Supplementary

Supplementary table 1. Participant characteristics in subgroups determined by baseline characteristics (ITT population).

Baseline subgroup	Age, years	Sex, female, %	Diabetes duration, years	Basal insulin dose, U/kg	HbA1c, %	HbA1c, mmol/mol	BMI, kg/m²	Diabetic nephropathy, %	Daily insulin dose, %	
									<30 U/day	≥30 U/day
Age, years										
<65 (n=573)	54.1 (7.7)	48.0	11.0 (6.1)	0.4 (0.1)	8.6 (0.7)	70.8 (7.4)	29.9 (5.0)	8.4	36.1	63.9
≥65 (n=314)	70.1 (4.1)	54.1	16.7 (7.6)	0.4 (0.1)	8.5 (0.7)	69.5 (7.2)	29.9 (4.7)	12.1	36.3	63.7
Duration of T2D, years										
<10 (n=305)	54.9 (10.3)	49.5	5.6 (2.4)	0.4 (0.1)	8.5 (0.7)	69.8 (7.1)	30.2 (5.3)	7.9	39.3	60.7
≥10 (n=582)	62.4 (9.1)	50.5	16.8 (5.8)	0.4 (0.1)	8.6 (0.7)	70.6 (7.3)	29.7 (4.7)	10.7	34.5	65.5
Basal insulin dose, U/day										
<30 (n=316)	59.6 (10.5)	47.8	12.3 (7.1)	0.3 (0.1)	8.6 (0.7)	70.0 (7.7)	28.9 (4.6)	26.3	99.4	1.2
≥30 (n=571)	59.9 (10.0)	51.5	13.4 (7.3)	0.5 (0.1)	8.6 (0.6)	70.5 (7.0)	30.4 (5.0)	28.5	0.6	98.8
HbA1c, % (mmol/mol)										
7.5–8.0 % (n=238) (58–64 mmol/mol)	60.7 (10.5)	50.8	13.1 (7.4)	0.4 (0.2)	7.8 (0.2)	61.6 (1.9)	30.1 (5.0)	8.8	40.3	59.7
>8.0–9.0 % (n=403) (>64–75 mmol/mol)	59.9 (10.1)	47.6	12.7 (7.0)	0.4 (0.1)	8.5 (0.3)	69.7 (3.0)	30.0 (4.9)	11.7	33.3	66.7
>9.0–10.0 % (n=246) (>75–86 mmol/mol)	58.7 (10.0)	53.7	13.4 (7.4)	0.4 (0.1)	9.5 (0.3)	79.8 (3.0)	29.5 (4.8)	7.3	37.0	63.0
BMI,ᵃ kg/m²										
<25 (n=148)	59.2 (10.1)	41.9	12.6 (8.1)	0.5 (0.2)	8.6 (0.7)	70.0 (7.2)	23.2 (1.3)	6.8	43.9	56.1
25 to <30 (n=345)	60.2 (10.2)	46.7	13.7 (7.1)	0.4 (0.1)	8.6 (0.7)	70.7 (7.3)	27.5 (1.4)	9.6	39.1	60.9
30 to <35 (n=237)	60.4 (9.9)	51.5	13.2 (6.7)	0.4 (0.1)	8.6 (0.7)	69.9 (7.8)	32.4 (1.5)	12.2	34.6	65.4
≥35 (n=156)	58.8 (10.2)	63.5	11.6 (7.3)	0.4 (0.1)	8.6 (0.7)	70.0 (7.1)	37.6 (1.5)	9.0	25.0	75.0
eGFR,ᵇ mL/min/1.73-m²										
≥90 (n=318)	55.2 (10.9)	51.3	11.5 (7.2)	0.4 (0.1)	8.6 (0.7)	70.6 (7.5)	29.5 (4.9)	5.3	39.9	60.1
60 to <90 (n=436)	62.0 (8.6)	49.5	13.4 (7.0)	0.4 (0.1)	8.6 (0.7)	70.3 (7.1)	30.1 (5.0)	8.3	32.8	67.2
<60 (n=106)	65.3 (8.1)	54.7	15.2 (7.2)	0.4 (0.1)	8.5 (0.7)	69.6 (7.1)	29.7 (4.5)	28.3	35.8	64.2

Mean (SD) unless otherwise stated.
ᵃFor one patient, BMI value was missing at baseline. ᵇFor 27 patients, eGFR values were missing at baseline.
BMI, body mass index; eGFR, estimated glomerular filtration rate; ITT, intent to treat; kg, kilogram; SD, standard deviation; T2D, type 2 diabetes; U, units.

Supplementary table 2. Change in HbA1c from baseline to Week 26 by baseline characteristics subgroups (ITT population).

