CKD-MBD Management in the CKD Patient

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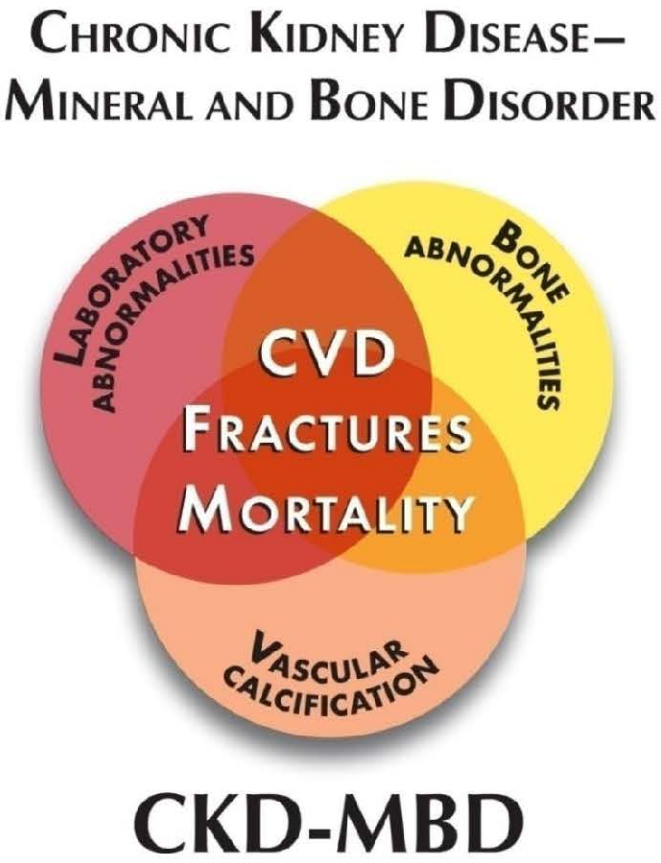
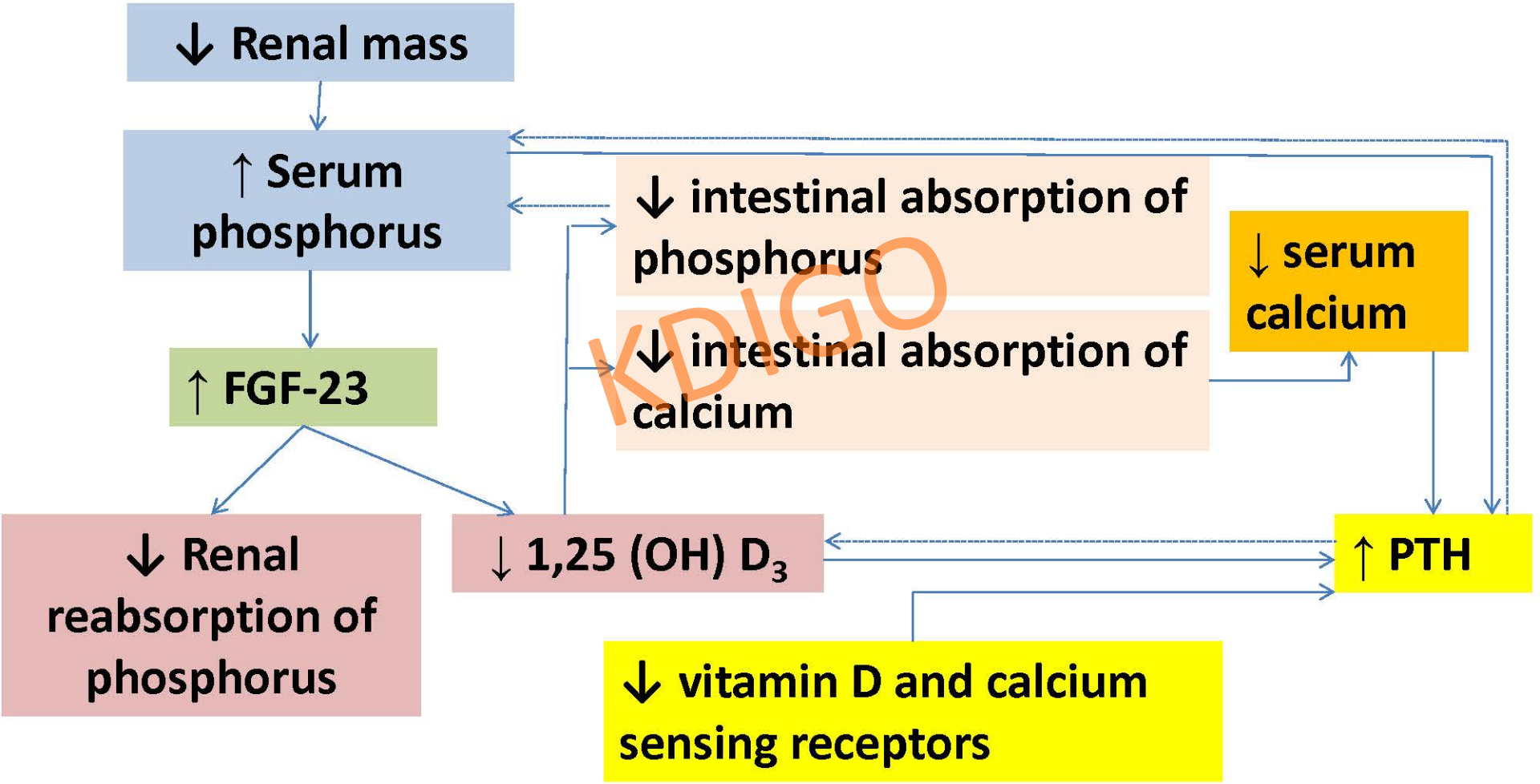
Conflict of Interest: Co-Chair of EVOLVE Nephrology partnership paid a stipend by Amgen

Definition



Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD) Moe S. *Kidney Int*. 2009;76(suppl 113):S1-S130.

Pathophysiology



Treatment of CKD-MBD: Phosphorus and Calcium

- **4.1.1. In patients with CKD stages 3–5, we suggest maintaining serum phosphorus in the normal range *(2C)*. In patients with CKD stage 5D, we suggest lowering elevated phosphorus levels toward the normal range *(2C)*.**

- **4.1.2. In patients with CKD stages 3–5D, we suggest maintaining serum calcium in the normal range *(2D)*.**

Treatment of CKD-MBD: Abnormal PTH Levels

- **4.2.3. In patients with CKD stage 5D, we suggest maintaining iPTH levels in the range of approximately two to nine times the upper normal limit for the assay *(2C)*.**

  We suggest that marked changes in PTH levels in either direction within this range prompt an initiation or change in therapy to avoid progression to levels outside of this range *(2C)*.

CKD-MBD Therapy

1. Control of hyperphosphatemia with phosphate binders
2. Correction of hypocalcemia
3. Administration of vitamin D sterol
4. Calcimimetic therapy
5. Parathyroidectomy

Although hyperphosphatemia has been clearly linked to increased mortality, increased progression of vascular calcification and progression of hyperparathyroidism, intervention studies leading to improved outcomes are not available at the present time.

Goldfarb and Martin, Neph SAP, 2012

Sevelamer vs Calcium-based phosphate binder RCTs in CK

	Author	Year	N	Follow-up	Risk of bias	HD
1	Chertow et al	2002	200	12	Unclear	Yes
2	Sadek et al	2003	31	5	Unclear	Yes
3	Braun et al	2004	113	12	High	Yes
4	Block et al	2005/7	99	18/44	Low	Yes
5	Russo et al	2007	55	24	High	Yes
6	Barreto et al	2008	101	12	Low	Yes
7	Qunibi et al	2008	203	12	Low	Yes
8	Suki et al	2008	2103	20	High	Yes
9	Takei et al	2008	46	24	High	Yes
10	Kabuta et al	2011	183	12	Unclear	Yes

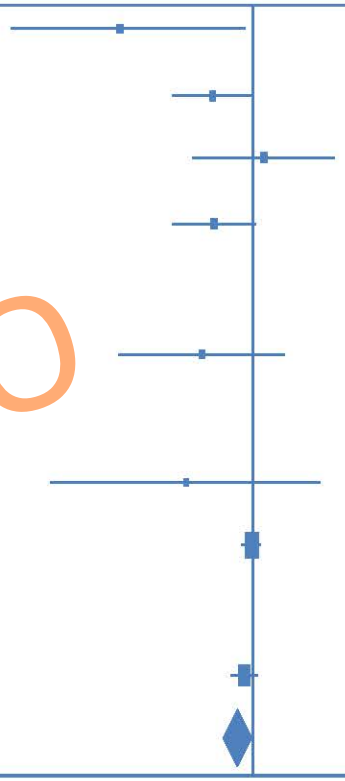
Jamal et al, Lancet 2013

Lanthanum vs calcium-based phosphate binder RCTs in CKD

	Author	Year	N	Follow-up	Risk of bias	HD
1	Wilson et al	2009	1354	24	High	Yes
2	Toussaint et al	2011	45	18	High	Yes
3	Block et al	2012	58	9	Low	Yes

Jamal et al, Lancet, 2013

RCTs	Non-calcium binders		Calcium binders		Weight	Risk ratio (95% CI)
	Events	Total patients	Events	Total patients		
Barreto et al (2008)[12]	1	52	8	49	0.3%	0.12 (0.02–0.91)
Block et al (2007)[9]	11	60	23	67	3.2%	0.53 (0.28–1.00)
Chertow et al (2002)[5]	6	99	5	101	1.0%	1.22 (0.39–3.88)
Di Iorio et al (2012)[22]	12	107	22	105	3.0%	0.54 (0.28–1.03)
Kakuta et al (2011)[20]	0	91	0	92		Not estimable
Qunibi et al (2008)[13]	3	100	7	103	0.8%	0.44 (0.12–1.66)
Russo et al (2007)[10]	0	27	0	28		Not estimable
Sadek et al (2003)[6]	1	21	3	21	0.3%	0.33 (0.04–2.95)
Suki (2008)[14]	267	1053	275	1050	24.5%	0.97 (0.84–1.12)
Takei et al (2008)[15]	0	22	0	20		Not estimable
Wilson et al (2009)[16]	135	680	157	674	17.9%	0.85 (0.70–1.05)
Subtotal	**436**	**2312**	**500**	**2310**	**50.9%**	**0.78 (0.61–0.98)**



Heterogeneity: τ^2=0.03; χ^2=12.35; df=7 (p=0.09); I^2=43%

Test for overall effect: Z=2.09 (p=0.04)

Jamal et al, Lancet, 2013

Studies have shown that low 25-hydroxyvitamin D levels are associated with increased mortality in nondialysis-dependent CKD patients; however, data are lacking regarding whether correcting this deficiency leads to improved outcomes.

