TRANSPLANT
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O1

USE OF BELATACEPT AS RESCUE IN KIDNEY GRAFT RECIPIENTS WITH INTOLERANCE TO CALCINEURIN INHIBITORS: A FRENCH EXPERIENCE OF 36 CASES

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Belatacept is indicated as an alternative in calcineurin inhibitors (CNI) for prophylaxis of graft rejection in *de novo* renal transplant recipients. Because this drug is known to avoid nephrotoxicity and some other adverse events of CNIs some physicians were tempted to use belatacept as a rescue molecule in case of intolerance to CNI.

We report 36 cases of a switch from CNI to belatacept in seven transplant centers in France.

Patients: We studied 16 male and 20 female transplant recipients (mean age 61 years, 31/36 deceased donors), with low immunological risk. Immunosuppressive regimen included induction therapy (22 anti IL-2R, 12 ATG), CNI (8 csa, 28 tac), steroids and mycophenolates. Two groups of patients were identified. In group 1 (G1, $n = 18$, 17/18 Extended Criteria donors) switch from CNI to belatacept was performed early, before 6 months postgraft (median date: day 96) and indications were delayed graft function or low GFR with evidence on biopsy of donor vascular lesions, tubular necrosis and in one case microangiopathy. Two patients were switched for extra indications: one for non compliance and diabetes, one for neurological toxicity of tac. In group 2 (G2, $n = 18$), switch was performed later (median date: day 500), indication was mainly deteriorating GFR, with evidence on biopsy of FIAT, vascular lesions and suspicion of CNI nephrotoxicity. One patient was switched because of pancreatitis due to tac. Belatacept was administrated every two weeks during two months and then monthly.

Results: In G1 only one graft was lost (primary nonfunction). The remaining grafts are functioning well with a decrease of the mean creatinine level respectively: 303, 164 and 206 μmol/l before switch, at nadir and at the last visit (median follow-up: 210 days). In G2 all grafts are functioning with a decrease of the mean creatinine level respectively: 228, 134 and 160 μmol/l before switch, at nadir and at the last visit (median follow-up: 287 days). The 2 cases of non renal toxicities of CNI improved as well. Tolerance of belatacept was good. Overall, only one patient had an acute rejection episode. Six patients had infectious complications: 2 norovirus diarrhoea, 1 pneumonia, 1 cutaneous cellulitis, 1 mycobacterium infection. One patient had a positive BK virus viremia.

Conclusions: Use of belatacept as rescue seems promising and improves GFR. In particular, early switch in low immunoligical risk patients receiving an ECD kidney and with severe CNI nephrotoxicity could save some grafts.

O2

THE IMPACT OF MTOR INHIBITION ON EVOLUTION OF RENAL FUNCTION AND URINARY PROTEIN EXCRETION – 24 MONTHS DATA FROM 719 *DE NOVO* LTX RECIPIENTS

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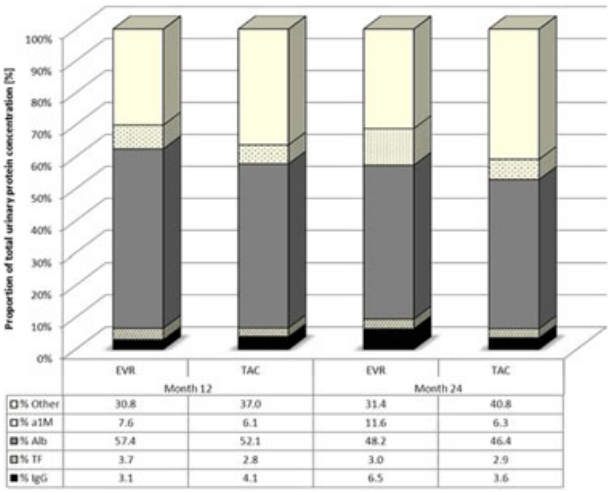
Background: The interplay of glomerular filtration and tubular absorption of proteins of dufferent size defines the pattern/magnitude of daily urinary protein excretion(UPE). Increased UPE, also called proteinuria, serves as a clinical surrogate for renal injury and progressive damage in a variety of diseases affecting different parts of the nephron. mTOR-inhibitor treatment has also been associated with increased UPE not only in KTx but also non-renal Tx recipients.

Method: Data were retrieved from study H2304 (NCT00622869), a 24-month (M), RCT in 719 *de novo* LTx recipients comparing everolimus(EVR, C0 3–8 ng/mL) plus reduced tacrolimus(rTAC, C0 3–5 ng/mL) to standard TAC (TAC-C, C0 6–10 ng/mL). Here, the total daily UPE, measured as urinary protein-to-creatinine ratio, as well as a set of differently sized urinary proteins will be described in order to allow a more detailed investigation of the origin/course of UPE in *de novo* LTx patients receiving EVR.

Results: UPE was higher with EVR+rTAC compared to standard TAC with highest values at M6 (290 mg/day) followed by decreasing values at M12 and a further decrease to 194 mg/day at M24. Daily UPE maintained stable in TAC Control at 158 mg/day. UPE 500 mg/day at any time point occurred in 18.1% of patients in TAC-C vs. 23.6% in EVR+rTAC (18.9% when EVR C0 was in the range of 3 ng/mL). Analysis of urinary protein electrophoresis determining the distribution pattern of alpha 1 microglobulin(26 kDa), albumin(70 kDa), transferrin(80 kDa), and immunoglobulinG(150 kDa) are shown in Fig 1 demonstrating similar patterns for EVR and TAC.



Discussion: Clinical observations suggest that mTOR-inhibitor treatment might be associated with increased UPE, potentially due to enhanced cell wall permeability and podocyte dysregulation. However, in case of mTOR-inhibitor facilitated reduction of CNI exposure, the improvement in glomerular blood flow and consequently a higher overall protein filtration in combination with mTOR-dependent reduction in tubular protein reabsorption may also contribute to increased urinary protein excretion without pathological significance.

O3

CNI AND STEROID-FREE IMMUNOSUPPRESSION AFTER SPK TRANSPLANTATION: ONE YEAR RESULTS OF A PROSPECTIVE AND RANDOMIZED STUDY

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Eviter l'utilisation des immunosuppresseurs nephrotoxiques et diabétogènes serait un avantage après une transplantation de pancréas-rein simultanée (SPK).Nous rapportons les résultats à un an d'uneétude prospective et randomisée évaluant l'efficacité et la sécurité d'un traitement comparant Tacrolimus (Tac) au Sirolimus (SRL) après une SPK. Il s'agit d'une étude dont le promoteur est le CHU de Nantes et désignée par les investigateurs avec un suivi à 5 ans. Cent patients diabétiques de type -1 (âge moyen de 40 ans, 21–56), avec une IRC furent inclus après avoir obtenu leur consentement écrit. Tous les 100 patients ont bénéficiés d'une greffe de pancréas avec dérivation portale et intestinale. Une randomisation en double aveugle avait lieu au moment e la greffe. Après une période commune de 3 mois d'immunosuppression à base de Thymoglobuline durant 5 jours et Tac/MMF et faible dose de prednisone, 50 patients ont été inclus dans le groupe SRL et 50 autres ont poursuivis avec Tac. A ce moment, la corticothérapie a été arrêtée. Une biopsie de routine du greffon rénal était programmée à un an. Tous les résultats sont présentés en intention de traiter. La survie actuelle à 12 mois du patient et du greffon rénal était de 100% dans les 2 groupes. La survie du pancréas à 12 mois a été de 82% dans le groupe Tac et 88% dans le groupe SRL; 12 pancréas (12%) ont été perdu durant les 3 premiers mois par thrombose; l'incidence de rejet aigu durant cette période commune a été de 5%. Apres randomisation, 4 pancréas ont été perdu (2 dans chaque groupe). L'incidence de rejet à été de 10% dans le groupe Tac versus 22% dans le groupe SRL. En raison des effets indésirables et/ou adverses, 50% des patients du groupe SRL ont interrompus le SRL et le Tac a été repris. Aucune différence significative n'a été retrouvée lors de l'évaluation de la fonction rénale, du métabolisme glucidique et lipidique durant toute la première année. L'analyse des biopsies rénales réalisée à un an a montré une plus forte incidence de lesions d'activité immune, associée à un taux significativement plus haut de DSA dans le groupe SRL (28 vs. 10%; $p < 0.05$). En conclusion, l'analyse des résultats observés au

terme d'un an de SPK révelent un taux très élevé d'arrêt du SRL en comparaison au Tac (50 vs. 4%), un pourcentage de rejet aigu évalué au double dans le groupe SRL (22 vs. 10%) et un profil histologique rénal et bio-humoral compatible avec une plus faible efficacité que le Tac. Le suivi à 5 ans est en cours d'étude.

O4 EPITHELIAL TO MESENCHYMAL TRANSITION MARKERS IN KIDNEY TRANSPLANT RECIPIENTS: THE CERTITEM TRIAL

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Background: A randomized trial was run to determine whether epithelial to mesenchymal transition (EMT) markers would help to identify kidney transplant (tx) patients (pts) at such a high risk of graft fibrogenesis that they would benefit from an early withdrawal of anticalcineurin (CNI).
Methods: Initial treatment consisted in CsA+MPS+Cs and basiliximab. We measured by IHC *de novo* expression of vimentin and β-catenin translocation in tubular epithelial cells, on a 3 months post-tx biopsy. A biopsy in which ≥10% of tubules expressed markers defined EMT+ pts. We randomly assigned both EMT+ ($n = 75$) and EMT- ($n = 119$) pts to either continue CsA+full dose MPS ($n = 98$), or to stop CsA and start on everolimus+low dose MPS (EVL/CNI-free) ($n = 96$).
Results: The objective was to evaluate if the progression of interstitial fibrosis (IF) between the 1st and a 2nd biopsy performed at 12 months post-Tx would be attenuated in EMT+ pts converted to a CNI-free regimen. The primary endpoint (PE) was the progression of IF and tubular atrophy (TA) score from M3 to M12 (ΔFI/AT≥1). In the modified ITT analysis (pts with adequate structural data at M3 & M12), the PE occurred in 16/31 EMT+ pts on CsA and in 12/26 EMT+ pts converted to EVL/CNI-free ($p = 0.68$). Biopsy proven acute rejection (BPAR) occurred more frequently in the EVL/CNI-free grp (25.0 vs. 5.1%, $p < 0.001$). Subclinical BPAR occurred on M12 biopsy in 10.4% of the EVL/CNI-free pts and 2.0% of the CsA pts ($p = 0.015$). Independent factor of BPAR was a MPS dose < to the recommended one (720 mg/d in the EVL/CNI-free, 1440 mg in the CsA grp) during >28 consecutive days. Pts with EVL trough level <7.0 ng/mL were also particularly at risk of BPAR (15/44, 34.1%). Graft loss occurred in 5 pts in the EVL/CNI-free grp vs. 1 in the CsA grp, $p = 0.12$.
Conclusion: An early CNI withdrawal with a switch from CsA to EVL does not prevent IF progression in patients at high fibrogenic risk and carries out a significant risk of rejection.

O5 RANDOMIZED, MULTICENTER STUDY OF EVEROLIMUS WITH EARLY REDUCTION OR ELIMINATION OF TACROLIMUS IN 719 *DE NOVO* LIVER TRANSPLANT RECIPIENTS: RESULTS AT 24 MONTHS

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Purpose: Optimizing renal function and avoiding chronic renal failure after liver transplantation is currently challenging. H2304 (NCT00622869) study evaluated the efficacy and safety of everolimus (EVR) facilitated reduction or elimination of tacrolimus (TAC) vs. standard TAC exposure (TAC-C) in *de novo* liver transplant recipients (LTxR). The 12-month (M) results showed that the regimen of EVR with reduced dose TAC had comparable efficacy and superior renal function vs. TAC-C. We present here the final 24M results from the H2304 study.
Methods: In this 24M, multicenter, open-label study, 719 *de novo* LTxR were randomized (1:1:1) after a 30-day (±5 days) run-in period with TAC-based regimen (± mycophenolate mofetil), to receive either EVR (C0 3–8 ng/mL) with reduced TAC (C0 3–5 ng/mL; EVR+rTAC, $N = 245$) or EVR (C0 6–10 ng/mL) with TAC withdrawal (TAC-WD; $N = 231$) at M4 or TAC control (TAC-C;C0 6–10 ng/mL; $N = 243$); all arms included corticosteroids. The main endpoints at 24M included composite efficacy failure rate (treated biopsy proven acute rejection [tBPAR], graft loss [GL], or death [D]) and its components, and renal function (assessed using glomerular filtration rate [eGFR] estimated by MDRD4 formula). Key safety endpoints included the incidence of adverse events (AEs) and serious AEs (SAEs).
Results: Enrollment in TAC-WD arm was prematurely terminated due to a higher rate of acute rejection and the protocol was amended accordingly. Mean TAC exposure at M24 was 3.94 vs. 6.71 ng/mL in EVR+rTAC vs. TAC-C, respectively. The incidence of composite efficacy failure (tBPAR/GL/D) was comparable for EVR+rTAC and TAC-C (Kaplan-Meier event rates: 10.3% vs. 12.5%; risk difference -2.2%; [97.5% CI: -8.8%, 4.4%]; $p = 0.452$). The EVR+rTAC arm achieved non-inferiority for the incidence of composite efficacy failure against the TAC-C arm ($p < 0.001$; pre-specified non-inferiority margin: 12%). The incidence of BPAR was significantly lower with EVR+rTAC compared with TAC-C (6.1% vs. 13.3%; risk difference: -7.2% [95% CI: -13.5%, -0.9%]; $p = 0.010$). Superior renal function was maintained at M24 with EVR+rTAC compared with TAC-C (mean difference in eGFR change: 6.66 mL/min/1.73 m^2 [97.5% CI: 1.9, 11.42]; $p = 0.0018$) (ITT population). For on-treatment patients, the difference in eGFR at M24 was 11.5 mL/min in favor of EVR+rTAC. At M24, the incidence rates for EVR+rTAC vs. TAC-C for AEs (96.3% vs. 97.9%) and SAEs (56.3% vs. 54.1%) were comparable.
Conclusion: The M24 results confirm that minimization of TAC by introduction of EVR at 1M after LTx achieves comparable overall efficacy and safety with superior renal function compared to standard immunosuppression with TAC.

O6 LONG-TERM EXPOSURE TO BELATACEPT IN RECIPIENTS OF EXTENDED CRITERIA DONOR KIDNEYS

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Background: BENEFIT-EXT randomized extended criteria donor kidney recipients to more (MI) or less intensive (LI) belatacept regimens, or cyclosporine (CsA). Patients continuing through year 3 could enter the long-term extension (LTE). We report 5-year outcomes in the LTE cohort.
Results: Of 304 (56% of intent-to-treat) patients entered the LTE and 260 (48% of ITT) continued through 5 years. From year 3 to year 5, 20 LTE patients died (5 MI; 9 LI;6 CsA) and 8 had graft loss (2 MI;1 LI; 5 CsA); 3 patients had an acute rejection episode (2 MI; 1 LI); 70 patients (20 MI; 26 LI; 24 CsA) had serious infections; and 27 (10 MI; 8 LI; 9 CsA) had malignancies. 4 post-transplant lymphoproliferative disorder (PTLD) cases occurred between year 3 and year 5 (3 LI; 1 CsA); 2/3 PTLD cases in LI were in EBV-negative patients. Mean cGFR (MDRD) at year 5 was 56 (MI), 59 (LI), and 45 (CsA) mL/min/1.73 m^2 (Figure).
Conclusions: For LTE patients, belatacept was associated with a consistent safety profile and sustained renal function improvement vs. CsA over time, with no new safety findings through year 5. The greatest risk for developing PTLD in belatacept patients remains EBV-negative serostatus.

O7 LONG-TERM BELATACEPT MAINTAINS EFFICACY AND SAFETY: 5-YEAR BENEFIT LONG-TERM EXTENSION (LTE) RESULTS

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Background: BENEFIT compared more (MI) or less intensive (LI) belatacept regimens to cyclosporine (CsA) in patients receiving a living or standard criteria donor kidney transplant. Patients completing 36 months could enter the long-term extension (LTE). We report 5-year results of the LTE.
Results: Four hundred and fifty-six (68% of intent-to-treat) patients entered the LTE at 36 months; 406 (89%) completed 60 months. Infection and malignancy rates from months 36–60 across MI, LI, and CsA were: fungal infections (14%, 15% and 12%), viral infections (21%, 18% and 16%), malignancies (7%, 6% and 9%); no additional post-transplant lymphoproliferative disorder occurred after 36 months. From months 36–60, death occurred in 2% MI, 1% LI, and 5% CsA patients and graft loss in 0 belatacept and 2% CsA patients. Mean cGFR (MDRD; ml/min/1.73 m^2) at month 60: 74 in MI, 76 in LI, and 53 in CsA patients (Figure). Acute rejection in month 36–60 was rare: 0 MI, 1 LI, and 1 CsA.

Conclusions: Early renal function benefits observed with belatacept were sustained through 5 years. There were few deaths or graft loss, and acute rejection was rare during the LTE. The belatacept LI regimen provides sustained renal function benefit and a favorable safety profile through 5 years.

O8 MTOR INHIBITORS THERAPY AFTER LIVER TRANSPLANTATION ALLOWS A SUSTAINED INCREASED IN REGULATORY T CELLS PRESERVING THEIR SUPPRESSIVE CAPACITY

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The mammalian targets of rapamycin (mTOR) inhibitors (sirolimus [SRL] and everolimus [EVR]) are used in liver transplantation for their immunosuppressive activity. Evidence indicates that $CD4^+CD25^+CD127^-FoxP3^+$ regulatory T cells (Tregs) have a crucial role in immune tolerance. Furthermore, mTOR inhibitors have been demonstrated to preserve Tregs and in contrast to Tacrolimus (Tac).

The aim of this study was to evaluate Tregs number and function, in liver transplanted recipients before and after conversion from Tac to mTOR inhibitors.

Fifteen patients with stable graft function where converted from Tac to SRL ($n = 5$) or EVR ($n = 10$). We prospectively analysed, at day 0, 14, 30 and 90 after conversion, using flow cytometry, Treg population (CD4 + CD25 + FoxP3 + CD127-) on blood cells and then performed a functional assay to test Treg ability to suppress $CD4^+$ Tcell activity.

mTOR inhibitors were well tolerated, no acute rejection was observed except. All patients displayed sustained rise in Treg levels after the introduction of mTOR inhibitors, in the two groups, SRL or EVE (mean peak Treg level at 3 months: 6.45 ± 1.24% of CD4 T cells, vs. a mean baseline level of 3.61 ± 1.32%, p = 0.0002; mean fold increase=2.04 ± 0.73); for SRL group: mean peak Treg level: 6.01 ± 0.92 vs. 3.79 ± 0.94, p = 0.019, and in the EVE group: 6.63 ± 2.67 vs. 3.54 ± 2.98, p = 0.0024. Moreover, Tregs preserved their functional ability to suppress activated CD4 + T cells.

Our results suggest that mTOR inhibitors introduction after liver transplantation induced sustain and significant increase in Tregs, and the suppressive capability of these cells was maintained. We thus confirmed their potential role in graft tolerance.

O9 CNI FREE IMMUNOSUPPRESSION IN HEART TRANSPLANT PATIENTS TREATED WITH EVEROLIMUS: RESULTS OF A MULTICENTER FRENCH REGISTRY

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Everolimus (EVL) is a mTOR antagonist preventing acute rejection after heart transplantation (HT). It has shown: 1) a non inferior efficacy in combination with low dose of cyclosporine (Cya) compared to Mycophenolate Mofetil (MMF) with standard dose of Cya, 2) a lower incidence of CMV infection, 3) a slower progression of chronic allograft vasculopathy (CAV). In selected patients, EVL could spare renal function and prevent some cancers.

Studies aiming at anticalcineurins (CNI) weaning after introduction of EVL are however inconsistent.

We analysed a retrospective registry of intend to treat HT patients with EVL and planned CNI weaning. Ten french HT centers participated to the registry reporting clinical and biological data before and at the time of EVL introduction, if failing EVL introduction, if failing CNI weaning, and at the end of the study period. 163 patients were included 104 + 73 months after HT. EVL had to be discontinued in 9 patients (6%) due to side effects including 2 moderate cellular acute rejection episodes. CNI were successfully weaned in 154 patients 14 ± 16 month after introducing EVL. CNI weaning however failed in 27 patients (17%) for various reasons including 2 humoral and 1 cellular rejections. 127 patients were weaned of CNI during the study period with a mean follow-up of 2 ± 1.7 year after discontinuation of CNI. Death occurred in 19 patients 19 ± 15 months after CNI weaning. Causes of death were cancer: 10 patients all diagnosed before EVL introduction, sudden death: 6 patients all with significant CAV diagnosed before introducing EVL, infection: 1, cerebral hemorrage: 1, unknown: 1. No patient died of rejection. One third of the patient improved significantly renal function after CNI discontinuation. Conclusion: EVL allows weaning of CNI treatment in maintenance HT patient with a low risk of rejection.

O10 EFFECT OF ECULIZUMAB ON THE FIBRINOLYTIC ACTIVITY OF MICROVESICLES IN A RECURRENCE OF ATYPICAL HEMOLYTIC UREMIC SYNDROME AFTER RENAL TRANSPLANTATION

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Background: Activated endothelial cell (EC) play a key role in the thrombotic microangiopathy (TMA) of atypical hemolytic uremic syndrome (aHUS). EC release microvesicles (MVs) with procoagulant activity in thrombotic thrombocytopenic purpura and HUS related Shiga toxin. Fibrinolytic properties in balance with procoagulant MVs could be involved in the lysis of intravascular microthrombi.
Aims: We hypothesized that, in patients with aSHU, eculizumab acted on the release of fibrinolytic microvesicles from endothelial cells. This study was carried out to estimate the release pattern of fibrinolytic microvesicles in a patient who had a recurrence of aHUS after renal transplantation and who was treated by Eculizumab.
Methods: Blood samples were drawn before and after each infusion of Eculizumab. MVs were isolated from the plasma sample by sequential centrifugation. MVs concentration was evaluated by microvolume protein quantitation ($A_{280\ nm}$). Fibrinolytic activity of MVs was detected by fibrin-agarose zymography and by measuring the generation of plasmin using a photometric microtitre play assay.
Results: Microvesicle concentration and fibrinolytic activity before Eculizumab were similar to the control group. A higher concentration of MVs and a parallel increase in fibrinolytic activity was observed after each infusion of Eculizumab during the whole treatment period (6 month). Plasminogen activator which explained fibrinolytic activity was identified as tPA. This finding was in support of the endothelial origin of the fibrinolytic activity.
Conclusions: Our study shows that Eculizumab therapy is associated with the release of fibrinolytic microvesicles. These MV may in part explain the effect of Eculizumab.

