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All 24 subjects are included in the intent-to-treat analyses but excluded from the per-protocol analyses.

(2) Intent-to-Treat and Per-Protocol Analyses

Intent-to-treat analyses include data from all 62 subjects who received 1α-OH-D_2. Per-protocol analyses include data on 38 subjects, and exclude data on the 24 subjects identified above.
Of the 104 patients enrolled in the study, 62 (55.6%) were admitted to the treatment protocol; 38 (36.5% of those enrolled, 61.3% of those admitted to protocol) were considered in the analyses.

b. Memphis

(1) Premature Terminations

Fifteen (19.7%) of the 76 subjects who entered the treatment period were discontinued prematurely from the study or were determined to be non-evaluable.

Seven subjects were discontinued during Treatment Period 1 as follows: two subjects (Subject Nos. 06106 and 13109) voluntarily withdrew, both experiencing GI symptoms; two subjects (Subject Nos. 15105 and 16111) transferred to another dialysis unit; Subject No. 13105 had a parathyroidectomy performed; Subject No. 18114 regularly received Basogel, an aluminum-based phosphate binder; Subject No. 19120 was discontinued for persistent hyperphosphatemia of dietary origin. **Three of the 7 should be considered "treatment failures."**

Four subjects were discontinued during Treatment Period 2 as follows: three subjects (Subject Nos. 16115, 16127, and 18103) died as a result of chronic medical conditions; one subject (Subject No. 17103) transferred to another dialysis unit.

Four subjects (Subject Nos. 16117, 17101, 17110, and 18102) completed the 32-week study but were determined to be non-evaluable based on an average serum phosphorous greater than 6.9 mg/dL during the two treatment periods. **All 4 are considered "treatment failures."**

All fifteen subjects are included in the intent-to-treat analyses but excluded from the per-protocol analyses.

(2) Intent-to-Treat and Per-Protocol Analyses
Of the 108 subjects enrolled, 76 (70.4%) were admitted to the treatment protocol; 96 (46.7% of those enrolled, 71.7% of those admitted to protocol) were subjected to per-protocol analyses.

c. Both Sites
Of the 212 subjects enrolled in both locations, 138 (65.1%) were admitted to the study protocol; 96 (46.7% of those enrolled, 71.7% of those admitted to protocol) were subjected to per-protocol analyses. There were marked differences in discontinuations between the two locations.

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2. Enrollment Demographic Data

a. Los Angeles

TABLE 1: SUMMARY OF DEMOGRAPHIC DATA FOR CLINICAL STUDY NO. H-108-LA.

Patient Group	*n*	Age at Enrollment	Post HD Weight at Baseline	Months on HD	Prior Rx w/Calcitriol	Sex	Race
All Patients Evaluated (Total Pool)	865						
Mean		55.7	NA	42.0	Y= 413	M= 481	AA= 262
SD		17.8	NA	53.8	N= 452	F= 384	A= 68
Range		0-92	NA	0.2-359			C= 302
							H= 211
All Patients Not Randomized	761						
Mean		56.3	NA	41.5	Y=327	M=421	AA=205
SD		17.8	NA	53.8	N=434	F=340	A=68
Range		0-92	NA	0.2-359			C=268
							H=199
All Patients Enrolled and Randomized To Drug	53						
Mean		52.9	NA	35.9	Y= 44	M= 30	AA= 27
SD		14.9	NA	34.8	N= 9	F= 23	A= 0
Range		23 -75	NA	4 - 139			C= 19
							H= 7
All Patients Enrolled and Randomized to Placeb	51						
Mean		49.9	NA	55.3	Y= 42	M= 30	AA= 30
SD		16.1	NA	54.4	N= 9	F= 21	A= 0
Range		22 - 81	NA	5-206			C= 15
							H= 5
All Intent to Treat Patients on Drug	30						
Mean		54.5	74.8	37.0	Y= 25	M= 17	AA= 17
SD		13.6	19.2	37.5	N= 5	F= 13	A= 0
Range		30-75	43.7-135.4	4-139			C= 10
							H= 3
All Intent to Treat Patients on Placebo	32						
Mean		49.7	71.1	67.8	Y= 26	M= 17	AA= 19
SD		15.8	18.6	59.1	N= 6	F= 15	A= 0
Range		22-73	36.5-130.8	7-206			C= 9
							H= 4
All Valid Completers on Drug	17						
Mean		54.0	73.9	36.5	Y= 14	M= 10	AA= 9
SD		14.3	21.8	38.2	N= 3	F= 7	A= 0
Range		30-75	43.7-135.4	4-139			C= 7
							H= 1
All Valid Completers on Placebo	21						
Mean		54.3	71.1	64.6	Y= 17	M= 8	AA= 15
SD		14.1	21.2	57.2	N= 4	F= 13	A= 0
Range		22-73	36.5-130.8	7-180			C= 4
							H= 2

The valid completer subjects were between 22 and 75 years old (mean ± SE = 52.0 ± 1.9 years) and had been on hemodialysis treatment for at least 4 months (mean ± SE = 52.9 ± 6.6 months). **I note, however, that the patients randomized to placebo had been on dialysis longer than those placed on active drug, which**

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suggests that they may have had longer lasting or more serious disease and introduces a bias in distribution. Thirty-four subjects were male and 28 female; 36 were Afro-American, 19 Caucasian, and 7 Hispanic. Fifty-one (82.3%) of the subjects had received prior treatment with oral or i.v. 1α,25-$(OH)_2D_3$. Of these 62 subjects, 38 completed the study and were evaluable for statistical purposes. All 38 subjects received open-label treatment with the active test medication during Treatment Period 1 (Weeks 1 - 15). Seventeen (44.7%) of these subjects received continued active medication during Treatment Period 2 (Weeks 16 - 23) and 21 (55.3%) received placebo. A comparison of the treatment groups at baseline with regard to physical and biochemical characteristics is shown in the table below.

The significant differences between the treatment groups included:

a) mean serum calcium was higher in those subsequently in the placebo group (P=0.04),

b) those on placebo had been on dialysis for 64.57 ± 12.47 months in contrast to those on drug, 36.53 ± months (P=0.09).

c) the patients subsequently assigned to placebo had lower serum levels of 1,25-diOH Vitamin D_3 than did those to active drug (P=0.06).

Table 2: COMPARISON OF TREATMENT GROUPS AT BASELINE (LOS ANGELES)

Characteristic	Active Treatment (n = 17)	Placebo Treatment (n = 21)	Difference (P value)
Age	54.00 ± 3.48	54.33 ± 3.07	P = .94
Sex			
Male	n = 10	n = 8	
Female	n = 7	n = 13	
Race			
African-American	n = 9	n = 15	
Caucasian	n = 7	n = 4	
Hispanic	n = 1	n = 2	
Weight (post hemodialysis)	73.88 ± 5.28	71.11 ± 4.62	p = .69
Months on hemodialysis	36.53 ± 9.27	64.57 ± 12.47	p = .09
Prior treatment with calcitriol	n = 14	n = 17	
Phosphate binder dosage	1737.35 ± 243.52	1367.67 ± 138.03	p = .18
Plasma PTH	832.47 ± 123.36	696.58 ± 67.06	p = .32
Serum calcium	8.79 ± 0.19	9.25 ± 0.11	p = .04
Serum phosphorus	4.98 ± 0.15	4.71 ± 0.26	p = .41
BUN	59.29 ± 3.65	57.52 ± 4.17	p = .76
Serum creatinine	10.14 ± 0.79	11.03 ± 0.70	p = .40
Serum alkaline phosphatase	222.59 ± 71.93	154.71 ± 16.73	p = .32
Serum albumin	4.07 ± 0.08	4.07 ± 0.06	p = .99
Serum 1α,25-$(OH)_2D_2$	5.03 ± 0.03	5.05 ± 0.05	p = .72
Serum 1α,25-$(OH)_2D_3$	11.94 ± 0.66	10.66 ± 0.36	p = .06
Serum osteocalcin	72.12 ± 7.98	68.19 ± 5.35	p = .68
Bone-specific alkaline phosphatase	75.35 ± 30.22	45.65 ± 7.25	p = .30

B. Memphis

TABLE 3: SUMMARY OF DEMOGRAPHIC DATA FOR CLINICAL STUDY NO.H-108-MEMPHIS

Patient Group	*n*	Age at Enrollment	Post HD Weight at Baseline	Months on HD	Prior Rx w/Calcitriol	Sex	Race
All Patients Evaluated (Total Pool)	1000						
Mean		54.6	NA	43	Y= 531	M= 470	AA= 892
SD		15.1	NA	49.4	N= 469	F= 530	A= 2
Range		16-92	NA	0.1-321			C= 99
							H= 0
All Patients Not Randomized	893						
Mean		54.8	NA	41.9	Y=438	M=417	AA=787
SD		15.1	NA	49.4	N=455	F=476	A=2
Range		16-92	NA	0.1-321			C=97
							O=7
All Patients Enrolled and Randomized To Drug	53						
Mean		54.4	NA	50.3	Y= 45	M= 26	AA= 51
SD		12.4	NA	50.5	N= 8	F= 27	A= 0
Range		26-84	NA	3-231			C= 2
							O= 0
All Patients Enrolled and Randomized to Placebo	54						
Mean		50.7	NA	54.6	Y= 48	M= 27	AA= 54
SD		13.4	NA	50.7	N= 6	F= 27	A= 0
Range		25-75	NA	4-251			C= 0
							H= 0
All Intent to Treat Patients on Drug	41						
Mean		55.2	84.7	50.6	Y= 34	M= 18	AA= 40
SD		11.7	20.7	49.1	N= 7	F= 23	A= 0
Range		32-74	54.6-153.0	4-231			C= 1
							H= 0
All Intent to Treat Patients on Placebo	35						
Mean		49.0	75.8	61.5	Y= 30	M= 16	AA= 35
SD		14.4	21.6	55.8	N= 5	F= 19	A= 0
Range		27-75	31.8-132.5	7-251			C= 0
							H= 0
All Valid Completers on Drug	31						
Mean		55.1	83.1	53.7	Y= 26	M= 11	AA= 31
SD		11.9	18.7	51.1	N= 5	F= 20	A= 0
Range		32-74	54.6-124.4	4-231			C= 0
							H= 0
All Valid Completers on Placebo	30						
Mean		48.4	78.9	52.0	Y= 28	M= 15	AA= 30
SD		14.5	21.1	40.4	N= 2	F= 15	A= 0
Range		27-75	43.4-132.5	7-148			C= 0
							H= 0

The valid completers at this site were similar to those at the LA site in that they were between 27 and 75 years old and had been on dialysis for a similar length of time. The Memphis group, however, did not show any difference between drug and placebo groups seen in the LA group in time on dialysis. All subjects at this site, however, were Afro-American, in contrast to the racial mix in the LA group.

