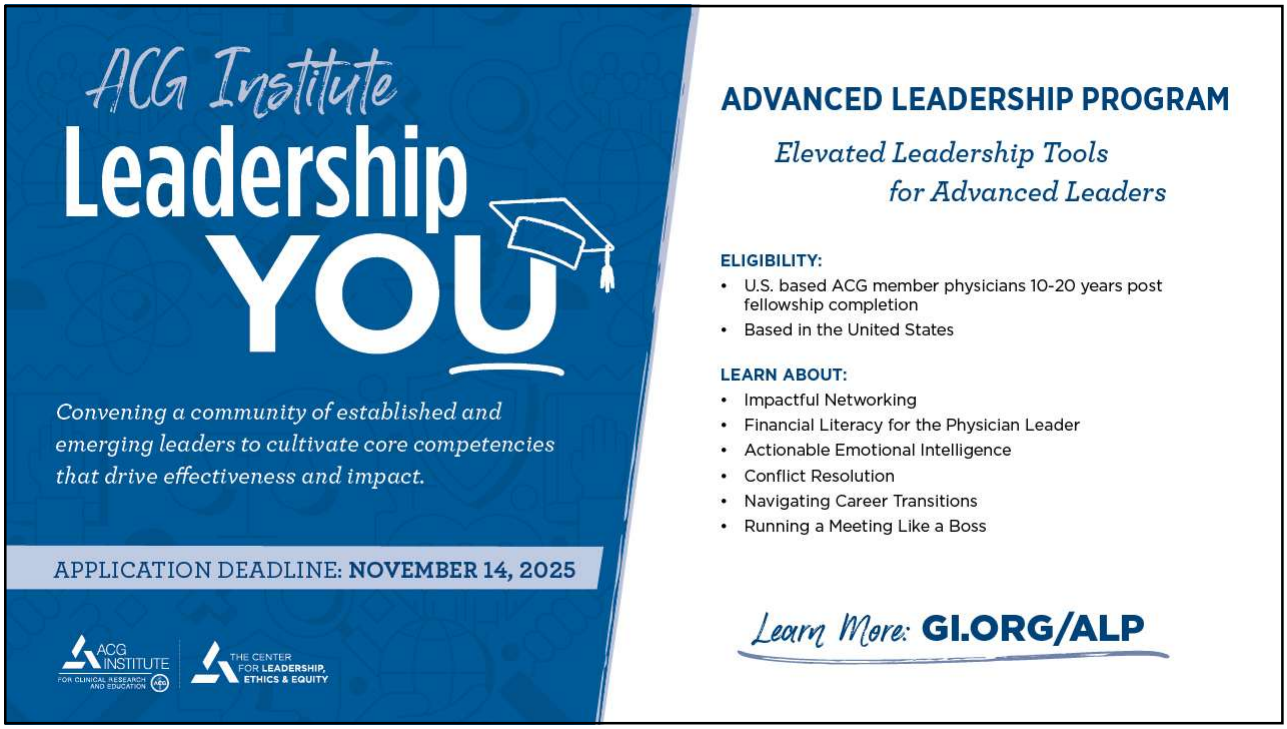
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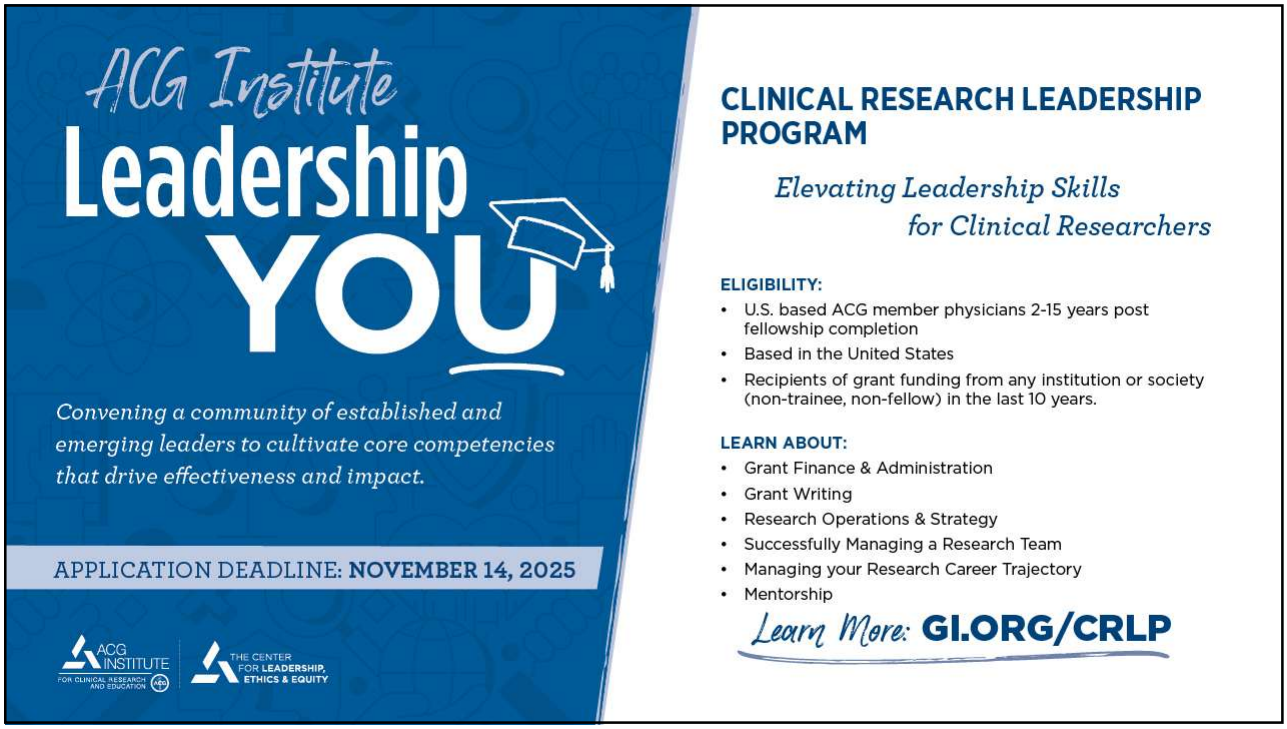
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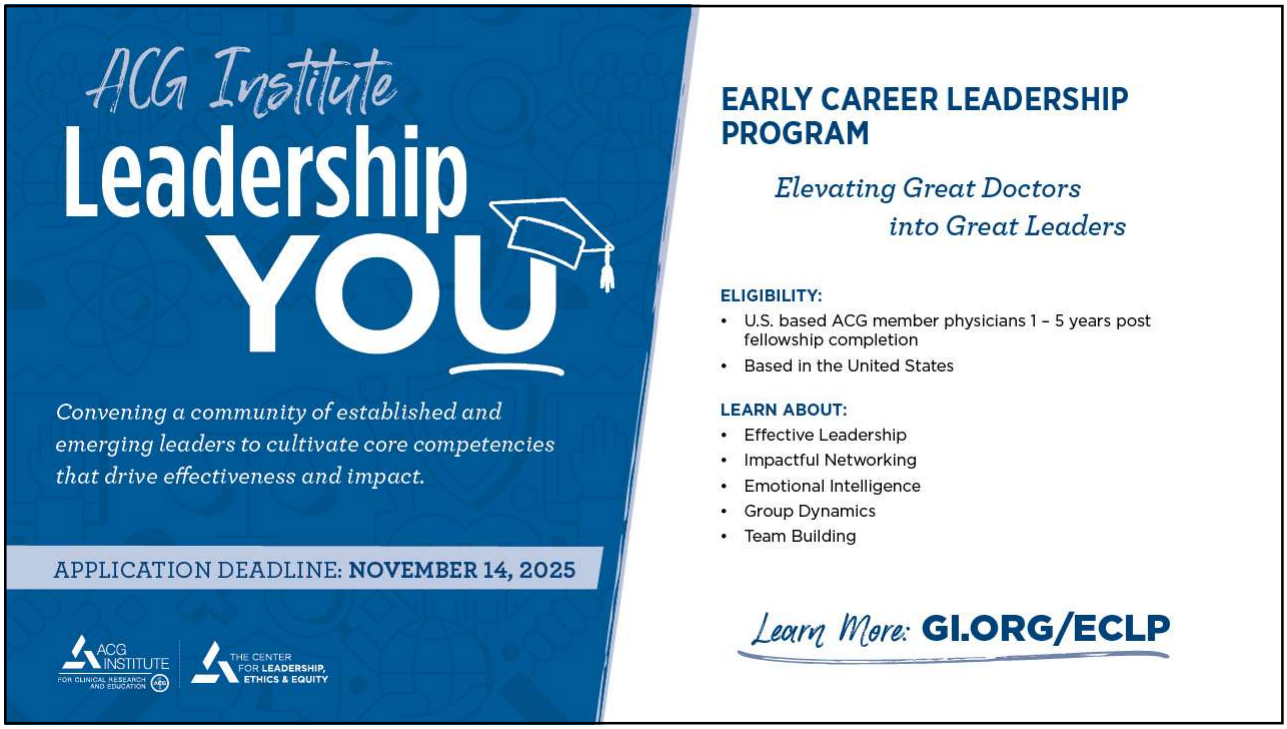
