ALL ABSTRACTS FOR AUSTROTRANSPLANT, OCTOBER 18–20, 2017, ZELL AM SEE – AUSTRIA

O 1 MANIPULATION OF THE T CELL COMPARTMENT WITH IL2MAB COMPLEXES FOR TOLERANCE INDUCTION

M. Wiletel[1], B. Mahr[1], N. Granofszky[1], M. Muckenhuber[1], T. Wekerle[1], J. Sprent[2], N. Pilat[1]
[1]MUW; [2]Garvan Institute of Medical Research, Vienna, Austria
E-mail: mario.wiletel@meduniwien.ac.at

Introduction: Treatment with IL2 combined with a specific antibody (IL2-cplx) has shown to selectively increase regulatory T cells (Tregs) but not other cells of the T cell compartment. Here we monitored the effect of different treatment protocols on the frequency on Tregs and other subtypes of the immune system (CD8 + cells and NK cells) to further develop and fine tune a Treg dependent tolerance approach. The aim of the project is to maintain long-term stability of Tregs for tolerance induction in transplantation.
Methods: Mice received IL2-cplx at different timepoints and concentrations (high-dose: HD 1/5 μg, i.p., for three consecutive days; low-dose: LD 0.5/2.5 μg, i.p., 3 × /week for 4 weeks). We used flow-cytometric analysis to investigate the frequency of immune cell subtypes (Tregs, NK cells and CD8 cells) in samples taken from blood and lymphoid tissues at different time points. Tolerance was assessed by skingrafting of MHC and minor histocompatibility (miHA) mismatched strain combinations.
Results: Here we demonstrate LD IL-2-cplx treatment as a successful way to maintain elevated frequencies of Tregs in peripheral blood for 4 weeks (d5 17.8% vs. 4.1% p = 0.004; d26 10.3% vs. 3.4% vs. naïve). Moreover, elevated Treg levels remained stable compared to high dose IL2 induction protocols. In contrast, significant reduction of NK cells (3.3% vs. 8.1% p = 0.024 vs. naïve, 26 days post treatment) and reduced levels of CD8 cells (18.1% vs. 22.2%) could be achieved. Preliminary data suggest long-term tolerance towards MHC mismatched (miHa matched) skingrafts with an IL2-cplx based tolerance protocol. CB6F1 grafts were used to investigate the impact of NK cells in skingraft rejection.
Discussion: We could show that LD IL2-cplx treatment leads to lasting elevated Treg levels and decreased NK and CD8 cell levels without IL2 mediated side effects. We think this protocol has huge potency in tolerance induction for transplantation.

O 2 LONGTERM RESULTS FOLLOWING ALEMTUZUMAB VERSUS ATG INDUCTION THERAPY IN COMBINED KIDNEY-PANCREAS TRANSPLANTATION: A SINGLE CENTER REPORT

C. Bösmüller[1], F. Messner[1], C. Margreiter[1], R. Öllinger[2], M. Maglione[1], D. Öfner[1], R. Margreiter[1], S. Schneeberger[1]
[1]Medizinische Universität Innsbruck, Innsbruck, Austria;
[2]Charité - Universitätsmedizin Berlin, Berlin, Germany
E-mail: claudia.boesmueller@tirol-kliniken.at

Objective: A retrospective long-term analysis of patient, pancreatic and kidney graft survival, graft function and major complications following a prospective randomized study comparing an induction therapy with Alemtuzumab to ATG.
Patients and methods: A total of 14 simultaneous kidney pancreas (SPK) transplants randomized to Alemtuzumab plus Tacrolimus-monotherapy (group A, *n* = 14) and 16 SPK randomized to ATG plus Tacrolimus + plus MMF + plus Steroids (group B, *n* = 16) performed at the Innsbruck transplant center between 2006 and 2010, were retrospectively analyzed within a mean follow up period of 9.5 (6.3–9.9) years post transplant.
Results: The 9 years patient survival in group A/B was 92.9/86.7%. The causes of death were tumor, sepsis (group A), cerebrovascular accident and unknown reason (group B). The 9 years pancreas survival in group A/B was 75.0/65.0%. The causes of totally 3 graft losses in group A were one case each of pancreatic vein thrombosis, arterial bleeding and chronic rejection. Three grafts were lost in group B for thrombosis and one for chronic rejection. The 9 years kidney survival in group A/B was 83.1/93.8%. The causes of totally 2 graft losses each in both groups were chronic rejection and initial non function (group A) and immunocomplex-GN and chronic rejection (group B), respectively. In the surviving grafts the mean long-term laboratory values were: creatinine (mg/dl) in group A/B 1.4/1.2, fastening glycaemia (mg/dl) 105/103 and HbA1c (g%) 5.5/5.6 in groups A/B, respectively. Apart from the 4 fatal complications mentioned, all other major complications were resolved: severe peripheral angiopathy (group A/B: 6/1), cerebrovascular ischaemia (2, group A), critical coronary heart disease (group A/B: 2/1), hemolytic anemia (1, group A) and partial portal vein thrombosis (1, group B). Totally 4 tumours occurred: lung cancer (group A, fatal); one case each of B-cell-lymphoma, prostate and cervix carcinoma (group B). Apart from one fatal sepsis (group A) all serious infections were reversible: one case each of pneumonia, bacteraemia, tuberculosis, recurrent cystitis in group A, and osteomyelitis, BK-nephropathy, recurrent condylomata, hepatitis B in group B.
Conclusion: Good long-term results in pancreatic and kidney graft survival were achieved in both groups. The long-term graft function, the patient survival and the incidence of severe infectious complications were comparable in both groups. A trend towards more serious vascular complications in group A might be explained by the individual grade of underlying angiopathy. More tumors occurred in group B, all survived, in contrast to one fatal malignancy in group A.

O 3 IMPLEMENTATION OF A SYSTEMATIC LIVER FIBROSIS SCREENING PROGRAM IN HEART TRANSPLANT CANDIDATES

A. Iscel, T. Reiberger, A. Zuckermann, A. Aliabadi-Zuckermann, M. Trauner, J. Riebandt, F. Wittmann, V. Paspalj
Medical University of Vienna, AKH Wien, Vienna, Austria
E-mail: ahmet.iscel@hotmail.com

Introduction: Both impaired hepatic perfusion and hepatic venous congestions potentially contribute to hepatic injury in patients with chronic heart failure (CHF). Pre-existing liver injury/fibrosis is a potential risk factor for post HTX-liver failure. Thus, we systematically implemented a liver screening program in selected heart transplant candidates.
Methods: Patients referred to the Heart Transplant Program of the Medical University of Vienna were screened for (a) signs of fibrosis/cirrhosis on abdominal imaging, (b) hyperbilirubinemia, (c) thrombocytopenia/splenomegaly. Selected patients underwent (i) hepatic venous pressure gradient (HVPG) measurements, (ii) indocyaningreen (ICG) clearance, (iii) transient elastography and (iv) transjugular liver biopsy.
Results: 13 patients underwent the liver screening program. Free hepatic venous pressures were elevated indicating venous congestion in all patients, however, HVPG was only increased in one patient – who also showed significant fibrosis in liver histology. ICG clearance was impaired in most patients, presumably due to impaired hepatic perfusion rather than impaired hepatic excretory function. Transient elastography indicated increased liver stiffness, however, all – except for one patient – presented with only mild perisinusoidal fibrosis. This suggests that hepatic venous congestion rather than advanced fibrosis may account for increased liver stiffness. No severe complications occurred during transjugular liver biopsy. Individual hemodynamic, laboratory and histological data will be presented at the conference.
Conclusions: Despite pathological imaging results and increased liver stiffness measurements, at the time of abstract submission only one of 13 patients showed advanced fibrosis as a contraindication against HTX. Perisinusoidal fibrosis was common, but is deemed reversible after improvement of hepatic congestion after HTX. Long-time data will show if a systematic hepatic screening program is able to predict post-HTX liver-related morbidity and mortality.

O 4 INVESTIGATION OF MESENCHYMAL STEM CELLS FOR PRECONDITIONING OF KIDNEY GRAFTS IN AN EX-VIVO MODEL OF HYPOTHERMIC MACHINE PERFUSION

N. Vallant, B. Sandhu, C. Pusey, V. Papalois
Imperial College London, London, United Kingdom
E-mail: n.vallant@imperial.ac.uk

Background: In transplantation, Hypothermic Machine Perfusion (HMP) has been shown to be superior to static cold storage (SCS). Delivery of drugs or active substances such as stem cells is one of the major benefits of this preservation method. Mesenchymal Stem Cells (MSCs) are multipotent cells with tissue repair capacities. The aim of this study was to introduce MSCs into a model of hypothermic machine perfusion and to directly compare outcomes at the time of reperfusion.
Methods: 12 porcine kidneys from 6 donor pigs were perfused at 4°C with or without 1–5 × 10^6 labelled human MSCs for 4 hours. The kidneys were then reperfused with whole autologous blood at 37°C for 2 hours. Functional parameters were compared between the groups and perfusate and biopsy samples were analysed for inflammatory cytokines by ELISA and qPCR. Additionally, 3 human kidneys were perfused with MSCs at different numbers to investigate the engraftment of the cells.
Results: MSCs could be traced within the kidneys using widefield microscopy. Physiological parameters were similar between the two groups in the porcine model. IL-1β levels were higher in perfusate and urine samples in the MSC group, with a median of 285.3 ng/ml (IQR 224.3–407.8 ng/ml) vs. 209.2 ng/ml (IQR 174.9–220.1), p = 0.51 and 105.3 ng/ml (IQR 71.03–164.7 ng/ml) vs. 307.7 ng/ml (IQR 190.9–349.6 ng/ml), p = 0.16, respectively. mRNA expression of the proinflammatory cytokines TNFα, NGAL and EDN-1 was higher in MSC pretreated kidneys after reperfusion.

Conclusions: MSCs can be delivered to a graft using ex-vivo HMP. Engraftment of the cells does not immediately influence functional parameters. Changes in levels of IL-1β as well as mRNA expression of cytokines suggest that MSCs do have an effect on the kidney grafts but whether this leads to a positive or a negative outcome on IRI in transplantation needs to be determined.

O 5 PREOPERATIVE ASSESSMENT OF MUSCLE MASS USING COMPUTERIZED TOMOGRAPHY SCANS TO PREDICT OUTCOMES FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION

H. Esser[1], T. Resch[1], M. Pamminger[2], M. Popovscaia[3], E. Gassner[2], M. Maglione[1], S. Schneeberger[1]
[1]Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Innsbruck, Austria; [2]Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria; [3]Department of Medical Statistics, Informatics and Health Economics, Medical University of Innsbruck, Innsbruck, Austria
E-mail: hannah.esser@tirol-kliniken.at

Introduction: To render recipient selection in view of the current shortage of donor organs, efforts to more accurately predict post-transplant outcome are advancing. Muscle mass has been shown to correlate with patient mortality and morbidity in chronic diseases. Herein we evaluate if preoperative assessment of muscle mass in liver transplant recipients aids in predicting post-transplant survival and morbidity.
Methods: We performed a retrospective analysis of all orthotopic liver transplants (OLT) performed between January 1st, 2011 and December 31st, 2013 at the Innsbruck Medical University. The pre-transplant contrast-enhanced CT scan showing the 3rd lumbar vertebra (L3) was used for measurements of total psoas area, the average psoas density, the psoas index (i.e. psoas area divided by body height2), the skeletal muscle index (i.e. total muscle area divided by body height2) and the average total muscle density at L3. A correlation with patient survival, post-operative morbidity (Clavien-Dindo classification grade III-V), and length of hospital stay was then established.
Results: From a total of 186 patients, a CT scan fitting the requirement was available in 172 cases. Patients below the 10th percentile of average psoas density and average total muscle density at L3 were found to have a significantly inferior patient survival. Muscle density also correlated with post-transplant morbidity (Clavien-Dindo classification grade III to V) and length of hospital stay. Patients with postoperative sepsis had a significantly lower total muscle density at L3 compared to patients without.
Conclusion: Assessing nutritional status in patients awaiting OLT by measuring the psoas density or the average total muscle density at L3 can aid in identifying patients at risk for post-transplant death and complications. Pre-transplant programs to improve the nutrition status and close postoperative monitoring are warranted to address this significant risk factor in liver transplantation.

O 6 TRANSFUSION OF STORED BLOOD INDUCES PULMONARY VASOCONSTRICTION IN CRITICALLY ILL PATIENTS AFTER CARDIAC SURGERY

D. Baron, J. Stefaniak-Baron, G. Leitner, R. Ullrich
Medizinische Universität Wien, Vienna, Austria
E-mail: david.baron@meduniwien.ac.at

Introduction: Experimental studies have shown that transfusion of packed red blood cells (PRBCs) stored for 40 days increases pulmonary arterial pressure (PAP) and pulmonary vascular resistance (PVR). We hypothesized that transfusion of stored blood would induce pulmonary vasoconstriction in critically ill patients after cardiac surgery.
Methods: This study was performed as a double-blind, parallel-group, randomized clinical trial at the Medical University of Vienna after ethics committee approval and registration (NCT02050230). Critically ill patients requiring one unit of PRBCs were randomized to receive PRBCs stored for ≤14 days (fresh PRBCs) or standard-issue PRBCs (the oldest compatible unit available from the blood bank) over 15 min. The increase of PAP during transfusion (ΔPAP) was defined as primary outcome parameter.

PAP, mean arterial pressure (MAP), and cardiac output (CO) were measured at baseline and after transfusion. PVR and systemic vascular resistance (SVR) were calculated. Concentrations of macrophage migration inhibitory factor (MIF) and syndecan-1 (SDC1) in serum and in supernatant of PRBCs were measured with ELISA. Statistical analysis was performed with Welch's test.
Results: Six patients received fresh PRBCs and five patients received standard-issue PRBCs. ΔPAP was greater after transfusion of standard-issue PRBCs than fresh PRBCs (7 ± 3 vs. 2 ± 2 mmHg, $p = 0.012$). Similarly, PVR (81 ± 50 vs. −1 ± 37 dyn s/cm^5, $p = 0.018$) and SVR (166 ± 61 vs. 9 ± 72 dyn s/cm^5, $p = 0.004$) increased to a greater extent after transfusion of standard-issue PRBCs than fresh PRBCs.

Standard-issue PRBCs increased systemic MIF concentrations by 56 ± 70% ($p = 0.02$), while transfusion of fresh PRBCs did not ($p = 0.54$). Systemic SDC1 concentrations increased after transfusion of fresh and standard-issue PRBCs ($p < 0.05$), but did not differ among groups ($p = 0.99$).
Conclusion: Transfusion of standard-issue PRBCs induces pulmonary vasoconstriction in critically ill patients after cardiac surgery.