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Table 4: COMPARISON OF TREATMENT GROUPS AT BASELINE
H-108 Memphis

Characteristic	Active Treatment (n = 31)	Placebo Treatment (n = 30)	Difference (P value)
Age	55.13 ± 2.13	48.37 ± 2.65	p = .05
Sex			
Male	n = 11	n = 15	
Female	n = 20	n = 15	
Race			
African-American	n = 30	n = 30	
Caucasian	n = 1	n = 0	
Weight (post hemodialysis)	83.13 ± 3.36	78.87 ± 3.86	p = .41
Months on hemodialysis	53.65 ± 9.18	51.97 ± 7.37	p = .89
Prior treatment with calcitriol	n = 26	n = 28	
Phosphate binder dosage	2052.58 ± 205.47	2235.03 ± 215.43	p = .54
Plasma PTH	961.42 ± 111.91	1009.43 ± 94.00	p = .75
Serum Ca	9.02 ± 0.11	8.99 ± 0.16	p = .86
Serum P	4.66 ± 0.15	4.90 ± 0.19	p = .33
BUN	59.94 ± 3.19	60.47 ± 2.63	p = .90
Serum Creatinine	11.90 ± 0.52	12.58 ± 0.70	p = .43
Serum alkaline phosphatase	208.29 ± 33.50	205.93 ± 35.80	p = .96
Serum albumin	4.05 ± 0.05	4.07 ± 0.07	p = .84
Serum 1α,25-$(OH)_2D_2$	5.01 ± 0.01	5.27 ± 0.19	p = .17
Serum 1α,25-$(OH)_2D_3$	10.80 ± 0.53	10.17 ± 0.13	p = .25
Serum osteocalcin	73.24 ± 7.87	81.28 ± 6.57	p = .44
Bone-specific alkaline phosphatase	57.98 ± 8.63	70.70 ± 15.00	p = .47

3. Medication

1. Dosing Compliance

Overall dosing compliance was above 80% for all evaluable subjects; mean (± SE) compliance was 99.0 ± 0.5%.

All subjects initiated 1α-OH-D_2 dosing in the dialysis unit at the rate of 10.0 μg (four 2.5 μg capsules) three times per week following hemodialysis. This dosage was adjusted, as needed, in order to bring the plasma PTH levels into the targeted range (150 to 300 pg/mL, inclusive). Subjects whose plasma PTH levels fell below 150 pg/mL immediately suspended test drug dosing and resumed dosing at one level below the previous dosage beginning at the mid-week hemodialysis of the following

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week. Conversely, subjects whose plasma PTH levels rose from the targeted range of 150 to 300 pg/mL increased their test drug dosage by one level at the next hemodialysis, provided that (1) the serum phosphorus level was ≤ 6.9 mg/dL, and (2) all dosage increases to levels greater than 10 μg per dialysis were followed by an 8-week evaluation period prior to further increases.

Beginning at Week 8, at the discretion of the Investigator, the dosage could be increased by up to 5.0 μg per hemodialysis for plasma PTH values that were not in the target range (150-300 pg/mL) and remained greater than 50% of the baseline value (defined as the average of values obtained during Weeks -2, -1 and 0). This increase was contingent on a serum phosphorus value ≤ 6.9 mg/dL at the time of the determining PTH value. If the phosphorus level was > 6.9 mg/dL, a dosage increase was considered based on the plasma PTH value obtained at the next opportunity when the phosphorus was ≤ 6.9 mg/dL. All dosage increases above 10.0 μg per dialysis were followed by an 8-week evaluation period prior to considering the subject for another increase of up to 5.0 μg per hemodialysis, to a maximum dosage of 20.0 μg per hemodialysis.

The allowed levels of test drug dosages are shown below:

Table 5. Dosing Regimen Table

Dosage Level	Dosing Regimen	Number of Capsules	Weekly Dosage (μg)
A (Maximum)	20.0 μg after each hemodialysis session	8	60.0
B	17.5 μg after each hemodialysis session	7	52.5
C	15.0 μg after each hemodialysis session	6	45.0
D	12.5 μg after each hemodialysis session	5	37.5
E (Initial Starting Dose)	10.0 μg after each hemodialysis session	4	30.0
F	7.5 μg after each hemodialysis session	3	22.5
G	5.0 μg after each hemodialysis session	2	15.0
H (Minimum)	2.5 μg after each hemodialysis session	1	7.5

Subjects who developed marked hypercalcemia (serum calcium > 11.2 mg/dL) or confirmed, marked hyperphosphatemia (two consecutive serum phosphorus values > 8.0 mg/dL) or a *persistent* serum calcium (mg/dL) X serum phosphorus (mg/dL) product > 75.0 immediately suspended treatment. ("Persistent" was defined as having a duration of three consecutive weeks.) Such subjects were monitored until the serum calcium and/or phosphorus were sufficiently lowered (serum calcium ≤ 10.5 mg/dL, serum phosphorus ≤ 6.9 mg/dL, and serum calcium X serum phosphorus product ≤70.0) and resumed test drug dosing at a rate which was one level below the previous dosage.

At the Investigator's discretion, the dosage of calcium-based dietary phosphate binders could be adjusted up or down to correct for moderate hyperphosphatemia (serum phosphorus > 6.9 to ≤ 8.0 mg/dL) or mild hypercalcemia (serum calcium > 10.5 to ≤ 11.2 mg/dL), respectively. In the case of *persistent* mild hypercalcemia and hyperphosphatemia when the phosphate binders could not be adjusted (i.e.,

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when serum calcium and serum phosphorus were both elevated), or of a serum calcium (mg/dL) X serum phosphorus (mg/dL) product *persistently* > 70.0, the dosage of test drug was reduced to a rate of one level below the previous dosage. In such this case, attention was given to ascertaining the cause of the hypercalcemia or hyperphosphatemia (e.g., dietary indiscretion or inappropriate dosage of calcium-based phosphate binders).

As during the washout period, the dietary phosphate binders were adjusted at the discretion of the Investigator to bring the serum phosphorus to a target range of 4.0 to 6.0 mg/dL.

If one of the dosage levels in the study was not optimum for maintenance dosing for a given subject (i.e., maintaining the plasma PTH in the target range), the Investigator, at his discretion, could vary the dosage administered at each hemodialysis according to a defined schedule (e.g., 2.5 μg at the first weekly dialysis and 0.5 μg at each of the subsequent dialyses) so that the total weekly dosage was optimized to the subject's needs.

The average (± SE) weekly prescribed dose progressively declined during Treatment Period 1 from 29.7 ± 0.3 μg for Week 0 to 16.1 ± 2.3 μg for Week 16 ($P < 0.001$). (The average prescribed weekly dose for Week 0 was less than 30.0 μg because five subjects started dosing on the second or third hemodialysis of Week 0 rather than on the first hemodialysis.) The average prescribed dose further decreased in subjects who continued treatment with active drug during Treatment Period 2 from 19.0 ± 4.1 for Week 16 to 15.3 ± 3.8 at Week 23. However, the average prescribed dose for subjects switched to placebo treatment rose from 13.8 ± 2.4 μg for Week 16 to 28.5 ± 2.6 for Week 23.

The primary reasons for suspensions and subsequent decreases in prescribed doses were over-suppression of plasma PTH (most common) and elevations of serum calcium and/or serum phosphorus. In a few cases, dosing with test medication was suspended for intercurrent illness and restarted, when possible, at the same level.

2. The following tables show the average weekly doses of drug administered in the two studies during the open label and placebo controlled phases

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TABLE 6: AVERAGE WEEKLY DOSES (μg) - PERIOD 1

WEEK NO. →		BASE	1	2	3	4	5	6	7	8
L.A.										
Per Protoc	N	38	38	38	38	38	38	38	38	38
	Mean	28.9	29.7	28.0	25.9	25.0	22.8	19.9	19.3	20.1
	SD	3.1	1.6	4.9	8.2	7.5	7.5	10.1	11.4	13.5
	SE	0.5	0.3	0.8	1.3	1.2	1.2	1.6	1.8	2.2
	Range	10.0-30.0	0.0-30.0	10.0-30.0	7.5-30.0	7.5-30.0	0.0-30.0	0.0-30.0	0.0-45.0	0.0-45.0
I.t.T.	N	62	61	60	60	58	58	58	58	58
	Mean	28.7	28.7	27.8	25.5	24.1	22.2	20.2	20.4	20.8
	SD	3.8	5.0	5.0	8.5	8.6	9.1	10.6	11.4	13.7
	SE	0.5	0.6	0.6	1.1	1.1	1.2	1.4	1.5	1.8
Memphis										
Per Protoc	N	61	61	61	61	61	61	61	61	61
	Mean	28.4	29.2	28.2	24.0	24.2	22.3	21.4	21.4	24.1
	SD	3.7	2.8	4.9	8.7	8.8	10.2	10.3	10.3	13.1
	SE	0.5	0.4	0.6	1.1	1.1	1.3	1.3	1.3	1.7
	Range	10.0-30.0	0.0-30.0	0.0-30.0	0.0-30.0	0.0-30.0	0.0-30.0	0.0-30.0	0.0-30.0	0.0-30.0
I.t.T.	N	76	76	76	75	75	73	73	73	72
	Mean	28.0	28.0	26.9	24.0	23.5	21.8	20.5	20.5	22.9
	SD	4.6	5.9	7.3	8.8	9.6	10.4	10.8	11.1	13.9
	SE	0.5	0.7	0.8	1.0	1.1	1.2	1.3	1.3	1.6

