

holigos[®]

MICROBIOME HEALTH

The Tolerability and Efficacy of Holigos[®] IBS Restore for Managing Irritable Bowel Syndrome

A Healthcare Professional
White Paper

A clinical trial presented at the 2019
American College of Gastroenterology
Annual Scientific Meeting

Holigos[®] IBS Restore Clinical Trial Overview

The gut microbiome is essential to the health of the GI tract. Some patients with irritable bowel syndrome (IBS) are known to have an abnormal microbiota composition. However, modulating the microbiota composition in a targeted, specific manner to improve symptoms is a challenge.

Holigos[®] IBS Restore is a proprietary formulation of glycans with specific structures that allow only certain beneficial bacteria (e.g., bifidobacteria) to digest them. Holigos[®] IBS Restore has been shown in previous studies to beneficially alter the composition and function of the gut microbiome. The objective of this trial was to determine whether administering once-daily Holigos[®] IBS Restore would improve the symptoms of IBS.

This trial demonstrated that Holigos[®] IBS Restore significantly benefited all IBS subtypes across multiple key endpoints:

- Changed IBS symptom severity from severe to mild
- Decreased the number of abnormal stools by 37% from baseline
- Increased the percentage of normal stools by 4.6-fold from a baseline of 9%
- Clinically significant improvement in IBS-SSS scores in over 86% of patients
- Decreased abdominal pain severity by 59%
- Reduced days with abdominal pain by over 58%
- Decreased bloating by 59%
- Increased quality-of-life scores by 48%

Holigos[®] IBS Restore is safe and well-tolerated

- 96% of patients considered Holigos[®] IBS Restore as tolerable, well-tolerable, or extremely well-tolerable
- Common side effects included mild local reactions in the gut, such as abdominal pain, distension, and flatulence

To learn more about Holigos[®] IBS Restore, please visit www.holigosibshcp.com.

Introduction

A balanced microbiome plays an essential role in the health of the GI tract.^{1,2} It supports the integrity of the intestinal barrier, maintains normal mucosal immune function, regulates gut motility, and modulates gut-brain signaling.³⁻⁵ At least a subset of patients with irritable bowel syndrome (IBS) has an abnormal microbiota composition.⁶ In particular, patients with IBS have lower bifidobacteria counts in the gut than those of healthy subjects.⁶ Increasing the bifidobacteria levels in the gut of patients with IBS is associated with improvement of IBS symptoms, including abdominal pain.⁶⁻⁸

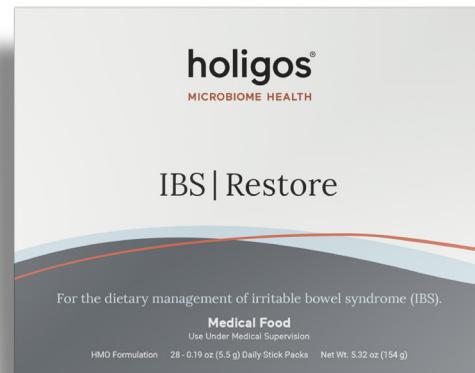
Holigos[®] IBS Restore is a proprietary formulation of glycans with specific structures that are identical to those found in human secretions, such as mother's milk (human milk oligosaccharides, or HMOs) and mucous, making them a key contributor to human health.⁹ In the gut, their specific structures mean that only certain beneficial bacteria (e.g., bifidobacteria) are able to digest them.¹⁰ Consequently, they have a very specific beneficial impact on the composition and function of the microbiota.

A prior study showed that Holigos[®] IBS Restore was both safe and well-tolerated in patients with IBS and can beneficially alter the composition and function of the gut microbiome, which includes increasing bifidobacteria populations.¹¹⁻¹³ Based on the outcomes of this study, we hypothesized that Holigos[®] IBS Restore may help manage symptoms in patients with IBS.

Trial Design

Holigos[®] IBS Restore was studied in a 12-week, multi-center, open-label trial in patients with IBS. The overall objective was to assess the potential for Holigos[®] IBS Restore to induce and support normal bowel habits and help manage symptoms of IBS.¹⁴

Holigos® IBS Restore is a medical food that is specifically formulated to provide nutritional support for IBS patients and help restore gut homeostasis.



