Advancing Patient Care in Nephrology a New Approach to Managing Parathyroid Health

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CKD = Chronic Kidney Disease
sHPT = Secondary Hyperparathyroidism

KWT-416-0125-80001

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Disclosure

No Disclosure

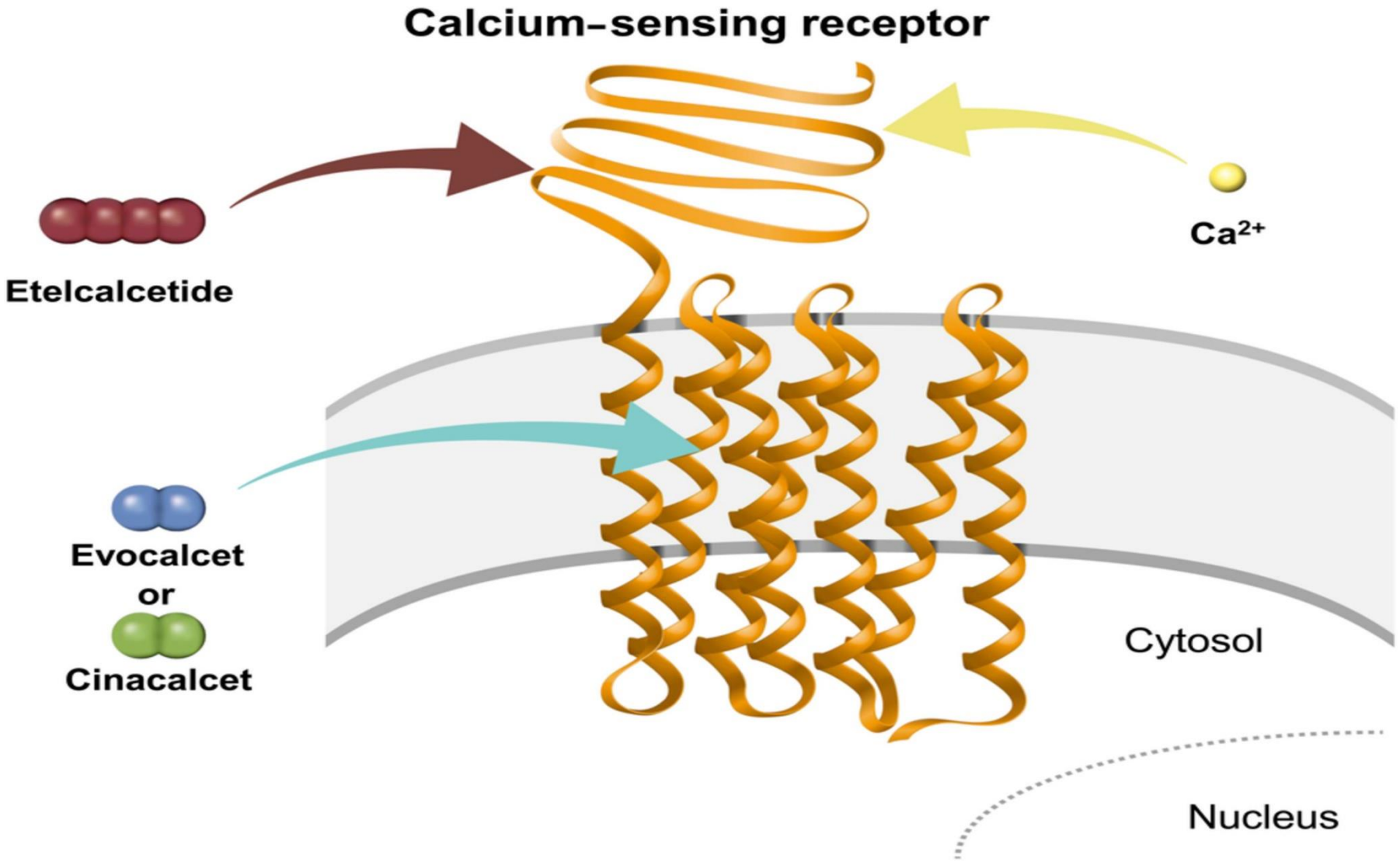
KDIGO guidelines 2017

CKD Stages	3A – 5D	3A – 5D *Receiving phosphate- lowering treatment*	5D *Requiring PTH- lowering treatment*
	Section 4.1.1 Treatments of CKD-MBD should be based on serial assessments of P, Ca, and PTH levels, considered together (NG)	**Section 4.1.6** Restrict the dose of Ca-based phosphate binders (2B)	**Section 4.2.4** Suggest calcimimetics, calcitriol, or vitamin D analogs, or a combination of calcimimetics and calcitriol, or vitamin D analogs (2B) Rationale: Given the lack of consensus among the Work Group and the higher acquisition cost of cinacalcet, it was decided to modify the 2009 recommendation to list calcimimetic therapy now first, in alphabetical order, among acceptable treatment options while still recognizing the utility and efficacy of active vitamin D compounds
	Section 4.1.2 Suggest lowering elevated phosphorus levels toward the normal range (2C)		
	Section 4.1.3 Avoid hypercalcemia (2C) Rationale: Mild and asymptomatic hypocalcemia (e.g., in the context of calcimimetic treatment) can be tolerated in order to avoid inappropriate calcium loading in adults.		

Acronyms: CKD: Chronic Kidney Disease, MBD: Mineral Bone Disease; PTH: Parathyroid Hormone,

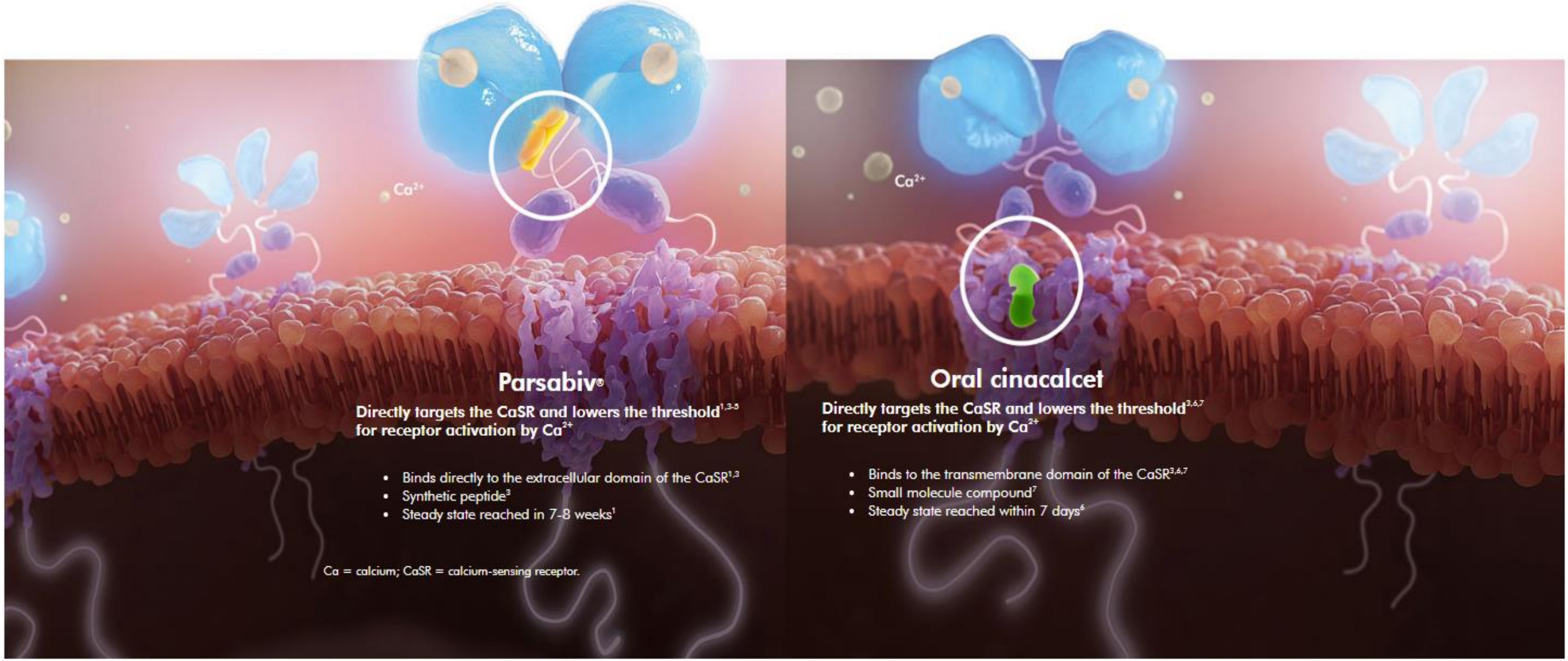
KDIGO 2017, *Kidney Int Suppl* 2017. 7(1): 1-60

Calcimimetics and the CaSR



from Therapeutic Apheresis and Dialysis, 2

Etelcalcetide and Cinacalcet: Calcimimetic Agents With Similar Characteristics but Different Structures and Routes of Administration



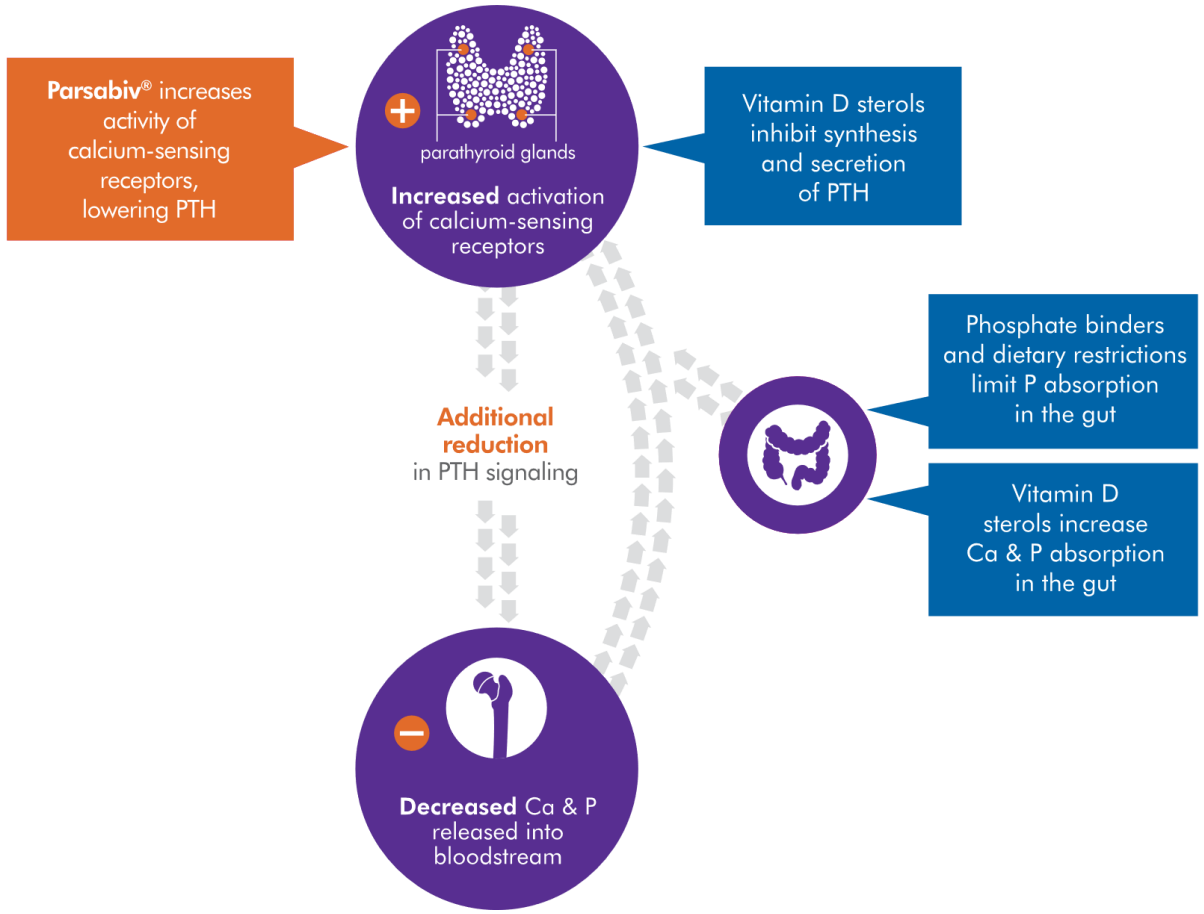
Parsabiv is available as alternative to mimpara

- Mimpara is no longer available in Kuwait after identification of higher Nitrosamine levels than accepted by FDA despite no safety concern or risk raised for development of malignancy
- Nitrosamines are organic compounds that form during chemical reactions and are widely present in many food and drugs, high doses and long term exposure may pose a risk of malignancy
- Mimpara is still available in some countries in generic formulations

Parsabiv™
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Treatment with Parsabiv® (etelcalcetide) vitamin D, and phosphate binders

Concomitant use of Parsabiv®, vitamin D, and phosphate binders has complementary effects on PTH, phosphorus, and calcium[1-7]



REFERENCES

Ca = calcium; P = phosphorus; PTH = parathyroid hormone

Behind the Scenes

Parsabiv® (etelcalcetide) lowers and maintains 3 key sHPT lab values.[1]

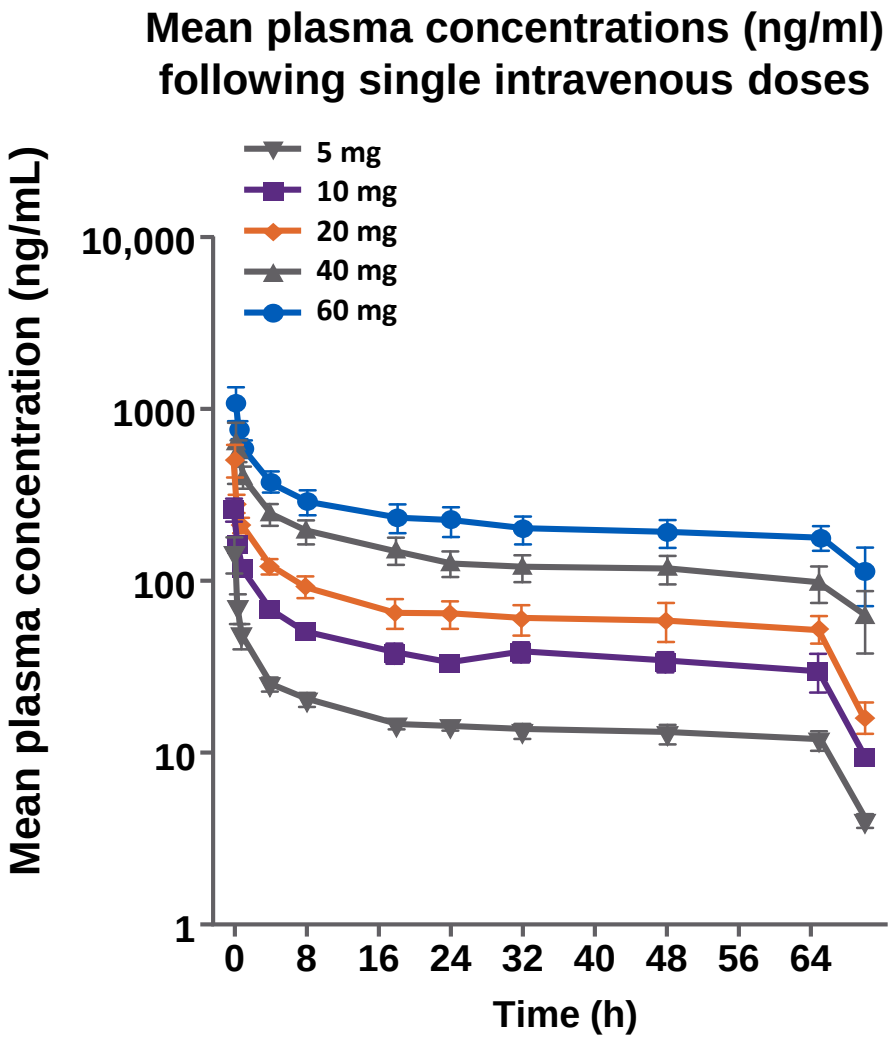
REFERENCES

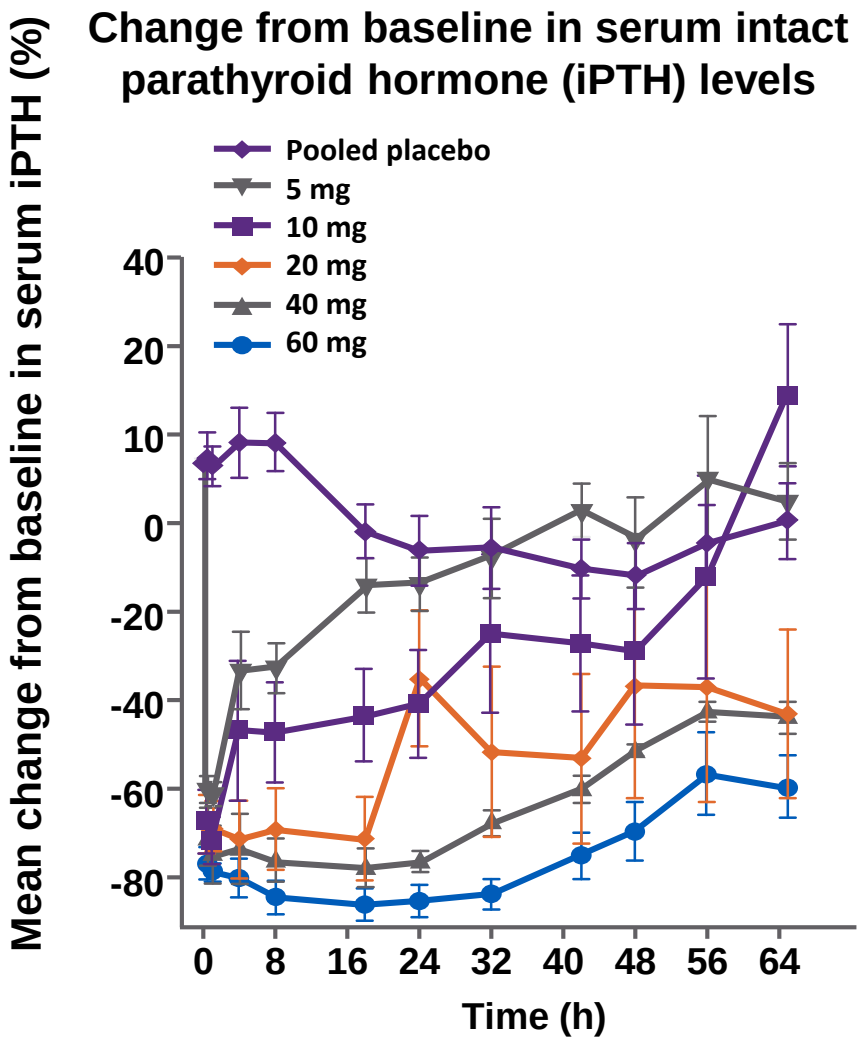
Etelcalcetide

- A synthetic peptide calcimimetic
- 7 D-amino acids linked to an L-cysteine *via* a disulfide bond
- Resistant to proteolysis – clearance mainly renal
- Dialysable in ESRD patients
- In ESRD the effective t/2 is 3-5 days
- Does not cross the blood-brain barrier

