

Supplemental Material

Supplemental Table 1. Patient's characteristics by heart failure history status and randomized treatment

Characteristic	HF		No HF	
	Placebo	Albiglutide	Placebo	Albiglutide
N.	968	954	3764	3776
Age, years	65.0 (58.0, 70.0)	65.0 (59.0, 71.0)	65.0 (58.0, 70.0)	64.0 (58.0, 70.0)
Women	352 (36.4%)	319 (33.4%)	1115 (29.6%)	1108 (29.3%)
NYHA I/II	820 (86.3%)	815 (87.4%)	0 (0.0%)	0 (0.0%)
Asian	42 (4.3%)	46 (4.8%)	200 (5.3%)	182 (4.8%)
Hispanic	93 (9.6%)	78 (8.2%)	895 (23.8%)	927 (24.5%)
Black or African American	21 (2.2%)	14 (1.5%)	93 (2.5%)	97 (2.6%)
White	798 (82.4%)	805 (84.4%)	2490 (66.2%)	2489 (65.9%)
Other	14 (1.4%)	11 (1.2%)	86 (2.3%)	81 (2.1%)
Asia Pacific	33 (3.4%)	41 (4.3%)	158 (4.2%)	144 (3.8%)
Eastern Europe	464 (47.9%)	466 (48.8%)	546 (14.5%)	571 (15.1%)
Latin America	62 (6.4%)	49 (5.1%)	783 (20.8%)	809 (21.4%)
North America	152 (15.7%)	131 (13.7%)	826 (21.9%)	835 (22.1%)
Western Europe	257 (26.5%)	267 (28.0%)	1451 (38.5%)	1417 (37.5%)
Current Smoker	125 (12.9%)	133 (13.9%)	626 (16.6%)	604 (16.0%)
CAD	790 (81.6%)	774 (81.1%)	2555 (67.9%)	2558 (67.7%)
CABG	208 (21.5%)	225 (23.6%)	634 (16.8%)	665 (17.6%)
PAD	192 (19.8%)	203 (21.3%)	967 (25.7%)	992 (26.3%)
Cerebrovascular disease	250 (25.8%)	249 (26.1%)	921 (24.5%)	922 (24.4%)
Atrial fibrillation/flutter	188 (19.4%)	186 (19.5%)	233 (6.2%)	235 (6.2%)
Weight, kg	92.3 (80.9, 105.6)	93.9 (81.9, 109.0)	89.9 (78.2, 103.0)	89.5 (78.0, 102.2)
BMI, Kg/m ²	32.4 (29.0, 36.7)	32.7 (29.1, 37.1)	31.2 (28.0, 35.2)	31.2 (28.0, 35.1)
Heart rate, bpm	72.0 (65.0, 78.0)	72.0 (66.0, 79.0)	72.0 (65.0, 79.0)	72.0 (65.0, 79.0)
Systolic BP, mmHg	134.0 (122.0, 143.0)	134.0 (123.0, 144.0)	135.0 (124.0, 145.0)	134.0 (124.0, 145.0)
Diastolic BP, mmHg	78.0 (70.0, 85.0)	79.0 (70.0, 85.0)	78.0 (70.0, 83.0)	77.0 (70.0, 83.0)
HbA1c, %	8.4 (7.7, 9.5)	8.5 (7.7, 9.6)	8.3 (7.6, 9.4)	8.3 (7.6, 9.5)
eGFR, ml/min/1.73m ²	72.0 (57.0, 88.0)	71.0 (55.0, 89.0)	79.0 (62.0, 95.0)	78.0 (63.0, 95.0)
eGFR <60 ml/min/1.73m ²	286 (29.5%)	307 (32.2%)	806 (21.4%)	758 (20.1%)
Diabetic eye disease	300 (31.0%)	315 (33.0%)	655 (17.4%)	667 (17.7%)
Diabetes duration, years	12.2 (6.9, 18.1)	12.6 (7.4, 18.7)	13.1 (7.8, 19.7)	13.0 (7.9, 19.3)
Insulin	565 (58.4%)	611 (64.0%)	2172 (57.7%)	2248 (59.5%)
Metformin	658 (68.0%)	651 (68.2%)	2848 (75.7%)	2811 (74.4%)
DPP4i	115 (11.9%)	116 (12.2%)	624 (16.6%)	582 (15.4%)

