Table 2. Weight-loss medications: Clinical trial information[32-39]

Study	Purpose	Methodology	Results
Torgerson et al, 2004 XENDOS study[32]	To assess the effects of adding orlistat to lifestyle changes in terms of body weight and T2DM risk	4-year, randomized, double-blind study of 3,305 patients who implemented lifestyle changes and received orlistat 120 mg or placebo 3 times/day. Participants had a BMI ≥30 and normal (79%) or impaired (21%) glucose tolerance.	After 4 years, cumulative incidence of DM was 9.0% with placebo and 6.2% with orlistat (risk reduction, 37.3%; *P* = .0032). The preventive effect was explained by the difference in subjects with IGT. Mean weight loss after 4 years was significantly greater with orlistat than placebo (5.8 vs. 3.0 kg; *P* <.001) and similar between orlistat recipients with IGT (5.7 kg) or NGT (5.8 kg) at baseline.
Smith et al, 2010 BLOOM study[33]	To assess the effects of lorcaserin on body weight	2-year, randomized, double-blind trial of 3,182 obese or overweight adults (mean BMI, 36.2) who underwent diet and exercise counseling and received lorcaserin 10 mg or placebo BID for 52 weeks. At week 52, patients in the placebo group continued to receive placebo; those in the lorcaserin group were randomized to receive placebo or lorcaserin.	At 1 year, 47.5% of lorcaserin recipients and 20.3% of placebo recipients lost ≥5% of their body weight (*P* <.001), corresponding to a mean loss of 5.8 kg with lorcaserin vs. 2.2 kg with placebo (*P* <.001). For lorcaserin recipients who had lost ≥5% of their baseline weight at 1 year, the loss was maintained in more of those who stayed on lorcaserin in year 2 (67.9%) than in those switched to placebo in year 2 (50.3%; *P* <.001). Outcomes for key secondary end points (e.g., WC, BP, TC, TG, IR) were more favorable for lorcaserin recipients.
O'Neil et al, 2012 BLOOM-DM study[34]	To assess the effects of lorcaserin on body weight and glycemic control	1-year, randomized trial of 604 OW/O patients with elevated HbA_{1C} assigned 1:1:1 to placebo, lorcaserin 10 mg QD, or lorcaserin 10 mg BID. Patients were also treated with metformin, an SFU, or both, and received diet and exercise counseling.	More patients lost ≥5% body weight with lorcaserin BID (37.5%; *P* <.001) or lorcaserin QD (44.7%; *P* <.001) than with placebo (16.1%). Mean weight change was –4.5% with lorcaserin BID and –5.0% with lorcaserin QD vs. –1.5% with placebo (*P* <.001 for each). HbA_{1c} decreased 0.9% with lorcaserin BID, 1.0% with lorcaserin QD, and 0.4% with placebo (*P* <.001 for each).
Gadde et al, 2011 CONQUER study[35]]	To assess efficacy and safety of two doses of PHEN/TPM CR as an adjunct to diet and lifestyle modification for weight loss and metabolic risk reduction	56-week phase 3 trial of 2,487 OW/O adults with ≥2 co-morbidities (e.g., HTN, dyslipidemia, DM/pre-diabetes) who were randomized in a 2:1:2 ratio to daily placebo, PHEN/TPM CR 7.5 mg/46 mg (7.5/46), or PHEN/TPM CR 15 mg/92 mg (15/92)	Mean change in body weight was –1·4 kg in the placebo group, –8·1 kg in the 7.5/46 group, and –10.2 kg in the 15/92 group. Cardiometabolic risk factors improved significantly in the PHEN/TPM CR groups as compared with the placebo group, with significant reductions in BP, TG, CRP, fasting glucose, and TC.
Garvey et al, 2012 SEQUEL	To evaluate the effects of long-term PHEN/TPM CR in patients with cardiometabolic disease	108-week, double-blind study of 676 OW/O patients who continued with original randomized daily treatment (placebo, PHEN/TPM CR 7.5 mg/46 mg [7.5/46], or PHEN/TPM CR 15 mg/92	PHEN/TPM CR, versus placebo, was associated with significant sustained weight loss. Mean changes from baseline in body weight were –1.8% for placebo, –9.3% for 7.5/46, and –10.5% for 15/92. PHEN/TPM