Etelcalcetide – an IV calcimimetic treatment of SHPT in HD patients

PK and PTH levels after a single IV dose in patients on haemodialysis





Martin KJ, et al. Kidney Int 2014;85:191–97

JAMA | Original Investigation

Effect of Etelcalcetide vs Placebo on Serum Parathyroid Hormone in Patients Receiving Hemodialysis With Secondary Hyperparathyroidism

Two Randomized Clinical Trials

Geoffrey A. Block; David A. Bushinsky; John Cunningham et al

JAMA. 2017;317(2):146-15

Etelcalcetide Phase 3 Clinical Trials

Background

Study design: two phase 3, 26-week, multicenter, randomized, double-blind, placebo-controlled clinical studies comparing Parsabiv® with placebo in patients with CKD on hemodialysis with iPTH >400 pg/mL and cCA ≥8.3 mg/dL (N=1023).[1,2]

Mean baseline iPTH was 847 pg/mL in the Parsabiv® group and 836 pg/mL in the placebo group.[3]

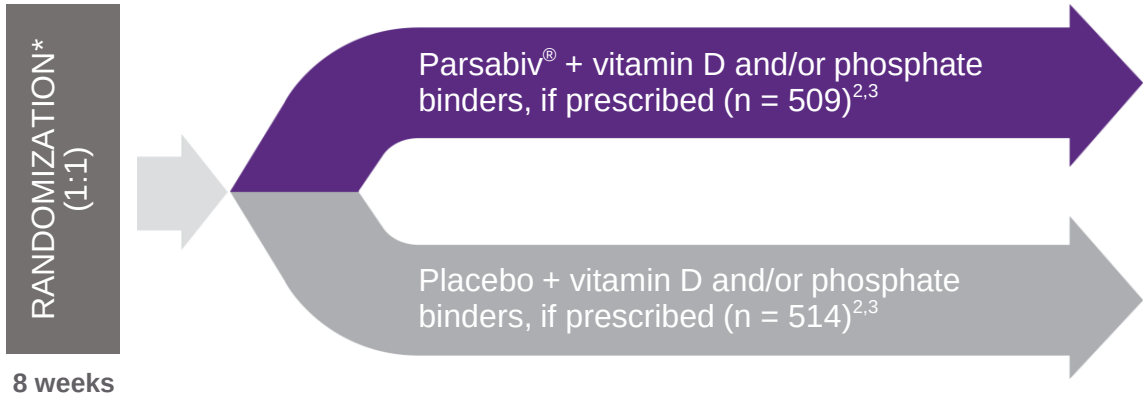
All information included on the placebo-controlled data reflect pooled data from both studies.

REFERENCES

iPTH = intact parathyroid hormone
cCA = corrected calcium
EAP = efficacy assessment phase

Parsabiv® was evaluated in two placebo-controlled studies[1-3]

Treatment phase—26 weeks[1,2]
(16 weeks titration followed by 10 weeks maintenance)

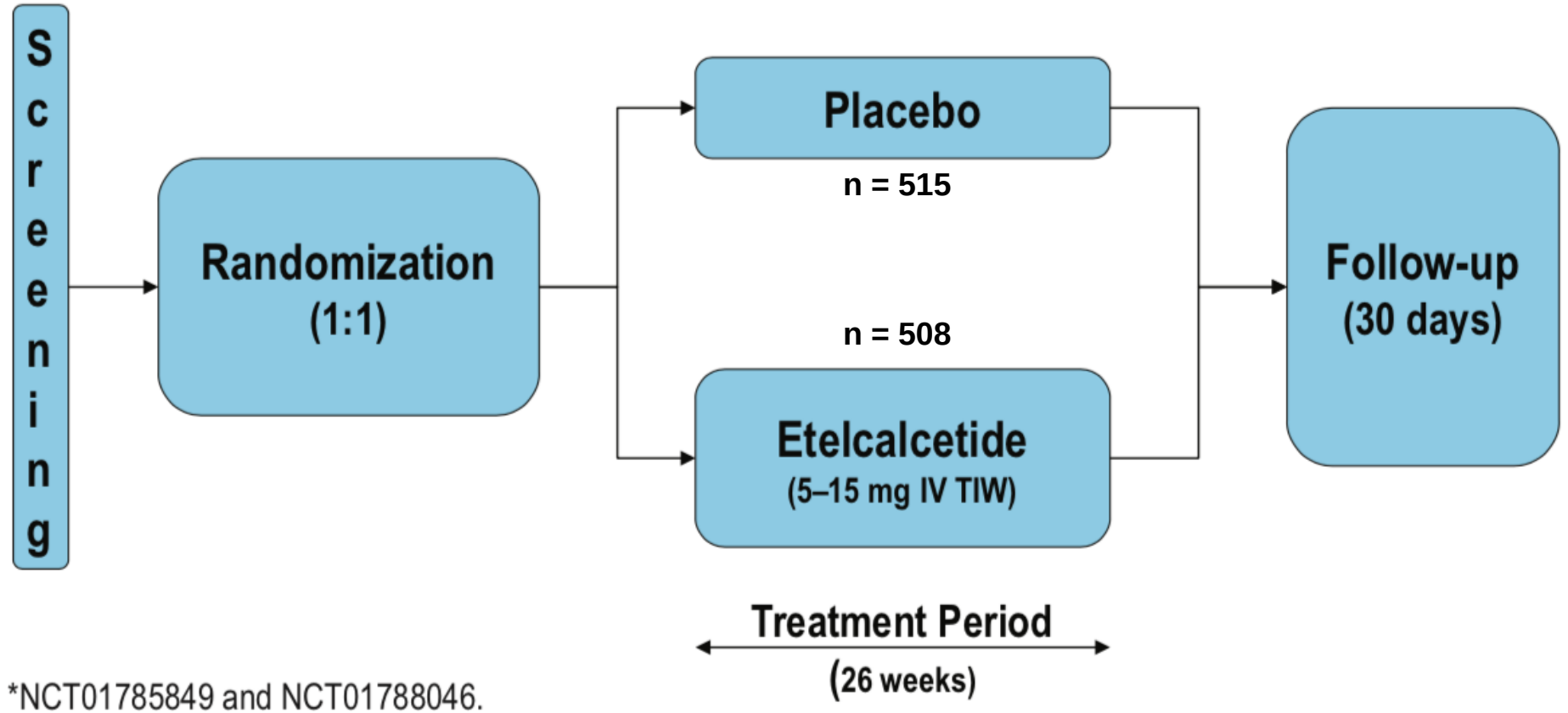


*Stratified by region, mean screening iPTH, and recent cinacalcet use.[2]

Primary endpoint: proportion of patients who achieved >30% reduction from baseline in mean iPTH during the EAP (defined as weeks 20 through 27, inclusive)[1,2]

References: 1. Parsabiv® (etelcalcetide) prescribing information, Amgen. 2. Block GA, et al. *JAMA*. 2017;317:146-155. 3.Data on file, Amgen; [Summary of Clinical Efficacy; 2015].

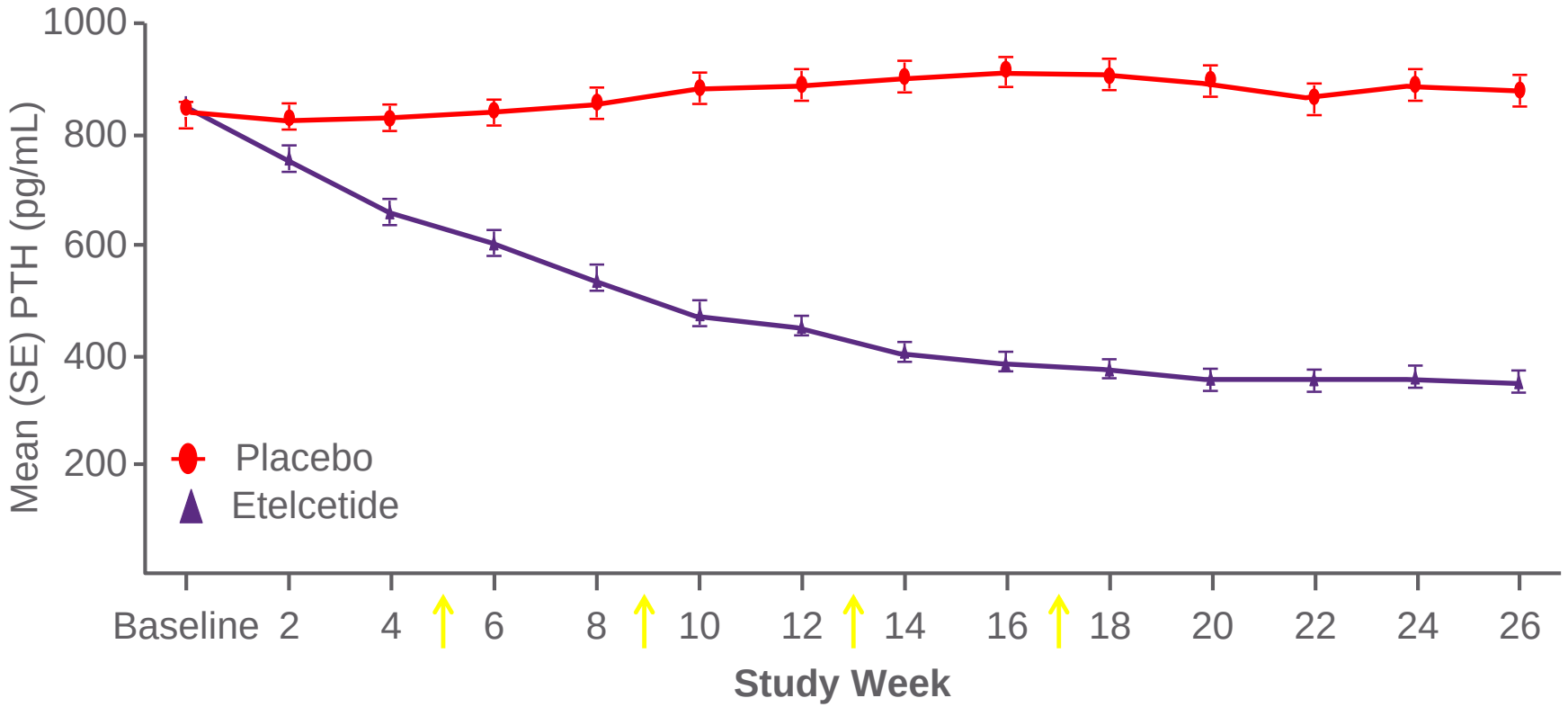
Study Design



*NCT01785849 and NCT01788046.
TIW = three times weekly.

Block GA, et al. *JAMA.* 2017;317:146-155.

Mean PTH Over Time



Placebo	**n**	513	490	488	480	471	466	456	457	440	427	416	402	383	368
Etelcalcetide	**n**	503	468	459	454	449	453	444	439	437	436	425	426	416	405

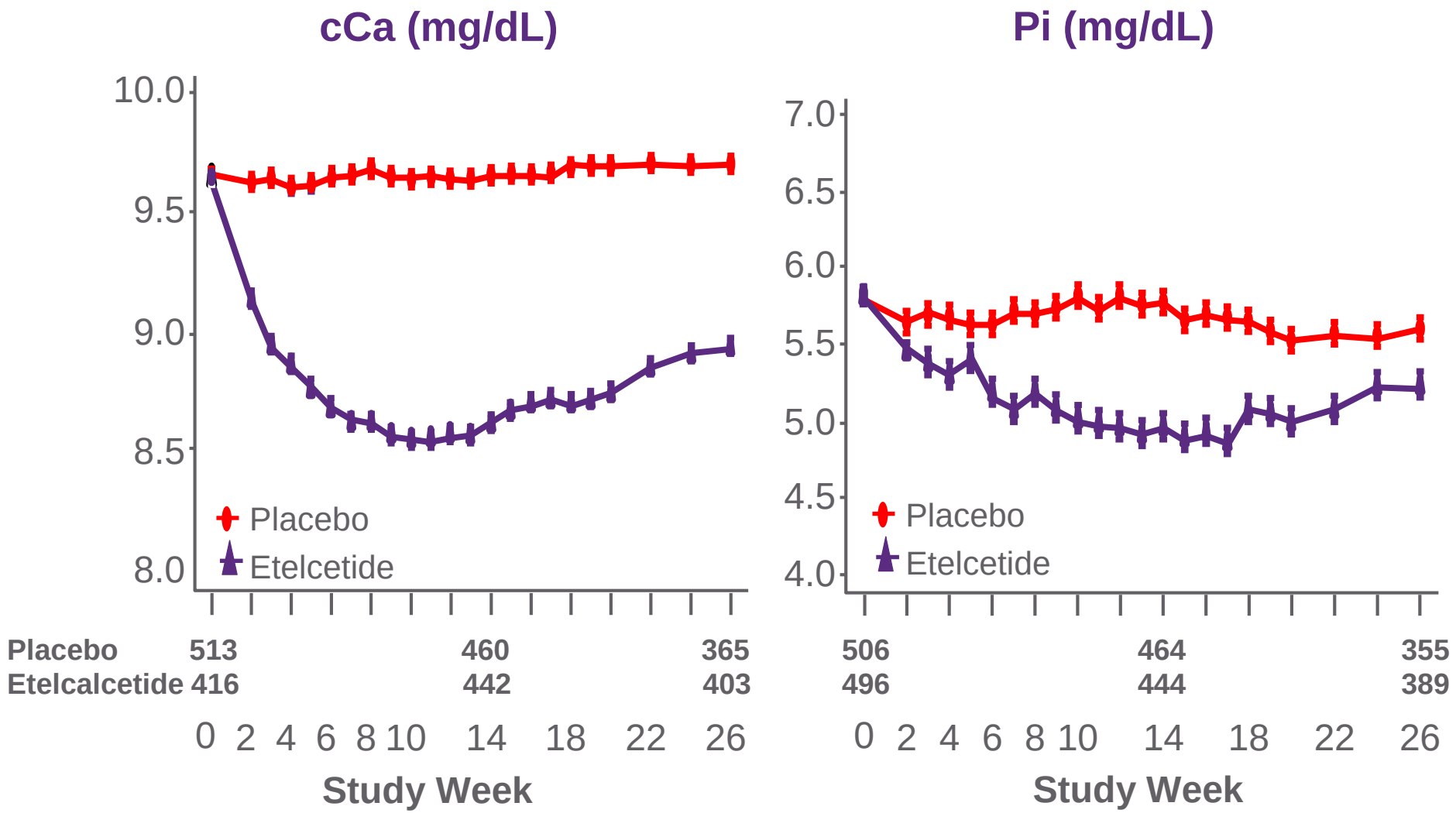
↑= dose titration points

PTH reduction > 30% (EAP)
Etelcalcetide 74.7%
Placebo 8.9%
p<0.001

PTH reduction ≤ 300 pg/mL (EAP)
Etelcalcetide 51.5%
Placebo 4.9%
p<0.001

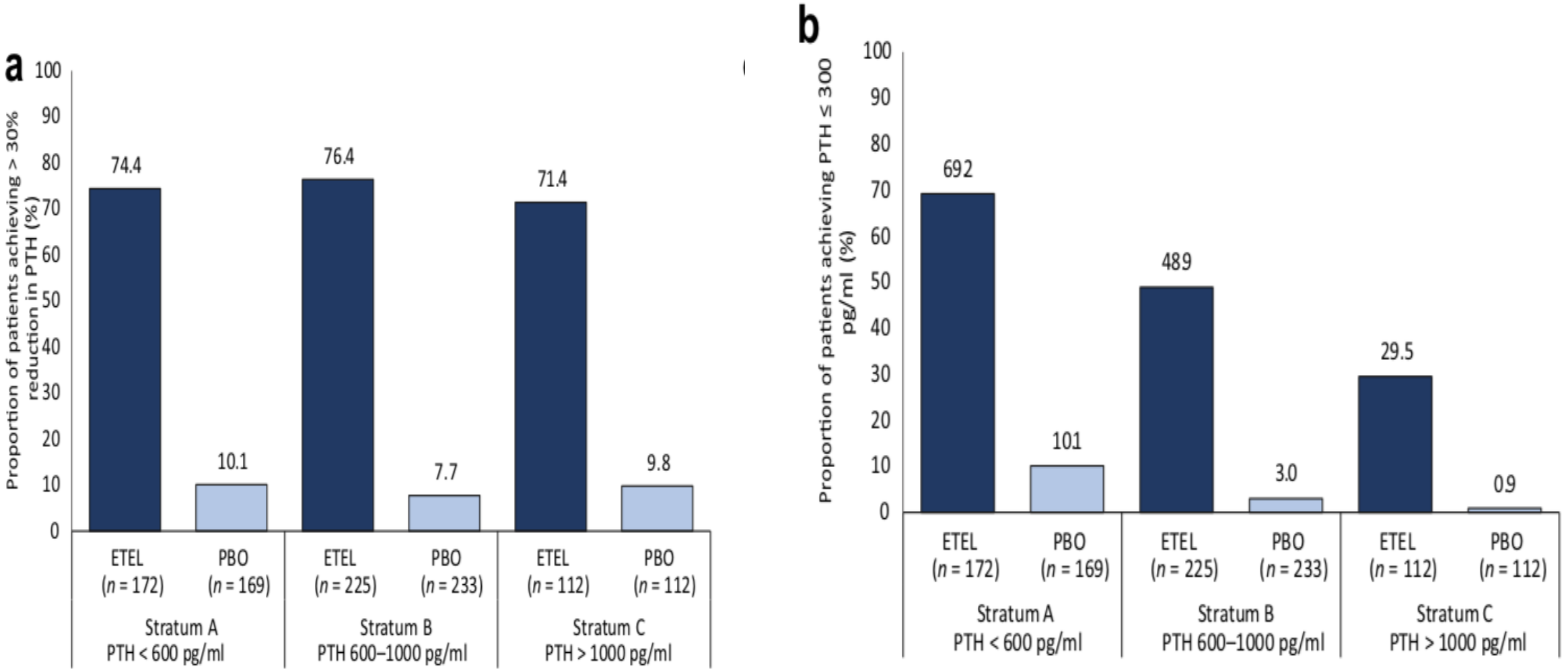
Cunningham J et al ERA – EDTA 2015
Block GA et al. JAMA 2016

