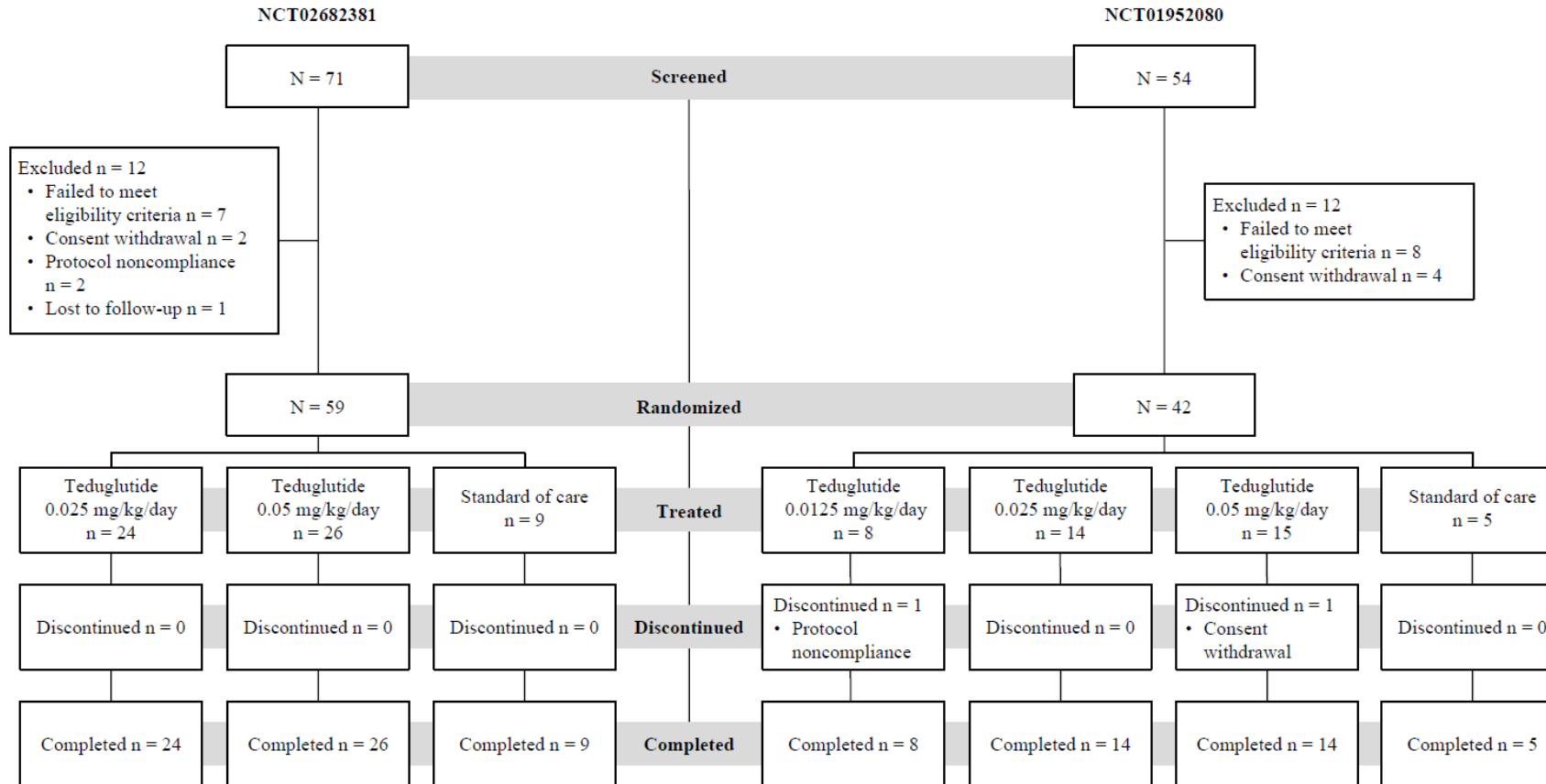


Figure, Supplemental Digital Content 1. CONSORT diagram.



Patients in the teduglutide treatment arms received a once-daily subcutaneous injection of teduglutide 0.0125 mg/kg (NCT01952080 only), 0.025 mg/kg, or 0.05 mg/kg (NCT01952080 and NCT02682381) (1,2).

