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1 CELL-BASED FLOW CYTOMETRY CROSSMATCH TEST DISCRIMINATES EFFECTIVELY BETWEEN PATHOGENIC AND NON- PATHOGENIC PREFORMED DSA

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Introduction: At the time of transplantation, solid phase-test tends to replace cell-based test. Flow Cytometry Crossmach (FCXM) may help to recognize pathogenic Donor Specific anti-HLA antibodies (DSA). This approach is not universally used. Here we reported our experience with DSA+FCXM+ transplantations.
Patients: We included 175 sensitized Kidney Transplant Recipients (KTR), transplanted with a current negative T-cell Complement Dependent Cytotoxicity crossmatch. FCXM were considered to be positive when Mean Chanel Shift (MCS) > 50 for T cells and MCS > 100 for B cells.
Results: Three profiles were identified: 41 DSA+FCXM+, 52 DSA+FCXM−, and 82 DSA−. Mean Fluorescence Intensity (MFI)-DSA were higher for DSA+FCXM+ (5544 ± 541) than for DSA+FCXM− (2581 ± 491), p = 0.02. To prevent antibody-mediated rejection (AMR), some patients received intravenous immunoglobulins (17% DSA−, 65% DSA+FCXM−, 83% DSA+FCXM+; p < 0.0001), rituximab (1% DSA−, 37% DSA+FCXM−, 24% DSA+FCXM+; p < 0.0001). Kaplan–Meier estimates over 24 months indicate a higher incidence of acute rejection (AR) and AMR in DSA+FCXM+ group [respectively 7.5% DSA−, 16% DSA+FCXM−, 40% DSA+FCXM+ for AR and 2.5% DSA−, 8% DSA+FCXM−, 27.5% DSA+FCXM+ for AMR] and a poorer graft survival [respectively 96% DSA−, 94% DSA+FCXM−, 85% DSA+FCXM+]. Outcome was not different between DSA− and DSA+FCXM− groups; as opposed to the DSA+FCXM+ group. Interestingly, only DSA+FCXM+ were still associated with AR in multivariate analysis (OR = 3.2 [1.2–9.3], p = 0.02), after adjustment for MFI-DSA.
Conclusion: Taken together, our data confirm the good prognosis of transplantation in sensitized KTR. Solid based tests enable the identification of DSA. Cell-based FCXM test discriminates between pathogenic and non-pathogenic DSA, even better than the MFI-DSA. Refinement of risk stratification through performing prospective FCXM may be useful and guide immunosuppressive strategies.

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Not attributed.

3 A NEW DIAGNOSTIC AND PRONOSTIC TOOL FOR ANTIBODY MEDIATED REJECTION IN KIDNEY TRANSPLANTATION: INTRAGRAFT DONOR SPECIFIC ANTI-HLA ANTIBODIES DETECTION

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Introduction: Antibody mediated rejection (AMR) is one of the main cause of loss of the kidney transplant. Despite the new BANFF classification, diagnostic difficulties and lack of prognosis factors persist. The detection of intra-graft DSA (gDSA) could be a diagnostic and prognostic tool of AMR.
Methodology: We looked for gDSA in 151 kidney graft biopsies from a monocentric, retrospective and transversal cohort of 87 sensitized recipients (sDSA+). gDSA were identified by Luminex SA assay on kidney biopsies eluates. Biopsies were reviewed and classified according to BANFF 2013 classification.
Results: On 87 patients, 65 had AMR. 103 biopsies are sDSA+/gDSA+: 19 in HLA class Iand 90 in HLA class II. We note a significant association of gDSA with both acute (p = 0.031) or chronic (p < 0.0001), with AMR histological features, in particular with C4d deposits p < 0.0001) and microcirculation inflammation (p = 0.002). Patients with gDSA+ have a significantly lower graft function (p = 0.045), a higher level of proteinuria (p = 0.09) and a lower renal survival 4 years after the biopsy (p = 0.09). A sDSA MFI > 3500 predicts the gDSA presence with a sensitivity of 70% and a specificity of 82%. Among 40 patients biopsied twice, we observed 4 cases of gDSA positivation and 4 cases of gDSA negativation. 14 patients are gDSA+/AMR− suggesting infra-histological diagnostic of AMR confirmed by histological diagnosis of AMR in 9 of the 10 patients biopsied later.
Conclusion: gDSA are frequently found in patients with sDSA; they are a witness of the interaction between sDSA and the graft endothelium. They could represent an additional argument for AMR diagnosis and could have a prognosis value that should be confirmed by a prospective study.

4 NEW ENDOTHELIAL ACTIVATION MARKERS HELP ANTIBODY-MEDIATED REJECTION DIAGNOSIS AND PREDICT LONG-TERM RENAL GRAFT DYSFUNCTION

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Introduction: Antibody-mediated rejection (ABMR) is a leading cause of allograft loss. The efficacy of treatment depends on an accurate diagnosis at an early stage. Sensitive, reliable, especially routinely applicable markers are still lacking.
Methods: Using immunohistochemistry, we retrospectively studied the diagnostic value of endothelial-to-mesenchymal transition (EndMT) markers (endothelial expression of vimentin, fascin and hsp47) for ABMR in 53 renal transplant biopsies including 20 ABMR, 24 with T cell-mediated rejection and 9 normal grafts. We validated our results in a second set of 74 non-selective biopsies.
Results: EndMT markers were very strongly expressed in the endothelial cells of peritubular capillaries in grafts with ABMR, and absent in normal renal grafts. The level of expression of EndMT markers was significantly associated with capillaritis ($\rho = 0.6$, $p < 0.0001$), glomerulitis ($\rho = 0.5$, $p = 0.0002$), peritubular capillary c4d deposition (EndMT score = 3.44 ± 0.18 vs. 1.8 ± 0.24 for c4d+ or c4d− groups, p = 0.0019), but not with i and t scores. In addition, EndMT identified ABMR at an early stage before clinical or histological features of ABMR, as well as C4d-negative ABMR. EndMT markers predicted significantly late (up to 4 years post biopsy) renal graft dysfunction ($\rho = -0.66$, $p < 0.0001$) and proteinuria ($\rho = 0.414$, $p = 0.023$). A prolonged cold ischemia time and a history of delayed graft function were the main risk factors associated with the occurrence of EndMT markers. In the second independent set of 74 biopsies, the level of EndMT marker expression was significantly higher in the patients with DSA than without (1.7 vs. 0.7, p = 0.0065). The diagnostic value of EndMT markers for ABMR was confirmed and showed a sensitivity of 100% and a specificity of 85%.
Conclusion: The capillary endothelial activation detected by the expression of EndMT markers is a sensitive and reliable diagnostic tool for ABMR, and predict late allograft function loss.

5 WHICH PLACE OF PANCREAS GRAFT BIOPSY IN THE MANAGEMENT OF PANCREAS TRANSPLANT RECIPIENTS?

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Introduction: Rejection or autoimmune recurrence is often difficult to diagnose in the field of pancreas transplantation. The place of pancreas graft biopsy in the management of pancreas transplant recipients is poorly defined. The aim of this study was to assess the contribution of pancreas graft biopsy in our cohort.
Methods: All recipients of pancreas transplant, with or without simultaneous kidney transplant, who had a pancreas graft biopsy for cause since 2011 were included. Biopsies were performed under ultrasound or computer tomographic guidance. We analyzed indications, results, concordance with kidney graft biopsies, and complications.
Results: Twenty-eight pancreas biopsies were performed in 24 patients. Six (21%) were non adequate. Twenty-one biopsies were performed for suspicion of rejection (increase in serum lipase *n* = 17, *de novo* DSA *n* = 2, kidney graft rejection *n* = 2). Among them, 14 showed rejection (grade I cell-mediated rejection *n* = 7, grade II cell-mediated rejection *n* = 6, antibody-mediated rejection *n* = 1) and only 3 were normal (4 non adequate). Evolution after treatment was favorable for all patients with grade I cell-mediated rejection. However, 5 out of 6 patients with grade II cell-mediated rejection lost their graft

within 6 months. Concordance of pancreas biopsy with kidney biopsy in patients having a kidney graft from the same donor was poor (3 of 8). Four biopsies were performed for abnormal oral glucose tolerance test or appearance of autoantibodies. Islets were seen in 3 of these biopsies, without any abnormality. Biopsies for unexplained inflammatory syndrome were normal. There were no complications of biopsies.
Conclusion: Pancreas graft biopsy is essential for the diagnosis and prognosis of pancreas rejection and must be performed in every case of increase in serum lipase or *de novo* DSA. Concordance with kidney biopsy is poor. The place of pancreas biopsy in autoimmune recurrence still has to be evaluated.

6 COMPLEMENT (C′) -BINDING ANTI-HLA DONOR SPECIFIC ANTIBODIES (DSA) IN HEART TRANSPLANTATION. CORRELATION WITH ANTIBODY MEDIATED REJECTION (AMR)

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Introduction: In heart transplantation (HTx), *de novo* DSA is a risk factor for AMR, but a high proportion of patients (pts) with DSA do not develop AMR. The purpose of this study is to test the accuracy of C′ –binding DSA to predict AMR.
Méthods: A cohort of 35 HTx pts from Rouen and Caen University hospitals, followed since January 2011, who developed *de novo* DSA, were tested for C′ –binding DSA on historical sera with DSA MFI > 1500. Test results were compared with AMR occurrence and graft dysfunction and/or chronic rejection. AMR definition was 2011 ISHLT pathological AMR classification. Two assays detecting C′ were used: C1q- and C3d-binding DSA and there results will be compared with AMR occurrence.
Résults: A first series of 25 HTx pts with *de novo* DSA were tested with the C3d-binding assay. C′ –DSA binding was correlated with AMR (pAMR equal or superior to 1) occurrence with a 77% sensitivity and a 71% specificity (PPV = 83%, NPV = 63%); and was correlated with graft dysfunction and/or chronic rejection with a 79% sensitivity and a 83% specificity (PPV = 92%, NPV = 63%). C1q-binding DSA study is ongoing and will be presented.
Conclusion: In HTx pts with *de novo* DSA, C′ binding seems to be correlated with AMR occurrence and graft dysfunction and/or chronic rejection, and should be tested in at least one serum sample.

7 CENTRIFUGATION, DOUBLE FILTRATION OR IMMUNOADSORPTION: WITCH TECHNIQUE FOR OUR DESENSITIZATION PROTOCOL?

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Introduction: We compared the efficiency of Immunoglobulin (Ig) removal and their consequences on haesmostasis of 3 different aphresis techniques in order to choose the one with best benefit/risk for our desensitization protocol in kidney transplantation.
Materials and Methods: We performed a prospective monocentric observational study to compare plasmatic exchanges by centrifugation (PE), double-filtration plasmapheresis (DFPP) and immunoadsoprtion (IA).
Results: 65 sessions of apheresis were performed in 11 patients, 23 by IA (LiFE-18 Milteniy), 19 in PE (Haemonetics-Terumo) and 21 by DFPP (Plasauto-ASHAi). Plasmatic volume (PV) treated by session was enhanced in IA with an increased IgG removal (PV: 73.1, removal: 70.1% ml/kg) compared to PE (PV: 42 ml/kg; removal 64.1%) and DFPP (PE: 39.7 ml/kg; removal 45.5%).

IgA et IgM removal remained higher in PE (IgA 61%, IgM 68%) and DFFP (IgA 52.4%, IgM 65.7%) than IA (IgA58.2%, IgM 51.9%). No bleeding adverse effect was reported. TP was reduced by 55% in PE, 48.1% by DFPP and 9% by IA ($p < 0.001$); fibrinogen by 65.2% in EP, 55.2% in DFPP and 24% in IA $p < 0.001$). Activated Cephalin Time was increased by 5.4 times in DFPP, 3.4 in EP and 3.3 times in IA. TCA increased 5.4 times in DFPP; 3.4 times in EP and 3.3 times in IA. Factors II, V and VIII were reduced respectively by 59.47% (EP), 36.8 (DFPP), 18.1% (IA) for factor II, by 63% (EP), 58.5% (DFPP) and 26.9% (IA) for factor V and by 57.3% (DFPP), 62.4% (EP) 19.8% (IA) for factor VIII.
Conclusion: IA was associated with a greater PV treated than EP or DFPP. So we couldn't conclude in a higher capacity to remove IgG in IA. Nevertheless we could confirm a better haemostasis tolerance during IA apheresis. Consequently, we choose this technique for our desensitization protocol.

8 A NEW DIAGNOSTIC TOOL FOR ANTIBODY MEDIATED REJECTION IN HEART AND LUNG TRANSPLANTATION: INTRAGRAFT DONOR SPECIFIC ANTI-HLA ANTIBODIES DETECTION

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Introduction: Antibody mediated rejection (AMR) is one of the causes of organ dysfunction and graft loss. The limited histological features, with a weak sensibility of c4d, make its diagnosis difficult to assess and its prognosis hard to evaluate. The detection of intragraf DSA (gDSA) could be a diagnostic and prognostic tool of AMR.
Methodology: We looked for gDSA in 15 biopsies of 7 heart transplant (HT) recipients of whom 6 were sensitized, and 12 biopsies of 10 lung transplant (LT) recipients of whom 7 were sensitized (sDSA+). AMR was defined by graft dysfunction and/or histological features of rejection and sDSA+. gDSA were identified by Luminex SA assay on heart or lung biopsy eluates.
Results: In HT recipients, 6 of the 15 biopsies have AMR features and 8 have gDSA. The concordance level between sDSA and gDSA was 60% (6 sDSA+/gDSA+). None of the gDSA+ patients was sDSA−. There is an 80% concordance level between gDSA and rejection (6 gDSA+/RH+, 6 gDSA−/RH−). The single case of gDSA−/RH+ was due to a very small size of the biopsy in a patient with a low MFI level of sDSA. The 2 cases of gDSA+/RH− came from a heart recipient without graft dysfunction. In one of the 2 HT biopsies, gDSA was present 2 months before rejection diagnosis. Among 3 patients who underwent a subsequent biopsy, gDSA disappeared in one case. In LT recipients, 5 cases of AMR were diagnosed among 12 biopsies. The concordance between sDSA and gDSA was 75% (5 sDSA+/gDSA+) and 100% between gDSA and AMR. Among the 7 gDSA− cases, 3 cases were cellular rejection (sDSA−) and 3 were diagnosed as pneumonia. The 4 gDSA+ patients evolved to chronic humoral rejection ($n = 3$) and/or death ($n = 3$). Among the 2 patients biopsied later, we note 1 case of gDSA positivation.
Conclusion: gDSA are detected in 86% of AMR+ in HT biopsies and 100% in LT biopsies when patients have DSA in serum. gDSA could represent a witness of the interaction between sDSA and the graft endothelium. They could become a new criteria for AMR diagnosis and could have a prognosis value that should be evaluated in a larger study.

9 COMPUTER-ASSISTED ANALYSIS OF RENAL GRAFT INFLAMMATION REVEALS HISTOPATHOLOGICAL HETEROGENEITY OF ANTIBODY-MEDIATED REJECTION

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Introduction: Kidney graft biopsy plays a key role in diagnosis of antibody-mediated rejection (AMR), which is the major cause of kidney graft failure. In AMR, the conventional assessment relies on Banff classification which faces limitations in terms of diagnostic accuracy and risk prediction. We have developed a new method of computerized image analysis in order to finely characterize the quality and intensity of graft inflammation.
Methods: Among the 69 kidney recipients, who fulfilled the Banff criteria for AMR between 2004 and 2012 at the Lyon University Hospitals, 57 had enough histological samples left for analysis. Double immunohistological stainings were performed with CD31 (capillaries) and respectively CD68 (macrophages), CD3 (T lymphocytes), CD66b (granulocytes), CD20 (B lymphocytes). Computerized image analysis was used to quantify the number of cell of each type in interstitium, glomeruli and peri-tubular capillaries. The ability of DSA to bind C3d was assessed using flow bead assays.
Results: 34 patients had C3d+ DSA and 23 had C3d− DSA. Banff score for humoral lesions (g + ptc) was similar in the two groups (3.4 ± 1.1 vs. 3.5 ± 1.2, $p = 0.65$). The number of B and T lymphocytes per 1000 pixels was similar between groups in glomeruli, interstitium and capillaries. Patients with C3d+ DSA had a higher number of monocytes per 1000 pixels in both peritubular capillaries (0.11 vs. 0.04, $p = 0.002$), glomeruli (0.03 vs. 0.01, $p = 0.018$) and interstitium (0.13 vs. 0.04, $p = 0.004$). The number of activated neutrophils (CD66b) in the interstitium was higher in the C3d+ group (0.004 vs. 0.0005, $p = 0.02$).
Conclusion: Using this novel reproducible approach for topological quantification of inflammation, we observed that histopathological features of complement-binding DSA are different from that of non-complement. Additional analyses are currently performed to investigate whether computer-assisted analysis of graft inflammation can stratify the risk of graft loss.

10 CAN WE REDUCE THE NUMBER OF KIDNEYS THAT ARE RETRIEVED BUT NOT TRANSPLANTED?

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Objective: Despite a growing organ shortage, a significant number of deceased donor kidneys is retrieved from deceased donors but not transplanted (RNTK). The aim of the study was to determine the main causes of refusal and analyze if it was justified or not.
Method: This multicenter national study included all RNTK from January 1, 2012 to December 31, 2012. Data were collected from the national database Cristal managed by the Agence de la Biomedecine. Each case was retrospectively analyzed by an urologist expert in transplantation, to determine, if possible, whether the refusal was justified or not.
Results: 252 retrieved kidneys (8.8%) were not transplanted. The main reasons for refusal were as follows: 107 vascular causes, (unsuitable artery (95) or vein (12); 48 tumor suspicion, within the graft (17) or at another site (31); pejorative graft biopsy findings (31); and multiple other factors (66). Among suspected tumors, one third were identified as benign. The refusal was due to iatrogenic lesions for 63 kidneys (25%): 29 complete artery section (main artery in 9 and polar artery in 20 cases) 11 venous injuries, 9 incident during cannulation, 6 kidney capsule lacerations, 5 complete ureteral section and 3 hematoma. Retrospective analysis of refusal causes suggested that 63 kidneys (25%) were probably improperly denied, 115 kidneys (46%) were duly turned down. The analysis was not feasible in 74 kidneys (29%), due to improper data collection.
Conclusion: A significant proportion of donated kidneys are unduly not transplanted. The solutions to reduce this unnecessary loss of grafts could be (i) the improvement of data collection and transmission, (ii) the evaluation by 2 experts in the field before turning down an organ, 3. an uropathologist on duty for urgent histology 24 h a day.