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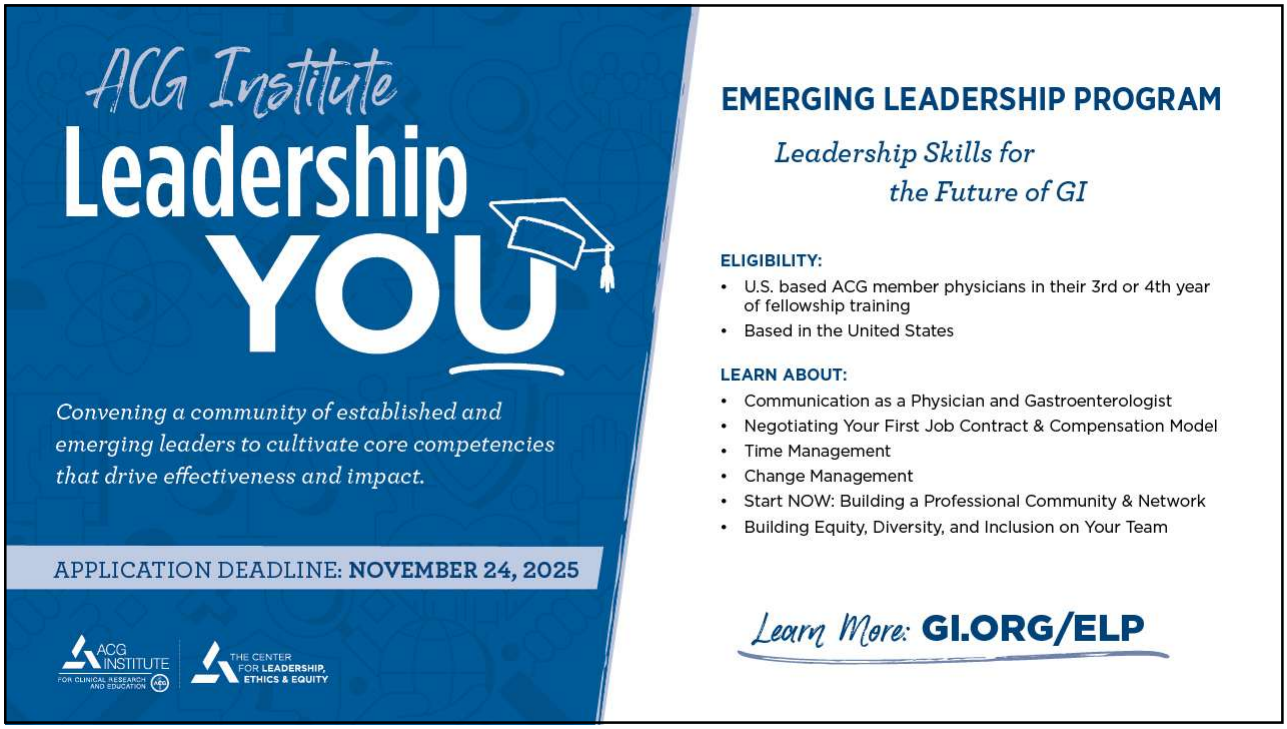
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NOTE: Must complete Prequalification Form (bit.ly/33guW6k) by November 3rd

