

Dr. Lorenzo Norsa, MD PhD

**Pediatric Department, Vittore Buzzi
children's hospital, University of Milan**

**DEFINING EARLY
MARKERS OF RESPONSE
AND PARENTERAL
NUTRITION WEANING FOR
CHILDREN WITH SHORT
BOWEL SYNDROME
TREATED WITH
GLUCAGON-LIKE PEPTIDE**

2

27 - 29 novembre 2025

Padova Congress
Via Carlo Goldoni 8, Cancellò C - Padova



Parenteral nutrition support



Spontaneous weaning expectancy in IF children

Goulet O, ClinNut 2021



TABLE 2 Univariable and multivariable analysis of predictors of 1-year enteral autonomy.

2023

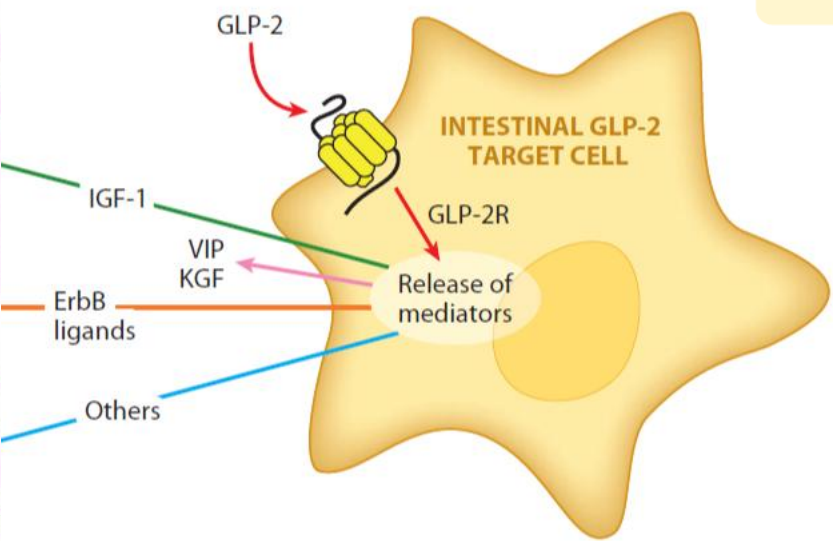
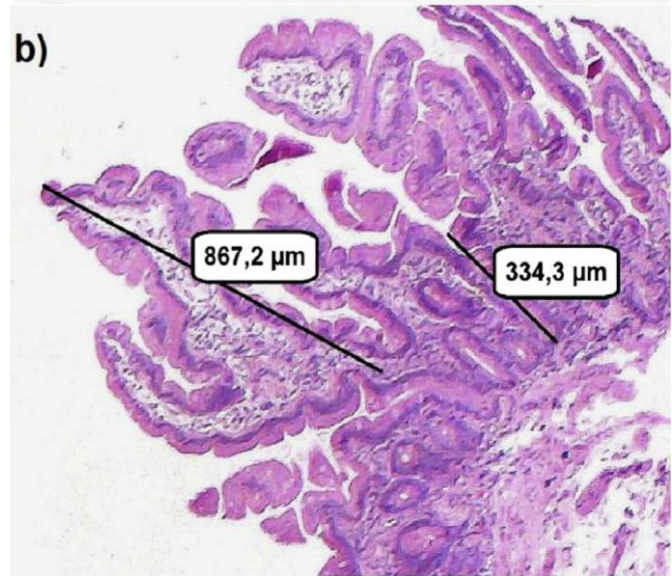
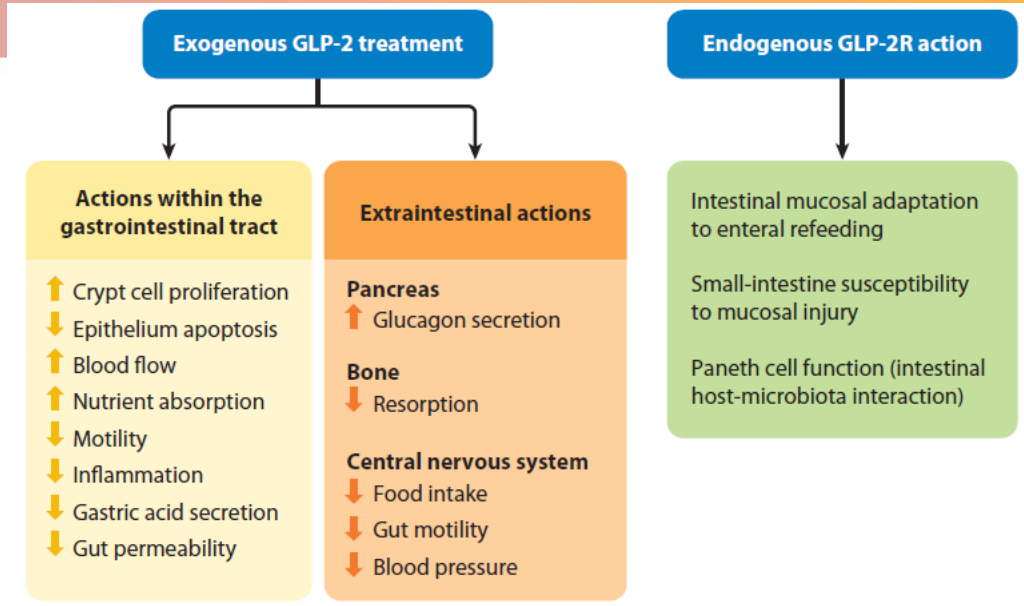
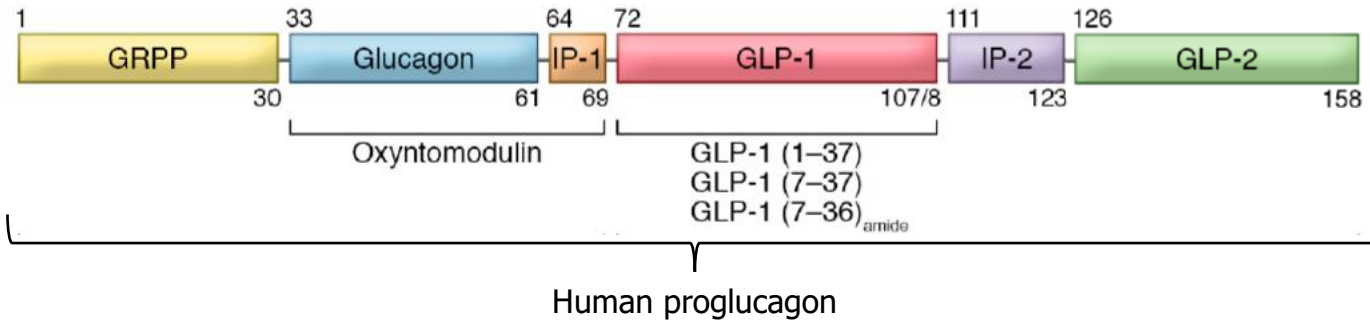
TABLE 1. Factors affecting parenteral nutrition (PN) weaning

