Intestinal Failure 3 (2024) 100027

Contents lists available at ScienceDirect

Intestinal Failure

journal homepage: www.sciencedirect.com/journal/intestinal-failure

# Real-life experience of teduglutide use in pediatric patients with short bowel syndrome in Argentina. A multicenter study

María Inés Martínez [b,*], Verónica Busoni [c], Carola Saure [d], Corina Dlugosewsky [a,e], Marcela Dalieri [f], Sandra Cosentino [g], Martín Balacco [h], Lorena Rudi [i], Adriana Fernandez [j], Carolina Rumbo [k]

[a] Unidad de Rehabilitación Intestinal y Trasplante de Intestino, Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina
[b] Servicio de Nutrición, Hospital de Niños Sor María Ludovica, La Plata, Argentina
[c] Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
[d] Servicio de Nutrición y Diabetes, Hospital JP Garrahan, Buenos Aires, Argentina
[e] Servicio de Clínica y Soporte Nutricional del Hospital Público Materno Infantil, Salta, Argentina
[f] Servicio de Nutrición, Hospital de Niños Sor María Ludovica, La Plata, Argentina
[g] Clínica Pediátrica San Lucas. Servicio de Nutrición, Neuquén, Neuquén, Argentina
[h] Unidad de Falla Intestinal Hospital de Niños Santísima Trinidad, Córdoba, Argentina
[i] Hospital Nacional Dr. Alejandro Posadas, El Palomar, Provincia de Buenos Aires, Argentina
[j] Human Nutrition, Faculty of Medical Siencies, National University of La Plata, Buenos Aires, Argentina
[k] Unidad de Rehabilitación Intestinal y Trasplante de Intestino Hospital, Universitario Fundación Favaloro, Buenos Aires, Argentina

ARTICLE INFO

*Keywords:*
Short bowel syndrome
Intestinal failure
Teduglutide
Children

ABSTRACT

*Introduction:* Current treatment of patients with chronic intestinal failure due to short bowel syndrome (CIF-SBS) attempts to promote the intestinal adaptation process. Teduglutide (TED) is the first successful pharmacological intervention which enhances natural intestinal adaptation.
*Aim:* To present the long-term results and follow up of all the children treated with TED at specialized intestinal failure units in Argentina.
*Methods:* Multicenter, descriptive, retrospective study of patients aged 1–18 years with CIF-SBS, that initiated TED in specialized centers in Argentina. Sex, age, SBS etiology/anatomy, remaining small bowel length (RBL), 20 % decrease in initial parenteral nutrition (PN) volume, and weaning at 3–6-12 months of treatment are described.
*Results:* Thirty-three patients (11 female) treated with TED between 1/2017 and 8/2023 in 9 centers were included. Median time of CIF-SBS prior to TED was 6.06 (IQR 3.8–10.4) years. Median age at starting TED was 7.5 (IQR 4.8–12.4), range 2.5–18 years. Anatomy types: type 1 in 1; type 2 in 22, and type 3 in 9. Median time of treatment was 1.5 (IQR 0.52–3.2) years.
A 20 % reduction of the initial weekly PN volume was obtained in 23 patients (70 %) and complete PN discontinuation without detriment of the nutritional status was achieved in 36 % during the entire follow-up period.
The most frequent adverse event was mild abdominal pain, and two patients discontinued the medication due to adverse events.
*Conclusions:* The Argentine experience with TED as part of the intestinal rehabilitation strategies showed good results and adverse events like those reported in other international series.

* Corresponding author.
*E-mail address:* mi.martinezbozzano@gmail.com (M.I. Martínez).

https://doi.org/10.1016/j.intf.2024.100027
Received 28 July 2024; Received in revised form 7 October 2024; Accepted 22 October 2024
Available online 28 November 2024

## Introduction

Intestinal failure (IF) has been defined as the reduction in gut function below the minimum necessary for the absorption of macronutrients, water, electrolytes, and micronutrients, requiring intravenous supplementation to maintain health and/or growth in children [1].

Short bowel syndrome (SBS) is the main cause of chronic IF (CIF) in pediatric patients. SBS occurs after a resection of a large segment of the small bowel, either by congenital or acquired lesions and secondary dysmotility and malabsorption/ maldigestion, resulting in loss of the absorptive area. The syndrome leads to diarrhea, dehydration, electrolyte disturbances, and malnutrition. In children, it results in the inability to maintain proper growth and development [2].

