swiss medical weekly

A diamond open access online journal | established in 1871 | published by the SMW supporting association
www.smw.ch

Supplementum 294
ad Swiss Med Wkly 2025;155
November 12, 2025

Abstracts of the 57th annual meeting of the Swiss Society of Nephrology

Interlaken (Switzerland), December 4–5, 2025

57TH ANNUAL MEETING OF THE SWISS SOCIETY OF NEPHROLOGY (SGN-SSN)

INTERLAKEN, DECEMBER 4–5, 2025

TABLE OF CONTENTS

LO-01 – LO-19	Long oral presentations	2 S
SO-01 – SO-29	Short oral presentations	12 S
EP-01 – EP-14	Elevator pitch	28 S
YSN-01 –YSN-04	YSN Award (Pecha Kucha)	38 S
Index of first authors		41 S

LONG ORAL PRESENTATIONS

LO-01

Antibody-Mediated Rejection in ABO-Incompatible Kidney Transplantation: The Role of Biopsy-Based Transcript Diagnostics in Differentiating Immune Accommodation from Alloimmune Injury

Dr. Lukas Weidmann [1], Dr. Kai Castrezana Lopez [1], Mr. Dusan Harmacek [1], Dr. Florian Westphal [1], Dr. Elena Rho 1, Dr. Kerstin Hübel 2, Dr. Seraina von Moos 3, Prof. Thomas Schachtner 4

1. Nephrology, University Hospital Zurich, Switzerland, 2. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 3. Department of Nephrology, Cantonal Hospital Luzern, Luzern, Switzerland, 4. University Hospital Zurich

Background: ABO-incompatible (ABOi) kidney transplantation has been associated with increased antibody-mediated rejection (AMR) risk. Since C4d deposition in this setting reflects immune accommodation, it cannot be evaluated. Consequently, according to Banff 2022 consensus, AMR diagnosis relies solely on microvascular inflammation (MVI) and the presence of donor-specific antibodies (DSAs), while both anti-HLA and anti-A/B antibodies are considered.

Methods: We analyzed 46 protocol biopsies from ABOi kidney transplant recipients at the University Hospital Zurich (2009–2024). Of these, 25 biopsies were assessed by the Molecular Microscope Diagnostics System (MMDx) and compared to control groups of 86 ABO-compatible (ABOc) biopsies: 35 protocol biopsies with MVI<2 and C4d-, 16 indication biopsies with MVI<2 but C4d+, and 35 indication biopsies with MVI = 1 (probable AMR, DSA+) and C4d-.

Results: Among ABOi biopsies, 5/46 (11%) met Banff 2022 criteria for active AMR, 8/46 (17%) for probable AMR, and 4/46 (9%) for chronic AMR. Overall, 37% (17/46) showed any form of AMR due to DSA-positivity (18% anti-HLA, 100% anti-A/B). In contrast, molecular AMR was detected in only 8% of cases assessed by MMDx, with no molecular rejection identified in ABOi biopsies exhibiting MVI<2. Despite being almost exclusively C4d-positive, transcriptomic profiles (molecular rejection and AMR classifier scores) of ABOi biopsies clustered with DSA-negative, C4d-negative ABOc controls ($p = 0.471$, $p = 0.832$). ABOi biopsies exhibited significantly lower molecular AMR classifier scores compared to both C4d-positive ABOc biopsies and ABOc cases with probable AMR ($p = 0.007$). However, in ABOc biopsies, even low-level C4d deposition (C4d1 by immunofluorescence) was associated with increased molecular AMR activity ($p = 0.011$).

Conclusion: Applying Banff 2022 criteria leads to an overdiagnosis of AMR in ABOi kidney allograft biopsies due to anti-A/B antibody presence. Here, biopsy-based transcript diagnostics help differentiate alloimmune injury from C4d deposition due to accommodation. However, in ABOc biopsies, C4d deposition drives molecular AMR activity already at the C4d1 level.

LO-02

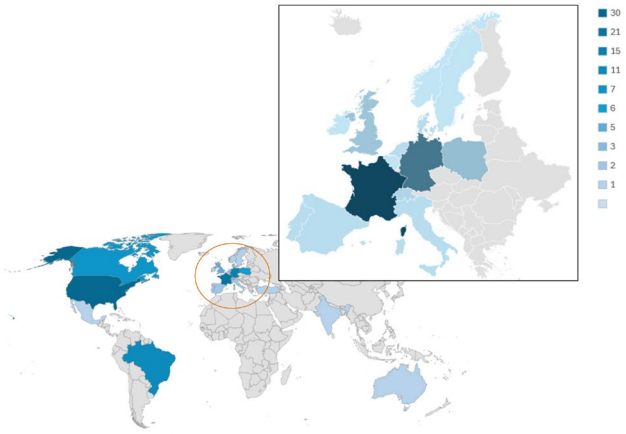
Atypical haemolytic uremic syndrome patients' perspective in the era of complement inhibitors.

Dr. Nora Schwotzer [1], Dr. Eva Jenny [2], Mrs. Stéphanie Sénéchal [3], Ms. Nadia Shine [4], Mr. Nicolas MULLIER [5], Mr. Jeff Schmidt [6], Prof. Véronique Frémeaux Bacchi [7], Prof. Fadi Fakhouri [8]

1. Service of nephrology and hypertension, Department of Medicine, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland;, 2. Service de néphrologie et d'hypertension, Centre hospitalier universitaire vaudois, Lausanne., 3. AIRG Switzerland, President, 4. AIRG Switzerland, Patients representative, 5. AIRG France, Board Member, aHUS advisor, 6. aHUS Alliance, 7. Department of Immunology, Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Paris University, Paris, France., 8. Lausanne University Hospital

Atypical haemolytic uremic syndrome (aHUS) is a complement-mediated disease due to dysregulation of the alternative pathway. C5 blockade has proven a remarkably effective but recently new complement modulators are rapidly developping. In the future, given the variety of therapeutic agents, patients' preferences will be central in the selection of a therapeutic regimen. This project supported by the AIRG grant assessed the patients perspective via an online questionnaire with global outreach to 23 countries including 122 patients. The results included 47% pediatric and 53% adult aHUS patients with detection of a genetic variant in 67%. From a patients' perspective, the most important factors influencing the choice of a treatment for aHUS were efficacy (score 90±23), safety (score 88±23 and accessibility (score 80±28 of 100). The preferred route of drug administration was oral (76%). Patients with childhood-onset aHUS showed less preference for intravenous administration (4% in childhood-onset aHUS vs 12% in adults). Long-acting medication (6-8 weeks) was preferred by most patients (63%) compared to short-acting (daily administration) in 24% and prolonged short-acting (1-3 weeks) in 13% of patients. Mean treatment and travel time was 8±17 hours and 5±13 hours per month, respectively. A large majority of patients (88%) were interested in home perfusion of aHUS medication. Only 30% of patients considered to be well informed on drug development. Antibiotic prophylaxis was prescribed in 69% of patients and 95% felt well informed about the risk of meningitis. Concern for future pregnancy was declared by 67% and 57% refrained from further pregnancy. In conclusion, this is the first large survey that assessed aHUS patients' perspective in the era of complement inhibitors. Overall, the survey confirms that patients with aHUS desire to be involved in therapeutic decision making and voice clear preferences on drug choice.

Figure 1: Outreach across 23 countries on 5 different continents.
Legend: Number of participants per country (blue scale 0-30).



LO-03

Calcium phosphate mineral formation and dynamics in bilateral ischemia-reperfusion injury

Dr. Miguel Correia [1], Dr. Stefan Rudloff [1], Prof. Uyen Huynh-Do [1]

Department of Nephrology and Hypertension, University of Bern and University Hospital Bern, Freiburgstrasse 15, CH-3010 Bern, Switzerland.

Background: Acute kidney injury (AKI) is a common clinical problem associated with high morbidity and mortality, yet effective strategies for early detection and treatment remain limited. Fetuin-A (FA), a circulating glycoprotein, regulates mineral metabolism and prevents soft tissue calcification by binding calcium phosphate minerals (CPM), which are normally cleared by the kidneys. We previously showed that unilateral ischemia-reperfusion injury (uIRI) in mice causes a sharp decline in endogenous FA, while supplementation with exogenous FA mitigates renal damage. Here, we investigate bilateral IRI (bIRI), examining how ischemia duration affects FA levels, kidney injury, and renal function, and present the first *in situ* characterization of CPM formation in the kidney.

Method: C57BL/6N mice (10-12 weeks) underwent bIRI with ischemia times of 10-22.5 minutes. Glomerular filtration rate (GFR) was measured pre- and post-intervention by transdermal FITC-sinistrin clearance, while serum inflammatory markers and FA levels were quantified by ELISA. CPM formation was visualized on PFA-fixed kidney sections via fluorescence microscopy, exploiting the affinity of FA for these particles.

Results: In male mice, GFR declined with increasing clamping duration, reaching significance at 17.5 minutes and beyond. Unlike upon uIRI or sham surgery, endogenous FA showed a less pronounced decline in prolonged bIRI, suggesting impaired renal clearance of systemic CPM. Moreover, CPM formation in the kidney tissue and inflammatory marker levels rose with longer clamping times, indicating more severe tissue damage.

Conclusion: Our findings highlight the contribution of CPM to the pathophysiology of bIRI, an AKI model that more closely reflects clinical settings where both kidneys are affected. Unlike uIRI or sham surgery, where at least one functional kidney remains, prolonged bIRI was associated with impaired FA/CPM clearance, reduced GFR, and greater tissue injury. Importantly, this study provides the first *in situ* visualization of renal CPM formation, establishing a novel mechanistic readout of injury severity.

LO-04

Characteristics and outcome of membranous nephropathy in Switzerland – data from the Swiss Transplant Cohort Study

Dr. Laila-Yasmin Mani [1], Mr. Matthias Berthold [1], Dr. Jaromil Frossard [2], Dr. Susanne Stampf [2], Prof. Thomas Müller [3], Prof. Thomas Schachtner [4], Prof. Michael Dickenmann [5], Prof. Dela Golshayan [6], Dr. Fadi Haidar [7], Dr. Carine Hadaya [7], Prof. Daniel Sidler [8], Dr. Isabelle Binet [9], Prof. Elion Hoxha [10], Prof. Uyen Huynh-Do [8]

1. University Clinic of Nephrology and Hypertension, Inselspital Bern, Bern, 2. Data Center of the Swiss Transplant Cohort Study, Basel University Hospital, Basel, Switzerland, 3. Department of Nephrology, USZ, University Hospital Zurich, Zurich, Switzerland, 4. University Hospital Zurich, 5. University Hospital Basel, 6. Lausanne University Hospital, 7. Department of Nephrology, HUG, University Hospital Geneva, University of Geneva, Geneva, Switzerland, 8. University Hospital Berne, 9. Departement of Nephrology and Transplantation Medicine, Kantonspital St. Gallen, St. Gallen, Switzerland, 10. III. Department of Internal Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background: Membranous nephropathy (MN) is among the commonest causes for nephrotic syndrome worldwide leading to end-stage kidney disease in roughly 40% of patients by 10-15 years. Kidney transplantation represents the therapy of choice with generally favorable outcomes. However, data for Swiss kidney transplant recipients with MN as the cause of ESKD are currently lacking. The purpose of this study was to analyze characteristics and outcome of patients transplanted for ESKD due to MN as compared to patients transplanted for other non-diabetic causes of ESKD and other glomerulonephritides (GN) in the Swiss Transplant Cohort Study (STCS).

Methods: This study nested within the prospective STCS identified patients with MN and GN as cause of ESKD among all adult kidney transplant recipients in the STCS database. Detailed phenotypisation including clinical, serological, histological, treatment and outcome parameters was performed by chart review and based on the STCS dataset as well as serological testing on plasma samples contained in the STCS biobank. We compared survival outcome with the log-rank test, cumulative incidence with the Gray test for cumulative incidence and continuous outcome using the Wilcoxon signed-rank test

Results: Among 943 patients transplanted for GN until 31.12.2020 in the STCS, 29 patients with MN fulfilled inclusion criteria. Patients within the MN group were mainly male and of Caucasian descent. Seropositivity was detected exclusively for phospholipase A2 receptor antibodies and thrombospondin type 1 domain containing protein 7A antibodies in a subset of patients. The majority of patients had received immunosuppressive therapy before transplantation. Overall, patients transplanted for MN had similar survival and graft outcomes compared to patients transplanted for non-MN GN or other non-diabetic kidney disease. Similarly, cumulative incidence of rejection episodes, infectious episodes and skin/non-skin cancer were similar across groups.

Conclusions: This analysis gives insight into characteristics and outcome of patients transplanted for MN in Switzerland.

LO-05

Chasing ghosts? – Osmotic Demyelination Syndrome in a high risk cohort of 110 patients with very profound hyponatremia (Serum-Na <110 mmol/l)

Dr. Florian Buchkremer [1], Prof. Nilufar Mohebbi [2]

NephroCare Dialysepraxis A. Staub AG, Luzern, 2. NephroCare Praxis und Dialysezentrum Zürich-City AG

Background: Osmotic demyelination syndrome (ODS) is a devastating neurologic syndrome linked to rapid correction of hyponatremia. Guidelines recommend limiting correction to no more than +10 mmol/l within 24 h and +18 mmol/l within 48 h. This practice has been challenged by recent reports that showed an association between these slow correction rates and increased mortality. Notably, most patients in these studies had only milder degrees of hyponatremia. Here, we analyzed a cohort of patients with very profound hyponatremia (<110 mmol/l).

Methods: We used data from MIMIC-IV, a large electronic health record dataset containing all admissions between 2008 and 2019 to the Beth Israel Deaconess Medical Center, a teaching hospital of Harvard Medical School in Boston.

Results: Overall, MIMIC-IV contained >4 million serum sodium measurements from ≈290000 patients. 11.4% of all measurements lay below the reference range, 0.8% were <125 mmol/l, and only about 1 in 6000 samples (n = 721) showed a value <110 mmol/l. Roughly one third of these were invalid, mostly caused by imputing errors or contamination with hypotonic infusions. The remaining 470 samples with valid sodium values <110 mmol/l came from 110 patients and 107 hospitalizations. ODS was diagnosed in only 1 patient, even though 68 patients (62%)

showed increases in serum sodium above the recommended range and 70 patients (64%) had additional risk factors for ODS. 30-day mortality (n = 17) was lower in patients with – according to the guideline – too rapid increases in serum sodium concentration (11.8%) compared to those without (21.4%), but the difference was not statistically significant (p = 0.28). During follow-up, head-CT/-MRI scans were done in 19 patients (17%) and rehospitalization occurred in 32 patients (29%). No additional cases of ODS were found.

Conclusion: ODS is rare in very profound hyponatremia, even in the presence of rapid increases in sodium concentration and additional risk factors.

LO-06

Deleterious effect of dietary potassium on kidney fibrosis in the UUO model and the POD ATTAC glomerular disease model

Dr. Thibaut CHARLEMAGNE [1], Dr. Valerie Olivier [2], Ms. Marylise Fernandez [1], Ms. Isabelle Roth [1], Dr. Ali Sassi [1], Ms. Alexandra Chassot [1], Mr. Raphael Yvon [1], Prof. Eric Feraille [1]

Universite de Geneve, Faculté de Médecine, Departement de physiologie cellulaire et métabolisme, 2. Department of Nephrology, HUG, University Hospital Geneva, University of Geneva, Geneva, Switzerland

The effect of a diet rich in potassium, such as the DASH diet, know to improve blood pressure, is unknown in kidney disease. In this setting, the spectre of hyperkalaemia, and the potential harm of aldosterone driven mineralocorticoid receptor (MR) activation could challenge potential beneficial effects. This study investigated the effect of dietary potassium on two murine models of kidney disease.

Mice were fed various levels of potassium, ranging from depleted (0.01% KCl in diet), normal NK (0.81%), moderately high mHK (1.31% KCl), to high HK (2% KCl). We induced renal injury (RI), by unilateral ureteral obstruction (UUO) in wild type C57/BL6 mice, or by induction of podocyte apoptosis in the transgenic POD-ATTAC model. We measured glomerular filtration rate (GFR). We sacrificed mice 7 days after UUO and 20 days after POD ATTAC induction and performed histological and biochemical analysis. We tested the involvement of MR activation with pharmacological MR antagonists (MRA), and MR tissue specific knock out (KO).

We found that dietary potassium was correlated to the level of kidney fibrosis in both UUO and POD ATTAC models, with a significant increase in Sirius red collagen staining (p = 0.043 / p = 0.034) and PDGFRB+ interstitial cells (p = 0.002) with the HK and mHK diets, compared to the NK control, as well as increased fibronectin protein amount (p = 0.006 / p = 0.004). POD ATTAC mice fed the mHK diet also had worse GFR than their NK fed littermates (p = 0.005). MRA significantly decreased fibrosis in HK/mHK fed mice in both models (p = 0.017 / p = 0.026). Tubular or myeloid KO of the MR failed to reproduce this effect.

Increased dietary potassium worsened kidney fibrosis in two unrelated models of murine kidney injury. MRA partially rescued this effect but not tubular or myeloid KO of the MR. These results discourage application of DASH style diets in chronic kidney disease.

LO-07

Determinants of Dialysis Modality Choice in End-Stage Chronic Kidney Disease: Patient and Healthcare Professional Perspectives

Prof. Nancy Helou [1], Mrs. Valentine Mach-Perrot [1], Dr. Audrey Linder [1], Prof. Olivier Bonny [2], Dr. Anne Dufey [3], Dr. Robin Chazot [4], Dr. Anne Cherpillod [5], Dr. David Fumeaux [5], Dr. Grzegorz Nowak [6], Dr. Ould Maouloud Hemett [7], Dr. Sophie Hügli [6], Dr. Olivier Phan [8], Dr. Floriane Seydtaghia [9], Prof. Daniel Teta [10], Prof. Menno Pruijm [11]

1. HESAV / HES-SO, 2. Service of Nephrology, Fribourg State Hospital and University of Fribourg, Fribourg, Switzerland, 3. Nephrology and Hypertension Division, University Hospital Geneva (HUG), Geneva, Switzerland, 4. Dialyse Riviera, 5. Clinique Cecil, 6. Hôpital du Valais – Centre Hospitalier du Valais Romand (CHVR), 7. Hôpital de Fribourg (HFR), Service of Nephrology and University of Fribourg, 8. Broye Intercantonal Hospital, Hemodialysis Center, 9. Etablissements Hospitaliers du Nord Vaudois (eHnv), Dialysis Center, 10. Service de Nephrology, Centre Hospitalier du Valais Romand, CHVR, Sion, Switzerland, 11. Service of nephrology and hypertension, Department of Medicine, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland;

Background: Chronic kidney disease (CKD) affects 8–16% of the global population and can progress to a stage requiring renal replacement therapy. While transplantation is the preferred treatment, when not immediately possible, patients must initiate dialysis. Several modalities exist (peritoneal dialysis, in-center, self-care, or home-based hemodialysis). How patients and professionals navigate this choice has been poorly studied in Switzerland.

Objective: To investigate how dialysis modality choices are made, and which factors influence the decision in the French-speaking part of Switzerland, from both patients' and healthcare professionals' perspectives.

Methods: A qualitative study was conducted in eight dialysis centers. Semi-structured interviews were recorded, transcribed, and thematically analyzed. Participants included 25 patients (mean age 61, SD 14; 72% men), five nurses, and seven nephrologists.

Results: Five themes emerged, largely consistent across patients and professionals:

1. Crisis-driven decision-making: Patients and healthcare professionals viewed modality choice as a process, but patients often experienced the moment of the decision as urgent, triggered by unbearable symptoms. They described four emotional stages (diagnosis shock, distancing from the silent disease, shock of impending dialysis, constrained acceptance).
2. Autonomy vs. safety: Choices were shaped by self-efficacy, family involvement, and trust in professionals.
3. Personal and social life alignment: Compatibility with work, routines, family dynamics, social engagement, and culture strongly influenced preferences.
4. Shared decision-making and ownership: Patients reported "owning" the decision, though families and professionals were key partners.
5. System-level influences: Medical contraindications, policies, economic incentives, and logistical constraints (e.g., storage space, transport) framed the options available.

Conclusions: When modalities are equally accessible, decisions are not driven by cost but by psychological readiness, perceived safety, and lifestyle compatibility. Despite comprehensive patient education, emotional preparedness was less emphasized. As patients frequently perceived they made their choice under crisis, early psychological support and system-level adaptations are needed to strengthen person-centered care.

LO-08

Factors affecting allosensitization before kidney retransplantation

Dr. Elena Rho [1], Ms. Madeleine Thommen [1], Dr. Lukas Weidmann [1], Mr. Dusan Harmacek [1], Dr. Seraina von Moos [2], Dr. Kai Castrezana Lopez [1], Dr. Florian Westphal [1], Dr. Kerstin Hübel [3], Prof. Britta George [1], Prof. Thomas Schachtner [4]

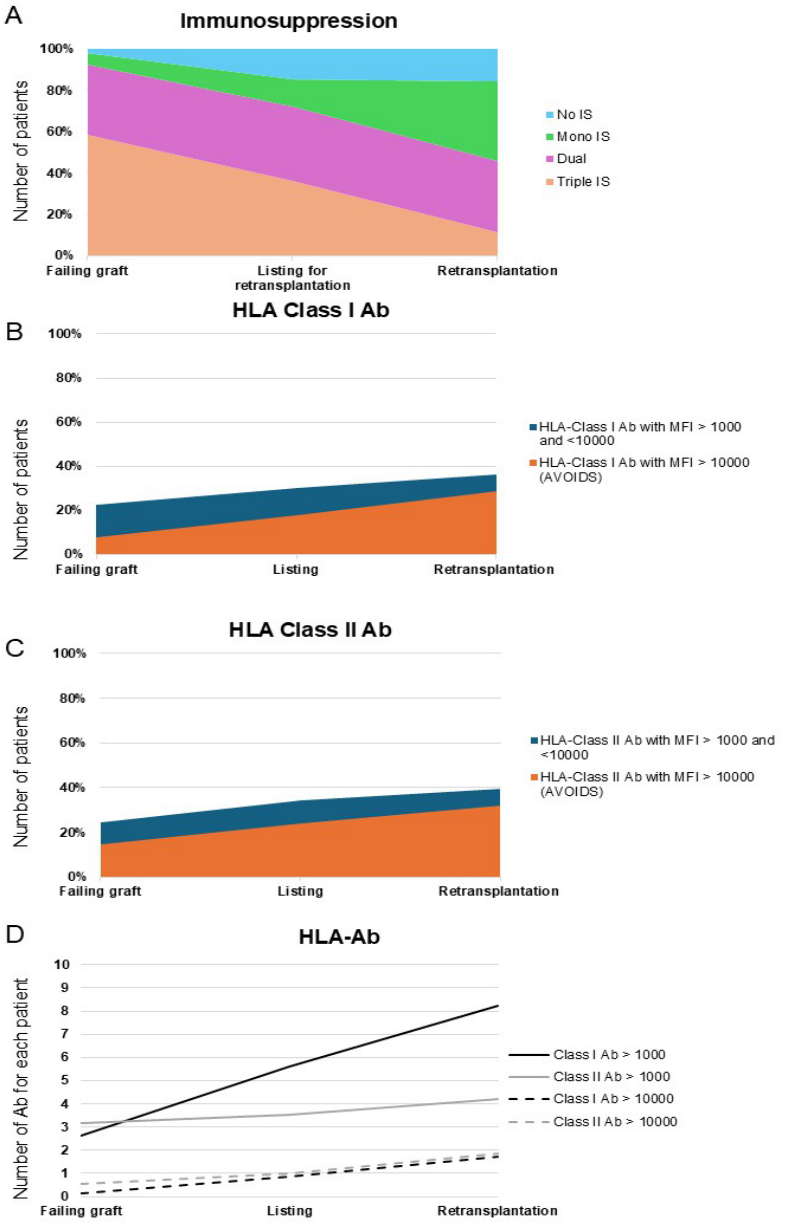
1. Nephrology, University Hospital Zurich, Switzerland, 2. Department of Nephrology, Cantonal Hospital Luzern, Luzern, Switzerland, 3. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 4. University Hospital Zurich

Background and aims: Retransplantation is becoming more common. Allosensitization might prolong time on the waiting list and worsen the outcome of a second transplant. Which is the best maintenance immunosuppression after graft failure is unclear.

Methods: Retrospective single-centre study including kidney transplanted recipients (KTR) who underwent a kidney retransplantation in the University Hospital of Zurich between 2012 and 2023. We analysed which factors and especially which kind of maintenance immunosuppression after transplant failure could affect allosensitization.

Results: In our cohort 129/1040 (12%) were retransplantations. Of these, 27/129 (20%) were living donations. The median waiting time for deceased donation was 2.8 years. The burden of immunosuppression decreased from transplant failure to retransplantation (triple immunosuppression 54 vs 12%, p <0.05), while the allosensitisation increased (number of HLA-Ab >1000/patient 5.8 vs 12.45 p >0.001), Figure 1. In the univariate analysis transplant nephrectomy was associated with a higher calculated panel reactive antibody (cPRA): 90 vs 29 (p <0.0001). Use of an antimetabolite at retransplantation was associated with lower cPRA (23 for azathioprine, 20 for MPA and 88 for no antimetabolite, p <0.001). The same was true for the use of prednisone (24 vs 66, p = 0.02), but it was not true for the use of calcineurin inhibitors (p = 0.2), Figure 2. First retransplantation was also associated to a lower cPRA if compared to a second or a third one (41 vs 78 vs 88, p = 0.02). In the multivariate analysis previous nephrectomy was associated with higher (OR 3.4, CI 1.1-10.4) and use of antimetabolite wit lower cPRA (OR 0.2, CI 0.07-0.43) at retransplantation. Surprisingly,

Figure 1

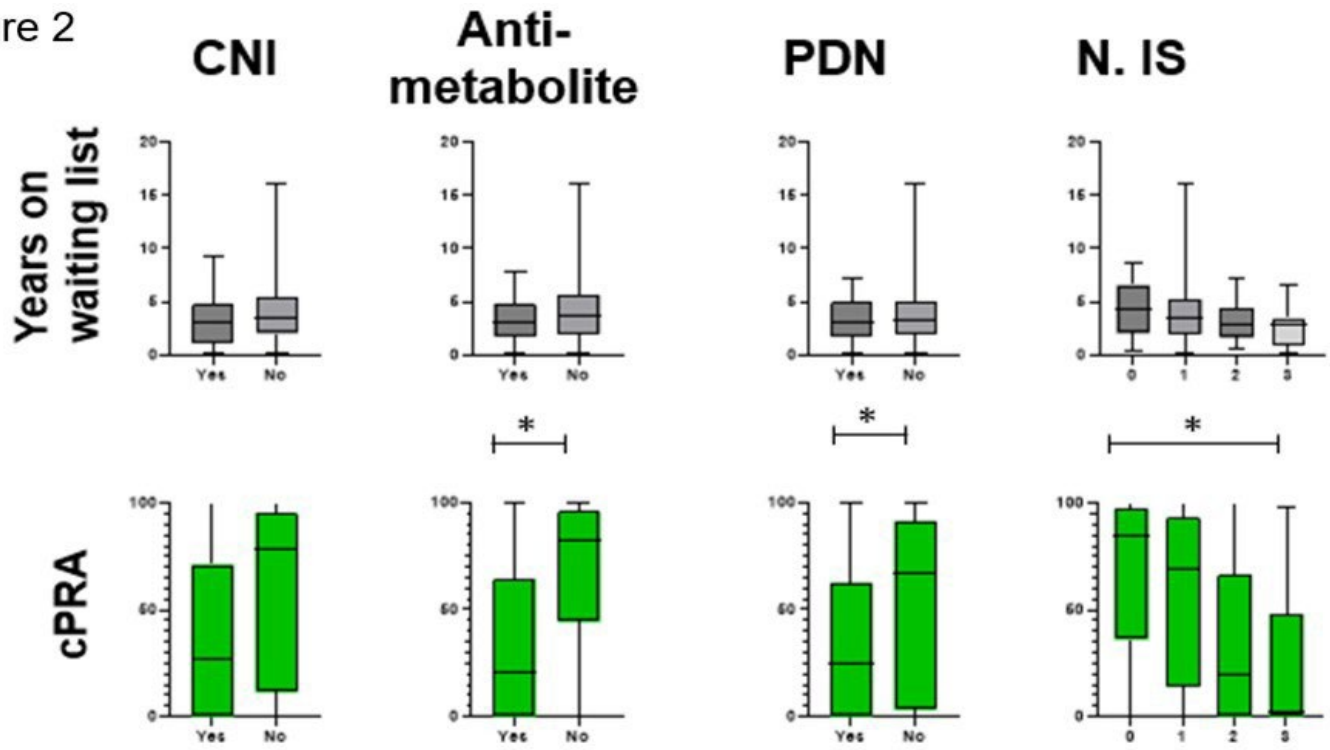


Burden of immunosuppression and allosensitisation from transplant failure to retransplantation

we could not find a correlation between cPRA and waiting time to retransplantation (r <0.2).

Conclusion: Nephrectomy has a deleterious, while antimetabolite at retransplantation has a protective effect on allosensitisation. Waiting time to retransplantation did not correlate with allosensitisation.

Figure 2



LO-09

Health care costs associated with chronic kidney disease in Switzerland: a retrospective claims analysis, 2015-2023

Dr. Michael Stucki [1], Ms. Louisa Cakir [1], Prof. Pietro Cippà [2], Dr. Harald Seeger [3], Prof. Simon Wieser [1]

1. Winterthur Institute of Health Economics, ZHAW Zurich University of Applied Sciences, Winterthur, 2. Nephrology and Transplantation Immunology, University Hospital Basel, Basel, 3. Institute for Nephrology and Dialysis, Cantonal Hospital Baden AG, Baden

Background: Chronic kidney disease (CKD) imposes substantial economic burden on health care systems worldwide, with treatment costs rising as disease progresses to advanced stages requiring renal replacement therapy. Comprehensive data on stage-specific healthcare costs in Switzerland remain limited. Understanding CKD costs by stage may help assess cost-effectiveness of early detection and screening.

Methods: We analyzed anonymized health insurance claims data from a major Swiss insurer between 2015 and 2023 to identify CKD patients and quantify associated healthcare costs. In absence of diagnostic coding, advanced CKD stages were identified using disease-specific indicators including high-dose diuretic prescriptions, dialysis, and kidney transplantation. Using retrospective patient trajectory analysis, we traced healthcare utilization and costs backward from advanced disease stages to estimate earlier stage costs. Total and CKD-specific per-patient monthly costs were estimated and stratified by disease stage.

Results: We identified 3'899 individuals presumably treated for advanced CKD. Preliminary results show CKD treatment costs increased substantially with disease progression. Mean monthly disease-specific costs per patient were CHF 612 (95% confidence interval 505-720) in early stage, CHF 729 (662-797) in advanced stage, and CHF 6'258 (6'128-6'388) in dialysis. Mean annual costs of patients receiving kidney transplantation amounted to CHF 83'663 (77'908-89'418) in the year of surgery. Post-transplantation monthly costs were roughly equivalent to advanced stage costs. CKD-specific costs represented 12% of patient's total costs in the early stage, 9% in the advanced stage, 50% in dialysis patients, and 46% in those undergoing transplantation.

Conclusions: CKD imposes a high economic burden on the Swiss healthcare system, with costs rising substantially in advanced stages. This study demonstrates the rising cost trajectory of advanced CKD, showing substantial economic potential of early detection and programs to delay progression. Systematic screening initiatives may reduce long-term healthcare costs in advanced stages.