Sulfonylureas	325 (33.6%)	283 (29.7%)	1054 (28.0%)	1063 (28.2%)
SGLT2i	37 (3.8%)	50 (5.2%)	228 (6.1%)	260 (6.9%)
Thiazolidinediones	13 (1.3%)	7 (0.7%)	89 (2.4%)	85 (2.3%)
ACEi/ARBs	830 (85.7%)	817 (85.6%)	2937 (78.0%)	2940 (77.9%)
Beta-blockers	806 (83.3%)	766 (80.3%)	2376 (63.1%)	2362 (62.6%)
MRAs	188 (19.4%)	206 (21.6%)	207 (5.5%)	207 (5.5%)
CCBs	308 (31.8%)	316 (33.1%)	1123 (29.8%)	1112 (29.4%)
Nitrates	222 (22.9%)	195 (20.4%)	568 (15.1%)	570 (15.1%)
Thiazides	200 (20.7%)	225 (23.6%)	837 (22.2%)	864 (22.9%)
Loop diuretics	378 (39.0%)	350 (36.7%)	521 (13.8%)	545 (14.4%)
Statins	851 (87.9%)	841 (88.2%)	3137 (83.3%)	3126 (82.8%)
Fibrates	62 (6.4%)	62 (6.5%)	283 (7.5%)	308 (8.2%)
Ezetimibe	36 (3.7%)	42 (4.4%)	255 (6.8%)	283 (7.5%)
Antiplatelet agents	768 (79.3%)	753 (78.9%)	2871 (76.3%)	2898 (76.7%)
Anticoagulants	147 (15.2%)	144 (15.1%)	267 (7.1%)	239 (6.3%)

Legend: CAD, coronary artery disease; CABG, coronary artery bypass grafting; PAD, peripheral artery disease; BMI, body mass index; HbA1c, glycated hemoglobin; eGFR, estimated glomerular filtration rate; DPP4i, dipeptidyl peptidase 4 inhibitors; SGLT2i, sodium glucose co-transporter 2 inhibitors; ACEi/ARBs, angiotensin converting enzyme inhibitors/angiotensin receptor blockers; MRAs, mineralocorticoid receptor antagonists; CCBs, calcium channel blockers.

Continuous variables are reported as medians and respective 25th to 75th percentiles.

Supplemental Table 2. Associations of NYHA class with cardiovascular events and mortality

Event	NYHA III/IV n. (%) IR 100py	NYHA I/II n. (%) IR 100py	No HF n. (%) IR 100py	HR (95%CI) * P-value NYHA I/II vs. No HF	HR (95%CI) * P-value NYHA III/IV vs. No HF
Cardiovascular death or HF hospitalization	46/248 (18.5) IR=12.7	123/1635 (7.5) IR=4.7	227/7540 (3.0) IR=1.9	2.16 (1.72-2.70) P <0.001	5.08 (3.65-7.06) P <0.001
Cardiovascular death, MI, or stroke	51/248 (20.6) IR =14.4	184/1635 (11.3) IR=7.2	512/7540 (6.8) IR =4.4	1.46 (1.23-1.74) P <0.001	2.67 (1.98-3.60) P <0.001
All-cause mortality	33/248 (13.3) IR=8.5	103/1635 (6.3) IR=3.8	260/7540 (3.4) IR =2.2	1.65 (1.31-2.09) P <0.001	3.63 (2.49-5.29) P <0.001

*Hazard ratio adjusted for age, sex, race, coronary artery disease, body mass index, systolic blood pressure, HbA1c, and eGFR.

Legend: IR, incidence-rate per 100 person-years; HF, heart failure; MI, myocardial infarction.

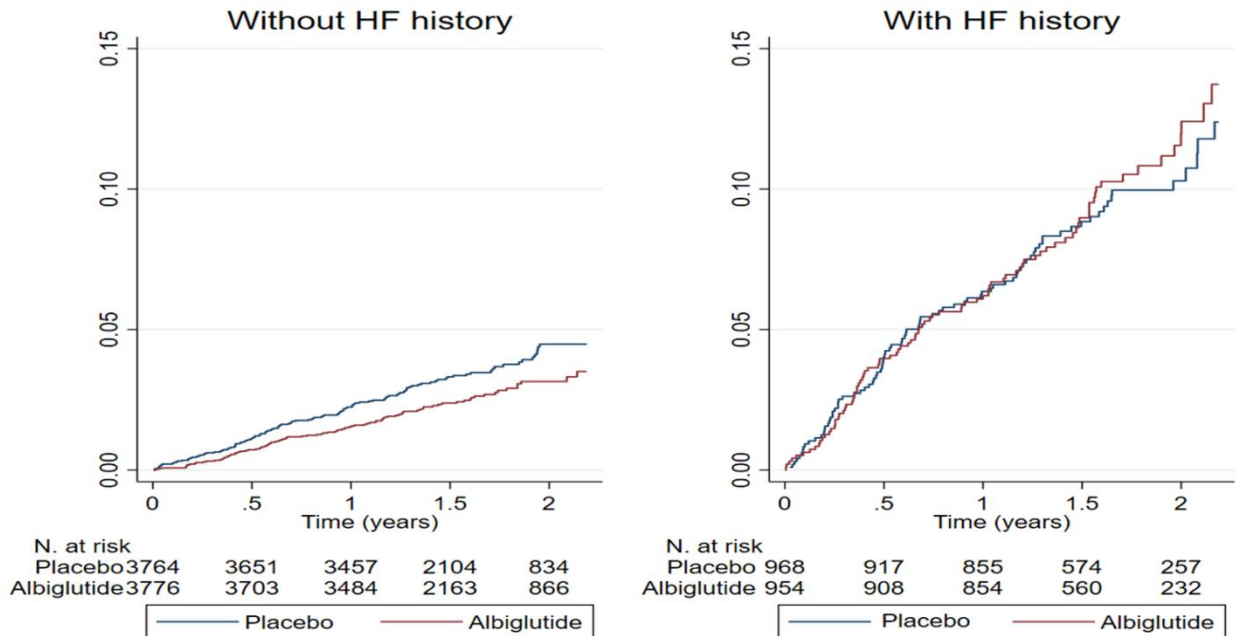
Supplemental Table 3. Effect of albiglutide vs. placebo on the study outcomes by HF history among patients who received at least one dose of the study drug

