Original Article

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Long-term renoprotective effect of luseogliflozin in type 2 diabetes patients: CHikushi Anti-diabetes mellitus Trial-Lusefi (CHAT-Lu)

Yosuke Takamiya[1,*], Chiyori Imanaga[1], Ichiro Abe[2], Kunihisa Kobayashi[2], Amane Ike[1], Akira Kawamura[1], Hidenori Urata[1]

[1] Department of Cardiovascular Diseases, Fukuoka University Chikushi Hospital, Fukuoka, Japan;
[2] Department of Endocrinology and Diabetes Mellitus, Fukuoka University Chikushi Hospital, Fukuoka, Japan.

SUMMARY Several sodium-glucose cotransporter 2 (SGLT2) inhibitors are known to have beneficial effects on renal function in patients with type 2 diabetes. However, the long-term effects of luseogliflozin, an SGLT2 inhibitor, remain uncertain in real-world settings. This multicenter, open-label, prospective observational study evaluated the long-term effects of luseogliflozin on renal function in Japanese patients with type 2 diabetes. Fifty-four outpatients initiated on luseogliflozin at Fukuoka University Chikushi Hospital or associated clinics were enrolled from April 2018 to December 2019, with 46 patients included in the final analysis set. The primary outcome was the change in estimated glomerular filtration rate (eGFR) from baseline to 104 weeks, and secondary outcomes included the change in eGFR at week 52 and changes in body weight and blood and urinary parameters at 52 and 104 weeks. The mean duration of diabetes was 8.1 years. Baseline eGFR was 75.8 ± 17.4 mL/min/1.73m^2, and no decline in eGFR was observed from baseline to 104 weeks. Decline in eGFR was suppressed in the two groups stratified by baseline eGFR (< 60 and ≥ 60 mL/min/1.73m^2). No changes were noted in urinary albumin excretion rate. Blood glucose, body weight, blood pressure, liver function, and uric acid levels showed significant improvements. There were four adverse events, but no serious adverse events closely related to luseogliflozin treatment. In type 2 diabetes patients, 2-year treatment with luseogliflozin provided beneficial metabolic effects and improved the rate of decline in eGFR, suggesting a renal protective effect.

Keywords Sodium-glucose cotransporter 2 inhibitor, renal function, multifaceted effects, practicing physician

1. Introduction

Many epidemiological analyses have shown that better glycemic control in patients with type 2 diabetes can suppress the onset and progression of microangiopathy more effectively. However, as shown in the United Kingdom Prospective Diabetes Study (UKPDS) 80, the post-trial monitoring of the UKPDS, the use of conventional sulfonylureas drugs and insulin does not improve mortality rates significantly compared to standard treatment unless the treatment is continued for ten years (*1*). Biguanides, pioglitazone, and α-glucosidase inhibitor drugs have demonstrated favorable effects on the short-term prognosis of macroangiopathy (*2-4*). However, until recently, there were no substantial reports on improved renal function in type 2 diabetes patients with diabetic nephropathy, and there is no clear evidence on whether conventional drugs improve renal prognosis. In the EMPA-REG study, the sodium-glucose cotransporter 2 (SGLT2) inhibitor empagliflozin improved the short-term prognosis of macroangiopathy, except for nonfatal stroke (*5*). Several large-scale studies (*5-8*) have also shown the effects of empagliflozin, dapagliflozin, and canagliflozin on improving renal prognosis. This study aimed to investigate whether luseogliflozin, an SGLT2 inhibitor, exhibits a class effect in protecting renal function. We also investigated whether there are differences in renal protective effects depending on the baseline estimated glomerular filtration rate (eGFR). We prospectively administered luseogliflozin to patients with type 2 diabetes, including those with renal dysfunction, to investigate the long-term renal prognosis.

2. Patients and Methods

2.1. Patients

Participants were patients with type 2 diabetes aged 20

years or older who were treated at the outpatient clinic of Fukuoka University Chikushi Hospital or by local physicians registered in the Chikushi Cardiovascular Clinical Research Network, who had provided written consent and who had been prescribed luseogliflozin (hemoglobin A1c [HbA1c] 6.5% or more but less than 10%, including those currently undergoing treatment), and whose eGFR immediately before starting treatment was 30-90 mL/min/1.73m^2.

