ABSTRACT

Objectives: Biologic therapy is commonly used to treat inflammatory bowel disease (IBD), but represents a significant cost in patient care. This pilot study analyzes the pharmacoeconomic benefit of utilizing a prescription oral medical food, serum-derived bovine immunoglobulin/protein isolate (SBI), for the management of IBD.

Study Design: Chart data from IBD patients who were administered SBI as part of an ongoing therapy (N = 21) were retrospectively collected from a gastrointestinal clinic.

Methods: Data regarding the management of IBD for the first 8 weeks in which patients used SBI were assessed and compared with the patients' history of current and past use of biologics. Literature-reported prices for biologics and SBI were applied to these data, and the potential total costs savings per patient over the 8 weeks of analysis were calculated.

Results: Seven patients had a history of primary or secondary nonresponsiveness to biologics and inadequate management with current therapeutic regimens, suggesting that they would likely have to begin another biologic therapy due to disease severity. Incorporation of SBI at 5 g/day resulted in better overall management of their disease, alleviating the cost of impending biologic therapy. The difference between patients' prior average 8-week biologic cost and the 8-week SBI cost equated to $5077 per nonresponder. This equated to $1692 per patient in the entire cohort.

Conclusions: Incorporation of SBI into the therapeutic regimen of this small cohort of IBD patients potentially correlates to a significant yearly savings, providing preliminary evidence for SBI as a cost-saving nutritive therapy to help manage IBD.


An estimated 1.8 million Americans are affected by inflammatory bowel disease (IBD),1 a chronic, lifelong illness that places medical and economic burdens on patients, their families, and the healthcare system. IBD is most commonly categorized as either Crohn’s disease (CD) or ulcerative colitis (UC). Many common IBD therapies are designed to target parts of the inflammatory response; these include aminosalicylates (5-ASAs), anti-inflammatory drugs (including locally acting and systemic steroids), immunomodulators, and biologic therapies.2 Antibiotics have also been employed for IBD treatment, particularly in CD. Other options for complicated cases or patients who do not respond to pharmaceutical therapy include surgery, particularly colectomy, bowel resections, strictureplasty, and abscess drainages.3 Treatment regimens for IBD represent a significant cost to US healthcare. Extrapolating from previous data, one recent study estimated that the total annual direct cost of UC and CD in the United States is at least $6.3 billion.4

The choice of a therapy for IBD can be challenging due to cycles of remission and relapse.4 The current primary goal of therapy for IBD is clinical remission, defined as a long period of time without symptoms or flares of disease, which ultimately improves the patient’s quality of life.5 This type of remission is often assessed through patient-reported outcomes. Historically, the severity of these symptoms dictates the patient’s therapeutic regimen; this is considered a “step up” or “bottom up” approach (Figure). Therapies like 5-ASAs and antibiotics are used to treat mild IBD, while immunomodulators and corticosteroids are employed for moderate conditions. Biologics and surgery are generally reserved for moderate to severe patients for whom less-aggressive treatments did not provide sufficient management. More recent approaches to IBD treatment, particularly in pediatrics, have described a “top down” method in which the order of therapy is reversed and biologics are administered early in disease in the attempt to prevent patients’ progression to severe disease.6 The “top down” approach involves longer administration of biologics, which can have both cost and safety implications, as discussed below.
The biologics category has seen significant development in recent years. The current biologics indicated for use in CD or UC are derivatives of antibodies and can be categorized by their binding properties. Anti-tumor necrosis factor alpha (TNF-alpha) therapies such as infliximab, adalimumab, golimumab, and certolizumab pegyl function by binding the proinflammatory cytokine TNF-alpha to dampen immune activation.\(^7\)\(^-\)\(^{10}\) Natalizumab and vedolizumab represent a newer class of anti-integrin biologic products that inhibit leukocyte recruitment to sites of inflammation.\(^11\)\(^-\)\(^{12}\) Both classes are recognized as effective therapies for moderate to severe cases of CD, UC, or both in patients with chronic, active disease with incomplete mucosal healing under conventional treatments.\(^7\)\(^-\)\(^{12}\) These provide a treatment option for patients with advanced disease who are refractory to aminosalicylates, antibiotics, steroids, and immunomodulators.