	Baseline, mean (SD)		Week 26, mean (SD)		Change from baseline to Week 26, LS mean (SE)		LS mean difference (95% CI)	Heterogeneity p-value
HbA1c, %								
	iGlarLixi (n=443)	BIAsp 30 (n=444)	iGlarLixi (n=443)	BIAsp 30 (n=444)	iGlarLixi (n=443)	BIAsp 30 (n=444)		
Age subgroups								
<65 years (n=573)	8.7 (0.7)	8.6 (0.7)	7.3 (1.1)	7.5 (1.0)	−1.3 (0.1)	−1.1 (0.1)	−0.3 (−0.4, −0.1)	0.991
≥65 years (n=314)	8.5 (0.7)	8.5 (0.6)	7.3 (1.0)	7.5 (1.0)	−1.3 (0.1)	−1.0 (0.1)	−0.3 (−0.5, −0.0)	
Diabetes duration subgroups								
<10 years (n=305)	8.6 (0.7)	8.5 (0.7)	7.2 (1.1)	7.5 (1.1)	-1.4 (0.1)	-1.1 (0.1)	-0.3 (-0.5, -0.1)	0.577
≥10 years (n=582)	8.6 (0.7)	8.6 (0.7)	7.3 (1.0)	7.5 (1.0)	-1.3 (0.1)	-1.1 (0.1)	-0.2 (-0.4, -0.0)	
Basal insulin dose subgroups								
<30 U/day (n=316)	8.6 (0.7)	8.5 (0.7)	7.3 (1.0)	7.5 (1.0)	-1.4 (0.3)	-1.2 (0.3)	-0.3 (-0.5, -0.0)	0.960
≥30 U/day (n=571)	8.6 (0.7)	8.6 (0.6)	7.3 (1.1)	7.5 (1.0)	-1.3 (0.1)	-1.0 (0.2)	-0.2 (-0.4, -0.1)	
HbA1c subgroups								
7.5–8.0 % (n=238)	7.8 (0.2)	7.8 (0.2)	7.0 (0.9)	7.1 (0.8)	-1.2 (0.1)	-1.1. (0.2)	-0.1 (-0.4, 0.1)	
>8.0–9.0 % (n=403)	8.5 (0.3)	8.5 (0.3)	7.1 (1.0)	7.5 (1.0)	-1.4 (0.1)	-1.1 (0.1)	-0.4 (-0.6, -0.2)	0.278
>9.0–10.0 % (n=246)	9.5 (0.3)	9.5 (0.3)	7.7 (1.2)	7.9 (1.1)	-1.3 (0.2)	-1.1 (0.2)	-0.2 (-0.4, 0.1)	
BMI subgroups								
<25 kg/m^2 (n=148)	8.5 (0.7)	8.6 (0.6)	7.2 (1.1)	7.4 (0.9)	-1.4 (0.1)	-1.2 (0.1)	-0.2 (-0.5, 0.2)	
25–<30 kg/m^2 (n=345)	8.7 (0.7)	8.6 (0.7)	7.2 (0.9)	7.5 (1.0)	-1.4 (0.1)	-1.1 (0.1)	-0.4 (-0.6, -0.1)	0.599
30–<35 kg/m^2 (n=237)	8.6 (0.6)	8.6 (0.7)	7.4 (1.1)	7.5 (0.9)	-1.2 (0.1)	-1.0 (0.1)	-0.2 (-0.4, 0.1)	
≥35 kg/m^2 (n=156)	8.6 (0.7)	8.6 (0.6)	7.4 (1.1)	7.6 (1.2)	-1.3 (0.1)	-1.0 (0.1)	-0.3 (-0.6, 0.1)	
eGFR subgroups								
≥90 mL/min/1.73-m^2 (n=318)	8.6 (0.7)	8.6 (0.7)	7.3 (1.2)	7.5 (1.0)	-1.2 (0.1)	-1.1 (0.1)	-0.1 (-0.3, 0.1)	
60 to <90 mL/min/1.73-m^2 (n=436)	8.6 (0.7)	8.5 (0.6)	7.2 (0.9)	7.5 (1.0)	-1.4 (0.1)	-1.1 (0.1)	-0.3 (-0.5, -0.1)	0.308
<60 mL/min/1.73-m^2 (n=106)	8.5 (0.7)	8.6 (0.5)	7.2 (1.1)	7.4 (1.0)	-1.4 (0.2)	-1.1 (0.2)	-0.3 (-0.7, 0.1)	

