

## SUPPLEMENTARY MATERIALS

**Supplemental Table 1.** Use of concomitant antidiabetic agents

	At start of teneligliptin administration (n = 10,696)	At 3 years of teneligliptin administration (n = 6,772)	During the observation period (n = 10,696)
Monotherapy	5,863 (54.8%)	3,511 (51.8%)	5,126 (47.9%)
Sulfonylurea	2,366 (22.1%)	1,493 (22.0%)	2,685 (25.1%)
Biguanide	1,765 (16.5%)	1,374 (20.3%)	2,294 (21.4%)
$\alpha$ -GI	1,074 (10.0%)	689 (10.2%)	1,251 (11.7%)
Thiazolidine	790 (7.4%)	489 (7.2%)	945 (8.8%)
Insulin	726 (6.8%)	392 (5.8%)	821 (7.7%)
Glinide	381 (3.6%)	299 (4.4%)	596 (5.6%)
SGLT2 inhibitor	28 (0.3%)	285 (4.2%)	429 (4.0%)

Values are number (%) of patients

$\alpha$ -GI,  $\alpha$ -glucosidase inhibitor; SGLT2, sodium–glucose cotransporter 2

**Supplemental Table 2.** Patient characteristics according to baseline renal function grade

	G1 (n = 2,008)	G2 (n = 5,015)	G3a (n = 1,525)	G3b (n = 561)	G4 (n = 217)	G5 (n = 56)	Patients on dialysis (n = 156)
Sex, male/female	1,194 (59.5%)/ 814 (40.5%)	3,113 (62.1%)/ 1,902 (37.9%)	900 (59.0%)/ 625 (41.0%)	308 (54.9%)/ 253 (45.1%)	118 (54.4%)/ 99 (45.6%)	29 (51.8%)/ 27 (48.2%)	113 (72.4%)/ 43 (27.6%)
Age, years	56.7 ± 12.9 (2,008)	65.6 ± 10.9 (5,015)	72.2 ± 9.7 (1,525)	74.3 ± 9.9 (561)	74.5 ± 10.8 (217)	69.2 ± 11.8 (56)	67.6 ± 10.2 (156)
Duration of T2DM, years	5.65 ± 6.32 (1,408)	7.04 ± 7.55 (3,541)	9.00 ± 8.76 (1,022)	10.48 ± 9.07 (392)	13.64 ± 9.78 (129)	13.12 ± 11.26 (35)	16.65 ± 9.23 (82)
HbA1c, %	8.51 ± 1.93 (1,889)	7.64 ± 1.35 (4,715)	7.37 ± 1.20 (1,432)	7.30 ± 1.21 (536)	7.34 ± 1.38 (202)	6.87 ± 1.10 (53)	6.73 ± 1.13 (103)
GA, %	21.73 ± 7.01 (89)	19.46 ± 7.08 (242)	19.82 ± 5.73 (70)	21.91 ± 8.30 (42)	19.53 ± 5.83 (26)	20.24 ± 5.68 (16)	23.40 ± 5.03 (92)
FBG, mg/dL	169.1 ± 64.0 (739)	147.5 ± 47.6 (1,849)	143.3 ± 46.2 (541)	148.6 ± 45.8 (205)	140.0 ± 39.1 (68)	121.3 ± 28.6 (20)	152.1 ± 57.3 (33)
BMI, kg/m <sup>2</sup>	25.88 ± 5.11 (1,454)	25.07 ± 4.14 (3,483)	25.18 ± 4.14 (1,011)	25.15 ± 4.38 (400)	24.83 ± 4.36 (139)	23.84 ± 3.70 (36)	22.89 ± 3.16 (98)
eGFR, mL/min/1.73 m <sup>2</sup>	106.00 ± 16.10 (2,008)	74.28 ± 8.20 (5,015)	53.55 ± 4.23 (1,525)	38.57 ± 4.23 (561)	23.97 ± 4.22 (217)	8.91 ± 4.29 (56)	—
Diet therapy	1,534 (76.4%)	3,877 (77.3%)	1,162 (76.2%)	437 (77.9%)	170 (78.3%)	42 (75.0%)	141 (90.4%)
Exercise therapy	1,250 (62.3%)	3,110 (62.0%)	847 (55.5%)	303 (54.0%)	106 (48.8%)	26 (46.4%)	54 (34.6%)
Any diabetic complication	398 (19.8%)	1,080 (21.5%)	512 (33.6%)	286 (51.0%)	161 (74.2%)	39 (69.6%)	145 (92.9%)
Retinopathy	154 (7.7%)	420 (8.4%)	179 (11.7%)	105 (18.7%)	54 (24.9%)	20 (35.7%)	74 (47.4%)
Neuropathy	133 (6.6%)	454 (9.1%)	198 (13.0%)	109 (19.4%)	48 (22.1%)	12 (21.4%)	49 (31.4%)
Nephropathy	249 (12.4%)	672 (13.4%)	393 (25.8%)	255 (45.5%)	150 (69.1%)	37 (66.1%)	144 (92.3%)

