 2007 and 2016 who received Leflunomide therapy. Graft function, viral clearance, immunosuppression level and risk of rejection were analysed.
Results: Of 57 patients were included with a mean follow up of 1138 ± 720 days. Median time from transplantation to diagnosis of BKVN was 213 days (48–1469 days) with a mean serum creatinine level of 193 ± 71 μmol/L at diagnosis. Leflunomide was introduced after failure of immunosuppression lowering (mean 37.7 ± 38%). The time from BKVN diagnosis to Leflunomide introduction was 41 ± 26 days (mean dose 28 ± 7 mg/days). At the end of the follow-up, 21% of the patients lost their graft and 5% deceased. Serum creatinine level was stable during the follow up.

BK-viremia clearance was obtained in 65% of patients after a median time of 277 days (21–1940 days). Graft rejection occurred in 32% of recipients after Leflunomide introduction. 19% of patients stopped Leflunomide (for side effects or rejection).
Conclusion: Leflunomide therapy seems to stabilize graft function but viral clearance was long to obtain and rate of rejection was substantial. A randomized control trial is necessary to definitely conclude about the effect of Leflunomide in NBKV treatment.

O70 SOFOSBUVIR-BASED REGIMEN FOR HCV RECURRENCE AFTER COMBINED LIVER-KIDNEY TRANSPLANTATION: RESULTS FROM THE ANRS CO23 CUPILT STUDY

S. Dharancy[9], A. Coilly[24], C. Fougerou-Leurent[19], C. Duvoux[6], N. Kamar[22], V. Leroy[14], A. Tran[14], P. Houssel-Debry[18], V. Canva[9], C. Moreno[3], F. Conti[16], J. Dumortier[11], V. Di Martino[1], S. Radenne[11], V. De Ledinghen[2], L. D'alteroche[23], C. Sylvain[17], C. Besch[21], P. Perre[8], D. Botta-Fridlund[12], C. Francoz[5], F. Habersetzer[21], H. Montialoux[20], A. Abergel[4], M. Debette-Gratien[10], A. Rohel[15], J.C. Duclos-Valle[24], G.P. Pageaux[13]
[1]Besançon; [2]Hépatologie, Bordeaux; [3]Hépatologie Erasme, Bruxelles; [4]Hépatologie, Clermond Ferrand; [5]Hépatologie Clichy, Clichy; [6]Hopital Henri Mondor, Créteil; [7]Grenoble; [8]Hépatologie, La Roche Sur Yon; [9]CHRU Lille, Lille; [10]Hépatologie, Limoges; [11]Hepatologie, Lyon; [12]Marseille; [13]Hépatologie, Montpellier; [14]Hepatologie, Nice; [15]ANRS; [16]Hopital Pitié Salpetriere, Paris; [17]Poitiers; [18]Hépatologie; [19]Pharmacologie, Rennes; [20]Rouen; [21]Hépatologie, Strasbourg; [22]Néphrologie, Toulouse; [23]Hépatologie, Tours; [24]Centre hépato-biliaire APHP, Villejuif, France

HCV infection is associated with lower patient survival following simultaneous combined liver kidney transplantation (CLKT). There are some concerns on renal function in transplanted patients treated with second generation direct acting antiviral (DAA). Study aims were to assess efficacy and tolerance of sofosbuvir (SOF)-based regimen in these difficult-to-treat patients.
Methodology: The ANRS CO23 CUPILT study is a prospective cohort including patients with HCV-recurrence following LT treated by second generation DAAs. The present work focused on patients treated for HCV recurrence after CLKT. Patients were followed at W0, W2, W4, W8, W12, W24, end of therapy (EOT), follow up W12 (FU12).
Results: The study population included 20 (15M/5W) patients, aged 57.5 years. CLKT were performed for dialyzed pts (32%) or for LT candidates with chronic renal dysfunction (68%). At baseline, liver fibrosis stage was F0–F2 in 45%, F3 in 15%, F4 in 25%, and 15% presented fibrosing cholestatic hepatitis. Median duration between CLKT and initiation of DAA was 58.7 months. At baseline, HCV viral load and glomerular filtration rate (GFR) (MDRD formula) were 6.4 log10 IU/mL and 50.9 mL/min. Median duration of therapy was 23.9 weeks. Among 20 pts who have completed the treatment, the EOT response was achieved in 100%. At time of analysis 19/19 (100%) pts achieved SVR12. In terms of tolerance, GFR decreased significantly from baseline value 50.9 mL/min to 41.8 mL/min at W12 ($p < 0.0001$), 41.4 mL/min at EOT ($p = 0.0001$) and to 42.7 at FU12 ($p = 0.0001$). 45% of pts presented, at least, one serious adverse event. Blood transfusion and EPO were required in 20% and 45% respectively. No pts experienced acute rejection and no pts deceased during the follow up.
Conclusion: SOF based regimen showed excellent results in terms of efficacy in CLKT pts. However, GFR significantly decreased during and after DAA treatment. Intensive renal function monitoring should be done in those patients.

