Supplementary Material

Title: Cardiovascular, metabolic, and safety outcomes with semaglutide by baseline age: post hoc analysis of SUSTAIN 6 and PIONEER 6

Authors: Stephen C. Bain (FRCP)[1], Nicolas Belmar (MD)[2], Søren T. Hoff (MD)[3], Mansoor Husain (MD)[4], Søren Rasmussen (PhD)[2], Tina Vilsbøll (MD)[5], Mark C. Petrie (MD)[6]

Author affiliations

[1]Swansea University Medical School, Swansea University, Swansea, UK

[2]Novo Nordisk A/S, Søborg, Denmark

[3]Novo Nordisk A/S, Bagsværd, Denmark

[4]Ted Rogers Centre for Heart Research, Department of Medicine, University of Toronto, Toronto, Canada

[5]Steno Diabetes Center Copenhagen, University of Copenhagen, Copenhagen, Denmark

[6]School of Cardiovascular and Metabolic Health, University of Glasgow, Glasgow, UK

Corresponding author

Stephen C. Bain, Swansea University Medical School, Swansea University, Swansea, SA2 8PP, UK; s.c.bain@swansea.ac.uk; +44(0)7710-641345

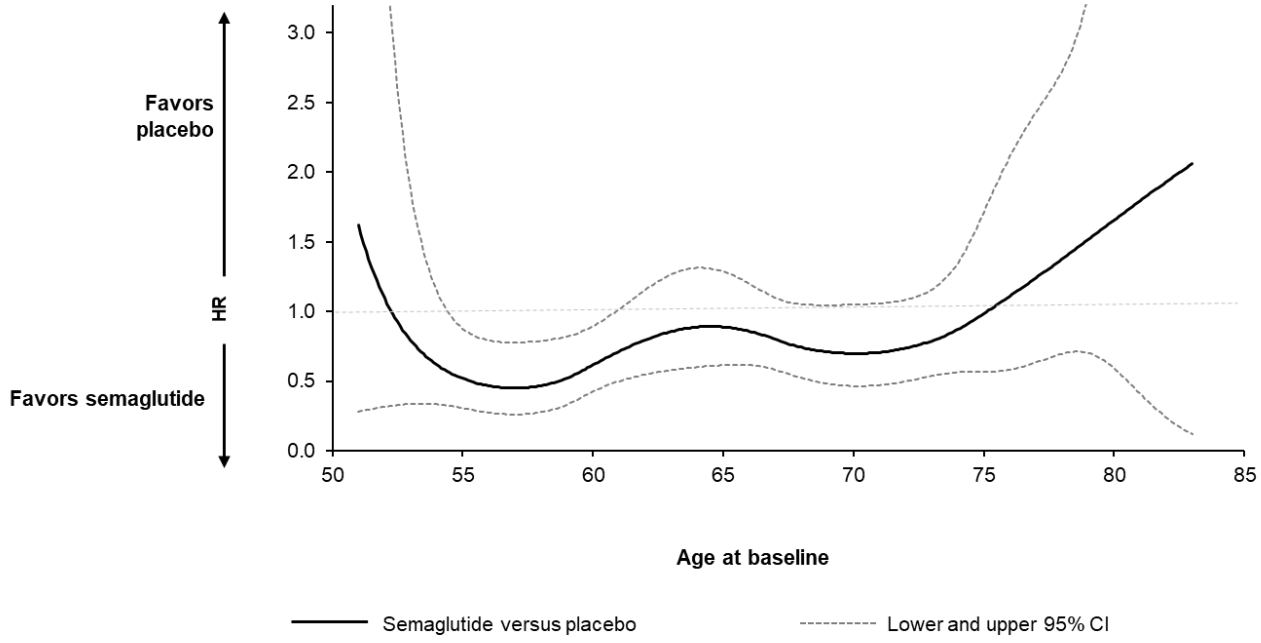
Supplementary Table 1. Concomitant medications at baseline by age subgroup

