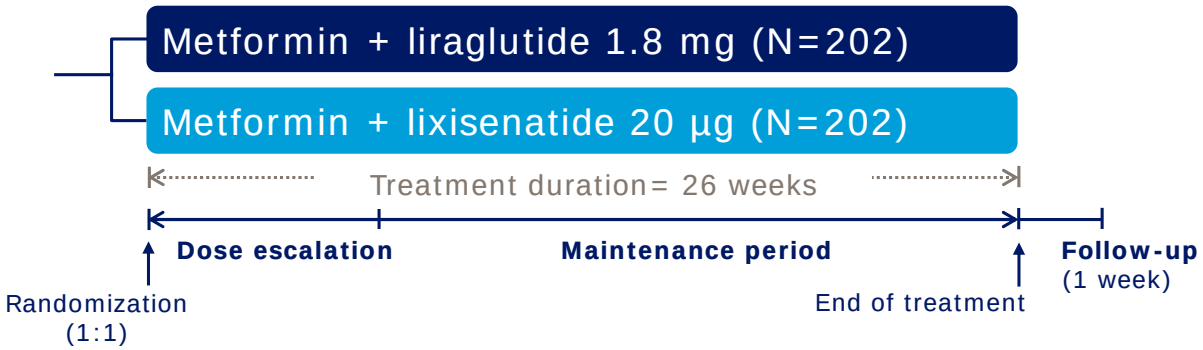
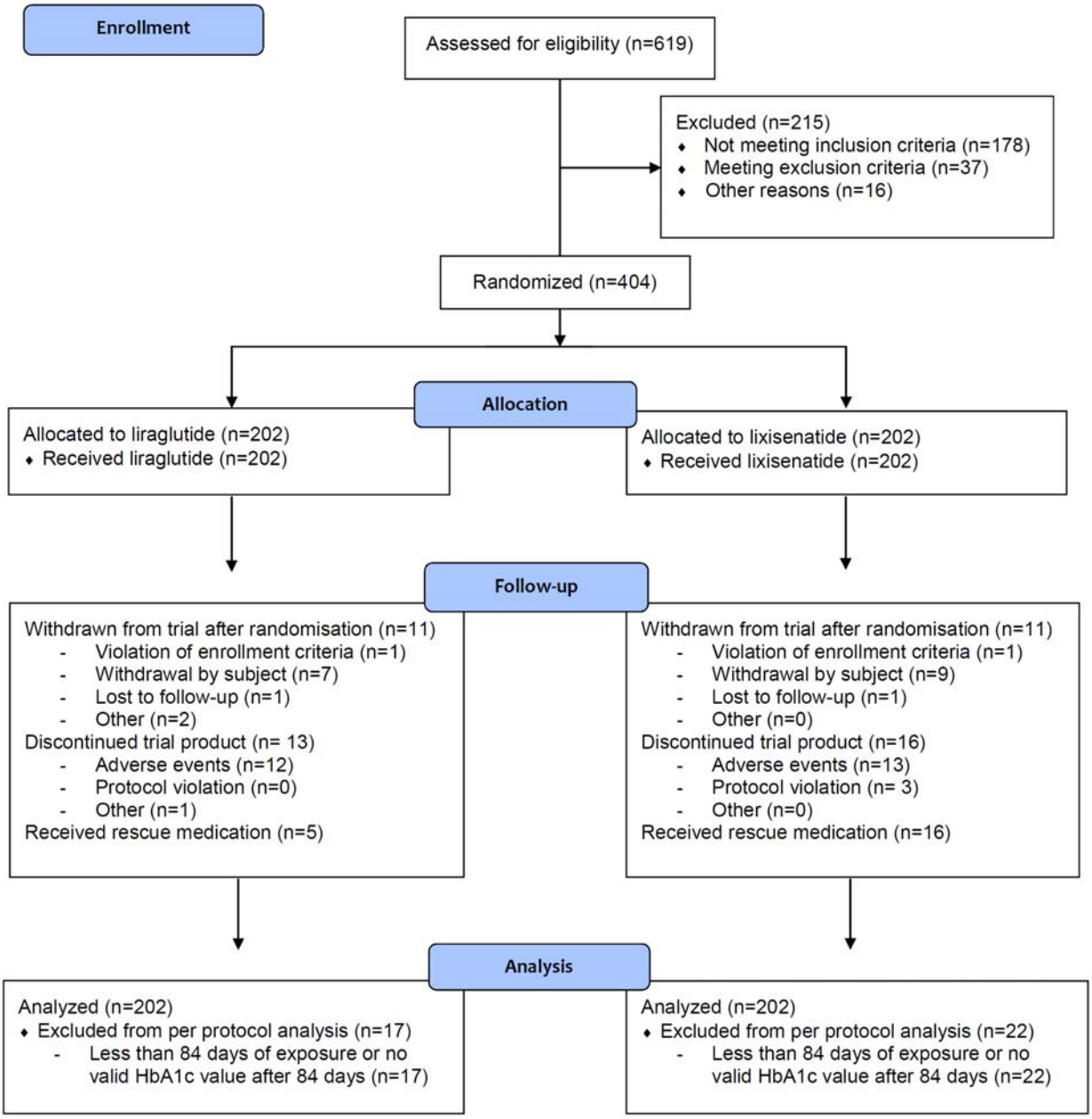
SUPPLEMENTARY DATA