O11 EVALUATION OF REGULATORY T CELLS IN RECURRENT HEPATITIS C AFTER LIVER TRANSPLANTATION

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Background: Immune response failure during HCV infection has been associated with the activity of regulatory T cells. Hepatitis C-related cirrhosis is the main reason for liver transplantation. However, 80% of transplanted patients present an accelerated recurrence of the disease.

The aim of this study was to assess the involvement of regulatory T-cell subsets, of T helper 1, 2 and 17 cells in recurrent hepatitis C after liver transplantation.
Methods: Forty four key molecules, related to Treg, T helper 1, 2 and 17 responses, have been analyzed in peripheral blood mononuclear cells (PBMC), obtained at day 0, 30 and 120 after transplantation, from 22 livers transplant recipients, by qRT-PCR. The results obtained in patients with severe hepatitis C recurrence ($n = 9$) were compared to those obtained in patients with mild recurrence ($n = 13$). The severity of hepatitis C recurrence was evaluated by the results METAVIR analysis on one year liver biopsy (mild: $F < 1$, severe: $F \geq 1$)
Results: Our results demonstrated a significant increase in mRNA levels of Treg markers within 30 days after LT in patients that will develop a severe recurrence when compared to those who will develop a mild recurrence of hepatitis C. Th1 markers, which could be implicated in antiviral response, were also elevated in severe recurrence. This could suggest that Tregs may play a role in the suppression of an antiviral response, early after liver transplantation.
Conclusion: These results suggest that Tregs are enhanced, immediately after liver transplantation, in patients that will develop a severe HCV recurrence. High levels of Treg could be predictive of severe recurrence, patients with this high production warrant more intensive management.

O12 IL-4 AND IL-13 OVER-EXPRESSION IN SEVERE RECURRENT HEPATITIS C AFTER LIVER TRANSPLANTATION

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Hepatitis C frequently recurs after liver transplantation, resulting in accelerated progression toward fibrosis.The mechanisms underlying accelerated liver

fibrosis after HCV recurrence are poorly understood but immunological factors are probably involved. Interleukin (IL)-4 and IL-13 have been shown to induce fibrogenesis using in vitro models.

To determine the role of IL-4 and IL-13, in the accelerated progression of fibrosis in recurrent hepatitis C after liver transplantation, we have retrospectively evaluated the in situ expression of IL-4 and IL-13 in transplanted patients with or without hepatitis C recurrence by using immunohistochemistry followed by semi-quantitative analysis of positive cells.

Fifteen patients have been analysed, five with severe recurrent hepatitis C (Metavir: $\geq$ F2) have been compared with 5 patients with minimal recurrence ($\leq$ F1) and with 5 stable HCV negative transplanted patients.

IL-4 and IL-13 in situ expression which was low in transplanted patients without HCV recurrence (2.3 ± 0.7, 1.2 ± 0.58 respectively), was significantly increased in mild HCV recurrence and further increased in severe recurrence. (for IL-4 23.4 ± 2.29 versus 7 ± 1.12, $p < 0.0001$; for IL-13 23.9 ± 5.18 versus 5 ± 1.21, $p = 0.001$ IL-4 and IL-13 protein were overexpressed in graft recipients with severe recurrent hepatitis C.

In conclusion, IL-4 and IL-13 expression is upregulated in severe recurrent hepatitis C, and may play a central role in the progression of hepatic lesions, particularly in fibrosis after liver transplantation. An immunointervention planned to inhibit IL-4 and IL-13 pathway could be helpful in the treatment of recurrent hepatitis C after liver transplantation.

O13 IL-22 DEFICIENCY IN DONOR T CELLS ATTENUATES MURINE ACUTE GRAFT-VERSUS-HOST DISEASE MORTALITY WHILE SPARING THE GRAFT-VERSUS-LEUKEMIA EFFECT

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Introduction: Acute graft-versus-host disease (aGVHD) remains a major complication following allogeneic hematopoietic cell transplantation (allo-HCT), limiting the success of this therapy. Many proinflammatory cytokines secreted following the conditioning regimen have been linked to aGVHD initiation. Interleukin-22 (IL-22) is a cytokine related to IL-10 for its structure and is secreted by TH17 cells and innate immune cells. Given the paradoxical role of IL-22 in inflammation with both protective or proinflammatory functions, we investigated whether IL-22 could play a role in aGVHD pathophysiology.
Methods: We used a mouse allo-HCT model in which BALB/C mice were administrated with allogenic bone-marrow cells from C57Bl/6 mice and T cells from wild-type (WT) or IL-22-/- C57Bl/6 mice. Survival and clinical scores were then evaluated. Immune effectors were characterized by flow cytometry at day 7 post allo-HCT. GVL effect was analyzed by bioluminescence method.
Results: We showed that IL-22 deficiency in donor T cells can decrease the severity of aGVHD while limiting systemic and local inflammation in aGVHD target organs. In addition, we found that Foxp3 + Treg cells were increased in recipient mice that received IL-22 deficient T cells, suggesting that Treg were involved in the reduced severity of GVHD. Finally, we found that the graft-versus-leukemia (GVL) effect mediated by donor T cells was preserved in the absence of IL-22.
Conclusion: Overall, these data indicate that IL-22 is involved in aGVHD and suggest that targeting of IL-22 may represent a valid approach towards decreasing aGVHD severity after allo-HCT while preserving the GVL effect.

O14 INCREASE SURVIVAL OF ALLOGENEIC SKIN GRAFT IN MICE BY TREATMENT WITH LOW-DOSE IL-2 COMBINED WITH RAPAMYCIN

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Introduction: Inducing $CD4^+CD25^+Foxp3^+$ regulatory T cells (Treg) is a major goal in the field of transplantation in order to promote tolerance toward donor alloantigens. IL-2, initially developed to improve immune response in cancer was recently tested to induce regulatory T cells and modulate immune diseases like diabetes and graft versus host disease. In a model of minor antigen mismatch skin graft in mice, we present experimental results on the effect of low-dose of IL-2 associated or not with rapamycin, an immunosuppressive molecule used in transplantation.
Methodology: DBA/2 recipient mice were treated by daily injections of IL-2 (64500UI) starting six days before donor BALB/c skin graft. Rapamycin (1 mg/kg/day) was given by gavage from day of transplantation. The effect of combined treatment was analyzed by graft survival as well as by the characterization of regulatory populations and conventional T cells.
Results: The low-dose IL-2 alone has no effect on the kinetics of graft rejection while a combined therapy with IL -2 and rapamycin allows a significant increase in survival graft. The median of rejection increased from day 11 without treatment to day 24 with the combined treatment ($p = 0.0002$). Some mice can retain their graft until D60. This effect on survival was associated with a significant increase in the frequency of Tregs six days after transplantation (17.98% of CD4 in the spleen of non- treated group versus 25.67% in the group treated with combined therapy) and with overexpression of CD25 and ICOS by Treg. This Tregs activation is accompanied by a decrease in activation of Teff evidenced by a decrease in expression of ICOS and CD44.
Conclusion: This work represents the first demonstration of the combined temporary effect of IL -2 and rapamycin in a mice model of skin grafts. Further studies are underway to optimize the results obtained, the necessary steps before considering the use of IL-2 in the control of alloreactivity in humans transplantation.

O15 EFFECT OF MELATONIN ON THE ENDOPLASMIC RETICULUM STRESS AND THE AKT PATHWAY ASSOCIATED WITH RENAL ISCHEMIA REPERFUSION: ROLE OF AMPK

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Introduction: Ischemia reperfusion (IR) syndrome remains a major cause of acute renal failure. This syndrome induces structural and functional damages including endoplasmic reticulum stress (ERS) and Akt pathway down regulation. Melatonin is an effective free radical scavenger and antioxidant and was shown to have protective effects against IR. However, the molecular mechanism by which melatonin affords protection remains unclear. This study was designed to investigate the effect of AMP-activated protein kinase (AMPK) inhibition on Akt phosphorylation and its downstream target glycogen synthase kinase 3b(GSK3b) and some ERS parameters after pre ischemic melatonin treatment in the rat kidney.
Methodology: 24 Wistar rats (180–250 g) were divided into 4 groups ($n = 6$ for each one) as follows: *Group Sham:* rats were not subjected to renal IR. *Group IR:* Rats were subjected to bilateral renal ischemia for 60 min followed by reperfusion for 6 h. *Group Mel+IR:* The same operation was done but animals were treated with melatonin (10 mg/kg i.p.) 30 min before renal clamping. *Group Mel+IR+ara a:* The same as group 3 but animals were perfused with ara a (p-AMPK inhibitor, 0.1 mg/kg/min) during 10 min just before melatonin injection. Tissue levels of p-Akt, p- GSK3b, heat shock protein 70 (HSP70), activating transcription factor-4 (ATF4) and necrosis factor receptor (TNFR)-associated factor-2 (TRAF 2) were determined by Western blot and were correlated with p-AMPK inhibition.
Results: A significantreduction in ATF4 and TRAF 2 was observed in melatonin treated rats when compared to IR group. This was consistent with a significant amelioration of Akt and GSK3b phosphorylation and HSP70 activation. The AMPK inhibition was shown to induce an important elevation of ATF4, TRAF2 while p-Akt, p- GSK3b and HSP70 levels remain unaltered.
Conclusions: The AMPK inhibition suppresses the beneficial effects of melatonin only regarding the ERS attenuation while the Akt pathway still unchanged.

O16 PRODUCTION OF ANTI-HLA ANTIBODIES INDEPENDENT OF CD4 + T CELLS IN ORGAN TRANSPLANTATION

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Background: It is widely accepted that anti-donor HLA antibodies (DSA) are major culprits for late allograft failure.

The current immunologic dogma predicts that B cells can only respond to protein antigen (such as donor HLA molecules) with the help of CD4 + T cells.

According to this theory, progress in T cell immunosuppression (IS) should have translated into similar results regarding recipient's humoral response. Yet a significant percentage of patients develop *de novo* DSA during the 1st year post-transplantation, a time when IS is maximal and observance usually good.

Understanding the mechanisms leading to DSA response in the absence of CD4 + T cell help might pave the way for innovative therapies aiming at extending graft life.
Method and Results: C57BL/6 mice genetically deficient in CD4 + T cells (MHC II KO mice) or wild type (WT) were used as recipients of a skin graft

(alloantigen drainage to lymph node) or a heterotopic heart transplant (alloantigen drainage to spleen). Donors were HLA A2 transgenic mice, i.e. C57BL/6 mice that express human HLA A2 molecule under the murine MHC I promoter. This trick allowed for the monitoring of DSA response with flow cross match and Luminex assays routinely used in the clinic.

WT recipients, all developed circulating anti-HLA A2 antibodies. Interestingly, while no MHCII KO recipients of a skin graft did, MHCII KO recipients of a heart transplant all developed a delayed DSA response at low titer.

Conclusion: Antibodies might be generated against protein antigen in the absence of CD4 + T cells. This atypical humoral response seems to require the drainage of antigen to the spleen, a condition met by solid organ transplantation because donor and recipient vessels are anastomosed.

The characteristics of CD4 + T cell independent humoral response, the immune mechanisms involved and its pathophysiological significance are currently under investigations.

O17 INVOLVEMENT OF TGFβ/IDO PATHWAY IN B CELL REGULATION MECHANISMS: APPLICATION TO CHRONIC HUMORAL REJECTION OF RENAL ALLOGRAFT

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Patients with chronic humoral rejection of renal allograft (cABMR) have B cell phenotypic abnormalities associated with functional dysfunctions (lack of inhibition of the T cell proliferation). In this work, we study the mechanism of this cooperation B / T, especially the TGFβ/IDO pathway.

Methods: We studied 12 stable patients (ST) (delay from graft> 12 months, no rejection, proteinuria < 0.5 g/24 h, PRA< 10%, no DSA and a one year biopsy without allograft glomerulopathy), 14 patients with cABMR (positive DSA, allograft glomerulopathy and/or C4d staining) and 17 controls (blood donors). B cell functions were analysed using coculture with autologous B and T cells. T cells were stimulated with anti CD3 and anti CD28, and co-cultured with CpG-activated B cells. Th1 (IFNγ et TNFα) and immunosuppressive (TGFβ et IL10) cytokines and the regulatory enzyme indoleamine 2,3 dioxygenase (IDO) were analyzed in the culture.

Results: Compared with ST and controls, cABMR B cells are defective in their ability to inhibit T cell proliferation (3.7 ± 8.1% inhibition of T cell proliferation vs. 39.5 ± 2.5% for ST, p = 0.004, 37.8% ± 3.8% for controls, p = 0.006). Th1 cytokine production is not inhibited in coculture for cABMR group compared to ST and controls (p = 0.004, p = 0.003 respectively for IFNγ and p = 0.0003, p = 0.002 respectively for TNFα).

In the control group, we show, for the first time in humans, that activated B cells produce IDO (0.3% B cells expressing IDO at day 0 vs. 25.5% at D4). T cell proliferation is restored in coculture in the presence of IDO blockers (1-methyl-tryptophane (1-MT)) and TGFβ blockers (anti-TGFβ) (51.3 ± 3.9% of inhibition of proliferation of T cells vs. 32.4% ± 6.9 with 1-MT, p < 0.001 vs. 33% ± 4.2 with anti-TGFβ vs. 12.3% ± 4.4 with the two blockers). In addition, IDO and TGFβ are involved in the generation of natural Treg (48.6% ± 2.1% induction of Treg at D4 without adding blockers vs. 37.9 ± 2 2% with 1-MT, p = 0.008).

cABMR B cells are deficient in TGFβ secretion at D4 (18% cABMR B cells secreting TGFβ vs. 58% for ST, p < 0.01, vs. 60% for controls, p < 0.001) and there is a significant decrease in the production of IDO (19.9% B cells secreting IDO at D4 for cABMR vs. 32.1% for ST, p = 0.004 vs. 36.5% for controls, p = 0.001).

These cytokine defects may explain the inability of activated cABMR B cells to induce natural Treg (15% of Treg at D0 vs. 13% at D4, p = ns), in contrast to ST and controls (18% of natural Treg at D0 vs. 30% at D4 for ST, p < 0, 001 and 20% vs. 40% for controls, p < 0, 001) or secreting IL-10 Treg (p = ns for cABMR, p = 0.008 for ST and p = 0.003 for controls).

Conclusion: In this study, we show for the first time that TGFβ/IDO pathway is involved in the B cells functional abnormalities in cABMR.

O18 GAMMA-DELTA T CELLS IN CELLULAR STRESS SURVEILLANCE IN TRANSPLANTATION

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Ischemia -reperfusion injury such as viral infections are stress conditions that impair renal graft. Our group has shown that gamma -delta T cells (LTγδ) increase in the peripheral blood of kidney transplant recipients after cytomegalovirus (CMV) infection, involved in the control of infection and correlated with a decreased incidence of cancer. In vitro, γδ TCR seems to recognize antigens common to different cellular stress (tumors, CMV), but these antigens remain poorly characterized.The aim was to study the TCR -dependent activation of LTγδ in different stress conditions encountered in transplantation.

Method: We used as a model a Tγδ clone, its TCR Vγ8Vδ3 was transferred to a transductant line (JRT3) and various tumor cell lines targets were studied. Specific monoclonal antibody (FMS- 01) recognizing the antigen of Vγ8Vδ3 TCR was generated. The activation of T effectors and antigen expression were measured by flow cytometry in different conditions of cellular stress: hypoxia at 0.1% of oxygen, heat-shock at 42°C or CMV infection.

Results: Stress of the target cells in these three conditions causes an increase in the TCR-specific activation of JRT3, blocked by the antibody (Ab) – FMS 01.Expression of the antigen targeted by the Ac FMS 01 increases in target cells with increasing stress. Intensity of JRT3 activation is correlated with the intensity of the expression. Inhibition of reactive oxygen species by N-Acetyl -cysteine decreases expression of the antigen targeted by the Ac FMS-01. The antigen targeted by the TCR Vg8Vd3 and recognized by the Ac-FMS 01 is currently being identified.

Conclusion: γδ T cells recognize antigens induced by oxidative stress conditions encountered in kidney transplantation. Identification of such antigens may well lead to new immunotherapies targeting mechanisms involved in the alteration of graft function.

O19 VERY LATE-ONSET CYTOMEGALOVIRUS DNAEMIA IN ASYMPTOMATIC RECIPIENTS: INCIDENCE, RISK FACTORS AND OUTCOME

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Introduction: Direct and indirect cytomegalovirus (CMV) effects after renal transplantation led clinicians to introduce universal prophylaxis in high risk patients, but its well-recognized drawback is a high incidence of late-onset CMV DNAemia and disease, which are both associated with a lower graft survival. There are no data evaluating the existence of asymptomatic DNAemia after the first year. The goals of this study were then to analyse the incidence, risk factors and consequences of very-late-onset CMV DNAemia in asymptomatic patients.

Method: We included 892 consecutive asymptomatic patients transplanted for at least 2 years and who came for their annual outpatient visit, in this single-center cross-sectional study. All of these patients were monitored for CMV using a whole blood CMV quantitative nucleic acid amplification testing (CMV-QNAT).

Results: Of 28 patients displayed a very-late-onset CMV DNAemia (3.1%) (Positive CMV-QNAT, mean viral load: 1355 copies/mL), while the 864 other patients had a negative CMV-QNAT. Using multivariate analysis, we found that female sex (OR=2.54, p = 0.02), past history of CMV mutation (OR=6.59, p = 0.04), and steroid at the visit (OR=2.39, p = 0.03) were independently associated with an increased risk of very-late-onset CMV DNAemia. Patients with a very-late-onset CMV DNAemia developed more frequently CMV disease over the year following the visit than the other patients (7% vs. 0.6%, p = 0.02). One year later, the median eGFR was lower in patients with a very-late onset CMV DNAemia than in both patients with or without post-transplant history of CMV infection (40 versus 51, p = 0.05 and 40 versus 53 mL/mn, p = 0.01, respectively).

Conclusion: Very-late-onset CMV DNAemia is a new rare entity associated with chronic graft dysfunction. It is frequently observed after a past history of CMV mutation and promoted by steroid use.

O20 MICROSPORIDIOSIS IN RENAL TRANSPLANT RECIPIENTS

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Introduction: Epidemiology and care of intestinal microsporidiosis (IM) in renal transplant recipients are not clearly defined.

Patients and Methods: This retrospective monocentric study included all patients with *Enterocytozoon bieneusi* IM diagnosed by quantitative PCR between 2007 and 2013. Patients were treated by fumagillin 60 mg/d (n = 13) or merely by tapering immunosuppressive drugs (n = 9).

Results: We included 22 patients, of whom 14 (64%) were males, aged 48 ± 13 years. IM occurred within 52 ± 55 months after kidney transplantation. Sequential quadritherapy with Thymoglobulin® induction was used in 64% of patients.

Symptoms always associated diarrhea (6.5 ± 4.3 stools/d) and weight loss of 8 ± 4% -similar among fumagillin-treated or untreated patients- and sometimes abdominal pain (27%) or fever (9%). Mean fumagilline therapy duration was reduced to 9 ± 3 days because of frequent thrombopenia. Clinical recovery occurred in 21 patients (95%), 38 ± 53 days after diagnosis. PCR became negative in 94% of patients, within 53 ± 111 days.

Compared to untreated patients, those receiving fumagillin recovered faster (23 ± 22 versus 63 ± 79 days) and showed less decrease in GFR (MDRD) at 3 months (-1.4 ± 10 versus -7.4 ± 11 ml/min/1.73 m²), though these results were not significant.

Regarding renal function, 17 patients (67%) exhibited acute renal failure (AKI classification), of whom 4 in stage 3. GFR (MDRD) decreased by 4.7 ± 11 ml/min/1.73 m² three months after IM and 4.9 ± 14 ml/min/1.73 m² at last follow up, done 19 ± 13 months after IM. When AKI occurred among patients with severe CKD, it sometimes led to end-stage renal disease: 2 patients required initiation of hemodialysis 194 and 347 days after IM. There were no rejection or death due to IM.

Conclusion: IM is often responsible of acute renal failure, sometimes irreversible. Tapering immunosuppression might be sufficient, however fumagillin could help to fasten clinical recovery and to improve renal prognosis.

O21 MICAFUNGIN AS ANTIFUNGAL PROPHYLAXIS IN HIGH-RISK LIVER TRANSPLANTATION: RANDOMISED, MULTICENTRE TRIAL

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Background: Amphotericin B (AmB) and fluconazole are recommended for antifungal prophylaxis after liver transplant (LTx). In this open-label, randomised, multicentre trial, the efficacy and safety of micafungin was compared with site-approved standard care prophylaxis (SC) in LTx pts at high risk of invasive fungal disease (IFD).

Methods: After LTx, pts were randomised 1:1 to iv micafungin 100 mg once daily (od) or iv SC (fluconazole 200–400 mg od; liposomal AmB 1–3 mg/kg/day; or caspofungin 70 mg loading, 50 mg maintenance od). The primary endpoint was clinical success (absence of a proven/probable IFD and no additional antifungals) at end of prophylaxis (EOP). Non-inferiority (10% margin) of micafungin vs. SC was assessed in the per protocol set (PPS) and confirmed in the full analysis set (FAS). Safety assessments were adverse events (AE) and liver and kidney function.

