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Interlaken (Switzerland), December 8–9, 2022

54TH ANNUAL MEETING OF THE SWISS SOCIETY OF NEPHROLOGY (SGN-SSN)

INTERLAKEN (SWITZERLAND), DECEMBER 8-9, 2022

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ELEVATOR PITCH PRESENTATIONS

OC 01

Complement C1s deficiency in a male caucasian patient with systemic lupus erythematosus

Dr. Jessica Kleer[1], Dr. Lillemor Skattum[2], Dr. Ingeborg Fischer[3], Dr. Min Jeong Kim[4], Prof. Marten Trendelenburg[1]

1. Laboratory of Clinical Immunology, Department of Biomedicine, University of Basel, Basel, Switzerland 2. Department of Laboratory Medicine, Section of Microbiology, Immunology and Glycobiology, Lund University, Lund, Sweden 3. Department of Pathology, Cantonal Hospital Aarau, Aarau, Switzerland, 4. Division of Nephrology, Cantonal Hospital Aarau, Aarau, Switzerland

Background: Deficiencies of the early complement components of the classical pathway are described to be associated with Systemic Lupus Erythematosus (SLE) or SLE-like syndromes and severe pyogenic infections. Among these deficiencies, C1s deficiency has been reported in 9 cases so far.

Methods or Case description: Here we describe a 34-year old, male patient who presented with severe, recurrent infections (meningitides, erysipelas, subcutaneous abscess, infections of the upper airways) since childhood as well as adult-onset SLE (6/11 ACR criteria) with proliferative lupus nephritis (LN). A screening of the complement cascade showed not measurably low CH50, while the function of the alternative pathway was normal. Subsequent determination of complement components revealed undetectable C1s with low levels of C1r and C1q and normal (C3) or slightly elevated (C2, C4, C1-inhibitor) concentrations of other complement proteins. The patient had no anti-C1q antibodies. A renal biopsy showed class IVA LN with positivity for complement C1q along the glomerular basement membranes and weak deposition of IgG, IgM and complement C3 in the mesangium and glomerular basement membranes. In an ELISA-based functional complement assay determining C4d deposition, the patients missing complement activity could be completely restored by the addition of active C1s. The genome of the patient was analyzed by whole genome sequencing showing two truncating variants in the C1s cDNA gene. One mutation was located at nucleotide 514 in exon 5, caused by a nucleotide substitution from G to T, resulting in a nonsense mutation from Gly172 (G172X). The other mutation was located at nucleotide 750 in exon 7, where C was replaced by a G, resulting in a nonsense mutation from Tyr250 (Y250X). Both mutations create a premature stop codon and have not previously been reported in the literature.

Results or Learning points: The genetic findings in combination with absent C1s in circulation strongly argue for a total C1s deficiency in our patient.

OC 02

Treatment challenges of recurrent multiple myeloma after kidney transplantation: a case study

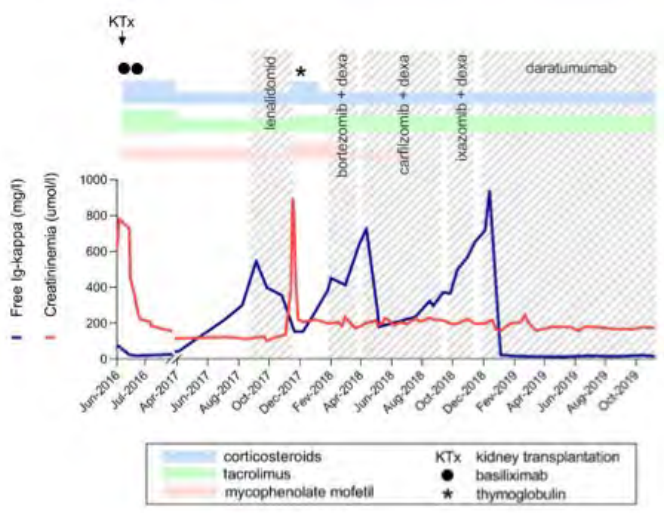
Dr. Anne-Catherine Saouli[1], Dr. Alice Horisberger[2], Dr. Mathilde Gavillet[3], Dr. Samuel Rotman[4], Dr. Jean-Pierre Venetz[5], Prof. Dela Golshayan[5]

1. Service of Nephrology and Hypertension, Lausanne University Hospital, Lausanne, Switzerland, 2. Service of Immunology and Allergy, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland., 3. Service of Hematology, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland., 4. Service of Clinical Pathology, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, 5. Transplantation Centre, Departments of Medicine and Surgery, Lausanne University Hospital (CHUV) and University of Lausanne (UNIL), Lausanne, Switzerland.

Background: Renal insufficiency is one of the disease-defining event in multiple myeloma (MM) (20-50% of cases) and 2-3% of the patients progress to ESRD requiring dialysis. New therapies have been introduced such as immunomodulatory drugs (IMIDs), proteasome inhibitors (PIs) and monoclonal antibodies (mAbs), used alone or in combination, leading to an improvement of overall survival. Autologous hematopoietic stem cells transplantation is also feasible for selected situations. In the past, kidney transplantation (KTx) was avoided for patients suffering from MM. However, reported KTx experiences describe encouraging mid-term results.

Methods or Case description: We report the clinical case of a 56 years-old patient suffering from kappa light-chain MM with ESRD (biopsy-proven cast nephropathy and monoclonal immunoglobulin deposit disease), describing the treatments before transplantation and the clinical course and management after KTx.

Results or Learning points: The patient received a cadaveric KTx and presented MM recurrence one year after. The disease escaped several lines of therapies, prompting the prescription of IMIDs. This treatment was associated with severe acute Banff IIA T-cell-mediated rejection and graft dysfunction, which partially recovered following high-dose steroids and Thymoglobulin. Considering this adverse event, the treatment was switched to successive PIs and eventually daratumumab (anti-CD38 antibody) with good tolerability and efficacy in the control of the MM. The mAb also prevented further anti-HLA immunization after severe allograft rejection.



Conclusions: Our case highlights the challenge in choosing the best MM therapy to improve progression- free survival without compromising the kidney allograft. Although KTx remains rare in MM patients, improvement in the therapeutic management of MM is leading to an increased number of cases. One crucial aspect is discussing beforehand the immunosuppressive protocol after KTx, systematic anti-infectious prophylaxis, as well as MM preventive and therapeutic strategies in case of recurrence.

OC 03

Eculizumab in typical hemolytic uremic syndrome: a systematic review

Dr. Paul de Zwart[1], Dr. Guiseppina Spartà[1], Dr. Valerie Luyckx[1]

1. University Childrens Hospital Zurich, Zurich, Switzerland

Background: Typical hemolytic uremic syndrome (HUS), most often associated with infection with Shiga-toxin-producing bacteria, mainly affects young children. It can be acutely life-

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threatening, as well as cause severe long-term renal and neurological morbidity. Specific treatment with proven efficacy is lacking. Since complement activation may be a driver of HUS, the monoclonal C5 antibody eculizumab is often used off-label once extra-renal complications (e.g. seizures) occur, with anecdotal success. Eculizumab is prohibitively expensive and carries risk of infection. Its utility has not been systematically studied.

Methods or Case description: PubMed, Embase and Web of Science were systematically searched for studies reporting the impact of eculizumab on long-term outcomes of typical HUS. Studies providing original data regarding long-term outcomes in patients with typical HUS, treated with at least one dose of eculizumab during the acute illness, were included. Studies were excluded if data overlapped substantially with other studies, included less than 5 relevant patients, or if outcomes of typical HUS patients were not reported separately. Study quality was assessed using the ROBINS-I tool for risk of bias in non-randomized studies of interventions.

Results or Learning points: 2944 studies were identified. 14 studies including 386 eculizumab-treated patients met inclusion criteria. Pooling of data across studies was not possible. No study reported a statistically significant positive effect of eculizumab on long-term outcomes. Most studies were however subject to critical risk of bias due to confounding by indication, with more severely ill patients receiving eculizumab, administered at variable time points and with variable dosing. Three studies attempted to control for confounding through patient matching, although residual bias persisted due to matching limitations.

Conclusions: Current observational evidence does not permit any conclusion regarding the impact of eculizumab in typical HUS given critical bias. Results of randomized clinical trials are eagerly awaited, as new therapeutic strategies are urgently needed to prevent long-term morbidity in these previously healthy individuals.

OC 04

A Case of Minimal Change Disease (MCD) in combination with Lupus-like features

Dr. Claudia Beerli[1], Prof. Bruno Vogt[1], Dr. Federica Bocchi[1]

1. University Clinic for Nephrology and Hypertension, Inselspital Bern, Bern, Switzerland

Background: There is a broad spectrum of glomerular diseases presenting histologically with incomplete lupus-like features (full-house immunofluorescence staining, extraglomerular immune deposits, intense C1q staining, endothelial tubuloreticular inclusions and combined mesangial, subendothelial and subepithelial deposits) without meeting clinical and laboratory criteria for Systemic Lupus Erythematosus (SLE). The etiopathogenesis is not fully elucidated and this poses a diagnostic challenge! The most common renal diseases reported in this context are membranous nephropathy followed by IgA nephropathy, infection-related glomerulonephritis, membranoproliferative glomerulonephritis, amyloidosis and C1Q nephropathy. No cases have been described in association with MCD.

Methods or Case description: A 19-year old male Caucasian presented with abdominal pain as the only symptom and severe nephrotic syndrome (hypoalbuminemia 2g/l, albuminuria 5g/d, anasarca and ascites) with bland urinary sediment. Additional analysis revealed an inflammatory syndrome, which was, considering the result of the paracentesis, compatible with bacterial peritonitis. Furthermore, renal function was normal, antinuclear and anti-double-stranded antibodies were negative and C3 and C4 reduced. Kidney biopsy showed a normal appearing glomerulus and widespread glomerular immune deposits (IgG, IgM, C3, C1q, C4d, kappa, and lambda light chains without IgA deposits) on direct immunofluorescence. Renal electron microscopy revealed diffuse effacement of visceral epithelial cell foot processes and mesangial and subendothelial dense deposits. Corticosteroids combined with calcineurin inhibitors were initiated.

Results or Learning points: Renal disease with lupus-like features could be used as an umbrella term for patients not matching the criteria for SLE. In some cases, these forms of glomerular disease are associated with a poor renal survival and therefore deserve careful consideration. Nephrologists should also be aware of the possible conversion to SLE during the follow-up of these patients.

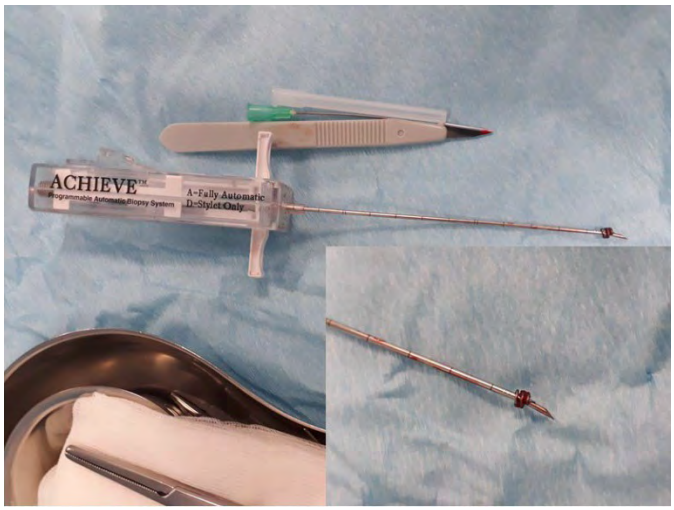
OC 05

On target- an unexpected complication of a kidney allograft biopsy *

Dr. Dusan Harmacek[1], Dr. Anna Lara Lavallée[2], Dr. Ante Katunaric[3], Dr. Daniel Ackermann[4], Prof. Bruno Vogt[4], Dr. Laila Mani[4]

1. Department of Biomedical Sciences, University of Lausanne, Lausanne, Switzerland 2. Department for Visceral Surgery and Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland 3. Department of Diagnostic, Interventional and Paediatric Radiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland 4. University Clinic for Nephrology and Hypertension, Inselspital Bern, Switzerland

Background: Kidney graft biopsy remains the gold-standard for the assessment of kidney transplant pathologies. The complication rate is generally lower than in native kidney biopsies ranging from 1.9 to 3.9% and has been shown to be higher among indication biopsies as opposed to protocol biopsies. Here, we present the case of an unusual complication of kidney allograft biopsy.



Methods or Case description: A 49-year-old female kidney allograft recipient was admitted for percutaneous transplant re-biopsy. She had received a deceased-donor kidney transplant into the right iliac fossa in 1999 and had recently been treated for T cell-mediated rejection by steroid pulses. Medical history was otherwise limited to laparoscopic hernia repair by Parietene® mesh. Following sonographic localization (Siemens Acuson 2000®), site marking, disinfection, local anesthesia and stab incision, an automated biopsy needle (16G, 15cm, Achieve®) placed into the ultrasound needle guide was smoothly advanced to the renal capsule. After releasing the trigger mechanism, an intrarenal needle track was visualized at the lower graft pole. However, during needle withdrawal, the needle-tip remained blocked 2 cm below the skin surface. While the needle could be advanced to the graft, it could not be re-

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trieved. Finally, a surgeon was able to extract the needle by exploring the puncture channel. As a surprise, the needle was found to be stuck within the coils of a helical tacker. The biopsy core could not be recovered from the damaged needle. The patient remained entirely asymptomatic with normal vital signs, hemoglobin, urine and ultrasound monitoring. No signs of macroscopic allograft damage, free air or fluid were detected on CT. Given the extraperitoneal mesh placement anterior to the kidney graft during hernia repair, this case suggests accidental penetration of a tacker by the biopsy needle during kidney graft biopsy.

Results or Learning points: We recommend that history of hernia repair should be routinely assessed before renal allograft biopsy.

*YSN paper

OC 06

An easy-to-perform assay to detect HLA-specific memory B cells: A missing tool in the HLA lab *

Dr. Caroline Wehmeier[1], Mrs. Aynur Gubelmann[2], Mr. Marc Kleiser[2], Mrs. Claudia Petit[2], Mrs. Amanda Puglia[2], Mrs. Dominique Roubaty[2], Dr. Patrizia Amico[1], Prof. Stefan Schaub[1], Dr. Gideon Hönger[3]

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland 2. HLA-Diagnostics and Immunogenetics, Department of Laboratory Medicine, University Hospital Basel, Basel, Switzerland 3. Department of Biomedicine, University of Basel, Basel, Switzerland

Background: Exposure to foreign HLA may lead to the formation of plasma cells (producing HLA antibodies) and dormant memory B cells. While screening for HLA antibodies is part of the pre-transplant immunological work-up in kidney transplantation, the presence of HLA-specific memory B cells is not yet routinely assessed. However, these cells can differentiate into antibody-producing cells upon antigen re-encounter, which may lead to antibody-mediated rejection (ABMR).

Methods or Case description: We present the case of a female patient who received a deceased donor transplant. As an HLA sensitizing event the patient had one previous pregnancy. Pre-transplant HLA antibody screening by Luminex single-antigen bead technology revealed HLA antibodies in the DR locus. No donor-specific HLA antibody (DSA) was found. After an uneventful early post-transplant course, the patient developed graft dysfunction and underwent transplant biopsy on day 7. The biopsy showed severe ABMR with thrombotic microangiopathy and endothelialitis. Repeated HLA antibody screening revealed a DSA against DR52 with high MFI. To assess a DR52 memory response, we performed a novel memory B cell assay using pre-transplant collected peripheral blood mononuclear cells (PBMC). In this assay, memory B cell-derived HLA antibodies can be detected following in-vitro polyclonal stimulation of PBMC and subsequent collection and evaluation of culture supernatants. Interestingly, this assay revealed the clear presence of DR52 memory. Moreover, analysis demonstrated immunization by only one eplet (104AK). Retrospectively, all detected DR antibodies in pre-transplant serum recognized this eplet but assignment based on only serum results was ambigious.

Results or Learning points: An alloimmune memory response can cause severe ABMR. Detection of HLA-specific memory by a novel method may help to refine the pre-transplant risk assessment and facilitate interpretation of serum HLA antibody analysis.

Conclusions: The novel easy-to-perform memory B cell assay is a missing tool in the HLA lab. Future studies should further explore the potential of this assay.

*YSN paper

OC 07

Zinc: A possible cause of acute tubulointerstitial nephritis?

Dr. Sarah Rosset[1], Dr. Sebastien Kissling[1], Dr. Samuel Rotman[2], Dr. Olivier Phan[1]

1. CHUV – Centre Hospitalier Universitaire Vaudois, Service de Néphrologie et Hypertension, Lausanne, Switzerland 2. Service of Clinical Pathology, Lausanne University Hospital and University of Lausanne, Switzerland

Background: Acute tubulointerstitial nephritis (ATN) remains a classic cause of acute renal failure; the causative agent may be difficult to identify especially in case of polymedication. We report an uncommon case of ATN possibly secondary to zinc intake.

Methods or Case description: A 25-year-old female patient, known to have polycystic ovarian syndrome treated by metformin, presents abdominal pains and fever with inflammatory syndrome treated successively with ceftriaxone, metronidazole, ciprofloxacin and non-steroidal anti-inflammatory drugs for suspected infectious gastro-enteritis. Prior to the initiation of this treatment, the first laboratory already showed acute kidney injury (AKI) without leukocyturia, hematuria or proteinuria on sediment. The renal function worsens rapidly, leading to a first renal biopsy showing acute and extremely active tubulointerstitial nephritis. Immunological and infectious panels are negative. A lymphocyte transformation test for ceftriaxone, ibuprofen and metformin is negative under corticosteroids. We conclude to an indeterminate drug-induced tubulointerstitial nephritis. The patient receives 1mg/kg/day of prednisone (PDN) with a tapering scheme, which allowed a clear decrease in creatinine. Under low dose PDN, without any known new drug exposure, she presents one more time an increase in creatinine. A second biopsy is performed, which shows again a 100% mononuclear and eosinophilic interstitial infiltrate without increase in fibrosis. PDN is increased to 1 mg/kg/day. Due to the severity of ATN, azathioprine is introduced to prevent recurrence. Four months later, the patient becomes pregnant and treatment with folic acid is started. At this point, she mentions the prolonged intake of zinc before both AKI episodes. Zinc is stopped.

Results or Learning points: The literature reports rare cases of association or causality between AKI and zinc.

Conclusions: This case illustrates the difficulty of identifying the exact drug cause of acute tubulointerstitial nephritis. The drug history should therefore extend to the use of pharmacological dietary substitution as zinc.

OC 08

Acute kidney injury in diabetic ketoacidosis in children and adolescents

Dr. Katrina Evers[1], Dr. Valerie Luyckx[1], Prof. Daniel Trachsel[2]

1. Pediatric Nephrology, University Children's Hospital Zurich, Zurich, Switzerland, 2. Pediatric Intensive Care and Pulmonology, University Children's Hospital of Basel UKBB, Basel, Switzerland

Background: Incidence rates of diabetes mellitus are rising globally. A serious complication is diabetic ketoacidosis (DKA). Paediatricians are often faced with this complication as the classical history of polyuria, polydipsia and weight loss is more difficult to obtain in younger children. Electrolyte disorders, brain oedema and acute respiratory distress due the metabolic acidosis must be recognized and treated promptly. Acute kidney injury (AKI) in patients with DKA is not a frequently discussed complication, although incidence rates are underestimated in clinical practice. The etiology of AKI in this setting may be complex and the long-term implications are underappreciated.

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Methods or Case description: Data sources: Literature review, clinical experience, and expert opinion

Study selection: A sampling of current evidence was accessed

Data extraction and synthesis: This narrative review summarizes the findings of around fifteen studies.

Results or Learning points: Literature review showed that the incidence of AKI in children with DKA admitted to a paediatric intensive care unit was 30-64.2% with the majority of patients presenting with stage 1 AKI. Suspected causes for AKI range from cortical necrosis over rhabdomyolysis to hypophosphataemia and hyperchloremia. A summary of results of four studies revealed that 3% of the affected children needed renal replacement therapy with a mortality rate of 2.5%.

Conclusions: The incidence of AKI in patients with DKA is high and volume depletion does not appear to be the only cause of its development. Despite the majority being AKI stage 1, mortality is significant among those with stage 3. Current recommendations for the initial assessment in DKA include the measurement of blood urea nitrogen (BUN) and creatinine as indicators for renal function but do not suggest repeated measurements if they lie in an age-appropriate range. In contrast to this urinary output should be carefully documented. Nevertheless little is known about the prevalence and prognosis of AKI in children and adolescents with DKA.

OC 09

Coexistence of autosomal recessive distal renal tubular acidosis and Sjogren syndrome: a coincidental finding? *

Dr. Alessio Raviola[1], Dr. Antonio Bellasi[1], Prof. Pietro Cippà[1], Dr. Silvio Pianca[1]

1. Division of Nephrology, Ente Ospedaliero Cantonale, Lugano, Switzerland

Background: Distal renal tubular acidosis (dRTA) is a defect of the urinary acidification process that limits the elimination of protons [H+] in the collecting duct. Various medical conditions spanning from anatomical alterations to genetic, autoimmune diseases or drugs toxicities can cause dRTA.

Methods or Case description: A 48 y.o. woman was referred to our centre for nephrology follow-up. At the age of 2 months she was diagnosed of a rare genetic cause of RTA due a mutation of ATP6V0A4, the gene coding for a component of the H+ transporting ATPase expressed by intercalated cells and critically involved in urine acidification. The patient presented over the years nephrolithiasis due to severe hypocitraturia, sensorineural hearing loss and CKD as well as dry mouth sensation, all features connected with the genetic mutation of the H+-ATPase proton pump channel in the kidneys, hear and salivary glands. However, as she also complained of ocular symptoms with lowered tears production and burning eyes sensation, she underwent a comprehensive auto-immune screening that documented high levels of ENA antibody titre (anti-SS-A and anti-SS-B), compatible with Sjogren syndrome, a cause of secondary dRTA.

Results or Learning points: Multiple medical conditions can be responsible of dRTA spanning from urological and anatomical alterations to renal, genetic or autoimmune diseases or drugs toxicities. Although the mutation of H+-ATPase proton pump channel can explain several of the medical findings, the coexistence of primary and secondary causes of dRTA questions whether a link between genetic and the autoimmune diseases exists.

Conclusions: Ad hoc studies should address the potential pathogenic link between the genetic and autoimmune disease in this patient.

*YSN paper

OC 10

Risk behaviors in teens can cause flank pain and acute kidney Injury (AKI) *

Mr. Chiara Sonnessa[1], Dr. Céline Kägi[1], Dr. Valerie Ann Luyckx[1]

1. Nephrologie, Kinderspital Zürich, Zürich, Switzerland

Background: Risk behaviors among young people are a concern. Positive developments are seen with regard to teenage smoking and alcohol consumption. No improvement is seen concerning heavy episodic drinking. New addictive behaviors are developing such as consumption of energy drinks. In addition, people are increasingly turning to the internet as an easy source of medication. Suicide is the second leading cause of death among 15-29 year-olds In Switzerland, often associated with harmful ingestions. We present 3 cases of teenage girls who developed severe flank pain and AKI after consumption of various substances not typically associated with AKI.

Methods or Case description: 3 teenage girls (13-, 15-, and 15-years-old) presented to our emergency room complaining of severe flank pain. In all 3 cases investigations revealed non-oliguric AKI (eGFR 19, 33 and 25 ml/min/1.73 m^2) with normal or swollen kidneys on ultrasound. No other cause of abdominal pain was found. The patients were managed conservatively. Severe abdominal pain persisted for several days, necessitating opiate analgesics. Kidney function improved slowly in all cases. After further questioning, Patient 1 admitted taking an intentional overdose of metamizol (2.5-5 g); Patient 2 consumed energy-drinks multiple times within 2 weeks, as well as 4g metamizol with the intention of self-harm; Patient 3 admitted to alcohol binges 4 and 7 days prior to admission.

Results or Learning points: Toxin-induced AKI should be considered as a differential diagnosis of sudden severe flank pain in teenagers. In addition to the classical causes of AKI, other commonly available substances and new addictive behaviors must be considered. Teenagers and their family should be informed of the risk of such behaviors, as an episode of AKI may have long term consequences in terms of increased risk of chronic kidney disease and hypertension.

Conclusions: Binge drinking, energy drink consumption and uncontrolled medication use can be causes of severe flank pain and AKI in teenage girls.

*YSN paper

OC 11

PORTRAY Study: A non-interventional study to investigate the real-world effectiveness, safety and adherence to extended-release calcifediol in stage 3–4 chronic kidney disease patients with secondary hyperparathyroidism

Prof. Arampatzis Spyridon[1], Prof. Markus Ketteler[2], Prof. Bover Sanjuan Jordi[3], Prof. Mario Cozzolino[4], Prof. João Frazão[5], Ms. Elodie Berger[6], Prof. Helmut Reichel[7]

1. Nephrological Center Bern and Dialysis Lindenhof Hospital Bern, Switzerland, 2. Robert Bosch Hospital, Stuttgart, Germany 3. University Hospital Germans Trias i Pujol, IGTP, Badalona (Barcelona), Catalonia, Spain 4. University of Milan, Milan, Italy 5. São João University Hospital Center, Porto, Portugal, 6. CSL Vifor, 7. Nephrological Center, Villingen-Schwenningen, Germany

Background: 42-80% of patients with stage 3 or 4 chronic kidney disease (CKD) have secondary hyperparathyroidism (SHPT) with low serum 25-hydroxyvitamin D (VitD) levels and other pathophysiological factors. Previous studies have shown that extended-release calcifediol (ERC) increases VitD to required levels (target of >50 ng/mL) and decreases inappropriately high parathyroid hormone (PTH) levels without clinically

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significant changes in serum calcium (sCa), serum phosphate (sP) and FGF-23. Marketing authorization for Rayaldee® (ERC) was granted in the USA in 2016 and in several European countries in 2022. It has been launched in Switzerland in March 2022 for the treatment of SHPT in adults with CKD stage 3 or 4 and serum VitD values <30 ng/ml (75 nmol/L). Limited evidence is currently available on ERC use outside of controlled trial settings, within European populations.

Methods or Case description: Based on routine clinical setting following initiation of ERC, PORTRAY aims to monitor key CKD mineral bone disease (MBD) laboratory parameters (iPTH, VitD, sCa, and sP) in CKD stage 3 and 4 patients with SHPT and low VitD. In addition, the PORTRAY research objectives include reasons for the use of ERC, its posology and adherence, PTH and VitD thresholds at study inclusion, evaluation of key CKD-MBD parameters, hospitalizations and health resource utilization in a real-life setting. Occurrence of adverse drug reactions, including hypercalcemia and hyperphosphatemia will also be monitored.

Results or Learning points: This is a non-interventional, prospective, multicentre, European, cohort study, with a prospective observational period per patient of 12 months, which is planned to start in October 2022 in 8 sites distributed across Switzerland, reflecting the prescribing patterns of the CKD population for ERC. Statistical analyses will be of an exploratory and descriptive nature.

Conclusions: Data analysis from this non-interventional study will provide additional information concerning the effectiveness and tolerability profile of ERC in routine medical practice.

OC 12

Uromodulin-associated kidney disease a rare but relevant medical condition*

Dr. Nathalie Merkel[1], Dr. Antonio Bellasi[1], Prof. Pietro Cippà[1], Dr. Silvio Pianca[1]

1. Division of Nephrology, Ente Ospedaliero Cantonale, Lugano, Switzerland

Background: ADTKD-UMOD (or uromodulin-associated kidney disease) is the most common form of Autosomal dominant tubulointerstitial kidney disease (ADTKD), a group of genetic disorders characterized by autosomal dominant inheritance and progressive kidney disease. ADTKD-UMOD is caused by the mutation of the gene encoding for uromodulin. In addition to slowly progressive kidney disease (usually with absent or minimal proteinuria and a bland urinary sediment), patients often present early-onset gout and a strong positive family history of CKD. As histological findings are often non-specific, genetic testing is required for a definitive diagnosis.

Methods or Case description: A 75-year old woman with CKD stage G4A1 and positive family history of end-stage kidney disease (mother and sister) was referred to our unit to investigate a progressive worsening in kidney function over the last year. The urine sediment was unremarkable. The patient underwent a thorough work-up to exclude, among other medical conditions, viral infections and auto-immune diseases. Kidney function loss was initially linked to NSAID abuse. However, chronic non-granulomatous interstitial nephritis and vascular sclerosis were documented in the kidney biopsy questioning the hypothesis of NSAID abuse. To further investigate CKD etiology and in light of the significant family history, genetic testing was performed confirming the presence of UMOD-mutation.

Results or Learning points: ADTKD should be suspected in patient with strong family history of CKD with absent or minimal proteinuria and unremarkable urinary sediment as well as in the presence of young-onset gout.

Conclusions: Even though there are currently no specific treatments, the diagnosis of ADTKD-UMOD is relevant as a patient might benefit from a kidney transplant. Similarly, genetic screening of family members may also be considered if a blood relative wishes to donate a kidney to a patient with ADTKD-UMOD.