Study	Population	Weaning	GEA	Length SB	ICV	Colon	Citrulline	Bilirubin	IR unit	Enteral tolerance > 50%	Lengthening surgery	SB diameter	IA	NEC	Sepsis
Andorsky DJ, 2001	30	67%		+											
Goulet O, 2005	87	88.5%		+	+										
Spencer AU, 2005	80	63.8%		+	+										
Daimond IR, 2010	106	66%		+					+						-
Infantino BJ, 2013	28 (<20cm SB)	48%			+	+									
Fallen EM, 2014	63 (<100 cm SB)	63%		+					+		-				
Demehri FR, 2015	171 (<50% SB)	64.3%		+	+								+	+	
Ives GC, 2016	42 (<30% SB)	55%										-			
Petit LM, 2016	98	58%		+	+	+									
Sparks EA, 2016	109	41.3%		+	+	+	+							+	
Capriati T, 2018	47	47%		+											
Belza C, 2019	139	68%		+	+	+		-		+					
Enman MA, 2020	158	89%	+	+	+									+	

GEA = gestational age; IA: intestinal atresia; ICV = ileocecal valve; IR = intestinal rehabilitation; NEC = necrotizing enterocolitis; SB = small bowel.

Norsa L, JPGN 2023

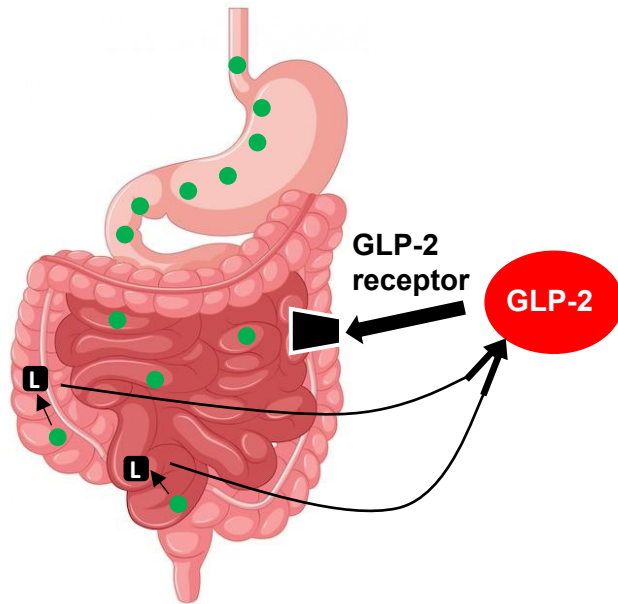
Pharmacological weaning



Drunker DJ, 2014
Drunker DJ, 2017

SBS-IF, GLP-2 and teduglutide

- Short bowel syndrome (SBS)-associated intestinal failure (IF) is a short bowel length below a critical value for adequate nutritional supply to support proper growth



Acute effects

- ↓ proximal motility
- ↑ mesenteric blood flow
- ↓ enteric secretions

Chronic effects

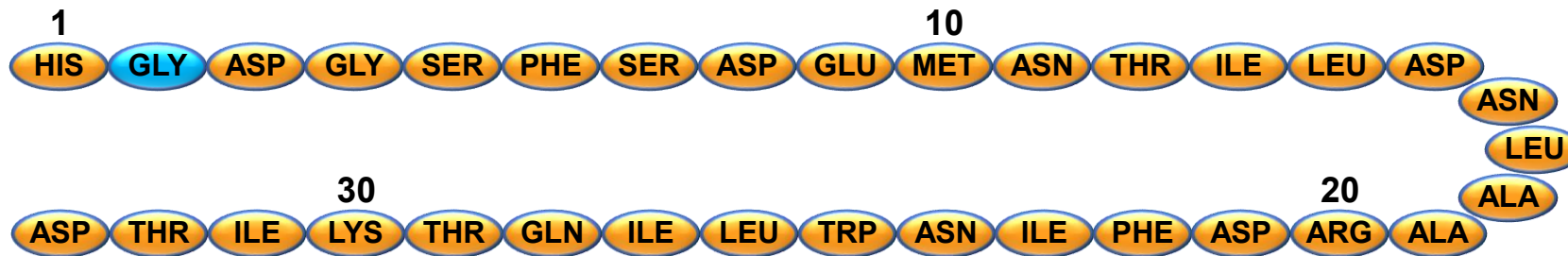
- ↑ crypt cell proliferation rate
- ↓ villous cell apoptosis
- ↑ intestinal mucosal hypertrophy

Elimination half-life

- GLP-2: 7 minutes
- Teduglutide: 2 hours in healthy individuals
1.3 hours in patients SBS-IF

Teduglutide

- Teduglutide is a GLP-2 agonist with an identical amino-acid sequence to endogenous GLP-2, except for the replacement of an alanine with glycine at position 2 ([Gly2]GLP-2)^{1,2}



- This single amino-acid substitution resists degradation by DPP-IV,²⁻⁴ increasing potency and lengthening mean half-life from ~7 min for endogenous GLP-2 to ~2 h in healthy subjects and 1.3 h in patients with SBS-IF^{1,2,4,5}

• DPP-IV, dipeptidyl peptidase intravenous; GLP-2, glucagon-like peptide-2; [Gly2]GLP-2, degradation-resistant analog of GLP-2 (teduglutide); IF, intestinal failure; SBS, short bowel syndrome.

1. Gattex [package insert]. Lexington, MA: Shire-NPS Pharmaceuticals, Inc., 7/16. 2. Revestive [summary of product characteristics]. Dublin, Ireland: Shire Pharmaceuticals Ireland Ltd, 7/17. 3. Drucker DJ, et al. *Nat Biotechnol.* 1997;15:673-7. 4. Tavares W, et al. *Am J Physiol Endocrinol Metab.* 2006 Jan;278(1):E134-9. 5. Hartmann B, et al. *J Clin Endocrinol Metab.* 2000;85:2884-8.

