POSTERS

KIDNEY

P001 UROMODULIN SERUM LEVELS IN KIDNEY GRAFT DONORS AND RECIPIENTS

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Background: Uromodulin is exclusively synthesized in the thick ascending limb cells of Henle's loop, and primarily released into urine, but to a lesser extent also transferred into the renal interstitium, subsequently entering the blood. Serum uromodulin (sUMOD) levels are associated with both estimated glomerular filtration rate and cell viability. Quantification of sUMOD promises new insights in post-transplant (post-Tx) graft function.
Methods: This retrospective study presents the results of sUMOD levels measured in pre- and post-Tx serum samples from 44 kidney graft recipients and 13 deceased kidney donors.
Results:
1. The donors' sUMOD levels ranged from 64 to 237 ng/ml (healthy adults: 30–552 ng/ml).
2. There was no association between donors' sUMOD level and post-Tx graft function (immediate/delayed).
3. The recipients' pre-Tx sUMOD level (3.1±1.9 ng/ml) was near the limit of detection (2 ng/ml).
4. Until day 5 post-Tx sUMOD levels were comparable in event-free recipients experiencing either immediate or delayed graft function (IGF vs. DGF = 69±44 vs. 72±35 ng/ml). However, sUMOD levels then diverged from day 9 to 21 (77±31 vs. 40±22 ng/ml, $p<0.01$) thus discriminating DGF from IGF.
5. Graft deteriorations were always associated with declined sUMOD levels.
6. In recipients with IGF urinary UMOD concentrations were positively correlated with sUMOD.

Conclusion: sUMOD is a novel indicator of kidney graft function. Further studies are in progress in order to assess tissue-specific sUMOD in comparison with other renal biomarkers

P002 LONG-TERM EFFECTS OF CMV IMMUNE GLOBULIN (CMVIG) PROPHYLAXIS IN KIDNEY GRAFT RECIPIENTS RECEIVING ANTI-LYMPHOCYTE GLOBULIN INDUCTION

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Background: Cytomegalovirus (CMV) remains the most common viral infection that causes morbidity, mortality, and graft loss among kidney graft recipients (KGR). The aim of this retrospective study was to evaluate the impact of CMVIG prophylaxis/therapy on 10-year graft/patient survival (Kaplan-Meier, patients deceased with functioning graft were censored) especially in KGR undergoing anti-lymphocyte globulin induction.
Methods: This study included 363 KGR with CMVIG prophylaxis (Cytotect®, Biotest) or treatment (plus ganciclovir) and 421 recipients without any immune globulin infusions. Subgroup analyses included recipients who had received intra-operative high dose ATG induction (9 mg/kg ATG-Fresenius®, HDI-ATG-F) in addition to a CyA-based triple-drug therapy (TDT).
Results: In the TDT cohort the incidences of CMV infections (only CMV-IgM seroconversion) or diseases were 25.2% resp. 15.5%, and 44.8% ($p<0.001$) resp. 18.6% ($p = 0.308$) in the TDT+ATG-F cohort.

Independent of the immunosuppression both patient and graft survival of the CMVIG ($n = 363$) versus non-IgG ($n = 421$) cohorts were not significantly different (cumulative 10-year patient survival, 95% Confidence Interval: 0.74 [0.69; 0.80] vs. 0.75 [0.70; 0.80], $p = 0.80$; graft survival 0.71 [0.65; 0.76] vs. 0.69 [0.54; 0.74], $p = 0.60$).

Comparing only TDT+HDI-ATG-F treated recipients there were also no significant differences in 10-yr graft/patient survival between the CMVIG ($n = 205$) and the non-IgG cohort ($n = 176$) (patient: 0.75 [0.67; 0.81] vs. 0.78 [0.69; 0.85], $p = 0.21$; graft 0.74 [0.66; 0.81] vs. 0.82 [0.74; 0.88], $p = 0.17$).

Comparing only the CMVIG prophylaxis cohort (D^+/R^-, $n = 100$) with the non-IgG cohort ($n = 176$) in TDT+HDI-ATG-F treated recipients there were also no differences in 10-yr graft/patient survival (patient: 0.77 [0.65; 0.85] vs. 0.78 [0.69; 0.85], $p = 0.40$; graft 0.81 [0.70; 0.89] vs. 0.82 [0.74; 0.88]; $p = 0.95$).
Conclusion: CMVIG is a safe preparation with no short- or long-term side effects. In the CMV high risk group (D^+/R^-) the prophylaxis with Cytotect guarantees a comparable high graft and patient survival than in recipients without CMV infection/disease. For CMV diseases pre-emptive or early therapy is efficient and recommendable.

P003 A CLINICAL REGISTRY FOR C3 GLOMERULOPATHY AND IMMUNE-COMPLEX MEDIATED MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

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Background: Following the invention of the nomenclature of C3 glomerulopathies (C3G) and immune-complex mediated forms of membranoproliferative glomerulonephritis (MPGN), a pathophysiology related classification of these orphan diseases became available. C3G has a high rate of recurrence after kidney transplantation and very little is known about the clinical time course, management and outcome of these patients.

Due to the rarity of these disorders, only multicenter registration will provide a data basis on diagnosed cases and their clinical time course and a necessary basis for targeted interventional trials.
Methods: We developed an open clinical registry for C3G and immune-complex mediated MPGN allowing the retrospective and prospective registration of cases. Data covers baseline information (age, sex, date of diagnosis), clinical follow-up data (renal function, proteinuria, nephrotic syndrome and specific diagnostic findings as well as the time course of disease (GFR slope, dialysis, transplantation and recurrence of disease). We thereby aim at the stimulation of adequate diagnostic procedures, combination of findings and a final evaluation of findings on an individual patient base.
Results: We expect 100–150 newly diagnosed patients per year in Germany. The registry is online since July 1st 2015 and accessible via the internet addresses "www.C3Gnet.de" and "www.C3G.website. All information regarding the participation and inclusion of patients are electronically available via the website. The database was developed in cooperation with the coordination center for clinical trials at the TU Dresden providing secured data entry and hosting and allows bi-lingual (German/English) data entry.

Therefore, this internet-based registry will collect and evaluate clinical data about patients with a diagnosis of C3G or immune-mediated MPGN in Germany and other countries in a multicentric fashion, thereby providing a data basis for therapeutic trials in the future.

P004 GLUCOSE CHEMICAL SATURATION TRANSFER MAGNETIC RESONANCE IMAGING FOR *IN-VIVO* DETECTION OF ACUTE RENAL ALLOGRAFT REJECTION

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Background: When acute renal allograft rejections (AR) occur, reliable diagnosis is crucial to minimize damage to the renal graft. During such AR episodes the resulting inflammation is accompanied by increased glucose consumption within the affected tissue. As of late, local tissue glucose can be assessed by magnetic resonance imaging through a procedure called glucose

chemical exchange saturation transfer (glucoCEST). Therefore, the aim of this study was to adapt the glucoCEST technique for the diagnosis of AR.
Methods: Three groups of animals underwent glucoCEST magnetic resonance imaging (MRI) four days after surgery, a time point at which the renal allograft shows marked signs of cellular AR: Adult, uni-nephrectomized, allogeneically transplanted rats undergoing AR, syngeneically transplanted rats without AR and rats with unilateral ischemia-reperfusion injury.
Results: *In-vivo* glucoCEST contrast (MTR_{asym}) could successfully be measured and calculated. Compared to syngeically transplanted (1.12 ± 0.21), and ischemia-reperfusion injury kidneys (1.32 ± 0.16) renal allografts undergoing AR exhibited significantly increased glucoCEST contrast (2.29 ± 0.39, p-value $\leq$ 0.005) in the renal cortex, when normalized to the healthy contralateral kidneys.
Conclusion: The glucoCEST MRI is a feasible method for *in-vivo* detection of acute cellular renal allograft rejection and allows differentiating between AR and ischemia-reperfusion injury.

P005 SUPERIOR RENAL FUNCTION IN AN EVEROLIMUS-BASED CALCINEURIN INHIBITOR FREE REGIMEN COMPARED TO STANDARD CYCLOSPORINE/MYCOPHENOLATE AND REDUCED CYCLOSPORINE/EVEROLIMUS: FOLLOW-UP OF THE HERAKLES STUDY AT MONTH 48

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Purpose: To follow up on renal function (GFR) at month 48 after kidney transplantation (Tx) in patients on immunosuppressive regimen with different calcineurin inhibitor (CNI) exposures.
Methods: 802 patients were included in this prospective, open-label, randomized multi-center study. After induction with basiliximab all patients received cyclosporine A (CsA), enteric-coated mycophenolate sodium (EC-MPS) and steroids. 3 months post Tx 499 patients were randomized 1:1:1 to either a) continue standard (STD) CsA(100–180 ng/ml) with EC-MPS (n = 166), b) convert to a CNI-free regimen with everolimus (EVR; 5–10 ng/ml) + EC-MPS (n = 171) or c) convert to CNI-reduced regimen CsA (50–75 ng/ml) with EVR(3–8 ng/ml) (n = 162).
Results: Here data from 48 months observational follow-up are presented: GFR (Nankivell, ITT) was similar at randomization 3 months post Tx and had significantly improved at month 12 by +5.6 mL/min (95%CI:[+2.9;+8.3]; p<0.001) and remained significantly improved by +6.8 mL/min in favor of CNI-free regimen at month 48 (p = 0.02). 54% of CNI-free, 36% of CNI-reduced and 44% of STD patients had an improvement in GFR at month 48 (p = 0.09 CNI-free versus STD). All 3 groups had similar rejection rate since randomization (13% STD, 16% CNI-free, 16% CNI-reduced) and overall comparable safety profile. Mean trough levels at month 48 were for CsA 111 ng/ml in STD and 86 ng/ml in CNI-reduced patients and for EVR 5.5 ng/ml in CNI-free and 5.5 ng/ml in CNI-reduced patients.
Conclusion: CNI-free as well as reduced CNI in combination with EVR represent both efficacious and safe regimen. CNI-reduced group had higher CsA levels than anticipated. The fact that CNI reduction was not fully accomplished might have prevented GFR differences compared to STD in this randomized treatment group. However, CNI-free regimen was associated with better GFR maintained for 4 years post Tx. The results of this large trial confirm previous reports of improved GFR after CsA withdrawal with EVR in combination with EC-MPS.

P006 MONTH 48 FOLLOW-UP RESULTS OF HERAKLES TRIAL ON THREE DIFFERENT TREATMENT REGIMEN AND SWITCHING OFF BEHAVIOUR IN DE NOVO RENAL TRANSPLANT PATIENTS

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Purpose: To compare switching off 3 different immunosuppressive (IS) regimen 4 years after renal transplantation (Tx).
Methods: 802 patients were included in this prospective, open-label, randomized, controlled multi-center study with observational follow-up (FU) until month 60 post Tx. After induction therapy all patients received cyclosporine A (CsA), enteric-coated mycophenolate sodium (EC-MPS) and steroids. At 3 months post Tx 499 patients were randomized 1:1:1 to either a) continue standard CsA (100–180 ng/ml) +EC-MPS(n = 166) (STD) or convert b) to a calcineurin inhibitor (CNI)-free regimen with everolimus (EVR) (5–10 ng/ml) + EC-MPS(n = 171) or c) to a CNI-reduced regimen with EVR (3–8 ng/ml) + reduced CsA (50–75 ng/ml) (n = 162). All patients continued on steroids.
Results: At 48 month post Tx, 40% of CNI-free, 30% of CNI-reduced, and 55% of standard treated patients were still on their initial assigned treatment and were available for month 48 analysis. Drop-out frequency among follow-up ITT population from randomization to month 48 was 17%, 15%, and 14% for standard, CNI-free, and CNI-reduced groups, respectively. Premature discontinuation due to adverse events occurred in 5 (3%) of standard, 5 (3%) of CNI-free and 1 (1%) of CNI-reduced patients (safety-population) from month 12 to 48. The CsA trough levels in CNI-reduced group were in the higher end of target levels (50–75 ng/ml) in non-switcher population; whereas in switcher population they were beyond the target levels. In non-switcher population, eGFR (Nankivell) was significantly improved by +13.7 ml/min/1.73m^{2}in favor of the CNI-free regimen at month 48 (p<0.001).
Conclusion: Month 48 results from HERAKLES show that immunosuppressive regimen using EVR with reduced-dose or without CNI-exposure reflect an efficacious and safe therapeutic approach offering the opportunity for an individualized immunosuppression to minimize CNI-exposure. Drop-out rates over 4 years post Tx showed relative similar adherence rates between groups. Patients that never switched off the assigned CNI-free regimen reached a markedly improved GRF.

P007 EXPLORATIVE *POST HOC* ANALYSIS OF ZEUS AFTER 5 YEARS: HISTOLOGICAL ASSESSMENTS FROM BIOPSIES

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Purpose: Analysis of pathologists' assessments and histological data allow for deeper insight on patient outcome when combined with investigator's final clinical diagnoses. Here we present 5 year data from de novo transplant recipients after conversion to an everolimus (EVR) based regimen and withdrawal of calcineurin inhibitor therapy versus continued CNI regimen.
Methods: Analysis of histological and pathologists' assessments from the prospective, open-label, controlled, multi-center study ZEUS. 300 renal transplant (Tx) patients were randomized at month 4.5 post Tx to either receive EVR plus enteric coated-mycophenolate sodium (EC-MPS) (n = 154) or cyclosporine (CsA) plus EC-MPS regimen (n = 146). After 12 months interventional core study an observational follow-up (FU) on patients safety and efficacy was performed until month 60 post Tx. As per study protocol graft core biopsies were indicated by suspected rejection episode, prior to or at the latest within 24 h after the initiation of anti-rejection therapy. Biopsies were read and interpreted by local pathologists.
Results: We will present the results of this *post hoc* analysis. In brief: total number (nr) of biopsies performed and mean nr of biopsies per patient are overall similar in both groups until month 60. Nr of pts with at least one rejection (as per final clinical diagnosis) was slightly higher in CNI group versus EVR group. Nr of patients with BPAR was higher in the EVR group especially due to mild, early acute rejections (mostly BANFF IA and IB). Number of patients with histological evidence of chronic/sclerosing allograft nephropathy was similar in both groups (both 10%), C4D staining positivity was found slightly higher in the EVR group (11% EVR vs. 7% CNI), however, patients with evidence of antibody mediated rejection was higher in the CNI group (2% EVR vs.4% CNI) as well as for CNI-induced toxicity lesions (16% EVR vs.23% CNI).
Conclusion: Data from histological assessments together with investigator reported final clinical patient outcomes show that an EVR-based regimen with early elimination of CNI-therapy is as safe and efficacious as a standard CNI-therapy offering the opportunity to reduce cumulative CNI-induced toxicities on the allograft.

P008 DISSEMINATED INFECTION WITH NOCARDIA FARCINICA AND SEVERE HYPONATREMIA AFTER KIDNEY TRANSPLANTATION

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Introduction: Nocardia is a species of gram-positive actinomycetes which is ubiquitous in decaying organic material, soil and water and usually gets ingested by airways. There are few reports of disseminated cutaneous, pulmonary, meningeal and lymphocutaneous infection which mostly affect immunocompromised patients, since intact T-cell mediated immunity is the major protection mechanism.
Case report: We report a case of disseminated pulmonary, cerebral and cutaneous infection with Nocardia farcinica in a 66 year old kidney transplant recipient. Initial admission was due to severe hyponatremia and pneumonia with radiologic signs of a septated pleural effusion. Isolation of agent was primary possible when cutaneous lesions developed. Treatment was difficult since oral trimethoprim/sulfomethoxacole led to severe hyponatremia so long term parenteral Amicazin and Minocyclin was initiated. After 7 months of consistent intravenous treatment disseminated lesions dissolved.

Conclusion: Disseminated infection with Nocardia in immunocompromised patients is a severe, life threatening and rare disease. Due to its infrequency, the variety of the clinical pattern and resistance situation diagnosis and treatment remain challenging and protracted.

P009 DESIGN AND RATIONALE OF ATHENA STUDY: A 12-MONTH STUDY EVALUATING EVEROLIMUS VERSUS STANDARD REGIMEN IN *DE NOVO* RENAL TRANSPLANT RECIPIENTS-BASELINE DATA

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Background: Long-term use of standard calcineurin inhibitor (CNI) post-kidney transplant (KTx) is associated with an increased risk for malignancies, cardiovascular disease, and renal failure. Previous studies have shown everolimus (EVR) to allow CNI reduction and thereby preserve renal function without affecting efficacy. ATHENA study is designed to evaluate the renal function comparing EVR with reduced CNI exposure (tacrolimus [TAC] or cyclosporine A [CsA]) versus a standard treatment protocol with mycophenolic acid (MPA) and TAC in *de novo* (day 0) KTx recipients (KTxR).
Methods: This is a 12-month (M), multi-centre, open-label, prospective study in KTxR (≥18 years) receiving renal allografts from deceased or living donors. Eligible patients were randomised prior to Tx to one of the three treatment arms (1:1:1): TAC+MPA+steroids ($n = 204$) or EVR+TAC+steroids ($n = 204$) or EVR+CsA+steroids ($n = 204$) all with basiliximab induction. The primary objective is to demonstrate non-inferiority in renal function (eGFR by Nankivell formula) in one of the EVR arms versus TAC+MPA+steroids arm at M12 post-KTx. The key secondary objective is to assess the incidence of treatment failure (BPAR, graft loss or death) at M12 post-KTx.
Study status: The study recruitment is completed in Germany and France. A total of 658 patients were enrolled, of which 614 patients were randomised in the study. To-date, baseline data was available for 367 treated patients (TAC+MPA, 125; EVR+TAC, 116; EVR+CsA, 126); of which 66% were male (65%, 67%, and 66%, respectively). The mean age was 54 years (TAC+MPA, 55 years; EVR+TAC, 54 years; EVR+CsA, 53 years) with 76% patients younger than 65 years (80%, 75%, and 74%, respectively). At baseline the mean BMI was 26.8 kg/m^2 (TAC+MPA, 26.7 kg/m^2; EVR+TAC, 26.7 kg/m^2; EVR+CsA, 26.8 kg/m^2). Overall, 18% patients received allograft from living donor (TAC+MPA, 18%; EVR+TAC, 17%; EVR+CsA, 20%). The mean HLA mismatch was 2.8 (TAC+MPA, 2.6; EVR+TAC, 2.8; EVR+CsA, 3.0). Patients with previous renal KTx 3 % in total (TAC+MPA 2 %, EVR+TAC 5%, EVR+CsA 2%. Updated data will be available at the congress and preliminary results of this ongoing trial are expected in 2016.
Conclusion: ATHENA is the largest European renal transplant study and the first study evaluating the non-inferiority of renal function as a primary objective in a *de novo* EVR-based immunosuppressive protocol.

P010 PROTEASE-ACTIVATED RECEPTOR (PAR-1) ANTIBODY, A NEW NON-HLA ANTIBODY WITH PRO-INFLAMMATORY ACTIONS

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Purpose: Microvascular endothelium is major target for antibodies directed against HLA and non-HLA antigens. Functional antibodies targeting G-protein coupled receptors (GPCRs) such as AT1R or ETAR are recently emerging as important mediators of antibody mediated rejection.
Methods: Beside AT1R and ETAR, high expression of protease-activated receptor-1 (PAR-1) was detected in the systematic screen for GPCR expression in quiescent and activated microvascular endothelium. Structural analysis of extracellular domains of screen positive GPCRs confirmed striking homology between second extracellular loops of AT1R, ETAR and PAR-1. Subsequently, solid phase assay using membrane extracts from PAR-1 overexpressing cells was developed for detection of PAR-1 antibodies. PAR-IgG was isolated from sera of patients with acute rejection with microvascular pathology and used for stimulation of human microvascular endothelial cells. Transcriptional regulation of interleukin 6 (IL-6) was studied by promoter deletion assay, transcription factor activation and binding by qRT-PCR, western blot, EMSA, cFOS knockdown and site directed mutagenesis. IL-6 secretion was determined by ELISA.
Results: PAR-1-IgG enhanced IL-6 release via increased IL-6 promoter activity which was dependent on cFos protein expression via its binding to the IL-6 promoter. Pretreatment with AP-1 inhibitor, cFos siRNA induced knock-down or site directed mutagenesis decreased IL-6 levels and IL-6 promoter activity. IL-6 secretion could be normalized by pretreatment with specific PAR-1 inhibitor. Specificity was further confirmed by peptide targeting of the 2nd extracellular loop of the PAR-1 which significantly decreased IL-6 release.
Conclusion: PAR-1 is a new target for functional antibodies in the context of microvascular rejection with deregulated IL-6 levels. Targeting PAR-1 and/or IL-6 could offer new therapeutic possibilites to withstand microvascular inflammation.

P011 INCREASED MORTALITY AND METASTATIC CANCER IN RENAL TRANSPLANT PATIENTS LACKING NATURALLY OCCURRING ANTI-ANGIOGENIC ANTIBODIES

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Purpose: We assessed the presence of naturally occurring blocking antibodies to mediators of vascularisation and metastasis in Kidney Transplant Recipients (KTR) with metastatic cancer ($n = 11$), non metastatic cancer ($n = 32$) and 38 KTR with no cancer history and 195 healthy controls.
Methods: The antibodies assessed were: PAR1-antibody, VEGF-A-antibody, VEGF-Receptor 1 antibody, VEGF-B antibody, VEGF-Receptor 2-Ab, EGF-Antibody and EGFR-Antibody. All KTR had stable graft function and there were no differences in immunosuppressive regimens, HLA mismatch, or duration of immunosuppression between KTR groups. KTR with metastatic cancer were significantly older than those without cancer ($p = 0.011$). KTR with non metastatic cancer were similar in age to KTR without cancer ($p = 0.071$). There was no correlation with age to any of the antibodies tested.
Results: Compared to healthy controls KTR without cancer had lower levels of PAR1-ab, VEGF-R1-Ab, VEGF-B-Ab, EGF-Ab and EGFR-Ab (all p values < 0.001). However KTR had similar levels VEGF-A-Ab and VEGF-R2-Ab. KTR with non metastatic cancer had similar antibody profiles to those KTR without cancer apart from having lower levels of PAR1-abs ($p = 0.043$). KTR with metastatic cancer had lower levels of antibodies to PAR1, VEGF and its receptors (all p values < 0.05) compared to those with no cancer history. Levels of antibodies to EGF and its receptor were similar between all KTR groups. These data show that KTR have lower levels of antibodies to mediators of tumour vascularisation compared to healthy controls. The reason for this is unknown but may relate to immunosuppression. KTR with metastatic cancer had further reduction in antibodies to PAR1 and the VEGF pathway but not EGF pathway.
Conclusion: We are assessing stored serum samples to confirm whether KTR with metastatic cancer lose these antibodies during the development of cancer or whether they historically had low levels. It is possible these antibodies could risk stratify KTR at risk of developing metastatic cancer.

P012 ANGIOTENSIN II RECEPTOR TYPE 1 (AT1R) ANTIBODY IGG1 SUBCLASS PREDICTS GRAFT OUTCOME IN PATIENTS WITH TRANSPLANT GLOMERULOPATHY

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Purpose: We assessed the presence or absence of angiotensin receptor antibodies (ATRab) in all those Kidney Transplant Patients who have had biopsy proven transplant glomerulopathy (TG) meeting Banff criteria at our institution between 1980–2011. All sera at the time of transplantation were assessed retrospectively. Out of 1729 transplant episodes there were 141 diagnoses of (TG). ATRab are implicated as independent risk factors for early vascular rejection, cellular rejection and late graft loss; even in the absence of HLA antibodies. ATRab however exist, like all antibodies, in the IgG subclasses 1 through 4.
Methods: We assessed the relationship of these sub classes to total ATRab levels and also to graft outcome in multivariate analysis.
Results: There was no correlation of total ATRab levels and IgG1 but there was a weak positive correlation with IgG2,3,4 subclasses. Although IgG2,3,4 subclasses did not correlate with graft outcome IgG1 subclass levels did. In multivariate analysis correcting for the effect of donor age, recipient age, HLA antibodies and graft number – the presence of ATRab IgG1 subclass above the median value (5 u/ml) was associated with accelerated graft loss (HR 1.91 [95% CI 1.01–3.6] $p = 0.045$). Total ATRab did not predict graft loss over and above the variables listed. The only other variable to independently predict outcome was graft number (HR 2.14 [95%CI 1.16–4.0] $p = 0.017$)
Conclusion: These data suggest that optimisation of the ATRab assay may be possible by focussing on the complement fixing IgG1 Angiotensin Receptor Antibody subclass.

P013 B-CELL AND T-CELL RESPONSES TO A SINGLE HEPATITIS B REVACCINATION WITH FENDRIX® IN RENAL TRANSPLANT PATIENTS WHO ARE PREVIOUS NONRESPONDERS

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Introduction: The aim of this ongoing study is to analyze the efficacy of a single hepatitis B revaccination with Fendrix®, especially the T-cell response, in kidney transplant patients who failed to develop hepatitis B surface antibodies after a standard regimen with conventional vaccines.
Methods: We recruited previous nonresponders ($n = 9$, 5 men, 4 women, age 33–67) to receive one dose of Fendrix®. AntiHBs titers were analyzed before and 1 month after the revaccination. For the analysis of specific T-cell responses, we used the lymphocyte transformation test (LTT) and the IFNγ-ELISpot assay.
Results: Three out of 9 kidney transplant patients (33%) showed hepatitis B specific B-cell and 2 out of 9 patients (22%) specific T-cell responses, none of the patients showed both. Mean anti-HBs titers increased from 0 to 40 (range 0–264) IU/l. Mean responses to the LTT remained stable (hepatitis B specific stimulation index of 1.5); but maximum responses increased (from 2.0 pre-vaccination to 3.6 at month 1). Mean ELISpot responses increased from 0 to 1 spot per 250 000 peripheral blood mononuclear cells.
Conclusion: The preliminary results showed that a single vaccination with Fendrix® could induce hepatitis B specific responses in 5 out of 9 kidney transplant patients.

P014 TRANSFORM STUDY TO EVALUATE THE EFFECT OF EVEROLIMUS WITH REDUCED CALCINEURIN INHIBITORS IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS: BASELINE DATA

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Purpose: The long-term graft and patient survival in kidney transplantation (KTx) remains an unmet need. The ability of everolimus (EVR) to allow substantial reduction of calcineurin inhibitor (CNI) exposure along with its antiproliferative properties may address many of the current limitations to long-term outcomes post-KTx. The TRANSFORM study is designed to evaluate the efficacy and safety of EVR+reduced (r) CNI versus mycophenolic acid (MPA)+standard (s) CNI in *de novo* KTx recipients (KTxR). Here, we present the baseline data of the patients who have been randomised till 17th February 2015.
Methods: TRANSFORM (NCT01950819) is an ongoing 24-month (M), multicentre, open-label study in which KTxR are randomised (1:1) to receive either EVR+rCNI or MPA+sCNI; all with induction and steroids. After completion, patients may enter into a further 3-year observational follow up. The primary objective is to evaluate the impact of these immunosuppressive regimens on a combined endpoint: a composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR <50 mL/min/1.73 m^2; MDRD4 formula) at M12 post-KTx. This endpoint represents a clinically meaningful approach to discriminate between immunosuppressive regimens in KTx. Key secondary objective is to evaluate the composite efficacy failure (tBPAR, graft loss or death) at M12 and M24 post-KTx.
Results: TRANSFORM is recruiting across 215 centres worldwide and of planned 2040 patients, 921 KTxR have been randomised to date. At baseline, the recipients' age (mean$\pm$SD) is 50.56$\pm$14.38 years and BMI (mean $\pm$ sd) is 25.58$\pm$4.42 kg/m^2. Most recipients are Caucasian (76.2%). For the CNIs, 12.4% of patients are receiving cyclosporine and 87.6% patients are on tacrolimus. Glomerular disease (15.9%) and polycystic disease (14.2%) are the major causes for KTx. Mean ($\pm$SD) cold ischemia time is 9.7$\pm$7.71 h.
Conclusion: TRANSFORM is the largest prospective clinical study in KTx that captures the key surrogate markers of long-term outcomes. The study has been designed to evaluate the short- and long-term outcomes of EVR+rCNI in *de novo* KTxR versus MPA+sCNI.

P015 RIGHT-SIDED HAND ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY. TECHNICAL EXPERIENCE.

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Introduction: Hand-assisted laparoscopic donor nephrectomy (HALDN) permits to combine the necessary extraction incision to manually assist the procedure. The left kidney has remained the preferred organ of choice, due to the greater vessel lengths.

We describe in this video the right side terminal HALDN with hand-assisted extension of the renal vessel, technique that allowed the exposure of the right aortorenal junction providing maximal length of both vein and artery. In a prospective study we compared 51 right and 40 left sided HALDN during a 7 year period with a 1 year followup.
Material and Methods: With the donor on the left flank we performed a 5-port transperitoneal approach: 11-mm umbilical port for laparoscope, two 5 and two 10-mm trocars as working ports. After superior retraction of liver, the peritoneum was opened laterocolically and the colon mobilized. Afterward follow the isolation of ureter, gonadal vessels and renal hilum. Then the ligation of the side branches of the renal vein and isolation of the vena cava and the aorta. Complete dissection of the kidney until it is only fixed by the hilar vessels. The renal vein is dissected down to its root from the cava and the renal artery. Then the surgeon's left hand is placed intra-abdominally via a lower pararectal incision. After further vessels preparation by using index and middle finger, the cava is pushed aside with identification and preparation of right artery down to its aortic origin. After IV heparin infusion, the ureter is cut between two clips and transected at level of pelvis minor. The renal vein is accordingly held between two fingers (index and thumb) and closed by a triple-row Endo-TA stapler. The same procedure followed for the artery. This simple maneuver results in recovery of the entire length of right artery making a safe and simple anastomosis possible.
Results: The median procedure time was 123 vs. 135 min for left procedure. The mean warm ischemia time was 44 vs. 41 s in left procedure. There were no conversions. Mean blood loss was 92 vs. 101 ml in left procedure. Mean Hospital discharge was 3.4 days. There was no vein thrombosis. Delayed graft function occurred in 2 recipients: one in the left and the other in the right group. No significant difference in creatinine was seen between the groups 1 year after the transplantation. One-year graft survival rate was 97.5% in the left vs. 98.1% in the right group.
Discussion/Conlusion: Even if laparoscopy has decreased the patient's morbidity the evaluation process for the kidney extraction must follow the principle that the best kidney, should always remain with the donor, independently from the surgical technique. HALDN approach results in a significative improvement in length of right renal vessels. Moreover, dissection first of right renal vein allows a retrocaval isolation of the artery, obtaining significative longer vessel.

