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Austrotransplant 2024: ‘Organ Transplant Tension - Possibilities and Reality’

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Introduction

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Dear colleagues,

It is a particular honor and pleasure for me to welcome you to this year's annual meeting of the Austrian Society for Transplantation, Transfusion and Genetics "AUSTROTRANSPLANT".

After last year's conference in Eisenstadt, we are holding this year's conference in beautiful Salzburg. The organizing committee is pleased to be able to present to you, as usual in just under three days, current developments and areas of discussion in the field of organ transplantation, both solid organ transplantation and stem cell transplantation.

The motto of this year's annual conference is "Organ Transplant Tension - Possibilities and Reality". Due to the increasingly pressing discrepancy between the need and supply of organs for a transplant, new innovative research is being pursued in many areas to deal with this situation, which is a focus of the program design at this year's annual conference.

There will again be an opportunity to discuss relevant developments in plenary sessions as well as to discuss them in detail in topic-related break-out sessions. There will also be separate poster sessions with space for exchange and discussion.

A particular concern of the society is the promotion of young talent in the field of transplantation, so that several prizes were announced as part of the conference, which are awarded in a separate young investigator session.

As a characteristic feature of the AUSTROTRANSPLANT annual conference, the scientific program is aimed particularly at nurses from the transplant centers. This time, the format planned here is interprofessional sessions in the organ-related parallel sessions, so that these sessions were designed together with nurses and doctors and we can hopefully create a forum for a common exchange.

We would also like to thank the industry for their generous support, without which the conference would not be possible.

The organizing committee would like to warmly welcome you to Salzburg!

Matthias Biebl (Congress President)
Christiane Rösch (Congress Secretary)
Manfred Kalteis (Congress Secretary)

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01

Targeting CD38 In Antibody-Mediated Kidney Transplant Rejection

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Background

Antibody-mediated rejection (AMR) is a leading cause of kidney transplant failure. Targeting of CD38 to inhibit alloantibody- and natural killer (NK) cell-driven injury may be a therapeutic option.

Methods

In this phase 2, double-blind, randomized, placebo-controlled trial, patients with late AMR (≥180 days after transplantation) received nine infusions of the CD38 antibody felzartamab (16 mg/kg) or placebo for 6 months, followed by a 6-month observation period. The primary outcome was safety and tolerability. Key secondary outcomes were renal-biopsy results at 24 and 52 weeks, donor-specific antibody levels, NK cell counts, and donor-derived cell-free DNA levels. After the finalization of the main trial, a subset of felzartamab or placebo patients with recurrent/persistent active AMR entered an open-label extension phase to assess the long-term safety/tolerability and efficacy of felzartamab. The extension phase includes immune monitoring in bone marrow aspirates at baseline and after 24 weeks.

Results

22 patients underwent randomization (felzartamab [n=11], placebo [n=11]). In the main trial, mild or moderate infusion reactions occurred in 8 patients in the felzartamab group. Serious adverse events occurred in one patient in the felzartamab group and in 4 patients in the placebo group; 1 patient in the placebo group had graft loss. At week 24, resolution of AMR was more frequent with felzartamab (9 of 11 patients [82%]) than with placebo (2 of 10 patients [20%]). The median microvascular inflammation score was lower in the felzartamab group than in the placebo group (0 vs. 2.5). Also lower was a molecular score reflecting the probability of AMR (0.17 vs. 0.77). At week 52, recurrence of AMR occurred in 3 of 9 felzartamab responders, with increases in molecular activity and biomarker levels toward baseline. Authors will also report baseline characteristics and first results of the open-label extension phase.

Conclusion

Felzartamab had acceptable safety and side-effect profiles.

02

Therapeutic Application Of Norursodeoxycholic Acid In Normothermic Machine Perfusion Reduces Perfusate Apoptosis Markers In Livers Rejected For Transplantation

Laurin Rauter[1], Dagmar Kollmann[2], Jule Dingfelder[1,2], Sertac Kacar[1], David Pereyra[1,2], Moriz Riha[1], Nikolaus Becker[1], Tina Saffarian[1], Konstantinos Mengrelis[1], Markus Wahrmann[3], Andreas Salat[1], Gerd Silberhumer[1,2], Thomas Soliman[1], Gabriela Berlakovich[1] and Georg Györi[1]

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Background
Nomothermic machine perfusion (NMP) can be used for viability assessment in extended criteria donor (ECD) livers. Additionally, NMP offers a platform for ex vivo therapeutic intervention. NorUrsodeoxycholic acid (norUDCA), an anti-inflammatory and anti-fibrotic bile acid, is investigated in the treatment of cholestatic and metabolic diseases. We aimed to investigate the therapeutic potential of norUDCA on ECD livers rejected for transplantation using NMP.

Methods
Over a period of 12 hours, apoptosis markers were evaluated in perfusate samples of 18 normothermic perfused, rejected livers. Nine livers were treated with 1500 mg of norUDCA after two hours. Apoptosis markers (Bcl-2, active caspase-3, cleaved PARP, Cytochrome c, p53) were measured using a commercially available human apoptosis panel on the Luminex platform. To account for donor heterogeneity the relative dynamic of apoptosis markers after application of norUDCA was determined for individual grafts.

Results
Apoptosis markers are present after 5 minutes and are increasing within the first two hours of NMP. NorUDCA treatment after two hours results in a significant reduction of apoptosis markers cleaved PARP ($p=0.0152$) and p53 ($p=0.0206$) at six hours, in addition to a significant reduction in delta 2h-6h values compared to control livers: Bcl-2 ($p=0.0360$), active caspase-3 ($p=0.0152$), cleaved PARP ($p=0.0206$) and Cytochrome c ($p=0.0208$). Of note is the dynamic reduction of apoptosis markers in the treatment group, whereas the control group remained constant or increased.

Conclusions
The present data suggests an anti-apoptotic effect of norUDCA during NMP of ECD liver grafts in a preclinical model. Use of norUDCA during NMP might be relevant for further improvement of outcome after liver transplantation.

03

Long-Term Tolerance In Heart Allografts Through Selective In-Vivo Expansion Of Regulatory T Cells

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Background
Chronic antibody-mediated rejection and the subsequent development of CAV are leading causes of late graft failure with specific treatment still being an unmet need. Regulatory T cells (Tregs) are essential for suppressing auto- and alloimmune responses, and their expansion can promote immunological tolerance. Selective *in vivo* expansion of Tregs can be achieved by treatment with interleukin-2 (IL-2) complexed to a specific anti-IL-2 antibody (IL-2cplx). This study aimed to induce long-term heart allograft tolerance by IL-2cplx based immunomodulation.

Methods
Female C57BL/6 mice were transplanted with fully mismatched BALB/c hearts and treated with IL-2/anti-IL-2 (1µg/5µg) and rapamycin (1µg/gBW) administered on d-3/-2/-1 and thrice a week until d29, and short-term anti-IL-6 (600µg d-1; 300µg d4/6). Cardiac allograft survival was monitored via palpation score, Treg frequencies in the blood were analyzed by flow-cytometry during follow-up period. Flow-cytometry crossmatch was performed to detect donor-specific antibodies (DSA).

Results
IL-2cplx protocol treatment led to indefinite survival (>150 days; $p<0.0001$) compared to untreated controls; MST= 7.5day) Interestingly, tolerance induction in a primarily vascularized HTX model was superior to a skin transplant model (MST=76d) in which all mice eventually rejected their grafts. Treg frequencies in peripheral blood were markedly increased compared to untreated heart graft recipients on d21 and d28 ($p<0.01$) post-HTX. Furthermore, IL-2cplx-based treatment prevented formation of donor-specific IgG1 ($p=0.0002$) and IgG2ab ($p<0.0001$).

Conclusions
We demonstrated that selective in vivo expansion of Tregs using IL-2cplx, combined with rapamycin and short-term anti-IL-6mAb treatment, leads to operational tolerance in a clinically relevant and stringent model of cardiac transplantation. Additionally, recipient mice treated with IL-2cplx exhibited significantly reduced levels of DSA suggesting the induction of humoral tolerance. Our findings indicate that the IL-2cplx-based treatment promotes immune tolerance in heart transplant recipients, as evidenced by indefinite survival in the absence of chronic immunosuppressive treatment and the absence of DSA throughout follow up.

04

Extended Preservation Of Kidneys At Subzero Temperature Using Nature-Inspired Cryoprotectants – A Pilot Study In A Large Animal Model

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Background
Limited supply and growing demand lead to a shortage of transplantable organs worldwide. Besides economic factors like increased healthcare costs, long waiting times, increased mortality and impaired quality of life are resulting from this shortage. Therefore, innovative preservation methods are explored in this context. Among these, subzero organ preservation and normothermic machine perfusion (NMP) are of great interest, as they may allow for extended viability, improved monitoring, increased quality, and better matching and transport logistics. In this study, we thus explored the feasibility of extended preservation (48hrs) of porcine kidneys with a nature-inspired anti-icing agent at -5°C followed by 6 hours of NMP.

Methods
Three porcine kidneys were retrieved using a living-donor procedure, flushed with a non-toxic peptoid based cryopreservative (XT-ViVo®, X-Therma Inc., California) and placed in a -5°C environment (TimeSeal®, X-Therma Inc., California) for 48 hours. Kidneys were subsequently

flushed and subjected to 6hrs of NMP using Kidney Assist (Organ Assist, Groningen) and an autologous whole-blood based perfusate. Before, during and after NMP, biopsies were taken for histological, viability and respiratory analysis. Perfusion was assessed using hyperspectral imaging (HSI) and biochemical parameters of perfusate and urine were analyzed.

Results

Hemodynamic flow remained stable throughout perfusion, with a renal resistance index around 0.6. The kidney metabolized oxygen at all times, with a peak at two hours of reperfusion, stabilizing thereafter. Physiologic pH, moderate perfusate lactate and ion levels were detected. All kidneys instantaneously produced urine upon reperfusion and during NMP (264 ml/h [256-298]; median [IQR]). High-resolution respirometry clearly revealed one preferred substrate pathway (succinate) and showed stable oxidative phosphorylation capacity after reperfusion. Kidney parenchyma and ureter were imaged using HSI, revealing stable micro-perfusion throughout 6 hours of NMP.

Conclusions

We show that ice-free subzero preservation combined with NMP is a promising method for extended organ storage that maintains organ quality and function. This could help ease logistical hurdles and allow for better donor-recipient matching. By combining two novel technologies, subzero preservation and NMP, time could be taken out of the equation in organ transplantation to ultimately help facilitate global organ exchange in the future.

05

Influence Of Preservation Method And Contamination During Preservation On Outcome After Liver Transplantation

Jule Dingfelder[1,2], Tina Saffarian[1], David Pereyra[1,2], Laurin Rauter[1], Sertac Kacar[1], Moriz Riha[1], Chiara Tortopis[1], Nikolaus Becker, Gerd Silberhumer[2], Andreas Salat[1], Thomas Soliman[1], Gabriela Berlakovich[1] and Georg Györi[1]

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Background

Infections are a known contributor to post-transplant morbidity and mortality in an especially vulnerable patient collective due to the necessary immunosuppression after liver transplantation. Our aim was to analyse if contamination during preservation and method of preservation influence outcome of recipients after transplantation.

Methods

In this retrospective cohort analysis, we included 247 transplantations performed between May 2018 and December 2022. Of those, 176 were transplanted after hypothermic oxygenated perfusion (HOPE) and 67 were transplanted after static cold storage (HOPE). Routine microbiological sampling during preservation includes preservation and perfusion solution. Infection related adverse events (AE) were defined as infections that needed treatment identified clinically or via positive culture, sepsis, infection related intervention, and infection related mortality.

Results

Out of 176 recipients in the HOPE group, only 29 (16%) had an infection related AE compared to 21 of 67 (31%) in the SCS group (p=0.010). Infection associated mortality

was observed in 8 recipients in each cohort (5% in HOPE vs 12% in SCS, p=0.038). Recipients of grafts with positive swabs during preservation experienced sepsis in7 of 36 cases during their postoperative course compared to only 17 of 210 recipients that did not have a positive culture during preservation (p=0.034). However, there was no significant difference in mortality between patients with or without positive preservation culture (14% vs 6%, p=0.101). The comprehensive complication index tended to be higher in recipients with positive preservation culture (43 [5.2-55.9] vs. 31.6 [11.8-47.9], p=0.522).

Conclusions

Recipients of grafts with contaminated preservation solution presented with higher rates of sepsis during hospitalization. Interestingly, recipients receiving grafts after HOPE presented with lower incidences of infection related AE as well as infection related mortality. Accordingly, preservation with HOPE seems to be associated with improved recipient outcomes not only due to mitigation of ischemia-reperfusion injury, but also via reduction of complications arising from bacterial contamination.

06

Nor-Ursodeoxycholic Acid Improves Biliary Markers During Normothermic Machine Perfusion

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Background

Normothermic machine perfusion (NMP) enables treatment of grafts and monitoring of regeneration. Nor-ursodeoxycholic acid (norUDCA) has antiinflammatory, antifibrotic, and antilipotoxic properties. It can modulate bile acid metabolism and was found to induce bile production with higher bicarbonate and lower cholesterol content, therefore possibly leading to reduced bile toxicity after ischemia. We aimed to investigate the therapeutic potential of norUDCA during NMP and monitor its effect on the perfused liver.

Methods

During NMP of 18 secondarily declined livers, 9 grafts were treated with a bolus of 1500mg norUDCA after 2h and for a total of 12h of perfusion. No graft met the criteria for transplantation at the 2h timepoint. Blood gas analysis of bile and perfusate including pH, bicarbonate, glucose, lactate, as well as additional analyses including lactate dehydrogenase (LDH), alanine-aminotransferase (ALT), aspartate-aminotransferase (AST), cholesterol, sodium, magnesium, calcium, was performed every hour. Liver and bile duct biopsies were collected before and after NMP.

Results

NorUDCA grafts presented with higher bile bicarbonate (180 min: 0.026, 240 min: p=0.016, 300 min: p=0.030) and trends in lower bile cholesterol content in norUDCA grafts. Bile AST and ALT was lower in norUDCA grafts (480: p=0.017 and p=0.004, 720 minutes ALT p=0.026); bile sodium was higher (180: p=0.004, 240: p=0.015) in norUDCA livers. Grafts treated with norUDCA presented with lower factor XIII activity in perfusate (240 min: p=0.034, 360 min: p=0.030). After treatment with norUDCA, more grafts met the criteria for transplantation at 6h and 12h (5 vs. 3 at both timepoints).

Conclusions

NorUDCA seems to have a similar effect on bile production during NMP compared to preclinical data. It might be able to ameliorate the detrimental effects of bile on the damaged biliary tree after ischemia. Its diverse therapeutic effects make it an immensely promising agent for application during NMP in the context of liver transplantation.

07

Improved Decision Making During Hypothermic Oxygenated Machine Perfusion Of Liver Grafts Via Simple Evaluation Of Perfusate Electrolytes And Lactate

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Background
While hypothermic oxygenated machine perfusion (HOPE) is associated with improved outcomes after liver transplantation (LTx), there is a lack of biomarkers to evaluate graft viability during perfusion. Currently, there are no broadly available and easily assessable parameters for monitoring HOPE.

Methods
This study included all patients who underwent LTx with liver grafts perfused via HOPE at the Medical University of Vienna between 2018 and 2023. HOPE was performed according to standard operating procedures using University of Wisconsin machine perfusion solution. Blood gas analysis was conducted every 30 minutes for up to 120 minutes during HOPE. Data on hospitalization was prospectively documented and retrospectively analyzed. Early allograft dysfunction (EAD) was assessed according to the criteria established by Olthoff et al.

