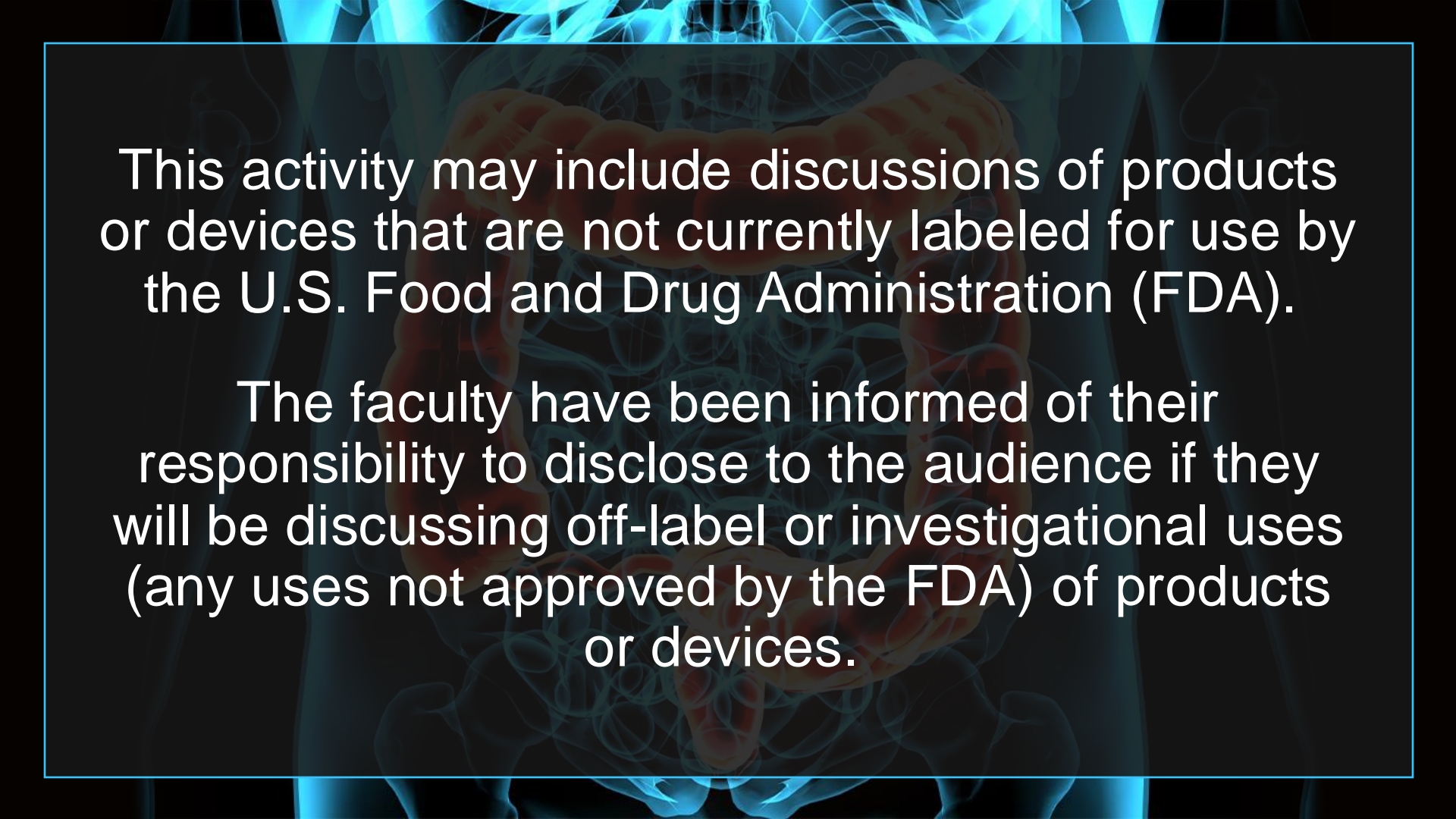




# Closing Gaps in Care for Short Bowel Syndrome in the Community Setting

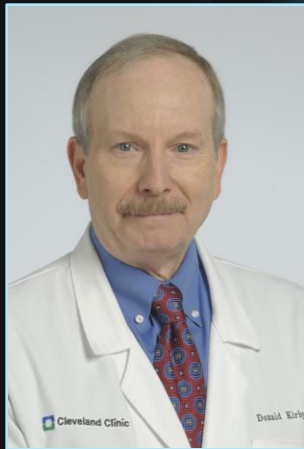
Supported by an educational grant from Takeda Pharmaceuticals U.S.A., Inc.



This activity may include discussions of products or devices that are not currently labeled for use by the U.S. Food and Drug Administration (FDA).

The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational uses (any uses not approved by the FDA) of products or devices.





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# LEARNING OBJECTIVE 1

Identify the pathophysiology and associated risk factors including disease-related complications of short bowel syndrome (SBS)



# LEARNING OBJECTIVE 2

Evaluate available and emerging SBS treatment strategies to promote enteral autonomy and reduce the need for parenteral nutrition (PN)





# LEARNING OBJECTIVE 3

Develop interdisciplinary  
and interprofessional  
coordinated care plans  
for patients with SBS  
being managed in the  
community setting



# Part 1

## Pathophysiology and Complications Associated with Intestinal Failure Due to SBS






# Audience Response



**Which of the following is the most common etiology for short bowel syndrome**

- A. Inflammatory bowel disease
- B. Malignancy
- C. Surgical complications
- D. Strangulated hernias
- E. I don't know

# Audience Response

 Which of the following is the most common etiology for short bowel syndrome

- A. Inflammatory bowel disease
- B. Malignancy
- C. Surgical complications
- D. Strangulated hernias
- E. I don't know



