AHRQ Healthcare Horizon Scanning System – Potential High Impact Interventions Report

Priority Area 11: Peptic Ulcer Disease and Dyspepsia

Potential High Impact Interventions Report

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Statement of Funding and Purpose

This report incorporates data collected during implementation of the Agency for Healthcare Research and Quality (AHRQ) Healthcare Horizon Scanning System by ECRI Institute under contract to AHRQ, Rockville, MD (Contract No. HHSA29020100006C). The findings and conclusions in this document are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

This report's content should not be construed as either endorsements or rejections of specific interventions. As topics are entered into the System, individual Topic Profiles are developed for technologies and programs that appear to be closer to diffusion into practice in the United States. Drafts of those reports are sent to various experts with clinical, health systems, health administration, and/or research backgrounds for comment and opinions about potential for impact. The comments and opinions received are then considered and synthesized by ECRI Institute to identify those interventions that experts deem, through the comment process, to have potential for high impact. Please see the methods section for more details about this process. This report is produced twice annually, and topics included may change depending on expert comments received on interventions issued for comment during the preceding six months.

A representative from AHRQ served as a Contracting Officer's Technical Representative and provided input during the implementation of the horizon scanning system. AHRQ did not directly participate in the horizon scanning, assessing the leads for topics, or provide opinions regarding potential impact of interventions.

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None of the individuals compiling this information has any affiliations or financial involvement that conflicts with the material presented in this report.

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Preface

The purpose of the AHRQ Healthcare Horizon Scanning System is to conduct horizon scanning of emerging health care technologies and innovations to better inform patient-centered outcomes research investments at AHRQ through the Effective Health Care Program. The Healthcare Horizon Scanning System provides AHRQ a systematic process to identify and monitor target technologies and innovations in health care and to create an inventory of target technologies that have the highest potential for impact on clinical care, the health care system, patient outcomes, and costs. It will also be a tool for the public to identify and find information on new health care technologies and interventions. Any investigator or funder of research will be able to use the AHRQ Healthcare Horizon Scanning System to select potential topics for research.

The health care technologies and innovations of interest for horizon scanning are those that have yet to diffuse into or become part of established health care practice. These health care interventions are still in the early stages of development or adoption except in the case of new applications of already-diffused technologies. Consistent with the definitions of health care interventions provided by the Institute of Medicine and the Federal Coordinating Council for Comparative Effectiveness Research, AHRQ is interested in innovations in drugs and biologics, medical devices, screening and diagnostic tests, procedures, services and programs, and care delivery.

Horizon scanning involves two processes. The first is identifying and monitoring new and evolving health care interventions that are purported to or may hold potential to diagnose, treat, or otherwise manage a particular condition or to improve care delivery for a variety of conditions. The second is the analysis of the relevant health care context in which these new and evolving interventions exist to understand their potential impact on clinical care, the health care system, patient outcomes, and costs. It is NOT the goal of the AHRQ Healthcare Horizon Scanning System to make predictions on the future utilization and costs of any health care technology. Rather, the reports will help to inform and guide the planning and prioritization of research resources.

We welcome comments on this Potential High Impact report. Send comments by mail to the Task Order Officer named in this report to: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to effectivehealthcare@ahrq.hhs.gov.

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Table of Contents

Figures

Executive Summary

Background

Horizon scanning is an activity undertaken to identify technological and system innovations that could have important impacts or bring about paradigm shifts. In the health care sector, horizon scanning pertains to identification of new (and new uses of existing) pharmaceuticals, medical devices, diagnostic tests and procedures, therapeutic interventions, rehabilitative interventions, behavioral health interventions, and public health and health promotion activities. In early 2010, the Agency for Healthcare Research and Quality (AHRQ) identified the need to establish a national Healthcare Horizon Scanning System to generate information to inform comparative-effectiveness research investments by AHRQ and other interested entities. AHRQ makes those investments in 14 priority areas. For purposes of horizon scanning, AHRQ's interests are broad and encompass drugs, devices, procedures, treatments, screening and diagnostics, therapeutics, surgery, programs, and care delivery innovations that address unmet needs. Thus, we refer to topics identified and tracked in the AHRQ Healthcare Horizon Scanning System generically as "interventions." The AHRQ Healthcare Horizon Scanning System implementation of a systematic horizon scanning protocol (developed between September 1 and November 30, 2010) began on December 1, 2010. The system is intended to identify interventions that purport to address an unmet need and are up to 7 years out on the horizon and then to follow them for up to 2 years after initial entry into the health care system. Since that implementation, more than 7,000 leads about topics have resulted in identification and tracking of more than 900 topics across the 14 AHRQ priority areas.