Despite the noted efficacy of biologics in treating IBD, there are challenges to this therapy option. Biologics have significant, low-frequency side effects that need to be noted when prescribed. These systemic therapies may reduce patients’ ability to fight off infection due to a dampening of the immune response. There have been reports of serious infections associated with infliximab, adalimumab, and certolizumab use, including tuberculosis and sepsis.\(^7\)\(^-\)\(^{10}\) Furthermore, biologics have been implicated as a risk factor for the development of blood disorders, lymphoma, and progressive multifocal leukoencephalopathy.\(^7\)\(^-\)\(^{12}\)

Therapeutic response and tolerability can also be challenges when treating IBD with biologics. It is believed that one-third of patients are refractory to anti–TNF-alpha therapy.\(^13\) Such patients are deemed primary nonresponders. Patients may also exhibit benefit from biologics initially, but then show recurrence of clinical symptoms due to loss of response or therapy intolerance. These types of patients are termed secondary nonresponders; it is estimated that up to 60% of patients in clinical practice who initially experience remission with anti–TNF-alpha biologics will fall into this category within a year of treatment.\(^14\) Interestingly, for both primary and secondary nonresponders, a common treatment strategy is to attempt biologic therapy again, especially with another anti–TNF-alpha agent.\(^15\)

Unfortunately, overall response and remission rates of primary nonresponders have been found to be lower when attempting the use of a second biologic agent.\(^13\) For secondary nonresponders, continuous biologic therapy may include escalation of dose or frequency, or switching to another class of biologics (ie, from anti–TNF-alpha to anti-integrin).\(^13\)

A third challenge to biological therapy is the cost. The direct price of these therapies is quite high, ranging from $25,000 to $60,000 per patient per year, according to wholesale reported costs and recommended dosing regimens.\(^7\)\(^-\)\(^{12}\) Agents such as infliximab and vedolizumab incur an additional charge of administering an intravenous infusion,\(^15\) further increasing the overall treatment cost. Furthermore, even though biologic therapy has been shown to be effective in improving the quality of life and reducing hospitalizations in patients with IBD who respond to the agents, this has not resulted in a decrease in the overall cost of managing IBD due to growing outpatient drug expenses.\(^16\) Thus, biologics significantly contribute to a substantial economic burden in patients with IBD.

There is still a need for a safe, cost-effective option that can reduce disease-related expenses and effectively manage IBD. Serum-derived bovine immunoglobulin/protein isolate (SBI) is a prescription medical food intended to meet the distinctive nutritional requirements unique to patients with intestinal disorders, particularly those who require management of chronic loose and frequent stools in such conditions as diarrhea-predominant irritable bowel syndrome (IBS-D), IBD, and enteropathy associated with HIV.\(^17\)\(^-\)\(^{19}\)

SBI was considered for therapy in patients with CD or UC in a private gastroenterology practice due to positive preclinical results,\(^20\)\(^-\)\(^{21}\) as well as findings from case studies of patients with IBD.\(^18\)\(^-\)\(^{22}\)\(^-\)\(^{24}\) This pilot retrospective analysis describes the estimated pharmacoeconomic impact of SBI on the biologic drug costs in a small group of patients with IBD.

**METHODS**

**Patients**

Patients in this analysis were from a single community-based gastroenterology practice near Orlando, Florida. Patients were prescribed SBI 5 g/day as a nutritional add-on therapy as part of their standard of care to manage chronic
loose and frequent stools associated with IBD. Patients who had used SBI for at least 8 weeks (N = 21) were included for analysis. This cohort was composed of patients with CD (n = 17) and UC (n = 4), ranging in age from 20 to 84 years (mean = 48; SD = 20.8), with 13 being male.

