DONOR SPECIFIC ANTIBODIES AND ANTIBODY-MEDIATED REJECTION

O1 NON-HLA AGONISTIC ANTI-ANGIOTENSIN II TYPE 1 RECEPTOR ANTIBODIES INDUCE A DISTINCTIVE PHENOTYPE OF ANTIBODY-MEDIATED REJECTION IN KIDNEY TRANSPLANT RECIPIENTS: AN OBSERVATIONAL COHORT STUDY

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The implementation of the HLA system in clinical practice was a breakthrough in transplant medicine. However, half of transplants fail within 15 years. We aimed to determine whether non-HLA anti-angiotensin II type 1 receptor (AT1R) antibodies (Abs) might identify kidney recipients at risk of graft rejection and loss.

We prospectively enrolled 1845 kidney recipients, who underwent graft evaluation in the first year post-transplant, including graft function, HLA DSAs, AT1R Abs and graft biopsy to assess rejection phenotype using histology and endothelial activation based on gene expression.

Overall, 371 (20.1%) patients had AT1R Abs, 334 (18.1%) had DSAs and 133 (7.2%) had both Abs. AT1R Abs were associated with an increased risk of graft loss: adjusted HR, 1.49 (95% CI, 1.07–2.06) for AT1R Abs alone and 2.26 (95% CI, 1.52–3.36) for AT1R Abs and DSAs. Patients with AT1R Abs showed a higher incidence of active Ab-mediated rejection (AMR) compared with patients without AT1R Abs (126/504 (25.0%) vs 173/1341 (12.9%); $p < 0.001$). AT1R Abs identified 51/77 (66.2%) patients as having AMR among patients with histological features of active AMR without DSAs. Compared to patients with prototypical DSA-mediated rejection, patients with AT1R Ab-associated rejection had more frequently hypertension (46/147 (31.3%) vs 32/51 (62.7%); $p < 0.001$), increased prevalence of vascular rejection with arterial inflammation (18/147 (12.2%) vs 22/51 (43.1%); $p < 0.001$), higher levels of endothelial-associated transcripts demonstrating the interaction of AT1R Abs with the vascular endothelium ($p = 0.013$), and lack of complement deposition in capillaries (73/147 (49.7%) vs 7/51 (13.7%); $p < 0.001$).

Thus, AT1R Abs identify kidney recipients at high risk of graft rejection and loss, independent of HLA system. Recognition of complement-independent AT1R Ab-mediated vascular rejection could lead to the development of new treatment strategies targeting circulating Abs and AT1Rs to improve graft survival.

O2 ROLE OF C1Q-BINDING DONOR-SPECIFIC ANTI-HLA ANTIBODIES IN PREMATURE AND ACCELERATED KIDNEY ALLOGRAFT INTERSTITIAL FIBROSIS

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The last Banff meeting held in 2017 has focused on the importance of a precise diagnosis of interstitial fibrosis and tubular atrophy (IF/TA) in kidney recipients by addressing specific etiological factors. This study investigated the role of anti-HLA antibodies DSAs and their characteristics in the progression of IF/TA.

We prospectively included 1004 kidney recipients with systematic assessment of injury phenotype and IF/TA Banff score on allograft biopsies performed at 1 year post-transplant. All pts were assessed for DSAs and their characteristics (specificity, de novo status, MFI, C1q binding) at 6 months post-transplant. We integrated all for cause biopsies performed beyond 1 year ($n = 539$) to assess IF/TA progression.

We identified 416 (41%) pts with IF/TA0 score, 278 (28%) pts with IF/TA1 score, 165 (16%) pts with IF/TA2 score and 145 (15%) pts with IF/TA3 score. The prevalence of DSAs increased with IF/TA severity: 19% in IF/TA0 pts, 24% in IF/TA1 pts, 28% in IF/TA2 pts and 36% in IF/TA3 pts. DSA MFI level was positively correlated with IF/TA severity ($\rho = 0.21$, $p = 0.001$), with MFI of 3543 ± 3167 in IF/TA0 pts, 4093 ± 4779 in IF/TA1 pts, 5071 ± 5391 in IF/TA2 pts and 7816 ± 6222 in IF/TA3 pts. C1q-binding DSA prevalence also increased with IF/TA severity: 3% in IF/TA0 pts, 5% in IF/TA1 pts, 10% in IF/TA2 pts and 17% in IF/TA3 pts ($p < 0.001$). Among all DSA characteristics, C1q binding was the most important one to predict the severity of IF/TA in random forest analysis (mean decrease in model accuracy: 22%). Pts with C1q-binding DSA had increased microvascular inflammation ($p < 0.001$) and C4d deposition capillaries ($p < 0.001$), and they exhibited accelerated progression of IF/TA ($p = 0.02$) beyond 1 year post-transplant.

C1q-binding DSAs are associated with premature and accelerated kidney allograft fibrosis, with a biological gradient between DSA C1q-binding ability and fibrosis severity, suggesting a causal effect of DSAs in an alloimmune subtype of allograft fibrosis.

O3 NON ADHERENCE, LOW IMMUNOSUPPRESSION AND DE NOVO DSA: A PLACE TO MONITOR NA BY SELF REPORT?

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Introduction: In kidney transplant recipients (KTR), non-adherence (NA) is associated with an increased risk of graft failure (GF). The goal of this study was to monitor NA in order to predict the subsequent occurrence of de novo DSA (dnDSA) and GF.

Methods: We included 301 adult KTR in a multicentric French NA study. NA was assessed at 3, 6, 12 and 24 months post transplantation by the Morisky scale. Under immunosuppression (IS) was assessed by low calcineurin inhibitor (CNI) trough levels or CNI withdrawal at 3, 6, 12 and 24 months. We studied with logistic regression the impact of NA and CNI regimen on apparition of dnDSA. Many Cox models included models with time-dependent variable for NA status were performed to study the impact of NA and the impact of CNI regimen on the hazard of GF defined as death, return in dialysis or retransplant whichever came first.

Results: Time of follow-up was 10 years post-transplantation, if GF did not occur before. Between 2 and 3 years post transplant, dnDSA occurred in 16 patients among the 226 tested (7.1%). After adjustment for recipient and donor age, expanded criteria donor, low CNI trough levels and CNI withdrawal, the hazard of GF was not increased in NA patients compared to adherent patients and we did not find any association between NA and dnDSA occurrence. After adjustment for recipient and donor age, expanded criteria donor and NA status, we found a significant association between under IS and apparition of dnDSA from 1 year post transplantation. The hazard of GF was also increased in patients with under IS at 24 months post-transplantation.

Conclusion: NA estimated by repeated self-reports was not associated with an increase of the hazard of GF and apparition of dnDSA but under IS from one year post transplantation was associated with apparition of dnDSA and an increase of the hazard of GF at 24 months. These data do not support the routine monitoring of NA with questionnaires.

O4 PREDICTING DSA RISK WITH EPLET-MISMATCHES IN KIDNEY TRANSPLANTATION

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Introduction: Median survival of a kidney transplant reaches 15 years but remains limited by chronic rejection, especially mediated by Donor Specific HLA Antibodies (DSA). The target of these antibodies remains difficult to define, with different definitions of HLA incompatibility. We here investigate the effect of eplet mismatches on the risk of DSA development.

Methods: We focused our work on kidney transplant recipients transplanted at Grenoble University Hospital between 2012 and 2014 included, enabling a 4 years follow-up period. These patients were DSA free at the time of transplantation. They received ATG or basiliximab induction, followed by maintenance therapy with tacrolimus and MMF, with early steroid withdrawal (day 3 or month 3). Trough levels for tacrolimus were 5–8 μg/L. A Luminex assay (Immucor) was used, with a MFI threshold at 1000 for positivity.

Results: Between 2012 and 2014, 323 patients received a kidney transplant at our center, among which the HLA 4 digits information was estimated in 231 patients using HLAMatchmaker. In this 231 patients cohort, 198 were first-time

kidney recipients. At least one DSA was identified in 29 patients (12%, with class I: 5, class II: 19, class I and II: 5). The DSA risk prediction with a logistic regression model based on 2 covariates showed a non-significant effect of classical mismatches ($p = 0.87$) but a significant effect of eplet-mismatches ($p = 0.03$, OR=1.05 for each eplet-mismatch).
Conclusion: The risk of DSA development is significantly associated with eplet-mismatch load. This confirms the usefulness of eplet-mismatches in assessing donor-recipient compatibility, like in the Eurotransplant program.

O5 HIGHLY VARIABLE SIALYLATION STATUS OF DONOR-SPECIFIC ANTIBODIES HAS NO IMPACT ON HUMORAL REJECTION OUTCOMES

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Introduction: Antibody-mediated rejection (AMR) is a major cause of kidney graft loss. Some patients however, maintain long-term graft function despite the presence of donor-specific antibodies (DSA) in their circulation. Identifying the parameters associated with DSA pathogenicity is therefore as important as detecting their presence. Recent experimental studies have shown that sugar content, in particular sialylation status of the Fc fragment of IgGs, is variable. This could change IgGs' ability to bind to C1q and to Fc receptor, thereby modulating IgGs' effector functions.

In the present study, the sialylation status of DSA was analysed and its relation with humoral rejection pathophysiology evaluated.
Methods: Among 938 kidney transplant recipients for whom a graft biopsy was performed between 2004 and 2012 at the Lyon University Hospitals, 69 fulfilled the diagnosis criteria for AMR and were enrolled. Sera banked at the time of the biopsy were screened for the presence of DSA by luminex. The sialylation of DSA was quantified using Sambucus nigra agglutinin-based chromatography.
Results: All patients had remarkably similar levels of sialylation of serum IgGs (~2%). In contrast, sialylation status of DSA were highly variable (median = 9%; range = 0–100%), allowing to distribute the patients in two groups: high DSA sialylation: n = 44 (64%) and low DSA sialylation: n = 25 (36%). The two groups differed neither on the intensity of rejection lesions (C4d, ptc and g; $p > 0.05$) on the biopsy nor on graft survival rates (Log rank test, $p = 0.99$). These clinical results were confirmed *in vitro* both in complement-dependent and antibody dependent cell-cytotoxicity assays.
Conclusion: DSA sialylation status is highly variable but does not correlate with pathogenicity.

O6 IMPACT OF GALACTOSYLATION OF DONOR-SPECIFIC ANTI-HLA ANTIBODIES IN RENAL TRANSPLANTATION: IN VITRO MODEL

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The interaction between anti-HLA antibodies (Ab) and graft endothelium is central to the pathophysiology of humoral rejection. Galactosylation (GL) of the IgG Fc fragment impacts the effector functions of Ab, as demonstrated in autoimmunity.

The objective of this work is to study the impact of GL of an anti-HLA I monoclonal Ab in an in vitro model of endothelial cells (EC) in culture, by studying EC activation and complement deposition (CPT) after binding of Ab to HLA class I molecules.

We generated degalactosylated forms of IgG1 anti-HLA I (DG) and hypergalactosylated forms (HG) using enzymes. The GL of these glycoforms, and that of the initial Ac were verified by mass spectrometry (MS). We have incubated interferon (IFN) pre-activated umbilical cord EC with these glycoforms in the presence or absence of normal human serum. Deposits of CPT fractions C1q, C4d, C3d and C5b9 were quantified by flow cytometry, as well as the membrane expression of ICAM and CD46, CD55 and CD59 complement regulators.

In MS, GL of the initial Ab is 41%, including 5.4% of HG forms, and the purity of DG and HG forms generated in vitro is 93.5% and 78%. GL changes do not alter antigen binding. IgG1 HG resulted in greater C1q, C4d and C3d deposition compared to DG IgG ($p = 0.049$, $p = 0.01$, $p = 0.0021$). Pre-activation increases the expression of CD46 and CD55 ($p < 0.0001$ and $p = 0.03$) but this is not affected by the different glycoforms. The expression of CD59 is not modified by pre-activation but decreases with exposure to HG IgGs ($p = 0.0007$). On pre-activated EC, DG IgGs induce 29% higher ICAM expression compared to HG IgGs ($p = 0.0071$).

HG leads to more activation of the classical complement pathway. CD59 expression of EC decreases with exposure of hypergalactosylated IgG. Direct endothelial activation is greater in case of degalactosylated IgG.

O7 REASSESSMENT OF THE CLINICAL IMPACT OF PREFORMED DONOR-SPECIFIC ANTI-HLA CW ANTIBODIES IN KIDNEY TRANSPLANTATION

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Introduction: Several studies reported that anti-denatured HLA-Cw (anti-dHLA-Cw) antibodies are highly prevalent in sensitized patients awaiting kidney transplantation, and that anti-native HLA-Cw antibodies (anti-nHLA) provide random T-lymphocytes flow cytometry crossmatch (T-FCXM) results. In this study, we aimed to 1) reassess T-FCXM prediction for anti-HLA-Cw with classical SAFB and iBeads® and 2) evaluate the pathogenic potential of preformed anti-dHLA-Cw.
Materials and methods: We performed 136 T-FCXM with sera reacting solely against one Cw donor antigen with a classical SAFB MFI $\geq$ 500. Twenty-eight (20.6%) were positive. Classical SAFB and iBeads® MFI were higher for antibodies inducing a positive T-FCXM ($p = 0.0008$ and $p < 0.0001$, respectively). Forty-three (31.6%) anti-Cw were identified as anti-dHLA (iBeads® MFI < 300) and all triggered negative T-FCXM. The correlation of SAFB MFI was very low with T-FCXM ratio ($\rho = 0.178$, $p = 0.04$) and slightly higher with iBeads® MFI ($\rho = 0.289$, $p = 0.0006$). For T-FCXM prediction, a classical SAFB MFI of 1095 provided sensitivity >95%, but specificity was only 22%. In comparison, an iBeads® MFI threshold of 441 provided similar sensitivity but 44% specificity. We retrospectively studied 43 kidney recipients transplanted with preformed anti-HLA-Cw donor-specific antibodies (DSA). At 2 years post-transplantation, recipients with preformed anti-nHLA had experienced more biopsy-proven acute AMR (11/25) than recipients with anti-dHLA (1/18) ($p = 0.014$). At 5 years, 8/25 (32.0%) recipients with anti-nHLA had experienced biopsy-proven chronic AMR versus 1/18 (5.6%) of those with anti-dHLA ($p = 0.046$). At 7 years, 9/25 (36%) recipients with anti-nHLA had lost their graft versus 2/18 (11.1%) of those with anti-dHLA ($p = 0.068$).
Conclusion: Anti-nHLA-Cw DSA but not anti-dHLA-Cw DSA seemed to be deleterious in kidney transplantation.

O8 POST-TRANSPLANT EVOLUTION OF PREFORMED DSA IN RECIPIENTS WITH HIGH IMMUNOLOGICAL RISK

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Introduction: Preformed DSA are associated with graft loss, yet their post-transplant evolution is poorly described. The aims of this study were 1/ to describe their evolution and 2/ their impact on graft loss.
Materials and methods: Among the 950 kidney recipients transplanted in our centre between 2009 and 2015, 75 had preformed DSA, without pre-transplant plasmapheresis. Induction therapy mainly consisted in anti-thymocytes globulins, rituximab and IVIg. DSA were measured at the day of the graft (day 0), day 40, months 3, 6 and 12.
Results: In pre-transplant sera, 16 recipients (21%) had historical DSA versus 59 (79%) having DSA detected in day 0 serum. Median of historical MFI sum was 4000 (quartiles 1861-10066) versus 1720 (955–3237) at day 0. In the post-transplant period, 74% of the recipients were DSA+ at day 0, 71% at day 40, 48% at M3 and M6, 42% at M12. SumMFI were at their peak at day 10 (1880, 1067–5084) and day 40 (1556, 1042–2565). Three evolution profiles were evidenced: the recipients being DSA- from day 10 to M12 (profile 1, 22.2%), the DSA+ recipients at day 10/40 who were DSA- at M12 (profile 2, 36.5%) and DSA+ recipients from day 10/40 to M12 (profile 3, 41.3%). The only pre-transplant DSA characteristic associated with a lower graft survival at 6 years was the peak historical sum MFI ($p = 0.01$). Post-transplant, recipients displaying profiles 2 or 3 had a lower graft survival at 6 years than recipients displaying profile 1 ($p = 0.04$). Furthermore, the recipients displaying profile 3 had a lower eGFR at 3 and 4 years post-transplant.

Conclusion: We identified three post-transplant evolution profiles for pre-formed DSA. The presence of DSA before day 40 is associated with a poor renal prognostic. An early therapeutic intervention for eliminating them could improve graft function.

O9 DESENSITIZATION FOR HLA-INCOMPATIBLE KIDNEY TRANSPLANTATION FROM LIVE OR DECEASED DONORS: IT IS WORTH IT

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In patients with end-stage renal disease, kidney transplantation is associated with a better quality of life and longer survival. HLA sensitization in these patients may result in a higher difficulty to access to a kidney transplant (KT) and in a longer time on the waiting-list. Recipient's desensitization is a procedure to remove donor-specific antibodies (DSAs). Kidney transplantation of recipients with one or more DSAs is called HLA incompatible. The aim of this study was to assess the results of KT recipients from HLA-incompatible living or deceased donors after desensitization.
Method: We included highly-sensitized recipients who received a KT in our hospital. Desensitization consisted in IV Rituximab and apheresis (double filtration plasmapheresis and/or semi-specific immunoadsorption). Immunosuppressive treatment was started prior to transplantation and included Tacrolimus, Mycophenolic acid and steroids. Induction therapy consisted in anti-thymocyte globulins, 0.5 to 1 mg/kg/day for 5 days).
Results: Since 2015, 24 recipients received a KT as such. Thirteen (54.2%) received a graft from a living-donor, 10 from brain-death donor and 1 from a cardiac-death donor (Maastricht-2 classification). Median time of follow-up (FU) was 15 months [1.5–33]. At last FU, mean serum creatinine level was 149 $\pm$ 45 μmol/L and proteinuria was 0.26 $\pm$ 0.22 g/L. Biopsy-proven rejections occurred in 5 patients (21%) at 4.5 months [0.7–16.8] but none of the recipients developed end-stage renal disease. One was cellular rejection, 3 were acute antibody-mediated rejections and 1 was chronic antibody-mediated rejection. C4d deposition was positive in the FU kidney biopsies in 42%. BK viremia occurred in 12.5% and cytomegalovirus viremia in 37.5% of patients at a median time of 4.3 months and 0.37 month respectively.
Conclusion: In our experience, kidney transplantation from HLA-incompatible living or deceased donors has shown its feasibility with good results.

HIGH RISK TRANSPLANTATIONS AND SURGICAL COMPLICATIONS

O10 LONG TERM CONSEQUENCES OF BOTH COLD ISCHEMIA AND ANASTOMOSIS TIME IN KIDNEY TRANSPLANTATION

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Introduction: Ischemia-Reperfusion is of major concern in the field of renal transplantation. It is well demonstrated that prolonged cold ischemia or anastomosis time is responsible for a higher rate of delayed graft function, but long-term consequences are more controversial, with no study so far analysing in a combined way the effects of these both ischemia times.
Methods: From a cohort of 491 patients transplanted between 1989 and 2000, we aimed to evaluate the prognostic impact (GFR measured with inulin clearance at 1, 5 and 10 years post-transplant, graft loss and all-cause mortality) of cold ischemia and anastomosis time, using a bifactorial analysis of ischemia's tertiles.
Results: During a median follow-up of 18.1 year occurred 194 graft loss and 188 deaths. Anastomosis time considered as an isolated continuous variable was only associated to all-cause mortality (HR = 1.02/min, p = 0.01). Bifactorial analysis showed a significant effect of anastomosis time among patients of the higher tertile of cold ischemia ($\geq$ 32 h), with an influence on GFR level (1-year mean mGFR = 49.0 mL/min/1.73 m^2 for an anastomosis time $\leq$ 21 min, similar to the reference group corresponding to the shorter cold ischemia and anastomosis time [p = 0.99], versus 40.6 for an anastomosis time $\geq$ 31 min [p = 0.02]). This beneficial effect of a short anastomosis time was also significant on renal function at 5 and 10 years, but not on graft or patient survival.
Conclusion: Our results suggest that a shorter anastomosis time has a protective effect on long-term renal function that compensate consequences of a prolonged cold ischemia. Expected anastomosis time could so be a useful parameter to optimize graft allocation.

O11 IMPACT OF ISCHEMIA-REPERFUSION-INDUCED EARLY REMOTE ORGAN DYSFUNCTIONS ON LONG-TERM OUTCOMES IN LIVER TRANSPLANTATION

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Introduction: Ischemia-reperfusion injury (IRI) to the graft is often put forward in the short- and long-term prognosis of liver transplantation (LT). Late extrahepatic organ dysfunction, mainly renal failure, significantly affects long-term results. The impact of early remote organ injury (EROD) on long-term results is disregarded but may be significant when leading or being a consequence of graft injury.
Method: A retrospective unicentric cohort study was conducted on patients transplanted (n = 294) to evaluate the impact and determinants of EROD on long-term outcomes of liver transplantation. EROD was defined as *de novo* renal failure needing renal replacement, cardiovascular event needing ICU and/or need for reintubation or ventilation time >7 days. Early allograft dysfunction was defined according to Olthoff's criteria. Graft IRI was studied by IL6 levels (ng/mL) at reperfusion and intra-graft lactate (mmol/g) at the time of back-table preparation.
Results: A major determinant of EROD was the level of IL6 at reperfusion. A threshold of 1000 ng/mL of IL6 was significantly associated to 1-year graft loss. EROD predicted long-term outcomes, specifically in patients experiencing concomitant EAD. However, even in the absence of EAD, the time to liver function tests normalization was longer in case of EROD. EAD was predicted by intrahepatic lactate content at backtable preparation (AUROC 0.906) which was associated to the level of IL6 at reperfusion (p = 0.0001). IL6 level was determined by cold ischemia time, anhepatic time and MELD. Graft survival was associated to the level of IL6 in a dose-dependent manner (p < 0.001). In multivariate analysis, EROD and EAD independently predicted graft survival (p = 0.0002 and 0.002)
Conclusion: Long-term graft survival is determined by both graft injury and preexisting or subsequent extrahepatic organ failure that can be predicted intraoperatively by intragraft lactate content and IL6 at reperfusion.