O 7 PREDICTORS AFFECTING SURVIVAL RATES AFTER PEDIATRIC LIVER TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

V. Berchtold[1], C. Margreiter[1], R. Oberhuber[1], M. Maglione[1], B. Cardini[1], J. Grahammer[2], T. Müller[3], R. Margreiter[1], S. Schneeberger[1], A. Weissenbacher[4]
[1]Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Innsbruck, Austria; [2]Department of Plastic and Reconstructive Surgery, Medical University Innsbruck, Innsbruck, Austria; [3]Department of Paediatrics I, Innsbruck Medical University, Innsbruck, Austria; [4]Nuffield Department of Surgical Sciences, Oxford Transplant Centre, Churchill Hospital, Oxford University, Oxford, United Kingdom
E-mail: valeria.berchtold@tirol-kliniken.at

Introduction: In this study we aim to assess factors influencing long-term patient and graft survival as well as surgical parameters and risk factors influencing organ function after pediatric liver transplantation.
Results: A total of 62 deceased donor liver transplantation (LTX), 17 deceased donor split-LTX, 45 LTX from living donors and 3 multivisceral transplantations performed in children between 3 months and 17 years were included in this study. The median cold ischemia time (CIT) was 426 min in the deceased donor group and 105 min in the living LTX group. The 10- and 20-year patient and graft survival in the early stage (1984–1994) was 50.0%/41.7% and 45.0%/37.5% in the deceased donor group and went up to 81.8%/75.0% and 81.8%/69.2% between 1995 and 2004 respectively. Patient and graft survival in the late stage (2005–2016) increased to 93.8%/83.1% (10 and 20 years) in the deceased donor group. Ten-year patient and graft survival after living-LTX were 81.6% and 83.3% in the era from 1997 to 2016.

A CIT above 6 hours, however, resulted in a significant lower patient survival. Living donor LTX is associated with a significant better outcome concerning the long-term patient and graft survival. Increased donor weight and advanced donor age impact patient survival. The MELD score as a good marker to size up the urgency for transplantation influenced the graft survival significantly whereas there is no effect on the patient survival.
Conclusion: Excellent long-term results could be achieved with pediatric liver transplantation during the last 30 years. Limited ischemia time, detailed surgical planning and deliberately organ selection considering living donor LTX are factors influencing the outcome.

O 8 SALVAGE OF AN EARLY HEPATIC ARTERY THROMBOSIS AFTER SPLIT LIVER TRANSPLANTATION IN A 4-YEAR-OLD GIRL – A CASE REPORT AND REVIEW OF THE LITERATURE

V. Berchtold[1], A. Weissenbacher[2], T. Müller[3], U. Klingowski[3], A. Entenmann[3], S. Straub[3], S. Eschertzhuber[4], R. Unterpertinger[4], F. Messner[1], S. Scheidl[1], C. Margreiter[1], R. Oberhuber[1], D. Öfner[1], S. Schneeberger[1]
[1]Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Innsbruck, Austria; [2]Nuffield Department of Surgical Sciences, Oxford Transplant Centre, Churchill Hospital, Oxford University, Oxford, United Kingdom; [3]Department of Paediatrics I, Innsbruck Medical University, Innsbruck, Austria; [4]Department für Anästhesie und Intensivmedizin, Universitätsklinik Innsbruck, Innsbruck, Austria
E-mail: valeria.berchtold@tirol-kliniken.at

Introduction: Early hepatic artery (eHAT) thrombosis after liver transplantation in children constitutes a dreaded complication and requires immediate revascularization by thrombectomy and/or surgical revision as well as anticoagulation therapy.
Presentation of case: We report the course of a 4 year-old girl submitted to split liver transplantation from a deceased donor for treatment of a cholestatic liver disease. After an early uneventful course and recovery, eHAT occurred after a sudden gastrointestinal bleeding and subsequent rapid blood transfusion on day 4 after transplantation. Arterial revascularization was achieved by renewing the arterial anastomosis with an accessory hepatic artery. A second eHAT occurred spontaneously on day 7. The attempted second revascularization by thrombectomy and re-anastomosis was unsuccessful and it became apparent, that intima dissection in the donor hepatic artery was the underlying cause. After deterioration of graft function, a high urgency retransplantation of yet another split liver graft with insertion of the hepatic artery including an aortic patch into the aorta of the recipient was successful.
Conclusion: The incidence of eHAT in children remains high and its impact significantly on graft loss. Rapid intervention and identification of fragility of the intima as a cause with subsequent retransplantation and reconstruction of the

artery by insertion into the aorta resulted in salvage of a complex situation. Close monitoring by ultrasound and immediate intervention seem to be the key to avoid graft failure but also late complication. Successful graft salvage results in similar patient survival rates comparable to liver transplantation without the occurrence of eHAT.

O 9 PERIOPERATIVE OUTCOME IN LIVING KIDNEY DONORS – RETROSPECTIVE ANALYSIS OF 289 CONSECUTIVE CASES

J. Feka, L. Unger, P. Sabler, S. Rasoul-Rockenschaub, G. Györi, M. Hofmann, C. Schwarz, T. Soliman, G. Böhmig, A. Kainz, A. Salat, G. Berlakovich, Wien, Austria

Medizinische Universität Wien, Innsbruck, Austria

E-mail: gabriela.berlakovich@meduniwien.ac.at

Background: Living Donor Kidney Transplantation is the best available treatment for End-Stage Renal Disease. Nevertheless, unilateral nephrectomy bears risks for the healthy, voluntary donor. As obesity is a known risk factor for surgical complications, we investigated the impact of BMI on perioperative complication rates and renal function during the short-term postoperative course.
Materials and Methods: We retrospectively analyzed patients scheduled for living donor kidney nephrectomy at our institution. We identified 289 donors that underwent unilateral nephrectomy between 01.01.2006 and 31.12.2015. Donors were categorized according to their BMI (BMI < 25 kg/m^2, BMI $\geq 25/<30$ kg/m^2, BMI ≥ 30 kg/m^2).
Results: 126 donors had a BMI < 25 (43.6%) while 120 (41.5%) had a BMI $\geq 25/<30$ and 43 (14.9%) were obese with a BMI ≥ 30. BMI did not influence the percentage of laparoscopic approaches (86.5% vs. 83.3% vs. 88.4%, respectively; $p = 0.6564$), on conversion rates (0% vs. 2.0% vs. 2.6%, $p = 0.2879$) or postoperative complication rates defined as Clavien Dindo $\geq$ II (8.7% vs. 13.3% vs. 14.0%, respectively; $p = 0.4474$). Notably, there were no Grade III or higher complications in any group. There was no difference in preoperative kidney function, postoperative surgical site infection or systemic infection. BMI and male sex, however, had a statistically significant influence on short-term decline of eGFR.
Conclusion: Obese donors do not suffer from an increased risk of intraoperative or perioperative complication rates. However, male sex and high BMI are associated with a more pronounced short-term decline in renal function. The impact of BMI on long-term consequences for kidney donors need to be defined in larger prospective cohorts.

O 10 RENAL AND SKIN SODIUM BALANCE AFTER KIDNEY TRANSPLANTATION

C. Kaltenecker[1], T. Shoumariyeh[1], F. Kopf[1], F. Pramhas[1], C. Kopecky[1], M. Antlanger[1], M. Säemann[1], H. Oberleithner[2], J. Kovarik[1]

[1]Department of Nephrology and Dialysis, Medical University of Vienna, Vienna, Austria; [2]Westfälische-Wilhelms-Universität, Münster, Germany

E-mail: christopher.kaltenecker@meduniwien.ac.at

Background: As recently discovered by nuclear magnetic resonance imaging, the skin and skeletal muscle are considerable sodium storage sites which are mobilized by B cells and macrophages. Immunosuppressants and reduced kidney function might even promote sodium accumulation, which is a cardiovascular risk factor independent of blood pressure. Here we assessed kidney transplant recipients regarding their blood salt sensitivity (SBTmini). We compared them to chronic kidney disease and healthy volunteers to determine their sodium handling profile in response to diuretic and anti-hypertensive treatment.
Methods: This cross-sectional single center study recruited patients from the Vienna General Hospital between September 2016 and July 2017 at the nephrology wards. Kidney transplant recipients were followed on a study the SGLT2-inhibitor empagliflozin (NCT03113110). Healthy volunteers and chronic kidney disease (CKD) patients were included as reference.
Results: Relative to healthy controls (mean $\pm$ SD, 137 $\pm$ 40%, $n = 50$) and CKD patients (152 $\pm$ 32%, $n = 6$), kidney transplant recipients had lowest salt sensitivity (116 $\pm$ 51%, $n = 15$). Two weeks on SGLT2-inhibitor therapy, salt sensitivity was reduced even more (97 $\pm$ 36%, $n = 14$).
Conclusion: The sodium handling in kidney transplant recipients even improved by SGLT2-inhibitor therapy, despite presence of anti-hypertensives at baseline. Healthy volunteers not receiving any medication showed highest salt sensitivity, likely due to sodium rich diet. Nevertheless, subcutaneous sodium storage might still be pronounced in these patients, which will be investigated in dedicated studies.

O 11 INFLUENCE OF DONOR AND RECIPIENT SEX ON LONG TERM FUNCTION AFTER PANCREAS TRANSPLANTATION

F. Messner, C. Bösmüller, M. Maglione, R. Oberhuber, B. Cardini, S. Schneeberger, C. Margreiter

Medical University of Innsbruck, Department of Visceral, Transplant and Thoracic Surgery, Innsbruck, Austria

E-mail: franka.messner@i-med.ac.at

Background: The combined kidney-pancreas transplantation is an established therapy for insulin dependent Diabetes mellitus with terminal kidney insufficiency. Studies in liver, kidney and pancreas transplantation have shown a correlation between gender-match and risk of graft loss. In this study we want to analyze the influence of recipient and donor sex on the incidence of pancreas graft loss in our cohort.
Methods: To evaluate the impact of gender on long term function after pancreas transplantation, we performed a retrospective analysis of all pancreas transplantations performed between January 1979 and December 2016 at the Medical University Innsbruck. After exclusion of patients without recent follow-up. 537 patients could be included in the study. Statistical analysis was performed using SPSS, a p-value <0.05 was considered statistically significant.
Results: Of the 537 pancreas transplantations, 199 (37.1%) female and 338 (62.9%) male recipients have been transplanted. In 290 (54%) cases a gender-matched and in 247 (46%) cases a non-gender-matched transplantation was performed. Kaplan-Meier analysis revealed a significantly superior pancreas graft survival ($p = 0.015$) in the gender-matched group. There was no significant difference between both groups in terms of cold ischemic time, HLA-match or type of pancreas transplantation. The gender-matched group had a higher recipient age (43.3 vs. 40.8 years; $p = 0.005$) and a lower donor age (28.9 vs. 31.3 years; $p = 0.024$). There was a higher rate of re-transplantations in the non-gender-matched group (17.1% vs. 10%; $p = 0.045$). After division of the different donor-recipient gender constellations only the male-donor-to-male-recipient group had a significant better pancreas graft survival than the female-donor-to-male-recipient group ($p = 0.019$).
Discussion: Our analysis shows, that gender-matched pancreas transplantations lead to a significant better long term graft survival. Factors, which might influence this result in our cohort, are a higher recipient and lower donor age as wells as a lower rate of re-transplantations in the gender-matched group.

O 12 LIVE TISSUE STAINING AS A NEW PREDICTING TOOL IN CLINICAL KIDNEY TRANSPLANTATION

A. Weissenbacher, M. Hermann, J. Troppmair, D. Öfner, S. Schneeberger, R. Oberhuber

Medical University of Innsbruck, Department of Visceral, Transplant and Thoracic Surgery, Innsbruck, Austria

E-mail: rupert.oberhuber@i-med.ac.at

The quest for objective graft assessment prior to transplantation is the Holy Grail of transplantation as it could predict graft outcomes.

The use of expanded-criteria donor kidneys demands careful pre-implantation assessment. However, histopathological analysis of the pre-transplant biopsy is time consuming. Our aim is to establish a rapid assessment tool of donor kidney quality and investigate its predictive value for clinical use.

Based on the Biopsychronology study using rodent kidneys (Hermann/Ashraf et al.) we started a prospective clinical trial at Innsbruck Medical University in October 2015 to implement live confocal real time analysis as a clinical tool for deceased donor kidney transplantation. A semiquantitative score for quantification purposes of the imaging results has been created and is compared to the biopsy-histology result. The score displays the sum of viable cells divided by the number of non-viable cells per examined area (glomerulus, proximal and distal tubules; with an overall score of -3 (nonviable) up to $+3$ (100% viable).

So far, 38 kidney transplant recipients (8 female, 21%; 9 re-transplants, 24%) have been recruited and successfully transplanted. The median recipient age was 59.2 years; the median donor age was 61.4 years. Mean $\pm$ SD cold ischemia time was 14 $\pm$ 4.9 hours. Overall, 14 patients developed DGF (36.8%). In the group with positive scores 1–3, DGF rate was 8/24, 33.3%. The DGF rate in the group with negative scores -3–0 was 6/14, 42.9%; $p = 0.73$. The mean $\pm$ SD serum creatinine and serum urea at discharge were 2.2 $\pm$ 1.1 mg/dl and 80.2 $\pm$ 36.8 mg/dl. No organ has been discarded so far on basis of the imaging result.

Our preliminary data confirm that real time imaging provides us detailed information about the organ quality prior to transplantation.

O 13 NK CELLS PREFERENTIALLY TARGET MATURE LYMPHOCYTES UNDER INFLAMMATORY CONDITIONS BY MISSING-SELF RECOGNITION

B. Mahr, N. Pilat, N. Granofszky, S. Maschke, K. Hock, T. Wekerle
Medizinische Universität Wien, Innsbruck, Austria
E-mail: benedikt.mahr@meduniwien.ac.at

Background: The classical hybrid resistance model allows investigating the basic principles of natural killer (NK) cell mediated bone marrow (BM) rejection including missing-self recognition. In this model F1 (BL6 × BALB/c) recipients are lethally irradiated and NK cells are pre-activated to reject parental BM. We recently showed that NK suppression/tolerization is a critical mechanism in an irradiation free regimen inducing mixed chimerism to achieve transplantation tolerance. Here, we now further investigate the detailed mechanisms how NK cells reject allogeneic BM.
Methods: To assess successful engraftment and chimerism, we bred F1 mice whose leukocytes concomitantly express both CD45.1 and CD45.2. Irradiated or non-irradiated F1 recipient mice received titrated doses (20-5 × 10^6) of unseparated parental BALB/c (CD45.2) or syngeneic CB6F1 (CD45.2) BM cells. Selected mice received total body irradiation (d-1), α-NK1.1 (d-1,d2,d5, d8) or poly(I:C) (d-1).
Results: 20 × 106 BALB/c BM cells readily engrafted in F1 mice receiving 3 Gy total body irradiation. We gradually decreased irradiation intensity and found that even in the absence of irradiation F1 mice were not able to reject parental BALB/c BM even at low doses (5 × 10^6). However, the effect of hybrid resistance became noticeable by lower chimerism levels of BALB/c donors compared to syngeneic F1 donors (1.4% ± 0.08 vs. 2.8% ± 0.17, p = 0.0003). Chimerism persisted for 150 days and recipient NK cells re-shaped their receptor repertoire to decrease reactivity to donor cells. Pre-activating NK cells with the TLR-3 agonist poly(I:C) significantly reduced parental chimerism but could not completely abolish it. In contrast, poly(I:C) treated mice were able to completely reject equal numbers of BALB/c lymph node cells.
Conclusion: Therefore we conclude that NK cell mediated BM rejection in non-irradiated recipients is markedly enhanced in the context of inflammation and is more effective against mature lymphocytes. In contrast, NK cells are relatively ineffective in mediating rejection under non-inflammatory conditions and rather gradually adapt to allogeneic cells.