Results: The FAS comprised 172 micafungin and 172 SC pts. Mean age was 51.2 yrs, 48.0% had a MELD score ≥20. Most common risk factors for IFD were post-operative renal impairment (31.4%), abdominal re-operation within 5 days of LTx (21.5%) and pre-operative renal impairment (20.3%). 60 (17.4%) pts had intra-operative transfusion of ≥20 units of cellular blood product. 13.4% of pts had a previous liver transplant. 22.7% of donors were >65 yrs old. At EOP (mean drug duration 17 days), clinical success was 98.6% for micafungin (n = 140) and 99.3% for SC (n = 137) (Δ [95% CI]: 0.7 [-2.7, 4.4]) in the PPS and 96.5% and 93.6% (-2.9 [-8.0, 1.9]) in the FAS. There were 4 *Aspergillus* and 8 *Candida* infections at EOP. 70% of pts completed prophylaxis. Incidences of drug-related AEs for micafungin and SC were 11.6% and 16.3%, leading to discontinuation in 6.4% and 11.6% of cases, respectively. Liver and kidney function were similar between groups.

Conclusions: Micafungin was shown to be safe and non-inferior to SC as antifungal prophylaxis in high-risk LTx patients.

O22 PREDICT THE EVOLUTION OF CMV INFECTION: A MODEL BASED ON GAMMA-DELTA T CELL KINETICS

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Introduction: Cytomegalovirus (CMV) infection in transplantation is associated with increased morbidity and mortality and increased if a mutant strain (UL97 or UL54) induces treatment failure. Our team showed that gamma -delta T cells (LTγδ) were involved in the control of CMV infection. However, the practical use of LTγδ assay in peripheral blood of patients to predict the resolution of infection or conversely the emergence of a mutant strain is not established.The objective was to assess if LTγδ kinetics can predict the resolution of CMV infection in kidney transplant recipients at high risk of infection (D + R- and R + with anti-thymocyte globulin – ATG), or the emergence of a mutant strain.

Method: LTγδ kinetics has been described in D + R or – R + / GAL patients between 2003 and 2011. This kinetics was compared between infected and non infected patients and between patients with and without mutation. LTγδ expansion was estimated by a linear mixed model, the time of expansion defined as the date of occurrence of this expansion from the beginning of infection.

Results: Of 167 patients D + R- and 104 R + patients were included, 93 D + R- and 75 R + with CMV infection. Time of LTγδ expansion was correlated with the duration of viremia ($r = 0.91$, $p < 0.0001$). The delay of LTγδ expansion was associated with the presence of a mutant strain ($p < 0.0001$). This mutation was predicted by a persistent viremia after 39 days of LTγδ expansion (AUC 0.76).

Conclusion: In high risk patients, LTγδ expansion is related to the resolution of CMV infection. Conversely, the delay of expansion and a persistence of viremia after expansion are predictive of the occurrence of a mutant strain. Monitoring LTγδ could be useful during CMV infection as to predict the resolution of the infection as the emergence of a mutant strain.

O23 NAÏVE AND TEMRA VD2^{NEG} GD T CELL SUBSETS DURING POST-TRANSPLANT CMV DNAEMIA: A PILOT STUDY

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Introduction: Monitoring of cytomegalovirus (CMV) immune response at baseline may help clinicians to better define the risk of post-transplant CMV infection or disease and then to better use prophylaxis. Vd2^{neg} gd T cells are induced after CMV infection and play a major role for controlling the virus. The goal of this study was then to determine whether these cells at baseline could predict post-transplant CMV DNAemia in R+ kidney transplant recipients receiving a preemptive treatment.

Patients and Methods: Vd2^{neg} gd T cells were longitudinally analysed at baseline, day 15, month 1, month 3, and month 6 in 34 kidney transplant recipients receiving a preemptive strategy. Naïve, central memory, TEMh and TEMRA subsets were also analysed within the Vd2^{neg} gd T cells compartment.

Results: The first part of the study was conducted in 11 D+R- patients, where a Vd2^{neg} gd T cell expansion was always observed after CMV primo-infection. At baseline, Vd2^{neg} gd T cells exhibited mainly a naïve phenotype, which move toward a predominantly TEMRA phenotype after CMV primoinfection. Among the 23 R+ patients, 17 developed post-transplant CMV DNAemia. At baseline and day 15, TEMRA Vd2^{neg} gd T cell percentages were significantly higher in patients who did not develop any CMV DNAemia when compared to patients with DNAemia <2000 copies/mL and those with DNAemia >2000 copies/mL (At day 15: 81.2%, 59%, 47.1%, respectively, $p = 0.04$ and $p = 0.03$, respectively). At day 15, 74.2% of TEMRA Vd2^{neg} gd T cells predicted the absence of post-transplant CMV DNAemia with a sensibility of 100% and a specificity of 90%.

Conclusion: This pilot study shows that TEMRA Vd2^{neg} gd T cell percentages could be a promising candidate for monitoring CMV immune response in R+ patients at baseline.

O24 IS MYCOPHENOLATE ACID EXPOSURE A RISK FACTOR FOR BK VIRUS INFECTION?

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Background: In this prospective study, we analysed the association between the Mycophenolate Acid (MPA) exposure and the occurrence of BK virus infection during the first year post-renal transplantation.

Methods: Of 179 consecutive patients transplanted between 2006 and 2009 were included. MPA area under the concentration-time curves (MPA AUC) were performed at day 7 and months 1, 3, 6 and 12. The detection of BK virus infection relied on count of urine decoy cells once a week until month 2 and at months 3, 6 and 12. A blood qPCR was done above 6 decoy cells by microscope slide. They all received an induction (thymoglobulin for 97%), steroids associated with MMF (100%) and a calcineurine inhibitor (CNI) (cyclosporine (65%) or tacrolimus (35%)).

Results: 34 (19%) patients have a BK virus infection (Gr1) after a mean delay of 57 days while 145 (81%) were free of BKVI at any time (Gr2). In Gr1, 18/34 patients have a positive blood qPCR and 5 of them (2.7%) developed a BKV nephropathy with only one graft loss. In Gr1, the MPA AUCs at the time of BK virus infection (63.74 mg.h.l) were not significantly different than time paired AUCs of Gr2 (55.93 mg.h.l) ($p = 0.095$). 48% of patients in Gr1 while only 30% of patients in Gr2 have a MPA AUC superior or equal to 60 mg.h.l. ($p = 0.055$). 12/37 (32.4%) patients receiving tacrolimus have a BK virus infection while only 22/144 (15.3%) patients receiving cyclosporine have ($p = 0.0086$).

Conclusion: These results suggest that the intensity of MPA exposure alone is not in itself a risk factor of BK virus infection.

O25 RISK FACTORS FOR SIGNIFICANT BK VIRURIA DURING EARLY POST-TRANSPLANT PERIOD

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Introduction: BK virus (BKv) infection is a threat to renal allograft survival. BKv nephropathy had largely been described since more potent immunosuppressive drugs appeared. An overimmunosuppression is often advocated for risk factor. Therapeutic drug monitoring may better assess individual immunosuppression. The aim of this study is to seek risk factors for significant BKviruria (> 10^5 copies/ml because there is no BK viremia under this threshold) and to determine whether a high AUC of mycophenolic acid (MPA) is one of them.
Method: we retrospectively observed 255 kidney recipients with a 1-year follow-up treated by mycophenolate mofetil between July 2006 and June 2011. BKv was regularly sought in blood and urine samples by quantitative PCR. Different risk factors were sought between group with significant BK viruria and without.
Results: Fifty recipients (19.9%) had a BK viruria, 38 (14.9%) had a sustained BK viruria during the first 3 months and 25 (9.8%) had a BK viremia during the first year. Six (2.6%) patients underwent BKv nephropathy. Threshold for significant BK viruria was 56 h.mg/L determined by ROC equation. In univariate analysis, significant BK viruria occured more frequently in male recipients (81.6 vs. 62.6%; $p = 0.02$), older (54.6 ± 14.3 vs. 49.5 ± 13.3 years; $p = 0.03$) with a greater MPA AUC (54.1 ± 21.1 vs. 44.6 ± 20.7 hr.mg/L; $p = 0.02$). Nephroangiosclerosis and focal segmental glomerular sclerosis were more frequent when significant BK viruria occurred: 18.4 vs. 7.1% ($p = 0.02$) and 13.2 vs. 4.3% ($p = 0.03$) respectively.

In multivariate analysis, male gender (relative risk (RR) 3.1; $p < 0.02$) age above 58 years old (RR 2.6; $p < 0.02$) and MPA AUC greater than 56 h.mg/l (RR 2.8; $p < 0.001$) were risk factors for significant BK viruria.
Conclusion: A high MPA AUC (>56 h.mg/l) seems to be a risk factor for significant BKviruria as male gender and age. It could be reasonable to not exceed MPA AUC > 55 h.mg/l to prevent significant BK viruria and BK viremia.

O26 SHOULD WE TRANSPLANT OR DIALYZE HIV-INFECTED PATIENTS WITH CHRONIC KIDNEY DISEASE STAGE V?

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Background: The renal replacement therapy modality associated with the best survival is not known for HIV-infected patients.
Methods: All HIV-infected patients from the French National REIN registry initiating renal replacement therapy (RRT) between 2005 and 2009 were included and prospectively followed until 31/12/2010. Survival (Kaplan Meier estimate) and prognosis factors (time-dependant covariate Cox model) were determined according to RRT modality.
Results: Of 280 HIV-infected patients initiated a RRT between 2005 and 2009 in France: haemodialysis 92%, peritoneal dialysis 6%, KT 2%, median age 47 yrs [min: 12.5, max: 86.2], males 69%. During follow up (median time 399 days), 39% of dialyzed patients were enrolled on a KT waiting list, and 16% of enrolled patients were transplanted. KT patients were younger (42.6 yrs) than listed non-transplanted patients (45.4 yrs, $p < 0.01$) who were younger than non-listed patients (49.8 yrs, $p = 0.06$). Two- and 3-yr survival was 80% and 68%, respectively for all RRT patients. Risk factors for death were age (HR=1.2 for each 5-yr period, 95CI[1.1, 1.3]), male sex (HR=2.3, [1.1, 4.6]), smoking (HR=2.3, [1.3, 3.9]), HCV infection (HR=2, [1.1, 3.6]), heart failure (HR=2.3, [1.2, 4.2]) and low BMI (HR=0.9 per kg/m^2,[0.8, <1]). Distribution of the 54 deaths was as follows: KT patients: 2/23 (3 and 64 days after KT), listed dialyzed patients: 3/107, and non-listed dialyzed patients: 49/167. Listed patients had a better survival than non-listed patients (HR=5.8 [1.8–18.9]) and than KT patients (HR=14.7 [1.5–144.1]). The latter advantage was only due to the 2 post-operative deaths in the KT patient group. After 64 days post-KT or post-enrolment on the waiting list, no death was recorded in the KT patient group, compared to 3 deaths among the 107 listed patients.
Conclusion: After an increased risk for death in the post-operative period, KT seems to be associated with the best survival in HIV-infected patients.

O27 PTLD RENAL TRANSPLANT PATIENTS DIE FROM CHEMOTHERAPY-INDUCED INFECTIOUS COMPLICATIONS RATHER THAN FROM LYMPHOMA PROGRESSION: A SINGLE CENTER STUDY

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Introduction: There is no consensus on post-transplant lymphoproliferative disorders (PTLD) best treatment strategy. Chemotherapy is considered as the therapeutic option with the higher response rate, but no study has compared features and outcomes of PTLD vs. lymphomas observed in the general population (non-PTLD). We performed a case-control (1:2) study to compare outcomes in PTLD vs. non-PTLD patients after chemotherapy.
Patients: Twenty-one PTLD diagnosed since 2000 in a French transplantation center were included and matched to 42 controls treated in the hematology center of the same institution. Cases and controls were matched on age, International Prognostic Index (IPI), cerebral localization and histological type. Sixteen diffuse large B-cell lymphoma (DLBCL) and their controls were treated with cyclophosphamide, doxorubicin, oncovin, prednisone and Rituximab (R-CHOP) and 5 primary cerebral lymphomas (PCL) and their controls received methotrexate-based chemotherapy.
Results: Two-year overall survival (OS) was 57% and 71% and 5-year survival was 44% and 58% respectively in PTLD vs. controls ($p = 0.20$). Response rate to first line chemotherapy was similar in both groups (71% in PTLD and 62% in controls, $p = 0.58$). Median dose intensity was less in PTLD than in controls (89% versus 100%, $p = 0.02$). Febrile neutropenia and death from infectious complications were significantly higher in PTLD vs. controls (respectively 57% vs. 19%, $p = 0.004$ and 31% vs. 0%, $p = 0.03$). A Performance Status beyond 1 was identified as the only independent risk factor for death (HR 2.68, CI95% [1.28–5.68], $p = 0.01$) in the multivariate analysis.
Conclusion: Our study shows that PTLD patients have a poorer prognosis as compared to controls but the difference didn't reach a statistical significance, probably due to the small sample. The poor outcomes observed in PTLD are attributed to chemotherapy-induced infectious complications more than disease's aggressiveness.

O28 NORMALIZATION OF URINARY CELL MRNA LEVELS FOR DIAGNOSIS OF TCMR IN RENAL TRANSPLANTATION

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Introduction: Prediction of T cell mediated rejection (TCMR) of renal allografts with non-invasive biomarkers is a major objective in renal transplantation. A composite score (CpScore) was recently validated in a multicenter prospective study, using the quantification of CD3ε and IP10 mRNAs, and 18S rRNA to distinguish TCMR from non-rejecting grafts. Normalization of urinary PCR remains a matter of debate. We made the hypothesis that testing multiple reference genes for normalization will help to optimize the diagnostic performance of urinary mRNAs.
Methods: We retrospectively studied 41 patients from 2 french renal transplantation centers, 15 with a biopsy-proven TCMR, 12 with IF/TA lesions and no rejection, and 14 with pristine biopsies. We measured CD3ε, IP10, GAPDH, HPRT, lactotransferrin (LTF, highly expressed in polymorphonuclear cells) and uroplakin (UPK, reflecting the presence of urothelial cells) urinary mRNAs, and 18S rRNA. We used CD3ε, IP10, and 18S as candidate genes, and 18S, GAPDH, HPRT, LTF and UPK as reference genes. ROC curves for every candidate gene and for the CpScore were compared with or without normalization by the reference genes.
Results: In our data, CD3, IP10 and CpScore, but not 18S mRNA expression levels were significantly associated with TCMR (ROC curve AUC 0.69, 0.71, 0.70 and 0.48, respectively). Normalization by a reference gene enhanced the diagnostic performance of CD3, IP10 and CpScore, with the best results obtained with GAPDH normalization (AUC: 0.77, 0.73 and 0.81, respectively). Unexpectedly, uroplakin was significantly correlated to classical reference genes, more than with rejection markers.
Conclusion: Normalization, especially with GAPDH, is an important step when measuring urinary cell mRNAs that may enhance their diagnostic performance.

O29 ECULIZUMAB IN ANTIBODY MEDIATED REJECTION

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Introduction: There is to date no gold standard treatment of antibody mediated rejection (AMR). Current therapeutic strategies rely on plasmapheresis combined with intravenous globulin (IVIg). Despite these treatments, 12%-37% of patients suffering from acute AMR eventually lose their grafts.

Eculizumab is a humanized monoclonal antibody that targets complement protein C5 and prevents the formation of the membrane attack complex. Therefore it could be efficient in treating complement mediated lesions during AMR. Few clinical cases describe the efficiency of Eculizumab in treating acute AMR.

Methodology: In this monocentric retrospective study we report 15 patients (7 men and 8 women) that have been treated between October 2011 and June 2013 for AMR using Eculizumab on top of plasmapheresis, IV Ig and a B-cell targeting agent. Patients were transplanted between January 2002 and November 2012. All AMR were documented by a graft biopsy according to the Banff 2009 criteria at diagnosis and we followed the patient and graft outcome after treatment. The biopsy was repeated whenever necessary. The mean follow up was 10.4 months.

Results: Seven patients out of 15 (47%) did not respond to the treatment and 5 lost their graft. 9 patients were diagnosed with AMR 27.2 months after their transplantation, out of which 6 (78%) did not respond to treatment. The remaining 6 were diagnosed with AMR in the first year following transplantation and only one lost its graft (17%), $p < 0.05$. Only one of the patients died and 7 experienced severe infections. In the responders group, the mean serum creatinine was 163 μmol/l 37.6 months after transplantation and 10.4 months after AMR diagnosis. No responding patients received eculizumab more than 3 months.

Conclusion: Eculizumab seems more efficient in early versus late AMR, which reflects a more prominent involvement of the complement cascade in early versus late AMR.

O30 THE PROGNOSTIC FACTORS IN CHRONIC ACTIVE ANTIBODY-MEDIATED REJECTION

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Chronic active antibody-mediated rejection (CAMR) is an important cause of chronic allograft dysfunction and kidney graft loss. CAMR treatment is not well established and its effectiveness is discussed.

The aim of our work was to study the risk factors of graft loss in patients with CAMR.

Methods: we conducted a retrospective study of CAMR diagnosed in our center between January 2007 and June 2013. We performed a Cox regression analysis of risk factors of graft loss, having as variables the recipient clinical and biological characteristics, histological lesions (Banff 2007) and the treatment of CAMR.

Results: From 837 patients transplanted, 24 patients were diagnosed as CAMR (Graft biopsy and DSA). Mean age was 48 ± 18.8 years. The median duration of the diagnosis of CAMR was 38.5 months (3–261). Creatinine at diagnosis was 254 ± 92.8 μmol/l and proteinuria 1.32 g/d. 7 patients (29.2%) received only plasma exchanges (PE), 6 patients (25%) PE + low doses IvIg and 11 patients (45.8%) PE+IvIg+Rituximab.

10 patients lost their graft after a mean period of 16.9 months (5–52). 3 patients died (including on death complicating lymphoma).

The factors associated with graft loss were: recipient age >50 years (HR 1.15 [1.001–1.32], $p = 0.04$), CMV infection before CAMR (HR 4.46 [1.2–16.4], $p = 0.024$), GFR < 20 ml/min at time of rejection (HR 10.7 [1.6- 61.6], $p = 0.012$) and histological grade of cg2 (HR 8.7 [1.03–74], $p = 0.047$). The presence of C4d on biopsy, the MFI and the class (I or II) of DSA and the treatment modality did not significantly influence graft survival.

Conclusion: The CAMR is frequently complicated by graft loss. Recipient age >50 years, renal dysfunction and allograft glomerulopathy at diagnosis and CMV infection before rejection was associated with poor prognostic.

O31 MANAGEMENT OF SENSITIZED PATIENTS IN KIDNEY TRANSPLANTATION. PROSPECTIVE SINGLE CENTER STRATEGY

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Introduction: Many patients (pts) awaiting for a KT in our institution are highly sensitized (HS) because of HLA antibodies in their serum. In order to avoid early alloantibody mediated rejection (AMR) leading to a early graft loss, we prospectively proposed a therapeutic strategy by plasmapheresis (PP) and IVIg .

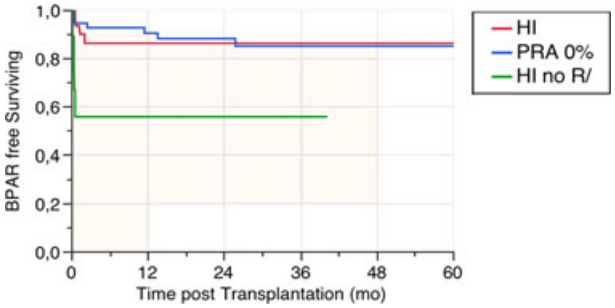
Materials and Methods: The first PP (1.4 X plasma volume of the patient) is performed before surgery. Then a total dose of 2gr/kg IVIG is infused during 48 hours postoperatively. At day5, PP are reinitiated (3/week for 1 month).

IS regimen include tacrolimus, MMF and low-dose steroids. Donors with extended criteria are excluded as well as positive virtual crossmatch.

This prospective study compares the evolution of three groups (G) of pts.

G1: 27 HS pts treated by PP and IVIg; G2: 54 pts without immunological risk (PRA 0%), paired with G1 for age, sex and year of KT and G3: 9 HS pts not treated by IVIG and PP. The mean follow-up is 24 months.

Results: Patient survival was similar in the three groups. In G1 and G2, we observe the same cellular acute rejection rate (10% at 1 year fig 1), none AMR, graft survival was 100% at the end of the follow-up, the GFR is equivalent (G1: 55, G2: 51 ml / min). In the other hand, G3 develops a high AMR rate (40%) and a significantly reduced graft survival.



The main morbidity in G1 is a high rate of hematoma arround the graft (in 9 cases) requiring further surgery in 6 pts.

Conclusion: AMR were avoided in pts HS treated by PP and IV Ig according to our therapeutic strategy started at the time of KT

The cellular acute rejection rate, the graft survival rate and renal function are similar in treated HS pts and in the reference population (without antibodies). HS pts in who we don't follow our strategy, a high AMR rate and a poor graft survival is observed.

O32 EVALUATION OF THE EFFICACY AND SAFETY OF BASILIXIMAB AS CURATIVE TREATMENT OF PERSISTENT OR COMPLICATED ACUTE REJECTION IN CARDIAC TRANSPLANTATION

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Basiliximab (Simulect) is a monoclonal antibody directed against the alpha chain (CD25) of the interleukin 2 receptor. It inhibits the activation of T lymphocytes and is indicated for prevention of acute rejection in *de novo* allogeneic renal transplantation in adults and children and is commonly used as induction therapy in solid organ transplantation.

Our retrospective study involved the treatment of 22 cellular rejection in 17 patients failing to control rejection by conventional strategies (corticosteroid resistant: $n = 12$; intolerance or contraindications to switched or increased immunosuppression $n = 8$). Basiliximab was administered in two doses of 20 mg IV over 20 min with 4 days intervals. A semi -quantitative score of rejection was used to compare the results of biopsies before and after treatment with basiliximab. We respectively assigned a score of 0, 1, 2, 3 or 4 to stages ISHLT 0R -1A- 1B -3A- 3B. The analysis is made from the patient records.