Teduglutide

- ✓ Approved for some country in Europe for SBS-IF in children >4 months of corrected age
- ✓ Daily morning subcutaneous injection of 0.05 mg/kg

Current recommendation

Children who have plateaued in their intestinal adaptation
(inability to reduce PN by >10% even when stable for > 3 months)

Only in children who would be expected to tolerate an increasing enteral nutrition

Data on predictors of real-world response are still scarce








Real-TEDUPediatricRegistry

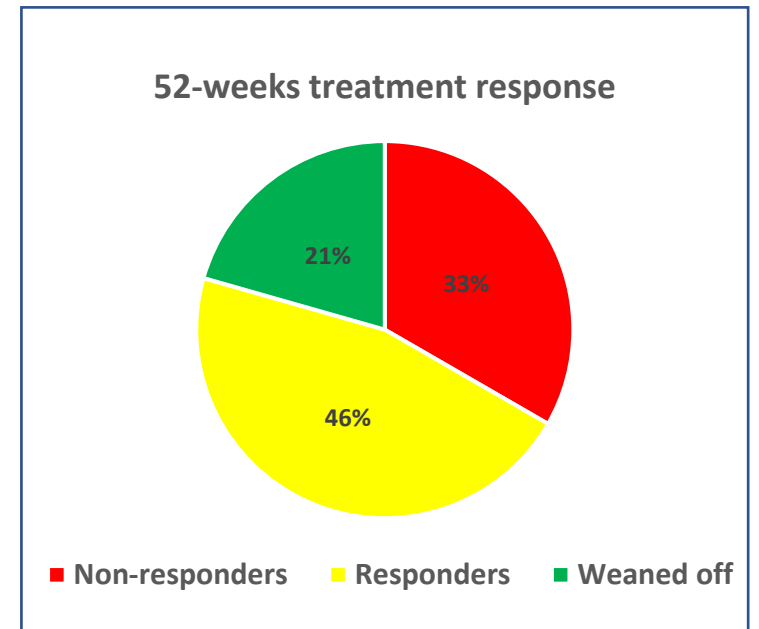
- ❖ A real-life, multicenter, retrospective and prospective cohort study
- ❖ To enroll prospectively children <18 years old who started teduglutide from June 2021 and collect data from previously treated patients

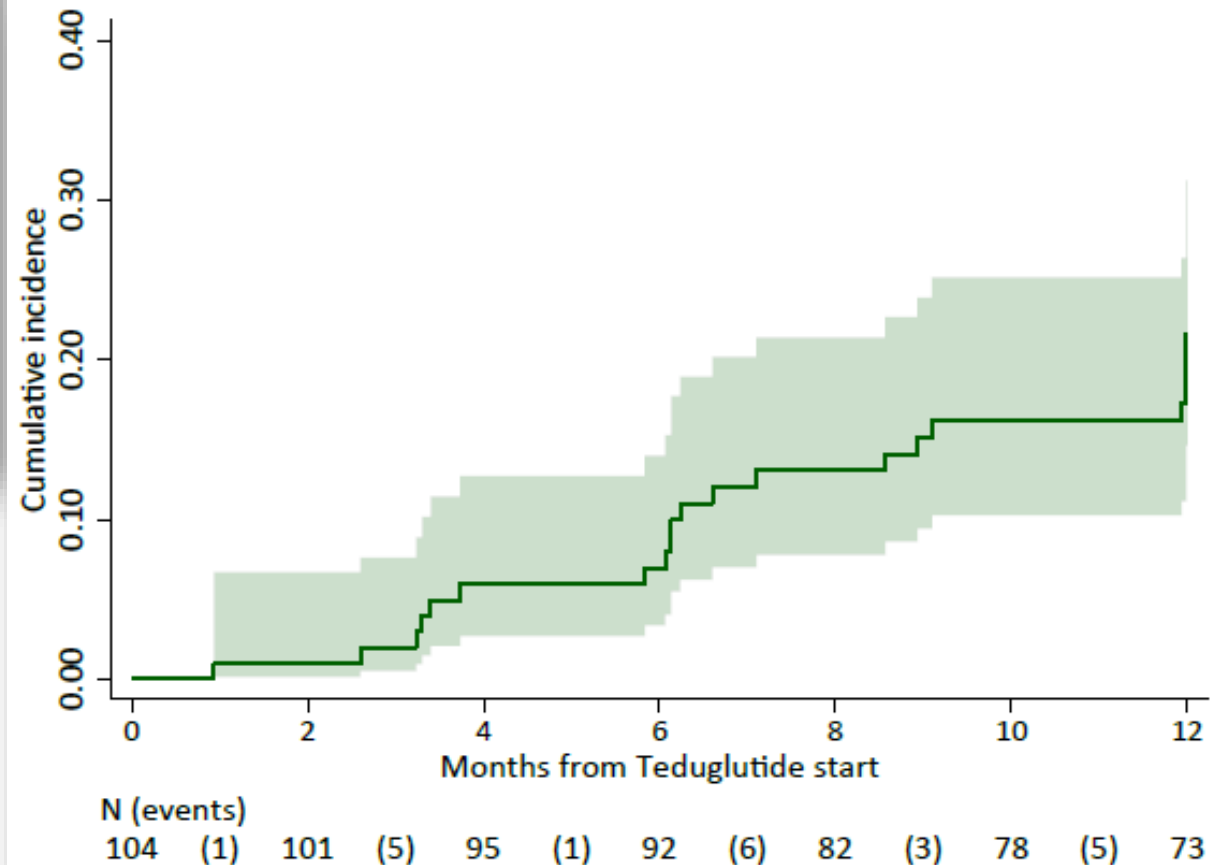
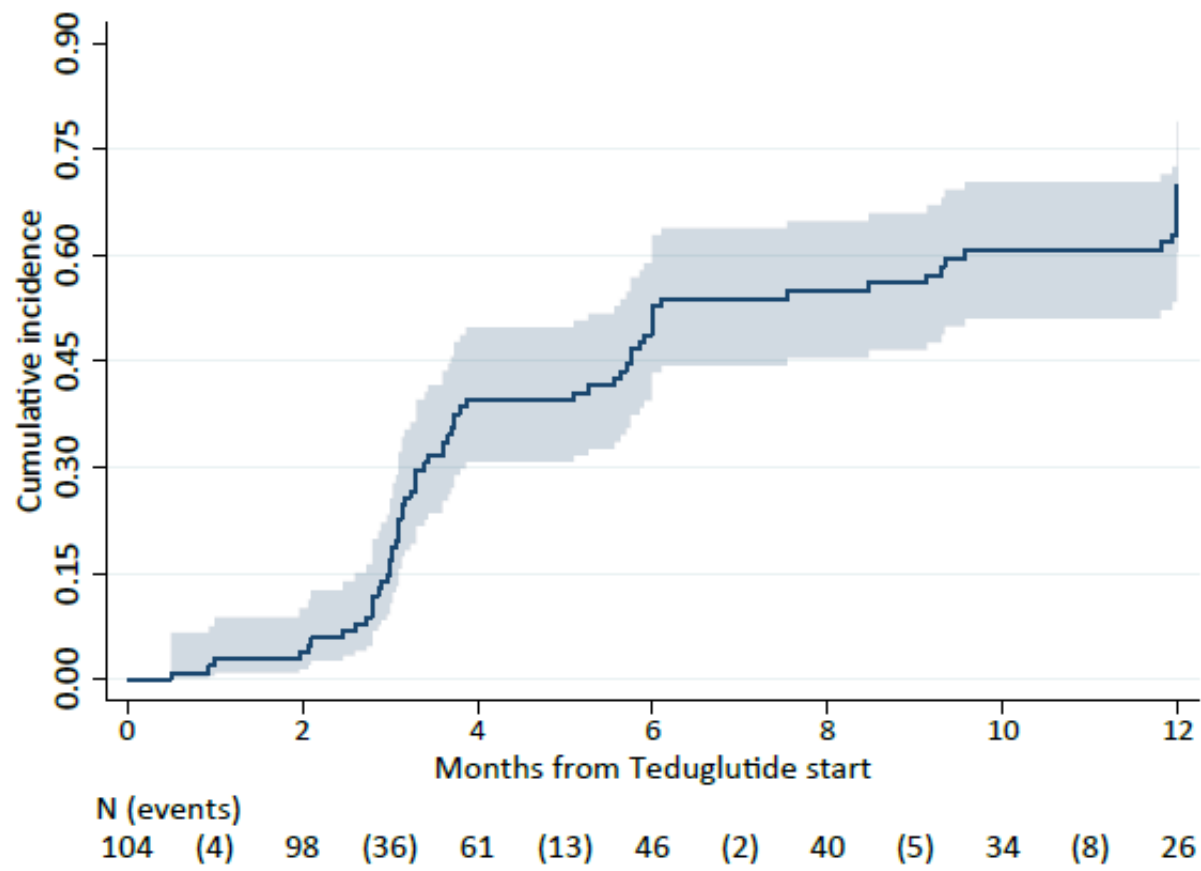