The length of the remaining small bowel that defines SBS in children is controversial. It has been proposed as the need for parenteral nutrition (PN) for more than 42 days after a bowel resection or a residual small-bowel length (RBL) of less than 25 % of that expected for gestational age [3].

Current treatment of patients with CIF-SBS includes home PN combined with a controlled oral/enteral diet, medical treatment with drugs aiming to reduce diarrhea and surgical treatment to restore intestinal transit or to lengthen the remaining intestine. All these therapies that intend to promote the intestinal adaptation process and to gain PN independence are called Intestinal Rehabilitation (IR) [4,5].

Within the mechanisms involved in intestinal adaptation, the role of enterohormones is strategic. Among them, glucagon-like peptide 2 (GLP-2) has the following effects: a) decreases gastric secretion and motility, b) regulates the intestinal transit, c) stimulates the intestinal blood flow, d) improves the intestinal barrier function, e) increases fluid and nutrients absorption [6]. The native GLP-2 has a short half-life due to enzymatic degradation by the dipeptidyl peptidase-IV. Various synthetic analogues with a longer half-life have been developed using recombinant DNA techniques for clinical use. Teduglutide (TED) is the first of these analogues used in the clinical practice and so far, it is the only one approved to be used by children [7]. In 2012 the European Medical Agency (EMA) and the Food and Drug Administration (FDA) approved the use of TED for adults with SBS [8]. Later in 2016 and in 2019, EMA and FDA respectively approved its use in children older than 1 year of age [9,10]. In 2023, Chiba et al. reported the first data on the efficacy and safety of TED in infants under 1 year of age (between 4 and 12 months of gestational age) and additional data on children with IF-SBS, reporting similar PN reductions, with comparative or fewer safety concerns in infants compared to children [11].

The aim of the present work is to present the long-term results and follow up of all the children treated with TED at specialized IF units in Argentina.

## Methods

This is a multicenter, descriptive, retrospective study of patients aged 1–18 years with CIF/SBS, that initiated TED in specialized centers in Argentina. Sex, age, SBS etiology/anatomy, intestinal length, follow-up period, 20 % decrease of initial PN volume, and weaning at 3–6-12 months of treatment are described.

Data was collected in a database constructed for this study and extracted from clinical records and/or databases, and it was completed prospectively at each participating center.

The data was expressed in absolute values, percentages, Median (M/IQR). For the statistical analysis, the SPSS version 20 program was used. Non-parametric tests were used. Mann Whitney for comparison between groups and Wilcoxon to compare the same group in two measurements.

The prescription criteria were uniform across the centers and were based on the recommendations of the Spanish Guidelines published in 2017 [12] and the ANMAT's endorsements [13]. These criteria included, a) medication prescription and follow-up to be performed by healthcare professionals with experience in the management of SBS; b) patients to be older than 1 year of age with baseline diagnosis of SBS and PN dependent, clinically stable, with a period of at least 3–6 months after the last abdominal surgery, and PN prescription stable; c) caregivers willing to administer the medication subcutaneously and capable to adhere to all clinical and laboratory follow up proposed to assess the efficacy and safety of the treatment.

Nevertheless, the follow-up protocols for patients under TED were specific to each center.

This study was approved by the institutional Ethics Committee DDI (1687) 0824.

## Results

Nine specialized pediatric centers in Argentina have reported treating patients with TED. Since the drug's approval in December 2020 [13], these centers have cared for a total of 104 children with SBS who had been dependent on PN for more than a year. Within this population, thirty-three patients (11 female) were treated with TED between 1/2017 and 8/2023, and those are the patients included in the present analysis. Nine of those patients started treatment before the Argentine drug agency's (ANMAT) approval. Each center had between 1 and 12 patients on TED.

The medication dose used was 0.05 mg/kg/day for all of them.