Outcome/HF history status	Albiglutide n. (%)	Placebo n. (%)	HR (95%CI)	Inter.P
Cardiovascular death or HF hospitalization				
No HF	97/3764 (2.6)	130/3749 (3.5)	0.73 (0.56-0.95)	0.063
HF	91/952 (9.6)	88/966 (9.1)	1.06 (0.79-1.42)	
Cardiovascular death				
No HF	74/3764 (2.0)	82/3749 (2.2)	0.89 (0.65-1.21)	0.54
HF	48/952 (5.0)	48/966 (5.0)	1.04 (0.70-1.55)	
HF hospitalization (first)				
No HF	29/3764 (0.8)	58/3749 (1.5)	0.49 (0.31-0.77)	0.025
HF	50/952 (5.3)	53/966 (5.5)	0.96 (0.66-1.42)	
Cardiovascular death, MI, or stroke				
No HF	234/3764 (6.2)	277/3749 (7.4)	0.83 (0.69-0.98)	0.29
HF	101/952 (10.6)	145/966 (15.0)	0.70 (0.54-0.90)	
All-cause mortality				
No HF	123/3764 (3.3)	135/3749 (3.6)	0.90 (0.70-1.14)	0.43
HF	71/952 (7.5)	70/966 (7.2)	1.06 (0.76-1.47)	

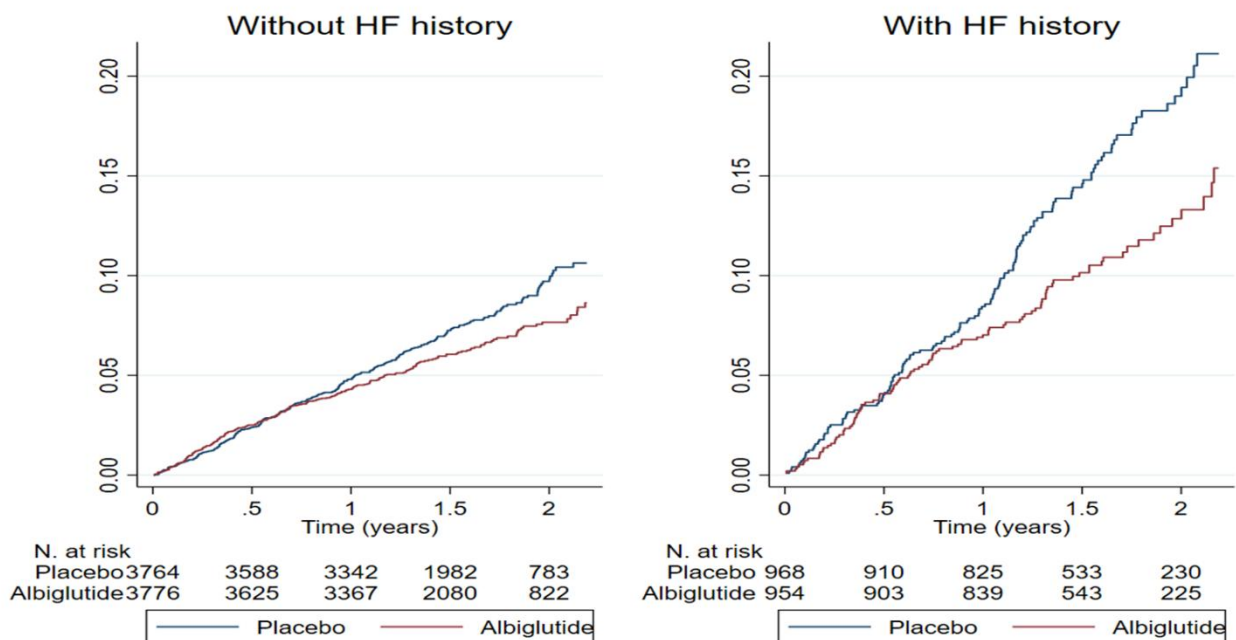
Legend: HF, heart failure; MI, myocardial infarction.

Supplemental Figure 1. Kaplan-Meier curves for the composite outcomes of cardiovascular death or heart failure hospitalization and cardiovascular death, myocardial infarction, or stroke

Cardiovascular death or HF hospitalization



Cardiovascular death, MI or Stroke



Legend: HF, heart failure; MI, myocardial infarction.