CONSORT = Consolidated Standards of Reporting Trials.

REFERENCES

- 1 Carter BA, Cohran VC, Cole CR, et al. Outcomes from a 12-week, open-label, multicenter clinical trial of teduglutide in pediatric short bowel syndrome. *J Pediatr* 2017;181:102-11.e5.
- 2 Kocoshis SA, Merritt RJ, Hill S, et al. Safety and efficacy of teduglutide in pediatric patients with intestinal failure due to short bowel syndrome: a 24-week, phase III study. *JPEN J Parenter Enteral Nutr* 2020;44(4):621-31.

Table, Supplemental Digital Content 2. Average BSFS score

Average BSFS score	Teduglutide			SoC (n = 9)
	0.025 mg/kg/day (n = 24)	0.05 mg/kg/day (n = 26)	Total (n = 50)	
Baseline				
n	19	24	43	8
Median (min, max)	7.0 (5.7, 7.0)	7.0 (4.8, 7.0)	7.0 (4.8, 7.0)	7.0 (6.5, 7.0)
Mean (SE)	6.6 (0.1)	6.6 (0.1)	6.6 (0.1)	6.9 (0.1)
Week 12				
Actual value				
n	18	23	41	5
Median (min, max)	3.5 (2.5, 7.0)	6.0 (1.0, 7.0)	5.5 (1.0, 7.0)	3.5 (3.0, 7.0)
Mean (SE)	4.6 (0.4)	4.9 (0.4)	4.8 (0.3)	4.8 (0.9)
Change from baseline				
n	18	23	41	5
Median (min, max)	-2.8 (-4.0, 0.0)	-1.0 (-6.0, 0.0)	-1.0 (-6.0, 0.0)	-3.0 (-4.0, 0.0)
Mean (SE)	-2.0 (0.4)	-1.7 (0.4)	-1.8 (0.3)	-2.1 (0.9)
P value	0.0001	0.0001	< 0.0001	0.0736
Week 24				
Actual value				
n	17	24	41	4
Median (min, max)	3.5 (2.0, 7.0)	3.5 (2.0, 7.0)	3.5 (2.0, 7.0)	4.8 (3.0, 7.0)
Mean (SE)	4.7 (0.5)	4.2 (0.4)	4.4 (0.3)	4.9 (1.0)
Change from baseline				

Average BSFS score	Teduglutide			SoC (n = 9)
	0.025 mg/kg/day (n = 24)	0.05 mg/kg/day (n = 26)	Total (n = 50)	
n	17	24	41	4
Median (min, max)	-3.0 (-4.0, 0.0)	-3.0 (-4.5, 0.5)	-3.0 (-4.5, 0.5)	-2.0 (-4.0, 0.0)
Mean (SE)	-2.0 (0.4)	-2.3 (0.4)	-2.2 (0.3)	-2.0 (0.9)
<i>P</i> value	0.0002	< 0.0001	< 0.0001	0.1162
Change from week 12				
n	16	23	39	4
Median (min, max)	0.0 (-3.5, 3.5)	0.0 (-3.5, 3.0)	0.0 (-3.5, 3.5)	0.0 (-4.0, 3.0)
Mean (SE)	0.2 (0.5)	-0.7 (0.4)	-0.3 (0.3)	-0.3 (1.4)
<i>P</i> value	0.6626	0.1273	0.3612	0.8729

P values were generated from a paired difference t-test comparing week 12 and week 24 with baseline values, or between week 12 and week 24 values.

Data were from NCT02682381.

BSFS scores were calculated based on the minimum value of the available scores in a 4-week period. Some patients may have only one available score for a particular 4-week period.

BSFS = Bristol Stool Form Scale; SoC = standard of care; SE = standard error.