*YSN paper

OC 13

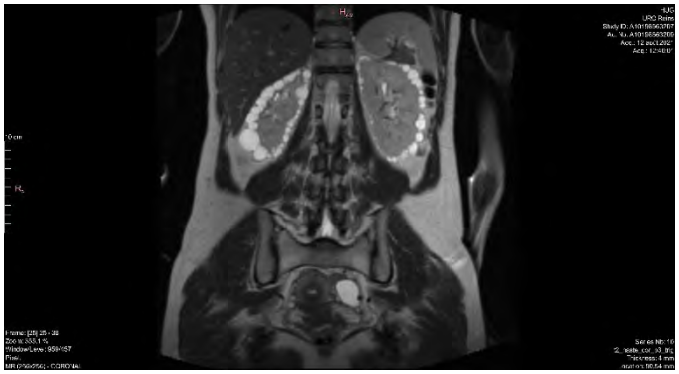
Glomerulocystic kidney disease*

Dr. Marc Scheen[1], Prof. Ariane Paoloni-Giacobino[2], Dr. Elsa Gonzalez Nguyen-Tang[3], Prof. Sophie De Seigneux[4], Dr. Fadi Haidar[1]

1. Hôpitaux universitaires de Genève, Service de Néphrologie, Rue Gabrielle-Perret-Gentil 4, 1205 Genève, Suisse, 2. Hôpitaux universitaires de Genève, Service de Génétique, Rue Gabrielle-Perret-Gentil 4, 1205 Genève, Suisse, 3. Hôpitaux universitaires de Genève, Unité Romande de Néphrologie Pédiatrique, Rue Gabrielle-Perret-Gentil 4, 1205 Genève, Suisse, 4. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland

Background: A 47 year old female patient of Afghan origin, with a history of hypertension and depression was addressed to the general nephrology clinic of Geneva University Hospital in august 2021, with uncontrollable hypertension and a suspected diagnosis of cystic kidney disease. She presented with persistent hypertension under a two drug regimen consisting of perindopril and amlodipine. An abdominal CT without contrast performed in 2019 for suspected symptomatic kidney stone disease, revealed multiple cysts in both kidneys. Family history was positive for a brother on hemodialysis for ESRD of unknown etiology in Afghanistan. Upon referral, the patient was asymptomatic with an unremarkable physical exam. Biological work-up revealed creatinine levels of 68 µmol/L, (eGFR of 108 ml/min/1.73 m^2 CKD-EPI).

Methods or Case description: The complete blood count and the routine serum chemistry were normal. Urinalysis was unremarkable. Whole exome sequencing was performed, followed by a targeted bioinformatics analysis of a panel of genes involved in cystic kidney diseases (https://panelapp.genomicsengland.co.uk/panels/283/). Variant filtering and classification was performed based on the guidelines for the interpretation of sequence variants from the American College of Medical Genetics and Genomics. No pathogenic or likely pathogenic variants were found.



Results or Learning points: Renal MRI with volumetry revealed normal sized kidneys with multiple bilateral cysts of atypical subcapsular and cortical distribution, that resembled a pearl necklace, with relative sparing of the renal medulla.

Conclusions: This case is compatible with renal Glomerulocystic kidney disease (GCKD), a rare form of cystic disease, caused by the dilation of the Bowman space and proximal tubule.

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OC 14

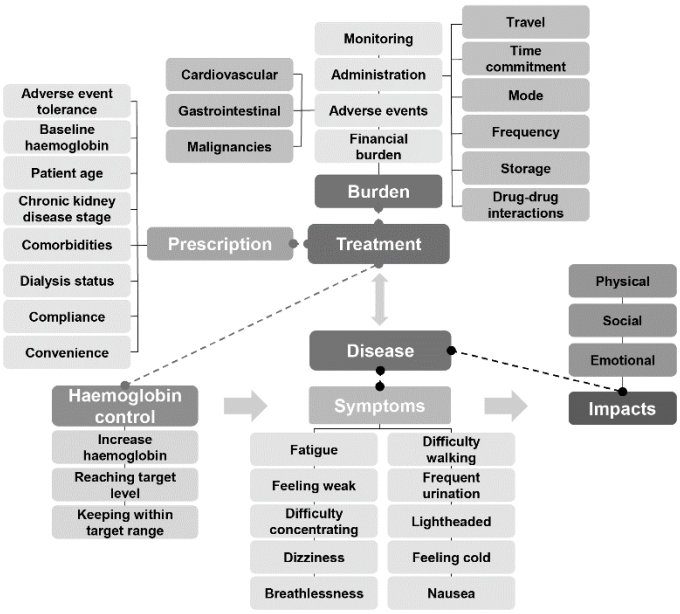
Identifying drivers of patients' and physicians' preferences for treatments of anaemia of chronic kidney disease: a qualitative study

Dr. Ember (Yiwei) Lu[1], Dr. Tony Okoro[1], Dr. Sebastian Heidenreich[2], Ms. Sarah Mulnick[3], Dr. Jaein Seo[3], Dr. Harjeet Dhillon[4], Dr. Rodrigo Refoios Camejo[4]

1. GSK, Collegeville, PA, US 2. Evidera, London, UK 3. Evidera, Bethesda, MD, US 4. GSK, London, UK

Background: Patients' treatment needs may be better addressed by improving understanding of patient and physician preferences for managing chronic kidney disease (CKD) anaemia.

Figure: Conceptual map of qualitative interview findings



Methods or Case description: Semi-structured qualitative telephone interviews, designed using targeted literature, were conducted with CKD patients (non-dialysis/peritoneal dialysis) and physicians from the United States, Germany and Japan. Interviews comprised 3 sections: (1) patients' symptoms and quality of life (QoL), or physicians' clinical experience; (2) treatment experience, concerns, benefits, adverse events and convenience; (3) a hypothetical treatment choice with benefit-risk trade-offs. Mixed deductive/inductive analyses were undertaken, and data visualised using conceptual mapping. At an attribute selection workshop, US and German nephrologists reviewed literature and qualitative interview findings to identify drivers of patient/physician preferences for anaemia treatments.

Results or Learning points: Overall, 18 patients (n = 6/country) and 12 physicians (n = 4/country) participated. Patients were ≥CKD stage 3 (50% stage 5), the majority (72%) received erythropoiesis-stimulating agent (ESA) treatment. Frequently reported comorbidities: hypertension (78%), type 2 diabetes (46%), hyperlipidaemia (22%). Physicians had 40–50 years' clinical experience, 75% were in private practice. Attributes were depicted by conceptual map (Figure). Haemoglobin control within target range was important to patients and physicians, connecting this to fewer symptoms/better QoL. Most physicians (n = 9, 75%) raised concerns about ESA-associated cardiovascular (CV) risks. Patients experienced several CKD anaemia symptoms, notably fatigue and dizziness; also recognised by physicians. Patients linked improved energy-levels to treatment success. Patients raised concerns about convenience of intravenous (time commitment) and subcutaneous (storage requirements, self-injection) administration, but considered oral pills convenient and familiar (once-weekly over thrice-weekly).

Conclusions: Patient/physician treatment preferences are multi-factorial, driven by clinically important attributes (haemoglobin target, symptom improvement, CV side effect risk). Treatment regimen attributes affected their perceived convenience. All aspects contributed to perceived value, however relative importance differed. These findings support a further survey to elicit trade-offs between treatment aspects and better understanding of patient/physician preferences.

(GSK-funded study; ERA2022 presentation ENCORE)

OC 15

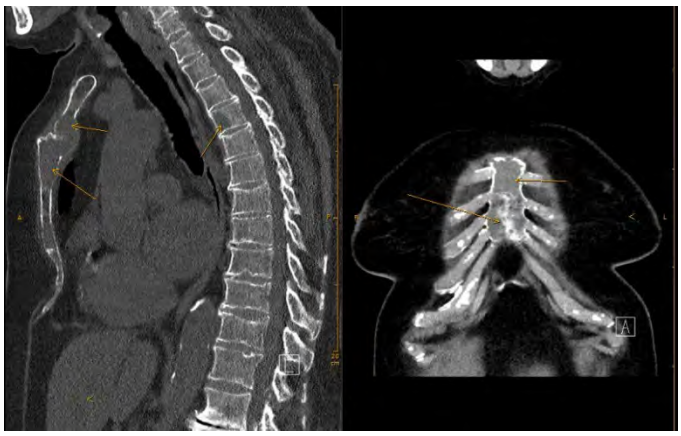
Rare corrective measure for the treatment of symptomatic hypercalcemia

Dr. Michael Moeddel[1], Dr. Barbara Nikolic[2]

1. Nephrologie – Hirslanden Klinik im Park, Zurich, Switzerland 2. Internal Medicine - Hirslanden Klinik im Park, Zürich, Switzerland

Background: Symptoms and treatment of hypercalcemia depend on its severity and chronicity. This case demonstrates that despite various drug treatment options, dialysis is rarely required to cure hypercalcemia and may be necessary under certain circumstances.

Methods or Case description: A 77-year-old patient had been suffering from fatigue, dyspnea and chest pain for several weeks. Laboratory findings revealed new-onset anemia (hemoglobin 81 g/l), renal failure (acute on chronic, eGFR of 36 ml/min/1.73 m^2) and mild hypercalcemia (2.87 mmol/l). Computed tomography showed marked osteolytic changes of the sternum and T5 (Fig. 1). Due to the clinical findings, the initial suspicion of multiple myeloma was confirmed by detection of high-titre light chains and early bone marrow aspiration. Calcium levels were increasing up to 3.17 mmol/l during hospitalization. For moderate-severe hypercalcemia, denosumab was administered twice in a total dose of 120 mg s.c. Bortezomib (2.5 mg s.c.) and dexamethasone (40 mg i.v.) had already been administered as part of the oncological treatment of myeloma. Despite these measures, the patient became symptomatic the same day with increasing hypercalcemia (3.48 mmol/l) and deterioration of renal function. Consecutively, two dialysis treatments were necessary to lower calcium levels. Initial myeloma treatment was successful as indicated by normalization of light chains (decrease of free light chain lambda from 10793 mg/l to 53 mg/l) and normalization of renal function. Early discharge and further out-patient treatment was possible.



Results or Learning points: Paraneoplastic hypercalcemia in the setting of multiple myeloma proved to be severe and refractory to standard therapy. Bisphosphonates were contrain-

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dicated due to renal failure. Denosumab, bortezomib/dexmethasone and radiotherapy required intermittent dialysis to control hypercalcemia. Dialysis treatment must be considered as therapy option in severe hypercalcemia or in refractory courses, especially in patients with renal insufficiency.

OC 16

Recurrent severe fluctuation of consciousness and cognition in a patient undergoing hemodialysis

Mrs. Ursina Lais[1], Dr. Marie-An Carstensen de Letter[2], Dr. Agnes Kneubühl[1]

1. Spital Lachen, Department of Nephrology and Dialysis, Lachen, Switzerland 2. Neuroclinic Spital Lachen, Switzerland

Background: There are different causes for impaired consciousness in chronic dialysis patients including hypoglycemia, stroke, dialysis disequilibrium syndrome, hypotension, seizures and opioid-intoxication. We report the case of a dialysis patient with impaired consciousness and cognition at the end of almost every long dialysis interval.

Methods or Case description: The 60-year-old male patient startet hemodialysis (HD) in 11/2021 after two years of peritoneal dialysis (PD), which was startet because of transplant kidney failure due to rejection. His original kidney disease was focal and segmental glomerulosclerosis according to kidney biopsy. The change in dialysis technique was made after nephrectomy in 12/2021 due to non metastatic renal cell carcinoma. Further diagnosis include liver disfunction because of biopsy proven toxic (Azathioprin) induced hepatopathy and thrombosis of the portal vein with daily ascites production of about 300 ml drained through Tenckhoff catheter. As of 01/2022 the patient experienced an impairment of consciousness with confusion and disorientation at the end of almost every long dialysis interval, starting already at home. Until 06/2022 he got hospitalized seven times.

Results or Learning points: We excluded infections, liver failure, diabetes mellitus as well as alcohol and substance abuse and performed cerebral CT-Angiography and MRI without finding an explanation. Encephalogram before, during and after events showed no seizures. Lumbar puncture showed no cells, normal protein, glucose, lactate, Tau-Protein, Phospho-Tau Protein and further neuroimmunologic parameters. Laboratory analysis in particular showed high PTH. Polygraphy showed obstructiv sleep disorder. In 07/2022 the patient had his first tonic-clonic seizure. After starting CPAP therapy at night and anti-epileptic medication (Levetiracetam) based on clinical seizure activity, the episodic acute disturbances of consciousness and cognition stopped.

Examination	Date	Status	Result
Liquor	13.02.2022	Impaired consciousness	Ec 1 10^3/µl, LC 0/µl, Glucose-Ratio normal, Beta Amyloids normal Glucose-Ratio normal, Lactate normal, Protein normal, Tau-Proteins normal
Polygraphy	14.02.2022	BMI 26 k/m^2	AHI 6.5/h
EEG	07.03.2022	Impaired consciousness	Nonspecific slow cortical activity of the brain
Immunology (Serum)	31.03.2022	Impaired consciousness	Amphiphysin, Anti-HU, -RI, -YO, -GAD65, -CV2, -MA, -TA/MA2, -SOX1, -TR, -ZIC4, -LGI1, -CASPR2, -GABA, -GluR1/2, -DPPX-IgG: all negative except Anti-CASPR2 1:10 (not diagnostic)
PTH	04.04.2022	Impaired consciousness	83.4 pmol/l (no 1-6.8)
Polygraphy	13.06.2022	BMI 26 kg/m^2	AHI 23.9/h
EEG	04.07.2022	First generalized tonic-clonic seizure	Postictal generalized slowing of critical pattern with mainly theta- and delta-activity
PTH	04.07.2022	Impaired consciousness	70 pmol/l (no 1-6.8)

Conclusions: Patients undergoing hemodialysis may have various causes of impairment of consciousness. Nonconvulsive status epilepticus should be considered even if encephalograms show no specific epileptic activity. The cause is usually multimodal as in our patient suffering from OSAS and hyperparathyreoidism in addition.

OC 17

Epidemiology, thrombolytic management, and outcomes of acute stroke among patients with chronic kidney disease: a systematic review and meta-analysis*

Dr. Ido Zamberg[1]

1. Division of Nephrology, department of medicine, McGill University, Canada

Background: The relative frequency of ischAemic versus haemorrhagic stroke among patients with chronic kidney disease (CKD) has not been clearly described. Moreover, no recent meta-analysis has investigated the outcomes of patients with CKD treated with thrombolysis for acute ischaemic stroke. We conducted a systematic review and meta-analysis to estimate the proportion of stroke subtypes and the outcomes of thrombolysis in CKD.

Methods or Case description: A PubMed, EMBASE and Cochrane literature research was conducted. The primary outcome was the proportion and incidence of ischaemic versus haemorrhagic strokes among patients with CKD. In addition, we assessed the impact of CKD on disability, mortality and bleeding among patients with acute ischaemic stroke treated with thrombolysis. The pooled proportion and the risk ratio were estimated using a random-effects model.

Results or Learning points: Thirty-nine observational studies were included: 22 on the epidemiology of stroke types and 17 on the outcomes of thrombolysis in this population. In the main analysis (>99 281 patients), ischaemic stroke was more frequent than haemorrhagic among patients with CKD [78.3%, 95% confidence interval (CI) 73.3–82.5%]. However, among patients with kidney failure, the proportion of ischaemic stroke decreased and was closer to that of haemorrhagic stroke (59.8%, 95% CI 49.4–69.4%). CKD was associated with worse clinical outcomes in patients with acute ischaemic stroke compared with patients with preserved kidney function.

Conclusions: The relative frequency of haemorrhagic stroke seems to increase as kidney function declines. Among patients with acute ischaemic stroke treated with thrombolysis, presence of CKD is associated with higher disability, mortality and bleeding, compared with patients with preserved kidney function.

Paper published in NDT.

*YSN paper

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SHORT ORAL & POSTER PRESENTATIONS

OC 18 / P 01

Kidney Function, Outcome and Pill Burden of Belatacept-Conversion in kidney-transplant recipients*

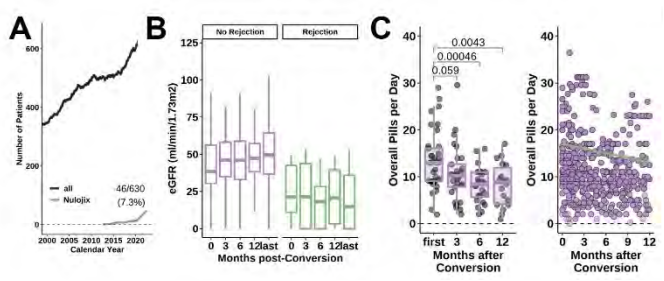
Dr. Federica Bocchi[1], Mr. Sascha Neuenschwander[2], Dr. Katarina Benackova[2], Dr. Daniel SIDLER[2]

1. University Hospital, Berne, Switzerland, 2. Klinik für Nephrologie und Hypertonie, Inselspital, Bern, Switzerland

Background: Belatacept is a treatment option for the prophylaxis of rejection after kidney transplantation (KT). Belatacept may prevent and/or revert side effects of conventional immunosuppression, notably Calcineurin Inhibitors (CNI) and thereby increase allograft survival, reduce pill burden and increase quality of life.

Methods or Case description: We conducted a retrospective study in 53 KT patients converted to Belatacept between July 2012 to June 2022 at our institution and assessed (1) allograft survival, (2) eGFR course, (3) pill burden and (4) treatment costs. Patients had a transplant history of 3.12 years (IQR: 0.74-9.9) and indication for conversion was clinical or histology proven Calcineurin Inhibitor Toxicity (CNT) (n = 44, 83%) or refractory rejection (n = 9, 17%).

Results or Learning points: Belatacept conversion rate increased in the last years (Figure A). At the end of the study, 46 of 630 (7.3%) patients with a functioning kidney allograft were under Belatacept. One year graft outcome was excellent in patients converted for CNT (98%, CI: 93-100%), but poor for patients converted for rejection (53%, CI: 28-100%). In the former group, after conversion 57% of patients (25/44) showed a eGFR slope of greater 2 ml/min/year (responders), 9% (5/44) of -0.5 to 2 ml/min/year (partial responders) and 32% (14/44) of below -0.5 ml/min/year (non-responders). Overall, eGFR increased from 38.5 ml/min/1.73 m^2 at conversion to 47.4 ml/min/1.73 m^2 at 12 months (Figure B). Clinical (type of KT, age) and biochemical parameters (baseline eGFR) were ineffective to predict eGFR response after conversion. One patient suffered from rejection with re-exposure of CNI, in two patients Belatacept was discontinued. Pill burden and monthly cost of treatment significantly dropped in the majority of patients (Figure C).



Conclusions: Belatacept-conversion is safe in patients with stable transplant function and may stabilize or increase eGFR in a majority of patients. Conversion leads to a reduction of pill burden for immunosuppressive drugs and supplementary therapies.

*Student paper

OC 19 / P 02

Impact of marginal donor to marginal recipient kidney transplantation on delayed graft function and outcome

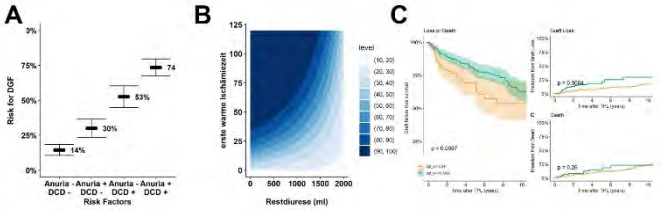
Dr. Federica Bocchi[1], Dr. Christian Kuhn[2], Mrs. Natalie Müller[2], Dr. Federico Storni[3], Prof. Guido Beldi[3], Dr. Daniel SIDLER[2]

1. University Hospital, Berne, Switzerland, 2. Klinik für Nephrologie und Hypertonie, Inselspital, Bern, 3. Klinik für Viszerale Chirurgie und Medizin, Inselspital, Bern, Switzerland

Background: The demographics of donor and recipient candidates for Kidney Transplantation (KT) have substantially changed recently: older and polymorbid. KT from marginal donors is associated with delayed graft function (DGF), prolonged hospitalization, inferior allograft function and patient survival. Similarly, KT to marginal recipients is associated with reduced outcomes. We assess the overall and combined impact of a KT from marginal donors to marginal recipients. We focused on 1) DGF; 2) hospital stay and number of dialysis days after KT; 3) allograft function at 3 and 6 months, and 4) patient and allograft survival.

Methods or Case description: Retrospective cohort study of deceased donor KT recipients in Bern, Switzerland, from 2008 to 2022. DGF was defined as the need of at least one dialysis session after KT. Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration 2009 creatinine equation. Following co-variables were considered: donor characteristics (age, acute kidney injury, comorbiditites, type of organ procurement), recipient characteristics (age, dialysis history, residual urine volume, previous KT history), cold and warm ischemia time. Exclusion criteria were multiorgan KT and patients with primary non-function.

Results or Learning points: 394 deceased donor KT were included. The overall DGF rate was 25% (n = 103) and median time from reperfusion to DGF resolution was 8.8 days (IQR: 3.4-14.5 days). Overall, patients with DGF received 4 dialysis sessions (IQR: 2-8). Pre-KT oliguria (<200 ml/24h) and donor with circulatory death (DCD) procurement predicted the risk for DGF independently and when combined in a synergistic manner compared to KT without such risk parameters (Figure A, B). Recipients with initial DGF showed an inferior overall outcome and events were attributed predominantly to early graft failures (Figure C).



Conclusions: Seized residual diuresis and DCD donation synergistically predict DGF events with risk for subsequent inferior outcomes.

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OC 20 / P 03

Effect of 2021-2022 vaccination on the seroprevalence of antibodies to Influenza A and B strains in kidney transplant recipients and health-care workers*

Dr. Stephanie Zappi[1], Dr. Francesco Muoio[2], Dr. Luca Bernasconi[3], Dr. Davide Corti[2], Dr. Luca Piccoli[2], Dr. Min Jeong Kim[1]

1. Division of Nephrology, Cantonal Hospital Aarau, Aarau, Switzerland, 2. Humabs Biomed SA, Vir Biotechnology, Switzerland 3. Institute of Laboratory Medicine Kantonsspital Aarau, Switzerland

Background: Since the beginning of the coronavirus 2 pandemic in 2019, incidence of influenza infections has significantly decreased mainly due to the COVID-19-related protective measures. We aimed to evaluate the prevalence of serum antibodies against Influenza A and B in kidney transplant recipients (KTRs) and health-care workers (HCWs) before and after receiving the 2021-2022 season vaccine.

Methods or Case description: In prospectively collected pre- and postvaccination sera from KTRs (n = 75) and HCWs (n = 28), vaccinated with Fluarix® tetra, IgG antibodies against influenza hemagglutinins of the strains included in the 2021-2022 vaccine (A/Victoria/H1N1; A/Cambodia/H3N2; B/Washington; B/PHUKET) were measured by ELISA. Same measurements were performed in the sera from unvaccinated KTRs (n = 28) and HCWs (n = 11) at 3-month interval during the same season. The half maximal effective dilution (ED50) was measured for all sera and fold-change variation of ED50 values before and after vaccination were calculated.

Results or Learning points: ED50 values of IgG against each strain from the serially collected sera are shown in Figure 1. Almost all study participants showed antibodies to all four strains prior to vaccination, whereby the ED50 values were mostly higher in the HCWs. There was no significant increase of ED50 values after vaccination in both KTRs and HCWs, and the increase was comparable in KTRs and HCWs. Unvaccinated subjects, especially HCWs, showed a slight increase of ED50 values over a 3-month interval, although this variation was not significant. During the study period no influenza infection was self-reported or diagnosed in all the enrolled subjects.

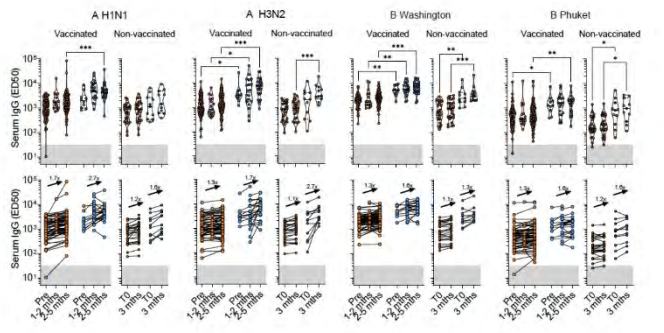

Figure 1. Serum IgG titers against influenza strains before and after vaccination. Pre, samples collected before vaccination. 1-2 and 2-5 mths, samples collected at the indicated months after vaccination. T0, samples collected from non-vaccinated individuals at the beginning of the vaccination season. 3 mths, samples collected from non-vaccinated individuals 3 months later than T0.

Conclusions: In our cohorts of KTRs and HCWs, we were able to show a wide prevalence of pre-vaccination antibodies against influenza vaccine strains of 2021-2022 season. IgG levels were significantly higher in HCWs compared to KTRs. There was no significant increase of antibodies after vaccination in both KTRs and HCWs.

*YSN paper

OC 21 / P 04

Hemodialysis and spirituality: exploring spiritual expectations of hemodialysis patients in a University Dialysis Center

Dr. Simon Mastrangelo[1], Mr. Etienne Rochat[1], Dr. Menno Prujim[1]

1. Lausanne University Hospital, Lausanne, Switzerland

Background: Previous American studies suggest that dialysis patients want dialysis caregivers to discuss spirituality and mobilize appropriate spiritual resources. Whether this also applies to the Swiss dialysis population, and whether patients' spiritual experiences contribute to their coping mechanisms is unknown. The objective of this pilot study was therefore to explore the spiritual expectations of hemodialysis patients in a Swiss Dialysis Center.

Methods or Case description: An experienced sociologist (SM) conducted 20 qualitative, semi-structured interviews with dialysis patients in the ambulatory chronic dialysis unit of the University Hospital of Lausanne. Among the questions asked were: “Do you have any spirituality, religion, belief, or interest in broader existential issues? If so, which one(s)? Did the COVID-19 pandemic influence your spiritual practices? Would you like health professionals to take note of what you have just told me?” All interviews were recorded, transcribed, and then coded and analyzed with Atlas.ti software.

Results or Learning points: In total, 14/20 (70%) patients practiced some form of religion (believers), 4 were agnosts, and 2 defined themselves as atheist. The majority (75%) consider that spirituality can play a positive role to preserve hope and to manage the difficulties caused by the disease and its treatment. However, only 25% of believers would appreciate support of a spiritual nature from dialysis caregivers. The majority of those who have spiritual practices wish to keep it private and outside the hospital structure. Their relationship to spirituality has generally not been significantly impacted by their changing health status, or the COVID-19 pandemic. The most frequently mentioned needs are related to social dimensions (isolation, loneliness, need to talk, financial problems).

Conclusions: In this pilot study, the majority of Swiss dialysis patients did not express the wish to discuss more often spiritual issues with dialysis caregivers, but they would appreciate more attention for social and socio-economic difficulties.

OC 22 / P 05

Gender differences in the dialysis population in Switzerland from 2014 to 2021

Mrs. Rebecca Guidotti[1], Prof. Patrice M. Ambühl[1]

1. Institute of Nephrology, Stadtspital Zurich, Zurich, Switzerland

Background: The Swiss Dialysis Registry (srrqap) collects nationwide data since 2013. The primary goal of the srrqap is to control and improve the quality of dialysis therapy in Switzerland. In the present analysis, the gender differences, analyzed over the years, of the dialysis population in Switzerland are presented and compared with international data.

Methods or Case description: All medical establishments in Switzerland (N = 96) providing chronic dialysis treatment, provided data from 2014-2021.

Results or Learning points: Women are on average one year younger than men at start of dialysis (64.7 vs. 65.6 years; p = 0.021) and in both sexes the starting age at dialysis increases slightly over the years. Two third of incident dialysis patients are men, with the percentage above 65 years getting even bigger reaching up to 73%. No obvious gender differences were found with regard to dialysis modality. Women are more likely

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than men to receive <12 hours/week of dialysis, and the use of catheters at the start of dialysis is more common in women than men. Men have a higher Charlson score and more comorbidities than women (incident and prevalent). Overall patient survival of women and men on dialysis is very similar in the first 4 years, however thereafter, the difference increases over time, with a survival advantage for women.

Table: Ranges of mean values from 2014-2021 for specific parameters, stratified by gender

Variables	Female	Male	p-value
Hemoglobin, g/dL	11.0 – 11.1	11.2 – 11.3	≤ 0.05
Parathyroid hormone, ng/L	341.8 – 405.2	303.7 – 391.3	ns
Iron substitution, %	73.0 – 78.8	72.5 – 77.6	≤ 0.05
Erythropoietin substitution %	83.8 – 86.9	76.7 – 79.8	≤ 0.05
Kt/V	1.70 – 1.80	1.49 – 1.57	≤ 0.05
Dialysis vintage, years	4.2 – 5.1	3.6 – 4.5	≤ 0.05
1 year survival probability*, %	90.7	90.3	
2 year survival probability*, %	80.8	79.1	
3 year survival probability*, %	71.3	69.9	
4 year survival probability*, %	60	59.3	
5 year survival probability*, %	51.9	48.8	
6 year survival probability*, %	44.7	40.1	
7 year survival probability*, %	38.1	30.6	
Cadaveric transplants*, OR	1.34	1	0.000

Conclusions: Unlike other countries, where women are 1-2 years older than men at dialysis start, incident female dialysis patients in Switzerland are one year younger than male patients. In contrast to other countries, deceased donor transplant rates were higher in women than in men. Women under 45 years on dialysis have a higher mortality risk than men, which is in line with other countries. However, the number in this age group is very low and we could not show that it's infection-related.