O12 IMPACT OF OBESITY IN KIDNEY TRANSPLANTATION IN FRANCE: PROSPECTIVE COHORT STUDY FROM THE REIN AND CRISTAL REGISTERS BETWEEN 2008 AND 2014

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Introduction: Consequences of obesity on post kidney transplantation outcomes are uncertain. The aim of this study is to compare patient and graft survival and post-transplant complications in obese patients and non obese patients and to evaluate the impact of pre-transplant weight loss of obese subjects on post transplantation outcomes.
Method: We performed a prospective cohort study from the REIN and CRISTAL registers on 12,094 kidney transplant patients between 2008 and 2014 in France. We compared obese patients with non obese and obese patients who have lost at least 10% of their weight before transplantation (OPP) with obese patients with stable weight (OPS).
Results: Patient survival is similar between obese and non obese (HR = 0.97, 95% CI [0.79, 1.19], p = 0.10) but obese subjects, compared to non-obese, have a lower graft survival (HR = 1.41, 95% CI [1.18; 1.69], p < 0.001), a greater risk of delayed function (OR = 2.10, 95% CI [1.73, 2.42], p < 0.001), of acute rejection (OR = 1.37, [1.14; 1.63], p < 0.001), of post-transplant diabetes (OR = 1.33, [1.16; 1.52], p < 0.001) and their length of hospital stay is longer (regression coefficient = 0.92, CI 95% [0.26, 1.58], p < 0.001). OPP, compared with OPS, have lower patient survival (HR = 1.50, 95% CI [1.001; 2.254], p = 0.049), such as graft survival (HR = 1.74, 95% CI [1.24; 2.43])., p = 0.001). They have as many post-transplant complications as OPS and their length of hospital stay is longer (regression coefficient = 2.97, 95% CI [1.45, 4.48], p < 0.001).
Conclusion: The results on patient survival are similar between obese and non obese. Pre-transplant weight loss in obese patients seems to be deleterious on both patient survival and graft survival and therefore does not appear to be recommended.

O13 ANTICOAGULATION AND RELATED BLEEDING COMPLICATIONS IN PATIENTS ON WAITING LIST FOR LIVER TRANSPLANTATION

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Background: In liver transplant candidates, anticoagulation is an effective and recommended treatment to recanalize, prevent rethrombosis, and avoid extension of portal vein thrombosis (PVT), but can be associated with bleeding complications. The aim of this study was to evaluate the safety of anticoagulation in a large series of liver transplant candidates.
Methods: In two tertiary care centers, all patients listed for liver transplantation (LT) from January 2010 to March 2018 were screened for anticoagulation therapy while on the waiting list. Patients' clinical characteristics, indication for anticoagulation, bleeding events, hospitalisation, transfusion requirements and surgical complications were collected.
Results: Of the 1052 patients listed for LT, 70 (6.7%) were treated with an anticoagulant and 62 (88.5%) had PVT. At inscription, the median MELD score was 17 (range: 7–37). During the waiting period, 28 (40.0%) bleeding events occurred: 23 (64.3%) required hospitalisation, with a median length stay of 16 days (range: 1–60), and 16 (57.1%) received blood transfusion. Bleeding complications were related to portal hypertension in 16 patients (57.1%), to lower gastro intestinal bleeding in 3 patients (10.7%), and to an extra-digestive source (hematoma, epistaxis, hemoperitoneum) in 9 patients (32.2%). Ten patients (35.7%) required endoscopic treatment and 3 (10.7%) patients had to undergo surgery. Ten patients (35.7%) stopped anticoagulation after haemorrhage. Among the 42 patients who underwent LT, 37 (88.0%) had PVT: 17 (45.9%) recanalized, 15 (40.5%) partially recanalized and 5 (13.5%) had complete PVT. Thrombectomy was performed in 14 cases (37.8%) and 39 (90.5%) had end-to-end portal anastomosis. During surgery, the median blood loss was 1500 mL (200–5000) and 18 patients (42.9%) received blood transfusion.
Conclusion: In liver transplant candidates, anticoagulation is associated with a risk of bleeding, mainly related to portal hypertension.

O14 PERCUTANEOUS COAXIAL RENAL GRAFT BIOPSY, AN ALTERNATIVE TO TRANSJUGULAR BIOPSY FOR PATIENTS AT HIGH RISK OF BLEEDING

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Introduction: Transjugular renal biopsy (TJRB) is the gold standard for patients with high haemorrhagic risk. TJRB is not devoid of complications with sometimes insufficient performance. Percutaneous coaxial renal biopsy (coaxial-PRB) could be a less invasive alternative. We report our experience of this technique applied to kidney transplant (KT).
Patients/Methods: TJRB is performed using a modified Colapinto-type needle inserted from the right internal jugular vein to the vein of the graft. The biopsy is carried out in aspiration until the capsule is exceeded. The coaxial-PRB uses a coaxial system allowing at the end of the procedure to embolize the biopsy path. Embolization can be performed under ultrasound or radioscopic control. We have identified cases of KT-TJRB and coaxial KT-PRB performed between 06/2015 and 08/2018
Results: 40 patients were biopsied: 8 KT-TJRB and 32 coaxial KT-PRB. Twenty-five patients were on antiplatelet therapy (APT). Nineteen patients had a pathological occlusion time (47.5%) related to APT (n = 13), thrombopathy (n = 4) or thrombocytopenia (n = 2). Of the 18 patients on anti-vitamin K, 13 had heparin relay and 5 had a short window without anticoagulation. Of the 32 coaxial KT-PRB, 13 samples were inadequate, 2 limits and 17 adequate according to the Banff 2017 classification. A histological diagnosis was established in 29 cases (91%). Three cases of coaxial KT-PRB were complicated (8%): 2 perirenal hematomas and 1 arteriovenous fistula. Among the 8 KT-TJRB performed: 6 samples were inadequate and 2 adequate allowing a histological diagnosis in 5 cases (62.5%). Two KT-TJRB were complicated by hematomas, one of which required transfusion.
Conclusion: Coaxial KT-PRB is an effective and safe alternative to KT-TJRB for patients at high risk of bleeding.

O15 ENDOSCOPIC POLYDIMETHYLSILOXANE INJECTION AS AN UPFRONT TREATMENT OF VESICOURETERAL REFLUX FOR PREVENTION OF RECURRENT ACUTE GRAFT PYELONEPHRITIS IN 103 RENAL TRANSPLANT RECIPIENTS

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Objectives: Acute graft pyelonephritis (AGPN) secondary to vesicoureteral reflux (VUR) may lead to graft loss. Currently, the gold standard treatment is open surgical re-implantation but it's associated at a potential high perioperative morbidity. The aim of this study was to evaluate the endoscopic polydimethylsiloxane injection (EPI) as an upfront treatment for VUR following renal transplantation in order to prevent recurrent AGPN.
Methods: A monocentric retrospective study was performed between 2000 and 2017. All patients with VUR associated to AGPN managed by EPI as an upfront treatment were included. VUR were clustered as low and high grade using voiding cystourethrography. AGPN relapse after EPI was considered as a treatment failure.
Results: 103 patients were included. EPI was successful in 59.2% of cases based on 43 months of follow up data. There was no difference between low and high grade VUR. In multivariate analysis, absence of residual diuresis (HR 2.4, CI 95%; p = 0.001), early AGPN post transplantation (HR 2.1; CI 95%; p = 0.020), and renal transplantation in left side (HR 2; CI 95%; p = 0.047) were associated to a failure of EPI. Patients with all of these risk factors had 100% occurrence of EPI treatment failure. Among patients in failure, a new EPI or an open surgical re-implantation was efficient in respectively 80% and 81.2%. No serious adverse effects were associated with EPI.
Conclusion: EPI is a suitable management of VUR after renal transplantation. Thus, endoscopic management should be used in the first line of treatment to prevent recurrent AGPN secondary to VUR except if a patient is positive for all risk factors for EPI failure.

O16 MAGNETIC BLACK-STAR® DOUBLE J STENT IN KIDNEY TRANSPLANTATION: COST ANALYSIS AND VALORIZATION VERSUS A STANDARD DOUBLE J STENT

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Introduction: Magnetic Black-Star® double J stent (MBS) UROTECH is a polyurethane medical device with a small magnet fixed to the endovesical loop of the stent. The removal of the MBS stent is performed by transurethral magnetic attraction using a magnetic retrieval catheter (MRC) allowing a simplified removal without fibroscope and extraction clamp. Our aim is to evaluate the reproducibility of the retrieval mode and the economic impact of the MBS stent in kidney transplantation assessing a comparative study of running costs, and economical valorisation of the JJ retrieval mode, in 'day hospital' (DH).
Methods: From 1 January to 30 April 2018, 64 kidney transplantations were performed utilizing a double J stent (JJ) to protect the vesicoureteral anastomosis. A MBS JJ 6 Fr.-15 cm, made under our request specifically for kidney transplantation, was utilized in 20 recipients (8M, 12F). 44 recipients had a standard JJ (SJJ). The MBS removal, comparable to a bladder voiding catheterisation, was realized in ambulatory by a nurse after a short training.
Results: The retrieval with the MRC was possible in all MBS recipients. Mean ureteral catheterization time was shorter in MBS vs SJJ group due to unused fibroscopes (23.8 j vs 49.8 j, p < 0.0001). The global cost of a SJJ including consumables, fibroscope and extraction clamp decontamination and sterilization, is 82€ vs 96€ for MBS. The amortization and maintenance expenses of fibroscopes weren't considered. Analyzing the different income of the procedures and 'diagnosis related group', according to the two JJ extraction modes, the MBS valorisation in DH is 270€ upper than SJJ.
Conclusions: MBS stent allows an easy retrieval without fibroscope with a simpler logistics. The procedure can be delegated to a nurse. The slight additional cost of MBS vs SJJ is widely covered by his better economical valorization.

O17 PROSTATE CANCER IN SOLID ORGAN TRANSPLANTATION

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Introduction: The prostate cancer (PC) is the commonest neoplasia in men. With aging of solid organ recipients (SOR), its incidence should grow. The aim

of this study was to analyse retrospectively our renal (RTR), hepatic (RTH) & cardiac (RTC) transplant recipients treated for PC.
Methodology: Retrospective monocentric study of PC diagnosed in the renal, hepatic or cardiac transplanted patients since 1989. All the patients were followed by digital rectal exam and PSA.
Results: 56 PC were diagnosed in 1567 men SOR(3.6%): 33 RTR, 15 RTH, & 8 RTC. The median age at the diagnostic was 64.4 (51.7–68) & the median interval transplantation – diagnostic was 68 (37.5–139) months. The median PSA rate was 6.9 (5.7–13) ng/mL. The clinical stages were T1, T2, & T3 respectively for 31, 20 & 5 patients. The diagnosis was done by screening, after prostatitis and a bone pain in respectively 51, 1 & 1 patients. 3 PC were discovered in prostate shavings. 2 patients were actively followed. 35 patients (23 RTR, 10 RTH & 3 RTC) were traited by radical prostatectomy (RP). The histological results were 26 pT2c & 9 pT3, with 5 positive surgical margins. The Gleason score (GS) was 5, 6, 7 & 9 in respectively 1, 27, 7 & 1 patients. 1 patient with positive pelvic ganglions was treated with hormonal therapy (HT). 1 had a biochemical relapse at 10 months & had radiotherapy. With a medial following of 63.4 ± 42.3 months (0.6–199.1), 2 RTR are deceased due to their PC, 3 & 11 years after respectively HT & RP.
Conclusion: The PC prevalence in SOR remains controversial even if we might assist to a significant growth in the future. It's why it is necessary to discuss about the systematic screening in SOR by mens after 50 years. The PR is feasible regardless of the solid organ transplanted.

O18 OVERALL, RENAL AND IMMUNOLOGIC OUTCOME OF KIDNEY TRANSPLANT RECIPIENTS ADMITTED IN THE TRANSPLANTATION INTENSIVE CARE UNIT (UNIVERSITY HOSPITAL OF TOULOUSE)

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Introduction: The outcomes of kidney transplant recipients admitted to the ICU in the modern era remain poorly described. Risk of over-immunosuppression or immunization to the ICU may also mitigate the longterm outcomes of these patients.
Methods: In this retrospective study, we addressed the outcomes of kidney transplant recipients admitted within the intensive care unit between January 2010 and June 2016. Predictive factors of death were identified.
Results: In a large cohort of 200 KTR admitted to the ICU between 2010 and 2016 (median age 61 years [50.7–68]), we showed that the short and long-term mortality rates (inhospital 20%, month-6 26.5%) were predicted by the severity of the acute condition but also by an EBV proliferation in the weeks preceding the admission to the ICU (i.e., a potential surrogate marker of an underlying immune paralysis and frailty), whereas the characteristics of the transplantation were not predictive. Acute kidney injury (AKI; 85%) and the need of renal replacement therapy (50%) were highly prevalent. Progression toward chronic kidney disease (CKD) was observed in 45% of survivors at 6 months and was predicted by the CKD stage at baseline and the severity of the AKI. Among survivors, 15.1% developed new anti-HLA antibodies (donor-specific antibodies in 9.2%).
Conclusion: Thus, survival of KTR admitted to the ICU is good but further interventional studies will need to address the risk of CKD progression and anti-HLA immunization to improve their long-term outcomes.

FROM KIDNEY DONATION TO TRANSPLANTATION

O19 ORIENTATION OF CO-MORBID PATIENTS TO RENAL TRANSPLANTATION: INTEREST OF A REGIONAL WEBMCM

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Introduction: Besides the rare consensual cases of absolute contra-indication, the HAS recommends that all patients with end-stage renal failure (ESRF), who are less than 85 years old, shall be assessed for transplantation.
However, the major risk of post-transplant complications in the elderly and / or co-morbid patients makes it sometimes futile to perform a pre-transplant assessment. The transplantologists from the Auvergne Rhône Alpes region, with the support of the ARS, has set up a telemedicine tool allowing nephrologists and transplantologists to discuss the relevance of starting or not a pre-transplant assessment in this population. Results of the first 12 months experience are presented herein.
Method: Since January 2017, nephrologists can present, in web-Multi-disciplinary Consultation Meetings (WebMCM), the files considered complex to the corresponding transplant teams of their choice.
Results: After 1 year, 95% of centers (18 nephrology centers and 4 transplant centers) were trained and 28% presented at least 1 record. During the 27 sessions, 90 files were discussed. In 51% of cases, the patient was referred to a transplant team to start a pre-transplant assessment, in 27% of cases the discussion resulted in a temporary or permanent contraindication to transplantation and in 22% of cases additional examinations were requested.
Conclusion: The "webMCM for transplantation" avoids loss of chance of transplantation while limiting the potentially useless examinations and consultations in case of systematic addressing. It therefore seems to be a promising tool to optimize the management of patients with ESRF.

O20 TRANSPLANT CENTER CHARACTERISTICS ASSOCIATED WITH LIVING-DONOR KIDNEY TRANSPLANTATION IN FRANCE: A HIERARCHICAL MODELING APPROACH

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Background: Living-donor kidney transplantation (LDKT) is the best option for end-stage renal disease patients with no contraindications to transplantation. In France, 16% of renal transplants are performed with a living donor (LD), which is lower than in other countries. The objective of this study was to identify the center characteristics associated with LDKT in France with a hierarchical modeling approach.
Patients and methods: This was a retrospective multicenter observational study of 8701 patients who received a renal graft between 2010 and 2014 in 32 transplantation centers. Hierarchical modeling was used to estimate the center effect associated with LDKT.
Results: Of the 8507 incident transplant patients, 1225 were transplanted with a LD kidney. The 9% LDKT rate variance was linked to the transplant center effect. After adjustment for patient and center characteristics, the variance decreased by 47%. Patients transplanted at a center with more than four nephrologists (1.81 [95% CI: 1.10–2.95]) and more than 1.5 nurse transplant coordinators (1.98 [95% CI: 1.26–3.13]) were more likely to be transplanted with a LD kidney. Patients transplanted at a center with an ABO-incompatible program had a higher chance of being transplanted with a LD kidney (2.23 [95% CI: 1.22–4.06]). There was no association between the center size and LDKT.
Conclusion: This study shows that, at the center level in France, both the number of nephrologists and the number of nurse transplant coordinators were positively associated with the patient undergoing a LDKT. Centers with an ABO-incompatible program had a greater rate of LDKT compared with other centers. Resources attributed to a transplant center should facilitate optimal transplant strategies such as LDKT.

O21 COMPARISON OF POST-DONATION KIDNEY FUNCTION BETWEEN CAUCASIAN DONORS AND LOW-RISK *APOL1* GENOTYPE LIVING KIDNEY DONORS OF AFRICAN ANCESTRY

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Some of the increased risk of end stage renal disease among living kidney donors of African descent is attributable to APOL1 gene variants. However, APOL1 genotype may not summarize by itself the totality of this risk. We wondered whether adaptation of the remaining kidney, after donation, was different between donors of African descent with low-risk APOL1 genotype and Caucasian donors. We matched 31 donors with African ancestry and low-risk APOL1 genotype with 62 Caucasian living kidney donors on age, sex, BMI and measured GFR. GFR was measured at baseline with ^{51}Cr-EDTA urinary clearance and kidney volume was measured on preoperative CT-scan. African and Caucasian donors had similar baseline mGFR (99.4 ± 11.3 mL/min/1.73 m^2 vs 97.4 ± 11.8 mL/min/1.73 m^2, p = 0.45), similar baseline eGFR

(98.0 ± 16.0 mL/min/1.73 m^2 vs 96.5 ± 14.4 mL/min/1.73 m^2, p = 0.67), and similar 1-year postdonation eGFR (62.4 ± 12.9 mL/min/1.73 m^2 vs 66.1 ± 14.1 mL/min/1.73 m^2, p = 0.22). Donors of African ancestry experienced lower post-donation eGFR increase than Caucasian donors (+13.2 ± 10.9 mL/min/1.73 m^2 vs +18.3 ± 11.2 mL/min/1.73 m^2 p = 0.03). Remaining-kidney baseline volume was lower for donors of African ancestry compared to Caucasian donors (122.4 ± 20.1 mL/1.73 m^2 vs 130.3 ± 18.8 mL/1.73 m^2, p = 0.04). Remaining kidney "mGFR/volume" ratio was higher in donors of African descent compared to Caucasian donors (0.42 ± 0.10 mL/min/mL vs 0.38 ± 0.06 mL/min/mL, p = 0.03). In conclusion living kidney donors of African ancestry with low-risk APOL1 genotype have lower post-donation eGFR increase and lower baseline kidney volume compared to Caucasian donors.

O22 WHAT IS THE INTEREST IN PROTOCOL BIOPSY THREE MONTHS AFTER RENAL TRANSPLANTATION?

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Introduction: The interest of protocol renal biopsy (PRB) after renal transplantation remains controversial. We studied the prognostic value of lesions observed on systematic PRB at 3 months (M3).
Material and method: This is a single-center, retrospective study of 1062 formal M3 PRBs, performed consecutively between February 2007 and February 2017, in adult renal transplant patients. Patients with acute rejection before M3 were analyzed separately. The predictive value of histological data (Banff 2015) on renal function (MDRDs) at 1 year and graft survival at 5 years was evaluated for each elemental lesion or after grouping into 5 scores (g + ptc, i + t, cg+cv, ci+ct, ah).
Results: 992 patients were analyzed after excluding 70 recipients who experienced an acute rejection before M3. In univariate analysis, chronic lesions appear to be predictive of renal function at 1 year and graft survival at 5 years, unlike glomerulitis or capillaritis lesions, acute tubular necrosis lesions, microcalcifications or percentage of glomerular sclerosis. The multivariate analysis confirms that a score ci + ct ≥ 2 (RR 2.2 [1.1–4.4], p = 0.03) and ah = 3 (RR 2.7 [1.2–6.3], p = 0.02) lead to a risk of graft loss at 5 years.
Conclusion: In patient without acute rejection, the 3-month PRB as a pronostic value because the presence of interstitial fibrosis and tubular atrophy lesions, as well as severe arteriolar hyalinosis, is associated with a decrease in graft survival. 5 years.

O23 EARLY EXPRESSION OF HEME-OXYGENASE-1 BY THE RENAL TRANSPLANT IS ASSOCIATED WITH PRONOUNCED ACUTE TUBULAR NECROSIS BUT A LOWER RISK OF SIGNIFICANT BK VIRURIA

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Introduction: Ischemia-reperfusion (I/R) may cause cellular damages and may increases the immunogenicity of the renal transplant, leading to delayed graft function (DGF) and acute rejection (AR). Heme-oxygenase-1 (HO-1) is a ubiquitous and inducible enzyme upon cellular stress. Thanks to the degradation of heme into carbon monoxide and biliverdin, HO-1 confers significant cell resistance to I/R. In humans, variations of its expression may influence the course of kidney transplant. The aim of this study was to analyze the HO-1 expression in renal tissue at the time of transplantation and its association with renal function, AR and infectious outcomes during the 1st year of transplantation.
Methods: A retrospective monocentric study has been conducted in our kidney transplant center between 2011 and 2016. HO-1 expression was determined in 236 renal biopsies by immunohistochemistry. Characteristics of both the recipients ant the renal transplants were studied.
Results: We identified 160 HO-1+ (68%) vs 76 HO-1- (32%) transplants. Ischemic times were not associated with HO-1 expression. In contrast, we observed more frequent DGF (10.6% vs 2.6%, p = 0.035) and acute tubular necrosis (ATN) (39.4% vs 36.3%, p = 0.049) in the HO-1+ group. The HO-1+ group exhibited a significant reduction of BK viruria >10^7 copies/mL (13.1% vs 23.7%, p = 0.026). No difference between HO-1 groups was noted in terms of renal function, AR or mortality.
Conclusion: Most of renal transplants did express HO-1 immediately after transplantation. The expression of HO-1 seems to correlate with the intensity of ATN and is associated with DGF. In our study, the expression of HO-1 may reflect the intensity of the underlying cellular ischemic stress and was not associated with a better outcome in terms of renal function or AR. However, HO-1 expression in the renal graft appears to be associated with less frequent BK viruria.

