Table 3. Adverse Events.*

Adverse Event	Semaglutide (N=1306)			Placebo (N=655)		
	No. of participants (%)	No. of events	Events/100 person-yr	No. of participants (%)	No. of events	Events/100 person-yr
Any adverse event	1171 (89.7)	9658	566.1	566 (86.4)	3302	398.0
Serious adverse events	128 (9.8)	164	9.6	42 (6.4)	53	6.4
Adverse events leading to discontinuation of drug or placebo	92 (7.0)	123	7.2	20 (3.1)	23	2.8
Gastrointestinal disorders	59 (4.5)	78	4.6	5 (0.8)	5	0.6
Fatal events†‡	1 (0.1)	1	0.1	1 (0.2)	3	0.3
Adverse events reported in ≥10% of participants§						
Nausea	577 (44.2)	1068	62.6	114 (17.4)	146	17.6
Diarrhea	412 (31.5)	766	44.9	104 (15.9)	138	16.6
Vomiting	324 (24.8)	636	37.3	43 (6.6)	52	6.3
Constipation	306 (23.4)	390	22.9	62 (9.5)	73	8.8
Nasopharyngitis	281 (21.5)	480	28.1	133 (20.3)	216	26.0
Headache	198 (15.2)	387	22.7	80 (12.2)	104	12.5
Dyspepsia	135 (10.3)	179	10.5	23 (3.5)	30	3.6
Abdominal pain	130 (10.0)	175	10.3	36 (5.5)	41	4.9
Upper respiratory tract infection	114 (8.7)	158	9.3	80 (12.2)	116	14.0
Safety focus areas¶						
Gastrointestinal disorders‖	969 (74.2)	4309	252.6	314 (47.9)	739	89.1
Gallbladder-related disorders	34 (2.6)	42	2.5	8 (1.2)	8	1.0
Hepatobiliary disorders‖	33 (2.5)	40	2.3	5 (0.8)	5	0.6
Cholelithiasis	23 (1.8)	24	1.4	4 (0.6)	4	0.5
Hepatic disorders	31 (2.4)	37	2.2	20 (3.1)	24	2.9
Acute pancreatitis**	3 (0.2)	3	0.2	0	—	—
Cardiovascular disorders†	107 (8.2)	134	7.2	75 (11.5)	96	10.5
Allergic reactions	96 (7.4)	108	6.3	54 (8.2)	63	7.6
Injection-site reactions	65 (5.0)	99	5.8	44 (6.7)	82	9.9
Malignant neoplasms†	14 (1.1)	14	0.8	7 (1.1)	7	0.8
Psychiatric disorders‖	124 (9.5)	160	9.4	83 (12.7)	113	13.6
Acute renal failure	3 (0.2)	4	0.2	2 (0.3)	2	0.2
Hypoglycemia	8 (0.6)	15	0.9	5 (0.8)	7	0.8

* Adverse events are shown for the safety analysis population (all randomly assigned participants exposed to at least one dose of trial drug or placebo); since all participants received at least one dose of drug or placebo, the safety population is the same as the full-analysis population. Included are all adverse events that occurred during the on-treatment period (i.e., the period during which any dose of semaglutide or placebo was administered within the previous 49 days, with any period of temporary interruption of a regimen excluded), unless indicated otherwise. Adverse events were classified by severity as mild (causing minimal discomfort and not interfering with everyday activities), moderate (causing sufficient discomfort to interfere with normal everyday activities), or severe (preventing normal everyday activities).

† Included are events that were observed during the in-trial period (the time from random assignment to last contact with a trial site, regardless of treatment discontinuation or rescue intervention).

‡ In the semaglutide group, sudden cardiac death occurred in one participant with a medical history of hypertension and obstructive sleep apnea who had discontinued semaglutide. In the placebo group, death due to glioblastoma, aspiration pneumonia, and severe sepsis occurred in one participant each who had discontinued placebo.

§ Shown are the most common adverse events, according to the preferred term in the Medical Dictionary for Regulatory Activities (MedDRA), version 22.1, reported in 10% or more of participants in either treatment group.

¶ On the basis of therapeutic experience with glucagon-like peptide-1 receptor agonists and regulatory feedback and requirements, a number of safety focus areas were prespecified as being of special interest in the safety evaluation. Identified through searches of MedDRA, these preferred terms were judged to be relevant for each of the safety focus areas.

‖ This is a system organ class. (For gallbladder-related disorders, hepatobiliary disorders is the system organ class and cholelithiasis is the preferred term.)

** Acute pancreatitis was confirmed by the event adjudication committee.

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