OC 23 / P 06

Real world (electronic) patient report outcome (ePROs): a quality tool for hemodialysis patients using Consilium Care Mobile App

Dr. Michael Moeddel 1, Prof. Andreas Trojan 2, Dr. Ingrid Schuller 1, Mr. Marek Peschel 1

1. Nephrologie – Hirslanden Klinik im Park, Zurich, 2. OnkoZentrum, Zürich, Switzerland

Background: Consilium care mobile app (CC-App) is an established digital self-monitoring for diseases, especially cancer. As a CE certified medical product, the app enables electronic recording of symptoms and self-reported events by patients (ePROs) and improvement of treatment quality through collaborative patient-doctor review of symptoms. The handling of the app in the context of dialysis patients is analyzed.

Methods or Case description: 10 dialysis patients were able to install the app on their smartphone. The CC-App offers 103 organ symptoms. Each patient could self-select symptoms; dialysis-specific symptoms such as itching, fatigue, dry mouth, numbness and tingling were recommended for recording. App functions such as vitals, weight, pulse, BP and blood glucose could be optionally monitored by each user, as well as medication and note function. Evaluation was planned for 4 weeks.

Results or Learning points: Results were obtained from 8 of 10 patients, average age was 65 years. 4 of 8 patients made entries in the app almost daily, the other four had breaks of up to several days at a time, one participant only used the app for a total of 7 days. A total of 259 vital signs were entered, 1301 symptoms such as itching, fatigue, dry mouth, numbness and tingling, as well as 38 entries on medication.

Conclusions: Consilium care app offers outpatients the possibility of accurate symptom and vital sign monitoring with digital transmission and low-threshold contact options to the respective treatment center. Targeted selection of users, introduction and active support in the initial phase significantly increases compliance and thus the benefit. While app use seems limited due to high treatment intensity of center treated hemodialysis patients, the application is particularly suitable for home/peritoneal dialysis patients and in kidney transplant patients. This allows a very good monitoring and connection possibility to the center without physical presence. Studies in this regard are still pending.

OC 24 / P 07

Complementary and alternative medicines, symptoms, and quality of life of patients undergoing haemodialysis: a complex relationship

Ms. Marie Kemnitz[1], Mr. Matteo Antonini[2], Prof. Philippe Delmas[2]

1. University of Lausanne, Switzerland 2. La Source School of Nursing, University of Applied Sciences and Arts Western Switzerland

Background: Patients requiring haemodialysis suffers from many symptoms that negatively impact their quality of life. Literature suggests that complementary and alternative medicines are used by chronic patients to cope with their situation and improve their quality of life. Nevertheless, the use of these practices is still taboo, so they are rarely integrated into overall patient care, making it difficult to assess their effects and their interactions with standard healthcare protocols. To help filling this gap, this study aims to explore the relationships between the perceived symptoms, the complementary and alternative medicine use, and the level of quality of life of patients undergoing haemodialysis.

Methods or Case description: Sequence analysis was used to create a typology of complementary and alternative medicines users. How the use of complementary and alternative medicines is linked to symptoms' presence and patients' quality of life was explored using regression analysis. Data come from questionnaires completed by 88 patients in French-speaking Switzerland.

Results or Learning points: We identified 5 profiles: (a) people who don't use any complementary and alternative medicine or use them sporadically, (b) patients that practice meditation, (c) people who practice prayer, (d) patients that takes plant-based products and use other complementary and alternative medicines, (e) people who use massage therapy. Complementary and alternative medicines use and symptoms appear unrelated, as well as complementary and alternative medicines use and the physical dimension of quality of life. Yet, the use of complementary and alternative medicines is linked to higher values of the psychological dimension of patients' quality of life. Meditating and praying appear to be the most effective practices.

Conclusions: Almost 2 out of 3 patients undergoing haemodialysis use complementary and alternative medicines. The use of these practices seems to be scarcely related to physical suffering and symptoms' experience, while it seems to be linked with the preservation of patients' psychological balance.

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OC 25 / P 08

InterACTIVE-HD 2.0 – Patient-specific prediction of intradialytic multi-solute plasmatic trends: preliminary results

Dr. Giustina Casagrande[1], Dr. Carlo Balsamello[1], Dr. Silvio Pianca[2], Dr. Antonio Bellasi[2], Dr. Carlo Jovane[3], Dr. Reto Venzin[4], Dr. Giuseppe Rombolà[5], Prof. Pietro Cippà[2], Dr. Gianvincenzo Melfa[3], Dr. Carla Colturi[6], Prof. Maria Laura Costantino[1]

1. Department of Chemistry, Materials and Chemical Engineering, Politecnico di Milano, Milan, Italy, 2. Division of Nephrology, Ente Ospedaliero Cantonale, Lugano, Switzerland, 3. Department of Nephrology and Dialysis, Sant'Anna Hospital, Como, Italy, 4. Nephrology, Kantonsspital Graubünden, Chur, Switzerland, 5. Nephrology Dialysis and Kidney Transplant Unit, ASST Settelaghi, Varese, Italy, 6. Nephrology and Dialysis UOC, ASST Valtellina e Alto Lario, Sondrio, Italy

Background: Elderly ESRD patients are characterized by multiple comorbidities. Thus, the use of predictive customized models to properly simulate in few minutes the patients' responses to the treatment, i.e., mass and fluids distributions within modelled compartments, by only using initial clinical data would be of great help in clinical hands to enhance efficiency of the treatment itself and improve their quality of life. The aim is to validate the available predictive model on the new data acquired for the Interreg project InterACTIVE-HD 2.0.

Methods or Case description: 5 hospitals were involved into the project. In Como, Lugano, Varese, Chur, and Sondrio Dialysis units respectively 45, 25, 45, 10 and 20 patients were enrolled. Phase 1 includes the monitoring of 6 consecutive sessions, Phase 2 the monitoring of other 3 sessions, 2 months later. Moreover, in Como, Lugano, and Varese other 3 adjunctive sessions will be monitored. Hourly hematic recordings and continuous machine acquisitions are required for model customization (3 sessions), to obtain an averaged set of patient-specific parameters. These will feed an available multi-solute, multi-pool predictive model, which can be run by using initial data of the session to be simulated. Model's predictive accuracy and reliability over time will be evaluated for each subsequent monitored session, in terms of normalized Root Mean Square Errors (nRMSEs). Preliminar phase 1 results were available for the centres of Lugano, Como, and Sondrio.

Results or Learning points: For the recorded sessions, median predictive nRMSE related to plasmatic [Na+], [Cl-], [Ca2+], and [HCO3-], and to hematic volume, is below 5%, while for [K+] it is below 7% and for [urea] below 12%.

Conclusions: This preliminary assessment represents a step forward for the development of decision support systems allowing treatment customization on each patient. Complete data deriving from the following phases will determine reliability over time and inter-centre applicability.

OC 26 / P 09

Daprodustat is not associated with an increased risk of cancer: results from the ASCEND-D and ASCEND-ND trials

Prof. Ajay K. Singh[1], Prof. Christoph Wanner[2], Prof. Andrzej Wiecek[3], Dr. Allison Blackorby[4], Dr. Tara Barker[4], Dr. Amy Meadowcroft[4], Dr. Alexander R. Cobitz[4]

1. Brigham and Women's Hospital, Harvard Medical School, Boston, US 2. University Hospital of Würzburg, Würzburg, Germany 3. Medical University of Silesia, Katowice, Poland, 4. GSK, Collegeville, PA, US

Background: We explored the risk of cancer development in 2 cardiovascular outcome trials in patients with chronic kidney disease (CKD) anaemia requiring dialysis (Anaemia Studies in CKD: Erythropoiesis via a novel prolyl hydroxylase inhibitor Daprodustat [ASCEND]-D1; NCT02879305) and those not on dialysis (ASCEND-ND2; NCT028768355).

Methods or Case description: Cancer-related adverse events (AEs) from the ASCEND studies were identified based on a predefined list of terms including new cancer events or tumour progression and recurrence for patients receiving ≥1 dose of daprodustat or erythropoiesis-stimulating agents (ESA; Safety Population). Patients were included, providing no: history of cancer within 2 years prior to screening, current cancer treatment, complicated kidney cyst. A post-hoc modified intention-to-treat approach was used, including on- and off-treatment events.

Results or Learning points: 2964 patients were randomised in ASCEND-D and 3872 in ASCEND-ND, with ~14,200 person-years of follow-up. At baseline, prior cancer history was reported in: 5.0% (daprodustat) and 4.9% (ESA) of patients in ASCEND-D; 5.2% (daprodustat) and 4.4% (darbepoetin), of patients in ASCEND-ND. Both the rate of cancer-related AEs and rate per 100 person-years were balanced for each study, with no pattern regarding location or type (Table). Of patients with cancer AEs (Table), fatal AEs occurred in: <1% (n = 11, daprodustat) and 1% (n = 15, ESA) in ASCEND-D; <1% (n = 6, daprodustat) and <1% (n = 11, darbepoetin) in ASCEND-ND. The number of patients with multiple cancer AEs, time to first onset, outcome of the event and event seriousness/severity were also similar between treatment groups for both trials.

Table: Cancer adverse events from the Anaemia Studies in Chronic Kidney Disease: Erythropoiesis via a novel prolyl hydroxylase inhibitor Daprodustat (ASCEND) -dialysis (D), and -non dialysis (ND) trials occurring in ≥10 patients per study

Safety Population, mITT approach*	ASCEND-D				ASCEND-ND			
	Daprodustat N=1482		ESA N=1474		Daprodustat N=1937		Darbepoetin alfa N=1933	
	n (%)	Rate/ 100 PY	n (%)	Rate/ 100 PY	n (%)	Rate/ 100 PY	n (%)	Rate/ 100 PY
Overall Cancer AEs	**65 (4)**	**1.89**	**77 (5)**	**2.26**	**87 (4)**	**2.50**	**84 (4)**	**2.40**
Neoplasms, malignant	57 (4)	1.66	69 (5)	2.02	80 (4)	2.29	75 (4)	2.14
Skin	7 (<1)	0.20	14 (<1)	0.40	22 (1)	0.62	15 (<1)	0.42
Site unspecified	3 (<1)	0.09	5 (<1)	0.14	11 (<1)	0.31	9 (<1)	0.25
Renal	10 (<1)	0.29	4 (<1)	0.12	3 (<1)	0.08	6 (<1)	0.17
Breast	3 (<1)	0.09	4 (<1)	0.11	8 (<1)	0.22	5 (<1)	0.14
Colorectal	4 (<1)	0.11	3 (<1)	0.09	5 (<1)	0.14	5 (<1)	0.14
Blood and lymphatic system disorders	6 (<1)	0.17	6 (<1)	0.17	5 (<1)	0.14	10 (<1)	0.28
Marrow depression and hypoplastic anemia	6 (<1)	0.17	6 (<1)	0.17	5 (<1)	0.14	10 (<1)	0.28

*Post-hoc; AE, adverse event; ESA, erythropoiesis-stimulating agent; mITT, modified intention-to-treat

Conclusions: In cardiovascular outcome trials comprised of patients requiring dialysis (ASCEND-D) and not requiring dialysis (ASCEND-ND) with CKD anaemia, daprodustat was not associated with an increased risk of cancer or cancer mortality, relative to ESA. Collectively, across these trials, cancer AEs were balanced.

References:

1. Singh AK, et al. NEJM 2021;385:2325–335

2. Singh AK, et al. NEJM 2021;385:2313–324

(GSK-funded study; ENCORE of presentation at ERA 2022)

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OC 27 / P 10

Iron Parameters in Patients Treated With Roxadustat for Anemia Associated With Chronic Kidney Disease: Post Hoc Analysis of the Non–Dialysis-Dependent or Incident Dialysis Population From Four Phase 3 Studies

Prof. Ciro Esposito[1], Dr. Jonathan Barratt[2], Dr. Frank Dellanna[3], Dr. Jose Portoles[4], Dr. Gabriel Choukroun[5], Dr. Luca De Nicola[6], Dr. Michael Reusch[7], Mr. James Young[8], Dr. Alina Jiletcovici[9], Dr. Nada Dimkovic[10]

1. Unit of Nephrology and Dialysis, ICS Maugeri, University of Pavia, Italy 2. Department of Cardiovascular Sciences, University of Leicester, UK 3. Department of Kidney and Dialysis, MVZ DaVita Rhein-Ruhr GmbH, Germany 4. Department of Nephrology, Hospital Universitario Puerta de Hierro, Department of Nephrology, Anemia Working Group Spanish Society of Nephrology, Spain 5. Department of Nephrology, CHU Amiens Picardie and Jules Verne University, France 6. Department of Biochemistry, Biophysics, and Bioinformatics, University of Campania, Italy 7. Department of Nephrology, Guard Therapeutics International AB, Germany 8. Department of Statistics, Astellas Pharma, Inc., US 9. Department of Medical Affairs, Astellas Pharma, Inc., US 10. Department of Nephrology, University of Belgrade, Serbia

Background: Anemia is a common complication in patients with chronic kidney disease (CKD) who are non–dialysis-dependent (NDD) or incident dialysis-dependent (ID-DD) (ie, initiated dialysis within the last 4 months). This post hoc analysis examined iron metabolism parameters in patients with anemia of CKD who were NDD/ID-DD and treated with either roxadustat or an erythropoiesis-stimulating agent (ESA).

Endpoint/parameter	Non–Dialysis-Dependent/Incident to Dialysis (NDD/ID-DD)	
	Roxadustat (n=1078)	ESA (n=1051)
CFB in hemoglobin (g/dL) to Weeks 28-52, regardless of rescue therapy		
Baseline, mean (SD)	9.04 (1.15)	9.05 (1.12)
CFB, mean (SD)	2.06 (1.36)	1.90 (1.31)
LS mean (95% CI)	1.85 (1.734, 1.966)	1.65 (1.534, 1.765)
LSMD (95% CI)	0.20 (0.038, 0.362)	
P-value	0.0153	
CFB in serum iron (µg/dL) to Week 20		
Baseline, mean (SD)	65.39 (26.56)	64.21 (26.76)
CFB, mean (SD)	5.04 (32.93)	-0.37 (32.76)
LS mean (95% CI)	6.93 (4.122, 9.735)	-0.29 (-3.065, 2.486)
LSMD (95% CI)	7.22 (3.337, 11.099)	
P-value	0.0003	
CFB in ferritin (µg/L) to Week 20		
Baseline, mean (SD)	384.75 (352.97)	373.63 (312.13)
CFB, mean (SD)	-139.92 (244.26)	-107.57 (230.93)
LS mean (95% CI)	-118.57 (-138.008, -99.140)	-108.50 (-127.885, -89.114)
LSMD (95% CI)	-10.07 (-37.031, 16.881)	
P-value	0.4837	
CFB in TIBC to Week 20		
Baseline, mean (SD)	44.62 (8.97)	44.57 (8.61)
CFB, mean (SD)	7.55 (8.03)	0.56 (6.05)
LS mean (95% CI)	6.77 (5.894, 7.651)	0.49 (-0.370, 1.358)
LSMD (95% CI)	6.28 (5.074, 7.484)	
P-value	<0.0001	
CFB in TSAT (%) to Week 20		
Baseline, mean (SD)	27.35 (10.91)	27.17 (10.40)
CFB, mean (SD)	-1.44 (12.47)	-0.66 (10.95)
LS mean (95% CI)	-0.17 (-1.176, -0.828)	-0.37 (-1.364, 0.617)
LSMD (95% CI)	0.20 (-1.184, 1.583)	
P-value	0.7774	
Proportion of patients using IV iron as rescue therapy up to Week 52		
IV iron, n (%)	36.5%	49.1%
95% CI	0.34, 0.39	0.46, 0.52
Odds ratio (95% CI)	0.52 (0.42, 0.63)	
P-value	<0.0001	

Methods or Case description: The results of four phase 3, randomized, open-label studies (NDD [DOLOMITES]; ID-DD [HIMALAYAS, SIERRAS, ROCKIES]) comparing oral roxadustat to an ESA (darbepoetin alfa or epoetin alfa) for patients with anemia of CKD were pooled in this post hoc exploratory analysis. Iron metabolism parameters (serum iron, ferritin, total iron binding capacity [TIBC], transferrin saturation [TSAT]), hemoglobin, and proportion of patients using intravenous (IV) iron supplementation were measured at various intervals within the 52-week efficacy evaluation period in patients with NDD or ID-DD CKD. The Table displays change from baseline (CFB), least squares mean difference (LSMD), 95% confidence interval (95% CI), and P-value for each iron metabolism parameter.

Results or Learning points: In total, 2129 patients were evaluated (1078 roxadustat, 1051 ESA). Hemoglobin levels increased from baseline to Weeks 28-52 for patients receiving roxadustat with NDD/ID-DD CKD compared to ESA active control (P = 0.0153). Treatment with roxadustat was associated with increased serum iron (P = 0.0003) and TIBC (P <0.0001) from baseline to Week 20 compared to treatment with ESA. Ferritin and TSAT did not significantly change from baseline to Week 20 in patients with NDD/ID-DD CKD receiving roxadustat. Fewer patients receiving roxadustat received IV iron supplementation at Week 52 (P <0.0001).

Conclusions: Compared with ESA, roxadustat treatment was associated with improvement in iron metabolism while achieving a statistically significant increase in hemoglobin levels in patients with anemia of NDD or ID-DD CKD.

OC 28 / P 11

SARS-CoV-2 breakthrough infections in patients with a history of anti-CD20 therapy during the Omicron variant waves in Switzerland (RituxiVac 3.0)

Dr. Matthias Moor[1], Prof. Britta Maurer[2], Dr. Cédric Hirzel[3], Dr. Daniel SIDLER[4]

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Department of Rheumatology and Immunology, Inselspital, University Hospital Bern, University of Bern, Bern, Switzerland., 3. Institute of Infectious Diseases, University of Bern, Bern, Switzerland., 4. Klinik für Nephrologie und Hypertonie, Inselspital, Bern, Switzerland

Background: Patients with B-cell depleting therapies show inferior immune responses to vaccines, including mRNA vaccines against SARS-CoV-2. Here, we investigated the incidence of SARS-CoV-2 breakthrough infections in the RituxiVac study cohort during the Omicron waves in Switzerland.

Methods or Case description: Using a questionnaire, we assessed vaccination history, self-reported adherence to protective measures, SARS-CoV-2 exposure, SARS-CoV-2 infection and COVID-19 complications in patients with a history of anti-CD20 therapies and healthy controls. Primary outcome was the hazard of self-reported positive SARS-CoV-2 PCR or antigen tests in patients vs. controls in association with protective measures, additional SARS-CoV-2 vaccine doses and biomarkers of vaccine-driven immunogenicity. Secondary outcomes were COVID-19 related hospitalizations and COVID-19 related mortality.

Results or Learning points: The present analysis included 81 patients with a history of anti-CD20 drugs and 24 healthy controls. The median follow-up duration was 3.5 months. Adherence to protective measures and rates of exposure to SARS-CoV-2 were similar among patients and healthy controls, as were self-reported SARS-CoV-2 infections (25/81 [31%] vs. 9/24 [38%], p = 0.54). Severe COVID-19 occurred in 8.6% (7/81) of patients and COVID-19 related mortality was 5.9% (4/81) whereas no severe or fatal cases occurred in the control group (p = 0.3 and 0.6, respectively). Neither vaccine elicited antibody levels nor the extent of the cell-mediated immune response (as by ELIspot assay) after the second vaccine dose were associated with the risk for SARS-Cov-2 infection. However, having had a third vaccine dose was associated with a reduced risk for SARS-CoV-2 infections among anti-CD20 treated patients (HR 0.19, 95%CI: 0.05-0.7, p <0.05).

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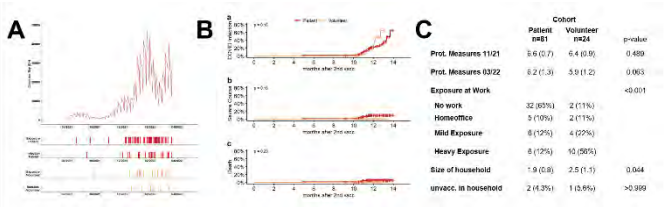


Conclusions: Breakthrough infections with SARS-CoV-2 were frequent in patients and healthy controls despite a high level of self-reported adherence to protective measures. Additional SARS-CoV-2 vaccine doses were associated with a lower risk for SARS-CoV-2 infection in this vulnerable patient population. (Funded by Bern University Hospital, ClinicalTrials.gov number, NCT04877496)

OC 29 / P 12

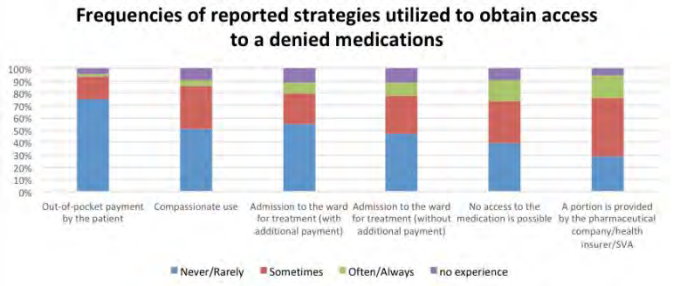
Swiss pre-approval process for pharmaceuticals and other medicinal products not covered by basic insurance: viewpoint of nephrologists *

Dr. Paul de Zwart[1], Prof. Thomas Müller[2], Dr. Guiseppina Spartà[1], Dr. Valerie Luyckx[1]

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

Background: In Switzerland, nephrologists must frequently obtain pre-approval from health insurers for certain medications/tests for individual patients. The current individualized approach raises equity concerns given that similar requests might be dealt with differently by different health insurers and/or evaluating physicians.

Methods or Case description: An anonymous survey regarding experiences in applying for pre-approvals for medications required for kidney disease care was distributed to all 400 registered nephrologists in Switzerland. Ethics approval was not required. No personal data was collected.



Results or Learning points: Responses were received from 95 nephrologists. Rituximab and SGLT2 inhibitors (reported by 75% and 40% of respondents respectively) most frequently required pre-approval. Rebuttals were most frequently required for Rituximab (49%), Eculizumab (41%) and SGLT2 inhibitors (32%), also the most frequently denied medications. Genetic testing was most frequently requested for complement (70%) and Alports spectrum (19%) genes. Requests for genetic testing were more frequently denied for cystic renal diseases (17%) and nephrotic syndrome (14%). Approaches used when medications were denied are illustrated in Figure 1. Most nephrologists found requests for further information from the health insurers were rarely/never reasonable (58%); 72% reported it was rarely/never possible to engage with the insurance physician; 69% were concerned insurance physicians did not have relevant expertise. Most respondents (58%) reported receiving different responses always/often from different insurers for similar patients, 73% reported sometimes/rarely receiving different responses from the same insurer. One in three nephrologists reported that the pre-approval process always/often results in a clinically relevant delay in treatment. Two thirds of respondents spend at least 1 -2 hours per week on pre-approvals. Most respondents (84%) reported that the pre-approval process sometimes/often/always makes them feel that they cannot do their best for the patient.

Conclusions: From the perspective of nephrologists, the pre-approval process in Switzerland is cumbersome, intransparent and inequitable, and may result in denial or delays of important treatment for patients.

*Student paper

OC 30 / P 13

Metabolic Acidosis in Cameroonian patients with Chronic Kidney Disease (CKD): preliminary results from an open-label randomised study

Dr. Martial Tsiazok[1], Dr. Maimouna Mahamat[1], Dr. Victorine Nzana[2], Dr. Hermine Fouda[3], Dr. Aristide Nono[1], Dr. Karla Mukwuelle[1], Dr. James Tataw[4], Dr. Emmanuelle Djong[2], Mrs. Falone Magoua[2], Prof. Pierre-Yves Martin[5], Prof. Sophie de Seigneux[6], Prof. François Kaze[2], Prof. Gloria Ashuntantang[1], Prof. Patrick Saudan[6]

1. Hôpital Général de Yaoundé, Cameroon 2. Centre Hospitalier Universitaire de Yaoundé, Cameroon 3. Centre Hospitalier Universitaire de Douala, Cameroon 4. Hôpital du Jura Bernois, Switzerland 5. Faculty of Medicine, Geneva University, Geneva, Switzerland 6. Service of Nephrology, Geneva University Hospitals, Geneva, Switzerland

Background: Metabolic acidosis is usually present in CKD and the effectiveness of oral bicarbonate supplementation in order to slow down its progression has been noted in patients with CKD living in western countries but is unknown in patients living in Africa. We started a prospective randomised trial in January 2020 to determine the impact of bicarbonate supplementation on top of local standard care in CKD Cameroonian patients.

Methods or Case description: Patients eligible for the study (eGFR <60 ml/min, aged >18 years old and enrolled in outpatient clinics of 2 hospitals (located in Yaoundé urban areas) are randomly assigned to an intervention group (bicarbonate + local standard nephrological care) or to a control group (local standard nephrological care only). The primary composite endpoint is a composite end-point associating severe decline in GFR (>3ml/min/yr) or need of dialysis or occurrence of end-stage CKD (eGFR <15 ml/min) measured at 24 months after inclusion. We aim at enrolling 133 patients.

Results or Learning points: At the end of August 2022, 90 patients have been randomised. Mean age is 58 + 11 yrs, male gender is 70%. Regarding CKD diagnoses, 67 had either diabetes or nephrosclerosis, 13 had chronic glomerulonephritis and 10 other diagnoses. Mean baseline eGFR was 30 + 13 ml/min, macroproteinuria was present in 53 patients, of whom 7 had nephrotic range proteinuria. Mean serum bicarbonate was 24 + 5 mmol/L. Twenty-six (29%) of the patients had a baseline serum bicarbonate <22 mmol/L.

Conclusions: These preliminary results indicate that chronic metabolic acidosis is uncommon among CKD patients in Yaoundé, Cameroon. This study may demonstrate whether bicarbonate supplementation even in African patients without overt metabolic acidosis could benefit them in terms of renal function decline.

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OC 31 / P 14

Low dose methadone for breathlessness in people with CKD≥ KDIG3b experiencing or at risk of morphine-neurotoxic effects – single-centre case series

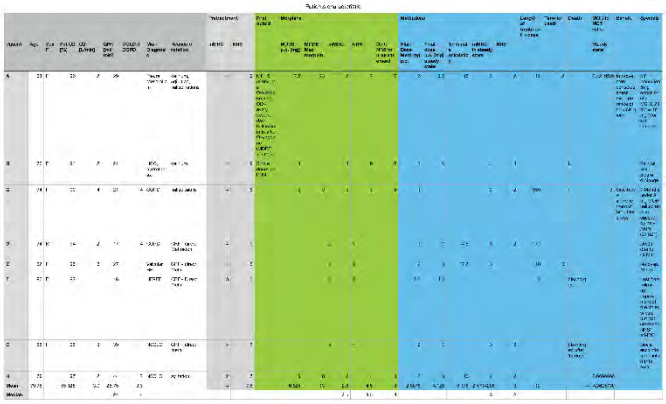
Dr. Piotr Sobanski[1]

1. Palliative Care Station und Kompetenzzentrum, Innere Medizin, Spital Schwyz, Switzerland

Background: Low-dose opioids are used for breathlessness management, commonly needed in advanced malignant and non-malignant illnesses. CKD is frequently seen in the advanced stages of other disease, requiring adjustment of ongoing treatment to avoid drug accumulation. In CKD, the most studied opioid for breathlessness, morphine (M), and even more its metabolites (morphine-6-glucuronide, M-6-G, and morphine-3-glucuronides, M-3-G) can accumulate. M is renally excreted, in 90% as: M-3-G (more hydrophilic cumulates more in CKD) and M-6-G. Effects of M-3-G (neurotoxicity) can dominate over desirable M-6-G effects (analgesia) in moderate and severe CKD. For this reason, morphine is contraindicated if GFR <30 ml/min. Prolonging intervals between doses of M can be insufficient to prevent M-3-G accumulation. Methadone in CKD accumulates, but not having neurotoxic metabolites, can after dose reduction, be more safe than M.

Methods or Case description: Retrospective analysis of records of 8 consecutive patients (6 females, 2 men) with neurotoxic effects after low-dose M (6.6mg/24h) or on the risk of those, with CKD stage ≥ 3b KDIGO, hospitalized from 09.2017-02.2022 in a palliative care unit (Schwyz, Schweiz). Mean age 79.8 (rate 63-94), mean GFR 27 ml/min (range 16–44). After discontinuation of previous opioids, methadone was started (1 mg methadone s.l. BID). If satisfactory improvement was continuously, the planned dose was postponed, to prevent overdosing. Rescue doses were allowed >3 h. After 3–4 days, if sufficient symptom alleviation was reached, fix daily dose was calculated and prescribed every 12h.

Results or Learning points: All patients experience a clinically meaningful improvement in breathlessness without neurotoxic side effects after starting methadon (mean effective dose 4.1mg/24h). In those who was previously under M the dose equivalence between M and methadone was 4.4:1. M, even in low dose, (6.6mg/24h p.o.) can evoke neurotoxic effects in people with CKD ≥3b KDIGO.



Conclusions: Low-dose methadone in people CKD (≥3b KDIGO) should be considered as an alternative to morphine.