O24 RESULTS OF KIDNEY TRANSPLANTATION FROM ABO-INCOMPATIBLE LIVING DONORS AFTER DESENSITIZATION

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Background: In patients with end-stage renal disease, kidney transplantation is associated with a better quality of life and longer survival. ABO-incompatible (ABOi) kidney transplantation across blood group barriers enables better kidney transplantation accessibility. Recipient's desensitization is a procedure to remove anti-A or anti-B antibodies in order to achieve ABOi transplantation. The aim of this study was to assess the results of kidney transplant recipients from ABOi living donor after desensitization in our center.
Methods: We included all recipients who received an ABOi kidney transplant in our hospital. Desensitization consisted in IV Rituximab and apheresis (i.e. double filtration plasmapheresis and/or semi-specific immunoadsorption, and/or specific immunoadsorption). Immunosuppressive treatment was started two weeks prior to transplantation and included Tacrolimus, Mycophenolic acid (MPA) and steroids. Induction therapy consisted in Basiliximab (20 mg Day-0 and Day-4). At post-transplant day 15, 11 (40 .7%) patients were converted from MPA to everolimus.
Results: Since 2015, 27 recipients received an ABOi kidney transplant. Median time of follow-up (FU) was 13.2 months [1.8–38.4]. At last FU, mean serum creatinine level was 119 ± 34 μmol/L and proteinuria was 0.27 ± 0.18 g/L. Biopsy-proven rejections occurred in 4 patients (14.8%) at 3.0 months [0.9–3.1]. One was chronic antibody-mediated rejection and 3 were borderline acute rejections. C4d deposition was positive in the FU kidney biopsies (M1 and M3) in 96%. One patient lost his graft due to a surgical complication. BK viremia occurred in 3.7%. BK viruria occurred in 18.5% and cytomegalovirus viremia in 18.5% of patients at a median time of 5 [0.6–25.4] months and 1.1 [−2.7–12.7] months respectively.
Conclusion: In our experience, kidney transplantation from ABOi living donors has shown its feasibility with good results.

O25 C5B9 DEPOSITION IN GLOMERULAR CAPILLARIES IS ASSOCIATED WITH POOR ALLOGRAFT SURVIVAL IN ANTIBODY-MEDIATED REJECTION

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Background: C4d deposition in peritubular capillaries (PTC) reflects complement activation in antibody-mediated rejection (ABMR). However, its association with allograft survival is controversial. We hypothesized that capillary deposition of C5b9 – indicative of complement- mediated injury – is a severity marker of ABMR. This study aimed to determine the frequency, the location and the prognostic impact of these deposits in ABMR.
Methods: We retrospectively selected patients with an ABMR diagnosis in two French transplantation centers from January 2005 to December 2014 and performed C4d and C5b9 staining by immunohistochemistry.
Results: Fifty-four patients were included, with a median duration of follow-up of 52.5 (34.25–73.5) months. Thirteen patients (24%) had C5b9 deposits along glomerular capillaries (GC). Among them, 7 (54%) had a global and diffuse staining pattern. All C5b9+ patients – except 1 – also had deposition of C4d in GC and PTC. C4d deposits along PTC and GC were not associated with death-censored allograft survival (p = 0.42 and 0.69, respectively). However, death-censored allograft survival was significantly lower in patients with global and diffuse deposition of C5b9 in GC than those with a segmental pattern or no deposition (median survival, 6 months, 40.5 months and 44 months respectively; p = 0.015). The duplication of glomerular basement membrane occurred earlier after transplantation in C5b9+ ABMR than in C5b9– ABMR (median time, 28 vs 85 months; p = 0.058).
Conclusion: We identified a new pattern of ABMR in a subgroup of patients with poor allograft survival. This severe phenotype associated deposits of C4d along peritubular and glomerular capillaries, glomerular C5b9 deposition and a quick onset of glomerular basement membrane duplication. The efficacy of complement inhibitors should be assessed in this subgroup of patients.

O26 DISTRIBUTION OF DE NOVO DSA SUBCLASSES DETERMINED BY MASS SPECTROMETRY (MS): ALL DSAS ARE COMPOSED OF THE FOUR IGG SUBCLASSES AND A HIGH PROPORTION OF IGG3 PREDICTS THE RISK OF ABMR

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DSAs are composed of different IgG subclasses whose distribution could have a major impact on their pathogenicity. Several teams were interested in the detection of these subclasses in flow cytometry by adapting the Luminex Single-Ag test. Some studies have reported that the detection of IgG3 with this technique was associated with poorer graft survival. However, this test does not allow a relative quantification of the different subclasses.

We have developed a new test to investigate the relative distribution of subclasses with MS after isolation of DSA on specific Single-Ag beads. We studied the distribution of DSA subclasses in all patients who developed a de novo DSA (with or without graft dysfunction) on a sample collected at time of graft biopsy. Patients were divided into two groups: DSA with ABMR and DSA without ABMR.

Between 2014 and 2017, 48 patients had developed a de novo DSA including 16 patients without ABMR and 32 patients with ABMR. All IgG subclasses were detected by MS for all analyzed DSA: 60.1% of IgG DSA were IgG1, 23.7% IgG2, 8.6% IgG3 and 7.3% IgG4. The proportion of IgG3 was significantly higher in the rejection group: 9% vs 5.8%, $p = 0.007$. In addition, patients with IgG3 > 7.25% had a higher C4d score (1.69 ± 1.3 vs 0.82 ± 1.2, $p = 0.017$), a tendency for more microvascular inflammation (g + cpt score: 3.3 ± 2.0 vs 2.2 ± 1.9, $p = 0.08$) and a significantly higher risk for a decrease of GFR > 25%: 46.2% vs 9.5%, $p = 0.006$.

In conclusion, de novo DSA are all composed of the four IgG subclasses but with a variable distribution. A higher proportion of IgG3 is associated with the risk of ABMR, C4d deposition and poor outcome.

O27 THROMBOTIC MICROANGIOPATHY AFTER RENAL TRANSPLANTATION: A CLINICOPATHOLOGICAL STUDY AND IDENTIFICATION OF PROGNOSTIC FACTORS

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Introduction: Thrombotic microangiopathy (TMA), whether *de novo* or recurrent, is a serious complication after renal transplantation, but prognostic factors and the role of complement inhibitors in the therapeutic strategy regarding *de novo* TMA are yet to be determined.
Methods: We retrospectively included all the patients with histopathologic lesions of TMA on for cause or screening kidney allograft biopsies performed between January 2004 and March 2016 in our center. The aims of our study were the description of clinicopathologic features and the identification of prognostic factors of *de novo* TMA.
Results: 98 patients experienced at least one episode of histological TMA, among which 90% were *de novo*, (4.8% of the kidney transplant population). The median time of occurrence was 198 ± 920 days. The majority (83.7%) of cases were localized in the graft. The etiological factors were multiple in 37% of cases, antibody-mediated rejection (ABMR) being the most frequent cause (46%), whereas underlying abnormalities of the alternative complement pathway were proved or suspected in 64% of *de novo* TMA patients with genetic testing. Graft survival was worst compared to kidney transplant recipients without TMA (84.7% vs 91.3% at 5 years; $p < 0.0001$). One-year graft loss in *de novo* and recurrent TMA patients was 8% and 10% respectively. The 2 main factors associated with graft loss were intimal arteritis and renal function at diagnosis. The histological pattern was not discriminative of any etiology, even if arteriolar pattern and glomerular pattern were more often associated with CNI toxicity and ABMR respectively.
Conclusion: These results confirm the theory of the "multiple hit" with often multiple causal factors and the implication of alternative complement pathway dysregulation in the pathogenesis of some cases of *de novo* TMA. It also underlines the prognostic value of histology but its current limits to provide the clinician with etiologic clues.

MEDICAL COMPLICATIONS

O28 PRE-TRANSPLANT POLYPHARMACY: AN ALERT ASSOCIATED WITH A HIGHER RISK OF HOSPITALIZATIONS AFTER KIDNEY TRANSPLANTATION IN OLDER RECIPIENTS

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Background: Age is no longer a limit to kidney transplantation (KT) access for patients with end stage renal disease, but recipients older age and frailty are associated with poor outcome after KT, especially hospitalizations for complications. Pre-KT comorbidity, polypharmacy and sarcopenia could be contributors to frailty. Our objective was to identify factors associated with a high number of days of hospitalizations during the first year post-KT.
Methods: Recipients older than 70 years who underwent KT between 2009 and 2016 in our center were included in this retrospective study. The burden of complications was assessed by the number of days of hospitalization during the first year post-KT. We tested pre-KT comorbidities, polypharmacy and sarcopenia, as well as KT characteristics, as potential factors associated with post-KT complications. Muscle mass was assessed by measuring the L4 psoas area on abdominal computed tomography.
Results: A hundred and thirteen patients were included. Median (range) age was 74 (70–85). Median (IQR) number of days of hospitalization during the first year post-KT was 32 (20–46). 5-year patient survival with a functioning graft was lower in recipients hospitalized more than 32 days during the first year post-KT ($p = 0.02$). Pre-KT polypharmacy >5 and 10 drugs was the only factor associated with a number of days of hospitalization higher than the median (OR = 3.7, 95% CI = 1.2–14.3 and 8.3, 95% CI 2.3–36.7, respectively), even after adjusting for age and Charlson comorbidity index in a multivariate analysis. Low muscle mass was not associated with an increased risk of hospitalization.
Conclusion: In older KT recipients, pre-transplant polypharmacy is associated with post-transplant complications and hospitalizations, independently of comorbidity. Pre-KT geriatric interventions should be implemented to reduce polypharmacy.

O29 FRENCH MULTICENTRIC RETROSPECTIVE STUDY OF ACUTE PANCREATITIS IN RENAL RECIPIENTS

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Introduction: Kidney transplantation is considered as the treatment of choice when it is possible compared as dialysis for patient with end-stage renal disease. Nevertheless, acute or chronic, transplant-related or unrelated complications can occur for these patients as cardiovascular diseases, neoplastic diseases and gastrointestinal disorders. We studied a serious digestive adverse event as acute pancreatitis (AP).
Method: In a retrospective study, all AP were collected in 7 French renal transplantation centers (some of Spiesser's team) from 2006 and 2016 thanks to data from medical information department after hospitalization.
Results: In this study, 42 AP were screened. Median of AP occurrence is 50 months [0–293] but 25% of AP occur during the first post-transplantation year. The most frequent etiology is gallstones (36%) as in general population whereas iatrogenic AP are 29% of etiologies (about 1% in general population). Acute alcohol consumption is less common (12%). Acute kidney failure occurs in 72% of AP occurrences with renal replacement in 26%. Significant difference exists between initial serum creatinine (159 μmol/L [103.2–218]) and serum creatinine after AP (282 μmol/L [121.5–479]) ($p = 0.011$). At 3 years, graft survival is 74% and mortality is 27%.
Conclusion: In renal recipients, etiologies are different from general population. AP occur mainly during the first year. AP seem impact renal and patient survival.

O30 MICROVASCULAR RAREFACTION AND LONG-TERM GRAFT DYSFUNCTION IN KIDNEY TRANSPLANT RECIPIENTS WITH DELAYED GRAFT FUNCTION

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Background: Acute kidney injury in the perioperative period, clinically called delayed graft function (DGF), is associated with decreased kidney graft

survival. As animal studies suggest that microvascular rarefaction is a key factor in the acute to chronic kidney disease transition, our primary aim was to assess whether DGF is associated with increased peritubular capillaries (PTC) loss compared to immediate graft function. Then, we set out to determine the impact of PTC loss on subsequent graft function and the predictors of PTC loss in patients with DGF.
Methods: In this single center retrospective cohort study, we compared the change in PTC density on pre- and post-transplant biopsies in patients with and without DGF, transplanted between June 2008 and June 2016. PTC density was evaluated through immunochemistry for CD34 and was expressed as the percentage of cortical area occupied by PTC. We used linear regression models to evaluate determinants of PTC loss and its impact on subsequent graft function.
Results: 220 patients were included in the study (75 with DGF and 145 with immediate graft function). We observed a greater decrease in PTC density in patients who experienced DGF compared to those with immediate graft function (-2.73%, $p < 0.0001$). PTC loss was associated with subsequent graft dysfunction up to 3 years post transplant ($\rho = 0.37$, $p < 0.0001$). In patients with DGF, statin use at the time of transplantation (-0.94%, $p < 0.05$) and donation after cardiac arrest versus after neurological death (-1.76%, $p < 0.05$) were protective for PTC loss while donor hypertension (1.23%, $p < 0.05$) was associated with enhanced PTC loss.
Conclusions: The adverse impact of delayed graft function on long-term graft function is at least partly explained by PTC loss. PTC loss represents a potential prognostic marker and/or a therapeutic target in kidney transplant recipients with DGF.

O31 MORTALITY CAUSES AFTER KIDNEY TRANSPLANTATION IN A MONOCENTRIC COHORT: A CHANGE OF PARADIGM?

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Introduction: Cardiovascular diseases represent the first cause of mortality after kidney transplantation but these data rely on old studies from US or Australian registries. Few studies have described outcomes and survival after kidney transplant in France and in a recent period. We wonder if the progressive changes in recipients demographic and medical characteristics have an impact of mortality causes.
Methods: we included all patients that received kidney transplantation between 01/01/2005 and 31/12/2014 in our center. Patients were followed until 31/12/2016. Death occurring during the transplant period and the 6 months following graft loss were included. Causes of death and risks factors were recorded.
Results: 124 deaths occurred among the 871 patients transplanted during the study period (15.8%). Infections were the first cause of death (33%), before cardiovascular diseases (29%) and cancer (20%). The patient survival was 95.9% at 1 year, 88.9% at 5 years, and 79.1% at 10 years respectively. Risk factors associated with a poor survival were age >50 years, BMI >30 kg/m^2, dialysis, diabetes, HCV seropositivity and deceased kidney donor.
Conclusion: Infections are the leading cause of death in patients receiving kidney transplantation in our center. This result should guide us toward a better management of our transplant patients, especially for patients with risk factors, in order to limit the infectious mortality.

O32 CHARACTERISTICS OF T/NK-CELL LYMPHOMAS AFTER RENAL TRANSPLANTATION: A FRENCH NATIONAL MULTICENTRIC RETROSPECTIVE STUDY

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Introduction: Post Transplant Lymphoproliferative Disorders (PTLD) encompass a spectrum of heterogeneous entities ranging from benign lymphocytic proliferations to high-grade malignant lymphomas. Because the vast majority of cases PTLD arise from B cells, available data on T/NK-cell PTLD are scarce, which limits the quality of the management of these patients.
Methods: All adult cases of PTLD diagnosed in the 35 kidney transplant centers in France were prospectively recorded in the national registry between 1998 and 2007. To ensure all cases of PTLD-T/NK were identified, registry data were cross-checked with those of 2 independent databases: K-ViroGref and Tenomic. Medical files of T/NK-cell PTLD were reviewed and data were compared with that of i) the 440 cases of B-cell PTLD from the registry, and of ii) a control cohort of 148 "conventional" T/NK-cell lymphomas.
Results: 58 cases of T/NK-cell PTLD were enrolled in the study. T/NK-cell PTLD occurred significantly later after transplantation and had a worse overall survival than B-cell PTLD ($p < 0.0001$). Depending on the clinical presentation, 2 subtypes of T/NK-cell PTLD could be distinguished: i) cutaneous ($n = 16$, 28%) and ii) systemic ($n = 42$, 72%), the latter being associated with a worse prognosis ($p < 0.0001$). Compared with systemic T/NK-cell lymphomas diagnosed in immunocompetent patients, overall survival of T/NK-cell PTLD was worse ($p < 0.0001$). This difference was neither entirely explained by the higher tumor mass at diagnosis, nor the more aggressive histological phenotype of systemic T/NK-cell PTLD, since multivariate analysis identified transplantation as an independent factor associated with death. Interestingly, transplanted patients were less intensively treated and responded less to immunochemotherapy than controls.
Conclusion: Systemic T/NK-cell are rare type of PTLD with bleak prognosis, likely because of suboptimal treatment and/or the detrimental impact of therapeutic immunosuppression.

O33 GROWING FREQUENCY OF TRANSPLANTED PATIENTS AMONG THE FRENCH COHORT OF ATYPICAL HEMOLYTIC UREMIC SYNDROME IN THE ERA OF ECULIZUMAB

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Introduction: Eculizumab has revolutionized the management of atypical Hemolytic Uremic Syndrome (aHUS). However, the lack of randomized trials and population-based studies precludes any assessment of the epidemiological impact of this biotherapy on aHUS natural history.
Methods: A nationwide, retrospective, multicenter study was conducted, involving 34 French nephrology centers. Clinicians were contacted to update follow-up. Inclusion criteria were the following: 1- An extensive complement work-up in a patient diagnosed with aHUS, 2- 18 or older between 01/01/2007 and 01/01/2016.
Results: Over the study decade, 397 patients were identified from 33 centers. Among them, 33 were lost to follow-up and 39 passed away before the end of the study period. In the meantime, 175 *de novo* cases and 43 transfers from pediatric to adult joined the cohort. Hence, the French aHUS cohort increased from 179 to 325 patients between 01/01/2007 and 01/01/2016. The frequency of aHUS patients under dialysis had steadily and significantly decreased between 2012 and 2016, dropping from 34% to 16% ($p < 0.0001$). In the meantime, the proportion of aHUS with a functional kidney transplant increased from 29% to 41%, while the frequency of those treated with eculizumab increased from 20% to 44% (from 38% to 83% in *CFH* mutation carriers). The distribution and frequency of complement abnormalities did not change over this period. Moreover, the greater proportion of transplanted patients was even more striking in the patients harboring a pathogenic variant in complement genes, associated with poor outcomes. Between 2012 and 2016, the frequency of transplanted patients increased from 16% to 41% and from 37% to 57.5% in *CFH* and *CFI* variants carriers, respectively.
Conclusions: This large multicenter study shows the dramatic change in aHUS natural history at the eculizumab era. The transplanted population has significantly increased over the dialysis aHUS population for the past 4 years.

O34 SEMI-SPECIFIC IMMUNOADSORPTION (IA) AND FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS (FSGS) RECURRENCE ON THE GRAFT

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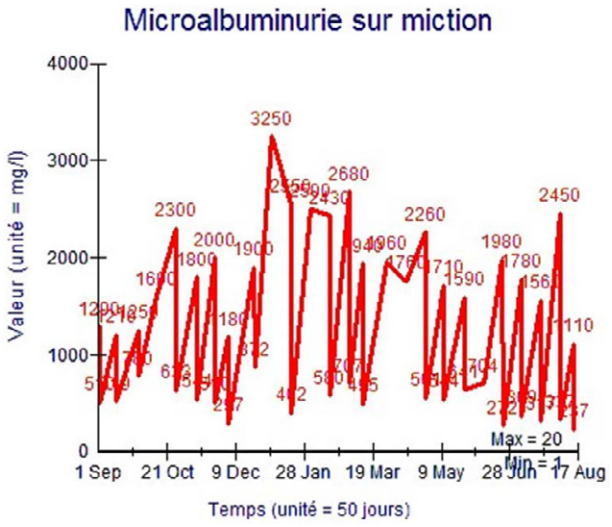
Introduction: FSGS recurrence on the kidney graft is a serious complication often leading to early graft loss. No specific treatment is known. Multiple strategies have been described (steroids, rituximab, iv cyclosporin, ACTH, galactose, plasmapheresis). IA has also been used with potential benefit.
Methods: We describe a series of six patients, whose primary kidney disease was FSGS, suffering from recurrence of the disease on the kidney graft. Recurrence was defined as new-onset albuminuria in the post-transplant period. Patients did not respond to traditional alternatives (steroids, rituximab and PP). Iterative semi-specific IA sessions (Globaffin, Fresenius®) were established. The degree of albuminuria and therapeutical response determined the interval between sessions. Treated plasma volume was >100 mL/kg.
Results: The average interval between transplantation and the first IA was 784 ± 531 days [3-1523]. The average albuminuria for each patient before each session was respectively 776 ± 512, 1986 ± 689, 1925 ± 1038, 2793 ± 1466, 834 ± 719 et 1048 ± 999 mg/L. Each patient achieved reductions of proteinuria during and after each session. The average reduction of albuminuria per session was respectively 49 ± 43%, 21 ± 21%, 63 ± 21%, 28 ± 16%, 55 ± 41% et 49 ± 53%. One patient has stopped IA treatment and now has a stable albuminuria <500 mg/L, the others are IA-dependent. No patient needs more than one session per week to maintain a stable proteinuria. Two hospitalizations for infection were necessary. One patient had a temporary interruption due to venous access problems. The sessions were generally well tolerated.
Conclusion: IA is an efficient solution to stabilize albuminuria in FSGS recurrence: the mechanism of action is unknown but certainly related to the apheresis treatment. Due to the induced immunosuppression, infectious risk must be taken into account. Fig. 1 Typical albuminuria evolution in a patient over one year.



O35 PATTERNS OF HYPERTENSION IN RENAL TRANSPLANT PATIENTS EVALUATED WITH 24 H AMBULATORY BLOOD PRESSURE MONITORING

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Objectives: Prevalence of the different patterns of hypertension in renal transplant recipients (RTR) using 24 h ambulatory blood pressure monitoring (ABPM) along with their determining factor are lacking. The aim of our study was to describe the epidemiology of hypertension in RTR, based on ambulatory blood pressure monitoring (ABPM).
Methods: In this cross-sectional study, prevalent RTR were proposed systematic blood pressure work-up consisting of ABPM, office blood pressure (3 consecutive blood pressure measurements performed by a nurse after 5 min of quiet rest) and detection of orthostatic hypotension. Optimal target was defined as BP < 130/80 mmHg for office BP. ABPM goals was defined using the ESH guidelines but we also defined another targets using only the 24 h average ABPM as seen in the literature.
Results: 258 RTR underwent ABPM. Mean ABPM was 132/76 mmHg not different from the mean office BP (132/73 mmHg). Prevalences of patients with resistant hypertension and uncontrolled BP when we considered day-time and night-time values were respectively 23% and 48% vs 20% and 41% when we take into consideration only the 24 h average ABPM. 20% of RTR had orthostatic hypotension. Office blood pressure did not detect resistant hypertension in 5% of patients.
Conclusion: Our results show a suboptimal control of BP in a cohort of RTR with 20% of patients with resistant hypertension and more than 50% of patients with uncontrolled BP. Prevalence of hypertension is underestimated in RTR because of the lack of established definition of blood pressure using ABPM in this population. ABPM goals need to be better define to assess correctly hypertension and improve the management of BP in RTR.

