The Durable Safety and Effectiveness of Lixisenatide in Japanese People with Type 2 Diabetes: The Post-Marketing Surveillance PRANDIAL Study

Authors: Yasuo Terauchi[1], Makiko Usami[2], Tomoyuki Inoue[3]

Affiliations:

[1] Department of Endocrinology and Metabolism, Graduate School of Medicine, Yokohama City University, Yokohama, Japan.

[2] Post-Authorization Regulatory Studies, Sanofi K.K., Tokyo, Japan.

[3] General Medicine Medical, Sanofi K.K., Tokyo, Japan.

Corresponding author:

Makiko Usami, Sanofi K.K., Opera City Tower, 3-20-2 Nishi-Shinjuku, Shinjuku-ku, Tokyo, 163-1488, Japan.

Phone: +81 (3)6301-3443

Email:Makiko.Usami@sanofi.com

Supplementary Material

Supplementary Table S1. Incidence and logistic regression analysis of ADRs by participant subgroup

Baseline characteristic		Univariate analysis			Multivariable analysis			
		N	ADR n (%)	*P*-value[a]	N	ADR, n (%)	Adjusted OR (95% CI)	*P*-value[b]
Age group – category 1	< 65 years	1,882	328 (17.4)	< 0.0001	1,831	318 (17.4)	1.202 (0.968–1.494)	0.0957
	≥ 65 years	1,154	270 (23.4)		1,104	263 (23.8)		
Age group – category 2	< 75 years	2,691	505 (18.8)	0.0005	2,599	488 (18.8)	1.299 (0.960–1.759)	0.0903
	≥ 75 years	345	93 (27.0)		336	93 (27.7)		
Hospitalization status	Inpatient	536	134 (25.0)	0.0012	513	124 (24.2)	–	–
	Outpatient	2,510	470 (18.7)		2,422	457 (18.9)		
Medical history	No	2,502	467 (18.7)	0.0007	2,413	451 (18.7)	1.173 (0.928–1.482)	0.1814
	Yes	544	137 (25.2)		522	130 (24.9)		
History of treatment for CVD	No	2,669	501 (18.8)	< 0.0001	2,655	497 (18.7)	1.445 (1.084–1.928)	0.0121
	Yes	295	89 (30.2)		280	84 (30.0)		
History of treatment for PAD	No	2,901	572 (19.7)	0.0211	2,885	565 (19.6)	–	–
	Yes	51	17 (33.3)		50	16 (32.0)		
Hepatic dysfunction	No	2,454	449 (18.3)	< 0.0001	2,354	435 (18.5)	1.366 (1.090–1.711)	0.0067
	Yes	592	155 (26.2)		581	146 (25.1)		

Renal dysfunction	No	2,836	551 (19.4)	0.0481	2,733	530 (19.4)	–	–
	Yes	210	53 (25.2)		202	51 (25.3)		
CVD	No	1,406	228 (16.2)	< 0.0001	1,352	224 (16.6)	–	–
	Yes	1,640	376 (22.9)		1,583	357 (22.6)		
Diabetic nephropathy	No	2,701	517 (19.1)	0.0097	2,597	496 (19.1)	–	–
	Yes	345	87 (25.2)		338	85 (25.2)		
Renal dysfunction, CVD, or	No	1,077	143 (13.3)	< 0.0001	1,030	140 (13.6)	1.740 (1.402–2.160)	< 0.0001
diabetic nephropathy	Yes	1,969	461 (23.4)		1,905	441 (23.2)		
Concomitant insulin	No	996	170 (17.1)	0.0077	1,097	177 (16.1)	1.163 (0.934–1.448)	0.1763
	Yes	2,050	434 (21.2)		1,838	404 (22.0)		
Concomitant long-acting	No	1,102	193 (17.5)	0.0159	1,202	200 (16.6)	–	–
insulin	Yes	1,944	411 (21.1)		1,733	381 (22.0)		
Concomitant rapid-acting	No	2,781	535 (19.2)	0.0098	2,733	528 (19.3)	1.282 (0.906–1.815)	0.1610
insulin	Yes	265	69 (26.0)		202	53 (26.2)		
Concomitant OADs	No	746	183 (24.5)	0.0003	929	219 (23.6)	–	–
	Yes	2,300	421 (18.3)		2,006	362 (18.1)		
Concomitant SU	No	1,948	434 (22.3)	< 0.0001	1,952	435 (22.3)	0.720 (0.573–0.906)	0.0051
	Yes	1,098	170 (15.5)		983	146 (14.9)		
Concomitant biguanide	No	1,545	345 (22.3)	0.0005	1,634	358 (21.9)	0.816 (0.669–0.997)	0.0467
	Yes	1,501	259 (17.3)		1,301	223 (17.1)		
Concomitant SGLT2	No	2,392	513 (21.5)	< 0.0001	2,618	534 (20.4)	0.732 (0.523–1.025)	0.0692

