SHORT PRESENTATIONS ON POSTERS

KIDNEY TRANSPLANTATION I

PV01 EUROPEAN KIDNEY TRANSPLANT TRIAL ATHENA – PATIENT AND ALLOGRAFT OUTCOME BY COUNTRY

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Purpose: The ATHENA trial* was conducted to compare efficacy and safety of everolimus [EVR] combined with tacrolimus [TAC] or cyclosporine A [CyA] vs. mycophenolic acid [MPA] plus TAC in *de novo* kidney transplant [KTx] recipients.
Methods: A 12-months [M] open-label, prospective randomized, controlled trial (RCT) enrolled $N = 612$ patients [pts] from 15 German [GER] and 12 French [FRA] sites randomized in a 1:1:1 ratio to either EVR (C0: 3–8 ng/mL M1-12) with TAC (C0: 4–8 ng/mL M1-3; 3–5 ng/mL M3-12), or EVR (C0: 3–8 ng/mL M1-12) with CyA (C0: 75–125 ng/mL M1-3; 50–100 ng/mL M3-12) or to Control treated with MPA and TAC (C0: 4–8 ng/mL M1-3; 3–5 ng/mL M3-12). This abstract reports M12 efficacy and safety data from $N = 208$, $N = 199$, and $N = 205$ pts treated with EVR+TAC, EVR+CyA, and MPA+TAC analyzed by country, respectively.
Results: Outcome by country varied from ITT study results (presented at DTG2017**): treated BPAR excluding BANFF IA occurred in 10.3/6.5%; 16.7/7.3%; and 5.3/13.2% in the GER/FRA cohorts with EVR+TAC, EVR+CyA, and MPA+TAC, respectively. CMV infections represented a key secondary endpoint and was observed in 6.2% of EVR+TAC, 2.5% of EVR+CyA vs. 20.6% of MPA+TAC treated pts, all of which were significantly less frequent with EVR treatment vs. TAC Control (ITT; $p < 0.01$). CMV infections occurred in 8.1/1.6%; 2.8/1.8%; and 22.5/15.1% in the GER/FRA cohorts with EVR+TAC, EVR+CyA, and MPA+TAC, respectively.
Conclusion: ATHENA as to date largest randomized European KTx study confirmed overall good efficacy outcomes across all treatment groups. Of note, that cohort analyses by country reflect variations in KTx populations observed in two neighbor countries. [Ref:*NCT01843348; **Thaiss et al. DTG2017, IDPV18; Sommerer et al. DTG2017,IDPV17; Suwelack et al. DTG2017,IDV128]

PV02 IMPACT OF DECEASED DONOR AGE ON THE OUTCOME OF KIDNEY ALLOGRAFT FUNCTION – AN ANALYSIS FROM THE ATHENA TRIAL

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Background: The ATHENA trial [NCT01843348] was conducted to compare efficacy, safety and outcomes on renal function [eGFR] of everolimus [EVR] combined with reduced exposure tacrolimus [TAC] or cyclosporine A [CyA] vs. standard treatment with mycophenolic acid [MPA]+TAC in *de novo* kidney transplant [KTx] recipients. Study results suggest a significant impact of deceased donor [DD] age on recovery, evolution and outcome of renal allograft function after 12 months [M] measured as eGFR after 12M.
Methods: A 12 months open-label RCT conducted in 15 German and 12 French study sites randomized $N = 612$ KTx patients [pts] in a 1:1:1 ratio to either EVR (3–8 ng/mL) + TAC (4–8 ng/mL M1-3; 3–5 ng/mL M3-12), or EVR (3–8 ng/mL) + CyA(75–125 ng/mL M1-3; 50–100 ng/mL M3-12) or to Control MPA+TAC (4–8 ng/mL M1-3; 3–5 ng/mL M3-12); all with steroids. This abstract assesses the impact of DD age on allograft function.
Results: Early recovery and allograft function at M12 was comparable in all 3 treatment groups with mean changes in eGFR (Nankivell) from M1 to M12 of +3.1 [CI: 0.4; 5.7], +4.3 [CI: 1.3; 7.3], and +6.5 [CI: 3.9; 9.2] mL/min in the EVR+TAC, EVR+CyA, and MPA+TAC group, respectively (p = n.s.). Analysis of DD age categories [<35; 35–49; 50–64; ≥65 years] showed that DD age had significant impact on change in allograft function to M12 ($p < 0.01$), regardless of treatment. Patients who received an organ from a DD ≥65 years showed significantly worse eGFR compared to other DD age categories ($p < 0.01$).
Conclusion: Data from ATHENA suggest that deceased donor age has significant impact on 12M eGFR outcomes, here presented for the first time from a large European RCT. Results appear especially relevant in light of the growing impact of organ shortage and increased numbers of elderly organ donors.

PV03 EVEROLIMUS WITH REDUCED CALCINEURIN INHIBITOR EXPOSURE IN *DE NOVO* KIDNEY TRANSPLANT RECIPIENTS: INFECTION AND WOUND HEALING OUTCOMES FROM THE TRANSFORM STUDY

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Background: Post-transplant (Tx) infections affect graft and patient survival. The protective effect of early introduction of everolimus (EVR) against viral infections has repeatedly been shown in kidney transplant recipients (KTxRs). However, including mTOR inhibitors (mTORi) into immunosuppressive regimen immediately after Tx was questioned because of their anti-proliferative properties and potential effects on the wound healing process. Here we report 12 months (M) results on the incidence of infections and wound healing in KTxRs receiving EVR + reduced calcineurin inhibitor (rCNI) vs. mycophenolic acid (MPA) + Standard CNI (sCNI) regimen from the TRANSFORM study.
Methods: TRANSFORM (NCT01950819) is a 24M, multicenter, open-label, 2-arm study in which de novo KTxRs were randomized (1:1) within 24 h post-Tx to receive either EVR+rCNI ($N = 1022$) or MPA+sCNI ($N = 1015$), with induction and steroids. Here we show outcomes on infections and on wound healing events (WHE).
Results: The overall infection rate was lower with EVR+rCNI than MPA+sCNI regimen (52.0% vs. 59.8%). The overall incidence of CMV infections was significantly lower with EVR+rCNI vs. MPA+sCNI regimen (3.6% vs. 13.3%, $p < 0.001$) The overall rates of BKV infection reported as adverse event were also significantly lower in EVR+rCNI vs. MPA+sCNI arm (4.3% vs. 8.0%, $p < 0.001$). The overall incidence of WHE was comparable between the groups (EVR+rCNI vs. MPA+sCNI: 39.0% vs. 33.7%).
Conclusions: M12 results from TRANSFORM, the largest KTx study to date, confirmed the benefit of early EVR introduction in preventing viral infection in de novo KTxRs and confirmed its safe profile with comparable risk of WHE between the EVR+rCNI and MPA+sCNI groups.

PV04 EVEROLIMUS WITH REDUCED CALCINEURIN INHIBITOR EXPOSURE IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS: EFFICACY, SAFETY AND RENAL FUNCTION OUTCOME FROM THE TRANSFORM STUDY

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Background: TRANSFORM (NCT01950819) is the largest study conducted in *de novo* KTxRs to evaluate the benefit of Everolimus (EVR) with reduced-dose CNI (rCNI) compared to mycophenolate (MPA) with standard CNI (sCNI) using a composite endpoint of antirejection efficacy and renal function. Here we present the data on efficacy, safety and renal function.
Method: TRANSFORM is a 24 month (M), multicenter, open-label, non-inferiority study in which KTxRs were randomized to receive EVR+rCNI ($n = 1022$) or MPA+sCNI ($n = 1015$) with induction and steroids. The primary objective was M12 incidence of binary composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) <50 mL/min/1.73 m2. Other assessments included incidence of donor-specific antibodies (DSA), adverse events (AEs), and infection.
Results: Overall, 76.9% KTxRs completed the study medication up to M12. Mean EVR trough level was within target range (3–8 ng/mL) throughout the study. At M12, only 57.9% and 62.1% of KTxRs were within the TAC target range in the EVR+rCNI and MPA+sCNI arms, respectively. Non-inferiority margin of 10% for the primary endpoint was achieved in EVR+rCNI vs. MPA+sCNI (48.2% vs. 45.1%, $p = 0.001$). Mean eGFR (53 vs. 54.4 mL/min/1.73 m^2), incidence of the composite endpoint of tBPAR/graft loss/death, and incidence of de novo DSA (EVR+rCNI: 10.2%; MPA+sCNI: 13.6%) were comparable between arms. Overall AEs were comparable between arms; incidence of AEs leading to study drug discontinuation was higher with EVR+rCNI vs. MPA+sCNI, but AEs requiring dose adjustment were higher in MPA+sCNI arm.

Conclusion: In comparison to MPA+sCNI-based regimen, EVR+rCNI-based regimen provides good and comparable efficacy, safety, and renal function in KTxRs. M24 follow-up data are awaited.

