Short Bowel Syndrome (SBS) Patient-led Listening Session
July 19, 2022

Objective of session

To further educate the FDA on the realities of short bowel syndrome (SBS), particularly the impact it has on patients and caregivers day-to-day and their quality of life; treatment options available, and the risks and benefits thereof; and the unmet needs of the SBS community.

Brief overall summary

In this FDA Patient Listening Session, adults with SBS and caregivers of children with SBS shared a broad spectrum of insights around what it is like to live with SBS. Through ninety minutes of highly engaged storytelling, participants shed light on the realities of their lives affected by the rare disease state, and the risks and benefits of current treatment options.

Participants shared heartbreaking and inspirational stories equally balanced by setback and success. Through the relentless pursuit of happiness and quality of life, the SBS community is eagerly and collectively advocating for ongoing innovation within the clinical landscape.

It is our hope that the Patient Listening Session had an actionable impact on the FDA participants and overall influence of innovation with the SBS landscape.

Summary of topics discussed

Overview of SBS, Sivan Kinberg, MD

- SBS is a serious and chronic malabsorption disorder that results from physical loss of bowel (often due to surgical resection) and/or function loss of bowel (bowel is present but does not work well)
- Clinical features include diarrhea or high stool outputs from an ostomy; gassiness, bloating; dehydration; malnutrition; electrolyte abnormalities; fatigue
- Complications can include liver disease, central venous catheter (CVC) complications (i.e., sepsis, clots, line breaks), vitamin/mineral deficiencies, metabolic bone disease, kidney disease, surgical complications; it affects social life, sleep, school, work
- Can result in “intestinal failure”: the inability of the gastrointestinal tract to sustain life without supplementation parenteral nutrition (PN) for at least 60 days
- Current management of SBS is intestinal rehabilitation, a multidisciplinary approach to making the remaining bowel work better
  - Nutritional: oral (specialized diet), enteral nutrition (tube feeding), and/or parenteral nutrition (specialized nutrition that goes directly into the bloodstream, bypassing the GI tract, via a CVC)
  - Medical: acid blockers, anti-motility agents, pro-motility agents, antibiotics, intestinal hormones (i.e., glucagon-like peptide 2 agonists [GLP-2])
  - Surgical: to restore continuity (put all functioning intestines back together); to lengthen remaining bowel (Bianchi, STEP); to fix complications (tapering of dilated bowel, obstruction, strictures, ostomy prolapse); intestinal transplant
Goals of management: maintain hydration and nutrition; ensure adequate weight gain and development (children); promote intestinal adaptation; minimize complications from SBS and long-term PN; wean from PN; optimize quality of life

Challenges and unmet needs: every SBS patient is different; an SBS patient’s needs change over time; there is a lack of evidence and consensus; prevention of SBS; optimizing remaining intestinal function and adaptation; preventing complications; product shortages; consideration of quality of life, mental health, neurocognitive outcomes

Caregiver 1, parent of ten-year-old son with SBS: Everyday life with SBS

Son’s nutrition needs are met with PN. The challenges, risks, and benefits of PN include:
- Challenges: administering PN via a pump (be “hooked up”) daily for 8 to 12 hours; requires a consistent daily schedule; you are dependent on DME suppliers, home care companies, and/or infusion pharmacies; shortages of lipids, multivitamins, ethanol locks, and tubing
- Risks: errors in sterile procedure can lead to line infections, hospital admissions, and life-threatening complications; possibility of liver complications with long-term PN; blood sugar complications
- Benefits: provides hydration; increases life expectancy while the patient undergoes other treatment options to rehab the intestines; keeps people alive

Sleep, for patients and caregivers. is affected by SBS and PN
- PN is typically administered overnight, to allow freedom from being “hooked up” to an IV and pump during the day. Leads to discomfort and frequent urination. Risks associated with child being attached to tubing while they sleep include danger of entanglement and strangulation, and occlusion (if tube gets kinked), with subsequent risk of blood sugar plummeting. SBS also causes frequent bowel movements and diarrhea, day and night.
- If the child has an ostomy, there is concern of possible leakage (challenging, but also potential cause of CVC infection, if CVC is soiled), and a need to wake up every few hours to check it.
- Lack of sleep impacts quality of life for patient and caregiver: tired all the time; need for naps/early bedtime, even in older children and adults

Patient 1, 32-year-old adult with SBS: Everyday life with SBS

Background
- Born in 1989, with first intestinal surgery within days of birth; on PN for 29 years; on tube feeding for 22 years; has had 31 CVCs, with 26 CVC infections; has had multiple surgeries; had intestinal transplant in 2014 when other options were limited or non-existent
- Health and day-to-day life: you need strong determination not to let symptoms and complications of SBS and PN interrupt life; you need a strong support system