	Semaglutide					Placebo				
Age subgroup, years	Overall	≤60	>60 to ≤65	>65 to ≤70	>70	Overall	≤60	>60 to ≤65	>65 to ≤70	>70
Glucose-lowering agents, n (%)	2,723 (84.1)	709 (85.3)	779 (86.6)	643 (85.5)	592 (78.3)	2,737 (84.4)	729 (87.6)	717 (87.4)	662 (83.7)	629 (78.8)
Metformin	2,434 (75.1)	652 (78.5)	705 (78.3)	578 (76.9)	499 (66.0)	2,447 (75.5)	668 (80.3)	665 (81.1)	592 (74.8)	522 (65.4)
SU	1,215 (37.5)	312 (37.5)	354 (39.3)	290 (38.6)	259 (34.3)	1,222 (37.7)	311 (37.4)	317 (38.7)	292 (36.9)	302 (37.8)
α-glucosidase inhibitors	52 (1.6)	19 (2.3)	9 (1.0)	10 (1.3)	14 (1.9)	69 (2.1)	19 (2.3)	18 (2.2)	18 (2.3)	14 (1.8)
TZD	100 (3.1)	22 (2.6)	19 (2.1)	32 (4.3)	27 (3.6)	94 (2.9)	28 (3.4)	20 (2.4)	25 (3.2)	21 (2.6)
DPP4i	5 (0.2)	1 (0.1)	0	3 (0.4)	1 (0.1)	2 (<0.1)	2 (0.2)	0	0	0
GLP-1RA	0	0	0	0	0	0	0	0	0	0
SGLT2i*	1 (<0.1)	1 (0.1)	0	0	0	4 (0.1)	1 (0.1)	3 (0.4)	0	0
Glinides	74 (2.3)	13 (1.6)	14 (1.6)	23 (3.1)	24 (3.2)	64 (2.0)	12 (1.4)	15 (1.8)	14 (1.8)	23 (2.9)
Other	166 (5.1)	50 (6.0)	49 (5.4)	35 (4.7)	32 (4.2)	140 (4.3)	43 (5.2)	36 (4.4)	33 (4.2)	28 (3.5)
Insulin-treated	1,751 (54.1)	418 (50.3)	486 (54.0)	419 (55.7)	428 (56.6)	1,730 (53.4)	431 (51.8)	417 (50.9)	440 (55.6)	442 (55.4)
Insulin-naïve	1,488 (45.9)	413 (49.7)	414 (46.0)	333 (44.3)	328 (43.4)	1,511 (46.6)	401 (48.2)	403 (49.1)	351 (44.4)	356 (44.6)

CV, n (%)										
Antihypertensives	3,048 (94.1)	770 (92.7)	854 (94.9)	714 (94.9)	710 (93.9)	3,022 (93.2)	758 (91.1)	762 (92.9)	737 (93.2)	765 (95.9)
Beta blockers	1,868 (57.7)	502 (60.4)	496 (55.1)	437 (58.1)	433 (57.3)	1,919 (59.2)	506 (60.8)	470 (57.3)	458 (57.9)	485 (60.8)
Ca channel blockers	1,019 (31.5)	213 (25.6)	255 (28.3)	269 (35.8)	282 (37.3)	1,064 (32.8)	247 (297)	253 (30.9)	276 (34.9)	288 (36.1)
ACE inhibitor	1,511 (46.7)	402 (48.4)	465 (51.7)	318 (42.3)	326 (43.1)	1,473 (45.4)	411 (49.4)	367 (44.8)	373 (47.2)	322 (40.4)
Angiotensin receptor blocker	1,183 (36.5)	271 (32.6)	296 (32.9)	305 (40.6)	311 (41.1)	1,187 (36.6)	251 (30.2)	319 (38.9)	287 (36.3)	330 (41.4)
Others	232 (7.2)	57 (6.9)	50 (5.6)	53 (7.0)	72 (9.5)	260 (8.0)	54 (6.5)	56 (6.8)	65 (8.2)	85 (10.7)
Diuretics	1,245 (38.4)	275 (33.1)	323 (35.9)	312 (41.5)	335 (44.3)	1,276 (39.4)	281 (33.8)	288 (35.1)	332 (42.0)	375 (47.0)
Loop diuretics	546 (16.9)	122 (14.7)	125 (13.9)	129 (17.2)	170 (22.5)	530 (16.4)	112 (13.5)	98 (12.0)	126 (15.9)	194 (24.3)
Thiazides	507 (15.7)	91 (11.0)	142 (15.8)	136 (18.1)	138 (18.3)	532 (16.4)	94 (11.3)	133 (16.2)	162 (20.5)	143 (17.9)
Thiazide-like diuretics	198 (6.1)	51 (6.1)	61 (6.8)	48 (6.4)	38 (5.0)	195 (6.0)	54 (6.5)	49 (6.0)	47 (5.9)	45 (5.6)
Aldosterone antagonists	199 (6.1)	50 (6.0)	50 (5.6)	51 (6.8)	48 (6.3)	195 (6.0)	59 (7.1)	47 (5.7)	36 (4.6)	53 (6.6)
Lipid-lowering	2,585 (79.8)	672 (80.9)	697 (77.4)	594 (79.0)	622 (82.3)	2,620 (80.8)	660 (79.3)	661 (80.6)	639 (80.8)	660 (82.7)
Anti-platelets	2,363 (73.0)	636 (76.5)	625 (69.4)	541 (71.9)	561 (74.2)	2,428 (74.9)	641 (77.0)	592 (72.2)	593 (75.0)	602 (75.4)
Oral anti-coagulants	235 (7.3)	34 (4.1)	48 (5.3)	58 (7.7)	95 (12.6)	208 (6.4)	34 (4.1)	46 (5.6)	39 (4.9)	89 (11.2)

*During the time of these trials, SGLT2is were not considered standard of care. Data are shown as n (%). ACE, angiotensin-converting enzyme; Ca, calcium; CV, cardiovascular; DPP4i, dipeptidyl peptidase 4 inhibitor; GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium–glucose cotransporter 2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione.

Supplementary Figure 1. Time to first MACE with age as a continuous variable



MACE was a composite of death from cardiovascular causes, nonfatal myocardial infarction, and nonfatal stroke. Quadratic spline regression was applied using Cox proportional hazard regression to analyse treatment differences in time-to-first MACE by continuous baseline age. CI, confidence interval; HR, hazard ratio, MACE, major adverse cardiovascular events.