**Nutritional Standard of Care**

SBI is the nutritional ingredient in a prescription medical food (EnteraGam) intended to supply the distinctive nutritional requirements unique to the clinical dietary management of intestinal disorders, particularly in patients with chronic loose and frequent stools.25 As a medical food, SBI must be used under physician supervision.26 SBI is a specially formulated protein source (~92% protein) purified from United States Department of Agriculture (USDA)-approved food-grade plasma with >50% immunoglobulin (Ig) G; it also includes ~1% IgA, 5% IgM, and other proteins typically found in plasma and milk. SBI is generally recognized as safe (GRAS), a safety requirement for medical food products.26

**Chart Review**

A retrospective chart review examined information from patients who were diagnosed with IBD and who received SBI for at least 8 weeks. Patients’ medical history, disease symptoms and status, concurrent medications, and failed therapies were recorded. Their patterns in the use, avoidance, primary nonresponsiveness, and secondary nonresponsiveness of biologics were assessed. Patient-reported disease management from when they began SBI until at least 8 weeks after they had been on therapy was compared with their biologic history.

**Assessment of Cost Difference**

The costs associated with biologic prescriptions administered to patients who had a history of biologic unresponsiveness were determined using the average wholesale price listed on the Medi-Span drug database. The prescribing information for infliximab, adalimumab, and certolizumab pegol27,8,10 was used to determine the suggested dosing regimen for the products. Literature-reported values for the additional costs incurred by infusion visits ($226 per visit) for infliximab were also determined15 and then added to the direct cost.

Length of therapy for biologics was determined by the practice’s standard of care (SOC) or from prescribing information for the respective biologics. Specifically, length of therapy for patients with CD with primary nonresponsiveness were: infliximab, 14 weeks7; adalimumab, 12 weeks (SOC); and certolizumab pegol, 8 weeks (SOC). Length of therapy in patients with UC with primary nonresponsiveness were assumed to be as follows: infliximab, 20 weeks (SOC); and adalimumab, 8 weeks.8 For secondary nonresponders in both CD and UC for all biologics, length of therapy was estimated at 1 year based on patient charts. Price, dosing, and length of therapy were then employed to calculate the total cost associated with biologic use for each primary and secondary nonresponder, and total cost was divided by total weeks of biologic therapy to determine average biologic cost per week for each patient. The average weekly cost was compared with the average weekly cost of 8 weeks of SBI therapy, as determined from the 5-g daily dosing regimen used in the practice and the average wholesale price listed on the Medi-Span drug database. The total difference in the 8-week cost of biologics and SBI was used to find the average cost savings per patient in the group (n = 7) and as well as the entire cohort (N = 21).

**RESULTS**

A retrospective chart review was performed on patients with IBD who used SBI for at least 8 weeks as part of their therapy regimen (N = 21). The analysis for this duration of therapy was chosen based on end-of-study time points in clinical trials of SBI use in IBS-D17 and HIV populations,19 as well as other IBD case study information regarding patient responsiveness to SBI.18,22-24 Patients included in the analyzed cohort encompassed diagnoses of CD and UC (Table 1). Reviews of medical records of the examined
Pharmacoceconomic Analysis: Oral Immunoglobulins in IBD

patients revealed that before SBI incorporation, patients were not experiencing complete clinical management on standard therapies such as biologics, immunomodulators, immunosuppressants, antibiotics, and steroids for their symptoms. SBI was added to the therapy regimen of these patients for the purpose of achieving disease management.

For the scope of this review, patients were specifically assessed and categorized according to their history with systemic biologic therapy prior to use of SBI (Table 2). Of the 21 patients with IBD, 9 had no history of use of biologics prior to beginning SBI (Group A). Five were actively taking biologics, but were inadequately managed and still experiencing clinical symptoms (Group B). There were also 7 patients in the cohort who had been prescribed or recommended biologics, but had a primary nonresponse (n = 5) or developed a secondary nonresponse and became intolerant (n = 2) (Group C).

Since there is no gold standard for the measurement of IBD disease activity, and because formal scales do not necessarily afford practicability in a real-world setting, practicing physicians often evaluate remission based on the prevalence and severity of disease symptoms, systemic manifestations, and response to current therapies.27,28 Thus, in this practice patient-reported outcomes of disease management on current therapy regimens is a method used to assess disease activity.