P018 PULMONARY ASPERGILLOMA – INCIDENTAL FINDING IN A RENAL TRANSPLANT RECIPIENT AFTER SUCCESSFUL CHEMOTHERAPY FOR POSTTRANSPLANT LYMPHOPROLIFERATIVE DISEASE (PTLD)

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We report the case of a 52-year old man with adult polycystic kidney disease, who preemptively received a living-donor renal transplant on July 14, 2010 (PRA max. 0%; basiliximab induction; tacrolimus/mycophenolic acid/prednisolone), with ongoing excellent graft function. A secondary highly malignant gastric MALT lymphoma was diagnosed in February 2014. Chemotherapy (4x CHOP, 6x Rituximab 375 mg/m^2) and local radiotherapy (36 Gy) induced complete remission since August 2014. Immunosuppressive therapy was switched to everolimus (ERL) and steroids. Late onset neutropenia, low CD4 cell counts < 200/µl and hypogammaglobulinemia – as side effects of chemotherapy – evolved as potential risk factors for infections. During in-hospital treatment for urosepsis, an X-ray and the following CT scan of the lung (Nov. 7, 2014) were highly suspective of an aspergilloma of the right upper lobe (4.5 × 3.5 × 4.0 cm, central cavernoma formation; potential second lesion in the lingula, diameter 1.5 cm). Bronchoscopy, BAL and the CT scan of the paranasal sinuses did not show pathological findings. Antifungal therapy comprised anidulafungin iv, amphothericin B per inhalation and voriconazol 2 × 4 mg/kg iv (then 2 × 300 mg po). Because of problems with drug monitoring, the necessary increase to the doubled dosage of oral voriconazol was delayed in time. Due to strong interactions with voriconazol, ERL treatment had to be reduced to 16% of the original dosage. As the suspected aspergilloma decreased in size only gradually, a video-assisted thoracoscopy with complete wedge excision of the histologically confirmed aspergilloma in the right upper lobe was performed on 07/01/2015.
Conclusion: Our case report shows that a 1:6 dose reduction of ERL is feasible and enables safe long-term voriconazol treatment for aspergilloma. As the initial subtherapeutic voriconazol trough levels may have compromised the success of antifungal therapy, monitoring of voriconazol trough levels is strongly recommended.

P019 MEDICATION ADHERENCE OF DIALYSIS PATIENTS WITH PHOSPHATE BINDERS ELECTRONICALLY MEASURED WITH MEMS™

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Introduction: The life of patients with severe renal failure is affected by nutritive restrictions and extensive dialysis sessions three times a week. By this

the patients' level of knowledge about the disease and medical treatment are assumed to be high. The aim of this study was to evaluate the medication adherence with phosphate binders in dialysis patients.
Methods: Dialysis patients taking phosphate binders three times daily, were eligible to be enrolled in the study. Adherence was measured electronically with MEMS™-containers over an observation period of 6 months per patient. Furthermore the influence of the amount of reported comorbidities on the adherence by using a questionnaire was evaluated.
Results: The mean dosing adherence rate with phosphate binders was 43 ± 5% in 36 dialysis patients. Patients who reported only their primary disease, the adherence rate was measured at 34 ± 9% (n = 11). For patients who reported 1–4 comorbidities and more than 5 comorbidities the adherence rate was at 42 ± 6% (n = 24) and 83 ± 11% (n = 3) $p < 0.036$) respectively.
Conclusion: The dosing adherence rates of dialysis patients with phosphate binders turned out to be low most probably because patients are afraid of the resorption of calcium from the phosphate binders and the negative effects. Dialysis patients need educational support to improve the right use of phosphate binders and to allay their fears.

P020 *DE NOVO* ANCA-ASSOCIATED VASCULITIS 20 MONTHS AFTER KIDNEY TRANSPLANTATION

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Background: *De novo* ANCA-associated vasculitis (AAV) after kidney transplantation is rare. To the best of our knowledge, the use of Rituximab or plasmapheresis in this setting has not been reported.
Methods: Case report.
Results: A 66-year-old asymptomatic woman, who had received a cadaveric kidney transplant 20 months previously for end-stage autosomal dominant polycystic kidney disease, was noted on follow-up to have a rise in creatinine from 2.0 to 2.6 mg/dl and increased proteinuria of 0.4 gram/gram creatinine.

Renal allograft biopsy revealed a glomerulonephritis with extracapillary proliferation and interstitial inflammation. Anti-proteinase 3 antibody in serum was strongly positive. No extrarenal manifestations of vasculitis were evident. Retrospective analyses of stored pre- and post-transplantation serum samples were negative for ANCAs, confirming a diagnosis of de novo AAV.

Treatment was commenced with high-dose steroid and Rituximab. As renal function deteriorated and repeat biopsy after 2 weeks showed persistent extracapillary proliferative glomerulonephritis, treatment was escalated to 7 sessions of plasmapheresis. Despite this, renal function remained impaired 4 months later with serum creatinine of 7.0 mg/dl.
Conclusion: Although Rituximab and plasmapheresis have proven efficacy in AAV, these treatments could not arrest deterioration of renal graft function in this case of de novo AAV after kidney transplantation.

P022 SPARTACUS: A MULTICENTRE, PROSPECTIVE RANDOMISED STUDY COMPARING TACROLIMUS HEXAL® VERSUS PROGRAF® BASED REGIMEN IN *DE NOVO* RENAL TRANSPLANT RECIPIENTS

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Background: In a transplant (Tx) setting, studies evaluating pharmacokinetic (PK) parameters and therapeutic equivalence of generic tacrolimus versus the reference drug are lacking. The SparTacus (NCT01649427) study was designed to compare the PK profile and clinical data of tacrolimus hexal® with prograf® in renal Tx recipients (RTxR).
Methods: In this prospective, two-phase open-label study, 76 *de novo* RTxR were randomised to receive either tacrolimus hexal® (n = 35) or prograf® (n = 41), both in combination with enteric-coated mycophenolate sodium + corticosteroids + induction therapy with basiliximab. Starting dose of tacrolimus was 0.15 mg/kg/day, adjusted to target plasma levels (C0) of 8–12 ng/ml from Tx to month (M) 1; 5–10 ng/ml up to M3; and 5–8 ng/ml up to M6. Primary objective of the study in phase I was to demonstrate comparable PK (ratio of the $AUC_{0\text{-}12\ h}$ over a period of 1-M post-Tx) of tacrolimus hexal® versus prograf®, and in phase II to demonstrate non-inferiority of renal function (GFR; Nankivell formula) between both treatment arms at M6 post-Tx. Here we present the PK results of the first month along with efficacy and safety data from this study.
Results: At M1, the dose-normalised tacrolimus 12-h-AUC (h/10^3XL) was comparable between tacrolimus hexal® versus prograf® (adjusted log-transformed LS mean, 2.9 vs. 3.0; difference, 0.076; 90% CI: −0.169, 0.321, p = 0.605; adjusted back-transformed LS mean, 19.0 vs. 20.5; ratio, 1.079; 90% CI: 0.844, 1.378, p = 0.605). LS mean value for Cmax (1/10^3XL) and mean 12 h tacrolimus C0 (μg/l) at M1 were comparable between tacrolimus hexal® versus prograf® (Cmax, 1.1 vs. 1.2; difference, 0.150; 90% CI: −0.134, 0.435; p = 0.377; C0, 12.2 vs. 11.1, respectively). Of 76 patients, 40 (PK-Set 40 pts.) actually completed 6-M treatment; tacrolimus hexal®, n = 19; prograf®, n = 21. At M6, tacrolimus hexal® versus prograf® had a comparable incidence of composite events (ITT, n = 76) (5.7% vs. 9.8%, p = 0.681) and its individual components (BPAR [5.7% vs. 7.3%], graft loss [0.0% vs. 2.4%], death [0.0% vs. 2.4%]). Incidence of adverse events (AEs) and serious AEs were comparable between tacrolimus hexal® and prograf® (AEs: 97.1% and 100%; serious AEs: 37.1% and 42.1%, respectively). Updated data will be shown at the congress.
Conclusion: Tacrolimus hexal® has a PK profile similar to that of prograf®, with comparable efficacy and safety in *de novo* RTxR.

P024 EBV NEGATIVE TRANSPLANT RECIPIENT WITH COMPLETE RECOVERY OF POSTRANSPLANT LYMPHATIC DISEASE AND SECONDARY OXALOSIS

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We present a 48-year-old, male recipient of a combined kidney and pancreas transplantation (KPTX) in 2010.

Immunosuppression was started with tacrolimus, MMF and steroids, induction therapy consisted of three doses of thymoglobulin (total 4.5 mg/kg). Due to EBV high risk constellation six doses of Cytotect (CMV/EBV hyperimmunoglobulin) were administered to prevent primary infection of EBV.

Six months after KPTX patient presented with fever, weight loss and severe diarrhea. Eventually EBV-associated postransplant lymphatic disease (PTLD) was diagnosed and eight doses of rituximab (375 mg/m^2) were administered. Because of high EBV-virus loads the patient also received six further doses of cytotect and immunosuppression was decreased.

Four months after diagnosis PET scan revealed complete – and up to now sustained – remission.

Renal function remained stable with baseline creatine about 200 umol/l, no requirement for insulin treatment.

Three years after KPTX patient presented with weight loss and diarrhea. A complete work-up was performed, which revealed no sign of recurrence of PTLD, infection, endocrine or autoimmune disease. Diarrhea were treated symptomatically, yet renal function declined constantly. Biopsy showed severe (secondary) oxalosis, probably due diarrhea.

Summarizing, we present the case of a EBV negative transplant recipient with complete recovery of PTLD, yet eventual graft loss due to secondary oxalosis.

P025 *DE NOVO* PANCA-ASSOCIATED VASCULITIS IN A RENAL TRANSPLANT RECIPIENT AFTER ADJUSTING IMMUNOSUPPRESSION

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We present a 73-year-old, male, cadaveric renal transplant recipient with elevated serum-creatinine levels (216 μmol/l). Renal transplantation took place in 1995. Underlying disease was unclear and retrospectively evaluated as chronic glomerulonephritis.

A kidney transplant biopsy (12/2014) showed histological signs of calcineurin-inhibitor induced toxicity. Immunosuppression consisted of cyclosporine A, azathioprine and methylprednisolone. Consecutive conversion on belatacept, mycophenolate mofetil, methylprednisolone was established.

In march 2015 re-hospitalization, due to hydropic decompensation with pericardial effusion, took place (creatinine 315 μmol/l). A subsequent kidney transplant biopsy revealed extracapillary-proliferating, pauci-immune glomerulonephritis. At this time perinucelar antineutrophil cytoplasmatic antibodies (pANCA) 1:160 and anti-myeloperoxidase (MPO) 90.5 U/ml were found to be elevated.

We think of it as de novo pANCA-associated vasculitis in a renal transplant recipient after conversion of immunosuppressive therapy to belatacept, alternatively relaps of primary disease cannot be ruled out.

Vasculitis remission-induction therapy using prednisolone and rituximab (375 mg/m^2 of body-surface area per week for 4 weeks) as well as conversion of immunosuppressive therapy back to cyclosporine A, was established.

Summarizing, we report an unusual observation of de novo pANCA-vasculitis with MPO-specificity in a renal transplant recipient, without history of prior antibody associated vasculitis, after switching immunosuppression to belatacept because of calcineurin-inhibitor induced toxicity.

P027 IL-34 MEDIATES ACUTE KIDNEY INJURY WORSENING SUBSEQUENT CHRONIC KIDNEY DISEASE

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Macrophages (Mø) are integral in ischemia/reperfusion injury (I/R) incited acute kidney injury (AKI) that leads to fibrosis and chronic kidney disease (CKD). IL-34 and Colony Stimulating Factor 1 (CSF-1) share a receptor (*c-fms*), and both cytokines mediate Mø survival and proliferation, but also have distinct features. CSF-1 is central to kidney repair and destruction, the role of IL-34 until now is not known. In renal I/R in mice, the time-related magnitude of Mø mediated AKI and the subsequent CKD is markedly reduced in IL-34 deficient mice compared with wild-type mice (WT). As I/R injury is an inevitable consequence of the kidney transplant procedure we probed for CSF-1 and IL-34 expression in human kidney transplant biopsies. CSF-1, IL-34, cfms and PTP-z in TEC are upregulated in the engrafted kidney and rises even higher during acute kidney rejection. Accompanying IL-34 expression by TEC, we detect a pronounced rise in serum IL-34 during rejection compared with engraftment and healthy controls. Consistent with the level of IL-34 expression in TEC, we detect far more Mø ($CD68^+$) and neutrophils ($Ly6G^+$) in the renal interstitium. In conclusion, IL-34 dependent Mø mediated, CSF-1 non-redundant, mechanisms may promote persistent ischemia incited AKI that worsens subsequent CKD.

P028 SUCCESSFUL TREATMENT WITH ECULIZUMAB IN A YOUNG PATIENT DEVELOPING A SEVERE AHUS CAUSED BY AN ACUTE SEVERE VASCULAR TRANSPLANT REJECTION

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We report a 22 year-old patient undergoing kidney transplantation in 2006 because of urethral valves.

2013 patient developed proteinuria and elevated creatinine. Biopsy showed rejection BANFF 1b possibly due to non-adherence. After treatment with steroids and reintroduction of Tacrolimus and MMF creatinine remained at 200 umol/l.

2015 he developed urosepsis, declining graft function and pancytopenia, especially hemoglobin of 2.8 mmol/l – initially without signs of hemolysis. Antibiotic therapy was administered, MMF paused to the suspected toxic effects on the bone marrow indicated by bone marrow cytology. Urinary tract infection and pancytopenia recovered, whereas graft function deteriorated. Biopsy revealed vascular rejection Banff IIa and interstitial fibrosis of 80%.

Within the following day patient became anuric, severe hemolysis with detection of fragmentocytes and thrombopenia appeared .

Patient developed seizures, was intubated and renal replacement therapy (RRT) was started. Despite RRT potassium rose to 8 mmol/l.

Atypical hemolytic uremic syndrome (aHUS) was diagnosed (normal ADAM TS 13), one session of plasma exchange (TPE) was performed and eculizumab was administered once weekly (900 mg) for four weeks.

Subsequently, clinical symptoms stabilized quickly and patient recovered without neurologic sequelae.

This demonstrates successful treatment with eculizumab in de novo aHUS probably triggered by vascular transplant rejection.

P029 LONG-TERM QUALITY OF LIFE OF LIVING KIDNEY DONORS: A SINGLE CENTER EXPERIENCE

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Background: Over the last few years, the evaluation of the health related quality of life (QoL) of living kidney donors (LKD) has become of particular interest. Although the overall results are excellent, there are some concerns about psychological impairments and other negative long-term effects. The present study sought to evaluate the QoL and various clinical and paraclinical parameters of LKD.
Methods: Between 1998 and 2010, 72 living kidney donations were performed at our institution. To follow-up, clinical data concerning the donors was analysed. To assess the QoL, two questionnaires — the Short-Form 36 (SF-36) and a general questionnaire — were sent to all 72 living donors.
Results: There was no change in systolic and diastolic blood pressure during the follow up ($p = 0.933$ and 0.381). Mild proteinuria (> 150 mg/l) was observed in 6 cases. Out of 72 donors, 55 (76.4 %) responded to the questionnaires. The mean values of the physical and mental summation scale (PCS and MCS, respectively) were 51.3 (SD = 7.6) and 50.6 (SD = 8.1). Kidney donors had a higher QoL compared to the general population. Peri- or postoperative complications were associated with lower values for physical function (PF) and PCS ($p = 0.016$ and 0.030).
Discussion: Although some changes like mild proteinuria can be observed, living donor kidney transplantation (LDKT) is safe for donors. The QoL is excellent and potentially better than in the general population. To ensure a positive outcome for donors, a good clinical evaluation of potential donors is essential.

P030 A CASE OF A RENAL TRANSPLANT RECIPIENT AFTER STEM CELL TRANSPLANTATION WHO SUFFERED FROM MULTIPLE (OPPORTUNISTIC) INFECTIONS IN SPITE OF LOW LEVEL OF IMMUNOSUPPRESSION

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We report a 54-year old patient after allogenic peripheral blood stem cell transplantation (2000) due to acute lymphoblastic leukemia in sustained remission. In 2012 kidney transplantation (KTX) with low immunological risk (PRA 0%, Mismatch: 0-0-0) was performed.

The immunosuppression consisted of Tacrolimus, MMF and Prednisolone as well as induction with basiliximab.

Best creatinine after KTX was 200 umol/l, protocol biopsy after three months revealed BKV-nephropathy, therefore tacrolimus was switched to everolimus and MMF dose reduced.

Nevertheless allograft function deteriorated further with eGFR declining to 20 ml/min, BK-virus load in the blood increased to 900 000 copies and histology showed ongoing destructing polyomavirus infection.

Hence high dose of intravenous immunoglobulin was administered, leading to acute graft failure due to hemolysis, which recovered after treatment with steroids.

Renal function stabilized at low level (eGFR 20 ml/min) with dual immunosuppressive therapy with everolimus and prednisolone.

01/2015 the patient suffered from severe enteritis with clostridium difficile, further aggravating graft dysfunction.

05/2015 pneumocystis-pneumonia was diagnosed, renal function decreased further and renal replacement therapy had to be initiated.

In Conclusion we present a case of a renal transplant recipient after stem cell transplantation who suffered from multiple (opportunistic) infections in spite of low level of immunosuppression.

P031 A CASE OF RECURRENT, PRIOR UNKNOWN AND RAPIDLY PROGRESSING C3 GLOMERULONEPHRITIS, ACUTE RENAL FAILURE AND GRAFTED AHUS SUCCESSFULLY TREATED WITH ECULIZUMAB

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Presentation of Case: A 69 years old patient underwent kidney transplantation (KTx) in January 2013. She was on dialysis since 10/2010 and had a diagnosis of mesangioproliferative glomerulonephritis. The immunosuppression consisted of an basiliximab induction therapy together with tacrolimus, MMF and steroids. In 09/ 2013, a biopsy was performed due to increasing proteinuria and a diagnosis of C3 glomerulonephritis (C3GN) was made. Subsequent workup of the two native kidney biopsies demonstrated presence of C3GN in her native kidneys. We performed close monitoring of renal function and proteinuria. Comprehensive analysis of the complement system (function and genetics and antibody-screening) was performed. No causative factor was found. Six months after the diagnosis of recurrent C3GN she developed nephrotic syndrome and eGFR declined. Biopsy now demonstrated extracapillary proliferative C3GN, transplant rejection was excluded. We initiated therapeutic plasma exchange (TPE) in an effort to correct complement dysregulation and stabilize renal function. Following the first sessions of TPE she rapidly became dialysis dependent and developed all signs of atypical hemolytic uremic syndrome with severe hemolysis (requiring blood transfusion) and thrombocytopenia. She also developed neurologic symptoms.

We decided to initiate eculizumab therapy to halt aHUS and possibly treat the progressive C3GN. Complement inhibition terminated aHUS and eGFR began to rise. She was weaned from dialysis and clinical symptoms stabilized.

The eGFR is now, almost 1 year after the event between 40 and 50 ml/min (initial 65 ml/mkin), proteinuria is within the microalbuminuric range.
Conclusions: This case demonstrates a) the relevance of a proper diagnosis and necessity to reclassify such cases b) the chance for a successful treatment of C3GN and c) the close proximity of pathologies in C3GN and aHUS with a possible conversion of disease.

P032 TIME-COURSE AND PRELAVENCE OF PREDIABETES AND POST-TRANSPLANTATION DIABETES MELLITUS AFTER KIDNEY TRANSPLANTATION

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Background: Posttransplantation diabetes mellitus is an increasing problem in solid organ transplantation with prediabetes being a major risk factor. Here we describe time-course and prevalence of disturbances in glucose metabolism after kidney transplantation at a large European university hospital transplant center.
Methods: All consecutive renal transplant recipients from 2007 to 2014 were included in the analysis. Disturbances in glucose metabolism were assessed by retrospective chart analysis using fasting plasma glucose and HbA1c. Anthropometric data as well as data on allograft function and immunosuppression were collected.
Results: A total of 361 patients were included in analysis with a maximum follow up of 2551 days. 71 had known diabetes mellitus prior to transplantation. The prevalence of PTDM was 20% in month 3–6 and remained subsequently at around 15%. The prevalence of prediabetes was as high as 60% throughout the periods of observation.
Conclusion: We demonstrate the prevalence of disturbances in glucose metabolism after kidney transplantation to be as high as 80% with a maximum in the early post-transplant period. Most patients displayed prediabetes. Given the prognostic implications of PTDM and the predicative role of prediabetes, continuous screening for patients at risk and preventive strategies are required in long-term post-transplant care.

P033 PATHOPHYSIOLOGY OF DISTURBED GLUCOSE METABOLISM IN PATIENTS ON KIDNEY TRANSPLANT WAITING LIST: COMPARISON TO MATCHED CONTROLS WITH NORMAL RENAL FUNCTION

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Background: Glucose metabolism prior to transplantation affects the risk of post transplantation diabetes mellitus. The aim of the present study was to compare the pathophysiology of glucose metabolism (normal glucose tolerance, prediabetes) in patients listed for kidney transplantation and matched controls with normal renal function.
Methods: Patients without known diabetes mellitus on active kidney transplant waiting list were metabolically phenotyped. Matched controls were non-diabetic individuals with normal renal function. Matches were for (i) gender, age and BMI as well as for (ii) gender, age, BMI, fasting plasma glucose and 2 h glucose in oral glucose tolerance test (OGTT).
Results: A total of 107 patients and 107 controls were investigated. Waiting list patients had significantly lower fasting plasma glucose. Additional matching for OGTT glucose concentrations revealed significantly lower insulin sensitivity, but higher insulin secretion in waiting list patients, as compared to controls. In subanalysis according to glucose tolerance status, this difference was only present in subjects with normal glucose tolerance but not in subjects with prediabetes.
Conclusion: The pathopyhsiology of disturbances in glucose metabolism differs among patients on kidney transplant waiting list and matched controls with normal renal function.

P034 ROLE OF γδ T-CELLS IN ISCHEMIA REPERFUSION INJURY

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Background: Graft outcome is markedly influenced by ischemia reperfusion injury (IRI) in solid organ transplantation. Delayed graft function (DGF) correlates with duration of cold ischemia time (CIT) and varies between 5% (in living donation with 2–3 h CIT) and 25% (in deceased donation with 16 h CIT) after kidney transplantation. Moreover, DGF prolonged CIT is also a risk factor for chronic allograft fibrosis. γδ T-cells are involved in inflammation and immunomodulation and in this project we focused on the role of γδ T-cells in IRI induced inflammation and fibrosis by investigating γδ T-cell receptor deficient mice in the model of renal IRI.
Methods: IRI was induced in γδ T-cell receptor (TCR-γδ) deficient and wildtype (WT) mice by transient unilateral clamping of the left renal pedicle for 45 min. 7 days after IRI TCR-γδ deficient, WT and the contralateral control kidney were compared by histology, immunohistochemistry, qPCR and FACS analysis for inflammation and fibrosis. Moreover, long term outcome 3 weeks after IRI was investigated.
Results: Severe inflammation and acute tubular injury occurred in WT mice within 7 days after IRI. TCR-γδ deficient mice developed a similar phenotype. In addition, enhanced fibronectin expression in WT as well as in TCR-γδ deficient mice was detected after 3 weeks of follow up. By FACS analysis the absence of γδ T-cells was confirmed in the TCR-γδ deficient mice and moreover reduced IL-17A production was detected.
Conclusion: γδ T-cell receptor deficiency did not alter the course of IRI. Inflammation and progressive renal fibrosis were similar in WT and in TCR-γδ deficient mice.

KIDNEY/PANCREAS

P035 FOLLICULAR T-HELPER-CELLS ARE EXPANDED IN RENAL TRANSPLANT PATIENTS WITH DONOR SPECIFIC ANTIBODIES

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Background/Aim: Renal transplantation (RTx) is the treatment of choice for patients with end-stage renal disease. Immunosuppressive therapy controlling the alloresponse is critical to long-term renal allograft survival. Despite immunosuppressive therapy, some patients develop donor-specific antibodies (DSA) and are at risk for humoral antibody-mediated rejecton (AMR). Recent evidence indicates that a specialized T-cell subset (follicular T-helper-cells,Tfh) has a central role in inducing and enhancing humoral immune responses. Tfh may facilitate the development of DSA. Thus, it is the aim of this study to investigate Tfh in renal transplant patients.
Method: 48 renal transplant patients with DSA, 39 renal transplant patients without DSA and 24 age-matched healthy controls (HC) were enrolled. PBMC were isolated from peripheral blood by ficoll gradient isolation or whole blood lysis. Tfh were defined as being CXCR5+ and/or IL-21 + . Furthermore, the cytokine profile of CXCR5+ Tfh was characterized. Tfh were analyzed by flow cytometry.
Results: IL-21 + Tfh were significantly increased in renal transplant patients with DSA as compared to HC (IL-21$^+$, % of T-helper-cells: 11.5 $\pm$ 6% vs. 7.9 $\pm$ 3.2%, p = 0.006). However, renal transplant patients without DSA were not different from HC (8.4 $\pm$ 11% vs. 7.9 $\pm$ 3.2%, p = 0.3). Interestingly, Th1-like Tfh correlated negatively with serum creatinine in patients with DSA (r=−0.33, p = 0.06).
Conclusion: Tfh are increased in renal transplant patients with DSA and may be associated with renal allograft function. Further investigations are needed to assess the impact of Tfh on DSA formation and renal allograft outcome.

P036 ROLE OF IL17A IN HYPOXIA INDUCED ACUTE KIDNEY INJURY

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Background: In solid organ transplantation acute kidney injury (AKI) is a relevant complication and increases post-operative morbidity and mortality. In addition, AKI contributes to the progression to chronic kidney disease (CKD). IL17A as a pro-inflammatory cytokine is involved in immunomodulation in several diseases. In this project, we tested if IL17A deficiency or therapeutic blockade attenuates AKI and the progression to CKD in a mouse model of ischemia reperfusion injury (IRI).
Methods: IRI was induced in IL17A deficient and wildtype (WT) mice by transient unilateral clamping of the left renal pedicle for 45 min. After 7 days IL17A deficient, WT and the contralateral control kidney were compared by FACS, histology and immunohistochemistry to investigate acute tubular damage, leukocyte infiltration and fibrosis at different time points (d1, 7, 21).
Results: IRI caused severe inflammation and acute tubular injury in WT mice within 7 days after IRI. Surprisingly, IL17A deficient mice were not protected from IRI. In addition, IRI caused up-regulation of renal fibrosis with enhanced fibronectin expression in WT as well as in knock out mice. As expected up-regulation of IL17A production after *in vitro* cell stimulation with PMA/Ionomycin was only observed in the clipped kidney of the WT mice. When WT mice were treated with a therapeutic IL17A blocking antibody, results were in line with the knock out results. Inflammation was similar as in WT mice with vehicle treatment.
Conclusion: IL17A deficiency as well as IL17A therapeutic inhibition did not attenuate inflammation or tissue fibrosis in a mouse model of ischemia induced AKI.

P038 EFFECTS OF EARLY ANTIHYPERTENSIVE THERAPY ON ACUTE RENAL ISCHEMIA REPERFUSION INJURY

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Background: Many patients undergoing kidney transplantation are on hypertensive medication. After kidney transplantation ischemic allograft injury is present in 5–25% of cases and contributes to the delayed graft function. In this experimental study we investigated whether antihypertensive treatment has an effect on the severity of renal ischemia reperfusion injury (IRI).
Methods: In a CD1 mouse model we performed renal pedicle clamping to induce IRI and treated the mice with an ACE inhibitor or with the soluble epoxyhydroxylase (sEH) inhibitor TPPU and compared the results to vehicle treatment alone. Functional MRI to measure renal perfusion and histology work up was done.
Results: IRI resulted in an increase of systolic blood pressure by +20 mmHg in the vehicle group. By ACE inhibitor and by sEH inhibitor treatment blood pressure elevation was successfully attenuated and less glomerulosclerosis developed. However, by functional MRI using arterial spin labelling we could show that at day 1 after IRI renal perfusion impairment was aggravated by antihypertensive treatment. By immunohistochemistry we could show that the treatments had no effect on later fibrosis and tubular atrophy which developed in the treatment groups and in the vehicle group within 14 days.
Discussion: Antihypertensive treatment with an ACE inhibitor and with the sEH-inhibitor TPPU after IRI was potent in attenuating blood pressure elevatation and glomerulosclerosis. However, tubulo-interstitial fibrosis and inflammation was not influenced by antihypertensive therapy. Importantly, early renal perfusion was negatively affected by lowering systemic blood pressure.
Conclusion: The timing, type and dose of antihypertensive treatment for kidney transplantat recipients needs careful consideration in order to avoid worsening of renal perfusion impairment. Individual therapy decisions need to be made taking the existing co-morbidities (e.g. cardiovascular conditions) and duration of cold ischemia time which aggravates IRI into account.