Other complications

Hypertension	1,020 (50.8%)	3,092 (61.7%)	1,123 (73.6%)	481 (85.7%)	198 (91.2%)	49 (87.5%)	140 (89.7%)
Dyslipidaemia	1,312 (65.3%)	3,405 (67.9%)	1,087 (71.3%)	412 (73.4%)	160 (73.7%)	32 (57.1%)	70 (44.9%)
Heart disease	157 (7.8%)	781 (15.6%)	409 (26.8%)	204 (36.4%)	88 (40.6%)	18 (32.1%)	73 (46.8%)

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Values are number (%) of patients or mean  $\pm$  standard deviation (number of patients)

G, renal function grade; T2DM, type 2 diabetes mellitus; HbA1c, haemoglobin A1c; GA, glycated albumin; FBG, fasting blood glucose;

BMI, body mass index; eGFR, estimated glomerular filtration rate

**Supplemental Table 3.** Use of concomitant agents according to baseline renal function during the observation period

	G1 (n = 2,008)	G2 (n = 5,015)	G3a (n = 1,525)	G3b (n = 561)	G4 (n = 217)	G5 (n = 56)	Patients on dialysis (n = 156)
<b>Antidiabetic agents</b>							
Monotherapy	910 (45.3%)	2,414 (48.1%)	713 (46.8%)	245 (43.7%)	95 (43.8%)	34 (60.7%)	91 (58.3%)
Sulfonylurea	489 (24.4%)	1,277 (25.5%)	421 (27.6%)	158 (28.2%)	54 (24.9%)	7 (12.5%)	1 (0.6%)
Biguanide	569 (28.3%)	1,136 (22.7%)	282 (18.5%)	58 (10.3%)	16 (7.4%)	3 (5.4%)	0
α-GI	208 (10.4%)	558 (11.1%)	215 (14.1%)	92 (16.4%)	41 (18.9%)	7 (12.5%)	22 (14.1%)
Thiazolidine	200 (10.0%)	430 (8.6%)	148 (9.7%)	58 (10.3%)	7 (3.2%)	2 (3.6%)	0
Insulin	152 (7.6%)	347 (6.9%)	120 (7.9%)	69 (12.3%)	39 (18.0%)	10 (17.9%)	36 (23.1%)
Glinide	94 (4.7%)	287 (5.7%)	83 (5.4%)	44 (7.8%)	19 (8.8%)	5 (8.9%)	19 (12.2%)
SGLT2 inhibitor	119 (5.9%)	213 (4.2%)	41 (2.7%)	8 (1.4%)	2 (0.9%)	1 (1.8%)	0
<b>Other agents</b>							
Antihypertensive agents	762 (37.9%)	2,497 (49.8%)	936 (61.4%)	420 (74.9%)	168 (77.4%)	39 (69.6%)	121 (77.6%)
Antidyslipidaemic agents	693 (34.5%)	2,191 (43.7%)	755 (49.5%)	266 (47.4%)	111 (51.2%)	25 (44.6%)	42 (26.9%)
Erythropoiesis- stimulating agents	0	1 (<0.1%)	1 (0.1%)	8 (1.4%)	11 (5.1%)	6 (10.7%)	33 (21.2%)

Values are number (%) of patients

G, renal function grade; α-GI, α-glucosidase inhibitor; SGLT2, sodium–glucose cotransporter 2

**Supplemental Table 4.** ADRs and AEs of special interest in  $\geq 2$  patients (any ADR) or  $\geq 1$  patient(serious ADR) and other ADRs in  $\geq 10$  patients