Mean (SE) calcium and phosphorous by study week



Cunningham J et al ERA – EDTA 2015
Block GA et al. JAMA 2016

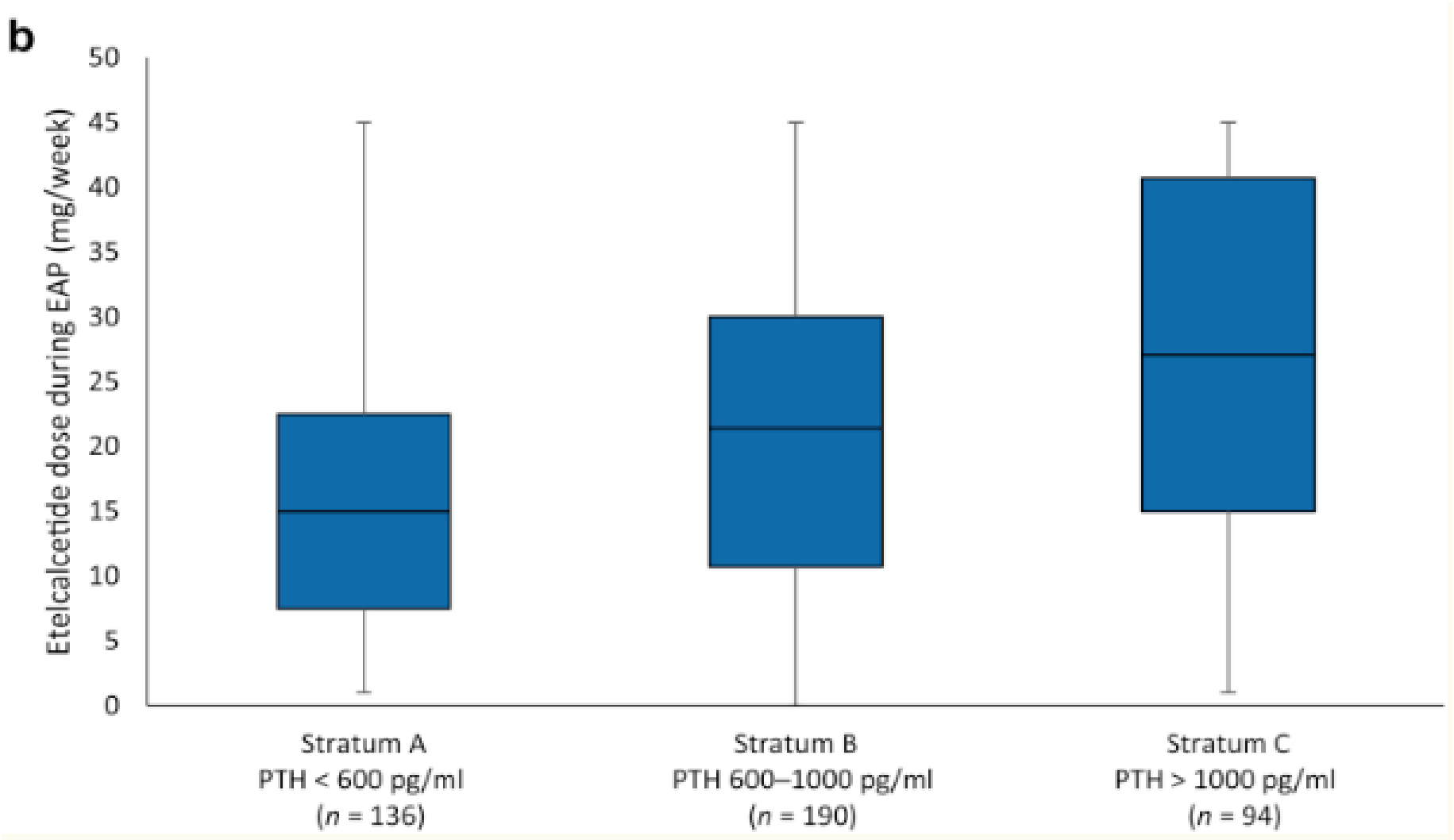
Etelcalcetide Is Effective at All Levels of Severity of Secondary Hyperparathyroidism in Haemodialysis Patients



Cunningham et al Kidney Int Reports, 2019

Etelcalcetide – dosing

higher dose needed in more severe disease



Cunningham et al. Kidney Int Rep 2019

Parsabiv® (etelcalcetide) Phase 3 Clinical Trials

Parsabiv® combined placebo-controlled studies – dosing and titration

Starting dose of Parsabiv® or placebo was 5 mg administered three times per week into the venous line of the dialysis circuit at the end of hemodialysis during rinse back or intravenously after rinse back.[1-4]

- The dose was actively titrated at weeks 5, 9, 13, and 17 to achieve predialysis serum iPTH ≤ 300 pg/mL
- The minimum dose was 2.5 mg and the maximum dose was 15 mg
- The dose could be increased in 2.5 mg or 5 mg increments based on predialysis iPTH and cCa concentrations

Parsabiv® was withheld if any of the following were observed: iPTH < 100 pg/mL (10.6 pmol/l)(two consecutive measurements), corrected calcium < 7.5 mg/dL (1.9mmol/l), symptomatic hypocalcemia, other ongoing adverse events.[5]

During the efficacy assessment phase, the average weekly dose of active vitamin D (IV paricalcitol equivalent) was 16.7 μg in the Parsabiv® group and 14.5 μg in the placebo group.[6]

The average dose of Parsabiv® at the time of the EAP (defined as weeks 20 through 27, inclusive) was 7.2 mg three times per week.[1]

REFERENCES

Parsabiv® Phase 3 Clinical Trials

3 out of 4 Patients on Parsabiv® (etelcalcetide) achieved >30% reduction in mean PTH[1]

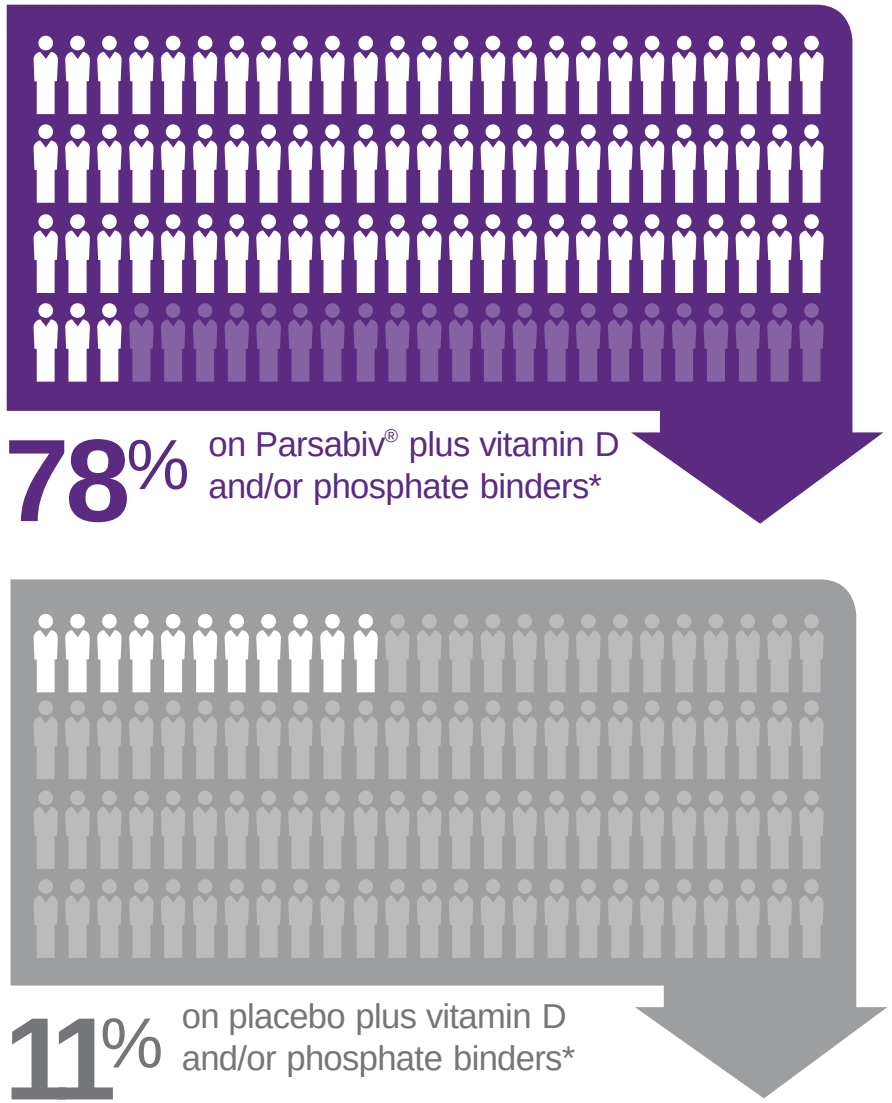
Study design: results are combined from two phase 3, 26-week, multicenter, randomized, double-blind, placebo-controlled clinical studies comparing Parsabiv® with placebo in patients with CKD on hemodialysis with iPTH >400 pg/mL and cCA ≥8.3 mg/dL (N=1023).[2,3]

Patients in both treatment arms could be treated with vitamin D sterols and/or phosphate binders. Mean baseline iPTH in the Parsabiv® group and placebo group were 847 pg/mL and 836 pg/mL, respectively.[4] The primary endpoint of each study was the proportion of patients who achieved a > 30% reduction from baseline in mean iPTH during the efficacy assessment period (defined as weeks 20 through 27, inclusive).[2,3]

Important Safety Information: Parsabiv® lowers serum calcium and can lead to hypocalcemia, sometimes severe.

REFERENCES

*Vitamin D and/or phosphate binders, if prescribed.[3]



P < 0.001

Parsabiv® Phase 3 Clinical Trials

73% of Patients

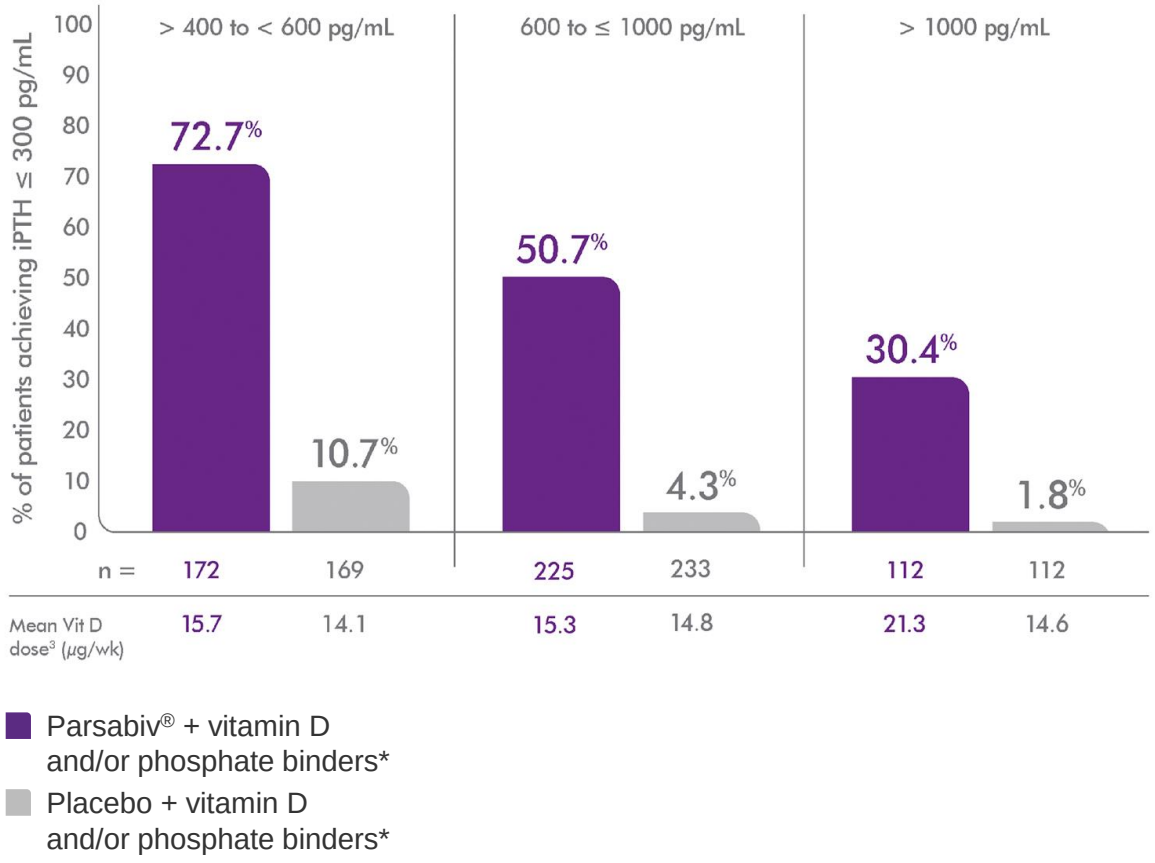
achieved the study PTH treatment goal when Parsabiv® was initiated when PTH was > 400 to < 600 pg/mL[1] (> 42 to < 63 pmol/l)

Secondary endpoint: in phase 3 trials, overall 53.4% of Parsabiv® patients achieved iPTH ≤ 300 pg/mL (31 pmol/l) vs 5.8% of placebo patients during the efficacy assessment period (P < 0.001)

REFERENCES

*Vitamin D and/or phosphate binders, if prescribed.[2]

Subgroup analysis:
Patients achieving study iPTH treatment goal by screening iPTH[1,2]



Parsabiv® Phase 3 Clinical Trials

1 out of 3 Patients

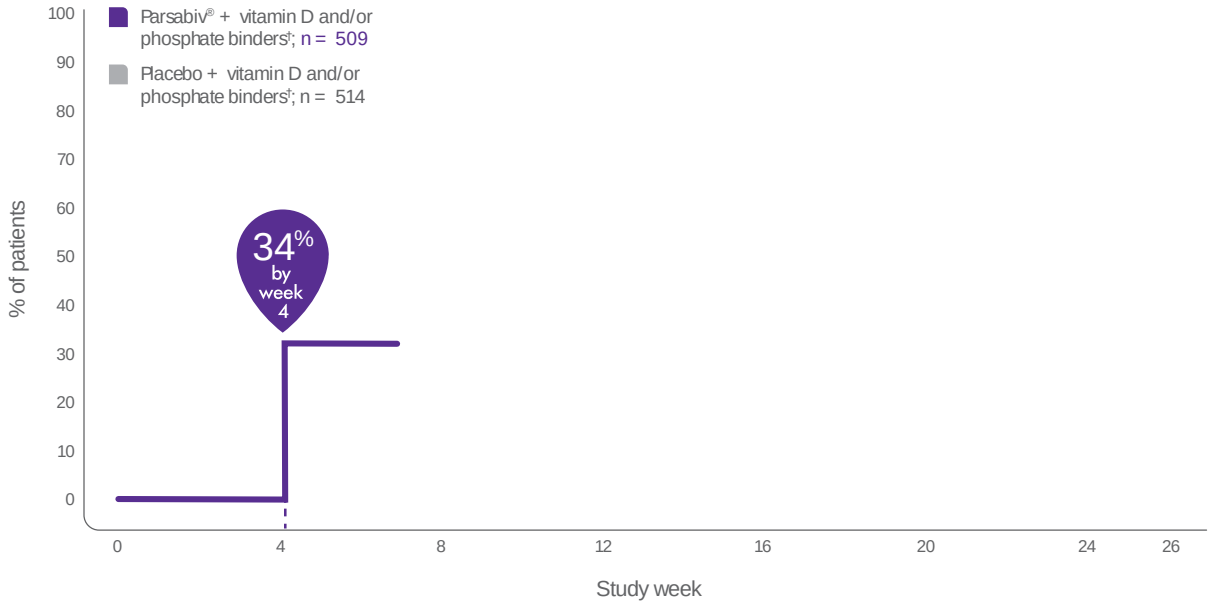
given Parsabiv® achieved a reduction in PTH by Week 4[1]

Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

REFERENCES

*Timepoint when > 30% reduction in iPTH was first observed.
†Vitamin D and/or phosphate binders, if prescribed.[2]

Post-hoc analysis:
Time to first occurrence* of >30% reduction in iPTH from combined placebo-controlled studies



Rolling averages: data are from combined placebo-controlled studies of 3 iPTH values (from previous, current, and next visit) were used.

