O1 DIAGNOSTIC VALUE AND CONFOUNDING FACTORS OF URINARY BIOMARKERS IN THE NON-INVASIVE SCREENING OF RENAL ALLOGRAFT INFLAMMATION

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Introduction: The diagnostic value of urinary biomarkers has already been demonstrated in the acute rejection (AR) of renal allograft, but confounding factors (like BK virus (BKV) reactivation) which may interfere with their interpretation, have been poorly evaluated. Our goal was to evaluate the respective impact of urinary tract infection (UTI), BKV reactivation and acute rejection on these biomarkers to optimize a noninvasive strategy of AR assessment.
Method: In this retrospective single center study, a total of 391 urine samples collected at time of graft biopsy and BKV blood nucleic acid testing were included. Urinary concentrations of BK viruria, CXCL9 and CXCL10 proteins and CD3ε, CXCL9, CXCL10, granzyme B, perforin mRNAs were quantified.
Results: Our results confirmed the impact of UTI and BKV reactivation on urinary chemokine protein levels. To determine the impact of different stages of BKV reactivation, 262 samples are evaluated (after samples exclusion with AR or UTI): 84 viruria, 26 viremia without proven BKV nephritis (BKVN) and 20 BKVN. While viruria had limited impact, concentrations of mRNAs and protein biomarkers were significantly increased and similar in viremic patients and patients with BKVN. In a multivariate analysis, after elimination of UTI and BK viremia, a 3-parameter diagnostic model (urinary proteins CXCL9 and CXCL10 and serum DSA status) diagnosed acute rejection with an area under the curve of 0.81 (p = 9.93E-13). Restricted to unstable patients at the time of indication biopsy (n = 168), the rejection prediction was even more robust with an AUC of 0.85 (p = 5.09E-12).
Conclusion: BK viremia with BKVN or not and UTI are two status to determine before urinary CXCL9 and CXCL10 use in AR diagnosis.

O2 VALUE OF DONOR-SPECIFIC-ANTIBODIES CHARACTERISTICS AT TIME OF KIDNEY ALLOGRAFT BIOPSY

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This study aimed to investigate for serum IgG donor-specific-antibodies, whether the mean fluorescence intensity with or without serum ethylenediamine tetraacetic acid treatment, the ability to bind C1q or C3d, and/or the intragraft detection, showed clinical utility at time of transplant biopsy. Seventy-seven kidney transplant recipients with an allograft biopsy for cause and serum donor specific antibodies were included. Median time between transplantation and biopsy was 25 months (range: 0.5–251), and median follow-up was 24 months (range 0–125). Antibody-mediated rejection was proven in 40% of biopsy specimens. Sensitivity and specificity of C1q, C3d and gDSA assays for predicting antibody-mediated rejection were 68% and 61%, 52% and 70%, 64.5% and 56.5%, respectively. In univariate analysis, donor-specific-antibodies mean fluorescence intensity, C3d positivity and intra-graft detection were associated with death-censored graft loss. In multivariate models, factors associated with death-censored graft loss were glomerular filtration rate, interstitial fibrosis/tubular atrophy score, and C4d positivity. In conclusion, at time of an allograft biopsy for cause, glomerular filtration rate and histopathologic criteria are the best prognosis factors for subsequent kidney allograft loss. Our findings weaken the rationale for implementing C1q, C3d or gDSA assays at the time of the biopsy because they do not independently predict antibody-mediated rejection and graft loss.

O3 FP7 BIOMARGIN: SMALL SETS OF URINARY CELL mRNAs LEADING TO A PARTITION TREE ON KIDNEY ALLOGRAFT LESIONS

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Background: FP7 Biomargin aimed at detecting and validating biomarkers of kidney graft lesions. In this study, we investigated the diagnostic potential of messenger RNAs (mRNAs) in urine samples.
Methods/Materials: Urine samples were collected at the time of protocol or for-cause biopsies in 4 European clinical centers. Patients were retrospectively selected after centralized histological reading of their biopsy by expert pathologists, and classified into 4 groups (normal, ABMR, TCMR or IF/TA). Absolute quantification of mRNAs was performed on urine cell pellets by qPCR. A statistical pipeline including 2 uni- and 5 multivariate analyses was applied to identify which biomarker candidates were associated with one of the 4 groups. Multivariate models were built to define parsimonious subsets of mRNAs that collectively were highly associated with graft lesions.
Results: A total of 24 mRNAs was quantified on 238 urine cell pellets from the case-control study, which included 73 Normal, 34 TCMR, 71 IF/TA and 60 ABMR samples. A set of 4 mRNAs differentiates patients with a biopsy showing acute rejection (AMBR or TCMR) from a normal biopsy (mean AUC = 0.73). Another set of 3 mRNAs discriminates the patients with a biopsy showing acute rejection from IFTA (mean AUC = 0.72). Finally, among the rejection group, a 4 gene signature enables to distinguish ABMR from TCMR (mean AUC = 0.77).
Conclusion: We identified small subsets of urine mRNAs, which enable a multistep approach to discriminate patients into 4 clinically relevant situations. These non-invasive molecular signatures could advise clinicians on the indication of performing a biopsy. The diagnostic performance of our mRNA signatures is currently been investigated in a trans-sectional set of urine samples, obtained at the time of 458 consecutive biopsies. Their predictive performance will then be assessed in a prospective Cohort Study.

O4 FP7 BIOMARGIN SHOWS THAT A SMALL SET OF BLOOD MICRO-RNAS IS ASSOCIATED WITH ACUTE KIDNEY ALLOGRAFTS REJECTION

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Background: FP7 Biomargin aimed at detecting and validating biomarkers of kidney graft lesions. In this study, we investigated the diagnostic potential of microRNAs (miRNAs) in whole blood samples.

Methods/Materials: Blood samples were collected at the time of protocol or for-cause biopsies in 4 European clinical centers. Biopsies were retrospectively selected after centralized histological reading by expert pathologists, and classified into 4 groups (Normal, ABMR, TCMR or IF/TA), to build two independent case-control studies (discovery- and selection sets). Global microRNA (miRNAs) profiling was performed on blood samples from the discovery set by microfluidic cards. A statistical pipeline including 2 uni- and 5 multivariate analyses was applied to identify a list of biomarker candidates associated with one of the 4 groups. This list of miRNAs was quantified using custom TLDA plates on the selection set. Multivariate models were then built to define miRNAs signature of graft lesions.
Results: A total of 754 miRNAs was quantified in the discovery set that included 42 Normal, 17 TCMR, 37 IF/TA and 30 ABMR samples. Our statistical pipeline identified 141 candidates that were assessed in the selection cohort of 37 Normal, 23 TCMR, 41 IF/TA and 37 ABMR samples. The table shows the association between histological phenotypes and miR-derived statistical models in the selection cohort.

Group comparison	Number of miRNAs in the best model	Mean AUC*
Rejection vs Normal	4	0.70
TCMR vs Normal	6	0.75
ABMR vs Normal	4	0.81
ABMR vs TCMR	5	0.64
ABMR vs IF/TA	5	0.72

*Estimated by resampling approaches.

Conclusion: We identified a small subset of miRNAs in the blood with a strong association with ABMR and/or TCMR, thus providing the basis for innovative non-invasive molecular tools development. Their diagnostic performance is currently being investigated in blood samples collected at time of 453 consecutive allograft biopsies in our BIOMARGIN trans-sectional study.

O5 FP7 BIOMARGIN SHOWS THAT SMALL SETS OF INTRA-GRAFT MICRORNAS ARE STRONGLY ASSOCIATED WITH RENAL ALLOGRAFT LESIONS

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Background: FP7 Biomargin aimed at detecting and validating biomarkers of kidney graft lesions. In this study, we investigated the diagnostic potential of microRNAs (miRNAs) in allograft biopsy samples.
Methods/Materials: Biopsies were collected from protocol or for-cause biopsies in 4 European clinical centers. Samples were retrospectively selected after centralized histological reading by expert pathologists, and classified into 4 groups (Normal, ABMR, TCMR or IF/TA), to build two independent case-control studies (discovery- and selection sets). Global miRNA profiling was performed by microfluidic cards (TLDA, Life Technologies) on the discovery set. A statistical pipeline including 2 uni- and 5 multivariate analyses was applied to identify an extended list of biomarker candidates associated with one of the 4 groups. This extended list of miRNAs was quantified using custom TLDA plates on the selection set. Multivariate models were then built to define miRNA signatures of graft lesions.
Results: A total of 754 miRNAs was quantified in the discovery set that included 32 Normal, 13 TCMR, 25 IF/TA and 18 ABMR samples. Our statistical pipeline identified 140 candidates that were assessed in the validation cohort of 32 Normal, 13 TCMR, 26 IF/TA and 28 ABMR samples. The table shows the association between histological phenotypes and miRNA-derived statistical models in the validation cohort.

Group comparison	Number of miRNAs in the best model	Mean AUC*
ABMR vs Normal	4	0.76
ABMR vs TCMR	3	0.90
ABMR vs IF/TA	6	0.94
TCMR vs Normal	6	0.96
Rejection vs Normal	3	0.95
Rejection vs No Rejection	4	0.86

*Estimated by resampling approaches.

Conclusion: We identified a small set of miRNAs within kidney allograft biopsies with a strong association with TCMR and ABMR. These miRNA signatures might provide useful molecular tools to improve allograft assessment. Their diagnostic performance is currently being investigated in our BIOMARGIN trans-sectional study of 312 consecutive allograft samples.

O6 ACTIVATABLILITY OF CIRCULATING TFH17 PREDICTS HUMORAL RESPONSE TO THYMODEPENDENT ANTIGENS

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Despite therapeutic immunosuppression, a significant proportion of transplanted patients develop donor-specific antibodies (DSA), which are currently recognized as the first cause of allograft failure. Generation of antibodies against protein antigens (including donor HLA) results from a thymus-dependent (TD) humoral response, which means that B cells need to receive a co-stimulation signal from activated follicular helper T cells (Tfh) to differentiate into plasma cells. In this study, we test whether profiling of circulating Tfh (cTfh) could predict the ability to mount a TD humoral response in 36 renal transplanted patients and 9 healthy controls. We took advantage of the 2015 influenza vaccination campaign, which provided a normalized setting of antigenic stimulation. The number of cTfh, their polarization profile, and ability to up-regulate i) helper molecules (CD40L and ICOS) and ii) the activation marker CD25 following in vitro stimulation in presence of patients' own plasma (with IS drugs) were measured prior vaccination. These parameters were then compared between responders and non-responders to influenza vaccine. While most of the characteristics of cTfh profile were similar between the two groups, we observed that responders showed a significantly higher proportion of cTfh17 that upregulated CD25 expression after in vitro stimulation. We performed a posteriori analysis of the cTfh profile of 15 transplanted patients at the time of DSA appearance and found that the proportion of cTfh17 cells that upregulated CD25 after in vitro stimulation was similar to responder to influenza vaccine. We concluded that the ability of the cTfh17 subset to be activated in vitro predicts TD antibody response and might be used as non-invasive biomarker to identify transplanted patients at risk to develop DSA.

O7 NEW SENSITIVE MARKERS FOR EARLY TRANSPLANT GLOMERULOPATHY DIAGNOSIS IN RENAL TRANSPLANTED RECIPIENTS

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Introduction: Chronic antibody mediated rejection (cABMR) with Transplant glomerulopathy (TG) remains a major contributor of renal graft loss in the long term. New sensitive markers are needed to make an early diagnosis of disease in order to improve graft outcome.
Materials and methods: Using immunohistochemistry, we studied the glomerular endothelial expression of fascin, glomerular basement membrane (GBM) deposition of fibronectin (FN) and type IV collagen (coll4), in 203 biopsies patients including 59 with ABMR and 144 without.
Results: We found FN and coll4 deposition in the GBM, combined with endothelial fascin expression in the glomeruli of the kidney transplanted patients with ABMR. This was more pronounced in cABMR than in acute ABMR. The level of expression of FN, coll4 and fascin was significantly correlated with Banff g, ptc, cg, c4d scores and DSA. Our analysis showed that the presence of these markers in the glomeruli is a strong predictor of long term graft dysfunction (up to 5 years post biopsy), much stronger than ABMR lesion itself. Logistic regression model showed FN deposition in the GBM to be a strong and independent predictor for graft loss with an odds ratio (OR) of 4.17 (95% CI: 1.5–11.6, $p = 0.006$) after adjustment for g+ptc, c4d, DSA and other known risk factors for graft loss. Positive biopsies for these markers expression also predict TG occurrence in late biopsies ($p < 0.0001$ by Fisher's exact test).
Conclusion: Glomeral fascin, fibronectin and collagen IV expressions are very sensitive markers for glomeral injury during ABMR, and early diagnosis of TG. They seem to predict very well long term graft loss.

O8 MOLECULAR ASSESSMENT BY RT-MLPA FOR THE DIAGNOSIS OF CELLULAR AND ANTIBODY MEDIATED REJECTION IN HEART TRANSPLANT

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Introduction: The distinction between cellular (RC) and humoral (RH) rejection is fundamental due to their different medical care and clinical outcome. Histology is the current gold standard for those distinctions but it is

limited. Studies using micro-arrays have identified specific and sensitive transcriptional signatures, however, those methods are not suitable to clinical practice. Development of a targeted transcriptional analysis suitable to formol-fixed-paraffin-embedded (FFPE) tissue is mandatory to implement the histologic analysis. We are studying RT-MLPA (Reverse Transcription Multiplex Ligase Dependant Probe Amplification) in this indication.
Methodology: Central histopathologic review of 54 EMB was realized. RNA from paraffin blocs of those sample was isolated and was quantified by spectrophotometry. 17 genes were incorporated into the RT-MLPA assay based on their ability to accurately classify between rejection types. Data analysis was performed using Unsupervised Hierarchical Clustering (UHC) and Principal Component Analysis (PCA).
Results: 2 biopsies were excluded from the analysis for insufficiency of myocardial tissue. 50 of the 52 other samples could be analyzed by RT-MLPA. The transcription profiles could accurately distinguish between RC, RH and control cases, as demonstrated by UHC and PCA. 3 cases initially classified as control presented a molecular signal of RH. The analysis of 2 mixed cases could detect RH and RC transcriptional signal in one case.
Conclusion: RT-MLPA is suitable to FFPE EMB analysis. The 17 transcripts signature could distinguish between RH, RC and absence of rejection. A more detailed analysis of 200 cases is currently studied. A classification algorithm will be elaborated.

O9 LONG-TERM FOLLOW-UP OF TORQUE TENO VIRUS VIREMIA AFTER KIDNEY TRANSPLANTATION

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Introduction: New biomarkers are needed to accurately assess the degree of immunosuppression in transplant recipients and provide an optimal personalized balance between rejection and infection risks. We investigated Torque teno virus (TTV) loads kinetics at transplantation and for 24 months thereafter in a well-characterized cohort of kidney transplant recipients (KTR).
Methods: Four hundred and twenty blood samples from 70 KTR were collected on the day of transplantation (D0), and at 1, 3, 6, 12 and 24 months (M) after transplantation. Among these KTR, 52 were viruric for BK virus (BKV), of which 28 were BKV viremic including 13 with biopsy-confirmed BKV associated-nephropathy. TTV viremia was measured using the TTV R-gene® kit (bioMérieux, Marcy l'Etoile, France). Bayesian methods were used to estimate TTV viremia distribution and ROC curve analysis was used to analyze the association of TTV viremia with acute rejection occurrence and BKV status.
Results: Positive TTV viremia was detected in 94% of KTR. Mean viral loads were 2.89, 4.23, 6.55, 5.99, 5.14 and 4.53 $\log_{10}$ copies/mL at D0, M1, M3, M6, M12 and M24, respectively. TTV viremia rose by $\geq$2 $\log_{10}$ copies/mL from baseline to M3 (probability of 98%), then declined by $\geq$1 $\log_{10}$ copies/mL from M3 to M24 (probability of 81%). Higher TTV viremia was associated with a deceased donor, a lower count of CD8 + T cells, and a higher BKV viremia (probability of 90%). D0 TTV viremia under 3.3 $\log_{10}$ copies/mL was associated with acute rejection occurrence in the post-transplantation period ($p = 0.008$). An increase of TTV viremia by 1 $\log_{10}$ copies/mL between D0 and M1 was associated with BKV viruria development ($p = 0.068$).
Conclusion: TTV viremia may adequately reflect the degree of immunosuppression and represent a useful predictor of acute rejection and BKV replication after kidney transplantation. Future studies on larger cohorts are needed to confirm these results.

O10 KIDNEY DONOR RISK EVALUATION: COMPARISON OF THREE INDEXES USING FRENCH DATA

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Background: US Kidney Donor Risk Index (Rao et al., 2009) and UK kidney donor risk index (Watson et al., 2012) were developed and validated on US and UK data respectively to quantify global graft failure risk. The aim of this study was to create a French donor risk index (FDRI) and compare it with the US and UK indexes on French data.
Methods: All adults who received a first kidney transplant from a donor after brain death aged over 18 in metropolitan France between 2007 and 2013 were included. Missing data were substituted by multiple imputation method. FDRI was built by identifying graft survival predictors with a Cox model and a bootstrap procedure (median follow-up: 54 months). FDRI was internally validated. The discriminatory ability of the three indexes was assessed using the concordance probability estimate (Gönen & Heller, 2005). Kaplan-Meier curves were constructed according to index intervals.
Results: At equivalent US-KDRI, graft survival observed in the French cohort is higher than the US one and similar to the UK one. French donors US-KDRI is also higher than US donors. The French index includes the following donor factors : age (continuous, hazard ratio = 1.01 [1.01–1.02]), hypertension (HR =1.33 [1.2–1.47]), vascular cause of death (HR = 1.18 [1.06–1.31]), and estimated glomerular filtration level (continuous, HR = 0.997 [0.995–0.998]), as well as use of antidiuretic hormone during intensive care (HR = 0.9 [0.81–0.99]). It was adjusted for recipient age, cause of ESRD, dialysis at registration and cold ischemia time. Concordance for the 3 tested indices ranged between 0.60–0.62.
Conclusion: In terms of global graft survival, the FDRI was as discriminative as US and UK indexes when applied on French data and allows better risk evaluation than simple standard versus expanded criteria donors.

O11 FRENCH DONOR RISK INDEX

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Context: In a context of organ shortage, transplantation with an expanded criteria donor (ECD) liver is becoming everyday practice. Different Liver donor risk indexes (LDRI) were developed to predict graft failure according to donor characteristics. An attempt to externally validate both the US DRI and the EuroTransplant DRI (Winter, Liver International 2017) showed their unsuitability in the French liver allocation system, thus suggesting the need for a French specific DRI.
Objective: The objective of this study was to determine donor characteristics associated with 1-year liver graft failure in France and to model a French LDRI.
Method: Using the French registry CRISTAL, we included all adult recipients transplanted between 2007 and 2013 and their donors (n = 5759). Study endpoint was 1-year post-transplant graft failure (recipient death or retransplant). Survival rates were estimated using the Kaplan-Meier method. Cox models were used for multivariate analysis and to construct the French LDRI (FLDRI).
Results: Donor factors associated with 1-year graft failure were: age >65, Hypertension, cerebro-vascular death, low GFR and height. Significant recipient factors included in the model were: Age, intensive care unit/intubation, indication, GFR/dialysis, viral C cirrhosis. The predictive accuracy of the model with recipient and donor factors was good (0.7). The highest FLDRI quartile had a 1-year survival of 78.6% whereas the lowest had 86.3%. Low and high-risk recipients receiving a graft from a high-risk donor had 1-year graft survival of 87.5% and 63.0% respectively versus 89.9% and 78.4% for a low risk donor.
Conclusion: The FLDRI may be used as a tool for donor-to-recipient matching, thus increasing the rate of ECD livers utilization without negatively impacting graft outcome. This score should now be validated on a prospective cohort. A root-cause analysis of liver offer refusal in low-risk donors is suggested.

O12 IS EUROPEAN DEPRIVATION INDEX ASSOCIATED WITH KIDNEY TRANSPLANTATION FAILURE AND MORTALITY IN FRANCE?

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Background: It is widely accepted that socioeconomic deprivation is associated with both mortality and comorbidity in the general population. In the United States poorer graft survival has been observed in kidney transplant recipient living in socially deprived area. The European Deprivation Index (EDI) is an indicator of deprivation which can be replicated in European countries. The main objective of the study was to assess whether EDI is associated with transplantation failure or death in transplantation in France.
Methods: All the patients who received a kidney transplant in one of the 29 French medical centers during the period 1 January 2010 to 31 December 2014 were studied. The European Deprivation Index (EDI) was estimated with the patient home address at registration on the waiting list. Patients were categorized by EDI quintiles that have been determined in the French population. The events of interest were graft failure, defined by a chronic dialysis initiation or a second transplantation, and death. As death on transplantation is a competing event of transplantation failure, a competing risk analysis has been performed with a Fine and Gray regression model.
Results: In multivariate analysis with a Cox model, the mortality was higher for the most precarious patients, defined as patients in the 5th quintile of the EDI (cs-HR: 1.31, 95%CI: [1.01–1.70]). However, after an adjustment on the recipient's comorbidities, the EDI was not associated with transplantation failure.
Conclusions: The specificities of the French care system could explain that our study did not find any link between the deprivation evaluated by the EDI and the graft failure but with higher mortality for patients in the most disadvantaged quintile. The French EDI is reproducible in all 26 European countries and may allow us to compare the results of our study with other countries to understand

the mechanisms of social disparities and try to reduce mortality in kidney transplantation.

O13 HAND-ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY, AN OUT-DATED TECHNIQUE ? RESULTS OF 270 CASES

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Minimally-invasive techniques for living donor nephrectomy have proved their superiority and actually replace the open surgical procedures. Can laparoscopy, with or without manual assistance, still be an alternative, at a lower cost, to robotic-assisted surgery which is booming? The objective of this study is to evaluate our results of hand-assisted living donor nephrectomy.

This monocentric work list all the procedures between 2002 and 2017. All the nephrectomies were realized by transperitoneal approaches with manual assistance Gel-Port system® after clipping the vessels with the Endo-TA® stapler. Kidneys were extracted by the manual assistance incision. The outcomes were retrospectively collected using the data system DIVAT and the medical records.