O36 CT SCAN-DERIVED MEASUREMENT OF TPI (TOTAL PSOAS INDEX) IS AN OBJECTIVE TOOL FOR THE ASSESSMENT OF CENTRAL SARCOPENIA AND IS A STRONG PREDICTOR OF FRAILTY IN SURGERY AND ONCOLOGY

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Introduction: CT scan-derived measurement of TPI (Total Psoas Index) is an objective tool for the assessment of central sarcopenia and is a strong predictor of frailty in surgery and oncology. The aim of this study was to determine the impact of TPI on kidney transplant outcomes.
Methods: We retrospectively included 264 kidney recipients who had abdomino-pelvic CT-scan in the 3-year prior to their first transplantation between January, 1st 2007 and December, 31st 2013 at University Hospital of Montpellier (France). Total psoas index (mm^2/m^2) was measured as the cross-sectional areas of the left and right psoas muscle (TPA (mm^2)), normalized for height, at the level of L3 vertebra. Patients were classed and analyzed in TPI terciles stratified for sex.
Results: Mean TPI was 61.7 ± 12.1 mm^2/m^2 for men and 42.4 ± 14.2 mm^2/m^2 for women. Length of stay at transplantation was higher in low-TPI group compared to high-TPI group (19.71 ± 13.32 vs 15.39 ± 7.13 respectively, p = 0.01). But after adjustment for age, Charlson index and delayed-graft function, this difference did not reach statistical significance. The number of rehospitalizations at one-year post-transplant and total rehospitalizations were higher in low-TPI group compared to high-TPI group (p = 0.03 and p = 0.003 respectively). In multivariate logistic regression models, small TPI was a strong risk factor for repeated rehospitalizations compared to large TPI (OR = 2.45 (1.26–4.76), p = 0.01); post-operative complications were also an independent risk for iterative rehospitalizations (OR = 1.88 (1–3.53), p = 0.05). Graft loss and death rate were not different between the terciles of TPI.
Conclusion: The measure of TPI seemed to be an objective and reproducible tool to assess central sarcopenia and frailty. It was associated with an increase of post-transplant morbidity.

REJECTION

O37 ACUTE ANTIBODY-MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION: PLASMAPHERESIS OR IMMUNOADSORPTIONS?

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Introduction: Apheresis-based therapy associated with corticosteroids and intravenous (IV) immunoglobulin (IG) is considered as standard-of-care of acute antibody-mediated rejection (AABMR), a major cause of kidney transplant loss. However, data to choose between plasmapheresis (PP), and immunoadsorption (IA) are lacking.
Methods: We retrospectively analyzed the cases of AABMR treated with PP and/or IA in Marseille University Hospital between 1/1/2013 and 6/30/2016. The treatment also included IV steroids and IG, and increasing of baseline immunosuppression. Until October 2013, only PP were performed and then, we could choose between PP and IA according to clinico-biological presentation and feasibility of the technique. We measured the rates of mortality, graft losses, patients that increased their serum creatinine (SCr) >30% compared to mean SCr before AABMR, after 2 years of follow-up. We also compared those outcomes and safety data between the PP and IA groups.

Results: We included 24 patients. Eleven patients were treated with PP, and 10 with IA (both techniques were used in 3 cases). The patients of both groups had similar baseline characteristics. We observed 4 deaths (16.7%) and 7 death-censored graft losses (29.2%). At the end of the study, 5/13 patients with a functional transplant had increased their SCr >30% (38.4%). There was no difference in these outcomes between the 2 groups. The rates of severe bleeding events and blood transfusions were not different between the 2 groups. There were 4 severe infections leading to hospitalization in both groups but the 3 infections leading to death occurred in the PP group only ($p = 0.21$).
Conclusion: In this study, 54% of patients had a functional transplant 2 years after AABMR and none of the apheresis technique was associated with better efficacy and safety results. Further studies are needed to clarify which apheresis-based therapy must be used, given their invasive aspects and cost.

O38 AN INTEGRATIVE APPROACH FOR THE ASSESSMENT OF PERITUBULAR CAPILLARITIS EXTENT AND SCORE IN MICROVASCULAR INFLAMMATION – ASSOCIATION WITH TRANSPLANT GLOMERULOPATHY AND GRAFT LOSS

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Background: In active antibody-mediated kidney allograft rejection (ABMR) the microvascular inflammation score (MVI), a positive C4d staining or gene transcripts of endothelial damage are currently seen as surrogates of HLA antibody-antigen interaction as they are strong predictors of transplant (TX)-glomerulopathy (TG) and TX-loss. We recently observed the association of diffuse extent of peritubular capillaritis (ptc – inflammation in >50% of cortical peritubular capillaries) with increased risk of TX-loss and higher DSA-values. We tested the suitability of this pattern as additional surrogate of on-going HLA-antibody interaction.
Methods: We retrospectively re-evaluated 616 patients for ptc morphology, TG in all biopsies (n = 1619) and death-censored TX-loss. We assessed more precisely our cases with a ptc score=1, diffuse ptc extent and no glomerulitis ($ptc1_{diffuse}$, n = 26), currently not diagnostic for ABMR.
Results: Positive C4d and MVI-scores≥2 were found in 11 and 19% of the samples, TG in 13% of the patients. Including $ptc1_{diffuse}$ in the group of MVI ≥ 2 significantly increased the AUC for TG (0.602, $p = 0.008$) compared to the current MVI ≥ 2 (0.560, $p = 0.12$). After adjustment for confounders (C4d or cellular rejection), $ptc1_{diffuse}$ remained independently associated with TG [OR 3.89, $p = 0.008$]. Patients with $ptc1_{diffuse}$ had significantly worse TX-survival than patients with MVI ≥ 2 and <2 (42 vs 59 vs 70%, $p = 0.002$).
Conclusion: Our integrated approach for ptc morphology, including the distribution of ptc (diffuse ptc) in the assessment of MVI, was better than current recommendations for the prediction of TG and subsequent TX-loss risk. It highlights a risk population currently not identified as such.

O39 ARCHETYPE ANALYSIS IDENTIFIES DISTINCT PROFILES IN RENAL TRANSPLANT RECIPIENTS WITH TRANSPLANT GLOMERULOPATHY ASSOCIATED WITH ALLOGRAFT SURVIVAL

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Introduction: Transplant glomerulopathy (TG) is a common glomerular lesion observed after kidney transplantation associated with bad prognosis. The heterogeneity of TG has not been precisely characterized to date.
Methods: Consecutive kidney transplant recipients from 3 Paris centers and 1 center in Canada presenting with a diagnosis of TG (Banff cg score ≥1 by light microscopy) January 2004 and January 2014 were included. Comprehensive pathology, clinical, immunological, and outcome data were used in unsupervised archetype analysis.
Results: Among the 8,207 post-transplant allograft biopsies performed during the inclusion period, 552 presented with TG (incidence of 6.7%). The median time to TG diagnosis post-transplant was 33.18 months (IQR: 12.12–78.72 months). Kidney allograft survival rates after TG diagnosis were 57.1% and 25.5% at 5 and 10 years, respectively. An unsupervised learning method integrating clinical, functional, immunological and histological parameters revealed 5 TG distinct archetypes. The 5 TG archetypes displayed distinct allograft survival profiles with incremental graft loss rates between archetypes, ranging from 88% to 22% allograft survival rates 5 years after TG diagnosis ($p < 0.0001$).
Conclusions: A probabilistic data-driven archetypical approach applied in a large well-defined multicentric cohort refines the diagnostic and prognostic features associated with TG. Reducing heterogeneity among TG cases can improve disease characterization, enable patient-specific risk stratification, and open new avenues for archetype-based treatment strategies in TG.

O40 RESPONSE TO TREATMENT AND LONG-TERM OUTCOMES IN KIDNEY RECIPIENTS WITH ANTIBODY-MEDIATED REJECTION (AMR): A DATA-DRIVEN APPROACH

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Early and reliable systems for evaluating response to treatment in AMR are lacking. We investigated the ability of combined clinical, histological and immunological markers for decision making in kidney recipients with AMR receiving standard of care (SOC) treatment.

Among 1196 kidney recipients (2008–2011), we prospectively enrolled all patients with biopsy-proven active AMR according to Banff criteria, who received SOC (plasma exchange, high-dose IVIG, rituximab and steroids) with assessment at the time of AMR diagnosis and 3-month post-treatment initiation for clinical data, histological characteristics and DSA characteristics.

We included 139 kidney recipients with active AMR (median time post-transplant: 15.5 months). At post-treatment evaluation, independent determinants of graft loss included: GFR (HR, 0.95; 95% CI, 0.93–0.98), peritubular capillaritis (HR, 2.08; 95% CI, 1.08–3.99), interstitial inflammation (HR, 2.70; 95% CI, 1.12–6.55), transplant glomerulopathy (HR, 3.37; 95% CI, 1.82–6.26) and C1q-binding DSAs (HR, 2.57; 1.29–5.12). A conditional inference tree for graft loss revealed 5 profiles of response to treatment with distinct outcomes as reflected by a 5-year graft survival going from 33% to 93% (cross-validated accuracy: 0.77; post-treatment variables included: GFR, transplant glomerulopathy and C1q-binding DSAs). For instance, patients with GFR >33 mL/min and without C1q-binding DSA (n = 63, 45.3%) showed a 5-year allograft survival of 93% compared with 35% in patients with GFR ≤33 mL/min, without transplant glomerulopathy and with C1q-binding DSA (n = 15, 10.8%).

Multidimensional assessment of response to SOC treatment of active AMR allowed to build a clinical decision tree showing accuracy in risk stratifying graft outcomes and uncover different profiles of response to treatment. Further studies are needed to define second-line strategies in patients with poor prognosis, such as complement targeting agents in patients with C1q-binding DSAs.

O41 IMPACT OF FCγR3A POLYMORPHISMS ON AMR OUTCOME IN KIDNEY TRANSPLANTATION

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Introduction: Antibody-mediated rejection (AMR) is widely recognized as the first cause of allograft failure. AMR outcome is however heterogeneous at the individual level, making difficult the assessment of the risk of graft loss at the time of diagnosis.

During AMR, the binding of donor specific antibodies (DSA) on graft endothelial cells is responsible for the recruitment of innate immune cells (in particular NK cells). These cells can damage graft endothelial cells by antibody-dependent cell-mediated cytotoxicity (ADCC). NK interact with Fc Fragment of DSA by a unique receptor: FcγR3A (CD16A). A SNP (FcγR IIIa*559A>C, rs396991) modulates FcγR3A binding capacity to Fc of IgG but its impact in AMR has never been assessed.
Method and results: Among the renal transplanted patients followed in Lyon University Hospital that had a graft biopsy between 2004 and 2015, 118 presented an AMR as defined by Banff: (i) presence of microvascular inflammation on biopsy, and (ii) circulating DSA. The 15.9% that were homozygous for the "high-binding" FcγR3A allele had an inferior allograft as compared with patients with a "low-binding" FcγR3A ($p = 0.03$). An in vitro model of ADCC, in which purified human NKs were co-cultured with endothelial cells coated with DSA, confirmed that NKs with a high-binding FcγR3A displayed stronger activation and promoted more endothelial damages.
Conclusion: Our work demonstrates that FcγR3A polymorphisms impact AMR outcome and suggest that this genetic biomarker could be useful to stratify the risk of graft loss at diagnosis of AMR.

O42 NK CELLS IN ALLOGRAFT KIDNEY REJECTION: DETECTION, QUANTIFICATION AND LOCALIZATION USING MULTIPLEX IMMUNOFLUORESCENCE

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Introduction: Recent transcriptomic studies of kidney allograft biopsies have highlighted the role of NK cell transcripts in the setting of antibody-mediated rejection (ABMR). We aimed to detect, quantify and localize NK cells *in situ* during ABMR, TCMR and non rejection biopsies using a multiparametric immunofluorescence technique (mIF) on paraffin-embedded sections.
Methods: Fifty biopsies (20 ABMR, 20 TCMR et 10 NR) were analyzed by mIF (Opal, Perkin Elmer) using anti-NKp46, CD3, CD163 and CD34 antibodies for NK cells, T lymphocytes, macrophages and endothelial cells respectively. The sections were acquired on Vectra 3.0® automated imaging system. Computerized quantification was performed with inForm® software (PerkinElmer). Messenger RNA of different immune cells (NK, T cells and macrophages) were quantified using qPCR in frozen biopsies from the same cohort (n = 26, 10 TCMR, 11 ABMR et 5 NR) for correlation with mIF results.
Results: NK cells density quantified by immunohistochemistry was significantly correlated to density quantified with mIF ($r = 0.91$, $p < 10^{-4}$). Total cell density with mIF was significantly higher in TCMR ($1303 \pm 254/mm^2$) than ABMR ($435 \pm 70/mm^2$) or NR biopsies ($46 \pm 20/mm^2$) ($p < 10^{-4}$). Percentage of NK cells during ABMR and TCMR was low compared to other cell types and comparable in the 2 types of rejection (2.87% in TCMR and 2.66% in ABMR, $p = 0.58$). Quantification of mRNA expression of different cell types was correlated to mIF results ($r = 0.52$, $p = 0.009$ for NK cells (NKP46); $r = 0.47$, $p = 0.019$ for T cells (CD3) and $r = 0.58$, $p = 0.003$ for macrophages (CD14)).
Conclusion: This study allowed us to develop a reliable technique of multiparametric immunofluorescence on paraffin-embedded sections and to show that NK cells are present during TCMR as well as ABMR but in very low proportions.

O43 TREATMENT OF NK MEDIATED REJECTIONS BY MTOR INHIBITORS: A TRANSLATIONAL STUDY

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Introduction: In a previous work, our group showed that some innate immune effectors: Natural Killer (NK) lymphocytes, could perceive the absence of expression of self HLA class (HLA-I) I molecules ("missing self") by graft endothelial cells and cause antibody-independent microvascular inflammation, which has the same detrimental prognosis as chronic humoral rejection. In this translational study, we aimed at identifying a possible molecular therapeutic target to treat this new type of rejection.
Methods and Results: Purified human NK were cocultured with K562 cells, which do not express HLA-I. Imaging flow cytometry analyses showed that the mTORC1 pathway was critical during missing self-induced NK activation. The use of a mouse model of missing self-induced NK-mediated rejection revealed that rapamycin (but not cyclosporin) was effective in blocking the mTORC1 pathway in NK and suppressing the development of microvascular lesions in cardiac graft. Based on these experimental results, we tested mTOR inhibitors in 2 transplant patients (1 heart and 1 kidney) diagnosed with missing self-induced NK-mediated rejection. At 6 months both patients showed a significant decrease in the intensity of the rejection lesions on biopsy.
Conclusions: Our work demonstrates that the mTORC1 pathway is critical for missing self-induced NK-activation and suggests that mTOR inhibitors may be a valid therapeutic option in this new type of rejection.

O44 DEFINING PROFILES OF RESPONSE TO TREATMENT AND PATTERNS OF PROGRESSION TO GRAFT FAILURE OF ACUTE T CELL-MEDIATED REJECTION (TCMR) IN KIDNEY RECIPIENTS: MAJOR IMPACT OF I-IF/TA AND DSAS

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While the natural history and impact of TCMR are being revisited with the recent recognition of chronic active TCMR by the Banff classification, response to treatment of acute TCMR is not defined and patterns of progression to graft failure after acute TCMR are unknown.

Among 2905 kidney recipients transplanted between 2004 and 2013, we prospectively included all pts with pure biopsy-proven acute TCMR, who received standardized treatment by steroids. Pts were systematically assessed at the time of diagnosis and at 3 months post-treatment for glomerular filtration rate (GFR), proteinuria, histology and anti-HLA DSAs.

We included 256 pts with pure acute TCMR, diagnosed at a median time of 3.5 months post-transplant. Distribution of TCMR grades was 90 (35%) grade IA, 113 (44%) grade IB, 36 (14%) grade IIA, 10 (4%) grade IIB and 7 (3%) grade III TCMR. At post-treatment evaluation, independent determinants of graft loss included GFR ($p < 0.001$), proteinuria ($p = 0.007$), time post-transplant ($p = 0.02$), peritubular capillaritis ($p = 0.02$), i-IF/TA ($p = 0.02$) and DSAs ($p = 0.001$). Based on a classification tree, we identified 5 profiles of response to treatment (cross-validated accuracy: 0.80). Non-responders included pts with persisting TCMR injury and failing allograft (n = 28, 10-yr graft survival: 12%), pts with preserved function and transition to chronic active TCMR (n = 40, 10-yr graft survival: 55%) and pts with preserved function, de novo DSAs and transition to AMR (n = 33, 10-yr graft survival: 57%). Responders included pts with intermediate (n = 69, 10-yr graft survival: 74%) and good graft function (n = 86, 10-yr graft survival: 93%) without rejection injury after treatment.

Clinical, histological and immunological assessment of response to treatment of acute TCMR allowed to uncover different profiles of response to treatment with distinct outcomes. Further studies are needed to define the efficacy of second-line strategies in patients evolving towards chronic active TCMR and AMR.

O45 INFLAMMATION IN FIBROTIC AREAS (I-IF/TA) IDENTIFIES A T CELL-MEDIATED REJECTION COMPONENT OF IF/TA WITH POOR KIDNEY ALLOGRAFT OUTCOME

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Addressing the etiological heterogeneity of interstitial fibrosis in kidney allografts is key to improve long-term transplant outcomes. We investigated the determinants, clinical and histological phenotype, and outcome of i-IF/TA in a prospective cohort of kidney recipients.

We prospectively enrolled 1539 kidney recipients (2004–2010), with systematic assessment of i-IF/TA Banff score and tubulitis in atrophic tubules (t-IF/TA), on allograft biopsies at 1-year post-transplantation. We considered donor, recipient and transplant baseline characteristics, immunosuppression, infectious diseases (CMV, pyelonephritis, BK virus), presence of anti-HLA DSAs and all the biopsy-proven diagnoses made in the first year post-transplant.

We identified 946 (61%) patients with IF/TA at 1-year post-transplant, among whom 394 (42%) patients showed i-IFTA, which was associated with t-IF/TA in 309 (78%) patients. Patients with i-IF/TA at 1-year post-transplant had significantly decreased 8-year allograft survival compared with patients with non-inflammatory IF/TA (81% vs 87%, $p = 0.002$). Independent risk factors for i-IF/TA included: TCMR (OR = 2.7, $p < 0.001$), BKVN (OR = 3.3, $p = 0.007$), HLA B (OR = 1.3, $p = 0.012$) and DR (OR = 1.2, $p = 0.044$) mismatch. Corticosteroids (OR = 0.6, $p = 0.039$), CNI (OR = 0.5, $p = 0.011$) and MMF/MPA (OR = 0.5, $p = 0.011$) had protective effects on i-IF/TA occurrence. Unsupervised hierarchical clustering based on the whole spectrum of Banff elementary lesions at 1-year post-transplant showed that i-IF/TA aggregated in the TCMR cluster (i, t, ti, t-IF/TA and i-IF/TA) but not in the AMR (g, ptc, C4d, cg) and chronicity clusters (cv, ci, ct, ah) with a positive gradient between increasing level of i-IF/TA and t-IF/TA Banff scores and the risk of allograft loss ($p < 0.001$).

i-IFTA may reflect a TCMR subcomponent of IF/TA related to under-immunosuppression and is associated with poor kidney transplant outcome compared to non-inflammatory IF/TA.

LIVER TRANSPLANTATION

O46 DE NOVO MALIGNANCIES SCREENING AFTER LIVER TRANSPLANTATION FOR ALCOHOLIC LIVER DISEASE: A COMPARATIVE OPPORTUNISTIC STUDY

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Background: Patients having received a liver transplant for alcoholic liver disease (ALD) have a high risk of *de novo* malignancies, especially in the upper aerodigestive tract and lungs due to their smoking history. The aim of this retrospective study was to evaluate the impact of an intensive screening program for tobacco-related cancers in this population.
Methods: We compared a group of patients transplanted for ALD who continue to smoke and who were included in an intensive screening program implemented in Centre 1, and a group of similar patients followed according to usual practice (chest CT-scan every five years) in Centre 2. The intensive screening program consisted of an annual checkup including a clinical examination by an otorhinolaryngologist, a chest CT-scan, and an upper digestive endoscopy.
Results: A total of 147 patients were included, 71 patients in Centre 1 and 76 in Centre 2. The mean adherence to intensive screening was 74.0% for chest CT-scan, 46.0% for otorhinolaryngologist examination, and 62.0% for upper digestive endoscopy. The cumulative incidence of a first tobacco-related cancer was 12.3% at 3 years, 20.6%, at 5 years, 42.6% at 10 years and 64.0% at 15 years. A curative treatment was possible in 80.0% of the patients in Centre 1 versus 57.9% in Centre 2 ($p = 0.068$). The rates of curative treatment were 63.6% vs 26.3% ($p = 0.062$) for lung cancers, 100.0% vs 87.5% ($p = 0.498$) for lip-mouth-pharynx-larynx cancers, and 66.7% vs 100.0% ($p = 1$) for esophageal cancers, respectively. In addition, for lung cancers, irrespective of study group, 68.7% received a curative treatment when the diagnosis was made by CT-scan screening versus 14.3% when it was made because of symptoms ($p = 0.008$).
Conclusion: Our study strongly suggests that the screening of lung cancer by annual chest CT-scan after LT for ALD could significantly increase the rate of curative treatment.