Goldfarb and Martin, Neph SAP, 2012

Efficacy and safety of paricalcitol therapy for CKD: a meta-analysis

- 9 RCTs in 2–5 CKD
- 832 patients

Cheng J et al, Clin J Am Soc Nephrol, 2012

Vitamin D treatment and mortality in CKD: a systematic review and meta-analysis

- 14 observational studies, 7 prospective
- No Blinding or randomization of patients

Duranton F et al, Am J Nephrology, 2013

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Cinacalcet on Cardiovascular Disease in Patients Undergoing Dialysis

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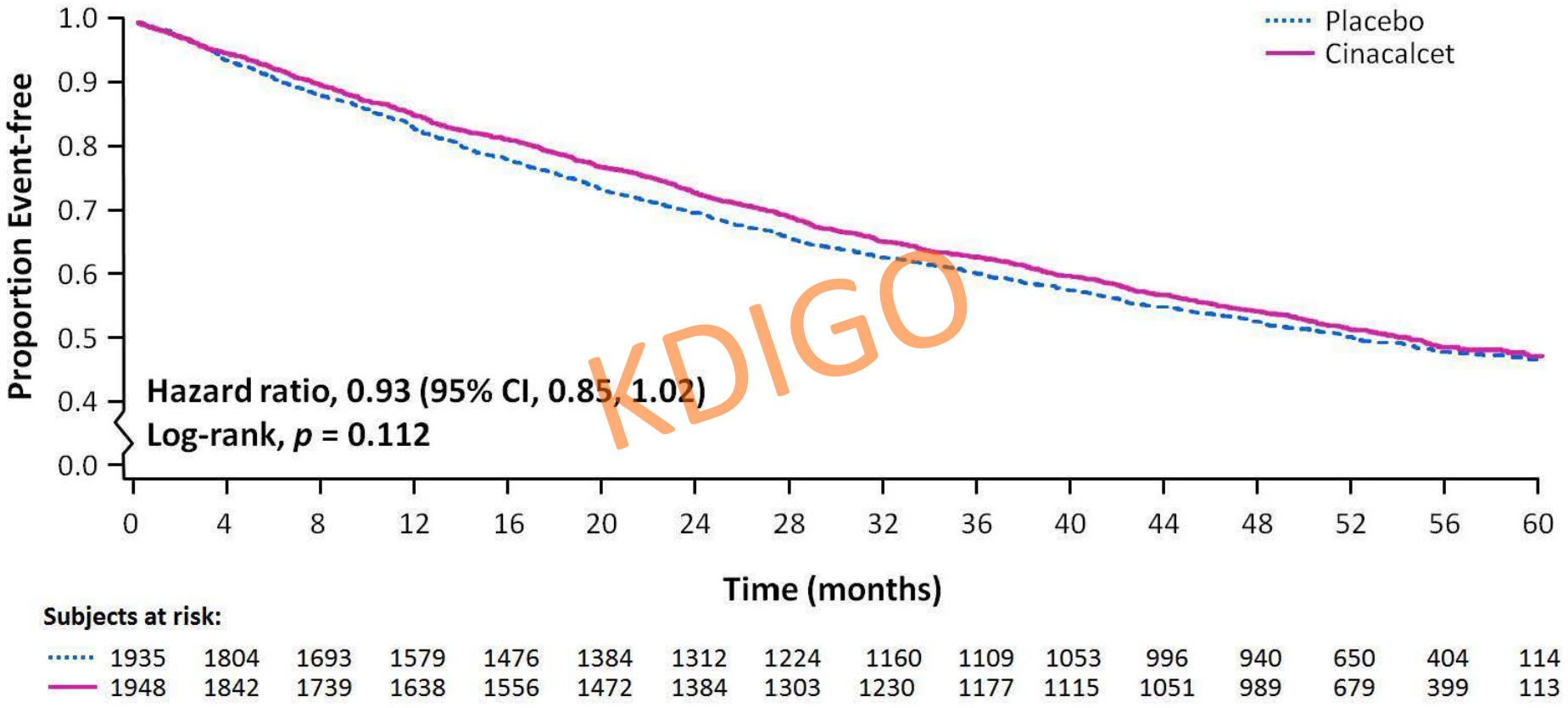
Kaplan-Meier Plot of Primary Composite Endpoint (ITT)



Age as a confounder and modifier

Baseline Patient Characteristics

Demographics	Cinacalcet (N = 1948)	Placebo (N = 1935)
Age (yr) – median (p10, p90)	55.0 (35.0, 74.0)	54.0 (35.0, 73.0)
Female sex	41.5%	39.7%
Race or ethnic group		
White	57.7%	57.7%
Black	21.0%	22.1%
Other	21.3%	20.2%
Quételet's (body mass) index (kg/m^2) – median (p10, p90)	26.3 (20.4, 36.4)	26.4 (20.6, 36.7)
Dialysis vintage (months) – median (p10, p90)	45.4 (8.5, 142.0)	45.1 (9.9, 149.6)
Blood pressure (mm Hg) – median (p10, p90)		
Systolic	140 (110, 176)	141 (111, 177)
Diastolic	80 (60, 100)	80 (60, 100)

Chertow et al. NEJM 2012.

Could age imbalance occur by chance?

- Observed 0.8 yrs difference in mean age at baseline (54.8 yrs in cinacalcet group vs 54.0 yrs in placebo group) despite enrolling almost 4000 subjects
- ~8% chance of difference in mean age ≥ 0.8 yrs
  - Standard deviation (SD) for age and sample size dictates likelihood of imbalance
  - SD larger in SHPT population than other CV trials

Age SD	Probability of |Age Diff| > 0.8 Yrs	Example Trial Populations (assume N's in EVOLVE)
20	0.20	
14	0.08	EVOLVE, HEMO, Cinacalcet Ph3, DCOR
12	0.04	SHARP
11	0.02	CHARM, MIRACLE, PRAISE, RED-HF
10	0.01	TREAT
8	0	4D, AURORA

Unadjusted and Adjusted ITT Analyses

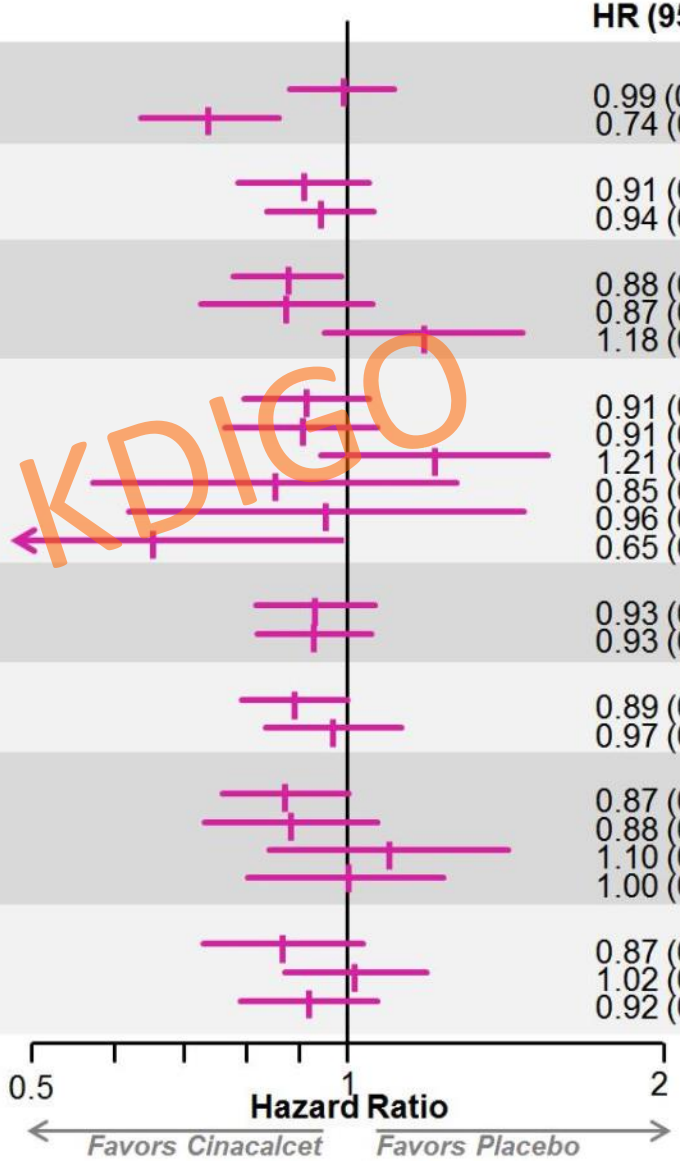
Model	Relative Hazard	95% CI	P-value
Unadjusted	0.93	0.85 to 1.02	0.11
Age-adjusted	0.88	0.81 to 0.97	0.007
Multivariable (best fit)	0.88	0.79 to 0.97	0.008
Multivariable-adjusted (all included)	0.88	0.80 to 0.98	0.02

* Unadjusted ITT was primary outcome
* MV adjusted ITT prespecified

Relative Hazards of Primary Composite Endpoint (Intent-to-Treat Analysis)

EVOLVE

Subgroup	N	HR (95% CI)	Interaction *p*-value
Age			0.007
< 65 yrs	2878	0.99 (0.88, 1.11)	
≥ 65 yrs	1005	0.74 (0.63, 0.86)	
Sex			0.784
Female	1578	0.91 (0.79, 1.05)	
Male	2305	0.94 (0.84, 1.06)	
Race Group			0.065
White	2240	0.88 (0.78, 0.99)	
Black	837	0.87 (0.72, 1.06)	
Other	806	1.18 (0.95, 1.47)	
Region			0.165
United States	1430	0.91 (0.80, 1.05)	
Europe	1188	0.91 (0.77, 1.07)	
Latin America	687	1.21 (0.95, 1.56)	
Russia	283	0.85 (0.57, 1.27)	
Canada	146	0.96 (0.62, 1.48)	
Australia	149	0.65 (0.43, 0.99)	
Diabetes			0.943
Yes	1302	0.93 (0.82, 1.06)	
No	2581	0.93 (0.82, 1.05)	
BL Vitamin D			0.337
Yes	2310	0.89 (0.79, 1.00)	
No	1573	0.97 (0.84, 1.13)	
PTH Group			0.255
300-600 pg/mL	1573	0.87 (0.76, 1.00)	
> 600-900 pg/mL	929	0.88 (0.73, 1.07)	
> 900-1200 pg/mL	550	1.10 (0.84, 1.43)	
>1200 pg/mL	831	1.00 (0.80, 1.24)	
Dialysis Vintage			0.432
< 2 years	1098	0.87 (0.73, 1.03)	
2 to < 5 years	1285	1.02 (0.87, 1.19)	
≥ 5 years	1499	0.92 (0.79, 1.07)	



