POS-828

WABISHKI BIZHIKO SKAANJ: A LEARNING PATHWAY TO FOSTER BETTER INDIGENOUS CULTURAL COMPETENCE WITHIN CANADIAN KIDNEY RESEARCH

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Introduction: Can-SOLVE CKD is a kidney research network in Canada within which Indigenous patients, caregivers, researchers, and community leaders have created an Indigenous Peoples' Engagement and Research Council (IPERC). A key component of IPERC's work is the creation of a new learning pathway, Wabishki Bizhiko Skaanj ("White Horse" in Anishinaabemowin), that will help researchers build respectful partnerships with Indigenous peoples within the health research setting. Wabishki Bizhiko Skaanj aims to enhance researchers' knowledge of racial biases, Indigenous voices and stories, the impact of colonization, and culturally safe health research practices.
Methods: A working group including members of the Can-SOLVE CKD Network, Diabetes Action Canada, First Nations Health Authority (BC), Provincial Health Services Authority (BC), and First Nations Health and Social Secretariat of Manitoba is leading the pathway's development. Two in-person workshops were held in October 2017 and March 2018 to develop the concept and identity of the curriculum, which consists of interactive learning exercises, facilitated online modules, and webinars. Several components of the pathway have been piloted and feedback is being gathered via surveys, pledges, and stories.
Results: The pathway's content is designed to help participants understand, recognize, and correct the racism that occurs in health care and research, in some cases caused by their own conscious and unconscious biases. Through enhanced knowledge, self-awareness and strengthened cultural competency, Wabishki Bizhiko Skaanj aims to support all partners in health care and research to close the gaps in health outcomes between Indigenous and non-Indigenous communities.
Conclusions: Wabishki Bizhiko Skaanj represents a novel learning platform for Indigenous cultural safety in Canadian health research. While Wabishki Bizhiko Skaanj was developed in the context of kidney health, the learning pathway can be adopted by networks and institutions across Canada, to help reduce and ultimately eliminate the racism that Indigenous people face within the health care system. The material presented in this abstract was previously submitted to the Canadian Society of Nephrology Annual General Meeting and the American Society of Nephrology Kidney Week.

No conflict of interest

POSTER SESSION: LATE BREAKING CLINICAL TRIALS

POS33
15/04/2021
Poster Area
05:00 – 06:00

POS-829

INCIDENCE AND PREDICTORS OF HYPERKALAEMIA IN PATIENTS WITH CKD AND T2D IN THE FIDELIO-DKD TRIAL

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Introduction: Patients with chronic kidney disease (CKD) and type 2 diabetes (T2D) have an increased risk of hyperkalaemia. Finerenone, a novel, selective, nonsteroidal, mineralocorticoid receptor antagonist, reduced the incidence of kidney and cardiovascular events in patients with CKD and T2D in the FIDELIO-DKD trial. This post hoc analysis describes the incidence and predictors of hyperkalaemia in FIDELIO-DKD.
Methods: FIDELIO-DKD was a phase III, multicentre, double-blind trial that randomised 5734 patients (1:1) to finerenone or placebo. Patients with CKD, T2D and serum potassium ($[K^+]$) ≤4.8 mmol/l at the run-in and screening visits, and treated with optimised renin–angiotensin system blockade were included. CKD was defined as a urine albumin-to-creatinine ratio (UACR) ≥30–<5000 mg/g and an estimated glomerular filtration rate (eGFR) ≥25–<75 ml/min/1.73 m^2. Initial dosing of study drug (10 mg or 20 mg once daily [od]) was based on eGFR at screening. During the trial, study drug dosing was based on serum $[K^+]$ levels and eGFR changes, which were monitored at every study visit; the study drug was temporarily withheld if $[K^+]$ >5.5 mmol/l and restarted at 10 mg od when $[K^+]$ ≤5.0 mmol/l. In this safety analysis, hyperkalaemia was defined as an investigator-reported adverse event (AE) or by serum $[K^+]$ levels (>5.5 and >6.0 mmol/l); events were considered treatment-emergent if they occurred after the start of study drug administration and until 3 days after any interruption of study drug. Multivariate Cox proportional hazards regression was used to examine associations between baseline characteristics and first post-baseline treatment-emergent $[K^+]$ >5.5 or >6.0 mmol/l, adjusting for treatment assignment and baseline covariates chosen *a priori* based on clinical factors known to affect serum $[K^+]$. A p-value <0.05 was used to determine a significant association.
Results: At baseline, 769/5658 (13.6%) and 390/5658 (6.9%) patients had $[K^+]$ >4.8 mmol/l and >5.0 mmol/l, respectively. After a median follow-up of 2.6 years, 44/2827 (1.6%) patients in the finerenone group and 12/2831 (0.4%) patients in the placebo group experienced a treatment-emergent hyperkalaemia-related serious AE. In the finerenone group, 64/2827 (2.3%) patients permanently discontinued the study drug due to hyperkalaemia, compared with 25/2831 (0.9%) patients in the placebo group. In total, 597/2785 (21.4%) and 256/2775 (9.2%) patients in the finerenone and placebo groups, respectively, had a treatment-emergent $[K^+]$ >5.5 mmol/l, while 126/2802 (4.5%) and 38/2796 (1.4%) patients, respectively, had a treatment-emergent $[K^+]$ >6.0 mmol/l. Selected baseline characteristics of patients with vs without any $[K^+]$ >5.5 or >6.0 mmol/l during the study are shown in the Table. The results of a multivariate analysis of hyperkalaemia risk factors will be presented.