Investigate factors (before and during treatment) which could predict treatment response* and PN weaning after 1 year of treatment



	n = 104
	n = 6
	n = 21
	n = 13
	n = 14
	n = 12
	n = 5
	n = 33





* Response to treatment was defined as reduction of PN volume or calories $\geq 20\%$.

Demographics	Total
	N = 104
Male	64 (61.5%)
Female	40 (38.5%)
Age at TED start (years, median, IQR)	6.7 (3.6-10.4)
Ethnicity	
Caucasian	87 (83.7%)
Latin/Hispanic	5 (4.8%)
African	5 (4.8%)
Arab	7 (6.7%)
Week of gestation at birth (median, IQR)	33.0 (30.0-34.0)
Term	37 (35.6%)
N° of missing observations	42
Major causes of short gut	
Volvulus	23 (22.1%)
Necrotizing enterocolitis (NEC)	29 (27.9%)
Hirschsprung	15 (14.4%)
Gastroschisis	15 (14.4%)
Intestinal atresia	11 (10.6%)
Ischemic	5 (4.8%)
Pseudobstruction	2 (1.9%)
Meconium ileus	1 (1.0%)
Mixed form	3 (2.9%)
Length of residual small intestine (cm, median, IQR)	25.0 (15.0-45.0)
N° of missing observations	6
Ileocecal valve	24 (23.1%)
Colon	88 (84.6%)
Type of SBS	
I	16 (15.4%)
II	64 (61.5%)
III	24 (23.1%)
Ending stoma	21 (20.2%)
Age at PN start (months)	0.5 (0.1-2.9)
Time from PN start-TED start (years, median, IQR)	5.9 (2.8-8.8)
Funding body of TED	
National Health Service	89 (100.0%)
N° of missing observations	15

	Total	1-year response		p
	N = 104	No (N = 36)	Yes (N = 68)	
6-months response				
No	47 (45.2%)	32 (88.9%)	15 (22.1%)	<0.001 ^a
Yes	57 (54.8%)	4 (11.1%)	53 (77.9%)	

^aSignificance level of p < 0.05.

Table 2: Association between 6-months vs. 12 months clinical response.

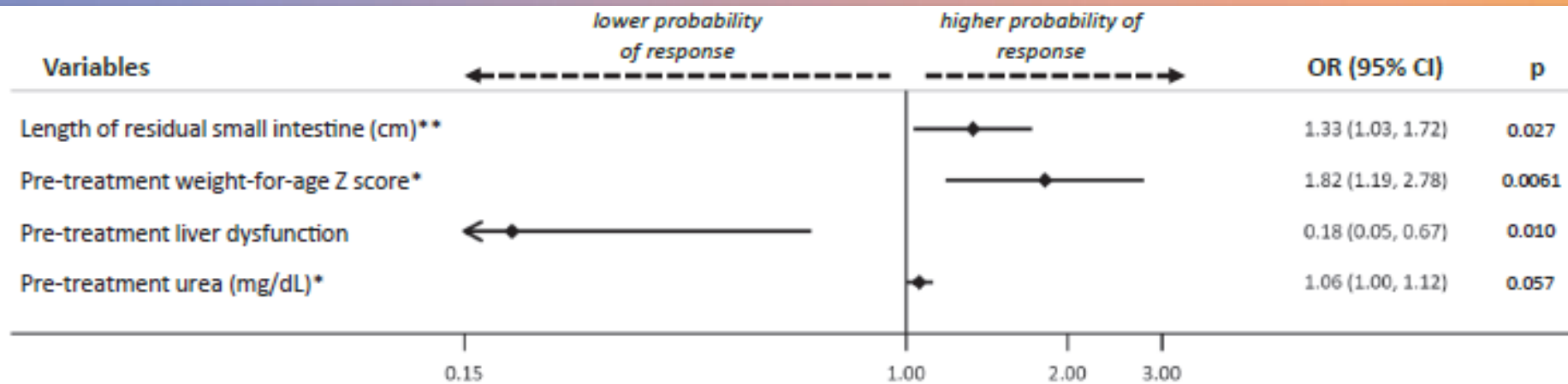


Fig. 3: Predictors of 1-year response obtained by a multivariable logistic regression model. Legend. OR: Odds ratio; CI: Confidence interval; *For 1-unit increase; **For 10 cm increase. Estimates were obtained using a multivariable logistic regression model. Odds ratios (ORs) for 1-year response (diamonds) were plotted with 95% confidence intervals (CIs) (solid lines).