270 nephrectomies were consecutively realized: 68 right kidneys, 40 with multiple arteries. The perioperative complications were: 5 vascular wounds, 2 jammings of the Endo-TA staplers and 1 pleural breach. No conversion into open surgery neither perioperative blood transfusion were necessary. We report: a median warm ischemia time of 3 min, a median length of hospital stay of 4.5 days, no breakdown of vascular suture line. A postoperative complication occurred among 84 patients: 76 Clavien I (14% of persistent pain at 1 month, 13% of parietal complication, 9% of intestinal disorder), 4 Clavien II, 3 Clavien III and 1 Clavien V (intestinal obstruction on bridle after 4 years). The rate of early graft function was 93%. With a median fallow-up of 4.5 years, none of the recipient developed vascular graft thrombosis.

Hand-assisted laparoscopic donor nephrectomy procures an optimal safety for the donors. This technique associated with the Endo-TA staple helps and secures the surgery, offering an effective vessels length which is essential for right kidney transplantations.

O14 KIDNEY TRANSPLANTS FROM DONORS AFTER CARDIO-CIRCULATORY DEATH (DCD) TYPE III MAASTRICHT, PRELIMINARY RESULTS OF A MONOCENTRIC SERIES OF 29 PATIENTS

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Background: The use of kidney transplants from using expanded criteria donors (ECD), including cardiac death (DDAC) develops in the current context of transplant shortages. The organ retrieval from DCD M3 has been authorized in France since 2014. The objective is to analyze the preliminary results of the first DCD M3 kidney transplants.
Methods: This monocentric retrospective study records all DCDM3 and all renal transplant patients with these transplants. Data collection was carried out using the local database for hospital coordination of organ and tissue sampling, patient records and the database "Computerized and Transplantated Data". The sampling procedures were carried out in accordance with the regulations defined by the DCDM3 protocol of the Agence de la Biomédecine after setting up a Regional Normothermal Circulation (CRN) in intensive care.
Results: Since the beginning of the program in our center in 2015, 57 potential DCDM3 have been identified, 29 procedures have resulted in a transplant. The characteristics of the donors were: an average age of 53.1 ± 2.21 years, an average hospital stay in intensive care units of 5.2 days (1–28 days). The mean functional ischemia was 32 minutes (58% ≤ 30 min). The mean CRN time was 178 min (± 11 min). The average cold ischemia was 476 minutes (348–1140 min). The characteristics of the recipients were: an average age of 60 ± 9 years, 35% pre-emptive transplant, 25% diabetic CKD, 27% ADPKD. 9% of patients had a delayed recovery of transplant function and no primary function was found. The mean rates of creatinemia at 3.6 and 12 months post-transplantation were respectively 129 μmol/L 135 μmol/L and 133 μmol/L.
Conclusion: The excellent results of renal transplants from DCDM3 reinforces the team to continue the development of this program.

O15 FOREGOING LIFE-SUSTAINING TREATMENTS IN THE ICU: PRACTICES EVOLVE OVER TIME

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Introduction: Significant variability exists in the decisions to withhold or withdraw (WhWd) treatments. Moreover practices may evolve over time. This study aims to compare the procedural features of foregoing treatments between two separate periods (2012 vs. 2016) in a single 16-bed ICU.
Methods: For each of the two periods considered, the characteristics and outcome of patients qualified for a WhWd procedure were collected.
Results: During the first and second periods, 596 and 600 patients were admitted to the ICU. The number of brain and circulatory deaths were 25 and 144 in 2012, 24 and 145 in 2016, respectively. Table 1 gives the characteristics of patients qualified for a WhWd procedure.

Table 1: Characteristics of patients qualified for a WhWd procedure

Period Admissions	2012 596	2016 600	p or odds ratio (CI 95%)
WhWd patients % (n)	14 (84)	30 (180)	2.4 (1.8–3.2)
Age (yrs.)	74 [63–82]	70 [63–79]	
SAPS II	69 [56–82]	67 [53–86]	
Length of stay (d)	8 [3–16]	3 [1–7]	$p < 0.001$
Sex ratio M/F	3.2	1.8	
Delay admission-first WhWd (d)	8 [3–16]	3 [1–7]	$p < 0.0001$
SOFA score on the day of first WhWd	8 [6–12]	8 [4–13]	
Mortality rate in the ICU % (n)	90 (76)	72 (129)	0.3 (0.1–0.6)
Delay first WhWd-death (d)	2 [0.5–6.5]	1 [0–4]	$p < 0.05$
% (n) of WhWd patients among the circulatory deceased patients	53 (64)	89 (129)	7.2 (3.9–13.3)

WhWd, withholding or withdrawal; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment Results given as median [IQR]
Conclusion: The rate of patients who die in the ICU after a WhWd decision significantly increases, while those of overall mortality and brain deaths remain stable. As a consequence, donation after circulatory arrest is expected to provide a growing proportion of organs for transplantation.

O16 EN BLOC KIDNEY TRANSPLANTATION OF PEDIATRIC DONORS LESS THAN 15 KG TO ADULT RECIPIENTS

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Introduction: The organ shortage has led to the expansion of the criteria used for donor selection. The high rate of vascular thrombosis in pediatric recipients explains that the pediatric donors less than 15 kg are often refused by transplantation teams. Those kidneys could be proposed to a "en bloc" kidney transplantation (EBKT) to adult recipients. Aim of this study was to evaluate the feasibility, survival and functional outcomes of these grafts.
Material and methods: Retrospective analysis of 12 EBKT of pediatric donors less than 15 kg performed from February 2002 to December 2016. All patients received antithrombotic prophylaxis. Glomerular Filtration Rate (GFR) was estimated by the simplified MDRD. The pre/per/post operative data, the complication rate, the functional and morphologic outcomes were also analysed.
Results:

Donor age (months)	15 ± 11.3
Donor sex ratio (male/female)	6 / 6
Mean donor weight (kg)	10 ± 5.37
Recipient age (months)	30 ± 10.2
Recipient sex ratio (male/female)	7 / 5
HLA mismatch	4 ± 0.7
Dialysis before transplantation (yes/no)	10 / 2
Dialysis duration (months)	54 ± 33.6
Total ischemia time (min)	669 ± 284
Mean vascular time (min)	32 ± 11
Mean MBI (kg/m²)	21 ± 1.8
Mean blood loss (ml)	313 ± 213
Mean Length of Stay (days)	17 ± 9.3

The mean follow-up was 45.5 (6–180) months. One patient was lost to follow-up at 24 months. There were no Primary Non Function and no Delayed Graft Function. The function recovery was immediate and the patient survival was 100%.

There were: 3 surgeries at day 1 for arterial thrombosis (n = 2) or compressive hematoma requiring a nephrectomy of one of the two kidneys (n = 1), one lymphocele, 2 arterial stenosis requiring surgical repair and one angioplasty/stent at M17 and M18 and one uretero-vesical reimplantation at M2 for necrosis of the bladder patch. At M3, M12 and at the end of latest news, mean MDRD was 76 + /-20.1, 93 + /-20.1 et 93.4 + /-16.3 respectively. There were 2 acute rejections treated at M3 and 2 proteinuria spontaneously resolving.

Conclusion: EBKT of pediatric donors less than 15 kg to adult recipients could be proposed to transplantation teams when pediatric transplantation teams refused them because of their good functional outcomes. Surgical complications are mainly vascular and should be screened during all the patient's follow-up.

O17 IMPACT OF A THERAPEUTIC PATIENT EDUCATION PROGRAM FOR ADULT KIDNEY TRANSPLANT RECIPIENTS ON MODIFICATION OF HEALTH BEHAVIORS AND QUALITY OF LIFE

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Introduction: Non-adherence to immunosuppressive medications is one of the causes of graft loss in adult kidney transplant recipients (KTR). Therapeutic patient education (TPE) is designed to enable patients to manage their treatment to prevent avoidable complications, and to maintain or improve quality of life. We aimed to assess the impact of a TPE program for adult KTR on modification of health behaviors and quality of life.

Patients and methods: Patients who received a kidney graft between January and October 2015 (period without TPE program)(group TPE-) were compared to KTR grafted and registered on TPE program from November 2015 to May 2016 (group TPE+). Learning, adherence to treatment (BAASIS survey) and quality of life (R-TRANS-QOL survey) were assessed one year post-transplantation and compared between the two groups.

Results: Within the 115 patients who received a kidney transplant between January and October 2015, 97 responded to the surveys (group TPE-). Among the 36 patients registered on TPE program, 32 responded to the surveys (group ETP+). TPE+ patients had significantly better knowledge about the immuno-suppressive medications and a better assessment of medical care than TPE- patients (1.85/2 versus 1.64/2, p = 0.002 and 84.4% versus 77.6%, p = 0.009 respectively). Feelings concerning physical health, mental health, fear of graft loss and/or adherence to treatment were not different between both groups.

Conclusion: Our TPE program shows an improvement of health behavior, medication understanding and relationship patients/carer. Thus the TPE program may be a step to increase therapeutic adherence.

O18 A NEW TOOL OF TRAINING AND EVALUATION IN THE MULTI-TAKING AN ORGAN: SIMLIFE

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Introduction: Before the transplant, it is necessary to obtain transplants during the taking of organ. The latter owes answers criteria of good practice. So we propose a new model of simulation using bodies with which a device of pulsatile circulation and ventilation is associated. This model is a tool of training and evaluation for the procedures of the multi-taking organ (PMO).

Material and Method: The model SimLife includes a body connected with a specific device allowing an arterial pulsatile circulation and a ventilation. SimLife System allows the ventilation of lungs leading the movements of the thorax and the diaphragm. The arterial drip allows to maintain a column of pressure in arteries. Solenoid valves assure the pulsatile dimension of this column of liquid, so miming for the surgeon the cardiac beatings transmitted in vessels. The passage of the blood feigned in organs restore to these a realistic recoloring, a temperature and a texture. This device adapts itself to the operating conditions. This model was estimated during 24 months, by 70 learners, during sessions of taking multi-organs within the framework of the French-speaking School of PMO by using a scale of Likert from 1 to 10. At the same time, the learners are estimated by means of a railing in the course of validation.

Results: For 4 criteria: possibility of learning of a procedure with this model, general realism of the model, the anatomical realism of the model and the global satisfaction, the rate of satisfaction is always upper to 80 % (83–98 %). The learners obtained scores in - above from 70 %, during their simulation.

Conclusion: In open surgery, SimLife is a device of education by simulation in very high degree of realism, usable to estimate the acquisition of performance of the learners in an educational program, as the PMO.

O19 HEPATITIS E VIRUS-ASSOCIATED CRYOGLOBULINEMIA IN SOLID-ORGAN-TRANSPLANT RECIPIENTS: A PROSPECTIVE STUDY

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Hepatitis E virus (HEV) is responsible for acute and chronic autochthonous hepatitis in developed countries, particularly in Western Europe. Conversely to hepatitis B or C, the association between HEV and cryoglobulinemia is less documented. We prospectively evaluated the prevalence of cryoglobulinemia in HEV infected solid-organ-transplant recipients with resolving and chronic hepatitis and assessed the evolution of cryoglobulinemia in patients given ribavirin therapy.

Between November 2005 to June 2016, 80 patients with HEV infection were enrolled in the study: kidney- (n = 55), liver- (n = 20), cardiac- (n = 3), pancreas- (n = 1) and kidney-pancreas (n = 1) transplant recipients. In this cohort, 36.3 % of patients cleared HEV within the first 3 months after HEV diagnosis (n = 29) while 63.7% developed chronic HEV infection (n = 51).

Overall, the prevalence of cryoglobulinemia at the acute phase of HEV infection (i.e. within the first month following HEV hepatitis diagnosis) was 36.4% (n = 24/66) and 52.9% (n = 27/51) at the chronic phase of HEV infection (i.e. HEV RNA detection more than 3 months after HEV infection diagnosis) (p = 0.09). No significant kidney function impairment or proteinuria was noticed in cryoglobulinemia positive patients. A 3-months ribavirin therapy (median duration, 3 [3–4] months) was given to all patients with chronic hepatitis and allowed HEV clearance in 81.4% of cases. After retreatment of relapsers, a sustained virological response was obtained for 100% of patients. In 14 out of the 23 patients (60.9%) of cryoglobulinemia disappeared within ribavirin therapy. Nevertheless, 39.1% of cryoglobulinemia remained positive 6 months after the end of ribavirin therapy.

Cryoglobulinemia is highly frequent during HEV infection in solid-organ-transplant recipients and could persist after viral clearance. Considering HEV endemicity in Western Europe with hyperendemic area, HEV markers should be check in case of cryoglobulinemia detection.

O20 SHOULD WE DRASTICALLY REDUCE IMMUNOSUPPRESSION TO TREAT BK VIREMIA AFTER KIDNEY TRANSPLANTATION? RESULTS FROM A MONOCENTRIC RETROSPECTIVE STUDY

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Introduction: Minimization of immunosuppression (IS) is the gold-standard treatment of BK viremia after kidney transplantation (KT). However its precise modalities remain to be clarified.

Methods: This is a retrospective study including 112 KT recipients between 04/2007 and 08/2015, with at least 2 consecutive positive plasma viremia (>2.7 log10) after KT. The cohort was divided into two groups: a less intensive tapering and monitoring group (LIg, n = 58) before 2012 and a more intensive tapering and monitoring group (MIg, n = 54) after 2012.

Results: Baseline demographic and immunologic characteristics were similar. The number of plasma BK PCRs performed during the first year was higher in the MIg (15 vs. 3, p < 0.001). BK viremia was detected sooner after KT (99 vs. 151 days, p = 0.033), was higher (5.4 vs. 4.6 log10, p = 0.023) but shorter (105 vs. 384 days, p < 0.001) in the MIg compared to LIg. At BK viremia onset, daily dose of mycophenolic acid (MPA, p = 0.151) and tacrolimus trough levels (Tac, p = 0.863) were similar. However, time to reach 50% of MPA dose reduction (16 vs. 39 days, p = 0.063) and to reach MPA withdrawal (43 vs. 92 days, p = 0.057) were shorter in the MIg compared to LIg. Tac trough levels

were also lower (5.3 vs. 6.3 ng/mL, p = 0.006) in the MIg 3 months after BK viremia onset. One year after BK viremia, incidence of graft loss (4% vs. 4%), biopsy-proven acute rejection (22% vs. 17%) and estimated glomerular filtration rate (45 vs. 45 mL/min/m²73) were similar in the MIg and LIg, respectively. Incidence of de novo donor-specific antibody (DSA) was higher (18% vs. 4%, p = 0.04) in the MIg and 1000-days de novo DSA free survival was lower in the MIg (log-rank, p = 0.067).
Conclusion: Intensive IS reduction shortens BKV, doesn't affect medium term graft outcome and is associated with increased incidence of de novo DSA.

O21 EVALUATION OF THE VACCINATION COVERAGE OF ORGAN TRANSPLANT CHILDREN'S FAMILY

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Introduction: Vaccine-specific recommendations were published by the HCSP in 2014 for immunosuppressed patients. In order to analyze the vaccination of the environment of children with organ transplants, we deed a retrospective study in 2016 at the CHU de la Timone Enfant in Marseille.
Method: A questionnaire was sent to parents of 89 transplanted children registered on the waiting list between 2005 and 2014. It included questions on their vaccination status and that of their children at registration, part on their medical follow-up and advice on vaccination in general. The results were analyzed according to the general recommendations (GR) of the vaccine schedule and according to specific recommendations (PR) for immunosuppressed patients.
Results: 56 families out of 89 could be analyzed, i.e. 106 adults and 87 brothers and sisters, or 193 people. According to the GR and PR, only 1.8% of the transplanted children had their entire family circle correctly vaccinated. Brothers and sisters were significantly better vaccinated according to GR than parents: 75.8% compared to 17.9% (p = 7.10–7). For MMR, 29.2% of parents were vaccinated, pertussis 22.6%, chickenpox 29.2% and influenza 47.2%. Factors influencing vaccination favorably include the involvement of the treating physician who informs parents and helps to overcome their fears about vaccines. 73.7% of adults in the GR and 60% in the PR were discussing vaccines with their treating physician. 72.7% of brothers and sisters following GR and 87.5% following PR had parents without fear about vaccination. PR monitoring was better if there were multiple doctors: 80% of the adults in the PR had multiple health care providers.
Conclusion: Vaccination of the transplant environment is very inadequate. To improve it, we propose a specific letter to help update the family's vaccination calendars for the treating physician.

O22 LOW BURDEN OF LATE INFECTIOUS COMPLICATIONS AFTER UPPER EXTREMITY ALLOTRANSPLANTATION

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Background: Upper extremity allotransplantation (UEA) significantly improves the quality of life of severely disabled patients. However, the risk-to-benefit ratio of this non-vital procedure that imposes a lifelong immunosuppression remains to be clarified. The aim of this study was to define the incidence and characteristics of infections after UEA, which have never been assessed before.
Methods: Included were all patients who received UEA between 1998 and 2016 according to the International Registry on Hand and Composite Tissue Transplantation. Infections were classified as "early" (EI) or "late" (LI) (≤180 or >180 days post-transplantation) and as opportunistic (OI) or not.
Results: Sixty-two patients were included. Median follow-up was 6.2 years (IQR: 2.4–10.1) and one patient died, not of infectious cause. Thirty-eight EI events (including 15 OI) occurred in 26 (41.9%) recipients, representing an incidence of 3.5 EI/1000 transplant-days. Twenty-six LI events (including 13 OI) occurred in 16 (25.8%) recipients, representing an incidence of 0.175 LI/1000 transplant-days. Sites of EI and LI events were distributed as follows: graft's muscle or bone (EI: 3/38 vs. LI: 3/26), graft's skin or subcutaneous tissues (4/38 vs. 1/26), skin or mucosa (8/38 vs. 9/26), systemic viral infection (6/38 vs. 3/26), lungs (5/38 vs. 1/26), urinary tract (5/38 vs. 2/26), catheter-related (2/38 vs. 2/26), other or unknown (5/38 vs. 5/26). Infections were of viral (EI: 12/38 including CMV n = 6, VZV n = 1, EBV n = 0 vs. LI: 12/26 including CMV n = 2, VZV n = 7, EBV n = 1), bacterial (20/38 vs. 11/26) or fungal (6/38 vs. 2/26) origin.
Conclusions: The incidence of LI is low after UEA. Burden of LI complications could be lower in UEA recipients than in solid-organ transplant recipients. This could be explained by the absence of chronic organ failure in UEA recipients. An ongoing analysis will compare the incidence of infection in this cohort and in a matched cohort of kidney transplant recipients (DIVAT).

O23 COMMERCIAL INTRAVENOUS IMMUNOGLOBULINS INDUCE HIGH BKV GENOTYPE- SPECIFIC NEUTRALIZING ANTIBODY TITERS IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: BK virus-associated nephropathy (BKVAN) represents a growing medical problem in kidney transplantation (KT). To date, there are no BKV-specific antiviral therapies available. Previously, we have showed that BKV genotype-specific neutralizing antibodies (NAbs) play a key role in protection against BKV replication after KT (Solis et al, SFT 2016).
Methods: We assessed the capacity of 3 commercial IVIG (Privigen®, Octagam ®, Clairyg®) to neutralize the 3 major BKV genotypes in vitro using a BKV pseudovirion system and BKV strains isolated from KTR with BKVAN. NAb titers were measured in plasma samples from KTR before and after IVIG administration for acute antibody-mediated rejection (1 g/kg/day, 1 cure/week, 3 weeks, n = 18) or for secondary immunodeficiency syndrome (0.4 g/kg/day, 1 cure, n = 11).
Results: In vitro, IVIG showed high and reproducible anti-BKV NAb titers ranging from: 5.05 to 6.68 $\log_{10}$, 4.36 to 5.51 $\log_{10}$, and 3.58 to 4.78 $\log_{10}$ for genotype I, II, and IV, respectively. Bayesian statistical analysis showed higher titers against genotype IV in Clairyg® than Privigen® and Octagam® with probabilities of 89% and 77%, respectively. Octagam® showed lower titers against genotype I and II than Privigen® and Clairyg® with probabilities ranging from 96 to 99%. In vivo, patients displayed a mean increase of NAb titers by 60 fold (genotype I) to 300 fold (genotype II and IV) after IVIg administration. Patients harboring NAb titers lower than 4 $\log_{10}$ reached high titers against the 3 genotypes (3.83 to 5.48 $\log_{10}$). These high titers persisted 3 months after the last administration (genotype I and II). We found a similar NAb titer increase in patients treated by 1 g/kg/day compared to those treated by 0.4 g/kg/day for genotypes I and II.
Conclusion: These data demonstrate that IVIG have an important anti-BKV neutralizing activity and pave the way towards the development of a new preventive strategy against BKVAN in KTR.

O24 RISK FACTORS FOR PNEUMOCYSTIS PNEUMONIA AFTER THE FIRST 6 MONTHS FOLLOWING RENAL TRANSPLANTATION

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Introduction: Pneumocystis pneumonia (PCP) incidence was decreased in renal transplant thanks to prophylaxis, recommended during the first months after transplantation. However, many late PCP cases are observed after the first 6 months and recommendations to maintain or reintroduce prophylaxis are lacking. The objective of the study was to identify risk factors to guide the individual prescription of prophylaxis, 6 months after renal transplantation.
Method: Thirty-three late PCP cases identified in our renal transplant unite between 1995 and 2012, were compared to 72 randomized controls transplant recipients.
Results: In univariate analysis, age of donor (> 48 years), retransplantation, a decrease glomerular filtration rate (≤45 mL/min), induction therapy mediated by anti-thymocyte globulin (ATG), steroid maintenance, high calcineurin inhibitors (CNI) doses (tacrolimus ≥ 0.5 mg/kg per day and cyclosporine ≥ 2.1 mg/kg per day) and cytomegalovirus (CMV) infection were significantly associated with PCP. In multivariate analysis, ATG (hazard ratio [HR]: 2.4 [1.1–5.4]), steroid therapy (HR: 3.1 [1.20–7.84], CNI (HR: 2.9 [1.28–6.38], and CMV (HR: 6.1 [2.74–16.33] remained associated with late PCP.
Conclusion: We confirm that intensive immunosuppressive regimen and CMV infection are critical risk factors for late PCP and should be taken into account to decide on maintenance or reintroduction of a prophylactic treatment.

