Title:

Overall efficacy and safety of sodium-glucose cotransporter 2 inhibitor luseogliflozin versus dipeptidyl-peptidase 4 inhibitors: multicenter, open-label, randomized-controlled trial (J-SELECT study)

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Table S1. Participating medical institutions

Participating medical institution	Responsible investigator	Number of enrolled patients
Caress Sapporo Hokko Memorial Clinic	Ichiro Sakuma	50
Wakasa Medical Clinic	Yutaka Wakasa	46
Sugawara Clinic	Masahiro Sugawara	43
Funayama Medical Clinic	Hideaki Funayama	34
Fukuda Clinic	Masahiro Fukuda	27
Seino Internal Medicine Clinic	Hiroaki Seino	20
Kondo Hospital	Akira Kondo	20
Itabashi Clinic	Naoki Itabashi	17
Iwatsuki-minami hospital	Yasuyuki Maruyama	17
Suisyoukai Murata Hospital	Kaori Murata	16
Hoya Hospital	Yasunori Utsunomiya	15
Suruga Clinic	Akira Yamauchi	15
Department of Diabetes and Endocrinology, Juntendo Tokyo Koto Geriatric Medical Center	Hidenori Yoshii	15
Yatagai Clinic	Shigeo Yatagai	14
Koyama Clinic	Hiroshi Koyama	14
Ooedo Orthopedics and Internal medicine	Takashi Kamiyama	12
Yamamoto Clinic	Hareaki Yamamoto	12
Mikokorokai Shimizu Clinic	Miho Shimizu	11
Kawada Clinic	Toshio Kawada	10
Yayoi Medical Clinic	Setsuya Sakagashira	10
Ozeki Clinic	Shigehiko Ozeki	9
Takeda Clinic	Tomoo Takeda	9
Katsuya Clinic	Tomohiro Katsuya	8
Oishi Clinic	Mariko Oishi	8

Doniwa Iin	Ken-ich Doniwa	7
Ueda Clinic for Internal Diseases	Nobuyuki Ueda	7
Sasamoto Medical Clinic	Makiko Sasamoto	7
Masaki Clinic	Hatsumi Masaki	6
Kamiyama Clinic	Takashi Kamiyama	5
Lee’s Clinic	Woon-Joo Lee	5
Chimori Clinic	Hiroko Chimori	5
Takeda Clinic	Hiroshi Takeda	5
Ikeda Clinic	Kazuo Ikeda	5
Mochizuki Naika Clinic	Koichi Mochizuki	4
Nishioka Clinic	Hiroaki Nishioka	4
Jintendo Iin	Kyoko Mitsuhashi	4
Kinugawa Cardiology Clinic	Toru Kinugawa	4
Ken Clinic	Motoko Miki	4
Kyoujokai Iin	Toshiyuki Horiuchi	4
Doi Naika	Kunihiro Doi	4
Shinagawa Naika Iin	Yuki Shinagawa	3
Shimozono Clinic	Isato Shimozono	3
Medical Corporation Keishinkai Ishizuka Clinic	Jinro Ishizuka	3
Sakurai Naika Clinic	Shunichiro Sakurai	3
Moritani Iin	Shigeki Moritani	3
Kase Iin	Norio Kase	3
Daiba Clinic	Shigeru Watanabe	3
Nakata Clinic	Shinsuke Nakata	3
Ekimae Tsunoda Clinic	Keiko Tsunoda	3
Konishibashi Clinic	Tadashi Sawanishi	3
Ogawa Naika Clinic	Yuji Ogawa	3

Kaisei Diabetes Clinic	Tomokazu Matsuda	3
HAT Kobe Tsuji Naika	Tomohiro Tsuji	3
H.E.C. Science Clinic	Shinichiro Shirabe	3
Ichou internal medicine Ashitomi	Satoshi Ashitomi	3
Mimihara Ohtori Clinic	Hiromi Ogata	3
Matsuo Kenko Clinic	Kaneyuki Matsuo	2
Sugie Internal medicine clinic	Takashi Sugie	2
Takenaka Clinic	Ken Takenaka	2
Shonankamakura General Hospital	Asami Tanaka	2
Hiyoko Clinic Medical Association Himawarikai	Yoshiro Suzuki	2
Sasazuka-Inoue Clinic	Masahiro Inoue	2
Hasegawa Clinic	Hiroshi Hasegawa	2
Nakao Medical Clinic	Haruyoshi Nakao	2
Nishikawa Clinic	Tetsuo Nishikawa	2
iryouhoujinsyadan jiboukai naikahihuka uematsuiin	Mikio Uematsu	2
Hotaruno Central Naika	Daigaku Uchida	2
Miyakawa Internal Medicine Pediatrics Clinic	Masaaki Miyakawa	1
Miura Central Clinic	Masahiro Takihata	1
Kato Internal Medicine Clinic	Hirotaka Ishii	1
Mizuno Medical Clinic	Kenji Mizuno	1
Inomata Clinic	Masahiko Inomata	1
Minamisawa Iin	Kosuke Minamisawa	1
Minami Hospital	Soichi Honda	1
Sisigui Clinic	Mitsuo Shirakawa	1
Uonuma Municipal Koide Hospital	Katsuya Fuse	1
Yamao Internal Medicine Clinic	Takuji Yamao	1
Licht Clinic	Akihiko Nakazima	1

Nagano Clinic	Masahiro Nagano	1
iryouhoujinzaidannukatakai nakamura clinic	Masahiko Nakamura	1
Nishidume Clinic	Suzuko Iwami	1
iryouhoujinsyadankeneikai miyamaetaiarakenei clinic	Hisakazu Degawa	1
Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital	Naoko Katayanagi	1
Okada Clinic	Yoshiharu Okada	1
Sawaki Internal Medicine and Diabetes Clinic	Hideaki Sawaki	1
Mimihara Takasago Clinic	Hiromi Ogata	1
Sennan Fujii Hospital	Motoshige Miyano	1
Clinic Matsuda	Yuki Matsuda	1

Table S2. Eligibility criteria

Inclusion criteria	Patients who meet all of the following criteria are included in this study. 1.Patients with type 2 diabetes mellitus 2.Male and female aged 20 years or older and younger than 75 years when giving their consent 3.Patients who did not use antidiabetic agents within 8 weeks before consenting, or patients who used antidiabetic agents other than SGLT2is and DPP-4is and who did not change the usage and the dose of them within 8 weeks before consenting. However, patients who use SU can be included in the study, if the patients meet all of the following criteria. i) Patients who regularly receive medical consultation more than once a month within 3 months before consenting. ii) Patients whose HbA1c was continuously 7.5% or higher within 3 months before consenting. iii) Patients who did not have hypoglycemia within 3 months before consenting. iv) Patients who use glimepiride of 2 mg/day or less, or gliclazide of 40 mg/day or less 4.Patients with HbA1c 6.5% or higher but no more than 10.0% within 8 weeks before consenting. 5.Patients who can give their consent in a written form.
Exclusion criteria	Patients who fall into any of the following criteria are excluded from participating in the study. 1.Type 1 diabetes mellitus or secondary diabetes 2.Patients who used insulin or GLP-1 analogs within 8 weeks before consenting 3.Patients who had myocardial infarction, cerebral infarction, or stroke within 12 weeks before giving their consent 4.Patients with severe liver disease (Patients with AST or ALT value five times or more of the upper limit of the stand value in each research institution) 5.Patients with serious renal disease (eGFR less than 30mL/min/1.73m^2)

6.Patients with unstable hypertension and dyslipidemia

7.Dehydrated patients (patients complain to have a symptom of dehydration)

8.Patients with urinary tract infection or genital infection

9.Patients who are breastfeeding, pregnant, possibly pregnant, or planning to be pregnant

10.Patients with contraindication or hypersensitivity to any medical component of each study drug

11.Patients who need legal representative for giving consent

12.Patients aged 65 years or older and 74 years or younger with geriatric syndrome (sarcopenia, cognitive dysfunction, ADL impairment, etc.)