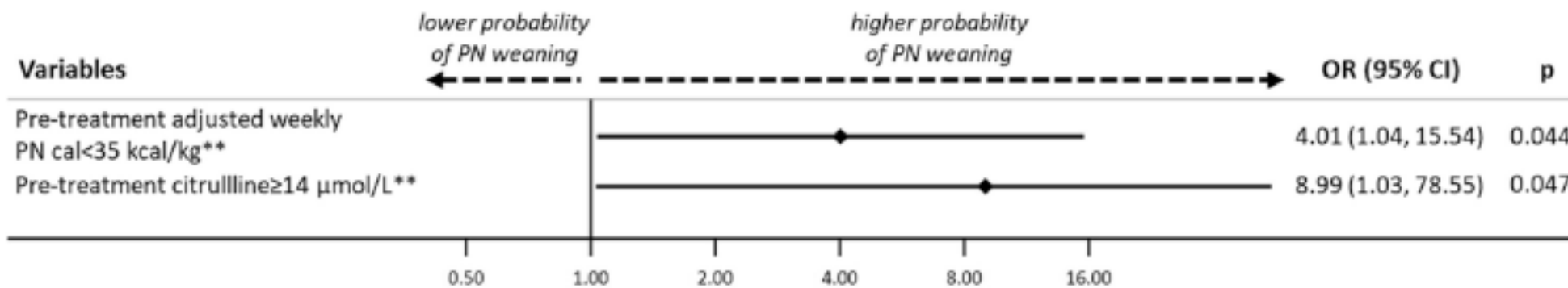


Fig. 4: Predictors of 1-year PN weaning estimated by a multivariable logistic regression model. Legend: OR: Odds Ratio; CI: Confidence interval; **Cutoff identified by the corresponding ROC curve. Estimates were obtained using a multivariable logistic regression model. Odds ratios (ORs) for 1-year PN weaning (diamonds) were plotted with 95% confidence intervals (CIs) (solid lines). Due to the small number of events and the quasi-complete separation in pretreatment citrulline $\geq 14 \mu\text{mol/L}$, the resulting odds ratios may be unstable and associated with wide confidence intervals. This reflects model uncertainty and should be interpreted with caution.

Mean Hb value during treatment

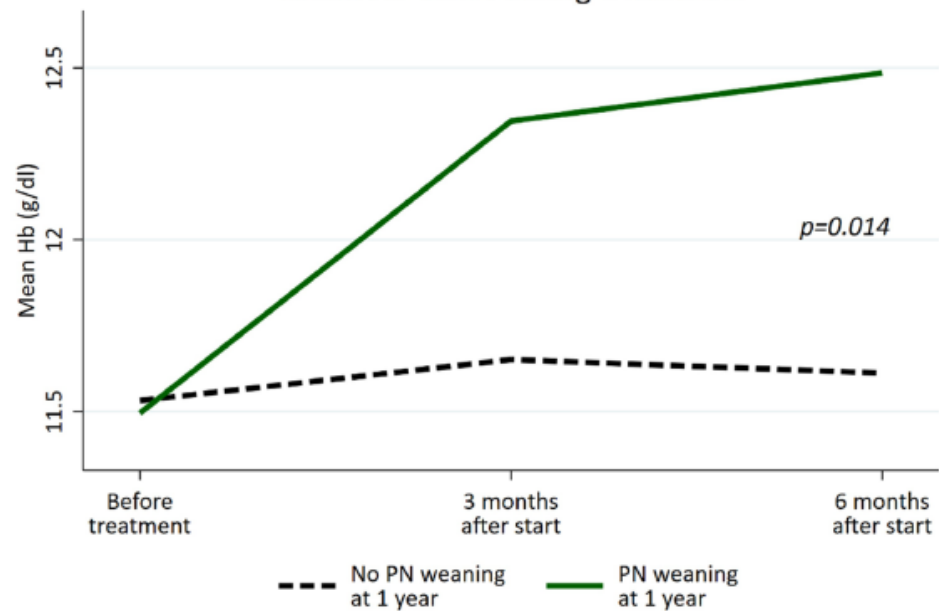


Fig. 5: Trend of haemoglobin (Hb) values over time according to PN weaning. Trends in haemoglobin (Hb) values during the first 6 months of Teduglutide therapy according to PN weaning at 1 year. A linear mixed-effects model was used to explore whether early changes in haemoglobin were different between patients weaned from PN compared to those not weaned. This model included group (PN weaning vs. no PN weaning), time and group-time interaction as fixed effects, and patient as random intercept (to account for patient variability). The p-value of 0.014 represents the p-value of the group-time interaction term, indicating that there is a significant interaction between PN weaning and time. This suggests that the two groups experienced different changes in Hb levels over time.