O25 ACTINOMYCOSIS: A RETROSPECTIVE STUDY IN RENAL TRANSPLANT RECIPIENTS IN FRANCE

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Introduction: Actinomycosis is an uncommon (1/300 000 à 1/1 000 000) and heterogeneous infection involving anaerobic bacteria Gram positive. Actinomyces are commensals of oral cavity and digestive tract. Our study is a review of cases of actinomycosis in renal transplant recipients in metropolitan France.
Methods: The French renal transplantation centres were contacted by email. We sent a survey to each centre which reported a case. Thanks to the survey, we collected information about actinomycosis (localisation, infection gate, diagnostic method, treatment and outcome) and transplantation (time between transplantation and infection, graft outcome).
Results: Eighteen of thirty-two centres (56%) answered. Seven cases (6 males, 1 female) were collected. The mean age of patients was 60 years. Actinomycosis was localised in the lung (n = 1), skin (n = 3), abdomen (n = 2) or brain (n = 1). Two patients (33%) had acute kidney injury. Diagnosis was made by microbiological examination (28%) or pathological examination (filaments and sulfur granules) (42%). Suspected infection gate was dental (50%) or abdominal (33%). All of the patients were treated with amoxicillin for 30 to 300 days. Surgical treatment was necessary for three patients (42%). One patient died (associated B lymphoma) and one had lung fibrosis after pulmonary actinomycosis. The other patients recovered completely in few months. The time between transplantation and infection was heterogeneous (4 to 204 months). Immunosuppressive therapy did not affect the severity of the infection. No grafts were rejected.
Conclusions: Actinomycosis is a low virulence infection mainly caused by mucosal breach. Its diagnosis leads to a prolonged antibiotherapy to prevent infection relapse. In renal transplantation, overall and renal survival do not appear to be impacted by this infection.

O26 PULMONARY TUBERCULOSIS AND MANAGEMENT OF CONTACT PATIENTS IN A DEPARTMENT OF NEPHROLOGY AND KIDNEY TRANSPLANTATION

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Introduction: European guidelines recommend that primary prophylactic treatment should be initiated in vulnerable high-priority contacts of a pulmonary tuberculosis (TB) case, as chronic kidney disease (CKD) patients and kidney transplanted recipients (KTR), even if the result of IGRA (Interferon Gamma Release Assay) is negative. The aim of our study was to report our management of a TB contact investigation in a nephrology unit in France, a low prevalence country.
Materiel and patients: 310 patients including 180 KTR and 130 CKD patients who were in contact with a pulmonary TB case in the nephrology department of the Bordeaux Hospital were included in an investigation based on a concentric circle (2 in the circle 1, 220 in the circle 2, and 88 in the circle 3). Patients of the circle 1 and 2 were considered as vulnerable high-priority contacts.
Results: Only few vulnerable high-priority contacts received an anti-TB treatment: the 2 patients of the circle 1, and 2.8% of KTR and 9% of CKD in the circle 2 who had a positive IGRA. With this strategy, no case of TB disease occurred during a 2-years follow-up.
Conclusion: This observation suggests that TB prophylaxis could be replaced by a comprehensive surveillance in vulnerable high-priority contacts of circle 2 with a negative IGRA in low prevalence countries.

O27 INFECTIONS REQUIRING HOSPITALIZATION AFTER SWITCH TO BELATACEPT IN KIDNEY TRANSPLANTATION

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Belatacept rescue therapy seems to be a valuable option in front of calcineurin inhibitor chronic toxicity in kidney transplantation. Nevertheless the risk of infectious adverse events after this switch is not well reported.

We report in this study the infectious complications requiring hospitalization after a switch to belatacept and we try to demonstrate the risk factors associated. All the patients of the Spiesser group (13 French kidney transplantation centres) switched to belatacept between July 2010 and May 2017 were included.

Two hundred and seventy five kidney transplant recipients (mean age 56.5± 14.5 years old) were switched to belatacept 10.8 months (median) after kidney transplantation. Sex ratio was 1.54 (M/F: 167/108) and 85.3% were recipients of a first kidney transplantation. There were 73 patients with an infection requiring hospitalization on average 9.7 months after the switch. Bacterial infections were diagnosed in 38 cases (52%), mainly acute allograft pyelonephritis (17 cases over 38: 44.7%). Parasitic or fungal infections were found in 14 cases (14%), mainly pneumocystis pneumonia (11 cases over 14: 78.5%). Viral infections in 33 cases (45.2%), mainly CMV disease in 17 cases over 33 (51.5%). The cause of infection was multiple in 28 cases over 73 (38.3%). The infection led to death in 8 cases over 73 (11%) and graft failure in 12 cases (11%) and belatacept was stopped in 15 others cases (20.5%).

In multivariate analysis, the age on the day of the switch (age > 60 years old: OR=22; CI 95% : 1.1-4.2), the treatment of a rejection before the switch (OR=2.1; CI 95% : 1-4.1) and the use of immunosuppressive agents before transplantation (OR=1.9; CI 95%: 1-3.88) were significantly associated with the occurrence of a serious infection requiring hospitalization.

The risk of infection requiring hospitalization after a switch to belatacept, used as a rescue therapy, seems to be high and justify a cautious monitoring and a prophylactic regimen in this population, particularly regarding the risk of pneumocystis pneumonia and CMV disease. These data have to be confirmed in a case control study.

O28 ACUTE KIDNEY DYSFUNCTION WITH NO REJECTION (ADNR) IS ASSOCIATED WITH POOR OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS

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Background: The entity "acute kidney dysfunction with no rejection (ADNR)" has been proposed for kidney transplant recipients (KTR) presenting with acute elevation of serum creatinine without histological evidence of acute rejection (AR). The prognosis of ADNR is unknown.
Methods: From 2007 to 2015, we retrospectively categorized all KTRs with for-cause kidney biopsy within 12 months post-kidney transplantation (KTx) into 2 groups: ADNR and biopsy-proven AR. Controls (C) included KTR with no ADNR or AR within 24 months post-KTx. BK virus nephropathy and primary nonfunction were excluded. Glomerular filtration rate (eGFR) was estimated using Modification of Diet in Renal Disease (MDRD) equation. Linear mixed models established intercepts and slopes of eGFR decline from 6 to 24 months post-KTx. Cubic spline analysis calculated the percentage of patients with a $\geq$ 30% reduction of eGFR from 6 to 24 months post-KTx.
Results: The mean age (yr) at KTx was 50.2 $\pm$ 14.2, 47.9 $\pm$ 17.8 and 53.6 $\pm$ 12.4 for ADNR (n = 93), AR (n = 22) and C (n = 135), respectively. The female/male ratio was 39.8% (ADNR), 45.5% (AR) et 34.1 (C). The median time for graft biopsy was 22 and 13 days post-KTx for ADNR and AR, respectively. ADNR included 21 patients with "borderline" histology. At 6 months post-KTx, eGFR was higher in C (55.2 $\pm$ 1.6 mL/min) versus ADNR (45.5 $\pm$ 1.9 mL/min; $p < 0.05$) and versus AR (48.6 $\pm$ 3.9 mL/min; $p = 0.13$). The eGFR slope from 6 to 24 months post-Tx was positive in C (0.16 $\pm$ 0.06 mL/min/month), but negative in ADNR (-0.04 $\pm$ 0.08 mL/min/month, $p < 0.05$) and in AR (-0,04 $\pm$ 0.16 mL/min/month, $p = 0.26$). The proportion of KTR with a $\geq$ 30% reduction of eGFR from 6 to 24 months post-KTx reached 7.4% in C versus 25.8% in ADNR ($p < 0.05$) and 19.1% in AR ($p < 0.05$).
Conclusion: In the present monocentric cohort, ADNR occurs frequently and early post KTx, and is associated with a significantly lower eGFR at 6 months and a significantly faster eGFR decline from 6 to 24 months post-KTx, in comparison to controls.

O29 ARE THERE FACTORS IN YOUNG PHYSICIANS THAT COULD REDUCE ORGAN DONATION?

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Introduction: In France, the high opposition rate to organ donation (33.6%) requires to engage all medical staff. The aim of this preliminary study was to identify factors in young physicians that could reduce organ donation.
Methods: An online questionnaire was sent to young physicians through the networks of the Junior Members of the French-Speaking Society of Transplantation and the Association of Young Specialists of Anesthesia and Intensive Care. Data were anonymous.

Results: One hundred and seventy persons answered to the questionnaire. One hundred and twenty-seven (74.7%) were residents and 25 (14.7%) were young seniors. Ninety-five (56.5%) were specialists of anesthesia and intensive care, 38 (22.4%) nephrologists and 28 (16.5%) urologists. One hundred and twenty-three (72.4%) considered that the last communication strategy of the French Biomedecine Agency was insufficient and 87 (51.2%) considered that its impact on the number of organ donors was uncertain. Fourteen (8.2%) participants were against the presumed consent approach and 7 (4.3%) were not themselves organ donors (2 owing to religious belief and 4 owing to negative work experience). One hundred and thirteen (66.5%) participants dreaded conflicting situation with families and 45 (26.5%) though that families should not be involved in the decision of organ donation. Thirty-eight (22.4%) participants though that it was legal to remove organs of an unwilling patient if his family agreed.
Conclusion: This study identified factors in young physicians that could reduce organ donation. Better information on donation process and better education for family management could help to reduce refusal for organ donation.

O30 CONVERSION FROM TACROLIMUS TWICE DAILY (PROGRAF™) TO TACROLIMUS ONCE DAILY (ADVAGRAF™) IN KIDNEY TRANSPLANT RECIPIENTS: 6 MONTH-INTERIM ANALYSIS OF A FRENCH MULTICENTER OBSERVATIONAL STUDY (OPALE)

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Introduction: Once daily formulation of Tacrolimus as Advagraf™ (ADV) has been proven to be comparable to twice daily formulation as Prograf™ (PRO) in terms of efficacy and safety for kidney transplantation (KT). However for patients (pts) under PRO modalities of midterm conversion to ADV have not been assessed in France for KT pts. This study aims to describe modalities of conversion (C) from PRO to ADV when deemed appropriate by physicians, during the first year after KT.
Methods: Multicentre, longitudinal observational 12-month study including data collection at baseline (BL), 6 and 12 months. 2 KT populations were analysed according to the time of C, before (early group-EG) and beyond (late group-LG) 6 months after KT. Primary objective included TAC dose ratio (DR), time to first TAC trough check (TT0) and additional visit (AV) due to C (if any). Interim analysis data at 6 months is presented.
Results: Out of 600 pts screened in 28 KT centres, 578 (451 (78%) in EG & 127 (22%) in LG) were included in analysis population. Main reasons for C were investigators decision (42.6%) and centre practice (28%). Mean age at inclusion was 51.5 ($\pm$ 14.1) yrs, 64.2 % were male. Cadaveric donor occurred for 79.9% pts. Main initial diagnosis was glomerulopathy including IgA nephropathy (24.7%). At BL, diabetes and dyslipidemia were reported for 19.7% and 28.3% in EG versus 27.9% and 37.6% in LG. Mean DR were 0.98 $\pm$ 0.17 mg in EG and 0.99 $\pm$ 0.09 mg in LG. More than 50% (EG: 49.33%; LG: 66.93%) had a DR = 1. Mean TT0 was 12.6 $\pm$ 15.4 days & 28.7 $\pm$ 28.7 days in EG & LG. AV were reported for 34 pts (6.2%). 14 BPAR were reported (50% borderline) in 14 pts (2.6%) after C with no graft loss. 2 deaths reported.
Conclusion: This interim analysis of the real-world OPALE study in KT recipients in France reported a conversion dose from PRO to ADV close to 1, especially when occurring beyond 6 months after KT, with very few additional visits due to conversion. The low rejection rate (2.6%) after conversion to ADV confirmed the procedure as safe.

O31 INCREASED BIOAVAILABILITY OF TACROLIMUS IN OBESE KIDNEY TRANSPLANT RECIPIENTS: A CASE-CONTROL STUDY

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Introduction: Immunosuppression adjustments in obese population are not consensual. Pharmacokinetics changes of Tacrolimus (Tac) induced by obesity are poorly studied.
Methods: We conducted a retrospective case-control study on the whole cohort of obese kidney transplant recipients (Ob) (BMI> 30 kg/m^2) treated by Tac followed at the University Hospital of Marseille, between 2013 and 2017. The non-obese control patients (NOb) were matched for age, sex and ethnic origin (ratio 1:1). Tac trough levels were weekly performed in the same laboratory by LC-MS/MS until month 3 (M3). Target trough levels were 8–10 ng/mL.
Results: Twenty-eight Ob were identified among 541 transplantations performed. The median BMI of the Ob was 31.6 (versus 23.2 kg/m^2 in 28 NOb), the mean age was 56 years old with a majority of women (57%). Each patient had the same immunosuppression: Thymoglobulin® (ATG), Tac (initial dose at 0.15 mg/kg/d), Mycophenolate Mofetil and steroids. Clinical data were similar between groups except a higher cumulative dose of ATG and a higher incidence of new-onset diabetes after transplantation (64 vs. 32 %, $p = 0.03$) in the Ob group. On an average of 22 dosages per patient, Tac trough levels were higher in Ob (mean: 9.9 vs. 8.7 ng/mL; $p = 0.008$) whereas Tac dose per weight ratios were lower (mean: 0.09 vs. 0.13 mg/kg/j; $p < 0.0001$). Tac trough levels per dose per weight ratios were higher in Ob group (mean: 116 vs. 76 (ng/mL)/(mg/kg); $p = 0.001$). A significant reduced dose between Tac initiation and M3 was observed in Ob group (-4.6 vs. -1.12; $p = 0.001$).
Conclusion: In this study, obesity seems to increase significantly bioavailability of Tac. Thus, an adjustment of the initial dose of Tac to achieve promptly trough levels range target should probably be discussed in Ob.

O32 INDUCTION THERAPY IN RENAL TRANSPLANTATION WITH MAASTRICHT TYPE III NON-HEART BEATING DONORS: COMPARISON BETWEEN ANTI-IL-2 RECEPTOR ANTIBODY AND POLYCLONAL ANTI-LYMPHOCYTE ANTIBODY

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Background: Anti-thymocyte globulin (ATG) induction therapy is recommended in recipients of kidneys from type III Maastricht controlled non-heart beating donors. No data are available in this population comparing ATG and anti-IL2 receptor (IL2R) antibody.
Methods: All kidney pairs from type III Maastricht donors were included if one recipient received an anti-IL2R antibody and the other matched recipient an ATG induction therapy. Retrospective analysis of the 6-month outcomes by Fisher's exact and Wilcoxon signed-rank tests for end-point variables, Mann-Whitney tests for demographic variables.
Results: Inclusion of 10 kidney pairs, i.e. 10 recipients with anti-IL2R antibody (group I) and 10 with ATG (group II) induction. Anti-IL2R was used in non-sensitized patients with no added risk of delayed graft function (DGF), and in one patient with HBV/HCV/HIV coinfection. Donors' mean age of 43 y. Mean agonal phase, asystolic phase and functional warm ischemia time (IT) of 36, 24 and 28 min. Recipients' mean age of 56 y. No differences in mean cold and warm IT (9.5 hours and 52 min in the cohort) and in last resistivity index (RI) recorded on the lifeport machine (mean RI 0.23). Maintenance with CNI (similar trough levels between day 15 and 6 months), MMF and steroids. DGF in 2 patients in group I and one patient in group II. Between day 5 and 6 months, similar renal function and proteinuria (serum creatinine at day 5: 269 vs. 324 μmol/L, eGFR at 6 months: 56 vs. 50 mL/min/1.73 m^2). No graft loss. 2 borderline cellular acute rejections (CAR) in group I, and one CAR in group II. No differences in histological data at 3 months including interstitial fibrosis and tubular atrophy. No difference in the incidence of infections.
Conclusion: In this small donor-matched cohort, an anti-IL2R antibody induction was not different than ATG at 6 months post-transplantation with type III Maastricht donors. The follow-up duration and the number of kidney pairs will progressively be incremented.

O33 THERAPEUTIC OBSERVANCE IN HEART TRANSPLANT: FRENCH COHORT AND IMPROVEMENT PERSPECTIVES

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Background: High risk of transplant rejection requires a life treatment, where morbidity and mortality might be affected by the patient's cooperation and compliance to medical prescriptions.
Method: An observational study based on heart transplant patient's compliance is going on at Louis Pradel hospital in Lyon. Throughout consultation and hospitalization, a survey was proposed to these patients since March 2017. This survey contained 6 questions about medication and two about smoking. Patients' score was established with the number of right answers: score = 6: good compliant, score 4–5: minor non-compliant, score £3: non-compliant.

Results: By now, 189 patients were included in the study. Among the patients tested, 28% were compliant and 6% non-compliant. The 45–55 age group showed the highest percentage of compliant and non-compliant patients simultaneously. 68% reported a delay with the regularly scheduled time of medication. 11% forgot from time to time their medication (memory issues). Finally, over 15% didn't know their medication's indications. Half of the patients before transplantation were active smokers. Following transplantation, 7% were active smokers including 10 former smokers and 4 new smokers.
Discussion: Among our cohort, in most cases patients were minor non-compliant (66%) and a few were non-compliant (6%). Compliance evaluation in the medical literature among heart transplanted patients shows bad performance as for Germani (1) (nonadherence: 38.5%) and Brocks (2) (nonadherence: 25%). This divergence might be explained by the different definitions of compliance and therapeutical adherence which implies an active implication of the patient towards his medications. (3)
Conclusion: Our data should be adding some adherence measurements to our current results. Furthermore, therapeutic education should be introduced in heart transplant service to enhance the patient compliance and therapeutical adherence.

O34 FACTORS INFLUENCING THE CHOICE OF NONDONOR FAMILIES IN A FRENCH ORGAN HARVESTING CENTER

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Objectives: Report the reasons that lead families to refuse organ donation during their close solicitation by hospital coordination.
Material and methods: A retrospective study was conducted between 2012 and 2015, including 148 (34%) refusal of organ donation among 426 patients identified in a state of brain death. A questionnaire of the family was completed for each interview. Collected data concerned patient characteristics, cause of death, description of the interview and reasons for refusal. A descriptive statistical analysis was performed.
Results: The median age of patients was 50 years with a sex ratio of 1.4 men to 1 woman. The most common reason for non-donor family was the desire to maintain the integrity of the body of the patient (28%) followed by a religious order pattern (11%), brutality and suddenness of death (9%), the denial of death (6%) and early age of the donor (5%). In 39% of cases, the family said that the donor had expressed a written or oral refusal in his lifetime.
Conclusion: A better understanding of the reasons leading to the refusal of non-donor family could provide assistance to the medical team on actions to general public with the aim to reduce the refusal rate.

O35 IMMUNE CHECKPOINT INHIBITORS IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Immune checkpoint inhibitors (ICIs) have emerged as powerful tools in the management of advanced cancers. As they stimulate immune responsiveness, their use can be difficult in kidney transplant recipients (KTR) under immunosuppressive therapy.
Methods: We describe the clinical course of a KTR with metastatic lung cancer treated with ICIs.
Results: A 56-year-old man was transplanted with a kidney from a deceased donor in 2014 for end-stage renal disease secondary to cholesterol embolization syndrome. His immunosuppressive treatment included tacrolimus, mycophenolic acid (MPA) and methylprednisolone. In 2015, he was diagnosed with stage IV non-small cell lung cancer (cT4N3M1a). MPA was discontinued and chemotherapy with pemetrexed and carboplatin was initiated in October 2015. After an initial partial response, the disease progressed, justifying second-line chemotherapy (docetaxel and nintedanib) in June 2016 that failed to induce a significant clinical response. A third-line treatment with nivolumab, a monoclonal antibody against the programmed cell death 1 (PD-1) receptor was considered. The risk of acute rejection and graft loss was discussed with the patient. Tacrolimus was switched to everolimus and methylprednisolone dose was increased. He received five cycles of nivolumab. His renal function remained stable during the treatment. Unfortunately, an unfavourable oncological evolution after the fourth cycle of ICIs was observed that led to reinitiate chemotherapy with pemetrexed and carboplatin. Subsequently, a significant regression of the disease was noted. The patient is still alive in June 2017, with a good performance status (ECOG 1).
Conclusion: Our case shows that although there is a risk of acute rejection, ICIs can be used in KTR after adjusting immunosuppression. The late favourable oncologic response might be a delayed response to the anti-PD1 but this remains to be investigated.

O36 FEVER AFTER KIDNEY TRANSPLANTATION: A PROSPECTIVE STUDY

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Introduction: Infections remain the second determined cause of mortality after kidney transplantation. Our objectives were to describe the frequency and the reasons of hospitalizations for fever after kidney transplantation.
Methods: It was a one year's prospective study. Included kidney recipients were hospitalized for fever higher than 38°C. Classical clinical parameters, risk factors and history of fever were collected. The etiologic diagnosis was supported by the results of microbiological and/or radiological analyzes.
Results: One hundred and twenty-nine hospitalizations for fever in 102 patients were analyzed. Infections were the cause of fever in 97% of cases. Acute urinary, respiratory and digestive infections accounted for 51%, 20% and 7% of events, respectively. Cystic infections and CMV diseases accounted for 5% of events, respectively. Two skin infections, 1 deep surgical site infection, 1 endocarditis and 1 central nervous system infection were diagnosed also. The 4 cases of non-infectious fever were associated with microcrystalline arthritis, acute graft rejection and myocardial infarction. For 96 events, 73 bacteria, 22 viruses, 1 fungus and 1 parasite were documented. Twenty-eight septicemia were recorded. In 6 cases of isolated fever of infectious origin, no microbiological documentation was obtained. Two deaths occurred during the study.
Conclusion: In our study, fever was a frequent cause of hospitalization after kidney transplantation and was associated with death in 2% of cases. Infection is the most frequent cause of fever and a microbe has been identified in 81% of cases of infection.