13.Patients with other conditions that the investigator/researcher thinks inappropriate for the study

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SGLT2i, sodium-glucose cotransporter 2 inhibitor; DPP-4i, dipeptidyl-peptidase 4 inhibitor; SU, sulfonylurea; HbA1c, hemoglobin A1c; GLP-1, glucagon-like peptide 1; AST, aspartate aminotransferase; ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate; ADL: Activities of Daily Living.

Table S3. Observation schedule and items

	consenting	week 0 (Baseline)	week 2 + 1 week	week 24 ± 2 weeks	week 52 ± 2 weeks
Eligibility information	○				
Characteristics of patients		○			
Medication information		○		○	○
Weight, blood pressure, pulse, abdominal circumference		○		○	○
General blood tests		○		○	○
OHA-Q		△		○	○
Special blood and urine tests		●	●	●	●
Adverse event		← ○ →			

○: mandatory; ●: optional; △: mandatory if the patient used any antidiabetic agents other than sodium-glucose cotransporter 2 inhibitor or dipeptidyl-peptidase 4 inhibitors within 8 weeks before consenting.

OHA-Q: Oral Hypoglycemic Agent Questionnaire;

Table S4. Primary and secondary endpoints

Primary endpoint	Proportion of patients who improved three or more endpoints among five endpoints listed below from baseline to week 52 (proportion of patients who achieved the composite endpoints) - HbA1c (change from baseline ≤ -0.37%) - Weight (percent change from baseline ≤ -3%) - eGFR (percent change from baseline ≥ -2.2%) - systolic blood pressure (change from baseline ≤ -4 mmHg) - pulse (change from baseline ≤ -3 bpm)
Secondary endpoints	1. Proportion of patients who achieved the composite endpoints from baseline to week 24 2. Change in HbA1c from baseline 3. Percent change in weight from baseline 4. Percent change in eGFR from baseline 5. Change in blood pressure from baseline 6. Change in pulse from baseline 7. Change in blood test values (or percent change in lipid biomarker values) from baseline - lipid biomarkers: HDL-chol, T-chol, LDL-chol, TG - hepatic biomarkers: AST, ALT, gamma-GTP - others: blood count (red blood cell, hemoglobin, hematocrit, leukocyte, platelet), uric acid, Amy 8. Change in specific test values from baseline - blood test values: NT-proBNP, erythropoietin, reticulocyte - urine test values: urinary albumin/creatinine ratio, urinary creatinine 9. Change in OHA-Q (questionnaire for patients QOL) score from baseline 10. Change in waist circumference and BMI from baseline

HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; T-chol, total cholesterol; LDL-chol, low-density lipoprotein cholesterol; TG, triglyceride; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyl transpeptidase; NT-proBNP, amino-terminal pro-brain natriuretic peptide; OHA-Q: Oral Hypoglycemic Agent Questionnaire

Table S5. Change in medication during the study

	Week	Luseogliflozin group	DPP-4i group	p value
Use of anti-diabetic agent	0	119 (43.0) / 277	111 (40.8) / 272	0.61
	24	277 (100.0) / 277	270 (99.6) / 271	0.49*
	52	273 (99.3) / 275	264 (98.9) / 267	0.68*
SGLT2i	0	0 (0.0) / 277	0 (0.0) / 272	-
	24	269 (97.1) / 277	5 (1.8) / 271	<0.001
	52	266 (96.7) / 275	9 (3.4) / 267	<0.001
DPP-4i	0	0 (0.0) / 277	0 (0.0) / 272	-
	24	2 (0.7) / 277	268 (98.9) / 271	<0.001
	52	7 (2.5) / 275	261 (97.8) / 267	<0.001
sulfonylurea	0	2 (0.7) / 277	3 (1.1) / 272	0.68*
	24	3 (1.1) / 277	3 (1.1) / 271	1.00*
	52	4 (1.5) / 275	5 (1.9) / 267	0.75*
biguanide	0	107 (38.6) / 277	103 (37.9) / 272	0.85
	24	113 (40.8) / 277	106 (39.1) / 271	0.69
	52	115 (41.8) / 275	109 (40.8) / 267	0.81
alfa-glucosidase inhibitor	0	8 (2.9) / 277	8 (2.9) / 272	0.97
	24	9 (3.2) / 277	8 (3.0) / 271	0.84
	52	9 (3.3) / 275	6 (2.2) / 267	0.47
glinide	0	4 (1.4) / 277	3 (1.1) / 272	1.00*
	24	5 (1.8) / 277	3 (1.1) / 271	0.72*
	52	3 (1.1) / 275	3 (1.1) / 267	1.00*
thiazolidine	0	15 (5.4) / 277	12 (4.4) / 272	0.59
	24	17 (6.1) / 277	13 (4.8) / 271	0.49
	52	18 (6.5) / 275	13 (4.9) / 267	0.40
GLP-1 receptor agonist	0	0 (0.0) / 277	0 (0.0) / 272	-

	24	0 (0.0) / 277	0 (0.0) / 271	-
	52	1 (0.4) / 275	0 (0.0) / 267	1.00*
insulin	0	0 (0.0) / 277	0 (0.0) / 272	-
	24	0 (0.0) / 277	0 (0.0) / 271	-
	52	1 (0.4) / 275	0 (0.0) / 267	1.00*
Antihypertensive agent	0	151 (54.5) / 277	157 (57.7) / 272	0.45
	24	156 (56.3) / 277	157 (57.7) / 272	0.74
	52	157 (57.1) / 275	156 (58.4) / 267	0.75
Hypolipidemic agent	0	117 (42.2) / 277	123 (45.2) / 272	0.48
	24	128 (46.2) / 277	132 (48.7) / 271	0.56
	52	130 (47.3) / 275	135 (50.6) / 267	0.44
Antiplatelet agent	0	19 (6.9) / 277	22 (8.1) / 272	0.58
	24	20 (7.2) / 277	22 (8.1) / 272	0.70
	52	20 (7.3) / 275	22 (8.2) / 267	0.67

