

Supplementary Material

Greater Combined Reductions of HbA_{1c} ≥ 1.0% and Body Weight Loss ≥ 5.0% or ≥ 10.0% with Orally Administered Semaglutide Versus Comparators

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Supplementary Table S1 Patient demographics and clinical characteristics at baseline in the PIONEER 1–5 and 8 trials

	PIONEER 1 [1]		PIONEER 2 [2]		PIONEER 3 [3]		PIONEER 4 [4]			PIONEER 5 [5]		PIONEER 8 [6]	
	Oral semaglutide 14 mg	Placebo	Oral semaglutide 14 mg	Empagliflozin 25 mg	Oral semaglutide 14 mg	Sitagliptin 100 mg	Oral semaglutide 14 mg	Liraglutide 1.8 mg	Placebo	Oral semaglutide 14 mg	Placebo	Oral semaglutide 14 mg	Placebo
People, <i>n</i>	175	178	411	410	465	467	285	284	142	163	161	181	184
Mean (SD) age, years	54 (11)	54 (11)	57 (10)	58 (10)	57 (10)	58 (10)	56 (10)	56 (10)	57 (10)	71 (8)	70 (8)	61 (10)	60 (10)
Mean (SD) duration of diabetes, years	3.4 (4.4)	3.4 (4.6)	7.2 (5.8)	7.7 (6.3)	8.7 (6.1)	8.8 (6.0)	7.8 (5.7)	7.3 (5.3)	7.8 (5.5)	14.1 (8.6)	13.9 (7.4)	14.1 (8.0)	14.8 (7.9)
Mean (SD) HbA _{1c} , %	8.0 (0.7)	7.9 (0.7)	8.1 (0.9)	8.1 (0.9)	8.3 (0.9)	8.3 (0.9)	8.0 (0.7)	8.0 (0.7)	7.9 (0.7)	8.0 (0.7)	7.9 (0.7)	8.2 (0.7)	8.2 (0.7)
Mean (SD) HbA _{1c} , mmol/mol	64 (8)	63 (7)	65 (10)	65 (10)	67 (10)	67 (10)	64 (8)	64 (7)	63 (8)	64 (8)	63 (8)	66 (8)	66 (8)
Mean (SD) body weight, kg	88.1 (22.1)	88.6 (23.4)	91.9 (20.5)	91.3 (20.1)	91.2 (21.7)	90.9 (21.0)	92.9 (20.6)	95.5 (21.9)	93.2 (20.0)	91.3 (17.8)	90.4 (17.5)	84.6 (21.0)	86.0 (21.4)
Background medication at randomisation, <i>n</i> (%)													
Metformin	–	–	411 (100.0)	410 (100.0)	465 (100.0)	467 (100.0)	285 (100)	284 (100)	142 (100)	132 (81.0)	110 (68.3)	121 (66.9)	125 (67.9)
Sulphonylureas	–	–	–	–	220 (47.3)	219 (46.9)	–	–	–	65 (39.9)	66 (41.0)	–	–
SGLT2i	–	–	–	–	–	–	74 (26.0)	73 (25.7)	36 (25.4)	–	–	–	–
Insulin													
Long-acting (basal)	–	–	–	–	–	–	–	–	–	45 (27.6)	43 (26.7)	74 (40.9)	81 (44.0)
Intermediate-acting	–	–	–	–	–	–	–	–	–	13 (8.0)	11 (6.8)	0	0
Fast-acting (bolus)	–	–	–	–	–	–	–	–	–	0	1 (0.6)	0	0
Pre-mixed	–	–	–	–	–	–	–	–	–	1 (0.6)	0	32 (17.7)	30 (16.3)
Basal + bolus	–	–	–	–	–	–	–	–	–	–	–	68 (37.6)	66 (35.9)
Other	–	–	–	–	–	1 (0.2)	–	–	–	0	1 (0.6)	–	–