After basiliximab, the semi- quantitative score of rejection dropped from 50 to 18 (64% reduction), reflecting improved histology. Rejection is considered resolved in 47.6% of cases. There were four treatment failures (unmodified rejection) and the use of two courses of basiliximab for five patients and three times in one case. The cure of basiliximab was the only intervention for 6 patients (28%) and accompanied by an adjustment or change of immunosuppressants in other cases. The global efficiency is 81%, taking into account both resolved rejections ($n = 10$) and improved ($n = 7$) after treatment with basiliximab. No adverse effects related to basiliximab have been observed.

This study reports the first use of basiliximab in heart transplantation for treatment of acute cellular rejection in the absence of alternative or in addition to an adjustment of the immunosuppressive treatment. No incidents have been observed and these encouraging results suggest the need for prospective studies.

O33 EARLY ACUTE HUMORAL REJECTION IN THE ABSENCE OF ANTI-HLA ANTIBODIES: CLINICO-PATHOLOGICAL DESCRIPTION FROM A FRENCH NATION-WIDE STUDY

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Antibody mediated rejection (ABMR) is usually associated with donor-specific anti-HLA antibodies (DSA). Evidence of ABMR in patients with no DSA strongly suggests the implication of non-HLA antibodies.

We implemented a retrospective nation-wide study to improve undertanding of non-HLA ABMR. Inclusion criteria were: *first or re-transplantion, deceased or living-donor; acute allograft dysfunction during the first three months; allograft biopsy showing a total score of glomerulitis and peritubular capillaritis g+ptc≥3 according to the Banff classification; absence of identified anti-HLA DSAs using Luminex®.*

Demographical and clinical parameters were collected *for* 36 cases. Recipient age was 53 ± 19 yrs. Male/female ratio was 3/1. Mean time of dialysis was 3 ± 3 yrs. Donor age was 53 ± 12 yrs. Cold ischemia time was 12 ± 8 hrs. All patients received induction therapy (94% basiliximab, 6% thymoglobuline), a CNI (69% tacrolimus, 31% cyclosporine), MPA and steroids. Rejection was diagnosed at day 12 ± 9 in the absence of graft function recovery in 30% of patients. The remaining 25 patients defined a poor serum creatinine nadir of 289 ± 169 μmol/L at day 15 ± 22. Acute graft dysfunction (393 ± 230 μmol/L) led to the diagnosis of acute rejection at day 25 ± 34. No anti-HLA DSA were observed. Mean g+ptc score was *3.8* [3–6]. In addition, intimal arteritis and interstitial inflammation (i ≥ 1) were observed in 50% and 69% of cases, respectively. Additional lesions included haemorragic suffusion and thrombotic microangiopathy in 26% and 9% of cases, respectively. Therapeutic strategies included steroids pulses (86%), thymoglobulines (37%), rituximab (31%), IVIG (49%) and plasmapheresis (49%). Primary non function was observed in 2 cases. At last follow up (3 ± 1 yrs) serum creatinine was 178 ± 92 μmol/l. 6% of patients were back to dialysis.

This study provides a close clinico-pathological description of non-HLA ABMR, and will be followed by additional histological and mechannistic analyses.

O34 EVALUATION OF THE TREATMENT'S EFFICACY OF ACUTE-MEDIATED REJECTION BY THE ASSOCIATION PP/IVIG/RITUXIMAB, IN KIDNEY TRANSPLANTATION

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Introduction: Antibody-mediated rejection (AMR) is a recognized cause of kidney allograft loss. The aim of this study is to evaluate the treatment's efficacy of AMR by the association PP/IVIg/Rituximab.
Methods: Retrospective study including all patients having AMR treated according to Marrakech protocol between January 2004 and December 2012 in Saint-Louis Hospital, Paris-France.
Results: Thirty-nine patients were included in this interim analysis. Two patients had a simultaneous kidney and pancreas graft, 13 were re-transplantations. All patients, except one, were treated by Thymo-Cellcept-Steroids-CNI (Cyclo or Tacro). AMR diagnosis was based upon Banff criteria. Mean serum creatinin level on diagnosis was 279 μM; proteinuria/creatininuria level was 0.22 g/mmol. Four patients didn't have any donor specific antibody (DSA). The mean occurrence of DSA was 2 and the mean MFI was 8520. The treatment included plasmapheresis, corticosteroids, intravenous immunoglobulins and Rituximab. Eighteen patients had an early rejection (less than 3 months) whereas 21 of them had a late one. The mean serum creatinin level, on diagnosis, was 259.9 ± 171.2 μM for early rejection and 295.8 ± 162.4 μM for late rejection (NS). The follow up period was 57.8 ± 33.3 months for the early group and 15.8 ± 13.6 months for the late one. At last follow up, the serum creatinine level was 165.1 ± 58.8 μM and 251.42 ± 101.0 μM, respectively ($p = 0.022$). In the early group, 16.7% of patients were switched back to dialysis versus 42.9% in the second group. The survival probability of the graft was 39.2% at 99 months in the early group versus 34% at 25 months in the late one. The survival curves were significantly different between both groups (log-rank $p = 0.0013$).
Conclusion: Better functional response to treatment and better survival of renal graft in the early AMR group in this interim analysis.

O35 CORTICOSTEROID AVOIDANCE IN ADULT KIDNEY TRANSPLANT RECIPIENTS RECEIVING ATG-F: 5 YEARS RESULTS OF A PROSPECTIVE AND RANDOMIZED STUDY

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Nous présentons les résultats à 5 ans d'une étude prospective, randomisée et multicentrique (CHU de Nantes, Toulouse, Besançon, Montpellier, Strasbourg et Nice), évaluant l'absence de corticostéroïde (Cs) après une première transplantation rénale chez l'adulte. 197 patients ont reçu une induction à base d'ATG-Fresenius durant 5 jours (en jours alternes), du mycophénolate mofétil (MMF) et de la ciclosporine (CsA; introduite à J5). 98 patients ont été randomisés dans le groupe Cs- et 99 dans le groupe Cs+ (pour une durée minimale de corticothérapie de 6 mois). L'efficacité et la tolérance de l'absence totale de Cs a été évaluée durant 5 ans après la greffe. La survie du greffon à 1 an et à 5 ans a été de 93.2% et de 80.6% dans le groupe Cs+ et de 94.9% et de 86.7% dans le groupe Cs- ($p = 0.276$). Le taux de patients sans épisode de rejet aigu à 1 et 5 ans a été de 86.9% et de 81.8% (Cs+) contre 74.5% et 74.5% (Cs-; $p = 0.144$). Aucun patient dans le groupe Cs- n'a présenté un épisode de rejet après la première année. A 5 ans, le poucentage de patients sans épisode de rejet aigu a été de 88.9% dans le groupe Cs+ et de 83.7% dans le groupe Cs-. La survie du greffon à 5 ans a été significativement plus basse chez les patients ayant présenté ou n'ayant pas présenté un rejet aigu dans le groupe Cs+ (55.6% contre 92%; $p = 0.005$), avec 8/18 échecs contre 2/25 dans le groupe Cs-. La fonction rénale est restée stable et sans différénce significative dans les 2 groupes durant les 5 années de suivi; à 5 ans la créatinine médianne était de 159 Umol/L dans le groupe Cs+ et de 145 Umol/L dans le groupe Cs-; l'estimation de la FG était de 53.5 ml/mn dans le groupe Cs+ et de 56.6 ml/mn dans le groupe Cs-. Un nombre plus élevé de patients dans le groupe Cs+ ont présenté un diabète *de novo*, une dyslipidémie et des tumeurs. Comme d'autres études ayant évalué l'arrêt ou l'absence d'une corticothérapie après une transplantation rénale, nous retrouvons une incidence de rejet aigu précoce significativement plus élevée en cas d'absence de Cs. Cependant, les patients du groupe Cs- n'ont pas présenté d'épisode tradif de rejet aigu et la survie du greffon n'a pas été négativement influencée à 5 ans par le nombre plus élevé de rejets aigu précoces. En revanche, le profil du rejet aigu chez les patients Cs+ était différent; il s'agit d'un rejet tardif avec un impact négatif sur la survie du greffon. Eviter toute corticothérapie depuis la greffe semble possible et sans effet négatif sur la survie du greffon à 5 ans sous un schèma immunosuppresseur à base d'ATG-F/CsA et /MMF, et avec un profil métabolique plus proche de la normale.

O36 UNCONTROLLED PATHWAYS ACTIVATION AFTER RENAL TRANSPLANTATION AND C5B9 DEPOSITS ON GRAFT PREDICT GRAFT OUTCOME IN ADULT RENAL TRANSPLANT WITH C3 GLOMERULOPATHY

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C3 glomerulopathy (C3G) is a severe disease strongly associated with abnormal control of complement alternative pathway activation. In renal posttransplantation, few data are available on recurrence risk and graft outcome. The aim of this study was to identify risk factors for recurrence and transplant outcome in particular the role of alternative pathways consumption and C5b9 staining after renal transplantation.

We retrospectively studied 47 patients with a history of DDD ($n = 15$), GNC3 (17) and MPGN type I ($n = 15$) who received renal transplantation (RT°. Plasma level of C3 and sMAC were performed by Elisa. C3 and C5b9 staining were done by immunochemistry on paraffin kidney slides.

Graft survival was 98% at one and 77% five years. 48% of patient had a clinical graft recurrence biopsy proven; 60% of them occurred in the first year after transplantation. The recurrence occurred in 33%, 47% and 60% of patients with DDD, GNC3 and MPGN type I respectively. At five years, 54% of graft lost was due to recurrence. Before transplantation, a low C3 levels and positive C3 Nef was found in 63% ($n = 18$ of 29 available data) and 60% of patients ($n = 14$ of 23 available data) respectively. After RT, a low C3 levels, positive C3 Nef and high sMAC were present in 20%, 33% and 37% of patient respectively. 70% of patients at time of recurrence had a low C3 or/and high sMAC. On the opposite only 8% of patient with no recurrence had low C3 or/and high sMAC. All patients who lost graft before 5 years due to recurrence had C3 low and/or sMAC high. Positive C3 staining was present in all biopsies from patients who had recurrence but C5b9 staining was positive in biopsies from patients who lost graft due to recurrence earlier. In conclusion, uncontrolled pathways activation and C5b9 deposits were associated with severe recurrence and poor graft outcome.

O37 ANALYSIS OF RENAL GRAFT ELASTOGRAPHY DOESN'T ALLOW FOR DETERMINATION OF INTERSTITIAL FIBROSIS

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Introduction: Kidney biopsy is an important invasive tool for the diagnosis of rejection and fibrosis, witch intensity is well correlated to chronic allograft nephropathy progression. Hepatic fibrosis quantification on histological section and the measurement of hepatic stiffness by elastography are highly correlated. This study was designed in order to seek a link between elastography and renal transplant fibrosis.
Methods: This is a monocentric, prospective, non interventional study. 100 consecutive transplanted patients who undergone a renal biopsy between January 2011 and May 2012 had transplant elastography measurement (ACUSON S2000 with ARFI software, SIEMENS) within a mean of 9 days.
Results: Of 97 were analyzed. 48 were protocol biopsies, 31 were done to diagnosed rejection and 18 to reevaluate immunosuppressive therapy. They were 32 women and 65 men with a mean age of 48 ± 14 year. 74 were on antihypertensive treatment and 24 were diabetics. At the time of renal biopsy, mean estimated GFR (MDRD) was 34.9 ± 18.6 ml/min and mean proteinuria was 76 ± 127 mg/mmol of UCr. According to Banff classification, 32 patients were ci0, 40 ci1, 13 ci2 and 12 ci3. The mean elastography of each fibrosis stages were respectively: 1.9; 1.96; 2.07; 2.02 kPa. There was no significant difference between elastography measurement and fibrosis stages, tubular atrophy or total score of chronic lesions on biopsy. Renal failure progress in 25 patients and 12 reach ESRD during the year after biopsy. Their mean eGFR at biopsy was 11.2 ml/min. Mean elastography for these patients was 1.88 kPa in patients ci1 ($n = 4$), 2.1 kPa in patients ci2 ($n = 2$) and 1.81 kPa in patients ci3 ($n = 6$). For these patients also, no correlation was found between histological analysis and elastography.
Conclusion: Elastography determination of renal graft doesn't seem to be an useful tool for the evaluation of interstitial fibrosis. Whether it is utile for the follow-up remain to be study.

O38 SURVIVAL AND POST TRANSPLANT COMPLICATIONS OF OBESE RENAL TRANSPLANT RECIPIENTS

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Objective: determining the survival and post transplant complications of a group of obese renal transplant recipients.
Methods: retrospective evaluation of clinical and biological data of obese renal transplant recipients transplanted during the period june 2006- june 2013. This group was matched with a group of non obese transplant recipients that received their grafts in the same period and with the same epidemiological charechteristics of donors and recipients.
Results: From the 553 kidney transplant recipients transplanted in our centre from june 2006- june 2013, we have included in our analysis a number of 40 patients wit a BMI >/= 30 kg/m^2 (group A) and we have matched them with a group of 40 patients with a BMI < 30 kg/m^2 (group B). Medium BMI in group A is 32 (30–39) kg/m^2 and in group B is 22(16.9–29) kg/m^2, with only 27.5% with BMI > 25 kg/m^2 in group B. Medium age is 56 versus 57 years, sex repartition is 57.5% female and 42.5 male in both groups,. Incidence of diabetes before transplantation is 42.5% in group A and 15% in group B (p value 0.01). Incidence of bariatric surgery pre- transplantation in group A is 7.5% (1 gastric ring and 2 sleeve interventions).

Incidence of delayed graft function was non significant between the 2 groups (p:0.3). Nadir of creatinine was 155 μmol/l in group A versus 132 μmol/l in group B (p:0.1). Incidence of NODAT was not significant between the 2 groups.

Parietal infections, lymphoceles and urinary tract infections were not different between the 2 groups. Also, there was no difference in cardio-vascular events between group A and group B.

Renal function and proteinuria were not different between the 2 groups at 1 year and at 5 years post transplantation.

Patient survival was similar (97.4% group A, IC 95 (82.8–99.6) versus 82% group B, IC 95 (64.1–91.5) (p 0.13). There was no difference in renal survival between the 2 groups (92.5% for both groups).
Conclusion: In this study, post transplant complications and survival are not different between obese and non – obese patients.

O39 EVALUATION OF THE MORBI-MORTALITY OF LIVER TRANSPLANT PATIENTS AT UNIVERSITY HOSPITAL OF LILLE. AN OBSERVATIONAL MONOCENTRIC RETROSPECTIVE STUDY

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Objectives: Firstly: To compare morbi-mortality after hepatic transplantation (HT)for decompensed cirrhosis patients, including alcoholic hepatitises, and of the patients operated for a hepatic tumour. Secondary: To compare the morbi-mortality of the patients transplanted for acute alcoholic hepatitis (AAH) and those transplanted for a decompensed cirrhosis of another origin.
Type of Study: Observational retrospective monocentric study between January 2008 and February 2013.
Patients and Methods: A total of 208 patients was analyzed during this period. The population was distributed according to the indication of transplantation: hépatocellulaire failure (HCF) including AAH or for hepatic tumour. We have compared mortality up to 6 months after HT; residence time and postoperative morbidity between the two groups. We also compared transplanted patients for a AAH vs. a decompensed cirrhosis not AAH.
Principal Results: I – The transplanted patients for HCF ($n = 73$) had a MELD score significantly higher (24 vs. 9.5). They have peroperative bleeding and transfusions, more postoperative complications (infectious, cardiovascular, renal, reintubations, reoperation) and long-term hospitalization (36 vs. 23 days). Mortality at 28 days and 6 months was not significantly different (6 vs. 4% and 10 vs. 4%).

II – The patients transplanted in AAH ($n = 16$) had MELD score of 30. They have a long-term hospitalisation around 11 days than patients with HCF not AAH. Only one death was indexed in 6 months.
Conclusion: In spite of the increased morbidity and long term hospitalisation, the absence of surmortality positions HT like a real therapeutic alternative among patients with serious hepatic dysfonction including those with a cortico-resistant AAH.

O40 LIVER RETRANSPLANTATION IN ADULTS: 25 YEARS EXPERIENCE IN A EUROPEANCENTER

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Background: Liver retransplantation (RLT) is the only therapeutic option in transplantation recipients with a failing graft showing inferior outcome when compared to primary liver transplantation.
Methods: We performed retrospective analysis of 143 adults retransplanted between 1987 and 2011.
Results: Indications for RLT were ischemic-type biliary lesions (ITBL) in 23%, primary non function (PNF) in 20%, hepatic artery thrombosis (HAT) in 17%, chronic rejection in 17%, and recurrent disease in 8%. One-, 5- and 10-years overall and graft survival were 60%, 52% and 39% and 55%, 46% and 32%, respectively. The 90-days mortality rate was 34% mainly due to septic complications (45%). Multivariate analysis showed transfusion requiring more than 7 units ($p = 0.005$) and preoperative dialysis ($p = 0.02$) to be associated with an impaired survival. ITBL was the main indication for RLT in our series and survival was significantly better in patients retransplanted for ITBL than for any other indication ($p < 0.02$). We also report the outcome of a subgroup of 14 recipients previously transplanted in childhood and requiring RLT in adulthood for ITBL to be superior when compared to the adult group (86% and 74% at 1- and 5-years and 57% and 49% for the overall adult group) ($p = 0.12$).

55% of the recipients experienced at least one complication after retransplantation, mainly biliary complications in 25% and arterial complications in 12, 5%.
Conclusion: Patients with ITBL usually have had good and stable graft function for many years and our findings suggest that this subgroup might greatly benefit from elective RLT with excellent long-term outcome.

O41 PROGNOSTIC FACTORS OF LONG-TERM SURVIVAL AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Background: Hepatocellular carcinoma (HCC) represents about 30% of indication of liver transplantation (LT). The aim was to study long-term prognosis and prognostic factors of patients transplanted for HCC.
Methods: In a monocentric cohort 293 patients were enrolled on the transplant list for HCC and 236 (81%) were transplanted (mean age at LT: 54 ± 10 years,

sex ratio M/F = 202/34). After analysis of the native liver, we concluded that 70 (32.2%) patients were transplanted outside Milan Criteria (MC) and with microvascular invasion (MVI) in 56 (25.8%) cases. Forty-nine of 87 patients (60.6%) transplanted outside MC or with MVI had adjuvant chemotherapy (Gemcitabin plus Oxaliplatin; GEMOX). Five and 10 years survival were studied according to pathological examination of the native liver (MC, MVI), etiologies of cirrhosis and adjuvant chemotherapy during the post LT period.
Results: Overall survival was 71% at 5 years and 60% at 10 years. There was no significant difference in survival according to etiology of cirrhosis. Survival in patients transplanted according to MC ($n = 147$) was 80% at 5 years and 68% at 10 years compared to 54% at 5 years and 44% at 10 years ($p < 0.0002$) in patients transplanted outside MC ($n = 70$). Survival in patients transplanted without MVI ($n = 161$) was 77% at 5 years and 68% at 10 compared to 51% at 5 years and 32% at 10 years ($p < 0.0002$) in patients transplanted with MVI ($n = 56$). Survival for patients outside MC or with MVI was 57% at 5 years and 52% at 10 years after adjuvant chemotherapy and 58% at 5 years and 40% at 10 years in the absence of chemotherapy (p = ns).
Conclusion: Long-term survival after LT for HCC was 74% at 5 years and 63% at 10 years. No difference in post LT survival according to the etiology of cirrhosis did exist. Pathological examination of Milan Criteria or vascular invasion of the native liver is the main pronostic factor. Adjuvant chemotherapy did not influence survival in patients above Milan criteria.

O42 PROGNOSTIC VALUE OF PROTOCOL GRAFT BIOPSY AT 3 MONTHS POST-GRAFT IN RENAL TRANSPLANTATION

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Introduction: In kidney transplantation, usefulness of protocol biopsies remains controversial. The aim of our study was to investigate the factors influencing renal histology and to assess the prognostic value of 3-month control biopsy on graft survival at 3 years.
Methodology: We retrospectively studied a cohort of 250 *de novo* consecutive renal transplant recipients between January 2008 and December 2010, who experimented protocol biopsy under ultrasound at 3 months post-graft (M3). All patients had a 3-year follow-up. Biopsies were analyzed according to the Banff's classification.
Results: Graft biopsy is a safe exam with <3% complications, all minor (hematuria with no need of blood transfusion). Only 6% of the biopsies were inadequate according to Banff's criteria. Twenty-seven percents of biopsies were considered to be normal by the nephropathologist. Eleven percents (27/250) displayed a cellular inflammation score (i + t) and/or a micro-vascular inflammation score (ptc+g+v) >1. We did not identify predictive factors for such lesions. However, in univariate analysis, the presence of a cellular or micro-vascular inflammation score above 1 on 3-month protocol biopsy was associated to a significantly reduced graft survival at 3 years (relative risk of graft loss 4.8 [1.2–17.44], p = 0.01). Multivariate analysis confirmed that inflammatory lesions was an independent risk factor (RR = 5.6 [1.2–23.5], p = 0.018) for graft loss, as well as early acute rejection (RR = 10.8 [1.8 to 54.1], p = 004).

Tubulo-interstitial and/or micro-vascular inflammation on 3-month protocol biopsies appear to be an independent risk factor for graft loss at 3 years post-graft. As we identified no predictive factors for these lesions, protocol biopsies remain an important tool for early graft assessment and subsequent management of immunosuppression.

