

## **Supplementary materials**

# **CLINICAL EFFECTIVENESS OF PHOSPHATE BINDERS FOR TREATING HYPERPHOSPHATEMIA IN END-STAGE RENAL DISEASE PATIENTS: A MULTICENTER REAL-WORLD STUDY**

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**Table S1.** List of study covariates

| Demographic variables                                                                              | Variable name | Type/format                                                                                    |
|----------------------------------------------------------------------------------------------------|---------------|------------------------------------------------------------------------------------------------|
| Age (year)                                                                                         | age           | number                                                                                         |
| Sex                                                                                                | sex           | male/female                                                                                    |
| Race                                                                                               | race          | text                                                                                           |
| Province                                                                                           | province      | text                                                                                           |
| Education (highest)                                                                                | education     | text                                                                                           |
| Marital status                                                                                     | mstatus       | text                                                                                           |
| Height (cm)                                                                                        | ht            | number                                                                                         |
| Body weight (kg)                                                                                   | Bw            | number                                                                                         |
| Boda mass index (BMI) (kg/m <sup>2</sup> )                                                         | bmi           | number                                                                                         |
| Reimbursement type                                                                                 | reimburse     | text                                                                                           |
| Renal replacement therapy (RRT) initiation date                                                    | drrtini       | DDMMYYYY                                                                                       |
| RRT Access date                                                                                    | daccess       | DDMMYYYY                                                                                       |
| Type of RRT                                                                                        | modeRRT       | No(0)/<br>Peritoneal dialysis (PD)(1)/<br>Hemodialysis (HD) (2)/<br>Kidney transplant (KT) (3) |
| Diagnostic variables                                                                               | ICD-9         | ICD-10                                                                                         |
| <i>ICD of target ESRD patients</i>                                                                 |               |                                                                                                |
| End stage renal disease                                                                            | -             | N180                                                                                           |
| Chronic kidney disease, stage 5                                                                    | -             | N185                                                                                           |
| End stage renal disease (require dialysis)                                                         | -             | N186                                                                                           |
| Chronic kidney disease, unspecified                                                                | -             | N189                                                                                           |
| Encounter for fitting and adjustment of extracorporeal dialysis catheter                           | -             | Z4901                                                                                          |
| Encounter for fitting and adjustment of peritoneal dialysis catheter                               | -             | Z4902                                                                                          |
| Breakdown (mechanical) of intraperitoneal dialysis catheter                                        | -             | T85611                                                                                         |
| Displacement of intraperitoneal dialysis catheter                                                  | -             | T85621                                                                                         |
| Leakage of intraperitoneal dialysis catheter                                                       | -             | T85631                                                                                         |
| Other mechanical complication of intraperitoneal dialysis catheter                                 | -             | T85691                                                                                         |
| Infection and inflammatory reaction due to peritoneal dialysis catheter                            | -             | T8571                                                                                          |
| Arteriovenous fistula, acquired                                                                    | -             | I770                                                                                           |
| Mechanical complication of vascular dialysis catheter                                              | -             | T824                                                                                           |
| Mechanical complication of other cardiac and vascular devices and implants                         | -             | T825                                                                                           |
| Infection and inflammatory reaction due to other cardiac and vascular devices, implants and grafts | -             | T827                                                                                           |

| <b>Diagnostic variables</b>                                                                   | <b>ICD-9</b>                                                                                                                                                                            | <b>ICD-10</b>                                                                                     |
|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Other specified complications of cardiac and vascular prosthetic devices, implants and grafts | -                                                                                                                                                                                       | T828                                                                                              |
| Unspecified complication of cardiac and vascular prosthetic device, implant and graft         | -                                                                                                                                                                                       | T829                                                                                              |
| Kidney Transplant status                                                                      | -                                                                                                                                                                                       | Z940                                                                                              |
| Venous catheterization for renal dialysis                                                     | 3895                                                                                                                                                                                    | -                                                                                                 |
| Arteriovenostomy for renal dialysis                                                           | 3927                                                                                                                                                                                    | -                                                                                                 |
| Revision of arteriovenous shunt for renal dialysis                                            | 3942                                                                                                                                                                                    | -                                                                                                 |
| Removal of arteriovenous shunt for renal dialysis                                             | 3943                                                                                                                                                                                    | -                                                                                                 |
| Hemodialysis                                                                                  | 3995                                                                                                                                                                                    | -                                                                                                 |
| Creation of cutaneoperitoneal fistula                                                         | 5493                                                                                                                                                                                    | -                                                                                                 |
| Peritoneal dialysis                                                                           | 5498                                                                                                                                                                                    | -                                                                                                 |
| Kidney transplantation                                                                        | 5569                                                                                                                                                                                    | -                                                                                                 |
| <i>ICD of comorbidities</i>                                                                   |                                                                                                                                                                                         |                                                                                                   |
| Diabetes (DM)                                                                                 | -                                                                                                                                                                                       | E10 - E149                                                                                        |
| Hypertension (HT)                                                                             | -                                                                                                                                                                                       | I10 - I159                                                                                        |
| Dyslipidemia                                                                                  | -                                                                                                                                                                                       | E780 - E789                                                                                       |
| Obesity                                                                                       | -                                                                                                                                                                                       | E660 - E669                                                                                       |
| Heart diseases                                                                                | 3601-3607, 3610-3617, 3619, 4109                                                                                                                                                        | I20, I200 - I259, I42, I420- I509                                                                 |
| Cerebrovascular accident (CVA)/stroke                                                         | -                                                                                                                                                                                       | I60 - I698                                                                                        |
| Peripheral vascular disease (PVD)                                                             | -                                                                                                                                                                                       | I70 - I798                                                                                        |
| Osteoporosis                                                                                  | -                                                                                                                                                                                       | M80 - M85                                                                                         |
| Fractures                                                                                     | 7812-7815, 7852-7855, 7901-7905, 7911-7915, 7921-7925, 7932-7935, 7941,7942, 7945, 7951, 7952, 7955, 7973, 7975, 7976, 7983, 7985, 7986, 8153, 8155, 8171, 8172, 8174, 8175, 8151, 8152 | S12-S1291, S22-S2291, S32-S3281, S42-S4291, S52-S5291, S62-S6281, S72-S7291, S82-S8291, S92-S9291 |
| Liver disease (cirrhosis, chronic hepatitis B, hepatitis C)                                   | -                                                                                                                                                                                       | B15 - B19, K70 - K77                                                                              |
| Chronic pulmonary disease                                                                     | -                                                                                                                                                                                       | J44 - J449, J45 - J46                                                                             |
| Any Cancer                                                                                    | -                                                                                                                                                                                       | C00 - C99                                                                                         |
| Acquired Immunodeficiency Syndrome (AIDS)                                                     | -                                                                                                                                                                                       | B20 - B24                                                                                         |
| Systemic Lupus Erythematosus (SLE)                                                            | -                                                                                                                                                                                       | M32                                                                                               |
| Gout                                                                                          | -                                                                                                                                                                                       | M10                                                                                               |
| Stone                                                                                         | -                                                                                                                                                                                       | N20 - N23                                                                                         |
| Dementia                                                                                      | -                                                                                                                                                                                       | F00 - F03                                                                                         |
| Any Handicapped                                                                               | -                                                                                                                                                                                       | G80 - G83                                                                                         |
| Pregnancy                                                                                     | -                                                                                                                                                                                       | O00 - O99, Z33                                                                                    |

|                                                   |                                                                                       |                                                                                               |
|---------------------------------------------------|---------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| Sleep disorder                                    | -                                                                                     | G47, F51                                                                                      |
| Periodontal disorder                              | -                                                                                     | K04 - K05                                                                                     |
| GI disorders                                      | -                                                                                     | K20-K31                                                                                       |
| <b>Standard Medication group</b>                  |                                                                                       |                                                                                               |
| Phosphodiesterase inhibitors                      | Angiotensin-converting enzyme inhibitors (ACEIs)/Aldosterone receptor blockers (ARBs) | Sodium-Glucose Co-Transporter 2 (SGLT2) inhibitors, Dipeptidyl peptidase-4 (DPP-4) inhibitors |
| Glycoprotein IIB/IIIA inhibitors                  | P2Y12 receptor blockers                                                               | Thiazolidinedione (TZD)                                                                       |
| Calcium-channel blockers                          | Beta-adrenergic antagonists                                                           | Sulfonylureas (SU)                                                                            |
| Diuretics, Erythropoietin Stimulating Agent (ESA) | Alpha-1 receptor antagonist                                                           | Glucagon-like peptide 1 (GLP-1) receptor agonists                                             |
| Vasodilators                                      | Uric lowering agents, Anti-dyslipidemia agents                                        | Metformin, insulin, and other antidiabetic agents                                             |
| Anticoagulants                                    | Cyclo-oxygenase inhibitors (COX) inhibitors                                           | Bisphosphonates, Vitamin D                                                                    |
| Antiarrhythmic agents                             | Antiparathyroid agents                                                                | Heparins                                                                                      |
| <b>Laboratory variables</b>                       | <b>Unit</b>                                                                           | <b>Lab code</b>                                                                               |
| Serum creatinine (sCr)                            | mg/dL                                                                                 | 200058                                                                                        |
| estimated Glomerular Filtration Rate (eGFR)       | ml/min                                                                                | 200718                                                                                        |
| Albumin                                           | g/dL                                                                                  | 200008                                                                                        |
| Phosphorus                                        | mg/dL                                                                                 | 200090                                                                                        |
| serum intact parathyroid hormone (iPTH)           | pg/dL                                                                                 | 200131                                                                                        |
| Calcium (corrected)                               | mg/dL                                                                                 | calcium + 0.8 (4.0 - albumin)                                                                 |
| Hemoglobin (Hb)                                   | g/dL                                                                                  | 250001                                                                                        |
| Hematocrit (Hct)                                  | %                                                                                     | 250002, 250003                                                                                |
| Sodium                                            | mEq/L                                                                                 | 200140                                                                                        |
| Potassium                                         | mEq/L                                                                                 | 200122                                                                                        |
| Chloride                                          | mEq/L                                                                                 | 200039                                                                                        |
| Bicarbonate (HCO <sub>3</sub> )                   | mEq/L                                                                                 | 200037                                                                                        |
| Fasting Blood Sugar (FBS)                         | mg/dL                                                                                 | 200076                                                                                        |
| HbA1C                                             | mg%                                                                                   | 100067                                                                                        |
| Cholesterol                                       | mg/dL                                                                                 | 200047                                                                                        |
| Triglyceride                                      | mg/dL                                                                                 | 200157                                                                                        |
| Low-Density Lipoprotein (LDL)                     | mg/dL                                                                                 | 200106                                                                                        |
| High-Density Lipoprotein (HDL)                    | mg/dL                                                                                 | 200085                                                                                        |
| Uric acid                                         | mg/dL                                                                                 | 200162                                                                                        |
| Serum Iron                                        | ug/dL                                                                                 | 200134                                                                                        |
| Ferritin                                          | ng/dL                                                                                 | 100072                                                                                        |
| Total iron-binding capacity (TIBC)                | Ug/dL                                                                                 | 100065                                                                                        |
| Transferrin saturation (TSAT)                     | %                                                                                     | iron/transferrin * 71.24                                                                      |
| Hepatitis B surface antigen (HbsAg)               | -                                                                                     | 100027                                                                                        |
| Hepatitis B surface antibody (HbsAb)              | -                                                                                     | 100028                                                                                        |
| Antibody to hepatitis C virus (AntiHCV)           | -                                                                                     | 100048                                                                                        |
| Antibody to HIV virus (AntiHIV)                   | -                                                                                     | 100034, 100035, 100036                                                                        |

**Table S2. Number of target patients by treatment approach**

| Approaches               | Treatments         | Number of patients (%) |               |                |
|--------------------------|--------------------|------------------------|---------------|----------------|
|                          |                    | OS                     | CVD           | bone disorders |
| ITT                      | No-PBs             | 3,736 (46.67)          | 3,233 (51.76) | 3,658 (48.96)  |
|                          | CBPBs              | 4,071 (50.86)          | 2,854 (45.69) | 3,623 (48.49)  |
|                          | NCBPBs             | 118 (1.47)             | 90 (1.53)     | 113 (1.51)     |
|                          | Aluminum hydroxide | 80 (1.00)              | 69 (1.10)     | 78 (1.04)      |
|                          | <b>Total</b>       | 8,005 (100)            | 6,246 (100)   | 7,472 (100)    |
| PPA                      | No-PBs             | 3,736 (53.52)          | 3,233 (59.03) | 3,658 (55.95)  |
|                          | CBPBs              | 3,184 (45.61)          | 2,193 (40.04) | 2,821 (43.15)  |
|                          | NCBPBs             | 54 (0.77)              | 46 (0.84)     | 52 (0.80)      |
|                          | Aluminum hydroxide | 7 (0.10)               | 5 (0.09)      | 7 (0.11)       |
|                          | <b>Total</b>       | 6,981 (100)            | 5,477 (100)   | 6,538 (100)    |
| Actual treatment-pattern | No-PBs             | 3,736 (48.63)          | 3,233 (53.82) | 3,658 (51.04)  |
|                          | CBPBs-CBPBs        | 3,361 (43.75)          | 2,449 (40.77) | 3,018 (42.11)  |
|                          | CBPBs-NCBPBs       | 487 (6.34)             | 240 (4.00)    | 400 (5.58)     |
|                          | CBPBs-aluminum     | 98 (1.28)              | 85 (1.42)     | 91 (1.27)      |
|                          | <b>Total</b>       | 7,682 (100)            | 6,007 (100)   | 7,167 (100)    |

Abbreviations: CBPBs; Calcium-based phosphate binders, CVD; cardiovascular disease, ITT; Intention to treat, OS; overall survival outcome, PBs; Phosphate binders, PPA; Per-protocol analysis,

**Table S3.** Baseline characteristics of patients included in the PPA by treatments approach

| Outcomes | Variables                               | N     | % Missing | Treatment group |               |               |                    | Total         | p-value |
|----------|-----------------------------------------|-------|-----------|-----------------|---------------|---------------|--------------------|---------------|---------|
|          |                                         |       |           | No-PBs          | CBPBs         | NCBPBs        | Aluminum hydroxide |               |         |
| OS       | <b>Total number of patients, n (%)</b>  |       |           | 3,736 (53.5)    | 3,184 (45.6)  | 54 (0.8)      | 7 (0.1)            | 6,981 (100)   |         |
|          | <b>Hospital, n(%)</b>                   | 6,981 | 0         |                 |               |               |                    |               | <0.001  |
|          | Ramathibodi Hospital                    |       |           | 3,283 (87.87)   | 2,192 (68.84) | 37 (68.52)    | 4 (57.14)          | 5,516 (79.01) |         |
|          | Bhumibol Hospital                       |       |           | 453 (12.13)     | 992 (31.16)   | 17 (31.48)    | 3 (42.86)          | 1,465 (20.99) |         |
|          | <b>age (years), mean(SD)</b>            | 6,981 | 0         | 48.50 (17.08)   | 62.02 (16.09) | 63.18 (14.64) | 53.11 (16.60)      | 54.78 (17.93) | <0.001  |
|          | <b>Female, n(%)</b>                     | 6,981 | 0         | 1,564 (41.86)   | 1,696 (53.27) | 23 (42.59)    | 4 (57.14)          | 3,287 (47.08) | <0.001  |
|          | <b>Reimbursement, n(%)</b>              | 6,981 | 0         |                 |               |               |                    |               | <0.001  |
|          | non-CSMBS                               |       |           | 2,723 (72.89)   | 1,752 (55.03) | 12 (22.22)    | 6 (85.71)          | 4,493 (64.36) |         |
|          | CSMBS                                   |       |           | 1,013 (27.11)   | 1,432 (44.97) | 42 (77.78)    | 1 (14.29)          | 2,488 (35.64) |         |
|          | <b>BMI (kg/m<sup>2</sup>), mean(SD)</b> | 3,053 | 56        | 24.15 (4.72)    | 24.95 (5.34)  | 24.24 (5.45)  | 23.35 (2.19)       | 24.42 (4.96)  | 0.001   |
|          | <b>Marital status, n(%)</b>             | 6,981 | 0         |                 |               |               |                    |               | <0.001  |
|          | Single                                  |       |           | 1,190 (31.85)   | 705 (22.14)   | 9 (16.67)     | 4 (57.14)          | 1,908 (27.33) |         |
|          | Married                                 |       |           | 2,178 (58.30)   | 2,012 (63.19) | 37 (68.52)    | 3 (42.86)          | 4,230 (60.59) |         |
|          | Divorced/widowed                        |       |           | 364 (9.74)      | 456 (14.32)   | 8 (14.81)     | 0 (0.00)           | 828 (11.86)   |         |
|          | Priest                                  |       |           | 0 (0.00)        | 2 (0.06)      | 0 (0.00)      | 0 (0.00)           | 2 (0.03)      |         |
|          | Unknown                                 |       |           | 4 (0.11)        | 9 (0.28)      | 0 (0.00)      | 0 (0.00)           | 13 (0.19)     |         |
|          | <b>Education levels, n(%)</b>           | 3,368 | 52        |                 |               |               |                    |               | <0.001  |
|          | Primary level or less                   |       |           | 589 (23.15)     | 256 (32.04)   | 6 (25.00)     | 0 (0.00)           | 851 (25.27)   |         |
|          | Secondary level                         |       |           | 766 (30.11)     | 166 (20.78)   | 3 (12.50)     | 0 (0.00)           | 935 (27.76)   |         |
|          | University level or more                |       |           | 1,189 (46.74)   | 377 (47.18)   | 15 (62.50)    | 1 (100.00)         | 1,582 (46.97) |         |
|          | <b>Renal replacement therapy, n(%)</b>  | 6,981 | 0         |                 |               |               |                    |               | <0.001  |
|          | No RRT                                  |       |           | 2,333 (62.45)   | 2,403 (75.47) | 25 (46.30)    | 2 (28.57)          | 4,763 (68.23) |         |
|          | RRT                                     |       |           | 1,403 (37.55)   | 781 (24.53)   | 29 (53.70)    | 5 (71.43)          | 2,218 (31.77) |         |
|          | <b>Comorbid, n(%)</b>                   |       |           |                 |               |               |                    |               |         |
|          | Hypertension                            | 6,981 | 0         | 1,874 (50.16)   | 3,077 (96.64) | 44 (81.48)    | 7 (100.00)         | 5,002 (71.65) | <0.001  |
|          | Diabetes                                | 6,981 | 0         | 871 (23.31)     | 1,722 (54.08) | 20 (37.04)    | 3 (42.86)          | 2,616 (37.47) | <0.001  |
|          | Dyslipidemia                            | 6,981 | 0         | 965 (25.83)     | 2,240 (70.35) | 32 (59.26)    | 4 (57.14)          | 3,241 (46.43) | <0.001  |