Methods

As part of the Healthcare Horizon Scanning System activity, a report on interventions deemed as having potential for high impact on some aspect of health care or the health care system (e.g., patient outcomes, utilization, infrastructure, costs) is aggregated twice annually. Topics eligible for inclusion are those interventions expected to be within 0 to 4 years of potential diffusion (e.g., in phase III trials for pharmaceuticals or biotechnologies or in phase II or a trial with some preliminary efficacy data on the target population for devices and programs) in the United States or that have just begun diffusing and that have completed an expert feedback loop.

The determination of impact is made using a systematic process that involves compiling a profile on topics and issuing topic profile drafts to a small group of various experts (selected topic by topic) to gather their opinions and impressions about potential impact. Those impressions are used to determine potential impact. Information is compiled for expert comment on topics at a granular level (i.e., similar drugs in the same class are read separately), and then topics in the same class of a device, drug, or biologic are aggregated for discussion and impact assessment at a class level for this report. The process uses a topic-specific structured form with text boxes for comments and a scoring system (1 minimal to 4 high) for potential impact in seven parameters. Participants are required to respond to all parameters.

The scores and opinions are then synthesized to discern those topics deemed by experts to have potential for high impact in one or more of the parameters. Experts are drawn from an expanding database ECRI Institute maintains of approximately 350 experts nationwide who were invited and agreed to participate. The experts comprise a range of generalists and specialists in the health care sector whose experience reflects clinical practice, clinical research, health care delivery, health business, health technology assessment, or health facility administration perspectives. Each expert uses

the structured form to also disclose any potential intellectual or financial conflicts of interest (COI). Perspectives of an expert with a COI are balanced by perspectives of experts without COIs. No more than two experts with a possible COI are considered out of a total of the seven or eight experts who are sought to provide comment for each topic. Experts are identified in the system by the perspective they bring (e.g., clinical, research, health systems, health business, health administration, health policy).

The topics included in this report had scores *and/or* supporting rationales at or above the overall average for all topics in this priority area that received comments by experts. Of key importance is that topic scores alone are not the sole criterion for inclusion—experts' rationales are the main drivers for the high impact potential designation. We then associated topics that emerged as having potentially high impact with a further subcategorization of "lower," "moderate," or "higher" within the potential high impact range. As the Healthcare Horizon Scanning System grows in number of topics on which expert opinions are received, and as the development status of the interventions changes, the list of topics designated as potential high impact is expected to change over time. This report is being generated twice a year.

For additional details on methods, please refer to the full AHRQ Healthcare Horizon Scanning System Protocol and Operations Manual published on AHRQ's Effective Health Care Web site.

Results

The table below lists the four topics for which (1) preliminary phase III data for drugs or phase II data for procedures were available; (2) information was compiled by November 2011 in this priority area; *and* (3) we received six to eight sets of comments from experts. (A total of 15 topics in this priority area were being tracked in the system as of November 2011.) For purposes of the Potential High Impact Interventions Report, we aggregated related topics for summary and discussion (e.g., individual drugs into a class). We present two summaries of topics (indicated below with an asterisk) that emerged as potential high impact on the basis of experts' comments and their assessment of potential impact. The material on interventions in this Executive Summary and report is organized alphabetically. Readers are encouraged to read the detailed information on each intervention that follows the Executive Summary.