Dosing

- Patients completing the trial took Holigos® IBS Restore (5 g) once daily for 12 weeks¹⁵
- Holigos® IBS Restore is a neutral powder that is provided in a carton box of 28 single-dose packets
- Holigos® IBS Restore is a proprietary formulation of 2 HMOs: 2'-FL (2'-fucosyllactose) and LNnT (lacto-N-neotetraose)¹⁵
- Holigos® IBS Restore does NOT contain gluten, added colors or flavors, or yeast¹¹
- Holigos® IBS Restore has little to no taste. It may be mixed with a drink, meal, or snack, and contains about 12 calories per dose¹¹

Food allergies and intolerances¹¹

- **Allergens:** Holigos® IBS Restore does not contain soy, peanuts, tree nuts, wheat, eggs, fish, shellfish, or gluten
- **Lactose intolerance:** Holigos® IBS Restore is suitable for consumption by people who are lactose intolerant due to the very small amount of lactose being ordinarily too low to trigger any symptoms of lactose intolerance
- **Milk protein:** Holigos® IBS Restore may contain traces of milk protein

Outcome Measures¹⁵

Primary outcome

Effect on stool consistency (Bristol type)

Key secondary outcomes

- Change in irritable bowel severity scoring system (IBS-SSS*) total score
- Change in IBS-SSS abdominal pain severity
- Change in number of days with abdominal pain
- Change in IBS abdominal distension severity
- Change in health-related quality of life (IBS-QOL†)

All results are based on the intention-to-treat population.

*The IBS-SSS assesses symptom severity by measuring abdominal pain intensity and frequency, abdominal distension, dissatisfaction with bowel habits, and life interference of IBS during the preceding 10 days. The total IBS-SSS score ranges between 0 and 500; a higher score indicates more severe symptoms.¹⁶

†The IBS-QOL is a self-reported quality-of-life measure specific to IBS that is used to assess the impact of IBS and its management.¹⁷

Results

Three hundred seventeen (317) patients were supplied with Holigos® IBS Restore (intention-to-treat, ITT) and 273 patients completed the study. In the ITT population, the predominant subtypes were: IBS-C (constipation), 42.9%; IBS-D (diarrhea), 26.7%; and IBS-M (mixed), 30.0%. Seventy-one percent (71%) of the ITT population was female, with a mean age of 44 years (range 18–93 years).¹⁵

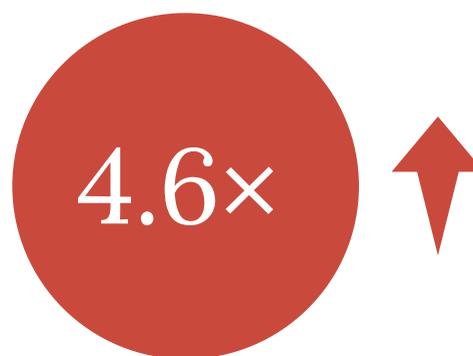
All IBS subtypes experienced similar efficacy outcomes.¹⁵