11 LONG-TERM OUTCOME OF RENAL ALLOGRAFT AFTER SEQUENTIAL LIVER-KIDNEY TRANSPLANTATION FROM A SINGLE LIVING DONOR

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Introduction: While the short-term results of solitary renal transplantation have improved considerably, favorable long-term outcomes have not yet been obtained because of chronic transplant nephropathy. We reviewed the long-term outcome of renal allografts in patients receiving sequential liver and kidney transplants from a single living donor.
Methods: Thirteen patients (3 adults, 10 children) underwent sequential liver (LTx) and kidney (KTx) transplantations from a single living donor between August 1996 and July 2014 at our center. The initial immunosuppressive agents used for the LTx were continued with dose modifications after the successive KTx.
Results: KTx was performed between 1.7 and 47.0 months after the LTx. One patient died two months after the KTx because of sepsis. The overall patient survival rate was 92.3% at 10 years. In 11 of 12 remaining patients, the renal allografts were found to be functioning, based on serum creatinine levels, after a mean follow-up period of 87.3 months (5–211 months). Only the first case, transplanted in 1996, exhibited allograft loss 17 years after transplantation because of chronic antibody-mediated rejection. The death-censored renal allograft survival rate at 10 years was 100%, which was better than that of KTx alone (84.9%) in Japan. Overall, only one case of biopsy-proven acute renal rejection requiring intensive treatment occurred within three years of the post-transplant period. The incidence of acute renal rejection was also lower after LTx/KTx than that after KTx alone at our center (8.3% vs. 13.6%, respectively).
Conclusions: Immunological protection conferred by the preceding liver allograft may have contributed to the long-term outcome of the renal allograft. In addition, the early suspension of steroid administration thanks to the occurrence of fewer rejection episodes might have contributed to the advancement of normal growth in pediatric transplant patients.

12 PEDIATRIC COMBINED KIDNEY-LIVER TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE OF 18 CASES

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Objectives: The experience of pediatric combined kidney/liver transplantation (CKLT) is limited but this strategy is required in specific diseases such as primary hyperoxaluria type 1 (PH1).
Methods: A retrospective study of the pediatric CKLTs performed at our institution between 1992 and 2013 was performed. Results are expressed as median [range].
Results: 18 children (9 boys, age 6.7 [1.0–18.6] years, body weight 13 [10–40] kg) underwent CKLT for PH1 (n = 14), Boichis syndrome (n = 3) and methylmalonic acidemia (n = 1).

Induction therapy consisted in anti-thymocyte globuline (N = 4) or basilixi-mab (N = 14). Hepatic and renal cold ischemia times were 9.4 [5.6–12.4] and 14.4 [9.3–19.6] h, respectively; 12 patients required per-operative dialysis. In the early post-operative period, dialysis was required in 7 patients; the stay in the PICU was 10 [6–29] days.

One patient died from cardiovascular disease 10 years after CKLT. No liver graft loss but 6 acute liver rejections were observed whereas 4 kidney grafts were lost (immediate post-operative period, N = 2). Five renal acute rejections were observed. Neither lymphoma nor solid tumor have been observed so far. At last follow-up (6.3 [0–21] years) for patients with functioning renal graft, renal function was 67 [25–103] ml/min per 1.73 m^2 and SDS for height was -2.3 [-7.2; 2.2].

A specific management was applied after CKLT in PH1 patients, namely citrate (n = 14) and hyperhydration (duration 4.0 [0.5–6.0] years). Oxaluria was normalized in 6 patients 3 years after CKLT, but 4 patients still presented with increased oxalaturia 1, 2, 3 and 10 years after Tx.
Conclusion: This series confirms the feasibility of pediatric CKLT with encouraging results in the long term, even in the youngest patients. In PH1, the underlying disease burden as assessed by urinary oxalate can persist for months/years, thus requiring specific follow-up and management.

13 COMPUTED TOMOGRAPHY ASSESSMENT OF MACROVESICULAR LIVER STEATOSIS IN CADAVERIC DONORS: A FRENCH SINGLE CENTER PROSPECTIVE OBSERVATORY STUDY

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Background: Metabolic disorders including liver steatosis are a major health problem all over the world. In liver transplantation, macrovesicular steatosis is probably the most difficult risk factor to appreciate and remains a major cause of graft failure. Computed tomography (CT) is commonly used in cadaveric donors' management teams to assess donors and to minimize the risk of complications in recipients. The purpose of our study was to validate the use of CT as a semi quantitative assessment of macrovesicular steatosis in cadaveric donors, using liver biopsy as a reference standard.
Methods: Our study obtained institutional approval by SRLF ethics committee No. 10-287. A total of 109 cadaveric donors were included between October 2009 and May 2011 (69 men and 40 women, mean age 55 $\pm$ 16 years, BMI 26.6 $\pm$ 5.0 kg/m^2). Brain death was diagnosed according to French law; afterwards liver biopsy and then CT were performed the same day to determine the degree of macrovesicular steatosis. All liver biopsies and CT were analyzed double blinded by one pathologist and one radiologist respectively. For CT, we used the liver to spleen (L/S) attenuation ratio which is a validated method to determine a 30% or greater steatosis in living liver donors.
Results: 14 out of 109 biopsies exhibited a macrovesicular steatosis >30%. No bleeding complication was observed. ROC curve was generated for L/S ratio to identify its ability to predict a steatosis >30%. Our results showed a cutoff value of 0.9 for CT L/S with sensitivity of 79% and specificity of 97%.
Conclusions: This study is the first performed in cadaveric donors, showing the same results as those found in living liver donors. CT provides high performance in diagnosis of macrovesicular steatosis >30% in cadaveric donors. The use of liver biopsy remains mandatory in donors with more than 30% of steatosis determined by CT to appreciate its severity as well as other histological abnormalities.

14 A SIMPLE MODEL TO PREDICT STEATOSIS >30% IN MORBIDLY OBESE LIVER DONORS

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Background: In the selection of marginal liver grafts most transplantation centers use a cut-off of 30% macrovesicular steatosis to define an acceptable risk of non-function. The quantification of steatosis still relies on macroscopic evaluation by the harvesting surgeon with the aid of a parenchymal biopsy, when available. The aim of this study was the creation of a non-invasive model to predict a steatosis degree >30%, based on simple clinical and biochemical markers available at the time of potential liver donor evaluation, in order to avoid futile and expensive procurement proceedings.
Methods: Data from 857 morbidly obese patients operated on for bariatric surgery in our center were prospectively collected. Liver biopsies were obtained and patients were divided in two groups according to the degree of steatosis classified as 30% and >30%. Univariate and multivariate analysis were performed in order to identify parameters associated with steatosis >30%.

Results: Steatosis >30% was found in 55% of the study population. Age, alanine aminotransferase (ALT) and waist circumference were found to be independently associated with steatosis >30%. Combining these parameters we developed a model to predict steatosis >30% with an area under the receiver operating characteristic (AUROC) of 0.78 (95% CI: 0.75–0.81). The best threshold was 0.06 offering a sensitivity of 72% a specificity of 70%.
Conclusions: a model combining 3 simples biological parameters can accurately predict steatosis >30% in morbidly obese patients and could be used to better select marginal grafts before activating the procurement proceeding.

15 LONG TERM IMPACT OF DISSEMINATED INTRAVASCULAR COAGULATION OF THE CADAVERIC DONOR ON KIDNEY TRANSPLANTATION

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Introduction: In 2013, the disseminated intravascular coagulation (DIC) was diagnosed in 19 of 1504 brain death kidney donors in France. The aim of this study was to evaluate the impact of donor DIC on kidney transplantation (KT).
Method: We identified 126 kidney recipients with DIC+ brain death donors between 01/01/1996 and 12/31/2012 in 4 French transplantation centers. They were matched to 126 recipients with DIC− donors according to donor age, gender, expanded criteria, transplantation date and center.
Results: DIC+ donors had a higher Creatinine than DIC− donors (134.5 vs. 90.0 μM, p = 0.001) and received more amines (p = 0.01) and transfusion (85.5 vs. 32.5%, p = 0.001).One and five years kidney survival was 92.7% and 83.5% in DIC+ donors recipients, and 95.3% and 85.2% in DIC− donors recipients (p = ns). eGFR median in DIC+ donors recipients and in DIC− donors recipients at M3 were 43.3 and 47.76 ml/min (p = 0.09); at M12: 45.48 vs. 48.3 ml/min (p = ns) and at M60: 37.54 vs. 38.56 ml/min (p = ns) respectively. Among recipients whose donor's creatinine was >133 μM, M3 eGFR medians were 46.5 in DIC+ and 46.1 ml/min in DIC− donors recipients (p = ns). Delayed graft function (DGF) was observed in 34.8% in DIC+ vs. 22.7% in DIC− (p = 0.04). Blood, platelet and fresh plasma frozen infusion frequency was not different between the two groups. The average period of hospital length of stay was similar in DIC+ (18.3 days) and DIC− donors recipients groups (17 d) (p = ns).
Discussion: DIC in cadaveric donors is associated with DGF and a tendency to a lower initial eGFR in kidney recipients. This is probably due to kidney damage in DIC+ donors (tubular necrosis, glomerular thrombi . . .). Analysis of the subgroup of DIC+ donors with thrombocytopenia remains to be done.
Conclusion: DIC of the donor does not affect graft survival or long-term graft function.

16 COMBINED PANCREATIC ISLET–LUNG TRANSPLANTATION: A NOVEL APPROACH TO THE TREATMENT OF END-STAGE CYSTIC FIBROSIS

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Introduction: Cystic fibrosis related-diabetes (CFRD) is a major factor of morbi-mortality in lung transplantation. We report the follow-up of five patients with end-stage cystic fibrosis and severe CFRD who were treated with combined pancreatic islet-lung transplantation.
Patients and Method: Bipulmonary bloc and pancreas are procured from the same donor. During the lung transplantation, slet isolation and culture are performed in the laboratory. Two weeks after lung transplantation, the islets are injected by percutaneous transhepatic catheterization of the portal vein under local anesthesia. Immunosuppression associates steroids and basiliximab for induction and then tacrolimus with mycofenolate mofetil and steroids.
Results: From October 2011 to May 2014, five CF patients (2 F/3M, age: 29 ± 5 years, IMC: 17 ± 2 kg/m^2) with respiratory insufficiency (FEV1:23 ± 3%) and brittle diabetes (diabetes duration: 10 ± 2 years, HbA1c = 8.2 ± 0.7%, insulin requirement = 43 ± 14 IU/day) underwent combined pancreatic islet- lung transplantation with an amount of 4564 ± 2418 Islets Equivalent/kg. Improvement in lung function was observed in five patients with a FEV1 reaching 96%, 75%, 90%, 68% and 85% respectively 30, 22, 15, 6 and 3 months after lung transplantation. The five patients showed immediately islet graft function with an increase in C peptide plasma levels. No complications related to the islet injection were observed. All patients presented an improvement in the metabolic control with a decrease in HbA1c to 6.3 ± 0.2% in absence of hypoglycemic events and a 50% decrease in the exogenous insulin needs.
Conclusion: In CF patients, combined pancreatic islet-lung transplantation restores both pulmonary function and metabolic control. Intra portal islet infusion does not increase the surgical morbidity of the lung transplantation. Further studies are required to evaluate the benefit risk ratio and the long term benefits of combined pancreatic islet-lung transplantation.

17 DONATION AFTER CARDIAC DEATH (DCD): A SOLUTION TO THE SHORTAGE OF KIDNEY TRANSPLANTS?

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Faced with the shortage of kidney transplants, donation after cardiac death (DCD) is an alternative with a risk of delayed graft function (DGF) and primary nonfunction (PNF) more important but long-term results comparable to deceased donation brain death (DBD). The objective of the study was to evaluate the DCD and identify risk factors for graft loss.

This retrospective monocentric study from 2007 to 2013 compared the DCD and DBD with standard criteria donors (SCD) and expanded criteria donors (ECD). The characteristics of donors, transplant and follow-up until 60 months were compared. The survival curves were performed by Kaplan-Meier test, and univariate and multivariate analysis were performed.

476 grafts were studied including 78 DCD, 198 SCD and 141 ECD. The study of serum creatinine level did not show any difference between the DCD and SCD at 5 years but was better than EDC. In DCD group, the transplant waiting times were significantly shorter compared to the SCD (p = 0.025) and EDC groups (p < 0.0001) as well as waiting times on dialysis. The ischemia time, the DGF and HLA incompatibilities were significantly higher in the DCD group (p < 0.0001 respectively), but did not appear to be risk factors for graft loss. The donor age appeared to be a risk factor for graft loss (p = 0.03) and death of recipients (p = 0.004), as well as cardiovascular risk factors. Five-years graft survival was similar in the three groups, but patient survival was better in SCD and DCD groups than in the ECD group (p = 0.0014).

DCD kidney transplantatin is a promising source of grafts with better results than EDC, and could increase up to 16–40% the number of donors. It is necessary to respect the protocol criteria established for this type of donors.

18 DUAL KIDNEY GRAFT VERSUS SINGLE TRANSPLANT IN OLD RECIPIENTS. RESULTS OF A CASE–CONTROL STUDY

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Introduction: The use of expanded criteria (EC) kidneys allows to old recipients, better access to transplantation. The BIGRE protocol witch gives the possibility to patients aged over 65 years to receive two kidneys, with moderate kidney failure, from the same EC donor, is a step to better access to grafts. But, should we continue doing it?
Material and Methods: It's a retrospective, case-control study, comparing dual transplants (DTX) to single transplants (STX) that were undertaken between the first September 2006 and the first September 2013. The matching has been done between the age of the donor and the recipient in each group, in the same 6 months of transplantation. We compare the postoperative complications and functional results observed in the two groups. Data were analyzed using SPSS 16.0.
Results: 42 patients (5.4% of transplantation activity in the same period) who received DTX (mean age = 71.7 ± 3.0 years) are matched to 42 patients who received STX (mean age = 70.5 ± 2.8 years). There were no differences in cold ischemia time and delayed graft function. The delay waiting was shorter in the DTX group than the STX group (7.1 ± 3.3 months vs. 13.9 ± 4.6; p < 0.01). The early reinterventions in the DTX group are more important without a statistic difference between the 2 groups. The indication of reoperation in the DTX group was transplantectomy of the second graft for venous thrombosis in three cases of four cases. STX recipients achieved better creatinine clearance at 7 days, 3, 6, and 12 months, although only significantly at 1 month (54.4 ± 19.5 vs. 44.5 ± 15.6 ml/min; p < 0.05). The patient and graft survival at 1 year was the same in the 2 groups.
Conclusion: DTX offered good results for graft survival and renal function compared to STX. The easy access to transplantation remains the strong point of the BIGRE protocol, offering better survival and quality of life to old patients with chronic kidney disease. Continuing this activity is a real gain for all patients in kidney graft waiting list.

19 ANALYSIS OF BRONCHOALVEOLAR LAVAGE FLUID WITH NMR SPECTROSCOPY IN A LUNG AUTOTRANSPLANTATION MODEL IN PIG

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Introduction: Evaluation of preservation protocols for organ transplantation is of primary importance regarding donor pool heterogeneity. We previously present NMR metabolomic analysis of preservation solution in the case of kidney. In the same manner, we propose a NMR analysis of bronchoalveolar lavage fluid (BALF) after an ischemia reperfusion sequence.
Materials and Methods: Bronchoalveolar lavage fluid (BALF) was collected after 5 h of reperfusion; explantation of the graft and an upper lobectomy was performed. Washing was done directly by instillation of 40 cc of physiological saline in the left upper bronchus. Samples were centrifuged and supernatant kept at −80°C until high resolution NMR acquisition on an Avance 500SB Spectrometer (Bruker) equipped with a 5 mm broadband inverse probe. Three groups of lung preservation protocol were studied: static preservation with Perfadex solution alone, static preservation with Perfadex solution with addition of an oxygen carrier and sham operated lung ($N = 5$ in each group).
Results: In the control lung, the BALF appears to be clean and we found only few metabolites in low concentrations as lactate. We also found in the NMR spectra metabolites from cell release as choline compounds. For sham operated group, all spectra were similar. BALF from lungs preserved with Perfadex alone showed spectra more complex with higher concentrations of lactate, addition of some metabolites aminoacids (valine, alanine) or sugar body (probably dextran-40 from prefadex solution). The last group with lung preserved with perfadex solution with addition of an oxygen carrier showed intermediate NMR profiles with intermediate concentration. The oxygen carrier seems to have a real impact on BALF composition.
Conclusion: We proposed descriptive and preliminary results on BALF analysis by NMR with a comparison of two lung preservation protocols versus healthy lung.

20 PRECLINICAL PORCINE MODEL OF ISCHEMIA-REPERFUSION INJURIES IN THE LUNG DURING CARDIOPULMONARY BYPASS

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Warm lung ischemia and reperfusion injuries in the lung are of great interest in both thoracic and cardiac surgery. During pulmonary transplantation, especially with non-heart beating donors, these lesions can lead to primary graft dysfunction. During cardiopulmonary bypass (CPB), lungs are vascularized only by the bronchial arteries: so lungs are in subtotal warm ischemia. We evaluated whether CPB is a pulmonary ischemia-reperfusion model by studying inflammation and ischemia-reperfusion injuries in the lungs of healthy swine.

We compared 3 groups of Large White swine ($n = 6$): the CPB group, in which CPB was established between the right atrium and the aorta; the sham group, animals underwent the same anesthetical and surgical procedure except CPB. The third group was a total cardio-circulatory arrest group. We evaluated an ischemic time of 120 min and a reperfusion time of 120 min. Hemodynamical datas were collected; blood and tissue samples were harvested for serical, proteomical and transcriptomical analyses.

Pulmonary arterial pressure was collapsed in the CPB group compared to sham group resulting in lung warm ischemia. IL-10 was greater in the sham group compared to CPB group at 120 min of reperfusion, and other markers of inflammation (TNFα, IL-6) were similar. We evaluated the HIF-1α pathway, specific of warm ischemia. In lung tissue sample, VEGF protein was increased significantly at 120 min of reperfusion after CPB and 120 min after total cardiac arrest.

That model is an accurate model of warm ischemia in the lungs. Results must be completed by further studies to assess the dynamical expression of genes of HIF-1α pathway. IL-10 may play a protective role in ischemia-reperfusion injuries in the lungs by counterbalancing the adverse effects of proinflammatory cytokines also expressed. That model may help to study warm ischemia during CPB or either during pulmonary transplantation with the development of non-heart beating donors programs.

