ORAL PRESENTATIONS

LIVER I: EXPANSION OF THE DONOR POOL/LIVER LIVING DONATION

V002 AB0 – INCOMPATIBLE LIVING DONOR LIVER TRANSPLANTATION (LDLTX) HINDERED BY ANTIBODY REBOUND

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Introduction: LDLT is an option to expand the donor organ pool for patients who can not be promptly supplied with a cadaver donor in spite of a potentially life-threatening disease. In Germany and Western Europe exist only a few small case series to AB0i LDLT.
Patient/ Method: We have prepared 10 patients for AB0i LDLTX. The donor recipient blood type combinations were A1→0 in four cases, A2→B one case, A1B→A three cases, A1B→B one case and B→A2 one case. The initial iso-titres at first examination time differ from 1:2048 to 1:8.
Results: On average, we performed four PTP (min 1, max 7) prior to TX and six PTP (min 0, max 12) after TX.
Conclusion: Surprisingly the TPE deplete the AB0 IgG antibodies in LDLTX better than IA. The TPE seems to be the PTP with the best ratio of cost and benefits in LDLTX. Most likely the outcome of AB0i LDLTX is more dependent on the antibody rebound than on the initial iso-titres. A LDLTX should not be performed when TRR<TI, TI>2 and not earlier than 7 days after the beginning of the desensitization therapy in carcinoma patients only.

V004 LIVING DONOR SEGMENT 2/3 LIVER GRAFT WITH ACCESSORY LEFT LIVER ARTERY TO SEGMENT 2: A TWO-STEP APPROACH USING LAPAROSCOPIC ARTERIAL LIGATION FOR FLOW MODULATION AND PRECONDITIONING

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Introduction: Despite recent advancements in surgical techniques, living-donor liver transplantation (LDLT) remains a challenging procedure – in particular when hepatic artery anomalies are present. An additional left hepatic artery is found in 12% to 21% of the population. The presence of accessory arteries is graded as unfavourable and may lead to an exclusion of potential donors. In the present case report we describe a surgical two-step approach to modify arterial perfusion of the graft before LDLT.
Methods: A 47-year-old mother qualified for left lobe donation for her child (8 months – biliary atresia). MRI diagnostic revealed an accessory left liver artery to liver segment II. The remaining left liver lobe was supplied with arterial blood through the common hepatic artery. To avoid arterial hypoperfusion of segment 2, we decided to perform an in-situ preconditioning of hepatic blood flow by ligation of the accessory left hepatic artery. Ligation was performed laparoscopically. Hepatic perfusion was re-evaluated by ultrasound and computed tomography (CT).
Results: Ultrasound and a CT-scan after one month revealed adequate arterial hepatic perfusion. Segment 2/3 transplantation was performed successfully. Posttransplant ultrasound revealed homogenic hepatic perfusion of the graft. The recipient was discharged on POD 37 with excellent graft function.
Conclusion: Preoperative conditioning via ligation of a left accessory artery for segment 2 facilitates successful living donor segment 2/3 pediatric liver transplantation despite vascular anomalies.

ECONOMY

V005 ECONOMIC IMPACT OF DONOR AND RECIPIENT QUALITY METRICS IN KIDNEY TRANSPLANTATION – AN INSTITUTIONAL PERIOPERATIVE COST ANALYSIS

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Background: End-stage renal disease (ESRD) has a major impact on health care costs. Kidney transplantation (KT) has been shown to be the most cost-effective therapy of ESRD. Donor organ shortage and growing waiting lists have led to strategies to expand the donor pools. The impact of these programs on hospital revenues is unclear. The aim of the study was to determine risk factors for increased expenditures after KT.
Methods: Analysis of hospital costs and revenues of KT recipients from January 2012 to January 2016 by investigating departmental financial accountings.
Results: A total of 174 KT were performed consisting of 92 (52.9%) expanded criteria donor (ECD) organs and 43 (24.7%) 'old-for-old' transplantation. Total costs estimated 22,865 ± 14,962€ for standard criteria donor (SCD) and 24,964 ± 13,191€ for ECD organs (Δ = 2,099€; $p = 0.327$). 'Old-for-old' transplantation showed highest costs with 26,973 ± 14,644€ (Δ = 3,982€; $p = 0.107$; compared to SCD). Donor's stroke or atraumatic intracranial bleeding as cause of death were associated with increased costs (OR 3.0 and 1.9; both $p < 0.05$). Recipient's obesity (OR 2.2) and age ≥ 65 years (OR 2.1), delayed-graft-function (OR 5.2) and reoperations (OR 24.6) were identified as independent predictors for increased costs (all $p < 0.05$).
Conclusion: ECD organs were not associated with considerable higher costs. Gross margins were slightly higher after ECD KT when compared to SCD. Medicare costs were significantly increased after "old-for-old" transplantations. Recipient characteristics seem to be more relevant parameters in cost prediction than donor characteristics.

BASIC SCIENCE I: VARIA

V006 SILENCING OF MHC CLASS I AS A NOVEL STRATEGY FOR REDUCTION OF ALLOREACTIVITY IN HEPATOCYTE TRANSPLANTATION – A PRELIMINARY *IN VITRO* STUDY

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Introduction and Background: Hepatocyte transplantation (HTx) is of large potential as an additional treatment modality for various liver diseases. However, primary hepatocytes seem to be highly antigenic *in vitro* and *in vivo* unlike the whole liver. Alternative strategies of immunomodulation thus are of special interest. Primary human hepatocytes (PHH) are known to constitutively express MHC class I, consequently silencing of MHC class I expression could potentially reduce the allogeneic immune responses induced upon transplantation and hence improve the outcome of HTx.
Methods: PHH were isolated using a 2-step-collagenase perfusion technique. Expression of MHC class I was silenced using lentiviral vectors encoding for β2-microglobulin (shβ2m) specific short hairpin RNA (shRNA). A non-specific shRNA (shNS) was used as control. Thereafter PHH were co-cultured with allogeneic lymphocytes (labeled with PKH-26) in terms of a mixed lymphocyte hepatocyte culture (MLHC). Proliferative responses were detected on day 10 of MLHC via flow-cytometry.
Results and Conclusions: The delivery of shβ2m into PHH caused a decrease by up to 96% in β2m transcript levels in comparison to shNS. This induced the downregulation of MHC class I cell surface expression by 73%±14% in comparison to shNS-expressing PHH. Subsequently, proliferative responses against silenced PHH were significantly lower than observed for unsilenced PHH (7.6%±3.2% vs. 15.6%±4.6%; $n = 9$). Preliminary *in vitro*

data thus indicate that silencing of MHC class I on PHH might represent a promising approach for immunomodulation in the transplant setting.