Priority Area 11: Peptic Ulcer Disease and Dyspepsia
1. *Helminthic therapy (pig whipworm) for treatment-resistant ulcerative colitis
2. Monoclonal antibody (vedolizumab) for treatment of moderate to severe inflammatory bowel disease
3. Rifaximin for treatment of nonconstipating irritable bowel syndrome
4. *Teduglutide (Gattex) for treatment of short bowel syndrome

Discussion

Compared with other priority areas, relatively few leads and topics have been identified in this priority area that meet inclusion criteria for the horizon scanning system and this report. Most research activity in this priority area is focusing on drugs and biologics for irritable bowel syndrome and inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis [UC]). Of the four topics experts provided comments on that are within 4 years of potential diffusion, two emerged as having the potential for high impact. One is notable for its novelty and ability to potentially address a serious unmet need for nonsurgical effective treatment for severe UC, the other for its potential to restore

bowel function in patients with short bowel syndrome, potentially improving quality of life and reducing cost and complications associated with parenteral nutrition (PN).

Helminthic Therapy

- **Key Facts**: Currently, there is no established "cure" for UC, a debilitating condition that can require surgery if it becomes severe and refractory to medical treatment. From 25% to 33% of patients with UC are reported to have an inadequate response to available medical therapy. For these patients, surgical colectomy is indicated. Patients sometimes also use alternative therapies. A biologic therapy, helminthic therapy (Trichuris Suis Ova [TSO] Suspension, Ovamed GmbH, Barsbuttel, Germany), is being used by some clinicians and patients as a nonsurgical therapeutic alternative for treatment-refractory UC. (The therapy has also recently been identified as being explored for other autoimmune diseases such as treatment-refractory multiple sclerosis, lupus, and rheumatoid arthritis.) The therapy involves self-infection with laboratory-grown parasitic worms (helminths), which are purported to counteract severe symptoms of the disease. The rationale for this treatment stems from the fact that inflammatory bowel diseases are rare in developing countries where helminths are common and the fact that people have altered immunologic responses in the gastrointestinal tract when infected with helminths. Reports from observational studies suggested that helminths might prevent or improve UC by inducing production of regulatory T cells and modulatory cytokines, which then reduce inflammation. The therapy has become available by mail order in the U.S. with a physician prescription. The U.S. Food and Drug Administration (FDA) recently issued guidance to its field district officers regarding helminthic therapy indicating that districts "may detain without physical examination all imported Trichuris suis ova (TSO); Pig Whipworm Eggs or Pig Whipworm Egg suspensions because these articles appear to be biological products for which a biologics license is not in effect under section 351 of the Public Health Service Act … ." It does not appear that the manufacturer intends to seek FDA regulatory approval for the therapy. Patients with severe UC report paying $300 to $4,700 for a 10-week dose of pig whipworms ordered from outside the U.S.
- **Key Expert Comments**: Overall, experts commenting on this topic were cautiously optimistic about the therapy's potential, based on preliminary data, although they noted the potential for high controversy and its potential to disrupt current care and cost models for UC treatment.
- **Potential for High Impact**: Moderately high

Teduglutide (Gattex) for Treatment of Short Bowel Syndrome

- **Key Facts**: Short bowel syndrome (SBS) encompasses a group of health problems, related to malnutrition, that occur in individuals who have lost at least half of their small intestines. Frequently SBS arises from the surgical removal of diseased portions of the bowel. A shortened bowel results in diarrhea, fatigue, abdominal pain, bloating, heartburn, and nutrient deficiencies. Treatment for severe SBS may involve oral rehydration solutions, intravenous nutrition delivery, and liquid food (PN) delivered through feeding tubes. An estimated 40,000 children and adults in the U.S. receive at-home intravenous nutritional support for SBS, based on data from the early 1990s, at a cost of more than $100,000 per patient per year. One study estimated that, in pediatric patients, the mean total cost of care per child with SBS over a 5-year period in the U.S. was $1.6 million. The estimated mortality rate in infants with SBS is 30%. Long-term PN can lead to serious side effects

such as liver damage, the risk of which increases the longer a patient is PN-dependent. No effective treatments are available to improve long-term nutritional absorption other than intestinal transplantation. Teduglutide (Gattex®, NPS Pharmaceuticals, Bedminster, NJ) is a subcutaneously administered glucagon-like peptide 2 analog, purported to induce repair and regeneration of the cells lining the intestine as well as increase nutrient absorption. In 2001, teduglutide received orphan drug designation for treatment of SBS. In August 2011, NPS began submitting data for a new drug application to FDA for the same indication and completed the submission in December. Reported results from small, clinical studies suggest that teduglutide reduces the need for PN in patients with SBS and is well tolerated.

