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Lorcaserin plus lifestyle modification for weight loss maintenance: Rationale and design for a randomized controlled trial

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ABSTRACT

Background/aims: Few studies have examined the efficacy of recently approved medications for chronic weight management in facilitating the maintenance of lost weight. This paper provides an overview of the design and rationale for a trial investigating whether lorcaserin, when combined with behavioral weight loss maintenance sessions (WLM), will facilitate the maintenance of losses of ≥ 5% of initial weight.

Methods: In this two-phase trial, participants with obesity will enroll in a 14-week run-in diet program consisting of weekly group lifestyle modification sessions and a 1000–1200 kcal/d meal replacement diet. Participants who complete this weight induction phase and lose at least 5% of initial weight will then be randomized to 52 weeks of WLM plus lorcaserin or WLM plus placebo. We hypothesize that at 52 weeks post randomization, participants assigned to WLM plus lorcaserin will achieve significantly better maintenance of the prior 5% weight loss.

Results: We will recruit 182 adults with obesity to participate in the diet run-in, 136 of whom (75%) are expected to become eligible for the randomized controlled trial. Co-primary outcomes include the percentage of participants who maintain a loss of at least 5% of initial weight at week 52 and change in weight (kg) from randomization to week 52.

Conclusions: This two-phase design will allow us to determine the potential efficacy of chronic weight management using lorcaserin for maintaining initial losses of at least 5% body weight, induced by the use of a structured meal-replacement diet. This combined approach holds promise of achieving larger long-term weight losses.

Clinical Trial Registration: NCT02388568 on ClinicalTrials.gov

1. Introduction

Comprehensive behavioral weight control interventions reliably induce mean losses of 5%–10% of initial weight [1]. Weight loss, however, is typically followed by steady regain over time [2,3]. Two interventions consistently prevent weight regain. The first is monthly or twice monthly weight loss maintenance (WLM) sessions, which support patients' continued efforts to consume a reduced-calorie diet, monitor their body weight regularly, and engage in high levels of physical activity (200–300 min/week) [1,4–6]. The second is the use of medications approved for chronic weight management [7]. Pharmacotherapy traditionally has been used to induce weight loss but may be of greater benefit in facilitating its maintenance [7,8]. The use of chronic weight management medications is analogous to the long-term (i.e., indefinite) use of medications to control hypertension and type 2 diabetes [9].

Since 2012, the U.S. Food and Drug Administration (FDA) has approved four new medications for chronic weight management [7,8]. They include two monotherapies: lorcaserin (Belviq), a selective serotonin receptor agonist [10]; and liraglutide 3.0 mg (Saxenda), a glucagon-like-peptide 1 (GLP-1) receptor agonist [11]. Two other new drugs represent combinations of medications originally approved for other purposes: phentermine-topiramate (Qsymia) and naltrexone-bupropion (Contrave) [12,13]. A fifth medication, orlistat (Xenical), received FDA approval was approved in 1999 for long-term weight management [14]. Table 1 summarizes the mechanisms of actions, side-effects, and efficacy of these medications.

Only two studies have examined the efficacy of these recently approved medications in facilitating the maintenance of lost weight

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Table 1
Pharmacotherapy currently approved for chronic weight loss.

Drug (generic)	Dose	Mechanism of action	Mean placebo-subtracted weight loss, % or kg[a]; duration of trial	Common side effects	Contraindications
Orlistat, prescription (120 mg)	120 mg TID	Pancreatic and gastric lipase inhibitor	2.9–3.4 kg, 2.9–3.4%; 1 y	Decreased absorption of fat-soluble vitamins, steatorrhea, oily spotting, flatulence with discharge, fecal urgency, oily evacuation, increase defecation, fecal incontinence	Cyclosporine (taken 2 h before or after orlistat dose), chronic malabsorption syndrome, pregnancy and breastfeeding, cholestasis, levothyroxine, warfarin, antiepileptic drugs
Orlistat, over-the-counter (60 mg)	60–120 mg TID	Pancreatic and gastric lipase inhibitor	2.9–3.4 kg, 2.9–3.4%; 1 y	See orlistat, prescription	See orlistat, prescription
Lorcaserin	10 mg BID	$5HT_{2C}$ receptor agonist	3.6 kg, 3.6%; 1 y	Headache, nausea, dry mouth, dizziness, fatigue, constipation	Pregnancy and breastfeeding Use with caution: SSRI, SNRI/MAOI, St John's Wort, triptans, bupropion, dextromethorphan
Phentermine (P)/ topiramate (T)	3.75 mg P/23 mg T ER QD (starting dose) 7.5 mg P/46 mg T ER QD (recommended dose) 11.25 mg P/69 mg T ER daily 15 mg P/92 mg T ER QD (high dose)	GABA receptor modulation (T) plus norepinephrine-releasing agent (P)	6.6 kg (recommended dose), 6.6% 8.6 kg (high dose), 8.6%; 1 y	Insomnia, dry mouth, constipation, paresthesia, dizziness, dysgeusia	Pregnancy and breastfeeding, hyperthyroidism, glaucoma, MAOIs, sympathomimetic amines
Naltrexone (N)/ Bupropion (B)	32 mg N/360 mg B BID	Reuptake inhibitor of dopamine and norepinephrine (B) and opioid antagonist (N)	4.8%	Nausea, constipation, headache, vomiting, dizziness	Uncontrolled hypertension, seizure disorders, anorexia nervosa or bulimia, drug or alcohol withdrawal, MAOIs
Liraglutide	3.0 mg injectable	GLP-1 agonist	5.8 kg; 1 y	Nausea, vomiting, pancreatitis	Medullary thyroid cancer history, multiple endocrine neoplasia type 2 history

Abbreviations: GABA, γ-aminobutyric acid; HR, heart rate; MAOI, monoamine oxidase inhibitors.
Table is reprinted with permission from reference [15].
[a] Mean weight loss in excess of placebo as percentage of initial body weight or mean kilogram weight loss over placebo.