P041 EFFECTS OF CYCLOSPORINE WITHDRAWAL ON GRAFT AND PATIENT SURVIVAL IN RENAL TRANSPLANT RECIPIENTS WITH PROGRESSIVE GRAFT DYSFUNCTION

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Objective: The effects of CNI withdrawal on graft loss and mortality in patients with progressive graft dysfunction remain elusive.
Methods: Adult patients who underwent kidney transplantation at the Charité-Universitätsmedizin Berlin were retrospectively included in the study. Progressive graft dysfunction yielding a creatinine value >3.5 mg/dl and a cyclosporibe based immunosuppressive triple regimen were defined as inclusion criteria. Patients were divided in two groups: in the CNI withdrawal group cyclosporine was stopped without prescription of another immunosuppressive agent. In the control group CNI was further administered.
Results: CNI was withdrawn at a mean of 72.8 $\pm$ 55.9 months after transplantation. eGFR did not differ between the groups at the time of CNI withdrawal ($p < 0.05$). However, at 120 months after transplantation patients without CNI demonstrated significant higher eGFR values compared to control patients ($p < 0.001$). CNI withdrawal was associated with a lower risk of graft loss (HR (95% CI) = 0.42 (0.27–0.66), $p < 0.001$) but not of all-cause mortality (HR (95% CI) = 0.63 (0.17–2.36), p = 0.49).
Conclusions: CNI withdrawal in patients with creatinine >3.5 mg and progressive graft dysfunction was associated with higher graft survival in this retrospective analysis.

P042 LONGTERM OUTCOME IN PANCREAS GRAFTS AFTER POLYOMAVIRUS INFECTION IN COMBINED KIDNEY-PANCREAS TRANSPLANTS: A SINGLE CENTER REPORT

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Purpose: We retrospectively analyzed the longterm survival and function in pancreas grafts after reduction of immunosuppression due to polyomavirus infection in simultaneous pancreas kidney transplants (SPK) performed at our center.
Methods: In totally 6 SPK recipients (among them one renal retransplant within a functioning pancreas) a polyomavirus infection was diagnosed by serum PCR in all cases (additionally biopsy proven in three patients) at mean 9.6 (1–30) months post transplant. The preceeding immunosuppression consisted of tacrolimus (TAC, $n = 5$) or cyclosporine A (CyA, $n = 1$) combined to MMF and steroids after an induction therapy with thymoglobuline ($n = 5$) or alemtuzumab ($n = 1$). The therapeutic regimens in the polyomavirus infection consisted of a dose reduction of TAC/CyA in all patients, conversion from TAC to CyA ($n = 2$), permanent discontinuation of MMF ($n = 1$) and application of Leflunomide ($n = 3$). The mean observation time was 35.3 (9–92) months.
Results: 5/6 (=83.3%) pancreas grafts remained at stable function within normoglycaemia without requirement of exogenous insulin and normal values of c-peptide. One pancreas was lost due to chronic rejection at month 21. Two kidneys were lost at month 11 and 13, respectively. The mean serum creatinine in the remaining renal grafts was 1.9 (1.0–2.6) mg/dl. The polyomavirus serum PCR turned completely negative in two patients at mean month 4.5 (2–7) after diagnosis and significantly decreased in four patients at mean month 12.0 (8–18).
Conclusion: a stable function in pancreas grafts can be kept if the immunosuppression is cautiously reduced in polyomavirus infected SPK patients. An early and regular post transplant screening of polyomavirus serum PCR is recommended.

P043 ONCE-DAILY MODIFIED-RELEASE TACROLIMUS IN DE NOVO SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT PATIENTS: A FIVE-YEAR PROSPECTIVE STUDY

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Backround: Data on the effectiveness of de novo once-daily tacrolimus (Advagraf) in simultaneous pancreas-kidney (SPK) transplant patients are limited.
Methods: From 09/2007 to 01/2011, 53 SPK recipients received an advagraf-based de novo immunosuppressive therapy. All patients received thymoglobuline induction, steroids and mycophenolate mofetil. Demographics, patient- and graft survival, rejection episodes, prescribed doses, trough levels, glomerular filtration rate (GFR, Cockroft-Gault formula), glucose-levels, and HbA1c values were collected prospectively.
Results: Overall patient, kidney, and pancreas graft survival were 87%, 81%, and 75% at a mean follow-up of 67.2 ± 18.3 months. Patient-, kidney- and pancreas survival rates at 1 and 5 years were 98%/90.5%, 92.4%/84.9% and 84.9%/79.2%. After a period of 5 years, 26 patients are still treated with Advagraf. After 1, 3 and 5 years mean GFR (ml/min) were 68.8 ± 30.2, 79.4 ± 20.1 and 81.3 ± 24.6; mean HbA1c-level (%) were 5.8 ± 0.9, 6.15 ± 1.1 and 6.2 ± 1.2 and mean fasting glucose-level (mg/dl) were 104.9 ± 26.6, 108.8 ± 36 and 99 ± 18.8. The incidence of biopsy proven acute rejection episodes within the first year was 37.7% ($n = 20$). In the early postoperative phase trough levels declined below determined target levels, despite significant increases in ADV dosage (mean dosage at postoperative day 14/21: 15.7/ 16.2 mg. Advagraf mean total daily dosage and whole-blood trough levels decreased over time.
Conclusion: Advagraf is an effective long-term immunosuppressant in simultaneous pancreas-kidney transplantation. Due to difficulties with the dose setting in the early postoperative phase, we recommend starting Advagraf not earlier than week 6 after SPK.

LIVER

P044 IMPACT OF ULTRASOUND ON DIAGNOSIS AND TREATMENT OF THE LIENALIS STEAL SYNDROME AFTER LIVER TRANSPLANTATION

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Introduction: The lienalis steal syndrom (LSS) is a know post transplant pathology with impaired arterial organ perfusion potentially leading to biliary complications and organ loss. We propose that routine ultrasound evaluation of liver hemodynamics after transplantation allows an early detection of LSS. The diagnosis is verified via angiography of the coeliac trunc and followed by an interventional plug embolization of the splenic artery. Postinterventional ultrasound depicts hemodynamic changes of the hepatic artery and the portal vein.
Methods: Between January 2012 and January 2015 all patients undergoing liver transplantation at our institution were routinely screened via ultrasound regarding the development of a LSS. The ultrasound examination encompasses resistive index (RI) measurement of the hepatic artery and flow velocity/volumetry investigation of the portal vein and the hepatic artery post transplantation and after splenic artery emobolization.
Results: In 218 patients 11 LSS (5%) were diagnosed and treated with interventional lienalis plug embolization. Ultrasound evaluation was suspicious in all patients showing elevated RI values of 0.72 (mean) and pathological portal vein hyperperfusion with 1.9 l/min (mean) flow volumetry. Postinterventional measurements showed a normalization of the hepatic artery RI with a mean value of 0.59 and a port venous flow of 1.1 l/min. Two patients developed non-anastomotic billiary strictures (NAS) and one patient died of subdural hematoma.
Conclusion: Routine ultrasound investigation allows an early detection of patients developing a lienalis steal syndrome after liver transplantation. Elevated resistance index (RI) values and portal vein hyperperfusion are solid markers to identify patients at risk. The therapeutic effects on liver hemodynamics after interventional lienalis coil embolization can be monitored via sonography.

P045 THE IMPACT OF PRE-TREATMENT ALPHA 1-FETOPROTEIN ON THE LONG-TERM PROGNOSIS AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Background: Alpha 1-fetoprotein (AFP) is an established diagnostic marker for hepatocellular carcinomas (HCC), but its role in the long-term prognosis after liver transplantation (LTX) is still unclear.
Methods: We reviewed 809 consecutive HCC patients treated at our department from 1995 to 2014, 143 of whom underwent LTX. The tumor register provided data on age, sex, treatment details, AFP, tumor diameter, number of tumors, Milan- and Duvoux-score and long term course. The Duvoux-score includes AFP in addition to number and diameter of tumors.
Results: The univariate analysis showed in palliatively treated patients a statistically significant influence of the pre-treatment AFP on the observed 10-year survival for all cut-off levels (7, 35, 400, 1000 ng/ml). None of those showed a statistically significant influence on the observed survival or the recurrence rate after LTX. The Milan-score had a statistically significant influence on the recurrence rate after LTX. The Duvoux-score had a statistically significant influence on the long-term survival and recurrence rates after LTX.
Conclusion: *Pre-treatment*: AFP provides in the univariate analysis no statistically significant information about the long-term survival after LTX. The Duvoux-score does have a statistically significant influence on the long-term survival as well as recurrence rate.

P046 FUNCTIONAL CHARACTERIZATION AND ANTI-COPPER RESPONSES TO ZINC AND D-PENICILLAMINE IN *ATP7B* MUTANT HEPATIC CELL LINES

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Background: In Wilson disease, mutations in liver copper transporter ATP7B result in copper (Cu) toxicity. D-penicillamine (DPA) and zinc (Zn) are commonly used to reverse toxic Cu. The impact of individual *ATP7B* mutations to treatment response is unknown.
Methods: Most common *ATP7B* mutations in Europe/USA, Asia and India were selected. Previously established *ATP7B* knockout HepG2 cell line was used to generate stable mutant cell lines (PLoS ONE, 9: e98809, 2014). Zn/DPA rescue from copper toxicity was determined.
Results: Mutant cell lines showed variable ATP7B protein expression compared to wild type. Co-localization studies with lamp2 marker suggested a trafficking defect. Cell viability assays showed different grades of activity for all mutant cell lines to evade toxic Cu with mutation p.H1069Q displaying moderate activity. Characteristic treatment responses were observed for individual cell lines on treatment. Overall, DPA was more effective as compared to Zn treatment. Interestingly, only Zn+DPA treatment could fully restore ATP7B activity as compared to wild type.
Conclusions: Different grades of ATP7B activity and a genotype-specific response on treatment were observed for individual mutations. The type of *ATP7B* mutation may modulate the efficacy of Zn and DPA treatment signifying that current regimens may benefit from knowledge of functional ATP7B parameters.

P048 5-YEAR FOLLOW-UP RESULTS OF THE PROTECT LIVER TRANSPLANTATION STUDY: EVEROLIMUS AND EARLY CALCINEURIN INHIBITOR WITHDRAWAL IS ASSOCIATED WITH SUPERIOR RENAL FUNCTION

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Background: After the 12 month (M) PROTECT core study, *de novo* liver transplant recipients (LTxR) randomized to switch from calcineurin inhibitor (CNI) based immunosuppression to everolimus (EVR) based regimen showed numerically higher renal function. This benefit was maintained for 3 years post LTx. Here we present the 5-year follow-up data from the PROTECT study.
Methods: PROTECT was an open-label, parallel-group, randomized controlled study in which LTxR received basiliximab and CNI-based immunosuppression +-steroids. Between Week 4 and 8, patients were randomized 1:1 to either EVR or continued CNI. In the EVR-group, CNI was tapered and completely withdrawn after 8 weeks. Patients who completed the core study were asked to enter the extension study and continue their randomized treatment. Key endpoints included change in renal function (eGFR by Cockcroft-Gault (CG)), efficacy failure (composite of BPAR, graft loss, death, or loss to follow-up), and incidence of adverse events and serious AEs.
Results: 81 patients entered the extension study (41, EVR; 40, CNI). At M 59 post randomization, the adjusted mean eGFR was significantly higher by 12.4 ml/min [95%CI: 1.2; 23.6; P = 0.0301] in the EVR group compared to the CNI-group. During the extension period, 3 deaths (1 EVR; 2 CNI) and no cases of graft loss occurred. Two BPARs occurred in the EVR group. SAEs occurred in 26 (63.4%) and 28 (70.0%) patients in the EVR and CNI-group, respectively. Commonly reported AEs were incisional hernia, nasopharyngitis, peripheral edema, diarrhea, and back pain.
Conclusion: Long-term EVR-facilitated CNI-free immunosuppressive regimen resulted in better renal function with as good patient and graft outcomes as compared to CNI standard.

P049 EFFICACY AND SAFETY OF GRAZOPREVIR AND ELBASVIR IN HEPATITIS C GENOTYPE 1-INFECTED PATIENTS WITH CHILD-PUGH CLASS B CIRRHOSIS

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Background: Improved treatments are needed for patients with hepatitis C virus (HCV) infection and advanced cirrhosis. The C-SALT study assessed the efficacy, safety and pharmacokinetics (PK) of grazoprevir (GZR) plus elbasvir (EBR) in patients with HCV infection and Child-Pugh class B (CP-B) cirrhosis.
Methods: CP-B patients with HCV infection received GZR (50 mg QD) and EBR (50 mg QD) for 12 weeks. Noncirrhotic patients with HCV infection were enrolled for PK analyses and received GZR (100 mg QD) plus EBR (50 mg QD) for 12 weeks. The primary end point was SVR12 in CP-B patients (HCV RNA

Results: 30 CP-B and 10 noncirrhotic patients were enrolled. Overall 27/30 (90.0%) of CP-B patients achieved SVR12: 1 patient developed spontaneous bacterial peritonitis and died because of hepatic failure and 2 patients relapsed. No patient had a treatment-related SAE, discontinued treatment, or had a grade 3/4 ALT elevation. Four patients had transient grade 3 total bilirubin elevations without increased ALT or AST. Geometric mean ratio (cirrhotic: noncirrhotic) for $AUC_{0\text{-}24}$ was 1.25 (0.70, 2.24) for grazoprevir and 0.90 (0.63, 1.60) for elbasvir.
Conclusions: High rates of SVR were observed in CP-B patients receiving GZR plus EBR. The regimen was well tolerated with no evidence of significant hepatotoxicity.

P050 EVEROLIMUS WITH REDUCED TACROLIMUS VERSUS STANDARD TACROLIMUS IN LIVING-DONOR LIVER TRANSPLANT RECIPIENTS: BASELINE DATA FROM THE H2307 STUDY

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Background: Living-donor liver transplant (LDLT) is a valuable option to bridge the gap for organ shortage. The CRAD001H2307 (NCT01888432) is an ongoing study that will evaluate for the first time the efficacy and safety of EVR + reduced TAC (rTAC) versus standard TAC (TAC-C) in LDLT recipients. Here, we present the baseline demographic characteristics of randomised patients evaluated by the Data Monitoring Committee (DMC) members.
Methods: H2307 is a 24-month (M), multicentre, controlled study aiming to randomise 280 LDLT recipients (1:1) into EVR (C_0 3–8 ng/ml) + rTAC (C_0 3–5 ng/ml) or TAC-C (6–10 ng/ml) after a 30-day run-in period with TAC (5–15 ng/ml) ± mycophenolate mofetil ± basiliximab and steroids as per study protocol. Primary objective is to compare the efficacy of EVR+rTAC versus TAC-C as measured by composite efficacy failure (treated biopsy-proven acute rejection, graft loss or death) at M12 post-LT. Secondary objectives are to compare changes in renal function assessed by estimated glomerular filtration rate (eGFR) from randomisation to M12, rate and time of hepatocellular carcinoma (HCC) recurrence, incidence of adverse events at M12 and M24 post-LT, among others.
Results: Patients are being recruited from 40 study centres across 12 countries. The DMC reviewed data from 103 randomised patients who are receiving study treatment, did not find any safety or efficacy concerns. The baseline data presented here includes age (53.1 ± 10.43 years), eGFR (108.5 ± 36.4 ml/min/1.73 m^2; $n = 93$) and model end-stage liver disease score of LDLT recipients (13.7 ± 5.3; $n = 101$).
Conclusion: H2307 study results will provide information on efficacy and overall safety as well as insights on HCC recurrence, and hepatitis viral replication in LDLT recipients treated with EVR+rTAC in comparison with those on TAC-C. Results are expected in 4th quarter of 2017.

P051 AGGRESSIVE SURGICAL MANAGEMENT IN COMBINATION WITH MTOR-INHIBITOR BASED IMMUNOSUPPRESSION ALLOWS SURVIVAL IN SELECTED PATIENTS WITH HCC RECURRENCE FOLLOWING LTX

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Introduction: Liver transplantation (LTX) for hepatocellular carcinoma (HCC) in cirrhosis represents a curative treatment in selected patients by elimination of the tumor together with the precancerotic liver cirrhosis. However, HCC recurrence after LTX occurring in 15–20% is a clinical challenge associated with poor outcome.
Methods: Retrospective analysis of all patients transplanted for HCC between 2001 and 2013 with special regard to patients with HCC recurrence (last follow-up 30 April 2015).
Results: 155 patients underwent primary LTX for HCC, thereof 29 (18.7%) developed HCC recurrence at a median of 14 (range 2–66) months after LTX. TNM-staging according to histology was T1:11.1%; T2:59.3%; T3:29.6%, N0:100%, M0:100%, V0:17.7%; V1:82.4%, G 1:14.8%; G2:66.7%; G3:18.5%, and R0:100% with a median maximum tumor diameter of 3.5 (1.5–17) cm and a median number of 2 (1–11) nodules. Localisation of recurrence included liver $n = 14$ (48%), lung $n = 17$ (59%), bone $n = 9$ (33%) and other intraabdominal localisation $n = 11$ (38%). At present, 19 (66%) patients have died due to HCC recurrence and 10 (34%) patients are alive (median follow-up 86 months). Dead patients experienced HCC recurrence earlier after LTX (median 13 (1–57) months), than patients still alive (median time LTX to recurrence 26 (2–66) months). At the time of recurrence 97% of the patients received a CNI-based immunosuppression (IS), thereof 21% in combination with an mTOR-inhibitor or mycophenolate mofetil, respectively, 3% of the patients were under m-TOR-inhibitor monotherapy. Immunosuppression after HCC recurrence included mTOR-inhibitors in 90% patients alive at the end of follow-up compared to 47% of patients who died. Survivors also underwent invasive treatment more frequently (70% tumor resection, 30% TACE, 10% ablation, 10 % radiation) than non-survivors (32% tumor resection, 16% radiation).
Conclusion: Analysis of our data showed that a multimodal concept after HCC recurrence including especially surgical recurrence resection and additionally switch of IS to an mTOR-based regiment enabled long-term survival in selected patients.

P052 EVEROLIMUS USE IMMEDIATELY AFTER LIVER TRANSPLANTATION

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Background: Clinical trials in LTX patients with randomization on day 30 to everolimus (EVR) show a benefit in renal function compared to calcineurin inhibitor (CNI) standard therapy. This late randomization was required due to a black box warning for hepatic artery thrombosis in trials using sirolimus, although no evidence existed with the use of everolimus based on phase II trials in LTX. Here we report our experience with EVR for different indications immediately after LTX in a number of patients.
Methods: Retrospective analysis of all adult LTX patients (2007–2012) in whom EVR was started within 3 month after LTX, divided in groups with de novo (≤5.pod) and delayed (>5.pod) EVR start.
Results: In 91 patients EVR therapy was started between pod 1–93 (target C0 3–8 ng/ml), median duration of EVR therapy 533 days. Concomitantly patients received low dose cyclosporine or tacrolimus (59.3%/25.3%; target C0 50–80/3–5 ng/ml). Main indication for EVR was impaired renal function (40%) and HCC (40%). EVR was discontinued due to AEs in 21 patients (23.1%), including hematological ($n = 5$) or dermatological ($n = 5$) side effects, wound healing disorder ($n = 2$), hypercholesterolemia ($n = 2$) or others ($n = 2$). 6 patients (6.6%) developed biopsy proven acute rejection (BPAR) after a median of 47 (range 27–356) days after LTX, there of 4 cases needed steroid therapy, all successfully treated. Overall 25 patients (27.5%) died after a median follow-up of 770 days, related to septicemia ($n = 7$), cardiorespiratory failure ($n = 7$) or HCC recurrence ($n = 4$). Comparing patients with de novo ($n = 50$) or delayed ($n = 41$) EVR start, we found no significant differences in terms of AEs, BPAR or death (p = 0.110–0.355). Wound infections or hernia were not more frequent in the group of patients with de novo (22%/22%) versus delayed EVR start (9.4%/29.3%). Renal function measured by creatinine/GFR was not different between both groups (de novo 1.2 mg/dl/56.4 ml/min/1.73 m^2;delayed 1.1 mg/dl/66 ml/min/1.73 m^2) and remained stable during follow-up (de novo 1.6 mg/dl/45.5 ml/min/1.73 m^2;delayed 1.2 mg/dl/57.4 ml/min/1.73 m^2; p = 0.092–0.210).
Conclusion: Our data show that EVR applied with very low dose CNI directly after LTX is safe and very effective resulting in a low rejection rate with the benefit of preserving renal function. There was no difference in wound healing complications between patients exposed to de novo or delayed EVR start.

P053 WHITE ADIPOSE TISSUE: A RESOURCE OF FUNCTIONAL PERIVENOUS AND PERIPORTAL HEPATOCYTE-LIKE CELLS FOR THE THERAPY OF LIVER DISEASE

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Background: Mesenchymal stem cells (MSC) may differentiate into hepatocyte-like cells *in vitro* and *in vivo* and may feature perivenous and periportal hepatocyte-specific functions. Thus they might be an alternative to hepatocyte transplantation in various liver diseases.
Methods: Adipose tissue-derived MSC from immunodeficient Pfp/Rag2$^{-/-}$ mice were isolated and differentiated. Morphology, cell surface markers and gene expression were documented.
Results: MSC changed their morphology into shapes of osteocytes, chondrocytes, adipocytes, and hepatocytes. Hematopoietic surface markers (CD45, CD14) were barely found. CD90, not expressed on mature mouse hepatocytes, decreased significantly after hepatocytic differentiation. Hepatic nuclear factor 4 alpha (HNF-4) involved in liver development or perivenous hepatocyte

enzymes like cytochrome P450 subtype 3a11 (CYP3a11) increased significantly. Similarly, periportal markers like carbamoylphosphate synthetase-1 (CPS-1), the key control enzyme of the urea cycle, were up-regulated. CYP450 enzyme activity and urea synthesis increased significantly to values comparable to cultured primary hepatocytes. *In vivo,* both perivenous and periportal qualities were preserved after hepatic transplantation.
Conclusion: Thus, adipose tissue-derived MSC differentiated into hepatocyte-like cells featuring periportal and perivenous functions. They might be promising candidates for the treatment of region-specific liver cell damage and support organ regeneration in acute and chronic liver diseases.

P054 GLUCOSE METABOLISM DURING INTRAHEPATIC SIZE REGULATION AFTER SIMULTANEOUS PORTAL VEIN LIGATION AND LIVER RESECTION

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Background: Despite the importance of glucose metabolism for regeneration and atrophy, the role of glucose metabolism is not well understood. The aim of this study was to evaluate intrahepatic spatially resolved glucose metabolism in case of two concurrent signals acting on a liver lobe.
Materials and Methods: Four male Wistar rats were subjected to right-PVL +70% partial-hepatectomy (rPVL+70%PHx). Animals underwent Fluordesoxyglucose (FDG) PET/MRI imaging to assess liver volume and FDG uptake before and 1, 2, 3 and 7 days after operation. The standardized uptake value (SUV) was calculated by dividing the mean radioactivity concentration in liver lobes by the injected dose per body weight.
Results: The ligated-right-lobe maintained its volume (93%) due to the concurrent regeneration signal, whereas the non-ligated-caudate-lobe increased substantially (590%). Decrease of total-glucose-uptake reflected the loss of total-liver-mass. The spatially resolved SUV reflected the volume of the respective liver lobe: almost unchanged in ligated-right lobe, increased in regenerating-remnant-liver.
Conclusion: Intrahepatic size regulation and glucose metabolism followed a different pattern in this model than observed in 80%PVL-substantial increase in SUV in atrophying-lobe and moderate increase in regenerating-lobe. The additional loss of liver mass and the relatively higher surgical stress due to the major liver resection probably contributed to the severely disturbed glucose homeostasis.

P055 VISUALIZATION OF LIVER PARENCHYMAL AND VASCULAR REGENERATION AFTER 70%PH IN MICE

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Background: The aim of this study was to establish a method to visualize and quantify vascular regeneration based on imaging data.
Methods : Vascular and territories reconstructions of portal and hepatic venous system were obtained by injecting a contrast agent (Microfil®) and subsequent μCT-imaging of the explanted regenerating mouse liver. Total liver volume (TLV), lobar volume, total vascular length and volume indicative of parenchymal and vascular liver regeneration was determined based on the 3D reconstructions using Imalytics ® and MevisLab®
Results: Up to now, we performed 49 microfil injections (22portal-vein, 27hepatic-vein) before, immediately, 2 and 7 days after 70%liver-resection. The increase in TLV was similar to the increase in liver weight. Vascular growth consisted of enlarging the diameter and length of the vascular stem with its main branches and outgrowth of additional terminal branches in both the portal-venous and hepatic-venous tree. Maximal vessel length of right-inferior-portal-vein increased by 1.2 fold whereas lobar volume increased by 2–3 fold, suggesting a nearly concentric growth.
Conclusion: CT imaging of explanted livers after contrasting the vascular tree with microfil represents a useful tool for visualizing and quantifying vascular regeneration. These data are of special value to generate scale-spanning system biology models of hepatic regeneration.

P056 ORTHOTOPIC LIVER TRANSPLANTATION FOR GIANT LIVER HEMANGIOMA: A CASE REPORT

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Background: In liver-hemangiomas, with increasing size, the risk of complications rises and treatment can be obligatory. Here we present the case of a 46 year old female who suffered from a giant hemangioma (size 21.7 x 23.7 x 25.5 cm, involving segments IV and V-VIII) causing severe portal hypertension and vena cava compression leading to therapy refractory ascites, hyponatremia and venostasis-associated thrombosis with pulmonary embolism. Tumor rupture or consumptive coagulopathy remained absent.
Methods: Surgical resection was impossible because of steatosis of the future liver-remnant. Orthotopic liver transplantation was identified as the only treatment option.
Results: Despite the progressing morbidity of the patient, her kidney-function remained stable and organ allocation according to the labMELD was improbable. Therefore a non-standard exception status was approved by the European organ allocation network "Eurotransplant". The patient received successful orthotopic liver transplantation 16 months after admission to our center. On outpatient follow-up, the patient presented well, with normal liver function tests and absence of ascites and had begun to resume a normal level of every day activity.
According to the SF30-Health Survey the life quality of our patient rose after transplantation in both tested categories. The physical score increased from 15.3 to 40.5; the value of the mental component grew 5.9 points and was 64.3 seven weeks after transplantation.
Conclusion: This case highlights the fact that liver transplantation should be considered early on in patients with non resectable, symptomatic benign liver tumors. Furthermore it indicates the necessity to promptly apply for a non-standard exception status to enable transplantation in patients with severe clinical condition but low labMELD score. Our case report therefore stands exemplarily for the underrepresentation of morbidity associated with refractory ascites in the labMELD-based transplant allocation system.

P057 TREATMENT WITH LITHIUM REDUCED ISCHEMIA-REPERFUSION INJURY IN STEATOTIC LIVER IN RATS VIA MODULATION OF AUTOPHAGY

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Background: Treatment with lithium can reduce ischemia-reperfusion (I/R) injury in liver via an upregulation of autophagy. In this study, we aimed to evaluate the effects of lithium in selective warm I/R model of steatotic liver in rats.
Methods: Moderate hepatic steatosis was induced in male Lewis rats by feeding a high fat and methionine-choline reduced diet for 14 days. Treatment groups received lithium (2 mmol/kg/day, 3 days before and after ischemia). Selective warm ischemia/ reperfusion was induced by clamping the hepatoduodenal ligament of the left lateral and median lobe for 60 min. Animals were observed for 30 min, 6 h, 24 h and 48 h (n = 6/group). Read-out parameters consisted of serum liver enzymes level, HMGB1 translocation and release, inflammatory cytokines level, liver neutrophil infiltration, MAPK, Caspase 3 and LC3 expression level.
Results: Treatment with lithium protected against I/R injury in steatotic liver, as indicated by lower serum aminotransferase levels, as well as higher MAPK-pathway-activation, lower inflammatory response, intracellular stress, less apoptosis and more autophagy.
Conclusion: Treatment with lithium may be a simple way for protecting against I/R injury in steatotic livers. The mechanism of action of lithium appears to involve its ability to activate MAPK pathways, induce autophagy, as well as to reduce inflammation, I/R-induced intracellular stress, and apoptosis.

P060 COMPARISON OF OUTCOMES FOLLOWING LIVER TRANSPLANTATION AND LIVER RESECTION FOR HEPATOCELLULAR CARCINOMA

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Background: The selection between liver transplantation (LT) and liver resection (LR), for the treatment of hepatocellular carcinoma (HCC) in patients with cirrhosis remains challenging, considering the donor organ shortage and the risk for liver insufficiency after resection. Therefore, the aim of this study was to compare the outcomes of LT and LR for HCC.
Methods: Clinicopathological data of patients who underwent LT and LR for HCC between 1989 and 2011 were retrospectively evaluated. Postoperative and long-term outcomes of patients with cirrhosis were compared between the two groups.
Results: During the study period, 361 and 85 patients ≤70 years old with cirrhosis underwent LT and LR for HCC, respectively. Postoperative morbidity (51% vs. 14%, P < .0001) and mortality (6% vs. 3%, P = .154) were higher after LR than after LT. Overall survival (OS) was significantly better following LT (n = 213) compared to LR (n = 37) (5y-OS: 75% vs. 57%; P = .001), in patients within Milan Criteria (MC). In patients beyond MC, there was no difference between LT (n = 148) and LR (n = 48) (5y-OS: 44% vs. 37%, P = .259). However, when analyzing younger patients ≤60 years old, OS after LT was better than after LR both within (5y-OS: 79% vs. 60%, P = .014) and beyond MC (5y-OS: 47% vs. 25%, P = .035).
Conclusions: LT for HCC within MC is associated with better postoperative and long-term outcomes in patients with cirrhosis compared to LR, and can thus be confirmed as the treatment of choice. Beyond MC, LT may provide a cancer-related survival benefit to younger patients with cirrhosis and should be considered in the living-donor setting, especially if tumor biology markers such as DNA-Index and α-fetoprotein are favorable.