O37 POLYOMAVIRUS INFECTION AFTER RENAL TRANSPLANTATION

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Introduction: Human polyomaviruses (BK virus and JC virus) are ubiquitous viruses. Polyomavirus (PyV) infection, which is frequent in transplantation, is often asymptomatic. This infection is burdened with a major risk of graft loss. The aim of our work is to describe the epidemiological and clinical aspects as well as the diagnostic and therapeutic means of PyV infections in renal transplant patients.
Materials and methods: This is a retrospective descriptive and analytical study that includes all renal transplant patients who had a PyV infection between 2013 and 2016 and who are monitored at the nephrology department of Sahloul hospital.
Results: During this period, we identified 73 kidney transplant patients with an average age of 28 years. The sex ratio of our population is 1.43. The prevalence of PyV infection is estimated at 35%. BKV was the most prevalent (18.6%), followed by JCV (10%) and co-infection by both viruses in 6% of cases. We detected 2 cases of JCV infection (viruria and viremia positive) of which one was complicated by death. Serum co-detection of 2 viruses was observed in one patient. The mean time to BKV infection was 9.8 months. Urinary viral loads ranged from less than 10^3 to more than 10^7 copies /mL, while those in plasma were less than 10^5 copies/mL. After confirmation of the diagnosis, the decrease in immunosuppression was adopted for all patients. The evolution was marked by the occurrence of renal insufficiency in 9 cases of PyV viremia, 6 cases of PyV-associated nephropathy (PVAN) and a case of ureteral stenosis.
Conclusion: The high frequency of this infection and its potential severity are arguments in favor of the implementation of preventive strategies, at least in those at risk.

O38 THE SPOUSE AS A SOURCE OF ORGANS IN RENAL TRANSPLANTATION

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Introduction: Renal transplantation is the treatment of choice for patients with end-stage renal disease. The first kidney samples were taken from living donors, the majority of which were genetically related. In recent years, there has been a diversification of the sources of grafts, in particular from the spouse.

The aim of our work is to evaluate the survival of grafts and patients and to identify the prognostic factors of graft function.
Material and methods: This is a retrospective study carried out from January 2012 to December 2016. The number of patients receiving a graft from the spouse was 50. The immunosuppressive treatment was based on induction by ATG or Anti-IL2 and CTC, MMF and CNI for maintenance treatment. We analyzed demographic characteristics, episodes of acute rejection, complications and survival of grafts and patients.
Results: There were 38 men (76%) and 12 women (24%) with a sex ratio of 3.16, the mean age was (43 ± 8.853 years) and the donor age was (40 ± 9.026 years) . 88% of the patients were dialyzed before the transplant, only six patients benefited from a pre-emptive transplant. Initial nephropathy was indeterminate in 72% of cases. 62% of patients had between 5 and 6 HLA mismatches with the donor, 18% were semi-identical. . The mean graft function at 1 year and 3 years was 11.82 and 12.21 mg/L creatinine, respectively.
Conclusion: Regarded the growing need for organs, renal transplantation from spouses is a viable option in our population, what allows to expand the circle of living donors, especially in the absence of a national program of tacking from deceased donors.

O39 POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE IN KIDNEY TRANSPLANT RECIPIENTS: A SINGLE CENTER EXPERIENCE

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Introduction: Post-transplant lymphoproliferative disorder (PTLD) is the second most common malignancy encountered after kidney transplantation. The aim of this study was to determine the prevalence, presentation, characteristics, and outcome of PTLD in our cohort of kidney transplant recipients (KTR).
Methods/Materials: Retrospective study including adult patients transplanted with a kidney between 1974 and 2012 who developed PTLD. Patients with combined transplantation were excluded.
Results: 2949 adults were transplanted with a kidney. 24 KTR developed PTLD (92% Caucasian; 50% male), a period prevalence of 0.81%. Age at first transplantation was 33 years (min 20–max 75). Two thirds of patients were treated with induction therapy at transplantation; 38% had a past history of treated acute rejection. Age at PTLD diagnosis was 51 years (min 33–max 75). Time from first transplantation to PTLD diagnosis was 13 years (min 0.6–max 30). Median duration of follow-up was 17 years (min 1.6–max 42). PTLD presented mainly with gastrointestinal (38%) and constitutional non-specific symptoms (21%); 79% with diffuse disease at time of diagnosis (Ann Arbor IV (75%)). Tumors were B-cell related in 92%. Histological subgroup included mainly monomorphic PTLD (n = 22) with a majority of Large Diffuse B-Cell Lymphoma (n = 18). In 21 KTR with available information, only 7 tumors were Epstein Barr Virus positive. Immunosuppression reduction was applied in all but 3 patients. 23 patients were treated: 16 achieved total remission; 3 relapsed; 4 failed to respond. 7 patients died from PTLD (29%). At last follow-up, 58% of KTR had died.
Conclusions: PTLD prevalence in our cohort of KTR is 0.81%. Tumors were mainly late-onset, monomorphic, high-grade invasive B lymphomas, not EBV-driven. Mortality from PTLD was 29%.

O40 THE TRANSFORM STUDY: LOWER VIRAL INFECTIONS WITH EVEROLIMUS AND REDUCED CALCINEURIN INHIBITOR VERSUS MYCOPHENOLATE AND STANDARD CALCINEURIN INHIBITOR IN DE NOVO KIDNEY TRANSPLANT PATIENTS AT MONTH 12

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Background: Infections, especially those caused by cytomegalovirus (CMV) and BK virus (BKV), remain a common cause of morbidity and mortality post kidney transplantation (KTx). Everolimus (EVR)-based regimens have shown a significant reduction of viraemia and incidence of CMV infections in de novo kidney recipients (KTxRs). Here, we present the incidence of infectious complications in de novo KTxRs receiving EVR plus reduced calcineurin inhibitor (rCNI) versus mycophenolic acid (MPA) plus standard CNI (sCNI) at 12 months.
Methods: TRANSFORM (NCT01950819) is a 24-month, multicentre, open-label, two-arm study, randomising de novo KTxRs 1:1 to receive EVR+rCNI (n = 1022) or MPA+sCNI (n = 1015), with induction and steroids within 24 h post-Tx. Pre-emptive CMV therapy and/or prophylaxis therapy for at least 6 months post-Tx was recommended for all donor-positive/recipient-negative and for all CMV-positive recipients. Incidence of CMV and BKV infections reported as adverse event (AE) were summarised by treatment.
Results: Overall, 72.1% of patients in the EVR+rCNI and 81.0% of patients in the MPA+sCNI arms completed the study medication. Incidence of AEs/infections (97.9% vs. 97.2%) and serious AEs/infection (54.9% vs. 56.1%) were comparable between EVR+rCNI and MPA+sCNI arms. Incidence of overall infections (52.0% vs. 59.8%), viral infections (17.2% vs. 29.2%), CMV (3.6% vs. 13.3%) and BKV (4.3% vs. 8.0%) infection were lower with EVR+rCNI versus MPA+sCNI, respectively.
Conclusions: TRANSFORM, the largest study in de novo KTxRs, showed lower incidence of all types of viral infections, including CMV and BKV infection in EVR+rCNI versus MPA+sCNI, confirming the antiviral benefits of EVR when introduced early. Further analyses of the level of viraemia and severity of CMV disease may provide additional evidence on the protective effect of the EVR+rCNI regimen.

O41 12 MONTHS DATA ON INFECTIONS FROM ATHENA STUDY SHOW SIGNIFICANTLY LESS CMV-AND BKV-EVENTS WITH EVEROLIMUS-BASED VERSUS TACROLIMUS-MPA REGIMEN IN DE NOVO RENAL TRANSPLANT RECIPIENTS

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Background: The ATHENA trial was designed to compare everolimus [EVR] in combination with tacrolimus [TAC] or cyclosporine A [CyA] vs. a standard of mycophenolic acid [MPA] and TAC in de novo kidney transplant [KTx] recipients.
Methods: In this 12 months [M], prospective, open-label, randomized study with 15 German and 12 French sites, 612 patients [pts] were randomized 1:1:1 at time of Tx to either EVR (C0 target: 3–8 ng/mL M1-M12) +TAC (C0 target levels: 4–8 ng/mL M1-M3; 3–5 ng/mL M3-M12), or EVR (3–8 ng/mL M1-M12) + CyA (C0 target: 75–125 ng/mL M1-M3; 50–100 ng/mL M3-M12) or to control TAC regimen (4–8 ng/mL M1-M3; 3–5 ng/mL M3-M12) with MPA. All pts continued on steroids. Herein we report M12 outcomes on infections and CMV events from ITT with 208 EVR+TAC pts, 199 EVR+CyA pts and 205 TAC+MPA pts.
Results: From randomization to M12 total incidences of infections were 73% in EVR+TAC and 72% in EVR+CyA treated pts versus 82% in TAC+MPA pts. Whilst incidences of bacterial infections were similar between the three treatment groups (44% EVR+TAC, 43% EVR+CyA, 42% TAC+MPA) major differences were seen for viral infections with incidences of 41% in TAC+MPA versus only 26% in EVR+TAC and 12% in EVR+CyA groups. Incidence of BKV events was 23% in TAC+MPA versus 17% in EVR+TAC versus 9% in EVR+CyA pts ($p < 0.01$). CMV events occurred two thirds less in EVR treated pts compared to TAC+MPA control group with an incidence of 21% in TAC+MPA versus 6% for EVR+TAC and 3% for EVR+CyA treatment pts ($p < 0.001$).
Conclusion: ATHENA as largest European KTx study confirmed comparable efficacy and safety together with less viral infections for EVR-based treatment groups compared to TAC+MPA group. A significant, protective effect of EVR-based regimens versus CMV-/BKV-events was robustly confirmed.

O42 TRANSFORM STUDY: IMPACT OF DONOR TYPE ON 12-MONTH OUTCOMES OF EVEROLIMUS AND REDUCED CALCINEURIN INHIBITOR VERSUS MYCOPHENOLATE AND STANDARD CALCINEURIN INHIBITOR IN DE NOVO KIDNEY TRANSPLANT PATIENTS

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Background: Allograft source (living or deceased donor) impacts long-term patient and graft survival, and renal function post kidney transplant (KTx). TRANSFORM (NCT01950819) is the largest prospective study evaluating the

efficacy and safety of everolimus (EVR) and reduced calcineurin inhibitor (rCNI) versus mycophenolate (MPA) and standard CNI (sCNI) in de novo KTx recipients (KTxRs). Here, we present the 12-month (M) results by donor type.
Methods: In this 24M, multicentre, open-label, two-arm, randomised (1:1) study, de novo KTxRs received EVR+rCNI (n = 1022) or MPA+sCNI (n = 1015), with induction and steroids within 24 h post-Tx. Patients were stratified at randomisation by donor type (living, deceased standard criteria, or deceased expanded criteria) and CNI usage (cyclosporine or tacrolimus). Primary objective was to evaluate rates of the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) <50 mL/min/1.73 m2. The study compared EVR+rCNI versus MPA+sCNI at M12 using a 10% non-inferiority margin.
Results: The study met its primary objective of the composite of tBPAR and eGFR (EVR+rCNI vs. MPA+sCNI: 48.2% vs. 45.1%; difference [CI]: 3.2% [-1.3%, 7.6%]). Of 2037 KTxRs, 1017 received grafts from living donors (LD) and 1014 from deceased donors (DD). At baseline, mean body mass index, end-stage disease leading to Tx (except for immunoglobulin A nephropathy), and mean panel reactive antibodies, were balanced between groups. Analysis of adherence to CNI C0, efficacy and safety outcomes in donor subgroups is currently underway.
Conclusions: In this largest study to date in de novo KTxRs, demographics and baseline characteristics were comparable between LD and DD subgroups. Additional data will provide insights on how EVR+rCNI performed versus MPA+sCNI in different donor types.

O43 12 MONTHS OUTCOMES ON ALLOGRAFT FUNCTION WITH EVEROLIMUS-CNI VS TACROLIMUS-MPA REGIMEN IN DE NOVO RENAL TRANSPLANT RECIPIENTS: THE ATHENA STUDY

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Background: The ATHENA study was designed to compare efficacy, safety and outcomes on renal function [GFR] of everolimus [EVR] combined with tacrolimus [TAC] or cyclosporine A [CyA] versus a standard regimen of mycophenolic acid [MPA] +TAC in de novo kidney transplant [KTx] recipients.
Methods: In this 12 months [M], prospective, open-label, randomized study with 15 German and 12 French sites, 612 patients [pts] were randomized 1:1:1 at time of Tx to either EVR (C0 target: 3–8 ng/mL M1-M12) +TAC (C0 target: 4–8 ng/mL M1-M3; 3–5 ng/mL M3-M12), or EVR (3–8 ng/mL M1-M12) + CyA (C0 target: 75–125 ng/mL M1-M3; 50–100 ng/mL M3-M12) or control TAC (C0 target: 4–8 ng/mL M1-M3; 3–5 ng/mL M3-M12) + MPA. Steroids were to be continued in all pts. Here we report M12 outcomes on allograft function from ITT full analysis set with 208 EVR+TAC versus 199 EVR+CyA versus 205 TAC+MPA pts.
Results: From randomization to M12 allograft recovery was good in all three treatment groups with increase in GFR (Nankivell) as ΔeGFR M1-M12: a) EVR+TAC +6.6 mL/min, b) EVR+CyA +9.6 mL/min, c) TAC+MPA +7.6 mL/min (not significantly different). Analysis of donor age categories [<35; 35–49; 50–64; >65 years] showed that donor age >65 years had worst renal allograft outcomes, regardless of treatment. Urinary protein excretion at M12 was not different between groups with a category analysis showing only 3.7% of TAC+MPA versus 1.3% of TAC+EVR versus 0.7% of CyA+EVR pts had proteinuria in nephrotic range [>339 mg/mmol] at M12.
Conclusion: Comparable improvement in renal allograft function between all treatment groups with no difference in measured urinary protein excretion after 12 Mo drug exposure was shown in ATHENA, the largest European KTx study. Strongest impact on post Tx GFR appears to be determined by donor age, which is shown here for the first time in a large prospective study.

O44 CONVERSION TO EVEROLIMUS (EVL) AFTER LIVER TRANSPLANTATION (LT) IN THE REAL LIFE: DATA FROM THE EVEROLIVER MULTICENTER OBSERVATIONAL REGISTRY

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Introduction: Conversion to EVL has been used to minimize CNI and optimize renal function. This multicenter study aims to analyze modalities of conversion and long-term renal outcome.
Patients and methods: From 2006 till 2016, LT patients from 10 centers who were converted to EVL were recruited. Clinical and biological data were collected at various time visits till 5 years. Indications of transplantation were mainly alcoholic (53.4%) and HCV cirrhosis (19.9%). 41% of the recipients had HCC.
Results: 930 adult recipients (74% male, 53.9 ± 10.4 y/o). EVL was introduced in 42.5% of the patients during the 1st year post-transplant. Main reasons of introduction of EVL were chronic renal failure (35.7%) treatment of recurrent HCC (6.8%) or de novo cancer (20.3%) and prevention of HCC recurrence (23.5%). Mean through levels of EVL were respectively 5.7 ± 4.4, 6.3 ± 3.1, 6.5 ± 2.6 ng/mL at M1, M36 and M60. CNI were withdrawn in 49.4% and 71% of the patients respectively at M3 and M12. In the group of patients with an eGFR at baseline ≥60 mL/mn/1.73 m2 (n = 438) mean eGFR from M3 till M60 didn't differ statistically from baseline. In the group of patients with at baseline a mean eGFR < 60 mL/mn/1.73 m2; n = 445), median time from transplant to conversion was 25.1 (0.1–35.2) months, mean eGFR improved statistically from 42.8 ± 10.5 at baseline to 51.4 ± 41.4 (p = 0.008) and 48.9 ± 16.8 (p = 0.027) mL/mn/1.73 m2 respectively at M36 and M60. Twenty patients (2.1%) developed a histologically proven acute rejection with a median delay of 4.3 months (extremes 1–30.8). Survival rates at 1 and 3 years were respectively 92 % and 77%, and when excluding patients with cancer, survival was respectively 97% and 87%.
Conclusion: This real life registry showed that conversion from CNI to EVL allowed a significant weaning of CNI and a significant improvement of GFR maintained at 5 years in patients with chronic renal failure, with a low risk of rejection.

O45 WHICH INDUCTION FOR IMMUNIZED KIDNEY TRANSPLANT RECIPIENTS WITHOUT DSA?

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Introduction: Basiliximab is usually given to non-immunized patients. Today, because of better characterization of DSA with sensible flow bead assays, some use basiliximab in immunized kidney transplant recipients (KTR) without DSA.
Methods: Among 1030 adults KTR transplanted between 07/2007 and 05/2016 in our institution, 218 (21%) were immunized without pretransplant DSA (MFI < 1000). We compared risk of acute rejection and appearance of DSA in KTR treated by either basiliximab or antithymocyte globulin (rATG). We performed Kaplan-Meier curves and univariate/multivariate cox regression analysis (R version 3.2.3, p < 0.05).
Results: Basiliximab and rATG were used in 60 and 158 KTR, respectively. As compared to rATG-KTR, basiliximab-ATG had a lower PRA (24 ± 26% vs. 66 ± 32%, p < 0.0001), receive more frequently a first graft (88 vs. 63%, p < 0.0001) or a transplant with a living donor (13% vs. 2%, p = 0.005). Immunosuppressive combination of everolimus, tacrolimus and steroids was used only in basiliximab group (8.3% vs. 0%, p = 0.001). During the follow up (3 ± 2 years), acute rejection risk was higher in basiliximab group (n = 16, 21.7%) than in rATG group (n = 20, 12.7%) (log rang, p = 0.004). This greater risk remained after adjustment for sex, age, number of HLA mismatches and initial immunosuppressive strategy (HR=1.99 [1.02–4.69], p = 0.044). The appearance of DSA was observed in 13 (21.7%) and 26 (16.4%) patients treated with basiliximab and rATG (p = 0.087), respectively.
Conclusion: These results suggest that basiliximab induction is associated with an increased risk of acute rejection for immunized kidney transplant recipients without pretransplant DSA.

O46 RENAL, EFFICACY AND SAFETY OUTCOMES USING AN EVEROLIMUS (EVR)-BASED CALCINEURIN INHIBITOR (CNI)-FREE REGIMEN VERSUS STANDARD TACROLIMUS (TAC) AFTER LIVER TRANSPLANT (LTX): TWO-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 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. In CERTITUDE, immunosuppression was at the investigators' discretion.
Results: 188 pts were randomized in SIMCER; 143 entered CERTITUDE (65/93 EVR, 78/95 TAC) with 138 pts followed to year 2 (63 EVR, 75 TAC). The leading indications for Ltx were alcoholic cirrhosis (75/143) and HCC (35/143). At year 2, 44/65 (67.7%) EVR patients and 67/78 (85.9%) TAC pts remained on study drug. Mean (SE) change in estimated GFR (eGFR; MDRD) from randomization (RND) to year 2 after adjusting for baseline eGFR was -8.0 (2.8) mL/min/1.73 m2 with EVR and -13.5 (2.6) mL/min/1.73 m2 with TAC; difference 5.5 mL/min/1.73 m2 (p = 0.150). Observed mean (SD) eGFR at year 2 was 83.6 (24.8) versus 75.3 (29.6) mL/min/1.73 m2 with EVR versus TAC (p = 0.089). Between RND and year 2, biopsy-proven acute rejection (BPAR) occurred in 15.4% and 7.7% of EVR and TAC pts, respectively (p = 0.146). BPAR was mild in all except 2 EVR pt and 3 TAC pts. Major adverse cardiac events (MACE) occurred in 0% and 3.8% of EVR and TAC pts, respectively (p = 0.251). Neoplasms occurred in 5 EVR pts (5 neoplasms) and 9 TAC pts (14 neoplasms). HCC recurred in 0 EVR patients and 8.7% TAC pts. Two pts died in each group. No grafts were lost. Study drug was discontinued due to adverse events in 23.1% of EVR pts and 10.3% of TAC pts.
Conclusions: EVR and MPA with early TAC withdrawal preserves renal function to year 2 post-Ltx, with a higher rate of mild BPAR. MACE, malignancies and HCC recurrence were less frequent with EVR versus TAC but numbers were low.

O47 CONVERSION FROM CALCINEURIN INHIBITOR- TO BELATACEPT-BASED MAINTENANCE IMMUNOSUPPRESSION IN HEART TRANSPLANT PATIENTS: A SINGLE-CENTER EXPERIENCE

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Calcineurin inhibitors (CNI) continue to be the mainstay of immunosuppression after heart transplantation. However CNI are associated with nephrotoxicity. Belatacept is an immunosuppressive drug approved for use in kidney transplantation but has not been yet studied after heart transplantation. Contrary to CNIs, belatacept has not been shown to cause nephrotoxicity. The aim of this study was to determine whether conversion from CNI- to belatacept-based maintenance immunosuppression improves renal function in heart transplant recipients with renal dysfunction without increasing acute rejection rate.

Between 10/2015 and 07/2016, 6 heart-only and 2 heart-kidney adult transplant patients were converted to a belatacept CNI-free immunosuppressive regimen as part of renal sparing protocol. Renal function and acute rejection were assessed at 1, 3 and 6 month after the switch. An improvement in renal function was defined as an estimated glomerular filtration rate (eGFR) increase >5 mL/min.

Mean renal function improved from an eGFR of 29.0 mL/min [range: 18.9; 38.0] prior to the switch to 35.0 mL/min [21.1; 43.7] at 1 month post-conversion, 38.3 mL/min [29.5; 58.0] at 3 month post-conversion and 38.6 mL/min [27.7; 54.7] at 6 month post-conversion. Renal function improved in 6 patients and remained stable in 2 patients. Five patients were diagnosed with 1R acute cellular rejection (ACR) and one patient was diagnosed with 2R ACR. No 3R ACR nor antibody-mediated rejection was noticed. Two patients developed an infection after belatacept initiation. One patient developed a nephrotic syndrome requiring CNI reintroduction.

This single-center study suggests that conversion to belatacept with CNI withdrawal in heart transplant patients with renal dysfunction led to improved renal function without increasing acute rejection rate.

O48 SUBSEQUENT NON-MELANOMA SKIN CANCERS AND IMPACT OF IMMUNOSUPPRESSION IN LIVER TRANSPLANT RECIPIENTS

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Background: Non-melanoma skin cancers (NMSC) are the most frequent cancers in solid organ transplant recipients, with a high rate of recurrence (subsequent tumors). The aims of the present retrospective study were to describe subsequent NMSC in a large cohort of liver transplant recipients (LTR) with long follow-up, and to analyse the factors influencing it, including immunosuppressive (IS) regimen.
Methods: Ninety-eight LTR (76 males) with a personal post-transplant history of spinocellular carcinoma (SCC), basocellular carcinoma (BCC) and Bowen's disease were included, with a median follow-up of 12.4 years (range 1.5–27.8) after LT.
Results: Median follow-up after first NMSC was of 6.4 years (0.17–22.1). Fifty-two (53.1%) patients developed 162 subsequent NMSC with a BCC/SCC ratio of 1.8:1. The actuarial risk of developing second NMSC was 13.7%, 28.4%, 49.4%, 65.7% and 88.4% at 1-, 2-, 5-, 10- and 15-years, respectively. Multivariate analysis disclosed that phototype I-II (Vs. III-IV) was a significant risk factor for second NMSC (HR: 2.556, 95%CI 1.45–4.48, p = 0.001), whereas calcineurin inhibitors (CNI) withdrawal was significantly protective (HR: 0.358, 95%CI 0.142–0.902, p = 0.029).
Conclusions: Our results confirm that subsequent NMSC are very frequent in LTR and strongly suggest that conversion from CNI-based IS regimen to mTORi/antimetabolite-based IS regimen can reduce subsequent NMSC.