Median time of CIF-SBS prior to start treatment with TED was 6.06 (IQR 3.8–10.4), range 1.2–17.9 years. Median age at starting TED was 7.5 (IQR 4.8–12.4), range 2.5–18 years. The etiology of SBS in patients with neonatal onset CIF was: gastroschisis in 8, atresia in 10, necrotizing enterocolitis in 1, volvulus in 3 and cloacal malformation in 1. In those with post-neonatal onset, 5 patients with volvulus were included, 2 with abdominal trauma, 2 postsurgical complications, 1 complicated Stevens-Johnson Syndrome. The

reported median of remmant bowel length (RBL) was 22 (IQR 15–37) cm. RBL was < 40 cm in 79 %, and ≤ 20 cm in 60 %; 1 patient had duodenum-colonic anastomosis, and 2 patients had an end colostomy. According to the type of remaining anatomy [14], 1 patient had anatomy type 1; 22 patients had type 2 [18 subtype A (<40 cm RBL) and 4 subtype B (> 40 cm)], 9 patients had type 3 (A 6, B 3) and 1 patient had duodenum-colic anastomosis.

All the patients included in the analysis were followed up until 8/2023. The median time of treatment was 1.5 (IQR 0.52–3.2) years, range 0.25–6.7 years. Fifteen patients received TED for ≤ 12 months, 6 patients received it between 12–24 months and 12 patients were treated for more than 24 months. Two patients electively discontinued TED after 3.6 and 4.6 years of treatment and 2.0 and 3.6 years after PN discontinuation respectively. Both patients maintained their nutritional status under oral supplementation after 1.33 and 0.26 years of TED discontinuation. A third patient has been electively on alternate days of TED treatment for 2.2 years with favorable progress, and 2 patients discontinued TED due to complications after 2.09 and 0.8 years of treatment respectively.

In terms of adaptability and response to TED treatment, a 20 % reduction of the initial PN volume was obtained 23/33 (70 %) of the entire series treated and it was achieved as follows, 14 /33 patients at month 3, in 23/29 patients at month 6, and in 19/19 at month 12. An overall adaptability of 12/33 (36 %) was observed in the entire follow-up period. Complete PN discontinuation without detriment of the nutritional status was achieved in 4/33 patients at month 3, in 6/29 patients at month 6 and in 8/19 patients at month 12 of TED treatment. Table 1 shows the changes in parenteral intake, stool output, and BMI z score and height for age in all treated patients.

Three patients required transient increases in PN during non-TED related complications and one patient required restarting PN for one month due to nutritional deterioration associated with pneumonia, after having discontinued it. Median time of TED treatment until weaning from PN in the 12 patients was 8.16 (IQR 2.8–20.2) months (range 3 −41). Changes in parenteral intake, stool output and anthropometric parameters at the beginning of TED treatment and at the last clinic visit, of all patients treated, can be seen in Table 1. When comparing different variables between rehabilitated vs PN dependent patients at the last follow up visit, longer duration of treatment was the only statistically significant variable, but it is likely that the non-weaned group contains patients who would adapt with longer follow up (Table 2).

The adverse events related to the GI tract registered during TED treatment were abdominal pain (9 patients), peri anastomotic ulcers (4), intestinal partial occlusion (1), small bowel adhesions (1), transient cholestasis (1). Two patients required cholecystectomy, one for cholesterolosis and another for acute cholecystitis due to pre-existing lithiasis. There were no systemic adverse events associated with the use of TED, such as volume overload in responding patients. Two patients discontinued TED due to adverse events. One patient, 3 months after weaning PN presented with repeated sub occlusive symptoms without evidence of mechanical obstruction, which determined nutritional and metabolic deterioration that was resolved by suspending TED and restarting PN. The other patient presented episodes compatible with severe d lactic acidosis that only improved with the interruption of TED.

## Discussion

TED is the first specific CIF-SBS drug approved for both adults and children over one year of age. Although the experience with its use in children is limited due to the small number of patients and shorter follow-up periods, it has demonstrated a comparable rate of positive outcomes to that seen in adults, with a low incidence of serious complications.

The first results of a clinical trial using TED in children were published in 2017 [15]. This 12-week multicenter study evaluated the safety and efficacy of different doses of TED compared to a control group receiving standard care. The authors found that TED showed a good safety profile and was well tolerated in pediatric patients at the tested doses (0.0125, 0.025 and 0.05 mg/kg). They also reported that treatment was associated with a reduction of PN requirements in the population studied. At week 12, PN had been discontinued in 4 patients, but it was restarted in 2 of them 4 weeks after discontinuation.

A 24-week follow-up study of pediatric patients was published in 2020 [14]. Of the 59 patients included, 54 % managed to reduce more than 20 % of the PN intake with a TED dose of 0.025 mg/kg/d, 69 % with a dose of 0.05 mg/kg/d, and 11 % with standard care. Additionally, five treated patients managed to discontinue PN [16].