**Table S3.** Baseline characteristics of patients included in the PPA by treatments approach (cont.)

| Outcomes | Variables                        | N     | %<br>Missing | Treatment group         |                         |                         |                         | Total                   | p-value |
|----------|----------------------------------|-------|--------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|          |                                  |       |              | No-PBs                  | CBPBs                   | NCBPBs                  | Aluminum<br>hydroxide   |                         |         |
| OS       | CVD                              | 6,981 | 0            | 503 (13.46)             | 991 (31.12)             | 13 (24.07)              | 2 (28.57)               | 1,504 (21.54)           | <0.001  |
|          | Bone disorder related ESRD       | 6,981 | 0            | 78 (2.09)               | 363 (11.40)             | 2 (3.70)                | 0 (0.00)                | 443 (6.35)              | <0.001  |
|          | Gout                             | 6,981 | 0            | 141 (3.77)              | 243 (7.63)              | 1 (1.85)                | 0 (0.00)                | 385 (5.51)              | <0.001  |
|          | Liver disease                    | 6,981 | 0            | 150 (4.01)              | 204 (6.41)              | 3 (5.56)                | 0 (0.00)                | 357 (5.11)              | <0.001  |
|          | SLE                              | 6,981 | 0            | 50 (1.34)               | 77 (2.42)               | 1 (1.85)                | 0 (0.00)                | 128 (1.83)              | 0.015   |
|          | Cancer                           | 6,981 | 0            | 27 (0.72)               | 36 (1.13)               | 1 (1.85)                | 0 (0.00)                | 64 (0.92)               | 0.217   |
|          | AIDS                             | 6,981 | 0            | 8 (0.21)                | 22 (0.69)               | 1 (1.85)                | 0 (0.00)                | 31 (0.44)               | 0.004   |
|          | GI disorder                      | 6,981 | 0            | 127 (3.40)              | 373 (11.71)             | 5 (9.26)                | 2 (28.57)               | 507 (7.26)              | <0.001  |
|          | Chronic pulmonary disease        | 6,981 | 0            | 55 (1.47)               | 122 (3.83)              | 2 (3.70)                | 0 (0.00)                | 179 (2.56)              | <0.001  |
|          | Tumor lysis syndrome             | 6,981 | 0            | 2 (0.05)                | 0 (0.00)                | 0 (0.00)                | 0 (0.00)                | 2 (0.03)                | 0.784   |
|          | Hypoparathyroidism               | 6,981 | 0            | 0 (0.00)                | 7 (0.22)                | 0 (0.00)                | 0 (0.00)                | 7 (0.10)                | 0.079   |
|          | Secondary hyperparathyroidism    | 6,981 | 0            | 314 (8.40)              | 924 (29.02)             | 32 (59.26)              | 2 (28.57)               | 1,272 (18.22)           | <0.001  |
|          | <b>Laboratory, median (IQR)</b>  |       |              |                         |                         |                         |                         |                         |         |
|          | eGFR, ml/min/1.73 m <sup>2</sup> | 6,963 | 0            | 5.0 (3.8, 8.0)          | 7.8 (4.8, 12.0)         | 5.9 (4.2, 9.4)          | 4.6 (3.4, 11.4)         | 6.0 (4.0, 10.4)         | <0.001  |
|          | Phosphorus, mg/dL                | 6,981 | 0            | 5.6 (5.0, 6.6)          | 5.1 (4.8, 6.2)          | 5.6 (5.0, 6.9)          | 6.2 (5.0, 8.1)          | 5.4 (4.8, 6.6)          | <0.001  |
|          | PTH, pg/dL                       | 3,924 | 44           | 319.6<br>(141.8, 639.2) | 165.8<br>(79.9, 330.5)  | 328.5<br>(150.6, 861.2) | 406.9<br>(44.0, 1304.4) | 237.8<br>(105.8, 499.0) | <0.001  |
|          | Calcium, mg/dL                   | 6,981 | 0            | 9.4 (8.8, 10.0)         | 9.4 (8.8, 9.9)          | 10.0 (9.6, 10.6)        | 10.4 (9.9, 11.8)        | 9.4 (8.8, 10.0)         | <0.001  |
|          | Hemoglobin, g/dL                 | 6,981 | 0            | 10.5 (9.1, 11.9)        | 9.7 (8.4, 11.1)         | 10.8 (9.3, 11.7)        | 9.6 (8.7, 11.5)         | 10.2 (8.8, 11.5)        | <0.001  |
|          | Hematocrit, %                    | 1,896 | 73           | 29.0<br>(25.0, 33.0)    | 28.9<br>(24.7, 33.0)    | 30.6<br>(29.0, 34.7)    | 31.4<br>(17.3, 38.0)    | 29.0<br>(24.9, 33.0)    | 0.246   |
|          | Albumin, g/dL                    | 6,981 | 0            | 3.6 (3.1, 4.0)          | 3.4 (2.8, 3.8)          | 3.6 (3.3, 3.9)          | 3.3 (3.2, 3.4)          | 3.5 (3.0, 3.9)          | <0.001  |
|          | Sodium, mEq/L                    | 6,932 | 1            | 138.0<br>(136.0, 140.0) | 138.0<br>(134.0, 140.0) | 139.0<br>(136.0, 141.0) | 138.0<br>(136.0, 140.0) | 138.0<br>(135.0, 140.0) | <0.001  |
|          | Potassium, mEq/L                 | 3,470 | 50           | 4.6 (4.0, 5.0)          | 4.5 (4.0, 5.0)          | 4.4 (4.0, 5.0)          | 4.4 (3.8, 4.8)          | 4.6 (4.0, 5.0)          | 0.144   |



**Table S3.** Baseline characteristics of patients included in the PPA by treatments approach (cont.)

| Outcomes | Variables            | N     | % Missing | Treatment group         |                         |                         |                         | Total                   | p-value |
|----------|----------------------|-------|-----------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|          |                      |       |           | No-PBs                  | CBPBs                   | NCBPBs                  | Aluminum hydroxide      |                         |         |
| OS       | Chloride, mEq/L      | 6,938 | 1         | 100.0<br>(97.0, 104.0)  | 103.0<br>(99.0, 107.0)  | 100.5<br>(97.0, 104.0)  | 100.0<br>(98.0, 105.0)  | 101.0<br>(98.0, 105.0)  | <0.001  |
|          | Carbondioxide, mEq/L | 6,943 | 1         | 22.8<br>(20.0, 25.5)    | 21.0<br>(18.0, 24.4)    | 21.1<br>(19.0, 24.2)    | 22.0<br>(16.0, 27.5)    | 22.0<br>(19.0, 25.0)    | <0.001  |
|          | Uric, mg/dL          | 6,197 | 11        | 7.0 (5.6, 8.5)          | 7.8 (6.2, 9.4)          | 6.6 (5.3, 8.2)          | 6.7 (6.2, 8.1)          | 7.3 (5.9, 8.9)          | <0.001  |
|          | Glucose, mg/dL       | 3,483 | 50        | 101.0<br>(87.0, 135.0)  | 102.6<br>(88.2, 138.0)  | 99.0<br>(90.0, 138.6)   | 90.0<br>(86.4, 108.0)   | 102.6<br>(88.2, 136.8)  | 0.741   |
|          | HbA1C, mg%           | 2,502 | 64        | 6.3 (5.6, 7.3)          | 6.3 (5.6, 7.3)          | 5.9 (5.4, 6.5)          | 6.6 (4.6, 12.4)         | 6.3 (5.6, 7.3)          | 0.304   |
|          | LDL, mg/dL           | 4,179 | 40        | 101.0<br>(79.0, 128.0)  | 104.0<br>(82.0, 133.0)  | 100.5<br>(83.0, 131.5)  | 135.0<br>(72.0, 217.0)  | 102.8<br>(80.6, 130.0)  | 0.042   |
|          | Cholesterol, mg/dL   | 6,492 | 7         | 179.0<br>(150.0, 215.0) | 181.0<br>(150.0, 217.9) | 157.0<br>(131.0, 204.0) | 194.0<br>(175.0, 281.8) | 180.0<br>(150.0, 216.0) | 0.042   |
|          | Triglyceride, mg/dL  | 6,029 | 14        | 115.5<br>(82.0, 158.0)  | 127.4<br>(92.0, 183.0)  | 107.5<br>(81.0, 159.0)  | 207.0<br>(109.0, 211.6) | 121.2<br>(86.8, 171.0)  | <0.001  |
|          | HDL, mg/dL           | 3,990 | 43        | 45.0<br>(37.0, 56.0)    | 45.0<br>(37.0, 56.0)    | 52.0<br>(47.0, 62.0)    | 43.0<br>(39.0, 53.0)    | 45.0<br>(37.0, 56.0)    | 0.114   |
|          | Iron, ug/dL          | 2,332 | 67        | 51.0<br>(34.5, 71.0)    | 52.0<br>(35.2, 72.1)    | 54.0<br>(34.6, 72.0)    | 35.0<br>(35.0, 35.0)    | 52.0<br>(35.0, 72.0)    | 0.81    |
|          | TIBC, ug/dL          | 2,343 | 66        | 208.9<br>(172.6, 245.0) | 207.0<br>(173.0, 246.0) | 230.0<br>(187.0, 244.0) | 171.3<br>(171.3, 171.3) | 207.0<br>(173.0, 246.0) | 0.937   |
|          | Ferritin, ng/dL      | 365   | 95        | 188.0<br>(165.0, 217.0) | 181.0<br>(156.0, 213.0) | 183.0<br>(183.0, 203.0) | 268.0<br>(268.0, 268.0) | 183.0<br>(157.0, 213.0) | 0.366   |
|          | antiHCV, n(%)        | 6,981 | 0         | 38 (1.02)               | 41 (1.29)               | 0 (0.00)                | 0 (0.00)                | 79 (1.13)               | 0.767   |
|          | antiHBs, n(%)        | 6,981 | 0         | 1041 (27.86)            | 173 (5.43)              | 1 (1.85)                | 0 (0.00)                | 1215 (17.40)            | <0.001  |

**Table S3.** Baseline characteristics of patients included in the PPA by treatments approach (cont.)

| Outcomes | Variables                               | N     | % Missing | Treatment group |               |               |                    | Total         | p-value |
|----------|-----------------------------------------|-------|-----------|-----------------|---------------|---------------|--------------------|---------------|---------|
|          |                                         |       |           | No-PBs          | CBPBs         | NCBPBs        | Aluminum hydroxide |               |         |
| CVD      | <b>Total number of patients, n (%)</b>  |       |           | 3,233 (59.0)    | 2,193 (40.0)  | 46 (0.8)      | 5 (0.09)           | 5,477 (100)   |         |
|          | <b>Hospital, n(%)</b>                   | 5,477 | 0         |                 |               |               |                    |               | <0.001  |
|          | Ramathibodi Hospital                    |       |           | 2,825 (87.38)   | 1,389 (63.34) | 26 (56.52)    | 4 (80.00)          | 4,244 (77.49) |         |
|          | Bhumibol Hospital                       |       |           | 408 (12.62)     | 804 (36.66)   | 20 (43.48)    | 1 (20.00)          | 1,233 (22.51) |         |
|          | <b>age (years), mean(SD)</b>            | 5,477 | 0         | 46.23 (16.11)   | 59.39 (16.49) | 62.22 (14.35) | 43.43 (10.00)      | 51.63 (17.50) | <0.001  |
|          | <b>Female, n(%)</b>                     | 5,477 | 0         | 1,353 (41.85)   | 1,187 (54.13) | 20 (43.48)    | 2 (40.00)          | 2,562 (46.78) | <0.001  |
|          | <b>Reimbursement, n(%)</b>              | 5,477 | 0         |                 |               |               |                    |               | <0.001  |
|          | non-CSMBS                               |       |           | 2,478 (76.65)   | 1,319 (60.15) | 11 (23.91)    | 4 (80.00)          | 3,812 (69.60) |         |
|          | CSMBS                                   |       |           | 755 (23.35)     | 874 (39.85)   | 35 (76.09)    | 1 (20.00)          | 1,665 (30.40) |         |
|          | <b>BMI (kg/m<sup>2</sup>), mean(SD)</b> | 2,391 | 56        | 24.06 (4.68)    | 24.72 (5.40)  | 26.51 (6.95)  | 22.20 (0.57)       | 24.25 (4.91)  | 0.006   |
|          | <b>Marital status, n(%)</b>             | 5,477 | 0         |                 |               |               |                    |               | <0.001  |
|          | Single                                  |       |           | 1,114 (34.46)   | 574 (26.17)   | 8 (17.39)     | 2 (40.00)          | 1,698 (31.00) |         |
|          | Married                                 |       |           | 1,833 (56.70)   | 1,317 (60.05) | 34 (73.91)    | 3 (60.00)          | 3,187 (58.19) |         |
|          | Divorced/widowed                        |       |           | 281 (8.69)      | 295 (13.45)   | 4 (8.70)      | 0 (0.00)           | 580 (10.59)   |         |
|          | Priest                                  |       |           | 0 (0.00)        | 1 (0.05)      | 0 (0.00)      | 0 (0.00)           | 1 (0.02)      |         |
|          | Unknown                                 |       |           | 5 (0.15)        | 6 (0.27)      | 0 (0.00)      | 0 (0.00)           | 11 (0.20)     |         |
|          | <b>Education levels, n(%)</b>           | 2,887 | 47        |                 |               |               |                    |               | <0.001  |
|          | Primary level or less                   |       |           | 503 (21.86)     | 166 (29.38)   | 6 (30.00)     | 0 (0.00)           | 675 (23.38)   |         |
|          | Secondary level                         |       |           | 712 (30.94)     | 111 (19.65)   | 3 (15.00)     | 0 (0.00)           | 826 (28.61)   |         |
|          | University level or more                |       |           | 1,086 (47.20)   | 288 (50.97)   | 11 (55.00)    | 1 (100.00)         | 1,386 (48.01) |         |
|          | <b>Renal replacement therapy, n(%)</b>  | 5,477 | 0         |                 |               |               |                    |               | <0.001  |
|          | No RRT                                  |       |           | 2,007 (62.08)   | 1,684 (76.79) | 27 (58.70)    | 0 (0.00)           | 3,718 (67.88) |         |
|          | RRT                                     |       |           | 1,226 (37.92)   | 509 (23.21)   | 19 (41.30)    | 5 (100.00)         | 1,759 (32.12) |         |
|          | <b>Comorbid, n(%)</b>                   |       |           |                 |               |               |                    |               |         |
|          | Hypertension                            | 5,477 | 0         | 1,406 (43.49)   | 2,091 (95.35) | 36 (78.26)    | 5 (100.00)         | 3,538 (64.60) | <0.001  |
|          | Diabetes                                | 5,477 | 0         | 588 (18.19)     | 1,024 (46.69) | 18 (39.13)    | 1 (20.00)          | 1,631 (29.78) | <0.001  |
|          | Dyslipidemia                            | 5,477 | 0         | 610 (18.87)     | 1,358 (61.92) | 25 (54.35)    | 2 (40.00)          | 1,995 (36.43) | <0.001  |

**Table S3.** Baseline characteristics of patients included in the PPA by treatments approach (cont.)

| Outcomes | Variables                        | N     | %<br>Missing | Treatment group         |                         |                         |                         | Total                   | p-value |
|----------|----------------------------------|-------|--------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|          |                                  |       |              | No-PBs                  | CBPBs                   | NCBPBs                  | Aluminum<br>hydroxide   |                         |         |
| CVD      | Bone disorder related ESRD       | 5,477 | 0            | 41 (1.27)               | 188 (8.57)              | 2 (4.35)                | 0 (0.00)                | 231 (4.22)              | <0.001  |
|          | Gout                             | 5,477 | 0            | 173 (5.35)              | 324 (14.77)             | 2 (4.35)                | 1 (20.00)               | 500 (9.13)              | <0.001  |
|          | Liver disease                    | 5,477 | 0            | 108 (3.34)              | 103 (4.70)              | 3 (6.52)                | 1 (20.00)               | 215 (3.93)              | 0.027   |
|          | SLE                              | 5,477 | 0            | 38 (1.18)               | 59 (2.69)               | 1 (2.17)                | 0 (0.00)                | 98 (1.79)               | 0.001   |
|          | Cancer                           | 5,477 | 0            | 19 (0.59)               | 24 (1.09)               | 1 (2.17)                | 0 (0.00)                | 44 (0.80)               | 0.072   |
|          | AIDS                             | 5,477 | 0            | 5 (0.15)                | 17 (0.78)               | 1 (2.17)                | 0 (0.00)                | 23 (0.42)               | <0.001  |
|          | GI disorder                      | 5,477 | 0            | 84 (2.60)               | 213 (9.71)              | 6 (13.04)               | 0 (0.00)                | 303 (5.53)              | <0.001  |
|          | Chronic pulmonary disease        | 5,477 | 0            | 23 (0.71)               | 41 (1.87)               | 1 (2.17)                | 0 (0.00)                | 65 (1.19)               | 0.002   |
|          | Tumor lysis syndrome             | 5,477 | 0            | 1 (0.03)                | 0 (0.00)                | 0 (0.00)                | 0 (0.00)                | 1 (0.02)                | <0.001  |
|          | Hypoparathyroidism               | 5,477 | 0            | 0 (0.00)                | 2 (0.09)                | 0 (0.00)                | 0 (0.00)                | 2 (0.04)                | 0.558   |
|          | Secondary<br>Hyperparathyroidism | 5,477 | 0            | 220 (6.80)              | 636 (29.00)             | 26 (56.5)               | 3 (60.00)               | 885 (16.16)             | <0.001  |
|          | <b>Laboratory, median (IQR)</b>  |       |              |                         |                         |                         |                         |                         |         |
|          | eGFR, ml/min/1.73 m <sup>2</sup> | 5,461 | 0            | 4.8 (3.6, 7.2)          | 7.4 (4.6, 11.8)         | 5.4 (4.2, 8.8)          | 3.4 (3.4, 4.0)          | 5.4 (3.8, 9.2)          | <0.001  |
|          | Phosphorus, mg/dL                | 5,477 | 0            | 5.6 (5.0, 6.6)          | 5.4 (4.8, 6.4)          | 5.7 (5.0, 7.0)          | 7.8 (6.6, 8.1)          | 5.6 (5.0, 6.6)          | <0.001  |
|          | PTH, pg/dL                       | 3,153 | 42           | 341.8<br>(157.0, 658.0) | 181.0<br>(84.0, 358.6)  | 400.2<br>(190.8, 852.8) | 943.5<br>(44.0, 2783.5) | 271.4<br>(120.0, 553.0) | <0.001  |
|          | Calcium, mg/dL                   | 5,477 | 0            | 9.6 (9.1, 10.2)         | 9.4 (8.9, 9.9)          | 10.2 (9.7, 10.6)        | 10.7 (10.6, 11.8)       | 9.6 (9.0, 10.1)         | <0.001  |
|          | Hemoglobin, g/dL                 | 4,825 | 12           | 10.6<br>(9.1, 11.9)     | 9.6<br>(8.3, 11.0)      | 10.8<br>(9.3, 11.7)     | 9.8<br>(9.2, 10.7)      | 10.2<br>(8.8, 11.6)     | <0.001  |
|          | Hematocrit, %                    | 1,432 | 74           | 28.9<br>(24.6, 33.0)    | 28.4<br>(24.0, 32.7)    | 32.2<br>(29.0, 36.4)    | 31.4<br>(31.4, 31.4)    | 28.7<br>(24.1, 32.9)    | 0.799   |
|          | Albumin, g/dL                    | 5,477 | 0            | 3.7 (3.2, 4.1)          | 3.5 (2.9, 3.9)          | 3.6 (3.3, 4.1)          | 3.3 (3.2, 3.3)          | 3.6 (3.1, 4.0)          |         |
|          | Sodium, mEq/L                    | 5,429 | 1            | 138.0<br>(136.0, 140.0) | 138.0<br>(135.0, 140.0) | 139.0<br>(136.0, 142.0) | 139.0<br>(138.0, 140.0) | 138.0<br>(135.0, 140.0) | 1.000   |
|          | Potassium, mEq/L                 | 2,520 | 54           | 4.6 (4.1, 5.2)          | 4.6 (4.1, 5.0)          | 4.4 (4.0, 5.0)          | 3.9 (3.4, 4.4)          | 4.6 (4.1, 5.1)          | <0.001  |

**Table S3.** Baseline characteristics of patients included in the PPA by treatments approach (cont.)

| Outcomes | Variables            | N     | % Missing | Treatment group         |                         |                         |                         | Total                   | p-value |
|----------|----------------------|-------|-----------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|          |                      |       |           | No-PBs                  | CBPBs                   | NCBPBs                  | Aluminum hydroxide      |                         |         |
| CVD      | Chloride, mEq/L      | 5,434 | 1         | 100.0<br>(97.0, 103.0)  | 103.0<br>(99.0, 107.0)  | 100.5<br>(98.0, 105.0)  | 99.0<br>(98.0, 100.0)   | 101.0<br>(98.0, 105.0)  | <0.001  |
|          | Carbondioxide, mEq/L | 5,439 | 1         | 23.0<br>(20.2, 25.8)    | 21.0<br>(18.0, 24.5)    | 21.0<br>(19.0, 24.0)    | 22.0<br>(16.8, 25.7)    | 22.3<br>(19.0, 25.2)    | <0.001  |
|          | Uric, mg/dL          | 4,843 | 12        | 7.0<br>(5.6, 8.4)       | 7.7<br>(6.1, 9.3)       | 6.6<br>(5.3, 8.3)       | 7.9<br>(3.3, 9.0)       | 7.2<br>(5.8, 8.8)       | <0.001  |
|          | Glucose, mg/dL       | 2,494 | 54        | 100.4<br>(86.4, 131.0)  | 102.0<br>(88.2, 134.0)  | 98.0<br>(90.0, 140.0)   | 85.5<br>(81.0, 90.0)    | 101.0<br>(87.0, 133.2)  | 0.779   |
|          | HbA1C, mg%           | 1,582 | 71        | 6.3 (5.6, 7.3)          | 6.2 (5.5, 7.3)          | 5.9 (5.3, 6.5)          | 4.6 (4.6, 4.6)          | 6.2 (5.5, 7.3)          | 0.096   |
|          | LDL, mg/dL           | 2,975 | 46        | 104.0<br>(81.0, 129.0)  | 108.0<br>(85.0, 137.0)  | 104.0<br>(90.8, 148.0)  | 72.0<br>(72.0, 72.0)    | 106.0<br>(83.0, 133.0)  | 0.061   |
|          | Cholesterol, mg/dL   | 5,024 | 8         | 180.8<br>(152.6, 216.0) | 185.0<br>(154.0, 221.0) | 164.0<br>(138.0, 222.0) | 182.5<br>(174.5, 235.9) | 182.0<br>(153.0, 218.0) | 0.105   |
|          | Triglyceride, mg/dL  | 4,658 | 15        | 115.0<br>(82.0, 157.0)  | 128.4<br>(92.0, 183.0)  | 116.0<br>(86.0, 173.0)  | 160.3<br>(109.0, 211.6) | 121.0<br>(86.0, 169.0)  | <0.001  |
|          | HDL, mg/dL           | 2,846 | 48        | 46.0<br>(37.0, 56.0)    | 45.1<br>(38.0, 58.0)    | 53.0<br>(45.0, 70.0)    | 39.0<br>(39.0, 39.0)    | 46.0<br>(37.8, 57.0)    | 1.000   |
|          | Iron, ug/dL          | 1,555 | 72        | 52.8<br>(36.0, 74.0)    | 54.5<br>(38.0, 75.0)    | 61.0<br>(34.6, 72.0)    | NA                      | 54.0<br>(37.4, 75.0)    | 0.124   |
|          | TIBC, ug/dL          | 1,561 | 71        | 209.0<br>(174.3, 244.0) | 207.0<br>(176.0, 246.0) | 234.0<br>(198.0, 246.0) | NA                      | 209.0<br>(176.0, 245.0) | 0.211   |
|          | Ferritin, ng/dL      | 284   | 95        | 190.0<br>(166.0, 218.0) | 181.0<br>(156.0, 212.0) | 183.0<br>(183.0, 203.0) | NA                      | 183.0<br>(157.0, 212.5) | 0.406   |
|          | antiHCV, n(%)        | 5,477 | 0         | 30 (0.93)               | 29 (1.32)               | 0 (0.00)                | 0 (0.00)                | 59 (1.08)               | 0.650   |
|          | antiHBs, n(%)        | 5,477 | 0         | 983 (30.41)             | 89 (4.06)               | 1 (2.17)                | 0 (0.00)                | 1073 (19.59)            | <0.001  |

