SUPPLEMENTARY DATA

Supplementary information

In total, 7 patients died during the study: 2 patients in the iGlarLixi group, 4 patients in the iGlar group, and 1 patient in the Lixi group. None of the fatal events were considered related to the investigational drugs by the investigator.

Six of 7 patients died due to treatment-emergent adverse events (TEAEs): 2 patients (0.4%) in the iGlarLixi group, 3 patients (0.6%) in the iGlar group, and 1 patient (0.4%) in the Lixi group; 1 patient in the iGlarLixi group and 1 patient in the iGlar group died post-treatment due to TEAEs.

In the iGlarLixi group: a 64-year-old male patient died from metastatic lung cancer and a 72-year-old male patient died from congestive cardiac failure. In the iGlar group, a 55-year-old male patient died from acute myocardial infarction and acute pulmonary edema, a 62-year-old male patient died from acute cardiac failure, and a 60-year-old male patient died about 3 months after the treatment period due to the worsening of undifferentiated keratinized squamous cell carcinoma in the mouth which was diagnosed during the on-treatment period. A 70-year-old male patient in the iGlar group died due to the post-treatment AE of gastrointestinal hemorrhage. In the Lixi group, a 63-year-old female patient was reported to be found dead on her bed due to unknown reasons 208 days after the first dose of the study drug. An autopsy was not performed.

Supplementary Table 1. Summary of clinical laboratory parameters

	iGlarLixi (n=468)	iGlar (n=467)	Lixi (n=233)
Lipase ≥3 × ULN	4/468 (0.9%)	6/462 (1.3%)	5/231 (2.2%)
Amylase ≥3 × ULN	1/468 (0.2%)	1/462 (0.2%)	1/231 (0.4%)
Calcitonin			
≤ULN	437/461 (94.8%)	427/456 (93.6%)	203/223 (91.0%)
>ULN – <20 ng/L [pg/mL]	23/461 (5.0%)	27/456 (5.9%)	20/223 (9.0%)
≥20 – <50 ng/L [pg/mL]	1/461 (0.2%)	1/456 (0.2%)	0/223
≥50 ng/L [pg/mL]	0/461	1/456 (0.2%)	0/223
Creatinine ≥150 µmol/L (1.70 mg/dL)	2 (0.4%)	1 (0.2%)	0
Alanine aminotransferase			
>3 × ULN	2/462 (0.4%)	2/456 (0.4%)	1/223 (0.4%)
>5 × ULN	0/462	0/456	1/223 (0.4%)
Aspartate aminotransferase			
>3 × ULN	1/461 (0.2%)	2/455 (0.4%)	2/222 (0.9%)
>5 × ULN	0/461	0/455	1/222 (0.5%)
Alkaline phosphatase >1.5 × ULN	2/462 (0.4%)	3/456 (0.7%)	2/223 (0.9%)
Total bilirubin >1.5 × ULN	1/462 (0.2%)	1/456 (0.2%)	0/223

ULN, upper limit of normal.