- The starting dose of Parsabiv® was 5 mg TIW at the end of hemodialysis
- The dose was titrated at weeks 5, 9, 13, and 17 to achieve predialysis serum iPTH ≤ 300 pg/mL. The dose could be increased in 2.5 mg or 5 mg increments based on predialysis iPTH and cCa concentrations increased in 2.5 mg or 5 mg increments based on predialysis iPTH and cCa concentrations

Parsabiv® Phase 3 Clinical Trials

Pooled Results

Week 4 response nearly doubled by Week 8[1]

Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

REFERENCES

*Timepoint when >30% reduction in iPTH was first observed.
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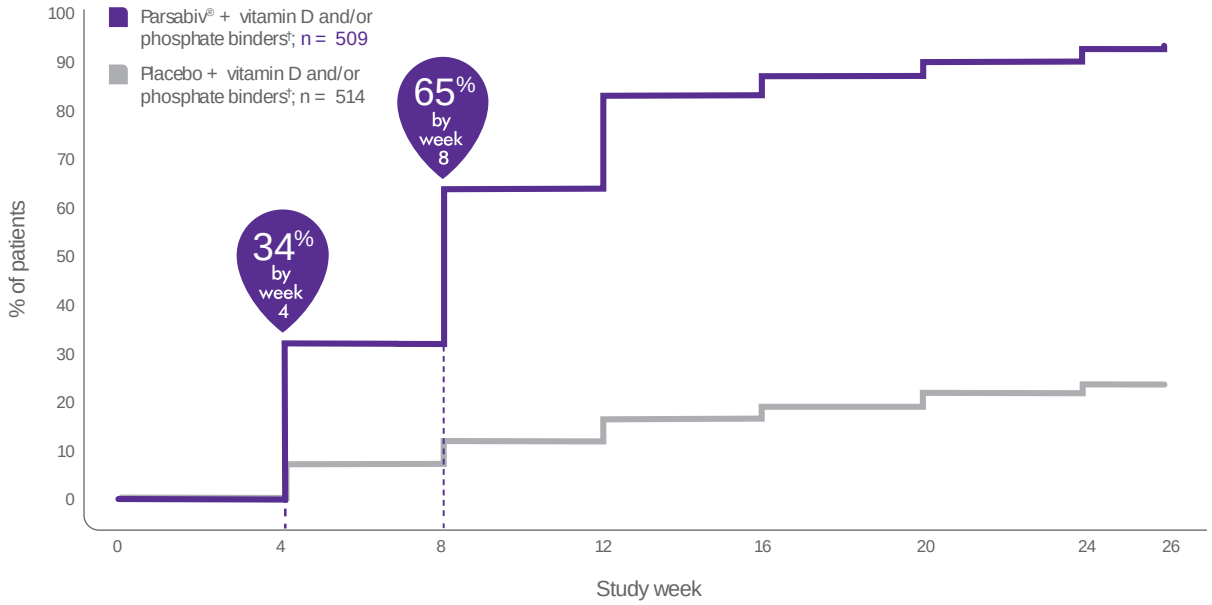

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Research

JAMA | Original Investigation

Effect of Etelcalcetide vs Cinacalcet on Serum Parathyroid Hormone in Patients Receiving Hemodialysis With Secondary Hyperparathyroidism

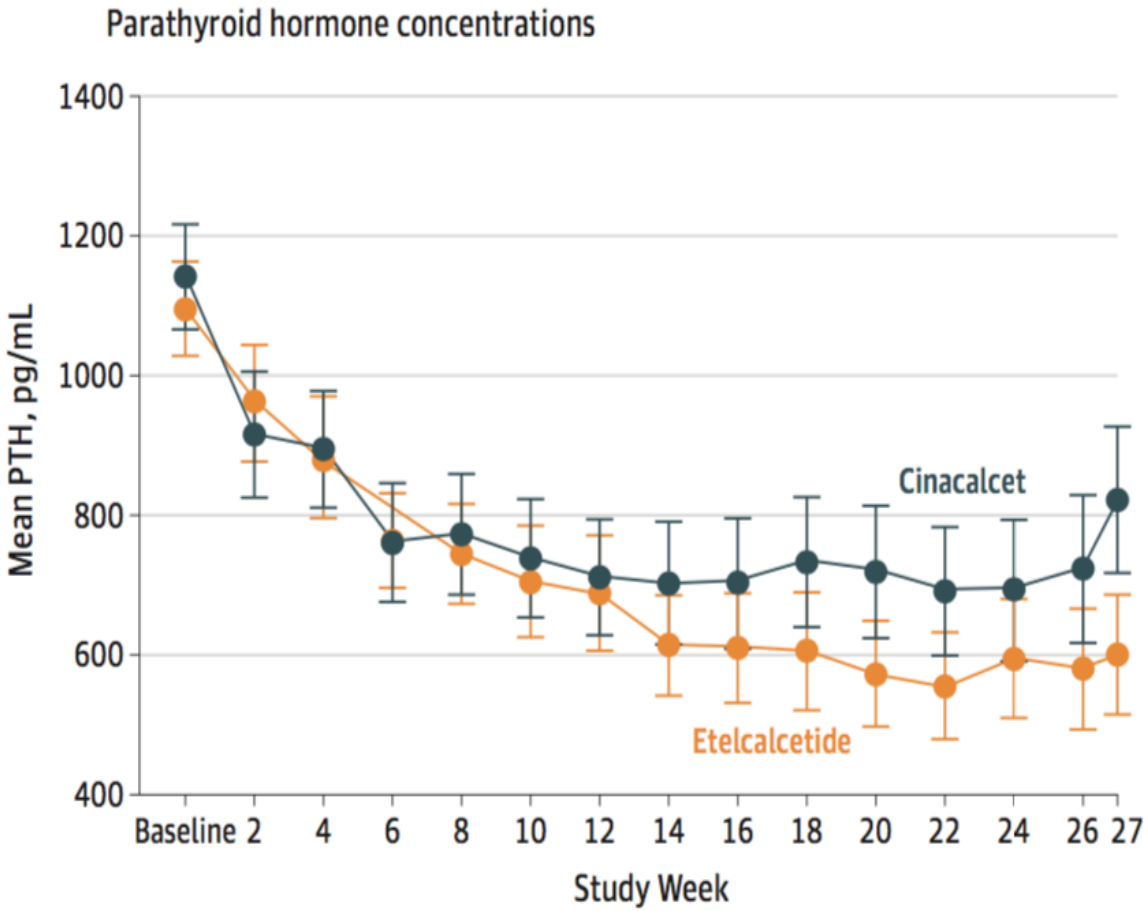
A Randomized Clinical Trial

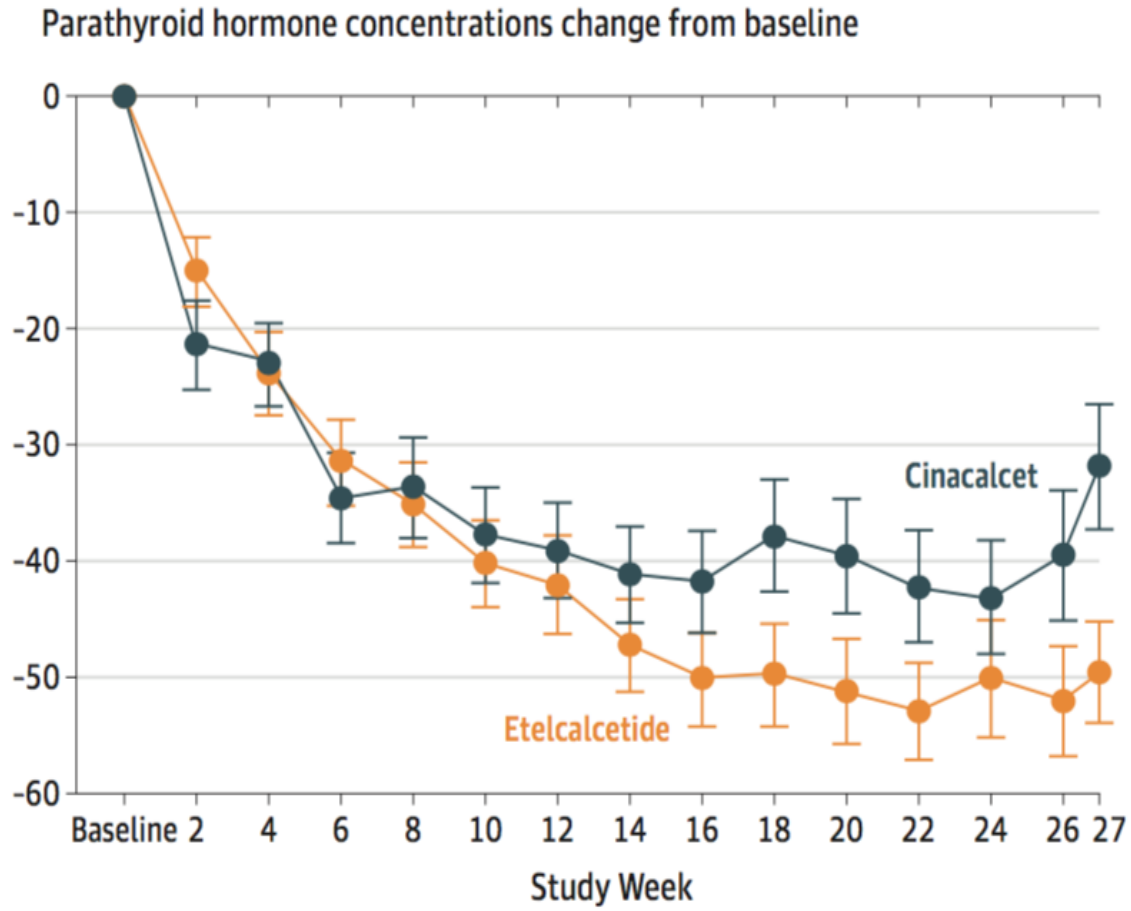
Block GA, et al.

JAMA 2017;317:156-

Etelcalcetide vs. cinacalcet

greater PTH reduction with etelcalcetide





No. of patients

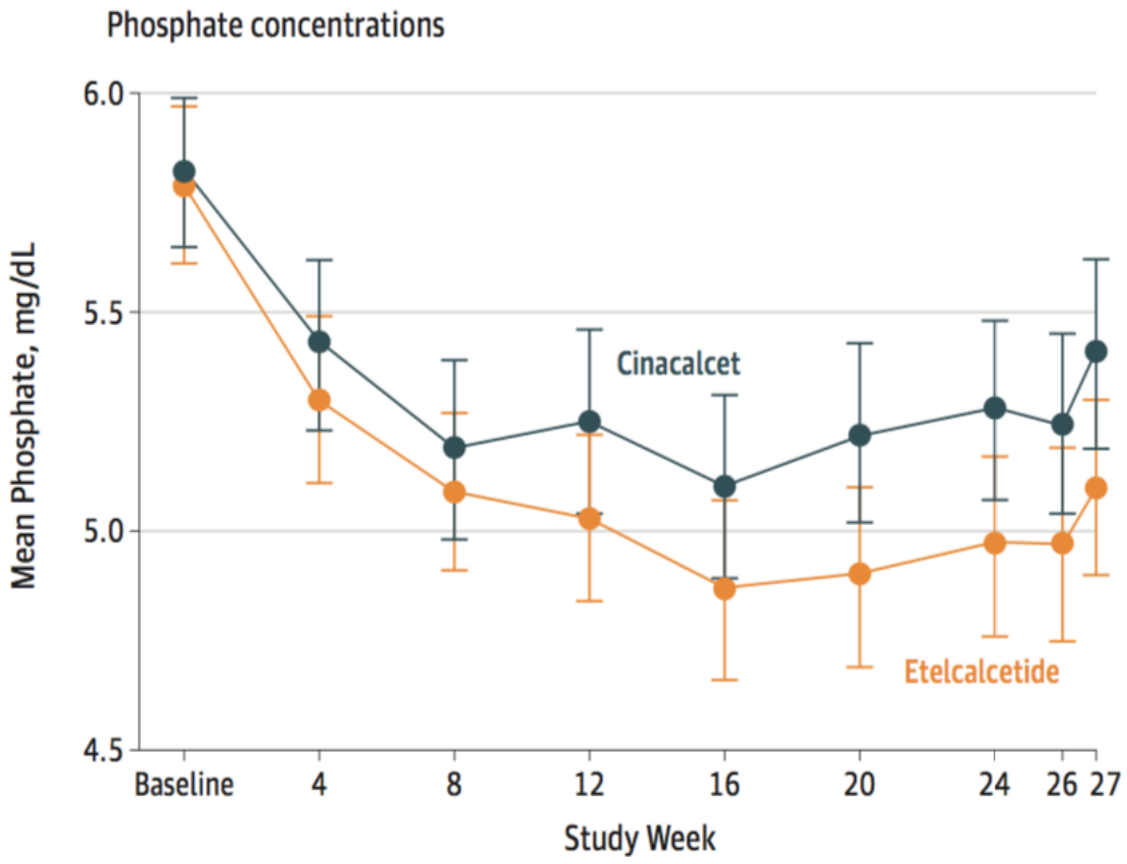
Etelcalcetide	338	293	300	304	303	291	288	288	277	277	270	256	265	255	276277
Cinacalcet	341	286	300	302	308	299	302	298	291	291	293	288	283	274	289287

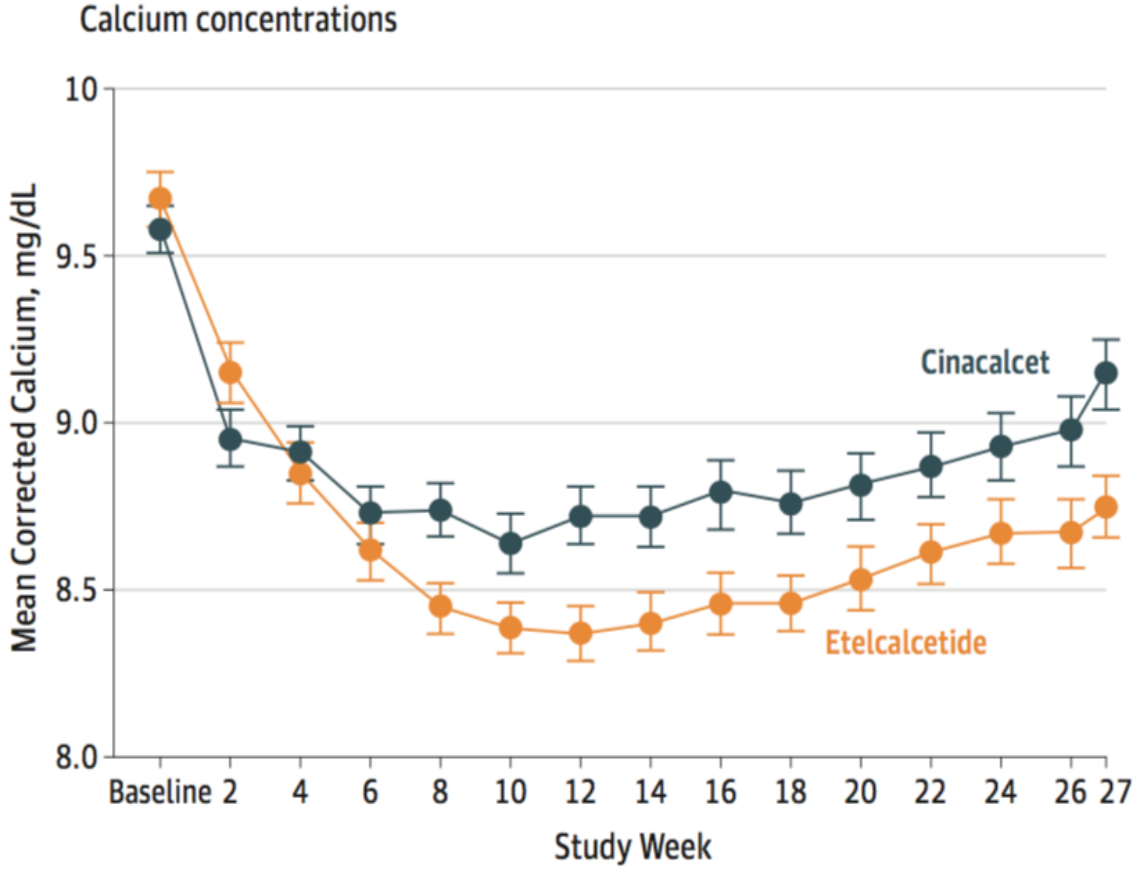
	293	300	304	303	291	288	288	277	277	270	256	265	255	276	
	286	300	302	308	299	302	298	291	291	293	288	283	274	289	

Block GA, et al. JAMA 2017;317:156–164.

Etelcalcetide vs. cinacalcet

greater Ca and Pi reduction with etelcalcetide





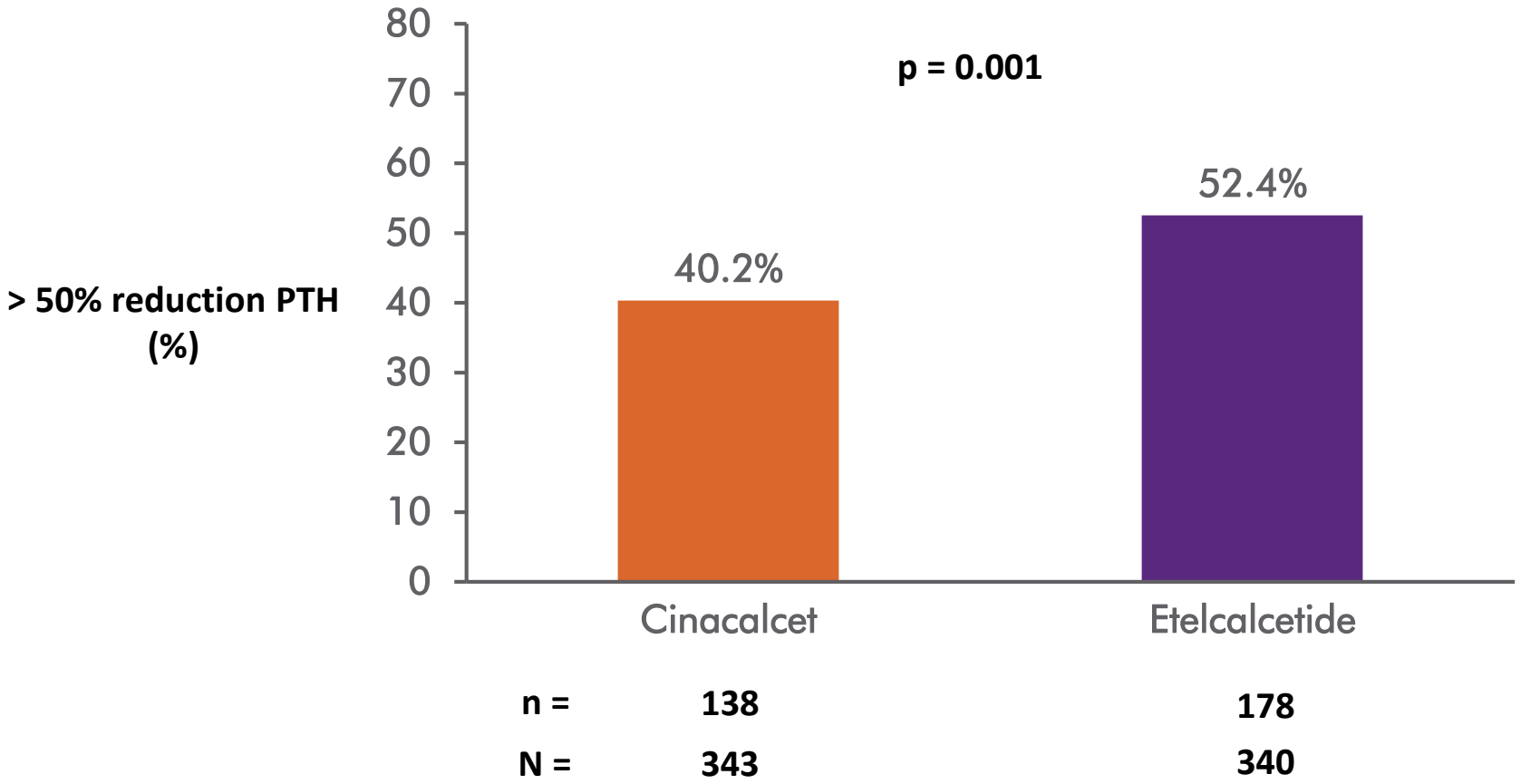
No. of patients

Etelcalcetide	335	301	304	288	274	269	265	255	277	338	290	299	308	300	290	291	291	274	279	266	257	267	251	273
Cinacalcet	339	304	310	298	295	293	284	276	287	341	291	304	304	312	296	298	301	291	292	289	284	283	272	284

Block GA, et al. JAMA 2017;317:156–164.

Etelcalcetide vs. cinacalcet

patients achieving > 50% PTH reduction from baseline



* Secondary endpoint.
EAP weeks 20–27

Block GA, et al. JAMA 2017;317:156–164.

