

Addition of Sevelamer and Mortality: The Worldwide DOPPS

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Background / Objective

Background

- Prior studies have shown that sevelamer attenuates progression of arterial calcification and may reduce the risk of death in a head-to-head comparison with calcium-based phosphate binders (PB)
- In the real world, however, sevelamer is often used as add-on therapy for hemodialysis (HD) patients already treated with Ca-based PB when dose escalation of the binder is limited to avoid hypercalcemia

Objective

- To test whether the addition of sevelamer to Ca-based PB therapy leads to improved survival

Methods

Study Population

- N=12,564 patients from 12 countries in DOPPS phases 3-4 (2005-2011)
- Patients who were prescribed a Ca-based PB at study enrollment or who initiated a Ca-based PB after enrollment, and who were not already prescribed sevelamer

Analysis

- Sequential stratification method to identify as-yet-untreated (with sevelamer) patients who were appropriate comparators to the newly treated patients based on their risk of death
- We computed a time-updated prognostic score of mortality from pre-treatment values of age, sex, vintage, BMI, Kt/V, 13 comorbidities, albumin, hemoglobin, pre-dialysis BUN, creatinine, Ca, phosphorus, intact PTH, total cholesterol, and use of the following meds: ESA, IV and oral vitamin D, Ca carbonate, lanthanum carbonate, CCB, and ACEI/ARB
- We matched 2501 treated patients with all as-yet-untreated patients (one-to-many matching) with a similar prognostic score at the same time interval and within the same country and phase, then assessed the association with mortality using Cox regression stratified by each set of matched patients

