Nasal Spray Formulation of Teriparatide Is in the Works

By Patrice Wending
Chicago Bureau

CHICAGO — A nasal spray formulation of the osteoporosis drug teriparatide has cleared its first scientific hurdle.

Inhalable parathyroid hormone (PTh1-34) demonstrated a similar absorption profile as the approved injectable product, Forteo, in a phase I, pharmacokinetics study. Dr. Gordon Brandt and colleagues reported in a poster at the annual meeting of the American Association of Clinical Endocrinologists.

Twelve healthy men and women, ages 20-40 years, received a 25-ng injection of teriparatide on day 1, followed by single doses of the nasal spray on 4 subsequent days. Two nasal formulations of teriparatide were evaluated: Formulation No. 1 was given at 200 mcg and 400 mcg, and No. 2 at 500 mcg and 1,000 mcg. Blood samples were taken up to 4 hours post treatment.

The times of maximal drug concentration for teriparatide nasal spray and Forteo were not statistically different, reported Dr. Brandt, executive vice president, clinical research and medical affairs, Nastech Pharmaceutical Co., Bothell, Wash., who sponsored the study.

While Forteo achieves a 50-pg/ml peak blood level after subcutaneous administration, the tested doses of nasal spray delivered up to 400 pg/ml peak blood level, Dr. Brandt said in an interview. “In this first-in-man study, we administered higher doses than are required, so in subsequent studies we will adjust the doses,” he said.

Single-Dose Zoledronic Acid Rapidly Improves Bone Markers

By Nancy Walsh
New York Bureau

TORONTO — A single intravenous dose of zoledronic acid reduced markers of bone resorption in postmenopausal women more rapidly and to a greater extent than did weekly oral alendronate, Dr. Kenneth Saag reported in a poster session at a world congress on osteoporosis.

Zoledronic acid is the most powerful of the available bisphosphonates, and its long duration of effect now has been shown in a multicenter double-blind trial that randomized 118 women aged 45-79 years to a single infusion of 5 mg zoledronic acid or 70 mg weekly oral alendronate for 24 weeks. Patients receiving IV zoledronic acid also received oral placebo, and those receiving oral alendronate also received IV placebo.

In the zoledronic acid group, mean urine cross-linked N-telopeptide of type I collagen (NTX) fell from 46.1 to 15.2 nmol bone collagen equivalent (BCE)/mmol creatinine at week 1, while the level of this marker of bone turnover fell from 45.8 to 35.5 nmol BCE/mmol creatinine in the alendronate group at 1 week. The greater reduction in urine NTX with zoledronic acid was significant and persisted throughout the 24 weeks of the study, according to Dr. Saag of the division of rheumatology, University of Alabama, Birmingham.

Levels of bone-specific alkaline phosphatase (BSAP) also decreased from baseline throughout week 24 in both groups. While reductions in BSAP levels were significantly greater in the zoledronic acid group at week 12, levels in both groups were within the pre-menopausal range of 6-12.8 ng/ml.

Overall, 91% of patients in the zoledronic acid group and 86% of those in the alendronate group experienced an adverse event. During the first 3 days after drug initiation, flu-like symptoms led to a greater frequency of adverse events in the zoledronic acid group than in the alendronate group (46% vs. 37%), but after 3 days the adverse event rates were similar in the two groups, Dr. Saag said.

Serious adverse events were reported by two patients in the zoledronic acid group (one report of osteoarthropathy and one of chest pain) and by none in the alendronate group (one report of patella fracture and two of osteoarthropathy). None of the reports was considered to be related to the treatment.

Patient preferences for the treatments also were analyzed, with study participants expressing a “strong preference” for the single infusion compared with the weekly regimen (66% vs. 20%), Dr. Robert Lindsay noted in another poster session at the meeting, which was sponsored by the International Osteoporosis Foundation.

Even among patients who experienced adverse events during the 3 days after the infusion, 74% expressed an overall preference for the single-dose treatment, according to Dr. Lindsay of the clinical research center, Helen Hayes Hospital, West Haverstraw, N.Y.

The study was funded by Novartis Pharma AG, Basel, Switzerland.