V007 ROLE OF CATS/PAR2 FOR THE REJECTION PROCESS IN MURINE RENAL TRANSPLANTATION

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Background: Cathepsin S is involved in peptide loading to the MHC class II and thus important for antigen presentation. CatS can also be secreted by activated macrophages and neutrophils and activates protease-activated receptor-(PAR)-2 on the endothelial cells. We hypothesized that targeting CatS/Par2 would have a dual suppressive effect on kidney allograft rejection by limiting alloantigen presentation as well as vascular damage.
Methods: Murine kidney transplantation was performed in the syngeneic (B6 to B6) and allogeneic setting (Balb/c to B6). Mice were either treated with CatS inhibitor or vehicle. To study the effects of *Par2* deficiency, we performed kidney transplantation using C57BL/6.*Par2*$^{-/-}$. Therapeutic effects were assessed by histopathology, immunohistochemistry and RT-PCR.
Results: At 10 days allografts showed severe acute rejection with strongly induced mRNA levels of CatS and numerous inflammatory genes. CatS inhibition significantly ameliorated the acute rejection process. Immunostaining showed suppressed $CD8^+$ cell infiltration into grafts, reduced mRNA expression levels of inflammatory genes. Allografts from *Par2*-deficient mice showed less histological damage and less graft infiltrating $CD8^+$ cells as compared to their wildtype controls.
Conclusions: These data show that CatS/Par2 is critically involved in the pathogenesis of allograft rejection.

V008 INNATE IMMUNE CELLS ARE ACTIVATED BY REGULATED CELL DEATH EVENTS IN EARLY HEPATIC ISCHEMIA REPERFUSION INJURY

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Background: Ischemia reperfusion injury (IRI) remains an important problem in clinical organ transplantation. There is growing evidence that innate unconventional effector T cells play a key role in mediating early hepatic IRI. Regulated cell death (RCD) events like ferroptosis and necroptosis are involved, but the mechanisms underlying the T cell-RCD crosstalk are poorly understood.
Methods: In this study we investigate early immunological events in a model of hepatic IRI in genetically targeted mice to study the role of RCD events. We used ferroptosis resistant *knockout* (KO) mice which underwent a 90 min partial warm ischemia, followed by 24 h of reperfusion. Furthermore, we used a clinically more relevant model where we blocked the pathway of RCD (inhibition of ferroptosis) by drugs. Hepatocellular injury was evaluated by HE-histology and serum-transaminase measurement. Hepatic leukocyte subsets and cytokine secretion were characterized by immunohistochemistry, ELISA, RT-PCR and FACS.
Results: Mice resistant to ferroptosis induction were protected from hepatic IRI (serum transaminase levels 920U/l vs. 2540U/l in wt controls; $p = 0.02$). We found that unconventional $CD27^-$ $\gamma\delta TCR^+$ and $CD4^-$ $CD8^-$ double-negative (DN) T cells (major effector cells in hepatic IRI) are significantly reduced in the livers of those mice, where the RCD pathway is blocked (genetically or by drugs). We further show that the proinflammatory cytokine TNFα, which can induce further necroptosis events, is reduced in these KO animals.
Conclusion: Ferroptosis events appear to be the initial activator for hepatic IRI and lead to further progression by activating innate unconventional CD27-$\gamma\delta TCR^+$ and CD4-CD8-DN T cells. This opens new therapeutic options to improve LTx outcomes.

V010 IMMUNOSUPPRESSIVE DRUGS QUANTITATIVELY AND FUNCTIONALLY IMPAIR HUMAN MUCOSAL ASSOCIATED INVARIANT T-CELLS IN LIVER TRANSPLANT RECIPIENTS

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Mucosal-associated invariant T- (MAIT-) cells constitute a recently identified unconventional T cell population characterized by expression of the TCRVα7.2 chain specifically recognizing bacterial and fungal vitamin B metabolites presented by the MHC-Ib molecule MR1. Being equally responsive to inflammatory cytokines, MAIT cells bridge innate and adaptive immunity. As these cells have been shown to play a role in severe infections, we investigated their phenotypical and functional properties under common immunosuppressive regimens (IR) in individuals after liver transplantation. Regardless of the type of IR, patients exhibited significantly reduced frequencies of peripheral MAIT cells as compared to healthy controls, characterized by an activated, exhausted $HLA\text{-}DR^+CD38^+PD1^+$ phenotype. Upon innate cytokine stimulation, we detected significantly reduced frequencies of TNFα+ MAIT cells in all investigated IR groups (e.g. Cyclosporine A, Tacrolimus and/or MMF), accompanied by a drop in polyfunctional $TNF\alpha^+IFN\gamma^+GranzymeB^+$ cells. In response to specific stimulation with bacterial antigen, $IFN\gamma^+$ MAIT cells were significantly reduced whereas other cytokines were unaffected. As MAIT cells serve important surveillance tasks at barrier tissues, our data paves way to decipher how MAIT cell impairment contributes to the development of opportunistic infections in patients under immunosuppressive therapy.

V011 MOLECULAR ARCHITECTURE OF ETAR ACTIVATION MEDIATED BY ENDOTHELIN-1 AND ETAR-AGONISTIC ANTIBODIES

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Endothelin-1 type A receptor (ETAR) exhibits multiligand binding abilities and signals upon natural ligand Endothelin-1 (ET-1)- and ETAR-agonistic IgG (ETAR-IgG)-mediated stimulation. Development of high-resolution methods allows for structural-functional relationship studies of specific receptor modules in the receptor activation. Elucidation of ETAR activation mechanisms could have broad clinical relevance for obliterative vasculopathies, at the example of vascular transplant rejection.

To distinguish the activation mediated by the natural ligand or the agonistic antibodies, we developed a GPCR activation assay in yeasts and signalling reporter assays in mammalian cells. ETAR activation was induced by addition of ET-1 or ETAR-IgG isolated from patients with associated transplant pathology.

Both, ET-1 and ETAR-IgG triggered a dose-dependent activation. ETAR-IgG stimulation induced stronger activation of the receptor than ET-1. Targeted mutagenesis was performed in order to identify which receptor regions govern the activation. Replacing the second extracellular loop (ECL2) abolished ET-1-mediated G12/13 signalling. The same results were observed when introducing point mutations in the first ECL. ECL3 mutation led to a constitutive activation of the receptor. We successfully created models allowing for structural and functional studies of molecular architecture modules appreciating ETAR receptor plasticity, which helped us to define the role of the specific extracellular domains. Better understanding of the molecular mechanisms responsible for ETAR activation holds great potential for design of more specific ETAR blockers.

THORACIC ORGANS I: HEART

V012 SUPERIOR RENAL FUNCTION WITH CNI-FREE EVEROLIMUS OVER STANDARD CNI-BASED REGIMEN: 18 MONTHS DATA FROM THE RANDOMIZED, MULTI-CENTER MANDELA TRIAL IN *DE NOVO* HEART TRANSPLANT RECIPIENTS

