

ERA 2023



Review of the 60th European Renal Association (ERA) Congress

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CELEBRATING 60 years of congresses, the European Renal Association (ERA) held their 2023 congress in Milan, Italy, and virtually. Primarily known for its fashion show, Milan has also welcomed medical innovations, such as rifampicin, an antibiotic drug that has been used to treat tuberculosis, and witnessed the first procedure using haematopoietic stem cells as vectors for gene therapy in hereditary diseases.

In their joint pre-congress statement, ERA President, Christoph Wanner, and ERA Local President, Piergiorgio Messa, acknowledged the difficulties caused by the COVID-19 lockdown, which prevented ERA from holding the 2020 congress in Milan. "Now, after 3 years, we are very happy to be able to welcome all of you face-to-face in Milan," they stated.

In the opening ceremony, Messa hoped that attendees would enjoy the congress, as well as the various Milanese attractions, both new and old. Messa was then followed onto the stage by Ronald Gansevoort, Paper Selection Committee Chair, who reminded attendees that the ERA Congress is international, with more than 2,196 submitted abstracts from 86 countries.

This year's programme had been streamlined. Instead of the many categories and sub-categories that made up previous congress, this one consisted of seven main topic areas:

dialysis; acute kidney disease and critical care nephrology; physiology, cell biology, and genetic diseases; chronic kidney disease; glomerular and tubule-interstitial diseases; kidney transplantation; and hypertension and diabetes. Gansevoort also noted that chronic kidney disease was the most popular topic, with 562 abstracts submitted.

Gansevoort went on to detail the new format of the focused oral sessions, where authors of the selected abstracts were to present their results orally, with a single slide and no paper poster. The presentations were presented in dedicated halls, and took a total of 4 minutes; 3 minutes for the presentation and 1 minute for questions. This change was due to the fact that the large halls would typically be empty of attendees, and oral presentations only would benefit the presenters.

Scientific Committee Chair, Francesca Mallamaci, noted the importance of including high profile female nephrologists in the Scientific Community. The current Scientific Committee has a good male–female balance, and every effort was made to include nephrologists from every European country, as well as non-European countries, with interests in different fields of nephrology.

"Gansevoort went on to detail the new format of the focused oral sessions."



This year's congress had three major themes: research, with a specific mission for education; governance; and equality, with each individual or group of people being given the same resources or opportunities.

A number of awards were presented this year, including the ERA Awards for Young Investigators, which are open to all ERA members aged 40 years and younger. These awards have been named after three well-known masters of nephrology. The Rosanna Gusmano Award is for young investigators in basic science; the Stanley Shaldon Award is for young investigators in translational science; and the Eberhard Ritz Award is for young investigators in clinical science.

The winners of the 2023 ERA Awards for Young Investigators included: Christoph Kuppe, Department of Nephrology, North Rhine-Westphalia Technical (RWTH) University of Aachen, Germany; Olivier Aubert, Department of Kidney Transplantation, Necker Hospital, Paris, France; Edouard Fu, Brigham and Women's

Hospital and Harvard Medical School, Boston, Massachusetts, USA; and Stefanie Steiger, Division of Nephrology, Ludwig Maximilian University (LMU) Hospital of Munich, Germany.

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Vladimir Tesar, Department of Nephrology, 1st Faculty of Medicine, Charles University of Prague, Czechia, was also awarded the ERA Award for Outstanding clinical contributions to the field, while Tobias B. Huber, Department of Medicine, University Medical Center Hamburg-Eppendorf, Germany, was given this award for their contributions to basic science in nephrology.

Next year's congress will be held in Stockholm, Sweden, between 23rd May–26th May. Until then, please enjoy highlights of the reviews presented at this year's congress. ●

Haemodiafiltration Reduces Mortality Risk Compared with Conventional Haemodialysis?

INSIGHTFUL findings from the prospective, multicentre, randomised controlled trial, CONVINCe, were presented during a late-breaking clinical trial session that took place at the ERA Congress 2023, in Milan, Italy, on Friday 16th June.