**Table S3.** Baseline characteristics of patients included in the PPA by treatments approach (cont.)

| Outcomes      | Variables                               | N     | % Missing | Treatment group |               |               |                    | Total         | p-value |
|---------------|-----------------------------------------|-------|-----------|-----------------|---------------|---------------|--------------------|---------------|---------|
|               |                                         |       |           | No-PBs          | CBPBs         | NCBPBs        | Aluminum hydroxide |               |         |
| Bone disorder | <b>Total number of patients, n (%)</b>  |       |           | <b>3,658</b>    | <b>2,821</b>  | <b>52</b>     | <b>7</b>           | <b>6,538</b>  |         |
|               | <b>Hospital, n(%)</b>                   | 6,538 | 0         |                 |               |               |                    |               | <0.001  |
|               | Ramathibodi Hospital                    |       |           | 3,229 (88.27)   | 1,905 (67.53) | 36 (69.23)    | 4 (57.14)          | 5,174 (79.14) |         |
|               | Bhumibol Hospital                       |       |           | 429 (11.73)     | 916 (32.47)   | 16 (30.77)    | 3 (42.86)          | 1,364 (20.86) |         |
|               | <b>age (years), mean(SD)</b>            | 6,538 | 0         | 48.05 (16.83)   | 60.74 (15.96) | 62.73 (14.73) | 53.11 (16.60)      | 53.65 (17.61) | <0.001  |
|               | <b>Female, n(%)</b>                     | 6,538 | 0         | 1,510 (41.28)   | 1,426 (50.55) | 22 (42.31)    | 4 (57.14)          | 2,962 (45.30) | <0.001  |
|               | <b>Reimbursement, n(%)</b>              | 6,538 | 0         |                 |               |               |                    |               | <0.001  |
|               | non-CSMBS                               |       |           | 2,691 (73.56)   | 1,627 (57.67) | 12 (23.08)    | 6 (85.71)          | 4,336 (66.32) |         |
|               | CSMBS                                   |       |           | 967 (26.44)     | 1,194 (42.33) | 40 (76.92)    | 1 (14.29)          | 2,202 (33.68) |         |
|               | <b>BMI (kg/m<sup>2</sup>), mean(SD)</b> | 2,840 | 57        | 24.13 (4.73)    | 24.97 (5.42)  | 23.75 (5.13)  | 23.35 (2.19)       | 24.38 (4.97)  | 0.001   |
|               | <b>Marital status, n(%)</b>             | 6,538 | 0         |                 |               |               |                    |               | <0.001  |
|               | Single                                  |       |           | 1,180 (32.26)   | 657 (23.29)   | 9 (17.31)     | 4 (57.14)          | 1,850 (28.30) |         |
|               | Married                                 |       |           | 2,128 (58.17)   | 1,765 (62.57) | 35 (67.31)    | 3 (42.86)          | 3,931 (60.13) |         |
|               | Divorced/widowed                        |       |           | 346 (9.46)      | 389 (13.79)   | 8 (15.38)     | 0 (0.00)           | 743 (11.36)   |         |
|               | Priest                                  |       |           | 0 (0.00)        | 2 (0.07)      | 0 (0.00)      | 0 (0.00)           | 2 (0.03)      |         |
|               | Unknown                                 |       |           | 4 (0.11)        | 8 (0.28)      | 0 (0.00)      | 0 (0.00)           | 12 (0.18)     |         |
|               | <b>Education levels, n(%)</b>           | 3,283 | 50        |                 |               |               |                    |               | <0.001  |
|               | Primary level or less                   |       |           | 580 (23.00)     | 230 (31.21)   | 5 (21.74)     | 0 (0.00)           | 815 (24.82)   |         |
|               | Secondary level                         |       |           | 760 (30.13)     | 156 (21.17)   | 3 (13.04)     | 0 (0.00)           | 919 (27.99)   |         |
|               | University level or more                |       |           | 1,182 (46.87)   | 351 (47.63)   | 15 (65.22)    | 1 (100.00)         | 1,549 (47.18) |         |
|               | <b>Renal replacement therapy, n(%)</b>  | 6,538 | 0         |                 |               |               |                    |               | <0.001  |
|               | No RRT                                  |       |           | 2,268 (62.00)   | 2,110 (74.80) | 23 (44.23)    | 2 (28.57)          | 4,403 (67.34) |         |
|               | RRT                                     |       |           | 1,390 (38.00)   | 711 (25.20)   | 29 (55.77)    | 5 (71.43)          | 2,135 (32.66) |         |
|               | <b>Comorbid, n(%)</b>                   |       |           |                 |               |               |                    |               |         |
|               | Hypertension                            | 6,538 | 0         | 1,803 (49.29)   | 2,720 (96.42) | 42 (80.77)    | 7 (100.00)         | 4,572 (69.93) | <0.001  |
|               | Diabetes                                | 6,538 | 0         | 837 (22.88)     | 1,485 (52.64) | 19 (36.54)    | 3 (42.86)          | 2,344 (35.85) | <0.001  |
|               | Dyslipidemia                            | 6,538 | 0         | 911 (24.90)     | 1,937 (68.66) | 31 (59.62)    | 4 (57.14)          | 2,883 (44.10) | <0.001  |

**Table S3.** Baseline characteristics of patients included in the PPA by treatments approach (cont.)

| Outcomes      | Variables                        | N     | %<br>Missing | Treatment group         |                         |                         |                         | Total                   | p-value |
|---------------|----------------------------------|-------|--------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|               |                                  |       |              | No-PBs                  | CBPBs                   | NCBPBs                  | Aluminum<br>hydroxide   |                         |         |
| Bone disorder | Bone disorder related ESRD       | 6,538 | 0            | 477 (13.04)             | 862 (30.56)             | 13 (25.00)              | 3 (42.86)               | 1,355 (20.72)           | <0.001  |
|               | Gout                             | 6,538 | 0            | 128 (3.50)              | 200 (7.09)              | 1 (1.92)                | 0 (0.00)                | 329 (5.03)              | <0.001  |
|               | Liver disease                    | 6,538 | 0            | 143 (3.91)              | 161 (5.71)              | 3 (5.77)                | 0 (0.00)                | 307 (4.70)              | 0.015   |
|               | SLE                              | 6,538 | 0            | 49 (1.34)               | 61 (2.16)               | 1 (1.92)                | 0 (0.00)                | 111 (1.70)              | 0.101   |
|               | Cancer                           | 6,538 | 0            | 25 (0.68)               | 26 (0.92)               | 0 (0.00)                | 0 (0.00)                | 51 (0.78)               | 0.802   |
|               | AIDS                             | 6,538 | 0            | 6 (0.16)                | 21 (0.74)               | 1 (1.92)                | 0 (0.00)                | 28 (0.43)               | 0.001   |
|               | GI disorder                      | 6,538 | 0            | 115 (3.14)              | 294 (10.42)             | 4 (7.69)                | 2 (28.57)               | 415 (6.35)              | <0.001  |
|               | Chronic pulmonary disease        | 6,538 | 0            | 47 (1.28)               | 90 (3.19)               | 2 (3.85)                | 0 (0.00)                | 139 (2.13)              | <0.001  |
|               | Tumor lysis syndrome             | 6,538 | 0            | 2 (0.05)                | 0 (0.00)                | 0 (0.00)                | 0 (0.00)                | 2 (0.03)                | 0.813   |
|               | Hypoparathyroidism               | 6,538 | 0            | 0 (0.00)                | 6 (0.21)                | 0 (0.00)                | 0 (0.00)                | 6 (0.09)                | 0.095   |
|               | Secondary hyperparathyroidism    | 6,538 | 0            | 275 (7.52)              | 788 (27.93)             | 30 (57.69)              | 2 (28.57)               | 1,095 (16.75)           | <0.001  |
|               | <b>Laboratory, median (IQR)</b>  |       |              |                         |                         |                         |                         |                         |         |
|               | eGFR, ml/min/1.73 m <sup>2</sup> | 6,523 | 0            | 5.0 (3.8, 7.8)          | 7.6 (4.8, 11.6)         | 5.9 (4.2, 9.8)          | 4.6 (3.4, 11.4)         | 5.8 (4.0, 10.0)         | <0.001  |
|               | Phosphorus, mg/dL                | 6,538 | 0            | 5.6 (5.0, 6.6)          | 5.3 (4.8, 6.3)          | 5.6 (5.0, 6.9)          | 6.2 (5.0, 8.1)          | 5.4 (4.9, 6.6)          | <0.001  |
|               | PTH, pg/dL                       | 3,583 | 45           | 322.6<br>(141.8, 640.6) | 174.0<br>(86.0, 348.8)  | 328.5<br>(140.8, 868.1) | 406.9<br>(44.0, 1304.4) | 249.6<br>(112.6, 518.8) | 0.715   |
|               | Calcium, mg/dL                   | 6,538 | 0            | 9.4 (8.8, 10.0)         | 9.3 (8.7, 9.8)          | 10.0 (9.6, 10.5)        | 10.4 (9.9, 11.8)        | 9.4 (8.8, 9.9)          | <0.001  |
|               | Hemoglobin, g/dL                 | 6,538 | 0            | 10.6<br>(9.1, 11.9)     | 9.7<br>(8.4, 11.1)      | 10.8<br>(9.3, 11.7)     | 9.6<br>(8.7, 11.5)      | 10.2<br>(8.8, 11.6)     | <0.001  |
|               | Hematocrit, %                    | 1,733 | 73           | 29.0<br>(25.0, 33.0)    | 28.8<br>(24.6, 33.0)    | 30.3<br>(28.1, 36.4)    | 31.4<br>(17.3, 38.0)    | 29.0<br>(24.8, 33.0)    | <0.001  |
|               | Albumin, g/dL                    | 6,538 | 0            | 3.6 (3.2, 4.0)          | 3.4 (2.9, 3.8)          | 3.6 (3.3, 3.9)          | 3.3 (3.2, 3.4)          | 3.5 (3.0, 3.9)          | 0.001   |
|               | Sodium, mEq/L                    | 6,492 | 1            | 138.0<br>(136.0, 140.0) | 138.0<br>(135.0, 140.0) | 139.0<br>(136.0, 141.0) | 138.0<br>(136.0, 140.0) | 138.0<br>(135.0, 140.0) | 0.954   |
|               | Potassium, mEq/L                 | 3,132 | 52           | 4.6 (4.0, 5.0)          | 4.5 (4.1, 5.0)          | 4.4 (4.0, 5.0)          | 4.4 (3.8, 4.8)          | 4.6 (4.1, 5.0)          | 0.239   |

**Table S3.** Baseline characteristics of patients included in the PPA by treatments approach (cont.)

| Outcomes       | Variables            | N     | % Missing | Treatment group         |                         |                         |                         |                         | p-value |
|----------------|----------------------|-------|-----------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|                |                      |       |           | No-PBs                  | CBPBs                   | NCBPBs                  | Aluminum hydroxide      | Total                   |         |
| Bone disorders | Chloride, mEq/L      | 6,498 | 1         | 100.0<br>(97.0, 103.0)  | 103.0<br>(99.0, 107.0)  | 100.0<br>(97.0, 104.0)  | 100.0<br>(98.0, 105.0)  | 101.0<br>(98.0, 105.0)  | <0.001  |
|                | Carbondioxide, mEq/L | 6,503 | 1         | 22.9<br>(20.0, 25.6)    | 21.0<br>(18.0, 24.5)    | 21.8<br>(19.1, 24.6)    | 22.0<br>(16.0, 27.5)    | 22.0<br>(19.0, 25.0)    | <0.001  |
|                | Uric, mg/dL          | 5,785 | 12        | 7.0 (5.6, 8.5)          | 7.8 (6.3, 9.4)          | 6.6 (5.3, 8.2)          | 6.7 (6.2, 8.1)          | 7.3 (5.9, 8.9)          | <0.001  |
|                | Glucose, mg/dL       | 3,115 | 52        | 101.0<br>(87.0, 135.0)  | 102.6<br>(88.2, 137.0)  | 99.0<br>(90.0, 138.6)   | 90.0<br>(86.4, 108.0)   | 102.6<br>(88.0, 136.8)  | <0.001  |
|                | HbA1C, mg%           | 2,203 | 66        | 6.3 (5.6, 7.3)          | 6.3 (5.6, 7.3)          | 6.0 (5.4, 6.7)          | 6.6 (4.6, 12.4)         | 6.3 (5.6, 7.3)          | <0.001  |
|                | LDL, mg/dL           | 3,810 | 42        | 101.8<br>(79.0, 128.0)  | 105.0<br>(82.0, 133.6)  | 100.5<br>(90.8, 139.0)  | 135.0<br>(72.0, 217.0)  | 103.0<br>(81.0, 131.0)  | <0.001  |
|                | Cholesterol, mg/dL   | 6,059 | 7         | 179.0<br>(151.0, 215.0) | 181.9<br>(150.1, 218.0) | 163.0<br>(125.0, 205.8) | 194.0<br>(175.0, 281.8) | 180.0<br>(150.0, 216.0) | 0.001   |
|                | Triglyceride, mg/dL  | 5,613 | 14        | 116.0<br>(82.0, 158.0)  | 128.0<br>(92.0, 184.0)  | 107.5<br>(80.0, 169.0)  | 207.0<br>(109.0, 211.6) | 121.0<br>(86.0, 170.8)  | <0.001  |
|                | HDL, mg/dL           | 3,626 | 45        | 45.0<br>(37.0, 56.0)    | 45.0<br>(37.0, 56.0)    | 52.0<br>(46.0, 62.0)    | 43.0<br>(39.0, 53.0)    | 45.0<br>(37.0, 56.0)    | 0.541   |
|                | Iron, ug/dL          | 2,073 | 68        | 51.0<br>(35.0, 71.5)    | 52.0<br>(35.9, 73.0)    | 51.0<br>(34.3, 71.8)    | 35.0<br>(35.0, 35.0)    | 52.0<br>(35.0, 72.0)    | 0.003   |
|                | TIBC, ug/dL          | 2,083 | 68        | 208.9<br>(173.0, 245.0) | 207.0<br>(174.0, 245.0) | 229.0<br>(179.5, 242.5) | 171.3<br>(171.3, 171.3) | 207.8<br>(174.0, 245.0) | 0.250   |
|                | Ferritin, ng/dL      | 335   | 95        | 188.0<br>(165.0, 217.0) | 181.0<br>(156.0, 212.0) | 183.0<br>(175.0, 193.0) | 268.0<br>(268.0, 268.0) | 183.0<br>(157.0, 212.0) | 0.308   |
|                | antiHCV, n(%)        | 6,538 | 0         | 37 (1.01)               | 35 (1.24)               | 0 (0.00)                | 0 (0.00)                | 72 (1.10)               | 0.077   |
|                | antiHBs, n(%)        | 6,538 | 0         | 1038 (28.38)            | 138 (4.89)              | 1 (1.92)                | 0 (0.00)                | 1177 (18.00)            | <0.001  |

Abbreviations: Body mass index; (BMI), CBPBs; Calcium-based phosphate binders, CVD; cardiovascular disease, CSMBs; Civil Servant Medical Benefit Scheme, eGFR; estimated Glomerular Filtration Rate, ESRD; End-stage renal disease, HbA1C; Hemoglobin A1C, HDL; High-Density Lipoprotein, HIV; human immunodeficiency virus, IQR; interquartile range, ITT; Intention to treat, GI; Gastrointestinal tract, LDL; Low-Density Lipoprotein, NCBPBs; N; number, Non-calcium-based phosphate binders i.e., lanthanum or sevelamer; OS; overall survival outcome, PBs; Phosphate binders, PPA; Per-protocol analysis, SLE; PTH; Parathyroid hormone levels, RRT, Renal Replacement Therapy, Systemic lupus erythematosus, TIBC; Total iron binding capacity

**Table S4.** Baseline characteristics of patients included in the actual treatment-pattern analysis by treatment approach

| Outcomes | Variables                               | N     | % Missing | Treatment group |              |               |                | Total        | p-value |
|----------|-----------------------------------------|-------|-----------|-----------------|--------------|---------------|----------------|--------------|---------|
|          |                                         |       |           | No-PBs          | CBPBs-CBPs   | CBPBs-NCBPs   | CBPBs-aluminum |              |         |
| OS       | <b>Total number of patients, n (%)</b>  | 8,005 | 0         | 3,736 (48.6)    | 3,361 (43.8) | 487 (6.34)    | 98 (1.28)      | 7,682        |         |
|          | <b>Hospital, n(%)</b>                   | 7,682 | 0         |                 |              |               |                |              | <0.001  |
|          | Ramathibodi Hospital                    |       |           | 3,283 (87.9)    | 2,315 (68.9) | 326 (66.94)   | 37 (37.8)      | 5,961 (77.6) |         |
|          | Bhumibol Hospital                       |       |           | 453 (12.1)      | 1,046 (31.1) | 161 (33.06)   | 61 (62.2)      | 1,721 (22.4) |         |
|          | <b>age (years), mean(SD)</b>            | 7,682 | 0         | 48.5 (17.1)     | 61.8 (16.1)  | 60.84 (14.74) | 53.6 (15.4)    | 55.4 (17.8)  | <0.001  |
|          | <b>Male, n(%)</b>                       | 7,682 | 0         | 2,172(58.1)     | 1,575 (46.9) | 251 (51.5)    | 49 (50.0)      | 4,047 (52.7) | <0.001  |
|          | <b>Reimbursement, n(%)</b>              | 7,682 | 0         |                 |              |               |                |              | <0.001  |
|          | non-CSMBS                               |       |           | 2,723 (72.9)    | 1,835 (54.6) | 97 (19.92)    | 84 (85.7)      | 4,739 (61.7) |         |
|          | CSMBS                                   |       |           | 1,013 (27.1)    | 1,526 (45.4) | 390 (80.08)   | 14 (14.3)      | 2,943 (38.3) |         |
|          | <b>BMI (kg/m<sup>2</sup>), mean(SD)</b> | 3,288 | 57        | 24.2 (4.7)      | 24.9 (5.3)   | 25.35 (4.80)  | 23.2 (4.2)     | 24.47 (4.9)  | <0.001  |
|          | <b>Marital status, n(%)</b>             | 7,682 | 0         |                 |              |               |                |              | <0.001  |
|          | Single                                  |       |           | 1,190 (31.9)    | 748 (22.3)   | 80 (16.43)    | 37 (37.8)      | 2,055 (26.8) |         |
|          | Married                                 |       |           | 2,178 (58.3)    | 2,121 (63.1) | 345 (70.84)   | 48 (49.0)      | 4,692 (61.1) |         |
|          | Divorced/widowed                        |       |           | 364 (9.7)       | 481 (14.3)   | 61 (12.53)    | 13 (13.3)      | 919 (12.0)   |         |
|          | Priest                                  |       |           | 0 (0.0)         | 2 (0.1)      | 0 (0.00)      | 0 (0.00)       | 2 (0.03)     |         |
|          | Unknown                                 |       |           | 4 (0.1)         | 9 (0.3)      | 1 (0.21)      | 0 (0.00)       | 14 (0.2)     |         |
|          | <b>Education levels, n(%)</b>           | 3,508 | 54        |                 |              |               |                |              | <0.001  |
|          | Primary level or less                   |       |           | 589 (23.2)      | 270 (32.1)   | 29 (25.00)    | 4 (57.1)       | 892 (25.4)   |         |
|          | Secondary level                         |       |           | 766 (30.1)      | 180 (21.4)   | 10 (8.62)     | 1 (14.3)       | 957 (27.3)   |         |
|          | University level or more                |       |           | 1,189 (46.7)    | 391 (46.5)   | 77 (66.38)    | 2 (28.6)       | 1,659 (47.3) |         |
|          | <b>Renal replacement therapy, n(%)</b>  | 7,682 | 0         |                 |              |               |                |              | <0.001  |
|          | No RRT                                  |       |           | 2,333 (62.5)    | 2,526 (75.2) | 359 (73.72)   | 33 (33.7)      | 5,061 (65.9) |         |
|          | RRT                                     |       |           | 1,403 (37.6)    | 835 (24.8)   | 128 (26.28)   | 65 (66.3)      | 2,621 (34.1) |         |
|          | <b>Comorbid, n(%)</b>                   |       |           |                 |              |               |                |              |         |
|          | Hypertension                            | 7,682 | 0         | 1,874 (50.2)    | 3,247 (96.6) | 480 (98.56)   | 92 (93.9)      | 5,693 (74.1) | <0.001  |
|          | Diabetes                                | 7,682 | 0         | 871 (23.3)      | 1,806 (53.7) | 253 (51.95)   | 38 (38.8)      | 2,968 (38.6) | <0.001  |
|          | Dyslipidemia                            | 7,682 | 0         | 965 (25.8)      | 2,351 (70.0) | 360 (73.92)   | 48 (49.0)      | 3,724 (48.5) | <0.001  |