- **Key Expert Comments**: Experts commenting on this drug believe that these reductions in PN could potentially improve health outcomes and quality of life as well as lower costs. However, three patients in a recent interim analysis were reported to have developed malignancies while enrolled in the study. Although two of the patients were smokers and presented with lung cancer, additional scrutiny regarding the safety of teduglutide is likely to be required going forward.
- **Potential for High Impact**: Moderately high

Peptic Ulcer Disease and Dyspepsia Interventions

Intervention

Helminthic therapy for treatment of ulcerative colitis

Currently, there is no established "cure" for ulcerative colitis (UC). From 25% to 33% of patients with UC fail to respond satisfactorily to available medical therapy. For these patients, surgical colectomy is indicated.[1] Helminthic therapy is intended to provide a nonsurgical therapeutic alternative for these treatment-refractory patients.

Helminthic therapy involves self-infection with parasitic worms (i.e., helminths), which are believed to counteract severe symptoms of the disease. The rationale for this treatment stems from the fact that inflammatory bowel diseases are rare in developing countries where helminths are common and the fact that people with helminths have an altered immunologic response to antigens.[2] Preclinical studies suggest that helminths prevent or improve UC by inducing production of regulatory T cells and modulatory cytokines, which then reduce inflammation.[3]

Trichuris Suis Ova (TSO) Suspension (Ovamed GmbH, Barsbuttel, Germany) contains microscopic porcine whipworm ova that have been grown in a laboratory.[3] According to the manufacturer, the suspension contains 500 ova per dose; it is packaged in a vial.[3] To administer the therapy, the patient mixes the ova with juice or an electrolyte drink and swallows the solution.[3] The company recommends a starting dose of 500 ova, taken orally once every 1 to 3 weeks, with titration to a 1,000 ova per dose if no response is seen after 8 weeks (four treatments).[3] The company notes that initial response may require several weeks and, because helminths are short-lived in humans, will require repeated dosing to maintain response.[3]

The TSO product is currently available and is shipped directly from the manufacturer to the patient. The company requires a letter from a physician and a statutory declaration from the importer stating that the worms are for personal use and constitute 3 or fewer months of treatment.[4] The company then directs patients to a Web site to order the product, at a cost of roughly $485 for three vials, plus shipping.[4] Patients with severe UC report paying $300 to $4,700 for a 10-week dose of pig whipworms ordered from outside the U.S.[5-7]

The U.S. Food and Drug Administration (FDA) has issued the following guidance to its field district officers regarding helminthic therapy:

> Districts may detain without physical examination all imported Trichuris suis ova (TSO); Pig Whipworm Eggs or Pig Whipworm Egg suspensions because these articles appear to be biological products for which a biologics license is not in effect under section 351 of the Public Health Service Act and thus appear to be new drugs under the meaning of section 201(p) of the FD&C Act without an effective new drug application approval, as required by section 505 of the FD&C Act. These unlicensed biological products appear to be offered for import for the treatment of Crohn's Disease and other inflammatory bowel diseases. [8]

It does not appear that the manufacturer intends to seek FDA regulatory approval for the therapy.

In a small study of four patients with UC who underwent a single dose (2,500 ova) of helminthic therapy, patients experienced an average reduction of the Clinical Colitis Activity Index to 57% of baseline, and no adverse events were seen during the 28-week followup period, the authors reported.[9] In a larger study of 54 patients with UC, patients improved in their Disease Activity Index scores, and again, no side effects were seen.[10]

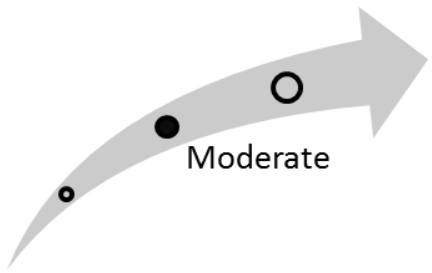
Clinical Pathway at Point of This Intervention