Parsabiv (etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Head-to-head study; etelcalcetide vs.cinacalcet in sHPT

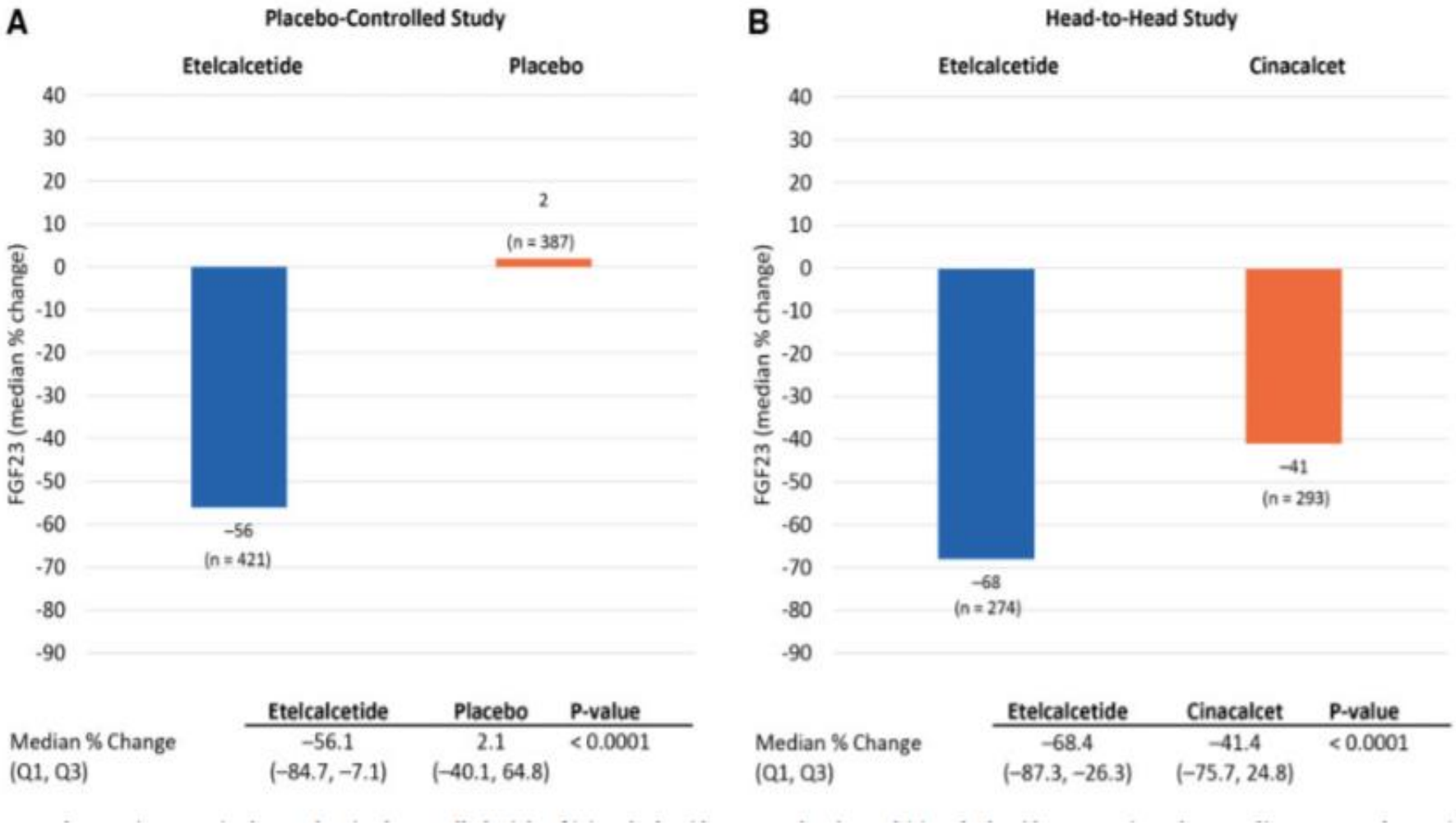
Table 2. Treatment Emergent Adverse Events[a]

Preferred Term	Patients, No. (%)	
	Etelcalcetide (n = 338)	Cinacalcet (n = 341)
Blood calcium decreased[b]	233 (68.9)	204 (59.8)
Nausea	62 (18.3)	77 (22.6)
Vomiting	45 (13.3)	47 (13.8)
Hypotension	23 (6.8)	10 (2.9)
Headache	22 (6.5)	24 (7.0)
Muscle spasms	22 (6.5)	20 (5.9)
Diarrhea	21 (6.2)	35 (10.3)
Hypertension	21 (6.2)	23 (6.7)
Anemia	17 (5.0)	15 (4.4)
Hypocalcemia	17 (5.0)	8 (2.3)
Pain in extremity	17 (5.0)	14 (4.1)
Bronchitis	5 (1.5)	17 (5.0)

Block, Bushinsky, Cheng, Cunningham et al JAMA. 2017;317(2):156-164

Etelcalcetide – effects on FGF23

Etelcalcetide – effects on FGF23

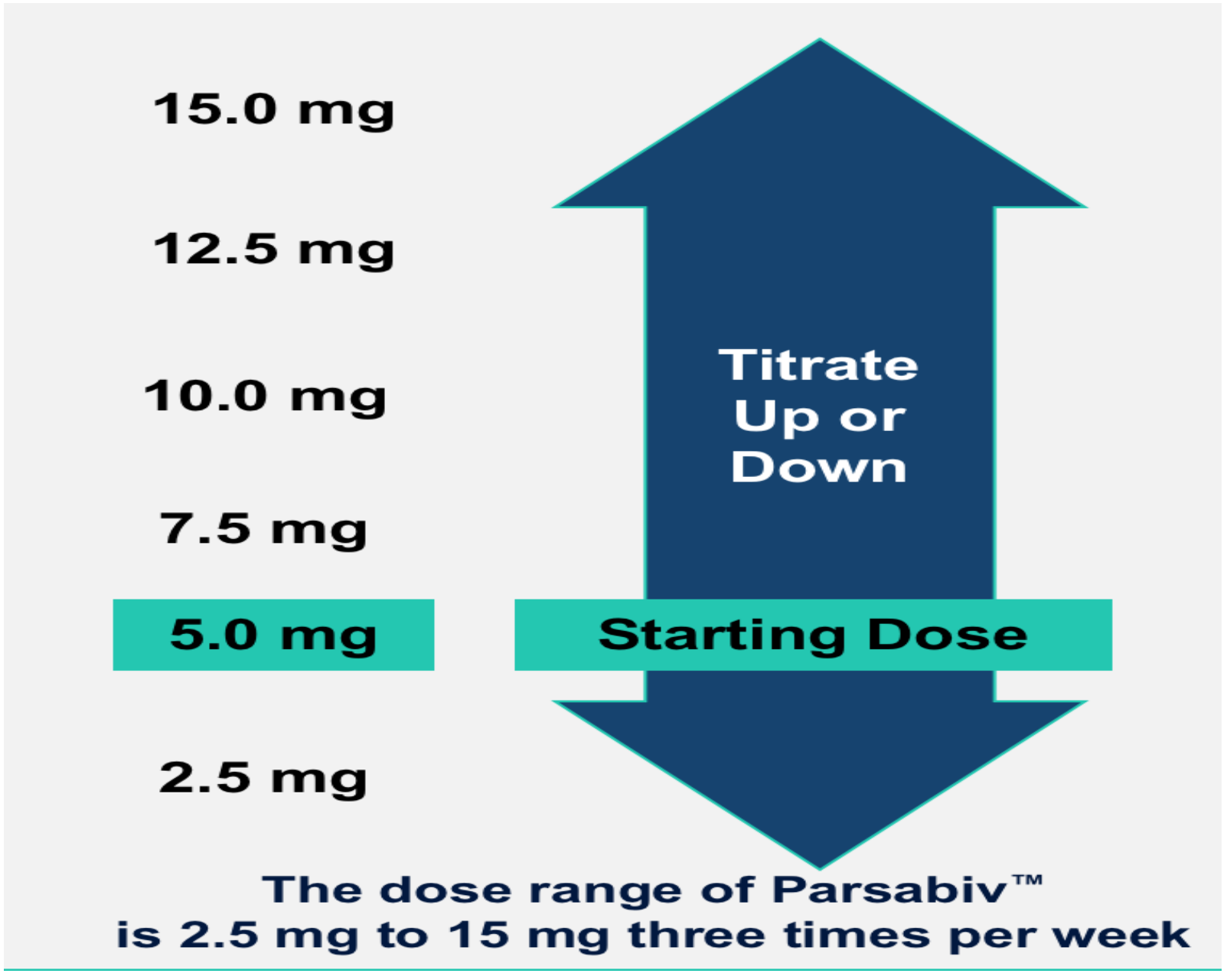


	Etelcalcetide	Placebo	P-value
Median % Change (Q1, Q3)	–56.1 (–84.7, –7.1)	2.1 (–40.1, 64.8)	< 0.0001

	Etelcalcetide	Cinacalcet	P-value
Median % Change (Q1, Q3)	–68.4 (–87.3, –26.3)	–41.4 (–75.7, 24.8)	< 0.0001

(A) etelcalcetide vs. placebo
(B) etelcalcetide vs. cinacalcet.

Wolf et al Clinical Kidney Journal, 2020


15.0 mg
12.5 mg
10.0 mg
7.5 mg
5.0 mg
2.5 mg
Titrate Up or Down
Starting Dose
The dose range of Parsabiv™ is 2.5 mg to 15 mg three times per week

Transplantation

Rapid loss of bone early

High fracture rate

Variable skeletal substrate/evolution

Toxic post transplant environment

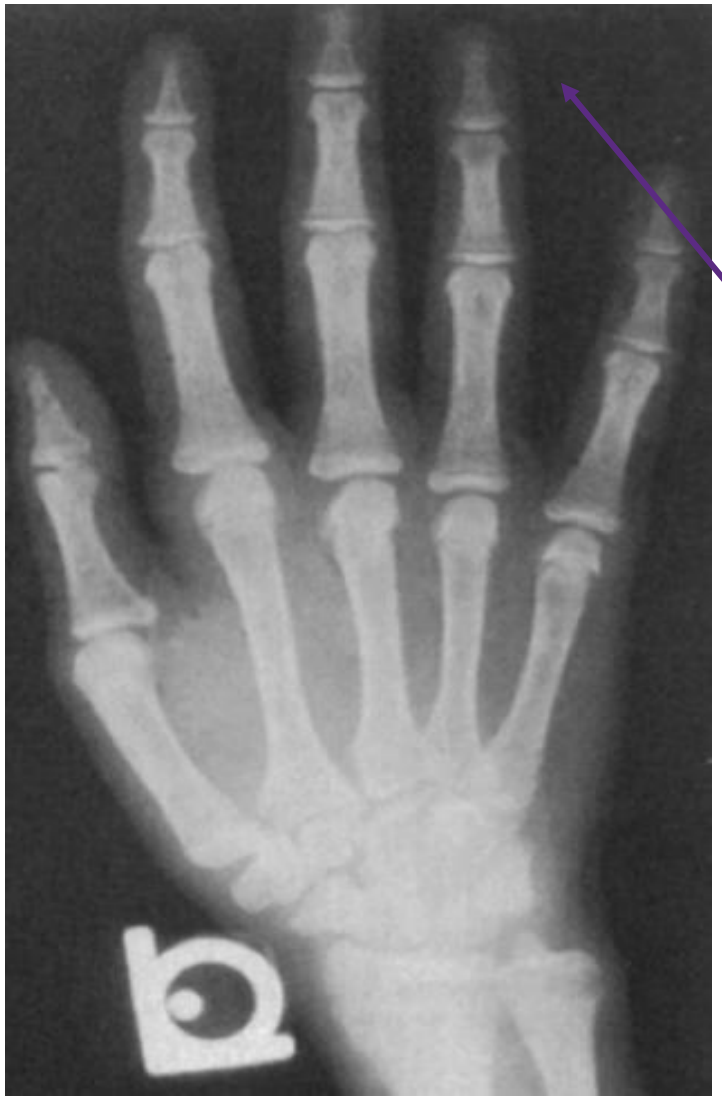
- steroids
- CNI's
- CKD

High prevalence of

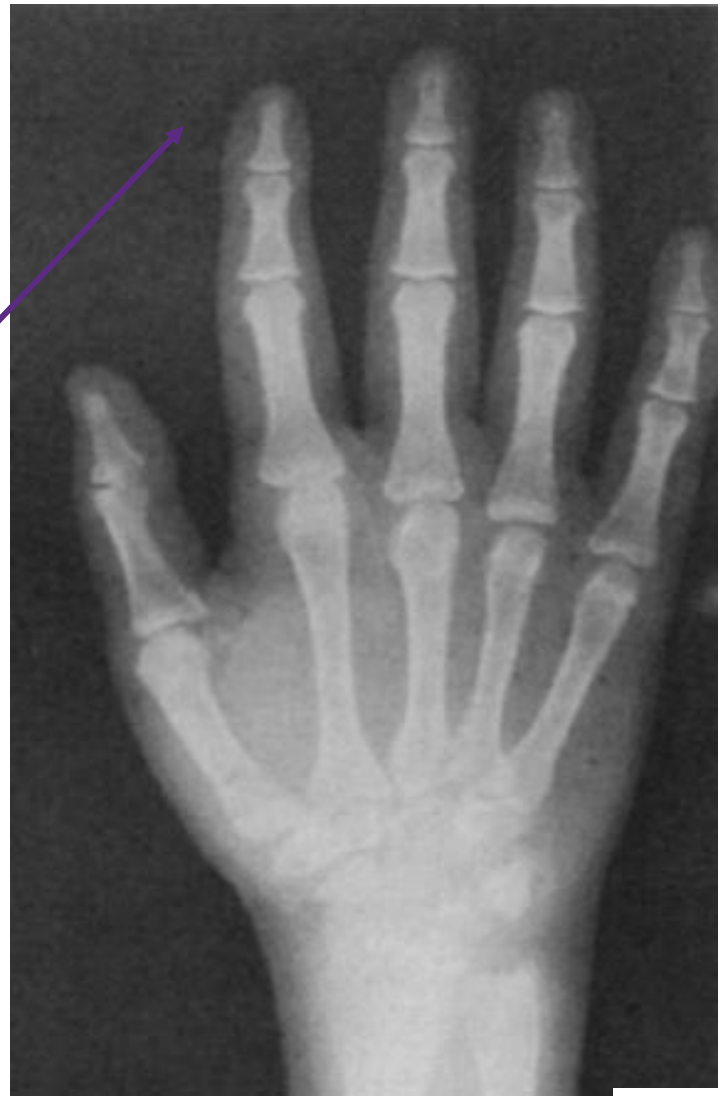
- vitamin D deficiency
- hyperparathyroidism

Clinical outcomes much better with advent of steroid sparing regimes

Resolution of hyperparathyroid bone disease after transplantation

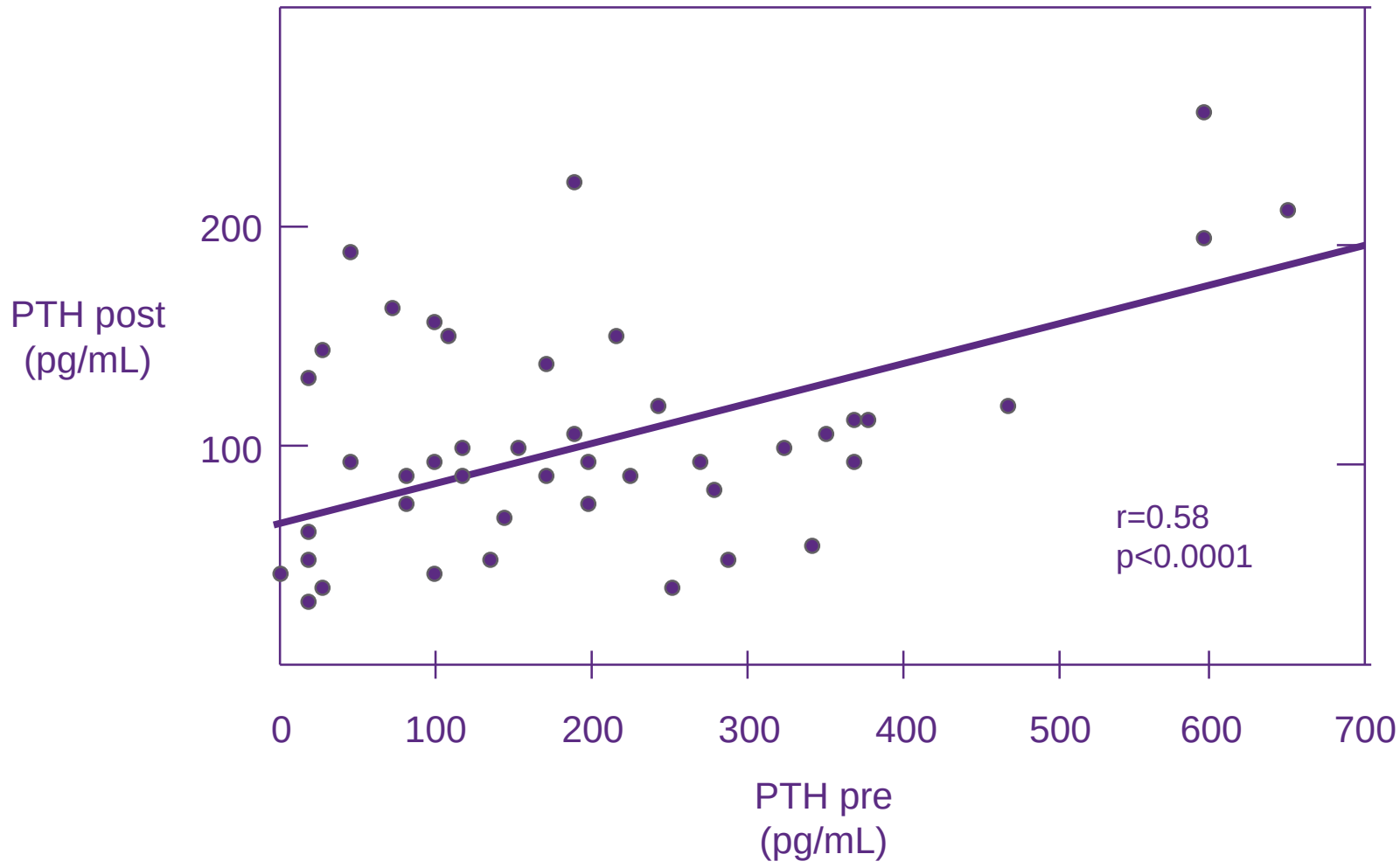


10 months



Alfrey AC, et al. N Engl J Med 1968;279:13–56

PTH – pre- versus post-transplant



Agüero-Torres H, et al. 1998;88:1452–6

Hypercalcaemia post renal Tp

- Usually PTH dependent
- Spontaneous resolution:
  - common early
  - uncommon late
- Persistence associated with big PT glands and nodular hyperplasia

