8 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

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Safety

Disposition: As shown in the table below, 90% of placebo-treated subjects and 97% of cinacalcet-treated subjects experienced adverse events during the study.

Study 20000236: Disposition

	Placebo n (%)	Cinacalcet n (%)
Subjects evaluable for safety	31	30
Deaths on study	0 (0)	0 (0)
Severe adverse events*	3 (10)	11 (37)
Serious adverse events	3 (10)	1 (3)
Withdrawal due to adverse events	2 (6)	2 (7)
All adverse events	28 (90)	29 (97)

* Includes severe, life-threatening and fatal adverse events

Exposure: A total of 61 (30 cinacalcet, 31 placebo) received study medication (see table below). The mean (range) number of days of exposure to study drug was 106 (19 to 116) days for the cinacalcet group and 105 (22, 115) days for the placebo group. The mean (range) cumulative dose of cinacalcet was 7293.7 ( ) mg.

Study 20000236: Summary of Exposure to Study Drug

	Placebo (N=31)	Cinacalcet (N=30)
Number of days of exposure		
Mean	105.4	106.4
SD	19.9	20.0
Min, Max	22 , 115	19 , 116
Cumulative dose of cinacalcet (mg)		
Mean	0.0	7293.7
SD	0.0	3272.6
Min, Max		

Study 20000236: Summary of Exposure to Study Drug		
	Placebo	Cinacalcet
Dose compliance (%)		
Mean	98.1	95.0
SD	3.5	7.9
Min, Max		

Dosing Compliance (%) = 100 x (number of days dose taken / number of days prescribed).

Deaths: No deaths occurred during the study.

Serious Adverse Events: Serious adverse events were reported by 3 (10%) placebo-treated subjects and one (3%) cinacalcet-treated subjects. None of the serious adverse events occurred in more than one subject.

Subject Incidence of Serious Adverse Events by Preferred Term		
	Placebo	AMG 073
	(N = 31)	(N = 30)
	n (%)	n (%)
Subjects	3 (10)	1 (3)
Events		
Fever	0 (0)	1 (3)
Infection	0 (0)	1 (3)
Overdose-No Sequelae	1 (3)	0 (0)
Pain Chest, Non-Cardiac	1 (3)	0 (0)
Hypotension Postural	1 (3)	0 (0)
Cerebrovascular Disorder	1 (3)	0 (0)

Adverse Events Leading to Withdrawal: A total of 4 subjects withdrew from the study due to adverse events [2 (7%) from the cinacalcet group and 2 (6%) from the placebo group]. In the cinacalcet group, both withdrawals were due to hypocalcemia in one subject who had a baseline calcium of 10.2, and an initial low calcium of 7.3 mg/dL with symptoms at week 5, on the 70mg dose. He continued to have calcium levels from 7.3 – 8.2 mg/dL despite supplementation and ultimately withdrew from the study at week 15. A second subject, receiving cinacalcet withdrew from the study due to nausea and vomiting while on the 50mg dose. In the placebo group, one subject withdrew due to nausea and anorexia and a second subject withdrew due to a cerebrovascular event.

Adverse Events: Ninety-seven percent of subjects in the cinacalcet group and 90% of subjects in the placebo group reported at least 1 adverse event during the study (see table below). Ninety-seven percent of subjects in the cinacalcet group and 90% of subjects in the placebo group reported at least 1 adverse event during the study. The most common adverse events reported by cinacalcet-treated subjects were (cinacalcet, placebo) hypocalcemia (47%, 0%), nausea (27%, 23%), myalgia (23%, 23%), diarrhea (20%, 16%), and vomiting (17%, 10%).

20000236: Adverse Events, by Body System		
	Placebo	Cinacalcet
Subjects Receiving Dose	31	30
Subjects Reporting AEs	28 (90)	29 (97)
Events:		
Body as a whole	12 (39)	16 (53)

20000236: Adverse Events, by Body System		
	Placebo	Cinacalcet
Gastrointestinal	18 (58)	20 (67)
Nervous	13 (42)	12 (40)
Cardiovascular	5 (16)	0 (0)
Myo/Endo/Pericardial	1 (3)	1 (3)
Respiratory	9 (29)	6 (20)
Endocrine/Metabolic	7 (23)	16 (53)
Musculoskeletal	12 (39)	13 (43)
Infectious	2 (6)	2 (7)
Blood and Lymphatic	1 (3)	4 (13)
Skin and Appendages	6 (19)	5 (17)
Urinary Disorders	4 (13)	3 (10)
Reproductive	1 (3)	0 (0)
Vascular Disorders	1 (3)	0 (0)
Vision Disorders	2 (6)	2 (7)
Hearing / Vestibular	1 (3)	2 (7)
Psychiatric	2 (6)	1 (3)

Adverse Events of Special Interest:

Convulsions: There were no reports of seizure activity during the study.

