

The OPTIMA study*:

Assessing a New Cinacalcet (Sensipar®/Mimpara®) Treatment Algorithm for Secondary Hyperparathyroidism (HPT)

“The OPTIMA treatment algorithm was designed to be a practical treatment paradigm that builds upon the properties of cinacalcet by increasing or decreasing vitamin D dosage to increase the achievement of treatment targets.”

—Messa et al¹

Sensipar® is indicated for the treatment of secondary hyperparathyroidism (HPT) in patients with chronic kidney disease (CKD) on dialysis.

Important Safety Information

- Sensipar® treatment should not be initiated if serum calcium is less than the lower limit of the normal range (8.4 mg/dL).
- Sensipar® lowers serum calcium; therefore, it is important that patients are carefully monitored for the occurrence of hypocalcemia.
- Significant reductions in calcium may lower the threshold for seizures. Secondary hyperparathyroidism (HPT) patients, particularly those with a history of seizure disorder, should be carefully monitored for the occurrence of low serum calcium or symptoms of hypocalcemia.
- In Sensipar® postmarketing use, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia were reported in patients with impaired cardiac function. The causal relationship to Sensipar® therapy could not be completely excluded and may be mediated by reductions in serum calcium levels.
- Adynamic bone disease may develop if intact parathyroid hormone (iPTH) levels are suppressed below 100 pg/mL.
- Patients with moderate to severe hepatic impairment should be monitored throughout treatment with Sensipar®, as cinacalcet exposure assessed by area under the curve (AUC) was higher than in patients with normal hepatic function.
- Serum calcium and serum phosphorus should be measured within 1 week and PTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar®. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and PTH every 1 to 3 months.
- The most commonly reported side effects were nausea, vomiting, and diarrhea.

Please refer to the accompanying Sensipar® Package Insert for full prescribing information.

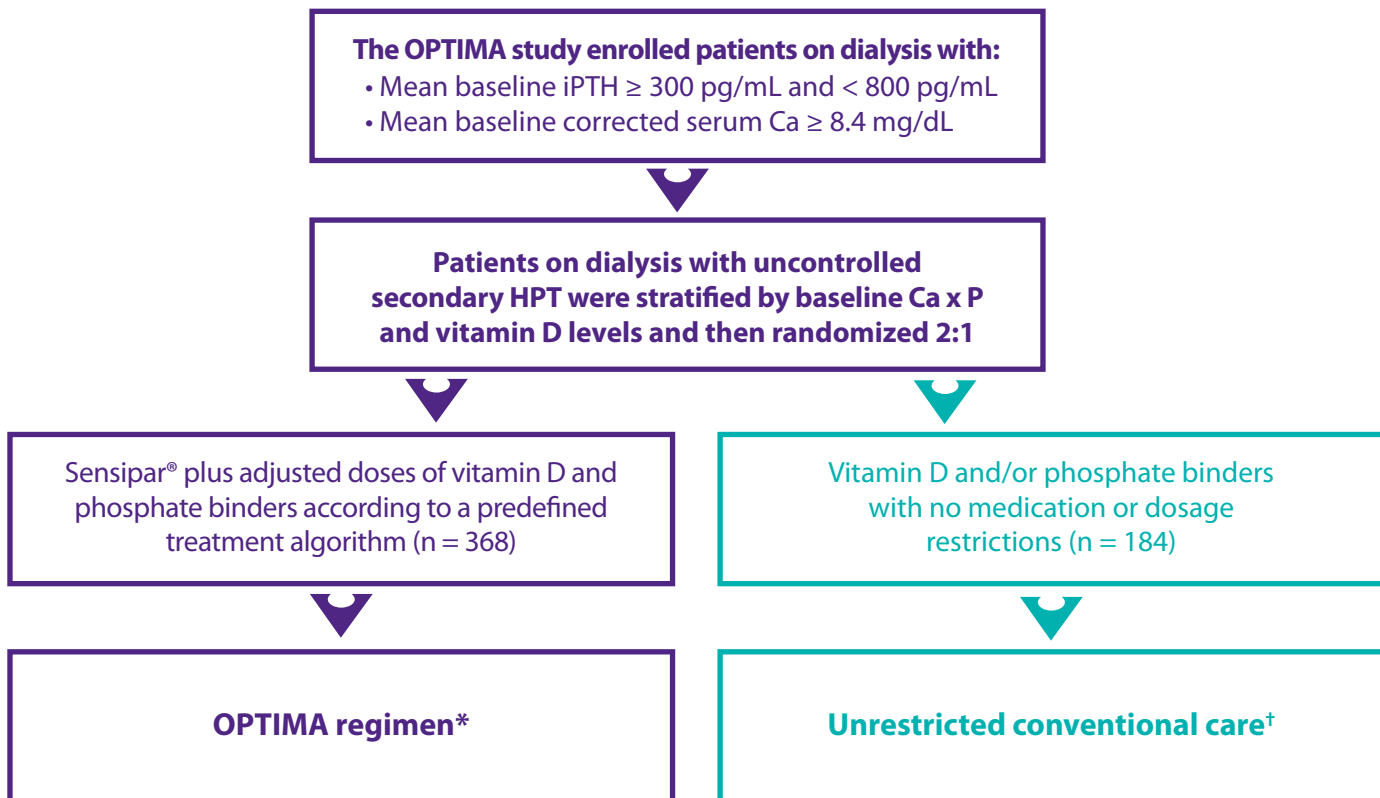
*The OPTIMA study: An **OP**en-label, randomized study using cinacalcet **To IM**prove **A**chievement of KDOQI™ targets in patients with end-stage renal disease.