Mean citrulline value during treatment

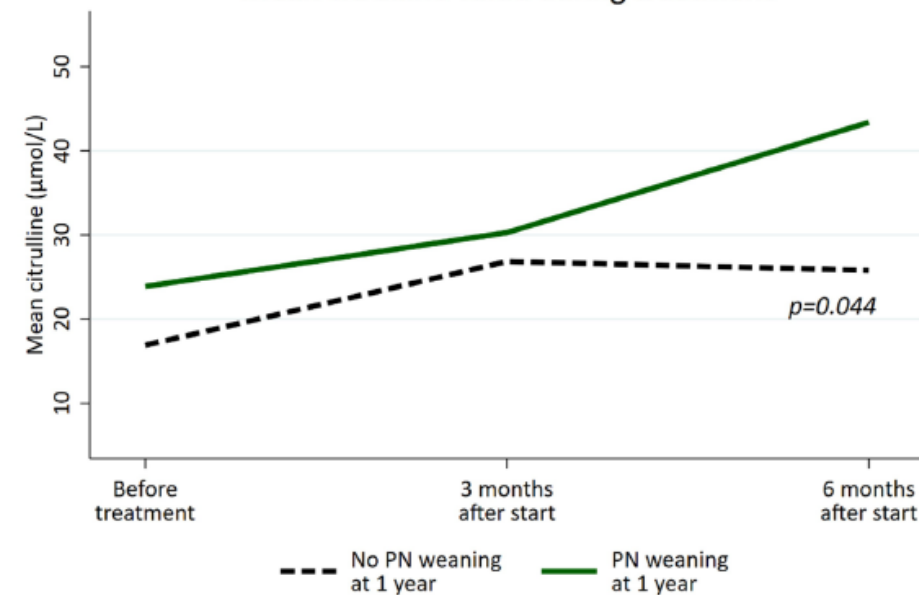
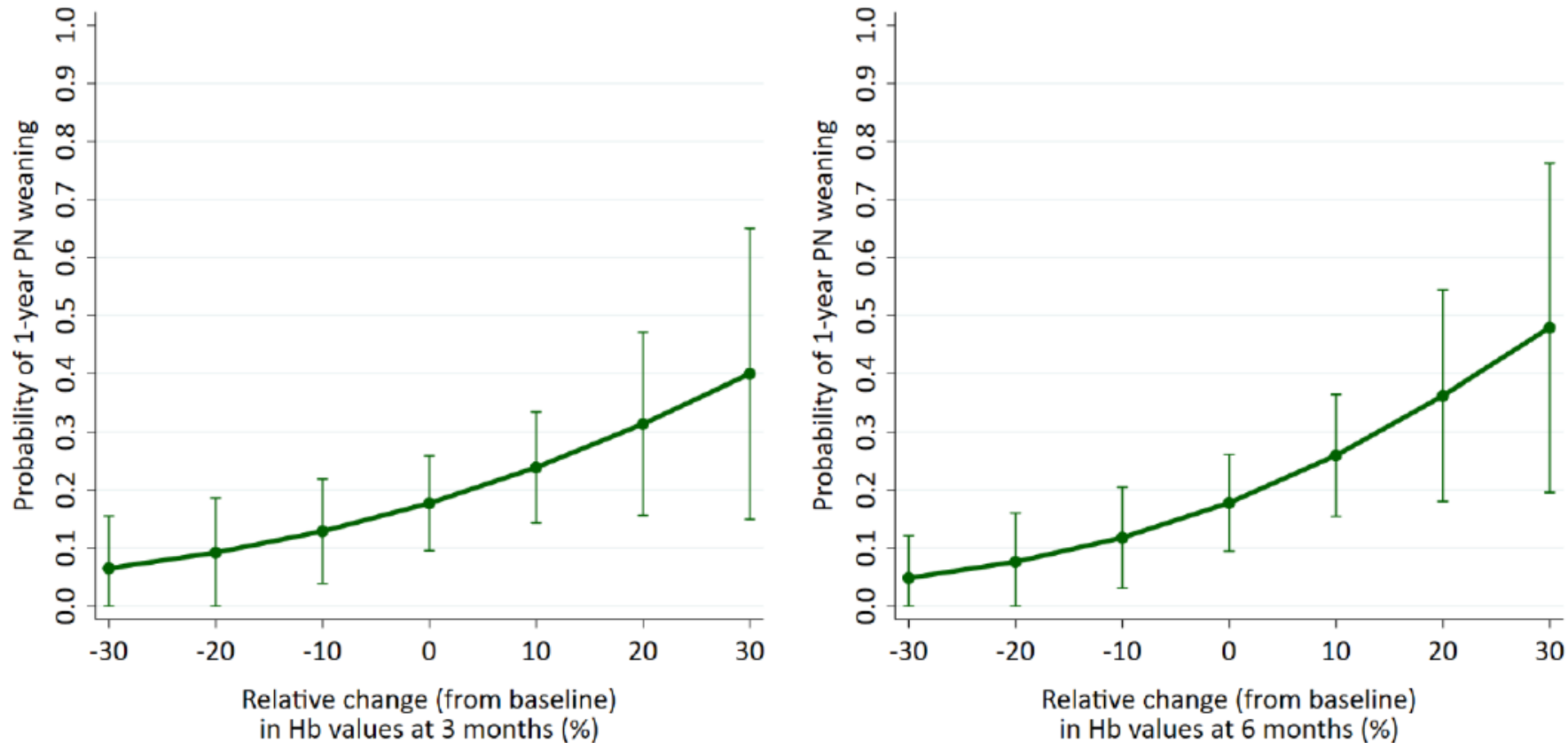


Fig. 6: Trend of citrulline values over time according to PN weaning. Trends in citrulline values during the first 6 months of Teduglutide therapy according to PN weaning at 1 year. A linear mixed-effects model was used to explore whether early changes in citrulline were different between patients weaned from PN compared to those not weaned. This model included group (PN weaning vs. no PN weaning), time and group-time interaction as fixed effects, and patient as random intercept (to account for patient variability). The p-value of 0.044 represents the p-value of the group-time interaction term, indicating that there is a significant interaction between PN weaning and time. This suggests that the two groups experienced different changes in citrulline levels over time. It should be noted that the 6-month citrulline values are only available for 41 and 43 patients, respectively.

Supplementary figure 1: Probability of 1-year PN weaning as a function of the relative change in hemoglobin values from baseline at 3 months (left panel) and 6 months (right panel).

The curves represent the estimated probability of 1-year PN weaning, with error bars indicating the 95% confidence interval for each interval of hemoglobin (Hb) change. A positive trend in PN weaning probability is observed with increasing relative change in Hb values.

The x-axis shows all possible values of relative changes in hemoglobin. Only one patient had an 83% increase in hemoglobin (from 6.5 g/dl at baseline to 11.9 g/dl at 3 and 6 months).



	Adverse events (AEs)	
	Any grade	Grade III-IV
Total number of AEs	33	12
Type of AE		
Upper-respiratory-tract infection	5 (15.2%)	1 (8.3%)
Abdominal distension	3 (9.1%)	–
Abdominal pain	4 (12.1%)	–
Congestive heart failure	1 (3.0%)	–
Catheter related blood stream infections (CRBSI)	5 (15.2%)	5 (41.7%)
Other	15 (45.5%)	6 (50.0%)
Specify		
Anastomotic stricture	1 (6.7%)	1 (16.7%)
Catheter obstruction	1 (6.7%)	–
Constipation and abdominal distension	1 (6.7%)	–
D-lactic acidosis	1 (6.7%)	1 (16.7%)
Elevated liver enzymes	1 (6.7%)	–
Enteritis	1 (6.7%)	–
Exit site infection (tunnelitis)	1 (6.7%)	–
Intestinal sub-obstruction	3 (20.1%)	2 (33.4%)
Occlusion	2 (13.3%)	2 (33.4%)
Swollen and painful joints	1 (6.7%)	–
Transient generalized pruritus	1 (6.7%)	–
Vomiting	1 (6.7%)	–
Serious Adverse Events (SAEs)	16 (48.5%)	11 (91.7%)
Relation with teduglutide		
No	9 (56.3%)	
Yes	7 (43.8%)	
Specify		
Unlikely related	1 (14.3%)	
Possible related ^a	1 (14.3%)	
Probable related ^b	5 (71.4%)	

^aThere is a possibility that Teduglutide is the cause of the AE, but it is not the most likely explanation and there are other potential explanations.

