

WHAT IS CLAIMED IS:

1. A method of treating or ameliorating hyperammonemia in a patient in need thereof, comprising:

assessing or receiving information on a baseline QT interval of the patient;

administering a first amount of ornithine phenylacetate to the patient during a first period of time; and

administering a second amount of ornithine phenylacetate to the patient during a second period of time;

wherein the first amount of ornithine phenylacetate is between about 10 g to about 30 g, and the second amount of ornithine phenylacetate is less than the first amount.

2. The method of claim 1, wherein the baseline QT interval is determined as an average of two or more measurements of QT intervals prior to the administration of the first amount of ornithine phenylacetate.

3. The method of claim 3, wherein two measurements of QT interval are taken 30 minutes and 15 minutes prior to the administration of the first amount of ornithine phenylacetate.

4. The method of any one of claims 1 to 3, further comprises assessing or receiving information on a change of QT interval from the baseline QT interval during or after the administration of the first amount of ornithine phenylacetate.

5. The method of claim 4, wherein the change of QT interval is the difference between one or more QT intervals during the first period of time and the baseline QT interval.

6. The method of claim 5, further comprises adjusting the first amount of ornithine phenylacetate when the change of QT interval is an increase of more than 20% from the baseline QT interval.

7. The method of claim 4, wherein the change of QT interval is the difference between one or more QT intervals during the second period of time and the baseline QT interval.

8. The method of claim 7, further comprises adjusting the second amount of ornithine phenylacetate when the change of QT interval is an increase of more than 20% from the baseline QT interval.

9. The method of any one of claims 1 to 8, wherein the QT interval is measured by an electrocardiogram (ECG).

10. The method of any one of claims 1 to 9, wherein the QT interval is corrected for heart rate using Fridericia's formula (QTcF).

11. The method of claim 10, wherein the assessed baseline QTcF of the patient is less than 500 ms.

12. The method of any one of claims 1 to 11, further comprises obtaining or having obtained information on whether the patient has one or more risk factors for QT prolongation prior to administering the first amount of ornithine phenylacetate.

13. The method of claim 12, wherein the risk factors for QT prolongation comprise hypokalemia, hypomagnesemia, congenital long-QT syndrome, suspected or actual acute myocardial infarction, or concurrent therapy with one or more QT-prolonging drugs, or combinations thereof.

14. The method of claim 12 or 13, wherein the patient does not have hypokalemia, hypomagnesemia, or congenital long-QT syndrome.

15. The method of claim 12 or 13, wherein the patient is not being administered any QT-prolonging drug concurrently.

16. The method of claim 13, wherein the suspected acute myocardial infarction is determined by elevated troponin I values in conjunction with evolving or new ECG signals.

17. The method of claim 16, wherein the patient has a troponin I (TnI) level of between 0 and about 0.4 ng/mL.

18. A method of treating or ameliorating hyperammonemia in a patient in need thereof, the method comprising:

receiving or having received information on the patient's concurrent therapy with one or more QT-prolonging drugs;

administering a first amount of ornithine phenylacetate to the patient during a first period of time; and

administering a second amount of ornithine phenylacetate to the patient during a second period of time;

wherein the first amount of ornithine phenylacetate is between about 10 g to about 30 g, and the second amount of ornithine phenylacetate is less than the first amount.

19. A method of treating or ameliorating hyperammonemia in a patient in need thereof, the method comprising:

administering a first amount of ornithine phenylacetate to the patient during a first period of time; and

administering a second amount of ornithine phenylacetate to the patient during a second period of time, wherein the first amount of ornithine phenylacetate is between

about 10 g to about 30 g, and the second amount of ornithine phenylacetate is less than the first amount; and

wherein the patient is not to take one or more QT-prolonging drugs concurrently.

20. The method of claim 13, 18 or 19, wherein the QT-prolonging drugs are selected from the group consisting of amiodarone, anagrelide, arsenic trioxide, astemizole, azithromycin, bepridil, chloroquine, chlorpromazine, cilostazol, ciprofloxacin, cisapride, citalopram, clarithromycin, cocaine, disopyramide, dofetilide, domperidone, donepezil, dronedarone, droperidol, erythromycin, escitalopram, flecainide, fluconazole, gatifloxacin, grepafloxacin, halofantrine, haloperidol, ibogaine, ibutilide, levofloxacin, levomepromazine (methotrimeprazine), levomethadyl acetate, levosulpiride, mesoridazine, methadone, moxifloxacin, ondansetron, oxaliplatin, papaverine HCl (intra-coronary), pentamidine, pimozide, probucol, procainamide, propofol, quinidine, roxithromycin, sevoflurane, sotalol, sparfloxacin, sulpiride, sultopride, terfenadine, telaprevir, terlipressin, terodiline, thioridazine, and vandetanib.