study,[36] an extension of the CONQUER study		mg [15/92]). All patients participated in a lifestyle-modification program.	CR, relative to placebo, improved CV and metabolic variables and decreased rates of incident T2DM.
Garvey et al, 2014 SEQUEL study[37]	To evaluate the effect of PHEN/TPM CR on progression to T2DM and/or cardiometabolic disease in patients with pre-diabetes and/or MetS at baseline	See Methodology section in the SEQUEL study above. 475 patients met criteria for pre-diabetes or MetS at baseline.	Among patients with pre-diabetes and/or MetS, mean changes from baseline in body weight were –2.5% for placebo, –10.9% for 7.5/46, and –12/1% for 15/92. This weight loss was associated with reductions of 70.5% and 78.7% in incidence rate of T2DM for those receiving 7.5/46 and 15/92, respectively, a significant effect versus placebo. The ability of PHEN/TPM CR to prevent T2DM was related to degree of weight lost and was accompanied by significant improvements in cardiometabolic parameters.
Greenway et al, 2010 COR-I study[38]	To assess the effect of SR naltrexone and bupropion on body weight	56-week double-blind phase 3 study of 1,742 patients who were obese or OW with dyslipidemia or HTN who were randomized in a 1:1:1 ratio to receive daily SR naltrexone 32 mg plus SR bupropion 360 mg (NB32 group), SR naltrexone 16 mg plus SR bupropion 360 mg (NB16 group), or placebo twice daily. All participants followed a mild hypocaloric diet and an exercise regimen.	Mean change in body weight was –1.3% in the placebo group, –6.1% in the NB32 group (P <.0001 vs. placebo) and –5.0% in the NB16 mg group (P <.0001 vs. placebo). In terms of risk factors, NB32, relative to placebo, had a favorable effect on WC, TG, HDL-C, CRP, and fasting insulin. A transient increase of ~1.5 mm Hg in mean BP was followed by a reduction of ~1 mm Hg below baseline in the NB groups.
Wadden et al, 2013 SCALE Maintenance Study[39]	To assess the efficacy of liraglutide in maintaining weight loss achieved with a low-calorie diet	56-week phase 3 study of 422 O/OW patients with co-morbidities who lost ≥5% of initial weight during a low-calorie diet run-in were randomized to liraglutide 3.0 mg/day or placebo given SC. Diet and exercise counseling were provided throughout the trial.	Patients lost a mean 6.0% body weight during the run-in. From randomization to week 56, weight decreased an additional 6.2% with liraglutide and 0.2% with placebo (P <.0001). More liraglutide recipients (81.4%) than placebo recipients (48.9%) maintained the ≥5% run-in weight loss (P <.0001) and more liraglutide recipients (50.5%) than placebo recipients (21.8%) lost ≥5% of randomization weight (P <.0001). Liraglutide, relative to placebo, produced small but significant improvements in several cardiometabolic risk factors.

BP, blood pressure; CRP, C-reactive protein; CV, cardiovascular; HDL-C, high-density lipoprotein cholesterol; HTN, hypertension; IGT, impaired glucose tolerance; IR, insulin resistance; MetS, metabolic syndrome; NGT, normal glucose tolerance; OW/O, overweight/obese; PHEN/TPM CR, controlled-release phentermine/topiramate; SC, subcutaneously; SFU, sulfonylurea; SR, sustained-release; T2DM, type 2 diabetes mellitus; TC, total cholesterol; TG, triglycerides; WC, waist circumference.