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Purpose: The MANDELA study (NCT00862979) was designed to assess the benefit on renal function of either a CNI-free or CNI-minimized everolimus [EVR]-based regimen after early conversion of de novo heart transplant recipients (HTxR).
Methods: MANDELA is a multi-center, randomized, controlled, open-label, 12 month study. In total 232 de novo HTxR were enrolled 3 months [M] post Tx, of whom 162 could be randomized (1:1) to receive either EVR (C0-h 5–10 ng/mL) with reduced CNI (TAC C0-h 3–8 ng/mL or CsA C0-h 50–150 ng/mL) + steroids (≤0.3 mg/kg) or EVR (C0-h 5–10 ng/mL) with mycophenolic acid (EC-MPS max. 2880 mg/day or MMF max. 3 g/day) + steroids (≤0.3 mg/kg). The primary objective was renal function [eGFR; MDRD] 12 M after randomization for assessment of superiority in CNI-free over CNI-reduced EVR group. Key secondary objectives included efficacy (composite of BPAR ISHLT1990 grade≥3A/ISHLT2004 grade≥2R, graft loss/re-transplant, death or loss to follow-up) and safety profiles including infections.
Results: Primary endpoint for superior renal function in CNI-free EVR arm was met with high significance: a difference of +11.3 mL/min in favor of CNI-free EVR group versus CNI-reduced group ($p < 0.001$) in full analysis set; per protocol analysis showed a difference of +16.8 mL/min in favor of CNI-free EVR arm ($p < 0.001$) [eGFR (ml/min) from MDRD formula; LS-mean from ANCOVA model]. Rate of MACE and BPAR was in line with international standards and the safety profile according to the patient set and drugs investigated herein. Data from full analysis will be presented at DTG2018 meeting.
Conclusion: MANDELA study showed improved renal function can be achieved by early conversion to an everolimus-based CNI-free regimen in HTxR without compromising safety and efficacy.

KIDNEY I: PUSHING THE LIMIT

V016 A CRITICAL ANALYSIS OF MODERN ULTRASOUND METHODS (INCL. CEUS) FOR THE EVALUATION OF BLOOD FLOW IN KIDNEY TRANSPLANTS

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Background: For the assessment of kidney transplants ultrasound is the first method of choice in daily routine and when problems are supposed. Modern ultrasound techniques e.g. contrast-enhanced ultrasound (CEUS) or digital flow methods (B-Flow) are developed recently. Aim of this study is to determine the applicability of different modern ultrasound methods including CEUS for the assessment of blood-flow in kidney transplants.
Methods: Fifty examinations of 41 renal transplanted patients were examined by B-Mode, color-coded Doppler sonography (CCDS), B-Flow, CEUS and contrast-enhanced B-Flow (ceB-Flow). All examinations were performed by one independent examiner with a high-end ultrasound device. The reading was done by two experienced examiners in consensus using rating scales.
Results: Compared to other ultrasound modalities, CEUS had the highest informative value with the best image quality and questions could be answered in 100%. The highest penetration depth was reached in CEUS (8.6 ± 1.6 cm). B-Flow allows only the assessment of superficial organ regions (5.0 ± 1.1 cm) and is very susceptible to imaging artefacts. By contrast agent administration, the penetration depth of B-flow could be increased significantly (7.0 ± 1.7 cm). The ability to visualize slow blood flow was limited in CCDS compared to B-flow and CEUS.
Conclusion: For the assessment of renal transplants CCDS is still important for the evaluation of the hemodynamic. Digital flow methods are promising but need further improvements in penetration depth. CEUS was able to show the capillary microperfusion with the highest image quality and the highest diagnostic value. Therefore, the combination of all ultrasound modalities is necessary for a complete assessment of renal transplants.

V017 SUCCESSFUL EARLY TREATMENT OF HCV VIREMIA AFTER TRANSPLANTATION OF HCV POSITIVE RENAL ALLOGRAFTS INTO HCV NEGATIVE RECIPIENTS

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Background: Kidneys from deceased donors with hepatitis C (HCV) viremia are usually not utilized for transplantation. Direct-acing antiviral agents have shown to be efficient for treatment of HCV infection. We report our experience on transplanting HCV- positive kidneys with detectable viremia into HCV-negative candidates with subsequent antiviral therapy.
Methods: Data from seven HCV-negative recipients receiving kidneys from five HCV-viremic donors were collected. All patients had given informed consent concerning acceptance of a HCV-positive donor organ prior to transplantation. Recipients were closely followed posttransplant by measuring HCV viremia, liver and renal function as well as trough levels of immunosuppressive drugs.
Results: A total of four donors exhibited HCV genotype 1 and one donor had HCV genotype 3a. HCV viremia was detectable in all seven renal transplant recipients within 3 days posttransplant. After determination of HCV genotype, antiviral treatment with a sofosbuvir-based regimen was started at a median time point of 7 (2–10) days after transplantation for 8–12 weeks (sofosbuvir/ledipasvir, $n = 5$; sofosbuvir/velpatasvir $n = 2$). All patients achieved complete virologic response at end of treatment. Sustained virologic response was 100% at 12 weeks follow-up. Levels of liver enzymes normalized at the end of treatment in all patients. Renal allograft function as well as trough levels of tacrolimus remained stable during and after antiviral treatment.
Conclusions: Early treatment of HCV-negative recipients receiving kidneys from HCV-viremic donors provides an effective and safe approach to expand the donor pool for selected patients.

LIVER II: ALLOCATION IN THE LIVER TRANSPLANTATION

V018 ORGAN SHORTAGE AND PATIENT SURVIVAL – DEVELOPMENTS SINCE IMPLEMENTATION OF MELD-BASED LIVER ALLOCATION IN GERMANY

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Introduction: The Model for End-stage liver disease (MELD) based allocation system has been implemented in Germany in 2006 in order to reduce waiting list mortality. Purpose of this study is to evaluate post-transplant outcome - especially under the aspect of increasing organ shortage in Germany.
Methods: All patients undergoing liver transplantation (LT) in Germany from 2004 to 2015 were assessed retrospectively using the electronic record system of Eurotransplant (ET). The study period was divided into three time sections (A: Pre-MELD 2004–2006; B: post-MELD low donor 2007–2010; C: post-MELD high donor 2011–2012).
Results: From 2004 to 2015 a total of 12762 LTs were performed in Germany. After MELD implementation, the median matchMELD at time of LT increased from 17 to 28 in 2015. Donation rate increased after 2004 and remained stable from 2006 to 2011 (around 14 per million inhabitants), but decreased afterwards considerably to 10.4 organ donors/million in 2015. Compensatory, during this period, median donor age increased from 44 to 53 years ($p < 0.001$) and the percentage extended donors (age≥65 years) increased from 11.1% to 25.4%. The ratio of used liver donors to reported donors was found to be notably higher in Germany (around 85% since MELD implementation) compared to other ET countries (around 77%). Comparing the different time periods 3-year patient survival in group A was 72.2%, 67.4% group B in group B and then remained constant at 69.1% in group C 2011–2012 (A vs. B, $p < 0.001$; B vs. C, $p = 0.282$).
Conclusion: Organ shortage lead to looser acceptance of marginal organs since MELD implementation. Despite an initial increase of organ donors survival declined after MELD implementation in Germany.

V019 OUTCOME ANALYSIS OF CRITICALLY ILL PATIENTS AFTER LISTING FOR LIVER TRANSPLANTATION. ARE WE DOING THE RIGHT THING?

