Patient Responder Analysis for a Total IBS Symptom Score (TISS) and Abdominal Pain with a Novel Peppermint Oil Site Specific Targeting (PO-SST) Formulation from the US-based IBSREST Randomized Controlled Trial

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Background

There are high placebo response rates with a large amount of variability in IBS clinical trials.[1] Recently, more restrictive outcome measures have been developed for IBS trials to distinguish between active treatment response and placebo response. However, a stringent responder endpoint may not accurately convey the degree of clinical improvement based on patient reported outcomes (PRO). The IBS Reduction Evaluation and Safety Trial (IBSREST) showed that a novel formulation of peppermint oil (PO) using solid-state microspheres (PO-SST) to target the small intestine, was an effective IBS therapy at 24 hours, with improved efficacy at 4 weeks. One previous PRO study, IBSACT*, showed an 80% plus response rate.[2]

Aims

This post-hoc analysis of IBSREST data was done to determine if there was a meaningful response difference between "any improvement" and the high hurdle of "40% improvement" with PO-SST versus placebo. The study was also designed to add to earlier RCT evidence to support the use of PO for IBS.[3]

Methods

IBSREST subjects met Rome III criteria for IBS-M or IBS-D, had average daily IBS related abdominal pain of ≥ 4 (0-10 scale), and a total IBS symptom score (TISS) of ≥ 2 (0-4 scale). Subjects were randomly allocated to PO-SST (IBgard) 180 mg TID or placebo for 4 weeks. The primary analysis was based on the TISS and a secondary analysis evaluated changes in abdominal pain. Supportive analyses were performed classifying subjects as responders if they experienced ≥ 40% improvement in TISS or abdominal pain. Seventy-two patients were evaluable for the 24 hour response population and 71 were evaluable for the 4 week response population.

TISS – Total IBS Symptom Score comprises the average of:

- Abdominal pain or discomfort
- Conastipation
- Urgency of BM
- Incomplete evacuation
- Pain at evacuation
- Bloating or distension
- Diarrhea
- Gas or mucus

*IBSACT – IBS Adherence and Compliance Trial

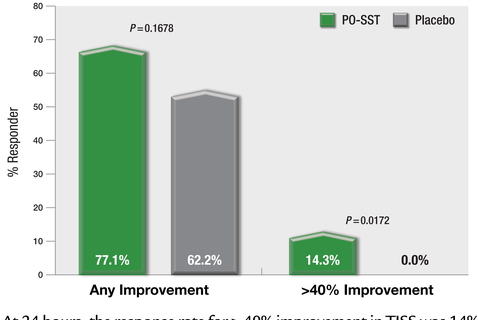
Table 1. Different IBS treatment options (adapted from Enck *et. al.*[4])

Drug	Number of Studies	Number of Patients	Number Needed to Treat	Odds Ratio
Peppermint Oil	4	392	2 - 3	4.11
Psychotherapy	22	1314	4 - 5	2.60
Probiotics	15	1838	7 - 8	2.24
TCA	9	575	5 - 6	2.10
SSRI	6	284	8 - 9	2.08
Spasmolytics	22	1718	5 - 6	1.97
Fibers, Bran	12	611	30	1.12

Treatments for IBS – Numbers Needed to Treat (NNT)
Compared to any alternative therapies for IBS, PO has been shown to have the lowest number-needed-to-treat (NNT) needed to achieve benefit in IBS patients.

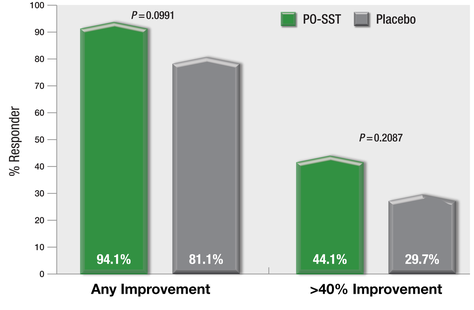
Results

Figure 1. Improvement in TISS at 24 hours



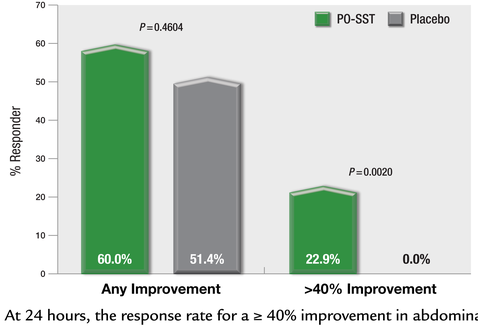
At 24 hours, the response rate for ≥ 40% improvement in TISS was 14% in patients receiving PO-SST vs. 0% receiving placebo (P=0.017), while 77% receiving PO-SST had "any improvement" vs. 62% receiving placebo (P=0.17; Figure 1).

Figure 2. Improvement in TISS at 4 weeks



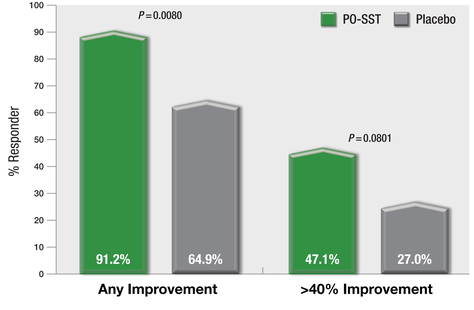
After 4 weeks of treatment, 44% receiving PO-SST were responders with ≥ 40% improvement in TISS vs. 30% receiving placebo (P=0.21), while 94% receiving PO-SST were responders with "any improvement" vs. 81% receiving placebo (P=0.099; Figure 2)

Figure 3. Improvement of abdominal pain at 24 hours



At 24 hours, the response rate for a ≥ 40% improvement in abdominal pain was 23% in patients receiving PO-SST vs. 0% with placebo (P=0.002), while 60% receiving PO-SST had "any improvement" vs. 51% receiving placebo (P=0.46; Figure 3).

Figure 4. Improvement of abdominal pain at 4 weeks



At 4 weeks, 47% receiving PO-SST and 27% receiving placebo were responders with ≥ 40% improvement in abdominal pain (P=0.008), while "any improvement" response rates for PO-SST were 91% vs. 65% for placebo (P=0.08; Figure 4).

Conclusions

- A higher percentage of patients responded to PO-SST vs. placebo
- The stringent "40% improvement" threshold tended to be pronounced within 24 hours for TISS and abdominal pain, while differences in "any improvement" were retained at 4 weeks for abdominal pain, supporting a consistent effect on abdominal pain with PO-SST
- This responder analysis confirmed the high response rates seen with PO-SST in the IBSACT trial[2]

References

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Disclosures

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