For patients with mild to moderate UC, treatment guidelines recommend the use of oral aminosalicylates, oral prednisone, topical agents (e.g., mesalamine, corticosteroids), and/or antiinflammatory treatments (sulfasalazine, olsalazine, mesalamine).[11] For patients with severe UC, or

UC that fails to respond to standard care, infliximab infusion is typically administered. Patients who experience toxicity require hospitalization and infusion of corticosteroids.[11] If the patient does not improve after 3 to 5 days, colectomy (i.e., surgical removal of the colon) can be necessary.[11]

Helminthic therapy is intended to be used in patients with treatment-resistant UC who have not undergone colectomy. However, in some clinical trials, patients who were given TSO also received concomitant corticosteroids in low to medium doses, and the manufacturer claims that this combination therapy was safe.[3] Therefore, helminthic therapy has the potential to either compete with or complement the use of antiinflammatory drugs, immunosuppressive drugs, and biological therapies that target the immune system, particularly in unresponsive patients. Helminthic therapy may also compete with over-the-counter drugs and herbal medications, which patients often seek out if standard treatment for UC fails to reduce their symptoms.[12]

Figure 1. Overall High Impact Potential: Helminthic therapy for treatment of ulcerative colitis (TSO)



Overall, experts were cautiously optimistic about TSO's potential to address the important unmet need of treatment-refractory UC. While the intervention has the potential to be highly controversial and markedly disruptive to current care and cost models, experts opined that more empirical data and patient education would be necessary before this intervention would become widely diffused for this indication. Based on this input, our overall assessment is that this intervention is in the moderate high potential impact range.

Results and Discussion of Comments

Seven experts, with clinical, research and health systems backgrounds, offered perspectives on this intervention.[13-19] While these experts agreed that the lack of curative or effective noninvasive therapies for UC represents an important unmet need, one expert with a research perspective was skeptical about the ability of helminthic therapy to meet this need, stating that lack of UC in underdeveloped countries (where helminths are common) was a "weak" correlation upon which to base a medical treatment. Furthermore, while some of the experts stated that the empirical data from clinical trials thus far has been promising, all commented on the small number of participants in these trials (n = 4 and n = 54). However, given that TSO can be obtained by mail order with a physician prescription, the incentive to perform trials may be lacking.

Experts with a clinical perspective believe that this therapy has a very high potential to disrupt current care models and the way patients with UC are treated, should the treatment be proven safe and effective and be adopted. Highlighted was TSO's potential for displacing currently available pharmacotherapy and surgery. Additional, less salient considerations included potential drug-drug interactions, the possibility of shortened hospital length-of-stay for UC exacerbations, and uncertainty about whether helminth-treated patients could become challenging colectomy candidates, should the surgery eventually be required.

Experts' opinions were divided in assessment of how TSO might affect the per-patient costs of treating UC. Some noted that this treatment is priced less expensively than some currently approved UC treatments (e.g., infusion therapy, surgery) and therefore has the potential to reduce costs associated with treatment; however, other experts stated that patients will pay for this treatment out of pocket, which would increase their financial burden.

All these experts agreed that helminthic therapy would be controversial and face barriers to clinical and patient acceptance. The first of four themes consistently addressed by the experts was that patients are likely to balk at the idea ingesting parasitic worms, and convincing patients to seek this therapy

will require thorough patient education practices. Second, because the ova are derived from pigs, many patients with religious or dietary restrictions might object to the treatment. Third, because of TSO's novelty and weak evidence base, clinicians might be reluctant to recommend this therapy until more data become available, particularly regarding the treatment's risk-benefit ratio. Finally, three clinical experts expressed concern about the potential for helminth "outbreaks" in both communities and livestock farms.

Despite these views, most of the experts commenting on this topic agreed that if this intervention were to become widely accepted, it has the potential to be easily integrated into current health care infrastructure models (because it is purchased and administered by the patient) and should not require any major training or learning curve on the part of the patient.