O43 IMPROVEMENT OF SENSORY NERVE CONDUCTION CORRELATES WITH CGMS MEAN GLUCOSE AND VARIABILITY REDUCTION FIVE YEARS AFTER ISLET TRANSPLANTATION FOR TYPE 1 DIABETES

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Long-term benefit-risk ratio of islet transplantation remains unclear. This study describes the evolution of peripheral and autonomic neuropathy 5 years after islet transplantation with the Edmonton protocol in type 1 diabetic patients (ClinicalTrial.gov: NCT00446264 / 01123187). Twenty-one consecutive patients (13 islet-alone, eight islet-after-kidney), transplanted for at least 5 years, underwent biological evaluation, continuous blood pressure and glucose monitoring (CGM), lower-limb electrophysiological and cardiovascular autonomic testing (R-R variation with paced breathing, Valsalva ratio, postural heart rate and blood pressure changes) before transplantation and yearly during 5 years. Ten/21 patients were insulin-independent 5 years post-transplantation with a median (IQR) A1c at 6.0 (5.8–6.7) vs. 7.8 (6.9–8.3)% in the insulin-requiring group $p < 0.001$). Three lost their islet graft, but were analyzed in intention-to-treat. The medians of sensory action potential ($p < 0.05$) and both sensory and motor nerve conduction velocities ($p < 0.01$) improved between 0 and 5 years. All 4 parameters significantly correlated negatively with CGM mean glucose and all except sensory nerve conduction velocity negatively with triglycerides ($p \leq 0.01$). Sensory conduction velocity correlated negatively with glucose variability (SD) on CGM ($p < 0.01$). Tacrolimus levels negatively correlated with motor conduction parameters ($p \leq 0.02$). All four parameters correlated positively with ß score or post-prandial C-peptide level ($p < 0.05$). *C*ardiovascular reflex testing did not change over the 5–year follow-up. Conclusion: islet-alone or after-kidney transplantation improved significantly sensory nerve conduction parameters. As previously demonstrated, mean glucose was the main factor influencing this improvement.

O44 OUTCOME OF ARISTOLOCHIC ACID NEPHROPATHY AFTER RENAL TRANSPLANTATION

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Background: In the early 1990s, intake of slimming pills containing Aristolochic Acids (AA) led to a rapidly progressive kidney failure. AA are nephrotoxins and a significant proportion of patients developed urothelial carcinoma. The aim of this study was to assess the outcome of patients with AA nephropathy (AAN) after kidney transplantation.
Methods: A case-control study in patients with AAN who underwent kidney transplantation. Patients' characteristics and outcomes were compared to a control group of patients with interstitial chronic nephropathy matched for gender and age at transplantation.
Results: Twenty patients were transplanted since 1992 for AAN. Nineteen were female. All but one were Caucasian. Mean age at diagnosis was 45 ± 2 years (39 ± 2 in controls, p = ns). Time on dialysis was 19 ± 4 months (28 ± 3 in controls, p = ns). Time from diagnosis to transplantation was significantly shorter in AAN patients (5 ± 0.7 vs. 11 ± 1 year). Mean age at transplantation was 50 ± 3 years (49 ± 2 in controls, p = ns). Mean time of follow-up was 13 ± 1 year. Immunosuppressive therapy was comparable in both groups. Seven patients presented with urothelial carcinomas of the upper-tract; two of them with additional bladder urothelial carcinomas. Of these two patients, one required radical cystectomy. In the control group, none suffered from urological complications. Cardiovascular complications were comparable in both groups. Patient survival was 100% in AAN patients compared to 100, 92 and 92% in the control group (p = ns) at 5, 10 and 15 years respectively after transplantation. Graft survival at 5, 10, and 15 years was 95, 83, and 75% in the AAN group compared to 100%, 92%, and 92% in the control group (p = ns).
Conclusion: AAN leads rapidly to end-stage renal disease requiring transplantation. Although 35% of patients presented urothelial carcinomas of the upper-tract and bladder, patients' survival is excellent and graft survival is not affected.

O45 LONG-TERM IMPACT OF SYMPTOMATIC VESICO-URETERAL RELFUX AFTER KIDNEY TRANSPLANTATION: RESULTS FROM A RETROSPECTIVE MONOCENTRIC STUDY

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Introduction: The aim of this study is to evaluate the effect of vesico-ureteral reflux (VUR) on graft function.
Methods: From March 1986 to October 2012, 27 patients who received a renal allograft and symptomatic VUR (recurrent graft infection) confirmed by cystography (VUR+ group) were retrospectively studied. Patients were classified in two groups according to treatment efficacy (medical, surgical, endoscopic): Success (no VUR after surgical treatment; $n = 12$) or Failure (persistent VUR; $n = 15$). Patients were compared to a cohort of control patients (no symptomatic VUR) matched for age and year of transplantation ($n = 54$).
Results: Women composed 78% of the VUR+ group (average follow-up: 8.1 ± 6 years); the most frequent primary kidney disease was reflux nephropathy (RN) (30%) and the VUR diagnosis was confirmed at 21 ± 20 months after transplantation. Treatment performed was endoscopic on 17 patients (five failures), surgical on two patients (no failure) and medical for ten patients exclusively. From the third month (M3) to 5 years post-transplantation, the rate of degradation of graft function (eGFR; MDRD) was lower in Success group than in Failure group (ΔeGFR: -9.7 ± 20.2 vs. -16.3 ± 21.4 ml/min/1.73 m^2).

Compared to the control group (average follow-up: 7.9 ± 7 years), there were more women and initial RN in VUR+ group (18/54 vs. 21/27 [p = 0.0002] and 3/54 vs. 8/27 [p = 0.005]; respectively). From M3 to final follow up, the rate of graft function degradation was lower in the controls than the VUR+ group (ΔeGFR: -12 ± 17.4 vs -18 ± 19.1 ml/min/1.73 m^2) and greater in the Failure group than in the controls (mean ΔeGFR: -22.1 ± 19.8 vs.

14.3 ± 16.4 ml/min/1.73 m^2). Renal function evolution was similar in the Success and the control groups during follow up.
Conclusion: Complete correction of post-transplantation VUR may decrease its impact on graft function. A prospective study including more patients needs to be done.

O46 RECOMBINANT C1 INHIBITOR LIMITS ISCHEMIA REPERFUSION INJURY AND IMPROVES GRAFT OUTCOMES IN A PIG MODEL OF KIDNEY TRANSPLANTATION

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Background: Ischemia reperfusion injury (IRI) remains a critical issue in transplantation. C1 inhibitor (C1INH) regulates complement and contact system activation, two key mechanisms of immune response development after IRI.
Methods/Materials: We investigated the benefits of treatment with a recombinant human C1INH (rhC1INH) before reperfusion in a pig model of kidney autotransplantation. This preclinical model permits us to obtain clinically relevant data on both the acute response and chronic outcome during a 3 months follow up.
Results: Treated animals recovered kidney function quickly, as serum creatinine (Fig 1) measurements showed that while Vehicle animals could never recover proper kidney function, rhC1INH-treated animals recovered pretransplant levels by Day 11 ($p < 0.05$ AUC comparison).

With regards to chronic graft outcome (Fig 2), rhC1INH treatment prevented chronic loss of function and fibrosis development compared to vehicle ($p < 0.05$). Immunohistochemistry analyses also showed a reduction of epithelial to mesenchymal transition activation as well as a decreased number of invading macrophages within the graft.
Conclusion: In this preclinical model of kidney transplantation, inhibition of complement activation by rhC1INH at reperfusion offers a high degree of protection against IRI and preserves graft integrity, significantly improving outcomes. This therapeutic strategy can easily be translated to the clinic due to the timing of treatment.

O47 EFFECT OF ISCHEMIA-REPERFUSION ON RENAL CORTEX VASCULAR NETWORK IN A PORCINE RENAL AUTOTRANSPLANTATION MODEL

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Purpose: Vascular integrity is a cornerstone of organ viability, particularly in cases of transplantation. The aim of this study is to describe the modifications of renal cortex vascular network due to an ischemia-reperfusion sequence (IR) in a preclinical pig kidney autotransplantation model.
Materials and Methods: The surgical and experimental protocols were performed in accordance with the guidelines of the French Ministries of Agriculture and Research for the use and care of laboratory animals. Three months after autotransplantation (grafts, $n = 5$) or simple contralateral nephrectomy (sham surgery, $n = 5$), porcine kidneys were perfused with a radio-opaque silicone polymer and the cortex studied by X-ray micro-computed tomography. Vessel morphology, density and complexity of the network (number of bifurcations and arborescence factor) were analyzed from a three dimensional (3D) -image analysis method, isolating three areas of the cortex: outer, middle and inner.
Results: Renal ischemia-reperfusion led to a decrease of the cortical vascular segment volume associated with a rarefaction of small vessels inferior to 30 μm particularly in the inner cortex (0.79 ± 0.54% vs. 7.06 ± 1.44%, $p = 0.0079$). In the total cortex, an increase of connectivity characterized by an increase of bifurcations (296 ± 42.7 vs. 139 ± 26 $p < 0.05$) and a rise of arborescence (0.90 ± 0.04 vs. 1.07 ± 0.05, $p < 0.05$) were also observed.
Conclusion: Three months after renal autotransplantation, ischemia-reperfusion leads to a decrease in number of small vessels of the inner cortex. The increase of vascular network complexity has never been reported but could be associated with an adaptive regenerative processes. Our work gives a new light on the impact of IR on vascular repair.

O48 SIRT1 PROTECTS THE LIVER AGAINST ISCHEMIA REPERFUSION INJURY: IMPLICATIONS IN STEATOTIC LIVER ISCHEMIC PRECONDITIONING

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Introduction: Steatotic livers show higher vulnerability against ischemia-reperfusion injury than normal livers, due to the altered microcirculation and the enhanced oxidative stress. Ischemic Preconditioning (PC) is the only surgical strategy that has been applied in patients with steatotic livers undergoing warm ischemia. Silent Information Regulator 1 (Sirt1) is an histone deacetylase that regulate a diverse array of cellular functions, including cellular stress response and metabolism. This study has evaluated the possible implication of Sirt1 in fatty livers.
Methodology: Homozygous (Ob) Zucker rats aged 12 weeks were classified as follows: Group 1 = Sham; Group 2 = I/R:Ob rats were subjected to 60 min of partial (70%) ischemia followed by 24-h reperfusion; Group 3 = PC:Hepatic inflow to the median and left lobes was occluded by a clamp for 5 min followed by a reflow for 10 min and then livers were subjected to I/R; Group 4 = PC + sirtinol: as in group 3, but treated with sirtinol, a sirtuin 1 inhibitor (0.9 mg/kg intravenously) 5 min before PC. Blood and liver samples were collected after 24 h of reperfusion. Liver injury (AST) and oxidative stress (MDA) were evaluated. Sirt1 and its direct substract Ac-p53, AMPK, eNOS and HSP70 were determined by Western blot. In addition, analysis of apoptosis parameters (Ac-p53, Caspase 9, Cytochrome C) was performed.
Results: (1) Sirt1 protein levels are enhanced in hepatic PC, (2) Inhibition of Sirt1during PC increases liver injury and oxidative stress, (3) Sirt1 enhanced levels associated with augmented eNOS, AMPK levels, whereas inhibition of Sirt1 reversed the activation of protective mechanisms. (4) Inhibition of Sirt1 increases levels of apoptosis markers.
Conclusions: Sirt1 regulates the protective effects of hepatic PC by eNOS and AMPK pathways.

O49 RELEVANCE OF CARBONIC ANHYDRASE II IN RAT FATTY LIVER PRESERVATION

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Intoduction: Liver ischemia and reperfusion injury (IRI) causes up to 10% of early organ dysfunction after transplantation. The switch to anaerobic metabolism during liver graft storage provokes accumulation of lactic acid and leads to lower pH which activates proteases and induces cell death. Carbonic anhydrases (CA) are ubiquitous metalloenzymes that catalyze the reversible conversion of carbon dioxide to bicarbonate and proton. The CA reaction is involved in many physiological and pathological processes, including pH and CO_2 homeostasis. However, the role of CA in liver graft preservation has been poorly investigated.

The aim of this work is to evaluate the benefits of the addition of CAII to the IGL-1 cold storage solution for increasing fatty liver graft preservation and to establish the relationship with well known protective factors such as AMPK and AKT.
Methodology: Steatotic livers from obese Zucker rats (9 weeks aged) were preserved for 24 h (4°C) in IGL-1 solution with and without CAII (10 μg/ml). Livers were then "ex-vivo" perfused for 2 h at 37°C. Liver injury (transaminases) and function (bile production and vascular resistance) were measured. ACII, AMPK, Akt, GSK3β, Casp3, Casp9 and MAPKs (p38, ERK and JNK) were also determined by western blot.
Results: Fatty livers preserved in IGL-1 + CAII showed lower injury (transaminases) and better function (bile production) compared to IGL-1 alone. We found that CAII was down regulated during cold ischemia. The preservation of fatty livers in IGL-1 + CAII induced a significant phosphorylation of AMPK and Akt. Also, a significant decrease in MAPKs (ERK, p38 and JNK) after 2 h of reperfusion was observed. This was consistent with a major decrease of liver apoptosis parameters (Casp3, Casp9, and GSK3β).
Conclusion: CAII seems to be a promising additive to IGL-1 solution for protecting steatotic livers from IRI. This effect is associated with the inhibition of MAPKs and the activation of Akt and AMPK pathways.

O50 RESULTS IN LIVING DONOR FOR HEPATIC TRANSPLANTATION

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The main problem of living donor liver transplantation is ethical, it is associated with risks for the donor (healthy subjects who will undergo major surgery, without any other benefit than saving the life of a loved one).

In Algeria, the use of liver transplantation living related donor, it was deemed necessary because of the impossibility of other therapeutic options for patients with end-stage liver failure often and no transplant program to donor brain death.

The goal of this presentation is to report the results of hepatectomy in living in a donated organ donor.

Material and Method: From 2003 to 2013, 34 liver transplants in living related donors were performed in our department.

The series includes 34 donors, divided into 15 men and 19 women, with a median age of 26 years (18–58 years) and a BMI of 27 (16–26.5) kg/m^2.

The relationship between donor and recipient was a relation of the first degree in 30 cases and second degree in four cases.

The potential donors were selected after evaluation psychological, clinical, biological, serologic, noninvasive imagery (angio IRM, bili IRM, spiral TDM) and hepatic biopsy.

The surgical procedure was a right hepatectomy in 32 cases, a left hepatectomy in one case. One donor was not taken, the right hepatectomy was unfinished, vascular and biliary division was not realized due of death of the recipient intraoperative by hemorrhagic shock.

Results: In our series, the living donor mortality was 0%.

The operational continuations were simple in 52% of the cases.

Forty-eight percent of donors showed early postoperative complications according to Clavien classification, was a major morbidity in 27% of cases, and minor morbidity in 73% of cases.

The duration of hospitalization was on average 19 days (11 and 30 days).

No remote complication has was noted, after a retreat varying 4 months to 10 years, the donors are well and took again their daily activities.

Conclusion: The results obtained in our series encourage us to continue this activity until a transplant program in cadaveric donor.

However, it is necessary to keep in mind that the safety of the living donor is a priority. The hepatectomy should be realized by an experienced team in liver surgery to minimize the morbidity and mortality of the living donor.

O51 OUTCOME OF THE DONOR LIVING IN KIDNEY TRANSPLANT: EXPERIENCE OF THE DEPARTMENT OF NEPHROLOGY CASABLANCA

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Introduction: Renal transplantation from living kidney donors is the oldest technique of transplantation. Furthermore it gives better results in terms of survival of transplants without exposing the donor to avoidable risks. The purpose of this work is to establish a systematic follow-up of the donor to estimate the impact of the donation on their physical and mental health.

Material and methods: It is about a prospective study concerning all kidney living donors since the beginning of the renal transplantation in department of nephrology of Casablanca. All were contacted to make a clinical examination, a biological and radiological assessement (an urinary tree without preparation and an abdominal echography).

Results: On 107 contacted donors, only 24 appeared in consultation with an average backward drop of 3.2 years. The average of their age is of 49.75 $\pm$ 11.8 years, with feminine ascendancy (66%). The donation was made by the parents in 50% of the cases and by the spouse in 8% of the cases. Three of the donors were smokers. a morbid obesity (IMC $>$ 30 kg/m^2) was noted at 25% of the donors. Two donors became hypertensive. One case of hematuria and three cases of proteinuria were found in the urinary strip, but not confirmed in the ponderal dosage, one case of dyslipidémia was also observed. the radiological assessement did not reveal abnormalities except bladder calcifications in hyperuricémia cases. The emotional links between donors and recipients strengthened in every case

Conclusion: In the light of these results, it seems imperative to make sensitive our donors to a regular medical follow-up to minimize the risks of kidney donnation in the same way as their meticulous selection. Necessary condition to success the kidney transplantion.

O52 RESULTS OF 64 LIVER TRANSPLANTATIONS WITH ELDERLY DONORS IN BORDEAUX

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Introduction: Donors older than 61 years-old represented 29% in 2007, 43% in 2012 (Agence de la Biomédecine). We report the evolution of patients and grafts older than 70 and 80 years in Bordeaux.

Methods: We analyzed our database since 2005. Quantitative data were analyzed with Mann–Whitney test, qualitative data with Chi-square or Fischer's exact test. $p < 0.05$ was considered significant. Graft survival was analyzed with Kaplan-Meier analysis and log-rank test.

Results: From 2005/01/01 to 2013/08/31 64 patients benefited from a graft of more than 70 years-old. Results are expressed as median (quartile 25–75) or number.

1-month, 1-year and 5-years graft survival was comparable.

Conclusion: With other risk factors limited, elderly liver grafts have good results. Most frequent liver transplant indications were alcoholic cirrhosis with or without HCC; these older grafts are exceptionally attributed to patients with hepatitis C.

	Donors 70–79 years	Donors ≥ 80 years	
	N = 47	*N* = 17	
Donors and grafts			
Age (years)	74 (72–78)	81 (80–83)	<0.0001
BMI (kg.m^{-2})	24.2 (22.0–26.6)	24.9 (22.8–26.6)	NS
Haemorrhagic stroke/ischemic stroke/trauma/anoxia	40/1/5/1	14/0/2/1	NS
Steatosis none/ ≤30%/ >30%	21/18/0	9/8/2000	NS
Recipients			
Age (years)	57 (52–62)	56 (53–62)	NS
MELD score	16 (8–21)	14 (10–19)	NS
HCC/cirrhosis OH/emergency/miscellaneous/cirrhosis HCV	19/16/5/5/2	7/3/1/6/0	NS
Waiting on list (d)	73 (27–244)	121 (32–269)	NS
ICU length of stay (d)	14 (7–22)	7 (5–11)	0.023
Hospital length of stay (d)	25 (19–41)	21 (19–26)	NS
Surgery			
Total ischemia time (min)	510 (375–750)	460 (315–530)	NS
Warm ischemia time (min)	60 (40–82)	75 (59–120)	0.042
Postoperative			
ASAT peak (IU l^{-1})	816 (467–1215)	503 (417–1469)	NS
Bilirubin peak (μmol l^{-1})	126 (93–209)	126 (86–201)	NS
Time to factor V ≥ 50% (d)	2 (1–2)	2 (1–2)	NS
Time to bilirubin ≤20 μmol l^{-1} (d)	21 (12–58)	29 (18–58)	NS

O53 RESULTS OF TRANSPLANTATION WITH KIDNEYS FROM UNCONTROLLED NON-HEART-BEATING DONORS. A FRENCH EXPERIENCE IN PAYS DE LA LOIRE

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Kidney donation after circulatory determination of death (DCDD) is an activity limited by logistical concerns and questioning concerning the evolution of the transplants.

We have started DCDD program in May 2008. In May 2011, in situ cold preservation was changed for normothermic regional extracorporeal circulation (NRC). From May 2008 to July 2013 we have performed 50 kidney transplantations in DCDD program (G1) The results of these transplantations (G1) were compared with those observed for patients having received the transplants of standard (G2, $n = 74$) or extended criteria (ECD, G3, $n = 74$) dead donors.

For G1, primary non-function was more frequent (6% vs. 0% and 2.7% for G2 and G3) and the delay to obtain a sCreatinine below 250 mmol/l longer (21.5 ± 11 days, vs. 5 ± 5 et 10 ± 9 for G2 et G3, $p < 10^{-4}$). Renal function at one and 2 years is similar between G1 and G3 (178 ± 68 et 166 ± 67 vs. 158 ± 60 et 163 ± 68 mmol/l for respectively G1 and G3) but remained significantly worse than G2 (138 ± 48 et 140 ± 66 mmol/l, $p < 0.01$). In addition, acute rejection incidence, 1 year patient and graft survivals are similar between the three groups. Patients of G3 presented more bacterial infections than other groups. Systematic one year graft biopsies (G1, $n = 24$, G2, $n = 41$ and G3, $n = 37$) evidenced a more severe progression of arterial fibrous intimal thickening (cv) in G1 than in G2 or G3 but scoring for other histological lesions remained similar. CNR use is associated with a shortened of delay graft function time and an improvement of renal function at one year (145 ± 35 vs. 187 ± 77 mmol/l).

In conclusion, the results of the kidney transplantations from DCDD program get closer to those from ECD and it seems coherent to propose these transplants to the recipients having the strongest probability to receive ECD transplants. However, the best quality of transplants taken under CNR will allow to widen this indication.

O54 THE DGFS: A USEFUL SCORING SYSTEM FOR THE PREDICTION AND MANAGEMENT OF DELAYED GRAFT FUNCTION FOLLOWING KIDNEY TRANSPLANTATION FROM CADAVERIC DONORS

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Delayed graft function (DGF) is a common complication of kidney transplantation and is known to impact short- and long-term graft outcomes. We explored the possibility of developing a simple tool that could predict with good confidence the occurrence of a DGF and could be helpful in current clinical practice. We built a score, tentatively called DGFS,from a French multicentric and prospective cohort of 1844 adult recipients of deceased donor kidneys collected since 2007, and computerized in the DIVAT databank. Only five explicative variables; cold ischemia time, donor age, donor serum creatinine, recipient body mass index and induction therapy, contributed significantly to the DGF prediction. These were associated with a good predictive capacity (area under the ROC curve at 0.73). The DGFS calculation is facilitated by an application available on smartphones, tablets or computers at www.divat.fr/en/softwares. The DGFS should allow the simple classification of patients according to their DGF risk at the time of transplantation, and thus allow tailored specific management or therapeutic strategies.