KDOQI™ is a trademark of the National Kidney Foundation, Inc.

Sensipar®
(cinacalcet) Tablets
30mg-60mg-90mg

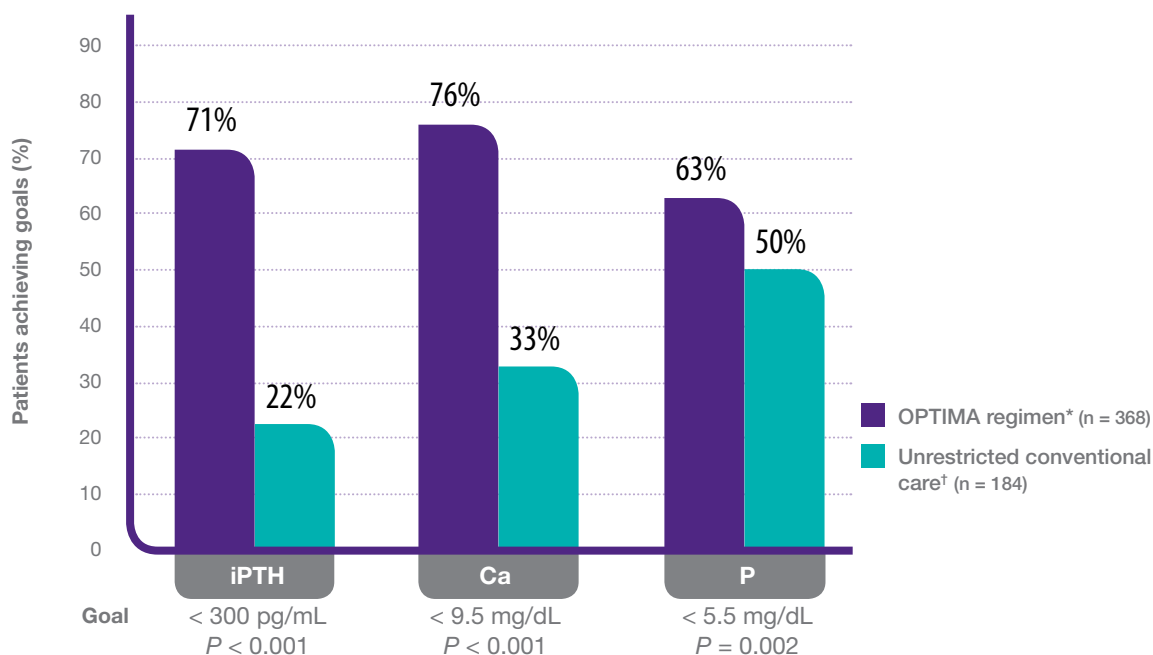
Study design¹

- The results of this multicenter, open-label study were published by Piergiorgio Messa et al in the *Clinical Journal of the American Society of Nephrology* in January 2008