	HbA1c, mmol/mol							
	Baseline, mean (SD)		Week 26, mean (SD)		Change from baseline to Week 26, LS mean (SE)		LS mean difference (95% CI)	Heterogeneity p-value
	iGlarLixi (n=443)	BIAsp 30 (n=444)	iGlarLixi (n=443)	BIAsp 30 (n=444)	iGlarLixi (n=443)	BIAsp 30 (n=444)		
Age subgroups								
<65 years (n=573)	71.1 (7.3)	70.5 (7.2)	55.8 (11.7)	58.1 (10.8)	-14.6 (0.7)	-12.0 (0.7)	-2.7 (-4.6, -0.8)	0.991
≥65 years (n=314)	69.7 (7.4)	69.4 (6.9)	55.8 (11.4)	58.5 (10.9)	-14.0 (0.9)	-11.3 (1.0)	-2.7 (-5.4, -0.1)	
Diabetes duration subgroups								
<10 years (n=305)	70.3 (7.1)	69.4 (7.2)	55.0 (12.5)	57.9 (11.6)	-14.9 (0.9)	-11.6 (1.0)	-3.3 (-5.8, -0.7)	0.577
≥10 years (n=582)	70.7 (7.5)	70.5 (7.1)	56.3 (11.0)	58.3 (10.4)	-14.2 (0.7)	-11.8 (0.7)	-2.4 (-4.3, -0.4)	
Basal insulin dose subgroups								
<30 U/day (n=316)	70.4 (7.8)	69.7 (7.5)	55.8 (11.0)	58.1 (10.4)	-15.5 (2.7)	-12.8 (2.7)	-2.7 (-5.4, -0.1)	0.960
≥30 U/day (n=571)	70.7 (7.1)	70.4 (6.9)	55.8 (11.8)	58.3 (11.0)	-13.9 (1.5)	-11.1 (1.6)	-2.6 (-4.6, -0.8)	
HbA1c subgroups								
7.5–8.0 % (n=238)	61.5 (1.9)	61.7 (1.9)	52.9 (9.4)	54.4 (8.5)	-13.3 (1.5)	-11.9 (1.6)	-1.4 (-4.3, 1.4)	
>8.0–9.0 % (n=403)	69.8 (3.0)	69.7 (3.1)	54.1 (10.6)	57.9 (10.7)	-15.5 (0.8)	-11.5 (0.9)	-4.0 (-6.3, -1.7)	0.278
>9.0–10.0 % (n=246)	79.8 (3.0)	79.8 (3.0)	60.9 (12.9)	62.8 (11.5)	-13.8 (1.6)	-11.9 (1.6)	-1.7 (-4.6, 1.0)	
BMI subgroups								
<25 kg/m^2 (n=148)	69.6 (7.5)	70.3 (6.9)	55.2 (12.4)	57.2 (10.1)	-15.0 (1.4)	-13.3 (1.3)	-1.7 (-5.3, 1.9)	
25–<30 kg/m^2 (n=345)	71.2 (7.5)	70.2 (7.1)	54.8 (10.2)	58.1 (10.5)	-15.7 (0.8)	-11.7 (0.9)	-3.96 (-6.4, -1.5)	0.599
30–<35 kg/m^2 (n=237)	70.6 (7.0)	69.9 (7.8)	56.9 (12.4)	58.5 (10.3)	-12.9 (1.0)	-11.2 (1.1)	-1.69 (-4.6, 1.2)	
≥35 kg/m^2 (n=156)	69.9 (7.5)	70.2 (6.8)	56.8 (12.2)	59.2 (12.7)	-13.8 (1.4)	-10.9 (1.3)	-2.89 (-6.5, 0.7)	
eGFR subgroups								
≥90 mL/min/1.73-m^2 (n=318)	70.6 (7.3)	70.7 (7.8)	56.8 (12.6)	58.3 (10.7)	-13.4 (0.9)	-12.3 (0.9)	-1.2 (-3.6, 1.3)	
60 to <90 mL/min/1.73-m^2 (n=436)	70.9 (7.2)	69.7 (6.9)	55.1 (10.3)	58.1 (11.0)	-15.3 (0.8)	-11.5 (0.8)	-3.7 (-5.9, -1.6)	0.308
<60 mL/min/1.73-m^2 (n=106)	69.4 (8.1)	70.0 (5.7)	54.9 (12.5)	57.3 (10.3)	-14.9 (1.6)	-11.7 (1.7)	-3.2 (-7.8, 1.5)	

BIAsp, biphasic insulin aspart; CI confidence interval; eGFR, estimated glomerular filtration rate; FRC, fixed-ratio combination; iGlarLixi, FRC of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; ITT, intent to treat; LS, least squares; SD, standard deviation; SE, standard error.

Supplementary table 3. Change in body weight from baseline to Week 26 by baseline characteristics subgroups (ITT population).

