More Weight Lost With Liraglutide Than Orlistat

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PHOENIX — Liraglutide, an investigational drug given once a day, produced significantly more weight loss than orlistat in a randomized, 20-week, placebo-controlled trial in obese patients, most of whom were not diabetic.

Participants on four different doses of liraglutide—1.2, 1.8, 2.4, and 3.0 mg—tested in the study lost significantly more weight, compared with a control group on placebo. Those treated at the two highest doses (2.4 and 3.0 mg per day) lost significantly more weight than did those given 120 mg of orlistat (Xenical) three times a day.

The mean weight loss ranged from 4.8 kg with the lowest 1.2-mg dose of liraglutide to 7.2 kg with the 3.0-mg dose, according to the investigators. The mean weight loss for placebo was little more than 2 kg and about 4 kg with orlistat.

"A very nice dose separation" was how Dr. Arne Astrup, the lead author and head of the department of human nutrition at the University of Copenhagen, described results of the six-arm, 564-patient study at the annual scientific meeting of NAASO, the Obesity Society.

Novo Nordisk A/S sponsored the trial. It announced in May that it had submitted a New Drug Application for liraglutide to the U.S. Food and Drug Administration and a marketing authorization application to the European Medicines Agency—both seeking an indication for liraglutide in the treatment of people with type 2 diabetes. These were followed in July by a request for marketing approval in Japan.

Liraglutide is a human analogue of glucagon-like peptide-1 (GLP-1). According to the company's Web site, liraglutide inhibits appetite and stimulates insulin production only when glucose levels become too high.

In September, The Lancet published the results of a 1-year phase III trial showing that patients with early type 2 diabetes achieved better glycemic control with liraglutide monotherapy (doi: 10.1016/S0140-6736(08)61246-5).

Nearly two-thirds of the participants in the current study did not have diabetes; most of the rest were classified with prediabetes, leaving about 3% with the disease. About three-quarters of the population were women, and the average age was in the mid-40s (range 18-65 years). Body mass index ranged from 30 kg/m^2 to 40 kg/m^2 and weight from about 96 kg to 98 kg. The protocol encouraged all participants to go on a reduced-calorie diet and be physically active.

The proportion who lost 5% or more of body weight was 44% with orlistat but 54%-76% with liraglutide.

DR. ASTRUP

The proportion of participants who lost 5% or more of body weight was 44% with orlistat but ranged from 54% to 76% with the liraglutide doses; and 28% of those on the highest dose lost more than 10% of their body weight. Waist circumference also went down significantly relative to placebo at the two highest liraglutide doses.

Pulse rates increased by up to four beats per minute with liraglutide but declined with placebo and orlistat. Mean systolic blood pressure decreased 5.6-8.8 mm Hg in the liraglutide groups, and declined 4 mm Hg with placebo and 5.4 mm Hg with orlistat.

Four patients had hypoglycemic symptoms with liraglutide. None required assistance. The most common events were nausea and vomiting. "In all the doses except the highest, [nausea] came down to the placebo level over time," Dr. Astrup said. A phase III trial is planned.

Dr. Astrup disclosed being a consultant to Novo Nordisk and receiving financial support for serving on advisory boards relative to liraglutide. The investigators also included Novo Nordisk employees, one of whom was a shareholder in the company, and other scientists who had received financial support and/or served on advisory boards. ■

Pages 14a—14b