WEEK NO. →		9	10	11	12	13	14	15	16
L.A.									
Per Protoc	N	38	38	38	38	38	38	38	38
	Me	18.3	16.8	18.3	18.7	18.9	16.3	16.3	14.2
	SD	14.5	14.7	15.1	15.5	15.1	13.0	13.6	12.2
	SE	2.4	2.4	2.4	2.5	2.5	2.1	2.2	2.0
	Ra	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0
I.t.T.	N	55	55	55	54	53	53	53	51
	Me	19.7	18.7	18.3	18.4	19.8	16.7	17.5	14.8
	SD	15.0	15.3	14.8	15.0	15.1	13.0	14.2	12.8
	SE	2.0	2.1	2.0	2.0	2.1	1.8	1.9	1.8
Memph									
Per Protoc	N	61	61	61	61	61	61	61	61
	Me	24.9	25.4	24.0	24.0	21.2	21.5	20.0	19.5
	SD	13.7	14.5	15.2	14.2	14.4	15.0	15.2	16.3
	SE	1.8	1.9	2.0	1.8	1.8	1.9	1.9	2.1
	Ra	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0	0.0-45.0
I.t.	N	72	71	71	71	71	71	69	69
	Me	23.3	24.6	23.9	23.7	20.9	21.0	19.6	19.2
	SD	14.6	14.8	15.0	14.3	14.5	15.0	15.0	16.1
	SE	1.7	1.8	1.8	1.7	1.7	1.8	1.8	1.9

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TABLE 7: AVERAGE WEEKLY DOSE (μg) - Period II- Drug Group

WEEK NO. →		16	17	18	19	20	21	22	23	24
L.A.										
Per Protoc	N	17	17	17	17	17	17	17	17	
	Mean	15.9	17.5	18.1	17.5	17.6	17.9	18.4	15.3	
	SD	13.0	16.5	16.0	16.2	16.9	16.5	16.1	15.8	
	SE	3.2	4.0	3.9	3.9	4.1	4.0	3.9	3.8	
	Range	0.0-45.0	2.5-60.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	2.5-60.0	0.0-60.0	
I.t.T.	N	26	26	26	26	26	26	26	25	
	Mean	16.0	17.1	18.3	16.7	16.6	17.1	18.4	13.2	
	SD	13.3	14.8	15.4	15.5	14.6	14.4	14.8	15.0	
	SE	2.6	2.9	3.0	3.0	2.9	2.8	2.9	3.0	
Memph										
Per Protoc	N	31	31	31	31	31	31	31	231	
	Mean	19.3	19.4	17.3	16.4	18.6	18.3	16.7	16.4	
	SD	16.7	15.5	13.7	14.2	14.9	15.9	16.4	15.6	
	SE	3.0	2.8	2.5	2.6	2.7	2.9	2.9	2.8	
	Range	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	
I.t.T.	N	37	36	36	36	36	35	35	35	
	Mean	18.2	18.3	16.5	15.6	17.4	18.1	16.5	15.5	
	SD	16.0	15.1	13.3	14.0	14.8	15.5	16.4	15.4	
	SE	2.6	2.5	2.2	2.3	2.5	2.6	2.8	2.6	

TABLE 8: AVERAGE WEEKLY DOSE (μg) - Period II- Placebo Group

WEEK NO. →		16	17	18	19	20	21	22	23	24
L.A.										
Per Protoc	N	21	21	21	21	21	21	21	21	
	Mean	12.9	15.4	18.0	21.4	22.9	24.4	27.7	28.0	
	SD	11.6	12.6	12.5	13.1	13.6	13.6	13.3	12.1	
	SE	2.5	2.8	2.7	2.9	3.0	3.0	2.9	2.6	
	Range	0.0-45.0	0.0-45.0	0.0-45.0	0.0-50.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	
I.t.T.	N	27	26	26	26	26	25	25	25	
	Mean	13.9	16.3	18.5	21.3	21.5	23.1	26.1	25.8	
	SD	12.4	13.9	13.6	14.0	13.4	13.9	13.9	13.5	
	SE	2.4	2.7	2.7	2.8	2.6	2.8	2.8	2.7	
Memph										
Per Protoc	N	30	30	30	30	30	30	30	30	
	Mean	19.8	21.5	22.6	23.8	26.5	27.2	28.2	28.3	
	SD	16.1	18.1	17.8	17.3	17.8	16.0	17.7	16.3	
	SE	2.9	3.3	3.3	3.2	3.3	2.9	3.2	3.0	
	Range	0.0-45.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	0.0-60.0	
I.t.T.	N	32	31	31	31	31	31	30	30	
	Mean	20.3	21.1	22.2	23.5	25.8	26.8	28.2	28.3	
	SD	16.3	18.0	17.7	17.0	17.9	15.9	17.7	16.3	
	SE	2.9	3.2	3.2	3.1	3.2	2.9	3.2	3.0	

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c. Phosphate Binder Dosages

The phosphate binders during this study were calcium carbonate and calcium acetate. The daily doses of phosphate binders were calculated from the subjects' reports of intake, There were inconsistencies between the sites' reporting of binder dosages and the dosage units available for the brand of product. If the inconsistencies were not resolved, dosages of elemental calcium were derived from the content listed in the *Physician's Desk Reference* 1997.

I find no record of how many "inconsistencies" occurred nor of how often imputed estimates of calcium intake were used. Thus, the table listing "calcium intake" contains data of questionable validity and these data certainly do not warrant the statistical precision or even analysis presented. Unfortunately, this also opens to question the significance of the efficacy data for the investigational drug!

(1) In the Los Angeles Study, the estimated intake of phosphate binder averaged 1533 ± 135 (mean ± SE) mg of elemental calcium/day at baseline (as shown in the table below). At the end of Treatment Period 1 (Week 16), the average phosphate binder dosage was 1847± 179 mg of elemental calcium/day. The change was statistically significant (P = 0.026). The average phosphate binder dosages remained unchanged in both treatment groups during Treatment Period 2, ranging from 1987 ± 280 mg and 1728 ± 235 mg of elemental calcium/day at Week 16 to 2119 ± 296 mg (P = 0.294) and 1703 ± 178 mg (P = 0.873) at Week 24 for subjects receiving active drug and placebo, respectively. No significant difference was observed in binder doses between active and placebo treatment groups at Week 16 (P = 0.480) or at Week 24 (P = 0.217). **In view of the questionable estimates of calcium intake, the conclusions drawn by the Sponsor are not warranted and the statistical analysis is not valid.**

Table 9: L.A. : Milligrams of Elemental Calcium per Day

		Treatment Period 1	Treatment Period 2	
			Active	Placebo
	n	38	17	21
Baseline:	mean	1533.1	1737.4	1367.7
	SD	828.8	1004.1	632.5
	SE	134.5	243.5	138.0
Week 16:	mean	1847.1	1986.9	1728.3
	SD	1091.2	1152.8	1051.0
	SE	179.4	279.6	235.0
	P-value Baseline:	0.026	0.161	0.092
	P-value comparison to placebo:		0.480	
Week 24:	mean		2118.6	1702.5
	SD		1219.2	815.7
	SE		295.7	178.0
	P-value Week 16:		0.294	0.873
	P-value comparison to Placebo:		0.217	

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(2) In the Memphis Study, as shown in the table below, the phosphate binder dose level averaged 2,142 ± 148 (mean ± SE) mg of elemental calcium/day at baseline. At the end of Treatment Period 1 (Week 16), the average phosphate binder dosage was 2,340 ± 162 mg of elemental calcium/day. This change during the 16 weeks of open-label treatment with 1α-OH-D_2 was statistically insignificant ($P = 0.210$). A decrease in average phosphate binder dosages was observed in subjects receiving active drug in Treatment Period 2, from 2,305 ± 207 mg of elemental calcium/day at Week 16 to 1,911 ± 245 mg at Week 24 ($P < 0.006$). For subjects randomized to placebo, there was an increasing trend in average phosphate binder dosage from 2,375 ± 255 mg of elemental calcium/day at Week 16 to 2,696 ± 369 mg at Week 24 ($P = 0.296$). No significant difference was observed in phosphate binder doses between active and placebo treatment groups at Week 16 ($P = 0.831$) at Week 24 ($P = 0.080$). **See comments under Section (1) above. The observations in the Memphis Study are, furthermore, different from those seen in the LA Study.**

Table 10: Memphis: Milligrams of Elemental Calcium per Day

		Treatment Period 1	Treatment Period 2	
			Active	Placebo
	n	61	31	30
Baseline:	mean	2142.3	2052.6	2235.0
	SD	1155.8	1144.0	1180.0
	SE	148.0	205.5	215.4
Week 16:	mean	2339.7	2305.1	2375.4
	SD	1267.8	1149.8	1398.4
	SE	162.3	206.5	255.3
	P-value Baseline:	0.210	0.460	0.304
	P-value comparison to placebo:		0.831	
Week 24:	mean		1910.7	2696.4
	SD		1366.5	2023.3
	SE		245.4	369.4
	P-value Week 16:		0.006	0.296
	P-value comparison to Placebo:		0.080	

4. Laboratory Assessments

There was significant intra- and inter- individual variation in laboratory measurements during the washout period and during the two treatment periods. Such variation was expected in this population where concomitant illnesses and complications related to renal disease are common. Variation in laboratory measurements occurred most frequently in hematologic and electrolyte parameters, probably due to hemodialysis itself. Laboratory abnormalities in individual subjects were not discussed unless attributed to the use of the test medication or related to a serious adverse event. **True assessment of safety of the drug based on laboratory studies cannot be done with confidence, particularly in view of the small numbers of subjects, questionable validity of randomization, and short duration of observation.**

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a. Plasma PTH Results

(1) Los Angeles Area

Table 11: Per Protocol Patients - Placebo Group

Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
1101	[redacted]								
2106									
2108									
2115									
3101									
3102									
3110									
5102									
5108									
5109									
8101									
8102									
8107									
8109									
8111									
8114									
8117									
10102									
1010									
1010									
1010									
1010									
2110									
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)									
N	21	21	21	21	21	21	21	21	21
Mean	511.6	605.81	656.87	654.54	719.62	797.89	696.2	683.86	717.74
SD	382.72	385.9	338	361.12	375.05	420.84	313.53	385.83	288.67
SE	83.52	84.21	73.76	78.8	81.84	91.84	68.42	84.2	62.99