	Body Weight, kg							
	Baseline, mean (SD)		Week 26, mean (SD)		Change from baseline to Week 26, LS mean (SE)		LS mean difference (95% CI)	Heterogeneity p-value
	iGlarLixi (n=443)	BIAsp 30 (n=444)	iGlarLixi (n=443)	BIAsp 30 (n=444)	iGlarLixi (n=443)	BIAsp 30 (n=444)		
Age subgroups								
<65 years (n=573)	81.8 (17.6)	83.0 (19.3)	81.3 (17.7)	84.1 (19.9)	-0.4 (0.2)	1.2 (0.2)	-1.7 (-2.2, -1.1)	0.188
≥65 years (n=314)	78.8 (14.5)	80.7 (16.6)	78.3 (14.4)	82.0 (17.2)	-0.8 (0.3)	1.4 (0.3)	-2.2 (-2.9 -1.5)	
Diabetes duration subgroups								
<10 years (n=305)	81.9 (19.0)	83.9 (20.3)	82.0 (19.0)	85.0 (20.8)	0.0 (0.3)	1.3 (0.3)	-1.3 (-2.0, -0.6)	0.052
≥10 years (n=582)	80.1 (15.1)	81.3 (17.4)	79.3 (15.2)	82.5 (18.0)	-0.9 (0.2)	1.3 (0.2)	-2.2 (-2.7, -1.6)	
Basal insulin dose subgroups								
<30 U/day (n=316)	78.9 (16.1)	77.8 (17.2)	78.4 (16.1)	79.3 (17.6)	-1.7 (0.7)	0.5 (0.7)	-2.1 (-2.8, -1.4)	0.362
≥30 U/day (n=571)	81.7 (16.7)	84.6 (18.7)	81.2 (16.8)	85.6 (19.4)	0.1 (0.4)	1.8 (0.4)	-1.7 (-2.2, -1.2)	
HbA1c subgroups								
7.5–8.0 % (n=238)	80.3 (17.4)	85.4 (20.2)	79.3 (17.2)	86.8 (20.9)	-0.9 (0.4)	1.6 (0.4)	-2.4 (-3.2, -1.6)	
>8.0–9.0 % (n=403)	82.3 (16.6)	81.9 (16.8)	81.7 (16.8)	82.8 (17.5)	-0.6 (0.3)	1.0 (0.3)	-1.6 (-2.2, -1.0)	0.243
>9.0–10.0 % (n=246)	78.8 (15.6)	79.4 (19.1)	78.9 (15.8)	80.6 (19.1)	-0.3 (0.3)	1.6 (0.3)	-1.8 (-2.6, -1.1)	
BMI subgroups								
<25 kg/m^2 (n=148)	62.0 (8.7)	61.7 (8.4)	62.0 (9.0)	63.0 (8.8)	0.2 (0.4)	1.7 (0.4)	-1.5 (-2.5, -0.6)	
25–<30 kg/m^2 (n=345)	75.0 (10.0)	74.9 (10.2)	74.4 (10.1)	76.1 (10.9)	-0.5 (0.2)	1.2 (0.3)	-1.7 (-2.4, -1.1)	0.609
30–<35 kg/m^2 (n=237)	88.0 (11.2)	90.1 (12.3)	87.4 (11.7)	91.6 (13.3)	-0.8 (0.3)	1.5 (0.3)	-2.3 (-3.1, -1.5)	
≥35 kg/m^2 (n=156)	102.2 (14.7)	103.9 (15.5)	101.4 (15.3)	105.1 (16.8)	-1.0 (0.4)	0.8 (0.4)	-1.8 (-2.8, -0.8)	
eGFR subgroups								
≥90 mL/min/1.73-m^2 (n=318)	77.3 (15.4)	81.7 (19.9)	77.4 (15.4)	83.4 (20.6)	-0.2 (0.3)	1.6 (0.2)	-1.7 (-2.4, -1.1)	
60 to <90 mL/min/1.73-m^2 (n=436)	82.5 (16.7)	82.7 (18.3)	81.8 (16.7)	83.5 (18.7)	-0.6 (0.2)	1.1 (0.2)	-1.7 (-2.3, -1.1)	0.300
<60 mL/min/1.73-m^2 (n=106)	79.4 (15.6)	80.9 (13.9)	77.8 (16.4)	81.6 (14.2)	-1.6 (0.4)	1.1 (0.5)	-2.7 (-3.9, -1.5)	

BIAsp, biphasic insulin aspart; CI confidence interval; eGFR, estimated glomerular filtration rate; FRC, fixed-ratio combination; iGlarLixi, FRC of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; ITT, intent to treat; LS, least squares; SD, standard deviation; SE, standard error.