O55 FUNGAL CONTAMINATION OF TRANSPLANT-ORGAN PRESERVATION FLUID: ANALYSIS OF 12 NEW CASES IN THREE TRANSPLANT-CENTERS

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Introduction: Fungal infection of transplant-organ preservation fluid, usually by Candida species, is a rare by serious event but with potentially dire consequences.
Methods: We reviewed all the organ preservation fluid contamination for all kidney and pancreas-kidney transplants at three French University Hospitals over a 5-year period between January 2008 and December 2012. The aim of this study was to evaluate the treatment which was use and the outcome.
Results: Fluid samples from 12 (11 renal and one renal and pancreatic) of the 1236 transplanted patients (0.97%), were positive for yeast, 11 with *Candida* sp. and one with both *Penicillium* sp. and Sporobolomyces Salmonicolor. There was one pediatric patient, a 2.5 year-old boy who had been on peritoneal dialysis for 14 months before transplantation, and eleven adults (eight males and three females) with a mean age of 53 ± 12 and whose mean time on dialysis prior to transplantation was 37 ± 33 months. All 12 patients received antifungal therapy, for an average of 11 ± 9 months (0.5–29 months), nevertheless in three of these cases serious complications were occurred: a ruptured artery in the pancreatic graft resulting in pancreatectomy; preemptive removal of the renal graft due to mycotic aneurysm within the artery; and one episode of acute rejection (eventually resolved) due to a miss adjustment of immunosuppressant dosage after cessation of the anti-fungal therapy. After an average of 22 ± 17 months of follow-up, all patients were alive and 10 grafts were functioning.
Conclusion: Also antifungal therapy and close monitoring are essential elements in the treatment of these patients, they failed to avoid serious graft-threatening complications, especially mycotic arteries aneurysms. We believe that it would be interesting to conduct a prospective study, under standardized treatment conditions, to help better identify the risk factors for the occurrence of such infections and the ideal duration of therapy.

O56 CAN WE OPTIMIZE THE ORGAN PROCUREMENT ORGANISATION IN FRANCE?

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Background: For historical reasons, the rule in France is that each transplant team performs its organ procurements, no matter the donor hospital location. This results in many travels by car or plane and entails a risk for the teams. In October 2006, two young surgeons were killed in an airplane crash. The aim of the study is to describe in details the current practices and to determine models of improvement.
Methods/Materials: The charts of all deceased donors in whom one organ at least has been procured in 2011 in France were included in the study. The following parameters were analyzed: distance between donor and recipient hospitals, teams performing the procurement and the transplant, transportation modalities, costs of transportation, salaries of procurement teams, costs of organ shipments. We recalculated the same parameters, applying two different organization models, the "organ-share model" (OSM), in which transplant teams of a same organ trust each other for procurement, the closest travelling to the donor hospital, and the "level-share model" (LSM), in which a single team (the closest one) procures all the organs of a given level (thoracic or abdominal).
Results: In 2011 in France, 3651 teams travelled 1 359 499 km across the country (3.5 times the distance earth-moon), generating 240 tons-equivalent CO2, using 2765 cars and 886 fixed-wing airplanes, on 1119 different routes. The costs were 19 821 000 €. The OSM would allow to reduce the distances by 29% and the costs by 21% but would not result in a reduction of the number of teams involved. The LSM would allow to reduce the number of teams by 38%, the distances by 69% and the costs by 52%.
Conclusion: The OSM is relatively easy to apply but would results in an unfair repartition of the procurement duties between small and large teams. The current training conditions of procurement surgeons do no allow applying the LSM model. However, the major savings generated by this model would allow to fund the three mandatory conditions to apply the model: specific training resulting in an accreditation for each organ for each surgeon, decent payment of the procurement teams (which is not the case currently) and permanent quality control of the organs (which does not exist).

O58 KIDNEY DONATION: THE OPINION OF MOROCCANS

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Introduction: In Morocco, each year, the list of patients waiting for kidney transplantation continues to grow while the offer remains below needs. Despite considerable efforts to promote kidney donation reticence persist. The objective of our work is to study the opinion of Moroccans and trying to understand what are the cultural and social obstacles to the development of the kidney transplantation in our country.
Materials and Methods: We conducted a survey on a representative sample of the adult population of Casablanca between July and September 2013. Our questions focused on the knowledge of citizens about end stage of kidney disease, their position relative to the kidney donation from a living person and after brain death and finally the explicit justification for refusal.
Results: In our survey of 500 people, 67% have heard of ESRD, 69% know kidney transplant in Morocco, 60% are convinced that it is an effective treatment, 70% agree to donate a kidney in lifetime and 52% agree to do it after death. The fear of renal failure after nephrectomy is the main reason for refusal of the donation for the living (88%), while the violation of the body integrity and the obstruction of religion are the principal reasons of refusal after brain death (57%) with a lack of argument in a quarter of those surveyed.
Conclusion: In Morocco, the limited number of kidney donors is mainly due to the lack of medical information as well as by religious considerations, hence the need for more awareness campaigns to persuade more people about the importance of this humanitarian gesture.

O59 KNOWLEDGE AND ATTITUDES OF MOROCCAN STUDENTS ABOUT ORGAN DONATION AND TRANSPLANTATION

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Introduction: Morocco stays far behind other countries in the domain of organ donation and transplantation. Improving the knowledge of Moroccan students, about organ donation, can be a key factor in the development of transplant activity. The aim of this study is to evaluate the knowledge, attitudes and beliefs of students concerning organ donation and transplantation.
Methods: The opinion poll was conducted in Marrakech city, with four high education structures (College of Medicine, College of Sciences, Applied Sciences School, a private school of business management), between June 2013 and September 2013 with a pre established questionnaire filled by the investigator himself. The 36 survey questions answered four main themes wich are: the evaluation of knowledge, the opinion and attitude of citizen, the explanation of refusal and the propositions to encourage organ donation in Morocco.
Results: One hundred percent of surveyed subjects answered the questionnaire. 89.4% of 503 surveyed students are aware of organ transplant in Morocco. 83.4% were informed of the existence of legislation governing organ donation and transplantation. Quarter of students believed that removal and transplant acts were realized just in public health establishment who have the authorization. Two persons of 3 were able to indentify transplantable organs and tissues. More than half of persons accepted to donate their organs after death. The religious reason was in the head list of refusal determinants of organ donation after death, with a prevalence of 39.7%.
Discussion and conclusion: Young Moroccans have limited knowledge relating organ donation. The development of this therapy needs to establish an adequate project of information and motivation of general population.

O60 PERCEPTION OF ORGANS REMOVAL FROM BRAIN-DEAD PATIENTS BY ANESTHESIOLOGISTS IN CHU IBN ROCHD CASABLANCA

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Introduction: The organ transplant is a very challenging medical subject. The objective of the study was to assess the level of knowledge as well as analyzing the attitudes of anesthesiologists' vis-à -vis organ donation or removal from brain-dead patients.
Materials and Methods: Our study population is represented by anesthesiologists practicing in both sectors (public and private). A survey was launched and covered three items as follow: the number of years in practice, the assessment of the level of knowledge and the analysis of health case staff attitudes towards the harvesting of organs from brain-dead patients.
Results: Of 65 surveys were collected, representing a response rate of 100%. The average age was 30 years old, ranging from 21 to 58 years. There is a male predominance (85%). The results show that 69% of anesthesiologists have not received the adequate training on brain death and harvesting of organs. On the other hand, 95% of anesthesiologists defined the brain death as an irreversible loss of all brain function; and the majority confirmed that there three existing clinical criteria to diagnose brain death; mainly the cranial trauma and stroke. Moreover, 74% of anesthesiologists are willing to donate their organs and 65% agree that their relatives do the same. The major reasons for refusal are religious (42%) and fear of mutilation of the human body (33%). 75% of anesthesiologists have already supported a brain-dead patient. Of 54% consider it ethically alive and potentially a source of life for others.
Discussion: Anesthesiologists are familiar with brain death and are, also, sensitive to the organ donation/ harvesting despite the lack of training. It is necessary to deepen and develop the knowledge of the health personal through an effective training and learning development plan on brain death, organ donation and organ harvesting in our country.

O61 PROCUREMENT OF CORNEAS: ROLE OF HOSPITAL COORDINATION

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Introduction: The transplant activity of corneas is essentially based on the importation. Despite a significant improvement in the activity of graft, it is still insufficient to meet the needs of patients suffering from corneal blindness, hence the importance of the establishment of the procurement activity of corneas in the hospital. An activity supported by the establishment of a hospital coordination whose primary role is to identify potential donors and organize the procurement of organs and tissues.

To guide the best efforts to be undertaken, by the hospital coordination team, for the improvement of corneal procurement, it became necessary to establish a research study for 22 months about the collection of non- opposition of families of potential donors.
Methodology: A survey of approaches to the families of potential donors is performed over a period of 22 months (from September 2011 to July 2013).The study realized the census of 223 potential donors in cardiac death and six potential donors in '' brain death '' state.
Results: Among the 223 reported cases of potential donors, 42% ($n = 94$) were not approached, in which 32% ($n = 72$) due to the presence of medical contraindications against the procurement and 10% ($n = 22$) not reachable or they arrive after 24 hours of death to their loved ones.

The approach of 129 families of potential donors has allowed us the collection of 12 consents of non opposition to procurement. This figure represents 9% of families approached with an opposition to procure of 91% ($n = 117$). The refusal of the families was mainly related to religion with a percentage of 64% ($n = 75$), While 17% of relatives would not take the responsibility to decide instead of "the deceased", 15% were hesitant and 4% refused without giving arguments.

Among the approached families only 6% have addressed the issue of the graft and the procurement of organs and tissues with the potential donor 's lifetime and only 1% of families approached knew the will of their loved one to organ donation and tissue after death. In our approach to families it was found that the majority of families have more ideas on the kidney transplant 98%, while only 2% have information corneal tissue is part of the procurement. .

The approach to families of potential donors in six brain-dead states allowed having the non opposition to procurement of kidneys and corneas of three donors. We noted two cases of refusal to the procurement, declared by the ascendants of the potential donor, despite the consent of the spouse which constitute the 33% of cases approached. Moreover, we had a case of the spouse to refusal of procurement. The concept of brain death was difficult to understand by the families approached as well those who signed the consent of non opposition than those who declared refusal to procurement.

It was found that the consent of non opposition from relatives of the donor, was always followed by a request for confidentiality of the act of procurement and good restitution of the body.

The ties of kinships between the potential donor and family members approached for consent of non opposition play an important role in decision making. We collected non- opposition to the procurement from spouses with rate of 69%, brothers-sisters 23% and cousins (s) / aunts 8%.

The socio-cultural level of families approached was not a limiting consent factor to families' non opposition to procurement. It was found that 68% of families who were not opposing to procurement are in rural areas and have a very low level of education.
Conclusion: The comprehensive census of approaches to potential donor's families will certainly allow us to develop the coordination activity in the hospital and significantly the corneas procurement.

O62 THE EPIDEMIOLOGICAL PROFILE OF BRAIN DEATH KIDNEY DONOR AT THE UNIVERSITY HOSPITAL OF CASABLANCA

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Introduction: Renal transplantation is the treatment of choice of the ESRD. It was only in 2010 that the first kidney transplantation from a brain death donor emerged, following the Moroccan law 16/1998, allowing better access to transplantation for patients on dialysis.
Methods: This is a descriptive retrospective study conducted on 3 years (September 2010-September 2013) including all potential donors brain death identified by the coordinating unit of the harvesting organs at the Casablanca University Hospital. The aim of our study is to describe the epidemiological characteristics of these donors.
Results: A serie of 54 cases was gathered during this 3 years. The mean donor age was 27.16 years (10–54ans), with a male predominance of 68%. The main cause of brain death was severe head trauma following a road accident in 51%, followed by hemorrhagic stroke in 20%. The average length of stay in reanimation was 3.16 days. 92% of patients needed noradrenalin with an average dose of 1.75 mg/h. The mean serum creatinine of all patients was 13.44 mg/l. Of the 54 potential donors, we have eight kidney harvesting (14%), the causes of not harvesting of the remaining cases (86%) were: five cases had contra-indication for donation (two cases of hepatitis B, two cases of HIV and one case of renal failure), 11 cardiac arrest; two cases without family and 28 cases of the opposition of the family (52%). The main reason given for this opposition was the violation on body integrity after death.
Conclusion: Although kidney transplantation from brain death donor is in its beginning stage in Morocco, it has given new hope to our ESRD patients to the shortage of living donors. Many efforts are still needed to raise awareness of our public to the importance of organ donation because the opposition is still the main obstacle to cadaveric donation.

O63 KIDNEY TRANSPLANTATION: HEMODIALYSIS AND ITS SURROUNDING ARE THEY INFORMED ENOUGH?

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Introduction: Kidney transplantation is the best treatment for chronic renal failure. However there is less donors compared to recipients whose number continues to increase. Ignorance of transplantation by hemodialysis patients and their families could be one of the cause. We aim to assess the knowledge and opinions of hemodialysis patient and his surrounding on renal transplantation.
Methodology: The survey conducted in August 2013 included 83 hemodialysis patients of our center and 70 members of their surroundings. They underwent a questionnaire that focused on the following themes: socio-economic status, willing to be transplanted or a donor, the kidney transplantation benefits, religion's point of view on transplantion. None of those interviewed had never been a transplanted or an organ donor.
Results: Out of the 83 hemodialysis patients we noted 49.4% of women with an average age of 41.4 $\pm$ 12 years, 66.7% had a low economic status. There was a lack of information among 62.7%. Only 41% reported to be transplant candidate with 12% noted on the transplant list. Transplantation was estimated to be more expensive by 50.6% of the patients and 71.1% think that it allowed a better life. For 20.5% of the patients, Islam is against the cadaveric donation and 10.9% for living donation. Out Of the 70 members of the surrounding questioned there were 56.8% of women with an average age of 44.4 $\pm$ 10.5 years. The low economic status represented 52.3%; 61.4% lacked information. 56.8% think that life is impossible with only one kidney, 13.6% were noted on the donation register. For 45.5% Islam is against the cadaveric donation and 27.3% for living donation.
Conclusion: It is important to increase awareness of hemodialysis patients and their families about kidney transplantation.

O64 PREVALENCE, INCIDENCE, AND RISK FACTORS FOR DONOR-SPECIFIC ANTI-HLA ANTIBODIES IN MAINTENANCE LIVER-TRANSPLANT PATIENTS

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Background: The pathogenic role of donor-specific antibodies (DSAs) remains unclear after liver transplantation (LT). Thus, we investigated the prevalence, incidence, and consequences of DSAs in maintenance liver-transplant patients.
Patients and Method: Two hundred sixty-seven patients who had been a liver-transplant recipient for at least for 6 months were screened at least twice for anti-HLA antibodies, using the Luminex single antigen technique.
Results: At 51 [6–220] months after a LT, 46/267 (17%) patients had anti-HLA DSAs [10 anti-class I, 33 anti-class II, 3 anti-class I and II]. Twenty-six patients (11.8%) had developed *de novo* DSAs [2 anti-class-I, 24 anti-class II] during the follow-up, i.e. 36.5 (2–65) months. Predictive factors for the emergence of *de novo* DSAs were a higher number of transplantations (OR 4.5; 95%CI 1.2–16.86, $p = 0.025$) and long-term use of steroids (OR 0.268; 95%CI 0.093–0.77, $p = 0.014$]. Four out these 26 patients (15.4%) developed an antibody mediated rejection. One of these patients had a very low immunosuppression regimen, and two others were non-compliant. After therapy, the outcome was good in three out of four patients.
Conclusion: Our data suggest that systematic monitoring was unnecessary in maintenance liver-transplant patients, but should be performed in cases of graft dysfunction.

O65 PRESENCE OF C3D FIXING HLA ANTIBODIES CARRY WORSE PROGNOSIS AND IS ASSOCIATED WITH INCREASED ALLOGRAFT VASCULOPATHY IN HEART TRANSPLANT (HT) PATIENTS

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HT patients survival is altered by chronic rejection including rapidly progressive cardiac allograft vasculopathy (CAV) and myocardial contractile dysfunction. Together with graft failure, death related to CAV is a leading cause of death or retransplantation in long survivors. Determinants of humoral rejection leading to CAV are still under investigation. Donor Specific Antibodies (DSA) have been associated with CAV. However not all DSA patients develop CAV. Identification of predictors of risk of CAV or graft failure is of major interest.

We tested whether *de novo* C3d fixing HLA DSA (C3dDSA) was associated with poor outcome or CAV. 271 files were screened and 242 patients included. Inclusion was based on presence of *de novo* Single Antigen HLA antibody within 365 days prior to coronarography and echocardiography (positive patients). Patients without HLA Ab at the time of or after angiography were negative patients. Coronarographies were blindly classified according to CAV ISHLT grading. Echo were analyzed for LV systolic or diastolic alteration. All patients with DSA-HLA antibodies were tested for C3d fixation (Lifecodes).

Of 27 patients (11%) had developed *de novo* HLA antibodies. Mean time between Ab detection and angiography was 47 days.Among 11 deceased positive patients (100%) were carrying DSA Ab and 6 (55%) were C3dDSA. Of 16 patients survived with HLAAb; 10 with DSA only 2 were C3dDSA (20%). Presence of DSA did not significantly affect LVEF (61.1% $\pm$ 18.5 vs. 59.9% $\pm$ 10.6). Kaplan-Meier showed reduced survival when HLA Ab were detected (log rang <0.02 vs. absence HLA Ab). While averaged CAV score increased in deceased patients versus alive (1.29 vs. 0.67; $p < 0.01$), it was also higher in patients with C3dDSA versus absence of HLA Ab (1.62 $\pm$ 0.46 vs. 0.84 $\pm$ 0.01; $p < 0.05$ LSD fisher). In conclusion we report that presence of HLAAb specifically when fixing C3d is associated with worse prognosis and more severe CAV in HT patients.

O66 EVOLUTION AND IMPACT OF PRE-EXISTING DONOR SPECIFIC ANTIBODIES IN A MONOCENTRIC COHORT OF ADULT KIDNEY TRANSPLANT RECIPIENTS

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Introduction: DSA (donor-specific antigen) are known to increase the risk of allograft rejection and graft failure. These antibodies could be pre-existing DSA or *de novo* DSA. Recent techniques like Luminex are more sensitive leading to a retrospective detection of pre-existing DSA in the sera of the day of transplantation (D0).
Patients and Methods: we analyzed retrospectively by Luminex analysis the D0 sera of all patients who received a kidney transplant in Strasbourg Universitary Hospital between 2005 and 2007, in a context of lymphocytotoxic negatif crossmatch. Our aim was to determine the evolution and the impact of pre-existing DSA on graft without specific preventive humoral treatment.
Results: Among 239 studied patients, 37 (15.5%) had pre-existing DSA detected only by Luminex assays in D0 serum: 22 (59.5%) had class I DSA (A, B, C), 8 (21.6%) class II DSA (DR, DQ, DP) and 7 (18.9%) class I and II DSA. Five year after transplantation, pre-existing DSA disappeared in 22 patients (principally during the first year), and persisted in 15 patients. In patients without pre-existing DSA ($n = 202$), 32 developed *de novo* DSA, 50 developed

non DSA anti-HLA antibodies and 120 stayed non- sensitized at 5 years. The presence of pre-existing DSA, only when they persist, increased significantly the risk of rejection and graft failure (58 vs. 85%, p = 0.0029). Patients with pre-existing DSA which disappeared during follow-up had a graft survival (78 vs. 85%, NS) and a risk of rejection comparable to non-sensitized patients. Persistent pre-existing DSA were more often class II DSA (11/15) and had a MFI superior to 3000 at D0 (12/15).
Conclusion: Pre-eexisting DSA are deleterious only when they persist during follow-up. Class I pre-existing DSA or with a MIF <3000 tend to disappear after transplantation and are not prejudiciable for graft survival.

O67 ANTI HLA-CW AND ANTI HLA-DP DSA ARE PATHOGENIC IN KIDNEY TRANSPLANTATION

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Introduction: It is widely accepted that HLA donor-specific antibodies (DSA) have a deleterious impact in kidney transplantation. However, preformed anti-Cw and anti-DP DSA are not considered in organ allocation policies and their clinical relevance is uncertain. We here asked whether they could impact graft outcome.
Methods: We conducted a retrospective study, comparing 41 patients transplanted with exclusive anti-Cw and/or anti-DP DSA, to 82 sensitized patients with no DSA, matched 2/1 for sex, year and rank of transplantation, recipient and donor age, and 52 "classical" certain DSA patients. DSA were characterized by single antigen flow beads assay and each donor was exhaustively HLA phenotyped for HLA A, B, Cw, DR, DQ, DP when anti Cw/DP sensitization was evidenced. Primary endpoint was the occurrence of rejection. Crossmatchs (XM) results, graft function, survival, infectious and tumoral complications were also registered.
Results: Acute rejection (AR), acute antibody mediated rejection (AAMR) and ptc+g lesions occurred more frequently in the anti-Cw/DP than in the no DSA group (AR 39% vs. 12%, AAMR 27% vs. 5%, ptc+g > 0 44% vs. 6%; p < 0.0001 for each). Anti Cw/DP profile appeared to be closer to the certain DSA group (AR 39% vs. 35%, AAMR 27% vs. 28%, ptc+g > 0 44% vs. 35%, p non significant). Positive flow cytometry XM were more frequent in the anti-Cw/DP than in the no DSA group (21/41–51% vs. 15/82–18%, p = 0.001) but not different from the certain DSA group (28/51–55%). Nevertheless, graft function, complications, graft and patient survival did not differ between the 3 groups during all the follow up (48 ± 27 months).
Conclusion: Taken together, our results suggest that preformed anti-Cw and anti-DP DSA can be pathogenic, with the same deleterious effects that classical DSA. It might justify the systematic identification of HLA-Cw and DP antigens, as the detection of anti-Cw and anti-DP antibodies, and their inclusion in the kidney allocation systems.

