## **Supplementary Materials**

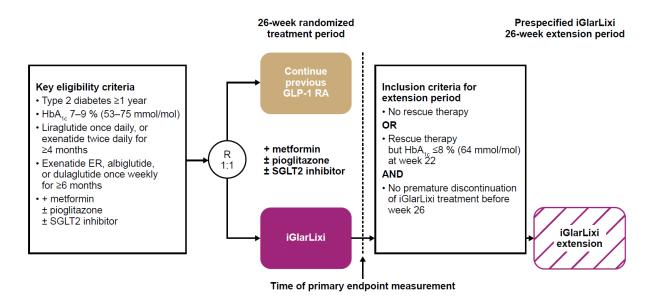
	Participants randomized to initial 26-week treatment period		Participants in the 26-week extension period (0–52 weeks)
	GLP-1 RA	iGlarLixi	iGlarLixi
	(n = 256)	(n = 255)	(n = 206)
Any AE	121 (47.3)	163 (63.9)	150 (72.8)
Participants with any serious AE	9 (3.5)	10 (3.9)	21 (10.2)
Participants with any AE leading to death	0	0	1 (0.5)
Gastrointestinal disorders (overall)	26 (10.2)	55 (21.6)	51 (24.8)
Nausea	6 (2.3)	22 (8.6)	19 (9.2)
Diarrhea	6 (2.3)	14 (5.5)	15 (7.3)
Vomiting	2 (0.8)	8 (3.1)	8 (3.9)
Documented symptomatic (≤3.9 mmol/L) hypoglycemia			
Number of participants with events	6 (2.3)	71 (27.8)	74 (35.9)
Events per participant-year	0.08	1.54	1.59
Documented symptomatic (<3.0 mmol/L) hypoglycemia			
Number of participants with events	1 (0.4)	24 (9.4)	37 (18.0)
Events per participant-year	<0.01	0.25	0.24

**Table S1**—AEs\* and hypoglycemic events in the safety population.

Data are n (%) unless otherwise stated. \*AEs listed are treatment-emergent AEs.

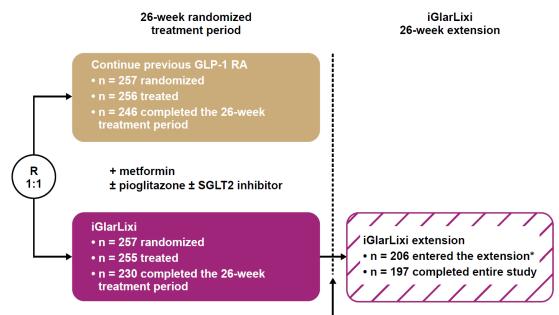
AE, adverse event; GLP-1 RA, glucagon-like peptide-1 receptor agonist; iGlarLixi, titratable fixed-ratio combination of basal insulin glargine 100 units/mL and the GLP-1 RA lixisenatide.

## Figure S1—Study design.



ER, extended release; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA<sub>1c</sub>, glycated hemoglobin; iGlarLixi, titratable fixed-ratio combination of basal insulin glargine 100 units/mL and the GLP-1 RA lixisenatide; R, randomization; SGLT2, sodium glucose cotransporter 2.

## Figure S2—Patient disposition.



Time of primary endpoint measurement

\*Five participants who entered the extension phase had received rescue therapy during the main treatment period but had an HbA<sub>1c</sub>  $\leq$ 8 % (64 mmol/mol) at week 22. The rescue therapies received were insulin glulisine (n=2), insulin lispro (n=1), glimepiride (n=1), and glipizide (n=1).

GLP-1 RA, glucagon-like peptide-1 receptor agonist; iGlarLixi, titratable fixed-ratio combination of basal insulin glargine 100 units/mL and the GLP-1 RA lixisenatide; R, randomization; SGLT2, sodium glucose co-transporter 2.