Supplementary Figure S1. Trial design diagram



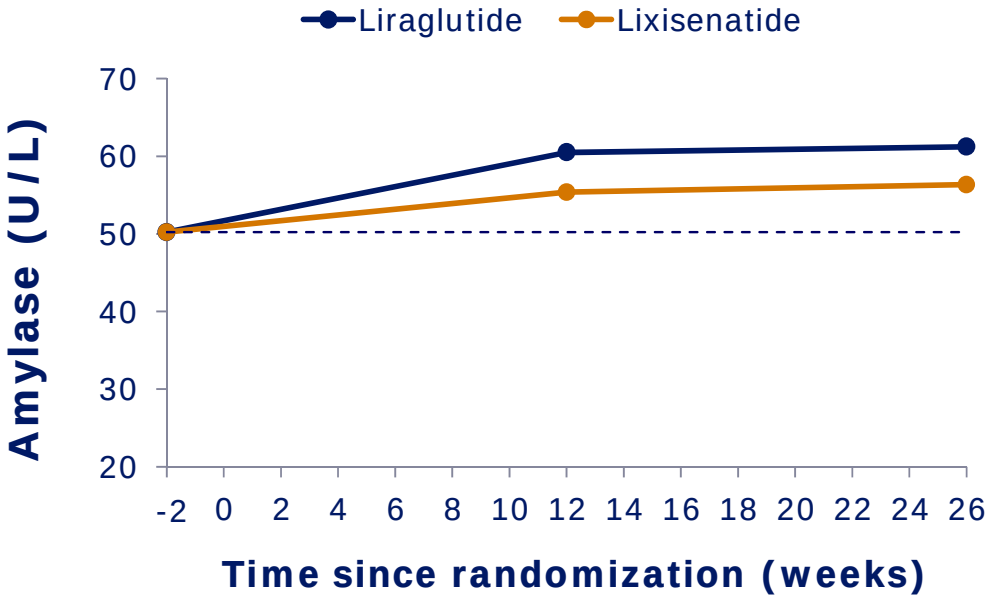
SUPPLEMENTARY DATA

Supplementary Figure S2. CONSORT trial flow diagram
CONSORT 2010 Flow Diagram



SUPPLEMENTARY DATA

Supplementary Figure S3. Amylase from week 0 to week 26
Normal range for amylase: 28-100 U/L;
Group mean estimated are from mixed model for repeated measurements (MMRM) log-transformed, with treatment, country and log-transformed baseline values, all nested within visit, and adjusted according to observed baseline distribution.