Chertow et al, NEJM, 2013

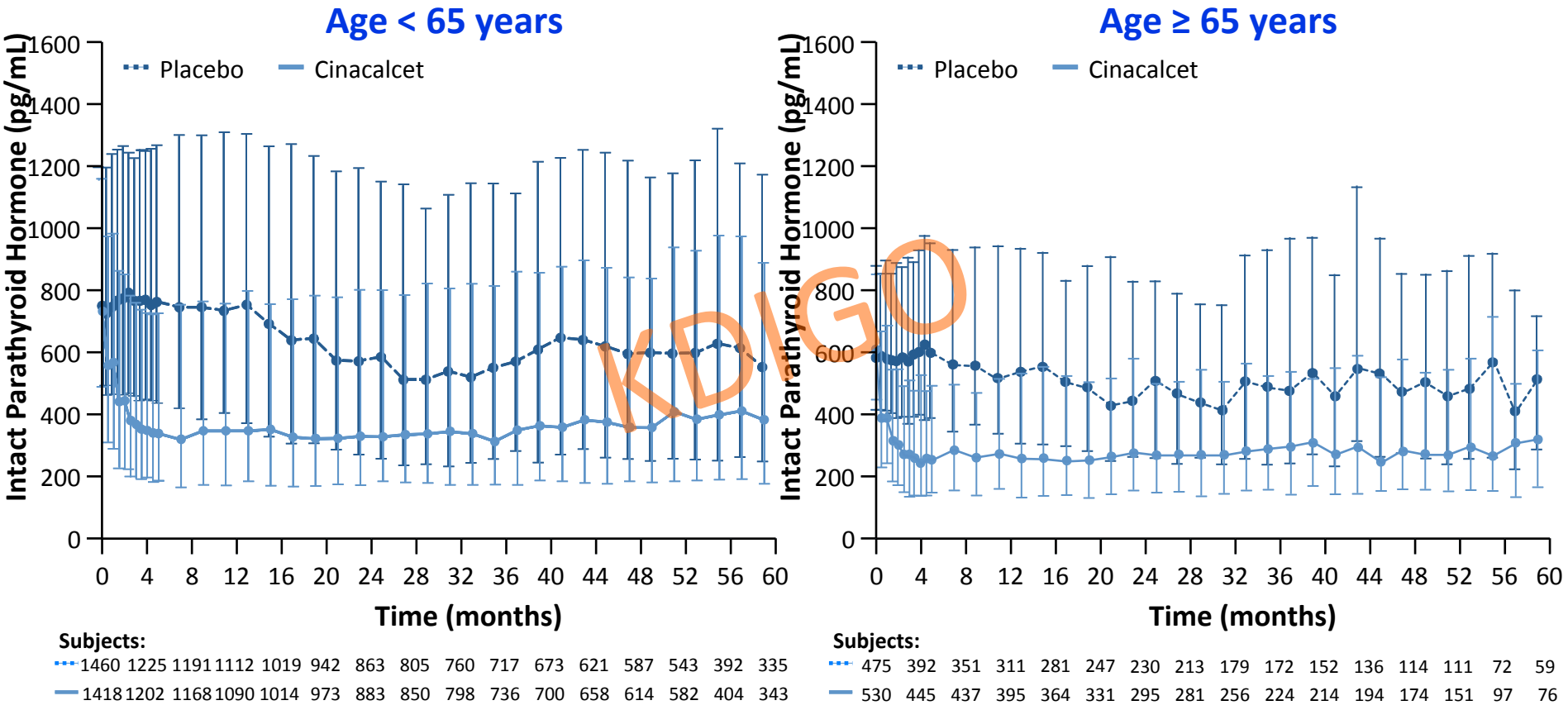
Background

- In a pre-specified subgroup analysis the effect of cinacalcet on CVD events more pronounced in older patients: treatment x age (continuous) interaction p = 0.03.

Hypothesis

- Lower baseline CVD risk and more frequent use of co-interventions that reduce PTH in younger patients may explain the age effects of Cinacalcet.

Median Plasma iPTH



Parfrey et al, CJASN, 2015

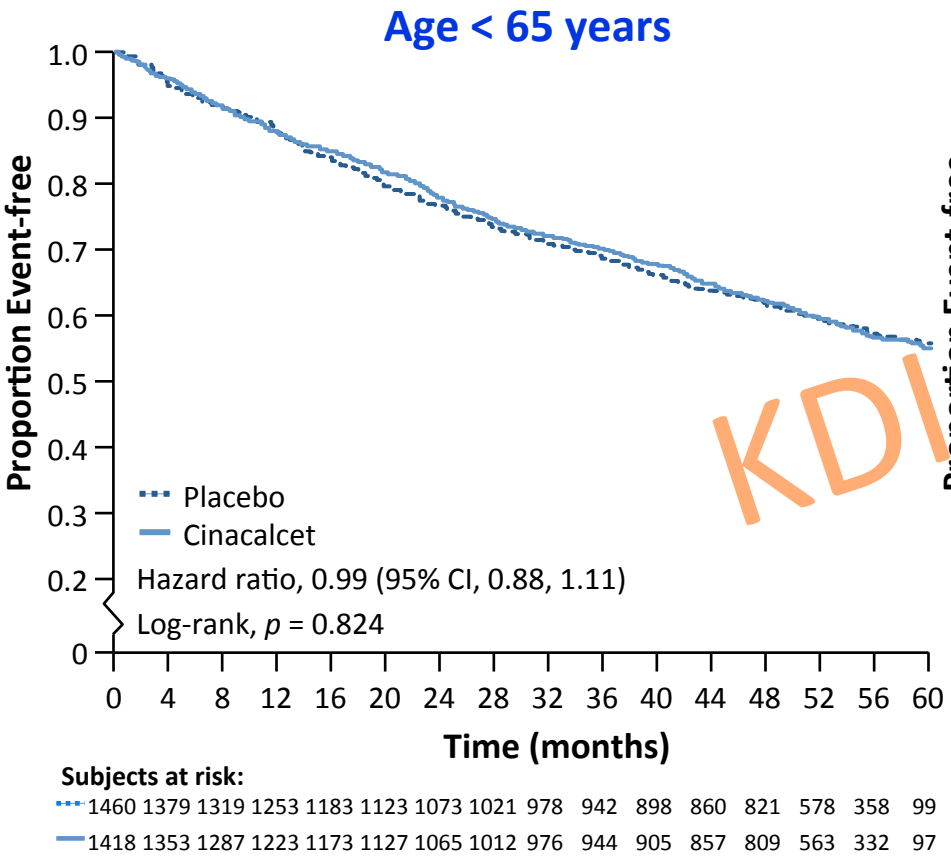
Baseline Characteristics by Age Group and by Treatment Arm

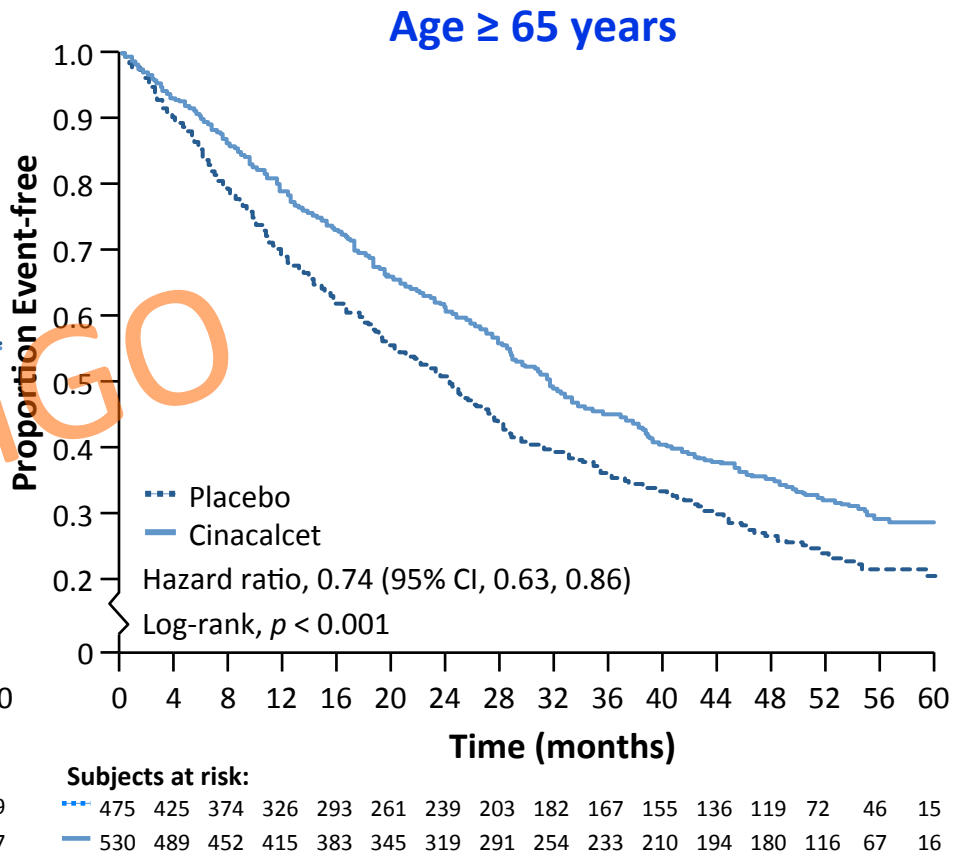
n (%)	< 65 years		≥ 65 years	
	Cinacalcet (N = 1418)	Placebo (N = 1460)	Cinacalcet (N = 530)	Placebo (N = 475)
Diabetes*	414 (29)	422 (29)	240 (45)	226 (48)
Heart failure*	281 (20)	294 (20)	169 (32)	162 (34)
Peripheral vascular disease*	181 (13)	194 (13)	132 (25)	128 (27)
Coronary artery bypass graft*	58 (4)	68 (5)	77 (15)	86 (18)
Percutaneous coronary intervention*	79 (6)	81 (6)	51 (10)	51 (11)
Myocardial infarction*	138 (10)	132 (9)	101 (19)	112 (24)
Stroke *	99 (7)	132 (9)	63 (12)	61 (13)
Transient ischemic attack*	54 (4)	40 (3)	46 (9)	34 (7)
Amputation*	86 (6)	89 (6)	35 (7)	40 (8)
Atrial fibrillation*	82 (6)	109 (8)	120 (23)	116 (24)

Parfrey et al, CJASN, 2015

*$P < 0.001$ between each age group, combining those randomized to placebo and to cinacalcet