LO-10

Immune Pathway Overlap in Recurrent IgA Nephropathy and T cell mediated rejection: A Proteomic Study

Dr. Matthieu Halfon [1], Prof. Manfredo Quadroni [2], Dr. Samuel Rotman [1], Dr. Mélanie Metrich [1], Prof. Thomas Schachtner [3], Dr. Dorothea Rutishauser [3], Dr. Caroline Wehmeier [4], Dr. Fadi Haidar [5], Prof. Uyen Huynh-Do [6], Dr. Laila-Yasmin Mani [6], Dr. Christian Bucher [7], Prof. Fadi Fakhouri [1], Prof. Manuel Pascual [1], Prof. Dela Golshayan [1]

1. Lausanne University Hospital, 2. University of Lausanne, 3. University Hospital Zurich, 4. University Hospital Basel, 5. Geneva University Hospitals, 6. University Hospital Berne, 7. Kantonsspital St. Gallen

Background: IgA nephropathy (IgAN) is the most common form of glomerulonephritis(GN) leading to kidney transplantation in

Switzerland. As with other types of GN, patients transplanted for IgAN (IgAN-KTx) remain at risk of disease recurrence in the graft.Previous studies have shown that recurrence is associated with an increased risk of allograft rejection. In addition, alloimmunization against the graft has been linked to a higher likelihood of IgAN recurrence.This study aims to explore potential shared molecular pathways between recurrence and rejection.

Methods: We performed untargeted proteomic profiling of kidney allograft biopsies using mass spectrometry. The study included three control biopsies from patients transplanted for autosomal dominant polycystic kidney disease (ADPKD) or hypertensive nephropathy without significant graft injury, three biopsies with severe recurrent IgA nephropathy (R-IgAN), three biopsies from patients transplanted for non-GN causes with T cell–mediated rejection (TCMR), and three biopsies from patients transplanted for IgAN who developed TCMR without recurrence. Protein abundance differences between groups were analyzed using volcano plots and heatmaps. Pathway enrichment analysis was performed using Gene Ontology (GO) annotations, based on results from the proteomic data.

Results: Untargeted proteomic analysis quantified a median of 8037 proteins per sample (IQR 7568–8123), including 380 proteins from the Banff Human Organ Transplant (B-HOT) panel .Pathway enrichment analysis of T cell activation revealed that similar pathways were differentially expressed in both R-IgAN and TCMR compared with controls.In the protein abundance analysis restricted to the B-HOT panel, proteins involved in T cell and B cell activation (interleukin-17 receptor B ,CD 81, tyrosine kinase 2), MHC presentation (vacuole membrane protein 1), and proinflammatory response (complement component 9) were significantly more abundant in R-IgAN and TCMR compared with control biopsies.

Conclusion: Our study demonstrates that R-IGAN and TCMR share overlapped immune pathway expression,notably involving lymphocyte activation and major histocompatibility complex (MHC) presentation.

LO-11

Incremental Dialysis in Switzerland: Trends, patient characteristics, regional variation and outcomes

Ms. Rebecca Guidotti [1], Prof. Patrice Ambühl [1], Mr. Linard Hoessly [2]

City Hospital Zurich, Institute of nephrology, 2. Basel University Hospital, Clinic for Transplantation Immunology and Nephrology

Background: Incremental dialysis (ID) involves stepwise initiation based on residual kidney function. Studies suggest it may preserve renal function and offer comparable outcomes to standard dialysis. Data from Switzerland are scarce. Given the increasing importance of patient-centered approaches, including quality of life, symptom management, and autonomy, we aimed to describe the use and outcomes of ID in Swiss clinical practice.

Methods: We analyzed data from the Swiss Dialysis Registry, including all incident hemodialysis patients between 2014–2024 (n = 7’480), with a mean follow-up of 1059±826 days.

Results: Between 2014 and 2024, the proportion of patients initiating dialysis with once- or twice-weekly treatment steadily increased, indicating growing implementation of ID nationally (Figure 1). The French-speaking region (FR) showed the steepest rise, with a seventeen-fold increase (1.5%—26.6%), followed by the Italian-speaking region (IT) with a ninefold increase. The German-speaking region (GER) experienced a more moderate increase, doubling from 2.2% to 4.7% (Figure 2). Patients undergoing incremental dialysis across different regions showed no significant differences in age or BMI. Renal function was significantly higher in patients from the German-speaking region (10.7 ml/min) compared to those from the French-speaking region (7.3 ml/min). Additionally, Charlson Comorbidity Index scores were significantly higher in Ticino (5.0) than in the French-speaking region (4.1). In a cause-specific Cox-regression model accounting for competing risks of recovery, transplantation, or change abroad and adjusted for age, sex, BMI, and comorbidities, incremental dialysis was not associated with a difference in mortality compared with the standard regimen (HR 1.02, 95% CI 0.87–1.20, p = 0.82).

Conclusions: ID has seen increasing implementation in Switzerland over the past decade, with higher use in the French-speaking versus the German-speaking region, likely reflecting practices in neighboring countries. Adjusted survival analyses showed no significant mortality difference versus standard hemodialysis, supporting ID as a feasible and safe option for adequately selected patients.

Table 1: Patient characteristics at dialysis initiation, by dialysis regimen

Characteristics	Total (n=7'480)	Incremental (n=490)	Standard (n=6'990)	P value
Age, yrs	67.7±14.7	71.0±13.7	67.5±14.8	0.000
Gender male, %	66.7	61.2	67.1	0.008
Caucasian, %	92.4	91.2	92.9	0.045
Public center/hospital, %	69.8	61.2	70.4	0.000
BMI, kg/m²	26.5±5.7	25.7±5.4	26.5±5.8	0.001
Residual kidney function, ml/min	6.3±5.2	8.4±5.5	6.1±5.1	0.000
Diabetes mellitus, %	39.6	39.0	39.6	0.784
Cancer, %	18.4	23.1	18.1	0.006
Charlson comorbidity index, n	4.3±2.2	4.3±2.2	4.3±2.2	0.934

Figure 1: Initial hemodialysis treatment frequency, 2014–2024

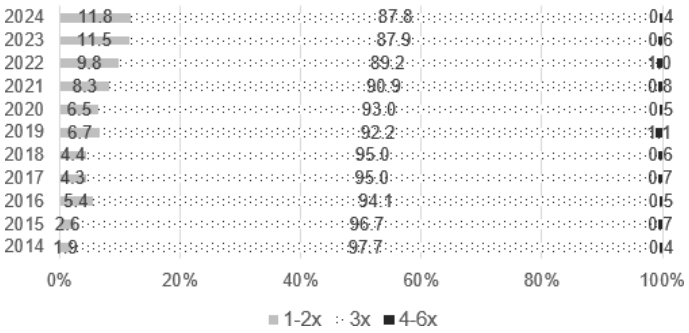
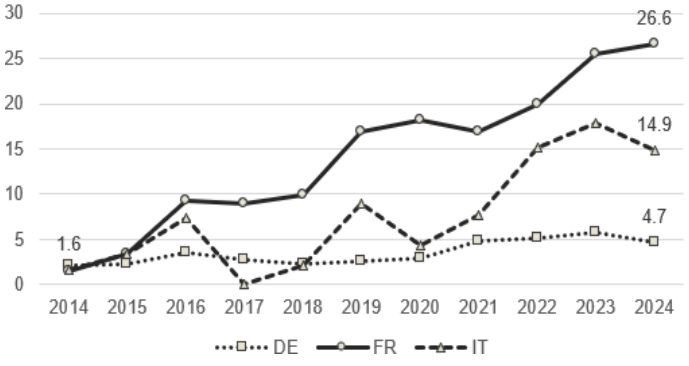


Figure 2: Percentage of incremental dialysis at start of dialysis by language region



LO-12

Long-term health risks in living kidney donors: 30 years of prospective experience from the Swiss Organ Living-Donor Health Registry

Dr. Joana Krättli [1], Ms. Deborah Buess [1], Dr. Matthias Diebold [1], Ms. Marie Flohr [1], Dr. Caroline Wehmeier [2], Prof. Daniel Sidler [3], Prof. Guido Beldi [4], Prof. Dela Golshayan [5], Dr. Tobias Zingg [6], Prof. Sophie de Seigneux [7], Dr. Fadi Haidar [8], Dr. Alexander Ritter [9], Dr. Isabelle Binet [10], Dr. Kerstin Hübel11, Dr. Fabian Rössler [12], Prof. Jürg Steiger [1], Prof. Patricia Hirt-Minkowski [2]

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland, 2. University Hospital Basel, 3. University Hospital Berne, 4. Clinic for Visceral Surgery and Medicine, University Hospital Insel, Abdominal Center Berne, Switzerland, 5. Lausanne University Hospital, 6. Department of Visceral and Transplant Surgery, Lausanne University Hospital (CHUV), Lausanne, Switzerland, 7. Nephrology and Hypertension Division, University Hospital Geneva (HUG), Geneva, Switzerland, 8. Department of Nephrology, HUG, University Hospital Geneva, University of Geneva, Geneva, Switzerland, 9. Division of Nephrology and Transplantation Medicine, HOCH Cantonal Hospital St.Gallen, St. Gallen, Switzerland, 10. Kantonsspital St. Gallen, 11. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 12. Department of Surgery and Transplantation, University Hospital Zurich, Zurich, Switzerland

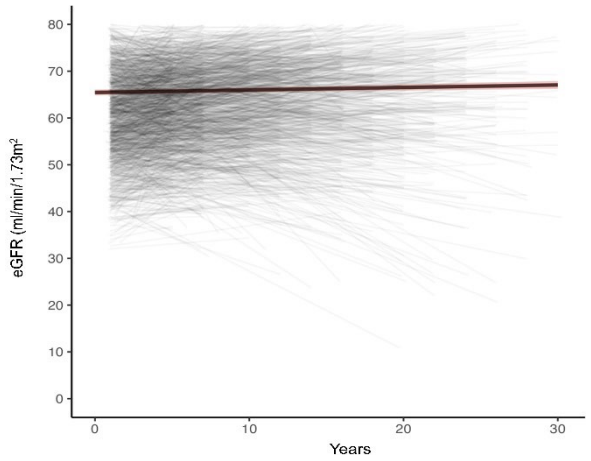
Background: Living kidney donor transplantation provides major benefits for recipients, but long-term safety of donors remains a critical concern.

Methods: We conducted a prospective, multicenter cohort study to characterize long-term kidney function trajectories and to identify risk factors for adverse outcomes. Using 30 years of prospective data from the Swiss Organ Living-Donor Health Registry, we investigated 1863 consecutive individuals after kidney donation between 04/1993 and 08/2018 with a minimum follow-up of five years. Kidney function trajectories were modelled using a linear mixed-effects model.

Results: In total, 1863 living kidney donors (median age 53 years, 66.2% female) were included, with 15.5% individuals presenting at donation with treated arterial hypertension. Predonation kidney function was generally normal (median eGFR 96 ml/min/1.73m²), with only 1% having eGFR <60 ml/min/1.73m². Median follow-up was 12 years (IQR 7-18 years). Over follow-up, kidney function increased slightly, with an average annual eGFR change of 0.14 ml/min/1.73m² (95% CI 0.10-0.18 ml/min/1.73m²; Figure 1). Slopes differed by donor characteristics: women, non-obese donors, and those without predonation hypertension had greater increases, while obese and hypertensive donors showed attenuated slopes. No significant differences were observed by age at donation or predonation eGFR. During the observation period only three donors (0.2%) progressed to kidney failure requiring dialysis. Altogether, 17 donors (0.9%) developed eGFR <30 ml/min/1.73m², 28 (1.5%) had persistent severe proteinuria, and 40 (2.1%) reached the combined endpoint. These donors were older, more frequently male, and had a higher prevalence of hypertension, obesity, and adverse cardiovascular or metabolic outcomes. Multivariable analysis identified male sex, older age, and predonation obesity as independent predictors of reaching the combined endpoint.

Conclusions: Our results underscore the overall safety of living kidney donation while highlighting the need for standardized and, when needed, tailored long-term surveillance to optimize donor care and counselling.

Fig. 1 Predicted eGFR over time



LO-13

Pegcetacoplan maintains proteinuria reduction and stable eGFR in pediatric patients over 52 weeks in the phase 3 VALIANT trial

Prof. Wesley Hayes [1], Dr. Larry Greenbaum [2], Dr. Carla Nester [3], Prof. Gema Ariceta [4], Dr. Bradley Dixon [5], Dr. Yael Borovitz [6], Prof. Christoph Licht [7], Dr. Antonio Mastrangelo [8], Dr. Nabil Melhem [9], Dr. Naoya Fujita [10], Dr. Nicole Van De Kar [11], Dr. Dean Wallace [12], Dr. Eli Khankin [13], Dr. Anwesha Mukherjee [13], Dr. Luis Lopez Lazaro [14], Mr. Johan Szamosi [14], Dr. Marina Vivarelli [15]

1. Department of Pediatric Nephrology, University Children's Hospital Zurich, Zurich, 2. Emory School of Medicine and Children's Healthcare of Atlanta, Atlanta, GA, 3. University of Iowa, Stead Family Children's Hospital, Iowa City, IA, 4. Hospital Vall d'Hebron, Barcelona, 5. University of Colorado School of Medicine, Aurora, CO, 6. Schneider Children's Medical Center of Israel, Petah-Tikva, 7. The Hospital for Sick Children and University of Toronto, Toronto, ON, 8. Unit Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, 9. Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, 10. Aichi Children's Health and Medical Center, Aichi, 11. Radboudumc Amalia Children's Hospital, Nijmegen, 12. Royal Manchester Children's Hospital, Manchester, United Kingdom, 13. Apellis Pharmaceuticals, Inc, Waltham, MA, 14. Swedish Orphan Biovitrum AB, Stockholm, 15. Bambino Gesù Children's Hospital, IRCCS, Rome

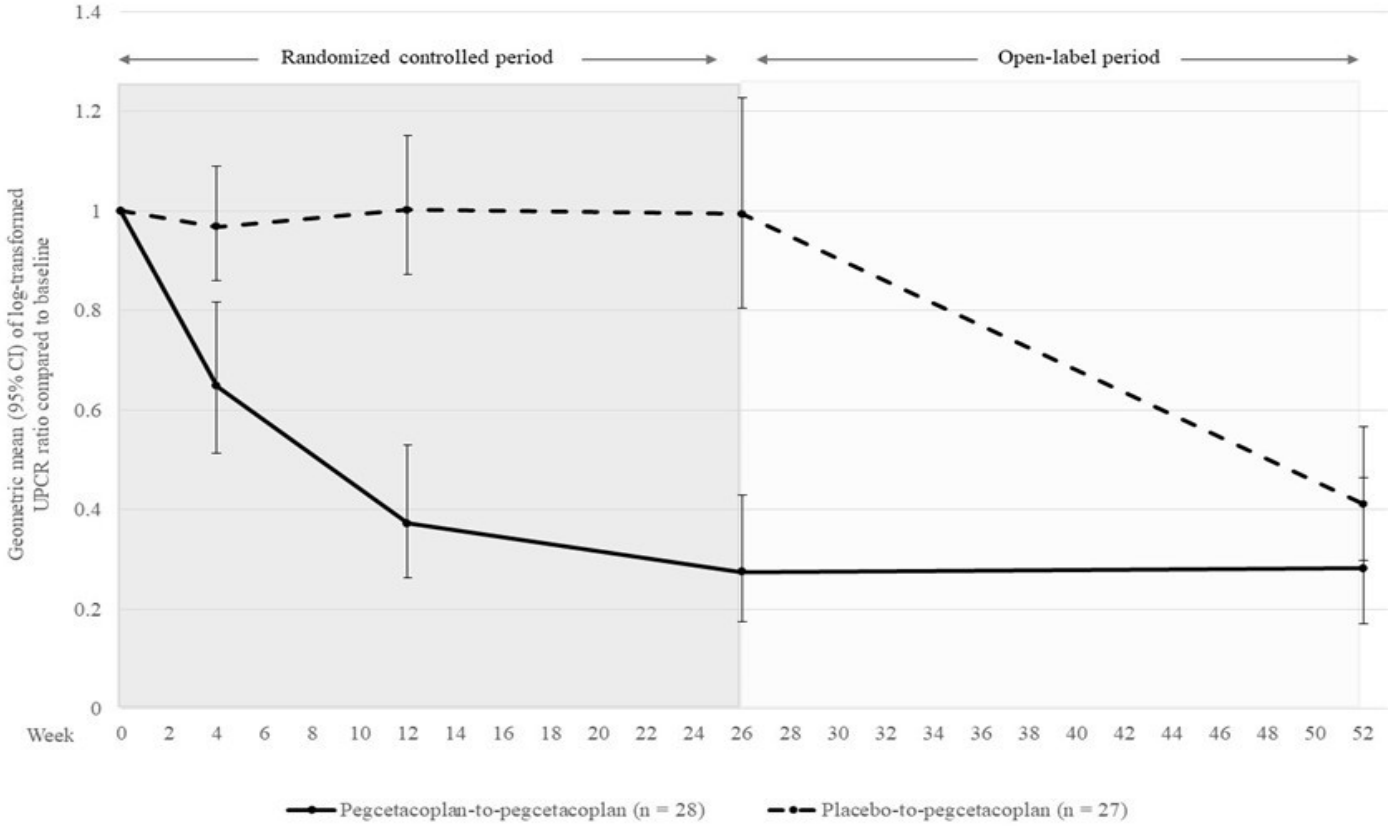
Background: C3 glomerulopathy (C3G) and primary immune-complex mediated membranoproliferative glomerulonephritis (IC-MPGN) are progressive kidney diseases often diagnosed in childhood, with nephrotic-range proteinuria posing a high risk of kidney failure. In the 26-week randomized controlled period (RCP) of VALIANT (phase 3; NCT05067127), pegcetacoplan, a C3/C3b inhibitor, significantly reduced proteinuria and stabilized estimated glomerular filtration rate (eGFR) in adolescents (12–17 years) and the overall population. During the subsequent 26-week open-label period (OLP), all patients received pegcetacoplan.

Methods: Adolescents received subcutaneous pegcetacoplan (n = 28) or placebo (n = 27) twice weekly during the RCP, followed by pegcetacoplan-to-pegcetacoplan (n = 27) or placebo-to-pegcetacoplan (n = 25) treatment in the OLP. Efficacy was assessed by changes in proteinuria (urine protein-to-creatinine ratio [UPCR]) and eGFR. The proportion of patients achieving a ≥50% reduction in UPCR, normalization of serum albumin, and improvement in complement biomarkers was also evaluated.

Results: Adolescents on pegcetacoplan during the RCP achieved −73.6% [−83.1, −58.6] reduction in UPCR and stable eGFR (+0.7 [3.6] mL/min/1.73 m²). Among 11 patients with nephrotic-range proteinuria, 10 (90.9%) achieved a ≥50% UPCR reduction, and 8 (72.7%) reduced UPCR to <3 g/g by week 26. Of 8 patients with hypoalbuminemia, 6 (75%) normalized serum

albumin (vs. 0 on placebo). Pegcetacoplan increased serum C3 and reduced sC5b-9 from Week 4 with no changes observed on placebo. By week 52, proteinuria reduction was sustained (–71.8% [– 82.9, –53.6]) in the adolescent population (Figure), with consistent results in placebo-to-pegcetacoplan patients. eGFR remained stable throughout (+3.2 [4.1] mL/min/1.73 m²). Safety profiles of the RCP and OLP were similar.

Conclusion: The VALIANT OLP confirmed pegcetacoplan's sustained efficacy and safety in adolescents, consistent with the overall cohort. Pegcetacoplan maintained proteinuria reductions, preserved kidney function, and prevented eGFR decline observed in the placebo group, with safety outcomes consistent with prior studies.



LO-14

Practice patterns of routine blood sampling in Swiss hemodialysis centers and their influence on laboratory data and patient outcome

Ms. Sophie Feuchter [1], Ms. Rebecca Guidotti [2], Prof. Andreas Kistler [1]

Department of Medicine, Cantonal Hospital Frauenfeld, Spital Thurgau AG, Frauenfeld, 2. Institute of Nephrology, City Hospital Zurich, Zurich

Background: We have previously reported considerable variability in routine blood sampling practices across Swiss hemodialysis centers, both in timing during the week and testing frequency, with a stunning East–West geographical difference. In this study, we examined the associations between practice patterns, patient laboratory parameters, and clinical outcomes.

Methods: Data for 2023 were obtained from the Swiss Renal Registry and Quality Assessment Program (SRRQAP) on all centers that completed our questionnaire survey about their blood sampling practice. The primary outcome was mortality in relation to early- versus mid-week blood sampling. Secondary outcomes comprised hemoglobin, ferritin, phosphate and parathyroid hormone levels.

Results: A total of 3149 patients treated in 60 dialysis centers were included in the analysis. Overall, annual mortality was 11.4% with no difference between the early- and mid-week routine blood sampling groups (HR = 1.07, 95% CI: 0.85–1.35, p = 0.54) after adjusting for potential confounders. Hemoglobin concentration was slightly higher in patients with mid-week blood sampling (11.2 vs. 11.1 g/dL), a difference that was statistically significant (p = 0.032) but clinically negligible. The proportion of patients within the target hemoglobin range (10.0 – 11.5 g/dL) did not differ between groups. Ferritin levels were significantly higher in the early-week group compared with the mid-week group (526 vs. 473 ng/mL; p = 0.00019), as were phosphate (1.56 vs. 1.40 mmol/L; $p = 6.16 \times 10^{-5}$) and parathyroid hormone concentrations (300.2 vs. 241.8 ng/L; $p = 1.12 \times 10^{-8}$).

Conclusions: The timing of routine blood sampling in hemodialysis patients had no effect on overall mortality, but it may affect certain biochemical parameters. Further study is needed to assess the clinical relevance of these laboratory effects.

LO-15

Predictors of Stone Recurrence in the NOSTONE Trial: Post Hoc Analysis

Dr. Matteo Bargagli [1], Dr. Nasser Dhayat [2], Prof. Olivier Bonny [3], Prof. Beat Roth [4], Prof. Andreas Christe [5], Dr. Alexander Ritter [6], Prof. Nifular Mohebbi [6], Dr. Nicolas Faller [3], Dr. Lisa Pellegrini [7], Dr. Giulia Bedino [7], Dr. Reto M. Venzin [8], Dr. Philipp Grosse [8], Dr. Carina Huesler [9], Dr. Irene Koneth [9], Dr. Christian Bucher [9], Dr. Rosaria Del Giorno [10], Dr. Luca Gabutti [10], Dr. Michael Mayr [11], Dr. Urs Odermatt [12], Dr. Florian Buchkremer [13], Dr. Thomas Ernandez [14], Dr. Catherine Stoermann [14], Prof. Daniel Teta [15], Prof. Bruno Vogt [1], Dr. Luca Tamo' [1], Dr. Grazia Cereghetti [1], Dr. Sven Trelle [16], Dr. Marie Roumet [16], Prof. Daniel G. Fuster [1]

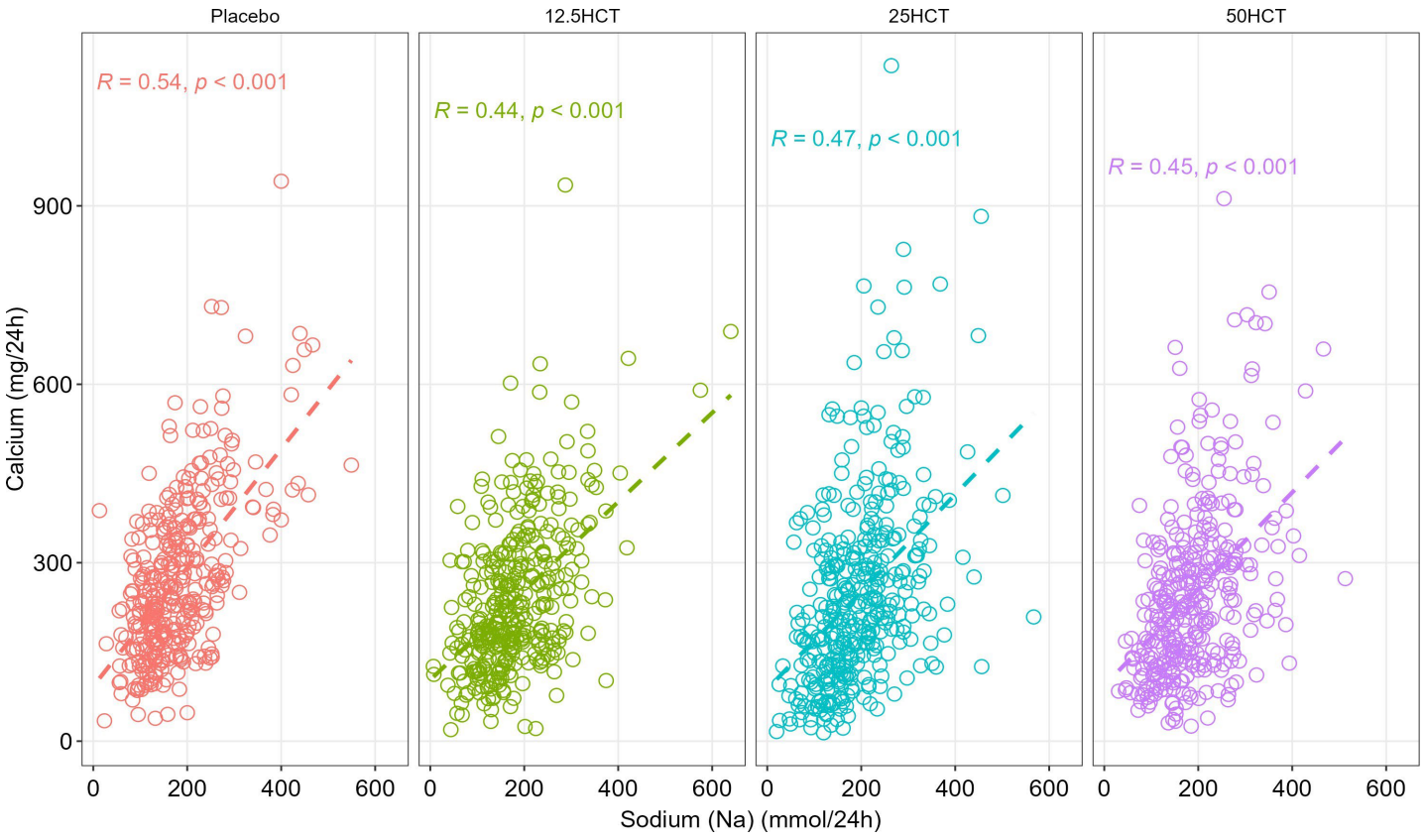
1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Nephrology and Dialysis Care Center, B. Braun Medical Care AG, Hochfelden, Zürich, Switzerland, 3. Service of Nephrology, Fribourg State Hospital and University of Fribourg, Fribourg, Switzerland, 4. Department of Urology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 5. Department of Radiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 6. Department of Nephrology, University Hospital Zürich, Zürich, Switzerland, 7. Department of Nephrology, Regional Hospital Lugano, Lugano, Switzerland, 8. Department of Nephrology, Cantonal Hospital Graubünden, Chur, Switzerland, 9. Department of Nephrology and Transplantation Medicine, Cantonal Hospital St. Gallen, St. Gallen, Switzerland, 10. Department of Internal Medicine, Regional Hospital Bellinzona, Bellinzona, Switzerland, 11. Medical Outpatient Department, University Hospital Basel, University of Basel, Basel, Switzerland, 12. Department of Nephrology, Cantonal Hospital Luzern, Luzern, Switzerland, 13. Division of Nephrology, Dialysis and Transplantation, Cantonal Hospital Aarau, Aarau, Switzerland, 14. Department of Nephrology, HUG, University Hospital Geneva, University of Geneva, Geneva, Switzerland, 15. Service de Nephrology, Centre Hospitalier du Valais Romand, CHVR, Sion, Switzerland, 16. Department of Clinical Research, University of Bern, Bern, Switzerland

Background: In the NOSTONE trial, hydrochlorothiazide (HCTZ) did not reduce stone recurrence and lowered urine calcium less than expected. Here we conduct a post-hoc analysis to examine the effect of HCTZ and additional risk factors affecting urine solute excretion and recurrence.

Methods: We aimed at investigating the effect of baseline urine sodium (an established proxy of intake), calcium and relative supersaturation ratios (RSRs) for CaOx and CaP on stone recurrence (symptomatic, radiologic or combined), and exploring the relationship between change in urine sodium, calcium and RSRs on recurrence. The effect of each predictor was tested separately on each stone outcome considering either baseline or follow-up (time-varying) values. The eventuality of an influence of the treatment group on the relationship between the outcomes was investigated by testing the interaction effect between the predictor and the treatment group.

Results: No significant association was observed between any baseline predictor and symptomatic recurrence. Radiologic recurrence was associated with baseline urinary sodium (OR = 1.36, p = 0.025), RSR CaP (OR = 5.57, p <0.001) but not RSR CaOx. For the composite outcome, only baseline RSR CaP predicted the risk of recurrence (HR = 2.27, p = 0.004). None of these effects differed significantly between treatment groups. In the time-varying analysis, RSR CaP but not urine sodium or urine calcium were significantly associated with symptomatic recurrence (HR = 2.21, 95%CI: 1.29–3.79, p = 0.004). No time-varying predictor was significantly associated with the composite outcome. Urinary sodium had a positive, treatment-dependent effect on the change in urine calcium with a stronger effect observed in the placebo vs HCTZ groups (interaction p = 0.007).

Conclusions: Our analysis reveals baseline RSR CaP as a strong predictor of radiologic stone recurrence. The effect of dietary sodium on urine calcium was attenuated in patients receiving HCTZ compared to patients receiving placebo. Composite and radiologic stone recurrence appear to be independent of dietary sodium intake.



LO-16

Sex-specific changes in tubular repair and immune responses after renal ischemia-reperfusion injury.

Dr. Louis Stavart [1], Dr. Arnaud Lyon [1], Dr. David Cune [2], Ms. Clarisse Simons [3], Dr. Monique Gannagé2, Dr. Florent Allagnat [3], Dr. Alban Longchamp [4], Prof. Dela Golshayan [1]

1. Transplantation Center and Transplantation Immunopathology Laboratory, Lausanne University Hospital (CHUV), Lausanne, 2. Service of Immunology and Allergy, Lausanne University Hospital, Lausanne, 3. Service of Vascular Surgery,Lausanne University Hospital, Lausanne, 4. Center for Engineering in Medicine, Harvard Medical School (HMS), and Transplant Center, Massachusetts General Hospital (MGH), Boston, MA

Context: Renal ischemia-reperfusion injury (IRI) contributes to poor kidney allograft outcomes through persistent inflammation and maladaptive repair. Epidemiological studies and preclinical models suggest that females are relatively protected against the progression to chronic kidney disease and fibrosis after an acute injury, yet the underlying biological mechanisms remain largely unexplored.

Methods: We investigated sex-specific pathways of kidney repair and fibrosis using a unilateral 45-minute renal IRI model without contralateral nephrectomy in male and female C57BL/6 mice. Kidneys were harvested at multiple time points to analyze injury, repair, and fibrotic responses through semi-quantitative PCR, bulk RNA sequencing, histological staining, immunofluorescence, and flow cytometry.

Results: Distinct temporal and spatial patterns of injury emerged between sexes. In female kidneys, there was a lower expression of proinflammatory and profibrotic genes, coupled with an improved metabolic gene signature and attenuated *Sox9* upregulation, a transcriptional regulator recently linked to tubular fate. Consistent with these molecular findings, histological analyses revealed reduced collagen deposition and tissue remodeling, and greater areas of uninjured tubules in females compared to males. Interestingly, expression of each of the three known estrogen receptors had marked sex-, spatial-, and time-dependent differences, suggesting a dynamic role in orchestrating tissue responses. Concomitantly, macrophage infiltration differed between sexes, in severity but also in polarization states, suggesting a link between innate immune responses and sex hormones-mediated signaling.