SUPPLEMENTARY DATA

Supplementary Table S1. Summary of adverse events and hypoglycemic episodes

	Liraglutide		Lixisenatide	
	N (%)	E	**N (%)**	E
Number of patients	202 (100)		202 (100)	
Total AE	145 (71.8)	540	129 (63.9)	435
Serious AEs	12 (5.9)	13	7 (3.5)	7
AE related discontinuations	13 (6.4)	20	15 (7.4)	20
Most common AEs (≥ 5% by preferred term)				
Nausea	44 (21.8)	67	44 (21.8)	60
Diarrhea	25 (12.4)	39	20 (9.9)	22
Vomiting	14 (6.9)	18	18 (8.9)	22
Dyspepsia	11 (5.4)	11	6 (3.0)	9
Nasopharyngitis	13 (6.4)	13	20 (9.9)	22
Headache	15 (7.4)	31	17 (8.4)	35
Lipase increased	17 (8.4)	17	5 (2.5)	5
Decreased appetite	13 (6.4)	13	5 (2.5)	5
Serious AEs (by preferred term)				
Coronary artery disease			1 (0.5)	1
Myocardial ischemia	1 (0.5)	1		
Atrial fibrillation			1 (0.5)	1
Cardiac failure			1 (0.5)	1
Gastric ulcer hemorrhage	1 (0.5)	1		
Esophageal ulcer hemorrhage	1 (0.5)	1		
Abdominal hernia	1 (0.5)	1		
Diabetic foot infection	1 (0.5)	1		
Lobar pneumonia			1 (0.5)	1
Influenza	1 (0.5)	1		
Ischemic stroke	1 (0.5)	1		
Syncope	1 (0.5)	1		
Pyrexia	1 (0.5)	1		
Cholecystitis acute	1 (0.5)	1		
Thermal burn			1 (0.5)	1
Rotator cuff syndrome	1 (0.5)	1		

SUPPLEMENTARY DATA

	Liraglutide		Lixisenatide	
	N (%)	E	**N (%)**	E
Acute myeloid leukemia	1 (0.5)	1		
Anxiety disorder due to a general medical condition			1 (0.5)	1
Prostatic dysplasia			1 (0.5)	1
Skin ulcer	1 (0.5)	1		
Hypoglycemic episodes				
Confirmed	3 (1.5)	4	5 (2.5)	8
ADA classification				
Severe	0	0	0	0
Documented symptomatic	7 (3.5)	11	8 (4.0)	21
Asymptomatic	8 (4.0)	16	5 (2.5)	18
Probable symptomatic	1 (0.5)	1	1 (0.5)	2
Relative	0	0	1 (0.5)	2
Unclassified	0	0	0	0

%, percentage of patients experiencing at least one event. Confirmed hypoglycemic episode: patients unable to treat themselves (severe hypoglycemic episode) and/or a plasma glucose reading <3.1 mmol/L (56 mg/dL). ADA, American Diabetes Association; AE, adverse event; E, number of events; N: number of patients experiencing at least one event

SUPPLEMENTARY DATA

Supplementary Table S2. Anti-drug antibodies

		Liraglutide		Lixisenatide	
		N	%	N	%
Week 0	Antibody negative	202	100.0	200	99.0
	Antibody positive	0		2	1.0
	Cross-reacting antibodies	0		1	0.5
	In vitro neutralizing	0		0	
Week 12	Antibody negative	186	100.0	64	35.8
	Antibody positive	0		115	64.2
	Cross-reacting antibodies	0		0	
	In vitro neutralizing	0		0	
Week 27	Antibody negative	182	98.9	45	24.6
	Antibody positive	2	1.1	138	75.4
	- Cross-reacting antibodies	0		1	0.5
	- Neutralizing antibodies	0		46	25.1

N, number of patients; %, percentage is based on visit group.

SUPPLEMENTARY DATA

List of investigators

From Czech Republic:
Alena Šmahelová, Klinika geriatrická a metabolická FNHK, Hradec Králové;
Martina Košková, Interní a diabetologická ordinace, Oblastní nemocnice, Mladá Boleslav;
Jitka Zemanová, Interní a diabetologická ordinace, Plzeň;
Renata Vetešníková, Diabetologická ordinace, Prostějov;
Anna Rancová, Interní a diabetologická ordinace, Olomouc;

From Finland:
Liisa Hiltunen, Oulun kaupungin diabetesvastaanotto, Keskustan terveysasema, Oulu;
Saale Pöykkö, Lapin Keskussairaala, Sisatautien poliklinikka, Rovaniemi;
Kirsi Sävelä, Porin kaupunginsairaala, Sisatautien poliklinikka, Pori;
Juha, Saltevo, Terveystalo Jyväskylä, Jyväskylä.