The OPTIMA study was designed to evaluate the ability of the OPTIMA regimen* to improve the achievement of PTH, Ca, and P goals compared with unrestricted conventional care.†

The OPTIMA regimen* allowed more patients to achieve treatment goals[‡] compared with patients receiving unrestricted conventional care^{1§}



Reported adverse events¹

- 80% of patients in the OPTIMA regimen* group and 59% of patients in the unrestricted conventional care[†] group experienced at least 1 adverse event (AE)
- The most common AEs were nausea (OPTIMA regimen* 32% vs unrestricted conventional care[†] 3%), vomiting (24% vs 7%) and diarrhea (13% vs 7%)
- Hypocalcemia (serum Ca < 7.5 mg/dL on at least 2 consecutive measurements during the study) occurred in 5% of patients in the OPTIMA regimen* group and 1% of patients in the unrestricted conventional care[†] group

Patients who received unrestricted doses of conventional care[†] experienced lower rates of goal achievement for PTH, Ca, and P.

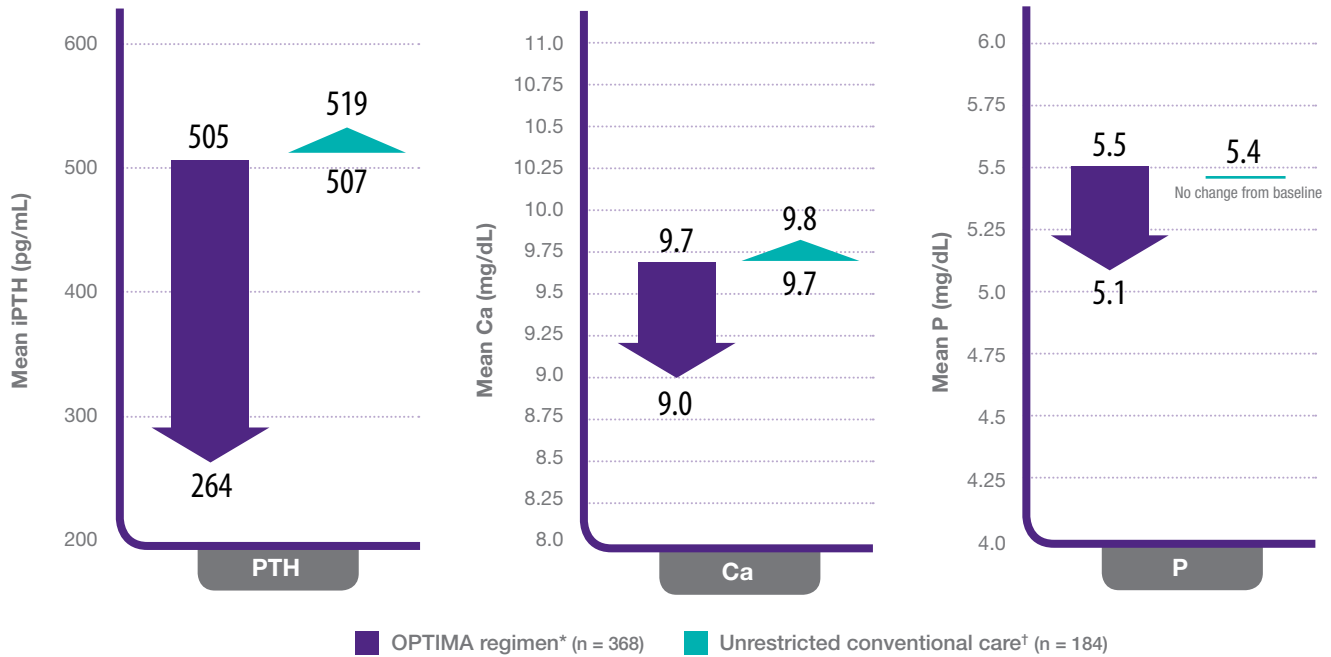
The Sensipar[®] PI recommends that if serum Ca falls below 7.5 mg/dL or if symptoms of hypocalcemia persist and the dose of vitamin D cannot be increased, withhold administration of Sensipar[®] until serum Ca levels reach 8.0 mg/dL and/or symptoms of hypocalcemia have resolved.³