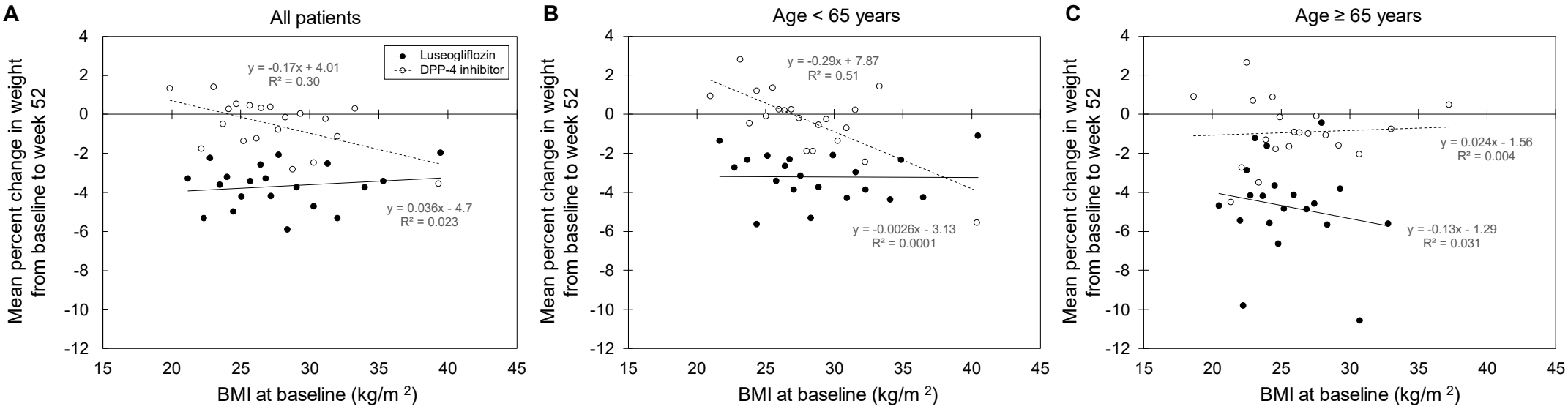
Data are presented as number of patients (%) / N.

Chi-squared test or Fisher's exact test for categorical variables and two-sample t-test for continuous variables were performed.

* Intergroup comparison was conducted using Fisher's exact test, as it did not meet the requirement of the chi-squared test.

DPP-4i, dipeptidyl peptidase 4 inhibitor; SGLT2i, sodium-glucose cotransporter 2 inhibitor; GLP-1 receptor agonist, glucagon-like peptide 1 receptor agonist

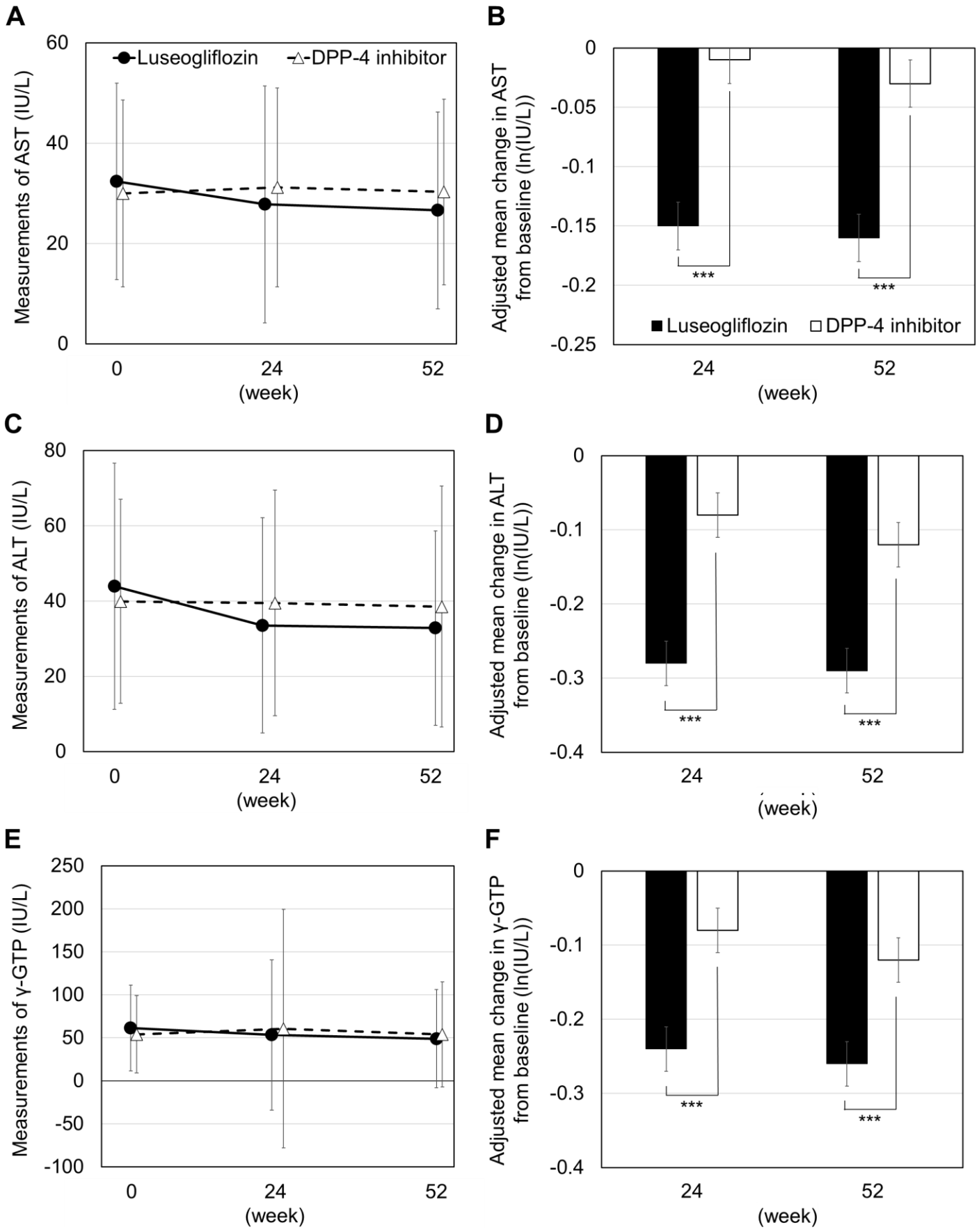
Figure S1. Correlation between BMI at baseline and percent change in weight from baseline to week 52



BMI at baseline was divided into 20 quartiles, and the mean BMI at each quartile as X value and mean percent change in weight from baseline to week 52 at each quartile as Y value were plotted.

DPP-4, dipeptidyl-peptidase 4; BMI, body mass index

Figure S2. Change in hepatic function biomarkers



Data are presented as mean ± standard deviation for measurements or mean ± standard error for adjusted mean change from baseline.

A two-sample t-test was performed for between-group comparisons of measurements. Since the measurements of AST, ALT, and γ-GTP did not distribute normally, the two-sample t-test was performed using log-transformed values.

The adjusted mean change of each continuous variable was estimated using models for repeated measures (MMRM) with an unstructured covariance structure with treatment group, time, interaction between treatment group and time, values at baseline, and allocation factors as fixed effects, and enrolled patients as random effects.

*, **, and *** represent $p<0.05$, $p<0.01$, and $p<0.001$, respectively.

DPP-4, dipeptidyl-peptidase 4; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyl transpeptidase.