Table, Supplemental Digital Content 3. Change in PN/IV volume

PN/IV volume, mL/kg/day	Teduglutide				SoC (n = 14)
	0.0125 mg/kg/day (n = 8)	0.025 mg/kg/day (n = 38)	0.05 mg/kg/day (n = 41)	Total (n = 87)	
Baseline					
n	7	34	39	80	14
Median (min, max)	50.4 (27.1, 100.0)	61.9 (12.3, 141.7)	56.3 (23.6, 132.9)	56.9 (12.3, 141.7)	82.5 (32.6, 125.9)
Mean (SE)	55.3 (9.1)	64.0 (4.8)	62.4 (4.5)	62.4 (3.1)	79.6 (6.9)
Week 12					
Actual value					
n	7	36	37	80	13
Median (min, max)	48.0 (10.9, 90.0)	44.5 (0.0, 108.8)	39.7 (0.0, 123.5)	42.2 (0.0, 123.5)	79.5 (27.6, 128.0)
Mean (SE)	50.2 (9.1)	44.8 (4.5)	45.6 (4.9)	45.6 (3.1)	78.5 (7.6)

PN/IV volume, mL/kg/day	Teduglutide				SoC (n = 14)
	0.0125 mg/kg/day (n = 8)	0.025 mg/kg/day (n = 38)	0.05 mg/kg/day (n = 41)	Total (n = 87)	
Change from baseline					
n	7	32	36	75	13
Median (min, max)	-2.4 (-16.3, 1.1)	-14.8 (-63.8, 4.1)	-11.8 (-49.9, -1.6)	-12.3 (-63.8, 4.1)	-2.3 (-5.8, 14.7)
Mean (SE)	-5.1 (2.3)	-19.1 (2.9)	-17.3 (2.1)	-16.9 (1.7)	0.1 (1.8)
<i>P</i> value	0.0701	< 0.0001	< 0.0001	< 0.0001	0.9375
Week 24					
Actual value					
n	N/A	24	26	50	9
Median (min, max)	N/A	43.0 (0.0, 121.4)	32.5 (0.0, 109.8)	38.4 (0.0, 121.4)	76.6 (18.0, 125.0)
Mean (SE)	N/A	45.8 (6.2)	36.5 (5.2)	40.9 (4.1)	73.6 (11.0)
Change from baseline					
n	N/A	20	25	45	9
Median (min, max)	N/A	-17.7 (-33.7, 2.8)	-18.8 (-61.4, 1.9)	-18.4 (-61.4, 2.8)	-5.9 (-14.6, 0.4)
Mean (SE)	N/A	-16.2 (2.4)	-23.3 (3.5)	-20.1 (2.3)	-6.0 (1.5)
<i>P</i> value	N/A	< 0.0001	< 0.0001	< 0.0001	0.0041

P values were generated from a paired difference t-test comparing mean week 12 and week 24 values with mean baseline values.

Data were pooled from NCT01952080 and NCT02682381.

N/A = not applicable; PN/IV = parenteral nutrition and/or intravenous fluids; SE = standard error; SoC = standard of care.

Table, Supplemental Digital Content 4. Change in enteral nutrition volume

Enteral nutrition volume, mL/kg/day	Teduglutide				SoC (n = 14)
	0.0125 mg/kg/day (n = 8)	0.025 mg/kg/day (n = 38)	0.05 mg/kg/day (n = 41)	Total (n = 87)	
Baseline					
n	8	32	39	79	14

Enteral nutrition volume, mL/kg/day	Teduglutide				SoC (n = 14)
	0.0125 mg/kg/day (n = 8)	0.025 mg/kg/day (n = 38)	0.05 mg/kg/day (n = 41)	Total (n = 87)	
Median (min, max)	20.5 (0.0, 109.6)	26.3 (0.0, 91.9)	17.9 (0.0, 111.9)	23.1 (0.0, 111.9)	12.8 (0.0, 86.8)
Mean (SE)	34.3 (14.6)	29.1 (4.9)	26.1 (4.3)	28.1 (3.2)	25.5 (8.3)
Week 12					
Actual value					
n	7	35	38	80	13
Median (min, max)	51.8 (0.0, 105.1)	37.6 (0.0, 127.2)	25.1 (0.0, 155.0)	33.6 (0.0, 155.0)	17.5 (0.0, 90.5)
Mean (SE)	51.9 (14.6)	40.1 (5.9)	35.3 (5.8)	38.9 (4.0)	29.7 (9.7)
Change from baseline					
n	7	30	37	74	13
Median (min, max)	10.8 (-4.5, 35.3)	1.2 (-6.4, 70.8)	4.6 (-6.6, 43.1)	3.4 (-6.6, 70.8)	0.0 (-2.2, 15.6)
Mean (SE)	12.7 (5.8)	10.0 (3.3)	7.9 (1.7)	9.2 (1.7)	2.8 (1.3)
P value	0.0709	0.0052	0.0001	< 0.0001	0.0617
Week 24					
Actual value					
n	N/A	23	26	49	9
Median (min, max)	N/A	17.3 (0.0, 94.1)	27.0 (0.0, 163.8)	23.8 (0.0, 163.8)	2.9 (0.0, 61.9)
Mean (SE)	N/A	29.1 (6.2)	40.2 (7.9)	35.0 (5.1)	14.8 (7.2)
Change from baseline					
n	N/A	18	25	43	9
Median (min, max)	N/A	3.3 (-14.8, 47.3)	5.8 (-7.1, 61.7)	5.1 (-14.8, 61.7)	0.0 (-11.8, 10.1)
Mean (SE)	N/A	7.7 (3.2)	11.0 (3.3)	9.6 (2.3)	0.7 (2.0)
P value	N/A	0.0269	0.0030	0.0002	0.7176
Change from week 12					
n	N/A	23	26	49	9