[‡]Treatment goals were defined as iPTH ≤ 300 pg/mL; Ca < 9.5 mg/dL; P < 5.5 mg/dL.
[§]These results were for patients with iPTH 300–800 pg/mL.
 iPTH = intact parathyroid hormone; Ca = calcium; P = phosphorus.

For secondary HPT patients on dialysis

The OPTIMA regimen* provided greater reductions of key laboratory parameters than unrestricted conventional care^{1,2†}

The OPTIMA regimen* lowered mean serum levels of PTH, Ca, and P over 23 weeks¹



The OPTIMA regimen* improved phosphorus reductions regardless of baseline PTH over 23 weeks²



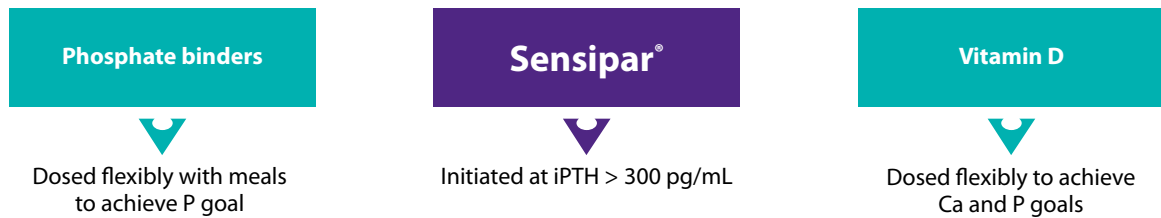
4 Please see Important Safety Information on the front cover.

*Sensipar® plus adjusted doses of vitamin D and phosphate binders, if prescribed.