^bTeduglutide is more likely to be the cause of the AE than other explanations. There are strong indications to support this relationship.

Table 3: Adverse Events (AEs) during 12 months of treatment with Teduglutide and relationship between serious adverse events (SAE) and treatment.



Growth trajectories in the first year of treatment

Table 1. Weight, height and BMI z-scores over time according to response to Teduglutide

	Total N=104	NON-RESPONDERS N=36	RESPONDERS N=68	p
3 months				
Weight z-score	-1.4 (-2.7, -0.5)	-2.2 (-3.6, -1.1)	-1.0 (-2.0, -0.0)	0.007
Height z-score	-1.1 (-2.5, -0.3)	-1.7 (-2.5, -1.1)	-0.8 (-2.2, -0.2)	
BMI z-score*	-0.7 (-1.7, -0.1)	-1.0 (-2.6, -0.7)	-0.4 (-1.4, 0.0)	
6 months				
Weight z-score	-1.4 (-2.6, -0.5)	-1.9 (-3.1, -1.2)	-1.0 (-2.5, -0.3)	
Height z-score	-1.2 (-2.4, -0.5)	-1.9 (-2.5, -1.0)	-0.9 (-2.3, -0.4)	
BMI z-score*	-0.8 (-1.8, -0.2)	-1.1 (-2.2, -0.4)	-0.5 (-1.7, 0.1)	
9 months				
Weight z-score	-1.1 (-1.9, -0.3)	-1.7 (-2.5, -1.1)	-0.9 (-1.5, -0.3)	
Height z-score	-1.0 (-1.5, -0.0)	-1.3 (-1.5, -0.2)	-0.8 (-1.4, -0.0)	
BMI z-score*	-0.7 (-1.4, 0.1)	-1.3 (-2.4, -0.5)	-0.3 (-1.0, 0.2)	
12 months				
Weight z-score	-1.3 (-2.5, -0.4)	-1.7 (-2.7, -1.1)	-1.2 (-2.5, -0.3)	
Height z-score	-1.2 (-2.3, -0.4)	-1.4 (-2.1, -0.4)	-1.0 (-2.3, -0.4)	
BMI z-score*	-0.7 (-1.6, -0.1)	-1.4 (-2.5, -0.6)	-0.4 (-1.1, 0.2)	

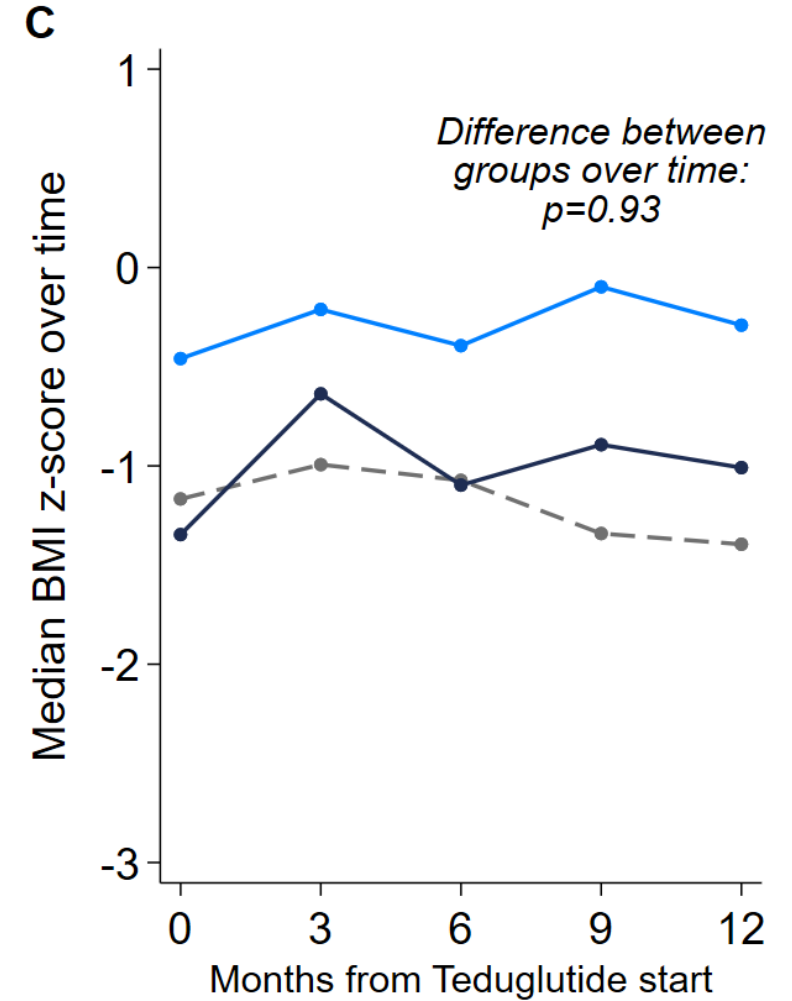
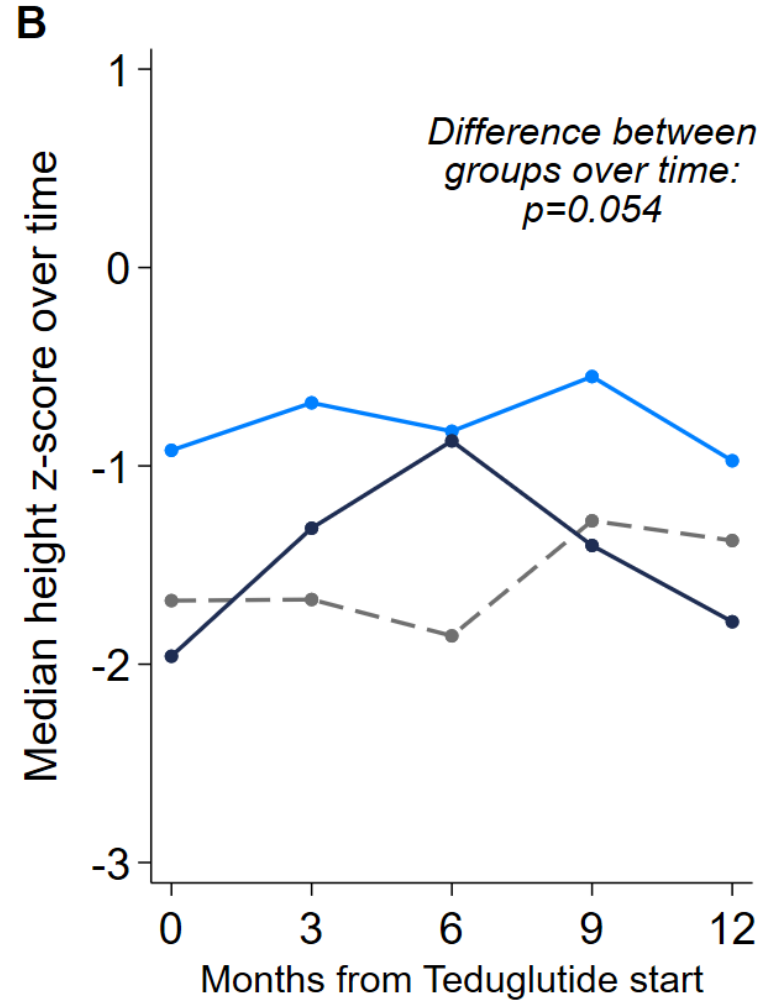
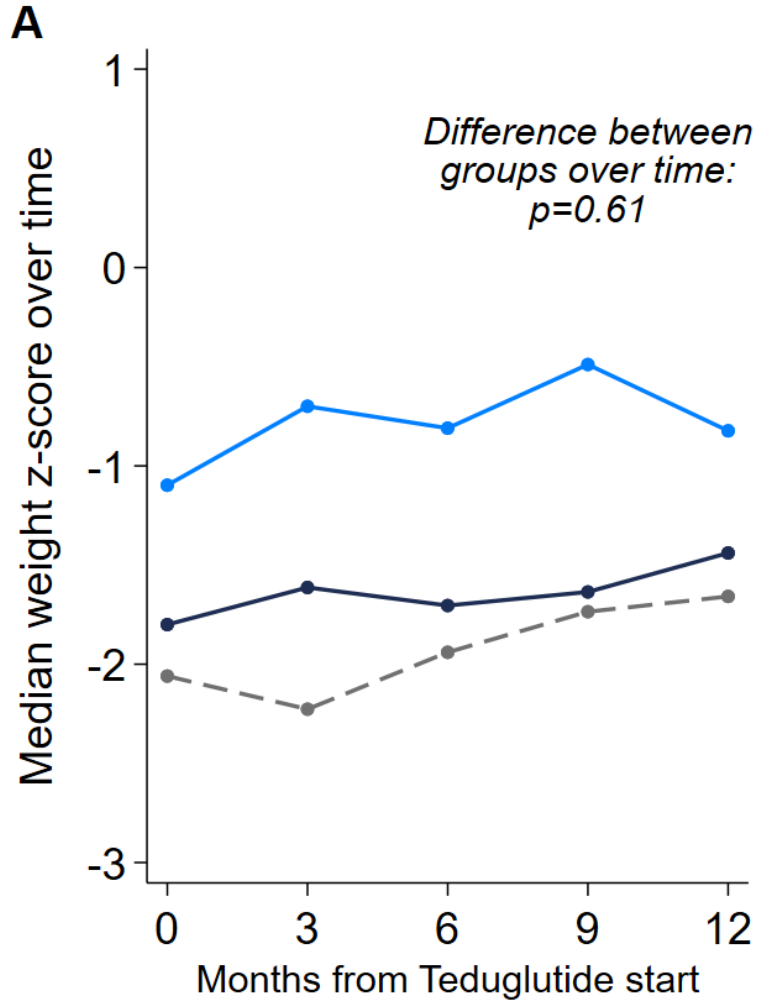
*For children under 2 years of age, the weight-for-length z-score was calculated