Table S6. Changes in other laboratory tests and vital signs

	Week	Luseogliflozin group		DPP-4i group		Intergroup difference in	
		Measurement (n)	adjusted mean change from baseline (SE)	Measurement (n)	adjusted mean change from baseline (SE)	adjusted mean change (95% CI)	p value
Red blood cell (x 10^4/μL)	0	486.3±44.1 (271)		480.0±41.8 (266)			
	24	505.4±47.2 (269)	16.7 (1.7)	478.5±44.1 (259)	-4.8 (1.7)	21.5 (17.1, 26.0)	<0.001
	52	499.5±50.3 (264)	11.0 (1.8)	477.5±43.8 (257)	-4.6 (1.9)	15.6 (10.7, 20.5)	<0.001
Hemoglobin (g/dL)	0	14.9±1.4 (271)		14.7±1.3 (266)			
	24	15.4±1.5 (269)	0.5 (0.0)	14.6±1.4 (259)	-0.2 (0.1)	0.7 (0.5, 0.8)	<0.001
	52	15.3±1.6 (264)	0.4 (0.1)	14.6±1.4 (257)	-0.2 (0.1)	0.6 (0.4, 0.7)	<0.001
Hematocrit (%)	0	45.1±3.8 (271)		44.6±3.6 (265)			
	24	46.9±3.9 (269)	1.6 (0.1)	44.4±3.8 (259)	-0.6 (0.2)	2.2 (1.8, 2.5)	<0.001
	52	46.7±4.4 (264)	1.4 (0.2)	44.4±3.8 (257)	-0.4 (0.2)	1.8 (1.4, 2.3)	<0.001
White blood cell (/μL)	0	6679.2±1707.4 (270)		6677.2±1791.9 (264)			
	24	6565.7±1684.4 (269)	-173.9 (76.4)	6702.9±1861.6 (259)	-46.1 (77.7)	-127.8 (-333.4, 77.8)	0.22
	52	6379.6±1587.3 (264)	-341.5 (72.9)	6779.9±1852.4 (256)	48.4 (73.5)	-389.9 (-584.6, -195.1)	<0.001
Platelet (x 10^4/μL)	0	24.6±6.3 (270)		24.9±5.8 (264)			
	24	24.0±6.3 (269)	-0.7 (0.2)	24.3±6.0 (259)	-0.6 (0.2)	-0.1 (-0.6, 0.5)	0.77

	52	23.7±6.4 (263)	-1.0 (0.2)	24.2±5.8 (255)	-0.5 (0.2)	-0.5 (-1.0, 0.1)	0.11
Uric acid (mg/dL)	0	5.53±1.32 (272)		5.39±1.37 (268)			
	24	4.99±1.39 (265)	-0.61 (0.05)	5.60±1.33 (259)	0.08 (0.05)	-0.69 (-0.84, -0.55)	<0.001
	52	5.03±1.25 (262)	-0.56 (0.05)	5.45±1.28 (256)	-0.06 (0.05)	-0.49 (-0.64, -0.35)	<0.001
Amy (IU/L)	0	64.5±27.2 (240)		65.3±31.1 (228)			
	24	70.1±29.7 (250)		70.7±35.2 (227)			
	52	69.1±29.6 (247)		72.7±43.1 (226)			
Amy (log-transformed) (ln(IU/L))	0	4.09±0.41 (240)		4.09±0.40 (228)			
	24	4.17±0.40 (250)	0.08 (0.02)	4.17±0.41 (227)	0.07 (0.02)	0.01 (-0.04, 0.05)	0.77
	52	4.15±0.41 (247)	0.06 (0.02)	4.18±0.44 (226)	0.10 (0.02)	-0.04 (-0.08, 0.01)	0.09
NT-proBNP (pg/mL)	0	33.6±33.0 (93)		38.7±40.0 (82)			
	2	27.3±20.6 (72)		40.3±52.3 (66)			
	24	35.6±31.1 (92)		39.5±56.9 (79)			
	52	30.2±23.8 (85)		39.4±47.6 (81)			
NT-proBNP (log-transformed) (ln(pg/mL))	0	3.13±0.90 (93)		3.22±0.96 (82)			
	2	3.00±0.86 (72)	-0.05 (0.08)	3.14±1.05 (66)	0.11 (0.08)	-0.17 (-0.37, 0.04)	0.11
	24	3.17±0.97 (92)	0.11 (0.07)	3.15±1.00 (79)	0.03 (0.08)	0.08 (-0.11, 0.27)	0.42
	52	3.14±0.76 (85)	0.09 (0.07)	3.16±1.03 (81)	0.08 (0.08)	0.00 (-0.18, 0.19)	0.98

Erythropoietin (mIU/mL)	0	9.3±5.2 (91)		9.6±4.8 (81)			
	2	11.2±4.5 (73)		10.1±5.4 (66)			
	24	10.1±5.4 (93)		10.8±9.7 (78)			
	52	10.9±10.2 (87)		11.1±9.8 (81)			
Erythropoietin (log-transformed) (ln(mIU/mL))	0	2.11±0.49 (91)		2.16±0.47 (81)			
	2	2.33±0.41 (73)	0.23 (0.04)	2.22±0.43 (66)	0.08 (0.04)	0.15 (0.05, 0.25)	0.004
	24	2.21±0.44 (93)	0.09 (0.04)	2.19±0.57 (78)	0.04 (0.05)	0.05 (-0.06, 0.17)	0.35
	52	2.23±0.49 (87)	0.12 (0.04)	2.24±0.52 (81)	0.11 (0.05)	0.01 (-0.10, 0.13)	0.81
Reticulocyte (%)	0	17.9±4.8 (93)		16.5±4.3 (81)			
	2	19.6±5.7 (73)	1.8 (0.5)	16.4±4.7 (66)	-0.4 (0.5)	2.3 (1.0, 3.6)	<0.001
	24	17.6±4.5 (92)	-0.2 (0.4)	16.5±5.1 (77)	-0.2 (0.4)	0.0 (-1.1, 1.1)	0.97
	52	17.4±4.9 (87)	-0.2 (0.4)	16.2±4.9 (80)	-0.4 (0.4)	0.2 (-0.9, 1.3)	0.72
UACR (mg/g･Cre)	0	356.2±2306.0 (91)		207.6±519.2 (79)			
	2	268.8±964.4 (74)		216.9±631.4 (65)			
	24	451.3±1603.9 (91)		250.5±697.0 (78)			
	52	880.4±6529.6 (86)		760.9±4193.7 (79)			
UACR (log-transformed) (ln(mg/g･Cre))	0	3.36±1.77 (91)		3.46±1.84 (79)			
	2	3.50±1.83 (74)	0.12 (0.10)	3.27±1.88 (65)	-0.29 (0.11)	0.41 (0.15, 0.67)	0.002

	24	3.50±2.11 (91)	0.27 (0.15)	3.39±1.96 (78)	-0.15 (0.16)	0.41 (0.00, 0.82)	0.048
	52	3.45±2.00 (86)	0.29 (0.17)	3.52±2.11 (79)	-0.02 (0.18)	0.30 (-0.17, 0.77)	0.21
Urinary creatinine (mg/dL)	0	113.4±77.6 (87)		118.1±87.4 (72)			
	2	79.2±57.3 (70)	-29.5 (7.8)	97.0±84.2 (59)	-14.3 (8.4)	-15.2 (-35.9, 5.5)	0.15
	24	90.4±69.2 (86)	-25.1 (9.1)	124.6±104.6 (72)	10.6 (9.9)	-35.7 (-60.7, -10.7)	0.005
	52	93.6±75.5 (83)	-23.3 (9.5)	110.7±100.2 (77)	-6.5 (10.0)	-16.8 (-42.6, 9.0)	0.20

Data are presented as mean ± standard deviation (n) for measurements or mean (standard error (SE)) for adjusted mean change from baseline.