Supplementary table 4. Change in insulin dose from baseline to Week 26 by baseline characteristics subgroups (ITT population).

	Total daily insulin dose, U/day							
	Baseline, mean (SD)		Week 26, mean (SD)		Change from baseline to Week 26, LS mean (SE)		LS mean difference (95% CI)	Heterogeneity p-value
	iGlarLixi (n=443)	BIAsp 30 (n=444)	iGlarLixi (n=443)	BIAsp 30 (n=444)	iGlarLixi (n=443)	BIAsp 30 (n=444)		
Age subgroups								
<65 years (n=573)	26.4 (5.9)	33.7 (11.3)	39.1 (13.5)	54.2 (27.6)	12.9 (11.2)	24.8 (17.5)	-11.9 (-47.4, 23.6)	0.991
≥65 years (n=314)	26.5 (6.8)	33.2 (10.5)	36.6 (14.6)	53.4 (26.8)	10.7 (19.2)	22.9 (10.6)	-12.2 (-48.9, 24.4)	
Diabetes duration subgroups								
<10 years (n=305)	26.2 (6.5)	32.3 (10.8)	38.6 (14.4)	54.5 (28.3)	11.7 (16.7)	26.2 (20.0)	-14.5 (-49.5, 20.4)	0.804
≥10 years (n=582)	26.5 (6.1)	34.2 (11.1)	38.0 (13.7)	53.6 (26.8)	12.4 (12.7)	23.1 (11.6)	-10.8 (-40.6, 19.1)	
Basal insulin dose subgroups								
<30 U/day (n=316)	20.2 (2.8)	23.4 (4.7)	30.7 (11.7)	40.4 (20.8)	4.7 (35.0)	15.4 (37.9)	-10.7 (-50.5, 29.2)	0.909
≥30 U/day (n=571)	29.9 (4.7)	39.1 (9.4)	42.4 (13.4)	61.4 (27.7)	16.0 (23.3)	29.3 (21.3)	-13.3 (-46.7, 20.1)	
HbA1c subgroups								
7.5–8.0 % (n=238)	25.4 (5.8)	31.9 (10.9)	34.7 (13.9)	50.1 (22.9)	10.6 (17.2)	23.0 (14.1)	-12.4 (-55.3, 30.6)	
>8.0–9.0 % (n=403)	27.0 (6.5)	34.2 (10.8)	39.6 (14.1)	55.3 (29.2)	12.1 (15.5)	24.0 (23.0)	-12.0 (-50.9, 27.0)	1.000
>9.0–10.0 % (n=246)	26.6 (6.2)	34.1 (11.5)	39.4 (13.3)	55.6 (27.9)	13.5 (14.7)	25.9 (15.2)	-12.3 (-45.6, 20.9)	
BMI subgroups								
<25 kg/m^2 (n=148)	25.9 (5.1)	30.9 (9.9)	34.5 (11.9)	48.9 (22.4)	7.1 (16.2)	18.5 (19.2)	-11.4 (-47.4, 24.5)	
25–<30 kg/m^2 (n=345)	26.0 (6.4)	33.0 (10.1)	36.0 (13.0)	50.9 (23.3)	10.1 (15.0)	21.8 (17.2)	-11.7 (-47.0, 23.6)	0.994
30–<35 kg/m^2 (n=237)	27.1 (6.9)	33.9 (11.7)	39.7 (14.7)	57.6 (33.4)	13.5 (18.8)	29.8 (14.3)	-16.3 (-60.2, 27.6)	
≥35 kg/m^2 (n=156)	27.0 (5.4)	36.6 (12.2)	45.5 (14.1)	59.5 (28.5)	18.5 (17.0)	28.2 (17.2)	-9.7 (-56.3, 37.0)	
eGFR subgroups								
≥90 mL/min/1.73-m^2 (n=318)	26.4 (6.3)	31.6 (10.8)	38.5 (13.4)	52.2 (25.7)	11.8 (17.6)	24.6 (15.3)	-12.8 (-50.0, 24.4)	
60 to <90 mL/min/1.73-m^2 (n=436)	26.2 (6.2)	34.7 (10.4)	38.9 (13.7)	55.8 (27.2)	12.5 (10.5)	25.0 (11.5)	-12.5 (-39.7, 14.8)	0.999
<60 mL/min/1.73-m^2 (n=106)	27.9 (5.8)	32.2 (10.5)	34.8 (16.3)	49.5 (27.1)	9.9 (32.2)	21.5 (31.9)	-11.6 (-82.5, 59.2)	

BIAsp, biphasic insulin aspart; CI confidence interval; eGFR, estimated glomerular filtration rate; FRC, fixed-ratio combination; iGlarLixi, FRC of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; ITT, intent to treat; LS, least squares; SD, standard deviation; SE, standard error.