Building on evidence suggestive that haemodiafiltration (HDF) confers a survival advantage in patients with end-stage kidney disease compared to conventional haemodialysis (HD) at ≥ 23 L/session convection volumes, researchers looked to clarify this further.

Lead study investigator, Peter Blankestijn, Department of Nephrology and Hypertension, University Medical Center Utrecht, the Netherlands, reported the main outcomes from the CONVINCe trial. The trial aimed to identify whether HDF delivered consistently at high-dose confers mortality benefit when compared with high-flux conventional HD.

The trial included a total of 1,360 patients from 61 different centres in eight European countries. Patients were included if they were deemed likely to achieve 23 L convection volumes and could complete patient-reported outcome assessments. Baseline characteristics were similar across both groups, and median follow-up time was 30 months.

Rates of all-cause mortality were higher in those treated with high-flux HD (n=677) than those treated with high-dose HDF (n=683), at 21.9% and 17.3%, respectively. The hazard ratio for this was 0.77 (95% confidence interval: 0.65–0.93),

which Blankestijn reported was highly statistically significant. Blankestijn further explained that although safety was not a specifically defined endpoint, no safety concerns were raised during the trial.

Blankestijn discussed conclusions from the study, highlighting that the findings show high-dose HDF (≥ 23 L convection volume per session) in post-dilution mode can be delivered over prolonged time periods, and confers a reduced risk of death when compared with standard high-flux HD.

In terms of limitations, patient selection limited generalisability as only those patients likely to achieve ≥ 23 L/session convection volume, and able to complete patient-reported outcome assessments, were included.

Blankestijn highlighted: "The CONVINCe study is a potential first step in identifying a new standard of care in chronic kidney disease. The advance of haemodiafiltration technology could change the way we treat specific patients living with chronic kidney disease." Looking towards the future, the team are looking to undertake a comprehensive analysis of the >10,000 sets of questionnaires to evaluate patient-reported outcomes, and hope to have the results later this year. ●

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Exercise During Haemodialysis Improves Physical Function

Exercise may significantly improve physical function in patients with kidney failure on haemodialysis, compared with usual care, according to a study presented at the ERA Congress 2023. This group of patients are at risk of progressive physical deconditioning and multi-morbidity, which represents a high health economic burden. New data shows that this progressive cycle may be prevented through exercise intervention.

The multicentre, cluster randomised, controlled interventional trial assessed whether combined endurance and resistance training during haemodialysis led to improvements in physical function compared to usual care. Change in 60 second sit-to-stand test (STS60) between baseline and 12 months was the primary outcome. In total, 917 patients from 21 ambulatory dialysis centres were included in the study.

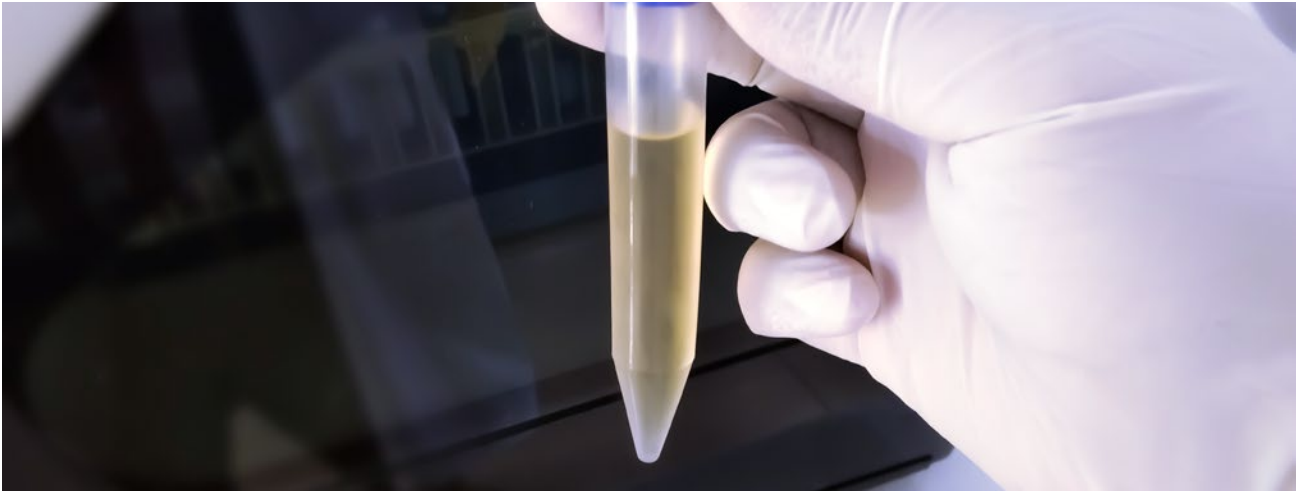
The team noted an improvement in STS60 repetitions from 16.2 ± 7.6 to 19.2 ± 9.1 in the exercise group, while the usual care group declined from 16.2 ± 7.1 to 14.7 ± 7.9 (95%