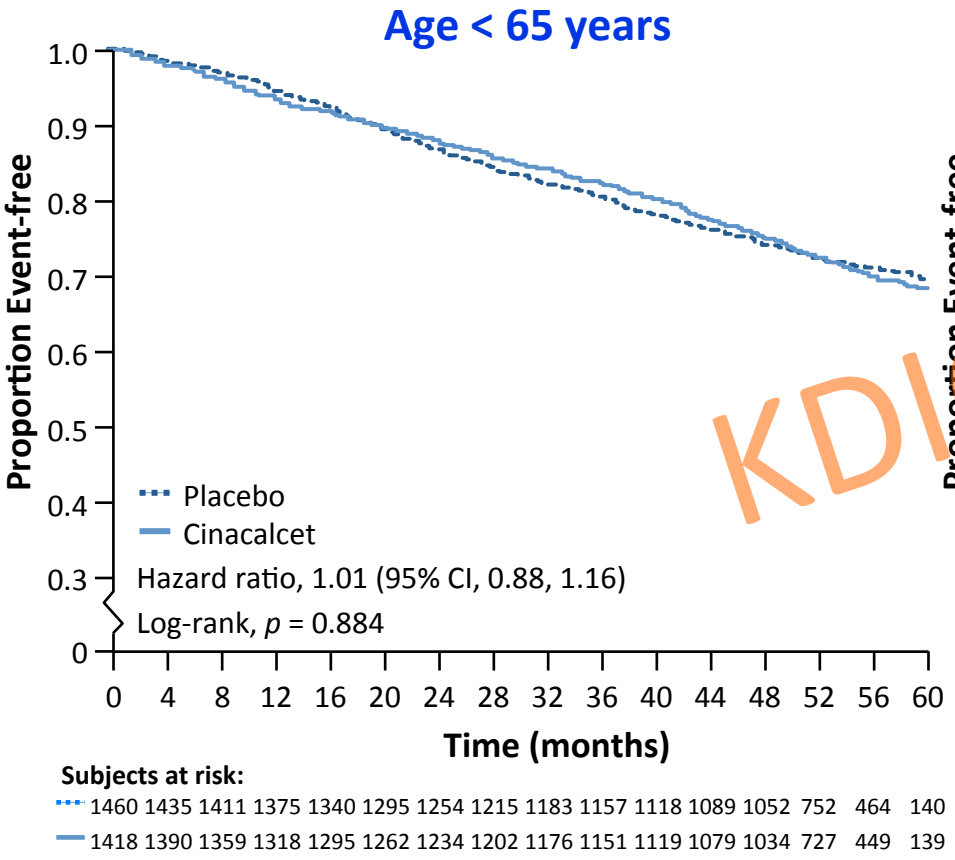
Time to Primary Composite Endpoint

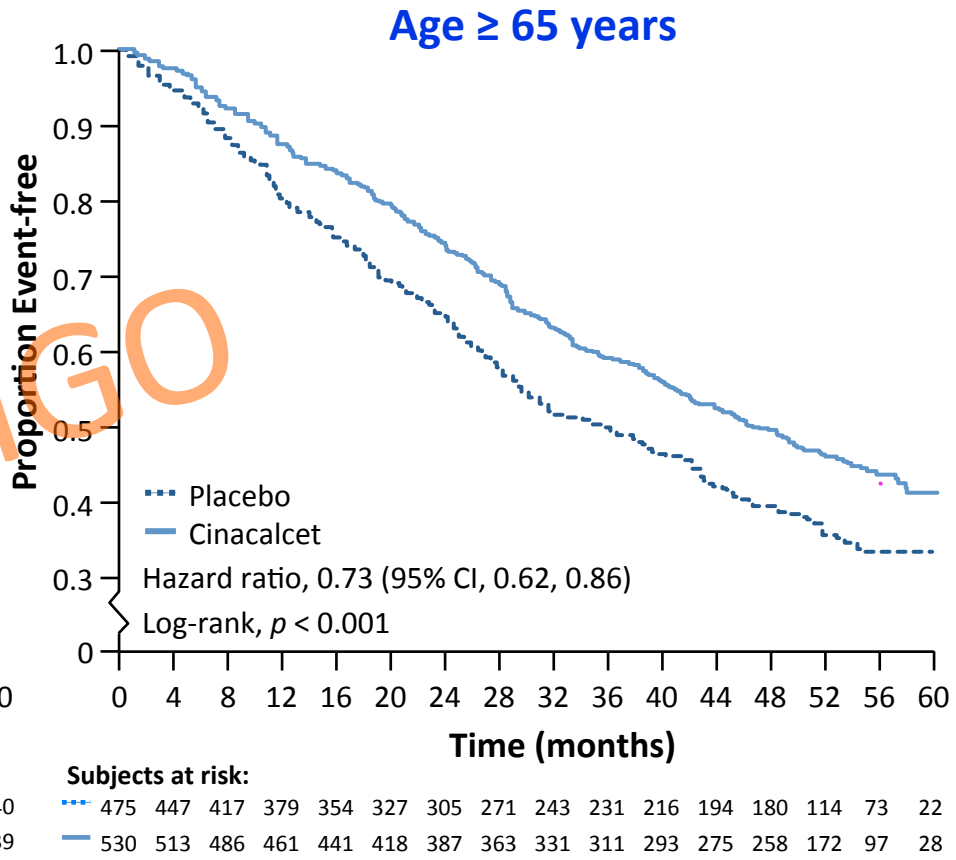




Parfrey et al, CJASN, 2015

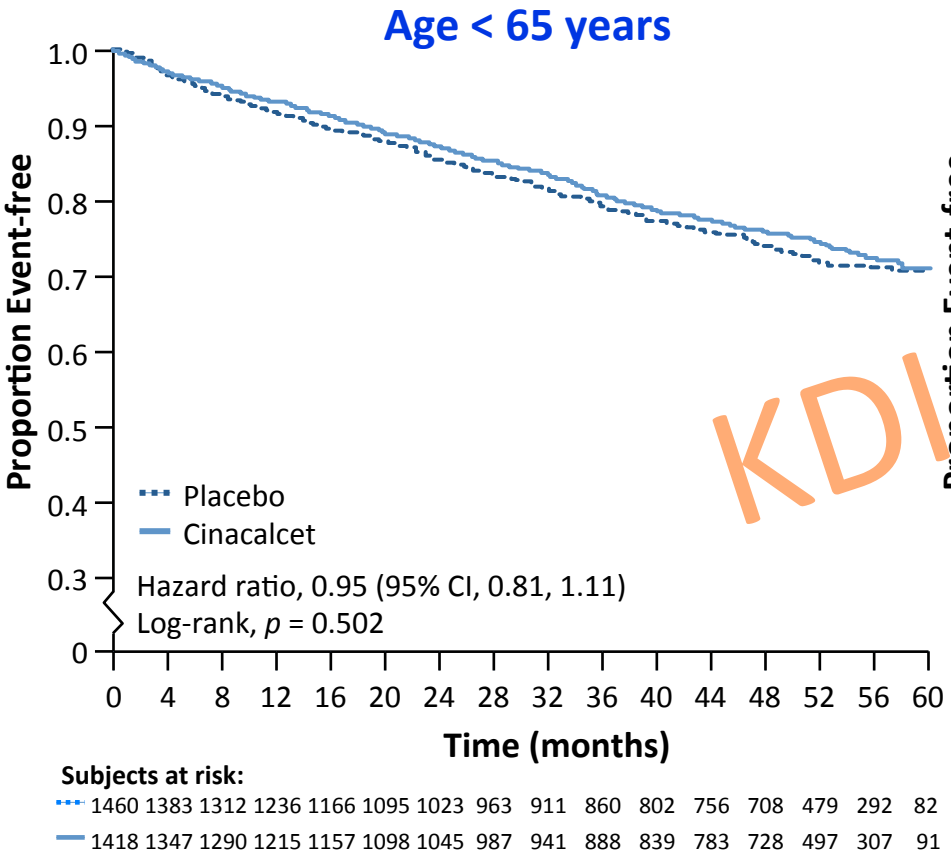
Time to Death

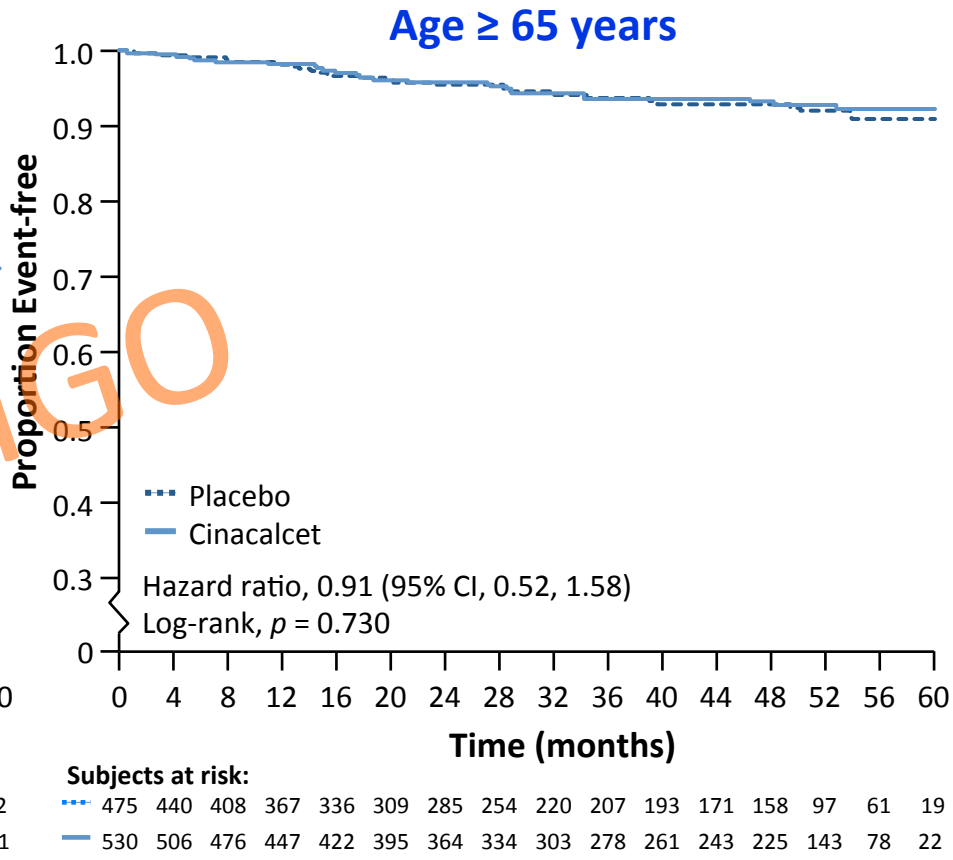




Parfrey et al, CJASN, 2015

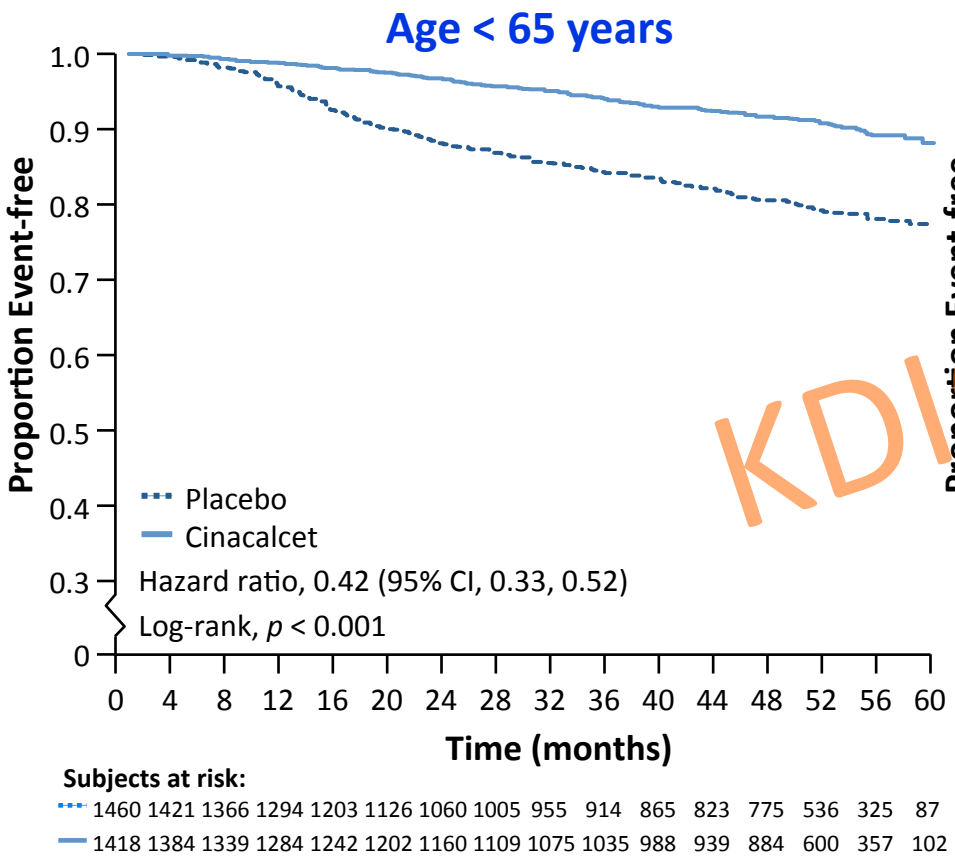
Time to Kidney Transplantation

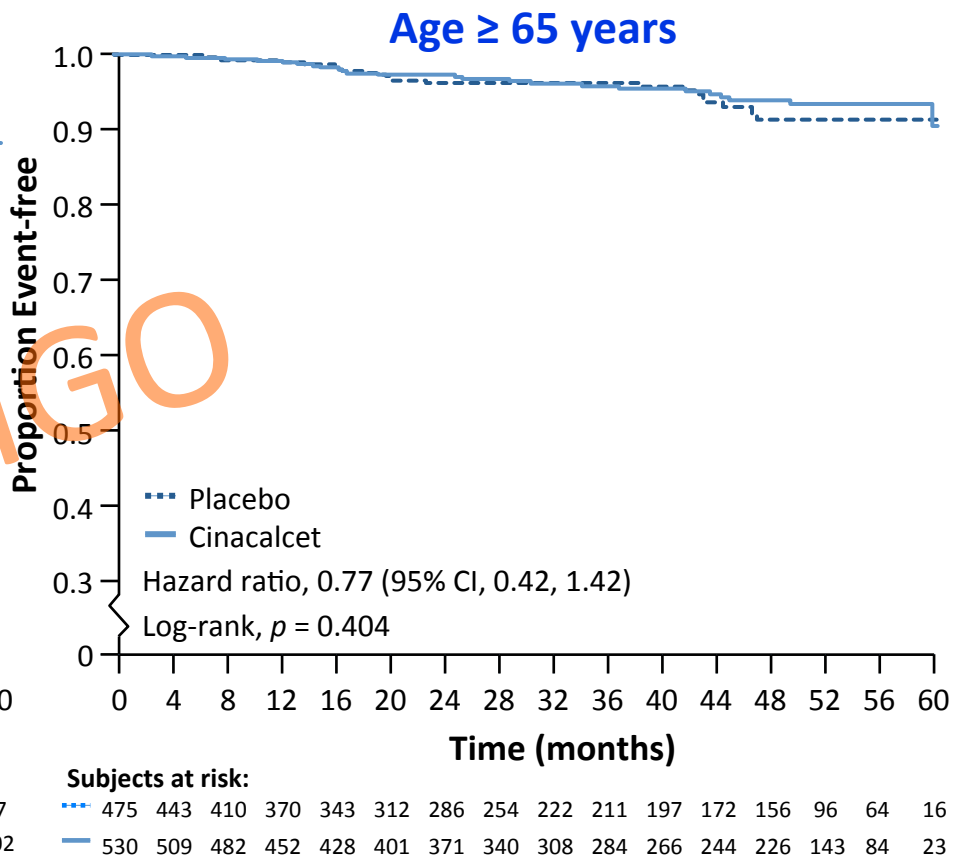




Parfrey et al, CJASN, 2015

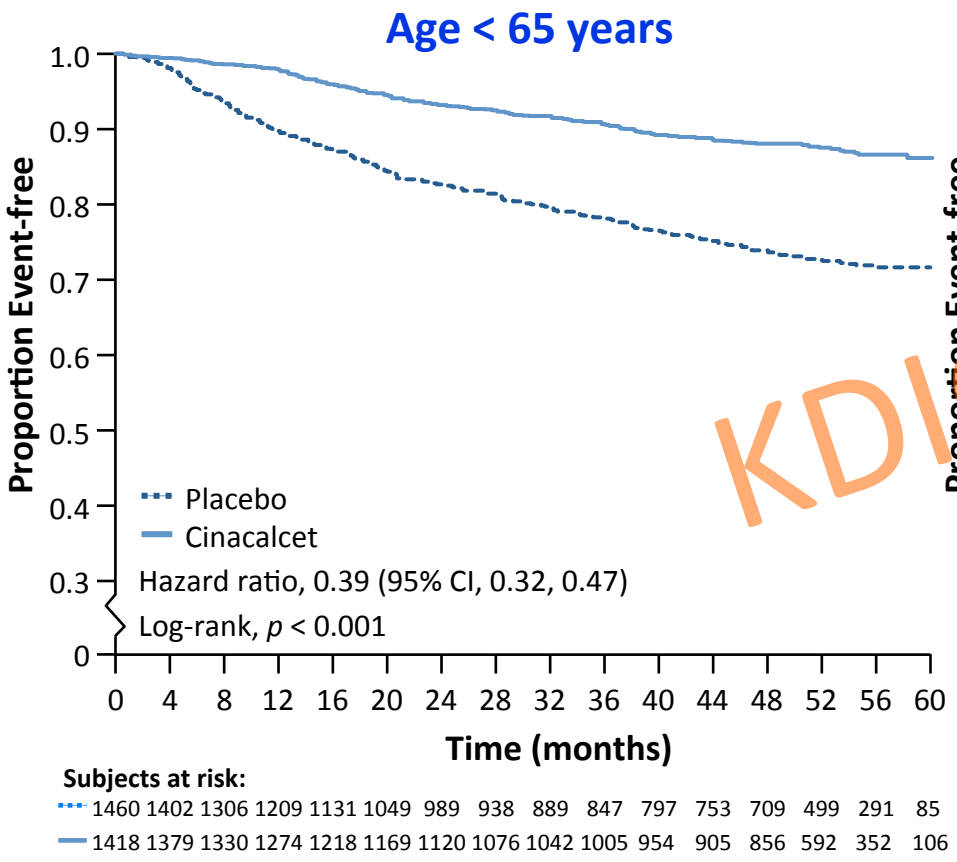
Time to Parathyroidectomy

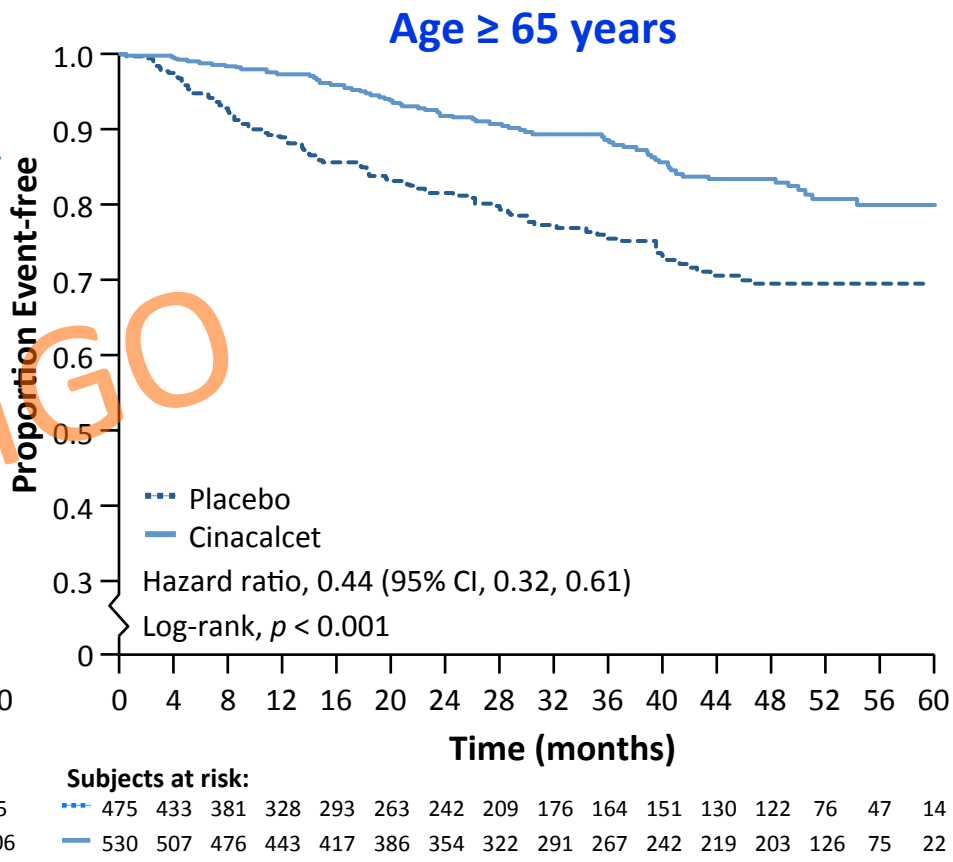




Parfrey et al, CJASN, 2015

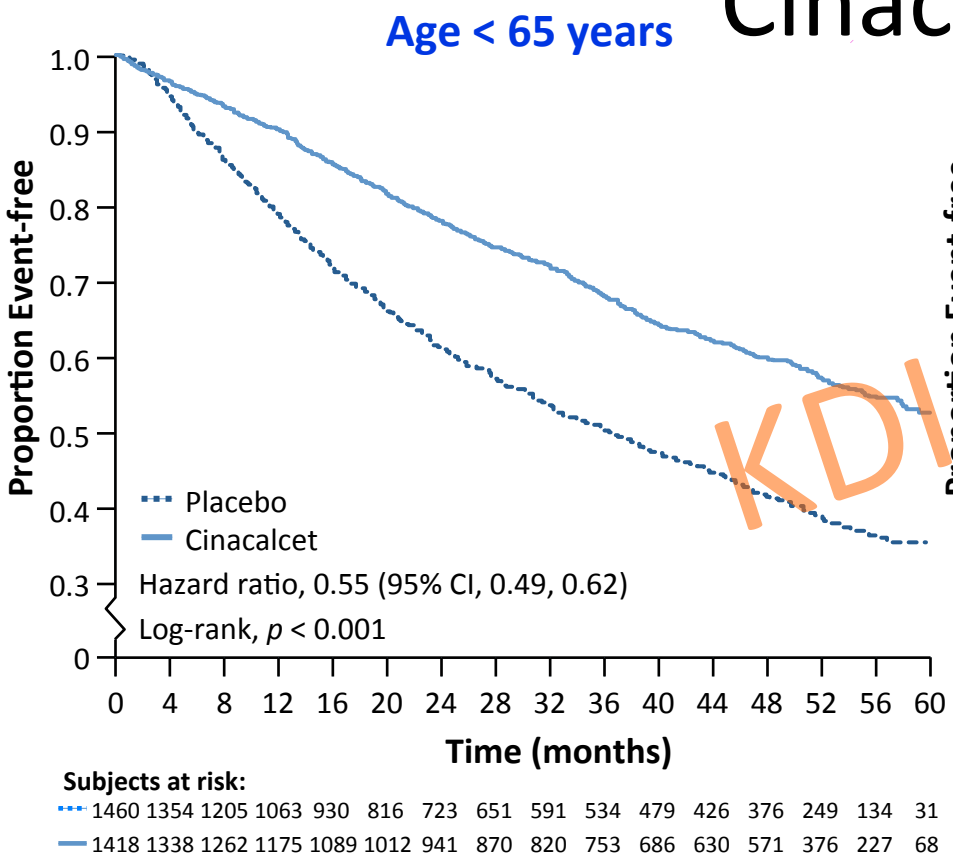