Enteral nutrition volume, mL/kg/day	Teduglutide			Total (n = 87)	SoC (n = 14)
	0.0125 mg/kg/day (n = 8)	0.025 mg/kg/day (n = 38)	0.05 mg/kg/day (n = 41)		
Median (min, max)	N/A	1.9 (-16.3, 30.9)	0.5 (-8.1, 38.1)	1.3 (-16.3, 38.1)	0.0 (-9.6, 2.7)
Mean (SE)	N/A	3.4 (2.1)	3.3 (1.6)	3.3 (1.3)	-0.7 (1.2)
<i>P</i> value	N/A	0.1221	0.0543	0.0133	0.5379

P values were generated from a paired difference t-test comparing mean week 12 and week 24 values with mean baseline values, or between mean week 12 and week 24 values.

Data were pooled from NCT01952080 and NCT02682381.

N/A = not applicable; SE = standard error; SoC = standard of care.

Table, Supplemental Digital Content 5. Change in stool frequency per day

Stool frequency per day	Teduglutide			SoC (n = 9)
	0.025 mg/kg/day (n = 24)	0.05 mg/kg/day (n = 26)	Total (n = 50)	
Baseline				
n	18	22	40	6
Median (min, max)	3.0 (0.5, 11.0)	3.0 (1.0, 8.5)	3.0 (0.5, 11.0)	4.8 (2.5, 7.5)
Mean (SE)	3.4 (0.5)	3.5 (0.4)	3.5 (0.3)	5.1 (0.8)
Week 12				
Actual value				
n	15	16	31	2
Median (min, max)	2.0 (1.0, 6.5)	2.8 (1.0, 5.5)	2.5 (1.0, 6.5)	5.8 (2.0, 9.5)
Mean (SE)	2.9 (0.4)	2.8 (0.4)	2.8 (0.3)	5.8 (3.8)
Change from baseline to week 12				
n	13	16	29	2
Median (min, max)	-0.5 (-4.5, 2.0)	-0.6 (-3.0, 1.5)	-0.5 (-4.5, 2.0)	-0.3 (-2.5, 2.0)
Mean (SE)	-0.7 (0.5)	-0.8 (0.4)	-0.8 (0.3)	-0.3 (2.3)

Stool frequency per day	Teduglutide			SoC (n = 9)
	0.025 mg/kg/day (n = 24)	0.05 mg/kg/day (n = 26)	Total (n = 50)	
<i>P</i> value	0.1456	0.0522	0.0133	0.9296
Week 24				
Actual value				
n	16	16	32	2
Median (min, max)	2.5 (0.5, 11.0)	3.0 (1.0, 10.5)	3.0 (0.5, 11.0)	1.3 (0.0, 2.5)
Mean (SE)	3.3 (0.6)	3.5 (0.6)	3.4 (0.4)	1.3 (1.3)
Change from baseline				
n	13	16	29	2
Median (min, max)	-0.5 (-5.5, 7.0)	0.0 (-3.5, 9.5)	-0.5 (-5.5, 9.5)	-2.0 (-2.5, -1.5)
Mean (SE)	-0.1 (0.8)	0.2 (0.7)	0.1 (0.5)	-2.0 (0.5)
<i>P</i> value	0.8986	0.7565	0.8846	0.1560

P values were generated from a paired difference t-test comparing mean week 12 and week 24 values with mean baseline values.