Results
In total, 158 patients were included in the analysis, with 44 patients (27.8%) developing EAD. Liver grafts that developed EAD had significantly lower sodium concentrations at all time points. Conversely, lactate levels were higher in EAD grafts at 60 and 90 minutes during HOPE. Sodium and lactate levels at 90 minutes showed the highest predictive potential for EAD, with an area under the receiver operating characteristic curve of 0.741 and 0.633, respectively. Optimal cut-off values were determined to be 85 mmol/L for sodium and 4.3 mmol/L for lactate at 90 minutes. Using these cut-offs, a low-risk cohort (high sodium, low lactate) with 17.6% EAD was identified, while the high-risk cohort (low sodium, high lactate) showed a striking EAD incidence of 69.2%.

Conclusion
A simple evaluation of sodium and lactate levels at 90 minutes during HOPE seems to effectively identify high-risk donor organs before LTx. Accordingly, pre-perfusion for 90 minutes and evaluation of graft suitibility using readily available blood gas analysis might lead to significant improvement of outcome in this cohot of patients.

08

Enhanced Renal Tissue Regeneration And Functional Recovery With IL-15 Treatment In Acute Kidney Injury

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09

Enhanced In Vitro Functionality Of Porcine Hepatocytes Using 3D Culture Techniques Including Precision-Cut Liver Slices

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Background
Three-dimensional (3D) cell culture techniques have gained considerable importance in recent years, especially in the field of liver research. Cultivating hepatocytes in two-dimensional (2D) environments is limited due to their rapid loss of functional properties and inability to maintain their native 3D architecture. In contrast, 3D cell cultures, including precision-cut liver slices (PCLS), aim to mimic cell-cell as well as cell-matrix interactions and thus in vivo liver conditions. This is critical for the study of liver function, toxicity testing, and the development of liver models for transplantation medicine. Due to the limited number of human organs available for transplantation research, porcine organs are commonly used for proof-of-concept studies, thus porcine hepatocytes serve as an excellent model for preliminary research.

Methods
Various 3D culture techniques, including spheroid cultures, hydrogel-based systems, and precision-cut liver

slices, are used to investigate primary porcine hepatocytes. Hepatocytes from porcine liver biopsies are cultured in 2D and 3D environments and PCLS are prepared by cutting liver tissue into thin, viable slices using a precision-cutting technique. Morphological and functional analyses are performed to assess cell viability, enzyme activities, and gene expression.

Expected Results

Hepatocytes in 3D cultures, including PCLS, are expected to exhibit higher activity, cell viability, and functional stability over an extended period of time compared to 2D cultures. Specifically, PCLS are expected to maintain a more physiological liver architecture and cell-cell interactions, providing a more accurate representation of in vivo liver conditions.

Conclusion

In conclusion, these experiments seek to demonstrate the efficacy of 3D cell culture methods, including PCLS, in preserving the physiological and functional characteristics of hepatocytes in vitro. These advanced culture systems provide valuable tools for liver research. Future studies should focus on further optimization and standardization of 3D culture techniques to enhance their application in biomedical research and translation into clinical practice.

10

Identifying The Cellular Source Of Donor-Specific Antibodies

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Background

Donor-specific antibodies (DSA) greatly restrict long-term outcomes in transplantation. Despite their impact on the field, the mechanisms that sustain the humoral immune responses against mismatched donor-MHC antigens in transplantation remain incompletely understood. Herein, we therefore aimed to identify the B cell subset(s) that are responsible for DSA secretion to gain insights into their biology and uncover potential therapeutic targets.

Methods

C57BL/6 mice received a syngeneic or fully mismatched BALB/c cardiac allograft without immunosuppression. DSA were assessed via flow-crossmatch and MHC-specific ELISA. Plasma cell subsets were quantified and purified using flow cytometry.

Results

Untreated C57BL/6 mice rapidly rejected fully mismatched BALB/c cardiac allografts, inducing a long-lasting humoral allo-immune response with DSA detectable for up to 15 months. Bone marrow and spleen cells isolated from cardiac allograft recipients 20 weeks after transplantation were cultured. A flow-crossmatch of the culture supernatants identified the bone marrow as the primary source of late DSA production. To identify the cellular source of these DSA, bone marrow plasma cell subsets were quantified via flow cytometry. Notably, plasma cells exhibiting a long-lived phenotype (i.e. long-lived plasma cells; LLPC; $CD138^{+}$ $B220^{-}$ $CD19^{-}$ $TACI^{+}$) were significantly enriched (as frequency within all bone marrow plasma cells and absolute cell number) in cardiac allograft recipients (median: $41.3\pm13.6\%$; n=22) compared to recipients of a syngeneic heart (median: $12.6\pm10.6\%$; n=7) or naïve mice (median: $13.6\pm17.3\%$; n=12) ($p<0.001$). Furthermore, cultures of flow-sorted bone marrow plasma cell subsets revealed that DSA were exclusively secreted by LLPC, but not other subsets. Ultimately, transplanting bone marrow of cardiac allograft recipients into syngeneic naïve mice induced DSA in the secondary bone marrow recipients, suggesting that LLPC persistently secrete DSA independent of antigen presence.

Conclusion

Bone marrow resident long-lived plasma cells are a critical source of late DSA and represent a potential therapeutic target in antibody-mediated rejection and de-sensitization.

11

Establishing An In Vitro Model With Precision-Cut Liver Slices With Extended Viability For Medical Research Applications

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Background

The limited availability of donor organs still poses a significant challenge in liver transplantation, leading to an urgent requirement for innovative approaches to enhance the donor pool. One promising in vitro model are Precision cut liver slices (PCLS) which have the advantage to preserve the complex cell diversity and cell-cell interactions mimicking the native environment of a liver. As a result, PCLS serve as an excellent model to effectively investigate the underlying cellular mechanisms of novel therapeutic treatment strategies aiming at organ reconditioning or regeneration.

Methods

The aim is the development of an optimized and standardized protocol for maintaining PCLS viability and functionality over a period of 7 to 14 days. PCLS are prepared from porcine biopsy samples with a diameter of 8 mm and a thickness of 250 µm using a vibrating microtome. These slices are than incubated on specific cell culture inserts with an optimized medium that mimics the conditions of the liver microenvironment. The viability is evaluated through multiple parameters like LDH leakage, AST/ALT measurements, morphological and immunohistochemical staining. Furthermore, gene expression analysis is conducted to quantify expression levels of key enzymes and regulatory systems involved in metabolic pathways.

Expected Results

It is hypothesized that by optimizing culture conditions, the viability of the liver slices can be significantly extended from several hours to at least one week. This would be supported by observing a decrease in LDH leakage, minimal histological degradation, as well as stable enzyme activities and gene expression levels.

Conclusion

Successful extension of PCLS viability would establish the basis for a robust and high-throughput model, enabling long-term studies by supporting more comprehensive investigations of liver regeneration, pathophysiology, and pharmacology compared to conventional 2D cell culture models.

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Costimulation-Independent Secretion Of IgM DSA By Marginal Zone B Cells

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Background

Costimulation blockade with CTLA4-Ig/belatacept is associated with a reduced incidence of IgG donor-specific antibodies (DSA) in kidney transplantation compared to standard of care calcineurin inhibitors (CNI). However, a notable fraction of patients on belatacept develop IgM DSA after transplantation, indicating that a distinct form of humoral allo-immune response persists under costimulation blockade. Within this project, we set out to characterize the nature of these costimulation-independent B cell responses and their consequence for transplantation in a mouse model for cardiac transplantation.

Methods

CCR5 knock-out mice (CCR5KO; C57BL/6 background, H-2b), which exhibit pronounced humoral allo-immunity,

received a fully mismatched BALB/c (H-2d) cardiac allograft under CTLA4-Ig monotherapy (1.25mg/dose on days 0, 4, 14, 26, 54, 86) and were followed for up to 100 days. Donorreactive B cell subsets were identified via flow cytometry using recombinant donor MHC tetramers. DSA were quantified via flow crossmatch and ELISA.

Results

Untreated CCR5KO recipients promptly rejected BALB/c cardiac allografts (MST= 8 days) and developed IgM and IgG DSA. CTLA4-Ig prolonged graft survival (MST>100 days) and prevented IgG but not IgM DSA formation, thus closely modeling the clinical situation. Bone marrow, spleen, and lymph node cells isolated from CTLA4-Ig treated cardiac allograft recipients 21 days after transplantation were cultured separately. An ELISA of the culture supernatants identified the spleen as primary source for costimulation-independent IgM DSA. To identify the cellular source of these IgM DSA, we tracked donor-reactive IgM^+ B cells in recipient spleens using fluorophore-conjugated recombinant donor MHC tetramers. Thereby we found that IgM^+ donor-reactive B cells predominantly display a marginal zone B cell phenotype ($CD1d^+$ $CD21^{high}$). Interestingly, while the formation of donorreactive germinal centers was completely abrogated by CTLA4-Ig, the number of donor-reactive marginal zone B cells remained unaffected.

Conclusion

These results demonstrate that marginal zone B cells are the source of costimulation independent IgM DSA.

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IONA – Interdisciplinary Oncological Follow-Up Clinic In Vienna, Updated Results After 4 Years Of Experience

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Background

Patients with cancer in childhood and adolescence show high cure rates, up to 90%. In Vienna, those patients are usually treated in the St. Anna Children`s Hospital or at the Department of Pediatrics and Adolescent Medicine, Medical University. During childhood, short-term follow-up is performed in the children`s hospitals. Afterwards patients had to organize further surveillance by themselves. This transition approach was not successful in many cases, with patients facing incomprehension and rejection due to a lack of experience with disease- and treatment-related complications.

Methods

"IONA – Interdisciplinary Oncological Follow-Up Clinic" is offering age-appropriate medical and psychosocial long-term follow-up since 2020. This outpatient department was established through a collaboration between the City of Vienna and the Austrian Health Insurance Fund (ÖGK). The City of Vienna finances the major part of the pilot project, with support from the Children's Cancer Aid Wien-NÖ-BGLD. A team of two hemato/oncologists, two clinical psychologists, a social worker and two case managers provides individualized care, including tailored medical check-ups and advisory services regarding risk factors and late effects, along with psychosocial and neuropsychological care. Two case managers ensure low-barrier contact and assist in scheduling necessary appointments. In addition, IONA is located in an ÖGK healthcare center with access to multidisciplinary medical departments.

Results

More than 600 survivors have been referred to IONA since 2020. The majority were diagnosed with CNS tumors, acute leukemia or lymphoma. Close cooperation between children`s hospitals and IONA with continuous exchange and joint conversations not only during transition but also in case of relapse or disease progression leads to a high transition rate, with 99% of patients successfully proceeding to long term-surveillance.

Conclusion

- IONA provides interdisciplinary standardized long-term follow-up care for patients aged 18 and older beeing diagnosed with a hemato/oncologic disease in childhood or adolescence and having completed treatment and short-term follow up care at children`s hospitals.

- IONA successfully accompanies patients in their transition process with 99% of referred patients receiving ongoing long-term surveillance at IONA thus far.
- Close cooperation among all disciplines ensures high-quality care and strong adherence to long-term follow-up for these patients.

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Influence Of ATG On Transferred And Endogenous Regulatory T Cells In Mice

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Background

ATG is widely used as induction therapy in solid organ transplantation. In the context of regulatory T cells (Treg) therapy, ATG is hypothesized to increase the cell products' efficiency by reducing the number of effector T cells. While the influence of ATG on endogenous Tregs is well described, the beneficial effect of ATG administration before adoptive Treg therapy remains to be discussed. Deploying a murine model of cell transfer we aim to shed light on the effects of ATG on adoptively transferred Tregs.

Methods

CD45.2 C57BL/6 mice received a single shot of 18mg/kg custom-made rabbit anti-mouse ATG on day 0 and $1x10^6$ CD45.1 C57BL/6 Tregs on day 5. Day 5 was selected since at this time point ATG serum levels have already declined to subtherapeutic levels to avoid depletion of transferred Tregs. Mice were sacrificed on day 10 for characterization of transferred and endogenous Tregs in secondary lymphoid organs. Results were compared to Tregs transferred to untreated recipients.

Results

Absolute cell numbers of transferred Tregs did not differ between ATG treated or untreated recipient mice 5 days after cell administration. Characterization of transferred Tregs in ATG treated mice indicated decreased levels of activated (CD44+) but increased levels of proliferating (Ki67+) cells and showed a trend towards increased Foxp3 expression compared to untreated recipient mice. ATG increased levels of proliferating endogenous Tregs and their Foxp3 expression, similar to what was shown for transferred Tregs, and had an additional positive effect on levels of Helios+ cells, while levels of CD44+ endogenous Tregs remained unchanged.

Conclusion

Here we show, that ATG might have a positive impact on the transferred cell product by increasing proliferation as well as Foxp3 expression. Nevertheless, the question of a beneficial effect of ATG induction for depletion of endogenous lymphocytes before cell transfer therapies remains and will be investigated further.

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Early Detection Of Postoperative Infections Via Continuous Temperature Monitoring

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Background

Approximately 91,000 deaths per year in Europe are caused by nosocomial infections. Especially transplant recipients are highly susceptible to infections, due to

immunosuppression. About 20% of transplant recipients need extra antibiotics after developing infections within the first week post-surgery.

Fever is one of the main symptoms of infection and therefore, a continuous measurement of body temperature could be crucial to improve overall outcome.

Here we used an adhesive axillary thermometer (SteadyTemp®) to investigate whether an earlier fever detection can reduce medication needs, shorten hospital stays and avoid additional invasive procedures and consequently improve overall outcome and patients' quality of life.

Methods
A total of 103 participants undergoing visceral surgery (including 6 transplant recipients) were included in the study. The patch (Steadytemp®) was placed centrally in the middle axillary line within 48h post-surgery. The body temperature was also measured via infrared thermometer. In addition, inflammatory markers (CRP, leukocytes, PCT) were tested regularly, as well as patient health and medication documented.

Results
Continuous body temperature measurement detected fever in 30 out of 103 patients (~29%), while routine measurement via infrared thermometer detected it only in 11 patients (~11%). In 5 of these cases, surgical revision was required subsequently.

When both the patch and the infrared thermometer detected fever in a patient, on average, the patch detected the fever 252 minutes earlier.

Conclusions
Our study points out the advantages of a continuous body temperature measurement, leading to a much more precise and reliable detection of increased body temperature. This finding has significant implications for temperature monitoring in general patient care, and especially for vulnerable transplant recipients.

These results highlight the importance of implementing the usage of continuous temperature monitoring for all hospitalized patients to enhance patient safety. However, further studies should be performed to include more transplant recipients, especially directly post-surgery.

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Hyperspectral Imaging For Evaluating Steatotic Liver Grafts

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Background
The increasing need for extended criteria donor (ECD) organs stems from the disparity between transplant waiting lists and organ availability. While donor livers with microsteatosis or moderate steatosis generally show favorable outcomes, severely macrosteatotic livers carry a higher risk of primary non-function or early allograft dysfunction, complicating clinical transferability due to subjective differentiation between steatosis types. Hyperspectral imaging (HSI) offers a non-invasive approach for assessing steatosis, potentially aiding in pre-transplant evaluation. This study investigated the feasibility and accuracy of using HSI in steatosis assessment.

Method
Livers from a previously established non-alcoholic steatosis pig model were utilized for this study. As part of this model, blood was retrieved prior to the start of perfusion. In this context, HSI data was collected using the TIVITA® 2.0 device to observe the consequent reduction in blood flow and precisely determine the onset of warm ischemia. The collected data was then analyzed to quantify steatosis levels, and the results were compared with histopathological findings to validate the correlation.