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ACG/ASGE Epidemiologic Research Award in Gastrointestinal Endoscopy

$50k/ 1- or 2-year award

To fund research using the GIQuIC registry

- **Request a Letter of Support from GIQuIC by November 3**
  - Email: research@giquic.org

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8

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- **Visit gi.org/research-awards** to learn more about the 8 grant categories & apply
- **New! Grant Writing Resources -** gi.org/grant-writing-resources
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Participating in the Webinar

Moderator:
John K. DiBaise MD, FACG

All attendees will be muted and will remain in "Listen Only Mode"

Type your questions here so that the moderator can see them.
Not all questions will be answered but we will get to as many as possible.

A handout with the slides and room to take notes can be downloaded from your control panel.

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ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

Week 41 – Thursday, October 9, 2025
ACG Clinical Guideline: Management of Crohn's Disease in Adults
Faculty: Gary R. Lichtenstein, MD, FACG
Moderator: Edward V. Loftus, Jr., MD, FACG
At Noon and 8pm Eastern

Week 42 – Thursday October 16, 2025
The Role of Social Determinants of Health in Gastroenterology Care
Faculty: Costas H. Kefalas, MD, MMM, MS-PopH, FACG
Moderator: Sonali Paul, MD, FACG
At Noon and 8pm Eastern

Visit **gi.org/ACGVGR** to Register

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Up Coming 2025-26 ACG SBS Series

- Small Bowel Nutrient and Fluid Absorption: Key Concepts to Manage Short Bowel Syndrome
- Inpatient Management of the Newly Diagnosed Short Bowel Patient: Consult to Discharge
- Short Bowel Syndrome/Intestinal Failure: Recognition, Complications, and Basic Management
- Short Bowel Syndrome: Maximizing Management to Convert Intestinal Failure to Intestinal Insufficiency
- Cases of Non-Short Bowel/Intestinal Failure: Pearls for Recognition and Management

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Disclosures

Shirley C. Paski, MD, MSc

Nutrishare: Advisory Committee/Board Member;
Takeda Pharmaceuticals Inc: Grant/Research Support

John K. DiBaise, MD, FACG

Takeda Pharmaceutics: Advisory Board;
Immunic Therapeutics: Consultant;
Zealand Pharmaceuticals: Research Grant,
Northsea Therapeutics: Research Grant

**All of the relevant financial relationships listed for these individuals have been mitigated*

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Advanced therapies for short bowel syndrome

Shirley C. Paski, MD, MSc
Staff Gastroenterologist, Cleveland Clinic

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56 yo. F with structuring, penetrating enterocolonic Crohn's disease

- s/p extended R hemicolectomy and multiple small bowel resections, most recently 9-2024
- Current anatomy: upper GI with 55cm proximal small bowel anastomosed to distal transverse colon thru rectum/anus. No ICV.
- On TPN since 8-2024, currently 1.8L daily containing 1350 kcal/d
- Crohns disease in endoscopic remission on risankizumab

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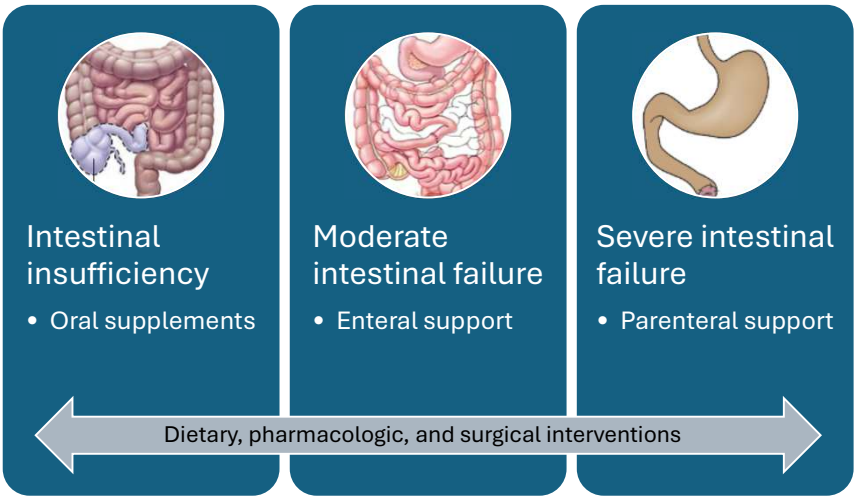
Intestinal insufficiency ⇔ intestinal failure



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Intestinal failure may be due to 1 or multiple etiologies

Surgical/Structural	Mucosal disease	Dysmotility	Obstruction

• Short bowel syndrome
• Malabsorptive bariatric surgery
• Surgical bypass
• Fistulas
	• Congenital/genetic
	• Crohn's disease
	• Celiac disease
	• NSAID enteropathy
	• CVID
	• GVHD
	• Vasculitis
	• Eosinophilic enteropathy
	• Autoimmune enteropathy
	• Whipple disease
	• HIV enteropathy
	• Severe malnutrition
		• Mitochondrial (e.g. MNGIE)
		• Neuropathy
		  • CNS lesions
		  • Autonomic failure
		  • Multiple sclerosis
		  • Parkinson's
		  • Guillen-Barre
		  • Paraneoplastic
		• Myopathy
		  • Scleroderma
		  • Muscular dystrophy
		  • Dermatomyositis
		  • Amyloidosis
		• Medications
		  • Opioids
		  • Anticholinergic
		  • Cathartics
			• Adhesions
			• Strictures
			• Radiation
			• Sclerosing peritonitis

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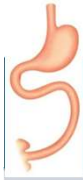
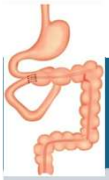
Estimate fluid needs based on remnant bowel



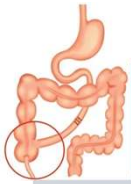
Type I
Enterostomy

- Fluid loss: high
- Poor jejunal adaptation
- Rapid transit and hypersecretion



Type II
Jejuno-colic

- Fluid loss: moderate-high
- Poor jejunal adaptation
- Rapid transit
- SIBO



Type III
Jejuno-ileocolic

- Fluid loss: mild
- Potential for ileal adaptation
- Fat malabsorption and calcium oxylate stones

Goulet O et al. Current Concepts of Intestinal Failure 2016 pp1-22.
Chakrabarty I & Burns D. Clinical Mgmt Intestinal Failure 2012 pp13-30