Patients analysed for safety	10,696	
	All ADRs	Serious ADRs
<b>Hypoglycaemia-related ADRs</b>		
N (%)	38 (0.36%)	8 (0.07%)
per 100 patient-years	0.15	0.03
Hypoglycaemia	28 (0.26%)	6 (0.06%)
Blood glucose decreased	9 (0.08%)	1 (0.01%)
Hypoglycaemic unconsciousness	1 (0.01%)	1 (0.01%)
<b>Skin and subcutaneous tissue disorders, ADRs</b>		
N (%)	44 (0.41%)	6 (0.06%)
per 100 patient-years	0.17	0.02
Rash	13 (0.12%)	1 (0.01%)
Pruritus	9 (0.08%)	0
Pemphigoid	5 (0.05%)	5 (0.05%)
Drug eruption	4 (0.04%)	0
Urticaria	4 (0.04%)	0
Eczema	2 (0.02%)	0
Rash generalised	2 (0.02%)	0
<b>Gastrointestinal disorders, ADRs</b>		
N (%)	73 (0.68%)	12 (0.11%)
per 100 patient-years	0.29	0.05
Constipation	29 (0.27%)	0
Abdominal distension	6 (0.06%)	0
Nausea	6 (0.06%)	0
Abdominal discomfort	5 (0.05%)	0
Diarrhoea	4 (0.04%)	0
Intestinal obstruction (ileus)	4 (0.04%)	4 (0.04%)
Abdominal pain	3 (0.03%)	0
Abdominal pain upper	3 (0.03%)	0
Dyspepsia	3 (0.03%)	0
Gastrointestinal disorders	3 (0.03%)	0
Gastrooesophageal reflux disease	2 (0.02%)	0
Gastric ulcer	1 (0.01%)	1 (0.01%)
Gastric ulcer haemorrhage	1 (0.01%)	1 (0.01%)

Inguinal hernia	1 (0.01%)	1 (0.01%)
Intestinal ischaemia	1 (0.01%)	1 (0.01%)
Large intestine perforation	1 (0.01%)	1 (0.01%)
Pancreatitis acute	1 (0.01%)	1 (0.01%)
Large intestine polyp	1 (0.01%)	1 (0.01%)
Oesophageal motility disorder	1 (0.01%)	1 (0.01%)
<b>Hepatic impairments, ADRs</b>		
N (%)	47 (0.44%)	4 (0.04%)
per 100 patient-years	0.18	0.02
Hepatic function abnormal	28 (0.26%)	3 (0.03%)
Aspartate aminotransferase increased	8 (0.07%)	0
Alanine aminotransferase increased	7 (0.07%)	0
Liver disorder	4 (0.04%)	0
Hepatic enzyme increased	3 (0.03%)	0
Blood bilirubin increased	2 (0.02%)	0
Hepatitis acute	1 (0.01%)	1 (0.01%)
<b>Renal impairments, ADRs</b>		
N (%)	34 (0.32%)	7 (0.07%)
per 100 patient-years	0.13	0.03
Renal impairment	7 (0.07%)	2 (0.02%)
Blood creatinine increased	7 (0.07%)	1 (0.01%)
Proteinuria	7 (0.07%)	0
Protein urine present	3 (0.03%)	0
Nephrotic syndrome	2 (0.02%)	2 (0.02%)
Blood urea increased	2 (0.02%)	0
Hyperkalaemia	2 (0.02%)	0
Diabetic nephropathy	2 (0.02%)	0
Acute kidney injury	1 (0.01%)	1 (0.01%)
Haemodialysis	1 (0.01%)	1 (0.01%)
Hypoalbuminaemia	1 (0.01%)	1 (0.01%)
<b>Cardiovascular events, AE</b>		
N (%)	85 (0.79%)	76 (0.71%)
per 100 patient-years	0.33	0.30
Cerebral infarction	24 (0.22%)	24 (0.22%)
Acute myocardial infarction	8 (0.07%)	8 (0.07%)
Angina unstable	7 (0.07%)	7 (0.07%)
Myocardial infarction	7 (0.07%)	7 (0.07%)

Subdural haematoma	6 (0.06%)	6 (0.06%)
Carotid artery stenosis	5 (0.05%)	3 (0.03%)
Cerebral haemorrhage	5 (0.05%)	5 (0.05%)
Blood creatine phosphokinase increased	4 (0.04%)	0
Lacunar infarction	3 (0.03%)	3 (0.03%)
Subarachnoid haemorrhage	2 (0.02%)	2 (0.02%)
Transient ischaemic attack	2 (0.02%)	1 (0.01%)
Carotid artery thrombosis	1 (0.01%)	1 (0.01%)
Cerebellar haemorrhage	1 (0.01%)	1 (0.01%)
Cerebral ischaemia	1 (0.01%)	1 (0.01%)
Cerebrovascular accident	1 (0.01%)	1 (0.01%)
Embolic stroke	1 (0.01%)	1 (0.01%)
Haemorrhage intracranial	1 (0.01%)	1 (0.01%)
Intracranial aneurysm	1 (0.01%)	1 (0.01%)
Subdural haemorrhage	1 (0.01%)	1 (0.01%)
Acute coronary syndrome	1 (0.01%)	1 (0.01%)
Putamen haemorrhage	1 (0.01%)	1 (0.01%)
<b>Cardiovascular events, ADRs</b>		
N (%)	18 (0.17%)	14 (0.13%)
per 100 patient-years	0.07	0.05
Cerebral infarction	3 (0.03%)	3 (0.03%)
Blood creatine phosphokinase increased	3 (0.03%)	0
Myocardial infarction	2 (0.02%)	2 (0.02%)
Acute myocardial infarction	1 (0.01%)	1 (0.01%)
Angina unstable	1 (0.01%)	1 (0.01%)
Carotid artery stenosis	1 (0.01%)	1 (0.01%)
Cerebellar haemorrhage	1 (0.01%)	1 (0.01%)
Cerebral haemorrhage	1 (0.01%)	1 (0.01%)
Cerebral ischaemia	1 (0.01%)	1 (0.01%)
Subarachnoid haemorrhage	1 (0.01%)	1 (0.01%)
Lacunar infarction	1 (0.01%)	1 (0.01%)
Putamen haemorrhage	1 (0.01%)	1 (0.01%)
<b>Malignant tumours, AEs</b>		
N (%)	111 (1.04%)	111 (1.04%)
per 100 patient-years	0.44	0.44
Pancreatic carcinoma	15 (0.14%)	15 (0.14%)
Colon cancer	14 (0.13%)	14 (0.13%)