PV05 CORRELATION OF TACROLIMUS METABOLISM RATE AND CALCINEURIN INHIBITOR NEPHROTOXICITY

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Introduction: The calcineurin (CNI) inhibitor tacrolimus (Tac) is an effective immunosuppressive drug after renal transplantation (RTx) but has a narrow therapeutic window. In previous studies, the Tac metabolism rate was defined as the Tac blood trough concentration (C) divided by the daily dose (D). A fast Tac metabolism rate (<1.05 ng/mL/mg) was associated with renal dysfunction. We herein hypothesize that CNI nephrotoxicity correlates to the Tac metabolism rate.
Methods: We analyzed 55 kidney biopsies containing acute CNI nephrotoxicity and correlated its severity (<25% or ≥25% CNI toxicity) with the corresponding Tac metabolism rate (C/D ratio) at the date of RTx biopsy. Only patients receiving immediate release Tac twice daily had been included. In addition, C0, C2 and C4 Tac levels of fast and slow Tac metabolizers were analyzed.
Results: 35 RTx recipients had <25% CNI nephrotoxicity, 20 patients ≥25%. The Tac metabolism rate correlated negatively with the severity of CNI nephrotoxicity ($p = 0.0001$). C2 Tac blood concentrations were significantly higher in the group of fast Tac metabolizers compared with slow metabolizers (18.75 (6.7–42.6) vs. 9.20 (4.2–18.7) ng/mL; $p = 0.004$). C0 and C4 Tac levels did not show differences between the groups.
Conclusions: Fast Tac metabolism was associated with higher Tac C2 level and negatively correlated to the severity of CNI nephrotoxicity. Calculation of the Tac C/D ratio early after RTx is a simple clinical tool for risk stratification to prevent renal dysfunction.

PV06 EARLY CONVERSION TO A CNI-FREE IMMUNOSUPPRESSION WITH SRL AFTER RENAL TX – LONGTERM DATA OF A MULTICENTER TRIAL AND IMPLICATIONS FOR THE PRODUCTION OF DNDSA

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Introduction: Early conversion to a CNI-free immunosuppression with SRL, MMF and steroids was shown to be safe 1- and 3-year post Tx in the SMART study. Recently, there have been reports on increased occurrence of (*dn*DSA) under mTORis.
Methods: We recruited patients from the SMART study to primarily investigate the development of *dn*DSA in a controlled setting. Secondary outcome parameter were kidney function, overall and graft survival and development of malignancies.
Results: We were able to recruit 53% of the core study population ($n = 74$), 39 SRL and 35 CsA from 6 centers with an average exposition time of 3.7 years for SRL and 7.0 years for CsA. Blood samples for DSA analysis were collected with a mean of 8.7 years after Tx. No significant difference between the therapeutic arms could be detected with respect *dn*DSA (6/39, 15.4% SRL vs. 10/35, 28.6% CsA, $p = 0.089$). GFR was significantly improved under SRL with 64 mL vs. 53 mL/min/1.73 m2 ($p = 0.044$). There was a trend towards a reduced graft failure rate under SRL (11.3% SRL vs. 24.6% CsA, $p = 0.056$).
Conclusions: An early conversion to SRL did not result in an increased incidence of *dn*DSA nor increased risk for the graft or recipient. Significant benefits remained under SRL regarding graft function and malignancy.

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LIVER TRANSPLANTATION

PV08 ROLE OF PERFUSION TIME AND PERFUSATE IN CONTROLLED OXYGENATED REWARMING OF LIVER GRAFTS PRIOR TO TRANSPLANTATION

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Introduction: Controlled oxygenated rewarming (COR) of cold stored livers by machine perfusion (MP) has shown promising results in experimental and clinical settings. In clinical routine it is often difficult to coordinate the time of implantation with the end of the preceding perfusion protocol. Therefore the present study investigated the influence of extending *ex vivo* graft perfusion beyond the established 90 min.
Methods: Porcine livers were subjected to 18 h cold storage and put on a MP device (LiverAssist®) with portal (3 mmHg, continuous flow) and arterial (30 mmHg, pulsatile flow) perfusion with gradual rewarming up to 20°C during the first 60 min using either Belzer MPS or Custodiol-N solution. Perfusion was continued at 20°C for additional 30 or 120 min. Organ function was evaluated in an established reperfusion model using diluted autologous blood.
Results: Endischemic reconditioning by COR resulted in a more than 2fold improvement of liver integrity (Bile, AST) upon reperfusion when compared with untreated livers. Extension of *ex vivo* MP at 20°C from 90 to 180 min did not change perfusate levels of AST or lactate. Upon reperfusion, no differences were observed between livers, previously reconditioned for 90 or 180 min with respect to transaminase release or bile production. The use of the colloid containing Belzer MPS instead of colloid free Custodiol-N as perfusate surprisingly resulted in slightly elevated weight gain during MP, but did not significantly change the results observed upon reperfusion.
Conclusion: It could be shown that *ex vivo* perfusion at 20°C can safely be perpetuated after gradual rewarming, at least up to 3 h. Thus, the surgical preparation of the recipient can be performed in temporal liberty while the machine is running in the background.

PV09 ONE-YEAR FOLLOW-UP AFTER LIVER TRANSPLANTATION IN CHILDREN WITH CYSTIC FIBROSIS

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Background: Liver disease and resulting biliary cirrhosis are important complications in patients with cystic fibrosis accounting for 2.7% of mortality.
Patients: We report on 7 children with cystic fibrosis (median age 13.5 years, range 8–18, 3 female, 4 male) who underwent liver transplantation (LTx) (6 whole organs, 1 living donation) at University Hospital, Essen from 2006 to 2017. Observation period was 12 months.
Results: Indications for LTX were biliary cirrhosis with portal hypertension 7, reduced liver function in 5 and dystrophy in 5 patients. Patient and graft survival after 12 months was 100%. Three operative revisions were required because of hematoma and leaking bile duct. Failure to thrive improved in all patients after LTX. Postoperative pulmonary infection occurred in 2 patients. Preoperative colonisation with pseudomonas aeruginosa aspergillus fumigatus and stenotrophomonas maltophilia was present in both patients. Pre-transplant impairment of lung function (FEV1 as % of predicted value) was normal (>80%) in 2 patients, moderately severe (40%–80%) in 4 and severe (below 40%) in 1 patient, and were preserved or improved within 12 months after transplantation in all patients. Mean maximum postoperative ascites production was 2.45 l/day and drainage was needed for a mean of 22 days (range 5–25 days). Insulin dependent diabetes, and antihypertensive drug therapy were documented in 2 and 3 patients, respectively. Elevated HbA1c-levels improved after switching immunosuppressive therapy from Tacrolimus to Cyclosporin A in two patients.
Conclusion: Children with cystic fibrosis requiring liver transplantation had a good overall and a good graft one-year survival. Pulmonary function was preserved or even improved and patients showed better thriving.

PV10 POSTOPERATIVE INFECTIONS FOLLOWING INTESTINAL TRANSPLANTATION

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Introduction: Due to high immunosuppression, recurring allograft rejections, and altered mucosal permeability, bacterial translocation and invasive fungal infections are significant challenges after intestinal transplantation. Additionally, the small bowel is the primary target organ of Rota-, Noro- and Adenovirus, so that the timely recognition of viral infections and differentiation from cellular rejection remain difficult.
Methods: Thirty-one patients (median age 39.5 ± 13.4 years) received an intestinal graft ($n = 18$) or a multivisceral transplantation ($n = 13$). We observed the 1-year postoperative course concerning bacterial, viral, and fungal infections, considering time of onset, treatment, immunosuppression, and survival.
Results: Most infections developed within 3 months posttransplant. Bacterial infections (39% of patients) appeared with a peak at 4 weeks. 46% were infections of the urinary tract, 32% blood stream, 11% wounds, 7% respiratory tract, 5% cholangitis. 60% of patients developed viral infections (peak 3 months posttransplant). They were often related to antirejection therapy and included CMV-infections (64%), Rota- (17%), Adeno- (12%) and Norovirus infections (7%). 4 patients developed invasive Aspergillosis within the first year, requiring triple antifungal therapy, and surgical debridement. Most patients cleared their infections under efficient treatment, 2 died of infection-related multiorgan failure following bacterial pneumonia.
Conclusion: The reduction of initial immunosuppression and the introduction of antibacterial, antifungal, and antiviral prophylaxis helped to reduce infection rates after intestinal and multivisceral transplantation.

PV11 THE INFLUENCE OF MICROVASCULAR INVASION ON SURVIVAL AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA – A 10-YEAR SINGLE CENTER EXPERIENCE

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Background: Liver transplantation (LTx) is the gold standard for non-metastatic hepatocellular carcinoma (HCC) without macrovascular invasion in cirrhosis. Although several studies show a negative impact of microvascular invasion on survival it is to date no contraindication for LTx. Aim of this retrospective single center study was to evaluate the significance of microvascular invasion (V1) on overall- (OS) and disease free survival (DFS) after LTx.
Methods: From 2007 to 2017 112 Patients with HCC in cirrhosis underwent LTx at our transplant center and were included into the study. Patient data was electronically collected and analysed regarding histopathologic staging, tumor reccurence and survival. Overall survival and diseases free survival rates were determined by Kaplan-Meier Analysis, significance was determined by log-rank testing.
Results: 1-, 3- and 5-year OS after LTx for patients with HCC was 86.3, 73.9 and 67.9% respectively. 1-, 3- and 5 year DFS was 84.5, 71.1 and 59.6%. 14 of 112 Patients presented with microvascular invasion. OS was significantly worse in patients with V1 status ($p = 0.032$) with 1-, 3- and 5 year OS of 86.4 vs. 76.9, 74.6 vs. 54.7 and 70.5 vs. 13.7% for patients without V1 status compared to patients with microvascular invasion. DFS was highly significantly reduced in case of V1 status ($p = 0.002$) with 1-, 3- and 5 year DFS of 85.4, 73.8 and 67.0% for patients without and 70.1, 42.1 and 10.5% with microvascular invasion.
Conclusion: Our results show a significantly worse prognosis for patients with microvascular invasion after LTx for HCC with especially bad results for 5-year OS and 5-year DFS. Obtaining a histological sample prior to listing for transplantation seems necessary for evaluation of vascular invasion status.