Discussion: Altogether, our results highlight that female kidneys are less prone to fibrosis and exhibit more regenerative potential after an ischemic injury, which appears to be mediated by estrogen receptor signaling and sex-specific innate immune responses. These findings open new perspectives for personalized targeting of immune interactions to enhance repair and reduce fibrosis after initial IRI in kidney transplantation.

LO-17

The Swiss Kidney Biopsy Registry: Results of the Pilot Phase

Prof. Andreas Kistler [1]

1. Department of Medicine, Cantonal Hospital Frauenfeld, Spital Thurgau AG, Frauenfeld

Background: Data on the incidence and prevalence of biopsy-proven kidney diseases in Switzerland are lacking. To close this gap and facilitate research on rare kidney diseases, we established a nationwide registry, the Swiss Kidney Biopsy Registry (SKBR). Here, we report the results of the pilot phase, performed in five nephrology units and three pathology institutes.

Methods: To minimize workload for physicians, we developed an electronic pathology order form to transfer clinical and laboratory data from nephrologists both to the pathology institutes and to the registry by HIN-secured e-mail (once-only principle of data entry). The pdf includes validation rules and automated translation into SNOMED CT codes for easy automated data import into electronic pathology reporting systems. Diagnostic codes according to the kidney biopsy coding system (kibico) are included in the routine pathology reports, sent in copy to the registry. A machine learning-based algorithm has been developed to extract these diagnostic codes. Likewise, clinical follow up data are transferred to the registry via e-mail copy of routine clinical reports.

Results: The centers were initiated between April 22 and Mai 27. Through September 15, 64 patients were included in the registry. Patient characteristics and indication for biopsy are shown in the Table. Transfer of pathology reports and diagnostic coding were initiated later. Of 31 reports, 26 were matched correctly to the corresponding pathology order form using an AI algorithm. Pathology codes were extracted correctly by the algorithm from all 9 reports containing codes.

Conlusions: We have established a versatile workflow to transfer clinical and pathological data to the SKBR, respecting the once-only principle and minimizing workload for physicians while obviating the need for an on-site data manager. Thus, the SKBR is ready to be rolled out to all Swiss nephrology units and renal pathology institutes.

Patient characteristics and indication for biopsy (n = 64)	
Age, median (IQR; range)	60 (45-74; 18-90)
Gender, % male	67
BMI, median (IQR; range)	24.8 (22.6-28.3; 16.7-58.6)
Diabetes mellitus, % (Type 1 / 2 / other)	17 (0, 16, 2)
Arterial hypertension, %	61
Serum creatinine, median (IQR; range)	168 (111-290; 47-2'500)
Protein-creatinine ratio, mg/mmol, median (IQR; range)	136 (24-315; 0-1'046)
Indication for biopsy (more than one may apply)	
acute decrease of kidney function (AKI)	16 (25%)
subacute or chronic decrease of GFR	24 (38%)
low GFR of unknown dynamic	4 (6.2%)
isolated asymptomatic microhematuria	1 (1.6%)
macrohematuria	2 (3.1%)
asymptomatic proteinuria	9 (14%)
nephritic syndrome	4 (6.2%)
nephrotic syndrome	7 (11%)
other	17 (27%)

LO-18

Association of Chronic Fatigue with Dialysis Recovery Time in Hemodialysis Patients

Dr. Paulo de Sousa [1], Dr. David Jaques [1], Dr. Thomas Ernandez [2], Dr. Vincent Bourquin [2], Dr. Nicola Marangon [3], Dr. Valérie Jotterand [3], Dr. Michael Zellweger [4], Prof. Sophie de Seigneux [1], Prof. Patrick Saudan [1]

1. Division of Nephrology, Geneva University Hospitals, 2. Quavitae rive droite, 3. Quavitae rive gauche, 4. Groupe médical d'Onex

Background: Chronic fatigue is a common complaint among patients undergoing regular hemodialysis and can be measured using the "Multidimensional Fatigue Inventory" (MFI) score. Dialysis recovery time (DRT) is likely a contributing factor to the overall sense of weakness these patients experience. We examined the relationship between chronic fatigue and DRT, as well as associated clinical and demographic factors.

Methods: Patients were recruited from four dialysis centers in Geneva. Chronic fatigue and health status perception were assessed using the MFI score (20 questions across four domains: general fatigue, mental fatigue, motivation, and reduced activities, scored on a scale from 0 to 100) and the EQ-5D questionnaire. DRT was categorized into four intervals (<2 hours, 2-6

hours, 7-12 hours, and > 12 hours, according to Rayner et al. AJKD 2014).

Results: In March 2023, we recruited 93 patients with an average age of 67 years. The median duration of dialysis was 36 months (ranging from 3 to 190 months), and 43% had diabetes. DRT was <2 hours in 34 patients, 2-6 hours in 31 patients, 7-12 hours in 17 patients, and >12 hours in 11 patients. The average MFI score was 61 (±17). A multiple regression analysis showed a highly significant association between MFI scores and DRT ($p < 0.001$). There was also a statistically significant association with the EuroQol score. Age, gender, and the modified Charlson comorbidity score were not linked to higher DRT, nor were hemodiafiltration or the volume of ultrafiltration during sessions.

Conclusions: In our cohort, chronic fatigue is strongly linked to the length of DRT. Key clinical and demographic factors, the use of hemodiafiltration, and the volume of ultrafiltration during dialysis sessions do not appear to influence DRT duration.

LO-19

Transcriptional mapping of thrombotic microangiopathy in human kidney

Dr. Anna Rinaldi [1], Prof. Marie Frimat [2], Dr. Viviane Gnemmi [3], Dr. Sarah Bruneau [4], Dr. Muriel Auberson [5], Dr. Sarah Ducastel [6], Dr. Claire Cartery [7], Dr. Lea Lutz [8], Ms. Cristina Torcasio [8], Dr. Moglie Le Quintrec [9], Dr. Simon Ville [4], Prof. Pietro Cippà [10], Prof. Fadi Fakhouri [11]

1. Institute for Translational Research USI-EOC, 2. Univ. Lille, CHU Lille, Nephrology Department, F-59000, Lille, France, 3. Pathology Department, Université de Lille, Lille, France, 4. Centre Hospitalier Universitaire de Nantes, Nantes Université, Inserm, Centre de Recherche en Transplantation et Immunologie, UMR 1064, ITUN, F-44000 Nantes, France, 5. Department of Biomedical Sciences, University of Lausanne, Lausanne, Switzerland, 6. Univ. Lille, Inserm, Institut Pasteur de Lille, U1167 – RID-AGE, F-59000 Lille, France, 7. Department of Nephrology, CH de Valenciennes, Valenciennes, France, 8. Division of Nephrology, Ente Ospedaliero Cantonale, Lugano, Switzerland, 9. Department of Nephrology, CHU de Montpellier, Montpellier, France, 10. University Hospital Basel, 11. Service de néphrologie et d'hypertension, Centre hospitalier universitaire vaudois, Lausanne.

Thrombotic microangiopathy (TMA) encompasses a group of severe disorders characterized by thrombosis in the microvasculature leading to thrombocytopenia, mechanical haemolytic anaemia and organ damage mainly in the kidney. The main driver of TMA is EC dysfunction that may arise from distinct types of injury. The molecular mechanisms underpinning EC dysfunction remain poorly defined. In this study, we applied single-nucleus RNA sequencing (snRNA-seq) to kidney biopsies from 16 TMA patients with diverse triggers – scleroderma renal crisis (SRC), complement-mediated atypical haemolytic uremic syndrome (aHUS), anti-VEGF therapy and gemcitabine-induced TMA – alongside three healthy controls, to map EC transcriptional responses and cell-cell interactions. We identified compartment-specific EC injury signatures, including angiogenesis and inflammatory pathways activation in glomerular, arteriolar, and capillary ECs. Dysregulation of angiogenic and EC permeability-associated genes such as KITL and PTGER3 was observed across subtypes. Analysis of glomerular crosstalk revealed subtype-specific alterations in VEGF signalling between podocytes and ECs, with compensatory upregulation in aHUS and GEM-TMA, and suppression in anti-VEGF-TMA. Podocyte gene dysregulation further highlighted their role in EC repair, particularly outside anti-VEGF context. SRC-TMA showed unique arteriolar signalling shifts, including activation of endothelin and downregulation of JAG1-NOTCH4 pathways. Kidney tubular and interstitial compartments exhibited injury-associated transcriptional states. These findings demonstrate TMA-induced multisegmental renal damage and underscore the diversity of EC responses. Overall, this study reveals shared and TMA subtype-specific EC injury mechanisms and highlights novel endothelial and glomerular signalling pathways, providing a foundation for future targeted therapeutic approaches in this heterogeneous group of severe disorders.

SHORT ORAL PRESENTATIONS

SO-01

Aggressive drug deprescribing in selected patients after belatacept conversion

Ms. Corinna Pietz [1], Prof. Daniel Sidler [1]

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, Bern, Switzerland

Background: Kidney transplantation (KT) is the preferred treatment for end-stage kidney disease. However, calcineurin inhibitors (CNI) contribute substantially to cardiovascular and metabolic complications. Belatacept-based immunosuppression (IS) enables CNI withdrawal and may allow for broader deprescribing in selected patients, though its feasibility and safety remain underexplored.

Methods: We retrospectively analyzed 467 KT recipients with stable graft function, stratified into three groups: (1) conventional IS (n = 326); (2) belatacept with dual or triple IS and/or co-medication (n = 127); and (3) a single-pill group (n = 14) receiving belatacept plus one additional IS without other co-medications. Clinical and laboratory parameters (BMI, blood pressure, serum creatinine, eGFR, LDL, HbA1c, fasting glucose) were assessed. Propensity score matching (age, sex, follow-up duration) was applied to reduce confounding.

Results: After matching, baseline characteristics were well balanced. The belatacept groups demonstrated significantly higher estimated glomerular filtration rate (eGFR, 59 and 45 mL/min/1.73m² vs. 55 ml/min/1.73m²) compared with the conventional IS group. Both blood pressure and BMI were lower in belatacept-treated patients. No significant differences were observed between the two belatacept groups regarding blood pressure, BMI, glucose, or HbA1c. Overall, medication burden (pill load) was markedly reduced in the belatacept cohorts, particularly in the single-pill group.

Discussion: Belatacept-based immunosuppression provides effective graft protection while enabling CNI-free regimens in KT recipients. In carefully selected patients, stepwise deprescribing – including reduction of non-immunosuppressive medications – is feasible without compromising graft function or metabolic stability. These findings support belatacept as a strategy for simplifying therapy and potentially improving long-term metabolic outcomes after kidney transplantation.

	overall	Belatacept minimal	Belatacept other	standard	minimal vs. other	minimal vs. Standard	other vs. Standard
	N = 81	n = 14	n = 31	n = 36			
Sex (male)	38 (47%)	8 (57%)	13 (42%)	17 (47%)	n.s.	n.s.	n.s.
Age (years)	49 (36, 58)	47 (31, 57)	53 (41, 59)	44 (36, 58)	n.s.	n.s.	n.s.
Donor Type (LDT)	57 (70%)	10 (71%)	23 (74%)	24 (67%)	n.s.	n.s.	n.s.
TPL years	3.9 (1.9, 7.7)	2.3 (1.6, 4.5)	5.2 (3.0, 8.2)	4.2 (1.9, 7.1)	<0.05	n.s.	n.s.
BD sys	131 (117, 140)	127 (113, 133)	131 (114, 139)	133 (124, 140)	n.s.	n.s.	n.s.
BD dia	80 (69, 90)	75 (67, 80)	76 (67, 89)	86 (74, 91)	n.s.	0.041	0.042
BMI (kg/m2)	25.2 (23.1, 25.2)	24.5 (22.5, 25.2)	24.5 (21.8, 25.3)	25.20 (25.20, 25.20)	n.s.	0.052	0.048
EPIGFR	51 (36, 62)	59 (46, 74)	45 (30, 58)	55 (42, 63)	0.018	n.s.	0.12
HBA1C	5.60 (5.30, 5.90)	5.60 (5.25, 5.88)	5.50 (5.20, 5.90)	5.60 (5.38, 6.00)	n.s.	n.s.	n.s.
IS	1.00 (1.00, 2.00)	1.00 (1.00, 1.00)	1.00 (1.00, 2.00)	2.00 (1.00, 3.00)	0.023	<0.001	<0.001
other meds	2.00 (1.00, 3.00)	0.00 (0.00, 0.00)	3.00 (2.00, 4.00)	2.50 (1.75, 3.25)	<0.001	<0.001	0.6

SO-02

Biochemical and molecular biological analysis of (likely) pathogenic NPHS2 missense variants

Ms. Blanda Beci [1], Dr. Carolin Eul [1], Dr. Luisa Bertgen [1], Dr. Sucheta Sridhar [2], Prof. Britta George [1]

1. Nephrology, University Hospital Zurich, Switzerland, 2. Department of Nephrology, University Hospital Zürich, Zürich, Switzerland

Identification of monogenic causes of steroid resistant nephrotic syndrome (SRNS) has revealed the glomerular podocyte as the centre of action in the pathogenesis of SRNS. Patients suffering from SRNS display symptoms such as proteinuria, which often results in kidney failure. Treatment options are limited to lifelong dialysis or kidney transplantation, as there are no other target-specific treatment options so far. One of the most common causes of monogenetic-associated SRNS are variants of the *NPHS2* gene, encoding the slit diaphragm protein podocin which interacts with nephrin and other SD proteins, thereby building a signaling platform for dynamic interactions between the slit diaphragm, the actin cytoskeleton, and focal adhesions.

Missense variants of the protein can lead to an altered topology and/or to its retention in the endoplasmic reticulum. Either way, pathogenic variants result in a loss of function subsequently result in a breakdown of podocytes' actin cytoskeleton and thus loss of their unique architecture, a process known as foot process effacement. The patho-mechanisms of missense variants are incompletely understood. Therefore, a systematic structure-function analysis of 13 podocin missense variants, all likely pathogenic *in vivo* was performed using HEK-293T cells. Cells stably expressing eGFP-tagged wildtype podocin or variants were analyzed by Western blot. Furthermore, podocin wildtype and variants were examined for their subcellular localization using live-cell imaging. This revealed retention in the ER for most of the variants. Moreover, human Podocin was injected into the fly genome and examined for its effect on the integrity of the nephrocyte diaphragm, a structure alike to the mammalian slit diaphragm, to get further insights into Podocin and its variants *in vivo*. This study helps to establish models useful in predicting the disease severity of variants of unknown pathogenicity.

SO-03

Case report: belatacept-induced colitis in a renal transplant recipient

Dr. Aurélie Huber [1], Dr. Ralph Briner [2], Dr. Suzanne Chartier [3], Dr. Fadi Haidar [4], Prof. Sophie de Seigneux [1], Dr. Lena Berchtold [1]

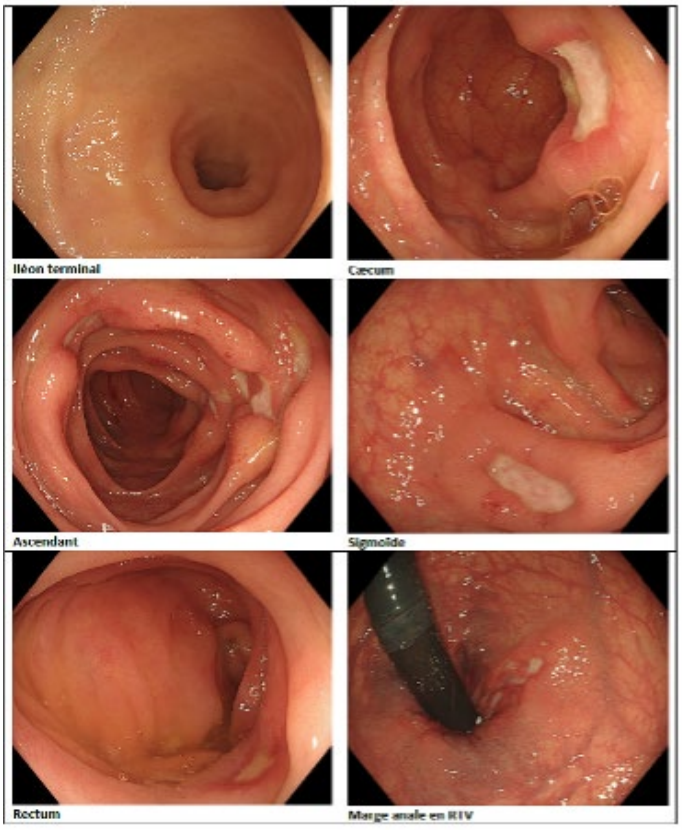
1. Nephrology and Hypertension Division, University Hospital Geneva (HUG), Geneva, Switzerland, 2. Department of Gastroenterology, HUG, University Hospital Geneva, University of Geneva, Geneva, Switzerland, 3. Department of Diagnostics, Division of Pathology, HUG, University Hospital Geneva, University of Geneva, Geneva, Switzerland, 4. Geneva University Hospitals

Background: Belatacept is a selective co-stimulation blocker increasingly used in kidney transplantation due to its favorable impact on long-term graft function and reduced nephrotoxicity compared to calcineurin inhibitors. While generally well tolerated, gastrointestinal adverse effects are rarely reported.

Case Presentation: We report the case of a 65-year-old kidney transplant recipient who developed subacute bloody diarrhea, abdominal pain, tenesmus, and weight loss while on maintenance immunosuppression with belatacept and everolimus. His post-transplant course was notable for opportunistic infections, an episode of acute cellular rejection, and chronic allograft dysfunction. Belatacept had been introduced seven months earlier, following the identification of significant interstitial fibrosis on protocol biopsy. At presentation, the patient exhibited inflammatory syndrome along with gastrointestinal symptoms. Stool cultures and an extensive microbiological workup were negative. Colonoscopy revealed multiple large, non-hemorrhagic ulcerations affecting all colonic segments, arising from otherwise macroscopically normal mucosa. Histological examination showed mild colitis with cryptitis and eosinophilic infiltration, suggestive of drug-induced colitis (Figure 1). Belatacept was discontinued and replaced with ciclosporin, and budesonide was initiated at 9 mg/day. The patient experienced rapid clinical and biological improvement. A follow-up colonoscopy performed six months later showed near-complete mucosal healing, with only a few residual ulcerations. Budesonide was gradually tapered over two months without symptom recurrence.

Conclusion: This is the second documented case of probable belatacept-induced colitis in a kidney transplant recipient. As belatacept becomes more widely used, clinicians should be aware of this rare but potentially reversible adverse effect.

Early colonoscopic evaluation and timely immunosuppressive adjustment can lead to favorable outcomes.



SO-04

CENSUS-EU: An observational study to investigate prevalence and burden of chronic kidney disease-associated pruritus in Europe, Switzerland included.

Dr. Fabienne Aregger [1], Dr. Marina Bantzi [2], Prof. Patrice Ambühl [3], Dr. Erwin Grüter [4], Dr. Stefan Flury [5], Dr. Davide Giunzioni [6], Dr. Despina Ruessmann [7]

1. Inselspital university hospital, department of nephrology and hypertension, Bern, Switzerland, 2. CSL Vifor, department of medical affairs, Villars-sur-Glâne, Switzerland, 3. Stadtspital Waid and Triemli, department of nephrology, Zurich, Switzerland, 4. Kantonsspital Baden, department of dialysis and nephrology, Baden, Switzerland, 5. Kantonsspital Frauenfeld, department of nephrology, Frauenfeld, Switzerland, 6. Hospital of Lugano, department of nephrology, Lugano, Switzerland, 7. CSL Vifor, department of medical affairs, Glattbrugg, Switzerland

Background: Chronic Kidney Disease-associated Pruritus (CKD-aP) is a common condition of patients undergoing haemodialysis (HD) which can impair health-related quality of life (HRQoL), causing sleep and mood disorders which are directly associated with severity of pruritus. Data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) demonstrated that the prevalence of at least moderate pruritus ranged from 26% (in Germany) to 48% (in the United Kingdom). Despite this, there has been a lack of clarity about its epidemiology which impacts the current standard of care. Herein, we present the key findings of CENSUS-EU study assessing the prevalence of CKD-aP and its impact on patients' HRQoL and choice of current treatments in Europe, including Switzerland.

Methods: CENSUS-EU is a prospective, cross-sectional, multicentre European study. Eligible patients (≥18 years under HD for ≥3 months), were asked to complete five questionnaires, one evaluating pruritus and four evaluating HRQoL. Additionally, all subjects completed a survey on the communication and management of their itching as well as current anti-pruritic medication. Finally, the medical records of the participants were analysed regarding dialysis characteristics, treatment, and healthcare patterns.

Results: In total, 2,963 patients (164 from 5 Swiss centres) were analysed. Overall CKD-aP affects 53.5% of patients receiving HD (56.7% in Switzerland), of which 18.0% revealed moderate and 13.2% severe pruritus (18.9% and 7.9% respectively in Switzerland). Increasing pruritus severity is associated with greater impact on HRQoL, sleeping disorders, social isolation and depression. Nevertheless, 40.9% (44.4% in Switzerland) of the HD patients with severe pruritus were not receiving anti-pruritus treatment and almost one third of them do not report their pruritus.

Conclusions: The results of CENSUS-EU suggest that 31% of HD patients (26.8% in Switzerland) experience moderate or severe CKD-aP. The study clearly shows that CKD-aP affects HRQoL and even if patients are identified many remain untreated.

SO-05

Correlation of Banff-based Activity and Chronicity Indices with Injury Dimension, Rejection Classifier, and Rejection Archetype Scores from Biopsy-based Transcript Diagnostics

Dr. Florian Westphal [1], Mr. Dusan Harmacek [1], Dr. Petra Hruba [2], Dr. Kai Castrezana Lopez [1], Dr. Kerstin Hübel [1], Dr. Elena Rho [1], Dr. Eva Girmanova [3], Prof. Britta George [1], Prof. Ondrej Viklicky [3], Dr. Lukas Weidmann [1], Prof. Thomas Schachtner [4]

1. Nephrology, University Hospital Zurich, Switzerland, 2. Institute for Clinical and Experimental Medicine, Transplant Laboratory, 3. Institute for Clinical and Experimental Medicine, Transplant Laboratory, IKEM, Prague, 4. University Hospital Zurich

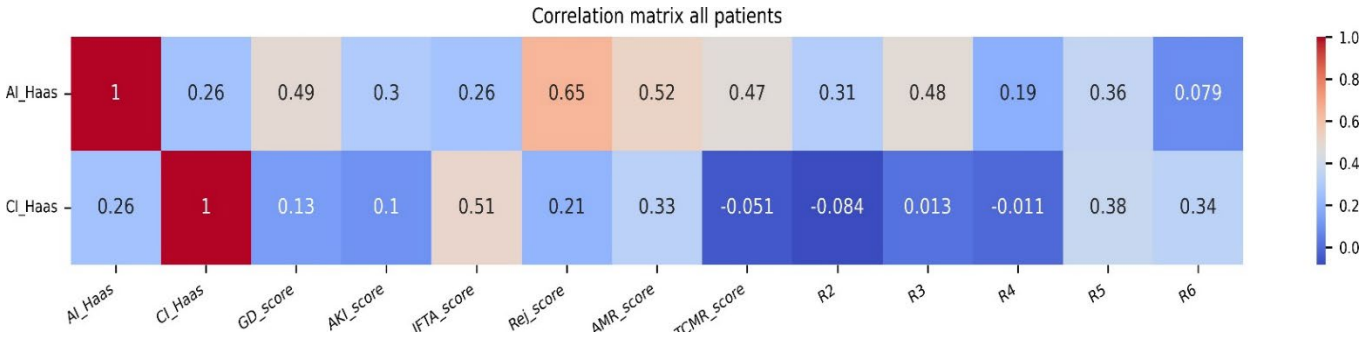
Background: The latest Banff meeting report states that indices for activity and chronicity based on the Banff classification (Haas et al.) provide useful information. Biopsy-based transcript diagnostics offer a novel approach to classify and quantify injury, rejection, and rejection phenotypes.

Methods: Our study utilized kidney allograft biopsies from Prague and Zurich, which were analyzed histologically according to Banff 2022 and by the Molecular Microscope Diagnostics System (MMDx). The activity (AI) and chronicity (CI) indices were calculated as linear combinations of Banff lesion scores according Haas et al. The molecular injury dimension scores, rejection classifier scores, and archetype scores were assessed. Data were analyzed with Python 3.9.

Results: In our cohort, a mean AI of 2.66 and a mean CI 4.8 was found. The molecular injury dimension scores of global disturbance (GD), and acute kidney injury (AKI), and atrophy-fibrosis (IFTA) had mean values of 0, 0.25, and 0.37. The global disturbance and acute kidney injury scores demonstrated a weak correlation with the histological activity indices (0.49 and 0.3). The molecular atrophy-fibrosis score (mean 0.37) showed a moderate correlation with the histological CI (0.51). The MMDx classifiers for rejection, AMR, and TCMR correlated moderately with histological activity indices (0.65, 0.52, and 0.47). Furthermore, the MMDx archetype scores for TCMR (R2), mixed rejection (R3), early-stage AMR (R4), fully developed AMR (R5), and late-stage AMR (R6) displayed weak correlation with the histological activity indices (0.08 to 0.48).

Conclusions: In conclusion, our findings underscore the complexities inherent in assessing kidney allograft pathology. While

molecular and histological analyses offer complementary insights, the observed weak to moderate correlations suggest that these techniques generate partially distinct information. Future research is needed to leverage the strengths of both methodologies to improve prognostication and patient outcome.



SO-06

Could TrkC activation provide a potential avenue for therapeutic intervention in AKI?

Dr. Carolin Eul [1], Dr. Sucheta Sridhar [2], Dr. Sarah Boedecker [3], Dr. Malte Krakow [3], Prof. Britta George1

1. Nephrology, University Hospital Zurich, Switzerland, 2. Department of Nephrology, University Hospital Zürich, Zürich, Switzerland, 3. University Hospital Muenster

Background: Acute tubular injury often progresses to chronic kidney disease (CKD). The neurotrophic tyrosine kinase receptor C (TrkC), known to regulate neuronal differentiation and survival, is also expressed in the murine kidney – predominantly by podocytes and to a lesser extent in specific tubular segments such as the cortical collecting duct and thick ascending limb. Loss of TrkC in nephrons leads to proteinuria and features of focal segmental glomerulosclerosis (FSGS), while the tubules remain histologically unaffected. However, TrkC expression varies in CKD biopsy samples across different etiologies. Therefore, this study aims to investigate the role of TrkC in tubular injury.

Methods: Three-months-old nephron-specific knockout mice (TrkC-KO) and littermate controls were subjected to adenine induced tubular injury. Mice were fed either 0.2% adenine-enriched or control diet for 8 days. Weight loss and blood urea nitrogen (BUN) levels were measured. Kidney tissue was analyzed using histology, electron microscopy, snRNA sequencing and immunofluorescence. Cell culture experiments were conducted assess the effects of adenine treatment on TrkC signaling *in vitro*.

Results: Adenine-enriched diet caused crystal deposition, tubular injury, and inflammation. Male TrkC-KO mice on the adenine diet experienced greater weight loss and higher BUN levels than corresponding TrkC controls. Immunofluorescence showed increased NFκB and Ki67 expression in distal tubules of TrkC-KO mice, along with elevated leukocyte and macrophage infiltration in the kidney cortex. These results were also recapitulated in single nuclei RNA sequencing analysis. *In vitro*, HEK293T cells overexpressing TrkC displayed enhanced TrkC phosphorylation and downstream signaling when activated with its ligand NT-3 and subsequently treated with adenine. Activation of TrkC in HEK293T cells with NT-3 enhanced cell viability when co-treated with adenine compared to cells without TrkC activation.

Conclusion: The results suggest that TrkC signaling may have a protective role in the kidney during acute tubular injury, with potential implications for CKD progression.

SO-07

Diagnostic and therapeutic management in severe hyponatremia: impact of guideline adherence on clinical outcomes

Mr. Michael Reuster [1], Prof. Thomas Fehr [2]

1. Department of Cardiology, University Hospital, Bern, 2. Department of Internal Medicine, Kantonsspital Graubunden, Chur

Background: Hyponatremia is the most common electrolyte disorder in hospitalized patients. Severe forms are associated with increased morbidity and mortality. Despite clear international guideline recommendations, adherence to diagnostic and therapeutic standards is often insufficient. We analyzed the management of patients with severe hyponatremia to evaluate the impact of guideline adherence on clinical outcomes.

Methods: We performed a retrospective single-center study at the Department of Internal Medicine, Cantonal Hospital Graubünden, Switzerland. Between September 2016–December 2019, 199 adult patients with severe hyponatremia (serum sodium <125 mmol/L) were included. Diagnostic work-up was assessed by stratifying patients according to completion of the minimal diagnostic standard. Interpretation and documentation of diagnostic results in the electronic health record were also analyzed. Therapeutic management was evaluated with emphasis on fluid intake, categorized into predefined volume groups. Outcomes included rate of overcorrection, length of hospital stay, rehospitalization, and mortality.

Results: A minimal diagnostic standard was completed in 61% of patients. Guideline-adherent work-up was associated with improved survival: odds of mortality were reduced by 75% in-hospital (p = 0.008), 76% within 6 months (p = 0.001), and 72% within 12 months (p = 0.002). Documentation quality was poor; complete diagnostic details (tonicity and volume status) were recorded in only 15%. Compared with patients with a fully documented diagnosis, those in whom hyponatremia was not mentioned had 5.33-fold higher odds of in-hospital death (p = 0.047), 9.88-fold higher odds within 6 months (p = 0.005), and 6.35-fold higher odds within 12 months (p = 0.01). Half of the patients received >2000mL fluids in 48h. Overcorrection occurred in 18% and was associated with higher volumes (2001–3000mL: OR 6.06, p = 0.029; >3000L: OR 10.32, p = 0.003). No osmotic demyelination was observed.

Conclusions: Patients with severe hyponatremia benefit from guideline-adherent diagnostics and thorough documentation. Both were associated with improved survival, while excessive fluid administration increased overcorrection. Improving adherence and documentation may enhance outcomes in this high-risk population.

SO-08

Diffusion and multiparametric MRI radiomics predict renal function decline in ADPKD

Dr. Matteo Bargagli [1], Dr. Luisa Altabella [2], Dr. Marina Fedon Vocaturo [2], Dr. Riccardo Negrelli [3], Dr. Maria Chiara Ambrosetti [3], Dr. Giovanni Puppini [3], Dr. Carlo Cavedon [2], Prof. Daniel G. Fuster [1], Prof. Pietro Manuel Ferraro [4]

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Medical Physics Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy, 3. Radiology Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy, 4. Section of Nephrology, Department of Medicine, Università degli Studi di Verona, Verona, Italy

Introduction: Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary kidney disorder and a leading cause of end-stage kidney disease. Current risk stratification relies on height-adjusted total kidney volume (htTKV) and the Mayo Classification, which capture cyst burden but not alterations in the non-cystic parenchyma. Radiomics applied to MRI offers the opportunity to extract quantitative features reflecting tissue microstructure. In this study, we investigated whether radiomic features from multiparametric MRI, including apparent diffusion coefficient (ADC) maps, improve prediction of renal function decline in ADPKD.