**Table S4** Baseline characteristics of patients included in the actual treatment-pattern analysis by treatment approach (cont.)

| Outcomes | Variables                        | N     | % Missing | Treatment group         |                         |                          |                         | Total                   | p-value |
|----------|----------------------------------|-------|-----------|-------------------------|-------------------------|--------------------------|-------------------------|-------------------------|---------|
|          |                                  |       |           | No-PBs                  | CBPBs-<br>CBPBs         | CBPBs-<br>NCBPBs         | CBPBs-<br>aluminum      |                         |         |
| OS       | CVD                              | 7,682 | 0         | 503 (13.5)              | 912 (27.1)              | 132 (27.10)              | 13 (13.3)               | 1,675 (21.8)            | <0.001  |
|          | Bone disorder related ESRD       | 7,682 | 0         | 78 (2.1)                | 343 (10.2)              | 49 (10.06)               | 7 (7.1)                 | 515 (6.7)               | <0.001  |
|          | Gout                             | 7,682 | 0         | 141 (3.8)               | 250 (7.4)               | 37 (7.60)                | 3 (3.1)                 | 431 (5.6)               | <0.001  |
|          | Liver disease                    | 7,682 | 0         | 150 (4.0)               | 216 (6.4)               | 32 (6.57)                | 2 (2.0)                 | 400 (5.2)               | <0.001  |
|          | SLE                              | 7,682 | 0         | 50 (1.3)                | 81 (2.4)                | 6 (1.23)                 | 1 (1.0)                 | 138 (1.8)               | 0.01    |
|          | Cancer                           | 7,682 | 0         | 27 (0.7)                | 38 (1.1)                | 1 (0.21)                 | 0 (0.0)                 | 66 (0.9)                | 0.122   |
|          | AIDS                             | 7,682 | 0         | 8 (0.2)                 | 24 (0.7)                | 1 (0.21)                 | 0 (0.0)                 | 33 (0.4)                | 0.018   |
|          | GI disorder                      | 7,682 | 0         | 127 (3.4)               | 395 (11.8)              | 54 (11.09)               | 9 (9.2)                 | 585 (7.6)               | <0.001  |
|          | Chronic pulmonary disease        | 7,682 | 0         | 55 (1.5)                | 131 (3.9)               | 18 (3.70)                | 2 (2.0)                 | 206 (2.7)               | <0.001  |
|          | Tumor lysis syndrome             | 7,682 | 0         | 2 (0.1)                 | 0 (0.0)                 | 0 (0.00)                 | 0 (0.0)                 | 2 (0.03)                | <0.001  |
|          | Hypoparathyroidism               | 7,682 | 0         | 0 (0.0)                 | 8 (0.2)                 | 0 (0.00)                 | 0 (0.0)                 | 8 (0.1)                 | 0.715   |
|          | Secondary hyperparathyroidism    | 7,682 | 0         | 314 (8.4)               | 979 (29.1)              | 150 (30.80)              | 23 (23.5)               | 1,466 (19.1)            | <0.001  |
|          | <b>Laboratory, median (IQR)</b>  |       |           |                         |                         |                          |                         |                         |         |
|          | eGFR, ml/min/1.73 m <sup>2</sup> | 7,667 | 0         | 5.0 (3.8, 8.0)          | 7.8 (4.8, 12.0)         | 6.4 (4.4, 9.8)           | 4.6 (3.4, 6.8)          | 6.0 (4.0, 10.2)         | <0.001  |
|          | Phosphorus, mg/dL                | 7,682 | 0         | 5.6 (5.0, 6.6)          | 5.5 (5.0, 6.3)          | 5.91 (1.61)              | 6.6 (6, 7.6)            | 5.7 (5.0, 6.6)          | <0.001  |
|          | PTH, pg/dL                       | 4,364 | 43        | 319.6<br>(141.8, 639.2) | 168.4<br>(81.0, 335.0)  | 319.59<br>(165.4, 696.1) | 314<br>(161.6, 705.3)   | 242.7<br>(110.2, 509.3) | <0.001  |
|          | Calcium, mg/dL                   | 7,682 | 0         | 9.4 (8.8, 10.0)         | 9.4 (8.8, 9.9)          | 9.33 (1.03)              | 9.9 (9.4, 10.6)         | 9.4 (8.8, 10.0)         | 0.002   |
|          | Hemoglobin, g/dL                 | 7,682 | 0         | 10.5 (9.1, 11.9)        | 9.7 (8.4, 11.1)         | 10.3 (8.9, 11.4)         | 9.2 (7.4, 10.5)         | 10.1 (8.8, 11.5)        | <0.001  |
|          | Hematocrit, %                    | 2,204 | 71        | 29.0<br>(25.0, 33.0)    | 29.0<br>(24.8, 33.0)    | 31.2<br>(26.4, 34.6)     | 28.2<br>(23.5, 31.4)    | 29.1<br>(25.0, 33.1)    | 0.001   |
|          | Albumin, g/dL                    | 7,682 | 0         | 3.6 (3.1, 4.0)          | 3.4 (2.9, 3.8)          | 3.6 (3.1, 4.0)           | 4.1 (3.7, 4.5)          | 3.5 (3.0, 3.9)          | <0.001  |
|          | Sodium, mEq/L                    | 7,639 | 1         | 138.0<br>(136.0, 140.0) | 138.0<br>(134.0, 140.0) | 138.0<br>(135.0, 141.0)  | 137.5<br>(135.0, 140.0) | 138.0<br>(135.0, 140.0) | <0.001  |
|          | Potassium, mEq/L                 | 4,025 | 48        | 4.6 (4.0, 5.0)          | 4.5 (4.0, 5.0)          | 4.6 (4.2, 5.0)           | 4.7 (4.2, 5.2)          | 4.6 (4.0, 5.0)          | 0.004   |
|          | Chloride, mEq/L                  | 7,645 | 0         | 100.0<br>(97.0, 104.0)  | 103.0<br>(99.0, 107.0)  | 103.0<br>(99.0, 106.0)   | 100.0<br>(97.0, 105.0)  | 101.0<br>(98.0, 105.0)  | <0.001  |

**Table S4** Baseline characteristics of patients included in the actual treatment-pattern analysis by treatment approach (cont.)

| Outcomes | Variables            | N     | % Missing | Treatment group         |                         |                         |                         | Total                   | p-value |
|----------|----------------------|-------|-----------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|          |                      |       |           | No-PBs                  | CBPBs-<br>CBPBs         | CBPBs-<br>NCBPBs        | CBPBs-<br>aluminum      |                         |         |
| OS       | Carbondioxide, mEq/L | 7,650 | 0         | 22.8<br>(20.0, 25.5)    | 21.0<br>(18.0, 24.4)    | 21.4<br>(18.6, 24.5)    | 21.0<br>(18.0, 24.0)    | 22.0<br>(19.0, 25.0)    | <0.001  |
|          | Uric, mg/dL          | 6,848 | 11        | 7.0 (5.6, 8.5)          | 7.8 (6.2, 9.5)          | N=487                   | 7.6 (6.2, 9.1)          | 7.4 (5.9, 9.0)          | <0.001  |
|          | Glucose, mg/dL       | 4,037 | 47        | 101.0<br>(87.0, 135.0)  | 102.6<br>(88.2, 137.0)  | 102.0<br>(90.0, 136.0)  | 101.0<br>(89.0, 128.0)  | 102.6<br>(88.2, 136.8)  | 0.769   |
|          | HbA1C, mg%           | 2,851 | 63        | 6.3 (5.6, 7.3)          | 6.3 (5.6, 7.3)          | 6.2 (5.4, 6.9)          | 6.1 (5.6, 7.4)          | 6.3 (5.6, 7.3)          | 0.039   |
|          | LDL, mg/dL           | 4,682 | 39        | 101.0<br>(79.0, 128.0)  | 104.0<br>(82.0, 132.8)  | 101.0<br>(78.0, 129.5)  | 103.0<br>(82.0, 135.0)  | 102.6<br>(80.0, 130.0)  | 0.043   |
|          | Cholesterol, mg/dL   | 7,160 | 7         | 179.0<br>(150.0, 215.0) | 181.0<br>(150.0, 218.0) | 177.0<br>(149.0, 211.0) | 185.0<br>(152.6, 218.2) | 180.0<br>(150.0, 216.0) | 0.156   |
|          | Triglyceride, mg/dL  | 6,643 | 14        | 115.5<br>(82.0, 158.0)  | 128.0<br>(92.0, 184.0)  | 126.0<br>(91.0, 178.0)  | 127.2<br>(94.0, 178.0)  | 122.0<br>(87.0, 172.0)  | <0.001  |
|          | HDL, mg/dL           | 4,479 | 42        | 45.0<br>(37, 56.0)      | 45.0<br>(37, 56.0)      | 45.0<br>(37.0, 55.0)    | 49.0<br>(42.0, 55.0)    | 45.0<br>(37.0, 56.0)    | 0.868   |
|          | Iron, ug/dL          | 2,746 | 64        | 51.0<br>(34.5, 71.0)    | 52.0<br>(35.0, 73.0)    | 56.5<br>(41.9, 78.0)    | 56.0<br>(42.5, 75.0)    | 52.0<br>(36.0, 73.0)    | 0.153   |
|          | TIBC, ug/dL          | 2,759 | 64        | 208.9<br>(172.6, 245.0) | 206.0<br>(173.0, 246.9) | 210.8<br>(171.3, 243.8) | 214.0<br>(185.0, 255.0) | 207.0<br>(173.0, 246.0) | 0.793   |
|          | Ferritin, ng/dL      | 441   | 94        | 188.0<br>(165.0, 217.0) | 181.5<br>(156.0, 213.0) | 175.0<br>(159.0, 196.0) | 193.0<br>(158.0, 211.5) | 182.0<br>(157.0, 211.0) | 0.775   |
|          | antiHCV              | 7,682 | 0         | 38 (1.02)               | 44 (1.31)               | 4 (0.82)                | 3 (3.06)                | 89 (1.16)               | 0.297   |
|          | antiHBs              | 7,682 | 0         | 1041 (27.86)            | 184 (5.47)              | 25 (5.13)               | 2 (2.04)                | 1252 (16.30)            | <0.001  |

**Table S4** Baseline characteristics of patients included in the actual treatment-pattern analysis by treatment approach (cont.)

| Outcomes | Variables                               | N     | % Missing | Treatment group |                 |                  |                    | Total         | p-value |
|----------|-----------------------------------------|-------|-----------|-----------------|-----------------|------------------|--------------------|---------------|---------|
|          |                                         |       |           | No-PBs          | CBPBs-<br>CBPBs | CBPBs-<br>NCBPBs | CBPBs-<br>aluminum |               |         |
| CVD      | <b>Total number of patients, n (%)</b>  |       |           | 3,233 (53.8)    | 2,449 (40.8)    | 240 (4.0)        | 85 (1.4)           | 6,007 (100.0) |         |
|          | <b>Hospital, n(%)</b>                   | 6,007 | 0         |                 |                 |                  |                    |               | <0.001  |
|          | Ramathibodi Hospital                    |       |           | 2,825 (87.38)   | 1,575 (64.31)   | 130 (54.17)      | 25 (29.41)         | 4,555 (75.83) |         |
|          | Bhumibol Hospital                       |       |           | 408 (12.62)     | 874 (35.69)     | 110 (45.83)      | 60 (70.59)         | 1,452 (24.17) |         |
|          | <b>age (years), mean(SD)</b>            | 6,007 | 0         | 46.23 (16.11)   | 59.45 (16.21)   | 56.88 (14.48)    | 50.69 (15.47)      | 52.20 (17.36) | <0.001  |
|          | <b>Female, n(%)</b>                     | 6,007 | 0         | 1,353 (41.85)   | 1,314 (53.65)   | 118 (49.17)      | 42 (49.41)         | 2,827 (47.06) | <0.001  |
|          | <b>Reimbursement, n(%)</b>              | 6,007 | 0         |                 |                 |                  |                    |               | <0.001  |
|          | non-CSMBS                               |       |           | 2,478 (76.65)   | 1,405 (57.37)   | 55 (22.92)       | 77 (90.59)         | 4,002 (66.62) |         |
|          | CSMBS                                   |       |           | 755 (23.35)     | 1,044 (42.63)   | 185 (77.08)      | 8 (9.41)           | 2,005 (33.38) |         |
|          | <b>BMI (kg/m<sup>2</sup>), mean(SD)</b> | 2,602 | 57        | 24.06 (4.68)    | 24.70 (5.30)    | 25.30 (4.99)     | 23.97 (4.49)       | 24.27 (4.86)  | 0.029   |
|          | <b>Marital status, n(%)</b>             | 6,007 | 0         |                 |                 |                  |                    |               | <0.001  |
|          | Single                                  |       |           | 1,114 (34.46)   | 614 (25.07)     | 46 (19.17)       | 41 (48.24)         | 1,815 (30.21) |         |
|          | Married                                 |       |           | 1,833 (56.70)   | 1,495 (61.05)   | 163 (67.92)      | 32 (37.65)         | 3,523 (58.65) |         |
|          | Divorced/widowed                        |       |           | 281 (8.69)      | 333 (13.60)     | 30 (12.50)       | 12 (14.12)         | 656 (10.92)   |         |
|          | Priest                                  |       |           | 0 (0.00)        | 1 (0.04)        | 0 (0.00)         | 0 (0.00)           | 1 (0.02)      |         |
|          | Unknown                                 |       |           | 5 (0.15)        | 6 (0.24)        | 1 (0.42)         | 0 (0.00)           | 12 (0.20)     |         |
|          | <b>Education levels, n(%)</b>           | 2,988 | 50        |                 |                 |                  |                    |               | <0.001  |
|          | Primary level or less                   |       |           | 503 (21.86)     | 186 (29.48)     | 12 (25.53)       | 2 (22.22)          | 703 (23.53)   |         |
|          | Secondary level                         |       |           | 712 (30.94)     | 123 (19.49)     | 5 (10.64)        | 3 (33.33)          | 843 (28.21)   |         |
|          | University level or more                |       |           | 1,086 (47.20)   | 322 (51.03)     | 30 (63.83)       | 4 (44.44)          | 1,442 (48.26) |         |
|          | <b>Renal replacement therapy, n(%)</b>  | 6,007 | 0         |                 |                 |                  |                    |               | <0.001  |
|          | No RRT                                  |       |           | 2,007 (62.08)   | 1,874 (76.52)   | 187 (77.92)      | 41 (48.24)         | 4,023 (66.97) |         |
|          | RRT                                     |       |           | 1,226 (37.92)   | 575 (23.48)     | 53 (22.08)       | 44 (51.76)         | 1,984 (33.03) |         |
|          | <b>Comorbid, n(%)</b>                   |       |           |                 |                 |                  |                    |               |         |
|          | Hypertension                            | 6,007 | 0         | 1,406 (43.49)   | 2,341 (95.59)   | 237 (98.75)      | 84 (98.82)         | 4,071 (67.77) | <0.001  |
|          | Diabetes                                | 6,007 | 0         | 588 (18.19)     | 1,144 (46.71)   | 103 (42.92)      | 38 (44.71)         | 1,890 (31.46) | <0.001  |

**Table S4** Baseline characteristics of patients included in the actual treatment-pattern analysis by treatment approach (cont.)

| Outcomes | Variables                        | N     | % Missing | Treatment group         |                        |                         |                         | Total                   | p-value |
|----------|----------------------------------|-------|-----------|-------------------------|------------------------|-------------------------|-------------------------|-------------------------|---------|
|          |                                  |       |           | No-PBs                  | CBPBs-<br>CBPBs        | CBPBs-<br>NCBPBs        | CBPBs-<br>aluminum      |                         |         |
| CVD      | Diabetes                         | 6,007 | 0         | 588 (18.19)             | 1,144 (46.71)          | 103 (42.92)             | 38 (44.71)              | 1,890 (31.46)           | <0.001  |
|          | Dyslipidemia                     | 6,007 | 0         | 610 (18.87)             | 1,526 (62.31)          | 158 (65.83)             | 40 (47.06)              | 2,357 (39.24)           | <0.001  |
|          | Bone disorder related ESRD       | 6,007 | 0         | 41 (1.27)               | 214 (8.74)             | 16 (6.67)               | 2 (2.35)                | 285 (4.74)              | <0.001  |
|          | Gout                             | 6,007 | 0         | 173 (5.35)              | 366 (14.94)            | 15 (6.25)               | 13 (15.29)              | 611 (10.17)             | <0.001  |
|          | Liver disease                    | 6,007 | 0         | 108 (3.34)              | 115 (4.70)             | 19 (7.92)               | 5 (5.88)                | 254 (4.23)              | <0.001  |
|          | SLE                              | 6,007 | 0         | 38 (1.18)               | 64 (2.61)              | 2 (0.83)                | 5 (5.88)                | 113 (1.88)              | <0.001  |
|          | Cancer                           | 6,007 | 0         | 19 (0.59)               | 24 (0.98)              | 0 (0.00)                | 0 (0.00)                | 43 (0.72)               | 0.240   |
|          | AIDS                             | 6,007 | 0         | 5 (0.15)                | 19 (0.78)              | 1 (0.42)                | 1 (1.18)                | 27 (0.45)               | 0.008   |
|          | GI disorder                      | 6,007 | 0         | 84 (2.60)               | 238 (9.72)             | 26 (10.83)              | 14 (16.47)              | 377 (6.28)              | <0.001  |
|          | Chronic pulmonary disease        | 6,007 | 0         | 23 (0.71)               | 44 (1.80)              | 8 (3.33)                | 0 (0.00)                | 78 (1.30)               | <0.001  |
|          | Tumor lysis syndrome             | 6,007 | 0         | 1 (0.03)                | 0 (0.00)               | 0 (0.00)                | 0 (0.00)                | 1 (0.02)                | 0.930   |
|          | Hypoparathyroidism               | 6,007 | 0         | 0 (0.00)                | 3 (0.12)               | 0 (0.00)                | 1 (1.18)                | 7 (0.12)                | <0.001  |
|          | Secondary<br>Hyperparathyroidism | 6,007 | 0         | 220 (6.80)              | 719 (29.36)            | 73 (30.42)              | 53 (62.35)              | 1,153 (19.19)           | <0.001  |
|          | <b>Laboratory, median(IQR)</b>   |       |           |                         |                        |                         |                         |                         |         |
|          | eGFR, ml/min/1.73 m <sup>2</sup> | 5,997 | 0         | 4.8 (3.6, 7.2)          | 7.2 (4.6, 11.6)        | 5.8 (4.2, 9.4)          | 4.0 (3.2, 5.4)          | 5.4 (3.8, 9.0)          | <0.001  |
|          | Phosphorus, mg/dL                | 6,007 | 0         | 5.6 (5.0, 6.6)          | 5.4 (4.8, 6.4)         | 5.4 (4.9, 6.6)          | 6.6 (5.7, 7.5)          | 5.6 (5.0, 6.6)          | <0.001  |
|          | PTH, pg/dL                       | 3,575 | 40        | 341.8<br>(157.0, 658.0) | 183.0<br>(86.4, 365.0) | 257.6<br>(118.0, 519.8) | 350.0<br>(170.0, 701.6) | 269.6<br>(120.0, 544.0) | <0.001  |
|          | Calcium, mg/dL                   | 6,007 | 0         | 9.6<br>(9.1, 10.2)      | 9.4<br>(8.9, 9.9)      | 9.4<br>(9.0, 10.0)      | 10.3<br>(9.6, 10.8)     | 9.6<br>(9.0, 10.1)      | <0.001  |
|          | Hemoglobin, g/dL                 | 5,296 | 12        | 10.6 (9.1, 11.9)        | 9.7 (8.4, 11.0)        | 10.2 (8.7, 11.2)        | 10.2 (8.8, 11.3)        | 10.2 (8.8, 11.6)        | <0.001  |
|          | Hematocrit, %                    | 1,693 | 72        | 28.9<br>(24.6, 33.0)    | 28.5<br>(24.0, 32.7)   | 31.2<br>(26.4, 34.4)    | 31.5<br>(27.9, 34.2)    | 29.1<br>(24.6, 33.1)    | <0.001  |
|          | Albumin, g/dL                    | 6,007 | 0         | 3.7 (3.2, 4.1)          | 3.5 (2.9, 3.9)         | 3.7 (3.3, 4.2)          | 4.2 (3.6, 4.6)          | 3.6 (3.1, 4.0)          | 0.815   |