THORACIC ORGAN TRANSPLANTATION

PV13 INFLUENCE OF ACUTE CELLULAR REJECTION AFTER HEART TRANSPLANTATION ON 3D-DEFORMATION PATTERNS OF THE LEFT VENTRICLE

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Background: Two-dimensional deformation parameters have been reported to be significantly decreased in acute cellular rejection (ACR). Our objective was to evaluate 3-dimensional speckle tracking echocardiography (3D STE) in pts with different grades of biopsy-proven rejection episodes.
Methods: Sixty heart transplant recipients with suitable 3D full volumes were prospectively examined by 3D STE shortly after endomyocardial biopsy (EMB) blinded to the results. Three groups were analysed: Group 1 = 20 pts. with ACR-grade 0R (no rejection, G0R), group 2 = 20 pts. with grade 1R (mild rejection, G1R) and group 3 = 20 pts with grade 2R (moderate rejection, G2R). No EMB was classified as grade 3 (severe rejection).
Results: Comparing group G0R with G2 significant differencies were increase of end systolic volume index (ESVI): G0R 17.5 mL/m^2 vs. G2R 21.5, $p = 0.04$), decrease of LV-EF: G0R 64% vs. G2R 57%, $p = 0.002$, decrease of GLS: G0R -22% vs. G2R -15.7%, $p < 0.001$, reduction of GCS: G0R -32.7% vs. G2R -27.9%, $p = 0.005$ and decrease of radial strain: G0R 42.4% vs. G2R 33.85%, $p < 0.001$. The twist was nearly significantly reduced (G0R 11.25° vs. G2R 8°, $p = 0.052$ and torsion with G0R 1.5°/cm LV vs. G2R 1.1°/cm, $p = 0.03$.
Conclusions: To our knowledge, this are the first insights in 3D STE in ACR after heart transplantation showing significant decrease of deformation patterns in all three dimensions of the LV. Further analyses have to evaluate cut-off values for relevant ACR and advantages over 2D STE.

PV14 EARLY POST-TRANSPLANT SURVIVAL IN PATIENTS RECEIVING HEARTMATE 3 LEFT VENTRICULAR ASSIST DEVICE

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Objectives: The HeartMate 3 (HM 3) has been commercially available since the end of 2015. As the clinical outcome of HM 3 continue to be evaluated, data on post-transplant survival are not available.
Methods: We evaluated early post-transplant survival in patients supported by the HM 3.
Results: From January 2017 to April 2018 2018 in our center 93 adult heart transplants (HTx) were performed. 10 patients were successfully bridged to HTx with the HM 3. All patients were in "high urgent" status at the time of transplant (right heart failure: $n = 3$; cardiac arrhytmias: $n = 1$; gastrointestinal bleeding: $n = 3$; device infection: $n = 3$; driveline infection: $n = 1$). The median age was 56 (46–62) years, the mean body mass index was 25.59. 80% patients had dilated cardiomyopathy, the median bridge-to-transplant waiting time was 6 (2–19.5) months. The overall 30-day survival was 90%.
Conclusion: To the best of our knowledge, this is the first study evaluating post-transplant survival of patients bridged with HM 3. The short-term post-HTx survival was 90%. An optimized selection algorithm using score systems and early decision making may improve post-transplant results. Prospective studies are needed in this matter.

PV15 SUPERIOR RENAL FUNCTION AT MONTH 12 IN THE EVR-BASED QUADRUPLE ARM EARLY AFTER LUNG TRANSPLANTATION – 4EVERLUNG STUDY, A PROSPECTIVE RANDOMIZED MULTICENTER TRIAL IN GERMANY

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The 4Everlung trial evaluates the benefit of an early everolimus-based quadruple low immunosuppressive (IS) regimen on renal function (RF), safety and efficacy in lung transplant patients.

4EVERLUNG is a prospective, randomized, open-label, 12 month multicenter trial conducted in 8 German sites with 180 screened and 130 randomized patients (pts) 1:1 (3–18 months post LTx). The full analysis set (ITT) consists of 67 EVR-based quadruple low CNI (EVR) pts and 63 standard triple IS (Std) regimen pts.

In the EVR-based regimen pts received: EVR (C0-h 4 ± 1 ng/mL) with reduced calcineurin inhibitor CNI (tacrolimus C0-h 3–5 ng/mL or cyclosporine C0-h 50 ± 25 ng/mL) and EC-MPA max. 1440 mg/day or MMF max. 2 g/day + prednisone (≤0.15 mg/kg). In the Std regimen pts received: standard CNI (tacrolimus C0-h > 5 ng/mL or CsA C0-h > 100 ng/mL) with mycophenolate (center-specific) + prednisone (≤0.2 mg/kg). Stratification of pts at randomization was done according to baseline cGFR values: ≥40–60 mL/min, >61–75 mL/min or >76–100 mL/min.

Primary endpoint of RF was met with high significance superiority: cGFR [CKD EPI] at M12 was +9.9 mL/min with 64.5 mL/min for the EVR group vs. 54.6 mL/min for the Std group (LS-mean, ANCOVA, $p < 0.001$). Key parameters for effctive immunosuppression (BPAR, graft Loss or death) were equal between both groups: 10 BPARs in each treatment group (p = n.s) with the majority of biopsies graded as A0 for both treatment groups and 1 graft loss per treatment group (all p = n.s.). Safety profiles were similar between both groups.

4EVERLUNG study proves a safe and efficacious IS profile for the EVR-based low CNI regimen, early after LTx with significant better renal function maintained 12 months compared to the standard IS regimen.

PV16 IMPACT OF HUMAN LEUCOCYTE ANTIGEN (HLA) MISMATCHING ON THE OUTCOMES OF HEART TRANSPLANTATION: IS THERE A NEED FOR MODIFICATION OF IMMUNOSUPPRESSION?

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Objective: Studies on HLA matching after heart transplantation revealed inconsistent results. However, it is still discussed to include HLA matching into allocation policies for cardiac transplantation. The aim of this retrospective analysis was to assess differences in outcome after htx according to the degree of HLA–matching.
Methods: Between 2011 and 05/2018 102 patients underwent htx in our department. HLA mismatches (MM) on the major antigen loci HLA-A,-B, and –DR were calculated, causing 0–6 mismatches. Patients were classified with regard to the number of MM: Group 1: 0–3 MM, and group 2: 4–6 MM.
Results: Htx was performed in 30 patients with 0–3 MM and in 72 patients with at least 4 MM. Thirty-day-mortality was 13.3% in patients of gr. 1, and 11.1% in gr. 2. Primary graft dysfunction could be observed in 20% of group 1-patients and 23.6% of patients with >3 MM. We did not find significant differences between the groups regarding incidence of rejection, renal failure, or severe infection. Duration of mechanical ventilation, stay on intensive care unit and in hospital were also comparable. 6 months after htx we found a trend towards a lower level of tacrolimus in patients of group 1. 1-year-follow up revealed a comparable morbidity. The 1-y-survival rate was 76.0% (19/25) and 75.0% (45/60) in groups 1 and 2. Tacrolimus levels were comparable at this time.
Conclusions: Based on our results, we could not find a significant impact of a better HLA compatibility on patients′outcome after cardiac transplant. However, due to the lower levels of tacrolimus in patients with fewer HLA-mismatches, further investigations are necessary to confirm the hypothesis that immunological similarity may allow for reduction of immunosuppressive therapy.

PV17 HUMAN CYTOMEGALY VIRUS (CMV) IMMUNOGLOBULIN INCREASED CMV-FREE SURVIVAL IN HIGH RISK PATIENTS AFTER HEART TRANSPLANTATION (HTX)

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Background: We compared a prophylactic to a preemptive treatment strategy against CMV regarding the incidence of CMV viremia, acute rejections (AR) or cardiac allograft vasculopathy (CAV) after HTx.
Methods: HTx patients (n = 56) were retrospectively studied regarding CMV-free survival viremia, AR, and CAV. Average follow-up was 4.15 years (355 days up to 7.5 years). Patients were classified into 3 groups according to their received CMV therapy: preemptive (n = 19), prophylactic monotherapy (either valganciclovir for 3 months or early single dose of 1 mg/kg/BW of CMV immunoglobulin, CMVIG, 2 weeks post-HTx, n = 18) or prophylactic double therapy (3 months valganciclovir plus early single dose of CMVIG, n = 19).
Results: Median patient survival was not significant different among the study groups. However, the median CMV-viremia free survival was different among the groups: 1817 days for prophylactic double, 1459 days for prophylactic mono and 1482 for preemptive (p = 0.52). Ssubanalysis of patients with high risk for CMV infection (donor+ and recipient– CMV status) showed that the CMV-free survival was significantly higher when patients received double prophylaxis therapy compared to the other two groups ($p < 0.01$). Whether the incidence of AR nor of CAV was not significantly influenced by the choice of CMV treatment regimen. Antiviral medication was discontinuated in 10.5% preemptive group, 38.9% prophylactic mono group, and 31.6% prophylactic double group, respectively.
Conclusion: Our results suggest that early therapy with CMVIG as adjunct to antiviral treatment could prolong CMV-free survival in high risk patients for CMV infection. If a repetitive CMVIG dosing post-HTx will further reduce CMV infection needs to be explored in the future.