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Background: About 15% of liver transplantations (LT) in the Eurotransplant region are performed in patients with a high-urgency (HU) status. That status is awarded to patients with acute liver failure or who require an acute re-transplantation. This study aims to evaluate the efficacy of this prioritization.
Methods: Patients were included that were either listed for HU liver transplantation or who reached a MELD score of ≥40 from 01.01.2007 up to 31.12.2015. Waiting list and post-transplantation outcomes were compared between both groups.
Results: In the study period, 2,299 patients received a HU status and 1,580 reached a laboratory MELD score of 40 during listing. At 30 days after listing 74% of all HU patients were transplanted and 15% died whilst waiting. In the MELD 40 group, 49% of patients were transplanted and 43% deceased. Analysis of post-transplantion outcome of patients without a previous LT, showed a higher 3-year survival in HU patients as compared to MELD 40 patients (69% vs. 57%, $p < 0.001$). The number of previous LTs and the "uncapped" MELD-score were the most important risk factors for survival in HU patients.
Conclusions: HU prioritization is highly effective in preventing mortality on the waiting list. In patients without a previous transplantation, survival of HU patients exceeds that of patients with a MELD score ≥40. For subgroups of HU patients - with previous LTs and a high MELD score- outcome is inferior to survival of MELD 40 patients. With the current scarcity of organs in mind, we should reevaluate HU prioritization of those patients over other potential recipients who have a better prognosis after transplantation.

V021 THE ROLE OF DONOR-SPECIFIC ANTI-HLA ANTIBODIES IN LIVER TRANSPLANT RECIPIENTS

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Background: The clinical role of donor-specific anti-HLA antibodies (DSAs) in liver transplantation (LT) is not clearly established. We investigated the impact of the presence of DSAs on morbidity and mortality of LT recipients.
Materials and Methods: Between 2008 and 2015 649 LTs were performed at our institute. DSAs were determined by the Luminex® assay for all patients. Patients with positive DSA results at time of LT and in the post-transplant period were included. Transplant outcome was compared to a matched control group with no appearance of DSAs. The normalized mean fluorescence intensity (MFI) was used to quantify DSA levels and was correlated with clinical courses.
Results: 162 cases with class-I and/or class-II DSAs were identified and matched. One-year mortality was significantly higher in DSA positive patients compared to the control group ($p = 0.037$). There was no significant difference in the mortality after three, five and seven years. In both groups the leading cause of death was sepsis (38%). Within the DSA group, a MFI level over 8000 was associated with a significantly higher overall mortality, when compared to patients with low MFI levels ($p = 0.042$).
Conclusion: DSAs were associated with negative short-term survival after LT. This effect diminished in the long-term observation. Although high MFI-levels seem to correlate with the mortality, further investigations have to be made to detect risk factors for a negative outcome in patients with DSAs. Sepsis was identified as the leading cause of death. Therefore, future research needs to focus on the optimization of immunosuppressive regimes and treatment algorithms in this sensitive cohort, as LT recipients with positive findings of DSAs seem to be particularly prone to inferior outcome.

IMMUNOLOGY I: THE HIGHLY IMMUNIZED PATIENT

V022 PREDICTION OF ANTIBODY- AND CELL-MEDIATED REJECTION OF KIDNEY TRANSPLANTS BY HLA EPITOPE MATCHING

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Our previous study has demonstrated that epitope matching as performed by both the HLAMatchmaker and the Predicted Indirectly Recognizable HLA Epitope (PIRCHE) algorithm is an independent predictor for de novo donor-specific HLA antibodies (DSA). Here, we analyzed the correlation between HLA epitope matching and allograft rejection following kidney transplantation. A total of 1,083 consecutive deceased and living kidney transplants performed between 1995 and 2015 were enrolled to the study cohort. All patients revealed having no DSA prior to transplantation as detected by solid-phase immunoassays. HLA epitope mismatches were determined by both the HLAMatchmaker and PIRCHE algorithm. Rejections were diagnosed according to current Banff criteria. During follow-up 63 (6%) patients developed antibody-mediated rejection (ABMR). T-cell-mediated rejection (TCMR) was observed for 226 (21%) patients during follow-up. There was a direct correlation between the degree of HLA epitope matching and the incidence of ABMR and TCMR. At 10 years of follow-up, patients with a HLAMatchmaker score <5 ($n = 123$), ≥5 to <18 ($n = 173$), ≥18 to <36 ($n = 469$) and ≥36 ($n = 318$) revealed a predicted incidence of ABMR and TCMR of 1% and 8%, 5% and 14%, 8% and 25% as well as 15% and 29%, respectively. Patients with a PIRCHE-II score <9 ($n = 107$), ≥9 to <35 ($n = 149$), ≥35 to <90 ($n = 504$) and ≥90 ($n = 323$) had a predicted incidence of ABMR and TCMR of 1% and 7%, 3% and 16%, 9% and 25% as well as 14% and 28%, respectively. These findings suggest a potential predictive value of HLA epitope matching for renal allograft rejection.

PANCREAS

V023 PREEMPTIVE VERSUS NON-PREEMPTIVE SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION: A COMPARATIVE ANALYSIS OF LONG-TERM RESULTS

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Background: Simultaneous pancreas-kidney transplantation (SPK) can be performed preemptively or following renal dialysis. In this study, we aimed to evaluate whether preemptive SPK has a favorable effect on long-term patient- and graft-survival.
Methods: This is a retrospective, single-centre study including 515 SPK patients treated between 1994 and 2017. 457 recipients were already on dialysis (DIA), 58 patients were transplanted preemptively (PRE). Both groups were compared by analyzing long-term patient- and graft survival, serum creatinine (SCr) and HbA1c, cardiovascular diseases, diabetes history as well as surgery- and donor-related factors.
Results: Cumulative 5-year patient-, kidney- and pancreas graft survival were 90.6%/82.7%/72.8% in DIA and 92.2%/81.4%/67.3% in PRE, respectively. Cumulative 10-year patient-, kidney- and pancreas graft survival were 81.5%/68.7%/62.8% in DIA and 89.8%/78.5%/64.9% in PRE. Cumulative 15-year patient-, kidney- and pancreas graft survival were 70.8%/54.6%/49.4% in DIA and 80.3%/65.8%/53.0% in PRE (log rank p = 0.270/0.409/0.831). Mean SCr and mean HbA1c after 5 years were 1.75 ± 1.55 mg/dl/5.97 ± 1.06% in DIA and 1.77 ± 1.62 mg/dl/6.15 ± 1.35% in PRE, p = 0.949/0.455. Mean SCr and mean HbA1c after 10 years were 1.85 ± 1.62 mg/dl/5.78 ± 0.85% in DIA and 1.85 ± 1.29 mg/dl/5.96 ± 0.89% in PRE, p = 0.998/0.439. Dialysis patients suffered from coronary heart disease more often than preemptively transplanted recipients (DIA: 121 (26.5%); PRE: 6 (10.3%), p = 0.007). 10- and 15-year patient- and kidney graft survival rates were each 10% worse in DIA, but did not differ significantly.
Conclusions: SPK should be performed if possible before beginning dialysis in type-1 diabetics.