22

SBS diet and lifestyle

- Separate fluids from solids.
- Eat every 2-3 hours.
- Avoid concentrated sweets. Limit sugars to 10g per serving.
- Chew well.
- Sip (not slurp) fluids between meals, ideally isotonic fluids and ORS

Oral/enteral nutrition requirements are higher in malabsorption

23

SBS basic medical management

- Electrolyte replacement
- Anti-diarrheals (loperamide, diphenoxylate → codeine, DTO)
- PPI, H2B
- Soluble fiber (psyllium)
- Anti-secretory (clonidine, somatostatin analogue)
- PERT, bile acid sequestrants (limited roles)
- SIBO treatment

Manage primary GI disease

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Nutrition support indicated when nutrition needs cannot be met orally

Enteral support
- Gastric/post-pyloric
- Jejunal

Parenteral support
- IV hydration
- Parenteral nutrition

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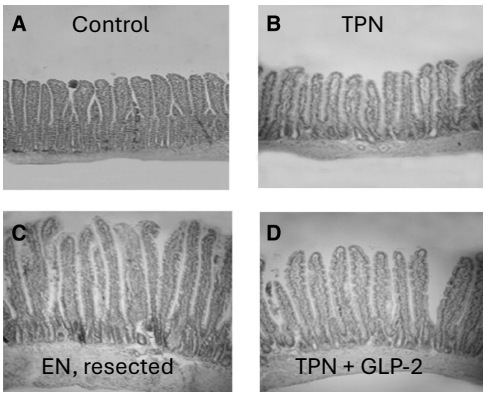
Trophic factors facilitate parenteral support weaning

- ~~Growth hormone~~
- GLP-2 agonists
  - Secreted from L-cells in ileum & proximal colon
    - Stimulated by intraluminal carbs & fat
  - "Ileal break"
    - Slows gastric emptying & intestinal transit
    - Reduces gastric secretion
  - Stimulates growth of small & large intestine
    - Increases mucosal blood flow
    - Increases epithelial proliferation
    - Inhibits apoptosis

Ileal morphology:



Martin GR et al., AJP 2004;286:G964.

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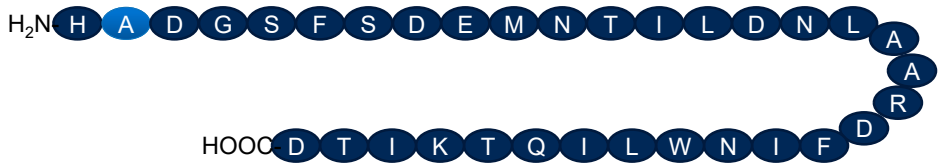
Teduglutide



- Teduglutide is a recombinant GLP-2 analogue
  - Alanine → Glycine
  - Resistant to dipeptidyl peptidase-4 (DPP-4) degradation; t½ 7mins → 2hrs
  - Same trophic, motility, and absorptive effects

Jeppesen PB et al. Gut 2005;54:1224.

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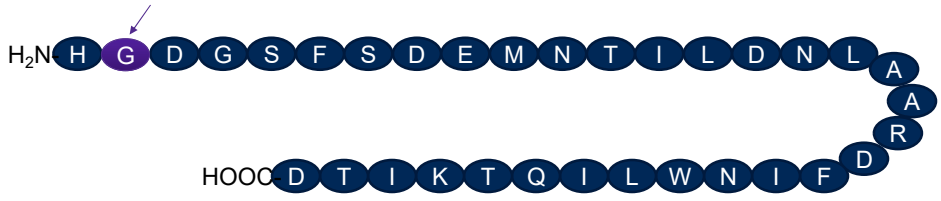
Teduglutide



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Jeppesen PB et al. Gut 2005;54:1224.

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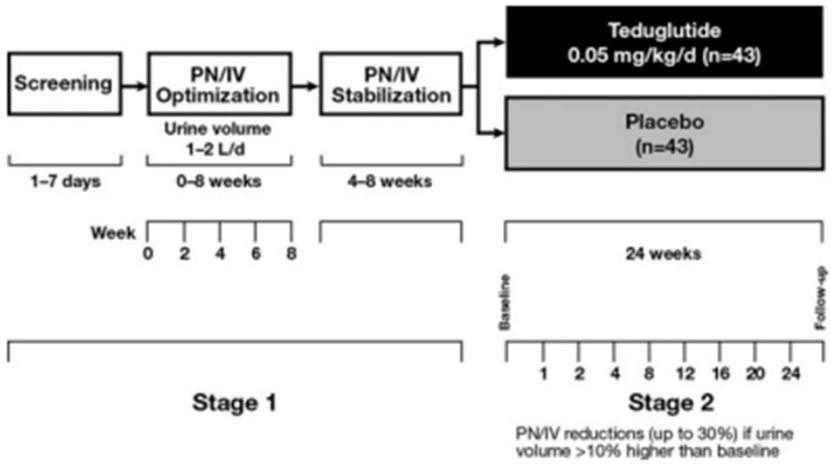
Teduglutide clinical trial study design



Gastro 2012;143:1473

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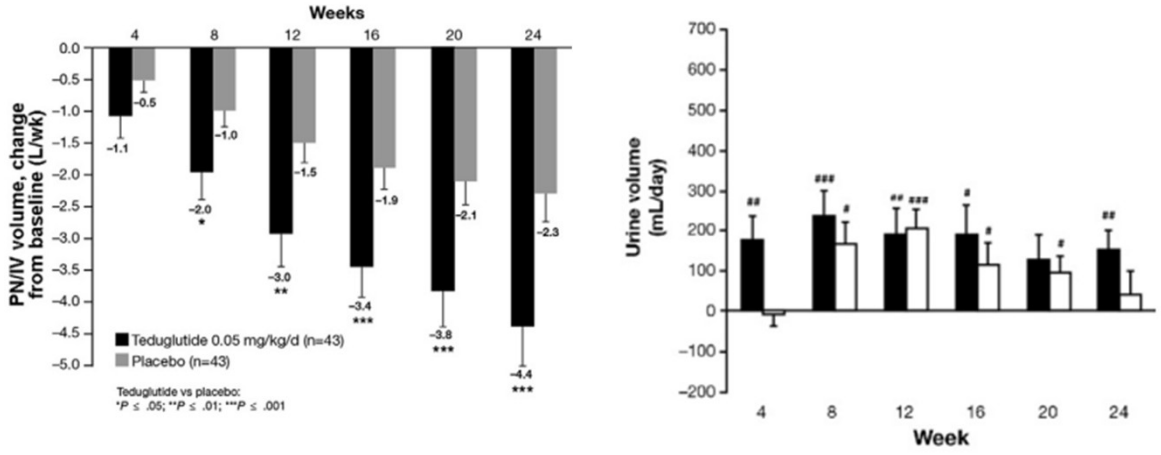
Teduglutide significantly reduced need for PS and improved urine output