Data from NCT02682381.

SE = standard error; SoC = standard of care.

Table, Supplemental Digital Content 6. Effects of disease and patient characteristics on stool consistency (BSFS)

Parameter	F-value	<i>P</i> value
Week 12		
Current age, year	1.99	0.1661
Age at diagnosis, year	2.26	0.1403
Baseline BMI, kg/m ²	0.17	0.6807
Reason for SBS	2.54	0.0552
Remaining small intestine length, cm	0.16	0.6944
Anti-diarrheal use between baseline and week 12	2.20	0.1455
Antibiotic use between baseline and week 12	3.86	0.0563
Change in enteral nutrition volume [†] , mL/kg/day	0.91	0.3471
Change in PN/IV volume [†] , mL/kg/day	0.98	0.3299
Change in urine output, mL/kg/day	0.09	0.7707

Week 24		
Current age, year	1.78	0.1894
Age at diagnosis, year	2.17	0.1485
Baseline BMI, kg/m ²	0.18	0.6739
Reason for SBS	1.98	0.1182
Remaining small intestine length, cm	0.57	0.4542
Anti-diarrheal use between week 12 and week 24	0.65	0.4244
Antibiotic use between week 12 and week 24	0.32	0.5739
Change in enteral nutrition volume [†] , mL/kg/day	0.12	0.7281
Change in PN/IV volume [†] , mL/kg/day	2.08	0.1573
Change in urine output, mL/kg/day	1.30	0.2657

[†]Based on diary data.

P values are from ANCOVA analysis modeling BSFS score change from baseline as the dependent variable and baseline BSFS score, treatment, and a third factor as independent variables.

Data from NCT02682381.

ANCOVA, analysis of covariance; BMI = body mass index; BSFS = Bristol Stool Form Scale; PN/IV = parenteral nutrition and/or intravenous fluids; SBS = short bowel syndrome.

Table, Supplemental Digital Content 7. Change in anti-diarrheal doses per day

Anti-diarrheal doses per day	Teduglutide			Total (n = 87)	SoC (n = 14)
	0.0125 mg/kg/day (n = 8)	0.025 mg/kg/day (n = 38)	0.05 mg/kg/day (n = 41)		
Baseline					
n	3	12	18	33	3
Median (min, max)	2.0 (2.0, 6.0)	3.0 (2.0, 6.0)	3.0 (1.0, 10.0)	3.0 (1.0, 10.0)	3.0 (2.0, 3.0)
Mean (SD)	3.3 (2.3)	3.3 (1.1)	3.1 (2.0)	3.2 (1.7)	2.7 (0.6)
Week 12					
n	2	12	17	31	3
Median (min, max)	4.0 (2.0, 6.0)	3.0 (2.0, 6.0)	3.0 (1.0, 10.0)	3.0 (1.0, 10.0)	3.0 (2.0, 3.0)
Mean (SD)	4.0 (2.8)	3.3 (1.1)	2.9 (2.1)	3.1 (1.8)	2.7 (0.6)
Week 24					

Anti-diarrheal doses per day	Teduglutide				SoC (n = 14)
	0.0125 mg/kg/day (n = 8)	0.025 mg/kg/day (n = 38)	0.05 mg/kg/day (n = 41)	Total (n = 87)	
n	N/A	10	11	21	2
Median (min, max)	N/A	3.0 (1.0, 4.0)	3.0 (1.0, 5.0)	3.0 (1.0, 5.0)	3.0 (3.0, 3.0)
Mean (SD)	N/A	2.6 (1.1)	2.8 (1.2)	2.7 (1.1)	3.0 (0.0)

Anti-diarrheal medications include loperamide, loperamide hydrochloride, lomotil, and hyoscyamine sulfate. Doses were counted as number of doses per day (e.g., twice daily, three times daily, four times daily) regardless of amount received. Doses received for multiple medications were added to obtain the total number of doses received per day.

Data were pooled from NCT01952080 and NCT02682381.

N/A = not applicable; SD = standard deviation; SoC = standard of care