O49 FACTORS INFLUENCING ISLET GRAFT SURVIVAL TEN YEARS AFTER ISLET TRANSPLANTATION (IT) IN TYPE 1 DIABETES (T1D)

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The pathogenic role of humoral autoimmunity post-IT remains debated. We compared the effect of seroconversion of GAD, IA2 and ICA in T1D patients on the long-term outcome post-IT.
Methods: 33 T1D patients received either an IT alone (ITA, n = 19) or an islet-after-kidney transplantation (IAK, n = 14), with the Edmonton regimen. Metabolic results, graft survival assessed by a fasting C-peptide > 0.3 ng/mL), insulin-independency with normal HbA1c, β-score (classified as optimal (β-score ≥ 7) or sub-optimal (β-score < 7) to define the primary graft function (PGF)), GAD and IA2 aAb (RIA-Cis-Bio), and ICA (IFI) were prospectively assessed yearly during 10 years. Seroconversion was defined when GAD levels increased by 5 units from baseline pre-IT and when IA2 or ICA doubled compared to baseline.
Results: The graft was functional in 25 patients (14 ITA, 11 IAK) among whom 11 patients still insulin-independent (4 ITA, 7 IAK) with a median follow-up duration of 10.2 [5.8–11.0)] years. In the whole group, the percentages of graft survival and insulin-independence (Kaplan-Meier) were respectively 76% and 28% at 10 years. The graft type (IAK or ITA) had no influence on the results. In contrast, graft survival (93% *vs.* 53%; p = 0.0008; log-rank test) and insulin-independence (42% *vs.* 0% (p = 0.0002)) rates were significantly higher in patients with optimal PGF (n = 21) *vs.* sub-optimal PGF (n = 12) at 10 years. The frequency of GAD, IA2 or ICA sero-conversions taken separately or together did not differ between ITA and IAK, or optimal-suboptimal PGF. The seroconversion of the 3 autoantibodies seemed however associated with a lower 10-year graft function survival in the whole (76 *vs.* 53%), ITA (72% *vs.* 40%), and optimal PGF (93% *vs.* 48%) groups.
Conclusion: In these IT patients, an individual seroconversion of GAD, IA2 or ICA autoantibodies did not influence the long-term outcome, in contrast with the seroconversion of the 3 antibodies, suggesting a possible biomarker for immunomodulation.

O50 IS PANCREAS RETRANSPLANTATION A GOOD OPTION FOR UNSTABLE DIABETES TREATMENT?

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Introduction: Pancreatic transplantation is a reference treatment for unstable diabetes. In case of failure, a second transplantation may be performed in selected patients.

The primary outcome of this study was to assess second pancreatic graft survival. The secondary outcomes were to evaluate patients survival, causes of graft loss, and the impact on kidney graft function in case of pancreas-kidney transplantation.
Methods: This single center retrospective study regroup all second pancreas transplantation performed from 1987 to 2017. Data were collected from patients files through the DIVAT database ("Données Informatisées et Validées en Transplantation").

The second transplantation was performed mostly with a common or external iliac artery anastomosis and an inferior vena cava implantation.

Graft survival, causes of graft loss and patient survival were evaluated.
Results: From January 1987 to February 2017, 38 pancreas retransplantation occurred in our center, in 9 women and 29 men. The mean age was 42 years old. 36 patients profited of a second pancreas transplantation after a first pancreas-kidney transplantation. 2 patients received a second pancreas graft after a first pancreas alone transplantation.

Graft survival was of 65% after 5 years, of 45% after 10 years. 11 patients (29%) lost their pancreatic graft, 3 of which from a early portal vein thrombosis.

Patients survival was of 85% after 5 years and 74% after 10 years. One patient death was directly related to his second pancreas transplantation. 5 patients had to go back on dialysis because of chronic rejection of the kidney transplant (with one non-compliance).
Conclusion: A second pancreas transplantation results in a reasonable graft survival, with a low impact on renal function. Its indeed a therapeutic option to be considered in selected patients after a first graft failure.

O51 LONG TERM FOLLOW-UP OF HEREDITARY HAEMORRHAGIC TELANGIECTASIA PATIENTS WHO UNDERWENT LIVER TRANSPLANTATION FOR SEVERE LIVER INVOLVEMENT

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Introduction: Liver transplantation (LT) has been reported as the only definitive curative treatment in hereditary haemorrhagic telangiectasia (HHT) with severe liver involvement leading to high-output cardiac failure and/or biliary ischemia and/or portal hypertension. The aim of this study was to evaluate HHT patients long-term follow-up after liver transplantation 10 to 24 years after transplant.
Methods: Patients who underwent liver transplant for HHT in the Lyon liver transplant Unit from 1993 to 2009 were followed prospectively at this centre and in the French reference centre for HHT.
Results: Fifteen patients were included in this study (14 women and 1 man). Mean age at transplant was 52 years (33–66). Main indication for LT was cardiac failure. Twelve patients are still alive (80%) 16 years (8–24) after LT. One patient died from cardiac failure 65 days after LT and two late deaths unrelated to the disease occurred. In patients with cardiac failure, mean cardiac index failed from 5 to 3 L/min respectively ($p = 0.001$). Eleven patients out of 15 also experienced a dramatic improvement in epistaxis and quality of life. Among the 14 long survivors, recurrent liver telangiectasia was found on CT scan in 8 patients (57.1%) and on histology in 2 patients (14.2%) after a mean delay after LT of 11.6 years (6–15).
Conclusion: LT is a successful option for the treatment of severe hepatic HHT with low mortality in this cohort. Although, long term follow-up also suggests that hepatic recurrence of the disease seems to happen in an increasing number of patients.

O52 IMPACT OF DIRECT ACTING ANTIVIRAL AGENTS (DAAS) FOR HEPATITIS C VIRUS (HCV)-INDUCED LIVER DISEASES ON REGISTRATION AND OUTCOME ON WAITING LIST (WL) FOR LIVER TRANSPLANT (LT)

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Context: The 2nd generation of DAAs has provided major progress in the therapeutic management of patients with HCV in demonstrating improved sustained virological response. In France, since 2013, the availability and extent use of DAAs for cirrhotic patients lead to eradicate HCV and avoid liver decompensation.
Objective: To determine the impact of the 2th-generation of DAAs on registration and outcome on the WL for LT.
Patients and Methods: The study included all adult candidates registered on WL for HCV-induced liver diseases between 2000 and 2016 ($N = 5580$). We compared kinetics over time of transplant indications, outcome on WL and 1-year post-transplant survival.
Results: The number of candidates listed for HCV-induced liver diseases has increased of 104% from 2000 ($n = 194$) to 2013 ($n = 395$). We observed an inversion of the indications of transplant, HCC becoming predominant and representing 54% of HCV-candidates in 2016 vs 30% in 2006. From now, decompensated HCV-cirrhosis represents 38% of candidates and listing for retransplantation decreased of 35% since 2013. We observed (i) a significant decrease of WL mortality from 7.4% in 2013 to 3.3% in 2016 (+62%), (ii) a decrease of 30% of delisting for worsening condition from 2014 to 2016, (iii) an increase of 82% of delisting for improving condition between periods 2011–2013 and 2014–2016, (iv) sharp increase of inactive patients on WL from 23% in 2013 to 60% in 2016. From now, HCV -induced liver diseases represents no more than 16% of liver transplant between 2014 and 2016, compared to 20% in 2011 and the 1-year graft survival rate is significantly improved between before 2010–2012 and after 2013–2014 extent use of DAAs.
Conclusion: Our study indicates that patients have been benefiting from therapeutic access to DAAs. The decrease of transplant needs for HCV-induced liver candidates has contributed to the decrease of global waiting list mortality and removal for worsening conditions observed in France since 2 years.

O53 IMPACT OF REVERSIBLE CARDIAC ARREST IN THE BRAIN-DEAD ORGAN DONOR ON THE RESULTS OF LIVER TRANSPLANTATION

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Introduction: Reversible cardiac arrest in brain deceased organ donor is often considered as prediction of poor results in liver transplantation (LT). The aim of this study was to analyse the impact of reversible cardiac arrest (CA) in the donor.
Material and Methods: We conducted a retrospective monocentric study including 330 liver transplantations between January 2008 and June 2017. We identified two groups: CA group (107 recipients of grafts from donors with reversible CA) and control group (323 recipients of grafts from donors without history of CA). exclusion criteria were: repeat LT, combined transplantations, split LT, LT with donors after circulatory death.
Results: Both groups were comparable regarding donor criteria except for the age (CA group younger than control group with median age 46 years versus 63 years). Recipient characteristics were similar between the two groups.

After LT, normalization of seric levels of factor V, creatinin, total bilirubin and GGT were comparable in both groups. ICU stay was of 9.9 ± 1.5 days in CA group and 11.4 ± 1.1 in control group (ns).

Overall survival and graft survival at 3 months, 1 year and 5 years were comparable between the two groups.

Arterial complications' rate was the same between the two groups. Primary biliary patency was better in CA group ($p = 0.028$).
Conclusions: Our study shows that LT with grafts from donors with CA is safe. It would even provide less biliary complications. Careful selection of donors with CA is mandatory not to jeopardize LT outcomes.

O54 MAY DE NOVO DONOR SPECIFIC ANTI HLA ANTIBODIES (DSA) AFFECT THE OUTCOME OF LIVER TRANSPLANT PATIENTS ON CALCINEURINE-INHIBITOR-FREE REGIMEN?

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Introduction: Calcineurin inhibitors (CNI) adverse effects have led to increasing interest in CNI withdrawal strategies. In this situation, the impact of de novo donor specific anti-HLA antibodies (DSA) on liver graft survival is debated. The aim of our study was to correlate the presence of DSA in liver transplant patients, on a CNI-free regimen, with the biological and histological features of the graft.
Methods: We conducted a retrospective study including liver transplant patients without preformed anti HLA antibodies prior to liver transplant and having a CNI-free immunosuppression. CNI withdrawal was performed after exclusion of infra-clinic rejection. DSA identification was performed with Luminex (SAP class I and II) MFI cut-off>1000. Liver biopsies were interpreted according to Banff 2016 Consensus on allograft pathology.
Results: We included a total of 67 patients. DSA testing was performed in 57 patients. The reasons for CNI withdrawal were: nephrotoxicity 55%, de novo neoplasia 30%, recurrent hepatocarcinoma 10%, diabetes, neurotoxicity and study protocol in 5% of patients. CNI withdrawal protocols consisted in mycophenolate mofetil (MMF) in 37 patients, MMF+everolimus in 12 patients (18%) and mTOR inhibitor in 16 patients (24%). Immune tolerance was achieved in 2 patients. 25 patients had DSA and 32 patients had no DSA. 91% of patients had class II DSA. Liver biopsy was performed within one month after DSA testing in 32 patients. Among 12 patients having DSA, liver biopsy was normal in 25% of patients, revealed steatosis in 41% of patients and advanced fibrosis or mixt rejection in 34% of patients versus the group of 20 patients without DSA where liver biopsy was normal in 60% of patients, mild fibrosis was seen in 30% of patients and chronic rejection in 5% patients. DSA MFI were > 10,000 in rejection and advanced fibrosis cases.
Conclusion: DSA could have a negative impact on liver allograft outcomes in patients on CNI-free regimens.

O55 CONVERSION FROM TACROLIMUS TWICE DAILY (PROGRAF™) TO TACROLIMUS ONCE DAILY (ADVAGRAF™) IN LIVER TRANSPLANT RECIPIENTS: 6 MONTH-INTERIM ANALYSIS OF A FRENCH MULTICENTER OBSERVATIONAL STUDY (COBALT)

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Introduction: Once daily formulation of Tacrolimus (TAC) as Advagraf™ (ADV) has been proven to be comparable to twice daily formulation as Prograf™ (PRO) in terms of efficacy and safety after liver transplantation (LT). However for patients (pts) under PRO, midterm modalities of conversion (C) to ADV have not been assessed in France for LT pts. This study aims to describe modalities of C from PRO to ADV when deemed appropriate by physicians, during the first year after LT.
Methods: Multicentre, longitudinal observational 12-month study including data collection at baseline (BL), 6 and 12 months. 2 LT populations were analysed according to the time of C, before (early group-EG) and beyond (late group-LG) 3 months after LT. Primary objective included TAC dose ratio (DR), time to first TAC trough check (TT0) and additional visit (AV) due to C (if any). Interim analysis data at 6 months is presented.
Results: 383 pts (8 excluded for analysis) were enrolled in 18 LT centres; 198 (53%) in EG & 177 (47%) in LG. Main reasons for C were investigators decision (54.9%) and centre practice (37.6%). Mean age at inclusion was 54.71 ± 11.10 years, 76.8% were male. DBD was performed in 96.3% pts. Main initial diagnosis was alcohol cirrhosis (57.6%) and HCC (42.1%). At BL, diabetes and dyslipidemia were reported in 39.4% and 7.6% in EG vs 33.9% and 10.2% in LG. Mean DR was 1.01 ± 0.29 mg in EG and 1.07 ± 0.29 mg in LG. 39.9% (EG) and 58.5% pts (LG) had DR = 1. Mean TT0 was 19.7 ± 34.04 days & 36.07 ± 37.65 days in EG & LG. AV were reported for 1 pt (0.03%). BPAR were reported for 7 pts (2.1%) after C (delay since C: 96.4 ± 53.15 days) with no graft loss. 1 death was reported (MOF).
Conclusion: This interim analysis of the real-world COBALT study in LT recipients in France reported a conversion dose from PRO to ADV close to 1, especially when occurring beyond 3 months after LT with no additional visits due to conversion. The low rejection rate (2.1%) after conversion to ADV confirmed safety of the procedure.

O56 IMPACT OF POTENTIAL RISK FACTORS AFTER LIVER TRANSPLANTATION – FRENCH STUDY OF 7290 PATIENTS

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De novo liver transplantation (TH) cancers are one of the leading causes of late post TH mortality with a cancer risk twice that of the general population. For patients transplanted from the liver in France we investigated the impact of prognostic factors associated with the occurrence of de novo cancer in patients who received (TH). We wanted to see the relationship between the characteristics of the recipients and the donors, and the appearance of de novo post-TH cancer.

This cohort study is based on a population including all primary liver transplants performed in France from January 1, 2000 to December 31, 2013 (n = 7290). An extension of the Cox model adapted to the identification of prognostic factors in a context of competitive risks was used.

Of the 7290 adult transplant recipients who had never had pre-transplant cancer between 2000 and 2013, 806 reported at least one post-transplant de novo cancer. The median age of patients without post-transplant cancer over the period was 50.39 years, the median age of patients with cancer was 55.66 years. The median (interquartile) follow-up time was 4.6 (1.88–8.10) years for patients not diagnosed with post-transplant cancer and 3.88 (1.99–6.65) years for Patients developing de novo cancer post-transplantation. The THs with alcoholic cirrhosis etiology accounted for 57.7% of the causes of TH in patients with cancer versus 40.9% in TH who had not developed cancer. We observed a significant increase in the risk of cancer Subdistribution Hazard Ratio (SHR) = 1.05 and death Hazard Ratio (HR) = 1.02 with age. Women have a significantly lower risk than men to declare a post TH cancer. Concerning results on initial disease, donor characteristics and immunosuppressor treatment in analysis.

O57 « HORS TOUR » LIVER GRAFT IS NOT A BAD GRAFT

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Introduction: When successively refused by five teams, a liver graft can still be allocated as « hors tour » rule. The team that accepts it can freely choose the recipient, allowing quicker access to liver transplantation. The experience of the transplant centers that accept these grafts is currently poorly broadcasted.
Methods: This retrospective monocentric work aims to compare "hors tour" graft liver transplantation results (n = 28) to patients with MELD lower than 20, transplanted with whole liver from brain-dead donor (n = 215) during the same period from 2008 to 2017.
Results: There was no difference between donor age (58.7 vs 54.3, p = 0.265). Donor Risk Index was higher in the "hors tour" group (1.75 vs 1.36, p = 0.003). There was no difference in terms of patient survival (p = 0.3575), graft survival (p = 0.4917), arterial patency (p = 0.6128) and biliary complications (p = 0.0565).
Conclusion: Thanks to careful recipient selection, results are similar. The use of such liver graft demands a better knowledge about the difference between a "hors tour" liver graft and extended criteria liver graft which expose the recipient to liver failure and long term complications.

O58 MRNA IL-17 EXPRESSION IN KIDNEY TRANSPLANTATION

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Introduction: To investigate the role of interleukin 17 (IL-17)/IL-23 pathway in the inflammatory process thus contributing to interstitial injury during acute allograft rejection, a IL-17 mRNA expression in renal allograft biopsy tissue was evaluated.
Methods: The gene expression of IL-17A in early allograft post-transplant biopsy (day 7: D7) was analyzed by quantitative real-time PCR (QUANTITEC IL-17A QIAGEN®) in 18 patients with acute rejection (GI) and 18 kidney recipients with stable renal function (GII) for at least one year. The relative expression for the target gene was given by 2^{-DDCT}. ELISA R&D systems kits were used to test the IL-17A, Il-17F and IL-23 levels in plasma at the day of transplantation (D0) and (D7).
Results: Functional exploration of allograft biopsy tissue of renal transplant revealed that recipients with (AR) have a significantly increased mRNA expression levels of IL-17A in D7 compared to patients with stable renal function (p = 0.037). Moreover, significant elevations of plasma IL-17A levels were noted in GI than in GII (p = 0.002) and serial study of this cytokine confirmed that increased IL-17A levels between D0 and D7 correlate to acute renal allograft rejection (p = 0.06). Nevertheless, ROC curves, used to evaluate the performance of plasma IL-17A in detecting AR showed that given 100% specificity, the highest sensitivity was only 35.4% at cutoff value of 40.87 pg/mL.
Conclusion: Based on these findings, significant increase of IL-17A mRNA and protein levels in AR patients highlights the role of this cytokine that can be a useful clinical biomarker to predict early acute renal allograft rejection

O59 INTERLEUKIN-34 AS A PROMISING REGULATORY CYTOKINE MEDIATING TRANSPLANT TOLERANCE THROUGH TREGS

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Cytokines are powerful tools to regulate immune responses. In transplantation, it is still important to identify new specific and powerful mediators of immune tolerance. Interleukin-34 (IL34) is a newly discovered cytokine that binds to CSF1R (the M-CSF receptor), CD138 and PTPz and involved in differentiation and survival of myeloid cells. Until recently, no link with T cell biology or transplantation had ever been reported for IL34. We previously showed that the cytokine IL34 was expressed by rodent $CD8^+CD45RC^{low}$Tregs, human $FOXP3^+CD45RC^{low}CD8^+$ and $CD4^+$Tregs and its overexpression was able to induce long-term allograft survival in a rat model through the modulation of macrophages. To further study the function of this cytokine in the immune system and alloreactive immune responses, we generated IL-34 deficient rats using the CRISPR/Cas9 technology. We showed that IL34 deficient animals present an increase of pro-inflammatory macrophages and have less $CD8^+CD45RC^{low}$ Tregs. Moreover, we demonstrated that human IL34 protein

administration into NSG mice infused with human PBMCs efficiently delayed in a dose dependent-manner GVHD when associated with a suboptimal 10-days dose of rapamycin. Furthermore, as IL34 is a cytokine that could be considered as biomarker of immune status of patients, we dosed this cytokine by ELISA in serum samples from kidney transplant recipients' cohort (CHU Nantes) with different outcomes. Data showed a trend of an increase in IL34 level in stable patients before transplantation compared to patients that will reject their graft. Moreover we analyzed $CD8^+CD45RC^{low}IL34^+$ Tregs in blood from a cord blood transplanted cohort (H. Mondor) in patients at low and high risk of developing a GVHD. Interestingly, low risk patients have a significantly higher rate of these cells compared to patients at high risk.

Thus, our data suggest the clinical relevance of IL34 in transplantation as a potent tolerance inducer.

O60 TRANSIENT ANTIBODY TARGETING OF CD45RC TO INDUCE TRANSPLANT TOLERANCE AND SUSTAINED ANTIGEN-SPECIFIC REGULATORY T CELLS

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Currently, the essential goal in transplantation is to develop therapy with specific immunosuppression to induce allograft tolerance without lifelong immunosuppression. The CD45RC molecule can be used to define two different subpopulations in rat and human, effector T cells express high level of CD45RC while regulatory T cells express low level of CD45RC. We hypothesize that targeting the CD45RC isoform with a short term anti-CD45RC mAb treatment could eliminate $CD45RC^{high}$ effector cells, enrich in $CD45RC^{low}$ regulatory T cells and thus induce tolerance in transplantation.

The effect of anti-CD45RC mAb was studied as a short-term treatment to prevent rejection in a heart allograft rat model and also to prevent graft versus host disease in a humanized mice model.

A 10d anti-CD45RC treatment induced allograft tolerance in 80% of treated recipient, with a transient decrease of both $CD4^+$ and $CD8^+$ $CD45RC^{high}$ T cells while the absolute number of both $CD4^+$ and $CD8^+$ $CD45RC^{low}$ Tregs is 5-fold increased. We also demonstrated the total absence of IgG humoral anti-donor immune responses in anti-CD45RC treated rats (n = 3), while, primary and memory immune responses against exogenous antigens were not affected (n = 3), demonstrating that anti-CD45RC mAb treatment induces a specific immunosuppression. In addition, we demonstrated that $CD45RC^{low}$ $CD4^+$ and $CD8^+$ Tregs from long-surviving anti-CD45RC-treated recipients were more suppressive in vitro and in vivo compared to those obtained from naive rats (n = 4).