All efficacy results were seen by Week 4, the first measured timepoint.¹⁵

Primary outcome

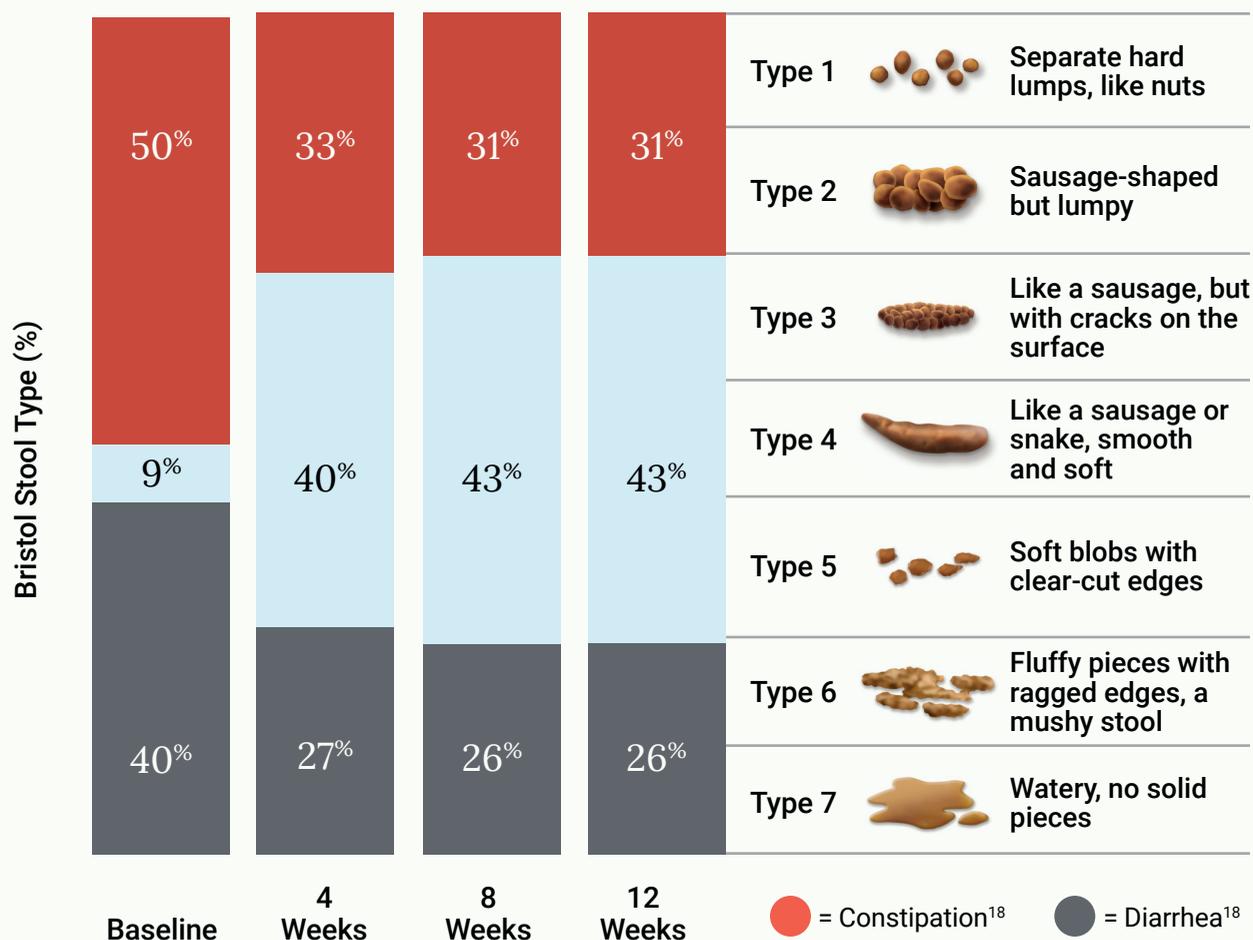


Holigos® IBS Restore significantly decreased the number of abnormal stools by 37% from baseline in all IBS subtypes.¹⁵



Holigos® IBS Restore increased the percentage of normal stools by 4.6-fold from a baseline of 9%.¹⁵

