These results are supplied for informational purposes only. Prescribing decisions should be made based on the approved package insert in the country of prescription.

NAME OF SPONSOR/COMPANY:

Genzyme Corporation, 500 Kendall Street, Cambridge, MA 02142
Bone Care International, Inc., Middleton, WI 53652 (Bone Care was acquired by Genzyme Corporation July 2005)

TITLE OF STUDY:

Protocol BCI-CH-110: Effect of High Pulse Dose Oral 1α -Hydroxyvitamin D_2 on Elevated Blood Parathyroid Hormone Levels in End Stage Renal Disease Patients on Hemodialysis

INVESTIGATORS AND STUDY CENTER(S):

This was a multi-center study conducted at two study sites in the United States.

STUDIED PERIOD:

First patient enrolled: 01 November 1995
Last patient completed: 08 May 1996

PHASE OF DEVELOPMENT:

Phase 2

OBJECTIVES:

To evaluate the efficacy and safety of high pulse Hectorol® (doxercalciferol capsules) as a therapy for secondary hyperparathyroidism in patients with Stage 5 Chronic Kidney Disease (CKD).

METHODOLOGY:

This was a Phase 2, open-label study in subjects who had completed Protocol BCI-CH-106**.** The study consisted of an 8-week washout period followed by oral Hectorol® treatment for up to 12 weeks or until intact parathyroid hormone (iPTH) levels were below 100 pg/mL.

NUMBER OF PATIENTS (PLANNED AND ANALYZED):

No. Enrolled: 12
No. Treated: 10
No. Completed: 10

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION:

Subjects included in this study were men and women, age 20 to 75 years, on three-times weekly hemodialysis treatment for at least four months, with a history of elevated iPTH values (>400 pg/mL), and had previously completed Protocol BCI-CH-106.

TEST PRODUCT, DOSE, AND MODE OF ADMINISTRATION:

Hectorol®: 1 mcg soft gelatin capsules
Dose: The initial dose was 10 mcg after each hemodialysis session (30 mcg/week).
Doses were administered orally.

DURATION OF TREATMENT:

8-week washout period followed by up to 12 weeks of treatment.

REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION:

Not applicable.

CRITERIA FOR EVALUATION:

Criteria for Evaluation - Efficacy:
Plasma iPTH response was evaluated for the test drug's efficacy.

Criteria for Evaluation - Safety:
Safety was evaluated on the basis of adverse events, serum calcium and serum phosphorus.

STATISTICAL METHODS:
Statistical significance was declared if the two-sided p-value was ≤ 0.05.

Statistical Methods - Efficacy:
Baseline values for plasma iPTH were defined as the data collected at the last visit during the washout period. At each post-baseline determination, the significance of the change from baseline for plasma iPTH was determined using either a paired t-test or a Wilcoxon one-sample test, as appropriate.

Statistical Methods - Safety:
All adverse experiences were recorded and their frequency determined.

Baseline values for serum calcium and phosphorus were defined as the data collected at the last visit during the washout period. At each post-baseline determination, the significance of the change from baseline for serum calcium and serum phosphorus was determined using either a paired t-test or a Wilcoxon one-sample test, as appropriate.

SUMMARY / CONCLUSIONS:

Summary / Conclusions - Demographics:
The 10 subjects who received treatment were between 28 and 73 years (mean = 53.6 years) and had been on hemodialysis treatment for at least 4 months (mean= 60.1months). Nine subjects were male and one was female. Nine (90.0%) of the subjects had received prior treatment with Iα,25$(OH)_2D_3$.

Summary / Conclusions – Efficacy:
At baseline, the mean plasma iPTH level was 820.2 pg/mL. Fifty percent of the subjects reached iPTH levels of < 100 pg/mL before the end of the study. This low iPTH value first occurred after 7 to 51 days on Hectorol® therapy. By the end of the study, the mean plasma iPTH was 322.8 pg/mL, a significant decrease of 60.6% ($p < 0.001$).

Summary / Conclusions - Safety Results:
Two treatment emergent adverse events occurred in two patients during the study. One serious, treatment emergent adverse event (chest pain) occurred in a single patient. The event resolved and was assessed as not related to study drug by the Investigator. The second treatment emergent adverse event was a non-serious event of hyperphosphatemia. The event was assessed as severe, resolved and was considered probably related to study drug by the Investigator. There was one episode of hypercalcemia (defined as serum calcium above 11.4 mg/dL). There were six episodes of hyperphosphatemia in four patients while on study drug.

Serum Calcium: The baseline mean serum calcium level was 8.79 mg/dL. At the end of treatment, the mean serum calcium was 9.62 mg/dL. The mean increase of 0.9 mg/dL during treatment was statistically significant ($p = 0.006$).

Serum Phosphorus: The mean serum phosphorus level at baseline was 5.38 mg/dL, compared to 4.98 mg/dL at the end of treatment ($p = 0.563$).

Clinical Chemistry and Hematology: There were no clinically significant changes in clinical chemistry or hematology measurements.

Based on report prepared on: 17 December 1997
Synopsis prepared on: 24 June 2006