Statistical Analysis Plan:

Gastric Artery Embolization Trial for Lessening Appetite Nonsurgically (GETLEAN)

NCT02248688

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I give my approval for the attached SAP entitled *GET LEAN* dated December 19th, 2021.

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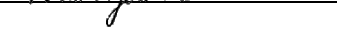
Signature: 

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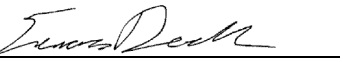
Signature: 

Date: December 28th, 2021

Abbreviations and Definitions

BMI	body mass index
CCK	cholecystokinin
EWL	excess body weight loss
Hg-A1c	hemoglobin-A1c
IBW	ideal body weight
LGA	left gastric artery
MCS	SF-36v2 Mental Component Summary
PCS	SF-36v2 Physical Component Summary
QOL	quality of life
SAP	Statistical Analysis Plan
SF-36v2	Short Form-36 Version 2

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Preface:

Morbid obesity, defined as a body mass index (BMI) of greater than 40kg/m^2, is a prevalent and deadly public health problem affecting 6.6% of the United States population[1]. Bariatric surgery is a commonly used procedure for morbidly obese patients in whom conservative weight loss measures such as diet and exercise have failed[2]. However, these surgical treatments have known serious complications, including anastomotic leaks, bowel obstruction, deep vein thrombosis, pulmonary embolism, gastrointestinal bleeding, dumping syndrome, and anesthesia risks resulting in morbidity and mortality[2]. The 30-day mortality rate associated with bariatric surgery is approximately 0.31% as of 2014, which is lower than previously reported in 2004[3]. However, the repeat operation rate is 7% and the overall complication rate is 17%[3]. It is estimated that only 1% of eligible patients elect to undergo bariatric surgery [4]. Left gastric artery (LGA) embolization may fulfill a role as a minimally invasive alternative to the current surgical treatment of gastric bypass or reduction surgery for morbidly obese patients. The LGA supplies the fundus of the stomach, where it is known that the hormone ghrelin (one of the hormones responsible for appetite) is produced. Ghrelin is a 28-amino acid hunger-stimulating peptide and hormone that is produced mainly by P/D1 cells lining the fundus of the stomach and epsilon cells of the pancreas [5]. Ghrelin is the only known circulating orexigenic, or appetite-enhancing, hormone [6].

Scope of Analysis

The purpose of the present study was to collect safety and efficacy data in patients undergoing LGA embolization for morbid obesity in the United States. As a secondary goal, the pilot study obtained other satiety-related hormones, and quality-of-life (QOL) data.

Arm:
Beadblock Embolization: Embolization of the LGA via embolic agent Beadblock, 300-500 Micron.

Participants/Study Length
A total of 5 patients started and completed the study within 13 months after enrollment from 2014-2017.

Data Source
Food and Drug Administration Investigational Device Exemption and institutional review board approval were obtained to perform this study on five patients.

Primary Outcomes *(measured at 6 months and 12 months post-procedure)*

1. Body Weight Average
2. Percentage of Excess Body Weight Loss (EWL)
3. Average Ghrelin Hormone Levels

Secondary Outcomes *(measured at 6 months and 12 months post-procedure)*

1. Average Leptin Hormone Levels
2. Average Cholecystokinin (CCK) Hormone Levels
3. QOL: Average Short Form-36 Version 2 (SF-36v2) Physical Component Summary (PCS)
4. QOL: Average SF-36v2 Mental Component Summary (MCS)
5. Hemoglobin-A1c (Hg-A1c) Levels*

* Only evaluated for sole diabetic patient in this trial.