O47 LIVER TRANSPLANTATION FOR NONALCOHOLIC STEATOHEPATITIS-RELATED CIRRHOSIS: PRELIMINARY RESULTS OF A FRANCOPHONE MULTICENTER COHORT

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Introduction: Nonalcoholic steatohepatitis is the most common liver disease in the world. Liver transplantation (LT) may be the treatment of the terminal phase of the disease, liver failure and/or hepatocellular carcinoma (HCC). Few long-term data after TH are available.
Methods: This multicenter retrospective francophone study will include all patients transplanted for nonalcoholic steatohepatitis-related cirrhosis since 2000 in France and participating francophone centers. We report here the preliminary results.
Results: In August 2018, 89 patients (including 56 men) have been included in 4 centers. The mean age of patients was 60.4 years (range 42–70) at LT, the mean MELD score was 15.9 (range 6–40) and 41 patients had HCC (46.1%). Before transplantation, 49.3% of the patients were obese, 65.0% diabetic, 65.0% had arterial hypertension and 12.0% had dyslipidemia. Mean follow-up after LT was 4.5 years (0.1–13.0). After LT, 63% of patients were obese, 70% had hypertension, 69% diabetes, and 60% dyslipidemia. Fourteen patients had a protocol liver biopsy at 5 years (out of 30 patients followed), disclosing a recurrence of steatosis in 100% of the cases, and a recurrence of cirrhosis in 35%. After LT, occurred 45 cardiovascular events (in 29 patients), as well as 23 cancers (in 18 patients). Patient survival was 93.9% at 1 year, 85.6% at 5 years and 71.4% at 10 years. Four re-transplantations were performed (none for recurrence of the initial disease). No patients had bariatric surgery (before or after LT).
Conclusion: These preliminary results suggest that patients transplanted for nonalcoholic steatohepatitis-related cirrhosis have liver and extra-hepatic complications associated with the underlying metabolic syndrome. Therefore, the role of bariatric surgery needs to be discussed and strongly evaluated.

O48 PIRCHE ALGORITHM MAY PREDICT DE NOVO DONOR SPECIFIC HLA ALLOANTIBODIES (DSA) FORMATION FOLLOWING LIVER TRANSPLANTATION. A SINGLE CENTER PILOT STUDY

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Background: In liver transplantation de novo anti HLA donor specific alloantibodies (dnDSA) have been reported to be associated with a high incidence of graft failure. Determinants of DSA specificity are generated via the indirect allorecognition pathway. The PIRCHE (predicted indirectly recognizable HLA epitopes) score is a novel HLA epitope matching tool to predict the alloimmune response and dnDSA formation following kidney transplantation. The aim of our study was to perform the PIRCHE score for the first time in liver transplant patients and to asses it's potential to predict de novo DSA formation in a cohort of liver transplant patients.
Methods: A total of 55 liver transplant patients, without preformed DSA were analyzed. The novo DSA were detected by single antigen bead assay. Twenty eight patients had de novo DSA whereas 27 patients had no serum DSA. HLA typing of the recipient and of the donor was achieved by serological and/or DNA-based techniques. Missing typings were extrapolated from HLA-ABCDRDQ-haplotype frequencies based on the National Marrow Donor Program database 2007 for Americans of European descent. Similarly, low-resolution typing data of patients and donors was extrapolated using a multiple imputation approach. The HLA-derived mismatched peptide epitopes that can be presented by the recipient's HLA-DRB1 molecules were calculated using the latest version of the PIRCHE algorithm.
Results: Patients in DSA group had a mean PIRCHE score of 100 comparing to no DSA group where the mean score was 86.5 ($p = 0.07$). On the subgroup analysis, HLA-A and HLA-B PIRCHE were significantly higher in the DSA group patients comparing to the non DSA patients (22 and 20 vs 18 and 16, $p < 0.05$).
Conclusion: PIRCHE score could be predictor of the novo DSA formation following liver transplantation. Using this approach DSA formation and consequently allograft injury could be prevented. Larger studies are needed to validate PIRCHE score in liver transplantation.

O49 LONG-TERM RESULTS OF LIVER TRANSPLANTATION FOR AUTO-IMMUNE HEPATITIS: FIRST RESULTS OF A FRENCH NATIONAL STUDY

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Introduction: Autoimmune hepatitis (AIH) is a rare indication for liver transplantation (LT), accounting for less than 5% of all LT in Europe. The aims of this retrospective study were, from a large nationwide cohort with long follow-up, (i) to evaluate the overall survival rate of patients and grafts after LT for AIH, (ii) to describe the rejection episodes and AIH recurrence, (iii) to identify the risk factors for disease recurrence, especially the role of immunosuppressive regimen. We report here the first results.
Methods: From databases of the French Agence de la Biomédecine and French LT centers, we selected all patients aged ≥16, transplanted for AIH in France.
Results: Were included 341 patients (73 males) transplanted from July 1987 to April 2018 in 21 French LT centers. Median age at LT was 43.8 years (16.4–72.6). The indication for LT was fulminant or subfulminant liver failure in 58 cases and liver cirrhosis for 280 patients, including 19 hepatocellular carcinoma (HCC). AIH was associated with another autoimmune disease in 27.9% of patients. Median time of follow-up was 77.2 months (0.1–363.7). Post-LT maintenance immunosuppression consisted of tacrolimus (73.9%), cyclosporine (12.3%), mTOR inhibitor (10.0%), MMF (66.6%) and/or azathioprine (17.3%). Long-term corticosteroid therapy was maintained in 2/3 of patients. The rates of acute rejection, chronic ductopenic rejection and disease recurrence were 31.9%, 5.6% and 23.1% respectively. Patient survival was 88.1%, 81.7%, 75.6%, 70.3% and 66.3% at 1, 5, 10, 15 and 20 years

respectively. The main causes of death were sepsis (n = 20), malignancies (n = 11, including 3 HCC recurrence) and liver failure (n = 9), secondary to AIH recurrence for 4 of them. During follow-up, 45 patients underwent retransplantation, including 9 for disease recurrence (3.7%).
Conclusion: Our results strongly confirm that survival after LT for AIH is excellent. Disease recurrence is frequent and needs further analysis.

O50 MTOR INHIBITORS IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS

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Background: During the past decade, mTOR inhibitors (mTORi), everolimus and sirolimus, have been increasingly used after adult liver transplantation (LT). The aim of the present study was to describe the use of mTORi in pediatric LT recipients.
Methods: All pediatric LT recipients who received mTORi before December 2017 from 4 European pediatric LT centers were included and analyzed.
Results: The present cross-sectional study included 30 patients; 21 were male (70%), median age was 9.3 years (range: 1.2–17.1 years) at mTORi introduction. Main indications for mTORi introduction were pre-existing liver malignancy (43.3%), calcineurin inhibitor (CNI) nephrotoxicity (26.7%), rejection (23.4%), PTLD (13.3%), or inclusion in a prospective study (3.3%). At last follow-up, mTORi CNIs were withdrawn in 10 patients (10/29, 34.5%). The median dose of mTORi was 1.8 mg/day (range: 0.3–5.0) or 0.058 mg/kg/day (range: 0.01–0.26), and the median trough level was 5.1 mg/L (range: 1.0–15.5). After a median follow-up of 2.8 years (range: 0.2–10.0), 50.0% of the patients presented with at least one adverse event. The main adverse events included hyperlipidemia, proteinuria, dermatitis, and mucitis. Overall mTORi discontinuation rate was 23.3% (10.0% because of adverse event). Among the 13 patients who received mTORi because of an initial malignant liver tumor, 3 presented recurrence and died. The 4 patients who presented with PTLD experienced a favorable outcome. Introduction of mTORi had no significant impact on renal function.
Conclusion: Our results suggest that mTORi can be used in pediatric LT recipients in different clinical situations, to reinforce immunosuppressive therapy, or to reduce CNI and related toxicity.

O51 HOW TO OPTIMIZE EARLY IMMUNOSUPPRESSION AFTER LIVER TRANSPLANTATION FOR ACLF 3 PATIENTS?

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Background: Liver transplantation (LT) for stage 3 acute-on-chronic liver failure (ACLF 3) patients is controversial and data are scarce regarding the postoperative management of these patients. The specific place of mTOR inhibitors (mTORi) in this special population has not been addressed.
Method: All consecutive patients admitted in a University hospital Intensive Care Unit for ACLF3 (excluding acute liver failure) were included. Initial immunosuppression protocol always included tacrolimus, corticosteroids and MMF. The impact of basiliximab induction, early tacrolimus exposure and early mTORi introduction and specifically everolimus. The primary endpoint was 1-year survival. Patients who died within the first postoperative week were excluded.
Result: 61 patients were included. Median CLIF-C score at admission and at LT and MELD were 64 (15–79), 67 (13–85) and 42 (20–58). Basiliximab induction was used in 39 (64%) patients, mTORi in 23 among whom 12 (20%) had everolimus. Median time to everolimus switch was 29 days (7–90). Patients with everolimus switch had higher admission CLIF-C (66 vs 61; p = 0.105), more frequent preLT dialysis (100% vs 18%; p = 0.108) and a significantly lower preLT platelet (p = 0.043). The causes for everolimus switch were neurological disorders (n = 5), renal failure (n = 4), thrombotic microangiopathy (n = 2), cancer (n = 1). A rejection episode was treated in 20% of cases. Basiliximab use and switch to everolimus were often associated (p = 0.027). Basiliximab use and treated rejection episodes were associated with higher 1-year survival (p = 0.022 and 0.005).There was no significant difference in the rate of surgical complications, reoperation or 1-year survival in patients receiving everolimus.
Conclusion: Early immunosuppression in ACLF 3 patients impacts 1-year survival. Basiliximab improves survival. Everolimus seems a safe and efficient alternative in case of tacrolimus toxicity even in the early postoperative period.

O52 EVEROLIMUS PLUS SORAFENIB AS A TREATMENT OPTION FOR HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION

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Background: Few authors reported on the outcome of patients with hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT). The aim of this study is to analyze predictive factors of survival for patients after HCC recurrence and best treatment strategies.
Methods: Consecutive patients who underwent LT for HCC between 2005 and 2015 at our center were recruited. Characteristics of patients with recurrence, modalities of treatment and outcome were collected retrospectively. Predictive factors for survival after recurrence were analyzed by Cox regression analysis.
Results: Among 306 patients underwent LT, 43 patients (14%) developed HCC recurrence with a median survival time after recurrence of 10.9 months (95% CI: 6.6–18.6). Main treatment for recurrence was chemotherapy (Sorafenib or Gemcitabine based, n = 33). Survival of patients treated with Sorafenib (SOR) and everolimus (EVL) (n = 19) was significantly better than that of the group treated with other strategies (n = 24) (p = 0.0006). Multivariate analysis demonstrated that SOR+EVL therapy and absence of dissemination at diagnosis of recurrence were independent predictive factors of prolonged survival after recurrence. Among the patient treated with EVL, survival of patients with controlled EVL blood trough levels ≥5 ng/mL was significantly better compared to those with EVL through levels <5 ng/mL (p = 0.021). Adverse events were comparable among groups treated with SOR in combination or not to EVL.
Conclusion: The combination therapy of SOR and EVL was an independent predictor for better survival after HCC recurrence. Patients with controlled everolimus trough level ≥5 ng/mL may get the best survival benefit.

O53 INCIDENCE AND TREATMENT OF BIOPSY PROVEN REJECTION IN PATIENTS CONVERTED TO EVEROLIMUS (EVL) AFTER LIVER TRANSPLANTATION (LT): LONGTERM HISTOLOGICAL DATA FROM THE EVEROLIVER MULTICENTER OBSERVATIONAL FRENCH REGISTRY

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The aim of this multicenter French observational study is to analyze incidence, histological features and treatment of rejection under EVL regimen.
Patients and methods: From 2006 till August 2017, LT patients from 9 centers who were converted to EVL were recruited in the study. Data from last liver biopsy performed prior to conversion and from all biopsies performed after conversion were collected. Indications of transplantation were mainly alcoholic cirrhosis (54.4%) and HCV cirrhosis (21.6%). HCC was present in 44.2% of the recipients.
Results: 1045 adult recipients (75.1% male) had a mean age of 54.3 ± 10.3 years. EVL was introduced in 45% of the patients during the 1st year. Main reasons of introduction of EVL were chronic renal failure (36.2%) treatment of recurrent HCC (6.2%) or de novo cancer (21.1%) and prevention of HCC recurrence (41.5%). Mean through EVL levels were respectively 5.6 ± 3.7, 6.3 ± 3.1 ng/mL at M1 and M36. CNI were withdrawn in 49.8% at M12. Under CNI regimen, 480/1045 (46%) patients had at least 1 liver biopsy prior to conversion to EVL. Biopsy-proven acute rejection (BPAR), treated BPAR and BP chronic rejection (BPCR) were respectively 9.6%, 6.9% and 2.1%. Under EVL regimen, 527/1045 (50.4%) patients had at least 1 liver biopsy after conversion to EVL with a median delay of 25.2 (0.4–359) months. BPAR, treated BPAR and BPCR were respectively 8.9%, 5.5% and 3.1%. In the 329 patients who had at least 2 biopsies prior and after conversion, only 14 patients (4.2%) without BPAR prior to conversion developed BPAR after conversion. Eight patients (0.8%) underwent retransplantation.
Conclusion: This real life registry showed in more than 1000 liver biopsies from patients converted to EVL, that the risk of treated BPAR under EVL based regimen with a long follow-up is low (≤ 5%). Conversion from CNI to EVL allowed a weaning of CNI in 50% of the patients at 1 year and a minimization of CNI in the others without increasing chronic rejection (3%).

O54 STUDY OF THE MANAGEMENT AND IMPACT ON OVERALL SURVIVAL AND GRAFTS OF ANASTOMOTIC BILIARY STENOSIS (AS) AFTER LIVER TRANSPLANTATION

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Objective: To study the management and impact on overall survival and grafts of anastomotic biliary stenosis (AS) after liver transplantation. PATIENTS AND METHODS: Monocentric retrospective study between 2010 and 2016 including all hepatic transplant patients in Toulouse. The management of SA was analyzed as well as the search for risk factors for stenosis and the impact on overall survival and grafts. Results: Of 225 patients included, 56 (25%) presented with stenosis. The median onset was 83 months, 70% in the first 6 months. A Liver score >800 points at the time of transplantation was the independent predictor of AS onset. Initial endoscopic management was decided in 87.5% of cases but was finally possible in only 66% of cases. With a median procedure duration of 12 months, a median of 4 procedures per patient. Surgical treatment accounted for 2% of initial decisions and 12.5% of final procedures. Percutaneous management had a high rate of failure, especially in the case of catching endoscopic treatment. The presence of an AS had no impact in terms of overall patient survival nor in terms of graft survival. Conclusion: SA do not have any impact on the survival of patients and grafts, at the cost of long endoscopic treatment with several procedures. In the event of failure of this treatment, it seems preferable to move directly towards the surgical repair.

IMMUNOSUPPRESSION

O55 TACROLIMUS DOSAGE ADJUSTMENT ACCORDING TO CYP3A5 GENOTYPE IN KIDNEY TRANSPLANTATION: LONG-TERM RESULTS

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Background: Tacrolimus exhibits pharmacokinetics variability partly explained by CYP3A5 activity. In contrast to *3/*3 genotype, those carrying at least one *CYP3A5*1* allele exhibit higher enzyme activity leading to lower Tac trough blood level despite higher daily dose. In this study, we aimed to evaluate the impact of CYP3A5 polymorphism on renal graft outcome
Methods: This monocentric cohort includes 1252 renal transplant recipients with a mean follow up (FU) of 4 years (up to 12.1y). Genotyping of the 6986A>G allelic variant corresponding to *CYP3A5*3* was systematically performed. After 3-months post-transplant, Tac trough blood level target range was 5–7 ng/mL. However in order to avoid Tac-induced nephrotoxicity, Tac daily dose was limited to a maximum of 0.1 mg/kg/day irrespective of CYP3A5 genotype
Results: Our sample includes 224 *CYP3A5*1/-* patients (13.9%) including 35 *1/*1 genotype recipients. During the FU, we observed 221 graft losses or deaths (17.65%). At baseline, there was no significant difference in characteristics between *3/*3 and *1/- groups. Despite higher daily dose, *1/- recipients exhibit systematically significant lower Tac trough blood level during the FU ($p < 0.01$). Multivariate analysis doesn't show any significant influence of *1/- genotype (HR=0.73, CI 95% 0.48–1.09, $p = 0.12$) on patient-graft survival. However, GFR decline was significantly lower for the *1/- group ($p = 0.004$). At five years, eGFR was significantly better for *1/- recipients (47 vs 42 mL/min/1.73 m2, $p < 0.001$). *CYP3A5* genotype doesn't impact the risk of rejection (HR for *1/- group=0.96, CI 95% 0.66–1.42, $p = 0.87$)
Conclusion: In this long-term study, *CYP3A5*1/-* recipients exhibited lower Tac trough blood level with no impact on the rejection rate. Renal survival was independent of CYP3A5 genotype. However, the kidney graft function was significantly better in this subgroup showing a lower Tac-induced nephrotoxicity.

O56 RENAL, EFFICACY AND SAFETY OUTCOMES USING AN EVEROLIMUS (EVR)-BASED CALCINEURIN INHIBITOR (CNI)-FREE REGIMEN VS STANDARD TACROLIMUS (TAC) AFTER LIVER TRANSPLANT (LTX): THREE-YEAR FINDINGS FROM CERTITUDE

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Background: EVR-based CNI-free therapy may preserve renal function and reduce CNI-related complications after Ltx but long-term data are sparse.
Methods: The prospective CERTITUDE trial follows Ltx patients [pts] to 5 years post-Ltx after completing the 6-month [M] SIMCER study, in which deceased-donor pts were randomized at month 1 post-Ltx to (i) EVR + TAC withdrawn by month 4 or (ii) standard TAC, both with basiliximab induction, mycophenolic acid (MPA) ± steroids to compare the glomerular filtration rate (GFR) after Ltx.
Results: 143 of the 188 pts randomized in SIMCER entered in CERTITUDE (65/93 EVR, 78/95 TAC) with 135 pts followed to M36 post-transplantation (62 EVR, 73 TAC). The leading indications for Ltx were alcoholic cirrhosis (75/143) and hepatocellular carcinoma [HCC] (35/143). Adjusted means (SEM) change in estimated GFR (eGFR; MDRD) from SIMCER randomization to M36 after adjusting for baseline eGFR was -13.4 (2.9) mL/min/1.73 m2 with EVR and -18.7 (2.6) mL/min/1.73 m2 with TAC; difference 5.2[-2.390;12.917] mL/min/1.73 m2 ($p = 0.177$). Observed mean (SD) eGFR at M36 was 77.3 ± 27.8 vs 69.2 ± 22.7 mL/min/1.73 m2 with EVR vs TAC ($p = 0.070$). Treated biopsy-proven acute rejection [BPAR] affected 4 everolimus-treated pts and 2 tacrolimus pts during M6-36. Major adverse cardiovascular events (MACE) occurred in 3.1% and 5.1% of EVR and TAC pts, respectively ($p = 0.689$). Global neoplasm occurred in 6 (7.7%) TAC pts and in 6 (9.2%) EVR pts. No patient under EVR experienced a recurrence for liver cancer whereas 5.1% under TAC treatment had HCC recurrence. Five pts died in TAC treatment group and 3 died in the EVR treatment group. Just one graft was lost for one TAC patient. Study drug was discontinued due to adverse events in 23.1% of EVR pts and 11.5% of TAC pts.
Conclusions: EVR and MPA with early TAC withdrawal preserves renal function to year 3 post-Ltx, without increased risk of rejection. MACE, malignancies and HCC recurrence were less frequent in the EVR group.

O57 EFFICACY AND SAFETY OF EVEROLIMUS [EVR] WITH REDUCED-DOSE CALCINEURIN INHIBITOR [RCNI] IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS [KTXRS]: M24 RESULTS FROM THE TRANSFORM STUDY

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Background: TRANSFORM is the largest prospective study in KTxRs comparing efficacy and safety of EVR+rCNI (tacrolimus [TAC] or cyclosporine [CsA]) to mycophenolic acid [MPA]+standard-dose of CNI [sCNI] using a composite endpoint: antirejection efficacy and renal function.
Methods: This is a multicenter, open-label, non-inferiority study. 2037 KTxRs were randomised to receive either EVR (1.5 and 3 mg/day [D] with CsA and TAC, respectively; trough level [C_0]: 3–8 ng/mL)+rCNI or MPA (1.44 and 2 g/d for enteric-coated mycophenolate sodium or mycophenolate mofetil respectively)+sCNI. Patients received basiliximab or anti-thymocyte globulin induction with steroids. The primary objective was incidence of binary composite of treated biopsy-proven acute rejection [tBPAR] or estimated glomerular filtration rate [eGFR] <50 mL/min/1.73 m²; key secondary objective was incidence of tBPAR, graft loss, or death at M24. Incidences of donor-specific antibodies [DSA], adverse events [AEs] and infections were also evaluated.
Results: Overall, 87.1% of KTxRs completed medication up to M24. Mean TAC C_0 was above in EVR+rTAC and within the target range in MPA+sTAC. EVR+rCNI was noninferior to MPA+sCNI (47.9% vs 43.7%, $p = 0.067$) for the primary endpoint. Incidence of tBPAR was low between arms. Graft loss,

deaths, AEs, mean eGFR and incidence of de novo DSA over M24 were comparable between arms. Incidence of AEs leading to study drug discontinuation was higher with EVR+rCNI, but more dose reduction/adjustment was reported in MPA+sCNI. BK virus and cytomegalovirus (CMV) infections were significantly less frequent in EVR+rCNI ($p < 0.001$).
Conclusion: EVR+rCNI-based regimen provides comparable efficacy, safety, and renal function to MPA+sCNI-based regimen in KTxRs along with benefit against viral infections.