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Comorbidities affecting ≥ 20% of people in any trial, <i>n</i> (%)													
Hypertension	90 (51.4)	98 (55.1)	298 (72.5)	305 (74.4)	357 (76.8)	339 (72.6)	222 (77.9)	215 (75.7)	97 (68.3)	154 (94.5)	153 (95.0)	138 (76.2)	147 (79.9)
Dyslipidaemia	54 (30.9)	44 (24.7)	97 (23.6)	95 (23.2)	136 (29.2)	141 (30.2)	54 (18.9)	74 (26.1)	36 (25.4)	42 (25.8)	51 (31.7)	75 (41.4)	67 (36.4)
Obesity (> 30 kg/m ²)	38 (21.7)	41 (23.0)	108 (26.3)	117 (28.5)	119 (25.6)	133 (28.5)	72 (25.3)	68 (23.9)	42 (29.6)	63 (38.7)	67 (41.6)	26 (14.4)	35 (19.0)
Diabetic neuropathy	14 (8.0)	9 (5.1)	53 (12.9)	64 (15.6)	115 (24.7)	129 (27.6)	52 (18.2)	53 (18.7)	32 (22.5)	80 (49.1)	81 (50.3)	61 (33.7)	62 (34.9)
Diabetic retinopathy	14 (8.0)	8 (4.5)	32 (7.8)	46 (11.2)	74 (15.9)	81 (17.3)	28 (9.8)	25 (8.8)	14 (9.9)	67 (41.1)	57 (35.4)	62 (34.3)	60 (32.6)
Diabetic nephropathy	9 (5.1)	6 (3.4)	17 (4.1)	15 (3.7)	52 (11.2)	40 (8.6)	23 (8.1)	21 (7.4)	14 (9.9)	133 (81.6)	131 (81.4)	30 (16.6)	38 (20.7)
Hyperlipidaemia	29 (16.6)	33 (18.5)	111 (27.0)	113 (27.6)	94 (20.2)	102 (21.8)	106 (37.2)	94 (33.1)	49 (34.5)	34 (20.9)	36 (22.4)	32 (17.7)	33 (17.9)
Ischaemic heart disease	14 (8.0)	15 (8.4)	57 (13.9)	46 (11.2)	77 (16.6)	81 (17.3)	38 (13.3)	32 (11.3)	12 (8.5)	75 (46.0)	69 (42.9)	35 (19.3)	37 (20.1)
Heart failure	4 (2.3)	5 (2.8)	22 (5.4)	16 (3.9)	41 (8.8)	42 (9.0)	19 (6.7)	17 (6.0)	3 (2.1)	56 (34.4)	61 (37.9)	12 (6.6)	10 (5.4)
Osteoarthritis	13 (7.4)	19 (10.7)	65 (15.8)	58 (14.1)	74 (15.9)	59 (12.6)	32 (11.2)	43 (15.1)	12 (8.5)	37 (22.7)	46 (28.6)	29 (16.0)	25 (13.6)
Cataract	9 (5.1)	11 (6.2)	22 (5.4)	27 (6.6)	54 (11.6)	45 (9.6)	13 (4.6)	21 (7.4)	13 (9.2)	51 (31.3)	55 (34.2)	26 (14.4)	22 (12.0)
Cholelithiasis	11 (6.3)	9 (5.1)	55 (13.4)	50 (12.2)	56 (12.0)	57 (12.2)	34 (11.9)	35 (12.3)	20 (14.1)	34 (20.9)	22 (13.7)	27 (14.9)	19 (10.3)
Gastro- oesophageal reflux disease	14 (8.0)	20 (11.2)	44 (10.7)	43 (10.5)	73 (15.7)	79 (16.9)	39 (13.7)	44 (15.5)	18 (12.7)	34 (20.9)	31 (19.3)	36 (19.9)	29 (15.8)

HbA_{1c} glycated haemoglobin, *SD* standard deviation, *SGLT2i* sodium-glucose co-transporter 2 inhibitor

References

1. Aroda VR, Rosenstock J, Terauchi Y, et al. PIONEER 1: randomized clinical trial of the efficacy and safety of oral semaglutide monotherapy in comparison with placebo in patients with type 2 diabetes. *Diabetes Care*. 2019;42:1724–32.
2. Rodbard HW, Rosenstock J, Canani LH, et al. Oral semaglutide versus empagliflozin in patients with type 2 diabetes uncontrolled on metformin: the PIONEER 2 trial. *Diabetes Care*. 2019;42:2272–81.
3. Rosenstock J, Allison D, Birkenfeld AL, et al. Effect of additional oral semaglutide vs sitagliptin on glycated hemoglobin in adults with type 2 diabetes uncontrolled with metformin alone or with sulfonylurea: the PIONEER 3 randomized clinical trial. *JAMA*. 2019;321:1466–80.
4. Pratley R, Amod A, Hoff ST, et al. Oral semaglutide versus subcutaneous liraglutide and placebo in type 2 diabetes (PIONEER 4): a randomised, double-blind, phase 3a trial. *Lancet*. 2019;394:39–50.
5. Mosenzon O, Blicher TM, Rosenlund S, et al. Efficacy and safety of oral semaglutide in patients with type 2 diabetes and moderate renal impairment (PIONEER 5): a placebo-controlled, randomised, phase 3a trial. *Lancet Diabetes Endocrinol*. 2019;7:515–27.
6. Zinman B, Aroda VR, Buse JB, et al. Efficacy, safety, and tolerability of oral semaglutide versus placebo added to insulin with or without metformin in patients with type 2 diabetes: the PIONEER 8 trial. *Diabetes Care*. 2019;42:2262–71.