Published evidence on the use of GLP-2 analogues in children is limited and recent. In June 2022, Gigola et al. published a systematic review covering studies up to November 2021 on the use of TED in patients under 18 years of age. Fourteen studies met the inclusion criteria, encompassing 223 patients who were treated for a median of 45 weeks (IQR 36–52.5). Thirty-six patients (16 %) were weaned from PN in a M of 24 weeks (IQR 24–48), 149/223 (67 %) patients reduced parenteral support in terms of volume, calories and hours of infusion. Complications were also reported in 11 of 14 publications, the most frequent were related to the

**Table 1**
Indicators of treatment response.

| | Basal | Last follow up | P Wilcoxon test |
|---|---|---|---|
| **PN infusion days/week*** | 7 (6 −7) | 3.5 (0 −5.75) | *< 0.001* |
| **Weekly NP volume (ml)*** | 9555 (3360 −12,150) | 3500 (0 −8025) | *< 0.001* |
| **NPEI/ BMR index*** | 0.92 (0.76 −1.01) | 0.52 (0 −0.91) | *< 0.001* |
| **Stool output (number/day)*** | 4 (3.25 −5) | 3 (2 −4) | 0.008 |
| **Z-score BMI/age*** | −0.68 (−1.3/0.14) | −0.61 (−1.2/−0.75) | *0.79* |
| **Z-score Height/age*** | −1.91 (−2.7/−1.3) | −1.73 (−2.5/−0.6) | *0.24* |

* M / IQR, NPEI = non protein energy intake;BMR basal metabolic rate

**Table 2**
Comparison between patients who achieved and did not achieve enteral autonomy during treatment.

| | Weaned from PN n 12 | Not weaned from PN n 21 | P (Mann Whitney) |
|---|---|---|---|
| **Patients** | 3 female (25 %)<br>9 neonatal onset (75 %) | 9 female (43 %)<br>13 neonatal onset (62 %) | |
| **Anatomy type** | | | |
| **1** | 0 | 1 | |
| **2A** | 7 | 11 | |
| **2B** | 1 | 3 | |
| **3A** | 2 | 4 | |
| **3B** | 2 | 1 | |
| **Duodeno-colic anastomosis** | 0 | 1 | |
| **SBS etiology** | | | |
| **Gastroschisis** | 3 | 5 | |
| **Atresia** | 5 | 5 | |
| **NEC** | 0 | 1 | |
| **Neonatal Volvulus** | 2 | 4 | |
| **Non-neonatal Volvulus** | 1 | 2 | |
| **Others** | 1 | 4 | |
| **RBL* M (IQR)**** | 24 (20-43.7) | 20 (10-35.5) | 0.39 |
| **Previous CIF time (years)*** | 7 (3.3-10.7) | 5.6 (3.8-9.8) | 0.57 |
| **Age at start of TED (years)*** | 8.1 (5.1-12.8) | 7.5 (4.7-12) | 0.68 |
| **Duration of TED treatment (years)*** | **3.3 (1.17-4.8)** | **0.92 (0.45-1.79)** | **0.006** |
| **Initial PN volume (ml/week)*** | 7875 (4450-11625) | 10010 (5912-12400) | 0.4 |
| **PN Days/week** | 6 (5.25-7) | 7 (6-7) | 0.048 |
| **Initial NPEI index*** | 0.83 (0.75-1) | 0.91 (0.76-1.01) | 0.79 |

* RBL Remnant Bowel Length
** Median/ IQR

gastrointestinal tract [17].

In Argentina, experience with TED in real life began in 2014 in adult patients and in 2017 in children. The ANMAT approved the use of TED for patients with SBS older than 1 year in December 2020; until that time its use was agreed for each individual patient under a regime of access to medications for compassionate use. In 2023, there was an extension of the ANMAT's approval to include patients starting at 4 months of age [18]. In 2021, a group of Argentine pediatric experts published guidelines for the management of IF-SBS, which included treatment with GLP2 analogues. Further on, this group published recommendations for the use of TED in children based on the evidence evaluated up to 2021. Both manuscripts used the Delphi methodology [19,20].