21 EMERGING ROLE OF SIRTUIN 1 IN RAT ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction: Cold Ischemia Reperfusion Injury (IRI) remains a major cause of primary dysfunction of liver grafts. Nicotinamide adenine dinucleotide (NAD^+) is a classical coenzyme mediating many redox reactions and its biosynthesis is mediated partially by nicotinamide phosphoribosyl transferase (NAMPT). Also, NAD^+ is the requiring cofactor for the activity of Sirtuin 1 (SIRT1). Sirtuins are known to play major roles in protecting against cellular stress and in controlling metabolic pathways. However, the role of SIRT1 in IRI has not yet been elucidated. Here, we investigate SIRT1 implication in orthotopic liver transplantation (OLT) using IGL-1 preservation solution supplemented with an anti-ischemic drug, trimetazidine (TMZ).
Methodology: Livers from Sprague-Dawley male rats were preserved for 8 h in IGL-1 solution enriched or not with TMZ (10^{-6} M) and then subjected to OLT (Kamada's technique). After 24 h of reperfusion, rats were sacrificed and liver injury (ALT), mitochondrial damage (GLDH), oxidative stress (MDA) and NAD/NADH levels were determined. SIRT1, ac-p53, ac-FoxO1 (its direct substrates), NAMPT, p-AMPK, autophagy parameters (beclin-1, LCB3), p-mTOR and p70s6K were determined by western blot. Caspase 3 and Tunnel analysis were also performed as liver apoptosis parameters.
Results: TMZ in IGL-1 solution reduced liver injury, oxidative stress and mitochondrial damage, as well as increased SIRT1 protein expression levels, NAD^+ and NAMPT. SIRT1 overexpression was accompanied by a significant increase in p-AMPK, an inhibition of p-mTOR and p70S6K and the subsequent activation of autophagy. SIRT1 activation was consistent with decreased liver apoptosis.
Conclusion: We evidenced, for the first time, that SIRT1 exerts a protective effect against IRI associated with rat OLT. Thus, the modulation of this protein could be a useful pharmacological target for the prevention of liver IRI.

22 FATE AND ROLE OF THE CYTOSKELETTON DURING COLD ISCHEMIA

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Objectives: Ischemia reperfusion lesions are an unavoidable consequence of organ transplantation. Researching new therapeutics against these require the definition of early mechanisms. The cytoskeleton is composed of 3 types of filaments: microfilaments, intermediate filaments and microtubules.
Methods: In an *in vitro* model using primary human endothelial cells reproducing the conditions of organ preservation, two aspects were explored: 1-function: using pharmaceutical agents to stabilize microfilaments (Jaspakinolide) and microtubules (Taxol), we determined if maintaining the filament structure could decrease cell death; 2-mechanism: to define the determining factor in cytoskeleton alteration, we separated each of the 3 parameters altered during preservation: solution (culture medium versus preservation solution), oxygen (normoxia versus anoxia) and temperature (37 vs. 4°C)
Results: (i) Intermediary filaments, made of vimentin in these cells, were unaffected. (ii) Microfilaments showed radical changes: progressive disappearance of the structure replaced by a disorganized array of nodules. (iii) Microtubules almost completely disappeared with time. The results of the first aspect showed that pharmaceutical intervention could indeed preserve fiber structure but did not alter survival. Regarding the second aspect, our study shows that temperature, and not oxygen deprivation or the solution, was the determining factor of the cytoskeleton's loss of integrity observed during preservation.
Conclusion: The impact of preservation on the cytoskeleton highlights the importance of this structure for the development of new therapeutics and the definition of biomarkers of graft quality.

23 INFLUENCE OF THE ENDOPLASMIC RETICULUM IN CELL SURVIVAL DURING COLD ISCHEMIA

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Objectives: Reseach into new therapeutics against preservation-induced ischemia reperfusion injury (IRI) require the definition of early mechanisms. During a stress, protein maturation mechanisms are altered, inducing an accumulation of misfolded proteins which stimulates the UPR (unfolded protein response) through 3 pathways: IRE1α-XBP1, PERK-eIF2α-ATF4 and ATF6. We studied the activation of the UPR in preservation and its consequences.
Methods: We used a porcine model of kidney preservation and an *in vitro* model of IRI using primary human endothelial cells.
Results: *In vivo,* during pig kidney preservation, we show that each pathway has a specific activation kinetic, suggesting a unique role for each in the response to IRI. *In vitro,* using specific pharmaceutical agents (STF083010 to inhibit the endoribonuclease IRE1α, Salubrinal to inhibit the dephosphorylation of EIF2S1 and activate PERK-eIF2α-ATF4, AEBSF to inhibit ATF6), we demonstrate that cell survival can be increased through signal modulation between the three UPR branches. Using siRNA, we show that this increase is dependent the ATF6 pathway and the presence of both IRE1α and XBP1.
Conclusion: To our knowledge, this is the first study showing the involvement of UPR in IRI physiopathology and the consequences of UPR pathways modulation. Our *in vitro* data on cell survival suggest the benefits that therapeutics modulating the UPR could bring to improve organ quality and increase the efficacy of transplantation, particularly in the current context of marginal donors with organs more exposed to IRI and the graft quality decrease.

24 ROLE OF MITOCHONDRIAL MODULATION DURING KIDNEY PRESERVATION: EVALUATION IN A PRECLINICAL MODEL OF DECEASED AFTER CIRCULATORY DEATH DONOR

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Objective: Trimetazidin (TMZ), a modulator of mitochondrial metabolism, has shown protective properties in several ischemia reperfusion settings. We evaluated TMZ as an additive to preservation solution in a preclinical pig kidney transplantation model of deceased after circulatory death donor (DCD).
Methods: Groups of 7 animals were studied: sham; uninephrectomized (left kidney nephrectomy); IC60VIA (preservation with Viaspan); IC60VIA + TMZ10 (Viaspan + 10 mg/l TMZ); IC60VIA + TMZ20 (Viaspan + 20 mg/l TMZ). Kidneys were subjected to 60 min warm ischemia prior to collection and flushing with cold preservation solution. Function recovery, oxidative stress, inflammation and histological lesions were evaluated.
Results: Addition of TMZ significantly improved acute kidney function recovery ($p < 0.05$), particularly the 20 mg/l dose, as evidenced by serum creatinine evaluation. Tubular function as well as urine concentration were significantly improved ($p < 0.05$) during the first 2 weeks post transplant. Histological analysis at the end of the first week showed a decrease in kidney necrosis lesions and improvement of repair. During this last week, plasma levels of 8 iso-prostane, lipid peroxydation marker, were also decreased in treated groups, particularly in the 20 mg/l group. Plasma levels of pro-inflammatory cytokines TNF and IL6 were also decreased.
Conclusion: Added to the preservation solution in a model of DCD, TMZ limits the main lesion mechanisms of ischemia reperfusion injury. This type of molecule could also be interesting in conditioning regiments such as abdominal normothermic recirculation.

25 ISCHEMIA REPERFUSION INDUCES A RAREFACTION OF THE KIDNEY MICROVASCULAR NETWORK IN RELATION WITH GRAFT FUNCTION DECAY: A STUDY IN A PRECLINICAL PORCINE MODEL OF KIDNEY TRANSPLANTATION

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Objectives: The microvascular network is a major target of ischemia reperfusion. The goal of our study was to characterize kidney cortex vascular remodeling after ischemia reperfusion and define the most affected area.
Methods: We used a pig kidney transplantation preclinical model with contro-lateral nephrectomy in which the graft is preserved 24 h at 4°C in University of Wisconsin solution. 3 months post-transplant, kidneys ($n = 5$) were studied *ex vivo* by microtomography and compared to native kidneys ($n = 5$, Figure 1a). Vascular network morphology and in particular the density and tortuosity of the vascular segments were analyzed in three dimensions. Cortical blood flow was also evaluated, as well as kidney function and tubular lesions.
Results: Kidney ischemia reperfusion lead to a decrease in vascular segment volume associated with a rarefaction of small vessels (<30 μm), particularly in the deep cortex (Figure 1b). This rarefaction was correlated with kidney function decrease, proteinuria and tubular dysfunction (Figure 1c). Graft cortical blood flow was decreased at 1 h and 3 months post transplant. In the full cortex of the graft, we showed a increase in vascular segment bifurcation number and the development of tissue fibrosis which contributes to vascular remodeling (Figure 1d).
Conclusion: This study provides observations on the lesional spectrum of kidney ischemia reperfusion and will permit the future development of therapeutics to improve preservation of the kidney graft microvascular network.

26 MECHANISTIC ANALYSIS OF MACHINE PERFUSION BENEFITS ON WARM ISCHEMIC KIDNEY UNCOVERS IMPROVED ENOS PHOSPHORYLATION DURING PRESERVATION AND VASODILATION AFTER REOXYGENATION

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Objectives: Protection of endothelial cell function may explain the benefits of machine perfusion (MP) for marginal kidneys preservation. However, this hypothesis remains to be tested with a preclinical model. We postulated that MP protects the nitric oxide (NO) signaling pathway, altered by static cold storage (CS), and improves renal circulation recovery compared to CS. The endothelium releases the vasodilator NO in response to flow *via* either increased endothelial NO synthase (eNOS) expression (KLF2 dependent) or activation of eNOS by phosphorylation.
Methods: We analyzed porcine kidneys subjected to 1 h of warm ischemia and preserved 24 h by CS or MP. The pathway study was conducted by Western Blot, completed with a contractibility study of the vessels and a laser Doppler analysis of revascularization at reperfusion.
Results: We reported that MP did not affect cortical levels of KLF2 and eNOS compared to CS. However, MP significantly increased eNOS activating phosphorylation in the renal cortex and increased NO-dependent vasodilatation of renal arteries at the end of preservation. eNOS activating phosphorylation was AMPK-dependent rather than Akt- or PKA-dependent. *In vivo*, at reperfusion, laser Doppler showed that cortical microcirculation was improved in MP kidneys.
Conclusion: We demonstrate for the first time in a large animal preclinical model that MP benefits kidney grafts through protection of the NO signaling pathway, confirming the value of MP for marginal kidney preservation.

27 PROGNOSTIC VALUE OF RESISTANCE INDEX DURING HYPOTHERMIC PULSATILE RENAL PRESERVATION OF KIDNEYS FROM UNCONTROLLED DECEASED DONORS AFTER CARDIAC ARRET

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The organ shortage has led to the use of marginal kidneys as those from uncontrolled deceased donors after cardiac arret (uDDCA). Their assessment is based on the analysis of donor's characteristics, perfusion parameters and biopsy if doubt. The aim of our study was to verify the prognostic value of the Resistance Index (RI) for the evaluation of the viability of these grafts.

Since 2006, 72 grafts were removed and perfused by the RM3 machine (Waters Medical®). Donors met the criterias of the French National protocol for uDDCA. 20 grafts were not transplanted because of poor perfusion parameters (RI > 0.5 mmHg/ml/min) or severe histological lesions or other. Before recovery, they were conserved *in situ* using a Gillot Sonde (GS) or using a Normothermic Regional Circulation (NRC). A dual kidney transplantation (DKT) was performed if RI were between 0.35 and 0.5. We studied the association between RI and donor's characteristics and functional outcomes.

Between 2006 and 2013, there were 46 patients transplanted from uDDCA including 6 DKT. Median follow-up was 48 ± 27.4 months. There were 86.9% Delayed Graft of Function (DGF) and no Primary Non Function (PNF). At 12 months, the mean calculated glomerular filtration rate and inulin clearance were 44.3 ± 14.6 and 45.4 ± 11.6 ml/min/1.73 m² respectively. RI of grafts preserved by GS ($n = 29$) were significantly higher than those by CRN ($n = 17$). RI were significantly associated with donor's sex and creatinine, duration of warm ischemia and of conservation by NRC/GS. The number of post transplant dialysis and the date of function recovery were significantly improved when the RI were <0.35. There was no association between RI and clearance at 12 months.

The absence of PNF and the good functional outcomes validate our strategy of acceptance of grafts from uDDCA according to the analysis of RI. RI are correlated with the degree of organ injury of these grafts.

28 FINAL RESULTS FROM THE LONG-TERM EXTENSION (LTE) OF THE BELATACEPT PHASE 2 STUDY IN KIDNEY TRANSPLANTATION

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Introduction: At 5 years post-transplant, data from the Phase 2 IM103-100 LTE study of belatacept (bela) in kidney transplantation demonstrated a favorable safety profile and improved renal function versus cyclosporine (CsA) (Vincenti F et al, *JASN* 2010;21(9):1587–96). Here we report outcomes in all randomized and treated patients through study close (approximately 10 years).
Methods: 218 patients were randomized to receive bela (n = 145) or CsA (n = 73). After 6 months, bela patients were randomized to 4-week (n = 62) or 8-week (n = 60) dosing intervals (5 mg/kg). Here we focus on the results from randomization to study end in bela patients randomized to 4- or 8-week treatment groups and all CsA patients.
Results: At month 3, mean MDRD cGFR was 66 (bela 4-week), 65 (bela 8-week), and 60 (CsA) ml/min/1.73 m^2; and at 10 years mean cGFR was 72 (bela 4-week), 67 (bela 8-week), and 52 (CsA) ml/min/1.73 m^2. From randomization to end of study, acute rejection occurred in 4, 4 and 5 patients in the bela 4-week, bela 8-week, and CsA groups, respectively. Death or graft loss occurred in 14 bela patients (10%) and 8 CsA patients (11%). The incidence rate of serious adverse events was 33 (bela 4-week), 48 (bela 8-week) and 55 (CsA) per 100 person-years; incidence of serious infections was 6 (bela 4-week), 10 (bela 8-week) and 15 (CsA) per 100 person-years. There were 3 cases of PTLD in bela-treated patients (2 EBV-negative, 1 EBV-unknown) that occurred by Month 13 and 1 case in a CsA-treated patient in Year 4 (EBV-unknown).
Conclusions: Data from this limited cohort suggest that the profile of bela is consistent over approximately 10 years of treatment: patients maintained renal function with no new safety findings and long-term outcomes were similar between 4-week and 8-week treatment groups. Results should be validated in a larger cohort.

29 OUTCOMES AT 3-YEARS IN EBV+ RECIPIENTS OF DECEASED DONOR KIDNEYS FROM TWO RANDOMIZED TRIALS (BENEFIT AND BENEFIT EXT) COMPARING BELATACEPT VERSUS CYCLOSPORINE

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Introduction: The less intensive (LI) regimen of belatacept (bela) is approved for use in EBV+ adult kidney transplant recipients. Here we present *post hoc* analyses of 3-year outcomes in EBV+ patients (pts) in the pooled population of BENEFIT and BENEFIT-EXT who received a deceased donor kidney.
Methods: In BENEFIT, pts received living donor (n = 385) or SCD kidneys (n = 281), and in BENEFIT-EXT (N = 543), pts received ECD kidneys (defined as UNOS criteria ECD, cold ischemia time 24 h, or donation after cardiac death). In both trials, pts were randomized to a more intensive (MI) or LI regimen of bela or CsA. In this analysis, the pooled cohort was evaluated for pt and graft survival, cGFR, acute rejection (AR), and a composite end point (EP): death, graft loss or GFR < 30.
Results: In this cohort, 250 MI, 247 LI, and 249 CsA pts were EBV+ at the time of transplant and received a deceased donor kidney. Pt/graft survival at Month (M) 36: 211 (84%) MI, 217 (88%) LI, and 205 (82%) CsA. The rate of AR through M36 was 22% MI, 17% LI, 14% CsA. Mean(SD) MDRD cGFR at M36 was 50.5(30) MI, 51.6(27) LI, 35.0(23) ml/min/1.73 m^2 CsA. Fewer bela-treated pts versus CsA reached the composite EP (Figure). Rates of serious adverse events were generally similar across treatment arms.
Conclusions: The results of this *post hoc* analysis demonstrate the following for EBV+ pts in BENEFIT and BENEFIT-EXT receiving a deceased donor kidney: similar pt/graft survival with bela versus CsA, improved renal function for both bela regimens versus CsA, and similar rate of AR for bela versus CsA (approved LI regimen only). For both bela regimens, the rate of composite EP was lower with bela versus CsA. The positive outcomes in this subset of EBV+ pts are consistent with the results observed with bela in the overall populations of BENEFIT and BENEFIT-EXT.

30 EVALUATION OF DONOR-SPECIFIC ANTIBODIES THROUGH 5 YEARS WITH BELATACEPT IN BENEFIT AND BENEFIT-EXT

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Introduction: Donor-specific antibodies (DSA) are associated with negative post-transplant outcomes, including increased risk of antibody-mediated rejection and graft failure. *De novo* (DN) DSA occur in ~11% of kidney transplant recipients by 1 year and in ~20% by 5 years (Everly et al, *Transplantation* 2013;95(3):410–7). The 3 year ITT results from BENEFIT and BENEFIT-EXT showed that belatacept (bela) was associated with lower rates of DN DSA than CsA (3% vs. 8%, Larsen C et al, ESOT 2011 [presentation O244]). Here we report the incidence of DN DSA through Year 5 in the long-term extensions (LTE) of these studies.
Methods: In BENEFIT, patients received living donor or SCD kidneys, and in BENEFIT-EXT, patients received ECD kidneys. Patients who received either the more intensive (MI) or less intensive (LI) bela or CsA regimen could enter the LTE after 3 years. The presence of DSA was established centrally by measuring the recipient's HLA antibodies, and then determining if any of those HLA antibodies were donor directed based on donor and recipient HLA type. HLA antibody screening was performed by solid phase flow cytometry (FLowPRA™), and specificity (Class I and II) assessed by LabScreen™ single antigen beads (One Lambda, Inc.).
Results: From baseline through Year 5 in the LTE cohort of both studies, numerically fewer bela- versus CsA-treated patients developed DN DSA (Table): in BENEFIT, 3 (1.9%) MI, 6 (3.6%) LI, and 16 (11.8%) CsA, and in BENEFIT-EXT, 7 (6.7%) MI, 1 (0.9%) LI, and 9 (10.3%) CsA-treated patients developed DN DSA. Mean fluorescent intensity was also assessed and data will be reported.
Conclusions: These data demonstrate a reduced rate of DN DSA with bela versus CsA from baseline through 5 years, consistent with the findings observed through 3 years.

31 OUTCOMES AT 3-YEARS IN EBV+ RECIPIENTS OF UNOS CRITERIA ECD KIDNEYS FROM A RANDOMIZED TRIAL (BENEFIT-EXT) COMPARING BELATACEPT VERSUS CYCLOSPORINE

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Introduction: The less intensive (LI) regimen of belatacept (bela) is currently approved for use in EBV+ adult kidney transplant recipients. Here we present *post hoc* analyses for the 3-year outcomes of EBV+ patients (pts) in BENEFIT-EXT who received deceased donor kidneys consistent with UNOS ECD criteria.
Methods: In BENEFIT-EXT, 543 pts received ECD kidneys per UNOS criteria, anticipated cold ischemia time (CIT) >24 h, or donation after cardiac death. UNOS criteria donors were defined as age 60 years or age 50–59 with 2 other risk factors (cerebrovascular accident, hypertension, or serum creatinine >1.5 mg/dl). Pts were randomized to receive CsA or a more intensive (MI) or LI bela regimen. In this *post hoc* analysis, the UNOS ECD cohort was evaluated for pt and graft survival, cGFR, acute rejection (AR), and a composite end point (EP) of time to death, graft loss or cGFR < 30 ml/min/1.73 m^2.
Results: In BENEFIT-EXT, 119 MI, 110 LI, and 123 CsA pts were EBV+ and received a UNOS criteria ECD kidney. At month (M) 36, survival with a functioning graft was similar across treatment arms: 95 (80%) MI, 90 (82%) LI, and 94 (76%) CsA. Mean (SD) MDRD cGFR at M36 was 40.0 (26) MI, 39.7 (24) LI, and 26.3 (21) ml/min/1.73 m^2 CsA. At M36, AR was 24 (20%) MI, 22 (20%) LI, 18 (15%) CsA. Fewer bela pts reached the composite EP compared with CsA (Figure). Rates of serious adverse events were generally similar across treatment arms.
Conclusions: The results of this *post hoc* analysis of EBV+ recipients of UNOS ECD kidneys in BENEFIT-EXT demonstrate similar pt and graft survival with both bela regimens versus CsA. Renal function was also improved with bela MI and LI despite numerically higher rates of AR, and the rates of the composite EP were lower with bela MI and LI versus CsA. The positive outcomes in this subset of EBV+ pts are consistent with those observed for bela in the overall BENEFIT-EXT population.