O 14 TOLL-LIKE RECEPTOR (TLR)-3 – A NOVEL TARGET FOR THE PREVENTION OF ISCHEMIA-REPERFUSION INJURY IN SOLID ORGAN TRANSPLANTATION

T. Resch[1], H. Esser[1], V. Mellitzer[1], S. Ebner[1], B. Cardini[1], R. Oberhuber[1], F. Primavesi[1], R. Moling[1], D. Öfner[1], J. Troppmair[1], S. Schneeberger[1], G. Schäfer[2], J. Holfeld[3], C. Tepeköylü[1]
[1]Center of Operative Medicine, Department for Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Innsbruck, Austria; [2]Department of Pathology, Medical University of Innsbruck, Innsbruck, Austria; [3]Department of Cardiac Surgery, Medical University of Innsbruck, Innsbruck, Austria
E-mail: t.resch@tirol-kliniken.at

Background: Toll-like receptor (TLR)-3 represents a pattern recognition receptor involved in the innate immune response. Recently it has been proposed as a candidate molecule for the modulation of cardiac ischemia reperfusion (IRI) *in vitro*.
Methods: In order to investigate the detailed effects of TLR3 on cardiac IRI *in vivo*, syngeneic heart transplantation was performed in either C57BL/6 wild type (WT) or TLR3 knockout ($TLR3^{-/-}$) mice following 9 hours of cold ischemia.
Results: TLR3 knockout significantly diminished IRI-related injury 48 hours after reperfusion as demonstrated by a cumulative histological damage score ($TLR3^{-/-}$: 5.8 ± 0.8 vs. WT: 8.8 ± 0.3; p = 0.006). In particular, epicardial and myocardial damage was alleviated (p < 0.05, respectively). Furthermore, the presence of infiltrating lymphocytes significantly decreased (p = 0.0009). This was accompanied by reduced intragraft (CCL3, CCL4) and splenic mRNA expression of pro-inflammatory cytokines (TNFα, IL1b, CCL4, CXCL10; all p < 0.05). Whereas elevated levels of anti-inflammatory factors (TGFβ) were observed, those indicating hypoxia (HIF1α) significantly declined (p < 0.05, respectively). Importantly, in contrast to the depletion of TLR3 expression in $TLR3^{-/-}$ recipient grafts and spleens, other toll-like receptors (TLR2, TLR4) remained unaffected, indicating that the observed protective effects were solely due to TLR3 deletion.
Conclusion: This study outlines for first time the detrimental influence of TLR3 signaling on the development of IRI after cardiac transplantation. Our data indicate that TLR3 represents a possible novel target for future pharmacologic therapies in solid organ transplantation.

O 15 CHRONIC CTLA4IG THERAPY LEADS TO PERMANENT HEART TRANSPLANT SURVIVAL IN THE ABSENCE OF CD40L

L. Unger, B. Mahr, C. Schwarz, M. Muckenhuber, N. Granofszky, N. Pilat-Michalek, T. Wekerle
Medical University of Vienna, Vienna, Austria
E-mail: thomas.wekerle@meduniwien.ac.at

Background: Costimulation-blockade using CTLA4Ig is clinically approved and leads to excellent long-term allograft survival in human kidney transplantation. However, an increased risk for acute rejection episodes still represents a major clinical problem. A combination with CD40L blockade has shown synergistical effects regarding long-term allograft survival but optimal timing and optimal dosing strategies need to be defined. After early termination of a clinical trial with an anti-CD40LmAb due to thromboembolic complications, new efforts are made to develop therapeutics interfering with the CD40/CD40L pathway. Therefore, a murine heterotopic heart transplantation model was used to investigate effects of combination therapies on chronic and late acute rejection.
Methods: Balb/c donor hearts were transplanted cervically into naïve C57Bl/6 or C57Bl/6 CD40L−/− mice. CTLA4Ig (0.25 mg on days 0, +4, +14, +28, +56, +84; equal to the clinically approved dosing regimen related to mg/kg body weight) as well as MR1 induction (anti-CD40L mAb on days 0, +4; in a dose of 0.2 mg, 0.5 mg or 1 mg/administration) were administered intraperitoneally. Grafts were assessed at least 3 times/week. Follow-Up was terminated at the time of rejection or 100 days post-transplant.
Results: CTLA4Ig or MR1 monotherapies led to a median survival time (MST) of 22 (CTLA4Ig; *n* = 7), 15 (0.2 mg MR1; *n* = 6) or 67 (0.5 mg MR1; *n* = 5) days. Combination of CTLA4Ig with MR1 induction therapy led to an increase of MST but rejection occurred in all groups (CTLA4Ig+0.2 mg MR1, +0.5 mg MR1 or +1 mg MR1). To test the effect of long-term CD40L interference, naïve CD40L−/− mice were transplanted and also rapidly rejected their allografts. Finally, long-term allograft survival was achieved in all recipients when CD40L−/− mice were treated with CTLA4Ig.
Conclusion: MR1 induction therapy, even in excessively high doses, does not lead to long-term allograft survival. However, "chronic" costimulation-blockade with CTLA4Ig leads to excellent long-term allograft survival in mice deficient of CD40L.

O 16 ALLOGRAFT REJECTION IS ASSOCIATED WITH THE DEVELOPMENT OF FUNCTIONAL IGE SPECIFIC FOR DONOR MHC ANTIGENS

A. Farkas[1], U. Baranyi[2], G. Böhmig[3], L. Unger[4], S. Hopf[1], M. Wahrmann[3], H. Regele[5], B. Mahr[1], C. Schwarz[1], K. Hock[6], N. Pilat[1], I. Kristo[4], C. Lupinek[7], J. Thalhamer[8], E. Wlodek[9], M. Clatworthy[10], J. Martin[9], G. Pettigrew[9], R. Valenta[7], T. Wekerle[1]
[1]Department of Surgery, Section of Transplantation Immunology, Medical University of Vienna, Vienna, Austria; [2]Department of Surgery, Cardiac Surgery Laboratory, Medical University of Vienna, Vienna, Austria; [3]Division of Nephrology and Dialysis, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria; [4]Department of Surgery, Medical University of Vienna, Vienna, Austria; [5]Institute of Clinical Pathology, Medical University of Vienna, Vienna, Austria; [6]Department of Surgery, Section of Transplantation Immunology, Medical University of Vienna, Vienna, Austria; [7]Divisions of Immunopathology, Department of Pathophysiology & Allergy Research, Medical University of Vienna, Vienna, Austria; [8]University of Salzburg, Salzburg, Austria; [9]Department of Surgery, University of Cambridge, Cambridge, United Kingdom; [10]Department of Medicine, University of Cambridge, Cambridge, United Kingdom
E-mail: andreas.m.farkas@gmail.com

Background: Donor-specific antibodies (DSA) of the IgG isotype are routinely measured for diagnostic purposes in transplant recipients and their occurrence is associated with antibody-mediated rejection and long-term graft loss. Besides the classical donor-specific IgG, donor-specific IgM and IgA were previously reported. IgE with specificity for donor-MHC-antigens has never been published so far.
Methods: Naïve mice received skin or heart grafts in several strain combinations (BALB/c to B6, BALB/c to C3H, C3H to BALB/c) and in a model of antibody-mediated-rejection (Bm12.Kd.IE to B6). S was collected and used for MHC I and II specific ELISA to detect DSA IgE. Furthermore, the serum of 6 kidney transplant patients with high DSA IgG was analyzed using an anti-human-IgE detection antibody and LABScreen kits (HLA I/II).Sera were also used for *in vitro* (human/murine) and *in vivo* (murine) degranulation assays. Additionally 7 kidney tissue samples obtained from organ donors were analyzed via flow-cytometry to detect cells expressing the high-affinity receptor for IgE (FcεRI).
Results: Donor-MHC I and II-specific IgE was found upon acute rejection of allogeneic skin and heart grafts (*n* = 6 and 4 per strain combination), as well as in humoral heart graft rejection by using a MHC-specific ELISA (*n* = 4). Anti-

HLA IgE, including donor-HLA I and/or II specificities, was identified in 5/6 patients. Mediator release was triggered *in vitro* by stimulating basophils that were coated with murine or human IgE-positive serum, respectively, with specific recombinant MHC or HLA antigens. Mast cell degranulation was also evident in sensitized mice *in vivo*. Additionally FcεRI+ cells were present in human renal cortex and medulla therefore providing targets for HLA-specific IgE.
Conclusion: These results demonstrate that MHC/HLA-specific IgE develops during an alloresponse and is functional in mediating effector mechanisms.

O17 INFLUENCE OF A PERIOPERATIVE STANDARD FOR LIVER TRANSPLANTATION

D. Kniepeiss, N. Homfeld, P. Schemmer
Klinische Abteilung für Transplantationschirurgie, Universitätsklinik für Chirurgie, Medizinische Universität Graz, Graz, Austria
E-mail: daniela.kniepeiss@medunigraz.at

Background: Standards are internationally accepted Quality Control-Mechanisms and are used to optimize how resources are used. The objective was to observe how the introduction of perioperative standards would influence both the quality of the results and the usage of resources.
Methods: The checklist for patient examinations prior to a liver transplantation were established and optimized. In addition interdisciplinary indication conferences, perioperative patient developments, therapy standards, 24/7 pathological - call service, utilization of innovative OP- techniques as well as mortality- and morbidity-conferences were applied. The influence of these measures on the quality of the results and the resource usage has been first documented and then evaluated and compared with publications.
Results: The quality of the results showed a clear improvement to a level that is equivalent to a high-volume transplant center. There was a positive influence on patients time spent both in the Intensive care unit and hospital overall as well as morbidity and mortality.
Conclusion: A continuous and well structured revision of medical content of transplant programs will result in improved patient care.

O 18 FIRST EXPERIENCES IN THE DE NOVO USE OF EXTENDED RELEASE TACROLIMUS (ENVARSUS®) AFTER ORTHOTOPIC LIVER TRANSPLANTATION

T. Soliman, G. Györi, M. Hofmann, A. Salat, S. Rockenschaub, G. Berlakovich
MedUniWien, Abteilung für Transplantation, Wien, Austria
E-mail: thomas.soliman@meduniwien.ac.at

Introduction: Regarding the low rates of rejection after OLT immunosuppression has reached a quite high standard. However, there is still room for improvement in achieving adherence of patients to daily immunosuppression. New formulations such as Envarsus® should contribute to that attempt but only little evidence is available in OLT.
Methods: In a retrospective single center study we analysed 57 OLT in 55 patients who received Envarsus® after induction therapy with ATG (1.5 mg/kg BW) together with steroids tapered within 3 months till withdrawal. Envarsus® was started on day 3po with 0.10 mg/kg BW and then adapted to blood levels of tacrolimus that were measured daily.
Results: All patients had first OLT between 3/2016 and 5/2017. Mean age of the recipients was 52 years (22–71 years), 78% ($n = 43$) male. Underlying disease was ALCI 29%, HCC 29%, CHOL 15%, CYCI 9%, PHC 7%, ACHF 4% and others 7%. One year patient and graft survival was 91% and 88%. Two patients had to be retransplanted for HAT and IBD respectively within six months after first OLT. During follow up one biopsy proven acute rejection (1.8%) was diagnosed and successfully treated with a three-day iv steroid administration. One patient had clinical suspected acute rejection but refused biopsy as well as iv steroid therapy. Maintenance immunosuppression had to be switched from Envarsus® to other CNIs in only 14.5% of the patients ($n = 8$). Reason for the switch was the need of iv drug administration for several reasons. No change of immunosuppression was induced by severe side effects.
Conclusion: Tacrolimus in its extended release formulation is a potent and easy to use immunosuppressant that is well tolerated by the patients showing strong adherence. The lower initial dose of Envarsus® might also have a positive effect on side effects in the early post-OLT phase but more data are needed to support this thesis.

O 19 BACKTABLE HEPATIC ARTERY RECONSTRUCTION IN ORTHOTOPIC LIVER TRANSPLANTATION

H. Esser, B. Mutschlechner, T. Resch, B. Cardini, R. Oberhuber, C. Margreiter, D. Öfner, S. Schneeberger, M. Maglione
Medical University of Innsbruck, Universitätsklinik für Visceral-, Transplantations- und Thoraxchirurgie, Innsbruck, Austria
E-mail: hannah.esser@tirol-kliniken.at

Background: In the context of orthotopic liver transplantation (OLT) variations of the hepatic artery often necessitate backtable hepatic artery reconstruction (HAR) to warrant good arterial blood flow after anastomosis. Meticulous reconstruction is crucial as arterial complications represent an important cause of morbidity and mortality after OLT. Herein, we analysed our own results with backtable HAR in adult liver transplant recipients.
Methods: We performed a retrospective analysis of all consecutive adult OLT performed at our centre between January 1st, 2007 and December 31st, 2013.
Results: In total we could include 374 patients in our analysis. 30 patients required backtable arterial reconstruction prior to implantation, 344 patients were managed without backtable hepatic artery reconstruction. Patients with arterial jumpgrafts or unknown arterial anastomosis were excluded.

There were no statistically significant differences in graft- and patient-survival in both groups. 1- and 3-year graft survival were 86.9% and 80.9% in the no HAR group vs. 80% and 69.6% in the HAR group; 1- and 5-year patient-survival were 90.4% and 85.6% in the no-HAR group vs. 86.7% and 76.4% in the HAR group.

Using the Spearman's rank correlation our data revealed a weak positive correlation between backtable HAR and arterial thrombosis ($rs = 0.146$, $p = 0.005$). There was no significant correlation between HAR and other analysed factors such as bile duct ischemia, bile duct anastomotic stricture, bile duct non-anastomotic stricture or arterial stenosis.
Conclusion: Though there is a weak correlation between backtable HAR and arterial dissection, we could not detect a significant difference in postoperative patient- and graft survival. These findings affirm backtable HAR as a safe option to utilize grafts with an anatomic variation of the hepatic artery.