Methods: We analyzed 112 ADPKD patients from the Bern ADPKD Registry with standardized baseline MRI (T1-weighted, T2-weighted, and diffusion-weighted). Kidneys were manually segmented, and radiomic features were extracted using PyRadiomics. Feature stability was assessed under segmentation perturbations, followed by redundancy reduction and selection through LASSO regression. Models were developed using support vector machines with 20-fold cross-validation. The primary outcome was rapid renal function decline, defined as eGFR ≤ –3 mL/min/1.73 m²/year over a median follow-up of 5.5 years. Clinical, imaging, and ensemble models were compared by mean AUC.

Results: Among single-modality models, ADC-based radiomics achieved the highest performance (AUC 0.82, 95%CI 0.74–0.90), outperforming clinical (AUC 0.77) and T1/T2 models (AUC 0.77). Fusion of ADC with clinical variables showed comparable performance (AUC 0.81). Direct combination of ADC with T1/T2 reduced accuracy, likely due to redundancy, whereas ensemble models integrating ADC, T1/T2, and clinical data achieved the best results (AUC 0.85, 95%CI 0.79–0.90) with improved calibration.

Conclusions: ADC-derived radiomic features were the most informative predictors of renal function decline in ADPKD, capturing both cystic and non-cystic tissue alterations. Ensemble models further enhanced stability and generalizability. These findings suggest that diffusion MRI-based radiomics may provide incremental prognostic value beyond htTKV and current clinical standards, supporting its potential use for early risk stratification and treatment decisions in ADPKD.

SO-09

Dysregulation of a Nephrin-Associated Phospho-Protein Network Impairs Filtration and Podocyte Adhesion

Dr. Carolin Eul [1], Dr. Luisa Bertgen [1], Dr. Blanda Beci [1], Prof. Britta George [1]

1. Nephrology, University Hospital Zurich, Switzerland

Minimal change disease (MCD) is characterized by the presence of nephrotic syndrome. In a subset of patients, pathogenic antibodies against the slit-diaphragm (SD) protein Nephrin were identified in blood and biopsy samples. The mechanisms in podocytes induced by antibody binding to Nephrin remain to be elucidated. An analysis of the phospho-proteome in cell culture was conducted using an antibody-mediated Nephrin clustering model of MCD. This analysis revealed 501 differentially phosphorylated peptides belonging to 431 unique proteins. Gene set enrichment analysis demonstrated that inter alia the biological process 'regulation of focal adhesion (FA) assembly' was enriched. We verified that a significant proportion of the identified proteins were indispensable for filtration *in vivo*, employing a knockdown approach with consecutive analysis of filtration in *Drosophila melanogaster* nephrocytes. One of the phosphorylated proteins identified by phosphor proteome analysis was Rapgef1, which has been shown to be an activating factor of the small GTPase Rap1. The knockout of the Rapgef1 gene in the metanephric mesenchyme of mice resulted in the manifestation of nephrotic syndrome. Bulk RNA sequencing of Rapgef1 knockout mice glomeruli demonstrated significant regulation of genes implicated in cell adhesion and extracellular matrix organization. Immunofluorescence analysis of glomeruli from Rapgef1 knockout mice confirmed alterations in glomerular basement membrane (GBM) and fibronectin (FN) composition. Overall, a Nephrin-associated phospho-protein network critical for podocyte adhesion and filtration was identified, and we hypothesize that perturbation of this network underlies MCD pathogenesis.

SO-10

Efficacy and Safety of Palopegteriparatide Treatment in Adults With Hypoparathyroidism: 3-Year Results From the Phase 3 PaTHway Trial

Prof. Aliya Khan [1], Prof. Bart Clarke [2], Dr. Mishaela Rubin [3], Prof. Peter Schwarz [4], Prof. Dolores Shoback [5], Prof. Claudia Gagnon [6], Prof. Andrea Palermo [7], Dr. Lisa Abbott [8], Dr. Lynn Kohlmeier [9], Dr. Elena Tsourdi [10], Prof. Filomena Cetani [11], Prof. Rajesh Jain [12], Dr. Carol Zhao [13], Dr. Bryant Lai [13], Dr. Michael A. Makara [13], Dr. Jenny Ukena [13], Dr. Christopher T. Sibley [13], Dr. Aimee D. Shu [13], Prof. Lars Rejnmark [14], Dr. Jean-Philippe Bertocchio [15]

1. McMaster University, Hamilton, ON, Canada, 2. Mayo Clinic, Rochester, MN, USA, 3. Columbia University, New York, NY, USA, 4. Rigshospitalet, Copenhagen, Denmark, 5. UCSF/VA Medical Center, San Francisco, CA, USA, 6. CHU de Québec-Université Laval Research Centre, Quebec City, QC, Canada and Department of Medicine, Université Laval, Quebec City, QC, Canada, 7. Unit of Metabolic Bone and Thyroid Disorders, Fondazione Policlinico Campus Bio-medico, Rome, Italy and Unit of Endocrinology and Diabetes, Campus Bio-medico University, Rome, Italy, 8. Northern Nevada Endocrinology, Reno, NV and University of Nevada, Reno, Reno, NV, USA, 9. Endocrinology and Spokane Osteoporosis, Spokane, WA, USA, 10. Technische Universität Dresden Medical Center, Dresden, Germany, 11. University of Pisa, Department of Clinical and Experimental Medicine, Endocrine Unit, Pisa Italy, 12. University of Chicago, Chicago, IL, USA, 13. Ascendis Pharma Inc, Palo Alto, CA, USA,14. Aarhus University Hospital, Aarhus N, Denmark, 15. Pitié-Salpêtrière Hospital, Paris, France

Introduction: Palopegteriparatide is a prodrug of PTH(1-34), administered once daily, designed to provide active PTH within the physiological range for 24 hours/day. It is approved in the US, EU, and several other countries.

Methods: This analysis evaluated the long-term efficacy and safety of palopegteriparatide in adults with chronic hypoparathyroidism through week 156 of PaTHway, a phase 3 trial with a 26-week randomized, double-blind, placebo-controlled period, followed by an open-label extension.

Results: At week 156, 89% (73/82) of participants remained in the trial; of those, 96% were independent from conventional therapy (no active vitamin D and ≤600 mg/day elemental calcium) and 88% had normal albumin-adjusted serum calcium (2.07-2.64 mmol/L) with mean (SD) of (2.2 (0.2) mmol/L). Mean (SD) serum phosphate (1.1 (0.2) mmol/L) and calcium x phosphate product (2.5 (0.4) $mmol^2/L^2$) remained within normal ranges. Mean (SD) eGFR was 78.0 (14.5) mL/min/1.73 m^2, reflecting a mean (SD) increase of 8.8 (11.9) mL/min/1.73 m^2 from

baseline (*P* <0.0001); 59% and 43% of participants had an increase in eGFR of ≥5 mL/min/1.73 m² and ≥10 mL/min/1.73 m², respectively. Mean (SD) 24-hour urine calcium levels normalized with palopegteriparatide treatment, remaining below the upper limit of normal (≤250 mg/day) through week 156 (162.1 [117.8] mg/day). TEAEs were mostly grade 1 or 2, with no new safety signals identified.

Conclusions: Through year 3 of the PaTHway trial, retention rate was high and palopegteriparatide demonstrated consistent longer-term safety and efficacy, which included the maintenance of serum and urine biochemistries within normal levels and sustained improvement in renal function.

SO-11

Epidemiological and Genetic Investigation of Pneumocystis jirovecii Pneumonia Outbreak in Kidney Transplant Recipients: Evidence for Human-to-Human Transmission?

Dr. Laura Cereghetti [1], Dr. Jennifer Scotti Gerber [1], Dr. Antonio Bellasi [2], Dr. Elia Lo Piore [1], Prof. Luigia Elzi [1], Dr. Carlo Balmelli [1]

Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale, Lugano, 2. Service of Nephrology, Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale, Lugano

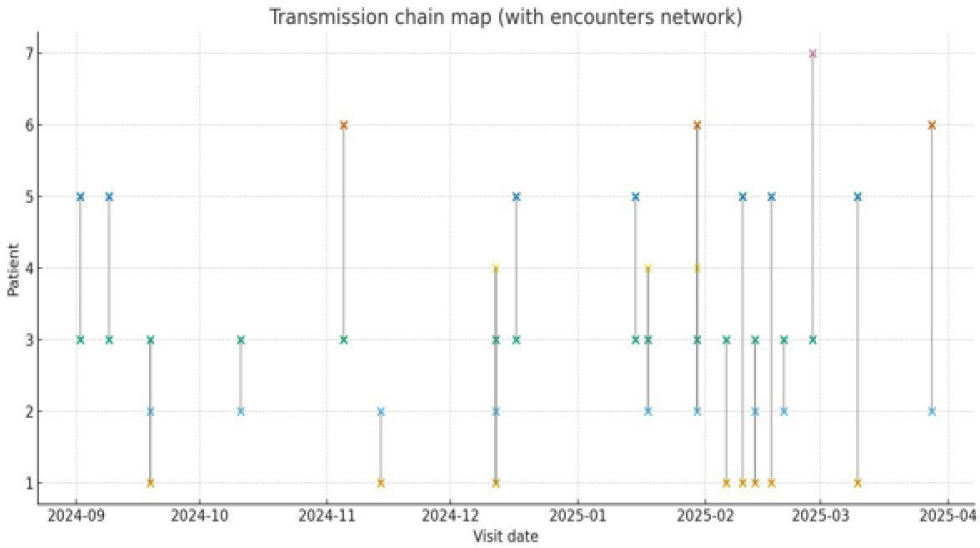
Background: *Pneumocystis jirovecii* (Pj) is an opportunistic pathogen causing pneumonia in immunocompromised hosts. Outbreaks have been reported among kidney transplant recipients (KTR). In February 2025, we observed a rise in cases of *Pj* pneumonia (PJP) in our outpatient clinic, prompting an outbreak investigation.

Methods: Clinical and epidemiological data were collected from September 2024 to June 2025. Multilocus Sequence Typing (MLST) of available samples was performed. Contact tracing was conducted to identify possible sources of transmission.

Results: Seven proven cases of PJP were identified (first case February 27, 2025; last case June 20, 2025), representing 8% (7/86) of our KTR cohort. Median age was 64 years (IQR 57–68); 3/7 were female; median time from transplantation was 72 months (IQR 55–116). Immunosuppressive regimens varied, but none had received corticosteroid therapy ≥20 mg/daily in the past six months. All patients were lymphopenic (median lymphocyte count 0.6 G/L; IQR 0.2–0.7), with severe lymphopenia (<0.5 G/L) in three cases. All presented with bilateral ground-glass infiltrates on CT and positive Pj PCR on BAL. Quantitative PCR showed a median of 1,263,556 cp/ml (IQR 241,488–10,223,607). MLST was successful in four cases and revealed high diversity (H-index 0.987, mt26S, CytB, SOD). Contact tracing six months prior to the index case highlighted multiple overlapping outpatient visits on the same days (Figure 1). Following these findings, mandatory surgical mask use was implemented in the clinic, and prophylactic trimethoprim–sulfamethoxazole (TMP-SMX) was prescribed to 77/79 patients (two refused).

Conclusions: We report a PJP outbreak in KTR. Molecular typing and contact tracing strongly suggest interhuman transmission in the outpatient setting. No specific individual risk factors differentiated affected from unaffected patients. After introduction of mask policy and TMP-SMX prophylaxis, no further cases occurred during the three months following the last case, with prevention measures still ongoing.

Figure 1



SO-12

Expanding Therapeutic Boundaries: First Experience with Obinutuzumab in a Dialysis Patient with systemic Lupus Erythematodes

Dr. Ilirjana Bajraktari [1], Dr. Simeon Schietzel [1], Prof. Uyen Huynh-Do [2]

1. University Clinic of Nephrology and Hypertension, Inselspital Bern, Bern, 2. University Hospital Berne

Therapy resistance in SLE (systemic Lupus Erythematodes) remains a major challenge, often associated with poor patient outcomes. Obinutuzumab is a glycoengineered, humanized type II anti-CD20 monoclonal antibody that – compared to rituximab – promotes enhanced antibody-dependent cellular cytotoxicity as well as direct cell death. It has been pproved in combination with chemotherapy for the treatment of chronic lymphocytic leukemia and follicular lymphoma.[1] FDA has just authorized Obinutuzumab as treatment for Lupus nephritis.[2] We report the case of a 44.yrs old female hemodialysis patient with severe therapy-resistant SLE who demonstrated a signjficant clinical and serological response following combination of Belimumab and Obinutuzumab. The patient had previously failed standard-of-care immunosuppressive strategies, including rituximab, with persistent systemic disease activity (severe musculoskelettal pain, arthritis, neutroand thrombocytopenia,

very active serological activity), which all decreased following combination treatment with obinutuzumab and belimumab. The treatment was well tolerated, with no adverse events observed. We conclude that

- SLE can persist with a severe course in patients on hemodialysis
- Obnituzumab is safe and efficient in anuric hemodialysis patient with severe sLEa.

This case underscores the potential of innovative therapeutic strategies to overcome resistance sLE, and supports further investigation into targeted approaches that modulate pathophysiological mechanisms beyond conventional pathways.

- Cameron, F., & McCormack, P. L. (2014). Obinutuzumab: First global approval. *Drugs, 74*(2), 147–154. https://doi.org/10.1007/s40265-013-0167-3
- Furie, R. A. REGENCY Trial Investigators. (2025). Efficacy and safety of obinutuzumab in active lupus nephritis. *New England Journal of Medicine, 392*(15), 1471-1483. https://doi.org/10.1056/NEJMoa2410965

SO-13

Feasibility of Implementing Electronic Patient-Reported Outcome Measures (ePROMs) in Hemodialysis: A Pilot Study in a Secondary Care Hospital in Switzerland

Dr. Thomas Reich [1], Dr. Olivier Linder [1], Prof. Stefan Zschiedrich [1]

1. Department of Nephrology, Bürgerspital Solothurn, Solothurn

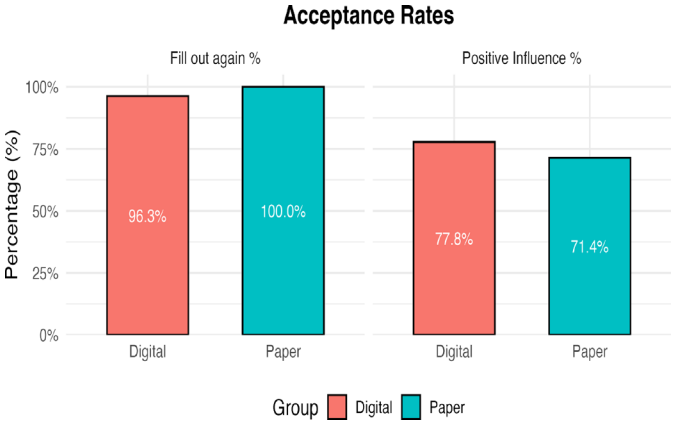
Background: Patients on hemodialysis frequently experience a high burden of physical and psychological symptoms, which are often underassessed. In Switzerland, few projects have evaluated patient-reported outcomes in dialysis, leaving a gap in practical implementation experience. This feasibility pilot study aimed to investigate whether implementing ePROMS is feasible, acceptable and generates useful data.

Methods: We used a tablet-based system to collect ePROMs using the KDQOL-36 questionnaire. Adult outpatients with ESRD on hemodialysis were screened and recruited. Acceptability was measured with a short survey after ePROM completion. Usability and data quality were assessed through predefined outcomes. Data were collected at baseline with follow-up data collection planned for 3 and 6 months. Patients who were unable to complete the electronic questionnaire after more than two attempts or due to a medical condition filled out a paper-based version.

Results: In the baseline assessment conducted in September 2025, a total of 38 patients were enrolled. Of these, 27 completed ePROMs on a tablet, while 11 used a paper-based version. The mean age was 60.5 years in the ePROM group and 73.4 years in the paper-based group. Average completion time was 21 minutes in the ePROM group compared to 47.6 minutes for the paper-based group. In the ePROM group, 11% required assistance. All patients in the ePROM group completed the questionnaire, whereas only 67% in the paper-based group did so. Acceptance and willingness to participate in future assessments were comparable in the two groups.

Discussion: These preliminary findings indicate that implementing ePROMs is feasible and efficient in hemodialysis patients. Reliable data were successfully collected in the ePROM group in less time, showing the usability of this approach. For older patients, strategies such as assisted completion, or paper-based alternatives remain necessary.

Group	n	Mean Age	Mean Duration	Needed Help	Finished Questionnaire
All	38	64.2	26.4	8.8%	89.5%
Digital	27	60.5	21.0	11.1%	100.0%
Paper	11	73.4	47.6	0.0%	63.6%



SO-14

First Swiss experience with Sparsentan in reducing proteinuria in a transplant recipient with recurrent IgA nephropathy – a case report

Dr. Rüdiger Eisel [1], Dr. Clemens Jäger [1], Dr. Annette Enzler-Tschudy [2], Dr. Christian Bucher [2]

1. Nierenzentrum Rheintal – Liechtenstein, 2. Kantonsspital St. Gallen

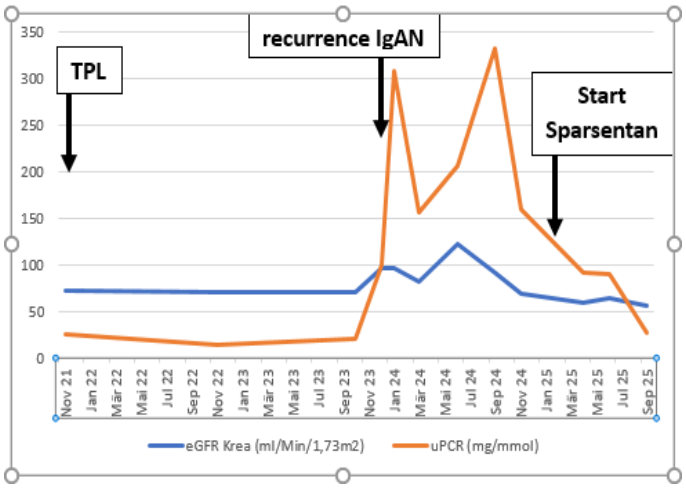
Background: IgA nephropathy is the most common primary glomerulonephritis and may recur after kidney transplantation, often leading to proteinuria and progressive graft dysfunction. Supportive therapy with RAAS inhibition and SGLT2 inhibitors may reduce but not eliminate this risk. Sparsentan, a dual endothelin-1 and angiotensin II receptor antagonist, has recently been approved for IgA nephropathy in native kidneys, but evidence in transplant recipients is lacking.

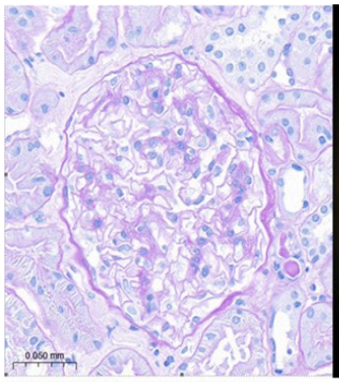
Methods: We describe the clinical course of a young kidney transplant recipient with recurrent IgA nephropathy. The patient underwent living donor kidney transplantation after a period of dialysis. Standard immunosuppression was administered, and protocol biopsies as well as regular laboratory monitoring were performed during follow-up.

Results: Initial graft function was excellent, with no proteinuria. Early protocol biopsies showed no signs of rejection or recurrence, allowing steroid withdrawal. Approximately two years after transplantation, the patient developed proteinuria and hematuria despite optimized supportive therapy, including maximal ACE inhibition, an SGLT2 inhibitor, and low-dose steroids. Biopsy confirmed recurrent IgA nephropathy. Proteinuria persisted and graft function began to decline gradually. At this stage, sparsentan was introduced, with simultaneous discontinuation of RAAS blockade. Treatment was well tolerated, without hepatotoxicity or other adverse events. Following initiation, a marked reduction in proteinuria of about 40% was observed within weeks. After six months, proteinuria was even reduced by as much as 80%. Graft function stabilized and no further decline was documented during the observation period.

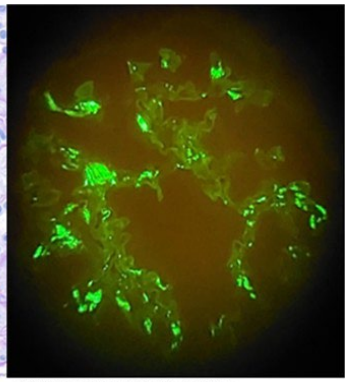
Conclusion: This is the first reported use of sparsentan in a kidney transplant recipient with recurrent IgA nephropathy in Switzerland. The drug induced a rapid and sustained reduction in proteinuria and stabilized graft function, without relevant side effects. Sparsentan appears to be a promising and well-tolerated therapeutic option for IgA nephropathy, potentially applicable to both native and transplanted kidneys. Further data on long-term efficacy, safety, and cost-effectiveness are needed.

Grafic 1: development of eGFR and Proteinuria





Picture 1: slightly broadend mesangium



Picture 2: mesangial IgA staining

Table 1: data

	Nov 21	Nov 22	Okt 23	Dez 23	Jan 24	Mär 24	Jun 24	Sep 24	Nov 24	03.04.2025	02.06.2025	22.09.2025
eGFR Krea (ml/Min/1,73m2)	73	71	71	96	97	82	123	92	69	60	65	56
uPCR (mg/mmol)	25	14	21	100	309	157	207	333	160	91	90	27
uACR (mg/mmol)	5	<3		66					134	74	71	17
Tac trough level (ug/l)		8.1		10.0	5.0	4.7	5.0	7.7	8.5	9.1	12.2	9.4
Office blood pressure (mmHg)			137/84			128/79		145/84		129/78	149/83	142/83

SO-15

HLA Class II on Urinary EVs: A Marker of Acute Renal Allograft Injury

Dr. Jakob E. Brune [1], Mr. Radoslaw Grochowski [2], Dr. Daniel Hagey [3], Dr. André Görgens [3], Prof. Stefan Schaub [4], Prof. Joel Nordin [5]

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel and Division of Biomolecular and Cellular Medicine, Karolinska Institutet, Stockholm, Sweden, 2. Division of Biomolecular and Cellular Medicine, Karolinska Institutet, Stockholm, Sweden, 3. Division of Biomolecular and Cellular Medicine, Karolinska Institutet, Stockholm, Sweden and Department of Cellular Therapy and Allogeneic Stem Cell Transplantation (CAST), Karolinska University Hospital, Stockholm, Sweden, 4. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland, 5. Division of Biomolecular and Cellular Medicine, Karolinska Institutet, Stockholm, Sweden and Department of Clinical Immunology and Transfusion Medicine (KITM), Karolinska University Hospital, Stockholm, Sweden

Background: Long-term survival of kidney allografts is limited by the risk of allograft rejection. To date, there remains an unmet need for non-invasive biomarkers to support surveillance of transplant function and early diagnosis of allograft rejection. In recent years, extracellular vesicle (EV)-based diagnostics have received increasing attention across a wide range of diseases. Here, we present data on the characterization of urinary EVs in patients with various biopsy-proven renal allograft pathologies.

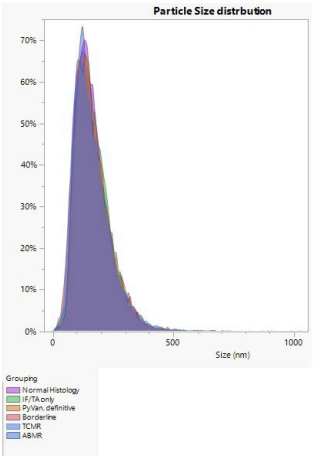
Methods: We analyzed urinary samples from 68 renal allograft recipients with T-cell mediated rejection (n = 18), antibody-mediated rejection (n = 10), BK polyomavirus-associated nephropathy (n = 10), borderline changes (n = 10), and no rejection (n = 20). Differential centrifugation and ultrafiltration were used to remove larger particles and enrich the fraction of small EVs (sEVs). Nanoparticle tracking analysis was performed to assess the number and size distribution of sEVs. Morphology was examined by electron microscopy. EV surface proteins were analyzed using a bead-based flow cytometry assay (MACSPlex EV Kit IO), which detects 39 different EV surface epitopes.

Results: The average particle size across all 68 samples was 164 nm, with no significant differences between the histologic groups (p = 0.93). Similarly, there were no differences in particle size distribution (Figure 1a). Electron microscopy confirmed the presence of spherical structures typical of sEVs (Figure 1b). Bead-based flow cytometry confirmed the presence of classical sEV marker proteins (CD9, CD63, CD81) (Figure 2). Of the remaining 36 EV surface proteins studied, only HLA class II showed signal intensities that significantly differed in patients with rejection (ABMR and TCMR), borderline changes, and PyVAN compared to patients with unremarkable histology (Figure 3a). HLA class II signal intensities also correlated with acute Banff lesion scores (At, Ati, Ag, PCTitis), but not with chronic Banff lesion scores (Figure 3b).

Conclusions: This study highlights the potential of urinary EV-based diagnostics for the detection of transplant allograft rejection.

Figure 1

a)



b)

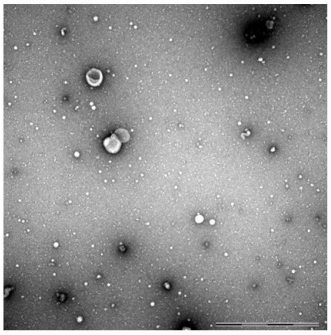


Figure 2

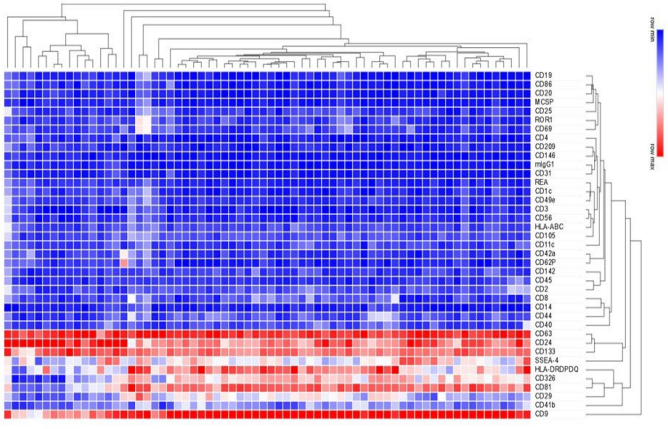
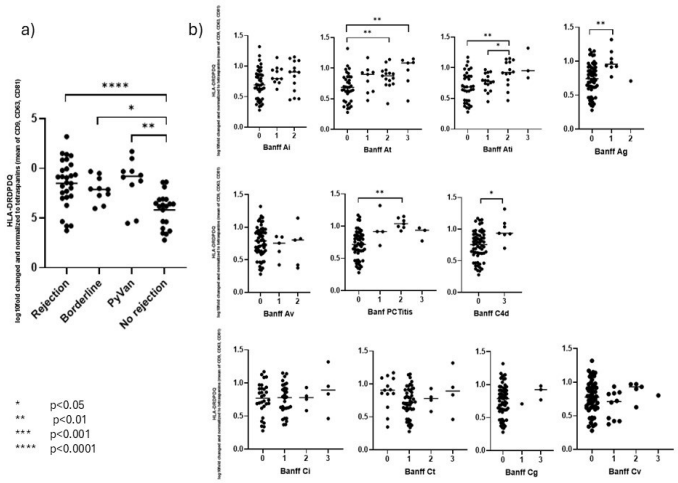


Figure 3



SO-16

Impact of Metamizol Exposure on Early Tacrolimus Levels in KT Recipients

Prof. Daniel Sidler [1], Ms. Diana Szücs [2]

1. University Hospital Berne, 2. Division of Nephrology and Hypertension, Inselspital, Bern

Introduction: Kidney transplantation (KT) is an effective treatment for advanced or dialysis-dependent kidney disease. Calcineurin inhibitors (CNI), particularly tacrolimus, have a narrow therapeutic window and undergo extensive metabolism via CYP3A enzymes and P-glycoprotein, making them vulnerable to drug–drug interactions. Metamizol, a non-opioid analgesic commonly used postoperatively, may alter tacrolimus exposure. We aimed to quantify the clinical interaction between metamizol and tacrolimus early after KT.

Methods: We performed a retrospective, single-centre study at the University Hospital Insel Bern. Patients without in-hospital exposure to tacrolimus or metamizol were excluded. Participants were stratified by timing of metamizol discontinuation: Early Stop (≤72 h post-reperfusion) vs Late Stop (>72 h or continued). The primary endpoint was time to first therapeutic tacrolimus trough (C0) ≥8 ng/mL. Secondary endpoints were failure to achieve target by postoperative day 7 and occurrence of supratherapeutic C0 >15 ng/mL during weeks 2–3.

Results: We analysed 2,579 treatment records (1,586 metamizol; 993 tacrolimus) and 3,671 tacrolimus C0 measurements from 151 patients (26.06.2015–16.12.2023). Metamizol was discontinued during hospitalisation in 55/124 (44.2%); median time to discontinuation was 92.8 h (IQR 66.4–118) after reperfusion; Early Stop occurred in 34%. Overall, 98.1% reached C0 ≥8 ng/mL with a median time of 2.68 days (IQR 1.66–6.51). Time to target did not differ significantly between Early Stop and Late Stop (2.44 vs 2.72 days; p = n.s.). However, failure to reach target by day 7 was more frequent with Late Stop (30.6% vs 14.7%, p = n.s). Supratherapeutic C0 >15 ng/mL in weeks 2–3 occurred more often with Late Stop (35.5% vs 26.5%, p = n.s.).

Discussion: Prolonged metamizol exposure predisposed to early tacrolimus underexposure and later overshoot, consistent with a clinically meaningful interaction. These findings support intensified therapeutic drug monitoring and pre-emptive tacrolimus dose adjustments around metamizol initiation and discontinuation in the early post-transplant period.

SO-17

Indapamide and Chlorthalidone to Reduce Urine Supersaturation for Secondary Prevention of Kidney Stones: a Randomized, Double-blind, Crossover Trial (INDAPACHLOR Trial)

Dr. Martin Scoglio [1], Dr. Matteo Bargagli [1], Dr. Felix Rintelen [2], Dr. Marie Roumet [2], Dr. Sven Trelle [2], Prof. Daniel G. Fuster [1]

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Department of Clinical Research, University of Bern, Bern, Switzerland

Background: Kidney stones constitute a major global healthcare problem characterized by high recurrence rates. The majority of kidney stones consist of calcium and a high urine calcium is the predominant metabolic abnormality in patients with kidney stones. The NOSTONE trial recently demonstrated that hydrochlorothiazide (HCT) has limited efficacy in preventing recurrence. Our objective is to assess whether indapamide or chlorthalidone are more effective than HCT in reducing urine supersaturations (RSRs) for calcium oxalate and calcium phosphate, which are validated predictors of stone recurrence.