32 TRANSCRIPTOMIC MICROARRAY ANALYSIS OF REGULATORY B LYMPHOCYTE POPULATIONS IDENTIFIED IN PATIENTS TREATED WITH BELATACEPT

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Introduction: The so-called regulatory B lymphocytes are involved in self-tolerance. Currently, no specific phenotypic or transcriptional markers are identified. In humans, transitional B cells, immature, are defined by phenotypic markers $CD24^{high}CD38^{high}$. These cells secrete IL-10 and can inhibit the T cell response *in vitro*. We have shown recently that kidney transplant recipients treated with Belatacept (CTLA4-Ig, co-stimulatory blocking agent) have significantly more $CD24^{high}CD38^{high}$ transitional B cells compared to recipients treated with calcineurin inhibitors (Leibler C et al, AJT. 2014). Here we present the results of the first transcriptomic analysis of this population.
Methodology: B cells were obtained from human PBMC by magnetic bead selection. Three populations were sorted by flow cytometry based on CD24 and CD38: transitional $CD24^{high}CD38^{high}$ population was compared with two control populations $CD24^{+}CD38^{-}$ (memory) and $CD24^{int}CD38^{int}$ (mature). A transcriptomic analysis of these three populations was performed by Agilent Whole human genome oligo microarrays.
Results: Bioinformatic analysis showed a particular signature in the population of interest $CD24^{high}CD38^{high}$ with around 500 genes up-regulated and 800 genes down-regulated compared to the two control populations. Twelve genes involved in signaling pathways, apoptosis, cell cycle arrest and metalloendopeptidase activity were specifically expressed in the population of interest.
Conclusion: Identification of specific candidate genes by flow cytometry may allow us to better characterize the regulatory B cells phenotype and to identify the mechanisms involved in the regulation process.

33 HIGH-DOSE IVIG WITHOUT CARBOHYDRATE EXCIPIENTS SAFETY IN THE EARLY KIDNEY POSTRANSPLANTATION PERIOD

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Intravenous immunoglobulins (IVIG) are widely used in kidney transplantation despite the risk of nephrotoxicity, usually attributed to carbohydrate excipients.

In this study, we assessed the safety of high-dose IVIG courses without carbohydrate excipients in kidney transplant recipients.

A first part of our retrospective study evaluated renal function after 180 high-dose (2 g/kg) IVIG courses without carbohydrate excipients delivered to 84 kidney recipients within 3 months after renal transplantation. A second study compared at 3 months and 1 year post-transplant renal function and histology in 50 patients who received IVIG without carbohydrate excipients and in 27 patients who received IVIG containing carbohydrate excipients.

According to the RIFLE criteria, no cases of AKI were reported after 180 courses of IVIG without carbohydrate excipient.

The two groups who received IVIG, with or without carbohydrate excipient, HAD similar serum creatinine at 3 months and 1 year after transplantation. However, histological analysis of protocol biopsies showed that the absence of carbohydrate excipient was associated with a decreased prevalence of tubular cytoplasmic macrovacuolisation at 3 months (63% vs. 12%, $p < 0.0001$) and one year (44.4% vs. 6.1%, $p < 0.001$). The IF/TA score at 3 months and one year was similar in both groups.

High-dose IVIg without carbohydrate excipients are safe in the early postransplantation period. The use of products without carbohydrate excipients appears to decrease tubular damage caused by osmotic nephrosis at 3 months and 1 year after transplantation.

34 EVEROLD: A MULTICENTER RANDOMIZED STUDY FOR THE USE OF EVEROLIMUS IN "OLD-FOR-OLD" RENAL TRANSPLANTATION

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Introduction: In elderly patients receiving a kidney graft from old donors, CNI-free protocols are interesting but expose to the risk of acute rejection. We conducted the Everold study for assessing the benefit of the use of everolimus in old- for-old renal transplantation (recipient and donor >60 years).

Methods: We included 304 patients with low immunological risk that were randomized to the CsA arm (Csa): anti-IL2R induction/CsA/MMF, or the everolimus switch arm (Evs): switch from CsA to everolimus after 6 weeks, or the *de novo* everolimus arm (Evd): thymoglobulins/everolimus *de novo*/MMF). In the 3 groups MPA exposure was normalized using MPA AUCs and steroids were withdrawn after 4 months.
Results: Patient characteristics were similar in the 3 groups, in particular mean age of the donors and the recipients (68 and 71 years) and cold ischemia time (16 h). We report data of 285/304 patients that completed the study. One year patient survival was identical in the 3 arms (94%). There were 12 graft losses in the Csa arm versus 7 in the Evs arm and 5 in the Evd arm. Delayed graft function (DGF) and particularly severe and prolonged DGF (more than one HD session) were significantly less frequent in the Evd arm. The 12 month biopsy-proven acute rejection rate was not different between groups: Csa 10%, Evs 15%, Evd 7%. Intent to treat analysis showed similar 1 year GFR (MDRD) respectively 34, 37 and 39 ml/min. The discontinuation rate was high in the everolimus groups: Evs 41%, Evd 62% versus Csa 26%, mainly due to adverse events. Lymphoceles, wound healing complications and neutropenia were more frequent in the Evd arm and mouth ulcers in the 2 everolimus groups.
Conclusion: Old-for-old renal transplantation provides good patient and graft survival. The 3 arms seems equivalent in terms of clinical outcome at one year however tolerance of everolimus in these populations was poor.

35 CONVERSION TO EVEROLIMUS DRAMATICALLY IMPROVES THE PROGNOSIS OF *DE NOVO* MALIGNANCIES AFTER LIVER TRANSPLANTATION FOR ALCOHOLIC LIVER DISEASE

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De novo malignancies are a main cause for late death after liver transplantation (LT). Everolimus (ERL) is an immunosuppressive agent with anti-tumoral properties. The aim of the present retrospective study was to identify prognostic factors, including conversion to ERL, for patients presenting non cutaneous *de novo* solid organ malignancy after LT for alcoholic cirrhosis. The study population consisted in 83 patients (presenting 100 tumours, including 75% of upper aero-digestive tract cancers), among the 398 patients who underwent LT for alcoholic cirrhosis in our centre. After diagnosis, ERL was introduced in 38 patients and calcineurin-inhibitor was discontinued in 64.1% of them. Tumour stage was a significant prognostic factor with a 1-year survival at 82.6% for early stages, 63.4% for intermediate stages (N+) and 27.4% for disseminated diseases ($p < 0.001$). Associated relative risk factor was 2.202 (95% CI 1.044–4.644) for intermediate stages and 5.743 (95% CI 2.436–13.541) for metastatic stages. One and 5-year survival was 77.4% and 35.2% in ERL group versus 47.2% and 19.4% in the non-ERL group, respectively ($p = 0.003$). The relative risk factor for ERL was 0.447 (95% CI 0.257–0.778). Our results strongly suggest that conversion to ERL improves the prognosis of *de novo* malignancies after LT for alcoholic cirrhosis. Prospective studies are needed to confirm this benefit.

36 TWENTY-FOUR MONTH POST TRANSPLANTATION FOLLOW UP OF THE CERTITEM TRIAL

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Background: CERTITEM has evaluated the effect of everolimus/calcineurin inhibitors free (CNI free) on fibrosis progression and results have been reported at 12 months (M12). Data at M24 have been collected as part of a 6 year post transplantation observational study (C4Ever), setup to evaluate the impact of CNI free versus cyclosporin + mycophenolic acid (CsA + MPA) on the incidence of cancer and major cardiovascular events (MACE) in renal transplant recipients (RTx).
Methods: In CERTITEM, patients were randomized into 2 treatment groups at M3: CNI-free and CsA + MPA. Patients who completed the CERTITEM M12 visit were included in C4Ever.
Results: At M24, 141 patients were evaluable (67 in CNI free, 74 in CsA + MPA); among those, 36 and 70 patients respectively remained on their randomization treatment. At M24, biopsy proven acute rejection (BPAR) and *de novo* donor specific antibodies (dnDSA) occurred more frequently in

the CNI-free group (31.3 vs. 5.4%, p < 0.001 and 34% vs. 11.6%). The mean eGFR by MDRD4 formula was comparable: 56.9 ml/min in the CNI-free group vs. 52.9 ml/min in the CsA + MPA group, p = 0.54. Independent factors of BPAR at M24 were a positive epithelial to mesenchymal transition status at M12 and the CNI-free group. The incidence of cancer at M24 was 4.5% in the CNI-free group vs. 4.1% in the CsA + MPA group (ns) and MACE 4.5% vs. 5.4% (ns) respectively. Basal or squamous cell cancer occurred in 1 (1.5%) patient in the CNI-free group vs. 3 (4.1%) in the CsA + MPA ns. Death occurred in 2 pts in the CNI-free group versus none in the CsA + MPA group, ns. No graft loss occurred. Safety was comparable in both groups.
Conclusion: At M24, an increased incidence of dnDSA was observed in both groups whilst BPAR increased in the CNI free group. A non-significant increase in the incidence of MACE was observed in the CsA + MPA group; incidence of cancer was similar. Longer follow up of this population could provide further evidence regarding incidence of cancer and MACE in RTx.

37 EFFICACY OF RITUXIMAB IN FOCAL SEGMENTAL GLOMERULOSCLEROSIS RECURRENCE IN ADULT KIDNEY TRANSPLANTATION RECIPIENT: A PRELIMINARY STUDY

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Introduction: In the literature, only 20 cases of adult renal transplant (RT) recipients with recurrent focal segmental glomerulosclerosis (HSF) treated with Rituximab (RTX) were described. We report a series of 14 adults in 4 transplantation units.
Patients: Patient characteristics are: 10M and 4F, age 38 ± 15 years, immunosuppressive regimen: Induction (7SAL, 7 anti-IL2R) then calcineurin inhibitors (8CsA, 6Tac) + mycophenolate + steroids. The time between the TR and HSF recurrence was 14.5 [0–247] days. Initial treatment of the recurrence was Plasmapheresis (PTX) + CsAiv + steroids. The RTX was started immediately (n = 5, G1 group) or after failure of initial treatment (n = 6, G2) or weaning failure from PTX (n = 3, G3). Complete remission (CR) is defined as proteinuria <0.3 g/day, a partial remission (PR) by proteinuria <2 g/day or decrease >50% in proteinuria.
Results: Overall, we observed 7CR and 3PR with 2CR + 1PR in G1, 4CR + 0PR in G2, 1CR + 2PR in G3, 1 dialysis dependant patient at M24 in G1 and another at M9 in G2. The median interval between the diagnosis of HSF and starting RTX was 32 days [24–113] in G2, 60 days [23–103] in G3. HSF relapse after remission post RTX was 0/3 in G1, 0/4 in G2 and 3/3 in G3. CD19 were >10/mm^3 at the time of relapse in the 3 Pts. A repeated course of RTX allowed 2CR in G3. During the 1st year, 10 patients developed severe infections (13 bacterial, 2 viral, 1 parasite).
Discussion: The success rate of RTX in our series (10/14) is comparable to that of literature. CD19 > 10/mm^3 may be an indicator of HSF relapse after RTX induced remission.
Conclusion: In RT recipients with recurrent HSF, Rituximab treatment maybe useful in case of failure of initial treatment (PTX/CsA/steroids) or weaning failure from PTX.

38 ACCESS TO THE PREEMPTIVE REGISTRATION ON THE WAITING LIST FOR CADAVERIC RENAL TRANSPLANTATION: A HIERARCHICAL MODELING APPROACH

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Background: Outcomes are significantly higher when kidney transplantation (KT) is preemptive rather than performed after dialysis. Enrolment on KT waiting list should be considered preemptively as much as possible. This study was carried out to estimate the association between the renal unit and the preemptive registration on the waiting list for first cadaveric KT in a French network of care.
Methods: From 2008 to 2012, 1529 adult-patients followed in 49 centers of the French North-West network, and registered on the waiting list for a first cadaveric KT, were included. We used a traditional logistic regression for bivariate analysis, and mixed logistic regression with dialysis center as random-effects term.
Results: Of the 1529 patients included in the study, 407 were placed on the waiting list preemptively. In bivariate analysis, cardiovascular disease (CVD), social deprivation score, ownership of the facility and the transplant center were associated with the preemptive registration. The non-adjusted mixed model showed a significant variability across dialysis centers. In multivariate analysis, factors independently associated with preemptive registration were CVD [OR 0.55 (95% IC 0.39–0.76)], social deprivation [OR 0.74 (95% IC 0.57–0.96)], ownership of the facility [University Hospital, reference – General Hospital, OR 0.48 (95% IC 0.24–0.95) – Private, OR 0.39 (95% IC 0.18–0.83)] and the transplant center (P < 0.05). Variability between dialysis centers was reduced after taking into account for their characteristics but was not influenced by patients characteristics.
Conclusion: Preemptive registration is associated with dialysis centers, transplant centers, social deprivation, and can be partly explained by disparities in practices. In view of these findings, public health actions should be implemented to facilitate the access to preemptive registration on the waiting list, especially among the most disadvantaged populations.

39 IMPACT OF WEIGHT LOSS BEFORE RENAL TRANSPLANTATION IN OBESE PATIENTS: RISK OF EARLY MORTALITY

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Introduction: Access to renal transplantation for obese patients is important because survival is significantly better after transplantation than if they remained on dialysis transplant list. Loosing weight before transplant to have a body mass index (BMI) < 30 or 35 is frequently required this weight loss could be more harmful than beneficial.
Methods: We have retrospectively studied the data of 893 transplant patients from 01/01/2007 to 31/12/10 in the Mayo Clinic Rochester, USA Data from non obese patients (NO group) were compared with those from patients with an history of obesity (O group). In the O group, dates from patients with a significant weight loss (WL group) were compared to those from obese patient who have not lost weight (NWL group). Significant weight loss is defined as a decrease in weight observed during the time spends on the waiting list of more than 10% of the initial weight.
Results: Most patients received a kidney transplant from a living donor, Of the O group (n = 380, 42%), 33% had a BMI > 30 and 17% a BMI > 35 at time of transplantation. In comparison with NO, O patients are older, have more comorbidities (stroke, hypertension and diabetes), warm ischemia time tends to be longer, surgical complications are more frequent. However the patients and grafts survivals do not differ between the two groups. Apart from a greater proportion of African-American in the WL (n = 78), no differences in demographic characteristics were observed between WL and NWL group. No difference in the incidence of surgical or medical complications was seen between the WL and NWL groups. However, the patients survival adjusted for age and comorbidities is better in NWL group first year post transplantation.
Conclusion: Weight loss before transplantation in obese do not decrease surgical complications and may be harmful.

40 EXCELLENT LONG-TERM OUTCOME OF RENAL TRANSPLANTATION IN CYSTINOSIS PATIENTS

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Cystinosis is a rare lysosomal disorder leading to end stage renal disease (ESRD) in more than 90% of patients before 20 years old. We report outcome of renal transplantation in cystinosis patients. Data were retrospectively analysed in 5 French university centres. A control cohort of 93 patients was constituted, matching to age, graft date, living/deceased donor and center to cystinosis patients. 31 transplantations were performed between 1980 and 2013. Median age at transplantation was 20.4 years (7–36.5). At transplantation, all cystinosis patients had corneal cystine deposits, 3 diabetes and 7 hypothyroidism. At 10 years graft survival was similar between the two groups (86.5 and 72% respectively). After a median follow up of 144 months (6–340), six cystinosis patients (19%) reached ESRD. At the end of follow up, graft survival was better in cystinosis group with 53% of graft survival at 340 months. Cystinosis complications occurred during follow up: diabetes mellitus (n = 4), hypothyroidism (n = 1), liver involvement (n = 1), neurologic involvement (n = 2). Diabetes after transplantation occurred as frequently in cystinosis than in control patients (13% and 5% respectively, p = 0.25), with no differences in term of calcineurin inhibitors treatment during follow-up. Renal transplantation appears to be safe and efficient in cystinosis patient.

41 FIVE-YEAR PROGNOSTIC VALUE OF THE EGFR AND ITS SLOPE OF EVOLUTION DURING THE FIRST YEAR POST-TRANSPLANTATION IN KIDNEY ALLOGRAFT RECIPIENTS

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Introduction: The 1-year estimated glomerular filtration rate (eGFR) and its evolution during the first year after the transplantation are prognostic markers associated with subsequent graft loss. The goal of our study was to evaluate their performance to predict 5-year allograft loss.
Patients and Methods: Demographic and immunologic characteristics of kidney donors and recipients, their 1-year eGFR and its slope during the first year computed by linear regression were analysed for each patient who received a first kidney allograft in our center between 1999-01-01 and 2011-08-31. Fine & Gray statistics and ROC curves were used to analyse the prognostic impact of all available variables, and the factors which incluenced the slope of eGFR were determined using a linear mixed model.
Results: During a mean follow-up period of 65 $\pm$ 41.3 months, 114 out of 961 patients lost their graft and 51 died. The only identified independant prognostic factors were the 1-year eGFR ($p = 7 \times 10^{-7}$) and its slope over the first year ($p = 3.5 \times 10^{-4}$). However these markers had poor predictive performances: area under ROC curves were 0.68 and 0.66 respectively. Between 1 and 5 year post-transplantation, the sign of the eGFR slope changed for 40.5% of the analysed patients: 27.2% had a negative 1-year eGFR slope but a positive 5-year slope, and 13.3% exhibited a symmetrical pattern. Marginal donors and class 2 allo-immunisation were associated with more negative eGFR slopes. A lower 1-year eGFR and a steeper decreasing eGFR slope were associated with an increased mortality.
Discussion: One-year eGFR and its slope during the 1st year post transplantation are the strongest prognostic factors for kidney allograft. Nevertheless, none of them is reliable to predict 5-year allograft survival. The analysis of eGFR trajectories suggests that long-term allograft outcome depends on events which occur later than 1 year post-transplantation and change the eGFR trajectory in 40.5% of patients.