PV18 THE MUNICH LUNG TRANSPLANT GROUP: 5-YEAR EXPERIENCE WITH THE LUNG ALLOCATION SCORE

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Objectives: The Lung Allocation Score (LAS) was implemented in Germany to improve lung transplant outcomes and waitlist mortality, after demonstrating favourable outcomes in the United States. The purpose of this study was to analyze our 5-year single-centre experience with the LAS within the influential area of the Eurotransplant Foundation.
Methods: After implementation of the LAS until December 2016, 294 patients underwent single (SLTX) or double lung transplantation (DLTX) at our centre. Patients were divided into 4 groups according to their diagnosis. Analyses of survival probabilities were performed to differentially compare transplant procedures, underlying diagnoses and LASs at time of transplantation. Waitlist characteristics, transplant procedures, perioperative mortality and morbidity, and up to 5-year post-transplant outcomes were analyzed.
Results: In the LAS-era, the proportion of lung transplants performed for interstitial lung disease (ILD) increased over time from 27% in 2012 to 54% in 2016 (p = 0.056). In reverse, the proportion of patients with chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF) undergoing lung transplantation declined over the 5-year period. We observed an increasing proportion of COPD patients on the waitlist without relevant changes in overall waiting times. Outcome was independent of diagnoses and LAS. DLTX was associated with better survival probality than SLTX ($p \leq 0.01$).
Conclusion: We demonstrate that the LAS is a valuable tool for the selection of lung transplant candidates, recognizing urgency and prognostic transplant benefit. However, the LAS did not shorten overall waiting times. Further long-term data respecting differential transplant centre activities have to be gathered.

ORGAN DONATION – ALLOCATION – RESULT ANALYSIS

PV20 COMPUTATIONAL SIMULATIONS DEMONSTRATE THE FEASIBILITY AND BENEFIT OF HLA EPITOPE MATCHING IN DECEASED DONOR KIDNEY ALLOCATION

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The Eurotransplant (ET) Kidney Allocation System (ETKAS) aims at allocating organs to patients on the waiting list (WL) fairly whilst optimizing HLA matching. Evidently, HLA epitope matching (EM) is biologically and clinically more relevant. Here, we performed ETKAS-based computer simulations to evaluate the potential benefit of EM on allocation efficacy.

A virtual European population of 400,000 individuals and a WL of 10,400 patients were constructed and maintained during simulation, matching the 2015 ET Annual Report characteristics. Within 10 simulated years, simulations allocated 22,600 kidneys. T-cell epitopes were calculated using the pirche.org algorithm. Besides comparing four EM scenarios, the impact of applying EM in all ET countries was compared to applying EM only in Germany.

The best-balanced scenario prioritized A-B-DR fully matched donors, replaced the HLA match grade by PIRCHE-II score and exchanged the HLA

mismatch probability (MMP) by an epitope MMP polynomial. This setup showed negligible impact on kidney exchange rates and waiting time, whilst HLA match grades decreased mildly. However, considering previously reported data, the projected 10-year incidence rate of *de novo* donor specific HLA antibodies (dnDSA) is expected to be relatively reduced by 13% in ET when EM is applied in all ET countries, and respectively by 10% in Germany when EM is only applied in Germany, with no further effect on other ET countries in terms of HLA matching, waiting time or transplant numbers.

The anticipated reduced graft loss rates may not only benefit transplanted patients but also patients on the WL while the reduced risk for dnDSA increases chances for a subsequent retransplant. We conclude that EM may lead to an improved outcome while keeping equal balances on the WL.

PV21 WAITING LIST DEVELOPMENT IN GERMANY SINCE INTRODUCTION OF MELD-BASED LIVER ALLOCATION

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In addition to the implementation of the Model of End-stage Liver Disease (MELD) score in Germany in 2006 other factors have also tremendously affected the liver transplantation (LTx) program, among others the all-time low of available donor organs. This study analyzes their impact on the waiting list.

The electronic record system of the Eurotransplant was analyzed retrospectively for all patients who underwent listing in Germany from 2004 to 2015. In addition, open accessible data from DSO was investigated.

In the investigated time period 21444 patients were registered for liver transplantation in Germany. In line with the development of organ donors the number of new subscriptions declined over time, having its maximum in the year 2010 with 2121 and decreasing to 1432 registrations in 2015. A similar trend could be observed in the number of actively listed patients (2010: 2161; 2015: 1280). Reregistrations displayed 10.4% of all cases (2226/21444). The median time spend on waiting list was 139 days (IQR 20-476). Reasons for removal from the waiting list in this era were transplantation (60.9%), death on waiting list (22.6%) or removal for other reasons (16.5%). These reasons included unfit for transplantation (3.8%), recovery (5.2%) or other/unknown causes (7.5%).

When analyzing patients who died on waiting list or were removed due to poor health status (= mortality), the absolute number was constant over the years (median 388; IQR 334–470; $p = 0.63$). However, the quotient of mortality and actively listed patients increased noticeably from 0.16 to 0.26 ($p = 0.0045$).

The MELD allocation as well as other environmental factors have tremendously changed waiting list statistics. Unfortunately, the goal of reducing waiting list mortality was not achieved in the long term.

PV22 TWO DECADES OF THE EUROTRANSPLANT SENIOR PROGRAM (ESP): THE GENDER GAP IN MORTALITY IMPACTS PATIENT SURVIVAL AFTER KIDNEY TRANSPLANTATION

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Background: Long-term outcomes of the Eurotransplant Senior Program (ESP) are urgently needed to improve selection criteria for kidney transplant recipients (KTRs), patient education, and allocation policies.
Methods: We analyzed 244 ESP-KTRs between 1999 and 2018. All ESP-KTRs were assessed by the standardized SF-8. A control of 82 dialysis patients waitlisted within the ESP was used for comparison.
Results: We observed 1-, 5-, and 10-year patient survival of 91.7, 66.3, and 38.0%. Independent mortality risk factors included male gender ($p = 0.006$) and acute cellular rejection ($p < 0.001$). Median patient survival of male ESP-KTRs was 80 vs. 131 months for female ESP-KTRs ($p = 0.006$). 1-, 5-, and 10-year death-censored allograft survival was 93.3%, 82.6%, and 70.4%. Independent risk factors included high BMI ($p < 0.001$) and acute cellular rejection ($p < 0.001$).

After re-initiation of dialysis median patient survival was 58 months (range: 0–152 months). No ESP-KTR underwent retransplantation. 45.1% of ESP-KTRs showed DGF, 3.7% primary non-function. Median kidney allograft function at 1-, 5-, and 10-years were 39.7, 39.5, and 41.2 mL/min.

Median physical and mental component scores (PCS/MCS) of ESP-KTRs were 40.2 (range: 16.9–62.5) and 48.3 (range: 21.1–62.5), significantly higher compared to dialysis patients ($p < 0.05$). 97% of ESP-KTRs who underwent successful transplantation would again do so.
Conclusion: Kidney transplantation within the ESP shows highly favorable outcomes independent of recipient and donor age. However, gender disparities in mortality of ESP-KTRs became obvious. These findings may reveal targets to improve gender-specific patient care.

PV24 WHO COVERS THE COSTS OF GUIDELINE DEMANDS?

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The German transplant guidelines for liver transplantation were established to select transplant candidates according to chance of success and medical urgency. Hepatocellular carcinoma in cirrhosis is a good example to evaluate the required time and effort to implicate accurate work flow and decisions.

Patients with HCC in cirrhosis are eligable for a standard exception (SE). The UNOS T2 criteria are determined by contrast media imaging either computed tomography or magnetic resonance tomography. The so called "Anlage 1 (analog to Liver Reporting and Data System (LiRADS))" needs to be filled out and has to be signed by a radiologist and a member of the transplant conference every 3 months to extend the SE. The work-flow includes the assessment of all radiological imaging in a HCC-conference prior to the tumor conference. Therafter, patients are discussed in the transplant conference. All three conferences take place weekly and require the presence of the experts including transplant surgeon, hepatologist, radiologist, oncologist, radiation, psychiatrist and patholgist. Transplant coordinators prepare the files.

The calculated amount of time was 1050 min for the HCC-conference and 1905 min for the transplant conference. The corresponding costs were 1200 € and 2400 €, respectively. The tumor conference was excluded, because this conference also discusses non-transplant indications. The extrapolation of total costs reflects 172.800 € per year.

In summary, transplantation medicine in Germany underlies strict guidelines that require immens investment of experts. The required time and undertaken efforts need to be covered to ensure that the transplant centres can perform according to the guidelines.

KIDNEY TRANSPLANTATION II

PV26 RISK FACTORS OF EPSTEIN-BARR VIRUS REACTIVATION AND POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS IN THE FIRST YEAR AFTER KIDNEY TRANSPLANTATION: RESULTS FROM A LARGE MULTI-CENTRE STUDY

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Epstein-Barr virus (EBV) can reactivate in transplant patients leading to post-transplant lymphoproliferative disorders (PTLD). Current recommendations suggest monitoring of EBV load at regular intervals. However, the predictive value of EBV load for EBV-associated complications in different risk populations is not clear so far. We performed a large prospective multicenter study on 541 renal transplant patients and analysed 3133 blood samples for EBV load by qPCR throughout 8 visits during the first post-Tx year. Patients with D+/R– EBV or CMV mismatch or the use of rabbit ATG received valganciclovir prophylaxis. 109 patients (20.1%) had detectable EBV viral load; 37 patients (6.83%) had an elevated load over 2000 copies/mL and 11 patients (2.03%) had a high load over 10000 copies/mL. At the end of the study, 85.7% of the patients with reactivation were negative for EBV load. Risk factors for reactivation were EBV and CMV mismatch. Interestingly, incidence of EBV was significantly associated with CMV reactivation, both for detectable viraemia ($p = 0.0231$; OR = 1.86) and for elevated viraemia ($p = 0.0413$; OR = 2.76). Immunosuppressive therapy was associated with EBV incidence, with highest incidence for patients under ATG ($p = 0.0225$; OR = 1.69) and lowest for patients under basiliximab and rapid steroid withdrawal) ($p = 0.0432$; OR = 0.59). However, no effect of further medication including valganciclovir prophylaxis was found for elevated EBV. There was only one case of serious PTLD in an ATG-treated patient with EBV viral load of 12,271 copies/mL. No EBV-associated transplant rejections were observed. Early onset of EBV-reactivations is not associated with severe complications and further studies are required to determine the long-term effect.