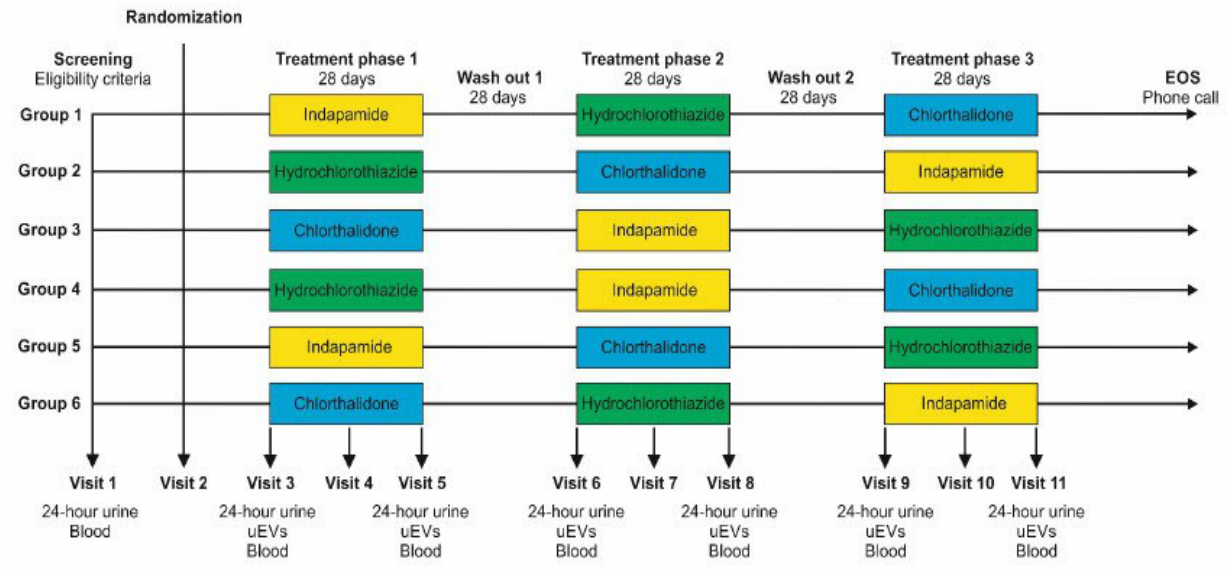
Methods: INDAPACHLOR is a single-center, randomized, double-blind, cross-over trial evaluating the efficacy of indapamide or chlorthalidone compared to hydrochlorothiazide in lowering urine RSRs for calcium oxalate and calcium phosphate in individuals with idiopathic calcium kidney stones. Participants will be allocated to indapamide 2.5 mg once daily, chlorthalidone 25 mg once daily, and hydrochlorothiazide 50 mg once daily in a random sequence. The three consecutive active treatment periods of 28 days each will be separated by wash-out periods of 28 days. The primary outcomes are the changes of the RSR calcium oxalate and RSR calcium phosphate from baseline to day 28 of each treatment period. Secondary outcomes include changes in 24 h urine and blood parameters from baseline to day 28 of each treatment period.

Results: The INDAPACHLOR trial is registered at ClinicalTrials.gov (NCT06111885). Approval of the cantonal Ethics Commission Bern was obtained on May 28 2024 (approval # 2024_00477), and authorization from Swissmedic was received on June 27 2024 (approval # 701824). Patient recruitment commenced in December 2024. As of end-August 2025, a total of 72 patients have been recruited (targeted enrolment 99 participants). Of these, 25 participants already completed the study. The study was initially expected to conclude by the end of 2027; however, current recruiting rates indicate it may finish earlier than anticipated.

Inclusion Criteria	
Patients fulfilling all the following inclusion criteria are eligible for the study:	
1	Written, informed consent
2	Age 18 years or older
3	Recurrent kidney stone disease (2 or more stone episodes in the last 10 years prior to randomization)
4	Past kidney stone containing 50% or more of calcium oxalate, calcium phosphate or a mixture of both
Exclusion Criteria	
The presence of any one of the following exclusion criteria will lead to exclusion:	
1	Patients with secondary causes of recurrent calcium kidney stones including severe eating disorders (anorexia or bulimia), chronic bowel disease, intestinal or bariatric surgery, sarcoidosis, primary hyperparathyroidism, chronic urinary tract infection
2	Patients taking the following medications: Thiazide or loop diuretics, carbonic anhydrase inhibitors (including topiramate), xanthine oxidase inhibitors, alkali, active vitamin D (calcitriol or similar), calcium supplementation, bisphosphonates, denusomab, teriparatide, sodium-glucose co-transporter 2 (SGLT2) inhibitors, strong CYP3A4 inhibitors or inducers (may affect indapamide metabolism), lithium.
3	Patients with chronic kidney disease (defined as CKD-EPI eGFR < 30ml/min)
4	Patients with glomerulonephritis
5	Patients with the following biochemical imbalances: severe hypercalcemia (>2.8 mmol/L), therapy-resistant hypokalemia or conditions with increased potassium loss, severe hyponatremia (<130 mmol/L), symptomatic hyperuricemia

Criteria for Withdrawal/Discontinuation	
Study participants must be withdrawn from the study if the following occurs:	
1	At the participants' own request
2	If, in the investigator's opinion, continuation of the study would be harmful to the participant's well-being
3	If the participant discontinues treatment before the assigned second treatment period is completed
4	Use of prohibited medication indicated during study
5	Severe hypokalemia (plasma potassium <2.5 mmol/L)
6	Start of uric acid lowering therapy
7	Pregnancy

Figure 1. Flow chart of the study design.



SO-18

Late-onset Cobalamin C deficiency associated atypical hemolytic uremic syndrome – diagnostic pitfalls: a case report.

Dr. Martha Stampfli [1], Dr. Sibylle Tschumi [1], Prof. Giacomo Simonetti [2], Prof. Corinne Benchimol [3], Dr. Gabriela Oesch [4], Dr. Alexander Lämmle [5], Prof. Matthias Baumgartner [6]

1. Division of Pediatric Nephrology, Inselspital, Bern University Hospital, Switzerland, 2. Pediatric Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Switzerland, 3. Division of Pediatric Nephrology, Mount Sinai Hospital, New York, NY, 4. Division of Neuropaediatrics, Development and Rehabilitation, Inselspital, Bern University Hospital, Switzerland, 5. Division of Pediatric Metabolism & Neurometabolics, Inselspital, Bern University Hospital, Switzerland, 6. Division of Metabolism, University Children's Hospital Zurich, Zurich, Switzerland

Background: Cobalamin C (CblC) deficiency as origin of atypical hemolytic uremic syndrome (HUS) is rare. CblC deficiency is multisystemic: failure to thrive, muscular hypotonia, multiple central nervous symptoms, retinopathy, megaloblastic anemia and around 10% of patients develop HUS. Treatment consists of substitution of hydroxocobalamin, betaine, carnitine and folinic acid.

Case presentation: A formerly healthy ten-year-old female Caucasian patient presented with acute emesis and abdominal pain. She then suffered a generalized tonic-clonic status epilepticus and hypertensive crisis. Cerebral imaging was normal and laboratory exams revealed renal insufficiency with creatinine at 506µmol/l (reference level <60µmol/l), intravascular hemolysis (hemoglobin 63g/l), thrombocytopenia (min. 100 G/l), hematuria and proteinuria. Atypical HUS was suspected and eculizumab was administered. She received intermittent hemodialysis. Genetic testing revealed two pathogenic variants in the *MMACHC* gene (frameshift insertion c.271_272insA, p.Arg91Lysfs*14 and intron deletion c.82-13_82-10delCTTT), consistent with CblC deficiency. Subsequent metabolic treatment consisted of the above-mentioned. In the following course, she suffered a relapse of hypertensive crisis despite stable metabolic values and controlled fluid management. Hypertension required a five-fold regimen and renal replacement therapy was performed for ten weeks. Her renal function is recovering, currently at 60ml/min/1.73m^2 (eGFR Schwartz), and she has no evident neurologic sequelae.

Conclusion: In pediatric atypical HUS patients, CblC deficiency should always be considered by measuring plasma total homocysteine and / or methylmalonic acid in blood or urine. Especially, since detection by Newborn Screening (NBS) has limitations and is not performed in every country. Molecular genetic disease confirmation is of utmost importance.

Keywords: Atypical hemolytic uremic syndrome, Cobalamin C deficiency, Late-onset form, Newborn Screening, Case report

SO-19

Model-based meta-analysis to inform chronic kidney disease drug development

Dr. Klervi Golhen [1], Dr. Monica Simeoni [1], Dr. Nicholas Medjeral-Thomas [2], Dr. Theodoros Papathanasiou [1], Dr. Anna Largajolli [3], Dr. Sinziana Cristea [3], Dr. Matt Zierhut [3], Dr. Chiara Zecchin [1]

1. Clinical Pharmacology Modelling and Simulation, GSK, 2. Translational Medicine, GSK, 3. Certara

Background: Chronic kidney disease (CKD) represents a significant unmet medical need, with diverse etiologies and disease severities requiring tailored treatments. This study leverages the CODEx CKD Database and Model-Based Meta-Analysis (MBMA) to explore the correlation between early surrogate endpoints, such as urinary albumin-to-creatinine ratio (UACR) and urinary protein-to-creatinine ratio (UPCR), and long-term composite clinical outcomes. The goal is to provide insights to inform clinical trial design, optimize drug development, and refine patient stratification for CKD and its subtypes.

Methods: The CODEx CKD Database was developed using systematic methods outlined in the Cochrane Handbook and PRISMA guidelines. Safety and efficacy average level data from randomized controlled trials (RCTs) investigating interventions such as ACE inhibitors, ARBs, SGLT2 inhibitors, and endothelin receptor antagonists were extracted. A MBMA assessed the relationship between UACR and UPCR changes at early timepoints (e.g., 6 months) and composite clinical endpoints over 2 years (e.g., progression to end-stage renal disease, renal death). The model accounted for inter-study heterogeneity and variability in CKD etiology and severity.

Results: Exploratory analyses suggest that reductions in UACR and UPCR at 6 months may correlate with improved composite clinical outcomes at 2 years. These findings highlight the potential of UACR and UPCR as intermediate markers to support futility analyses and adaptive trial designs in early-phase studies, enabling early Go/No-Go decisions in interim analyses with smaller sample sizes. These approaches could enhance trial design and improve efficiency, while addressing limitations in prior studies, including heterogeneity in CKD progression, variability across patient populations and between Ph2 and Ph3 trials.

Conclusions: The integration of CODEx CKD Database and MBMA offers a promising framework to explore surrogate endpoint correlations in CKD drug development. Early insights into UACR and UPCR-clinical outcome relationships may enhance clinical trial design and accelerate development of targeted therapies for CKD and its subtypes.

SO-20

Nephrologists' Survey on the Management of Chronic Kidney Disease-associated Mineral and Bone Disorders in Switzerland

Mrs. Noemi Galliker [1], Dr. Marco Bonani [2], Dr. Antonio Bellasi [3], Prof. Daniel Teta [4], Prof. Andrea Trombetti [5], Dr. Matthias Moor [6]

1. Department of Medicine, Emmental Regional Hospital, Burgdorf, 2. Department of Nephrology, University Hospital Zurich, University of Zurich, Zurich, 3. Service of Nephrology, Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale, Lugano, 4. Service de Nephrology, Centre Hospitalier du Valais Romand, CHVR, Sion, Switzerland, 5. Division of Bone Diseases, Department of Medicine, Geneva University Hospitals and Faculty of Medicine, Geneva, 6. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern

Background: Management of chronic kidney disease-associated mineral and bone disorders (CKD-MBD) remains controversial even in high-income countries. Here, we assessed nephrologists' practice patterns, and considerations regarding bone biopsies, biochemical markers, and antiresorptive or osteoanabolic treatments in patients with chronic kidney disease.

Methods: We conducted a cross-sectional survey with 41 questions among members of the Swiss Society of Nephrology. Responses were analyzed by descriptive statistics.

Results: The survey included 75 respondents, corresponding to a response rate of 25-30%. Participants were predominantly male (61%) and worked mainly in the German-speaking Switzerland (67%). Among the respondents, 37 (52%) stated that they have access to a center that could perform bone biopsies, and 22 (31%) have in the past 5 years referred patients for a bone biopsy. Most respondents indicated that the bone biopsies in their CKD-MBD patients were performed by orthopedic surgeons (55%) and were analyzed in Switzerland, France or Germany. Most nephrologists commonly prescribed bisphosphonates and denosumab. 88% and 42% have never yet used

romosozumab and PTH analogues, respectively. Most participants voiced general concerns using antiresorptive or osteoanabolic treatments in CKD-MBD due to lack of data in advanced CKD, and due to unknown bone turnover status (76% each), yet bone biopsies were only rarely performed before initiating anti-osteoporotic therapies (in less than 25%). Participants were only somewhat confident in biochemical biomarkers of osteodystrophy subtypes. Overall, 97% participants indicated that better access to bone biopsies could change their prescribing patterns of anti-osteoporotic therapies in CKD-MBD.

Conclusion: Most nephrologists in Switzerland would welcome better access to bone biopsies, have concerns about bone turnover, and yet they feel obliged to prescribe medications with insufficiently defined bone turnover. Thus, efforts are warranted to increase awareness and knowledge of diagnosis tools and novel therapeutics regarding CKD-MBD in Switzerland.

SO-21

Oral Glucocorticoid Burden in Lupus Nephritis: A Swiss Cohort Analysis

Dr. Maria Wallner [1], Dr. Kristin Schmiedeberg [1], Prof. Johannes von Kempis [1], Prof. Camillo Ribi [2], Dr. Yanic Heer [3], Dr. Jana Jarecki [3], Prof. Uyen Huynh-Do [4], Prof. Frauke Förger [1]

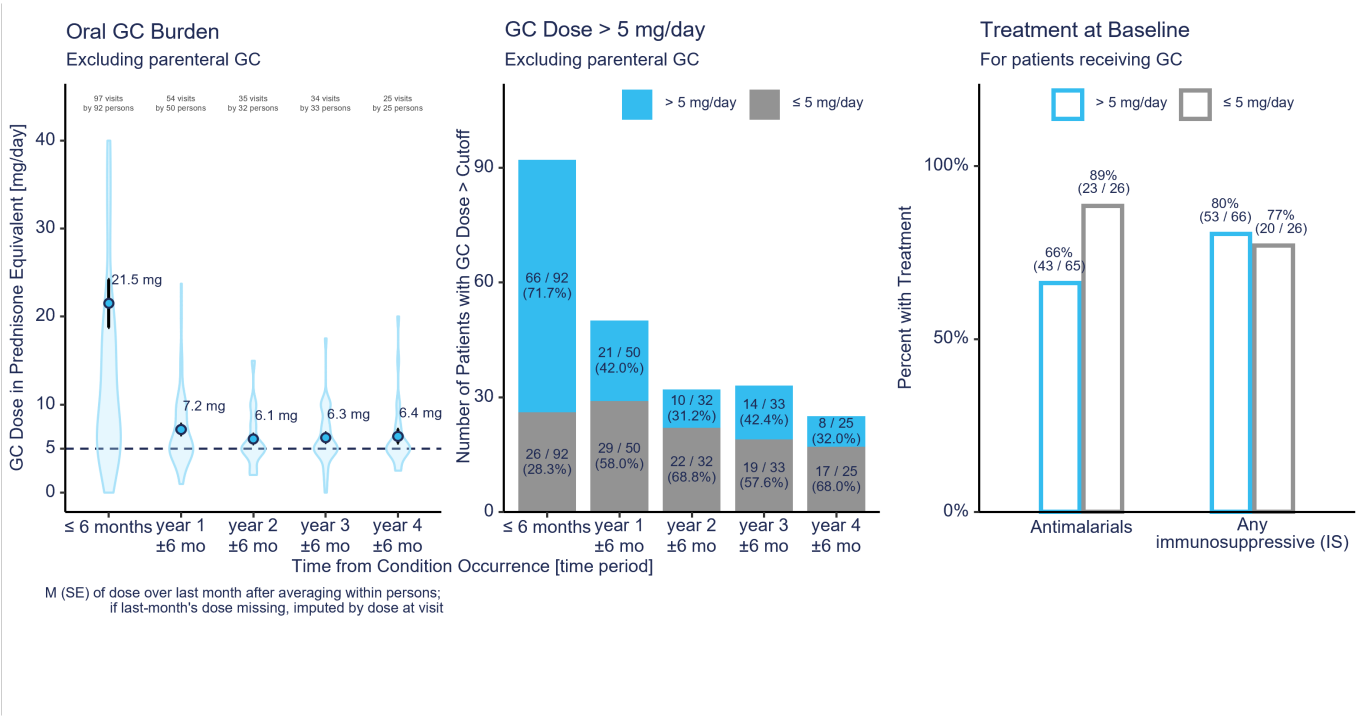
1. Department of Rheumatology, Cantonal Hospital St.Gallen, 2. Department of clinical Immunology and Allergology, University Hospital Lausanne, 3. Rewoso AG – real-world solution, Zurich, 4. University Hospital Berne

Background: Swiss real-world data for the treatment of lupus nephritis (LN) are limited. We describe exposure to oral glucocorticoids (GC) and other lupus medication in patients with LN during four years of follow-up.

Methods: This retrospective study included patients with LN enrolled in the Swiss SLE Cohort Study (SSCS) during 2007 to 2024. Analysis was performed on patients with biopsy-confirmed LN on baseline urinary protein-creatinine ratio (uPCR), GC exposure, concomitant use of antimalarials (HCQ) and other immunosuppressive agents (IS), in addition to GC exposure within four years following diagnosis.

Results: The cohort of 144 LN patients was predominantly female (83%) and Caucasian (65%), with a mean disease duration of 8.8 years and a median uPCR of 92.5 mg/mmol. Treatments at baseline comprised oral GC in 92 patients, of whom 72% were on HCQ, 75% on IS and 7% on biologics. The mean GC dose around LN diagnosis was 21.5 mg/day, with 71.7% (66/92 patients) receiving > 5 mg/day. At baseline, LN patients who received GC showed a median uPCR of 92.1 mg/mmol, those with a GC dose > 5mg/day had 110.2 mg/mmol while those with a GC dose ≤ 5 mg/day had 35.5 mg/mmol. After approximately 1.5 years, the mean GC dose was 7.2 mg/day (42%, 21/50 receiving > 5 mg/day). After about 2.5 years it was 6.1 mg/day (31%, 10/32 receiving > 5 mg/day). Among patients on GC dose > 5 mg/day, 66% received HCQ and 80% IS (most frequently mycophenolate mofetil, followed by azathioprine).

Conclusion: In the Swiss cohort of LN patients, a higher burden of oral GC was associated with proteinuria of about 1 g/day at baseline, yet the average dose declined to around 7 mg/day within one year. This reduction is likely due to the high proportion of patients taking combination treatment.



SO-22

Oxygenation at birth restores NKCC2 and NCC expression, partially explaining the transient nature of Bartter Syndrome type 5

Dr. Stefan Rudloff [1], Ms. Nadine Schumacher [1], Dr. Kamel Laghmani [2], Prof. Uyen Huynh-Do [1]

Department of Nephrology and Hypertension, University of Bern and University Hospital Bern, Freiburgstrasse 15, CH-3010 Bern, Switzerland., 2. Renal physiology and tubulopathies, Centre de Recherche des Cordeliers, Sorbonne Université, 15 rue de l'École de Médecine, 75006 Paris, France

Background: Bartter syndrome (BS) is a rare inherited kidney disorder caused by defective sodium, potassium, and chloride reabsorption. Most cases result from mutations in genes encoding renal salt transporters, including *Slc12a1* (NKCC2), *Kcnj1* (ROMK), or *Clcnkb* (ClC-Kb), but over 20% of patients long lacked a molecular diagnosis. This gap was partly closed by the discovery that mutations in the X-linked stress-response gene *Mage-d2* cause BS type 5, a severe but transient form presenting prenatally with fetal polyuria, massive salt loss, polyhydramnios, extreme prematurity, and high mortality. Disease severity results from impaired surface expression of NKCC2 and NCC in fetal kidneys, where MAGE-D2 protects these transporters by promoting hypoxia-response signaling and limiting endoplasmic reticulum (ER) stress-induced degradation. However, a detailed analysis of their perinatal expression dynamics has not yet been performed, which we address here.

Methods: Using Western blotting, we analyzed perinatal expression levels of NKCC2, NCC, MAGE-D2, and ER stress-related proteins in total kidney lysates form wild-type mice under three conditions: physiological hypoxia during pregnancy, pathological hypoxia induced by maternal oxygen restriction, and normoxia in newborn pups.

Results: NKCC2 and NCC expression was reduced under pathological hypoxia but rose sharply after birth, coinciding with improved oxygenation. In contrast, most ER stress-related proteins (HSP13, OS9, AUP1, MAN1A1) showed the opposite pattern, with increased expression during fetal hypoxia and marked reduction postnatally. MAGE-D2 and HSP40, however, displayed differential protein maturation pattern under both conditions.

Conclusion: Our findings strongly support the hypothesis that oxygenation at birth is a crucial event for the robust upregulation of NKCC2 and NCC, providing a mechanistic basis for the transient course of BS type 5. Conversely, ER stress-related proteins and chaperones appear to preserve basal expression levels, counteracting hypoxic stress. Together, these results lay the groundwork for future studies in conditional *Mage-d2* knockout mice.

SO-23

Pegcetacoplan demonstrates sustained 52-week efficacy and safety across subgroups in C3G and primary IC-MPGN: results from the VALIANT trial

Prof. Fadi Fakhouri [1], Dr. Carla Nester [2], Dr. Andrew Bomback [3], Prof. Gema Ariceta [4], Dr. Yahsou Delmas [5], Dr. Bradley Dixon [6], Prof. Daniel Gale [7], Dr. Larry Greenbaum [8], Prof. Seung Hyeok Han [9], Prof. Nicole Isbel [10], Prof. Christoph Licht [11], Dr. Antonio Mastrangelo [12], Prof. Masashi Mizuno [13], Dr. Maria Izabel Neves de Holanda [14], Prof. Matthew Pickering [15], Prof. Giuseppe Remuzzi [16], Dr. Nicole Van De Kar [17], Dr. Marina Vivarelli [18], Dr. Patrick Walker [19], Dr. Dean Wallace [20], Prof. Daniel Zecher 21, Dr. Moglie Le Quintrec [22], Dr. Yael Borovitz [23], Dr. Nabil Melhem [24], Ms. Katie Gordon [25], Dr. Anwesha Mukherjee [25], Mr. Johan Szamosi [26], Dr. Lucia Quintana-Gallardo [26]

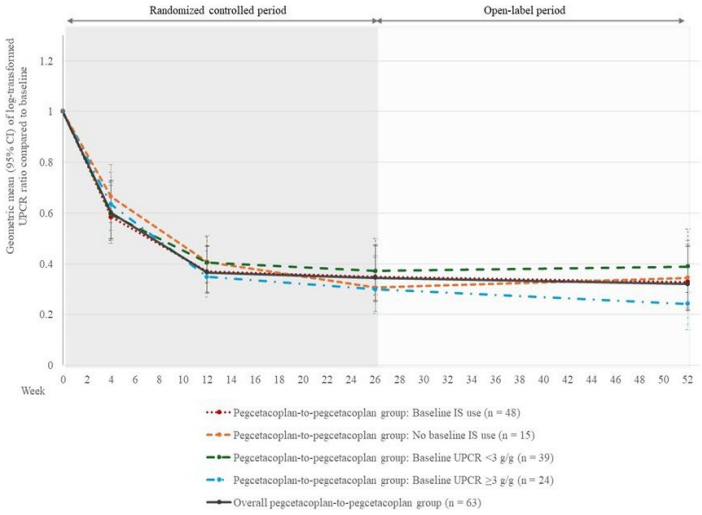
1. Lausanne University Hospital, 2. University of Iowa, Stead Family Children's Hospital, Iowa City, IA, 3. Columbia University Irving Medical Center, New York, NY, 4. Hospital Vall d'Hebron, Barcelona, 5. Bordeaux University Hospital, Bordeaux, 6. University of Colorado School of Medicine, Aurora, CO, 7. University College London, London, 8. Emory School of Medicine and Children's Healthcare of Atlanta, Atlanta, GA, 9. Yonsei University College of Medicine, Seoul, 10. Princess Alexandra Hospital, Brisbane, 11. The Hospital for Sick Children and University of Toronto, Toronto, ON, 12. Unit Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, 13. Department of Renal Replacement Therapy, Nagoya University Graduate School of Medicine, Nagoya, 14. Hospital Federal de Bonsucesso, Ruschel Medicina, Rio de Janeiro, 15. Imperial College, London, 16. Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo, 17. Radboudumc Amalia Children's Hospital, Nijmegen, 18. Bambino Gesù Children's Hospital, IRCCS, Rome, 19. Arkana Laboratories, Little Rock, AR, 20. Royal Manchester Children's Hospital, Manchester, United Kingdom, 21. Regensburg University Hospital, Regensburg, 22. Department of Nephrology, CHU de Montpellier, Montpellier, France, 23. Schneider Children's Medical Center of Israel, Petah-Tikva, 24. Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, 25. Apellis Pharmaceuticals, Inc, Waltham, MA, 26. Swedish Orphan Biovitrum AB, Stockholm

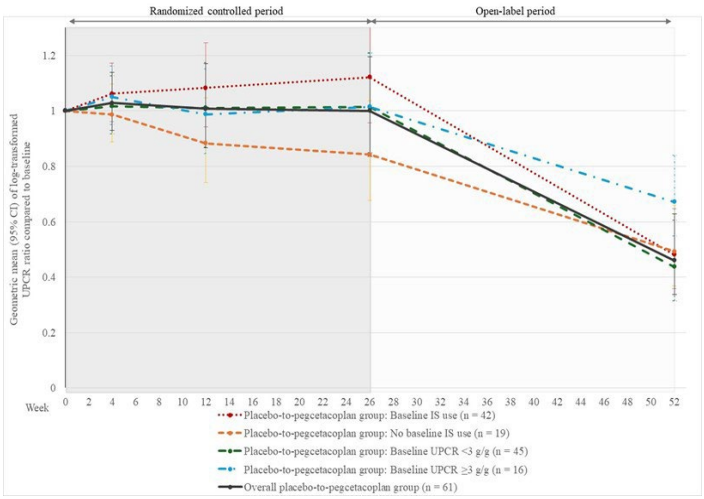
Background: Pegcetacoplan, a targeted C3/C3b inhibitor, has shown significant efficacy in reducing proteinuria and stabilizing kidney function in patients with C3 glomerulopathy (C3G) and primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN). The phase 3 VALIANT trial (NCT05067127) evaluated pegcetacoplan over a 26-week randomized controlled period (RCP) followed by a 26-week open-label period (OLP), during which all patients received pegcetacoplan. This analysis focuses on sustained efficacy, safety, and subgroup responses.

Methods: During the RCP, patients received pegcetacoplan (n = 63) or placebo (n = 61). In the OLP, all patients received pegcetacoplan-to-pegcetacoplan, n = 59; placebo-to-pegcetacoplan, n = 55). Efficacy was assessed by changes in proteinuria (urine protein-to-creatinine ratio [UPCR]) and estimated glomerular filtration rate (eGFR). Safety and treatment-emergent adverse events (TEAEs) were monitored.

Results: Pegcetacoplan-treated patients achieved robust proteinuria reductions by week 26 (mean [95% CI] UPCR change: –68.3% [–75.7, –58.4]), with 20 (31.8%) patients achieving complete remission (≤0.5 g/g), and 11 (17.5%) achieving normalization (≤0.2 g/g). Proteinuria reductions were sustained at week 52 (–67.2% [– 75.8, –55.4]). Placebo-to-pegcetacoplan patients experienced similar reductions during the OLP (week 52: –51.3% [–62.1, –37.5]). At week 52, 54.0% of pegcetacoplan-to-pegcetacoplan patients and 41.0% of placebo-to-pegcetacoplan patients achieved ≥50% proteinuria reduction. Subgroup analyses showed consistent proteinuria reductions regardless of baseline nephrotic proteinuria or immunosuppressant use (Figure). eGFR remained stable in the pegcetacoplan group (week 52: –3.7 [2.7] mL/min/1.73 m²), while placebo patients showed eGFR stabilization after switching to pegcetacoplan. TEAEs were mostly mild or moderate, with improved tolerability over time. No new safety signals were identified.

Conclusion: Pegcetacoplan demonstrated sustained efficacy in reducing proteinuria and stabilizing kidney function over 52 weeks, regardless of baseline proteinuria or immunosuppressant use. Safety outcomes were consistent with prior studies, supporting pegcetacoplan as a durable treatment option for C3G and primary IC-MPGN.





SO-24

Prediction and outcome of recurrent membranous nephropathy after kidney transplantation – data from the Swiss Transplant Cohort Study

Dr. Laila-Yasmin Mani [1], Mr. Matthias Berthold [2], Dr. Jaromil Frossard [3], Prof. Pierre-Yves Bochud [4], Prof. Thomas Müller [5], Prof. Thomas Schachtner [6], Prof. Michael Dickenmann [7], Prof. Dela Golshayan 8, Dr. Fadi Haidar [9], Dr. Carine Hadaya [9], Prof. Daniel Sidler [1], Dr. Isabelle Binet [10], Prof. Elion Hoxha 11, Prof. Uyen Huynh-Do [1]

1. University Hospital Berne, 2. University Clinic of Nephrology and Hypertension, Inselspital Bern, Bern, 3. Data Center of the Swiss Transplant Cohort Study, Basel University Hospital, Basel, Switzerland, 4. Infectious Diseases Service, University Hospital and University of Lausanne., 5. Department of Nephrology, USZ, University Hospital Zurich, Zurich, Switzerland, 6. University Hospital Zurich, 7. University Hospital Basel, 8. Lausanne University Hospital, 9. Department of Nephrology, HUG, University Hospital Geneva, University of Geneva, Geneva, Switzerland, 10. Departement of Nephrology and Transplantation Medicine, Kantonspital St. Gallen, St. Gallen, Switzerland, 11. III. Department of Internal Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background: Membranous nephropathy (MN) is among the commonest causes for nephrotic syndrome worldwide leading to end-stage kidney disease (ESKD) in roughly 40% by 10-15 years. Kidney transplantation represents the therapy of choice. However, recurrence of MN occurs in 40-50% of cases increasing the risk for graft loss. The purpose of this analysis was to identify clinical and biological markers predictive for recurrence of MN after kidney transplantation.

Methods: This study nested within the prospective Swiss Transplant Cohort Study (STCS) identified patients with MN as the cause of ESKD by individual chart review among all adult kidney transplant recipients transplanted for ESKD due to glomerulonephritis in the STCS database. Only biopsy-proven recurrence of MN was considered. The presence of 20 selected single nucleotide polymorphisms (snp) stemming from genome-wide association studies performed within the STCS were compared between patients with and without recurrence using Cox's regression with false discovery rate correction.

Results: Among 943 patients transplanted for glomerulonephritis until 31.12.2020 in the STCS, 29 patients with MN fulfilled inclusion criteria. During a median follow up-time of 6 years, 5 patients (17%) were diagnosed with recurrence of MN on the kidney graft. Baseline characteristics were majorly balanced between the groups of recurrent and non-recurrent patients with however a majority of male donors and by trend more living-related donors among recurrent patients. Patients with recurrence lost their grafts in 1 out of 5 during follow-up. Among 20 snps associated with the development of MN on native kidneys, 3 were found to be significantly associated with MN recurrence on the kidney graft.

Conclusions: This analysis gives insight into characteristics and outcome of patients with recurrent MN after kidney transplantation in Switzerland and suggests genetic markers predictive for disease recurrence.

SO-25

Prediction of NPHS1 Variant Pathogenicity in Monogenic Nephrotic Syndrome

Dr. Luisa Bertgen [1], Dr. Carolin Eul [1], Dr. Blanda Beci [1], Dr. Sucheta Sridhar [1], Prof. Britta George [1]

1. Nephrology, University Hospital Zurich, Switzerland

Steroid resistant nephrotic syndrome (SRNS) is one of the most frequent causes of chronic kidney disease in children and young adults. SRNS is often caused by mutations in one single gene. *NPHS1*, encoding for the slit diaphragm (SD) protein Nephrin is the first to be identified as a cause for monogenic kidney disease. Loss-of-function variants of *NPHS1* cause congenital nephrotic syndrome, typically requiring renal replacement therapy within the first year of life. To date, more than 200 pathogenic variants have been described, most of them missense variants. However, the underlying pathogenic mechanisms of these missense variants remain incompletely understood. Therefore, a systematic structure-function analysis of 21 different Nephrin missense variants, all (likely) pathogenic *as stated by ClinVar* was performed. We therefore generated MDCKII cell lines stably expressing either wild-type Nephrin or missense variants. Immunoblotting (IB) and immunofluorescence microscopy revealed a correlation between protein expression patterns and cellular localization of the protein. Wild-type Nephrin and variants that are fully glycosylated in IB were able to localize to the plasma membrane, whereas variants that were only rudimentary glycosylated failed to reach the plasma membrane. Knockdown of *sns* the Drosophila ortholog of Nephrin results in disruption of the nephrocyte diaphragm (ND). Consistently, we could show that human wild-type Nephrin, as well as fully glycosylated variants were able to (partially) rescue the disruption of NDs, whereas Nephrin variants with glycosylation defects failed. Thus, we may predict the impact of Nephrin variants of unknown pathogenicity on the SD *in vivo* from the presentation in IB.