Gastric cancer	13 (0.12%)	13 (0.12%)
Lung neoplasm malignant	11 (0.10%)	11 (0.10%)
Bladder cancer	8 (0.07%)	8 (0.07%)
Hepatocellular carcinoma	7 (0.07%)	7 (0.07%)
Lymphoma	6 (0.06%)	6 (0.06%)
Breast cancer	5 (0.05%)	5 (0.05%)
Rectal cancer	5 (0.05%)	5 (0.05%)
Prostate cancer	5 (0.05%)	5 (0.05%)
Gallbladder cancer	3 (0.03%)	3 (0.03%)
Acute leukaemia	2 (0.02%)	2 (0.02%)
Renal cancer	2 (0.02%)	2 (0.02%)
Hepatic cancer	2 (0.02%)	2 (0.02%)
Bile duct cancer	1 (0.01%)	1 (0.01%)
Cholangiocarcinoma	1 (0.01%)	1 (0.01%)
Chronic myeloid leukaemia	1 (0.01%)	1 (0.01%)
Gallbladder cancer recurrent	1 (0.01%)	1 (0.01%)
Lung carcinoma cell type unspecified recurrent	1 (0.01%)	1 (0.01%)
Malignant neoplasm of conjunctiva	1 (0.01%)	1 (0.01%)
Malignant neoplasm of renal pelvis	1 (0.01%)	1 (0.01%)
Metastases to liver	1 (0.01%)	1 (0.01%)
Oesophageal carcinoma	1 (0.01%)	1 (0.01%)
Ovarian cancer	1 (0.01%)	1 (0.01%)
Plasma cell myeloma	1 (0.01%)	1 (0.01%)
Prostate cancer metastatic	1 (0.01%)	1 (0.01%)
Uterine cancer	1 (0.01%)	1 (0.01%)
Small intestine carcinoma	1 (0.01%)	1 (0.01%)
Thyroid cancer metastatic	1 (0.01%)	1 (0.01%)
Salivary gland cancer	1 (0.01%)	1 (0.01%)
Thyroid cancer	1 (0.01%)	1 (0.01%)
Renal cell carcinoma	1 (0.01%)	1 (0.01%)

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**Malignant tumours, ADRs**

N (%)	27 (0.25%)	27 (0.25%)
per 100 patient-years	0.11	0.11
Pancreatic carcinoma	5 (0.05%)	5 (0.05%)
Colon cancer	4 (0.04%)	4 (0.04%)
Gastric cancer	4 (0.04%)	4 (0.04%)
Bladder cancer	2 (0.02%)	2 (0.02%)

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Breast cancer	2 (0.02%)	2 (0.02%)
Gallbladder cancer	2 (0.02%)	2 (0.02%)
Lymphoma	2 (0.02%)	2 (0.02%)
Lung neoplasm malignant	2 (0.02%)	2 (0.02%)
Bile duct cancer	1 (0.01%)	1 (0.01%)
Ovarian cancer	1 (0.01%)	1 (0.01%)
Plasma cell myeloma	1 (0.01%)	1 (0.01%)
Rectal cancer	1 (0.01%)	1 (0.01%)
Prostate cancer	1 (0.01%)	1 (0.01%)
<b>Other ADRs (in ≥10 patients)</b>		
Dizziness, N (%)	11 (0.10%)	0

Values are number (%) of patients. ADRs were defined as adverse events for which a causal relationship with teneligliptin could not be excluded (i.e., related or unknown)