Change in Bristol Stool Type

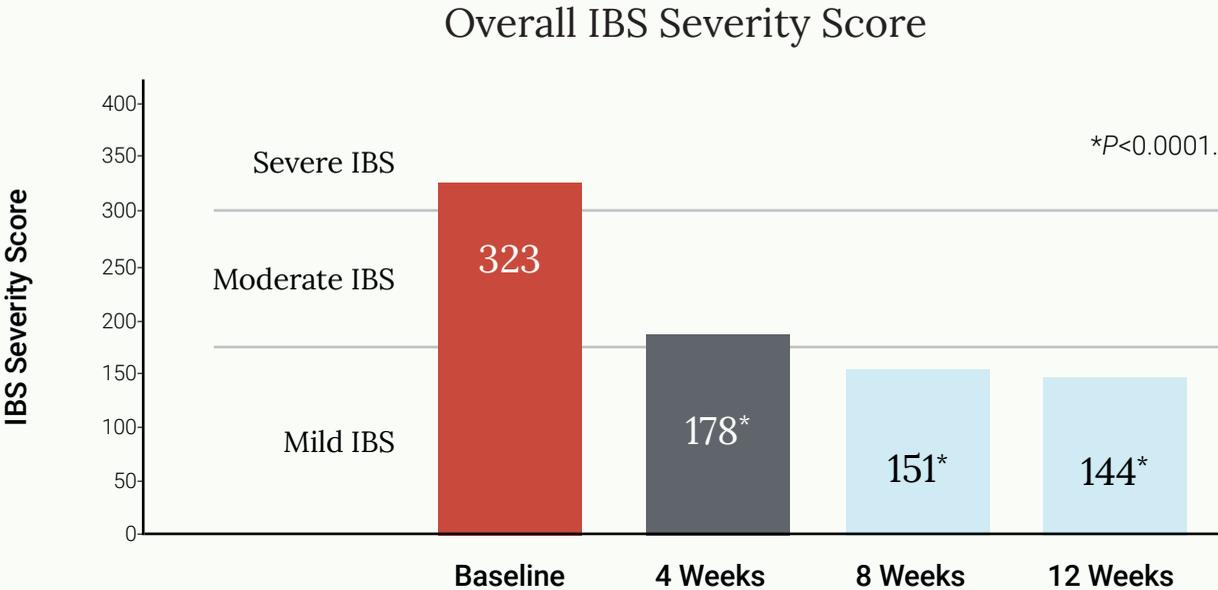


Over 86% of patients had a clinically significant improvement in their IBS-SSS total score by Week 12.¹⁵

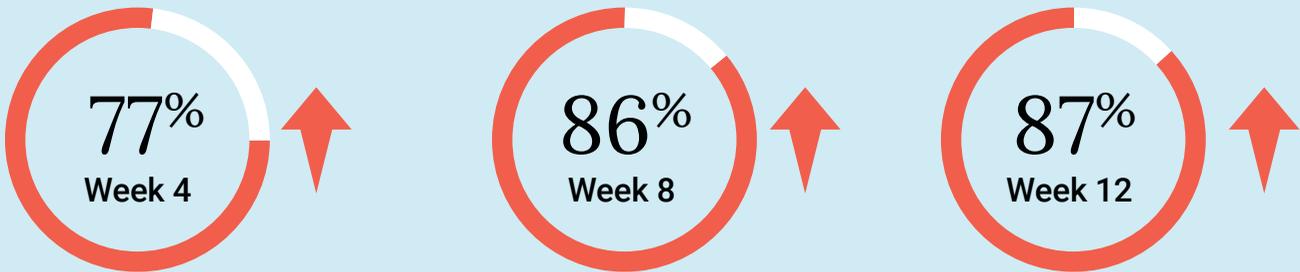
A reduction of 50 points or more in the IBS-SSS total score is considered clinically significant.¹⁶

Key secondary outcomes

IBS symptom severity changed from severe to mild by Week 12, as measured by the IBS-SSS¹⁵



Percentage of Patients with >50-Point Improvement in IBS-SSS Total Score¹⁵





Holigos® IBS Restore significantly decreased abdominal pain severity^{15,16†}

59% ↓



Holigos® IBS Restore significantly reduced days with abdominal pain^{15‡}

58% ↓



Holigos® IBS Restore significantly decreased bloating^{15,16*}

59% ↓



Holigos® IBS Restore significantly increased quality-of-life scores^{15,17*§}

48% ↑

* $P < 0.0001$, ITT.

†The abdominal pain severity component of the IBS-SSS measures the occurrence of abdominal pain for 10 days preceding taking the questionnaire.

‡Reduced from an average of 6.0 to 2.5 days within the prior 10 days.

§IBS-QOL, $P < 0.0001$, ITT.

Safety and Tolerability

The ingredients in Holigos® IBS Restore have been positively reviewed by the Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA) and are accepted as safe.^{19-22*}

- 96% of patients who completed the trial considered Holigos® IBS Restore as tolerable, well-tolerable, or extremely well-tolerable¹⁵
- The ingredients in Holigos® are very well tolerated by infants, children, adults, and patients with IBS^{13,23-25}
- Common side effects associated with Holigos® IBS Restore included mild local reactions in the gut, such as abdominal pain, distension, and flatulence¹¹

In a placebo-controlled clinical trial, Holigos® IBS Restore demonstrated no aggravation of gastrointestinal symptoms compared with placebo.^{11,13}

Summary



The results of this trial demonstrate that once-daily oral administration of Holigos® IBS Restore can provide nutritional support to help significantly reduce the symptoms of IBS, including abdominal pain and bloating, while significantly decreasing abnormal stool consistency. Holigos® IBS Restore was shown to be safe and well-tolerated in patients with IBS.¹⁵

To learn more about Holigos® IBS Restore, please visit www.holigosibshcp.com.

Medical food product: Holigos® IBS Restore should be used under medical supervision. The information provided in this white paper should not be used for diagnosis of IBS or other health problems or diseases. Only doctors can diagnose IBS and information provided is not intended as a substitute for care and advice by a healthcare professional. Medical foods do not require approval by the FDA and should not be viewed as alternatives to FDA-approved drugs. Medical foods marketing does not require prior approval by the FDA but must comply with regulations.

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