O71 PREDICTIVE FACTORS OF SPONTANEOUS CMV VIRAL LOAD CLEARANCE IN KIDNEY TRANSPLANTATION

J. Noble[3], P. Gatault[3], H. Longuet[3], C. Baron[3], J.M. Halimi[3], C. Gaudy-Graffin[2], E. Mounteanu[1], S. Alain[1], M. Buchler[3]
[1]CNR des cytomegalovirus, CHU Dupuytren, Limoges; [2]Laboratoire de Virologie; [3]Service Néphrologie-transplantation, CHU Tours, Tours, France

Introduction: In kidney transplantation, cytomegalovirus (CMV) reactivation is associated with increased morbidity and mortality. The threshold of PCR value to benefit a curative treatment is not known. The purpose of this study was to assess predictive factors associated with spontaneous clearance of CMV viremia in kidney transplant recipient
Material and methods: All kidney recipients in a single center were recruited. Patients with at least one positive CMV viremia were included in our analysis. CMV infection was identified by PCR to detect CMV DNA in whole blood, using Abbott® RealTi*m*e CMV, calibrated according to WHO standard and expressed in log IU/mL (Detection = 1.79 UI log/mL). Prophylaxis was given for 3 months for R+ and 6 months for D+R-. Clinical and biological symptoms attributable to CMV were collected. We defined as rapid spontaneous CMV clearance when PCR became undetectable before the fourth control. Results were expressed as mean ±SD
Results: Three hundred and ninety patients were transplanted between 05/2012 and 05/2015. 150 patients had at least one positive CMV PCR. 55 (36%) had spontaneous undetectable viral load. PCR was still positive after four controls in 29 patients (19%). Sixty-six (45%) patients were treated. D+R- patients were less frequent in the group of patients with spontaneous undetectable viral load (12.7 vs 34.7%, $p = 0.004$). Factors associated with CMV clearance without treatment were initial PCR level lower than 4 log UI/mL (1.8 vs 20%, $p = 0.001$), absence of increase of the viral load more than 1 log UI/mL (4.2 vs 39.7%, $p < 0.0001$), absence of clinical symptoms (fever, asthenia and diarrhea, $p = 0.036$, $p = 0.011$ and $p = 0.0001$ respectively) and absence of biological abnormalities (acute thrombopenia and leukopenia, $p = 0.0001$ and $p = 0.0001$)
Conclusion: A score using these factors may be used to predict spontaneous clearance of CMV viral load after a first viremia in kidney transplantation and avoid treatment and/or hospitalization

O72 VALGANCICLOVIR FOR EBV PREVENTION IN PEDIATRIC RENAL TRANSPLANTATION

E. Cheyssac[5], V. Baudoin[7], R. Novo[2], M. Charbit[6], B. Ranchin[3], M. Fila[4], S. Decramer[10], E. Merieau[11], J. Harambat[1], A. Zaloszyc[9], A. Ryckewaert[8], G. Roussey[5]
[1]Service de Néphropédiatrie, CHU Bordeaux, Bordeaux; [2]Service de Néphropédiatrie, CHRU Lille, Lille; [3]Service de Néphropédiatrie, Hospices Civils de Lyon, Lyon; [4]Service de Néphropédiatrie, CHU, Montpellier; [5]4, CHU Nantes, Nantes; [6]Service de Néphropédiatrie, Hopital Necker Enfants Malades; [7]Service de néphropédiatrie, Hopital Robert debré, Paris; [8]Service de pédiatrie, CHU Rennes, Rennes; [9]Service de Néphropédiatrie, CHU Strasbourg, Strasbourg; [10]Service de Néphropédiatrie, CHU Toulouse, Toulouse; [11]Service de Néphropédiatrie, CHU Tours, Tours, France