# What Is Intestinal Failure?

## Intestinal Failure (IF)

Reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes such that **IV supplementation is required\*** to maintain health and/or growth

\*If IV supplementation is not required, it is termed intestinal insufficiency

- Heterogeneity of IF
  - Acquired or congenital
  - Gastrointestinal or systemic
  - Benign or malignant etiology
  - Abrupt onset or from a slowly progressive chronic illness
  - Self-limiting short-term or long-lasting

# Classification of Intestinal Failure

## Type I

Acute, short-term, often self-limiting

## Type II:

Prolonged acute condition, often in metabolically unstable patients, requiring complex multidisciplinary team care and IV supplementation over periods of weeks or months

## Type III (Chronic IF):

Chronic condition in metabolically stable patients requiring IV supplementation over months or years; may be reversible or irreversible



# Short Bowel Syndrome

- Most common cause of chronic intestinal failure
- Patients with < 200 cm of functional small bowel
  - Important to get an accurate length of remaining bowel either during surgery or radiologically via opisometer
- Clinical features may vary depending on the extent and anatomy of intestine lost and the ability of the patient and remaining intestine to compensate for the loss
- Treatment needs may vary depending on disease severity and resection type
  - Potential for rehabilitation from intestinal failure to intestinal insufficiency

# Etiologies of SBS

**Surgical complications are the most common cause of SBS**

Malignancy/  
Radiation

Trauma

Mesenteric  
ischemia

Bariatric  
disasters

Vascular  
disease

Strangulated  
hernias

Surgical  
complications

Inflammatory  
bowel  
disease



# Normal Intestinal Function

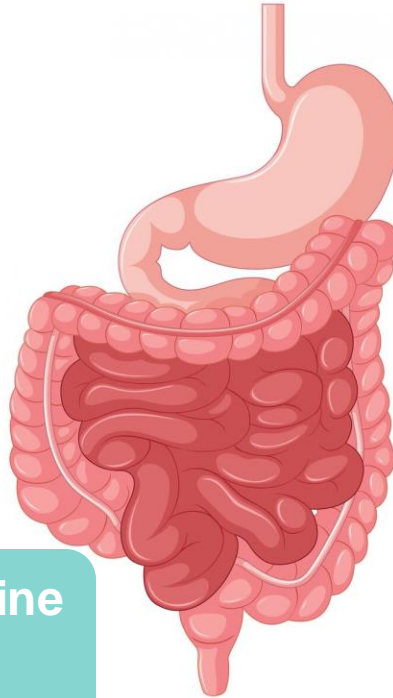
## Fluid Entering (per day)

- Oral intake 2 L
- Salivary 1.5 L
- Gastric 2.5 L
- Biliary 0.5 L
- Pancreatic 1.5 L
- Intestinal 1 L

Total: 8 to 9 L per day

## Small & Large Intestine

- Water
- Electrolytes



## Fluid Reabsorbed (per day)

- Small intestine 7 L
- Large intestine 1.4 L

## Small Intestine

- Carbohydrates
- Fats
- Proteins
- Calcium
- Magnesium
- Trace elements
- Vitamins

# SBS Bowel Anatomy Types and Functions

End-Jejunostomy



Type 1

- Rapid transit
- Acid hypersecretion
- Poor adaptation
- Large fluid losses
- Malabsorption
- Worst prognosis
- < 100 cm

Jejuno-colonic



Type 2

- Rapid transit
- Poor adaptation
- B12 and bile salt malabsorption
- Variable calorie and fluid absorption
- < 65 cm

Jejunioileo-colonic



Type 3

- Adequate absorption until about 75% resected
- Good adaptation
- Slower transit
- Uncommon; best prognosis
- < 30 cm

# Intestinal Malabsorption in SBS

## Rapid intestinal transit

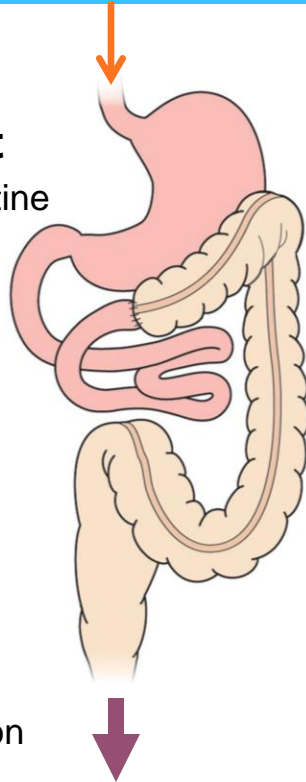
- No time to mix w/food in intestine

## Bacterial overgrowth

- Obstruction
- Sluggish peristalsis
- Loss of valve
- ↓ pH

## Bile acid wasting

- Deconjugation of bile acids with impaired micelle formation



## Acid hypersecretion

- Inactivation of endogenous pancreatic enzymes
- Decreased Peptide YY

## Loss of surface area

- Secretion of secretin and CCK (failure to stimulate release of pancreatic enzymes)



# Clinical Presentation of SBS

## Pediatrics

- Diarrhea
- Reflux
- Gas and abdominal pain
- Poor growth or weight gain
- Vitamin and mineral deficiencies

## Adults

- Diarrhea
- Dehydration
- Gas, bloating, and abdominal pain
- Fatigue
- Malnutrition
- Vitamin and mineral deficiencies

# Achieving Early and Accurate Diagnosis

- High index of suspicion based on patient history
- Laboratory studies
- Fecal fat test
- Imaging
- Endoscopy
- Colonoscopy

# Impact of SBS on QoL and Family

## Adults with SBS on PN

- Most intense concern is being a burden to others
- Loss of independence
- Activities require intense planning and are negatively impacted