The results presented in this study are consistent with those reported by other groups in North America and Europe. In our cohort, atresia and gastroschisis were the most common causes of SBS, unlike other series where NEC was more prevalent. Regarding the remaining anatomy, the RBL was similar to other reports, indicating extensive intestinal resections in all cases. A significant proportion of our patients had unfavorable anatomy (jejunum-colon anastomosis with less than 40 cm of jejunum), and only 1 patient had type 1 anatomy, which was more common in the other publications. The response rate in our patient population, assessed by significant reduction in weekly PN volume, was similar the other reports. Regarding the achievement of intestinal autonomy in this series more than one third of the patients were weaned from PN. This proportion is greater than those reported by the Finnish and Israeli series [21, 22], but much lower than the first real life report published by the Spanish group in 2017 [23]. The prospective study conducted at Hospital Necker in Paris during 48 used carefully selected clinical, nutritional, biochemical and functional indicators; the PN weaning rates within 48 weeks were similar to those in our series [24].

As reported in pivotal studies and real-life reports, mild and self-limited abdominal pain was the most commonly encountered treatment-related adverse event. In the two patients whose treatment was suspended, the adverse events described later resolved. Table 3 compares the indications, results, and adverse events in different case series of the use of TED in real life.

TED is another tool in the intestinal rehabilitation treatment, it does not replace other medical, nutritional, and surgical strategies. The novelty of the use of this GLP-2 analogue in intestinal rehabilitation is that it pushes the limits of natural intestinal adaptation. This medication can a priori benefit different groups of patients: 1) Those who have prolonged PN dependence (several years), as a *2nd chance of Intestinal adaptation.* 2) Patients with shorter duration of PN who could probably achieve adaptation over time but develop nutritional failure (serious complications of IF and its treatment) that prevent them from adapting: *early indication.* 3) Patients with low chances of adaptation and daily PN dependence, in whom less dependency would be the goal: *Indication to improve quality of life and reduce PN related complications.* Finally, indications in special situations have yet to be defined and should be considered on a case-by-case basis for the time being.

To objectively assess the results of TED treatment, it would be necessary to define an indicator or group of reliable, accessible, and reproducible indicators of the severity of intestinal failure/insufficiency. At present, TED is a drug with relatively short time of use worldwide. Long-term adverse and side effects remain to be described. In the same way, time of maintenance of efficacy after drug

**Table 3**
Summary of real-life experience with the use of teduglutide.

| **Publication/year** | *JPGN* 2020 [23] | *Am J Clin Nutr* 2023 [24] | *Transplantation* 2023 [25] | *Transplantation* 2023 [21] | *JPGN* 2022 [22] | *Present series* |
|---|---|---|---|---|---|---|
| **Authors** | Ramos Boluda E et al. | Lambe C et al. | Norsa L et al. | Merras-Salmio L et al. | Guz-Mark A et al. | *Martinez et al.* |
| **Type of study** | Spanish Multicenter Prospective | French Single center Prospective | European Multicenter Retro and prospective | Finnish | Israeli Multicenter | Argentine, Multicenter Retrospective |
| **Patients N** | 17 | 25 | 69 | 19 | 13 | *33* |
| **Period of treatment** | N/A | 07/2018-07/2019 | Starting 07/2021 | 2016-2022 | N/A | *01/2017- 08/2023* |
| **Diagnosis** | | | | | | |
| NEC | 6 | 3 | 27 % | 21 % | 38 % | *1* |
| Gastroschisis | 2 | 5 | | 21 % | | *8* |
| Atresia | 3 | 4 | | 21 % | | *10* |
| Volvulus | 3 | 7 | | 26 % | | *8* |
| Others | 2 | 6 | | 21 % | | *6* |
| **RBL** | X 52 (14-144) cm | M 26 (12-40) cm | M 26 (14-55) cm | Median 16 % small bowel remaining 78 % had ICV removed | M 20 (15-40) cm | *M 22 (15-37) cm* |
| **Anatomy Type** | | | | | | |
| **1** | N/A | | | N/A | N/A | |
| **2** | | 6 | 16 % | | | *1* |
| **3** | | 12 | 59 % | | | *22* |
| | | 7 | 24 % | | | *9* |
| **Age at starting TED (Years)** | X 5.6 | M 9.4 (8-11) | M 5.4 (3-9) | M 2.8 (1.1-17) | M 6 (4.7-7) | *M 7.5 (4.8-12.4)* |
| **Results** | | | | | | |
| Response + | 15 (88 %) | At week 24: 96 % ↓ PN volume ang energy intake Energy absorption increase from 59 to 73 % All ↓stool frequency, ↑stool consistency | ↓ 20 % NPEI in 73 % ↓ 50 % NPEI in 46 %, ↓75 % NPEI in 33 % | 14 (74 %) | 8 (62 %) | *23 (70 %) vol ↓ ↓ NPEI* *2* |
| **Results PN weaning** | 12 (70 %) | 8 (32 %) | N/A | 4 (21 %) | 2 (15%) | 12 (36%) |
| **Results No response** | 1 | N/A | N/A | 1 | NA/A | N/A |
| **Results Withrawal due to adverse events** | 1 | 0 | N/A | 1 | N/A | 2 |
| **Adverse events (number)** | Heart failure 1 Cholecystitis 1 Abdominal pain Stoma swelling | Mild Abdominal pain 16 Stoma changes 3 Redness at injection site 7 Leg muscle pain 2 | N/A | Intestinal bleeding 4 Tubular nephropathy 3 Stomal prolapse4/4 | N/A | *Abdominal pain 9 Cholecystitis 1 Cholesterolosis 1 Cholestasis 1 Bowel obstruction 1 D lactic acidosis 1 Perianastomotic ulcers 4* |
| **Duration of TED treatment** | N/A | 48 weeks | N/A | 15 (2-52) months | 18 (12-30) months 77 % > 1 year | *M 1.5 (0.53-3.2) years* |