Intervention

Teduglutide (Gattex) for treatment of short bowel syndrome

Short bowel syndrome (SBS) encompasses a group of health problems related to malnutrition that occurs in individuals who have lost at least half of their small intestines. The primary cause of SBS is surgical removal of more than half of the small intestine because of disease, injury, or birth defects.[20] Approximately 70% of patients with Crohn's disease require at least one surgical procedure during their lifetimes to remove damaged intestine, leaving them at risk for complications such as SBS.[21] SBS can cause diarrhea, fatigue, abdominal pain, bloating, heartburn, and nutrient deficiencies.[20] An estimated 40,000 people in the United States receive at-home intravenous nutritional support for SBS based on data from the early 1990s, at a cost of more than $100,000 per patient per year.[22,23] One study estimated that, in pediatric patients, the mean total cost of care per child with SBS over a 5-year period was $1.6 million.[23] The estimated mortality rate in infants with SBS is 30%.[24] Long-term parenteral nutrition (PN) can lead to serious side effects such as liver damage, the risk of which increases the longer a patient is PN-dependent.[25] No effective long-term treatments are available to improve nutritional absorption other than intestinal transplant.

Teduglutide (Gattex®, NPS Pharmaceuticals, Bedminster, NJ) is intended to provide several critical actions throughout the gastrointestinal tract for the treatment of SBS, including suppressing gastric motility; stimulating intestinal nutrient transport, intestinal blood flow, and crypt cell proliferation; inhibiting crypt cell apoptosis (programmed cell death); and enhancing gut barrier function.[26] Teduglutide is a subcutaneously administered (0.05 mg/kg of body weight, per day) glucagon-like peptide 2 (GLP-2) analog, containing a single amino-acid substitution which is purported to render it resistant to dipeptidyl peptidase IV, thus significantly increasing the biologic half-life and activity of teduglutide.[21] As a GLP-2 agonist, teduglutide is purported to induce repair and regeneration of the cells lining the intestine as well as increase the size and density of intestinal villi in the intestinal epithelial layer, resulting in better absorption of nutrients.[21]

In 2001, NPS Pharmaceuticals received orphan drug designation for teduglutide for the treatment of SBS.[21] In August 2011, NPS began submitting data for a new drug application to FDA for the same indication and completed the submission in December.[21] Teduglutide is not approved for any indication by the FDA or European Medicines Agency.[21,27]

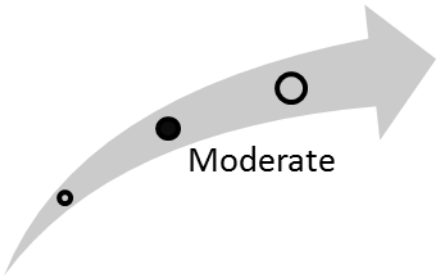
In results of a randomized, double blind, placebo-controlled, phase III trial, investigators reported that 63% of patients (n = 43) given teduglutide (subcutaneous injections 0.05 mg/kg, daily) responded to treatment (≥20% reduction from baseline in weekly PN and/or intravenous fluid volumes) versus 30% of patients (n = 43) given placebo (p = 0.002).[28] At week 24, patients who received teduglutide experienced an average 4.4 liter reduction in weekly parenteral support/PN (baseline 12.9 liters) compared with patients who received placebo, who experienced an average 2.3-liter reduction in fluids required (baseline of 13.2 liters; (p ≤0.001). After 24 weeks of treatment, 54% of patients treated with teduglutide were able to reduce the number of infusion days per week by 1 or more days, compared with 23% of patients treated with placebo (p = 0.005).[28] In a second study, an interim analysis of patients with SBS (n = 34) treated with either teduglutide or placebo for 12 months reported that 91% of patients given teduglutide were responders (achieved 20% to 100% reduction in PN and/or intravenous volume from baseline). Additionally, after 12 months of treatment with teduglutide, 53% of patients reduced their infusion days per week, and 24% of patients reduced their infusion days per week by 3 or more days. Three patients in the study were able to completely discontinue PN and/or intravenous fluids.[29] The mean reduction in the volume of PN and/or intravenous fluids was 5.2 liters per week from pretreatment baseline.[29] Nine subjects discontinued the trial because of adverse events. Additionally, three cases of cancer (a metastatic adenocarcinoma of probable gastrointestinal origin, nonsmall cell lung carcinoma, and squamous cell lung carcinoma) were observed during the study.