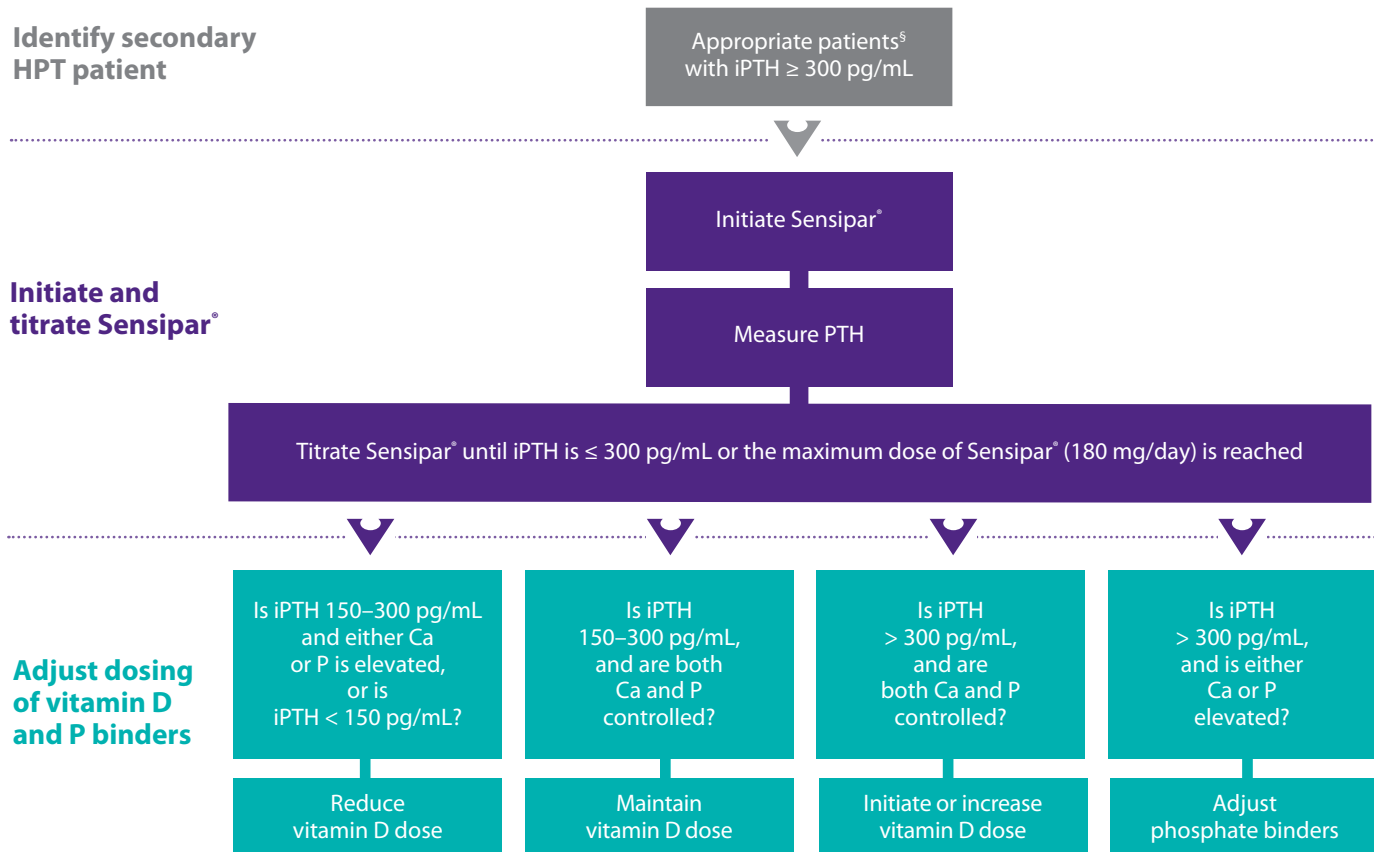
†Unrestricted use of vitamin D and phosphate binders, if prescribed.

The OPTIMA regimen* achieved better PTH, Ca, and P results than unrestricted conventional care[†] while requiring low mean doses of vitamin D¹

The OPTIMA regimen* utilized this targeted approach



The OPTIMA treatment regimen**



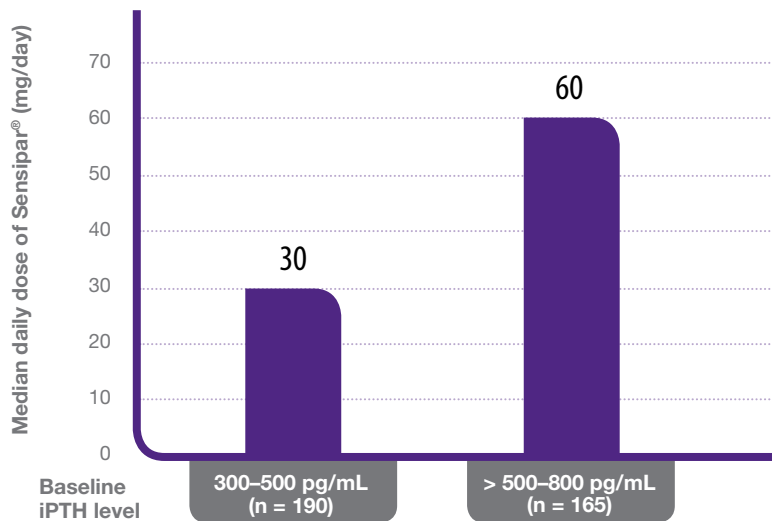
Serum Ca and serum P should be measured within 1 week, and PTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar[®]. Once the maintenance dose has been established, serum Ca and serum P should be measured approximately monthly, and PTH every 1 to 3 months.³

*See insert in pocket for full description of treatment algorithm.