Introduction: EBV primoinfection (PI) or reactivation is a serious concern in pediatric renal transplantation because of the frequency of EBV-seronegative (EBV-) recipients and seropositive (EBV+) donors. Valganciclovir (VGC) is commonly used for CMV prophylaxis but its efficacy for EBV prevention is questionable.
Patients and Methods: Inclusion criteria were: recipients under 18 years, renal transplantation performed between 01/01/2012 and 30/06/2013, EBV- recipient with an EBV+ donor (group at risk of PI) or EBV + recipients (group at risk of reactivation). VGC was administered for EBV or CMV prophylaxis, according to the common use in each center. A severe EBV infection was defined as a PTLD, a symptomatic infection and/or a high blood viral load (>4.5 log/mL). Groups with prophylaxis (P+) or not (P-) were compared with Chi-2, Fischer, Student or Wilcoxon tests, according to the data.
Results: 79 children were included, 57 of them (72%) in the P+ group, 22 (28%) in the P- group. 25 (31%) were in the group at risk of PI, 54 (69%) in the group at risk of reactivation. Incidence of severe EBV infection was 22.8% in the P+ group, and 22.7% in the P- group, ($p = 0.99$). In the group at risk of PI, 42% of the patients of P+ had a severe EBV infection vs 33.3% in the P- group ($p = 1$). There was no significant difference for severe EBV infection in the group at risk of reactivation (13% in P+ vs 18% in P-, $p = 0.68$). Neutropenia was more frequent in the P+ group than in the P- group (66.7% vs 33.4%, $p = 0.005$)
Discussion and conclusion: The results of this small cohort do not support the effectiveness of VGC for the prevention of EBV infection in pediatric renal transplantation. However the risk of neutropenia is more frequent.

O73 HEPATIC ISCHEMIA-REPERFUSION INJURY ASSOCIATED WITH ACUTE KIDNEY INJURY IN LIVER TRANSPLANTATION: PROSPECTIVE COHORT STUDY

I. Jochmans[1], N. Meurisse[2], D. Monbaliu[1], J. Pirenne[1]
[1]Department of Abdominal Transplant Surgery, University Hospitals Leuven, KU Leuven, Belgium, Leuven; [2]Department of Abdominal Transplant Surgery, University of Liege Academic Hospital, ULg CHU, Belgium, Liege, Belgium

Acute kidney injury (AKI), a major risk factor for poorer outcome after liver transplantation (LT), is usually attributed to renal ischemia and drug toxicity. In rodents, hepatic ischemia-reperfusion injury (HIRI) has been shown to cause AKI but solid clinical prospective evidence is missing. We investigated the association between HIRI and AKI during LT in a prospective cohort study. In 80 adult LT recipients with normal pre-transplant renal function, AKI was assessed by RIFLE-criteria from baseline to hepatectomy, reperfusion, and early postreperfusion until postoperative day (POD) 5. Urinary kidney-injury-molecule-1 (KIM-1) and plasma heart-type-fatty-acid-binding-protein (H-FABP), were compared between Injury/Failure-patients and matched cohort without AKI. Cardiac output (CO) was measured throughout LT and peak AST reflected HIRI. Logistic regression determined AKI risk factors. 21 patients (26%) developed AKI at 12 h (IQR: 6 h-POD1) postreperfusion; 13 progressed from Risk to Injury; 5 to Failure. Demographics were similar between

AKI-patients and those without AKI. Cold ischemia time was longer in AKI-patients ($p = 0.004$) with higher peak AST ($p < 0.001$), more early allograft dysfunction ($p < 0.001$), and longer ICU/hospital stay. In AKI-patients, creatinine (Scr) started to increase during LT and was higher vs baseline at 6 h-POD4 while preoperative Scr remained stable in those without AKI. CO and tacrolimus trough levels were similar in both groups. H-FABP at 12 h was higher in AKI-patients. Peak AST, occurring at 6 h, was the only independent risk factor for AKI [adjusted odds ratio 2.42 (1.24–4.91), $p < 0.001$]. The occurrence of chronic kidney disease stage 2 or higher at 1 year was more frequent in AKI-patients (89% vs 58%). Patient survival at 1 year did not differ (90% in AKI vs 98% in no-AKI). In conclusion, AKI is initiated during OLT and its association with peak AST suggests HIRI as determinant.

O74 DUAL KIDNEY TRANSPLANTS AS POLICY TO OPTIMIZE THE ALLOCATION OF MARGINAL DONOR KIDNEYS: ANALYSIS OF THE FRENCH COHORT 2002–2014

E. Savoye[7], R. Snanoudj[5], C. Hiesse[8], M.N. Peraldi[4], A. Durrbach[1], N. Ouali[6], M. Durand[3], L. Badet[2], M.M. Macher[7]

[1]Hôpital Bicêtre, Le Kremlin-Bicêtre; [2]Chirurgie de la transplantation pav V et immuno clinique et TX pav p, groupe de l'hôpital Edouard Herriot, Lyon; [3]Hôpital Pasteur de Nice, Nice; [4]Hôpital de Saint Louis; [5]Hopital Necker; [6]Hôpital Tenon, Paris; [7]4, Agence de la biomédecine, Saint Denis; [8]Hôpital Foch, Suresnes, France

The aim of this national multicentre cohort study was to assess the outcomes of dual kidney transplantation (DKT) in terms of patient and graft survival and renal function, and to compare these results with those obtained from single kidney transplantation (SKT). Our analysis was restricted to first transplants performed between May 2002 and December 2014, with marginal donors, defined as brain death donors older than 65 years, with an estimated glomerular filtration rate (eGFR) lower than 90 mL/min. Recipients aged less than 65 with a PRA over 25% were excluded.