Subject	Base	1	2	3	4	5	6	7	8	9
1101	[redacted]									
2106										
2108										
2115										
3101										
3102										
3110										
5102										
5108										
5109										
8101										
8102										
8107										
8109										
8111										
8114										
8117										
10102										
10103										
10104										
10106										
10107										
21103										
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	21	21	21	21	21	21	21	21	21	21
Mean	696.58	511.34	430.68	399.11	334.28	286.51	362.45	352.41	332.25	349.4
SD	307.31	330.13	335.63	325.56	252.33	265.56	333.4	343.03	307.81	369.27
SE	67.06	72.04	43.24	71.04	55.06	57.95	72.75	74.85	67.17	80.58
P vs. Base		<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001

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Subject	10	11	12	13	14	15	16	17	18	19
1101	[redacted]									
2106										
2108										
2115										
3101										
3102										
3110										
5102										
5108										
5109										
8101										
8102										
8107										
8109										
8111										
8114										
8117										
10102										
10103										
10104										
10106										
10107										
21103										
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	21	21	21	21	21	21	21	21	21	21
Mean	341.67	342.35	340.07	359.96	290.71	333.69	317.81	473.1	563.22	563.94
SD	162.93	231.59	198.03	204.61	148.96	230.41	253.6	299.76	346.73	328.92
SE	35.55	50.54	43.21	44.65	32.51	50.28	55.34	65.41	75.66	71.78
P vs. Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	0.001	0.072	0.134

Subject	20	21	22	23	24
1101	[redacted]				
2106					
2108					
2115					
3101					
3102					
3110					
5102					
5108					
5109					
8101					
8102					
8107					
8109					
8111					
8114					
8117					
10102					
10103					
10104					
10106					
10107					
21103					
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)					
N	21	21	21	21	21
Mean	700.35	707.37	687.04	708.86	662.29
SD	353.83	412.72	397.32	352.44	356.34
SE	77.21	90.06	86.7	76.91	77.76
P vs Base	0.96	0.967	0.88	0.776	0.801

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Table 12: Per Protocol, Active Group

Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
1102	[redacted]								
1103									
1105									
2101									
2105									
2110									
2113									
3106									
5101									
5105									
5106									
8105									
10108									
10109									
20114									
21102									
21109									

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	17	17	17	17	17	17	17	17	17
Mean	578.66	630.44	705.77	704.97	746.78	747.01	758.05	818.91	868.1
SD	413.72	330.47	477.82	444.28	368.98	413.7	361.93	467.69	578.81
SE	100.34	80.15	115.89	107.75	89.49	100.34	87.78	113.43	140.38
P vs Base	.	.	.	.	.	.	.	.	.
P vs Plac	0.432	0.029	0.965	0.965	0.734	0.646	0.584	0.183	0.734

Subject	Base	1	2	3	4	5	6	7	8	9
1102	[redacted]									
1103										
1105										
2101										
2105										
2110										
2113										
3106										
5101										
5105										
5106										
8105										
10108										
10109										
20114										
21102										
21109										

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	17	17	17	17	17	17	17	17	17	17
Mean	832.47	603.32	611.42	530.98	460.58	470.18	462.29	464.46	422.25	468.3
SD	508.61	366.05	535.46	496.78	419.63	517.94	502.44	535.47	492.41	546.76
SE	123.36	88.78	129.87	120.49	101.78	125.62	121.86	129.87	119.43	132.61
P vs Base		<0.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	0.001
P vs Plac	0.668	0.397	0.334	0.432	0.277	0.194	0.848	0.668	0.929	0.894

Subject	10	11	12	13	14	15	16	17	18	19
1102	371.7	412.7	327.3	318.4	300.4	2	[redacted]			
1103	1027.1	1039.5	716.4	265.5	320					
1105	182.2	55.7	50.1	30.6	65.9	4				
2101	934.4	1623.7	990	1083.9	788.4	7				
2105	129.4	203.1	41.8	189.5	383	3				
2110	170.4	255.9	153.6	206.2	488.6	1				
2113	581.7	257.9	204.2	238.6	202.8	1				
3106	313.2	352	394.5	670.6	347.7	7				
5101	597.8	190.5	121.3	146.8	151.5					
5105	268.6	293.6	180.3	146.7	239.1	2				
5106	306	162.7	206.6	301.3	279.9	2				
8105	1535.5	1730.		1336	1863.5					
10108	378.7	246.5	294.8	231.5	115	1				
10109	311.9	180.4	243	237.2	115.5	1				
20114	144.7.		190.1	324.5	213	6				
21102	55.4	42.5	203.6	159.9	289.7	3				
21109	131.3	232.5	314.4	246.7	348.5	2				

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Subject	10	11	12	13	14	15	16	17	18	19
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	17	17	17	17	17	17	17	17	17	17
Mean	437.65	436.7	374.24	360.82	383.09	423.69	386.66	333.95	395.7	366.66
SD	394.37	515.84	422.04	348.19	416.8	391.36	452.38	383.36	542.26	398.07
SE	95.65	125.11	102.36	84.45	101.09	94.92	109.72	92.98	131.52	96.55
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.825	0.779	0.334	0.365	0.941	0.668	0.894	0.008	0.003	0.003

Subject	20	21	22	23	24
1102	[redacted]				
1103					
1105					
2101					
2105					
2110					
2113					
3106					
5101					
5105					
5106					
8105					
10108					
10109					
20114					
21102					
21109					
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)					
N	17	17	17	17	17
Mean	326.51	336.14	399.92	395.48	394.33
SD	353.79	352.81	380.86	365.87	289.59
SE	85.81	85.57	92.37	88.74	70.24
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	0.001	0.004	0.001	0.012

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Table 13: Los Angeles: Serum PTH, All Subjects- Placebo Group

Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
1101	[redacted]								
2102									
2103									
2104									
2106									
2108									
2111									
2112									
2115									
2117									
2118									
3101									
3102									
3103									
3105									
3108									
3109									
3110									
5102									
5104									
5108									
5109									
8101									
8102									
8107									
8109									
8111									
8113									
8114									
8115									
8117									
8119									
9101									
10102									
10103									
10104									
10106									
10107									
20101									
20102									
20103									
20104									
20108									
20113									
20116									
21103									
21106									
21107									
21108									
21110									
21113									
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)									
N	31	31	31	31	32	32	32	32	32
Mean	547.83	602.52	632.78	663.91	640.32	674.31	603.68	633.73	943.77
SD	391.15	349.5	326.24	348.95	695.27	626.85	602.33	805.77	941.23
SE	70.25	62.77	58.6	62.67	122.91	110.81	106.48	142.44	166.39
P vs Base	.	.	.	.	.	.	.	.	.
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)									
N	31	31	31	31	32	32	32	32	32
Mean	547.83	602.52	632.78	663.91	640.32	674.31	603.68	633.73	943.77
SD	391.15	349.5	326.24	348.95	695.27	626.85	602.33	805.77	941.23
SE	70.25	62.77	58.6	62.67	122.91	110.81	106.48	142.44	166.39
P vs Base	.	.	.	.	.	.	.	.	.
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)									
N	21	21	21	21	21	21	21	21	21
Mean	511.6	605.81	656.87	654.54	719.62	797.89	696.2	683.86	717.74
SD	382.72	385.9	338	361.12	375.05	420.84	313.53	385.83	288.67
SE	83.52	84.21	73.76	78.8	81.84	91.84	68.42	84.2	62.99
P vs Base	.	.	.	.	.	.	.	.	.

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Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)									
N	49	48	47	47	48	48	47	43	33
Mean	465.57	508.46	536.34	570.1	702.96	706.61	677.74	738.81	950.76
SD	366.59	332.52	323.03	340.94	627.8	575.65	547.81	730.69	927.28
SE	52.37	48	47.12	49.73	90.61	83.09	79.91	111.43	161.42
P vs Base	.	.	.	.	.	.	.	.	.

Subject	Base	1	2	3	4	5	6	7	8	9
1101	.	[redacted]								
2102.										
2103										
2104										
2106										
2108										
2111										
2112.										
2115										
2117.										
2118										
3101										
3102										
3103.										
3105										
3108.										
3109.										
3110										
5102										
5104.										
5108										
5109										
8101										
8102										
8107										
8109										
8111										
8113.										
8114										
8115.										
8117										
8119										
9101.										
10102										
10103										
10104										
10106										
10107										
20101.										
20102.										
20103.										
20104										
20108.										
20113.										
20116										
21103										
21106.										
21107.										
21108.										
21110.										
21113										
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)										
N	32	31	30	30	30	30	30	30	30	29
Mean	847.1	744.19	692.33	647.36	546.36	497.07	543.25	574.1	478.08	543.48
SD	765.46	946.3	926.51	970.45	805.41	640.31	671.71	843.56	574.67	895.67
SE	135.32	169.96	169.16	177.18	147.05	116.9	122.64	154.01	104.92	166.32
P vs Base	.	0.003	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)										
N	32	32	32	32	32	32	32	32	32	32
Mean	847.1	744.54	682.77	640.61	545.93	499.72	543.01	571.93	481.91	541.01
SD	765.46	930.91	898.59	940.61	780.92	621.63	651.99	817.78	558.73	853.09
SE	135.32	164.56	158.85	166.28	138.05	109.92	115.26	144.57	98.77	150.81
P vs Base	.	0.003	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001

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Subject	Base	1	2	3	4	5	6	7	8	9
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	21	21	21	21	21	21	21	21	21	21
Mean	696.58	511.34	430.68	399.11	334.28	286.51	362.45	352.41	332.25	349.4
SD	307.31	330.13	335.63	325.56	252.33	265.56	333.4	343.03	307.81	369.27
SE	67.06	72.04	73.24	71.04	55.06	57.95	72.75	74.85	67.17	80.58
P vs Base	.	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)										
N	32	31	30	30	30	30	30	30	30	29
Mean	847.1	744.19	692.33	647.36	546.36	497.07	543.25	574.1	478.08	543.48
SD	765.46	946.3	926.51	970.45	805.41	640.31	671.71	843.56	574.67	895.67
SE	135.32	169.96	169.16	177.18	147.05	116.9	122.64	154.01	104.92	166.32
P vs Base	.	0.003	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001