Results

Figure 1: Change in lab values in patients receiving sevelamer

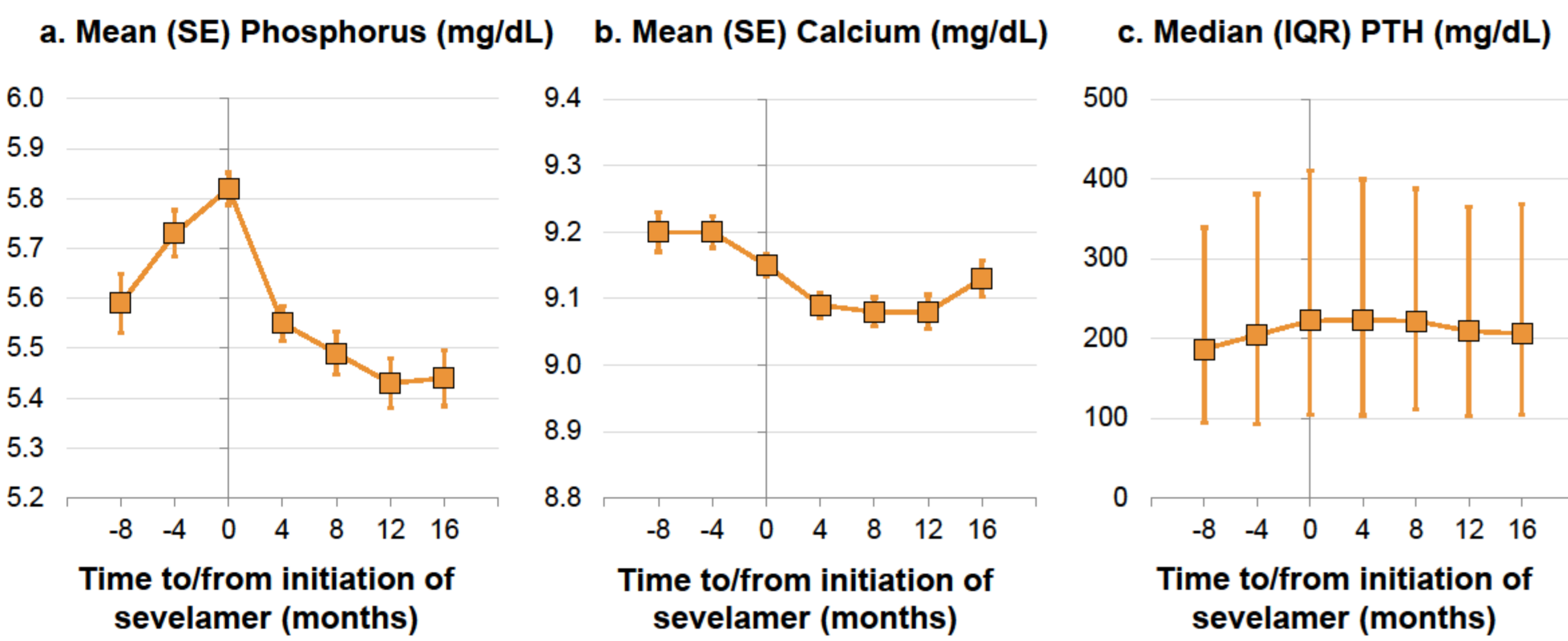
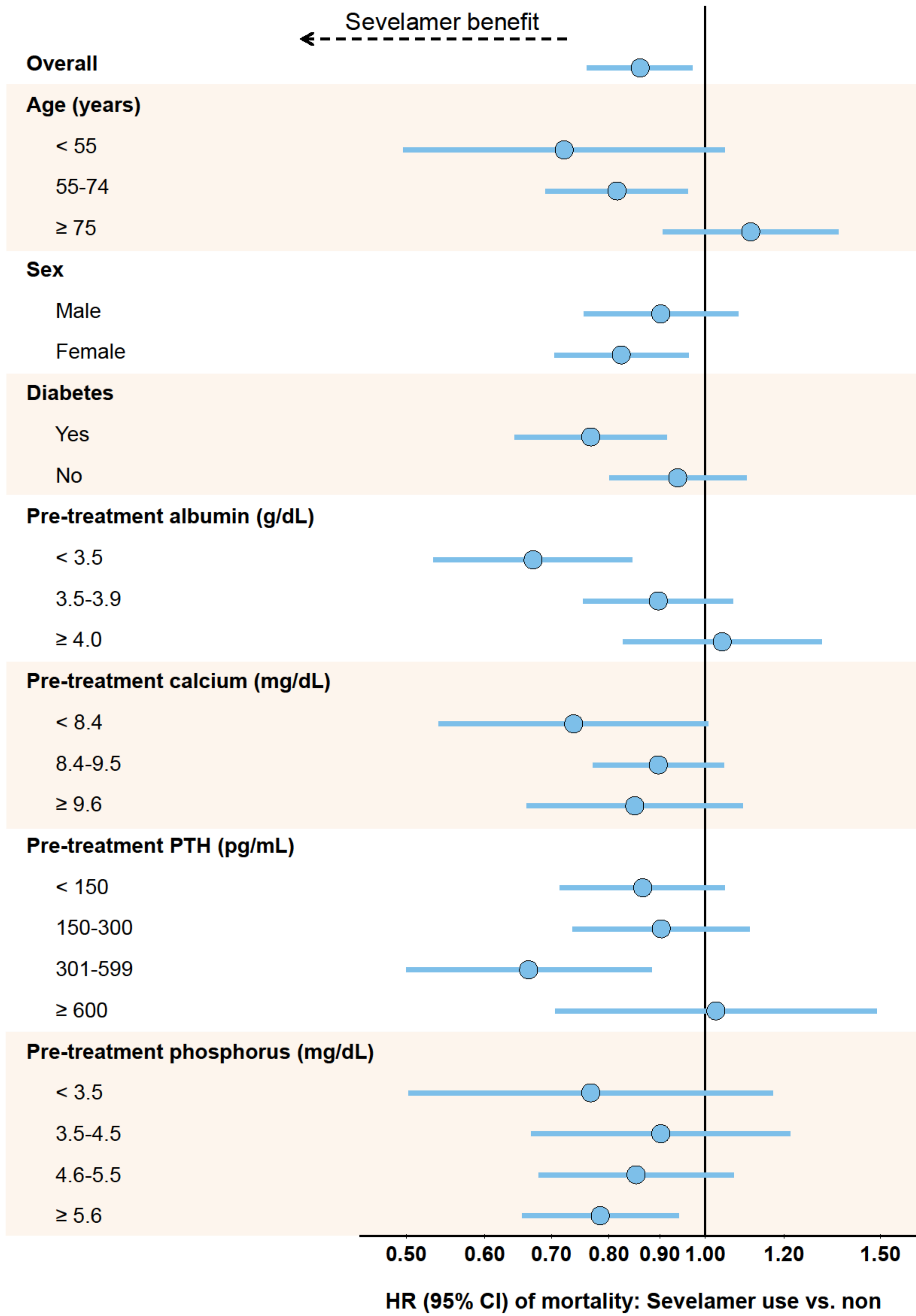