Patients are asked to rate improvement in their disease as none, minimal, moderate, significant, or complete, and responses are noted in their charts. Recordings of patient-reported assessments and resulting physician evaluations of clinical remission were obtained for these groups of patients. Although patients in Group B cited chronic loose and frequent stools, abdominal pain, and gas prior to SBI incorporation, 4 out of 5 had self-reported moderate to significant management of IBD upon making the medical food part of their therapy. Patients in Group C also had ongoing incomplete responses to traditional therapies, including biologics, and reported experiencing chronic loose and frequent stools, bloating, distension, and rectal bleeding. However, after incorporation of SBI into the therapy regimens of these patients, 5 of 7 had moderate to significant disease management according to physician and patient evaluation of clinical remission. Group C patient histories and their responses to SBI are shown in Table 3.

Whereas the patients in Group C were not actively taking biologics, they were not being completely managed on their current therapies at the beginning of the analysis, indicating biologic intervention may have eventually been necessary. Specifically, this would likely have included a second attempt at biologic therapy for the patients experiencing a primary nonresponse and possibly a different type of biologic therapy and/or increased dose for those who had developed intolerance in the form of a secondary nonresponse. However, because Group C patients had good clinical management throughout the 8 weeks following incorporation of SBI, these patients did not require biologic use during this time.

To determine the pharmacoeconomic impact of SBI use in these patients, their previous treatments were used to estimate the average historical biologic cost for 8 weeks and then were compared with the cost of SBI administered 5 g/day for 8 weeks (Table 4). In both primary and secondary nonresponders (Group C), the $848 spent on 8 weeks of SBI therapy was at least $4000 less than the amount patients historically spent on biologic therapy. When the per-patient cost differences were averaged across the primary and secondary nonresponders, estimated savings afforded by SBI during the time of analysis totaled $5077. In considering the savings across the entire cohort of IBD patients (Groups A, B, and C) the average was $1692 per patient during the 8-week period.

DISCUSSION

IBD creates a significant pharmacoeconomic burden on US healthcare. The cost of pharmaceuticals and management of associated adverse events (AEs) greatly impacts the expense accompanying these diseases. For patients on biologic therapy, regular maintenance dosing is recommended because this method of administration is less

<table>
<thead>
<tr>
<th>Table 1. Demographics of Analyzed Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>Diagnosis: n (%)</td>
</tr>
<tr>
<td>CD</td>
</tr>
<tr>
<td>UC</td>
</tr>
<tr>
<td>Male: n (%)</td>
</tr>
<tr>
<td>Age in years: mean (SD)</td>
</tr>
<tr>
<td>Senior (≥65 years) age group: n (%)</td>
</tr>
</tbody>
</table>

CD indicates Crohn’s disease; UC, ulcerative colitis.

<table>
<thead>
<tr>
<th>Table 2. History of Biologic Use Prior to Beginning SBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>A</td>
</tr>
<tr>
<td>B</td>
</tr>
<tr>
<td>C</td>
</tr>
<tr>
<td>Total:</td>
</tr>
</tbody>
</table>

SBI indicates serum-derived bovine immunoglobulin/protein isolate.
immunogenic than episodic therapy.27,28 The cost of regular maintenance therapy can be quite significant, as demonstrated in the total historical cost of biologic therapies in this analysis. New, safe, efficacious, and cost-effective therapies are needed for the management of IBD to counter this increased expense. SBI, a specially formulated nutritional ingredient, is GRAS, which is an FDA requirement for medical foods. This indicates that SBI has the same safety of food that is commercially available.