confidence interval [CI]: 2.22–5.48; $p < 0.0001$). Furthermore, the distance walked in 6 minutes ($+37.5$ m; 95% CI: 14.7–60.4; $p = 0.0013$), as well as the timed up and go test (-1.1 s; 95% CI: -1.9 – 0.3 ; $p = 0.0078$) improved in the exercise group. Data further showed that those in the exercise group spent a median of 2 days in hospital annually, compared with 5 days in the usual care group. The vitality subscale and physical summary score were also found to improve in the exercise group; however, other subscales on the 36-item Short Form Survey (SF-36) quality of life instrument did not change.

The team concluded that physical function was significantly improved with 12 months of exercise in patients with kidney failure on haemodialysis, compared to usual care. ●

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Reducing Urinary Albumin–Creatinine Ratio in Chronic Kidney Disease: A New Approach?



RESULTS from CONCORD, a multicentre, randomised, double-blind, placebo-controlled Phase II study were presented by Ronald Gansevoort, Division of Nephrology, University Medical Center, Groningen, the Netherlands, at the ERA Congress 2023, on Friday 16th June, in Milan, Italy.

The trial enrolled a total of 170 patients, and investigated the safety and efficacy of a soluble guanylate cyclase activator, runcaciguat. Soluble guanylate cyclase activators are a novel class of therapeutics that help dilate renal blood vessels, and therefore have the potential to enhance renal blood flow and slow chronic kidney disease (CKD) progression.

The inclusion criteria were: aged ≥ 45 years; had a diagnosis of chronic kidney disease with an estimated glomerular filtration rate of 25–60 mL/min/1.73m²; a urine albumin–creatinine ratio (UACR) of 30–3,000 mg/g; established atherosclerotic cardiovascular and/heart failure (New York Heart Association Class I–II); stable antihypertensive treatment with maximum tolerated angiotensin-converting enzyme inhibitor /angiotensin II receptor antagonist treatment; and any of the following: ≥ 2 -year history of Type 2 diabetes (T2D); \pm stable dose

of sodium-glucose co-transporter-2 inhibitor [SGLT2i] ≥ 3 months), and/or hypertension receiving medication for ≥ 5 years.

Patients were categorised into three strata: patients with CKD and T2D not treated with SGLT2i; patients with CKD and T2D treated with SGLT2i for ≥ 3 months; and patients with CKD without T2D. Reduction in UACR from baseline to the average of Days 22, 29, and 57, was the primary efficacy endpoint, according to a per-protocol analysis for Phase II trials.

In each stratum, patients were randomised on a 3:1 basis to receive either once daily runcaciguat or placebo. Following this, doses were up-titrated weekly over a 4-week period from 30 mg to 120 mg. In the subsequent maintenance phase, patients received the maximum tolerated dose for ≥ 4 weeks. This was followed by a safety follow-up period of 30 days.

The researchers found that patients with CKD who were on maximum tolerated dose of angiotensin-converting enzyme inhibitor/angiotensin II receptor antagonist displayed significantly reduced UACR, irrespective of concomitant SGLT2i use, and that runcaciguat was well tolerated. ●

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Novel Disease-Modifying Treatment for IgA Nephropathy

A POTENTIAL disease-modifying treatment for patients with IgA nephropathy was explored in a presentation delivered by Richard Lafayette, Stanford University, California, USA, during a late-breaking clinical trial session at the ERA Congress 2023, on 17th June.