SO-26

Proteomic Profiling Reveals Complement and Endothelin Pathway Activation in Recurrent IgA Nephropathy

Dr. Matthieu Halfon [1], Prof. Manfredo Quadroni [2], Dr. Samuel Rotman [1], Dr. Mélanie Metrich [1], Prof. Thomas Schachtner [3], Dr. Dorothea Rutishauser [3], Dr. Caroline Wehmeier [4], Dr. Fadi Haidar [5], Prof. Uyen Huynh-Do [6], Dr. Laila-Yasmin Mani [6], Dr. Christian Bucher [7], Prof. Fadi Fakhouri [1], Prof. Manuel Pascual [1], Prof. Dela Golshayan [1]

1. Lausanne University Hospital, 2. University of Lausanne, 3. University Hospital Zurich, 4. University Hospital Basel, 5. Geneva University Hospitals, 6. University Hospital Berne, 7. Kantonsspital St. Gallen

IgA nephropathy (IgAN) is the most common glomerulonephritis (GN) leading to kidney transplantation in Switzerland. As with other forms of GN, patients transplanted for IgAN (IgAN-KTx) are at risk of disease recurrence in the graft. Recurrence is associated with significantly worse graft outcomes compared to non-recurrent cases. Moreover, unlike native kidney IgAN, there are currently no approved treatments for recurrent IgAN after transplantation. This study aims to identify potential therapeutic targets for recurrent IgAN in the transplant setting.

Methods: We conducted an untargeted proteomic analysis of kidney allograft biopsies using mass spectrometry. The study compared three control biopsies – from patients transplanted for autosomal dominant polycystic kidney disease (ADPKD) or hypertensive nephropathy without significant graft injury – with three biopsies showing severe recurrent IgA nephropathy (R-IgAN) (characterized by extracapillary proliferation). Protein abundance differences between groups were analyzed using volcano plots and heatmaps. Pathway enrichment analysis was performed using Gene Ontology (GO) annotations, based on results from the proteomic data.

Results: Untargeted proteomics analysis quantified a median of 8,389 (IQR: 7,983–8,652) proteins per samples. Compared to controls, R-IgAN showed significant complement pathway enrichment (Normalized Enrichment Score: 1.68; adj. p = 0.03), with overabundance of membrane attack complex proteins and CFHR5. in addition, protein abundance analysis showed a significantly higher abundance of endothelin receptor A in R-IgAN compared to controls ($\log_2$ fold change: 2.3; p = 0.008).

Conclusion: To our knowledge, this is the first study to report an enhanced proteomic signature of key complement proteins in kidney allografts affected by recurrent IgAN. This finding is important, as complement inhibitors are already approved for use in native IgAN and could potentially be repurposed for recurrent disease. Similarly, endothelin receptor A – recently targeted by sparsentan, a novel therapy for native IgAN – was also overabundant in recurrent IgAN, suggesting a possible therapeutic benefit.

SO-27

Regression of proteinuria during pregnancy in women with proteinuric nephropathy: impossible or uncommon?

Dr. Domenico Cozzo [1], Dr. Valentina Forni Ogna [2], Dr. Eileen DM Gallery [3], Prof. Bruno Vogt [4], Dr. Claudia Ferrier Guerra [3]

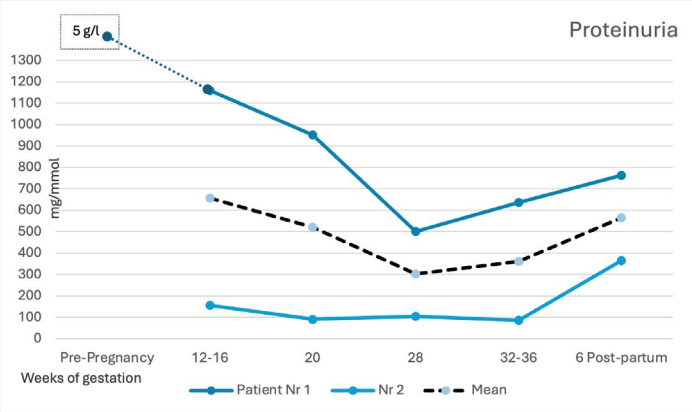
1. Nephrology and Hypertension Division, University Hospital Geneva (HUG), Geneva, Switzerland, 2. Service of Nephrology, Ente Ospedaliero Cantonale, Ticino, Switzerland, 3. Nefrocentro Ticino, 4. University Hospital Bern

Background: In healthy women, pregnancy is associated with a physiological increase in glomerular filtration rate (GFR). In women with pre-existing proteinuric nephropathy, proteinuria often increases during pregnancy, boosting feto-maternal risks and renal complications. However, regression of pre-existing proteinuria during pregnancy in patients with stable nephropathy and preserved renal function, has been seldom reported in literature. The underlying mechanisms are unclear, but the possibility of proteinuria remission could change the approach to proteinuric nephropathy in pregnancy.

Cases-study: We report the case histories of two pregnant women with proteinuric nephropathy who attended our renal outpatient clinic in the first trimester of gestation, because of a significant risk for feto-maternal complications. Patient Nr.1 suffered from primary FSGS and patient Nr.2 had proven diabetic nephropathy. Both patients had undergone in-vitro fertilization. Patient Nr.1 was treated with LMW-heparin throughout pregnancy and patient Nr.2 received labetalol for pre-existing hypertension and low-dose aspirin.

Results: In the first trimester of pregnancy, clinical examination of both patients was unremarkable with blood pressure (BP) within the normal range. No evidence of liver disease was found. Laboratory data confirmed normal renal filtration function and significant proteinuria. Investigations revealed a reduction in creatinine (secondary to the physiological pregnancy-related increase in GFR). By contrast, initial proteinuria decreased progressively during the entire gestation and returned close to pre-pregnancy levels in the postpartum period (Table 1, Figure 1).

Conclusions: Regression of proteinuria during pregnancy is uncommon, but not impossible in the presence of stable kidney disease and normal renal function. Many factors may contribute to reduction of proteinuria, including improved patient lifestyle, better dietary/treatment compliance, optimal BP and glycemic control. A possible pathophysiological mechanism could be the activation of renal reserve of normal nephrons, which in turn reduces hyperfiltration burden in the affected glomeruli, thus resulting in reduced protein leakage.



	Proteinuria (protein/creatinine, mg/mmol)					
wks	*Pre-Pregnancy*	*12-16*	*20*	*28*	*32-36*	*Post-Partum (6 wks)*
Nr 1	5 g/L	1158	951	500	636	762
Nr 2	301	155	90	104	85.7	365
	Plasma Creatinine (µmol/l)					
wks	*Pre-Pregnancy*	*12-16*	*20*	*28*	*32-36*	*Post-Partum (6 wks)*
Nr 1	unknown	36.4	37.3	36	38.6	47.8
Nr 2	96	66.3	66.3	66.9	81.7	83.1

wks = weeks of gestation

SO-28

The use of SGLT-2 inhibitors in kidney transplant recipients with diabetes: a single-centre experience

Dr. Patrizia Amico [1], Ms. Katarina Liskova [1], Dr. Caroline Wehmeier [1], Dr. Matthias Diebold [1], Prof. Patricia Hirt-Minkowski [1], Prof. Stefan Schaub [1]

1. University Hospital Basel

Background: Sodium-glucose co-transporter-2 inhibitors (SGLT-2i) have shown to improve cardiorenal outcomes in patients with and without diabetes. Evidence on the efficacy and safety of SGLT-2i in kidney transplant recipients (KTRs) is limited since this subgroup of patients was excluded from the main outcome studies due to concerns related to risk of infection. We present the results of SGLT-2i use in KTRs with type 2-diabetes or new-onset diabetes mellitus after transplantation (NODAT) at the University Hospital Basel.

Methods: In this retrospective analysis, 102 KTRs with type 2 diabetes/NODAT and SGLT-2i treatment were included. We evaluated the following outcomes: estimated glomerular filtration rate using CKD-EPI (eGFR), hemoglobulin (Hb), glycated hemoglobin (HbA1c), body mass index (BMI), uric acid, urine protein-creatinine ratio/urine albumin-creatinine ratio (UPCR/UACR), adverse events (UAEs), and the reason for treatment discontinuation.

Results: Allograft function was preserved over a median follow-up of 12.3 months (range 2.2-74) and until end of follow-up (EFU): baseline; 53ml/min/1.73 m^2 ± 17 vs. EFU; 52ml/min/1.73 m^2 ± 19, p = 0.96). HbA1c decreased by 0.7% (baseline: 7.7% ± 1.5 vs. EFU 7.0% ± 1.2, p <0.0001) and Hb improved (baseline: 128 g/l ± 18 vs. EFU: 136 g/l ± 24, p <0.0001). No significant changes were observed regarding uric acid and UPCR/UACR. BMI showed a non-significant reduction (baseline: 28.2 kg/m^2 ± 4.5 vs. EFU: 27.8 ± 4.8 kg/m^2, p = 0.2). UAEs occurred in 30/102 (29%) of KTRs: urinary tract infections (n = 11), skin infections (n = 10), and blood pressure drops (n = 4), hypoglycemia (n = 3), metabolic acidosis (n = 1), and acute pancreatitis (n = 1). The KTR's age was independently associated with a higher risk of UAEs (OR 1.58, p = 0.03). The rate of SGLT-2i discontinuation was 12.7% (13/102).

Conclusions: SGLT-2i in KTRs appear to be an effective medication with no negative impact on allograft function. The predominant UAE was infection-related, and risk of UAE significantly increased with recipient's age.

SO-29

Urinary biomarker analysis reveals rapid intra-renal anti-inflammatory and anti-fibrotic effects of sparsentan in IgA nephropathy (IgAN) in the SPARTAN study

Dr. Stéphane Genoud [1]

1. CSL Vifor

Background: SPARTAN (NCT04663204) is an experimental medicine study evaluating sparsentan (SPAR), a dual endothelin and angiotensin receptor antagonist, in adults newly diagnosed with IgA nephropathy (IgAN). The study uses a biomarker-focused approach and includes repeat kidney biopsy. Prior data showed ~70% reduction in proteinuria over 24 weeks.

Methods: Twelve adults with biopsy-confirmed IgAN within 6 months, proteinuria ≥0.5 g/day, eGFR ≥30 mL/min/1.73 m^2, and no ACEi/ARB use in the past year were enrolled. SPAR treatment lasts 110 weeks. One patient discontinued before 24 weeks due to hypotension. Urinary biomarkers (inflammation, fibrosis, B cell and complement activation) were measured by ELISA and normalized to urine creatinine at baseline, 6, 12, and 24 weeks.

Results: In 11 patients, SPAR led to rapid and sustained reductions in urinary biomarkers by week 12. Protein-protein interaction mapping revealed close relationships among affected biomarkers, suggesting coordinated modulation of intra-renal inflammatory and fibrotic pathways by SPAR. Notable reductions were observed in urinary sCD163 and IL6, as well as in BAFF and C5b9, indicating effects on B cell and complement activation.

Conclusion: Dual endothelin and angiotensin receptor antagonism with SPAR modulates key intra-renal pathways beyond haemodynamic effects. These include inflammation, fibrosis, B cell, and complement activation, potentially limiting the consequences of IgA immune complex deposition in both glomerular and tubular compartments.

Figure 1B: Percent (SEM) change from baseline in urinary sCD163, IL-6, BAFF & C5b-9 over 24 weeks of SPAR treatment

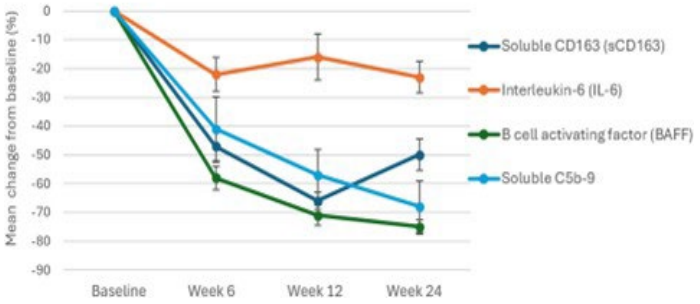


Figure 1A	n	Change from baseline at Week 12 % (SEM)
Alpha-2 macroglobulin	11	-83 (8)
B cell activating factor (BAFF)	9	-71 (7)
Chitinase-3-like protein-1 (CHI3L1; YKL-40)	7	-71 (11)
Clusterin	11	-47 (12)
C-X-C motif chemokine ligand-10 (CXCL10)	6	-51 (15)
C-X-C motif chemokine ligand-16 (CXCL16)	11	-18 (9)
Growth differentiation factor-15 (GDF-15)	11	-46 (7)
Interleukin-6 (IL-6)	7	-16 (16)
Monocyte chemoattractant protein-q (MCP-1)	11	-23 (9)
Plasminogen	11	-85 (5)
Soluble C5b-9	9	-57 (18)
Soluble CD163 (sCD163)	11	-66 (6)

* Patients excluded from analysis if baseline biomarker concentration lower than second lowest calibration point on standard curve

ELEVATOR PITCH

EP-01

Isolated v-lesions" do not show molecular rejection, but in combination with microvascular inflammation, increase the probability of molecular mixed rejection

Dr. Evelyn Kowarik [1], Dr. Lukas Weidmann [2], Mr. Dusan Harmacek [2], Dr. Kai Castrezana Lopez [2], Dr. Elena Rho [2], Dr. Florian Westphal [2], Dr. Kerstin Hübel [3], Prof. Britta George [2], Dr. Ariana Gaspert [4], Ms. Birgit Helmchen [4], Dr. Petra Hruba [5], Dr. Eva Girmanova [6], Prof. Ondrej Viklicky [6], Prof. Thomas Schachtner [7], Dr. Seraina von Moos [1]

1. Department of Nephrology, Cantonal Hospital Luzern, Luzern, Switzerland, 2. Nephrology, University Hospital Zurich, Switzerland, 3. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 4. Department of Pathology and Molecular Pathology, University Hospital Zurich, 5. Institute for Clinical and Experimental Medicine, Transplant Laboratory, 6. Institute for Clinical and Experimental Medicine, Transplant Laboratory, IKEM, Prague, 7. University Hospital Zurich

Background: The threshold for intimal arteritis (v-lesion) is low, and detection of v1 is sufficient for a diagnosis of TCMR Grade II-III, and in the presence of DSA for a diagnosis of probable AMR. Banff 2024 questions the significance of so-called isolated v-lesions when tubulointerstitial inflammation or microvascular inflammation is absent. Biopsy-based transcript diagnostics might help with clarification.

Methods: We analyzed 675 kidney allograft biopsies assessed by histology and biopsy-based transcript diagnostics using the Molecular Microscope Diagnostics System (MMDx) platform from two centers (Zurich and Prague). 133 kidney allograft biopsies with v-lesions (isolated v-lesion, n = 32; v-lesion with TCMR/Borderline, n = 10; v-lesion with AMR/MVI, n = 64; and v-lesion with mixed rejection, n = 27) were compared to 542 biopsies without v-lesions (no rejection, n = 244; TCMR/Borderline, n = 42; AMR/MVI, n = 228; and mixed rejection, n = 28).

Results: Isolated v-lesions showed molTCMR in 1/32 and molAMR in 1/32 cases, comparable to non-rejection (11/244, p = 0.25; 19/244, p = 0.94). V-lesions with TCMR/Borderline showed molTCMR in 3/10 (30%) comparable to 13/42 (31%) cases with TCMR/Borderline w/o v-lesions (p = 0.34). Interestingly, v-lesions with AMR/MVI showed molTCMR in 9/64 (14%) compared to only 7/228 (3%) cases with AMR/MVI w/o v-lesions (p <0.001). Among 55 cases with mixed rejection, v-lesions significantly increased the median molTCMR score (0.24 (IQR 0.04-0.77) vs 0.06 (IQR 0.01-0.41), p = 0.02), with no difference in AMR score (0.37 (IQR 0.08-0.8) vs 0.37 (0.15-0.84), p = 0.6). MolAKI categories were consistently higher in biopsies with v-lesions across all groups.

Conclusion: V-lesions are associated with molAKI. With respect to rejection, biopsies with isolated v-lesions are molecularly comparable to non-rejection biopsies, supporting the new Banff 2024 category of "isolated v" instead of TCMR grade II-III. Interestingly, v-lesions appear to be a driver of molTCMR among cases with microvascular inflammation, but not tubulointerstitial inflammation. Biopsy-based transcript diagnostics have the potential to clarify mixed rejection phenotypes in the presence of v-lesions.

EP-02

Acute kidney injury after catheter-directed thrombolysis versus thrombo-aspiration by AngioJet in patients with acute lower limb ischaemia

Dr. Antonio Ulpiano [1], Mrs. Melanie Saul [2], Dr. Céline Deslarzes [3], Dr. Elisabeth Côté [3], Dr. Sebastien Déglise [3], Prof. Menno Pruijm [4]

1. Service de néphrologie et d'hypertension, Centre hospitalier universitaire vaudois, Lausanne., 2. University of Lausanne, 3. Service of Vascular Surgery, Lausanne University Hospital, Lausanne, 4. Service of nephrology and hypertension, Department of Medicine, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland;

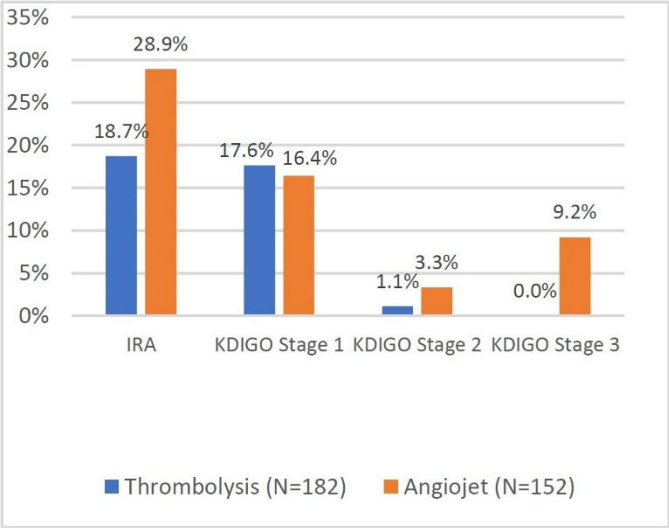
Background: Catheter-directed thrombolysis (CDT) and AngioJet percutaneous pharmaco-mechanical thrombectomy (APMT) are endovascular treatments of acute lower limb ischemia (ALI). Acute kidney injury (AKI) is a recognized complication, but its prevalence has been insufficiently studied. The aim of this study was to compare the rates of AKI after CDT and APMT in patients suffering from ALI.

Methods: In this retrospective monocentric observational study, we included all ALI patients treated by CDT or PMT between January 2010 and December 2020 in the Centre Hospitalier Universitaire Vaudois (CHUV). AKI was evaluated using values of serum creatinine pre- and post-intervention and at discharge. Association of CDT and APMT with AKI was further explored with baseline demographic data, ALI stage, interventional data and hemolysis markers.

Results: A total of 182 patients (aged 68 y, 79.1% men) were treated by CDT and 152 (aged 70.8 y, 63.8% men) by APMT. There were more hypertensive patients in the CDT group (75.8 vs 62.8%, p = 0.012); other co-morbidities were similar. ALI stages were more severe in the APMT group (Rutherford I: 59.2% in APMT vs 59.3% in CDT, IIa 23 vs 35.2%%, IIb 17.8 vs 5.5%, p <0.001), but needed less reinterventions (34.2% vs 66.5%, p <0.001). The AKI rate was significantly higher in the APMT group (28.9% vs 18.7%, p <0.001). KDIGO stage III AKI occurred only in the APMT group (9.2% vs. 0%, p <0.001, see Figure). Elevation of hemolysis markers was higher in the APMT group (15.1% vs 2.2%, p <0.001).

Conclusion: In our study APMT treatment of ALI was associated with a significantly higher rate of AKI compared to CDT.

This risk should be balanced against the possibility to use APMT in more severe ALI, its higher success rate and lower need for reinterventions. Patient-related factors associated with AKI after endovascular treatment of ALI need further study.



EP-03

Donor-derived metatastatic tumor presenting six years after kidney transplantation

Dr. Unal Tokkuzun [1], Prof. Thomas Schachtner [2], Dr. Vittoria Espeli [3], Dr. Jessica Barizzi [4], Dr. Milo Frattini [4], Dr. Francesca Molinari [4], Dr. Alexandra Valera [4], Dr. Jennifer Scotti Gerber [1]

1. Ospedale Regionale di Lugano EOC, Department of nephrology, Lugano, Switzerland, 2. Department of Nephrology, University Hospital Zürich, Zürich, Switzerland, 3. Oncology Institute of Southern Switzerland, 4. Cantonal pathology Institute EOC, Bellinzona

Background: Donor-derived tumors are a rare but serious complication of kidney transplantation. We report a case of a 67-yo kidney transplant recipient who developed a donor-derived tumor six years after transplantation.

Methods: The patient was found to have hepatic lesions, peritoneal carcinomatosis, and a lesion within the transplanted kidney, detected incidentally on a CT scan. He was asymptomatic but rapidly presented ascites. Immunosuppression consisted of belatacept (due to tacrolimus-related neurotoxicity) and mycophenolate mofetil. Diagnostic workup included imaging, multiple biopsies (peritoneal and liver metastasis, renal graft lesion, and normal graft parenchyma), and molecular analyses to determine tumor origin.

Results: Biopsy of a peritoneal metastasis revealed papillary adenocarcinoma. Microsatellite analysis of ascitic fluid and the biopsy specimen displayed a discordant profile compared with the patient, raising concerns about tumor heterogeneity or sample exchange. Further biopsies of the graft lesion and adjacent non-tumoral parenchyma demonstrated identical molecular characteristics, distinct from the recipient's genotype, confirming the donor-derived origin. Immunohistochemical analysis suggetsed adenocarcinoma features, most likely of pulmonary origin. It is hypothesized that the donor harbored a clinically silent pulmonary carcinoma with micrometastasis to the kidney, which later developed into overt malignancy in the recipient. Other recipients from the same donor included a liver recipient, who died shortly after transplantation from unrelated causes, and another kidney recipient without any oncological history. The patient was treated with 2 cycles of carboplatin, well tolerated but with progression disease. We administered a second line chemotherapy (paclitaxel) with clinical benefit (ascites resolution). Given the patient's wish to avoid returning to dialysis and the aggressiveness of the disease, for which stopping immunosuppression was not expected to improve prognosis, monotherapy with belatacept was maintained.

Conclusions: This case highlights the challenges of donor-derived malignancies and the importance of molecular investigations to guide management and ensure the safety of other organ recipients.

EP-04

It is never too late – recovery of kidney function with complement inhibition

Dr. Jan Bruegger [1], Prof. Andrea Vicelli [1], Dr. Petra Rhyn [1], Dr. Bernhard Hess [2], Prof. Thomas Müller [1]

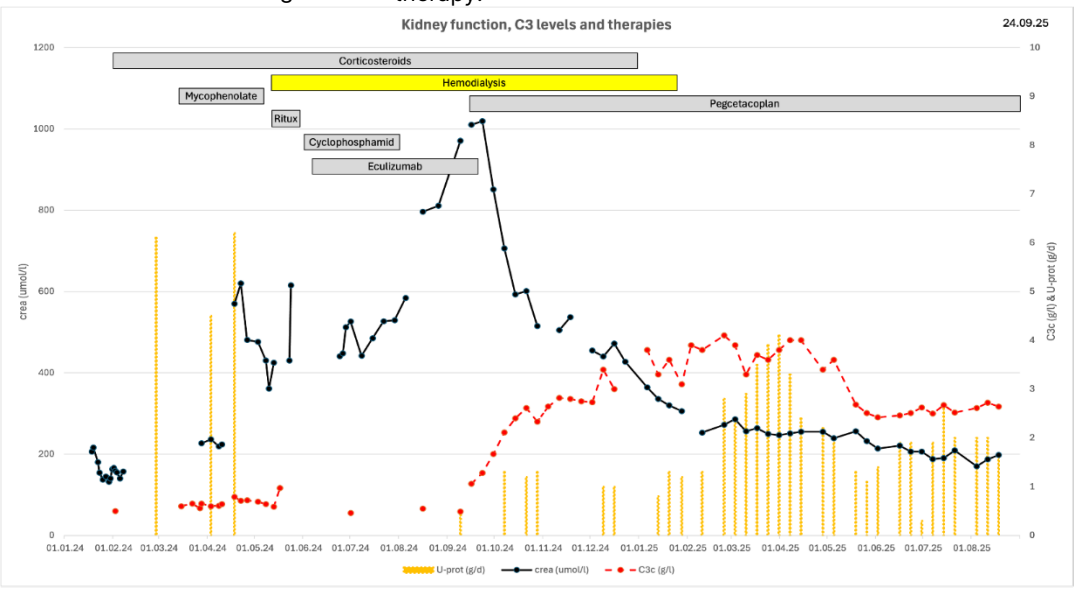
1. Nephro am See Praxis und Dialyse, Seestrasse 85, 8810 Horgen, 2. Hirslanden, Innere Medizin, Bellariastrasse 38, 8038 Zürich

Background: The decision to continue, to change or to stop immunosuppressive treatments in situations of unresponsive and progressive renal deterioration is a well known clinical dilemma, for patients and their doctors. This decision becomes even more difficult when the patient has reached a state when dialysis is necessary and biopsy findings are inconclusive. The following case and discussion of the literature presents diagnostic and therapeutic approaches in this distressing scenario.

Method: Retrospective analysis of a clinical case with regular monitoring of markers of kidney function and complement activation during different treatment approaches over 2 years and literature review of similar scenarios.

Results: Beginning of 2024 a 40 yr old, previously healthy patient presented with acute onset of weight gain, edema and tiredness. The tests showed renal insufficiency (eGFR 24 ml/min/1.73m2), nephrotic syndrome and microhematuria. Otherwise, no abnormalities for platelets, ANA, p/c-ANCA, anti-GBM, anti-PLA2R, anti-dsDNA, C3-nephritis, hepatitis serologies, viral serologies (apart from indeterminate EBV-IgM and low C3 levels) were seen. Two biopsies showed a proliferative IC-GN, with a differential of infection-associated or very early MPGN-IC (IF IgG 2+, C3 3+). The figure shows the immunosuppressive treatments: steroids, Mycophenolate, Rituximab, Cyclophosphamide and Eculizumab. All failed and the patient finally required dialysis 5 months after her first presentation. Despite 4 months of ongoing dialysis and against significant resistance finally a treatment with anti-C3 complement inhibitor Pegcetacoplan was started. 3 months later dialysis could be stopped and the patients has been now off dialysis for more than 8 months with a stabilized GFR between 25 to 30 ml/min. The literature does not describe a similar case of recovery after such a long dialysis period.

Conclusions: It is never too late – at least in situations of persistent complement activation a trial of specific inhibitor therapies might be justified, despite ongoing and long-term dialysis therapy.



EP-05

Long-Term Efficacy and Safety of Palopegteriparatide Treatment in Adults With Chronic Hypoparathyroidism: 4-Year Results From the Phase 2 PaTH Forward Trial

Prof. Andrea Palermo [1], Prof. Aliya Khan [2], Dr. Mishaela Rubin [3], Prof. Peter Schwarz [4], Prof. Bart Clarke [5], Prof. Uberto Pagotto [6], Dr. Elena Tsourdi [7], Prof. Filomena Cetani [8], Prof. Rajesh Jain [9], Dr. Carol Zhao [10], Dr. Michael Ominsky [10], Dr. Bryant Lai [10], Dr. Jenny Ukena [10], Dr. Christopher T. Sibley [10], Dr. Aimee D. Shu [10], Prof. Lars Rejnmark [11], Dr. Jean-Philippe Bertocchio [12]

1. Unit of Metabolic Bone and Thyroid Disorders, Fondazione Policlinico Campus Bio-medico, Rome, Italy and Unit of Endocrinology and Diabetes, Campus Bio-medico University, Rome, Italy, 2. McMaster University, Hamilton, ON, Canada, 3. Columbia University, New York, NY, USA, 4. Rigshospitalet, Copenhagen, Denmark, 5. Mayo Clinic, Rochester, MN, USA, 6. Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna, Italy, 7. Technische Universität Dresden Medical Center, Dresden, Germany, 8. University of Pisa, Department of Clinical and Experimental Medicine, Endocrine Unit, Pisa Italy, 9. University of Chicago, Chicago, IL, USA, 10. Ascendis Pharma Inc, Palo Alto, CA, USA, 11. Aarhus University Hospital, Aarhus N, Denmark, 12. Pitié-Salpêtrière Hospital, Paris, France

Background: Palopegteriparatide is a prodrug of PTH (1-34), administered once daily, designed to provide active PTH within the physiological range for 24 hours/day. It is approved in the US, EU, and several other countries.

Methods: This analysis investigated the efficacy and safety of palopegteriparatide in adults with chronic hypoparathyroidism through week 214 of PaTH Forward, a phase 2 trial with a 4-week randomized, double-blind, placebo-controlled period, followed by open-label extension through week 266.

Results: At week 214, 95% (56/59) of participants remained in the trial; of those, 93% were independent from conventional therapy (no active vitamin D and ≤600 mg/day elemental calcium) and 98% had normocalcemia (2.07-2.64 mmol/L). Mean bone turnover markers C-terminal telopeptide of type 1 collagen (CTx) and procollagen type 1 N-terminal propeptide (P1NP) increased from low end of normal at baseline, peaked by week 26, and declined thereafter, remaining stable above baseline. Elevated baseline mean BMD Z-scores trended towards age- and sex-matched norms at lumbar spine, femoral neck, and total hip, largely stabilized after week 26 and remained above zero. At week 214, mean (SD) eGFR was 86.0 (21.7) mL/min/1.73 m^2, reflecting a mean (SD) increase of 7.6 (13.7) mL/min/1.73 m^2 from baseline. Mean (SD) 24-hour urine calcium levels normalized with palopegteriparatide and were maintained (≤6.2 mmol/day). TEAEs were mostly mild/moderate; no new safety signals were identified.

Conclusions: These results demonstrate sustained efficacy and safety of palopegteriparatide in adults with chronic hypoparathyroidism through week 214 of PaTH Forward, suggesting continued benefits in skeletal dynamics and renal function.