Results
HSI successfully differentiated between steatotic livers and healthy control livers, providing quantitative data on steatosis with high correlation to histopathological results. During blood retrieval, HSI detected changes in tissue composition and accurately identified the onset of warm ischemia by assessing the decline in blood flow and oxygen supply, with the real-time data limited to the time needed for taking one picture.

Conclusions
Additionally, HSI demonstrated its capability to assess microperfusion, oxygenation, and organ morphology, including steatosis. This highlights its potential to enhance clinical decision-making by enabling non-invasive and nearly continuous monitoring regarding organ suitability during various stages of the transplantation process. The implementation of HSI in the clinical settings could improve the assessment of liver grafts prior to transplantation, potentially increasing the pool of acceptable organs and improving transplant outcomes.

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Non-Alcoholic Steatohepatitis Pig Model For Transplantation Research

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Background
Steatosis, characterized by the accumulation of lipids in hepatocytes, markedly affects liver transplantation outcomes. The development of a reliable and reproducible animal model of steatosis facilitates research using not only healthy but also steatotic pig livers, thereby advancing the understanding of extended criteria donor organs. This study aimed to establish an effective pig model of steatosis to further evaluate the performance of these organs during different machine perfusion techniques, in comparison to healthy livers.

Methods
A cohort of pigs was subjected to a specifically designed high-fat diet over a median of 32 weeks to induce steatosis, with dietary intake and health parameters continuously monitored. Liver biopsies were performed at defined time points to assess steatosis progression. Post-induction, livers were evaluated using conventional laboratory values to confirm steatosis. Following these assessments, the livers were explanted according to standard clinical protocols and subjected to sub-normothermic machine perfusion (SNMP) after cold ischemia. Key perfusion metrics were monitored throughout the process.

Results
The high-fat diet successfully induced several degrees of steatosis in the pig model, with histopathological analysis revealing macrovesicular steatosis similar to human non-alcoholic fatty liver disease, along with signs of inflammation and commencing fibrosis. Additionally, immunofluorescence staining was performed. During SNMP, steatotic livers exhibited impaired perfusion dynamics compared to healthy controls.

Conclusions
The study successfully established a pig steatosis model that aimed to mimic steatosis in humans, providing a valuable tool for transplantation research. The model demonstrated consistent and reproducible induction of steatosis. Comparative analysis under SNMP revealed differences in the performance of steatotic versus healthy livers. This model holds potential to serve as a platform for investigating steatosis pathophysiology and improving machine perfusion strategies of such livers.

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Performance Of Steatotic Pig Livers During Sub-Normothermic Machine Perfusion

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Background
Sub-normothermic machine perfusion (SNMP) is used to preserve and evaluate liver grafts at temperatures above hypothermic and below normothermic conditions, especially evaluating its temperature stage in controlled oxygenated rewarming in combined perfusion protocols such as DHOPE-COR-NMP. However, the experience in preserving and assessing steatotic livers during SNMP is limited. This study focused on comparing the performance of steatotic versus healthy liver grafts during SNMP to provide a more comprehensive understanding during this specific temperature setting.

Methods
Steatotic livers were obtained from pigs fed with a specifically designed high-fat diet over a median of 32 weeks to induce steatosis. Healthy liver grafts were obtained from pigs receiving a standard diet. Both steatotic and healthy livers underwent SNMP for 12 hours. During perfusion, key parameters such as perfusion dynamics, biliary tree secretion and lactate clearance were monitored. Histopathological analysis and immunofluorescence assays were performed post-hoc to assess steatosis levels and liver condition.

Results
Steatotic livers exhibited impaired perfusion dynamics compared to healthy livers, with higher vascular resistance and lower flow rates. Biliary tree secretion and overall metabolic activity, measured by lactate clearance and glucose metabolism, was also lower in steatotic livers compared to healthy controls. Histopathological analysis confirmed the presence of macrovesicular steatosis, with associated cellular damage.

Conclusions
SNMP showed differences in the performance of steatotic versus healthy liver grafts. Steatotic livers showed a tendency of impaired perfusion highlighting the challenges associated with steatotic livers for transplantation. This study underscores the importance of individualized assessment and optimization of liver grafts during machine perfusion. Further research is needed to refine SNMP techniques and improve the viability of steatotic liver grafts.

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Multimodal Photoacoustic And Ultrasound Imaging System During Ex-vivo Organ Perfusion

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Background
Machine perfusion techniques represent promising tools for evaluating organ quality prior to transplantation. They facilitate the evaluation of microperfusion – a key factor influencing graft outcomes – through the integration of additional modalities and techniques. Photoacoustic (PA) and ultrasound (US) imaging have emerged as techniques for providing detailed insights into the vascular conditions of an organ. This study aimed to investigate the use of a multimodal PA/US imaging system to evaluate the perfusion kinetics of livers during machine perfusion.

Methods
A previously developed multimodal PA/US imaging system, equipped with a dual-wavelength pulse laser (532nm/1064nm) and a wavelength-switchable fibre bundle coupling unit, was used to assess perfusate flow through the organ during machine perfusion. The system also included two transparent US sensors positioned on the organ to capture integral microperfusion measurements from A-line signals. Imaging experiments were performed on porcine liver subject to sub-normothermic and normothermic machine perfusion. Additionally, to investigate perfusion kinetics, indocyanine green (ICG) was investigated as a contrast agent.

Results

Experiments carried out with acellular perfusate showed no significant contrast at wavelengths 532nm and 1064nm, with PA-B-scan images primarily depicting unstable blood residues. US images provided morphological contrast, clearly showing liver lobe interfaces, larger vessels, and fat accumulations. During normothermic machine perfusion, PA/US benefited from high absorption in the visible wavelength range but faced challenges due to surface absorption. Using ICG as a contrast agent, significant perfusion kinetics were observed. After injecting ICG PA/US-B scan images revealed a notable increase in contrast, followed by a gradual decay. Overall, the system effectively monitored perfusion dynamics in larger vessels.

Conclusions

This study demonstrated the potential of multimodal PA/US imaging for monitoring perfusion dynamics and assessing microperfusion. Further research is required to investigate diverse perfusion conditions and to conduct continuous comparative evaluations with other techniques to determine clinical applicability. A notable limitation of this study is that the imaging system was developed de novo, leading to a prototype that, while functional, was not as refined or user-friendly as established commercial systems.

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Serum Proteomics Analysis Of Lung Transplant Patients Receiving Different Induction Therapies

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Background

Induction therapy in lung transplantation is crucial for immune modulation and graft survival. Despite its widespread use, the impact of different induction therapies on serum proteomics profiles is understudied. This study investigates these profiles in lung transplant patients receiving alemtuzumab, anti-thymocyte globulin (ATG), or no induction therapy.

Methods

Using mass spectrometry and the LIMMA platform for data analysis, we compared serum samples from pre-transplantation and one year post-transplantation. Our cohort included 97 patients (47 received alemtuzumab, 32 received ATG, and 18 received no induction therapy).

Results

Comparing samples one year post-transplantation to pre-transplantation, we identified 40 dysregulated proteins in the alemtuzumab group, 22 in the ATG group, and none in the no-induction group. The most significantly dysregulated proteins in the alemtuzumab group included upregulation of apolipoprotein A-I, and downregulation of multiple complement factors and immunoglobulin subunits, fetuin-B, fibulin-1, and Intracellular adhesion molecule1, suggesting reduced inflammation and immune response. In the ATG group, significant changes included upregulation of immunoglobulin heavy constant mu, indicating enhanced primary antibody responses, and downregulation of complement factors and extracellular matrix protein 1, indicating modulation of the complement pathway and inflammation. Inter-group comparisons at one year post-transplantation revealed downregulation of fibulin-1 and fetuin-B between alemtuzumab and no induction, suggesting a more favorable proteomic pattern for graft survival, while no significantly dysregulated proteins were found between alemtuzumab and ATG. In contrast, ATG versus no induction showed no significant differences.

Conclusions

Alemtuzumab and ATG induction therapies modulate key proteins in immune response, inflammation, and complement regulation, creating an immunosuppressive

environment critical for preventing rejection and ensuring long-term graft survival. Alemtuzumab showed more extensive dysregulation in serum proteomics, indicating more robust immune system inhibition. The lack of significant proteomic changes in the no-induction group underscores the potential benefits of induction therapy in managing post-transplant immune responses.

Keywords: Lung transplantation, induction therapy, serum proteomics, mass spectrometry, alemtuzumab, anti-thymocyte globulin

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The Effect Of Hemolysis During Normothermic Machine Perfusion Of The Kidney In RPTEC Cells

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Background
Ex situ normothermic machine perfusion (NMP) of the kidney may aid in reducing the organ shortage. However, during prolonged preservation periods, red blood cells (RBC) in the perfusion solution are damaged and free hemoglobin and hemin are released. Oxidative stress and mitochondrial damage are induced and may trigger acute and chronic kidney dysfunction. Herein, we investigated the effect of hemolysis in an *in vitro* model cell culture model of renal proximal tubular epithelial cells (RPTEC).

Methods
RPTEC cells were seeded in 6-well plates (1x10^6/well) and were allowed to attach for 3h. Cells were then treated with hemin (50µM dissolved in 10% DMSO) or control (1% DMSO) and incubated for 24h. Next, cell viability was assessed by ATP quantification and metabolic activity was evaluated by MTS assay. High resolution respirometry was performed to assess mitochondrial function parameters as oxidative phosphorylation (OXPHOS) capacity, efficiency of ATP production and integrity of the outer mitochondrial membrane.

Results
The OXPHOS capacity was decreased three fold by hemin treatment when compared to the control (64.86$\pm$22.39 vs 24.07$\pm$5.25 pmol/s·m, p-value <0.0002, paired t test). The efficiency of ATP production was also impaired (0.83$\pm$0.02 vs 0.73$\pm$0.05, p-value <0.0003, paired t test) and lower ATP levels were found (p-value <0.0001, paired t test). In line, the metabolic activity was reduced revealed by MTS assay (p-value <0.0001, paired t test). Interestingly, the outer mitochondrial membrane integrity remained intact reflected by cytochrome c control efficiencies <0.1 in both groups.

Conclusion
Free heme leads to a compromised bioenergetic state in RPTEC cells. Thus, hemolysis during kidney NMP may contribute to mitochondrial damage and impaired kidney function.

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Induced Pluripotent Stem Cell Derived Hepatocyte-Like Cells To Enhance Liver Regeneration During Normothermic Machine Perfusion

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Background
Prolonged *ex situ* normothermic machine perfusion (NMP) may serve as a platform for regeneration of marginal livers. Due to their high proliferative capacity induced pluripotent stem cell (iPSC) derived cells may be applied during NMP to regenerate marginal donor organs. We herein aimed to investigate the impact and conditions of iPSC-derived definitive endoderm (DE) in a precision-cut liver slice (PCLS) model.

Methods
Liver punch biopsies (8mm) were obtained to generate precision-cut liver slices (300µm). 0.1 x 10^6 mCherry-labeled DE were added and incubated for 7 days with a continued differentiation protocol towards hepatocyte progenitor-like cells (HPC). Immunofluorescence microscopy was performed daily; immunohistochemistry (Ki-67, alpha-fetoprotein (AFP)), and fluorescence-activated cell sorting (FACS) was performed on day 1, 4 and 7. Culture supernatant was analyzed for albumin, lactatedehydrogenase (LDH) and aspartateaminotransferase (AST) daily.

Results
mCherry-labeled DE did attach on PCLS and could be traced during 7 days of co-cultivation by immunofluorescence microscopy. After tissue dissociation and FACS of PCLS, viable mCherry-positive transplanted cells could be sorted. They showed proliferative capacity as confirmed by Ki-67 positivity. In addition, they differentiated towards HPC revealed by AFP signal. When compared to control PCLS (without DE co-cultivation), no significant differences for AST (283 ± 117 U/L vs 324 ± 141 U/L, p=0.7566) and LDH (163 ± 100 U/L vs 165 ± 103 U/L, p=0.9590) as well as Albumin secretion (278 ± 3 g/L vs 280 ± 2 g/L, p=0.9638) were found.

Conclusions
iPSC derived DE may be used to regenerate livers while undergoing NMP, while the function impact remains under investigation.

03_Kidney TX

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Evaluation Of The Most Common Microorganisms Causing Surgical Site Infections After Renal Transplantation

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Introduction
Renal transplant recipients are highly susceptible to infections due to surgical complexity and immunosuppression, with surgical site infections (SSI) being a significant early postoperative complication. This study aimed to identify the common microorganisms causing SSI after renal transplantation and evaluate their susceptibility to standard antibiotics.

Methods
We conducted a single-center, observational cohort study of adult renal transplant patients from January 2017 to December 2019 (n=231). Cephalosporins were used for prophylaxis. We evaluated risk factors for SSI (age, gender, BMI, type of donation) and clinical outcomes (organ function, patient survival, SSI occurrence, hospital stay). Patients were grouped by BMI (<25, 25-30, >30). Microbial specimens from SSI cases (n=46) were analyzed using conventional methods and antibiotic sensitivity tests.

Results
Among 231 kidney transplant recipients (56 12.8 years, male 149, living donation 41), 46 developed SSIs (55 years, male 31, living donation 11). SSIs occurred in 15.4% of BMI group 1, 18.5% of group 2, and 28.8% of group 3. While higher BMI was linked to more SSIs, it wasn't statistically significant. Of the 46 SSIs, 29 (63%) were monomicrobial, and 17 (37%) were polymicrobial. Predominant organisms included Staphylococcus epidermidis (23.9%), Enterococcus faecalis (21.7%), coagulase-negative staphylococci (26.1%), and Candida albicans (21.7%). However, numerous other bacteria and fungi against which the routine antibiotic was not effective, were found, especially in patients with a higher BMI. As a result, the anti-infective substances were switched, so effective therapy was started late.

Conclusion
SSI is an early complication after renal transplantation, which brings a great burden to patients. Therefore, preventing wound infection is extremely important. Routinely used anti-infective substances do not cover all bacteria and fungi, which especially occur in patients with a higher BMI. Therefore, routine anti-infective therapy should be re-evaluated in further studies and possibly expanded in high-risk patients.

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Spatial Transcriptomics Of Glomeruli From Kidney Transplant Biopsies With Microvascular Inflammation With And Without The Presence Of DSA

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Background
Microvascular inflammation (MVI), and in particular glomerulitis (g), in the presence of donor-specific antibodies (DSA) is considered a diagnostic hallmark of antibody-mediated rejection (ABMR) in kidney transplant (KTX) biopsies. However, in a substantial number of cases with MVI, DSA cannot be detected and the degree of pathophysiological connection between these two entities is a matter of debate. We selectively applied spatial transcriptomics in glomeruli with glomerulitis to investigate molecular differences between DSA+ and DSA- cases.

Methods
We selected biopsies from six DSA+ and eight DSA- cases with g≥2 and two healthy controls. Spatial transcriptomic analysis was done with GeoMx from Nanostring®. Glomeruli were annotated as region of interest and incubated with the "whole transcriptome atlas panel". Analysis was done using "R" with packages including "limma" (identify differentially expressed genes), "fgsea" (enrichment analysis) and "SpatialDecon" (cell deconvolution with the "safeTME" annotation matrix).

Results
After filtering for rarely expressed genes and ROI with low sum counts, 174 glomeruli were left in total. Looking at the top 300 upregulated genes of DSA+ and DSA- cases compared to controls, we noticed only partial overlap between the two conditions. Next, we looked at gene set enrichment analysis of pathogenesis-based transcript (PBT) sets (gene lists obtained from https://www.ualberta.ca/medicine/institutes-centres-groups/atagc/research/gene-lists.html). In direct comparison "immunoglobulin" - and "DSA-selective" transcript sets were enriched in the DSA+ group, whereas DSA- cases showed enrichment in most other PBT's, e.g. "macrophage-associated" transcripts. The "NK-cell transcript burden" PBT was not different. Immune cell deconvolution showed higher macrophage abundancy in DSA- cases and higher CD8 T-cell abundancy in DSA+ cases. The NK cell abundancy was not significantly different.