42 KIDNEY TRANSPLANTATION IN PATIENTS WITH SYSTEMIC SCLEROSIS: A FRENCH MULTICENTER STUDY

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Introduction: La transplantation rénale est une des options thérapeutiques de la prise en charge de l'insuffisance rénale chronique terminale des patients sclérodermiques. Cependant les données actuellement disponibles montre une survie du patient et du greffon inférieures aux autres néphropathies.
Méthodologie: Un questionnaire a été adressé à chaque centre de transplantation rénale français afin de recenser les patients sclérodermiques transplantés rénaux. Leurs caractéristiques cliniques et paracliniques ont été répertoriées et leurs survies analysées.
Résultats: Trente quatre patients âgés en moyenne de 52.9 ans (27.7–75.5) ont bénéficié de 36 greffes rénales entre 1987 et 2013. L'atteinte rénale initiale était liée à une crise rénale sclérodermique dans 76.4% des cas. Le délai entre la prise en charge en dialyse et l'inscription sur liste d'attente est de moins de 24 mois dans 76% des cas et le délai moyen avant greffe de 45 mois (5–153 mois). Au décours de la greffe on note une seule non fonction primaire (récidive de la maladie) et 5 reprises retardées de fonction (13.9%). Le traitement immunosuppresseur a comporté des anticalcineurines dans 92% des cas. Les stéroïdes ont été prescrits dans 89% des cas et arrêtés en moyenne à 6 mois dans seulement 36.7% des cas. Les atteintes extra-rénales sclérodermiques restent stables en majorité au décours de la greffe. La survie des patients à 1 an, 3 ans, 5 ans et 10 ans est respectivement de 100%, 93.8%, 85.7% et 77.1%. La survie du greffon censurée pour le décès à 1 an, 3 ans, 5 ans et 10 ans est respectivement de 97.2%, 93.6%, 89.4%, 73.3%. Trois suspicions de récidive de crise rénale sclérodermique sont rapportées.
Conclusion: La survie des patients et des greffons après transplantation rénale est excellente dans notre étude. En l'absence de contre indication extra-rénale à l'inscription sur liste d'attente, la transplantation rénale nous paraît devoir être privilégiée dans cette population.

43 KIDNEY TRANSPLANT AND ANTECEDENT OF PSYCHIATRIC ILLNESS

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Introduction: No data are available on the outcome of kidney transplantation in patients with chronic psychosis or bipolar disorder.
Materials and Methods: We conducted a retrospective multicenter study from 1989 to 2012 of three French centers with a sole inclusion criterion of renal transplantation with antecedent of bipolar disorder (BD) or progressive chronic psychosis. Our objective was to evaluate the results of kidney transplantation and the development of psychiatric illness.
Results: Twenty-three patients (12 men) aged 30.0–73.0 years (median 51.9 years) were included. Six had been diagnosed with schizophrenia, 2 with chronic paranoid schizophrenia (CPS) and 15 with BD. Twenty-two patients were dialyzed at the time of transplantation with a median time on dialysis of 2.5 years (0.8–11.9).

After transplantation, 18 (78.3%) patients experienced at least one psychiatric decompensation including 2 immediately after transplantation and 12 (52.1%) were hospitalized in a specialized environment. Twelve (66.6%) of these patients had a BD and 6 (33.3%) schizophrenia or PHC. An attempt of suicide was reported among the patients with BD.

Discontinuation of immunosuppressive therapy was noted in four (17.4%) patients (2 BD and 2 schizophrenics) and for three of them, this cessation was the cause of graft loss.

At the end of follow-up [median 5.0 years (0.2–17.9)], 8 patients had an episode of acute rejection. The patient survival was 82.6% and graft survival was 78.3% vs. 83.3 and 77.3% respectively in the control group. The median of estimated GFR was 77.5 ml/min/1.73 m^2 (40–120).
Conclusion: We report for the first time the feasibility of kidney transplantation in a population suffering from a severe psychiatric illness. Kidney transplantation is often complicated with psychiatric decompensation justifying an assessment prior to transplantation and post transplantation medical and psychiatric optimal monitoring.

44 RECURRENCE OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS ON THE GRAFT: INTEREST OF PLASMA EXCHANGE AND IMMUNOADSORPTION – ABOUT 11 CASES

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Primary focal segmental glomerulosclerosis recurrence on a graft: Interest of plasma exchanges and immuno-adsorption – 11 case studies.
Introduction: Primary focal segmental glomerulosclerosis (FSGS) is a nephropathy progressing to terminal kidney disease. Recurrence on a graft is common. In order to reduce relapses, plasma exchanges (PE) are proposed. We report our experiences since 2009.
Materials and Methods: We prospectively included all patients with primary FSGS who received a kidney transplant since 2009. Immunosuppressive therapy includes an induction (Thymoglobulin), intraveinous cyclosporine, mycophenolate mofetil and corticosteroids. The PE are carried out according to the Niaudet protocol[1]. If unsuccessful, the PE are stopped and replaced by immuno-adsorption (IA) then Rituximab if proteinuria persists.
Results: We included 11 patients (4 men). FSGS on native kidneys occurred as nephrotic syndrom (9/11) mean age was 21 (4 months to 55 years). Evolution time to dialysis was 11 years and 6 months (3 months to 32 years). Two patients were transplanted for the second time after graft loss due to recurrence. Mean follow-up after transplantation was 18 months (38 months$\pm$). Eight patients had no recurrence with PE. The others received IA with two partial responses and one complete remission. The mean creatinine at 1 year was 122 μM and proteinuria/creatininuria ratio was 1.6 g/g.
Conclusion: Intensive EP changed the prognosis of primary FSGS transplant. We report a series of 11 patients with eight successes due to PE. Three patients relapsed, IA permitted partial (2) and complete remission (1).If EP and IA fail, the role of rituximab in the treatment of recurrent FSGS remains to be determined.
Reference: 1. Canaud G, Zuber J, Sberro R, Royale V, Anglicheau D, Snanoudj R, et al. Intensive and prolonged treatment of focal and segmental glomerulosclerosis recurrence in adult kidney transplant recipients: a pilot study. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. mai 2009;9(5):1081–6.

45 CLINICAL AND BIOLOGICAL STATE IN PATIENTS WHO RESUME DIALYSIS: COMPARISON BETWEEN KIDNEY TRANSPLANTED AND INCIDENT PATIENTS

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Introduction: The number of patient returning on dialysis after kidney allograft failure (KA) is increasing and little is known about their characteristics. In this study we compared them with the incident patients during the year before the initiation of dialysis.
Material and Methods: We collected all the clinical and the biological datas related to the last year before the patients started dialysis in patients who resume dialysis at CHRU from Montpellier between 2008-01-01 and 2012-12-31.
Results: On 521 patients who began dialysis, 103 were KA patients and 202 were incident. The mean age was 53.6 years in KA patients vs. 63.9 years in incident patients at the time of initiation of dialysis. Hemodialysis was the most used technic (94.2% in KA vs. 90.6%, ns) and the frequency of the initiation of the dialysis for emergency indications was the same in the two groups. KA patients were more registered on the transplant-waiting list (81% vs. 60%, $p = 0.001$) but had less consultation (2.9 vs. 3.3 consults per patients, $p = 0.004$). The BMI was lower in KA patients (23 vs. 26.8 kg/m², $p < 0.0001$). KA patients were more anemic (hemoglobin 9.7 vs. 10.7 g/dl; $p < 0.0001$) and required a greater EPO dosing (106 vs. 63 ui/kg/sem, $p < 0.0001$). They were more acidotic ($HCO3-$ 16.7 vs. 18.5 mM, $p < 0.0001$), had lower albumin levels and lower cholecalciferol levels (37.5 vs. 36.9 g/dl, $p < 0.0001$ and 15.3 vs. 20.6 nmol/ml, $p < 0.0001$ respectively). The CRP levels were similar. The Charlson's score was more elevated in incident patients at the start of the dialysis ($p < 0.0001$).
Conclusion: Glomerular filtration rate is decreasing faster in transplanted patients during the year before resuming on dialysis. Anemia is more severe despite the greater medical prescription in EPO and the nutritional state seems to be more precarious.

46 COMPARISON OF INTERLEUKIN-2 BLOCKADE IN KIDNEY TRANSPLANT PATIENTS RANDOMIZED TO 40 OR 80 MG BASILIXIMAB WITH CYCLOSPORINE OR 80 MG BASILIXIMAB WITH EVEROLIMUS

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Background: The IL-2 receptor antibody basiliximab (BSX) at a total dose of 40 mg is known to achieve saturation of the CD25 antigen on T-cells (TC) for approximately 5 weeks (W) in kidney transplant patients (KTP) receiving CsA, an inhibitor of IL-2 production. A total BSX dose of 40 mg may be inadequate to achieve CD25 saturation without concomitant CsA. The effect of higher BSX doses in CsA-free patients is unknown.
Methods: In a 12-week, randomized, trial of BSX pharmacodynamics, 16 *de novo* KTP at low immunological risk received BSX at a total dose of 40 mg + CsA (controls, $n = 3$), 80 mg + CsA ($n = 6$) or 80 mg + EVR ($n = 7$), all with mycophenolic acid and steroids. The primary endpoint was the saturation kinetics of CD25 receptors by BSX to W12, measured by the % of CD25+ TC at specified time points and expressed as saturation area under the effect (AUE, W). The AUE to W12 for the % of TCL binding BSX was also studied. Study recruitment ended prematurely due to a high number of biopsy-proven acute rejections (BPAR) in BSX 80 mg + EVR group.
Results: Mean [SD] AUE of CD25 saturation was 8.4 [1.6] W for control, 11.1 [1.1] W for BSX 80 mg + CsA, and 9.7 [0.7] W for BSX 80 mg + EVR. Mean [SD] AUE of BSX binding to CD25 receptors was 7.0 [1.8] W, 9.9 [2.2] W and 8.4 [0.8] W, respectively. BPAR occurred in one control patient, one BSX 80 mg + CsA patient and four BSX 80 mg + EVR patients. There were no deaths and one graft loss (control group). One adverse event (AE) with a suspected relation to BSX was reported, in the BSX 80 mg + EVR group (BK virus infection).
Conclusion: BSX at a total dose of 80 mg with a CsA-free regimen may achieve similar CD25 saturation to 40 mg with concomitant CsA during the first 3 months post-transplant. Although the total dose of BSX was doubled it did not seem to provide adequate immunosuppression in KTP to prevent early acute rejection when combined with EVR in CsA-free regimen. BSX at a dose of 80 vs. 40 mg does not appear to be associated with increased BSX-related AEs.

47 ANTI-HLA ANTIBODIES AND HUMAN DENDRITIC CELL: *IN VITRO* EFFECTS ON CELL MATURATION AND SURVIVAL

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Background: Anti-HLA antibodies are a major cause of graft loss through acute and chronic antibody-mediated rejection, and a determinant of graft survival. In addition to Fc-dependant effects responsible for antibody dependant cell mediated cytotoxicity and complement-dependant effects, anti-HLA antibodies are also able to alter cell functions by transducing signals. Such mechanisms have mostly been described for activation, proliferation and survival in endothelial and smooth muscle cells, thus participating in allograft vasculopathy. The impact of anti-HLA antibodies on professional antigen-presenting cells is currently unknown.
Methods: Setting-up of an *in vitro* model of human monocyte-derived dendritic cells expressing an HLA-A2 allele and observation of phenotype modifications and cell survival in the presence of monoclonal mouse anti-HLA-A2 or anti-pan-MHC class I or II antibodies from BD Pharmingen™.
Results: Dendritic cells lipopolysaccharide, TNFα and CD40 ligand-induced maturation was non specifically inhibited by anti-HLA-A2 or anti-pan-MHC class I antibodies, with suspected Fc-dependant effect. With anti-HLA-A2 antibody $F(ab)'_2$ fragments, we observed a moderate increase of maturation markers expression with low titers and a loss of this maturation process with high titers. Immature and mature dendritic cells survival was unaffected while targeting MHC class I. In contrast, we showed the induction of a dose-dependant maturation of dendritic cells and mature dendritic cell apoptosis by anti-pan-MHC class II.
Conclusion: The differential effect when triggering MHC class I or class II suggests the possibility of different signaling and regulation pathways.

48 POSITIVE IMPACT OF EVEROLIMUS ON REGULATORY T CELLS AFTER LIVER TRANSPLANTATION

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Liver transplantation remains the only treatment for terminal liver disease. However, immunosuppressive drugs required for allograft acceptance are intrinsically toxic and may be responsible for severe side effects. Modulating the immune system of the host to induce tolerance of the graft is a promising new approach to reduce or even eliminate non specific immunosuppressive regimen. More particularly, promoting Tregs could be crucial in achieving operational tolerance. Standard immunosuppressive treatments using calcineurin inhibitors such as tacrolimus have been shown to have a deleterious effect on Treg population. On the contrary, reports indicate that mTOR inhibitors may have a positive impact on Tregs and thus could favor the establishment of operational tolerance.

Here we present the first randomized prospective clinical study comparing Tregs levels from liver transplanted patients receiving either tacrolimus or everolimus. A total of 30 patients from four centers were monitored. Blood samples were obtained before transplantation, then 1, 3 and 6 months after transplantation. Flow-cytometry immunophenotyping of Tregs was performed using freshly isolated PBMC. Tregs were isolated from PBMC using magnetic sorting to assess their immunosuppressive capacities.

Levels of Tregs were significantly reduced after 1 month of standard tacrolimus-based immunosuppressive regimen ($p < 0.05$). Six months after transplantation, levels of Treg from patients converted to everolimus were significantly higher than patients who remained under tacrolimus treatment ($p < 0.02$). Additionnally, we observed a strong tendency ($p = 0.057$) for higher level of Tregs in HCV-infected patients compared to non infected patients. Tregs conserved their suppressive capacities independently of the treatment and the time point.

This is the first clinical study to formally demonstrate the positive impact of everolimus on Tregs levels for liver transplanted patients compared to tacrolimus.

49 EXPRESSION OF TH17 PATHWAY IN ACUTE T-CELL MEDIATED REJECTION AFTER RENAL TRANSPLANTATION WITH ECD IS A DETERMINANT FACTOR OF RESPONSE TO ANTI REJECTION THERAPY

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Introduction: People aged 65 years reach up to 20% of patients listed for a kidney transplant. In an attempt to meet this rapidly increasing demand, organs from so-called expanded criteria donors (ECD) have been used more frequently. Immune response related to immunosenescence in kidney allografts from ECD has not been studied yet in human.
Methods: We profiled 43 kidney biopsies samples presented with acute T-cell mediated rejection (Banff 2013) (ACR), 25 from 23 > 50 years-old recipients engrafted with ECD (ECD group) and 18 from 17 < 50 years-old recipients engrafted with optimal donor (control group). We measured relative expression of a pre-specified panel of 18 mRNAs by quantitative RT-PCR assay. IL-17 protein expression in kidney biopsies has been studied by immunohistochemistry ($N = 10$).
Results: Donor and recipient ages were significantly higher in ECD group (donors: 70 ± 9 vs. 37 ± 8 years, $p < 0.0001$; recipients: 64 ± 8 vs. 36 ± 10 years, $p < 0.0001$). ACR histology was similar in both groups.

Relative expression of IL-17 mRNA, RORgt mRNA and t-bet mRNA were significantly higher in ECD allografts. Immunochemistry confirmed IL-17 protein expression in old recipients engrafted with ECD presented with ACR.

In marginal group, IL-17 mRNA expression in kidney biopsies in marginal group was a negative risk factor for ACR treatment response (classified as resistant if the eGFR did not return to within 20% of the baseline within 4 weeks after initiation of antirejection treatment) with eight ACR resistant in IL-17 positive recipients (54%) and no ACR resistant in IL-17 negative recipients ($p = 0.01$).
Conclusion: Th-17 pathway is increased in ACR in >50 years-old recipients engrafted with ECD. So more, presence of IL-17 expression in those kidney allografts represents a negative impact on ACR treatment response.

50 IDENTIFICATION OF BIOMARKERS PREDICTIVE OF ACUTE REJECTION IN TRANSPLANT PATIENTS TREATED WITH BELATACEPT

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Introduction: In renal transplantation, treatment with Belatacept in non immunized patients is associated with the same rate of graft loss or death, an improved renal function, a reduction of cardiovascular risk compared to cyclosporin A. However, an increased risk of acute cellular rejection was observed without an increased frequency of DSA. We analyzed biomarkers at the day of the transplant, associated with high risk of developing acute rejection in patients treated with belatacept.
Methods: 38 patients were included. All had a lymphocyte phenotyping at D0, D15, D30, D90 and D180. Renal biopsy was performed when an increase of 20% of serum creatinine was observed and systematically J365. The analysis of biopsies was made according to Banff classification. All patients received treatment with Simulect, cellcept (2 g/day) and steroids. Patients were randomized to receive Belatacept or cyclosporin A (BMS IM103-100).
Results: 38 patients were included. 26 were receiving belatacept and 12 cyclosporine. 8 patients have developed acute rejection during the first year (7 treated with belatacept and 1 with cyclosporine). The rate of CD4, CD8, CD20, CD56 was comparable during transplantation in the 2 groups. In the patient group treated with Belatacept, only the rate of CD4+ CD57+ (7.1% vs. 1.9%, $p < 0.03$) and the rate of CD4+ CD62L+ CD45RA+ were higher (9.5% vs. 1.3%, $p < 0.007$) at day 0 in patients receiving belatacept and up who developed rejection. Other lymphocyte populations were comparable.
Conclusions: For patients treated with belataceptfor renal transplantion, the presence of CD4+ CD57+ and CD4+ CD45RA+ CD27− is associated with a higher rejection rate. Their presence at high levels may lead to changes in treatment regimens associated with belatacept.

51 TACROLIMUS AND SIROLIMUS DIFFERENTIALLY PROMOTE APOPTOSIS AND PREMATURE SENESCENCE IN EXOCRINE AND ENDOCRINE PANCREATIC CELLS

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Background: New-onset diabetes after transplantation (NODAT) is a major complication in transplanted patients. Cellular mechanisms by which two immunosuppressive drugs, Tacrolimus (TAC) and Sirolimus (SIR) alter the pancreatic exocrine and endocrine cell fate and function were examined.
Methods: Human exocrine PANC-1, rat endocrine insulin-secreting RIN-m5f cells, and isolated rat islets were submitted to 100 nM TAC or SIR. In cultures, apoptosis was assessed by annexin-5-FITC and propidium iodide staining, expression of Bax and active Caspase-3, and p53 and p21 senescence markers by Western blot. Cell cycle, and SA-beta-galactosidase (SA-β-gal) activity were analyzed by flow cytometry or fluorescence microscopy.
Results: In exocrine PANC-1 cells, TAC and SIR increased Bax (3-fold) and cleaved Caspase-3 (5-fold) expression but only TAC induced early apoptosis. Simultaneously, $\Delta\Psi m$ was decreased, and p53 and p21 were up-regulated (2.5- and 2-fold increase, respectively). Only SIR prompted cell cycle arrest in G1 phase. In endocrine RIN-m5F cells, TAC and SIR increased apoptosis. Only p53 (TAC: 1.8-fold, SIR 1.7-fold) and p21 (TAC: 2.3-fold, SIR: 3.8-fold) were upregulated. Cell cycle arrest was induced only by SIR. The induction of premature senescence in all pancreatic cells and islets was confirmed by SA-beta-galactosidase activity.
Conclusions: TAC and SIR can induce pancreatic cell dysfunction, followed by senescence or apoptosis, but differentially alter endocrine and exocrine pancreatic cells.