M median (IQR), X Mean (SD), N/A not available, NPEI Non protein energy intake

discontinuation has been scarcely studied. So far, it is unknown if TED treatment is needed for life as a replacement therapy or if it is possible to completely discontinue it in adapted patients at a certain point. A safe and effective way to discontinue medication should also be investigated.

Although treatment with TED in children appears to be helpful and safe, an important issue to consider when deciding its indication is the price, which adds to the already high expenses of home PN and related complications [5,18,19]. For this reason, it is important to discuss the use of strategies to reduce costs. In a recent study published by the Necker Hospital group in Paris on costs of IF treatment in real life, the authors compare a group of children with SBS-IF on home PN treated with subcutaneous TED with another group of children with SBS-IF on home PN followed during the same period who were eligible for TED but were not treated. They describe a gradual reduction in the budget of home PN and its complications (home-care visits, PN bags, hospital admissions) that were significantly lower in the group of patients treated with TED. Nevertheless, the model was not cost-effective when the price of TED was included in the expenses [26]. In a Canadian publication with a theoretical cost analysis model, they propose that a presentation with a smaller dose per vial could contribute to price reduction [27].

This study presents the experience with TED in children collected from nine IF/IR specialized centers. Given the low prevalence of

the disease and the short time that this enterohormone has been in the market, the results are valuable. However, the authors acknowledge that the number of patients included is insufficient to draw conclusions about predictors of adaptation under TED treatment or to make definitive statements about discontinuing the drug in pediatric patients once adaptation is achieved. Other limitations of this work are the retrospective nature of the data collection, the lack of a uniform follow up protocol among the centers involved and the varying treatment duration among patients.

## Conclusions

TED is the first pharmacological option that effectively enhances intestinal adaptation. It is recommended to be prescribed by physicians specialized in managing CIF-SBS. The results and adverse events observed in this series align with those reported in the literature, showing a positive response in over two-thirds of cases and successful weaning from PN in one-third of treated patients.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

## Ethical clearance

The study was approved by the Bioethics Committee of the Hospital Universitario Fundación Favaloro DDI (1687) 0824.

## Patient's/Guardian's consent

Retrospective study, informed consent was not requested.

## CRediT authorship contribution statement

**Dalieri Marcela:** Writing – review & editing, Validation, Data curation. **Sandra Cosentino:** Visualization, Validation, Data curation. **Martin Balacco:** Visualization, Validation, Data curation. **Lorena Rudi:** Visualization, Validation, Data curation. **Adriana Fernández:** Writing – review & editing, Validation, Supervision, Investigation, Data curation. **Carolina Rumbo:** Writing – review & editing, Validation, Methodology, Data curation, Conceptualization. **María Inés Martínez:** Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Veronica Busoni:** Writing – review & editing, Methodology, Investigation, Data curation, Conceptualization. **Carola Saure:** Writing – review & editing, Investigation, Data curation, Conceptualization. **Corina Dlugosewsky:** Validation, Investigation, Data curation.

