ENDOBAR

EndoBar

Study Title: Efficacy and Safety of EndoBar Bariatric Embolization for Weight Management in People with Obesity

Sponsor:	Endobar Solutions, LLC
Office Address:	Ramland Road 40 Orangeburg NY 10962, USA
Protocol No:	CZ01
Product:	The Endobar Infusion Catheter System
Investigational Device:	The Endobar Infusion Catheter System (consisting of an occlusion balloon catheter, a Smart Manifold delivery system and microspheres)
Revision Number:	Rev B
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Revision History

Section	Change	Reason For Change
Changes below to version A resulting in version B		
All document	Document update according EN ISO 14155:2011	

1 PROTOCOL SUMMARY

Efficacy and Safety of EndoBar Bariatric Embolization for Weight Management in People with Obesity

Study Objective

To evaluate the efficacy and safety of the Endobar gastric embolization system for the treatment of obesity before continuing to a larger Pivotal Trial.

Investigational Device

The investigational device in this clinical study is the Endobar Infusion Catheter System – a disposable system consisting of an occlusion balloon catheter, a Smart Manifold delivery system.

Study Design/Planned Number of Subjects

This study is a prospective, sham controlled, single-blind 12-month trial with 1:1 randomization. A maximum of 40 subjects (obese men and women who have a body mass index (BMI) of 35.0–55.0 kg/m^2) will be enrolled in the study. Eligible subjects will be randomized to treatment with Endobar Therapy (n = 20) or sham procedure control (n = 20). Endobar Therapy involves catheter-based embolization of the left gastric artery. All subjects in both Endobar Therapy and Sham Control groups will receive Lifestyle Therapy (behavioral and diet education). At the end of 6 months all subjects randomized to the Sham Control group will receive catheter-based embolization of the left gastric artery. Both Endobar Therapy and Sham Control crossover to Endobar Therapy groups will be followed for a total of 12 months.

Study Duration

The duration of the study is expected to last approximately 18 months from the first enrollment. An additional 12 months to the study closeout after the last follow-up.

Sample Size

This study is powered to detect a differential change in total body weight loss between groups. Briefly, 18 patients are required in each group to have an 85% chance of detecting, as significant at an alpha of 5%, a change in total body weight loss of 5% in the Control group to 10% in the GAE group (assuming a standard deviation of 5%), and 1:1 randomization. Again, assuming a 10% loss to follow-up, a total of 20 patients are required per group. Secondary endpoints will be evaluated using descriptive statistics.

Primary Endpoints

Percent total body weight loss at 6 months and at 12 months are the primary endpoints intended to provide efficacy and safety of investigational device.

- Efficacy Endpoints: The primary efficacy endpoints of the study will be difference in percent total body weight loss at 6 months between Sham Control and Endobar Therapy groups and percent total body weight loss at 12 months in the group randomized to initial Endobar Therapy. Success will be defined as: 1) ≥5%total body weight loss at 6 months with statistical superiority to the Sham Control group and 2) ≥5%total body weight loss at 12 months.

- Safety Endpoints: All participants will be carefully monitored by a physician and research nurse during this study. Safety will be monitored by:
    - Incidence of device-, procedure- and therapy- related adverse events
    - Incidence of device related, or unrelated, serious adverse events, including unanticipated adverse device effects

Secondary Endpoints

The secondary outcomes measured at 6 and 12-months are:

- Percent excess weight (%EWL), defined as absolute weight loss divided by baseline excess weight and multiplied by 100, at 6 months and at 12 months. Excess weight will be determined from ideal body weights based on a BMI=25 kg/m^2
- Proportion of subjects who achieve ≥5% and ≥10% total body weight loss from baseline at 6 months and at 12 months.
- Percent change in selected coronary heart disease risk factors (plasma triglyceride and HDL-cholesterol, and systolic and diastolic blood pressure) at 6 months and at 12 months)
- Success of performing the radiological procedure