Patients were excluded if they had any of the following conditions: severe ketosis, diabetic coma or precoma, type 1 diabetes, severe infection, preoperative/postoperative state, severe trauma, pregnancy or possible pregnancy (for women), breastfeeding, or known hypersensitivity to any of the ingredients of luseogliflozin. In addition, patients were excluded if they had taken SGLT2 inhibitors within 6 months before starting luseogliflozin treatment or were deemed unsuitable for any other reason by the study investigators.

Patients were discontinued from the study if they withdrew consent, experienced adverse events, including severe hypoglycemia that prevented them from continuing treatment, missed outpatient visits, or if a physician deemed it inappropriate for them to continue in the study.

This study was approved by the Kyoto Prefectural University of Medicine Clinical Research Review Board (file number: 201822). The study protocol and patient informed consent forms were included in the ethics committee application documents, and written consent was obtained from each patient before enrollment. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was registered in the Japan Registry of Clinical Trials (registration number: jRCTs051180060).

2.2. Evaluation endpoints

The primary endpoints were changes in eGFR from baseline to 104 weeks overall, further stratified by baseline eGFR (eGFR < 60 mL/min/1.73m^2 or eGFR ≥ 60 mL/min/1.73m^2). Secondary endpoints were changes in eGFR from baseline to week 52, changes in resting double product (calculated as systolic blood pressure × pulse rate) at week 52 and week 104, and changes in body weight, blood test values (*e.g.*, hemoglobin, HbA1c, hepatic biomarkers, lipids, and uric acid) and urine test values (*e.g.*, urinary albumin excretion rate) at week 52 and week 104. Safety endpoints included type, severity, and causality of adverse events.

2.3. Diabetes mellitus, hypertension, dyslipidemia and obesity

Diabetes, hypertension, and dyslipidemia were determined based on prescription status or according to Japanese guidelines (*9-11*). Obesity was defined according to Japanese standards as a body mass index of 25 kg/m^2 or higher.

2.4. Statistical analysis

Statistical analysis was performed at Fukuoka University with IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, US). Significant differences were tested using the Student's *t*-test for items with normal variation and the Mann-Whitney test for items without normality. Equality of variance was tested with the Levene test, and when equal variance was not assumed, Welch's test was performed. Correlations were tested with Spearman's rank correlation coefficient. Numerical results are presented as mean ± standard deviation (SD), median with interquartile range (IQR), or frequency ratio. A *P*-value of less than 0.05 was considered significant.

3. Results

Between April 2018 and December 2019, 54 patients were enrolled across five facilities. Three patients discontinued luseogliflozin due to adverse events, two patients deviated from the protocol, and three patients dropped out. The remaining 46 patients continued luseogliflozin up to week 104 and were included in the analysis (Figure 1). Reported adverse events included death, cerebral infarction, elevated blood glucose (with luseogliflozin continued), and skin rash in one patient each. The dosage of luseogliflozin at week 104 was 2.5 mg/day in 30 patients, 5 mg/day in 15 patients, and 1.25 mg/day in one patient.

Table 1 presents the background characteristics of participants. The mean age was 66.2 years, and the mean duration of diabetes was 8.1 years. The proportion of obese patients was high, with a mean body mass index of 27 kg/m^2. Approximately 60% of patients had hypertension and dyslipidemia as comorbidities. Dipeptidyl peptidase 4 inhibitors were the most commonly used oral hypoglycemic drugs (37%), followed by biguanides (26%). Renin-angiotensin-

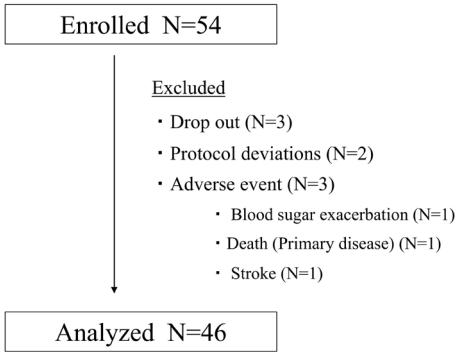

Figure 1. Participant flow in the study.

aldosterone system (RAS) inhibitors were used in approximately 46% of patients.