PV27 PRE-EXPOSURE PROPHYLAXIS (PREP) WITH DACLATASVIR PLUS SOFOSBUVIR BEFORE TRANSPLANTATION OF HCV-POSITIVE DONOR KIDNEYS TO HCV-NEGATIVE KIDNEY TRANSPLANT RECIPIENTS – A PROOF OF CONCEPT STUDY

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In a controlled prospective trial, we investigated the use of a pre-exposure prophylactic (PrEP) regimen with direct-acting antivirals to prevent chronic hepatitis C (HCV) infection from HCV serologic positive (seropos) kidney donor organs to HCV serologic negative (seroneg) kidney transplant recipients (KTR). $N = 39$ HCVseroneg waitlisted patients (pts) will receive an HCVseropos kidney transplant (KT) in a multi-phase staggered design. PrEP with daclatasvir 60 mg and sofosbuvir 400 mg is performed for 12 weeks, starting at the time of KT. Primary endpoint is sustained virological negativity (SVN) 12 weeks after the end of PrEP. Here we report the first interim results of this study (phase I). So far, six pts received a KT from three HCVseropos donors between 15.12.17–20.02.18. Mean donor age was 43.3 years, mean recipient age was 57.2 years. Mean waiting time on dialysis was 72.6 ± 30.5 months. Of note, after pts agreed to the study to receive an HCVseropos kidney, mean waiting time was 24.6 ± 14.7 days only. PrEP was well tolerated in all KTR without signs of drug-related adverse events or discontinuations. One HCVseropos donor was viraemic at the time of explantation (>2xE5 IU/mL HCV RNA, genotype 2a) while the other two have been tested RNA negative; thus the PrEP in the KTR of RNA negative donor was reduced to 4 weeks. At the end of therapy (EOT) no HCV transmission was detected in all recipients. 4/6 KTR have reached the interim efficacy endpoint SVN 4 weeks after the end of PrEP. 2/6 KTR presented with delayed graft function initially. At EOT all pts had stable graft function (mean creatinine 1.3(±0.4) mg/dL). Optional HCV organ allocation enables additional KTs by reducing waiting time. PrEP was safe and prevented HCV transmission to negative KTR.

PV28 EPIDEMIOLOGY OF AND RISK FACTORS FOR BK POLYOMAVIRUS REPLICATION AND NEPHROPATHY IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS: AN INTERNATIONAL CERTAIN REGISTRY STUDY

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Background: BK polyomavirus-associated nephropathy (BKPyVAN) constitutes a serious cause of kidney allograft failure, but large-scale data in pediatric renal transplant recipients and a comprehensive analysis of specific risk factors in this patient population are lacking.
Methods: We analyzed data of 313 pediatric patients in the Cooperative European Paediatric Renal Transplant Initiative (CERTAIN) registry research network, with an observation period of up to five years. The net state of immunosuppressive therapy was assessed by the modified Vasudev score.
Results: Presumptive BKPyVAN (defined as sustained high-level BK viremia $>10^4$ copies/mL) within 5 years post-transplant occurred in 15.8% of patients, and biopsy-proven BKPyVAN in 4.9%. New-onset BKPyV viremia was observed in 115 patients (36.7%), of whom 11 (9.6%) developed viremia late, i.e. after the second year post-transplant. In 6/48 patients (12.5%) with high-level viremia and in 3/14 (21.4%) with BKPyVAN this respective event occurred late. BKPyV viremia and/or BKPyVAN were associated with a higher net state of immunosuppression (OR 1.3, $p < 0.01$) and with tacrolimus-based immunosuppression (OR 3.3, $p < 0.001$), but also with younger recipient age (OR 1.1 per year younger, $p < 0.001$) and obstructive uropathy (OR 12.4, $p < 0.01$) as primary renal disease.
Conclusions: Uncontrolled BKPyV replication affects a significant proportion of pediatric renal transplant recipients, and is associated with unique features of epidemiology and risk factors such as young recipient age, obstructive uropathy as primary renal disease and over-all intensity of immunosuppressive therapy. BKPyV surveillance should be considered beyond two years post-transplant in pediatric patients at higher risk.

PV29 THE PRESENCE OF RARE BKPYV GENOTYPES AFTER RENAL TRANSPLANTATION IS ASSOCIATED WITH WORSE TRANSPLANT OUTCOME

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Background: The BK-polyomavirus (BKPyV) associated nephropathy (PyVAN) is observed in 1–10% of renal transplant recipients, of which up to 80% undergo graft failure. BKPyV reactivation after renal transplantation was associated with donor-derived genotypes (GT), against the recipient has no immunological protection. Thus, the risk for PyVAN appears to be higher in BKPyV seroconcordant donors and receivers' pairs. Since genotype I is the most prevalent genotype, we analyzed the impact of the detection of non-genotype I on intermediate clinical outcome after renal transplantation.
Methods: Fifty-six patients who were renal transplanted between January 2015 and October 2016 and tested positive for BKPyV viremia were included into the study. The BKPyV-VP1 coding sequences were PCR-amplified, sequenced, and subjected to genotyping. For further evaluation, patients were divided in genotype I ($n = 46$) and non genotype I ($n = 10$) groups.
Results: The most abundant genotype I was detected in 46 of 56 (82%) patients, while genotypes II and IV were detected in 2 (4%) and 8 of 56 (14%) patients. Genotype III was not detected in our cohort. In comparison to the genotype I group, PyVAN was significantly more frequent in the non genotype I group (8 of 10 (80%) vs. 17 of 46 (37%); $p = 0.001$) 24 months after transplantation. Accordingly, graft failure was significantly more frequent in the non-genotype I group (3 of 10 (30%) vs. 2 of 46 (4%); $p = 0.007$).
Conclusion: The detection of rare BKPyV genotypes appears to be associated with higher rates of PyVAN diagnosis and worse intermediate transplant outcome after renal transplantation.

PV30 IMMUNE RESPONSES IN RENAL TRANSPLANT RECIPIENTS AT RISK OF BK-VIRUS ASSOCIATED NEPHROPATHY – IMPACT OF THREE IMMUNOSUPPRESSIVE REGIMENS

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Introduction: Early detection of patients at risk of BK virus-associated graft nephropathy would allow prevention by early adjusting immunosuppressive treatment.
Materials and Methods: We analyzed intracellular cytokine responses, CD4 helper function and B cell responses up to 24 months post-transplant in a prospective randomized study of 105 renal transplant recipients ($n = 35$, CsA/MMF; $n = 37$, Tacr/MMF; $n = 33$, Tacr/ERL; 18 drop-outs).
Results: Risk of BK viremia was lowest in Tacr/ERL patients (4/30 (13%), CsA/MMF; 14/36 (39%), Tacr/MMF; 1/21 (5%), Tacr/ERL; $p = 0.005$). Tacr/ERL patients showed increased T-dependent B cell responses ($p = 0.004$, 4 months; $p = 0.019$, 1 year), and lowest CD4, CD19 and CD14 cell IL10 responses (CD4: PMA; $p = 0.009$, 1 year; CD19: PMA; $p = 0.002$, 4 months; CD14: LPS; $p = 0.048$, 2 years) compared to CsA/MMF and Tacr/MMF patients. Pretransplant, increased IL-10R expression was detected in patients developing BK viremia ($CD4^+$ T cells, $p = 0.005$; $CD8^+$ T cells, $p = 0.004$; $CD14^+$ monocytes, $p = 0.004$). Post-transplant, CD4 helper activity ($p = 0.008$, 4 months) and CD4 and CD8 cell IL10 responses were increased (PMA; CD4: $p = 0.003$, 1 year; $p = 0.038$, 2 years; CD8: $p = 0.013$, 1 year) in these patients.
Conclusion: Our data demonstrate a significantly lower risk of BK viremia on Tacr/ERL compared to CsA/MMF and Tacr/MMF treatment. The previously reported increased risk of donor-specific antibody (DSA) formation on everolimus treatment is supported by our finding of significantly increased T-dependent B cell responses. Whereas pretransplant increased IL-10R expression may predict an increased risk of developing BK viremia, the increased post-transplant Th2 responses (CD4 helper activity and IL10 responses) found in these patients may increase the risk of DSA formation.

PV31 INDICATIONS AND POSSIBILITIES FOR CONTRAST-ENHANCED ULTRASOUND (CEUS) IN KIDNEY TRANSPLANT RECIPIENTS: A SINGLE CENTER EXPERIENCE

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Background: For the assessment of kidney transplants (KTX) ultrasound is the first method of choice in daily routine and when problems are supposed. Contrast-enhanced ultrasound (CEUS) plays an increasing role in kidney imaging. The used contrast agent is not nephrotoxic and has no relevant side-effects. Aim of this study was to describe the indications and possibilities of CEUS in renal transplanted patients.
Methods: 265 CEUS examinations of the kidneys and KTX were performed at the University Hospital Regensburg between September 2014 and April 2018. 121 examinations of renal transplanted patients were included for the analysis. CEUS was performed by experienced sonographers after bolus injection of 1.0–2.4 mL sulphur hexafluoride microbubbles using a high-end ultrasound device with multifrequency probes at a low mechanical index.
Results: The average age was 58 ± 14 years (20–76 years). 88.9% of the patients had GFR below 60 mL/min/1.73 m² and therefore a relative or absolute contraindication against contrast-enhanced CT or MRI. No adverse events were observed after the injection of contrast-agent. 70.5% of all examinations (n = 87) were related to pathologies of the KTX and in 29.5% (n = 36) to pathologies of the native kidneys. In KTX the assessment of the renal perfusion was the main issue (57.0% of all cases), followed by the evaluation of complex renal cysts (25.6%), infectious diseases (7.4%) and solid renal masses (4.7%). The objectives in the native kidneys were in 89.0% the evaluation of complex renal cysts and the assessment of solid renal masses (8.3%).
Conclusion: CEUS is a safe and excellent diagnostic tool for renal transplanted patients. It could be applied easily bedsides and allows an immediate assessment of a variety of indications.