The adjusted mean change of each continuous variable was estimated using models for repeated measures (MMRM) with an unstructured covariance structure with treatment group, time, interaction between treatment group and time, values at baseline, and allocation factors as fixed effects, and enrolled patients as random effects.

DPP-4i, dipeptidyl peptidase 4 inhibitor; Amy, amylase; NT-proBNP, amino-terminal pro-brain natriuretic peptide; UACR, urinary albumin-to-creatinine ratio

Table S7. Changes in laboratory tests and vital signs stratified by baseline BMI

	BMI < 25kg/m^2			BMI ≥ 25kg/m^2		
	Luseogliflozin group	DPP-4i group	p value	Luseogliflozin group	DPP-4i group	p value
HbA1c (%)	-0.7±0.7 (84) (p<0.001)	-0.6±0.6 (82) (p<0.001)	0.86	-0.8±0.8 (180) (p<0.001)	-0.6±0.9 (179) (p<0.001)	0.031
Weight (kg)*	-3.8±3.7 (85) (p<0.001)	0.2±4.8 (80) (p=0.71)	<0.001	-3.6±4.0 (178) (p<0.001)	-0.8±4.2 (177) (p=0.008)	<0.001
eGFR (mL/min/1.73m^2)*	-0.7±12.1 (84) (p=0.58)	-4.7±10.2 (80) (p<0.001)	0.024	-1.9±12.1 (178) (p=0.035)	-2.5±13.1 (175) (p=0.011)	0.64
Systolic blood pressure (mmHg)	-3.9±16.1 (84) (p=0.029)	-4.2±14.0 (81) (p=0.009)	0.90	-4.6±15.7 (178) (p<0.001)	-1.8±17.3 (178) (p=0.17)	0.11
Diastolic blood pressure (mmHg)	-3.7±11.4 (84) (p=0.004)	-0.9±9.6 (81) (p=0.41)	0.09	-1.9±11.0 (178) (p=0.023)	-2.3±12.0 (178) (p=0.010)	0.71
Pulse (bpm)	-0.9±9.1 (84) (p=0.35)	-0.2±9.7 (79) (p=0.86)	0.62	-0.5±10.6 (173) (p=0.57)	1.1±10.4 (164) (p=0.16)	0.16
HDL-chol (mg/dL)*	10.5±15.8 (81) (p<0.001)	2.0±16.2 (78) (p=0.27)	0.001	7.2±13.9 (175) (p<0.001)	4.1±17.6 (173) (p=0.002)	0.07
T-chol (mg/dL)*	0.7±13.5 (75) (p=0.65)	-0.7±14.3 (66) (p=0.68)	0.54	0.0±14.7 (154) (p=0.99)	-0.3±14.1 (149) (p=0.78)	0.83
LDL-chol (mg/dL)*	0.2±19.7 (54) (p=0.95)	2.9±26.9 (48) (p=0.45)	0.55	0.9±23.8 (118) (p=0.68)	1.2±24.9 (105) (p=0.61)	0.92
TG (log-transformed) (ln(mg/dL))*	-3.47±9.50 (62) (p=0.006)	-2.68±11.39 (63) (p=0.07)	0.67	-0.62±10.20 (139) (p=0.47)	-0.96±8.62 (122) (p=0.22)	0.77
AST (log-transformed) (ln(IU/L))	-0.05±0.32 (83) (p=0.13)	-0.01±0.32 (79) (p=0.75)	0.41	-0.21±0.44 (176) (p<0.001)	0.00±0.39 (174) (p=0.99)	<0.001

ALT (log-transformed) (ln(IU/L))	-0.15±0.40 (83) (p=0.001)	-0.08±0.46 (79) (p=0.13)	0.30	-0.31±0.55 (176) (p<0.001)	-0.08±0.49 (175) (p=0.037)	<0.001
γ-GTP (log-transformed) (ln(IU/L))	-0.19±0.40 (81) (p<0.001)	-0.13±0.47 (79) (p=0.018)	0.35	-0.28±0.51 (174) (p<0.001)	-0.07±0.43 (171) (p=0.032)	<0.001
Red blood cell (x 10^4/μL)	7.5±39.3 (82) (p=0.09)	-2.1±22.1 (78) (p=0.40)	0.06	15.5±30.6 (176) (p<0.001)	-1.9±25.9 (174) (p=0.33)	<0.001
Hemoglobin (g/dL)	0.4±1.0 (82) (p<0.001)	-0.1±0.7 (78) (p=0.20)	<0.001	0.5±0.9 (176) (p<0.001)	-0.1±0.8 (174) (p=0.28)	<0.001
Hematocrit (%)	1.3±3.1 (82) (p<0.001)	-0.2±2.0 (77) (p=0.46)	<0.001	1.8±2.8 (176) (p<0.001)	-0.1±2.4 (174) (p=0.61)	<0.001
White blood cell (/μL)	-233.5±981.3 (82) (p=0.034)	32.2±1303.8 (77) (p=0.83)	0.15	-263.1±1323.9 (175) (p=0.009)	137.3±1162.4 (173) (p=0.12)	0.003
Platelet (x 10^4/μL)	-1.1±3.5 (82) (p=0.005)	-0.7±4.0 (76) (p=0.13)	0.50	-0.8±2.9 (175) (p<0.001)	-0.4±3.2 (173) (p=0.07)	0.34
Uric acid (mg/dL)	-0.54±0.93 (82) (p<0.001)	0.08±0.71 (78) (p=0.32)	<0.001	-0.50±0.96 (175) (p<0.001)	0.01±0.98 (174) (p=0.93)	<0.001
Amy (log-transformed) (ln(IU/L))	0.01±0.17 (70) (p=0.57)	0.11±0.28 (66) (p=0.001)	0.011	0.08±0.25 (148) (p<0.001)	0.09±0.22 (140) (p<0.001)	0.69
FLI	-9.5±13.8 (53) (p<0.001)	-3.9±17.3 (51) (p=0.11)	0.07	-8.6±12.7 (123) (p<0.001)	-3.6±14.3 (104) (p=0.013)	0.005
FIB-4 index (log-transformed)	0.10±0.21 (82) (p<0.001)	0.06±0.31 (76) (p=0.08)	0.46	-0.01±0.26 (175) (p=0.71)	0.08±0.24 (173) (p<0.001)	0.001

Data are presented as mean ± standard deviation (n).

Two-sample t-tests were performed for between-group comparisons and one-sample t-tests for within-group comparisons.

* Percentage change was calculated instead of change.