Figure 2 shows the changes in eGFR over time. Overall eGFR (mL/min/1.73m^2) was 75.8 ± 17.4 at baseline, 75.4 ± 20.7 at week 52, and 75.8 ± 20.8 at week 104, with no significant decline observed during the study period. To assess changes in eGFR, patients were divided into two groups based on baseline eGFR (≥ 60 mL/min/1.73m^2 and < 60 mL/min/1.73m^2). Patients with renal dysfunction (eGFR < 60 mL/min/1.73m^2) accounted for 8.7% of the total. No significant decline in eGFR was observed in either group.

Table 1. Patient characteristics

Characteristics	N (%)
N	46
Mean age (SD), y (*n* = 46)	66.2 ± 13.2
Male (*n* = 46)	27 (58.6)
Duration, y (*n* = 45)	8.1 ± 6.8
Body mass index, kg/m^2 (*n* = 46)	27 ± 3.7
Clinical presentation	
Hypertension (*n* = 43)	29 (67.4)
Dyslipidemia (*n* = 43)	28 (65.1)
Hyperuricemia (*n* = 43)	6 (14.0)
Smoking (*n* = 46)	23 (50.0)
Drinking (*n* = 46)	28 (60.9)
Ischemic heart disease (*n* = 43)	4 (9.3)
Previous stroke (*n* = 43)	1 (2.3)
Diabetic microangiopathy (*n* = 43)	1 (2.3)
Medication	
Antidiabetic drugs	
DPP4 inhibitors (*n* = 46)	17 (37.0)
Biguanides (*n* = 46)	12 (26.0)
Sulfonylureas (*n* = 46)	7 (15.2)
α-Glucosidase inhibitors (*n* = 46)	0 (0)
Glinides (*n* = 46)	0 (0)
Thiazolidinediones (*n* = 46)	2 (4.3)
Insulin (*n* = 46)	1 (2.2)
GLP1 RAs (*n* = 46)	0 (0)
Antihypertensive drugs (*n* = 46)	29 (63.0)
Renin-angiotensin system inhibitors (*n* = 46)	21 (45.7)
Antidyslipidemic drugs (*n* = 46)	18 (39.1)
Antithrombotic agents (*n* = 46)	4 (8.7)

Data are presented as numbers (%) or means ± standard deviation. DPP4, dipeptidyl peptidase 4; GLP1 RAs, glucagon-like peptide-1 receptor agonists, SD, standard deviation.

Secondary endpoints are shown in Table 2. No significant change was observed in urinary albumin excretion rate over time. Baseline HbA1c was 7.5% and was significantly decreased at week 52 and week 104 (week 52, 7.0%; week 104, 7.0%; $P < 0.01$ for each). Body weight significantly decreased by 3.6 kg at week 52, and this effect was maintained at week 104. Systolic and diastolic blood pressure significantly decreased at week 52, and diastolic blood pressure also significantly decreased at week 104. Hepatic biomarkers significantly improved at week 52 and week 104. Serum uric acid levels significantly decreased at week 104.

As shown in Figure 3, eGFR demonstrated no significant decrease over time regardless of urinary albumin excretion rate or use of RAS inhibitors.

Table 3 shows the correlation matrix table for each parameter at week 104. Changes in eGFR did not correlate with changes in HbA1c, body weight, or blood pressure. The only parameter negatively correlating with eGFR changes at week 104 was uric acid.

4. Discussion

This multicenter study conducted in local residents demonstrated that administering luseogliflozin, an SGLT2 inhibitor, to patients with type 2 diabetes in clinical practice provides long-term renal protective effects. Several large-scale studies (*5-8*) have shown that dapagliflozin, empagliflozin, and canagliflozin improve renal prognosis. While primary endpoints of large-scale clinical trials often include end-stage renal