From France:
Bertrand Cariou, Hôpital Nord- Laënnec, Service d'Endocrinologie, Saint Herblain;
Pierre Serusclat, Groupe Hospitalier, Mutualiste des Portes du sud, Service d'Endocrinologie, Venissieux;
Sébastien Czernichow, Hôpital Ambroise Paré, Unité de nutrition, Billancourt;
Nathan Abenhaim, Cabinet Médical, Strasbourg;
Stéphane Le Mouel, Cabinet Médical, Hinx;
Guillaume Charpentier, Centre Hospitalier Sud, Francilien, Service d'Endocrino- Diabétologie, Corbeilessonnes;

From Germany:
Alain Barakat, Diabetologische Schwerpunktpraxis, Duisburg;
Hans-Peter Kempe, Diabetologie-Ludwigshafen, Ludwigshafen;
Babette Lorra, Diabetes- und Stoffwechselpraxis, Bochum, Bochum;
Michael Nauck, Diabeteszentrum Bad Lauterberg, Bad Lauterberg;
Armin Sammler, Gemeinschaftspraxis, Friedrichsthal;
Regina Tosch-Sisting, Studienzentrum in Berlin, Berlin;
Nicola Matejek, Internistische Gemeinschaftspraxis, Lampertheim;
Alexander Segner, Ingbert;

From Hungary:
Robert Takacs, SZTE I. Belgyógyászati, Klinika, Szeged;
Mihaly Dudas, Pandy Kalman Korhaz, Gyula;
Albert Szocs, Szocs Depot, Egészségügyi, Szolgáltató Kft., Budapest;
Gábor Fülöp, Pécsi Tudományegyetem, Klinikai KözpontII, Belgyógyászati Klinika, és Nephrológia Centrum, Pécs;
Gábor Nyirati, Bajai Szent Rókus, Kórház, II Belgyógyászat, Baja;
Krisztina Wudi, ClinDiab Egészségügyi, Szolgáltató és, Kereskedelmi Kft., Budapest;

From Italy:
Manfredi Rizzo, Universitario di Palermo, Palermo;
Annunziata Lapolla, UOC Diabetologia e, Dietetica, Padova;
Natalino Simioni, Servizio di Diabetologia, Azienda, Cittadella (PD);
Sebastiano Squatrito, Azienda Ospedaliera, Garibaldi, Diabetologia U.O.S., Catania;
Giuseppe Fatati, Struttura Semplice di, Diabetologia, Dietologia e, Nutrizione Clinica, Terni;

From Latvia:
Valdis Pirags, Pauls Stradins Clinical, University Hospital, Centre of Endocrinology, Riga;
Andra Valtere, Ambulatory part of Clinic, “Gailezers” of Riga Eastern Clinical University Hospital, Riga;

SUPPLEMENTARY DATA

Dace Teterovska, Private Practice of Endocrinology, Ogre;
Inese Strautina, Health Centre 4, Kr.Barona Street 117, Riga;
Inguta Stura, Jugla Medical Center, Riga;
Inta Leitane, Tornakalna Outpatient Clinic, Riga;

From Lithuania:
Natalija Denisova, Public establishment “Kauno Silainiu Outpatient Clinics”, Kaunas;
Romena Laukiene, Vilnius University Hospital, “Santariskiu Klinikos”, Centre of Endocrinology, Vilnius;
Andrej Levinger, Republican Klaipeda Hospital, Public Enterprise Consulting Clinic, Klaipeda;
Diilda Velickiene, Lithuanian Health Sciences University Hospital, Kaunas;
Ausra Sirutaviciene, Republican Siauliai Hospital, Siauliai;

From the United Kingdom:
Andrew Johnson, Southmead Hospital, Bristol;
Robert Andrews, Musgrove Park Hospital, Taunton;
Bijay Vaidya, Royal Devon & Exeter Hospital, Devon;
Thomas Barber, University Hospitals of Coventry and Warwickshire NHS Trust, Coventry;
Ann Millward, Diabetes Clinical Research Unit, Plymouth;
Glennis Williams, Grove Park Terrace, Chiswick;
Jeff Stoker, Bermuda Practice, Popley Basingstoke;
Khin Swe-Myint, James Paget University Hospital, Great Yarmouth;
Neil Paul, Ashfields Primary Care Centre, Sandbach;
Iskandar Idris, Royal Derby Hospital, Derby;
Sunil Nair, Diabetes Centre, Countess of Chester NHS Foundation Trust, Chester.