P061 IMPACT OF DIFFERENT IMMUNOSUPPRESSIVE REGIMENS ON THE HEALTH-RELATED QUALITY OF LIFE FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION

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Background: The influence of immunosuppression on the recipients' quality of life (QoL) is of major importance after orthotopic liver transplantation (OLT) has not yet been evaluated.
Methods: The impact of different immunosuppression regimens after OLT was evaluated in 275 patients using the Short Form 36 (SF-36) survey. Following immunosuppressive strategies were compared: (a) CNI, (b) mTOR inhibitors and (c) mTOR combined with CNI. All regimes were prescribed alone (mono) or in combination (+) with prednisolone and/or mycophenolate mofetil (MMF).
Results: Highest scores were evident in patients in the mTOR+ group. There were significantly higher values for general health perceptions (GH, p = 0.049), vitality (VIT, p = 0.020) and physical component summary (PCS, p = 0.041) when compared to CNImono and for GH (p = 0.042) and VIT (p = 0.043), when compared to mTORmono. Early conversion to mTOR inhibitors (< 2 months after OLT) was associated with higher values for 7 of 10 scales, when compared to a late conversion (> 2 months after OLT), with a statistically significant improvement for the dimension role-emotional (RE, p = 0.027).
Discussion: mTOR inhibitor-based regimens appear to have beneficial effects on QoL after OLT, especially after an early conversion.

P062 TREATMENT OF HEV INFECTIONS IN SOLID ORGAN TRANSPLANT RECIPIENTS WITH RIBAVIRIN

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Background: Ribavirin has been shown to be effective in solid organ transplant recipients with hepatitis E virus (HEV) infections. However, the effectivity and safety of this treatment needs further evalution.
Methods: We retrospectively studied 23 HEV-infected solid organ transplant recipients receiving ribavirin-therapy. Ribavirin-therapy was initiated a mean of 75 months (range 3–303) after transplantation at a median dose of 800 mg/day (range 400 to 1000). Patients received ribavirin for a median of 4.5 months (range 3–10).
Results: Successfull ribavirin-therapy leading to sustained virological response (SVR) was observed in 87% of the patients. Treatment failure was observed in three patients (one breakthrough, 2 relapses). In one of these patients a second course of ribavirin for 8 months led to SVR (initial treatment duration: 6 months), while prolonged treatment and retreatment failed to achieve SVR in the two remaining patients. One patient died from complications of liver cirrhosis after experiencing a virological breakthrough. All three patients with initial treatment failure were carrying an HEV-strain with the G1634R-mutation, which has previously been associated with improved viral replication.
Conclusions: This retrospective analysis confirms that ribavirin is a safe and efficent treatment option in solid organ transplant recipients. However, treatment failure may occur.

P063 ANXIETY, DEPRESSION, OPTIMISM AND PESSIMISM IN PATIENTS BEFORE AND AFTER LIVER TRANSPLANTATION

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Background: Liver transplantation can be life-saving for patients but is related to high morbidity rates as well. The current study seeks to evaluate the influence of liver transplantation on anxiety, depression and dispositional optimism.
Material and Methods: Depression and anxiety were assessed with the HADS questionnaire. Dispositional optimism was measured using the LOT-R test. The findings were compared with the results from the general population.
Results: The number of returned questionnaires was 292 of 689 (235 liver transplant recipients: OLT group, 57 patients on the liver transplant waiting list: waiting group). Both depression and anxiety scores were significantly higher in the waiting group compared to the OLT group (p < 0.05) and compared to the general population (anxiety: p < 0.001, depression: p < 0.05)

The OLT group showed significantly higher anxiety scores (p < 0.001) than the general population with no differences in the depression and summation scores (p > 0.05).

The scores for dispositional optimism were higher in the OLT group (15.8, SD = 4.1) compared to the waiting group (14.0, SD = 3.9, p < 0.05). The general population had equal values as the waiting group (p > 0.05). The optimism score was higher in the OLT group than in the reference population (p < 0.01).
Conclusion: Liver transplantation significantly reduces depression and anxiety and appears to lead to a more optimistic view of life.

P065 MACROPHAGE INVASION IN HEPATOCELLULAR CARCINOMA ASSOCIATES WITH RECURRENCE AND GRAFT REJECTION AFTER LIVER TRANSPLANTATION

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Introduction: Tumor-associated macrophages (TAMs) promote tumor progression and have an effect on survival in human cancer. However, little is known regarding their influence on tumor progression, graft rejection and prognosis after orthotopic liver transplantation for hepatocellular carcinoma (HCC).
Methods: We analyzed tumor specimens of HCC (n = 32) in hepatectomy specimens for distribution and localization of TAMs, as defined by expression of CD68. Abundance of TAMs was correlated with clinicopathologic characteristics, tumor recurrence and patients' survival after liver transplantation. None of the patients received neoadjuvant radio- and/or chemotherapy prior to transplantation. Statistical analysis was performed using SPSS software.
Results: Patients with high prevalence of TAMs in tumorous tissue (TT) of hepatectomy specimen showed significantly higher graft tumor recurrence following liver transplantation (ρ < 0.05). Furthermore, high expression of TAMs in tumor invasive front (TIF) of hepatectomy specimen was associated with increased incidence of graft acute rejection after liver transplantation (ρ < 0.05). Tumor recurrence and graft rejection, respectively, were confirmed as independent prognostic variables in the multivariate survival analysis (both ρ < 0.05).
Conclusion: Our study provides first evidence that CD68 associates with clinicopathological parameters following liver transplantation for HCC. Tumor recurrence in graft and acute rejection after transplantation were significantly higher in patients with high expressions of CD68 in HCC of hepatectomy specimen. CD68 might serve as a potential biomarker in HCC in the setting of liver transplantation, whereas further studies are needed to elucidate its functional role.

P068 ABO MISMATCH INCREASES BILE DUCT COMPLICATION RATE IN DECEASED DONOR LIVER TRANSPLANTATION

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Background: Acceptance of liver allografts with a blood group mismatch in high urgency allocation (HUA) is common practice and helps to receive an organ in time. While patient and graft survival in patients transplanted with an ABO incompatible graft have been previously described, we herein present novel insights into bile duct complications in this setting.
Methods : This retrospective analysis included 413 consecutive adult recipients of deceased donor liver grafts between 1/2005 and 12/2012 at our centre. Statistical analysis was performed with fisher´s exact and Mann-Whitney test, survival was estimated with Kaplan-Meier plot. Linear regression was performed using backwards model and Wald-test.
Results: A total of 13 (3.1%) patients received liver grafts with ABO mismatch. Patient characteristics differed in hospital discharge (35 vs. 23 days; $p = 0.004$), cirrhosis (69.2 vs. 93.5%; $p = 0.01$), CMV mismatch (76.9 vs. 48.0%; $p = 0.04$), Re-transplantation (46.2 vs. 9.0%; $p = 0.001$), HUA (30.8 vs. 4.3%; $p = 0.003$) and gender mismatch (61.5 vs. 33.0%; $p = 0.04$). Five-year patient and graft survival for ABO mismatch (76.9, 76.9%) was not significantly different (79.5, 75.9%; $p = 0.26$, $p = 0.47$). Bile duct complications (53.8 vs. 19.8%; $p = 0.008$), leakage (30.8 vs. 10.3%; $p = 0.04$), non anastomotic stenosis (23.1 vs. 4.8%; $p = 0.03$), anastomotic stenosis (28.6 vs. 10.3%; $p = 0.04$), re-operation rate (23.1 vs. 4.8%; $p = 0.04$) and mortality (23.1 vs. 2.0%; $p = 0.003$) were higher in ABO mismatch recipients. Linear regression model identified ABO mismatch (HR 4.518; $p = 0.02$), recipient BMI (HR 1.078; $p = 0.03$), hepaticojejunostomy (HR 3.975; $p = 0.001$), arterial complication (HR 3.975; $p = 0.001$) and venous thrombosis (HR 10.432; $p = 0.002$) as independent factors for bile duct complications.
Conclusion: Patients receiving liver grafts with ABO mismatch showed similar patient and graft survival compared to the control group. ABO mismatch was identified as independent factor for the development of bile duct complications.

P070 SAFETY AND EFFICACY OF DACLATASVIR PLUS SOFOSBUVIR WITH OR WITHOUT RIBAVIRIN FOR HEPATITIS C POST-TRANSPLANT: INTERIM RESULTS FROM THE COMPASSIONATE USE PROGRAM

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Background: Recurrence of hepatitis C in the post-liver transplant (LT) setting is a significant concern and interferon-free therapies are needed. We report here results for a subgroup of LT recipients with HCV recurrence from a compassionate use program of DCV+SOF±RBV.
Methods: Adult patients with chronic HCV infection at high risk of hepatic decompensation or death within 12 months, with no available treatment options, received DCV 60 mg+SOF 400 mg QD for 24 weeks; RBV was added at physicians' discretion. This interim analysis includes 87 LT recipients with recurrent hepatitis C with available data at 16/03/2015.
Results: Most patients were male (60; 69%); median age: 58 years (39, 75). Most were infected with HCV genotype-1 (76; 87%) and 26 (30%) received RBV. Median time since LT: 3.3 years (0.3, 21.5). Thirty-five (40%) patients had cirrhosis; Child-Pugh B/C: 13 (37%); MELD score $\geq$ 15: 8 (23%). Of 38 patients with available HCV-RNA at 12 weeks posttreatment, all achieved virologic response (SVR12 100%). Severe adverse events (AEs) occurred in 18 (21%) patients; 6 patients discontinued therapy for AE; 3 patients died (1 liver-disease; 2 sepsis).
Conclusion: In this preliminary analysis DCV+SOF±RBV demonstrated high rates of SVR12 and was well tolerated in this difficult-to-treat LT population.

P071 MONTH 12 SUBGROUP ANALYSIS OF THE H2304 STUDY: GENDER-EFFECT ON TRANSPLANT-RELATED OUTCOMES

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Background: There is growing evidence towards gender specific differing outcomes between male and female liver Tx recipients (LTxR). At month (M) 12 after LTx, the H2304 study showed that everolimus (EVR) facilitates early tacrolimus (TAC) reduction with comparable efficacy and superior renal function versus standard TAC (TAC-C) regimen. Here, we present *post hoc* analysis on effect of gender on efficacy, renal function and the safety outcomes at M12 post-LTx.
Methods: H2304 is a 24-M, randomized, multicenter, open-label study in 719 *de novo* LTxR. After a 30-day post-LTx run-in period with TAC±mycophenolate LTxR were randomized 1:1:1 to either convert to EVR (C0 3–8 ng/ml) + reduced TAC (C0 3–5 ng/ml; EVR+rTAC; $n = 245$) or EVR (C0 6–10 ng/ml) and TAC withdrawal (TAC-WD; $n = 231$) at M4 or remain on TAC-C (C0 6–10 ng/ml; $n = 243$) with steroids. Primary endpoint at M12 was the composite efficacy failure rate of treated biopsy-proven acute rejection (tBPAR), graft loss or death. Key secondary endpoint was evolution of eGFR from randomization (RND) to M12 by MDRD4.
Results: Overall, 180 male (73.5%) and 65 female (26.5%) LTxR were randomized to EVR+rTAC and 179 male (73.7%) and 64 female (26.3%) to TAC-C. At M12, all patients showed lower incidence of tBPAR with EVR+rTAC (female 3.1% and male 2.8%) than with TAC-C (female 7.8% and male 6.7%). Change in eGFR from RND to M12 was +1.55 and −1.47 ml/min/1.73 m^2 for female and male recipients in the EVR+rTAC arm vs. −14.60 and −7.76 ml/min/1.73 m^2 for female and male recipients in the TAC-C arm. Overall incidence of adverse events (AEs) at M12 were comparable between gender and treatment arms (EVR+rTAC; female: 93.8% and male: 95.0 % vs. TAC-C; female: 92.1% and male: 96.1). The incidence of peripheral edema was higher in female in the EVR+rTAC arm (29.2%) than in male (13.3%) recipients, whereas the incidences were 7.9% for females and 11.8% for males in the TAC-C arm.
Conclusions: M12 data showed that both male and female recipients have improved eGFR with EVR+rTAC compared to those with TAC-C, as well as lower incidence of tBPAR. Although patient number is small and should be interpreted with caution, a better eGFR was observed in females receiving EVR+rTAC versus TAC-C. AE profile was comparable between genders and treatment arms.

P072 MONTH 12 SUBGROUP ANALYSIS OF THE H2304 STUDY: CLINICAL OUTCOMES OF TRANSPLANTATION BY MELD SCORE

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Background: The H2304 study demonstrated that everolimus (EVR) provides similar efficacy and superior renal function versus standard tacrolimus (TAC-C) in de novo liver transplant recipients (LTxR). Pre-planned subpopulation analyses by model-for end-stage liver disease (MELD) strata were performed. Here, we present the efficacy and safety parameters at month (M) 12 post-LTx by MELD score.
Methods: H2304 is a 24-M, multicenter, open-label, randomized study in de novo LTxR to compare the efficacy and safety of EVR (C0 3–8 ng/ml) + reduced-exposure tacrolimus (C0 3–5 ng/ml; EVR+rTAC) or EVR (C0 6–10 ng/ml) with TAC withdrawal (TAC-WD) at M4 to TAC-C (C0: 6–10 ng/ml); all arms include corticosteroids. Following 30 ± 5 day run-in period with TAC-based immunosuppression (± mycophenolate), LTxR were randomized 1:1:1 to the 3 arms. Primary endpoint at M12 was the composite efficacy failure rate of treated biopsy-proven acute rejection (tBPAR), graft loss or death. Secondary endpoint was evolution of renal function from randomization (RND) to M12 using eGFR measured by Modification of Diet in Renal Disease 4 (MDRD4).
Results: At M12, the composite efficacy failure rates across MELD scores (categories: <14; 15-<19; 20-<24; 25-<29; ≥30) in the EVR+rTAC arm were better than in the TAC-C arm ($n = 243$), with lower incidence of tBPARs in the EVR+rTAC versus TAC-C. Rate of graft loss or death was in favor of TAC-C. The eGFR from RND to M12 was better with EVR+rTAC even in the category of highest MELD score. The overall safety profile was similar between the two treatment groups at different MELD scores.
Conclusions: Across MELD categories including MELD ≥30, M12 data from the H2304 study showed better renal function with EVR+rTAC versus TAC-C, as well as lower incidence of tBPAR. The overall safety profile was comparable between treatment arms. Since patient numbers are small in the highest MELD categories, results should be interpreted with caution. Further research is needed to confirm results in the group of sickest patients.

P074 GLYCINE IS GRAFT PROTECTIVE AND PRESERVES KIDNEY FUNCTION AFTER LIVER TRANSPLANTATION: DATA OF THE HEGPOL-TRIAL [ISRCTN69350312]

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Background: Glycine, a non-essential amino acid, prevents tissues from several types of injury in various experimental models. Thus the HEGPOL-Trial was designed to assess both the efficacy and safety of glycine in liver transplantation (LTx).
Methods/Materials: A total of 130 patients undergoing primary LTx were randomized in a two-arm placebo-controlled multicenter double-blinded trial. While sixty six recipients were treated with i.v. glycine (4.4 %; 250 ml) controls ($n = 64$) received injectable water (250 ml) during the anhepatic phase. The same infusion was repeated once a day for the following 7 postoperative days (POD 1–7). Primary endpoints were peak levels of aspartate-aminotransaminase (AST), alanine-aminotransaminase (ALT) and graft survival. Secondary endpoints were liver injury based on histology, liver perfusion, AUC of both AST and ALT, early graft dysfunction and cyclosporine A-induced nephrotoxicity.
Results: Per protocol analysis has shown no difference between groups; however, patients with cut off plasma glycine values of ≥7000 μmol/l ($n = 29$) prior to reperfusion showed significantly lower serum ALT levels during the first 25 h after LTx. Further the eGFR was significantly better with glycine during the study. Patient survival was 86.2% compared with 72.6% in controls ($p = 0.08$).
Conclusion: Although the per protocol analysis could not verify the hypothesized effects of glycine, very high plasma concentrations of glycine achieved after its i.v. administration at the anhepatic phase and early after liver transplantation proved not only to be safe, but also hepatoprotective and nephroprotective. Trial Registration: HEGPOL; ISRCTN69350312.

PS, AN and GP have equally contributed to this work.

P075 RESULTS OF LIVER TRANSPLANTATIONS AND LIVER RESECTIONS IN PATIENTS WITH CAROLI-SYNDROME

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Introduction: Caroli-Syndrome is a congenital intrahepatic bile duct dilatation which can lead to fibrotic and cirrhotic liver morphology and is associated with recurrent infectious complications due to cholangitis. The aim of this study was to analyse outcome of patients with Caroli-Syndrome undergoing liver resection or transplantation.
Materials and Methods: Between 2004 and 2013 in total 924 liver resections and 547 liver transplantation were performed. Of patients with Caroli syndrome perioperative parameters, postoperative course and complications were retrospectively collected in a data base.
Results: Two patients (0.4%) underwent liver transplantation and in 11 patients (0.8%) anatomical liver resection was necessary due to Caroli-Syndrome. One liver transplantation was a living split-liver-transplantation, the other one was a postmortal transplantation. Except of a biliary stricture, which was treated successfully with biliary stenting, the postoperative follow-up over five years was uneventful. In comparison to other entities, patients resected due to Caroli-Syndrome were predominantly young females with low ASA score. Length of operation and hospital stay was shorter and postoperative morbidity was lower. There was no death. In three patients intrahepatic carcinoma was histologically confirmed.
Conclusion: Liver transplantation and liver resections in Caroli-Syndrome are rare, but overall associated with a low postoperative morbidity and mortality. In case of extensive biliary affection liver transplantation should be performed as early as possible to avoid recurrent septic cholangitis or development of intrahepatic carcinoma.

P076 POSTTRANSPLANT PEAK C-REACTIVE PROTEIN CORRELATES WITH ISCHEMIA-REPERFUSION INJURY AND RISK OF TUMOR RECURRENCE IN LIVER TRANSPLANT PATIENTS WITH HCC

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Background: Ischemia reperfusion (I/R) injury was shown to promote intra- and extrahepatic tumor outgrowth in liver transplant patients with hepatocellular carcinoma (HCC). C-reactive protein (CRP) is a parameter of inflammatory response to surgical trauma. The aim of this study was correlate posttransplant peak CRP-level with I/R-induced hepatocellular damage and recurrence-free survival following liver transplantation (LT) for HCC.
Material/Methods: 103 liver transplant patients with HCC were included. Based on explant histopathology, patients were classified as Milan In and Milan Out. ROC-analysis was used for determination of most optimal cut-off post-LT peak CRP-level. Peak CRP values along with other established clinicopathologic variables were correlated with early hepatocellular damage (transaminases, hepatic artery resistive index) and tumor-specific outcome.
Results: An optimal cut-off peak CRP-level of 3.5 mg/dl for overall and recurrence-free survival was assessed. In the high CRP-group (< 3.5 mg/dl), hepatocellular damage was higher and hepatic artery perfusion more compromised than in the low CRP-group (≤ 3.5 mg/dl; $p < 0.001$). Five patients in the low CRP-group (7.8%), but 19 patients of the high CRP-subset (48.7%) developed HCC relapse post-LT ($p < 0.001$). The 1- and 5-year disease-free survival rates were 95.3% and 91.7% in the low CRP-group, but 89.5% and 48.7% in high CRP-subset ($p < 0.001$). In multivariate analysis, presence of microvascular invasion (Hazard ratio [HR] 10.9), peak CRP >3.5 mg/dl (HR 4), AFP-level >400 IU/ml (HR 3) and total ischemia time >450 min (HR 3.4) were identified as independent predictors of HCC relapse. While CRP level had no predictive value in Milan In recipients, peak CRP-value (HR 5.8) together with microvascular invasion (HR 8.3) were identified as the only independent predictors of recurrence-free survival in Milan out patients. The 1- and 5-year tumor-free survival rates in this special subset were 94.4% and 88% the low ($n = 36$), but only 87.8% and 29.3% in the high CRP-patients ($n = 25$; $p < 0.001$).
Conclusion: Early posttransplant peak CRP values correlate with both, I/R-induced hepatocellular injury and risk of HCC recurrence. In particular patients with HCC exceeding the Milan criteria might, thus, benefit from targeting inflammatory mechanisms.

P077 OUTCOME OF PATIENTS WITH BUDD-CHIARI-SYNDROM AFTER LIVER TRANSPLANATION

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Background: Budd Chiari syndrome (BCS) is a rare disease with occlusion of the hepatic venous outflow tract. Aim of this study was to evaluate the outcome and thrombophilic risk factors in such patients undergoing liver transplantation (LT).
Patients and Methods: Between October 2001 and February 2012 thirteen patients (11 f/2 m) with BCS (11 acute, 2 subacute or chronic) underwent LT at the University Hospital of Regensburg. JAK-2 mutation analysis, thrombophilic screening, and outcome analysis were performed in all patients.
Results: Mean age at time of LT was 36 + 12 years. Eight of thirteen patients (61.5%) additionally had an acute portal vein thrombosis at time of diagnosis and presented with acute liver failure. The following thrombophilic risk factors were found: polycythemia vera ($n = 3$), essentiell thrombocythemia ($n = 5$), protein C deficiency ($n = 2$), others ($n = 3$). After LT all patients were on lifelong anticoagulation. Mean follow-up was 72 + 36 months, 11 patients are alive (causes of death: mamma carcinoma 3 years post-LT, recurrence of BCS 7 years post-LT). Three patients underwent re-LT (1 recurrent BCS). 6 of 13 patients are on cytoreductive therapy (hydroxyurea or anagrelide).
Conclusion: BCS is a good indication for LT in patients with liver failure, but recurrence of BCS may rarely occur.

P079 FRIEND OR FOE? T-TUBES DECREASING BILIARY COMPLICATIONS AFTER ORTHOTOPIC LIVER TRANSPLANTATION! AN ANALYSIS OF 1463 CONSECUTIVE PATIENTS UNDERGOING ORTHOTPIC LIVER TRANSPLANTATION

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Introduction: The application of T-Tubes for biliary tract reconstruction in orthotopic liver transplantation (OLT) still remains controversial. The aim of this study was to evaluate the impact of T-Tube placement during biliary tract reconstruction in orthotopic liver transplants on postoperative biliary complications (e.g. stenosis and leakage) and overall outcome.
Methods: A retrospective analysis of 1463 consecutive adult liver transplants with side-to-side choledocho-choledochostomy was performed using specific statistical regression tests on donor and recipient data obtained from a prospectively collected database.
Results: Biliary tract reconstruction with a T-Tube was performed in 89.6% (n = 1311) of all patients. Overall biliary complication rate was 16.6% (stenosis: 13%, (n = 190); leakage: 3.6%, (n = 52)). The incidence for both stenosis and leakage were significantly higher in patients without T-tubes ($p < 0.001$). Multivariate regression analysis revealed presence of T-Tube, donor age and preservation solution (UW) as significant independent prognostic factors/predictors for development of both biliary stenosis and leakage (all $p < 0.001$).
Conclusion: Our data demonstrate favorable outcomes for the use of T-Tubes for biliary tract reconstruction in orthotopic liver transplantation. A standardized utilization of T-Tubes should therefore be considered to further decrease the incidence of postoperative biliary complications.

P080 PORCINE DERMAL COLLAGEN GRAFTS FOR ABDOMINAL CLOSURE IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS ≤2 YEARS OF AGE WITH BILIARY ATRESIA

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Introduction: Primary wound closure after pediatric liver transplantation cannot always be achieved due to lack of intraabdominal space. At worst, excessive pressure from post-anhepatic small bowel edema or oversized grafts can lead to a compartment syndrome, which ultimately culminates in impaired graft perfusion and graft loss. Synthetic materials used for wound closure are frequently fertile soil for infections. Here we describe our experience of abdominal wound closure in pediatric liver transplant recipients using a biodegradable porcine dermal collagen graft (PDCG).
Patients and Methods: We performed a retrospective review of our pediatric liver transplant database targeting patients under ≤2 years and with previous Kasai portoenterostomies that received a PDCG for abdominal closure after liver transplantation.
Results: Between 2011 and 2013 seven patients with previous Kasai portoenterostomies received a PSCG for wound closure following liver transplantation. Recipient's age at time of transplantation was 9.08 (±5.49) month. Mean body weight and height were 6.6 (±1.1) kg and 63.1 (±7.8) cm respectively. 71.43% (5/7) received a living donor liver allograft (Seg. II, III) and 14.29% (1/7) received a deceased donor split (Seg. II, III) or a full size liver allogaft respectively. Mortality and re-transplantation rate was 0%. One (14.29%) patient with intestinal perforation required reoperation and one PDCG hat to be removed due to superinfection. No intraabdominal compartment syndrome, bile leakage and portal or hepatic artery thrombosis occurred.
Conclusion: PDCGs are key to successful abdominal closure in pediatric liver transplant recipients where primary wound closure cannot be achieved.

THORACIC ORGANS

P081 SURVIVAL ANALYSIS AND POSTOPERATIVE COMPLICATIONS AFTER VENTRICULAR ASSIST DEVICE IMPLANTATION; PROGNOSTIC VALUE OF INTERMACS SCALE

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Background: Ventricular assist devices (VADs) have been proven to be effective in improving survival in patients with refractory heart failure. This study evaluates retrospectively the patients' profiles, clinical outcomes, postoperative complications and mortality in patients who underwent VAD implantation in our center taking into account preoperative Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) levels.
Methods: Between August 2010 and March 2015, 104 patients underwent VAD implantation in our center. Patients were divided in 3 groups: Group A which includes patients at INTERMACS level 1. Group B which includes patients at INTERMACS level 2, 3 and group C which includes INTERMACS Level 4, 5 and 6. Patients' characteristics, incidence and time of onset of postoperative complications and mortality were compared between groups.
Results: Total mortality was higher in group A than in group C ($p = 0.03$), but not between groups B and C ($p = 0.1$). Early mortality (at 30 days after VAD) was higher in group A than in group B ($p = 0.02$) and group C ($p = 0.02$). After 30 days mortality was not different between groups. Sepsis, bleeding and ischemic stroke were among the most frequent post-operative complications.
Conclusion: INTERMACS scale correlates with outcomes after VAD implantation in our single center study.

P082 EXTRACORPOREAL LIFE SUPPORT (ECLS) AFTER HEART TRANSPLANTATION: IMPACT ON MORBIDITY AND MORTALITY

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Objective: The use of extracorporeal life support (ECLS, veno-arterial ECMO) in the early period after heart transplantation (htx) has enormously increased during the last years. Representing a very helpful, short-term device in patients with primary graft dysfunction (PGD), its consequences for the further course are still controversially discussed. We aimed to compare patients with and without ECLS early following htx.
Methods: 53 patients underwent htx in our department between 2010 and 4/2015. 12 patients were treated with ECLS due to graft dysfunction, with 7 intraoperative implantations (group ECLS-I) and 5 after arrival on ICU (ECLS-P). ECLS and noECLS patients were comparable regarding pre- and intraoperative parameter.
Results: In the ECLS group 6 patients died within 30 days (ECLS-I:3, ECLS-P:3). Survival at one year ($n = 44$) was 82.4 % (28/34) in noECLS patients compared to 50 % (5/10) after ECLS. The incidence of renal failure (no ECLS 17.6 % vs. 20 %) or of at least one graft rejection >I° (5.9 vs. 10 %) was comparable between both groups. Ventricular assist device before htx did not cause significant differences postoperatively between the groups.

However, in addition to a higher mortality, postoperative morbidity (mechanical ventilation, inotropic support, renal failure) was also increased in patients receiving ECLS on ICU compared to those with intraoperative implantation.
Conclusions: In patients with graft dysfunction after htx, ECLS represents a hemodynamic support which should be considered early in the intraoperative setting. Delayed application may significantly impair patients´outcome, more than ever in times of an increasing number of marginal donor organs.

P083 LUNG TRANSPLANTATION IN A MULTIDRUG-RESISTANT ACINETOBACTER BAUMANII COLONIZED PATIENT

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Background: Colonization or infection with various pathogens can frequently be found in patients listed for lung transplantation. Increased incidence of multi-resistant pathogens can aggravate peri-transplantation management or may even be prohibitive for transplantation.
Methods: Outbreak of multidrug-resistant Acinetobacter baumanii (MDR-*Ab*) was detected at our hospital. Management of a 50-year old patient with alpha-1-antitrypsin deficiency, listed for double-lung transplantation, receiving continuous intensive-care-unit treatment due to severe pneumonia with requirement for interventional-lung-assist (iLA) therapy over several months is presented. Along with the ICU-course, skin colonization with MDR-*Ab* occurred. Collaboratively in our interdisciplinary transplant conference and in concordance with official institutions, the patient was still considered as transplantable.
Results: The patient could successfully be double-lung transplanted. The initial need for further assisted ventilation or oxygen insufflation could be weaned off after the first month. Colistin (Polymyxine) was administered intravenous and inhalative in the first month. MDR-*Ab* was still detectable in skin swabs without evidence of systemic infection. After good recovery and clinically inapparence, the patient could be moved to a rehab-clinic two months after transplantation.
Conclusion: Transplantation with multidrug resistant colonized patients is feasible but should be evaluated on an individual basis. Collaborative interdisciplinary transplant teams are necessary for decision making and treatment of those high-risk patients.