V024 PROTOCOL DUODENAL GRAFT BOPSIES FOR PANCREAS GRAFT SURVEILLANCE

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Background: Reliable means to monitor pancreas grafts are do not exist. Histological evaluation of pancreas grafts is usually done on demand rendering risk of procedure related complications and late diagnosis.
Methods: Protocol duodenal graft biopsies in 18 consecutive pancreas transplant recipients with a follow-up of a minimum of 12 months were performed at days 14, 30, 90, 180, 360, 430. UPMC classification for intestinal rejection was used. C4d staining and HLA screen for development of de novo DSA was performed when antibody mediated rejection was suspected.
Results: Patient survival was 100% and pancreas graft survival was 88% at a mean follow-up of 2 years. A total of 113 endoscopic biopsy procedures were performed in 17 grafts without a single complication. Adherence to protocol and successful intention to biopsy were 100%. Biopsies revealed rejection in one out of five SPK recipients at 1 year, whereas 9 out of 10 PAK were rejecting as early as 14 days post-transplant. Both pancreas after kidney re-transplant recipients developed a single rejection episode rejection at day 180. All rejections treated could be reversed. Following transient treatment success, 2 grafts were lost secondary to ongoing rejection at 7 and recurrent rejection at 15 months post-transplantation. Additionally, biopsies detected other complications such as portal venous thrombosis and over-immunosuppression (CMV infection).
Conclusions: Protocol graft duodenal biopsies are a safe measure to monitor pancreas allografts. Rejection, graft thrombosis and CMV disease can be recognized and treatment success can be monitored.

V025 PANCREAS TRANSPLANTATION USING DUODENODUODENOSTOMY: MANAGEMENT OF DUODENAL COMPLICATIONS IN PATIENTS AFTER GRAFT PANCREATECTOMY

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Backround: Enteric drainage in pancreas transplantation (PT) using duodenoduodenostomy (DD) is controversial. Possible disadvantages appear in cases of anastomotic insufficiency or graft loss because subsequent leaks at the native duodenal site are more difficult to repair.
Patients and Methods: A total of 246 DD during PT were performed between 2005 and 2017. Out of these patients, 35 recipients had a pancreas-graft loss and necessity of graft pancreatectomy. We retrospectively analyzed our experience with the management of the resulting duodenal leakage after graft pancreatectomy.
Results: The hole in the recipient duodenum resulting from graft pancreatectomy was primarily treated in all the cases with a transverse, double-layer, interrupted suture using polydioxanone (3-0 or 4-0). 28 (80%) of the 35 patients had no enteric complications during the postoperative course. Seven (20%) patients developed insufficiencies of the duodenal suture with consecutive duodenal leak. 4 patients were treated with a Roux-en-Y-constructed duodenojejunostomy, forming a side-to-side anastomosis. In case of one patient a further suture of duodenum was successful, while in another case we were able to treat the duodenal leak conservatively keeping the retroperitoneal drain in place for longer.
Conclusion: DD is technically feasible with no increase in enteric complications. Longitudinal incision of the native duodenum should not exceed 3 cm. Further studies are needed to compare potential complications of DD and the benefits conferred by this technique.

V026 DEVELOPMENT OF THE WAITING TIME FOR A PANCREAS TRANSPLANT OVER THE LAST 11 YEARS: A CENTER ANALYSIS

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Introduction: Pancreas transplantation has a special role among the transplantation of solid organs because of the very small number of patients receiving this kind of operation. Therefore, one might consider that the decrease in organs donors seen in Germany over the last years would not affect this particular group of patients at first hand.
Methods and Results: From 2006 to 2017 we performed 275 pancreas transplantations in our center. The mean waiting time for a transplant organ was 705.92 ± 611.90 days (median 569 days). Looking separately at the respective years of transplantation, there is no significant increase in waiting time over the last years. However, there is a considerable fluctuation range between the years taken into account for this study and the individual waiting time in one year can vary extensively.
Conclusion: According to the results in our center we cannot confirm that there is a clear increase in waiting time for a pancreas transplant over the last years. This is probably due to a certain detachment of this kind of transplantation from the general development of the number of organ donors. This observation, though, might be misleading because there might be further influences like the acceptance of organs in a recipient oriented extended allocation procedure or in a rescue allocation process. Anyhow, there seemed to have been little change in the average waiting time for a pancreas transplant for the patients on the waiting list of our center over the last 11 years. As mentioned in the literature before, there is a marked underutilization of potential pancreas transplants in general organ procurement. So there might be an additional leeway for this special kind of transplantation.

IMMUNOPATHOLOGY

V028 INTRA-GRAFT B CELLS – FACTORS DETERMINING IMMIGRATION, PROLIFERATION, AND ACTIVATION

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Intra-graft lymphocytes may be associated with reduced allograft outcome. Here, we investigate factors influencing survival, proliferation and activation of intra-graft B cells. We applied optimal and suboptimal doses of Cyclosporine A with or without the addition of an anti-BAFF antibody in a rat RTX model. B/T cells were measured by FACS in blood, spleen, and allografts. Intra-graft B-/T-cell proliferation was analysed by immunohistochemistry (Ki67). Expression of BAFF and T cell costimulatory molecules (CD40L/ICOS) was assessed by qPCR. Intra-renal B cell differentiation and activation markers were analysed by qPCR and FACS. Optimal CNI dosage led to a significant decrease in intra-graft T cells compared to subtherapeutic CNI treatment, but B cell numbers remained unaffected, and consisted primarily of recirculating follicular B cells. However, the proliferation of B cells was significantly reduced in optimal CNI treated groups. This correlated with a reduced expression of costimulatory molecules expressed by T cells, e.g.CD40L/ICOS. Systemic depletion of soluble BAFF led to a reduction of B cells in all compartments including the graft, however, the rate of B cell proliferation ($Ki67^+$ B cells) was not affected. We demonstrated immigration and proliferation of B-/T-cells within allografts in the setting of suboptimal CNI and chronic rejection. BAFF was not required for

proliferation of intra-graft B cells, but reduced infiltration/survival of B cells. CNI mediated blockade of T cells reduced the rate of intra-graft B cell proliferation but did not reduce intra-graft B cell numbers. Our results highlight the role of T cell dependent/independent mechanisms of B cell immigration, proliferation and activation.

V029 PREFORMED DONOR-REACTIVE T-CELLS THAT PERSIST AFTER ABO DESENSITIZATION INDEPENDENTLY PREDICT SEVERE ACUTE CELLULAR REJECTION AFTER LIVING DONOR KIDNEY TRANSPLANTATION

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Donor-reactive T-cells impact allograft outcome due to higher incidences of acute rejection early after transplantation. These donor-reactive T-cells rapidly acquire effector functions and are relatively resistant to standard immunosuppression.

We analyzed 150 first living-donor KTRs (KTRs) between 2008 to 2016, 92 ABO-compatible (ABOc) and 58 ABO-incompatible (ABOi) KTRs. Samples were collected at 6 timepoints, before rituximab, before immunoadsorption, before transplantation, at +1, +2, and +3 months posttransplantation, and donor-reactive T-cells were measured using an interferon-γ Elispot assay.