## Declaration of Competing Interest

- María Inés Martínez and Carolina Rumbo have received honoraria from TAKEDA for scientific support in educational activities.
- Verónica Busoni: Speaker and Advisory borad. Research /educational support.Takeda
- Carola Saure: Speaker and Advisory board. Takeda
- Adriana Fernández: has received honoraria from TAKEDA for scientific support in educational activities. AF works in Research Area in Nutri-Home (Fresenius- kabi) CABA Argentina.

None of the authors received fees for preparing this paper. Takeda has not participated in the collection and analysis of the data of this retrospective research work nor in the writing of the manuscript.

## Acknowledgments

The authors appreciate the collaboration of the interdisciplinary teams that treat patients with chronic intestinal failure at each Institution.

## References

[1] Pironi L, Arends J, Baxter J, Bozzetti F, Peláez RB, Cuerda C, et al. ESPEN endorsed recommendations. Definition and classification of intestinal failure in adults. Home Artif Nutr Chronic Intest Fail; Acute Intest Fail Spec Interest Groups ESPEN Clin Nutr 2015;34:171–80. https://doi.org/10.1016/j.clnu.2014.08.017.

[2] O'Keefe SJD, Buchman AL, Fishbein TM, Jeejeebhoy KN, Jeppesen PB, Shaffer J. Short bowel syndrome and intestinal failure: consensus definitions and overview. Clin Gastroenterol Hepatol 2006;4:6–10. https://doi.org/10.1016/j.cgh.2005.10.002.

[3] Wales PW, de Silva N, Kim J, Lecce L, To T, Moore A. Neonatal short bowel syndrome: population-based estimates of incidence and mortality rates (https://) J Pedia Surg 2004;39:690–5. https://doi.org/10.1016/j.jpedsurg.2004.01.036.

[4] Norsa L, Goulet O, Alberti D, DeKooning B, Domellöf M, Haiden N, et al. Nutrition and intestinal rehabilitation of children with short bowel syndrome: A position paper of the ESPGHAN committee on nutrition. Part 1: From intestinal resection to home discharge. J Pedia Gastroenterol Nutr 2023;77:281–97. https://doi.org/10.1097/MPG.0000000000003849. Epub 2023 May 31.

[5] Norsa L, Goulet O, Alberti D, DeKooning B, Domellöf M, Haiden N, et al. Nutrition and intestinal rehabilitation of children with short bowel syndrome: A position paper of the ESPGHAN committee on nutrition. Part 2: Long-term follow-up on home parenteral nutrition. J Pedia Gastroenterol Nutr 2023;77:298–314. https://doi.org/10.1097/MPG.0000000000003850.

[6] Sigalet DL. Advances in glucagon like peptide-2 therapy. physiology, current indications and future directions. Semin Pedia Surg 2018;27:237–41. https://doi.org/10.1053/j.sempedsurg.2018.07.008. Epub 2018 Jul 29.

[7.] Rosete BE, Wendel D, Horslen SP. Teduglutide for pediatric short bowel syndrome patients. Expert Rev Gastroenterol Hepatol 2021;15:727–33. https://doi.org/10.1080/17474124.2021.1913052. Epub 2021 Apr 26.

[8] Drug Approval Package. [cited 14 Apr 2024]. Available: ⟨https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203441Orig1s000TOC.cfm⟩.

[9] Revestive. [cited 14 Apr 2024]. Available: ⟨https://www.ema.europa.eu/en/medicines/human/EPAR/revestive#authorisation-details⟩.

[10] [No title]. [cited 22 Apr 2024]. Available: ⟨https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/203441s013lbl.pdf⟩.

[11] Chiba M, Masumoto K, Kaji T, Matsuura T, Morii M, Fagbemi A, et al. Efficacy and safety of teduglutide in infants and children with short bowel syndrome dependent on parenteral support. J Pedia Gastroenterol Nutr 2023;77:339–46. https://doi.org/10.1097/MPG.0000000000003867. Epub 2023 Jun 26.

[12] Moreno J.M., Polo B., Prieto G., et al, eds. Tratamiento Del Síndrome De Intestino Corto. Guía De Inicio Y Seguimiento De Un Paciente Pediátrico Tratado Con Revestive®; 2017.