SBI has also been tested for efficacy in both pre-clinical models and human case studies of IBD. In an multi-drug resistant protein 1 knockout (mdr1a/-) mouse model of spontaneous colitis, SBI attenuated an increase in colon crypt permeability and reduction of E-cadherin, changes that are characteristic of inflammation in this model.21 SBI also led to statistically significant improvements in colonic markers of inflammation, such as percentage of regulatory T-lymphocytes and expression of IL-17, IL-6, MIP-1beta, and IFN-gamma. In addition, TNF-alpha, IFN-gamma, and inducible nitric oxide synthase (iNOS) expression trended lower in this model. SBI was also tested in another animal model of colitis.20 Altered Schaedler flora mice, when exposed to oral dextran sodium sulfate and a human E. coli LF82 provocateur associated with Crohn's disease, develop colitis and altered morphology in cecum and colon tissue. Oral SBI attenuated inflammation by helping to maintain normal colon mucosal height and cecum tissue structure, as well as by preventing cecum stromal collapse in this model.20

Clinically, SBI has been shown to manage IBD in other retrospective case studies.19,22–24 In a review of 45 patients with IBD (CD, n = 38; UC, n = 7) who were not fully controlled on traditional therapies, SBI was able to provide further management of overall patient health when added to patients' therapy regimen. Specifically, patients were 2.8-times more likely to report condition management after 12 weeks of SBI therapy.18 Another review of 4 patients with CD and 3 patients with UC who were struggling with clinical remission despite traditional treatments reported that the addition of SBI as nutritional support to their current therapy regimens afforded benefit in regard to ileostomy output, stool frequency and consistency, abdominal discomfort, rectal bleeding, biologic dose, and steroid use.25

In addition to improvements in clinical endpoints, 2 recent reports have shown that adding SBI to ongoing therapy regimens leads to normal-appearing colonic tissue in patients with refractory UC.22,24 For a patient with UC who refused biologic therapy after treatment of septic arthritis due to infection during a surgical procedure, SBI administration reduced watery, bloody stools from 10-15 per day to normal stool frequency and consistency with no reported bleeding.22 The patient was also able to taper

Table 3. Summary of Patients in Group C

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Gender, Age in Years</th>
<th>Diagnosis</th>
<th>Biologic History</th>
<th>Therapeutic History Before SBI</th>
<th>Outcome After SBI Incorporation</th>
<th>Patient-reported Disease Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female, 20 CD NR IFX; NR ADA; NR CTZ</td>
<td>MTX sensitivity leading to restricted management options</td>
<td>Overall improvement when added to regimen of rifaximin and probiotic formulation</td>
<td>Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Male, 48 UC NR IFX; NR ADA</td>
<td>Oral 5-ASA and 5-ASA/NAC enemas, but still experiencing high frequency of bowel movements</td>
<td>Reduction in bowel movements; decline beginning vedolizumab because of adequate symptom management</td>
<td>Significant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Male, 21 UC NR IFX</td>
<td>Steroids and 5-ASA but reporting nocturnal diarrhea and rectal bleeding; recommendation of biologic therapy</td>
<td>Successful taper of steroids, no nocturnal symptoms, less rectal bleeding. No longer considered biologic candidate</td>
<td>Minimal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Male, 84 CD NR ADA</td>
<td>Steroids and rifaximin, but experiencing disease flares and malnutrition</td>
<td>Overall improvement</td>
<td>Complete</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Male, 25 CD NR ADA; LR IFX</td>
<td>Minimally symptomatic but experiencing tachyphylaxis with IFX; 5-ASA being used as adjunctive therapy</td>
<td>Incorporated with rifaximin and probiotic formulation; reduction in bloating, gas, distension, and stool frequency</td>
<td>Significant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Male, 36 CD IFX intolerance; CTZ intolerance</td>
<td>Intolerant to rifabutin, biaxin, and mycobutin; partially controlled with steroids</td>
<td>Improvement in chronic loose and frequent stools</td>
<td>Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Male, 35 CD IFX intolerance</td>
<td>Complications from immunomodulatory products; primary therapy rifaximin</td>
<td>Little clinical improvement</td>
<td>Minimal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5-ASA indicates aminosalicylate; ADA, adalimumab; CD, Crohn's disease; CTZ, certolizumab pegol; IFX, infliximab; LR, losing response; MTX, methotrexate; NAC, N-acetylcysteine; NR, nonresponsive; SBI, serum-derived bovine immunoglobulin/protein isolate; UC, ulcerative colitis.
prednisone from 40 to 5 mg/day and experienced complete clinical management. A repeat colonoscopy demonstrated normal mucosal tissue after SBI administration (a Mayo UC score of 2 before SBI was reduced to 0 after SBI).