## Parents of children with SBS

- More likely to be physically tired, annoyed, and report problems sleeping
- Difficulty in spending time with partners, shopping, or taking holidays

## Family QoL outcomes

- Those with children age < 5 scored worse on daily family activities, household tasks, and family relationships



# Parenteral Nutrition: Patient Burden

## Requires significant time

- 10-15 hours of infusion time/day
- Negative psychosocial and mental health impact overall

## Resource intensive

- Obtaining, storing, and preparing PN for administration
- Operation of infusion pump
- Catheter maintenance

## Risk of complications

- Line-associated infection
- Line-associated thromboembolism
- PN associated liver failure

## Significant direct and indirect costs

- Direct costs of PN therapy (copays, insurance premiums)
- Time to manage PN by patient and/or caregivers (uncompensated time)
- Loss of employment

# Potential Complications of SBS



Central venous catheter: infection, occlusion, thrombosis, breakage

Hepatobiliary: steatosis, cholestasis, cirrhosis

Metabolic bone disease: osteoporosis, osteopenia, osteomalacia

Kidney injury: oxalate kidney stones, acute kidney disease, chronic kidney disease

Nutrition deficits: malnutrition, dehydration, electrolyte and micronutrient imbalances, vitamin deficiencies

# Part 2

**Available and Emerging  
Treatment Options to Promote  
Enteral Autonomy and Reduce  
Parenteral Support**





# Audience Response

 Which of the following would be the most appropriate first-line treatment for managing gastric hypersecretion in patients with SBS?

- A. Proton pump inhibitors
- B. H<sub>2</sub>RAs
- C. Octreotide
- D. Clonidine
- E. I don't know

# Audience Response

 Which of the following would be the most appropriate first-line treatment for managing gastric hypersecretion in patients with SBS?

- A. Proton pump inhibitors
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- D. Clonidine
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# Dietary Approaches to Rehabilitating the Gut

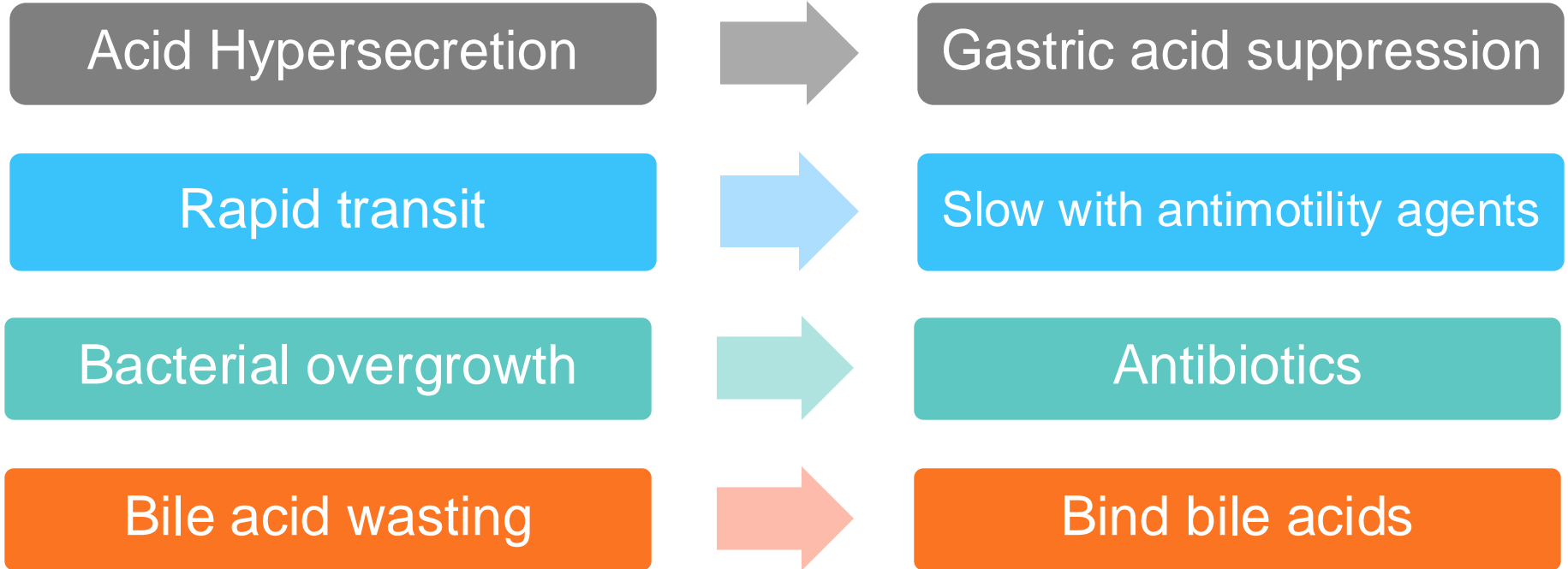
- To enhance absorptive capacity, improve nutritional status, and reduce need for parenteral nutrition
- Dietary strategy
  - 5-6 smaller meals or snacks/day
  - Avoid simple carbohydrates
  - Limit lactose and artificial sweeteners
  - Major emphasis on maintaining hyperphagia vs excessive dietary restrictions
- Oral fluid intake
- Vitamin and mineral supplements
- Enteral nutrition
  - Use as a supplement to oral feeding to avoid PN requirement

