

The Ratio of Administered Paricalcitol Dose to Serum PTH Level Is Associated with Survival in Maintenance Hemodialysis Patients

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Background

- Vitamin D receptor activators (VDRA) including *paricalcitol* are associated with greater survival in maintenance hemodialysis (MHD) patients.
- However, patients with higher serum PTH, indicative of a more severe secondary hyperparathyroidism and higher death risk, are usually given higher VDRA doses.
- This can lead to **bias by medical indication** in observational studies.

Hypothesis

- We hypothesized that the **ratio** of administered **paricalcitol dose to PTH level** can disclose the underlying dose-survival association with less bias.
- Working Concepts:
 - Relationship between ratio of administered paricalcitol/PTH level (**paricalcitol dose index**) and survival will allow investigation of survival benefit with less confounding by disease severity
 - Paricalcitol index represents paricalcitol dose adjusted by SHPT severity

Results

- Characteristics of 36,970 MHD patients:
 - 60.8 +/- 15.4 years old
 - 47% women
 - 42% blacks
 - 34% diabetics
 - 12% incident (dialysis vintage < 6 mo)
- The paricalcitol (mcg/week) to PTH (pg/ml) ratio [x1,000] was divided into 4 groups:
 - Zero (reference group); 1 to 30; 30 to 60; and >=60 (mcg/wk) / (pg/mL) x 1000
 - Higher paricalcitol dose index was incrementally associated with greater survival.**

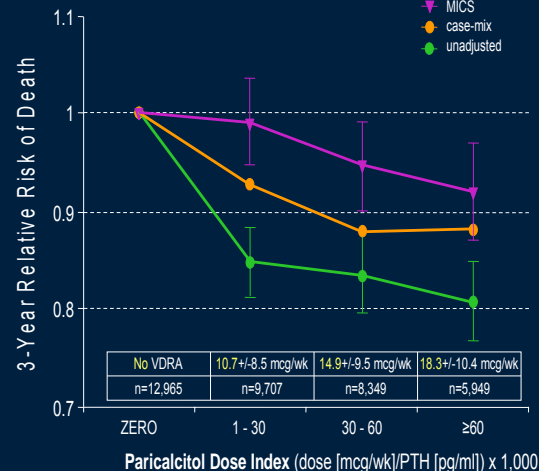
	Paricalcitol to iPTH ratio: (mcg/wk) / (pg/mL) x 1000			
Paricalcitol Index	ZERO	1 – 30	30 – 60	>= 60
Number of Patients	n = 12,965	n = 9,707	n = 8,349	n = 5,949
Paricalcitol Dose mcg/wk	No VDRA	10.7 +/- 8.5	14.9 +/- 9.5	18.3 +/- 10.4

Methods

- We examined survival of MHD patients in a 3-year national cohort (7/2001-6/2004)
- Outcome measure: All-Cause Mortality
- Predicting Variable: Paricalcitol Index, i.e., administered paricalcitol dose during the first 3 months of the cohort divided by the averaged serum intact PTH over the same period
- Study Population: 36,970 MHD patients from all DaVita dialysis clinics across the nation.
- Analytical Method: Cox survival modeling
- The death hazard ratio (and 95% CI) of the paricalcitol/PTH groups were calculated at 3 levels of multivariate adjustments:

- Unadjusted**
- Case-mix adjusted:** Demographics and comorbidity (age, gender, race/ethnicity, diabetes, vintage, insurance, marital status) and dialysis dose (Kt/V)
- Malnutrition-inflammation complex syndrome (MICS) adjusted:** Protein intake (nPNA or nPCR), administered EPO dose, serum albumin, creatinine, phosphorus, calcium, ferritin, TIBC, hemoglobin, WBC, and lymphocyte%

Association between Paricalcitol Dose Index and Survival



Conclusions

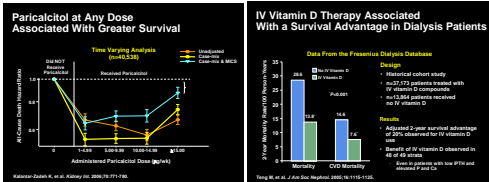
The observed dose-response phenomenon may indicate that higher weekly paricalcitol dose per each pg/ml of intact PTH has incremental association with greater survival in MHD patients.

These results may indicate a dose-related survival benefit with paricalcitol treatment that appears independent of SHPT severity..

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Study	Number of patients	Examined treatment	Results	Comments
Shoji et al.	242	oral alfalcidol vs. no treatment	Lower cardiovascular mortality with alfalcidol treatment.	Prevalent HD patients from Japan; all cause mortality similar in the two groups.
Teng et al.	51,037	any VDRA vs. no treatment	20% lower all-cause mortality in the vitamin D group.	Prevalent HD patients from a single for-profit dialysis chain; benefit present in 48 of 49 examined subgroups.
Young et al. [Abstract]	29,582	any VDRA vs. no treatment	No difference in all-cause mortality in fixed-effect model, 9% lower mortality in time-dependent model.	Prevalent HD patients from DOPPS study, data only published in abstract format.
Melamed et al.	1,007	calcitriol vs. no treatment	Lower all-cause mortality associated with calcitriol use.	Incident HD and PD patients from CHOICE study.
Kalantar-Zadeh et al. and Lee et al.	58,058	paricalcitol vs. no treatment	Lower all-cause mortality associated with paricalcitol use in time-dependent models.	Prevalent HD patients from a single for-profit dialysis chain. Benefit present in all examined subgroups.
Naves et al. [Abstract]	16,004	oral calcitriol vs. no treatment	Lower all-cause, CV, infectious and cancer-related mortality with calcitriol.	Prevalent HD patients from six Latin American countries.
Tentori et al.	7,731	any VDRA vs. no treatment	Lower all-cause mortality with activated vitamin D.	Prevalent HD patients from a single non-profit dialysis chain.
Kovessy et al.	520	calcitriol vs. no treatment	Lower all-cause mortality with calcitriol.	CKD stage 2-5, not yet on dialysis. Also showed trend toward lower ESRD incidence with calcitriol.