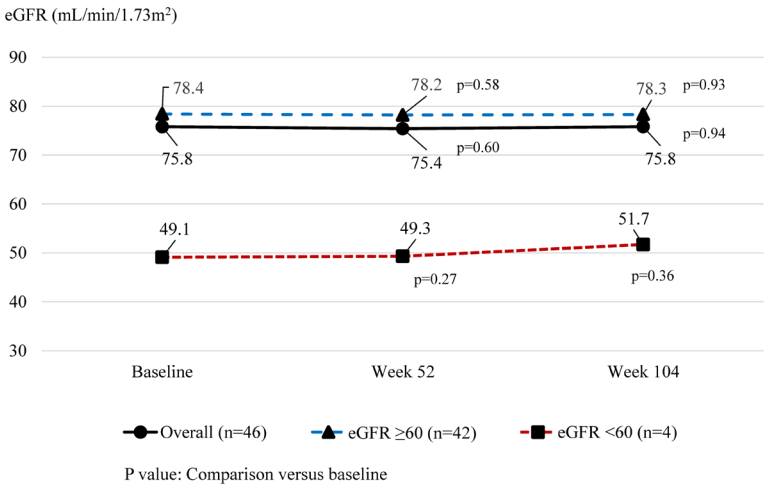

Figure 2. Change of eGFR. Week 52, after 52 weeks of treatment; week 104, after 104 weeks of treatment. eGFR, estimated glomerular filtration rate; G ≥ 60, eGFR ≥ 60 mL/min/1.73m^2; G < 60, eGFR < 60 mL/min/1.73 m^2.

Table 2. Changes in parameters at week 52 and week 104

	Week 0	Week 52	*P*-value *vs.* Week 0	Week 104	*P*-value *vs.* Week 0
Body weight, kg (*n* = 44)	70.6 ± 12.7	67.0 ± 12.0	< 0.01	66.8 ± 12.5	< 0.01
SBP, mmHg (*n* = 45)	133.1 ± 13.0	129.5 ± 9.7	0.02	130.0 ± 10.2	0.18
DBP, mmHg (*n* = 45)	76.2 ± 8.4	73.8 ± 8.6	< 0.01	73.8 ± 9.5	0.02
HR, bpm (*n* = 40)	74.3 ± 10.0	73.2 ± 8.9	0.27	73.6 ± 8.3	0.46
Double product (*n* = 41)	9982 ± 1696	9607 ± 1350	0.12	9572 ± 1202	0.14
HbA1c, % (*n* = 46)	7.5 ± 0.6	7.0 ± 0.7	< 0.01	7.0 ± 0.6	< 0.01
Glucose, mg/dL (*n* = 46)	176.7 ± 56.0	148.3 ± 36.6	< 0.01	141.9 ± 37.4	< 0.01
LDL-C, mg/dL (*n* = 42)	115.7 ± 32.0	115.6 ± 29.1	0.22	110.7 ± 26.2	< 0.01
HDL-C, mg/dL (*n* = 41)	50.8 ± 12.8	54.2 ± 14.8	< 0.01	53.0 ± 13.2	0.05
Triglyceride, mg/dL (IQR) (*n* = 43)	162 (110-233)	153 (111-203)	0.18	155 (107-221.5)	0.19
AST, U/L (IQR) (*n* = 43)	24 (21-35)	21 (17-26)	< 0.01	22 (17-26.5)	< 0.01
ALT, U/L (IQR) (*n* = 43)	29 (21-43)	23 (15-27)	< 0.01	22 (16.5-27.5)	< 0.01
γ-GTP, U/L (IQR) (*n* = 43)	35 (24-50)	27 (18-37)	< 0.01	27 (21-36.5)	< 0.01
UA, mg/dL (*n* = 43)	5.3 ± 1.3	5.0 ± 1.1	0.06	4.9 ± 1.2	0.01
WBC,×10^3 /μL (*n* = 42)	6.5 ± 1.4	6.1 ± 1.3	0.10	6.3 ± 1.5	0.39
Ht, % (*n* = 42)	42.4 ± 3.6	43.5 ± 4.1	0.02	43.1 ± 3.6	0.50
Plt, ×10^4/μL (*n* = 42)	23.0 ± 5.9	22.7 ± 6.0	0.14	22.7 ± 6.3	0.10
ALB, mg/dL (*n* = 32)	4.2 ± 0.3	4.3 ± 0.3	0.60	4.3 ± 0.3	0.90
Na, mmol/L(*n* = 43)	140.1 ± 2.5	140.3 ± 2.4	0.07	140.0 ± 2.1	1.00
K, mmol/L(*n* = 43)	4.2 ± 0.4	4.3 ± 0.4	0.48	4.2 ± 0.4	0.68
Urinary albumin/urinary creatinine (mg/g • Cr) (*n* = 34)	18.0 (8.0-61.2)	20.5 (8.4-58.4)	0.99	14.5 (6.6-43.2)	0.48

Data are presented as means ± standard deviation or medians (interquartile range). Week 0, 0 week (baseline); week 52, after 52 weeks of treatment; week 104, after 104 weeks of treatment. γ-GTP, gamma-glutamyl transpeptidase; ALB, albumin; ALT, alanine transaminase; AST, aspartate transaminase; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HR, heart rate; Ht, hematocrit; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; Plt, platelets; SBP, systolic blood pressure; UA, uric acid; WBC, white blood cells.

