

Table S1. Differences in baseline characteristics between the improved group and the deteriorated group based on changes in HOMA2-R in the pemafibrate group during the 52-week study period.

Variable	Improved group (n=83)	Deteriorated group (n=58)	<i>P</i> -value
Age (years)	60.1 ± 12.7	60.1 ± 11.7	0.979
Female sex	27 (32.5)	18 (31.0)	1.000
BMI (kg/m ²)	27.4 ± 4.2	27.2 ± 3.8	0.718
FPG (mg/dL)	140.1 ± 32.1	128.3 ± 26.3	0.023
HbA1c (%)	7.02 ± 0.84	6.79 ± 0.68	0.085
Triglyceride (mg/dL)	180 (137, 249)	163 (130, 218)	0.226
HDL-C (ng/mL)	52.6 ± 12.4	52.1 ± 11.2	0.825
AST (IU/L)	32.7 ± 17.5	29.8 ± 12.8	0.281
ALT (IU/L)	31 (21, 48)	29 (19, 43)	0.404
γ-GTP (IU/L)	45 (31, 84)	34 (22, 56)	0.007
eGFR (mL/min/1.73m ²)	71.1 ± 20.1	67.4 ± 15.4	0.941
HOMA2-R	2.30 (1.74, 3.14)	1.75 (1.32, 2.37)	<0.001
HOMA2-β	74.4 (61.1, 90.6)	76.5 (53.1, 97.7)	0.695
Fibrates	28 (33.7)	24 (41.4)	0.379
Statins	60 (72.3)	39 (67.2)	0.576
α-glucosidase inhibitors	0 (0)	2 (3.4)	0.168
Biguanides	50 (60.2)	40 (69.0)	0.373
DPP-4 inhibitors	35 (42.2)	31 (53.4)	0.234
GLP-1 receptor agonists	3 (3.6)	4 (6.9)	0.446
SGLT2 inhibitors	37 (44.6)	29 (50.0)	0.608
Thiazolidines	4 (4.8)	3 (5.2)	1.000

Data are shown as mean ± SD, median (25% percentile, 75% percentile), or number (%). *P*-values for pemafibrate group versus control group were obtained using Student's *t*-test, the Mann–Whitney test, or Fisher's exact test. BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; γ-GTP, γ-glutamyl transpeptidase; eGFR, estimated glomerular filtration rate; HOMA, Homeostatic model assessment; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT2, sodium glucose cotransporter 2.

Table S2. Differences in baseline characteristics between the improved group and the deteriorated group based on changes in disposition index in the pemafibrate group during the 52-week study period.

Variable	Improved group (n=79)	Deteriorated group (n=62)	P-value
Age (years)	60.0 ± 12.7	60.2 ± 11.8	0.930
Female sex	30 (38.0)	15 (24.2)	0.102
BMI (kg/m ²)	27.4 ± 4.2	27.3 ± 3.8	0.920
FPG (mg/dL)	142.6 ± 34.8	126.8 ± 19.8	<0.001
HbA1c (%)	7.08 ± 0.88	6.72 ± 0.59	0.007
Triglyceride (mg/dL)	171 (132, 237)	170 (138, 232)	0.935
HDL-C (ng/mL)	52.5 ± 11.6	52.2 ± 12.3	0.888
AST (IU/L)	32.1 ± 16.9	30.8 ± 14.2	0.640
ALT (IU/L)	30 (21, 54)	30 (20, 41)	0.443
γ-GTP (IU/L)	44 (24, 84)	35 (25, 64)	0.377
eGFR (mL/min/1.73m ²)	71.7 ± 20.8	66.8 ± 14.2	0.112
HOMA2-R	2.30 (1.66, 3.09)	1.97 (1.39, 2.59)	0.033
Disposition index	0.33 (0.25, 0.44)	0.38 (0.30, 0.49)	0.004
Fibrates	23 (29.1)	29 (46.8)	0.036
Statins	58 (73.4)	41 (66.1)	0.360
α-glucosidase inhibitors	0 (0)	0 (0)	1.000
Biguanides	50 (63.3)	40 (64.5)	1.000
DPP-4 inhibitors	35 (44.3)	31 (50.0)	0.610
GLP-1 receptor agonists	1 (1.3)	6 (9.7)	0.446
SGLT2 inhibitors	37 (46.8)	29 (46.8)	1.000
Thiazolidines	3 (3.8)	4 (6.5)	0.699

Data are shown as mean ± SD, median (25% percentile, 75% percentile), or number (%). *P*-values for pemafibrate group versus control group were obtained using Student's *t*-test, the Mann–Whitney test, or Fisher's exact test. BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; γ-GTP, γ-glutamyl transpeptidase; eGFR, estimated glomerular filtration rate; HOMA, Homeostatic model assessment; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT2, sodium glucose cotransporter 2.

Table S3. Changes from baseline in key endpoints for the participants.

Variables	Pemafibrate (n=141)	Control (n=138)	<i>P</i> -value
	Mean change at 52 wks	Mean change at 52 wks	
Body mass index (kg/m ²)	0.0 (−0.1 to 0.2)	−0.1 (−0.2 to 0.1)	0.489
Total cholesterol (mg/dL)	−6.4 (−10.4 to −2.4) **	−1.1 (−5.4 to 3.1)	0.076
Triglycerides (mg/dL)	−46 (−60 to −30) ***	−14 (−20 to 0) *	< 0.001
HDL-cholesterol (mg/dL)	2.0 (0.3 to 3.8) *	−0.2 (−1.2 to 0.9)	0.035
AST (IU/L)	−3.5 (−5.4 to −1.6) ***	0.7 (−1.4 to 2.7)	0.003
ALT (IU/L)	−6 (−9 to −4) ***	−1 (−2 to 0)	< 0.001
γ-GTP (IU/L)	−10 (−14 to −5) ***	−1 (−2 to 1)	< 0.001
eGFR (mL/min/1.73m ²)	2.5 (0.6 to 4.4)	−0.7 (−2.2 to 0.8)	0.009

Data are shown as mean or median change (95% confidence interval). *P*-values for pemafibrate group versus control group were obtained using Student's *t*-test, the Mann–Whitney test. * *P* < 0.05, ** *P* < 0.01, *** *P* < 0.001 vs baseline. AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transpeptidase; eGFR, estimated glomerular filtration rate.

Table S4. Relationships between changes in indices for glucose metabolism and changes in metabolic parameters in the pemafibrate group evaluated by multiple linear regression analysis.

Δ HOMA-2R	Regression coefficients	95% confidence interval	<i>P</i> value
Δ HDL-C	−0.058	−0.101, −0.022	0.003
$\Delta\gamma$ -GTP	0.004	−0.001, 0.009	0.113
Δ ALT	0.002	−0.011, 0.015	0.772
Δ DI	Regression coefficients	95% confidence interval	<i>P</i> value
Δ TG	−0.00022	−0.00038, −0.00005	0.011
Δ BMI	−0.03373	−0.06252, −0.00494	0.022
$\Delta\gamma$ -GTP	−0.00047	−0.00112, 0.00019	0.164
Δ eGFR	−0.00138	−0.00363, 0.00086	0.226

Multiple linear regression was adjusted for age, sex, high-density lipoprotein cholesterol (HDL-C), γ -glutamyl transpeptidase (γ -GTP) and alanine aminotransferase (ALT) for homeostatic model assessment (HOMA)-2R, and age, sex, triglyceride (TG), body mass index (BMI), γ -GTP, and estimated glomerular filtration rate (eGFR) for disposition index (DI).