Experimental drug achieves unprecedented weight loss

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An investigational combination of drugs already approved to treat obesity, migraine and epilepsy produced up to a 10 percent weight loss in obese individuals participating in a one-year clinical trial, according to researchers at Duke University Medical Center.

Appearing online in The *Lancet* today, the study found that treatment with the controlled-release combination therapy consisting of phentermine and topiramate also achieved significant reductions in blood pressure and hemoglobin A1C. Study participants also experienced improvements in cholesterol, triglycerides and inflammatory markers, including C-reactive protein, when taking either of two doses of the combination when compared to placebo.

"Patients receiving this combination experienced 8.6 percent greater weight loss, on average, compared to those patients receiving placebo," says Kishore M. Gadde, M.D., director of Duke's obesity clinical trials program. "This kind of weight loss, coupled with significant reductions in cardiometabolic risk factors represents a potentially important advancement in the management of obesity."

Currently, orlistat is the only drug available for the long-term treatment of obesity. It is marketed in prescription strength as Xenical, and available over the counter as Alli. Meta-analysis studies have shown that treatment with orlistat, at maximum strength, can lead to approximately seven-pound greater weight loss compared to treatment with placebo after one year. "The combination drug achieves about 19 pounds of

weight loss relative to placebo at one year," Gadde says.

The 56-week, phase 3 study was conducted in 93 U.S. centers with 2487 patients who had a BMI of 27-45kg/m2, and two or more co-morbidities such as diabetes or heart disease. Patients were randomly assigned to receive either a placebo or one of two low-dose drug combinations. The study tested phentermine, a short-term obesity treatment available since 1959, and topiramate, marketed under the trade name Topamax, in doses up to 400mg to treat epilepsy and prevent migraines. Patients in the study also received diet and exercise advice.

The study was funded by Vivus, which is seeking FDA approval to market the combination therapy under the trade name Qnexa. In October 2010, the FDA ruled that the New Drug Application could not be approved in its current form, and asked the company for more safety data.

In March, the FDA issued a warning regarding the use of topiramate during pregnancy stating that pregnant women who take the drug are at considerably increased risk of having babies born with cleft lip and/or cleft palate. Topiramate has also been associated with memory problems and mood changes, including depression and anxiety.

Gadde says 34 women became pregnant while in Qnexa clinical trials, and "no birth defects were reported for the babies born." Even so, Gadde says pregnant women would not be candidates for use of this drug because "there is no reason for women to use weight loss drugs while they are pregnant or trying to become pregnant."

The study used once-daily oral doses of the combined drugs. Phentermine 7.5mg plus topiramate CR 46mg achieved 7.8 percent weight loss (p