Finally, we tested an anti-human CD45RC mAb in a GVHD model of human PBMCs infusion in humanized mice and demonstrated through cell sorting and co-transfer of $CD45RC^{low}$ cells or direct administration of the mAb into NSG mice that this protocol prevented GVHD occurrence in most of the mice (n = 6).

Our results highlighted the potential of anti-CD45RC mAb as a new innovative therapy in transplantation to induce specific immune tolerance without any other treatment.

O61 AUTOLOGOUS ADIPOSE-DERIVED STEM CELLS WITH IMMUNOMODULATORY PROPERTIES CAN BE GENERATED IN ALLOGRAFT RECIPIENTS UNDER IMMUNOSUPPRESSION

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Introduction: Infusions of autologous adipose-derived mesenchymal stem cells (ASC) may become an important option for the management of allograft rejection. This is explained by the immunomodulatory properties of ASC, in particular their ability to inhibit innate immune cells (especially monocytes) and to induce regulatory B cells (Breg). Whether it is possible or not to generate ASC with potent immunomodulatory properties in allograft recipients under immunosuppression is unknown. We analysed the *in vivo* immunomodulatory effect of ASC generated in an upper-extremities transplantation (UET) recipient.

Methods: A 34-year-old woman who underwent UET in 2007 received ASC as salvage therapy for relapsing rejection. At time of ASC preparation, immunosuppressive treatment included prednisone, tacrolimus, sirolimus and MMF. The patient received ASC (2×100.10^6 IV 1 week apart) in 2014 and 2015 at time of severe skin rejections. Immunosuppressive treatment remained unchanged until day 14. Prednisone were then increased to 20 mg/day. PBMC were isolated at days 0, 14, 30 and 90. An extensive analysis of monocytes, T and B cells subpopulations and a functional assay to quantify Breg were performed.

Results: No side effect was reported. At day 7, skin biopsies showed a milder dermal infiltrate. At day 14, there was no additional clinical lesion but pre-existing lesions were still present. At day 42, grafted skin was almost normal. After each ASC infusion, expression of the activation marker CD62 by monocytes decreased and the proportion of Breg significantly increased. Data were similar to those observed in non-transplanted patients who received ASC for scleroderma or rheumatoid arthritis in clinical trials.

Conclusion: This study provides the first evidence that ASCs with potent immunomodulatory properties can be generated in allograft recipients under immunosuppression.

O62 STUDY OF IMMUNOREGULATORY T LYMPHOCYTES IN TOLERANT TRANSPLANTED PATIENTS WITH LONG-TERM MINIMIZED IMMUNOSUPPRESSION

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Background: The long-term immunosuppressive therapy required to maintain host tolerance of a transplanted organ contributes to an increased risk for malignancy in organ transplant recipients. A variety of factors, including the intensity and duration of immunosuppression, can influence the likelihood of development of cancer in these patients. Here, we focused on two regulatory T cell populations, namely regulatory T cells CD4(+)CD25(+)FoxP3(+) (Treg) and CD4(+)CD8aa(+) double positive (DP8a) T cells as possible targets for immunosuppressive therapy.

Methods: Monocentric study including 52 renal transplant recipients (mean age: 64 year old) for more than 10 years (mean duration: 28 years), without clinical or biological signs of rejection, treated with minimized immunosuppression: azathioprine+steroids (Aza n = 5) or calcineurin inhibitor monotherapy (CNI, n = 33). Patients were subdivided into two subgroups (with (P+Ca) vs without cancer (P-Ca)). Healthy donors served as controls (HC n = 15).

Results: The mean frequency of Treg among the CD4 (+) T cells increased in the Aza group compared to the CNI ($p < 0.05$) and the HC groups ($p = 0.07$). Treatment with CNI seems to be associated with a decrease of Treg frequency ($p = 0.07$) and a lower stability of their phenotype (Helios(+) Treg $p < 0.05$).Whatever the treatment, the Treg frequency increased in the P+Ca group compared to the P-Ca group ($p = 0.05$), as well as their Helios(+) ($p = 0.05$) and effector-memory FoxP3(bright)CD45RA(−) ($p = 0.12$) fractions. Although there was no significant difference in the T DP8a frequency regarding the treatment and the occurrence of cancer, we observed a very high frequency of DP8a in two patients of the Aza+Ca group (n = 4) (arbitrary fold change cut-offs of > 10 as referred to the mean value of HC).

Conclusion: Our results reveal in tolerant transplanted patients under minimized immunosuppression an increase of Treg-memory cells with stable phenotype preferentially associated with cancer and Aza.

O63 MARKERS OF MICRO-VASCULAR ENDOTHELIAL CELL ACTIVATION IDENTIFY POOR RENAL GRAFT OUTCOME IN EARLY BIOPSY WITH ACUTE TUBULAR NECROSIS IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Acute tubular necrosis (ATN), a frequent histopathological feature in the early post renal transplant biopsy, affects graft function on the

long term. Appropriate markers to identify patients at risk of absent or incomplete recovery after delayed graft function are lacking.
Materials and Methods: Using immunohistochemistry, we detected micro-vascular endothelial (fascin, vimentin) and tubular epithelial (vimentin, kim1) activation/injury markers in 41 kidney transplant recipients who had a graft biopsy during the first month after transplantation showing ATN lesions.
Results: We found a significant association of microvasculature endothelial activation in early biopsies of patients with no or partial graft recovery (rho= −0.55, p = 0.0005 for spearman's correlation of endothelial activation marker fascin expression with eGFR at 24 month post transplant). A strong correlation between extensive ATN, scored by morphometry, and a poor graft function at 24 month post transplant, (spearman's correlation with rho= −0.64, p = 0.003) was found only in the patients with the endothelial activation markers but not in those without these markers. The predictive value of micro-vascular endothelial activation for worse renal graft outcome was confirmed in a second transplant center with 40 early biopsies with ATN.
Conclusion: Our results suggest a detrimental role of endothelial cell activation at the early phase of kidney transplantation and the implication of micro-vascular injury in early ATN and late graft loss.

O64 TIME-DEPENDENT RECONDITIONING EFFECT OF ABDOMINAL NORMOTHERMIC OXYGENATED RECIRCULATION (ANOR) IN A PORCINE PRECLINICAL DCD MODEL KIDNEY TRANSPLANTATION

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Introduction: Kidneys from donation after circulatory death (DCD) are exposed to ischemia reperfusion injuries. Abdominal Normothermic Oxygenated Recirculation (ANOR; also called NRP: normothermic regional perfusion) is a reconditioning method, clinically approved to improve DCD organ quality. The aim of this study is to evaluate the optimal duration of ANOR which remain unknown, as ANOR duration varies from 2 h until 6 h in Europe.
Methods: The ANOR was modeled in a DCD porcine model. After 30 min of cardiac arrest, ANOR was run for 0, 2, 4 or 6 h (n = 6 *per* group); kidneys were machine-preserved for 18 h and allotransplanted (n = 6 *per* group).
Results: At the end of kidney machine perfusion, kidneys submitted to 2, 4 or 6 h ANOR present a better flow and lower organ resistance compared to 0 h ANOR. In term of kidney function after transplantation, from day 0 to day 14 post-transplantation, kidneys submitted to 6 h ANOR present a lower creatininemia compared to 0, 2 and 4 h ANOR, and kidneys submitted to 4 and 6 h ANOR present a more physiological glomerular filtration rate (GFR) compared to 2 and 0 h ANOR. From day 0 to day 90 post-transplantation, kidneys submitted to 4 or 6 h ANOR present a lower creatininemia and fractional excretion of sodium compared to 0 and 2 h ANOR. At day 90 after transplantation (Day 90), kidneys submitted to 4 and 6 h ANOR present a more physiological kidney function and a lower ratio proteinuria/creatininuria, compared to 2 and 0 h ANOR. A day 90, kidneys submitted to 0 h ANOR present a higher fractional excretion of sodium compared to 2, 4 and 6 h ANOR. In term of kidney fibrosis at day 90, kidneys submitted to 6 h ANOR present a lower fibrosis level compared to 0 and 2 h ANOR.
Conclusion: Processing ANOR between 4 and 6 h duration appears beneficial to improve early and tardive kidney graft function recovery and limit fibrosis development.

O65 *EX VIVO* NORMOTHERMIC HEMO-PERFUSION OF PIG KIDNEYS AFTER STATIC COLD-STORAGE: FUNCTIONAL EXPLORATIONS AND ENERGETIC PERFORMANCES

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Background: *Ex vivo* normothermic perfusion (EVNP) allows to preserve/recondition lower quality organs, but mechanisms are unclear and experimental studies heterogeneous. We explore hemodynamic, filtration, reabsorption and O_2 consumption of cold-stored kidneys next submitted to EVNP with Krebs (K) *versus* whole-blood (WB), with or without heparin (Hep). To reduce animal number (3R), we use Pig contralateral kidneys from transplantation studies and WB from end-protocol controls.
Methods: Kidneys flushed and cold-stored (SCOT15®; 2–4 h); blood cold-stored in CPDA-1 bags. After catheterization of renal artery and ureter (urine production, UP, mL/min), the kidney was mounted for perfusion flow monitoring (PEF mL/min), at 37°C, at constant 80 mmHg pressure (PP); resistance RR=PP/PEF. Perfusion media equilibrated with 95%O2/5%CO2 (K + 60% BSA). Na fractional reabsorption (FR%) calculated from creatinine-based glomerular filtration rate (GFR; mL/min), Na transport (mmol/min) and excretion; av-QO2 consumption ($QO2_{,m}$mol/min) calculated from PEF and arterial and venous O2 levels. Results, mean ± SD (n), expressed for 100 g kidney weight.
Results: (Hep, IU/L): (i) K-BSA yields the highest perfusion flow and QO2, but low GFR and urine flow, and insignificant FR% and TNa/QO2 –a measure of transport efficiency. (ii) With WB-250Hep, PEF decreases but GFR, FR% and UP increase; conversely, QO2 is reduced (TNa/QO2 increased). (iii) Increasing Hep 5,000, PEF remains similar, but GFR, UP, TNa, FR%, and transport efficiency strongly increase (2–6 fold).
Conclusion: Using a Pig preclinical model of static cold storage, we show strong decoupling, with Krebs, between (high) perfusion and (poor) function: thus, artificial medium appears unsuitable for renal function. Conversely, heparinized whole-blood yields better function, approaching "physiological" values, especially in terms of transport "respiratory" efficiency.

O66 IMPACT OF ACTIVE OXYGENATION AND AN OXYGEN CARRIER DURING PRESERVATION OF KIDNEY TRANSPLANTS IN MACHINE PERFUSION PRIOR TO TRANSPLANTATION

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Introduction: Experimental and clinical data indicate that the preservation in a machine perfusion (MP) is beneficial for the renal graft from non-heart beating donors (NHBD). However, this method requires improvement to minimize the ischemia lesions. The addition of O_2 and an O_2 carrier during the perfusion could optimize the preservation.
Method: We used a porcine NHBD model: kidneys were exposed to one hour of warm ischemia in situ then preserved in a MP Waves® for 24 h +/− active oxygenation and supplemented or not with 2 g/L of HbAm (hemoglobin of marine worm (*Arenicola marina*)) before transplantation and follow up for 3 months post-transplantation (4 groups, n = 6 per group).
Results: During perfusion, the kidneys preserved in MP HbAm with or without active oxygenation showed a lower resistance and lower diastolic pressure, compared to the kidneys preserved in MP without HbAm without oxygenation. At the same time, the perfusion flow is significantly higher in the HbAm group with active oxygenation. Regarding the post-transplant kidney function, the animals with kidneys MP HbAm without active oxygenation show significantly lower serum creatinine than the animals with kidneys MP alone and kidneys MP HbAm active oxygenation. Three months after transplantation, the proteinuria/creatininuria ratio was higher in the group kidneys MP without supplementation of HbAm, compared to the groups kidneys MP active oxygenation. The interstitial fibrosis evaluated 3 months after transplantation was significantly lower in the group kidneys MP HbAm active oxygenation compared to the group kidneys MP without active oxygenation.
Conclusion: Our results suggest that the addition of active oxygenation during kidney perfusion machine provide an increased level of protection during preservation of the renal graft. This protection appears to be increased with addition of marine worm hemoglobin at the dose of 2 g/L.

O67 POST-TRANSPLANT REDUCTION IN PRE-EXISTING DONOR-SPECIFIC ANTIBODY LEVELS AFTER BELATACEPT- VS CYCLOSPORINE-BASED IMMUNOSUPPRESSION

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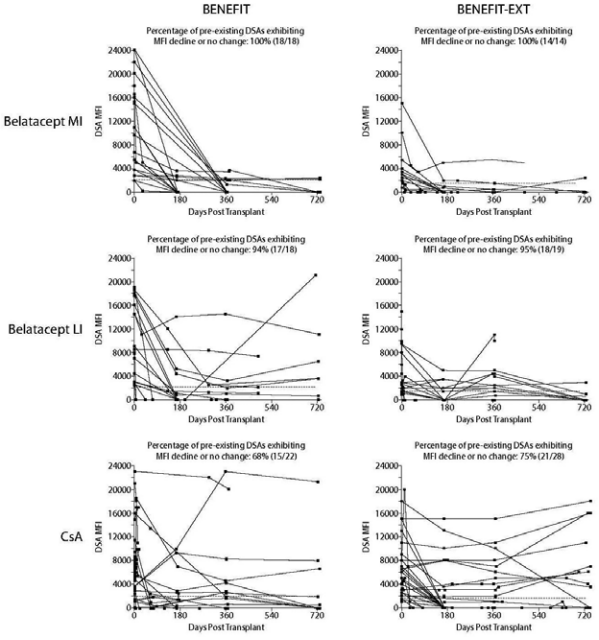
Introduction: We explored the effect of belatacept (bela)- and cyclosporine (CsA)-based immunosuppression (IS) on pre-existing donor-specific antibody (DSA) levels by monitoring mean fluorescence intensity (MFI) in patients (pts) enrolled to BENEFIT and BENEFIT-EXT.
Methodology: For both studies, cytotoxic T-cell–negative crossmatch kidney transplant recipients were randomized to bela more intense (MI)-, bela less intense (LI)-, or CsA-based IS. Pre-existing DSAs were assessed centrally at baseline via solid-phase assays: flow cytometry screen and Luminex single-antigen bead assays. DSA was determined by comparing antibody specificity to donor mismatched antigens.
Results: In BENEFIT, pre-existing DSAs were detected in 4.6%, 4.9%, and 6.8% of pts randomized to bela MI, bela LI, and CsA, respectively. In BENEFIT-EXT, these values were 6.5%, 5.7%, and 9.2%, respectively. The HLA class distribution of DSAs by treatment arm was similar in each study [table]. In both studies, more pts assigned to bela MI had baseline PRA <20% than ≥20%.

Over the first 2 years, pre-existing DSAs in bela-treated pts exhibited greater decreases in MFI vs pre-existing DSAs in CsA-treated pts [figure]. The effect of bela-based IS on DSA levels was more pronounced in BENEFIT-EXT vs BENEFIT. In both studies, MFI decline was more apparent with bela MI vs bela LI. Total IgG, IgM, and IgA levels were also reduced in bela-treated pts. Due to small sample sizes, clinical outcomes were not assessed.

Conclusions: Bela-based IS leads to greater decreases in DSA MFI, post-transplant in pts with pre-existing DSAs vs CsA-based IS.

	BENEFIT			BENEFIT-EXT		
	Bela MI (n=10)	Bela LI (n=11)	CsA (n=15)	Bela MI (n=12)	Bela LI (n=10)	CsA (n=17)
Mean age, y	49.6	45.0	44.1	55.2	53.8	57.7
Antibody class						
I	7 (70)	7 (64)	10 (67)	9 (75)	7 (70)	12 (71)
II	2 (20)	3 (27)	4 (27)	2 (17)	2 (20)	2 (12)
Both	1 (10)	1 (9)	1 (7)	1 (8)	1 (10)	3 (18)
PRA, n (%)						
<20%	7 (70)	4 (36)	6 (40)	12 (100)	8 (80)	14 (82)
≥20%	1 (10)	3 (27)	5 (33)	0 (0)	1 (10)	2 (12)
Missing	2 (20)	4 (36)	4 (27)	0 (0)	1 (10)	1 (6)



O68 INCIDENCE OF ACUTE REJECTION AND DONOR SPECIFIC ANTIBODIES IN LOW-IMMUNOLOGICAL RISK PATIENTS TREATED BY TACROLIMUS AND MYCOPHENOLIC ACID WITH OR WITHOUT INDUCTION THERAPY

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The need for using induction therapy in *de novo* non-HLA sensitized kidney-transplant patients receiving tacrolimus-based therapy is a matter of debate. The aims of this study were to assess the incidence of donor-specific antibodies (DSAs) and acute rejection in this setting.

All non-HLA sensitized de novo kidney-transplant patients who have received maintenance immunosuppression based on tacrolimus and mycophenolic acid with or without steroids, with or without induction therapy, and who had undergone a first kidney transplantation between Mars 2008 to June 2015 were included in the study (n = 450). 325 patients had received induction therapy (281 with basiliximab, and 44 with polyclonal antibodies). The remaining patients did not receive induction therapy (n = 125).

During the first year post-transplant, the incidence of acute rejection was 10.2% (46 out of 450 patients). Acute rejection episodes occurred in 38 patients who had been given induction therapy (11.7%) and 8 patients who have not be offered induction therapy (6.4%) (p = ns). During the first year post-transplant, 12 patients who received induction developed at least one DSA (3.6%) versus two in the group without induction therapy (1.6%) (p = ns). Estimated glomerular filtration rate at one year post-transplant did not differ between both groups.

Induction therapy is not required in low-immunological risk patients given tacrolimus and mycophenolic acid maintenance immunosuppression.

O69 FIVE-YEAR OUTCOMES AFTER RANDOMIZED TREATMENT BY RITUXIMAB IN EARLY ACUTE ANTIBODY-MEDIATED REJECTION IN RENAL TRANSPLANTATION – LONG TERM OUTCOMES OF THE RITUX ERAH STUDY

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Background: The treatment of acute antibody-mediated rejection (ABMR) is still a matter of debate. The place of rituximab is still controversial. The French multicenter double-blind, placebo-controlled RITUX ERAH study included 38 patients with biopsy proven early ABMR in the first year of renal transplantation. All patients received plasma exchanges, IVIg, and corticosteroids and were assigned to rituximab infusion (375 mg/m²) or placebo at day 5. Additional infusions of rituximab were allowed. In the intention-to-treat analysis, graft survival and renal function were not different between the groups treated by placebo or rituximab at 12 months. Long-term data are needed to conclude on the place of rituximab.

Methods: Evaluation of the five-year outcomes of the patients from the RITUX ERAH study according to the rituximab or placebo treatment received (independently of the initial randomized arm).

Results: All 38 patients were included. 11 received placebo (P group) and 27 at least one infusion of rituximab (R group). At 5 years after ABMR, death-censored kidney allograft survival was not different between the groups (64% in the P group, 54% in the R group). For patients with a functional graft, renal function (serum creatinine level, proteinuria, the evolution from the time of ABMR) was not different 5 years after ABMR (mean serum creatinine 148 μmol/L (eGFR 47 mL/min/1.73 m²) in the P group vs 164 μmol/L (44 mL/min/1.73 m²) in the R group; mean proteinuria 0.9 g/L in the P group vs 0.3 g/L in the R group). There was no difference in the incidence of bacterial and viral infectious complications, neoplastic complications 5 years after ABMR. The evolution of anti-HLA sensitization is currently being evaluated.

Conclusion: In our cohort, there was no benefit 5 years after ABMR of rituximab in addition with plasma exchanges, IVIg and steroids.

O70 HLA INCOMPATIBLE KIDNEY TRANSPLANTATION: DESENSITIZATION BY USING SEMISPECIFIC IMMUNOADSORPTION

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HLA incompatible (HLAi) kidney transplantation is defined by the presence at pretransplant of donor-specific alloantibody (ies) -DSA-. DSAs significantly increase the risk of antibody-mediated rejection.

We report on our desensitization experience on (i) 8 highly sensitized (HS) kidney-transplant candidates (TGI > 95%, waitlisted for at least 3 years) who did not have a live-donor, and (ii) on 8 kidney transplant candidates who had a live-donor against which they had a positive cross-match.

Desensitization protocol for the 8 HS patients relied on semispecific immunoadsorption (SSIA) with or without membrane filtration (Monet), in association with rituximab (375 mg/m² twice), tacrolimus, mycophenolic acid and steroids. Seven have been transplanted with a current negative cross-match even though there were DSA(s). Two of them presented with early acute antibody-mediated rejection that required eculizumab therapy. At last follow-up 6 have a functioning graft.

The 8 sensitized with a potential live-kidney donor had an historical and/or current positive cross-match. They have been desensitized with SSIA ± membrane filtration ± double filtration plasmapheresis, in association with rituximab (375 mg/m^2 twice), tacrolimus, mycophenolic acid and steroids. Seven were eventually transplanted; the last one presented during desensitization a myocardial infarction. None of them has had antibody-mediated rejection; at last follow-up all have a functioning graft with a very good renal function.

We conclude that in the setting of HLAi kidney transplantation pretransplant desensitization enables to transplant (highly) sensitized patients with very good results, at least in the short term.