20/92 ABOc-KTRs (21%) and 12/58 ABOi-KTRs (26%) showed detectable donor-reactive T-cells pretransplantation. 8/20 ABOc-KTRs (40%) with preformed donor-reactive T-cells and 17/72 ABOc-KTRs (24%) without preformed donor-reactive T-cells developed acute cellular rejection ($p = 0.163$). 7/12 ABOi-KTRs (57%) with preformed donor-reactive T-cells, but only 3/46 ABOi-KTRs (7%) without preformed donor-reactive T-cells showed acute cellular rejection. Interestingly, 6/7 ABOi-KTRs (86%) with preformed donor-reactive T-cells that persist after ABO desensitization developed acute cellular rejection, whereas only 1/5 ABOi-KTRs (20%) with preformed donor-reactive T-cells that disappeared during ABO desensitization ($p = 0.072$). Among 118 KTRs without preformed donor-reactive T-cells, 10/72 ABOc-KTRs (14%), but 0/46 ABOi-KTRs (0%) showed development of de-novo donor-reactive T-cells ($p = 0.006$).

Preformed donor-reactive T-cells that persist despite initiation of CNI-based maintenance immunosuppression and rituximab identifies KTRs at highest risk of acute cellular rejection. Less de-novo donor-reactive T-cells after ABO desensitization may account for less acute cellular rejection among ABOi-KTRs.

PSYCHOSOMATICS II

V031 A SYSTEMATIC REVIEW OF ASSESSMENTS USED FOR THE PSYCHOSOCIAL EVALUATION OF PATIENTS BEFORE ADMISSION TO THE ORGAN TRANSPLANT WAITING LIST – A STUDY PROTOCOL

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Background: There is a common agreement that not only somatic factors, but also psychosocial variables have predictive value for patients" post-transplant outcomes. Patients" adherence to life-long necessary medications and medical follow-up should be considered as well as underlying psychological disorders before admission to the waiting list. In order to take these and further relevant psychiatric and psychosocial information into account, a structured evaluation is necessary. Still, this process is being performed mostly in a non-standardized way and the existing assessment strategies are inconsistently used.
Aim: The main objective of this review is to provide an overview of the existing instruments that are used for the psychosocial evaluation of patients before admission to the waiting list with regard to their content and psychometric properties.
Method: A systematic literature search will be carried out, including all studies that used a standardized assessment for evaluating patients with a medical indication for solid organ transplantation and report their psychometric properties. The review will include studies with adult patients (> 18 years) who have been evaluated for a liver, kidney, heart, lung, pancreas, small intestine and multi-visceral transplantation. Recipients of a living donor transplant and studies related to stem cell recipients will be excluded. We will use the COSMIN checklist in order to rate the quality of the studies and the psychometric properties of the measures in question.
Implications: Insights gained from this review can be used as a first reference point for clinicians to structure and standardize the psychosocial evaluation. By using validated instruments, the accuracy and prognostic value of this process could be improved.

V032 QUALITY OF LIFE, ANXIETY, DEPRESSION, AND FATIGUE IN LIVING KIDNEY DONATION – A PROSPECTIVE STUDY

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Objectives: Prospective data regarding the psychosocial outcome of living kidney donation (LKD) in Germany is rare. The present study analyzed relevant variables before and 1 year after LKD.
Methods: Health-related quality of life (HRQOL) was evaluated with the *Short-Form 36-Item Health Survey* (*SF-36*), anxiety and depression with the *Hospital Anxiety and Depression Scale* (*HADS*), and fatigue with the *Multidimensional Fatigue Inventory* (*MFI-20*).
Results: Of 106 German-speaking donors (LKD 2/2012–3/2017), pre- and postoperative data were available from 85 donors (80%). Mean age at LKD was 53 yrs (SD = 11.0), 66% donors were female. The "physical component summary" of the SF-36 showed no significant HRQOL changes. A significant HRQOL decrease was observed in the "mental component summary" ($p = 0.01$, $d = 0.42$), esp. the subscale "vitality" ($p < 0.001$, $d = 0.52$). The MFI-20 showed corresponding increases in "general fatigue" ($p = 0.01$, $d = 0.33$) and "physical fatigue" ($p = 0.02$, $d = 0.35$). In the affected domains, the preoperative score was superior to the general population, while the postoperative score was similar to the general population. No significant pre to post changes were noted in the HADS; 5 donors showed slightly elevated depression scores and 1 donor a clinically relevant score 1 yr after LKD. The preoperative vitality score explained 41% variance of the postoperative vitality score. Moderate correlations ($r = 0.3$–0.4) were observed between donor-rated well-being of the recipient and changes in donors' mental HRQOL and vitality.
Conclusions: Small to medium effect sizes indicate only moderate mean changes. Nevertheless, the psychosocial outcome of LKD should be routinely assessed, and affected donors should receive specialized treatment. Risk factors should be further explored.

V034 MEASUREMENTS OF ADHERENCE IN RENAL TRANSPLANT RECIPIENTS: WHAT IS THE BEST METHOD?

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Aims: Aim of this presentation is to provide a detailed overview of current measurement methods of adherence in renal transplant recipients, evaluating their benefits and disadvantages.
Methods: Our investigation is based on current literature on adherence measurement in renal transplant recipients from 2000 to 2018. We will survey the most common methods of measurement and make comparisons concerning their accuracy, practicability and economy.
Results: Most common methods in current research are electronic monitoring, self-reports, collateral reports and examination of trough levels. Although self-reports as well as collateral reports are economic, they tend to overestimate adherence. The use of trough levels is complex and its accuracy depends on the specific medical regimen. Electronic monitoring provides a dynamic and long-term measurement on adherence behavior and is frequently considered the best method. However, it can misestimate adherence, due to its potential interventional effect. The diverse measurement methods display only low to moderate correlations.
Conclusion: Since contemporary measurement methods display diverse features and correlate remotely, current literature suggests a combination of methods ("Triangulation") to enhance accuracy.

KIDNEY II: CLINICAL STUDIES IN NEPHROLOGY

V035 CD40 INHIBITION WITH CFZ533 – A FULLY HUMAN, NON-DEPLETING, FC SILENT MAB - IMPROVES RENAL ALLOGRAFT FUNCTION WHILE DEMONSTRATING COMPARABLE EFFICACY VS. TRACROLIMUS AFTER KIDNEY TRANSPLANTATION

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Purpose: To assess the potential of CFZ533 (CFZ) as primary immunosuppressant in a calcineurin-inhibitor (CNI)-free regimen in de novo kidney transplant (KTx) patients(pts).

Method: CFZ533 is a fully human, Fc-silenced, non-depleting, IgG1 mAb preventing CD40 pathway signaling and activation of $CD40^+$ cell types. NCT02217410 is a 12-month multicenter randomized controlled Phase 2a clinical trial evaluating efficacy, safety, tolerability, and pharmacokinetics of CFZ in combination with mycophenolate mofetil (MMF) and corticosteroids (CS) compared with tacrolimus (TAC), MMF and CS in de novo KTx recipients. All pts received aIL-2 induction with basiliximab and CS as per center practice.
Results: $N = 51$ pts were transplanted and randomized (2:1) to either CFZ ($N = 33$) or TAC ($N = 18$). 25 of 51 pts (49%) received a living donor allograft. After CD40 target saturation, CFZ was dosed every 4 weeks. CFZ was well tolerated with no infusion related nor thromboembolic events. Month 6 interim results demonstrated comparable efficacy on the composite endpoint of treated biopsy proven acute rejection, graft loss, or death (21.2 vs. 22.2%) and better renal function (55.8 vs. 45.5 mL/min), less serious adverse events (SAE) (47.1 vs. 61.1%) and fewer infectious complications (50.0 vs. 77.8%) with no increase of opportunistic infections (viral overall: 26.5 vs. 50.0%; SAE CMV: 2.9 vs. 11.1%; BKV: 15.2 vs. 22.2%), and a lower rate of new-onset diabetes mellitus (14.7 vs. 38.9%) with CFZ versus TAC. 12-month final study data will be available until DTG.
Conclusion: CFZ533, a new anti-CD40 monoclonal antibody may have potential to become an effective CNI- free treatment for KTx recipients improving transplant outcomes by preventing graft rejection without nephrotoxic (and other) CNI adverse effects.