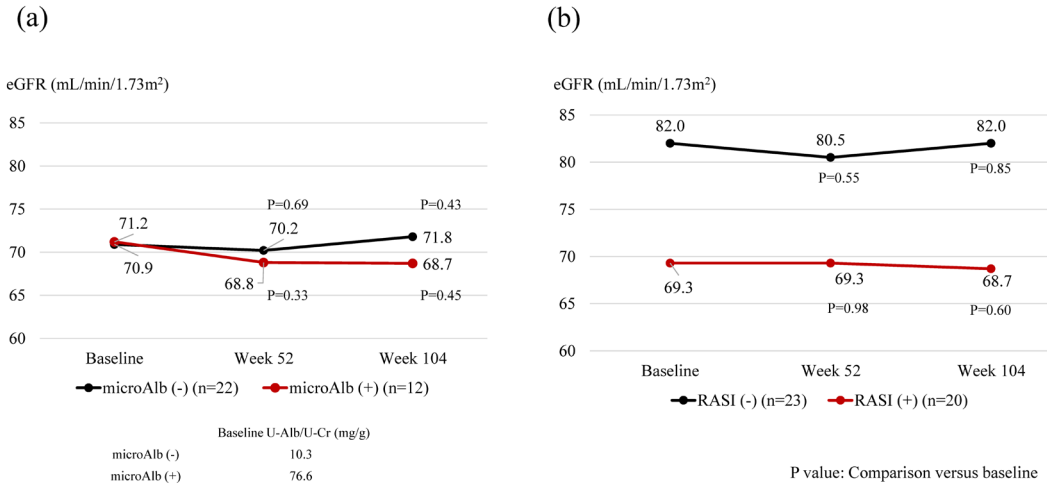

Figure 3. Change of eGFR with or without microalbuminuria (a) and renin-angiotensin-aldosterone system inhibitors (b) at baseline. Week 52, after 52 weeks of treatment; week 104, after 104 weeks of treatment. eGFR, estimated glomerular filtration rate; microAlb, microalbuminuria; RASI, renin-angiotensin system inhibitor; U-Alb, urinary albumin; U-Cr, urinary creatinine.

disease, renal death, and cardiovascular death, the evaluation of these endpoints requires a large sample size of around several thousand participants. It would be difficult to conduct such large clinical trials in routine clinical settings; for this reason, we focused on the eGFR slope following long-term treatment with SGLT2 inhibitors. The eGFR slope is associated with renal prognosis, and a decline of 0.5-1.0 mL/min/1.73m^2/year in eGFR has been reported as a surrogate endpoint for the progression of renal disease (*12*). The average annual decline in eGFR in Japanese patients is 0.36 mL/min/1.73m^2 (*13*), and the annual decline in eGFR in patients with type 2 diabetes has been reported to be as high as 1.67 mL/min/1.73m^2 in a large-scale study (*14*). This accelerated decline indicates diabetes as a factor that worsens renal prognosis.

This study aimed to demonstrate the renal protective effects of luseogliflozin, which has not been shown to improve renal prognosis in large-scale studies. In this study, no significant decline in eGFR was