21. The method of claim 13, 18 or 19, wherein the QT-prolonging drugs are selected from the group consisting of amantadine, amisulpride, amitriptyline, amphotericin B, atazanavir, bendroflumethiazide, bendrofluazide, chloral hydrate, diphenhydramine, doxepin, esomeprazole, famotidine, fluoxetine, fluvoxamine, galantamine, garenoxacin, hydroxychloroquine, hydroxyzine, indapamide, itraconazole, ivabradine, ketoconazole, loperamide, metoclopramide, metolazone, metronidazole, nelfinavir, olanzapine, omeprazole, paroxetine, piperacillin, tazobactam, posaconazole, propafenone, quetiapine, quinine sulfate, ranolazine, sertraline, solifenacin, trazodone, torsemide (torasemide), voriconazole, and ziprasidone.

22. The method of claim 13, 18 or 19, wherein the QT-prolonging drugs are selected from the group consisting of alfuzosin, apomorphine, aripiprazole, artenimol, piperazine, asenapine, atomoxetine, bedaquiline, bendamustine, benperidol, betrixaban, bortezomib, bosutinib, buprenorphine, cabozantinib, capecitabine, ceritinib, clofazimine, clomipramine, clozapine, crizotinib, cyamemazine (cyamepromazine), dabrafenib, dasatinib, degarelix, delamanid, desipramine, deutetrabenazine, dexmedetomidine, dolasetron, efavirenz, eliglustat, epirubicin, eribulin mesylate, ezogabine (retigabine), felbamate, fingolimod, fluorouracil (5-FU), flupentixol, gemifloxacin, granisetron, hydrocodone, iloperidone, imipramine (melipramine), inotuzumab ozogamicin, isradipine, ketanserin, lapatinib, lenvatinib, lithium, lopinavir, ritonavir, melperone, midostaurin, mifepristone, mirabegron, mirtazapine, moexipril, hydrochlorothiazide, necitumumab, nifedipine, nilotinib, norfloxacin, nortriptyline, nusinersen, ofloxacin, osimertinib, oxytocin, paliperidone, palonosetron, panobinostat, pasireotide, pazopanib, perflutren lipid microspheres, perphenazine, pilsicainide, pimavanserin,

pipamperone, primaquine phosphate, promethazine, prothipendyl, ribociclib, rilpivirine, risperidone, romidepsin, saquinavir, sertindole, sorafenib, sunitinib, tacrolimus, tamoxifen, telavancin, telithromycin, tetrabenazine, tiapride, tipiracil, trifluridine, tizanidine, tolterodine, toremifene, tramadol, trimipramine, tropisetron, valbenazine, vardenafil, vemurafenib, venlafaxine, vorinostat, and zotepine.

23. The method of any one of claims 18 to 22, further comprises assessing or receiving information on a change of QT interval during the administration of the first amount or the second amount of ornithine phenylacetate, as compared from a baseline QT interval prior to the administration of the first amount of ornithine phenylacetate.

24. The method of claim 23, further comprises adjusting the first amount of ornithine phenylacetate when the change of QT interval is an increase of more than 20% from the baseline QT interval.

25. The method of claim 23, further comprises adjusting the second amount of ornithine phenylacetate when the change of QT interval is an increase of more than 20% from the baseline QT interval.

26. The method of any one of claims 1 to 25, wherein the first amount of ornithine phenylacetate is about 20 g and the first period of time is about 6 hours.

27. The method of any one of claims 1 to 26, wherein the second amount of ornithine phenylacetate is about 15 g and the second period of time is about 18 hours.

28. The method of any one of claims 1 to 27, wherein the second amount of ornithine phenylacetate is administered immediately after the completion of the administration of the first amount of ornithine phenylacetate.

29. The method of any one of claims 1 to 28, further comprises administering a third amount of ornithine phenylacetate immediately following the completion of the administration of the second amount of ornithine phenylacetate during a third period of time.

30. The method of claim 29, wherein the third period of time is about 4 days and the third amount of ornithine phenylacetate administered per day (24 hours) is the same or less than the second amount of ornithine phenylacetate.

31. The method of claim 29 or 30, further comprises assessing or receiving information on a change of QT interval from the baseline QT interval during or after the administration of the third amount of ornithine phenylacetate

32. The method of claim 31, wherein the change of QT interval is determined as the difference between one or more QT intervals during the third period of time and the baseline QT interval.

33. The method of claim 32, further comprises adjusting the third amount of ornithine phenylacetate when the change of QT interval is an increase of more than 20% from the baseline QT interval.

34. The method of any one of claims 1 to 33, wherein ornithine phenylacetate is administered via continuous intravenous infusion.

35. The method of any one of claims 1 to 34, wherein the patient is also receiving standard of care.

36. The method of claim 35, wherein the standard of care comprises lactulose with or without rifaximin.

37. The method of any one of claims 1 to 36, wherein the patient has liver cirrhosis, liver decompensation, an acute liver disease, a chronic liver disease, portal hypertension, or urea cycle disorder.

38. The method of any one of claims 1 to 37, wherein the patient is suffering from or has suffered from one or more episodes of hepatic encephalopathy.