Table

Baseline characteristics and medications*	No $[K^+]$ >5.5 mmol/l (n=4604)	Any# $[K^+]$ >5.5 mmol/l (n=1054)	No $[K^+]$ >6.0 mmol/l (n=5430)	Any# $[K^+]$ >6.0 mmol/l (n=228)
Sex, male	3279 (71.2)	694 (65.8)	3831 (70.6)	142 (62.3)
Age, years	65.8 ± 9.0	64.5 ± 9.1	65.4 ± 9.0	63.6 ± 9.7
Serum $[K^+]$, mmol/l	4.3 ± 0.4	4.7 ± 0.5	4.4 ± 0.5	4.7 ± 0.6
eGFR, ml/min/1.73 m^2	44.8 ± 12.4	42.2 ± 12.9	44.5 ± 12.5	40.2 ± 12.6
Median UACR (IQR), mg/g	820 (440–1565)	957 (479–1918)	840 (443–1608)	1083 (563–2073)
Haemoglobin, g/dl	13.1 ± 1.7	12.5 ± 1.7	13.0 ± 1.7	12.2 ± 1.7
History of CV disease	2097 (45.5)	503 (47.7)	2494 (45.9)	106 (46.5)
ACEi	1563 (33.9)	371 (35.2)	1855 (34.2)	79 (34.6)
ARB	3034 (65.9)	683 (64.8)	3568 (65.7)	149 (65.4)
β-blocker	2405 (52.2)	560 (53.1)	2855 (52.6)	110 (48.2)
Diuretic	2677 (58.1)	527 (50.0)	3102 (57.1)	102 (44.7)
Treatment assignment				
Finerenone	2151 (46.7)	676 (64.1)	2680 (49.4)	147 (64.5)
Placebo	2453 (53.3)	378 (35.9)	2750 (50.6)	81 (35.5)

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; IQR, interquartile range

Conclusions: The K^+ management protocol implemented in FIDELIO-DKD minimised the clinical impact of hyperkalaemia, as demonstrated by the low frequency of clinically meaningful hyperkalaemia-related serious AEs. (Funded by Bayer AG; FIDELIO-DKD clinicaltrials.gov number NCT02540993)

Conflict of Interest: RA reports personal fees and non-financial support from Bayer Healthcare Pharmaceuticals Inc., during the conduct of the study he also reports personal fees and non-financial support from Akebia Therapeutics, Janssen, Relypsa, Vifor Pharma, Boehringer Ingelheim, Sanofi, Eli Lilly, AstraZeneca, and Fresenius he has received personal fees from Ironwood Pharmaceuticals, Merck & Co., Lexicon, and Reata, and non-financial support from Otsuka America Pharmaceutical, Opko Pharmaceuticals, and E. R. Squibb & Sons he is a member of data safety monitoring committees for Amgen, AstraZeneca, and Celgene a member of steering committees of randomised trials for Akebia Therapeutics, Bayer, Janssen, and Relypsa a member of adjudication committees for AbbVie, Bayer, Boehringer Ingelheim, and Janssen he has served as associate editor of the American Journal of Nephrology and Nephrology Dialysis and Transplantation and has been an author for UpToDate and he has received research grants from the U.S. Veterans Administration and the National Institutes of Health. AJ and RL are full-time employees of Bayer AG, Division Pharmaceuticals, Germany.PR reports personal fees from Bayer, during the conduct of the study he has received research support and personal fees from AstraZeneca and Novo Nordisk, and personal fees from Eli Lilly, Boehringer Ingelheim, Astellas, Gilead, Mundipharma, Sanofi, and Vifor. All fees are given to Steno Diabetes Center, Copenhagen. He has an equity interest in Novo Nordisk.BP reports consultant fees for Bayer, AstraZeneca, Sanofi/Lexicon, scPharmaceuticals, SQ Innovation, G3 Pharmaceuticals, Sarfez, Phasebio, Vifor/Relypsa, Cereno Scientific, Ardelyx, KBP Biosciences, Boehringer Ingelheim, Brainstorm Medical, and Tricida he has stock options for Ardelyx, KBP Biosciences, SQ Innovation, Sarfez, scPharmaceuticals, Cereno Scientific G3 Pharmaceuticals, Vifor/Relypsa, Brainstorm Medical, and Tricida he also holds a patent for site-specific delivery of eplerenone to the myocardium (US patent #9931412) and a provisional patent for histone-acetylation-modulating agents for the treatment and prevention of organ injury (provisional patent US 63/045,784). SDA has received research support from Abbott Vascular and Vifor International, and personal fees from Abbott Vascular, Boehringer Ingelheim, Bayer, BRAHMS, Novartis, Servier, Vifor International, Impulse Dynamics, and Cardiac Dimensions. GF reports lectures fees and/or that he is a committee member of trials and registries sponsored by Bayer, Novartis, Vifor, Medtronic, Servier, Amgen, and Boehringer Ingelheim. He is a Senior Consulting Editor for JACC Heart Failure, and he has received research support from the European Union.LMR has no disclosures. PK is a full-time employee of Bayer AG, Division Pharmaceuticals, Germany. He is the co-inventor of finerenone and holds US and European patents relating to finerenone (US8436180B2 and EP2132206B1).CS is a full-time employee at Bayer PLC, Data Science and Analytics, United Kingdom. GLB reports research funding, paid to the University of Chicago Medicine from Bayer, during the conduct of the study he also reports research funding, paid to the University of Chicago Medicine from Novo Nordisk and Vascular Dynamics he acted as a consultant and received personal fees from for Merck, Relypsa, and Alnylam he is an Editor of the American Journal of Nephrology, Nephrology, and Hypertension, and Section Editor of UpToDate and he is an Associate Editor of Diabetes Care and Hypertension Research.