Diarrhea
- Common and persistent with SBS
Need to always plan around it, i.e., know where bathrooms are, be prepared for emergencies
As anti-diarrheal medications take effect, diarrhea can turn to constipation, and it becomes a cycle; it is difficult to find balance
Odor and sounds of defecation can draw unwanted attention, especially for children and youth; it is often accompanied by or causes pain
Hydration is a constant concern
Bacterial overgrowth is also common with SBS

Transplant
It is not a cure. It can be an exchange of hardships.
The patient presented an overview of her life eight years post-transplant, both the good and the bad:
- No pain before, during, or after eating
- Can eat to her heart’s desire
- Permanent ileostomy
- Chyle leak
- Post-transplant lymphoproliferative disorder (PTLD)
- Aspergiloma in the right lung
- Bilateral hip replacements; avascular necrosis of hips and shoulders
- Shoulder replacement (was pending at the time)
- Chronic ureteral stent
- Daily PN and IV fluid management
- Daily tube feedings (20 hrs./day)
- Disordered eating

Conclusion
With SBS, the options become more limited as you live longer with it
You wait until the last minute possible to go forward with the next treatment option, because future options are limited
There are complications from both surgical options and from long-term PN, including loss of vascular access (from multiple CVCs); when you lose vascular access, you can no longer have a CVC, and so can no longer receive PN
There comes a time when more surgery is not possible
You need access to the right care, at the right time, at the right place, which is challenging with SBS
This patient’s definition of “success” has changed throughout her journey
Multiple surgeries have resulted in medical trauma

Caregiver 2, mother of teenaged daughter with SBS: Everyday life with SBS

- Supplies (PN, tube feeding, ostomy, etc.) are a big part of life with SBS
  - Difficult to manage, order, organize, and store the many supplies needed
  - They must be ordered at different cadences and may involve different home care companies and/or DMEs; medications may also come from multiple pharmacies
  - Must always plan ahead and anticipate needs and emergencies
There are out-of-pocket expenses for supplemental or new products.

Due to shortages, availability, and recalls, supplies delivered may be different; even slight differences can affect routines.

Abbott infant formula recall (Elecare, Jr.) has had a big impact. This caregiver’s daughter has not been able to tolerate replacements and has not been getting adequate nutrition at a critical time of growth.

- **Risks**
  - PN and CVCs
    - Sterile equipment and technique must be used to minimize infectious risk; compromise may lead to severe illness and hospitalization; could lead to sepsis
    - Care must be taken with routine care, by whomever accesses the CVC, and with choice of activities; constant weighing of risk/benefits
    - In addition to infection, risks include dislodgement and blockage or breakage.
  - Ostomies (gastrostomy [G-tube]; gastrojejunostomy [GJ-tube]; ileostomy/jejunostomy/colostomy)
    - Managing equipment malfunction, leakage, local irritation, infection, high outputs, strictures, fistulas

- **Diarrhea, a mainstay of SBS**
  - Must maintain hydration status, whether through supplemental IV hydration, or supplement oral or enteral hydration
  - Can lead to vitamin and micronutrient deficiencies
  - May necessitate extra medications

**Caregiver 3, father of two-year-old son with SBS: Risks and benefits within the SBS treatment landscape in relation to surgery and devices**

- **Surgery**
  - May be part of the natural course due to the cause of the SBS and may include bowel exploration, resection, reanastomosis, CVC placement (or repair or removal), reconstruction
  - May be correctional or a treatment option: bowel lengthening, bowel transplant
  - For parents and caregivers, there is no choice; surgery is part of life. It is more a matter of when or who or where—how do we improve quality of life quickly?
  - Risk is measured differently when it is risk against risk
  - Risks that weigh into the balance include lifelong exposure to PN; poor quality of life; surgical exposure (high short-term risk for long-term potential change); pharmaceutical exposure (may aid adaptation or absorption but not replace)
  - Complications may include negative side effects and reactions
  - It is a very fragmented landscape; the field lacks data

- **Devices**
  - Devices used in managing SBS include G-tubes, CVCs, ostomies, feeding pumps, IV pumps. There are risks and complications with each device.

- **Conclusion:** There are a lot of solutions around maintaining life, but not a lot of innovation regarding intestinal adaptation. There is a need for innovation to improve rather than maintain.
Patient 2, 33-year-old adult with SBS: Risks and benefits within the SBS treatment landscape in relation to pharmaceutical options

- Background: Now in his thirties, he has been living with SBS since birth; he has never known anything different than life with SBS and on PN. His family was able to find creative solutions to overcome challenges of growing up (traveling, going to college, having a job, etc.) with SBS and while PN-dependent. Notes value of strong family support, and the benefit of his mother being a nurse.
- Tried different options for symptom management, with varying levels of success
- GLP-2 was suggested when he was a teenager, but PN was working OK so they chose the “known” over the “unknown.”
- Ran out of options for venous access and had to have a CVC placed through his liver; placement not ideal, and difficult for him to access when hooking himself up to/unhooking himself from PN.
- Began GLP-2
  - Benefits include being weaned off PN. Patient notes that while he was able to live a good life while on PN—go to college, do work he loved, live independently, travel, etc.—after several years without PN, he says he finds the idea of having to go back on PN “unacceptable.”