O 20 A NEW PREDICTING TOOL FOR EXPERIMENTAL LIVER TRANSPLANTATION – LIVE TISSUE STAINING

M. Fodor, B. Cardini, S. Schneeberger, M. Maglione, J. Troppmair, M. Hermann, R. Oberhuber
Medical University of Innsbruck, Department of Visceral, Transplant and Thoracic Surgery, Innsbruck, Austria
E-mail: rupert.oberhuber@i-med.ac.at

The ischemia reperfusion injury is a main contributor to early graft dysfunction, which leads to costly and lengthy follow-up treatments or even organ loss in clinical liver transplantation. To address the ever-increasing gap between patients on waiting list and organs available for transplantations, more and more marginal grafts are transplanted.

Methods to monitor graft quality prior to transplantation are therefore highly desirable to optimize clinical outcome.

In an experimental model we used life confocal microscopy to assess murine liver graft quality. Six to ten-week-old male animals were subjected to a methionine-choline-deficient (MCD) diet causing non-alcoholic fatty liver disease (NAFLD), or to the Lieber DeCarli diet producing alcohol-induced liver injury. Untreated animals served as control. In each group liver biopsies were analyzed after 45 min' warm ischemia time (WIT) induced by liver pedicle occlusion, 24 hours' cold ischemia time (CIT) respectively. All clamped livers were reperfused for 4 hours. Graft quality assessment was performed by measurement of serum transaminases, standard histopathology, assessment of cytokine expression profiles, assessment of oxidative stress and live confocal microcopy.

After CIT and WIT liver grafts showed a decrease in cell viability when compared to naïve animals ($p < 0.05$) as assessed using life confocal microscopy. Animals exposed to the MCD diet showed significantly lower cell viability within the liver biopsies after CIT as well as after WIT when compared to control animals ($p < 0.05$). Similar results were obtained from the analysis of cell viability of animals fed with the LDC diet. Results from confocal microscopy were then correlated with the results from detection of serum transaminases of, standard H&E staining the expression of proinflammatory cytokines as well as markers for oxidative stress.

Our data demonstrate that confocal microscopy is well suitable to detected organ damage prior to transplantation.

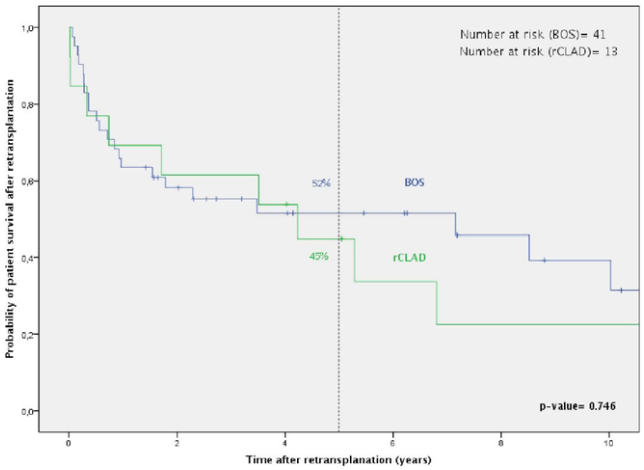
O 21 LUNG RETRANSPLANTATION FOR CLAD- DOES THE PHENOTYPE OF CLAD AFFECT THE SURVIVAL? A RETROSPECTIVE EXPLORATIVE STUDY

M.M. Schuster[1], A. Benazzo[2], G. Muraközy[2], C. Lambers[2], S. Schwarz[2], W. Klepetko[2], P. Jaksch[2]

[1]Medizinische Universität Wien, Innsbruck, Austria; [2]Klinische Abteilung für Thoraxchirurgie/Allgemeines Krankenhaus Wien/Medizinische Universität Wien/Wien, Innsbruck, Austria

E-mail: schuster_magdalena@yahoo.com

Background: Chronic lung allograft dysfunction (CLAD) is the major factor limiting the long-term outcome after lung transplantation (LuTX). The two main phenotypes are bronchiolitis obliterans syndrome (BOS) and restrictive CLAD (rCLAD). Patients, who develop rCLAD after primary LuTX, have a significantly worse survival, than recipients with BOS. Still, it is not fully clear so far, whether the CLAD-phenotypes also affect the outcome of patients, who had been retransplanted for CLAD. Existing evidence shows, that rCLAD might be associated with a worse survival after retransplantation (ReTX) than BOS. Aim of this study was, to investigate the influence of the CLAD-phenotypes, BOS and rCLAD, on survival after ReTX.
Material and Methods: Patients, who received ReTX for CLAD from 2000 to 2014, were retrospectively analysed and allocated to a BOS and rCLAD group. CLAD was defined as irreversible decline in peak forced expiratory volume in 1 second (FEV1) <80% of baseline. rCLAD was defined as CLAD with a persistent decline in TLC at <90% of baseline and thus, restrictive functional change; BOS as CLAD without rCLAD. The Kaplan–Meier-method and Cox-proportional hazards model were used to assess time-to-event rates (e.g., survival).



Results: Among 54 candidates, 41 (76%) had developed BOS after primary LuTX and 13 (24%) patients rCLAD.

Unadjusted overall survival after ReTX was not statistically different for BOS and rCLAD ($p = 0.746$). The 5-year survival of BOS patients after ReTX was 52% compared to 45% in rCLAD patients. rCLAD could not be identified as independent risk factor of death after ReTX in the adjusted analysis ($p = 0.119$; hazard ratio 2.14; confidential interval 0.82–5.55).
Conclusion: In our experience survival after ReTX for rCLAD is not significantly different in comparison to survival of patients, who were retransplanted for BOS. Further research is necessary to validate these results.

O 22 CLINICAL-SCALE MANUFACTURE OF ANTI-FUNGAL T-CELLS EVALUATED IN A COMPARATIVE STUDY USING BOTH DIRECT SELECTION AND EXPANSION

R. Geyeregger[1], S. Tischer[2], N. Frank[3], C. Hoffmann-Freimüller[3], J. Stemberger[3], B. Maecker-Kolhoff[4], R. Blasczyk[5], G. Fritsch[6], B. Eiz-Vesper[7]

[1]St Anna Kinderkrebsforschung, Vienna, Austria; [2]Institute for Transfusion Medicine, Hannover Medical School, Hannover, Germany; [3]St. Anna Kinderkrebsforschung e.V.; [4]Integrated Research and Treatment Center (IFB-Tx), Department of Pediatric Hematology and Oncology, Hannover Medical School, Hannover, Germany; [5]Institute for Transfusion Medicine, Integrated Research and Treatment Center (IFB-Tx), Hannover Medical School, Hannover, Germany; [6]St. Anna Kinderkrebsforschung e.V., Children's Cancer Research Institute, Medical University, Vienna, Austria; [7]Institute for Transfusion Medicine, Integrated Research and Treatment Center (IFB-Tx), Hannover Medical School, Hannover, Germany

E-mail: rene.geyeregger@ccri.at

Introduction: A*spergillus-fumigatus* (Aspf) infections constitute a major cause of morbidity and mortality in patients after haematopoietic-stem-cell-transplantation. Using blood from identical volunteers, we compared two different strategies, the Interferon-gamma (IFN-g) Cytokine-Capture-System (CCS) versus short-term expansion (STE), to evaluate the most suitable approach for the clinically in-time generation of Aspf-T-cells.
Materials/Methods: Donor-derived PBMCs from leukapheresis ($n = 6$) were prepared in Hannover for the IFN-g-CCS, remaining cells were sent to Vienna to perform STE. For the IFN-g-CCS, 1×10^7 cells were stimulated for 16 hours with GMP-conform Aspf-lysate followed by magnetic selection of IFN-g-producing T-cells. Cells were characterized for phenotype and function by flow cytometry. For the STE, 2×10^7 cells were stimulated for 12 days with either the Aspf-lysate alone or with pepmixes and IL-15. The final cell products were characterized via flow cytometry, IFN-g-EliSpot and IFN-g/granzyme-B Fluro-Spot analyses.
Results: IFN-g-CCS: Frequency of IFN-g+ Aspf-T-cells (pre-enrichment) ranged between 0.07 and 0.16% which was above the eligibility threshold of ≥0.03%. The purity of Aspf-T-cells, obtained from five donors after enrichment was 49% ± 6 (range: 33–69%). The absolute number of selected IFN-g+ CD3 + T-cells was 724 ± 256. This could be approximately multiplied by a factor of 100, if $>1 \times 10^9$ PBMCs were used. STE: After 12 days, Aspf-T-cells ($n = 6$) showed highly specific activity against the lysate (856 ± 223 spot forming colonies (SFC)/105 cells) and pepmixes (892 ± 276 SFC/105 cells). In both methods, predominantly CD4 + T-cells were expanded (84% ± 2.3 vs. 82% ± 5.3) compared to CD8 + T-cells (12.6% ± 2.9 vs. 14.7% ± 5.3) among CD3. Whereas CD4 + T-cells were mainly of central-memory type (mean 40% of CD3), 27% of CD8 + T-cells were effector-memory T-cells (27%). Target cells were highly functional and cytotoxic as determined by secretion of granzyme-B and IFN-g.
Conclusion: Based on the purity of up to 69% after the IFN-g-CCS and the high number of SFC after STE, both methods seem to be suitable for clinical-scale productions.

O 23 EXTRACORPOREAL PHOTOPHERESIS AS TREATMENT OF CHRONIC LUNG ALLOGRAFT DYSFUNCTION: A SINGLE CENTRE EXPERIENCE

A. Benazzo, S. Schwarz, T. Schweiger, K. Hoetzenecker, C. Lambers, G. Muraközy, S. Taghavi, W. Klepetko, P. Jaksch
Medizinische Universität Wien, Vienna, Austria
E-mail: alberto.benazzo@meduniwien.ac.at

Lung transplantation is the only therapeutic procedure for end-stage lung pathologies, however, long-term outcome is still impaired by chronic lung allograft dysfunction (CLAD). To date, there is no curative treatment available but Extracorporeal Photopheresis (ECP) has been increasingly used as second-line therapy, showing promising results. It improves pulmonary function tests and graft survival.

We retrospectively analyzed our experience with ECP as treatment of CLAD. As primary outcome we studied graft survival from the beginning of ECP treatment. Moreover the following data were collected: perioperative data, lung function parameters at different time points, kidney function parameters and immunosuppression protocol.

Since 2011, 106 patients (male = 51, female = 55) who developed CLAD were treated with ECP. Among them, 80 had a diagnosis of BOS, 15 of RAS and 11 a combined form of them. 63 Patients responded to ECP either with a stabilization or improvement of lung function. We observed a significantly better graft survival in responders: 82.9% at 5 years compared to 75% in non responders group. We couldn't find an higher prevalence of RAS patients in non responders group. 50% of the patients didn't receive any induction therapy, 20% received ATG and 18% Alemtuzumab. 28 Patients required a retransplantation. In 22 cases a double lung transplantation was performed, in all other cases a single lung transplantation was preferred.

ECP is currently a second-line therapy of CLAD. In this single-centre large series, we show its great potential to stop further worsening of graft function. Further studies are necessary to clarify its immunological mechanisms.

O 24 BODY COMPOSITION AS ASSESSED BY 3 COMPARTMENT MODEL BIOELECTRICAL IMPEDANCE ANALYSIS PREDICTS LUNG FUNCTION IN ADULT PATIENTS WITH CYSTIC FIBROSIS AFTER LUNG TRANSPLANTATION

K. Staufer, E. Halilbasic, P. Hillebrand, S. Harm, S. Schwarz, P. Jaksch, W. Klepetko, M. Trauner, L. Kazemi-Shirazi
Medizinische Universität Wien, Vienna, Austria
E-mail: Katharina.Staufer@meduniwien.ac.at

Nutritional status is an important prognostic factor in patients with cystic fibrosis (CF). This study investigated the impact of nutritional status on lung function (LF) in adult CF patients after LT.

Therefore, body composition measured by 3 compartment model - bioelectrical impedance analysis (BIA), body mass index (BMI), as well as 25-hydroxy(OH)-vitamin D-levels were longitudinally assessed in consecutive adult double-lung transplanted CF patients.

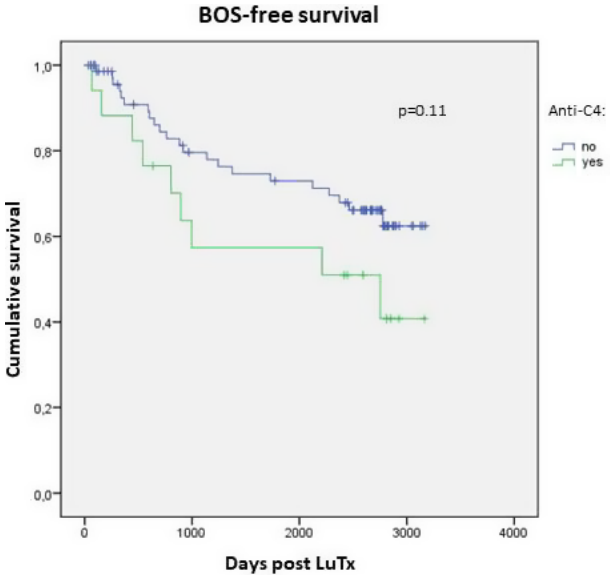
In total, 147 LF tests and BIAs were performed in 58 patients (59% female, median age: 30.1 years, median BMI: 19.6 kg/m^2). Malnourished patients (BMI < 18.5 kg/m^2; 28%) had a significantly reduced LF compared to normal/overweight patients (FEV1%pred, 57% vs. 77%; p = 0.024). BMI, as well as the BIA parameters phase angle, total body water, fat free mass, body cell mass (BCM), extracellular mass (ECM)/BCM ratio were univariate predictors of FEV1%pred. When included in a linear mixed model ECM/BCM ratio remained the only significant predictor (p = 0.012). Vitamin D-deficiency was present in 93.1% of patients and significantly correlated with maximum vital capacity and total lung capacity.

BIA was superior to BMI in prediction of LF. Continuous care by dietitians and gastroenterologists trained in CF care might improve nutritional status and LF in CF patients after LT.