O58 IMPACT OF CYCLOSPORIN ON INNATE CD8$^+$ T-CELLS IN TRANSPLANT PATIENTS WITH MINIMIZED IMMUNOSUPPRESSION

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Background: Neoplasia associated with the loss of antitumor immunosurveillance is a major long-term complication of organ transplantation. Our laboratory study innate CD8$^+$ T-cells, an unconventional $\alpha\beta$-T cell subset, expressing markers of both innate immune cells (receptors of Natural Killer cells (KIR)) and memory T-cells, particularly the transcription factor Eomesodermin (Eomes). These features, along with our description of their numerical and functional restoration in chronic myeloid leukemia patients responding to treatment, support the hypothesis that innate CD8$^+$ T-cells have a role in cancer immunosurveillance, including in transplant patients.
Methods: Peripheral Blood Mononuclear Cells (PBMCs) were collected from 23 patients (mean age: 64 years) of a single-center study (CHU Poitiers), who had received renal transplantation for more than 10 years (mean time: 28 years), with no clinical or biological sign of rejection under minimized immunosuppression (low dose of calcineurin inhibitor). Innate CD8$^+$ T-cells (CD3$^+$CD8$^+$panKIR$^+$Eomes$^+$) from patients and 16 healthy donors (HD) were immunolabeled and analyzed by flow cytometry. Furthermore, HD's PBMCs were cultured *in vitro* for 7 days with cyclosporine (0.1 μg/mL) prior to flow cytometry analysis.
Results: *Ex vivo*, transplant patients have an increased frequency of innate CD8$^+$ T-cells as compared to healthy donors (5.1% ± 3.1 and 12.0% ± 9.8 of CD3$^+$ CD8$^+$ T-cells in HD and patients, respectively, $p < 0.01$). No difference between patients based on their history of cancer was observed. *In vitro*, the frequency of innate CD8$^+$ T-cells is increased after cyclosporin treatment (6.7% ± 4.3 and 11.8% ± 5.6 of CD3$^+$ CD8$^+$ T-cells before treatment and after treatment, respectively, $p < 0.05$).
Conclusion: Our study provides the first demonstration of an *in vivo* effect of cyclosporine on innate CD8$^+$ T-cells. Moreover, our *in vitro* results suggest a direct action of cyclosporin on this cell population.

O59 MEASUREMENT OF IMMUNOSUPPRESSIVE DRUGS ADHERENCE USING PHARMACEUTICAL FILE AND PHARMACY RECORDS

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Introduction: In France, the pharmaceutical file (PF) and the pharmacy records (PR) list the drugs delivered to patients and could be reliable measurement tools for non-adherence to immunosuppressant medication (NA-IS). The objective of our study was to test the feasibility of measuring NA-IS by PF and PR in recent renal transplant patients.
Methods: 92 patients treated by tacrolimus were included in this study between M4 and M12 post-transplantation. The NA-IS was measured twice, at inclusion visit (V1) and 4 months later (V2), by: 1/ the proportion of days covered by IS drugs (PDC) calculated from the PF, 2/ the PDC calculated from PR, 3/ the coefficient of variation of tacrolimus levels (CV), 4/ the percentage of tacrolimus levels <5 ng/mL (%Tac < 5), and 5/the Morisky Scale (MS).
Results: At V1, 34 patients (37%) did not have an accessible PF. For the remaining 58 patients, the median PDC-PF was 89% (72%–99%). At least one pharmacy delivery was not reported for 34 patients (58%). In contrast, the median PDC-PR (obtained in 100% of patients) was 100% (98%–100%). The median CV was 25% (20%–31%), the %Tac < 5 median was 0% (0%–5%), and the percentage of NA-IS patients measured by the MS was 21.7% (forgetting: 15.2%, delay taking medication: 9.8%). Similar results were found at V2. At V2, the group with a PDC-PR < 90% ($n = 9$) had more forgotten doses with QM ($p = 0.03$), higher CV ($p = 0.02$), more visits missed ($p = 0.01$), and more readmissions ($p = 0.05$) than the group with PDC-PR > 90% ($n = 82$).
Conclusion: The proportion of days covered by immunosuppressive drugs calculated from the pharmaceutical file is not trustworthy. However, the proportion of days covered by immunosuppressive drugs calculated from pharmacy records seems to be a very reliable tool for measuring the NA-IS. It is also associated with appointment non-adherence and more complications leading to readmissions.

O60 IMPACT OF PHARMACEUTICAL INTERVIEW FOR RECENT RENAL TRANSPLANT PATIENTS

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Introduction: Clinical pharmacists are involved in the follow-up of renal transplant patients for the management of their immunosuppressive therapy (IS). The objective of this study was to assess the impact of a pharmaceutical interview (PI) on treatment knowledge and immunosuppressive therapy non-adherence (IS-NA).
Material and methods: 92 patients treated by tacrolimus were included between M4 and M12 post-transplantation. The first 48 patients were able to participate in a post-transplant therapeutic education program (PI- group). The other 44 had an additional PI when they were included (PI+ group). Treatment knowledge (100 points questionnaire) and IS-NA were measured at baseline and 4 months later with: the proportion of days covered by IS calculated from pharmacy records (PDC), the coefficient of variation of tacrolimus levels (CV), the percentage of tacrolimus levels <5 ng/mL (%Tac < 5), and the Morisky Scale (MS).
Results: At baseline, the 2 groups (PI− vs PI+) were comparable in terms of demographic data, treatment knowledge (73.3% vs 65.8%, $p = 0.2$), and measurement of IS-NA: PR: 100% vs 100% ($p = 0.6$), CV: 26% vs 25% ($p = 0.9$), %Tac < 5: 0% vs 0% ($p = 0.6$), MS: 19% vs 25% ($p = 0.6$). Four months later, the measure of IS-NA was similar between the groups: PR: 100% vs 100% ($p = 0.9$), CV: 17% vs 17% ($p = 0.5$), %Tac < 5: 0% vs 0% ($p = 0.3$), MS: 19% vs 33% ($p = 0.3$). However, the PI+ group had a better knowledge of its treatment (72.2% vs 83.3%, $p = 0.001$).
Conclusion: Pharmaceutical interview of renal transplant patient improves treatment knowledge but has shown no impact on early adherence. It is necessary to reassess this intervention in late renal transplant patients.

O61 INCIDENCE OF ACUTE REJECTION, *DE NOVO* DONOR SPECIFIC ANTIBODIES AND GRAFT LOSS IN LOW-IMMUNOLOGICAL RISK PATIENTS TREATED BY TACROLIMUS AND MYCOPHENOLIC ACID WITH OR WITHOUT INDUCTION THERAPY

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Introduction: The benefits of induction therapy in primary non-sensitized kidney transplant recipients receiving tacrolimus-based maintenance immunosuppressive regimen are debatable. In this retrospective study, we assessed the incidence of acute rejection, *de novo* donor-specific antibodies (*dn*DSA) and graft loss in a cohort of low-immunological risk patients.
Methods: From March 2008 to December 2015, 448 non-HLA sensitized patients undergone a first kidney transplantation and received maintenance immunosuppression based on tacrolimus, mycophenolic acid and steroids in our institution. Among the 297 kidney recipients who received induction therapy, 269 patients received IL-2 receptor blockers and 28 polyclonal antibodies. The remaining patients did not receive any induction therapy ($n = 151$).
Results: At two years following kidney transplant, biopsy-proven acute rejection occurred in 42 patients who had been given induction therapy (14.1%) and 13 patients who have not be offered induction therapy (8.6%, $p = 0.092$). Eighteen patients who received induction therapy developed *dn*DSA within the first 2 years following transplant (6.1%). Conversely, three patients without induction therapy developed at least one *dn*DSA during the same period (2.1%, $p = 0.060$). A history of T-cell mediated rejection was the main risk factor for the development of *dn*DSA in multivariate analysis (OR: 64.00 [12.46–328.67], $p < 0.001$). Patients receiving induction therapy had higher rate of graft loss than those receiving no induction therapy (HR: 6.68 [2.21–20.20], log rank test $p = 0.034$). In multivariate analysis, the main determinants of graft loss at 2 years were the recipients' age (OR: 1.10 [1.03–1.16], $p = 0.003$), the donors' creatinine level (OR: 1.01 [1.00–1.02], $p = 0.009$) and the CMV status D+/R− (OR: 12.74 [3.48–46.65], $p < 0.001$).
Conclusions: Induction therapy is not mandatory in low-immunological risk patients receiving a tacrolimus-based maintenance immunosuppression.

O62 THE MADELEINE STUDY: IMPACT OF AN DAY 1 LOW-DOSE TACROLIMUS AND EVEROLIMUS MAINTENANCE IMMUNOSUPPRESSION

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Introduction: Tacrolimus is the reference immunosuppressive drug in solid organ transplant. Its nephrotoxicity requires limiting drug exposure. An association with everolimus allows an early minimization of trough levels and offers an antiviral protection. In this study, we evaluate an immunosuppression based on tacrolimus (envarsus©) and everolimus (certican©) from day 1 in kidney transplantation.
Methods: We included 60 consecutive kidney transplant recipients transplanted in our center, provided they were DSA free and had no or a low HLA sensitization, excluding CMV D+/R− patients. An ATG induction was used in all cases. Tacrolimus and everolimus were given from POD 1, with trough levels from 5 to 7 μg/L and from 3 to 5 μg/L during the first month for tacrolimus and everolimus respectively, then from 4 to 5 and 5 to 7 from month 1. Steroids were weaned at month 3 post-transplant. No valganciclovir prophylaxis was used.
Results: Sixty patients were included in the study. Everolimus was maintained over month 3 in 53 patients (88%). Among the 60 patients, 50 had a protocol kidney biopsy at month 3, with 38 (76%) normal biopsies, 3 (6%) borderline lesions and 9 (18%) IF/TA grade 1 or 2. There was no cellular or humoral rejection. Four (6.6%) developed a DSA (max. MFI was 4845). The number of CMV replication (PCR > 3 logs/mL) was 8 (13%), without any case of CMV disease. There were 3 (6%) BK-virus replications. The median serum creatinine at time of last follow-up was 136 μmol/L. There was one single case of allograft loss (primary non-function).
Conclusion: An initial immunosuppression with low-dose tacrolimus, together with everolimus, after ATG induction, is immunologically safe and interesting from the viral point of view, in order to limit the risk of CMV and BKV replications.

O63 RESOLUTION OF RITUXIMAB POSITIVE INTERFERENCE ON COMPLEMENT-DEPENDENT CYTOTOXICITY AND FLOW CYTOMETRY B CELL CROSSMATCHES IN ALLOGENEIC KIDNEY TRANSPLANTATIONS

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Background: Therapeutic antibodies (Abs), such as Rituximab (RTX) may interfere with the lymphocytotoxicity (LCT) and flow cytometry (FC) crossmatches (XM). RTX, the first anti-CD20 monoclonal Ab released, mimics a donor-specific anti-HLA Ab, resulting in false-positive B cells LCT or FC XM. In the setting of kidney transplantation, RTX is currently used in ABO or HLA desensitization protocols, in humoral rejection and in ANCA-associated vasculitis or other autoimmune diseases. Access to transplantation may be delayed for some kidney transplantation candidates, especially those treated by multiple infusions of RTX, because of difficulties in the interpretation of the XM results.
Methods: A RTX immunodepletion protocol using a specific anti-RTX Ab (clone MB2A4, Bio-Rad©) coupled with magnetic beads (BioMag®Plus, COOH, Bangslab©) was developed. Measurement of RTX concentration in serum samples was performed by solid-phase assay (ELISA). LCT and FC XM were processed simultaneously on the original sera and the depleted ones. Identification of anti-HLA Abs by Luminex© Single Antigen assay was performed in the sera to ensure that depletion was restricted to RTX and preserved other Abs, like anti-HLA Abs.
Results: We were able to fully deplete without any dilution, up to 3 μg/mL of RTX corresponding of 100 days after 2 infusions (375 mg/m² of body surface area each). LCT and FC XM turned negative with depleted sera. Thus, the interference of RTX on XM techniques can be resolved. Of note, specificities and MFI of anti-HLA Abs were unchanged after depletion.
Conclusion: RTX can be effectively removed from sera using magnetic beads conjugated with a specific anti-RTX Ab. These results demonstrate the feasibility and the efficacy of our fast, easy and routinely-suitable method. By restoring the interpretability of the XM, the patients awaiting for a kidney transplant and treated by multiple infusions of RTX may beneficiate of improved access to transplantation.

BASIC TRANSPLANTATION

O64 DYNAMIC TRANSCRIPTOMIC ANALYSIS OF ISCHEMIC INJURY IN A PORCINE PRE-CLINICAL MODEL MIMICKING DONORS DECEASED AFTER CIRCULATORY DEATH

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Introduction: Due to organ shortage, clinicians are prone to consider alternative type of organ donors among them donors deceased after circulatory death (DCD). However, especially using these organs which are more prone to graft dysfunction, there is a need to better understand mechanistic events occurring during ischemia phase and leading to ischemia/reperfusion injuries (IRI). The aim of this study is to provide a dynamic transcriptomic analysis of preclinical porcine model kidneys subjected to ischemic stress mimicking DCD donor.
Methods: We compared cortex and corticomedullary junction (CMJ) tissues from porcine kidneys submitting to 60 min warm ischemia (WI) followed by 0, 6 or 24 h of cold storage in University of Wisconsin solution versus control non-ischemic kidneys (n = 5 per group).
Results: 29 cortex genes and 113 CMJ genes were significantly up or down-regulated after WI versus healthy kidneys, and up to 400 genes were regulated after WI and more 6 or 24 h of cold storage ($p < 0.05$). Home selected gene kinetic classification, Gene-ontology-biological processes and Gene-ontology-molecular-function functional enrichment analysis revealed relevant genes implication during WI and cold storage.
Conclusion: We uncovered targets which we will further validate as biomarkers and new therapeutic targets to optimize graft kidney quality before transplantation and improve whole transplantation outcome.

O65 PREVENTIVE GC7 REDUCES BRAIN DEATH-INDUCED RENAL INJURIES IN A PRECLINICAL KIDNEY TRANSPLANTATION PORCINE MODEL

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Introduction: N1-guanyl-1,7-diaminoheptane (GC7), an inhibitor of eIF5A hypusination, protects from ischemic injuries. Thus, GC7 could be useful in order to precondition kidneys from donors before transplantation process.
Methods: Using a pig brain-death (BD) donation preclinical model, we carried out the *in vivo* evaluation of GC7 pre-treatment (3 mg/kg iv bolus, 5 min after BD), at the beginning of the 4 h-donor management, after which kidneys were collected, cold-stored (18 h in UW), and one was allo-transplantated in a double-nephrectomized recipient. Groups were defined as following: (n = 6 per group): healthy (CTL), untreated BD (Vehicle) and GC7-treated BD (GC7).
Results: At the end of 4 h-management, GC7 decreased BD-induced markers (i) eIF5A hypusination, (ii) tissue levels of reactive oxygen species markers, and (iii) the mitochondrial-dependent apoptosis pathway (Bax and cleaved Caspase-9). In addition, GC7 increased (2 to 6-fold, $p < 0.05$) the expression of anti-oxidant proteins (SOD2, HO-1, PGC1a, NRF2, and total & phosphorylated-Sirtuin1 & 3). At the end of cold storage, GC7 treatment induced an increase of NRF2 and PGC1a mRNA and a better mitochondrial integrity/homeostasis with an increase of the Bcl-2/Bax anti-apoptotic ratio, MFN2 and mTOR proteins ($p < 0.05$). GC7 treatment significantly improved the kidney outcome during 3 months follow up after transplantation, decreasing NGAL and creatinine blood levels, as well as fibrosis.
Conclusion: At the brain-death donor management phase, GC7 treatment protected kidneys from brain-death-induced injuries; during the cold storage phase, GC7 appeared to preserve antioxidant defences and to protect mitochondria. Thus, pre-treatment with GC7 can be used to precondition the graft leading to better early and long-term function post-transplantation.

O66 GENETIC DELETION OF DUSP3 PHOSPHATASE ATTENUATES KIDNEY DAMAGE AND INFLAMMATION FOLLOWING ISCHEMIA/REPERFUSION IN MOUSE

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Background: Renal ischemia-reperfusion (I/R) injury is the leading cause of acute kidney injury (AKI). Dual Specificity Phosphatase 3 (DUSP3, also called *Vaccinia*-H1 Related (VHR)) is highly expressed in endothelial cells, as well as in platelets, monocytes and macrophages. Since DUSP3 is a positive regulator of the innate immune response, its inactivation/deletion may attenuate kidney inflammation and damage caused by I/R.
Methods: Ten-weeks-old C57BL/6 wild-type (WT, n = 10) versus DUSP3 systemic knock-out (KO, n = 10) mice underwent unilateral left renal ischemia for 30 min. Right nephrectomy was simultaneously performed. The left kidney was excised and blood sample was collected from *inferior vena cava* at 48 h *post* reperfusion. Renal function was assessed upon blood urea nitrogen (BUN) levels. Expressions of inflammatory and immune markers were comparatively quantified at both mRNA and protein levels in I/R kidneys in DUSP3 WT vs KO mice. Renal distribution of DUSP3 was established by immunofluorescence.
Results: DUSP3 was detected in glomeruli and endothelial cells of outer and inner medulla. Following renal I/R, BUN was significantly lower in KO mice. DUSP3 KO I/R kidneys showed a reduced number of PCNA-, CD11b- and F4-80-positive cells compared to WT. The protein levels of CD11b and HSP70, as well as PCNA, were significantly lower in DUSP3 KO vs WT I/R kidneys. Conversely, an increase of anti-inflammatory M2 macrophages was observed in DUSP3 KO I/R kidneys. At transcriptional levels, DUSP3 KO I/R kidneys showed a significant downregulation of IL-6, *CD11b*, IL-1b, *TNF-a* and *KIM-1* compared to WT. Quantification of *DUSP3* mRNA showed a significant increase in I/R kidneys, as confirmed by immunofluorescence.
Conclusions: Genetic deletion of DUSP3 attenuates renal I/R-associated damage and inflammation.

O67 EARLY FUNCTIONAL RECOVERY OF ISCHEMIC PORCINE KIDNEYS PERFUSED *EX VIVO* WITH AUTOLOGOUS WHOLE-BLOOD, AFTER NORMOTHERMIC PRESERVATION WITH IMPROVED AQIX® RS-I SOLUTION – COMPARISON TO OXYGENATED HYPOTHERMIC MACHINE PRESERVATION

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Background: To preserve high-risk kidneys, Ex Vivo Normothermic Perfusion (EVNP) gains momentum, but optimal conditions need to be defined. We explore functional recovery of ischemic ("high-risk") grafts perfused with autologous whole-blood, after preservation with a modified Aqix solution versus oxygenated Hypothermic Machine Perfusion (HMP).
Methods: *Warm ischemia* 80 min. *Preservation*: Normothermic Perfusion, NP (80 mmHg, carbogen, 6 h) with Aqix supplemented with PEG (35kD, 30 g/L) and Amino Acids (1%; n = 5) or Hypothermic perfusion, HP (4°C, KPS, 100% O_2, KidneyAssist®, 12 h; n = 5). *Perfusion*: whole-blood EVNP-perfusion (37°C, heparin 5000 UI/L, 80 mmHg, carbogen, 3 h).
Results (Perfusion phase): R1. Aqix-EVNP kidneys (group NP) are less resistive (0.8 vs 2.0 mmHg.min/mL, $p < 0.01$) and less injured (LDH: 0.6 vs 15.0 U/min; urine proteins: 1.0 vs 2.2 g/L, $p < 0.05$), than KPS-hypothermic kidneys (group HP), but they consume more O_2 (82 vs 26 μmol/min, $p < 0.005$). R2. Glomerular filtration (0.9 vs 1.4 mL/min), urine production (0.4 et 0.7 mL/min) and sodium reabsorption (80 vs 102 μmol Na/min) are similar. R3. HMP kidneys (HP) present better transport efficiency TNa/QO_2: 3.9 vs 1.0 μmol Na/μmol O_2, $p < 0.01$) and urine acidification (7.07 vs 7.8 upH, $p < 0.05$)
Conclusion: On general grounds, EVNP-preserved grafts exhibited a comparable renal functional panel to KPS-HMP grafts', but their resistance was lower and closer to current clinical evaluation criterium. With appropriate modifications (colloid, metabolites,...), remaining to be improved, the interstitial-like solution Aqix® RS-I appears as a possible solution to be used for normothermic preservation. A porcine autotransplantation study, comparing Aqix-EVNP vs KPS-HMP preservation, is under analysis. Preliminary observations point at the feasibility and viability of improved Aqix for NT preservation/reconditioning of high-risk renal grafts.

O68 ROLE OF γδ T CELLS IN DONOR SPECIFIC ANTIBODY GENERATION

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Introduction: The generation of donor-specific antibodies (DSA), the leading cause of failure in transplantation, requires that alloreactive B cells receive T-cell (LT) help. According to the molecular nature of the TCR, two main types of LT are distinguished: α/β or γ/δ.

While the importance of LTα/β in the generation of DSA is well established, the implication of LTγδ is unknown. Data from the literature suggest that LTγδ could i) directly help B cells (like LTα/β follicular helper) or contribute indirectly by activating LTα/β by presenting them with antigen.
Methodology: The heart of Balb/c (H2d) mice was transplanted to 4 types of C57BL/6 (H2b) recipients: (i) wild type (with LTα/β and γ/δ), (ii) CD3ε KO (deficient for both LTα/β and LTγ/δ), (iii) TCRα KO (deficient in LTα/β only), or iv) TCRδ KO (deficient in LTγδ only). The DSA titre was quantified before and after each week post-transplant by flow crossmatch.
Results: The 4 recipient strains had the expected T cell phenotype and a B cell compartment quantitatively and functionally normal. Unlike wild-type mice, mice without T cells did not develop DSA after heart transplantation. While mice without LTα/β did not develop DSA, mice without LTγδ showed a similar DSA response to wild-type mice.
Conclusion: Our results confirm the importance of LTα/β in DSA generation and suggest that LTγ/δ are not involved in this process. A clinical study is underway to validate this hypothesis clinically.