**Table S4** Baseline characteristics of patients included in the actual treatment-pattern analysis by treatment approach (cont.)

| Outcomes | Variables           | N     | % Missing | Treatment group         |                         |                         |                         | Total                   | p-value |
|----------|---------------------|-------|-----------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|          |                     |       |           | No-PBs                  | CBPBs-CBPBs             | CBPBs-NCBPBs            | CBPBs-aluminum          |                         |         |
| CVD      | Chloride, mEq/L     | 5,973 | 1         | 100.0<br>(97.0, 103.0)  | 103.0<br>(99.0, 107.0)  | 103.0<br>(99.0, 106.0)  | 98.0<br>(95.0, 101.0)   | 101.0<br>(97.0, 105.0)  | <0.001  |
|          | Uric, mg/dL         | 5,363 | 11%       | 7.0 (5.6, 8.4)          | 7.8 (6.2, 9.3)          | 7.8 (6.5, 9.6)          | 6.9 (5.7, 8.6)          | 7.3 (5.9, 8.8)          | <0.001  |
|          | Glucose, mg/dL      | 2,921 | 51%       | 100.4<br>(86.4, 131.0)  | 102.0<br>(88.2, 134.0)  | 99.0<br>(88.0, 136.0)   | 96.0<br>(86.0, 119.0)   | 100.8<br>(87.0, 133.0)  | 0.122   |
|          | HbA1C, mg%          | 1,889 | 69%       | 6.3 (5.6, 7.3)          | 6.2 (5.5, 7.3)          | 6.1 (5.4, 6.9)          | 5.8 (5.2, 6.7)          | 6.2 (5.5, 7.2)          | <0.001  |
|          | LDL, mg/dL          | 3,395 | 43%       | 104.0<br>(81.0, 129.0)  | 108.0<br>(85.0, 136.2)  | 101.5<br>(80.0, 135.0)  | 96.0<br>(78.0, 134.0)   | 105.0<br>(82.0, 132.8)  | 0.296   |
|          | Cholesterol, mg/dL  | 5,555 | 8%        | 180.8<br>(152.6, 216.0) | 184.0<br>(154.0, 221.0) | 179.0<br>(150.5, 211.0) | 180.0<br>(149.0, 218.0) | 182.0<br>(153.0, 218.0) | 1.000   |
|          | Triglyceride, mg/dL | 5,156 | 14%       | 115.0<br>(82.0, 157.0)  | 128.0<br>(92.0, 181.4)  | 133.0<br>(96.4, 187.0)  | 117.0<br>(92.0, 157.0)  | 121.0<br>(86.0, 168.6)  | 0.015   |
|          | HDL, mg/dL          | 3,254 | 46%       | 46.0<br>(37.0, 56.0)    | 45.0<br>(38, 58.0)      | 47.0<br>(37.0, 57.0)    | 49.9<br>(41.0, 61.0)    | 46.0<br>(37.8, 57.0)    | 1.000   |
|          | Iron, ug/dL         | 1,941 | 68%       | 52.8<br>(36.0, 74.0)    | 54.1<br>(38.0, 75.0)    | 60.0<br>(44.0, 83.0)    | 61.0<br>(45.0, 82.0)    | 55.0<br>(39.0, 75.0)    | 0.008   |
|          | TIBC, ug/dL         | 1,950 | 68%       | 209.0<br>(174.3, 244.0) | 207.0<br>(175.0, 247.5) | 212.5<br>(172.2, 239.5) | 205.0<br>(179.0, 239.0) | 208.0<br>(176.0, 244.0) | 0.951   |
|          | Ferritin, ng/dL     | 403   | 93%       | 190.0<br>(166.0, 218.0) | 179.0<br>(157.0, 210.0) | 179.0<br>(167.0, 197.0) | 179.5<br>(158.0, 203.5) | 181.0<br>(157.0, 209.0) | 0.474   |
|          | antiHCV             | 6,007 | 0%        | 30 (0.93)               | 32 (1.31)               | 2 (0.83)                | 5 (5.88)                | 71 (1.18)               | 0.001   |
|          | antiHBs             | 6,007 | 0%        | 983 (30.41)             | 98 (4.00)               | 11 (4.58)               | 9 (10.59)               | 1144 (19.04)            | <0.001  |

**Table S4** Baseline characteristics of patients included in the actual treatment-pattern analysis by treatment approach (cont.)

| Outcomes       | Variables                               | N     | % Missing | Treatment group |               |               |                | Total         | p-value |
|----------------|-----------------------------------------|-------|-----------|-----------------|---------------|---------------|----------------|---------------|---------|
|                |                                         |       |           | No-PBs          | CBPBs-CBPBs   | CBPBs-NCBPBs  | CBPBs-aluminum |               |         |
| Bone disorders | <b>Total number of patients, n (%)</b>  |       |           | 3,658 (51.0)    | 3,018 (42.1)  | 400 (5.6)     | 91 (1.3)       | 7,167 (100.0) |         |
|                | <b>Hospital, n(%)</b>                   | 7,167 | 0         |                 |               |               |                |               | <0.001  |
|                | Ramathibodi Hospital                    |       |           | 3,229 (88.27)   | 2,046 (67.79) | 256 (64.00)   | 32 (35.16)     | 5,563 (77.62) |         |
|                | Bhumibol Hospital                       |       |           | 429 (11.73)     | 972 (32.21)   | 144 (36.00)   | 59 (64.84)     | 1,604 (22.38) |         |
|                | <b>age (years), mean(SD)</b>            | 7,167 | 0         | 48.05 (16.83)   | 60.60 (15.97) | 61.42 (14.66) | 50.81 (15.81)  | 53.98 (17.46) | <0.001  |
|                | <b>Female, n(%)</b>                     | 7,167 | 0         | 1510 (41.28)    | 1,524 (50.50) | 180 (45.00)   | 45 (49.45)     | 3,259 (45.47) | <0.001  |
|                | <b>Reimbursement, n(%)</b>              | 7,167 | 0         |                 |               |               |                |               | <0.001  |
|                | non-CSMBS                               |       |           | 2,691 (73.56)   | 1,714 (56.79) | 88 (22.00)    | 78 (85.71)     | 4,571 (63.78) |         |
|                | CSMBS                                   |       |           | 967 (26.44)     | 1,304 (43.21) | 312 (78.00)   | 13 (14.29)     | 2,596 (36.22) |         |
|                | <b>BMI (kg/m<sup>2</sup>), mean(SD)</b> | 3,041 | 58        | 24.13 (4.73)    | 2,4.93 (5.36) | 25.28 (4.86)  | 23.21 (4.16)   | 24.42 (4.95)  | <0.001  |
|                | <b>Marital status, n(%)</b>             | 7,167 | 0         |                 |               |               |                |               | <0.001  |
|                | Single                                  |       |           | 1,180 (32.26)   | 703 (23.29)   | 73 (18.25)    | 33 (36.26)     | 1,989 (27.75) |         |
|                | Married                                 |       |           | 2,128 (58.17)   | 1,886 (62.49) | 284 (71.00)   | 47 (51.65)     | 4,345 (60.63) |         |
|                | Divorced/widowed                        |       |           | 346 (9.46)      | 419 (13.88)   | 42 (10.50)    | 11 (12.09)     | 818 (11.41)   |         |
|                | Priest                                  |       |           | 0 (0.00)        | 2 (0.07)      | 0 (0.00)      | 0 (0.00)       | 2 (0.03)      |         |
|                | Unknown                                 |       |           | 4 (0.11)        | 8 (0.27)      | 1 (0.25)      | 0 (0.00)       | 13 (0.18)     |         |
|                | <b>Education levels, n(%)</b>           | 3,417 | 52        |                 |               |               |                |               | <0.001  |
|                | Primary level or less                   |       |           | 580 (23.00)     | 245 (31.17)   | 23 (22.55)    | 4 (57.14)      | 852 (24.93)   |         |
|                | Secondary level                         |       |           | 760 (30.13)     | 170 (21.63)   | 9 (8.82)      | 1 (14.29)      | 940 (27.51)   |         |
|                | University level or more                |       |           | 1,182 (46.87)   | 371 (47.20)   | 70 (68.63)    | 2 (28.57)      | 1,625 (47.56) |         |
|                | <b>Renal replacement therapy, n(%)</b>  | 7,167 | 0         |                 |               |               |                |               | <0.001  |
|                | No RRT                                  |       |           | 2,268 (62.00)   | 2,221 (74.46) | 141 (35.52)   | 29 (31.87)     | 4,659 (65.35) |         |
|                | RRT                                     |       |           | 1,390 (38.00)   | 762 (25.54)   | 256 (64.48)   | 62 (68.13)     | 2,470 (34.65) |         |
|                | <b>Comorbid, n(%)</b>                   |       |           |                 |               |               |                |               |         |
|                | Hypertension                            | 7,167 | 0         | 1,803 (49.29)   | 2,876 (96.41) | 297 (99.25)   | 90 (98.90)     | 5,166 (72.46) | <0.001  |

**Table S4** Baseline characteristics of patients included in the actual treatment-pattern analysis by treatment approach (cont.)

| Outcomes       | Variables                        | N     | % Missing | Treatment group         |                         |                         |                         | Total                   | p-value |
|----------------|----------------------------------|-------|-----------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|                |                                  |       |           | No-PBs                  | CBPBs-CBPs              | CBPBs-NCBPs             | CBPBs-aluminum          |                         |         |
| Bone disorders | Diabetes                         | 7,167 | 0         | 837 (22.88)             | 1,560 (52.30)           | 238 (59.50)             | 44 (48.35)              | 2,679 (37.58)           | <0.001  |
|                | Dyslipidemia                     | 7,167 | 0         | 911 (24.90)             | 2,033 (68.15)           | 329 (82.25)             | 52 (57.14)              | 3,325 (46.64)           | <0.001  |
|                | CVD                              | 7,167 | 0         | 477 (13.04)             | 901 (30.20)             | 185 (46.25)             | 28 (30.77)              | 1,591 (22.32)           | <0.001  |
|                | Gout                             | 7,167 | 0         | 128 (3.50)              | 207 (6.94)              | 45 (11.25)              | 7 (7.69)                | 387 (5.43)              | <0.001  |
|                | Liver disease                    | 7,167 | 0         | 143 (3.91)              | 173 (5.73)              | 41 (10.33)              | 2 (2.20)                | 341 (4.76)              | 0.002   |
|                | SLE                              | 7,167 | 0         | 49 (1.34)               | 64 (2.12)               | 9 (2.27)                | 1 (1.10)                | 119 (1.66)              | 0.139   |
|                | Cancer                           | 7,167 | 0         | 25 (0.68)               | 28 (0.93)               | 3 (0.76)                | 0 (0.00)                | 53 (0.74)               | 0.261   |
|                | AIDS                             | 7,167 | 0         | 6 (0.16)                | 23 (0.76)               | 2 (0.50)                | 0 (0.00)                | 30 (0.42)               | 0.004   |
|                | GI disorder                      | 7,167 | 0         | 115 (3.14)              | 313 (10.37)             | 15 (7.35)               | 9 (9.89)                | 480 (6.70)              | <0.001  |
|                | Chronic pulmonary disease        | 7,167 | 0         | 47 (1.28)               | 96 (3.18)               | 14 (3.50)               | 0 (0.00)                | 157 (2.19)              | <0.001  |
|                | Tumor lysis syndrome             | 7,167 | 0         | 2 (0.05)                | 0 (0.00)                | 0 (0.00)                | 0 (0.00)                | 2 (0.03)                | 0.751   |
|                | Hypoparathyroidism               | 7,167 | 0         | 17 (0.46)               | 44 (1.46)               | 3 (0.75)                | 3 (3.30)                | 67 (0.93)               | 0.282   |
|                | Secondary Hyperparathyroidism    | 7,167 | 0         | 275 (7.52)              | 833 (27.92)             | 195 (48.75)             | 54 (59.34)              | 1,357 (19.03)           | <0.001  |
|                | <b>Laboratory, median(IQR)</b>   |       |           |                         |                         |                         |                         |                         |         |
|                | eGFR, ml/min/1.73 m <sup>2</sup> | 7,155 | 0         | 6.2 (4.2, 17.8)         | 6.6 (4.6, 11.4)         | 4.2 (3.4, 5.6)          | 4.8 (3.6, 6.6)          | 6.4 (4.4, 12.6)         | <0.001  |
|                | Phosphorus, mg/dL                | 7,167 | 0         | 5.6 (5.0, 6.6)          | 5.3 (4.8, 6.4)          | 6.2 (5.4, 7.4)          | 6.6 (6.0, 7.7)          | 5.6 (5.0, 6.6)          | <0.001  |
|                | PTH, pg/dL                       | 4,071 | 43        | 322.6<br>(141.8, 640.6) | 178.0<br>(89.0, 357.4)  | 289.0<br>(146.0, 634.6) | 313.5<br>(164.9, 657.6) | 253.0<br>(115.8, 527.6) | <0.001  |
|                | Calcium, mg/dL                   | 7,167 | 0         | 9.4<br>(8.8, 10.0)      | 9.3<br>(8.7, 9.8)       | 9.7<br>(9.1, 10.5)      | 9.8<br>(9.3, 10.5)      | 9.4<br>(8.8, 10.0)      | <0.001  |
|                | Hemoglobin, g/dL                 | 7,167 | 0         | 10.6 (9.1, 11.9)        | 9.7 (8.4, 11.1)         | 10.9 (9.6, 11.8)        | 9.1 (7.4, 10.5)         | 10.2 (8.8, 11.5)        | <0.001  |
|                | Hematocrit, %                    | 2,014 | 72        | 29.0<br>(25.0, 33.0)    | 29.0<br>(24.7, 33.0)    | 32.9<br>(29.8, 36.4)    | 28.2<br>(23.2, 31.6)    | 29.1<br>(25.0, 33.1)    | 0.009   |
|                | Albumin, g/dL                    | 7,167 | 0         | 3.6 (3.2, 4.0)          | 3.4 (2.9, 3.8)          | 3.7 (3.3, 4.3)          | 3.7 (3.2, 4.3)          | 3.5 (3.0, 3.9)          | <0.001  |
|                | Sodium, mEq/L                    | 7,127 | 1         | 138.0<br>(136.0, 140.0) | 138.0<br>(135.0, 140.0) | 138.0<br>(136.0, 140.0) | 138.0<br>(135.0, 140.0) | 138.0<br>(135.0, 140.0) | <0.001  |

**Table S4** Baseline characteristics of patients included in the actual treatment-pattern analysis by treatment approach (cont.)

| Outcomes       | Variables           | N     | % Missing | Treatment group         |                         |                         |                         | Total                   | p-value |
|----------------|---------------------|-------|-----------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|---------|
|                |                     |       |           | No-PBs                  | CBPBs-CBPBs             | CBPBs-NCBPBs            | CBPBs-aluminum          |                         |         |
| Bone disorders | Potassium, mEq/L    | 3,617 | 50        | 4.6 (4.0, 5.0)          | 4.5 (4.1, 5.0)          | 4.7 (4.2, 5.1)          | 4.7 (4.2, 5.2)          | 4.6 (4.1, 5.0)          | 0.012   |
|                | Chloride, mEq/L     | 7,133 | 0         | 100.0<br>(97.0, 103.0)  | 103.0<br>(99.0, 107.0)  | 99.0<br>(97.0, 102.0)   | 101.0<br>(97.0, 105.0)  | 101.0<br>(98.0, 105.0)  | <0.001  |
|                | Uric, mg/dL         | 6,365 | 11        | 7.0 (5.6, 8.5)          | 7.8 (6.3, 9.4)          | 6.7 (5.6, 8.0)          | 7.6 (6.2, 9.1)          | 7.4 (5.9, 9.0)          | <0.001  |
|                | Glucose, mg/dL      | 3,609 | 50        | 101.0<br>(87.0, 135.0)  | 103.0<br>(88.2, 137.0)  | 98.0<br>(86.0, 133.2)   | 104.4<br>(89.0, 128.0)  | 102.6<br>(88.0, 136.0)  | 0.415   |
|                | HbA1C, mg%          | 2,501 | 65        | 6.3 (5.6, 7.3)          | 6.3 (5.6, 7.3)          | 5.8 (5.3, 6.6)          | 6.0 (5.5, 7.1)          | 6.3 (5.6, 7.3)          | 0.018   |
|                | LDL, mg/dL          | 4,247 | 41        | 101.8<br>(79.0, 128.0)  | 104.3<br>(82.0, 133.0)  | 94.0<br>(71.0, 119.0)   | 102.0<br>(78.0, 144.0)  | 103.0<br>(81.0, 131.0)  | 0.013   |
|                | Cholesterol, mg/dL  | 6,656 | 7         | 179.0<br>(151.0, 215.0) | 182.0<br>(150.0, 218.0) | 168.0<br>(141.0, 199.0) | 184.5<br>(148.0, 223.0) | 180.0<br>(150.0, 216.0) | 0.046   |
|                | Triglyceride, mg/dL | 6,157 | 14        | 116.0<br>(82.0, 158.0)  | 128.0<br>(92.0, 185.0)  | 113.0<br>(80.0, 160.0)  | 127.0<br>(91.0, 178.0)  | 122.0<br>(86.8, 172.0)  | <0.001  |
|                | HDL, mg/dL          | 4,056 | 43        | 45.0 (37.0, 56.0)       | 45.0 (37, 56.0)         | 45.0 (36.0, 55.0)       | 49.0 (41.0, 56.0)       | 45.0 (37.0, 56.0)       | 0.897   |
|                | Iron, ug/dL         | 2,447 | 66        | 51.0<br>(35.0, 71.5)    | 52.0<br>(35.9, 73.0)    | 58.0<br>(43.0, 75.0)    | 55.0<br>(42.0, 73.0)    | 52.0<br>(36.0, 73.0)    | 0.087   |
|                | TIBC, ug/dL         | 2,459 | 66        | 208.9<br>(173.0, 245.0) | 206.7<br>(174.0, 245.0) | 209.0<br>(182.7, 240.0) | 208.6<br>(184.0, 253.0) | 207.8<br>(173.7, 245.0) | 0.825   |
|                | Ferritin, ng/dL     | 405   | 94        | 188.0<br>(165.0, 217.0) | 181.0<br>(156.0, 212.0) | 178.0<br>(157.0, 202.0) | 192.0<br>(151.0, 226.0) | 181.0<br>(157.0, 211.0) | 0.863   |
|                | antiHCV             | 7,167 | 0         | 37 (1.01)               | 38 (1.26)               | 3 (0.75)                | 3 (3.30)                | 81 (1.13)               | 0.244   |
|                | antiHBs             | 7,167 | 0         | 1038 (28.38)            | 147 (4.87)              | 19 (4.75)               | 2 (2.20)                | 1206 (16.83)            | <0.001  |

Abbreviations: Body mass index; (BMI), CBPBs; Calcium-based phosphate binders, CVD; cardiovascular disease, CSMBS; Civil Servant Medical Benefit Scheme, eGFR; estimated Glomerular Filtration Rate, ESRD; End-stage renal disease, HbA1C; Hemoglobin A1C, HDL; High-Density Lipoprotein, HIV; human immunodeficiency virus, IQR; interquartile range, ITT; Intention to treat, GI; Gastrointestinal tract, LDL; Low-Density Lipoprotein, NCBPBs; N; number, Non-calcium-based phosphate binders i.e., lanthanum or sevelamer; OS; overall survival outcome, PBs; Phosphate binders, PPA; Per-protocol analysis, SLE; PTH; Parathyroid hormone levels, RRT, Renal Replacement Therapy, Systemic lupus erythematosus, TIBC; Total iron binding capacity



**Table S5.** Median (IQR) follow-up time by treatment approach and outcomes

| Treatment approaches                             | Median (Q1, Q3) follow-up time |                       |                         |                                       |
|--------------------------------------------------|--------------------------------|-----------------------|-------------------------|---------------------------------------|
|                                                  | No-PBs<br>No-PBs*              | CBPBs<br>CBPBs-CBPBs* | NCBPBs<br>CBPBs-NCBPBs* | Aluminum hydroxide<br>CBPBs-aluminum* |
| <b>Primary outcome: OS</b>                       |                                |                       |                         |                                       |
| ITT                                              | 3.88<br>(1.97, 6.31)           | 4.14<br>(1.93, 7.19)  | 2.77<br>(1.43, 5.48)    | 4.72<br>(1.91, 8.90)                  |
| PPA                                              | 3.88<br>(1.97, 6.31)           | 3.41<br>(1.54, 6.05)  | 2.29<br>(0.89, 3.93)    | 0.79<br>(0.45, 1.85)                  |
| Actual treatment-pattern*                        | 3.88<br>(1.97, 6.31)           | 3.77<br>(1.74, 6.69)  | 5.14<br>(3.04, 8.28)    | 6.36<br>(3.52, 9.24)                  |
| <b>Primary outcome: Time to CVD</b>              |                                |                       |                         |                                       |
| ITT                                              | 1.98<br>(0.77, 4.13)           | 2.22<br>(0.72, 4.83)  | 2.07<br>(0.67, 3.99)    | 2.06<br>(0.54, 6.21)                  |
| PPA                                              | 1.98<br>(0.77, 4.13)           | 1.92<br>(0.64, 4.51)  | 1.35<br>(0.57, 2.61)    | 0.77<br>(0.33, 0.78)                  |
| Actual treatment-pattern*                        | 1.98<br>(0.77, 4.13)           | 1.79<br>(0.60, 4.34)  | 4.16<br>(2.45, 6.49)    | 3.84<br>(2.58, 7.10)                  |
| <b>Secondary outcome: Time to bone disorders</b> |                                |                       |                         |                                       |
| ITT                                              | 3.84<br>(1.94, 6.28)           | 3.82<br>(1.77, 6.79)  | 2.57<br>(1.37, 5.44)    | 3.75<br>(1.73, 8.19)                  |
| PPA                                              | 3.84<br>(1.94, 6.28)           | 3.14<br>(1.37, 5.75)  | 2.29<br>(0.81, 4.01)    | 0.79<br>(0.45, 1.85)                  |
| Actual treatment-pattern*                        | 3.84<br>(1.94, 6.28)           | 3.56<br>(1.59, 6.35)  | 4.88<br>(2.78, 7.90)    | 6.17<br>(3.51, 8.74)                  |