OC 32 / P 15

Altered lipid metabolism in ADPKD patients treated with Tolvaptan *

Dr. Matteo Bargagli[1], Dr. Manuel Anderegg[2], Prof. Uyen Huynh-Do[2], Prof. Bruno Vogt[2], Prof. Pietro Manuel Ferraro[3], Prof. Daniel Fuster[2]

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Freiburgstrasse 15, 3010, Bern, Switzerland, 3. U.O.S. Terapia Conservativa della Malattia Renale Cronica, Fondazione Policlinico Universitario A. Gemelli IRCCS, 00168, L. A. Gemelli 8, Rome, Italy

Background: Dyslipidemia is a common finding in Autosomal Dominant Polycystic Kidney Disease patients and lower HDL was associated with disease progression. Since vasopressin can interact with both glucose and lipid regulation pathways, Tolvaptan treatment might affect metabolic derangements in ADPKD patients.

Methods or Case description: We conducted an exploratory analysis in the Bern ADPKD registry, a prospective observational cohort study. Glucose and lipid metabolism parameters were measured at baseline and every 12 months thereafter. Patients taking Tolvaptan at baseline were excluded from the analysis. Multivariable mixed-effects regression models adjusted for age, sex, baseline BMI, eGFR, TSH and multiple medications use including insulin, oral antidiabetic drugs, statins and ezetimibe were used to assess changes in glucose and lipid metabolism parameters associated with Tolvaptan treatment.

Results or Learning points: A total of 189 participants (122 without and 67 with subsequent Tolvaptan treatment) were included in the analysis. At baseline, 31% (n = 58) of patients had increased total cholesterol, 14% (n = 26) low HDL, 32% (n = 61) high LDL and 22% (n = 41) high triglycerides concentrations. During follow-up, Tolvaptan treatment was associated with reduced HDL (β -0.186; 95% CI −0.260, -0.111; p <0.001), increased LDL (β 0.216; 95% CI 0.014, 0.430; p = 0.048) and triglycerides (β 0.381; 95% CI 0.130, 0.633; p = 0.003) levels. No significant changes were observed in total cholesterol, glucose or hemoglobin A1c.

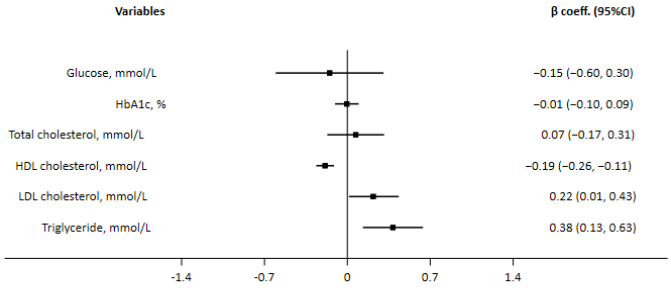


Figure 1. Beta coefficients of the association between glucose and lipid metabolism parameters with Tolvaptan administration

Conclusions: Chronic Tolvaptan treatment is associated with worsening dyslipidemia in ADPKD patients. Lipid metabolism parameters testing should be increased in patients taking Tolvaptan.

*YSN paper

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OC 33 / P 16

Cancer and survival of patients transplanted for glomerulonephritis in the Swiss kidney transplant cohort*

Dr. Matthieu Halfon[1], Dr. Patrick Taffe[2], Dr. Christian Bucher[3], Prof. Uyen Huynh-Do[4], Dr. Laila Mani[4], Dr. Edin Muradbegovic[5], Dr. Fadi Hadar[5], Dr. Thomas Schachtner[6], Dr. Caroline Wehmeier[7], Prof. Manuel Pascual[1], Prof. Fadi Fakhouri[8], Prof. Dela Golshayan[1]

1. Organ Transplant Center, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland., 2. Center for Primary Care and Public Health, Lausanne university, Switzerland 3. Clinic for Nephrology and Transplantation, Cantonal Hospital St. Gallen, Switzerland 4. University Clinic for Nephrology and Hypertension, Inselspital Bern, Switzerland 5. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 6. University Hospital Zurich, Department of Nephrology, Zurich, Switzerland 7. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland 8. Service of Nephrology and Hypertension, Department of Medicine, Lausanne University Hospital and University of Lausanne, Switzerland

Background: The incidence of cancer is 2 to 5 times higher in kidney transplant (KTx) recipients as compared to the general population, mostly because of the chronic use of immunosuppressive drugs. In the setting of solid organ transplantation, an oncological diagnosis is associated with poor outcome. As KTx recipients are a heterogeneous population, data on cancer screening recommendations are scarce. Nevertheless, due to previous exposure to immunosuppressive therapies, patients transplanted for glomerulonephritis(GN-KTx) might represent a high-risk group.

Methods or Case description: The purpose of our study is to provide such data. We compared the rates of non-skin cancer, skin cancer and patients' survival between GN-KTx, patients transplanted for diabetic nephropathy (DM-KTx), for ADPKD, or for other causes. Only kidney alone transplantation and first allograft recipients were included. Statistical differences between groups were assessed by a flexible parametric modelling of the cause-specific cumulative incidence function.

Results or Learning points: 2621 patients were included in the analysis,of whom 702 were GN-KTx. We compared subgroups of patients based on the cause de nephropathy. For non-skin cancers, the probability to present a cancer was 21% at 12 years post transplantation and was similar in all groups(P = 0.6).There was no statistical difference across subtypes of GN-KTx.When skin cancers were considered, There was also no difference between groups(P:0.4). When overall survival was considered, compared to other groups, DM-KTx had the worse outcome, while GN-KTx had the best (47% and 72% at a mean follow-up of 5.5 years, respectively;P = 0.02). cardiovascular diseases were the major cause of death for DM-KTx (27%). Survival across the GN-KTx group showed significant differences, with IgAN-KTx having the best prognosis as compared to ANCA-KTx(P = 0.02) who had an increased risk of death (OR 3.2;CI 95%, 1.2-8; P = 0.001).

Conclusions: The overall prognosis of GN-KTx in the STCS is good but there are significant differences depending of the type of GN. Notably, ANCA-KTx have the worst prognosis.

*YSN paper

OC 34 / P 17

HLA antibody affinity determination: from HLA-specific monoclonal antibodies to donor-specific HLA antibodies (DSA) in patient sera

Ms. Melanie N Hug[1], Ms. Sabrina Keller[1], Ms. Talea Marty[1], Prof. Daniel Gygax[1], Prof. Dominik Meinel[1], Mr. Peter Spies[1], Mrs. Joelle Handschin[2], Mr. Marc Kleiser[3], Ms. Noemi Vazquez[2], Ms. Janina Linnik[2], Dr. Rico Buchli[4], Prof. Frans Claas[5], Prof. Sebastiaan Heidt[5], Dr. Jar How Lee[6], Prof. Stefan Schaub[7], Dr. Gideon Hönger[2]

1. School of Life Sciences Muttenz, University of Applied Sciences and Arts Northwestern Switzerland, Muttenz, Switzerland 2. Department of Biomedicine, University of Basel, Basel, Switzerland 3. Department of Laboratory Medicine, University Hospital Basel, Basel, Switzerland 4. PureProtein LLC, Oklahoma City, US 5. Department of Immunology, Leiden University Medical Center, Leiden, The Netherlands 6. Terasaki Innovation Center (TIC), Glendale, US 7. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland

Background: Organs transplanted across donor-specific HLA antibodies (DSA) are associated with various clinical outcomes. However, neither the route of pre-sensitization nor readily available DSA-characteristics allow the discrimination between potentially harmless DSA and DSA with detrimental effect. DSA affinity has the potential to provide better information to predict the hazardous potential of circulating DSA. Several biophysical technologies allow the assessment of antibody binding strength, but prior knowledge of antibody concentration is required. The objective of the present study was therefore to develop an approach that combines DSA-affinity with DSA-concentration determination for patient sample evaluation.

Methods or Case description: We first investigated several platforms including bio-layer interferometry (BLI), surface plasmon resonance (SPR), flow induced dispersion analysis (FIDA), and a Luminex Single Antigen Bead (SAB) titration assay, testing representative sets of HLA-specific monoclonal antibodies (mAbs) by incubating them with their cognate recombinant HLA molecules. Binding affinities were assessed either based on real time antibody on- (ka) and off-rate (kd) determinations (BLI, SPR) or by end-point measurements using the steady state equilibrium dissociation constant (steady state KD) (FIDA, SAB).

Results or Learning points: FIDA is particularly suitable for measuring DSA-affinities in patient serum samples and simultaneously determines DSA-concentration. We investigated DSA of twenty pre-transplant patient samples, all with negative complement-dependent cytotoxicity (CDC)-crossmatch results and SAB signals ranging between 571 and 14899 MFI. DSA-concentration ranged between 11.2 – 1223nM (median 81.1nM) and their measured affinities were between 0.055 – 24.7nM (median 5.34nM; 449-fold difference). In 13/20 patients (65%), DSA accounted for more than 0.1% of total serum antibodies, and 4/20 sera (20%) revealed a proportion of DSA even higher than 1%.

Conclusions: This study strengthens the presumption that pre-transplant patient DSA consists of various concentrations and different net affinities. Clearly, validation of these results in larger patient cohorts is the critical next step in assessing the clinical relevance of the two measures.

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OC 35 / P 18

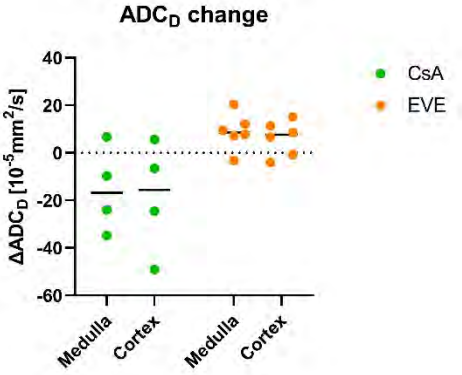
Influence of Immunosuppressive Regimen on Diffusivity and Oxygenation of Kidney Transplants-Analysis of Functional MRI Data from the Randomized ZEUS Trial

Ms. Jasna Cotting[1], Prof. Bruno Vogt[2], Prof. Ute Eisenberger[3], Prof. Peter Vermathen[1], Dr. Laila Mani[2]

1. Departments of Biomedical Research and Radiology, University of Bern, 3010 Bern, Switzerland 2. University Clinic for Nephrology and Hypertension, Inselspital Bern, Switzerland 3. Nephrological Centre Lower Saxony, Hospital Hann. Münden, 34346 Hann. Münden, Germany

Background: The ZEUS study was a multi-center randomized controlled trial investigating the effect of early conversion from a ciclosporin (CsA)-based to an everolimus (EVE)-based regimen on kidney graft function twelve months post-transplantation. The purpose of this investigator-initiated sub-study was the evaluation of additional aspects of graft function using functional magnetic resonance imaging (fMRI) methods. Considering calcineurin inhibitor nephrotoxicity, we hypothesized that graft diffusivity and micro-perfusion measured by diffusion-weighted imaging (DWI) as well as oxygenation measured by blood oxygen level-dependent (BOLD)-MRI differ between patients under ciclosporin or everolimus.

Methods or Case description: De novo kidney graft recipients were randomized to continue CsA or be converted to EVE at 4.5 months posttransplant. In this sub-study, fMRI of kidney grafts including DWI and BOLD was prospectively performed at month 4.5 and 12 post-transplantation on 3 and 1.5 (n = 3) Tesla MR scanners. Image analysis was blinded involving up to 24 regions of interest placed in cortex and medulla.



Results or Learning points: Sixteen patients underwent fMRI protocol. After exclusion due to image quality, outlier values or missing data, DWI and BOLD were analyzed for ten and eight subjects respectively. The diffusion coefficient ADCD decreased in the CsA-treated group over time, whereas it increased in the EVE group ($p = 0.046$, medulla). The change in ADCD from months 4.5 to 12 significantly differed between groups in the cortex ($p = 0.033$) and medulla ($p = 0.019$). In BOLD, cortico-medullary transverse relaxation rate R2* increased (decreased tissue oxygen) in the CsA-treated and decreased in EVE-treated groups over time. Similarly, R2* values at month 12 were higher in the CsA-treated group compared to the EVE-treated group. There was no significant difference for the perfusion fraction FP.

Conclusions: This prospective sub-study of the ZEUS trial suggests an impact of immunosuppressive regimen on fMRI parameters of the kidney graft.

OC 36 / P 19

SC5b-9 and Bb factor levels as potential novel biomarkers in crescentic IgA nephropathy*

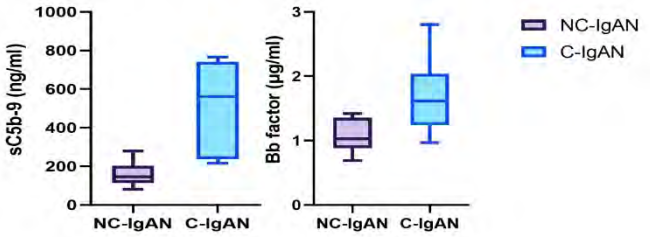
Dr. Gabriella Guzzo[1], Dr. Salima Sadallah[2], Mrs. Isabelle Bassi[1], Prof. Giuseppe Pantaleo[2], Prof. Manuel Pascual[3], Prof. Daniel TETA[1]

1. 1. Service of Nephrology, Valais Hospital, Sion, Switzerland., 2. 2. Service of Immunology and Allergy, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland., 3. 3. Organ Transplant Center, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland.

Background: IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide and the first cause of end-stage kidney disease among primary glomerulonephritis. Local and systemic evidence of complement activation (CA) are prognostic markers of severe IgAN. Both the alternative and lectin pathway are responsible for CA in IgAN, they converge into the generation of C5 convertase, which forms the membrane attack complex (MAC), also called C5b-9. The C5b-9 complex perforates glomerular basement membranes, which may lead to crescent formation. A soluble form of C5b-9 complex can be detected in human plasma (SC5b-9). We hypothesize that SC5b-9 may be a novel biomarker in crescentic IgAN.

Methods or Case description: To measure SC5b-9, and complement fragment Bb, a plasma marker of complement alternative pathway activation, in patients with IgAN with crescents compared to patients with IgAN without crescents.

Figure 1. SC5b-9 and Bb factor levels compared between the non-crescentic (NC-IgAN) and the crescentic IgAN (C-IgAN) group.



Results or Learning points: Twenty-seven patients, with IgAN confirmed by kidney biopsy (KB), underwent complement analysis during three years in our institution. Seventeen patients were included in the study and gave informed consent to participate, of whom 6 patients had active crescents at the moment of KB. Creatinine, 24 hours proteinuria, albuminuria and systolic blood pressure were higher in the group with crescents. SC5b9 and Bb factor levels were markedly higher in the crescentic group (514 + 236 vs 163 + 61 ng/ml and 1.7 + 0.6 vs 1.1 + 0.3 µg/ml, p of 0.002 and 0.02, Figure 1). A serum C3 splitting activity was found giving rise to C3c in 4 patients with crescents.

Conclusions: In this pilot study, only patients with severe and crescentic forms of IgAN, showed a strong CA (SC5b9), which appeared to be mediated also by the alternative pathway of complement (Bb factor). Thus, SC5b9 and factor Bb may represent novel plasma biomarkers, predictive of crescentic IgAN. A large multicentre trial is needed to confirm our preliminary findings.

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OC 37 / P 20

Hot spot for aHUS of rare variant p.Ile357Met of complement factor I

Dr. Nora Schwotzer[1], Prof. Fadi Fakhouri[2], Prof. Véronique Fremeaux-Bacchi[3], Dr. Carine El-Sissy[3]

1. Service of Nephrology and Hypertension, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, 2. Service of Nephrology and Hypertension, Department of Medicine, Lausanne University Hospital and University of Lausanne, Switzerland, 3. Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Service d'Immunologie, Paris, France

Background: Atypical haemolytic uremic syndrome (aHUS) and C3 glomerulopathy (C3GP) are two rare renal diseases that involve dysregulation of the alternative pathway in the complement system. Pathogenic role of complement factor I (CFI) in aHUS has been debated. CFH and MCP mutations are identified as the main genetic driver of aHUS and CFI variants occur more often as a co-mutations, adding to the risk constellation. In this analysis, we describe 10 cases of aHUS where rare variant p.Ile357Met of CFI was identified.

Methods or Case description: Clinical and biological data of 10 patients with p.Ile357Met missense variant were reviewed based on patient files. All genetic testing was performed at the Laboratoire d'Immunologie Biologique of Hôpital Européen Georges Pompidou, Paris; a reference laboratory for the investigation of the complement system.

Results or Learning points: We identified 10 individuals with aHUS that carry the same rare variant p.Ile357Met of CFI. A majority (70%) were women with median age of 36.5years at diagnosis. All (100%) presented initially with aHUS and 3 (30%) developed C3GP during follow-up. All C3GP occurred on kidney allograft. End-stage renal disease due to aHUS and/or C3GP occurred in 5 native kidneys and 2 kidney allograft. Two patients presented aHUS in peripartum and both recovered. Two patients presented multiple TMA recurrence that were associated with shigatoxine in 2 cases and with intraocular anti-VEGF injections in 1 case. Four (40%) patients received eculizumab.

Conclusions: Enrichment of the rare variant p.Ile357Met of CFI in a aHUS cohort affecting 10 patients underline its pathogenic role and highlight a hot-spot region in the serine protease domain. All presented with aHUS and 30% developed C3G. Classic triggers such as kidney transplantation, pregnancy, CNI exposure, Shiga toxin or anti-VEGF treatment where identified for most episodes underlining that the pathogenic potential of the rare variant p.Ile357Met is strongly dependent on the magnitude of the trigger.

OC 38 / P 21

The role of hypoxia-inducible factor asparaginyl hydroxylase (FIH) in chronic kidney disease*

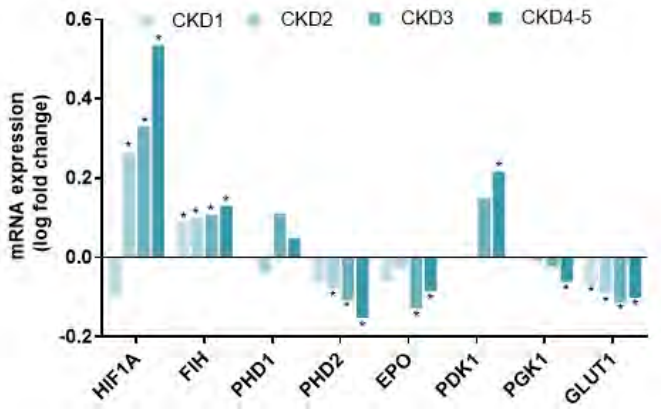
Dr. Anna Faivre[1], Dr. Romain Dissard[1], Dr. Willy Kuo[2], Dr. Thomas Verissimo[1], Dr. David Legouis[3], Dr. Grégoire Arnoux[1], Dr. Ngoc An Le[2], Dr. Bernhard Spingler[2], Dr. Bert Mueller[4], Dr. Georg Schulz[4], Dr. Maja Lindenmeyer[5], Dr. Clemens Cohen[6], Prof. Joseph M. Rutkowski[7], Dr. Carsten Scholz[2], Prof. Vartan Kurtcuoglu[2], Prof. Sophie De Seigneux[1]

1. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 2. Institute of Physiology, University of Zurich, Zurich, Switzerland, 3. Division of Intensive Care, Department of Acute Medicine, Geneva University Hospitals, Geneva, Switzerland, 4. Biomaterials Science Center, Department of Biomedical Engineering, University of Basel, Gewerbestrasse 14, 4123 Allschwil, Switzerland, 5. III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, 6. Nephrological Center, Medical Clinic and Polyclinic IV, University of Munich, Munich, Germany, 7. Department of Medical Physiology, Texas A&M University Health Science Center, Bryan, Texas, United States of America

Background: The roles of hypoxia and hypoxia inducible factor (HIF) during chronic kidney disease (CKD) are much debated. Interventional studies with HIF-α activation in rodents yielded contradictory results. The HIF pathway is regulated by prolyl and asparaginyl hydroxylases; while prolyl hydroxylase inhibition is a well-known method to stabilize HIF-α, little is known about the effect asparaginyl hydroxylase Factor Inhibiting HIF inhibiting (FIH).

Methods or Case description: We used a model of progressive proteinuric CKD and a model of obstructive nephropathy with unilateral fibrosis. In these models, we assessed hypoxia with pimonidazole and vascularization with three-dimensional micro-CT imaging. We analyzed a database of 217 CKD biopsies from stage 1 to 5 and we randomly collected 15 CKD biopsies from various severity degrees to assess FIH expression. Finally, we modulated FIH activity in vitro and in vivo using a pharmacologic approach, to assess its relevance in CKD.

Results or Learning points: In our model of proteinuric CKD, we show that early CKD stages are not characterized by hypoxia or HIF activation. At late CKD stages, some areas of hypoxia are observed, but these are not colocalizing with fibrosis. In mice and in humans, we observed a downregulation of the HIF pathway, together with an increased FIH expression in CKD, according to its severity. Modulating FIH in vitro affects cellular metabolism, as described previously. In vivo, pharmacologic FIH inhibition increases the glomerular filtration rate of control and CKD animals and is associated with a reduced development of fibrosis.



Conclusions: The causative role of hypoxia and HIF activation in CKD progression is questioned. A pharmacological approach of FIH downregulation seem promising in proteinuric kidney disease.

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OC 39 / P 22

Immuno-metabolic and sex-specific responses to renal ischemia-reperfusion injury*

Mr. Arnaud Lyon[1], Mr. Thomas Agius[2], Mr. Kevin Kiesworo[2], Dr. Matthieu Halfon[1], Dr. Sebastien Deglise[3], Dr. Florent Allagnat[2], Dr. Alban Longchamp[2], Prof. Dela Golshayan[1]

1. Organ Transplant Center, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland., 2. department of vascular surgery, Lausanne University Hospital, Lausanne, Switzerland 3. department of vascular surgery, lausanne university hospital, Lausanne, Switzerland

Background: Substantial ischemia-reperfusion injury (IRI) occurs in 30% to 50% of kidney transplantations from deceased donor organs. IRI usually manifests as delayed graft function but can promote acute rejection and the evolution towards chronic allograft dysfunction. Previous experimental and clinical studies have highlighted sex-specific susceptibility to IRI in kidney and other organs. While sex hormones seem to be important, the precise underlying mechanisms still need to be uncovered.

Methods or Case description: IRI was modelled in mice using unilateral nephrectomy, followed by 23min ischemia and reperfusion. Kidney function was evaluated over time by measuring plasma urea and creatinine levels. Histology, immunohistochemistry and Spatial total mRNA sequencing was carried out on paraffin-embedded tissue. Kidney ischemic damage was quantified using a validated semi-quantitative score. qPCR was performed on RNA extracted from flash-frozen organ samples. Time-course CyTOF was applied on peripheral blood mononuclear cells.

Results or Learning points: Following IRI, females had a significantly better renal function. Renal histology showed increased tubulointerstitial lesions in males, together with significantly increased expression of genes associated with renal damage and specific cytokines such as IL-6 and TNF-α. Consistently, the secretion of pro-inflammatory cytokines was followed by a significantly higher increase of blood neutrophils counts in males at postoperative day 2. In males, this was associated with the infiltration of an immune cluster at the corticomedullary junction and global downregulation of metabolism, proliferation and survival related genes.

Conclusions: Our data show an increased recruitment of neutrophils at the onset of IRI, particularly in males. IL-6 and TNF-α seem to be sex-specific key regulators of the early immune response. If these pathways are confirmed, they could be targeted by approved drugs with, therefore, rapid translation into clinical trials to improve graft outcome. Therapeutics against IRI could also increase the number of transplantable cadaveric kidneys, by enabling an extended and safer use of marginal organs.

*YSN paper

OC 40 / P 23

A transfer learning framework for single cell transcriptomics reveals the role of altered proximal tubule cell states in kidney disease*

Dr. Daniele Malpetti[1], Dr. Anna Rinaldi[2], Dr. David Legouis[3], Dr. Gregoire Arnoux[3], Dr. Thomas Verissimo[3], Dr. Anna Faivre[4], Dr. Francesca Mangili[1], Dr. Andrea Rinaldi[5], Dr. Marco Bolis[5], Dr. Maarten Naesens[6], Mr. Lorenzo Ruinelli[7], Dr. Jerome Pugin[3], Dr. Solange Moll[8], Dr. Laura Azzimonti[1], Prof. Sophie De Seigneux[4], Prof. Pietro Cippà[2]

1. Istituto Dalle Molle di Studi sull'Intelligenza Artificiale (IDSIA), USI/SUPSI, Lugano, Switzerland, 2. Division of Nephrology, Ente Ospedaliero Cantonale, Lugano, Switzerland, 3. Division of Intensive Care, Department of Acute Medicine, Geneva University Hospitals, Geneva, Switzerland, 4. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 5. Institute of Oncology Research, Bellinzona, 6. Department of Microbiology, Immunology and Transplantation, KU Leuven, Leuven, Belgium, 7. ICT, Ente Ospedaliero Cantonale, Lugano, Switzerland 8. Clinical Pathology Division, University Hospital of Geneva, University of Geneva, Geneva, Switzerland

Background: Single-cell transcriptomics introduced a new level of granularity in our understanding of tissue composition and disease characterisation. However, current single-cell technologies are not applicable in the clinical routine because of major challenges related to tissue processing and data analysis.

Methods or Case description: We first generated an atlas of human renal cells (and cell states), including all published single-cell studies and newly generated single-nucleus RNAseq data to cover the poorly characterized early phase after acute kidney injury. In parallel, we developed a transfer learning approach to link single-cell transcriptome signatures to clinical samples analysed by bulk RNAseq: the model was trained in a large gene expression dataset and then applied to five independent clinical datasets for which both bulk RNAseq and clinical data were available.

Results or Learning points: The computational framework was first validated in kidney cancer samples to predict histological diagnosis, clinical outcome and response to therapy. We confirmed a substantial dimensionality reduction without loss of information, the applicability to small clinical datasets and the direct interpretability of the results, opening the opportunity to link clinical data to single-cell information extracted from bulk RNAseq. The application of this approach to kidney biopsies obtained from patients with diabetic nephropathy and after kidney transplantation revealed specific cell types and ecosystems associated with chronic kidney disease progression. Among others, we found evidence for an association between altered states in proximal tubule cells after kidney injury with the progression to kidney fibrosis. Further characterization of those peculiar cell states highlighted cell states transitions of tubular injury and repair in human acute kidney injury and their potential role in the transition to chronic kidney disease.

Conclusions: Machine learning techniques defined a novel strategy to translate the power of single-cell transcriptomics into clinical practice and identify cells states clinically relevant across kidney diseases.

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OC 41 / P 24

Lectin-aided sorting of intact tubular nephron segments – a novel tool in kidney research

Dr. Stefan Rudloff[1], Ms. Jessica Roskosch[1], Dr. Anne-Christine Uldry[2], Prof. Uyen Huynh-Do[3]

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Core Facility Proteomics and Mass Spectrometry, Department for BioMedical Research, University of Bern, Switzerland, 3. University Clinic for Nephrology and Hypertension, Inselspital Bern, Bern, Switzerland

Background: The study of individual intact renal tubule segments is far from trivial and still mostly relies on the manual microdissection of the nephron. This is not only very laborious, requiring years of practice, but often also yields only small quantities of usable material, usually restricted to one specific nephron segment. In this study, we assessed the usability of fluorescently labeled lectins or agglutinins to efficiently sort abundant quantities of several intact nephron segments from the same kidney in a relatively short time frame.

Methods or Case description: To find a suitable combination of lectins, their binding pattern was assessed on paraffin and fresh-frozen kidney sections. Tubular nephron fragments from collagenase-digested kidneys were consequently labeled with 3 lections (SNA-Cy3, SBA-Cy5, and LTL-FITC), and using a 200um nozzle 4 different nephron segments were sorted with a MoFlo ASTRIOS EQ. The segments were subsequently validated by mRNA expression analysis, assessed for sex differences by proteomic profiling, or used in primary cell culture.

Results or Learning points: Gene expression analysis confirmed the identity of the 4 sorted segments to be PT (FITC), TAL (triple negative), DCT (Cy3-Cy5 double positive), or more distal nephron segments (Cy3). Proteomics revealed differences in energy metabolism between the PT and DCT, but also sex differences in drug metabolism or evasion of cellular stress. Primary cells derived from DCT segments seem to depend on canonical Wnt signaling to maintain their identity in culture.

Conclusions: We established a new, broadly applicable technique to tissue sort abundant quantities of different nephron segments from the same kidney based on fluorescently labeled lectins or agglutinins. This method may provide the basis for a wide range of applications including the derivation of novel cell lines, the elucidation of sex-specific differences in renal diseases, or as a source of "building blocks" for ex vivo kidneys systems for drug screening and testing purposes.