Time to Commercial Cinacalcet

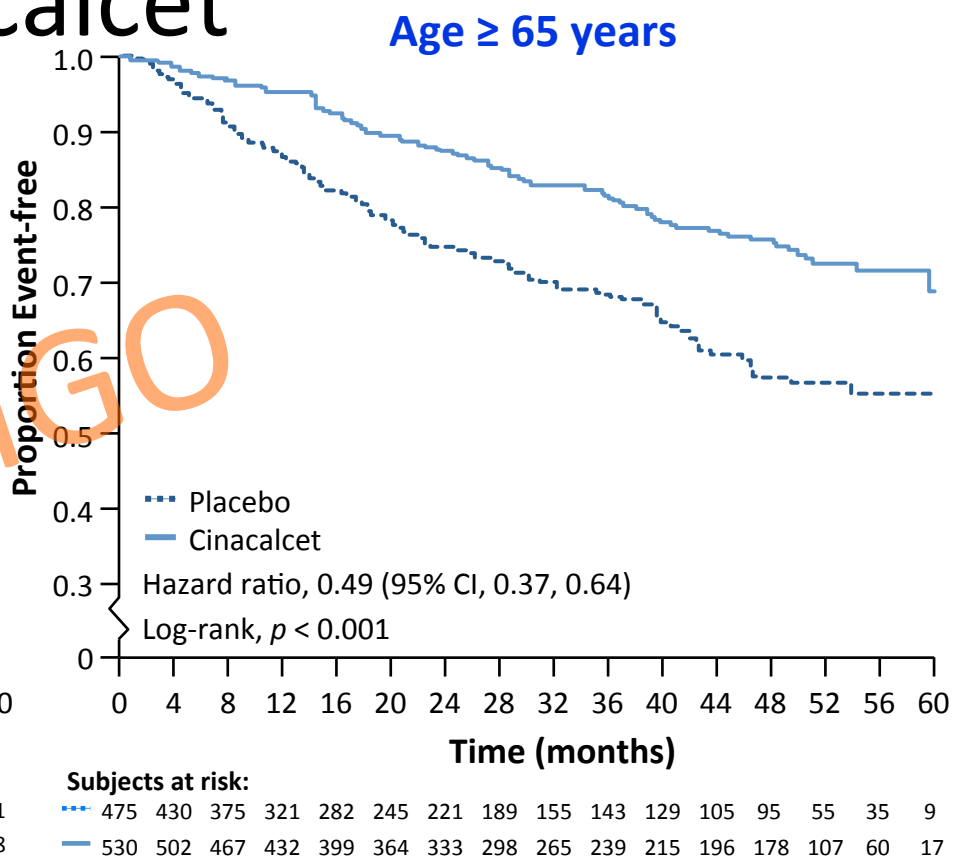




Parfrey et al, CJASN, 2015

Time to Kidney Transplant, Parathyroidectomy or Commercial Cinacalcet





Parfrey et al, CJASN, 2015

Treatment Effect by Age Group and by Baseline Cardiovascular History

Censoring at co-interventions	< 65 years, n		≥ 65 years, n	
	Placebo	Cinacalcet	Placebo	Cinacalcet
With baseline CV history (N = 1775)	**568**	**543**	**322**	**342**
HR (95% CI)	0.84 (0.71, 1.00)		0.66 (0.54, 0.80)	
Without baseline CV history (N = 2108)	**892**	**875**	**153**	**188**
HR (95% CI)	0.97 (0.79, 1.18)		0.83 (0.59, 1.18)	