Gastro 2012;143:1473

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Features of patients who weaned off TPN

- 11/173 patients treated by teduglutide were weaned off TPN
  - 63% were able to wean off ≥1-day TPN
- Healthy remaining bowel
  - 5 with mucosal disease (Crohn's, radiation enteritis)
  - 6 with infarction/injury
- PN volume <7L/week at baseline (9/11)
- Preservation of colon (8/11)

O'Keefe et al., Clin Nutr 2012

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Real world teduglutide experience: higher % wean off TPN and lower % death

	Control	Teduglutide	P
Outcome, pts (n)	3081	269	
Still on PN	49.5%	63.2%	
Weaned off PN	18.2%	30.5%	<0.001
Deceased	21.8%	4.8%	
Lost to follow up	10.5%	1.5%	
PS volume (ml), pts (n)	2987	252	
Weekly, median (IQR)	12, 292 (10,500)	9000 (9000)	<0.001
Daily, median (IQR)	1756 (1500)	1285 (1265)	<0.001
Days of PS/wk, pts (n)	2992	254	
Median (IQR)	7 (2)	5 (3)	<0.001
Type of oral feeding, pts (n)	1277	88	
NPO	5.6%	0	
Only water	0.5%	0	<0.001
Clear liquids	1.7%	0	
Small amount of food/drink	23.3%	6.8%	
Unrestricted food/drink	68.7%	93.2%	

Clin Nutr 2025;47:54-67

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Some can maintain PN volume reduction after discontinuing teduglutide

- Follow-up after teduglutide discontinuation:
  - 15 had rapid weight loss, treated with increased PN
  - 15 patients maintained stable BMI & PN volume
    - *3 had discontinued TPN during study and remained off*
  - 7 had further PN volume reductions
- Predictive features:
  - Longer small bowel & colon
  - Lower PN volume reduction on drug
  - Lower BMI

Compher et al., JPEN 2011;35:603.

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Teduglutide improved QOL vs controls at 24 wks.

	TED				Placebo				P b/w groups
	Median baseline	Median week 24	Change	P	Median baseline	Median week 24	Change	P	
GI symptoms	4.9	3.9	-1.2	**0.007**	4.1	3.3	0	0.83	0.116
Sleep	5.1	3.3	-0.9	**0.003**	4.2	3.3	0	0.527	0.0811
Leisure activity	5.0	3.3	-0.9	**0.024**	4.6	4.3	0	0.972	0.123
Everyday activity	4.8	33.8	-0.9	**0.007**	5.0	4.3	-0.3	0.157	0.499
Energy	5.0	4.7	-0.9	0.051	4.8	4.5	0.1	0.476	0.455
MSK symptoms	4.4	3.6	-0.6	**0.002**	3.8	3.6	-0.1	0.445	0.240
Social life	5.4	4.0	-0.5	**0.018**	5.2	3.9	-0.1	0.469	0.301
Physical health	5.2	4.1	-0.4	**0.021**	4.4	3.9	-0.4	0.325	0.354

Clin Nutr 2013;32:713

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Warnings and Precautions (REMS)

- **Neoplastic growth**
  - Pre-treatment colonoscopy and polypectomy
  - Repeat colonoscopy at 1 year
  - Screening/surveillance prn, minimum q5 years
  - Contraindicated in colon cancer, GI malignancy
- **Intestinal obstruction**
  - Hold teduglutide
- **Biliary & pancreatic**
  - Baseline bilirubin, alk phos, lipase, amylase; then q6 mo.
- **Volume overload**
  - Regular volume assessment, TPN volume adjustment
- **Increased absorption of concomitant oral medication**
  - Benzodiazapines, psycotropic toxicity reported

Product Monograph

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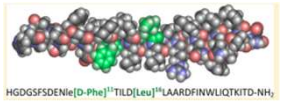
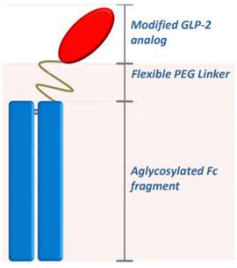
Upcoming GLP-2 agonists & combination GLP-1/GLP-2 agonist

- Apraglutide
  - GLP-2 modified positions 2, 10, 11, and 16
  - GLP-2 agonist + selective GLP-1 and GCG agonist
  - Weekly injection
- Glepaglutide
- HM15912
  - Modified GLP-2 analog conjugated with human IgG Fc fragment via flexible linker
  - Monthly injection
- HM15912/efpeglenatide
  - GLP-2 analog/GLP-1 receptor agonist





Wisniewski et al J Med Chem 2016;59:3129.
Choi et al ESPEN 2022

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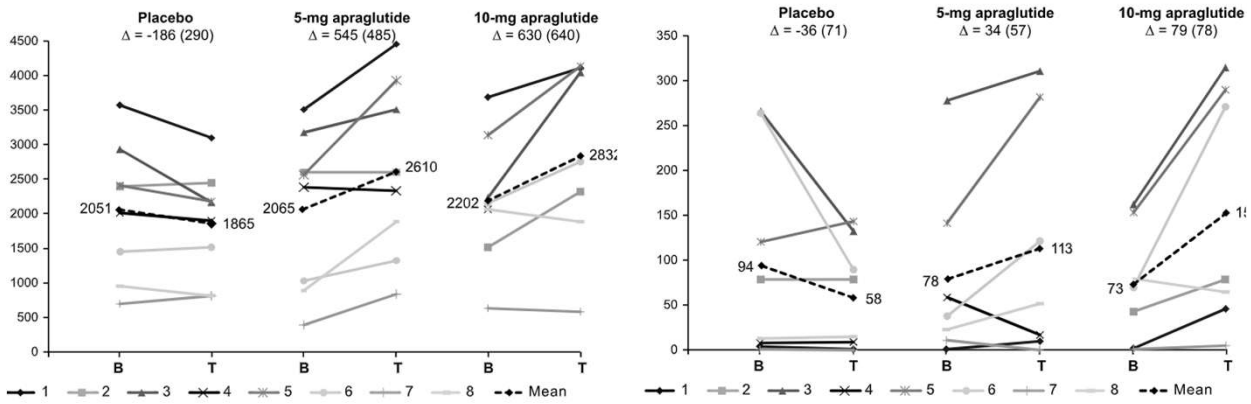
Apraglutide improved urine output and sodium