OC 42 / P 25

Circadian urinary excretion of water, and not salt, is affected by stress hypertension*

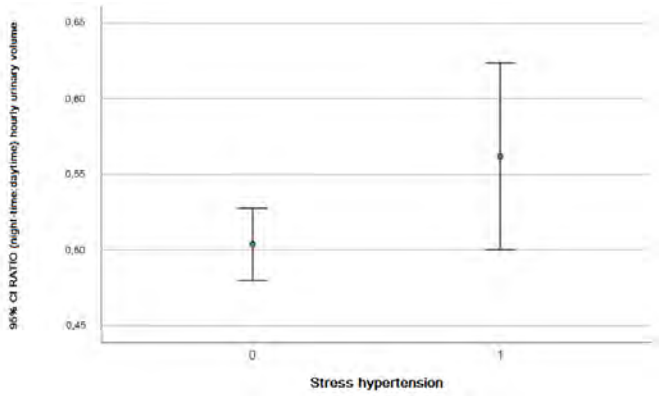
Dr. Vanessa Gagliano[1], Mr. Fabio Moretti[2], Dr. Rosaria Del Giorno[3], Prof. Luca Gabutti[1]

1. Internal Medicine, Cantonal Hospital Bellinzona, Switzerland 2. Faculty of Biomedicine, Università della Svizzera Italiana, Lugano, Switzerland 3. Angiology Service, University Hospital of Lausanne, Switzerland

Background: The circadian rhythm of urinary sodium excretion and blood pressure (BP) are known to be correlated. However, the underlying physiological mechanisms, as well as the role of the sympathetic nervous system (SNS) on this, are still a matter of debate. The literature about the influence of the adrenergic activity on the catabolic/anabolic balance is also limited. Therefore, in this cross-sectional study, we aimed to investigate the impact of stress hypertension, otherwise called "white coat hypertension", on the patterns of circadian urinary sodium and water excretion, expressed as night-time/day-time ratios, as well as to explore the relationship with elevated blood pressure and body mass index (BMI).

Methods or Case description: We analysed data from a Swiss population-based research project, conducted during the years 2017 and 2018. Participants underwent 24h blood pressure monitoring using a Mobil-O-Graph device, together with a 24-hour split urine collection (daytime and night-time urine collected separately). The final sample was composed of 1023 subjects, and it was divided into two groups according to the presence or absence of "stress hypertension", defined as an in-office systolic BP increase of ≥ 15 mmHg and/or diastolic BP increase of ≥ 10 mmHg, compared to home blood pressure monitoring (HBPM) values.

Results or Learning points: Results mainly showed that people affected by stress hypertension have higher night/day urinary volume excretion ratio (p = 0.006) and higher BMI, while the night/day urinary sodium excretion ratio is not statistically different in the two groups.



Conclusions: In conclusion, the present study suggests that stress hypertension affects circadian urinary excretion of water, but not sodium output, and that there is an interconnection between SNS activation and body weight, which is worth further investigation.

*YSN paper

OC 43 / P 26

Prevalence of hypertension and uncontrolled hypertension after solid organ transplantation in the Swiss Transplant Cohort Study: a 5-year follow-up.

Dr. Nora Schwotzer[1], Dr. Yimin Lu[2], Dr. Matthieu Halfon[3], Prof. Manuel Pascual[3], Prof. Pedro Marques-Vidal[4], Prof. Dela Golshayan[3], Dr. Grégoire WUERZNER[5]

1. Service of Nephrology and Hypertension, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, 2. Service of Nephrology and Hypertension, Department of Medicine, Lausanne University Hospital and University of Lausanne, Switzerland, 3. Transplantation Center, Department of Medicine and Surgery, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, 4. Department of Medicine, Internal Medicine, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, 5. Division of Nephrology and Hypertension, Department of Internal Medicine, Lausanne University Hospital, Switzerland

Background: Graft survival has drastically improved in solid organ transplantation (SOT) and long-term outcomes are now mainly associated with cardio-vascular morbidity. Hypertension (HTN) is a frequent complication after SOT. We describe the prevalence of HTN, uncontrolled HTN and details on pharmacologic treatment of HTN across SOT recipients using data from the Swiss Transplant Cohort Study (STCS). The STCS enrolls prospectively >90% of all SOT recipients in Switzerland since 2008.

Methods or Case description: Data extracted from the STCS in December 2019 was used for this study, with analysis of follow-

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up data of the first 5 years post-transplantation. HTN was defined as BP >140/90 mmHg or the use of antihypertensive drugs.

Results or Learning points: A total of 3865 adult recipients of a single SOT during the study period were included (2287 kidneys, 859 livers, 392 lungs and 327 hearts). Global prevalence of HTN was high at 5 years follow-up (90.4% in kidney, 85.8% in heart, 84.9% in lung and 76.1% in liver transplantation).The proportion of untreated HTN was highest in liver and lung transplant recipients at 5 years post-transplantation (23.5% in liver, 16.7% in lung, 9.4% in heart and 5.4% in kidney transplantation). Uncontrolled HTN was more frequent in kidney, lung and liver transplant recipients at 5 years (38.9% in kidney, 36.8% in lung, 30.5% in liver, and 18.5% in heart transplantation), but with lower pill burden in lung and liver transplant recipients (>3 antihypertensive drugs in 8.8% of kidney, 7.6% of heart, 0.91% in lung and 0.75% in liver transplant recipients).

Conclusions: Prevalence of HTN after SOT is high in all SOT types. Awareness to avoid untreated HTN should be raised especially in liver and lung transplantation. Moreover, uncontrolled HTN remains an important issue across SOT recipients. Specific antihypertensive strategies should be developed in patients after SOT, who already have a high pill burden.

OC 44 / P 27

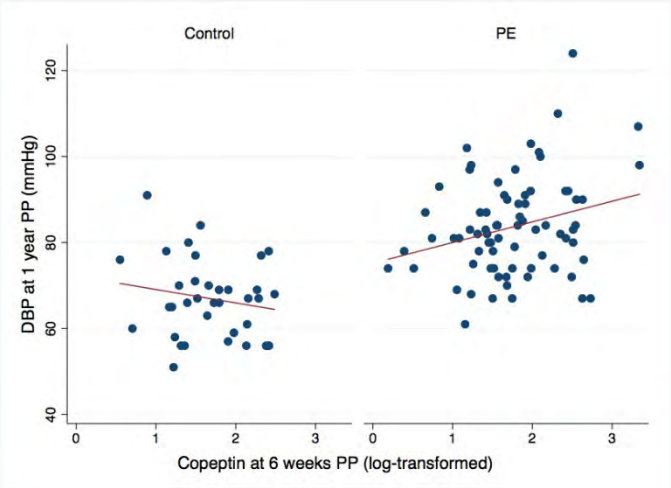
Serum copeptin as a prognostic marker in pre-eclampsia*

Dr. David Jaques[1], Dr. Anne Dufey[2], Dr. Grégoire WUERZNER[3], Ms. Véronique Othenin[4], Dr. Begona Martinez De Tejada[5], Dr. Antoinette Pechere[2], Prof. Bélen PONTE[6]

1. Hôpitaux universitaires de Genève, Service de Néphrologie, Rue Gabrielle-Perret-Gentil 4, 1205 Genève, Suisse, 2. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 3. Division of Nephrology and Hypertension, Department of Internal Medicine, Lausanne University Hospital, Switzerland, 4. geneva university hospitals, 5. geneva univesity hospitals, Switzerland 6. Nephrology and Hypertension Service. University Hospitals of Geneva, Switzerland

Background: Background: Pre-eclampsia (PE) is as a risk factor for subsequent cardiovascular and kidney disease. Serum copeptin correlates with adverse kidney outcomes in the general population and is increased during PE as compared to healthy pregnancy. We describe the association between copeptin and subsequent kidney outcomes in pregnant women.

Methods or Case description: Methods: We enrolled 372 patients with PE and 82 with healthy pregnancy in this prospective cohort study. Serum copeptin was measured at 6 weeks postpartum (PP). Office blood pressure (BP), eGFR and albuminuria were measured at 6 weeks as well as at 1 year PP in a subgroup of 110 patients. Interaction effect was tested using likelihood ratio test (LRT).



Results or Learning points: Results: As compared to healthy controls, patients with PE were less frequently Caucasian, more likely smokers and had higher body mass index ($p < 0.05$). At 6 weeks PP, copeptin levels were similar between groups. At one year PP, systolic BP (SBP), diastolic BP (DBP) and albuminuria were higher in PE as compared to control patients ($p < 0.05$) while eGFR was similar between groups. A significant interaction existed between copeptin and PE status regarding DBP at 1 year PP ($p = 0.045$ for LRT). A similar but borderline interaction existed between copeptin and PE status for albuminuria at 1 year PP ($p = 0.126$ for LRT).

Conclusions: Conclusions: At 6 weeks PP, women who suffered from PE do not have increased copeptin levels as compared to healthy controls. However, in case of PE only, copeptin levels are associated with subsequent adverse kidney outcome. Whether this association is causal and would represent a potential therapeutic target remains to be tested.

*YSN paper

OC 45 / P 28

New therapeutic perspectives for blood pressure control: dexfadrostat phosphate, a novel aldosterone synthase inhibitor, in patients with primary aldosteronism

Dr. Grégoire WUERZNER[1], Prof. Paolo Mulatero[2], Dr. Michael Groessl[3], Dr. Christoph Schumacher[4], Prof. Hans Brunner[5], Prof. Bruno Vogt[3]

1. Division of Nephrology and Hypertension, Department of Internal Medicine, Lausanne University Hospital, Switzerland, 2. Division of Internal Medicine and Hypertension, University of Torino, Torino, Italy 3. University Clinic for Nephrology and Hypertension, Inselspital Bern, Switzerland 4. Damian Pharma AG, Switzerland 5. Service of Nephrology and Hypertension, Department of Medicine, Lausanne University Hospital and University of Lausanne, Switzerland

Background: Aldosterone synthase (CYP11B2) is the rate-limiting enzyme for aldosterone biosynthesis. Patients with primary aldosteronism (PA) are characterized by an uncontrolled production of aldosterone and are at higher risk of stroke, heart failure and death compared to patients with essential hypertension. Previous attempts to eliminate the excessive aldosterone synthesis defining PA have been unsuccessful, particularly due to unintended inhibition of other steroid hormones. Dexfadrostat phosphate is a novel ASI that acts directly on CYP11B2.

Methods or Case description: Dexfadrostat phosphate was investigated in patients with PA diagnosed within 1 year of study entry according to medical guidelines including a suppression test to demonstrate autonomous aldosterone production. Eligibility was verified by a Central Review panel. Following a pla-

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cebo-controlled run-in period, enrolled patients were randomized to one of three doses of dexfadrostat phosphate taken orally, once daily. After 8 weeks, patients were switched to placebo and followed for an additional 2 weeks. Blood samples were taken at 2-week intervals and evaluated in a central laboratory for steroid and peptide hormones as well as electrolytes. Blood pressure was measured during each clinic visit. Ambulatory systolic blood pressure (aSBP) was monitored over 24-hours at baseline and after 8 weeks of treatment.

Results or Learning points: All endpoints of the study were met with high significance. Dexfadrostat phosphate treatment was generally safe and well tolerated. We present the effects on the aldosterone-to-renin ratio (ARR) and blood pressure reduction, correction of hypokalemia, and reversal of therapeutic effects upon drug withdrawal.

Conclusions: The phase 2 study evaluated the ability of dexfadrostat phosphate to deliver both biochemical (ARR, potassium) and subsequent clinical (aSBP) correction of the consequences of uncontrolled aldosterone production. By demonstrating clinical utility in an indication of extreme aldosterone dysregulation, the potential of dexfadrostat phosphate may well expand to address essential hypertension, chronic kidney disease, hypokalemia, volume expansion and organ remodeling.

OC 46 / P 29

Living kidney donor evaluation and coronary risk assessment with low radiation dose computed tomography as a one-stop-shop examination*

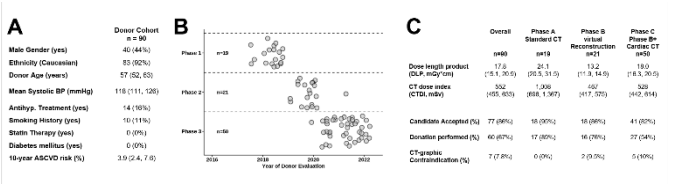
Ms. Nicole Yacob[1], Prof. Adrian Huber[2], Dr. Daniel Sidler[1]

1. Klinik für Nephrologie und Hypertonie, Inselspital, Bern, Switzerland 2. Klinik für Diagnostische, Interventionelle und Pädiatrische Radiologie, Inselspital, Bern, Switzerland

Background: To compare a standard triple phase computer tomography (CT) protocol with a combined dual-energy, split-bolus CT protocol with cardiothoracic assessment of living kidney donor candidates.

Methods or Case description: This was an analysis of pre-selected living kidney donor candidates in a single transplantation center in Switzerland. CT scans of candidates were analyzed and compared between patients with a standard abdominal triple phase CT acquisition (Protocol A), an abdominal dual phase CT acquisition with virtual non-contrast reconstruction and a split-bolus contrast medium administration for assessment of the urinary tract (Protocol B) and a protocol B with additional cardiothoracic CT acquisition (Protocol C). Cardiothoracic and abdominal CT findings, as well as CT dose estimations were compared between the groups.

Results or Learning points: A total of 90 kidney donor candidates were included. The highest radiation dose was observed with CT protocol A (n = 19, DLP 1008 mGy*cm; CTDI 24.1 mGy), while radiation dose was lower in the dual energy, split bolus CT protocol B (n = 21, 467 mGy*cm; CTDI 13.2 mGy), even when combined with the additional cardiothoracic CT in protocol C (n = 50, DLP 528 mGy*cm; CTDI 18.0 mGy; p <.001). 17/50 (34%) donor candidates with the combined cardiothoracic and abdominal CT protocol C had coronary artery calcifications, while 3/50 (6%) had previously unknown significant coronary stenosis that led to subsequent invasive coronary angiography and coronary stent insertion. Other relevant cardiothoracic findings included aortic root ectasia (12%), bicuspid aortic valve (2%) and emphysema (8%). Abdominal CT findings were not significantly different between the three groups (p = >.81). Overall, 77/90 (86%) of donor candidates were accepted as kidney donors. In 7 donors (7.8%), CT-graphic contraindications were identified.



Conclusions: Combined cardiothoracic and abdominal CT assessment with low radiation dose is feasible and shows a relevant prevalence of clinically significant cardiothoracic findings in kidney donor candidates. This procedure allows identification of contraindications for kidney donation with high precision.

*Student paper

OC 47 / P 30

Cardiovascular Safety of Roxadustat Versus Erythropoiesis-Stimulating Agents for Treatment of Anemia in Patients With Chronic Kidney Disease Incident to or Not Receiving Dialysis: Pooled Subgroup Analysis of Four Phase 3 Studies

Prof. Ciro Esposito[1], Dr. Jonathan Barratt[2], Dr. Frank Dellanna[3], Dr. Jose Portoles[4], Dr. Gabriel Choukroun[5], Dr. Luca De Nicola[6], Dr. Michael Reusch[7], Mr. James Young[8], Dr. Alina Jiletcovici[9], Dr. Nada Dimkovic[10]

1. Unit of Nephrology and Dialysis, ICS Maugeri, University of Pavia, Italy 2. Department of Cardiovascular Sciences, University of Leicester, UK 3. Department of Kidney and Dialysis, MVZ DaVita Rhein-Ruhr GmbH, Germany 4. Department of Nephrology, Hospital Universitario Puerta de Hierro, Department of Nephrology, Anemia Working Group Spanish Society of Nephrology, Spain 5. Department of Nephrology, CHU Amiens Picardie and Jules Verne University, France 6. Department of Biochemistry, Biophysics, and Bioinformatics, University of Campania, Italy 7. Department of Nephrology, Guard Therapeutics International AB, 8. Department of Statistics, Astellas Pharma, Inc., US 9. Department of Medical Affairs, Astellas Pharma, Inc., 10. Department of Nephrology, University of Belgrade, Serbia

Background: Cardiovascular safety of roxadustat is established in the non–dialysis-dependent (NDD) and incident-to-dialysis (ID)- dialysis-dependent (DD) chronic kidney disease (CKD) populations compared to erythropoiesis-stimulating agents (ESAs); however, the effect of baseline characteristics on cardiovascular safety requires further elucidation.

Methods or Case description: In this post hoc exploratory analysis, cardiovascular safety results from eligible patients with anemia of CKD enrolled in four phase 3, randomized, open-label studies (NDD [DOLOMITES] or ID-DD [SIERRAS, HIMALAYAS, ROCKIES]) were pooled and compared between roxadustat and an ESA. Time to major adverse cardiovascular event (MACE), MACE+ (MACE plus congestive heart failure or unstable angina requiring hospitalization), and all-cause mortality (ACM) was evaluated in subgroups established from baseline characteristics. These endpoints were evaluated descriptively for consistency with the main cardiovascular safety analyses in the pooled NDD or ID-DD CKD population previously reported. Hazard ratios derived using a meta-analysis method that combined individual study log-hazard ratios with weights inversely proportional to the variance of the study-specific log-hazard ratios and 95% confidence intervals were compared between roxadustat and ESA.

Results or Learning points: In total, 2142 patients were evaluated (1083 roxadustat, 1059 ESA; 616 NDD, 1526 ID-DD). Roxadustat was comparable to ESA for risk of MACE and MACE+ with a consistent finding for ACM in most subgroups, which was consistent with outcomes from the main cardiovascular safety analyses, including male sex, United States region, prior smoker, baseline hemoglobin ≥8 g/dL, prior statin use, peritoneal dialysis, no history of diabetes mellitus, no history of coronary artery disease, no history of congestive heart failure, transferrin saturation ≥20%, and ferritin ≥100 mcg/L (Figure).

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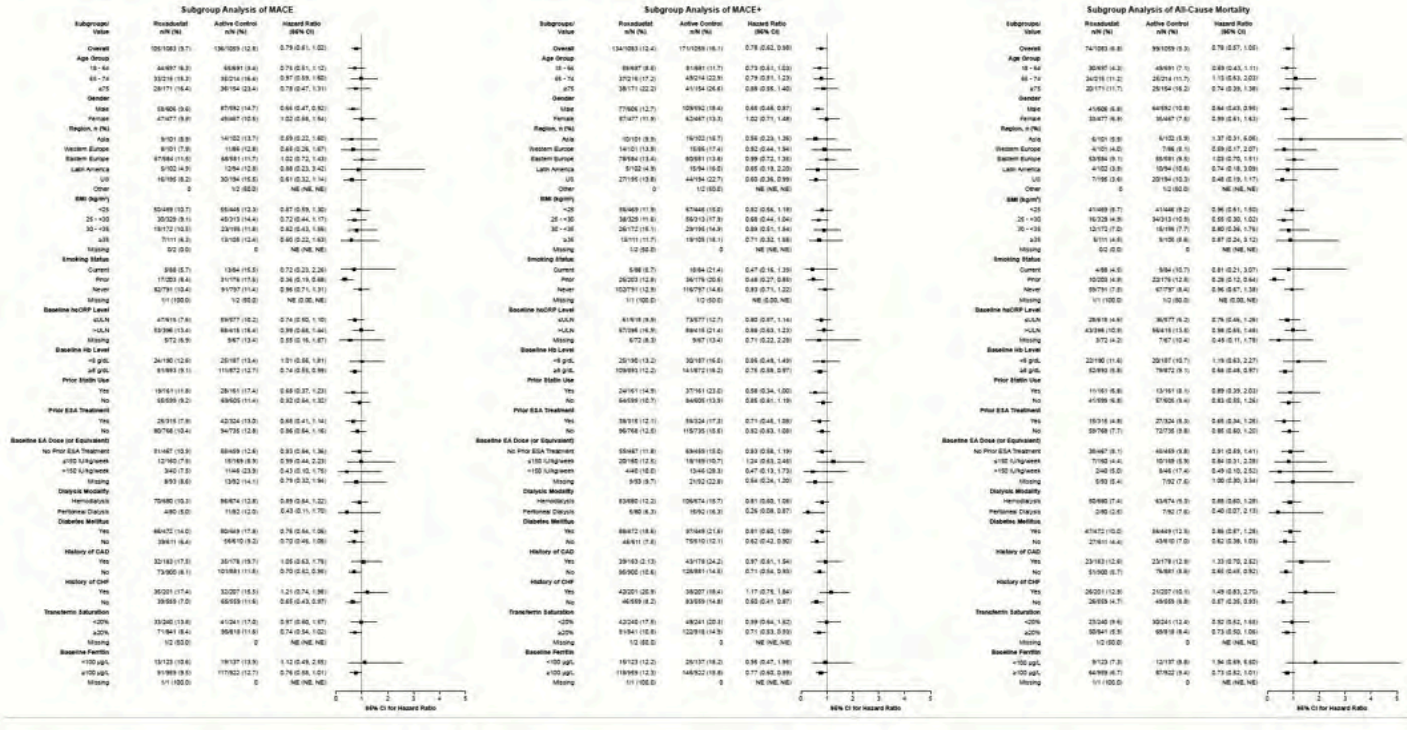
Conclusions: The risks of MACE, MACE+, and ACM between roxadustat and ESA were consistent with the main cardiovascular safety analyses in the pooled NDD or ID-DD CKD population across most baseline characteristic subgroups with no evidence of increased cardiovascular risk compared with ESA.



OC 48 / P 31

Association of Renin Angiotensin System (RAS) Gene Polymorphisms in Type 2 Diabetic Subjects with Proteinuric and Non-proteinuric Nephropathy

Dr. MM Iqbal[1], Dr. MS Hassan[2], Dr. MZA Bhuiyan[3], Dr. MAA Chowdhury[4], Dr. MZ Hassan[5], Dr. AN Malik[6]

1. n, Bangladesh 2. BIRDEM, Bangladesh 3. CHUV – Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland 4. nikdu, Bangladesh 5. BUHS, Bangladesh 6. KCL, UK

Background: The genotype frequency of polymorphisms in RAAS genes are varied in different types of nephropathies. Their polymorphic variations may have association with magnitude of proteiuria and progression of disease. In this study the SNPs in ACE, AGT and Aldosterone Synthase gene (CYP11B2) is compared between type 2 diabetic subjects with nephropathy having proteinuria or not.

Methods or Case description: In pre-diagnosed diabetic subjects nephropathy was defined by presence of albuminuria (UrAlb >30 mg/day) and/or CCr <60 ml/min without significant hematuria, pyuria and disproportionate kidneys. The proteinurics are designated as PDN and non-proteinuric nephropathy as NPDN. Genomic DNA was extracted from blood and then amplified using appropriate primers by PCR for evaluation. The insertion-deletion of ACE (ID, DD, II); polymorphisms of AGT in M235T (MM,TT,MT) and Aldosterone Synthase (CYP11B2) gene (TT,CC,TC) was investigated in this study.

Results or Learning points: The nephropathy subjects with proteinuria (PDN) vs normo-proteinuria (NPDN) were 379 vs. 115; age 57±8 vs 58±8 years (p = NS); CCR 58±38 vs. 50±25 ml/min (p = NS) and 24hr UrAlb 956±1452 vs. 11±8 mg/d (p <0.001). The distribution of genotype frequencies for ACE and AGT were similar between PDN vs. NPDN (p = 0.37 and p = 0.959). The distribution of polymorphysms for CYP11B2 was significantly different between the two study groups (TC was 45 vs. 69%; CC 11 vs. 6% and TT 44 vs. 25%; p <0.001) respectively for PDN vs NPDN

Conclusions: The genotype frequency of angiotensinogen (AGT) gene and angiotensin converting enzyme (ACE) gene is not different among diabetic subjects with or without proteinuric nephropathy. The significant difference in Aldosterone synthase (CYP11B2) gene polymorphisms need further exploration for development and progression of nephropathy among Bangladeshi type 2 diabetics with nephropathy.

OC 49 / P 32

Is nephrolithiasis a systemic disorder ? Evidence from a prospective cohort study.

Prof. Bernhard Hess[1]

1. Kidney Stone Center Zurich, Klinik im Park, 8038 Zurich, Switzerland

Background: There is increasing evidence that many renal stone formers (SF) exhibit 'non-urologic' abnormalities such as metabolic syndrome (MS) or cardiovascular disease.

Methods or Case description: A disease is defined as systemic if several organs/tissues or the whole body are affected. We analyzed additional anthropometric/metabolic data from 531 non-selected consecutive renal stone formers investigated over 11 years for incomplete distal renal tubular acidosis (idRTA) [1]. Eight cystine stone patients and 130 calcium stone formers with various secondary causes [1] including idRTA

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were considered having a systemic disease. The remaining 393 SF (321 calcium, 63 uric acid, 9 infection) were screened for full MS/features thereof (definition IDF [2]), LDL-cholesterol (LDL-C) >3.0 mmol/l (- risk for coronary death [3]), urine volume <1.2 L/d likely caused by reduced thirst sensitivity/AVP dysregulation [4], and low bone mass.

Results or Learning points: Only 1 (1.6%) of 63 uric acid SF (UA-SF) was without any abnormality, compared with 9% of calcium SF (CaSF, p <0.0001, Table). Full MS (p <0.0025) or features thereof (p <0.0001) were more prevalent in UA-SF, whereas elevated LDL-C was more often present in CaSF (p <0.005). Only 1 of 9 infection SF had no metabolic/cardiovascular abnormality. Altogether, just 30 out of 531 SF (5.6%) did not show any marker of systemic disease.

Parameters	Calcium SF (321)	Uric acid SF (63)	p value*
sBP ≥ 130 mmHg	106/281 (38%)	44/59 (75%)	< 0.0001
dBP ≥ 85 mmHg	96/281 (34%)	28/59 (47%)	< 0.0001
Full MS	43/321 (13%)	13/63 (21%)	< 0.0025
Any feature of MS	166/321 (52%)	41/63 (65%)	< 0.0001
Low HDL-chol.	61/315 (19%)	15/62 (24%)	< 0.05
High triglycerides	92/315 (29%)	33/62 (53%)	< 0.0001
Fast. Gluc. ≥ 5.6 mM	47/306 (15%)	17/60 (28%)	< 0.0001
LDL-chol. ≥ 3.0 mM	197/314 (63%)	34/62 (55%)	< 0.005
U-vol. < 1200 ml/d	38/321 (12%)	8/63 (13%)	NS
Low bone mass	22/321 (7%)	4/63 (6%)	NS
NO abnormalities	28/321 (9%)	1/63 (1.6%)	< 0.0001

Conclusions: 1) Nephrolithiasis should be considered a systemic disease, as >90% of SF exhibit markers of systemic disease. 2) Primarily recurrent CaSF and UA-SF should be referred to nephrologists for evaluation not only of urine chemistries, but systemic pathologies such as traits of MS, elevated LDL-C, hyperparathyroidism, incomplete dRTA, bone disease, medullary sponge kidney, inflammatory bowel disease, bariatric surgery and lithogenic drugs.

1. J Nephrol 35: 1619-, 2022;
2. Lancet 366: 1059-, 2005;
3. Circulation 136: 2315-, 2018;
4. J Am Soc Nephrol 7: 1802, 1996

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LONG ORAL PRESENTATIONS

OC 50

Hydrochlorothiazide for the prevention of kidney stone recurrence

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

1. University Clinic for Nephrology and Hypertension, Inselspital Bern, Switzerland 2. Lausanne University Hospital, Switzerland 3. Inselspital, 4. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 5. Nephrology, Catonal Hospital Lugano, Switzerland 6. Nephrology, Cantonal Hospital Chur, Switzerland 7. Nephrology, Cantonal Hospital St. Gallen, Switzerland 8. Clinic for Nephrology and Transplantation, Cantonal Hospital St. Gallen, Switzerland 9. Internal Medicine, Cantonal Hospital Bellinzona, Switzerland 10. Medical Outpatient Clinic, University Hospital Basel, Switzerland 11. Nephrology, Cantonal Hospital Luzern, Switzerland 12. Division of Nephrology, Cantonal Hospital Aarau, Aarau, Switzerland, 13. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 14. 1. Service of Nephrology, Valais Hospital, Sion, Switzerland., 15. CTU, University of Bern, Switzerland

Background: Nephrolithiasis is one of the most frequent conditions affecting the kidney and characterized by a high risk of recurrence. Thiazide diuretics are widely used for kidney stone recurrence prevention, but data are limited regarding their efficacy as compared with placebo and any dose–response relationship.

Methods or Case description: In this double-blind trial, we randomly assigned patients with recurrent calcium-containing kidney stones to 12.5 mg, 25 mg or 50 mg hydrochlorothiazide or placebo once daily. The main objective was to investigate the dose–response relationship for prevention of the primary end point, a composite of symptomatic or radiologic recurrence.

Results or Learning points: A total of 416 patients underwent randomization, median duration of follow-up was 2.92 years. A primary end point occurred in 60 of 102 patients (59%) receiving placebo, in 62 of 105 patients (59%) receiving 12.5 mg (rate ratio, 1.33; 95% confidence interval [CI], 0.92 to 1.93), in 61 of 108 patients (56%) receiving 25 mg (rate ratio, 1.24; 95% CI, 0.86 to 1.79), and in 49 of 101 patients (49%) receiving 50 mg hydrochlorothiazide (rate ratio, 0.92; 95% CI, 0.63 to 1.36). There was no linear relationship between hydrochlorothiazide dose and the primary end point (P = 0.66). Hypokalemia, gouty arthritis and new onset diabetes mellitus occurred more frequently in patients assigned to hydrochlorothiazide compared to placebo.

Conclusions: Among patients with recurrent kidney stones, recurrence rates were not different between patients receiving once daily 12.5 mg, 25 mg or 50 mg hydrochlorothiazide or placebo. (Funded by the Swiss National Science Foundation; NOSTONE ClinicalTrials.gov number, NCT03057431).