Table 3. Correlation between amounts of change in each parameter at week 104

	ΔeGFR	ΔHbA1c	ΔDBP	ΔBW	ΔLDL-C	ΔHDL-C	ΔAST	ΔALT	ΔγGTP	ΔUA
ΔeGFR										
ΔHbA1c	*r* = -0.03 *P* = 0.85									
ΔDBP	*r* ≤ 0.01 *P* = 0.97	*r* = 0.35 *P* = 0.82								
ΔBW	*r* = 0.15 *P* = 0.34	*r* = 0.21 *P* = 0.18	*r* = 0.29 *P* = 0.053							
ΔLDL-C	*r* = 0.06 *P* = 0.75	*r* = 0.22 *P* = 0.19	***r = 0.41*** ***P = 0.01***	*r* = 0.24 *P* = 0.16						
ΔHDL-C	*r* = 0.14 *P* = 0.37	*r* = 0.01 *P* = 0.95	*r* = 0.25 *P* = 0.11	*r* = -0.29 *P* = 0.06	*r* = 0.29 *P* = 0.91					
ΔAST	*r* = -0.15 *P* = 0.35	*r* = -0.72 *P* = 0.65	*r* = -0.25 *P* = 0.12	*r* ≤ -0.01 *P* = 0.99	***r = -0.38*** ***P = 0.02***	*r* = -0.30 *P* = 0.056				
ΔALT	*r* = -0.20 *P* = 0.21	*r* = 0.27 *P* = 0.87	*r* = -0.21 *P* = 0.19	*r* = 0.06 *P* = 0.72	*r* = -0.30 *P* = 0.07	***r = -0.31*** *P* = 0.05	***r = 0.91*** ***P < 0.01***			
ΔγGTP	*r* = -0.05 *P* = 076	*r* = -0.29 *P* = 0.06	*r* = -0.24 *P* = 0.13	*r* = -0.14 *P* = 0.36	*r* = -0.09 *P* = 0.61	***r = -0.36*** ***P = 0.02***	***r = 0.41*** ***P < 0.01***	***r = 0.42*** ***P < 0.01***		
ΔUA	***r = -0.32*** ***P = 0.04***	*r* = 0.29 *P* = 0.053	*r* = -0.22 *P* = 0.17	*r* = -0.02 *P* = 0.92	*r* = -0.09 *P* = 0.58	*r* = -0.12 *P* = 0.44	*r* = 0.17 *P* = 0.28	*r* = 0.17 *P* = 0.30	***r = 0.32*** ***P = 0.04***	

ΔeGFR = (estimated glomerular filtration rate at week 104 - estimated glomerular filtration rate at baseline), ΔHbA1c = (hemoglobin A1c at week 104 - hemoglobin A1c at baseline), ΔDBP = (diastolic blood pressure at week 104 - diastolic blood pressure at baseline), ΔBW = (body weight at week 104 - body weight at baseline), ΔALT=(alanine transaminase at week 104 - alanine transaminase at baseline), ΔAST = (aspartate transaminase at week 104 - aspartate transaminase at baseline), Δγ-GTP = (gamma-glutamyl transpeptidase at week 104 - gamma-glutamyl transpeptidase at baseline), ΔHDL-C = (high-density lipoprotein cholesterol at week 104 - high-density lipoprotein cholesterol at baseline), ΔLDL-C = (low-density lipoprotein cholesterol at week 104 - low-density lipoprotein cholesterol at baseline), ΔUA = (uric acid at week 104 - uric acid at baseline).

observed in the two years after starting luseogliflozin treatment. eGFR remained stable, and the group with reduced renal function (eGFR < 60 mL/min/1.73m^2) showed an increase in eGFR of 2.6 mL/min/1.73m^2. Among patients with type 2 diabetes, administration of luseogliflozin did not result in decreased eGFR or increased urinary albumin excretion rate, suggesting its potential to improve renal prognosis. Among the six SGLT2 inhibitors available in Japan, luseogliflozin has the lowest prescribed dose (*15*). A previous *in vivo* study revealed that luseogliflozin has a high renal transfer rate (*16*), which may enable luseogliflozin's pharmacological effects to be exerted efficiently. Luseogliflozin utilizes multiple metabolic pathways, which means there are minimal changes in plasma exposure even in patients with hepatic or renal dysfunction (*17,18*), thus reducing the risk of side effects. These characteristics suggest that luseogliflozin has at least equal or greater efficacy than that of other SGLT2 inhibitors. The results of this study suggest that the renal protective effect of SGLT2 inhibitors, including luseogliflozin, is a class effect, supporting the findings of Suzuki *et al.* (*19*). Large-scale studies have reported that SGLT2 inhibitors improve renal function to a greater extent in patients with reduced renal function than in patients with normal renal function (*7,8*). In this study, over 90% of patients had an eGFR of 60 mL/min/1.73m^2 or higher, and 65% (22 of 34 patients) were in the normoalbuminuric phase. In patients with normal renal function, luseogliflozin suppressed decreases in eGFR and increases in urinary albumin, demonstrating a renal protective effect. In the normoalbuminuric phase, glycemic control was initially insufficient, with an HbA1c of 7.5%, and it is said that diabetic nephropathy develops 10 years after the onset of diabetes (*20*). In this study, the mean duration of diabetes was approximately 8 years, so this patient population is considered to be at high risk of progressing to the microalbuminuria phase. In view of this, it may be beneficial to administer SGLT2 inhibitors to all patients with type 2 diabetes, including those before the onset of nephropathy, unless use is contraindicated for some reason.