EP-06

Long-term prediction of renal function decline using diffusion MRI in kidney transplant and CKD patients

Dr. Aurélie Huber [1], Ms. Lindsey Crowe [2], Prof. Sophie de Seigneux [1], Dr. Thomas De Perrot [2], Prof. Jean-Paul Vallée [2], Dr. Lena Berchtold [1]

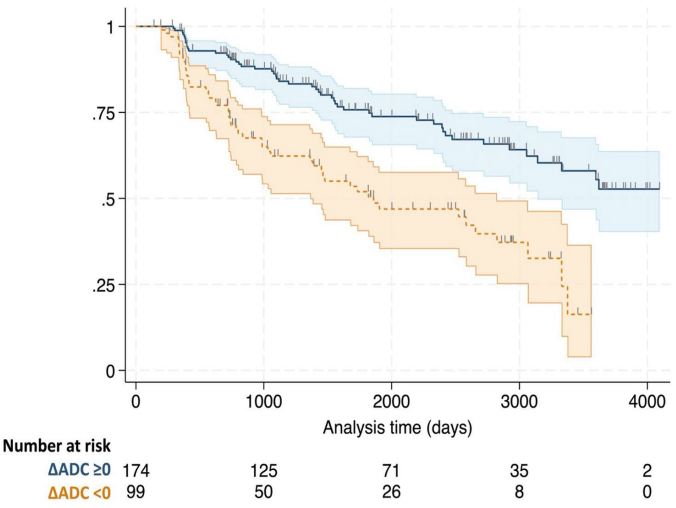
1. Nephrology and Hypertension Division, University Hospital Geneva (HUG), Geneva, Switzerland, 2. Department of Radiology, HUG, University Hospital Geneva, University of Geneva, Geneva, Switzerland

Introduction: Early identification of patients at risk for renal function decline is crucial for personalized management. While interstitial fibrosis is a key prognostic marker, it is typically assessed via invasive biopsy. Diffusion-weighted MRI offers a promising non-invasive alternative. In previous work[1], we demonstrated that the cortico-medullary difference in apparent diffusion coefficient (ΔADC) correlates with fibrosis severity and independently predicts renal function decline over 2 years. This study aims to validate these findings in a larger cohort with up to 10 years of follow-up and subgroup analyses.

Methods: This prospective study included kidney transplant recipients and patients with chronic kidney disease (CKD) undergoing clinically indicated renal biopsy. All participants underwent diffusion MRI within one week. Renal function was tracked annually. The primary endpoint was rapid renal function decline, defined as either ≥30% reduction in eGFR or initiation of dialysis or transplantation. Univariate survival analyses and multivariate Cox regressions were performed, adjusting for baseline eGFR (<45 vs. ≥45 mL/min/1.73 m²) and proteinuria (<0.3 vs. ≥0.3 g/24h), both in the overall cohort and in subgroups.

Results: A total of 299 patients were included (70% transplant recipients, 30% CKD), with a median age of 52 years. Median follow-up was 9.1 years (95% CI: 7.2–11.0). Rapid decline occurred in 101 patients (34%). Kaplan-Meier analysis showed that patients with ΔADC<0 had a 2.5-fold increased risk of functional decline or need for dialysis/transplantation (95% CI: 1.70–3.75). In multivariate analysis, ΔADC remained a strong independent predictor (HR 2.14, p <0.001). Subgroup analyses confirmed ΔADC as predictive in both CKD (p = 0.012) and transplant recipients (p <0.001), although statistical significance in multivariate models was retained only in the transplant subgroup (HR 2.23, p <0.001).

Conclusion: ΔADC measured by diffusion MRI independently predicts long-term renal function decline. This imaging biomarker may provide a valuable non-invasive tool for risk stratification, particularly in kidney transplant recipients.



EP-07

Metabolic risk after living kidney donation: An analysis of the Swiss Organ Living-Donor Health Registry

Dr. Joana Krättli [1], Ms. Deborah Buess [1], Dr. Matthias Diebold [1], Dr. Caroline Wehmeier [1], Prof. Daniel Sidler [2], Prof. Dela Golshayan [3], Dr. Tobias Zingg [4], Prof. Sophie de Seigneux [5], Dr. Fadi Haidar [6], Dr. Isabelle Binet [7], Dr. Alexander Ritter [7], Dr. Kerstin Hübel [8], Dr. Fabian Rössler [9], Prof. Jürg Steiger [1], Prof. Patricia Hirt-Minkowski [1]

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland, 2. Department for Nephrology and Hypertension, University Hospital Insel, Berne, Switzerland, 3. Transplantation Center, Department for Medicine, Lausanne University Hospital (CHUV), Lausanne, Switzerland, 4. Department of Visceral and Transplant Surgery, Lausanne University Hospital (CHUV), Lausanne, Switzerland, 5. Nephrology and Hypertension Division, University Hospital Geneva (HUG), Geneva, Switzerland, 6. Department of Nephrology, HUG, University Hospital Geneva, University of Geneva, Geneva, Switzerland, 7. Clinic for Nephrology and Transplantation Medicine, HOCH Health Ostschweiz, Cantonal Hospital St. Gallen, St. Gallen, Switzerland, 8. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 9. Department of Surgery and Transplantation, University Hospital Zurich, Zurich, Switzerland

Background: Due to persistent organ shortage worldwide, the selection criteria for living kidney (LK) donors have broadened to include elderly donors, and those with co-morbidities as hypertension and obesity. As little is known about the metabolic health after living kidney donation (LKD), this prospective, multi-center cohort study explored metabolic changes among LK donors, with a particular focus on weight trajectories.

Methods: We analyzed metabolic and cardiovascular parameters before and after LKD in 466 consecutive LK donors recorded in the Swiss Organ Living-Donor Health Registry between January 2018 and August 2022. Outcomes included weight, blood pressure, hemoglobin A1c levels, and the occurrence of new-onset type 2 diabetes mellitus (T2DM), arterial hypertension, and cardiovascular diseases. Donors were stratified by pre-donation body mass index (BMI) and by post-donation weight change.

Results: Obese donors (BMI ≥30 kg/m²) more frequently had pre-existing hypertension at baseline than non-obese donors (31.6% vs. 18.3%, p = 0.03). During follow-up (median 2.9 years), 6% of LK donors developed arterial hypertension, 2.6% developed cardiovascular disease, and 1.1% developed T2DM. Obese donors had a higher incidence of post-donation T2DM than non-obese donors (p = 0.01). Changes in BMI post-donation were not correlated with age or pre-donation BMI (Figure 1). Donors with post-donation weight gain had numerically slightly higher and statistically different follow-up blood pressure values (p≤0.006), but no clear differences in rates of new-onset hypertension or T2DM were observed between weight-change groups.

Fig. 1

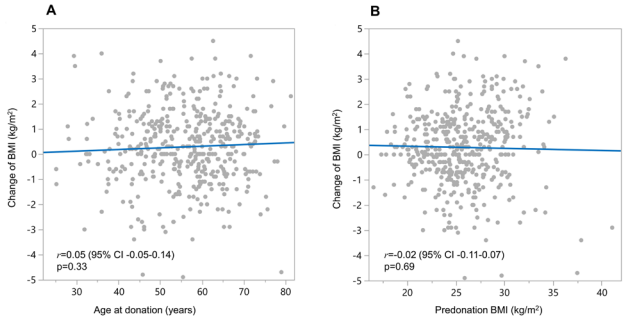


Figure 1: The relationship for age at donation (A) and predonation BMI (B) with change of BMI after LKD is visualized in correlation plots.

Conclusions: This exploratory analysis suggests that LKD is generally metabolically safe. While metabolic changes were modest overall, obesity at the time of donation was associated with a slightly higher frequency of post-donation T2DM, underscoring the importance of counseling on lifestyle modification before donation, particularly for individuals with elevated BMI.

EP-08

Metabolic safety of long-term citrate therapy in high-risk kidney stone formers

Dr. Alexander Ritter [1], Mrs. Lea Bührer [2], Prof. Daniel G. Fuster [3], Dr. Nasser Dhayat [4], Prof. Olivier Bonny [5], Prof. Gregoire Wuerzner [6], Dr. Thomas Ernandez [7], Dr. Florian Buchkremer [8], Prof. Stephan Segerer [9], Mr. Maximilian Sabev [10], Dr. Daniel S. Engeler [11], Prof. Beat Roth [12], Mrs. Laura Keller [10], Prof. Pietro Manuel Ferraro [13], Prof. Ulrike Held [14], Prof. Nifular Mohebbi [15], Prof. Carsten A. Wagner 16, Dr. Harald Seeger [17]

1. Division of Nephrology and Transplantation Medicine, HOCH Cantonal Hospital St.Gallen, St. Gallen, Switzerland, 2. Centre for Computational Health, Institute of Computational Life Sciences, Zurich University of Applied Sciences (ZHAW), Wädenswil, 3. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 4. Nephrology and Dialysis Care Center, B. Braun Medical Care AG, Hochfelden, Zürich, Switzerland, 5. Service of Nephrology, HFR Fribourg, Fribourg, 6. Service of nephrology and hypertension, Department of Medicine, Lausanne University Hospital and University of Lausanne, Lausanne, 7. Division of Nephrology and Hypertension, University Hospital Geneva, Geneva, 8. Division of Nephrology, Dialysis and Transplantation, Cantonal Hospital Aarau, Aarau, Switzerland, 9. Nephrologie, Kantonsspital Aarau, Aarau, 10. Division of Nephrology, University Hospital Zurich, Zurich, 11. Division of Urology, HOCH Cantonal Hospital St.Gallen, St. Gallen, 12. Department of Urology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 13. Section of Nephrology, Department of Medicine, Università degli Studi di Verona, Verona, Italy, 14. Department of Biostatistics at Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, 15. Department of Nephrology, University Hospital Zürich, Zürich, Switzerland, 16. Institute of Physiology, University of Zurich, Zurich, 17. Institute for Nephrology and Dialysis, Cantonal Hospital Baden, Baden

Background: Citrate is frequently prescribed to kidney stone formers (KSFs), but evidence on long-term metabolic safety is limited. We investigated the impact of extended citrate therapy on metabolic health, urinary stone risk, and stone recurrence in high-risk Swiss KSFs.

Methods: The Swiss Kidney Stone Cohort (SKSC) is a prospective, multicenter study enrolling KSFs and non-stone formers. Baseline blood and urine tests were obtained in all participants; KSFs had repeated assessments over three years with telephone follow-up for stone events. We analyzed 654 KSFs (110 on citrate, 544 without) and 207 controls. Outcomes included anthropometric measures (BMI, body roundness index, waist-to-hip ratio), metabolic markers (HbA1c, glucose, lipids), urinary relative supersaturation ratios by EQUIL2 (calcium oxalate, brushite, uric acid), recurrence, and kidney stone composition.

Results: Body composition remained stable across groups. HbA1c increased in untreated patients but not in citrate users. HDL cholesterol rose in both groups, while LDL declined only with citrate. Urine relative super-saturation ratios showed a stronger fall in brushite among untreated patients, whereas citrate therapy led to a greater decline in uric acid relative supersaturation ratio while the ratio for calcium oxalate declined in a similar fashion in both groups. Recurrence occurred more often in citrate users, with compositional shifts in 43% compared to 30% of untreated patients. No increase in calcium phosphate stones was observed under citrate therapy in patients with repeated analyses of kidney stone composition.

Conclusions: Long-term citrate use was metabolically safe and lowered uric acid relative supersaturation ratio, while untreated patients exhibited stronger reductions in brushite risk. The higher recurrence rate in patients treated with citrate may derive from greater baseline risk. Randomized trials are required

to determine risks and benefits of citrate therapy on top of standard counseling.

EP-09

Molecular Rejection Signals in Chronic-Active T Cell-Mediated Rejection: Histological Drivers and Potential Outcome Implications

Dr. Lukas Weidmann [1], Dr. Petra Hruba [2], Dr. Eva Girmanova [2], Mr. Dusan Harmacek [1], Dr. Kerstin Hübel [3], Dr. Elena Rho [1], Dr. Kai Castrezana Lopez [1], Dr. Ariana Gaspert [4], Ms. Birgit Helmchen [4], Dr. Florian Westphal [1], Prof. Britta George [1], Dr. Seraina von Moos [5], Prof. Ondrej Viklicky [2], Prof. Thomas Schachtner [6]

1. Nephrology, University Hospital Zurich, Switzerland, 2. Institute for Clinical and Experimental Medicine, Transplant Laboratory, IKEM, Prague, 3. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 4. Department of Pathology and Molecular Pathology, University Hospital Zurich, 5. Department of Nephrology, Cantonal Hospital Luzern, Luzern, Switzerland, 6. University Hospital Zurich

Background: Chronic-active T cell-mediated rejection (caTCMR) remains debated within the TCMR continuum. The possible aid of molecular diagnostics in detecting TCMR signatures and potential treatment indications remains underinvestigated.

Methods: This two-center study (total cohort 755 biopsies) analyzed 374 kidney allograft biopsies excluding cases with microvascular inflammation (MVI), antibody-mediated rejection (AMR), or overlapping pathologies, yielding 26 *Banff* -defined caTCMR, 40 borderline/acute TCMR, 177 subthreshold, and 131 negative controls. All biopsies underwent histopathological (*Banff* classification) and transcriptomic (Molecular Microscope Diagnostic System, MMDx) evaluation.

Results: Among the 26 caTCMR cases, those with concomitant acute TCMR showed higher median TCMR classifier scores ($TCMR_{prob}$: 0.54 [0.30, 0.83]) than "pure" caTCMR (0.03 [0.01, 0.28]; p = 0.012). 13 (50%) had $TCMR_{prob}$ >0.2, including 7 (27%) with additional AMR_{prob} >0.2. Molecular sign-outs classified 9/13 (69%) as molecular TCMR and 4/13 (31%) as mixed molecular AMR/TCMR. Within the TCMR continuum, only ti-lesions were independently associated with $TCMR_{prob}$ >0.2 (OR 2.295, 95% CI 1.063-5.433; p = 0.042), while i-IFTA aligned with molecular chronicity (IFTA score). $TCMR_{prob}$, other molecular rejection/injury markers, and histological chronicity were significantly associated with allograft failure.

Conclusion: In conclusion, molecular TCMR in caTCMR is linked to active inflammation (i, t, ti), not i-IFTA- or t-IFTA-lesions. MMDx revealed TCMR and AMR signals in caTCMR, even without MVI. Molecular and histological parameters were outcome relevant. Therefore, molecular diagnostics might support current practices in identifying cases at risk.

EP-10

Prognostic value of proteinuria and kidney function in patients with newly diagnosed multiple myeloma

Mr. Davide Spica [1], Dr. Min Jeong Kim [2]

1. Nephrologie, Kantonsspital Aarau, 2. Kantonsspital Aarau

Background: Renal impairment is a common complication of multiple myeloma (MM), affecting 20 to 50% of patients at diagnosis. We aimed to evaluate the prognostic value of proteinuria and kidney function at the time of MM diagnosis in the era of advanced therapeutic options for MM.

Methods: In a single-center cohort of 110 patients with newly diagnosed MM from 2015 – 2023 clinical and laboratory data were retrospectively analyzed for the effect of various proteinuria and kidney function on the kidney outcome, MM course and patient survival. The statistical analyses were performed using Stata 18 by descriptive statistics and regression modelling.

Results: Acute kidney injury (AKI) was observed in 76 of 110 patients at the MM diagnosis (Table 1). Proteinuria was significantly higher in patients with AKI (PCR 297 vs. 79 mg/mmol, p <0.001). Whereas tubular proteinuria (both alpha1-microglobulin and retinol-binding-protein) was significantly higher in patients with AKI (p <0.001 and 0.009 respectively), glomerular proteinuria (both albumin and IgG) was not different in both groups. After the first-line therapy, which was similar in patients with or without AKI, higher initial tubular proteinuria was significantly associated with lower eGFR (r = -0.755, p = 0.002 for alpha1-microglobulinuria in mg/mmol). The same was also true for the eGFR after the mean follow-up of 3.2 years (r = -0.600, p = 0.017). However, there was no significant association of tubular proteinuria with hematological response and patient survival. Lower initial eGFR was associated with lower patient survival at last follow-up (odds ratio = 1.018, p = 0.025), but not with hematological response.

Conclusions: Our data demonstrate that higher tubular proteinuria at the MM diagnosis correlates with worse kidney function both at diagnosis and on the further course. However, hematological response and patient survival under current therapeutic options did not vary according to the degree of proteinuria.

	Overall (n = 110)	AKI (n = 76)	No AKI (n = 34)	p-value
Age (yrs), mean (SD)	70.0 (10.3)	70.2 (10.6)	69.5 (9.9)	0.74
Sex, No. of male patients (%)	61 (55.5%)	43 (56.6%)	18 (52.9%)	0.72
Baseline creatinine (µmol/l)	77.0 (20.3)	77.7 (18.2)	75.5 (24.7)	0.61
Baseline eGFR CKD-EPI (ml/min/1.73m^2)	79.9 (15.6)	78.8 (14.2)	82.4 (18.2)	0.27
Creatinine at MM diagnosis	201.9 (226.0)	254.1 (254.9)	85.1 (26.1)	<0.001
eGFR CKD-EPI at MM diagnosis	45.9 (26.4)	33.4 (18.3)	73.9 (19.6)	<0.001
AKI, No. of patients (%)	76 (69.1%)			
stage 1	33 (30.0%)			
stage 2	20 (18.2%)			
stage 3	19 (17.3%)			
Kidney replacement therapy	4 (3.6%)			
Pathogenic Kappa-FLC, No of patients (%)	73 (66.4%)	49 (64.5%)	24 (70.6%)	0.53
Pathogenic Lambda-FLC, No of patients (%)	37 (33.6%)	27 (35.5%)	10 (29.4%)	0.53
FCL ratio involved/uninvolved	566.7 (1181.5)	784.2 (1367.0)	80.7 (109.4)	0.003
total Serum calcium (mmol/l)	2.5 (0.5)	2.5 (0.6)	2.3 (0.2)	0.022
Albumin-corrected serum calcium (mmol/l)	2.7 (0.5)	2.8 (0.6)	2.5 (0.2)	0.006
Clinical diagnosis of cast nephropathy	40 (36.4%)	40 (52.6%)	0 (0.0%)	<0.001
Proteinuria (spot-urine ratio to creatinine, mg/mmol)				
Protein to creatinine	230.1 (325.7)	297.3 (354.1)	79.9 (178.0)	<0.001
Albumin ti creatinine	52.0 (185.5)	59.5 (196.7)	35.3 (159.0)	0.53
IgG to creatinine	8.3 (22.6)	10.8 (26.7)	2.9 (4.7)	0.092
alpha 1-MG to creatinine	9.8 (10.5)	12.3 (11.6)	4.1 (3.1)	<0.001
Retinol binding protein to creatinine	1.7 (4.4)	2.5 (5.2)	0.1 (0.2)	0.009
Co-morbidity and medication, No. of patients (%)				
hypertension	64 (58.2%)	45 (59.2%)	19 (55.9%)	0.74
diabetes	13 (11.9%)	9 (12.0%)	4 (11.8%)	0.97
obesity	33 (30.0%)	18 (23.7%)	15 (44.1%)	0.031
smoking	32 (29.4%)	21 (28.0%)	11 (32.4%)	0.64
loop diuretics	6 (5.5%)	4 (5.3%)	2 (5.9%)	0.89
RAASi	45 (40.9%)	33 (43.4%)	12 (35.3%)	0.42
other antihypertensive meds	46 (41.8%)	31 (40.8%)	15 (44.1%)	0.74
NSAR	26 (23.6%)	22 (28.9%)	4 (11.8%)	0.050
Chemotherapy performed, No. of patients (%)	106 (96.4%)	76 (100.0%)	30 (88.2%)	0.002
Bortezomib	75 (68.2%)	54 (71.1%)	21 (61.8%)	0.33
Revlimid	75 (68.2%)	50 (65.8%)	25 (73.5%)	0.42
Melphalan	7 (6.4%)	4 (5.3%)	3 (8.8%)	0.48
Daratumumab	36 (32.7%)	24 (31.6%)	12 (35.3%)	0.70
Cyclophosphamid	15 (13.6%)	12 (15.8%)	3 (8.8%)	0.33
Dexamethason	95 (86.4%)	68 (89.5%)	27 (79.4%)	0.16
Prednisolon	7 (6.4%)	4 (5.3%)	3 (8.8%)	0.48
others	6 (5.5%)	4 (5.3%)	2 (5.9%)	0.89

EP-11

Single-Kidney Transplantation with Discarded Partner Kidney vs. Dual Kidney Transplantation: Results from a National Cohort Study

Ms. Stephanie Näf [1], Mr. Simon Schwab [2], Dr. Isabelle Binet [3], Dr. Alexander Ritter [4], Dr. Max Rieger [5], Prof. Dela Golshayan [6], Dr. Fadi Haidar [7], Dr. Franz Immer [2], Prof. Thomas Schachtner [5], Prof. Stefan Schaub [8], Dr. Thomas Wolff [8], Mr. Rafal Porzucek [9], Dr. Christian Kuhn [3], Prof. Daniel Sidler [10]

1. BESAS Bern Hospital Center for Geriatric Medicine Siloah, Gümligen, Bern, Switzerland, 2. Swisstransplant, 3. HOCH Kantonsspital St. Gallen, 4. Division of Nephrology and Transplantation Medicine, HOCH Cantonal Hospital St.Gallen, St. Gallen, Switzerland, 5. University Hospital Zurich, 6. Lausanne University Hospital, 7. Geneva University Hospitals, 8. University Hospital Basel, 9. Patient Advisory Board, 10. University Hospital Berne

Background: The transplantation of a single kidney, while its partner kidney is discarded despite both having been initially offered (dual-offered, single-transplanted; DOST), represents a missed opportunity to preserve nephron mass and optimize donor utilization. Dual kidney transplantation (DKT) preserves nephron mass by transplanting both kidneys from a marginal donor, but its benefits relative to DOST remain underexplored.

Methods: In this nationwide multicenter cohort (2008–2021), we analyzed 36 DKT and 20 DOST recipients. Both groups were propensity-matched 1:2 to 112 regular single-kidney transplant recipients (RegT) based on donor and recipient characteristics. The primary endpoint was estimated glomerular filtration rate (eGFR) at 12 months. Secondary endpoints included eGFR through 5 years, death-censored graft and patient survival, perioperative metrics, and 12-month quality of life (EQ-5D).

Results: At 12 months, median eGFR was higher in DKT (50.8 ml/min/1.73 m²) than DOST (33.5 ml/min/1.73 m²) or RegT (38.0 ml/min/1.73 m²; p >0.001), with differences sustained through 5 years. Graft and patient survival were similar. DKT involved longer surgery (270 vs. 163 min; p >0.001), greater blood loss (550 vs. 300 ml; p = 0.084), and more transfusions (75% vs. 30%; p = 0.0017) but no increase in delayed graft function or major complications. EQ-5D scores were higher in DKT (85.0) than DOST (70.0) and RegT (71.0; p = 0.048).

Conclusion: DKT is a safe and effective approach for marginal donor kidneys, offering superior graft function and quality of life without added perioperative risk. Broader adoption may reduce unnecessary organ discards and improve transplant outcomes.

EP-12

Sodium bicarbonate and volume retention in metabolic acidosis after kidney transplantation – a post hoc analysis

Mrs. Pierina Sara Staub [1], Mr. David Kronthaler [2], Dr. Anna Wiegand [3], Dr. Suzan Dahdal [4], Prof. Daniel Sidler [4], Prof. Spyridon Arampatzis [4], Dr. Karine Hadaya [5], Dr. Harald Seeger [6], Prof. Rudolf P. Wüthrich [3], Prof. Ulrike Held [2], Prof. Carsten A. Wagner [7], Prof. Nifular Mohebbi [8], Dr. Alexander Ritter [9]

1. Institute of Physiology, University of Zurich, Zurich, Switzerland, 2. Department of Biostatistics at Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, 3. Division of Nephrology, University Hospital Zurich, Zurich, 4. Division of Nephrology and Hypertension, Inselspital, Bern, 5. Clinique des Grangettes, Hirslanden, Geneva, 6. Institute for Nephrology and Dialysis, Cantonal Hospital Baden, Baden, 7. Institue of Physiology, University of Zurich, Zurich, 8. Department of Nephrology, University Hospital Zürich, Zürich, Switzerland, 9. Division of Nephrology and Transplantation Medicine, HOCH Cantonal Hospital St.Gallen, St. Gallen, Switzerland

Background: Metabolic acidosis is common after kidney transplantation and typically managed with sodium bicarbonate (SB). Concerns exist, however, that SB may induce sodium retention and fluid overload. Data in kidney transplant recipients (KTRs) are scarce. This analysis examined the effect of SB on markers of volume status.

Methods: This post-hoc analysis used data from the Preserve-Transplant Study, a randomized, single-blind, placebo-controlled, multicenter trial. A total of 242 KTRs with metabolic acidosis were randomized 1:1 to SB (1.5–4.5 g/day) or placebo for 24 months. Primary outcomes were body weight, NT-proBNP, plasma renin, aldosterone, aldosterone-to-renin ratio (log-transformed), nocturnal systolic blood pressure (SBP) dipping, and use of antihypertensives. Secondary endpoints included incident hypertension, admissions for fluid overload/hypertension, and sodium/potassium balance. Mixed-effects regression models were applied.

Results: We identified weak evidence for treatment effects in the SB group compared to placebo for body weight (BGD: 1.23 kg; p = 0.09), and no evidence for NT-proBNP, plasma renin, or aldosterone-to-renin ratio. Substantial evidence was found for lower plasma aldosterone (BGD: -0.17 ng/L; p = 0.007), the latter four log-transformed. Weak evidence was seen for increased nocturnal SBP dipping (OR: 2.28; p = 0.09). Antihypertensive and diuretic use was similar between groups. Weak evidence for higher serum sodium (BGD: 0.51 mEq/L; p = 0.02) and strong evidence for higher log-transformed 24h sodium excretion (BGD: 0.16 mEq/24h; p <0.001) were found with SB treatment. No or weak evidence was observed for other secondary outcomes. Subgroup analyses revealed no relevant differential effects.

Conclusions: In this cohort of kidney transplant recipients with metabolic acidosis, our findings do not indicate clinically relevant adverse effects of SB on volume status in KTRs. Nevertheless, targeted studies are warranted to better delineate safety, in particular in high-risk patients.

EP-13

Two Cases of Hyperacute Rejection After AB0 Incompatible Kidney Transplantation: What Lurks Behind the Titre?

Dr. Kerstin Hübel [1], Prof. Anne Halpin Halpin [2], Dr. Elena Rho [3], Dr. Fabian Rössler [4], Mr. Dusan Harmacek [3], Dr. Kai Castrezana Lopez [3], Dr. Lukas Weidmann [3], Dr. Lukas Frischknecht [5], Dr. Jakob Nilsson [6], Mr. Bruce Motyka [7], Prof. Thomas Schachtner [8], Prof. Lori West [9]

1. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 2. Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, 3. Nephrology, University Hospital Zurich, Switzerland, 4. Department of Surgery and Transplantation, University Hospital Zurich, Zurich, Switzerland, 5. Klinik für Immunologie, Universitätsspital Zurich, 6. Klinik für Immunologie, Universitätsspital Zuerich, 7. University of Albtera, Edmonton, 8. University Hospital Zurich, 9. Department of Pediatrics, University of Alberta, Edmonton

Purpose: Although ABO-incompatible (ABOi) living donor kidney transplantation is performed on a routine basis, it remains a procedure with a high immunologic risk requiring immunosuppression aimed at diminishing antibody production and removal of circulating antibodies from the recipient.The current method used to determine ABOi immune risk is the red cell agglutination method, developed in 1901, this test is known to lack reproducibility and specificity for ABO antibody measurement.

Methods: Retrospective measurement of ABO IgG and IgM antibodies was per formed using a novel bead-based ABO antibody detection assay.

Results: Two recent cases were assessed for ABOi transplant and found to have low IgG and IgM titres following non-specific antibody removal by Therasorb column. Despite lack of HLA donor-specific antibodies pre- and post-transplant, both patients experienced pathology-confirmed hyperacute rejection. Allograft nephrectomy was performed at day 2 for patient 1. Patient 2 was treated with pheresis, high dose ste roids, IVIG and eculizumab and graft nephrectomy was performed seven days post transplant. ABO antibodies decreased following Therasorb treatment but there were remaining IgG donor-specific ABO antibodies in the pre-transplant samples. Data shown in Figure 1. IgG subclass analysis using the bead-based assay revealed a high proportion of IgG2 anti-A antibody in both patients. Hyperacute antibody-mediated rejection in these two ABO-A-incompatible kidney transplant cases was likely due to insufficient removal of anti-A antibodies, despite the low red cell agglutination titres. The reagents used to detect IgG agglutination titres may not be optimized for IgG2subclass detection and may underappreciate the level of IgG ABO antibodies.

Conclusions: These cases highlight the need for better diagnostics for ABO anti body detection to support ABOi transplantation. The use of non-selective Therasorb columns for ABO antibody removal also requires further investigation.

EP-14

Unraveling a mechanism underlying hepatitis E-associated kidney disease: the discovery of HEV ORF2 capsid protein-associated immune complex glomerulonephritis

Ms. Birgit Helmchen [1], Dr. Anne-Laure Leblond [2], Dr. Maliki Ankavay [3], Dr. Daniela Lenggenhager [4], Dr. Jasna Jetzter [5], Prof. Fritjof Helmchen [6], Dr. Hüseyin Yurtsever [7], Dr. Rosella Parrotta [5], Dr. Marc Eamonn Healy [8], Dr. Amiskwia Poeschel [9], Prof. Enni Markkanen [9], Prof. Nasser Semmo [10], Mr. Martin Ferrie [11], Prof. Laucence Cocquerel [12], Dr. Harald Seeger [13], Dr. Helmut Hopfer [14], Prof. Beat Müllhaupt 15, Prof. Jerome Gouttenoire [16], Prof. Darius Moradpour [17], Dr. Ariana Gaspert [18], Prof. Achim Weber [19]

1. Department of Pathology and Molecular Pathology, University Hospital Zurich (USZ), 2. Department of Pathology and Molecular Pathology, University Hospital Zurich (USZ) and University Hospital Zurich (USZ), 3. Division of Gastroenterology and Hepatology, CHUV Lausanne, 4. Department of Pathology and Molecular Pathology, University of Zurich (USZ), 5. Department of Pathology and Molecular Pathology, University of Zurich (UZH) and Hospital Zurich (USZ), 6. Brain Research Institute, University of Zurich (UZH), 7. Institute of Pathology, Cantonal Hospital, Aarau, 8. Department of Pathology and Molecular Pathology, University of Zurich (UZH) and University Hospital Zurich (USZ), 9. Institute of Veterinary Pharmacology and Toxicology, University of Zurich (UZH), 10. Department of Visceral Surgery and Medicine, Inselspital, Bern University Hospital, University of Bern, 11. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, U1019 – UMR 9017 – CIIL – Center for Infection and Immunity of Lille., 12. Univ. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, U1019 – UMR 9017 – CIIL – Center for Infection and Immunity of Lille., 13. Institute for Nephrology and Dialysis, Cantonal Hospital Baden, Baden, 14. Institute of Medical Genetics and Pathology, University Hospital Basel, University of Basel., 15. Department of Gastroenterology and Hepatology, University Hospital Zurich (USZ), 16. Division of Gastroenterology and Hepatology, Lausanne University Hospital and University of Lausanne., 17. Division of Gastroenterology and Hepatology, Lausanne University Hospital and University of Lausanne, 18. Department of Pathology and Molecular Pathology, University Hospital Zurich, 19. Department of Pathology and Molecular Pathology, University of Zurich (UZH) and University Hospital Zurich (USZ).

Background and Aims: Hepatitis E virus (HEV) infection is one of the most common viral hepatitis worldwide and can be associated with extrahepatic manifestations, particularly affecting the kidneys. The underlying mechanisms remain unclear, with both direct viral infection and indirect immune-mediated processes proposed. We present a case of de novo immune complex-mediated (GN) with a membranoproliferative (MPGN) pattern linked to glomerular deposition of a previously unknown form of the HEV open reading frame 2 (ORF2) capsid protein in patients with acute or chronic hepatitis E.

Methods: Immunostaining, electron microscopy, deconvolution microscopy, and laser-capture microdissection combined with mass spectrometry were used to specifically investigate the glomerular compartment.