IMMUNOLOGY

PV32 INDUCTION OF BILIARY EPITHELIAL WOUND HEALING AND ANGIOGENESIS THROUGH IL6 IN DONOR BILE DUCTS AFTER LIVER TRANSPLANTATION

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Background: Impaired epithelial cell proliferation and angiogenesis after ischemia/reperfusion injury may compromise wound healing of the donor bile duct and may lead to later biliary complications. It is known that IL6 can induce VEGFA and biliary epithelial cell proliferation. The aim of this study was to examine IL6 and VEGFA mRNA expression in the common bile duct at the time of organ retrieval, after cold storage, and during transplantation.
Methods: Common bile duct samples during donor hepatectomy, after cold storage, and after reperfusion were compared by novel RNAscope in-situ hybridization (ISH) for IL6 and VEGFA mRNA expression. Additional immunohistochemistry for CD45 was done, followed by whole-slide scanning and automated digital image analysis. ISH signal and $CD45^+$ cells were quantified and expressed as spot-area μm^2/1000 μm^2 and cells/1000 μm^2, respectively.
Results: Donor hepatectomy bile ducts (n = 5) showed a baseline IL6 (0.3 ± 0.2) and VEGFA (0.6 ± 0.4) mRNA expression that was comparable to the expression levels detected following cold storage for both IL6 (0.5 ± 0.1) and VEGFA (0.8 ± 0.4). However, after reperfusion (n = 5), IL6 expression was markedly increased (1.2 ± 0.2, p = 0.007) and VEGFA expression levels were also elevated (1.5 ± 2.0). A co-localization of IL6 and VEGFA was observed in epithelial cells during cold storage and in the sub epithelial region after reperfusion. $CD45^+$ cell count decreased from donor hepatectomy (2.5 ± 1.4) to reperfusion (1.3 ± 1.0).
Conclusions: Increased expression of IL6 and VEGFA mRNA in the common bile duct after reperfusion may facilitate wound healing. Impaired expression of IL6 and VEGFA may have a deleterious effect on wound healing and mitigating preservation injury in donor livers via the IL6 pathway should be considered.

PV33 *EX VIVO* ADMINISTRATION OF ATGS BEFORE REPERFUSION REDUCES THE EXTENT OF VASCULAR INFLAMMATION IN HUMAN VESSELS

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Introduction: Polyclonal antithymocyte globulins (ATGs) are widely used in induction of immunosuppression and treatment of acute rejection. Previously, we demonstrated that ATG bind to endothelial cells in vivo. We investigated the effect of the early application of ATGs on the vascular response of human vessels after ischemia-reperfusion.
Material and Methods: Human vessels (saphenous vein/internal thoracic artery segments discarded from CABG surgical procedures) were obtained after informed consent and Ethics approval. The vessels were preserved in a NaCl/Heparin solution and after 4 h ischemia connected to a customized bioreactor consisting on a double roller-pump with oxygenator and reperfused for 120 min with compatible human blood. Vessels were treated with 1 mg/kg ATG (Thymoglobulin). Untreated vessels served as control group. Vitality of the vessels was measured through oxygen consumption during reperfusion. Cytokines (IL-6, TNF-alpha) as well as VEGF were analysed by ELISA. Immunohistochemical analysis of CD11 and CD31 was performed to evaluate the reduction of the vascular inflammation.
Results: Vitality of the vessels could be demonstrated with adequate oxygen consumption and stable pH values. Treatment with ATGs prevented increase of IL-6 in serum. No differences regarding the concentration of TNF-alpha and VEGF were observed within the groups. Immunohistochemical analyses showed a significant reduction of positive reactions to CD11b and CD31 after treatment with ATG when compared to control vessels.
Conclusion: Down-regulation of adhesion molecules by ATG may be responsible for decreased expression of CD11b and CD31 after reperfusion. We could demonstrate local modulation of endothelial response, despite little activity on circulating cytokines.

PV34 THE IMPACT OF HUMAN LEUKOCYTE ANTIGEN G GENE POLYMORPHISMS ON ACUTE CELLULAR REJECTION AFTER LIVER TRANSPLANTATION

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Human leukocyte antigen G (HLA-G) is a nonclassical HLA class I molecule. Expression of HLA-G has been associated with increased graft survival and decreased rejection episodes. It has been reported that the HLA-G 14-base pair (bp) insertion/deletion (ins/del) (rs66554220) and +3142C>G (rs1063320) gene polymorphisms modify the expression level of HLA-G. The aim of the case control study was to investigate whether these HLA-G polymorphisms have an impact on acute cellular rejection after liver transplantation. In total, 146 liver transplant recipients (57 with acute cellular rejection and 89 without acute cellular rejection) and 99 corresponding liver donors were genotyped for both polymorphisms. The 14-bp ins/ins and the +3142GG genotypes are more frequent in recipients without acute cellular rejection compared to recipients with acute cellular rejection (3.5% vs. 31.5%, p = <0.001; 12.3% vs. 41.6%, p = <0.001) displaying an association with protection from acute cellular rejection. In contrast, in liver donors we could not reveal an association. We conclude that 14-bp ins/ins and +3142GG genotypes of HLA-G in liver transplant recipients are of importance for prediction of acute cellular rejection after liver transplantation. Thus genotyping of liver recipients for both polymorphisms might be useful to stratify liver transplant recipients according to the risk of acute cellular liver transplant rejection.

PV35 PREVALENCE AND IMPACT OF PREFORMED ANTI-HLA ANTIBODIES OF THE IGA ISOTYPE IN KIDNEY TRANSPLANTATION

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Introduction: Preformed donor-specific anti-HLA antibodies (DSA) detected by solid-phase assays have been associated with early kidney allograft loss. Until now, mostly antibodies of the IgG isotype have been studied, whereas other isotypes, in particular IgA, have not yet been thoroughly investigated.
Methods: Pre-transplant sera from 295 patients receiving a CDC-cross-match-negative kidney transplant were retrospectively analyzed for anti-HLA antibodies using Luminex technology. The presence of anti-HLA IgG and IgA was determined using screening beads. HLA specificity was determined for IgG

using single antigen beads applying an MFI cutoff of 1000 for positive results. Antibody results were then correlated with the incidence of graft loss. All patients received basiliximab induction and tacrolimus-based maintenance immunosuppression.
Results: Upon screening, anti-HLA IgG were found in 55.9% and anti-HLA IgA in 28.9% of patients, respectively. 70.2% of anti-HLA IgA-positive patients also had anti-HLA IgG. Whereas anti-HLA IgG targeted both class I and II HLA, those of the IgA isotype preferentially targeted class I HLA. 63 patients (21.4% of the total cohort) had IgG DSA. Allograft survival was significantly shorter in DSA-positive compared to DSA-negative patients during a median follow-up of 4.9 years ($p = 0.007$). The presence of anti-HLA IgA had no impact on graft survival in IgG DSA-positive patients. However, in IgG DSA-negative patients, the presence of anti-HLA IgA was associated with a higher incidence of graft failure (13.6 vs. 6.5%) during follow-up ($p = 0.086$).
Conclusions: These results suggest a negative effect of anti-HLA IgA on kidney allograft survival in IgG DSA-negative patients. Donor-specificity of anti-HLA IgA is currently being studied.

PV36 FOLLICULAR HELPER T CELL EXPANSION AND DSA FORMATION IN A RAT RENAL TRANSPLANT MODEL

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DSA are associated with reduced graft survival. Effective generation of high affinity antibodies depends on B cell activation by follicular Helper T cells (Tfh). We examined Tfh expansion, germinal centre B cell proliferation, generation of long-lived plasma cells, as well as DSA features in a rat model of chronic renal allograft rejection.

We compared transplanted rats with full CNI mediated immunosuppression for 28 and 56 days with prolonged CNI underdosing, which was previously shown to induce DSA formation and ongoing rejection. Splenic Tfh, B cell proliferation and plasma cells were quantified by immunofluorescence, and splenic T and B cell subsets were analysed by FACS. Regulation of specific molecules relevant to B-/Tfh-cell interaction and function (Bcl-6,CD40/CD40L, ICOS/ICOSL) and cytokines were determined by RT-PCR, IHC, or FACS. Serological DSA were analysed regarding Ig isotype, subclass as well as complement-mediated cytotoxicity by flow cytometry.

Splenic Tfh cells were expanded in our RTX model of chronic rejection compared to standard CNI treatment and untreated control groups. This correlated with increased follicular germinal centre B cell proliferation and generation of long-lived plasma cells. Standard, but not under-dosed CNI prevented formation of germinal centres and blocked the formation of DSA. Analysis of the IgG subclass revealed an early dominance of complement-activating IgG subclass 2b (IgG2b > IgG2a > IgG1 > IgG2c), which correlated with detection of complement-dependent cytotoxicity. Levels of IgG1, 2a and 2c increased over time in rejecting rats. Tfh cells may play a role in generation of deleterious DSA and may represent a specific target for therapeutic intervention to treat ABMR.