BMI, body mass index, DPP-4i, dipeptidyl-peptidase 4 inhibitor; HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; HDL-cholesterol, high-density lipoprotein cholesterol; T-chol, total cholesterol; LDL-cholesterol, low-density lipoprotein cholesterol; TG, triglyceride; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyl transpeptidase; Amy, amylase; FLI, fatty liver index; FIB-4 index: fibrosis-4 index

Table S8. Changes in laboratory tests and vital signs stratified by baseline age

	Age < 65 years			Age ≥ 65 years		
	Luseogliflozin group	DPP-4i group	p value	Luseogliflozin group	DPP-4i group	p value
HbA1c (%)	-0.7±0.9 (183) (p<0.001)	-0.5±0.9 (176) (p<0.001)	0.046	-0.8±0.6 (82) (p<0.001)	-0.7±0.8 (86) (p<0.001)	0.53
Weight (kg)*	-3.2±3.5 (180) (p<0.001)	-0.3±4.7 (174) (p=0.35)	<0.001	-4.7±4.4 (83) (p<0.001)	-0.9±3.7 (83) (p=0.028)	<0.001
eGFR (mL/min/1.73m^2)*	-2.0±11.6 (181) (p=0.021)	-2.7±13.0 (172) (p=0.006)	0.58	-0.5±13.1 (81) (p=0.74)	-4.2±10.6 (83) (p<0.001)	0.045
Systolic blood pressure (mmHg)	-4.5±15.2 (182) (p<0.001)	-2.2±16.9 (174) (p=0.09)	0.17	-4.0±16.9 (81) (p=0.035)	-3.6±15.6 (86) (p=0.034)	0.88
Diastolic blood pressure (mmHg)	-2.2±10.5 (182) (p=0.006)	-2.0±12.0 (174) (p=0.028)	0.91	-3.1±12.6 (81) (p=0.030)	-1.8±10.0 (86) (p=0.10)	0.47
Pulse (bpm)	-0.3±10.2 (177) (p=0.71)	0.9±10.8 (162) (p=0.31)	0.32	-1.4±10.1 (81) (p=0.22)	0.3±8.7 (82) (p=0.74)	0.25
HDL-chol (mg/dL)*	7.8±13.5 (176) (p<0.001)	2.7±15.3 (170) (p=0.024)	0.001	9.2±16.7 (80) (p<0.001)	5.1±20.5 (81) (p=0.027)	0.18
T-chol (mg/dL)*	1.2±14.8 (157) (p=0.30)	-0.2±15.9 (141) (p=0.88)	0.42	-1.9±12.8 (72) (p=0.21)	-0.9±10.2 (74) (p=0.44)	0.60
LDL-chol (mg/dL)*	1.6±24.2 (119) (p=0.46)	4.0±26.9 (100) (p=0.14)	0.49	-1.4±18.3 (53) (p=0.57)	-2.4±22.0 (53) (p=0.43)	0.80
TG (log-transformed) (ln(mg/dL))*	-0.74±10.29 (142) (p=0.39)	-1.10±9.74 (125) (p=0.21)	0.77	-3.33±9.27 (59) (p=0.008)	-2.47±9.47 (60) (p=0.048)	0.62
AST (log-transformed) (ln(IU/L))	-0.19±0.39 (178) (p<0.001)	0.00±0.42 (172) (p=0.95)	<0.001	-0.09±0.46 (81) (p=0.07)	-0.02±0.23 (81) (p=0.55)	0.18
ALT (log-transformed) (ln(IU/L))	-0.30±0.49 (178)	-0.07±0.54 (172)	<0.001	-0.18±0.53 (81)	-0.09±0.33 (82)	0.24

	(p<0.001)	(p=0.09)		(p=0.004)	(p=0.012)	
γ-GTP (log-transformed) (ln(IU/L))	-0.26±0.47 (175)	-0.06±0.50 (169)	<0.001	-0.23±0.49 (80)	-0.15±0.30 (81)	0.24
	(p<0.001)	(p=0.12)		(p<0.001)	(p<0.001)	
Red blood cell (x 10^4/μL)	16.4±29.0 (177)	-0.9±25.6 (172)	<0.001	5.4±41.5 (81)	-4.2±22.7 (80)	0.07
	(p<0.001)	(p=0.63)		(p=0.25)	(p=0.10)	
Hemoglobin (g/dL)	0.5±0.8 (177)	-0.1±0.9 (172)	<0.001	0.3±1.2 (81)	-0.1±0.6 (80)	0.020
	(p<0.001)	(p=0.23)		(p=0.037)	(p=0.29)	
Hematocrit (%)	2.0±2.6 (177)	-0.1±2.4 (171)	<0.001	0.9±3.4 (81)	-0.2±2.0 (80)	0.014
	(p<0.001)	(p=0.66)		(p=0.019)	(p=0.39)	
White blood cell (/μL)	-191.6±1247.5 (176)	165.5±1177.2 (170)	0.007	-388.5±1164.8 (81)	-23.9±1263.0 (80)	0.06
	(p=0.043)	(p=0.07)		(p=0.004)	(p=0.87)	
Platelet (x 10^4/μL)	-0.6±3.0 (176)	-0.3±3.2 (169)	0.39	-1.4±3.2 (81)	-1.0±3.8 (80)	0.40
	(p=0.008)	(p=0.21)		(p<0.001)	(p=0.025)	
Uric acid (mg/dL)	-0.44±0.94 (178)	-0.02±0.97 (170)	<0.001	-0.69±0.94 (79)	0.13±0.76 (82)	<0.001
	(p<0.001)	(p=0.80)		(p<0.001)	(p=0.13)	
Amy (log-transformed) (ln(IU/L))	0.06±0.25 (149)	0.10±0.26 (139)	0.25	0.04±0.17 (69)	0.10±0.19 (67)	0.09
	(p=0.003)	(p<0.001)		(p=0.038)	(p<0.001)	
FLI	-7.7±14.0 (125)	-3.4±17.2 (106)	0.040	-11.8±9.4 (51)	-4.2±10.3 (49)	<0.001
	(p<0.001)	(p=0.043)		(p<0.001)	(p=0.006)	
FIB-4 index (log-transformed)	0.00±0.24 (176)	0.07±0.28 (169)	0.015	0.08±0.26 (81)	0.08±0.21 (80)	0.90
	(p=0.92)	(p=0.001)		(p=0.008)	(p=0.001)	

Data are presented as mean ± standard deviation (n).

Two-sample t-tests were performed for between-group comparisons and one-sample t-tests for within-group comparisons.

* Percentage change was calculated instead of change.