Abbreviations: CBPBs; Calcium-based phosphate binders, CVD; cardiovascular disease, CSMBs; IQR; interquartile range, ITT; Intention to treat, NCBPBs; N; number, Non-calcium-based phosphate binders i.e., lanthanum or sevelamer; OS; overall survival outcome, PBs; Phosphate binders, PPA; Per-protocol analysis, Q; quartile

**Table S6.** Factors associated with treatment assignments: multi-logit regression

| Variables                     | Univariate analysis     |         | Multivariate analysis |         |
|-------------------------------|-------------------------|---------|-----------------------|---------|
|                               | OR (95%CI)              | P-value | OR (95%CI)            | P-value |
| <b>CBPBs vs No-PBs</b>        |                         |         |                       |         |
| Age, years                    | 1.048 (1.045, 1.051)    | <0.001  | 1.044 (1.041, 1.048)  | <0.001  |
| Sex                           |                         |         |                       |         |
| Female                        | 1                       |         | 1                     |         |
| Male                          | 0.635 (0.578, 0.698)    | <0.001  | 0.756 (0.683, 0.837)  | <0.001  |
| Reimbursement                 |                         |         |                       |         |
| Non CSMBS                     | 1                       |         | 1                     |         |
| CSMBS                         | 2.235 (2.025, 2.468)    | <0.001  | 1.253 (1.120, 1.403)  | <0.001  |
| Mode of RRT                   |                         |         |                       |         |
| No RRT                        | 1                       |         | 1                     |         |
| RRT                           | 0.550 (0.496, 0.609)    | <0.001  | 0.782 (0.700, 0.874)  | <0.001  |
| Phosphorus, mg/dL             | 0.911 (0.881, 0.942)    | <0.001  | 1.023 (0.987, 1.061)  | 0.213   |
| Calcium, mg/dL                | 0.914 (0.875, 0.955)    | <0.001  | 0.846 (0.807, 0.888)  | <0.001  |
| Hospitals                     |                         |         |                       |         |
| Bhumibol Hospital             | 1                       |         | n/a                   | n/a     |
| Ramathibodi Hospital          | 0.289 (0.256, 0.325)    | <0.001  | n/a                   | n/a     |
| Hypertension                  | 13.112 (8.687, 19.789)  | <0.001  | n/a                   | n/a     |
| Diabetes                      | 3.114 (2.838, 3.416)    | <0.001  | n/a                   | n/a     |
| Dyslipidemia                  | 4.336 (3.907, 4.811)    | <0.001  | n/a                   | n/a     |
| CVD                           | 2.818 (2.512, 3.162)    | <0.001  | n/a                   | n/a     |
| Bone disorders related ESRD   | 5.381 (4.530, 6.392)    | <0.001  | n/a                   | n/a     |
| Secondary Hyperparathyroidism | 0.846 (0.772, 0.928)    | <0.001  | n/a                   | n/a     |
| <b>NCBPBs vs No-PBs</b>       |                         |         |                       |         |
| Age, years                    | 1.046 (1.038, 1.055)    | <0.001  | 1.035 (1.022, 1.049)  | <0.001  |
| Sex                           |                         |         |                       |         |
| Female                        | 1                       |         | 1                     |         |
| Male                          | 0.745 (0.572, 0.969)    | 0.028   | 1.014 (0.691, 1.488)  | 0.943   |
| Reimbursement                 |                         |         |                       |         |
| Non CSMBS                     | 1                       |         | 1                     |         |
| CSMBS                         | 14.934 (10.397, 21.450) | <0.001  | 5.880 (3.724, 9.286)  | <0.001  |

**Table S6.** Factors associated with treatment assignments: A multi-logit regression (cont.)

| Variables                           | Univariate analysis   |         | Multivariate analysis |         |
|-------------------------------------|-----------------------|---------|-----------------------|---------|
|                                     | OR (95%CI)            | P-value | OR (95%CI)            | P-value |
| <b>NCBPBs vs No-PBs (cont.)</b>     |                       |         |                       |         |
| Mode of RRT                         |                       |         |                       |         |
| No RRT                              | 1                     |         | 1                     |         |
| RRT                                 | 4.108 (3.076, 5.487)  | <0.001  | 3.352 (2.271, 4.950)  | <0.001  |
| Phosphorus, mg/dL                   | 1.209 (1.129, 1.295)  | <0.001  | 1.238 (1.110, 1.381)  | <0.001  |
| Calcium, mg/dL                      | 1.411 (1.267, 1.571)  | <0.001  | 1.484 (1.292, 1.704)  | <0.001  |
| Hospitals                           |                       |         |                       |         |
| Bhumibol Hospital                   | 1                     |         | n/a                   | n/a     |
| Ramathibodi Hospital                | 0.321 (0.183, 0.564)  | <0.001  | n/a                   | n/a     |
| Hypertension                        | 4.784 (0.659, 34.682) | 0.121   | n/a                   | n/a     |
| Diabetes                            | 1.848 (1.107, 3.087)  | 0.019   | n/a                   | n/a     |
| Dyslipidemia                        | 3.942 (1.521, 7.604)  | 0.038   | n/a                   | n/a     |
| CVD                                 | 1.765 (0.948, 3.286)  | 0.073   | n/a                   | n/a     |
| Bone disorders related ESRD         | 4.221 (2.104, 8.469)  | <0.001  | n/a                   | n/a     |
| Secondary Hyperparathyroidism       | 3.167 (2.074, 6.307)  | <0.001  | n/a                   | n/a     |
| <b>Aluminum hydroxide vs No-PBs</b> |                       |         |                       |         |
| Age, years                          | 1.018 (1.006, 1.030)  | 0.003   | 1.038 (1.024, 1.052)  | <0.001  |
| Sex                                 |                       |         |                       |         |
| Female                              | 1                     |         | 1                     |         |
| Male                                | 0.720 (0.482, 1.076)  | 0.109   | 0.737 (0.487, 1.115)  | 0.148   |
| Reimbursement                       |                       |         |                       |         |
| Non CSMBS                           | 1                     |         | 1                     |         |
| CSMBS                               | 3.275 (2.143, 5.006)  | <0.001  | 0.352 (0.195, 0.635)  | 0.001   |
| Mode of RRT                         |                       |         |                       |         |
| No RRT                              | 1                     |         | 1                     |         |
| RRT                                 | 3.275 (2.143, 5.006)  | <0.001  | 4.010 (2.575, 6.245)  | <0.001  |
| Phosphorus, mg/dL                   | 1.313 (1.200, 1.437)  | <0.001  | 1.392 (1.257, 1.541)  | <0.001  |

**Table S6.** Factors associated with treatment assignments: A multi-logit regression (cont.)

| Variables                                   | Univariate analysis   |         | Multivariate analysis |         |
|---------------------------------------------|-----------------------|---------|-----------------------|---------|
|                                             | OR (95%CI)            | P-value | OR (95%CI)            | P-value |
| <b>Aluminum hydroxide vs No-PBs (cont.)</b> |                       |         |                       |         |
| Calcium, mg/dL                              | 1.532 (1.322, 1.775)  | <0.001  | 1.437 (1.226, 1.685)  | <0.001  |
| Hospitals                                   |                       |         |                       |         |
| Bhumibol Hospital                           | 1                     |         | n/a                   | n/a     |
| Ramathibodi Hospital                        | 0.168 (0.107, 0.264)  | <0.001  | n/a                   | n/a     |
| Hypertension                                | 7.891 (0.345, 12.321) | 0.265   | n/a                   | n/a     |
| Diabetes                                    | 2.969 (1.859, 4.741)  | <0.001  | n/a                   | n/a     |
| Dyslipidemia                                | 2.486 (1.504, 4.108)  | <0.001  | n/a                   | n/a     |
| CVD                                         | 1.354 (0.755, 2.428)  | 0.309   | n/a                   | n/a     |
| Bone disorders related ESRD                 | 4.477 (2.464, 8.133)  | <0.001  | n/a                   | n/a     |
| Secondary Hyperparathyroidism               | 1.993 (1.275, 3.115)  | 0.002   | n/a                   | n/a     |

Abbreviations: CBPBs, calcium-based phosphate binders; CI, confidence interval; CSMBS, civil servant medical benefit scheme; CVD, cardiovascular disease; ESRD, end-stage renal disease; OR, Odd ratio; PBs, phosphate binders; RRT, renal replacement therapy.

**Table S7.** Summary of covariate balance before and after weighting by propensity score for OS by treatment approach

| Treatment approaches | Covariates                       | Standardized mean difference (SMD) |                | Variance ratio  |                | p-value |
|----------------------|----------------------------------|------------------------------------|----------------|-----------------|----------------|---------|
|                      |                                  | Before weighted                    | After weighted | Before weighted | After weighted |         |
| ITT                  | CBPBs versus No-PBs              |                                    |                |                 |                |         |
|                      | Age                              | 0.779                              | -0.050         | 0.875           | 0.823          | 0.040   |
|                      | Sex (Male)                       | -0.213                             | 0.007          | 1.025           | 0.999          | 0.154   |
|                      | CSMBS                            | 0.480                              | -0.026         | 1.265           | 0.990          | 0.009   |
|                      | Receiving RRT                    | -0.270                             | 0.029          | 0.802           | 1.026          | 0.015   |
|                      | Serum phosphate                  | -0.102                             | 0.003          | 1.232           | 1.153          | 0.241   |
|                      | Serum calcium                    | -0.095                             | 0.035          | 1.048           | 1.088          | 0.011   |
|                      | NCBPBs versus No-PBs             |                                    |                |                 |                |         |
|                      | Age                              | 0.782                              | 0.029          | 0.795           | 0.615          | 0.071   |
|                      | Sex (Male)                       | -0.061                             | 0.010          | 1.024           | 0.999          | 0.125   |
|                      | CSMBS                            | 1.101                              | 0.127          | 0.946           | 1.029          | 0.091   |
|                      | Receiving RRT                    | 0.463                              | -0.041         | 1.030           | 0.961          | 0.081   |
|                      | Serum phosphate                  | 0.185                              | 0.121          | 1.162           | 0.981          | 0.046   |
|                      | Serum calcium                    | 0.654                              | 0.429          | 0.935           | 0.669          | 0.021   |
|                      | Aluminum hydroxide versus No-PBs |                                    |                |                 |                |         |
|                      | Age                              | 0.296                              | 0.028          | 0.688           | 0.682          | 0.015   |
|                      | Sex (Male)                       | -0.138                             | 0.054          | 1.039           | 0.994          | 0.048   |
|                      | CSMBS                            | 0.144                              | -0.099         | 1.145           | 0.956          | 0.004   |
|                      | Receiving RRT                    | 0.050                              | 0.069          | 1.036           | 1.060          | 0.002   |
|                      | Serum phosphate                  | 0.919                              | 0.378          | 1.565           | 1.108          | <0.001  |
|                      | Serum calcium                    | 0.649                              | 0.259          | 1.241           | 0.940          | <0.001  |
| PPA                  | CBPBs versus No-PBs              |                                    |                |                 |                |         |
|                      | Age                              | 0.814                              | -0.033         | 0.888           | 0.864          | 0.036   |
|                      | Sex (Male)                       | -0.230                             | 0.002          | 1.023           | 1.000          | 0.251   |
|                      | CSMBS                            | 0.379                              | -0.016         | 1.252           | 0.976          | 0.026   |
|                      | Receiving RRT                    | -0.284                             | 0.011          | 0.789           | 1.010          | 0.416   |
|                      | Serum phosphate                  | -0.133                             | 0.006          | 1.197           | 1.229          | 0.080   |
|                      | Serum calcium                    | -0.099                             | 0.022          | 1.066           | 1.099          | 0.042   |

**Table S7.** Summary of covariate balance before and after weighting by propensity score for OS by treatment approach (cont.)

| treatment approaches         | Covariates                                                | Standardized mean difference (SMD) |                | Variance ratio  |                | p-value |
|------------------------------|-----------------------------------------------------------|------------------------------------|----------------|-----------------|----------------|---------|
|                              |                                                           | Before weighted                    | After weighted | Before weighted | After weighted |         |
| PPA                          | NCBPBs versus No-PBs                                      |                                    |                |                 |                |         |
|                              | Age                                                       | 0.923                              | 0.153          | 0.734           | 0.557          | 0.046   |
|                              | Sex (Male)                                                | -0.015                             | 0.046          | 1.023           | 0.994          | 0.019   |
|                              | CSMBS                                                     | 1.172                              | 0.105          | 0.891           | 1.047          | 0.053   |
|                              | Receiving RRT                                             | 0.327                              | -0.185         | 1.080           | 0.817          | 0.039   |
|                              | Serum phosphate                                           | 0.032                              | 0.220          | 0.855           | 1.044          | 0.011   |
|                              | Serum calcium                                             | 0.717                              | 0.448          | 0.690           | 0.554          | <0.001  |
|                              | Aluminum hydroxide versus No-PBs (excluded from analysis) |                                    |                |                 |                |         |
|                              | Actual treatment-pattern approach                         | CBPBs-CBPBs versus No-PBs          |                |                 |                |         |
| Age                          |                                                           | 0.803                              | -0.053         | 0.890           | 0.846          | <0.001  |
| Sex                          |                                                           | -0.227                             | 0.004          | 1.023           | 1.000          | 0.251   |
| CSMBS                        |                                                           | 0.387                              | -0.028         | 1.254           | 0.988          | 0.093   |
| Mode of RRT                  |                                                           |                                    |                |                 |                | 0.0256  |
| PD                           |                                                           | -0.178                             | -0.018         | 0.445           | 0.919          |         |
| HD                           |                                                           | -0.272                             | -0.030         | 0.698           | 1.041          |         |
| KT                           |                                                           | 0.124                              | -0.014         | 1.873           | 0.933          |         |
| Serum phosphate              |                                                           | -0.127                             | 0.004          | 1.192           | 1.181          | 0.474   |
| Serum calcium                |                                                           | -0.096                             | 0.085          | 1.065           | 1.105          | 0.446   |
| CBPBs-NCBPBs versus No-PBs   |                                                           |                                    |                |                 |                |         |
| Age                          |                                                           | 0.774                              | 0.066          | 0.744           | 0.789          | 0.029   |
| Sex                          |                                                           | -0.133                             | 0.041          | 1.028           | 0.996          | 0.033   |
| CSMBS                        |                                                           | 1.253                              | -0.022         | 0.809           | 0.990          | 0.043   |
| Mode of RRT                  |                                                           |                                    |                |                 |                | 0.074   |
| PD                           |                                                           | -0.292                             | -0.0004        | 0.167           | 0.998          |         |
| HD                           |                                                           | -0.116                             | -0.019         | 0.882           | 0.973          |         |
| KT                           |                                                           | -0.047                             | 0.044          | 0.733           | 1.218          |         |
| Serum phosphate              |                                                           | -0.051                             | 0.021          | 1.356           | 1.004          | 0.215   |
| Serum calcium                |                                                           | -0.068                             | -0.008         | 0.924           | 0.819          | 0.158   |
| CBPBs-aluminum versus No-PBs |                                                           |                                    |                |                 |                |         |
| Age                          |                                                           | 0.169                              | 0.019          | 0.862           | 0.839          | <0.001  |
| Sex                          |                                                           | -0.163                             | -0.190         | 1.038           | 0.959          | 0.007   |
| CSMBS                        |                                                           | 0.320                              | 0.026          | 0.626           | 1.009          | 0.080   |

**Table S7.** Summary of covariate balance before and after weighting by propensity score for OS by treatment approach (cont.)

| Treatment approaches              | Covariates                           | Standardized mean difference (SMD) |                | Variance ratio  |                | p-value |
|-----------------------------------|--------------------------------------|------------------------------------|----------------|-----------------|----------------|---------|
|                                   |                                      | Before weighted                    | After weighted | Before weighted | After weighted |         |
| Actual treatment-pattern approach | CBPBs-aluminum versus No-PBs (cont.) |                                    |                |                 |                |         |
|                                   | Mode of RRT                          |                                    |                |                 |                | 0.015   |
|                                   | PD                                   | -0.109                             | 0.030          | 0.648           | 1.144          |         |
|                                   | HD                                   | -0.294                             | 0.194          | 0.677           | 1.184          |         |
|                                   | KT                                   | 0.176                              | -0.060         | 2.343           | 0.737          |         |
|                                   | Serum phosphate level                | 0.264                              | -0.029         | 2.123           | 1.042          | 0.122   |
|                                   | Serum calcium level                  | -0.0145                            | -0.044         | 1.220           | 0.815          | 0.357   |

Abbreviations: CBPBs, calcium-based phosphate binders; CI, confidence interval; CSMBS, civil servant medical benefit scheme; ESRD, end-stage renal disease; HD; Hemodialysis, ITT; Intention to treat, KT; kidney transplant, OR; Odd ratio; OS; overall survival, PBs, phosphate binders; PPA; Per-protocol analysis, PD; Peritoneal dialysis, RRT, renal replacement therapy, SMD; standardized mean difference

**Table S8.** Summary of covariate balance before and after weighting by propensity score for time to CVD event by treatment approach

| Treatment approaches | Covariates                       | Standardized mean difference (SMD) |                | Variance ratio  |                | p-value |
|----------------------|----------------------------------|------------------------------------|----------------|-----------------|----------------|---------|
|                      |                                  | Before weighted                    | After weighted | Before weighted | After weighted |         |
| ITT                  | CBPBs versus No-PBs              |                                    |                |                 |                |         |
|                      | Age                              | 0.784                              | -0.046         | 1.002           | 0.834          | 0.096   |
|                      | Sex (Male)                       | -0.225                             | -0.0002        | 1.023           | 1.000          | 0.769   |
|                      | CSMBS                            | 0.477                              | -0.021         | 1.384           | 0.987          | 0.004   |
|                      | Receiving RRT                    | -0.321                             | 0.022          | 0.759           | 1.019          | 0.037   |
|                      | Serum phosphate                  | -0.061                             | -0.008         | 1.376           | 1.087          | 0.124   |
|                      | Serum calcium                    | -0.229                             | 0.079          | 1.244           | 1.207          | 0.026   |
|                      | NCBPBs versus No-PBs             |                                    |                |                 |                |         |
|                      | Age                              | 0.887                              | 0.066          | 0.909           | 0.642          | 0.032   |
|                      | Sex (Male)                       | -0.097                             | -0.041         | 1.033           | 1.001          | 0.039   |
|                      | CSMBS                            | 1.257                              | 0.167          | 1.010           | 1.071          | 0.019   |
|                      | Receiving RRT                    | 0.312                              | -0.035         | 1.069           | 0.967          | 0.041   |
|                      | Serum phosphate                  | 0.150                              | -0.001         | 1.040           | 0.622          | 0.103   |
|                      | Serum calcium                    | 0.575                              | 0.486          | 0.854           | 0.567          | <0.001  |
|                      | Aluminum hydroxide versus No-PBs |                                    |                |                 |                |         |
|                      | Age                              | 0.314                              | -0.050         | 0.717           | 0.882          | 0.046   |
|                      | Sex (Male)                       | -0.091                             | 0.015          | 1.036           | 0.999          | 0.241   |
|                      | CSMBS                            | 0.252                              | -0.036         | 1.285           | 0.977          | 0.069   |
|                      | Receiving RRT                    | 0.112                              | 0.049          | 1.058           | 1.040          | 0.038   |
|                      | Serum phosphate                  | 1.060                              | 0.384          | 1.411           | 1.043          | <0.001  |
|                      | Serum calcium                    | 0.706                              | 0.366          | 1.521           | 0.947          | <0.001  |
| PPA                  | CBPBs versus No-PBs              |                                    |                |                 |                |         |
|                      | Age                              | 0.807                              | 0.029          | 1.048           | 0.899          | 0.315   |
|                      | Sex (Male)                       | -0.248                             | -0.006         | 1.020           | 1.001          | 0.412   |
|                      | CSMBS                            | 0.361                              | -0.008         | 1.339           | 0.991          | 0.269   |
|                      | Receiving RRT                    | -0.323                             | 0.011          | 0.757           | 1.007          | 0.056   |
|                      | Serum phosphate                  | 0.949                              | 0.009          | 0.857           | 1.156          | 0.116   |
|                      | Serum calcium                    | -0.245                             | 0.052          | 1.257           | 1.174          | 0.039   |