Caregiver 4, mother of eighteen-year-old daughter with SBS: Risks and benefits of SBS treatment landscape in relation to devices

- Daughter lost most of her small intestine when she was four years old due to a volvulus; parents were told (“like many still are”) that she would likely only live for five more years because of the damage PN would do to her liver.
- Different devices: At different times and at different stages of development, the type of medical devices and care she has needed has changed. Lots of changes of devices and surgeries over the years. For example,
  - Initially, in hospital she had CVC, G-tube, and ostomy. The ostomy was taken down and she was discharged with a CVC and G-tube.
  - During young childhood, she came off PN twice, thus she had a CVC removed, a new one surgically placed, and then the new CVC removed. She retained the G-tube.
  - During young childhood, she had another ostomy placed and taken down.
  - At points during childhood and adolescence, she was able to maintain her weight and health with oral nutrition. However, she was not comfortable having the G-tube removed. Mom notes, “It had become part of her, and was often a way to give her fluids and keep her out of the hospital. Although she was good for the moment, this chronic illness fluctuates. And sure enough, her caloric need increased prior to puberty, and she began needing tube feeds again.”
  - At eighteen, she has another new CVC, a G-tube, and another ostomy.
  - Mom notes, “Currently there is discussion of an ostomy take down. However, she is fearful of doing that only to need it again. Each time these devices are needed, she has
to have surgery again. That brings a whole new set of risks and benefits as was discussed earlier.”

• Complications:
  o The G-tube
    ▪ Has to be changed out regularly. Can be done at home or in the hospital, depending on circumstances and type of tube. Complications can require painful dilation of the G-tube stoma and even surgical revision.
    ▪ Pain and discomfort from intolerance of formula
    ▪ Infections
  o All devices involved a lack of sleep: Mom says, “I don’t think I slept all night for years. The pumps beeped, diapers overflowed from the all-night fluids and there were lots of poop explosions.”
  o CVC: Painful weekly dressing changes
  o Ostomy: leakage
  o Shortages: Recent shortages have included tubing. They had to switch pumps to administer PN because they couldn’t get tubing for the one they had. The new tubing is thinner and has broken on different occasions, leaving her at risk for a bloodstream infection.

• Conclusion:
  o Devices improve quality of life, but no not offer a cure.
  o Mom says, “As a child, my daughter wanted her central line removed more than anything. She hated the painful dressing changes and limitations it placed on her. As a young adult who can feel and recognize the benefits of it—she is grateful for her central line. It keeps her from dehydrating and helps keep her heart rates and weight stable. The benefits far outweigh the risks…. These devices have saved her life and improved her quality of life, but they are sometimes difficult to deal with as well. My daughter says that with all the devices covering her from chest to pelvis, she often feels claustrophobic in her own body. But life without them would be so limiting, painful, and not much of a life at all.”

Patient 3, 62-year-old adult with SBS: Risks and benefits of SBS treatment landscape in relation to PN

• Background: Has been on PN for thirty-six years, after a volvulus cut off blood supply to her intestines. Was newly married, and concerned about how scars, tubing, ostomy, pump, etc. would affect her life. She just celebrated her 39th wedding anniversary.

• Innovation and research trials haves had positive impact on her quality of life. For example,
  o Portable pumps you can carry in a backpack
  o Lidocaine numbing ointment (for inserting needle into a port, for PN administration)
  o Early research trial of human growth hormone and food education allowed her to eat without getting sick, after nine years of not being able to eat anything by mouth without vomiting
  o Has been able to reduce PN calories and get one night off from PN per week, which has helped improve liver function and gives her one good night’s sleep per week, and, she adds, “what I call a mental health day!"
  o Premixed, shelf stable, PN
• Quality of life
  o Need to weigh risks vs benefits when choosing what is important or what activities are worth the risk, and how to minimize risk
  o Travels extensively
    o Lives in Florida and travels to Alaska for 3.5 months each year
      ▪ Needs to adhere to a time schedule and gradually adjust PN to accommodate for four-hour time change (to maintain glucose levels).
      ▪ Infuses on airplane, endures pat down by TSA with many medical supplies, pumps, backpack, and excessive fluids