Conclusions
Analyzing glomerulitis in DSA- and DSA+ KTX biopsies using spatial transcriptomics revealed differences in PBT set enrichment scores and immune cell abundancies.

Further research is needed to better characterize these differences and understand their potential consequences.

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Effect Of Felzartamab Anti-CD38 Treatment On The Molecular Phenotype And Donor Derived Cell Free DNA In Antibody-Mediated Rejection In Kidney Transplant Biopsies

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Background
A recent randomized trial found that treatment with CD38 antibody felzartamab suppressed histologic antibody-mediated rejection activity (ABMR), with recurrence post treatment in some patients.

Methods
The present study examined the molecular effects felzartamab treatment using microarray analysis of kidney biopsies, comparing baseline to week 24 and week 52 of 10 felzartamab and 10 placebo patients.

Results
Of 10 felzartamab-treated patients with histologic ABMR, 9 had molecular ABMR activity: IFNG-induced and NK cell transcripts. Felzartamab suppressed IFNG-induced and NK cell transcripts in all 9, with recurrence of ABMR activity post treatment in 8, with minimal effect on the ABMR-induced endothelial transcripts that reflect ABMR stage. Molecular responses were often incomplete when ABMR activity was intense. There was no association of treatment or follow-up date for molecular TCMR classifier scores. Felzartamab also slowed the trajectories of molecular injury scores, suggesting slowing of progression to renal failure. Geneset enrichment analysis showed suppression of all enriched pathways. From baseline to week 24, 12 immune response pathways were suppressed. Between weeks 24 and 52, 6 pathways related to cellular development and metabolism were suppressed. From baseline to week 52, 47 pathways related to cellular development, regulation, metabolism, and immune response were suppressed, indicating significant impacts on immune and cellular processes.

Conclusions
We conclude that felzartamab treatment selectively suppresses molecular ABMR activity but not stage in ABMR patients with recurrence of activity post treatment in 8/9, and that molecular responses and recurrences were more widespread than histologic responses.

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Long-Term Outcome Following Pediatric Kidney Transplantation Is Similar To Adult Kidney Transplantation

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Background
Even though graft and patient outcomes following pediatric kidney transplantation have improved considerably over the last decades, there are concerns regarding benefits of pediatric kidney transplantation due to the technical complexity of the surgery in small recipients. We investigated the outcomes of pediatric kidney transplantation in comparison to adult kidney transplantation.

Methods
A retrospective analysis of all pediatric kidney transplantations performed at the Medical University of Innsbruck between 2002 and 2022 was conducted. Patient and graft survival was compared to a cohort of 1578 adult recipients undergoing kidney transplantation from a standard criteria donor.

Results
Between 2002 and 2022, 85 pediatric kidney transplantations were performed. 54 children (63.5%) were male, median age was 13 years (range: 7 months - 18 years). Preemptive kidney transplantation was performed in 25 pediatric recipients (30.1%), and 47.6% of transplants were living donor organs. Over the same period, 1578 adult patients received a kidney transplant from a standard criteria donor. 65.1% of patients were male, median age was 48 years (range: 19 - 75 years). In the adult cohort, living donor kidney transplantation accounted for only 14.4%. 228 transplantations (14.4%) were performed preemptively.

In pediatric recipients, overall graft survival was 96.9% at 1 year and 90.8% at 5 years compared to 95.5% and 83.4% in adult recipients, respectively. Similarly, patient survival was 94.7% at 1 year and 87.5% at 5 years in the pediatric cohort compared to 94% and 83.4% in adults, respectively. Furthermore, graft survival following pediatric kidney transplantation did not differ between recipients of a living and a deceased donor graft.

Conclusions
Long-term outcome following pediatric kidney transplantation is comparable to adult kidney transplantation with respect to patient and graft survival. No difference regarding long-term graft survival between living and deceased donor organs was observed in pediatric kidney transplantation.

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Targeting CD38 In Antibody-Mediated Rejection – The Potential Of Noninvasive Biomarkers To Detect Rejection Reversal And Recurrence

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Background
In a recent phase 2 trial (Mayer et al, NEJM, doi: 10.1056/NEJMoa2400763), the CD38 antibody felzartamab showed to reverse antibody-mediated rejection (AMR) after kidney transplantation, presumably due to natural killer (NK) cell depletion. Here, we evaluated whether distinct noninvasive biomarkers - known to reflect plasma cell activity (donor-specific antibodies [DSA]), graft injury (donor-derived cell-free DNA [dd-cfDNA]), inflammation

(C-X-C motif chemokine ligand [CXCL]9 and 10), or NK cell integrity - can accurately mirror the resolution and, after treatment discontinuation, the recurrence of rejection.

Methods
Twenty-two recipients were randomized to receive either felzartamab (n=11) or placebo (n=11) for 6 months, followed by a 6-month observational period. Follow-up biopsies were performed after 24 and 52 weeks. Concurrently, DSA mean fluorescence intensities (MFI) and titers, as well as serum and urinary CXCL9/10 levels, were assessed using microbead assays. NK cell counts and dd-cfDNA levels were quantified via flow cytometry and digital droplet PCR, respectively.

Results
At week 24, treatment with felzartamab led to a profound reduction of $CD16^{bright}$ NK cell counts (median percentage from baseline: -84.7% vs. 18.1% in placebo patients; p<0.001) and absolute levels of dd-cfDNA (-80.7% vs. 9.4%; p=0.002), with increases towards baseline levels by week 52. DSA MFI levels and titers of the immunodominant DSA, as well as chemokine levels in serum and urine showed no meaningful changes, except for a numerical, nonsignificant decrease in serum CXCL9 (percentage from baseline) (-26.5% vs. 0.0%; p=0.231).

Conclusions
Our results suggest that the assessment of NK cell counts and dd-cfDNA release, but not DSA or chemokine levels, could be useful for monitoring responsiveness to felzartamab treatment. It remains to be established whether monitoring of these biomarkers allows for individualized guidance of CD38 antibody-based anti-rejection treatment.

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Establishing A DCD Program In The Region North: First Experiences

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Background
Today, organ shortage is the major issue in transplantation medicine. In Austria the utilization of DCD organ donors has the biggest potential to increase the number of organs available for transplantation. Since 2013 health care authorities request the implementation of a DCD program in all transplant regions. In the transplant region North, after intensive preparation, now a DCD program was started in April 2024.

Methods
For preparing a DCD program in our region we had vivid information exchange with other Austrian transplant centers and got a lot of support. Numerous documents were provided and information about their experience with DCD was generously shared. We also could visit DCD procedures in the region east and west.

Official regulatory documents and guidelines of the involved scientific societies were reviewed.

In cooperation with the regional transplant delegate and the major donor centers we created information material and a step-by-step checklist for the management of a DCD case.

Finaly intensive information was given to potential donor hospitals and the local transplant delegates.

Results
After the official start of the Program, two DCD doners were reported to our center within the first two months.

In both cases DCD was executed and the whole procedure was done exactly according to the protocol without any problems.

Indication for comfort terminal care was a severe hypoxic brain damage after resuscitation and a massive intracerebral hemorrhage respectively. Times from termination of the ventilation to circulatory arrest was 16 and 19 minutes, the functional warm ischemia time was 27 and 16 minutes, the absolute warm ischemia time was 15 and 14 minutes respectively.

The liver and both kidneys were explanted in both cases, however the right kidney artery of the second donor had a subtotal stenosis and consecutively this kidney was not transplanted.

Conclusions
After structured preparation, a DCD organ donation program successfully started in the region Noth. Further efforts will be made to expand the program over all potential donor hospitals.

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Diaphragmal Leak With Pleural Effusion 1 Year After Peritoneal Dialysis (PD)

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Background
A 67-year-old man with end-stage renal disease developed massive right-sided pleural effusion ½ year after the initiation of peritoneal dialysis (PD) presented with dyspnea on exertion that progressed.

Methods
Although pleuroperitoneal communication was suspected, computer tomographic peritoneography on usual breath holding did not show leakage. After methylenblue was given by PD, the diaphragmal defect was detectable in VATS.

Results
CT scan and fast treatment consisted in thoracoscopic approach is treatment of choice. Repair methods in thoracal approach with simple sutures is possible.

Conclusion
In subacute chest pain concomitant with pleural effusion after peritonealdialysis diaphragmal defects should be considered. Ultimately, surgical corrections of diaphragmatic defects may be necessary for definitive management in selected patients. Although these scenarios are rare, clinicians should be aware of these possibilities as early collaboration between medical and surgical services is essential for optimal patient care.

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"YouTube" For Surgical Training And Education In Donor Nephrectomy: Friend Or Foe?

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Background
The COVID-19 pandemic has accelerated the shift toward e-learning in surgical training. With rising cases of end-stage chronic kidney disease, the demand for kidney transplants is high. Donor safety in nephrectomy procedures is crucial, emphasizing the need for effective training. This study evaluates the quality and effectiveness of YouTube videos on laparoscopic and robotic donor nephrectomy for surgical education.

Methods
On October 24, 2023, YouTube searches for "laparoscopic live donor nephrectomy" and "robotic live donor nephrectomy" returned 123 videos, with 63 included in the study. Popularity was evaluated using the Video Power Index (VPI), while reliability and quality were assessed with the LAP-VEGaS Video Assessment Tool and JAMA criteria. A structured checklist, the "Live Donor Nephrectomy Scoring System (LDNSS)," was created to evaluate the completeness and educational value of procedural steps.

Results
Out of 63 videos reviewed, laparoscopic surgical procedures were depicted in 71.4% of them, while robotic approaches were shown in 28.6%. Academic backgrounds were associated with 54% of the videos, and individual physician backgrounds with 46%. Mean scores were LAP-VEGaS 9.79 +/- 3.87, VPI 6.32 +/- 3.31, and LDNSS 9.68 +/- 1.97. Academic videos scored significantly higher in LAP-VEGaS and LDNSS (all $p<0.01$). While LAP-VEGaS, VPI, and LDNSS scores correlated significantly (all $p<0.05$), no correlation was found between JAMA score and other scoring systems. Videos with more clicks and likes showed significantly better scores across all measures (all $p<0.05$).

Conclusion
Amidst pandemic challenges on surgical education, YouTube has become a valuable resource for learning about laparoscopic and robotic donor nephrectomy for living kidney donation. However, the quality and reliability of these videos vary greatly, often lacking thorough reviews and leading to incomplete information. To enhance their educational value, it's proposed that videos undergo professional evaluation before publication and adhere to standardized scoring systems to ensure logical structure and improved quality.

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Analysis Of Donor Factors In Post-Mortem Kidney Transplantation Over The Years

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Background
The COVID-19 pandemic set back kidney transplantation (KT) programs leading to declining number of KTs ever since. The causes are speculated to be not only a general organ-shortage but also a worsening donor/organ quality. The aim of this study is to evaluate the quality trends of post-mortem donor kidneys offered to our center.

Methods
We evaluated all post-mortem kidney donors (n=1461) between 2018 and 2023 offered by the ETKAS to our center. We categorized allocation types into individual or non-individual (extended or competitive) allocations. Donor variables to calculate the "Kidney Donor Risk Index" (KDRI) as well as acceptance/rejection rates and reasons were collected. Differences in KDRI and donor age were compared using the Kruskal-Wallis test.

Results
The analysis revealed significant differences in the KDRI during the years, with the highest in 2019 (median 1.48; IQR 1.09-1.74), however, without the confirmation of a negative trend. Likewise, donor age showed a similar pattern. Notably, there was an increase in non-individual allocations from 56% to 72% and a decline in individual offers from 44% to 28%. The KDRI of individual allocations (median 1.33; IQR 1.02-1.70) was significantly lower compared to that of extended (1.48; IQR 1.09-1.74) or competitive allocations (median 1.41; IQR 1.11-1.77). The most common reason for offer rejection was poor organ and/or donor quality, with an increasing trend over the years from 60% to 72%.

Conclusion
The KDRI and age of kidney donors offered to our center did not exhibit a negative trend. This refutes the initial assumption of a decline in organ quality. However, the increase in non-individual offers at the expense of individual offers might create a subjective perception of declining organ quality. Additionally, the parameters used to calculate the KDRI do not solely reflect the complexity of a kidney offer, on which the decision of acceptance or rejection is based.

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The Potential Of Hematocrit And Albumin Correction To Uncover Adverse Effects Of Tacrolimus Through Level Variability In Pediatric Kidney Transplant Recipients

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Background
The narrow therapeutic index of tacrolimus requires frequent monitoring after kidney transplantation. Studies in adults and pediatric kidney transplant recipients suggest associations between high intrapatient tacrolimus trough level variability (TAC-IPV) and poor graft outcomes and donor-specific antibody formation. Tacrolimus trough levels are routinely measured in whole blood where hematocrit and serum albumin, major binding sites for tacrolimus, are potential confounders for TAC-IPV interpretation. The aim of this study was to investigate whether hematocrit and serum albumin represent relevant confounders for the interpretation of TAC-IPV.

Methods
This was a retrospective single-center study at the Medical University of Vienna, including all pediatric patients who received their kidney graft between 2010 and 2020. Exclusion criteria were insufficient follow-up data and non-tacrolimus-based immunosuppression. Hematocrit tacrolimus through level correction was conducted as previously published and modified for a combined correction with albumin. TAC-IPV was calculated in six month moving windows. Mixed-effects models were utilized to assess associations between TAC-IPV and corrected TAC-IPV with estimated glomerular filtration rate (eGFR) six months later.

Results
39 patients followed for a median of 552 days (IQR 517-561) were included in this study. 72% were male with 75% living donors, a median age of 10 years (IQR 5-16) and a median HLA mismatch of 3 (IQR 2-3). While whether crude TAC-IPV nor hematocrit-corrected TAC-IPV were associated with eGFR six months later (est.=0.03 p=0.67, est.=-0.06 p=0.27), combined hematocrit- and albumin-correction of TAC-IPV unveiled a significant association with eGFR (est.=-0.14 p=0.01).

Conclusions
This is the first study to assess the potential of hematocrit and albumin correction to uncover adverse effects of TAC-IPV in pediatric kidney transplant recipients. We have shown a relevant underestimation of TAC-IPV, and its association with graft function, in pediatric kidney transplant recipients without appropriate hematocrit- and albumin-correction.

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Preoperative Evaluation Of The Iliac Calcification Score Before Kidney Transplantation And Its Impact On Postoperative Complications

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Background
Patients with renal insufficiency have an elevated incidence and progression of arteriosclerosis compared to the general population. Before kidney transplantation, ensuring adequate vascular quality in the pelvic region is crucial for graft anastomosis.

Methods
In our retrospective study (2018–2022), we analyzed data from 266 kidney transplant patients who underwent preoperative NTX evaluation. Using CT scans, we detected vascular calcification in various pelvic vessel segments abdominal aorta (AO), common iliac arteries (AICd/AICs), and external iliac arteries (AIEd/AIEs) considered for potential anastomosis. Our investigation aimed to correlate vessel calcification with short- and long-term graft function and outcome.

Results
The median patient age was 53.31 ± 13.37 years, with 94 (35.3%) females and 172 (64.7%) males. Calcifications were observed in the following vessel segments: AO in 173 patients (65%), AICd in 155 patients (62%), AICs in 151 patients (60.5%), AIEd in 99 patients (37.2%) and AIEs in 97 patients (36.5%). Notably, iliac calcification significantly correlated with delayed graft function (odds ratio 2.541, p=0.001). A trend was observed between iliac calcification and graft loss (odds ratio 4.315, p=0.068). However, it did not show significant associations with graft rejection (p=0.522) or postoperative complications (p=0.365).