§Secondary HPT patients on dialysis with iPTH ≥ 300 pg/mL and < 800 pg/mL, and corrected serum Ca ≥ 8.4 mg/dL.

Therapy utilization¹

Doses of Sensipar[®] used in the OPTIMA regimen^{*†}

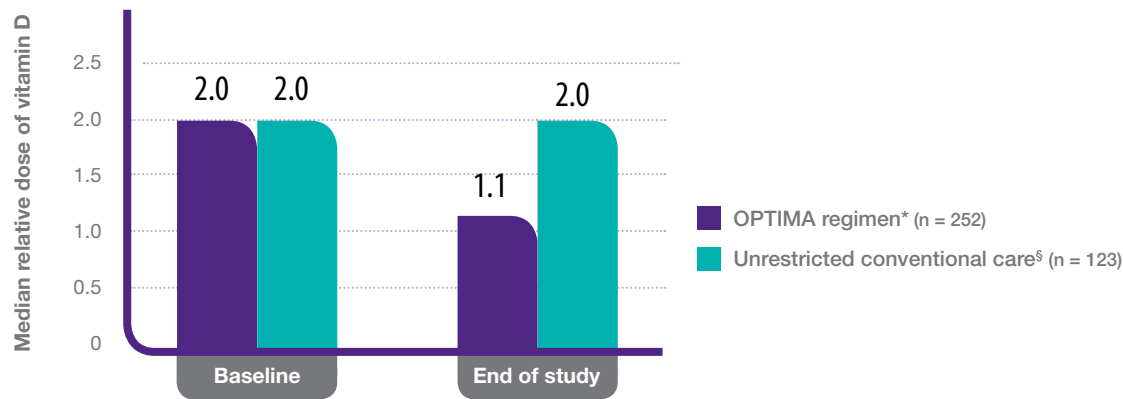


[†]At the end of the efficacy assessment phase.

- Mean and median doses of Sensipar[®] were 56 mg/day and 30 mg/day, respectively
- 65% of patients received Sensipar[®] 60 mg/day or less
- A total of 6% of the patients used the maximum 180 mg/day dose most often compared with other dosages throughout the efficacy assessment phase
- Patients with less severe disease required lower doses of Sensipar[®] to control PTH (median dose 30 mg/day in patients with baseline iPTH 300–500 pg/mL and 60 mg/day in those with iPTH > 500–800 pg/mL)
- In three additional clinical studies conducted in CKD patients on dialysis, the median dose of Sensipar[®] at end of study was 90 mg. Patients with milder disease typically required lower doses³
- The most commonly reported side effects were nausea, vomiting, and diarrhea³