GI Adverse Events: Gastrointestinal adverse events are common with cinacalcet treatment. Nausea was reported in 27% of cinacalcet-treated patients and 23% of placebo treated patients. Vomiting was reported in 17% of cinacalcet-treated patients and 10% of placebo-treated patients. Diarrhea was reported in 20% of cinacalcet-treated patients and 16% of placebo treated patients. Dyspepsia was reported in 4 (13%) of cinacalcet-treated subjects and 1 (4%) of placebo-treated subjects. There were no reports of esophagitis, gastritis or gastric ulcer.

Cataracts: Cataract formation associated with cinacalcet use was reported in animal studies. There were no reports of cataract in this trial.

Laboratory: Safety laboratory assessments were performed at screening and follow-up. Shift tables demonstrated no evidence of a treatment effect in hematologic and blood chemistry variables. Specific relevant laboratory evaluations are discussed below.

Serum Calcium: Mean (SE) serum calcium concentrations at baseline were 9.5 (0.1) mg/dL and 9.4 (0.1) mg/dL in the cinacalcet and placebo groups, respectively. At week 16, mean serum calcium concentrations were 8.3 mg/dL in the cinacalcet group and 9.3 mg/dL in the placebo group. These values represent a 13% decrease from baseline in the cinacalcet group and a 2% decrease in the placebo group.

Serum Phosphorus: The mean (SE) serum phosphorus concentrations at baseline were 4.2 (0.1) mg/dL in the cinacalcet group and 4.1 (0.1) mg/dL in the placebo group. Modest increases in serum phosphorus occurred in the cinacalcet group, reflective of reductions in plasma iPTH concentrations. At week 16, the mean (SE) serum phosphorus concentrations were 4.9 (1.2)

mg/dL in the cinacalcet group and 4.3 (1.2) mg/dL in the placebo group (normal range: 2.2 to 5.1 mg/dL).

Creatinine Clearance: The mean (SE) CrCl at baseline was 34.8 (1.6) mL/min in the cinacalcet group and 33.1 (1.9) mL/min in the placebo group. The mean CrCl was stable during the study in both treatment groups.

Ca x P: The mean (SE) Ca x P values at baseline were 39.6 (1.1) $(mg/dL)^2$ in the cinacalcet group and 38.9 (1.2) $(mg/dL)^2$ in the placebo group. Ca x P values and percentage change from baseline were similar between treatment groups throughout the study. At week 16, the mean (SE) Ca x P value was 41.0 (1.4) $(mg/dL)^2$ for the cinacalcet group and 40.0 (1.6) $(mg/dL)^2$ for the placebo group. At week 16, Ca x P had increased by 5% in the cinacalcet group and by 2% in the placebo group.

Vitamin D (1,25[OH]2D3): The mean (SE) 1,25(OH)2D3l at baseline was 31.3 (3.4) pg/mL in the cinacalcet group and 30.1 (2.9) pg/mL in the placebo group. The mean 1,25(OH)2D3 levels were stable during the study in both treatment groups.

Bone Alkaline Phosphatase (BALP): Median baseline BALP concentrations were 16.4 and 18.6 ng/mL in the cinacalcet and placebo groups, respectively (normal range: 2.9 to 20.1 ng/mL). At week 16, median BALP was 33% lower than baseline in the cinacalcet group and 6% higher than baseline in the placebo group.

Urine Calcium: Mean (range) baseline values for urine calcium excretion were below normal at baseline: 42.0 (4.2 to 228.6) mg/24 hours in the cinacalcet group and 39.7 (4.9 to 153.4) mg/24 hours in the placebo group (normal range: 50 to 300 mg/24 hours). At week 16, the mean 24-hour urine calcium values were increased from baseline in both treatment groups but remained in the normal range with mean values of 63.2 (10.2 to 303.9) and 49.7 (7.9 to 373.5) mg/24 hours in the cinacalcet and placebo groups, respectively.

Urine Phosphorus: Mean baseline 24-hour urine phosphorus excretion was 753.4 (range: 320.0 to 1244.0) mg/24 hours in the cinacalcet group and 683.7 (range: 291.0 to 1038.0) mg/24 hours for the placebo group (normal range: 400 to 1300 mg/24 hours). At week 16 (the end of the efficacy-assessment phase) the mean 24-hour urine phosphorus excretion was 759.4 (range: 119.0 to 3218.0) and 758.5 mg/24 hours (range: 278.0 to 1374.0) mg/24 hours in the cinacalcet and placebo groups, respectively.

Urine Protein: Mean (SE) 24-hour urine protein excretion at baseline was 2089 (325) mg/24 hours in the cinacalcet group and 2060 (531) mg/24 hours in the placebo group. At week 16, the corresponding values were 1643 (297) mg/24 hours in the cinacalcet group and 2385 (691) mg/24 hours in the placebo group. The mean percentage change from baseline at week 16 was a decrease of 12% (with a median decrease of 30%) in the cinacalcet group and an increase of 32% (with a median decrease of 16%) in the placebo group.

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