O69 QUANTIFICATION AND PHENOTYPIC ANALYSIS OF CIRCULATING FOLLICULAR HELPER T-CELLS IN IMMUNIZED KIDNEY TRANSPLANT PATIENTS: CASE-CONTROL STUDY

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Introduction: The leading cause of renal transplant failure is antibody-mediated rejection due to donor-specific anti-HLA antibodies (DSA). The currently limited efficacy of the treatments indicates the need for individual predictive markers of the DSA appearance. The production of DSA requires the prior activation of follicular helper T-cells (TFH, $CXCR5^+CD4^+$) and some of their subfamilies in lymphoid tissues. There are circulating TFHs (cTFH) expressing the same markers whose number and activation characteristics may vary according to those of their lymphoid organ counterparts. The aim of this work was to study if there was a correlation between the presence of DSA and the quantification of these different populations of cTFH. Methodology: we performed a case-control study including 17 "case" patients presenting *de novo* DSA and 26 non-immunized "control" patients matched for time since transplantation, age, number of HLA mismatches, immunosuppression at the time of transplantation and at the sampling day. We quantified the cTFHs and their TFH1 ($CXCR3^+CCR6^-$), TFH2 ($CXCR3^-CCR6^-$), TFH17 ($CXCR3 \pm CCR6^+$), TFH regulatory ($foxp3^+$) subpopulations and we analyzed activation markers (PD1, ICOS) and proliferation markers (ki67) as well. Results: we did not observe any difference between the two groups for the proportion of cTFH among $CD4^+$ T lymphocytes nor for their subpopulations among cTFH. We found no correlation between cTFH level and time since transplantation. Conclusion: our study found no correlation between the characteristics of cTFH and the presence of DSA. A prospective study analyzing individual kinetics of cTFH and anti-HLA antibodies may be able to highlight such a correlation.

O70 DONOR-SPECIFIC CAR REGULATORY T CELLS RESTRAIN HUMORAL ALLOREACTIVITY IN DRUG-FREE IMMUNOCOMPETENT ALLOGRAFT RECIPIENTS

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Introduction: Administration of regulatory T cells with direct donor specificity (dTreg) limits cellular alloreactivity in preclinical allograft models. These data have led to phase I clinical trials in transplant recipients with the aim of using this approach to minimize immunosuppression. However, immunosuppression minimization comes with the increased risk of alloantibody-mediated graft loss and the ability of dTreg to limit humoral alloreactivity is unknown. We analyzed the impact of dTreg generated with a chimeric antigen receptor (CAR) on the humoral alloimmune response in fully immunocompetent murine skin allograft recipients in the absence of immunosuppressive drugs.
Methodology: FOXP3^{+} Tregs were sorted from B6$^{Foxp3\text{-}Gfp}$ reporter mice, TCR stimulated and transduced with a HLA-A2-specific CAR (A2-CAR dTreg) or a HER-2-specific CAR (control-CAR Treg). After 7 days, 1.10^{6} of A2-CAR or control-CAR Treg were intravenously injected to WT B6 mice. Mice received a skin graft from a HLA-A2 transgenic B6 donor the day of Treg injection and the anti-HLA-A2 humoral response was monitored by ELISA and ELISPOT (n = 14 mice/group).
Results: A2-CAR dTreg significantly prolonged skin allograft survival as compared to control-CAR Tregs ($p < 0.001$). A2-CAR dTreg recipients had significantly lower levels of circulating donor-specific IgG antibodies (anti-HLA-A2 DSA, 7499 $\pm$ 4850 vs 19069 $\pm$ 19068 A.U. for A2-CAR dTreg and control-CAR Treg respectively, $p = 0.02$). At the peak of the humoral response (day 21), the frequency of anti-HLA-A2-secreting cells was significantly lower in A2-CAR dTreg recipients (19.5 $\pm$ 14.7 vs 63.2 $\pm$ 30.0 for A2-CAR dTreg and control-CAR Treg respectively, $p = 0.049$).
Conclusion: These data are the first evidence that CAR dTregs therapy restrains humoral immunity in allograft recipients in the absence of adjunct immunosuppression and support the design of immunosuppression minimization strategies in transplant patients receiving dTreg therapy.

O71 VALIDATION OF AN INTEGRATIVE PROGNOSTIC SCORE FOR RESPONSE TO THERAPY IN SOLID ORGAN TRANSPLANTS

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Introduction: Drug development in transplantation has diminished due to the lack of suitable endpoints. We sought to validate the performance of an integrative scoring system for predicting long-term kidney allograft loss in the setting of therapeutic interventions.
Methods: We used an integrative risk-scoring system previously derived and validated in an international cohort comprising 5,125 kidney transplant recipients. The risk score is based on clinical, biochemical, immunological and histological parameters measured after transplant. We included patients who underwent therapeutic interventions following standardized protocols for antibody-mediated rejection (ABMR), T-cell mediated rejection (TCMR) and CNI toxicity.
Results: 484 patients were included: 224 receiving SOC ABMR treatment; 143 SOC TCMR treatment and 117 receiving Belatacept. The prognostic risk score was significantly modified by the therapeutic interventions (mean risk score of 3.01 $\pm$ 0.79 at the time of treatment versus 2.71 $\pm$ 0.82 after treatment, $p < 0.001$). 2 prototypes of patients were identified by the risk score: i) Group 1 showing decreasing predicted probability of graft loss after treatment (responders, 68%); ii) Group 2 showing stable or increased predicted probability of graft loss after treatment (non-responders, 32%). The risk score prediction capability of individual patient allograft loss was highly accurate (C-index 0.84; 95% CIs = 0.80–0.89). The calibration plot showed an optimal agreement between the risk score and the actual observation of kidney allograft loss.
Conclusion: This integrative risk scoring system for allograft loss showed high performance in the setting of therapeutic interventions. Our result suggests that this scoring system could be used as a valid surrogate endpoint for next-generation multicenter trials and in the approval of drugs in solid organ transplantation.

O72 POPULATION-BASED MODELING OF PROTOTYPES AND DETERMINANTS OF ALLOGRAFT FUNCTION TRAJECTORIES AFTER KIDNEY TRANSPLANTATION: IMPACT FOR PATIENT MONITORING AND RISK STRATIFICATION

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Introduction: Although the current gold standard of kidney allograft patients monitoring relies on glomerular filtration rate (GFR) assessment, little is known about the profiles of long-term GFR trajectories and their determinants at a population level. Such information would have substantial value for improving risk stratification in kidney transplantation.
Methods: We assembled an international cohort of kidney transplant recipients at 15 referral centers (10 in Europe and 5 in the US) from 2001 to 2016. Patients underwent assessment of clinical, histological and immunological parameters, as well as repeated estimated GFR measurements (eGFR, MDRD equation). Latent class mixed models (LCMM) were performed to determine profiles of patient's eGFR trajectories. Multinomial regression models were used to assess patient and allograft characteristics associated with the eGFR trajectory profiles.

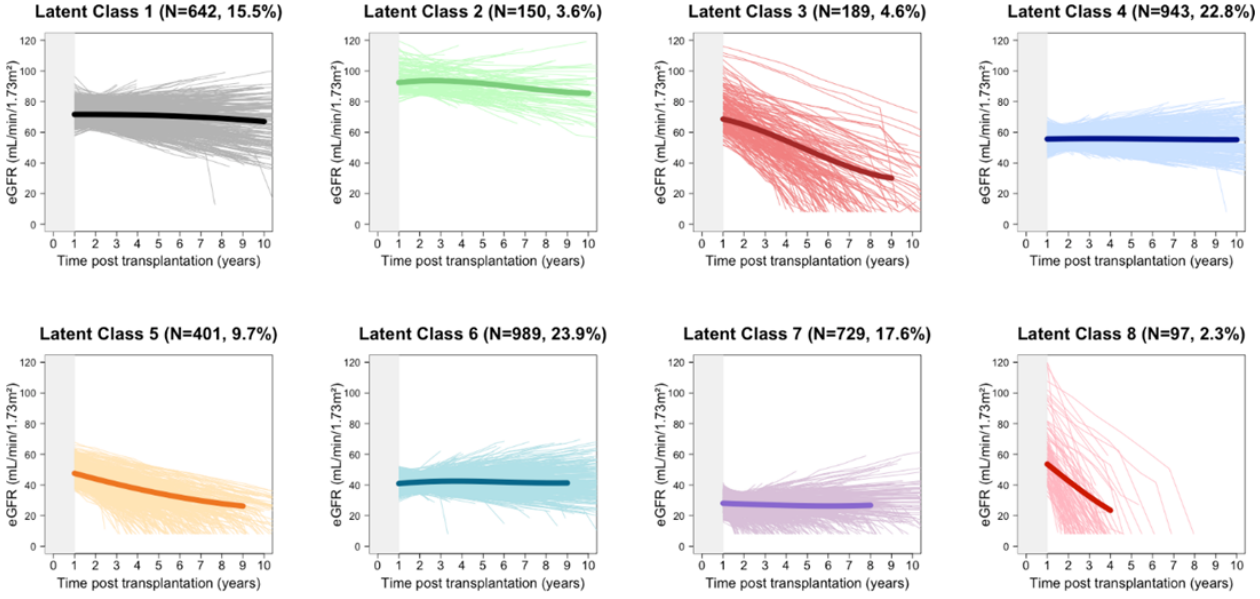

Figure 1 Latent classes of eGFR in the development cohort.

Results: A total of 10,194 patients were included (n = 4,140 in the development cohort, n = 6,054 in the validation cohorts), with 116,328 eGFR measures analyzed (median follow-up time post-transplant of 6.5 years). Overall, we identified 8 latent classes of eGFR (fig 1). The determinants of the latent classes were the recipient age and gender, the expanded criteria donor, the delayed graft function, and assessed at 1-year: the microvascular inflammation, the presence of DSA, the proteinuria and the first value of eGFR. We confirmed that the same 8 phenotypes of eGFR trajectories were conserved in validation cohorts.
Conclusion: With this population-based study, we identified for the first time universal profiles of eGFR trajectories. These profiles allow to stratify the long-term evolution of renal function in kidney recipients. Our results provide the basis for a dynamic approach of the risk stratification in kidney transplantation.

INFECTIONS

O73 THE TRANSFORM STUDY: INFECTION OUTCOMES WITH EVEROLIMUS PLUS REDUCED CALCINEURIN INHIBITOR AND MYCOPHENOLATE PLUS STANDARD CALCINEURIN INHIBITOR REGIMENS IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS

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Background: Post-transplant [Tx] bacterial and viral infections are known to affect graft and patient survival. Accumulating evidence supports the protective effect of everolimus [EVR] against viral infections, especially cytomegalovirus [CMV] infections, in kidney transplant recipients [KTxRs]. Here, we report 24 months [M] results on the incidence of infections in de novo KTxRs receiving EVR+reduced calcineurin inhibitor [rCNI] versus mycophenolic acid [MPA]+standard CNI [sCNI] regimen from the TRANSFORM study.
Methods: TRANSFORM (NCT01950819) is a 24M, multicenter, open-label, two-arm study in which de novo KTxRs were randomized (1:1) within 24 h post-Tx to receive either EVR+rCNI (N = 1022) or MPA+sCNI (N = 1015), with induction and steroids. Viral (CMV and BKV) and bacterial infection rates were assessed by treatment and/or serology type.
Results: The overall infection rate was lower with EVR+rCNI than MPA+sCNI regimen (57.6% vs 65.6% respectively, $P < 0.001$). EVR+rCNI regimen also showed lower incidence of viral (20.5% vs 35.3%, $P < 0.001$) and bacterial infections (37.9% vs 40.6%, $P < 0.001$) than MPA+sCNI. The overall incidence of CMV infections was significantly lower with EVR+rCNI vs MPA+sCNI regimen (3.6% vs 13.3%, $P < 0.001$). Though baseline CMV status was comparable between arms, CMV incidence was significantly lower in EVR+rCNI vs MPA+sCNI arm among high risk patients with serology status D+/R+ (5.4% vs 12.8%, $P = 0.004$) and D+/R− (18.8% vs 43.7%, $p < 0.001$). The overall rates of BKV infection reported as adverse event were also significantly lower in EVR+rCNI vs MPA+sCNI arm (10.2% vs 15.2%, $p < 0.001$).
Conclusions: M24 results from TRANSFORM, the largest KTx study to date, confirmed the benefit of early EVR introduction in preventing viral infection in de novo KTxRs.

O74 REAPPRAISAL OF ANTI-THYMOCYTE GLOBULIN INDUCTION DURING CMV INFECTION: THE RISK IS INCREASED IN R+ BUT NOT IN D+R- KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Cytomegalovirus (CMV) guidelines consider that induction therapy with rabbit anti-thymocyte globulin (rATG) is at increased risk of CMV infection, particularly in the most exposed group (D) positive, recipient (R) negative (D+R−) kidney transplant recipients (KTR). Nevertheless, analysis on a consequent cohort comparing rATG and anti-interleukin 2-receptor antibody (IL2RA), separately in D+R− and R+ patients have not been performed yet to reappraise this risk in those two populations.
Methods: We compared the incidence of CMV infection in R+ and D+R− KTR in three cohorts of 1214 KTR, receiving either rATG or anti-IL2RA. We performed survival curve analysis, and a multivariate analyse for CMV incidence in each group and in each cohort. Then, we analyzed CMV incidence with rATG and anti-IL2RA in patients separately with or without preformed IE1 CMV-specific cell-mediated immunity (CMV-specific CMI). To finish, we analyzed longitudinally the CMV-specific CMI comparing patients with rATG or anti-IL2RA in the whole cohort, then separately in patients with and without preformed CMV-specific CMI.
Results: We showed, in a first discovery set, then confirmed, in two replication sets, that rATG increases the risk of CMV infection in R+ but not in D+R- KTR, regardless the type of CMV preventive strategy. Following multivariate analysis, rATG was an independent and reproducible risk factor for CMV infection, only in R+ and not in D+R- KTR. Thereafter, we found that within patients with preformed CMV-specific CMI, those receiving rATG exhibited higher CMV infection risk than those treated with anti-IL2RA. Longitudinal analysis of CMI showed that rATG, only in R+ KTR, was associated with a severe abrogation of the preformed CMV-specific CMI.
Conclusion: rATG induction therapy, compared to anti-IL2RA, adds no further risk of CMV infection in D+R- KTR but an increased risk in R+ KTR, who requires a risk-adapted preventive strategy and closer follow-up.

O75 MONITORING HEPATITIS E VIRUS IN STOOLS TO ADJUST RIBAVIRIN THERAPY DURATION IN CHRONICALLY INFECTED SOLID-ORGAN-TRANSPLANT RECIPIENTS

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Introduction: Hepatitis E virus (HEV) is a leading agent of viral hepatitis worldwide. Even if most HEV infections cause self-limiting hepatitis in immunocompetent subjects, HEV genotype 3 can progress to chronic hepatitis in immunosuppressed patients. Ribavirin has been shown to be efficient for treating chronic HEV infection but the optimal duration of therapy is still undetermined. In this setting, persistence of HEV shedding has been related to relapse after ribavirin cessation.
Methods: Between September 2009 and September 2017, 48 chronically infected solid-organ-transplant recipients for whom HEV RNA was assessed in blood and stools at the end of the scheduled ribavirin therapy were included in this retrospective study. We compared the sustained virological response at 24 weeks after ribavirin cessation (SVR24) in patients for whom ribavirin treatment was prolonged when HEV RNA was still detectable only in the stools at 12 weeks, to a historical group of patients in whom ribavirin was systematically stopped at the end of scheduled therapy.
Results: All patients were given initially ribavirin for 12 weeks. Thirty-five had undetectable HEV RNA in the blood and stools at the end of scheduled therapy. Three of them relapsed after ribavirin cessation (SVR24: 91.4%). Thirteen had undetectable HEV RNA in the blood but persistent HEV shedding at the end of

scheduled therapy. Six of these 13 patients stopped ribavirin as scheduled, and all of them relapsed (SVR24: 0%), while in the 7 other patients ribavirin therapy was prolonged to 24 weeks and all but one achieved SVR (SVR24: 85.7%, p = 0.005).
Conclusions: This retrospective study shows that monitoring HEV RNA in the stools can be a useful tool in determining the optimal duration for ribavirin therapy for chronic HEV infections. Prolonging ribavirin therapy in patients with persistent HEV shedding in feces is efficient to improve SVR24 rate.

O76 HEPATITIS E VIRUS GENOTYPE 3 AND CAPSID PROTEIN IN URINE OF INFECTED SOLID-ORGAN-TRANSPLANT RECIPIENTS

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Introduction: Hepatitis E virus genotype 3 (HEV3) is responsible for acute and chronic hepatitis in solid-organ-transplant recipients. HEV was recently found in the urine of some acutely and chronically genotype 4-infected patients. We investigated the urinary excretion of HEV3 by solid-organ-transplant recipients during the acute phase of infection. We also assessed the values of urinary and serum HEV antigen (Ag) concentrations as indicators of the development of a chronic infection.
Methods: We examined the urinary excretion of HEV3 by 24 consecutive solid-organ-transplant recipients at the acute phase of HEV hepatitis and characterized the excreted virus.
Results: Urinary HEV RNA was detected in half of the patients (12 out of the 24) and urinary HEV Ag was detected in all but one (96%). The density of RNA-containing HEV particles in urine was low (1.11–1.12 g/cm^3), corresponding to lipid-associated virions. The urinary HEV Ag and HEV RNA sedimented independently in iodixanol density gradients, suggesting that most of the HEV Ag was not associated with infectious virions. The urinary HEV RNA/Ag detected was not associated with impaired kidney function or *de novo* proteinuria. Finally, there was more HEV Ag in the serum at the acute phase of HEV infection in solid-organ-transplant recipients whose infection became chronic.
Conclusions: HEV is frequently excreted in the urine of HEV3-infected solid-organ-transplant recipients without impairing renal function. The excreted urinary particles has a lipid envelope. Urinary HEV Ag was a sensitive indicator of HEV infection as was HEV Ag in serum. Acute phase serum HEV Ag was a good prognostic marker for the development of a chronic HEV infection.

O77 SUSTAINED VIROLOGICAL RESPONSE AT WEEKS 12 FOR PREDICTING OVERALL THERAPEUTIC SUCCESS AFTER RIBAVIRIN TREATMENT IN CHRONICALLY HEPATITIS E VIRUS-INFECTED SOLID-ORGAN-TRANSPLANT RECIPIENTS

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Introduction: Hepatitis E virus (HEV) is a major causative agent of chronic hepatitis in immunocompromised patients. A 12-weeks ribavirin treatment is currently recommended as first-line therapy for immunosuppressed patients with persisting HEV replication. The sustained virological response 24 weeks after ribavirin cessation (SVR24) has been mostly used to define overall SVR by analogy to hepatitis C virus infection management. In this retrospective study, we assessed the concordance between SVR24 and SVR12 in a cohort of chronically HEV-infected solid-organ-transplant patients.
Methods: Between September 2009 and August 2017, 70 solid-organ-transplant recipients developed a chronic HEV infection in Toulouse University Hospital and benefited of ribavirin therapy. All patients were treated for at least 3 months with a median ribavirin dose of 600 [600–800] mg per day. A relapser was defined as a patient who achieved an end-of-treatment response (HEV RNA undetectable in blood after a 12-week ribavirin treatment) but in whom HEV RNA reappeared in the blood after ribavirin cessation.
Results: Among the 70 patients, 3 were non-responders with persistence of HEV RNA detection in the blood at the end of a prolonged 24 weeks ribavirin therapy and were excluded from the subsequent analysis. Fifty-four among the 67 remaining patients achieved an SVR24 (80.6%). Thirteen patients experienced a relapse within 73 [30–90] days following the end of ribavirin treatment. All relapses occurred within 12 weeks post-ribavirin cessation, thus the concordance between SVR12 and SVR24 was 100%. Time to relapse was not different between patients with persisting HEV RNA in feces at the end of treatment (52 [21–86] days, n = 6) and those without (83 [45–92] days, n = 7; p = 0.331).
Conclusions: In this large retrospective study, we showed that an SVR at weeks 12 post-ribavirin cessation was concordant to SVR at weeks 24.

O78 MICROBIOLOGICAL EPIDEMIOLOGY OF PRESERVATION FLUIDS IN KIDNEY TRANSPLANT RECIPIENTS: A NATIONWIDE OBSERVATIONAL STUDY

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Introduction: During the immediate aftermath of a kidney transplantation, there is a risk of nosocomial infections transmitted from the donor to the recipient. Microbiology of kidney graft preservation fluid (PF) is systematically analyzed. In case of a positive culture, the risk for the recipient is poorly known. The indication of antibiotic therapy is discussed.
Methods: Based on data recorded by the French Biomedicine Agency (CRISTAL), we conducted a retrospective study between October 2015 and December 2016 analysing donor characteristics, presence of infection in the donor, transplantation data, recipient data (age, patient and graft survival) and microbiological analysis of PF.
Results: Of 4 487 kidney transplants, including 725 (16.2%) from living donors (LD), 20.5% were performed with kidney graft whose PF microbiological analysis were positive (1.8% with LD, 24.1% with deceased donor). 59.9% of positive PF were polymicrobial. Main germs identified were coagulase-negative Staphylococci (65.8%) followed by *Enterobacteriaceae* (28%). PF culture matched with donor germs in 1.1% of cases. In multivariate analysis, risk factors of positive culture of PF from deceased kidney donors were : digestive perforation during procurement (OR 4.4 (2.1; 9.1)), multi-organ versus renal procurement alone (OR 1.4 (1.1; 1.7)), *en bloc* kidney transplantation (OR 2.5 (1.3; 4.9)). Perfusion pump and antibiotic therapy of the donor were associated with a lower risk of positive PF culture (OR 0.4 (0.3; 0.5; 0.5) and 0.6 (0.5; 0.7) respectively).
Conclusion: PF does not appear to be a vector of infections transmitted from donor to recipient. Contamination of PF appears to occur at the surgical time of procurement.