# Rehydration Strategies for SBS-IF

- Dehydration is a major concern in IF as increased liquid may not be absorbed appropriately
- Rehydration strategies
  - Avoid hypertonic fluids such as fruit juices, sodas, or other sweetened drinks (including commercial nutritional supplements)
  - Hypotonic fluids such as water, coffee, tea, and diet drinks may be appropriate in small quantities
  - Preference for isotonic oral rehydration solutions
    - Commercial solutions (e.g. DripDrop, Pedialyte, EquaLyte, CeraLyte, Liquid IV, or WHO rehydration packets)
    - Homemade solutions including water, salt, and low amounts of sugar
      - Recipe: 4 cups water +  $\frac{3}{4}$  teaspoon salt + 2 tablespoons sugar + flavoring (Crystal Light, Mio drops, sugar-free Kool Aid)



# Therapeutic Opportunities in SBS



# Medications for the Spectrum of SBS

## Anti-motility agents

- Loperamide\*
- Diphenoxylate\*
- Codeine\*, tincture of opium\*

## Gastric acid suppression medications

- Proton pump inhibitors\*
- H<sub>2</sub>RAs\*

## Anti-secretory agents

- Octreotide\*
- Clonidine\*

## Small intestinal bacterial overgrowth treatment

- Antibiotics\*
- Probiotics\*

## Bile acid sequestrants

- Cholestyramine\*

## Trophic agents

- rGH
  - Somatropin
- GLP-2 analog
  - Teduglutide

\*Not approved by the U.S. Food and Drug Administration (FDA) for the treatment of SBS.

GLP-2 = glucagon-like peptide-2; H<sub>2</sub>RAs = histamine 2 receptor antagonists; rGH = recombinant human growth hormone.

Cuerda C, et al. *Clin Nutr.* 2021;40(9):5196-5220. Matarese L, et al. *J Parenter Enteral Nutr.* 2013;37(2):161-170.

# Growth Hormone for SBS-IF

- Recombinant human growth hormone
  - Promotes crypt cell proliferation
  - Decreases parenteral nutrition needs
  - Use limited by adverse effects
  - Somatropin: approved by the FDA for treatment of SBS in patients receiving specialized nutrition support
    - Glutamine: approved by the FDA for treatment of SBS in patients receiving specialized nutrition support when used in conjunction with recombinant human growth hormone

# Glucagon-like-peptide 2 (GLP-2) in SBS-IF

## GLP-2 Function

- Secreted mainly by cells in distal small bowel and proximal colon
- Mediates increased jejunal absorption through induction of jejunal epithelial proliferation
- Slows gastric emptying and increases intestinal transit time

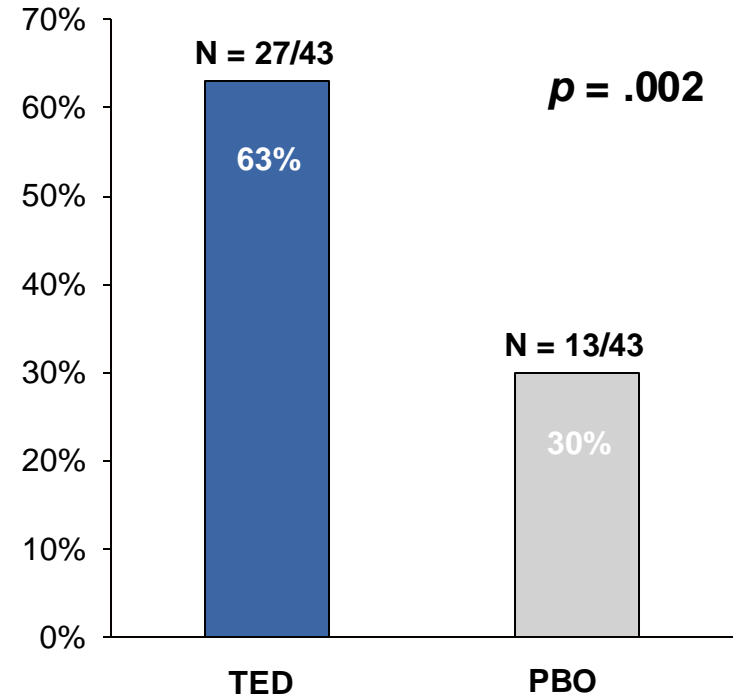
## GLP-2 Analog Therapies

- Teduglutide
  - Approved by FDA for adult and pediatric patients age  $\geq 1$  who are dependent on PN
- Options in development (not FDA approved)
  - Apraglutide: phase III clinical trial completed
  - Glepaglutide: phase III clinical completed
  - Dapiglutide: phase Ib clinical ongoing