P084 MODIFIED RIGHT ATRIAL ANASTOMOSIS (CAVOATRIAL TECHNIQUE) IN ORTHOTOPIC HEART TRANSPLANTATION: FOLLOW UP AND COMPARISON WITH THE BIATRIAL TECHNIQUE

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Background: In 1997, cavoatrial technique for orthotopic heart transplantation (oHTx) was first developed in our institution. The purpose of this study is reporting our experiences with this technique compared to biatrial technique.
Methods: Retrospectively 180 oHTx between 1997 and 2013 were analyzed. The applied transplantation techniques were biatrial technique ($n = 108$) and cavoatrial technique ($n = 72$). Intraoperative and postoperative data based on echocardiography and rhythm analysis.
Results: Demographic data were similar in both groups. Ischemic time, cardiopulmonary bypass and cross-clamp time were significantly shorter in biatrial group. Postoperatively, signs for right ventricular dysfunction were lower in the cavoatrial group (16.4% vs. 26.2%). Follow-up echocardiographic examination showed excellent results with no significant differences. After 5 years, occurrence of mild tricuspid regurgitation (TR) was low in both groups (35.4% vs. 24.9%). Rate of severe TR was also low (0% vs. 0%), similar to rate of permanent pacemaker implantations (13.3% vs. 10.0%). There were no significant differences in survival at one (77.6% vs. 81.2%) or five (69.6% vs. 72.4%) years between the groups.
Conclusion: This study showed excellent findings for both groups. Cavoatrial technique can be a safe and simple alternative for heart transplantation. Reduced postoperative rate of severe TR and implantations of permanent pacemaker encourage the use of this technique.

P085 NOVEL MINIMALLY-INVASIVE TECHNIQUE OF TRICUSPID VALVE RECONSTRUCTION IN A HEART TRANSPLANT RECIPIENT

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Objective: Tricuspid valve regurgitation represents a typical problem in heart transplant recipients. In severe cases conventional tricuspid valve reconstruction is high risk. We reasoned that a minimally-invasive strategy through a right sided mini-thoracotomy provides access to the tricuspid valve without the need for resternotomy total cardiopulmonary bypass and cross clamping.
Case Report: We report the case of a 57-year-old patient with ischemic cardiomyopathy and consecutive heart transplantation in 2008. Due to terminal renal failure he has been on dialysis. During the last two years our patient has developed increasing tricuspid valve regurgitation due to annulus dilatation, which was severe at the last presentations with ascites, cirrhosis of the liver, gastrointestinal bleeding, pleural effusions and dyspnoea. We performed tricuspid valve annuloplasty with a 28 mm Cosgrove band through a right sided mini-thoracotomy, single groin cannulation, without cross clamping or bicaval occlusion. The incision into the right atrium was made through the pericardium without further dissection. While the atrium was open, drainage was balanced by the perfusionist so that air drainage was kept to a minimum and visibility was good. The procedure was free of problems and the patient recovered uneventfully. So he could be discharged 9 days later with improved clinical conditions and minimal tricuspid valve regurgitation.

Conclusions: Tricuspid valve reconstruction using a minimally-invasive beating-heart technique without bicaval occlusion is possible also in heart transplant recipients. This technique is a valid treatment option for these and other high risk patients.

P086 ORGANISATIONAL STRUCTURES AND PRINCIPLES OF A STUDENT HEART AND LUNG TRANSPLANT PERFUSION SERVICE AT THE UNIVERSITY OF JENA

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Background: From 2000–2015, 209 thoracic organ transplantations were performed at the University Hospital Jena. For thoracic organ harvesting, cardiothoracic surgeons are supported by a medical-student run perfusion service, which differs from other services in Germany in various aspects: 1) All students are recruited directly by the department of cardiothoracic surgery during clinical traineeships. 2) These students are exclusively used for thoracic explantations for Jena. 3) The students assist in a wide-ranging remit during the explantation: Packaging of materials; communication with the surgical team at Jena and pilots/drivers during explantation; organ perfusion and surgical assistance at the operating table. The purpose of this abstract is to analyse the structures of the student perfusion service and its applicability to other centres.
Methods: We analysed the training structure, recruitment strategies, protocols of the explantations and students' contracts from 2000–2015.
Results: In total 32 medical students participated in the perfusion service within the last 15 years, with an average of 4.5 students being concomitantly active. Most students were recruited during clinical traineeship in cardiothoracic surgery or clinical rotations. Following recruitment, students received theoretical and practical training regarding the explantation process and observed ≥ 3 explantations. Median time to completed training was 64 (interquartile range [IQR]: 34–109) days with a median time of occupation of 23 (IQR: 15–31) months and 9 (IQR: 8–12) explantations. To improve incorporation of students into the team, many were simultaneously employed as operating assistants. Although students are recruited at the University of Jena, employment and payment per explantation are provided by the "Deutsche Stiftung für Organtransplantation" (DSO).
Conclusion: The student perfusion service is an integral part of the transplantation process at the department of cardiothoracic surgery in Jena and is funded by the DSO. The concept is cost-efficient and provides profound integration of students into the surgical transplantation process. It might be superior to a system relying on external students unrelated to the transplantation team and presents an alternative for other thoracic transplantation centres.

P087 SHORT-TERM VENTRICULAR ASSIST DEVICE AS A BRIDGE TO LONG-TERM ASSIST DEVICE – HEART TRANSPLANTATION IN CARDIOGENIC SHOCK: IS IT A JUSTIFIED STRATEGY?

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Background: Low cardiac output syndrome is associated with significant mortality. In patients with refractory low cardiac output left ventricular assist devices (VAD) are used to re-establish cardiac output and to prevent death. However, long term LVAD implantation in these is complicated by a high rate of right heart failure and mortality. Therefore our strategy is to implant a short term VAD (left or biventricular) as a bridge to long term LVAD or heart transplantation (HTx).
Methods: We retrospectively analysed data from patients who received a short term LVAD support prior to implantation of a long term LVAD or HTx between 2013 and 2014. We performed short term LVAD (CentriMag, Levotronix) implantation via median sternotomy with percutaneous cannulas. Patients were included regardless of perioperative status and severity of heart failure.
Results: A total of 14 patients were supported with a LVAD and 5 patients with a biventricular VAD. Duration of support ranged from 4 to 109 days, mean 25 ± 24 days. The overall survival to myocardial recovery, upgrade to long term VAD and Htx was 58 % ($n = 11$).
Conclusions: Currently short term VAD owing its capacity for full ventricular support represents an ideal solution for bridge to bridge or HTx.

P088 MALIGNANT TUMORS IN LUNG TRANSPLANT RECIPIENTS – A RETROSPECTIVE ANALYSIS

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Background: Immunosuppression after lung transplantation (LuTx) in patients with end-stage pulmonary disease consists of a fine line between organ tolerance and prevention of infections. Cancer immunosurveillance is considered to comprise crucial immune responses to arising tumor cells and is potentially restricted by immunosuppressive therapy.
Methods: We analyzed 238 patients, who were followed up after LuTx, regarding the occurrence of malignant diseases between 2000 and 2015. Therefore, we collected data on surgical procedure for Tx (single, double, or combined heart-lung Tx), smoking status, immunosuppressive therapy, infections, presence of chronic lung allograft dysfunction, interval from LuTx to establishment of tumor diagnosis, and histology of tumor according to TNM stage (7^{th} edition).
Results: We identified nine patients (3.8%, five men and four women) with one or more tumors following LuTx. Of these, pulmonary end-stage disease was due to chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), and pulmonary arterial hypertension (PAH), in three, five, and one patient, respectively. Six patients developed lung cancer, two non-melanoma skin cancer, one Epstein-Barr virus-positive primary central nervous system posttransplant lymphoproliferative disorder, one cholangiocarcinoma, and one prostate cancer. Lung cancer had developed in the graft of four (67.7%) and in the native lung of two single LuTx patients (33.3%). Seven lung transplant recipients (77.8%) had a smoking history including all lung cancer patients. One patient presented with three different tumors (lung, prostate, and skin cancer) and five had previously been treated for chronic lung allograft dysfunction. The median interval LuTx to tumor was 4.5 years (range 0.4–5.9), the shortest in ILD patients (1.9 years, 1.0–5.9) and for pulmonary adenocarcinoma (0.4 years). Only three tumors (27.3%) were diagnosed in a metastatic stage with a median interval of 0.8 years (0.4–4.5) from Tx to diagnosis. The median overall survival for all tumors was 3.9 years (0.1–7.7).
Conclusion: Lung cancer was the most frequent malignant tumor following LuTx in our study and its early diagnosis requires thorough post-Tx follow-up.

IMMUNOLOGY

P089 THE OPERATIONAL TRANSPLANT TOLERANCE AXIS: MSC – MDSC – TREG/TH17

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Prolonged use of pharmacological immunosuppression is associated with severe detrimental side-effects not least neurotoxicity and increased risk of opportunistic infections of de novo malignancies. Additionally, pharmacotherapy is also dependent on patient adherence. The immunomodulatory capacities of mesenchymal stem cells (MSCs) and multipotent adult progenitor cell (MAPCs) are currently the subject of preclinical and clinical assessment in solid organ transplantation. We have demonstrated that in a fully allogenic, rat heterotopic heart transplantation model, 3rd party MAPCs treatment (drug-free immunosuppression) can induce long-term, transferable acceptance and that tolerance was dependent on myeloid-derived immunosuppressive cells (MDSC). Recently we have shown that MSC induced long-term acceptance of allogeneic heart grafts in mice acts via MDSC-mediated conversion of Th17 cells into T(reg) cells. This is consistent with our current clinical observations that exposure to low-dose third-party MAPC is associated with an increased T (reg) frequency. Currently, the long term consequences of modulating the host immune system with allogenic MSC are unknown.

P090 CONCERTED T-CELL ACTIVITY AGAINST EARLY AND LATE BKV-ANTIGENS IS NECESSARY FOR VIRAL CLEARANCE

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Polyomavirus-BK (BKV) associated nephropathy is a known cause of graft failure. No specific therapy is established so far and viral load monitoring accompanied by adjustment of immunosuppression is the only known effective therapeutic option. We previously demonstrated BKV-specific T-cells as a factor predicting BKV-clearance and disease recovery. However, due to technical limitations, data on the role and specificity of different T-cell subsets including cytolytic/helper CD4 and CD8 T-cells is scarce and their specificity to early and late viral antigens is not defined.

We implemented a multi-parameter flow cytometry protocol and investigated the sensitivity and robustness of variable effector molecules (IFNg, TNFa, IL2, IL4, IL17, GranzymeB) and receptors (4-1BB, CD40L, PD1) as BKV-specific activation markers under immunosuppression. By detecting BKV-specific T-cells according to the expression of the receptors CD137 and CD154 in combination with the effector molecule GranzymeB, we were able to detect specific T-cells more sensitively (compared to IFNg-based approaches) and categorized them into cytolytic/helper T-cells. Subsequently, antiviral immunity of 37 kidney transplant patients in clinical follow up and of 15 healthy volunteers was dissected into cytolytic and helper T-cell responses. Next, we dissected cytolytic and helper T-cell responses according to early and late BKV-antigen specificity.

Our approach increased the sensitivity of detecting of BKV-specific T-cells by 4.2-fold (median) in comparison to previously used INFg-based detection by flow cytometry. Of importance, we showed that BKV clearance was observed when both, cytolytic and helper, T-cells were simultaneously detected. Interestingly, CD4 T-cells significantly contribute to viral clearance. Additionally we could assign Tbet driven CD4 T-cell responses to late BKV-antigens.

By using surface markers together with the cytolytic molecule GranzymeB we showed for the first time a necessary concerted action of cytolytic and helper T-cells against early and late BKV-antigens. This new approach allows a more sensitive and reliable monitoring of BKV-specific T-cells. It can prevent underestimation of BKV-specific immunity and improve the adjustment of immunosuppression, minimizing the risk of graft rejection.

P091 SUCCESSFUL MANAGEMENT OF "PASSENGER LYMPHOCYTE SYNDROME" IN AN AB0 COMPATIBLE, NON-IDENTICAL ISOLATED BOWEL TRANSPLANT

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Background: "Passenger Lymphocyte Syndrome" (PLS) is a rare disorder encountered in all types of compatible, non-identical AB0 organ transplantation. By definition activated donor (or "passenger") B-lymphocytes produce antibodies to the recipient's red cell antigens triggering hemolysis in some cases. Regarding small bowel transplantation (SBTx) four cases of PLS have been published so far. We here report the fifth case of PLS in SBTx and the first one describing the successful management of PLS in a cadaveric, isolated SBTx.
Methods: A 60-year old Caucasian female with blood type A Rh(D)+ suffered from short bowel syndrome after extensive mesenteric ischemia and subsequent total small bowel resection. Two years later she received a small bowel transplant from a 32-year old Caucasian female with blood type 0 Rh(D)+. The initial postoperative course was uneventful until on POD 9 a hemoglobin-drop of 4 g/dl (10 to 5.9) was noticed without signs of active bleeding. Laboratory results implied massive hemolysis and the DAT was strongly positive with Anti-IgG and Anti-C3d. Antibodies reacting to A1- and A2 erythrocytes could be demonstrated via IAT and eluation from the surface of the recipient's red blood cells (RBC). The presumptive diagnosis of "Passenger Lymphocyte Syndrome" was made and only donor-specific 0 Rh(D)+ packed red blood cells (PRBC) were infused from that point on. Subsequently the patient received three cycles of prednisolone and two cycles of plasmapheresis on POD 10 and 11. During the second cycle of plasmapheresis (POD 11) the patient became hemodynamically instable and fresh blood was noticed in the abdominal drains. Angiographically a bleeding aneurism of the pancreaticoduodenal artery could be coiled. In the following course the patient's hemoglobin levels were stable and laboratory results showed no more signs of hemolysis. The DAT and IAT turned negative on POD 33. Anti-A in the red blood cell eluate stayed weak positive until the patient was discharged from the hospital.
Results: The PLS in this patient could be successfully managed by a combination of increased immunosuppression, plasmapheresis and transfusion of PRBC of BG 0. The patient is in well being 12 months postoperatively without signs of hemolysis.
Conclusion: PLS is a rare but severe complication of AB0 compatible, non-identical organ transplantation. It should be included in the differential diagnosis of hemolysis in the non-BG identical setting of SBTx.

P093 AB0-INCOMPATIBLE PEDIATRIC HEART TRANSPLANTATION - SIGN OF INDUCED TOLERANCE AGAINST THE DONOR BLOOD GROUP AFTER PERMANENT AND IMPERMANENT ANTIGEN EXPOSURE

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Background: In pediatric heart transplantation AB0-incompatible transplantation is possible because of the immature immune system. There is no higher risk of hyperacute rejection. Studies revealed permanent absence of donor specific isohemagglutinins as sign of induced B-cell tolerance. Whether continues exposure to the donor antigen is necessary to induce and maintain B-cell tolerance is unknown.
Method: Analyse of the development of donor specific isohemagglutinins after AB0-incompatible pediatric heart transplantation.
Results: Between 2004 and 2014 six patients underwent AB0-incompatible heart transplantation (3 male). The mean age at transplantation was 7.7 months. None of the patients suffered from hyperacute rejection. However one patient (number 1) needed retransplantation because of hypertrophic obstructive cardiomyopathy. None of the patients developed normal isohemagglutinins against the donor blood group (maximum 1:16), despite a normal amount of isohemagglutinins against the third blood group. Patient number one underwent AB0-compatible retransplantation four years after AB0-incompatible transplantation. Also over the next four years the patient did not develop a normal isohemagglutinine titer against the donor blood group.
Conclusion: There is absence of donor specific isohemagglutinins after AB0-incompatible pediatric heart transplantation, perhaps as a sign of induced B-cell tolerance. The absence was provable after permanent and impermanent exposure to donor antigen.

P094 RENAL TRANSPLANTATION IN HIV-POSITIVE RENAL TRANSPLANT RECIPIENTS: EXPERIENCE AT THE MANNHEIM UNIVERSITY HOSPITAL

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Renal transplantation in HIV-positive patients with end-stage renal disease has in recent years become a successful treatment option.

We report two patients that underwent renal transplantation using a combination of basiliximab, CNIs, MMF and steroids with a "non-interacting" antiretroviral combination therapy consisting of stavudine or abacavir, lamivudine, and nevirapine.

We observed no acute rejection but a BKV infection in both patients.

In conclusion, a quadruple immunosuppression with an IL-2 receptor antagonist, a CNI, MMF and steroids appears to be advisable to prevent high rates of acute rejection, but if possible thereafter immunosuppression should be tapered rapidly (e.g. MMF stop, prednisolone dose 5 mg/day). The selection of antiretroviral agents should avoid compounds that interact severely with the immunosuppression used.

P096 DE NOVO DSA FORMATION - A POSSIBLE TRIGGER FOR ITBL IN LIVER ALLOGRAFTS

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Introduction: In time of an actual lack of grafts and the wider use of marginal organs, we have to meet the challenge of performing a liver transplantation by going of without a hitch. We have to consider long-term problems and how we could avoid them. Biliary complications still remain a severe clinical problem not only in the early postoperative course, but also in clinical follow-up. In particular the development of ITBL with a high morbidity and mortality rates requires complex therapeutic concepts.

Patients and Methods: We performed a retrospective analysis with collected consecutive database from 2008 to 2012 in 395 patients. The solid-phase Luminex® assay was used. We performed an examination of recipient blood at special time points

Results: We made an analysis of patients after OLT, which developed allograft complications due to a ITBL. We picked out patients in this population for de novo DSA, which were detected by standardized Luminex® assays at several time points after transplantation. We revealed 15 patients with ITBL out of the population group of 395 patients. Here 47% of 15 patients with ITBL provably developed de novo DSAs. We made matched pair analysis of these patients to patients, who developed no ITBL specific problems. The 15 patients with ITBL revealed a significant ($p = 0.03$) higher amount of de novo donor-specific Anti-HLA antibodies after OLT. In regard of the postoperative course concerning the endoscopic interventions after OLT there were high significant differences in the ITBL versus the control group: ERC ($p = 0.000$) and stenting (0.001).

Conclusion: This study demonstrates that an early de novo formation of donor-specific Anti-HLA antibodies after orthotopic liver transplantation results in increased development of ITBL. A founding prospective study for pre- and postoperative screening methods should be one of the new challenges in avoiding this complications in future patients.

BASIC SCIENCE

P097 THE LIPIDOME OF PANCREATIC ISLETS - BIOMARKER FOR ISLET QUALITY AND FUNCTION?

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Transplantation of pancreatic islet cells is nowadays applied as a successful treatment of type-1 diabetic patients. The quality control of human islets prior to transplantation is crucial for the clinical outcome. Remarkably, the field is still lacking sensitive tests or valid biomarkers that characterize the quality and predict the effectiveness of islets transplanted into diabetic patients. Several lipid classes are known to be critically involved in apoptosis, inflammation and stress response- major pathogeneic factors for pancreatic islets during organ procurement, isolation and transplantation. Within this project, we therefore aim at evaluating the sensitivity and predictive potential of lipidomic analysis for rodent and human islets and correlate results with established *in vitro* and *in vivo* assays.

Lipids were extracted with methyl-tert-butyl ether (MTBE), directly infused into a LTQ Orbitrap mass spectrometer, and subsequently identified and quantified by LIPID X software. The shotgun lipidomic analysis showed that stress response of isolated rat and human islets is accompanied by increased levels of ceramides, decreased levels of diacylglycerols, and concurrently by the increased abundance of phosphatidylserin. The consistent alterations of the lipidomic profile significantly correlated with, and positively predicted, islet viability (analysed by DNA-binding dye exclusion) and islet function (analysed by glucose stimulated insulin release) *in vitro*.

We assume that alterations of the lipidomic profile reflect various stress response pathways in a single multi-parametrical readout, thus representing a novel quality control assay with predictive value for pancreatic islets prior to transplantation.

P098 SPECIFIC INHIBITION OF RECEPTOR-TYROSIN-KINASE AND MTOR IMPROVES THE LONG-TERM OUTCOME AFTER EXPERIMENTAL LUNG TRANSPLANTATION

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Chronic lung allograft dysfunction (CLAD) is the main risk factor after lung transplantation (LTx). CLAD can be recognized as bronchiolitis obliterans syndrome (BOS) or restrictive allograft syndrome (RAS) or both. The pathogenesis remains unclear. Uncontrollable repair mechanisms with the release of growth factors are discussed and might be responsible for these processes. The aim was to confirm the efficacy of the combination therapy of two receptor-tyrosine-kinase-inhibitors (imatinib and vatalanib) in addition to an mTOR-inhibitor (everolimus) to attenuate the development of CLAD in a rat LTx model.

To evaluate the antifibrotic effects of imatinib (20 mg/kg/day i.g.), vatalanib (20 mg/kg/day i.g.) and everolimus (2.5 mg/kg/day i.g.) after LTx, a rat model of left lung allo-transplantation (F344-to-WKY) was used. Allogenic transplanted rats were treated with imatinib/vatalanib from day 0 to 60 and with everolimus from day 7 to 60. Non-treated animals were used as a reference.

In the non-treated control group, severe chronic rejection (ISHLT-C2R/D2R) was recognized in all rats on day 60. All allografts of the therapy group exhibited a significant reduction of chronic bronchiolar rejection (ISHLT-C; $p \leq 0.05$), chronic vascular rejection (ISHLT-D; $p \leq 0.05$) and interstitial fibrosis (IF; reduction of $p \leq 0.05$).

In conclusion, specific inhibition of receptors for plated-derived growth factor by imatinib and vascular endothelial growth factor by vatalanib combined with inhibition of mTOR by everolimus might delay the development of CLAD after LTx. This combination might be an interesting therapy for patients after LTx.

P099 HEMOCOMPATIBILITY TESTING ACCORDING TO ISO 10993-4: FUNCTIONALIZATION OF POLYCARBONATURETHANE CONSISTING OF A POLYETHYLENEIMINE HYDROGEL AND ANTI-THROMBIN III USING A CHANDLER-LOOP MODEL

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Purpose: Usage of polymers in cardiac surgery (e. g. small diameter vascular bypass grafts, pump chambers of ventricular assist systems) remains critical due to increased risk of thrombosis because of poor hemocompatibility of the polymer material. Polycarbonateurethane (PCU) is an attractive polymer for cardiac prosthesis because of its excellent mechanical properties. However, PCU is highly thrombogenic. Therefore, PCU was functionalized to improve anti-thrombotic properties.
Methods: Small diameter PCU grafts were modified using plasma treatment and immobilization of different hydrogels made of (1) polyethyleneglycoldiamine (PEG) and methyl-carboxy-dextran (coated with anti-thrombin III, PEG-Dex-ATIII), (2) PEG alone (connected with laminin nonapeptide (CDPGYIGSR) PEG-L), and (3) polyethyleneimine branched (coated with ATIII, PEI-ATIII). The grafts were circulated in a Chandler-loop model for 90 min at 37°C with human blood. Before and after circulation, parameters of the hemostatic system including coagulation, platelets, complement and leukocyte activation were investigated.
Results: PCU-PEI-ATIII significantly inhibited activation of coagulation (thrombin-anti-thrombin complex) and activation of platelets (ß-thromboglobulin). Furthermore, PCU-PEI-ATIII prevented activation of leukoyctes (PMN-elastasis) and complement activation (complement factor SC5b-9).
Conclusions: Surface modification using polyethylenimine hydrogels and covalent binding of ATIII seems to be an attractive chemical modification of PCU biomaterials for use as small-diameter bypass graft or as a pump chamber in ventricular assist devices.

P100 CHEMICAL MODIFICATIONS OF POLYCARBONATURETHANE TO IMPROVE ENDOTHELIALIALIZATION PROPERTIES- EFFECT OF SHEER STRESS

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Purpose: Pump chambers from ventricular assist devices were frequently made of polycarbonaturethane (PCU) because of its excellent mechanical properties. However, its restricted hemocompatibility required surface modification and/or endothelialization.
Methods: The surface of PCU was modified using nitrogen plasma treatment and/or binding of different hydrogels that were covalently connected with cell-active molecules (e.g. heparin, anti-thrombin III, argatroban, fibronectin, laminin, peptides with RGD binding motif). Biocompatibility of modified PCU was verified under blinded conditions using static and dynamic cell culture techniques.
Results: Platelet adhesion / endothelial cell (EC) adhesion (under *in vitro* conditions) was significantly reduced / increased in 13/35 and 14/35 modifications, respectively. Concomitance was documented in 6/35 modifications. 3/6 functionalized PCUs (direct coating of anti-thrombin III; polyethyleneglycol hydrogel; polyethyleneimine hydrogel connected with heparin) allowed not only EC adhesion but EC proliferation. Under sheer stress, only the 3rd modification improved EC density compared with non-modified PCU. However, ECs did not arrange in flow direction as observed for a polyetherurethane graft and cell anchorage was reduced.
Conclusion: Despite large variation in surface modification chemistry and improved EC adhesion under static culture conditions, additional introduction of sheer stress foiled promising preliminary data. Therefore, biocompatibility testing required not only static tests but also usage of physiological conditions such as sheer stress in the case of vascular grafts or ventricular pump chambers.

P101 SCREENING ANALYSIS OF FUNCTIONALIZED POLYURETHANE TO IMPROVE ITS BIOCOMPATIBILITY

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Progenitor cells were mobilized during extracorporeal membrane oxygenation (ECMO) as a response to pulmonary injury or blood-foreign surface interactions. Mononuclear cells were removed from the surface of explanted PMPMOs ($n = 16$), cultivated in endothelial cell medium, and characterized by flow cytometry using different surface markers. Native cells from the MOs were monocytoid and included a small subpopulation (<1%) of endothelial progenitor cells (CD45+/CD31+/VEGFRII+/CD133+ Spindle-shaped attaching cells were identified early, but without proliferative activity. After long-term cultivation palisading and cobblestone type outgrowth cells with high proliferative activity appeared and were characterized as (1) leukocytoid CD45+/CD31+ (CD133+/VEGFRII+/CD90+CD14+/CD146dim/CD105dim), (2) endothelial-like CD45-/CD31+ (VEGFRII+/CD146+/CD105+/CD133-/CD14-/CD90-), and (3) mesenchymal-like CD45-/CD31- (CD105+/CD90+/CD133dim/VEGFRII-/CD146-/

CD14-) cells. The distribution of the cell populations depended on the MO and cultivation time. Endothelial-like cells formed capillary-like structures and did update Dil-acetylated low-density lipoprotein. In conclusion, endothelial- and mesenchymal-like cells adhered on the surface of PMP-MOs. Further research is needed to assign the different outgrowth subpopulations to the disease state of the patient or the biocompatibility of the polymer surfaces.

P102 IMMUNOSUPPRESSIVE DRUGS MODULATE THE MICROENVIRONMENT IN SOLID ORGAN TRANSPLANTATION BY SUPPRESSING THE MTOR SIGNALING PATHWAY AND CHEMOKINE SECRETION IN PRIMARY HUMAN HEPATOCYTES

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Introduction: In the context of liver transplantation, NK-cells may play an important role by targeting the allogeneic organ. However, immunosuppression is supposed to control both T and NK cell-mediated alloreactivity. Since recent evidence suggests that immunosuppressive drugs may also affect non-immune cells, we investigated their suppressive capacity on signaling, proliferation and chemokine production of primary human hepatocytes and liver epithelial cells.
Materials & methods: Primary human hepatocytes (PHH) and hepatic epithelial cells were incubated with calcineurin (CNI) or mTOR inhibitors (mTORi) for 48 h and surface expression of T/NK cell ligands was analyzed by FACS. Phosphorylation of Akt/mTOR pathway components and chemokine production was assessed by multiplex techniques. Moreover, PHH were co-cultured with isolated NK cells under different proinflammatory conditions and NK cell activation was analyzed by FACS and cytokine arrays.
Results: Both CNI and mTORi blocked phosphorylation of kinases within the PI3K/Akt pathway in liver epithelial cells and chemokine secretion (e.g. CXCL1, 8, 12) was significantly suppressed. Surface expression of HLA class I and CD166 was slightly down-regulated. Under pro-inflammatory conditions like TLR or interferon stimulation, liver cells secreted cytokines (IL-6) and chemokines (CXCL8). Surprisingly, PHH suppressed NK cell activation, shown by DNAM-1 down-modulation and decreased IFN-γ, TNF-αexpression under IL-2- and IFN-α-but not IL-12/IL-15-mediated activation.

In conclusion, the suppressive capacity of CNI and mTORi on epithelial cells may represent underestimated mechanism with strong impact on tolerance/rejection after liver transplantation. Moreover, hepatic epithelial cells may contribute to immunomodulation after liver transplantation by suppressing NK cell responses depending on the inflammatory condition.

P103 CYTOPLASMIC HMGB1 INTERACTS WITH PARTNER PROTEINS RESULTING IN HEPATOCELLULAR DAMAGE IN WARM ISCHEMIA/REPERFUSION INJURY

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Introduction: Warm ischemia/reperfusion (WI/R) injury occurs in liver transplantations and results in liver dysfunction. During WI/R, HMGB1 translocate from the nucleus to the extracellular space, leading to aggravation of inflammatory responses. However, functions of cytoplasmic HMGB1 are unknown, though it promotes autophagy in cell lines.

We hypothesize that cytoplasmic HMGB1 interacts with partner proteins involved in WI/R by interfering with autophagy. The aim of this study is, (i) to identify the partner proteins of HMGB1 in cytoplasm, and (ii) to investigate the role of the cytoplasmic HMGB1-partner protein complex in autophagy pathways during WI/R.
Method: Normal and WI/R liver tissues were used for cytoplasmic protein extraction. The protein extract was subjected to enrich HMGB1-protein complexes by co-immunoprecipitation. To separate and identify the immunoprecipitated proteins in eluates, two-dimensional electrophoresis (2-DE) and Obitrap-mass-spectrometry (MS) detection were performed. Identified candidate proteins were verified using Western blotting.
Result: 2-DE using eluates prepared with samples from normal versus WI/R liver tissues resulted in different protein distribution patterns. MS detection and 2-DE image analysis revealed 4 candidate proteins (ASS1, CTH, ATP5B and BHMT).
Conclusion: Specific partner proteins interact with HMGB1 in cytoplasm during hepatic WI/R injury. These candidate proteins might interfere with autophagy during hepatic WI/R.