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Subject	10	11	12	13	14	15	16	17	18	19
1101	[redacted]									
2102.										
2103										
2104.										
2106										
2108										
2111										
2112.										
2115										
2117.										
2118.										
3101										
3102										
3103.										
3105										
3108.										
3109.										
3110										
5102										
5104.										
5108										
5109										
8101										
8102										
8107										
8109										
8111										
8113.										
8114										
8115.										
8117										
8119										
9101.										
10102										
10103										
10104										
10106										
10107										
20101.										
20102.										
20103.										
20104										
20108.										
20113.										
20116.										
21103										
21106.										
21107.										
21108.										
21110.										
21113										

Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)										
N	29	29	29	29	29	29	29	26	26	26
Mean	569.87	578.81	670.59	486.88	553.2	593.8	526.5	629.42	755.9	729.5
SD	1078.8	1131.64	1492.27	638.79	1083.41	1134.07	872.18	833.08	970.29	860.66
SE	200.33	210.14	277.11	118.62	201.18	210.59	161.96	163.38	190.29	168.79
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	0.097	0.038
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)										
N	32	32	32	32	32	32	32	32	32	32
Mean	564.93	573.03	656.21	489.73	549.82	586.62	525.63	629.61	732.37	710.92
SD	1026.91	1077.09	1420.04	609.71	1031.21	1079.48	830.78	768.18	890.01	793.3
SE	181.53	190.4	251.03	107.78	182.29	190.83	146.86	135.8	157.33	140.24
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	0.053	0.023
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	21	21	21	21	21	21	21	21	21	21
Mean	341.67	342.35	340.07	359.96	290.71	333.89	317.81	473.1	563.22	563.94
SD	162.93	231.59	198.03	204.61	148.96	230.41	253.6	299.76	346.73	328.92
SE	35.55	50.54	43.21	44.65	32.51	50.28	55.34	65.41	75.66	71.78
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	0.001	0.072	0.134
Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)										
N	29	29	29	29	29	29	29	26	26	26
Mean	569.87	578.81	670.59	486.88	553.2	593.8	526.5	629.42	755.9	729.5

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Subject	10	11	12	13	14	15	16	17	18	19
SD	1078.8	1131.64	1492.27	638.79	1083.41	1134.07	872.18	833.08	970.29	860.66
SE	200.33	210.14	277.11	118.62	201.18	210.59	161.96	163.38	190.29	168.79
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	0.097	0.038

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Subject	20	21	22	23	24
1101	[redacted]				
2102.					
2103.					
2104.					
2106					
2108					
2111					
2112.					
2115					
2117.					
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3101					
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8119					
9101.					
10102					
10103					
10104					
10106					
10107					
20101.					
20102.					
20103.					
20104.					
20108.					
20113.					
20116.					
21103					
21106.					
21107.					
21108.					
21110.					
21113					

Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)

N	26	25	25	25	24
Mean	916.42	716.63	709.97	732.82	672.57
SD	1081.13	403.66	397.53	418.71	356.93
SE	212.03	80.73	79.51	83.74	72.86
P vs Base	0.853	0.845	0.969	0.845	0.698

Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)

N	32	32	32	32	32
Mean	862.8	863.54	858.34	876.19	827.7
SD	992.92	1007.05	1005.95	1009.92	996.91
SE	175.53	178.02	177.83	178.53	176.23
P vs Base	0.878	0.804	0.969	0.939	0.546

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	21	21	21	21	21
Mean	700.35	707.37	687.04	708.86	662.29
SD	353.83	412.72	397.32	352.44	356.34
SE	77.21	90.06	86.7	76.91	77.76
P vs Base	0.96	0.987	0.88	0.776	0.801

Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)

N	26	25	25	25	24

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Subject	20	21	22	23	24
Mean	916.42	716.63	709.97	732.82	672.57
SD	1081.13	403.66	397.53	418.71	356.93
SE	212.03	80.73	79.51	83.74	72.86
P vs Base	0.853	0.845	0.969	0.845	0.698

Table 14: Los Angeles, All Subjects - Active Group, Serum PTH

Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
1102	[redacted]								
1103									
1104									
1105									
1106									
2101									
2105									
2107									
2109									
2110									
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2116									
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3107									
3111									
3112									
3113									
5101									
5103									
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8110									
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10101									
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20111									
20112									
20114									
21101									
21102									
21104									
21105									
21109									
21111									
21112									
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)									
N	30	30	30	30	30	30	30	30	30
Mean	553.49	614.34	690.1	690.17	687.7	736.21	745.36	767.24	862.86
SD	416.26	322.59	425.56	380.7	392.27	435.07	397.02	422.82	494.63
SE	76	58.9	77.7	69.51	71.62	79.43	72.49	77.2	90.31
P vs Base									
P vs Plac	0.794	0.468	0.602	0.828	0.496	0.479	0.955	0.804	0.849
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)									
N	30	30	30	30	30	30	30	30	30
Mean	553.49	614.34	690.1	690.17	687.7	736.21	745.36	767.24	862.86

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Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
SD	416.26	322.59	425.56	380.7	392.27	435.07	397.02	422.82	494.63
SE	76	58.9	77.7	69.51	71.62	79.43	72.49	77.2	90.31
P vs Base	.	.	.	.	.	.	.	.	.
P vs Plac	0.794	0.468	0.602	0.828	0.496	0.479	0.955	0.804	0.849
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)									
N	17	17	17	17	17	17	17	17	17
Mean	578.66	630.44	705.77	704.97	746.78	747.01	758.05	818.91	868.1
SD	413.72	330.47	477.82	444.28	368.98	413.7	361.93	467.69	578.81
SE	100.34	80.15	115.89	107.75	89.49	100.34	87.78	113.43	140.38
P vs Base	.	.	.	.	.	.	.	.	.
P vs Plac	0.432	0.29	0.965	0.965	0.734	0.646	0.584	0.183	0.734
Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)									
N	53	51	51	50	50	49	47	46	31
Mean	453.07	495.15	561.72	539.79	557.38	587.66	584.28	596.52	642.65
SD	403.64	351.84	424.14	396.07	397.94	441.33	438.27	453.4	499.16
SE	55.44	49.27	59.39	56.01	56.28	63.05	63.93	66.85	69.65
P vs Base	.	.	.	.	.	.	.	.	.
P vs Plac	0.822	0.888	0.96	0.447	0.227	0.254	0.249	0.289	0.882

Subject	Base	1	2	3	4	5	6	7	8	9
1102	[redacted]									
1103										
1104.										
1105										
1106.										
2101										
2105										
2107										
2109										
2110										
2113										
2114.										
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3104										
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20111										
20112.										
20114										
21101.										
21102										
21104.										
21105										
21109										
21111.										
21112.										

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Subject	Base	1	2	3	4	5	6	7	8	9
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)										
N	30	30	30	29	28	27	27	27	26	26
Mean	797.18	588.51	560.84	489.09	426.85	415.81	409.19	416.2	406.17	445.62
SD	443.75	375.51	463.72	449.47	359.42	455.22	438.66	460.88	418.33	465.07
SE	81.02	68.56	84.66	83.47	67.92	87.61	84.42	88.7	82.04	91.21
P vs Base	.	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.966	0.674	0.699	0.552	0.938	0.63	0.291	0.421	0.557	0.879
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)										
N	30	30	30	30	30	30	30	30	30	30
Mean	797.18	588.51	560.84	486.11	440.04	438.3	432.35	438.66	416.56	450.75
SD	443.75	375.51	463.72	441.96	355.36	440.5	425.49	445.72	406.54	447.57
SE	81.02	68.56	84.66	80.69	64.88	80.42	77.68	81.38	74.22	81.72
P vs Base	.	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.966	0.61	0.661	0.505	0.955	0.788	0.435	0.6	0.605	0.832
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	17	17	17	17	17	17	17	17	17	17
Mean	832.47	603.32	611.42	530.98	460.58	470.18	462.29	464.46	422.25	468.3
SD	508.61	366.05	535.46	496.78	419.63	517.94	502.44	535.47	492.41	546.76
SE	123.36	88.78	129.87	120.49	101.78	125.62	121.86	129.87	119.43	132.61
P vs Base	.	<.001	<.001	<.001	<.001	0.001	<.001	<.001	<.001	0.001
P vs Plac	0.668	0.397	0.334	0.432	0.277	0.194	0.848	0.668	0.929	0.894
Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)										
N	30	30	30	29	28	27	27	27	26	26
Mean	797.18	588.51	560.84	489.09	426.85	415.81	409.19	416.2	406.17	445.62
SD	443.75	375.51	463.72	449.47	359.42	455.22	438.66	460.88	418.33	465.07
SE	81.02	68.56	84.66	83.47	67.92	87.61	84.42	88.7	82.04	91.21
P vs Base	.	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.966	0.674	0.699	0.552	0.938	0.63	0.291	0.421	0.557	0.879

Subject	10	11	12	13	14	15	16	17	18	19
1102	[redacted]									
1103										
1104.										
1105										
1106.										
2101										
2105										
2107										
2109										
2110										
2113										
2114.										
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20111										
20112.										
20114										
21101.										
21102										
21104.										

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Subject	10	11	12	13	14	15	16	17	18	19
21105.	[redacted]									
21109										
21111.										
21112.										
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)										
N	26	26	24	24	24	24	24	24	24	24
Mean	373.48	404.42	387.77	357.69	385.85	423.51	384.31	326.6	365.6	356.55
SD	347.09	437	398.71	307.66	367.66	358.38	397.78	323.04	460.82	353.34
SE	68.07	85.7	81.39	62.8	75.05	73.15	81.2	65.94	94.06	72.13
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.213	0.576	0.137	0.233	0.914	0.872	0.719	0.003	<.001	<.001
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)										
N	30	30	30	30	30	30	30	30	30	30
Mean	388.24	415.04	384.52	360.46	382.98	413.11	381.75	335.58	366.79	359.54
SD	344.97	423.17	381.78	307.79	356.19	349.21	380.99	320.52	433.65	344.51
SE	62.98	77.26	69.7	56.19	65.03	63.76	69.56	58.52	79.17	62.9
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.255	0.552	0.103	0.162	0.681	0.788	0.487	0.001	<.001	<.001
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	17	17	17	17	17	17	17	17	17	17
Mean	437.65	436.7	374.24	360.82	383.09	423.69	386.66	333.95	395.7	366.66
SD	394.37	515.84	422.04	348.19	416.8	391.36	452.38	383.36	542.26	398.07
SE	95.65	125.11	102.36	84.45	101.09	94.92	109.72	92.98	131.52	96.55
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.825	0.779	0.334	0.365	0.941	0.668	0.894	0.008	0.003	0.003
Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)										
N	26	26	24	24	24	24	24	24	24	24
Mean	373.48	404.42	387.77	357.69	385.85	423.51	384.31	326.6	365.6	356.55
SD	347.09	437	398.71	307.66	367.66	358.38	397.78	323.04	460.82	353.34
SE	68.07	85.7	81.39	62.8	75.05	73.15	81.2	65.94	94.06	72.13
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.213	0.576	0.137	0.233	0.914	0.872	0.719	0.003	<.001	<.001

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Subject	20	21	22	23	24
1102	[redacted]				
1103					
1104.					
1105					
1106.					
2101					
2105					
2107					
2109					
2110					
2113					
2114.					
2116.					
3104					
3106					
3107.					
3111.					
3112.					
3113.					
5101					
5103.					
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10101.					
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20105					
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20107.					
20109					
20110					
20111.					
20112.					
20114					
21101.					
21102					
21104.					
21105.					
21109					
21111.					
21112.					

Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)

N	24	24	24	22	21
Mean	323.7	322.01	374.53	377.69	404.39
SD	320.51	298.93	330.24	327.74	262.94
SE	65.42	61.02	67.41	69.88	57.38
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	<.001	<.001	<.001	0.008

Intent-to-Treat Analysis (All Treated Subjects; Last Valued Carried to End of Study)

N	30	30	30	30	30
Mean	333.27	331.91	373.93	367.93	381.3
SD	318.57	301.51	325.78	314.74	265.4
SE	58.16	55.05	59.48	57.46	48.46
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	<.001	<.001	<.001	<.001

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	17	17	17	17	17
Mean	326.51	336.14	399.92	395.48	394.33
SD	353.79	352.81	380.86	365.87	289.59
SE	85.81	85.57	92.37	88.74	70.24
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	0.001	0.004	0.001	0.012

Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)

N	24	24	24	22	21
Mean	323.7	322.01	374.53	377.69	404.39
SD	320.51	298.93	330.24	327.74	262.94
SE	65.42	61.02	67.41	69.88	57.38
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	<.001	<.001	<.001	0.008

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At baseline, mean (± SE) plasma PTH was 757.4 ± 66.4 pg/mL (range of 289.1 to 2299.6 pg/mL). Mean PTH decreased after starting drug, yielding statistically significant reductions (P < 0.001) at Weeks 1 through 16. The range of values at Week 16 was 75.4 to 2011.7 pg/mL. At Week 24, after 8 additional weeks of either drug or placebo, the range was 58.7 to 1331.4 for those receiving drug and 136.6 to 1346.7 for those on placebo.

The Sponsor interprets the data as demonstrating that 34 (89.5%) of the subjects reached the pre-determined target PTH range of 150 to 300 pg/mL during treatment with 1α-OH-D_2 after 7 to 93 days of therapy (mean ± SE = 27.5 ± 3.7 days).

Because the number of subjects for whom data are available are small, the values for each subject were examined.

During the washout phase, 5 subjects had values within the "target" range for at least 2 measurements after the start; 4 of these were subsequently in the placebo group and 1 in the drug group.

During the second phase (16 of open-label drug), 21 of the 34 subjects who had a PTH level within the "target" range subsequently had values above the range with values thereafter above and below. Of the 34 subjects who achieved "target" values at any time, 14 had values above the range at least once during the 3 last 3 weeks of treatment. Therefore, the value given for "time to show efficacy" is not clinically meaningful.

During the third phase (double-blind, placebo-controlled), 15 of the 17 subjects who continued on drug had PTH levels above the target range at least once. Of the 21 switched to placebo, 2 remained below the target range for the entire period.

The Sponsor claims further that all of the 38 subjects (100.0%) achieved PTH suppression of ≥ 30% on or before Week 8 of the study, with response occurring after 7 to 56 days of therapy (mean ± SE = 15.5 ± 2.0 days). The average dose of 1α-OH-D_2 administered to achieve ≥ 30% PTH suppression was 9.9 ± 0.1 (mean ± SE) μg per hemodialysis, ranging from 0.0 to 10.0 μg. By the end of Treatment Period 1 (Week 16), mean plasma PTH was reduced to 348.6 ± 57.2 pg/mL from a baseline of 757.4 ± 66.4 (P < 0.001). The mean reduction in plasma PTH, relative to baseline, was 52.9 ± 4.6% (P < 0.001). The mean plasma PTH level at Week 16 for subjects randomized to active drug was 386.7 ± 109.7 pg/mL. By the end of study (Week 24), plasma PTH remained unchanged (suppressed) at 394.3 ± 70.2 pg/mL (P = 0.911). In contrast, the mean plasma PTH at Week 16 for subjects randomized to placebo drug was 317.8 ± 55.3 pg/mL, and rose to 662.3 ± 77.8 pg/mL at Week 24 (P < 0.001).

I note, however, that 24 of the 38 patients who had achieved a 30% reduction in serum PTH levels by week 8 had subsequent rises in the concentrations within 1 to 8 weeks following the reduction. Furthermore, some of the "responses" noted, while impressive numerically when expressed as "% decreases," are of no clinical significance. As examples:

Subject 1103: baseline, 1235.3; Week 8, 840.8, 30% reduction.

Subject 3106: baseline, 758; Week 7, 283.9, 62.5% reduction; Week 8, 514.6, 321.% reduction from baseline and 81.3% increase from previous week!

Subject 8105: baseline, 2299.6; Week 5, 1275, 55% reduction.

In subjects randomized to active drug (n=17), the change in mean plasma PTH from a baseline value of 832.5 ± (SEM) 123.4 pg/mL to 394.3 ± 70.2 pg/mL at Week 24 was significant (P < 0.001). For subjects randomized to placebo (n=21), the change in mean plasma PTH from the mean baseline level of 696.6 ± 67.1 pg/mL to 662.3 ± 77.8 pg/mL at Week 24 was statistically insignificant. Significant differences in mean PTH were noted between treatment groups beginning at Week 20 through Week 24 (P < 0.050).

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In view of the small number of subjects studied, the effects of the drug in each subject were examined in addition to the differences between means (as reported). There was large variability in serum PTH levels, not only from patient to patient, but also from week to week in the same patient. High variability is to be expected in this category of patients, but demands a larger number of study subjects for clinical validity. The following table lists the number of subjects at specific time points in the study who achieved "target" levels of PTH; these are evaluated according the group to which they had been randomized.

PTH (pg/mL) WEEK No.	<150		150-300		300-500		>500	
	P	A	P	A	P	A	P	A
(-8)	3	0	5	3	5	7	10	5
(-4)	0	0	1	1	8	5	12	9
0	0	0	3	1	4	5	16	11
+4	3	2	5	5	12	6	3	3
+8	5	4	11	8	3	1	3	4
+12	2	3	9	8	8	3	2	2
+16	6	2	7	10	5	1	5	4
+20 (III 4)	1	6	2	5	4	4	16	2
+24 (III 8)	1	2	3	5	5	8	14	2

Subjects in the "target" range of PTH values include some on drug and some on placebo. There are insufficient numbers of individuals to perform sub-group analyses. Those who have responded to calcitriol in the past may be more or less likely to respond to hectorol. The responses noted in the Table above suggest an imbalance in the groups. The group receiving placebo at week 16 had more subjects with higher PTH levels at weeks (-8) to 0 and fewer who achieved "target" levels on drug by week 16.

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(2) Memphis Area

Table 15: Serum PTH: Memphis Area - Active Drug Group - Per Protocol

Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
6101	[redacted]								
6103									
6104									
6107									
12103									
13101									
13102									
13103									
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19101									
19102									
19105									
19106									
19109									
19111									

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	31	31	31	31	31	31	31	31	31
Mean	737.36	722.86	773.27	983.35	829.77	783.49	937.66	998.15	963.55
SD	488.34	374.95	424.46	812.58	510.83	634.75	709.37	721.54	612.67
SE	87.71	67.34	76.24	145.94	91.75	114	127.41	129.59	110.04
P vs Base									
P vs Plac	0.643	0.125	0.514	0.908	0.817	0.244	0.504	0.612	0.323

Subject	Base	1	2	3	4	5	6	7	8	9
6101	[redacted]									
6103										
6104										
6107										
12103										
13101										
13102										
13103										
13104										
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18109										
18113										
19101										
19102										
19105										
19106										
19109										
19111										

BEST POSSIBLE COPY

Subject	Base	1	2	3	4	5	6	7	8	9
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	31	31	31	31	31	31	31	31	31	31
Mean	961.43	887.59	671.21	707.49	626.1	627.98	537.6	545.19	531.84	526.17
SD	623.09	766.37	502.13	621.98	523.88	648.24	558.84	581.84	476.91	621.53
SE	111.91	137.64	90.19	111.71	94.09	116.43	100.37	104.5	85.65	111.63
P vs Base		.064	<.001	0.001	<.001	0.001	<.001	<.001	<.001	<.001
P vs Plac	0.523	1.000	0.965	0.653	0.337	0.622	0.250	0.179	0.582	0.161

Subject	10	11	12	13	14	15	16	17	18	19
6101	[redacted]									
6103										
6104										
6107										
12103										
13101										
13102										
13103										
13104										
14102										
14103										
16101										
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18109										
18113										
19101										
19102										
19105										
19106										
19109										
19111										
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	31	31	31	31	31	31	31	31	31	31
Mean	436.46	421.56	348.06	357.05	374.33	395.03	402.45	446.24	347.15	383.65
SD	481.17	426.59	344.02	478.13	380.74	425.01	405.24	412.31	339.54	319.48
SE	86.42	76.62	61.79	85.87	68.38	76.33	72.78	74.05	60.98	57.38
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.772	0.717	0.084	0.029	0.205	0.856	0.653	0.071	<.001	0.011

Subject	20	21	22	23	24
6101	[redacted]				
6103					
6104					
6107					
12103					
13101					
13102					
13103					
13104					
14102					
14103					
16101					
16102					
16104					
16107					
16109					
16113					
16124					
16125					
16126					
17102					

BEST POSSIBLE COPY

Subject	20	21	22	23	24
18101	[redacted]				
18108					
18109					
18113					
19101					
19102					
19105					
19106					
19109					
19111					

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	31	31	31	31	31
Mean	376.97	348.21	271.64	304.43	373.09
SD	364.34	298.28	230.9	284.93	380.57
SE	65.44	53.57	41.47	51.17	68.35
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	<.001	<.001	<.001	<.001

Table 16: Per Protocol - Placebo

Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
6102	[redacted]								
6105									
6109									
6110									
13108									
13111									
15101									
15103									
16105									
16108									
16114									
16119.									
16121									
16122									
17104									
17105									
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17108									
17109									
18107									
18110									
19104									
19107									
19108									
19114									
19117									
19118									
19119									
19122									
19123									

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	30	30	30	30	30	30	30	30	30
Mean	835.13	961.43	872.82	912.93	920.52	927.46	962.67	1019.54	1062.21
SD	572.31	519.5	456.72	547.52	661.59	632.96	567.35	589.21	641.27
SE	104.49	94.85	83.39	99.96	120.79	115.56	103.58	107.57	98.82
P vs Base	.	.	.	.	.	.	.	.	.