6 **Please see Important Safety Information on the front cover.**

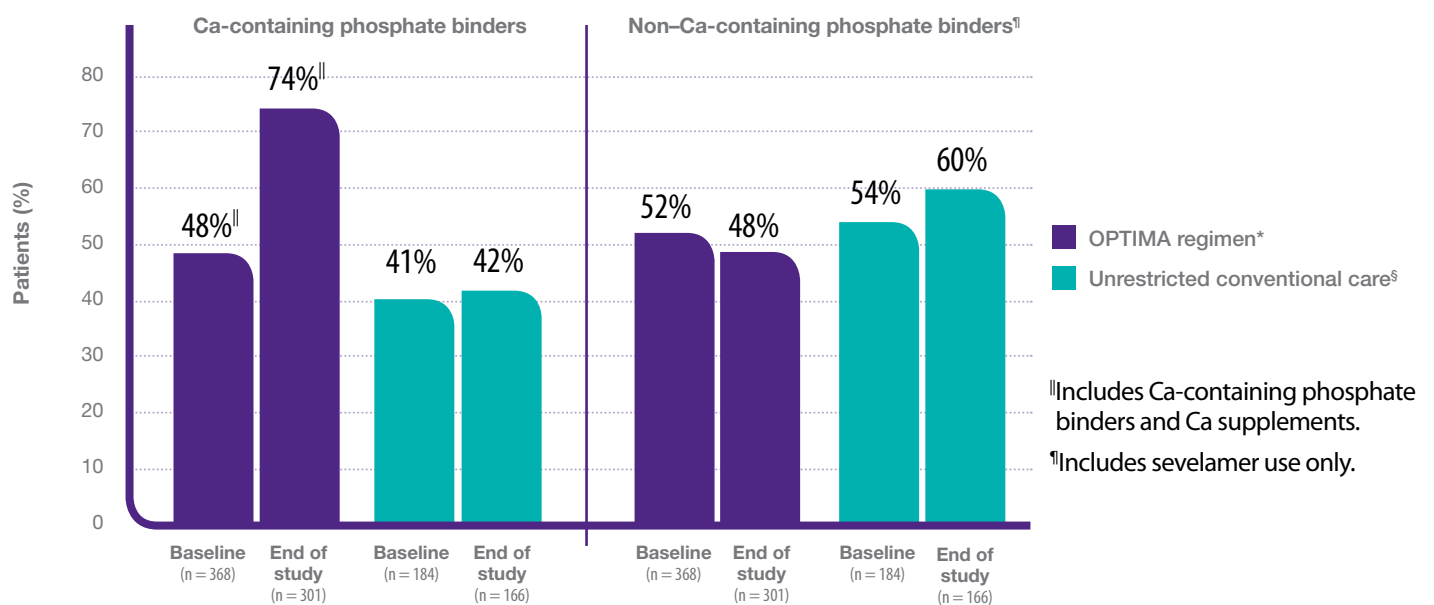
Change in relative dose[‡] of vitamin D in patients receiving vitamin D at baseline



[‡]Due to the multiple vitamin D analogs permitted in the study, vitamin D dose comparisons were based on conversion of each dose a patient received into a multiple of the protocol-defined minimum dose for a particular sterol. Minimum doses were defined as IV calcitriol 0.5 µg TIW, IV alfacalcidol 1 µg TIW, paricalcitol 2 µg TIW, oral calcitriol 0.25 µg TIW, or oral alfacalcidol 0.25 µg/day. A relative dose of 1 represents a minimum dose of each vitamin D analog as defined by the study protocol.

- In those patients receiving vitamin D at baseline:
 - OPTIMA regimen*—the median relative dose of vitamin D decreased from 2.0 to 1.1
 - Unrestricted conventional care§—there was no change in median relative dose of vitamin D from baseline
- In all patients:
 - OPTIMA regimen*—the mean relative dose of vitamin D decreased by 6%
 - Unrestricted conventional care§—there was a 14% increase in the mean relative dose of vitamin D

Changes in the use of Ca-containing phosphate binders in the OPTIMA study



- Use of aluminum-based phosphate binders decreased from 19% to 12% in the OPTIMA regimen* group and increased from 20% to 21% in the unrestricted conventional care[§] group

Conclusions¹

- The OPTIMA regimen* used a targeted approach that initiated Sensipar® primarily to lower PTH, phosphate binders primarily to lower P, and vitamin D primarily to modulate changes in Ca and P
- The OPTIMA regimen* allowed more patients to achieve PTH, Ca, and P goals compared with unrestricted conventional care[†]
- The OPTIMA regimen* resulted in changes in the utilization of Sensipar®, vitamin D, and phosphate binders

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References:

1. Messa P, Macário F, Yaqoob M, et al. The OPTIMA study: assessing a new cinacalcet (Sensipar®/Mimpara®) treatment algorithm for secondary hyperparathyroidism. *Clin J Am Soc Nephrol*. 2008;3:36-45.
2. Data on file, Amgen.
3. Sensipar® (cinacalcet) prescribing information, Amgen.

*Sensipar® plus adjusted doses of vitamin D and phosphate binders, if prescribed.

[†]Unrestricted use of vitamin D and phosphate binders, if prescribed.

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