52 CD4+ T CELL HELP IS MANDATORY FOR NAÏVE AND MEMORY B CELLS TO GENERATE DONOR-SPECIFIC ANTIBODIES

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Background: Antibody-mediated rejection (AMR) is the leading cause of kidney transplant failure. Current immunologic dogma predicts that B cells respond to protein antigen (such as HLA molecules) only with the help of CD4+ T cells.

Yet, despite progress in T cell immunosuppression, about 10% of patients develop *de novo* donor-specific antibodies (DSA) during the first year post-transplantation, a time when IS is maximal and observance usually good.

In the present project we aimed at determining whether DSA can be generated in the absence of CD4+ T cell help.
Methods and Results: We first investigated the importance of CD4+ T cell for naive humoral allogeneic response. B6 mice genetically deficient in CD4+ T cells (MHC II KO mice) or wild type (WT) were used as recipient of a skin graft (alloantigen drainage to lymph node) or a heterotopic hear transplant (drainage to spleen). Donors were HLA A2 transgenic mice, i.e. B6 mice that express human HLA A2 molecule under the murine MHC I promoter. This trick allowed for the monitoring of DSA response with assays routinely used in the clinic (Luminex). While WT recipients, all developed circulating anti-HLA A2 antibodies, no MHCII KO recipients did whatever the location of alloantigen drainage.

We then determined whether CD4+ T cell help was dispensable for memory B cells to respond to a second challenge with the alloantigen. Balb− (3rd party) or A2-specific memory B cells were purified from the spleen of recipient WT mice, 45 days after the rejection of 2 successive skin grafts. 5×10^6 purified splenic B cells were transferred IV to RAG KO mice that were then transplanted with A2 heart. None of the RAG recipients developed circulating anti-A2 antibodies.
Conclusion: CD4+ T cell help is mandatory for the generation of DSA by naïve and memory B cells. These results led us to initiate a clinical study evaluating whether the monitoring of circulating CD4+ T cell allow identifying patients at risk for DSA generation.

53 TREG CELL THERAPY IN ORGAN TRANSPLANTATION: IS IT ONLY A MATTER OF RATIO BETWEEN TREG AND CONVENTIONAL T CELLS?

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Thymus-derived CD4+ CD25+ Foxp3+ regulatory T cells play a pivotal role in the control of alloreactivity. Since their discovery, several reports have shown that Tregs are involved in tolerance induction to allogeneic skin, islet, and heart transplantation as well as in fetal tolerance. In the context of Graft versus host disease (GVHD), we and others have shown that Tregs specific for allogeneic Ag are far more capable of suppressing effector T cells and controlling the GVHD compared to polyclonal Tregs. Surprisingly, in mice, similar approach does not permit to prevent organ rejection. In bone marrow transplantation, due to irradiation of recipient mice, the Teff/Treg ratio is strictly controlled. This is not the case in solid organ transplantation where infusion of therapeutic Tregs, even at high dose remains less represented compared to conventional T cells.

Here, we hypothesized that the ratio between Teffs and Tregs should be the main factor for Tregs functionality. To test this hypothesis, *ex-vivo* expanded donor specific Tregs from B6 mice were used to control B6C3F1 skin graft rejection in B6 WT or B6 CD3-KO recipients.

In wild type C57BL/6 recipients graft rejection occurs in 1 week (MST = 7 days). When 2 million donor specific Tregs were added, we did not observe any delay in skin graft rejection.

Using CD3KO recipients first we determined that infusion of 1 million CD3+ effector Tcells is enough to induce acute rejection in 9 days. When Tregs were added at a ratio of 1:1, rejection occurred in 17 days ($p = 0.0017$).

Thus, in this very stringent model of skin rejection, controlling the Treg/Tconv ratio dramatically ameliorates skin graft survival but is not sufficient to fully control the rejection.

54 TOLERANT KIDNEY TRANSPLANT PATIENTS DISPLAY B CELLS WITH A PLASMA CELL-LIKE PHENOTYPE THAT EXPRESS GRANZYME B AND SHOW REGULATORY PROPERTIES

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Whereas a B cell transcriptional profile has been recorded for operationally tolerant kidney graft patients, the role that B cells play in this tolerance has not been reported yet. In this study, we analyze the role of B cells from operationally tolerant patients, healthy volunteers and kidney-transplant recipients with stable graft function on T cell response. Proliferation, apoptosis and type I pro-inflammatory cytokine production by effector $CD4^+CD25^-$ T cells were measured after anti-CD3/anti-CD28 stimulation with or without autologous B cells. We report that B cells are able to inhibit $CD4^+CD25^-$ effector T cell response in a dose dependent manner. This effect needs B cells to interact with their T cell targets and acts through a GzmB dependent pathway. Tolerant recipients harbor a higher number of B cells expressing GzmB and displaying a plasma cell-phenotype. Finally, $GzmB^+$ B cell number is dependent on IL-21 and B cells regulate both the number of $IL\text{-}21^+$ T cells and IL-21 production, suggesting a negative feedback loop in these patients which increases excessive B cell activation and allows regulation to take place. These data provide novel insights into the characterization of B cell–mediated immunoregulation in tolerance in clinic and show for the first time a potential regulatory role for B cells on effector T cells in blood from patients with operationally tolerant kidney grafts.

55 INFECTIOUS COMPLICATIONS IN HIV- INFECTED RENAL TRANSPLANT PATIENTS

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Introduction: The aim of this study is to evaluate the incidence and the type of infectious complications and graft and patient survival in HIV- infected renal transplant patients

Méthods: Retrospective evaluation of prospectively gathered data, between January 2004 and June 2014. Only the infectious complications that needed hospitalisation were studied.

Results: We have studied 23 renal transplant patients infected by HIV and compared them with 20 renal transplant patients non-infected by HIV. All patients had the same induction therapy (anti IL-2). The groups were matched for age, sex and race.

Follow-up was 44 months. There was no difference between the 2 groups in the incidence of bacterial infectious complications: respiratory infections: 30.4% vs. 15%, ($p = 0.29$), urinary infections: 43.4% vs. 25% ($p = 0.33$), sepsis: 8.7% vs. 8.7%, ($p = 1$).

There was no difference between the 2 groups in the incidence of viral infections:

CMV infection: 47.8% vs. 35% ($p = 0.53$), BKV infection: 17.4% vs. 25%, ($p = 0.71$). Incidence of Kaposi sarcoma is 8.7% in the HIV group vs. 5% in the control group (p = NS). Genital herpes is more frequent in the HIV group: 26% vs. 0% ($p = 0.02$).

There is no difference in parasitary infections: intestinal cryptosporidiosis: 13.3% vs. 5% (p value: 0.61).

Renal function at 3 months, 1 year and 5 years is no different between the 2 groups, also there is no difference in proteinuria (p = NS).

5- year graft survival is: 95.6% in the HIV group vs. 85%, (p: 0.32) and patient survival is 95.6% vs. 100%, (p: 1).

Conclusion: Within the limits of the small number of patients and limited follow-up, infectious complications do not seem to be different between the HIV- infected and the non HIV- infected renal transplant patients.

56 PROGNOSTIC VALUE OF LOW PCR CYTOMEGALOVIRUS LOAD IN KIDNEY TRANSPLANT RECIPIENTS

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Cytomegalovirus (CMV) is associated with an increase of morbidity and mortality after transplantation. Use of Polymerase Chain Reaction (PCR) has been recommended to diagnosis and/or monitoring of CMV infection. Nevertheless the PCR value threshold to start treatment has not yet been defined.

Material and Methods: We included all kidney recipients between 05/2012 and 07/2013 in this retrospective monocenter study. CMV PCR (whole blood, threshold = 1.79 log, Abbott® RealTi*m*e CMV) was performed weekly during the first 4 months after transplantation and then monthly during one year except for low risk patients (D−R−). Prophylaxis (valganciclovir) was given for 3 months for R+ and 6 months for D+R−. All patients with at least one positive PCR were included in our analysis. Curative treatment (ganciclovir iv or oral valganciclovir) was started in case of high CMV load (>4 log) and/or clinical/biological abnormalities associated with positive CMV DNA load (whatever the level). We assessed indications and incidence of curative treatment. Results were expressed as mean ± SD.

Results: During the 14-month period, a positive CMV viremia using PCR occurred in 59/140 patients after 6.4 ± 5.2 months (5 patients under prophylaxis). Twenty seven (45%) received a treatment (55.5% D+R−; 33.3% D−R+; 11.1% D+R+). Within these 27 patients, 16 (59%) were treated because of a PCR level higher than 4 log whereas the others were treated because of clinical and/or biological abnormalities associated with positive CMV DNAemia. Thirty two patients (55%) were not treated (50% D+R+; 40.6% D−R+; 6.25% D+R−; 3.12% D−R−). Interestingly, 29/32 (87.8%) non-treated patients had spontaneous undetectable CMV load after two controls (15.3% in the treated group, $p < 0.0001$). No further positive CMV PCR load was observed during the follow-up in these patients.

Conclusion: We suggest that a "wait-and-see" attitude may be indicated for patients with low positive CMV load (threshold < 4log on whole blood) in the absence of clinical or biological abnormalities.

Keywords: Cytomegalovirus, Kidney transplantation, PCR.

57 TRANSPLANTATION OF KIDNEY WITH CYTOMEGALOVIRUS (CMV) SEROPOSITIVE DONORS DURABLY AFFECTS THE LONG TERM ANTI-CMV RESPONSE IN RECIPIENTS

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Introduction: Cytomegalovirus (CMV) infection is associated in solid organ transplantation with increased morbidity and mortality. We have recently shown that CMV seropositivity of the donor (D+) is an independent risk factor for renal graft loss. IThe purpose of this study was to assess CMV specific CD8 T-cell response in D+ patients compared to D−R+.

Methods: Fifty-two kidney transplant patients grafted between January 2009 and December 2011 in Tours and expressing either HLA A2 or B7 were identified. Further analyses performed: numbers of anti-CMV CD8 T-cell (PE-conjugated CMVpp65-dextramers), percentage of numbers anti-pp65 CD8 T-cell with TEMRA phenotype (CCR7-neg and CD45RA-pos) and the response to pp65 peptide

(TNF-α, IFN-γ and granzyme B) measured by ELISpot. Results are expressed as mean ± SD. Mann–Whitney test was applied for group comparison.
Results: Today, 39 patients (29 D+ and 10 D−R+) were included. Mean follow-up was 45 ± 11.7 months. Number of anti-CMV CD8 T cells seems increased in D+ group compared to D−R+ group (12 223 ± 22 625 vs. 2967 ± 4374 respectively, p = 0.26). However, D+ as compared to D−R+ patients had a higher anti pp65 immune response as assessed for TNF-α (13 904 ± 13 234 vs. 2520 ± 3215 p = 0.00026), INF-γ (12 653 ± 14 193 vs. 2218 ± 4069, p = 0.0019), and granzyme B (3387 ± 5423 vs. 275 ± 367, p = 0.0024). Numbers of CMV specific TEMRA cells (dextramer+/CCR7−/CD45RA+) were similar between the two groups.
Conclusion: This study indicates that receiving a kidney from a CMV infected donor durably affects the long term anti-CMV response. This may suggest recurrent CMV replication episodes inside the graft.

58 NO RELATION BETWEEN HYPOGAMMAGLOBULINEMIA AND SEVERE INFECTION POST RENAL TRANSPLANTATION: COHORT STUDY OF 189 PATIENTS

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Introduction: Recently, a link between hypogammaglobulinemia (HGG) and infection has been demonstrated in kidney transplant recipients. A meta-analysis has suggested the benefit of IgIV administration. However, these studies have analyzed all type of infections regardless their severity. In our study, we analyzed the relationship between HGG and the risk of severe infection.
Methods: We conducted a monocentric cohort study (kidney graft recipients between 2007 and 2013). Ig subtypes (IgG, IgM, IgA) were available prospectively at day 15 (D15), month 6 (M6), M12 posttransplant. Two posttransplant periods were distinguished: P1 (D15-M6) and P2 (M6-M12). Two different persons blinded to each other retrospectively retrieved infectious events from medical records.
Results: The study included 189/315 patients with available Ig determination at D15. IgG HGG was observed in 62% and 37% of patients at D15 and M6 respectively.

Risk factors (RF) for HGG at D15 were age (OR 1.03) and past history of glomerulonephritis (OR 2.97) in multivariate analysis. RF for HGG at M6 were age (OR 1.03), HGG at D15 (OR 3.49) and acute rejection (OR 4.45) in both uni and multivariate analysis.

Most infections occurred during P1 (n = 70). RF of all type of infections between D15 and M24 were age (HR 1.04) and previous transplantation (HR 2.07). Basiliximab induction (HR 0.47) was associated with lower infection risk. Survival free all type infection, bacterial infection and viral infection was not different between patients with or without HGG at D15. Finally, the frequency of infections at P1 and P2 was not different between patients with or without HGG.
Conclusion: Our study does not support a link between HGG and severe infection post renal transplantation. The use of IgIV in order to minimize the risk of severe infections in kidney transplant recipients with HGG needs to be evaluated in prospective studies.

59 ACUTE CELLULAR REJECTION AFTER TREATMENT OF BK VIREMIA IN RENAL TRANSPLANT RECIPIENTS

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Background: BK virus is an emerging pathogen in kidney transplant recipients, and often leads to poor graft outcomes. Immunosuppression (IS) reduction is mainly performed in case of BK viremia (BKv), with the risk of acute cellular rejection (ACR).
Methods: We retrospectively analyzed 32 kidney recipients with BK viremia from 2006 to 2011. Among them, 34% had ACR after reduction of IS. The aim of this study was to compare patients who had ACR (ACR+, n = 11) with those who had not (ACR−, n = 21).
Results: ACR occurred in a median time of 18 (10–29) weeks after IS reduction. ACR+ patients had lower glomerular filtration rate at the 1st BKv detection compared to ACR− patients: 29 (22–39) vs. 42 (32–53) ml/min/1.73 m^2 (p < 0.01). The *area under* the *curve* of *mycophenolic* acid (AUC-MPA) was 17 ± 11 in ACR+ group vs. 29 ± 11 mg h/l in ACR− group (p < 0.05) with a 26.5 mg h/l threshold evaluated by ROC equation below which ACR risk increased. No patient treated with leflunomide developed ACR (n = 3). BKv was still present in 6/11 patients when ACR occurred. ACR were treated with steroid pulses. After a 5 ± 1.6 year mean follow-up, graft and patient survivals were lower in ACR+ patients compared to ACR− patients (respectively 45% and 73% vs. 90% and 90%).
Conclusions: ACR must be considered as a serious event after IS reduction in transplant recipients with BKv. Graft dysfunction and AUC-MPA < 26.5 mg h/l seem associated with higher risk of ACR. Use of leflunomide remains to be defined: at early BKv stage if an AUC-MPA < 26.5 mg h/l is needed to obtain viral clearance or as an adjunctive ACR treatment.

60 HIGH RATES OF VIROLOGICAL RESPONSE AND MAJOR CLINICAL IMPROVEMENT DURING SOFOSBUVIR AND DACLATASVIR-BASED REGIMENS FOR THE TREATMENT OF FIBROSING CHOLESTATIC HCV-RECURRENCE AFTER LIVER TRANSPLANTATION: THE ANRS CO23 CUPILT STUDY

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Introduction: Fibrosing cholestatic hepatitis (FCH) is a rare but severe form of HCV-recurrence following liver transplantation (LT) leading to poor short term survival. Therapeutic options are limited. Study aims were to assess efficacy and tolerance of sofosbuvir (SOF) and daclatasvir (DCV)-based regimens in this setting.
Methods: The CUPILT study is a prospective nationwide cohort including patients with HCV-recurrence following LT treated by new antivirals. The present work focused on 21 patients diagnosed with FCH and included between October 2013 and February 2014. FCH diagnosis was based on strict criteria including histological review by an expert pathologist. Treatment regimens were prescribed at investigator's discretion.
Results: FCH was diagnosed after a median duration of 6 months [range 1–18] following LT and therapy started at 10 months [2–38] post LT. Features of patients at W0 were: median age: 53 years [36–67], men: 81%, G1: 76%, bilirubin: 6.0 mg/dl [0.6–19]. Ascites was observed in 8 (38%) patients. The following regimens were used: Peg-IFNa + SOF + RBV (n = 2), SOF + RBV (n = 6), SOF + DCV (n = 1) and SOF + DCV + RBV (n = 12) for 24 weeks. All patients were alive without re-transplantation at W12. At W12, 20 (95%) patients had HCV RNA <15 IU/ml and 17 (81%) were not detectable. The rates of ALT and gGT normalization at W12 were 76% and 52%, respectively. Median bilirubin serum levels rapidly decreased from 6.0 to 3.6 at W1 and 2.6 mg/dl at W2. Ascites disappeared in 4/8 patients. Complete clinical response (no ascites and bilirubin < 2 mg/dl) was observed at W12 in 15 (71%) patients. Tolerance was satisfactory.
Conclusion: SOF and DCV based regimens show promising results combining high rates of virological response and major clinical improvement at W12. Durability of virological and clinical response will be presented.

61 PREDICTION OF RECURRENCE AFTER LIVER TRANSPLANTATION FOR HCC: VALIDATION OF THE AFP MODEL IN AN ITALIAN COHORT

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Background and Aims: The AFP model (pre LT AFP, size, number), was shown superior to Milan criteria for prediction of HCC recurrence in a French population. Our aim was to test the AFP model in an Italian population of HCC candidates.

Methods: 560 patients transplanted for HCC (2002–2010) in 4 Italian centres were studied. AFP score was assessed at last evaluation before LT (median waiting time: 8.8 mths). Probabilities of recurrence and death were estimated by the log rank test or competing risk analysis and compared according to the AFP score cut-off of 2.
Results: Study population: males: 86%, age: 56 ± 7 years, median AFP: 9 (range 0.4–17 500), median tumour number and size: 2 and 2.5 cm, pts beyond Milan criteria: 24%, pre LT treatment: 86%, post-operative mortality: 7.1%.

Five-year probabilities of recurrence:

Milan in versus Milan out: 14.1% vs. 27.4% ($p < 0.001$).
AFP score < 2 vs. > 2: 11.4% vs. 40.2% ($p < 0.001$, competing risk analysis) overall.
13.2% vs. 36.4%, for pts within Milan ($p < 0.005$).

Five-year survival rates according to AFP score <2 or >2:

73.5% vs. 40.4% ($p < 0.001$).
Censoring HCC-related deaths, competing risk analysis show similar incidence of non HCC-related deaths in both groups (19.0% and 21.9% for AFP score < 2 and > 2).