Table. Patient characteristics in the prognostic score-matched cohort comparing sevelamer-treated patients with those as-yet-untreated

Characteristic	Control strata N strata = 2,501 ^a	Treated patients N patients = 2,501
Age, years	63.8 ± 9.7	61.5 ± 14.0
Male, %	59	58
Time on dialysis, months	44 (30-71)	25 (6-65)
Body mass index, kg/m ²	25.5 ± 3.5	26.1 ± 6.3
Single-pool Kt/V	1.5 ± 0.2	1.4 ± 0.3
Comorbidities, %		
Coronary heart disease	43	44
Cancer	13	12
Other cardiovascular disease	31	31
Cerebrovascular disease	16	14
Congest heart failure	31	34
Diabetes	43	45
GI bleeding	4	4
Hypertension	84	85
Lung disease	11	12
Neurologic disease	10	8
Psychiatric disorder	13	13
Peripheral vascular disease	24	25
Recurrent cellulitis/gangrene	7	9
Albumin, g/dl	3.8 ± 0.3	3.8 ± 0.4
Hemoglobin, g/l	11.4 ± 0.8	11.3 ± 1.4
BUN (pre-dialysis), mg/dl	60.9 ± 9.2	63.5 ± 18.5
Creatinine, mg/dl	8.8 ± 2.2	9.3 ± 2.9
Calcium, mg/dl	9.0 ± 0.4	9.2 ± 0.9
Phosphorus, mg/dl	5.1 ± 0.8	5.8 ± 1.7
Intact PTH, pg/ml	243 (172-324)	217 (105-380)
Total cholesterol, mg/dl	159 ± 23	159 ± 42
ESA	88	88
Active vitamin D derivatives		
Oral	37	34
IV	22	24
Calcium carbonate	63	61
Lanthanum carbonate	6	6
Calcium channel blocker	38	40
ACEI/ARB	41	44

^aN control patients per strata ranged from 1-91 for a total of 9594 distinct patients; note that patients could contribute to more than 1 stratum. Each stratum was assigned equal weight for calculating means.

