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Add-on to current guidelines for monitoring of SBS patients treated with teduglutide

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By inducing growth of the intestinal epithelium, the drug teduglutide, used for the treatment of short bowel syndrome-associated intestinal failure, could feasibly promote growth of pre-existing colonic neoplasms and incite the development of new ones. A baseline screen for colonic lesions and a 1-year follow-up have therefore been recommended, although an ongoing global prospective registry has, to date, shown no promotion of colonic neoplasms. Most recently, there have been reports of patients developing upper intestinal polyps while on the drug, including ones with malignant potential. To ensure patient safety, the Committee overseeing the global registry therefore recommends that monitoring strategies be updated to include screening for small intestinal lesions as well.

Short bowel syndrome (SBS) is a rare disease resulting from extensive intestinal resection. It is the leading cause of chronic intestinal failure (CIF), defined as "the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth"[1]. Home parenteral support (PS) is the standard treatment for SBS-CIF, but it can lead to several complications and can significantly impair patients' quality of life (QoL). The pharmacological management of SBS has recently changed with the advent of proadaptive factors, in particular gastrointestinal peptide hormones.

SBS-CIF management requires a multidisciplinary team in an expert center, with the aim to reduce PS dependence. Teduglutide, a glucagon-like peptide-2 analog, is approved for once-daily treatment of SBS patients (in adults and children ≥1 year old) by the U.S. Food and Drug Administration (FDA) and European Medicines Agency. Several clinical trials and real-life studies have shown the efficacy and safety of teduglutide in SBS-CIF, including an improved intestinal absorptive capacity and a reduction in PS volumes, allowing improving SBS patients' QoL[2–5]. Also, a recent meta-analysis has confirmed the efficacy of teduglutide on PS reduction and/or discontinuation in SBS adult patients, with a benefit increasing over time up to at least 1 year after treatment initiation[6]. Finally, according to the European Society of Clinical Nutrition and Metabolism (ESPEN) guidelines, teduglutide shall be the first choice for carefully selected SBS patients who are candidates for growth factor treatment[1].

Rationale for colonic screening

While the teduglutide Summary of Product Characteristics and package leaflet clearly define its benefits, contraindications, and target populations, its long-term risks remain under investigation. By inducing histological changes, including increased crypt depth, villus height, and plasma citrulline levels[2], it enhances intestinal absorption and promotes gut repair and growth, but in theory by doing so can feasibly promote the growth of pre-existing neoplasms or even incite the development of new ones. In a *post hoc* analysis of the STEPS studies, 18% of patients who received long-term teduglutide and underwent post-exposure colonoscopy had colonic polyps *versus* 12% at baseline, supporting recommendations for colonoscopic screening before teduglutide therapy and subsequent on-therapy colonoscopic monitoring[7]. Accordingly, the current ESPEN guidelines recommend a colonoscopy (if remnant colon and/or rectum is present), abdominal ultrasound, and gastroscopy when considering administration of intestinal growth factors in all patients before treatment initiation, to detect polyps and exclude neoplastic disease, as well as to clarify unclear anatomic situations (e.g. suspected strictures, blind loops, and unclear anastomotic sites) or disease activity in the gastrointestinal remnant (e.g.