Conclusions: The AFP model discriminates better than Milan criteria between patients at low and high risk of recurrence in a non French population of HCC candidates.
The AFP model can be proposed as a new selection tool in an Italian population.

62 PROGRESSION OF ARTERIAL PULSE PRESSURE, A POTENTIAL MECHANISM AND BIOMARKER FOR CSA ASSOCIATED NEPHROTOXICITY AND RENAL GRAFT FAILURE

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Introduction: The benefits of cyclosporine A (CsA) are partly counterbalanced by its chronic vascular nephrotoxicity, which compromises renal graft outcome in the long term.
Method: In a previous clinical trial with 108 *de novo* renal transplanted patients under tri-therapy (CsA, mycophenolate mofetil (MMF) and corticoid) randomized, withdrawn either from CsA ($n = 54$) or MMF ($n = 54$) at 3 months (M) post graft, we analyzed, in their 3 and 12 M protocol biopsies, the influence of pulse blood pressure progression (Δpp) from 3 to 12 M post transplant on the expression of two tubular epithelial phenotypic change (EPC) markers (β catenin and vimentin), two graft suffering markers associated with graft fibrogenesis and predicting renal graft dysfunction.
Results: Δpp from 3 to 12M was higher in the CsA than in MMF group (Δpp = +4.5 ± 2.2 vs. −2 ± 2.6 mmHg, $p < 0.05$). We found a significant pp progression (52.6 ± 12–61 ± 15 mmHg, $p = 0.0061$) in the patients expressing EPC markers on their 12M biopsy, but pp was slightly regressed in the patients without EPC marker expression (57.5 ± 13–53 ± 12 $p = 0.09$). We noticed a significant pp increase (54.7 ± 11–62 ± 15 mmHg, $p = 0.028$) in the patients who had cv progression (Δcv 1) from 3 to 12M, but pp remained stable (55.5 ± 13–55 ± 13, $p = 0.8$) in those without. Δcv was significantly correlated with ΔEPC scores between 3 and 12M post transplant ($r = 0.32$, $p = 0.01$). These results suggest that the association between Δpp and EPC markers could be mediated by tubular chronic hypoxia due to the development of arteriolosclerosis under increased pp. Multivariate analysis confirmed that CsA based therapy, Δpp and donor's age were 3 independent risk factors for EPC marker expression at 12M. In addition, pp progression associated 12M EPC marker expression predicted renal graft dysfunction up to 4 years post transplant.
Conclusion: pp progression post-transplant seems a new interesting marker for the surveillance of CsA associated graft failure.

63 BK VIRUS NEPHROPATHY: INVOLVEMENT OF DONNOR AND/OR IMMUNOSUPRESSIVE THERAPY ?

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Background: BK Virus Nephropathy (BKVN) is an increasingly complication of renal transplant that can threaten graft's survival. As there is no specific antiviral curative treatment. Determining risk factors for BKVN is a keypoint for management. Several risk factors have been mentioned, linked either to the donor or to the immunosuppressive therapy (IST). The main objective of our work was to study the outcome of remaining transplanted kidney of patients presenting with BKVN, looking for involvement of donor and/or of IST in the onset of the disease.
Methods: Our study was limited to renal transplant patients above 18 years of age, with histology-proved BKVN, in the Lille University Hospital between 2006 and 2013, and to transplant patients with contralateral kidney. Clinical biological and histological data was recovered at distinct periods of the follow-up period.
Results: Out of 800 kidney transplant patients, 28 cases of BKVN were found (3.5%) and 25 patients had the contralateral kidney. BKVN appeared at 20.0 ± 12.5 months after transplant, with median GFR of 28.1 ± 11.6 ml/min/1.73 m^2. Graft was lost in 50% of cases, with a median delay of 11.1 ± 10.6 months. GFR at diagnosis was lower in the group of patients who lost their graft ($p = 0.01$). Patients with persisting viremia 3 months after diagnosis lost their graft more often (60% vs. 25%). No case of BKVN was diagnosed in the contralateral kidney's group. Graft failure was less frequent in this group (12%). There is a difference in immunosuppressive treatment between the two groups, with more Cyclosporine being used in the contralateral kidney's group (32% vs. 0%).
Conclusion: We did not find involvement of donor in BKVN. Impact of IST is confirmed, especially with calcineurin inhibitors. Tacrolimus provides more cases of BKVN, whereas Cyclosporine is a protective agent.

64 ANEMIA CORRECTION USING ERYTHROPOIESIS-STIMULATING AGENT HAD NO EFFECT ON LEFT VENTRICULAR MASS IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Anemia is an important contributor of left ventricular hypertrophy (LVH) in patients with chronic kidney disease. However, the benefits of anemia correction on left ventricular mass are not known in kidney transplant recipients. The objective of this study was to determine the impact of complete anemia correction on LVH in anemic kidney transplant recipient with chronic renal dysfunction.
Methods: The Correction of Anemia and Progression of Renal Insufficiency in Transplant patients study (CAPRIT study) was a prospective multicenter clinical trial in which 128 kidney transplant recipients with anemia and stage 3–4 CKD were included. They were randomized into two groups with different target hemoglobin levels, the treatment group in witch we aim to obtain a complete anemia correction (Hb level 13–15 g/dl) and the control group in witch anemia was partially corrected (10.5–11.5 g/dl). Left ventricular mass (LVM) was determined by successive EKG and echocardiograms. We also analyzed the association between LVM and hemoglobin at baseline and evaluated the occurrence of cardiovascular events during follow-up.
Results: Characteristic of the patients were similar between the two groups. After 6 months of randomization, Hb level were significantly different between the two groups. We did not found any statistically significant difference on LVM or cardiovascular events incidence between the two groups after a 2 years follow-up. Moreover LVM has not significantly changed over time. Finally LVM at inclusion was not statistically associated with hemoglobin level.
Conclusion: This randomized study shows that the complete correction of anemia in kidney transplant recipient had no impact on left ventricular hypertrophy and cardiovascular events. The safety was excellent in this population.

65 CONTRIBUTION OF INFRARED SPECTROSCOPY TO THE IDENTIFICATION OF KIDNEY TRANSPLANT CRYSTAL DEPOSITS

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Introduction: Composition, consequences and aetiology of crystal deposits in kidney allograft still unclear. The aim of this study was to characterize the physicochemical aspects and clinical circumstances of such calcifications.
Materials and Methods: It is a monocentric, retrospective, observational study. From 1996 to 2012, 1621 biopsies were performed in 1040 kidney

recipients. Crystals were observed in 130 biopsies (8.1%) in 78 patients (7.5%). 55 patients with crystal (Pcx+) were compared to 100 kidneys recipients without crystal (Pcx−). Physicochemical characterisation of crystals was performed using infrared spectroscopy.
Results: No difference was observed between Pcx+ and Pcx− for clinical characteristics of donors, recipients before and after graft and their treatment. Biological screening at D15, M3, M6, M12 et M24 showed more significant hyperparathyroidism in Pcx+ than in Pcx−: D15: 278 vs. 160 pg/ml ($p = 0.001$); M3: 211 vs. 123 pg/ml ($p = 0.003$); M6: 193 vs. 105 pg/ml ($p = 0.001$); M12: 198 vs. 117 pg/ml ($p = 0.005$). PTH upper 75th was associated with a relative risk of calcification of 4.2 at D15 (IC 1.9–9.17, $p < 0.001$), 3.88 at M3 (IC 1.79–8.43; $p < 0.001$) and 3.04 at M6 (IC 1.2–7.6; $p = 0.016$). We found no correlation between calciuria and PTH levels or tubular crystals. Infrared spectroscopy found calcium phosphates in 89.8% of cases (46.9% CA and 42.9% PACC) versus whewellite in 8.2% and other in 2%. No difference of eGFR was observed at 2 years of follow up.
Conclusion: Infrared spectroscopy confirmed that 89.8% of kidney transplant crystal deposits were calcium phosphates. They were associated with a worse persistent hyperparathyroidism

66 NEPHRON SPARING SURGERY FOR *DE NOVO* KIDNEY GRAFT TUMOR: RESULTS FROM A MULTICENTER NATIONAL STUDY

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Objective: To study the French experience of renal sparing surgery for *de novo* kidney graft renal cell tumors in a multicenter cohort.
Material and Methods: National retrospective, multicenter study. Data collected from 32 French transplantation centers. Cases of renal graft *de novo* tumors, treated as RCC since the beginning of their transplantation activity were included. Only renal transplant recipients with functional renal graft were included from January 1988 to April 2012.
Results and Limitations: Seventy-nine *de novo* tumors of allograft kidney were diagnosed. 43 patients (54.4%) underwent renal sparing surgery. Mean age of grafted kidney at the time of diagnosis was 47.5 year old (26.1–72.6). The mean time between transplantation and tumor diagnosis was 142.6 months (12.2–300). Fifteen tumors were clear cell carcinomas (34.9%), 25 (58.1%) were papillary carcinomas. One (2.3%) was a mixt RCC (clear cell and papillary carcinoma) and two were oncocytomas (4.65%). Respectively 10 (24.4%), 24 (58.3%) and 8 (19.5%). tumors were Fuhrman grade 1, 2 and 3. Nine patients had postoperative complications (20.9%) including 4 requiring surgery (Clavien IIIb). All surgical margins were negative with a mean tumoral size of 26 mm. The mean time of follow up was up to 29.6 months (0.65–100.6). At the last time of follow up, 41 patients had a functional kidney graft, without dialysis and no long-term complications.
Conclusions: Nephron sparing surgery is a safe and appropriate indication for all small tumors of transplanted kidney with very good long term functional and oncological outcomes preserving patients from returning on dialysis.

67 CHARACTERIZATION OF MESENCHYMAL STEM CELLS FROM PORCINE ADIPOSE TISSUE AND THEIR EFFECTS ON KIDNEY GRAFT RECOVERY IN A PRECLINICAL PORCINE MODEL OF RENAL AUTO-TRANSPLANTATION MIMICKING THE DECEASED AFTER CARDIAC ARREST DONOR CONDITIONS

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Introduction: Ischemia reperfusion (IR) is a key process involved in acute and chronic renal graft dysfunction. The objective of this study was to characterize mesenchymal stem cells from porcine adipose tissue (pASC) and their role in the graft function recovery in conditions mimicking deceased after cardiac arrest donors (DCD).
Materials and Methods: Morphology, proliferative capacities, phenotype by flow cytometry and the metabolic profile in Nuclear Magnetic Resonance (NMR) of porcine ASC (pASC) were determined. Their resistance to a sequence of hypoxia-reoxygenation (HR) was tested by analyzing their viability and metabolic profile in NMR. Feasibility, functional and histological outcomes of an autologous injection of 106 pASC/kg in the renal artery of 3 auto-transplants kidneys after 1 h of warm ischemia and 24 h of storage at 4°C in UW solution and contralateral nephrectomy were compared to a group of autotransplanted pigs without injection of pASC.
Results: The cell extraction technique is reproductible and allows having sufficient pASC with the characteristics of mesenchymal stem cells. The metabolic profile in NMR of pASC was not changed with the passages, characterizing stability lines. The cell viability after a sequence of HR exceeded 70%. The injection of 106 pASC/kg is practicable 15 days after removal of adipose tissue. The function recovery was significantly improved and the histological lesions were reduced in the group treated by pASC.
Conclusion: Injection of pASC in renal graft artery at reperfusion of the grafts in a porcine model mimicking deceased after cardiac arrest donor conditions improves graft function recovery and limits tubular damages at day 7. These therapeutic potentials will be confirmed by further studies at the end of the follow-up at 3 months of 6 animals.

68 IMPACT OF THE AGE OF DONOR ON ENDOTHELIAL FUNCTION IN GRAFT AND RECIPIENT'S NATIVE AORTA IN A RAT MODEL OF AORTIC TRANSPLANTATION

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Introduction: A major complication of transplantation is graft vasculopathy in which endothelial dysfunction participates. We investigated the impact, in a rat model of aortic transplantation, of both surgical procedure and age of the donor on endothelial function in recipient's native aorta and graft.
Methods: Fifteen Wistar male rats aged 3–4 months were divided into three groups: autograft ($n = 5$), allograft from older donors (5 Wistar male rats aged 13–14 months) and control ($n = 5$). One month after surgery, vascular reactivity was assessed in aortic rings from both graft and recipient's native aorta by measuring changes in isometric tension in response to phenylephrine and acetylcholine in isolated organs chambers. We investigated the presence of endothelium-derived contracting factor (EDCF) by the addition of indomethacin, an inhibitor of prostanoids formation. Vascular oxidative stress was determined by epifluorescence microscopy in frozen sections of aortas using the redox-sensitive probe dihydroethidium.
Results: Vascular reactivity of graft and recipient's native aorta in the autograft group was comparable to the control. In contrast, grafts from older rats presented significant blunted endothelium-dependent relaxations, without an increase in oxidative stress ($-28.5 \pm 39.4\%$ vs. $79.4 \pm 7.1\%$, $p < 0.0001$). In the allograft group, a decrease in the contraction of recipients' native aortas was found in the presence of indomethacin (2.9 ± 0.7 g vs. 5 ± 0.6 g, $p < 0.01$), demonstrating the formation of EDCFs in these rings.
Conclusion: Aortic allograft from old donor and young recipient's native aorta suffered impairments in the endothelial function that cannot be attributed to the surgical procedure. Thus donor's age and allo-immune reaction might be involved in the local mechanisms of endothelial dysfunction observed in the graft but also in the recipient's native aorta.

69 INFLUENCE OF PRESERVATION TEMPERATURE ON ENDOTHELIAL CELLS AND KIDNEY PHENOTYPES

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Introduction: Ischemia reperfusion (IR) injury is unavoidable during organ transplantation and leads to complications. With the increased use of marginal donors, more sensitive to IR, solutions must be found to improve outcome. We

hypothesized that a higher preservation temperature could offer better protection against IR.
Methods: We tested this in an *in vitro* model of IR using primary endothelial cells and in *ex vivo* preserved pig kidneys. In both, 24 h preservation in University of Wisconsin solution was used.
Results: *In vitro*, compared to 4°C, temperatures between 19 and 32°C provided higher protection against cell death (LDH release test), permitting better mitochondrial function (complexes II and V activity tests) and a lower expression of endothelial activation and inflammation markers TLR4, MCP1 and ICAM1. *Ex vivo,* however, the superiority of 19 or 32°C was lost, as preserved pig kidneys showed similar levels of tissue damage (both tubular dilatation, loss of brush border and endoluminal detachment) during preservation, and at 24 h the 4°C kidneys displayed a trend towards less damage. In addition, the tissular Monocyte/Macrophage infiltration was increased in the 19°C and more in the 32°C temperature conservation as compared to 4°C storage.
Conclusion: Our study shows that although a higher preservation temperature is preferable for cell survival and function, whole organ testing demonstrates that conceptual work needs to be performed to harness the potential of sub-normothermia.

70 INHIBITION OF THE COAGULATION PROTEASES XA AND IIA DURING THE EXTRACORPOREAL PORCINE KIDNEY PRESERVATION

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Introduction: Organs from donors deceased after cardiac death represent an important "pool" to reduce organ shortage in transplantation. However, these organs are particularly exposed to ischemia/reperfusion injuries (IRI). We propose to reduce IRI by targeting coagulation, one of the major target during IRI, in the objective to limited the inflammation response.
Method: We evaluated the effect of anti IIa (Melagatran) or anti-Xa + IIa molecule (EP) in an autotransplanted kidney pig model. Kidneys were clamped during 60 min (warm-ischemia) and then preserved 24 h in 4°C UW solution. Melagatran or EP molecules were used during cold storage (UW-M or UW-EP), compared to UW + unfractionated-heparin (UW-UFH) or UW alone (UW).
Results: In our *in vivo* model of ischemia-reperfusion, we improved the early kidney function recovery in the anti-IIa and anti-Xa + IIa groups as compared to UFH and UW alone groups. Using the anti-IIa we observed a decrease of RANTES, CXCR3, IL-1b and TRAIL mRNA expression in blood leukocytes in early time after reperfusion. Using the anti-Xa + IIa we showed a decrease of plasma IL-6 and TNFa mRNA in blood leukocytes in early time after reperfusion. At 3 months after transplantation we observed a better kidney function in the anti-IIa and antiXa + IIa treated groups than compared to UW-UFH and UW in correlation with the fibrosis and inflammation. In addition, we observed a reduction of IFNg, TNFa, IL-2 in the anti-IIa group, and a decrease of IL-1b, MCP-1 expression in the antiXa + IIa group, in association with a decrease of tissue leukocyte infiltration in these two groups as compred to UW-UFH and UW groups.
Conclusion: We conclude that anti-IIa or anti Xa-IIa, use during organ preservation, is beneficial for kidney function and that they may be used as protectors against chronic renal dysfunction, like inflammation.

71 EVALUATION OF DIFFERENT ISOTYPES OF VEGF IN VASCULAR REPAIR DURING PRESERVATION: ANALYSIS IN A PRECLINICAL MODEL

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Objectives: The vascular network is a major target during ischemia reperfusion, with both acute and chronic consequences on graft outcome. It has been shown that the negative evolution of kidney graft function could be linked to a deregulated Hypoxia Inducible Factor 1α (HIF1α) and vascular endothelium growth factor (VEGF) response. We thus investigated the different isotypes of VEGF.
Methods: Two VEGF isotypes (165 and 121) were added to Viaspan solution (25 μg/l). Evaluation took place in a kidney autotransplantation model in Large White pigs (n = 6) with a 3 month follow up. Treated groups were compared to sham and uninephrectomized groups. Function recovery, inflammation (pro-inflammation markers measurements) and tubular lesions were evaluated. At 3 months, animals were euthanized and we analyzed the expression of HIF1α, VEGF and TGFβ as well as interstitial fibrosis development.
Results: After 24 h of preservation, function recovery was observed earlier in the VEGF 121 group, a benefit observed during the full follow up. Tubular functions were also significantly improved. At the tissue level, edema was less pronounced in the VEGF 121 group. Use of VEGF 121 significantly limited the expression of pro-inflammatory markers TNFα and HMGB1. Urine and plasma NGAL were lower in both treated groups, with a more definite improvement in VEGF 121 animals. 3 months after transplant, interstitial fibrosis and tubular atrophy were most markedly decreased in the VEGF 121 group.
Conclusion: This study highlights the importance of vascular lesion factors and their interest in regards to repair. Moreover, the type of molecule used is important, with a different impact for each isotype. Our work highlights the fact that the endothelial cell is an invaluable target for therapeutic intervention, with effects on the tubules.