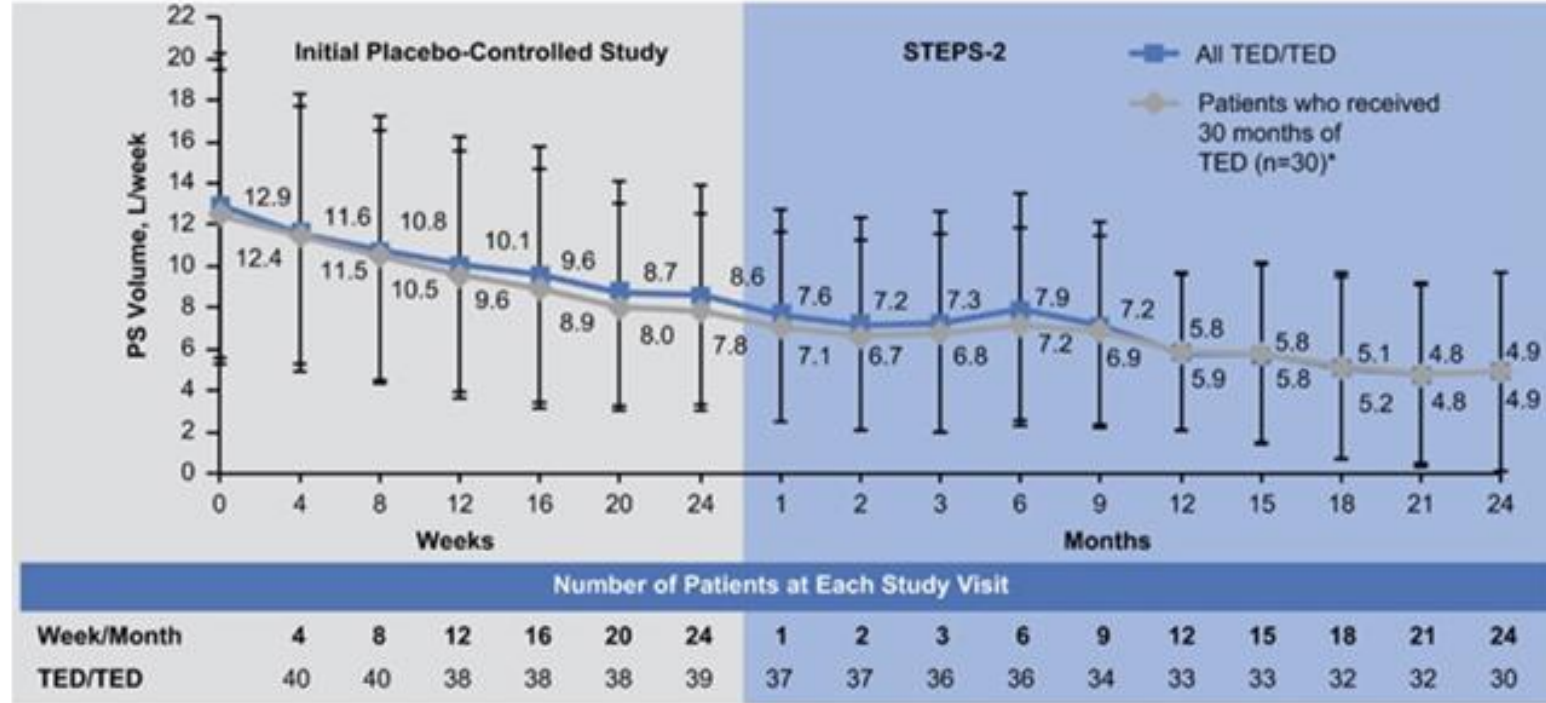
# Teduglutide Efficacy in Adult Patients with SBS-IF

- 24-week study of patients with SBS-IF, N = 86
- Administered SQ teduglutide or placebo QD
- Response = % of patients with > 20% reduction in PN volume from baseline at weeks 20 and 24



Teduglutide is approved for patients age  $\geq 1$  with SBS who need parenteral support.  
QD = every day; SQ = subcutaneous; TED = teduglutide.  
Jeppesen PB, et al. *Gastroenterology*. 2012;143(6):1473-1481.e3.

# Teduglutide: Long-Term Efficacy in Adults



Teduglutide is approved for patients age  $\geq 1$  with SBS who need parenteral support.  
 Schwartz LK, et al. *Clin Transl Gastroenterol.* 2016;7(2):e142.

# Teduglutide and PS Independence

Pooled analysis of 5 adult clinical trials:  
134 patients included

16 patients (12%)  
achieved enteral independence

Baseline PS requirements  
Duration: range 2-18 years  
Days per week: range 3-6 days

75% of patients required  $\geq 1$  year of  
TED treatment before PS  
elimination

One patient weaned off PS after  
2.5 years of treatment with TED

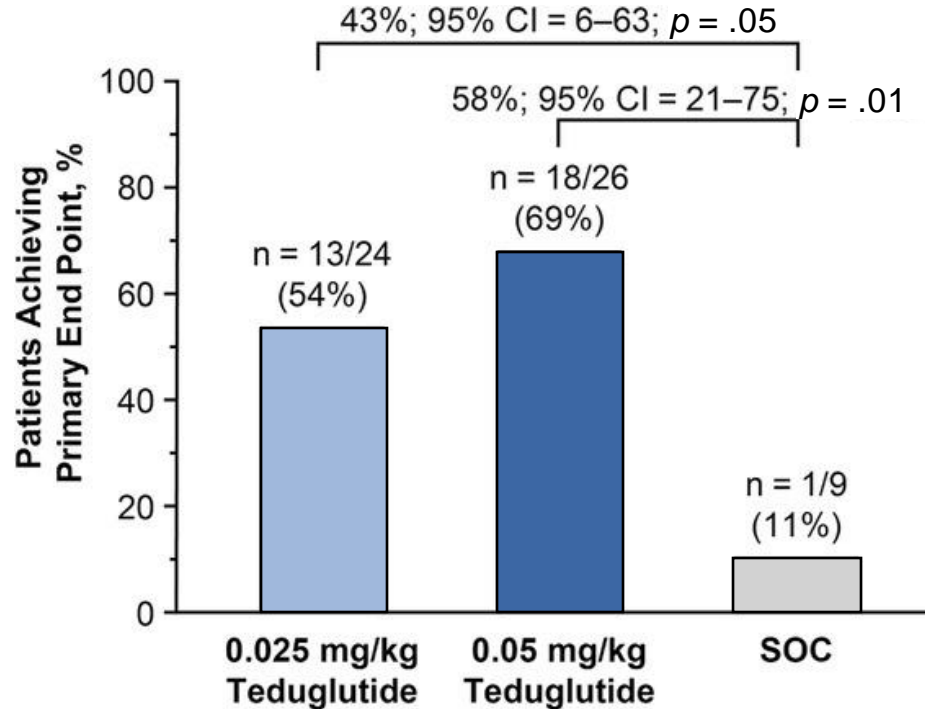
Teduglutide is approved for patients age  $\geq 1$  with SBS who need parenteral support.