Another patient with UC incorporated SBI into his therapy regimen after prolonged attempts to gain control of loose watery stools and cramping on a regimen of biologics, steroids, and 5-ASAs. SBI afforded reduction in stool frequency and significant management of chronic loose and frequent stools (1-2 normally formed stools/day) and no other symptomatology over the course of 8 weeks. The patient was removed from oral steroids after 16 weeks. A follow-up colonoscopy after approximately 1 year of SBI, adalimumab, and oral mesalamine showed normal-appearing colonic tissue and no sign of active disease. Although not yet observed in a well-controlled clinical trial, these clinical and endoscopic findings served as the basis for utilization of SBI as standard of care in the IBD population analyzed herein.

The proteins found in SBI are hypothesized to have a multifaceted mode of action that is facilitated by the high immunoglobulin content of the product. As with the immunoglobulin-like proteins found in biologics, the immunoglobulins in SBI are thought to function through their binding properties. Each lot of SBI is derived from the USDA-approved food-grade plasma of more than 3000 bovine donors, creating a polyclonal pool of immunoglobulins that has been shown to bind to a variety of microbial components. The ability of oral SBI to bind these microbial components (ie, lipopolysaccharide, flagellin, etc) results in a downstream maintenance of immune balance in the gut through steric and immune exclusion of these antigens from the gut-associated lymphoid tissue. Another postulated downstream effect of SBI binding to and excluding luminal antigens from the lamina propria is management of gut barrier function, with resulting improvement in tight junction protein expression. Overall, by acting to reestablish homeostasis in the gut, the immunoglobulins and other proteins in SBI are believed to improve nutrient utilization.

In addition to lower cost, SBI also has a lower AE profile compared with biologics. The reported AEs for SBI in clinical trials (2%-5%) included mild nausea, constipation, stomach cramps, headache, and increased urination. SBI is not absorbed systemically as intact protein and thus does not travel through the circulatory or hepatic systems. This reduces the likelihood of AEs associated with long-term use. Furthermore, SBI does not directly dampen the normal systemic immune response and thus, unlike biologics, does not increase susceptibility to infection or cause other serious complications. Patients in this practice reported SBI use for up to 28 weeks with no AEs. The product has been used safely for up to 48 weeks in clinical studies. SBI has also been shown to be well-tolerated for a duration of up to 8 months in fragile patient populations, such as adults with HIV and infants aged as young as 6 months.

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Gender, Age in Years</th>
<th>Diagnosis</th>
<th>Biologic</th>
<th>Response</th>
<th>Total Cost/ Patient</th>
<th>Average 8-week Cost</th>
<th>Difference Between Cost of SBI* and Biologic*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female, 20</td>
<td>CD</td>
<td>IFX</td>
<td>NR</td>
<td>$31,766</td>
<td>$7474</td>
<td>$6626</td>
</tr>
<tr>
<td>2</td>
<td>Male, 48</td>
<td>UC</td>
<td>ADA</td>
<td>NR</td>
<td>$22,931</td>
<td>$6115</td>
<td>$5267</td>
</tr>
<tr>
<td>3</td>
<td>Male, 21</td>
<td>UC</td>
<td>IFX</td>
<td>NR</td>
<td>$15,065</td>
<td>$5478</td>
<td>$4630</td>
</tr>
<tr>
<td>4</td>
<td>Male, 84</td>
<td>CD</td>
<td>ADA</td>
<td>NR</td>
<td>$9614</td>
<td>$6409</td>
<td>$5561</td>
</tr>
<tr>
<td>5</td>
<td>Male, 25</td>
<td>CD</td>
<td>ADA</td>
<td>LR</td>
<td>$27,692</td>
<td>$5538</td>
<td>$4690</td>
</tr>
<tr>
<td>6</td>
<td>Male, 36</td>
<td>CD</td>
<td>CTZ</td>
<td>INT</td>
<td>$37,857</td>
<td>$5827</td>
<td>$4979</td>
</tr>
<tr>
<td>7</td>
<td>Male, 35</td>
<td>CD</td>
<td>IFX</td>
<td>INT</td>
<td>$30,130</td>
<td>$4635</td>
<td>$3787</td>
</tr>
</tbody>
</table>

Total: $35,540
Average Group C: $5077
Average Entire Cohort: $1692

ADA indicated adalimumab; CD, Crohn’s disease; CTZ, certolizumab pegol; IFX, infliximab; INT, intolerant; LR, losing response; NR, nonresponsive; SBI, serum-derived bovine immunoglobulin/protein isolate; UC, ulcerative colitis.