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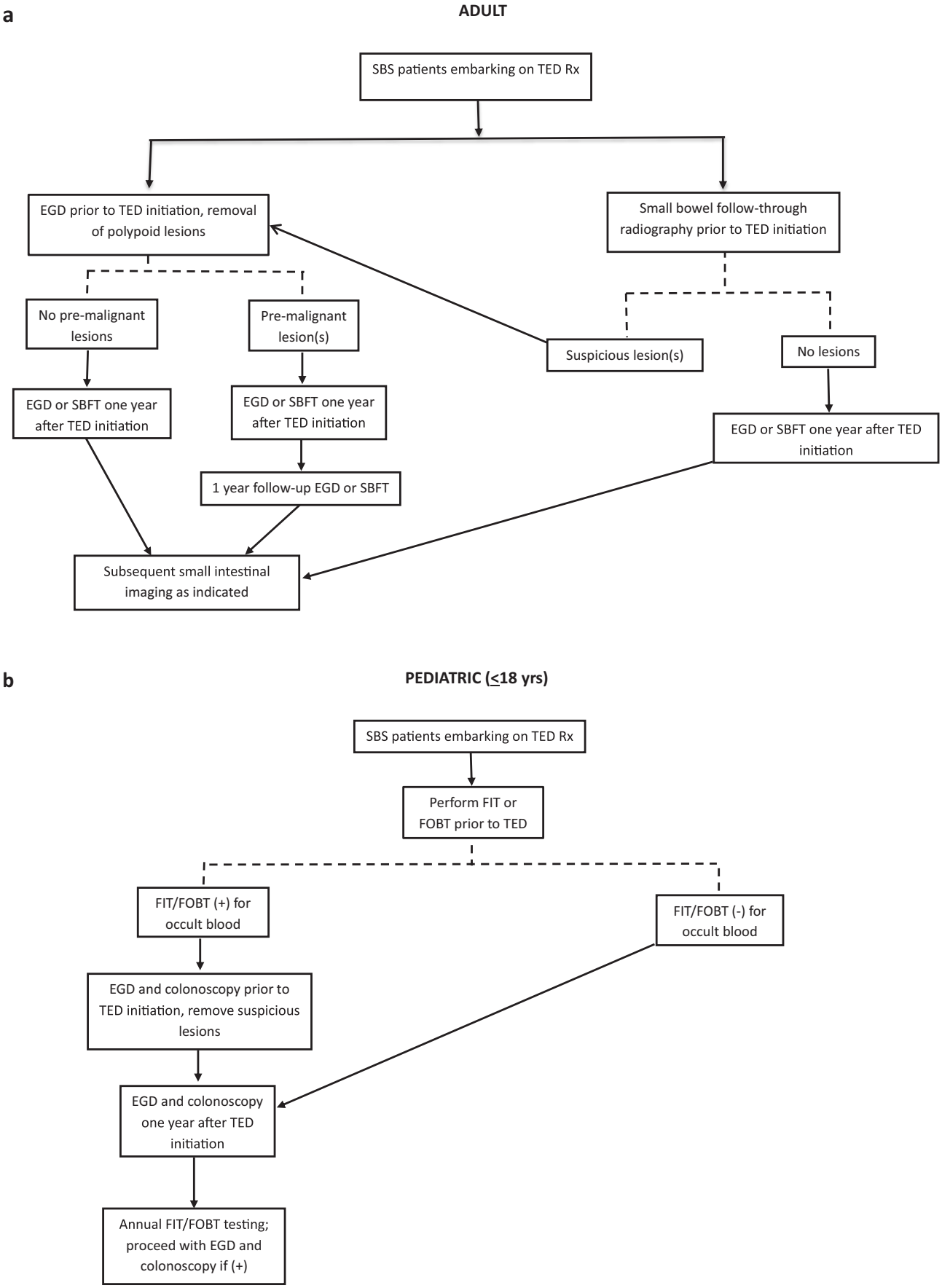

Fig. 1 | Recommended additions of small bowel screening and monitoring onto existing colon guidelines. a Adult. TED = teduglutide; SBFT = small bowel follow-through; EGD = upper endoscopy; solid arrow = proceed to next step; dotted line = possible outcome. **b** Pediatric (<18 yrs). FOBT = fecal occult blood test, FIT: fecal immunochemical blood test; EGD = upper endoscopy; TED = teduglutide; solid arrow = proceed to next step; dotted line = possible outcomes.

Crohn's disease)[1]. Moreover, the potential risks of neoplastic growth acceleration and colonic polyp growth enhancement could result in gastrointestinal obstruction, and biliary and pancreatic disorders among teduglutide-treated patients. To ensure that the benefits of teduglutide outweigh the potential risks, the FDA determined that a Risk Evaluation and Mitigation Strategy was necessary. Therefore, a global, prospective, observational, multi-center registry is ongoing to assess the long-term safety profile and clinical outcomes of SBS patients with a remnant colon treated with teduglutide, the detailed protocol of which is described in a recent publication[8]. To date, no carcinogenic effect has been associated with the use of teduglutide.

New concerns for small intestinal neoplasia

However, focusing concern solely on polyps of the colon may be shortsighted: isolated instances of de novo upper gastro-intestinal polyps have also been reported in the literature, including hamartomatous polyps in an adult, which are lesions not considered to be pre-malignant, as well as gastric foveolar hyperplastic polyps in two children and adenomas in a second adult (both of which do possess malignant potential)[9–11]. Perhaps of greater concern is a recent observational study that identified polypoid lesions, especially in the duodenum and jejunum, in 10 SBS patients treated with teduglutide for >1 year, detected by upper and/or lower intestinal endoscopy, highlighting the importance of performing regular gastrointestinal endoscopy for early detection of induced neoplasia in teduglutide-treated patients[12]. These ten polypoid lesions were identified 11–66 months after initiation of teduglutide; none of the ten presented any clinical signs or symptoms, and, very importantly, four were traditional adenomas containing low-grade dysplasia.

Recommendations

Based on the highlighted risks of upper gastrointestinal polyps, the SBS Registry Global Scientific Steering Committee--the members of which are the signatories of this letter--recommends that after considering the details of each adult patient's case, the clinician should choose to proceed with either an upper endoscopic exploration or comparable radiologic imaging both before and then one year after teduglutide initiation with removal of polypoid lesions, and thereafter as needed based on the findings (see Fig. 1a). This is in addition to the established guidelines for colonic screening. In choosing between an upper endoscopy and radiologic imaging, the clinician needs to bear in mind that a conventional upper endoscopy may not visualize the entire remnant small bowel, but a radiologic study may require a subsequent endoscopy. For pediatric patients (≤18 years of age), we recommend either a fecal immunochemical test (FIT) or fecal occult blood test (FOBT) before teduglutide initiation, followed by a colonoscopy and upper endoscopy if the occult blood testing is positive, a colonoscopy and upper endoscopy 1 year after initiation, and annual FIT/FOBT testing thereafter (Fig. 1b). Newer DNA-based fecal tests (e.g. Cologuard®) could feasibly be used instead of a FIT/FOBT, although, to date, the accuracy with which this newer molecular detection technique detects lesions in the small intestine has not been established.