O71 NON-ACTIVE DESENSITIZATION IN HIGHLY IMMUNIZED PATIENTS WAITING FOR A KIDNEY TRANSPLANT. A 9 YEARS MONOCENTER STUDY

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Hyperimmunized patients have a bad access to renal transplantation. We designed a protocol of non-active desensitization (NAD), where forbidden HLA specificities are withdrawn if the MFI of HLA antibodies identified in a Single Antigen Bead Assay is less than 3000 during the last 3 years, except those directed against former transplants. The efficacy of NAD was evaluated by the evolution of the TGI and NFAG, indicators of access to transplant of the French Agency of Biomedecine: TGI is a calculated PRA (> 85% for Hyperimmunized patients) and NFAG is the number of potential donors during the 5 last years for a given patient. Over a 9-years period, we have included 82 highly sensitized patients, waiting for a transplant during a median time of 4.6 years. We have withdrawn a median of 2 HLA-A, 6 HLA-B, 2 HLA-DR and 0 HLA-DQ antibodies. The TGI decreased from 98.5% to 94.5% and the NFAG rose from 2 to 17.5. Twenty one patients out of 82 were transplanted, 10 patients with at least one DSA in the historical sera (hDSA). Six patients were transplanted with 1 hDSA, 1 with 2 hDSA, 2 with 3 hDSA and 1 with 6 hDSA (4 with class I only, 3 with class II, and 3 with both classes I and II). The median MFI of the DSA on the current serum was 661, and the sum of MFI for those with several DSA was 1792. The median historical MFI peak was 8421 with a median of 7 years between the day of the peak and the transplantation. When patients transplanted with (10) and without hDSA (11) were compared for clinical data, no difference was seen. Two patients underwent acute humoral rejection within 3 months in both groups, with good response to treatment. One patient in each group died and 1-year post transplant serum creatinine was identical (respectively 165 μmol vs 164.5 μmol). Our results suggest that our NAD protocol improves patient access to a transplant and seems safe when the patient is transplanted even with hDSA

O72 VASCULAR SEQUESTRATION OF DONOR-SPECIFIC ANTIBODIES AND ENDOTHELIAL CHIMERISM PROTECT ALLOGENEIC ISLETS FROM HUMORAL REJECTION

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Introduction: Antibody-mediated rejection (AMR) is widely recognized as the first cause of transplant failure. Patients grafted with allogeneic islets for type-1 diabetes can develop donor specific antibodies (DSA). However, we recently reported that DSA did not accelerate the rate of graft attrition in a large cohort of islet recipients.

We undertook this translational study to identify the molecular mechanisms underlying the resistance of allogeneic islets to AMR.

Methods and Results: *In vitro*, DSA, both polyclonal immune sera and murine anti H-2^k mAb, were able to bind to CBA (H-2^k) islets and induce complement-dependent destruction of islet cells.

In contrast, repeated IV injections of DSA to C57BL/6 RAG2 KO (H-2^b) diabetic mice, did not impact CBA islet grafts function *in vivo*, reproducing what observed in patients.

Live imaging studies demonstrated that DSA were sequestrated in recipients' vascular bed and were unable to reach islet parenchyma. Interestingly, islet graft vasculature did not develop AMR lesions upon DSA transfer, in contrast with what observed in heart transplants. This difference was explained by the fact that donor endothelial cells were progressively replaced by endothelial cells from recipient origin (i.e. endothelial chimerism) in islet grafts but not heart transplants.

Conclusion: Our experimental study demonstrates that vascular sequestration of DSA and endothelial chimerism combine to protect allogeneic islets from humoral rejection. This study could have important clinical implications not only for islet grafted patients but also to understand the limitations of some biotherapies.

O73 POST TRANSPLANT DIABETES MELLITUS IN KIDNEY TRANSPLANT RECIPIENTS: METABOLIC STATUS ONE YEAR LATER

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Post-transplant diabetes mellitus (PTDM) is a frequent and severe complication (morbimortality, graft loss) of renal transplantation (RT) for which therapeutic strategies are discussed.

Aim: To retrospectively assess PTDM patients' abilities to withdraw from insulin at M12 according to their anterior metabolism state.

Methods: Within the RT unit, all patients above 18 years old with a renal transplant received between 01/01/2011 and 10/31/2015 and with a consequent PTDM were included.

Results: 674 RT were completed over the period with 65 consequent PTDM (prevalence 9.6%). 48 patients received early insulin therapy (73.8%), 30 of them were able to be weaned (62.5%) at M12. From all 17 patients on oral antidiabetic as initial therapy, 10 remained insulin-free to M12 (58.8%).

	Without insulin to M12 n = 41	With insulin to M12 n = 24	p
Graft weight kg	66.3 ± 13.9	77.1 ± 18.3	0.01
M6 weight kg	65.2 ± 14.3	76.8 ± 15.4	0.003
M12 weight kg	65.9 ± 13.4	79.3 ± 19.2	0.002
Graft BMI kg/m^2	24.0 ± 4.5	26.0 ± 4.6	0.09
M6 BMI kg/m^2	23.6 ± 4.3	26.0 ± 3.8	0.025
M12 BMI kg/m^2	23.9 ± 3.8	26.5 ± 5.2	0.028
Glycaemia mmol/L	6.1 ± 1.4	7.2 ± 2.9	0.039
HbA1c %	5.9 ± 0.7	6.6 ± 1.3	0.04
Triglycerides mmol/L	1.6 ± 0.8	2.6 ± 1.5	0.04
Uric acid μmol/L	409 ± 99	497 ± 182	0.029
Initial insulin %	73	75	0.87

In multivariate analysis, M6 weight predicted the possibility of insulin withdrawal before M12 (p = 0.012).

Conclusion: In line with Hecking's results (*J Am Soc Nephrol*, 2012)., insulin therapy showed good results to treat PTDM. Nevertheless, these data also showed that for insulin-resistant patients, initial insulin therapy may not be the only available choice to successfully treat PTDM.

O74 CARDIOVASCULAR LONG-TERM FOLLOW-UP AFTER PEDIATRIC KIDNEY TRANSPLANTATION

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Purpose: Chronic kidney disease stage 5 is an orphan disease in pediatric population. The best treatment is kidney transplantation. Those children are exposed to uremic complications and immunosuppressive treatment during their whole life.

Methods: Children who have been transplanted before 18 years old at Marseille have been included. Children born after 12/31/1995 and transplanted after 12/31/2010 have been excluded. The principal outcome was occurrence of major cardiovascular events (myocardial infarction, stroke, lower limbs arteriopathy and death of a cardiovascular cause).

Results: 69 patients have been included with 12 years of median follow-up (0–37 years). 53 patients had one transplantation, 17 had two transplantations and 3 patients had three transplantations. The average of transplantation follow-up was 16 years. Ten cardiovascular events (5 stroke, 2 lower limbs arteriopathy, 2 cardiovascular death and one myocardial infarction) occurred during the follow-up. 48% presented high blood pressure, 23% were smokers. 4 patients presented dyslipidemia and one patient had NODAT. 20 years renal graft survival was 80% for children who were transplanted between 3 and 9 years old, 82% for children who were transplanted between 10 and 14 years old. And only 55% for children who were transplanted after 15 years old.

Conclusion: Cardiovascular events are a frequent complication of long term follow-up after kidney transplantation in young patients. It seems to be important to study this kind of event and to manage cardiovascular morbidity early in their life.

O75 HIGH PREVALENCE OF POOR LOCOMOTOR FUNCTION AFTER KIDNEY TRANSPLANTATION: RESULTS OF A FRENCH PROSPECTIVE STUDY

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Objective: Chronic kidney disease is strongly associated with Poor Locomotor Function (PLF) and sarcopenia. However, few studies have evaluated them after Kidney Transplantation (KT). The main objective of this study was to define the prevalence of PLF 3 months after successful KT.
Patients and Methods: Since February 2016, locomotor and cognitive tests are routinely performed for all KT recipients in the KT unit. The 5-repeat-sit-to-stand test (5STS), Timed Up and Go test, walking speed, unipedal stance time with opened and closed eyes, handgrip strength and Frailty index are performed 3 months after KT. We defined PLF if at least 2 tests out of 6 deviated of more than 2SD or 10 percentile from the expected age-specific mean in the same population matched for age and sex (LOCNORM study established French norms).
Results: Over a one-year period (February 2016 to February 2017), tests were analysed on 133 KT recipients (aged 20–81 years). 65% of patients had PLF, 25% had 1 pathological test and only 10% had normal locomotor function. 29% of patients had more than 4 pathological locomotor tests and then were considered with High PLF (HPLF). Finally, 100% of the patients diagnosed as frail had one or more deficient locomotor tests. Time on dialysis before KT was associated with PLF ($p < 0.04$). 5STS added to walking speed found 87% of HPLF. This association might be appropriate to quickly detect deficient patients.
Conclusion: A majority of patients have poor locomotor function independently of age. This functional limitation is under estimated and associated with frequent falls, higher mortality and poor quality of life. Screening before and after KT must be developed especially in young patients, in order to propose personalized rehabilitation programs after KT as in other solid organ transplantation.

O76 CLASSIFICATION OF THE DIAGNOSES OF THE PRIMARY KIDNEY DISEASE IN PATIENTS ENROLLED ON WAITING LIST FOR KIDNEY TRANSPLANTATION – PROPOSITION OF A DIAGNOSTIC ALGORITHM FOR PATIENTS WITH « UNDETERMINED » NEPHROPATHY

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Introduction: Chronic renal failure is a public health issue. Primary kidney disease is unknown in 16% of cases at initiation of replacement therapy in France (REIN 2015).
Methodology: The purpose of this cross-sectional observational study is to identify and classify the primary kidney disease of patients enrolled on the waiting list for a renal transplant in our center and to study the cases of « undetermined » nephropathy. After conducting an exhaustive diagnostic approach based on surveys to validate or invalidate the diagnosis of initial nephropathy extracted from our databases, we classified the diagnoses into two categories: « determined » nephropathy or « undetermined » nephropathy. We compared the prevalence of diagnoses of kidney disease of our population with that of the prevalent cases who received a kidney transplantation in 2015 (REIN 2015).
Results: 329 patients were analyzed. We classified the diagnoses of primary kidney disease in: « determined » nephropathy (61.7%) or « undetermined » nephropathy (35.3%) (3% missing data). We corrected the diagnosis of kidney disease in 85 patients. For cases of « undetermined » nephropathy, we were able to determine the origin of the disease (glomerular, vascular, tubulo-interstitial and/or hereditary) in 69% of cases. We propose a diagnostic algorithm to support the diagnosis of these cases. We had no diagnosis for 10.9% of the cases (9.7% of the prevalent cases grafted in 2015 in France).
Conclusion: This study shows the importance of an exhaustive and systematized diagnostic approach continually updated in the light of scientific advances, allowing the establishment of the diagnosis of primary kidney disease in order to reduce the cases of « undetermined » nephropathy.

O77 AUTOIMMUNITY BIOMARKERS CAN PREDICT THE RELAPSE OF IGA NEPHROPATHY ON KIDNEY TRANSPLANT

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IgA Nephropathy (IgAN) frequently relapses on kidney transplants and can cause graft losses. The aim of our study was to determine the ability of specific autoimmunity biomarkers, Gal-deficient IgA1 (Gd-IgA1, autoantigen) and IgG- or IgA-anti-Gd-IgA1 (autoantibody) to predict the recurrence of the disease.

Every patient who met the retrospective inclusion criteria were analyzed. These criteria were: biopsy proven IgAN as native kidney disease, a minimal follow-up of 10 years, a first kidney transplantation and a calcineurin inhibitor based immunosuppressive regimen. Serum samples at diagnosis and from the first day of kidney transplantation were analyzed by IgA1-Gd and anti-IgA1-Gd ELISA. Thirty control samples were also analyzed. Judgment criteria were death, graft loss and clinicopathologic recurrence.

Ninety-six recipients were finally retrospectively included. Among them, 92 were transplanted from deceased donors, with a mean age of 48.1 years old. During follow-up, 13 patients died, 34 recipients lost their graft (17 caused by IgAN recurrence), and 34 patients had a clinico-histological recurrence after a mean interval of 5.85 years. IgG anti-Gd-IgA1 was high at time of transplantation as well as at diagnosis and was significantly associated with clinicopathologic recurrence (hazard ratio 2.68 [1.26–5.71], $p = 0.01$). Area under ROC curve was 0.622 [0.505–0.739], $p = 0.05$. These predictive performances remained significant after multivariate adjustment. IgA anti-Gd-IgA1 was significantly associated with graft loss from recurrence.

This study shows that in our population, the quantitative assessment of serum auto-antibodies specific to Gd-IgA1 at time of transplantation can predict IgAN recurrence on kidney transplants.

O78 DISTINGUISHING INFLAMMATORY BK VIRUS NEPHROPATHY FROM T CELL MEDIATED REJECTION: THE ROLE OF PLASMA CELLS AND HUMORAL IMMUNITY

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Introduction: BK virus nephropathy (BKVN) occurs in up to 10% of renal transplant recipients and can result in graft loss. The early diagnosis of BK virus viremia and the rapid decrease in immunosuppression can prevent the development of BKVN. Given the possible presence of tubulitis lesions and interstitial mononuclear inflammatory infiltrate, the differential diagnosis with T cell mediated rejection (TCMR) can be difficult.
Methods: Here, we tried to determine if the subtypes of immune cells in biopsy samples could reliably differentiate between BKVN and TCMR. BKVN biopsy (plasma pcr BKV > 4 log) samples with moderate to severe tubular (> t2) and interstitial lesions (> i2) (n = 15) were assessed for characterization and quantification of the different leukocyte populations by immunohistochemical staining, and were compared with TCMR (plasma pcr BKV=0) samples (> i2 and >t2) (n = 19).
Results: Macrophages and B cells were equally represented in both the BKVN and TCMR groups. Plasma cells were significantly more represented in the BKVN infiltrate (25.49% *vs* 5.78%, $p < 0.0001$) while T cells were more represented in the TCMR infiltrate (40.9% *vs* 51.76%, $p = 0.0093$).
Conclusion: The predominance of plasma cells might be a criterion for the diagnosis of inflammatory BKVN and suggests the important role of humoral immunity in the development of the disease.

O79 RENAL ALLOGRAFT TRANSPLANTECTOMY: MORBIDITY, MORTALITY AND IMPACT ON ALLOIMMUNIZATION ABOUT 180 CASES

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Background: Number of unfunctional kidney graft is actually growing up. 10% of patients returning to dialysis have still a non-functional graft. Role of renal transplantectomy and allo-immune impacts are poorly understood.
Material/Methods: This retrospective monocentric study of 180 transplantectomy was conducted from the first January 2000 to the 31 may 2016. Data were collected retrospectively and analyzed with statistical software SPSS 21.0.
Results: Population was 48.3% female and 51.7% male. The average age was 48 ± 15 years (7–76). The average running time of the kidney graft was 5.89 years (0–25.57). 38.33% of procedures were made by extracapsular approach and 61.67% by intracapsular. Transplantectomy were performed for: graft intolerance syndrome 47.2%, graft infection 22.2%, artery or vein thrombosis 15.5% and tumor 8.33%. The surgery time was 84.13 ± 40.12 min. Blood loss were 258.10 ± 601.32 mL. Morbidity was evaluate at 38% and mortality at 2.79%.

Complications was higher in surgery perform after 12 months ($p = 0.006$). Complications were also more important in several risky indications such as sepsis, venous/arterial thrombosis, non primary graft function, and kidney transplant removal in order to make space ($p < 0.05$). It has not been demonstrated significant difference in the evolution of anti-HLA antibodies according to the technique, based on transfusions, or for different groups of patients transplanted or not. At the end of more than half of patients re-enrolled study on the waiting list were transplanted. The average time for the new transplant was 28.1 months (1.8–95).
Conclusion: Transplantectomy is a highly morbid procedure. It must be considered after optimizing anesthesiologic patient conditions. It must be done away from a septic episode which increases the complications and mortality.

O80 RENAL GRAFT IMPLANTATION ON VASCULAR PROSTHESIS. A LARGE MULTICENTER STUDY

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Kidney transplantation with renal artery implanted on a vascular prosthesis is no comment, hard and risky. The objective of this study was to evaluate the overall survival and the specific survival of the transplant in this context.

Patients included in this study were drawn from the multicentric cohort from 10 transplantation centers. This was a retrospective study. The different complications were reported and a prognostic score was created. The Transplantation Committee of the French Association of Urology (CTAFU) has given its support in the collection of data.

Group 1 consisted of patients with kidney transplantation using artery anastomosis on a vascular prosthesis (figure 1). Group 2 consisted of patient with the same vascular profile than group 1 but with artery anastomosis performed on a native artery. And group 3 consisted of patients without any history of arteriopathy.

Thirty-four patients were included in group 1, 108 patients were included in group 2 and 1713 patients were included in group 3. Transplant's overall survival in group 1 was lower than group 2 and group 3 ($p = 0.1107$). Transplant's median survival was 9 years in group 1 and respectively 7.7 years and 12 years in group 2 and 3.

In group 1, graft dysfunction was mostly caused by a nephrologic dysfunction and come back in hemodialysis (80%) or mortalis. In group 1, the transplant function stops were mainly linked a nephrologist degradation and a return to dialysis (80%) and following a recipient of deaths directly attributable to renal transplantation (10%). In group 2, it was found excess mortality ($p = 0.0016$), more serious complications ($p > 0.0001$) and vascular complications ($p < 0.0001$) in comparison to groups 1 and 3.

Kidney transplantation with arterial anastomosis of vascular prosthesis, in selected patients, would give the same results if not higher than those observed in patients with vascular same profile (group 2) but whose arterial anastomosis is remote of the prosthesis.

O81 OUTCOMES IN KIDNEY RECIPIENTS FROM DECEASED DONORS OLDER THAN 70 YEARS: A RETROSPECTIVE MONOCENTRIC STUDY

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Outcomes in kidney recipients from deceased donors older than 70 years: a retrospective monocentric study.
Introduction: Considering the shortage of organs for transplantation, there is an urge to find ways to increase the pool of donor organs. In order to provide new sources, extended-criteria donors have been already proved to be useful for transplantation. Our goal is to assess the prognosis in kidney recipients transplanted from deceased donors older than 70 years.
Methods: Kidney recipients from deceased kidney donors aged over 70 years were included from 2005 to 2015, in a single-center retrospective study. Outcomes were survival, graft survival, censored or not for death, mean glomerular filtration rate (MDRD), and histological data on kidney biopsies. We looked then for factors that could impact these kidney prognosis (i.e. comorbidities, cold-storage vs hypothermic machine perfusion, ...).
Results: 116 patients were included. The mean age for donors was 74.83 (71.35–78.31), and 66.72 (58.72–74.73) for recipients. The mean KDPI for donors was 97.09 (93.56 – 100), whereas the mean EPTS for recipients was 70.27 (48.26 – 92.28). The means of glomerular filtration rate were 27.20 mL/min (13.33–39.52) at 15 days, 37 mL/min (23.62–60.02) at 3 months, 36 mL/min (23.34–60.56) at 1 year. Hypothermic perfusion had a strong impact on protocol kidney biopsies at 3 months, as 20 biopsies out of 38 kidneys not perfused showed tubular injuries, whereas only 4 kidneys perfused out of 40 presented these injuries. Yet, the global outcomes still need to be determined with statistical analysis.
Conclusion: The global results are not yet analyzed but the graft survival censored for death is acceptable. We think that very old deceased kidney donors may be an interesting source of organs and that the score to help decision-making shouldn't be the unique tool to accept or not a renal transplant.

O82 ENDOSCOPIC POLYDIMETHYLSILOXANE INJECTION IN PREVENTION OF RECURRENT GRAFT PYELONEPHRITIS FOR TRANSPLANTED KIDNEY WITH VESICOURETERAL REFLUX

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Objectives: evaluate the success rate of endoscopic injection of polydimethylsiloxane (EIP) for transplanted kidney with vesicoureteral reflux (VUR) and predictive factors of recurrence of acute graft pyelonephritis (AGPN).
Methods: 48 patients with recurrent AGPN associated to radiological VUR treated by EIP between 2000 and 2012 were retrospectively included. VUR were classified in low grade (LG) for I and II radiological type and high grade (HG) for types III, IV and V. Treatment failure was defined as recurrence of AGPN.

Free graft pyelonephritis (FGP) survival was calculated. Duration of dialysis, presence of native kidneys VUR, number of pretreatment AGPN, time to onset after transplantation, radiological grade of reflux, time to VUR management, experience of the endoscopist, voiding dysfunction and pretreatment creatinine levels were evaluated as predictors of failure.
Results: 24 patients were included in LG group (4 grade I and 20 grade II) and 27 patients in HG group (respectively 21, 5 and 1 reflux grades III to V).The 2 groups were comparable for all studied variables ($p < 0.05$). No obstruction was observed after EIP. The overall success rate was 70.6% ($n = 36$). The FGP rates at 1 and 3 years of EIP were 70.6% and 64.2%, with no difference between the two groups ($p = 0.549$). Recurrence ($n = 15$) occurred at a median of 5 months (3–9) regardless of grade group ($p = 0.131$), with 75% of persistent reflux. Three independent prognostic factors for EIP failure were identified: lack of residual diuresis before transplantation ($p = 0.014$), presence of voiding dysfunction ($p = 0.001$) and limited experience of the endoscopist ($p = 0.006$). For patients treated by a trained endoscopist ($n = 32$),the absence and the presence of 1, then 2 of the other risk factors were associated respectively with FGP rates at 2 years of 100%, 51.9% and 33.3% ($p < 0.001$).
Conclusion: EIP is a safe and effective first-line method to decrease recurrent graft pyelonephritis for patient with VUR.

O83 URETERO-ILEOPLASTY FOR URINARY TRACT SALVAGE AFTER KIDNEY TRANSPLANTATION

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Introduction: Urinary tract complications after kidney transplantation (KT) occur in 2–10% of cases. Their treatments can be complex. Aim of our study was to evaluate the feasibility and functional outcomes of salvage uretero-ileoplasty after KT.
Material and Methods: Retrospective and monocentric study from 2005 to 2017 including all of the salvage uretero-ileoplasty (sUI) performed in last-line treatment of complications of the urinary tract of the kidney graft.

6 male and 1 female were included. Mean age was 54.7 (20–73) and mean BMI was 25.4 (18.6–36) kg/m^2. The average time between the KT and the sUI was 21.3 (1–65) months. There were there living donors, one standard criteria donor, three extended criteria donors. No one were transplanted preemptively. Initial urinary anastomosis techniques were Lich-Grégoir ($n = 2$), pyelo-ureteral ($n = 4$) and uretero-ileal ($n = 1$) in bricker. All of cases, there were a stenosis and/or an ischemic necrosis of the urinary tract.
Results: Mean operative time and mean length of stay were 287.2 (247–337) min et 21.2 (13–36) days respectively. Blood losses were 415 (10–750) mL. There was no transfusion and no perioperative complications. The mean follow-up was 92.8 (29–189) mois. 2 patients have had a Hyperbaric Oxygen Therapy. 6 patients have had post-operative complications (grade 2 ($n = 4$), grade 1 ($n = 2$) according to Clavien-Dindo Classification). 6 patients have been rehospitalized at least once during the follow-up (one for infectious endocarditis at M15 and one for internal hernia at 6 years postoperatively. At day 0, M1, M6, M12 and at the date of the last news, mean serum creatinine was 240, 158, 160, 168, 170 micromol/L, respectively. There was no digestive fistula, no graft loss and no death.
Conclusion: Salvage uretero-ileoplasty is helpful, feasible and efficient. This technique has to be reserved as last-line treatment in cases of urinary tract complications after kidney transplantation.