inhibitor	Yes	654	91 (13.9)		317	47 (14.8)		
Concomitant rapid-acting insulin secretagogue	No	2,879	554 (19.2)	0.0013	2,833	550 (19.4)	1.583 (1.009–2.485)	0.0458
	Yes	167	50 (29.9)		102	31 (30.4)		

[a]Between-group comparison by Fisher's exact test

[b]Between-group comparison by Chi-squared test

ADR adverse drug reaction, *CI* confidence interval, *CVD* cardiovascular disease, *OAD* oral antidiabetic drug, *OR* odds ratio, *PAD* peripheral arterial disease, *SGLT2* sodium-glucose cotransporter-2, *SU* sulfonylurea

Supplementary Table S2. Body weight, BMI, and laboratory values during the 3-year study, and in the LOCF analysis

Variable		Baseline	Week 24	Week 78	Week 156	LOCF			
						Baseline	Final evaluation	Mean±SD change	*P*-value[a]
Body weight, kg	*n*	2426	1725	973	616	2339[b]			
	Mean±SD	75.71±17.49	74.22±17.17	74.17±16.95	72.89±16.39	75.84±17.56	73.54±17.14	–2.30±4.76	<0.0001
BMI, kg/m^2	*n*	2341	1659	935	592	2255[b]			
	Mean±SD	28.65±5.62	28.08±5.44	28.01±5.37	27.43±5.19	28.71±5.65	27.82±5.46	–0.88±1.81	<0.0001
Blood CPR, ng/ml	*n*	476	87	27	21	173[b]			
	Mean±SD	2.57±2.40	2.82±2.27	2.40±1.83	3.28±2.68	2.47±1.91	2.63±2.03	0.16±1.81	0.2613
Fasting blood	*n*	295	30	8	6	62[b]			
CPR, ng/mL	Mean±SD	2.02±1.74	2.59±2.25	2.19±2.25	2.84±3.05	2.17±1.94	2.16±1.73	–0.01±1.37	0.9394
AST, IU/L	*n*	1987	1316	740	439	1881[b]			
	Mean±SD	27.7±17.7	24.9±13.6	24.8±18.4	23.1±10.6	27.7±17.7	25.8±22.4	–1.9±23.6	0.0007
ALT, IU/L	*n*	2018	1344	757	445	1919[b]			
	Mean±SD	32.2±24.3	28.1±19.5	27.3±19.1	24.9±16.3	32.1±24.0	28.4±23.4	–3.7±23.2	<0.0001
Serum creatinine,	*n*	2007	1332	752	461	1913[b]			
mg/dL	Mean±SD	0.90±1.06	0.97±2.00	0.91±1.01	1.02±1.20	0.90±1.06	0.94±1.57	0.05±0.82	0.0092
eGFR,	*n*	1997	1325	751	460	1903[b]			
mL/min/1.73 m^2	Mean±SD	76.13±27.58	75.57±28.43	75.14±26.44	71.42±26.45	76.28±27.71	74.65±27.17	–1.63±14.05	<0.0001
Amylase, IU/L	*n*	656	336	193	105	520[b]			
	Mean±SD	69.2±43.2	72.1±32.3	74.2±26.4	76.3±29.4	70.7±45.9	72.6±34.6	1.9±33.9	0.1916

Lipase, IU/L	*n*	80	11	6	5	26[b]			
	Mean±SD	42.15±34.79	41.42±30.66	31.47±10.41	31.16±10.51	43.42±29.66	49.30±31.33	5.88±22.51	0.1945
Calcitonin, pg/mL	*n*	38	3	1	2	12[b]			
	Mean±SD	10.1±19.9	24.3±19.0	36.4	27.3±7.5	22.8±29.3	23.5±30.1	0.7±2.5	0.3297

[a]Comparison to baseline by paired *t*-test

[b]Data are for participants for whom both baseline and a final value were available allowing for LOCF analysis

ALT alanine aminotransferase, *AST* aspartate aminotransferase, *BMI* body mass index, *CPR* C-peptide immunoreactivity, *eGFR* estimated glomerular filtration rate, *IU* international unit, *LOCF* last observation carried forward, *SD* standard deviation