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Subject	Base	1	2	3	4	5	6	7	8	9
6102	[redacted]									
6105										
6109										
6110										
13108										
13111										
15101										
15103										
16105										
16108										
16114										
16119										
16121										
16122										
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18110										
19104										
19107										
19108										
19114										
19117										
19118										
19119										
19122										
19123										

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	30	30	30	30	30	30	30	30	30	30
Mean	1008.73	801.97	698.18	667.17	793.86	711.43	794.42	745.42	768.19	671.56
SD	614.57	498.9	566.63	633.31	656.96	784.8	1036.79	1025.31	1094.48	645.01
SE	93.95	91.09	103.45	115.63	119.94	143.28	189.29	187.2	199.82	117.76
P vs Base	.	<.001	<.001	<.001	0.006	<.001	0.001	<.001	0.002	<.001

Subject	10	11	12	13	14	15	16	17	18	19
6102	[redacted]									
6105										
6109										
6110										
13108										
13111										
15101										
15103										
16105										
16108										
16114										
16119										
16121										
16122										
17104										
17105										
17106										
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18107										
18110										
19104										
19107										
19108										
19114										
19117										
19118										
19119										
19122										
19123										

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	30	30	30	30	30	30	30	30	30	30
Mean	640.96	473.14	501.72	476.43	499.26	454.93	454.05	622.39	750.49	621.22
SD	576.69	528.52	500.69	466.01	501.51	420.93	385.46	532.66	539.23	453
SE	105.29	96.49	91.41	85.08	91.56	76.85	70.38	97.25	98.45	82.71
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001

BEST POSSIBLE COPY

Subject	20	21	22	23	24
6102	[redacted]				
6105					
6109					
6110					
13108					
13111.					
15101					
15103					
16105.					
16108					
16114					
16119					
16121					
16122					
17104					
17105					
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19108					
19114					
19117					
19118					
19119					
19122					
19123					

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	30	30	30	30	30
Mean	828.94	861.31	822.46	747.4	871.88
SD	700.84	648.18	628.04	568.34	623.56
SE	127.96	118.34	114.66	103.76	113.85
P vs Base	0.004	0.002	0.003	<.001	0.065

Table 17. Memphis Area: Serum PTH - Active Drug, All Subjects

Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
6101	[redacted]								
6103									
6104									
6107									
6108									
12103									
12105									
13101									
13102									
13103									
13104									
13109									
14102									
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15102									
15105									
16101									
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16103									
16104									
16107									
16109									
16111									
16112									
16113									
16117									
16124									
16125									
16126									
16127									
17101									
17102									
17103									
17107									
17110									

BEST POSSIBLE COPY

Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
17111	[redacted]								
18101									
18102									
18104									
18108									
18109									
18112									
18113									
19101									
19102									
19103									
19105									
19106									
19109									
19111									
19115									
19116									
19120									
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)									
N	41	41	41	41	41	41	41	41	41
Mean	753.58	755.88	802.71	989.95	874.57	801.18	954.38	986.96	985.09
SD	467.38	417.14	451.63	725.86	516.66	574.18	650.48	665.33	551.9
SE	72.99	65.15	70.53	113.36	80.69	89.67	101.59	103.91	86.19
P vs Base	.	.	.	.	.	.	.	.	.
P vs Plac	0.506	0.221	0.583	0.822	0.734	0.194	0.672	0.54	0.888
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)									
N	41	41	41	41	41	41	41	41	41
Mean	753.58	755.88	802.71	989.95	874.57	801.18	954.38	986.96	985.09
SD	467.38	417.14	451.63	725.86	516.66	574.18	650.48	665.33	551.9
SE	72.99	65.15	70.53	113.36	80.69	89.67	101.59	103.91	86.19
P vs Base	.	.	.	.	.	.	.	.	.
P vs Plac	0.506	0.221	0.583	0.822	0.734	0.194	0.672	0.54	0.888
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)									
N	31	31	31	31	31	31	31	31	31
Mean	737.36	722.86	773.27	983.35	829.77	783.49	937.66	998.15	963.55
SD	488.34	374.95	424.46	812.58	510.83	634.75	709.37	721.54	612.67
SE	87.71	67.34	76.24	145.94	91.75	114	127.41	129.59	110.04
P vs Base	.	.	.	.	.	.	.	.	.
P vs Plac	0.643	0.125	0.514	0.908	0.817	0.244	0.504	0.612	0.323
Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)									
N	53	53	52	52	51	50	50	50	41
Mean	671.51	686.56	715.6	885.12	781.69	731.09	887.09	919	985.09
SD	474.13	449.66	467.73	695.88	516.69	559.75	657.99	668.7	551.9
SE	65.13	61.77	64.86	96.5	72.35	79.16	93.05	94.57	86.19
P vs Base	.	.	.	.	.	.	.	.	.
P vs Plac	0.98	0.683	0.944	0.42	0.624	0.586	0.605	0.658	0.888

Subject	Base	1	2	3	4	5	6	7	8	9
6101	[redacted]									
6103										
6104										
6107										
6108.										
12103										
12105.										
13101										
13102										
13103										
13104										
13109										
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16109										
16111										
16112.										
16113										
16117										
16124										
16125										
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Subject	Base	1	2	3	4	5	6	7	8	9
16127	[redacted]									
17101										
17102										
17103										
17107.										
17110										
17111.										
18101										
18102										
18104.										
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19103.										
19105										
19106										
19109										
19111										
19115.										
19116.										
19120										

Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)

N	41	41	40	40	40	40	40	40	40	40
Mean	973.88	908.48	676.08	701.9	638.98	646.4	576.19	618.55	578.83	594.62
SD	567.04	710.34	497.59	592.18	527.17	606.32	536.32	573.06	489.28	622.95
SE	88.56	110.94	78.68	93.63	83.35	95.87	84.8	90.61	77.36	98.5
P vs Base		0.048	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.806	0.774	.84	0.898	0.448	0.905	0.36	0.422	0.707	0.38

Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)

N	41	41	41	41	41	41	41	41	41	41
Mean	973.88	908.48	704.56	729.75	668.37	675.6	607.11	648.44	609.69	625.09
SD	567.04	710.34	524.09	611.33	553.52	627.23	565.38	597.34	521.97	645.32
SE	88.56	110.94	81.85	95.47	86.44	97.96	88.3	93.29	81.52	100.78
P vs Base		0.048	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.806	0.774	0.971	0.766	0.561	0.962	0.454	0.513	0.703	0.387

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	31	31	31	31	31	31	31	31	31	31
Mean	961.43	887.59	671.21	707.49	626.1	627.98	537.6	545.19	531.84	526.17
SD	623.09	766.37	502.13	621.98	523.88	648.24	558.84	581.84	476.91	621.53
SE	111.91	137.64	90.19	111.71	94.09	116.43	100.37	104.5	85.65	111.63
P vs Base		0.064	<.001	0.001	<.001	0.001	<.001	<.001	<.001	<.001
P vs Plac	0.523	1.00	0.965	0653	0.337	0.622	0.25	0.179	0.582	0.161

Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)

N	41	41	40	40	40	40	40	40	40	40
Mean	973.88	908.48	676.08	701.9	638.98	646.4	576.19	618.55	578.83	594.62
SD	567.04	710.34	497.59	592.18	527.17	606.32	536.32	573.06	489.28	622.95
SE	88.56	110.94	78.68	93.63	83.35	95.87	84.8	90.61	77.36	98.5
P vs Base		0.048	<.001	<.001	<.001	<.001	<.001	<.001	<.001	0.001
P vs Plac	0.806	0.774	0.84	0.898	0.448	0.905	0.36	0.422	0.707	0.38

Subject	10	11	12	13	14	15	16	17	18	19
6101	[redacted]									
6103										
6104										
6107										
6108.										
12103										
12105.										
13101										
13102										
13103										
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16102										
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16111										

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Subject	10	11	12	13	14	15	16	17	18	19
16112.	[redacted]									
16113										
16117										
16124										
16125										
16126										
16127										
17101										
17102										
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19115.										
19116.										
19120										

Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)										
N	40	39	39	39	38	38	37	37	37	37
Mean	500.93	498.21	443	442.15	457.02	449.39	476.13	501.53	423.2	452.9
SD	477.72	449.98	410.43	497.78	437.52	432.35	444.53	437.13	408.63	371.76
SE	75.53	72.05	65.72	79.71	70.98	70.14	73.08	71.86	67.18	61.12
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.865	0.737	0.45	0.126	0.484	0.79	0.913	0.162	0.001	0.079
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)										
N	41	41	41	41	41	41	41	41	41	41
Mean	533.69	528.02	475.5	474.69	499.06	491.99	511.03	533.95	463.26	490.07
SD	516.24	486.94	456.22	532.5	477.4	473.67	478.56	470.71	452.91	420.84
SE	80.62	76.05	71.25	83.16	74.56	73.97	74.74	73.51	70.73	65.72
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.971	0.798	0.429	0.126	0.533	0.818	0.904	0.18	0.001	0.088
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)										
N	31	31	31	31	31	31	31	31	31	31
Mean	436.46	421.56	348.06	357.05	374.33	395.03	402.45	446.24	347.15	383.65
SD	481.17	426.59	344.02	478.13	380.74	425.01	405.24	412.31	339.54	319.48
SE	86.42	76.62	61.79	85.87	68.38	76.33	72.78	74.05	60.98	57.38
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.772	0.717	0.084	0.029	0.205	0.856	0.653	0.071	<.001	0.011
Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)										
N	40	39	39	39	38	38	37	37	37	37
Mean	500.93	498.21	443	442.15	457.02	449.39	476.13	501.53	423.2	452.9
SD	477.72	449.98	410.43	497.78	437.52	432.35	444.53	437.13	408.63	371.76
SE	75.53	72.05	65.72	79.71	70.98	70.14	73.08	71.86	67.18	61.12
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
P vs Plac	0.865	0.737	0.45	0.126	0.484	0.79	0.913	0.162	0.001	0.079