**Table S8.** Summary of covariate balance before and after weighting by propensity score for time to CVD event by treatment approach (cont.)

| treatment approaches              | Covariates                                                          | Standardized mean difference (SMD) |                | Variance ratio  |                | p-value |
|-----------------------------------|---------------------------------------------------------------------|------------------------------------|----------------|-----------------|----------------|---------|
|                                   |                                                                     | Before weighted                    | After weighted | Before weighted | After weighted |         |
| PPA                               | NCBPBs versus No-PBs                                                |                                    |                |                 |                |         |
|                                   | Age                                                                 | 1.048                              | 0.194          | 0.793           | 0.826          | 0.044   |
|                                   | Sex (Male)                                                          | -0.033                             | -0.002         | 1.031           | 1.000          | 0.196   |
|                                   | CSMBS                                                               | 1.234                              | 0.191          | 1.039           | 1.114          | 0.081   |
|                                   | Receiving RRT                                                       | 0.069                              | -0.201         | 1.052           | 0.986          | 0.012   |
|                                   | Serum phosphate                                                     | 0.034                              | 0.175          | 0.829           | 0.688          | <0.001  |
|                                   | Serum calcium                                                       | 0.612                              | 0.225          | 0.670           | 0.926          | <0.001  |
|                                   | Aluminum hydroxide versus No-PBs (excluded from analysis: no event) |                                    |                |                 |                |         |
| Actual treatment-pattern approach | CBPBs-CBPBs versus No-PBs                                           |                                    |                |                 |                |         |
|                                   | Age                                                                 | 0.817                              | -0.041         | 1.012           | 0.860          | 0.125   |
|                                   | Sex (Male)                                                          | -0.237                             | -0.002         | 1.021           | 1.0002         | 0.119   |
|                                   | CSMBS                                                               | 0.418                              | -0.016         | 1.366           | 0.988          | 0.030   |
|                                   | Receiving RRT                                                       | -0.317                             | 0.028          | 0.763           | 1.022          | 0.019   |
|                                   | Serum phosphate                                                     | 0.131                              | -0.015         | 1.493           | 1.078          | 0.072   |
|                                   | Serum calcium                                                       | -0.236                             | 0.057          | 1.234           | 1.024          | 0.082   |
|                                   | CBPBs-NCBPBs versus No-PBs                                          |                                    |                |                 |                |         |
|                                   | Age                                                                 | 0.836                              | -0.180         | 0.829           | 0.766          | 0.248   |
|                                   | Sex (Male)                                                          | -0.147                             | 0.122          | 1.031           | 0.976          | 0.115   |
|                                   | CSMBS                                                               | 1.469                              | -0.079         | 0.810           | 0.943          | 0.053   |
|                                   | Receiving RRT                                                       | 0.417                              | -0.155         | 1.036           | 0.855          | 0.011   |
|                                   | Serum phosphate                                                     | 0.227                              | -0.029         | 1.507           | 1.019          | 0.004   |
|                                   | Serum calcium                                                       | -0.235                             | -0.152         | 1.205           | 0.661          | 0.042   |
|                                   | CBPBs-aluminum versus No-PBs                                        |                                    |                |                 |                |         |
|                                   | Age                                                                 | 0.285                              | -0.092         | 0.923           | 0.724          | 0.025   |
|                                   | Sex (Male)                                                          | -0.151                             | -0.111         | 1.039           | 0.995          | 0.024   |
|                                   | CSMBS                                                               | 0.382                              | 0.066          | 0.481           | 0.925          | 0.124   |
|                                   | Receiving RRT                                                       | 0.304                              | -0.024         | 1.070           | 0.980          | 0.031   |
|                                   | Serum phosphate                                                     | 0.581                              | 0.121          | 1.783           | 0.570          | 0.002   |
|                                   | Serum calcium                                                       | -0.277                             | 0.119          | 1.764           | 1.147          | 0.010   |

Abbreviations: CBPBs, calcium-based phosphate binders; CI, confidence interval; CSMBS, civil servant medical benefit scheme; CVD, cardiovascular disease; ESRD, end-stage renal disease; HD; Hemodialysis, ITT; Intention to treat, KT; kidney transplant, OR; Odd ratio; PBs, phosphate binders; PPA; Per-protocol analysis, PD; Peritoneal dialysis, RRT, renal replacement therapy, SMD; standardized mean difference

**Table S9.** Summary of covariate balance before and after weighting by propensity score for time to bone disorder by treatment approach

| Treatment approaches | Covariates                       | Standardized mean difference (SMD) |                | Variance ratio  |                | p-value |
|----------------------|----------------------------------|------------------------------------|----------------|-----------------|----------------|---------|
|                      |                                  | Before weighted                    | After weighted | Before weighted | After weighted |         |
| ITT                  | CBPBs versus No-PBs              |                                    |                |                 |                |         |
|                      | Age                              | 0.740                              | -0.045         | 0.886           | 0.810          | 0.121   |
|                      | Sex (Male)                       | -0.173                             | 0.006          | 1.031           | 0.999          | 0.252   |
|                      | CSMBS                            | 0.445                              | -0.023         | 1.282           | 0.989          | 0.014   |
|                      | Receiving RRT                    | -0.260                             | 0.026          | 0.816           | 1.021          | 0.231   |
|                      | Serum phosphate                  | -0.081                             | 0.004          | 1.276           | 1.158          | 0.131   |
|                      | Serum calcium                    | -0.133                             | 0.042          | 1.040           | 1.080          | 0.030   |
|                      | NCBPBs versus No-PBs             |                                    |                |                 |                |         |
|                      | Age                              | 0.780                              | 0.045          | 0.820           | 0.617          | 0.089   |
|                      | Sex (Male)                       | -0.060                             | 0.015          | 1.027           | 0.998          | 0.059   |
|                      | CSMBS                            | 1.089                              | 0.147          | 0.989           | 1.043          | 0.540   |
|                      | Receiving RRT                    | 0.473                              | -0.057         | 1.018           | 0.949          | 0.031   |
|                      | Serum phosphate                  | 0.199                              | 0.128          | 1.179           | 0.996          | 0.025   |
|                      | Serum calcium                    | 0.642                              | 0.398          | 0.924           | 0.662          | <0.001  |
|                      | Aluminum hydroxide versus No-PBs |                                    |                |                 |                |         |
|                      | Age                              | 0.312                              | 0.040          | 0.716           | 0.705          | 0.062   |
|                      | Sex (Male)                       | -0.123                             | 0.059          | 1.041           | 0.988          | 0.451   |
|                      | CSMBS                            | 0.177                              | -0.102         | 1.178           | 0.945          | 0.015   |
|                      | Receiving RRT                    | 0.0617                             | 0.084          | 1.040           | 1.066          | 0.601   |
|                      | Serum phosphate                  | 0.941                              | 0.391          | 1.570           | 1.128          | 0.001   |
|                      | Serum calcium                    | 0.643                              | 0.207          | 1.278           | 0.947          | <0.001  |
| PPA                  | CBPBs versus No-PBs              |                                    |                |                 |                |         |
|                      | Age                              | 0.775                              | -0.027         | 0.896           | 0.853          | 0.050   |
|                      | Sex (Male)                       | -0.194                             | 0.001          | 1.030           | 1.000          | 0.564   |
|                      | CSMBS                            | 0.344                              | -0.128         | 1.255           | 0.991          | 0.002   |
|                      | Receiving RRT                    | -0.278                             | 0.007          | 0.799           | 1.005          | 0.158   |
|                      | Serum phosphate                  | -0.121                             | 0.005          | 1.221           | 1.233          | 0.274   |
|                      | Serum calcium                    | -0.135                             | 0.028          | 1.048           | 1.067          | 0.004   |

**Table S9.** Summary of covariate balance before and after weighting by propensity score for time to bone disorder by treatment approach (cont.)

| treatment approaches              | Covariates                                                          | Standardized mean difference (SMD) |                | Variance ratio  |                | p-value |
|-----------------------------------|---------------------------------------------------------------------|------------------------------------|----------------|-----------------|----------------|---------|
|                                   |                                                                     | Before weighted                    | After weighted | Before weighted | After weighted |         |
| PPA                               | NCBPBs versus No-PBs                                                |                                    |                |                 |                |         |
|                                   | Age                                                                 | 0.929                              | 0.150          | 0.766           | 0.559          | 0.165   |
|                                   | Sex (Male)                                                          | -0.021                             | 0.069          | 1.026           | 0.984          | <0.001  |
|                                   | CSMBS                                                               | 1.165                              | 0.112          | 0.930           | 1.059          | 0.014   |
|                                   | Receiving RRT                                                       | 0.360                              | -0.194         | 1.067           | 0.871          | 0.121   |
|                                   | Serum phosphate                                                     | 0.022                              | 0.268          | 0.842           | 1.113          | 0.001   |
|                                   | Serum calcium                                                       | 0.687                              | 0.406          | 0.658           | 0.535          | <0.001  |
|                                   | Aluminum hydroxide versus No-PBs (excluded from analysis: no event) |                                    |                |                 |                |         |
| Actual treatment-pattern approach | CBPBs-CBPBs versus No-PBs                                           |                                    |                |                 |                |         |
|                                   | Age                                                                 | 0.766                              | -0.047         | 0.897           | 0.845          | 0.001   |
|                                   | Sex (Male)                                                          | -0.192                             | 0.006          | 1.030           | 0.999          | 0.521   |
|                                   | CSMBS                                                               | 0.360                              | -0.020         | 1.260           | 0.989          | 0.412   |
|                                   | Receiving RRT                                                       | -0.271                             | 0.023          | 0.805           | 1.020          | 0.124   |
|                                   | Serum phosphate                                                     | -0.111                             | 0.008          | 1.217           | 1.212          | 0.098   |
|                                   | Serum calcium                                                       | -0.129                             | 0.025          | 1.048           | 1.032          | 0.113   |
|                                   | CBPBs-NCBPBs versus No-PBs                                          |                                    |                |                 |                |         |
|                                   | Age                                                                 | 0.700                              | 0.074          | 0.754           | 0.794          | 0.429   |
|                                   | Sex (Male)                                                          | -0.075                             | 0.011          | 1.023           | 0.998          | 0.151   |
|                                   | CSMBS                                                               | 1.204                              | -0.021         | 0.884           | 0.989          | 0.096   |
|                                   | Receiving RRT                                                       | -0.214                             | -0.019         | 0.858           | 0.983          | 0.312   |
|                                   | Serum phosphate                                                     | 0.003                              | 0.0003         | 1.492           | 1.004          | 0.825   |
|                                   | Serum calcium                                                       | -0.110                             | -0.005         | 0.962           | 0.840          | 0.165   |
|                                   | CBPBs-aluminum versus No-PBs                                        |                                    |                |                 |                |         |
|                                   | Age                                                                 | 0.164                              | -0.049         | 0.878           | 0.736          | 0.279   |
|                                   | Sex (Male)                                                          | -0.163                             | -0.149         | 1.042           | 0.995          | 0.040   |
|                                   | CSMBS                                                               | -0.306                             | -0.071         | 0.635           | 0.958          | 0.251   |
|                                   | Receiving RRT                                                       | -0.224                             | 0.119          | 0.855           | 1.091          | 0.002   |
|                                   | Serum phosphate                                                     | 0.262                              | -0.048         | 2.238           | 1.035          | 0.653   |
| Serum calcium                     | -0.174                                                              | 0.045                              | 1.268          | 0.809           | 0.124          |         |

Abbreviations: CBPBs, calcium-based phosphate binders; CI, confidence interval; CSMBS, civil servant medical benefit scheme; CVD, cardiovascular disease; ESRD, end-stage renal disease; HD, Hemodialysis, ITT, Intention to treat, KT, kidney transplant, OR, Odd ratio; PBs, phosphate binders; PPA, Per-protocol analysis, PD, Peritoneal dialysis, RRT, renal replacement therapy, SMD, standardized mean difference

**Table S10.** Estimation of PB effects on bone disorder: Parametric survival analysis with Weibull survival distribution (ITT approach)

| Factors                       | Adjusted HR<br>(95%CI) | p-value |
|-------------------------------|------------------------|---------|
| Treatments                    |                        |         |
| No-PBs                        | 1                      |         |
| CBPBs                         | 2.639 (2.114, 3.296)   | <0.001  |
| NCBPBs                        | 2.028 (1.102, 3.732)   | 0.023   |
| Aluminum hydroxide            | 4.113 (2.348, 7.204)   | <0.001  |
| Age (years)                   | 1.014 (1.007, 1.020)   | <0.001  |
| Sex                           |                        |         |
| Female                        | 1                      |         |
| Male                          | 0.644 (0.542, 0.764)   | <0.001  |
| Mode of RRT                   |                        |         |
| No RRT                        | 1                      |         |
| PD                            | 0.831 (0.525, 1.315)   | 0.429   |
| HD                            | 1.198 (0.975, 1.468)   | 0.084   |
| KT                            | 1.533 (1.160, 2.034)   | 0.003   |
| CVD                           | 1.390 (1.164, 1.661)   | <0.001  |
| Secondary Hyperparathyroidism | 1.555 (1.280, 1.891)   | <0.001  |
| Phosphorus, mg/dL             | 0.889 (0.840, 0.942)   | <0.001  |
| Calcium, mg/dL                | 1.195 (1.107, 1.290)   | <0.001  |
| Anti-PTH agents               | n/a                    | n/a     |
| Reimbursement                 |                        |         |
| Non CSMBS                     | n/a                    | n/a     |
| CSMBS                         | n/a                    | n/a     |
| Hospital                      |                        |         |
| Bhumibol Hospitals            | n/a                    | n/a     |
| Ramathibodi Hospitals         | n/a                    | n/a     |
| Hypertension                  | n/a                    | n/a     |
| Diabetes                      | n/a                    | n/a     |
| Dyslipidemia                  | n/a                    | n/a     |
| Anemia                        | n/a                    | n/a     |
| Gout                          | n/a                    | n/a     |

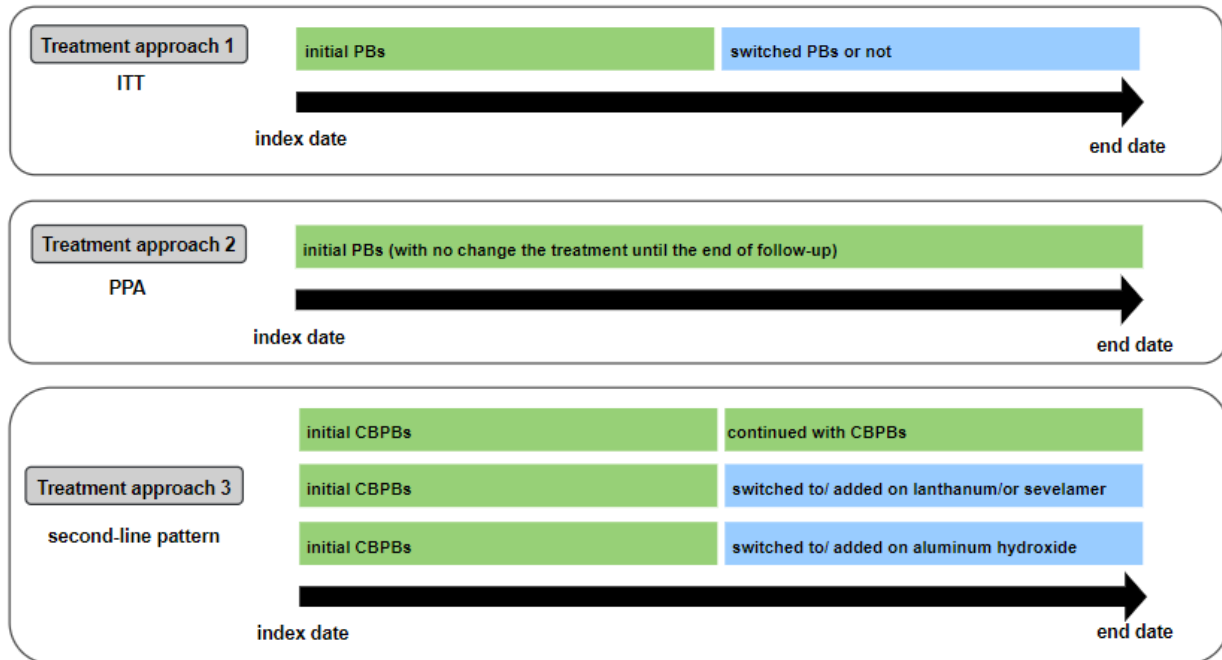
Abbreviations: CBPBs, calcium-based phosphate binders; CI, confidence interval; CSMBS, civil servant medical benefit scheme; CVD, cardiovascular disease; ESRD, end-stage renal disease; HD; Hemodialysis, HR; Hazard ratio, KT; Kidney transplantation; PBs, phosphate binders; PD; peritoneal dialysis, PTH; Parathyroid hormone, RRT, renal replacement therapy.

**Table S11.** Summary E-value point estimates and confidence intervals by treatment approach: actual treatment-pattern approach

| Treatments                    |               | E-value for point estimate<br>( $E_{est}$ ) | E-value for confidence limit<br>( $E_{CI}$ ) |
|-------------------------------|---------------|---------------------------------------------|----------------------------------------------|
| <b>OS</b>                     |               |                                             |                                              |
| CBPBs-CBPBs                   | No-PBs        | 1.550                                       | 1.353                                        |
| CBPBs-NCBPBs                  |               | 5.741                                       | 4.715                                        |
| CBPBs-aluminum                |               | 1.710                                       | 1.524                                        |
| CBPBs-NCBPBs                  | CBPBs-CBPBs   | 4.448                                       | 3.642                                        |
| CBPBs-aluminum                |               | 1.291                                       | 1.000                                        |
| CBPBs-aluminum                | CBPBs- NCBPBs | 4.253                                       | 3.804                                        |
| <b>Time to CVD</b>            |               |                                             |                                              |
| CBPBs-CBPBs                   | No-PBs        | 1.865                                       | 1.218                                        |
| CBPBs-NCBPBs                  |               | 2.376                                       | 1.621                                        |
| CBPBs-aluminum                |               | 1.421                                       | 1.000                                        |
| CBPBs-NCBPBs                  | CBPBs-CBPBs   | 3.331                                       | 2.679                                        |
| CBPBs-aluminum                |               | 1.345                                       | 1.175                                        |
| CBPBs-aluminum                | CBPBs- NCBPBs | 1.515                                       | 1.173                                        |
| <b>Time to bone disorders</b> |               |                                             |                                              |
| CBPBs-CBPBs                   | No-PBs        | 5.441                                       | 3.458                                        |
| CBPBs-NCBPBs                  |               | 4.195                                       | 3.138                                        |
| CBPBs-aluminum                |               | 1.991                                       | 1.378                                        |
| CBPBs-NCBPBs                  | CBPBs-CBPBs   | 3.108                                       | 2.482                                        |
| CBPBs-aluminum                |               | 1.541                                       | 1.326                                        |
| CBPBs-aluminum                | CBPBs- NCBPBs | 1.744                                       | 1.386                                        |

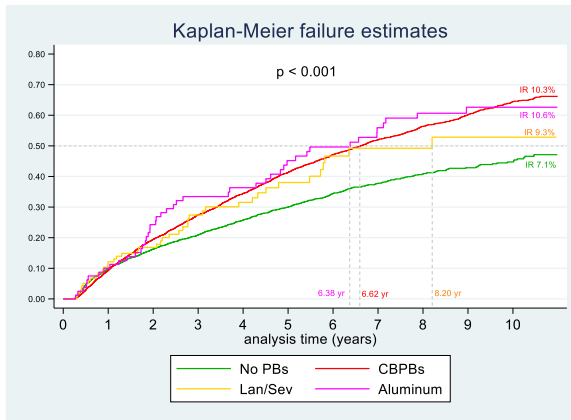
Abbreviations: CBPBs; Calcium-based phosphate binders, CI; confidence interval, CVD; cardiovascular disease, est; estimation, IQR; interquartile range, NCBPBs; N; number, Non-calcium-based phosphate binders i.e., lanthanum or sevelamer; OS; overall survival outcome, PBs; Phosphate binders