PS = parenteral support.

Iyer K, et al. *J Parenter Enteral Nutr.* 2017;41(6):946-951.

# Pediatric Teduglutide: Efficacy

Primary endpoint:  
Number of patients who  
achieved a  $\geq 20\%$   
reduction in parenteral  
support (PS) from  
baseline at week 24

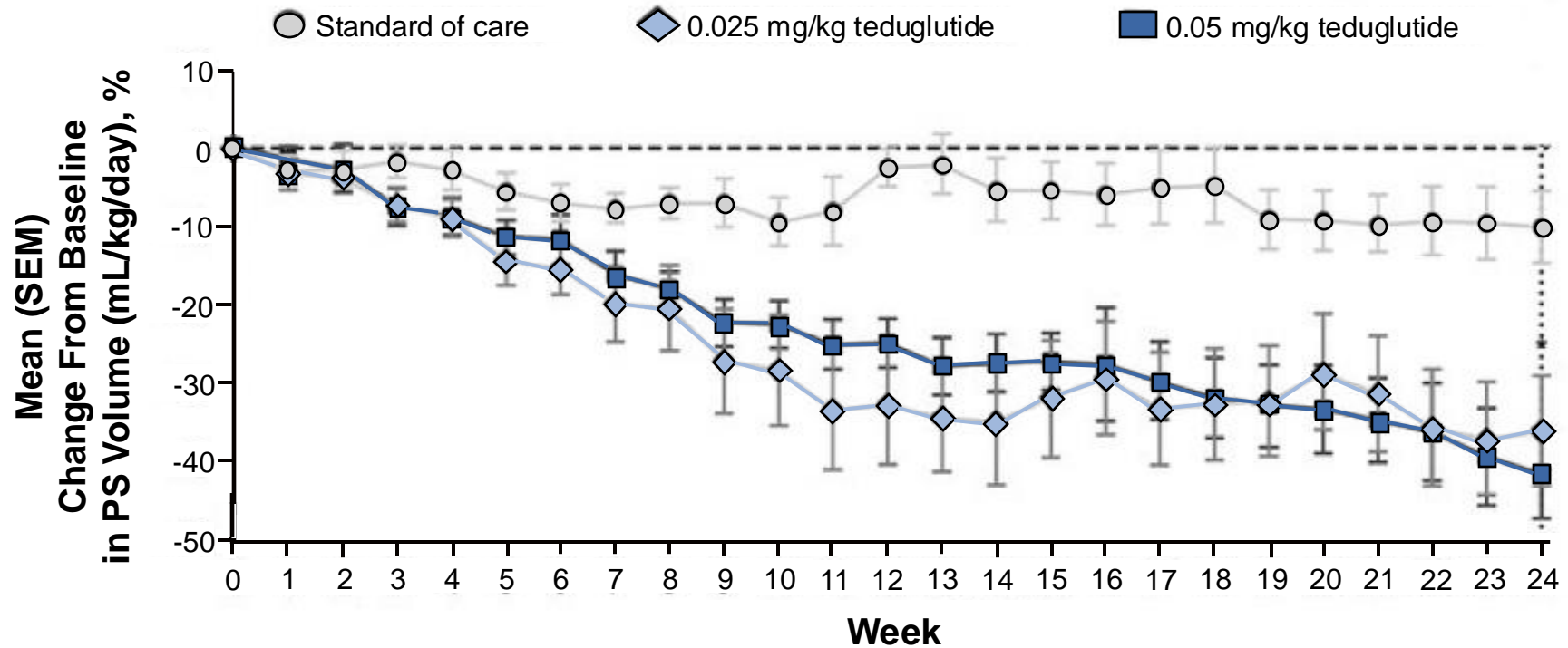


SOC = standard of care

Teduglutide is approved for patients age  $\geq 1$  with SBS who need parenteral support.

Kocoshis SA, et al. *J Parenter Enteral Nutr.* 2020;44(4):621-631.

# Pediatric Teduglutide: Efficacy in Reducing Parenteral Support (PS)



Teduglutide is approved for patients age  $\geq 1$  with SBS who need parenteral support.  
Kocoshis SA, et al. *J Parenter Enteral Nutr.* 2020;44(4):621-631.



# Most Commonly-Reported Teduglutide Adverse Events

	RCT Group (n = 109) n (%)	RCT Extension (n = 173) n (%)	RCT Placebo (n = 59) n (%)
GI stoma complication	17 (37.8)*	31 (45.6)	3 (13.6)
Abdominal pain	42 (38.5)	72 (41.6)	16 (27.1)
Upper respiratory tract infection	30 (27.5 )	50 (28.9)	8 (13.6)
Catheter sepsis events	17 (15.6)	47 (27.2)	10 (16.9)
Nausea	29 (26.6)	46 (26.6)	12 (20.3)
Headaches	18 (16.5)	35 (20.2)	9 (15.3)
Asthenic conditions	14 (12.8)	35 (20.2)	7 (11.9)
Injection site reactions	22 (20.2)	33 (19.1)	7 (11.9)

Teduglutide is approved for patients age ≥ 1 with SBS who need parenteral support.

\*Of 45 patients with a stoma.

RCT = randomized controlled trial.

Pape UF, et al. *Therap Adv Gastroenterol.* 2020;13:1756284820905766.

# Teduglutide: Monitoring Recommendations

- Risk for accelerated neoplastic growth
  - Pediatric screening: baseline and annual fecal occult blood screening; 1 year colonoscopy/sigmoidoscopy with a repeat every 5 years or if blood in stool
  - Adult screening: baseline colonoscopy/sigmoidoscopy with repeat at 1 year and then 5 years thereafter
- Intestinal obstruction
- Fluid overload
- Pancreaticobiliary disease
  - Lab monitoring every 6 months
- Monitor for changing drug effects from increased absorption
- Active malignancy (< 5 years) is contraindication to GLP-2

Teduglutide is approved for patients age  $\geq 1$  with SBS who need parenteral support.