Conclusions
Our study underscores the importance of assessing pelvic vascular quality before kidney transplantation. We demonstrated that iliac calcification had a significant impact on short- and long-term graft function and outcome. Future research should explore preventive strategies and interventions for patients with iliac calcification to optimize transplant outcomes and enhance patient care.

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Potential Impact Of *Strongyloides Stercoralis* For Future Kidney Transplant Recipients

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Background
Strongyloides stercoralis (*S. stercoralis*) infection, a frequently overlooked parasitic disease, is widespread in tropical regions and considered rare in Europe. However, globalization, migration and global warming contribute to an increase of cases of this nematode worm in Central Europe. Specifically, individuals undergoing high-dose corticosteroid treatment, such as kidney transplant (KTX) recipients, are at risk of the potentially life-threatening hyperinfection syndrome if they harbor latent *S. stercoralis* infection. This syndrome is characterized by autoinfection, leading to massive worm burden, hyperinflammation, and possibly death, but can be easily prevented by ivermectin-treatment. This raises the question of whether transplant candidates should undergo routine screening for *S. stercoralis* infection. Thus, we aimed to assess the prevalence of *S. stercoralis* infection in future KTX recipients.

Methods
Blood samples were collected from 108 hemodialysis patients and analyzed for IgG-antibodies using serology testing. A questionnaire was used to determine prior soil exposition, medical history including transplant status, travel history, symptoms indicative of helminthic infection, and immunosuppressive therapy.

Results
Of the 108 patients, 37 (34.3%) had a history of organ transplantation (26 KTX, 6 multiple KTX, 2 heart transplants, and 3 liver transplants). IgG-antibodies against *S. stercoralis* were detected in 16 patients (14.8%), including five with prior KTX. Among IgG-positive patients, gastrointestinal symptoms in 25% (n=4), and pruritus 18.8% (n=3). Notably, 81.3% (n=13) had a travel history to endemic areas, 50% (n=8) were pet owners, and 37.5% (n=6) reported soil contact. However, there were no statistically significant differences in these variables between IgG-positive and IgG-negative individuals (all p>0.05).

Conclusions
With globalization, migration, and climate change facilitating the spread of helminth infections, the prevalence of *S. stercoralis* in Austria is increasing. Therefore, *S. stercoralis* screening in pre-transplant protocols should be considered. A larger study encompassing all hemodialysis patients in Vienna is currently underway to further elucidate these findings.

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Robotic Assisted Nephrectomy For Living Kidney Donation: Experience And Results Of A Single Centre – University Hospital Of Graz

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Background
Minimally invasive nephrectomy for living kidney donation has become the standard of care in most centres, significantly reducing postoperative morbidity and hospital stay duration for donors. Robot-assisted nephrectomy for living donors (RANLD) has gained significant ground and is increasingly used in daily practice. We present our institutional experience, detailing the surgical technique and outcomes at the University Hospital of Graz.

Methods
We conducted a retrospective analysis of perioperative and short-term outcomes for the initial 18 RANLDs procedures performed using the DaVinci Xi surgical platform from November 2022 to June 2024. Data collected included patient sociodemographics, perioperative and postoperative outcomes, and procedural video recordings.

Results
During the observation period, the number of living kidney donations at our hospital doubled. A total of 18 RANLD procedures were performed. The mean patients age was 51.06±11.48 years (range: 27 - 64 years). Operative time did not differ significantly between left and right nephrectomies. There were no conversions to open surgery, and no intraoperative or postoperative complications were recorded. The mortality rate was 0%. Notably, 13 out of 18 procedures were performed by the same surgeon, indicating a proficient learning curve and a median operating time of 150 minutes.

Conclusions
RANLD is an emerging minimally invasive surgical technique that demonstrate safety and low rates of mortality and morbidity. Robotic-assisted living donor nephrectomy is poised to play a pivotal role in the future of transplantation surgery.

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Monitoring Of Medical Adherence To Immunosuppressive Drugs By Electronic Healthcare Data In Kidney Transplant Recipients – A Prospective Study

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Background
Medication non-adherence is a major challenge in the management of kidney transplant recipients, leading to graft rejection and allograft loss. Current guidelines advocate for routine monitoring of medication adherence as a critical component of post-transplant care, but the optimal strategy to detect non-adherence has yet to be defined. Utilizing electronic healthcare data e.g. pharmacy refill records (PRR) offers a practical, widely accessible, and cost-effective method to evaluate adherence.

Methods
The AdTorque cohort study was initiated to conduct an extensive, multimodal longitudinal evaluation of adherence to immunosuppressive medications among kidney transplant recipients. This included PRR, self-reports by questionnaires, electronic drug monitoring, psychological assessments, immunosuppressive drug levels and immune monitoring. All 226 adult kidney graft recipients transplanted at the Medical University of Vienna between 2018 and 2019 were monitored for 2 years with a clinical follow-up of 4 years.

Results
This preliminary analysis includes data on PRR presented as continuous measures of adherence (CMA) of 147 patients during the first post-transplant year for the immunosuppressive drugs tacrolimus (TAC) and mycophenolic acid (MPA). CMA is defined as days› supply obtained divided by the days of observation, whereas 1 indicates perfect adherence. The observation in CMA1 spans from first to last dispensation and in CMA2 from first dispensation to end of observation (end of month 12 post-transplant). CMA3 and CMA4 correspond to CMA1 and CMA2, with all values >1 being capped at 1. For TAC the following CMAs were calculated: CMA1 0.86, CMA2 0.79, CMA3 0.87 and CMA 4 0.80 and for MPA: CMA1 1.28, CMA2 1.05, CMA3: 0.97 and CMA4 0.92. We also compared these results to the patient reported BAASIS® questionnaire and patient outcomes.

Conclusions
High levels of adherence based on PRR were calculated for TAC and MPA in the first year post-transplant with higher rates for MPA.

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Proteinuria In Deceased Kidney Transplant Donors For Prediction Of Chronic Lesions In Pre-Transplant Biopsies – An Ongoing Prospective Multi-Center Study

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Background
Proteinuria is an established biomarker in native kidney disease, there is, however, a lack of data on its significance for assessing organ quality in the setting of deceased kidney donors. Donor urinary protein-to-creatinine ratio (UPCR) has been associated with the extent of chronic lesions in pre-transplant kidney graft biopsies in a prospective single center study. Validating this association in a larger multicenter cohort and assessing its value in addition to known clinical predictors might help to improve evaluation of organ quality and organ utilization.

Methods
We are currently conducting a prospective observational multi-center study including 300 consecutive adult deceased kidney donor and adult kidney graft recipient pairs procured and transplanted in four Austrian university based transplant centers. The primary aim is to validate donor UPCR for assessing graft quality of kidney grafts from deceased donors by examining the association of donor UPCR with the extent of chronic lesions in pre-implant kidney grafts (glomerulosclerosis, arteriosclerosis/arteriolosclerosis, interstitial fibrosis and tubular atrophy = total chronic lesion score). The secondary objective is the evaluation of donor UPCR for the prediction of graft function after one year, and building of a donor urine biobank. The study in currently ongoing; the expected end of study is by the last quarter of 2027.

Results
The trial centers at the Medical University Vienna, Medical University Innsbruck, Ordensklinikum Elisabethinen Linz and Medical University Graz have started including patients and samples in January 2023, March 2024, April 2024 and June 2024, respectively.

Conclusion/Outlook
While proteinuria in donor reports is often noted semi-quantitatively and not linked to graft quality, a preliminary study has shown that a quantitative and qualitative assessment of donor proteinuria can predict chronic graft damage. Confirming these findings through a large multicenter study, alongside known graft quality predictors, could help develop better prediction models for graft quality. These models have the potential to enhance pre-implant risk assessment and organ utilization. The established of a large comprehensive donor urine bio-database will enable further research.

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The Impact Of Immunosuppression On The Occurrence Of Malignancies After Kidney Transplantation

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Background
Kidney transplantation is associated with in an increased incidence of malignancies due to immunosuppressive drugs. Tacrolimus is suggested to promote tumorigenesis by inhibiting T-cell-mediated immunosurveillance. The aim of this study was to differentiate the impact of exposure to tacrolimus from the cumulative immunosuppressive burden.

Methods
Therefore, all consecutive patients, receiving a single kidney transplant between 2016 and 2019 at Medical University of Vienna, Austria with tacrolimus-based immunosuppression were analyzed. The occurrence of post-transplant malignancies and tacrolimus trough level were noted until the end of 2023. Overall immunosuppression was assessed by Torque Teno virus (TTV) plasma load. Joint modelling of linear mixed models and Cox proportional hazards models was used for statistical analysis.

Results
A total of 441 patients with 60 de-novo malignancies were analyzed. Among baseline variables, only age at

transplant was associated with an increased risk for a malignancy (HR 1.98, 95% CI 1.58-2.48 per decade). In unadjusted analysis, the hazard ratios for tacrolimus exposure and malignancy risk were 2.99 (95% CI 1.47-7.69) and 2.55 (95% CI 0.85-8.52) for area under the trajectory and slope, respectively. The area under the trajectory for TTV plasma load was not associated with malignancy risk (HR 1.13, 95% CI 0.91-1.42). In a multivariable model tacrolimus exposure was associated with the risk for malignancies (HR for area under trajectory 2.04, 95%CI 1.04-4.23 and for slope 2.6, 95% CI 1.5-4.9) while TTV was not (HR for area under trajectory 1.04, 95%CI 0.86-1.28).

Conclusions

Tacrolimus toxicity might have a stronger effect on the incidence of malignancies after kidney transplantation than the net degree of immunosuppression defined by TTV load. Minimization of tacrolimus exposure might decrease the burden of malignancies after kidney transplantation.

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Modifiable Risk Factors For The Development Of BKPyV-associated Complications: A Systematic Meta-Analysis

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Background

BK virus associated nephropathy (BKPyVAN) remains a significant cause of renal graft injury. Several risk factors have been proposed, mostly based on monocentric- or retrospective studies. We performed a systematic meta-analysis with broad inclusion criteria to provide better understanding of the existing evidence and to build solid assumptions about the importance of each proposed risk factor.

Methods

Pubmed, Medline and Embase were used for literature search. If present, odds ratios (OR) were collected from published data or otherwise calculated from provided baseline parameters. Forest plots were created to illustrate summative ORs for the endpoints: BKPyV-DNAemia (<10,000 or >10,000 copies/mL), biopsy-proven BKPyVAN, and infection leading to treatment.

Results

Literature searches identified 4,705 publications of which 113 were finally included. Significant risk factors for BKPyVAN were tacrolimus (versus cyclosporine OR 1.93, 95% CI: 1.41-2.65), tacrolimus levels (OR 1.65, CI: 1.01-2.68), corticosteroid use (OR 1.76, CI: 1.12-2.75), HLA-MM $\geq$4 (OR 1.27, CI: 1.07-1.52), PRAs >50% (OR 2.58, CI: 1.4-4.8) and AB0 incompatible transplantation (OR 1.98, CI: 1.34-2.91). We did not find an increased risk for anti-thymocyte globulin- versus anti-interleukin 2 induction (OR: 0.99, CI 0.66-1.49), ureteral stent implantation (OR 2.39, CI: 0.99-5.77), mycophenolate (OR 1.76, CI: 0.88-3.52) or mTOR inhibitors (OR 0.82, CI: 0.57-1.19).

Conclusion

With this large meta-analysis we were able to quantitatively confirm that tacrolimus, corticosteroids, high HLA mismatch and ABOi transplantation significantly increase the risk for BKPyVAN. We could not reproduce a protective effect of mTOR-inhibitors and did not find an increased risk with ATG induction.

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Early Progression Of Chronic Histologic Lesions In Kidney Transplant Biopsies Is Not Associated With HLA Histocompatibility

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Background
Early progression of chronic histologic lesions in kidney allografts represents the main finding in graft attrition. The objective of this retrospective cohort study was to elucidate whether HLA histocompatibility is associated with progression of chronic histologic lesions in the first year post-transplant. Established associations of *de novo* donor-specific antibody (dnDSA) formation with HLA mismatch and microvascular inflammation (MVI) were calculated to allow for comparability with other study cohorts.

Methods
We included 117 adult kidney transplant recipients, transplanted between 2016 and 2020 from predominantly deceased donors, who had surveillance biopsies at 3 and 12 months. Histologic lesion scores were assessed according to the Banff classifica- tion. HLA mismatch scores [i.e. eplet, predicted indirectly recognizable HLA-epitopes algorithm (PIRCHE-II), HLA epitope mismatch algorithm (HLA-EMMA), HLA whole antigen A/B/DR] were calculated for all transplant pairs. Formation of dnDSAs was quantified by single antigen beads.

Results
More than one-third of patients exhibited a progression of chronic lesion scores by at least one Banff grade in tubular atrophy (ct), interstitial fibrosis (ci), arteriolar hyalinosis (ah) and inflammation in the area of interstitial fibrosis and tubular atrophy (i-IFTA) from the 3- to the 12-month biopsy. Multivariable proportional odds logistic regression models revealed no association of HLA mismatch scores with progression of histologic lesions, except for ah and especially HLA-EMMA DRB1 [odds ratio (OR) = 1.10, 95% confidence interval (CI) 1.03–1.18]. Furthermore, the established associations of dnDSA formation with HLA mismatch and MVI (OR = 5.31, 95% CI 1.19–22.57) could be confirmed in our cohort.

Conclusions
These data support the association of HLA mismatch and alloimmune response, while suggesting that other factors contribute to early progression of chronic histologic lesions.

04_Liver TX

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Hyperspectral Imaging For Organ Quality Assessment Of A Machine Perfused Donor Liver

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Introduction
Hyperspectral Imaging (HSI) offers useful information on organ quality and has already been successfully used in kidney and liver transplantation to assess transplanted organs. Few studies have shown that HSI technology is also a viable tool for the evaluation of a machine-perfused donor liver.

Methods
The allocated liver from a 49-year-old female donor (161cm, 70kg) was perfused with the OrganOx® normothermic machine perfusion system in the recommended way. Organ quality assessment was performed based on laboratory values at defined time points and HSI. After discarding the organ, biopsies were taken and correlated with the results of the HSI.

Results
The donor liver's size (29x17x11cm) and weight of 2180 grams posed challenges for adequate placement within the organ container. A baseline biopsy of the liver revealed no evidence of fibrosis, steatosis, or inflammation. An hour after perfusion started, measurements of the perfusate indicated a pH of 7.18, a glucose level of 404 mg/dl, and a lactate level of 1.7 mmol/l. During perfusion lactate levels steadily rose, peaking at 4.9 mmol/l after the total perfusion time of 12 hours. Macroscopic alterations (signs of congestion and reduced blood circulation) on the liver's surface were noted, particularly pronounced in segments 2, 3, and 8. HSI of these areas unveiled significantly reduced oxygenation.

Consequently, based on all these observations, the decision was made to discard the organ. Histological examination of the altered regions revealed congestion, necrotic changes, and dissociation of sinusoidal lining cells from liver cell cords. The histological findings correlated well with the HSI.

Conclusion
This case report describes the integration of HSI in the decision-making of the decline of a 49-year-old machine-perfused donor liver. HSI offered useful information concerning tissue morphology and graft viability and therefore, could be a useful additional tool in assessing donor liver quality before transplantation.