AE, adverse event; ADR, adverse drug reaction

**Supplemental Table 5.** Complete listing of adverse drug reactions by system organ

class/preferred term

<b>Patients analysed for safety</b>	<b>10,696</b>	
	<b>All ADRs</b>	<b>Serious ADRs</b>
<b>Number of patients with ADRs</b>	<b>412 (3.85%)</b>	<b>117 (1.09%)</b>
<b>Number of events of ADRs</b>	<b>489 events</b>	<b>133 events</b>
<b>Infections and infestations</b>	<b>19 (0.18%)</b>	<b>7 (0.07%)</b>
Herpes zoster	6 (0.06%)	1 (0.01%)
Pneumonia	3 (0.03%)	2 (0.02%)
Upper respiratory tract infection	3 (0.03%)	0
Cystitis	2 (0.02%)	0
Peritonitis	1 (0.01%)	1 (0.01%)
Pyelonephritis acute	1 (0.01%)	1 (0.01%)
Sepsis	1 (0.01%)	1 (0.01%)
Pneumonia bacterial	1 (0.01%)	1 (0.01%)
Angular cheilitis	1 (0.01%)	0
Bronchitis	1 (0.01%)	0
Gastroenteritis	1 (0.01%)	0
Otitis media	1 (0.01%)	0
<b>Neoplasms benign, malignant and unspecified, including cysts and polyps</b>	<b>29 (0.27%)</b>	<b>29 (0.27%)</b>
Pancreatic carcinoma	5 (0.05%)	5 (0.05%)
Colon cancer	4 (0.04%)	4 (0.04%)
Gastric cancer	4 (0.04%)	4 (0.04%)
Bladder cancer	2 (0.02%)	2 (0.02%)
Breast cancer	2 (0.02%)	2 (0.02%)
Gallbladder cancer	2 (0.02%)	2 (0.02%)
Lymphoma	2 (0.02%)	2 (0.02%)
Lung neoplasm malignant	2 (0.02%)	2 (0.02%)
Bile duct cancer	1 (0.01%)	1 (0.01%)
Ovarian cancer	1 (0.01%)	1 (0.01%)
Plasma cell myeloma	1 (0.01%)	1 (0.01%)
Rectal cancer	1 (0.01%)	1 (0.01%)
Prostate cancer	1 (0.01%)	1 (0.01%)
Brain neoplasm	1 (0.01%)	1 (0.01%)
Ureteral neoplasm	1 (0.01%)	1 (0.01%)

<b>Blood and lymphatic system disorders</b>	<b>7 (0.07%)</b>	<b>1 (0.01%)</b>
Iron deficiency anaemia	3 (0.03%)	0
Anaemia	2 (0.02%)	0
Eosinophilia	1 (0.01%)	1 (0.01%)
Polycythaemia	1 (0.01%)	0
<b>Metabolism and nutrition disorders</b>	<b>44 (0.41%)</b>	<b>9 (0.08%)</b>
Hypoglycaemia	28 (0.26%)	6 (0.06%)
Decreased appetite	2 (0.02%)	2 (0.02%)
Hyperkalaemia	2 (0.02%)	0
Hypertriglyceridaemia	2 (0.02%)	0
Hypoalbuminaemia	1 (0.01%)	1 (0.01%)
Diabetic ketosis	1 (0.01%)	1 (0.01%)
Dehydration	1 (0.01%)	0
Diabetes mellitus	1 (0.01%)	0
Diabetes mellitus inadequate control	1 (0.01%)	0
Electrolyte imbalance	1 (0.01%)	0
Hypercholesterolaemia	1 (0.01%)	0
Hyperglycaemia	1 (0.01%)	0
Hyperuricaemia	1 (0.01%)	0
Hyponatraemia	1 (0.01%)	0
Lipid metabolism disorder	1 (0.01%)	0
Hyperamylasaemia	1 (0.01%)	0
Hypo HDL cholesterolaemia	1 (0.01%)	0
<b>Psychiatric disorders</b>	<b>4 (0.04%)</b>	<b>0</b>
Insomnia	2 (0.02%)	0
Anger	1 (0.01%)	0
Eating disorder	1 (0.01%)	0
<b>Nervous system disorders</b>	<b>37 (0.35%)</b>	<b>11 (0.10%)</b>
Dizziness	11 (0.10%)	0
Headache	5 (0.05%)	0
Cerebral infarction	3 (0.03%)	3 (0.03%)
Somnolence	3 (0.03%)	0
Hypoaesthesia	2 (0.02%)	0
Carotid artery stenosis	1 (0.01%)	1 (0.01%)
Cerebellar haemorrhage	1 (0.01%)	1 (0.01%)
Cerebral haemorrhage	1 (0.01%)	1 (0.01%)
Cerebral ischaemia	1 (0.01%)	1 (0.01%)