[13] Administración Nacional de Medicamentos, Alimentos y Tecnología Médica. Expediente Nº: 1–47-1110–717-16–8. En: ⟨https://bit.ly/3tJy8lG⟩; consulted in June 2022.

[14] Goulet O, Abi Nader E, Pigneur B, Lambe C. Short bowel syndrome as the leading cause of intestinal failure in early life: Some insights into the management. Pedia Gastroenterol Hepatol Nutr 2023 Jun 26;22(2019):303–29. https://doi.org/10.1097/MPG.0000000000003867 (https://).

[15] Carter BA, Cohran VC, Cole CR, Corkins MR, Dimmitt RA, Duggan C, et al. Outcomes from a 12-week, open-label, multicenter clinical trial of teduglutide in pediatric short bowel syndrome. J Pedia 2017;181:102–111.e5. https://doi.org/10.1016/j.jpeds.2016.10.027. Epub 2016 Nov 15.

[16] Kocoshis SA, Merritt RJ, Hill S, Protheroe S, Carter BA, Horslen 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 Parent Enter Nutr 2020;44:621–31. https://doi.org/10.1002/jpen.1690. Epub 2019 Sep 8.

[17] Gigola F, Cianci MC, Cirocchi R, Ranucci MC, Del Riccio M, Coletta R, et al. Use of teduglutide in children with intestinal failure: a systematic review. Front Nut 2022;9:866518. https://doi.org/10.3389/fnut.2022.866518.

[18] [No title]. [cited 22 Apr 2024]. Available: ⟨https://boletin.anmat.gob.ar/octubre_2023/Dispo_8872–23.pdf⟩.

[19] Fernández A, Desantadina V, Balacco M, Busoni V, Cabral A, Cosentino S, et al. Clinical guidelines for the managment of intestinal failure secondary to pediatric short bowel syndrome. Arch Argent Pedia 2021;119:e441–72. https://doi.org/10.5546/aap.2021.e441.

[20] Martínez MI, Balacco M, Busoni V, Fernández A, Rumbo C. Expert recommendations on the use of teduglutide in pediatric patients with short bowel syndrome. Med (B Aires) 2023;83:114–21.

[21] Merras-Salmio L, Riikka G, Mutanen A, Pakarinen M. Abstract 82: teduglutide in 19 pediatric SBS patients – single center real world data on clinical efficacy and treatment associated challenges. Transplantation 2023;107(7S):48–9.

[22] Guz-Mark A, Hino B, Berkowitz D, Hartman C, Millman PN, Orlanski-Meyer E, et al. The variable response to teduglutide in pediatric short bowel syndrome: a single country real-life experience. J Pedia Gastroenterol Nutr75 2022:293–8. https://doi.org/10.1097/MPG.0000000000003541. Epub 2022 Aug 9.

[23] Ramos Boluda E, Redecillas Ferreiro S, Manrique Moral O, García Romero R, Irastorza Terradillos I, Nuñez Ramos R, et al. Experience with teduglutide in pediatric short bowel syndrome: first real-life data. J Pedia Gastroenterol Nutr 2020;71:734–9. https://doi.org/10.1097/MPG.0000000000002899.

[24] Lambe C, Talbotec C, Kapel N, Barbot-Trystram L, Brabant S, Nader EA, et al. Long-term treatment with teduglutide: a 48-week open-label single-center clinical trial in children with short bowel syndrome. Am J Clin Nutr 2023;117:1152–63. https://doi.org/10.1016/j.ajcnut.2023.02.019.

[25] Norsa L, Ramos Boluda E, Guz-Mark A, Hojsak I, Hilberath J, Broekaert I, et al. Abstract 85: preliminary results of the registry of European children treated with teduglutide. Transplantation 2023;107(7S):50.

[26] Cucinotta U, Acunzo M, Payen E, Talbotec C, Chasport C, Alibrandi A, et al. The impact of teduglutide on real-life health care costs in children with short bowel syndrome. J Pedia 2023;20:20. https://doi.org/10.1016/j.jpeds.2023.113882.

[27] Gattini D, Belza C, Kraus R, Avitzur Y, Ungar WJ, Wales PW. Cost-utility analysis of teduglutide compared to standard care in weaning parenteral nutrition support in children with short bowel syndrome. Clin Nutr 2023;42:2363–71. https://doi.org/10.1016/j.clnu.2023.10.001. Epub 2023 Oct 5.