CV history: cardiovascular (heart failure, peripheral vascular disease, amputation, stroke, transient ischemic attack, myocardial infarction or coronary artery revascularization at baseline.)

The Creditability of the Age Subgroup effect in EVOLVE

Design

1. Age ≥ and < 65 years was a baseline characteristic
2. The subgroup was not a stratification factor at randomization
3. The age subgroup analysis was pre-specified
4. It was one of a small group (N=7) of pre-specified subgroup hypotheses tested

Analysis

5. The test of treatment x age interaction was significant
6. The age interaction effect was significant and independent of other significant interactions
7. The direction of the age subgroup effect was not pre-specified

The Creditability of the Age Subgroup effect in EVOLVE

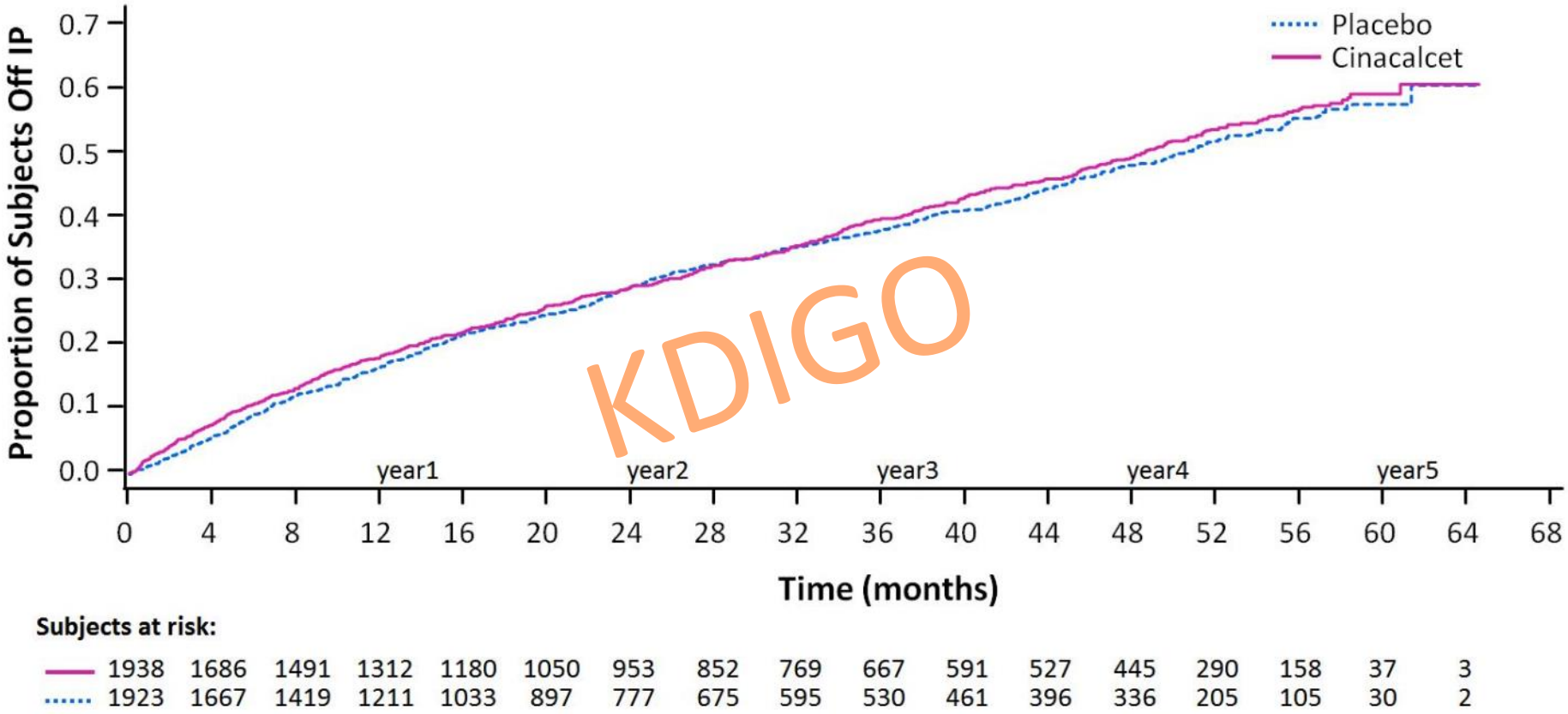
Context

8. The age subgroup effect is consistent with that in RCT of sevalamer v calcium-based phosphate binders
9. The age subgroup effect was consistent across related outcomes
10. The biological rationale for the effect is logical

Sun et al, BMJ, 2012

Impact of non-adherence

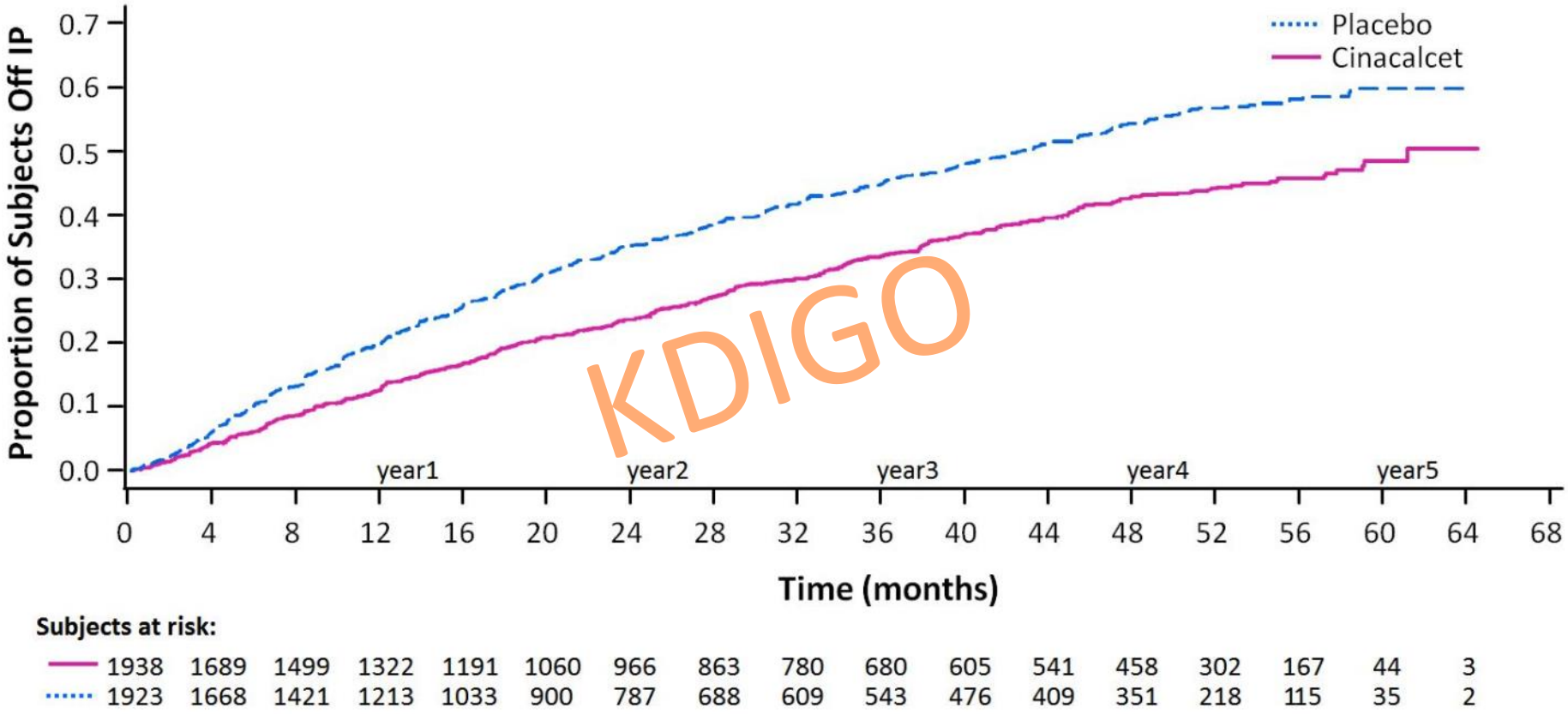
Time to First Discontinuation of Study Drug due to Protocol-specified Reasons*



Chertow et al, NEJM, 2013

*Safety Analysis Set

Time to First Discontinuation from Study Drug due to Non-protocol Specified Reasons*



Chertow et al, NEJM, 2013

*Safety Analysis Set

Treatment of HPT in Placebo Group of EVOLVE

- 80% reached max daily dose of placebo
- At year 2:
  - Vit D sterol use
    - 66% in placebo
    - 52% in cinacalcet
  - Calcium based phosphate binders
    - 49% in placebo
    - 58% in cinacalcet
  - Non-calcium based phosphate binders
    - 37% in placebo
    - 28% in cinacalcet
- PTX 14%
- Commercial cinacalcet 23%

Parfrey et al. JCEM, 2013.