P106 PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR γ ACTIVATION COUNTERACTS SEPSIS-INDUCED CYTOTOXIC T CELL CYTOTOXICITY TOWARDS ALLOANTIGENIC TARGET CELLS

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Background: Patients receiving an immune suppressive therapy to sustain organ transplantation are known to be at high risk to develop a sepsis. As this is known to be linked to cytotoxic T cell (CTL)-dependent toxicity, strategies to break this vicious cycle are needed.
Methods: Therefore, we designed this study to first analyze whether sepsis activates $CD8^+$-T cells towards alloantigenic target cells and second, to test whether a CTL-dependent cytotoxicity can be blocked by PPARγ activation. To mimic septic conditions $CD8^+$-T cells were isolated from cecal ligation and puncture (CLP)-operated mice compared to sham-treated mice. Cytotoxicity of $CD8^+$-T cells was analyzed following a classical alloantigenic activation regime or directly in an *ex vivo* cytotoxicity assay.
Results: We noticed that $CD8^+$ T cells derived from septic mice enhanced cytotoxicity towards alloantigenic P815 target cells, which was effectively lowered by 1 μM of the PPARγ agonist rosiglitazone. With CTLs derived from T-cell specific Lck-Cre PPAR$\gamma^{fl/fl}$ mice rosiglitazone was ineffective, proving a PPARγ-dependent mechanism. At the molecular level PPARγ activation reduced Fas, Fas-L, and granzyme B expression of activated CTLs.
Conclusion: Our study suggests PPARγ activation to prevent alloantigenic $CD8^+$-T cell activation.

RISK ASSESSMENT AND MANAGEMENT OF THE IMMUNISED PATIENT

P108 DESPITE INTENSIFIED IMMUNOSUPPRESSION FLOW CYTOMETRY CROSSMATCH RESULTS ARE PREDICTIVE OF ANTIBODY-MEDIATED REJECTION

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Background: The flow cytometry crossmatch (FCXM) appears as more sensitive than a conventional lymphocytotoxic crossmatch.
Methods: We here addressed the question whether a positive B and/or T cell FXCM (B-FCXM and T-FCXM) prior to living donor kidney transplantation was associated with antibody-mediated rejection when using intensified immunosuppression. In all patients, lymphocytotoxic crossmatches for B and T cells were negative. 105 recipients (211 data sets) were analyzed; of whom 16 recipients received ABO incompatible transplants.
Results: Overall B- and T-FXCM results (donor-specific median fluorescence intensity) were approximately twofold higher in nine recipients with versus 96 patients without antibody-mediated rejection. B- and T-FCXM results were significantly higher prior to ABO incompatible versus compatible transplantation ($p < 0.0001$). B-FCXM results were significantly higher within 30 days versus earlier than 30 days prior to ABO incompatible transplantation; which most likely reflects an effect of rituximab treatment. None of patients with positive B-FCXM result after rituximab treatment suffered from antibody-mediated rejection. T-FCXM results within the two time periods did not differ. A single positive versus a single negative B- and T-FCXM result predicted antibody-mediated rejection with a relative risk of 3.2 and 2.0, respectively.
Conclusion: Despite intensified immunosuppression FCXM results are predictive of antibody-mediated rejection.

P109 HEPARIN-INDUCED THROMBOCYTOPENIA (HIT-II) IN DOUBLE-LUNG TRANSPLANT PATIENTS - EXPERIENCE WITH PREOPERATIVE PLASMAPHERESES AND TWO TIMES INTRAOPERATIVE HEPARIN

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Rationale: Heparin-induced thrombocytopenia (HIT) poses a tremendous surgical challenge, as heparin is the only anticoagulant drug that can be antagonized, especially in sequential double-lung transplantation where heparin is used two times. Alternative anticoagulants may pose great bleeding risks. Based on the antibody-mediated nature of HIT, we reasoned that it may be possible to eliminate HIT antibodies by plasmaphereses, allowing heparin and protamin to be used during surgery.
Objective: We report our experience with plasmaphereses in 7 HIT II-positive patients undergoing double-lung transplantation using heparin/protamin.
Methods: All seven patients underwent sequential double-lung transplantation. HIT II was confirmed in all 7 patients. The patients received a single run of plasmaphereses immediately after the donor organ was accepted and before transplantation. The surgical procedures were then performed using standard heparin/protamin for each side, two times in each patient.
Results: All patients survived the operation and are still alive. There were no complications or side effects during the plasma exchange. The use of heparin during the transplantation was free of complications. No thromboembolic or bleeding complications were observed.
Conclusions: The results suggest that preoperative plasma exchange in HIT-II positive patients and using heparin two times during lung transplantation is safe and efficient.

P110 AN ANTIBODY RESPONSE TO VACCINATION WITH HEPATITIS B SURFACE ANTIGEN DOES NOT CORRELATE WITH THE DEVELOPMENT OF DENOVO ANTI-HLA ANTIBODIES AFTER RENAL TRANSPLANTATION

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Introduction: Response rates to HBV vaccination in dialysis patients vary between 50–80%. Time on dialysis, age and gender are factors influencing response rates. A impaired response to HBV vaccination during dialysis may predict a reduced alloresponse after renal transplantation and thus a decreased risk to develop deNovo anti-HLA antibodies.
Methods: We analyzed 193 non-immunized renal transplant recipients. Response to HBV vaccination was evaluated by measuring the anti-HBs Titer at time of transplantation. DeNovo Anti-HLA antibodies post-transplant were detected using Luminex. Acute rejection episodes, graft loss and renal function were assessed within a median follow-up of 5.5 years.
Results: 75% patients exhibited an adequate immune response to HBV vaccination on dialysis. Vaccine responder (R) and none responder (NR) did not differ with respect to age, gender and time on dialysis. However, more NR developed deNovo donor-specific (23 vs. 14.5%, p = n.s) and none donor-specific (8.3 vs. 6.3%, p = n.s) anti-HLA antibodies in comparison to R. Accordingly, the number of acute rejections was higher in NR as compared to R (37.5 vs. 23.4%, p = n.s.) while graft survival was comparable.
Conclusion: Contrary to our hypothesis antibody response to HBV vaccination on dialysis is not associated with the development of anti-HLA antibodies post transplant.

P111 DONOR DERIVED CELL-FREE DNA, DONOR-SPECIFIC HLA-ANTIBODIES AND CLINICAL OUTCOME AFTER LIVER TRANSPLANTATION

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Background: The immunological and clinical consequences of circulation donor-derived DNA (dd-DNA) and donor -specific HLA-antibodies (DSA) are not well understood. Dd-DNA may serve as an early graft integrity marker but may also be associated with cellular chimerism and immune-regulatory property. DSA indicate humoral immune response.
Methods: We analyzed dd-DNA and DSA in a random sample of 63 liver transplant recipients between 2009 and 2012. Dd-DNA was measured in serum by quantitative PCR, DSA by Luminex Single Antigen Bead Assay at day 3, week 3 and month 3 post-transplant. Both, dd-DNA and DSA were correlated with 1y graft survival, rejection rates and complications of large (anastomotic strictures [AS]) and the small bilary ducts (ITBL).
Results: Dd-DNA was found in 98% of the patients at day 3 after transplantation. In all patients the amount of dd-DNA decreased until month 3. Forty-nine percent of patients showed a macrochimerism, defined as more than 1% of dd-DNA. Alloantibodies were found in 27 of 63 (42%) patients. The vast majority (81%) of alloantibodies were donor specific (DSA), directed against HLA-class II (87%). DSA are associated with the development of ITBL (29% vs. 8%, p = 0.03) but not with AS. High levels of dd-DNA seem to be protective for bilary complications (ITBL 6% vs. 37.5% and AS 9.6% vs. 37.5%, p = 0.01). Both, DSA and ddDNA did not correlate with 1y graft survival and rejection episodes. Interestingly, low levels of dd-DNA are a risk factor to develop DSA (72% vs. 39%, p = 0.01).
Conclusion: Our first results suggest that evolution of DSA is dependent of the release of ddDNA. DSA may play a causal role for small bilary complications while high levels dd-DNA seems to be protective.

P112 EVOLUTION OF CARDIOVASCULAR RISK FACTORS IN LONG-TERM LIVER-TRANSPLANT RECIPIENTS: RELEVANCE OF PROCAM SCORE AND SMOKING STATUS

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Background & Aims: Although cardiovascular disease (CVD) is the leading cause of long-term mortality in liver transplant recipients (LTRs) a reliable scoring system and risk factors to define patients at risk of a cardiovascular event (CVE) are needed.
Methods: The aim of this retrospective clinical study was to identify risk factors and a scoring system for long-term LTRs with risk for CVD/CVE. We studied whether basic Procam score as tool for cardiovascular risk assessment and its parameters (LDL/HDL-cholesterine, systolic blood pressure, triclycerides, age, gender, diabetes, smoking status, positive cardiovascular family history) reflect efficiently LTRs with a risk for CVE.
Results: 190 matched LTRs (matched for gender, age, indication for liver transplantation) from 1987–2013 with 1–27 years of follow up (middle age 54.39 ± 14.2) were included to the study. 24.2% with mid-long term survival of 5–10 years and 29.5% with long-term survival >10 years were compared to 46.3% short-term survivors. Procam score was calculated and matched to corresponding risk levels. 23.7% had a Procam score level 2 or 3 representing medium (10–20% risk) to high (>20% risk) risk of CVE, suffering myocardial infarction or sudden heart failure within 10 years of follow up. In univariate analysis absolute Procam score showed a significant correlation with survival time post liver transplantation ($p = 0.001$) and incidence of CVE ($p = 0.003$) during follow up. Comparing the several factors that contribute to Procamscore, especially smoking ($p = 0.003$), age ($p = 0.000$) and new onset diabetes ($p = 0.010$) were independent risk factors for survival. When choosing liver transplant survival/time to re-transplantation as end-point, HDL ($p = 0.003$) and smoking status ($p = 0.013$) revealed to be independent risk factors. Thus, smoking status can be filtered as an independent risk factor for liver re-transplantation and survival.
Conclusions: In conclusion Procam score reflects CVEs and survival of LTR and can be used in the clinical setting, to screen LTRs before complications e.g. CVE and liver failure become manifest. Especially for elderly LTRs, early diagnosis/treatment of abnormal factors of Procam score and severe recommendation of smoking abstinence post liver transplantation are able to minimize cardiovascular risk.

P114 CYTOMEGALOVIRUS-SPECIFIC IMMUNITY IN LUNG TRANSPLANT RECIPIENTS

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Monitoring the cellular immunity for Cytomegalovirus (CMV) in lung transplant recipients is a promising tool to support prevention strategies for posttransplant CMV-infection or reactivation. Commercially available *in vitro* test systems differ in their capacity to stimulate subpopulations of T-lymphocytes. We compared two assays for CMV-immune monitoring regarding their clinical practicability and significance.

Blood samples of 30 lung transplant recipients (LuTRs) were examined before transplantation and six months afterwards with T-Track® CMV (Lophius Biosciences GmbH, Regensburg) and QuantiFERON®-CMV (Cellestis GmbH, Darmstadt). T-Track® CMV is based on ELISpot allowing quantification of interferon-gamma (IFN-γ) secreting CD4+ and CD8+ T-cells. QuantiFERON®-CMV is restricted to detection of IFNγ producing CD8+ T-cells with ELISA. The data are compared to viral load by qPCR.

Both approaches exhibit advantages and limitations. QuantiFERON®-CMV often generates indeterminate results as depletion of T-cells is not taken into account. T-Track® CMV circumvents this drawback albeit needing large blood volumes. Individual patient data suggest that CMV-specific cellular immunity could serve as indicator for save removal of antiviral prophylaxis in high risk patients or to determine the time-point of safe withdrawal of antiviral therapy in intermediate-risk patients.

Determination of CMV-specific cellular immunity may help to adjust antiviral therapy in lung transplant patients.

P115 A NOVEL STRATEGY FOR THE DETECTION OF ACTIVE TUBERCULOSIS

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Background: The fast diagnosis of active Tuberculosis (TB) disease and differentiation from latent infection is a major challenge. Particularly latently infected transplant patients are of increased risk to develop active TB infection due to immunosuppression. Active TB is also a contraindication for transplantation.
Method: The Reverse T cell Technology (RTT) represents a novel strategy for detection of *in vivo* activated antigen-specific T helper (Th) cells. These cells transiently appear in the periphery during active microbial replication and serve as marker for an active infection. Encounter of TB antigen-pulsed antigen-presenting cells (APC) with *in vivo* activated antigen-specific Th cell induces an APC-intrinsic maturation process leading to the up-regulation of the RTT-marker mRNA that is quantified using qRT-PCR.
Result: We were able to correctly identify 13 out of 16 patients with diagnosed active TB disease resulting in a test sensitivity of 81%, whereas 1 of 8 tested healthy control subjects and patients with latent TB showed a positive test result, indicating a test specificity of 88%.
Conclusion: Data provide evidence that *in vivo* activated TB antigen-specific T cells may represent a reliable and early marker for the detection of active tuberculosis that would allow the rapid diagnosis before and after transplantation.

P116 DIVERTICULITIS IN IMMUNOSUPPRESSED PATIENTS - A FATAL OUTCOME?

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Introduction: Morbidity and mortality of sigmoid diverticulitis is significantly higher in immunosuppressed patients compared to immunocompetent patients. Given the significance in in-hospital mortality, early diagnosis and treatment is crucial to prevent death. The approach of elective sigmoid resection for patients with diverticulosis at the time of transplant listing should be discussed, in particular because the first episode of diverticulitis can already be fatal.
Purpose: The purpose of this study was to evaluate immunosuppressed patients´ in-hospital mortality and morbidity from diverticulitis compared to non-immunosuppressed patients and identification of risk factors for lethal course.
Methods: This retrospective study included 227 patients who received inpatient treatment for colonic diverticulitis between 04/2008 and 04/2014. The groups were divided into immunocompetent and immunosuppressed patients. Primary endpoints were mortality and morbidity during treatment. Risk factors for death were evaluated.
Results: 227 patients were diagnosed with diverticulitis, amongst them 15 (6.6%) were receiving immunosuppressive therapy due to solid organ transplantation ($n = 10$), autoimmune disease ($n = 4$) or cerebral metastasis ($n = 1$). Baseline characteristics were similar. However, 13 of 15 immunosuppressed patients suffered of colonic perforation and showed higher morbidity ($p = 0.04$). Further, immunosuppressed patients showed longer in-hospital (27.6 vs. 14.5 days; $p = 0.02$) and ICU stay (9.8 vs. 1.1 days; $p < 0.001$), a higher rate of emergency operations (66% vs. 29.2%; $p = 0.02$) and in-hospital mortality (20% vs. 4.7%; $p = 0.04$). Age and emergency operations were significant predictors for death.
Conclusion: Morbidity and mortality of diverticulitis is higher in immunosuppressed patients. Early diagnosis and treatment is crucial to prevent death. The approach of elective sigmoid resection for patients with diverticulosis at the time of listing should be discussed, in particular because the first episode of diverticulitis can already be fatal.

P118 RELEVANCE OF SMOKING STATUS IN LIVER TRANSPLANT RECIPIENTS: RISK FACTOR FOR ANASTOMOTIC STRICTURE AND RE-TRANSPLANTATION

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Background & Aims: Most commonly occurring complications following orthotopic liver transplantation (LTX) are associated with the biliary tract. Especially biliary anastomotic stricture (AS) remains a persistent problem in the long-term follow up of liver transplant recipients (LTRs).
Methods: The aim of this retrospective clinical study was to identify risk factors for long-term LTRs with risk for anastomotic stricture. We studied whether smoking status of LTRs in long- term follow up is associated with AS and re-LTX.
Results: 190 matched LTRs (matched for gender, age, indication for liver transplantation) from 1987–2013 with 1–27 years of follow up (middle age 54.39 ± 14.2) were included to the study. 24.2% with mid-long term survival of 5–10 years and 29.5% with long-term survival >10 years were compared to 46.3% short-term survivors. Positive smoking status was evaluated for 36 LTRs including 16 smokers as short-term survivors, 12 as mid-long term and 8 as long-term survivors. In univariate analysis, smoking status of LTRs revealed a significant correlation with survival time post LTX and the occurrence of AS ($p = 0.02$). When choosing Kaplan Meier survival analysis, positive smoking status seems to be a significant factor for the appearance of AS ($p = 0.017$), especially for the mid- and long-term outcome of LTRs. Comparing re-LTX to smoking status, smokers showed a significant correlation to re-LTX in univariate analysis ($p = 0.01$) as well as in Kaplan Meier survival analysis ($p = 0.007$). In multivariate analysis, smoking remained an independent risk factor for re-LTX ($p = 0.009$) when including cholangitis, bacterial, viral or fungal infection, portal vein thrombosis, portal hypertension and anastomotic stricture.
Conclusions: In conclusion smoking status of LTRs should be assessed to predict a poor clinical outcome. Advice of smoking abstinence post liver transplant might be able to minimize risk of re-LTX and biliary complications, especially AS in the long-term outcome of LTRs.

P120 INFLUENCE OF THE TACROLIMUS METABOLISM RATE ON URINARY TRACT INFECTIONS AFTER RENAL TRANSPLANTATION

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Introduction: Urinary tract infection (UTI) is the most common complication after renal transplantation (RTx). We hypothesize that the tacrolimus (tac) metabolism rate impacts on occurrence of UTI.
Methods: The study included RTx outpatients with UTI and germ identification. Non-UTI patients presenting at our RTx office during the same time period (August 2012–September 2014) served as a control group in a matched-pair analysis. The tac metabolism rate was expressed as the blood concentration normalized by the dose (C/D ratio).
Results: 102 UTI patients were compared with 102 non-UTI patients. Female gender ($p = 0.0001$) and advanced age ($p = 0.0181$) were identified as risk factors as reported in the literature. Further risk factors were low body weight ($p = 0.0001$) and minor height ($p < 0.0001$). Patients also suffered from significant more UTI ($p = 0.0047$) in case of previously reduced mycophenolate mofetil dose (due to former infections). Interestingly, the weight adjusted tac C/D ratio ($p = 0.034$) but not the non-weight adjusted C/D ratio ($p = 0.446$) had a significant influence on the development of UTI.
Conclusion: We conclude from our data that especially older female recipients with low body weight and a C/D ratio ≤95 ng per mL/mg per kg are at risk for developing UTI and may therefore profit from alternative immunosuppressive regimens.

AGE IN TRANSPLANTATION MEDICINE

P121 CONSEQUENCES OF PROLONGED CIT AND DGF IN ELDERLY KIDNEY TRANSPLANT RECIPIENTS

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Background: In kidney transplantation (Ktx), the association of cold ischemia time (CIT) and delayed graft function (DGF) is particularly detriemental in graft from marginal donors. However, actual cutoff criteria are still being debated. In this study, the association of immunological factors and ischemic times and longterm survival following KTx were analyzed in young and elderly recipients.
Methods: Data from 1247 patients transplanted between 2000 and 2010 at the Department of Surgery, Innsbruck, were retrospectively analyzed. The age-dependent shortterm and longterm outcome were investigated.
Resultats: Patients >65 years ($n = 193$) had a significantly lower 10 year graft and patient survival ($p < 0.001$) than younger patients <65 years ($n = 1054$). However, graft survival censored for death with a functioning graft was age-independent. In a univariate analysis, patients >65 years received significantly more ECD and DCD grafts, a higher donor age, had a higher CMV mismatch rate, a higher BMI, a higher rate of DGF but a shorter CIT. Interestingly, acute rejection rates (AR) were comparable in young and old recipients.

Next, the age-dependent impact of DGF on graft and patient survival was analyzed. In patients <65 years with DGF, 10 year patient and graft survival was significantly lower compared to patients without DGF ($p < 0.05$). Similarly, graft survival was impaired by DGF in patients >65 years.

Furthermore, the association of CIT and the type of donor (DCD, ECD versus SCD) was examined. The risk of graft loss for ECD grafts but not SCD grafts was markedly increased beyond 800 min CIT. Consequently, prolonged CIT (cutoff: >878 min) was associated with reduced graft survival of ECD but not SCD grafts.

On multivariate analysis, recipient age and DGF were independent risk factors for patient survival in younger recipients ($p < 0.0005$). Likewise, recipient age, donor age, induction therapy and DGF were risk factors for impaired graft survival. In contrast, in patients >65 years, age and induction therapy were associated with inferior patient survival. Graft survival was independently affected by donor age, induction therapy and DGF.
Conclusion: DGF rates and CIT have a negative independent impact on graft and patient survival following kidney transplantation. Thus, it is particularly important to further reduce cold ischemia times in elderly transplant recipients of ECD grafts.

P122 DONOR AGE ≥65 YEARS IS THE MAJOR RISK FACTOR FOR ALLOGRAFT LOSS IN A GERMAN TRANSPLANT POPULATION

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Aim of our study was to analyze the risk factors (RF) for 3-year allograft loss in a typical German transplant population. We retrospectively analyzed 422 adult single kidney transplants between 2007 and 2012, including 192 patients from the ETKAS, 94 patients from the ESP and 136 living donor (LD) kidney transplants. The 3-year patient and graft survival was 96.9% and 90.6% in ETKAS and 88.1% and 73.2% in the ESP. In recipients of a LD kidney the graft survival with younger donors was 95.5%, while it was 65.4% in patients with LD above 65 years.

In a multivariate analysis we identified donor age ≥ 65 years (OR 9.7 [3.4;27.8]; $p < 0.001$)., severe surgical complications (OR 7.6 [2.8;20.3]; $p < 0.001$) and intense immunosuppression (OR 5.2 [1.6;17.5]; $p = 0.008$) as independent RF for immediate graft loss. Donor age above 65 years was the only and highly significant RF for long-term allograft loss (HR 4.1 [2.5;7.0]; $p < 0.001$).

While we achieved an excellent patient and graft survival in our ETKAS patients and recipients of LD younger than 65 years, the graft survival was lower not only in the ESP recipients but also in recipients of living donor grafts older then 65 years.

We conclude that a donor age above 65 years is a significant RF for long-term allograft loss not only in DBD but also in LD.

P125 RECIPIENT'S BUT NOT DONOR'S AGE AND BMI ARE ASSOCIATED WITH LONG TERM SURVIVAL AFTER LIVER TRANSPLANTATION

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Background: Over the last decades survival after LTX strongly improved, but factors associated with long time survival have not been well defined yet.
Methods: Medical charts of all adult de novo LTX recipients who were transplanted at our center between 1997 and 1999 were reviewed.
Results: Overall 114 patients were analysed (male: $n = 70$, 61%). Twenty-six patients were lost of follow-up, 68 (59.6%) were followed >14 years after transplantation.

At the time of transplantation age and BMI of patients ranged from 16–69 years (mean: 49.1) and from 15.1–33.3 kg/m^2 (mean: 24.0 kg/m^2). Age and BMI were identified as risk factors for mortality ($p = 0.011$ and $p = 0.009$, respectively). Kaplan Meier analysis comparing patients with BMI and age above and below the median confirmed these factors as predictors of decreased survival ($p = 0.008$ and $p = 0.009$). Furthermore, hepatitis B as underlying liver disease was associated with an improved survival (Kaplan-Meier analysis $p = 0.036$).
Conclusion: Age and BMI of recipients, but not of donors were predictors of long term survival. Patients with hepatitis B as underlying disease had an improved survival.

P126 THE EFFECT OF TACROLIMUS (FK506) IN THE ELDERLY TRANSPLANT RECIPIENT

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Background: Immunosenescence is anticipated to have major implications for immunosuppressant drugs following organ transplantation, albeit barely explored in experimental and clinical studies.
Methods: To investigate the impact of aging on the effect of Tacrolimus (TAC), we dissected immune response and T cell phenotype by using a fully mismatched mouse skin transplant model. Young (3 months) and old (18 months) C57BL/6 mice underwent skin transplantation either treated with TAC or PBS intraperitoneally.
Results: TAC resulted into a significantly prolonged allograft survival in old recipients, while half of the dose was applied to provide the same bioavailability as in young recipients. Moreover, TAC was able to suppress IL2 more efficiently in old $CD4^+$ T cells that led to a lower proliferation and repopulation rate. Hence, the absolute number of $CD4^+$ T cells was reduced in old recipients while showing higher apoptotic rate. At the same time, cytokine production was changed by TAC in an age-specific manner; systemic IFNγ production was lowest in the old recipients. Interestingly, the production of the anti-inflammatory cytokine IL10 showed a reciprocal relationship between young and old mice since the frequency of $CD4^+$ $IL10^+$ $IFN\gamma^-$ increased in old but decreased in young mice. To elucidate changes in IL10 production, old naïve $CD4^+$ T cells were cultured in TH1 polarizing conditions, the predominant immune state after transplantation. Strikingly, old TH1 cells were able to produce significant amount of IL10 enhanced by TAC noticeably not observed in young $CD4^+$ T cells.
Conclusion: Collectively, our results demonstrated a prolonged allograft survival in old recipients when treated with TAC, while lower doses were applied than in young recipients. The potent effect of TAC modified the immunoreactive capacities of $CD4^+$ T cells leading to a reduced cell repopulation with higher apoptotic rate and increased levels of IL10.

PERSONALISED MEDICINE IN TRANSPLANTATION

P128 MONTH 48 FOLLOW-UP RESULTS OF THE HERAKLES TRIAL: EFFICACY AND SAFETY OF THREE DIFFERENT TREATMENT REGIMEN IN DE NOVO RENAL TRANSPLANT PATIENTS

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Purpose: To compare safety and efficacy of 3 different immunosuppressive regimen at month 48 after renal transplantation (Tx).
Methods: 802 patients were included in this 1 year, prospective, open-label, randomized, controlled multi-center study with observational follow-up until month 60 post Tx. After induction therapy all patients received cyclosporine A (CsA), enteric-coated mycophenolate sodium (EC-MPS) and steroids. 3 months post Tx 499 patients were randomized 1:1:1 to either a) continue standard CsA (100–180 ng/ml)+EC-MPS (n = 166) (STD) or convert b) to a calcineurin inhibitor (CNI)-free regimen with everolimus (EVR) (5–10 ng/ml) + EC-MPS (n = 171) or c) to a CNI-reduced regimen with EVR (3–8 ng/ml) + reduced CsA (50–75 ng/ml) (n = 162). All patients continued on steroids. At time of month 48 follow-up interims-analysis data were available from 110 (73%) STD, 117 (79%) CNI-free and 111 (76%) CNI-low treated patients of the follow-up ITT population.
Results: From randomization to month 48 BPAR was reported in 19/151 (13%) STD, 24/149 (16%) CNI-free and in 23/147 (16%) CNI-reduced patients (ITT; p = ns). 5 deaths (3%) occurred in STD, 3 (2%) in CNI-free and 6 (4%) in the CNI-reduced group. 9 (6%) graft losses were observed in the STD, 6 (4%) in the CNI-free and 2 (1%) in the CNI-reduced group. Composite failure (BPAR, death, graft loss, loss to follow-up) occurred in 32 (21%) STD, 36 (24%) CNI-free and in 39 (27%) CNI-reduced treated patients. Premature discontinuation due to AEs was reported for 5 (3%) of STD, 5 (3%) of CNI-free and 1 (1%) of CNI-reduced patients (safety-population) since month 12 to month 48. Renal function (cGFR, Nankivell, LOCF) was significantly improved by +6.8mLmin/1.73 m2 in favor of the CNI-free regimen at month 48 (ITT; p = 0.02).
Conclusion: Month 48 results from HERAKLES show that immunosuppressive regimen using EVR with reduced-dose or without CNI-exposure reflect an efficacious and safe therapeutic approach offering the opportunity for an individualized immunosuppression to minimize CNI-exposure.

P129 FIRST CLINICAL RESULTS OF A SALIVA TESTING ON INFLAMMATION IN TRANSPLANT PATIENTS

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Introduction: Ideal biomarker should be specific, sensitive, non-invasive, mirror the benefit of therapy and offer prognostic potential. We developed a test using a colorimetric assay to detect kynurenine (Kyn) changes in patients. Kynurenine [EC 1.13.11.42] is generated downstream in the tryptophan metabolism and one of the key players concerning inflammatory response and known for immune-modulation not only on T-regulatory and NK cells.
Materials and Methods: Blood samples were measured retrospectively from 442 renal transplant patients (n = 5100) and prospectively from 114 patients (n = 790). 292 healthy blood donors served as normal controls. In a second step we developed a test method in saliva first on basis of the colorimetric assay including the normal controls and prospectively in 66 (n = 290) patients after renal transplantation with 18 rejection episodes.
Results: Test-recovery rate was 97–99.8%, intra-assay variance 1.53% and inter-assay variance 2.77%. Values in normal controls were 2.7 + 0.4 μM for serum and 0.9 + 0.4 μM for saliva. Mean values in patients with rejection (BPAR) was 17.4 + 8.4 μM in serum (s) and 4.6 + 1.6 μM in saliva (sal) compared to uneventful patients 4.3 + 1.6 μM (s) and 1.3 + 0.6 μM (sal). The proportion rate was equal between normal controls, uneventful patients after transplantation and rejection. We found a) a significant correlation of Kyn and rejection episodes (BPAR) early in the beginning, b) a predictive information concerning the long-term run of the transplant (up to 144 mos) and c) excellent tool for monitoring therapeutic interventions especially on individual basis (drug minimization). In serum testing we could differentiate significant between steroid-sensitive, steroid-resistant and antibody mediated rejection and infection. In saliva we found no circadian behavior for kynurenine.
Conclusion: This test fulfills the given prerequisites. It is a safe and reliable method, is easy and quick to perform and not costly. The test enables the individual monitoring of patients under immunsupressive therapy. The test set-up is under evaluation and further development. Further validation is planned in prospective clinical observational and interventional studies.