Survival rates were estimated using the Kaplan-Meier method. Cox and logistic models were used in multivariate analysis.

461 DKT and 1131 SKT were included in the analysis. DKT recipients had lower BMI, shorter waiting time and dialysis duration. DKT donors were older, had higher BMI, more frequently a history of hypertension and lower eGFR. Mean cold ischemia time (21 h) was 3 h longer for DKT.

While primary non function (PNF) (6%) and delayed graft function (DGF) (30%) did not differ between SKT and DKT, 1 year eGFR was lower in SKT recipients (39.5 vs 49.3 mL/min, $p < 0.001$). Graft survival and death-censored graft survival were significantly better in DKT even after adjustment for recipient and donor risk factors. Nevertheless no difference was found concerning patient survival. Three-years graft and patient survival rates for DKT vs SKT were respectively as follows: 79% vs 73% ($p = 0.003$) and 86% vs 85% ($p = 0.55$).

Good results obtained by DKT encourage teams to develop DKT whenever it's feasible. In a context of organ shortage, DKT appears to be a good option to optimize the use of kidneys from marginal donor otherwise discarded. When a kidney from a marginal donor is proposed, national regulation and transplant teams should decide between SKT or DKT by taking into account two main objectives: maximizing the use of grafts and reducing cold ischemic time.

O75 ORGAN PROCUREMENT FROM DCD III DONORS: EXPERIENCE OF A LOCAL COORDINATION TEAM FOR ORGAN DONATION

X. Merny[2], M. Bourguignon[2], M. Homerin[2], C. Schwartz[2], T. Panier[2], E. Henry De Frahan[2], C. Toumpsin[2], P. Hantson[2], D. Van Deynse[2], M. Mourad[2]

[1]Centre de transplantation; [2]Coordination locale de don, Cliniques St Luc, Université catholique de Louvain, Bruxelles, Belgium

Objective: To report, in an university transplantation centre, the experience of a local coordination team for organ donation from donors belonging to the Maastricht III category (DCD III).
Material and Methods: A retrospective analysis was performed from the medical charts of the DCD III donors between 01/01/2006 and 31/12/2015.
Results: 33 DCD III procedures could be performed within this period, while 80 procedures were performed from donors in brain death (DBD). The ratio between DCD III and DBD donors remained unchanged over the years. The mean age of the donors (20 M, 13 F) has ranged from 36.5 (2011) and 55.7 years (2013). Thirty donors were initially admitted in the Emergency Department and 19/33 could be considered as potential donors from hospital admission due to illness severity. During the same period, 73 potential procedures could not be achieved for various reasons: medical contra-indications (n = 31), non-identification of potential donors (n = 24), family refusal (n = 9), medico-legal issue (n = 3), logistic problems (n = 3), other (n = 3). The main diagnosis on admission was pre-hospital cardiac arrest in men, and intracranial haemorrhage in women. The mean length of ICU stay was 4.5 days; the decision of treatment withdrawal occurred after a mean interval of 3.6 days (mean delay between withdrawal decision and DCD III procedure: 0.9 day). The assessment of the neurological prognosis always involved multiple investigations. For the half of the patients (n = 16), hemodynamic conditions were not supported pharmacologically. In contrast, 32/33 patients were still mechanically ventilated. The delay for "switch off" during DCD III procedures varied from 2 to 25 min, with a median value of 13 min. The DCD procedures allowed the procurement of 57 kidneys, 17 livers, 10 lungs, 31 cardiac valves, 26 bones and tendons, 2 hepatocytes, 8 pancreas islets cells. The graft and patient survival at 1 and 5 years is under analysis.

O76 ALLOREACTIVITY DRIVES THE REPOPULATION AND THE MAINTENANCE OF HUMAN INTESTINAL GRAFT TISSUE-RESIDENT MEMORY CELLS

J. Zuber, B. Shonts, S.P. Lau, A. Obradovic, J. Fu, S. Yang, S. Coley, J. Weiner, J. Thome, S. Dewolf, D. Farber, Y. Shen, G. Bhagat, A. Griesemer, M. Martinez, T. Kato, M. Sykes

Columbia University Medical Center, New York, United States

Introduction: Large numbers of donor tissue-resident memory T cells are transferred within intestinal grafts. However, little is known about how Host-vs-Graft (HvG) and Graft-vs-Host (GvH) responses influence the turnover, phenotype and repertoire of graft-resident T-cell populations following transplantation and how the balance between HvG to GvH responses correlates with clinical outcomes.
Methodology: Phenotype and donor /recipient origin of graft-resident lymphocytes were investigated prospectively with multicolor flow cytometry from 183 fresh ileum graft biopsies from 14 intestinal transplant recipients. To investigate intra-graft HvG and GvH responses, we identified (pre-transplant) and tracked the donor- and recipient-reactive TCR repertoire in 18 post-transplant biopsies, including 6 with overt rejection, using a recently developed high-throughput sequencing approach.
Results: In the absence of rejection, donor T cells persisted long term in the graft and were enriched for GvH-reactive clones. Early expansion of GvH clones in the graft correlated with rapid graft infiltration by recipient antigen presenting cells. Over time, T cell replacement rates in the graft were significantly faster over the first 3 and 6 months post-transplant in patients with mixed (humoral plus cellular) rejection compared to those without. Rejection was associated with transient infiltration by blood-like recipient CD28 + $NKG2D^{Hi}$ CD8 + alpha beta T cells, marked predominance of HvG clones (up to 80% of recipient mappable T-cell clones), and accelerated T cell turnover in the graft. Ultimately, recipient T cells eventually acquired tissue-resident phenotypic markers (CD103 + CD69 + CD28−) yet still contained HvG clones at low frequency.
Conclusion: To conclude, we found that the replacement rate and the phenotype of intestinal graft-resident T cells correlates strongly with both clinical outcome and the dynamics of the two-way alloimmune response.

O77 PREDICTING 90-DAY MORTALITY FOLLOWING LIVER TRANSPLANTATION IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE: A DECISION-TREE MODEL FROM THE FRENCH NATIONAL LIVER TRANSPLANTATION SYSTEM, THE OPTIMATCH STUDY, 2008–2014

E. Levesque[1], E. Audureau[3], C. Duvoux[4], A. Winter[5], C. Jacquelinet[7], D. Azoulay[2], C. Feray[4], G. Optimatch[6]

[1]Anesthsélie-réanimation; [2]Chirurgie digestive, Hôpital Henri Mondor, Creteil; [3]santé publique, Hôpital Heni Mondor; [4]Hépatologie, Hôpital henri Mondor, Créteil; [5]Santé publique, Université de Montpellier, Montpellier; [6]Direction de la Recherche Clinique, APHP, Paris; [7]Agence de Biomédecine, Saint Denis, France

Introduction: Cirrhotic patients undergoing an initial liver transplantation (LT) have a 1-year survival exceeding 85%. Some cirrhotic patients present organ failures at the time of LT defining Acute-On-Chronic Liver Failure (ACLF). The aim of this study was to build a decision-tree algorithm for predicting 90-day mortality in transplanted patients, by assessing the independent prognostic contribution of ACLF.
Methods: All patients transplanted between 2008 and 2014 (N = 4789) were included as part of the OPTIMATCH study, yielding 4010 patients with complete data for the present analysis. Data collected comprised clinical and biological features at the time of LT for recipients and their donors, assessing ACLF status according to ACLF/CANONIC criteria to categorize patients. A survival Classification and Regression Analysis (CART) algorithm was applied to build the prognostic model for 90-day mortality. .
Results: 1657 patients (41%) met the CANONIC criteria of ACLF with at least one organ failure (1: 20.3%; 2: 12.6%; 3 and more: 8.4%). Overall 90-day mortality rate was 7.6%, with corresponding rates of 5.4%, 7.2%, 10.2% and 20.1% in patients with 0, 1, 2, 3 and more organ failures, respectively. Decision-tree modelling identified 12 subgroups further classified in 4 increasing risk classes (Figure), highlighting the prognostic importance of respiratory failure and acute renal failure at the time of LT, as well as complex interactions between donor and recipient features.

Conclusion: Ventilator support and/or acute renal failure at the time of LT are major predictors of mortality but complex recipients/donors relationships may moderate these associations, as demonstrated by our CART analysis.

O78 FRENCH CONTROLLED DONATION AFTER CIRCULATORY DEATH (CDCD) PROGRAM: FIRST RESULTS

C. Antoine[10], M. Videcoq[5], B. Riou[8], D. Dorez[1], G. Cheisson[3], L. Martin-Lefevre[4], L. Durand[10], E. Savoye[10], G. Karam[6], O. Skowron[2], E. Savier[7], B. Barrou[9], P. Comité De Pilotage[10]
[1]CHPOT; [2]Urologie, CH Annecy, Annecy; [3]CHPOT, CHU Bicêtre, Kremlin Bicêtre; [4]CHPOT, CH la Roche sur Yon, La Roche Sur Yon; [5]CHPOT; [6]Urologie, CHU Nantes, Nantes; [7]Chirurgie hépato-biliaire; [8]CHPOT; [9]Urologie, CHU Pitié La Salpétrière, Paris; [10]DPGOT, Agence de la biomédecine, Saint Denis La Plaine, France

The national protocol for the cDCD program authorized in France since 2014 includes selection criteria as donor age ≤60 years, functional warm ischemia time (fWIT) <30 min (liver), <90 min (lung), <120 min (kidney), in situ kidney perfusion performed by normothermia regional perfusion (nRP), machine perfusion use (except liver) and short cold ischemia times (CIT). Only non-urgent recipients awaiting a 1st transplant were eligible.

The aim of this study was to compare primary non function (PNF), delayed graft function (DGF) and length of stay in hospital after kidney transplantation (KTR) according to 2 types of donors: cDCD (53 KTR from 12/2014 to 5/2016) and brain death donors (DBD) aged ≤60 years (3756 KTR from 1/2013 to 4/2016), only for patients awaiting 1st transplant.

Out of 60 potential cDCD donors, 29 have been retrieved, mean age 48 years. Causes of death are mainly hypoxic brain damage (48%) and trauma/head injury (26%). Procurement failure are secondary to Relative's opposition (30%), agonal delay >180 min (7.6%) and logistical problem (7.6%). Mean fWIT are 30 min (kidney), 21 min (liver) and 85 min (lung). nRP was used in all utilized donors after mean circulatory arrest delay of 25 min. Mean renal CIT is 10.7 h.

Rate of PNF (2%), mean creatinin (150 vs 176 μmol/l) and renal clearance (54 vs 47 ml/mn) at discharge are comparable. DGF rate (3.4% vs 19.5%), dialysis number and length of stay in hospital are significantly improved in case of cDCD. 13 liver transplants and 1 lung transplant are also performed without EAD.

These good results ensue from national and consensual protocol, with aim to limit war ischemia times and injuries, thanks to nRP use, optimal graft preservation and recipient selection. cDCD program represents an optimal and additional source of valuable transplants.

O79 350 PEDIATRIC LIVING DONOR LIVER TRANSPLANTATIONS

A. Pire, C. De Magnée, B. D'hondt, M. Janssen, R. Reding
3, Cliniques universitaires Saint Luc, Bruxelles, Belgium

Introduction: Due to the shortage of and/or lack of access to deceased donors, living donor liver transplantation (LDLT) has contributed to allow the transplantation of children in a timely fashion regarding the evolution of their diseases. We reviewed our 23 years experience in LDLT.
Patients and Methods: Between July 1993 and December 2015, 350 LDLT were performed (median age: 1.25 years; range: 0.3–16.5 years). The first indication for LT was biliary atresia (n = 218, 62%).
Results: No mortality or persisting disability was encountered in the 350 living donors of this series. Overall patient and graft survivals in the recipients were 96% and 95% at one year, and 94% and 92% at five years, respectively. The retransplantation rate was 8/350 (2.3%), including two children who finally died. No ABO-incompatible graft was lost in this series. To better evaluate our learning curve, the results were further analyzed considering five eras. A striking feature was the progressive increase of the proportion of LDLT/total paediatric LT along the eras as follows: 1993–7: 57/152 (38%); 1998–2001: 38/100 (38%); 2002–7: 66/161 (41%); 2008–11: 80/101 (79%); 2012–15: 108/122 (88%). When comparing 1993–7 and 2007–11 eras, 5 year patient and graft survival rates increased from 89% to 98%, and 86% to 96%, respectively.
Conclusions: Our results indicate: (1) the increasing recourse to LDLT at our pediatric LT program; (2) the safety of living donor surgery and management; (3) the improvement of overall results of LDLT along the eras; (4) the judicious use of ABO-incompatible LDLT due to an adequate protocol for isoagglutinin depletion. A detailed assessment of the risks/benefits balance of steroid-free immunosuppression in pediatric LT is ongoing.

O80 EFFECT OF THE DIFFERENT SENSITIZATION EVENTS ON HLA ALLOIMMUNIZATION AND ACCESS TO TRANSPLANTATION IN KIDNEY TRANSPLANT CANDIDATES

A. Cros, I. Szwarc, V. Garrigue, J.E. Serre, C. Rene, A. Ramounau-Pigot, J.F. Eliaou, G. Mourad, M. Le Quintrec, V. Pernin
4, CHU de Montpellier, Montpellier, France

HLA allo-immunization is caused by sensitization events such as transfusions, pregnancies or previous transplantations. The objective of our work was to analyze the consequences of each sensitization event on HLA immunization and on access to transplantation.

We investigated HLA immunization (by Luminex single bead Ag, One lambda, positivity if MFI > 1000) of 461 patients registered on the waiting list between 01/01/2009 and 31/12/2013, with only one type of sensitization event (123 transfused, 68 with pregnancies, 19 previous transplants) or without sensitization event (251 patients; control group).

The percentage of immunized patients was respectively 41% in the control group, 39% in the transfused group, 59% in group pregnancy, 89% in the transplantation group ($p < 0.001$) for class I HLA antibodies, and 26%, 25%, 43% and 83% ($p < 0.001$) for class II HLA antibodies. The mean number of anti-HLA specificities (class I and class II) was respectively 1.6 ± 3.0 ; 2.2 ± 6.1 ; 8.5 ± 15.5 ; 27.4 ± 8.9 ($p < 0.001$). Mean MFI were 2385 ± 1931 ; 2245 ± 1729 ; 3036 ± 3375 ; 5697 ± 4784 ($p < 0.001$) for class I antibodies and mean MFI were 2031 ± 1456 ; 2013 ± 1346 ; 4321 ± 4346 ; 9102 ± 6870 ($p < 0.001$) for class II antibodies. cPRA (calculated Panel Reactive Antibodies) were 10%, 12%, 35% and 65% ($p < 0.001$) for the different groups respectively. At 01.05.2016, 89% in the control group, 85% in the group transfused, 85% in the group pregnancy but only 47% in the group transplantation were transplanted ($p < 0.001$). Mean waiting time (month) was 20.3 ± 16.0, 23.6 ± 18.7, 24.8 ± 18.2 et 29.1 ± 20.3 in the different groups respectively ($p = 0.006$).

HLA immunization risk depends on the sensitization event. Previous transplantations had the strongest effect on HLA immunisation and significantly restricted the access to a new transplant, followed by pregnancies. The prevalence of HLA sensitization in the transfusion group is not very different compare to the group without classical sensitization event.

O81 A CONSECUTIVE SERIES OF 125 CONTROLLED DCD-LIVER TRANSPLANTATIONS

O. Detry[2], N. Meurisse[2], M.F. Hans[2], M.H. Delbouille[2], J. Monard[2], A. Deroover[2], J. Joris[1], A. Kaba[1], P. Honoré[2]
[1]Service d'Anesthésie & Réanimation; [2]Service de Chirurgie & Transplantation, CHU Liege, Liege, Belgium

Introduction: Donation after circulatory death (DCD) has been proposed to partially overcome the organ donor shortage. DCD-LT remains controversial, with reported increased risk of graft loss and retransplantation. The authors retrospectively reviewed a single centre experience with controlled DCD-LT in a 14-year period.
Patients and Methods: 125 DCD-LT were consecutively performed between 2003 and 2016. All donation and procurement procedures were performed as controlled DCD in operative rooms. Data are presented as median (ranges). Median donor age was 56 years (16–84). Most grafts were flushed with HTK solution in the first part of experience, and more recently with IGL1. Allocation was centre-based. Median follow-up was 52 (1–164) months. No patient was lost to follow-up.
Results: Median total DCD warm ischemia was 19 min (9–39). Median cold ischemia was 238 min (105–576). Patient survivals were 90.2%, 77.5% and 74.5 % at 1.3 and 5 years, respectively. Graft survivals were 87.7%, 76.3% and 73.2% at 1.3 and 5 years, respectively. Biliary complications included anastomotic strictures and extrahepatic main bile duct ischemic obstruction, that were managed either by endoscopy or hepatico-jejunostomy. No PNF was observed in this series and one graft was lost due to ischemic cholangiopathy.
Discussion: In this series, DCD LT appears to provide results similar to classical LT. Short cold ischemia and recipient selection with low MELD score may be the keys to good results in DCD LT, in terms of graft survival and avoidance of ischemic cholangiopathy.

O82 SOFOSBUVIR AND NS5A INHIBITORS WITHOUT RIBAVIRIN DURING 12 WEEKS ARE EFFICIENT TO TREAT HEPATITIS C RECURRENCE AFTER LIVER TRANSPLANTATION ONLY IN GENOTYPE 1. RESULTS FROM THE CO23 ANRS CUPILT STUDY

P. Houssel-Debry[22], A. Coilly[28], C. Fougerou-Leurent[21,20], C. Jezequel[22], C. Duvoux[6], V. De Ledinghen[2], S. Radenne[12], N. Kamar[26], V. Leroy[7], V. Di Martino[1], L. D'alteroche[27], V. Canva[9], F. Conti[17], J. Dumortier[11], H. Montialoux[23], P. Lebray[18], D. Botta-Fridlund[13], R. Anty[15], C. Moreno[3], C. Silvain[19], C. Besch[25], P. Perre[8], C. Francoz[5], A. Abergel[4], F. Habersetzer[24], M. Debette-Gratien[10], A. Rohel[16], A. Diallo[16], E. Rossignol[20,21], A. Veislinger[20,21], H. Danjou[20,21], J.C. Duclos-Vallée[28], G.P. Pageaux[14]

[1]Hepatology Unit, University Hospital Minjoz, Besançon; [2]Hepatogastroenterology Unit, University Hospital Haut-Lévêque, Bordeaux; [3]Hepatogastroenterology University Hospital Erasme, Université Libre de Bruxelles, Bruxelles; [4]Digestive Department, University Hospital Estaing, Clermont-Ferrand; [5]Hepatology unit, University Hospital Beaujon, Clichy; [6]Hepatogastroenterology Unit, University Hospital Henri-Mondor, Creteil; [7]Hepatogastroenterology Unit, University Hospital Michallon, Grenoble; [8]Internal Medicine unit, Vendée Departmental Hospital, La Roche Sur Yon; [9]Digestive tract Diseases Unit, University Hospital Huriez, Lille; [10]Hepatogastroenterology Unit et Nutrition, University Hospital Dupuytren, Limoges; [11]Digestive tract diseases Department, University Hospital Edouard Herriot; [12]Hepatogastroenterology Unit, University Hospital Croix-Rousse, Lyon; [13]Hepatogastroenterology Unit, University Hospital La Timone, Marseille; [14]Hepatogastroenterology and Liver transplantation Department, University Hospital Saint Eloi, Montpellier; [15]Hepatogastroenterology Unit, University Hospital Archet, Nice; [16]ANRS; [17]Hepatobiliary surgery and liver transplantation Unit, University Hospital Pitié-Salpêtrière; [18]Hepatogastroenterology Unit, University Hospital Pitié-Salpêtrière, Paris; [19]Hepatogastroenterology Unit, University Hospital Milétrie, Poitiers; [20]Pharmacology Unit, University hospital Pontchaillou; [21]INSERM, CIC 1414 Clinical Investigation Centre; [22]Liver diseases Unit, University Hospital Pontchaillou, Rennes; [23]Hepatogastroenterology Unit, University Hospital Charles Nicolle, Rouen; [24]Hepatogastroenterology Unit, University Hospital Nouvel hôpital civil; [25]Transplantation, hepatic and endocrine surgery Unit, University Hospital Hautepierre, Strasbourg; [26]Nephrology, Hypertension and Dialysis Unit, University Hospital Rangueil, Toulouse; [27]Hepatogastroenterology Unit, University Hospital Trousseau, Tours; [28]Centre Hépato-Biliaire, University Hospital Paul-Brousse, Villejuif, France

Introduction: Sofosbuvir (SOF) with NS5A inhibitors has shown efficacy to treat hepatitis C (HCV) recurrence after liver transplantation (LT). But the duration of treatment and the use of RBV are not clear after LT. We aimed to assess which patients can be treated with this therapeutic regimen without RBV during 12 weeks after LT.

Methods: From October 2013 to October 2015, 699 patients with HCV recurrence after LT have been enrolled in the prospective multicentric ANRS CO23 CUPILT cohort. We selected patients receiving SOF and NS5A inhibitor +/- RBV. The primary efficacy end point was a sustained virological response 12 weeks after the end of treatment (SVR12). We identified four groups of patients according to treatment' regimens and duration: SOF+NS5A ± RBV during 12 or 24 weeks. Logistic regression with adjustment was used.

Results: 386 patients fulfilled the inclusion criteria with the following characteristics: genotype 1: 75.1%, treatment-naïve 62.2%, fibrosis stage F3/F4 in 155 patients and decompensated cirrhosis: 5.2%. 143 patients were treated during 12 weeks (105 without RBV). The rate of F3–F4 fibrosis stage (47.7%, $p = 0.0006$), previously treated (45.3%, $p = 0.0008$) and non-responders patients (19.3%, $p = 0.0442$) was higher in 24 weeks treatment groups. The SVR12 was 97.1%, 100%, 98.9%, 95.5% in the 12 weeks without RBV group, the 12 weeks with RBV group, the 24 weeks without RBV group and the 24 weeks with RBV group, respectively ($p = 0.27$). By multivariate analysis, the factors such fibrosis stage, previous treatment, HCV genotype, HCV viral load at baseline did not influence the rate of SVR12 among the four study groups ($p = 0.38$). However the risk of failure was higher in G3 group (OR = 4.92, (1.19–20.20) ($p = 0.03$).

Conclusion: SOF+NS5A inhibitors without RBV regimen during 12 weeks was efficient to treat HCV recurrence after liver transplantation including F3–F4 and previously treated patients in genotype 1.