Results: In a kidney transplant recipient with proteinuria and raising creatinine level (Fig1a), immune complex GN with a membranoproliferative pattern developed alongside increasing glomerular deposits of HEV ORF2 protein (Fig1b-c). The HEV ORF2 protein co-localized with IgG, thus forming immune complexes. Notably, the glomerular HEV ORF2 protein was found to be a truncated, non-glycosylated form rather than a secreted, glycosylated capsid protein. HEV RNA was not detected in kidney cells. Unlike in liver cells, no evidence of productive HEV infection was detected in the kidney. Patients with acute hepatitis E exhibited similar albeit less pronounced deposits (Fig2). These findings link the production of HEV ORF2 protein production to the development of hepatitis E-associated GN.

Conclusion (Fig3): The formation of glomerular IgG-HEV ORF2 immune complexes provides a mechanistic explanation for the renal manifestations of HEV infection. This immediately offers a diagnostic tool for hepatitis E-associated GN and establishes hepatitis E-associated GN as a distinct clinical entity. Furthermore, our findings emphasize that renal involvement should always be considered in cases of hepatitis E.

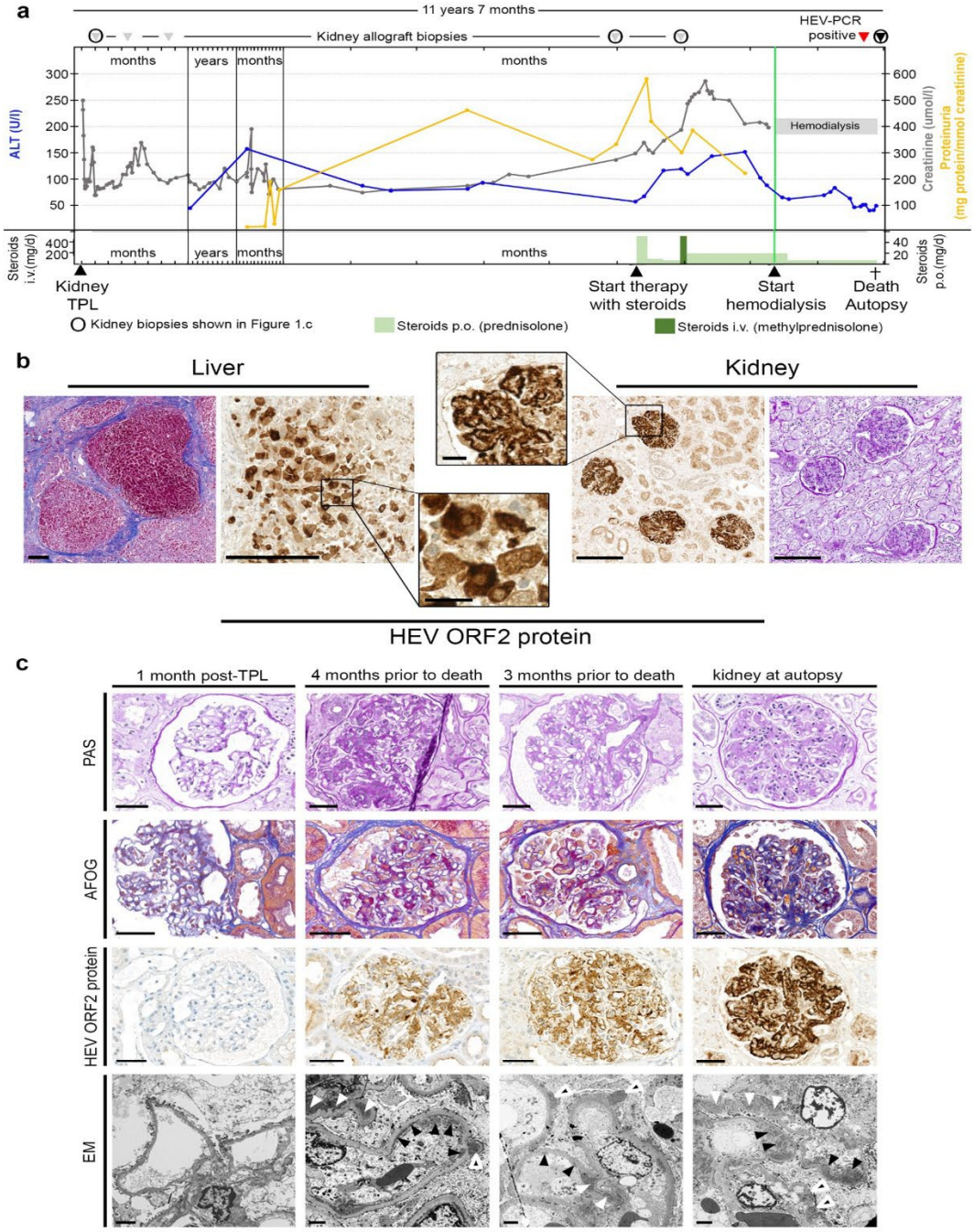


Figure 1: Clinical course, autopsy findings and gradual development of immune complex glomerulonephritis with membranoproliferative pattern in a kidney transplant recipient with hepatitis E (a) Course of alanine transaminase (ALT, blue), proteinuria (yellow) and creatinine (grey), time points of therapeutic and diagnostic interventions as well as death / autopsy. (b) Histology of autopsy liver showing cirrhosis (Masson trichrome stain) and hepatitis with immune reactivity for HEV ORF2 protein in hepatocytes (left). Histology of transplant kidney at autopsy showing glomerulonephritis (periodic acid Schiff [PAS] stain) and (extracellular) immune reactivity for HEV ORF2 protein in glomeruli (right). Scale bars in overviews, 200 µm; scale bars in detail, 25 µm. Stainings performed more than 5 times on different tissues blocks. (c) Kidney histology. One month post transplantation: inconspicuous glomeruli on light microscopy (PAS and acid fuchsin-Orange G [AFOG] stains), no HEV ORF2 protein deposits, no electron dense deposits on electron microscopy (EM). Four months prior to death (biopsy 4): glomerulus with mild mesangial and endocapillary hypercellularity, segmental sclerosis and prominent podocytes (PAS stain). Mostly mesangial and few glomerular basement membrane protein deposits (AFOG stain). Moderate mesangial and glomerular basement membrane positivity for HEV ORF2 protein. Mesangial (white arrowheads), subendothelial (black arrowheads) and subepithelial (black and white arrowheads) on EM. Three months prior to death (biopsy 5): glomerulus with mild mesangial and endocapillary hypercellularity (PAS stain). Mostly mesangial and few glomerular basement membrane protein deposits (AFOG stain). Moderate to strong mesangial and glomerular basement membrane positivity for HEV ORF2 protein. Mesangial (white arrowheads), subendothelial (black arrowheads) and subepithelial (black and white arrowheads) on EM. Kidney at autopsy: glomerulus with mild mesangial and endocapillary hypercellularity (PAS stain). Mostly mesangial and few glomerular basement membrane protein deposits (AFOG stain). Strong mesangial and glomerular basement membrane positivity for HEV ORF2 protein. Mesangial (white arrowheads), subendothelial (black arrowheads) and subepithelial (black and white arrowheads) on EM. Scale bars in PAS, AFOG, and HEV ORF2 protein images: 50 µm; scale bars in EM images: 2 µm.

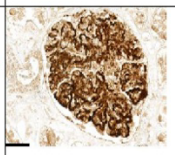
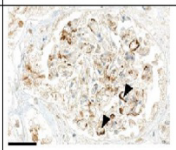
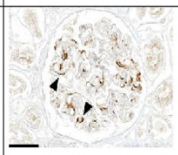
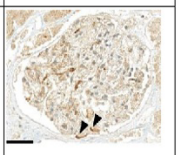
	Chronic hepatitis E	Acute hepatitis E		
	Patient 1	Patient 2	Patient 3	Patient 4
HEV genotype	HEV-3h_s	HEV-3h_s	HEV-3	HEV-3h_s
Age: 63 ± 5 years Sex: 3 males, 1 female	50-59 / male	50-59 / male	60-69 / female	70-79 / male
History of liver disease Viral load in liver	chronic HEV infection 4.4 x 10^6	cirrhosis due to NASH n.a.	cirrhosis due to NASH/ASH n.a	cirrhosis due to ASH n.a
History of kidney disease Viral load in kidney	IgA nephropathy, kidney TPL 0	unknown n.a.	unknown n.a.	unknown n.a
Immunosuppression (IS)	yes	no	no	no
basis IS / add on IS	tacrolimus, MMF / corticosteroids	-	-	-
Urea max. (mmol/)	hemodialysis	n.a.	25	n.a.
Creatinine max. (umol/l)	573	188	180	> 200
eGFR min. (ml/min/1.73m²)	hemodialysis	33	25	n.a.
Serum albumin min. (g/l)	11	26	26	24
Proteinuria	yes	yes	yes	n.a.
HEV RNA in blood	1.2 x 10^8 IU/mL	4.0 x 10^6 IU/mL	4.6 x 10^4 IU/mL	2.2 x 10^3 IU/mL
HEV ORF2 immunohistochemistry on autopsy kidney (scale bar: 50 µm)				
Staining intensity, semiquantitative	+++	+	+	+

Figure 2: Clinical findings, laboratory values and HEV ORF2 IHC on autopsy kidneys, patients 1-4. ASH, alcoholic steatohepatitis; HEV, hepatitis E virus; MMF, mycophenolate mofetil; NASH, nonalcoholic steatohepatitis; TPL, transplantation. Viral load expressed as HEV genome copy number/µg total RNA. n.a., information not available. Scale bars: 50µm.

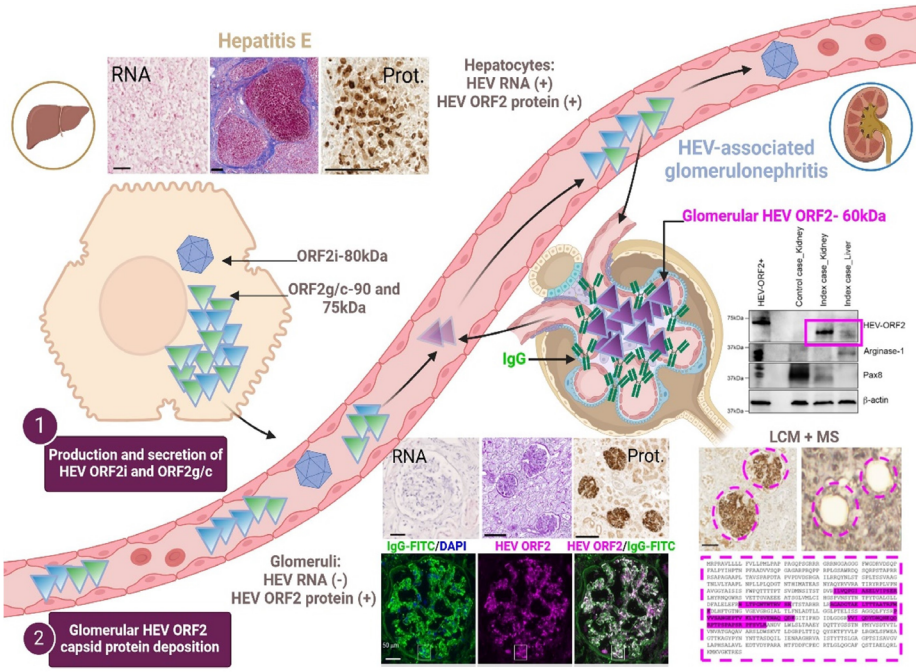


Figure 3: Graphical summary of the patho-mechanisms underlying the development of renal manifestations upon HEV infection in immunocompromised patients.

YSN AWARD (PECHA KUCHA)

YSN-01

Inter-Center Variability Of Biopsy-Based Transcript Diagnostics – Comparison Of Banff Lesions With Molecular Scores

Mr. Dusan Harmacek [1], Mr. David Kronthaler [2], Mrs. Petra Hruba [3], Mrs. Eva Girmanova [3], Mr. Lukas Weidmann [1], Mrs. Seraina von Moos [1], Mr. Kai Castrezana Lopez [1], Mrs. Elena Rho [1], Mrs. Kerstin Hübel [1], Mr. Florian Westphal [1], Mrs. Ariana Gaspert [4], Mrs. Birgit Helmchen [4], Mr. Ludek Voska [3], Mrs. Katerina Jaklova [3], Mrs. Ulrike Held [2], Mr. Ondrej Viklicky [3], Mr. Thomas Schachtner [1]

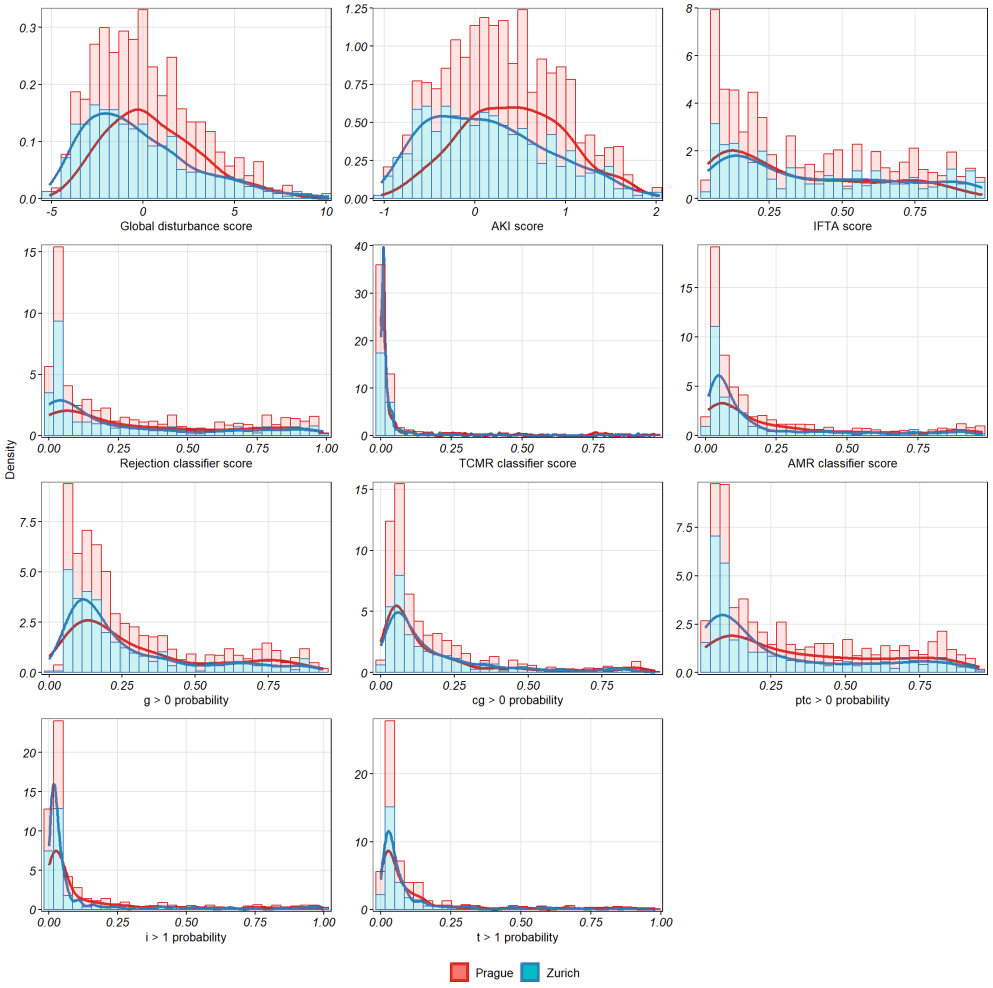
1. Department of Nephrology, University Hospital Zurich, Zurich, Switzerland, 2. Epidemiology, Biostatistics and Prevention Institute, Department of Biostatistics, University of Zurich, Zurich, Switzerland, 3. Institute for Clinical and Experimental Medicine, Prague, Czechia, 4. Department of Pathology and Molecular Pathology, University Hospital Zurich, Zurich, Switzerland

Background: Biopsy-based transcript diagnostics should objectively evaluate kidney allograft biopsies. Banff 2022 Work Plan calls for validation of biopsy-based transcript assays in different centers to help define universally applicable molecular classifier thresholds.

Methods: 755 kidney allograft biopsies from 2 European centers were assessed by the Molecular Microscope Diagnostics system (MMDx®) at 2 laboratories in Portland, USA, and Prague, Czechia. We compared histological lesions to the MMDx classifier and probability scores using the cumulative link proportional model. The cohort comprised 145 cases of active/chronic-active antibody-mediated rejection (AMR), 117 probable AMR, and 64 DSA-neg. (donor-specific antibodies), C4d-neg. microvascular inflammation (MVI); and 93 T-cell mediated rejection (TCMR).

Results: Glomerulitis (g), peritubular capillaritis (ptc), interstitial inflammation (i), and tubulitis (t) drive the corresponding molecular lesion scores, rejection, AMR, and TCMR classifiers. Adjusting for multiple variables, histological g lesions were associated with transplant vintage (p <0.001) but not with the presence of DSA at the time of biopsy. Transplant vintage did not affect histological ptc or v lesions. Histological v lesions showed modest negative association with DSA in the model with molecular rejection (p = 0.024) and AMR classifier (p = 0.043), but not the TCMR classifier (p = 0.13). MVI lesions were positively associated with DSA (OR 1.54, 95% CI 1.17 to 2.03, p = 0.002) only in the model with TCMR classifier. Glomerular basement membrane double contours (cg) drive the molecular cg>0 probability only when MVI is present (p <0.05). In the multivariate adjusted analysis, we observed significantly higher odds for almost all histological lesions in Zurich compared to Prague.

Conclusions: Histological lesions drive the molecular probability and classifier scores across the 2 centers. The inter-center variability might be explained by different biopsy policies and inter-observer variability of renal pathologists. Our data suggest that the added value of the MMDx must be assessed in the context of a center's individual characteristics.



YSN-02

Short-term effects of an SGLT2 inhibitor on divalent ions in autosomal dominant polycystic kidney disease (ADPKD): the SIDIA trial

Ms. Lorena Roth [1], Mr. Dusan Harmacek [2], Prof. Thomas Schachtner [2], Prof. Britta George [2], Dr. Cornelia Hofmann [3], Dr. Argyrios Georgalis [4], Dr. Reto M. Venzin [4], Mr. Patrick Hofmann [5], Prof. Thomas Fehr [1]

1. Department of Internal Medicine, Cantonal Hospital Graubuenden, Chur, Switzerland, 2. Department of Nephrology, University Hospital Zurich, Zurich, Switzerland, 3. Zurich University of Applied Sciences, Institute of Computational Life Sciences, Wädenswil, Switzerland, 4. Department of Nephrology, Cantonal Hospital Graubuenden, Chur, Switzerland, 5. Renal Division, Department of Medicine, Brigham and Women's Hospital, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts

Clinical Phase: Phase 2

Study design: Investigator-initiated randomised, single-blind, placebo-controlled, cross-over study

Support: This study was supported by research funding from Vontobel Foundation Zurich and Boehringer Ingelheim

Background: SGLT2 inhibitors (SGLT2i) are a cornerstone of CKD therapy, lowering progression, CV events, and mortality. ADPKD patients were excluded from major trials, and data on electrolyte handling with SGLT2i, especially with tolvaptan, are lacking.

Methods: SIDIA was a randomized, double-blind, placebo-controlled, two-period crossover trial in 15 ADPKD patients (mean eGFR 68, median age 43). Participants received empagliflozin 10 mg or placebo for 14 days with washout. Primary endpoints were 24-h urinary phosphate, calcium, and magnesium; secondary endpoints included other electrolytes, inflammation, vitamin D metabolism, tolerability, and safety. Effects were analyzed with a generalized linear mixed model.

Results: No significant differences were seen in 24-h urinary phosphate, calcium, or magnesium with empagliflozin vs. placebo (26 vs. 22.9 mmol/d, p = 0.21; 4.0 vs. 2.3, p = 0.56; 4.6 vs. 4.3, p = 0.18). Empagliflozin lowered uric acid (– 26%), increased serum magnesium (+5.7%) and urinary citrate (+79%), and reduced BP (–4/–7 mmHg). A small, expected dip in eGFR (–7.1%) was noted; urine volume was 4.6 vs. 3.8 L, with no safety signals.

Conclusions: In ADPKD patients with and without tolvaptan, short-term empagliflozin was safe, showing no significant effects on urinary calcium, phosphate, or magnesium. Increased serum magnesium, along with higher urinary citrate and lower uric acid, may provide long-term benefits by slowing disease progression and reducing stone and gout risk.

Figure Legends

Figure 1
Forest plot of the effect of empagliflozin versus placebo on primary outcomes. Median and IQR are shown. The forest plot represents the treatment effect and estimated relative difference (%) derived from a GLMM with treatment and treatment period included as fixed effects and patient as a random intercept to account for the cross-over design. Error bars show associated 95% CIs. Analysis of primary outcomes was performed with *P* values and hypothesis testing with a two-sided-significance level of 0.05.
GLMM, generalized linear mixed model.

Figure 2
Forest plot of the effect of empagliflozin versus placebo on secondary outcomes. Median and IQR are shown. The forest plot represents the treatment effect and estimated relative difference (%) derived from a GLMM with treatment and treatment period included as fixed effects and patient as a random intercept to account for the cross-over design. Error bars show associated 95% CIs. GLMM, generalized linear mixed model.

Figure 1

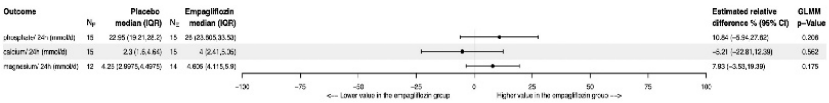
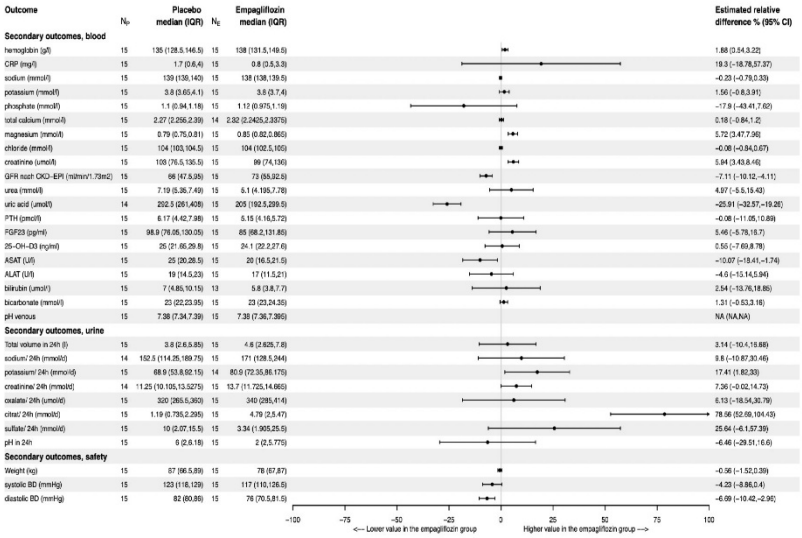


Figure 2



YSN-03

The role of casts in proximal tubule injury and atrophy

Dr. Anna Faivre [1], Dr. Anders M. Kristensen [1], Dr. Xiang Zheng [1], Dr. Qi Wu [1], Mrs. Hanne Kidmose [1], Prof. Robert A. Fenton [1], Prof. Ina M. Schiessl [1]

1. Aarhus University, Department of Biomedicine, Aarhus, Denmark

Background: Acute kidney injury (AKI) is common and associated with high morbidity and mortality. A substantial proportion of patients do not fully recover and progress toward chronic kidney disease (CKD). The mechanisms driving this failed repair remain unclear. During AKI, granular casts frequently appear and correlate with tubular injury severity, but whether they actively contribute to tubular injury is unknown.

Methods: We investigated the ischemia–reperfusion injury (IRI) model in C57BL/6J male mice (8–12 weeks). Unilateral IRI was induced by 30-min renal artery clamping. Granular casts and adjacent epithelium were isolated by laser microdissection for spatial proteomics, with contralateral kidneys serving as controls. Longitudinal intravital two-photon (2PM) imaging was used to track cast formation, as well as tubular injury and fibrosis development. This was done in PDGFRβCreER^{T2} x Salsa6F mice, which allow tracking of PDGFRβ-cells (main precursors renal myofibroblasts). Cast removal was attempted with osmotic diuresis (mannitol, 1 g/kg intraperitoneally twice daily for 4 days plus 20% in drinking water for 7 days).

Results: Preliminary proteomic analysis in n = 3 mice revealed that casts share much of their protein content with adjacent epithelium but also contain injury-associated markers, such as KIM1 of ICAM1. Serial intravital imaging of IRI kidneys demonstrated intratubular material from day 2 and mature granular casts by day 4. Mannitol reduced urine osmolality as expected with this regimen. We are currently performing 2PM longitudinal imaging of mice with IRI, treated or not with mannitol. Preliminary data in n = 7 mice seem to indicate a protective effect of mannitol over vehicle treatment.

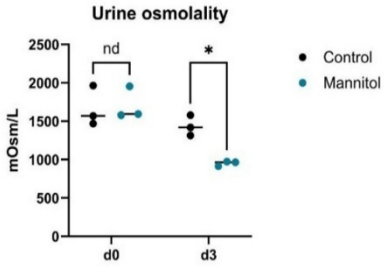


Figure 1. Urine osmolality measured in mice after vehicle or mannitol treatment

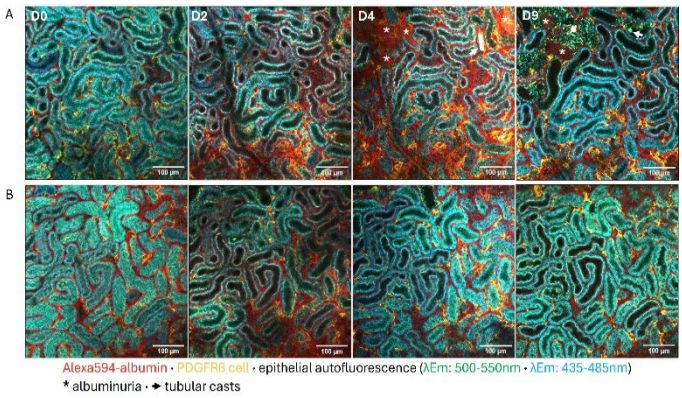


Figure 2. Serial intravital imaging in (A) vehicle and (B) mannitol-treated mice after ischemia-reperfusion injury

Conclusions: Granular casts may not only reflect injury but also exacerbate proximal tubule damage and maladaptive repair, potentially through obstruction and direct signaling on the adjacent epithelium. Cast removal with osmotic diuretics represents a feasible strategy that warrants further evaluation.

YSN-04

Unravelling the critical role of Wdr72 for kidney function

Ms. Hannah Auwerx [1], Dr. Xiaoxu Li [2], Dr. Anna Rinaldi [3], Dr. Maysam Mansouri [1], Dr. Chenyu Li [4], Dr. Felix Gantenbein [1], Prof. Katalin susztak [4], Prof. Pietro Cippà [5], Dr. Soline Bourgeois [1], Prof. Carsten A. Wagner [6]

1. Institute of Physiology, University of Zurich, Zurich, 2. Laboratory of Integrative Systems Physiology, École Polytechnique Féderale de Lausanne, Lausanne, 3. Department of Biomedicine, University of Basel, Basel, 4. Department of Medicine, University of Pennsylvania, Philadelphia, 5. University Hospital Basel, 6. Institue of Physiology, University of Zurich, Zurich

WDR72 is broadly expressed along the renal tubular system. In humans, rare biallelic loss-of-function mutations cause amelogenesis imperfecta and distal renal tubular acidosis (dRTA). GWAS revealed a strong association between *WDR72* variants and kidney function decline, with credible set analysis highlighting coding loss-of-function variants, suggesting a causal role in kidney function. Our group previously characterized young *Wdr72*$^{-/-}$ mice which displayed a dRTA phenotype upon acid loading and established the role of WDR72 in the H^+-ATPase activity of the collecting duct. However, the role of WDR72 in the remaining tubular segments and its precise role in kidney health and disease remains unknown.

We studied 18 months-old *Wdr72*$^{-/-}$ mice and their wild-type littermates to characterize the role of *Wdr72* in age-related kidney function decline. In aged mice, *Wdr72*-deficiency led to kidney function decline, with increased BUN and creatinine and decreased measured GFR. Old mice also developed spontaneous dRTA. Importantly, these phenotypes were not observed in young *Wdr72*$^{-/-}$ under baseline conditions and were uncovered with aging. Additionally, old *Wdr72*$^{-/-}$ mice showed evidence for mitochondrial dysfunction, such as increased lactate, decreased mitochondrial to nuclear DNA ratio, and severe downregulation of mitochondrial gene sets in bulk-RNA sequencing data. Seahorse assays on proximal tubular opossum kidney cells confirmed decreased mitochondrial respiration in the absence of WDR72. In humans, co-expression analysis strongly correlated WDR72 expression with mitochondrial related pathways. Moreover, *Wdr72*-deficient mice seem to display a strong pro-inflammatory signature on transcriptome and protein levels. Finally, human transcriptome and proteome data showed a globally decreased kidney expression of *WDR72*/WDR72 during CKD.

Altogether, our data establish *Wdr72* as a key determinant for kidney function and acid-base balance. Loss of *Wdr72* impairs mitochondrial integrity and triggers pro-inflammatory signaling pathways in mice, offering promising leads for future mechanistic investigations..

INDEX OF FIRST AUTHORS

The numbers refer to the numbers of the abstracts.

Amico P SO-28
Aregger F SO-04
Auwerx H YSN-04

Bajraktari I SO-12
Bargagli M LO-15, SO-08
Beci B SO-02
Bertgen L SO-25
Bruegger J EP-04
Brune JE SO-15
Buchkremer F LO-05

Cereghetti L SO-11
Charlemagne T LO-06
Correia M LO-03
Cozzo D SO-27

de Sousa P LO-18

Eisel R SO-14
Eul C SO-06, SO-09

Faivre A YSN-03
Fakhouri F SO-23
Feuchter LO-14

Galliker N SO-20
Genoud S SO-29
Golhen K SO-19
Guidotti R LO-11

Halfon M LO-10, SO-26
Harmacek D YSN-01
Hayes W LO-13
Helmchen B EP-14
Helou N LO-07
Hübel K EP-13
Huber A EP-06, SO-03

Khan A SO-10
Kistler A LO-17
Kowarik E EP-01
Krättli J EP-07, LO-12

Mani LY LO-04
Mani LY SO-24

Näf S EP-11

Palermo A EP-05
Pietz C SO-01

Reich T SO-13
Reuster M SO-07
Rho E LO-08
Rinaldi A LO-19
Ritter A EP-08
Roth L YSN-02
Rudloff S SO-22

Schwotzer N LO-02
Scoglio M SO-17
Sidler D SO-16
Spica D EP-10
Stampfli M SO-18
Staub PS EP-12
Stavart L LO-16
Stucki M LO-09

Tokkuzun U EP-03

Ulpiano A EP-02

Wallner M SO-21
Weidmann L LO-01
Weidmann L EP-09
Westphal F SO-05

SWISS MEDICAL WEEKLY

Editor in chief:
Prof. Gérard Waeber

Deputy editor in chief:
Prof. Stefan Weiler

Academic editors: see www.smw.ch

Managing editors:
Natalie Marty, MD
Jan Roth, MD

doi: https://doi.org/10.57187/s.5090
ISSN online supplement: 2504-1622

Guidelines for authors and online submission: www.smw.ch

Cover image: © Erozhnov | Dreamstime.com