JPEN 2022;46:896

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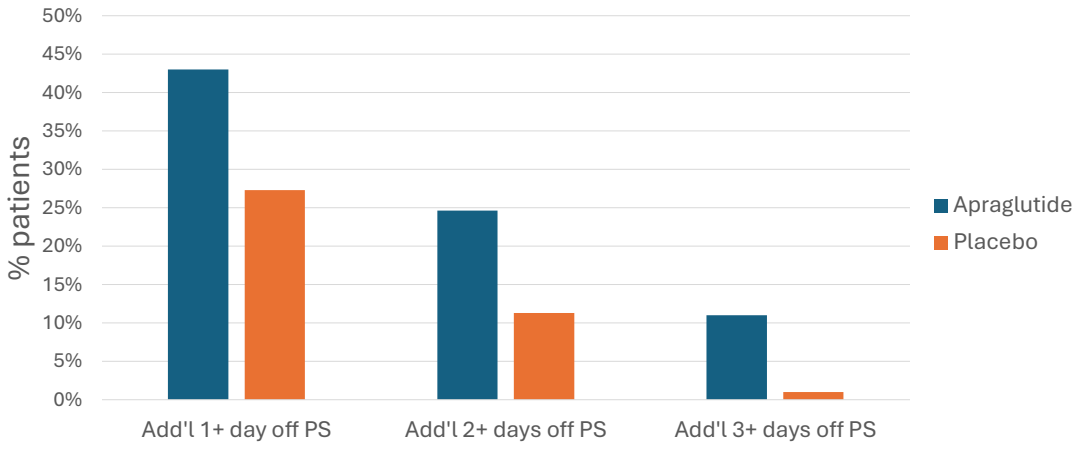
Apraglutide increased days off TPN at week 24



CIIRTA 2025 Abstract

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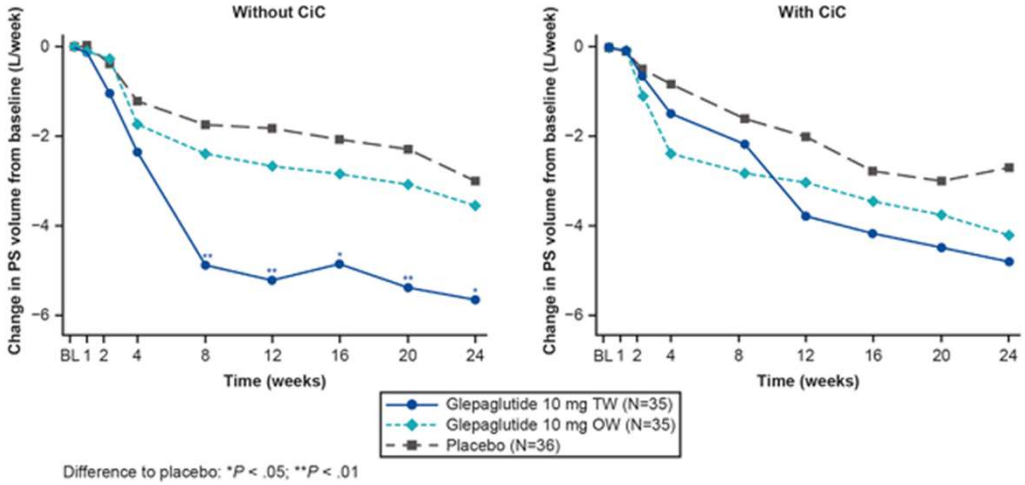
Glepaglutide reduced PN volume significantly starting week 8 in SBS without CIC



Difference to placebo: *$P < .05$; **$P < .01$

Gastro 2025;168:701-13

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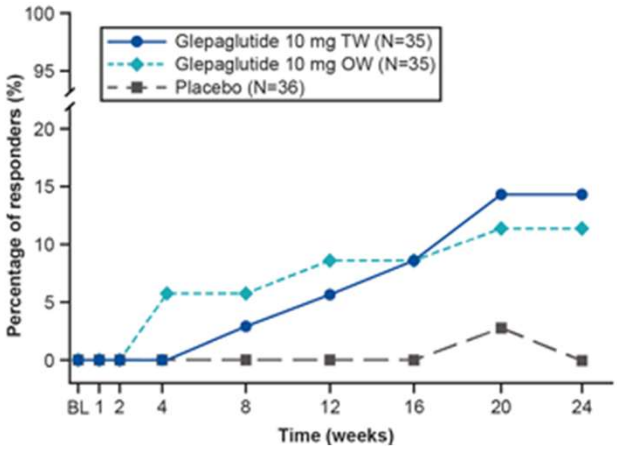
Glepaglutide increased enteral autonomy



	Glepaglutide 10 mg TW (N=35)	Glepaglutide 10 mg OW (N=35)	Placebo (N=36)
n/N (%)	5/35 (14.3)	4/35 (11.4)	0/36 (0)
Difference vs. placebo [95% CI]	14.1 [2.5; 25.6]	11.2 [0.7; 21.6]	–
Nominal *P* value	.0160	.0424	–

Gastro 2025;168:701-13

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Additional medications (off label)

Medication	Mechanism of action	Current Indication	Usual Dosing
Eluxadoline	Mixed opioid effects on GI tract	IBS-D	100mg po bid with food
Exenatide Liraglutide	GLP-1 agonist	Type 2 diabetes, metabolic syndrome	5mcg subQ bid (Byetta) 2mg subQ every 7 days (Bydureon) 0.6-1.8mg subQ daily (Liraglutide)
Crofelomer	Blocks Cl- secretion via CFTR & CaCC	Non-infectious HIV diarrhea	125mg po bid