SGLT2 inhibitors inhibit the sodium-glucose cotransporter 2 in the kidneys, suppressing the reabsorption of Na and glucose. As one of the renal protective mechanisms of SGLT2 inhibitors in type 2 diabetes, the inhibition of SGLT2 suppresses Na reabsorption in the proximal tubule, increasing Na delivery to the macula densa surrounding the distal tubule; this causes the afferent arteriole to constrict, reducing hyperfiltration and lowering intraglomerular pressure, thus preventing glomerular injury (*21*). At the cellular level, it has been reported that SGLT2 inhibitors improve energy metabolism in proximal tubule cells, suppress Na/K ATPase consumption on the vascular side of the proximal tubule, and protect tubule cells (*22*), and that increased expression of SGLT2 leads to injury in glomerular epithelial cells (podocytes) (*23*). In this study, luseogliflozin not only improved glycemic

control but also reduced body weight, diastolic blood pressure, liver function parameters, and uric acid at week 52, and these effects were maintained at week 104. The changes in eGFR at weeks 52 and 104 showed no correlation with baseline HbA1c or with the amount of HbA1c reduction over the 2-year period, suggesting that the renal protective effect of luseogliflozin is independent of glycemic control. The pleiotropic effects of luseogliflozin were weight loss, diuresis, uric acid reduction, and blood pressure reduction, which did not show a direct correlation with renal function, except for uric acid reduction. However, it is already known that hypertension, hyperglycemia, and worsening uric acid can cause renal dysfunction (*24,25*); thus, improvements in these factors may have contributed synergistically to renal protection.

In patients with type 2 diabetes, angiotensin II type 1 (AT1) receptor expression is increased in efferent arterioles compared to afferent arterioles, and RAS inhibitors dilate efferent arterioles more, lowering intraglomerular pressure (*26*). Combining the use of RAS inhibitors with SGLT2 inhibitors may provide additional correction of intraglomerular pressure. On the other hand, there is a concern that this combination may reduce eGFR. In this study, there was no decrease in eGFR regardless of RAS inhibitor use, suggesting that combined use with RAS inhibitors does not excessively reduce intraglomerular pressure and continues to provide renal protection, and further suggests that luseogliflozin offers a renal protective effect independent of RAS inhibitor treatment.

Patients with type 2 diabetes have a high rate of nonalcoholic fatty liver disease (approximately 70%) (*27*), and the incidence of hypertension is twice as high as that of nondiabetic patients (*28*). Obesity contributes to hyperinsulinemia, which can lead to the onset of diabetes and elevated blood glucose. In this study, luseogliflozin reduced body weight, lowered diastolic blood pressure, improved liver damage, and reduced uric acid levels, resulting in long-term improvement of lifestyle-related conditions commonly associated with diabetes. This suggests that luseogliflozin may also be useful in improving and maintaining comprehensive health.

Adverse events occurred in four patients. One adverse event was death due to malignant brain lymphoma which was not related to luseogliflozin. There was no evidence of urinary ketone bodies or lactic acidosis, indicating that luseogliflozin was safe for long-term use.

A limitation of this study is that it was a single-arm, open-label study, and a placebo effect could not be ruled out.

In this multicenter, prospective, observational study conducted in a real-world clinical setting by general practitioners, luseogliflozin demonstrated renal protective effects in patients with type 2 diabetes regardless of the baseline eGFR value or the presence or absence of microalbuminuria. The study showed that luseogliflozin demonstrates multifaceted favorable effects on blood glucose, liver function, body weight, and uric acid.

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**Address correspondence to:*
Yosuke Takamiya, Department of Cardiovascular Diseases, Fukuoka University Chikushi Hospital, 1-1-1, Zokumyoin, Chikushino-shi, Fukuoka, 818-8502, Japan.
E-mail: takamiya2011@cis.fukuoka-u.ac.jp

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