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Immunosuppressive Induction Therapy Using The Antithymocyteglobulin Grafalon® – A Single-Center Non-Interventional Study

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Background
An important part of the post-transplant care is the optimal immunosuppression, i.e. a balance between over- and undersuppression. Immunosuppressive (IS) therapy can be divided into maintenance therapy on the one hand and induction therapy on the other hand. The latter has been discussed controversially since 1984, when Thymoglobulin®, a T-cell depleting antithymocyteglobulin (ATG), was introduced.

Methods
Aim of this non-interventional study was to evaluate safety and efficacy of induction therapy following liver transplantation (LT) using Grafalon®, a novel ATG. From March 2021 to November 2022 a cohort of 80 patients receiving induction therapy with Grafalon® after LT at Medical University of Vienna was prospectively included in the study. During the first postoperative week incidence of thrombocytopenia and leukocytopenia was assessed. In total the follow-up period was one year, during which bacterial infections, incidence and severity of biopsy proven acute rejection (BPAR) and overall survival were evaluated. A cohort of 249 patients receiving Thymoglobulin® as induction therapy after LT from

August 1998 to August 2003 was used for qualitative comparison of BPAR and overall survival.

Results
Grafalon® induction resulted in a peak incidence of thrombocytopenia and leukocytopenia on the fourth postoperative day of 64% and 31% of patients, respectively. During follow-up the rate of BPAR was 12.5%, the one-year survival rate was 90%. Furthermore, incidence of bacteremia was 21% and the rate of local infections (i.e. surgical site infections and pneumonia) was 49% during the first postoperative year. In comparison with the historic cohort, a reduction in the rate of BPAR could be observed.

Conclusion
In conclusion, the results of this study offer reassuring evidence for the safety and efficacy of Grafalon® as an IS induction agent following LT. Continued research is necessary to evaluate potential long-term benefits of induction therapy and to compare different IS regimens.

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Dual Hypothermic Oxygenated Perfusion Of Liver Grafts Before Transplantation Is Associated With Reduction Of Severe Biliary Complications

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Background
Supporting evidence for the use of hypothermic oxygenated machine perfusion (HOPE) before liver transplantation (LTx) indicates a positive impact on biliary complications. In this study, we aim to assess whether perfusion through the portal vein alone (sHOPE) or with additional hepatic artery perfusion (dHOPE) differently affects outcomes after LTx.

Methods
We retrospectively analyzed consecutive patients who underwent LTx at the Medical University of Vienna from 2018 to 2023. Donor organs were either preserved using static cold storage (SCS) or subjected to end-ischemic sHOPE or dHOPE. The in-hospital course and post-discharge visits at the department's outpatient clinic were documented, with a focus on the development of biliary complications. The severity of these complications was categorized based on the required therapeutic interventions, such as endoscopic retrograde cholangiopancreatography (ERCP) or surgical revision.

Results
A total of 247 patients were included in the study (69 SCS, 76 sHOPE, 102 dHOPE). Hospitalization was shorter for patients who underwent HOPE (median days: SCS = 25 vs. HOPE = 20, p = 0.019). Biliary complications were less common in the HOPE group (SCS = 37.7% vs. HOPE = 22.5%, p = 0.015). There was a significantly lower incidence of surgical revisions for biliary complications in the HOPE cohort (24.6% vs. 11.8%, p = 0.012). When comparing outcomes based on HOPE modality, a significant reduction in biliary complications (p = 0.006) and surgical revisions (p = 0.002) was observed only in dHOPE patients compared to SCS. Additionally, dHOPE was significantly associated with a reduced need for surgical revision for biliary complications in both univariate and multivariable logistic regression analyses (odds ratio = 0.336, p = 0.011).

Conclusions
HOPE reduces biliary complications and the need for surgical revisions. The reduction in surgical revisions is especially notable with dHOPE, though both methods are effective for preconditioning donor grafts before LTx.

A New Classification Of Biliary Complications After Liver Transplantation – Consensus Guidelines From The BileducTx Meeting

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Background

Injury to the bile ducts during liver retrieval and the transport process can lead to the development of biliary complications (BC) following orthotopic liver transplantation (OLT). Consistency in how to diagnose and report BC in OLT is currently lacking and therefore clinical studies are often non-comparable, hampering advances in the field. Thus, a consensus on how to define, grade, report and monitor BC after OLT is urgently needed to guide future clinical trial design and improve post-OLT outcomes.

Methods

The reporting guidelines and grading of BC presented here were established after a consensus meeting held on 14th and 15th December 2023 in Innsbruck, Austria, with experts in the field followed by a voting according to a modified Delphi method.

Results

After the in-person meeting, three rounds of online-voting and a subsequent online discussion the panel agreed on recommendations for classifying, grading and reporting post-OLT BC. BC not affecting the anastomotic area should be classified as hilar or intrahepatic post-transplant cholangiopathy. BC affecting the anastomotic area should be classified as anastomotic stricture/leakage. BC should be graded according to a modified Clavien Dindo classification into grade I to V. BC rates should be assessed 12 months post OLT.

Conclusion

The established guidelines provide clarity on the definition, grading, monitoring and reporting of post-OLT BC aiming to facilitate future clinical trial development.

Improving Adherence To Immunosuppression After Liver Or Kidney Transplantation In Individuals With Impairments In Personality Functioning – A Randomized Controlled Single Center Feasibility Study

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Background/Significance
Although adherence to immunosuppressive medication is the key factor for long-term graft survival today, 20-70% of transplant recipients are non-adherent to their immunosuppressive medication.

Methods
A prospective, randomized, controlled single-center feasibility study was designed to evaluate the impact of a step guided multicomponent interprofessional intervention program for patients after kidney or liver transplantation on adherence to their immunosuppressive medication in daily clinical practice.

The intervention consisted of group therapy and daily training as well as individual sessions in a step guided approach. The primary endpoint of the study was adherence to immunosuppression as assessed with the "Basel Assessment of Adherence to Immunosuppressive Medications Scale" (BAASIS). The coefficient of variation (CV%) of Tacrolimus (TAC) through levels and the level of personality functioning was a secondary endpoint. We conducted six monthly follow-up visits.

Results
Forty-one age- and sex-matched patients [19 females, 58.5 (*SD* = 10.56) years old, 22 kidney- and 19 liver transplantation] were randomized to the intervention- (*N* = 21) or control-group (*N* = 20). No differences between intervention- and control groups were found in the primary endpoint adherence and CV% of TAC. However, in further exploratory analyses, we observed that individuals with higher impairments in personality functioning showed higher CV% of TAC in the controls. The intervention might compensate personality-related susceptibility to poor adherence as evident in CV% of TAC.

Discussion
The results of the feasibility study showed that this intervention program was highly accepted in the clinical setting. The Intervention group could compensate higher CV% of TAC after liver or kidney transplantation in individuals with lower levels of personality functioning and non-adherence.

Conclusion/Implications
A step guided multicomponent (combining education, motivational interviewing, and psychodynamic therapy) interprofessional (consisting of psychiatrists, psychotherapists, nursing scientists, nurses) intervention could be integrated into daily clinical routine to increase adherence to medical and behavioral recommendations in liver or kidney transplant recipients. The multilevel intervention program is using clinically feasible methods of screening and tracking adherence and activities that empower patients in order to improve their self-management with focus on non-adherence. In our experience, there is a strong influence of personality functioning on emotional regulation, the doctor-patient relationship and consequently health management.

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Association Of Inflammatory Parameters And Complement Activity On Torque Teno Virus Load In Liver Transplant Patients And Healthy Volunteers

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Background
Torque Teno Virus (TTV) load reflects the immune function of its host and is proposed to guide immunosuppression in solid organ transplantation. Known factors determining TTV load are Immunosuppressive drugs and patient age, sex and BMI. Other factors accounting for individual TTV load variation remain to be explored. This study explores the impact of inflammatory parameters and the activity of the classical pathway of complement on TTV load.

Methods
Serum samples from 45 stable liver transplant patients, 6 months post-transplantation, and 48 healthy volunteers were analyzed for 25 cytokines and adipokines, along with classical pathway complement activity, using Luminex technique and ELISA. Data on tacrolimus (TAC) dosage, trough levels, age, gender, BMI, and TTV titer were collected. Multivariable regression analysis was performed using three models: model 0 included known TTV load determinants (age, sex, BMI, TAC trough level); model 1 included additional potential variables excluded stepwise; model 2 allowed exclusion of variables from model 0 by the selection algorithm. Results were validated by jackknife resampling.

Results
Univariable regression revealed correlations between TTV levels and sex, age, BMI, TAC level, factor D (fD), PAI-1, factor P (fP), CXCL10, C3a, and classical complement activity. Most variables, except PAI-1 and fP, showed a positive correlation with TTV. Multiple regression analysis indicated that model 2, which included age, TAC level, classical complement activity, fP, CXCL10, and C3a, explained the most variance in TTV load (61%). This was higher compared to model 0 and model 1, which explained 43% and 26% of the variance, respectively.

Conclusions
The positive correlation of C3a and fD, in context along with the negative correlation of fP, suggest a link between alternative complement pathway activation and TTV load. These results indicate that both literature-known parameters and factors like complement activity and CXCL10 are significantly associated with TTV levels.

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Probiotic Intervention To Reduce Postoperative Inflammation In Liver Transplantation

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Background
End-stage liver failure as an indication for liver transplantation (LT) and the associated changes in the microbiome can lead to the entry of potentially pathogenic pathogens and their metabolites from the intestine into the bloodstream and thus to pathologically increased inflammation, which can be critical in the context of major surgical procedures such as LT. Associated postoperative infections lead to increased morbidity and mortality, which are also associated with high treatment costs. Prophylactic perioperative pro- and synbiotics are intended to influence the postoperative inflammatory reactions in LT patients.

A meta-analysis of studies on the administration of pro-/synbiotics in LT [1] showed a reduction in postoperative clinical infections with a treatment duration of >10 weeks preoperatively to 14 days postoperatively with a pooled relative risk of 0.24, 95% CI: 0.12– 0.24, and improved postoperative liver function in one of 3 studies.

Methods
We performed a randomized, controlled, clinical pilot study including cirrhotic patients listed for LT. 5 patients were randomized in the intervention group with multispecies probiotic for at least 2 months before LT, 5 patients in the control group without probiotic therapy. Endotoxin concentration and inflammatory markers in peripheral and portal venous blood were measured pre-, peri- and postoperatively, as well as parameters of the intestinal barrier and liver function, clinical outcome, and additional assessment of QoL was performed.

Results
There was no significant difference regarding intestinal translocation based on the measured surrogate parameters cluster of differentiation 14 (CD14) and lipopolysaccharide-binding protein (LBP), as well as the inflammatory and liver function parameters after LT and zonulin as a marker for intestinal barrier function between the two groups. Surgical site infection (SSI) rate was 20% in the intervention and 40% in the control group, duration of antimicrobial therapy after LT was 10 (0-109) days in the intervention group and 20 (0-39) days in the control group. Brief symptom inventory (BSI-18) showed significantly less somatization in the intervention group as compared with the control group.

Conclusions
These results provide important insights for the planning of future clinical trials to investigate the influence of probiotic intervention on the outcome after LT.

Reference
1 Kahn J, Pregartner G, Schemmer P. Effects of both Pro- and Synbiotics in Liver Surgery and Transplantation with Special Focus on the Gut-Liver Axis-A Systematic Review and Meta-Analysis. Nutrients. 2020;12(8):2461.

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A Translational Model For Long-Term Normothermic Machine Perfusion Of Porcine Livers

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Background
Whereas short-term (24 hours) normothermic machine perfusionm (NMP) is used as diagnostic tool of livers prior to transplantation, long-term NMP offers the potential for modification, regeneration and repair of marginal grafts.

Methods
Aiming to establish a clinical approved protocol for long-term NMP, livers from domestic pigs (60-121 kg body weight) were subjected to NMP (OrganOx Metra) and consequences of protocol alterations on liver viability and function were monitored.

Results
NMP was initiated in 29 livers. Whereas priming of the NMP system with donor derived whole blood alone resulted in a stable organ function only to a maximum of 48 hours, daily substitution could prolong NMP to

156 hours (total: 13 livers). Further protocol refinements, including anti-infective therapy and bile excretion stabilization, resulted in optimal liver function and integrity in eight livers after one week. Graft perfusion was evaluated by hyperspectral imaging (HSI), indicating stable oxygen saturation levels (StO2), organ hemoglobin (THI), near infrared perfusion (NIR) and tissue water (TWI). Real-time confocal microscopy (SYTO16/PI, WGA staining) revealed a stable cell viability score (day 0: 0±0 vs. day1: 0.4±0.5; day 5: 0.3±0.5; day 7: 0.3±0.5; all p>0.05 respectively). Graft functionality remained high, as observed by continuous bile production (day 1: 231.9±82.7ml vs. day 7: 320.7±179.2ml), stable bile pH (day 7: 7.8±0.14), decline of serum transaminases (ALT on day 1: 250.5±131.6 vs. 7: 84.4±42.9; p<0.01) and lactate levels (day 0: 40.6±21.1 vs. day 7: 13.0±18.9; p<0.05). Assessment of mitochondrial function by high-resolution respirometry indicated stable ATP production efficiency (P-L control efficiency: day 1: 0.80±0.08 vs. day 7: 0.79±0.09; p>0.05) and no additional damage to the outer mitochondrial membrane (cytochrome c control factor: day 0: 0.28±0.18 vs. day 7: 0.23±0.09; p>0.05).

Conclusions
The establishment of translatable long-term preservation protocols could pave the way for NMP-based organ repair strategies.

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Development Of A Telemedicine Model (*TXMobile App*) To Support The After-Care Of Patients After Liver Transplantation

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Background
The success of a liver transplantation depends to a large extent on good postoperative follow-up care over many years. Aims of the after-care program comprise monitoring of the transplanted organ, screening of side-effects from immunosuppressive therapy and life-style optimization. To support patients in their everyday lives after liver transplantation, we developed the transplant app *TXMobile*.

Methods
Results and experiences from a previously conducted study were used as basis for the development of the new app. With participative methods like focus group meetings, questionnaires, and targeted interviews we conducted three different FHIR care plans for different stages after transplantation. Items of the different care plans represent the look of the *TXMobile* data management system (DMS) for professional users and the look of the patient's app flexibly, while providing the usability to manage the extent of after-care patients in the outpatient department.

Results
The transplant app *TXMobile* comprises an individualized curated list of medication, a reminder for medication intake, calendar function for standard visits and reminders for follow-up examinations in the outpatient department as well as in the routine healthcare system. Furthermore, it offers telemonitoring options for e.g. blood pressure and an ePRO function. All information attains the DMS in a structured way based on internationals standards (e.g. SNOMED) and can be registered in the national electronic health record ELGA.

Conclusions
With the support of the *TX Mobile* app patients after transplantation have a structured after-care program which should help to improve adherence, support self-management, optimize lifestyle and eases the transition from the clinic to standard care. The next goals of our project are a pilot study with 60 patients after liver transplantation, further adaptations of the app and ultimately implementation into routine care.

Acknowledgement
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Liver Transplantation In Metastatic Colorectal Cancer: First Case From The Medical University Graz

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Background
Liver metastases (LM) from colorectal cancer (CRC) are associated with high mortality, especially if metastasectomy is not possible. Liver transplantation (LT) as treatment for high selected patients is still under evaluation. Here we present our first case of LT in a patient with colorectal LM.

Case Report
A 62-year-old male patient with paraplegia after traumatic aortic dissection was randomly diagnosed with CRC and synchronous LM as part of an evaluation of wheelchair-associated decubitus ulcers. Workup demonstrated metastatic lesions to both liver lobes and a microsatellite-stable adenocarcinoma of the sigma with positive KRAS mutation.