Lafayette presented results from the ORIGIN study, a Phase IIb, randomised, double-blind, placebo-controlled trial that sought to investigate the safety and efficacy of atacicept, a dual anti-BLyS/APRIL fusion protein.

A total of 116 patients with biopsy-proven IgA nephropathy; either a 24 hour urine protein of >0.75 g/day or a urine protein-creatinine ratio of >0.75 g/g; an estimated glomerular filtration rate of ≥ 30 mL/min/1.73m²; and optimised blockade of the renin-angiotensin system, were recruited to the trial. The trial involved randomisation to a 36-week course of subcutaneous self-administered atacicept (n=82) or placebo (n=34). Although three different doses of atacicept were evaluated for safety and efficacy, the presentation focused on the 150 mg atacicept dose option.

The primary and secondary efficacy endpoints of the study were 24-week and 36-week proteinuria, respectively. Lafayette explained that the study met both of these endpoints, with atacicept displaying reductions in proteinuria that were statistically and clinically significant.

Upon safety evaluation, a favourable safety profile was noted. Throughout the 36 weeks, there was a low rate of serious adverse events (2%), no increase in rate of infections compared to placebo, and no discontinuation or interruption of drug delivery due to hypogammaglobulinaemia.

Following on from the results of this Phase IIb study, the safety and efficacy of weekly atacicept 150 mg subcutaneous injection is now being investigated in a pivotal Phase III study. ●

"The primary and secondary efficacy endpoints of the study were 24-week and 36-week proteinuria, respectively."





Anticoagulation Using Factor Xla Inhibition in Patients Receiving Haemodialysis

CLINICAL trial results investigating the efficacy, safety, and optimal dose of osocimab, a factor Xla inhibitor, in patients with end-stage kidney disease (ESKD) on haemodialysis, were presented by Wolfgang Winkelmayer, Baylor College of Medicine, Houston, Texas, USA, during a late-breaking clinical trial session at the 60th ERA Congress on 16th June 2023.

Thromboembolic risk is greater in patients with ESKD on haemodialysis; however, there is currently a lack of safe and effective anticoagulants for these patients. Winkelmayer discussed CONVERT, a Phase IIb, double-blind, placebo-controlled, randomised trial which, after initial enrolment and application of exclusion criteria, involved 704 patients with ESKD receiving haemodialysis three times per week for ≥ 9 hours per week.

"Osocimab yielded rapid, dose-dependent, and sustained inhibition of factor Xla."

The trial included three arms: lower-dose subcutaneous osocimab (loading dose of 105 mg followed by monthly doses of 52.5 mg; n=235); higher-dose subcutaneous osocimab (loading dose of 210 mg followed by monthly doses of

105 mg; n=234); or placebo (n=235). Patients were randomised on a 1:1:1 basis, and received treatment for up to 18 months.

Clinically relevant bleeding, a composite of major and clinically relevant non-major bleeding, was the primary trial outcome. Other outcomes evaluated were the extent of factor Xla inhibition; incidence of major adverse vascular events (composite of symptomatic venous thromboembolism, acute limb ischaemia, major limb amputation, non-fatal myocardial infarction or stroke, and vascular death); and extent of dialysis circuit clotting.

The researchers found that osocimab yielded rapid, dose-dependent, and sustained inhibition of factor Xla. In the lower-dose osocimab group, 16/232 (6.9%) experienced clinically relevant bleeding, compared with 11 out of 224 (4.9%) in the higher-dose osocimab group, and 18 out of 230 (7.8%) in the placebo group. The relative risk for moderate to complete dialysis circuit clotting at ≥ 1 visit was found to be significantly lower with osocimab than placebo and major adverse event rates were 3.0% in the placebo group, 2.7% in the higher-dose osocimab group, and 1.3% in the lower-dose osocimab group. For the future, further trials will be needed to determine if this novel therapeutic reduces thromboembolic risk in this patient cohort. ●