O68 *DE NOVO* DONOR SPECIFIC HLA ANTIBODIES IN NON-SENSITIZED KIDNEY TRANSPLANT RECIPIENTS AFTER T-CELL MEDIATED REJECTION: A LONGITUDINAL COHORT ANALYSIS

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Introduction: Local inflammation has recently emerged as a potential cause of humoral alloimmune response in renal transplantation and *de novo* donor specific anti-human leucocyte antigens antibodies (dnDSA) have been associated with history of acute rejection. We aimed at investigating frequencies and consequences of dnDSA occurrence following a fisrt episode of acute T cell mediated rejection (index TCMR) in a cohort of previously unsensitized kidney transplant recipients.
Methods: Among 1054 patients who underwent kidney transplantation between September 2004 and December 2010 in our center, we identified 75 unsensitized patients who experienced at least one episode of TCMR and we used highly sensitive Luminex technique to detect the presence of dnDSA in the year following the first rejection episode.
Results: Index TCMR occured a mean time of 4.4 ± 6.8 months post-transplantation. *De novo* DSA were detected in 16 (21%) patients one year thereafter, most of them being class II dnDSA (94%). Patients who subsequently developed dnDSA were undistinguishable by clinical, biological or histological variables at the time of transplantation or index TCMR, even if interstitial inflammation score (p = 0.09) and tubulitis score (p = 0.08) tended to be higher. These patients experienced significantly more susbequent antibodies mediated rejection (ABMR) episodes (0.3 ± 0.5 vs. 0.0 ± 0.1, p < 0.001) but this did not translate into a reduced death censored graft survival (p = 0.439). Follow-up biopsies after the index TCMR showed increased antibody-mediated changes in patients who subsequently developed dnDSA with significantly higher scores of glomerulitis and numerically higher scores of peritubular capilaritis and C4d staining.
Concluion: TCMR occurrence in previously unsensitized patients triggers the development of dnDSAs that increase the cumulative incidence of ABMR without affecting short-term graft survival.

O69 C1Q FIXING ABILITY OF *DE NOVO* DONOR SPECIFIC ANTIBODIES PREDICTS EARLY BUT NOT LONG-TERM KIDNEY ALLOGRAFT LOSS

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Background: *De novo* donor-specific antibodies (dnDSA) are not always associated with graft loss. C1q fixation assays could help identifying clinically relevant dnDSA. However, long-term datas of C1q fixing dnDSA (C1q+ dnDSA) are lacking. The aims of our study were then to describe incidence, risk factors and long-term impact of C1q+ dnDSA.
Methods: 346 non-sensitized kidney transplant recipients were screened at two and five years post-transplantation for dnDSA using Luminex Single Antigen Beads. Sera containing DSA underwent further testing using a C1q-Luminex assay.
Results: Twelve (3.5%) and 8 (2.5%) patients had C1q+ dnDSA at 2 and 5 years post-transplantation, respectively. All C1q+ dnDSA were class II DSA and found when class II DSA MFI were higher than 6237 and 10000 at 2 and 5 year, respectively. Number of HLA mismatches and cyclosporine at transplantation were independently associated with an increased risk of for C1q+ dnDSA occurrence (OR = 1.78, p = 0.007, and OR = 7.65, p = 0.01, respectively). Patients with class II C1q+ dnDSA detected at 2 and 5 years had a poorer 10-years death-censored graft survival than patients without DSA (p = 0.0001 and p = 0.02, respectively). There was no difference in graft survival between class II C1q+ dnDSA and class II C1q– dnDSA patients. However, graft losses occurred much more earlier in patients with C1q+ dnDSA detected at 2 years.
Conclusion: C1q+ dnDSA are observed in patients with high class II DSA MFI. They are not better than dnDSA to predict long-term graft survival. However, graft losses occurred much more earlier in patients with C1q+ dnDSA.

O70 AUTOANTIBODY MONITORING IN THE FOLLOW-UP OF PANCREAS TRANSPLANT RECIPIENTS

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Introduction: Whether autoimmune recurrence plays an important role in pancreas graft failure remains a matter of debate, mainly because of the lack of reliable diagnostic tools. Although devoid of a pathogenic role, circulating autoantibodies could be a useful marker. The aim of this study is to analyze the value of circulating autoantibodies to predict pancreas graft outcome.
Methods: Recipients of technically successful first pancreas transplantations performed in Lyon between January 2000 and December 2004 were enrolled. The immunosupressive regimen consisted in anti-thymocyte globulin, mycophenolate mofetil, tacrolimus, and prednisolone. Autoantibodies to glutamic acid decarboxylase, insulinoma associated protein 2 and zinc transporter eight antigen were measured before, at 1 year and then every 2 years after transplantation and at the time of graft dysfunction. Graft survivals were compared using a Log-rank test.
Results: Seventy-six patients (73 SPK and 3 PAK recipients) were included, with a median follow-up duration of 7.5 years (range: 0.4–11.8). Thirty-eight (50%) patients had one or more autoantibodies before transplantation with no difference in pancreas graft survival, versus patients without autoantibodies (5-year survival 83.6% vs. 83.9% respectively, p = 0.90). Autoantibodies appeared or significantly increased in 10 (13%) patients with a median onset of 3 years (range: 0.5–7). Graft survival was significantly lower in these patients with 5-year survival at 67.5% vs. 86.1% in the other 66 patients (p = 0.01). The median period between the appearance or increase of autoantibodies and graft loss was 1.4 years (range 0–2.4).
Conclusion: While the presence of autoantibodies before pancreas transplantation has no impact on graft survival, their appearance or increased titer

after transplantation is associated with lower graft survival. Autoantibody monitoring seems to be useful in the follow-up of pancreas transplant recipients.

O71 INCIDENCE AND COMPLICATIONS OF *DE NOVO* DSAS AFTER ABO COMPATIBLE LIVER TRANSPLANTATION

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Background: The incidence and consequences of occurrence of *de novo* DSAs after LT is not well known. So, we investigate the incidence, kinetic of occurrence, and complications associated with *de novo* DSAs.
Patients and Method: Between February 2008 and February 2012, all liver transplant recipients were tested for anti-HLA antibodies, with the Luminex SA™ assay, at Day 0, M1, M3, M6, M9, 1 year and every year until the last follow-up.
Results: A total of 119 patients were included in this study. At last follow-up, realized at 25(1–51) months post-transplantation, 15 patients (12.6%) without preformed anti-HLA DSAs had developed DSAs.

Of 10/15 patients (67%) with *de novo* DSAs have presented at least one episode of rejection, vs. only 20/ 104 patients (19%) without *de novo* DSAs ($p = 0.0003$). 4/15 patients (27%) with *de novo* DSAs have developed an early acute rejection, and 10/104 patients without DSAs (10%), (p = ns). 7/15 patients (47%) with DSAs have presented at least one episode of late acute rejection, and 7/104 (7%) DSAs-free patients ($p = 0.0002$). Patients with *de novo* DSAs have presented more episodes of steroid resistant rejections than patients without DSAs (8/10 vs. 7/19, $p = 0.05$).

Patients with *de novo* DSAs and steroid resistant rejection episode received an appropriated treatment based on B-cell targeting agents.

14/15 patients have developed DSAs before graft rejection.

No difference was observed between the two groups concerning survival after LT.
Conclusion: Occurrence of DSAs after LT is a frequent complication and is associated with an increased risk of rejection. Detection of anti-HLA DSAs allows an appropriated treatment, based on B-cell targeting agents, wich is effective in this situation.

O72 IMPACT OF RENAL GRAFT NEPHRECTOMY ON SECOND KIDNEY TRANSPLANTATION SURVIVAL

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Objectives: To determine the impact of renal graft nephrectomy on second kidney transplantation survival.
Methods: We performed a retrospective single-center study from January 2000 to December 2011. Retransplanted patients who underwent previous allograft nephrectomy more than 3 months post-transplantation (Group 1) were compared with those who did not (Group 2) in terms of graft survival, incidences of acute rejection and delayed graft function. Multivariate Cox proportional hazard models were used to assess risk factors of graft loss after retransplantation.
Results: Among the 146 patients included, 52 (35.6%) underwent graft nephrectomy (Group 1) and 94 (64.4%) did not (Group 2). Group 1 had a significantly shorter first graft survival (0.8 vs. 8.6 years, $p < 0.001$) and more anti-class I antibodies (90.5% vs. 74.2%, $p = 0.03$). Ten patients (19%) in group 1 and 16 patients (17%) in group 2 had at least one acute rejection episode ($p = 0.74$). Delayed graft function was observed in 13 patients (25%) in Group 1 and 17 patients (18%) in Group 2 ($p = 0.32$).

Graft survival at 1, 5 and 10 years was respectively 94%, 81% and 58% in Group 1 and 99%, 93% and 66% in Group 2 ($p = 0.10$). Graft survival was decreased by increased donor age and serum creatinine and tended to be associated with post-transplantation presence of anti-class I and II antibodies. Graft nephrectomy was not associated with graft survival in multivariate analysis.
Conclusions: Graft nephrectomy, probably a marker of high immunological risk patients, is not a risk factor of increased retransplant failure.

O73 THE OUTCOME OF PATIENTS RETURNED TO DIALYSIS AFTER KIDNEY TRANSPLANT FAILURE

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Introduction: The return to dialysis after renal transplant (Tx) is often seen as a painful failure by both the patient and the nephrologist. This explains the often late management of these patients on chronic dialysis when many comorbidities are present.
Methods: We conducted a retrospective, single-center, showing the clinical and laboratory data of renal transplant patients at the University Hospital and returned to dialysis (M0) between January-1-2000 and August-31-2010. The data analyzed concerns the year before the return to dialysis (M -12 and M-3) and the 12 following months (M3, M12). The objective of the study was to evaluate the presence of complications at M0 and the outcome at 12 months.
Results: Seventy renal transplant patients were included, 45 men. At M0 the mean age was 44.6 ± 12.2 years, duration of Tx was 75.6 ± 53.9 months and the age at Tx was 38.2 ± 12.5 years. At M0 the estimated GFR was 8.5 ± 4.4 ml/min and graft loss was in 74% of cases secondary to chronic allograft nephropathy. The majority of patients were receiving hemodialysis (98.6%) on FAV (89%). Metabolic complications of CKD settled significantly during the 3 months prior to M0. We have seen between M-12 and M0 a fall in hemoglobin (Hb) from 11.6 ± 1.4 to 9.9 ± 1.9 g/dl (50% of the cohort had a Hb < 10 g/dl), a decrease in serum calcium from 2.32 ± 0.21 to 2.06 ± 0.26 mmol/l and an increase in serum phosphate from 1.28 ± 0.08 to 1.95 ± 0, 57 mmol/l. Seventy-nine percent of patients had vitamin D deficiency and serum albumin decreased from 38.2 ± 2.2 to 34.2 ± 6.5 g/dl. Nearly 30% of patients had an infectious and/or cardiovascular complication within 12 months following the return to dialysis and six patients died during this period, mainly from infectious causes. Due to a toxic syndrome graft, 27.1% of patients were detransplanted.
Conclusion: The management of patients with graft failure before returning to dialysis needs to be optimized. Dialysis allows correction of a majority of metabolic disorders and should not be delayed. Mortality of infectious origin is certainly favored by the immunosuppressive therapy and the poor nutritional status of these patients.

O74 RETROSPECTIVE STUDY COMPARING URETEROVESICAL AND PYELOURETERAL ANASTOMOSIS PERFORMED DURING KIDNEY TRANSPLANTATION COMING FROM EXTENDED CRITERIA DONORS

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The aim of this study was to evaluate the rate of complications according to the type of urinary anastomosis after kidney transplantation from expanded criteria donors (ECD) according to UNOS criteria.
Materials and Methods: From January 2008 to December 2012, 343 cases of patients transplanted with ECD kidneys were reviewed. 176 transplantations were performed in Lyon and had a ureterovesical anastomosis (group 1) and 167 patients were transplanted in Necker hospital in Paris and had a pyeloureteral anastomosis (group 2). Urological complications were evaluated: fistulas and strictures
Results: Demographic data and history of donors and recipients are similar in the two groups. The overall complication rates were respectively 16.5% (group 1) and 16.5% (group 2). There are more fistulas in group 2 (7.8% vs. 3.4%). In the two groups, 50% of fistulas are operated. Moreover, in group 2 seven of the 13 fistulas are characterized by extensive necrosis of the ureter. The number of stenosis is comparable (5.7% vs. 6.6%, Group 1 vs. Group 2 respectively) with more rate of surgical corrections in group 1. The rate of endoscopic or radiological approach was 40% in group 1 and 90% in group 2.
Conclusion: The rate of urinary complication is superimposed in both groups. However, there is more urinary fistula after pyeloureterale anastomosis than after uretero vesical anastomosis. There is a close correlation between the risk of fistula and stenosis and the presence of anuria. The surgical strategy will depend on the anatomy of the recipient and the fact that the recipient has a conserved diuresis.

O75 PRETAGREF STUDY. PREVALENCE OF TOBACCO USE AND FACTORS ASSOCIATED WITH SMOKING CESSATION IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Tobacco use increases the risk of mortality, cancers and cardiovascular diseases in transplanted patients. Transplanted patients are encouraged to quit tobacco use before and after renal transplantation. This study was carried out to evaluate the prevalence of tobacco consumption in transplanted patients in one French region. This survey was also conducted to identify factors associated with the failure of smoking cessation.
Materials and Method: A questionnaire was sent by mail to transplanted patients followed in our center between the 01/01/95 and the 31/12/10. A second mail was sent to increase the response rate.

Results: During the study period, 544 questionnaires were sent to kidney transplant recipients. Among these 544, they were 362 responders. Of these 362 patients, 121 patients (33.4%) were past smokers, and 21 (5.8%) were active smokers. Among the smokers, 20% were exposed to second hand smoke. Of 48% had criteria for tobacco moderate to high dependency, 13.4% were addicted to alcohol. In the multivariate analysis, exposure to second hand smoke and living alone at home were associated with the failure of smoking cessation.
Conclusion: This study confirms that the prevalence of tobacco use is high in transplanted patients. Environmental factor are associated with the failure of tobacco cessation. Therefore, in transplantation centers, program devoted to tobacco cessation should be implemented.

O76 VITAMIN D DEFICIENCY AS A NOVEL RISK FACTOR OF NODAT

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Introduction: Vitamin D affects insulin secretion as well as insulin sensitivity and is involved in the differentiation and the proliferation of the keratinocyte. New Onset Diabetes After Transplantation (NODAT) and Non Melanoma Skin Cancer (NMSC) are two frequent complications that follow kidney transplantation. We studied the association between the vitamin D level at time of the transplantation and the occurence of complications on a large population of kidney recipients.
Patients and Method: Of 444 subjects who underwent a first transplantation in Nantes University Hospital between 2000 and 2011 were included in the study and prospectively followed. We analysed the association between vitamin D concentration at transplantation (<10 ng/ml, [10–30 ng/ml], >30 ng/ml) and the time of occurence of three events: NODAT treated within the first year, NMSC, and graft failure (death or return to dialysis) using Cox models.
Results: Cumulative incidence of NODAT was estimated to 13% at one year post transplantation. The multivariate analysis indicated that a patient with a vitamin D concentration <10 ng/ml had more than two times risk of NODAT in the first year post-transplantation than a patient with a aconcentration >30 ng/ml (HR = 2.62; p = 0.032). Other risk factors identified were tacrolimus, older age, corticosteroids and BMI. Cumulative incidence of NMSC was 6% at 5 years. Independently from traditional risk factors, patients with vitamin D level <10 ng/ml tended to develop less NMSC than patients with concentration >30 ng/ml (HR = 0.41; p = 0.18). In our study, vitamin D status was not significantly associated with the time of occurence of caner, patient survival or graft failure.
Conclusion: Vitamin D deficiency is a new independent risk factor of NODAT in the first year following a first kidney transplantation. Attention should be given to patients with chronic kidney disease and a correct vitamin D status, which means high rate of sunlight exposition and risk of NMSC.

O77 ROTATIONAL THROMBOELASTOMETRY FOR MANAGEMENT OF BLEEDING AND TRANSFUSION DURING LIVER TRANSPLANTATION: NOT BETTER THAN A TRAINED TEAM?

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Introduction: Liver transplantation could be a haemorrhagic surgery. Management of bleeding and transfusion could be helped by the use of thromboelastometry (ROTEM™). We have tested the utilization of a transfusion algorithm based on ROTEM™ results, at the CHU of Bordeaux.
Methods: After ethics local committee approval and consent, 60 consecutive liver transplant patients were included: 30 in the « before » group with our usual management of bleeding and transfusion avec, 30 in the « after» group, with a transfusion algorithm based on ROTEM™ results. Quantitative data were analyzed with Mann-Whitney test, qualitative data with Chi-square test or Fisher's exact test (XLSTAT 2013 software). $p < 0.05$ was considered significant.
Results: Of 60 patients were included between 2012/06/01 and 2013/06/18. The two groups were comparable as regard to donors, recipients, per operative surgical data and preoperative biological values. Results are expressed as median (quartile 25–75) or number.
Conclusion: Whereas ROTEM™ allows coagulation study in the operating theatre and its use leads to a tendency to increase fibrinogen use, this has no impact on bleeding or blood products transfusion. Other studies are warranted to confirm these results and to refine ROTEM™ utilization.

	"Before" group	"After" group	
	N = 30	*N* = 30	p
Per operative bleeding (ml)	3000 (1700–4000)	3000 (2125–4875)	0.39
Per operative autologous transfusion (ml)	545 (288–751)	490 (251–1122)	0.65
Per operative Albumin 4%	6 (5–8)	7 (5–10)	0.25
Transfusion until H24			
RBC units	3 (2–7)	5 (2–6)	0.57
FFP	0 (0–4)	0 (0–0)	0.29
Platelets units	0 (0–1)	0 (0–1)	0.6
Fibrinogen (g)	0 (0–3)	3 (0–6)	0.05
Tranexamic acid (g)	0.0 (0.0–1.4)	0.0 (0.0–0.8)	0.56
Patients exposed to blood products	25	24	0.74
Patients receiving fibrinogen	11	18	0.07
Patients receiving tranexamic acid	10	8	0.78

O78 INFLUENCE OF RECIPIENT CYTOCHROME *P450 3A5* POLYMORPHISM ON THE METABOLISM OF ADVAGRAF ADMINISTERED *DE NOVO* AFTER RENAL TRANSPLANTATION

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Advagraf (Adv), a prolonged release formulation of tacrolimus (tac) permits a once a day administration and improves medication adherence.

Patients (pts) possessing at least one *CYP3A5*1* allele have an increased tac metabolism.

This prospective study evaluates the clinical interest of a new simplified starting dose protocol of Adv after renal transplantation (RT) according to the recipient *CYP3A5* polymorphism.
Material and Method: *CYP3A5* genotype (*CYP3A5*1/*1*, *CYP3A5*1/*3*, *CYP3A5*3/*3*) was determined at the time of HLA typing. All pts received 0.1 mg/kg of Adv prior to RT. On day 1, the Adv dose was adapted according to *CYP3A5* genotype: 0.35 and 0.30 mg/kg/day in *CYP3A5*1/*1* and *CYP3A5*1/*3* respectively. CYP3A5 non expressors (*CYP3A5*3/*3*) were stratified to receive either 0.20 (control group) or 0.25 mg/kg/day. The daily dose (dd) remained unchanged during the first 3 days.The first tac trough level (TL) was determined at day 3 and the first dose adaptation performed on day 4. Associated therapy included MMF and CS. Pts needing plasma exchange because of prior sensitization were excluded.
Results: From January 2011 to July 2012, 84 consecutive pts (mean age:48 ± 21 years, 53M/31F) were included. Median Follow up (FU) was12 mo (3–21).

In the12 pts expressing CYP3A5 (two**1/*1*, ten**1/*3*), the dd remained significantly higher than in *CYP3A5*3/*3* pts all along the FU to achieve a similar tac TL.

Among pts CYP3A5 non expressors (*n*:72), 34 and 38 received a starting Adv dose of 0.2 and 0.25 mg/k/day respectively. After dose adaptation intended to reach a similar tac TL in both groups, we observed a significantly higher infratherapeutic tac TL rate in control group ($p < 0.02$).
Conclusion: The use of Adv "*de novo*" after RT is effective when *CYP3A5* polymorphism is taken into account. CYP3A5 expressors need a higher dd. In *CYP3A5*3/*3* pts a higher starting dose than the recommended one seems also preferable to avoid infratherapeutic TL that increases the risk of acute rejection.

O79 IMPAIRED RESPONSE TO CLOPIDOGREL IN PATIENT WITH KIDNEY TRANSPLANTATION

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Patients with decreased glomerular filtration rate (GFR) present higher cardiovascular morbidity and mortality following percutaneous coronary intervention, likely related to endothelial dysfunction, inflammation, coronary calcification, platelet activation and under-use of evidence-based therapies. Combined pharmacological inhibition of the $P2Y_{12}$ receptor by thienopyridines and of the cyclooxygenase pathway by aspirin is currently considered the reference anti-platelet strategy to prevent thrombotic complication of PCI with stent. Residual platelet reactivity is associated with adverse cardiovascular outcome especially in patients with decreased glomerular filtration rate. The cardio-vascular prognosis is improved after kidney transplantation, but immunosuppressive treatments are responsible for enhanced platelet activation, endothelial and smooth muscle cells dysfunction (arteriolopathy) leading to decrease in clopidogrel efficiency.

36 patients with kidney transplantation taking clopidogrel treatment 75 mg/day were enrolled. The platelet VASP phosphorylation state was assessed in all patients using a standardized flow cytometric assay with a cutoff value of 61%. Residual platelet reactivity occurs when >61%. Controls were 126 patients with chronic renal failure.

Patients with kidney transplantation are younger (58.3 vs. 72.6 years, p = 0.57), with less diabetes, (38% vs. 57%, p = 0.001), a lower BMI (25.2 sv 27.2 p = 0.78), 89% patients are on anti-calcineurin and 50% on steroids at low dose. VASP result is significantly higher in the transplantation group versus controls (60.0% vs. 51.2% p = 0.013). Transplantation is a risk factor of residual platelet reactivity: OR 2.9 [1.35–6.43], p = 0.006. This difference remains after adjustment for GFR with the MDRD formula (p = 0.04).

After kidney transplantation patients present platelet hyperreactivity. Mechanisms need further investigation: are immunosuppressive treatments providing endothelial and platelet activation?