Persistent HPT in long-term (>6 months) Tp recipients

	Transplant n = 25	Control n = 25
Cr clearance (mL/min)	92	92
PTH (pM)	5.2*	2.8
Serum calcitriol (pM)	142*	107
Serum calcium (mM)	2.35	2.35
TRP	0.77*	0.83

Some patients have a phenotype similar to primary hyperparathyroidism

Dumoulin G, et al. Am J Kid Dis 1997;29:746–53

Supplementary Slides

Parsabiv™
(etelcalcetide) Injection for intravenous use
2.5 mg/0.5 mL | 5 mg/1 mL | 10 mg/2 mL

Parsabiv® Phase 3 Clinical Trials

Open Label Extension Study
(OLE) Background

Study design: Data were pooled across 2 placebo-controlled parent studies and a subsequent OLE study.[1]

- OLE started from the baseline of the placebo-controlled parent study until the end or the pre-specified cutoff date of the OLE, whichever was earlier[1]
- Weeks 27 to 31 were the 30-day drug-free period (the 30-day follow-up period of the phase 3 study before entry into the extension study)[1]

Starting dose for Parsabiv® was 5 mg for all subjects, TIW

Dose was actively titrated at OLE weeks 5, 9, 17, 25, 33, 41, and 49 to a maximum dose of 15 mg to achieve predialysis serum iPTH ≤300 pg/mL while maintaining appropriate serum cCa concentrations[2]

Investigators were blinded to iPTH results during the first 10 weeks of treatment

Subsequent dose adjustment was determined by the investigator per protocol guidelines[2]

Average Parsabiv® weekly dose

The average weekly dose of Parsabiv® was 21.3 mg at 6 months and 20.0 mg at 12 months[2]

REFERENCES

TIW = three times a week

Parsabiv® Phase 3 Clinical Trials

Parsabiv® provided **Significant Reductions** in 3 key sHPT lab values vs placebo[1,2‡]

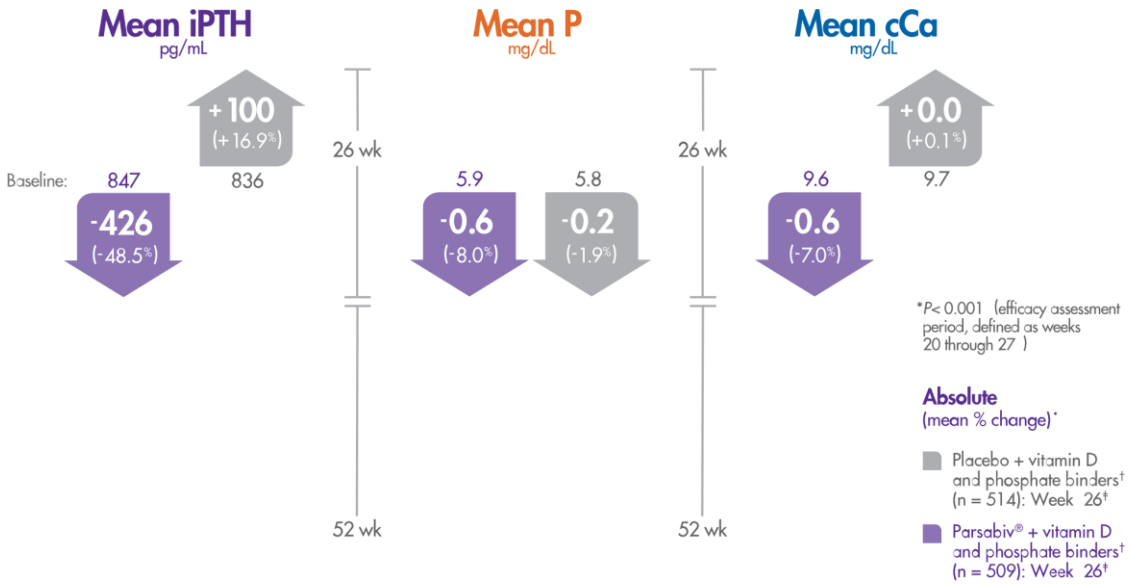
Placebo-controlled treatment period: results are combined from two 26-week, randomized, double-blind, placebo-controlled studies comparing Parsabiv® with placebo in patients with CKD on hemodialysis with iPTH > 400 pg/mL and corrected calcium ≥ 8.3 mg/dL (N = 1023).[3,4] Patients in both treatment arms could be treated with vitamin D sterols and/or phosphate binders. Mean baseline iPTH in the Parsabiv® group and placebo group were 847 pg/mL and 836 pg/mL, respectively.[5] The primary endpoint of each study was the proportion of patients who achieved a > 30% reduction from baseline in mean iPTH during the efficacy assessment period (defined as weeks 20 through 27, inclusive).[3,4]

Open-label extension: data pooled for patients receiving Parsabiv® across two placebo-controlled parent studies and a subsequent OLE study, starting from the baseline of the parent study until the end or the prespecified cutoff date of the OLE study, whichever was earlier. Weeks 27 to 31 were the 30-day drug-free period (the 30-day follow-up period of the phase 3 study before entry into the extension study).[5] During the OLE, the starting dose of Parsabiv® for all subjects was 5 mg. The Parsabiv® dose could be increased at OLE weeks 5, 9, 17, 25, 33, 41, and 49 to a maximum dose of 15 mg to achieve predialysis serum iPTH ≤ 300 pg/mL while maintaining appropriate serum cCa concentrations. Investigators were blinded to iPTH results during the first 10 weeks of treatment. Subsequent dose adjustment was determined by the investigator per protocol guidelines.[6]

REFERENCES

P = phosphorous
†Vitamin D and/or phosphate binders, if prescribed.[4]
‡Values represent mean iPTH, P, cCa during efficacy assessment period, defined as weeks 20 through 27, inclusive.[2]

Absolute and percent change in mean iPTH, phosphate, and corrected calcium over time



Parsabiv™ (etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Parsabiv® Phase 3 Clinical Trials

Lasting Results

Reductions in iPTH, phosphate and corrected serum calcium were maintained for up to 78 weeks[1,2‡]

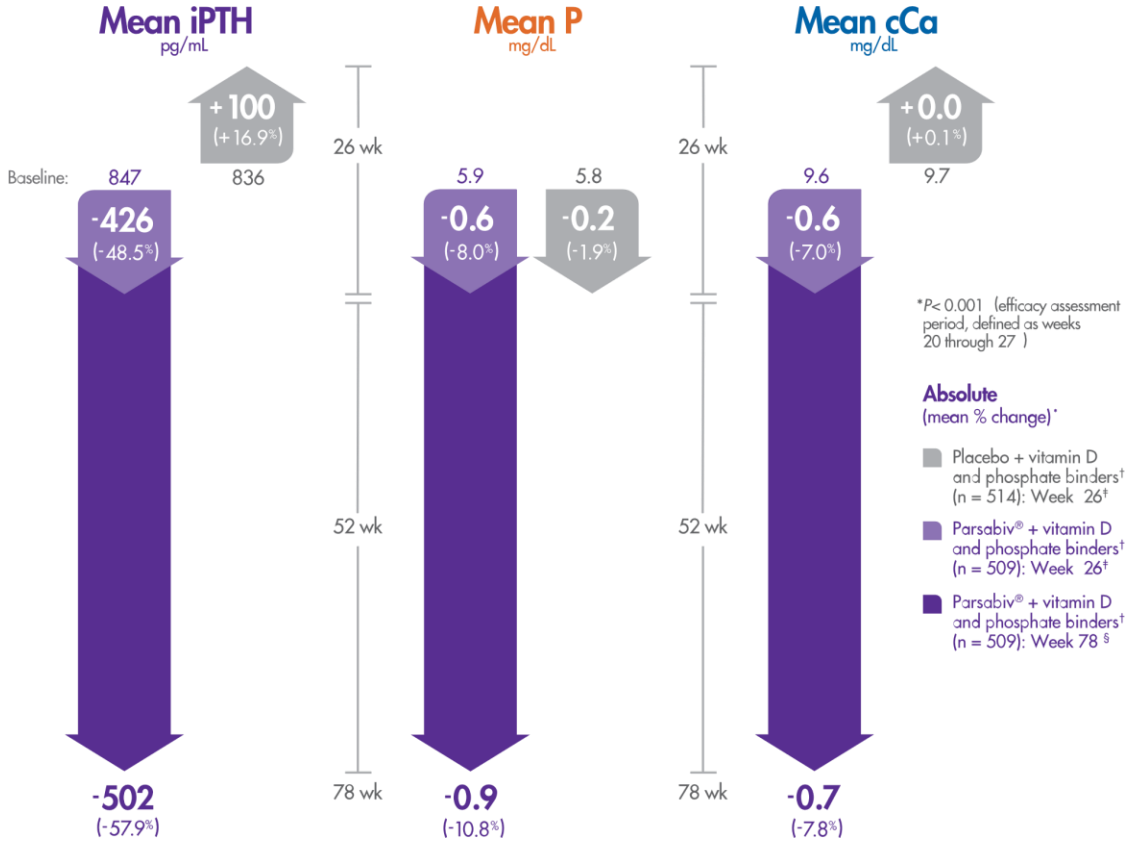
Placebo-controlled treatment period: results are combined from two 26-week, randomized, double-blind, placebo-controlled studies comparing Parsabiv® with placebo in patients with CKD on hemodialysis with iPTH > 400 pg/mL and corrected calcium ≥ 8.3 mg/dL (N = 1023).[3,4] Patients in both treatment arms could be treated with vitamin D sterols and/or phosphate binders. Mean baseline iPTH in the Parsabiv® group and placebo group were 847 pg/mL and 836 pg/mL, respectively.[5] The primary endpoint of each study was the proportion of patients who achieved a > 30% reduction from baseline in mean iPTH during the efficacy assessment period (defined as weeks 20 through 27, inclusive).[3,4]

Open-label extension: data pooled for patients receiving Parsabiv® across two placebo-controlled parent studies and a subsequent open-label extension (OLE) study, starting from the baseline of the parent study until the end or the prespecified cutoff date of the OLE study, whichever was earlier. Weeks 27 to 31 were the 30-day drug-free period (the 30-day follow-up period of the phase 3 study before entry into the extension study).[5] During the OLE, the starting dose of Parsabiv® for all subjects was 5 mg. The Parsabiv® dose could be increased at OLE weeks 5, 9, 17, 25, 33, 41, and 49 to a maximum dose of 15 mg to achieve predialysis serum iPTH ≤ 300 pg/mL while maintaining appropriate serum cCa concentrations. Investigators were blinded to iPTH results during the first 10 weeks of treatment. Subsequent dose adjustment was determined by the investigator per protocol guidelines.[6]

REFERENCES

†Vitamin D and/or phosphate binders, if prescribed.[4]
‡Values represent mean iPTH during EAP, defined as weeks 20 through 27, inclusive.[2]
§Value represents iPTH measured at the first hemodialysis session in week 79.[1]

Absolute and percent change in mean iPTH, phosphate, and corrected calcium over time



Parsabiv™ (etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Parsabiv® Phase 3 Clinical Trials

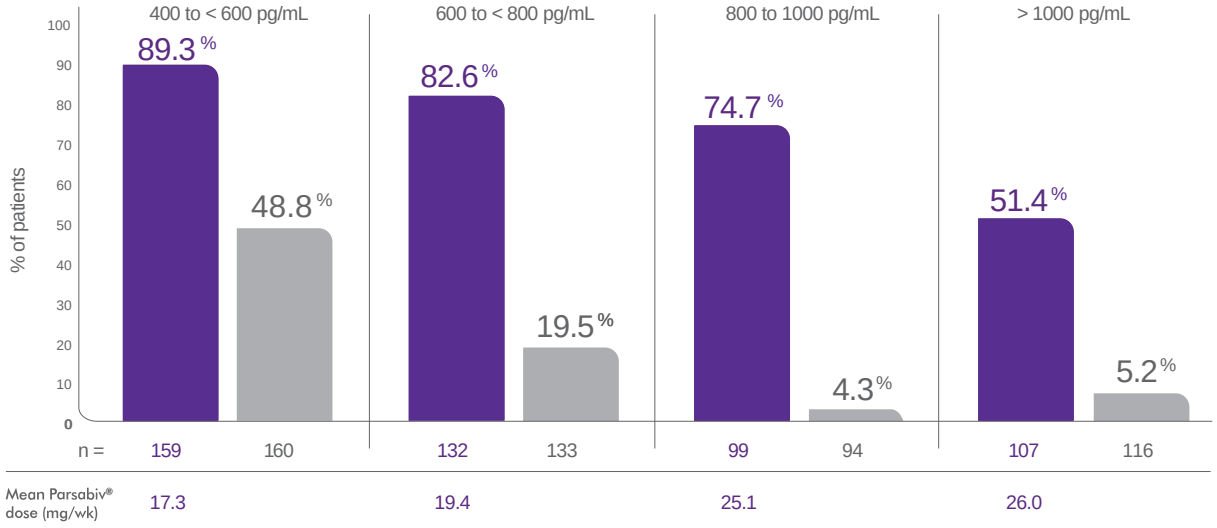
Most patients given Parsabiv® **achieved the KDIGO® goal range*** for PTH[1,2]

Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

REFERENCES

*KDIGO® guidelines suggest maintaining PTH in the range of 2x to 9x the upper limit of normal for the assay, defined as approximately 130 pg/mL to 600 pg/mL[2,5]
†Vitamin D and/or phosphate binders, if prescribed.[3]
Note: All references to KDIGO® guidelines for CKD-MBD set forth herein are intended to be informational only and do not reflect KDIGO®'s endorsement or support of Parsabiv® and/or Amgen. KDIGO® is a registered trademark of the National Kidney Foundation, Inc.

Subgroup analysis:
Patients achieving iPTH <600 pg/mL during EAP by screening iPTH[3]



- Overall, 76.5% of Parsabiv® patients achieved PTH <600 pg/mL (n=497) during the combined phase 3 trials[1]
- Secondary endpoint: in phase 3 trials, 53.4% of Parsabiv® patients achieved iPTH ≤300 pg/mL vs 5.8% of placebo patients during the EAP (*P*<0.001)[4]

Parsabiv™ (etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Parsabiv® Phase 3 Clinical Trials

Adverse Reactions

reported in ≥5% of patients given Parsabiv® (etelcalcetide) in combined placebo-controlled studies[1]

Discontinuations

- Overall, in placebo-controlled studies, 1.8% of patients in the Parsabiv® group and 2.5% of patients in the placebo group discontinued treatment due to an adverse event[2]

Low serum calcium

- Most events of blood calcium decrease or hypocalcemia were mild or moderate in severity in both the placebo and Parsabiv® groups[2,3]
- In combined placebo-controlled studies, 1% of patients given Parsabiv® discontinued treatment due to low corrected serum calcium vs 0% with placebo[1]

	Parsabiv® n = 503	Placebo n = 513
Adverse Reaction*	%	%
Blood calcium decreased†	64	10
Muscle spasms	12	7
Diarrhea	11	9
Nausea	11	6
Vomiting	9	5
Headache	8	6
Hypocalcemia	7	0.2
Paresthesia	6	1

*Included adverse reactions reported with at least 1% greater incidence in the Parsabiv® group compared to the placebo group.

†Asymptomatic reductions in corrected serum calcium between 8.3 mg/dL and >7.5 mg/dL (clinically significant reductions that required medical management) or reductions in calcium below 7.5 mg/dL.

‡Symptomatic reductions in corrected serum calcium <8.3 mg/dL.

§Paresthesia includes preferred terms of paresthesia and hypoesthesia.

REFERENCES

Real-World Evidence

Background

Collection criteria

Retrospective analysis of patients from large and medium dialysis organizations, which traditionally have more protocol restrictions.

ALADIN data reports include lab values for 1,983 adult patients new to Parsabiv® between February 2018 through June 2020.*

Parsabiv® dosing consistent with prescribing information[1]

- First Parsabiv® prescription required 5 mg TIW dosing.
- Baseline cCa ≥ 8.3 mg/dL for all patients[1]

REFERENCES

*ALADIN is a 3rd-party national database of lab values of patients with CKD and sHPT being treated with hemodialysis.

Included =	Parsabiv® treatment period for analysis defined as: ≥ 90 days on treatment
	Concomitant therapies such as phosphate binders and vitamin D were permitted, if prescribed
Excluded ≠	Patients with more than a 2-month gap in reported lab results for PTH at any point during a 6- or 9-month tracking period
	Patients with observed gaps in therapy greater than 12 doses in 6 months or 24 doses in 9 months
	Patients with evidence of other calcimimetic therapy within 90 days of Parsabiv® initiation

Real-World Evidence

64% of patients

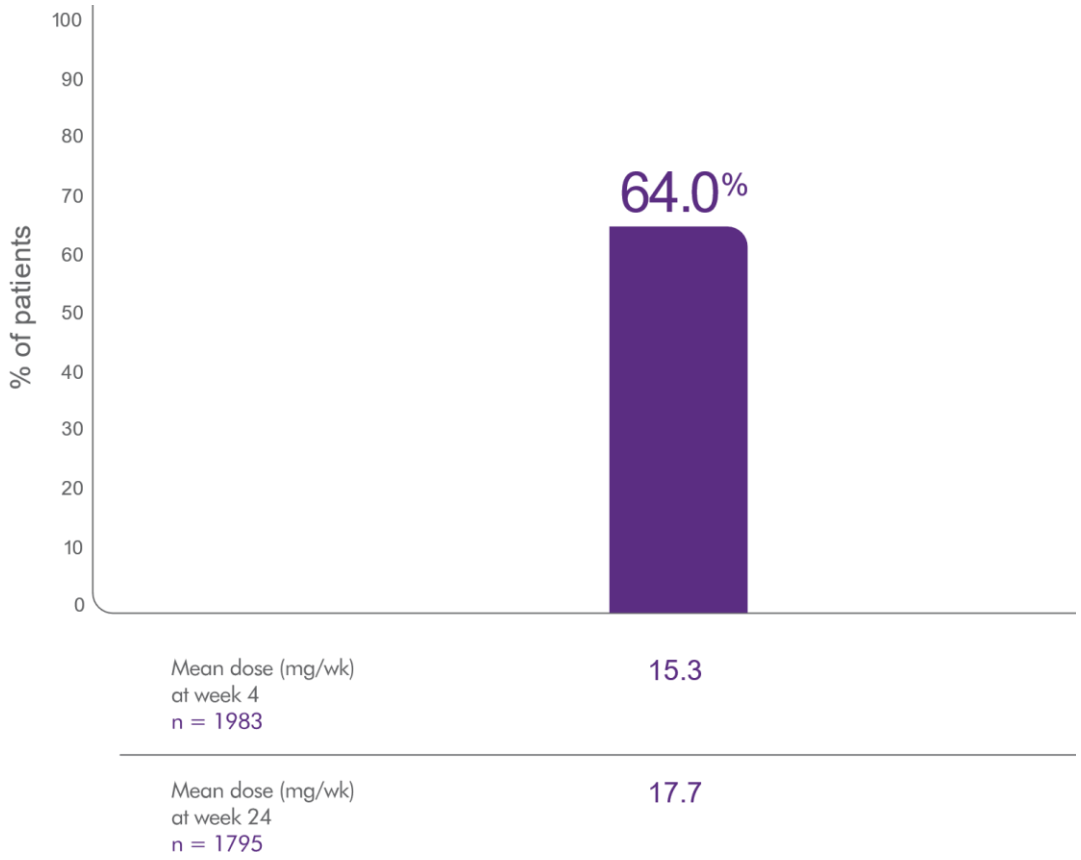
prescribed Parsabiv® (etelcalcetide) achieved a >30% reduction in PTH by week 24[1]

Data are derived from real-world sources and not from a controlled clinical study. Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusion of statistical or clinical significance can be drawn.