Non-adherence to Study Drug

- Defined as patients who prematurely stop study drug and assume risk similar to the opposite treatment group:
  - Dropin: placebo patients who prematurely stop study drug and start commercial cinacalcet prior to experiencing a primary endpoint
  - Dropout: cinacalcet patients who prematurely stop taking study drug prior to experiencing a primary endpoint

Total (N=3883)	n (%)	Observed Rates (%/yr)	Protocol Rates (%/yr)
Drop-in (Placebo)	384 (20%)	7.4	10.0
Drop-out (Cinacalcet)	1207 (62%)	27.3	10.0

Time off Study Drug vs Time on Study

Months	Cinacalcet (N=1948)	Placebo (N=1935)
Time on study Median (Q1, Q3)	50.6 (31.3, 56.4)	50.4 (26.7, 56.4)
Time on study drug Median (Q1, Q3)	21.2 (8.1, 40.8)	17.5 (7.1, 37.9)

Time on study drug was less than half of the time patients were on study

Pre-specified Adjustment for Non-adherence

- In an attempt to adjust for non-adherence to study drug in the estimates of treatment effect, different methods were implemented:
  - Lag Censoring Analysis
  - Iterative Parameter Estimation (IPE)
  - Inverse Probability Censoring Weight (IPCW)

Inverse Probability of Censoring Weight (IPCW) – Overview

- IPCW method censors data when non-adherence occurs (ie, weight=0 for time periods after this timepoint)
- For patients who were adherent and had similar characteristics to those who were not, IPCW method assigns bigger weights to these patients to "re-create" the population that would have been observed
- Weights are calculated based on the inverse of the probability that patients remains adherent using a logistic regression model
- Final hazard ratio is derived from a weighted Cox regression model

Pooled Logistic Regression Analysis of Baseline Predictors and Time-varying Confounders on Remaining Adherent to Study Drug

		Model 1: Baseline Predictors		Model 2: Baseline Predictors and Time-varying Confounders	
		Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Treatment (Cinacalcet vs Placebo)		1.25 (1.15, 1.36)	<0.001	0.79 (0.70, 0.89)	<0.001
Interval		0.93 (0.92, 0.93)	<0.001	0.94 (0.93, 0.95)	<0.001
Age per 5 years		1.02 (1.00, 1.04)	0.024	1.00 (0.97, 1.02)	0.631
Sex (Male vs Female)		1.07 (0.99, 1.17)	0.099	0.98 (0.88, 1.10)	0.735
Race group (ref: White)	Black	1.28 (1.11, 1.47)	<0.001	1.41 (1.17, 1.70)	<0.001
	Other	0.96 (0.84, 1.09)	0.005	1.00 (0.85, 1.18)	0.026
Country (ref: USA)	Australia	0.90 (0.71, 1.14)	0.100	0.84 (0.63, 1.13)	0.017
	Canada	0.90 (0.72, 1.13)	0.094	1.03 (0.77, 1.39)	0.527
	Europe	0.98 (0.86, 1.12)	0.133	1.05 (0.88, 1.25)	0.338
	Latin America	1.43 (1.24, 1.65)	<0.001	1.70 (1.41, 2.05)	<0.001
	Russia	1.19 (0.98, 1.44)	0.082	1.22 (0.95, 1.56)	0.330
History of diabetes		0.93 (0.84, 1.03)	0.140	0.91 (0.80, 1.04)	0.161
Baseline PTH per 100 pg/mL increase		0.98 (0.98, 0.99)	<0.001	1.02 (1.01, 1.03)	0.002
Baseline corrected serum calcium per 1 mg/dL increase		0.86 (0.81, 0.91)	<0.001	1.03 (0.94, 1.13)	0.491
Baseline serum phosphorus per 1 mg/dL increase		1.00 (0.97, 1.03)	0.856	0.99 (0.94, 1.03)	0.528
PTH per 100 pg/mL increase		—	—	0.96 (0.95, 0.97)	<0.001
Corrected serum calcium per 1 mg/dL increase		—	—	0.81 (0.76, 0.87)	<0.001
Serum phosphorus per 1 mg/dL increase		—	—	1.05 (1.01, 1.09)	0.010
Adverse event of nausea/vomiting		—	—	0.54 (0.44, 0.65)	<0.001
Adverse event of hypocalcemia		—	—	0.83 (0.47, 1.46)	0.517

Kubo et al, Pharm Stats, 2015

IPCW (cont'd)

- In EVOLVE, demographics, adverse events and lab assessments were used in the logistic regression model to estimate the probability of adherence:
  - Age
  - Sex
  - Race group (white, black, other)
  - Country
  - History of diabetes
  - Randomized treatment group
  - Time dependent covariates of PTH, adverse events of hypocalcemia, nausea/vomiting

IPCW PROs/CONs

PROs	CONs
Preserves randomization	Difficult model specification; must have no unknown confounders for adherence •Missing data may cause biased weights (eg, PTH)
Takes into account informative censoring	Computationally difficult to implement: creation of dataset is difficult; parameter estimates may not be stable since model may not converge
Adjusts for time dependent confounders	Sensitive to amount of non-adherent patients, results may be biased or unstable

Results – Primary Composite Endpoint

Method	Hazard Ratio	95% CI
ITT (primary analysis)	0.93	(0.85, 1.02)
Lag censoring	0.85	(0.76, 0.95)
IPE	0.87	(0.75, 1.02)
IPCW	0.76	(0.66, 0.88)

Kubo et al, Pharm Stats, 2015

Primary Composite Endpoint: Sensitivity Analyses

Analysis Type	Placebo (N=1935)	Cinacalcet (N=1948)	HR (95% CI)	p-value
ITT (primary analysis)	952 (49.2)	938 (48.2)	0.93 (0.85, 1.02)	0.112
Lag Censoring (6 mos)	658 (34.0)	638 (32.8)	0.85 (0.76, 0.95)	0.003
Censor at PTX	911 (47.1)	916 (47.0)	0.90 (0.82, 0.99)	0.031
Censor at KTX	907 (46.9)	891 (45.7)	0.90 (0.82, 0.99)	0.029
Censor at Commercial Cinacalcet Use	818 (42.3)	870 (44.7)	0.90 (0.82, 0.99)	0.032
Censor at PTX or Commercial Cinacalcet Use	786 (40.6)	854 (43.8)	0.87 (0.79, 0.96)	0.006
Censor at PTX, Commercial Cinacalcet, or KTX	748 (38.7)	812 (41.7)	0.84 (0.76, 0.93)	<0.001

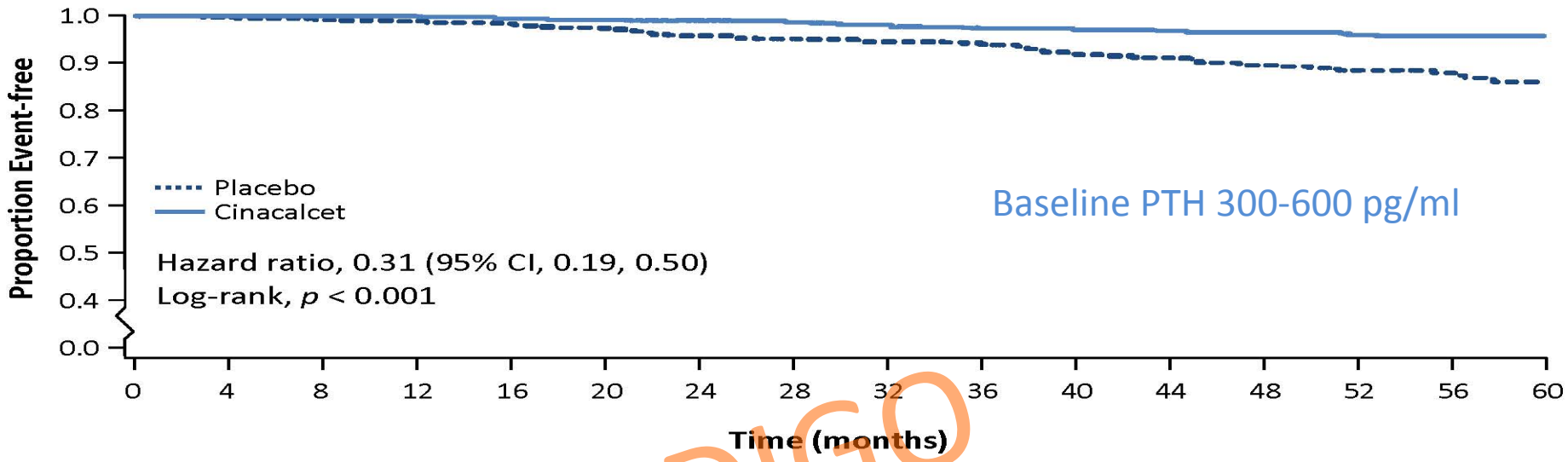
Chertow et al, NEJM, 2013

Summary of Unremitting Severe Secondary Hyperparathyroidism Based on Biochemical Criteria, Parathyroidectomy and Commercial Cinacalcet Use (Efficacy Analysis Set)

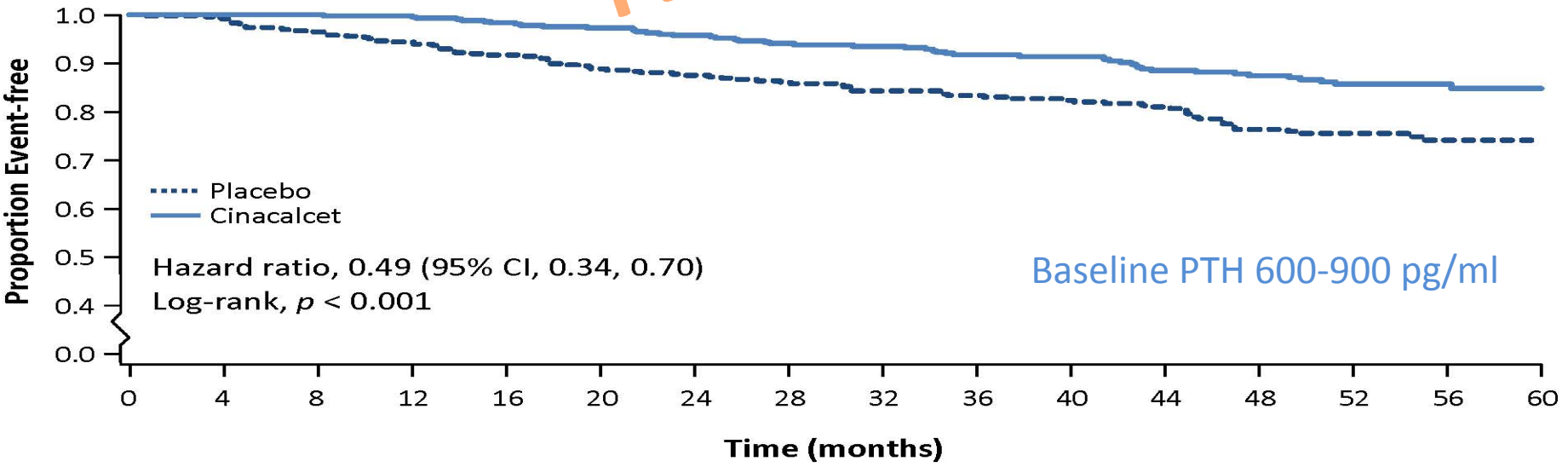
n (%)	Placebo (N = 1935)	Cinacalcet (N = 1948)
Number of subjects with severe secondary HPT – N_1(%)	470 (24.3)	240 (12.3)
PTH > 1000 pg/mL with serum calcium > 10.5 mg/dL on 2 consecutive occasions	279 (59.4)	138 (57.5)
PTH > 1000 pg/mL with serum calcium > 10.5 mg/dL on a single occasion and subsequent commercial cinacalcet use within 2 months of the laboratory assessment	60 (12.8)	22 (9.2)
Parathyroidectomy	278 (59.1)	140 (58.3)

Parfrey et al. JCEM, 2013.

