Supplemental Digital Content 4. Treatment-emergent adverse events by system organ class and preferred term based on safety populations

Category	Infants n (m)			Children* n (m)	
	Core study		Extension study	Core study	Extension study‡
	SoC (n = 5)	Teduglutide† (n = 7)	(N = 2)	(N = 8)	(N = 7)
Any TEAE	**5 (29)**	**7 (125)**	**2 (12)**	**8 (93)**	**7 (101)**
Blood and lymphatic system disorders	**-**	**2 (2)**	**-**	**-**	**1 (1)**
Anemia	-	1 (1)	-	-	1 (1)
Iron deficiency anemia	-	1 (1)	-	-	-
Eye disorders	**-**	**-**	**-**	**-**	**2 (3)**
Conjunctivitis allergic	-	-	-	-	1 (2)
Eye discharge	-	-	-	-	1 (1)
Gastrointestinal disorders	**3 (6)**	**4 (25)**	**1 (1)**	**6 (11)**	**7 (15)**
Abdominal discomfort/pain	-	1 (2)	-	2 (2)	1 (1)
Abdominal distension	-	1 (3)	-	1 (1)	-

Abnormal feces discolored	-	1 (1)	-	-	-
Cheilitis	-	-	-	-	1 (1)
Colonic hematoma	-	-	-	-	1 (1)
Constipation	1 (1)	-	-	2 (2)	-
Dental caries	-	-	-	1 (1)	2 (2)
Diarrhea	-	2 (3)	-	-	-
Enteritis	-	-	-	1 (1)	1 (3)
Enterocolitis	-	1 (1)	-	2 (2)	1 (2)
Flatulence	-	1 (1)	-	-	-
Frequent bowel movements	-	2 (2)	-	-	-
Gastritis	-	-	-	1 (1)	-
Gastric disorder	-	-	-	-	1 (1)
Gastrointestinal sounds abnormal	-	1 (1)	-	-	-
Lip dry	-	-	-	-	1 (1)
Mucous stools	-	1 (1)	-	-	-
Pancreatitis acute	-	-	1 91)	-	-

Proctalgia	-	-	-	1 (1)	-
Retching	-	1 (1)	-	-	-
Stomatitis	-	-	-	-	2 (2)
Teething	2 (3)	-	-	-	-
Vomiting	1 (2)	3 (8)	-	-	-
General disorders and administration site conditions	**1 (1)**	**4 (8)**	**1 (1)**	**5 (33)**	**3 (4)**
Catheter site granuloma	-	-	-	1 (1)	-
Injection site erythema	-	-	-	3 (12)	-
Injection site bruising	-	-	-	2 (9)	-
Injection site pain	-	-	1 (1)	1 (1)	-
Injection site rash	-	-	-	1 (1)	-
Injection site reaction	-	-	1 (1)	1 (1)	-
Injection site hematoma	-	-	-	1 (1)	-
Injection site induration	-	-	-	1 (1)	-

Pyrexia	1 (1)	4 (7)	-	2 (3)	3 (3)
Secretion discharge	-	1 (1)	-	-	-
Immune system disorder	**-**	**1 (1)**	**-**	**2 (2)**	**1 (4)**
Anaphylactic reaction	-	-	-	1 (1)	-
Food allergy	-	-	-	1 (1)	1 (4)
Immunization reaction	-	1 (1)	-	-	-
Infection and infestations	**3 (6)**	**6 (14)**	**2 (6)**	**7 (24)**	**6 (34)**
Adenoviral conjunctivitis	-	-	-	-	1 (1)
Adenovirus infection	-	-	-	1 (1)	-
Beta hemolytic streptococcal infection	-	-	-	-	1 (1)
Conjunctivitis	-	-	-	-	1 (1)
Device-related infection	2 (2)	1 (2)	-	4 (5)	2 (3)
Gastroenteritis	-	-	-	1 (1)	1 (1)
Gastroenteritis adenovirus	-	-	1 (1)	-	-
Gastroenteritis norovirus	-	1 (1)	-	-	-

Gingivitis	-	-	-	1 (1)	-
Hand-foot-and-mouth disease	1 (1)	-	-	2 (2)	1 (1)
Infected bite	-	-	-	-	1 (1)
Influenza	-	-	-	1 (1)	2 (2)
Medical device site infection	-	1 (1)	1 (1)	2 (5)	1 (1)
Nasopharyngitis	-	2 (2)	-	-	-
Oral candidiasis	-	-	1 (1)	-	-
Otitis media	-	-	-	1 (1)	-
Respiratory tract infection	-	1 (2)	-	-	-
Pharyngitis streptococcal	-	-	-	1 (1)	-
Rhinitis	-	-	-	1 (1)	-
Upper respiratory tract infection	2 (2)	2 (3)	1 (2)	-	-
Viral infection	1 (1)	1 (1)	-	-	-
Viral pharyngitis	-	-	-	-	1 (1)