These malignancies have been reviewed by an independent safety review board and no changes to the study protocol have been requested.[29]

Clinical Pathway at Point of This Intervention

Mild SBS can be treated by eating small and frequent meals, taking nutritional supplements, and using medication to manage diarrhea. Moderate SBS may also require the use of intravenous electrolyte and fluid supplements. Severe SBS treatment may involve oral rehydration solutions, intravenous nutrition delivery, and liquid food delivered through feeding tubes. In very severe cases, intravenous nutrition can be required indefinitely.[20] In cases where there is an obstruction in the intestine or extreme shortening of the small intestine, surgical options can enhance the surface area of the intestines or lengthen the time food spends in the intestines, which increases the absorption of nutrients.[30] Recombinant human somatropin (Zorbtive®, EMD Serono, Inc., Rockland, MA) can also be used to increase absorption of nutrients; however, somatropin has not been evaluated in patients with SBS for longer than 4 weeks.[31] Patients with SBS who cannot be maintained on PN are potential candidates for intestine transplantation.[25]

Figure 2. Overall High Impact Potential: Teduglutide (Gattex) for treatment of short bowel syndrome



Teduglutide has been evaluated in only a small number of patients, yet most experts who commented were optimistic about its potential to reduce the frequency of administration of PN in patients with SBS. A reduction in PN might significantly improve patient outcomes and quality of life. It might also reduce the cost of home care and complications associated with PN. SBS affects a relatively small number of patients, but those with SBS are significantly affected and have few treatment options. However, teduglutide is unlikely to obviate completely the need for PN in most SBS patients. Based on this input, our overall assessment is that this intervention is in the moderate high potential impact range.

Results and Discussion of Comments

Seven experts, with clinical, research, and health systems backgrounds, offered comments on this intervention.[32-38] The experts noted that although SBS affects a small population of patients, treatments that can reduce the need for PN are important because of its impact on quality of life and its high costs. Overall, experts were optimistic regarding the ability of teduglutide reduce the need for PN and improve patient health outcomes; however, two experts representing a research perspective stated the need for larger studies, and one of these experts thought teduglutide should be evaluated in an active comparator trial against an agent such as somatropin, which is indicated to increase nutrient absorption in patients with SBS. One expert representing a research perspective stated that PN is difficult to administer to patients with poor access to care and thus daily self-administered injections of teduglutide could reduce health disparities.

Experts stated self-administered teduglutide might disrupt current models of patient management by reducing the frequency of homecare visits for PN and inpatient/outpatient admissions due to complications from PN therapy. However, because the population of patients is relatively small, there might not be a large impact to the health care system.

In general, the experts expected teduglutide to be widely accepted by clinicians if the drug continues to show favorable efficacy and tolerability, because of the limited options for SBS. The drug is also expected to be widely accepted by patients. Two experts representing a clinical perspective stated that patients with SBS are usually quite savvy regarding treatment options, and teduglutide might be viewed by patients as a treatment option that is safer and more effective than PN alone.

Additionally, patients might view teduglutide as potentially improving quality of life by providing more "freedom" in the form of reduced administration of PN. Some of the experts also stated that the reduction in PN due to teduglutide use might decrease costs, increasing acceptance from clinicians, patients, and third-party payers. However one expert representing a clinical perspective stated that pediatric patients might have difficulty with a treatment that requires self- (or parental-) injection.

Although teduglutide has been evaluated in only a small patient population, most of the reviewers were optimistic regarding the potential for teduglutide to reduce the need for PN, which could significantly improve patient outcomes and quality of life as well as reduce the cost of care for this condition by reducing home care and complications associated with PN. Although SBS is seen in only a small patient population, those with the disease are significantly affected and have few treatment options, and thus it would likely be welcomed. Additionally medical advances are now allowing children with conditions that put them at risk for SBS to lead longer lives, providing a greater need for improved long-term treatment options for SBS.

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