Teduglutide [package insert]. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/203441Orig1s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/203441Orig1s000lbl.pdf).

# Considerations Before Using GLP-2

- Patient meets criteria for SBS-IF
- PN/IV fluids required  $> 3\text{x/week}$  for  $\geq 1$  year
- Patient has been optimized on:
  - Diet therapy
  - Anti-secretory drugs
  - Anti-diarrheal drugs
- Malignancy contraindication
- Partnership exists between treatment team and patient

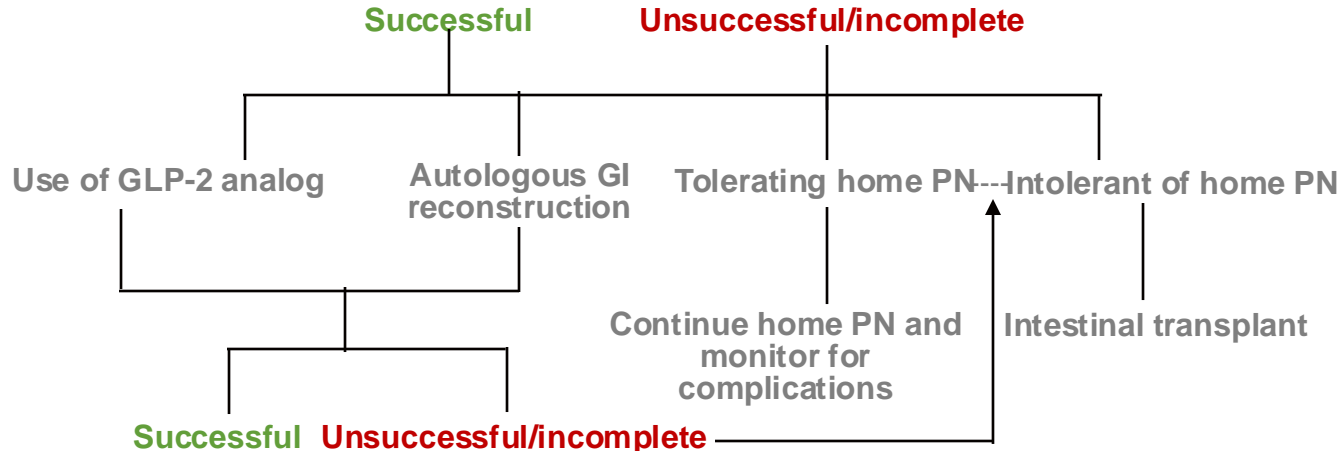
# Managing SBS-IF: Overview

PN still frequently necessary

- Does not enhance bowel function
- Costly (> \$100,000/year)
- Reduced quality of life
- 1-2 hospitalizations annually per patient

## Attempt to wean PN

- Optimize oral diet and fluids
- Aggressive use of antisecretory and antimotility agents
- Maximize function of remnant bowel surgically if possible
- Careful monitoring of status
- Micronutrient supplementation




# Part 3

## Coordinating Care with Interdisciplinary and Interprofessional SBS Specialists




# Audience Response

 What is one of the greatest barriers to smooth transition between pediatric and adult care?

- A. Patient unwillingness to move to a new provider
- B. Failure to initiate transition in a timely manner
- C. Lack of providers who care for adult patients with SBS
- D. Loss of social support networks
- E. I don't know

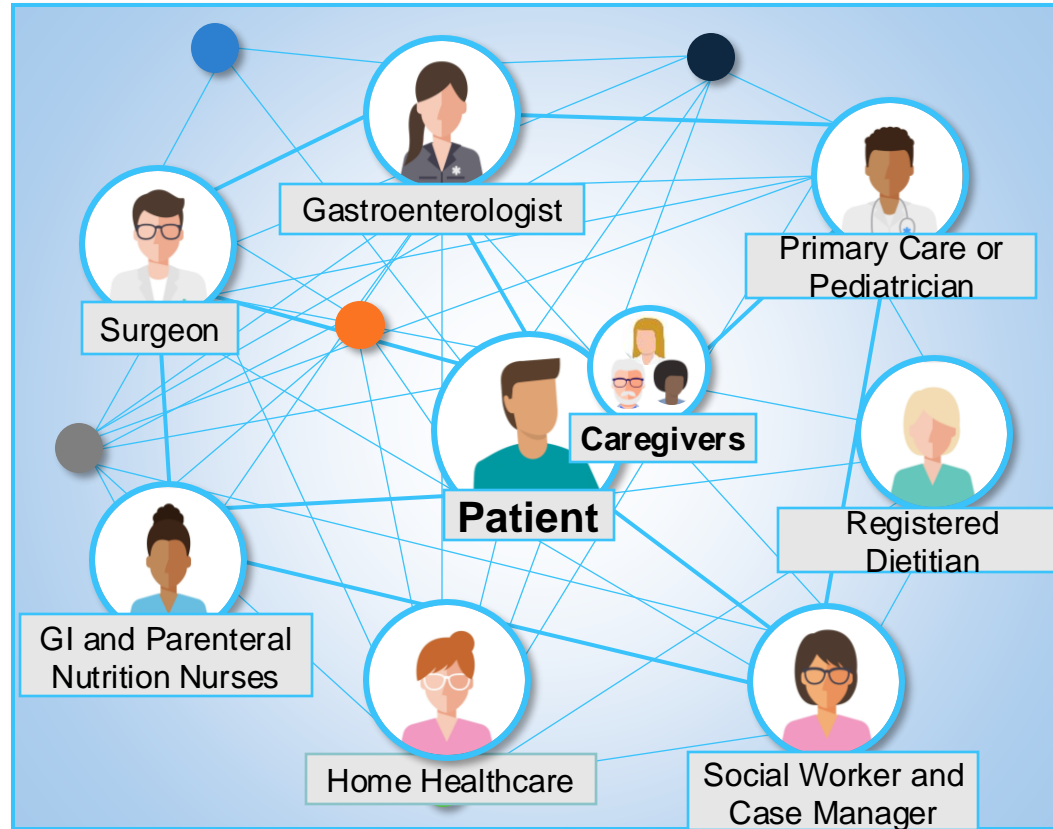


# Audience Response

 What is one of the greatest barriers to smooth transition between pediatric and adult care?