Table 2. Weight, height and BMI z-scores over time according to PN weaning

	Total N=104	NO PN WEANING N=83	PN WEANING N=21	p
3 months				
Weight z-score	-1.4 (-2.7, -0.5)	-1.3 (-2.6, -0.3)	-1.6 (-4.1, -0.7)	0.23
Height z-score	-1.1 (-2.5, -0.3)	-1.1 (-2.4, -0.3)	-1.3 (-3.2, -0.3)	0.59
BMI z-score*	-0.7 (-1.7, -0.1)	-0.7 (-1.6, -0.0)	-0.6 (-1.9, -0.3)	0.33
6 months				
Weight z-score	-1.4 (-2.6, -0.5)	-1.4 (-2.5, -0.5)	-1.7 (-3.9, -0.8)	0.27
Height z-score	-1.2 (-2.4, -0.5)	-1.2 (-2.4, -0.5)	-0.9 (-2.6, -0.7)	0.78
BMI z-score*	-0.8 (-1.8, -0.2)	-0.8 (-1.7, -0.1)	-1.1 (-2.0, -0.2)	0.37
9 months				
Weight z-score	-1.1 (-1.9, -0.3)	-0.9 (-1.7, -0.3)	-1.6 (-2.4, -1.1)	0.028
Height z-score	-1.0 (-1.5, -0.0)	-0.9 (-1.5, -0.0)	-1.4 (-2.4, -1.2)	0.034
BMI z-score*	-0.7 (-1.4, -0.1)	-0.5 (-1.5, -0.2)	-0.9 (-1.2, -0.5)	0.63
12 months				
Weight z-score	-1.3 (-2.5, -0.4)	-1.3 (-2.3, -0.3)	-1.4 (-2.9, -0.8)	0.15
Height z-score	-1.2 (-2.3, -0.4)	-1.2 (-2.1, -0.4)	-1.8 (-3.1, -0.6)	0.19
BMI z-score*	-0.7 (-1.6, -0.1)	-0.7 (-1.6, -0.1)	-1.0 (-1.7, -0.3)	0.56

*For children under 2 years of age, the weight-for-length z-score was calculated

DATA UNPUBLISHED – DO NOT REPLICATE



—●— Non responders —●— Responders non weaned —●— Weaned

DATA UNPUBLISHED – DO NOT REPLICATE

Congresso Nazionale SINPE 2025

CLINICAL NUTRITION: shaping a better future of health care

Conclusions

- Children with a better nutritional status, a longer residual small bowel and without liver impairment have a higher probability to respond to Teduglutide treatment
- Increase in haemoglobin in the first 6 months predict 1 year treatment response
- Children with higher baseline citrulline and lower PN dependancy have higher probability of 1-year PN weaning
- Increase in haemoglobin in the first 6 months predict weaning from parenteral nutrition at 1 year.
- TED treatment was associated with improved weight and BMI trajectories, particularly in responders.



Grazie per l'attenzione

27 - 29 novembre 2025

Padova Congress
Via Carlo Goldoni 8, Cancellò C - Padova