• Daily challenges
  o Need to pace yourself
  o Fatigue; scheduled naps
  o Need to know where public bathrooms are at all times
  o Need to travel with CVC line repair kit, in case of emergency
    ▪ Hospitals don’t have repair kits for all CVCs
    ▪ Many ED doctors not familiar with long-term PN and don’t realize how important it is to salvage a line (vs pulling it) when possible, to preserve vascular access. Patient notes, “I fight for every line at this point in my PN journey, every remaining site is precious! ER docs are quick to want to pull my line when I have a fever and chills because it’s a quick fix for them, but I must refuse and fight with antibiotics... I don’t have the luxury to ‘pull every line’ at an ER doctor’s recommendation and I have a team of experts to help me.”
  o Must manage, organize, and order PN supplies, and anticipate problems
  o Shortages cause problems; recent shortage of tubing meant needing to learn how to operate a new pump

• Risk vs benefit: She has considered GLP-2, but says, “At this point of my journey, I feel the devil of PN I know is better than a devil I don’t know. Every therapy has its risks, and so far, PN has allowed me to have a good quality of life.”

• Continuing research and innovation: She says, “I have participated in various research studies to both help myself and those that must travel this life after me. I most recently tried infusing eleven hours during the day to see if better sleep would improve my quality of life .... I discovered that I was too active to haul around two liters of fluid during the day. Nights are better for me, but their data may help pave the way for those in the future [such as the children we’ve heard about today] .... Continued innovation gives us new options and opens up HOPE.”

Partner Advocacy Organizers
The Oley Foundation (www.oley.org) and the father of an SBS patient
This session is a result of collaboration within the SBS community.

FDA divisions represented
FDA staff from a total of 24 different offices from across 5 FDA Centers attended this session.

Office of the Commissioner (OC) – 4 offices
• OC/OCPP/PA – Office of Clinical Policy and Programs/Patient Affairs (organizer)
• OC/OCPP/OOPD – Office of Clinical Policy and Programs/Office of Orphan Products Development
• OC/OCPP/OPT – Office of Clinical Policy and Programs/Office of Pediatric Therapeutics
• OC/OCPP/OCiP – Office of Clinical Policy and Programs/Office of Clinical Policy

Center for Biologics Evaluation and Research (CBER) – 3 offices/divisions
• CBER/OCD – Office of the Center Director
• CBER/OD/PS - Office of the Center Director/Policy Staff
• CBER/OVRR/DVRPA/CRB2 - Office of Vaccines Research and Review/Division of Vaccines and Related Products Applications/Clinical Review Branch 2

Center for Drug Evaluation and Research (CDER) – 8 offices/divisions
• CDER/OCD/DSS - Office of the Center Director/ Drug Shortages Staff
• CDER/OND/OII/DG - Office of New Drugs/Office of Immunology & Inflammation/Division of Gastroenterology
• CDER/OND/OII/DPTI - Office of New Drugs/Office of Immunology and Inflammation/ Division of Pharmacology Toxicology for Immunology & Inflammation I
• CDER/OND/OII/DPTII - Office of New Drugs/Office of Immunology and Inflammation/ Division of Pharmacology Toxicology for Immunology & Inflammation II
• CDER/OND/ORDPURM/DRDMG - Office of New Drugs/Office of Rare Diseases, Pediatrics, Urology, & Reproductive Medicine/Division of Rare Diseases & Medical Genetics
• CDER/ORO/DROI - Office of New Drugs/Office of Regulatory Operations/Division of Regulatory Operations for Immunology & Inflammation
• CDER/OTS/OB/DBIII - Office of Translational Sciences/Office of Biostatistics/Division of Biometrics III
• CDER/OTS/OCP/DIIP - Office of Translational Sciences/Office of Clinical Pharmacology/Division of Inflammation & Immune Pharmacology

Center for Devices and Radiological Health (CDRH) – 8 offices/divisions
• CDRH/OPEQ/OHTI - Office of Product Evaluation and Quality/Office of Health Technology I
• CDRH/OPEQ/OHTI/DHTIB - Office of Product Evaluation and Quality/Office of Health Technology I/Division of Health Technology IB
• CDRH/OPEQ/OHTI/DHTIC - Office of Product Evaluation and Quality/Office of Health Technology I/ Division of Health Technology IC
Patients represented

Four parents who are, or have been, caregivers for their children with SBS and three adults with SBS participated in the Patient Listening Session. The children range in age from two to eighteen, and the adults include individuals who have had SBS since birth and another who has had SBS since she was in her twenties. All of the patients have significant experience with home parenteral nutrition.

Participants did not identify financial interests relevant to this meeting and are not receiving compensation for this listening session.

Disclaimer

Discussions in FDA Patient Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report reflects the Oley Foundation’s account of the perspectives of patients and caregivers who participated in the Patient Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of short bowel syndrome, health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire short bowel syndrome patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.