

Vibrating Capsules for Chronic Constipation: The New Non-Pharmacologic Approach



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This summary reviews Rao S, Quigley EMM, Chey WD, et al. Randomized Placebo-Controlled Phase 3 Trial of Vibrating Capsule for Chronic Constipation. *Gastroenterology* 2023; In Press. doi.org/10.1053/j.gastro.2023.02.013

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STRUCTURED ABSTRACT

Question: Is a vibrating capsule superior to placebo in chronic idiopathic constipation for symptoms based on FDA-defined responder endpoints?

Design: Multicenter, 8-week, double-blind, placebo-controlled randomized controlled trial (RCT).

Setting: Ninety-five United States centers, conducted from April 2019 through July 2021

Patients: Included 312 outpatients meeting Rome III criteria for chronic idiopathic constipation (CIC).

Interventions/Exposure: Vibrating capsule swallowed 5 evenings per week (skipped Wednesday and Saturday) vs sham dissolvable placebo capsule. Each capsule was programmed to begin vibrating at noon the following day, with 2 separate vibration cycles over 2 days. Each vibration cycle consisted of 3 seconds of oscillation followed by 16 seconds of rest (3 stimulations per minute) for 2 hours.

Outcome: Co-primary endpoints were the proportion of patients with: (a) increase of ≥ 1 weekly complete spontaneous bowel movements (CSBM) from baseline for

≥ 6 of 8 weeks (FDA-defined endpoint); and, (b) increase of ≥ 2 weekly CSBM from baseline for ≥ 6 of 8 weeks. Key secondary endpoints included changes in stool consistency, based on Bristol stool scale, straining, and bloating. A spontaneous bowel movement (SBM) was defined as a spontaneous bowel movement that occurred without using rescue medication in the preceding 48 hours and without use of digital maneuvers, and a CSBM was a SBM with a sense of complete evacuation.

Data Analysis: Intention-to-treat analyses were performed. Co-primary endpoints were assessed with Chi-square test and secondary endpoints which were continuous variables were assessed with analysis of covariance. A hierarchical approach was used for the co-primary and secondary endpoints to control for Type I errors due to multiple endpoints.

Funding: Vibrant Ltd, the manufacturer of the vibrating capsule Vibrant.

Results: Overall, 312 CIC patients were randomized (mean age: 46-47 years old; 85%-88% female; 40%-47% White; baseline symptoms: 0.4 CSBMs/week; 1.6-1.7 SBMs/week, mean Bristol stool scale=2.1). Patients using the vibrating capsule were more likely than placebo-treated patients to achieve both co-primary endpoints of increase of ≥ 1 weekly CSBM for ≥ 6 of 8 weeks (39.3% vs 22.1%, respectively, $P < 0.0001$) and increase of ≥ 2 weekly CSBM for ≥ 6 of 8 weeks (22.7% vs 11.4%, respectively, $P < 0.0008$). Significant improvements were also noted for adjusted mean change in Bristol stool scale score (0.92 vs 0.44, respectively, $P < 0.001$) and straining score, but not for bloating or change in mean SBMs per week. Adverse event data reported that 11% of vibrating capsule-treated patients reported vibrating sensation in abdomen, but this did not lead to study discontinuation. Diarrhea as an adverse event was uncommon in both groups (1.2% vs 0%, respectively).

COMMENTARY

Why Is This Important?

Although our therapeutic armamentarium for CIC has expanded in the past decade, many CIC patients fail to achieve adequate relief and seek out new treatments.¹ Vibrating capsules as a means to stimulate colonic motility while minimizing diarrhea is an intriguing idea. This trial reports the Phase 3 data which led to FDA-approval for

this first-in-class vibrating capsule system, and this is a welcome addition to our treatment options.

This is a very well-designed trial, and the investigators should be congratulated for devising a trial with a rigorous definition of CSBM and utilizing a dissolvable sham capsule for use in the placebo group. Although the system to activate the capsules require an "Activation Pod" and a downloadable

app in addition to the capsules, more than 90% of study patients found the system easy to use.

Key Study Findings

Patients using the vibrating capsule were more likely than placebo-treated patients to achieve both co-primary endpoints of increase of ≥ 1 weekly CSBM for ≥ 6 of 8 weeks (39.3% vs 22.1%, respectively, $P < 0.0001$) and increase of ≥ 2 weekly CSBM for ≥ 6 of 8 weeks (22.7% vs 11.4%, respectively, $P < 0.0008$).

Caution

The study duration is relatively short (8 weeks) for a chronic condition. Appropriate blinding to treatment group could have been impacted in the 11% of vibrating capsule-treated patients who noted a vibrating sensation in their abdomen. However, exclusion of these patients did not change reported outcomes. The current trial only examined 1 activation mode or vibration cycle starting at noon on the day following administration, although a preliminary phase of the trial did assess efficacy of activating vibrations at 6 AM on the morning following ingestion.

My Practice

I have many CIC patients who are dissatisfied with currently available therapies, and many of these patients will be intrigued by a non-

pharmacologic option that may trigger colonic motility. Since these vibrating capsules just became available, I have not prescribed them yet. I do plan to use it soon in CIC patients who have failed over-the-counter and prescription agents for CIC. For these difficult-to-treat patients, it is important to rule out pelvic floor dysfunction, which is best treated with bio-feedback and not an appropriate option for IBS-C patients who have clinically important abdominal discomfort. Although combination therapy was not studied in this trial, I may combine this with other CIC treatments in some patients. I am uncertain about insurance coverage for this, although the manufacturer currently advertises a self-pay option for \$89/month.

For Future Research

Longer clinical trials and real-world data is needed to define efficacy in this chronic condition. Since the vibrating capsule is programmable, further research may identify optimal vibration cycles, which might vary by patient. Identifying the sub-group of CIC patients most likely to benefit from this treatment will also be beneficial.

Conflict of Interest

Dr. Schoenfeld reports serving on advisory boards, consultant and speakers bureau for Ironwood Pharmaceuticals, AbbVie Pharmaceuticals, and Ardelyx Pharmaceuticals, and serving as an advisory board member for Salix Pharmaceuticals.

Note: The authors of the article published in *Gastroenterology* are active on social media. Tag the to discuss their work and this EBGI summary!

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REFERENCES

1. Oh SJ, Fuller G, Patel D, et al. Chronic Constipation in the US: Results from a Population-Based Survey Assessing Healthcare Seeking and Use of Pharmacotherapy. *Am J Gastroenterol* 2020; 115: 895-905.