O80 RESULTS OF ROBOTIC PROSTATECTOMY AFTER KIDNEY TRANSPLANTATION

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Objective: To evaluate the oncologic and functional results of robotic prostatectomy in patients already having a kidney transplant.
Patients and Methods: We analyzed retrospectively preoperative settings, per operative, functional and oncologic results of 12 patients operated on between 2009 and 2013. Prostatectomy was performed via a transperitoneal approach without any changing in the ports position. The average age was 61.91 ± 2.98 years. The period between transplant and the diagnosis of adenocarcinoma was 79.7 months. The mean PSA was 7.34 ng/ml (4.9–11).
Results: The operative time was 241.3 ± 35.6 min with only one conversion and one transfusion. The intervention has been difficult due to adhesions on the side of the graft in 50% of cases. There was a case of obstructive acute renal failure resulting from a hematoma of the Retzius treated by percutaneous nephrostomy at D20. There was a majority of pT2c (72.7%) including 3 positive margins (27.3%) and 2 biochemical relapse treated by radiotherapy for one patient and hormonotherapy for the second one. The end-point PSA was undetectable. There was no significant difference between pre-operative and J7 creatinine (p = 0. 22).
Conclusions: Robotic Prostatectomy in renal transplant recipients is a safe technique without any specific serious effect on the allograft.

O81 PREGNANCY AND KIDNEY TRANSPLANT

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Introduction: The purpose of this work is to report our experience concerning the occurrence of a pregnancy in renal transplanted patients (RT), its progress, its effect on the renal graft at medium and long-term, as well as the maternal fetal complications.
Patients and Methods: We collected 20 pregnancies for 11 RT patients, followed during their pregnancies and three years after. We studied the various clinical and biological characteristics before and during the pregnancy as well as the impact of this one on the medium and long-term renal transplant, we also analyzed the obstetrical data and the new born health at birth.
Results: The mean age was 30.25 ± 5.23 years, the average deadline between the renal transplantation and the pregnancy was 47.7 ± 29.22 [7–102] months. The pregnancy was authorized in 30%. At the time of the diagnosis of the pregnancy, all the patients were under corticosteroids and cyclosporin, 16.7% under mycophenolate mofetil and 72.2% under azathioprine. The high blood pressure was present before the pregnancy in 35%. During the pregnancy, the proteinuria appeared in three cases, the urinary tract infection in 29%, and none preeclampsia nor diabetes. The anemia is present in all the patients during the pregnancy. Cyclosporine T0 in the 1st quarter was 182.81 ± 42.56 mg/l, and in the 3rd quarter 245.31 ± 48.48 mg/l. The mean term of delivery was after 37.5 ± 2 week of amenorrhea. A premature delivery is observed in 23.5% of the cases, a fetal death in utero in 2 cases, and an abortion in three cases. The number of living children is 15, with a mean birth weight of 3.18 ± 0.3 kg, the weight was lower than 2500 g in 5% of the cases. In the long-term follow-up, we noticed two cases of acute rejection related to the bad patients' compliance, and three cases of chronic allograft nephropathy, without a switch to dialysis.
Conclusion: The pregnancy in RT is at high risk one, requiring a multidisciplinary care because of the increased risks of maternal and fetal complications. Each pregnancy needs to be planned, all the parameters have to be studied and evaluated before a positive answer to a pregnancy request, which will allow to optimize its outcome and to minimize the complications.

O82 NEGATIVE ASSOCIATION OF BLOOD ANTICARDIOLIPIDS ANTIBODIES DETECTION BEFORE RENAL TRANSPLANT AND KIDNEY ALLOGRAFT FUNCTION: A COHORT STUDY

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The aim of this study was to test association between blood anticardiolipin antibodies (ACA) detection and thromboembolic risk, graft and patient survivals in renal transplant recipients.

All renal transplant recipients grafted between 01/2008 and 10/2012 without APS or systemic lupus were included in this retrospective cohort study. ACA were screened before renal transplant (positivity threshold >10). Donor and recipient characteristics were collected. Occurrence of three events was analyzed: venous thromboembolism, graft and patient survival.

Among 268 included (mean age 52 years ± 14; donor mean age 55 years ± 16 (88% deceased donors)), 112 (42%) patients have an ACA. After a median follow-up of 24.5 months, 69 (26%) venous thromboembolism (29 graft venous thromboses and 36 deep venous thromboses), 27 (10%) graft losses and 13 (5%) deaths were reported. Patients with events did not have more frequently ACA than the others. However, estimated GFR was significantly lower in ACA + group (46 (±19) ml/min/1.73 m^2 vs. (54 (±20) ml/min/1.73 m^2 in ACL- group; p = 0.005). Independent factors associated with graft loss were extended cold ischemia time (OR adjusted (a) = 1.00; CI 95% 0.99–1.00; p = 0.04), donor eGFR (0.95; 0.91–0.99; p = 0.02), and previous renal transplant (21.0; 2.54–173.0; p = 0.01); those independently associated with thromboembolic risk were recipient positive CMV serology (8.64; 1.06–70.07; p = 0.04) and anticoagulant treatment before transplant (8.95; 1.66–48.21; p = 0.01). ACA detection was not an independent factor of graft loss (OR adjusted 1.39, CI 95% (0.2–9.2); p = 0.74), neither venous thromboembolism (0.88, 0.37–2.08, p = 0.77).

Detection of ACA before renal transplant was not an independent risk factor of graft loss neither venous thromboembolism. However, patients with ACA have had a significantly lower eGFR than patients without ACA.

O83 PREVALENCE OF DONOR SPECIFIC ANTIBODIES IN LIVER TRANSPLANT RECIPIENTS WITH UNEXPLAINED LIVER GRAFT ABNORMALITIES IS EXTREMELY HIGH AND SIGNIFICANTLY HIGHER THAN IN CONTROL GROUPS: ROLE OF ANTIBODY-MEDIATED REJECTION IN LONG TERM GRAFT DYSFONCTIONS

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Introduction: Chronic antibody-mediated rejection (AMR) which is well-defined in kidney transplantation, is much less documented after liver transplantation (LT). The aim of this study was to analyze the prevalence of donor specific antibodies (DSA) in LT recipients on the long term according liver graft function.
Patients and Methods: Inclusion criteria: consecutive outpatient LT recipients diagnosed between 01 and 07/2012 with unexplained LFT abnormalities or unexplained liver fibrosis as assessed by Fibroscan, where tested for DSA (G0). Four control groups: matched on age and time post LT: pts with normal LFT and no reLT (G1), pts with abnormal LFT and no reLT (G2), pts with abnormal LFT and reLT (G3) and pts with HCV recurrence (G4). G1-G4 referred to control pts overall.

Exclusion criteria: ischemic cholangiopathy, infection with HBV or HEV post LT and AIH.
Results: Of 91 pts (males:67:24, age: 47.2 ± 11.3 years) 22 patients G0, 31, 19, 3, 16, pts in G1, G2, G3, G4, respectively investigated, 9.6 ± 6.2 years after LT. Indications for LT: AC 25.3%, HCV 25.3%PCS 14.3%, HCC 4.4%, FH 8.8%, HBV 6.6%, NASH 6.6%, PBC 4.4% and others 4.4%. Anti HLA class I and class II antibodies: 86% and 100%, respectively in G0, and in 62 and 70% in G1–G4. DSA: 95.5% in G0, anti class II in all cases, median MFI 11973. DSA: 50.7% in G1–G4 with a median MFI of 3443. The prevalences of DSA in G1, G2, G3 and G4 were 45.2%, 52.6%, 33.3%, and 68.8% respectively.
Conclusion: Prevalence DSA (mainly anti class II) extremely high (95%) and significantly higher than in control groups (50%).

MFI of DSA in patients with unexplained liver graft dysfunction are significantly higher than in control groups whitch highly uggest the responsibility of DSA and therefore the involvement of a late humoral rejection process in late unexplained allograft dysfunctions.

In HCV positive pts, the prevalence of DSA was also high and raises the issue of DSA as a contributor to fibrosis progression.

O84 IDENTIFICATION AND CONSEQUENCES OF ANTIBODIES WHICH BOUND C1Q IN 118 KIDNEY TRANSPLANT RECIPIENTS WITH DONOR SPECIFIC ANTIBODIES

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Introduction: Donor specific antibodies (DSA) play an important role in antibody-mediated rejection (ABMR) and graft dysfunction. Newer antibody detection assay like Luminex® is highly sensitive but it is not accurately predictive of clinical outcomes. A more precise characterization of DSA potentially harmful for the graft is still a matter of concern.
Patients and Methods: Of 118 recipients (8%) among 947 adult kidney transplant followed in Universitary Strasbourg Hospital had a functional graft and DSA in 2011. We identified and analyzed DSA by Single Antigen Beads (SAB), with the potential to activate the complement by binding C1q using a novel Luminex® C1q assay. We correlate these results with the presence of ABMR, morphological features, C4d staining and graft function.
Results: Median follow up of sensitized patients was 9 ± 7.4 years (6 months to 35 years). There were 65 sensitized patients before transplantation (55%). DSA identified in SAB were mainly class II (72%). 55 patients (47%) had antibodies that bound C1q (DSA C1q+) and in 45 patients DSA were *de novo*. SAB mean fluorescence intensity (MFI) was not a good marker for the prediction of complement binding. Of 80 patients among 118 underwent allograft biopsy for cause. Of 48 patients meet criteria for ABMR and in 30 cases there were chronic active antibody mediated rejection. Of 73% of these patients had DSA C1q+. Of 84% of patients who didn't have ABMR had DSA C1q−. C4d staining was positive in 69% of patients DSA C1q+ and negative in 52% of patients DSA C1q−. Patients with DSA C1q+ had a poorer graft function (SCr 164 ± 75 μmol/l) compared with those having DSA C1q− (SCr 146 ± 57 μmol/l). Five out of seven patients with graft loss had DSA C1q+.
Conclusion: DSA that bound C1q are mainly HLA class II and *de novo* DSA. Our data suggests that these DSA, as determined by this novel C1q assay, are associated with greater risk of ABMR, severe chronic tissue injury and allograft dysfunction.

O85 DONOR-SPECIFIC ANTIBODIES AGAINST DENATURED HLA CLASS I: DESCRIPTION, INCIDENCE, AND CLINICAL IMPACT

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Not only class I intact HLA but also denatured-HLA class I antigens are present on the surface of class I single antigen flow bead (SAFB) assays. Identification of antibodies specific for these denatured antigens is based on the acid-denaturation of the HLA antigen bound to the SAFB. Pre-transplant donor specific antibodies (DSA) detected by SAFB are associated with a higher risk of acute antibody-mediated rejection (AAMR) and graft loss. However, the incidence and the clinical impact of these denatured-HLA antibodies, identified as DSA, are still unknown.

We included 179 HLA class I sensitized kidney recipients transplanted with a deceased donor between January 2000 and December 2008 in this retrospective study and they were followed until February 2013. The sera of the day of transplantation were tested with the class I and class II SAFB to identify class I and class II DSA. Then, acid-denatured SAFB was used to detect DSA recognizing denatured-HLA among patients having class I DSA.

Sixty-seven patients were found with class I SAFB DSA in their pre-transplant serum. We found that 15 out of these 67 patients only had DSA against denatured-HLA, without any intact-HLA DSA, representing 50% of class I DSA with a 500–999 MFI and 10% of class I DSA with a MFI over 1000. All exhibited a negative T-cell flow crossmatch. Denatured-HLA DSA represented 44% of HLA-Cw DSA. Five-year AAMR incidence was higher in patients with class I intact HLA DSA than in patients with denatured-HLA DSA or no DSA (23.4% vs. 6.7% vs. 13.4%, p = 0.04). Five-year graft survivals were 78.1%, 91.7% and 86% in patients with class I intact HLA DSA, denatured-HLA DSA, and no class I DSA, respectively, but the difference was not statistically significant (p = 0.6).

Denatured-HLA DSA represent a significant fraction of class I DSA, and are not associated with an increased risk of AAMR or graft loss. They should not be a contra-indication to transplantation.

O86 ANTIBODY-MEDIATED REJECTION IN ABO INCOMPATIBLE AND POSITIVE CROSSMATCH TRANSPLANTATIONS: A SIMILAR PHENOTYPE BUT A DIFFERENT OUTCOME

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Introduction: The results of ABO-incompatible (ABOi) and positive crossmatch (HLAi) renal transplantations appear very different but have never been directly compared. The aims of this study were then to compare graft survival, and the incidence and the outcome of antibody-mediated rejection (AMR) between them. We also analysed a third group of patients who received a combined ABOi+HLAi transplantation.
Patients and Methods: Of 69 ABOi, 27 HLAi, and 10 combined ABOi+HLAi patients undergoing living-donor transplantations were included. AMR was defined by C4d deposition and microcirculation inflammation, C4d-negative AMR only by microcirculation inflammation.
Results: Five-year death-censored graft survival was better in ABOi than in HLAi and ABOi+HLAi patients (99%, 69%, and 64%, p = 0.0002). However, incidence of AMR was not significantly different between ABOi and HLAi, but higher in ABOi+HLAi patients (25%, 41%, and 80%, respectively). Incidence of C4d-negative AMR was lower in ABOi than in HLAi patients (9% vs. 37%, p = 0.002). Moreover after AMR, the percentages of patients experiencing a declining eGFR and graft loss were lower in ABOi than in both HLAi and ABOi/HLAi patients (declining eGFR: 29% vs. 73% and 87%; graft loss: 6% vs. 36% and 38%, respectively). The poorer prognosis of AMR in HLAi and ABOi+HLAi transplantations was not explained by a difference in the severity of AMR histological lesions, or a less use of plasma exchanges in HLAi patients.
Conclusion: Despite a similar Banff phenotype, AMR are associated with a good prognosis in ABOi patients and a bad one in HLAi patients. This finding partly explains the poorer graft survival observed in HLAi transplantion and highlights the limits of the Banff classification.

O87 OUTCOME OF EARLY ANTIBODY-MEDIATED HISTOLOGIC LESIONS IN BLOOD GROUP-INCOMPATIBLE KIDNEY TRANSPLANTATION

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Introduction: Antibody-mediated rejection (AMR) is defined by microcirculation inflammation (MI, g+ptc) and C4d deposition (C4d+MI+). It may be responsible for the excess of early graft loss in ABO incompatible transplantation (ABOi). However, the incidence and the outcome of C4d-negative AMR (C4d-MI+) and C4d deposition without morphological evidence of rejection (C4d+MI-) needs to be clarified.
Patients and Methods: Sixty four early biopsies in 50 ABOi patients were scored again according to the Banff classification and classified according to the presence of MI and C4d deposition.
Results: 13 (26%), 17 (34%), 6 (12%), and 14 (28%) of patients were C4d+MI−, C4d+MI+, C4d−MI+, and C4d-MI-, respectively. C4d+MI+ patients and C4d−MI+ patients had a lower 3-month eGFR when compared with C4d−MI− patients. However after 3 months, more patients in the C4d+MI− group experienced a declining eGFR when compared with the C4d+MI+, C4d−MI+, and C4d−MI− groups (69%, 29%, 33%, and 29%, respectively). In the C4d+MI− group, interstitial inflammation was strongly associated with a declining eGFR ($i > 0$:100% vs. $i = 0$:43%, p = 0.03). Finally, baseline antibody titre ≥1/16 was associated with C4d deposition (p = 0.01).
Conclusion: Isolated C4d deposition associated with interstitial inflammation may lead to chronic graft dysfunction and should not be considered as accommodation. Characterisation of this indolent inflammatory process may influence post-transplant treatment.

O88 THREE-YEARS OUTCOMES AFTER SWITCHING TO BELATACEPT FROM CALCINEURIN INHIBITOR IN STABLE KIDNEY TRANSPLANT RECIPIENTS

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Background: We report 3-year open-label data in kidney transplant recipients 6–36 Mo posttransplant who were randomized to continue calcineurin inhibitor (CNI) (n = 81) or switch to belatacept (n = 81). After 1 year, patients could enter the long-term extension (LTE) and after 2 years, patients randomized to CNI could switch to belatacept.
Results: 162/173 randomized patients entered LTE; 16 CNI patients converting to belatacept at year 2 are excluded from the year 3 CNI group (n = 65). At year 3, 79/81 belatacept and 64/65 CNI patients survived with a functioning graft. Three-year outcomes are in the table. Among patients with acute rejection (AR), 1 belatacept patient and 1 CNI patient had graft loss subsequent to AR by year 3. Malignancies occurred in 10% of belatacept and 8% of CNI patients. No post-transplant lymphoproliferative disorder was reported in either study arm.
Conclusions: Renal function improved at 3 years for kidney transplant recipients switching to belatacept from either CNI. Adherence remained high. No new safety signals were identified through 3 years follow-up. This exploratory trial indicates that switching patients from a CNI to belatacept may represent an effective clinical approach that should be validated in a large-scale trial.

O89 INITIATION OF ONCE DAILY FORMULATION OF TACROLIMUS (TAC-OD) IN KIDNEY AND LIVER TRANSPLANT RECIPIENTS: 3 MONTH-INTERIM ANALYSIS OF A FRENCH MULTICENTER OBSERVATIONAL STUDY

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Introduction: (TAC-OD) has been proven to be comparable to twice daily formulation (TAC-BID) in terms of efficacy and safety for Kidney (K) and Liver (L) transplantation (Tx).
Purpose: To describe TAC-OD initiation practices after KTx and LTx either during post-Tx hospitalization (gr1) or throughout follow-up (gr2), and to evaluate patient acceptability and compliance.
Methods: Multicentre, longitudinal observational 6-months study including clinical data collection and patient self questionnaire at inclusion, 3 and 6 months follow-up (compliance was evaluated with TEO® questionnaire from Girerd). Interim analysis data at 3 months is presented.
Results: A total of 1190 patients (75% K, 24%L, 1% K&L) were included by 78 physicians among 34 Tx centres. TAC-OD was initiated after surgery in 7% of patients at a mean of 14 days and during follow-up in 93% (n = 1097) at a mean of 4.8 years (range 1–25). 95% of gr2 patients were switched from TAC-BID, mg:mg associated with a mean decrease of 10% C0. Only 9% of patients needed a dose change during the first 45 days post initiation. Reducing the daily pill intake was the main reason for switching.

At 3 months after initiation, 98% of patients were still on TAC-OD. Systemic exposure remained stable and only four acute rejections were reported between 46 and 84 days after TAC-OD initiation with no graft loss. Initiation of TAC-OD increased compliance in 20% of patients as self-assessed by patients questionnaires (At 3 months, 19.6% of patients presented a "poor", 69% a "mild" and 11.5% a "good" compliance vs. 27.7%, 68.3% and 4% respectively at inclusion).
Conclusion: In this study, initiation of TAC-OD-based immunosuppression in a large cohort of KTx and LTx recipients was associated with a 20% improvement of treatment compliance without any safety concerns. Dosage and systemic exposure remained stable after an initial 10% decrease in systemic exposure.

O90 RITUX-ERAH: MULTICENTER RANDOMIZED TRIAL OF RITUXIMAB ON ACUTE ANTIBODY MEDIATED REJECTION IN TRANSPLANTATION

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Background: Treatment of acute antibody mediated rejection (AMR) is based on the association of plasma exchanges (PE), intravenous immunoglobulins (IVIg) and corticosteroids (CS). The efficiency of Rituximab in acute AMR has only been suggested by case series.
Methods: In this phase 3, multicenter, double-blind, placebo-controlled trial, we randomly assigned patients with biopsy-proven acute AMR, to receive Rituximab (R) (375 mg/m^2) or placebo (P). All patients received PE, IVIg, and CS. Primary endpoint was a composite criterion (graft loss or no improvement of renal function at day 12).
Results: Among the 38 patients included, the primary end point in the R group was 52.6% vs. 57.9% (p = 0.744). At 1 year, no death and one graft loss were observed in each group. Supplementary injection of Rituximab, total number of IVIg and PE were not different in the two groups. There was a significant decrease of serum creatinine with no difference between the two groups. There was no difference in the evolution of proteinuria between the two groups. There was no difference in the evolution of acute and chronic histological lesions between the two groups. There was a significant decrease of DSA with no difference between the two groups with a decrease of DSA ≥50% during the study of 53.3% in the P group versus 82.4% in the R group (p = 0.080).
Conclusion: The association of Rituximab to standard of care didn't improve renal function nor made difference on histological lesions. There was a trend towards a more important decrease in DSA in the R group.

O91 *NOROVIRUS* DIARRHEA IN RENAL TRANSPLANT RECIPIENTS

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Introduction: Diarrhea is a common complication of renal transplantation. It hampers the quality of life and increases the risk of graft loss. The exact role of *Norovirus* (*NoV*) infection in this population is unknown.
Patients and Methods: We undertook a monocentric consecutive prospective study, enrolling all consecutive patients investigated for diarrhea between January 2010 and August 2011.
Results: In this study 195 patients, aged 48 ± 15 years, were explored for diarrhea (more than four stools per day). The onset of diarrhea occurred after an average of 54 ± 70 months following the transplantation. Induction with anti-thymocyte globulin (48%) or anti-IL2R Ab (43%) had been used in most cases.

Infectious pathogens were identified in 43% of the patients: *NoV* (n = 54), C*lostridium difficile* (n = 8), microsporidium (n = 7), cryptosporidium (n = 3), *Campylobacter jejuni* (n = 6), *Adenovirus* or *Enterovirus* (n = 4) and CMV (n = 2). In the other cases, investigations failed to identify a cause in 97 patients (47.7%), or found less frequently iatrogenic causes (n = 5) or two lymphomas.

NoV infection was diagnosed by stool PCR in 54 patients, so that is the most prevalent cause of post-transplant diarrhea (28%).

A significant weight loss (7 ± 4% of baseline weight) was observed in 64% of the population. When compared with others, patients infected with Nov had a greater rate of weight loss (83 vs. 56%, p = 0.0001), acute renal failure (59 vs. 38%, p = 0.006) and consequently a higher requirement of diarrhea-related hospitalization (61 vs. 38%; p = 0.002). The persistence of diarrhea (190 ± 167 days) led to a tapering of immunosuppressive drugs in 85% of the *NoV* cases. Despite this tapering, 62% of *NoV* infected patients had long-term viral shedding after symptoms had resolved.
Conclusion: *NoV* infection is the most frequent cause of diarrhea in renal transplanted patients. This infection is severe and often needs a tapering of immunosuppression. Optimal treatment of *NoV*-related diarrhea warrants further studies.