Supplementary table 5. Incidence and rate of hypoglycaemia ADA Level 2[a] by baseline characteristics subgroups (safety population).

	Incidence, % (n)		OR (95% CI)	Heterogeneity p-value	Rate per participant year		RR (95% CI)	Heterogeneity p-value
	iGlarLixi	BIAsp 30			iGlarLixi	BIAsp 30		
Age subgroups								
Number of participants	442	441			442	441		
<65 years (n=572)	5.0 (14)	11.6 (34)	0.40 (0.21, 0.77)	0.665	0.11	0.49	0.23 (0.10, 0.49)	0.102
≥65 years (n=311)	8.6 (14)	15.5 (23)	0.50 (0.24, 1.01)		0.51	0.69	0.58 (0.25, 1.35)	
Diabetes duration subgroups								
Number of participants	442	441			442	441		
<10 years (n=303)	4.6 (7)	7.3 (11)	0.64 (0.24, 1.71)	0.408	0.14	0.34	0.34 (0.12, 0.97)	0.722
≥10 years (n=580)	7.2 (21)	15.9 (46)	0.40 (0.23, 0.69)		0.31	0.67	0.42 (0.22, 0.82)	
Basal insulin dose subgroups								
Number of participants	442	441			442	441		
<30 U/day (n=313)	9.6 (15)	14.7 (23)	0.62 (0.31, 1.24)	0.248	0.50	0.61	0.92 (0.40, 2.13)	0.011
≥30 U/day (n=570)	4.6 (13)	11.9 (34)	0.35 (0.18, 0.68)		0.11	0.53	0.21 (0.10, 0.45)	
HbA1c subgroups								
Number of participants	442	441			442	441		
7.5–8.0 % (n=238)	8.5 (10)	10.0 (12)	0.84 (0.34, 2.03)		0.32	0.40	0.72 (0.25, 2.08)	
>8.0–9.0 % (n=401)	5.7 (11)	15.4 (32)	0.33 (0.16, 0.68)	0.275	0.27	0.67	0.37 (0.16, 0.85)	0.407
>9.0–10.0 % (n=244)	5.3 (7)	11.5 (13)	0.43 (0.16, 1.11)		0.16	0.52	0.26 (0.09, 0.79)	
BMI subgroups[b]								
Number of participants	441	441			441	441		
<25 kg/m^2 (n=147)	10.1 (7)	19.2 (15)	0.46 (0.18, 1.22)		0.31	0.86	0.27 (0.07, 0.97)	
25–<30 kg/m^2 (n=344)	7.8 (14)	14.0 (23)	0.52 (0.25, 1.04)	0.803	0.32	0.62	0.48 (0.21, 1.10)	0.707
30–<35 kg/m^2 (n=236)	3.2 (4)	10.8 (12)	0.27 (0.08, 0.86)		0.21	0.35	0.54 (0.17, 1.72)	
≥35 kg/m^2 (n=155)	4.5 (3)	8.0 (7)	0.55 (0.14, 2.24)		0.09	0.42	0.22 (0.04, 1.10)	
eGFR subgroups[c]								
Number of participants	427	429			427	429		
≥90 mL/min/1.73-m^2 (n=317)	4.0 (6)	10.1 (17)	0.38 (0.15, 1.00)		0.13	0.32	0.40 (0.14, 1.13)	
60 to <90 mL/min/1.73-m^2 (n=433)	6.3 (14)	14.6 (31)	0.38 (0.20, 0.75)	0.661	0.25	0.71	0.31 (0.14, 0.67)	0.655
<60 mL/min/1.73-m^2 (n=106)	12.3 (7)	16.3 (8)	0.68 (0.22, 2.07)		0.61	0.80	0.66 (0.16, 2.80)	

[a]All confirmed <54 mg/dL (<3.0 mmol/L). [b]For one patient, BMI value was missing at baseline. [c]For 27 patients, eGFR values were missing at baseline.

ADA, American Diabetes Association; BIAsp, biphasic insulin aspart; CI confidence interval; eGFR, estimated glomerular filtration rate; FRC, fixed-ratio combination; iGlarLixi, FRC of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; OR, odds ratio; RR, rate ratio.

Supplementary table 6. Incidence and rate of hypoglycaemia ADA Level 1[a] by baseline characteristics subgroups (safety population).