O79 MANAGEMENT OF CULTURE-POSITIVE PRESERVATION FLUIDS BY KIDNEY ORGAN TRANSPLANT SPECIALISTS: A NATIONWIDE QUESTIONNAIRE SURVEY

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Introduction: During peri kidney transplantation (KT) period, there is no recommendations about preventive antibiotic therapy, who are based on local or individual practices. The objective of our survey is to establish an overview of these practices in KT centers in France.
Methods: We conducted a national questionnaire survey sent by email to a panel of hospital practitioners involved in the perioperative management of KT recipients. Results are analyzed according to microbiological results of the preservation fluid (PF) and associated comorbidities.
Results: 182/427 (42.6%) recipients replied. 167 were eligible to participate in the survey (residents N = 68/134 (50.7%), seniors N = 99/293 (33.8%)). Positivity of PF to *Staphylococcus aureus* methicillin sensitive leads to the prescription of antibiotics in 35% of respondents. The presence of diabetes, obesity or delayed graft function does not modify the use of antibiotic therapy (36%, 35% and 37%). Bacteria that provide the most antibiotic therapy are *Pseudomonas aeruginosa* (67%) and extended spectrum beta-lactamase-producing *Klebsiella pneumoniae* (57%). 77% of respondents report the existence in their center of a surgical antibioprophylaxis protocol for KT, 16% of respondents report a formalized prescription procedure in the event of positive PF bacteriological culture, and 13% of respondents report a protocol for systematic prescription of antibiotics as preventive measure in immediate post-KT.
Conclusion: Individual preventive antibiotic prescribing practices in the peri-KT period vary a lot in France. Microbiology of PF seems impact practices. To prevent antibiotic overuse and bacterial resistance, recommendations based on these practice data compared to biovigilance data should be established.

O80 NEW INSIGHT ON ESRD AND HEALTHY INDIVIDUALS' GUT BACTERIAL TRANSLOCATION

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Introduction: Chronic kidney disease (CKD) induces a structural and functional disruption of the intestinal epithelial barrier, leading to a gut bacterial translocation (GBT). The exposure to bacterial structures such as lipopolysaccharides (LPS) from Gram-negative bacterial cell wall yields an inflammatory response mediated by the innate immunity. LPS structure, especially the structural variations of its lipid A, determines LPS immunogenicity and therefore its biological function. In this study, we compared the activity and the quantity of circulating LPS between end-stage renal disease (ESRD) patients and healthy volunteers (HV).
Method: Plasma samples from 20 HV and 68 patients with ESRD were collected in the GABII cohort. Bioactivity and quantification of LPS was performed by the *Limulus amebocyte* lysate (LAL) assay, and high performance liquid chromatography coupled to mass spectrometry (HPLC/MS/MS) method respectively.
Results: Surprisingly, total LPS concentration was higher in the healthy group (817.9 ± 34.3 vs 445.8 ± 19.6pmol/mL; $p < 0.0001$) with a significant difference in the composition of translocated LPS according to the length of lipid A carbon chains. Moreover, the LPS activity to mass ratio was significantly lower in HV than ESRD patients ($4.7 \times 10^{-4} \pm 1.1 \times 10^{-4}$ vs $9.3 \times 10^{-4} \pm 0.7 \times 10^{-4}$ EU/pmol; $p < 0.0001$). In summary, the amount of total LPS is higher for HV than ESRD patients but its activity remains relatively lower, suggesting a better LPS neutralization in this control group.
Conclusion: Hence, GBT exists even in healthy context. Septic inflammation observed in ESRD is not related to higher amount of GBT but to difference in circulating LPS subtypes and to a lesser capacity of LPS neutralization compared to healthy individuals. This suggests that interventions should focus on both modification of gut microbiota and improvement in LPS neutralization.

O81 NATURAL HISTORY AND DETERMINANTS OF INFECTIOUS COMPLICATIONS AFTER KIDNEY TRANSPLANTATION: A NATIONWIDE PROSPECTIVE POPULATION BASED COHORT

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Background: Although Infectious complications are a major cause of morbidity and mortality in KTR, little is known about their natural history and determinants at a population level.
Methods: Nationwide cohort including all consecutive KTR from 6 French centers from 2000 to 2012 with prospective uniform and quality-checked extensive data collection including a systematic record of post-transplant infectious complications (site and pathogen involved).
Results: 7,621 KTR were included with a median follow-up time post-transplant of 6 years (IQR 4–10. During the follow-up, 9,457 infectious complications were diagnosed in 4307 patients. The first infection episode occurred after a median 230 days (IQR 35–1094) after KT. Infections were bacterial (n = 4951, 52%), viral (n = 1,556 16%), fungal (n = 327, 3%), parasitic (60, 0.4%) and from unknown pathogen (2,726, 29%). Main sites were upper genito-urinary tract (n = 3,365, 36%), followed by lower respiratory tract (2,726, 29%), skin and soft tissue (960, 10%), GI tract (n = 770, 8%). Main pathogens were Enterobacteriaceae (2,772, 29%), Staphylococcus (520, 5%), VZV (479, 5%), Pseudomonas (351, 3.7%), CMV (412, 4.3%), BK virus nephritis (184, 2%), norovirus (134, 1.4%); Candida (110, 1.2%), P. jirovecii (107, 1.1%), and Aspergillus (69, 0.7%). The main independent determinants of infection were: recipient and donor age, female gender, history of diabetes, hypertension, major cardiovascular events, cold ischemia, induction treatment, eGFR at 1-year post KT, acute rejection, and graft rank.
Conclusion: This is the first population-based assessment of infections after KT. These results suggest the potential for a data driven approach of infectious disease for improving patients risk stratification that would help clinicians in the clinical management and immunosuppressive regimens adaptation.

BEST ABSTRACTS

O82 BELATACEPT FOR HEART AND LUNG RECIPIENTS

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Introduction: Belatacept (BTC) is a CTLA4Ig available since 2011 for prophylaxis of graft rejection in adult renal transplantation (Tx). Data in heart and lung Tx are scarce. The aim of this study was to describe terms and conditions of BTC use as an option in these recipients.
Methods: Observational study in 2 French centers including all patients receiving BTC after heart or lung Tx from 01/2014 to 06/2018. The primary outcome was the evaluation of tolerance, the secondary the management of other immunosuppressive therapies.
Results: 25 patients (4 females) included (2 lung- and 23 heart-recipients, including 4 heart+kidney and 1 heart+liver), mean age 45.9 ± 13.3 years [23–67] when Tx occurred, at 9 [0–317]months after Tx (early introduction in 9 patients), EBV+, with a mean GFR of 40 ± 22 mL/min. BTC was prescribed to spare renal function for 72% of the patients, and 12% for TMA, 2 cases of Press Syndrome, leading to drastic decrease or withdrawal in anti-calcineurin for 75% of the patients, with adjustment of other immunosuppressive therapies. Infection and organ rejection occurrences during the year after BTC introduction were stable compared to the year before. Median treatment duration was 19 months. After 1 month with BTC, GFR was increased to 63 ± 51 mL/min (Δmean = +54%; $p = 0.003$) and remained stable during the 11 following months. Eleven BTC discontinuations were recorded: 2 for adverse events (cough and vertigo), 1 death due to organ rejection after 1 year, 1 failure on renal function, 2 non-compliance, 1 vein problem, 1 patient decision, 2 kidney function recoveries, and 1 hyperimmunisation recovery. A Burkitt lymphoma occurred 16 months after BTC withdrawal in a patient with a 4.5 month-treatment. A total of 4 patients experienced de novo DSA during BTC treatment (MFI<1500) with a mean time of 7 months.
Conclusion: BTC could be an alternative in post-op transient kidney failure, TMA, Press syndrome or to stabilize delayed renal insufficiency, with an acceptable tolerance.

O83 NATURAL HISTORY OF RECURRENT ALCOHOLIC CIRRHOSIS AFTER LIVER TRANSPLANTATION

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Background: Alcoholic liver disease (ALD) is one of the main indications for liver transplantation (LT) in Europe. Severe alcoholic relapse can lead to the recurrence of alcoholic cirrhosis (RAC) on the graft within a few years. The aim of the present study was to describe the natural history of RAC.
Methods: From 1992 to 2012, 812 patients underwent primary LT for ALD in 5 French transplant centres. All patients with severe alcoholic relapse and a diagnosis of RAC on the graft were included. The diagnosis of cirrhosis was based on the analysis of liver biopsy or on the association of clinical, biological, radiological, and/or endoscopic features of cirrhosis.
Results: RAC was diagnosed in 57/162 patients (35.2%) with severe alcoholic relapse. The diagnosis of RAC was based on histology for 38 patients (66.6%). Thirty-one patients (54.4%) had at least one episode of liver decompensation during follow-up. The main types of the first decompensation were ascites (70.9%), jaundice (58.0%), and hepatic encephalopathy (9.6%). The cumulated probability of decompensation was 23.8% 5 years after LT, 50.1% at 10 years, and 69.9% at 15 years. Thirty-six patients (63.1%) died during follow-up and the main cause of death was liver graft failure for 23 patients (64.1%). After diagnosis of cirrhosis, the survival rate was 66.3% at 1 year, 37.8% at 5 years, and 20.6% at 10 years. There was no significant difference in survival after LT ($p = 0.25$) and post diagnosis of cirrhosis ($p = 0.08$) according to whether the diagnosis of cirrhosis was histological or non-histological. Overall survival at 1 year and 5 years after diagnosis of RAC were 83.4% and 45.4%, in patients with compensated cirrhosis vs 52.6% and 31.5%, respectively, in patients with an episode of decompensation ($p = 0.04$).
Conclusion: RAC is associated with a high risk of liver decompensation and poor prognosis. Prevention of severe alcoholic relapse after LT is a major goal in order to improve patient survival.

O84 PROPHYLACTIC USE OF ECULIZUMAB IN PATIENTS AT HIGH RISK OF POST-TRANSPLANT AHUS RECURRENCE IMPROVES GRAFT OUTCOMES

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Introduction: Eculizumab has revolutionized the management of atypical Hemolytic Uremic Syndrome (aHUS). In 2012, the French aHUS Study Group issued recommendations to advocate the prophylactic use of eculizumab in the kidney transplant recipients with high risk of post-transplant aHUS recurrence.
Methods: A nationwide retrospective multicenter study was conducted, involving 32 centers. Inclusion criteria were the following: 1- aHUS diagnosed before the transplantation; 2- An extensive complement work-up undertaken at the French reference laboratory; 3- At least one adult-onset kidney transplantation with post-transplant follow-up.
Results: Overall, 216 kidney transplantations, performed in 162 patients were included into the study. Immunogenetic analysis unveiled complement abnormalities in 117 of 162 patients (72%). Out of a total of 216 transplantations, 55 had been preceded by a recurrence on previous allografts. Eculizumab and plasma therapy were used as prophylaxis for 52 and 26 kidney transplantations, respectively. The aHUS recurrence rate was significantly lower in patients treated with eculizumab compared to those with no or plasma therapy-based prophylaxis ($p < 0.0001$). Multivariate analysis identified complement abnormalities and acute rejection as independent risk factors for recurrence, whereas eculizumab prophylaxis was the sole independent factor associated with a reduced risk ($p < 0.0001$). Regarding graft survival, eculizumab prophylaxis was associated with a reduced risk of graft failure, especially in the patients with the greatest risk of recurrence (post-transplant recurrence and high-risk mutations)
Conclusions: This large multicenter study supports the of eculizumab as prophylaxis to prevent post-transplant aHUS recurrence and to improve graft outcomes, especially for transplantations associated with a high risk of recurrence.

O85 THYMOGLOBULIN INDUCTION DECREASES RISK OF ABMR AND DEATH IN KIDNEY RECIPIENTS

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Anti-thymocyte globulin (ATG) is currently the preferential induction treatment in kidney recipients at high risk for allograft rejection. No study has evaluated the benefits of this induction strategy in terms of patient survival.

We conducted a multicentric prospective study including unselected kidney recipients from 4 centers (2004–2014). We assessed the type of induction therapy (IL2R inhibitors (IL2R) or ATG) and the dose of ATG (mg/kg). All donor, recipient and transplant baseline characteristics were recorded. Patients were screened for anti-HLA DSAs at the time of transplantation, at any clinical event and yearly. We considered all allograft biopsies (N = 10,293) performed.

4,700 kidney recipients were included: 2,250 (48%) patients received ATG (mean dose 7.2 ± 3.1 mg/kg) and 2,450 (52%) patients received IL2R. The median follow-up was 7.0 (IQR, 4.4–9.6) years. ATG induction was the main protective factor for ABMR occurrence at 1 year (N = 680, HR = 0.69; 95% CI = 0.58–0.81) and at 5 years (N = 869, HR = 0.76, 95% CI = 0.66–0.88), when adjusted for clinical, histologic and immunologic factors. The protective effect of ATG was only observed in patients receiving at least 5 mg/kg (1-year HR = 0.667, 95% CI = 0.55–0.81; 5-year HR = 0.775 0.66–0.92). We generated a propensity score to match patients according to the induction treatment (ATG vs IL2R) with similar risk factors (DSA at day 0, HLA mismatches, graft rank, donor's age, type of donor and cold ischemia time). The matched sample was composed of 2,390 patients (1,200 ATG; 1,190 IL2R). Patients with pre-transplant DSAs receiving ATG (N = 176) showed better patient survival at 5 years compared to patients receiving IL2R (N = 171): 92% vs 84%, $p = 0.008$. Those without pre-transplant DSAs (N = 2,043) had similar survival according to induction therapy (ATG: 88% vs IL2R: 89%).

ATG is the main protective factor for ABMR occurrence in kidney recipients and improves patient survival in recipients with pre-transplant anti-HLA DSAs.

O86 OXYOP STUDY: FIRST USE IN HUMANS OF THE OXYGEN CARRIER (HEMO2LIFE®) FOR ORGAN PRESERVATION

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Introduction: Preventing ischemia/reperfusion injuries (IRIs) is a major issue in organ transplantation. The medical device $HEMO_2life^®$ is a marine oxygen carrier extracted from *Arenicola Marina* featuring high oxygen carrying capabilities and anti-oxidant properties.
Methods: OxyOp is a multicenter open-labeled study evaluating the safety of the use of $HEMO_2life^®$. Any donor in the 6 participating centers was eligible for inclusion. $HEMO_2life^®$ was added (1 g/L) to the preservation solution only for one of the 2 kidneys (the one transplanted locally).
Results: 58 kidney grafts were included, preserved in static mode (64%) or machine perfusion (36%). Mean ages of donors and recipients were 50 years (18 to 89) and 51 years (21 to 72) and 23 (38%) of the donors were ECD donors. The mean cold ischemia time (CIT) was 740 min +/- 258. At 3 months, the patient survival was 100%. There were 2 graft losses and 2 acute rejections (3.4%). No immunological, allergic or infectious complications related to the product were reported. Analysis of the adverse events by the IDSMB showed that they were in line with what was expected according to the donors and recipients population. Paired comparison with the contralateral group (kidneys allocated elsewhere in France) showed less DGF in the HEMO2life® group: more than 1 hemodialysis session 7 versus 26% (0.03), time for creatinine level <250 μmol/L 7 vs 13 days (0.02). Similarly, recovery of renal function (creatinine and eGFR AUCs) was better during the first 15 days. Cold ischemia was longer in the contralateral group but could not explain the difference alone.
Conclusion: The use of HEMO2life® in preservation solution is safe for the recipients and the grafts and improves renal function recovery, arguing for a randomized trial.

O87 DEPLETION OF ANTI-HLA ANTIBODIES IN ORGAN TRANSPLANTATION: IMMUNOADSORPTION OR PLASMAPHERESIS?

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Introduction: In transplantation, apheresis are used to rapidly remove anti-HLA antibodies, but there is no consensus on which one to prefer: immunoadsorption (IA) or plasmapheresis (PP)?
Material and methods: Our retrospective cohort included all solid organ transplanted (n = 38) or wait-listed (n = 5) patients, treated with IA or PP between 01/01/2010 and 31/05/2018, and for whom serum was available at the beginning of the treatment (D0) and after 8 + /- 1 sessions (S8). These sera were tested with Single Antigen Luminex.
Results: Twenty-nine patients were treated with PP and 14 with IA. Their D0 sera contained a total of 1840 positive beads (MFI≥500). The percentage of antibodies depletion at S8 was positively correlated with the use of IA ($p < 0.0001$) and negatively with the D0 MFI ($p < 0.0001$). To obtain a 50% or higher reduction in MFI, the odds ratio of IA compared with PP, adjusted to D0 MFI, was 2.74 (95% CI, 2.09–3.57). Then the depletion capacity of IA appeared higher than PP, but D0 MFI modulated this difference. Indeed, for a D0 MFI <4000, 86% of the antibodies had a MFI reduced by half or more and 80% became negative with PP against respectively 92% ($p = 0.001$) and 85% ($p = 0.05$) with IA. PP enabled to obtain a S8 MFI <2000 with a positive predictive value of 82% for a D0 MFI <3315. Finally, using IA did not ensure the success of the depletion. As an example, the negative predictive value of IA was 94% to obtain a negative S8 MFI for an antibody with a D0 MFI >6226 and 90% to obtain a S8 MFI <2000 for an antibody with a D0 MFI >10915.
Conclusion: IA are more effective than PP to remove anti-HLA antibodies. Nevertheless, the D0 MFI could help identify situations where IA would not be cost-effective.

O88 MISSING-SELF TRIGGERS NK-MEDIATED MICROVASCULAR INJURIES AND CHRONIC REJECTION OF ALLOGENIC KIDNEY TRANSPLANTS

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Introduction: Organ transplantation is the best treatment for terminal organ failure. However, long-term outcome of organ transplantation remains limited by inexorable loss of graft function, which the prevalent dogma links to the microvascular inflammation triggered by the recipient's antibody response against alloantigens (chronic antibody-mediated chronic rejection, cAMR).
Methods and Results: Analysing a cohort of 129 renal transplant patients with microvascular inflammation on graft biopsy, we found that, in half of the cases, histological lesions were not mediated by allo or auto-antibodies. In these patients, genetic studies revealed a higher prevalence of mismatches between donor HLA-I and inhibitory Killer-cell immunoglobulin-receptors (KIR) of recipient's NK cells. We hypothesized that the allogeneic nature of graft endothelium could create a "pseudo-missing self" situation, thereby the recipient's NK cells exposed to inflammatory stimuli would not receive HLA I-mediated inhibitory signals from donor endothelial cells. In co-culture experiments with human NK cells and endothelial cells, we demonstrated that the lack of self HLA-I on endothelial cells can activate NKs. In return, these NKs can kill endothelial cells. Finally, we confirmed the existence of missing-self induced NK-mediated rejection in a murine heart transplantation model.
Conclusion: Our work identifies a new type of chronic rejection, exclusively mediated by innate NK cells, that has the same detrimental impact on graft survival as cAMR.

O89 HIGH DOSE STEROID THERAPY FOR THE TREATMENT OF RECURRENT IGA NEPHROPATHY ON KIDNEY ALLOGRAFT (RIGACORT STUDY, RECURRENT IGA AND CORTICOSTEROIDS)

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IgA nephropathy (IgAN) is the most frequent glomerulonephritis leading to ESRD and kidney transplantation. Recurrences can occur on kidney allograft leading to graft loss in about 7 to 55% of the cases according to studies. There is no guideline for the treatment of recurrences. We compared the outcome of patients receiving supportive treatment alone (ST) to that of patients receiving supportive treatment associated with high dose steroids (HDS).

Here, we report a retrospective multi-center French study (January 1998 to December 2012) on kidney transplant recipients with active and histologically proliferative form of IgAN recurrence. Primary end point was the following composite criteria: more than 50% increase in creatinine from baseline, eGFR < 20 mL/min/1.73 m^2, dialysis or inscription on transplantation's waiting list evaluated at 6 months, 1, 3, 5 and 10 years. We screened 212 biopsy reports and reinterpreted them according to Oxford's classification, 35 patients met the inclusion criteria, 16 in the HDS group and 19 in the ST group.

We found a greater graft survival in the HDS group ($p = 0.01$). Univariate analysis found a significant risk reduction of the occurrence of the primary outcome in the HDS group: (HR 0.19, [0.04–0.86], $p = 0.03$). HDS treatment was associated with significant reduction in proteinuria starting 6 months after the treatment ($p < 0.05$). We found a significant preservation of the eGFR in the HDS group ($p < 0.01$) at 3, 5 and 10 years after the treatment. There was no significant difference in the frequency of adverse events.

These findings indicate that high dose steroid adjunctive therapy is statistically associated with a better kidney allograft survival among patients with proliferative forms of IgAN recurrence. Nevertheless, due to restrictive inclusion criteria only a limited number of patients were included. Hence, prospective randomized controlled studies in larger cohorts are required to confirm these results.

O90 URINARY PROTEIN BIOMARKERS OF ACUTE REJECTION IN RENAL TRANSPLANT PATIENTS: RESULTS FROM THE EUROPEAN RESEARCH PROGRAM BIOMARGIN

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Introduction: Biomargin aimed to discover and validate non-invasive biomarkers of kidney graft lesions in blood, urine or in the graft. We present here the results concerning urinary proteins.
Methods: All clinical studies were approved by ethics committees, complied with the Helsinki declaration amended in 2008, and patients provided informed consent. Urine samples were collected just before protocol or for-cause kidney graft biopsies, following a case-control (discovery and confirmation sets) and then a cross-sectional (performance assessment) design. Urine was consecutively submitted to protein reduction with dithiothreitol, alkylation with iodoacetamide, tryptic digestion and then solid-phase extraction for desalting before analysis by high resolution Micro-LC-QTOF. After untargeted screening, biomarker candidates were selected if linked ($p < 0.05$ after FDR correction) with one of the 4 groups (normal, AbMR, TCMR or IF/TA) assigned after centralized reading by expert pathologists, and had an AUC under the ROC curve AUCROC>0.6. Finally, the most pertinent combinations of proteins were selected using SPLS-DA.
Results: 2378 different urinary proteins were identified. In the discovery set, different combinations of 3 proteins for rejection, TCMR or AbMR showed the highest diagnostic performance against all other groups. In the independent confirmation set ($n = 109$) and cross-sectional study ($n = 339$), the AUROC were 0.81 and 0.81 for rejection, 0.85 and 0.81 for AbMR and 0.68 and 0.72 for TCMR. Sensitivity/specificity as calculated in the cross-sectional study were 77/69%, 80/59% and 56/71%, respectively. Combination of biomarkers with clinical data even improved these results.
Conclusion: We identified and validated urine protein signatures of rejection and AbMR. Their predictive performance is now being tested in the BIOMARGIN European prospective Cohort Study (>600 patients).