Viral upper respiratory tract infection	-	1 (1)	1 (1)	6 (6)	4 (21)
Injury, poisoning, and procedural complications	**2 (2)**	**2 (2)**	**-**	**2 (3)**	**4 (6)**
Contusion	1 (1)	-	-	-	-
Fall	-	-	-	-	1 (1)
Fracture	-	-	-	-	1 (1)
Frostbite	-	-	-	1 (2)	-
Gastrostomy tube site complication	-	-	-	1 (2)	1 (2)
Injury corneal	-	-	-	-	1 (1)
Lip injury	-	1 (1)	-	-	-
Skin abrasion	1 (1)	-	-	-	-
Vaccination complication	-	1 (1)	-	-	-
Wound complication	-	-	-	-	2 (2)
Investigations	**3 (5)**	**2 (4)**	**1 (1)**	**1 (1)**	**3 (3)**

Alanine aminotransferase increased	-	1 (2)	-	-	-
Amylase increased	-	-	-	1 (1)	1 (1)
Blood alkaline phosphatase increased	-	-	1 (1)	-	-
Blood iron decreased	1 (1)	-	-	-	-
Fecal volume increased	-	1 (1)	-	-	-
Lipase increased	-	-	-	-	1 (1)
Respiratory rate increased	1 (1)	-	-	-	-
Serum ferritin decreased	-	1 (1)	-	-	-
Transaminases increased	1 (3)	-	-	-	1 (1)
Metabolism and nutrition disorders	**2 (2)**	**2 (3)**	**-**	**4 (4)**	**3 (6)**
Decreased appetite	-	1 (2)	-	-	-
Dehydration	-	-	-	1 (1)	2 (2)
Hyperlipasemia	-	-	-	1 (1)	-
Hypertriglyceridemia	-	-	-	1 (1)	-
Hyperzincemia	-	-	-	1 (1)	1 (1)

Hypoglycemia	1 (1)	-	-	-	-
Hypophagia	-	1 (1)	-	-	-
Hypomagnesemia	-	-	-	-	1 (1)
Metabolic acidosis	1 (1)	-	-	-	1 (2)
Musculoskeletal and connective tissue disorders	**-**	**-**	**-**	**-**	**2 (2)**
Joint swelling	-	-	-	-	1 (1)
Myalgia	-	-	-	-	1 (1)
Nervous system disorders	**1 (1)**	**-**	**1 (1)**	**1 (1)**	**-**
Ataxia	1 (1)	-	-	-	-
Headache	-	-	-	1 (1)	-
Seizures	-	-	1 (1)	-	-
Product issues[§]	**2 (2)**	**3 (4)**	**-**	**3 (3)**	**5 (7)**
Device breakage	1 (1)	2 (2)	-	-	3 (5)
Device damage	-	-	-	3 (3)	2 (2)

Device leakage	-	1 (1)	-	-	-
Device occlusion	1 (1)	1 (1)	-	-	-
Psychiatric disorders	**-**	**2 (2)**	**-**	**-**	**1 (1)**
Head banging	-	-	-	-	1 (1)
Irritability	-	1 (1)		-	
Sleep disorder	-	1 (1)		-	
Reproductive system and breast disorders	**-**	**-**	**-**	**1 (1)**	**-**
Balanoposthitis	-	-		1 (1)	
Respiratory, thoracic, and mediastinal disorders	**2 (2)**	**3 (5)**	**-**	**-**	**3 (4)**
Asthma	-	-	-	-	1 (1)
Cough	1 (1)	1 (1)	-	-	2 (2)
Rhinorrhea	1 (1)	1 (1)	-	-	1 (1)
Upper respiratory tract inflammation	-	1 (3)	-	-	-

Skin and subcutaneous tissue disorders	**1(1)**	**3 (6)**	**1 (2)**	**7 (10)**	**5 (10)**
Dermatitis	-	-	-	-	1 (1)
Dermatitis allergic	-	-	-	-	1 (1)
Dermatitis contact	-	1 (1)	-	-	-
Dermatitis diaper	-	2 (3)	1 (1)	1 (1)	-
Dry skin	-	1 (1)	-	2 (2)	2 (2)
Eczema	-	1 (1)	-	1 (1)	-
Hemorrhage subcutaneous	-	-	-	-	2 (2)
Miliaria	-	-	-	-	1 (1)
Rash	-	-	-	4 (6)	1 (1)
Rash papular	1 (1)	-	-	-	-
Skin erosion	-	-	-	-	1 (1)
Urticaria	-	-	-	-	1 (2)
Vascular disorder	**1 (1)**	**-**	**-**	**-**	**-**
Hypertension	1 (1)	-	-	-	-

*For study NCT02980666 and its extension NCT03268811, six of eight children were enrolled and received teduglutide treatment after protocol amendment, which included improved training for parents to administer doses of teduglutide to patients.

[†]Data pooled from studies NCT03571516 (n = 5; patients randomized to receive teduglutide treatment compared with SoC group) and NCT02980666 (N = 2; patients only received teduglutide).

[‡]Of the children enrolled in the extension study, one child did not receive teduglutide owing to ongoing enteral autonomy from the core study.

[§]Device-related TEAEs and TESAEs were considered to be complications of central venous catheters used to prepare and administer PS, not the device used to prepare or administer teduglutide.

m = number of events; n = number of patients experiencing the event; PS = parenteral support; SoC = standard of care; TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event.