PV38 LOW-DOSE ALEMTUZUMAB INDUCTION IN SENSITIZED KIDNEY TRANSPLANT RECIPIENTS – ALLOGRAFT SURVIVAL AND INFECTION RATES

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Rationale: Alemtuzumab is a CD52-specific depleting antibody with T and B cell activity used for induction in kidney transplantation. In standard protocols (30–60 mg), efficacy is comparable to ATG in patients with high immunological risk, with prolonged lymphocyte depletion up to 12 months. Current concepts aim at optimized dosing strategies to reduce side effects. Here we report data from our experience with low-dose alemtuzumab for induction in sensitized patients.
Methods: Low-dose alemtuzumab (20 mg i.v. single dose, intraoperatively) was used for induction, followed by tacrolimus-based immunosuppression and corticosteroids, with mycophenolic acid added upon total lymphocyte count (TLC) >5% or 200/μL, respectively.
Results: Between 2007 and 2017, 46 patients received alemtuzumab induction in 48 kidney transplantations, five of which were HLA-incompatible living donor transplantations. Median PRAmax was 43 [22–76;IQR] %; all patients had negative CDC XM prior to transplantation. Low-dose alemtuzumab was well tolerated. Median time to TLC recovery was 65 [47–100] days, with no increase in hospitalisation due to infectious complications. During follow-up of 3.2 [1.5–5.6] years, 16 (33%) patients developed BPAR, 10 of which were antibody-mediated (3 acute, 7 chronic AMR). Death-censored allograft survival was 79.2%, allograft function in these patients at end of follow-up was excellent with an eGFR of 47 [39–65] mL/min/1.73 m². There was no increased rate of infections, especially viral infections.
Conclusion: Low-dose alemtuzumab induction followed by standard maintenance immunosuppression provides good patient and allograft outcome with low rate of rejection and infectious complications in sensitized renal allograft recipients.

LIVING DONATION

PV39 PERIOPERATIVE AND SHORT-TERM OUTCOMES OF ROBOTIC ASSISTED LIVING KIDNEY DONATION

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Background: Robotic assisted kidney donor surgery represents one of the most advanced surgical techniques for living kidney donation.
Material and Methods: We present our initial experience with 37 consecutive patients who underwent robotic assisted living kidney donation from September 2013 to May 2018.
Results: Within the last 5 years the amount of robotic assisted living kidney donation almost quintupled in our institution. A total of 19 left (51%) and 18 (49%) right kidneys were used for transplantation. Mean donor age was 53 (range: 35–70). The average total operative time was 151 ± 27 min with no difference between patients with single 153 ± 27 or multiple ($n = 8$; 22%) 144 ± 29 renal arteries or veins. Interestingly, right donor nephrectomy (139 ± 22) was significantly faster than left (163 ± 27) nephrectomy. Postoperative blood transfusions were necessary in $n = 1$ (2.7%) patient. No conversion to open surgery was performed. Clavien Dindo Grade <IIIb complication occurred in ($n = 4$) 10.8%. Grade IV and V complications did not occur. Mortality was 0%.

10 kidneys (27%) were transplanted across the AB0 barrier, requiring therapeutic apheresis as well as T and B cell directed immunosuppressive therapy. One year graft survival was 97%.
Discussion: Robotic assisted living kidney donation is an emerging minimally invasive surgical technique which facilitates excellent perioperative and short-term outcomes.

PV41 LONG-TERM OUTCOME AFTER LIVING KIDNEY DONATION

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Background: Living renal donation represents an excellent therapeutic strategy for patients with end-stage renal disease. However, living kidney donation is a special situation in medicine, since healthy persons undergo an invasive treatment. Careful analysis of long-term donor outcome is necessary with respect to the physical and clinical condition.
Methods: All living kidney donors (11/1967–12/2016) of the Transplant Center at Heidelberg were enrolled. Renal function and co-morbidities were assessed.
Results: Only 60% of the long-term donors participated in regular follow-up visits at the transplant center. A few donors refused follow-up visits completely. Renal function was about 30% lower compared to pre-donation, whereas proteinuria increased marginally. Blood pressure remained stable with an increase of donors receiving antihypertensive treatment. Socioeconomic status remained unchanged in most of the donors.
Conclusions: As expected, renal function decreased significantly after donation and incidence or severity of hypertension increased. However, long-term clinical outcome after living kidney donation was acceptable. The need of regular follow-up visits of living renal donors at transplant centers has to be emphasized.

PV42 SURGICAL COMPLICATIONS OF AB0-INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION – SINGLE CENTER EXPERIENCE 2004–2014 (FREIBURG-GERMANY)

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Introduction: In Germany AB0-incompatible (AB0i) kidney transplantation (KTx)is relatively widespread, due to organshortage and legal constrains concerning altruistic living kidney donation. Approximately 20% of living donations can be traced back to AB0i KTx donors. The long-term evidence

shows comparable results to AB0-compatible (AB0c) KTx in terms patient and graft survival. Studies on surgical complications are scarce and this study focuses on this aspect.
Methods: Between April 2004 and September 2015 106 consecutive AB0i and 277 AB0c KTx were performed. % AB0i KTx and 159 AB0c KTx recipients were excluded from our cohort due to differences in immunosuppression.101 AB0i and 118 AB0c receiving an immunosuppressive protocol including basiliximab, tacrolimus,mycophenol acidand corticosteroids were analyzed. Additionally, all AB0i recipients received rituximab 4 weeks prior to schedulded transplantation and immunoadsorption (IA).
Results: Surgical complications show no statistically relevant difference between the two cohorts with one exeption. In AB0i KTx recipients the incidence of lymphocele formation was 23% and thereby significantly higher in contrast to ABoc KTx cohort with 9.3% ($p < 0.01$). A main risk factor was more frequent preoperative IA sessions (AB0i KTx without lymphocele ($n = 77$):5.84 $\pm$ 3.58; AB0iKTx with lymphocele ($n = 23$):7.96 $\pm$ 5.18; ($p = 0.03$).
Conclusion: In AB0i KTx the incidence of lymphocele formation is significantly increased compared to AB0c KTx and leads to more frequent surgical reinterventions. Other surgical complications are not significantly increased adding to the evidence that AB0i KTx is a safe technique and viable option for increasing the donor pool specially for recipients whose only willing donor is blood group incompatible.

PV43 OUTCOMES FOLLOWING LIVING DONOR KIDNEY TRANSPLANTATION IN PATIENTS WITH DONOR-SPECIFIC HLA ANTIBODIES AFTER DESENSITIZATION WITH IMMUNOADSORPTION

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Living donor kidney transplantation is increasingly performed over human leukocyte antigen (HLA) barriers. Uncertainty still exists concerning the risk for antibody-mediated rejection episodes, possibly limiting long-term graft survival. The present study aimed to evaluate the outcomes of kidney transplantations performed after desensitization in patients with donor-specific HLA antibodies. Thirty-eight sensitized patients were included in the study. Sixteen patients had a positive CDC and/or ELISA crossmatch result with their prospective living donor and 32 patients had Luminex-detected donor-specific HLA antibodies (DSA). Patients were successfully desensitized by immunoadsorption treatment (median of 8 treatments) and anti-CD20 antibody rituximab ($N = 36$) combined with antithymocyte globulin ($N = 20$) or anti-IL2 receptor antibody therapy ($N = 18$). Twelve patients were additionally treated by plasmapheresis. The outcomes of the 38 patients were retrospectively compared to 76 standard risk recipients (2:1 matching). After transplantation, sensitized patients showed comparable death-censored graft survival and patient survival compared to standard risk recipients. Infectious complications, surgical complications and rejection rates (18% in both groups) were not significantly different between groups. Median 1-year serum creatinine was with 1.31 mg/dL in sensitized recipients not significantly different to the 1.38 mg/dL in standard risk recipients. One-year urinary protein excretion was also not significantly different with a low 10.8 and 10.5 g/mol creatinine, respectively. Our desensitization protocol for sensitized living donor kidney transplant recipients results in good graft outcomes with comparable side effects and rejections rates to standard risk recipients.

PV44 SOLID ORGAN TRANSPLANTATION FOLLOWING ALLOGENEIC HAEMATOPOIETIC CELL TRANSPLANTATION: EXPERIENCE FROM A REFERRAL ORGAN TRANSPLANTATION CENTER AND SYSTEMATIC REVIEW OF LITERATURE

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Background: Solid organ transplantation (SOT) following haematopoietic cell transplantation (HCT) is a rare event. Uncertainty exists whether such recipients are at higher risk of relapse of underlying haematological disease or at increased risk of developing infectious or immunological complications and malignancies following SOT.
Methods: The experience at our referral organ transplantation center ($n = 7$) and the present literature of SOT ($n = 198$) in recipients following previous HCT was systematically reviewed.
Results: Outcome analysis of 206 SOT recipients following HCT challenges the validity of the frequently stated comparable outcome with recipients without prior HCT. SOT recipients after HCT are younger and have a higher mortality and morbidity in comparison with "standard" recipients. Rejection rates for SOT recipients following HCT appear to be lower for all organs, but for liver transplantation. In the setting of liver transplantation following HCT, mortality for recipients of deceased donor grafts appears to be exceptionally high, although experience with grafts of living donors are favourable. Morbidity was mostly associated with infectious and malignant complications. Of note some SOT recipients who received solid organ donation from the same HCT donor were able to achieve successful withdrawal of immune suppression.
Conclusions: Despite limited follow-up, recipients with prior HCT show a different course after SOT, necessitating attention and closer follow-up.

