Intern Organs, 29:38-43). This phenomenon has been referred to as "phosphate rebound." In some cases, phosphate rebound produces higher phosphate levels than were initially present.

[010] The control of phosphorus often remains unsatisfactory in dialyzed patients. Accordingly, there is a continuing need for methods for treating hyperphosphatemia in hemodialysis patients. In particular, methods for reducing phosphate rebound are desired.

BRIEF SUMMARY

[010a] In one aspect, there is provided the use of a compound comprising the formula:

Ac-c(C)arrrar-NH_2 (SEQ ID NO:3)

in the manufacture of a medicament for treating chronic kidney disease-mineral and bone disorder (CKD-MBD) in a patient receiving hemodialysis,

wherein the medicament is to be administered within the period beginning about 15 minutes prior to completion of hemodialysis and ending about 3 hours after completion of hemodialysis, and wherein said administration is effective to maintain a post-hemodialysis serum phosphorus level that is lower than a pre-hemodialysis serum phosphorus level for a period of at least about 6 hours after dialysis.

[011] Disclosed is~~In one aspect,~~ a method ~~is provided~~ for treatment of hyperphosphatemia in hemodialysis patients.

[012] Disclosed is~~In another aspect,~~ a method ~~is provided~~ for reducing phosphate rebound in hemodialysis patients.

[013] Disclosed is~~In another aspect,~~ a treatment method compris~~e~~sing administering to a patient receiving dialysis (hemodialysis or peritoneal dialysis) a compound comprising the formula X_1 - X_2 - X_3 - X_4 - X_5- X_6 - X_7 wherein X_1 is a subunit comprising a thiol-containing group; X_5 is a cationic subunit; X_6 is a non-cationic subunit; X_7 is a cationic a subunit; and at least two of X_2, X_3 and X_4 are independently a cationic subunit. The compound is administered within about 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours after hemodialysis or within about 3 hours, 2 hours, 1 hour, 45 minutes, 30 minutes, 20 minutes, 15 minutes, 10 minutes, 5 minutes before completion of a hemodialysis session, and wherein the administration is effective to maintain a post-hemodialysis serum phosphorus level that

is lower than a pre-hemodialysis serum phosphorus level for a period of at least about 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 24 hours, 48 hours, 72 hours after completion of dialysis, or the time until the next hemodialysis session.

[014] In one embodiment, the compound is administered within a period beginning about 15 minutes prior to completion of hemodialysis and ending about 3 hours after completion of hemodialysis, and wherein said administering is effective to maintain a post-hemodialysis serum phosphorus level that is lower than a pre-hemodialysis serum phosphorus level for a period of at least about 6 hours after completion of dialysis

[015] In one embodiment, the agonist is Ac-c(C)arrrar-NH_2 (SEQ ID NO:3).

[016] In another embodiment, the agonist is a pharmaceutically salt of SEQ ID NO:3. An exemplary embodiment is an agonist that is a hydrochloride salt of SEQ ID NO:3.

[017] In one embodiment, the agonist is administered within about 1 hour after dialysis

or within about 30 minutes after dialysis. In a preferred embodiment, the agonist is administered during the rinse back procedure at the end of dialysis. In another embodiment, the agonist is administered within 5 hours before completion of dialysis, daily at least about 1 hour before completion of a dialysis session. In one embodiment, the dialysis is hemodialysis.

[018] In another embodiment, the agonist is administered during a rinse back procedure at the end of dialysis.

[019] In other embodiments, the patient has been diagnosed with end stage renal disease or chronic kidney disease and receives a treatment as described herein.

[020] In other embodiments, the patient is being treated with a drug that binds phosphate prior to and/or at the time of being treated as described herein.

[021] In yet other embodiments, the patient has chronic kidney disease associated with diabetes. In still other embodiments, the patient has chronic kidney disease associated with hypertension that is being treated by dialysis and receives a treatment as described herein. In other embodiments, the patient is being treated via dialysis for secondary hyperparathyroidism or primary hyperparathyroidism and receives a treatment as described herein.

[022] Also disclosed is a~~In yet another aspect, a method is provided, the~~ method comprising administering to a patient undergoing hemodialysis a calcium sensing receptor agonist, wherein the agonist is administered within about 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours after conclusion of hemodialysis or within about 3 hours, 2 hours, 1 hour, 45 minutes, 30 minutes, 20 minutes, 15 minutes, 10 minutes, 5 minutes before completion of hemodialysis, and wherein the administering is effective to maintain a post-hemodialysis serum phosphorus level that is lower than a pre-hemodialysis serum phosphorus level for a period of at least about 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 24 hours, 48 hours, 72 hours or the time until the next hemodialysis is commenced. In a preferred embodiment, the agonist is administered during the rinse back procedure at the end of dialysis.

[023] In one embodiment~~ of this aspect~~, the calcium sensing receptor agonist is not a compound of the form X_1 - X_2 - X_3 - X_4 - X_5- X_6 - X_7 wherein X_1 is a subunit comprising a thiol-containing group; X_5 is a cationic subunit; X_6 is a non-cationic subunit; X_7 is a cationic a subunit; and at least two of X_2, X_3 and X_4 are independently a cationic subunit.