Data represent patient lab outcomes provided to Amgen by large and mid-sized dialysis organizations. All patients were initiated on calcimimetics between February 2018 and June 2020, had ≥ 90 days on treatment, with no observed gaps in therapy greater that 12 doses in 6 months or 24 doses in 9 months, no evidence of other calcimimetic therapy within 90 days of Parsabiv® therapy initiation, and no more than a 2-month gap in reported lab results for PTH. Patients with baseline PTH < 400 were excluded. All patients were initiated at Parsabiv® 5 mg TIW and had a baseline cCa ≥ 8.3 mg/dl.[1]

REFERENCES

Percentage of patients achieving >30% reduction in mean iPTH from index state[1]



Real-World Evidence

Parsabiv® (etelcalcetide) Achieved Reductions in 3 key sHPT lab values[1]

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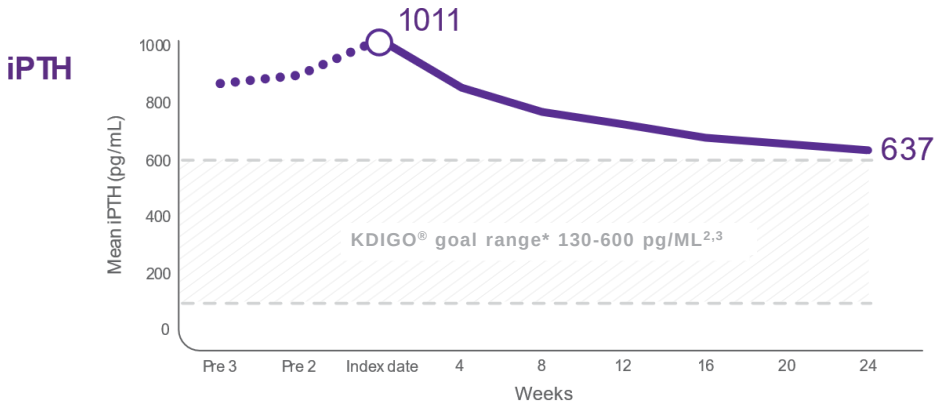
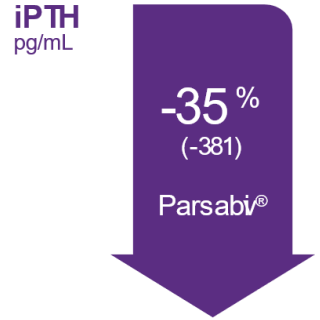
REFERENCES

*KDIGO® guidelines suggest maintaining PTH in the range of 2x to 9x the upper limit of normal for the assay, defined as approximately 130 pg/mL to 600 pg/mL.[2,3]
†Vitamin D and/or phosphate binders, if prescribed.[1]

Parsabiv achieved reductions in iPTH[1]



Mean % (absolute) change from baseline



n = 1795

• • • Before Parsabiv® initiated†
○ Parsabiv® initiated†

Real-World Evidence

Parsabiv® (etelcalcetide) Achieved Reductions in 3 key sHPT lab values[1]

Data are derived from real-world sources and not from a controlled clinical study. Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusion of statistical or clinical significance can be drawn.

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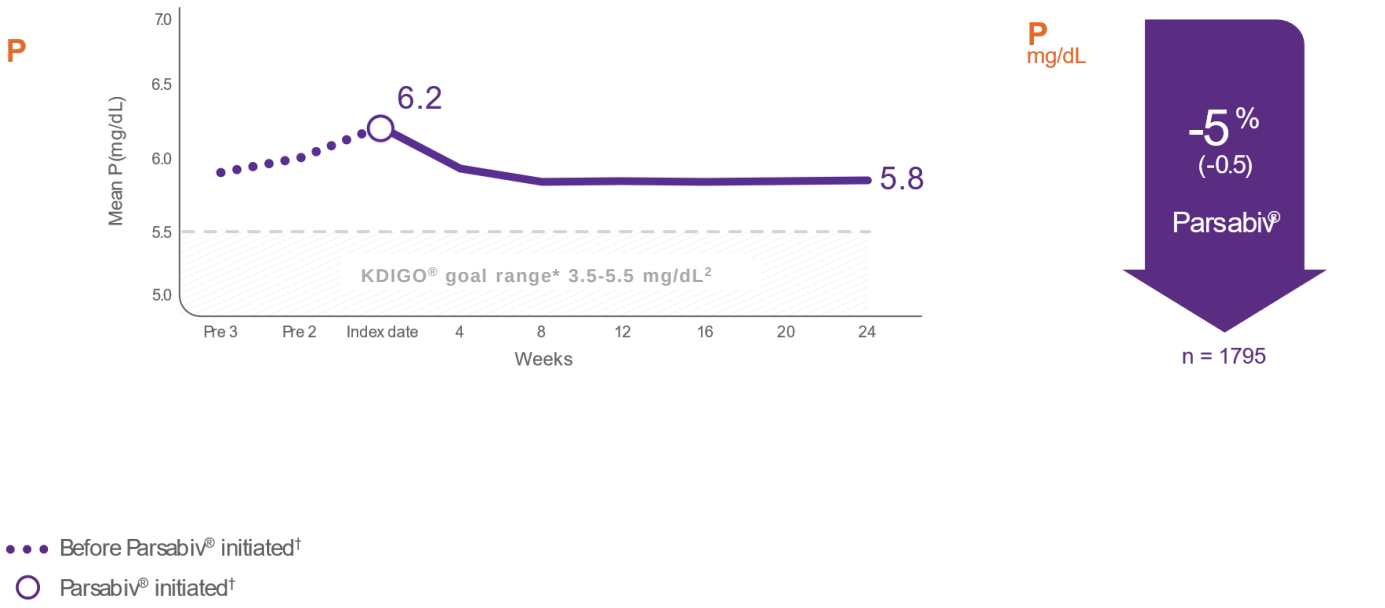
REFERENCES

*KDIGO® guidelines suggest maintaining PTH in the range of 2x to 9x the upper limit of normal for the assay, defined as approximately 130 pg/mL to 600 pg/mL.[2,3]
†Vitamin D and/or phosphate binders, if prescribed.[1]

Parsabiv achieved reductions in phosphorous[1]



Real-World Evidence

Parsabiv® (etelcalcetide) Achieved Reductions in 3 key sHPT lab values[1]

Data are derived from real-world sources and not from a controlled clinical study. Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusion of statistical or clinical significance can be drawn.

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REFERENCES

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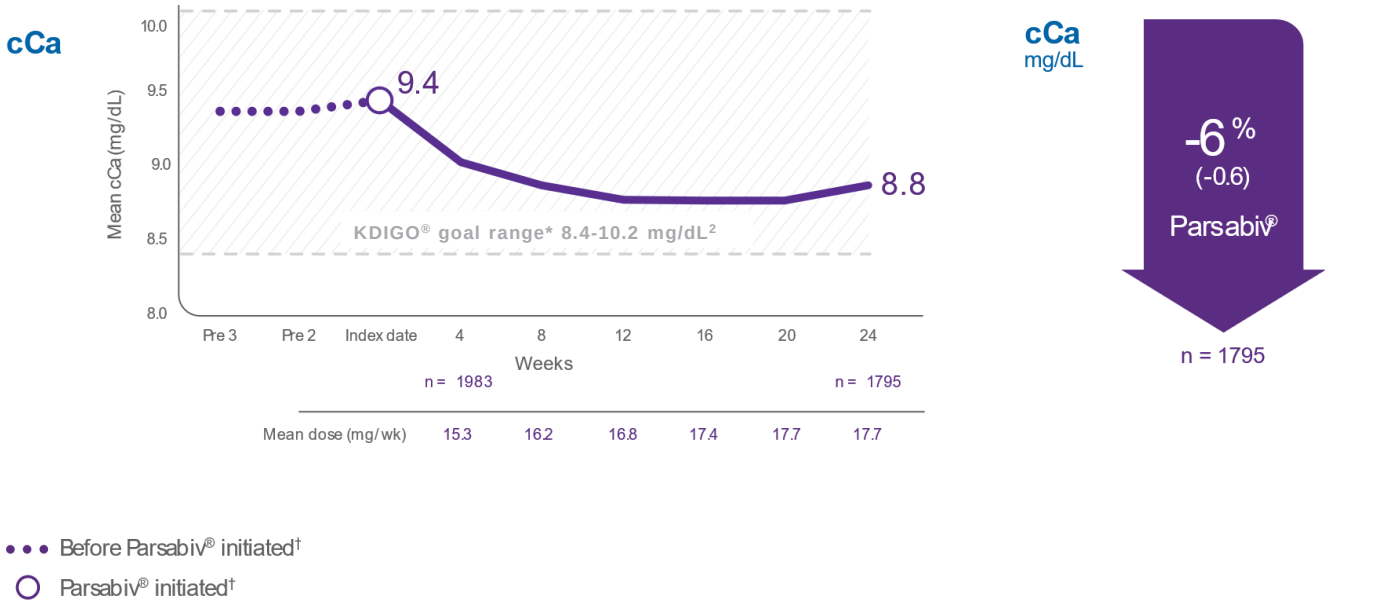
†Vitamin D and/or phosphate binders, if prescribed.[1]

Parsabiv achieved reductions in corrected calcium[1]



● ● ● Before Parsabiv® initiated†
○ Parsabiv® initiated†

Real-World Evidence

with Parsabiv® (etelcalcetide)

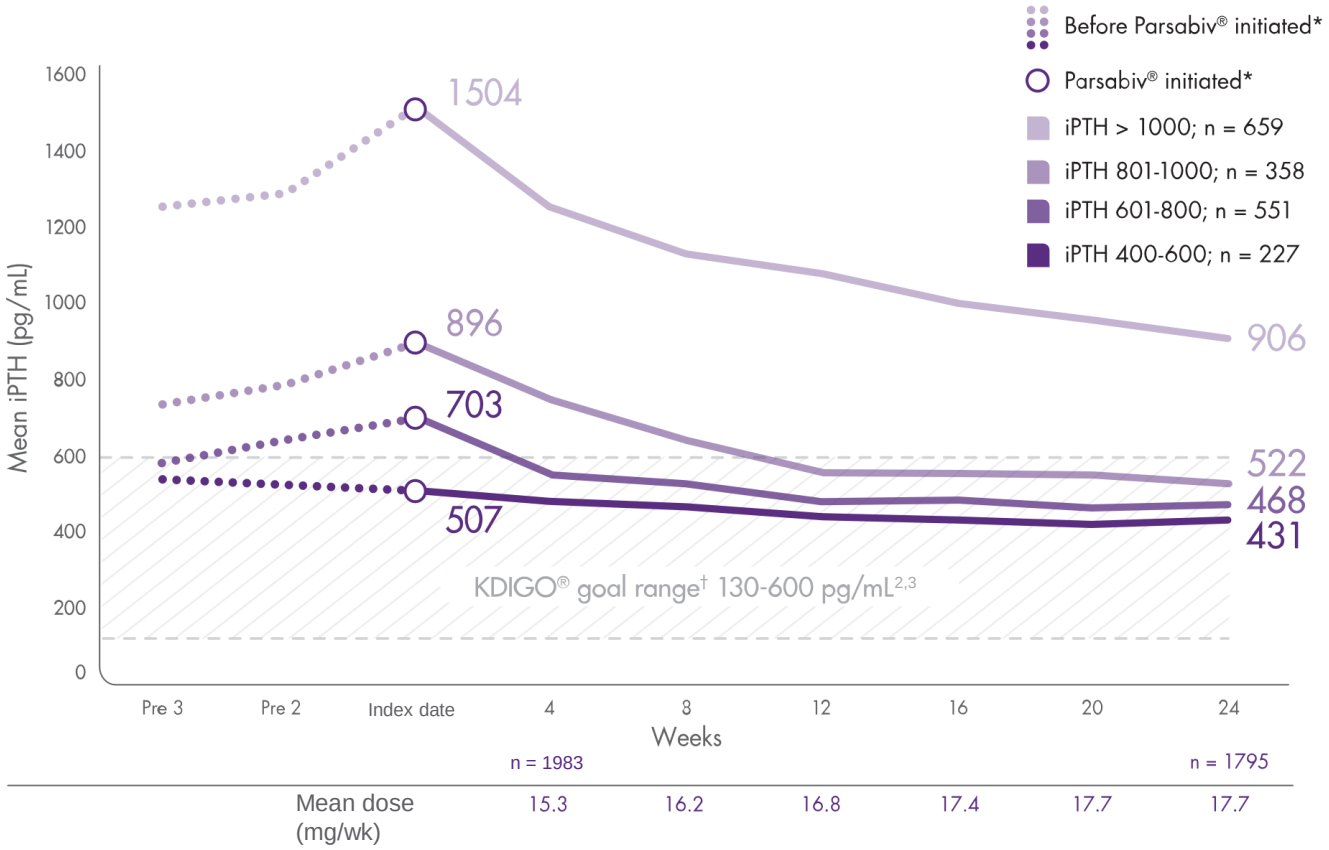
Data are derived from real-world sources and not from a controlled clinical study. Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusion of statistical or clinical significance can be drawn.

Data represent patient lab outcomes provided to Amgen by large and mid-sized dialysis organizations. All patients were initiated on calcimimetics between February 2018 and June 2020, had ≥ 90 days on treatment, with no observed gaps in therapy greater than 12 doses in 6 months or 24 doses in 9 months, no evidence of other calcimimetic therapy within 90 days of Parsabiv® therapy initiation, and no more than a 2-month gap in reported lab results for PTH. Patients with baseline PTH < 400 were excluded. All patients were initiated at Parsabiv® 5 mg TIW and had a baseline cCa ≥ 8.3 mg/dL.[1]

REFERENCES

*Vitamin D and/or phosphate binders, if prescribed.[1]
†KDIGO® guidelines suggest maintaining PTH in the range of 2x to 9x the upper limit of normal for the assay, defined as approximately 130 pg/mL to 600 pg/mL. [2,3]

Patients given Parsabiv® achieved PTH <600 pg/mL at Week 24 when initiated at baseline PTH ≤1000 pg/mL[1]



Real-World Evidence

The majority of patients given Parsabiv® **achieved the KDIGO® goal range*** for PTH[1-3]

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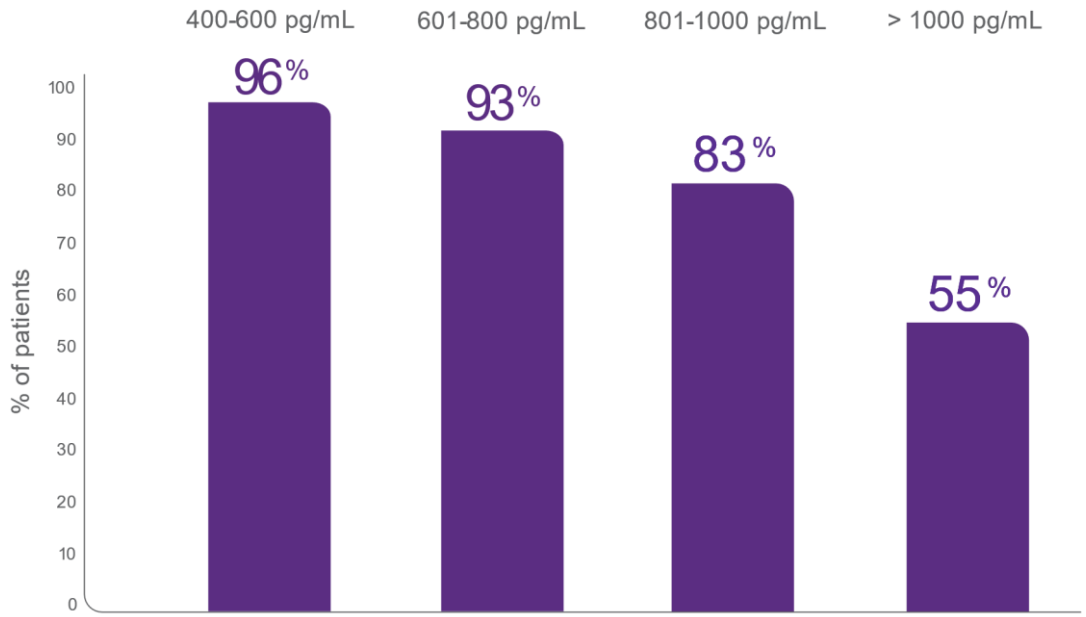
REFERENCES

*KDIGO® guidelines suggest maintaining PTH in the range of 2x to 9x the upper limit of normal for the assay, defined as approximately 130 pg/mL to 600 pg/mL.[1,4]

Patients achieving iPTH <600 pg/mL by week 24[2,3]



	400-600 pg/mL	601-800 pg/mL	801-1000 pg/mL	> 1000 pg/mL
Mean dose (mg/wk) at week 4 n = 1983	15.0	15.0	15.3	15.3
Mean dose (mg/wk) at week 24 n = 1795	16.2	15.6	16.8	20.7

Values represent percent of patients achieving the iPTH goal of <600 pg/mL within 24 weeks. Overall, 77% of patients achieved PTH <600 pg/mL (n = 1535) and 43% of patients achieved PTH ≤300 pg/mL (n = 859).[3]

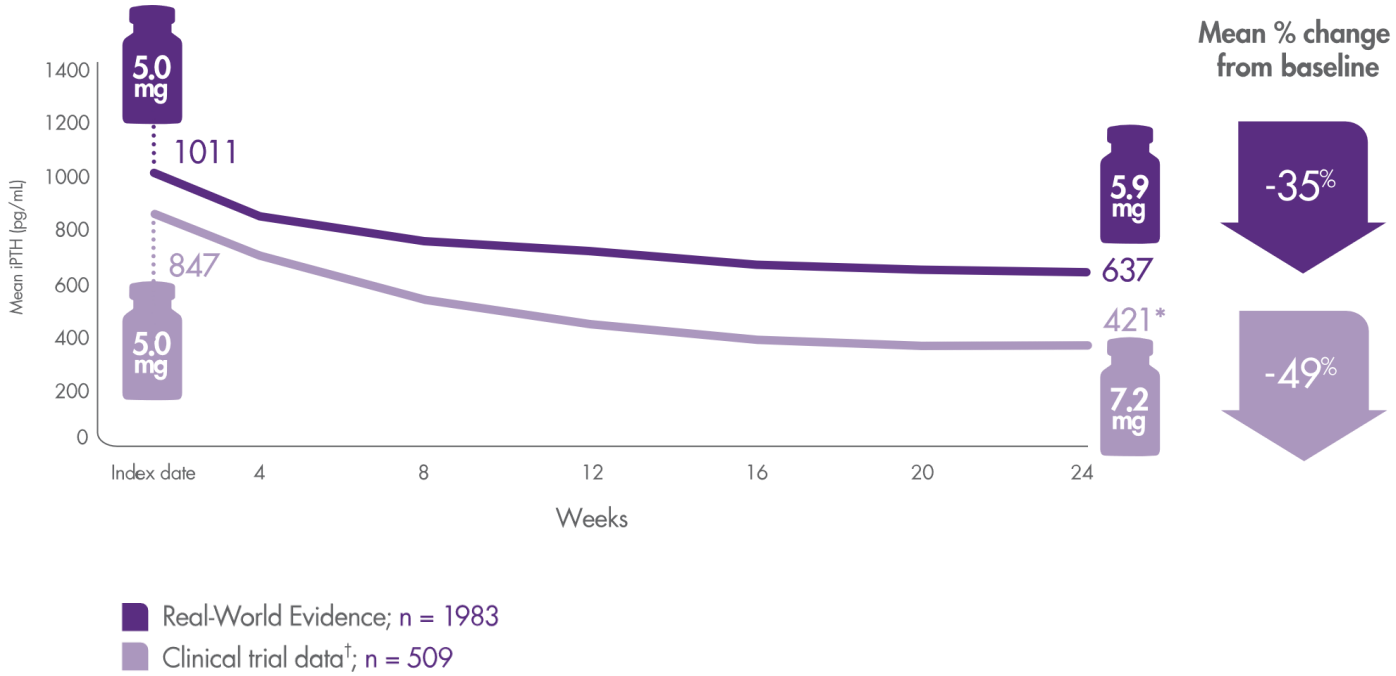
Real-World Evidence:

PTH lab levels and average Parsabiv® (etelcalcetide) dose[1-4]

REFERENCES

*Values represent mean iPTH during EAP, defined as weeks 20 through 27, inclusive.[2]
†Results are combined from two 26-week, randomized, double-blind, placebo-controlled studies comparing Parsabiv® with placebo in patients with CKD on hemodialysis.