O 25 PREVALENCE AND CLINICAL IMPACT OF ANTI-C4 ANTIBODIES IN A LUNG TRANSPLANT COHORT

S. Camovic[1], A. Scheed[2], F. Eskandary[1], M. Stadlberger[1], H. Haslacher[3], S. Geleff[4], G.F. Körmöczi[5], G. Bond[1], G.A. Böhmig[1], P. Jaksch[2], M. Wahrmann[1]
[1]Department of Medicine III, Division of Nephrology and Dialysis, Medical University Vienna, Vienna, Austria; [2]Department of Thoracic Surgery, Medical University Vienna, Vienna, Austria; [3]Department of Laboratory Medicine, Medical University Vienna, Vienna, Austria; [4]Clinical Institute of Pathology, Medical University Vienna, Vienna, Austria; [5]Department of Blood Group Serology and Transfusion Medicine, Medical University Vienna, Vienna, Austria
E-mail: markus wahrmann@meduniwien.ac.at

Introduction: Human leukocyte antigens (HLA) are the most prominent immunological targets in antibody-mediated rejection (AMR). However, in recent years non-HLA antigens have gained increasing interest. In this retrospective study we have screened for antibodies towards the highly polymorphic complement component 4 (C4) in lung transplanted patients by a novel bead-based assay.
Methods: The C4 gene status of 48 healthy volunteers was determined by sequence-specific primer PCR and next generation sequencing. The C4 protein of 8 genetically diverse subjects was isolated by ion exchange chromatography and immobilized to different bead populations. This panel was incubated with a pre-transplant serum and three post-transplant sera of 99 patients with a first-time lung transplantation (LuTx). Deposited IgG was detected by rabbit anti-human IgG and phycoerythrin-coupled goat anti-rabbit IgG on a Luminex 200 System.
Results: Nine of 94 tested pre-transplant sera had anti-C4 antibodies while 6/83, 6/81 and 3/71 of the respective post-transplant sera (2, 6 and 12 months post LuTx) were positive. Overall, 18 of 99 patients had anti-C4 antibodies in any of the four tested sera. Positive anti-C4 test results were not associated with rejections or graft survival, but there was a trend to an earlier occurrence of bronchiolitis obliterans syndrome (BOS) (Figure 1: $\chi^2 = 2.55$, p = 0.11).
Discussion: Our finding of an association of low-frequent anti-C4 antibodies with an earlier development of BOS, a chronic condition leading to early graft loss, is in line with previous reports that link anti-HLA antibodies to BOS. The only weak association may be due to a small case number and a low grade of pre-sensitization (only first-time LuTx). Our study emphasizes the importance of non-HLA antibodies in AMR and should prompt further studies using our novel C4 panel assay analyzing larger cohorts or subjects with higher pre-sensitization like kidney transplant patients.



O 26 ANTI-IL6 SYNERGIZES WITH IL2CPLX TREATMENT TO PROMOTE TRANSPLANTATION TOLERANCE BY MECHANISMS INVOLVING TREGS AND APCS

N. Pilat[1], M. Wiletel[1], B. Mahr[1], N. Granofszky[1], M. Muckenhuber[1], T. Wekerle[1], K. Webster[2], J. Sprent[2]
[1]Medical University of Vienna, Vienna, Austria; [2]Garvan Institute of Medical Research, Darlinghurst, NSW, Australia
E-mail: nina.pilat@meduniwien.ac.at

Introduction: Interleukin-2 (IL2) complexed with a specific antibody against IL2 (IL2cplx) rapidly expands and activates Tregs *in vivo*. Treatment with IL2cplx has shown potency in inducing tolerance towards islet (but not skin) allografts. Here we investigated the potency of IL2cplx based therapy to prolong skin allograft survival and the mechanisms of tolerance.
Methods: Mice received fully or MHC mismatched skingrafts, tolerogenic therapy with IL2cplx and mTOR inhibition (3 × /week for 4 weeks) and short-term treatment with anti-IL6. Tolerance was assessed by skingrafting, analysis of DSA, flow-cytometric analysis and MLRs. Groups of mice were challenged with a second skingraft to test for infectious tolerance and for memory responses.
Results: We could show that combination of IL2cplx, rapamycin and anti-IL6 significantly prolongs survival of fully mismatched skingrafts (MST = 76 days, p < 0.0001) and leads to prevention of acute rejection, even after complete stop of treatment at d29. Importantly, the absence of minor antigens led to graft survival >100 days. Analysis of sera revealed complete absence of donor-

specific antibodies ($p < 0.01$) and kinetics of rejection of a second graft suggested additional absence of Tmem response. Operational tolerant mice challenged with a 2nd graft and MLRs suggest absence of systemic tolerance or general immunosuppression. Flow cytometric analysis of the graft indicates increased frequencies of intragraft Tregs and active regulatory mechanisms as graft survival was critically dependent on Tregs. Anti-IL6 treatment was shown to synergize with IL2cplx to boost Treg proliferation and prevent NK and CD8 activation. Moreover anti-IL6 treatment leads to downregulation of MHCII and increased PDL-1 expression on APCs.
Discussion: We could show that Treg expansion via IL2cplx synergizes with rapamycin and anti-IL6, leading to significantly prolonged skin allograft survival and prevention of acute. We think these results will have significant impact on the development of new protocols for tolerance induction.

O 27 *IN VIVO* TREG EXPANSION OVERCOMES CTLA4IG-RESISTANT REJECTION AND LEADS TO PERMANENT GRAFT SURVIVAL BY DECREASING B7 EXPRESSION ON ANTIGEN PRESENTING CELLS

C. Schwarz, B. Mahr, L. Unger, N. Pilat, H. Regele, K. Aumayr, T. Wekerle
Medical University Vienna, Vienna, Austria
E-mail: christoph.a.schwarz@meduniwien.ac.at

Background: Early allograft rejection is a major obstacle under costimulation blockade-based immunosuppression. We have previously shown that the immunosuppressive effect of CTLA4Ig monotherapy is Treg-dependent at low (LD) but not high doses. Therefore, we aimed at increasing CTLA4Ig's efficacy by targeting recipient's Tregs through adoptive transfer and *in vivo* Treg expansion.
Methods: Cardiac allograft transplantation was performed (Balb/C on C57BL6) under CTLA4Ig monotherapy, modeled after the clinically approved dosing regimen (LD). In groups of mice treated with LD CTLA4Ig, 3×10^6 recipient Tregs were transferred early (D-1, $n = 6$) or late (D8, $n = 10$) or Tregs were expanded *in vivo* by using IL2/aIL2 complexes (D-3, D-2, D-1; $n = 5$).
Results: Transferred Tregs were viable and traceable in various compartments including the spleen, lymph nodes, blood and bone marrow. However, neither early, nor late Treg transfer prolonged allograft survival under LD CTLA4Ig therapy (MST 24.5 vs. 33.5 vs. 52.5; p = n.s.). In contrast, addition of IL2/aIL2 complexes significantly prolonged heart graft survival (MST > 100 days) compared to CTLA4Ig monotherapy (MST: 52.5 days) or IL2/aIL2 complexes only (MST: 14 days) ($p < 0.001$). Notably, the addition of IL2/aIL2 complexes abolished the deleterious effect on Treg numbers under costimulation blockade. Moreover, CD80 expression on dendritic cells, which was significantly increased by CTLA4Ig treatment, was lowered to levels observed in naïve animals.
Discussion: Whereas Treg transfer didn't result in an improved allograft outcome, *in vivo* Treg expansion by using IL2/aIL2 complexes resulted in long-term graft survival with low dose CTLA4Ig treatment. These results suggest a clinically promising strategy to improve outcome with costimulation-blockade-based immunosuppression.

O 28 MYOGENIC STEM CELLS IN MUSCLE REGENERATION AFTER HIND-LIMB ISCHEMIA IN THE MOUSE

F. Messner[1], M. Thurner[2], J. Müller[1], T. Hautz[1], M. Hermann[1], M. Blumer[1], R. Marksteiner[3], S. Schneeberger[1]
[1]Medizinische Universität Innsbruck, Innsbruck, Austria; [2]Medizinische Universität Innsbruck/Innovacell Biotechnology AG, Innsbruck, Austria; [3]Innovacell Biotechnology AG, Innsbruck, Austria
E-mail: franka.messner@i-med.ac.at

Background: Muscle tissue is most susceptible to ischemic injury but has a remarkable potential to recover. Myogenic stem cells are thought to be responsible for this phenomenon. The aim of the proposed study is to investigate the regenerative potential of *in-vitro* cultivated satellite cells and their effect on muscle tissue damage after limb ischemia in a mouse model.
Methods: A hind limb clamp model was applied in 6–10 week-old C57b/6J mice. After 2 hours of warm ischemic time (WIT), reperfusion was performed and transgenically labeled satellite cells (TdTomato or Luci-GFP, Innovacell Biotechnologie AG, VAT ID No: ATU 52015000) were injected in the anterior tibial muscle. Bioluminescence imaging (IVIS® Lumina II) and confocal microscopy enabled to track the cells and quantify the engraftment as well as to analyze functional integration *in-vivo*. After 3, 7, 14 and 100 days, muscle biopsies were obtained for histopathologic assessment.
Results: GFP labeled satellite cells were visualized early but also late (postoperative day 100) after two hours of WIT and cell injection via IVIS® *in vivo* imaging. Intramuscularly injected cells remained at the injection site and no migration was noted. Confocal imaging showed that TdTomato labeled satellite cells differentiated into muscle fibers. Furthermore, a significantly higher signal of Luci_GFP cells was found in mice that underwent 2 hours WIT compared to control mice, suggesting higher engraftment of cells due to WIT.
Conclusion: We could demonstrate that after moderate WIT, locally injected myogenic stem cells (satellite cells) did differentiate into muscle fibers and remained vital until postoperative day 100. Our results suggest that WIT allows more stem cells to engraft, suggesting a rational for cell therapy after ischemia. Further investigations are ongoing to evaluate their regenerative capacity in the setting of ischemic limb injury.

O 29 P66SHC A NOVEL TARGET IN THE PREVENTION OF ISCHEMIA-REPERFUSION INJURY (IRI)

S. Khalid[1], T. Furlan[1], J. Günther[1], A. Drasche[1], M. Hermann[2], J. Troppmair[1]
[1]Daniel Swarovski Research Laboratory, Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Innsbruck, Austria; [2]Department for Anesthesiology and Intensive Care, Medical University of Innsbruck, Innsbruck, Austria
E-mail: jakob.troppmair@i-med.ac.at

Excessive production of reactive oxygen species (ROS) has been causally linked to cell death resulting in the loss of cognitive or organ function in many disease settings ranging from neurodegeneration, stroke, diabetes, to ischemia/reperfusion injury (IRI) during solid organ transplantation. Antioxidants so far largely failed in the clinical setting. Also the direct inhibition of mitochondrial and non-mitochondrial ROS producing system is not clinically feasible. p66Shc is unique among ROS producing systems as its knockout did not affect normal signaling and thus survival while it prevented pathophysiological conditions caused by excessive ROS production. p66Shc, the longest form of the ShcA adaptor proteins normally resides in the cytoplasm. Previous work suggested that the activation of the pro-oxidant and pro-death function of p66Shc required phosphorylation on serine 36 (S36) followed by mitochondrial import and PKCβ has been proposed as S36 kinase. Due to the lack of inhibitors of its oxidoreductase function we pursue a strategy to inhibit p66Shc by interfering with its upstream activation. To this end we initiated a detailed analysis of the signaling interaction controlling p66Shc activation and function under cellular stress.

In our work we could confirm the requirement of PKCβ for ROS production and cell death but not for p66ShcS36 phosphorylation. Our searches for a *bona fide* S36 kinase lead to JNK1/2, whose involvement was confirmed through the use of inhibitors and JNK1/2-deficient cells. Moreover, expression of a S36E mutant in p66Shc-deficient cells restored ROS production under the stress conditions tested here. Additionally, we identified S139, T206 and S213 as critical PKCβ target sites regulating the pro-oxidant and pro-death function of p66Shc. Both, JNK1/2 and PKCβ, are normally activated under cellular stress and targeting them may provide a novel therapeutic approach to prevent diseases associated with excessive ROS production.

O 30 BORTEZOMIB IN LATE ANTIBODY-MEDIATED KIDNEY TRANSPLANT REJECTION - A DOUBLE-BLIND RANDOMIZED PLACEBO-CONTROLLED TRIAL (BORTEJECT STUDY)

F.-A. Eskandary[1], H. Regele[2], G. Bond[1], N. Kozakowski[2], M. Wahrmann[1], L. Hidalgo[3], H. Haslacher[4], C. Kaltenecker[1], M.-B. Aretin[5], R. Oberbauer[1], J. Reeve[6], P. Halloran[6], G. Böhmig[1]
[1]Klinische Abteilung für Nephrologie und Dialyse, Medizinische Universität Wien, Innsbruck, Austria; [2]Klinische Abteilung für Pathologie, Medizinische Universität Wien, Innsbruck, Austria; [3]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB, Canada; [4]Klinisches Institut für Labormedizin, Medizinische Universität Wien, Innsbruck, Austria; [5]Anstaltsapotheke, AKH Wien, Vienna, Austria; [6]Alberta Transplant Applied Genomics Centre, ATAGC, University of Alberta, Edmonton, AB, Canada
E-mail: farsad.eskandary@meduniwien.ac.at

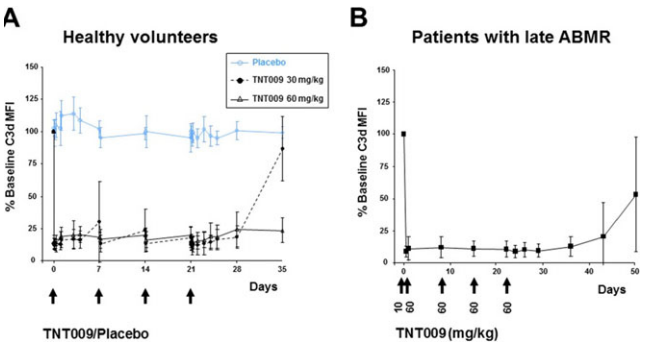
Background: Antibody-mediated rejection (ABMR) is a leading cause of long-term kidney transplant loss. Optimal treatment of late ABMR is unclear, and our current knowledge is mostly based on uncontrolled studies.
Methods: In this randomized, double-blind, placebo-controlled, single-center phase 2 trial (NCT01873157), we investigated whether two cycles of the proteasome inhibitor bortezomib (each cycle: 1.3 mg/m^2 on days 1, 4, 8 and 11) can stop the progression of late ABMR, using eGFR slope (Over 0, 3, 6, 12, 18 and 24 months) as primary endpoint (44 patients; 1:1 randomization). Secondary outcomes were mGFR at 24 months, donor-specific antibody (DSA) course and morphological/molecular results of 24-month follow-up biopsies.
Results: Upon systematic cross-sectional HLA antibody screening of 741 recipients [criteria: age >18a, eGFR >20 ml at ≥180 days post-transplantation] we identified 111 recipients with DSA. Forty-four DSA+ recipients with morphological evidence of ABMR were included in the trial. Twenty-one patients were allocated to receive bortezomib, and 23 placebo. Despite a trend in reduction of DSA levels, bortezomib neither affected eGFR decline (bortezomib vs. placebo: -4.6 ± 2.7 vs. -4.8 ± 2.5 ml/min/1.73 m^2/year), nor median mGFR at 24 months [33 ml (IQR: 28–40) vs. 43 ml (26–51), p = 0.2]. There were also no differences regarding two-year overall graft survival (81% vs. 96%, p = 0.1) and morphological (ABMR category, g+ptc

score, IFTA score, C4d) and molecular results (Molecular-ABMR score, MMDx) of 24-month follow-up biopsies. Bortezomib treatment was associated with a higher rate of GI adverse events (diarrhea: 67% vs. 22%, p = 0.005) and thrombo- and leukocytopenia.
Conclusion: The BORTEJECT trial demonstrates that proteasome inhibition does not ameliorate the two-year course of late ABMR. Our results underscore the need for randomized trials to dissect the efficiency and safety of new treatment strategies in this context.

O 31 MULTIPLE DOSING OF ANTI-C1S ANTIBODY TNT009 – EFFECT ON HLA ANTIBODY-TRIGGERED COMPLEMENT ACTIVATION IN HEALTHY VOLUNTEERS AND KIDNEY TRANSPLANT RECIPIENTS WITH ANTIBODY-MEDIATED REJECTION

J. Mühlbacher[1], B. Jilma[2], M. Wahrmann[3], F. Eskandary[3], James.C. Gilbert[4], S. Panicker[4], G. Böhmig[3]
[1]Department of Surgery, Medical University Vienna, Vienna, Austria; [2]Department of Clinical Pharmacology, Medical University Vienna, Vienna, Austria; [3]Department of Medicine III, Medical University Vienna, Vienna, Austria; [4]True North Therapeutics, Inc., South San Francisco, CA, USA
E-mail: jakob.muehlbacher@meduniwien.ac.at

Study Purpose: Complement inhibition may be an attractive strategy to prevent antibody-mediated allograft injury. One promising therapeutic target may be the enzymatic activity of key classical pathway (CP) component C1. In this first-in-human trial (NCT02502903) we evaluated the impact of 4 weeks treatment with TNT009, a humanized anti-C1s antibody on CP activity in healthy individuals and kidney transplant recipients with late antibody-mediated rejection (ABMR).
Methods: Sixteen healthy volunteers received 4 weekly IV doses of TNT009 or placebo (6:2 randomization, two cohorts: 30 or 60 mg/kg). Subsequently, 10 kidney transplant recipients diagnosed with late ABMR were treated with TNT009 (initial test dose of 10 mg/kg followed by 4 weekly doses of 60 mg/kg). To assess ex vivo HLA antibody-triggered complement activation, sera from dosed subjects were analysed on microbeads sensitized with HLA antibodies using the read-out of C3d fixation.
Results: Baseline C3d deposition levels were not significantly different between healthy volunteers and transplant recipients (mean C3d MFI: 4882 ± 754 vs. 4367 ± 1030, p = 0.15). In healthy volunteers, multiple doses of TNT009 led to a persistent (≥4 weeks) and >80% inhibition of HLA antibody-triggered C3d deposition (and in parallel CH50 activity) [figure 1]. Similarly, sustained complement inhibition was also achieved in the cohort of ABMR patients, with a comparable degree of CP blockade [figure 1]. CP inhibition tightly correlated with plasma levels of TNT009.
Conclusion: Multiple doses of TNT009 allowed for a prolonged and near complete CP inhibition both in healthy volunteers and ABMR patients. Our results provide a valuable basis for future studies evaluating the effect of prolonged C1s blockade on the course of antibody-mediated rejection.



O32 REFRACTORY ACUTE ABMR: EFFECTIVE TREATMENT BY A NOVEL STRATEGY OF MEMBRANE FILTRATION PLUS IMMUNOADSORPTION FOR CLASSICAL COMPLEMENT INTERFERENCE IN ADDITION TO ANTIBODY DEPLETION

K. Doberer[1], H. Regele[2], G. Scheriau[1], G. Böhmig[1], F. Eskandary[1]
[1]Department of Nephrology and Dialysis, Medical University Vienna, Vienna, Austria; [2]Department of Clinical Pathology, Medical University Vienna, Vienna, Austria
Corresponding author: E-mail: konstantin.doberer@meduniwien.ac.at

Background: Apheresis for IgG depletion represents an effective strategy for the prevention and treatment of antibody-mediated rejection (ABMR). We have earlier shown that membrane filtration (MF), added to the circuit of conventional immunoadsorption (IA), may specifically interfere with alloantibody-triggered complement activation, by eliminating C1q, the key component of the classical pathway (CP). Here we report on the effect of combined apheresis in four cases of severe refractory C4d-positive ABMR.
Methods: For IA we used a semiselective double-column device (146-GAM peptide adsorber; 2–3 plasma volumes per session). For combined apheresis, a porous membrane filter (MONET®) was connected to the extracorporeal circuit. ABMR was classified and scored according to the Banff 2013 update.
Results: Four kidney allograft recipients (transplantation between 2014 and 2016; two re-transplants, two female recipients, age 47–71 years, pre-Tx CDC-PRA 0–44%) were transplanted across preformed donor-specific antibodies (DSA, HLA class I and/or II) using a local standard protocol of peri-transplant IA and ATG induction. Despite desensitization, studied patients developed severe acute/active ABMR (g+ptc score: 2–4; TMA in 2 cases) 14 to 17 days after transplantation (two of the patients were dialysis-dependent). Signs of intra-graft CP activation (diffuse C4d staining in all four cases) prompted us to add MF to IA treatment. Upon 2–8 combined treatment sessions, recipients showed reversal of rejection, two within the first week. Remarkably, follow-up allograft biopsies showed marked morphological improvement (g+ptc: 0–2, no TMA), with negative C4d staining in three cases. Last serum creatinine 3–20 months post-Tx was 1.42 mg/dl (median; range: 0.97–3.1).
Conclusion: Our findings illustrate that MF as an add-on to IA may be an effective strategy to reverse refractory acute ABMR, presumably as a result of CP interference.

O 33 TENCKHOFF-CATHETER REMOVAL – WITHOUT OPERATION POSSIBLE?

R. Langer
Ordensklinikum Linz, Krankenhaus der Elisabethinen, Linz, Austria
E-mail: roblanger@hotmail.com

The removal of the peritoneal dialysis catheter happens to the majority after a successful kidney transplantation in form of an overnight hospital stay operatively.

One can sometimes see the complication of oozing ascites which is very uncomfortable for the immunosuppressed patient and could be even dangerous from the infectious point of view.

The alternative way to the classic method is demonstrated in a short video. One can see as the Tenckhoff-catheter is carefully pulled out from the anaesthesized patient. The drain gets loose from the cuffs which remain in the body and the silicon catheter can be removed in toto. After the short anaesthesia the patients can be discharged from the hospital on the same day. The only contraindication to the method is the metallic-olive ended catheter.

The method which originates to our knowledge from the UK could be successful established at the Linz Transplant Center.

O 34 REGRESSION OF LEFT ATRIAL DIAMETER AFTER KIDNEY TRANSPLANTATION IS ASSOCIATED WITH PROLONGED SURVIVAL

F. Regele[1], A. Kainz[1], M. Kammer[1], A. Beer[2], R. Steringer-Mascherbauer[3], T. Binder[1], R. Oberbauer[1]
[1]Medizinische Universität Wien, Vienna, Austria; [2]Medizinische Universität Innsbruck, Innsbruck, Austria; [3]Ordensklinikum Linz, Linz, Austria
E-mail: Alexander.Kainz@meduniwien.ac.at

The risk of cardiovascular death in patients on dialysis is dramatically elevated but can be reduced by renal transplantation. We previously showed that left atrial diameter at time of transplantation predicts cardiovascular and overall mortality. Now we investigated the association of changes in cardiac morphology after transplantation and mortality.

We retrospectively analyzed data from the Austrian dialysis and transplant repository which was merged with the echocardiography data repositories at the transplant centers. Of the 414 patients with at least two sequential echocardiograms and a median post-transplant follow-up of 8.0 years, we observed a significant progression of mean diameter of the left atrium (LA),

right atrium and right ventricle, and a significant regression of left ventricular diameter (LV). Patients, who showed a regression of initially enlarged LA diameter had a significantly lower risk of mortality compared to patients who progressed in LA diameter (HR 0.47, 95% CI 0.31–0.70, $p < 0.001$). Regression of LV was not associated with survival. Of the examined clinical covariables, only age at transplantation (OR 0.67, CI 0.52–0.87, $p = 0.007$) and pre-transplant peritoneal dialysis (PD) (OR 2.27, 95% CI 1.08–4.76, $p = 0.031$) were significantly associated with a regression of LA diameter.

In conclusion, we found that renal transplantation did not result in a regression of left atrial diameter in the majority of patients who had an enlarged atrial diameter at time of transplantation. However, those 36% with regression of LA exhibited a longer overall survival. Besides age, peritoneal dialysis and antihypertensive therapy were mediators of LA regression.

O 35 NOVEL GENETIC MUTATION OF DSP AND TTR GENES IN A CARDIAC ALLOGRAFT RECIPIENT WITH FAMILIAL HYPERTROPHIC-RESTRICTIVE CARDIOMYOPATHY: A CASE REPORT

K. Freystaetter, M. Andreas, A. Aliabadi-Zuckermann, F. Wittmann, F.-M. Kainz, K. Uyanik-Uenal, F. Laccone, A. Zuckermann
Medizinische Universität Wien, Vienna, Austria
E-mail: kathrin.freystaetter@gmail.com

We report of a 41-year old patient, who developed severe exercise intolerance during childhood. Later, she presented with palpitations and repeated syncopes, requiring cardiac transplantation due to end-stage hypertrophic-restrictive cardiomyopathy when 30 years old. The patient's mother died of heart failure when she was 60 years old. Due to the positive family history we performed next generation sequencing with a cardiomyopathy panel analysis, assessing 34 genes.

We identified two genetic mutations in our patient. Sequence analysis showed a heterozygotic base pair substitution in the coding sequence of the *DSP* gene from guanine to adenine (c.88G>A), resulting in the exchange of valine to methionine in position 30 of the amino acid sequence (p.Val30Met). The *DSP* gene encodes desmoplakin, found in desmosomes of cardiac cells, required for the stabilisation of tissues and signalling pathways. Mutations in this gene have previously been linked to the development of arrhythmogenic right-ventricular dysplasia. The pathogenicity of this specific mutation has been described variably in literature. Additionally, we found a heterozygotic base pair substitution in the coding sequence of the *TTR* gene from cytosine to thymine (c.370C>T), exchanging arginine to cysteine in position 124 of the amino acid sequence (p.Arg124Cys). The *TTR* gene encodes transthyretin, a transport protein for retinol and thyroxine. Genetic alterations have previously been implicated in the pathogenesis of transthyretin amyloidosis. This specific mutation has not been described in literature and computer algorithms provide varying results regarding its pathogenicity.

The development of cardiomyopathy is a highly complex and multifactorial process. The specific combination of genetic mutations detected in our patient has not previously been described and can therefore not be clearly linked to a causative effect. We will analyse further family members to differentiate between de novo changes or possible causative variants of cardiomyopathy.

O 36 INITIAL EXPERIENCE WITH MELTDOSE®-TACROLIMUS IN HEART TRANSPLANT RECIPIENTS WITHIN THE FIRST 12 POSTOPERATIVE MONTHS

V. Paspalj, J. Riebandt, F. Wittmann, K. Uyanik-Ünal, A. Aliabadi-Zuckermann, G. Laufer, A. Zuckermann
Medizinische Universität Wien, Vienna, Austria
E-mail: valentina.paspalj@akhwien.at

Introduction: Once-daily dosing of Tacrolimus retard formulations has already been shown to improve patient adherence in liver and kidney transplantation. We recently presented our experience with the MeltDose®-Tacrolimus (Envarsus) for long-term heart transplant patients and now started an early conversion protocol. The aim of this study was to evaluate the development of the kidney function and possible adverse events.
Methods: Between September 2016 and July 2017, overall 16 patients within their first postoperative year were switched from Prograf to Envarsus (mean age 49.6 years; 37.5% female; 37.5% ICMP, 37.5% DCMP, 25% other). Most patients (81.3%) were induced with ATG (Thymoglobulin®), calcineurin inhibitor (CNI) therapy was started after a cumulative dose of 4.97 ± 1.03 mg/kg of ATG, using either the regular Tacrolimus formulation (Prograf) per os or as continuous intravenous therapy. All patients were under triple immunosuppressive therapy consisting of CNI, Mycophenolate Mofetil and corticosteroid. Due to promising results of late switch from Prograf to Envarsus we started an early conversion protocol within the first 3 months after transplantation.
Results: Switching to the retard formulation (Envarsus) took place after a mean of 76 days (median 35 days, ranging from 10–355 days) post heart transplantation. Mean dose of Prograf was 8.2 ± 6.1 mg, the mean tacrolimus level was 11.6 ± 4.4 ng/dl. Initial dose of Envarsus was 5.3 ± 3.2 mg and the first tacrolimus level after switching was 9.3 ± 2.7 ng/dl. Renal parameters remained stable (eGFR 62.9 ± 27.9 ml/min/1.73 m^2 vs. 66.6 ± 27.2 ml/min/1.73 m^2). Rejection occurred in one patient on postoperative day 212, 202 days after switching to Envarsus. No patient had to be switched back.
Conclusion: These preliminary results indicate that the Tacrolimus retard formulation is a safe and effective alternative to the regular formulation in heart transplant patients within the early postoperative phase.

O 37 SALVAGE ECMO AS BRIDGE TO HEART TRANSPLANT – SINGLE CENTER EXPERIENCE

F. Wittmann, J. Riebandt, V. Paspalj, T. Haberl, A. Aliabadi-Zuckermann, G. Laufer, A. Zuckermann
AKH Wien, Vienna, Austria
E-mail: franziska.wittmann@akhwien.at

Introduction: Heart transplantation is the gold standard treatment of end-stage heart failure. In critically ill patients (INTERMACS level 1 and 2), ECMO implantation is an accepted therapy option. Possible following therapy options include implantation of a VAD or primary heart transplantation. Aim of this study was to evaluate the outcome of our transplant patients that were bridged with ECMO.
Methods: Between 2002 and 2017 a total of 611 patients were transplanted at our institution. 109 patients were listed high urgently (HU)– multi-organ transplantations, patients under 16 and those bridged with a durable mechanical circulatory support (MCS) device were excluded. We identified 12 patients (11.3%) with ECMO device in place before heart transplantation.
Results: The overall mean age of the HU listed patients was 48 ± 16 years, 73.6% of the patients were male. The 30-day and in hospital mortality were low with 5.7% and 8.5%, respectively. The overall one-year survival was 95.6%. There was no significant difference for patients being bridged to transplant with ECMO compared to those INTERMACS level 1 or 2 patients without temporary MCS device. All except for one ECMO patients were in single organ failure at the time of listing (creatinine 1.04 ± 0.48 mg/dl; BUN 24.6 ± 13.1 mg/dl; eGFR median >90 ml/min/1.73 m^2; AST 152.0 ± 181.7 U/l; ALT 188.9 ± 202.7 U/l; GGT 140.8 ± 142.9 U/l; bilirubin 1.91 ± 2.24 mg/dl).
Conclusion: In a high volume center, critically ill patients with biventricular failure or severe ventricular arrhythmias can successfully be bridged to transplant using ECMO, with similar short- and long-term survival, compared to other HU patients. Adequate patient selection is crucial, secondary end-organ damage should be avoided.

O 38 CARDIOPROTECTIVE EFFECTS OF PARACRINE FACTORS IN STEM CELL THERAPY FOR MYOCARDIAL INFARCTION: DIFFERENCES IN THE SECRETOME AS A POSSIBLE EXPLANATION FOR DIFFERENTIAL RESULTS OF PREVIOUS CLINICAL TRIALS

B. Wernly
PMU Salzburg, Salzburg, Austria
E-mail: b.wernly@salk.at

Introduction: Stem cell therapy for acute myocardial infarction (AMI) seemed to be a promising novel therapy, however large clinical trials brought differential outcome. More recently, it has been shown that paracrine effects of the secretome of stem cells rather than cell therapy might play a fundamental role in angiogenesis, cytoprotection and cell migration. The present study sought to compare cell processing protocols of clinical trials and investigated (i) effects of differential cell culture conditions on chemokine secretion of bone marrow mononuclear cells (BMSCs) and also peripheral blood mononuclear cells (PBMCs) and (ii) secretome mediated functional effects on angiogenesis, cell survival and cell migration.
Methods: Secretome of PBMCs and BMSCs cultured according to ASTAMI vs. REPAIR-AMI conditions was compared regarding IL-8, VEGF, MCP-1 and TNF-alpha secretion. Moreover, secretome mediated effects were evaluated on endothelial cell (HUVEC) tube formation and migration. Cardioprotective signalling kinases in human cardiomyocytes determined by Western Immunoblotting.
Results: Cells processed according to the REPAIR-AMI protocol secreted significantly higher amounts of IL-8 (487.3 ± 1231.1 pg/ml vs. 9.1 ± 8.2 pg/ml; $p < 0.05$). REAPIR-AMI supernatants led to significantly pronounced tube formation and migration on HUVEC and enhanced the phosphorylation of Akt, ERK, and CREB in cultures of human cardiomyocytes.
Conclusion: Cell processing conditions had a major impact on the composition of the BMSC/PBMC secretome. The REPAIR-AMI secretome significantly enhanced proangiogenic chemokine secretion, angiogenesis, cell migration and cardioprotective signalling pathways. These results might explain differential outcomes between the ASTAMI and REPAIR-AMI trial. Of importance, optimizing cell processing protocols with special regards to paracrine factors, might open a new therapeutic concept for improved clinical outcome in patients after AMI.

O 39 OUTCOME AFTER COMBINED HEART AND KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

J. Dumfarth, T. Weinberger, M. Kofler, C. Bösmüller, A. Weißenbacher, D. Öfner, D. Höfer, G. Pölzl, M. Grimm, S. Schneeberger, S. Eschertzhuber, H. Antretter
Medical University of Innsbruck, Innsbruck, Austria
E-mail: Julia.Dumfarth@i-med.ac.at

End-stage heart failure is frequently accompanied by secondary organ failure, most frequently chronic kidney disease. In recent years, numbers of simultaneous heart and kidney transplantation (HKT) have increased significantly. Aim of this study was to review the outcome of patients undergoing HKT between 1998 to 2017.

A total of 20 patients (85% men, mean age 55.2 ± 8.9 years; mean donor age 35.2 ± 11.5 years) underwent HKT. Seven patients (35%) had undergone cardiac surgery prior to heart transplantation. Only one patient was bridged to transplantation on a mechanical circulatory assist (total artificial heart). Nine patients (45%) were on dialysis prior to transplantation. Time on waiting list was 6.3 months (range 1–24).

Mean cardiac allograft ischemic time was 174 ± 41 min, kidney allograft ischemic time was 534 ± 148 min. 18 patients (90%) underwent hemofiltration or hemodialysis postoperatively, of which 11 (55%) had delayed renal graft dysfunction - defined as the need for dialysis during the first 7 days after transplant. Three patients (15%) underwent rethoracotomy due to bleeding, one patient was put on extracorporeal membrane oxygenation (ECMO) for four days postoperatively.

Induction therapy was performed with thymoglobulin in all patients; later on, all patients received triple immunosuppression therapy (steroids, calcineurin-inhibitors and azathioprine or mycophenolate). One patient died 30 days after transplantation due to invasive candidiasis and subsequent multi-organ failure.

During a mean follow up period of 62.3 months (range 5–170 months) two patients required dialysis due to chronic renal allograft dysfunction. Cardiac allograft rejection requiring medical treatment occurred in two cases, one patient developed coronary allograft vasculopathy requiring percutaneous coronary intervention. Overall survival after 6 months, 1 and 3 years after HKT was 95 ± 4.9%, 89.4 ± 7.1% and 83.5 ± 8.8%.

In selected patients suffering from end stage heart and kidney failure, HKT can be performed safely with excellent outcome and stable long term graft function.

O 40 ARTERIAL HYPERTENSION AS RISK FACTOR FOR RENAL DISEASE IN LIVING KIDNEY DONORS

J. Kerschbaum, S. Bitter, M. Weitlaner, K. Kienzl-Wagner, H. Neuwirt, C. Bösmüller, G. Mayer, S. Schneeberger, M. Rudnicki
Medizinische Universität Innsbruck, Innsbruck, Austria
E-mail: julia.kerschbaum@i-med.ac.at

Background: Living kidney donation represents the optimal renal replacement therapy, but recent data suggest an increased long-term risk for the donor. Here, we evaluated the risk for adverse events in 305 donors, who underwent live donor nephrectomy between 1985 and 2014.
Methods: Different outcomes during follow-up were evaluated. All covariates showing univariate association with the outcome variable were entered into a multivariable cox regression model.
Results: The median follow-up time was 8.9 years (1.0–29.1). In multivariate analysis age and arterial hypertension at baseline were significantly associated with a higher risk of adverse renal outcomes, such as (1) eGFR <60 ml/min/1.73 m^2 or new onset of albuminuria/proteinuria during follow-up (age per year: HR 1.05; 95% CI: 1.03–1.08), hypertension: HR 2.07; 1.17–3.64), (2) eGFR <60 ml/min/1.73 m^2 (age: HR 1.05; 1.03–1.08, hypertension: HR 2.25; 1.22–3.98), (3) eGFR <45 ml/min/1.73 m^2 (age: HR 1.12; 1.05–1.20, hypertension: HR 5.06; 1.49–17.22), and (4) eGFR <60 ml/min/1.73 m^2 and loss of ≥40% from baseline (age: HR 1.08; 1.03–1.13, hypertension: HR 4.22; 1.72–10.36). Age was the only significant predictor for death/major cardiovascular event (HR 1.06; 1.00–1.12). Donors with arterial hypertension at baseline were significantly older (median age: 55 years, range 30–68 years vs. 45 (21–71), p < 0.001), had a higher BMI (26.6 (17.4–34.2) vs. 24.2 (17.4–38.3, p = 0.020), and were less frequently related to the recipient compared to donors without hypertension (48.8% vs. 71.4%, p = 0.008).
Conclusion: Arterial hypertension and age at time of donation are strong predictors for adverse renal outcomes in living kidney donors.

P 1 COMBINED HEART AND KIDNEY TRANSPLANTATION IN MELAS SYNDROME

M. Kofler, J. Dumfarth, G. Pölzl, D. Höfer, S. Eschertzhuber, M. Rudnicki, C. Bösmüller, D. Öfner, M. Grimm, S. Schneeberger, H. Antretter
Medical University of Innsbruck, Department of Visceral, Transplant and Thoracic Surgery, Innsbruck, Austria
E-mail: ma.kofler@tirol-kliniken.at

Mitochondrial respiratory chain diseases represent a complex disease involving multiple organs. Mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS) is a maternally inherited disorder. MELAS syndrome causes reduced life-expectancy due to brain and cardiac involvement. In rare cases the disease can be associated with kidney disease and can present as Fanconi syndrome or focal segmental glomerulosclerosis.
Case Report: We report a case of a 39-year old woman diagnosed with MELAS syndrome suffering from end-stage heart failure requiring heart transplantation. Initially the patient's kidney function was stable but deteriorated while being listed. Histologic analysis revealed diffuse interstitial fibrosis and tubular atrophy. Due to these findings the patient was listed for combined heart and kidney transplantation, which could successfully be performed after a waiting time of 9 months.

The patient underwent uneventful combined transplantation and could be weaned from the respirator on the first postoperative day. Within the first 4 postoperative days, the patient underwent hemofiltration which was no longer needed afterwards due to stable graft function. After induction therapy with Anti-Thymocyte Globulines, the patient was switched to Tacrolimus, Mycophenolate and Prednisolone. Kidney as well as heart function normalized during the first few postoperative weeks and the patient could be discharged under stable conditions four weeks after transplantation. During the first year after the transplantation endomyocardial biopsies as well as echocardiographies were performed. During 31 months follow up there was no evidence of rejection or graft vasculopathy and the patient is stable and in NYHA class I. Kidney function is stable with serum creatinine levels of 1.2 mg/dl and calculated creatinine clearance of 49 ml/min.
Summary: We present the successful postoperative course of a patient suffering from MELAS syndrome undergoing combined heart and kidney transplantation. While these patients can be challenging due to encephalopathy, organ transplantation can provide excellent survival and good quality of life.

P 2 HIGHER DOSE NOREPINEPHRINE DONOR SUPPORT IS NOT ASSOCIATED WITH OUTCOMES FOLLOWING HEART TRANSPLANTATION

P. Angleitner[1], A. Kaider[2], J. Gökler[1], R. Moayedifar[1], E. Osorio[1], A. Zuckermann[1], G. Laufer[1], A. Aliabadi-Zuckermann[1]
[1]Division of Cardiac Surgery; [2]Center for Medical Statistics, Informatics and Intelligent Systems (CeMSIIS)
E-mail: philipp.angleitner@meduniwien.ac.at

:
Background: Higher dose norepinephrine donor support is a frequent reason for donor heart decline although its associations with outcomes following heart transplantation are unclear.
Methods: We retrospectively analysed patients transplanted between 1992 and 2015 at the Heart Transplant Program Vienna. Recipients (n = 965) were stratified depending on respective donor norepinephrine doses administered before organ procurement (group 0: 0 μg/kg/min; group 1: 0.01–0.1 μg/kg/min; group 2: >0.1 μg/kg/min). Associations between groups and outcome variables were investigated using a multivariable Cox proportional hazards model and logistic regression analyses.
Results: Donor norepinephrine dose groups were not associated with overall mortality (group 1 vs. 0: Hazard Ratio (HR) 1.12, 95% Confidence Interval (CI): 0.87–1.43; group 2 vs. 0: HR 1.07, 95% CI: 0.82–1.39; p = 0.669). No significant group differences were found for rates of 30-day mortality (group 0: 10.5%; group 1: 8.3%; group 2: 7.4%; p = 0.35), 1-year mortality (15.8% vs. 16.3% vs. 14.9%, p = 0.897), primary graft dysfunction (17.4% vs. 16.2% vs. 16.4%, p = 0.898), prolonged ventilation (> 7 days) (18.9% vs. 24.5% vs. 24.2%, p = 0.133), and renal replacement therapy (20.0% vs. 22.4% vs. 24.9%, p = 0.324). Groups 1 and 2 showed higher rates of prolonged intensive care unit stay (> 14 days) (18.9% vs. 28.5% vs. 27.5%, p = 0.005).
Conclusions: Acceptance of selected donor hearts supported by higher doses of norepinephrine may be a safe option to increase the donor organ pool.

P 3 CONVERSION FROM ADVAGRAF OR PROGRAF TO ENVARSUS IN STABLE LUNG TRANSPLANT (LUTX) PATIENTS

A. Kulu, T. Stork, G. Muraközy, E. Hielle-Wittmann, C. Lambers, W. Klepetko, P. Jaksch
MUW, Thoraxchirugie, Vienna, Austria
E-mail: peter.jaksch@meduniwien.ac.at

Objectives: The aim of the present study was to evaluate the safety of conversion from Advagraf or Prograf (Astellas Pharma) to once-daily extended-release tacrolimus (Envarsus; Chiesi) in stable adult lung transplant recipients.
Material and Methods: The observational included 53 stable lung transplant recipients (31 m/22 w) with mean age of 52.9 ± 13.9 (range 21.2–73.6) years, 39 were on Prograf and 14 on Advagraf based maintenance medication. Time after LuTX were 3.6 ± 2.9 years, the underlying disease was COPD in 22, IPF in 11, Alpha 1 ATM in 7, CF in 12 and IPH in 1 case. Through blood FK levels were measured before switch (baseline) and on day 10 (±3), day 30 (±10), day 90 (±10) and day 180 (±10). Lung function, serum Creatinine, side effects were documented at each visit. Conversion was based on a 1:0.70 proportion.
Results: Creatinine values were 1.33 ± 0.41 mg/dl, Tacrolimus dose 4.5 ± 2.5 mg/day, FK level (C0) 6.7 ± 2.2 ng/ml and FEV1 2.89 ± 0.9 l before switch to Envarsus. Within the first 2 months after switch 10 patients had to be re-switched to their prior medication due to side effects.

Analyzed parameters 180 ± 10 days after switch to Envarsus (p-values: pre-switch vs. 6 months post switch): Creatinine 1.57 ± 0.95 mg/dl ($p = 0.16$), Envarsus – dose 3.0 ± 1.8 mg ($p = 0.001$), FK- level 5.5 ± 1.4 ng/dl ($p = 0.03$), FEV1 2.58 ± 0.8 l ($p = 0.15$).
Conclusion: Conversion from Advagraf/Prograf to Envarsus in stable lung transplant patients is safe and efficient; however, initially, dose adaptations and careful monitoring are required.

P 4 SPECIFIC ROLE OF CD40/CD40 L SIGNALING DURING ALLOGRAFT REJECTION

N. Granofszky, B. Mahr, N. Pilat, L. Unger, T. Wekerle
Medizinische Universität Wien, Vienna, Austria
E-mail: nicolas.granofszky@meduniwien.ac.at

Background: While interrupting CD40 costimulation is particularly powerful in inhibiting alloresponses, the precise function on distinct T cell subsets and the mechanisms how CD40 modulates alloimmunity remain to be fully delineated.
Methods: CD40KO mice were used for allograft rejection experiments and the role of effector/memory subsets as well as distinct activation, migration and proliferation markers (Ki-67, CXCR3, CCR6, CD69) within this model were followed over time. Furthermore *in vitro* MLR experiments were done and protein expression of CD40 and CD40L on T cells was analyzed by FACS.
Results: Interestingly, only a small subset of T-cells express CD40 upon activation and within those around 12–13% were single positive for CCR6 while no expression was observed in CD40 negative T cells. In an *in vitro* study early and transient CD40L expression on T cells was observed with maximum expression only in the first generations during T cell division, followed by a decline thereafter. Treg frequency in CD40 and CD40KO mice was significantly lower compared to WT mice, however, CD40L expressing Tregs demonstrated a different expression pattern of Helios, CTLA4, ICOS and CD62L compared to CD40L negative Tregs. Skin grafts from CD40KO to WT mice revealed no difference in graft survival; however CD40KO background in both donor and recipient demonstrated a slight graft prolongation which is associated with differences in T cell priming and memory generation as well as a decrease in CXCR3/CCR6 expression on PBMCs 10 days after transplantation.
Conclusion: Upon activation CD40 is low expressed on T-cells and this CD40 + population exhibit improved migration potential during inflammatory processes. CD40L is very quick and transient expressed on activated T-cell subsets, including FoxP3 Tregs. CD40KO skins grafted onto CD40KO recipients demonstrated better graft survival which is associated with a disorder in the memory development.

P 5 AN INTEGRATIVE APPROACH OF ASSESSING PERITUBULAR CAPILLARITIS EXTENT AND SCORE IN MICROVASCULAR INFLAMMATION IS SUPERIOR IN PREDICTING TRANSPLANT GLOMERULOPATHY AND GRAFT LOSS

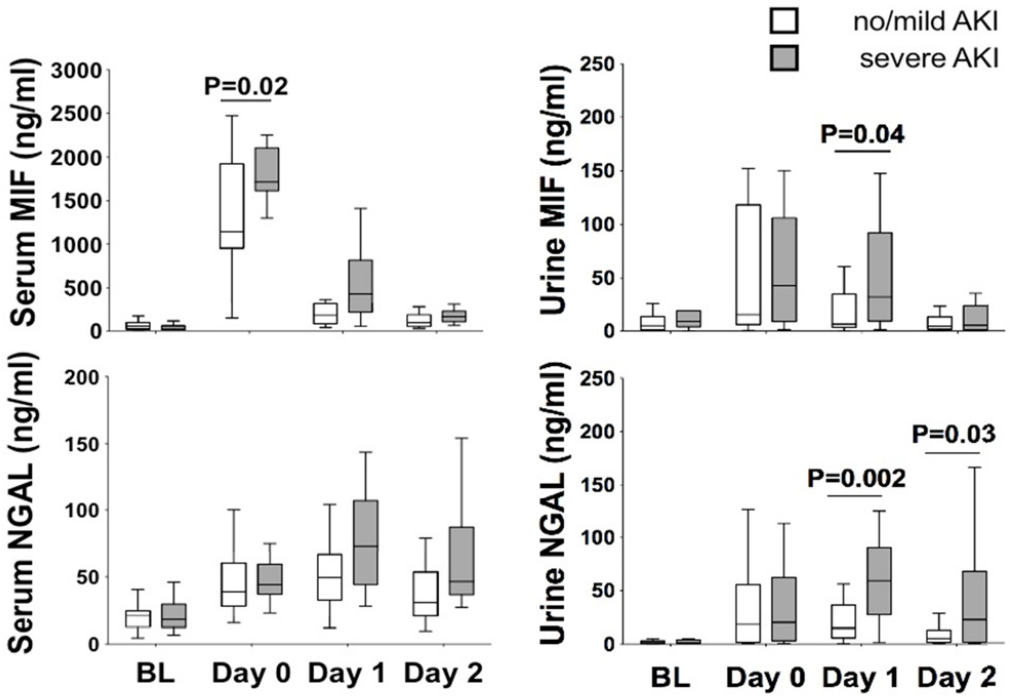
N. Kozakowski[1], H. Herkner[2], F. Eskandary[3], G. Bond[3], Z. Kikic[3]
[1]Kl. Institut für Pathologie, MUW, Vienna, Austria; [2]Universitätsklinik für Notfallmedizin, MUW, Vienna, Austria; [3]Innere Medizin III, Kl. Abt. für Nephrologie und Dialyse, MUW, Vienna, Austria
E-mail: nicolas.kozakowski@meduniwien.ac.at

Background: Banff Classification accepts following features as surrogates of HLA Antibody-Antigen interaction on renal endothelium: C4d staining and microvascular inflammation scores (MVI sum score:ptc+g ≥ 2), both strong predictors of transplant glomerulopathy (TG) and subsequent graft loss. However, increasing evidence questions the ability of the ptc score to solely mirror all relevant aspects of ptc morphology. Recently we observed a significant relationship of diffuse extent of ptc (inflammation of>50% the renal cortex) with graft loss and significantly higher DSA levels suggesting potential inclusion of diffuse ptc as an additional surrogate of antibody-antigen interaction.
Methods: We included 616 patients with adequate material for interpretation of MVI and C4d staining in first indication biopsies. Alternatively we assessed MVI with an integrated view of ptc morphology including both results of ptc score and extent: additionally to MVI scores, cases with a ptc score of 1 but diffuse extent of ptc ($ptc\ 1_{diffuse}$, $n = 26$) and no glomerulitis were added as surrogates of antigen-antibody interaction. Outcomes were prediction of any TG and death-censored graft loss.
Results: C4d+ and MVI scores ≥ 2 were observed in 11% and 19% of the specimens. TG was found in 13% of patients. The incorporation of $ptc\ 1_{diffuse}$ in addition to the MVI score ≥ 2 significantly increased the ROC curve for TG [AUC: 0.613 (95%CI 0.54–0.69), $p = 0.002$] compared to the Banff MVI score ≥ 2 [AUC: 0.571 (95%CI 0.49–0.64), $p = 0.046$] or C4d + [AUC: 0.540 (95%CI 0.47–0.61), $p = 0.26$]. In multivariate analysis $ptc\ 1_{diffuse}$ remained independently related to TG [OR 2.13 (CI: 1.22–3.72), $p = 0.008$]. $Ptc\ 1_{diffuse}$ and MVI score ≥ 2 subjects had worse graft survival (44%) compared to $ptc\ 1_{focal}$ or patients without MVI (70% and 68%; mean follow-up 9 years).
Conclusion: An integrated view of ptc morphology including diffuse ptc in assessing MVI is superior for TG and subsequent graft loss risk prediction.

P 6 MACROPHAGE MIGRATION INHIBITORY FACTOR VERSUS NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN-2 TO PREDICT ACUTE KIDNEY INJURY AFTER LIVER TRANSPLANTATION

J. Baron[1], J. Schiefer[1], G. Berlakovich[2], D. Baron[1], P. Faybik[1]
[1]Klinik für Anästhesie, Intensivmedizin und Schmerztherapie, Medizinische Universität Wien, Vienna, Austria; [2]Klinik für Chirurgie, Abteilung für Transplantation, Medizinische Universität Wien, , Vienna, Austria
E-mail: joanna.baron@meduniwien.ac.at

Introduction: Several biomarkers have been suggested as early predictors of acute kidney injury (AKI) after orthotopic liver transplantation (OLT). Systemic and urinary neutrophil gelatinase-associated lipocalin-2 (NGAL) appear to be promising predictors of AKI after OLT, but their clinical benefit remains to be proven [1,2]. Recently, systemic macrophage migration inhibitory factor (MIF) has been proposed as an early indicator for requirement of renal replacement therapy after OLT [3]. We hypothesized that either systemic or urinary MIF can predict the development of AKI after OLT with comparable power as systemic and urinary NGAL.
Methods: Concentrations of MIF and NGAL were measured in serum and urine samples collected from patients undergoing OLT. Acute kidney injury was classified according to the KDIGO criteria, with stages 2 and 3 summarized as severe AKI. Areas under the receiver operating curves (AUC) were calculated to assess predictive values of MIF and NGAL for the development of severe AKI.
Results: Forty-five patients (mean age 55 ± 8 years) were included. Nineteen patients (38%) developed severe AKI within 48 hours after OLT. After OLT, MIF concentrations in serum and urine were greater in patients with AKI than those without AKI. In contrast, only urine NGAL concentrations, but not serum NGAL concentrations were greater in patients with AKI than those without AKI. At the end of OLT, serum MIF was predictive of AKI (AUC 0.73; 95% confidence intervals, CI [0.55–0.90]; $p = 0.03$), while urinary MIF, serum NGAL, and urinary NGAL were not. On the first postoperative day, serum MIF (AUC 0.78; CI [0.62–0.93]; $p = 0.006$), urinary MIF (AUC 0.71; CI [0.53–0.88]; $p = 0.03$), and urinary NGAL (AUC 0.79; CI [0.64–0.93]; $p = 0.02$) were predictive for AKI, while serum NGAL was not.
Conclusion: In the setting of OLT, serum MIF predicted severe AKI earlier than serum NGAL and urinary NGAL.



ROC curve analysis

	Serum MIF	Serum NGAL	Urine MIF	Urine NGAL
Day 0				
AUC	0.73	0.59	0.58	0.5
95% CI	0.55-0.90	0.41-0.77	0.40-0.75	0.33-0.68
P Value	0.03	0.34	0.4	0.98
Day 1				
AUC	0.78	0.68	0.71	0.79
95% CI	0.62-0.93	0.50-0.85	0.53-0.88	0.64-0.93
P Value	0.006	0.06	0.028	0.002
Day 2				
AUC	0.71	0.75	0.58	0.65
95% CI	0.54-0.89	0.60-0.90	0.37-0.78	0.47-0.84
P Value	0.03	0.009	0.43	0.08

P 7

MINIMIZATION OF IMMUNOSUPPRESSION IN RENAL TRANSPLANTATION - FIFTEEN-YEAR-SINGLE-CENTER-EXPERIENCE IN 1,000 PATIENTS

K. Hohenstein[1], *H. Herkner*[2], *P. Hlavac*[1], *S. Scherr*[1], *B. Watschinger*[1]
[1]*Department of Nephrology and Dialysis, MUW, Vienna, Austria;* [2]*Department of Emergency Medicine, MUW, Vienna, Austria*
E-mail: katharina.hohenstein@meduniwien.ac.at

Background: The fear of patient and graft threatening side effects of immunosuppressants has led to long-term minimization strategies in renal allograft recipients. It remains unclear however, if very low intensities of immunosuppression are truly beneficial. We therefore evaluated the long-term outcomes of various degrees of immunosuppression in a large cohort of renal transplant recipients in a retrospective single center study.
Methods: 1,000 patients who received a kidney transplant (January 2000 to December 2012) fulfilled the study's inclusion criteria (age > 18 years, stable graft function - serum creatinine <2.5 mg/dl @ 1 year, continuous follow up at our center). Drug dosages and CNI levels were recorded at every visit. More than 100,000 drug level measurements were available for calculating CNI exposure. An algorithm was established to grade the cumulative intensity (CI) of immunosuppression (in mono, dual, triple therapy) at each time point. Exposure time and intensity of immunosuppression was calculated from the respective time and dosage recordings at each visit.
Results: 50.7% of patients had a very low or low, 16.7% a moderate and 22.8% a high or very high CI score. After adjustment for age, gender, baseline immunological risk, and other relevant donor and recipient characteristics, graft survival was significantly lower in the very high CI group when compared to the very low CI group (1,452.7 ± 867.6 vs. 2,605.9 ± 1,511.7 days, p = 0.006).
Conclusion: In renal transplant patients with stable graft function at one year, minimization of cumulative immunosuppression is associated with a better long term graft survival, than more intense treatment regimens.

P 8 SAPOVIRUS - A RARE CAUSE FOR CHRONIC DIARRHEA IN A PATIENT AFTER RENAL TRANSPLANTATION

S. Duchek[1], S. Grillenberger[2], R. Klauser-Braun[1], J. Kletzmayr[1]
[1]3. Medizinische Abteilung, SMZ-Ost Donauspital; [2]Institut für Pathologie und Bakteriologie, SMZ-Ost Donauspital Vienna, Austria
E-mail: stefanie.duchek@wienkav.at

Introduction: Gastroenterological complaints, especially diarrhea, occur frequently in patients after renal transplantation. Whether caused by immunosuppressors or infectious agents, e.g. invasive CMV, exsiccosis or reduced immunosuppression threaten transplant function.
Case Report: On March 20 2017 a 70-year-old patient, who underwent renal transplantation in 2012, was seen for a routine check in our outpatient clinic. He was suffering from diarrhea since 4 weeks, leading to a weight loss of 6 kilograms but presented without fevers or other symptoms. His grandchild, who is in Kindergarten, has had similar symptoms. Oral Rifaximin had ameliorated his complaints.

Lab results included stable Creatinine, negative CRP, CMV-PCR and fecal culture, hence mycophenolate mofetil was paused while tacrolimus and low-dose aprednislon were continued. After initial improvement we introduced low-dose mycophenolic acid.

In the following 8 weeks the patient continued having intermittent diarrhea, he lost another 10 kilograms including massive loss of muscle mass. Further searching for a cause included a gastro-/colonoscopy, thoracic and abdominal CT- and PET-scan without any pathological findings.

On May 31 his condition had worsened massively and while all lab results were still normal, faecal PCR testing (BioFire FilmArray ™) detected Sapovirus as culprit. Discontinuing mycophenolic acid and minimizing tacrolimus-levels resulted in normal stools in less than a week, followed by quick improvement of his condition and steady weight gain, although Sapovirus is still present in his stool.
Discussion: Within the family of Caliciviridae the most prevalent are Noro- and Sapovirus causing diarrhea in humans, Sapovirus mostly in little children but occasionally reported as culprit for severe chronic enteritis in transplant patients. The only therapeutic option is reducing immunosuppression.
Conclusion: Sapovirus is a rare but within immunosuppressed patients possibly serious infection and is not detected by routine diagnostics. When facing chronic enteritis in (renal) transplant patients PCR-analysis of the stool is strongly recommended.

P 9 SWIMMING AGAINST THE CURRENT: LIMITED NUMBERS OF ORGAN DONORS DESPITE A LONG-TIME ACTION PROGRAMME. CURRENT FIGURES AND FUTURE PERSPECTIVES

T. Unger, M. Willinger, U. Fischer
GOG
E-mail: Theresia.Unger@goeg.at

The number of organ donors in Austria is traditionally high. In an international ranking comparing the numbers of transplanted organs per million people, Austria was number four after Spain, Croatia and the US in 2015, and held the top position in 2014. However, despite a long-time action programme since 2001 the intended increase to 30 (utilized) donors per million people has not been accomplished. This target has been achieved by most regions at some point, but with the exception of Carinthia not on a sustainable basis. The numbers of donor reports and utilized donors vary widely in regional terms. Nation-wide the number of donor reports is nearly twice the number of utilized donors. The documentation of the 25 local transplant coordinators (LTXB) shows the causes for this discrepancy with objections against organ procurement expressed by relatives and a negative assessment of donor organs by the transplantation centres being the most prominent ones. But there are also demographic reasons why keeping the numbers of organ donors high is like swimming against the current: since the beginning of the action programme the number of hospital deaths with diagnoses relevant for organ donation has been constantly decreasing in combination with a growing number of deceased patients being 75 years and older, an age group that is rarely considered for organ donation.

To draw conclusions for a further development of the action programme critical success factors of Carinthia as the national model of success and Spain as its international counterpart are highlighted:
(1) improving communication skills and information of the public,
(2) hospital-wide co-ordination of intensive care beds and staff training,
(3) taking into account the admission of patients with impending death to the ICU to facilitate organ donation,
(4) broader acceptance of expanded criteria and nonstandard risk donors and
(5) promotion of DCD.