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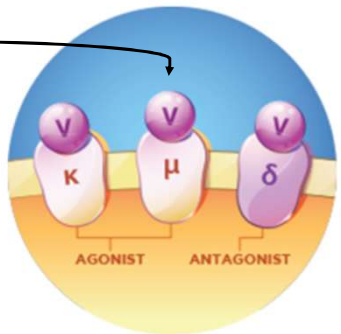
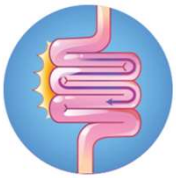
Eluxadoline for IBS-D

- Binds to opioid receptors in the GI tract



Mu- and kappa- receptor agonist
Delta-opioid receptor antagonist

- Decreases visceral hypersensitivity
- Slows GI motility

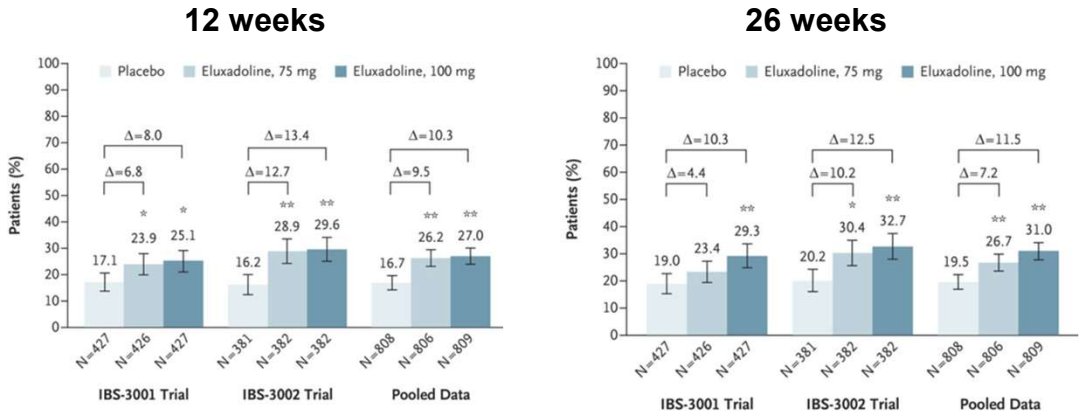


- High 1st pass metabolism
- Low systemic exposure

Lembo A et al NEJM 2016;374:242.

42

Eluxadoline 75-100mg po bid reduced pain and stool more formed after 12 and 26 weeks



Lembo A et al NEJM 2016;374:242.

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Eluxadoline cautions & contraindications

Adverse effects

- Nausea, constipation, abdominal pain in 5.8-8.6%
- Pancreatitis in 0.3%

Contraindications

- Without a gallbladder
- Known/suspected biliary obstruction, SOD dysfunction, Hx pancreatitis, structural disease of the pancreas
- Alcoholism or 3+ drinks/d
- Severe hepatic impairment
- Hx chronic/severe constipation, mechanical bowel obstruction

Lembo A et al NEJM 2016;374:242.
Product monograph

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GLP-1 agonists

- GLP-1 is produced by L-cells in the ileum that regulate proximal gut transit (ileal break)
- Enhance intestinal growth via crypt fission
- Enhances insulin secretion, inhibits glucagon secretion
- Extensive ileal resection → GLP-1 levels may be deficient
- Retained gastric contents associated with anesthesia complications
- Currently indicated for type 2 diabetes, metabolic syndrome, and weight loss

Drucker JCI 2024;134:e175634.
Hashah et al Clin Gastro Hep 2023.

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Exenatide 5mcg subQ bid improved bowel function in SBS

Before exenatide	Immediately after exenatide
Bowel movement within 10 mins of eating	Bowel movement 3-6 hours after eating
TPN in 3 patients	No TPN
Malnutrition without TPN in 3 patient	No malnutrition despite not having TPN
Urine frequency 1-2 times per day	Urine frequency 4-6 times per day plus increased volume
Repetitive gastric contractions in 3 patients	Reduced gastric contractions

Kunkel et al. Neurogastroenterol Motility 2011;23:739

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Liraglutide 0.6-1.8mg sc daily reduced jejunostomy output and improved absorption in 8 weeks

Measure	Baseline (mean)	8 wks liraglutide (mean)	P
Wet weight PN	3721 ml/d	3671 ml/d	0.79
Wet weight diet	2743 g/d	2733 g/d	0.83
Wet weight ostomy output	3249 g/d	2775 g/d	0.049
Wet weight absorption	-506 g/d	-42 g/d	0.05
Diuresis	1543 g/d	2308 g/d	0.02
Ostomy output sodium	309 mmol/d	272 mmol/d	0.04
Urinary sodium	132 mmol/d	197 mmol/d	0.03
Energy ostomy absorption	3243 kJ/d	4146 kJ/d	0.02
Carbohydrate absorption	53 ± 23%	62 ± 21%	0.002
Lipid absorption	20 ± 24%	30 ± 24%	0.09
Protein absorption	24 ± 25%	31 ± 28%	0.15

Hvistendahl et al JPEN 2018;42:112.

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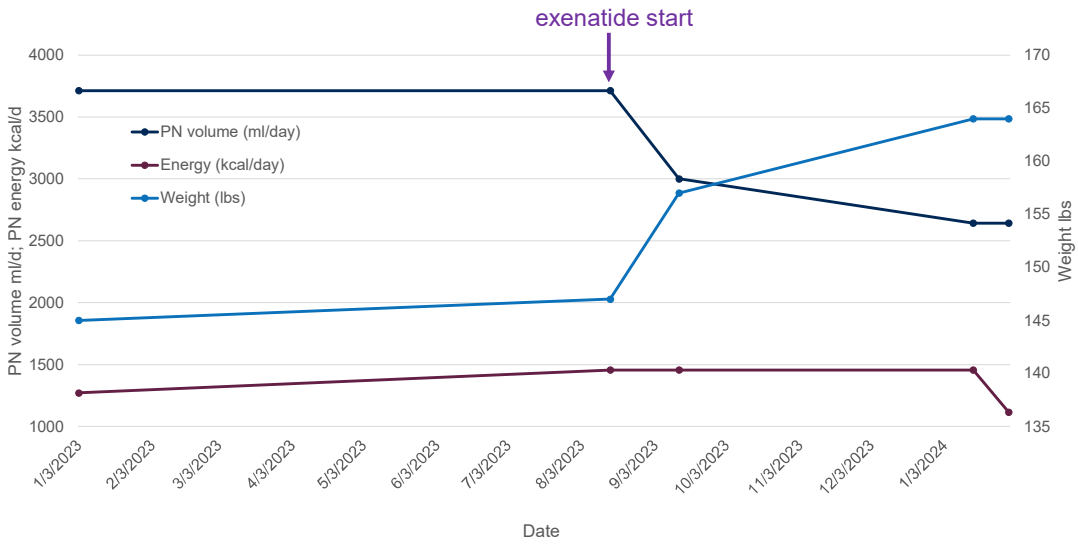
Long acting exenatide 2mg weekly ↓ TPN 30%