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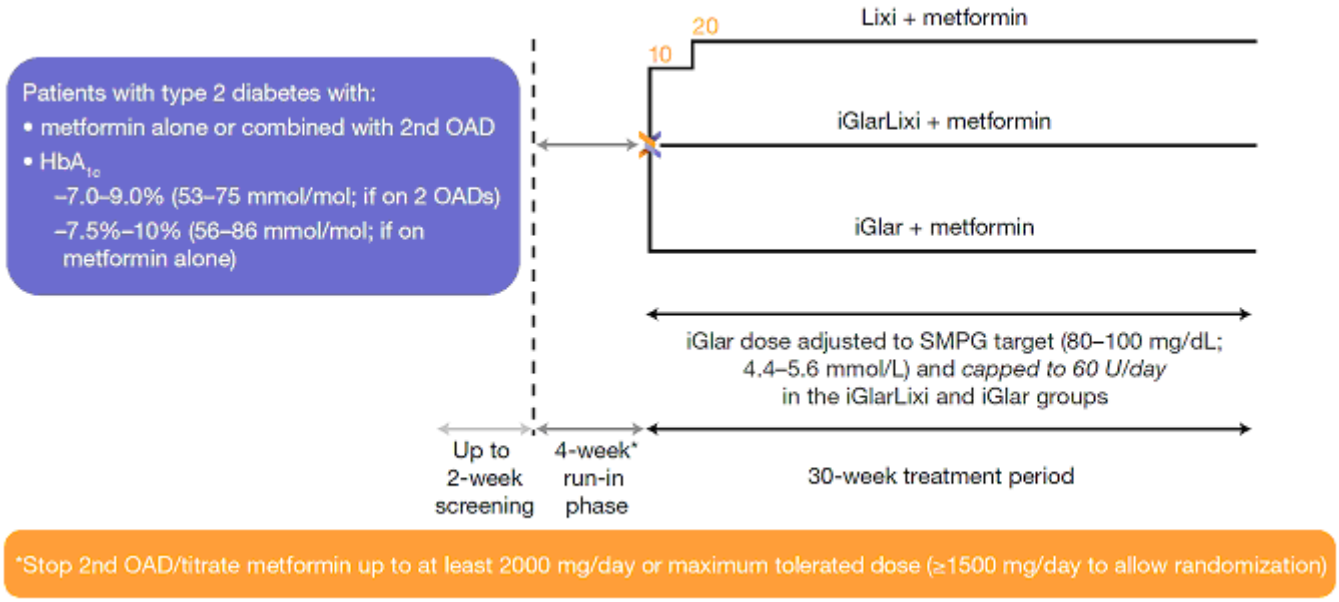
SUPPLEMENTARY DATA

Supplementary Figure 1. Schematic of study design



FPG, fasting plasma glucose; **iGlarLixi, titratable fixed-ratio combination iGlar:Lixi;** OAD, oral antidiabetic drug

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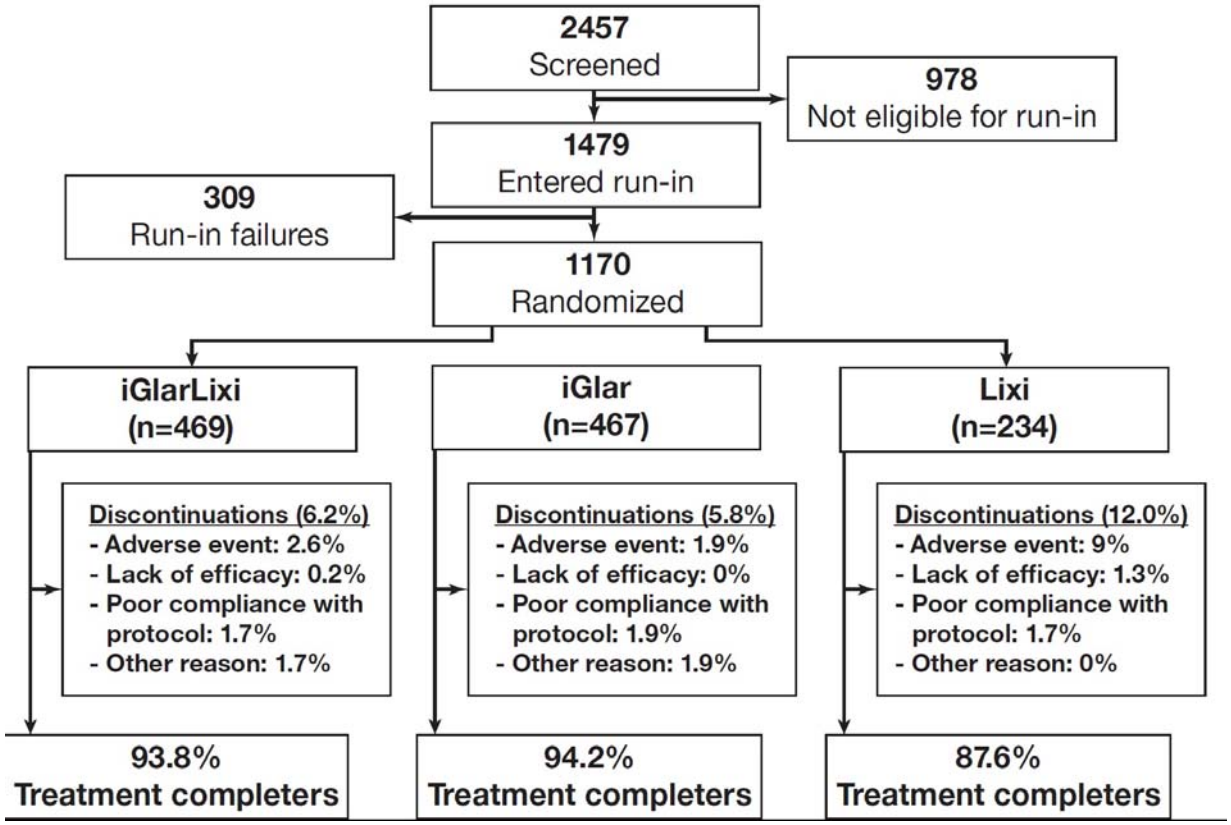
SUPPLEMENTARY DATA

