More Weight Lost With Liraglutide Than Orlistat

B JANE SALDOF MACNEIL, Senior Editor

PHOENIX — Liraglutide, an investigational drug given once a day, produced significantly more weight loss than orlistat in a randomized, 2-week, placebo-controlled trial of overweight or 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 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.

“Another 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 the 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 US 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 reviews 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/m² to 40 kg/m² 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 of participants who lost more than 5% of body weight was 44% with orlistat but 54%-76% with liraglutide.

DR. ASTRUP

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

was in the mid-40s (range 18-65 years).

Body mass index ranged from 30 kg/m² to 40 kg/m² 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 of participants who lost more than 5% of body weight was 44% with orlistat but 54%-76% with liraglutide.

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 by 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 is shown to the placebo group 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 noted that two employees, one of whom was a shareholder in the company, and other scientists who had received financial support and/or served on advisory boards.