	Incidence, % (n)		OR (95% CI)	Heterogeneity p-value	Rate per participant year		RR (95% CI)	Heterogeneity p-value
	iGlarLixi	BIAsp 30			iGlarLixi	BIAsp 30		
Age subgroups								
Number of participants	442	441			442	441		
<65 years (n=572)	24.0 (67)	35.5 (104)	0.57 (0.40, 0.82)	0.711	1.41	2.27	0.65 (0.44, 0.98)	0.726
≥65 years (n=311)	28.8 (47)	44.6 (66)	0.51 (0.32, 0.81)		3.13	3.94	0.74 (0.44, 1.24)	
Diabetes duration subgroups								
Number of participants	442	441			442	441		
<10 years (n=303)	19.7 (30)	30.5 (46)	0.56 (0.33, 0.95)	0.953	1.36	1.95	0.76 (0.43, 1.33)	0.819
≥10 years (n=580)	29.0 (84)	42.8 (124)	0.55 (0.39, 0.77)		2.39	3.27	0.70 (0.47, 1.03)	
Basal insulin dose subgroups								
Number of participants	442	441			442	441		
<30 U/day (n=313)	26.1 (41)	32.7 (51)	0.73 (0.45, 1.19)	0.176	2.45	3.00	0.87 (0.51, 1.49)	0.354
≥30 U/day (n=570)	25.6 (73)	41.8 (119)	0.48 (0.34, 0.68)		1.79	2.73	0.64 (0.43, 0.95)	
HbA1c subgroups								
Number of participants	442	441			442	441		
7.5–8.0 % (n=238)	27.1 (32)	35.0 (42)	0.69 (0.40, 1.20)		2.90	2.57	1.16 (0.63, 2.14)	
>8.0–9.0 % (n=401)	25.4 (49)	41.3 (86)	0.48 (0.31, 0.74)	0.594	1.70	3.02	0.59 (0.36, 0.95)	0.171
>9.0–10.0 % (n=244)	25.2 (33)	37.2 (42)	0.57 (0.33, 0.99)		1.74	2.74	0.57 (0.31, 1.06)	
BMI subgroups[b]								
Number of participants	441	441			441	441		
<25 kg/m^2 (n=147)	39.1 (27)	47.4 (37)	0.70 (0.36, 1.36)		4.33	4.60	0.85 (0.41, 1.77)	
25–<30 kg/m^2 (n=344)	27.8 (50)	43.4 (71)	0.50 (0.32, 0.78)	0.419	1.95	3.59	0.54 (0.33, 0.88)	0.368
30–<35 kg/m^2 (n=236)	16.8 (21)	33.3 (37)	0.40 (0.22, 0.74)		1.26	1.28	1.09 (0.57, 2.07)	
≥35 kg/m^2 (n=155)	23.9 (16)	28.4 (25)	0.81 (0.39, 1.69)		1.26	1.73	0.79 (0.36, 1.73)	
eGFR subgroups[c]								
Number of participants	427	429			427	429		
≥90 mL/min/1.73-m^2 (n=317)	26.8 (40)	34.5 (58)	0.68 (0.42, 1.10)		1.75	2.41	0.75 (0.44, 1.28)	
60 to <90 mL/min/1.73-m^2 (n=433)	24.0 (53)	39.6 (84)	0.49 (0.32, 0.74)	0.485	1.74	3.06	0.57 (0.36, 0.91)	0.419
<60 mL/min/1.73-m^2 (n=106)	28.1 (16)	46.9 (23)	0.43 (0.19, 0.96)		4.16	3.61	1.10 (0.45, 2.73)	

[a]All confirmed <70 mg/dL (<3.9 mmol/L) and ≥54 mg/dL (≥3.0 mmol/L). [b]For one patient, BMI value was missing at baseline. [c]For 27 patients, eGFR values were missing at baseline.
ADA, American Diabetes Association; BIAsp, biphasic insulin aspart; CI confidence interval; eGFR, estimated glomerular filtration rate; FRC, fixed-ratio combination; iGlarLixi, FRC of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; OR, odds ratio; RR, rate ratio.

Supplementary table 7. Proportion of participants reaching target HbA1c and composite endpoints by subgroups (ITT population).