Subarachnoid haemorrhage	1 (0.01%)	1 (0.01%)
Lacunar infarction	1 (0.01%)	1 (0.01%)
Putamen haemorrhage	1 (0.01%)	1 (0.01%)
Hypoglycaemic unconsciousness	1 (0.01%)	1 (0.01%)
Dementia Alzheimer's type	1 (0.01%)	0
Dysgeusia	1 (0.01%)	0
Head discomfort	1 (0.01%)	0
Loss of consciousness	1 (0.01%)	0
Dysstasia	1 (0.01%)	0
<b>Eye disorders</b>	<b>5 (0.05%)</b>	<b>4 (0.04%)</b>
Cataract	2 (0.02%)	2 (0.02%)
Diabetic retinal oedema	1 (0.01%)	1 (0.01%)
Retinal detachment	1 (0.01%)	1 (0.01%)
Vitreous haemorrhage	1 (0.01%)	1 (0.01%)
Vitreous floaters	1 (0.01%)	0
<b>Ear and labyrinth disorders</b>	<b>2 (0.02%)</b>	<b>1 (0.01%)</b>
Sudden hearing loss	1 (0.01%)	1 (0.01%)
Tinnitus	1 (0.01%)	0
<b>Cardiac disorders</b>	<b>18 (0.17%)</b>	<b>9 (0.08%)</b>
Ventricular extrasystoles	4 (0.04%)	0
Atrial fibrillation	3 (0.03%)	1 (0.01%)
Cardiac failure congestive	2 (0.02%)	2 (0.02%)
Myocardial infarction	2 (0.02%)	2 (0.02%)
Acute myocardial infarction	1 (0.01%)	1 (0.01%)
Angina unstable	1 (0.01%)	1 (0.01%)
Cardiac failure acute	1 (0.01%)	1 (0.01%)
Cardiac tamponade	1 (0.01%)	1 (0.01%)
Coronary artery stenosis	1 (0.01%)	1 (0.01%)
Cardiomyopathy acute	1 (0.01%)	1 (0.01%)
Palpitations	1 (0.01%)	0
Atrial flutter	1 (0.01%)	0
Atrioventricular block second degree	1 (0.01%)	0
<b>Vascular disorders</b>	<b>4 (0.04%)</b>	<b>2 (0.02%)</b>
Peripheral arterial occlusive disease	2 (0.02%)	1 (0.01%)
Aortic dissection	1 (0.01%)	1 (0.01%)
Hypertension	1 (0.01%)	0

<b>Respiratory, thoracic and mediastinal disorders</b>	<b>7 (0.07%)</b>	<b>5 (0.05%)</b>
Cough	2 (0.02%)	0
Dyspnoea	1 (0.01%)	1 (0.01%)
Interstitial lung disease	1 (0.01%)	1 (0.01%)
Pneumothorax	1 (0.01%)	1 (0.01%)
Pulmonary oedema	1 (0.01%)	1 (0.01%)
Respiratory disorder	1 (0.01%)	1 (0.01%)
Sputum retention	1 (0.01%)	0
<b>Gastrointestinal disorders</b>	<b>73 (0.68%)</b>	<b>12 (0.11%)</b>
Constipation	29 (0.27%)	0
Abdominal distension	6 (0.06%)	0
Nausea	6 (0.06%)	0
Abdominal discomfort	5 (0.05%)	0
Diarrhoea	4 (0.04%)	0
Abdominal pain	3 (0.03%)	0
Abdominal pain upper	3 (0.03%)	0
Dyspepsia	3 (0.03%)	0
Gastrointestinal disorders	3 (0.03%)	0
Ileus	3 (0.03%)	3 (0.03%)
Gastrooesophageal reflux disease	2 (0.02%)	0
Gastric ulcer	1 (0.01%)	1 (0.01%)
Gastric ulcer haemorrhage	1 (0.01%)	1 (0.01%)
Inguinal hernia	1 (0.01%)	1 (0.01%)
Intestinal ischaemia	1 (0.01%)	1 (0.01%)
Intestinal obstruction	1 (0.01%)	1 (0.01%)
Large intestine perforation	1 (0.01%)	1 (0.01%)
Pancreatitis acute	1 (0.01%)	1 (0.01%)
Large intestine polyp	1 (0.01%)	1 (0.01%)
Oesophageal motility disorder	1 (0.01%)	1 (0.01%)
Anal haemorrhage	1 (0.01%)	0
Pancreatic cyst	1 (0.01%)	0
Flatulence	1 (0.01%)	0
Faeces soft	1 (0.01%)	0
<b>Hepatobiliary disorders</b>	<b>39 (0.36%)</b>	<b>9 (0.08%)</b>
Hepatic function abnormal	28 (0.26%)	3 (0.03%)
Liver disorder	4 (0.04%)	0
Cholecystitis	2 (0.02%)	2 (0.02%)