POS-830

NEFECON FOR THE TREATMENT OF IgA NEPHROPATHY IN PATIENTS AT RISK OF PROGRESSING TO END-STAGE RENAL DISEASE: THE NEFIGARD PHASE 3 TRIAL RESULTS

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Introduction: Peyer's patches located within the gut-associated lymphoid tissue have been identified as a major source of poorly *O*-galactosylated immunoglobulin A (IgA)1, which triggers the formation of nephritogenic immune complexes in IgA nephropathy (IgAN). The therapeutic potential of targeting Peyer's patches in patients with IgAN was demonstrated in the Phase 2 NEFIGAN trial, which assessed the safety and efficacy of a novel targeted-release formulation of budesonide (NEFECON), designed to deliver budesonide to the Peyer's patches in the ileum. Patients treated for 9 months with NEFECON 16 mg/day demonstrated a significant (~30%) reduction in urine protein-to-creatinine ratio (UPCR) compared with placebo, and stabilization of estimated glomerular filtration rate (eGFR). Based on these data, the Phase 3 NefIgArd trial is a two-part design: Part A evaluates proteinuria reduction as a surrogate of the effect of NEFECON on long-term kidney function preservation.

Methods: NefIgArd is a randomized, double-blind, placebo-controlled clinical trial recruiting a total of 360 patients across 155 nephrology clinics in 20 countries. Patients must be aged ≥18 years with biopsy-confirmed primary IgAN, proteinuria >1 g/24 h and eGFR 35–90 mL/min/1.73 m^2 despite optimized renin–angiotensin system blockade. Patients are randomized on a 1:1 ratio to NEFECON 16 mg/day or placebo. The primary endpoint, based on the first 199 patients, is the percentage decrease in proteinuria (UPCR) after 9 months of treatment. The secondary objectives include the difference in kidney function between NEFECON-treated subjects and those on placebo, as measured using eGFR, and the urine albumin-to-creatinine ratio (UACR) at 9 months compared with baseline.

Results: Between September 2018 and October 2020, 657 subjects were screened. Of these, 306 patients were randomized and 199 with 9 months of follow-up were included in the efficacy analyses of Part A of the study. At 9 months, the geometric mean UPCR was reduced by 27% in the NEFECON group compared with the placebo group (p=0.0005). At 9 months, the NEFECON group provided a statistically significant 7% (3.87 mL/min/1.73m^2) treatment benefit on eGFR (p=0.0029), compared with placebo. There was a similar overall incidence of adverse events in the two treatment groups.

Conclusions: The NefIgArd study met its primary endpoint and demonstrated a favorable safety profile. These results are indicative of a clinically meaningful reduced risk of future progression to end-stage renal disease in patients with IgAN treated with NEFECON. This trial will continue in order to validate UPCR reduction as a surrogate of long-term renal function preservation.

Conflict of interest Corporate sponsored research or other substantive relationships:JB: Chair of the Study Steering Committee for the NefIgArd trialAS: Employee of Stone Biostatistics Ltd. Consultant for: BioSight, BVF Partners, Calliditas Therapeutics AB, Carrick, Cullinan, Deciphera, IO Botech, iTeos, Maverick, PsiOxus, Repare and RhoVac JK: Consultant for Calliditas Therapeutics AB

POS-831

THE EFFECT OF DAPAGLIFLOZIN IN PATIENTS WITH EGFR <30 ML/MIN/1.73M2: FINDINGS FROM THE DAPA-CKD TRIAL

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