**Figure S1.** Treatment approaches considered

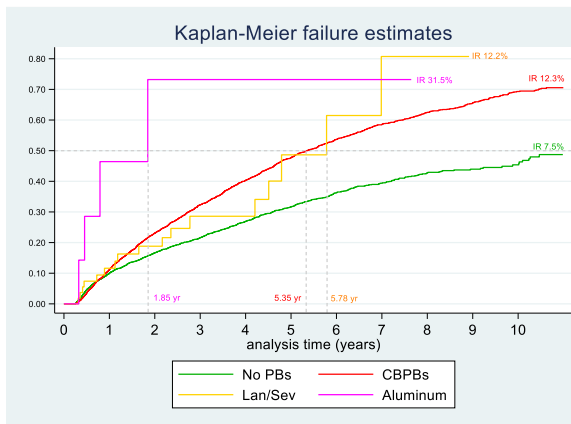


**Figure S2. KM curves for all-cause mortality by treatment approach**

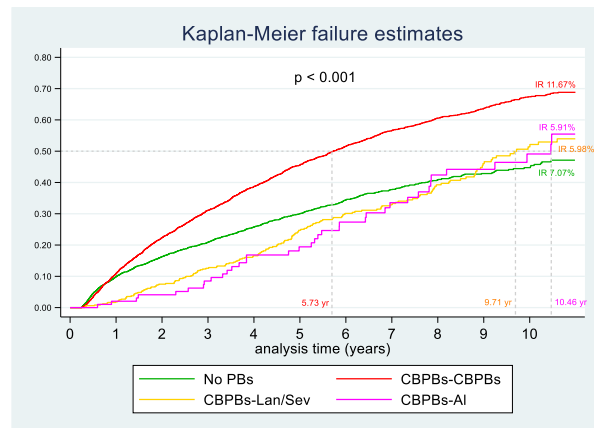
**A) ITT approach**



**B) PPA approach**

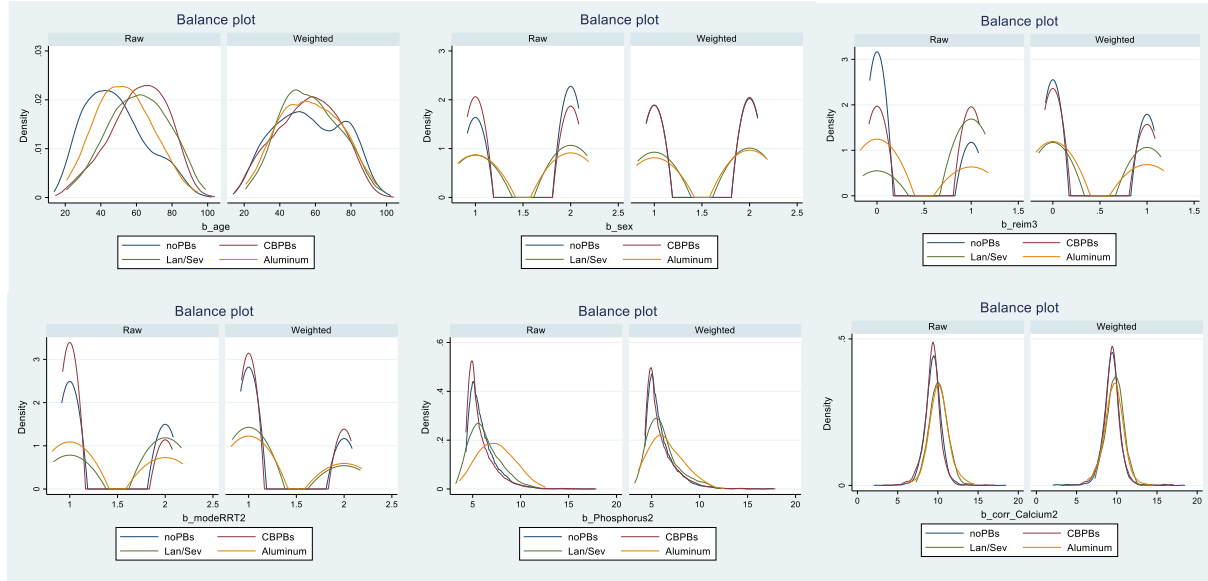


**C) Actual treatment-pattern approach**

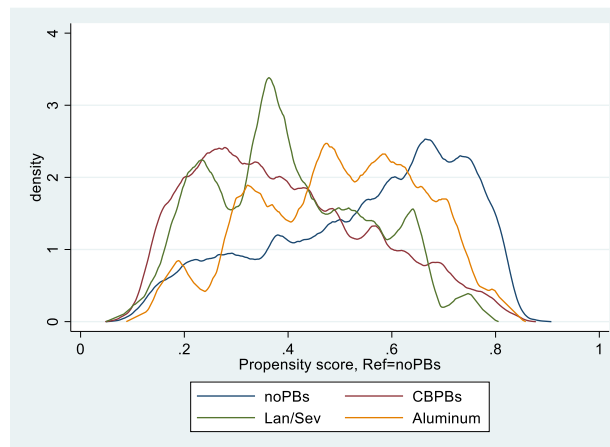


**Figure S3.** Assumptions check after weighting for OS in ITT approach A) Co-variate balance density plots, B) Overlapping plots

A) Balance density plot



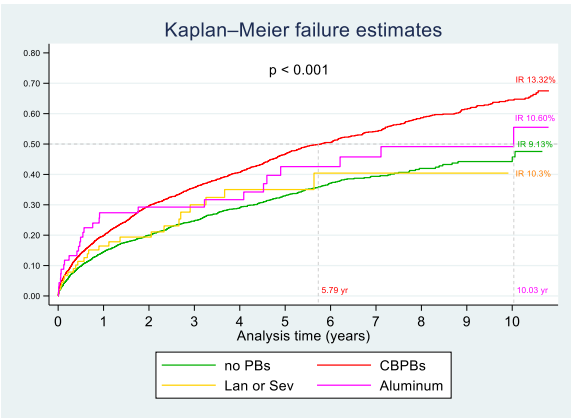
B) Overlapping plot



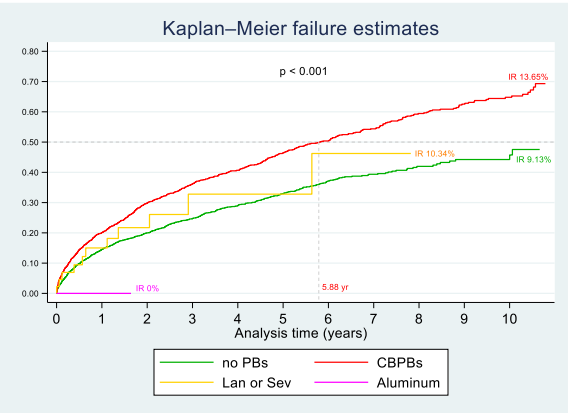


**Figure S4.** KM curves for CVD events by treatment approach

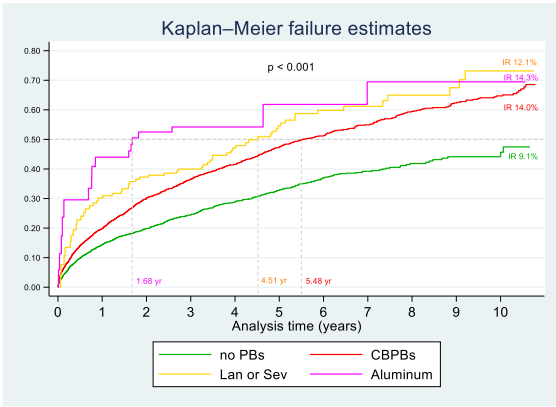
A) ITT approach



B) PPA approach

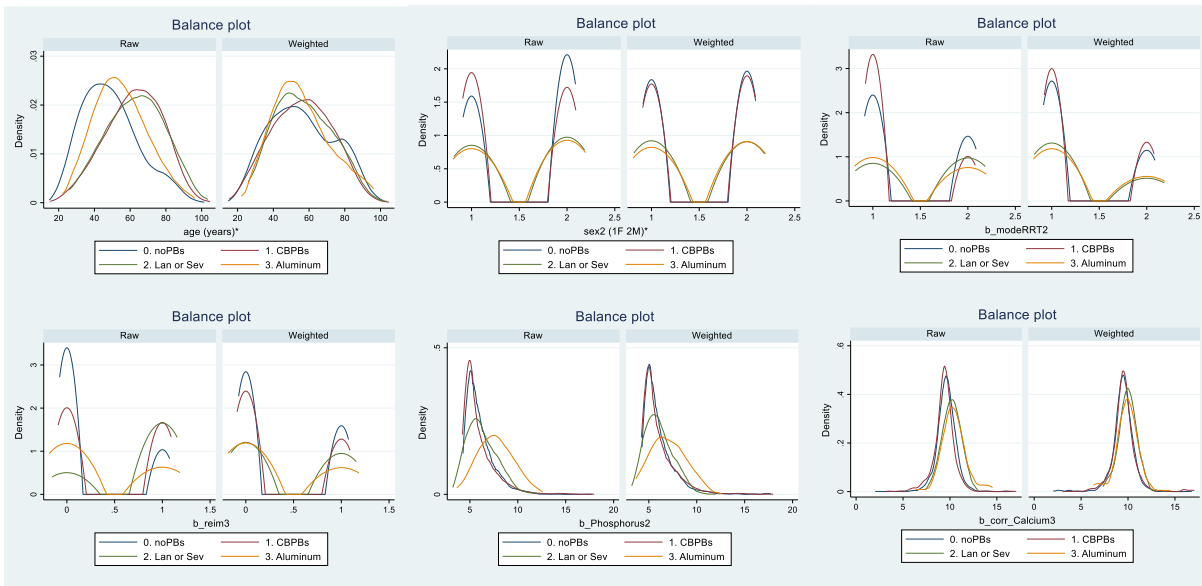


C) Actual treatment-pattern approach

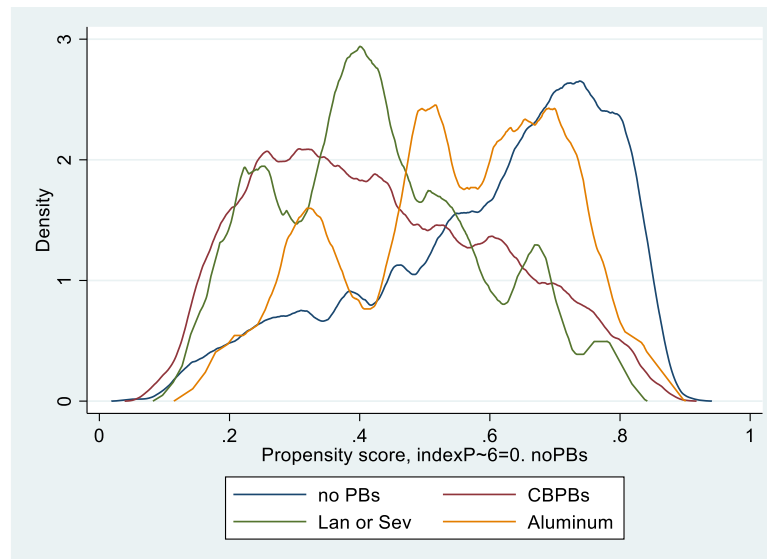


**Figure S5.** Assumptions check after weighting for time to CVD events in ITT approach A) Co-variate balance density plots, B) Overlapping plots

A) Balance density plot

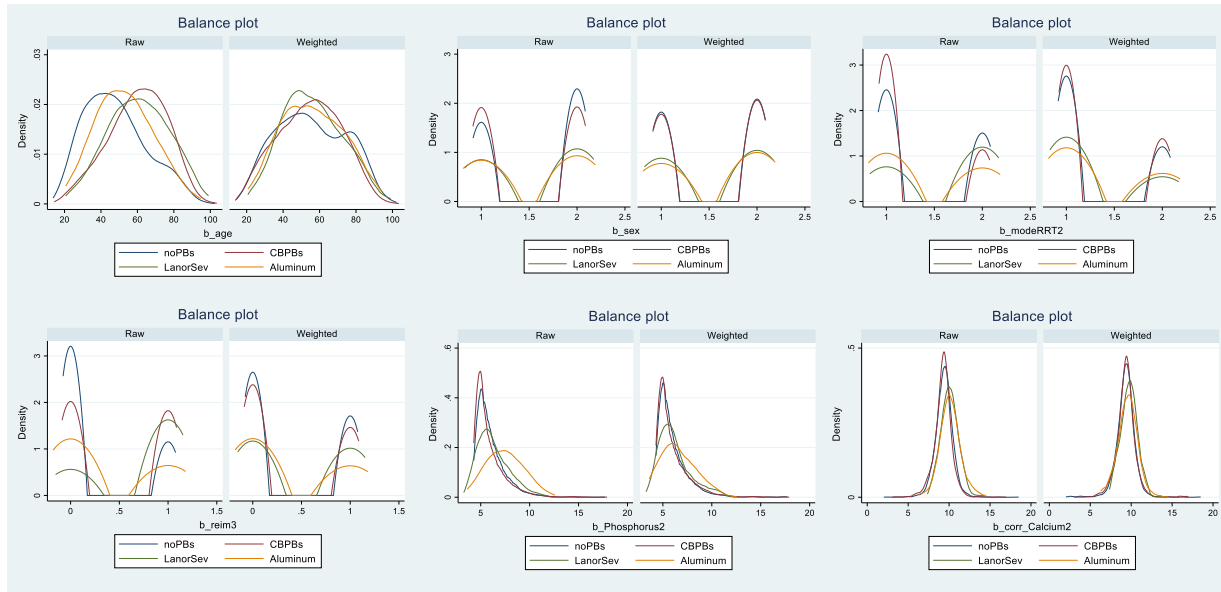


B) Overlapping plot

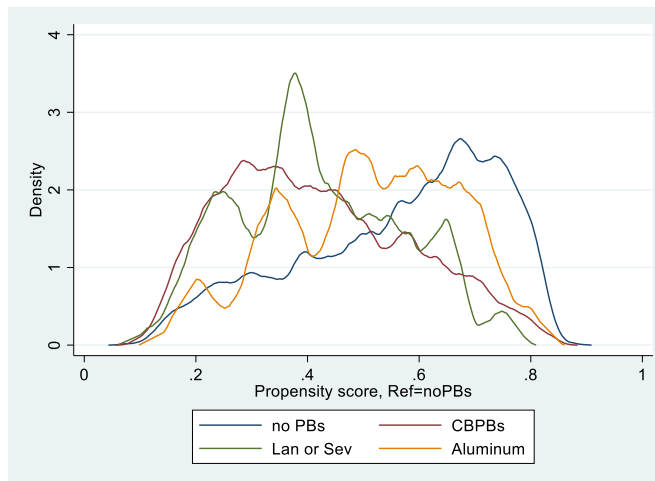


**Figure S6.** Assumptions check after weighting for time to bone disorder events in ITT and modified ITT approaches A) Co-variate balance density plots, B) Overlapping plots

A) Balance density plot



B) Overlapping plot



## Method S1. Clinical trial emulation and treatment approaches

Real-world End stage renal disease (ESRD) patients with hyperphosphatemia may be eligible for different treatment options predicated on serum phosphate levels, therapeutic goals, availability, and affordability. Treatment option data were retrieved from electronic records. Therefore, three approaches were considered to address variation in the potential prescribing patterns observed, see [Figure S1](#).

### ***A) Approach 1: Intention to treat (ITT)***

Data was analyzed on an ITT approach, i.e., patients were initially assigned to treatment groups regardless of adherence levels and/or, change or termination of treatment. Four treatment groups were considered (no-phosphate-binders (PBs) (control group), calcium-based phosphate-binders (CBPBs), lanthanum/or sevelamer, and aluminum hydroxide initiation).

### ***B) Approach 2: Per-protocol analysis (PPA)***

This PPA approach considered only patients in receipt of PBs only for the duration of the study period. Therefore, individual patients who switched treatments or were included in another treatment group were excluded from this analysis. Four treatment groups were generated (no-PBs (control group), persistent CBPBs, persistent lanthanum/or sevelamer, and persistent aluminum hydroxide).

### ***C) Approach 3: Actual treatment-pattern analysis***

CBPBs are commonly prescribed as the first-line treatment option for patients with ESRD and hyperphosphatemia in line with Thai health policy given the higher costs associated with non-CBPBs or NCBPBs (lanthanum and sevelamer) compared to CBPBs (except aluminum hydroxide). NCBPBs are not reimbursed to healthcare providers unless NCBPBs are recommended as a secondary treatment option if patients have not responded to treatment with CBPBs, or contraindications arise, or alternatively patients are in apposition to pay. As such, this approach differentiates the effectiveness of PBs as an actual treatment pattern when treatment with CBPBs is unsuccessful, which is not an uncommon occurrence.

We focused on patients initially treated with CBPBs and then switched to/or additionally received NCBPBs (i.e., lanthanum/or sevelamer, and aluminum hydroxide) if a target serum phosphate level was not maintained, for comparisons with patients not in receipt of any PBs.

Four groups were compared in this approach including no-PBs (control group), CBPBs-CBPBs, CBPBs-lanthanum/or sevelamer, and CBPBs-aluminum hydroxide.

- *No-PB patients (control group)*
- *CBPBs-CBPBs patients* were defined as those were initially treated with CBPBs and did not switch to/or additionally received any other PBs (i.e., lanthanum/sevelamer or aluminum hydroxide), or those received persistent CBPBs treatment in order to maintain serum phosphate levels within the normal range.
- *CBPBs-NCBPBs, and CBPBs-aluminum hydroxide* were defined as those were initially treated with CBPBs but were then switched to/or additionally received any NCBPBs (i.e., lanthanum or sevelamer), or aluminum hydroxide for a period greater than three months in order to maintain serum phosphate levels within the normal range.

## Method S2 Statistical analysis

### **A) Propensity score (PS) using a counterfactual approach by likelihood-adjusted-censoring with inverse-probability-weighted regression adjustment (LAC-IPWRA)**

The LAC-IPWRA estimators were derived from treatment assignment and outcome models as follows:

1. *Treatment models* were constructed using multi-logit equations to estimate individual probability for receipt of any PBs (i.e., PS). A total of 12 covariables (i.e., age, sex, reimbursement scheme, renal replacement therapy (RRT) modalities, hypertension (HTN), diabetes mellitus (DM), dyslipidemia (DLP), cardiovascular disease (CVD), hyperphosphatemia, serum phosphate, serum calcium (Ca) level, and study sites) were considered as a potential confounder for treatment assignment. Simple multi-logit regression analyses were used by fitting treatment assignment against each covariable. Any covariables with a univariate p-value  $< 0.1$  were then simultaneously included within a multivariate multi-logit regression with backward elimination approach. Finally, significant covariables and those clinically associated with treatment assignments were retained within the treatment model. Covariate balance across treatments was explored and appropriate adjustment undertaken, where required.
2. *Outcome models* were constructed using parametric survival approaches similar to conventional survival analysis.

Potential outcome means (POMs) (i.e., the average time to death/CVD events/bone disorders for each treatment group) were estimated. Additionally, adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated by weighted parametric survival models.

### **B) Assumptions checking**

Two model assumptions were considered to determine the most appropriate treatment effect model for observational survival-time data:

- 1) *The conditional independence*

This assumption requires that the potential outcomes should be independent from the treatment assignments conditioning on the covariates. This is analogous to a process of randomization in a randomized controlled trial (RCT). If the treatment

model is well specified, it should be able to balance all covariates among treatment groups. This assumption was verified to ensure that treatment assignments after weighting by PS were performed in a manner as efficient as randomization conditioning on the covariates. This assumption can be assessed by estimating the weighted standardized mean difference (SMD) and its variance ratio between the treatment and control groups for each covariate. We expect that the weighted SMD was closed to 0 or  $\leq 0.2$  and a variance ratio was 1. The density plot of each covariate was also constructed to check balancing after weighting. Additionally, the overall balance test was performed using Chi-square.

- 2) *Treatment overlap assumption* was checked to ensure that each patient has a positive probability of being assigned to each treatment option. This can be checked by plotting a graph of PS score or probability of treatment assignment on the x-axis and a density of propensity score on the y-axis between the treatment and control groups.

## Method S3 Sensitivity analysis

### *Sensitivity analysis for unmeasured confounders*

E-value was reported to assess the treatment effects on unmeasured confounders in real-world study data. E-value is defined as the minimum strength of association that an unmeasured confounder would need to have with both the treatment assignment and the outcome to fully explain a specific treatment-outcome association, conditional on the measured covariates.

The E-value is computed on the risk ratio (RR) scale, so results of statistical models other than the RR must be converted to the RR scale. The treatment effects on average treatment effects (ATE) and number of patients for each treatment groups after weighting, were used to estimate SMD using *esize regi*. The SMD was converted to the RR scale to estimate an E-value, as follows:

*Approximation RR and CIs:*

$$RR \approx e^{[0.91 \times SMD]}$$

$$\text{Lower limit (LL) for the RR} \approx e^{[0.91 \times SMD - 1.78 \times SD]}$$

$$\text{Upper limit (UL) for the RR} \approx e^{[0.91 \times SMD + 1.78 \times SD]}$$

*E-value for the point estimate and CI:*

*If  $RR > 1$ :*

$$E - \text{value (point estimate)} = RR + \sqrt{RR \times (RR - 1)}$$

$$E - \text{value (LL)} = 1 \text{ if } LL \leq 1, \text{ else } LL + \sqrt{LL \times (LL - 1)}$$

*If  $RR < 1$ :*

$$E - \text{value (point estimate)} = 1/RR + \sqrt{1/RR \times (1/RR - 1)}$$

$$E - \text{value (UL)} = 1 \text{ if } UL \geq 1, \text{ else } 1/UL + \sqrt{1/UL \times (1/UL - 1)}$$

E-values for the point estimate and CI indicate the magnitude of unmeasured confounding required to cause a shift in the treatment estimation. If the E-value for a point estimate and CI are large, this indicates a weak effect of unmeasured confounding. If the E-value for a point estimate and CI are small, it is possible that unmeasured confounding is influencing the treatment effects observed.