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GLP-1

Adverse effects

- Nausea, vomiting, GI dysmotility
- Hypoglycemia
- Pancreatitis
- Acute gallbladder disease
- Drug-induced ITP
- Injection site and hypersensitivity reactions

Contraindications

- Personal or family Hx of thyroid C-cell tumors (including medullary thyroid cancer), patients with MEN 2
- Hx of drug induced ITP from GLP-1 products
- Hx of hypersensitivity reaction to GLP-1 or product components

Product monograph.

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Crofelemer

- Inhibits:
  1) Cyclic adenosine monophosphate (cAMP)-stimulated cystic fibrosis transmembrane conductance regulator (CFTR) chloride ion (Cl^-) channel, and
  2) Calcium-activated Cl^- channels (CaCC) at the luminal membrane of enterocytes
- CFTR Cl^- channel and CaCC regulate Cl^- and fluid secretion by intestinal epithelial cells
- Crofelemer blocks Cl^- secretion and associated diarrhea water losses and normalizes flow of Cl^- and water in GI tract
- Currently indication: non-infectious diarrhea in patients with HIV on HAART

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Crofelemer improved electrolyte and fluid balance in patient with SBS without colon

- 55yo F s/p multiple ileocolonic resections → type II SBS
- Diarrhea and malnutrition refractory to antidiarrheals, opioids, antibiotics, eluxadoline
- Crofelemer 125mg bid → tid → crushed
- Over 6-18 months, developed formed stool 2-3/d, weight gain

Powers W J Clin Gastroenterol Treat 8:086.

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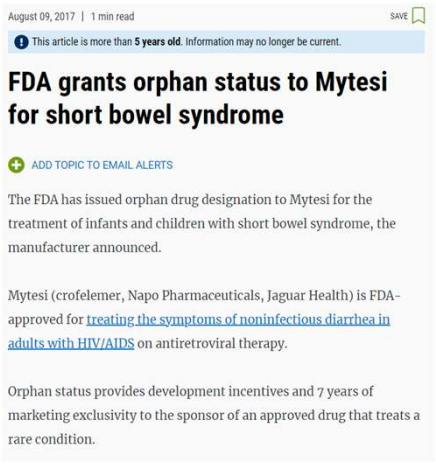
Crofelemer is safe to use

- Only contraindication is infectious diarrhea because it hasn't been tested in this population



August 09, 2017 | 1 min read SAVE

This article is more than **5 years old**. Information may no longer be current.

FDA grants orphan status to Mytesi for short bowel syndrome

ADD TOPIC TO EMAIL ALERTS

The FDA has issued orphan drug designation to Mytesi for the treatment of infants and children with short bowel syndrome, the manufacturer announced.

Mytesi (crofelemer, Napo Pharmaceuticals, Jaguar Health) is FDA-approved for treating the symptoms of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy.

Orphan status provides development incentives and 7 years of marketing exclusivity to the sponsor of an approved drug that treats a rare condition.

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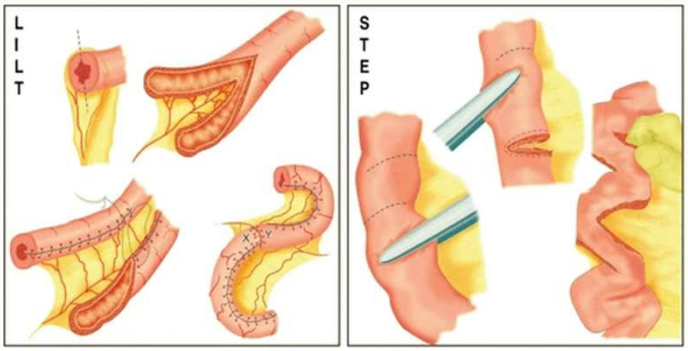
Surgical management of short bowel syndrome

- Restore luminal continuity/motility
  - Fistula repair
  - Stricturoplasty
  - Re-connection of existing bowel
- Lengthening procedures
  - STEP Serial transverse enteroplasty
  - LILT Longitudinal intestinal lengthening and tapering



Goulet O et al. Current Concepts of Intestinal Failure 2016 pp1-22.

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Imaging, motility and stool studies to help guide therapy

- Gastric emptying time
- Small bowel transit time
- Dilated bowel
- Partial bowel obstruction
- Colon transit studies
- Endoscopy, enteroscopy, capsule endoscopy, colonoscopy
- Evaluation of primary GI disease activity
- Stool studies

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Positioning of therapies for intestinal malabsorption

- Start with diet and lifestyle
  - No amount of medication can overcome gross excess consumption of free water/hyperosmotic beverages and a terrible diet
  - Physical activity to build/maintain lean body mass & strength
- Early resection, start PPI empirically
- Add anti-diarrheals ac meals and hs
- Assess appropriateness for anti-secretagogues and/or hormonal therapy
- Concurrent treatment of SIBO, PEI, micronutrient deficiencies, and surgical rehabilitation +/- intestinal transplant

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Intestinal transplant

Isolated small bowel

Multivisceral

Intestinal transplant indications:

- Intestinal failure associated liver disease
- Loss of central venous access of 2+ central veins
- 2+ catheter related sepsis
- 1+ line related fungemia, septic shock, or ARDS
- Recurrent severe dehydration despite IV fluid in addition to TPN
- Underlying disease with high morbidity (e.g. ultrashort bowel syndrome, microvillous inclusion disease)

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Take Home Points

1. Intestinal malabsorption symptoms vary significantly based on GI anatomy, structure, motility, and GI disease.
2. Treat symptoms, nutritional deficits, and underlying disease
3. Start nutrition support if oral intake fails to meet nutrition requirements
4. Consider advanced therapies for patients needing parenteral support
5. Refer to a specialized center for nutrition & medical optimization, surgical management, and/or transplant evaluation

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Thank you!

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Questions

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John K. DiBaise, MD, FACG

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