Cholecystitis acute	2 (0.02%)	2 (0.02%)
Cholangitis	1 (0.01%)	1 (0.01%)
Hepatitis acute	1 (0.01%)	1 (0.01%)
Biliary colic	1 (0.01%)	0
<b>Skin and subcutaneous tissue disorders</b>	<b>44 (0.41%)</b>	<b>6 (0.06%)</b>
Rash	13 (0.12%)	1 (0.01%)
Pruritus	9 (0.08%)	0
Pemphigoid	5 (0.05%)	5 (0.05%)
Drug eruption	4 (0.04%)	0
Urticaria	4 (0.04%)	0
Eczema	2 (0.02%)	0
Rash generalised	2 (0.02%)	0
Alopecia areata	1 (0.01%)	0
Dermatitis	1 (0.01%)	0
Dermatitis allergic	1 (0.01%)	0
Eczema asteatotic	1 (0.01%)	0
Hyperhidrosis	1 (0.01%)	0
Chronic pigmented purpura	1 (0.01%)	0
<b>Musculoskeletal and connective tissue disorders</b>	<b>7 (0.07%)</b>	<b>2 (0.02%)</b>
Rheumatoid arthritis	2 (0.02%)	1 (0.01%)
Myalgia	2 (0.02%)	0
Collagen disorder	1 (0.01%)	1 (0.01%)
Back pain	1 (0.01%)	0
Musculoskeletal pain	1 (0.01%)	0
Neck pain	1 (0.01%)	0
Periarthritis	1 (0.01%)	0
<b>Renal and urinary disorders</b>	<b>24 (0.22%)</b>	<b>7 (0.07%)</b>
Renal impairment	7 (0.07%)	2 (0.02%)
Proteinuria	7 (0.07%)	0
Ureterolithiasis	3 (0.03%)	2 (0.02%)
Nephrotic syndrome	2 (0.02%)	2 (0.02%)
Diabetic nephropathy	2 (0.02%)	0
Acute kidney injury	1 (0.01%)	1 (0.01%)
Hypertonic bladder	1 (0.01%)	1 (0.01%)
Haematuria	1 (0.01%)	0
Pollakiuria	1 (0.01%)	0
Renal disorder	1 (0.01%)	0

<b>Reproductive system and breast disorders</b>	<b>1 (0.01%)</b>	<b>0</b>
Gynaecomastia	1 (0.01%)	0
<b>Congenital, familial and genetic disorders</b>	<b>1 (0.01%)</b>	<b>0</b>
Epidermolysis bullosa	1 (0.01%)	0
<b>General disorders and administration site conditions</b>	<b>24 (0.22%)</b>	<b>6 (0.06%)</b>
Feeling abnormal	5 (0.05%)	0
Malaise	5 (0.05%)	0
Death	4 (0.04%)	4 (0.04%)
Oedema peripheral	3 (0.03%)	0
Pyrexia	2 (0.02%)	1 (0.01%)
Multiple organ dysfunction syndrome	1 (0.01%)	1 (0.01%)
Asthenia	1 (0.01%)	0
Feeling hot	1 (0.01%)	0
Hunger	1 (0.01%)	0
Oedema	1 (0.01%)	0
Physical deconditioning	1 (0.01%)	0
<b>Investigations</b>	<b>64 (0.60%)</b>	<b>5 (0.05%)</b>
Blood glucose decreased	9 (0.08%)	1 (0.01%)
Aspartate aminotransferase increased	8 (0.07%)	0
Blood creatinine increased	7 (0.07%)	1 (0.01%)
Alanine aminotransferase increased	7 (0.07%)	0
Blood triglycerides increased	4 (0.04%)	1 (0.01%)
Blood glucose increased	3 (0.03%)	1 (0.01%)
Amylase increased	3 (0.03%)	0
Blood creatine phosphokinase increased	3 (0.03%)	0
Protein urine present	3 (0.03%)	0
Hepatic enzyme increased	3 (0.03%)	0
Platelet count decreased	2 (0.02%)	1 (0.01%)
Blood bilirubin increased	2 (0.02%)	0
Blood pressure increased	2 (0.02%)	0
Blood urea increased	2 (0.02%)	0
Heart rate increased	2 (0.02%)	0
Blood pressure systolic increased	1 (0.01%)	0
Electrocardiogram abnormal	1 (0.01%)	0
Electrocardiogram QT prolonged	1 (0.01%)	0
Electrocardiogram T wave inversion	1 (0.01%)	0
Glycosylated haemoglobin increased	1 (0.01%)	0