*Average 8-week cost of SBI = $848. Other costs determined as described in Methods.
Patients in this analysis had diverse backgrounds and used multiple agents to treat their disease. Although the group was small, the patients’ demographics and therapeutic history were representative of a real-world population of patients with IBD. Incorporation of SBI into the therapeutic regimen in this small cohort of patients with moderate to severe IBD resulted in better overall disease management, as indicated by both patient-reported outcomes and clinician assessments. In the subset of patients who were primary and secondary nonresponders to biologics, patients were able obtain an additional cost benefit from SBI use. This correlated to a net 8-week cost savings of $1692 per patient across the entire cohort. If projected on an annual basis, cost savings could amount to $10,998 per patient across the entire group or $33,003 per patient if considering just primary and secondary nonresponders. To assess SBI’s longer-term impact, dose-range studies are planned to determine if the savings demonstrated in this study can be replicated in a larger group.

It is important to note that the patients in this study were maintained on a low dose of 5 g/day. The recommended dosing strategy is 5 g twice daily for the first 2 weeks, with an optional taper to once daily thereafter, based on clinical reports in patients with IBS-D 17 or IBD. 23 A higher dose—up to 20 g/day—may help manage a larger number of patients with IBD, as found recently in several very seriously ill patients who experienced excellent outcomes when SBI was used with 5-ASAs, immunomodulators, and short-course steroids. 22,24 Thus, the patients in this analysis may have had an even stronger response to SBI if a modified dosing strategy was used. Furthermore, patients not having a response or experiencing flares of disease after the 8 weeks of analysis could have been increased to additional doses of SBI to maintain the clinical management observed during the assessed time frame. Even with increased dosing to 20 g/day, the 8-week cost of SBI ($3392) would still be less than the 8-week cost of biologics (Table 4).

Limitations

Despite the potential economic benefits in broad areas, this analysis only takes into account the direct costs of biologics. We did not discuss the costs of other medications, including immunomodulators, and other direct medical costs, such as decreased hospitalizations and costs associated with managing serious AEs. Also, we did not consider increases in productivity or indirect cost benefits from improvements in overall quality of life. Prevention of surgery has been reported as an outcome of SBI use in patients with UC, 22 further illustrating its potential pharmacoeconomic benefit. Future analysis of SBI-mediated management of IBD, quality of life, productivity, and surgery prevention would provide a better estimate of the overall SBI-mediated savings in this population.

Other limitations of this study include the size of the analyzed cohort, lack of an optimized dose, and the duration of analysis. A larger national patient cohort and a longer study period in which the broad spectrum of costs are accounted for would be beneficial to get a more accurate assessment of the long-term pharmacoeconomic benefit of SBI in this patient population.

CONCLUSIONS

This pilot analysis offers a real-world example of the potential savings related to the use of SBI for the nutritional management of IBD, and it demonstrates that more pharmacoeconomic investigation regarding SBI use is merited. This pilot study provides the first evidence that SBI is a cost-saving, nutritive therapy to help manage IBD, showing that in this small cohort, it potentially afforded an overall reduction of $1692 per patient across 8 weeks. Furthermore, it supports previous reports suggesting that SBI should be considered for disease management in patients who do not respond fully to or refuse the use of biologics.

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Authorship Information: Concept and design (GLK, BPP); acquisition of data (HEY); analysis and interpretation of data (HEY, DW, BPP, GLK); drafting of the manuscript (HEY); critical revision of the manuscript for important intellectual content (GLK, BPP); statistical analysis (DW); provision of patients or study materials (IS, PB).

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