Baseline subgroup	Participants who reached HbA1c <7.0 %[a]				Participants who reached HbA1c <7.0 % without weight gain[a]				Participants who reached HbA1c <7.0 % without weight gain and without hypoglycaemia[a]			
	iGlarLixi n (%)	BIAsp 30 n (%)	OR (95% CI)	P value	iGlarLixi n (%)	BIAsp 30 n (%)	OR (95% CI)	P value	iGlarLixi n (%)	BIAsp 30 n (%)	OR (95% CI)	P value
Age, years												
<65	118 (42.3)	94 (32.0)	1.65 (1.16, 2.35)	0.965	74 (26.5)	34 (11.6)	2.94 (1.87, 4.63)	0.764	56 (20.1)	20 (6.8)	3.68 (2.13, 6.37)	0.635
≥65	69 (42.1)	47 (31.3)	1.67 (1.04, 2.70)		48 (29.3)	21 (14.0)	2.63 (1.47, 4.70)		30 (18.3)	11 (7.3)	2.95 (1.41, 6.17)	
Diabetes duration, years												
<10	72 (47.1)	56 (36.8)	1.63 (1.02, 2.61)	0.929	43 (28.1)	21 (13.8)	2.62 (1.45, 4.73)	0.754	35 (22.9)	12 (7.9)	3.79 (1.86, 7.71)	0.706
≥10	115 (39.7)	85 (29.1)	1.67 (1.17, 2.38)		79 (27.2)	34 (11.6)	2.95 (1.89, 4.62)		51 (17.6)	19 (6.5)	3.18 (1.82, 5.57)	
Basal insulin dose, U/day												
<30	61 (38.6)	49 (31.0)	1.49 (0.92, 2.40)	0.596	45 (28.5)	21 (13.3)	2.76 (1.54, 4.96)	0.923	32 (20.3)	14 (8.9)	2.77 (1.40, 5.48)	0.436
≥30	126 (44.2)	92 (32.2)	1.75 (1.23, 2.48)		77 (27.0)	34 (11.9)	2.87 (1.83, 4.50)		54 (18.9)	17 (5.9)	3.95 (2.21, 7.05)	
HbA1c, %												
7.5–8.0 (58–64 mmol/mol)	60 (50.8)	57 (47.5)	1.13 (0.68, 1.88)	0.194	45 (38.1)	26 (21.7)	2.21 (1.24, 3.93)	0.566	30 (25.4)	14 (11.7)	2.72 (1.35, 5.50)	0.655
>8.0–9.0 (>64–75 mmol/mol)	91 (47.2)	64 (30.5)	2.06 (1.37, 3.11)		53 (27.5)	22 (10.5)	3.27 (1.90, 5.63)		40 (20.7)	14 (6.7)	3.69 (1.93, 7.04)	
>9.0–10.0 (>75–86 mmol/mol)	36 (27.3)	20 (17.5)	1.77 (0.96, 3.29)		24 (18.2)	7 (6.1)	3.39 (1.40, 8.20)		16 (12.1)	3 (2.6)	5.11 (1.45, 18.04)	
BMI, kg/m²												
<25	24 (34.3)	23 (29.5)	1.20 (0.59, 2.44)	0.675	16 (22.9)	6 (7.7)	3.54 (1.28, 9.74)	0.585	8 (11.4)	4 (5.1)	2.34 (0.67, 8.21)	0.626
25–<30	80 (44.4)	52 (31.5)	1.92 (1.22, 3.03)		51 (28.3)	23 (13.9)	2.68 (1.54, 4.68)		35 (19.4)	12 (7.3)	3.33 (1.65, 6.70)	
30–<35	55 (44.0)	36 (32.1)	1.80 (1.04, 3.11)		37 (29.6)	12 (10.7)	3.80 (1.84, 7.83)		30 (24.0)	7 (6.3)	5.18 (2.15, 12.46)	
≥35	28 (41.8)	30 (33.7)	1.40 (0.71, 2.75)		18 (26.9)	14 (15.7)	1.83 (0.83, 4.12)		13 (19.4)	8 (9.0)	2.38 (0.91, 6.21)	
eGFR, mL/min/1.73-m²												
≥90	62 (41.3)	52 (31.0)	1.59 (0.99, 2.55)	0.692	34 (22.7)	15 (8.9)	3.10 (1.59, 6.01)	0.919	23 (15.3)	11 (6.5)	2.78 (1.29, 5.99)	0.850
60 to <90	96 (43.4)	71 (33.0)	1.75 (1.17, 2.62)		64 (29.0)	31 (14.4)	2.62 (1.61, 4.27)		48 (21.7)	16 (7.4)	3.69 (2.00, 6.78)	
<60	24 (42.1)	18 (36.7)	1.18 (0.53, 2.64)		21 (36.8)	9 (18.4)	2.63 (1.05, 6.60)		12 (21.1)	4 (8.2)	3.11 (0.92, 10.51)	

[a]Logistic regression model adjusting for treatment groups, randomization strata at screening visit, subgroup and subgroup-by-treatment group interaction, as well as fixed continuous covariates of baseline values of HbA_{1c}. Imputed as not reaching target (non-responder) in case of missing Week 26 HbA_{1c} values.

BIAsp, biphasic insulin aspart; BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; iGlarLixi, fixed-ratio combination of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; ITT, intent to treat; OR, odds ratio.