DPP-4i, dipeptidyl-peptidase 4 inhibitor; HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; HDL-cholesterol, high-density lipoprotein cholesterol; T-chol, total cholesterol; LDL-cholesterol, low-density lipoprotein cholesterol; TG, triglyceride; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyl transpeptidase; Amy, amylase; FLI, fatty liver index; FIB-4 index: fibrosis-4 index

Table S9. Changes in laboratory tests and vital signs stratified by baseline eGFR

	45 ≤ eGFR < 60 mL/min/1.73m^2			eGFR ≥ 60 mL/min/1.73m^2		
	Luseogliflozin group	DPP-4i group	p value	Luseogliflozin group	DPP-4i group	p value
HbA1c (%)	-0.7±0.8 (27) (p<0.001)	-0.6±0.9 (23) (p=0.006)	0.66	-0.7±0.8 (233) (p<0.001)	-0.6±0.8 (233) (p<0.001)	0.06
Weight (kg)*	-5.3±4.9 (28) (p<0.001)	-2.1±5.4 (22) (p=0.08)	0.034	-3.5±3.7 (232) (p<0.001)	-0.4±4.3 (230) (p=0.16)	<0.001
eGFR (mL/min/1.73m^2)*	5.1±16.2 (27) (p=0.11)	2.5±11.7 (22) (p=0.32)	0.53	-2.4±11.3 (233) (p=0.001)	-4.1±11.4 (231) (p<0.001)	0.11
Systolic blood pressure (mmHg)	-3.2±19.5 (27) (p=0.40)	-5.2±18.0 (23) (p=0.18)	0.72	-4.3±15.0 (231) (p<0.001)	-2.5±16.3 (231) (p=0.023)	0.21
Diastolic blood pressure (mmHg)	-6.0±12.7 (27) (p=0.021)	-2.2±12.1 (23) (p=0.39)	0.29	-2.0±11.0 (231) (p=0.005)	-2.0±11.3 (231) (p=0.009)	0.93
Pulse (bpm)	-2.2±9.5 (27) (p=0.24)	3.2±12.5 (22) (p=0.25)	0.09	-0.3±10.2 (226) (p=0.65)	0.5±10.0 (216) (p=0.48)	0.41
HDL-chol (mg/dL)*	4.1±18.3 (25) (p=0.28)	3.3±12.7 (19) (p=0.27)	0.87	8.6±14.2 (228) (p<0.001)	3.4±17.6 (230) (p=0.003)	<0.001
T-chol (mg/dL)*	-4.7±15.9 (23) (p=0.17)	-1.2±12.5 (16) (p=0.70)	0.47	0.8±14.1 (203) (p=0.42)	-0.4±14.4 (197) (p=0.71)	0.41
LDL-chol (mg/dL)*	-2.9±18.8 (17) (p=0.53)	-1.1±17.3 (13) (p=0.83)	0.79	1.1±22.9 (155) (p=0.56)	2.1±26.2 (139) (p=0.36)	0.73
TG (log-transformed) (ln(mg/dL))*	-2.67±11.03 (19) (p=0.31)	-1.95±6.18 (16) (p=0.23)	0.82	-1.38±9.97 (182) (p=0.06)	-1.49±9.99 (167) (p=0.06)	0.92
AST (log-transformed) (ln(IU/L))	-0.19±0.39 (26) (p=0.021)	-0.07±0.32 (21) (p=0.33)	0.27	-0.15±0.42 (230) (p<0.001)	0.00±0.38 (230) (p=0.89)	<0.001
ALT (log-transformed) (ln(IU/L))	-0.28±0.49 (26)	-0.17±0.36 (21)	0.40	-0.25±0.51 (230)	-0.07±0.49 (231)	<0.001

	(p=0.006)	(p=0.038)		(p<0.001)	(p=0.033)	
γ-GTP (log-transformed) (ln(IU/L))	-0.28±0.48 (25)	-0.09±0.52 (20)	0.21	-0.24±0.48 (227)	-0.09±0.44 (228)	<0.001
	(p=0.007)	(p=0.42)		(p<0.001)	(p=0.003)	
Red blood cell (x 10^4/μL)	8.4±43.9 (26)	5.2±21.9 (21)	0.77	13.3±32.6 (229)	-2.5±24.9 (229)	<0.001
	(p=0.34)	(p=0.29)		(p<0.001)	(p=0.13)	
Hemoglobin (g/dL)	0.1±1.4 (26)	0.1±0.7 (21)	0.90	0.5±0.9 (229)	-0.1±0.8 (229)	<0.001
	(p=0.72)	(p=0.38)		(p<0.001)	(p=0.08)	
Hematocrit (%)	0.9±3.8 (26)	0.1±2.5 (21)	0.41	1.7±2.8 (229)	-0.1±2.3 (228)	<0.001
	(p=0.23)	(p=0.83)		(p<0.001)	(p=0.40)	
White blood cell (/μL)	-247.7±941.9 (26)	355.7±1198.4 (21)	0.06	-229.2±1234.7 (228)	95.4±1197.7 (227)	0.005
	(p=0.19)	(p=0.19)		(p=0.006)	(p=0.23)	
Platelet (x 10^4/μL)	-0.8±2.4 (26)	-0.1±4.0 (21)	0.46	-0.9±3.2 (228)	-0.6±3.4 (226)	0.33
	(p=0.10)	(p=0.90)		(p<0.001)	(p=0.015)	
Uric acid (mg/dL)	-0.47±1.31 (26)	-0.21±0.83 (20)	0.44	-0.51±0.89 (228)	0.06±0.91 (230)	<0.001
	(p=0.08)	(p=0.27)		(p<0.001)	(p=0.35)	
Amy (log-transformed) (ln(IU/L))	0.06±0.14 (20)	0.12±0.25 (17)	0.34	0.05±0.24 (196)	0.10±0.24 (187)	0.08
	(p=0.07)	(p=0.06)		(p=0.001)	(p<0.001)	
FLI	-10.6±9.0 (17)	-5.3±11.4 (13)	0.16	-8.7±13.3 (159)	-3.5±15.8 (140)	0.002
	(p<0.001)	(p=0.12)		(p<0.001)	(p=0.009)	
FIB-4 index (log-transformed)	0.01±0.24 (26)	0.05±0.26 (21)	0.63	0.03±0.25 (228)	0.08±0.26 (226)	0.048
	(p=0.82)	(p=0.43)		(p=0.07)	(p<0.001)	

Data are presented as mean ± standard deviation (n).

Two-sample t-tests were performed for between-group comparisons and one-sample t-tests for within-group comparisons.

* Percentage change was calculated instead of change.

DPP-4i, dipeptidyl-peptidase 4 inhibitor; HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; HDL-cholesterol, high-density lipoprotein cholesterol; T-chol, total cholesterol; LDL-cholesterol, low-density lipoprotein cholesterol; TG, triglyceride; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma-glutamyl transpeptidase; Amy, amylase; FLI, fatty liver index; FIB-4 index: fibrosis-4 index.

Table S10. Adverse events

	Luseogliflozin group		DPP-4i group	
Number of patients in the safety analysis set	300		299	
Death	0 (0.0)		0 (0.0)	
Any adverse event	56 (18.7)		52 (17.4)	
Any serious adverse event	10 (3.3)		5 (1.7)	
Name of adverse event	total	serious	total	serious
genital pruritus	6 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)
hepatic dysfunction	5 (1.7)	0 (0.0)	2 (0.7)	0 (0.0)
dyslipidemia	5 (1.7)	0 (0.0)	1 (0.3)	0 (0.0)
cystitis	5 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
hyperglycemia	4 (1.3)	0 (0.0)	7 (2.3)	0 (0.0)
upper respiratory tract infection	4 (1.3)	0 (0.0)	10 (3.3)	0 (0.0)
pancreatic cancer	3 (1.0)	3 (1.0)	0 (0.0)	0 (0.0)
frequent urination	3 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
increased red blood cells	3 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
hypertension	2 (0.7)	0 (0.0)	2 (0.7)	0 (0.0)
hyperuricemia	2 (0.7)	0 (0.0)	2 (0.7)	0 (0.0)
peripheral arterial occlusive disease	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)
acute cholangitis	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)
inguinal hernia	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)
myocardial infarction	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)
pyelonephritis	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)
trigeminal neuralgia	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)
urosepsis	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)
uterine leiomyoma	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)
hypoglycemia	1 (0.3)	0 (0.0)	3 (1.0)	0 (0.0)