OC 51

Monogenic Forms of Kidney Stone Disease in 800 adult Kidney Stone Formers from the Bern Kidney Stone Registry

Dr. Manuel Anderegg[1], Dr. Eric Olinger[2], Dr. André Schaller[3], Dr. Lea Taylor[4], Dr. Matteo Bargagli[5], Dr. Rob Geraghty[2], Prof. John A. Sayer[2], Prof. Daniel Fuster[6]

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Freiburgstrasse 15, 3010, Bern, Switzerland, 2. Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne UK 3. Department of Medical Genetics, Inselspital, Bern University Hospital, University of Bern, Switzerland 4. Interfaculty Bioinformatics Unit, University of Bern, Bern, Switzerland 5. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 6. University Clinic for Nephrology and Hypertension, Inselspital Bern, Switzerland

Background: Kidney stone disease is increasing worldwide, leads to high morbidity and represents a substantial economic burden to health systems. The detection of monogenic forms of kidney stone disease provides crucial pathophysiological insights and enables precision medicine approaches in affected patients. Previous genetic analysis by whole exome sequencing (WES) or kidney stone disease gene panels in relatively small cohorts of selected stone formers detected monogenic forms of kidney stone disease in 8-30% of patients studied.

Methods or Case description: We conducted WES in 800 adult kidney stone formers participating in the Bern Kidney Stone Registry (BKSR). The BKSR is an unselected cohort of kidney stone formers with detailed phenotypic data available. Inclusion criteria are: ≥ 1 stone episode and age ≥ 18 years. For the initial analysis, we applied a virtual panel of 33 genes previously implicated in monogenic kidney stone disease. Variants in the 33 genes were filtered according to gnomAD allele frequencies (MAF <1%) and predicted consequence on the canonical transcript and were then curated against in silico pathogenicity tools, variant databases and previously reported modes of inheritance.

Results or Learning points: We detected 184 distinct predicted pathogenic variants in 19 of 33 analyzed genes. Taking into account likely mode of inheritance, this led to a molecular diagnosis for 12.1% of all patients. 30% of the detected variants with predicted pathogenicity have not been previously reported. 70% of kidney stone formers with likely monogenetic etiology showed monoallelic inheritance, fitting with previous data showing more dominant inheritance patterns in adults. Age at first stone was lower in patients with molecular diagnosis than patients without.

Conclusions: In an unselected cohort of adult kidney stone formers, we identified a surprisingly high prevalence of monogenetic forms of kidney stone disease. The next steps are to investigate potential multiallelic inheritance patterns and extend the genetic analysis to candidate genes.

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OC 52

Impact of alkali therapy on eGFR in kidney transplant recipients (Preserve-Transplant Study)

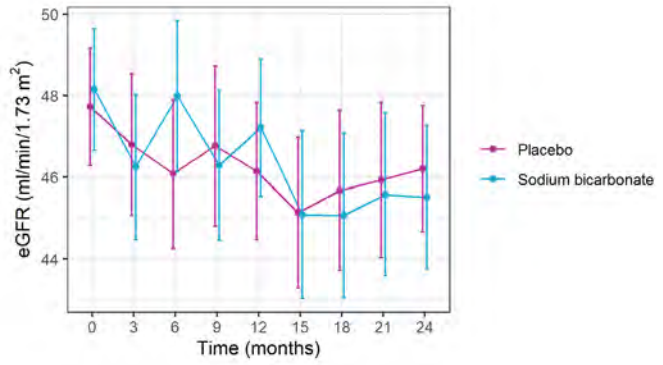
Dr. Nilufar Mohebbi[1], Dr. Alexander Ritter[1], Dr. Anna Wiegand[1], Ms. Nicole Graf[2], Dr. Suzan Dahdal[3], Dr. Daniel Sidler[4], Prof. Spyridon Arampatzis[3], Dr. Karine Hadaye[5], Prof. Thomas Müller[6], Prof. Carsten Wagner[7], Dr. Rudolf Wüthrich[1]

1. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 2. Graf Biostatistics, Switzerland 3. University Clinic for Nephrology and Hypertension, Inselspital Bern, Switzerland 4. Klinik für Nephrologie und Hypertonie, Inselspital, Bern, Switzerland 5. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 6. University Hospital Zurich, Department of Nephrology, Switzerland 7. Physiologisches Institut, Universität Zürich, Switzerland

Background: Kidney transplantation is the treatment of choice for patients with ESRD but long-term graft survival is still a challenging task. Observational studies have shown that metabolic acidosis is associated with graft loss and mortality. However, no interventional trial has been conducted yet to test if alkali treatment may preserve graft function.

Methods or Case description: We performed a prospective, multi-center, randomized, single-blinded, placebo-controlled trial to test the superiority of a 2-year alkali treatment with sodium bicarbonate in comparison to placebo for preservation of allograft function. Main inclusion criteria were: >12 months after renal transplantation, eGFR between 15 and 89 ml/min, and bicarbonate ≤22 mmol/l. The primary outcome was the creatinine-based yearly eGFR slope within 2 years. A subgroup analysis was performed for different CKD stages, baseline bicarbonate, type of immunosuppression, immunization, transplantation vintage, and type of graft.

Results or Learning points: 240 patients were included in the modified ITT population with an average age ± sd of 55±13.5 years. 92.5% of the study population received a calcineurin inhibitor-based immunosuppressive treatment and living donations accounted for 39.6%.The groups were well matched, as indicated by similar mean ± sd baseline eGFR (47.7±15.8 in the placebo group versus 48.2±16.3 ml/min/1.73 m^2 in the verum group) and similar mean ± sd serum bicarbonate levels at baseline (21.0±2.7 versus 21.3±2.6 mmol/l). The eGFR course of the 2-year treatment phase did not show a difference between the groups (Fig.1). The calculated yearly eGFR slopes over the 2 year treatment period amounted to -0.722 (5.521) in the placebo versus -1.413 (5.642) ml/min/1.73 m^2 per year in the bicarbonate group (median; IQR; P = 0.506). Furthermore, there were no significant differences in eGFR slopes in the subgroup analysis. Adverse events and serious adverse events were similar in both groups.



Conclusions: In adult kidney transplant recipients treatment with sodium bicarbonate over 2 years had no impact on creatinine-based eGFR slopes.

OC 53

Classifying hyponatremia by projected treatment effects – a new, quantitative approach for clinical practice and research

Dr. Florian Buchkremer[1], Dr. Bettina Winzeler[2], Prof. Philipp Schütz[3], Prof. Beat Müller[3], Prof. Stephan Segerer[1], Prof. Mirjam Christ-Crain[2]

1. Division of Nephrology, Kantonsspital Aarau, Aarau, Switzerland, 2. Department of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland, 3. Division of General Internal and Emergency Medicine, Kantonsspital Aarau, Aarau, Switzerland

Background: Current diagnostic recommendations and guidelines for hypotonic hyponatremia strongly focus on the pathogenesis of impaired urinary dilution (IDU). High net free water intake (HNFWI) and low non-electrolyte solute excretion (LNESE) are only considered when urine osmolality is very low. Here we present a new approach, that defines each case of hyponatremia concurrently by these three mechanisms.

Methods or Case description: Our classification is based on the Edelman equation and the external balance of sodium, potassium, and water. Using data from a large, prospective hyponatremia cohort (Co-Med Study), we calculated 'standard delta sodium' (SDNA) values. This newly developed measure provides the theoretical change to the serum sodium concentration, that would result from altering either HNFWI, IDU, or LNESE to an equivalent target with no other modification to the balance of water, sodium, or potassium.

Results or Learning points: With target levels at the 5th/95th percentile of the Co-Med study, median SDNA values (IQR) were 7.7 (5.1-11.2) for HNFWI, 11.8 (6.9-19.1) for IDU and 2.8 (1.7-4.7) mmol/l/24h for LNESE. At a minimum SDNA value of 4 mmol/l/24h, 79.8% of patients had 2 or 3 mechanisms present, the prevalence of HNFWI was 80.1%, IDU was found in 85.2% of patients, and LNESE in 31.2%. SDNA results in individual patients were highest with IDU in 65.2%, HNFWI in 33.0% and only 1.8% with LNESE. Hyponatremia was found to be multifactorial in most classic categories (primary polydipsia, hypovolemic hyponatremia, diuretic-induced hyponatremia, hypervolemic hyponatremia, SIADH) and typical underlying diseases (central nervous system disease, congestive heart failure, pulmonary disease, liver cirrhosis, and chronic kidney disease) as well.

Conclusions: Most hyponatremias are multifactorial and can be quantitatively defined by three dimensions: (1) high net free water intake, (2) impaired dilution of the urine and (3) low non-electrolyte solute excretion.

OC 54

Primary Hyperparathyroidism induces Erythropoitein resistance through FGF23

Prof. Bélen PONTE[1], Dr. Marco Demarchi[2], Dr. Thomas Verissimo[3], Dr. Samira Sadowski[4], Prof. Frederic Triponez[2], Prof. Sophie De Seigneux[1]

1. Nephrology and Hypertension Service. University Hospitals of Geneva, Switzerland 2. Thoracic surgery service. University Hospitals of Geneva, Switzerland 3. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 4. NIH Clinical Center. Bethesda, US

Background: In advanced CKD, secondary hyperparathyroidism (hPTH) could explain anemia resistance to erythropoietin (EPO) through a toxic effect on the bone marrow. However mechanisms are not well demonstrated. Anemia is present in 5% of the patients suffering from primary hPTH. Therefore, in order to understand the interplay between parathormone (PTH), EPO and haemoglobin, we studied patients undergoing parathyroidectomy for primary hPTH.

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Methods or Case description: We performed a prospective study over 6 months. We measured haemoglobin (Hb), PTH, FGF23, EPO, calcium and phosphate before (day 0), and after surgery at days 1, 10 and 180. We calculated de predicted EPO (pEPO) for the corresponding Hb levels. We then compared the evolution of those parameters during the follow-up and looked for correlations.

Results or Learning points: We included 111 patient, mostly women (81%) of median age 64 (56-74) and median eGFR 85ml/min (68-95).As expected, we observed a decrease in PTH, calcium and increase in phosphate after surgery (p <0.01). Regarding the other parameters of interest: Hb increased (p <0.01), while pEPO (p <0.01) and FGF23 decreased (p = 0.03). PTH increase correlated positively with FGF23 and calcium, but inversely with phosphate. There was a stronger positive correlation between EPO and FGF23, than with PTH. Although there was a trend for an inverse non-linear association between PTH and Hb, the association was clearly linear and stronger between FGF23 and Hb.

Conclusions: Those results suggest that in primary hPTH, Hb are lower despite higher EPO. This EPO resistance might be be mediated by an increased in FGF23 secretion during primary hPTH, which is itself likely associated to elevated calcium level.

OC 55

Withdrawal from dialysis in Switzerland between 2014 and 2021

Mrs. Rebecca Guidotti[1], Dr. Menno PRUIJM[2], Prof. Patrice M. Ambühl[1]

1. Institute of Nephrology, Stadtspital Zurich, Zurich, Switzerland 2. Lausanne University Hospital, Lausanne, Switzerland

Background: A recent Dutch study suggests that dialysis withdrawal has increased over the last years. The aims of this study were to investigate whether this is also the case in Switzerland, and to identify factors associated with withdrawal.

Methods or Case description: In this retrospective study, data were retrieved from the Swiss Dialysis Registry (srrqap). Annual death rates and causes of death were analyzed between 2014-2021. We compared clinical characteristics of patients who were withdrawn for medical/other reasons or who withdrew from dialysis with those who had another cause of death and with those who stayed alive.

Results or Learning points: A total of 7'246 incident patients on hemodialysis or peritoneal dialysis between 2014-2021 were included; of those, 2'325 patients died. In 2020, there was an above-average number of deaths, due to the coronavirus pandemic. Dialysis withdrawal because the patient refused further treatment represented 8.3-13.3% of all causes of death. Withdrawal by the patient did not increase throughout the study period, but withdrawal for medical/other reasons increased from 6.2 to 8.9% (see figure). Patients who died because of withdrawal from dialysis were significantly older and longer on dialysis than those with other causes of death, and had suffered less often from COVID-19. In multivariate regression analysis adjusted for age, sex, and Charlson score, testing negative for coronavirus was the only factor associated with withdrawal by the patient, whereas withdrawal for medical or other reason was also associated with higher age.

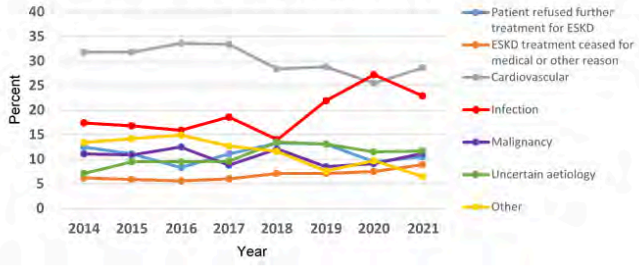
Conclusions: Unlike the Netherlands, dialysis withdrawal is not the leading cause of death in Switzerland, and withdrawal by the patient has not increased, not even during the COVID-19 epidemic. However, the percentage of patients who was withdrawn for medical/other reasons increased during this period, for unclear reasons. The only risk factors for withdrawal were higher age and – surprisingly – testing negative for the coronavirus.

Table: Characteristics (given as mean±SD or percentage) in incident dialysis patients according to their cause of death (patient withdrawal vs. others)

Characteristics	Patients alive (N=4'921)	Patient refused further treatment for ESKD* (N=209)	ESKD treatment ceased for medical or other reason (N=153)	Other causes of death (N=1963)	P-value†
Age at end follow up (years), mean±SD	64.3 ± 16.7	77.6 ± 9.1	78.4 ± 9.4	74.4 ± 11.6	**0.000**
Age at start of dialysis (years), mean±SD	61.8 ± 16.6	75.0 ± 9.0	75.6 ± 9.1	72.2 ± 11.5	**0.000**
Sex (male), n (%)	3223 (65.5)	134 (64.1)	98 (64.1)	1370 (69.8)	0.091
Charlson Score, mean±SD	4.01 ± 2.04	5.74 ± 2.68	5.60 ± 2.40	5.96 ± 2.62	0.244
Primary renal diagnosis, n (%)					
Renal vascular disease	1048 (21.3)	55 (26.3)	58 (37.9)	563 (28.7)	
Glomerulonephritis	874 (17.8)	17 (8.1)	15 (9.8)	175 (8.9)	
Diabetes mellitus	876 (17.8)	54 (25.8)	30 (19.6)	471 (24.0)	
Others/unknown aetiology	2121 (43.1)	83 (39.7)	50 (32.7)	754 (38.4)	
Dialysis vintage (days), mean±SD	939 ± 716	966 ± 638	1036 ± 705	826 ± 607	**0.002**
Modality (HD versus PD), n (%)	4353 (88.6)	193 (92.3)	142 (93.4)	1767 (90.0)	0.281
Modality Self care, n (%)	158 (3.6)	1 (0.5)	1 (0.7)	15 (0.8)	0.646
Vascular access (AVF*), n (%)	2578 (59.2)	94 (48.7)	64 (45.1)	780 (44.2)	0.231
Covid-19 infection, n (%)	317 (8.1)	5 (5.6)	4 (5.8)	115 (15.7)	**0.011**
Location (in-centre versus home), n (%)	4278 (87.0)	191 (91.4)	142 (93.4)	1744 (88.8)	0.262

*AVF=arteriovenous fistula; *ESKD=End stage kidney disease; †p-value: patients who died because of refusal vs other causes of death

Figure: Cause of death (grouped) per year of death; unadjusted



OC 56

Performance of Synacthen test in chronic hemodialysis patients*

Dr. Manuela Nickler[1], Dr. Susanne Stampf[2], Dr. Luca Bernasconi[3], Dr. Claudine Blum[4], Prof. Stephan Segerer[5], Dr. Min Jeong Kim[6]

1. Department of Nephrology & Transplantation Immunology, University Hospital Basel, Basel, Switzerland, 2. STATSperson, University Hospital Basel, Basel, Switzerland, 3. Institute of Laboratory Medicine Kantonsspital Aarau, Aarau, Switzerland, 4. Division of Endocrinology, Diabetes & Metabolism, Kantonsspital Aarau, Aarau, Switzerland, 5. Division of Nephrology, Kantonsspital Aarau, Aarau, Switzerland, 6. Division of Nephrology, Cantonal Hospital Aarau, Aarau, Switzerland

Background: Currently adrenal function tests (Synacthen test) in chronic hemodialysis (HD) patients are performed off dialysis. Performing the test during ongoing HD would considerably reduce additional efforts of patients and nursing staffs. The study therefore aims to show equivalence of cortisol concentrations pre- and during HD, each for low and standard dose Synacthen test.

Methods or Case description: In a single-center cross-over diagnostic equivalence study, Synacthen test was performed in four settings, in low (1µg) and standard dose (250µg) as well as pre- and during HD. Cortisol concentration was measured at 30 and 60 minutes after Synacthen administration, and additionally at 20 minutes in low dose test. Based on multivariable linear mixed model with random intercept for subjects, means of cortisol concentration on log-scale were estimated in each dose and test time combination. Differences in means were calculated and the TOST approach was applied to test for equivalence. In our study, equivalence was proven if the 90% confidence interval of the difference of two cortisol means on log-scale is entirely between -0.22 and 0.22.

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Figure 1: Cortisol concentration of 28 study participants under the four scenarios for Synacthen dose and time of Synacthen test.

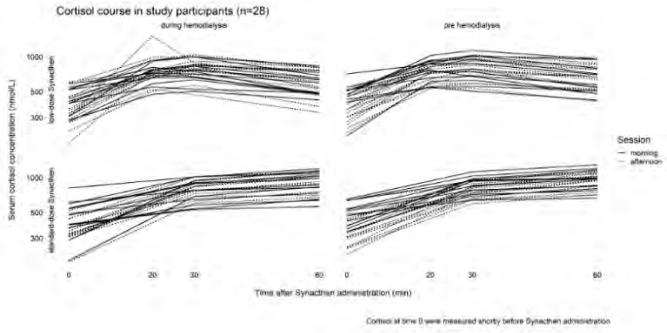
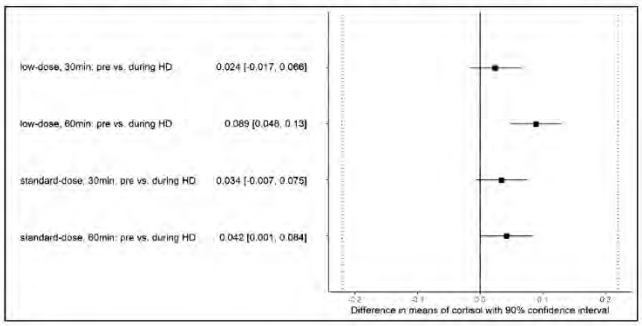


Figure 2: Differences of means of cortisol concentration (nmol/L) on log-scale in each Synacthen dose measured at 30 and 60 minutes after Synacthen administration. All 90% confidence intervals are entirely in equivalence region of (-0.22, 0.22) shown as the region between the two dotted vertical lines. Equivalence was thus proven in all four scenarios.



Results or Learning points: 28 chronic hemodialysis patients were enrolled and serum cortisol concentrations at 20 (in low dose), 30 and 60 minutes after Synacthen administration were shown to be equivalent pre- and during HD (Figure). Model-based estimates for mean cortisol on log-scale were adjusted by cortisol measured shortly before Synacthen, serum albumin at start of dialysis, glucose after Synacthen, daytime and within-subject variability (random intercept). In 10 tests, the cortisol peak after low dose Synacthen was already reached after 20 minutes, more often during HD (7 of 10 cases).

Conclusions: We found equivalent performance of Synacthen test during and off hemodialysis in chronic HD patients. These results suggest that the adrenal function test may be carried out during a HD session, leading to less organizational effort and thus earlier diagnosis of adrenal insufficiency.

*YSN paper

OC 57

Haemoglobin efficacy and cardiovascular safety data from the ASCEND-ND, -D, and -ID trials

Prof. Christoph Wanner[1], Prof. Ajay K. Singh[2], Dr. Adrian Liew[3], Dr. Anjali Acharya[4], Prof. Anjay Rastogi[5], Dr. Arnold Silva[6], Dr. Carmel Hawley[7], Dr. Gearoid McMahon[2], Prof. Indranil Dasgupta[8], Prof. Laura Mulloy[9], Prof. Lucia Del Vecchio[10], Dr. Marcelo Orias[11], Prof. Muh Geot Wong[12], Dr. Nicole Stankus[13], Dr. Osvaldo Merege Vieira Neto[14], Dr. Rafael Alberto Gomez Acevedo[15], Dr. Ricardo Correa-Rotter[16], Dr. Sergio Godoy[17], Dr. Shruti Gupta[2], Prof. Vladimír Tesař[18], Dr. Allison Blackorby[19], Dr. Amy Meadowcroft[19], Dr. Alexander R. Cobitz[19]

1. University Hospital of Würzburg, Würzburg, Germany 2. Brigham and Women's Hospital, Harvard Medical School, Boston, US 3. Mount Elizabeth Novena Hospital, Singapore 4. Albert Einstein College of Medicine, NYC, US 5. UCLA Health, LA, US 6. Boise Kidney and Hypertension Institute, Meridian, US 7. Department of Nephrology, Princess Alexandra Hospital, South Brisbane, Australia 8. Renal Medicine – University Hospitals Birmingham NHS Foundation Trust Heartlands Hospital, Birmingham, UK 9. Amedical College of Georgia, Augusta, US 10. Azienda Socio Sanitaria Territoriale Lariana, Italy 11. Yale University, Stamford, US 12. Royal North Shore Hospital, Sydney; Univeristy of Sydney, Sydney, Australia 13. University of Chicago Medicine, Chicago, US 14. Sociedade Brasileira de Nefrologia, São Paulo, Brazil, 15. RTS San Fernando, Renal Unit, Carrera, Cali-Valle del Cauca, Colombia 16. National Medical Science and Nutrition Institute Salvador Zubiran; National Autonomous University of Mexico; National Researcher III Conacyt, 17. George Clinical, Pilar, Mexico 18. Charles University, Prague, Czech Republic 19. GSK, Collegeville, PA, US

Background: The Anaemia Studies in Chronic Kidney Disease (CKD): Erythropoiesis via a novel prolyl hydroxylase inhibitor Daprodustat (ASCEND) phase 3 program investigated efficacy and safety of daprodustat, versus a conventional erythropoiesis-stimulating agent (ESA) across the CKD patient spectrum. We report haemoglobin and cardiovascular (CV) safety data for ASCEND-non-dialysis (ND; NCT02876835),1 -dialysis (D; NCT02879305),2 and -incident dialysis (ID; NCT03029208)3 trials.

Methods or Case description: This analysis included 2 multicentre, open-label randomised CV outcome trials in non-dialysis and dialysis patients (daprodustat once-daily versus ESA comparator) with a time-to-first adjudicated major adverse CV event (MACE) co-primary safety endpoint (non-inferiority margin: 1.25). ASCEND-ID was a 52-week study reporting adjudicated MACE but was not designed for formal MACE evaluation. MACE was defined as a composite of all-cause mortality, non-fatal myocardial infarction, and non-fatal stroke. All had a primary endpoint of mean change in haemoglobin between baseline and evaluation period (Weeks 28–52; non-inferiority margin: -0.75 g/dL).

Results or Learning points: 7148 patients were randomised across the 3 trials, including ~14,200 person years of follow-up in these CV outcome trials. Baseline characteristics were balanced across treatment groups. Non-inferiority was met for the CV outcome trials' MACE endpoint, and non-inferiority between daprodustat and ESA was demonstrated in all trials for haemoglobin (Table). Rates of adverse events were similar between daprodustat and ESA.

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Table: Cardiovascular safety and haemoglobin efficacy results from the Anaemia Studies in Chronic Kidney Disease: Erythropoiesis via a novel prolyl hydroxylase inhibitor Daprodustat (ASCEND) -non dialysis (ND), -dialysis (D), and -incident dialysis (ID) trials

ITT population	Daprodustat	ESA[a]	Treatment effect
Study	**First occurrence of adjudicated MACE[b], n/N (%)**		**Adjusted HR (95% CI)[c]**
ASCEND-ND[1]	378/1937 (19.5)	371/1935 (19.2)	1.03 (0.89, 1.19)
ASCEND-D[2]	374/1487 (25.2)	394/1477 (26.7)	0.93 (0.81, 1.07)
ASCEND-ID[3]	19/157 (12.1)	15/155 (9.7)	N/A
Study	**MACE rate per 100 PY (95% CI)**		**Absolute rate difference per 100 PY (95% CI)**
ASCEND-ND	10.86 (9.80, 12.02)	10.63 (9.58, 11.77)	0.23 (-1.31, 1.77)
ASCEND-D	11.07 (9.98, 12.26)	11.86 (10.72, 13.09)	-0.78 (-2.41, 0.84)
ASCEND-ID[3]	11.65 (7.02, 18.20)	9.24 (5.17, 15.24)	2.41 (-4.61, 9.43)
Study	**Mean (SD) baseline Hb (g/dL) / adjusted mean (SE) change in Hb (g/dL) from baseline to Week 28–52 (g/dL)[d]**		**Adjusted mean difference (95% CI)[d,e]**
ASCEND-ND[1]	9.9 ± 0.9 / 0.74 (0.02)	9.8 ± 0.9 / 0.66 (0.02)	0.08 (0.03, 0.13)
ASCEND-D[2]	10.3 ± 1.0 / 0.28 (0.02)	10.4 ± 1.0 / 0.10 (0.02)	0.18 (0.12, 0.24)
ASCEND-ID	9.5 ± 1.0 / 1.02 (0.09)	9.5 ± 1.0 / 1.12 (0.09)	-0.10 (-0.34, 0.14)

[a]Darbepoetin alfa (ASCEND-ND[1], -D peritoneal dialysis[2], -ID[3]), epoetin alfa (ASCEND-D hemodialysis[2])
[b]MACE includes all events occurring during the study (ITT approach)
[c]Pre-specified non-inferiority margin of 1.25. Based on a Cox proportional hazards model: ASCEND-ND, adjusted for treatment group, use or nonuse of an ESA and geographic region;[1] ASCEND-D, adjusted for treatment group, dialysis type and geographic region[2]
[d]Based on an ANCOVA model: ASCEND-ND, adjusted for baseline hemoglobin, treatment group, use or nonuse of an ESA and geographic region;[1] ASCEND-D, adjusted for baseline hemoglobin, treatment group, dialysis type and geographic region;[2] ASCEND-ID, adjusted for baseline Hb, dialysis type, and dialysis start manner (urgent, planned)
[e]Non-inferiority was declared if the lower bound of the two-sided 95% CI exceeded -0.75 g/dL
ANCOVA, analysis of covariance; CI, confidence interval; ESA, erythropoiesis-stimulating agent; HR, hazard ratio; ITT, intention-to-treat; MACE, major adverse cardiovascular event; n, number of patients with event of interest; N, total number of patients; N/A, not available; PY, person year; SD, standard deviation

Conclusions: Daprodustat demonstrated similar haemoglobin efficacy versus ESA in patients with anaemia of CKD in prevalent and incident dialysis patients, as well as patients with non-dialysis CKD. The CV outcome trials demonstrated daprodustat was non-inferior to ESA for CV safety. Daprodustat was well-tolerated in patients enrolled in all 3 trials and could be an effective alternative to conventional ESA.

References:

1. Singh AK et al. NEJM 2021;385:2313–324
2. Singh AK et al. NEJM 2021;385:2325–335
3. Singh AK et al. JAMA Intern Med 2022;182:592–602

(GSK-funded study; ENCORE of presentation at NKF 2022)

OC 58

A population-based scoring system to assess the impact of individual risk factors on vascular health*

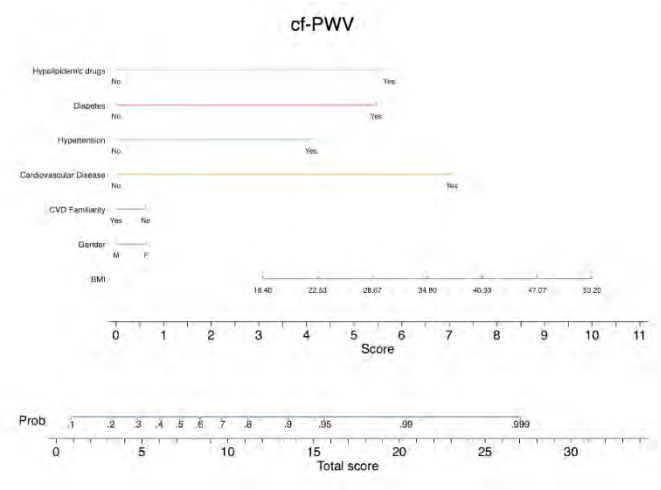
Dr. Vanessa Gagliano[1], Mr. David Gehrig[2], Dr. Rosaria Del Giorno[3], Prof. Luca Gabutti[1]

1. Internal Medicine, Cantonal Hospital Bellinzona, Switzerland 2. Faculty of Biomedicine, Università della Svizzera Italiana, Lugano, Switzerland 3. Angiology Service, University Hospital of Lausanne, Switzerland

Background: Arterial stiffness is an indicator of vascular health, influenced by both pathological conditions and physiological determinants, noticeably age. Augmentation index (AI) and pulse wave velocity (PWV) are used to assess arterial stiffness. However, data about their reference values are limited due to few large population-based studies and the lack of standardization of the measurement methods. Our study aims to establish population PWV and AI values in a cohort of adult people with and without modifiable cardiovascular risk factors.

Methods or Case description: We performed a retrospective analysis of a Swiss population-based research project, which took place in 2017 and 2018. Of the 1202 participants originally enrolled, 1097 were included in the final sample. The population was divided into "normal" (n = 390) and at-risk (n = 707), based on the presence of the following: smoking, diabetes, previous cardiovascular disease (CVD), LDL cholesterol ≥ 4.11 or treatment with hypolipidemic drugs, and hypertension or treatment with antihypertensive drugs. Tonometric and oscillometric devices were employed to measure PWV non-invasively, and the 75th percentiles of PWV and AI in the "normal" population were calculated to identify cut-offs for the logistic regression analysis.