V036 A PHASE-I CLINICAL TRIAL OF DONOR-DERIVED MIC CELL INFUSION FOR THE INDUCTION OF DONOR-SPECIFIC HYPORESPONSIVENESS AFTER LIVING DONOR KIDNEY TRANSPLANTATION (TOL-1 STUDY)

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MIC cells are donor-derived monocytes that gain immunosuppressive properties after incubation with the proliferation inhibitor mitomycin C.

PBMCs were harvested from living donors by leukapheresis and MIC cells were manufactured under GMP conditions. Kidney transplant recipients received either $1.5 \times 10E6$ MIC cells/kg body weight on day -2 ($N = 3$, group A), or $1.5 \times 10E8$ MIC cells/kg body weight on day -2 ($N = 3$, group B) or day -7 ($N = 4$, group C) before living donor kidney transplantation. Patients received immunosuppressive therapy with CyA, EC-MPS and CS. Primary outcome measure was the frequency of adverse events (AE) on day 30.

72 AEs (3 severe AEs) occurred in treated patients that were unrelated to MIC cell infusion. No positive cross match results, de novo donor specific antibodies or rejection episodes but 2 infectious complications were recorded. Median serum creatinine on day 30 was 1.4 mg/dL. In vitro, MIC cells were capable of inducing tolerogenic dendritic cells with low expression of costimulatory molecules CD80, CD86 and a 30% increase of immunosuppressive molecule CD103. Beyond day 30 after surgery, serum creatinine remained stable (median 1.48 mg/dL on day 180) with no significant proteinuria (median 10 g/mol creatinine on day 180) and no rejection episodes. $CD19^+$ B cells increased to a median of 300/μL until day 30 but decreased to a median of 35/μL on day 180. $CD19^+$ $CD24^{high}$ $CD38^{high}$ transitional Bregs increased from a median of 2% on day 30 to a median of 20% of the total $CD19^+$ B cell pool on day 180. There was a strong increase in the plasma IL-10/TNFα ratio from a median of 0.05 before cell therapy to a median of 0.11 on day 180.

MIC cell therapy represents a promising option for individualized immunosuppression after living donor kidney transplantation.

V038 DEFINITION AND SEVERITY GRADING OF POST-KIDNEY TRANSPLANTATION LYMPHATIC COMPLICATIONS

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Background: Post-kidney transplantation lymphatic complications (PKTL) are one of the most common surgical complications after kidney transplantation (KTx). Due to the lack of a universally accepted definition of PKTL, the reported incidence, as well as the associated morbidity varies considerably in the literature. Our aim was to propose a standardized definition and grading of severity of PKTL (lymphorrhea/lymphocele).
Methods: After a comprehensive literature review, a generally agreed and easy to apply definition and grading of severity for PKTL was provided and sent to all members of the international consensus team, from high-volume and well-known transplantation centers. After mail discussion, the definition and grading were revised and the final versions were drafted.
Results: Post KTx Lymphorrhea is outflow of more than 50 mL/day fluid after the 7th post KTx day from the drain, or the site of the removed drain, or surgical wound which is not blood, pus, or urine. Post KTx lymphocele was defined as a fluid collection near to the transplanted kidney in a non-epithelialized cavity of variable size, after rule out of hematoma, abscess, and urinoma. Three different grades of PKTL were defined according to management approach. Grade A PKTLs need non-invasive approaches and have minor effect on patient management. A grade B PKTL requires non-surgical interventions including external drainage and sclerotherapy for lymphocele and medical therapy, sclerotherapy, radiotherapy, or replacement of drain after remove of the first one for lymphorrhea. In grade C PKTL surgery is inevitable.
Conclusion: We present a definition and grading of severity of PKTL, which is easily applicable and standardizes comparisons between the results from different clinical studies.

IMMUNOLOGY II

V039 KIDNEY TRANSPLANT SURVIVAL IN PATIENTS WITH PREFORMED DONOR-SPECIFIC HLA ANTIBODIES (DSA) IN SOLID-PHASE ASSAYS – RESULTS OF A MULTICENTER STUDY FROM 18 GERMAN TRANSPLANT CENTERS

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Background: The prognostic value of preformed donor-specific HLA antibodies (DSA) detected by solid-phase assays, especially those with low reactivity, is still discussed controversially. This multicenter study aims to elucidate the effect of DSA detected during routine antibody screening prior to transplantation on outcome of kidney allografts in Germany. Preliminary results had been presented last year.
Methods: 1305 living donations (LD) and 2779 deceased donations (DD) between 2012 and 2015 were evaluated. Data on preformed DSA, clinical outcome and possible covariates including kidney donor risk index (KDRI) for DD were collected retrospectively. Outcome was analyzed in the prespecified groups of patients (1) without DSA, (2) with DSA <3000 mean fluorescence intensities (MFI), and (3) with DSA ≥3000 MFI.
Results: Antithymoglobulin (ATG) was used more often in DD than in LD (40% vs. 25% of patients with DSA). Median follow-up was 2 years. Preformed DSA were associated with decreased not-death-censored transplant survival in LD (HR 2.0 for DSA<3000 MFI and 3.6 for ≥3000 MFI, $p = 0.09$ and <0.001). In DD, crossing survival curves prevented Cox regression analysis for the whole follow-up period. Therefore, 3-month and long-term transplant survival were analyzed separately. While only DSA<3000 MFI tended to decrease 3-month DD transplant survival (HR 1.6, $p = 0.09$), only DSA ≥3000 MFI were associated with significantly decreased DD transplant survival after the 3rd month (HR 2.4, $p < 0.001$).
Conclusion: Preformed DSA were associated with decreased graft survival after kidney transplantation. As the antibody tests were already performed prior to transplantation, different clinical consequences (e.g. less induction with ATG) may have caused the stronger effect of DSA in LD.