Subject	20	21	22	23	24
6101	[redacted]				
6103					
6104					
6107					
6108.					
12103					
12105.					
13101					
13102					
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13104.					
13109.					
14102					
14103					
15102.					
15105.					
16101					

BEST POSSIBLE COPY

Subject	20	21	22	23	24
16102	[redacted]				
16103.					
16104					
16107					
16109					
16111.					
16112.					
16113					
16117					
16124					
16125					
16126					
16127					
17101					
17102					
17103.					
17107.					
17110					
17111.					
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19111					
19115.					
19116.					
19120.					
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)					
N	36	35	35	35	35
Mean	442.63	447.19	363.34	395.43	459.78
SD	413.37	419.06	362.9	381.66	443.02
SE	68.89	70.83	61.34	64.51	74.88
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	<.001	<.001	<.001	<.001
Intent-to-Treat Analysis (All Treated Subjects; Last Value Carried to End of Study)					
N	41	41	41	41	41
Mean	480.5	478.22	406.65	434.04	488.97
SD	450.53	452.24	415.51	426.87	470.55
SE	70.36	70.63	64.89	66.67	73.49
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	<.001	<.001	<.001	<.001
Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)					
N	31	31	31	31	31
Mean	376.97	348.21	271.64	304.43	373.09
SD	364.34	296.28	230.9	284.93	380.57
SE	65.44	53.57	41.47	51.17	68.35
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	<.001	<.001	<.001	<.001
Intent-to-Treat Analysis (All Randomized Subjects; Last Value Carried to Discontinuation)					
N	36	35	35	35	35
Mean	442.63	447.19	363.34	395.43	459.78
SD	413.37	419.06	362.9	381.66	443.02
SE	68.89	70.83	61.34	64.51	74.88
P vs Base	<.001	<.001	<.001	<.001	<.001
P vs Plac	<.001	<.001	<.001	<.001	<.001

Table 18: Serum PTH: Memphis Area, Placebo Patients (All)

Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
6102	[redacted]								
6105									
6106									
6109									
6110									
6111									

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Subject	-8	-7	-6	-5	-4	-3	-2	-1	0
12101	[redacted]								
12104									
12106									
13105									
13106									
13107									
13108									
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19123									

Intent toTreat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)

N	35	35	35	35	35	35	35	35	35
Mean	856.2	932.91	868.6	953.39	950.72	945.05	960.35	1024.18	1002.38
SD	558.65	510.85	453.92	562.54	626.91	604.99	535.34	566.53	533.63
SE	94.43	86.35	76.73	95.09	105.97	102.26	90.49	95.76	90.2
P vs Base									

Intent toTreat Analysis (All Treated Subjects; Last Value Carried to End of Study)

N	35	35	35	35	35	35	35	35	35
Mean	856.2	932.91	868.6	953.39	950.72	945.05	960.35	1024.18	1002.38
SD	558.65	510.85	453.92	562.54	626.91	604.99	535.34	566.53	533.63
SE	94.43	86.35	76.73	95.09	105.97	102.26	90.49	95.76	90.2
P vs Base									

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	30	30	30	30	30	30	30	30	30
Mean	835.13	961.43	872.82	912.93	920.52	927.46	962.67	1019.54	1062.21
SD	572.31	519.5	456.72	547.52	661.59	632.96	567.35	589.21	541.27
SE	104.49	94.85	83.39	99.96	120.79	115.56	103.58	107.57	98.82
P vs Base	.	.	.	.	.	.	.	.	.

Intent to Treat Analysis (All Randomized Subjects; Last Value Carried toDiscontinuation)

N	54	53	53	52	52	51	51	49	35
Mean	709.27	757.15	714.82	790.14	784.52	801.63	803.09	855.98	1002.38
SD	571.03	546.11	485.31	571.19	627.26	603.00	547.01	588.63	533.63
SE	77.71	75.01	66.66	79.21	86.99	84.44	76.60	84.09	90.2
P vs Base									

Subject	Base	1	2	3	4	5	6	7	8	9
6102	[redacted]									
6105										

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Subject	Base	1	2	3	4	5	6	7	8	9
6106	[redacted]									
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Intent toTreat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)

N	35	35	35	35	35	34	33	33	32	32
Mean	990.43	796.96	710.51	689.36	756.2	690.81	793.58	755.65	805.72	802.64
SD	488.25	484.57	543.09	606.08	626.64	748.87	995.40	981.83	1103.03	1051.94
SE	82.53	81.91	91.8	102.45	105.92	128.43	173.28	170.91	194.99	185.96
P vs Base		<.001	<.001	<.001	0.001	<.001	<.001	<.001	0.008	0.002

Intent toTreat Analysis (All Treated Subjects; Last Value Carried to End of Study)

N	35	35	35	35	35	35	35	35	35	35
Mean	990.43	796.96	710.51	689.36	756.2	684.32	772.92	737.16	789.01	786.20
SD	488.25	484.57	543.09	606.08	626.64	738.77	969.46	955.59	1057.39	1008.76
SE	82.53	81.91	91.80	102.45	105.92	124.88	163.87	161.52	178.73	170.51
P vs Base		<.001	<.001	<.001	0.001	<.001	<.001	<.001	0.003	0.001

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	30	30	30	30	30	30	30	30	30	30
Mean	1006.73	801.97	698.18	667.17	793.86	711.43	794.42	745.42	768.19	671.56
SD	514.57	498.90	566.63	633.31	656.96	784.80	1036.79	1025.31	1094.48	645.01
SE	93.95	91.09	103.45	115.63	119.94	143.28	189.29	187.2	199.82	117.76
P vs Base		<.001	<.001	<.001	0.006	<.001	0.001	<.001	0.002	<.001

Intent to Treat Analysis (All Randomized Subjects; Last Value Carried toDiscontinuation)

N	35	35	35	35	35	34	33	33	32	32
Mean	990.43	796.96	710.51	689.36	756.2	690.81	793.58	755.65	805.72	802.64
SD	488.25	484.57	543.09	606.08	626.64	748.87	995.40	981.83	1103.03	1051.94
SE	82.53	81.91	91.8	102.45	105.92	128.43	173.28	170.91	194.99	185.96
P vs Base		<.001	<.001	<.001	0.001	<.001	<.001	<.001	0.008	0.002

Subject	10	11	12	13	14	15	16	17	18	19

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Intent toTreat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)

N	32	32	32	32	32	32	32	32	32	32
Mean	644.05	603.79	531.12	527.41	511.81	469.51	485.91	629.23	747.77	618.04
SD	834.21	936.09	549.84	559.91	501.68	428.62	443.41	526.51	524.67	447.63
SE	147.47	165.48	97.20	98.98	88.68	75.77	78.39	93.07	92.75	79.13
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001

Intent toTreat Analysis (All Treated Subjects; Last Value Carried to End of Study)

N	35	35	35	35	35	35	35	35	35	35
Mean	641.20	604.39	537.95	534.55	520.29	481.61	496.61	627.65	736.03	617.42
SD	800.18	897.02	530.90	540.45	458.75	418.10	431.53	508.40	508.13	434.04
SE	135.25	151.62	89.74	91.35	82.11	70.67	72.94	85.94	85.89	73.37
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	30	30	30	30	30	30	30	30	30	30
Mean	540.96	473.14	501.72	476.43	499.26	454.93	454.05	622.39	750.49	621.22
SD	576.69	528.52	500.69	466.01	501.51	420.93	385.46	532.66	539.23	453
SE	105.29	96.49	91.41	85.08	91.56	76.85	70.38	97.25	98.45	82.71
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001

Intent to Treat Analysis (All Randomized Subjects; Last Value Carried toDiscontinuation)

N	32	32	32	32	32	32	32	32	32	32
Mean	644.05	603.79	531.12	527.41	511.81	469.51	485.91	629.23	747.77	618.04
SD	834.21	936.09	549.84	559.91	501.68	428.62	443.41	526.51	524.67	447.63
SE	147.47	165.48	97.20	98.98	88.68	75.77	78.39	93.07	92.75	79.13
P vs Base	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001

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Subject	20	21	22	23	24
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Intent toTreat Analysis (All Treated Subjects; Last Value Carried to Discontinuation)

N	32	32	31	31	30
Mean	844.99	872.62	849.48	772.36	871.88
SD	712.18	652.79	635.54	575.82	623.56
SE	125.90	115.40	114.15	103.42	113.85
P vs Base	0.011	0.007	0.011	0.001	0.065

Intent toTreat Analysis (All Treated Subjects; Last Value Carried to End of Study)

N	35	35	35	35	35
Mean	824.91	850.17	814.68	746.38	853.08
SD	687.44	632.27	610.96	552.42	602.90
SE	116.20	106.87	103.27	93.38	101.91
P vs Base	0.004	0.002	0.002	<.001	0.040

Per-protocol Analysis (All Evaluable Subjects; Last Value Carried to End of Study)

N	30	30	30	30	30
Mean	828.94	861.31	822.46	747.40	871.88
SD	700.84	648.18	628.04	568.34	623.56
SE	127.96	118.34	114.66	103.76	113.85
P vs Base	0.004	0.002	0.003	<.001	0.065

Intent to Treat Analysis (All Randomized Subjects; Last Value Carried toDiscontinuation)

N	32	32	31	31	30
Mean	844.99	872.62	849.48	772.36	871.88
SD	712.18	652.79	635.54	575.82	623.56
SE	125.90	115.40	114.15	103.42	113.85
P vs Base	0.011	0.007	0.011	0.001	0.065