[024] In one embodiment, the calcium sensing receptor agonist is a calcimimetic. In other embodiments, the calcimimetic is cinacalcet hydrochloride ($C_{22}H_{22}F_3N$•HCl).

[025] Further disclosed is~~In still another aspect,~~ a method for treating hyperphosphatemia in a patient who

receives at least on a periodic basis hemodialysis ~~is provided~~. The method comprises administering to the patient an effective amount of a calcium sensing receptor (CaSR) agonist, wherein the agonist is administered within about 18 hours after conclusion of hemodialysis or less than about 3 hours before completion of hemodialysis, and wherein the administering is effective to maintain a post-hemodialysis serum phosphorus level that is lower than a pre-hemodialysis serum phosphorus level for a period of at least about 6 hours.

[026] In one embodiment, the agonist is administered less than 30 minutes before completion of dialysis.

[027] In one embodiment, the agonist is cinacalcet hydrochloride. In another embodiment, the agonist is a compound of the form X_1 - X_2 - X_3 - X_4 - X_5- X_6 - X_7 wherein X_1 is a subunit comprising a thiol-containing group; X_5 is a cationic subunit; X_6 is a non-cationic subunit; X_7 is a cationic a subunit; and at least two of X_2, X_3 and X_4 are independently a cationic subunit.

[028] In one embodiment, the agonist is Ac-c(C)arrrar-NH_2 (SEQ ID NO:3) or a salt thereof.

[029] Disclosed is ~~In other aspects,~~ a method for regulating serum phosphorus concentration in a patient receiving at least on a periodic basis hemodialysis ~~is provided~~. The method comprises administering to the patient an effective amount of a calcium sensing receptor (CaSR) agonist, wherein the agonist is administered within about 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours after conclusion of hemodialysis or less than about 3 hours, 2 hours, 1 hour, 45 minutes, 30 minutes, 20 minutes, 15 minutes, 10 minutes, 5 minutes before completion of hemodialysis. In one embodiment, the administration is effective to maintain a post-hemodialysis serum phosphorus level that is lower than a pre-hemodialysis serum phosphorus level for a period of at least about 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 24 hours ,48 hours, 72 hours, or the time until the next hemodialysis session is begun. In a preferred embodiment, the agonist is administered during the rinse back procedure at the end of dialysis.

[030] After oral administration of cinacalcet hydrochloride, Cmax is achieved in approximately 2 to 6 hours. Accordingly, in another embodiment, the method comprises administering to the patient an effective amount of cinacalcet hydrochloride, wherein the cinacalcet hydrochloride is administered within about 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours after conclusion of hemodialysis or less than about 9 hours, 8 hours, 7 hours, 6 hours, 5 hours, 4 hours, 3

hours, 2 hours, 1 hour, 45 minutes, 30 minutes, 20 minutes, 15 minutes, 10 minutes, 5 minutes before completion of hemodialysis. In one embodiment, the administration is effective to maintain a post-hemodialysis serum phosphorus level that is lower than a pre-hemodialysis serum phosphorus level for a period of at least about 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 24 hours ,48 hours, 72 hours, or the time until the next hemodialysis session is begun.

[031] Also disclosed is~~In another aspect,~~ a dosing regimen for administration of a compound for treating hyperparathyroidism in a patient undergoing hemodialysis~~is provided~~. The dosing regimen comprises administering to the patient a calcium sensing receptor agonist, wherein the agonist is administered within about 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours after conclusion of hemodialysis or less than about 3 hours, 2 hours, 1 hour, 45 minutes, 30 minutes, 20 minutes, 15 minutes, 10 minutes, 5 minutes before completion of hemodialysis. In a preferred embodiment, the agonist is administered during the rinse back procedure at the end of dialysis. The regimen is effective to maintain a post-hemodialysis serum phosphorus level that is lower than a pre-hemodialysis serum phosphorus level ~~for a~~ period of at least about 6 hours.

[032] Further disclosed is~~In another aspect,~~ a method for treating hyperphosphatemia in a subject that receives dialysis~~is provided~~, wherein the subject is treated with a CaSR agonist compound as described herein. The treatment is effective to provide a post-dialysis serum phosphorus level that is less than a pre-dialysis serum phosphorus level for the duration of a period between dialysis sessions, i.e, the interdialytic period. In one embodiment, the post-dialysis serum phosphorus level is at least about 10%, 15%, 20% or 25% less than a pre-dialysis serum phosphorus level for the duration of the interdialytic period. The CaSR agonist compound is administered in accord with any of the treatment embodiments described herein, for example, before completion of a dialysis session or within about 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, or 4 hours after a dialysis session.

[033] In any of the embodiments~~of any of the aspects~~ noted herein, the CaSR agonist can be a compound comprising the sequence carrrar (SEQ ID NO:2). In other embodiments, the CaSR agonist is a conjugate comprised of the peptide carrrar (SEQ ID NO:2), where the peptide is conjugated at its N-terminal residue to a Cys residue. In a preferred embodiment, the conjugate is Ac-c(C)arrrar-NH_2 (SEQ ID NO:3).