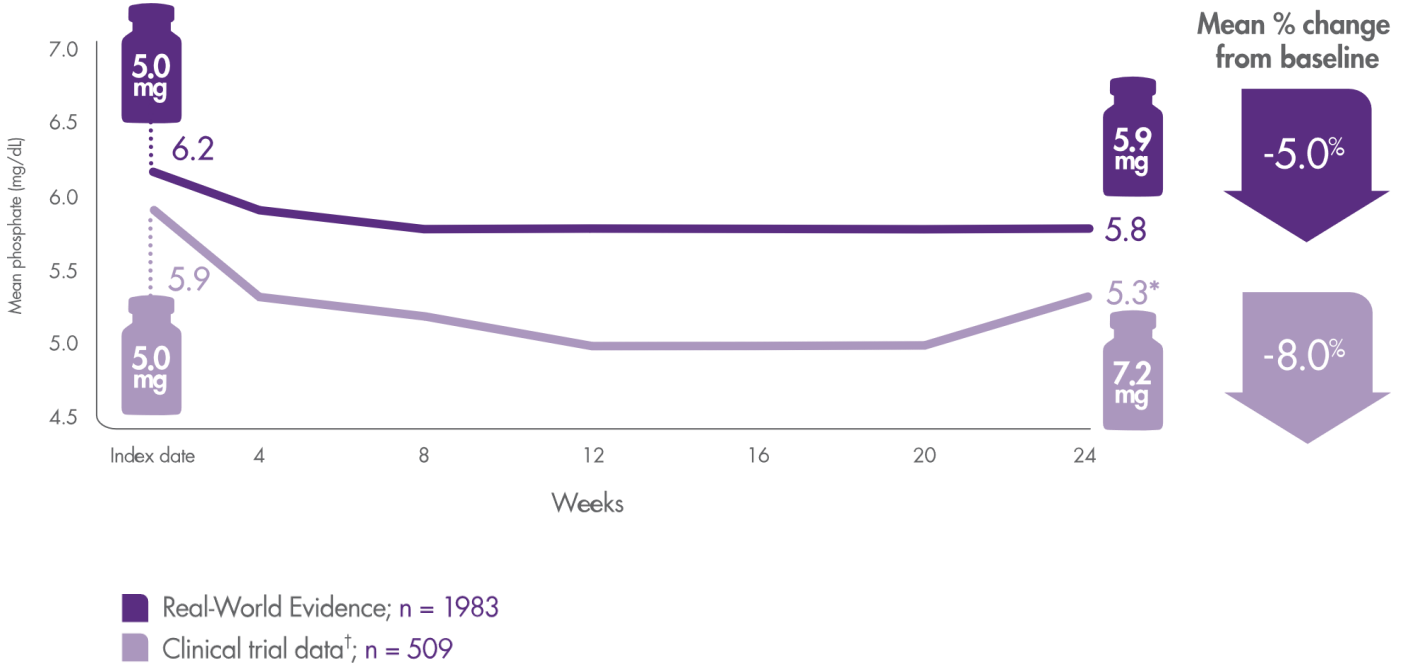
Mean iPTH levels over time and average dose



Real-World Evidence:

Phosphorus lab levels and average Parsabiv® (etelcalcetide) dose[1-4]

Mean P levels over time and average dose



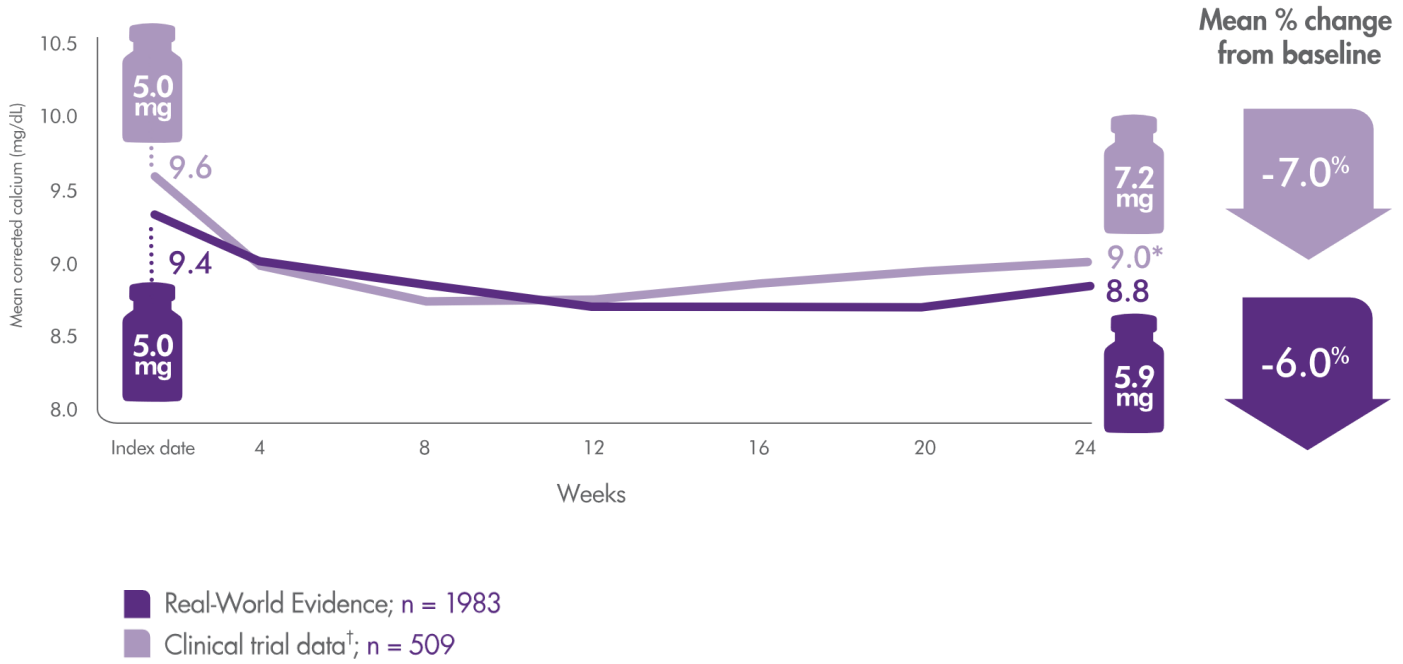
REFERENCES

*Values represent mean iPTH during EAP, defined as weeks 20 through 27, inclusive.[2]
†Results are combined from two 26-week, randomized, double-blind, placebo-controlled studies comparing Parsabiv® with placebo in patients with CKD on hemodialysis.

Real-World Evidence:

Calcium lab levels and average Parsabiv® (etelcalcetide) dose[1-4]

Mean cCa levels over time and average dose



REFERENCES

*Values represent mean iPTH during EAP, defined as weeks 20 through 27, inclusive.[2]
†Results are combined from two 26-week, randomized, double-blind, placebo-controlled studies comparing Parsabiv® with placebo in patients with CKD on hemodialysis.

The calcimimetic that gives you control over administration

Parsabiv® is the first and only IV-administered calcimimetic

Calcium Management

Managing calcium in patients taking Parsabiv® (etelcalcetide)[1]

≥ 8.3 mg/dL*

Initiate Parsabiv®

- Do not initiate Parsabiv® if corrected serum calcium is less than the lower limit of normal*
- **Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with Parsabiv®**. Educate patients on the symptoms of hypocalcemia and advise them to contact a healthcare provider if they occur

< 8.3 mg/dL to ≥ 7.5 mg/dL* without symptoms of hypocalcemia

Adjust Treatment as Needed

- **Consider decreasing or temporarily discontinuing Parsabiv® or use concomitant therapies to increase corrected serum calcium** (including calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration)

- **Throughout the studies, dialysate calcium concentration could be adjusted but had to remain ≥ 2.25 mEq/L[1]**
- **Significant lowering of serum calcium can cause paresthesias, myalgias, muscle spasms, seizures, QT interval prolongation, and ventricular arrhythmias[1]**

REFERENCES

*Lower limit of reference range in phase 3 trials was 8.3 mg/dL.[1,2]

Calcium Management

Managing calcium in patients taking Parsabiv® (etelcalcetide)[1]

< 7.5 mg/dL
or with symptoms of hypocalcemia

Withhold Parsabiv® and Monitor

- **Stop Parsabiv® and treat hypocalcemia**
- **Start or increase calcium supplementation** (including calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration)

When cCa returns ≥ 8.3 mg/dL*—**reinitiate Parsabiv®**

- **When corrected serum calcium levels are within normal limits, symptoms of hypocalcemia have resolved**, and predisposing factors for hypocalcemia have been addressed, reinitiate Parsabiv® at a dose 5 mg lower than the last administered dose. If patient's last administered dose of Parsabiv® was 2.5 mg or 5 mg, reinitiate at a dose of 2.5 mg

- **Throughout the studies, dialysate calcium concentration could be adjusted but had to remain ≥ 2.25 mEq/L[1]**
- **Significant lowering of serum calcium can cause paresthesias, myalgias, muscle spasms, seizures, QT interval prolongation, and ventricular arrhythmias[1]**

REFERENCES

*Lower limit of reference range in phase 3 trials was 8.3 mg/dL.[1,2]

Dosing and Administration

Before you initiate Parsabiv® (etelcalcetide)

REFERENCES

*Lower limit of reference range in phase 3 trials was 8.3 mg/dL.[1,2]

Switching to Parsabiv® from oral cinacalcet[1]

Discontinue for at least 7 days

Ensure your patient discontinues use of oral cinacalcet for at least 7 days prior to starting Parsabiv®.

Initiate Parsabiv® after day 7, if corrected serum calcium is at or above the lower limit of normal.*

Dosing and Administration

The FDA-approved starting dose

Initiate Parsabiv® at 5 mg, 3 times per week[1]

5 mg starting dose

3x a week

- Do not administer Parsabiv® more frequently than 3 times per week[1]
- Ensure corrected serum calcium is at or above the lower limit of normal* prior to Parsabiv® initiation, a dose increase, or reinitiation after a dose interruption
- If a regularly scheduled hemodialysis treatment is missed, DO NOT administer any missed doses. Resume Parsabiv® at the end of the next hemodialysis treatment at the prescribed dose[1]
- If doses of Parsabiv® are missed for more than 2 weeks, reinitiate Parsabiv® at the recommended starting dose of 5 mg (or 2.5 mg if that was the patient's last dose)[1]

REFERENCES

*Lower limit of reference range in phase 3 trials was 8.3 mg/dL.

Dosing and Administration

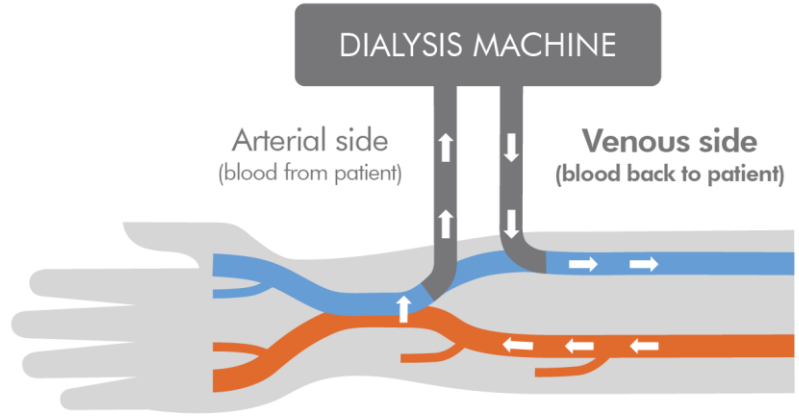
How to administer Parsabiv®

HOW

By intravenous bolus injection[1]

WHERE

Into the **venous** line of the dialysis circuit[1]



WHEN

Only at the end of hemodialysis, during rinse back or IV after rinse back[1]

- This is important to prevent the medication from being dialyzed

Flush with saline to make sure all medication reaches systemic circulation[2]

If giving during rinse back, flush with at least 150 mL of saline

OR

If giving IV after rinse back, flush with at least 10 mL of saline

REFERENCES

Dosing and Administration

How to monitor and titrate Parsabiv® (etelcalcetide)

Check their labs and know where they stand[1]

	PTH	Corrected Serum Calcium
Lab measurements after initiation or dose adjustment	after 4 weeks	at 1 week
Lab measurements once maintenance dose is established	per clinical practice	every 4 weeks

REFERENCES

Dosing and Administration

Start at 5 mg—then titrate up or down

Adjust dose based on PTH and corrected serum calcium[1]

Reductions too great? Titrate down

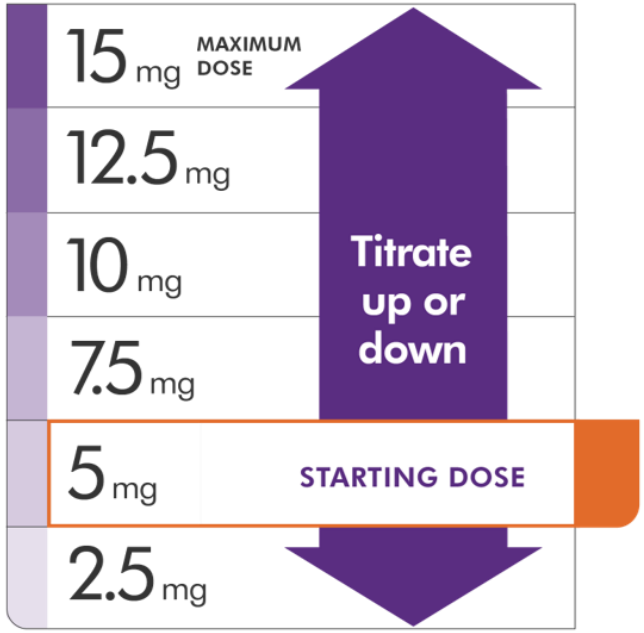
- Decrease or temporarily discontinue Parsabiv® when PTH is below target range
- Consider decreasing or temporarily discontinuing Parsabiv®, or use concomitant therapies,* when corrected serum calcium is below lower limit of normal† but ≥ 7.5 mg/dL without symptoms of hypocalcemia

Need greater reductions? Titrate up

- Increase the dose of Parsabiv® in 2.5 mg or 5 mg increments until PTH is within recommended target range and corrected serum calcium is within normal range
- Increase no more frequently than every 4 weeks up to a maximum dose of 15 mg three times per week

Reinitiating Parsabiv®

- If dose is stopped, reinitiate Parsabiv® at a lower dose when PTH is within target range and hypocalcemia has been corrected



REFERENCES

*Concomitant therapies include calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration.
†Lower limit of reference range in phase 3 trials was 8.3 mg/dL.[1,2]

Dosing and Administration

3 different vials—many dosing options

Parsabiv® is available in 3 different, single-use, single-dose vials[1]

2.5 mg/
0.5 mL

5 mg/
1 mL

10 mg/
2 mL

Always start with 5 mg dose, but use the other dose sizes when a different dose is required.

REFERENCES

Vials shown are not actual size.

Dosing and Administration

Parsabiv® (etelcalcetide) storage & handling

Protect from light[1]

- **DO NOT remove the carton lid**
- Keep Parsabiv® in the original closed carton, in the refrigerator, until you're ready to use it (2°C to 8°C [36°F to 46°F])
- Once removed from the refrigerator:
  - Use within 7 days if stored in the original carton
  - Use within 4 hours and do not expose to light if removed from original carton

Keep cold[1]

- Once removed from the refrigerator, DO NOT expose to temperatures above 25°C (77°F)
  - **DO NOT** place Parsabiv® on warm/hot surfaces

REFERENCES

Your clinical decision to prescribe Parsabiv® (etelcalcetide) is supported

Calcimimetics are part of the bundle for all ESRD patients[1]

CMS ESRD Bundle increase in 2021 reflects a Parsabiv® national average utilization of ~6.3% of dialysis treatments from Q3 2018 to Q4 2019[2]

Yet providers will receive the same amount of additional reimbursement ($10.09) for every Medicare patient, whether the patient is taking a calcimimetic or not[1]

The providers are responsible for patient outcomes, regardless of reimbursement. You can continue to prescribe Parsabiv® to those patients who need it

REFERENCES

THANK YOU

This concludes our
promotional presentation.

Parsabiv™
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL