Cinacalcet Helps Dialysis Patients Achieve KDOQI Targets

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June 25, 2007 (Barcelona) — The calcimimetic agent cinacalcet counteracts secondary hyperparathyroidism (SHPT) and improves calcium and phosphorous metabolism in renal dialysis patients, according to data presented at the 44th congress of the European Renal Association–European Dialysis and Transplantation Association.

Patients taking cinacalcet were able to achieve metabolic targets established by the Kidney Disease Quality Outcomes Initiative (KDOQI), results that should also be attainable in real-world practice, said investigators Denis Fouque, MD, PhD, and Emanuel Zitt, MD, PhD.

However, only patients with mild SHPT showed sustained benefits after 12 months of therapy, indicating that use of cinacalcet should begin as soon as possible, said Dr. Zitt.

Disruptions of calcium and phosphorous homeostasis contribute to the bone and cardiovascular disease associated with end-stage renal disease, so better mineral metabolism may decrease morbidity and mortality among these patients, said the researchers. They presented the interim findings of a multicenter, pan-European observational study in which clinical practice data were collected on dialysis patients with SHPT before and after treatment with cinacalcet.

In this analysis, the investigators studied the effect of cinacalcet according to severity of SHPT. Mild disease was defined as serum intact parathyroid hormone (iPTH) levels ranging from 300 to 499 pg/mL, levels from 500 to 800 pg/mL were considered moderate disease, and anything over 800 pg/mL was deemed severe. The upper limit of normal is 65 pg/mL.

The analysis included data from 1638 patients, 58% men and 42% women, with a mean age of 58 years. Twenty-one percent of the patients had undergone a kidney transplant, and 31% more were on a transplant waiting list. Eight percent had undergone a parathyroidectomy. Almost all of the patients (91%) had been treated with some type of phosphate binder. Sevelamer was the phosphate binder most commonly used, followed by calcium-based binders, aluminum-based binders, and lanthanum carbonate.

Only patients with data going back at least 6 months before starting cinacalcet treatment were included in the analysis, said Dr. Fouque, who presented an overview of the study.

At baseline, defined as the time at which cinacalcet was initiated, the patients’ median serum iPTH levels were 76.5 pmol/L, with a range of 53.2 pmol/L and 112.7 pmol/L in the lowest and third-highest quartiles, respectively. These levels were higher than those seen 6 months previously, when the median iPTH was about 62 pmol/L. The median serum calcium was 2.4 mmol/L, and the median serum phosphorous was 1.9 mmol/L. The median calcium–phosphorous multiplication product (CaxP) was 4.6 mmol/L. These values did not differ significantly with severity of hyperparathyroidism.

Within 3 months of beginning cinacalcet treatment, the patients’ serum iPTH levels “did decrease nicely,” said Dr. Fouque. The levels fell steadily, decreasing by a median of 35% from baseline by month 3, 45% by month 6,
and 52% at month 12. Yet the resulting iPTH values did not quite achieve the KDQOI target levels.

Median serum calcium levels did decrease 8% from baseline by month 3, putting the patients within the KDQOI target range. The levels started rising again almost immediately, however, to a median of 7% and 5% less than baseline at months 6 and 12, respectively, although they remained at KDQOI target levels. Median serum phosphorous achieved KDQOI target levels by dropping 10% from baseline by month 3 and remaining constant for the remainder of the analysis.

Patients were started on a dose of 30 mg/day and slowly titrated upward until the desired results were achieved. By 6 months, 59% of the patients were receiving 60 mg or less per day, and only 1% required the maximum dose of 180 mg/day, said Dr. Fouque, professor of nephrology at the Hôpital Edouard Herriot Lyon in France.

“This prospective study confirms that cinacalcet can achieve KDQOI targets,” he maintained.

However, the degree of hyperparathyroidism must be accounted for when considering these results, noted Dr. Zitt, of the Academic Teaching Hospital Feldkirch and a research fellow in the clinical division of nephrology at the Medical University of Innsbruck, Austria. Only a minority of patients in any of the groups achieved target levels of iPTH or phosphorous, although more than 55% of patients in all groups achieved and maintained target calcium levels by 6 months. A similar pattern was seen with CaxP, for which more than 70% of patients in all groups were still at target levels by 6 months. By 12 months, only in the mildest group did more than 50% of the patients maintain these target levels. “These findings suggest that earlier use of cinacalcet might result in a higher response rate and better control of SHPT," said Dr. Zitt.

Danilo Fliser, MD, associate professor of medicine in the division of nephrology, Medical School Hannover, in Hannover, Germany, and cochair of the session at which these findings were presented, pointed out that 10% of the patients stopped taking cinacalcet at some point in the study. "That may have been due to the side effects, such as nausea and vomiting," Dr. Zitt said.

None of the speakers disclosed any relevant financial relationships.