Although our committee's function is not intended to establish policy, the abovementioned observations in conjunction with our collective experience and expertise motivate us to disseminate this information since it has potentially important ramifications for patient management. Dissemination to health care professionals and the public through regulatory agencies has only recently been initiated, and on a very limited basis: in September 2024, the U.S. Food and Drug Agency (FDA) approved updates to the United States Prescribing Information (USPI) to include information about the evaluation and testing prior to starting teduglutide (known as GATTEX in the U.S.) treatment, and additional monitoring during GATTEX treatment. (https://www.shirecontent.com/PI/PDFS/Gattex_USA_ENG.pdf) To our knowledge, comparable changes in prescribing information have not yet occurred in other countries. Since teduglutide is distributed globally, and since health professionals elsewhere, as well as in the U.S,. are often not aware of updates in the USPI, our intent with this communication is to effect a more widespread and prompt dissemination of these new insights in order to strive for the highest quality of health care and to ensure the welfare of patients using the drug.

Data availability

This document represents the opinions of the SBS Registry Global Scientific Steering Committee. These opinions are based on the clinical expertise of the Committee members in conjunction with the observations cited in the references section. No novel data generation or analysis was involved.

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References

1. Pironi, L. et al. ESPEN Guideline on Chronic Intestinal Failure In Adults - Update 2023. *Clin. Nutr.* **42**, 1940–2021 (2023).
2. Jeppesen, P. B. et al. Teduglutide reduces need for parenteral support among patients with short bowel syndrome with intestinal failure. *Gastroenterology* **143**, 1473–1481 (2012).
3. Schwartz, L. K. et al. Long-term teduglutide for the treatment of patients with intestinal failure associated with short bowel syndrome. *Clin. Transl. Gastroenterol.* **7**, e142 (2016).
4. Pevny, S. et al. Experience with teduglutide treatment for short bowel syndrome in clinical practice. *Clin. Nutr.* **38**, 1745–1755 (2019).
5. Joly, F. et al. Six-month outcomes of teduglutide treatment in adult patients with short bowel syndrome with chronic intestinal failure: A real-world French observational cohort study. *Clin. Nutr.* **39**, 2856–2862 (2020).
6. Bioletto, F. et al. Efficacy of teduglutide for parenteral support reduction in patients with short bowel syndrome: a systematic review and meta-analysis. *Nutrients* **14**, 796 (2022).
7. Armstrong, D. et al. Colon polyps in patients with short bowel syndrome before and after teduglutide: Post hoc analysis of the STEPS study series. *Clin. Nutr.* **39**, 1774–1777 (2020).
8. Gondolesi, G. E. et al. Baseline characteristics of adult patients treated and never treated with teduglutide in a multinational short bowel syndrome and intestinal failure registry. *Nutrients* **16**, 2513 (2024).
9. Ukleja, A., Alkhairi, B., Bejarano, P. & Podugu, A. De novo development of hamartomatous duodenal polyps in a patient with short bowel syndrome during teduglutide therapy: a case report. *JPEN J. Parenter. Enter. Nutr.* **42**, 658–660 (2018).
10. Pevny, S. et al. De novo development of distal jejunal and duodenal adenomas after 41 months of teduglutide treatment in a patient with short-bowel syndrome: a case report. *JPEN J. Parenter. Enter. Nutr.* **45**, 652–656 (2021).
11. Salazar, J. A. et al. Gastric Foveolar Hyperplastic Polyps in 2 children with short bowel syndrome on long-term teduglutide. *JPGN Rep.* **4**, e389 (2023).
12. de Dreuille, B. et al. Unexpected upper gastrointestinal polyps in patients with short bowel syndrome treated with teduglutide: need for close monitoring. *Am. J. Clin. Nutr.* **117**, 1143–1151 (2023).

Author contributions

A group discussion, including F.J., J.P.A., G.E.G., P.B.J., M.K-S., U.-F.P., L.P., L.K.S., and J.B.M., first determined the content of the perspective. F.J. constructed an initial draft of the perspective, and J.P.A., G.E.G., P.B.J., M.K.-S., U.-F.P., L.P., L.K.S., and J.B.M. provided suggested edits. J.B.M. created a revised draft that integrated the suggested edits. F.J., J.P.A., G.E.G., P.B.J., M.K.-S., U.-F.P., L.P., L.K.S., and J.B.M. have read and approved the final version.

Competing interests

Each of the listed authors receives financial compensation as members of the SBS Registry Global Scientific Steering Committee, as well as funding to support research expenses in their roles as site PIs in the SBS Global Survey.

Additional information

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