bronchitis	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)
hypotension	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)
influenza	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)
insomnia	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)
rash	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)
bacterial vaginosis	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
balanoposthitis	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
diabetic retinopathy	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
diarrhea	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
fever	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
foot fracture	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
hematuria	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
increased hematocrit	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
injury	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
macrocytic anemia	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
parotitis	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
periodontal disease	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
thirst	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
thrombophlebitis	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
urethritis	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
vertigo	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
constipation	0 (0.0)	0 (0.0)	3 (1.0)	0 (0.0)
atrial flutter	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
bacterial pneumonia	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
pancreatitis	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
uterine cancer	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
asteatotic eczema	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)

back pain	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
diabetic nephropathy	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
disc protrusion	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
drug eruption	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
gastroesophageal reflux disease	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
headache	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
hypesthesia	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
increased blood triglyceride	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
increased NT-proBNP	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
increased pancreatic enzyme	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
increased platelet count	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
joint injury	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
joint pain	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
lymph node metastasis	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
malaise	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
myalgia	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
optic disc cupping	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
pityriasis rosea	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
psoriasis	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
spondylolisthesis	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
urolithiasis	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
zinc deficiency	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)

Data are represented as n (%).

DPP-4i, dipeptidyl-peptidase 4 inhibitor; NT-proBNP, amino-terminal pro-brain natriuretic peptide

Table S11. Adverse events stratified by baseline BMI

	BMI < 25kg/m^2				BMI ≥ 25kg/m^2			
	Luseogliflozin group		DPP-4i group		Luseogliflozin group		DPP-4i group	
Number of patients in the safety analysis set	94		93		203		203	
Death	0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	
Any adverse event	15 (16.0)		14 (15.1)		41 (20.2)		36 (17.7)	
Any serious adverse event	4 (4.3)		1 (1.1)		6 (3.0)		4 (2.0)	
Name of adverse event	total	serious	total	serious	total	serious	total	serious
upper respiratory tract infection	2 (2.1)	0 (0.0)	3 (3.2)	0 (0.0)	2 (1.0)	0 (0.0)	7 (3.4)	0 (0.0)
cystitis	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)
dyslipidemia	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)
pancreatic cancer	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	2 (1.0)	2 (1.0)	0 (0.0)	0 (0.0)
increased red blood cells	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
hypertension	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.5)	0 (0.0)
hyperuricemia	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.5)	0 (0.0)
acute cholangitis	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
peripheral arterial occlusive disease	1 (1.1)	1 (1.1)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
trigeminal neuralgia	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
balanoposthitis	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
bronchitis	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
hematuria	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
hypotension	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
injury	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
macrocytic anemia	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
parotitis	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

thirst	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
vertigo	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
genital pruritus	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)
hepatic dysfunction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.5)	0 (0.0)	1 (0.5)	0 (0.0)
hyperglycemia	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	4 (2.0)	0 (0.0)	6 (3.0)	0 (0.0)
frequent urination	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)
inguinal hernia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
myocardial infarction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
pyelonephritis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
urosepsis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
uterine leiomyoma	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
bacterial vaginosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
diabetic retinopathy	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
diarrhea	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
fever	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
foot fracture	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
hypoglycemia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	3 (1.5)	0 (0.0)
increased hematocrit	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
influenza	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
insomnia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.5)	0 (0.0)
periodontal disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
rash	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.5)	0 (0.0)
thrombophlebitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
urethritis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
asteatotic eczema	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
atrial flutter	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)
back pain	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)

bacterial pneumonia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)
constipation	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)	0 (0.0)
diabetic nephropathy	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
disc protrusion	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
drug eruption	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
gastroesophageal reflux disease	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
headache	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
hepatic dysfunction	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
hypesthesia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
increased blood triglyceride	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
increased NT-proBNP	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
increased pancreatic enzyme	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
increased platelet count	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
joint injury	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
joint pain	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
lymph node metastasis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
malaise	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
myalgia	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
optic disc cupping	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
pancreatitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)
pityriasis rosea	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
psoriasis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
spondylolisthesis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
urolithiasis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
uterine cancer	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)
zinc deficiency	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)

Data are represented as n (%).

DPP-4i, dipeptidyl-peptidase 4 inhibitor; NT-proBNP, amino-terminal pro-brain natriuretic peptide

Table S12. Adverse events stratified by baseline age

	Age < 65 years				Age ≥ 65 years			
	Luseogliflozin group		DPP-4i group		Luseogliflozin group		DPP-4i group	
Number of patients in the safety analysis set	206		205		94		94	
Death	0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	
Any adverse event	47 (22.8)		37 (18.0)		9 (9.6)		15 (16.0)	
Any serious adverse event	8 (3.9)		4 (2.0)		2 (2.1)		1 (1.1)	
Name of adverse event	total	serious	total	serious	total	serious	total	serious
genital pruritus	5 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
cystitis	4 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
dyslipidemia	4 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)
hepatic dysfunction	4 (1.9)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
hyperglycemia	4 (1.9)	0 (0.0)	6 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
upper respiratory tract infection	4 (1.9)	0 (0.0)	8 (3.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	0 (0.0)
increased red blood cells	3 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
frequent urination	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
hypertension	2 (1.0)	0 (0.0)	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
hyperuricemia	2 (1.0)	0 (0.0)	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
pancreatic cancer	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	2 (2.1)	2 (2.1)	0 (0.0)	0 (0.0)
acute cholangitis	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
inguinal hernia	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
myocardial infarction	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
peripheral arterial occlusive disease	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
pyelonephritis	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
trigeminal neuralgia	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

urosepsis	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
uterine leiomyoma	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
bacterial vaginosis	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
balanoposthitis	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
bronchitis	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
diabetic retinopathy	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
diarrhea	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
fever	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
foot fracture	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
hypoglycemia	1 (0.5)	0 (0.0)	3 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
hypotension	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
increased hematocrit	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
influenza	1 (0.5)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
injury	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
parotitis	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
periodontal disease	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
thrombophlebitis	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
urethritis	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
vertigo	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
hematuria	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
hepatic dysfunction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)
insomnia	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
macrocytic anemia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
rash	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
thirst	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
asteatotic eczema	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
atrial flutter	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

back pain	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
bacterial pneumonia	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
constipation	0 (0.0)	0 (0.0)	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
diabetic nephropathy	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
disc protrusion	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
drug eruption	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
gastroesophageal reflux disease	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
headache	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
hypesthesia	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
increased blood triglyceride	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
increased NT-proBNP	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
increased pancreatic enzyme	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
increased platelet count	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
joint injury	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
joint pain	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
lymph node metastasis	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
malaise	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
myalgia	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
optic disc cupping	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
pancreatitis	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
pityriasis rosea	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
psoriasis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
spondylolisthesis	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
urolithiasis	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
uterine cancer	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
zinc deficiency	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)

Data are represented as n (%).

DPP-4i, dipeptidyl-peptidase 4 inhibitor; NT-proBNP, amino-terminal pro-brain natriuretic peptide