O84 CHRONIC KIDNEY DISEASE AFTER LUNG TRANSPLANTATION: INCIDENCE, CHARACTERISTICS AND RISK FACTORS

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Background: Chronic kidney disease (CKD) is a frequent complication after lung transplantation, characterized by an increased mortality.
Methods: We retrospectively analyzed clinical and laboratory data from 188 patients who underwent lung transplantation at between 2009 and 2014 and survived more than 3 months. The prognostic value of variables for the occurrence of stage 3b CKD was calculated by univariate and multivariate analysis.
Results: Cumulative incidence of stage 3b or higher CKD was 18.4% at 1 year, 34.3% at 3 years and 42.1% at five years after LT. Cumulative incidences of stages 4 and 5 CKD were 12.8% and 5% at 3 years, and 22.5% and 12% at 5 years follow-up, respectively. Fifteen patients (8%) were on dialysis at the end of follow up. In CKD patients, proteinuria was 1.1 $\pm$ 1.4 g/24 h and biological thrombotic microangiopathy (TMA) occurred in 31% of patients. Using univariate analysis, we showed that risk factors associated with DFG < 45 mL/min were: age > 50 years ($p = 0.002$), smoking ($p = 0.006$), early acute kidney injury (AKI) ($p = 0.013$), early hemodialysis ($p = 0.002$), M1 creatininemia > 75 μmol/L ($p < 0.001$), M1 eGFR <80 mL/min/1.73 m^2 ($p < 0.001$), AKI occurring after 1 month ($p = 0.002$), CMV ($p < 0.001$), EBV ($p = 0.028$) and BKV ($p = 0.017$) replications, chronic diarrhea ($p = 0.003$), biological signs of TMA ($p = 0.006$), mean tacrolimus overdosages (over 12 ng/mL) higher than 4 ng/mL ($p = 0.045$) and everolimus treatment ($p = 0.005$). By multivariate analysis, age > 50 years (OR 2.44), early stage 3 AKI (OR 2.1), mean tacrolimus overdosages > 4 ng/mL (OR 1.71), TMA (OR 1.69) and CMV replication (OR 1.79) stayed associated with stage 3b CKD occurrence. CKD stages had no significant influence on patient survival in this cohort after a median follow up of 43 months ($p = 0.437$).
Conclusions: CKD is frequent after lung transplantation. We highlighted short as well as long term risk factors for CKD occurrence, including TMA, viral replications and tacrolimus overdosages.

O85 12 MONTHS SAFETY AND EFFICACY DATA FROM ATHENA STUDY ON EVEROLIMUS-BASED VS TACROLIMUS-MPA REGIMEN IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS

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Background: The ATHENA study was set up to compare everolimus [EVR] in combination with tacrolimus [TAC] or cyclosporine A [CyA] compared to mycophenolic acid [MPA] combined with TAC in de novo kidney transplant [KTx] recipients.
Methods: In this 12 months [M] prospective, open-label, multi-center study 612 patients [pts] were randomized 1:1:1 at time of Tx to either EVR (C0 target: 3–8 ng/mL M1–M12) + TAC(C0 target: 4–8 ng/mL M1–M3; 3–5 ng/mL M3–M12), or EVR (3–8 ng/mL M1–M12) + CyA (C0 target: 75–125 ng/mL M1–M3; 50–100 ng/mL M3–M12) or TAC (4–8 ng/ml M1–M3; 3–5 ng/mL M3–M12) + MPA. All pts were to continue on steroids. Here we report M12 efficacy and safety outcomes from 208 EVR+TAC, 199 EVR+CyA, 205 TAC+MPA pts (ITT).
Results: M12 Kaplan Meier estimates for treated BPAR were 6.7% in EVR+TAC, 17.6% in EVR+CyA and 3.9% in TAC+MPA group, with most events graded BANFF IA (1.9%; 9%; 1.5%) and only few (1.5%, 2% vs 0.5%) BANFF IIB/III. 5 pts in EVR+TAC, 5 in EVR+CyA and 6 in TAC+MPA died. Graft losses occurred as: 10 pts (4.8%) in EVR+TAC, 13 (6.5%) in EVR+CyA, 6 (2.9%) in TAC+MPA arm, including 5 primary non-functioning grafts in each EVR-group and 1 in TAC+MPA arm. Safety profiles were comparable, incidences of AEs/infections leading to study drug discontinuation or dose adjustment/interruption were 56.7% in EVR+TAC, 55.5% in EVR+CyA vs 61.3% in TAC+MPA arm. Main reasons for changes were infections (7.1% EVR+TAC, 4.5%EVR+CyA, 23.5%TAC control) and lympho-/leucopenia (3.3%, 3.5%, 13.2%). No differences in AEs on wound complications were seen (sum-incidences: 41.9% EVR+TAC, 38.9% EVR+CyA, 43.2% TAC+MPA).
Conclusion: ATHENA as the largest European KTx study confirmed good efficacy and event rates within international standards for all 3 groups with no unexpected safety events for this patient population. There were no differences in reported AEs on wound healing and less leucopenia with EVR-based regimens.

O86 PROTOCOL BIOPSIES IN PATIENTS WITH SUBCLINICAL DE NOVO DSA IN KIDNEY TRANSPLANTATION

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Introduction: De novo donor-specific antibody (DSA) is associated with antibody-mediated rejection (ABMR) and allograft loss. The aim of the study we present here, was to examine the histology associated with subclinical de novo DSA and to identify predictive factors of subclinical ABMR.
Methods: Retrospective multicentric study (9 French kidney transplant units of the Spiesser Group). All patients with a de novo DSA (One Lambda, MFI > 1000) without acute graft dysfunction and biopsied for DSA apparition were included in the study. Clinical, biological and histological characteristics of the patients were studied.
Results: 107 patients (76M/31F; mean age: 49.3 $\pm$ 12.7 years old) were biopsied 3.7 months (median) after the occurrence of a de novo DSA and after 65.3 months (median) after kidney transplantation. Graft function was stable during the 3 months before biopsy: MDRD = 57.3 $\pm$ 18.7 mL/min/1.73 m^2; proteinuria = 0.16 $\pm$ 0.14 g/g. DSA was in a large part a class 2 DSA (class 2 alone: 70.3%; class 1 + 2: 17.6%; class 1 alone: 12.1%). Biopsy led to the diagnosis of ABMR according to Banff classification (2013) in 42 cases (39.2%) with peritubular C4d deposition in only 15 cases (35.7%). Univariate analysis showed that the absence of steroids on the day of biopsy, presence of both class 1 and 2 DSA, the MFI of immunodominant DSA and the sum of the MFI of the DSA were associated with the diagnosis of subclinical ABMR. In multivariate analysis, only the sum MFI were still predictive (MFI > 7832: OR = 5.92, 1.63–21.46, $p = 0.006$).
Conclusion: Performing a kidney graft biopsy for the occurrence of de novo DSA without renal dysfunction lead to the diagnosis of a subclinical ABMR process in about 40%. This screening, guided by antibodies intensity, might allow the clinicians to initiate early a treatment before the organ dysfunction.

O87 INTRAVENOUS IMMUNOGLOBULINS FOR PREVENTION OF BK VIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENTS ACCORDING TO PRE-TRANSPLANT BK VIRUS NEUTRALIZING ANTIBODY TITERS: A PILOT STUDY

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Background: In kidney transplantation (KT), BK virus (BKV) replication could lead to BKV-associated nephropathy and graft loss. We and others have demonstrated that BKV replication post-KT is mostly of donor's origin. In a previous work, we demonstrated that BKV genotype-specific neutralizing antibodies (NAb) are protective against BKV replication above the threshold of 4 $\log_{10}$ (Solis et al, JASN) and intravenous immunoglobulins (IVIg) have an important anti-BKV neutralizing activity (Velay et al, personal communication).
Methods: We investigated the efficiency of IVIg for prevention of BKV replication after KT. Patients undergoing KT in Strasbourg were prospectively included from January 1 to March 2, 2017. Donors and recipients NAb were measured the day of KT. Patients at high risk of BKV replication were defined as those having BKV NAb titer below 4 $\log_{10}$ against the donor's BKV genotype or against the most common genotype (genotype I) if the sample of the donor was unavailable. Patients at risk received 3 cures of IVIg spaced by 3 to 4 weeks at a dose of 0.4 g/kg. The first cure was started at day 21 $\pm$ 7 after KT. BKV Nab titer, viruria and viremia were monitored until 6 months (M6) of KT. Bayesian method was used to estimate the posterior distribution of NAb titer against the target genotype after the 3 cures of IVIg at 3 months (M3) of KT. Bayesian method with data from a previous cohort was also used to estimate the posterior distribution of the risk of viruria and viremia at M6.
Results: 22 patients were included. 12 patients were at high risk for BKV replication and were treated by IVIg. At M3, NAb titer against the target BKV genotype increased above 4 $\log_{10}$ (probability: 73%). At M6, the risk of viruria and viremia was decreased in treated patients with a probability of 94% and 87%, respectively.
Conclusion: IVIg may represent an important strategy to prevent BKV replication after KT. A larger cohort study is needed to confirm these results.

O88 REAPPRAISAL OF THE LIVING KIDNEY DONOR SELECTION BASED ON THE RISK OF KIDNEY FAILURE

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Introduction: International recommendations have adopted a threshold of glomerular filtration rate (GFR) below 80 mL/min/1.73 m^2 to refuse a living kidney donation. As kidney donors are exposed to an increased risk of end-stage renal disease (ESRD), the KDIGO also recommend the determination of this risk based on a composite profile of many risk factors in living donor candidates.
Patients and Method: The main goals of our study were 1/ to compare both the projected 15-years and lifetime ESRD risks between a cohort of living kidney donors (n = 151) and a cohort of patients disqualified (GFR < 80 mL/min/1.73 m^2, n = 27), and 2/ to determine how many living kidney candidates would have been cleared for donation for each thresholds of ESRD risks.
Results: A complete overlap in both the 15-year and projected lifetime ESRD risks was observed between the two groups. Moreover, the use of these ESRD risks would deeply modify the donor selection by increasing the percentage of candidates cleared for living donation among those over 61 years-old, and decreasing those between 18–35 years-old, regardless the threshold of risk chosen. For instance, the use of the 15-year ESRD risk at 1% or 2% would increase the percentage of candidates cleared for living donation among those over 61 years-old by 25.1% and 42.4%, respectively. On the opposite, only 5.5% and 33% of patients between 18–35 years-old would be cleared for living donation using a post-donation projected lifetime ESRD risk below 1% or 2%, respectively.
Conclusion: In summary, the integration of these ESRD risks in the evaluation of living kidney donor candidates would allow reclassifying as living kidney donors older candidates with GFR below 80 mL/min/1.73 m^2 and exclude some young donor despite high GFR.

O89 10-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL IN KIDNEY TRANSPLANTATION COMPARING 2 IMMUNOSUPPRESSIVE STRATEGY WITH STEROIDS AND ANTITHYMOCYTE GLOBULINS: CYCLOSPORINE/AZATHIOPRINE VERSUS TACROLIMUS/MYCOPHENOLATE MOFETIL (CATM2)

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Introduction: The prospective randomized trial (CATM2 comparing Cyclosporin/Azathioprine (CsA/Aza) versus Tacrolimus/Mycophenolate Mofetil (Tac/MMF) treatments associated with steroids and antithymocyte globulins (ATG) did not prove superiority of immunosuppressive strategy after 3 kidney transplantation's years. Our objective was to evaluate the outcome of the CATM2 population after 10 years of follow-up.
Methods: This is an observational 10-years' follow-up study of CATM2. We analysed in 289 kidney transplant recipients, outcomes in terms of graft and patient survivals, particularly.
Results: Graft survival in the CsA/Aza group was 72.2% vs. 69.5% in the Tac/MMF group (p = 0.34). The death-censored graft survival was 83.3% vs. 78.9% (p = 0.61), respectively. The patient survival was 86.7% in the CsA/Aza group vs. 88% in the Tac/MMF group (p = 0.74). eGFR was 46.9 ± 1.8 mL/min/1.73 m^2 in the CsA/Aza group vs. 55.8 ± 2.2 mL/min/1.73 m^2 in the Tac/MMF group (p = 0.002). The acute rejection rate was higher in CsA/Aza group (17.8%) than in the Tac/MMF group (9.1%) (p = 0.03). There were more opportunistic parasitic infections and digestive intolerance in the Tac/MMF group than in the CsA/Aza group. *De novo* Donor Specific Antibodies were more frequent in the CsA/Aza group than in the Tac/MMF group (13.9% vs 2.9%, p = 0.001). However, immunosuppressive treatments were more modified in the CsA/Aza group (54.1% of cases) than in the Tac/MMF group (25.5%) (p = 0.005). Finally, the cost of one year's treatment was higher with Tac/MMF than CsA/Aza.
Conclusions: After 10 years of follow-up of the CATM2 population study, graft and patient survivals are not different between CsA/Aza and Tac/MMF treatments associated with ATG and steroids. In the Tac/MMF group, renal function is better, whereas infectious non-fatal complications are higher. According to these results, CsA/Aza association remains feasible.

O90 INVERTED DIRECT ALLORECOGNITION: A NEW PATHWAY TO GENERATE DONOR-SPECIFIC ANTIBODY AFTER SOLID ORGAN TRANSPLANTATION

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Donor specific antibody (DSA) is recognized as the first cause of transplant failure. Current immunologic dogma supports that DSA generation requires the help of recipient's CD4+ T cells of indirect specificity, which recognize donor-specific HLA molecules presented in recipient's MHC II molecules on the surface of alloreactive B cells.

In total opposition with this canonical model, we observed that C57BL/6 (H-2^b) KO for CD3ε, and therefore devoid of T cells, exhibited a normal DSA response after transplantation with CBA (H-2^k) heart.

Flow cytometry analyses of cell suspensions from murine heart allografts revealed the presence of "passenger CD4+ T cells" from donor origin. Administration of anti-CD4 mAb to the donors totally abrogated DSA response of CD3ε KO recipients, demonstrating the crucial role of passenger CD4+ T cells for DSA generation in this model.

In vitro co-culture experiments were then used to get insights into the molecular mechanisms underlying this unconventional T/B cooperation. Ligation of BCR with a mAb, mimicked antigen recognition and induced the upregulation of MHC II expression at the surface of B cells. Co-culture of activated C57BL/6 B cells with allogeneic CBA (but not syngeneic C57BL/6) CD4+ T cells induced B cell survival and proliferation. This T/B cooperation was abrogated when B cells from C57BL/6 MHC II KO were used or when anti-CD40L blocking mAb was added to the culture.

We concluded that donor's CD4+ T cells, able to directly recognize intact recipient MHC II molecules expressed on surface of activated B cells, can provide help to the latter and induce their differentiation into DSA-producing plasma cells. The relevance of this new pathway in the clinic is suggested by the presence of CD4+T cell from donor origin in human kidney allografts.

O91 MISSING-SELF TRIGGERS NK-MEDIATED MICROVASCULAR INJURIES AND CHRONIC REJECTION OF ALLOGENEIC KIDNEY TRANSPLANTS

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Background: Natural Killer cells (NK) are effectors of the innate immune system carrying inhibitory KIR (inh KIR), which regulate the killing function of these cells by interacting with MHC class I molecules (MHC-I). The "missing-self" hypothesis proposes that NK can sense the absence of self MHC-I on the surface of allogeneic cells. This unique characteristic suggests that NK could promote innate-driven rejection, a concept that has not been validated in clinical transplantation.
Methods and Results: 938 kidney transplant recipients had a graft biopsy between 2004 and 2012 in our center. 130 had microvascular inflammation (mvi), which is usually attributed to humoral rejection. Only 75 had donor-specific antibodies (DSA) susceptible to explain the mvi. We hypothesize that "missing-self" could be responsible for the lesions of the 55 remaining patients (mvi+DSA-). A matched control group of 55 patients with no mvi and no DSA was constructed (mvi-DSA-). Recipients' KIR genes and donors' and recipients' HLA ligands were genotyped and the licensing of the 5 inh KIR with known MHC-I ligands (KIR2DL1/C2, 2DL2-3/C1, 3DL1/Bw4, 3DL2/A3, A11) was assessed for both groups. The proportion of patients with at least 1 inh KIR-ligand mismatch was higher in mvi+DSA- group (64% vs 36%, p = 0.009).

In a human *in vitro* model, we demonstrated that the lack of self MHC-I on endothelial cells can activate NK. This activation triggers mTOR pathway in NK, which can be blocked by rapamycin. Using a murine *in vivo* cellular model of missing-self mediated killing, we found that rapamycin (but not CNI) can prevent the killing of targets. Finally, we confirmed the existence of missing-self induced rejection in a murine heart transplantation model and its sensitivity to mTOR inhibition.
Conclusion: "Missing-self" seems sufficient to trigger NK-mediated chronic vascular rejection of allogeneic kidneys. mTOR inhibitors might be of interest to prevent this rejection.

O92 PURITY OF ISLET PREPARATIONS AND LONG-TERM METABOLIC SUCCESS OF DIABETES CELL THERAPY

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Background: Carbohydrate antigen CA19.9 is a circulating mucin-type glycoprotein, witness of ductal cells proliferation. In islet transplantation (IT), the purity of infused preparations reflects the amount of ductal and alpha cells, of which CA19.9 and glucagon are blood markers. The post-IT outcome of these non-islet cells remains unknown.
Methods: This case-control, open-label, longitudinal study was designed to compare the 5-year evolution of graft function and markers of non-islet cells according to the purity of the preparations. 24 type 1 diabetic patients were included between 2003 and 2010, with at least a 5-year follow-up. CA19.9 and glucagon levels, metabolic parameters, β-score and daily insulin requirement were prospectively measured before and after IT and compared according to the extent of purity: Low (< 50%) or High (≥50%).
Findings: CA19.9 and glucagon levels, which were in the normal range before IT, significantly increased post-IT and were both inversely correlated with the degree of purity ($p < 0.0001$). At 5 years, HbA1c ($p = 0.01$) and daily insulin requirement ($p = 0.03$) were lower, whereas the percentage of insulin-independent patients ($p < 0.05$) and the β-score ($p = 0.07$) were higher in the Low compared to the High groups.
Interpretation: CA19.9 and glucagon levels increased post-IT. This increase was strongly and inversely correlated to islet purity with better metabolic results in the group having received the less pure preparations. This suggests that the presence of ductal cells in islet preparations could have a beneficial effect thanks to environmental factors or transdifferentiation from ductal or alpha-cells, which remain to be demonstrated.

O93 COMPARISON OF 4 PRESERVATION SOLUTIONS IN LIVER TRANSPLANTATION. A MULTICENTER FRENCH REGISTRY STUDY

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Background: In the last years, the rate of marginal grafts used in liver transplantation (LT) dramatically increased. Preservation quality plays a key role in LT outcome: to date, static cold storage is the gold standard. Despite, data on the equivalence of preservation solutions are divergent. The aim of the study was to evaluate the prognostic role of 4 PS in LT.
Methods: A retrospective study of the prospective French Biomedicine Agency National Database was held from 2008 to 2013: From 6347 LT in 22 centers, 4928 LT were included. Exclusion criteria were mismatch or unknown solution and HTK solution (3%). Statistic calculation used survival analysis and linear models for the log-duration of stay in the intensive care unit (ICU).
Results: Solutions used were Celsior (n = 1452), IGL-1 (n = 2191), SCOT 15 (n = 477), UW (n = 808). Patient survival was 86%, 80% and 74% at 1, 3 and 5 year respectively, without difference between the 4 groups ($p = 0.78$). Graft survival was 82%, 75% and 69% at 1, 3 and 5 year respectively ($p = 0.80$). In multivariate analysis liver cancer was preditor of patient survival. Retransplantation, recipient age and sex, dialysis, UNOS status, mechanical ventilation before LT, HCV positive antibody, HIV positive antibody were predictor of mortality and graft loss. The solution used was not an independent predictor of mortality ($p = 0.23$) or graft loss ($p = 0.37$) but was predictor of the stay in ICU at the multivariate analysis ($p < 0.001$): SCOT (median 6 days [3–12]) CELSIOR and UW (no statistical difference, median 7 days [4–14] and 7 days [3–13]) IGL1 (median 9 [6–17]). Protective factors associated with a shorter ICU stay were receiver's height ($p < 0.001$), presence of liver cancer ($p = 0.022$), donor's rescued cardiac arrest ($p = 0.003$).
Conclusion: Each solution was associated to different length of stay in ICU after LT, but their use had no influence on patient or graft survival at 1, 3 and 5 years after LT.

O94 IMMUNOSUPPRESSIVE REGIMEN AND RISK FOR *DE NOVO* MALIGNANCIES AFTER LIVER TRANSPLANTATION FOR ALCOHOLIC LIVER DISEASE: A RETROSPECTIVE ANALYSIS OF 368 PATIENTS OVER 25 YEARS

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Introduction: Long-term prognosis after liver transplantation for alcoholic liver disease is impaired because of occurrence of *de novo* malignancies and recurrent disease on liver graft. The aims of the present retrospective study were to evaluate the risk of *de novo* malignancy and to identify the significant predictive factors, from a large cohort of liver transplanted patients, with a long follow-up, in the setting of alcoholic liver disease.
Methods: From December 1985 to October 2010, 368 patients with alcoholic liver disease underwent liver transplantation in our centre and survived more than 6 months. There were 284 males and 84 females, with a median age of 52.6 years. Survival, incidence of *de novo* malignancies and several clinical and biological parameters were studied.
Results: From the study cohort of 368 patients, the cumulative incidence of a first solid organ *de novo* malignancy after LT was 8.7% at 5 years, 22.3% at 10 years, 31.5% at 15 years and 33.1% at 20 years. Tobacco consumption (both past and active) was associated with a significant increased risk of solid organ *de novo* malignancy (HR 3.35 and 4.62, respectively), whereas immunosuppressive regimen including mTORi was associated with a decreased risk (post-transplant time under mTORi-including immunosuppressive regimen was significantly longer in patients who did not present *de novo* malignancy (10.6% vs. 2.3%, p = 1.4 10–5)).
Conclusion: Our present retrospective study gives additional evidence that *de novo* malignancies in ALD LT patients are the major long term complication and that conversion from to mTORi-including immunosuppressive regimen could reduce this risk.