Additional Endpoints of Interest (assessed at baseline and at 6 and 12 months)

- Changes in mood (depression/anxiety)
- Change in quality-of-life
- Change in eating behavior
- Change in volume of Ensure consumed to achieve satiation
- Change in plasma ghrelin and glucagon-like peptide 1 concentrations
- Change in oral glucose tolerance and insulin sensitivity

Key Inclusion Criteria

- BMI 35.0–50.0 kg/m^2 at time of screening
- 21–60 years of age at time of screening

- Women of childbearing potential must agree to use at least one form of birth control (prescription hormonal contraceptives, diaphragm, IUD, condoms with or without spermicide, or voluntary abstinence) from time of study enrollment through study exit.
- Willing and able to provide informed consent

Key Exclusion Criteria

- Previous bariatric, gastric pancreatic, hepatic, and/or splenic surgery
- History of duodenal or gastric ulcers or regularly taking medications (therapy >1 day per week) that can cause ulcers (e.g. aspirin, non-steroidal anti-inflammatory drugs)
- Prior radiation to the upper abdomen
- Prior embolization to the stomach, spleen or liver
- Portal venous hypertension
- Active H. pylori infection
- Uncontrolled hypertension (> 160/100 with or without medication).
- Diabetes (determined by medical history, fasting blood glucose or results of an oral glucose tolerance test)
- Serum triglyceride > 400 mg/dL at screening.
- Class 4 or 5 surgical risk based on standard ASA criteria (Saklad M. Grading of patients for surgical procedures. Anesthesiol. 1941; 2:281–4). Need to define these criteria here
- Severe pulmonary or cardiovascular disease defined as a history or evidence of serious cardiovascular disease, including myocardial infarction, acute coronary syndrome, coronary revascularization, heart failure requiring medications, history of sudden cardiac death, or NYHA (New York Heart Association) class III or IV heart failure (defined below):
    - Class III: patients with marked limitation of activity; they are comfortable only at rest.
    - Class IV: patients who should be at complete rest, confined to bed or chair; any physical activity brings on discomfort and symptoms occur at rest.
- Coagulation disorders (platelets < 100,000, PT > 2 seconds above control or INR > 1.5 at screening).
- Anemia (Hb $\leq$ 10.0 g/dL) at screening.
- Malignancy in the last 5 years (except for non-melanoma skin cancer).
- Evidence of other significant organ system dysfunction (e.g. cirrhosis, renal failure)
- Pregnant or lactating.
- History of substance abuse in last 3 years.
- Thyroid Stimulating Hormone (TSH) >2.0 x upper limit of normal at screening.
- Taking prescription or over-the-counter medications for weight loss in the last 3 months before screening, or planning to participate in a commercial weight loss program in the next 5 years.
- Taking diuretic medication for congestive heart failure or edema.
- Evidence of significant mucosal inflammation, ulceration or ischemia detected on endoscopy, and those with unsuitable left gastric anatomy as judged by the study site physician will be excluded.

- Psychiatric illness that could affect compliance with the study, as judged by the site principle investigator.
- Unable to complete screening requirements (compliance with visits and dietary record)
- Taking medication once or more per week that causes weight gain (e.g. atypical antipsychotics, monoamine oxidase inhibitors, lithium, selected anticonvulsants, tamoxifen, glucocorticoids)
- Chronic abdominal pain that would potentially complicate management.
- Unstable weight (>3% change; self-reported) over the previous 2 months at time of screening.
- Subjects whom the site investigator, research team, or the study medical monitor feel is not able to participate in the study for any reason, including poor general health or unable/unwilling to follow the study protocol.

Follow-up Schedule

- Screening
- Baseline visit
- Interventional Radiology Procedure
- Randomization
- Left Gastric Artery Occlusion / Placebo
- Follow-up Visits Week: 1, 2, 3, 4, 6, 8, 10, 12, 14, 16, 20, 24, 26, 28, 32, 36, 40, 44, 52