Supplementary Figure 2. Patient disposition



One patient randomized to the Lixi group requested not to be treated and was excluded from the safety population.

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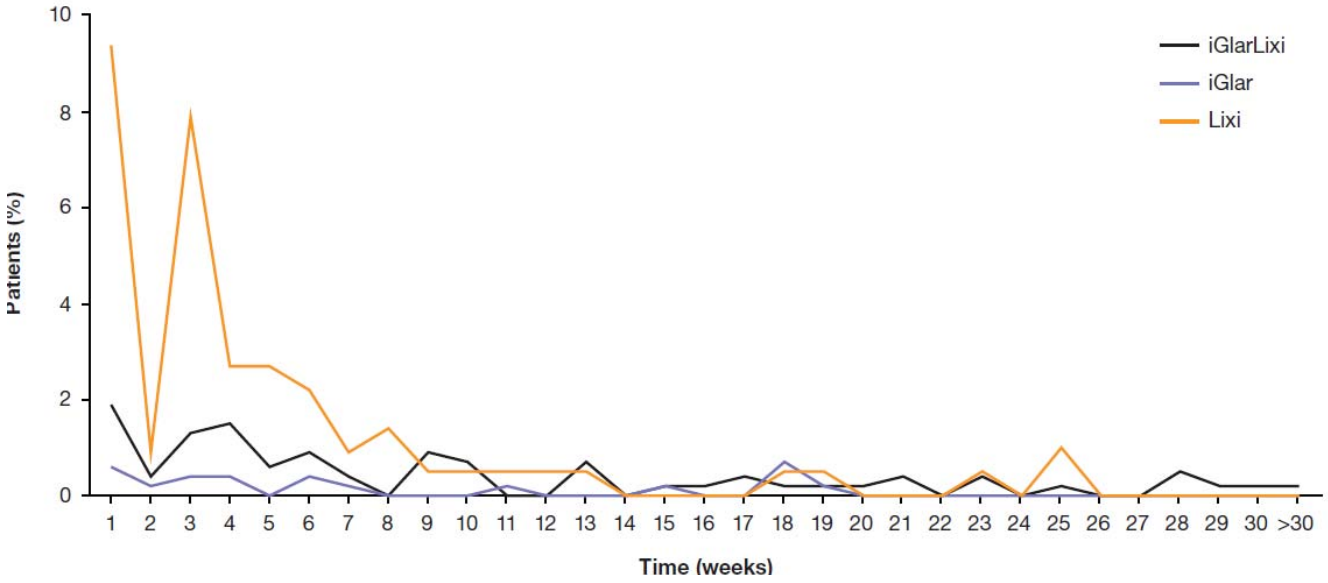
SUPPLEMENTARY DATA

Supplementary Figure 3. Nausea over time



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