First, induction chemotherapy with FOLFOX and Bevacizumab was given. After 10 cycles, the lesions showed partial remission and the patient was switched to maintenance therapy with Capecitabine and Bevacizumab. Because of diarrhea, he was switched to FOLFIRI and Aflibercept and referred to our department to evaluate for sigma-resection and metastasectomy.

The most recent staging showed neither progression of the liver lesions nor of the primary tumor and there were no distant metastases to other organs. Due to extensive spread in both liver lobes, metastasectomy was not feasible. According to International Hepato-Pancreato-Biliary Association guidelines, we evaluated the patient for LT. First, the resection of the primary tumor was performed, and three months later he was listed. Successful LT was performed after a waiting time of three months (22 months after primary diagnosis). The postoperative course was largely uneventful, and the patient was discharged on postoperative day 20. The immunosuppressive concept comprised induction with Tacrolimus, Corticosteroids and Mycophenolate-Mofetil. After completed wound healing, Everolimus was initiated. Three months after LT the patient presented in a good condition with excellent graft function and no signs of recurrence.

Conclusion
Liver transplantation could present a promising treatment for well-selected patients with CRC with "liver-only" metastases.

05_Stem Cell TX

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CD34 Positive Selection Of Cryopreserved Stem Cell Concentrates

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Background
Immunomagnetic CD34 positive (CD34+) selection is a graft manipulation technique to lower the risk of graft versus-host-disease (GvHD) in patients receiving stem cell boosts for graft failure after allogeneic hematopoietic cell transplantation (HCT). We report about the successful administration of stem cell boosts with CD34+ selected cells from a portion of previously cryopreserved stem cell products in three children.

Methods
Cryopreserved stem cells were thawed carefully, supplemented with Citrate, DNase and MgCl2, and centrifuged to reduce DMSO and platelets to a minimum. The cells were incubated with immunomagnetic beads against CD34. Subsequently, two washing steps were performed. Before selection, the cells were volume adjusted and filtered through a transfusion filter system to reduce cell aggregates and clots. CD34+ selection was performed using the CliniMacs plus device (Miltenyi Biotec). CD34+/CD45+ cells were analyzed by flow cytometry and sterility was tested by bacterial culture.

Results
Two cryopreserved haploidentical allogeneic peripheral stem cell grafts and one cryopreserved erythrocyte depleted bone marrow graft from an unrelated HLA-identical donor were thawed and CD34+ selected. Indications were secondary graft failure, cytopenia due to meta-iodobenzylguanidine (miBG) therapy and prolonged cytopenia after CAR-T-cell infusion, respectively. Basic values were 88, 129, and 39 x10^6 and after selection 44, 63, and 16 x10^6 viable CD34+ cells, which results in a CD34 recovery rate of 51, 49, and 42%. Sterility testing was negative. The patients were transfused with 1.2, 4.5, and 0.9 x10^6 CD34+ cells /kg body weight. The transfusions were well tolerated. All three patients engrafted and no GvHD occurred.

Conclusions
CD34+ selection of cryopreserved stem cell grafts was safe and efficient in three cases of allogeneic stem cell boost. Despite of extra-addition of anticoagulant aggregates and clots may occur and may hamper the processing. Thus, grafts should be filtered through a transfusion filter system before selection.

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Ruxolitinib In Acute And Chronic Graft-Versus-Host Disease - Extended Follow-Up Of A Named Patient Use Cohort Including Overlap- And Donor Lymphocyte Induced GvHD

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Background
Acute and chronic GvHD are frequent and serious complications after allogeneic haematopoietic stem cell transplantation.

Methods
We retrospectively evaluated 118 patients with acute (n=61), classical chronic (n=43) and overlap cGvHD (n=14) who received Ruxolitinib (RUX) as second line (2L) therapy or beyond 2L. In 22 patients, GvHD occurred after donor lymphocyte infusion (DLI). The cohort included heavily pretreated patients, with 26,2% of aGvHD in 3rd line or beyond and 29,8% of cGvHD in 4th line or beyond.

Results
Best overall response rate (ORR) to RUX was 68,9% in aGvHD, 62,8% in classical cGvHD and 78,6% in overlap cGvHD. The ORR increased to 78,7% in aGvHD, 74,4% in

classical cGvHD and 85,7% in overlap cGvHD upon the addition other agents to RUX in a proportion of patients. Most patients in any GvHD type could discontinue glucocorticoids. During RUX treatment, grade 3/4 infections occurred in 39,8%, and CMV reactivation in 22,0%. In 9 patients (7,6%) relapse occurred during or after RUX treatment. With a median survivors' follow up of 46,2 (range, 13,8 – 85,8) months from initiation of RUX, the 2-year probability of survival was 57,0% in aGvHD, 86,0% in classical cGvHD, and 78,6% in overlap cGvHD. Only 22 patients (18,6%) met all in-/exclusion criteria of the respective pivotal phase III studies. The most frequent incompatibilities were unmet SR-criteria, excessive pretreatment lines, DLI-associated GvHD, overlap GvHD, and medical and/or haematological exclusion criteria.

Conclusions

Our findings confirm the favourable efficacy profile of RUX established by the prospective phase III studies. Real-world use of RUX may differ from the use in the prospective studies in terms of an earlier and more liberal initiation, particularly with regard to SR-criteria. On the other hand, our cohort also demonstrated efficacy in patients with excessive pretreatment, and in patients with DLI-induced and/or overlap GvHD.

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Stepwise Implementation Of A Risk Factor-Based Algorithm For The Use And Dosage Of Anti-T-lymphocyte globulin (ATLG) For The Prevention Of Severe Graft-Versus-Host Disease (GVHD) In A Single Stem Cell Transplant Center – A Retrospective Analysis

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Background

ATLG is used to reduce severe aGvHD and cGvHD. Indication and dosage of ATLG varied over time and between transplant centers. In this retrospective single-center study, we describe the algorithms of ATLG use and dosing, and transplant outcomes from 2001 through 2023.

Methods

750 patients included in this study were allocated to either cohort0 (n=321, 2001-2015; ATLG predominantly restricted to unrelated transplants), cohort1 (n=226, 2014-2019; considering the risk factors, unrelated-donor, sex-mismatch, MMF-vs-MTX, KIR-L-status and disease-stage), or cohort2 (n=203, 2019-2023; additionally considering recipient's lymphocyte-count).

Results

Overall, 3-year-outcomes in the cohorts1&2, using risk. adapted ATLG-dosing were superior to cohort0 regarding OS (C0, 41%, C1, 66%, C2, 67%; p<0.001), PFS (C0, 37%; C1 64%; C2, 64%; p<0.001), NRM (C0, 32%; C1, 12%; C2, 17%; p<0.01), relapse (C0, 31%; C1; 24%; C2, 19%; p=0.01), aGvHD (C0, 30%; C1, 22%; C2, 33%; p=0.01), and cGvHD (3-year-cGvHD-probability C0, 26%; C1, 21%; C2, 20%; p=0.32). With matched-unrelated donors 3-year-OS increased from 45% in C0 to 65% in C1 and 78% in C2 (p<0.001). With matched-sibling donors, 3-year OS improved from 44% in C0 to 70% in C1 (p<0.001), but not further improved in C2 (59%). By multivariable analysis, the ATGL algorithms in C1 and in C2, as compared to C0, were confirmed as independent variables associated with improved OS, in matched-sibling and matched-unrelated transplants, respectively. Although the median ATGL dose has increased from 35mg/kg in C1 to 40mg/kg in C2 in unrelated transplants but decreased from 32.5mg/kg in C1 to 25mg/kg in C2 in matched-sibling transplantats, differential outcomes in C1 versus C2 were not significantly influenced by the respective ATLG algorithm.

Conclusions

Stepwise introduction of risk-adapted and subsequently also lymphocyte-based dosing of ATLG has contributed to significant improvements in HSCT outcomes in HLA-matched related and unrelated transplantation in this retrospective single-center study.

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Donor C1 Group KIR-Ligand Inferiority Is Linked To Increased Mortality In Haploidentical Hematopoietic Stem Cell Transplantation With Post-Transplant Cyclophosphamide

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Background

In HLA-identical hematopoietic stem cell transplantation (HSCT), HLA-C1 group killer cell immunoglobulin-like receptor (KIR) ligands have been linked to graft-versus-host disease, while C2 homozygosity was associated with increased relapses. The individual impact of the recipient's versus the donor's KIR ligands remains unclear.

Methods

We retrospectively investigated the effect of recipient versus donor C1 ligand content on survival and complications in post-transplant cyclophosphamide (PTCy)-based haploidentical HSCT (n = 170). HSCT were categorized as donor C1 supremacy (n = 34), C1 balance (n = 98), or donor C1 inferiority (n = 38).

Results
Following HSCT from C1-inferior donors, overall mortality (HR 2.10; P=0.02) and nonrelapse mortality (sHR, 2.97; P=0.02) were significantly increased. Following HSCT from C1-superior donors, a low 1-year relapse incidence and favorable 1-year progression-free survival were observed. C1 supremacy did not significantly impact acute or chronic graftversus-host disease, natural killer cell reconstitution, or day 21 chimerism. Infection was a more common cause of death among recipients with a C1-inferior donor compared to C1- superior or C1-balanced donors.

Conclusions
These findings suggest an increased risk for non-relapse mortality and particularly infectionrelated deaths, associated with C1-inferior donors. Upon independent confirmation, C1- inferior donors should be avoided in PTCy-based haploidentical HSCT.

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Long-term Outcome After Reduced Intensity Conditioning (RIC)- Based Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) In Pediatric Sickle Cell Disease (SCD)

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Background
HSCT is a curative intervention for SCD with OS of ≥90% after matched sibling donor (MSD) - and OS of ≥73% after matched unrelated donor (MUD) transplantation. Implementation of RIC has reduced organ toxicity but mixed chimerism (MC), graft failure (GF), and GVHD remain major obstacles. We evaluated uni-centric outcome after RIC-HSCT, and the influence of early granulo-monocyte donor chimerism (DC) in peripheral blood.

Methods
All SCD-patients (pts, n=13) after first RIC-HSCT between 2008 and 2019 were included.

Results
Median age was 7,5 (range 2-14) years with a median follow-up of 7,1 years. All pts received RIC (FLU, THIO, MEL) and bone marrow HSCT. 3/13 pts were transplanted from MUD and 10/13 from MSD. GvHD prophylaxis was FK-506 and MMF, but 61% (8/13) received ATG and 39% (5/13) PT-CY. No primary GF was observed and OS was 100%. DFS was 87,5% (7/8) in the ATG group and 40% (2/5) in the PT-CY group. One pt developed aGvHD (grade IV) and severe (CTCAE 4) complications. Secondary GF(sGF) was detected in 4/13 pts (30%,median day+205), all in MSD transplants.

In the ATG group DC was found in 90% of pts at day+100, remaining constant; sGF occurred in 1/8 pts, with increasing MC day+60>+100. In the PT-CY group DC was observed in 2/5 pts at day+100, remaining stable. 3/5 of pts experienced sGF, showing increased MC at day+60>+100 (table). Overall, sGF was significantly associated with MC (day+60 p=0,0001, day+100 p=0,009).

Discussion
Our results confirm excellent outcome (OS1 00%) after RIC with superior DFS for ATG vs PT-CY (87,5 vs 40%). Predictive value of early, increasing MC seems promising and needs to be confirmed in a prospective study.

GVHD-Prophylaxis	Donor	Day+60	Day+100	
ATG	MSD/Trait	51/73	>90/90	MC
		>90/90	>90/90	
		87/74	>90/90	MC
		>90/90	>90/90	
		>90/90	81/87	MC≤10%
	MSD	>90/90	>90/90	
		71/83	17/29	MC, **sGF**
	MUD	>90/90	>90/90	
PT-CY	MSD/trait	62/89	34/30	MC, **sGF**
	MSD	40/60	13/17	MC, **sGF**
		87/82	57/71	MC, **sGF**
	MUD	>90/90	>90/90	
		>90/90	>90/90	

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From Tumor Board Decision To Infusion: Timeline Of CD19 CAR-T Cell Therapy At The Medical University Of Vienna

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Background
CD19-directed CAR-T cells have demonstrated remarkable efficacy in relapsed/refractory B-cell lymphoma. In our center, all approved products (axicabtagene ciloleucel, tisagenlecleucel, brexucabtagene autoleucel, lisocabtagene maraleucel) are available. Published data suggest that longer time-to-infusion intervals ("brain-to-vein time") are associated with inferior survival, therefore we aimed to analyze our patients with respect to the treatment timelines.

Methods
We retrospectively analyzed all consecutive patients who underwent apheresis for commercially available CD19-CAR-T cell products since 2019. Patients participating in clinical CAR-T trials were excluded.

Results
Seventy-two patients (67% male) with a median age of 61 years (range, 20-83 years), diagnosed with diffuse large B-cell lymphoma (DLBCL; n=52), follicular lymphoma (FL; n=9), mantle cell lymphoma (n=3), acute lymphoblastic leukemia (n=3) and other lymphomas (n=5) were identified. The median time between tumor board (TB) decision and apheresis was 17 days, the median time from apheresis to infusion 46 days. The majority of DLBCL patients (n=36) received axicabtagene ciloleucel, whereas most patients with FL (n=8) received tisagenlecleucel. Thirty-one patients received bridging therapy with rituximab and polatuzumab ± bendamustine, 32 patients received bridging consisting of PI3K or TK inhibitors, bispecific antibodies, cytostatic drugs, or irradiation. In 9 patients bridging therapy was unknown. 7 of 72 patients died before CAR-T cell infusion mainly due to disease progression between 14 and 131 days after apheresis, in 9 patients CAR-T infusion is still pending. Fourteen of 56 patients (25%) infused with CAR-T cells died between 24 and 1073 days after infusion. Analysis of response is currently evaluated. After a median follow-up of 19 months, 42 patients (75%) are still alive.

Conclusions
The median brain-to-vein time is 63 days and is therefore comparable to recently published European data (Bücklein et al, 2024). However, a detailed analysis is necessary to evaluate reasons for the long intervals between TB to CAR-T cell infusion.

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EU-CAYAS-NET: The European Network Of Youth Cancer Survivors

Schneider, Carina[1], Gsell, Hannah[1], Brunmair, Barbara[1], Rizvi, Katie[2], Kienesberger, Anita[1] and Narbutas, Šarunas[2], on behalf of the EU-CAYAS-NET Consortium: https://beatcancer.eu/about-us/

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Background
In Europe, there are almost 500.000 childhood and adolescent cancer survivors[1]. 50.000 - 70.000 adolescents and young adults (AYA) are newly diagnosed per year[2], with a survival rate of 82%[3,4]. This population has a greater risk of health problems and other survivorship related issues, and need comprehensive long-term follow-up (LTFU) care, psychosocial support, equitable access to

AYA-specific oncology services, taking into account minorities and underrepresented groups (EDI approach).

Involving youth cancer survivors as central stakeholders is essential in defining targeted services and developing means to deliver them, in partnership with experts from healthcare, psychosocial care and policy. Europe's Beating Cancer Plan commits to improving the quality of life (QoL) for survivors - the EU Network of Youth Cancer Survivors (EU-CAYAS-NET) developed under a flagship initiative of the EU supports this mission.

Methods
EU-CAYAS-NET is a patient-advocate led, EU-co-funded project that unites CAYA-cancer organizations and institutions from 18 European countries to map resources for the CAYA-cancer community, create new European guidelines, position papers, toolkits, and to empower cancer survivors to advocate for their rights and needs.