Safety Outcomes

1. Adverse Events: Reported at each clinical visit.

Study Design

The following table displays Safety and Efficacy Data collected at designated intervals from trial participants undergoing LGA embolization with 300-500µm Bead Block (Biocompatibles, Farnham, United Kingdom) for the treatment of morbid obesity:

Procedure	Baseline	During Procedure	Post-Procedure					
			3-Day	1-week	1-Month	3-Month	6-Month	12-Month
BMI	X				X	X	X	X
Weight	X				X	X	X	X
Stool Guaiac	X				X			
Complete Blood Count	X		X	X	X			
BUN/Creatinine	X		X	X	X			
CT-Angiogram	X							
Prothrombin time (PT)/ partial thromboplastin time (PTT)	X							
Nuclear Medicine Gastric Emptying Study	X					X		
Evaluation by gastroenterologist with upper endoscopy*	X		X					
Certified Anesthesia Evaluation	X							
Evaluation by diabetologist or endocrinologist with experience in patients undergoing bariatric treatment evaluation*, **	X							
Ghrelin	X			X	X	X	X	X
Leptin	X			X	X	X	X	X
CCK	X			X	X	X	X	X
SF-36v2 Questionnaire	X							X
Hemoglobin A1c**	X					X	X	
Urine pregnancy Test***	X	X						

* = familiar with study protocol and part of study team
** = only if diabetic
*** = only if female

Analysis

All outcomes will be presented using descriptive statistics (namely by means and full range), no statistical models were run. For analyses regarding the hormones Ghrelin, Leptin and CCK, mean differences between baseline to time points where it is measured during the study (6 and 12 months). Counts are presented for categorical variables. Microsoft® Excel® Version 2017 will be used for all statistical analyses.

Primary Outcomes:

The following primary outcomes were analyzed:

1) Body Weight
2) EWL (calculated using the equations depicted below) and
3) Ghrelin Hormone Levels (reported as a percentage of the baseline value)

Results of this analysis were the difference in mean values of participants' baseline measurements and at time points where the primary outcomes are measured during the study (6 and 12 months).

$$EWL: \quad \frac{Baseline\ Weight\ in\ lbs. - Followup\ Weight\ in\ lbs.}{(Baseline\ Weight\ in\ lbs. - IBW)}$$

$$IBW: \quad (50 + (2.3 * ((Height\ in\ inches) - 60)$$

Secondary Outcomes
Satiety-related hormones:

1) Leptin and
2) CCK

Were analyzed in the same manner as Ghrelin hormone levels were analyzed, i.e., the difference in mean values between baseline and time point during the study (6 months and 12 months) reported as a percentage of the baseline value.

QOL: Data for QOL measurements were analyzed for differences in the mean values of participant's SF-36v2 PCS and MCS from baseline to time points where it was measured during the study (6 and 12 months).
Ranging from 0-100, higher scores on either PCS or MCS indicate better health status. The SF-36v2 contains 8 sections total which are each calculated into individual scale scores. A z-score is then determined for each scale score by subtracting the mean scale score of a sample of the national general population from the scale score of the individual participant being analyzed. Each of the 8 z-scores are then multiplied by the PCS scoring coefficient, added together, multiplied by 10 and added to 50.

Hg-A1c: Reported as the raw difference in percentage of Hg-A1c between baseline to time points where it is measured during the study (6 and 12 months) for the sole diabetic trial participant.

Missing Data

No relevant data was missing from the analyses described above. All relevant baseline measurements, primary and secondary outcomes were collected from the 5 participants.

Bibliography

1. Sturm R, Hattori A. Morbid obesity rates continue to rise rapidly in the United States. Int J Obes (Lond) 2013;37:889–891.
2. DeMaria EJ. Bariatric surgery for morbid obesity. N Engl J Med 2007; 356:2176–2183.
3. Chang SH, Stoll CR, Song J, Varela JE, Eagon CJ, Colditz GA. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003-2012. JAMA Surg 2014;149:275–287.
4. Ponce J. New procedure estimates for bariatric surgery: what the numbers reveal. Connect, May 2014. Available at: http://connect.asmbs.org/may-2014-bariatric-surgery-growth.html , Accessed June 26, 2016.
5. Seim I, Amorim L, Walpole C, Carter S, Chopin LK, Herington AC. Ghrelin gene-related peptides: multifunctional endocrine/autocrine modulators in health and disease. Clin Exp Pharmacol Physiol 2010; 37:125–131.
6. Dixit VD, Schaffer EM, Pyle RS, et al. Ghrelin inhibits leptin-and activation-induced proinflammatory cytokine expression by human monocytes and T cells. J Clin Invest 2004;114:57–66.