BASIC SCIENCE

PV45 ANTAGONISM OF PLATELET-DERIVED SEROTONIN (5-HT) MODULATES MACROPHAGE-MEDIATED TRANSPLANT VASCULOPATHY AFTER AORTIC TRANSPLANTATION BUT NOT LARGE AIRWAY REMODELING IN MURINE TRACHEAL ALLOGRAFTS

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Objectives: Recent advances have implicated serotonin (5-HT) as a regulator of inflammation, proliferation, regeneration, and repair. 5-HT may have a role in transplant vasculopathy (TV) and airway remodeling because it exerts effects via its subtype 2A receptor (5-HT2AR) on cells involved in these pathologies. The aim of this study was to evaluate the role of 5-HT2AR blockade on the development of TV and airway remodeling.
Methods: Orthotopic aortic and tracheal transplantation was performed in a fully allogeneic mouse model (C57BL/6 (H2b) in CBA (H2k)). Recipients were treated with 5-HT2AR-antagonist sarpogrelate (10 mg/kg/d) and sacrificed on day 14 for cytokine PCR analysis of the graft or on day 30 for (immuno-) histological measurement.
Results: In aortic grafts sarpogrelate led to markedly reduced vessel lumen occlusion (41% $\pm$ 7% vs. 55% $\pm$ 13%; $p < 0.05$) accompanied by a significantly lower amount of macrophages in the neointima (5.8% $\pm$ 0.8% vs. 9.3% $\pm$ 1.7%; $p < 0.05$). This correlates with PCR results showing significantly lesser expression of monocyte attracting chemokines MCP-1 and TGF-β ($p < 0.01$). Additionally we found drastically reduced 5-HT2AR expression (6% $\pm$ 3% vs. 55% $\pm$ 12%). In tracheal allografts epithelium-lamina propria-ratio was not influenced by sarpogrelate (0.45 $\pm$ 0.08 vs. 0.38 $\pm$ 0.05 (sarpogrelate); $p = 0.08$). Amounts of macrophages did not differ in sarpogrelate and untreated groups (32.8% $\pm$ 5.2% vs. 32.8% $\pm$ 1.7%; $p = 0.23$).
Conclusion: The results indicate a role for 5-HT in the development of TV after aortic transplantation via influencing macrophage activity. In large airway remodeling after tracheal transplantation this mechanism could not be found demonstrating basic differences in the pathomechanisms of these two transplantation models.

PV46 INVISIBLE ORGANS MADE BY GENETIC ENGINEERING TO TURN OFF MHC PRIOR TO ALLOGENEIC TRANSPLANTATION PREVENT A PRO-INFLAMMATORY CYTOKINE RESPONSE IN THE RECIPIENT

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HLA remains a main cause of allograft rejection. Previously, we have shown that MHC silenced cells and tissues are protected against immune rejection and the feasibility to silence MHC expression on lungs. Now, we evaluated the effect of MHC I silencing prior to allogeneic lung transplantation (Tx) model by monitoring the cytokine response during the first 12 weeks after Tx with immunosuppression given only in the first 4 weeks. SLA I was silenced during normothermic ex vivo perfusion with lentiviral vectors encoding short hairpin RNAs targeting β2m. A lentivirally transduced non-specific shRNA was used as control and NanoLuc as reporter gene. In each transplant experiment both donor lungs were genetically engineered with one lung being transplanted and the other lung used for quality control. Levels of β2m mRNA and SLA were quantified by RT-PCR and flow cytometry. SLA downregulation of the endothelial cells was designed to reach a level of 70%. Cytokines were monitored using multiplex technology. Already 1 h after Tx the serum levels of IL-1beta, IL-6 and IL-8 increased significantly in all animals by up to 0.263, 1.370 and 0.497 pg/mL, respectively. On POD 1, the cytokine secretion in the SLA silenced group decreased to pre-transplant levels whereas those of the control group remained significantly elevated ($p < 0.01$). On POD 14, levels of

IL-12 increased significantly by up to 0.286 pg/mL in the controls whereas it remained at pre-transplant levels in the SLA silenced lung recipients. Levels of IL-2, IL-10 and TNF-α were significantly higher ($p < 0.01$) in animals receiving SLA expressing in comparison to SLA silenced lungs. These data indicate that MHC silenced grafts are immunologically invisible and may successfully combat the burden of rejection and immunosuppression.

PV48 HEPATOCYTE TRANSPLANTATION FOLLOWING MAJOR LIVER RESECTION – PRELIMINARY RESULTS OF A PORCINE LARGE ANIMAL STUDY

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Introduction and Background: Hepatocyte transplantation (HTx) is of large potential as treatment modality for various liver diseases including acute liver failure. Post-hepatectomy liver failure remains a feared complication after liver resection with high morbidity and mortality despite advances in perioperative management and surgical technique. Therefore, we developed a porcine animal model to investigate if HTx after liver resection can improve postoperative liver function and bridge the patient to sufficient regeneration of the liver remnant.
Methods: Porcine hepatocytes were isolated using a 3-step-collagenase perfusion technique from whole donor livers procured according to protocols applied in humans (i.e. arterial perfusion with HTK-solution). Impairment of liver function was induced by major hepatectomy (subtotal resection of left median and lateral lobes as well as right median lobe) in 8 pigs. HTx was performed postoperative via an exteriorized portal venous catheter.
Results and Conclusions: An average of 8.4 $\times$ 108 hepatocytes with a mean viability of 77.5% were isolated from procured livers. A mean volume of 181.9 mL with 50.4 $\times$ 107 viable hepatocytes (1.2 $\times$ 107 hepatocytes/kgBW) was infused per animal at a flow rate of 1.9 mL/min. Portal venous pressure increased from 15.0 mmHg prior to liver resection to 16.1 mmHg after resection when HTx was started. HTx eventually was performed pressure controlled (initially one animal was lost due to pulmonary embolism) with tolerated increase of portal venous pressure up to 25 mmHg with temporary reduction/stoppage of infusion. Portal venous pressure peaked at 30.4 mmHg during HTx and was 29.1 mmHg at the end of cell infusion. All animals remained stable concerning vital parameters during HTx.

PV49 ANTI-ANGIOTENSIN II TYPE 1-RECEPTOR ANTIBODIES (AT1R-AB) INDUCE A SPECIFIC PHENOTYPE OF C4D NEGATIVE REJECTION DISTINCT FROM HLA ANTIBODIES

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AT1R-Ab have been associated with kidney allograft rejection; however, their ability to induce a specific rejection phenotype, independent of the presence of HLA-DSAs, has not been defined. In a prospective cohort of 881 kidney recipients, we performed systematic screening for AT1R-Ab and HLA-DSAs, together with concomitant allograft biopsy. The allograft rejection phenotype was assessed by histopathology, immunochemistry for C4d, and allograft gene expression measurement using microarray.

We identified 233/881 (26%) pts with post-transplant AT1R-Ab (>10 U/mL). Compared to negative pts, AT1R-Ab positive pts showed significant increased levels of glomerulitis, peritubular capillaritis, endarteritis. Level of interstitial inflammation and tubulitis were similar and so was prevalence of C4d deposition and TG. After adjusting for the detection of HLA-DSAs, AT1R-Ab were independently associated with glomerulitis, peritubular capillaritis and intimal arteritis. AT1R-Ab+/HLA-DSA− pts showed increased prevalence of intimal arteritis and decreased prevalence of C4d positivity compared to other groups. Compared to AT1R-Ab-/HLA-DSA+ pts, AT1R-Ab+/HLA-DSA− pts exhibited increased expression of endothelial cell associated transcripts in allograft. Histomolecular rejection phenotype in AT1R-Ab+/HLA-DSA− pts was distinct from that of AT1R-Ab-/HLA-DSA+ pts revealing stronger expression of endothelial damage transcripts.

AT1R-Ab are associated with a specific histo-molecular phenotype of C4d negative kidney allograft rejection, characterized by microvascular and arterial inflammation, high expression of endothelial cell associated transcripts and low prevalence of complement deposition in capillaries, independent of the presence of HLA-DSAs on a population level.

PV50 PRIMARY HUMAN HEPATOCYTES INDUCE A CD4$^+$ T CELL ALLORESPONSE *IN VITRO* WHICH IS ASSOCIATED WITH MHC CLASS II UPREGULATION AND SUPPRESSIBLE BY T_{REG}

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Background: Hepatocyte transplantation has developed into an encouraging approach for the treatment of several liver diseases. As engraftment and long-term acceptance could not be achieved yet, new methods need to be established to ensure reduction of post-transplant cell loss. In order to characterise hepatocyte induced immune reactions in the transplant setting and evaluate the regulatory potential of T_{reg}, *in vitro* experiments with primary human hepatocytes (PHH) were performed.
Methods: Immune reactions induced by PHH were analysed. Immunological potential of T_{reg} in mixed lymphocyte and mixed lymphocyte and hepatocyte cultures were examined using peripheral blood mononuclear cells and PHH. T_{reg} were polyclonally expanded to CD4$^+$ CD25^{high} CD127^{low} phenotype and added to co-cultures in single-/trans-well setups with/without supplementation of anti-interferon γ (IFNγ). Alloresponses induced by PHH were analysed by flow cytometry.
Results: Hepatocyte induced T cell response was observed as primarily CD4$^+$ T cell mediated and associated with IFNγ-induced up-regulation of major histocompatibility complex (MHC) class II on hepatocytes. Experiments with fragmented hepatocytes and culture supernatants could rule out indirect antigen presentation routes. Secretion of inflammatory cytokines accompanied the allospecific proliferation. Though CD8$^+$ T cells lacked proliferation during the course of co-culture, early up-regulation of CD69 was observed. T_{reg} supplementation successfully inhibited hepatocyte induced alloresponses. This effect was shown to be primarily cell contact dependent.
Conclusion: The hepatocyte induced alloresponse is CD4$^+$ T cell mediated and associated with MHC class II up-regulation on hepatocytes. All responses are suppressible by T_{reg}.