P130 MPA-INHIBITION: NEED FOR INDIVIDUALIZED TREATMENT?

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There is evidence that optimized MPA dosing could be central in achieving improved results. Significant relationships between the uptake of mycophenolic acid and the risks for acute rejection have been reported. Aim of this prospective study was either the evaluation of IMPDH-measurement as pharmacodynamic (inhibition-) profile in the first postoperative period or wether long term exposure for mycophenolate mofetil (MMF) / enteric coated mycophenolic acid (EC-MPS) is leading to an enzyme induction for IMPDH, thus decreasing MPA immunosuppressive properties and increasing the hazard for rejection.
Patients and Methods: By application of an IMPDH assay (HPLC based), enzyme activity was investigated in whole blood for the substrate xanthine monophosphate (XMP) and for xanthine (X) in isolated lymphocytes from renal transplant patients: A: Group of 52 patients for the short term and B: (56p.) for the long term evaluation. Gr.BI (MMF, n = 23; medication: 111 + 31 mos); Gr.BII (EC-MPS, n = 33; med.: 109 + 27 mos). Dosage was comparable in each group. Basic data from 24/36 healthy volunteers were included. Follow up measurements were performed at week 1, 2, 4 and month 3–120.
Results: Comparing in A the two groups (Gr.A I: rejection, n = 17, mean age 51 + 15 year) vs. (Gr. A II: no rejection, n = 35, mean age 51 + 14 year) we found a significant ($p < 0.001$) lower inhibition of IMPDH in Gr. A I (26.5 + 11% vs. 56.7 + 18%) already in the first week after transplantation. There was no correlation of IMPDH with MPA values (6.85 + 4 vs. 4.1 + 3 mg/l; first week), nor with the CNI trough blood levels (CsA: 144 + 39 vs. 168 + 52 ng/ml; TAC: 7.5 + 3 vs. 7.8 + 3 ng/ml, first week).

IMPDH activity increased in B with a high variability nearly 8 fold (mean 318 vs. 2100 pmol/min/ml) in whole blood. In isolated lymphocytes the increase was up to 340% and significant higher in patients with rejection episodes. A decrease of IMPDH inhibition was found 3 to 43 months post transplantation. There was a high inter- and intrapatient variability. We found a correlation (not linear) between duration of therapy and IMPDH-activity.
Conclusion: The data suggests that the measurement of the biological response may provide a more useful adjunct than traditional TDM of MPA .We found an increase of IMPDH activity. Additional dose reductions in maintenance treatment might lead to under-immunosuppression. Drug "minimization" for MMF/EC-MPS might be hazardous for the graft.

P131 NON-INVASIVE MONITORING OF RENAL ALLOGRAFT FUNCTION BY NMR-BASED URINE METABOLOMICS

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Background: Renal function monitoring after transplantation, to a large part, relies on serum creatinine, proteinuria and kidney biopsies. Most experts agree that additional diagnostic biomarkers for rejection and impaired renal function are highly desirable.
Methods: We applied metabolic profiling by NMR spectroscopy to discover and test novel urinary biomarkers for non-invasive monitoring of renal allograft function. Our modeling cohort comprised 1276 urine samples from 174 patients who had undergone kidney transplantation at the University Hospital Regensburg. The prospective UMBRELLA study recruited a test cohort consisting of more than 100 patients from which we collected a total of 1331 urine samples.

A statistical classification model was built to distinguish cases from controls based on the metabolic profiles. Cross-validation was used to estimate performance in the training cohort. Model performance was tested on the samples of the confirmation study.
Results: In the training set, cross-validation yielded an AUC-estimate of >0.9 in the ROC analysis. In the prospective confirmation study, an AUC of >0.75 was found.
Conclusion: NMR spectroscopy is a promising tool for non-invasive monitoring of patients after kidney transplantation and we are in the process of developing a commercially available multi-parameter test based on these data.

P132 LOW ASCITES LEVELS OF CELL MEMBRANE-DERIVED MICROPARTICLES INDICATE WORSE SHORT-TERM PROGNOSIS IN PATIENTS WITH DECOMPENSATED CIRRHOSIS

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Background: Microparticles (MP) are small vesicles (<1 μm) that are derived from cells after stress or cellular activation. Plasma MP levels have recently been associated with disease severity and outcome of patients with liver failure. We here retrospectively evaluated the prognostic value and clinical relevance of MP levels in the ascites fluid (AF) of patients with decompensated liver cirrhosis.
Material and Methods: AF samples of 163 cirrhotic patients (index paracentesis $n = 163$, follow up paracentesis within 30 days after index paracentesis $n = 75$) were collected between February 2011 and December 2012 and stored at 20°C. MP were isolated from AF samples of index paracentesis by 2-step ultracentrifugation and identified according to their size using fluorescence activated cell sorting (FACS). MP levels were correlated with clinical and laboratory parameters. Bacterial DNA in ascites was detected by using a quantitative 16S-rRNA gene based PCR method.
Results: MP could be detected in all ascites samples with a median quantification of 281.5 MP/μl (range 17.5–32557.1). High ascites MP levels (>500/μl; $n = 103$) were associated with a significantly better 30-day survival in decompensated liver cirrhosis, when compared to low ascites MP levels (<500/μl; $n = 60$; 94.5% vs. 76%, $p = 0.001$). At baseline, MP levels correlated with the MELD score (MELD ≥ 20: median 217.11 MP/μl versus MELD < 20 335.71 MP/μl), INR ($r = -0.206$, $p = 0.019$) and thrombocytes ($r = 0.295$, $p = 0.0001$) as well as with the administration of beta-blockers (OR 2.115 (1.055–4.239) for >500 MP/μl; $p = 0.034$). Interestingly, patients with bactDNA positive AF at index paracentesis and high level MP quantification (>500/μl) were characterized by a decreased ability for bactDNA clearance at follow-up paracentesis (>500MP/μl 100% vs. <500MP/μl 45.5%, $p = 0.012$). However, clinically evident infections such as spontaneous bacterial peritonitis did not correlate with ascites MP levels.
Conclusion: Ascites levels of cell membrane-derived microparticles are suitable to identify patients with cirrhosis and poor short-term prognosis. We propose ascites MP as an easily detectable biomarker with a considerable impact on patients' management especially with regard to the indication for transplantation.

P133 MONITORING OF CALCINEURIN INHIBITORS BY NFAT-REGULATED GENE EXPRESSION IN DE NOVO RENAL ALLOGRAFT RECPIENTS

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Background: Calcineurin inhibitors are critical-dose drugs with a narrow therapeutic range and the optimal monitoring strategies are discussed in terms of safety and efficacy. A new pharmacodynamic monitoring tool - assessing the expression of nuclear factor of activated T cells (NFAT)-regulated genes - has been established tomeasure directly the functional effect ofciclosporin A (CsA) in an individual patient. Until now, only sparse data on NFAT-regulated gene expression within the early post-transplant period are available.
Methods: Altogether 80 de novo renal transplant patients were enrolled in this prospective observational trial. The immunosuppression consisted of IL-2 receptor antagonist induction, CsA, mycophenolic acid and steroids. The expression of the NFAT-regulated genes (interleukin 2, granulocyte-macrophage colony stimulating-factor, interferon y) was determined by qRT-PCR at CsA C0 and C2 at regular follow-up visits within 6 months after transplantation.
Results: The median age of all patients was 47.9 ± 13.7 years (54 male). Residual NFAT-regulated gene expression showed a high interindividual variability. Inversely to reduction of CsA doses expression of NFAT-regulated genes increased from 1.78 ± 1.33% to 8.04 ± 7.36% in month 1 to month 6. Despite of comparable CsA C0 levels NFAT-regulated gene expression was significantly less inhibited in patients with treated biopsy-proven acute rejections (2.9 ± 2.2% vs. 2.0 ± 1.7%, $p = 0.047$). Patients with very low residual expression on NFAT-regulated genes were on increased risk of early infectious episodes. Residual expression of IFNy and GM-CSF genes correlated most significantly with clinical outcome.
Conclusions: NFAT-regulated gene expression is highly inhibited in the early post-transplant period in renal allograft recipients on CsA treatment. High residual NFAT-regulated gene expression was related to acute rejection episodes but low residual expression with infectious complications. Thus, NFAT monitoring has the potential to support pharmacokinetic monitoring in the early post-transplant period.

FUTURE OF IMMUNOSUPPRESSION

P136 EFFICACY AND SAFETY OF A CONVERSION FROM THE ORIGINAL FORMULATIONS TO THE GENERICS TACPAN® AND MOWEL®

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Background: Expensive pharmaceuticals are one of the most important causes for cost intensive health care systems. In western countries immunosuppressive agents approved for the prevention of rejection following solid organ transplantation (SOT), play a relevant role. Patents of original drugs expired and cheaper products are available. But only few data exists evaluating efficacy and safety of the generic drugs in Europe.
Methods: We treated 25 patients, who were clinically stable for a minimum of two years after liver transplantation (LT), with a combination of the generic tacrolimus formulation Tacpan® (TAP) and generic MMF, Mowel® (MOW). Patients were treated prospectively and followed up for 6 months. Tacrolimus through levels, transplant and kidney function and costs were compared to 25 age and gender matched control patients treated with the original formulations Prograf® or Advagraf® (TAC) and Cellcept® (MMF).
Results: In the matched-pair analysis of tacrolimus through level/dose ratio no significant difference was found between TAP/MOW and TAC/MMF groups at the beginning and at the end of the study 6 months later. The intra-individual comparison of tacrolimus through levels at the beginning and at the end of the study showed a slight increase in tacrolimus through levels in the TAP/ MOW group (in median +13.89%). Six months after the beginning of the study no significant difference for blood parameters between TAP/ MOW and TAC/ MMF was found. In total, 17 patients reported mild side effects in the TAP/MOW group after switching to the generics. The most common side effects were gastrointestinal symptoms. No acute rejection occurred in either group. Intra-individual analysis of costs revealed a considerable cost reduction ($p < 0.001$) in the TAP/MOW group (in median 25.03%).
Conclusion: In summary the use of the generics TAP/MOW seems to be safe and cost-effective in stable LT patients.

P137 COMET: EVALUATION OF COMPLIANCE AND TOLERABILITY OF ONCE DAILY TACROLIMUS (ADVAGRAF) IN KIDNEY TANSPLANT-PATIENTS

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Background: COMET was the first nationwide (D) study to evaluate adherence (compliance) in adult renal transplant recipients in a real-world-setting. As a novel approach, a composite primary variable (CPV) was chosen to assess whether patients adhered to the once daily tacrolimus dosing regimen.
Methods: 18 months observation period, 4 scheduled Visits (V). CPV: 4-item BAASIS self-report interview, investigator adherence assessment and tacrolimus-trough-levels. Secondary variables included analyses of individual adherence components and patient satisfaction.
Results: 153 patients [average time since transplantation 5.8 (SD = 4.6) years] were enrolled. Non-adherence, defined as lack of adherence with one of the composite variables reached 67.7%; 95% CI (%); [58.93; 75.63] at V4. Adherence according to the 4 BAASIS-dimensions taking, drug holiday, timing and dose reduction was observed for 86.9%, 100.0%, 58.2% and 98.7% of patients at V1 and 91.3%, 97.6%, 58.3% and 98.4% at V4. Adherence assessed by tacrolimus-trough-levels was 86.5%. Investigators rated Adhärenz as good in 85.6% of patients (V4). 94.7% of patients favored the convenience of once daily tacrolimus dosing.
Conclusions: Adherence based on CPV assessments appeared low, but was primarily caused by non-adherence to timing of medication intake. There was little evidence of missed doses or drug holidays.

K. Budde und P. Reinke contributed equally to this paper.

P138 B-CELL DEPLETION DOES NOT PREVENT ACUTE MIXED HUMORAL AND CELLULAR REJECTION IN A RAT RENAL TRANSPLANT MODEL

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Background: B-cells are increasingly recognized as important players in alloimmunity. Depletion of B-cells is performed in immunological high-risk renal transplant patients and in those with antibody-mediated rejection, usually together with other therapeutic measures. We established a rat renal transplant model with B-cell depleting induction but without maintenance immunosuppressive treatment to exclusively study the effects of B-cell depletion on allograft rejection.
Methods: The rat model LEW.1W on LEW (allo) has an exclusive but complete MHC disparity. Anti-rat CD20 antibody was injected into transplanted rats (allo+ab) directly after abdominal closure and animals were sacrificed on day 7 (d7) ($n = 5$ allo, $n = 5$ allo+ab). Syngeneic transplanted LEW rats served as additional controls (iso $n = 3$). Duration of experiment was prolonged to 4 weeks after beneficial effects of B-cell depletion on humoral component of rejection were observed ($n = 15$ allo, $n = 10$ allo+ab, $n = 3$ iso). Lymphocyte subpopulations, chemokines/cytokines and MHC-antibodies were analysed by flow cytometry. Mixed lymphocyte culture (non-radioactive) was performed. Grafts were examined by pathological analysis, immunohistochemistry (T-, B-, NK-cells and macrophages) and RT-PCR.
Results: In allo+ab animals peripheral B-cells were successfully depleted and on d7 less signs of humoral rejection were seen, whereas cellular graft infiltrates did not differ significantly from the allo group. B-cell depleted animals surviving for more than 7 days (significantly less than in the allo group, $p = 0.02$) had less cellular graft infiltration at d21, still they had signs of mixed acute humoral and cellular rejection comparable to the allo-controls. All allo and allo+ab animals tested had donor-specific MHC-antibodies. *In-vitro* T-cell reactivity and serum cytokines/chemokines remained fairly unaffected by B-cell depletion.
Conclusion: Despite influencing cellular graft infiltration, B-cell depleting treatment does neither prevent formation of MHC-antibodies and humoral rejection nor does it affect T-cell reactivity and cellular rejection.

P139 DIFFERENT PROCOAGULANT ACTIVITY OF THERAPEUTIC MESENCHYMAL STROMAL CELLS DERIVED FROM BONE MARROW AND PLACENTA DECIDUA

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While therapeutic mesenchymal stromal/stem cells (MSCs) have usually been obtained from bone marrow, perinatal tissues have emerged as promising new sources of cells for stromal cell therapy. Here we present a first safety follow-up on our clinical experience with placenta-derived decidual stromal cells (DSCs), used as supportive immunomodulatory and regenerative therapy for patients with severe complications after allogeneic hematopoietic stem cell transplantation (HSCT).

We found that DSCs are smaller, almost half the volume of MSCs, favoring microvascular passage. DSCs also show different hemocompatibility, with increased triggering of the clotting cascade after exposure to human blood and plasma *in vitro*. After infusion of DSCs in HSCT patients, we observed a weak activation of the fibrinolytic system, but the other blood activation markers remained stable, excluding major adverse events. Expression profiling identified differential levels of key factors implicated in regulation of hemostasis, such as a lack of prostacyclin synthase and increased tissue factor expression in DSCs, suggesting that these cells have intrinsic blood-activating properties. The stronger triggering of the clotting cascade by DSCs could be antagonized by optimizing the cell graft reconstitution before infusion, e.g. by using low-dose heparin anticoagulant in the cell infusion buffer.

We conclude that DSCs are smaller and have stronger hemostatic properties than MSCs, thus triggering stronger activation of the clotting system, which can be antagonized by optimizing the cell graft preparation before infusion. Our results highlight the importance of hemocompatibility safety testing for every novel cell therapy product before clinical use, when applied using systemic delivery.

P141 BELATACEPT-TREATED PATIENTS HAD SUPERIOR GRAFT SURVIVAL COMPARED WITH CYCLOSPORINE-TREATED PATIENTS: FINAL RESULTS FROM BENEFIT

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Background: No prospective, phase 3, randomized studies of immunosuppressive regimens have shown a survival advantage over cyclosporine-containing regimens. At 3 years post-transplant in BENEFIT, renal function was improved in belatacept-treated versus cyclosporine-treated kidney transplant recipients. We report the final 7-year results from BENEFIT.
Methods: Patients were randomized to more (MI) or less intensive (LI) belatacept-based or cyclosporine-based immunosuppressive regimens. Outcomes were assessed for all randomized and transplanted patients at year 7. In a prospective analysis, time to death or death-censored graft loss was compared between treatment arms using Cox regression.
Results: In total, 153/219 of belatacept MI-treated, 163/226 of belatacept LI-treated, and 131/221 of cyclosporine-treated patients were evaluable for this analysis. Hazard ratios comparing time to death/graft loss were 0.573 for belatacept MI versus cyclosporine ($p = 0.02$) and 0.570 for belatacept LI versus cyclosporine ($p = 0.02$)—a 43% risk reduction in death/graft loss for belatacept (MI or LI) versus cyclosporine. Mean MDRD calculated GFR significantly favored belatacept versus cyclosporine at all time points. Serious AE rate was similar across treatment arms.
Conclusions: In this analysis of 7-year results from BENEFIT, belatacept conferred statistically better graft survival and renal function versus cyclosporine. The belatacept safety profile was consistent with previous reports.

P142 LONG-TERM SURVIVAL OUTCOMES IN BELATACEPT-TREATED VERSUS CYCLOSPORINE-TREATED PATIENTS: FINAL RESULTS FROM BENEFIT-EXT

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Background: At 3 and 5 years post-transplant in BENEFIT-EXT, renal function benefits were seen for belatacept-treated versus cyclosporine-treated kidney transplant recipients. We report the final 7-year results from BENEFIT-EXT.
Methods: Recipients of ECD kidneys received more (MI) or less intensive (LI) belatacept-based or cyclosporine-based immunosuppressive regimens. Assessments included all randomized and transplanted patients through 7 years. In this prospective analysis, time to death or death-censored graft loss was compared between treatment arms using Cox regression.
Results: In total, 128/184 of belatacept MI-treated, 138/175 of belatacept LI-treated, and 108/184 of cyclosporine-treated patients were evaluable for this analysis. Hazard ratios comparing time to death/graft loss were 0.915 for belatacept MI versus CsA ($p = 0.65$) and 0.927 for belatacept LI versus CsA ($p = 0.70$). Mean MDRD calculated GFR significantly favored belatacept versus cyclosporine at all time points. Hazard ratios comparing the rates of freedom from death, graft loss, or cGFR <30 ml/min/1.73 m^2 were 0.589 for belatacept MI versus CsA ($p = 0.0003$) and 0.585 for belatacept LI versus CsA ($p = 0.0002$). Serious AE rate was similar across treatment arms.
Conclusions: At 7 years post-transplant, belatacept was associated with similar death/graft loss and improved renal function versus cyclosporine. The belatacept safety profile was consistent with previous reports.

P143 BELATACEPT-TREATED PATIENTS HAD SUPERIOR ESTIMATED GLOMERULAR FILTRATION RATE VERSUS CYCLOSPORINE-TREATED PATIENTS: RESULTS FROM A MIXED EFFECTS MODELING ANALYSIS OF BENEFIT

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Background: Prior analyses of BENEFIT showed significantly higher mean calculated GFR (cGFR) with belatacept versus cyclosporine. Here we report cGFR derived from a longitudinal modeling analysis of BENEFIT over 7-years.
Methods: Recipients of living or standard criteria donor kidneys received belatacept-based more (MI) or less (LI) intensive or cyclosporine-based immunosuppressive regimens. Mean cGFR was estimated from months 1–84 for all randomized and transplanted patients using a repeated measures model with an unstructured covariance matrix. The cGFR difference between treatment arms at each time point was also estimated. Time was regarded as a categorical variable. There was no imputation for death or graft loss.
Results: Mean cGFR increased slightly over 7 years for both belatacept regimens but declined for cyclosporine. The differences in mean cGFR between belatacept MI and cyclosporine at years 1, 3, 5, and 7 were 14.5, 20.3, 23.3, and 25.6 ml/min/1.73 m^2, respectively. The corresponding values for belatacept LI versus cyclosporine were 13.5, 20.4, 23.4, and 27.3 ml/min/1.73 m^2. These differences statistically significantly favored each belatacept regimen versus cyclosporine at all time points.
Conclusions: The significant improvement in renal function seen with belatacept versus cyclosporine is sustained over 7 years, with increasing divergence between treatment arms over time.

FUTURE OF IMMUNOSUPPRESSION/INTERDISCIPLINARITY IN TRANSPLANTATION MEDICINE

P144 PHARMACOKINETICS AND PHARMACODYNAMICS OF TACROLIMUS AND NFAT REGULATED GENE EXPRESSION IN KIDNEY TRANSPLANT PATIENTS

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Background : Suppression of genes that are regulated by the nuclear factor of activated T-cells (NFAT) is a direct effect of calcineurin inhibitors [Sommerer C. Transplantation. 2010; 89: 1417–23]. We correlated the pharmacodynamic effect on NFAT to the pharmacokinetics of tacrolimus.
Patients and Methods : This study was undertaken in the University Hospitals of Ulm and Heidelberg. Our protocol has been approved by the local ethics committee (# 329/12). The patients were on triple immunosuppression with low dose prednisolone (2.5–5 mg/d), mycophenolate (2 × 500 mg/d or equivalent) and tacrolimus (2 × 2 – 2 × 5 mg/d) adjusted to target trough levels (5–8 ng/ml). Tacrolimus trough levels (Ctrough) and 1.5–2 h later peak concentrations (Cpeak) were measured by LCMS. Simultaneously, the NFAT trough effect (Etrough) and after 1.5–2 h the NFAT nadir effect (Enadir) were determined by established methods [Giese T. Clin Immunol. 2009; 132: 305–11].

The pharmacokinetic half-life (T1/2) was estimated from peak (Cpeak) and trough concentrations (Ctrough) considering the time distance between peak and troughs (10.5–10 h). The pharmacodynamic concentration producing the half-maximum effect (CE50) and the Hill coefficient (H) were estimated from trough effect (Etrough) at trough concentrations and from nadir effect (Enadir) at peak concentrations.

$CE50 = Ctrough \times (Emax/Etrough - 1)^{(-1/H)} = Cpeak \times (Emax/Enadir - 1)^{(-1/H)}$

The two equations were solved by numerical iteration for an estimate of the two unknown parameters (CE50, H).
Results : A total of 10 stable kidney transplant patients were included. The median age was 58 years and the median serum creatinine was 306 mcmol/l. The pharmacokinetics of tacrolimus were estimated with T1/2 = 11 h, the apparent clearance Cl/F = 64 l/h and volume of distribution Vd/F = 480 l, respectively. The median value for NFAT was 89% (Etrough) of normal gene expression at trough levels, and the nadir effect was 43% (Enadir) representing the strongest immunosuppression of basal gene expression at peak levels (Figure 1). The pharmacodynamics of tacrolimus were estimated with CE50 = 7.7 ng/ml and the Hill coefficient with H = 4.6, respectively.
Conclusion : While on triple immunosuppression, the NFAT pharmacodynamics indicate a low concentration producing the half-maximum effect and a high Hill coefficient. These findings suggest a narrow trough-to-peak target concentration range of 4.0-to-9.5 ng/ml for tacrolimus.

P145 EVEROLIMUS - RETROSPECTIVE ANALYSIS OF 55 PATIENTS UNDER IMMUNOSUPPRESSIVE THERAPY WITH EVEROLIMUS AFTER PEDIATRIC HEART TRANSPLANTATION

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Background: The minimization of the immunosuppressive side effects as nephrotoxicity, infections and malignancies is a very important aim in the follow up after pediatric heart transplantation. The mTor-inhibitor might minimize these problems because of the lower nephrotoxicity and their antiproliferative effect. Therefor they are getting more and more a component of the standard immunosuppressive therapy after pediatric heart transplantation.
Methods: Retrospective analysis of all of our patients under immunosuppressive therapy with everolimus. We focused on the reasons for the switch of the immunosuppressive therapy to everolimus and the side effects that led to an interruption or termination of the therapy with everolimus.
Results: 55 patients after pediatric heart transplantation had a switch of their immunosuppressive therapy to everolimus between 2007 and 2014. Only five patients were switched to calcineurin inhibitor free therapy. The most important reasons for changing the immunosuppressive therapy to everolimus were renal insufficiency, vasculopathy and gastrointestinal problems. The renal function showed a quite variable development after the change of the immunosuppressive therapy. The vasculopathy remained quite stable in most of the cases. Almost one third of the patients ($n = 15$) discontinued the treatment with everolimus. The most important reasons were stomatitis, leukopenia, and atopic eczema. Interestingly almost two third of the patients tolerated everolimus good after a second try.
Conclusion: The immunosuppressive therapy with everolimus is a save possibility after pediatric heart transplantation especially in patients with renal insufficiency and vasculopathy.

P146 EARLY LEUKOCYTE INFILTRATION AND EXPRESSION OF B-CELL ACTIVATING FACTORS IN A KIDNEY TRANSPLANT MODEL

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Background: Subclinical inflammation, *de novo* Donor-specific antibodies (dnDSA), and non-adherence to immunosuppressive therapy are associated with reduced graft survival. We examined intra-graft leukocyte infiltration, expression of B-cell activating factors (BAFF/APRIL) and chemokines in a rat renal transplant model.
Methods: We compared ischemia-reperfusion (IR), syngeneic and allogeneic transplantation (Tx), and standard versus staggered immunosuppression (Cyclosporine daily or on alternating days) in analogy to non-adherence to therapy. Intra-graft leukocyte infiltration and BAFF/APRIL expression were assessed at days 6 and 28 by immunohistochemistry or FACS-analysis. Chemokine transcription and dnDSA were measured by RT-PCR and FACS, respectively.
Results: IR and syngeneic Tx did not effect T-/B-cell infiltration, while allogeneic Tx lead to an increase in both populations at d6, which was sustained until d28 if immunosuppression was staggered. An early increase in BAFF/APRIL expression (d6) was seen in IR and allogeneic Tx, but this only remained elevated in allogeneic Tx (d28), not in IR. RT-PCR revealed differential chemokine transcription.
Conclusion: Allogeneic transplantation leads to an increase of T-/B-cell infiltration and expression of B-cell factors when compared to ischemia-reperfusion; infiltration was sustained when immunosuppression was staggered. These findings demonstrate early changes in B-cell infiltration and B-cell factors and illustrate the effect of non-adherence to therapy.

P147 EVEROLIMUS - CALCINEURIN INHIBITOR FREE IMMUNOSUPPRESSIVE THERAPY. SECURE ALTERNATIVE IN SPECIAL CASES AFTER PEDIATRIC HEART TRANSPLANTATION

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Background: The standard immunosuppressive therapy after pediatric heart transplantation is a calcineurin inhibitor based immunosuppressive therapy combined with mycophenolic acid or mTor-inhibitor. A calcineurin inhibitor free therapy is not recommended because of a higher risk of acute rejection. However especially the calcineurin inhibitor associated side effects sometimes pose the hugest problems after pediatric heart transplantation. Particularly renal insufficiency and posttransplantat lymphoproliferative disease have to be mentioned here. Is a calcineurin inhibitor free immunosuppressive therapy a secure alternative in special cases after pediatric heart transplantation?
Methods: Retrospective analysis of all patients after pediatric heart transplantation under temporary or permanent calcineurin inhibitor free therapy. The analysis focused on the causes for change of the immunosuppressive therapy and the incidence of acute rejection.
Results: Between 2007 and 2014 five patients after pediatric heart transplantation were treated with a calcineurin inhibitor free immunosuppressive therapy. This special immunosuppressive regime was started on average 9 years after transplantation (range 4 to 17 years). Posttransplant lymphoproliferative disease (PTLD) ($n = 2$) and renal insufficiency ($n = 3$) made a calcineurin inhibitor free therapy necessary. The two patients with PTLD received a monotherapy with everolimus or a combination therapy with everolimus and prednisolone for seven or twenty months respectively. The target level of everolimus was 4–5 ng/ml. The patients with renal insufficiency received a permanent calcineurin inhibitor free immunosuppressive therapy with everolimus and mycophenolic acid. The target level of everolimus was 5–8 ng/ml. None of the patients suffered from acute rejection.
Conclusion: In special cases a calcineurin inhibitor free immunosuppressive therapy seems to be a secure alternative after pediatric heart transplantation.

P148 LATE ONSET OF TACROLIMUS AFTER ORTHOTOPIC HEART TRANSPLANTATION: BURDEN OR BOON?

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Background: One novel immunosuppressive therapeutic strategy after heart transplantation (HTX) is the use of a CNI-free regimen to preserve renal function. Unfortunately, a small number of patients suffers from late acute cellular rejection after CNI withdrawal. Late onset of low dose retarded Tacrolimus (TAC) (Advagraf®) can be used, despite of multiple distinct adverse side effects.
Methods: We analyzed 16 patients (female $n = 3$) who were switched to a CNI-free therapy consisting of everolimus (C0-level: 3–8 ng/ml), mycophenolat mofetil (C0-level: 2–4 ng/ml) and steroids (0.05 mg/kg body weight) between 1–117 months after HTX because of worsening kidney function. These patients were followed closely by echocardiography and myocardial biopsy. In case of recurrent, steroid-resistent acute cellular rejection, low dose TAC was added to therapy (C0-level: 3–5 ng/ml). Focus was set on histo-pathologic findings, renal function and survival.
Results: In a total of 16/158 patients, low dose TAC was added 735 days (401; 1669) after switch to a CNI-free regimen and frustrating application of pulsed steroids due to recurrent rejections (ISHLT (1990): Grade 1A/B: 18; 2A: 17; 3A: 13; 4A: 9). All patients presented clinically asymptomatic, echocardiography did not reveal significant impairment of LV-function.