High density lipoprotein decreased	1 (0.01%)	0
Lipids abnormal	1 (0.01%)	0
Weight increased	1 (0.01%)	0
White blood cell count decreased	1 (0.01%)	0
Blood elastase increased	1 (0.01%)	0
Electrocardiogram Q wave abnormal	1 (0.01%)	0
Blood alkaline phosphatase decreased	1 (0.01%)	0
Electrocardiogram ST-T change	1 (0.01%)	0
Liver function test increased	1 (0.01%)	0
<b>Injury, poisoning and procedural complications</b>	<b>1 (0.01%)</b>	<b>1 (0.01%)</b>
Femur fracture	1 (0.01%)	1 (0.01%)
<b>Surgical and medical procedures</b>	<b>1 (0.01%)</b>	<b>1 (0.01%)</b>
Haemodialysis	1 (0.01%)	1 (0.01%)

Values are number (%) of patients.

ADRs were defined as adverse events for which a causal relationship with teneligliptin could not be excluded, i.e., causal or unknown.

ADR, adverse drug reaction



**Supplemental Table 6.** Outcomes of ADRs and AEs of special interest

Category of ADR/AE	Number of patients	Recovered	Recovering	Not recovered	Recovered with sequelae	Death	Unknown
Hypoglycaemia-related ADRs	38	32	6	0	0	0	0
Skin and subcutaneous tissue disorders, ADRs	45	35	9	0	0	0	1
Gastrointestinal disorders, ADRs	80	49	24	3	0	2	2
Hepatic impairment, ADRs	54	25	13	12	0	1	3
Renal impairment, ADRs	37	15	8	12	0	0	2
Cardiovascular events, AEs	85	18	25	6	13	16	7
Cardiovascular events, ADRs	18	6	4	2	3	2	1
Malignant tumours, AEs	116	20	23	11	3	43	16
Malignant tumours, ADRs	28	7	9	1	1	5	5

Values are number of patients

ADR, adverse drug reaction; AE, adverse event

**Supplemental Table 7.** Changes in body weight and lipids over time

		0 months	6 months	12 months	24 months	36 months	Last visit
<b>Body weight</b>	N	6,401	4,881	4,296	3,600	3,039	6,401
	Value (kg)	65.46 ± 14.28	65.15 ± 14.29	65.06 ± 14.00	64.87 ± 13.61	64.80 ± 13.56	64.72 ± 14.15
	Change (kg)	–	–0.37 ± 3.60	–0.24 ± 3.54	–0.49 ± 3.98	–0.86 ± 4.37	–0.73 ± 4.60
	p-value*	–	<0.001	<0.001	<0.001	<0.001	<0.001
<b>Triglycerides</b>	N	7,351	5,672	5,014	4,093	3,377	7,351
	Value (mg/dL)	164.1 ± 126.2	151.7 ± 100.7	147.2 ± 93.9	148.7 ± 95.8	146.6 ± 87.5	151.6 ± 102.7
	Change (mg/dL)	–	–11.3 ± 109.6	–13.5 ± 106.7	–13.0 ± 114.9	–15.1 ± 112.0	–12.5 ± 117.2
	p-value*	–	<0.001	<0.001	<0.001	<0.001	<0.001
<b>HDL-C</b>	N	6,907	5,304	4,659	3,782	3,114	6,907
	Value (mg/dL)	53.5 ± 16.0	53.1 ± 15.4	54.2 ± 16.6	53.9 ± 14.8	54.3 ± 14.9	53.6 ± 15.6
	Change (mg/dL)	–	–0.4 ± 12.5	0.5 ± 13.2	0.1 ± 12.1	0.3 ± 13.4	0.1 ± 12.6
	p-value*	–	0.024	0.015	0.693	0.211	0.387
<b>LDL-C</b>	N	6,553	4,973	4,422	3,632	3,009	6,553
	Value (mg/dL)	113.7 ± 32.1	107.1 ± 28.8	106.7 ± 28.9	106.2 ± 28.3	105.9 ± 36.7	107.0 ± 33.6
	Change (mg/dL)	–	–6.2 ± 28.2	–6.3 ± 29.0	–6.4 ± 29.1	–6.8 ± 39.3	–6.7 ± 35.3
	p-value*	–	<0.001	<0.001	<0.001	<0.001	<0.001

Values are means ± standard deviation

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

\*p-value was estimated by paired *t*-test