V040 MODULATION OF IMMUNOGENICITY BY N-OCTANOYL-DOPAMINE (NOD): AN *IN VITRO* STUDY USING ENDOTHELIAL CELLS AND ALLOGENEIC T-CELLS

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Background: Since immunogenicity of organ allografts is strongly influenced by IFNγ we assessed in the present study 1) if NOD impairs IFNγ mediated signalling, 2) if this influences MHC expression on endothelial cells, 3) if NOD impairs T-cell adherence to endothelial cells and 4) if this is due to a reduced expression of adhesion molecules and their ligands on endothelial and T-cells.
Methods: Genome-wide gene-expression profiles were generated by Affymetrix. Westernblot and qPCR were used for assessment of CIITA. FACS analysis was performed to assess if NOD influences MHC class II. For the interaction of T-cells with endothelial cells, T-cells were first stimulated with Streptamere in the presence or absence of NOD and subsequently used in adhesion assays with TNFα or IFNγ stimulated endothelial cells. Supernatants were collected for measuring cytokines and part of the T-cells were used in FACS analysis to assess CD11a, CD18, CD49d, CD29 and CD25 expression.
Results: Pathway analyses revealed a major influence of NOD on the "antigen processing and presentation"-,"allograft rejection"- and "graft vs. host disease"-pathways. This was reflected by a reduced HLA-DR, CD74 and CIITA mRNA and protein expression. NOD treatment of T-cells inhibited adhesion to unstimulated and TNFα or IFNγ stimulated endothelial cells. Supernatants of these cells were less potent to induce endothelial expression of VCAM-1 and ICAM-1, due to strongly diminished levels of TNFα and IFNγ. T-cells stimulated in the presence of NOD also demonstrated a reduced expression of CD11a, CD18, CD49d, CD29 and CD25 in FACS analysis.
Conclusion: Our findings disclose the influence of NOD on IFNγ signalling and suggest a potential clinical use for modulating anti-donor immune responses in allograft recipients.

LIVER III: VARIA

V041 BILE DUCT DAMAGE AFTER COLD STORAGE OF DECEASED DONOR AND LIVING DONORS LIVERS AFTER LIVER TRANSPLANTATION

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Introduction and Background: Biliary lesions belong to a group of disorders that are regarded as the major complication in patients with orthotopic liver transplantation (OLT). It is suspected, that vascular damage of the donor bile duct might play a major role in the pathogenesis of postoperative biliary complications or the occurrence of ischemic-type biliary lesions (ITBL).
Methods: We performed histological evaluation of biopsy specimens from the donor bile duct received during OLT prior to recirculation of the hepatic artery and prior to biliary anastomosis. Organ retrieval was performed according to the protocol of the Deutsche Stiftung für Organtransplantation. After retrieval, the cystic duct was ligated and the bile ducts were rinsed with HTK solution. We looked for mucosal loss ≥ 50%, intramural bleeding ≥ 50%, Thrombi, Vascular lesions, Arteriolonecrosis, duct necrosis, and inflammation. Lesions were correlated with donor age, and type of transplantation. Statistical evaluation was performed by chi-square analysis.
Results: Between January 2013 and March 2018 67 biopsies were evaluable, 49 biopsies of deceased donors and 18 biopsies of living donors. Median donor age was 56 (14–80) years. Mucosal Loss ≥ 50%, intramural bleeding ≥ 50%, Thrombi, Vascular lesions, Arteriolonecrosis, duct necrosis, and inflammation occurred in 81%, 5%, 18%, 37%, 18%, 37%, and 45% respectively. Only two specimens showed no lesions. One, two, three, four and five different lesions were seen in 25%, 30%, 19%, 15%, and 8% respectively. Neither number nor kind of lesion was statistically significant correlated with the donor age or the type of transplantation. Vascular lesions of the donor bile duct occur very frequently during liver transplantation. Donor age and type of type of transplantation seem to have no influence on kind and frequency of bile duct damage.

V043 HCC RECURRENCE IN HCV PATIENTS AFTER LIVER TRANSPLANTATION: SILVER STUDY SUBGROUP ANALYSIS REVEALS SIROLIMUS TREATMENT IN COMBINATION WITH CNIS IS AN EFFECTIVE TREATMENT OPTION

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Background: While new treatment with DAAs are effective in eliminating HCV, recent studies have reported a high rate of HCC recurrence. In this context, results from the SiLVER Study are of interest, since this trial tested whether sirolimus improves outcomes in LTx recipients with HCC. In the present study, we examined the HCV+ sub-group. We compared those patients that received a mTOR inhibitor-free, CNI–based, immunosuppression (group A, $n = 83$) to those that received sirolimus (group B; $n = 77$).
Results: First, we wanted to assess if sirolimus had an effect on HCV replication, as reported from in vitro studies. However, we did not detect any difference in HCV-RNA between group A and B. We then speculated that the lack of an effect in group B could be due to variable sirolimus dosing. Therefore, we split group B into patients receiving sirolimus without CNIs for either less than (group B1; $n = 44$) or more (group B2; $n = 34$) than 50% of the time. While there still was no difference in the HCV-RNA titer between the three groups, we were surprised to find that HCC recurrence-free survival (RFS) in group B1 (81.8%) was significantly better compared to both group A (62.7%, $p = 0.0136$) and B2 (64.7%, $p = 0.0326$) at study end. Interestingly, further analysis of our subgroups revealed that there was a significant increase ($p = 0.0012$) in ALT values throughout the first three years in group B2 [111; 61–206], compared to group A (55; 33–93) and B1 (58.5; 30–96), raising the possibility that HCV patients with uncontrolled liver inflammation relate to substantially poorer outcomes due to less potent immunosuppression.
Conclusion: In HCV patients with HCC and a liver transplant mTOR inhibitors may best be used in combination with CNIs to reduce liver inflammation and improve outcomes.

V044 24-MONTH RESULTS FROM THE H2307 PIVOTAL STUDY: MTOR INHIBITION WITH EVEROLIMUS IN *DE NOVO* LIVING DONOR LIVER TRANSPLANTATION

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Purpose: Everolimus (EVR) with reduced-exposure tacrolimus (rTAC) has been shown to maintain an efficacy and safety profile and improve renal function in living donor LT recipients (LDLTRs) up to 12 months (M) post-LT compared to standard exposure TAC (sTAC). Here, we provide 24M follow-up results from the H2307 study.
Methods: H2307 (NCT01888432) was a 24M, multicenter, open-label trial with 284 *de novo* adult LDLTRs randomized 1:1 to EVR+rTAC or sTAC after a run-in period of 30 $\pm$ 5 days post-LT. Primary objectives comprised the composite efficacy failure (CEF) of treated biopsy-proven acute rejection (tBPAR), graft loss (GL) or death (D). Other important objectives encompassed evaluation of renal function in all patients and in patients bearing hepatocellular carcinoma (HCC) as well as (renal) adverse events (AEs).
Results: In both arms, 88% accomplished the 24M study. EVR+rTAC was found non-inferior to sTAC treatment. CEF rate (9.0% vs. 8.0%; $p < 0.001$) and its components (tBPAR: 3.1% vs. 4.4%; GL: 0 vs. 0.8%; D: 6% vs. 3%), were comparable between the two arms at M24. In the total study population, eGFR did not differ between EVR+rTAC and sTAC regimens (78.4 and 75.3 mL/min/1.73 m^2). However, proportion of patients with eGFR $\geq$ 60 mL/min/1.73 m^2 was higher in EVR+rTAC versus sTAC (76.4% and 66.9%). Within the HCC patient group, eGFR was significantly higher in EVR+rTAC arm ($p = 0.009$). AE incidence was comparable between both arms. Less renal AE occurred in EVR+rTAC compared to sTAC arm.
Conclusions: At M24, we observed comparable efficacy and safety profiles upon EVR+rTAC versus sTAC regimen in LDTRs. Importantly, EVR+rTAC treatment significantly improved renal function within the HCC subgroup compared to sTAC.