In the follow-up (61–1020 days), we performed altogether 33 biopsies, the majority was without severe pathological findings (ISHLT (1990): Grade 0: 26; 1A/B: 3; 2A: 4; 3A: 0; 4A: 2). One patient presented initially with high-grade rejection, which was, in the following course, declining to grade 0. Serum creatinine levels (mean values: before TAC: 1.66 mg/dl, after TAC:1.60 mg/dl) were commonly stable, only two patients are dependent on dialysis, but presented with severe renal insufficiency before change of immunosuppression. All patients were alive during follow-up.
Conclusion: Addition of low dose retarded TAC in patients suffering from acute rejection after switch to a CNI-free immunsuppression after HTX prevents re-occurance of late acute cellular rejection and does not impair improvement of renal function gained after withdrawal of standard dose CNI based therapy.

P150 CCR5 EXPRESSION ON PERIPHERAL MONOCYTES IN RENAL TRANSPLANT RECIPIENTS

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Background: Cellular rejection of renal allografts is mediated via CCR5 signaling. However, the degree to which circulating CCR5+ monocytes influence the clinical phenotype of chronic graft dysfunction remains incompletely defined. We therefore investigated CCR5 expression on peripheral classical, intermediate and non-classical monocytes in human transplant recipients.
Methods: PBMCs were freshly isolated from heparinzed blood, stained for CD14, CD16 and CCR5, and analyzed using the BD FACSCanto II flow cytometer. Statistical analysis was determined by two-way ANOVA with Bonferroni *post hoc* test.
Results: We studied ten asymptomatic transplant recipients (aRTR) and five transplant recipients hospitalized for acute infection (iRTR). Patients did not differ with respect to age, gender, time after transplantation, CNI through levels, leucocyte counts and serum creatinine. Compared to healthy controls, aRTR exhibited significantly lower monocyte counts ($49 \pm 23\%$ vs. $12 \pm 9\%$, $p < 0.01$). In iRTR monocyte counts were similar to healthy controls. CCR5 expression on non-classical monocytes was comparable for all individuals. However, significantly more aRTR exhibited expression of CCR5 compared to iRTR or healthy controls on intermediate ($93 \pm 18\%$ vs. $53 \pm 24\%$ and $30 \pm 32\%$, $p < 0.01$) and classical monocytes ($73 \pm 17\%$ vs. $7.4 \pm 6.5\%$ and $5.5 \pm 7.4\%$, $p < 0.01$).
Conclusion: CCR5 expression on PBMCs differs significantly between human renal transplant recipients with or without active infection.

P151 RARE CASE OF COMPLETE IVC THROMBOSIS AFTER LIVER TRANSPLANTATION

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The main post-transplant complications are biliary or arterial, with have been reported to occur in 15–35% of patients (5–8). Venous steno-occlusions are much rarer, and depending on the series, the frequency is 1–5% (7.8). Stenosis or Torsion of inferior vena cava at the level of the anastomosis following orthotopic liver transplantation is an even rarer complication and occurs with a frequency of roughly 1–2% of transplants (5–8). Occlusion of the IVC might result in edema of the lower body parts, ascites and hepatic dysfunction. While surgical revision has been the mainstay of treatment for venous complications after liver transplantation, percutaneous interventional techniques have made steady progress over the past several years.

Although venoplasty and stenting are affective in many cases, patients who fail first-line treatment may require surgical intervention or re-transplantation. Scheduled sequential balloon dilatation, an approach frequently used to treat fibrotic, benign biliary strictures, but less common treating vascular lesions, may avert the need for such high-risk life-threatening alternatives while achieving favorable clinical and angiographic response.

Herein we describe a case of a complete IVC thrombosis after liver transplantation treated successfully by catheter-directed thrombolysis with removal of the thrombotic material, percutaneous transluminal angioplasty (PTA) without intravascular stent placement and initiating of arterio-venous fistulas of the common iliac vessels.

Complete IVC thrombosis due to stenotorsion of suprahepatic caval anastomosis is an unusual complication after liver transplantation. Sequential balloon angioplasty may produce a favorable outcome in cases of initially angioplasty-resistant IVC obstruction. In this case, catheter- directed open thrombectomy and sequential PTA resulted in an excellent angiographic and clinical outcome. Although the report of a single case does not constitute evidence of efficacy, clinicians should not consider non-response after one session of balloon dilatation as a treatment failure, and may consider use of sequential interventional procedures to achieve therapeutic success.

CHALLENGE SHORTAGE OF DONATED ORGANS AND RECIPIENT'S ALLOCATION

P153 CARDIOGENIC SHOCK AS A LONG-TERM-CONSEQUENCE 14 YEARS AFTER ANTHRACYCLINE-BASED CHEMOTHERAPY IN T-ALL

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Significant advances in cancer treatment have markedly improved survival rates of children diagnosed with cancer. However, chemotherapeutic or radiologic treatments may result in long-term health consequences.

Anthracyclines like doxorubicin are one of the most widely used antineoplastic agents with application that is limited by cardiotoxicity. Risk factors for the development of cardiac dysfunction include younger age at cancer diagnosis and a cumulative-dose of greater than 500 mg/m^2. Nonetheless, latest findings suggest that there is no safe dose of anthracyclines to avoid the risk of reduced cardiac function.

Here, we report on a 20-year old man with sudden onset of multi-organ-failure due to a severe cardiogenic shock with initiating multi-organ-failure and the urgent need for the implantation of a left ventricular assist device (LVAD).

Of note, fourteen years before, he had been diagnosed with childhood T-cell acute lymphoblastic leukaemia (T-ALL) implying the application of the ALL-BFM-2000-protocol with a cumulative dose of 240 mg/m^2 of anthracyclines (120 mg/m^2 daunorubicin + 120 mg/m^2 doxorubicin). Post-chemotherapeutic maintenance lasted for two years, but was ended after diagnosis of constant complete remission of T-ALL. Last visit of a cardiologist was four years after T-ALL had been successfully treated showing normal echocardiography and electrocardiogram.

Present biopsies of the myocardium demonstrated strong fibrosis and vacuolated cardiomyocytes conformable with late-onset anthracycline-induced cardiomyopathy. After live-saving LVAD implantation he recovered remarkably well and could be transferred to rehabilitation twenty days postoperatively.

Our case emphasizes the need for a consistent and detailed follow-up in cancer survivors of the childhood to assess their global risk of long-term health consequences including the development of congestive heart failure.

P154 TRANSPLANTING A TRANSPLANTED KIDNEY - A NEW CHALLENGE IN TIMES OF DONOR ORGAN SHORTAGE

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Renal transplants may be damaged by immunological and non-immunological mechanisms over time so that the outcome of an already transplanted kidney is difficult to predict. We report the case of a 67 year old patient with end-stage renal disease due to IgA nephropathy, who was succesfully transplanted in March 2014 (PRA max. 0%, 5 HLA-A/B/C/DR/DQ matches). The donor was a 67 year old woman with chronic glomerulonephritis, who received her first kidney transplant in January 2005 from an ideal donor (20 years old, polytrauma; only one HLA-A/B/C/DR/DQ mismatch). She died after cerebral infarction (potential graft damage by arterial hypertension, urinary tract infections and cyclosporine A). The last outpatient visit (11/2013) showed good graft function (serum creatinin (S-Cr) 1.0 mg/dl, proteinuria 90 mg/24 h). The kidney function was well preserved (S-Cr 0.79 mg/dl). After transplantation (two arteries, basiliximab induction, tacrolimus/MMF/steroids) with a short cold ischemia time (10h12 min), duplex ultrasound showed a moderately reduced perfusion, without renal artery stenosis (confirmed by MR scan). Graft function was delayed (one posttransplant dialysis) but reached satisfactory and stable values (S-Cr 2.6 mg/dl, 1-year posttransplant) without acute rejection episodes. The 4-month protocol biopsy showed a reactive focal segmental and focal global glomerulosclerosis (4/13 and 4/13 glomeruli) and a 20% chronic tubulo-interstitial damage without signs of rejection or cyclosporine toxicity. Our case report shows that chronic damage of a long-term transplanted kidney is difficult to predict without biopsy. Significant chronic damage was detected in the 4-month protocol biopsy, despite well preserved predonation graft function and an ideal young original donor with nearly full HLA match. Nevertheless, 1-year graft outcome is satisfactory and encourages evaluation of organ donors bearing a transplanted kidney for kidney retransplantation in times of organ shortage.

P155 HEART TRANSPLANTATION WITH DONORS 60 YEARS OF AGE AND OLDER

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Objective: Despite numerous potential options, the most effective immediate solution for an increased donor pool is the expansion of acceptance criteria for donor age and medical condition. We aimed to compare the outcome after HTx with regard to the age of donor organs.
Methods: Between 2010 and April 2015, 11 patients underwent htx in our department using donor hearts 60 years of age and (group 1). Those were compared with 42 patients receiving younger donor organs (gr.2).
Results: We did not find differences between the groups with regard to epidemiologic data, comorbidities, clinical status and transplant status at transplantation. Donor criteria, including ejection fraction, CMV status, time of ischemia as well as sex were also comparable.

30-day mortality was similar in the groups (18.2% in gr.1 vs. 14.3% in gr.2; $p > 0.05$). Survival after 1 and 2 years also did not differ significantly. In both groups there were 2 patients requiring additional CABG during htx ($p < 0.05$). During follow-up, coronary artery vasculopathy occurred in 1 patient in gr. 1, not in group 2. There were no patients requiring re-htx.

After 1 year, ejection fraction was satisfying in both groups. Midterm cardiac morbidity was lower in group II ($p = 0.03$). However, there was only one CMV-infection during follow-up in both groups. Freedom from rejection episodes (>°1R) was similar.
Conclusions: Donor age did not significantly influence midterm outcome after htx. Carefully selected, older donor hearts can be used for heart transplantation with survival and outcome similar to those of younger donor organs.

P156 NORMOTHERMIC *EX VIVO* KIDNEY PERFUSION REPRESENTS A NOVEL PRESERVATION METHOD FOR HEART BEATING DONOR KIDNEY GRAFTS

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Background: The ongoing organ shortage has resulted in an increased interest to recover marginal kidney grafts for transplantation. Recently, Normothermic *Ex Vivo* Kidney Perfusion (NEVKP) has been developed as a novel preservation technique for kidney transplantation. We assessed the safety and efficacy of NEVKP in pig kidney transplantation.
Methods: Normothermic *Ex Vivo* Kidney Perfusion (NEVKP) at 37° was compared with cold storage (CS) at 4° in a model of heart beating porcine kidney autotransplantation (male Yorkshire pigs, 30 kg) ($n = 5$ each group). NEVKP and CS were performed for 8 h respectively. Continuous normothermic perfusion circuit characteristics, hourly blood gas samples, and renal real-time injury markers were investigated. Following autotransplantation, serum creatinine and blood urea nitrogen (BUN) were measured as markers of kidney function. After ten days, tissue biopsies were taken and stained (H&E, PAS, TUNEL) to investigate renal injury.
Results: Perfusion circuit characteristics such as temperature, arterial and venous pressure, renal blood flow (RBF), and intrarenal resistance (IRR) were maintained at a physiologic level throughout NEVKP. High rates of oxygen consumption revealed the metabolic activity of the perfused kidney grafts (89.1 ± 10.9 ml/min/g at 6 h). Aspartate aminotransferase, lactate, and lactate dehydrogenase values, as renal real-time injury markers, were below analyzer range throughout perfusion. Following contralateral kidney resection and renal autotransplantation, peak serum creatinine and BUN values on day one after surgery demonstrated a trend towards improved graft function in NEVKP versus CS preserved grafts (creatinine 2.1 ± 0.51 mg/dl vs. 2.8 ± 0.71 mg/dl and BUN: 19.8 ± 3.5 mg/dl vs. 25.3 ± 7.4 mg/dl; $p = 0.16$ and $p = 0.22$). Histological investigation demonstrated slight alterations in tubular morphology and no signs of necrosis in both groups.
Conclusion: This study demonstrates feasibility and safety of NEVKP as a novel preservation method for heart beating donor grafts. It provides a platform to further improve storage, assessment, and repair of marginal kidney grafts.

P161 ALCOHOL-SCREENING ON THE WAITING LIST FOR LIVER TRANSPLANTATION

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Optimal selection of liver transplant candidates and early detection of alcohol relapse is necessary to improve long-term outcomes. In this study, we screened our patients (n = 213) on the waitinglist between 2011 and 2014. We controlled the sobriety on each consultation by interrogation and supportive by biomarkers (blood alcohol, urinary ethyl glucuronid, Carbohydrate-deficient transferrin [CDT]).On the alcohol-liver-disease (ALD) group of 83 patients, we tested 76% by biomarker, which were positive in 22 patients (35%) for at least one test. On the other group (non-ALD) we tested only 51% with biomarker, which were positive for 4 (correspond to 6%) patients. None of the patient admitted the alcohol consumption by interrogation. All positive tested patients were reported inactive to eurotransplant and underwent a re-evaluation including a psychiatric setting. In case of a renewed psychiatric release a 6 month period of sobriety was necessary before reactivating the notification to eurotransplant. In case of no psychiatric release or relapse during the new sobriety-period the patients were removed from the waitinglist.
Conclusion: Even after at least six month of sobriety, we detected in 35% of the patient an alcohol relapse. This shows clearly that the use of biomarkers is necessary to control the sobriety.

CHALLENGE SHORTAGE OF DONATED ORGANS AND RECIPIENT'S ALLOCATION/POLITICAL, ECONOMIC, LEGAL ASPECTS

P164 EFFECTIVENESS OF ORGAN DONATION INFORMATION CAMPAIGNS IN GERMANY - A FACEBOOK BASED ONLINE SURVEY

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Background: The German transplantation system is in a crisis due to a lack of donor organs. One of the main approaches to increase organ donation rates are information campaigns. Since 2012 German health insurance funds are obliged by law to inform their members about organ donation. We raised the hypothesis: The willingness to sign a donor card rises by receiving the information material of the health insurance funds due to the subsequent increase of specific knowledge.
Objective: To assess the influence of information campaigns on the specific knowledge and the willingness to organ donation.
Methods: We conducted an online survey based on recruitment via Facebook groups and advertisement using the snowball effect and based on mailing lists of medical faculties in Germany. Besides the demographic data, the willingness to hold an organ donor card was investigated. Specific knowledge regarding transplantation was explored using five factual questions resulting in a specific knowledge score.
Results: We recruited a total of 2484 participants, of which 32.7% (300/917) had received information material. Mean age was 29.9 (SD = 11.0, median 26.0). There were 65.81% (1594/2422) of the participants that were female. The mean knowledge score was 3.28 of a possible 5.00 (SD = 1.1, median 3.0). Holding a donor card was associated with specific knowledge ($p < 0.001$), but not with the general education level ($p = 0.155$). Receiving information material was related to holding a donor card ($p < 0.001$), but not to a relevant increase in specific knowledge (difference in mean knowledge score 3.20 to 3.48, $p = 0.006$). The specific knowledge score and the percentage of organ donor card holders showed a linear association ($p < 0.001$).
Conclusions: The information campaign was not associated with a relevant increase in specific knowledge, but with an increased rate in organ donor card holders. This effect is most likely related to the feeling of being informed, together with an easy access to the organ donor card.

P165 VAD INFECTION: DOES IT ALWAYS JUSTIFY HIGH URGENCY STATUS?

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Background: VAD infection is a devastating complication in patients on VAD support and usually treated by device removal, thus requiring transplantation or VAD re-implantation. In patients bridged to transplant, it may appear more reasonable to aim for transplantation as VAD exchange carries considerable morbidity and mortality. However, this raises questions with regard to the justification of HU listing for VAD infection.
Methods: Among our population of VAD recipients bridged to transplant, three were diagnosed with VAD infection consisting of a combination of intrapericardial empyema and intrathoracic abscesses in each. They were treated by a combined surgical and anti-infective approach with a view to retaining the hardware until transplantation.

When the first patient presented with culture-negative VAD infection, his listing status was immediately set to HU. He remained in the ICU/IMC for a total of 46 days and underwent several debridements combined with underpressure therapy and anti-infective treatment. As no donor organ became available, therapy was continued until infection was successfully eradicated. In the second case, aspergillus device infection occurred very early after implantation so that VAD exchange rather than HU listing was considered but finally turned out to be unnecessary as infection was once again successfully eradicated. Given the experience from the first two cases, HU listing in the third patient was deferred in favor of an attempt at device preservation and finally turned out to be unnecessary when Staphylococcus aureus infection was found to be amenable to a combination of surgical and anti-infective treatment.
Results: VAD infection was eradicated by a combined surgical and anti-infective approach in all three patients. With anti-infective treatment terminated, they have now been free from recurrence for > 6–10 months and are listed for regular heart transplantation.
Conclusions: An approach combining surgical and anti-infective therapy, with close monitoring for deterioration, may allow hardware to be retained and infection to be eradicated while waiting for heart transplantation. Our cases suggesting little benefit of HU listing, VAD infection as a justification for HU listing may be challenged unless infection turns out to be unmanageable by other resources.

P167 DONOR-DERIVED TUBERCULOSIS AFTER SOLID ORGAN TRANSPLANTATION IN TWO PATIENTS AND A STAFF MEMBER

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Because of global mobility and migration resulting in a growing diversity of the donor pool the risk for donor-derived tuberculosis (TB) in solid-organ transplant (SOT) recipients becomes more and more relevant, even in countries with a low overall TB-incidence. Here we describe a case series of donor-derived TB in 2 of 3 SOT recipients and one medical staff member in Germany resulting in the death of one recipient. This case series highlights the relevance of this topic to clinicians. It advocates for a better communication between OPOs and TPCs regarding donor information and transplant recipient outcome. Furthermore it underpins the necessity for a German transplant registry to improve short and long-term recipient's safety, health and survival.

P168 IS IT POSSIBLE TO PREDICT RENAL TRANSPLANT FUNCTION BY AN ESTIMATION OF THE GFR USING THE AVAILABLE DONOR DATA?

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Introduction: Allocation of marginal organs is still a dilemma. On the one hand, organ shortage calls for the best possible use of organs, on the other hand futile transplantation should be avoided. Therefore, a reliable way of predicting organ function by using the available donor data would be of great help in daily allocation practice.
Methods: We retrospectively studied if we could predict the outcome of a renal transplant by calculating the GFR using the best available donor data from the Eurotransplant Organ report. We restricted our investigation to the patients who had be transplanted in the ESP in our center between 2005 and 2014 ($n = 176$). GFR was calculated according to the Cockroft-Gault formula. We correlated the GFR to the serum creatine levels of our recipients at discharge ($n = 176$) and 1 year ($n = 119$), 3 years ($n = 85$) and 5 ($n = 54$) years after transplantation. Analysis was performed using a linear regression method.
Results: We could demonstrate a correlation between the GFR calculated from the donor data and the subsequent renal transplant function which was more marked regarding the creatine levels at discharge ($r = 0.79$) and 1 year after transplantation ($r = 0.82$). It declined at 3 years ($r = 0.77$) and 5 years ($r = 0.74$) following the transplant operation.
Conclusion: It is not surprising to find a correlation between donor renal function and the later function in the recipients. The question is, however, if a decision in the allocation process based only on the calculated GFR is sufficient or if it is necessary to used more refined scoring systems. Our data suggest that is possible to get a general idea of the expected renal function in the recipient by calculationg the GFR in the donor, although it was not always helpful regarding the single patient. We also acknowledge that our analysis has its drawbacks since it considers only the accepted organs. Nevertheless, the method is easy to use and poses only a minimal additional workload on the staff concerned with organ allocation.

P169 **HEALTH ECONOMIC ANALYSIS OF RABBIT ANTITHYMOCYTE GLOBULIN (THYMOGLOBULIN) VERSUS BASILIXIMAB IN RENAL TRANSPLANTATION - A GERMAN PERSPECTIVE**

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Introduction: Kidney transplantation is now accepted as a proven therapeutic modality prompting a greater need to understand the cost-effectiveness of differing treatment approaches.
Methods: Primary objective was to quantify the economic consequences of acute rejection and adverse events in cadaveric kidney transplant recipients treated with thymoglobulin (Thymo) compared with those receiving basiliximab. Direct health economic data were collected according to clinical trial observation from 3 German sites in an existing database (Brennan et al NEJM, 2006)
Results: Based on the clinical data from the Brennan trial, the study quantified current data and changes in treatment patterns. Results demonstrate that at 12 months the cost of the Thymo regimen is €5753 more than that of the basiliximab regimen. However, costs of delayed graft function, nonfatal graft failure events and post-graft failure dialysis are lower among Thymo- treated patients (p = ns). Infection treatment costs are nearly identical in the two groups. Thymo treated patients incurred higher graft maintenance costs, consistent with their longer graft survival (p = ns). The associated cost from lower rejection events with Thymo offset the added cost from drug treatment and therefore Thymo is a more cost-efficient resource versus basiliximab due to cost-avoidance.
Conclusion: This analysis intended to provide information about costs and benefits of two immunosuppressive regimens and to investigate if treatment changes might result in more cost-effective care.

LIVING DONATION/PSYCHOSOMATICS, ETHICS

P171 *POST HOC* SUBGROUP ANALYSIS OF ZEUS: OUTCOME ON RENAL FUNCTION, EFFICACY AND SAFETY IN LIVING-DONOR KIDNEY TRANSPLANT RECIPIENTS AFTER CONVERSION FROM A CALCINEURIN INHIBITOR TO AN EVEROLIMUS BASED REGIMEN: 5 YEAR FOLLOW-UP DATA

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Purpose: To study renal function and patient outcome after 5 years in living donation subgroup of kidney de novo transplant recipients after conversion to an everolimus (EVR) based regimen and withdrawal of calcineurin inhibitor therapy.
Methods: *Post hoc* subgroup analysis from the prospective, open-label, controlled, multi-center study ZEUS. 300 renal transplant (Tx) patients were randomized at month 4.5 post Tx to either receive EVR plus enteric coated-mycophenolate sodium (EC-MPS) or cyclosporine (CsA) plus EC-MPS regimen. Of these were 80 living donor (LD) recipients (EVR group $n = 42$; CsA group $n = 38$). Patients could enter an observational follow-up (FU) period where outcome on patients' safety and efficacy was recorded until month 60 post Tx.
Results: Adjusted eGFR (Nankivell) in living donation subpopulation at month 60 was 67.2 (95% CI [62.5, 71.9]) mL/min/1.73 m2 in EVR versus 60.8 (95% CI [56.0, 65.6]) mL/min/1.73 m2 in CsA patients, resulting in a difference of +6.4 ml/min/1.73 m2 in favor of EVR patients ($p = 0.031$, ANCOVA). Unadjusted mean eGFR after 5 years was 69.5 ml/min for EVR versus 60.6 ml/min for CsA ($p = 0.006$, Wilcoxon). BPARs during FU since month 12 occurred in 4 patients of the EVR and 3 of the CsA group, all BANFF grade IA except one BANFF grade IIA among EVR patients. From randomization to month 60 one death occurred in CsA living donor recipients, two in the EVR living donation subgroup; one graft loss occurred in the EVR, none in the CsA group. Overall safety profile was similar between both treatment groups.
Conclusion: The presented analysis shows that EVR-based regimen with early elimination of CNI-therapy in living donor kidney transplant recipients is associated with a significant benefit on renal function maintained over 5 years post Tx without compromising safety and efficacy.

P172 ROBOTIC-ASSISTED DONOR NEPHRECTOMY FOR LIVING DONOR KIDNEY TRANSPLANTATION - UPDATE OF THE OUTCOME OF THE FIRST PATIENTS IN GERMANY

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Introduction: The emerging organ shortage raises the focus on living donation in many Transplantcenters. Transplantation after living kidney donation offers longer graft survival. In order to reduce the significant trauma for the donor, caused by the conventional retrieval procedure, the robotic-assisted donor nephrectomy was introduced in our center. The system allows a greater freedom of movement and recreates the hand-eye coordination and 3D-vision that is lost in standard laparoscopy. Here we provide an update of our series.
Methods: The daVinci ® system was used for a transperitoneal laparoscopic nephrectomy. All patients ($n = 27$) were positioned in an elevated-side-position. The intra-abdominal pressure was 12 mmHg, five trocars were used. The camera was positioned supra-umbilically pararectal. Vessels were ligated with two haemoloc ® clips. The organs were retrieved hand assisted via pfannenstiel incision, or via mini laparotomy.
Results: Operation time ranged between 127 and 284 min, blood-loss in all cases <300 cc. The warm ischemia time reached from 1 min 30sec to 6 min. No serviere postoperative complications (Charlston grade >2) occurred, expect one donor who developed a GERD who needed additional gastroenterological intervention. Donors stayed for 6.1 days in hospital (Median range 4–14 days).
Conclusion: The application of minimal invasive techniques allow an increased acceptance of the living kidney donation and may decrease the burden the recipients feel for their donors. The introduction of the robotic system holds the potential for a remarkable technical achievement in this matter. In our opinion it may therefore lead to a further increase of the numbers of donors for this life-saving transplant. The results are encouraging and clearly prove feasibility and safety.

P175 QUALITY OF LIFE 1 YEAR AFTER LIVING KIDNEY DONATION

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Background: Health-related quality of life (QOL) is an important outcome parameter in living kidney donation (LKD), but prospective data is still rare.
Methods: We prospectively evaluated QOL with the WHOQOL-Bref questionnaire in 72 donors 1 year after LKD. Furthermore, we analyzed potential influencing factors including kidney function.
Results: The sample consisted of 72% female donors. Mean age at donation was 53.8 years (SD = 10.4). The majority of recipients were adults (90%), most of them being the donor's child (43%) or spouse/partner (42%). QOL prior to LKD was higher than in the age-adjusted general population. After LKD, there was a significant decrease in all domains ("physical health": $p = 0.001$, "psychological": $p = 0.01$, "social relationships": $p = 0.03$, "environment": $p = 0.004$, "global QOL": $p = 0.001$). Postoperative QOL remained above that in the general population in "physical health" ($p = 0.001$), "environment" ($p < 0.001$), and "global QOL" ($p < 0.001$), while in "psychological" ($p = 0.21$) and "social relationships" ($p = 0.06$) it was not significantly different from the general population. Neither surgical technique (retroperitoneoscopic versus mini-incision) nor age, gender, BMI, or serum creatinine 1 year after LKD were significantly associated with QOL.
Conclusion: QOL 1 year after LKD was lower than preoperative QOL but at least comparable to the general population. QOL was not associated with socio-demographic or clinical variables.

P176 PSYCHOSOCIAL DIFFERENCES BETWEEN LIVING AND DECEASED DONOR RENAL TRANSPLANT RECIPIENTS

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The specific impact of living-related renal transplants as compared to deceased donor (DD) transplants on psychosocial functioning has received surprisingly little attention.

The present study aimed to assess whether living donor (LD) and DD recipients differ in socio-demographic variables, time since transplantation, emotional variables, knowledge about immunosuppressant (IS) intake, and self-reported adherence to IS.

A questionnaire study was performed among 72 LD and 169 DD recipients who attended the Department of Nephrology for a follow-up visit at least 1 year after transplantation.

Emotional responses were assessed using the Hospital Anxiety and Depression Scale (HADS) and the Transplant Effect Questionnaire (TxEQ). Patients' knowledge about IS intake was examined with a newly developed test consisting of 8 multiple choice questions, and IS adherence was measures by self-report (BAASIS), physicians' estimation, IS serum level variability, and allograft rejection.

Overall, LD recipients were younger and had a shorter duration since transplantation. Our results indicate that LD and DD transplantation may lead to different emotional responses with more feelings of guilt towards the donor and perceived responsibility to do well and with a generally higher anxiety level in LD recipients. LD recipients apparently had more knowledge about IS medication; however, they did not report more adherence to IS. No differences between LD and DD recipients were found for gender, educational level, depression, perceived social support, and allograft rejection. Feelings of guilt and anxiety may be an important focus for interventions to improve emotional adjustment to transplantation especially in LD recipients.

P178 AVOIDANCE OF LIVER TRANSPLANTATION IN SEVERE ALCOHOLIC LIVER DISEASE PATIENTS ABSTINENT FOR 6 MONTHS - A PROPOSAL FOR A PROSPECTIVE, MULTICENTRIC, OBSERVATIONAL STUDY (PROLIVIT)

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Background: Alcoholic cirrhosis remains the second most common indication for liver transplantation. Most transplant centers worldwide demand a 6 months period of full alcohol abstinence prior listing. The 6-months rule was frequently challenged since the 6-months period is arbitrary and there are probably multiple other factors that predict alcohol relapses. Clinical experience, however, shows that many patients who stop drinking alcohol recompensate to a stage where they do not need a liver transplantation. In these cases detoxification and not liver transplantation would be indicated.

We propose a prospective, multicentric observational study to examine the recovery of liver function of patients with alcoholic liver cirrhosis who stopped drinking in their 6 months probatory waiting time prior liver transplantation.

Study protocol: Patients with alcoholic liver cirrhosis and an indication for liver transplantation will be included. During their primary assessment patients are seen by a transplant psychiatrist and a heptologist. Professional detoxification therapy and the inclusion to a structured short-term cessation therapy are offered. Indication for liver transplantation will be confirmed by the local multidisciplinary transplant conference, usually based on a CHILD B/C cirrhosis and a MELD score $\geq$ 15 at the time of assessment. Patients will be explained that listing for transplantation will only be offered after a strict 6 months alcohol free period. Compliance will be tested by serum alcohol and ETG testing on a regular basis.

The primary endpoint is improvement of liver function at 6 months after the cessation of alcohol. Patients will be reevaluated for an indication for liver transplantation at this time (MELD $<$ 15, no other indication). Secondary endpoints will include the rate of recidivism and mental health status during waiting time, as well other objective parameters of liver function.

From this study we expect an answer to the question whether transplantation can be avoided by consequent 6 months alcohol abstinence.