Results or Learning points: We developed nomograms by assigning a numerical score to each independent prognostic factor; the total score estimated the probability of PWVs and AIs being over the defined cut-offs. Patients with hypertension, diabetes, and obesity showed higher PWV values ($p < 0.001$). In the univariate logistic regression, factors predictive for higher PWV values were diabetes, CVDs, hypercholesterolemia, and hypertension, while CVDs, antihyperlipidemic treatment, hypertension, and increase in BMI were predictive in the multivariate logistic regression. Smoking did not significantly influence arterial stiffness parameters.



Conclusions: The present study provides reference values for PWV and AI in subjects with and without modifiable cardiovascular risk factors and, through nomograms, a risk score stratification to assess the impact of individual risk factors on vascular health.

*YSN paper

OC 59

Prevalence and Consequences of Incidental Findings on Low Dose Native Abdominal Computed Tomography in a Population without History of Nephrolithiasis*

Dr. Alexander Ritter[1], Mr. Maximilian Sabev[1], Prof. Olivier Bonny[2], Dr. Grégoire WUERZNER[3], Dr. Thomas Ernandez[4], Dr. Catherine STOERMANN-CHOPARD[4], Dr. Florian Buchkremer[5], Prof. Stephan Segerer[6], Dr. Lena Jellestad[7], Prof. Carsten Wagner[8], Dr. Harald Seeger[9]

1. Klinik für Nephrologie, Universitätsspital Zürich, Switzerland 2. CHUV – Centre Hospitalier Universitaire Vaudois, Service de Néphrologie et Hypertension, Lausanne, Switzerland 3. Division of Nephrology and Hypertension, Department of Internal Medicine, Lausanne University Hospital, Switzerland, 4. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 5. Division of Nephrology, Cantonal Hospital Aarau, Aarau, Switzerland, 6. Division of Nephrology, Kantonsspital Aarau, Aarau, Switzerland, 7. Klinik für Konsiliarpsychiatrie und Psychosomatik, Universitätsspital Zürich, Switzerland 8. Physiologisches Institut, Universität Zürich, Switzerland 9. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland

Background: The use of sectional imaging techniques is increasing, including low dose abdominal computed tomographies of the abdomen in the context of nephrolithiasis. To weigh the risks and benefits of an imaging test, clinicians need to know not only the risk of the imaging procedure itself but also the potential consequences of incidental findings. To our knowledge, there have been no prior large cohort studies investigating "incidentalomas" and their consequences in non-contrast low-dose abdominal computed tomographies.

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Methods or Case description: This study is a multicenter, retrospective analysis of non-contrast low-dose abdominal computed tomography scans obtained as screening measure for the control group of the Swiss Kidney Stone Cohort (SKSC). The outcome of primary interest is the prevalence of incidental findings according to the American college of Radiology (ACR) incidental findings committee.

Results or Learning points: A total of 229 participants with mean age of 42.9 (±13.4) years were included in our preliminary analysis - 56.3% were male. 154 individual findings could be detected in 108 participants (47.2%). 38 (16.6%) participants had more than one finding. 55 (35.7%) findings were classified as "incidentalomas" according to the ACR findings committee – findings in 18 participants (7.9%) warranted further follow up. The kidneys accounted for most incidental findings – 55 in total. There were more male study subjects with incidental findings and they were significantly older than participants without findings.

Conclusions: Incidental findings are frequent in low-dose abdominal computed tomographies of individuals in the above age range. A relevant number of "incidentalomas" warrants further work-up. In the coming months, we aim to assess the costs and the psychologic impact of these findings on affected individuals.

*YSN paper

OC 60

Adenine-Induced Nephropathy Reduces Atherosclerosis in ApoE Knockout Mice*

Ms. Laeticia Scherler[1], Ms. Sofia Verouti[1], Dr. Daniel Ackermann[1], Prof. Bruno Vogt[1], Prof. Geneviève Escher[1]

1. University Clinic for Nephrology and Hypertension, Inselspital Bern, Bern, Switzerland

Background: Cardiovascular events are the main cause of death in patients with chronic kidney disease. We hypothesize that the protective effects of renal cholesterol and vitamin D3 metabolism are lost under this condition. Nephropathy was induced by adenine in Apolipoprotein E knockout mice. The atherosclerotic phenotype was compared to mice with normal renal function.

Methods or Case description: Mice were fed a western diet ±0.15% adenine. Urine and feces were collected to assess renal function and fecal output. Atherosclerosis, serum lipoprotein composition and functionality, hepatic lipids, and expression of genes involved in lipid metabolism, vitamin D3 and Na+ homeostasis, were assessed. Bones were analyzed by microCT.

Results or Learning points: Mice fed with adenine showed enhanced urinary Na+, Ca2+, and Pi excretion, reduced urinary pH, UreaUrine/UreaSerum, and CreatinineUrine/CreatinineSerum ratios. They developed less atherosclerosis. Lipoproteins in serum and hepatic lipids remained unchanged. Cholesterol efflux increased. Fecal output of cholesteryl ester and triglycerides increased. In the liver, mRNA levels of Cyp27a1, Cyp7a1, and Scarb1 increased; in the kidneys, Slc9a3, Slc12a3, Vdr, and Cyp24a1 decreased. Adenine increased cholesterol efflux in vitro. Tibias were shorter.

Conclusions: Adenine induced tubular damage and was athero-protective because of enhanced cholesterol efflux and lipids elimination in feces. Bone growth was also affected

*Student paper

OC 61

An open-label, non-randomized extension study to evaluate the long-term efficacy, safety and tolerability of LNP023 in subjects with C3 glomerulopathy: Interim analysis of a Phase 2 study

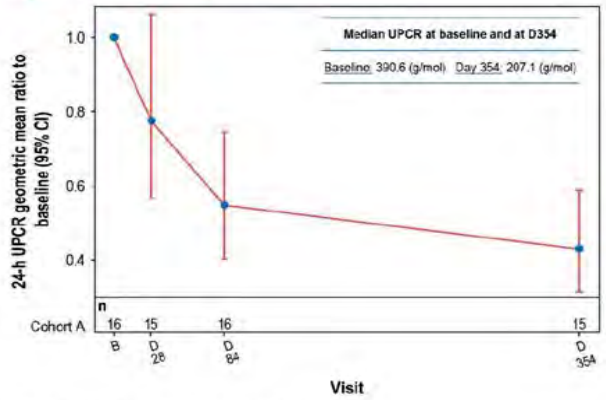
Dr. Matthias Meier[1]

1. Novartis, Switzerland

Background: Iptacopan (LNP023) is an oral, first-in-class, selective inhibitor of factor B, a key component of the alternative complement pathway (AP). We have previously reported data from a Ph2 study in native and recurrent C3G (NCT03832114) showing that 12W iptacopan treatment results in a 45% reduction in proteinuria in native C3G. Here we present the effects of 12M iptacopan treatment.

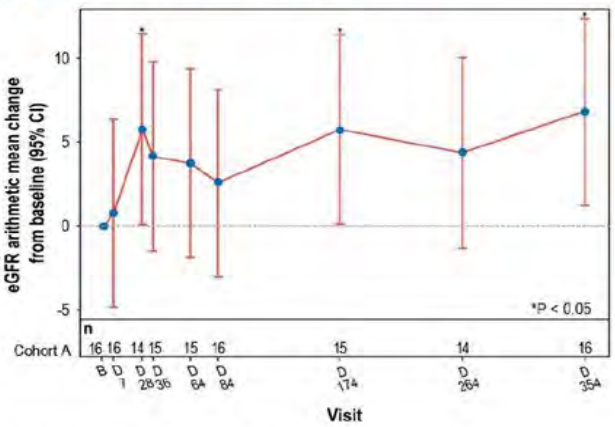
Methods or Case description: Adults with native (CoA) or recurrent C3G post kidney transplant (CoB) received iptacopan for at least 12W before entering this Ph2 extension trial (NCT03955445). The primary efficacy objective was to assess the effect of iptacopan on a composite endpoint of 1) stable/improved eGFR [≤10% reduction from baseline], 2) ≥50% reduction from baseline in UPCR, and 3) ≥50% increase from baseline in serum C3 after 12M treatment.

Figure 1: Primary endpoint Cohort A – UPCR



57% reduction in UPCR **(p<0.0001)**

Figure 2: Primary endpoint Cohort A – eGFR



+6.83 mL/min/1.73 m² **(p=0.0174)** increase in eGFR

Results or Learning points: Of 27 patients completing the 12W Ph2 study, 26 (16CoA, 10CoB) entered the extension for treatment with iptacopan 200 mg b.i.d. 53% of CoA patients met the

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composite renal endpoint criteria at 12M; proteinuria was reduced by 57% (p <0.0001; Fig1), eGFR increased by 6.83 mL/min/1.73 m^2 (p = 0.0174; Fig 2) and C3 increased by 253% (p <0.0001). eGFR was stable and C3 levels increased by 96% in CoB. Proteinuria reduction was not assessed in CoB as median baseline proteinuria was normal (18.4g/moL). Iptacopan was generally well-tolerated and most AEs were of mild severity in both cohorts. Biomarkers demonstrated substantial AP inhibition.

Conclusions: Long-term treatment with iptacopan results in further proteinuria reduction and eGFR improvement beyond that previously reported following 12W treatment in native C3G. Stable eGFR was seen in recurrent C3G, with stable increases in serum C3 levels found in both cohorts. The ongoing Ph3 APPEAR-C3G (NCT04817618) study is evaluating the efficacy of iptacopan in native C3G patients.

OC 62

Determinants of renal microperfusion as assessed with contrast-enhanced ultrasound in healthy men and women*

Dr. Antonio Ulpiano[1], Ms. Marielle Hendriks-Balk[1], Ms. Wendy Brito[1], Mr. Jonas Garessus[1], Prof. Michel Burnier[1], Dr. Grégoire WUERZNER[1], Dr. Menno PRUIJM[1]

1. Division of Nephrology and Hypertension, Department of Internal Medicine, Lausanne University Hospital, Switzerland

Background: Renal microcirculation is essential to maintain renal function, but its determinants in humans have been poorly studied. Contrast-enhanced ultrasound (CEUS) and its outcome measure, the perfusion index (PI), now allows non-invasive quantification of cortical micro-perfusion at the bedside. The aims of this study were to assess whether gender-differences exist in renal microperfusion, and to identify clinical determinants in healthy individuals.

Methods or Case description: Healthy, normotensive volunteers (eGFR >60 ml/min/1.73 m^2, no albuminuria) underwent CEUS under standardized conditions according to the destruction-reperfusion (DR) technique. The mean PI of four DR sequences was reported as primary outcome measure. Student's t-test or Wilcoxon tests were performed to compare groups. Associations between PI and clinical characteristics were assessed with Spearman tests and multivariate linear regression.

Results or Learning points: A total of 117 participants completed the study. We dropped 2 outliers (PI >10.000 arbitrary units (a.u.)) leaving 115 subjects (77 women and 38 men) for analysis; mean±SD age was respectively 37.1±12.2 and 37.1±12.7 years in women and men, mean eGFR 105.9±15.1 and 91.0±17.4 ml/min/1.73 m^2. PI was higher in women than men (3129± 212 vs 2470± 274 a.u, p = 0.036). Correlation analysis showed positive associations between PI and eGFR, systolic blood pressure, heart rate, and plasma renin activity (PRA) and a negative association between PI and potassium, but no associations with BMI, aldosterone or salt intake. In multivariate linear regression analysis, only PRA remained significantly associated with PI.

Conclusions: Although the perfusion index was higher among women, this was largely explained by gender differences in eGFR in our sample. PI is only weakly influenced by classic clinical variables, but is positively associated with PRA, suggesting that the renin-angiotensin system plays a role in the regulation of cortical micro-perfusion in humans. Which other factors contribute to the large variations in micro-perfusion across individuals needs further study.

*YSN paper

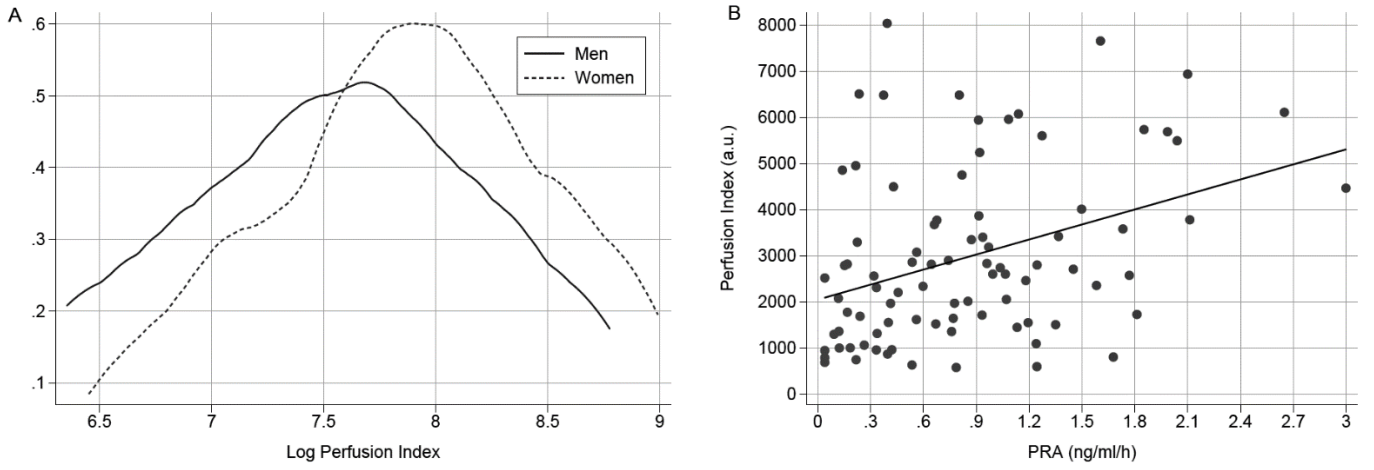

Figure 1: (A) Kernel density plot showing the distribution of the perfusion index in men and women (logarithmic scale); (B) Scatter plot showing the association between the perfusion index and plasma renin activity

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OC 63

Intrinsic TGF-b Signaling Attenuates Proximal Tubule Mitochondrial Injury and Inflammation in Chronic Kidney Disease*

Ms. Merve Kayhan[1], Ms. Judith Vouillamoz[1], Ms. Dayme Gonzalez Rodriguez[2], Dr. Milica Bugarski[3], Dr. Yasutaka Mitamura[4], Ms. Julia Gschwend[1], Prof. Christoph Schneider[1], Prof. Andrew Hall[3], Dr. David Legouis[5], Prof. Cezmi Akdis[4], Prof. Leslie Gewin[6], Prof. Roland Wenger[1], Dr. Stellor Nlandu Khodo[1]

1. Institute of Physiology, University of Zurich, Zurich, Switzerland, 2. University of Zurich, 3. Institute of Anatomy, UZH, Zurich, Switzerland 4. Swiss Institute of Allergy and Asthma Research, University of Zurich, Davos, Switzerland 5. Department of Medicine and Cell Physiology, University of Geneva, Switzerland 6. Department of Internal Medicine, Division of Nephrology, Washington University St. Louis, US

Background: Excessive TGF-b signaling and mitochondria dysfunction fuel chronic kidney disease (CKD) progression. However, inhibiting TGF-b failed to mitigate CKD in humans. The proximal tubule (PT), the most vulnerable renal segment, is packed with giant mitochondria and injured PT is pivotal in CKD progression. How TGF-b signaling affects PT mitochondria in CKD remained unknown.

Methods or Case description: Mice lacking the TGF-b receptor 2 (Tgfbr2 or TbRII) were injured with aristolochic acid (AA) and we combined spatial transcriptomics (Visium), microscopy and biochemical approaches to determine how TGF-b signaling affects PT mitochondrial homeostasis and tubulo-interstitial interactions in CKD.

Results or Learning points: Spatial transcriptomics with biochemical approaches reveal that specific deletion of Tgfbr2 in the PT worsens mitochondrial injuries and the Th1 immune response in CKD, partly, by impairing complex I expression and mitochondrial quality control leading to a metabolic rewiring towards aerobic glycolysis (Warburg-like effect). We identified injured S3 type 2 cells as the main mediators of the maladaptive macrophage/dendritic cell activation in the absence of Tgfbr2. snRNAseq database analysis confirmed decreased TGF-b receptors and metabolic deregulation in the PT of CKD patients.

Conclusions: This study unexpectedly uncovers the role of TGF-b signaling in PT mitochondrial homeostasis and inflammation in CKD, and identifies potential (molecular and cellular) therapeutic targets to hamper CKD progression.

*YSN paper

OC 64

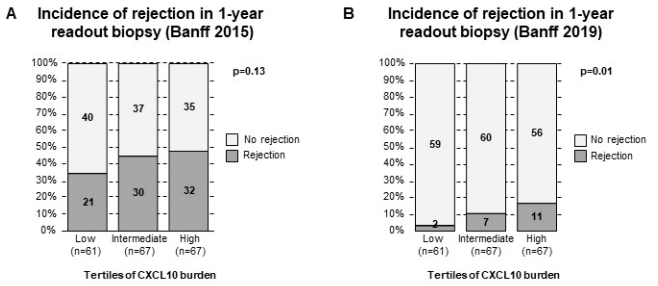
Randomized trial to assess the clinical utility of renal allograft monitoring by urine CXCL10 chemokine

Dr. Patricia Hirt-Minkowski[1], Mrs. Joelle Handschin[2], Dr. Susanne Stampf[3], Dr. Helmut Hopfer[4], Dr. Thomas Menter[5], Mrs. Lisa Senn[6], Dr. Gideon Hönger[2], Dr. Patrizia Amico[6], Dr. Caroline Wehmeier[6], Prof. Jürg Steiger[6], Dr. Michael T. Koller[3], Prof. Michael Dickenmann[6], Prof. Stefan Schaub[6]

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland, 2. Department of Biomedicine, University of Basel, Basel, Switzerland 3. STATSperson, University Hospital Basel, Basel, Switzerland, 4. Department of Medical Genetics and Pathology, University Hospital Basel, University of Basel, Basel, Switzerland, 5. Department of Pathology, University Hospital Basel, Basel, Switzerland, 6. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland

Background: Urine CXCL10 is a promising non-invasive biomarker for detection of renal allograft rejection. The aim of this study was to investigate the clinical utility of renal allograft monitoring by urine CXCL10 in a prospective clinical trial.

Methods or Case description: We randomized 120 patients into an intervention, and 121 patients into a control arm. In both arms, urine CXCL10 levels were monitored at three specific time points (1, 3, and 6 months posttransplant). In the intervention arm, elevated values (i.e., with a predefined cutoff for a positive result of ≥3ng/mmol creatinine) triggered performance of an allograft biopsy with therapeutic adaptations according to the result. In the control arm, urine CXCL10 was measured, but the results concealed. The primary outcome was a combined endpoint at one-year posttransplant (graft loss, death, clinical rejection, subclinical rejection in one-year readout biopsy, development of de novo donor-specific HLA-antibodies, estimated GFR <25 ml/min).



Results or Learning points: The primary outcome was not different between the intervention and the control arms (51% vs 48%; RR 1.06 [95% CI 0.82-1.37]; p = 0.70). When including only 201/241 (83%) patients having an adequate one-year readout biopsy, the primary outcome was also not different (55% vs 47%; RR 1.16 [95% CI 0.88-1.52]; p = 0.32). Furthermore, the per-protocol analysis revealed no significant difference (57% vs 46%; RR 1.20 [95% CI 0.90-1.61]; p = 0.24). The urine CXCL10 burden, calculated as the mean of measurements at the three monitoring time points, significantly correlated with rejection in one-year readout biopsies defined by the Banff 2019 classification (p = 0.01) as illustrated in figure 1. Urine CXC10 values often followed inflammation processes in the allograft (e.g., rejection, polyomavirus BK infection).

Conclusions: A urine CXCL10 monitoring strategy failed to improve one-year outcomes. However, urine CXCL10 can provide important information on the inflammatory status of the renal allograft (ClinicalTrials.gov_NCT03140514).

OC 65

Kidney Transplantation and its outcomes in Switzerland*

Ms. Yuansheng Zhang[1], Mr. Marlo Stadler[1], Prof. Thomas Müller[2], Prof. Sophie De Seigneux[3], Prof. Uyen Huynh-Do[4], Dr. Patrizia Amico[5], Prof. Dela Golshayan[6], Dr. Aurelia Schnyder[7], Prof. Vartan Kurtcuoglu[1], Dr. Diane de Zelicourt[1]

1. Institute of Physiology, University of Zurich, Zurich, Switzerland, 2. University Hospital Zurich, Department of Nephrology, Zurich, Switzerland 3. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 4. University Clinic for Nephrology and Hypertension, Inselspital Bern, Switzerland 5. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland 6. Transplantation Centre, Departments of Medicine and Surgery, Lausanne University Hospital (CHUV) and University of Lausanne (UNIL), Switzerland., 7. Clinic for Nephrology and Transplantation, Cantonal Hospital St. Gallen, Switzerland

Background: While kidney transplantation is generally associated with increased patient survival and improved health-related quality of life compared with long-term dialysis, outcomes after transplantation vary considerably. The prediction of individual risks is currently challenging, thus, understanding the burden of outcomes in Swiss transplant recipients may help frame national-level guidelines.

Methods or Case description: We extracted pre-, peri- and post-operative disease history, medications and outcomes for all adult kidney transplant recipients enrolled in the prospective Swiss Transplant Cohort Study (STCS) between May 2008 and

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December 2018 (2718 patients; 2767 transplantations). The primary outcome was all-cause mortality, with graft loss and major adverse cardiac events (MACE) as secondary outcomes.

Results or Learning points: The mean (+/-SD) age at transplantation was 54 (+/-13.5) years old. Prior to transplantation, 2241 (82%) patients underwent dialysis (hemodialysis: n = 1855 (68%), peritoneal dialysis: n = 383 (14%)) for a mean duration of 3.01 years. Of the 2767 transplantations, 56% were from brain-dead donors, followed by living unrelated (21%), living related (17%) and non-heart beating (6%) donors. A total of 322 patients died during the median follow-up of 3.57 years (IQR: 1.26–6.02). Cardiovascular disease was listed as one of the causes of death for 91 patients (28%). 469 patients (17%) experienced MACE, 50% of which were de novo MACE, and 231 patients (9%) experienced graft lost, 20% of which were acute renal allograft rejection (occur within the first 3 months post-transplantation). The median time to first MACE after transplantation was 1.95 (IQR: 0.35–4.79) years and the median to graft loss was 2.35 (IQR: 0.45–5.08) years. Using multivariate Cox regression, risk factors associated with poorer patient survival included age at transplantation, number of previous renal transplants, previous MACE and diabetes mellitus.

Conclusions: This study is the first systematic analysis of the STCS in the recent decade, providing insights into the prevalence of key comorbidities and predictors of survival after kidney transplantation.

*YSN paper

OC 66

Donor-specific tolerance induction by combined kidney and hematopoietic stem cell transplantation

Dr. Kerstin Hübel[1], Dr. Daniel SIDLER[2], Prof. Thomas Müller[3], Prof. Pietro Cippà[4], Prof. Thomas Fehr[5]

1. Klinik für Nephrologie, Universitätsspital Zürich, Switzerland 2. Klinik für Nephrologie und Hypertonie, Inselspital, Bern, Switzerland 3. University Hospital Zurich, Department of Nephrology, Switzerland 4. Division of Nephrology, Ente Ospedaliero Cantonale, Lugano, Switzerland, 5. Kantonsspital Graubünden, Switzerland

Background: Long-term survival of kidney allografts is limited by either inadequately controlled rejection and/or by side effects of long-term immunosuppression (drug toxicity, infections and neoplasia). Induction of donor-specific tolerance would resolve most, if not all of these limitations. Here, we report on 6 patients included in the first European trial of combined kidney and hematopoietic stem cell transplantation (HSCT; swisstolerance.CH).

Methods or Case description: Six patients (3 female / 3 male) underwent combined kidney and hematopoietic stem cell transplantation from their HLA-identical living siblings between 2016 and 2022. Conditioning therapy for HSCT and immunosuppression was performed according to the Stanford protocol including total lymphoid irradiation, anti-thymocyte globulin followed by corticosteroids (3 days), mycophenolate (1 months) and cyclosporine for 6-15 months. After 9-15 months all immunosuppression was withdrawn.

Results or Learning points: Five out of six patients were completely withdrawn from all immunosuppression (follow-up between 6 years and 4 months). No rejection or graft-versus-host disease episodes and no relevant infections occurred. Initial donor chimerism was seen in all patients. However, in 5/6 patients the chimerism level was declining, whereas one patient remained a stable mixed chimera. Specificity of tolerance was tested by molecular microscope analysis (absence of rejection signature) and by successful SARS CoV2 vaccination in some of the patients. One patient experienced a relapse of her primary glomerulonephritis in the allograft. She developed proteinuria, but renal function remained normal so far.

Conclusions: Combined HSCT and kidney transplantation from the same living donor provides tolerance to a kidney allograft. This tolerance is donor-specific, as shown by protective immune responses against a SARS-CoV2-specific vaccine and absence of "molecular rejection".

OC 67

Association of Kidney Graft Long Term Outcome with Recipient Hydrogen Sulfide Production and Cystathionine Gamma-Lyase Polymorphisms: a Cohort Study*

Dr. Matthieu Halfon[1], Dr. Raffaella Emsley[2], Mr. Thomas Agius[2], Mr. Arnaud Lyon[1], Dr. Florent Allagnat[3], Prof. Pierre-Yves Bochud[4], Dr. Sebastien Deglise[5], Prof. Manuel Pascual[1], Prof. Dela Golshayan[1], Dr. Alban Longchamps[3]

1. Organ Transplant Center, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland., 2. Department of Biomedical Sciences, University of Lausanne, Switzerland, 3. department of vascular surgery, Lausanne University Hospital, Switzerland 4. department of infectious diseases,Lausanne university hospital, Switzerland 5. department of vascular surgery, lausanne university hospital, Switzerland

Background: More than half of the transplanted kidneys in Switzerland come from deceased donors, with an increasing proportion of marginal organs, at increased risk of delayed graft function (DGF) and acute rejection. Thus, early organ-protective measures would improve transplantation outcome. Hydrogen sulfide (H2S) is produced endogenously by the cystathionine gamma-lyase, coded on the CTH gene. In pre-clinical models, H2S protected from renal ischemia-reperfusion injury and improved kidney graft survival. Here, we hypothesized that CTH genetic polymorphisms (SNP) and H2S production in the recipient could influence graft outcome.

Methods or Case description: Using the Swiss Transplant Cohort Study, we included all patients with a first kidney transplant and with available genotyping (Rs6677781 SNP, CTH gene). In addition, 192 cadaveric kidney transplant recipients were randomly selected to measure serum H2S levels. The primary composite endpoint was transplantation failure (graft loss, eGFR <30 ml/min/m2 or proteinuria>1 g/d), with time after transplantation. Statistical differences between groups were assessed by Kaplan-Meier analysis and Cox multivariable model.

Results or Learning points: 1243 patients were included in the main analysis and 604 (48%) harbored the CTH*592C>T mutation. During median follow-up (66.5 months, IQR 47.6-106.2), transplantation failure and graft loss occurred in 499 (40%) and 129 (10.3%) patients, respectively. Transplantation failure free survival at 10 years was 52% for the control (WT) and 56% for the SNP group, respectively (p = 0.023). Freedom from graft loss was 84% at 10 years for WT and 89% for SNP, respectively (p = 0.012). This association was robust to correction for potential confounding variables, for both transplantation failure (HR = 0.88, 95%CI:0.69-0.99,p = 0.037) and graft loss (HR = 0.61, 95%CI:0.43-0.88, p = 0.007). Interestingly, in the subgroup of patients with DGF, transplantation survival was improved in patients with high serum H2S levels (HR = 4.92, 95%CI:1.07-22.5, p = 0.04).

Conclusions: We found that kidney graft survival was improved in recipients harboring the CTH*592C>T genotype. Further research is needed to understand the underlying mechanisms

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OC 68

Muscle mass in renal transplant recipients - a cross-sectional analysis within the RenOS single center cohort

Dr. Simeon Schietzel[1], Prof. Dominik Uehlinger[1], Prof. Kurt Lippuner[2], Prof. Bruno Vogt[3], Prof. Uyen Huynh-Do[1], Prof. Spyridon Arampatzis[1], Dr. Matthias Moor[1]

1. Division of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland., 2. Department of Osteoporosis, Bern University Hospital, Bern, Switzerland, 3. Division of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

Background: As the age of renal transplant recipients (RTRs) increases and as transplantation becomes a valid therapeutic option for end-stage kidney disease in older age, attention must be put towards the evolution of functional status. Here, we report on gold standard measurements of skeletal muscle quantity in a well-defined cohort of RTRs.

Methods or Case description: In this cross-sectional study, we analyzed dual-energy x-ray absorptiometry (DEXA) derived body composition measurements of RTRs participating in the RenOS single center registry of Bern. We assessed relevant demographic and clinical parameter for descriptive statistics. We calculated appendicular lean mass indices (ALMI) in Kg/m2 and applied low muscle mass cut-offs of <5.5 and <7.25 Kg/m2 for women and men respectively.