Development of Severe Unremitting HPT

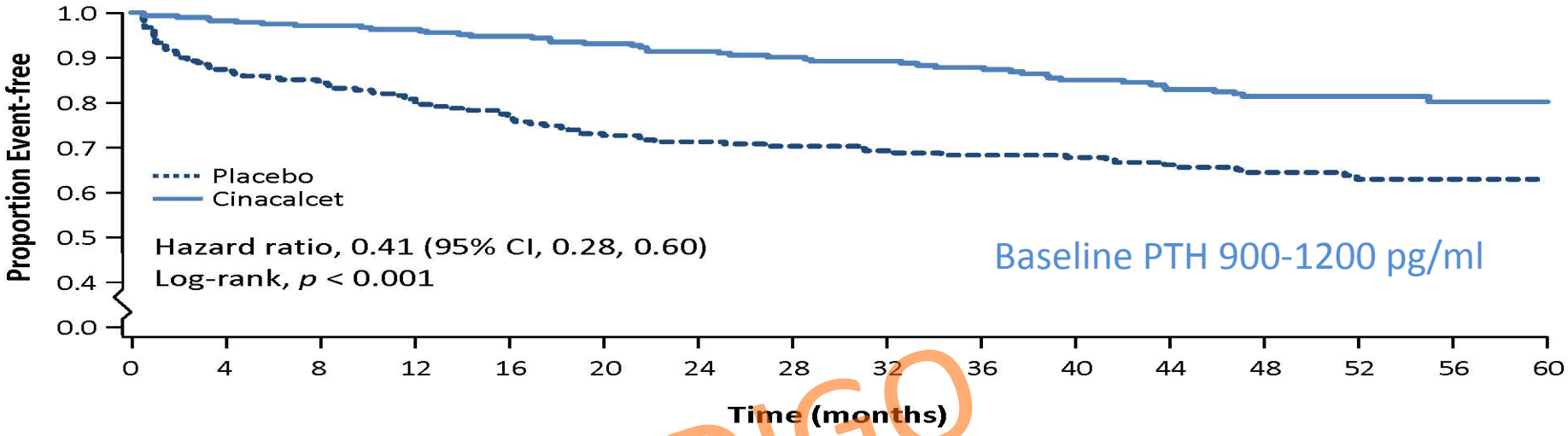


Baseline PTH 300-600 pg/ml

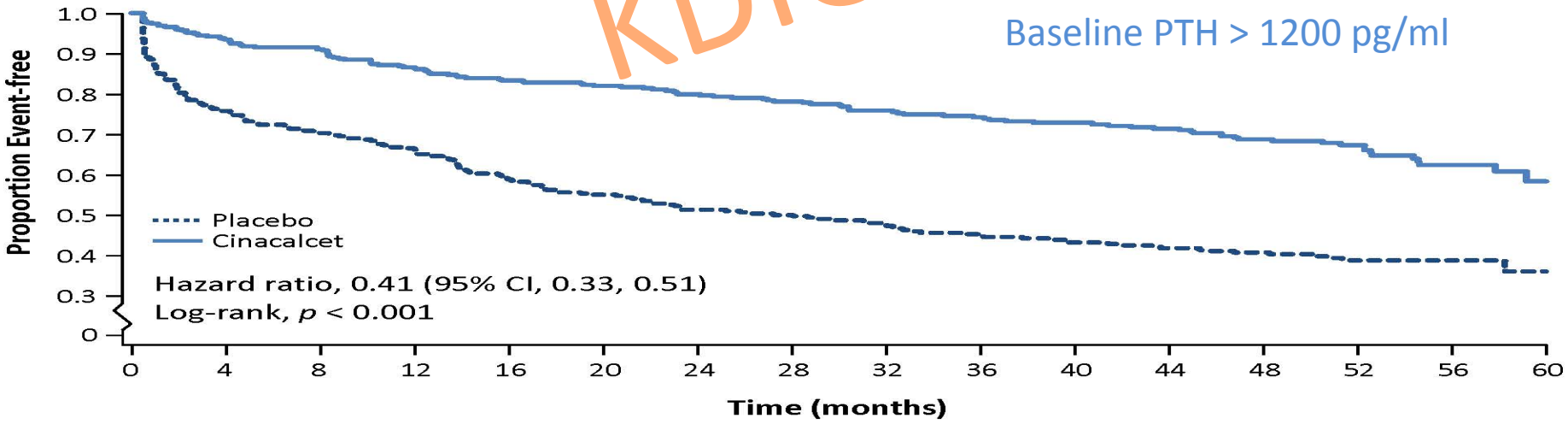


Baseline PTH 600-900 pg/ml

Development of Severe Unremitting HPT



Baseline PTH 900-1200 pg/ml



Baseline PTH > 1200 pg/ml

Calcific uremic arteriolopathy while on cinacalcet

	Events N	%	HR	95% CI	P
Placebo 1923	18	0.94			
Cinacalcet 1938	6	0.31	0.31	0.13-0.79	0.014

Cinacalcet is not licensed for the treatment of CUA

Floege et al, CJASN, 2015

MV model of calcific uremic arteriolopathy in EVOLVE

	HR	95% - CI
Cinacalcet v placebo	0.25	0.10 - 0.67
Male Sex	0.33	0.14 - 0.75
BMI (per kg/m²)	1.09	1.05 - 1.13
Diastolic BP (per 10mmHg)	1.50	1.19 - 1.90
Hx of parathyroidectomy	5.79	1.79 - 1.87
Baseline Tobacco use		
Current	1.79	0.54 - 5.89
Former	3.04	1.19 - 7.74

Floege et al, CJASN, 2015

Vitamin K antagonists and calcific uremic arteriolopathy

CUA	11/24 (46%)
Non-CUA at 1 year	196/3837 (5.1%)

Floege et al, CJASN, 2015

Effect of Cinacalcet on fracture events: pre-specified secondary endpoint unadjusted ITT analysis

	N	%	HR	95% CI
Placebo 1935	255	13.2		
Cinacalcet 1948	238	12.2	0.89	0.75-1.07

Moe et al, JASN, 2014

Effect of Cinacalcet on fracture events

Model	HR	95% CI
Adjusted ITT	0.84	0.69 – 1.01
Lag Censoring (>6 months)	0.72	0.58 – 0.90
Censoring at co-interventions that reduce PTH	0.71	0.58 - 0.87
Adjusted ITT in <65 yrs	0.92	0.73 - 1.16
Adjusted ITT in ≥ 65 yrs	0.69	0.49 - 0.95
RX by age interaction P = 0.06		

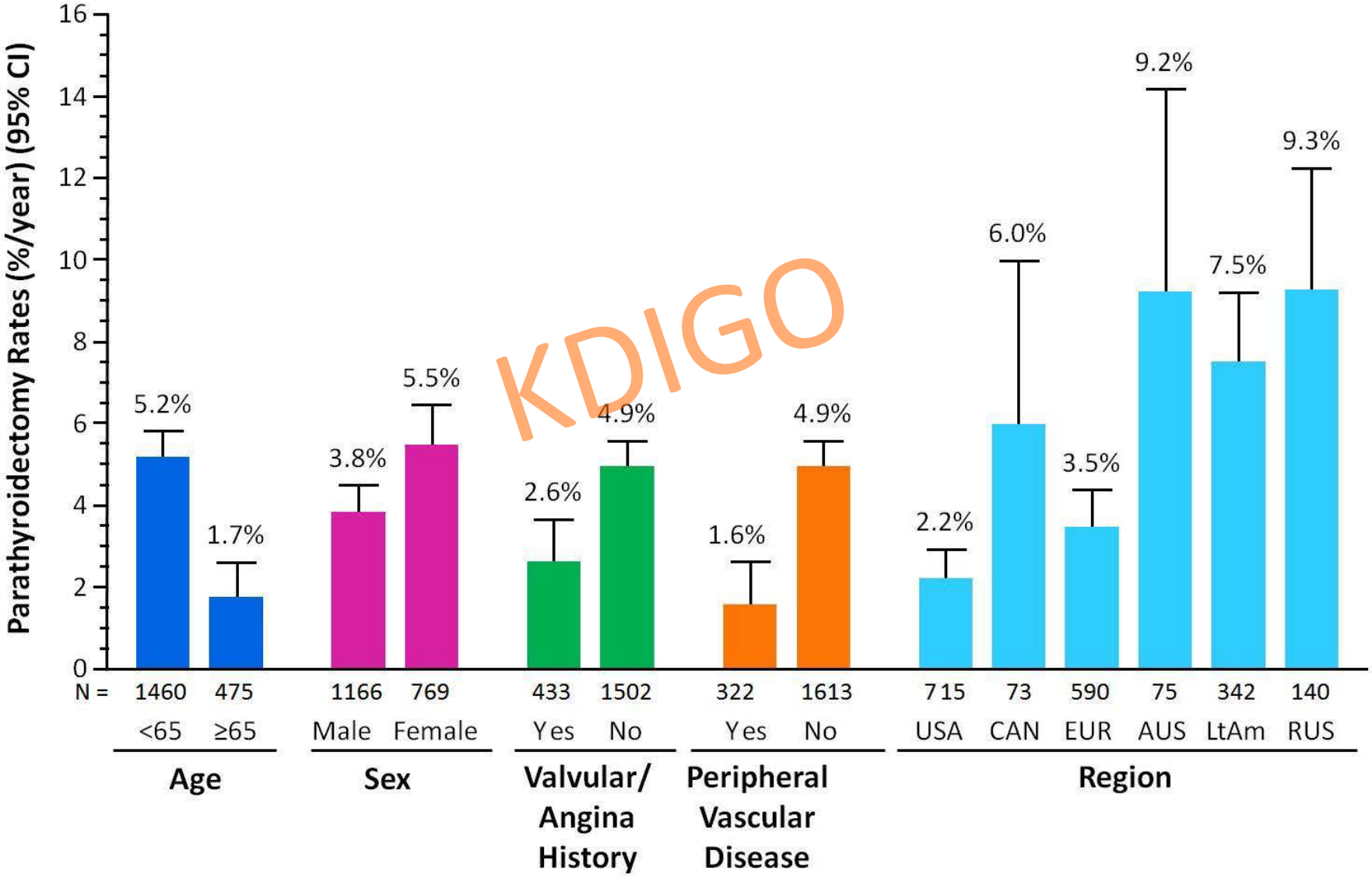
Moe et al, JASN, 2014

Summary of Adverse Events

- Exposure-adjusted rates (per 100 patient-years), cinacalcet v. placebo
  - Serious AE [53.3 v. 56.9]
  - All AE [273.2 v. 217.8]*
  - Hypocalcemia [6.7 v. 0.9]*
  - Nausea [18.3 v. 9.1]*
  - Vomiting [15.4 v. 8.0]*
  - Neoplastic events [2.9 v. 2.5]
  - Seizure [1.2 v. 0.8]
- 7-fold increase in hypocalcemia, 2-fold increase in nausea/ vomiting

*P < 0.001

Annualized Parathroidectomy Rates in the Placebo Arm by Subgroup



Biochemical Markers of CKD–BMD, Within 12 Weeks Prior to Clinical Events Associated With HPT, in Patients Randomized to Placebo

Markers, Median (P10, P90)	Commercial Cinacalcet	Parathyroidectomy	Severe Unremitting HPT
PTH (pg/mL)	1108 (455, 2310)	1872 (760, 3706)	1510 (810, 2991)
Corrected Serum Calcium (mg/dL)	10.0 (8.9, 10.8)	10.3 (9.3, 11.4)	10.4 (9.4, 11.3)
Serum Phosphorus (mg/dL)	5.9 (4.0, 8.1)	6.3 (3.9, 8.8)	6.1 (4.3, 8.5)

Parfrey et al. JCEM, 2013.

Conclusions

- Severe, unremitting HPT develops frequently in patients on HD, despite the use of conventional therapy with vitamin D sterols and phosphate binders
- Clinical outcome data on the use of phosphate binders and vitamin D is limited
- Treatment with cinacalcet significantly reduces the occurrence of severe unremitting HPT
- Cinacalcet likely reduces cardiovascular events
- Any potential benefits of cinacalcet must be balanced against risks
- PTX is used in younger patients, those with less co-morbidity, with high levels of PTH, and the rate varies by region