72 EXPERIMENTAL PIG MODEL OF HEPATIC HEMODYNAMIC OPTIMIZATION

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Introduction: Portal hypertension is the major hemodynamic consequence of cirrhosis. Liver transplantation treated the cirrhotic liver and the portal hypertension. Graft inflow (hepatic arterial flow, portal vein flow and pressure) modulation is of major concern during liver transplantation and had great repercussion on recipient outcomes. The aim of our study was to determine, in a non-pathologic reproducible pig model, the hemodynamics parameters that could influence and modulate hepatic inflow.
Materials and Method: Ten Large White pigs, weighting between 39 and 50 kg were operated under general anesthesia. Systemic and splanchnic hemodynamics parameters were measured before and 3 min after 8 hemodynamics modifications. Flows were measured by transit-time flowprobes (Transonic®) and pressure by catheter introduced in vessel. Modifications were systematically applied: close-open of hepatic artery, splenic artery, splenic vein, hypo-volemia/hyper-volemia, increased positive end-expiratory pressure (PEEP), close-open of portal vein and parietal closure.
Results: Animals characteristics and all the hemodynamics modifications were reproducible. Hepatic arterial flow was significantly modified by variation of central vein pressure, increased in PEEP and portal vein closing. Portal vein flow (PVF) depended on 3 factors: (i) aortic coeliac flow (about 20% of it), (ii) mesenteric superior arterial flow (about 140% of it), and (iii) splenic artery flow (closing it decrease PVF of 18%). Portal vein pressure (PVP) depended on 4 factors: (a) splenic vein (closing it decrease PVP of 15%), (b) central vein pressure (porto-caval gradient remains stable for each pig during experimentation) (c) portal vein, (d) increased PEEP.
Conclusion: In this study, we demonstrate for the first time in a large animal model that systemic parameters influence directly the hemodynamic flows into the liver and could play major role for this optimization.

73 EARLY CYCLOSPORINE WITHDRAWAL WITH MYCOPHENOLATE MOFETIL AFTER KIDNEY TRANSPLANTATION: *TEN YEARS AFTER*

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Introduction: Calcineurin inhibitors (CNI) carry long-term side effects, especially renal toxicity. However CNI discontinuation was associated in many studies with an increased risk of acute rejection in the short term and, about 40 years after their first use, CNI remain a cornerstone of immunosuppressive regimen in renal transplantation. We report the 10-year follow-up of a randomized trial comparing cyclosporine (CsA) or mycophenolate mofetil (MMF) withdrawal at 3 months post-graft.
Patients and Methods: One hundred and eight patients were randomly converted from a triple drug regimen (CsA-MMF-Prednisone) to a dual therapy (CsA-Prednisone or MMF-Prednisone) at 3 months post-graft. Immunosuppressive therapy, long-term complications, renal function and survival rates at 10 years were analyzed.

Results: In the CsA group, 3.7% remained under their randomized treatment compared to 35.2% in the MMF group, at 10 years ($p < 0.001$). Estimated glomerular filtration rate was significantly improved in the MMF group (64.4 ± 21 vs. 49.7 ± 14.7 ml/min/1.73 m², $p < 0.001$), even though the acute rejection rate was higher (11 in the MMF group, 4 in the CsA group, $p = 0.011$). Class II *de novo* donor-specific HLA antibodies occurred more frequently in the MMF group. Transplant biopsies after one year post-graft revealed higher rates of CNI-related toxicity ($p = 0.019$), and moderate-to-severe interstitial fibrosis and tubular atrophy ($p = 0.004$) in the CsA group. Ten-year graft and patient survivals were not different in the 2 groups. Multivariate regression analysis showed that acute rejection remained the strongest predictor of graft loss at 10 years (HR = 11.64, 95% CI [5.05–26.79], $p < 0.0001$).
Conclusion: Despite a significant improvement of renal function up to 10 years post-graft, early CsA withdrawal failed to increase graft survival. This result is not only due to an increased incidence of acute rejection in the short term but could also be related to chronic rejection.

74 EFFICACY AND SAFETY OF EVEROLIMUS IN COMBINATION WITH REDUCED TACROLIMUS IN *DE NOVO* LIVER TRANSPLANT RECIPIENTS: 36-MONTH RESULTS FROM THE RANDOMIZED H2304 STUDY

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Purpose: Long-term renal function (RF) preservation is one major challenge for liver transplant (LTx) recipients. The 24-month (M) results from the H2304 study have shown that everolimus (EVR) in combination with reduced tacrolimus (rTAC) provided superior RF and comparable efficacy and safety versus standard exposure TAC (TAC-C). Here we present the M36 results.
Methods: The study enrolled 719 patients, randomized 1 M after LTx to EVR + rTAC, EVR with TAC withdrawal at M4 (TAC-WD) or TAC-C. Patients who completed the 24M period on treatment continued the same treatment in the extension phase. At M 36 the key endpoints included composite efficacy failure rate (treated biopsy proven acute rejection [tBPAR], graft loss, or death), RF (estimated glomerular filtration rate [eGFR], MDRD4 formula) and incidence of AEs and serious AEs (SAEs).
Results: A total of 282 patients entered the extension phase (EVR + rTAC, $N = 106$; TAC-WD, $N = 51$; TAC-C, $N = 125$). At M36, the incidence of efficacy failure was numerically lower for EVR + rTAC versus TAC-C (11.5% vs. 14.6%; $p = 0.334$). BPAR incidence was significantly lower in the EVR + rTAC arm versus TAC-C (7.3% vs. 17.7%; $p = 0.006$). During the extension phase, there were no tBPAR events in the EVR + rTAC group versus 2 events in the TAC-C group. At M36 the difference in mean eGFR was 15.2 ml/min/1.73 m² in favor of EVR + rTAC versus TAC-C ($p < 0.001$). The incidence of AEs (82.1% vs. 76.8%) and SAEs (30.2% vs. 22.4%) in the EVR + rTAC and the TAC-C arms were comparable. In the TAC-WD arm only one tBPAR has been reported and incidence of SAEs was 31.4%. Difference in eGFR in the TAC-WD compared to TAC-C being 22.0 ml/min/1.73 m².
Conclusion: The H2304 extension data demonstrated that EVR facilitated TAC reduction regimen started 1 M post-LTx, resulted in superior RF maintained throughout the study period up to M 36 with better protection against tBPAR and comparable adverse events compared to standard TAC regimen.

75 PROSTATE CANCER BEFORE RENAL TRANSPLANTATION: A MULTICENTER STUDY

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Objective: To study the surgical risks of renal transplantation (RT) after treatment of localized prostate cancer (PC) and the oncological outcomes after transplantation in patients on the waiting list with a history of PC.
Method: We conducted a retrospective multicenter study (9 centers) including all patients with PC diagnosed before renal transplantation from December 1993 to July 2011.
Results: Forty-three patients were included. Age at diagnosis of PC was 60.6 ± 6.2 years (45.6–72.9). PSA at diagnosis was 8.1 ± 4.3 ng/ml (4.8–20). Thirty-eight patients were treated with prostatectomy: 28 by open surgery, 10 by laparoscopy, with 16 lymph nodes dissection. Five patients were treated by external radiotherapy and two by brachytherapy. Eight patients had adjuvant radiotherapy. Twenty-three, 19, and 1 PC were respectively low, intermediate or high risk according to the classification of D'Amico. The time lapse between PC treatment and RT was 44.4 ± 29.8 months (14–71). Seven recipients (16%) were transplanted within 24 months after the PC. 29 TR have been described as difficult by the operators (13 external iliac vascular dissections, 16 bladder, and 8 both). Surgical complications post- transplantation were not significantly related to dissections difficulties ($p = 0.2$). No recurrence of PC was observed after a mean follow-up after TR of 36 months.
Conclusion: CP discovered before the TR should be treated with RA to assess the risk of recurrence and reduce pending TR. If the CP is at low risk of recurrence, it seems possible to shorten the waiting period before the TR.

76 CHARACTERIZATION OF MICROPARTICLES DURING LUNG ISCHEMIA IN AN *EX VIVO* RAT LUNG PERFUSION MODEL

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Introduction: Post-operatively to lung transplantation, lung ischemia reperfusion injury is only graded by means of radiological and oxymetric characteristics. There is no actual relevant biomarker of ischemic insult in lungs. Microparticles (MPs) are sub-micronic fragments shed from stimulated and stressed cells measured as biomarkers of cell injury. We aimed at the assessment of MPs released during ischemic lung injury in an *ex vivo* rat lung perfusion model (EVrLP).
Method: We used an *ex vivo* rat lung perfusion and ventilation model. Following anesthesia, lungs were harvested from adult male Wistar rats. Lungs were placed in the EVrLP model either immediately (no ischemia [NI]; $n = 6$) either following 1 h warm ischemia ([WI]; $n = 6$). We used acellular Perfadex® as a perfusate. Lungs were ventilated and perfused for 1 h. Lung function was assessed with hemodynamic and oxymetric criteria. Alveolar and circulating MPs were assessed in the broncho-alveolar lavage and in the perfusate respectively.
Results: In [NI], the relative oxygenation ratio was significantly higher in comparison to [WI] ($p < 0.05$). In [WI], mean pulmonary artery pressure and wet to dry weight ratio were significantly increased in comparison to [NI] ($p < 0.01$ both). Besides, in [WI], alveolar MPs were significantly higher after 10 min and after 60 min of perfusion in comparison to alveolar MPs in [NI] ($p < 0.05$). The rate of detected alveolar MPs also significantly increased along reperfusion in [WI] ($p < 0.05$). We could not bring out circulating MPs in either both groups.
Conclusion: Alveolar MPs could reveal as a relevant biomarker for lung ischemia related injury.

77 URINARY CXCL10 INDEPENDENTLY IMPROVES THE NON-INVASIVE DIAGNOSIS OF ANTIBODY-MEDIATED KIDNEY ALLOGRAFT REJECTION

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Introduction: The urinary levels of CXCL9 and CXCL10 can noninvasively diagnose T cell-mediated rejection (TCMR) of renal allografts. Their performance as diagnostic/prognostic markers of antibody-mediated rejection (ABMR) is unknown.
Methods: We investigated urinary CXCL9 and CXCL10 levels in 244 renal allograft recipients with 281 indication biopsies. We assessed the benefit of adding these biomarkers to conventional models for diagnosing/prognosticating ABMR.
Results: Urinary CXCL9 and CXCL10 levels, normalized (CXCL9: Cr and CXCL10: Cr ratios) or not to urine creatinine levels, correlated well with the extent of tubulointerstitial (i + t score, all $p < 0.0001$) and microvascular (g + ptc score, all $p < 0.0001$) inflammation. Both chemokines were in favour of of ABMR (CXCL9 [area under the curve {AUC}] = 0.69; 95% confidence interval [CI]: 0.62–0.77; $p = 1.1E-8$), CXCL9: Cr [AUC = 0.68; 95% CI: 0.60–0.76; $p = 3.8E-6$], CXCL10 [AUC = 0.747; 95% CI: 68.0–81.4; $p = 5.5E-10$], and CXCL10: Cr [AUC = 0.755; 95% CI: 69.0–82.1; $p = 1.5E-10$]). Although the mean fluorescence intensity of the immunodominant donor- specific

antibody (iDSA) noninvasively diagnosed ABMR (AUC = 0.75; 95% CI: 0.68–0.82; p = 5.6E-12), combining the urinary CXCL10: Cr ratio with iDSA levels significantly improved the noninvasive diagnosis of ABMR (AUC = 0.83; 95% CI: 0.77–0.89; p = 2.5E-15), with a bootstrap mean difference of 0.080 (p = 0.002), a continuous net reclassification index of 0.6718 (p < 0.01) and an integrated discrimination improvement of 0.0854 (p < 0.01). Multivariate Cox regression showed that the CXCL10: Cr ratio was independently associated with an increased risk of graft loss.
Conclusion: Compared with conventional assessments, the addition of the urinary CXCL10: Cr ratio in the evaluation of kidney transplant recipients with ABMR improves noninvasive diagnosis and stratification of patients at high risk for graft loss.

78 CHARACTERIZATION OF HUMORAL REJECTION IN LIVER PEDIATRIC TRANSPLANTATION

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Objective: The aim of the study is to correlate C4d immunostaining and pathological features in liver grafts from pediatric transplant recipients with the presence of donor specific antibodies (DSA).
Methods: 31 grafts biopsies (27 ten-year biopsies and 5 biopsies on indication) from 31 pediatric transplant recipients were reviewed for histological features according to Banff recommandations. Immunostaining for C4d was performed on deparaffinized tissue sections and analyzed quantitatively and semiquantitatively. DSA were quantified by Luminex Single Antigen.
Results: C4d immunostaining was positive in 28/31 biopsies. It was distributed as follows: diffuse stroma portal (7/31) and focal stroma portal (13/31), portal vein endothelial cells (7/31 = 23%), peribiliary capillar plexus (18/31 = 58%), centrilobular vein endothelial cells (9/31 = 29%) and sinusoïdal cells (19/31 = 69%). 11/31 biopsies were classified as chronic rejection, defined by centrilobular fibrosis with hepatocellular loss. Diffuse portal stromal (p = 0.0036) and associated stroma portal and portal vein endothelial cells (p = 0.012) C4d immunostaining were significantly associated to chronic rejection. DSA were searched in 20 among the 31 children. 30% did not have any DSA. Among positive patients, 25% had DSA class 1 and 70% DSA class 2 C4d immunostaining of portal stroma (p = 0.016) and sinusoïdal cells (p = 0.0018) was significantly associated with the presence of DSA score 8.
Conclusion: The C4d immunostaining of portal stroma and of endothelial cells is correlated on the one hand with the pathological lesions of chronic rejection, on the other hand with the presence of DSA. These results strongly suggest the participation of humoral mechanisms in liver graft chronic rejection in pediatric population.

79 EVOLUTION OF THE DSA ABILITY TO FIX C1Q IN A COHORT OF 118 SENSITIZED KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Donor specific antibodies (DSA) able to fix C1q are probably harmful for kidney allograft. Nevertheless their main characteristics are not yet well established. A better characterization of these DSA is important for a better understanding of their real implication in allograft antibody mediated rejection (ABMR).
Patients and Methods: In our monocentric cohort, 118 out of 947 adult patients (8%) had a functional allograft kidney and presence of DSA in 2011. In these patients, kidney biopsies were made for cause or due to the DSA occurrence (19 in 2011, 53 before 2011 and 64 after 2011). Sera taken the days of biopsies stored in HLA laboratory were analyzed by Single Antigen Beads (SAB) and C1q assays. We identified patients who had multiple analyses in SAB and C1q assays and studied the evolution of the MFI of immunodominant DSA (iDSA) and its ability to fix C1q.
Results: 114 sera were available the day of the first kidney biopsy and at least one serum was available subsequently with an average of 18.3 ± 16 months between the two samples. In these 114 initial sera: iDSA were C1q+ in 60 cases (53%) among which 49 biopsies showed acute or chronic antibody mediated rejection (82%); iDSA were C1q- in 54 cases (47%) among which 20 biopsies showed acute or chronic humoral rejection (37%). Forty five out of 60 C1q+ iDSA remained c1q+ in the second serum (75%) whereas 15 became C1q negative. DSA lost their ability to fix c1q in 9 cases after ABMR treatment by IgIV+/− Rituximab and in 6 cases without treatment. We observed a decrease in SAB MFI (12 747 ± 6439 vs. 6439 ± 3396, p = 0.03). Among C1q negative iDSA in the first serum, 47 remained negative, DSA were no longer found in 4 patients by SAB and 3 iDSA acquired the ability to fix C1q.
Conclusion: It seems that the ability to fix c1q is not a stable characteristic of the DSA. Many factors like ABMR treatment and although DSA MFI level, could contribute to this capacity and need to be better understood. The clinical and histological impact of these changes should be studied in a larger cohort.

80 DETECTION OF C3D-BINDING DONOR-SPECIFIC ANTI-HLA ANTIBODIES AT DIAGNOSIS OF HUMORAL REJECTION PREDICTS RENAL GRAFT LOSS

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Introduction: Antibody-mediated rejection (AMR) is widely recognized as a major cause for kidney-graft loss. Yet assessment of individual risk at diagnosis is impeded by the lack of a reliable prognosis assay. In the present study, we tested whether the capacity of anti-HLA antibodies to bind complement components can allow for accurate risk stratification at the time of AMR diagnosis.
Methodology: Among the 938 kidney transplant recipients for whom a graft biopsy was performed between 2004 and 2012 at the Lyon University Hospitals, 69 fulfilled the diagnosis criteria for AMR and were enrolled. Sera banked at the time of the biopsy were screened for the presence of donor-specific anti-HLA antibodies (DSA) and their ability to bind C1q and C3d using flow bead assays.
Results: In contrast with C4d graft deposition, the presence of C3d-binding DSA was associated with a higher risk of graft loss (p < 0.001). Despite a similar trend the difference did not reach significance with a C1q-binding assay (p = 0.061). The prognosis value of a C3d-binding assay was further confirmed in an independent cohort of 39 AMR patients (p = 0.038). Multivariate analysis identified only eGFR under 30 ml/min per 1.73 m2 [HR = 3.56 (1.46–8.70); p = 0.005] and the presence of circulating C3d-binding DSA [HR = 2.80 (1.12–6.95); p = 0.027] as independent predictors for allograft loss at AMR diagnosis.
Conclusion: We conclude that assessment of the C3d-binding capacity of DSA at the time of AMR diagnosis allows for identification of patients at risk for allograft loss.

81 PREVALENCE AND PROGNOSIS OF RECURRENT ALCOHOLIC CIRRHOSIS AFTER LIVER TRANSPLANTATION

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Background: Alcoholic liver disease (ALD) is a major indication for liver transplantation (LT). Recurrent alcoholic cirrhosis (RAC) after LT can occur but has not been studied. The aims of this study were to estimate the prevalence, predictors and natural history of RAC after LT.
Methods: All patients transplanted for ALD between 1990 and 2007 in 3 French centers were included. Alcohol relapse after LT was detected by clinical, biological and histological follow-up. The diagnosis of RAC was based on histological proof or an array of features in a context of alcohol heavy relapse.
Results: Among 1894 adult LT patients, 696 were transplanted for alcoholic cirrhosis and survived more than 6 months. After a mean follow-up of 9.0 years, 81.6% of patients were abstinent or occasional drinker and 128 patients (mean age at LT 47.2 ± 7.1 years, male 78.9%) experienced heavy alcohol relapse (18.4% of cases). Heavy alcohol relapse occurred after a mean of 2.4 ± 2.1 years after LT. Among heavy drinkers, the diagnosis of RAC was performed in 41 patients (32%). The diagnosis of RAC was done 6.1 ± 4.1 years after LT and 4.2 ± 2.7 years after alcohol relapse. Occurrence of RAC was significantly associated with younger age and shorter period of pre-LT abstinence. One-, 5-, 10- and 15-year survivals were 100%, 87.6%, 49.7% and 21.0%, respectively for the patients with RAC vs. 100%, 89.4%, 69.9% and 41.1%, respectively for the patients without RAC (p < 0.001).
Conclusions: RAC affect <6% of transplanted patients for ALD. One third of heavy alcohol relapsers develop RAC in <5 years with a very poor prognosis.