Results or Learning points: The population comprised 194 patients, 71 women and 123 men, with a median age of 57 (IQR 44; 66) and 55 (44; 64) years. Median duration of renal replacement therapy was 16 (IQR 2; 36) years and muscle mass was measured 7 (IQR 3; 14) years after transplantation. Median ALMI values were 6.01 (IQR 5.38; 6.61) Kg/m2 in women and 7.27 (6.67; 8.18) Kg/m2 in men. Prevalence of low muscle mass was 28.2% in women and 49.6% in men. From the 5th to the 7th decade of age, median ALMI of women decreased from 6.33 (IQR 5.31; 6.76) to 5.17 (4.88; 6.10) Kg/m2, with a prevalence of low muscle mass rising from 23.3% to 35.3%. In men, ALMI decreased from 7.69 (IQR 6.62; 8.46) to 6.89 (6.19; 7.13) Kg/m2, with a low mass prevalence rising from 29.3% to 44%.

Conclusions: Our results suggest, that prevalence of low muscle mass in RTRs is worryingly high. Additional work is required to better understand the drivers of declining skeletal muscle mass in RTRs.

OC 69

Serum creatinine increase after starting RAAS blockade has the potential to identify kidney transplant recipients at risk of hyperfiltration damage*

Mr. Lukas Mosimann[1], Dr. Seraina von Moos[1], Mr. Laurenz Matter[1], Prof. Thomas Müller[1], Dr. Thomas Schachtner[1]

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

Background: In the situation of kidney transplantation hyperfiltration is physiologic, yet with large interindividual differences. Early identification of kidney transplant recipients (KTRs) with supraphysiologic hyperfiltration leading to hyperfiltration associated non-immunologic graft loss is important to improve long-term allograft outcome. We hypothesize that a serum-creatinine increase of ≥ 25% after starting renin-angiotensin-aldosteron system (RAAS) blockade is a surrogate marker for KTRs at risk of graft failure associated with hyperfiltration damage.

Methods or Case description: We analyzed a total of 264 KTRs transplanted between 2008 and 2018 in Zürich. To identify KTRs with hyperfiltration we calculated the expected serum-creatinine (ExpSCr) range considering the recipients metabolic demand and the donor organ supply as well as the adaptive capacity of a single kidney. Outcome of patients with analyzed depending on the extent of serum-creatinine increase after starting RAAS blockade.

Results or Learning points: A total of 178/266 KTRs (67%) were treated with RAAS blockade and 153/178 (86%) were hyperfiltrating according to ExpSCr range. Upon multivariate analysis, only recipient/donor BMI was associated with hyperfiltration (p = 0.001, Exp(B) 0.011). A serum-creatinine increase of ≥25% was observed in 30/153 KTRs (19.6%) with hyperfiltration as compared to 0/25 (0%) KTRs without hyperfiltration (p = 0.009). eGFR decline was highest after RAAS blockade in those with hyperfiltration and serum-creatinine increase of ≥25% (-3.2 ml/min/year) as compared to those with hyperfiltration and serum-creatinine increase <25% (-1.1 ml/min/year, p = 0.025) and those without hyperfiltration (-1ml/min/year, p = 0.1.64). Discontinuation of RAAS blockade was not associated with improvement but tendency to worsening allograft function.

Conclusions: Serum creatinine increase ≥ 25% after initiation of RAAS blockade has the potential to unmask KTRs at risk of hyperfiltration damage accelerating long-term allograft loss.

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YOUNG SWISS NEPHROLOGY PRESENTATIONS

OC 70

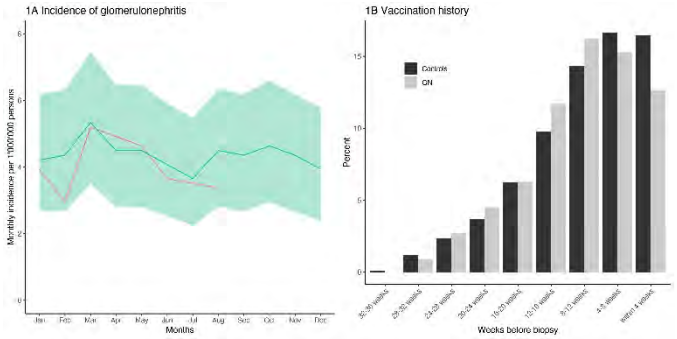
Incidence of Glomerulonephritis after SARS-CoV-2 mRNA Vaccination*

Dr. Matthias Diebold[1], Ms. Eleonore Locher[2], Dr. Philipp Boide[3], Dr. Anette Enzler-Tschudy[4], Dr. Anna Faivre[5], Dr. Ingeborg Fischer[6], Dr. Birgit Helmchen[7], Dr. Helmut Hopfer[8], Dr. Min Jeong Kim[9], Dr. Solange Moll[10], Dr. Giliane Nanchen[11], Dr. Samuel Rotman[12], Dr. Charalampos Saganas[13], Dr. Harald Seeger[14], Dr. Andreas Kistler[15]

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, 2. University Hospital Zurich, Department of Nephrology, 3. Clinic for Nephrology and Transplantation, Cantonal Hospital St. Gallen, 4. Institute of Pathology, Cantonal Hospital St. Gallen, Switzerland, 5. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland, 6. Department of Pathology, Cantonal Hospital Aarau, Aarau, Switzerland, 7. Institute of Pathology and Molecular Pathology, University Hospital Zurich, Zurich, Switzerland, 8. Department of Medical Genetics and Pathology, University Hospital Basel, University of Basel, Basel, Switzerland, 9. Division of Nephrology, Cantonal Hospital Aarau, Aarau, Switzerland, 10. Clinical Pathology Division, University Hospital of Geneva, University of Geneva, Geneva, Switzerland, 11. Service of Nephrology and Hypertension, Department of Medicine, Lausanne University Hospital and University of Lausanne, Switzerland, 12. Service of Clinical Pathology, Lausanne University Hospital and University of Lausanne, Switzerland, 13. Institute of Pathology, University of Bern, 14. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland, 15. Department of Medicine, Cantonal Hospital Frauenfeld, Spital Thurgau AG, Frauenfeld, Switzerland

Background: Numerous cases of glomerulonephritis manifesting shortly after SARS-CoV-2 vaccination have been reported, but causality remains unproven.

Methods or Case description: We studied the association between mRNA-based SARS-CoV-2 vaccination and new-onset glomerulonephritis using a nationwide retrospective cohort and a case-cohort design. Data from all Swiss pathology institutes processing native kidney biopsies served to calculate the expected incidence of IgA nephropathy, pauci-immune necrotizing glomerulonephritis, minimal change disease and membranous nephropathy in the adult Swiss population using a Bayesian model. A case-cohort study was used to calculate the risk ratio for the development of new-onset glomerulonephritis.



Results or Learning points: The observed incidence during the vaccination campaign (January to August 2021) was not different from the expected incidence based on the years 2015 to 2019 (incidence rate ratio 0.86, 95%-credible interval 0.73–1.02) and did not cross the upper boundary of the 95% credible interval for any month (Figure 1A). Among 111 patients aged >18 years with newly diagnosed glomerulonephritis between January and August 2021, 38.7% had received at least one vaccine dose before biopsy, compared to 39.5% of the general Swiss population matched for age and calendar-time (Figure 1B). The estimated risk ratio for the development of new-onset biopsy-proven glomerulonephritis was 0.97 (95%-confidence interval 0.66–1.42, P = 0.95) in vaccinated vs. unvaccinated individuals. Patients with glomerulonephritis manifesting within 4 weeks after vaccination did not differ clinically from those manifesting temporally unrelated to vaccination. Results were consistent across all types of glomerulonephritis.

Conclusions: In these two complementary studies in Switzerland, vaccination against SARS-CoV-2 was not associated with an increased incidence of glomerulonephritis. Most temporal associations between SARS-CoV-2 vaccination and glomerulonephritis are likely coincidental.

*YSN paper

OC 71

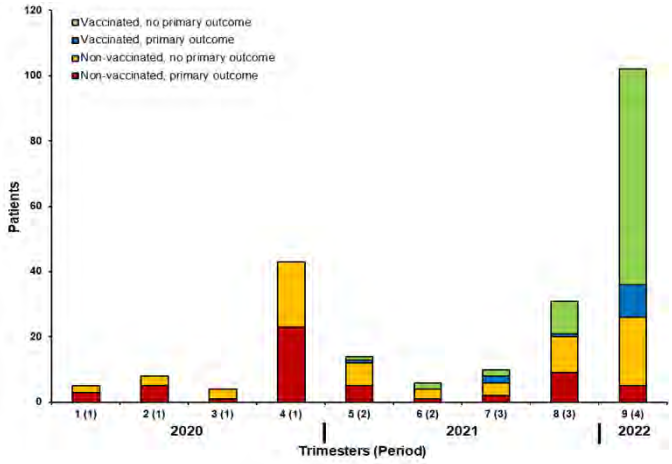
Clinical outcomes of SARS-CoV-2 infection in kidney transplant recipients in a Swiss University Hospital; role of anti-SARS-CoV-2 vaccination and monoclonal antibodies*

Dr. Matthaios Papadimitriou-Olivgeris[1], Dr. Ana Cipriano[1], Dr. Nicolas Guggisberg[1], Dr. Jonathan Tschopp[1], Prof. Oriol Manuel[1], Prof. Dela Golshayan[1]

1. Lausanne University Hospital, Lausanne, Switzerland

Background: Kidney transplant recipients (KTR) are at increased risk for COVID-19-associated complications. Few data are available on the impact of vaccination, the use of anti-Spike monoclonal antibodies (mAbs) and infection with the omicron variant on clinical outcomes after KTR.

Methods or Case description: We aimed to describe the epidemiology and outcomes of PCR-documented SARS-CoV-2 infection in KTR followed at our institution from March 2020 to February 2022. The primary endpoint was hospitalization for COVID-19-related symptoms or death within 28 days from diagnosis.



Results or Learning points: Overall, 64/189 (34%) patients developed the primary outcome. A significant decrease in the primary outcome was observed in the later periods of our study (54% in earlier vs. 15% in later periods; P <0.001, r -0.344), concomitant to the availability of novel preventive and therapeutic strategies such as vaccination and mAbs. Monoclonal Abs were administered as pre-emptive treatment in 72 patients (14 with casirivimab/imdevimab and 58 with sotrovimab). In our cohort of patients, 67/189 (35%) of patients were considered as adequately vaccinated. Multivariate analysis revealed that Charlson comorbidity index (P 0.001; OR 1.29, CI 1.12-1.50) was associated with adverse outcome, while preemptive administration of mAbs (P 0.013; OR 0.30, CI 0.12-0.77) was associated with better outcome, but not infection with the omicron variant or adequate vaccination. Figure 1 shows the number of patients

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with the primary outcome depending on adequate vaccination and timing of SARS-CoV-2 infection.

Conclusions: In this study, the use of anti-spike mAbs was associated with improved outcomes in KTR. Larger prospective studies are needed to confirm these results.

*YSN paper

OC 72

Soluble-Klotho derived from renal distal-convolution regulates calcium but not phosphate homeostasis*

Dr. Ganesh Pathare[1], Dr. Klaudia Kopper[1], Dr. Adisa Trnjanin[1], Dr. Dominique Loffing-Cueni[1], Mrs. Agnieszka Wengi[1], Prof. Johannes Loffing[1]

1. Institute of Anatomy, UZH, Zurich, Switzerland

Background: Klotho (Kl) is a proteohormone that delays aging in mice and that had been linked to sequalae of chronic kidney disease. Klotho is expressed as a full-length membrane-bound form and a circulating soluble form (sKl). The renal distal tubule is thought to be the main source of sKl, but the specific site of its origin remains elusive. Secondly, the role of sKl in regulating mineral-metabolism and ageing is poorly understood.

Methods or Case description: Mice with expression of the Cre-recombinase under the control of the distal convoluted tubule (DCT)-specific NaCl-cotransporter (NCC) and the late DCT (DCT2) and connecting tubule (CNT)-expressed TRPV5-Ca2+ channel were crossed with Ai14 (Tomato) reporter mice to isolate fluorescent DCT and CNT cells for single-cell RNA-seq. Moreover, Ncc-Cre and Trpv5-cre mice were crossed with a newly developed mouse line with a “floxed” Kl allele to generate a DCT- and a DCT2/CNT specific Kl deletion (Kl-KONcc-Cre and Kl-KOTrpv5-Cre, respectively).

Results or Learning points: The single-cell RNA-seq data revealed that the expression of Kl highly correlates with the expression of Trpv5 and other DCT2/CNT markers, but little with Ncc and other DCT markers. Immunohistochemistry further confirmed the predominant expression of Kl in DCT2 and CNT. Consistently, Kl-KONcc-Cre and Kl-KOTrpv5-Cre mice showed ~20% and ~80% reduction in systemic sKl levels, respectively. Moreover, deletion of Kl along the entire distal-convolution (i.e. DCT+CNT) in Kl-KONcc+Trpv5-Cre mice abolishes systemic sKl levels (sKl-KO). Compared to control mice, sKl-KO mice exhibited reduced renal TRPV5 expression, profound calciuria, and loss of bone mineral density. However, sKl-KO mice had unchanged serum FGF23, serum phosphate, urinary phosphate excretion, and renal NaPi-IIa expression.

Conclusions: Our findings demonstrate that systemic sKl levels mainly derive from the late DCT and CNT with a minor contribution from the early DCT. Mice lacking sKl have disturbed calcium homeostasis, but a normal phosphate balance.

*YSN paper

OC 73

Impaired fatty acid metabolism perpetuates lipotoxicity along the transition to chronic kidney injury*

Dr. Anna Rinaldi[1], Dr. Helene Lazareth[2], Dr. Virginie Poindessous[2], Dr. Ivan Nemazanyy[3], Dr. Julio Sampaio[4], Dr. Daniele Malpetti[5], Dr. Yohan Bignon[6], Dr. Maarten Naesens[7], Dr. Marion Rabant[8], Dr. Dany Anglicheau[9], Prof. Pietro Cippà[1], Prof. Nicolas Pallet[2]

1. Division of Nephrology, Ente Ospedaliero Cantonale, Lugano, Switzerland, 2. University Paris Cité, INSERM UMRS1138, Centre de Recherche des Cordeliers, F-75006 Paris, France, 3. PMM: The Metabolism-Metabolome Platform, Necker Federative Research Structure, INSERM US24/CNRS UMS3633, Paris, France, 4. CurieCoreTech Metabolomics and Lipidomics Technology Platform, Institut Curie, Paris, France, 5. Istituto Dalle Molle di Studi sull'Intelligenza Artificiale (IDSIA), USI/SUPSI, Lugano, Switzerland, 6. . Department of Biomedical Sciences, University of Lausanne, Lausanne, Switzerland, 7. Department of Microbiology, Immunology and ransplantation, KU Leuven, Leuven, Belgium, 8. Department of Pathology, Assistance Publique Hôpitaux de Paris, Necker Hospital, Paris, France, 9. Department of Nephrology and Kidney Transplantation, Assistance Publique Hôpitaux de Paris, Necker Hospital, Paris, France

Background: Understanding the cell-intrinsic mechanisms contributing to the maintenance of a dysfunctional cellular state in chronic kidney disease (CKD) and identifying therapeutic targets are research priorities in renal medicine. A key contributor to chronic kidney histological damage is acute kidney injury, especially ischemia-reperfusion injury (IRI). Persistent cell-extrinsic perturbations generated upon IRI, for example hypoxia, impair the energetic metabolism of Proximal Tubular Cells (PTC) participating in the process of transition from acute to chronic kidney injury. Here, we propose to investigate the PTC intrinsic factors involved in the perpetuation of an impaired cellular state which contribute to CKD progression.

Methods or Case description: We combined single nucleus transcriptomic, metabolomic and lipidomic approaches in experimental models and patient cohorts to investigate the molecular bases of the progression to chronic kidney allograft injury initiated by IRI.

Results or Learning points: The urinary metabolome of kidney transplant recipients with chronic allograft injury and who experienced severe IRI was significantly enriched with long chain fatty acids (FA). We identified a renal FA-related gene signature with low levels of Cpt2 and Acsm5 and high levels of Acsl4 and Acsm5 associated with IRI, transition to chronic injury, and established CKD in mouse models and kidney transplant recipients. The findings were consistent with the presence of Cpt2-, Acsl4+, Acsl5+, Acsm5- PTC failing to recover from IRI as identified by single nucleus RNA sequencing. In vitro experiments indicated that endoplasmic reticulum (ER) stress contributes to CPT2 repression, which, in turn, promotes lipids accumulation, drives profibrogenic epithelial phenotypic changes, and activates the unfolded protein response.

Conclusions: ER stress through CPT2 inhibition and lipid accumulation, engages an auto-amplification loop leading to lipotoxicity and self-sustained cellular stress. Thus, IRI imprints a persistent FA metabolism disturbance in the proximal tubule sustaining the progression to chronic kidney allograft injury.

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POSTER PRESENTATIONS

P 33

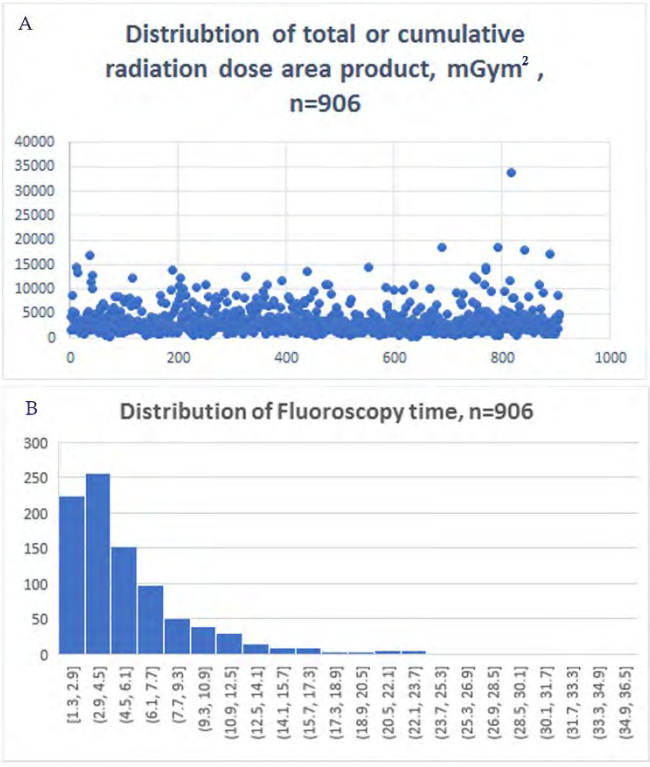
Coronary Angioplasty and Stenting in Acute Coronary Syndromes Using Very Low Contrast Volume and Radiation Dosage with improved Renal and Cardiovascular Outcomes

Prof. Mark Christopher Arokiaraj[1]

1. Pondicherry Institute of Medical Sciences, Puducherry, India

Background: Use of Cordis 6F Infiniti Thrulumen diagnostic catheters for coronary angioplasty and stenting in acute coronary syndrome (ACS) may improve clinical outcomes.

Methods or Case description: In 1,993 patients with ACS (2,580 lesions/2,884 stents), angioplasty was performed with Cordis 6F Infiniti Thrulumen diagnostic catheters. Follow-up was performed at 30 days. Primary angioplasty was performed in 610 cases, and only balloon angioplasty in another 74 patients. All procedures were performed through the femoral route, and switch-over to the radial route was made in 5 cases. Iodixanol was used in 75% of cases, and tirofiban in 99% of cases with adjusted dosages based on creatinine values. The mean contrast volume used per patient was 28 mL (± 6 mL) including the angiogram prior to the angioplasty. In renal failure patients the mean was lesser (≅20 ml). Creatinine >2mg/dl was seen in 140 patients at baseline and cardiogenic shock in 129 cases.



Results or Learning points: The median fluoroscopy time was 4.4 min (IQR 3–6.8), mean was 5.68 min (± 4.2), median dose-area product or kerma-area product was 1,526 µGym2 (IQR 918–2,667), median total or cumulative dose including backscatter was 2,759 µGym2 (IQR 1,788–4,255), and median cumulative skin dose was 475 mGy (IQR 295–740) in 906 consecutive patients. Groin hematoma was seen in 11 cases, proximal mild edge dissection in the deployed stent in 3 cases, and acute in-hospital stent thrombosis in 8 cases. Mild reversible contrast induced nephropathy was seen in 7 patients only. A minor fall (<5%) in creatinine was observed in a significant number of patients after the procedures. In total, 35 deaths were registered and 20 of these patients had cardiogenic shock, of which 11 subjects were late presenters. Three patients died after discharge due to possible acute stent thrombosis.

Conclusions: Angioplasty and stenting using Cordis 6F diagnostic catheters can improve clinical outcomes in patients with acute coronary syndromes.

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The Prevalence of CKD and Pattern of Renal Dysfunction in a Rural Community of Bangladesh

Dr. MM Iqbal[1], Dr. MAA Chowdhury[1], Dr. SK Banerjee[2], Dr. S Iqbal[3], Dr. S Islam[2], Dr. MZ Hassan[4], Dr. MS Hassan[3], Dr. SR Choudhury[5], Dr. RM Hossain[2], Dr. DK Adhikary[2], Dr. T Ahmed[3], Dr. MI Arslan[4], Dr. MZA Bhuiyan[6]

1. nikdu, Bengladesh,2. BSMMU, Bengladesh 3. BIRDEM, Bengladesh 4. BUHS, Bengladesh 5. NHF&RI, Bengladesh 6. CHUV – Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Background: The prevalence of CKD in rural communities, especially in developing countries, is largely unknown. Aim was to survey a rural community to see the prevalence of CKD and association with major risk factors

Methods or Case description: A geographically well-defined rural area (Baidyer Bazar union in Bangladesh) was selected. Listing of all households and the number of residents in that area was done. One subject from each household was done by applying KISH table. For participant selection and sample collection a number of field enumerators (FE), visitors (FV), attendants, local and central coordinator (CO) are recruited and trained. Information on prevailing NCDs and related risk factor of all dwellers were collected by a translated WHO-STEPS questionnaire by face-to-face interview. Serum creatinine was measured by standardized enzymatic method and urinary spot ACR by immunoturbidimetric method after collection of samples on a separate day early morning in fasting status. Abnormal results were repeated after 3 months.

Results or Learning points: Total 1889 adults is included here in whom repeat measurements was done when needed. The male-female ratio was 47:53. Mean BMI was 24±7 kg/m^2 and mean age 41±13 years where highest group was in 25-54 years (74%) and lowest in >65 years (5%). The study subjects were distributed in 4 renal function categories as- 1) eGFR≥ 60 ml/min/1.73 m^2 and ACR <30 mg/g 2) eGFR <60 ml/min/1.73 m^2 and ACR>30 mg/g 3) eGFR <60 ml/min/1.73 m^2 4) ACR>30 mg/g. The distribution pattern of renal functions based on these 4 categories was 89 vs. 1.5 vs. 2.2 vs. 7.3% respectively. When the abnormal results were repeated the pattern changed to 92.3 vs. 1.5 vs. 2.2 vs. 4% (p <0.001).

Conclusions: The prevalence of CKD in a rural community of Bangladesh, based on eGFR and ACR, was 11% initially and after repeat measurements came down to 7.7%. The pattern indicates that albuminuria-based nephropathy is the predominant cause.

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The challenging diagnosis of Pseudohyperkalemia: Report of two clinical cases

Dr. Claudia Ferrier-Guerra[1], Dr. Francesca Como[2], Dr. Federica Bocchi[3], Prof. Bruno Vogt[4]

1. University Hospital, Berne & NefrocentroTicino, Switzerland, 2. General Medical Practice Agno, Switzerland, 3. University Hospital, Berne, Switzerland, 4. University Clinic for Nephrology and Hypertension, Inselspital Bern, Switzerland

Background: Hyperkalemia is often due to renal failure-associated decrease in potassium (K+) excretion. Other causes include acidosis induced K+ transcellular shift, increased tissue catabolism and/or adverse response to medications. Since hyperkalemia may require emergency treatment, in the absence of an apparent cause it must be distinguished from pseudohyperkalemia, resulting from an artefactual rise in serum K+ (SK+). This allows avoidance of unnecessary therapy.

Methods or Case description: We report the case histories of two women who attended our renal outpatient clinic because of recurrent finding of hyperkalemia on several occasions (up to 5.8 mmol/L). One had mild untreated hypertension and asymptomatic renal calculi, the other woman had no clinical disorders. Neither had a history of impaired renal function, diabetes, hematological disturbances, malignancies or adverse response to medications.

Results or Learning points: Clinical examination was unremarkable in both women. Laboratory data confirmed normal renal function and the absence of metabolic acidosis. Renal and Doppler ultrasound were normal in both women with intraparenchymal RI in normal range. Potassium determination performed on whole blood sample gas analysis was compared to serum SK+ determination in two different laboratories. The results are listed below:

	Pat. No 1, age 57	Pat. No 2, age 47
eGFR (ml/min/1.73 m^2)	94	105
K+ (gas analysis) mmol/l	4.2	3.7
SK+ (laboratory nr 1) mmol/l	5.1	4.6
SK+ (laboratory nr 2) mmol/l	5.46	5.41

Conclusions: In patients who lack clinical evidence of hyperkalemia, pseudohypekalemia should be suspected. Various factors including phlebotomy methods, specimen handling and processing errors, as well as an isolated familial pseudohyperkalemia (related to erythrocytes fragility) should also be considered. Subsequent blood collection and handling should be performed with care to avoid red cell trauma/leakage. If unexpected hyperkalemia is found, results should be compared with those from whole blood gas analysis. If familial occurrence of pseudohyperkalemia is thought likely genetic counseling should be considered.

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Kt/v, mortality and risk of complications*

Dr. Kaspars Kivlenieks[1], Dr. Anda Grigāne[2], Prof. Jūlija Voicehovska[1], Dr. Eva Bormane[1], Dr. Dace Trumpika[1], Dr. Regīna Baufāle[1]

1. Riga East Clinical University Hospital, Nefrology and kidney replacement therapy clinic, Latvia, 2. Riga East Clinical University Hospital, Nefrology and kidney replacement therapy clinic, Latvia

Background: Dialysis quality ismeasured by Kt/V, it is one of the most important parameter for assessing hemodialysis for patients. Decreased Kt/V is associated with increased mortality and increased risk of complications, normal or increased Kt/V is associated with decreased mortality and complication rates. Guidelines have recommended Kt/V of 1.2 as the minimum dose for thrice-weekly HD. We analyzed the Kt/v, mortality and risk of complications in our hemodialysis center patients

Methods or Case description: We analyzed patients from 2021-2022, within 1 year 50 patients undergoing hemodialysis 3 times a week were analyzed.

Results or Learning points: The average Kt/V was 1.38. Patient mortality was minimal during this period and was related to Covid 19 infection, 3 patients died, one from sepsis and two from Covid 19 infection. 5 patients were hospitalized several times with hyperhydration and accompanying consequences, which were not related to dialysis, but with non-compliance with the regimen and increased fluid intake.

Conclusions: In general, the patients felt satisfactory and there were no complaints. Therefore, it can be considered that Kt/V above 1.3 is satisfactory and reduces the risk of mortality and complications.

*YSN paper

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Covid-19 2 years of experience in a Riga East Clinical University Hospital Nefrology and kidney replacement therapy clinic in Latvia*

Dr. Kaspars Kivlenieks[1], Dr. Anda Grigāne[2], Dr. Emīls Kokars[1]

1. Riga East Clinical University Hospital, Nefrology and kidney replacement therapy clinic, Latvia
2. Riga East Clinical University Hospital, Nefrology and kidney replacement therapy clinic, Latvia

Background: The Covid-19 infection caused a wide spectrum of symptoms, starting from the asymptomatic course of the disease and ending with severe lung damage that required artificial lung ventilation. Hemodialysis patients are at high risk. These patients are older, most often with several co-morbidities, immunosuppression and have more frequent contact with doctors and other patients. We will review our experience with chronic hemodialysis patients.

Methods or Case description: From 2020-2022, 128 patients received chronic hemodialysis. Of these, 30 patients were infected with Covid-19, all infections occurred at home from family members, none were confirmed in hospital, 8 patients were hospitalized in a period of 2 years. 21 IHD were performed in the inpatient department, while 22 patients were treated in the day inpatient mode, who underwent a total of 98 IHD procedures. Out of 30 patients, 7 patients died, 7 hemodialysis patients.

Results or Learning points: Of these 7 patients, 6 were unvaccinated. Therefore, the 2-year mortality is only 5.4% over two years. Such results were achieved by implementing the split flow of patients. Patients were divided into vaccinated and unvaccinated; procedures were performed on different shifts and patient flows did not cross. Also, Covid-19 positive and negative and strict quarantine for contacts. Also, every time the patients came for the procedure, a questionnaire, monitoring of active symptoms and body temperature, and a Covid-19 antigen test were performed before the procedure. Vaccination coverage among HD patients was very high at 95.6%.

Conclusions: In the group of hemodialysis patients' morbidity and mortality are not significant even in a 2-year period, although the patients are immunosuppressed and polymorbid. At this time, the solutions of the epidemiological regime are of decisive importance for control and motivation of patients to vaccinate and for its implementation, which gave a positive result. Mortality appeared to be associated with comorbidities and their complications.

*YSN paper

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