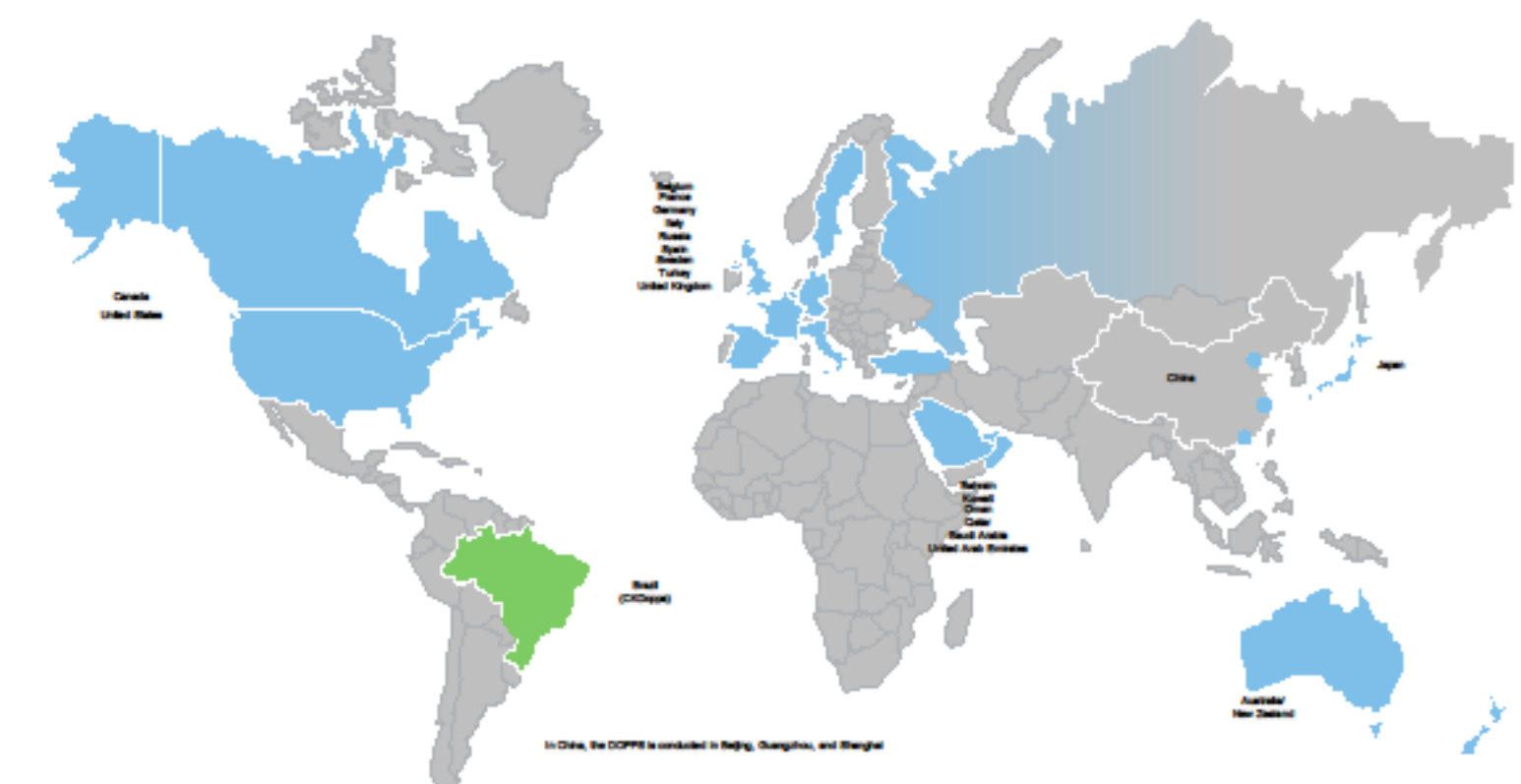
Figure 2: Sevelamer addition vs. as-yet-untreated with sevelamer



Summary / Conclusions

- Serum phosphorus levels decreased during the first 8 months of sevelamer treatment from a mean of 5.8 to 5.5 mg/dL; there were no clinically meaningful changes in serum levels of calcium or PTH during the study.
- Addition of sevelamer was associated with decreased mortality among patients treated with Ca-based phosphate binders.
- The survival benefit of sevelamer was more pronounced among younger patients and those with lower serum albumin; there was no evidence of interaction between sevelamer use and serum phosphorus levels.
- Additive therapy with sevelamer for treating hyperphosphatemia may improve survival in maintenance HD patients.

DOPPS The Dialysis Outcomes and Practice Patterns Study



DOPPS is an international prospective cohort study of hemodialysis treatment and patient outcomes:

- DOPPS 1 (1996-2001): 308 dialysis facilities and 17,034 patients in 7 countries (France, Germany, Italy, Japan, Spain, UK, and US)
- DOPPS 2 (2002-2004), DOPPS 3 (2005-2008), DOPPS 4 (2009-2011): ≥300 facilities and 11,000 - 13,000 patients per study phase in 12 countries (DOPPS 1 countries + Australia, Belgium, Canada, New Zealand, and Sweden)
- DOPPS 5 (2012-2015): ~500 facilities and 17,000 patients in nine new countries (Bahrain, China, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates, Russia, and Turkey) in addition to the 12 countries represented in DOPPS 4
- The DOPPS Program is supported by research grants from Amgen (founding sponsor, since 1996), Kyowa HAKKO Kirin (since 1999, in Japan), AbbVie Inc. (since 2009), Sanofi Renal (since 2009), Baxter Healthcare (since 2011), and Vifor Fresenius Medical Care Renal Pharma, Ltd (since 2011). Additional support is provided for specific projects and/or countries by a number of organizations. Additional information and slides available at www.dopps.org.
- Support for the DOPPS Program is provided without restrictions on publications.
- The DOPPS is coordinated by Arbor Research Collaborative for Health, Ann Arbor, MI USA.

Abstract #: MP348

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