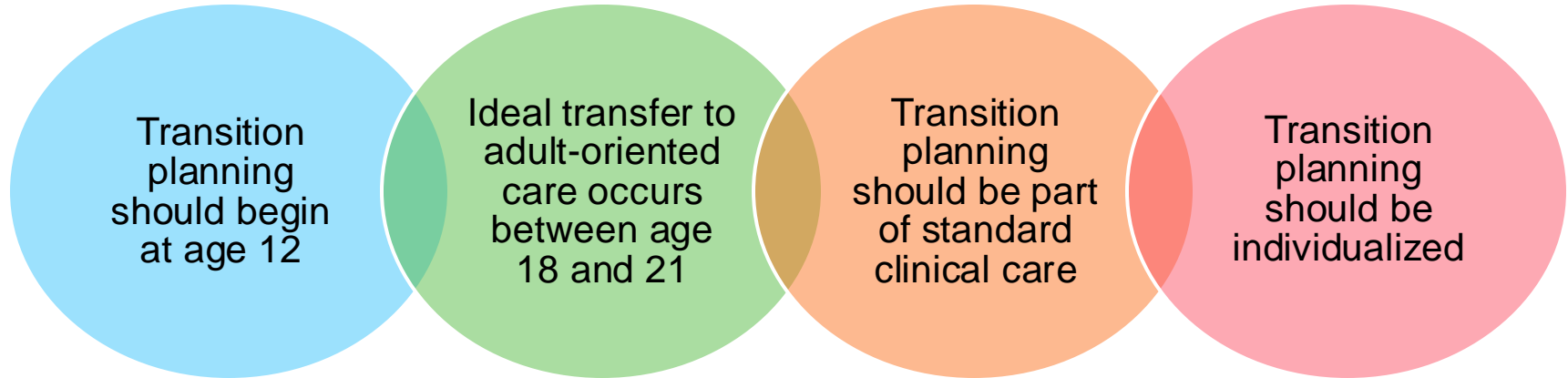
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- B. Failure to initiate transition in a timely manner
- C. Lack of providers who care for adult patients with SBS
- D. Loss of social support networks
- E. I don't know

# Creating Communities of Practice in SBS



# Transition of Care

## Guideline-Recommended Best Practices



# Strategies for a Smooth Transition

- Identify a provider
  - Shortage of adult providers is a major challenge for patients with SBS
  - Initiate a structured hand-off appointment including both pediatric and adult providers when possible (may be telehealth)
- Transition appointments for adult doctors for all medical problems including recent issues
- Transition summary note
  - Written summary of the medical history and treatment course
  - Surgical history
  - Amount of remaining small bowel, active problems, complete set of nutritional labs
- Identification of cultural and linguistic support if necessary
- Engage a social worker to ensure continuity of care

# Barriers to Transitions of Care

- Lack of planning or communication surrounding transition
- Lack of training in disease state and PN care
- Lack of social support to replace previous caregiver support
- Inability to locate an adult specialist with knowledge of pediatric SBS
- Patient or caregiver reluctance to transition
- Loss of insurance or financial assistance

# Supporting Under-Resourced Communities

- Home parenteral nutrition
  - Increases sense of normalcy in patients lives
  - Decreases need for distant travel
- Telehealth opportunities
  - Allows community providers to create team of providers
    - Facilitates multidisciplinary care team visits with multiple specialists
    - Increases access to specialists who may not be available locally
  - Access to urgent evaluations for complications
  - Increased access to clinical trials



# Resources to Help with Care Transitions



**Transition to Adulthood for Young Adults with Chronic GI Conditions Program**

<https://www.chop.edu/services/chop-penn-transition-program-digestive-liver-and-pancreatic-medicine>



Doc4me App

[www.doc4me-app.com](http://www.doc4me-app.com)

# Support for SBS: Patients and Providers

- Short Bowel Syndrome Foundation website: Lists support groups for patients with SBS as well as their caregivers

<http://shortbowelfoundation.org/>



- The Oley Foundation: Supports patients on home PN

<https://oley.org/>

- Programs and resources to support

- Competency
- Normalcy
- Advocacy



- American Society for Parenteral and Enteral Nutrition

<https://nutritioncare.org/>



# SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Develop a plan to manage the risks and complications associated with SBS-IF and parenteral nutrition
  - Consider socioeconomic barriers that might prevent patients from receiving parenteral nutrition or advanced pharmacotherapy
- Optimize nutrition and rehydration plans for patients with SBS-IF
- Utilize advanced pharmacotherapy, such as GLP-2 analogs, in appropriate patients with SBS dependent on parenteral nutrition
- Assemble a care transition team to support smooth transitions between pediatric and adult care



# Closing Gaps in Care for Short Bowel Syndrome in the Community Setting

Supported by an educational grant  
from Bristol Myers Squibb

Supported by an educational grant from Takeda Pharmaceuticals U.S.A., Inc.