Results
i) Interactive platform beatcancer.eu generates 40.000+ visits/month and hosts 600+ users: CAYA cancer survivors, carers, health care professionals and researchers; ii) 55 CAYA cancer survivors recruited as "Ambassadors" to advocate for survivorship issues; iii) 12 webinars, 10 educational videos, several social media campaigns; iv) joint white paper on three QoL topics LTFU, Transition and Mental Health & Psychosocial Support submitted for publication; v) map on Education & Career Support in Europe plus Train-the-Trainer Toolkit; vi) position paper "Recommendation and Implementation Roadmap for Minimum Standards of Specialist AYA Cancer Care Units"; vii) position paper launched at European Parliament: "Recommendations for Equitable, Diverse, and Inclusive Cancer Care".

Conclusions
EU-CAYAS-NET developed highly relevant outcomes of patient-advocate co-led research like toolkits, train-the-trainer-programmes and EU-level recommendations. The network will be funded by the EU for another three years in 2025 to establish the current results at national level throughout Europe.

References

(1) THE SIOPE STRATEGIC PLAN - A European Cancer Plan for Children and Adolescents (2015).

(2) Cancer World, The big challenge of treating adolescents and young adults with cancer, (https://archive.cancerworld.net/cancerworld-plus/the-big-challenge-of-treating-adolescents-and-young-adults-with-cancer/).

(3) A. Ferrari, R. D. Barr, Pediatr. Blood Cancer. 64, e26528 (2017).

(4) A. Trama et al., Lancet Oncol. 17, 896–906 (2016).

06_Heart TX

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Extracorporeal Membrane Oxygenation As A Bridge-To-Heart Transplantation: An In-Depth Analysis

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Background
ECMO as Bridge to Transplant (BTT) is increasingly used, especially in the US after the change in the UNOS heart allocation policy of 2018, where short-term MCS received the highest priority. After this change, the reported outcomes for this group of patients improved drastically. In Austria ECMO BTT always had the highest priority status. To our knowledge, no comprehensive evaluation of ECMO related adverse events (AE) in these patients exists.

Methods
A retrospective analysis of a prospectively maintained registry of all patients aged >16 years, undergoing OHT between 01/2012 and 01/2022 at our institution was performed. Patients were compared after division into two groups: ECMO BTT vs No ECMO BTT. Two-sided p-values of 0.05 were considered statistically significant.

Results
Of 394 patients 21 were bridged with ECMO. This group had a higher infection-rate post-transplant while on ICU (76.2% vs 45.6%, p=0.006), a longer median ICU length-of-stay [16 (8-30) vs 8 (6-16) days, p=0.017] and a longer length-of-intubation [3 (1-9) vs 1 (1-3) days, p=0.015]. No difference in long-term mortality was found between both groups. Multivariate Cox regression analysis revealed that ECMO BTT was not an independent predictor for one-year mortality [Hazard ratio (HR) 0.5 (95% CI: 0.1-2.45), p=0.39], whereas ECMO after OHT had a HR of 4.18 (CI :2.07-8.46, p<0.01), gender mismatch of 2.97 (CI: 0.71-12.44, p=0.136), total bilirubin of 1.19 (CI: 1.03-1.38, p=0.017) and need for renal replacement therapy after OHT of 3.29 (CI: 1.58-6.84, p=0.001).

Conclusions
Patients that survived the bridging phase and received OHT had a comparable survival to all other OHT patients but faced high AE rates. This observation could be attributed to thorough patient selection and short waiting times highlighting the importance of an individualized bridging strategy for critically ill OHT candidates.

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Torque-Teno Viral Load - A New Tool To Predict Donor-Specific Antibodies In Pediatric Heart Transplantation Recipients

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Background
In pediatric solid organ transplantation, individual clinical immunosuppression varies despite standardized and trough level controlled immunosuppressants. Assessment of Torque-Teno virus (TTV) has recently been proposed as a surrogate parameter for this purpose. We report the first worldwide experience with TT viral load in pediatric heart transplant recipients.

Methods
We retrospectively evaluated TT viral load in pediatric heart transplant recipients over the course of 6.5 years at our pediatric heart transplant center regarding the development of donor-specific antibodies (DSA) and biopsy-proven rejection.

Results
360 TTV measurements from 43 pediatric heart transplant recipients were analyzed. Median viral load was 107 copies/mL +/- 1.8 (IQR 5-8, range 0-10). Patients who developed donor-specific antibodies had significantly lower TTV values. This was also true for those with biopsy-proven humoral or cellular rejection. Multivariate regression uncovered TTV levels as the leading predictor for DSA development. Patients with TTV log10 levels of 5 or less had a threefold increased relative risk for DSA development compared to those with TTV of log10 of 7 or more (Odds Ratio 7.15).

Conclusions
We evaluated TTV as a possible surrogate parameter for individualized guidance of immunosuppression over a period of 6.5 years in our pediatric heart center in an observational study. Data suggest that patients with TTV log10 levels of less than 6 are at a significantly increased risk for DSA development and allograft rejection independent of tacrolimus trough levels.

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Heart Transplantation In Propionic Acidemia – Two Successful Cases

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Background
Propionic acidemia (PA) is an autosomal recessive disorder caused by a deficiency of propionyl-CoA carboxylase, a mitochondrial enzyme essential for metabolizing propionyl-CoA. Typically, PA manifests in the neonatal period due to protein intake via breastfeeding. PA can affect multiple organ systems and, over time, may lead to dilative cardiomyopathy.

Case Summary
We present two male patients with propionic acidemia (PA) who developed advanced heart failure (HF) due to dilated cardiomyopathy, necessitating heart transplantation (HTx). The first patient, a 14-year-old male with a M373K mutation in the PCCA gene, was diagnosed with PA in the neonatal period and first noted to have dilated cardiomyopathy at age 3. Despite initial stabilization, he developed acute HF at age 14 and underwent successful HTx after 15 days on the waiting list. Three years post-transplant, he remains stable with normal graft function. The second patient, a 24-year-old male with a homozygous V205D mutation in the PCCB gene, also diagnosed with PA in the neonatal period, remained asymptomatic until age 22 when he experienced his first acute HF episode. After three acute HF episodes at age 24, he underwent successful HTx following 30 days on the waiting list. Two years post-transplant, he is in very good condition with good graft function. Both patients faced challenging perioperative periods due to their special nutritional needs, necessitating continuous monitoring of ammonia and L-carnitine levels.

Conclusion
Heart transplantation can be a successful treatment for patients with propionic acidemia (PA), as evidenced by stable graft function post-transplant. However, the perioperative management is challenging due to the patients' special nutritional needs, requiring continuous monitoring of ammonia and L-carnitine levels.

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Extended 24-Hour EVLP For Human Donor Lungs: Overcoming Electrolyte Imbalances And Potentially Extending Perfusion Times With Added Hemodiafiltration

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Background
Ex vivo lung perfusion (EVLP) allows for assessing marginal donor lungs for transplantation, potentially extending the donor pool. Challenges such as electrolyte imbalances and the accumulation of perfusion solution in the lung tissue can, however, limit its effectiveness. In an effort to stabilize perfusate composition and extend perfusion times, additional dialysis has been tested in porcine models. This study reports the first case of a 24-hour EVLP run in human donor lungs with added hemodiafiltration (HDF).

Methods
Human lungs from a 46-year-old male donor, declined for transplantation due to pneumonia, were ventilated and perfused for 24 hours using acellular normothermic perfusion following an adapted Toronto protocol. HDF was incorporated into the circuit with an ultrafiltra-

tion rate of 400 mL/h after achieving target flow. Blood gas analyses, and perfusate and bronchoalveolar lavage (BAL) samples were collected at regular intervals.

Results
The lungs maintained stable electrolyte levels over the 24-hour perfusion without the need for substitution or buffering. Initial poor oxygenation (PaO2 70mmHg during retrieval) improved during EVLP, reaching a maximum ΔpO2 of 349 at 6 hours, and 211 at 24 hours respectively. Lactate levels remained stable, averaging 4mmol/L. The lungs' weight increased from a baseline of 980g to a total of 2,003g over 24 hours. Glucose supplementation began in the ninth hour to maintain levels above 70 mg/dL.

Conclusions
The addition of HDF during this extended EVLP demonstrated the potential to stabilize electrolyte levels effectively, however fluid removal from previously damaged lung tissue was not feasible. Continuous glucose consumption indicated ongoing metabolic activity, even after 24 hours. This was the first case of 24 hours EVLP perfusion of human donor lungs, signifying an important first step towards extended perfusion times, which could open up possibilities for therapeutic strategies for lung repair on EVLP.

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Initial Experience With Remote ECMO Implantation As Bridge-To-Lung Transplant Or Bridge-To-Decision

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Background
Extracorporeal membrane oxygenation (ECMO) often remains the only life-saving intervention for patients with end-stage lung disease experiencing severe cardiorespiratory failure, acting as bridge-to-recovery, bridge-to-decision, or bridge-to-transplant. However, ECMO resources are frequently centralized in larger hospitals with dedicated intensive care and thoracic surgery units. Therefore, several countries have established programs to facilitate remote ECMO implantation using mobile devices, allowing stable patient transport to these facilities. This study presents the first experience with remote veno-venous ECMO (vvECMO) implantation for patients with acute respiratory failure in Austria.

Methods
Patients with acute respiratory failure, deemed potential lung transplant candidates, and located at institutions without possibility for ECMO support, were considered eligible. A protocol was developed allowing for structured ECMO implantation and transport between hospitals. We retrospectively report our initial experience from April 2020 to May 2024.

Results
Six patients in respiratory failure due to Covid19-ARDS (n=1), exacerbation of interstitial lung disease (n=4), and COPD (n=1) were included. vvECMO cannulation was performed at the remote intensive care unit, using dual-lumen cannulas in the right jugular vein (n=4) or conventional femoro-jugular cannulation (n=2). Three patients were awake during implantation, whilst three were sedated and ventilated. Patients were transported to our facility via helicopter (n=4) or ambulance car (n=2) over a median distance of 75km (range 7-614). ECMO implantation and transportation were carried out without complications or adverse events. After a median ECMO runtime of 9.5 days (range 4-36), three patients deceased, one recovered, and two underwent double lung transplantation. Both transplant patients are currently still alive.

Conclusions
Herein we demonstrate the feasibility for safe remote vvECMO implantation and subsequent transport to specialized treatment facilities for patients with respiratory failure. Further protocol standardization in collaboration with other institutions could enhance ECMO indication and timing for critically ill patients at hospitals without direct access to ECMO resources.

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The Impact Of Preformed Donor-Specific Antibodies On Outcome After Lung Transplantation: A Retrospective Single-Center Experience

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Objective
Patients with pre-existing antibodies against donor human leukocyte antigens (HLA) present a significant immunological challenge for most lung transplant centers. Management of these patients varies significantly across centers. This study aimed to analyze the long-term outcomes of pre-sensitized patients at our institution.

Methods
This is a retrospective analysis including lung transplant recipients with preformed donor-specific antigens (DSAs) and post-transplant de novo DSAs (dnDSAs), transplanted in our institution between 2016 and 2021. Presence of pre-existing antibodies was first screened with complement-dependent lymphocytotoxicity assay at the time of listing. In case of positivity, single antigen bead assay was used and unacceptable antigens (UAGs) were defined. On the day of transplantation, all patients underwent a single antigen bead assay. Outcomes were overall survival, freedom from chronic lung allograft dysfunction (CLAD), incidence of acute cellular rejection (ACR) and antibody mediated rejection (AMR).

Results
Within the study period, 572 patients have been transplanted at our institution. 205 patients developed dnDSAs during the post-transplant follow-up. 5.9% of these patients (n=11) had UAGs, all of which received an organ from an HLA-matched donor. Incidence of AMR (p=0.818) and ACR (p=0.492) was not increased, and overall survival and freedom from CLAD were similar (p=0.070 and p=0.623, respectively). 28 patients (13.6%), initially screened as negative, displayed preformed DSAs on their day of transplantation and were not matched. Post-transplant crossmatch in all these patients was negative. ACR and AMR showed no significantly higher incidence compared to non-presensitized patients (p=0.341 and p=0.580, respectively). Although no differences in overall survival could be observed (p=0.636), freedom from CLAD was significantly lower in these unmatched, presensitized patients (p=0.018).

Conclusion
Based on our findings, matching of patients with UAGs is possible and leads to excellent results. Undetected and unmatched patients showed shorter freedom from CLAD and should be considered for post-transplant desensitization protocols.

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Beyond The Organ: Lung Microbiome Shapes Transplant Indications And Outcomes

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Background
The lung microbiome plays a crucial role in the development of chronic lung diseases, which may eventually necessitate lung transplantation. Additionally, perioperative outcomes appear to be connected with altered lung microbiomes and their dynamic changes, presenting a potential target for optimizing short-term outcomes post-transplantation.

Methods
A literature review was conducted using MEDLINE, PubMed Central, and Bookshelf.

Results
Chronic lung allograft dysfunction (CLAD) appears to be influenced and partly triggered by changes in the pulmonary microbiome and dysbiosis, such as increased bacterial load or the prevalence of specific species like Pseudomonas aeruginosa. Furthermore, the specific indications for transplantation, which involve diverse changes and impact the pulmonary microbiome, affect long-term outcomes. In addition to the composition and measurable bacterial load, dynamic changes in the allograft's microbiome can also negatively impact long-term outcomes. This review examines the "new" microbiome after transplantation and possible associations with immediate postoperative outcomes. Understanding these principles allows for the discussion of the impact of pulmonary microbiome alterations concerning CLAD and potential therapeutic implications.

Conclusions
This review aims to summarize the current literature regarding pre- and postoperative lung microbiomes and how they influence different lung diseases on their progression to failure of conservative treatment. It provides a comprehensive summary of current literature for centers looking for further options in optimizing lung transplant outcomes and highlights possible areas for further research activities investigating the pulmonary microbiome in connection to transplantation.

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Impact Of Extracorporeal Photopheresis On Soluble Factors In Serum Of Lung Transplant Recipients: Preliminary Findings

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Background
Chronic lung allograft dysfunction (CLAD) negatively affects outcome after lung transplantation. Prophylactic extracorporeal photopheresis (ECP) might reduce the incidence of CLAD. However, the mechanisms of ECP are poorly defined and its potential effect on soluble serum markers remains to be determined.

Methods
In a prospective, randomized, controlled single-center trial, lung transplant patients were assigned to either an intervention group or a control group. Both groups received standard immunosuppression (tacrolimus, mycophenolate mofetil, and steroids) (n= 30 per group). The intervention group underwent additionally 8 cycles of ECP within the first three months post-transplant. Serum samples were collected at baseline (pre-transplant) and 3 months post-transplantation. A broad array of soluble,

immunologically relevant factors was measured in these serum samples using the ProcartaPlex Human Immune Monitoring Panel 65plex immunoassay. Data were normalized to baseline levels to adjust for variability. Given the low levels of most individual mediators, we applied unsupervised clustering using FlowSOM and UMAP to identify distinct immune patterns. Subsequently, a Random Forest model was trained to pinpoint key factors driving these distinctions. All data were analyzed in R Studio.

Results

In our ongoing analysis BLC, MCP1, and Eotaxin emerged as key soluble factors influencing cluster distinctions (BLC: mean decrease in accuracy = 3.36, Gini = 2.59; MCP1: mean decrease in accuracy = 2.69, Gini = 2.47; Eotaxin: mean decrease in accuracy = 3.36, Gini = 1.90). These preliminary results indicate a potential role in immunological processes post-transplantation, possibly modulated by ECP.

Conclusions

Systemic serum levels of immune mediators only reflect major systemic immune alterations. Therefore, to better define ECP's impact on immune modulation in the ongoing project, we will examine in vitro supernatants from stimulated PBMCs and will use bulk RNA sequencing of peripheral blood mononuclear cells (PBMCs).

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